ANTIGEN BINDING MOLECULES TARGETING THYMIC STROMAL LYMPHOPOIETIN (TSLP)

RELATED APPLICATION(S)

[0001] This application claims the benefit of U.S. Provisional Application No. 63/369,152, filed on July 22, 2022; U.S. Provisional Application No. 63/369,158, filed on July 22, 2022; U.S. Provisional Application No. 63/369,165, filed on July 22, 2022; U.S. Provisional Application No. 63/369,175, filed on July 22, 2022; U.S. Provisional Application No. 63/369,202, filed on July 22, 2022; U.S. Provisional Application No. 63/369,203, filed on July 22, 2022; U.S. Provisional Application No. 63/369,204, filed on July 22, 2022; and U.S. Provisional Application No. 63/369,206, filed on July 22, 2022.

[0002] This application claims the priority to and is a continuation-in-part of U.S. Application No. 18/356,891, filed on July 21, 2023.

[0003] The entire teachings of the above applications are incorporated herein by reference. Without limiting the foregoing, this application incorporates by reference the Sequence Listing and code of respective Appendices A and B for the forgoing applications. For example the files claim.txt and fit_model.txt of U.S. Application No. 18/356,891.

INCORPORATION BY REFERENCE OF MATERIAL IN XML

[0004] This application incorporates by reference the Sequence Listing contained in the following eXtensible Markup Language (XML) file being submitted concurrently herewith:

a) File name: 57081061002_Sequence_Listing.xml; created July 21, 2023, 212,394 Bytes in size.

INCORPORATION BY REFERENCE OF MATERIAL IN AN ASCII FILE

[0005] This application incorporates by reference the Computer Program Listing contained in the following ASCII file being submitted concurrently herewith:

a) File name: claim.py; uploaded July 22, 2023 and available at https://zenodo.org/record/8174726/files/claim.py?download=1 or at https://doi.org/10.5281/zenodo.8174726 and selecting “claim.py” , 4,774 Bytes in size. The entire teachings of the above file are incorporated herein by reference in their entirety.

b) File name: fit_model.etab; , uploaded July 22, 2023 and available at https://zenodo.org/record/8174726/files/fit_model.etab?download=1 or at https://doi.org/10.5281/zenodo.8174726 and selecting "fit_model.etab", 2,888,059 Bytes in size. The entire teachings of the above file are incorporated herein by reference in their entirety.

[0006] The entire teachings of the above files are incorporated herein by reference in their entirety. The script in claim.py is intended to be run in a Python environment in the same folder as fit_model.etab to use the data of fit_model.etab.

BACKGROUND

[0007] Thymic stromal lymphopoietin (TSLP) is a cytokine that has been implicated in the pathogenesis of a variety of inflammatory conditions. Released upon epithelial exposure to "insults" such as allergens, TSLP initiates a cascade of downstream inflammation. TSLP receptors (TSLPRs) are expressed in a wide range of cell types, including airway smooth muscle cells (ASMCs), basophils, dendritic cells, eosinophils, group 2 innate lymphoid cells (ILC2s), hematopoietic progenitor cells, lymphocytes, macrophages, mast cells and monocytes (Gauvreau *et al.*, *Thymic stromal lymphopoietin: its role and potential as a therapeutic target in asthma*, Expert Opin Ther Targets 24(8):777-92 (2020)). There is compelling evidence that dysregulated TSLP expression can lead to allergic disease through the development of type 2 inflammatory responses (Ziegler *et al.*, *The biology of thymic stromal lymphopoietin (TSLP)*, Adv Pharmacol. 66:129-55 (2013)).

SUMMARY

[0008] There is a critical need for therapeutic agents for modulating (*e.g.*, reducing or neutralizing) thymic stromal lymphopoietin (TSLP) binding and/or activity. The disclosure provides such agents.

[0009] The disclosure provided herein is based, in part, on the discovery that polypeptides disclosed herein specifically bind to TSLP and demonstrate various additional beneficial properties. Accordingly, the disclosure generally relates to polypeptides (*e.g.*, antibodies), compositions (*e.g.*, pharmaceutical compositions) and methods that are useful for modulating (*e.g.*, reducing or neutralizing) TSLP function and/or activity (*e.g.*, *in vivo*).

[0010] Provided herein, among other things, are polypeptides (*e.g.*, antibodies and antigen binding fragments thereof) that specifically bind TSLP (*e.g.*, a full-length human

TSLP) or a variant thereof. In some embodiments, a polypeptide disclosed herein binds TSLP at an AB-loop region and C-terminal region of helix D.

[0011] In some embodiments, a polypeptide modulates (*e.g.*, reduces, such as inhibits) binding between TSLP and TSLPR (*e.g.*, alone or in a heterodimeric complex with interleukin 7 receptor alpha (IL-7Rα)). In some embodiments, a polypeptide modulates (*e.g.*, reduces, such as inhibits) TSLP-mediated signaling *in vitro* and/or *in vivo*.

[0012] The disclosure provides, among other things, a polypeptide (*e.g.*, an antibody or an antigen binding fragment thereof) that specifically binds a TSLP, wherein the polypeptide has one or more properties selected from:

a binding affinity for a TSLP characterized by a K_D of 10 pM or less (*e.g.*, as measured by KinExA);

a binding specificity for the AB-loop region and the C-terminal region of helix D of a TSLP;

a neutralizing activity against a TSLP (*e.g.*, a full-length human TSLP); or

an inhibitory activity against TSLP-mediated signaling,

or a combination of the foregoing.

[0013] The disclosure also provides, among other things, a polypeptide (*e.g.*, an antibody or an antigen binding fragment thereof) that comprises a paratope that is substantially similar to the paratope of an antibody comprising an immunoglobulin heavy chain variable domain (V_H)/an immunoglobulin light chain variable domain (V_L) combination selected from:

SEQ ID NO:4 and SEQ ID NO:20 (AB-1);

SEQ ID NO:5 and SEQ ID NO:21 (AB-2);

SEQ ID NO:6 and SEQ ID NO:20 (AB-3);

SEQ ID NO:7 and SEQ ID NO:22 (AB-4);

SEQ ID NO:8 and SEQ ID NO:23 (AB-5);

SEQ ID NO:9 and SEQ ID NO:24 (AB-6);

SEQ ID NO:10 and SEQ ID NO:25 (AB-7);

SEQ ID NO:11 and SEQ ID NO:20 (AB-8);

SEQ ID NO:12 and SEQ ID NO:20 (AB-9);

SEQ ID NO:13 and SEQ ID NO:26 (AB-10);

SEQ ID NO:14 and SEQ ID NO:27 (AB-11);

SEQ ID NO:15 and SEQ ID NO:28 (AB-12);

SEQ ID NO:16 and SEQ ID NO:29 (AB-13); or

SEQ ID NO:17 and SEQ ID NO:30 (AB-14), or

a combination of the foregoing,

wherein the polypeptide does not comprise a heavy chain comprising SEQ ID NO:81 and a light chain comprising SEQ ID NO:82.

[0014] In some embodiments, a polypeptide comprises a paratope that is substantially similar to a paratope of an antibody comprising a V_H/V_L combination selected from:

SEQ ID NO:4 and SEQ ID NO:20 (AB-1);

SEQ ID NO:5 and SEQ ID NO:21 (AB-2);

SEQ ID NO:6 and SEQ ID NO:20 (AB-3); or

SEQ ID NO:7 and SEQ ID NO:22 (AB-4), or

a combination of the foregoing,

wherein the polypeptide does not comprise a heavy chain comprising SEQ ID NO:81 and a light chain comprising SEQ ID NO:82.

[0015] The disclosure also provides, among other things, a polypeptide (*e.g.*, an antibody or an antigen binding fragment thereof) comprising:

a V_H amino acid sequence comprising a heavy chain complementarity determining region 1 (HCDR1), a heavy chain complementarity determining region 2 (HCDR2) and a heavy chain complementarity determining region 3 (HCDR3) that are substantially similar to a HCDR1, a HCDR2 and a HCDR3, respectively, of the amino acid sequence of any one of SEQ ID NOs:4-17; and

a V_L amino acid sequence comprising a light chain complementarity determining region 1 (LCDR1), a light chain complementarity determining region 2 (LCDR2) and a light chain complementarity determining region 3 (LCDR3) that are substantially similar to a LCDR1, a LCDR2 and a LCDR3, respectively, of the amino acid sequence of any one of SEQ ID NOs:20-30,

wherein the polypeptide does not comprise a heavy chain comprising SEQ ID NO:81 and a light chain comprising SEQ ID NO:82.

[0016] In some embodiments, a polypeptide comprises:

a V_H amino acid sequence comprising a HCDR1, a HCDR2 and a HCDR3 that are substantially similar to a HCDR1, a HCDR2 and a HCDR3, respectively, of the amino acid sequence of any one of SEQ ID NOs:4-7; and

a V_L amino acid sequence comprising a LCDR1, a LCDR2 and a LCDR3 that are substantially similar to a LCDR1, a LCDR2 and a LCDR3, respectively, of the amino acid sequence of any one of SEQ ID NOs:20-22.

[0017] In some embodiments, a polypeptide comprises a HCDR1, a HCDR2 and a HCDR3, and a LCDR1, a LCDR2 and a LCDR3, of an antibody comprising a V_H/V_L combination selected from:

SEQ ID NO:4 and SEQ ID NO:20 (AB-1);
SEQ ID NO:5 and SEQ ID NO:21 (AB-2);
SEQ ID NO:6 and SEQ ID NO:20 (AB-3);
SEQ ID NO:7 and SEQ ID NO:22 (AB-4);
SEQ ID NO:8 and SEQ ID NO:23 (AB-5);
SEQ ID NO:9 and SEQ ID NO:24 (AB-6);
SEQ ID NO:10 and SEQ ID NO:25 (AB-7);
SEQ ID NO:11 and SEQ ID NO:20 (AB-8);
SEQ ID NO:12 and SEQ ID NO:20 (AB-9);
SEQ ID NO:13 and SEQ ID NO:26 (AB-10);
SEQ ID NO:14 and SEQ ID NO:27 (AB-11);
SEQ ID NO:15 and SEQ ID NO:28 (AB-12);
SEQ ID NO:16 and SEQ ID NO:29 (AB-13); or
SEQ ID NO:17 and SEQ ID NO:30 (AB-14).

[0018] In some embodiments, a polypeptide further comprises a paratope that has 100% sequence identity to a paratope of an antibody comprising a V_H/V_L combination selected from:

SEQ ID NO:4 and SEQ ID NO:20 (AB-1);
SEQ ID NO:5 and SEQ ID NO:21 (AB-2);
SEQ ID NO:6 and SEQ ID NO:20 (AB-3);
SEQ ID NO:7 and SEQ ID NO:22 (AB-4);
SEQ ID NO:8 and SEQ ID NO:23 (AB-5);
SEQ ID NO:9 and SEQ ID NO:24 (AB-6);
SEQ ID NO:10 and SEQ ID NO:25 (AB-7);
SEQ ID NO:11 and SEQ ID NO:20 (AB-8);
SEQ ID NO:12 and SEQ ID NO:20 (AB-9);
SEQ ID NO:13 and SEQ ID NO:26 (AB-10);

SEQ ID NO:14 and SEQ ID NO:27 (AB-11);

SEQ ID NO:15 and SEQ ID NO:28 (AB-12);

SEQ ID NO:16 and SEQ ID NO:29 (AB-13); or

SEQ ID NO:17 and SEQ ID NO:30 (AB-14).

[0019] In some embodiments, a polypeptide comprises a HCDR1, a HCDR2 and a HCDR3, and a LCDR1, a LCDR2 and a LCDR3, of an antibody comprising a V_H/V_L combination selected from:

SEQ ID NO:4 and SEQ ID NO:20 (AB-1);

SEQ ID NO:5 and SEQ ID NO:21 (AB-2);

SEQ ID NO:6 and SEQ ID NO:20 (AB-3); or

SEQ ID NO:7 and SEQ ID NO:22 (AB-4).

[0020] In some embodiments, a polypeptide comprises a paratope that has 100% sequence identity to a paratope of an antibody comprising a V_H/V_L combination selected from:

SEQ ID NO:4 and SEQ ID NO:20 (AB-1);

SEQ ID NO:5 and SEQ ID NO:21 (AB-2);

SEQ ID NO:6 and SEQ ID NO:20 (AB-3); or

SEQ ID NO:7 and SEQ ID NO:22 (AB-4).

[0021] The disclosure also provides, among other things, a polypeptide (*e.g.*, an antibody or an antigen binding fragment thereof) that comprises a V_H comprising SEQ ID NO:2, wherein:

X_1 is not I;

X_2 is not W;

X_3 is not D;

X_4 is not S;

X_5 is not N;

X_6 is not K;

X_7 is not A;

X_8 is not A;

X_9 is not L;

X_{10} is not V;

X_{11} is not H,

X_{12} is not A;

X_{13} is not F;

X_{14} is not I,

or any combination of the foregoing.

[0022] In some embodiments, a polypeptide comprises a V_L comprising SEQ ID NO:18, wherein:

X_{15} is not N;

X_{16} is not L;

X_{17} is not S;

X_{18} is not K;

X_{19} is not S;

X_{20} is not V;

X_{21} is not W;

X_{22} is not D;

X_{23} is not S;

X_{24} is not S;

X_{25} is not S;

X_{26} is not D;

X_{27} is not H,

or any combination of the foregoing.

[0023] The disclosure also provides, among other things, a polypeptide (*e.g.*, an antibody or an antigen binding fragment thereof) comprising a V_H sequence that has at least 70% sequence identity to SEQ ID NO:3, a V_L sequence that has at least 70% sequence identity to SEQ ID NO:19, or both, wherein the V_H sequence does not comprise SEQ ID NO:3, the V_L sequence does not comprise SEQ ID NO:19, or both.

[0024] The disclosure also provides, among other things, a polypeptide comprising:

a) a HCDR 1 comprising the amino acid sequence of SEQ ID NO:31, a HCDR2 comprising the amino acid sequence of SEQ ID NO:35, and a HCDR3 comprising the amino acid sequence of SEQ ID NO:50; and

b) a LCDR 1 comprising the amino acid sequence of SEQ ID NO:60, a LCDR2 comprising the amino acid sequence of SEQ ID NO:67, and a LCDR3 comprising the amino acid sequence of SEQ ID NO:71,

wherein the polypeptide is an antibody or an antigen-binding fragment thereof.

[0025] The disclosure also provides, among other things, a polypeptide comprising:

a) a HCDR 1 consisting of the amino acid sequence of SEQ ID NO:31, a HCDR2 consisting of the amino acid sequence of SEQ ID NO:35, and a HCDR3 consisting of the amino acid sequence of SEQ ID NO:50; and

b) a LCDR 1 consisting of the amino acid sequence of SEQ ID NO:60, a LCDR2 consisting of the amino acid sequence of SEQ ID NO:67, and a LCDR3 consisting of the amino acid sequence of SEQ ID NO:71,

wherein the polypeptide is an antibody or an antigen-binding fragment thereof.

[0026] In some embodiments, a polypeptide comprises:

a) a V_H that is humanized, contains human framework regions, or a combination thereof;

b) a V_L that is humanized, contains human framework regions, or a combination thereof, or

both a) and b).

[0027] In some embodiments, a polypeptide comprises:

a) a V_H comprising the amino acid sequence of SEQ ID NO:5;

b) a V_L comprising the amino acid sequence of SEQ ID NO:21, or

both a) and b).

[0028] In some embodiments, an antigen-binding fragment comprises a single-chain fragment variable (scFv), a variable heavy domain of heavy chain (V_{HH}), a fragment antigen-binding (Fab), a Fab' or a $F(ab')_2$.

[0029] In some embodiments, a polypeptide comprises:

a) an antibody heavy chain constant domain;

b) an antibody light chain constant domain,

or both a) and b).

[0030] In some embodiments, an antibody heavy chain constant domain is an IgG1, IgG2, IgG3 or IgG4 constant domain.

[0031] In some embodiments, an antibody heavy chain constant domain is an IgG1 or IgG2 constant domain.

[0032] In some embodiments, an antibody heavy chain constant domain comprises one or more mutations which increase serum half-life of the antibody or antigen-binding fragment thereof in humans. In some embodiments, an antibody heavy chain constant domain comprises, relative to a wild-type human IgG constant domain, amino acid substitutions with

tyrosine, threonine and glutamic acid at amino acid residues 252, 254 and 256, respectively, wherein the amino acid residues are numbered according to the EU index as in Kabat.

[0033] In some embodiments, a polypeptide comprises:

a) an antibody heavy chain (HC) comprising the amino acid sequence of SEQ ID NO:92;

b) an antibody light chain (LC) comprising the amino acid sequence of SEQ ID NO:120, or

both a) and b).

[0034] In some embodiments, a polypeptide comprises:

a) an antibody heavy chain (HC) comprising the amino acid sequence of SEQ ID NO:106;

b) an antibody light chain (LC) comprising the amino acid sequence of SEQ ID NO:120, or

both a) and b).

[0035] In some embodiments, a polypeptide specifically binds TSLP.

[0036] In some embodiments, a polypeptide is a fusion protein.

[0037] In some embodiments, the disclosure provides a polynucleotide encoding a polypeptide disclosed herein, a vector comprising such a polynucleotide, and/or a host cell comprising such a polynucleotide and/or vector.

[0038] In some embodiments, the disclosure provides a composition (*e.g.*, a pharmaceutical composition) comprising a polypeptide disclosed herein. In some embodiments, a composition further comprises one or more pharmaceutical excipients, diluents, or carriers. In some embodiments, a composition further comprises one or more additional therapeutic agents (*e.g.*, an anti-inflammatory agent). In some embodiment, a polypeptide is conjugated (directly or by a linker) to one or more additional therapeutic agents (*e.g.*, an anti-inflammatory agent). In some embodiments, one or more additional therapeutic agents comprise a corticosteroid, a beta-agonist, a muscarinic antagonist, an anti-inflammatory agent, an IL-4 and/or IL-13 antagonist (*e.g.*, an antibody or antigen-binding fragment thereof targeting IL-13, IL-4 or IL-4R), or a combination thereof.

[0039] The disclosure also provides, among other things, a method of treating a subject in need thereof (*e.g.*, a subject having a TSLP-associated disease or condition), comprising administering to the subject an effective amount of a polypeptide disclosed herein and/or a

composition (*e.g.*, pharmaceutical composition) comprising one or more polypeptides disclosed herein.

[0040] The disclosure also provides, among other things, a method of modulating (*e.g.*, reducing) a TSLP-mediated signaling in a cell (*e.g.*, a cell in a subject), comprising contacting the cell with a polypeptide disclosed herein and/or a composition (*e.g.*, pharmaceutical composition) comprising one or more polypeptides disclosed herein.

[0041] In some embodiments, a subject has asthma, atopic dermatitis (AD), allergic conjunctivitis, chronic obstructive pulmonary disease (COPD), chronic spontaneous urticaria (CSU), rheumatoid arthritis (RA), rhinosinusitis (RS), eosinophilic esophagitis (EE), or a food-hypersensitivity reaction. In some embodiments, a subject has moderate asthma. In some embodiments, a subject has severe asthma. In some embodiments, a subject has COPD. In some embodiments, a subject has COPD and/or either moderate asthma or severe asthma.

[0042] The disclosure also provides, among other things, a method of reducing binding of TSLP to a TSLP receptor (TSLPR) on a cell in a subject, comprising contacting the cell with an effective amount of a composition (*e.g.*, pharmaceutical composition) comprising one or more polypeptides disclosed herein.

[0043] The disclosure also provides, among other things, a method of making a polypeptide disclosed herein, comprising culturing a host cell comprising a nucleotide sequence encoding the polypeptide under conditions where the polypeptide is expressed in the host cell.

[0044] The disclosure also provides, among other things, a computer-implemented method that comprises scoring a polypeptide comprising an amino acid sequence with a computationally binding optimized (CBO) model. The CBO model, for each amino acid position of the amino acid sequence of the polypeptide, calculates multiple energy scores, the multiple energy scores based on having substituted the amino acid at a given position in the amino acid sequence with each of a plurality of different amino acids. The CBO model further adds each energy score calculated to an array. The CBO model further generates a normalized sum of the energy scores for each position. The CBO model further calculates a logarithm of each energy score calculated. The CBO model further generates a score of the polypeptide by summing the logarithms of each energy score calculated, the score representing a functional property of the polypeptide.

[0045] The disclosure also provides, among other things, a system that includes a processor and a memory with computer code instructions stored thereon. The processor and

the memory, with the computer code instructions, are configured to cause the system to score a polypeptide sequence with a CBO model. The CBO model, for each amino acid position of the amino acid sequence of the polypeptide, calculates multiple energy scores, the multiple energy scores based on having substituted the amino acid at a given position in the amino acid sequence with each of a plurality of different amino acids. The CBO model further adds each energy score calculated to an array. The CBO model further generates a normalized sum of the energy scores for each position. The CBO model further calculates a logarithm of each energy score calculated. The CBO model further generates a score of the polypeptide by summing the logarithms of each energy score calculated, the score representing a functional property of the polypeptide.

[0046] Also provide herein, among other things, is a polypeptide that specifically binds a thymic stromal lymphopoietin (TSLP) and comprises an amino acid sequence that is assigned a score above a predetermined threshold by a computationally binding optimized (CBO) model upon scoring the amino acid sequence of the polypeptide.

[0047] The disclosure also provides, among other things, a polypeptide that binds human thymic stromal lymphopoietin (TSLP) and which is designed by a method comprising generating a polypeptide sequence with a CBO model. In some embodiments, the polypeptide is further designed by verifying the generated polypeptide sequence using the CBO model by, for each amino acid position of the polypeptide sequence, calculating a plurality of energy scores. The energy scores can be based on having substituted the amino acid at a given position in the polypeptide sequence with each of a plurality of different amino acids. In some embodiments, the polypeptide is further verified by adding each energy score calculated to an array. In some embodiments, the polypeptide is further verified by generating a normalized sum of the energy scores for each position. In some embodiments, the polypeptide is further verified by calculating a logarithm of each energy score calculated. In some embodiments, the polypeptide is further verified by generating a score of the polypeptide sequence by summing the logarithms of each energy score calculated. The score represents a functional property of the polypeptide's ability to bind to human TSLP. In some embodiments, the polypeptide sequence is verified if the polypeptide scores above a particular threshold.

BRIEF DESCRIPTION OF THE DRAWINGS

[0048] The patent or application file contains at least one drawing executed in color. Copies of this patent or patent application publication with color drawing(s) will be provided by the Office upon request and payment of the necessary fee.

[0049] The foregoing will be apparent from the following more particular description of example embodiments, as illustrated in the accompanying drawings in which like reference characters refer to the same parts throughout the different views. The drawings are not necessarily to scale, emphasis instead being placed upon illustrating embodiments.

[0050] In the drawings, "Reference" refers to the Reference Antibody.

[0051] FIG. 1 depicts the amino acid sequence of human thymic stromal lymphopoietin (TSLP) (SEQ ID NO:1). The epitope residues bound by the Reference Antibody disclosed herein are indicated by asterisks.

[0052] FIGs. 2A-2B depict an alignment of heavy chain variable domain (V_H) amino acid sequences of the Reference Antibody and example antibodies AB-1 to AB-14. The heavy chain complementarity determining region (HCDR) amino acid sequences as determined by ImMunoGeneTics (IMGT) numbering are indicated using underlining. The bold letters indicate variable residues (designated throughout this disclosure by "X_n") in the Reference Antibody and AB-1 to AB-14. "*" indicates paratope residues. *See* also V_H consensus sequence (SEQ ID NO:2) in Table 1. Paratope residues were defined as antibody residues in the Reference Antibody that, when bound to human TSLP, are within 5 angstroms of the antigen.

[0053] FIGs. 3A-3B depict an alignment of light chain variable domain (V_L) amino acid sequences of the Reference Antibody and example antibodies AB-1 to AB-14. The heavy chain complementarity determining region (LCDR) amino acid sequences as determined by ImMunoGeneTics (IMGT) numbering are indicated using underlining. The bold letters indicate variable residues (designated throughout this disclosure by "X_n") in the Reference Antibody and AB-1 to AB-14. *See* also V_L consensus sequence (SEQ ID NO:18) in Table 2.

[0054] FIGs. 4A-4B show binding profiles of non-limiting examples of anti-TSLP antibodies to human TSLP (hTSLP), generated using a direct enzyme-linked immunosorbent assay (ELISA).

[0055] FIGs. 5A-5B show binding profiles of non-limiting examples of anti-TSLP antibodies to cynomolgus monkey TSLP (cynoTSLP), generated using a direct ELISA.

[0056] FIGs. 6A-6B show binding profiles of non-limiting examples of anti-TSLP antibodies to hTSLP, generated using a blocking ELISA.

[0057] FIGs. 7A-7B show binding profiles of non-limiting examples of anti-TSLP antibodies to cynoTSLP, generated using a blocking ELISA.

[0058] FIGs. 8A-8C show that non-limiting examples of anti-TSLP antibodies neutralizing binding of hTSLP to TSLP receptor (TSLPR). Ba/F3-STAT5-Luc cells, STAT5 reporter cells that express hTSLPR and hIL-7Rα, were used to assess binding between hTSLP and TSLPR based on hTSLP-induced STAT5 activity. FIG. 8A shows TSLP-mediated STAT5 signaling as a function of hTSLP concentration. FIGs. 8B-8C show effects of the anti-TSLP antibodies on TSLP-mediated STAT5 signaling.

[0059] FIGs. 9A-9B are graphs showing that example anti-TSLP antibodies block TSLP binding to human myeloid dendritic cells (mDCs) from peripheral blood. The curves show effects of the anti-TSLP antibodies on TSLP-induced CCL17 expression by mDCs from one representative donor.

[0060] FIGs. 10A-10D are graphs showing binding profiles of AB-2a, AB-2b, the Reference Antibody, IgG1 isotype control, and IgG2 isotype control, generated using a direct ELISA. FIG. 10A shows binding profiles to hTSLP. FIG. 10B shows binding profiles to cynoTSLP. FIG. 10C shows binding profiles to mouse TSLP. FIG. 10D shows binding profiles to human IL-7.

[0061] FIGs. 11A-11B are graphs showing Ba/F3 assay results for AB-2a, AB-2b, the Reference Antibody, IgG1 isotype control, and IgG2 isotype control. FIG. 11A shows human TSLPR/IL-7Rα Ba/F3 assay results. FIG. 11B shows cyno TSLPR/IL-7Rα Ba/F3 assay results.

[0062] FIG. 12A is a diagram illustrating zero-order (1002), first-order (1004), and second-order (1006) models.

[0063] FIG. 12B is a flow diagram illustrating an example of the process used by embodiments of this disclosure to determine claimed sequences.

[0064] FIG. 13 illustrates a computer network or similar digital processing environment in which embodiments of the present invention may be implemented.

[0065] FIG. 14 is a diagram of an example internal structure of a computer (*e.g.*, client processor/device or server computers) in the computer system of FIG. 13.

DETAILED DESCRIPTION

[0066] A description of example embodiments follows.

[0067] Several aspects of the disclosure are described below, with reference to examples for illustrative purposes only. It should be understood that numerous specific details, relationships, and methods are set forth to provide a full understanding of the disclosure. One having ordinary skill in the relevant art, however, will readily recognize that the disclosure can be practiced without one or more of the specific details or practiced with other methods, protocols, reagents, cell lines and animals. The disclosure is not limited by the illustrated ordering of acts or events, as some acts may occur in different orders and/or concurrently with other acts or events. Furthermore, not all illustrated acts, steps or events are required to implement a methodology in accordance with the disclosure. Many of the techniques and procedures described, or referenced herein, are well understood and commonly employed using conventional methodology by those skilled in the art.

Definitions

[0068] Unless otherwise defined, all terms of art, notations and other scientific terms or terminology used herein are intended to have the meanings commonly understood by those of skill in the art to which this disclosure pertains. In some cases, terms with commonly understood meanings are defined herein for clarity and/or for ready reference, and the inclusion of such definitions herein should not necessarily be construed to represent a substantial difference over what is generally understood in the art. It will be further understood that terms, such as those defined in commonly-used dictionaries, should be interpreted as having a meaning that is consistent with their meaning in the context of the relevant art and/or as otherwise defined herein.

[0069] The terminology used herein is for the purpose of describing particular embodiments only and is not intended to be limiting.

[0070] When introducing elements disclosed herein, the articles “a,” “an,” “the,” and “said” are intended to mean that there are one or more of the elements. Further, the one or more elements may be the same or different. For example, unless the context clearly indicates otherwise, “a polypeptide” includes a single polypeptide, and two or more polypeptides.

[0071] Throughout this specification and the claims which follow, unless the context requires otherwise, the term “comprise,” and variations such as “comprises” and “comprising”, will be understood to imply the inclusion of, *e.g.*, a stated integer or step or

group of integers or steps, but not the exclusion of any other integer or step or group of integer or step. When used herein, the term "comprising" can be substituted with the term "containing" or "including."

[0072] As used herein, the term "consisting of" excludes any element, step, or ingredient not specified in the claim element. When used herein, the term "consisting essentially of" does not exclude materials or steps that do not materially affect the basic and novel characteristics of the claim.

[0073] Also provided herein are corresponding embodiments for each and every embodiment featuring the term "comprising," "containing," "including," or "having," wherein those terms are replaced by the term "consisting of" and/or "consisting essentially of".

[0074] As used herein, the conjunctive term "and/or" between multiple recited elements is understood as encompassing both individual and combined options. For instance, where two elements are conjoined by "and/or," a first option refers to the applicability of the first element without the second. A second option refers to the applicability of the second element without the first. A third option refers to the applicability of the first and second elements together. Any one of these options is understood to fall within the meaning, and, therefore, satisfy the requirement of the term "and/or" as used herein. Concurrent applicability of more than one of the options is also understood to fall within the meaning, and, therefore, satisfy the requirement of the term "and/or."

[0075] It should be understood that for all numerical bounds describing some parameter in this application, such as "about," "at least," "less than," "fewer than," and "more than," the description also necessarily encompasses any range bounded by the recited values. Accordingly, for example, the description "at least 1, 2, 3, 4, or 5" also describes, *inter alia*, the ranges 1-2, 1-3, 1-4, 1-5, 2-3, 2-4, 2-5, 3-4, 3-5, and 4-5, *et cetera*.

[0076] When a list is presented, unless stated otherwise, it is to be understood that each individual element of that list, and every combination of that list, is a separate embodiment. For example, a list of embodiments presented as "A, B, or C" is to be interpreted as including the embodiments, "A," "B," "C," "A or B," "A or C," "B or C," or "A, B, or C."

[0077] As used herein, the term "about" means within an acceptable error range for a particular value, as determined by one of ordinary skill in the art. Typically, an acceptable error range for a particular value depends, at least in part, on how the value is measured or determined, *e.g.*, the limitations of the measurement system. For example, "about" can mean

within an acceptable standard deviation, per the practice in the art. Alternatively, "about" can mean a range of ± 20%, *e.g.*, ± 10%, ± 5% or ± 1% of a given value. It is to be understood that the term "about" can precede any particular value specified herein, except for particular values used in the Exemplification. When "about" precedes a range, as in "90-99.9%," the term "about" should be read as applying to both given values of the range, such that "about 90-99.9%" means about 90% repeats to about 99.9%.

[0078] As used herein, the term "polypeptide" refers to a polymer of at least two amino acids covalently linked by an amide bond, regardless of length or post-translational modification (*e.g.*, glycosylation or phosphorylation). A polypeptide can comprise any suitable L-and/or D-amino acid, for example, common α-amino acids (*e.g.*, alanine, glycine, valine), non-α-amino acids (*e.g.*, β-alanine, 4-aminobutyric acid, 6-aminocaproic acid, sarcosine, statine), and unusual amino acids (*e.g.*, citrulline, homocitruline, homoserine, norleucine, norvaline, ornithine). The amino, carboxyl, and/or other functional groups on a polypeptide can be free (*e.g.*, unmodified) or protected with a suitable protecting group. Suitable protecting groups for amino and carboxyl groups, and methods for adding or removing protecting groups are known in the art and are disclosed in, for example, Green and Wuts, *"Protecting Groups in Organic Synthesis,"* John Wiley and Sons, 1991. The functional groups of a polypeptide can also be derivatized (*e.g.*, alkylated) or labeled (*e.g.*, with a detectable label, such as a fluorogen or a hapten) using methods known in the art. A polypeptide can comprise one or more modifications (*e.g.*, amino acid linkers, acylation, acetylation, amidation, methylation, terminal modifiers (*e.g.*, cyclizing modifications), *N*-methyl-α-amino group substitution), if desired. In addition, a polypeptide can be an analog of a known and/or naturally-occurring peptide, for example, a peptide analog having conservative amino acid residue substitution(s).

[0079] As used herein, a "polynucleotide" is defined as a plurality of nucleotides and/or nucleotide analogs linked together in a single molecule. In some embodiments, a polynucleotide disclosed herein comprises deoxyribonucleotides. In some embodiments, the polynucleotide comprises ribonucleotides. Non-limiting examples of polynucleotides include single-, double- or multi-stranded DNA or RNA, DNA-RNA hybrids (*e.g.*, each "T" position may be independently substituted by a "U" or vice versa), or a polymer comprising purine and pyrimidine bases, or other natural, chemically, or biochemically modified, non-natural, or derivatized nucleotide bases. The backbone of the polynucleotide can comprise sugars and

phosphate groups, modified or substituted sugar or phosphate groups, a polymer of synthetic subunits such as phosphoramidates, or a combination thereof.

[0080] As used herein, the term "sequence identity" refers to the extent to which two nucleotide sequences have the same residues at the same positions when the sequences are aligned to achieve a maximal level of identity, expressed as a percentage. For sequence alignment and comparison, typically one sequence is designated as a reference sequence, to which test sequences are compared. Sequence identity between reference and test sequences is expressed as a percentage of positions across the entire length of the reference sequence where the reference and test sequences share the same nucleotide or amino acid upon alignment of the reference and test sequences to achieve a maximal level of identity. As an example, two sequences are considered to have 70% sequence identity when, upon alignment to achieve a maximal level of identity, the test sequence has the same nucleotide residue at 70% of the same positions over the entire length of the reference sequence.

[0081] Alignment of sequences for comparison to achieve maximal levels of identity can be readily performed by a person of ordinary skill in the art using an appropriate alignment method or algorithm. In some instances, alignment can include introduced gaps to provide for the maximal level of identity. Examples include the local homology algorithm of Smith & Waterman, *Adv. Appl. Math.* 2:482 (1981), the homology alignment algorithm of Needleman & Wunsch, *J. Mol. Biol.* 48:443 (1970), the search for similarity method of Pearson & Lipman, *Proc. Nat'l. Acad. Sci. USA* 85:2444 (1988), computerized implementations of these algorithms (GAP, BESTFIT, FASTA, and TFASTA in the Wisconsin Genetics Software Package, Genetics Computer Group, 575 Science Dr., Madison, Wis.), and visual inspection (see generally Ausubel *et al., Current Protocols in Molecular Biology*).

[0082] When using a sequence comparison algorithm, test and reference sequences are input into a computer, subsequent coordinates are designated, if necessary, and sequence algorithm program parameters are designated. The sequence comparison algorithm then calculates the percent sequence identity for the test sequence(s) relative to the reference sequence, based on the designated program parameters. A commonly used tool for determining percent sequence identity is Protein Basic Local Alignment Search Tool (BLASTP) available through National Center for Biotechnology Information, National Library of Medicine, of the United States National Institutes of Health. (Altschul *et al.*, 1990).

[0083] As used herein, the term "substantially similar to" refers to a polypeptide disclosed herein that is substantially similar in amino acid sequence (*e.g.*, has at least about 80%, at least about 90%, at least about 95%, at least about 96%, at least about 97%, at least about 98%, or at least about 99% of the amino acid residues amino acid sequence identity) and substantially preserves one or more functional properties of a specified polypeptide disclosed herein (*e.g.*, AB-1). In some embodiments, the one or more functional properties are selected from, without limitation, a substantially similar binding affinity, a substantially similar binding specificity, a substantially similar inhibitory activity, a substantially similar neutralization activity, and a substantially similar self-association property.

[0084] As used herein, a "complementarity determining region (CDR)" encompasses any CDR defined by an art-recognized method for identifying the CDR residues on an antibody. *See*, *e.g.*, Kabat, E.A., *et al.*, (1991) Sequences of Proteins of Immunological Interest, Fifth Edition, U.S. Department of Health and Human Services, NIH Publication No. 91-3242, Chothia *et al.*, (1989) Nature 342:877; Chothia, C. *et al.*, (1987) J. Mol. Biol. 196:901-917; Al-lazikani *et al.*, (1997) J. Molec. Biol. 273:927-948; and Almagro, J. Mol. Recognit. 17:132-143 (2004). *See* also hgmp.mrc.ac.uk and bioinf.org.uk/abs. Two antibodies are determined to have the same CDR as one another with respect to a HCDR1, HCDR2, HCDR3, LCDR1, LCDR2 and/or LCDR3, when the identity of that CDR is determined for both antibodies using the same method.

[0085] The extent of the framework region and the CDRs of an antibody can be identified using one of several suitable methodologies that are well known in the art, for example, by the Kabat definition, the Chothia definition, the AbM definition, and/or the contact definition. Publicly and/or commercially available tools for identifying framework and/or CDR regions include, IgBlast (accessible at www.ncbi.nlm.nih.gov/igblast/), Scaligner (available from drugdesigntech at www.scaligner.com/), IMGT rules and/or tools (*see*, for example, www.imgt.org/IMGTScientificChart/Nomenclature/IMGT-FRCDRdefinition.html, also accessible at www.imgt.org/), Chothia Canonical Assignment (accessible at www.bioinf.org.uk/abs/chothia.html), Antigen receptor Numbering And Receptor CalssificatiIon (ANARCI, accessible at opig.stats.ox.ac.uk/webapps/newsabdab/sabpred/anarci/), or the Paratome web server (accessible at www.ofranlab.org/paratome/, or the Paratome web server (accessible at www.ofranlab.org/paratome/ see Vered Kunik, *et al*, Nucleic Acids Research, Volume 40, Issue W1, 1 July 2012, Pages W521-W524).

[0086] For example, for AB-2, the HCDR1, HCDR2, HCDR3, LCDR1, LCDR2 and LCDR3 amino acid sequences: (1) comprise SEQ ID NO:31, SEQ ID NO:35, SEQ ID NO:50, SEQ ID NO:60, SEQ ID NO:67, and SEQ ID NO:71, respectively, as determined by IMGT numbering; (2) comprise SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, and SEQ ID NO:71, respectively, as determined by Kabat numbering; and (3) comprise SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, and SEQ ID NO:71, respectively, as determined by Chothia numbering.

[0087] As used herein, the term "paratope" refers to a set of amino acid residues in an antibody or an antigen-binding fragment thereof that contribute to a binding interaction with an epitope of a target protein. The binding interaction can be a hydrogen bond, a salt bridge, a van der Waal interaction, an ionic bond or a combination thereof. A binding interaction may be direct, or indirect, *e.g.*, via a coordinated intermediate molecule, such as an ion or water. The residues of a paratope, in some embodiments, comprise only residues that are part of a defined CDR. In other embodiments, the residues of a paratope further comprise one or more residues that are not part of a defined CDR.

[0088] As used herein, the term "antibody mimetic" refers to polypeptides capable of mimicking an antibody's ability to bind an antigen, but structurally differ from native antibody structures. Examples of antibody mimetics include, but not limited to, Adnectins, Affibodies, Affilins, Affimers, Affitins, Alphabodies, Anticalins, Avimers, DARPins, Fynomers, Kunitz domain peptides, monobodies, nanobodies, nanoCLAMPs, and Versabodies.

[0089] As used herein the term "K_D," also referred to as "binding constant," "equilibrium dissociation constant" or "affinity constant," is a measure of the extent of a reversible association between two molecular species (*e.g.*, antibody and target protein) and includes both the actual binding affinity as well as the apparent binding affinity. Binding affinity can be determined using methods known in the art including, for example, by measurement of surface plasmon resonance, *e.g.*, using a Biolayer interferometry (Octet, ForteBio) or a surface plasmon resonance (Biacore) system and assay. A reference that compares various surface technologies for measuring binding affinity and kinetics is Yang, D., Singh, A., Wu, H., & Kroe-Barrett, R., *Comparison of biosensor platforms in the evaluation of high affinity antibody-antigen binding kinetics*, Analytical Biochemistry 508: 78-96 (2016), the contents of which are incorporated by reference herein in their entirety.

[0090] The term "subject" or "patient" refers to an animal (*e.g.*, a mammal such as a human), diagnosed with or suspected of having a TSLP-associated disease or condition (*e.g.*, a disease or condition associated with dysregulated TSLP expression such as, asthma or atopic dermatitis (AD)), or one at risk of developing such conditions. Diagnosis may be performed by any method or technique known in the art. One skilled in the art will understand that a subject to be treated according to the present disclosure may have been subjected to standard tests or may have been identified, without examination, as one at risk due to the presence of one or more risk factors associated with the disease or condition.

[0091] The phrase "pharmaceutically acceptable" means that the substance or composition the phrase modifies is, within the scope of sound medical judgment, suitable for use in contact with the tissues of humans and lower animals without undue toxicity, irritation, allergic response, and the like, and are commensurate with a reasonable benefit/risk ratio.

[0092] As used herein, the term "pharmaceutically acceptable salt" refers to those salts which are, within the scope of sound medical judgment, suitable for use in contact with the tissues of mammals without undue toxicity, irritation, allergic response, and the like, and are commensurate with a reasonable benefit/risk ratio. Pharmaceutically acceptable salts are well known in the art. For example, S. M. Berge *et al.*, describe pharmaceutically acceptable salts in detail in J. Pharmaceutical Sciences, 1977, 66, 1-19, the relevant teachings of which are incorporated herein by reference in their entirety. Pharmaceutically acceptable salts of the agents/compounds described herein include salts derived from suitable inorganic and organic acids, and suitable inorganic and organic bases.

[0093] Examples of salts derived from suitable acids include salts of an amino group formed with inorganic acids such as hydrochloric acid, hydrobromic acid, phosphoric acid, sulfuric acid and perchloric acid, or with organic acids such as acetic acid, oxalic acid, maleic acid, tartaric acid, citric acid, succinic acid or malonic acid or by using other methods used in the art, such as ion exchange. Other pharmaceutically acceptable salts derived from suitable acids include adipate, alginate, ascorbate, aspartate, benzenesulfonate, benzoate, bisulfate, borate, butyrate, camphorate, camphorsulfonate, cinnamate, citrate, cyclopentanepropionate, digluconate, dodecylsulfate, ethanesulfonate, formate, fumarate, glucoheptonate, glycerophosphate, gluconate, glutarate, glycolate, hemisulfate, heptanoate, hexanoate, hydroiodide, hydroxybenzoate, 2-hydroxy-ethanesulfonate, hydroxymaleate, lactobionate, lactate, laurate, lauryl sulfate, malate, maleate, malonate, methanesulfonate, 2-naphthalenesulfonate, nicotinate, nitrate, oleate, oxalate, palmitate, pamoate, pectinate,

persulfate, 2-phenoxybenzoate, phenylacetate, 3-phenylpropionate, phosphate, pivalate, propionate, pyruvate, salicylate, stearate, succinate, sulfate, tartrate, thiocyanate, p-toluenesulfonate, undecanoate, valerate salts, and the like.

[0094] Either the mono-, di- or tri-acid salts can be formed, and such salts can exist in either a hydrated, solvated or substantially anhydrous form.

[0095] Salts derived from appropriate bases include salts derived from inorganic bases, such as alkali metal, alkaline earth metal, and ammonium bases, and salts derived from aliphatic, alicyclic or aromatic organic amines, such as methylamine, trimethylamine and picoline, or $N^+((C_1\text{-}C_4)alkyl)_4$ salts. Representative alkali or alkaline earth metal salts include sodium, lithium, potassium, calcium, magnesium, barium and the like. Further pharmaceutically acceptable salts include, when appropriate, nontoxic ammonium, quaternary ammonium, and amine cations formed using counterions such as halide, hydroxide, carboxyl, sulfate, phosphate, nitrate, lower alkyl sulfonate and aryl sulfonate.

[0096] "Pharmaceutically acceptable carrier" refers to a non-toxic carrier or excipient that does not destroy the pharmacological activity of the agent with which it is formulated and is nontoxic when administered in doses sufficient to deliver a therapeutic amount of the agent. Pharmaceutically acceptable carriers that may be used in the compositions described herein include, but are not limited to, ion exchangers, alumina, aluminum stearate, lecithin, serum proteins, such as human serum albumin, buffer substances such as phosphates, glycine, sorbic acid, potassium sorbate, partial glyceride mixtures of saturated vegetable fatty acids, water, salts or electrolytes, such as protamine sulfate, disodium hydrogen phosphate, potassium hydrogen phosphate, sodium chloride, zinc salts, colloidal silica, magnesium trisilicate, polyvinyl pyrrolidone, cellulose-based substances, polyethylene glycol, sodium carboxymethylcellulose, polyacrylates, waxes, polyethylene-polyoxypropylene-block polymers, polyethylene glycol and wool fat.

[0097] "Treating" or "treatment," as used herein, refers to taking steps to deliver a therapy to a subject, such as a mammal, in need thereof (*e.g.*, as by administering to a mammal one or more therapeutic agents). "Treating" or "treatment" includes inhibiting the disease or condition (*e.g.*, as by slowing or stopping its progression or causing regression of the disease or condition) and relieving the symptoms resulting from the disease or condition.

[0098] The term "treating," or "treatment" refers to the medical management of a subject with the intent to improve, ameliorate, stabilize (*i.e.*, not worsen), prevent, or cure a disease, pathological condition, or disorder—such as the particular indications exemplified herein.

This term includes active treatment (treatment directed to improve the disease, pathological condition, or disorder), causal treatment (treatment directed to the cause of the associated disease, pathological condition, or disorder), palliative treatment (treatment designed for the relief of symptoms), preventative treatment (treatment directed to minimizing or partially or completely inhibiting the development of the associated disease, pathological condition, or disorder); and supportive treatment (treatment employed to supplement another therapy). Treatment also includes diminishment of the extent of the disease or condition; preventing spread of the disease or condition; delay or slowing the progress of the disease or condition; amelioration or palliation of the disease or condition; and remission (whether partial or total), whether detectable or undetectable. "Ameliorating" or "palliating" a disease or condition means that the extent and/or undesirable clinical manifestations of the disease, disorder, or condition are lessened and/or time course of the progression is slowed or lengthened, as compared to the extent or time course in the absence of treatment. "Treatment" can also mean prolonging survival as compared to expected survival if not receiving treatment. Those in need of treatment include those already with the condition or disorder, as well as those prone to have the condition or disorder or those in which the condition or disorder is to be prevented.

[0099] A "pharmaceutical composition" refers to a formulation of one or more therapeutic agents and a medium generally accepted in the art for delivery of a biologically active agent to subjects, *e.g.*, humans. In some embodiments, a pharmaceutical composition may include one or more pharmaceutically acceptable excipients, diluents, or carriers. In some embodiments, a pharmaceutical composition suitable for use in methods disclosed herein further comprises one or more pharmaceutically acceptable carriers.

[00100] "Pharmaceutically acceptable carrier, diluent, or excipient" includes any adjuvant, carrier, excipient, glidant, sweetening agent, diluent, preservative, dye/colorant, flavor enhancer, surfactant, wetting agent, dispersing agent, suspending agent, stabilizer, isotonic agent, solvent, or emulsifier which has been approved by the United States Food and Drug Administration as being acceptable for use in humans or domestic animals.

[00101] "Pharmaceutically acceptable carrier" refers to an ingredient in a pharmaceutical composition, other than an active ingredient, which is nontoxic to a subject. A pharmaceutically acceptable carrier includes, but is not limited to, a buffer, excipient, stabilizer, or preservative. In some embodiments, the carrier may be a diluent, adjuvant, excipient, or vehicle with which the agent (*e.g.*, polynucleotide) is administered. Such

vehicles may be liquids, such as water and oils, including those of petroleum, animal, vegetable or synthetic origin, such as peanut oil, soybean oil, mineral oil, sesame oil, and the like. For example, 0.4% saline and 0.3% glycine can be used. These solutions are sterile and generally free of particulate matter. They may be sterilized by conventional, well-known sterilization techniques (*e.g.,* filtration). The compositions may contain pharmaceutically acceptable auxiliary substances as required to approximate physiological conditions such as pH adjusting and buffering agents, stabilizing, thickening, lubricating, and coloring agents, *etc.* The concentration of the agent in such pharmaceutical formulation may vary widely, *i.e.*, from less than about 0.5%, to at least about 1%, or to as much as 15% or 20%, 25%, 30%, 35%, 40%, 45% or 50% by weight. The concentration will be selected primarily based on required dose, fluid volumes, viscosities, *etc.*, according to the mode of administration. Suitable vehicles and formulations, inclusive of other human proteins, *e.g.,* human serum albumin, are described, for example, in Remington: The Science and Practice of Pharmacy, 21st Edition, Troy, D.B. ed., Lipincott Williams and Wilkins, Philadelphia, PA 2006, Part 5, Pharmaceutical Manufacturing: 691-1092 (*e.g.,* pages 958-89).

[00102] Non-limiting examples of pharmaceutically acceptable carriers are solvents, dispersion media, coatings, antibacterial and antifungal agents, isotonic and absorption delaying agents, and the like that are physiologically compatible, such as salts, buffers, antioxidants, saccharides, aqueous or non-aqueous carriers, preservatives, wetting agents, surfactants or emulsifying agents, or combinations thereof.

[00103] Non-limiting examples of buffers are acetic acid, citric acid, formic acid, succinic acid, phosphoric acid, carbonic acid, malic acid, aspartic acid, histidine, boric acid, Tris buffers, HEPPSO, and HEPES.

[00104] Non-limiting examples of antioxidants are ascorbic acid, methionine, cysteine hydrochloride, sodium bisulfate, sodium metabisulfite, sodium sulfite, lecithin, citric acid, ethylenediamine tetraacetic acid (EDTA), sorbitol, and tartaric acid.

[00105] Non-limiting examples of amino acids are histidine, isoleucine, methionine, glycine, arginine, lysine, L-leucine, tri-leucine, alanine, glutamic acid, L-threonine, and 2-phenylamine.

[00106] Non-limiting examples of surfactants are polysorbates (*e.g.*, polysorbate-20 or polysorbate-80); polyoxamers (*e.g.*, poloxamer 188); Triton; sodium octyl glycoside; lauryl-, myristyl-, linoleyl-, or stearyl-sulfobetaine; lauryl-, myristyl-, linoleyl- or stearyl-sarcosine; linoleyl-, myristyl-, or cetyl-betaine; lauroamidopropyl-, cocamidopropyl-,

linoleamidopropyl-, myristamidopropyl-, palmidopropyl-, or isostearamidopropyl-betaine (*e.g.*, lauroamidopropyl); myristamidopropyl-, palmidopropyl-, or isostearamidopropyl-dimethylamine; sodium methyl cocoyl-, or disodium methyl oleyl-taurate; and the MONAQUA™ series (Mona Industries, Inc., Paterson, N.J.), polyethyl glycol, polypropyl glycol, and copolymers of ethylene and propylene glycol (*e.g.*, PLURONICS™, PF68, *etc.*).

[00107] Non-limiting examples of preservatives are phenol, m-cresol, p-cresol, o-cresol, chlorocresol, benzyl alcohol, phenylmercuric nitrite, phenoxyethanol, formaldehyde, chlorobutanol, magnesium chloride, alkylparaben (methyl, ethyl, propyl, butyl, and the like), benzalkonium chloride, benzethonium chloride, sodium dehydroacetate, and thimerosal, or mixtures thereof.

[00108] Non-limiting examples of saccharides are monosaccharides, disaccharides, trisaccharides, polysaccharides, sugar alcohols, reducing sugars, nonreducing sugars such as glucose, sucrose, trehalose, lactose, fructose, maltose, dextran, glycerin, dextran, erythritol, glycerol, arabitol, sylitol, sorbitol, mannitol, mellibiose, melezitose, raffinose, mannotriose, stachyose, maltose, lactulose, maltulose, glucitol, maltitol, lactitol, or iso-maltulose.

[00109] Non-limiting examples of salts are acid addition salts and base addition salts. Acid addition salts include those derived from nontoxic inorganic acids, such as hydrochloric, nitric, phosphoric, sulfuric, hydrobromic, hydroiodic, phosphorous, and the like, as well as from nontoxic organic acids such as aliphatic mono- and dicarboxylic acids, phenyl-substituted alkanoic acids, hydroxy alkanoic acids, aromatic acids, aliphatic and aromatic sulfonic acids, and the like. Base addition salts include those derived from alkaline earth metals, such as sodium, potassium, magnesium, calcium, and the like, as well as from nontoxic organic amines, such as N,N'-dibenzylethylenediamine, N-methylglucamine, chloroprocaine, choline, diethanolamine, ethylenediamine, procaine, and the like. In some embodiments, the salt is sodium chloride (NaCl).

[00110] Agents (*e.g.*, polynucleotides) described herein may be prepared in accordance with standard procedures and are administered at dosages that are selected to reduce, prevent, or eliminate, or to slow or halt progression of, a condition being treated (see, *e.g.*, Remington's Pharmaceutical Sciences, Mack Publishing Company, Easton, PA, and Goodman and Gilman's The Pharmaceutical Basis of Therapeutics, McGraw-Hill, New York, N.Y., the contents of which are incorporated herein by reference, for a general description of methods for administering various agents for human therapy).

[00111] "Administering" or "administration," as used herein, refers to providing a compound, composition, or pharmaceutically acceptable salt thereof described herein to a subject in need of treatment or prevention. Administering can be performed, for example, once, a plurality of times, and/or over one or more extended periods. Administration includes both direct administration (including self-administration), and indirect administration (including an act of prescribing a drug or directing a subject to consume an agent). For example, as used herein, one (*e.g.*, a physician) who instructs a subject (*e.g.*, a human patient) to self-administer an agent (*e.g.*, a drug), or to have an agent administered by another and/or who provides a patient with a prescription for a drug is administering an agent to a subject.

[00112] "A therapeutically effective amount," "an effective amount" or "an effective dosage" refers to an amount effective, at dosages and for periods of time necessary, to achieve a desired therapeutic result (*e.g.*, treatment, healing, inhibition or amelioration of physiological response or condition, *etc.*). A full therapeutic effect does not necessarily occur by administration of one dose and may occur only after administration of a series of doses. Thus, a therapeutically effective amount may be administered in one or more administrations. A therapeutically effective amount may vary according to factors such as the disease state, age, sex, and weight of a mammal (*e.g.*, a human patient), mode of administration, and the ability of a therapeutic or a combination of therapeutics to elicit a desired response.

[00113] An effective amount of an agent to be administered can be determined by a clinician of ordinary skill using the guidance provided herein and other methods known in the art. Relevant factors include the given agent, the pharmaceutical formulation, the route of administration, the type of disease or disorder, the identity of the subject (*e.g.*, age, sex, weight) or host being treated, and the like. For example, suitable dosages can be from about 0.001 mg/kg to about 100 mg/kg, from about 0.01 mg/kg to about 100 mg/kg, from about 0.01 mg/kg to about 10 mg/kg, from about 0.01 mg/kg to about 1 mg/kg body weight per treatment. Determining the dosage for a particular agent, subject and disease is well within the abilities of one of skill in the art. Preferably, the dosage does not cause or produces minimal adverse side effects.

[00114] Desired response or desired results include effects at the cellular level, tissue level, or clinical results. As such, "a therapeutically effective amount" or synonym thereto depends upon the context in which it is being applied. For example, in some embodiments it is an amount of the composition sufficient to achieve a treatment response as compared to the response obtained without administration of the composition. In other embodiments, it is an

amount that results in a beneficial or desired result in a subject as compared to a control. As defined herein, a therapeutically effective amount of a composition (*e.g.*, a pharmaceutical composition) disclosed herein may be readily determined by one of ordinary skill by routine methods known in the art. Dosage regimen and route of administration may be adjusted to provide the optimum therapeutic response.

Thymic Stromal Lymphopoietin (TSLP)

[00115] As used herein, TSLP includes wild-type TSLP proteins (*e.g.*, wild-type human TSLP proteins or homologs thereof) and truncated forms thereof, mutant, and engineered versions of full-length and truncated TSLP proteins, and modified forms (*e.g.*, post-translationally modified forms) of full-length and truncated TSLP proteins.

[00116] A non-limiting example of human TSLP sequences is GenBank: AAK67490.1 (SEQ ID NO:1).

[00117] MFPFALLYVLSVSFRKIFILQLVGLVLTYDFTNCDFEKIKAAYLSTISKDLIT YMSGTKSTEFNNTVSCSNRPHCLTEIQSLTFNPTAGCASLAKEMFAMKTKAALAIWC PGYSETQINATQAMKKRRKRKVTTNKCLEQVSQLQGLWRRFNRPLLKQQ (SEQ ID NO:1).

[00118] A non-limiting example of cyno monkey TSLP sequences is GenBank: EHH54440.1 (SEQ ID NO:83).

[00119] MKSLGQSKKEEVSFRKFFIFQLVGLVLTYDFTNCDFQKIEADYLRTISKDLI TYMSGTKSTDFNNTVSCSNRPHCLTEIQSLTFNPTPRCASLAKEMFARKTKATLALW CPGYSETQINATQAMKKRRKRKVTTNKCLEQVSQLLGLWRRFIRTLLKKQ (SEQ ID NO:83).

[00120] In some embodiments, a polypeptide binds to a wild-type TSLP protein (*e.g.*, a TSLP protein having the amino acid sequence of SEQ ID NO:1, SEQ ID NO:83, or both). In some embodiments, a polypeptide binds to a TSLP protein comprising the amino acid sequence of SEQ ID NO:1. In some embodiments, a polypeptide binds to a TSLP protein comprising the amino acid sequence of SEQ ID NO:1 and a TSLP protein comprising the amino acid sequence of SEQ ID NO:83.

[00121] In some embodiments, a polypeptide binds to a mutant or engineered TSLP protein. In some embodiments, a mutant or engineered TSLP protein comprises an amino acid sequence that has at least about 90% sequence identity to a wildtype TSLP protein, for example, at least about: 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.1%, 99.2%,

99.3%, 99.4%, 99.5%, 99.6%, 99.7%, 99.8%, or 99.9% sequence identity to a wildtype TSLP protein (*e.g.*, SEQ ID NO:1 or SEQ ID NO:83). In some embodiments, a mutant or engineered TSLP protein comprises an amino acid sequence that has about 90-99.9%, 90-99.8%, 92-99.8%, 92-99.6%, 94-99.6%, 94-99.5%, 95-99.5%, 95-99.4%, 96-99.4%, 96-99.2%, 97-99.2% or 97-99% sequence identity to a wildtype TSLP protein.

[00122] In some embodiments, a polypeptide binds to a modified TSLP protein.

[00123] In some embodiments, a polypeptide is capable of binding to one or more epitope residues in a TSLP protein (*e.g.*, a full-length human TSLP), for example, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 epitope residues of a TSLP protein. In some embodiments, a polypeptide is capable of binding to one or more epitope residues (*e.g.*, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or all 15 residues) selected from N64, N65, T66, V67, S68, C69, S70, N71, R72, H74, C75, E78, R150, F151 and R153 of SEQ ID NO:1.

[00124] In some embodiments, a polypeptide binds to one or more epitope residues of a TSLP protein (*e.g.*, one or more epitope residues in SEQ ID NO:1). In some embodiments, a polypeptide binds to one or more epitope residues (*e.g.*, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or all 15 residues) selected from N64, N65, T66, V67, S68, C69, S70, N71, R72, H74, C75, E78, R150, F151 and R153 of SEQ ID NO:1.

Comparator Polypeptides

[00125] As used herein, the term "comparator" or "comparator polypeptide" refers to a polypeptide (*e.g.*, immunoglobulin molecule) that specifically binds to a TSLP protein and is not a polypeptide disclosed herein. The sequence of a comparator polypeptide and a polypeptide disclosed herein may be compared to illustrate structural differences between them (*e.g.*, differences at one or more amino acid positions, such as amino acid substitutions). Polypeptides disclosed herein have more than insubstantial differences (*e.g.*, one or more substantial differences) in comparison to a comparator polypeptide, such that, polypeptides disclosed herein will, under controlled conditions, exhibit one or more (*i.e.*, one, two, or all three) of: a different function, in a different way, to achieve a different result, in comparison to a comparator polypeptide. A comparator polypeptide may vary from a polypeptide disclosed herein by one or more amino acids, *e.g.*, in some embodiments, by 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20 or more amino acids. In some embodiments, a comparator polypeptide diverges from a polypeptide disclosed herein by at least about: 0.4%,

0.8%, 1%, 2%, 3%, 4%, 5%, 6%, 7%, 8%, 9%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, or more amino acid percent identity.

[00126] In some embodiments, a comparator polypeptide is an antibody comprising:

a) a heavy chain complementarity determining region 1 (HCDR1), a heavy chain complementarity determining region 2 (HCDR2) and a heavy chain complementarity determining region 3 (HCDR3) sequences of SEQ ID NO:31, SEQ ID NO:33 and SEQ ID NO:48, respectively;

b) a light chain complementarity determining region 1 (LCDR1), a light chain complementarity determining region 2 (LCDR2) and a light chain complementarity determining region 3 (LCDR3) sequences of SEQ ID NO:59, SEQ ID NO:67 and SEQ ID NO:69, respectively, or

both a) and b).

[00127] In some embodiments, a comparator polypeptide is an antibody comprising:

a) a HCDR1, a HCDR2 and a HCDR3 sequences of SEQ ID NO:31, SEQ ID NO:33 and SEQ ID NO:48, respectively; and

b) a LCDR1, a LCDR2 and a LCDR3 sequences of SEQ ID NO:59, SEQ ID NO:67 and SEQ ID NO:69, respectively.

[00128] *See* Table 3 and FIG. 2 for SEQ ID NOs:31, 33 and 48. *See* Table 3 and FIG. 3 for SEQ ID NOs:59, 67 and 69.

[00129] In some embodiments, a comparator polypeptide is an antibody comprising:

a) an immunoglobulin heavy chain variable region (V_H) domain comprising the amino acid sequence of SEQ ID NO:3;

b) an immunoglobulin light chain variable region (V_L) domain comprising the amino acid sequence of SEQ ID NO:19, or

both a) and b).

[00130] In some embodiments, a comparator polypeptide is an antibody comprising:

a) an immunoglobulin heavy chain variable region (V_H) domain comprising the amino acid sequence of SEQ ID NO:3; and

b) an immunoglobulin light chain variable region (V_L) domain comprising the amino acid sequence of SEQ ID NO:19.

[00131] *See* Table 1 and FIG. 2 for SEQ ID NO:3. *See* Table 2 and FIG. 3 for SEQ ID NO:19.

[00132] In some embodiments, a comparator polypeptide is an antibody referred to herein as the "Reference Antibody." The Reference Antibody comprises:

a) a heavy chain comprising the amino acid sequence of SEQ ID NO:81; and

b) a light chain comprising the amino acid sequence of SEQ ID NO:82.

[00133] *See* Table 4 for SEQ ID NO:81. *See* Table 5 for SEQ ID NO:82.

[00134] The Reference Antibody binds and neutralizes TSLP.

Polypeptides

In some embodiments, a polypeptide specifically binds a TSLP.

In some embodiments, a polypeptide is an antibody or antigen-binding fragment thereof.

Variable Domains

[00135] In some embodiments, a polypeptide (*e.g.*, an antibody or antigen-binding fragment thereof) comprises an immunoglobulin heavy chain variable region (V_H), an immunoglobulin light chain variable region (V_L), or both. In some embodiments, a polypeptide comprises a V_H having less than 100% sequence identity to the amino acid sequence of SEQ ID NO:3, a V_L having less than 100% sequence identity to the amino acid sequence of SEQ ID NO:19, or both.

[00136] In some embodiments, a polypeptide comprises a V_H (*e.g.*, a mammalian V_H such as a rodent (*e.g.*, mouse) V_H, a primate (*e.g.*, a human) V_H). In some embodiments, a polypeptide comprises a V_H that is humanized (*e.g.*, at least about: 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 95%, 98% or 99% humanized), contains human framework regions, or both.

[00137] In some embodiments, a polypeptide comprises a V_H that has less than 100% sequence identity to the amino acid sequence of SEQ ID NO:3.

[00138] In some embodiments, a polypeptide comprises a V_H that has at least about 70% sequence identity to the amino acid sequence of SEQ ID NO:3. In some embodiments, a polypeptide comprises a V_H that has at least about: 71%, 72%, 73%, 74%, 75%, 76%, 77%, 78%, 79%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% sequence identity to the amino acid sequence of SEQ ID NO:3. In some embodiments, a polypeptide comprises a V_H that has at least about 85% sequence identity to the amino acid sequence of SEQ ID NO:3. In some embodiments, a

polypeptide comprises a V_H that has at least about 90% sequence identity to the amino acid sequence of SEQ ID NO:3.

[00139] In some embodiments, a polypeptide comprises a V_H that comprises at least one amino acid substitution (*e.g.*, at least one conservative substitution such as highly conservative substitution) relative to the amino acid sequence of SEQ ID NO:3. For example, the number of amino acid substitutions can be at least about: 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19 or 20, or about: 1-20, 1-19, 2-19, 2-18, 2-17, 3-17, 3-16, 4-16, 4-15, 5-15, 5-14, 6-14, 6-13, 7-13, 7-12, 8-12, 8-11 or 9-11. In some embodiments, a polypeptide comprises a V_H that comprises about 1-10 amino acid substitutions, relative to the amino acid sequence of SEQ ID NO:3. In some embodiments, the at least one amino acid substitution replaces only a heavy chain complementarity determining region 1 (HCDR1), a heavy chain complementarity determining region 2 (HCDR2), and/or a heavy chain complementarity determining region 3 (HCDR3) residue, of SEQ ID NO:3. In some embodiments, the at least one amino acid substitution replaces only a non-CDR residue (*e.g.*, within a framework region), of SEQ ID NO:3.

[00140] In some embodiments, an amino acid substitution is a conservative substitution. The term "a conservative amino acid substitution" or "a conservative substitution" refers to an amino acid substitution having a value of 0 or greater in BLOSUM62.

[00141] In some embodiments, an amino acid substitution is a highly conservative substitution. The term "a highly conservative amino acid substitution" or "a highly conservative substitution" refers to an amino acid substitution having a value of at least 1 (*e.g.*, at least 2) in BLOSUM62.

[00142] In some embodiments, a polypeptide comprises a V_H that has 100% sequence identity to the amino acid sequence of SEQ ID NO:3. In some embodiments, a polypeptide comprises a V_H that comprises the amino acid sequence of SEQ ID NO:3.

[00143] In some embodiments, a polypeptide comprises a V_H that has at least about 70% sequence identity to the amino acid sequence of any one or more of SEQ ID NOs:4-17. The sequences identified as SEQ ID NOs:4-17 are shown in Table 1, which correspond to human V_H domains. In some embodiments, a polypeptide comprises a V_H that has at least about: 71%, 72%, 73%, 74%, 75%, 76%, 77%, 78%, 79%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% sequence identity to the amino acid sequence of any one or more of SEQ ID NOs:4-17. In some embodiments, a polypeptide comprises a V_H that has at least about 85% sequence identity to

the amino acid sequence of any one or more of SEQ ID NOs:4-17. In some embodiments, a polypeptide comprises a V_H that has at least about 90% sequence identity to the amino acid sequence of any one or more of SEQ ID NOs:4-17.

[00144] In some embodiments, a polypeptide comprises a V_H that comprises at least one amino acid substitution relative to the amino acid sequence of any one or more of SEQ ID NOs:4-17. For example, the number of amino acid substitutions can be at least about: 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19 or 20, or about: 1-20, 1-19, 2-19, 2-18, 2-17, 3-17, 3-16, 4-16, 4-15, 5-15, 5-14, 6-14, 6-13, 7-13, 7-12, 8-12, 8-11 or 9-11. In some embodiments, a polypeptide comprises a V_H that comprises about 1-10 amino acid substitutions, relative to the amino acid sequence of any one or more of SEQ ID NOs:4-17.

[00145] In some embodiments, a polypeptide comprises a V_H that has 100% sequence identity to the amino acid sequence of any one of SEQ ID NOs:4-17. In some embodiments, a polypeptide comprises a V_H that comprises the amino acid sequence of any one of SEQ ID NOs:4-17.

[00146] In some embodiments, a polypeptide comprises a V_H that has at least about 70% sequence identity to the amino acid sequence of any one or more of SEQ ID NOs:4-7. In some embodiments, a polypeptide comprises a V_H that has at least about: 71%, 72%, 73%, 74%, 75%, 76%, 77%, 78%, 79%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% sequence identity to the amino acid sequence of any one or more of SEQ ID NOs:4-7. In some embodiments, a polypeptide comprises a V_H that has at least about 85% sequence identity to the amino acid sequence of any one or more of SEQ ID NOs:4-7. In some embodiments, a polypeptide comprises a V_H that has at least about 90% sequence identity to the amino acid sequence of any one or more of SEQ ID NOs:4-7.

[00147] In some embodiments, a polypeptide comprises a V_H that comprises at least one amino acid substitution relative to the amino acid sequence of any one or more of SEQ ID NOs:4-7. For example, the number of amino acid substitutions can be at least about: 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19 or 20, or about: 1-20, 1-19, 2-19, 2-18, 2-17, 3-17, 3-16, 4-16, 4-15, 5-15, 5-14, 6-14, 6-13, 7-13, 7-12, 8-12, 8-11 or 9-11. In some embodiments, a polypeptide comprises a V_H that comprises about 1-10 amino acid substitutions, relative to the amino acid sequence of any one or more of SEQ ID NOs:4-7.

[00148] In some embodiments, a polypeptide comprises a V_H that has 100% sequence identity to the amino acid sequence of any one of SEQ ID NOs:4-7. In some embodiments, a

polypeptide comprises a V_H that comprises the amino acid sequence of any one of SEQ ID NOs:4-7.

[00149] In some embodiments, a polypeptide comprises a V_L (*e.g.*, a mammalian V_L such as a rodent (*e.g.*, mouse) V_L, a primate (*e.g.*, a human) V_L). In some embodiments, a polypeptide comprises a V_L that is humanized (*e.g.*, at least about: 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 95%, 98% or 99% humanized), contains human framework regions, or both.

[00150] In some embodiments, a polypeptide comprises a V_L that has less than 100% sequence identity to the amino acid sequence of SEQ ID NO:19.

[00151] In some embodiments, a polypeptide comprises a V_L that has at least about 70% sequence identity to the amino acid sequence of SEQ ID NO:19. In some embodiments, a polypeptide comprises a V_L that has at least about: 71%, 72%, 73%, 74%, 75%, 76%, 77%, 78%, 79%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% sequence identity to the amino acid sequence of SEQ ID NO:19. In some embodiments, a polypeptide comprises a V_L that has at least about 85% sequence identity to the amino acid sequence of SEQ ID NO:19. In some embodiments, a polypeptide comprises a V_L that has at least about 90% sequence identity to the amino acid sequence of SEQ ID NO:19.

[00152] In some embodiments, a polypeptide comprises a V_L that comprises at least one amino acid substitution (*e.g.*, at least one conservative substitution such as highly conservative substitution) relative to the amino acid sequence of SEQ ID NO:19. For example, the number of amino acid substitutions can be at least about: 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19 or 20, or about: 1-20, 1-19, 2-19, 2-18, 2-17, 3-17, 3-16, 4-16, 4-15, 5-15, 5-14, 6-14, 6-13, 7-13, 7-12, 8-12, 8-11 or 9-11. In some embodiments, a polypeptide comprises a V_L that comprises about 1-10 amino acid substitutions, relative to the amino acid sequence of SEQ ID NO:19. In some embodiments, the at least one amino acid substitution replaces only a light chain complementarity determining region 1 (LCDR1), a light chain complementarity determining region 2 (LCDR2), and/or a light chain complementarity determining region 3 (LCDR3) residue, of SEQ ID NO:19. In some embodiments, the at least one amino acid substitution replaces only a non-CDR residue (*e.g.*, within a framework region), of SEQ ID NO:19.

[00153] In some embodiments, an amino acid substitution is a conservative substitution.

[00154] In some embodiments, an amino acid substitution is a highly conservative substitution.

[00155] In some embodiments, a polypeptide comprises a V_L that has 100% sequence identity to the amino acid sequence of SEQ ID NO:19. In some embodiments, a polypeptide comprises a V_L that comprises the amino acid sequence of SEQ ID NO:19.

[00156] In some embodiments, a polypeptide comprises a V_L that has at least about 70% sequence identity to the amino acid sequence of any one or more of SEQ ID NOs:20-30. The sequences identified as SEQ ID NOs:20-30 are shown in Table 2, which correspond to human V_L domains. In some embodiments, a polypeptide comprises a V_L that has at least about: 71%, 72%, 73%, 74%, 75%, 76%, 77%, 78%, 79%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% sequence identity to the amino acid sequence of any one or more of SEQ ID NOs:20-30. In some embodiments, a polypeptide comprises a V_L that has at least about 85% sequence identity to the amino acid sequence of any one or more of SEQ ID NOs:20-30. In some embodiments, a polypeptide comprises a V_L that has at least about 90% sequence identity to the amino acid sequence of any one or more of SEQ ID NOs:20-30.

[00157] In some embodiments, a polypeptide comprises a V_L that comprises at least one amino acid substitution relative to the amino acid sequence of any one or more of SEQ ID NOs:20-30. For example, the number of amino acid substitutions can be at least about: 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19 or 20, or about: 1-20, 1-19, 2-19, 2-18, 2-17, 3-17, 3-16, 4-16, 4-15, 5-15, 5-14, 6-14, 6-13, 7-13, 7-12, 8-12, 8-11 or 9-11. In some embodiments, a polypeptide comprises a V_L that comprises about 1-10 amino acid substitutions, relative to the amino acid sequence of any one or more of SEQ ID NOs:20-30.

[00158] In some embodiments, a polypeptide comprises a V_L that has 100% sequence identity to the amino acid sequence of any one of SEQ ID NOs:20-30. In some embodiments, a polypeptide comprises a V_L that comprises the amino acid sequence of any one of SEQ ID NOs:20-30.

[00159] In some embodiments, a polypeptide comprises a V_L that has at least about 70% sequence identity to the amino acid sequence of any one or more of SEQ ID NOs:20-22. In some embodiments, a polypeptide comprises a V_L that has at least about: 71%, 72%, 73%, 74%, 75%, 76%, 77%, 78%, 79%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% sequence identity to the amino acid sequence of any one or more of SEQ ID NOs:20-22. In some embodiments, a

polypeptide comprises a V_L that has at least about 85% sequence identity to the amino acid sequence of any one or more of SEQ ID NOs:20-22. In some embodiments, a polypeptide comprises a V_L that has at least about 90% sequence identity to the amino acid sequence of any one or more of SEQ ID NOs:20-22.

[00160] In some embodiments, a polypeptide comprises a V_L that comprises at least one amino acid substitution relative to the amino acid sequence of any one or more of SEQ ID NOs:20-22. For example, the number of amino acid substitutions can be at least about: 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19 or 20, or about: 1-20, 1-19, 2-19, 2-18, 2-17, 3-17, 3-16, 4-16, 4-15, 5-15, 5-14, 6-14, 6-13, 7-13, 7-12, 8-12, 8-11 or 9-11. In some embodiments, a polypeptide comprises a V_L that comprises about 1-10 amino acid substitutions, relative to the amino acid sequence of any one or more of SEQ ID NOs:20-22.

[00161] In some embodiments, a polypeptide comprises a V_L that has 100% sequence identity to the amino acid sequence of any one of SEQ ID NOs:20-22. In some embodiments, a polypeptide comprises a V_L that comprises the amino acid sequence of any one of SEQ ID NOs:20-22.

[00162] In some embodiments, a polypeptide comprises a V_H (*e.g.*, a mammalian V_H such as a rodent (*e.g.*, mouse) V_H, a primate (*e.g.*, a human) V_H) and a V_L (*e.g.*, a mammalian V_L such as a rodent (*e.g.*, mouse) V_L, a primate (*e.g.*, a human) V_L). In some embodiments, a polypeptide comprises a V_H and V_L that are humanized (*e.g.*, at least about: 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 95%, 98% or 99% humanized), contain human framework regions, or both.

[00163] In some embodiments, a polypeptide comprises:

a) a V_H that has less than 100% sequence identity to the amino acid sequence of SEQ ID NO:3;

b) a V_L that has less than 100% sequence identity to the amino acid sequence of SEQ ID NO:19, or

both a) and b).

[00164] In some embodiments, a polypeptide comprises:

a) a V_H that has less than 100% sequence identity to the amino acid sequence of SEQ ID NO:3; and

b) a V_L that has less than 100% sequence identity to the amino acid sequence of SEQ ID NO:19.

[00165] In some embodiments, a polypeptide comprises:

a) a V_H that has at least about 55% (*e.g.*, at least about: 60, 65, 70, 75, 80, 85, 90, 95, 98, or 99%) sequence identity to the amino acid sequence of SEQ ID NO:3;

b) a V_L that has at least about 55% (*e.g.*, at least about: 60, 65, 70, 75, 80, 85, 90, 95, 98, or 99%) sequence identity to the amino acid sequence of SEQ ID NO:19, or

both a) and b),

wherein the polypeptide does not comprise all 6 CDRs of an antibody comprising a V_H amino acid sequence of SEQ ID NO:3 and a V_L amino acid sequence of SEQ ID NO:19.

[00166] In some embodiments, a polypeptide comprises:

a) a V_H that has at least about 55% (*e.g.*, at least about: 60, 65, 70, 75, 80, 85, 90, 95, 98, or 99%) sequence identity to the amino acid sequence of SEQ ID NO:3; and

b) a V_L that has at least about 55% (*e.g.*, at least about: 60, 65, 70, 75, 80, 85, 90, 95, 98, or 99%) sequence identity to the amino acid sequence of SEQ ID NO:19,

wherein the polypeptide does not comprise all 6 CDRs of an antibody comprising a V_H amino acid sequence of SEQ ID NO:3 and a V_L amino acid sequence of SEQ ID NO:19.

[00167] In some embodiments, a polypeptide comprises:

a) a V_H that comprises at least one amino acid substitution (*e.g.*, at least one conservative substitution such as highly conservative substitution) relative to the amino acid sequence of SEQ ID NO:3;

b) a V_L that comprises at least one amino acid substitution (*e.g.*, at least one conservative substitution such as highly conservative substitution) relative to the amino acid sequence of SEQ ID NO:19, or

both a) and b).

[00168] In some embodiments, a polypeptide comprises:

a) a V_H that comprises at least one amino acid substitution (*e.g.*, at least one conservative substitution such as highly conservative amino acid substitution) relative to the amino acid sequence of SEQ ID NO:3; and

b) a V_L that comprises at least one amino acid substitution (*e.g.*, at least one conservative substitution such as highly conservative amino acid substitution) relative to the amino acid sequence of SEQ ID NO:19.

[00169] In some embodiments, a polypeptide comprises:

a) a V_H that comprises at least one amino acid substitution (*e.g.*, at least one conservative substitution such as highly conservative amino acid substitution) of a HCDR1, a HCDR2 and/or a HCDR3 residue, of SEQ ID NO:3;

b) a V_L that comprises at least one amino acid substitution (*e.g.*, at least one conservative substitution such as highly conservative amino acid substitution) of a LCDR1, a LCDR2 and/or a LCDR3 residue, of SEQ ID NO:19, or

both a) and b).

[00170] In some embodiments, a polypeptide comprises:

a) a V_H that comprises at least one amino acid substitution (*e.g.*, at least one conservative substitution such as highly conservative amino acid substitution) of a HCDR1, a HCDR2 and/or a HCDR3 residue, of SEQ ID NO:3; and

b) a V_L that comprises at least one amino acid substitution (*e.g.*, at least one conservative substitution such as highly conservative amino acid substitution) of a LCDR1, a LCDR2 and/or a LCDR3 residue, of SEQ ID NO:19.

[00171] In some embodiments, a polypeptide comprises:

a) a V_H that comprises at least one amino acid substitution (*e.g.*, at least one conservative substitution such as highly conservative amino acid substitution) of a non-CDR residue (*e.g.*, within a framework region), of SEQ ID NO:3;

b) a V_L that comprises at least one amino acid substitution (*e.g.*, at least one conservative substitution such as highly conservative amino acid substitution) of a non-CDR residue (*e.g.*, within a framework region), of SEQ ID NO:19, or

both a) and b).

[00172] In some embodiments, a polypeptide comprises:

a) a V_H that comprises at least one amino acid substitution (*e.g.*, at least one conservative substitution such as highly conservative amino acid substitution) of a non-CDR residue (*e.g.*, within a framework region), of SEQ ID NO:3; and

b) a V_L that comprises at least one amino acid substitution (*e.g.*, at least one conservative substitution such as highly conservative amino acid substitution) of a non-CDR residue (*e.g.*, within a framework region), of SEQ ID NO:19.

[00173] In some embodiments, a polypeptide comprises:

a) a V_H that has at least about 70% (*e.g.*, at least about: 75, 80, 85, 90, 95, 98, or 99%) sequence identity to the amino acid sequence of any one or more of SEQ ID NOs:4-17;

b) a V_L that has at least about 70% (*e.g.*, at least about: 75, 80, 85, 90, 95, 98, or 99%) sequence identity to the amino acid sequence of any one or more of SEQ ID NOs:20-30, or

both a) and b).

[00174] In some embodiments, a polypeptide comprises:

a) a V_H that has at least about 70% (*e.g.*, at least about: 75, 80, 85, 90, 95, 98, or 99%) sequence identity to the amino acid sequence of any one or more of SEQ ID NOs:4-17; and

b) a V_L that has at least about 70% (*e.g.*, at least about: 75, 80, 85, 90, 95, 98, or 99%) sequence identity to the amino acid sequence of any one or more of SEQ ID NOs:20-30.

[00175] In some embodiments, a polypeptide comprises:

a) a V_H that comprises at least one amino acid substitution (*e.g.*, at least one conservative substitution such as highly conservative amino acid substitution) relative to the amino acid sequence of any one or more of SEQ ID NOs:4-17;

b) a V_L that comprises at least one amino acid substitution (*e.g.*, at least one conservative substitution such as highly conservative amino acid substitution) relative to the amino acid sequence of any one or more of SEQ ID NOs:20-30, or

both a) and b).

[00176] In some embodiments, a polypeptide comprises:

a) a V_H that comprises at least one amino acid substitution (*e.g.*, at least one conservative substitution such as highly conservative amino acid substitution) relative to the amino acid sequence of any one or more of SEQ ID NOs:4-17; and

b) a V_L that comprises at least one amino acid substitution (*e.g.*, at least one conservative substitution such as highly conservative amino acid substitution) relative to the amino acid sequence of any one or more of SEQ ID NOs:20-30.

[00177] In some embodiments, a polypeptide comprises:

a) a V_H that comprises at least one amino acid substitution (*e.g.*, at least one conservative substitution such as highly conservative amino acid substitution) of a HCDR1, a HCDR2 and/or a HCDR3 residue, of any one or more of SEQ ID NOs:4-17;

b) a V_L that comprises at least one amino acid substitution (*e.g.*, at least one conservative substitution such as highly conservative amino acid substitution) of a LCDR1, a LCDR2 and/or a LCDR3 residue, of any one or more of SEQ ID NOs:20-30, or

both a) and b).

[00178] In some embodiments, a polypeptide comprises:

a) a V_H that comprises at least one amino acid substitution (*e.g.*, at least one conservative substitution such as highly conservative amino acid substitution) of a HCDR1, a HCDR2 and/or a HCDR3 residue, of any one or more of SEQ ID NOs:4-17; and

b) a V_L that comprises at least one amino acid substitution (*e.g.*, at least one conservative substitution such as highly conservative amino acid substitution) of a LCDR1, a LCDR2 and/or a LCDR3 residue, of any one or more of SEQ ID NOs:20-30.

[00179] In some embodiments, a polypeptide comprises:

a) a V_H that comprises at least one amino acid substitution (*e.g.*, at least one conservative substitution such as highly conservative amino acid substitution) of a non-CDR residue (*e.g.*, within a framework region), of any one or more of SEQ ID NOs:4-17;

b) a V_L that comprises at least one amino acid substitution (*e.g.*, at least one conservative substitution such as highly conservative amino acid substitution) of a non-CDR residue (*e.g.*, within a framework region), of any one or more of SEQ ID NOs:20-30, or

both a) and b).

[00180] In some embodiments, a polypeptide comprises:

a) a V_H that comprises at least one amino acid substitution (*e.g.*, at least one conservative substitution such as highly conservative amino acid substitution) of a non-CDR residue (*e.g.*, within a framework region), of any one or more of SEQ ID NOs:4-17; and

b) a V_L that comprises at least one amino acid substitution (*e.g.*, at least one conservative substitution such as highly conservative amino acid substitution) of a non-CDR residue (*e.g.*, within a framework region), of any one or more of SEQ ID NOs:20-30.

[00181] In some embodiments, a polypeptide disclosed herein comprises:

a) a V_H comprising the amino acid sequence of any one of SEQ ID NOs:4-17; and

b) a V_L comprising the amino acid sequence of any one of SEQ ID NOs:20-30.

[00182] In some embodiments, a polypeptide comprises:

a) a V_H comprising the amino acid sequence of any one of SEQ ID NOs:4-17; and

b) a V_L comprising the amino acid sequence of SEQ ID NO:19.

[00183] In some embodiments, a polypeptide comprises:

a) a V_H comprising the amino acid sequence of SEQ ID NO:3; and

b) a V_L comprising the amino acid sequence of any one of SEQ ID NOs:20-30.

[00184] In some embodiments, a polypeptide comprises:

a) a V_H that has at least about 70% (*e.g.*, at least about: 75, 80, 85, 90, 95, 98, or 99%) sequence identity to the amino acid sequence of any one or more of SEQ ID NOs:4-7;

b) a V_L that has at least about 70% (*e.g.*, at least about: 75, 80, 85, 90, 95, 98, or 99%) sequence identity to the amino acid sequence of any one or more of SEQ ID NOs:20-22, or

both a) and b).

[00185] In some embodiments, a polypeptide comprises:

a) a V_H that has at least about 70% (*e.g.*, at least about: 75, 80, 85, 90, 95, 98, or 99%) sequence identity to the amino acid sequence of any one or more of SEQ ID NOs:4-7; and

b) a V_L that has at least about 70% (*e.g.*, at least about: 75, 80, 85, 90, 95, 98, or 99%) sequence identity to the amino acid sequence of any one or more of SEQ ID NOs:20-22.

[00186] In some embodiments, a polypeptide comprises:

a) a V_H that comprises at least one amino acid substitution (*e.g.*, at least one conservative substitution such as highly conservative amino acid substitution) relative to the amino acid sequence of any one or more of SEQ ID NOs:4-7;

b) a V_L that comprises at least one amino acid substitution (*e.g.*, at least one conservative substitution such as highly conservative amino acid substitution) relative to the amino acid sequence of any one or more of SEQ ID NOs:20-22, or

both a) and b).

[00187] In some embodiments, a polypeptide comprises:

a) a V_H that comprises at least one amino acid substitution (*e.g.*, at least one conservative substitution such as highly conservative amino acid substitution) relative to the amino acid sequence of any one or more of SEQ ID NOs:4-7; and

b) a V_L that comprises at least one amino acid substitution (*e.g.*, at least one conservative substitution such as highly conservative amino acid substitution) relative to the amino acid sequence of any one or more of SEQ ID NOs:20-22.

[00188] In some embodiments, a polypeptide comprises:

a) a V_H that comprises at least one amino acid substitution (*e.g.*, at least one conservative substitution such as highly conservative amino acid substitution) of a HCDR1, a HCDR2 and/or a HCDR3 residue, of any one or more of SEQ ID NOs:4-7;

b) a V_L that comprises at least one amino acid substitution (*e.g.*, at least one conservative substitution such as highly conservative amino acid substitution) of a LCDR1, a LCDR2 and/or a LCDR3 residue, of any one or more of SEQ ID NOs:20-22, or

both a) and b).

[00189] In some embodiments, a polypeptide comprises:

a) a V_H that comprises at least one amino acid substitution (*e.g.*, at least one conservative substitution such as highly conservative amino acid substitution) of a HCDR1, a HCDR2 and/or a HCDR3 residue, of any one or more of SEQ ID NOs:4-7; and

b) a V_L that comprises at least one amino acid substitution (*e.g.*, at least one conservative substitution such as highly conservative amino acid substitution)

of a LCDR1, a LCDR2 and/or a LCDR3 residue, of any one or more of SEQ ID NOs:20-22.

[00190] In some embodiments, a polypeptide comprises:

a) a V_H that comprises at least one amino acid substitution (*e.g.*, at least one conservative substitution such as highly conservative amino acid substitution) of a non-CDR residue (*e.g.*, within a framework region), of any one or more of SEQ ID NOs:4-7;

b) a V_L that comprises at least one amino acid substitution (*e.g.*, at least one conservative substitution such as highly conservative amino acid substitution) of a non-CDR residue (*e.g.*, within a framework region), of any one or more of SEQ ID NOs:20-22, or

both a) and b).

[00191] In some embodiments, a polypeptide comprises:

a) a V_H that comprises at least one amino acid substitution (*e.g.*, at least one conservative substitution such as highly conservative amino acid substitution) of a non-CDR residue (*e.g.*, within a framework region), of any one or more of SEQ ID NOs:4-7; and

b) a V_L that comprises at least one amino acid substitution (*e.g.*, at least one conservative substitution such as highly conservative amino acid substitution) of a non-CDR residue (*e.g.*, within a framework region), of any one or more of SEQ ID NOs:20-22.

[00192] In some embodiments, a polypeptide disclosed herein comprises:

a) a V_H comprising the amino acid sequence of any one of SEQ ID NOs:4-7; and

b) a V_L comprising the amino acid sequence of any one of SEQ ID NOs:20-22.

[00193] In some embodiments, a polypeptide comprises:

a) a V_H comprising the amino acid sequence of any one of SEQ ID NOs:4-7; and

b) a V_L comprising the amino acid sequence of SEQ ID NO:19.

[00194] In some embodiments, a polypeptide comprises:

a) a V_H comprising the amino acid sequence of SEQ ID NO:3; and

b) a V_L comprising the amino acid sequence of any one of SEQ ID NOs:20-22.

[00195] In some embodiments, a polypeptide comprises:

a) a V_H that has at least about 70% (*e.g.*, at least about: 75, 80, 85, 90, 95, 98, or 99%) sequence identity to the amino acid sequence of SEQ ID NO:5;

b) a V_L that has at least about 70% (*e.g.*, at least about: 75, 80, 85, 90, 95, 98, or 99%) sequence identity to the amino acid sequence of SEQ ID NO:21, or

both a) and b).

[00196] In some embodiments, a polypeptide comprises:

a) a V_H that has at least about 70% (*e.g.*, at least about: 75, 80, 85, 90, 95, 98, or 99%) sequence identity to the amino acid sequence of SEQ ID NO:5; and

b) a V_L that has at least about 70% (*e.g.*, at least about: 75, 80, 85, 90, 95, 98, or 99%) sequence identity to the amino acid sequence of SEQ ID NO:21.

[00197] In some embodiments, a polypeptide comprises:

a) a V_H that comprises at least one amino acid substitution (*e.g.*, at least one conservative substitution such as highly conservative amino acid substitution) relative to the amino acid sequence of SEQ ID NO:5;

b) a V_L that comprises at least one amino acid substitution (*e.g.*, at least one conservative substitution such as highly conservative amino acid substitution) relative to the amino acid sequence of SEQ ID NO:21, or

both a) and b).

[00198] In some embodiments, a polypeptide comprises:

a) a V_H that comprises at least one amino acid substitution (*e.g.*, at least one conservative substitution such as highly conservative amino acid substitution) relative to the amino acid sequence of SEQ ID NO:5; and

b) a V_L that comprises at least one amino acid substitution (*e.g.*, at least one conservative substitution such as highly conservative amino acid substitution) relative to the amino acid sequence of SEQ ID NO:21.

[00199] In some embodiments, a polypeptide comprises:

a) a V_H that comprises at least one amino acid substitution (*e.g.*, at least one conservative substitution such as highly conservative amino acid substitution) of a HCDR1, a HCDR2 and/or a HCDR3 residue, of SEQ ID NO:5;

b) a V_L that comprises at least one amino acid substitution (*e.g.*, at least one conservative substitution such as highly conservative amino acid substitution) of a LCDR1, a LCDR2 and/or a LCDR3 residue, of SEQ ID NO:21, or

both a) and b).

[00200] In some embodiments, a polypeptide comprises:

a) a V_H that comprises at least one amino acid substitution (*e.g.*, at least one conservative substitution such as highly conservative amino acid substitution) of a HCDR1, a HCDR2 and/or a HCDR3 residue, of SEQ ID NO:5; and

b) a V_L that comprises at least one amino acid substitution (*e.g.*, at least one conservative substitution such as highly conservative amino acid substitution) of a LCDR1, a LCDR2 and/or a LCDR3 residue, of SEQ ID NO:21.

[00201] In some embodiments, a polypeptide comprises:

a) a V_H that comprises at least one amino acid substitution (*e.g.*, at least one conservative substitution such as highly conservative amino acid substitution) of a non-CDR residue (*e.g.*, within a framework region), of SEQ ID NO:5;

b) a V_L that comprises at least one amino acid substitution (*e.g.*, at least one conservative substitution such as highly conservative amino acid substitution) of a non-CDR residue (*e.g.*, within a framework region), of SEQ ID NO:21, or both a) and b).

[00202] In some embodiments, a polypeptide comprises:

a) a V_H that comprises at least one amino acid substitution (*e.g.*, at least one conservative substitution such as highly conservative amino acid substitution) of a non-CDR residue (*e.g.*, within a framework region), of SEQ ID NO:5; and

b) a V_L that comprises at least one amino acid substitution (*e.g.*, at least one conservative substitution such as highly conservative amino acid substitution) of a non-CDR residue (*e.g.*, within a framework region), of SEQ ID NO:21.

[00203] In some embodiments, a polypeptide disclosed herein comprises:

a) a V_H comprising the amino acid sequence of SEQ ID NO:4, and

b) a V_L comprising the amino acid sequence of SEQ ID NO:20 (AB-1).

[00204] In some embodiments, a polypeptide disclosed herein comprises:

a) a V_H comprising the amino acid sequence of SEQ ID NO:5, and

b) a V_L comprising the amino acid sequence of SEQ ID NO:21 (AB-2).

[00205] In some embodiments, a polypeptide disclosed herein comprises:

a) a V_H comprising the amino acid sequence of SEQ ID NO:6, and

b) a V_L comprising the amino acid sequence of SEQ ID NO:20 (AB-3).

[00206] In some embodiments, a polypeptide disclosed herein comprises:

a) a V_H comprising the amino acid sequence of SEQ ID NO:7, and

b) a V_L comprising the amino acid sequence of SEQ ID NO:22 (AB-4).

[00207] In some embodiments, a polypeptide disclosed herein comprises:

a) a V_H comprising the amino acid sequence of SEQ ID NO:8, and

b) a V_L comprising the amino acid sequence of SEQ ID NO:23 (AB-5).

[00208] In some embodiments, a polypeptide disclosed herein comprises:

a) a V_H comprising the amino acid sequence of SEQ ID NO:9, and

b) a V_L comprising the amino acid sequence of SEQ ID NO:24 (AB-6).

[00209] In some embodiments, a polypeptide disclosed herein comprises:

a) a V_H comprising the amino acid sequence of SEQ ID NO:10, and

b) a V_L comprising the amino acid sequence of SEQ ID NO:25 (AB-7).

[00210] In some embodiments, a polypeptide disclosed herein comprises:

a) a V_H comprising the amino acid sequence of SEQ ID NO:11, and

b) a V_L comprising the amino acid sequence of SEQ ID NO:20 (AB-8).

[00211] In some embodiments, a polypeptide disclosed herein comprises:

a) a V_H comprising the amino acid sequence of SEQ ID NO:12, and

b) a V_L comprising the amino acid sequence of SEQ ID NO:20 (AB-9).

[00212] In some embodiments, a polypeptide disclosed herein comprises:

a) a V_H comprising the amino acid sequence of SEQ ID NO:13, and

b) a V_L comprising the amino acid sequence of SEQ ID NO:26 (AB-10).

[00213] In some embodiments, a polypeptide disclosed herein comprises:

a) a V_H comprising the amino acid sequence of SEQ ID NO:14, and

b) a V_L comprising the amino acid sequence of SEQ ID NO:27 (AB-11).

[00214] In some embodiments, a polypeptide disclosed herein comprises:

a) a V_H comprising the amino acid sequence of SEQ ID NO:15, and

b) a V_L comprising the amino acid sequence of SEQ ID NO:28 (AB-12).

[00215] In some embodiments, a polypeptide disclosed herein comprises:

a) a V_H comprising the amino acid sequence of SEQ ID NO:16, and

b) a V_L comprising the amino acid sequence of SEQ ID NO:29 (AB-13).

[00216] In some embodiments, a polypeptide disclosed herein comprises:

a) a V_H comprising the amino acid sequence of SEQ ID NO:17, and

b) a V_L comprising the amino acid sequence of SEQ ID NO:30 (AB-14).

Complementarity Determining Regions (CDRs)

[00217] A CDR (*e.g.*, HCDR1, HCDR2, HCDR3, LCDR1, LCDR2 and/or LCDR3) can be a CDR defined by any art-recognized method for identifying CDR residues of an antibody, as described further herein (*e.g.*, a CDR as defined by Kabat, a CDR as defined by Chothia, or a CDR as defined by IMGT).

[00218] In some embodiments, a polypeptide (*e.g.*, an antibody or antigen-binding fragment thereof) does not comprise all six CDRs of an antibody that comprises a V_H amino acid sequence of SEQ ID NO:3 and a V_L amino acid sequence of SEQ ID NO:19. In some embodiments, a polypeptide does not comprise all six sequences of SEQ ID NO:31, SEQ ID NO:33, SEQ ID NO:48, SEQ ID NO:59, SEQ ID NO:67 and SEQ ID NO:69. *See* Table 3 for SEQ ID NO:31, SEQ ID NO:33, SEQ ID NO:48, SEQ ID NO:59, SEQ ID NO:67 and SEQ ID NO:69. In some embodiments, a polypeptide does not comprise all four sequences of SEQ ID NO:33, SEQ ID NO:48, SEQ ID NO:59, and SEQ ID NO:69.

[00219] In some embodiments, a polypeptide comprises fewer than six (*e.g.*, 1, 2, 3, 4 or 5) CDRs of an antibody that comprises a V_H amino acid sequence of SEQ ID NO:3 and a V_L amino acid sequence of SEQ ID NO:19. In some embodiments, a polypeptide comprises 1, 2, 3, 4 or 5 sequences, but not all 6 sequences, selected from SEQ ID NO:31, SEQ ID NO:33, SEQ ID NO:48, SEQ ID NO:59, SEQ ID NO:67 and SEQ ID NO:69. In some embodiments, a polypeptide comprises 1, 2, or 3 sequences, but not all 4 sequences, selected from SEQ ID NO:33, SEQ ID NO:48, SEQ ID NO:59, and SEQ ID NO:69.

[00220] In some embodiments, a polypeptide comprises all six CDRs of a specific polypeptide disclosed herein. In some embodiments, a polypeptide comprises fewer than six (*e.g.*, 1, 2, 3, 4 or 5) of CDRs of a specific polypeptide disclosed herein.

[00221] In some embodiments, a polypeptide comprises:

a) a V_H amino acid sequence comprising a HCDR1, a HCDR2, and a HCDR3 that are substantially similar (*e.g.*, having at least about 90% sequence identity) in amino acid sequence to a HCDR1, a HCDR2 and a HCDR3, respectively, of a V_H amino acid sequence of any one or more of SEQ ID NOs:4-17;

b) a V_L amino acid sequence comprising a LCDR1, a LCDR2 and a LCDR3 that are substantially similar (*e.g.*, having at least about 90% sequence identity) in amino acid sequence to a LCDR1, a LCDR2 and a LCDR3, respectively, of a V_L amino acid sequence of any one or more of SEQ ID NOs:20-30, or

both a) and b).

[00222] In some embodiments, a polypeptide comprises:

a) a V_H amino acid sequence comprising a HCDR1, a HCDR2, and a HCDR3 that are substantially similar (*e.g.*, having at least about 90% sequence identity) in amino acid sequence to a HCDR1, a HCDR2 and a HCDR3, respectively, of a V_H amino acid sequence of any one or more of SEQ ID NOs:4-17; and

b) a V_L amino acid sequence comprising a LCDR1, a LCDR2 and a LCDR3 that are substantially similar (*e.g.*, having at least about 90% sequence identity) in amino acid sequence to a LCDR1, a LCDR2 and a LCDR3, respectively, of a V_L amino acid sequence of any one or more of SEQ ID NOs:20-30.

[00223] *See* Tables 2-3 and FIGs. 2A-3B for SEQ ID NOs:4-17 and 20-30, and non-limiting examples of corresponding HCDR1, HCDR2, HCDR3, LCDR1, LCDR2, and LCDR3 sequences.

[00224] In some embodiments, a polypeptide comprises:

a) a V_H amino acid sequence comprising a HCDR1, a HCDR2, and a HCDR3 that substantially preserve one or more functional properties of a HCDR1, a HCDR2 and a HCDR3, respectively, of a V_H amino acid sequence of any one or more of SEQ ID NOs:4-17; or

b) a V_L amino acid sequence comprising a LCDR1, a LCDR2, and a LCDR3 that substantially preserve one or more functional properties of a LCDR1, a LCDR2 and a LCDR3, respectively, of a V_L amino acid sequence of any one or more of SEQ ID NOs:20-30, or

both a) and b).

[00225] In some embodiments, a polypeptide comprises:

a) a V_H amino acid sequence comprising a HCDR1, a HCDR2, and a HCDR3 that substantially preserve one or more functional properties of a HCDR1, a HCDR2 and a HCDR3, respectively, of a V_H amino acid sequence of any one or more of SEQ ID NOs:4-17; and

b) a V_L amino acid sequence comprising a LCDR1, a LCDR2, and a LCDR3 that substantially preserve one or more functional properties of a LCDR1, a LCDR2 and a LCDR3, respectively, of a V_L amino acid sequence of any one or more of SEQ ID NOs:20-30.

[00226] In some embodiments, a polypeptide comprises:

a) a V_H amino acid sequence that comprises a HCDR1, a HCDR2, and a HCDR3 comprising only one or more conservative substitutions (*e.g.*, only one or more highly conservative substitutions), relative to a HCDR1, a HCDR2 and a HCDR3, respectively, of a V_H amino acid sequence of any one or more of SEQ ID NOs:4-17; or

b) a V_L amino acid sequence that comprises a LCDR1, a LCDR2, and a LCDR3 comprising only one or more conservative substitutions (*e.g.*, only one or more highly conservative substitutions), relative to a LCDR1, a LCDR2 and a LCDR3, respectively, of a V_L amino acid sequence of any one or more of SEQ ID NOs:20-30, or

both a) and b).

[00227] In some embodiments, a polypeptide comprises:

a) a V_H amino acid sequence that comprises a HCDR1, a HCDR2, and a HCDR3 comprising only one or more conservative substitutions (*e.g.*, only one or more highly conservative substitutions), relative to a HCDR1, a HCDR2 and a HCDR3, respectively, of a V_H amino acid sequence of any one or more of SEQ ID NOs:4-17; and

b) a V_L amino acid sequence that comprises a LCDR1, a LCDR2, and a LCDR3 comprising only one or more conservative substitutions (*e.g.*, only one or more highly conservative substitutions), relative to a LCDR1, a LCDR2 and a LCDR3, respectively, of a V_L amino acid sequence of any one or more of SEQ ID NOs:20-30.

[00228] In some embodiments, a polypeptide comprises:

a) a V_H amino acid sequence that comprises a HCDR1, a HCDR2, and a HCDR3 comprising up to 1, 2, or 3 conservative substitutions (*e.g.*, up to 1, 2, or 3 highly conservative substitutions), relative to a HCDR1, a HCDR2 and a HCDR3, respectively, of a V_H amino acid sequence of any one or more of SEQ ID NOs:4-17; or

b) a V_L amino acid sequence that comprises a LCDR1, a LCDR2, and a LCDR3 comprising up to 1, 2, or 3 conservative substitutions (*e.g.*, up to 1, 2, or 3 highly conservative substitutions), relative to a LCDR1, a LCDR2 and a

LCDR3, respectively, of a V_L amino acid sequence of any one or more of SEQ ID NOs:20-30, or

both a) and b).

[00229] In some embodiments, a polypeptide comprises:

a) a V_H amino acid sequence that comprises a HCDR1, a HCDR2, and a HCDR3 comprising up to 1, 2, or 3 conservative substitutions (*e.g.*, up to 1, 2, or 3 highly conservative substitutions), relative to a HCDR1, a HCDR2 and a HCDR3, respectively, of a V_H amino acid sequence of any one or more of SEQ ID NOs:4-17; and

b) a V_L amino acid sequence that comprises a LCDR1, a LCDR2, and a LCDR3 comprising up to 1, 2, or 3 conservative substitutions (*e.g.*, up to 1, 2, or 3 highly conservative substitutions), relative to a LCDR1, a LCDR2 and a LCDR3, respectively, of a V_L amino acid sequence of any one or more of SEQ ID NOs:20-30.

[00230] In some embodiments, a polypeptide comprises:

a) a V_H amino acid sequence that comprises a HCDR1, a HCDR2, and a HCDR3 having 100% sequence identity to a HCDR1, a HCDR2 and a HCDR3, respectively, of a V_H amino acid sequence of any one or more of SEQ ID NOs:4-17; or

b) a V_L amino acid sequence that comprises a LCDR1, a LCDR2, and a LCDR3 having 100% sequence identity to a LCDR1, a LCDR2 and a LCDR3, respectively, of a V_L amino acid sequence of any one or more of SEQ ID NOs:20-30, or

both a) and b).

[00231] In some embodiments, a polypeptide comprises:

a) a V_H amino acid sequence that comprises a HCDR1, a HCDR2, and a HCDR3 having 100% sequence identity to a HCDR1, a HCDR2 and a HCDR3, respectively, of a V_H amino acid sequence of any one or more of SEQ ID NOs:4-17; and

b) a V_L amino acid sequence that comprises a LCDR1, a LCDR2, and a LCDR3 having 100% sequence identity to a LCDR1, a LCDR2 and a LCDR3, respectively, of a V_L amino acid sequence of any one or more of SEQ ID NOs:20-30.

[00232] In some embodiments, a polypeptide comprises a HCDR1, a HCDR2, a HCDR3, a LCDR1, a LCDR2 and a LCDR3, of an antibody comprising a V_H/V_L combination selected from:

SEQ ID NO:4 and SEQ ID NO:20 (AB-1);
SEQ ID NO:5 and SEQ ID NO:21 (AB-2);
SEQ ID NO:6 and SEQ ID NO:20 (AB-3);
SEQ ID NO:7 and SEQ ID NO:22 (AB-4);
SEQ ID NO:8 and SEQ ID NO:23 (AB-5);
SEQ ID NO:9 and SEQ ID NO:24 (AB-6);
SEQ ID NO:10 and SEQ ID NO:25 (AB-7);
SEQ ID NO:11 and SEQ ID NO:20 (AB-8);
SEQ ID NO:12 and SEQ ID NO:20 (AB-9);
SEQ ID NO:13 and SEQ ID NO:26 (AB-10);
SEQ ID NO:14 and SEQ ID NO:27 (AB-11);
SEQ ID NO:15 and SEQ ID NO:28 (AB-12);
SEQ ID NO:16 and SEQ ID NO:29 (AB-13); or
SEQ ID NO:17 and SEQ ID NO:30 (AB-14).

[00233] In some embodiments, a polypeptide comprises:

a) a HCDR1 comprising the amino acid sequence set forth in SEQ ID NO:31;
b) a HCDR2 comprising at least one amino acid substitution relative to at least one amino acid sequence set forth in SEQ ID NOs:33-46 (*e.g.*, at least one amino acid sequence set forth in SEQ ID NOs:34-46);
c) a HCDR3 comprising at least one amino acid substitution relative to at least one amino acid sequence set forth in SEQ ID NOs:48-57 (*e.g.*, at least one amino acid sequence set forth in SEQ ID NOs:49-57);
d) a LCDR1 comprising at least one amino acid substitution relative to at least one amino acid sequence set forth in SEQ ID NOs:59-66 (*e.g.*, at least one amino acid sequence set forth in SEQ ID NOs:60-66);
e) a LCDR2 comprising the amino acid sequence set forth in SEQ ID NO:67;
f) a LCDR3 comprising at least one amino acid substitution relative to at least one amino acid sequence set forth in SEQ ID NOs:69-80 (*e.g.*, at least one amino acid sequence set forth in SEQ ID NOs:70-80);

or any combination of the foregoing.

[00234] In some embodiments, a polypeptide comprises:

a) a V_H amino acid sequence comprising a HCDR1, a HCDR2, and a HCDR3 that are substantially similar (*e.g.*, having at least about 90% sequence identity) in amino acid sequence to a HCDR1, a HCDR2 and a HCDR3, respectively, of a V_H amino acid sequence set forth in any one of SEQ ID NOs:4-7;

b) a V_L amino acid sequence comprising a LCDR1, a LCDR2 and a LCDR3 that are substantially similar (*e.g.*, having at least about 90% sequence identity) in amino acid sequence to a LCDR1, a LCDR2 and a LCDR3, respectively, of a V_L amino acid sequence set forth in any one of SEQ ID NOs:20-22, or

both a) and b).

[00235] In some embodiments, a polypeptide comprises:

a) a V_H amino acid sequence comprising a HCDR1, a HCDR2, and a HCDR3 that are substantially similar (*e.g.*, having at least about 90% sequence identity) in amino acid sequence to a HCDR1, a HCDR2 and a HCDR3, respectively, of a V_H amino acid sequence of any one or more of SEQ ID NOs:4-7;

b) a V_L amino acid sequence comprising a LCDR1, a LCDR2 and a LCDR3 that are substantially similar (*e.g.*, having at least about 90% sequence identity) in amino acid sequence to a LCDR1, a LCDR2 and a LCDR3, respectively, of a V_L amino acid sequence of any one or more of SEQ ID NOs:20-22, or

both a) and b).

[00236] In some embodiments, a polypeptide comprises:

a) a V_H amino acid sequence comprising a HCDR1, a HCDR2, and a HCDR3 that are substantially similar (*e.g.*, having at least about 90% sequence identity) in amino acid sequence to a HCDR1, a HCDR2 and a HCDR3, respectively, of a V_H amino acid sequence of any one or more of SEQ ID NOs:4-7; and

b) a V_L amino acid sequence comprising a LCDR1, a LCDR2 and a LCDR3 that are substantially similar (*e.g.*, having at least about 90% sequence identity) in amino acid sequence to a LCDR1, a LCDR2 and a LCDR3, respectively, of a V_L amino acid sequence of any one or more of SEQ ID NOs:20-22.

[00237] In some embodiments, a polypeptide comprises:

a) a V_H amino acid sequence comprising a HCDR1, a HCDR2, and a HCDR3 that substantially preserve one or more functional properties of a HCDR1, a HCDR2 and a HCDR3, respectively, of a V_H amino acid sequence of any one or more of SEQ ID NOs:4-7; or

b) a V_L amino acid sequence comprising a LCDR1, a LCDR2, and a LCDR3 that substantially preserve one or more functional properties of a LCDR1, a LCDR2 and a LCDR3, respectively, of a V_L amino acid sequence of any one or more of SEQ ID NOs:20-22, or

both a) and b).

[00238] In some embodiments, a polypeptide comprises:

a) a V_H amino acid sequence comprising a HCDR1, a HCDR2, and a HCDR3 that substantially preserve one or more functional properties of a HCDR1, a HCDR2 and a HCDR3, respectively, of a V_H amino acid sequence of any one or more of SEQ ID NOs:4-7; and

b) a V_L amino acid sequence comprising a LCDR1, a LCDR2, and a LCDR3 that substantially preserve one or more functional properties of a LCDR1, a LCDR2 and a LCDR3, respectively, of a V_L amino acid sequence of any one or more of SEQ ID NOs:20-22.

[00239] In some embodiments, a polypeptide comprises:

a) a V_H amino acid sequence that comprises a HCDR1, a HCDR2, and a HCDR3 comprising only one or more conservative substitutions (*e.g.*, only one or more highly conservative substitutions), relative to a HCDR1, a HCDR2 and a HCDR3, respectively, of a V_H amino acid sequence of any one or more of SEQ ID NOs:4-7; or

b) a V_L amino acid sequence that comprises a LCDR1, a LCDR2, and a LCDR3 comprising only one or more conservative substitutions (*e.g.*, only one or more highly conservative substitutions), relative to a LCDR1, a LCDR2 and a LCDR3, respectively, of a V_L amino acid sequence of any one or more of SEQ ID NOs:20-22, or

both a) and b).

[00240] In some embodiments, a polypeptide comprises:

a) a V_H amino acid sequence that comprises a HCDR1, a HCDR2, and a HCDR3 comprising only one or more conservative substitutions (*e.g.*, only one or more

highly conservative substitutions), relative to a HCDR1, a HCDR2 and a HCDR3, respectively, of a V_H amino acid sequence of any one or more of SEQ ID NOs:4-7; and

b) a V_L amino acid sequence that comprises a LCDR1, a LCDR2, and a LCDR3 comprising only one or more conservative substitutions (*e.g.*, only one or more highly conservative substitutions), relative to a LCDR1, a LCDR2 and a LCDR3, respectively, of a V_L amino acid sequence of any one or more of SEQ ID NOs:20-22.

[00241] In some embodiments, a polypeptide comprises:

a) a V_H amino acid sequence that comprises a HCDR1, a HCDR2, and a HCDR3 comprising up to 1, 2, or 3 conservative substitutions (*e.g.*, up to 1, 2, or 3 highly conservative substitutions), relative to a HCDR1, a HCDR2 and a HCDR3, respectively, of a V_H amino acid sequence of any one or more of SEQ ID NOs:4-7; or

b) a V_L amino acid sequence that comprises a LCDR1, a LCDR2, and a LCDR3 comprising up to 1, 2, or 3 conservative substitutions (*e.g.*, up to 1, 2, or 3 highly conservative substitutions), relative to a LCDR1, a LCDR2 and a LCDR3, respectively, of a V_L amino acid sequence of any one or more of SEQ ID NOs:20-22, or

both a) and b).

[00242] In some embodiments, a polypeptide comprises:

a) a V_H amino acid sequence that comprises a HCDR1, a HCDR2, and a HCDR3 comprising up to 1, 2, or 3 conservative substitutions (*e.g.*, up to 1, 2, or 3 highly conservative substitutions), relative to a HCDR1, a HCDR2 and a HCDR3, respectively, of a V_H amino acid sequence of any one or more of SEQ ID NOs:4-7; and

b) a V_L amino acid sequence that comprises a LCDR1, a LCDR2, and a LCDR3 comprising up to 1, 2, or 3 conservative substitutions (*e.g.*, up to 1, 2, or 3 highly conservative substitutions), relative to a LCDR1, a LCDR2 and a LCDR3, respectively, of a V_L amino acid sequence of any one or more of SEQ ID NOs:20-22.

[00243] In some embodiments, a polypeptide comprises:

a) a V_H amino acid sequence that comprises a HCDR1, a HCDR2, and a HCDR3 having 100% sequence identity to a HCDR1, a HCDR2 and a HCDR3, respectively, of a V_H amino acid sequence of any one or more of SEQ ID NOs:4-7; or

b) a V_L amino acid sequence that comprises a LCDR1, a LCDR2, and a LCDR3 having 100% sequence identity to a LCDR1, a LCDR2 and a LCDR3, respectively, of a V_L amino acid sequence of any one or more of SEQ ID NOs:20-22, or

both a) and b).

[00244] In some embodiments, a polypeptide comprises:

a) a V_H amino acid sequence that comprises a HCDR1, a HCDR2, and a HCDR3 having 100% sequence identity to a HCDR1, a HCDR2 and a HCDR3, respectively, of a V_H amino acid sequence of any one or more of SEQ ID NOs:4-7; and

b) a V_L amino acid sequence that comprises a LCDR1, a LCDR2, and a LCDR3 having 100% sequence identity to a LCDR1, a LCDR2 and a LCDR3, respectively, of a V_L amino acid sequence of any one or more of SEQ ID NOs:20-22.

[00245] In some embodiments, a polypeptide comprises a HCDR1, a HCDR2, a HCDR3, a LCDR1, a LCDR2 and a LCDR3, of an antibody comprising a V_H/V_L combination selected from:

SEQ ID NO:4 and SEQ ID NO:20 (AB-1);
SEQ ID NO:5 and SEQ ID NO:21 (AB-2);
SEQ ID NO:6 and SEQ ID NO:20 (AB-3); or
SEQ ID NO:7 and SEQ ID NO:22 (AB-4).

[00246] In some embodiments, a polypeptide comprises:

a) a HCDR1 comprising the amino acid sequence set forth in SEQ ID NO:31;

b) a HCDR2 comprising at least one amino acid substitution relative to at least one amino acid sequence set forth in SEQ ID NOs:33-37 (*e.g.*, at least one amino acid sequence set forth in SEQ ID NOs:34-37);

c) a HCDR3 comprising at least one amino acid substitution relative to at least one amino acid sequence set forth in SEQ ID NOs:48-52 (*e.g.*, at least one amino acid sequence set forth in SEQ ID NOs:49-52);

d) a LCDR1 comprising at least one amino acid substitution relative to at least one amino acid sequence set forth in SEQ ID NOs:59-61 (*e.g.*, at least one amino acid sequence set forth in SEQ ID NO:60 or SEQ ID NO:61);

e) a LCDR2 comprising the amino acid sequence set forth in SEQ ID NO:67;

f) a LCDR3 comprising at least one amino acid substitution relative to at least one amino acid sequence set forth in SEQ ID NOs:69-72 (*e.g.*, at least one amino acid sequence set forth in SEQ ID NOs:70-72);

or any combination of the foregoing.

[00247] In some embodiments, a polypeptide comprises:

a) a V_H amino acid sequence comprising a HCDR1, a HCDR2, and a HCDR3 that are substantially similar (*e.g.*, having at least about 90% sequence identity) in amino acid sequence to a HCDR1, a HCDR2 and a HCDR3, respectively, of a V_H amino acid sequence of SEQ ID NO:5;

b) a V_L amino acid sequence comprising a LCDR1, a LCDR2 and a LCDR3 that are substantially similar (*e.g.*, having at least about 90% sequence identity) in amino acid sequence to a LCDR1, a LCDR2 and a LCDR3, respectively, of a V_L amino acid sequence of SEQ ID NO:21, or

both a) and b).

[00248] In some embodiments, a polypeptide comprises:

a) a V_H amino acid sequence comprising a HCDR1, a HCDR2, and a HCDR3 that are substantially similar (*e.g.*, having at least about 90% sequence identity) in amino acid sequence to a HCDR1, a HCDR2 and a HCDR3, respectively, of a V_H amino acid sequence of SEQ ID NO:5; and

b) a V_L amino acid sequence comprising a LCDR1, a LCDR2 and a LCDR3 that are substantially similar (*e.g.*, having at least about 90% sequence identity) in amino acid sequence to a LCDR1, a LCDR2 and a LCDR3, respectively, of a V_L amino acid sequence of SEQ ID NO:21.

[00249] In some embodiments, a polypeptide comprises:

a) a V_H amino acid sequence comprising a HCDR1, a HCDR2, and a HCDR3 that substantially preserve one or more functional properties of a HCDR1, a HCDR2 and a HCDR3, respectively, of a V_H amino acid sequence of SEQ ID NO:5; or

b) a V_L amino acid sequence comprising a LCDR1, a LCDR2, and a LCDR3 that substantially preserve one or more functional properties of a LCDR1, a LCDR2 and a LCDR3, respectively, of a V_L amino acid sequence of SEQ ID NO:21, or

both a) and b).

[00250] In some embodiments, a polypeptide comprises:

a) a V_H amino acid sequence comprising a HCDR1, a HCDR2, and a HCDR3 that substantially preserve one or more functional properties of a HCDR1, a HCDR2 and a HCDR3, respectively, of a V_H amino acid sequence of SEQ ID NO:5; and

b) a V_L amino acid sequence comprising a LCDR1, a LCDR2, and a LCDR3 that substantially preserve one or more functional properties of a LCDR1, a LCDR2 and a LCDR3, respectively, of a V_L amino acid sequence of SEQ ID NO:21.

[00251] In some embodiments, a polypeptide comprises:

a) a V_H amino acid sequence that comprises a HCDR1, a HCDR2, and a HCDR3 comprising only one or more conservative substitutions (*e.g.*, only one or more highly conservative substitutions), relative to a HCDR1, a HCDR2 and a HCDR3, respectively, of a V_H amino acid sequence of SEQ ID NO:5; or

b) a V_L amino acid sequence that comprises a LCDR1, a LCDR2, and a LCDR3 comprising only one or more conservative substitutions (*e.g.*, only one or more highly conservative substitutions), relative to a LCDR1, a LCDR2 and a LCDR3, respectively, of a V_L amino acid sequence of SEQ ID NO:21, or

both a) and b).

[00252] In some embodiments, a polypeptide comprises:

a) a V_H amino acid sequence that comprises a HCDR1, a HCDR2, and a HCDR3 comprising only one or more conservative substitutions (*e.g.*, only one or more highly conservative substitutions), relative to a HCDR1, a HCDR2 and a HCDR3, respectively, of a V_H amino acid sequence of SEQ ID NO:5; and

b) a V_L amino acid sequence that comprises a LCDR1, a LCDR2, and a LCDR3 comprising only one or more conservative substitutions (*e.g.*, only one or more highly conservative substitutions), relative to a LCDR1, a LCDR2 and a LCDR3, respectively, of a V_L amino acid sequence of SEQ ID NO:21.

[00253] In some embodiments, a polypeptide comprises:

a) a V_H amino acid sequence that comprises a HCDR1, a HCDR2, and a HCDR3 comprising up to 1, 2, or 3 conservative substitutions (*e.g.*, up to 1, 2, or 3 highly conservative substitutions), relative to a HCDR1, a HCDR2 and a HCDR3, respectively, of a V_H amino acid sequence of SEQ ID NO:5; or

b) a V_L amino acid sequence that comprises a LCDR1, a LCDR2, and a LCDR3 comprising up to 1, 2, or 3 conservative substitutions (*e.g.*, up to 1, 2, or 3 highly conservative substitutions), relative to a LCDR1, a LCDR2 and a LCDR3, respectively, of a V_L amino acid sequence of SEQ ID NO:21, or

both a) and b).

[00254] In some embodiments, a polypeptide comprises:

a) a V_H amino acid sequence that comprises a HCDR1, a HCDR2, and a HCDR3 comprising up to 1, 2, or 3 conservative substitutions (*e.g.*, up to 1, 2, or 3 highly conservative substitutions), relative to a HCDR1, a HCDR2 and a HCDR3, respectively, of a V_H amino acid sequence of SEQ ID NO:5; and

b) a V_L amino acid sequence that comprises a LCDR1, a LCDR2, and a LCDR3 comprising up to 1, 2, or 3 conservative substitutions (*e.g.*, up to 1, 2, or 3 highly conservative substitutions), relative to a LCDR1, a LCDR2 and a LCDR3, respectively, of a V_L amino acid sequence of SEQ ID NO:21.

[00255] In some embodiments, a polypeptide comprises:

a) a V_H amino acid sequence that comprises a HCDR1, a HCDR2, and a HCDR3 having 100% sequence identity to a HCDR1, a HCDR2 and a HCDR3, respectively, of a V_H amino acid sequence of SEQ ID NO:5; or

b) a V_L amino acid sequence that comprises a LCDR1, a LCDR2, and a LCDR3 having 100% sequence identity to a LCDR1, a LCDR2 and a LCDR3, respectively, of a V_L amino acid sequence of SEQ ID NO:21, or

both a) and b).

[00256] In some embodiments, a polypeptide comprises:

a) a V_H amino acid sequence that comprises a HCDR1, a HCDR2, and a HCDR3 having 100% sequence identity to a HCDR1, a HCDR2 and a HCDR3, respectively, of a V_H amino acid sequence of SEQ ID NO:5; and

b) a V_L amino acid sequence that comprises a LCDR1, a LCDR2, and a LCDR3 having 100% sequence identity to a LCDR1, a LCDR2 and a LCDR3, respectively, of a V_L amino acid sequence of SEQ ID NO:21.

[00257] In some embodiments, a polypeptide comprises:

a) a V_H comprising a HCDR1, a HCDR2 and a HCDR3 amino acid sequences of SEQ ID NO:4, and

b) a V_L comprising a LCDR1, a LCDR2 and a LCDR3 amino acid sequences of SEQ ID NO:20 (AB-1).

[00258] In some embodiments, a polypeptide comprises:

a) a V_H comprising a HCDR1, a HCDR2 and a HCDR3 amino acid sequences of SEQ ID NO:5; and

b) a V_L comprising a LCDR1, a LCDR2 and a LCDR3 amino acid sequences of SEQ ID NO:21 (AB-2).

[00259] In some embodiments, a polypeptide comprises:

a) a V_H comprising a HCDR1, a HCDR2 and a HCDR3 amino acid sequences of SEQ ID NO:6; and

b) a V_L comprising a LCDR1, a LCDR2 and a LCDR3 amino acid sequences of SEQ ID NO:20 (AB-3).

[00260] In some embodiments, a polypeptide comprises:

a) a V_H comprising a HCDR1, a HCDR2 and a HCDR3 amino acid sequences of SEQ ID NO:7; and

b) a V_L comprising a LCDR1, a LCDR2 and a LCDR3 amino acid sequences of SEQ ID NO:22 (AB-4).

[00261] In some embodiments, a polypeptide comprises:

a) a V_H comprising a HCDR1, a HCDR2 and a HCDR3 amino acid sequences of SEQ ID NO:8; and

b) a V_L comprising a LCDR1, a LCDR2 and a LCDR3 amino acid sequences of SEQ ID NO:23 (AB-5).

[00262] In some embodiments, a polypeptide comprises:

a) a V_H comprising a HCDR1, a HCDR2 and a HCDR3 amino acid sequences of SEQ ID NO:9; and

b) a V_L comprising a LCDR1, a LCDR2 and a LCDR3 amino acid sequences of SEQ ID NO:24 (AB-6).

[00263] In some embodiments, a polypeptide comprises:

a) a V_H comprising a HCDR1, a HCDR2 and a HCDR3 amino acid sequences of SEQ ID NO:10; and

b) a V_L comprising a LCDR1, a LCDR2 and a LCDR3 amino acid sequences of SEQ ID NO:25 (AB-7).

[00264] In some embodiments, a polypeptide comprises:

a) a V_H comprising a HCDR1, a HCDR2 and a HCDR3 amino acid sequences of SEQ ID NO:11; and

b) a V_L comprising a LCDR1, a LCDR2 and a LCDR3 amino acid sequences of SEQ ID NO:20 (AB-8).

[00265] In some embodiments, a polypeptide comprises:

a) a V_H comprising a HCDR1, a HCDR2 and a HCDR3 amino acid sequences of SEQ ID NO:12; and

b) a V_L comprising a LCDR1, a LCDR2 and a LCDR3 amino acid sequences of SEQ ID NO:20 (AB-9).

[00266] In some embodiments, a polypeptide comprises:

a) a V_H comprising a HCDR1, a HCDR2 and a HCDR3 amino acid sequences of SEQ ID NO:13; and

b) a V_L comprising a LCDR1, a LCDR2 and a LCDR3 amino acid sequences of SEQ ID NO:26 (AB-10).

[00267] In some embodiments, a polypeptide comprises:

a) a V_H comprising a HCDR1, a HCDR2 and a HCDR3 amino acid sequences of SEQ ID NO:14; and

b) a V_L comprising a LCDR1, a LCDR2 and a LCDR3 amino acid sequences of SEQ ID NO:27 (AB-11).

[00268] In some embodiments, a polypeptide comprises:

a) a V_H comprising a HCDR1, a HCDR2 and a HCDR3 amino acid sequences of SEQ ID NO:15; and

b) a V_L comprising a LCDR1, a LCDR2 and a LCDR3 amino acid sequences of SEQ ID NO:28 (AB-12).

[00269] In some embodiments, a polypeptide comprises:

a) a V_H comprising a HCDR1, a HCDR2 and a HCDR3 amino acid sequences of SEQ ID NO:16; and

b) a V_L comprising a LCDR1, a LCDR2 and a LCDR3 amino acid sequences of SEQ ID NO:29 (AB-13).

[00270] In some embodiments, a polypeptide comprises:

a) a V_H comprising a HCDR1, a HCDR2 and a HCDR3 amino acid sequences of SEQ ID NO:17; and

b) a V_L comprising a LCDR1, a LCDR2 and a LCDR3 amino acid sequences of SEQ ID NO:30 (AB-14).

[00271] In some embodiments, a polypeptide comprises:

a) a HCDR1 comprising the amino acid sequence of SEQ ID NO:31;

b) a HCDR2 comprising the amino acid sequence of SEQ ID NO:34;

c) a HCDR3 comprising the amino acid sequence of SEQ ID NO:49;

d) a LCDR1 comprising the amino acid sequence of SEQ ID NO:60;

e) a LCDR2 comprising the amino acid sequence of SEQ ID NO:67;

f) a LCDR3 comprising the amino acid sequence of SEQ ID NO:70, or

any combination of the foregoing.

[00272] In some embodiments, a polypeptide comprises:

a) a HCDR1 comprising the amino acid sequence of SEQ ID NO:31;

b) a HCDR2 comprising the amino acid sequence of SEQ ID NO:35;

c) a HCDR3 comprising the amino acid sequence of SEQ ID NO:50;

d) a LCDR1 comprising the amino acid sequence of SEQ ID NO:60;

e) a LCDR2 comprising the amino acid sequence of SEQ ID NO:67;

f) a LCDR3 comprising the amino acid sequence of SEQ ID NO:71, or

any combination of the foregoing.

[00273] In some embodiments, a polypeptide comprises:

a) a HCDR1 comprising the amino acid sequence of SEQ ID NO:31;

b) a HCDR2 comprising the amino acid sequence of SEQ ID NO:36;

c) a HCDR3 comprising the amino acid sequence of SEQ ID NO:51;

d) a LCDR1 comprising the amino acid sequence of SEQ ID NO:60;

e) a LCDR2 comprising the amino acid sequence of SEQ ID NO:67;

f) a LCDR3 comprising the amino acid sequence of SEQ ID NO:70, or

any combination of the foregoing.

[00274] In some embodiments, a polypeptide comprises:

a) a HCDR1 comprising the amino acid sequence of SEQ ID NO:31;

b) a HCDR2 comprising the amino acid sequence of SEQ ID NO:37;

c) a HCDR3 comprising the amino acid sequence of SEQ ID NO:52;

d) a LCDR1 comprising the amino acid sequence of SEQ ID NO:61;

e) a LCDR2 comprising the amino acid sequence of SEQ ID NO:67;

f) a LCDR3 comprising the amino acid sequence of SEQ ID NO:72, or

any combination of the foregoing.

[00275] In some embodiments, a polypeptide comprises:

a) a HCDR1 comprising the amino acid sequence of SEQ ID NO:31;

b) a HCDR2 comprising the amino acid sequence of SEQ ID NO:38;

c) a HCDR3 comprising the amino acid sequence of SEQ ID NO:53;

d) a LCDR1 comprising the amino acid sequence of SEQ ID NO:59;

e) a LCDR2 comprising the amino acid sequence of SEQ ID NO:67;

f) a LCDR3 comprising the amino acid sequence of SEQ ID NO:73, or

any combination of the foregoing.

[00276] In some embodiments, a polypeptide comprises:

a) a HCDR1 comprising the amino acid sequence of SEQ ID NO:31;

b) a HCDR2 comprising the amino acid sequence of SEQ ID NO:39;

c) a HCDR3 comprising the amino acid sequence of SEQ ID NO:53;

d) a LCDR1 comprising the amino acid sequence of SEQ ID NO:60;

e) a LCDR2 comprising the amino acid sequence of SEQ ID NO:67;

f) a LCDR3 comprising the amino acid sequence of SEQ ID NO:74, or

any combination of the foregoing.

[00277] In some embodiments, a polypeptide comprises:

a) a HCDR1 comprising the amino acid sequence of SEQ ID NO:31;

b) a HCDR2 comprising the amino acid sequence of SEQ ID NO:40;

c) a HCDR3 comprising the amino acid sequence of SEQ ID NO:49;

d) a LCDR1 comprising the amino acid sequence of SEQ ID NO:62;

e) a LCDR2 comprising the amino acid sequence of SEQ ID NO:67;

f) a LCDR3 comprising the amino acid sequence of SEQ ID NO:75, or

any combination of the foregoing.

[00278] In some embodiments, a polypeptide comprises:

a) a HCDR1 comprising the amino acid sequence of SEQ ID NO:31;

b) a HCDR2 comprising the amino acid sequence of SEQ ID NO:41;

c) a HCDR3 comprising the amino acid sequence of SEQ ID NO:54;

d) a LCDR1 comprising the amino acid sequence of SEQ ID NO:60;

e) a LCDR2 comprising the amino acid sequence of SEQ ID NO:67;

f) a LCDR3 comprising the amino acid sequence of SEQ ID NO:70, or

any combination of the foregoing.

[00279] In some embodiments, a polypeptide comprises:

a) a HCDR1 comprising the amino acid sequence of SEQ ID NO:31;

b) a HCDR2 comprising the amino acid sequence of SEQ ID NO:41;

c) a HCDR3 comprising the amino acid sequence of SEQ ID NO:51;

d) a LCDR1 comprising the amino acid sequence of SEQ ID NO:60;

e) a LCDR2 comprising the amino acid sequence of SEQ ID NO:67;

f) a LCDR3 comprising the amino acid sequence of SEQ ID NO:70, or

any combination of the foregoing.

[00280] In some embodiments, a polypeptide comprises:

a) a HCDR1 comprising the amino acid sequence of SEQ ID NO:31;

b) a HCDR2 comprising the amino acid sequence of SEQ ID NO:42;

c) a HCDR3 comprising the amino acid sequence of SEQ ID NO:53;

d) a LCDR1 comprising the amino acid sequence of SEQ ID NO:63;

e) a LCDR2 comprising the amino acid sequence of SEQ ID NO:67;

f) a LCDR3 comprising the amino acid sequence of SEQ ID NO:76, or

any combination of the foregoing.

[00281] In some embodiments, a polypeptide comprises:

a) a HCDR1 comprising the amino acid sequence of SEQ ID NO:31;

b) a HCDR2 comprising the amino acid sequence of SEQ ID NO:43;

c) a HCDR3 comprising the amino acid sequence of SEQ ID NO:55;

d) a LCDR1 comprising the amino acid sequence of SEQ ID NO:64;

e) a LCDR2 comprising the amino acid sequence of SEQ ID NO:67;

f) a LCDR3 comprising the amino acid sequence of SEQ ID NO:77, or

any combination of the foregoing.

[00282] In some embodiments, a polypeptide comprises:

a) a HCDR1 comprising the amino acid sequence of SEQ ID NO:31;

b) a HCDR2 comprising the amino acid sequence of SEQ ID NO:44;

c) a HCDR3 comprising the amino acid sequence of SEQ ID NO:56;

d) a LCDR1 comprising the amino acid sequence of SEQ ID NO:65;

e) a LCDR2 comprising the amino acid sequence of SEQ ID NO:67;

f) a LCDR3 comprising the amino acid sequence of SEQ ID NO:78, or

any combination of the foregoing.

[00283] In some embodiments, a polypeptide comprises:

a) a HCDR1 comprising the amino acid sequence of SEQ ID NO:31;

b) a HCDR2 comprising the amino acid sequence of SEQ ID NO:45;

c) a HCDR3 comprising the amino acid sequence of SEQ ID NO:57;

d) a LCDR1 comprising the amino acid sequence of SEQ ID NO:66;

e) a LCDR2 comprising the amino acid sequence of SEQ ID NO:67;

f) a LCDR3 comprising the amino acid sequence of SEQ ID NO:79, or

any combination of the foregoing.

[00284] In some embodiments, a polypeptide comprises:

a) a HCDR1 comprising the amino acid sequence of SEQ ID NO:31;

b) a HCDR2 comprising the amino acid sequence of SEQ ID NO:46;

c) a HCDR3 comprising the amino acid sequence of SEQ ID NO:48;

d) a LCDR1 comprising the amino acid sequence of SEQ ID NO:63;

e) a LCDR2 comprising the amino acid sequence of SEQ ID NO:67;

f) a LCDR3 comprising the amino acid sequence of SEQ ID NO:80, or

any combination of the foregoing.

Paratopes

[00285] Amino acid residues of a paratope contribute to an antibody's interaction with an epitope of its target protein. An interaction can be a hydrogen bond, a salt bridge, a van der Waals interaction, an electrostatic interaction, a hydrophobic interaction, pi-interaction effects, an ionic bond, and/or any combination thereof. An interaction can be direct, or indirect, *e.g.*, via a coordinated intermediate molecule, such as an ion or water. The residues of a paratope, in some embodiments, comprise only residues that are part of a defined CDR. In some embodiments, the residues of a paratope further comprise one or more residues that are not part of a defined CDR (*e.g.*, residues within a defined framework region).

[00286] In some embodiments, a paratope is oriented less than about 5.0 angstroms from an epitope on a target antigen when a polypeptide is bound to the target antigen, *e.g.*, less than about: 4.5, 4.0, 3.5, 3.0, 2.5, 2.4, 2.3, 2.2, 2.1, 2.0, 1.9, 1.8, 1.7, 1.6, 1.5, 1.4, 1.3, 1.2,

1.1, 1.0 or 0.9 angstroms, or about: 0.9-5.0, 0.9-4.8. 1.0-5, 1.0-4.5, 1.0-4.0, 1.0-3.5, 1.1-3.5, 1.1-3.0, 1.2-3.0, 1.2-2.5, 1.3-2.5, 1.3-2.4, 1.4-2.4, 1.4-2.3, 1.5-2.3, 1.5-2.2, 1.6-2.2, 1.6-2.1, 1.7-2.1, 1.7-2.0 or 1.8-2.0 angstroms, from the epitope. In some embodiments, less than all of the amino acid residues constituting a paratope (*e.g.*, about 40%, about 50%, about 60%, about 70%, about 80%, about 90%, about 95%, about 96%, about 97%, about 98%, or about 99% of the amino acid residues) in the paratope are oriented less than about 5.0 angstroms from an epitope on a target antigen when a polypeptide is bound to the target antigen.

[00287] In some embodiments, a polypeptide (*e.g.*, an antibody or antigen-binding fragment thereof) comprising a paratope disclosed herein comprises a V_H and a V_L. In some embodiments, paratope residues are contained within the V_H and V_L of a polypeptide.

[00288] In some embodiments, a polypeptide comprises a paratope that differs from a paratope of an antibody comprising a V_H/V_L combination of SEQ ID NO:3/SEQ ID NO:19.

[00289] In some embodiments, a polypeptide comprises a paratope that differs from a paratope of an antibody comprising a V_H/V_L combination of SEQ ID NO:3/SEQ ID NO:19, by substitution (*e.g.*, conservative substitution such as highly conservative substitution) of from 1 to 3 (*e.g.*, 1, 2 or 3) residues.

[00290] In some embodiments, a polypeptide comprises a paratope that is substantially similar (*e.g.*, having at least about 90% sequence identity) to a paratope of an antibody comprising a V_H/V_L combination of SEQ ID NO:3/SEQ ID NO:19. In some embodiments, a polypeptide comprises a paratope that is substantially similar (*e.g.*, having at least about 90% sequence identity) to, and substantially preserves one or more functional properties of, a paratope of an antibody comprising a V_H/V_L combination of SEQ ID NO:3/SEQ ID NO:19.

[00291] In some embodiments, a polypeptide comprises a paratope that has 100% sequence identity to a paratope of an antibody comprising a V_H/V_L combination of SEQ ID NO:3/SEQ ID NO:19

[00292] In some embodiments, a polypeptide comprises a paratope that differs from a paratope of an antibody comprising a V_H/V_L combination selected from: SEQ ID NO:4/SEQ ID NO:20 (AB-1), SEQ ID NO:5/SEQ ID NO:21 (AB-2), SEQ ID NO:6/SEQ ID NO:20 (AB-3), SEQ ID NO:7/SEQ ID NO:22 (AB-4), SEQ ID NO:8/SEQ ID NO:23 (AB-5), SEQ ID NO:9/SEQ ID NO:24 (AB-6), SEQ ID NO:10/SEQ ID NO:25 (AB-7), SEQ ID NO:11/SEQ ID NO:20 (AB-8), SEQ ID NO:12/SEQ ID NO:20 (AB-9), SEQ ID NO:13/SEQ ID NO:26 (AB-10), SEQ ID NO:14/SEQ ID NO:27 (AB-11), SEQ ID NO:15/SEQ ID NO:28

(AB-12), SEQ ID NO:16/SEQ ID NO:29(AB-13) or SEQ ID NO:17/SEQ ID NO:30 (AB-14).

[00293] *See* Table 1 for SEQ ID NOs:4-17 and FIGs. 2A-2B for the paratope residues of antibodies comprising a V_H sequence set forth in any one of SEQ ID Nos:4-17. *See* Table 2 for SEQ ID NOs:20-30.

[00294] In some embodiments, a polypeptide comprises a paratope that differs from a paratope of an antibody comprising a V_H/V_L combination selected from: SEQ ID NO:4/SEQ ID NO:20 (AB-1), SEQ ID NO:5/SEQ ID NO:21 (AB-2), SEQ ID NO:6/SEQ ID NO:20 (AB-3), SEQ ID NO:7/SEQ ID NO:22 (AB-4), SEQ ID NO:8/SEQ ID NO:23 (AB-5), SEQ ID NO:9/SEQ ID NO:24 (AB-6), SEQ ID NO:10/SEQ ID NO:25 (AB-7), SEQ ID NO:11/SEQ ID NO:20 (AB-8), SEQ ID NO:12/SEQ ID NO:20 (AB-9), SEQ ID NO:13/SEQ ID NO:26 (AB-10), SEQ ID NO:14/SEQ ID NO:27 (AB-11), SEQ ID NO:15/SEQ ID NO:28 (AB-12), SEQ ID NO:16/SEQ ID NO:29(AB-13) or SEQ ID NO:17/SEQ ID NO:30 (AB-14), by substitution (*e.g.*, conservative substitution such as highly conservative substitution) of from 1 to 3 (*e.g.*, 1, 2 or 3) residues.

[00295] In some embodiments, a polypeptide comprises a paratope that is substantially similar (*e.g.*, having at least about 90% sequence identity) to a paratope of an antibody comprising a V_H/V_L combination selected from:

SEQ ID NO:4 and SEQ ID NO:20 (AB-1);
SEQ ID NO:5 and SEQ ID NO:21 (AB-2);
SEQ ID NO:6 and SEQ ID NO:20 (AB-3);
SEQ ID NO:7 and SEQ ID NO:22 (AB-4);
SEQ ID NO:8 and SEQ ID NO:23 (AB-5);
SEQ ID NO:9 and SEQ ID NO:24 (AB-6);
SEQ ID NO:10 and SEQ ID NO:25 (AB-7);
SEQ ID NO:11 and SEQ ID NO:20 (AB-8);
SEQ ID NO:12 and SEQ ID NO:20 (AB-9);
SEQ ID NO:13 and SEQ ID NO:26 (AB-10);
SEQ ID NO:14 and SEQ ID NO:27 (AB-11);
SEQ ID NO:15 and SEQ ID NO:28 (AB-12);
SEQ ID NO:16 and SEQ ID NO:29 (AB-13); or
SEQ ID NO:17 and SEQ ID NO:30 (AB-14), or
a combination thereof.

[00296] In some embodiments, a polypeptide comprises a paratope that is substantially similar (*e.g.*, having at least about 90% sequence identity) to, and substantially preserves one or more functional properties of, a paratope of an antibody comprising a V_H/V_L combination selected from:

SEQ ID NO:4 and SEQ ID NO:20 (AB-1);
SEQ ID NO:5 and SEQ ID NO:21 (AB-2);
SEQ ID NO:6 and SEQ ID NO:20 (AB-3);
SEQ ID NO:7 and SEQ ID NO:22 (AB-4);
SEQ ID NO:8 and SEQ ID NO:23 (AB-5);
SEQ ID NO:9 and SEQ ID NO:24 (AB-6);
SEQ ID NO:10 and SEQ ID NO:25 (AB-7);
SEQ ID NO:11 and SEQ ID NO:20 (AB-8);
SEQ ID NO:12 and SEQ ID NO:20 (AB-9);
SEQ ID NO:13 and SEQ ID NO:26 (AB-10);
SEQ ID NO:14 and SEQ ID NO:27 (AB-11);
SEQ ID NO:15 and SEQ ID NO:28 (AB-12);
SEQ ID NO:16 and SEQ ID NO:29 (AB-13); or
SEQ ID NO:17 and SEQ ID NO:30 (AB-14), or
a combination thereof.

[00297] In some embodiments, a polypeptide comprises a paratope comprising only one or more conservative substitutions (*e.g.*, only one or more highly conservative substitutions) relative a paratope of an antibody comprising a V_H/V_L combination selected from:

SEQ ID NO:4 and SEQ ID NO:20 (AB-1);
SEQ ID NO:5 and SEQ ID NO:21 (AB-2);
SEQ ID NO:6 and SEQ ID NO:20 (AB-3);
SEQ ID NO:7 and SEQ ID NO:22 (AB-4);
SEQ ID NO:8 and SEQ ID NO:23 (AB-5);
SEQ ID NO:9 and SEQ ID NO:24 (AB-6);
SEQ ID NO:10 and SEQ ID NO:25 (AB-7);
SEQ ID NO:11 and SEQ ID NO:20 (AB-8);
SEQ ID NO:12 and SEQ ID NO:20 (AB-9);
SEQ ID NO:13 and SEQ ID NO:26 (AB-10);
SEQ ID NO:14 and SEQ ID NO:27 (AB-11);

SEQ ID NO:15 and SEQ ID NO:28 (AB-12);
SEQ ID NO:16 and SEQ ID NO:29 (AB-13); or
SEQ ID NO:17 and SEQ ID NO:30 (AB-14), or
a combination thereof.

[00298] In some embodiments, a polypeptide comprises a paratope comprising up to 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14 or 15 conservative substitutions (*e.g.*, up to 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14 or 15 highly conservative substitutions), relative a paratope of an antibody comprising a V_H/V_L combination selected from:

SEQ ID NO:4 and SEQ ID NO:20 (AB-1);
SEQ ID NO:5 and SEQ ID NO:21 (AB-2);
SEQ ID NO:6 and SEQ ID NO:20 (AB-3);
SEQ ID NO:7 and SEQ ID NO:22 (AB-4);
SEQ ID NO:8 and SEQ ID NO:23 (AB-5);
SEQ ID NO:9 and SEQ ID NO:24 (AB-6);
SEQ ID NO:10 and SEQ ID NO:25 (AB-7);
SEQ ID NO:11 and SEQ ID NO:20 (AB-8);
SEQ ID NO:12 and SEQ ID NO:20 (AB-9);
SEQ ID NO:13 and SEQ ID NO:26 (AB-10);
SEQ ID NO:14 and SEQ ID NO:27 (AB-11);
SEQ ID NO:15 and SEQ ID NO:28 (AB-12);
SEQ ID NO:16 and SEQ ID NO:29 (AB-13); or
SEQ ID NO:17 and SEQ ID NO:30 (AB-14), or
a combination thereof.

[00299] In some embodiments, a polypeptide comprises a paratope that has 100% sequence identity to a paratope of an antibody comprising a V_H/V_L combination selected from:

SEQ ID NO:4 and SEQ ID NO:20 (AB-1);
SEQ ID NO:5 and SEQ ID NO:21 (AB-2);
SEQ ID NO:6 and SEQ ID NO:20 (AB-3);
SEQ ID NO:7 and SEQ ID NO:22 (AB-4);
SEQ ID NO:8 and SEQ ID NO:23 (AB-5);
SEQ ID NO:9 and SEQ ID NO:24 (AB-6);
SEQ ID NO:10 and SEQ ID NO:25 (AB-7);

SEQ ID NO:11 and SEQ ID NO:20 (AB-8);
SEQ ID NO:12 and SEQ ID NO:20 (AB-9);
SEQ ID NO:13 and SEQ ID NO:26 (AB-10);
SEQ ID NO:14 and SEQ ID NO:27 (AB-11);
SEQ ID NO:15 and SEQ ID NO:28 (AB-12);
SEQ ID NO:16 and SEQ ID NO:29 (AB-13); or
SEQ ID NO:17 and SEQ ID NO:30 (AB-14), or
a combination thereof.

[00300] In some embodiments, a polypeptide comprises a paratope that differs from a paratope of an antibody comprising a V_H/V_L combination selected from: SEQ ID NO:4/SEQ ID NO:20 (AB-1), SEQ ID NO:5/SEQ ID NO:21 (AB-2), SEQ ID NO:6/SEQ ID NO:20 (AB-3) or SEQ ID NO:7/SEQ ID NO:22 (AB-4).

[00301] In some embodiments, a polypeptide comprises a paratope that differs from a paratope of an antibody comprising a V_H/V_L combination selected from: SEQ ID NO:4/SEQ ID NO:20 (AB-1), SEQ ID NO:5/SEQ ID NO:21 (AB-2), SEQ ID NO:6/SEQ ID NO:20 (AB-3) or SEQ ID NO:7/SEQ ID NO:22 (AB-4), by substitution (*e.g.*, conservative substitution such as highly conservative substitution) of from 1 to 3 (*e.g.*, 1, 2 or 3) residues.

[00302] In some embodiments, a polypeptide comprises a paratope that is substantially similar (*e.g.*, having at least about 90% sequence identity) to a paratope of an antibody comprising a V_H/V_L combination selected from:

SEQ ID NO:4 and SEQ ID NO:20 (AB-1);
SEQ ID NO:5 and SEQ ID NO:21 (AB-2);
SEQ ID NO:6 and SEQ ID NO:20 (AB-3); or
SEQ ID NO:7 and SEQ ID NO:22 (AB-4), or
a combination thereof.

[00303] In some embodiments, a polypeptide comprises a paratope that is substantially similar (*e.g.*, having at least about 90% sequence identity) to, and substantially preserves one or more functional properties of, a paratope of an antibody comprising a V_H/V_L combination selected from:

SEQ ID NO:4 and SEQ ID NO:20 (AB-1);
SEQ ID NO:5 and SEQ ID NO:21 (AB-2);
SEQ ID NO:6 and SEQ ID NO:20 (AB-3); or
SEQ ID NO:7 and SEQ ID NO:22 (AB-4), or

a combination thereof.

[00304] In some embodiments, a polypeptide comprises a paratope comprising only one or more conservative substitutions (*e.g.*, only one or more highly conservative substitutions) relative a paratope of an antibody comprising a V_H/V_L combination selected from:

SEQ ID NO:4 and SEQ ID NO:20 (AB-1);

SEQ ID NO:5 and SEQ ID NO:21 (AB-2);

SEQ ID NO:6 and SEQ ID NO:20 (AB-3); or

SEQ ID NO:7 and SEQ ID NO:22 (AB-4), or

a combination thereof.

[00305] In some embodiments, a polypeptide comprises a paratope comprising up to 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14 or 15 conservative substitutions (*e.g.*, up to 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14 or 15 highly conservative substitutions), relative a paratope of an antibody comprising a V_H/V_L combination selected from:

SEQ ID NO:4 and SEQ ID NO:20 (AB-1);

SEQ ID NO:5 and SEQ ID NO:21 (AB-2);

SEQ ID NO:6 and SEQ ID NO:20 (AB-3); or

SEQ ID NO:7 and SEQ ID NO:22 (AB-4), or

a combination thereof.

[00306] In some embodiments, a polypeptide comprises a paratope that has 100% sequence identity to a paratope of an antibody comprising a V_H/V_L combination selected from:

SEQ ID NO:4 and SEQ ID NO:20 (AB-1);

SEQ ID NO:5 and SEQ ID NO:21 (AB-2);

SEQ ID NO:6 and SEQ ID NO:20 (AB-3); or

SEQ ID NO:7 and SEQ ID NO:22 (AB-4), or

a combination thereof.

[00307] In some embodiments, a polypeptide comprises a paratope comprising amino acid residues corresponding to each of M2, G26, F27, T28, R30, T31, Y32, Y53, R98, P100, Q101, W102, E103, and E107 of SEQ ID NO:2, or a subset thereof. In some embodiments, a polypeptide comprises a paratope comprising amino acid residues corresponding to each of T28, T31, Y32, Y53, R98, W102, and E107 of SEQ ID NO:2.

Consensus Sequences

[00308] In some embodiments, a polypeptide (*e.g.*, an antibody or antigen-binding fragment thereof) comprises a V_H comprising the amino acid sequence of SEQ ID NO:2, wherein:

X_1 is not I;

X_2 is not W;

X_3 is not D;

X_4 is not S;

X_5 is not N;

X_6 is not K;

X_7 is not A;

X_8 is not A;

X_9 is not L;

X_{10} is not V;

X_{11} is not H;

X_{12} is not A;

X_{13} is not F; or

X_{14} is not I, or

any combination of the foregoing.

[00309] The sequence identified as SEQ ID NO:2 is shown in Table 1, which is a consensus V_H sequence for SEQ ID Nos:3-17 herein.

[00310] In some embodiments:

X_1 is I or V;

X_2 is W or S;

X_3 is D or S;

X_4 is S, T, Y or A;

X_5 is N, Y, D or T;

X_6 is K, T or I;

X_7 is A, S or T;

X_8 is A or S;

X_9 is L, D, E or S;

X_{10} is V or I;

X_{11} is H, F or Y;

X_{12} is A or S;

X_{13} is F, M or L;

X_{14} is I or V,

or any combination of the foregoing.

[00311] In some embodiments:

X_1 is V;

X_2 is S;

X_3 is S;

X_4 is T, Y or A;

X_5 is Y, D or T;

X_6 is T or I;

X_7 is S or T;

X_8 is S;

X_9 is D, E or S;

X_{10} is I;

X_{11} is F or Y;

X_{12} is S;

X_{13} is M or L;

X_{14} is V,

or any combination of the foregoing.

[00312] In some embodiments, X_1 is not I. In some embodiments, X_1 is I or V. In some embodiments, X_1 is V. In some embodiments, X_1 is I.

[00313] In some embodiments, X_2 is not W. In some embodiments, X_2 is W or S. In some embodiments, X_2 is S. In some embodiments, X_2 is W.

[00314] In some embodiments, X_3 is not D. In some embodiments, X_3 is D or S. In some embodiments, X_3 is S. In some embodiments, X_3 is D.

[00315] In some embodiments, X_4 is not S. In some embodiments, X_4 is S, T, Y or A. In some embodiments, X_4 is T, Y or A. In some embodiments, X_4 is T. In some embodiments, X_4 is Y. In some embodiments, X_4 is A. In some embodiments, X_4 is S.

[00316] In some embodiments, X_5 is not N. In some embodiments, X_5 is N, Y, D or T. In some embodiments, X_5 is Y, D or T. In some embodiments, X_5 is Y. In some embodiments, X_5 is D. In some embodiments, X_5 is T. In some embodiments, X_5 is N.

[00317] In some embodiments, X_6 is not K. In some embodiments, X_6 is K, T or I. In some embodiments, X_6 is T or I. In some embodiments, X_6 is T. In some embodiments, X_6 is I. In some embodiments, X_6 is K.

[00318] In some embodiments, X_7 is not A. In some embodiments, X_7 is A, S or T. In some embodiments, X_7 is S or T. In some embodiments, X_7 is S. In some embodiments, X_7 is T. In some embodiments, X_7 is A.

[00319] In some embodiments, X_8 is not A. In some embodiments, X_8 is A or S. In some embodiments, X_8 is S. In some embodiments, X_8 is A.

[00320] In some embodiments, X_9 is not L. In some embodiments, X_9 is L, D, E or S. In some embodiments, X_9 is D, E or S. In some embodiments, X_9 is D. In some embodiments, X_9 is E. In some embodiments, X_9 is S. In some embodiments, X_9 is L.

[00321] In some embodiments, X_{10} is not V. In some embodiments, X_{10} is V or I. In some embodiments, X_{10} is I. In some embodiments, X_{10} is V.

[00322] In some embodiments, X_{11} is not H. In some embodiments, X_{11} is H, F or Y. In some embodiments, X_{11} is F or Y. In some embodiments, X_{11} is F. In some embodiments, X_{11} is Y. In some embodiments, X_{11} is H.

[00323] In some embodiments, X_{12} is not A. In some embodiments, X_{12} is A or S. In some embodiments, X_{12} is S. In some embodiments, X_{12} is A.

[00324] In some embodiments, X_{13} is not F. In some embodiments, X_{13} is F, M or L. In some embodiments, X_{13} is M or L. In some embodiments, X_{13} is M. In some embodiments, X_{13} is L. In some embodiments, X_{13} is F.

[00325] In some embodiments, X_{14} is not I. In some embodiments, X_{14} is I or V. In some embodiments, X_{14} is V. In some embodiments, X_{14} is I.

[00326] In some embodiments, the polypeptides comprise a V_L comprising the amino acid sequence of SEQ ID NO:18, wherein:

X_{15} is not N;

X_{16} is not L;

X_{17} is not S;

X_{18} is not K;

X_{19} is not S;

X_{20} is not V;

X_{21} is not W;

X_{22} is not D;

X_{23} is not S;

X_{24} is not S;

X_{25} is not S;

X_{26} is not D; or

X_{27} is not H, or

any combination of the foregoing.

[00327] The sequence identified as SEQ ID NO:18 is shown in Table 2, which is a consensus V_L sequence for SEQ ID NOs:19-30 herein.

[00328] In some embodiments:

X_{15} is N or Y;

X_{16} is L or I;

X_{17} is S or R;

X_{18} is K, F or Y;

X_{19} is S or N;

X_{20} is V or I;

X_{21} is W or Y;

X_{22} is D, V or S;

X_{23} is S, M or E;

X_{24} is S, A or T;

X_{25} is S, D or E;

X_{26} is D, S, R or F;

X_{27} is H, L, K or E,

or any combination of the foregoing.

[00329] In some embodiments:

X_{15} is Y;

X_{16} is I;

X_{17} is R;

X_{18} is F or Y;

X_{19} is N;

X_{20} is I;

X_{21} is Y;

X_{22} is V or S;

X_{23} is M or E;

X_{24} is A or T;

X_{25} is D or E;

X_{26} is S, R or F;

X_{27} is L, K or E,

or any combination of the foregoing.

[00330] In some embodiments, X_{15} is not N. In some embodiments, X_{15} is N or Y. In some embodiments, X_{15} is Y. In some embodiments, X_{15} is N.

[00331] In some embodiments, X_{16} is not L. In some embodiments, X_{16} is L or I. In some embodiments, X_{16} is I. In some embodiments, X_{16} is L.

[00332] In some embodiments, X_{17} is not S. In some embodiments, X_{17} is S or R. In some embodiments, X_{17} is R. In some embodiments, X_{17} is S.

[00333] In some embodiments, X_{18} is not K. In some embodiments, X_{18} is K, F or Y. In some embodiments, X_{18} is F or Y. In some embodiments, X_{18} is F. In some embodiments, X_{18} is Y. In some embodiments, X_{18} is K.

[00334] In some embodiments, X_{19} is not S. In some embodiments, X_{19} is S or N. In some embodiments, X_{19} is N. In some embodiments, X_{19} is S.

[00335] In some embodiments, X_{20} is not V. In some embodiments, X_{20} is V or I. In some embodiments, X_{20} is I. In some embodiments, X_{20} is V.

[00336] In some embodiments, X_{21} is not W. In some embodiments, X_{21} is W or Y. In some embodiments, X_{21} is Y. In some embodiments, X_{21} is W.

[00337] In some embodiments, X_{22} is not D. In some embodiments, X_{22} is D, V or S. In some embodiments, X_{22} is V or S. In some embodiments, X_{22} is V. In some embodiments, X_{22} is S. In some embodiments, X_{22} is D.

[00338] In some embodiments, X_{23} is not S. In some embodiments, X_{23} is S, M or E. In some embodiments, X_{23} is M or E. In some embodiments, X_{23} is M. In some embodiments, X_{23} is E. In some embodiments, X_{23} is S.

[00339] In some embodiments, X_{24} is not S. In some embodiments, X_{24} is S, A or T. In some embodiments, X_{24} is A or T. In some embodiments, X_{24} is A. In some embodiments, X_{24} is T. In some embodiments, X_{24} is S.

[00340] In some embodiments, X_{25} is not S. In some embodiments, X_{25} is S, D or E. In some embodiments, X_{25} is D or E. In some embodiments, X_{25} is D. In some embodiments, X_{25} is E. In some embodiments, X_{25} is S.

[00341] In some embodiments, X_{26} is not D. In some embodiments, X_{26} is D, S, R or F. In some embodiments, X_{26} is S, R or F. In some embodiments, X_{26} is S. In some embodiments, X_{26} is R. In some embodiments, X_{26} is F. In some embodiments, X_{26} is D.

[00342] In some embodiments, X_{27} is not H. In some embodiments, X_{27} is H, L, K or E. In some embodiments, X_{27} is L, K or E. In some embodiments, X_{27} is L. In some embodiments, X_{27} is K. In some embodiments, X_{27} is E. In some embodiments, X_{27} is H.

[00343] In some embodiments,

a) X_1 is V, X_2 is W, X_3 is S, X_4 is S, X_5 is Y, X_6 is T, X_7 is S, X_8 is S, X_9 is D, X_{10} is I, X_{11} is F, X_{12} is A, X_{13} is M, X_{14} is I, X_{15} is N, X_{16} is I, X_{17} is S, X_{18} is K, X_{19} is S, X_{20} is V, X_{21} is W, X_{22} is D, X_{23} is S, X_{24} is S, X_{25} is S, X_{26} is S, or X_{27} is L, or a combination thereof;

b) X_1 is V, X_2 is W, X_3 is D, X_4 is S, X_5 is Y, X_6 is T, X_7 is A, X_8 is S, X_9 is E, X_{10} is I, X_{11} is F, X_{12} is A, X_{13} is M, X_{14} is I, X_{15} is N, X_{16} is I, X_{17} is S, X_{18} is K, X_{19} is S, X_{20} is I, X_{21} is W, X_{22} is D, X_{23} is S, X_{24} is S, X_{25} is S, X_{26} is S, or X_{27} is L, or a combination thereof;

c) X_1 is I, X_2 is W, X_3 is D, X_4 is T, X_5 is Y, X_6 is T, X_7 is A, X_8 is S, X_9 is S, X_{10} is I, X_{11} is F, X_{12} is A, X_{13} is F, X_{14} is I, X_{15} is N, X_{16} is I, X_{17} is S, X_{18} is K, X_{19} is S, X_{20} is V, X_{21} is W, X_{22} is D, X_{23} is S, X_{24} is S, X_{25} is S, X_{26} is S, or X_{27} is L, or a combination thereof;

d) X_1 is I, X_2 is W, X_3 is S, X_4 is S, X_5 is D, X_6 is T, X_7 is A, X_8 is S, X_9 is D, X_{10} is I, X_{11} is F, X_{12} is S, X_{13} is M, X_{14} is V, X_{15} is Y, X_{16} is I, X_{17} is S, X_{18} is F, X_{19} is S, X_{20} is I, X_{21} is Y, X_{22} is V, X_{23} is S, X_{24} is A, X_{25} is S, X_{26} is R, or X_{27} is L, or a combination thereof;

e) X_1 is V, X_2 is W, X_3 is D, X_4 is Y, X_5 is D, X_6 is T, X_7 is S, X_8 is S, X_9 is D, X_{10} is I, X_{11} is F, X_{12} is S, X_{13} is M, X_{14} is I, X_{15} is N, X_{16} is L, X_{17} is S, X_{18} is K, X_{19} is S, X_{20} is V, X_{21} is W, X_{22} is D, X_{23} is M, X_{24} is S, X_{25} is S, X_{26} is D, or X_{27} is L, or a combination thereof;

f) X_1 is V, X_2 is W, X_3 is D, X_4 is S, X_5 is D, X_6 is I, X_7 is S, X_8 is S, X_9 is D, X_{10} is I, X_{11} is F, X_{12} is S, X_{13} is M, X_{14} is I, X_{15} is N, X_{16} is I, X_{17} is S, X_{18} is K, X_{19} is S, X_{20} is I, X_{21} is W, X_{22} is D, X_{23} is S, X_{24} is S, X_{25} is S, X_{26} is D, or X_{27} is H, or a combination thereof;

g) X_1 is I, X_2 is W, X_3 is S, X_4 is A, X_5 is Y, X_6 is I, X_7 is S, X_8 is S, X_9 is D, X_{10} is I, X_{11} is F, X_{12} is A, X_{13} is M, X_{14} is I, X_{15} is N, X_{16} is L, X_{17} is S, X_{18} is Y,

X_{19} is S, X_{20} is V, X_{21} is W, X_{22} is D, X_{23} is M, X_{24} is S, X_{25} is S, X_{26} is S, or X_{27} is L, or a combination thereof;

h) X_1 is I, X_2 is W, X_3 is D, X_4 is S, X_5 is Y, X_6 is T, X_7 is A, X_8 is S, X_9 is D, X_{10} is I, X_{11} is F, X_{12} is A, X_{13} is F, X_{14} is I, X_{15} is N, X_{16} is I, X_{17} is S, X_{18} is K, X_{19} is S, X_{20} is V, X_{21} is W, X_{22} is D, X_{23} is S, X_{24} is S, X_{25} is S, X_{26} is S, or X_{27} is L, or a combination thereof;

i) X_1 is I, X_2 is W, X_3 is D, X_4 is S, X_5 is Y, X_6 is T, X_7 is A, X_8 is S, X_9 is S, X_{10} is I, X_{11} is F, X_{12} is A, X_{13} is F, X_{14} is I, X_{15} is N, X_{16} is I, X_{17} is S, X_{18} is K, X_{19} is S, X_{20} is V, X_{21} is W, X_{22} is D, X_{23} is S, X_{24} is S, X_{25} is S, X_{26} is S, or X_{27} is L, or a combination thereof;

j) X_1 is I, X_2 is W, X_3 is S, X_4 is T, X_5 is T, X_6 is T, X_7 is S, X_8 is S, X_9 is D, X_{10} is I, X_{11} is F, X_{12} is S, X_{13} is M, X_{14} is I, X_{15} is N, X_{16} is I, X_{17} is S, X_{18} is K, X_{19} is N, X_{20} is V, X_{21} is W, X_{22} is D, X_{23} is S, X_{24} is S, X_{25} is D, X_{26} is F, or X_{27} is L, or a combination thereof;

k) X_1 is I, X_2 is S, X_3 is S, X_4 is S, X_5 is Y, X_6 is I, X_7 is T, X_8 is S, X_9 is E, X_{10} is V, X_{11} is Y, X_{12} is A, X_{13} is L, X_{14} is I, X_{15} is N, X_{16} is I, X_{17} is S, X_{18} is F, X_{19} is S, X_{20} is V, X_{21} is W, X_{22} is S, X_{23} is S, X_{24} is T, X_{25} is S, X_{26} is R, or X_{27} is H, or a combination thereof;

l) X_1 is V, X_2 is W, X_3 is D, X_4 is S, X_5 is N, X_6 is T, X_7 is A, X_8 is A, X_9 is S, X_{10} is V, X_{11} is H, X_{12} is A, X_{13} is F, X_{14} is I, X_{15} is N, X_{16} is I, X_{17} is R, X_{18} is F, X_{19} is S, X_{20} is V, X_{21} is W, X_{22} is V, X_{23} is S, X_{24} is T, X_{25} is S, X_{26} is D, or X_{27} is K, or a combination thereof;

m) X_1 is I, X_2 is S, X_3 is D, X_4 is S, X_5 is T, X_6 is K, X_7 is A, X_8 is A, X_9 is S, X_{10} is V, X_{11} is Y, X_{12} is A, X_{13} is F, X_{14} is I, X_{15} is N, X_{16} is L, X_{17} is S, X_{18} is F, X_{19} is S, X_{20} is V, X_{21} is W, X_{22} is D, X_{23} is S, X_{24} is S, X_{25} is E, X_{26} is D, or X_{27} is L, or a combination thereof; or

n) X_1 is I, X_2 is W, X_3 is D, X_4 is S, X_5 is T, X_6 is K, X_7 is A, X_8 is A, X_9 is L, X_{10} is V, X_{11} is H, X_{12} is A, X_{13} is F, X_{14} is I, X_{15} is N, X_{16} is I, X_{17} is S, X_{18} is K, X_{19} is N, X_{20} is V, X_{21} is W, X_{22} is D, X_{23} is E, X_{24} is S, X_{25} is S, X_{26} is D, or X_{27} is E, or a combination thereof.

[00344] In some embodiments:

X_1 is I or V;

X_2 is W;

X_3 is D or S;

X_4 is S or T;

X_5 is N, Y or D;

X_6 is K or T;

X_7 is A or S;

X_8 is A or S;

X_9 is L, D, E or S;

X_{10} is V or I;

X_{11} is H or F;

X_{12} is A or S;

X_{13} is F or M; or

X_{14} is I or V, or

any combination of the foregoing.

[00345] In some embodiments:

X_1 is V;

X_2 is W;

X_3 is S;

X_4 is T;

X_5 is Y or D;

X_6 is T;

X_7 is S;

X_8 is S;

X_9 is D, E or S;

X_{10} is I;

X_{11} is F;

X_{12} is S;

X_{13} is M;

X_{14} is V,

or any combination of the foregoing.

[00346] In some embodiments, X_1 is not I. In some embodiments, X_1 is I or V. In some embodiments, X_1 is V. In some embodiments, X_1 is I.

[00347] In some embodiments, X_2 is W.

[00348] In some embodiments, X_3 is not D. In some embodiments, X_3 is D or S. In some embodiments, X_3 is S. In some embodiments, X_3 is D.

[00349] In some embodiments, X_4 is not S. In some embodiments, X_4 is S or T. In some embodiments, X_4 is T. In some embodiments, X_4 is S.

[00350] In some embodiments, X_5 is not N. In some embodiments, X_5 is N, Y or D. In some embodiments, X_5 is Y or D. In some embodiments, X_5 is Y. In some embodiments, X_5 is D. In some embodiments, X_5 is N.

[00351] In some embodiments, X_6 is not K. In some embodiments, X_6 is K or T. In some embodiments, X_6 is T. In some embodiments, X_6 is K.

[00352] In some embodiments, X_7 is not A. In some embodiments, X_7 is A or S. In some embodiments, X_7 is S. In some embodiments, X_7 is A.

[00353] In some embodiments, X_8 is not A. In some embodiments, X_8 is A or S. In some embodiments, X_8 is S. In some embodiments, X_8 is A.

[00354] In some embodiments, X_9 is not L. In some embodiments, X_9 is L, D, E or S. In some embodiments, X_9 is D, E or S. In some embodiments, X_9 is D. In some embodiments, X_9 is E. In some embodiments, X_9 is S. In some embodiments, X_9 is L.

[00355] In some embodiments, X_{10} is not V. In some embodiments, X_{10} is V or I. In some embodiments, X_{10} is I. In some embodiments, X_{10} is V.

[00356] In some embodiments, X_{11} is not H. In some embodiments, X_{11} is H or F. In some embodiments, X_{11} is F. In some embodiments, X_{11} is H.

[00357] In some embodiments, X_{12} is not A. In some embodiments, X_{12} is A or S. In some embodiments, X_{12} is S. In some embodiments, X_{12} is A.

[00358] In some embodiments, X_{13} is not F. In some embodiments, X_{13} is F or M. In some embodiments, X_{13} is M. In some embodiments, X_{13} is F.

[00359] In some embodiments, X_{14} is not I. In some embodiments, X_{14} is I or V. In some embodiments, X_{14} is V. In some embodiments, X_{14} is I.

[00360] In some embodiments:

X_{15} is N or Y;

X_{16} is L or I;

X_{17} is S;

X_{18} is K or F;

X_{19} is S;

X_{20} is V or I;

X_{21} is W or Y;

X_{22} is D or V;

X_{23} is S;

X_{24} is S or A;

X_{25} is S;

X_{26} is D, S or R;

X_{27} is H or L,

or any combination of the foregoing.

[00361] In some embodiments:

X_{15} is Y;

X_{16} is I;

X_{17} is S;

X_{18} is F;

X_{19} is S;

X_{20} is I;

X_{21} is Y;

X_{22} is V;

X_{23} is S;

X_{24} is A;

X_{25} is S;

X_{26} is S or R;

X_{27} is L,

or any combination of the foregoing.

[00362] In some embodiments, X_{15} is not N. In some embodiments, X_{15} is N or Y. In some embodiments, X_{15} is Y. In some embodiments, X_{15} is N.

[00363] In some embodiments, X_{16} is not L. In some embodiments, X_{16} is L or I. In some embodiments, X_{16} is I. In some embodiments, X_{16} is L.

[00364] In some embodiments, X_{17} is S.

[00365] In some embodiments, X_{18} is not K. In some embodiments, X_{18} is K or F. In some embodiments, X_{18} is F. In some embodiments, X_{18} is K.

[00366] In some embodiments, X_{19} is S.

[00367] In some embodiments, X_{20} is not V. In some embodiments, X_{20} is V or I. In some embodiments, X_{20} is I. In some embodiments, X_{20} is V.

[00368] In some embodiments, X_{21} is not W. In some embodiments, X_{21} is W or Y. In some embodiments, X_{21} is Y. In some embodiments, X_{21} is W.

[00369] In some embodiments, X_{22} is not D. In some embodiments, X_{22} is D or V. In some embodiments, X_{22} is V. In some embodiments, X_{22} is D.

[00370] In some embodiments, X_{23} is S.

[00371] In some embodiments, X_{24} is not S. In some embodiments, X_{24} is S or A. In some embodiments, X_{24} is A. In some embodiments, X_{24} is S.

[00372] In some embodiments, X_{25} is S.

[00373] In some embodiments, X_{26} is not D. In some embodiments, X_{26} is D, S or R. In some embodiments, X_{26} is S or R.In some embodiments, X_{26} is S. In some embodiments, X_{26} is R. In some embodiments, X_{26} is D.

[00374] In some embodiments, X_{27} is not H. In some embodiments, X_{27} is H or L. In some embodiments, X_{27} is L. In some embodiments, X_{27} is H.

[00375] In some embodiments,

a) X_1 is V, X_2 is W, X_3 is S, X_4 is S, X_5 is Y, X_6 is T, X_7 is S, X_8 is S, X_9 is D, X_{10} is I, X_{11} is F, X_{12} is A, X_{13} is M, X_{14} is I, X_{15} is N, X_{16} is I, X_{17} is S, X_{18} is K, X_{19} is S, X_{20} is V, X_{21} is W, X_{22} is D, X_{23} is S, X_{24} is S, X_{25} is S, X_{26} is S, or X_{27} is L, or a combination thereof;

b) X_1 is V, X_2 is W, X_3 is D, X_4 is S, X_5 is Y, X_6 is T, X_7 is A, X_8 is S, X_9 is E, X_{10} is I, X_{11} is F, X_{12} is A, X_{13} is M, X_{14} is I, X_{15} is N, X_{16} is I, X_{17} is S, X_{18} is K, X_{19} is S, X_{20} is I, X_{21} is W, X_{22} is D, X_{23} is S, X_{24} is S, X_{25} is S, X_{26} is S, or X_{27} is L, or a combination thereof;

c) X_1 is I, X_2 is W, X_3 is D, X_4 is T, X_5 is Y, X_6 is T, X_7 is A, X_8 is S, X_9 is S, X_{10} is I, X_{11} is F, X_{12} is A, X_{13} is F, X_{14} is I, X_{15} is N, X_{16} is I, X_{17} is S, X_{18} is K, X_{19} is S, X_{20} is V, X_{21} is W, X_{22} is D, X_{23} is S, X_{24} is S, X_{25} is S, X_{26} is S, or X_{27} is L, or a combination thereof; or

d) X_1 is I, X_2 is W, X_3 is S, X_4 is S, X_5 is D, X_6 is T, X_7 is A, X_8 is S, X_9 is D, X_{10} is I, X_{11} is F, X_{12} is S, X_{13} is M, X_{14} is V, X_{15} is Y, X_{16} is I, X_{17} is S, X_{18} is F, X_{19} is S, X_{20} is I, X_{21} is Y, X_{22} is V, X_{23} is S, X_{24} is A, X_{25} is S, X_{26} is R, or X_{27} is L, or a combination thereof.

Constant Domains

[00376] In some embodiments, a polypeptide (*e.g.*, an antibody or antigen-binding fragment thereof) comprises:

a) an antibody heavy chain constant domain sequence;

b) an antibody light chain constant domain sequence; or

both a) and b).

[00377] In some embodiments, a polypeptide comprises an antibody heavy chain constant domain sequence. In some embodiments, an antibody heavy chain constant domain is selected from the group consisting of an IgA constant domain, an IgD constant domain, an IgE constant domain, an IgG constant domain and an IgM constant domain.

[00378] In some embodiments, an IgG constant domain is an IgG1 constant domain (*e.g.*, any one of SEQ ID NOs:84-86), an IgG2 constant domain (*e.g.*, SEQ ID NO:87 or SEQ ID NO:88), an IgG3 constant domain or an IgG4 constant domain. In some embodiments, the IgG2 constant domain is an IgG2a, an IgG2b constant domain or an IgG2c constant domain. In some embodiments, an IgA constant domain is an IgA1 constant domain or an IgA2 constant domain. In some embodiments, the antibody heavy chain constant domain is an IgG1 constant domain (*e.g.*, IGHV1-5 or IGHV5-51).

[00379] ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGV HTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEPKSCDKTHT CPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGV EVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISK AKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTP PVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK (SEQ ID NO:84).

[00380] ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGV HTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEPKSCDKTHT CPPCPAPELLGGPSVFLFPPKPKDTLYITREPEVTCVVVDVSHEDPEVKFNWYVDGVE VHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKA KGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPP VLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK (SEQ ID NO:85).

[00381] ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGV HTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHT

CPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGV EVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISK AKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTP PVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK (SEQ ID NO:86).

[00382] ASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGVH TFPAVLQSSGLYSLSSVVTVPSSNFGTQTYTCNVDHKPSNTKVDKTVERKCCVECPP CPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVQFNWYVDGVEVHN AKTKPREEQFNSTFRVVSVLTVVHQDWLNGKEYKCKVSNKGLPAPIEKTISKTKGQP REPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPMLDS DGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK (SEQ ID NO:87).

[00383] ASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGVH TFPAVLQSSGLYSLSSVVTVPSSNFGTQTYTCNVDHKPSNTKVDKTVERKCCVECPP CPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVQFNWYVDGVEVHN AKTKPREEQFNSTFRVVSVLTVVHQDWLNGKEYKCKVSNKGLPAPIEKTISKTKGQP REPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTFPPMLDS DGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK (SEQ ID NO:88).

[00384] In some embodiments, a polypeptide comprises an antibody heavy chain constant domain sequence that has at least about 60% sequence identity to the amino acid sequence of any one of SEQ ID NOs:84-88 (*e.g.*, any one of SEQ ID NOs:84-86). For example, a polypeptide can comprise an antibody heavy chain constant domain sequence that has at least about: 61%, 62%, 63%, 64%, 65%, 66%, 67%, 68%, 69%, 70%, 71%, 72%, 73%, 74%, 75%, 76%, 77%, 78%, 79%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% sequence identity to the amino acid sequence of any one of SEQ ID NOs:84-88 (*e.g.*, any one of SEQ ID NOs:84-86). In some embodiments, a polypeptide comprises an antibody heavy chain constant domain sequence that has at least about 70% or at least about 80% sequence identity to the amino acid sequence of any one of SEQ ID NOs:84-88 (*e.g.*, any one of SEQ ID NOs:84-86).

[00385] In some embodiments, a polypeptide comprises an antibody heavy chain constant domain sequence that comprises at least one amino acid substitution relative to the amino acid sequence of any one of SEQ ID NOs:84-88 (*e.g.*, any one of SEQ ID NOs:84-86). For

example, the number of amino acid substitutions can be at least about: 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19 or 20, or about: 1-20, 1-19, 2-19, 2-18, 2-17, 3-17, 3-16, 4-16, 4-15, 5-15, 5-14, 6-14, 6-13, 7-13, 7-12, 8-12, 8-11 or 9-11. In some embodiments, a polypeptide comprises an antibody heavy chain constant domain sequence that comprises about 1-10 amino acid substitutions, relative to the amino acid sequence of any one of SEQ ID NOs:84-88 (*e.g.*, any one of SEQ ID NOs:84-86).

[00386] In some embodiments, a polypeptide comprises an antibody heavy chain constant domain sequence that has 100% sequence identity to the amino acid sequence of any one of SEQ ID Nos:84-88 (*e.g.*, any one of SEQ ID NOs:84-86).

[00387] In some embodiments, a polypeptide comprises an antibody heavy chain constant domain sequence that has at least about 60% sequence identity to the amino acid sequence of SEQ ID NO:84. For example, a polypeptide can comprise an antibody heavy chain constant domain sequence that has at least about: 61%, 62%, 63%, 64%, 65%, 66%, 67%, 68%, 69%, 70%, 71%, 72%, 73%, 74%, 75%, 76%, 77%, 78%, 79%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% sequence identity to the amino acid sequence of SEQ ID NO:84. In some embodiments, a polypeptide comprises an antibody heavy chain constant domain sequence that has at least about 70% or at least about 80% sequence identity to the amino acid sequence of SEQ ID NO:84.

[00388] In some embodiments, a polypeptide comprises an antibody heavy chain constant domain sequence that comprises at least one amino acid substitution relative to the amino acid sequence of SEQ ID NO:84. For example, the number of amino acid substitutions can be at least about: 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19 or 20, or about: 1-20, 1-19, 2-19, 2-18, 2-17, 3-17, 3-16, 4-16, 4-15, 5-15, 5-14, 6-14, 6-13, 7-13, 7-12, 8-12, 8-11 or 9-11. In some embodiments, a polypeptide comprises an antibody heavy chain constant domain sequence that comprises about 1-10 amino acid substitutions, relative to the amino acid sequence of SEQ ID NO:84.

[00389] In some embodiments, a polypeptide comprises an antibody heavy chain constant domain sequence that has 100% sequence identity to the amino acid sequence of SEQ ID NO:84. Antibodies disclosed herein using a designation "AB-[]a" (*e.g.*, AB-2a, *see*, *e.g.*, Table 4)) comprise the heavy chain constant domain amino acid sequence of SEQ ID NO:84, *i.e.*, comprising M135, S137, and T139.

[00390] In some embodiments, a polypeptide comprises (*e.g.*, an antibody or antigen-binding fragment thereof) an antibody heavy chain constant domain sequence that has at least

about 60% sequence identity to the amino acid sequence of SEQ ID NO:85. For example, a polypeptide can comprise an antibody heavy chain constant domain sequence that has at least about: 61%, 62%, 63%, 64%, 65%, 66%, 67%, 68%, 69%, 70%, 71%, 72%, 73%, 74%, 75%, 76%, 77%, 78%, 79%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% sequence identity to the amino acid sequence of SEQ ID NO:85. In some embodiments, a polypeptide comprises an antibody heavy chain constant domain sequence that has at least about 70% or at least about 80% sequence identity to the amino acid sequence of SEQ ID NO:85.

[00391] In some embodiments, a polypeptide comprises an antibody heavy chain constant domain sequence that comprises at least one amino acid substitution relative to the amino acid sequence of SEQ ID NO:85. For example, the number of amino acid substitutions can be at least about: 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19 or 20, or about: 1-20, 1-19, 2-19, 2-18, 2-17, 3-17, 3-16, 4-16, 4-15, 5-15, 5-14, 6-14, 6-13, 7-13, 7-12, 8-12, 8-11 or 9-11. In some embodiments, a polypeptide comprises an antibody heavy chain constant domain sequence that comprises about 1-10 amino acid substitutions, relative to the amino acid sequence of SEQ ID NO:85.

[00392] In some embodiments, a polypeptide comprises an antibody heavy chain constant domain sequence that has 100% sequence identity to the amino acid sequence of SEQ ID NO:85. Antibodies disclosed herein using a designation "AB-[]b" (*e.g.*, AB-2b, *see*, *e.g.*, Table 4)) comprise the heavy chain constant domain amino acid sequence of SEQ ID NO:85, *i.e.*, comprising Y135, T137, and E139).

[00393] In some embodiments, a polypeptide comprises an Fc polypeptide, or Fc domain (*e.g.*, an IgG1 domain, an IgG2 domain or an IgG4 domain). In some embodiments, an Fc domain comprises one or more mutations that, for example, decreases (*e.g.*, inhibits, ablates) an effector function of the Fc domain, increases half-life of an antibody or antibody fragment that comprises the Fc domain, or a combination thereof. *See, e.g.*, Dumet et al., *Insights into the IgG heavy chain engineering patent landscape as applied to IgG4 antibody development*, Mabs. 11(8):1341-50 (2019) (particularly Tables 1 and 2 therein) and WO02060919, the contents of which are incorporated by reference herein in their entirety. In some embodiments, an Fc domain comprises a LS modification (i.e., M428L/N434S substitutions with numbering determined by Kabat) or a YTE modification (i.e., M252Y/S254T/T256E substitutions as determined by Kabat numbering, corresponding to M135Y/S137T/T139E

when comparing SEQ ID NO:84 with SEQ ID NO:85). In some embodiments, an Fc domain comprises a YTE modification.

[00394] In some embodiments, a polypeptide (*e.g.*, an antibody or antigen-binding fragment thereof) comprises an antibody light chain constant domain sequence.

[00395] In some embodiments, a polypeptide comprises an antibody light chain constant domain sequence that is selected from the group consisting of a κ constant domain (*e.g.*, SEQ ID NO:89) and a λ constant domain (*e.g.*, SEQ ID NO:90).

[00396] RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSG NSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC (SEQ ID NO:89).

[00397] GQPKAAPSVTLFPPSSEELQANKATLVCLISDFYPGAVTVAWKADSSPVK AGVETTTPSKQSNNKYAASSYLSLTPEQWKSHRSYSCQVTHEGSTVEKTVAPTECS (SEQ ID NO:90).

[00398] In some embodiments, a polypeptide comprises an antibody light chain constant domain sequence that has at least about 60% sequence identity to the amino acid sequence of SEQ ID NO:89 or SEQ ID NO:90. For example, a polypeptide can comprise an antibody light chain constant domain sequence that has at least about: 61%, 62%, 63%, 64%, 65%, 66%, 67%, 68%, 69%, 70%, 71%, 72%, 73%, 74%, 75%, 76%, 77%, 78%, 79%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% sequence identity to the amino acid sequence of SEQ ID NO:89 or SEQ ID NO:90. In some embodiments, a polypeptide comprises an antibody light chain constant domain sequence that has at least about 70% or at least about 80% sequence identity to SEQ ID NO:89 or SEQ ID NO:90.

[00399] In some embodiments, a polypeptide comprises an antibody light chain constant domain sequence that comprises at least one amino acid substitution relative to the amino acid sequence of SEQ ID NO:89 or SEQ ID NO:90. For example, the number of amino acid substitutions can be at least about: 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19 or 20, or about: 1-20, 1-19, 2-19, 2-18, 2-17, 3-17, 3-16, 4-16, 4-15, 5-15, 5-14, 6-14, 6-13, 7-13, 7-12, 8-12, 8-11 or 9-11. In some embodiments, a polypeptide comprises an antibody light chain constant domain sequence that comprises about 1-10 amino acid substitutions, relative to the amino acid sequence of SEQ ID NO:89 or SEQ ID NO:90. In some

embodiments, the at least one amino acid substitution is a conservative substitution. In some embodiments, the at least one amino acid substitution is a highly conservative substitution.

[00400] In some embodiments, a polypeptide comprises an antibody light chain constant domain sequence that has 100% sequence identity to the amino acid sequence of SEQ ID NO:89 or SEQ ID NO:90.

[00401] In some embodiments, a polypeptide comprises an antibody light chain constant domain sequence that has at least about 60% sequence identity to the amino acid sequence of SEQ ID NO:90. For example, a polypeptide can comprise an antibody light chain constant domain sequence that has at least about: 61%, 62%, 63%, 64%, 65%, 66%, 67%, 68%, 69%, 70%, 71%, 72%, 73%, 74%, 75%, 76%, 77%, 78%, 79%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% sequence identity to the amino acid sequence of SEQ ID NO:90. In some embodiments, a polypeptide comprises an antibody light chain constant domain sequence that has at least about 70% or at least about 80% sequence identity to SEQ ID NO:90.

[00402] In some embodiments, a polypeptide comprises an antibody light chain constant domain sequence that comprises at least one amino acid substitution relative to the amino acid sequence of SEQ ID NO:90. For example, the number of amino acid substitutions can be at least about: 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19 or 20, or about: 1-20, 1-19, 2-19, 2-18, 2-17, 3-17, 3-16, 4-16, 4-15, 5-15, 5-14, 6-14, 6-13, 7-13, 7-12, 8-12, 8-11 or 9-11. In some embodiments, a polypeptide comprises an antibody light chain constant domain sequence that comprises about 1-10 amino acid substitutions, relative to the amino acid sequence of SEQ ID NO:90. In some embodiments, the at least one amino acid substitution is a conservative substitution. In some embodiments, the at least one amino acid substitution is a highly conservative substitution.

[00403] In some embodiments, a polypeptide comprises an antibody light chain constant domain sequence that has 100% sequence identity to the amino acid sequence of SEQ ID NO:90.

[00404] In some embodiments, a polypeptide comprises:

a) an antibody heavy chain constant domain sequence; and

b) an antibody light chain constant domain sequence.

[00405] In some embodiments, a polypeptide comprises an antibody heavy chain constant domain that is an IgG1 constant domain (*e.g.*, SEQ ID NO:84 or SEQ ID NO:85), and an antibody light chain constant domain that is a λ constant domain (*e.g.*, SEQ ID NO:90).

[00406] In some embodiments, a polypeptide comprises:

a) an antibody heavy chain constant domain comprising SEQ ID NO:85; or

b) an antibody light chain constant domain comprising SEQ ID NO:90,

or both a) and b).

[00407] In some embodiments, a polypeptide comprises:

a) an antibody heavy chain constant domain comprising SEQ ID NO:85; and

b) an antibody light chain constant domain comprising SEQ ID NO:90,

[00408] In some embodiments, a polypeptide comprises:

a) an antibody heavy chain constant domain comprising SEQ ID NO:84; or

b) an antibody light chain constant domain comprising SEQ ID NO:90,

or both a) and b).

[00409] In some embodiments, a polypeptide comprises:

a) an antibody heavy chain constant domain comprising SEQ ID NO:84; and

b) an antibody light chain constant domain comprising SEQ ID NO:90,

Antibodies and Antigen Binding Fragments

[00410] In some embodiments, a polypeptide is an immunoglobulin molecule, such as an antibody (*e.g.*, a whole antibody, an intact antibody) or an antigen-binding fragment of an antibody.

[00411] In some embodiments, a polypeptide is an antibody. As used herein, the term "antibody" refers to an immunoglobulin molecule capable of specific binding to a target, such as a carbohydrate, polynucleotide, lipid, polypeptide, etc., through at least one antigen recognition site, located in the variable domain of the immunoglobulin molecule. As used herein, the term "antibody" refers to a full-length antibody.

[00412] In some embodiments, a polypeptide is an antibody comprising two heavy (H) chains and two light (L) chains inter-connected by disulfide bonds or multimers thereof (for example, IgM). Each heavy chain comprises a V_H and a heavy chain constant domain (comprising domains CH1, hinge CH2 and CH3). Each light chain comprises a V_L and a light chain constant domain (CL). V_H and V_L regions may be further subdivided into regions of hypervariability, termed complementarity determining regions (CDRs), interspersed within

framework regions (FRs). V_H and V_L each comprises three CDRs and four FRs, arranged from the amino-terminus to the carboxy-terminus in the following order: FR1, CDR1, FR2, CDR2, FR3, CDR3, and FR4. An antibody can be of any species, such as a murine antibody, a human antibody, or a humanized antibody.

[00413] In some embodiments, a polypeptide comprises a heavy chain amino acid sequence that has at least about 60% sequence identity to the amino acid sequence of any one or more of SEQ ID NOs:91-118. For example, a polypeptide can comprise a heavy chain amino acid sequence that has at least about: 61%, 62%, 63%, 64%, 65%, 66%, 67%, 68%, 69%, 70%, 71%, 72%, 73%, 74%, 75%, 76%, 77%, 78%, 79%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% sequence identity to the amino acid sequence of any one or more of SEQ ID NOs:91-118. In some embodiments, a polypeptide comprises a heavy chain amino acid sequence that has at least about 70% or at least about 80% sequence identity to the amino acid sequence of any one or more of SEQ ID NOs:91-118.

[00414] In some embodiments, a polypeptide comprises a heavy chain amino acid sequence that comprises at least one amino acid substitution relative to the amino acid sequence of any one or more of SEQ ID NOs:91-118. For example, the number of amino acid substitutions can be at least about: 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19 or 20, or about: 1-20, 1-19, 2-19, 2-18, 2-17, 3-17, 3-16, 4-16, 4-15, 5-15, 5-14, 6-14, 6-13, 7-13, 7-12, 8-12, 8-11 or 9-11. In some embodiments, a polypeptide comprises a heavy chain amino acid sequence that comprises about 1-10 amino acid substitutions, relative to the amino acid sequence of any one or more of SEQ ID NOs:91-118.

[00415] In some embodiments, a polypeptide comprises a heavy chain amino acid sequence that has 100% sequence identity to the amino acid sequence of any one of SEQ ID NOs:91-118.

[00416] In some embodiments, a polypeptide comprises a heavy chain amino acid sequence that has at least about 60% sequence identity to the amino acid sequence of any one or more of SEQ ID NOs:91-94 and 105-108. For example, a polypeptide can comprise a heavy chain amino acid sequence that has at least about: 61%, 62%, 63%, 64%, 65%, 66%, 67%, 68%, 69%, 70%, 71%, 72%, 73%, 74%, 75%, 76%, 77%, 78%, 79%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% sequence identity to the amino acid sequence of any one or more of SEQ ID NOs:91-94 and 105-108. In some embodiments, a polypeptide comprises a heavy chain amino acid

sequence that has at least about 80% sequence identity to the amino acid sequence of any one or more of SEQ ID NOs:91-94 and 105-108.

[00417] In some embodiments, a polypeptide comprises a heavy chain amino acid sequence that comprises at least one amino acid substitution relative to the amino acid sequence of any one or more of SEQ ID NOs:91-94 and 105-108. For example, the number of amino acid substitutions can be at least about: 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19 or 20, or about: 1-20, 1-19, 2-19, 2-18, 2-17, 3-17, 3-16, 4-16, 4-15, 5-15, 5-14, 6-14, 6-13, 7-13, 7-12, 8-12, 8-11 or 9-11. In some embodiments, a polypeptide comprises a heavy chain amino acid sequence that comprises about 1-10 amino acid substitutions, relative to the amino acid sequence of any one or more of SEQ ID NOs:91-94 and 105-108.

[00418] In some embodiments, a polypeptide comprises a heavy chain amino acid sequence that has 100% sequence identity to the amino acid sequence of any one of SEQ ID NOs:91-94 and 105-108.

[00419] In some embodiments, a polypeptide comprises a heavy chain amino acid sequence that has at least about 60% sequence identity to the amino acid sequence of any one or more of SEQ ID NOs:91-94. For example, a polypeptide can comprise a heavy chain amino acid sequence that has at least about: 61%, 62%, 63%, 64%, 65%, 66%, 67%, 68%, 69%, 70%, 71%, 72%, 73%, 74%, 75%, 76%, 77%, 78%, 79%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% sequence identity to the amino acid sequence of any one or more of SEQ ID NOs:91-94. In some embodiments, a polypeptide comprises a heavy chain amino acid sequence that has at least about 70% or at least about 80% sequence identity to the amino acid sequence of any one or more of SEQ ID NOs:91-94.

[00420] In some embodiments, a polypeptide comprises a heavy chain amino acid sequence that comprises at least one amino acid substitution relative to the amino acid sequence of any one or more of SEQ ID NOs:91-94. For example, the number of amino acid substitutions can be at least about: 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19 or 20, or about: 1-20, 1-19, 2-19, 2-18, 2-17, 3-17, 3-16, 4-16, 4-15, 5-15, 5-14, 6-14, 6-13, 7-13, 7-12, 8-12, 8-11 or 9-11. In some embodiments, a polypeptide comprises a heavy chain amino acid sequence that comprises about 1-10 amino acid substitutions, relative to the amino acid sequence of any one or more of SEQ ID NOs:91-94.

[00421] In some embodiments, a polypeptide comprises a heavy chain amino acid sequence that has 100% sequence identity to the amino acid sequence of any one of SEQ ID NOs:91-94.

[00422] In some embodiments, a polypeptide comprises a heavy chain amino acid sequence that has at least about 60% sequence identity to the amino acid sequence of SEQ ID NO:92. For example, a polypeptide can comprise a heavy chain amino acid sequence that has at least about: 61%, 62%, 63%, 64%, 65%, 66%, 67%, 68%, 69%, 70%, 71%, 72%, 73%, 74%, 75%, 76%, 77%, 78%, 79%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% sequence identity to the amino acid sequence of SEQ ID NO:92. In some embodiments, a polypeptide comprises a heavy chain amino acid sequence that has at least about 70% or at least about 80% sequence identity to the amino acid sequence of SEQ ID NO:92.

[00423] In some embodiments, a polypeptide comprises a heavy chain amino acid sequence that comprises at least one amino acid substitution relative to the amino acid sequence of SEQ ID NO:92. For example, the number of amino acid substitutions can be at least about: 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19 or 20, or about: 1-20, 1-19, 2-19, 2-18, 2-17, 3-17, 3-16, 4-16, 4-15, 5-15, 5-14, 6-14, 6-13, 7-13, 7-12, 8-12, 8-11 or 9-11. In some embodiments, a polypeptide comprises a heavy chain amino acid sequence that comprises about 1-10 amino acid substitutions, relative to the amino acid sequence of SEQ ID NO:92.

[00424] In some embodiments, a polypeptide comprises a heavy chain amino acid sequence that has 100% sequence identity to the amino acid sequence of SEQ ID NO:92.

[00425] In some embodiments, a polypeptide comprises a heavy chain amino acid sequence that has at least about 60% sequence identity to the amino acid sequence of any one or more of SEQ ID NOs:105-108. For example, a polypeptide can comprise a heavy chain amino acid sequence that has at least about: 61%, 62%, 63%, 64%, 65%, 66%, 67%, 68%, 69%, 70%, 71%, 72%, 73%, 74%, 75%, 76%, 77%, 78%, 79%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% sequence identity to the amino acid sequence of any one or more of SEQ ID NOs:105-108. In some embodiments, a polypeptide comprises a heavy chain amino acid sequence that has at

least about 70% or at least about 80% sequence identity to the amino acid sequence of any one or more of SEQ ID NOs:105-108.

[00426] In some embodiments, a polypeptide comprises a heavy chain amino acid sequence that comprises at least one amino acid substitution relative to the amino acid sequence of any one or more of SEQ ID NOs:105-108. For example, the number of amino acid substitutions can be at least about: 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19 or 20, or about: 1-20, 1-19, 2-19, 2-18, 2-17, 3-17, 3-16, 4-16, 4-15, 5-15, 5-14, 6-14, 6-13, 7-13, 7-12, 8-12, 8-11 or 9-11. In some embodiments, a polypeptide comprises a heavy chain amino acid sequence that comprises about 1-10 amino acid substitutions, relative to the amino acid sequence of any one or more of SEQ ID NOs:105-108.

[00427] In some embodiments, a polypeptide comprises a heavy chain amino acid sequence that has 100% sequence identity to the amino acid sequence of any one of SEQ ID NOs:105-108.

[00428] In some embodiments, a polypeptide comprises a heavy chain amino acid sequence that has at least about 60% sequence identity to the amino acid sequence of SEQ ID NO:106. For example, a polypeptide can comprise a heavy chain amino acid sequence that has at least about: 61%, 62%, 63%, 64%, 65%, 66%, 67%, 68%, 69%, 70%, 71%, 72%, 73%, 74%, 75%, 76%, 77%, 78%, 79%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% sequence identity to the amino acid sequence of SEQ ID NO:106. In some embodiments, a polypeptide comprises a heavy chain amino acid sequence that has at least about 70% or at least about 80% sequence identity to the amino acid sequence of SEQ ID NO:106.

[00429] In some embodiments, a polypeptide comprises a heavy chain amino acid sequence that comprises at least one amino acid substitution relative to the amino acid sequence of SEQ ID NO:106. For example, the number of amino acid substitutions can be at least about: 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19 or 20, or about: 1-20, 1-19, 2-19, 2-18, 2-17, 3-17, 3-16, 4-16, 4-15, 5-15, 5-14, 6-14, 6-13, 7-13, 7-12, 8-12, 8-11 or 9-11. In some embodiments, a polypeptide comprises a heavy chain amino acid sequence that comprises about 1-10 amino acid substitutions, relative to the amino acid sequence of SEQ ID NO:106.

[00430] In some embodiments, a polypeptide comprises a heavy chain amino acid sequence that has 100% sequence identity to the amino acid sequence of SEQ ID NO:106.

[00431] In some embodiments, a polypeptide comprises a light chain amino acid sequence that has at least about 60% sequence identity to the amino acid sequence of any one or more of SEQ ID NOs:119-129. For example, a polypeptide can comprise a light chain amino acid sequence that has at least about: 61%, 62%, 63%, 64%, 65%, 66%, 67%, 68%, 69%, 70%, 71%, 72%, 73%, 74%, 75%, 76%, 77%, 78%, 79%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% sequence identity to the amino acid sequence of any one or more of SEQ ID NOs:119-129. In some embodiments, a polypeptide comprises a light chain amino acid sequence that has at least about 70% or at least about 80% sequence identity to the amino acid sequence of any one or more of SEQ ID NOs:119-129.

[00432] In some embodiments, a polypeptide comprises a light chain amino acid sequence that comprises at least one amino acid substitution relative to the amino acid sequence of any one or more of SEQ ID NOs:119-129. For example, the number of amino acid substitutions can be at least about: 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19 or 20, or about: 1-20, 1-19, 2-19, 2-18, 2-17, 3-17, 3-16, 4-16, 4-15, 5-15, 5-14, 6-14, 6-13, 7-13, 7-12, 8-12, 8-11 or 9-11. In some embodiments, a polypeptide comprises a light chain amino acid sequence that comprises about 1-10 amino acid substitutions, relative to the amino acid sequence of any one or more of SEQ ID NOs:119-129.

[00433] In some embodiments, a polypeptide comprises a light chain amino acid sequence that has 100% sequence identity to the amino acid sequence of any one of SEQ ID NOs:119-129.

[00434] In some embodiments, a polypeptide comprises a light chain amino acid sequence that has at least about 60% sequence identity to the amino acid sequence of any one or more of SEQ ID NOs:119-121. For example, a polypeptide can comprise a light chain amino acid sequence that has at least about: 61%, 62%, 63%, 64%, 65%, 66%, 67%, 68%, 69%, 70%, 71%, 72%, 73%, 74%, 75%, 76%, 77%, 78%, 79%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% sequence identity to the amino acid sequence of any one or more of SEQ ID NOs:119-121. In some embodiments, a polypeptide comprises a light chain amino acid sequence that has at least about 80% sequence identity to the amino acid sequence of any one or more of SEQ ID NOs:119-121.

[00435] In some embodiments, a polypeptide comprises a light chain amino acid sequence that comprises at least one amino acid substitution relative to the amino acid sequence of any

one or more of SEQ ID NOs:119-121. For example, the number of amino acid substitutions can be at least about: 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19 or 20, or about: 1-20, 1-19, 2-19, 2-18, 2-17, 3-17, 3-16, 4-16, 4-15, 5-15, 5-14, 6-14, 6-13, 7-13, 7-12, 8-12, 8-11 or 9-11. In some embodiments, a polypeptide comprises a light chain amino acid sequence that comprises about 1-10 amino acid substitutions, relative to the amino acid sequence of any one or more of SEQ ID NOs:119-121.

[00436] In some embodiments, a polypeptide comprises a light chain amino acid sequence that has 100% sequence identity to the amino acid sequence of any one of SEQ ID NOs:119-121.

[00437] In some embodiments, a polypeptide comprises a light chain amino acid sequence that has at least about 60% sequence identity to the amino acid sequence of SEQ ID NO:120. For example, a polypeptide cann comprise a light chain amino acid sequence that has at least about: 61%, 62%, 63%, 64%, 65%, 66%, 67%, 68%, 69%, 70%, 71%, 72%, 73%, 74%, 75%, 76%, 77%, 78%, 79%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% sequence identity to the amino acid sequence of SEQ ID NO:120. In some embodiments, a polypeptide comprises a light chain amino acid sequence that has at least about 70% or at least about 80% sequence identity to the amino acid sequence of SEQ ID NO:120.

[00438] In some embodiments, a polypeptide comprises a light chain amino acid sequence that comprises at least one amino acid substitution relative to the amino acid sequence of SEQ ID NO:120. For example, the number of amino acid substitutions can be at least about: 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19 or 20, or about: 1-20, 1-19, 2-19, 2-18, 2-17, 3-17, 3-16, 4-16, 4-15, 5-15, 5-14, 6-14, 6-13, 7-13, 7-12, 8-12, 8-11 or 9-11. In some embodiments, a polypeptide comprises a light chain amino acid sequence that comprises about 1-10 amino acid substitutions, relative to the amino acid sequence of SEQ ID NO:120.

[00439] In some embodiments, a polypeptide comprises a light chain amino acid sequence that has 100% sequence identity to the amino acid sequence of SEQ ID NO:120.

[00440] In some embodiments, a polypeptide comprises:

a) a heavy chain amino acid sequence that has at least about 60% sequence identity to the amino acid sequence of any one or more of SEQ ID NOs:91-118; or

b) a light chain amino acid sequence that has at least about 60% sequence identity to the amino acid sequence of any one or more of SEQ ID NOs:119-129, or

both a) and b).

[00441] In some embodiments, a polypeptide comprises:

a) a heavy chain amino acid sequence that has at least about 60% sequence identity to the amino acid sequence of any one or more of SEQ ID NOs:91-118; and

b) a light chain amino acid sequence that has at least about 60% sequence identity to the amino acid sequence of any one or more of SEQ ID NOs:119-129.

[00442] In some embodiments, a polypeptide comprises:

a) a heavy chain amino acid sequence comprising at least one amino acid substitution relative to the amino acid sequence of any one or more of SEQ ID NOs:91-118; or

b) a light chain amino acid sequence comprising at least one amino acid substitution relative to the amino acid sequence of any one or more of SEQ ID NOs:119-129, or

both a) and b).

[00443] In some embodiments, a polypeptide comprises:

a) a heavy chain amino acid sequence comprising at least one amino acid substitution relative to the amino acid sequence of any one or more of SEQ ID NOs:91-118; and

b) a light chain amino acid sequence comprising at least one amino acid substitution relative to the amino acid sequence of any one or more of SEQ ID NOs:119-129.

[00444] In some embodiments, a polypeptide comprises:

a) a heavy chain amino acid sequence comprising about 1-10 amino acid substitutions, relative to the amino acid sequence of any one or more of SEQ ID NOs:91-118; or

b) a light chain amino acid sequence comprising about 1-10 amino acid substitutions, relative to the amino acid sequence of any one or more of SEQ ID NOs:119-129, or

both a) and b).

[00445] In some embodiments, a polypeptide comprises:

a) a heavy chain amino acid sequence comprising about 1-10 amino acid substitutions, relative to the amino acid sequence of any one or more of SEQ ID NOs:91-118; and

b) a light chain amino acid sequence comprising about 1-10 amino acid substitutions, relative to the amino acid sequence of any one or more of SEQ ID NOs:119-129.

[00446] In some embodiments, a polypeptide comprises:

a) a heavy chain amino acid sequence that has 100% sequence identity to the amino acid sequence of any one of SEQ ID NOs:91-118; or

b) a light chain amino acid sequence that has 100% sequence identity to the amino acid sequence of any one of SEQ ID NOs:119-129, or

both a) and b).

[00447] In some embodiments, a polypeptide comprises:

a) a heavy chain amino acid sequence that has 100% sequence identity to the amino acid sequence of any one of SEQ ID NOs:91-118; and

b) a light chain amino acid sequence that has 100% sequence identity to the amino acid sequence of any one of SEQ ID NOs:119-129.

[00448] In some embodiments, a polypeptide comprises:

a) a heavy chain amino acid sequence that has at least about 60% sequence identity to the amino acid sequence of any one or more of SEQ ID NOs:91-94 and 105-108; or

b) a light chain amino acid sequence that has at least about 60% sequence identity to the amino acid sequence of any one or more of SEQ ID NOs:119-121, or

both a) and b).

[00449] In some embodiments, a polypeptide comprises:

a) a heavy chain amino acid sequence that has at least about 60% sequence identity to the amino acid sequence of any one or more of SEQ ID NOs:91-94 and 105-108; and

b) a light chain amino acid sequence that has at least about 60% sequence identity to the amino acid sequence of any one or more of SEQ ID NOs:119-121.

[00450] In some embodiments, a polypeptide comprises:

a) a heavy chain amino acid sequence comprising at least one amino acid substitution relative to the amino acid sequence of any one or more of SEQ ID NOs:91-94 and 105-108; or

b) a light chain amino acid sequence comprising at least one amino acid substitution relative to the amino acid sequence of any one or more of SEQ ID NOs:119-121, or

both a) and b).

[00451] In some embodiments, a polypeptide comprises:

a) a heavy chain amino acid sequence comprising at least one amino acid substitution relative to the amino acid sequence of any one or more of SEQ ID NOs:91-94 and 105-108; and

b) a light chain amino acid sequence comprising at least one amino acid substitution relative to the amino acid sequence of any one or more of SEQ ID NOs:119-121.

[00452] In some embodiments, a polypeptide comprises:

a) a heavy chain amino acid sequence comprising about 1-10 amino acid substitutions, relative to the amino acid sequence of any one or more of SEQ ID NOs:91-94 and 105-108; or

b) a light chain amino acid sequence comprising about 1-10 amino acid substitutions, relative to the amino acid sequence of any one or more of SEQ ID NOs:119-121, or

both a) and b).

[00453] In some embodiments, a polypeptide comprises:

a) a heavy chain amino acid sequence comprising about 1-10 amino acid substitutions, relative to the amino acid sequence of any one or more of SEQ ID NOs:91-94 and 105-108; and

b) a light chain amino acid sequence comprising about 1-10 amino acid substitutions, relative to the amino acid sequence of any one or more of SEQ ID NOs:119-121.

[00454] In some embodiments, a polypeptide comprises:

a) a heavy chain amino acid sequence that has 100% sequence identity to the amino acid sequence of any one of SEQ ID NOs:91-94 and 105-108; or

b) a light chain amino acid sequence that has 100% sequence identity to the amino acid sequence of any one of SEQ ID NOs:119-121, or

both a) and b).

[00455] In some embodiments, a polypeptide comprises:

a) a heavy chain amino acid sequence that has 100% sequence identity to the amino acid sequence of any one of SEQ ID NOs:91-94 and 105-108; and

b) a light chain amino acid sequence that has 100% sequence identity to the amino acid sequence of any one of SEQ ID NOs:119-121.

[00456] In some embodiments, a polypeptide comprises:

a) a heavy chain amino acid sequence that has at least about 60% sequence identity to the amino acid sequence of any one or more of SEQ ID NOs:105-108; or

b) a light chain amino acid sequence that has at least about 60% sequence identity to the amino acid sequence of any one or more of SEQ ID NOs:119-121, or

both a) and b).

[00457] In some embodiments, a polypeptide comprises:

a) a heavy chain amino acid sequence that has at least about 60% sequence identity to the amino acid sequence of any one or more of SEQ ID NOs:105-108; and

b) a light chain amino acid sequence that has at least about 60% sequence identity to the amino acid sequence of any one or more of SEQ ID NOs:119-121.

[00458] In some embodiments, a polypeptide comprises:

a) a heavy chain amino acid sequence comprising at least one amino acid substitution relative to the amino acid sequence of any one or more of SEQ ID NOs:105-108; or

b) a light chain amino acid sequence comprising at least one amino acid substitution relative to the amino acid sequence of any one or more of SEQ ID NOs:119-121, or

both a) and b).

[00459] In some embodiments, a polypeptide comprises:

a) a heavy chain amino acid sequence comprising at least one amino acid substitution relative to the amino acid sequence of any one or more of SEQ ID NOs:105-108; and

b) a light chain amino acid sequence comprising at least one amino acid substitution relative to the amino acid sequence of any one or more of SEQ ID NOs:119-121.

[00460] In some embodiments, a polypeptide comprises:

a) a heavy chain amino acid sequence comprising about 1-10 amino acid substitutions, relative to the amino acid sequence of any one or more of SEQ ID NOs:105-108; or

b) a light chain amino acid sequence comprising about 1-10 amino acid substitutions, relative to the amino acid sequence of any one or more of SEQ ID NOs:119-121, or

both a) and b).

[00461] In some embodiments, a polypeptide comprises:

a) a heavy chain amino acid sequence comprising about 1-10 amino acid substitutions, relative to the amino acid sequence of any one or more of SEQ ID NOs:105-108; and

b) a light chain amino acid sequence comprising about 1-10 amino acid substitutions, relative to the amino acid sequence of any one or more of SEQ ID NOs:119-121.

[00462] In some embodiments, a polypeptide comprises:

a) a heavy chain amino acid sequence that has 100% sequence identity to the amino acid sequence of any one of SEQ ID NOs:105-108; or

b) a light chain amino acid sequence that has 100% sequence identity to the amino acid sequence of any one of SEQ ID NOs:119-121, or

both a) and b).

[00463] In some embodiments, a polypeptide comprises:

a) a heavy chain amino acid sequence that has 100% sequence identity to the amino acid sequence of any one of SEQ ID NOs:105-108; and

b) a light chain amino acid sequence that has 100% sequence identity to the amino acid sequence of any one of SEQ ID NOs:119-121.

[00464] In some embodiments, a polypeptide comprises:

a) a heavy chain amino acid sequence that has at least about 60% sequence identity to the amino acid sequence of SEQ ID NO:106; or

b) a light chain amino acid sequence that has at least about 60% sequence identity to the amino acid sequence of SEQ ID NO:120, or

both a) and b).

[00465] In some embodiments, a polypeptide comprises:

a) a heavy chain amino acid sequence that has at least about 60% sequence identity to the amino acid sequence of SEQ ID NO:106; and

b) a light chain amino acid sequence that has at least about 60% sequence identity to the amino acid sequence of SEQ ID NO:120.

[00466] In some embodiments, a polypeptide comprises:

a) a heavy chain amino acid sequence comprising at least one amino acid substitution relative to the amino acid sequence of SEQ ID NO:106; or

b) a light chain amino acid sequence comprising about 1-10 amino acid substitutions, relative to the amino acid sequence of SEQ ID NO:120, or

both a) and b).

[00467] In some embodiments, a polypeptide comprises:

a) a heavy chain amino acid sequence comprising at least one amino acid substitution relative to the amino acid sequence of SEQ ID NO:106; and

b) a light chain amino acid sequence comprising about 1-10 amino acid substitutions, relative to the amino acid sequence of SEQ ID NO:120.

[00468] In some embodiments, a polypeptide comprises:

a) a heavy chain comprising the amino acid sequence of SEQ ID NO:105; and

b) a light chain comprising the amino acid sequence of SEQ ID NO:119 (AB-1b).

[00469] In some embodiments, a polypeptide comprises:

a) a heavy chain comprising the amino acid sequence of SEQ ID NO:106; and

b) a light chain comprising the amino acid sequence of SEQ ID NO:120 (AB-2b).

[00470] In some embodiments, a polypeptide comprises:

a) a heavy chain comprising the amino acid sequence of SEQ ID NO:107; and

b) a light chain comprising the amino acid sequence of SEQ ID NO:119 (AB-3b).

[00471] In some embodiments, a polypeptide comprises:

a) a heavy chain comprising the amino acid sequence of SEQ ID NO:108; and

b) a light chain comprising the amino acid sequence of SEQ ID NO:121 (AB-4b).

[00472] In some embodiments, a polypeptide comprises:

a) a heavy chain comprising the amino acid sequence of SEQ ID NO:109; and

b) a light chain comprising the amino acid sequence of SEQ ID NO:122 (AB-5b).

[00473] In some embodiments, a polypeptide comprises:

a) a heavy chain comprising the amino acid sequence of SEQ ID NO:110; and

b) a light chain comprising the amino acid sequence of SEQ ID NO:123 (AB-6b).

[00474] In some embodiments, a polypeptide comprises:

a) a heavy chain comprising the amino acid sequence of SEQ ID NO:111; and

b) a light chain comprising the amino acid sequence of SEQ ID NO:124 (AB-7b).

[00475] In some embodiments, a polypeptide comprises:

a) a heavy chain comprising the amino acid sequence of SEQ ID NO:112; and

b) a light chain comprising the amino acid sequence of SEQ ID NO:119 (AB-8b).

[00476] In some embodiments, a polypeptide comprises:

a) a heavy chain comprising the amino acid sequence of SEQ ID NO:113; and

b) a light chain comprising the amino acid sequence of SEQ ID NO:119 (AB-9b).

[00477] In some embodiments, a polypeptide comprises:

a) a heavy chain comprising the amino acid sequence of SEQ ID NO:114; and

b) a light chain comprising the amino acid sequence of SEQ ID NO:125 (AB-10b).

[00478] In some embodiments, a polypeptide comprises:

a) a heavy chain comprising the amino acid sequence of SEQ ID NO:115; and

b) a light chain comprising the amino acid sequence of SEQ ID NO:126 (AB-11b).

[00479] In some embodiments, a polypeptide comprises:

a) a heavy chain comprising the amino acid sequence of SEQ ID NO:116; and

b) a light chain comprising the amino acid sequence of SEQ ID NO:127 (AB-12b).

[00480] In some embodiments, a polypeptide comprises:

a) a heavy chain comprising the amino acid sequence of SEQ ID NO:117; and

b) a light chain comprising the amino acid sequence of SEQ ID NO:128 (AB-13b).

[00481] In some embodiments, a polypeptide comprises:

a) a heavy chain comprising the amino acid sequence of SEQ ID NO:118; and

b) a light chain comprising the amino acid sequence of SEQ ID NO:129 (AB-14b).

[00482] In some embodiments, a polypeptide is a single-domain antibody or an antigen-binding fragment thereof. As used herein, the term "single-domain antibody (sdAb)" or "nanobody" refers to an immunoglobulin molecule consisting of a single monomeric variable antibody domain and capable of specific binding to a target. A single-domain antibody can be of any species, such as a murine antibody, a human antibody or a humanized single-domain antibody.

[00483] In some embodiments, a V_H domain and a V_L domain may be linked together via a linker (*e.g.*, a synthetic linker) to form various types of single-chain antibody designs in which the V_H/V_L domains pair intramolecularly, or intermolecularly in those cases when the V_H and V_L domains are expressed by separate chains, to form a monovalent antigen binding site.

[00484] In some embodiments, a polypeptide is a heavy-chain antibody comprising two or more heavy chains, but lacking light chain, or an antigen-binding fragment thereof. Non-limiting examples of heavy chain antibodies include camelid Vhh (also referred to as VHH or V_HH) antibodies. Camelid antibodies are antibodies from the *Camelidae* family of mammals that include llamas, camels, and alpacas.

[00485] In some embodiments, a polypeptide is an antibody mimetic. The term "antibody mimetic" refers to polypeptides capable of mimicking an antibody's ability to bind an

antigen, but structurally differ from native antibody structures. Non-limiting examples of antibody mimetics include Adnectins, Affibodies, Affilins, Affimers, Affitins, Alphabodies, Anticalins, Avimers, DARPins, Fynomers, Kunitz domain peptides, monobodies, nanobodies, nanoCLAMPs, and Versabodies.

[00486] In some embodiments, a polypeptide is an antigen-binding fragment of an antibody. The term "antigen-binding fragment" refers to a portion of an immunoglobulin molecule (*e.g.*, antibody) that retains the antigen binding properties of the full-length Reference Antibody. Non-limiting examples of antigen-binding fragments include a V_H region, a V_L region, an Fab fragment, an $F(ab')_2$ fragment, an Fd fragment, an Fv fragment, and a domain antibody (dAb) consisting of one V_H domain or one V_L domain, *etc*. V_H and V_L domains may be linked together via a synthetic linker to form various types of single-chain antibody designs in which the V_H/V_L domains pair intramolecularly, or intermolecularly in those cases when the V_H and V_L domains are expressed by separate chains, to form a monovalent antigen binding site, such as single chain Fv (scFv) or diabody. In some embodiments, a polypeptide disclosed herein is an antigen binding fragment selected from Fab, $F(ab')_2$, Fab', scFv, or Fv. In some embodiments, a polypeptide is a scFv.

[00487] In some embodiments, a polypeptide is an isolated polypeptide.

[00488] In some embodiments, a polypeptide (*e.g.*, an isolated polypeptide) is recombinantly produced. In some embodiments, a polypeptide (*e.g.*, an isolated polypeptide) is synthetically produced.

[00489] In some embodiments, a polypeptide is linked to a second polypeptide. The term "linked" means attached, via a covalent or noncovalent interaction. Conjugation can employ a suitable linking agent. Non-limiting examples include peptide linkers, compound linkers, and chemical cross-linking agents. In some embodiments, the linker is a disulfide bond.

[00490] In some embodiments, a polypeptide is conjugated to a heterologous moiety. The term "conjugated" refers to attached, via a covalent or noncovalent interaction. Conjugation can employ any one or more of suitable linking agents. Non-limiting examples include peptide linkers, compound linkers, and chemical cross-linking agents.

[00491] In some embodiments, a heterologous moiety comprises a therapeutic agent, a diagnostic agent, or both. In some embodiments, a heterologous moiety is selected from polyethylene glycol (PEG), hexadecanoic acid, hydrogels, nanoparticles, multimerization domains and carrier peptides.

[00492] In some embodiments, a nanoparticle is a lipid nanoparticle. In some embodiments, a nanoparticle is a polymer nanoparticle. In some embodiments, a polymer is an amphiphilic polymer. In some embodiments, a polymer is a hydrophobic or hydrophilic polymer. Non-limiting examples of polymers include poly(lactic acid)-poly(ethylene glycol), poly(lactic-co-glycolic acid)-poly(ethylene glycol), poly(lactic-co-glycolic) acid (PLGA), poly(lactic-co-glycolic acid)-d-α-tocopheryl polyethylene glycol succinate, poly(lactic-co-glycolic acid)-ethylene oxide fumarate, poly(glycolic acid)-poly(ethylene glycol), polycaprolactone-poly(ethylene glycol), or any salts thereof. In some embodiments, a polymer nanoparticle comprises poly(lactic-co-glycolic) acid (PLGA).

[00493] In some embodiments, a carrier polypeptide is albumin or an Fc polypeptide.

[00494] In some embodiments, a polypeptide:

a) binds to a TSLP protein with a K_D of 10 pM or less (*e.g.*, as measured by KinExA);

b) binds to AB-loop region and C-terminal region of helix D of a TSLP protein;

c) binds to an epitope in a TSLP protein (*e.g.*, a full-length human TSLP);

d) competes with the Reference Antibody for binding to a TSLP protein;

e) reduces binding of a TSLP protein to a TSLPR;

f) modulates (*e.g.*, reduces, inhibits, neutralizes) against a TSLP-mediated biological activity, or

a combination of the foregoing.

[00495] In some embodiments, a polypeptide binds to a TSLP (*e.g.*, human)with a K_D of 10 pM or less (*e.g.*, as measured by KinExA).

[00496] In some embodiments, a polypeptide binds (*e.g.*, has a binding affinity for, has a binding specificity for) an AB-loop region and a C-terminal region of helix D of a TSLP.

[00497] In some embodiments, a polypeptide has neutralizing activity against a TSLP (*e.g.*, a full-length human TSLP). In some embodiments, the polypeptides have inhibitory activity against TSLP-mediated signaling.

[00498] In some embodiments, a polypeptide binds to a TSLP protein (*e.g.*, SEQ ID NO:1) with a K_D of about: 10 pM, 8 pM, 5 pM, 4 pM, 3 pM, 2 pM, 1.8 pM, 1.5 pM, 1.2 pM, 1.0 pM, 0.9 pM, 0.8 pM, 0.7 pM, 0.6 pM, 0.5 pM, 0.4 pM, 0.3 pM, 0.2 pM or 0.1 pM, or less; or about: 0.1-10 pM, 0.2-10 pM, 0.2-8 pM, 0.3-8 pM, 0.3-5 pM, 0.4-5 pM, 0.4-4 pM, 0.5-4 pM, 0.5-3 pM, 0.6-3 pM, 0.6-2 pM, 0.7-2 pM, 0.7-1.8 pM, 0.8-1.8 pM, 0.8-1.5 pM, 1.0-1.5 pM or

1.2-1.5 pM. In some embodiments, a polypeptide binds to a TSLP protein (*e.g.*, SEQ ID NO:1) with a K_D of 2 pM or less.

[00499] In some embodiments, a polypeptide binds to a TSLP protein (*e.g.*, SEQ ID NO:1) with a K_D of about: 2.0 pM, 1.9 pM, 1.8 pM, 1.7 pM, 1.6 pM, 1.5 pM, 1.4 pM, 1.3 pM, 1.2 pM, 1.1 pM, 1.0 pM, 0.9 pM, 0.8 pM, 0.7 pM, 0.6 pM, 0.5 pM, 0.4 pM, 0.3 pM, 0.2 pM or 0.1 pM, or less; or about: 0.1-2.0 pM, 0.2-2.0 pM, 0.2-1.9 pM, 0.3-1.9 pM, 0.3-1.8 pM, 0.4-1.8 pM, 0.4-1.7 pM, 0.5-1.7 pM, 0.5-1.6 pM, 0.6-1.6 pM, 0.6-1.5 pM, 0.7-1.5 pM, 0.7-1.4 pM, 0.8-1.4 pM, 0.8-1.3 pM, 0.9-1.3 pM, 1.0-1.3 pM, 1.0-1.2 pM or 1.1-1.2 pM. In some embodiments, a polypeptide binds TSLP with a K_D of about 1 pM or less.

[00500] In some embodiments, a polypeptide binds to AB-loop region and C-terminal region of helix D of a TSLP protein.

[00501] In some embodiments, a polypeptide binds to an epitope in a TSLP protein (*e.g.*, a full-length human TSLP).

[00502] In some embodiments, a polypeptide competes with the Reference Antibody for binding to a TSLP protein (*e.g.*, SEQ ID NO:1). Techniques and assays for assessing competition between antibodies are known in the art.

[00503] In some embodiments, a polypeptide reduces binding of a TSLP protein (*e.g.*, a full-length TSLP protein such as SEQ ID NO:1) to its receptor TSLPR (alone or in a heterodimeric complex with the IL-7Rα). In some embodiments, a polypeptide reduces binding of a TSLP protein to a TSLPR with an IC_{50} of about 500 pM or less, *e.g.*, about: 450 pM, 400 pM, 350 pM, 300 pM, 250 pM, 200 pM, 150 pM, 100 pM, 50 pM, 20 pM, 10 pM, 5 pM, 2 pM, 1 pM, 0.5 pM, 0.2 pM or 0.1 pM or less; or about: 0.1-500 pM, 0.1-450 pM, 0.2-450 pM, 0.2-400 pM, 0.5-400 pM, 0.5-350 pM, 1-350 pM, 1-300 pM, 2-300 pM, 2-250 pM, 5-250 pM, 5-200 pM, 10-200 pM, 10-150 pM, 20-150 pM, 20-100 pM or 50-100 pM.

[00504] In some embodiments, a polypeptide reduces binding of a TSLP protein (*e.g.*, a full-length TSLP protein such as SEQ ID NO:1) to TSLPR by at least about 10%, *e.g.*, by at least about: 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99%. In some embodiments, a polypeptide reduces binding of a TSLP protein (*e.g.*, a full-length TSLP protein such as SEQ ID NO:1) to TSLPR by at least about 30%.

[00505] In some embodiments, a polypeptide modulates (*e.g.*, reduces, inhibits, neutralizes) against a TSLP-mediated biological activity.

[00506] Non-limiting examples of TSLP-mediated activities include TSLPR-binding, TSLP-induced signal transducer and activator of transcription 5 (STAT5) signaling, TSLP-induced STAT3 signaling, TSLP-induced nuclear factor kappa-light-chain-enhancer of activated B cells (NFκB) signaling, TSLP-induced phosphoinositide-3-kinase (PI3K) signaling, TSLP-induced mitogen-activated protein kinase (MAPK) signaling, activation of one or more genes encoding interleukin-4 (IL-4), IL-5, IL-9, IL-13 and mitogen-activated protein kinase kinase 2 (MEK2), and dendritic cell activation. In some embodiments, a TSLP-mediated activity comprises one or more innate immune mechanisms of action and/or one or more adaptive immune mechanisms of action.

[00507] TSLP-mediated activities can be determined, for example, by measuring STAT5 reporter activity, dendritic cell activation, proliferation of cells expressing TSLPR and CCL17 production (*see*, *e.g.*, Verstraete *et al.*, *Structure and antagonism of the receptor complex mediated by human TSLP in allergy and asthma*, Nat Commun. 8:14937 (2017), the contents of which are incorporated herein by reference).

[00508] In some embodiments, a polypeptide neutralizes an activity mediated by a TSLP protein (*e.g.*, a full-length TSLP protein such as SEQ ID NO:1).

[00509] In some embodiments, a polypeptide neutralizes a TSLP-mediated activity with an IC_{50} of about 500 pM or less, *e.g.*, about: 450 pM, 400 pM, 350 pM, 300 pM, 250 pM, 200 pM, 150 pM, 100 pM, 50 pM, 20 pM, 10 pM, 5 pM, 2 pM, 1 pM, 0.5 pM, 0.2 pM or 0.1 pM, or less; or about: 0.1-500 pM, 0.1-450 pM, 0.2-450 pM, 0.2-400 pM, 0.5-400 pM, 0.5-350 pM, 1-350 pM, 1-300 pM, 2-300 pM, 2-250 pM, 5-250 pM, 5-200 pM, 10-200 pM, 10-150 pM, 20-150 pM, 20-100 pM or 50-100 pM.

[00510] In some embodiments, a polypeptide reduces a TSLP-mediated activity by at least about 10%, *e.g.*, by at least about: 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99%. In some embodiments, a polypeptide reduces a TSLP-mediated activity by at least about 30%.

[00511] In some embodiments, a polypeptide reduces a T2 inflammatory response mediated by one or more innate immune mechanisms of action of TSLP.

[00512] Non-limiting examples of T2 inflammatory responses include activation of group 2 innate lymphoid cells (ILC2s); activation, migration and/or local differentiation of eosinophil progenitor cells (EoPs) (*e.g.*, via upregulation of ICAM-1 and/or CD18, and/or via suppression of L-selectin surface expression); increase of eosinophil viability (*e.g.*, via production of IL-6, eosinophil-derived neurotoxin, and chemokines (including C-X-C Motif

Chemokine Ligand 8 (CXCL8), CXCL1 and chemokine (C-C motif) ligand 2 (CCL2)); basophil differentiation; production of T2 cytokines by mast cells; production of chemokine CXCL8 and/or CCL1 by mast cells; and macrophage differentiation (*e.g.*, via enhancing CD80 activation marker expression).

[00513] In some embodiments, a polypeptide reduces a T2 inflammatory response mediated by one or more innate immune mechanisms of action of TSLP by at least about 10%, *e.g.*, by at least about: 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99%. In some embodiments, a polypeptide reduces a T2 inflammatory response mediated by one or more innate immune mechanisms of action of TSLP by at least about 30%.

[00514] In some embodiments, a polypeptide reduces a T2 inflammatory response mediated by one or more adaptive immune mechanisms of action of TSLP.

[00515] Non-limiting examples of said T2 inflammatory responses include increased expression of major histocompatibility complex class II in dendritic cells; increased expression of one or more co-stimulatory molecules (*e.g.*, CD40, CD86, CD54, CD90, CD83 and/or CD-LAMP) in dendritic cells; increased expression of one or more chemokines (*e.g.*, CXCL8, CCL24, CCL17, CCL22 and CCL1) in dendritic cells; increased expression of OX40 ligand (OX40 L); naive T-cell differentiation and/or polarization (*e.g.*, differentiation of naive $CD4^+$ T cells into TNF-α^+IL-10^- T helper (Th) 2 cells); proliferation and/or differentiation of naive $CD4^+$ T cells into Th2 cells or memory T cells; and increased expansion of $CD8^+$ T cells upon TCR stimulation.

[00516] In some embodiments, a polypeptide reduces a T2 inflammatory response mediated by an adaptive immune mechanism of action of TSLP by at least about 10%, *e.g.*, by at least about: 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99%. In some embodiments, a polypeptide reduces a T2 inflammatory response mediated by an adaptive immune mechanism of action of TSLP by at least about 30%.

[00517] In some embodiments, a polypeptide has a lower poly-specificity for a non-specific target (*e.g.*, DNA) than the Reference Antibody. A DNA polyspecificity reagent (PSR) score is a measure of antibody binding to a non-specific DNA target. A DNA PSR score is calculated by dividing an ELISA or DELFIA score by a background score of a secondary antibody alone. A lower DNA PSR score, indicative of a lower poly-specific binding activity, is preferred for a polypeptide of the invention.

[00518] In some embodiments, a polypeptide has a DNA PSR score of no more than about: 1, 2, 3 or 4. In some embodiments, a polypeptide has a DNA PSR score of about: 1, 2, 3 or 4. In some embodiments, a polypeptide has a DNA PSR score of about: 1-4, 1-3, 1-2, 2-4, 2-3 or 3-4. In some embodiments, a polypeptide has a DNA PSR score of about: 2-4, 2-3 or 3-4.

[00519] In some embodiments, a polypeptide has a DNA PSR score that is at least about 10% lower than that of the Reference Antibody, for example, by at least about: 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% lower. In some embodiments, a polypeptide has a DNA PSR score that is at least about 30% lower than that of the Reference Antibody.

[00520] In some embodiments, a polypeptide has a DNA PSR score that is less than about 90% of that of the Reference Antibody, for example, less than about: 85%, 80%, 75%, 70%, 65%, 60%, 55%, 50%, 45%, 40%, 35%, 30%, 25%, 20%, 15%, 10%, 9%, 8%, 7%, 6%, 5%, 4%, 3%, 2% or 1% of that of the Reference Antibody.

[00521] In some embodiments, a polypeptide has a DNA PSR score that is about 1-90% relative to that of the Reference Antibody, for example, about: 2-90%, 2-85%, 3-85%, 3-80%, 4-80%, 4-75%, 5-75%, 5-70%, 6-70%, 6-65%, 7-65%, 7-60%, 8-60%, 8-55%, 9-55%, 9-50%, 10-50%, 10-45%, 15-45%, 15-40%, 20-40%, 20-35%, 25-35% or 25-30%, relative to that of the Reference Antibody.

[00522] In some embodiments, a polypeptide has a weaker self-association than the Reference Antibody, for example, as determined by an affinity-capture self-interaction nanoparticle spectroscopy (AC-SINS) value. The AC-SINS value is the change in maximum absorbance wavelength in the coated-nanoparticle absorption spectra compared to the spectra of the nanoparticle alone. Thus, the greater the change in maximum absorbance wavelength, the more self-interaction of the antibody coated on the nanopartical. Self-association is an unwanted property that correlates with poor viscosity and poor PK properties. Techniques and assays for assessing self-association of proteins are known in the art. *See*, *e.g.*, Patro & Przybycien, Biotechnol Bioeng. 52(2):193-203 (1996), the contents of which are incorporated herein in their entirety.

[00523] In some embodiments, a polypeptide has an AC-SINS value of no more than about: 0, 1, 2, 3, 4, 5, 6 or 7. In some embodiments, a polypeptide has an AC-SINS value of no more than about: 0, 1, 2, 3 or 4. In some embodiments, a polypeptide has an AC-SINS value of about: 0, 1, 2, 3, 4, 5, 6 or 7. In some embodiments, a polypeptide has an AC-SINS

value of about: 0, 1, 2, 3 or 4. In some embodiments, a polypeptide has an AC-SINS value of at least about: 0, 1, 2, 3, 4, 5, 6 or 7. In some embodiments, a polypeptide has an AC-SINS value of about 0-4.

[00524] In some embodiments, a polypeptide has an AC-SINS value that is at least about 10% lower than that of the Reference Antibody, for example, by at least about: 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% lower than that of the Reference Antibody. In some embodiments, a polypeptide has an AC-SINS value that is at least about 30% lower than that of the Reference Antibody.

[00525] In some embodiments, a polypeptide has an AC-SINS value that is less than about 90% of that of the Reference Antibody, for example, less than about: 85%, 80%, 75%, 70%, 65%, 60%, 55%, 50%, 45%, 40%, 35%, 30%, 25%, 20%, 15%, 10%, 9%, 8%, 7%, 6%, 5%, 4%, 3%, 2% or 1% of that of the Reference Antibody.

[00526] In some embodiments, a polypeptide has an AC-SINS value that is about 1-90% relative to that of the Reference Antibody, for example, about: 2-90%, 2-85%, 3-85%, 3-80%, 4-80%, 4-75%, 5-75%, 5-70%, 6-70%, 6-65%, 7-65%, 7-60%, 8-60%, 8-55%, 9-55%, 9-50%, 10-50%, 10-45%, 15-45%, 15-40%, 20-40%, 20-35%, 25-35% or 25-30%, relative to that of the Reference Antibody.

Fusion Proteins

[00527] The disclosure also provides, among other things, a fusion protein comprising one or more of the polypeptides disclosed herein.

[00528] The term “fusion protein” refers to a synthetic, semi-synthetic or recombinant single protein molecule. A fusion protein can comprise all or a portion of two or more different proteins and/or polypeptides that are attached by covalent bonds (*e.g.*, peptide bonds).

[00529] Fusion proteins of the disclosure can be produced recombinantly or synthetically, using routine methods and reagents that are well known in the art. For example, a fusion protein of the disclosure can be produced recombinantly in a suitable host cell (*e.g.*, bacteria) according to methods known in the art. *See, e.g.*, *Current Protocols in Molecular Biology*, Second Edition, Ausubel *et al.* eds., John Wiley & Sons, 1992; and *Molecular Cloning: a Laboratory Manual*, 2nd edition, Sambrook *et al.*, 1989, Cold Spring Harbor Laboratory Press. For example, a nucleic acid molecule comprising a nucleotide sequence encoding a

fusion protein described herein can be introduced and expressed in suitable host cell (*e.g.*, *E. coli*), and the expressed fusion protein can be isolated/purified from the host cell (*e.g.*, in inclusion bodies) using routine methods and readily available reagents. For example, DNA fragments coding for different protein sequences (*e.g.*, a light-responsive domain, a heterologous peptide component) can be ligated together in-frame in accordance with conventional techniques. In another embodiment, the fusion gene can be synthesized by conventional techniques including automated DNA synthesizers. Alternatively, PCR amplification of nucleic acid fragments can be carried out using anchor primers that give rise to complementary overhangs between two consecutive nucleic acid fragments that can subsequently be annealed and re-amplified to generate a chimeric nucleic acid sequence (see Ausubel *et al.*, Current Protocols in Molecular Biology, 1992).

Nucleic Acids, Vectors, Host Cells

[00530] The disclosure also provides, among other things, one or more polynucleotides (*e.g.*, DNA, RNA, or analogs of either, *e.g.*, optionally including one or more modified nucleotides; a polynucleotide may be linear or circular, *e.g.*, a linear or circular RNA) encoding any one of the polypeptides or fusion proteins described herein. In some embodiments, a polypeptide or fusion protein disclosed herein is encoded by a single polynucleotide. In some embodiments, a polypeptide or fusion protein disclosed herein is encoded by multiple polynucleotides.

[00531] In some embodiments, a polynucleotide comprises a nucleotide sequence that is codon-optimized for a chosen host cell.

[00532] The disclosure also provides, among other things, a vector (*e.g.*, an expression vector, including a viral-delivery vector) comprising any one or more of the polynucleotides disclosed herein.

[00533] The term “expression vector” refers to a replicable nucleic acid from which one or more proteins can be expressed when the expression vector is transformed into a suitable expression host cell.

[00534] In some embodiments, a vector (*e.g.*, expression vector) further comprises an expression control polynucleotide sequence operably linked to the polynucleotide, a polynucleotide sequence encoding a selectable marker, or both. In some embodiments, an expression control polynucleotide sequence comprises a promoter sequence, an enhancer sequence, or both. In some embodiments, an expression control polynucleotide sequence

comprises an inducible promoter sequence. The term "promoter" refers to a region of DNA to which RNA polymerase binds and initiates the transcription of a gene. The term "operably linked" means that the nucleic acid is positioned in the recombinant polynucleotide, *e.g.*, vector, in such a way that enables expression of the nucleic acid under control of the element (*e.g.*, promoter) to which it is linked. The term "selectable marker element" is an element that confers a trait suitable for artificial selection. Selectable marker elements can be negative or positive selection markers.

[00535] The disclosure also provides, among other things, an expression host cell comprising any one or more of the polynucleotides or expression vectors disclosed herein.

[00536] The term "expression host cell" refers to a cell useful for receiving, maintaining, reproducing and/or amplifying a vector. Non-limiting examples of expression host cells include mammalian cells such as hybridoma cells, Chinese hamster ovary (CHO) cells, COS cells, human embryonic kidney (HEK), yeast cells such as *Pichia pastoris* cells, or bacterial cells such as *E. coli*, including DH5α, etc.

Compositions

[00537] The disclosure also provides, among other things, a composition comprising any one of the polypeptides or fusion proteins disclosed herein. In some embodiments, a composition is a pharmaceutical composition.

[00538] In some embodiments, a composition (*e.g.*, pharmaceutical composition) further comprises pharmaceutically acceptable carriers, excipients, stabilizers, diluents or tonifiers (Remington's Pharmaceutical Sciences 16th edition, Osol, A. Ed. (1980)). Suitable pharmaceutically acceptable carriers, excipients, or stabilizers are nontoxic to recipients at the dosages and concentrations employed. Non-limiting examples of pharmaceutically acceptable carriers, excipients, stabilizers, diluents or tonifiers include buffers (*e.g.*, phosphate, citrate, histidine), antioxidants (*e.g.*, ascorbic acid or methionine), preservatives, proteins (*e.g.*, serum albumin, gelatin or immunoglobulins); hydrophilic polymers, amino acids, carbohydrates (*e.g.*, monosaccharides, disaccharides, glucose, mannose or dextrins); chelating agents (*e.g.*, EDTA), sugars (*e.g.*, sucrose, mannitol, trehalose or sorbitol), salt-forming counter-ions (*e.g.*, sodium), metal complexes (*e.g.*, Zn-protein complexes); non-ionic surfactants (*e.g.*, Tween), PLURONICS™ and polyethylene glycol (PEG).

[00539] In some embodiments, a composition (*e.g.*, a pharmaceutical composition) is formulated for a suitable administration schedule and route. Non-limiting examples of

administration routes include oral, rectal, mucosal, intravenous, intramuscular, subcutaneous, and topical, etc. In some embodiments, a composition (*e.g.*, a pharmaceutical composition) is stored in the form of an aqueous solution or a dried formulation (*e.g.*, lyophilized).

[00540] In some embodiments, a composition is formulated to be administered by infusion (*e.g.*, intravenous infusion). In other embodiments a composition is formulated for subcutaneous administration.

[00541] In some embodiments, a composition is provided in a dosage form, *e.g.*, in a prefilled syringe or autoinjector.

[00542] In some embodiments, a pharmaceutical composition comprises from about 50 mg to about 300 mg of a polypeptide or fusion protein disclosed herein, for example, about: 50 mg, 60 mg, 70 mg, 80 mg, 90 mg, 100 mg, 120 mg, 140 mg, 150 mg, 160 mg, 180 mg, 200 mg, 220 mg, 240 mg, 250 mg, 260 mg, 280 mg, or 300 mg. In some embodiments, a pharmaceutical composition comprises from about 60 mg to about 300 mg of a polypeptide or fusion protein disclosed herein, for example, about: 60-280 mg, 80-280 mg, 80-260 mg, 100-260 mg, 100-250 mg, 120-250 mg, 120-240 mg, 140-240 mg, 140-220 mg, 150-250 mg, 150-200 mg, 160-220 mg, 160-200 mg, or 180-200 mg.

[00543] In some embodiments, a pharmaceutical composition comprises from about 50 mg/ml to about 200 mg/ml of a polypeptide or fusion protein disclosed herein, for example, about: 50 mg/ml, 60 mg/ml, 70 mg/ml, 80 mg/ml, 90 mg/ml, 100 mg/ml, 120 mg/ml, 140 mg/ml, 150 mg/ml, 160 mg/ml, 180 mg/ml, or 200 mg/ml of a polypeptide or fusion protein disclosed herein. In some embodiments, a pharmaceutical composition comprises from about 60 mg/ml to about 200 mg/ml of a polypeptide or fusion protein disclosed herein, for example, about: 60-180 mg/ml, 80-180 mg/ml, 80-160 mg/ml, 100-160 mg/ml, 100-150 mg/ml, 120-150 mg/ml or 120-140 mg/ml.

[00544] In some embodyments, a composition is formulated to be administered with a second therapeutic agent as a combination therapy. In some embodiments, a second therapeutic agent comprises a corticosteroid, a beta-agonist (*e.g.*, a long-acting beta-agonist), a muscarinic antagonist, an anti-inflammatory agent, an IL-4 and/or IL-13 antagonist (*e.g.*, an antibody or antigen-binding fragment thereof targeting IL-13, IL-4 or IL-4R), or any combination thereof. In some embodiments, a second therapeutic agent comprises a corticosteroid (*e.g.*, an inhaled corticosteroid). Non-limiting examples of inhaled corticosteroids include beclomethasone dipropionate, budesonide, ciclesonide, fluticasone furoate, fluticasone propionate, mometasone, and mometasone furoate. In some

embodiments, a combination therapy comprises a beta-agonist (*e.g.*, a long-acting beta-agonist). Non-limiting examples of long-acting beta-agonists include albuterol sulfate, formoterol fumarate, salmeterol xinafoate, arformoterol tartrate, olodaterol, and combinations thereof. In some embodiments, a combination therapy comprises a muscarinic antagonist. In some embodiments, a combination therapy comprises an IL-4 and/or IL-13 antagonist (*e.g.*, for the treatment of allergic and/or asthmatic conditions). Non-limiting examples of IL-4 and/or IL-13 antagonists include Pitrakinra, anti-IL-13 antibodies or antigen-binding fragments thereof, anti-IL-4 antibodies or antigen-binding fragments thereof, and anti-IL-4R antibodies or antigen-binding fragments thereof. Non-limiting examples of antibodies or antigen-binding fragments thereof include anti-IL-13 antibodies or antigen-binding fragments thereof (*e.g.*, Lebrikizumab, Tralokinumab, and Anrukinzumab), anti-IL-4 antibodies or antigen-binding fragments thereof (*e.g.*, Pascolizumab (SB 240683)), anti-IL-4R antibodies or antigen-binding fragments thereof (*e.g.*, Dupilumab).

[00545] In some embodyments, a composition is formulated to be administered with an inhaled corticosteroid (ICS), a long-acting β2-agonist (LABA), a long-acting muscarinic antagonist (LAMA), or any combination thereof.

[00546] In some embodiments, a composition (*e.g.*, a pharmaceutical composition) comprises a polypeptide comprising:

a) a V_H comprising a HCDR1, a HCDR2 and a HCDR3 amino acid sequences of SEQ ID NO:5; and

b) a V_L comprising a LCDR1, a LCDR2 and a LCDR3 amino acid sequences of SEQ ID NO:21 (AB-2).

[00547] In some embodiments, a composition (*e.g.*, a pharmaceutical composition) comprises a polypeptide comprising:

a) a V_H comprising the amino acid sequence of SEQ ID NO:5, and

b) a V_L comprising the amino acid sequence of SEQ ID NO:21 (AB-2).

[00548] In some embodiments, a composition (*e.g.*, a pharmaceutical composition) comprises a polypeptide comprising:

a) a heavy chain comprising the amino acid sequence of SEQ ID NO:106; and

b) a light chain comprising the amino acid sequence of SEQ ID NO:120 (AB-2b).

[00549] In some embodiments, a composition (*e.g.*, a pharmaceutical composition) comprises a polypeptide comprising:

a) a heavy chain comprising the amino acid sequence of SEQ ID NO:92; and

b) a light chain comprising the amino acid sequence of SEQ ID NO:120 (AB-2a).

Methods of Use

[00550] The disclosure also provides, among other things, a method of neutralizing a TSLP protein (*e.g.*, a full-length TSLP protein) in a subject, comprising administering to the subject an effective amount of a pharmaceutical composition comprising a pharmaceutically acceptable carrier and, wherein as an active ingredient, any one of the polypeptides or fusion proteins disclosed herein.

[00551] In some embodiments, neutralizing a TSLP protein in a subject comprises administering to the subject an effective amount of a pharmaceutical composition comprising a pharmaceutically acceptable carrier and a polypeptide comprising:

a) a V_H comprising a HCDR1, a HCDR2 and a HCDR3 amino acid sequences of SEQ ID NO:5; and

b) a V_L comprising a LCDR1, a LCDR2 and a LCDR3 amino acid sequences of SEQ ID NO:21 (AB-2).

[00552] In some embodiments, neutralizing a TSLP protein in a subject comprises administering to the subject an effective amount of a pharmaceutical composition comprising a pharmaceutically acceptable carrier and a polypeptide comprising:

a) a V_H comprising the amino acid sequence of SEQ ID NO:5, and

b) a V_L comprising the amino acid sequence of SEQ ID NO:21 (AB-2).

[00553] In some embodiments, neutralizing a TSLP protein in a subject comprises administering to the subject an effective amount of a pharmaceutical composition comprising a pharmaceutically acceptable carrier and a polypeptide comprising:

a) a heavy chain comprising the amino acid sequence of SEQ ID NO:106; and

b) a light chain comprising the amino acid sequence of SEQ ID NO:120 (AB-2b).

[00554] In some embodiments, neutralizing a TSLP protein in a subject comprises administering to the subject an effective amount of a pharmaceutical composition comprising a pharmaceutically acceptable carrier and a polypeptide comprising:

a) a heavy chain comprising the amino acid sequence of SEQ ID NO:92; and

b) a light chain comprising the amino acid sequence of SEQ ID NO:120 (AB-2a).

[00555] In some embodiments, a subject is a mammal. In some embodiments, a subject is a mammal selected from the group consisting of a dog, a cat, a mouse, a rat, a hamster, a guinea pig, a horse, a pig, a sheep, a cow, a chimpanzee, a macaque, a cynomolgus, and a human. In some embodiments, a subject is a primate. In some embodiments, a subject is a human.

[00556] In some embodiments, a subject is 18 years of age or older, for example, about: 20, 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75 or 80 years of age or older. In some embodiments, a subject is 65 years of age or older. In some embodiments, a subject is about: 18-80, 20-80, 20-75, 25-75, 25-70, 30-70, 30-65, 35-65, 35-60, 40-60, 40-55, 45-55 years of age. In some embodiments, a subject is about 18-65 years of age.

[00557] In some embodiments, a subject is about 18 years of age or younger. In some embodiments, a subject is about: 16, 14, 12, 10, 8, 6, 4 or 2 years of age or older. In some embodiments, a subject is two years of age or older, for example, about: 2-18, 3-18, 3-16, 4-16, 4-14, 5-14, 5-12, 6-12, 6-10 or 8-10 years of age.

[00558] In some embodiments, a subject is a pediatric patient. In some embodiments, a subject is a pediatric patient who is 12 years of age or older.

[00559] In some embodiments, a subject has a blood eosinophil count of less than 150 cells/μL. In some embodiments, a subject has a blood eosinophil count of 150 to less than 300 cells/μL. In some embodiments, a subject has a blood eosinophil count of 300 cells/μL or above.

[00560] In some embodiments, a subject has, or is suspected of having, a TSLP-associated disease or condition (*e.g.*, a disease or condition associated with dysregulated TSLP expression such as overexpression of TSLP). In some embodiments, a subject has a TSLP-associated disease or condition. In some embodiments, a subject has been diagnosed with a TSLP-associated disease or condition. In other embodiments, a subject is at risk of developing a TSLP-associated disease or condition.

[00561] Non-limiting examples of TSLP-associated diseases and/or conditions (*e.g.*, diseases and/or conditions associated with dysregulated TSLP expression) include asthma, AD, allergic conjunctivitis, chronic obstructive pulmonary disease (COPD), chronic spontaneous urticaria (CSU), nasal polyposis, rheumatoid arthritis (RA), rhinosinusitis (RS) (*e.g.*, allergic rhinosinusitis, severe chronic rhinosinusitis (*e.g.*, severe chronic rhinosinusitis with nasal polyposis)), cancer and food-hypersensitivity reactions. Non-limiting examples of TSLP-associated cancer (*e.g.*, a cancer associated with dysregulated TSLP expression)

include lymphoma, acute lymphocytic leukemia (ALL), multiple sclerosis, and solid tumors (*e.g.*, cervical, ovarian, pancreatic, gastric cancer, or colorectal cancer (*e.g.*, colon cancer, rectal cancer, and variants thereof)).

[00562] In some embodiments, a subject has an inflammatory disorder (*e.g.*, an allergic inflammatory disorder). In some embodiments, a subject has a pulmonary inflammatory disease or condition. In some embodiments, a subject has asthma (*e.g.*, severe and/or uncontrolled asthma). In some embodiments, a subject has mild, moderate, moderate-to-severe, or severe asthma. In some embodiments, a subject has uncontrolled asthma (*e.g.*, uncontrolled moderate asthma, uncontrolled moderate-to-severe asthma, or uncontrolled severe asthma), allergic asthma (*e.g.*, mild allergic asthma, moderate allergic asthma, or severe allergic asthma), oral corticosteroid dependent asthma, or any combination thereof.

[00563] In some embodiments, a subject has been previously treated with one or more therapeutic agents prior to being administered a composition (*e.g.*, a polypeptide, or a pharmaceutical composition disclosed herein).

[00564] In some embodiments, a subject previously received a therapeutic or prophylactic agent. For example, a COPD patient may have received an inhaled corticosteroid (ICS), a long-acting β2-agonist (LABA), a long-acting muscarinic antagonist (LAMA), or any combination thereof.

[00565] The disclosure also provides, among other things, a method of treating a TSLP-associated disease or condition in a subject, comprising administering to the subject an effective amount of a pharmaceutical composition comprising a pharmaceutically acceptable carrier and, wherein as an active ingredient, any one of the polypeptides or fusion proteins disclosed herein.

[00566] In some embodiments, treating a TSLP-associated disease or condition in a subject comprises administering to the subject an effective amount of a pharmaceutical composition comprising a pharmaceutically acceptable carrier and a polypeptide comprising:

a) a V_H comprising a HCDR1, a HCDR2 and a HCDR3 amino acid sequences of SEQ ID NO:5; and

b) a V_L comprising a LCDR1, a LCDR2 and a LCDR3 amino acid sequences of SEQ ID NO:21 (AB-2).

[00567] In some embodiments, treating a TSLP-associated disease or condition in a subject comprises administering to the subject an effective amount of a pharmaceutical composition comprising a pharmaceutically acceptable carrier and a polypeptide comprising:

a) a V_H comprising the amino acid sequence of SEQ ID NO:5, and

b) a V_L comprising the amino acid sequence of SEQ ID NO:21 (AB-2).

[00568] In some embodiments, treating a TSLP-associated disease or condition in a subject comprises administering to the subject an effective amount of a pharmaceutical composition comprising a pharmaceutically acceptable carrier and a polypeptide comprising:

a) a heavy chain comprising the amino acid sequence of SEQ ID NO:106; and

b) a light chain comprising the amino acid sequence of SEQ ID NO:120 (AB-2b).

[00569] In some embodiments, treating a TSLP-associated disease or condition in a subject comprises administering to the subject an effective amount of a pharmaceutical composition comprising a pharmaceutically acceptable carrier and a polypeptide comprising:

a) a heavy chain comprising the amino acid sequence of SEQ ID NO:92; and

b) a light chain comprising the amino acid sequence of SEQ ID NO:120 (AB-2a).

[00570] In some embodiments, treating a TSLP-associated disease or condition comprises treating asthma (*e.g.*, severe and/or uncontrolled asthma). In some embodiments, treating a TSLP-associated disease or condition comprises treating moderate-to-severe asthma. In some embodiments, treating a TSLP-associated disease or condition comprises treating severe asthma. In some embodiments, treating a TSLP-associated disease or condition comprises treating uncontrolled asthma. In some embodiments, treating a TSLP-associated disease or condition comprises treating severe, uncontrolled asthma. In some embodiments, treating a TSLP-associated disease or condition comprises treating AD.

[00571] In some embodiments, treating a TSLP-associated disease or condition is a prophylactic therapy.

[00572] In some embodiments, an effective amount is sufficient to prevent the subject of developing a TSLP-associated disease or condition (*e.g.*, a disease or condition associated with dysregulated TSLP expression).

[00573] In some embodiments, an effective amount is sufficient to reduce TSLPR occupancy in a subject. In some embodiments, an effective amount is sufficient to reduce TSLPR occupancy by at least about 10%, *e.g.*, by at least about: 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99%. In some embodiments, an effective amount is sufficient to reduce TSLPR occupancy by about 10-99%, *e.g.*, by about: 10-98%, 15-98%, 15-97%, 20-97%, 20-

96%, 25-96%, 25-95%, 30-95%, 30-94%, 35-94%, 35-93%, 40-93%, 40-92%, 45-92%, 45-91%, 50-91%, 50-90%, 55-90%, 55-85%, 60-85%, 60-80%, 65-80%, 65-75%, or 70-75%.

[00574] In some embodiments, an effective amount is sufficient to reduce a TSLP receptor complex in the subject. In some embodiments, an effective amount is sufficient to reduce a TSLP receptor complex by at least about 10%, *e.g.*, by at least about: 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99%. In some embodiments, an effective amount is sufficient to reduce a TSLP receptor complex by about 10-99%, *e.g.*, by about: 10-98%, 15-98%, 15-97%, 20-97%, 20-96%, 25-96%, 25-95%, 30-95%, 30-94%, 35-94%, 35-93%, 40-93%, 40-92%, 45-92%, 45-91%, 50-91%, 50-90%, 55-90%, 55-85%, 60-85%, 60-80%, 65-80%, 65-75%, or 70-75%.

[00575] In some embodiments, an effective amount is sufficient to reduce an activity of a TSLP protein in a subject. In some embodiments, an effective amount is sufficient to reduce an activity of a TSLP protein by at least about 10%, *e.g.*, by at least about: 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99%. In some embodiments, an effective amount is sufficient to reduce an activity of a TSLP protein by about 10-99%, *e.g.*, by about: 10-98%, 15-98%, 15-97%, 20-97%, 20-96%, 25-96%, 25-95%, 30-95%, 30-94%, 35-94%, 35-93%, 40-93%, 40-92%, 45-92%, 45-91%, 50-91%, 50-90%, 55-90%, 55-85%, 60-85%, 60-80%, 65-80%, 65-75%, or 70-75%.

[00576] In some embodiments, an effective amount is sufficient to reduce airway inflammation (*e.g.*, the number and/or density of one or more types of airway submucosal inflammatory cells) in a subject. In some embodiments, an effective amount is sufficient to reduce airway inflammation by at least about 10%, *e.g.*, by at least about: 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99%. In some embodiments, an effective amount is sufficient to reduce airway inflammation by about 10-99%, *e.g.*, by about: 10-98%, 15-98%, 15-97%, 20-97%, 20-96%, 25-96%, 25-95%, 30-95%, 30-94%, 35-94%, 35-93%, 40-93%, 40-92%, 45-92%, 45-91%, 50-91%, 50-90%, 55-90%, 55-85%, 60-85%, 60-80%, 65-80%, 65-75%, or 70-75%.

[00577] In some embodiments, an effective amount is sufficient to reduce airway remodeling (*e.g.*, reticular basement membrane thickening, airway epithelial integrity) in a subject. In some embodiments, an effective amount is sufficient to reduce airway remodeling

by at least about 10%, *e.g.*, by at least about: 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99%. In some embodiments, an effective amount is sufficient to reduce airway remodeling by about 10-99%, *e.g.*, by about: 10-98%, 15-98%, 15-97%, 20-97%, 20-96%, 25-96%, 25-95%, 30-95%, 30-94%, 35-94%, 35-93%, 40-93%, 40-92%, 45-92%, 45-91%, 50-91%, 50-90%, 55-90%, 55-85%, 60-85%, 60-80%, 65-80%, 65-75%, or 70-75%.

[00578] In some embodiments, an effective amount is sufficient to treatment nasal polyps (*e.g.*, reducing the size and/or number of nasal polyps) in a subject. In some embodiments, an effective amount is sufficient to reduce the size of nasal polyps by at least about 10%, *e.g.*, by at least about: 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99%. In some embodiments, an effective amount is sufficient to reduce the size of nasal polyps by about 10-99%, *e.g.*, by about: 10-98%, 15-98%, 15-97%, 20-97%, 20-96%, 25-96%, 25-95%, 30-95%, 30-94%, 35-94%, 35-93%, 40-93%, 40-92%, 45-92%, 45-91%, 50-91%, 50-90%, 55-90%, 55-85%, 60-85%, 60-80%, 65-80%, 65-75%, or 70-75%. In some embodiments, an effective amount is sufficient to reduce the number of nasal polyps by at least about 10%, *e.g.*, by at least about: 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99%. In some embodiments, an effective amount is sufficient to reduce the number of nasal polyps by about 10-99%, *e.g.*, by about: 10-98%, 15-98%, 15-97%, 20-97%, 20-96%, 25-96%, 25-95%, 30-95%, 30-94%, 35-94%, 35-93%, 40-93%, 40-92%, 45-92%, 45-91%, 50-91%, 50-90%, 55-90%, 55-85%, 60-85%, 60-80%, 65-80%, 65-75%, or 70-75%.

[00579] A therapeutic agent disclosed herein can be administered via a variety of routes of administration, including, for example, topical, transdermal, parenteral (*e.g.*, intra-arterial, intravenous, intramuscular, subcutaneous injection, intradermal injection), intravenous infusion and inhalation (*e.g.*, intrabronchial, intranasal or oral inhalation, intranasal drops) routes of administration, depending on the compound and the particular disease to be treated.

[00580] Administration can be local or systemic as indicated. A preferred mode of administration can vary depending on a particular compound chosen.

[00581] In some embodiments, a composition (*e.g.*, a polypeptide or pharmaceutical composition) is administered to a subject as a monotherapy.

[00582] In some embodiments, a composition (*e.g.*, a polypeptide or pharmaceutical composition) is administered to a subject in combination with one or more additional

therapeutic agents (*e.g.*, concurrently, or sequentially with one or more additional therapeutic agents) or prophylactic agents (*e.g.*, concurrently, or sequentially with one or more prophylactic agents).

[00583] In some embodiments, treating a TSLP-associated disease or condition further comprises administering a therapeutically effective amount of one or more additional therapeutic agents to a subject at the same time as, or following administration of a composition (*e.g.*, a polypeptide or pharmaceutical composition). In some embodiments, treating a TSLP-associated disease or condition further comprises administering a therapeutically effective amount of one or more prophylactic agents to a subject before, at the same time as, or following administration of a composition (*e.g.*, a polypeptide or a pharmaceutical composition).

[00584] Administration of two or more therapeutic agents encompasses co-administration of the therapeutic agents in a substantially simultaneous manner, such as in a pharmaceutical combination. Alternatively, such administration encompasses co-administration in multiple containers, or separate containers (*e.g.*, capsules, powders, and liquids) for each therapeutic agent. Such administration also encompasses use of each type of therapeutic agent in a sequential manner, either at approximately the same time or at different times. A composition and a second therapeutic agent can be administered via the same administration route or via different administration routes.

[00585] The disclosure also provides, among other things, a method of reducing (*e.g.*, inhibiting) binding of TSLP to TSLPR in a cell, comprising contacting the cell an effective amount of any one or more of the polypeptides or fusion proteins disclosed herein.

[00586] In some embodiments, reducing (*e.g.*, inhibiting) binding of TSLP to TSLPR in a cell comprises contacting the cell an effective amount of a polypeptide comprising:

a) a V_H comprising a HCDR1, a HCDR2 and a HCDR3 amino acid sequences of SEQ ID NO:5; and

b) a V_L comprising a LCDR1, a LCDR2 and a LCDR3 amino acid sequences of SEQ ID NO:21 (AB-2).

[00587] In some embodiments, reducing (*e.g.*, inhibiting) binding of TSLP to TSLPR in a cell comprises contacting the cell an effective amount of a polypeptide comprising:

a) a V_H comprising the amino acid sequence of SEQ ID NO:5, and

b) a V_L comprising the amino acid sequence of SEQ ID NO:21 (AB-2).

[00588] In some embodiments, reducing (*e.g.*, inhibiting) binding of TSLP to TSLPR in a cell comprises contacting the cell an effective amount of a polypeptide comprising:

a) a heavy chain comprising the amino acid sequence of SEQ ID NO:106; and

b) a light chain comprising the amino acid sequence of SEQ ID NO:120 (AB-2b).

[00589] In some embodiments, reducing (*e.g.*, inhibiting) binding of TSLP to TSLPR in a cell comprises contacting the cell an effective amount of a polypeptide comprising:

a) a heavy chain comprising the amino acid sequence of SEQ ID NO:92; and

b) a light chain comprising the amino acid sequence of SEQ ID NO:120 (AB-2a).

[00590] The disclosure also provides, among other things, a method of inhibiting TSLP-induced signaling in a cell, comprising contacting the cell an effective amount of any one of the polypeptides or fusion proteins disclosed herein.

[00591] In some embodiments, inhibiting TSLP-induced signaling in a cell comprises contacting the cell an effective amount of a polypeptide comprising:

a) a V_H comprising a HCDR1, a HCDR2 and a HCDR3 amino acid sequences of SEQ ID NO:5; and

b) a V_L comprising a LCDR1, a LCDR2 and a LCDR3 amino acid sequences of SEQ ID NO:21 (AB-2).

[00592] In some embodiments, inhibiting TSLP-induced signaling in a cell comprises contacting the cell an effective amount of a polypeptide comprising:

a) a V_H comprising the amino acid sequence of SEQ ID NO:5, and

b) a V_L comprising the amino acid sequence of SEQ ID NO:21 (AB-2).

[00593] In some embodiments, inhibiting TSLP-induced signaling in a cell comprises contacting the cell an effective amount of a polypeptide comprising:

a) a heavy chain comprising the amino acid sequence of SEQ ID NO:106; and

b) a light chain comprising the amino acid sequence of SEQ ID NO:120 (AB-2b).

[00594] In some embodiments, inhibiting TSLP-induced signaling in a cell comprises contacting the cell an effective amount of a polypeptide comprising:

a) a heavy chain comprising the amino acid sequence of SEQ ID NO:92; and

b) a light chain comprising the amino acid sequence of SEQ ID NO:120 (AB-2a).

[00595] In some embodiments, a cell is selected from the group consisting of an airway smooth muscle cell (ASMC), a basophil, a dendritic cell, an eosinophil, a Group 2 innate

lymphoid cell (ILC2), a hematopoietic progenitor cell, a lymphocyte, a macrophage, a mast cell, and a monocyte.

AB-2

[00596] The disclosure also provides, among other things, a polypeptide comprising:

a) a HCDR 1 comprising the amino acid sequence of SEQ ID NO:31, a HCDR2 comprising the amino acid sequence of SEQ ID NO:35, and a HCDR3 comprising the amino acid sequence of SEQ ID NO:50; and

b) a LCDR 1 comprising the amino acid sequence of SEQ ID NO:60, a LCDR2 comprising the amino acid sequence of SEQ ID NO:67, and a LCDR3 comprising the amino acid sequence of SEQ ID NO:71,

wherein the polypeptide is an antibody or an antigen-binding fragment thereof.

[00597] The disclosure also provides, among other things, a polypeptide comprising:

a) a HCDR 1 consisting of the amino acid sequence of SEQ ID NO:31, a HCDR2 consisting of the amino acid sequence of SEQ ID NO:35, and a HCDR3 consisting of the amino acid sequence of SEQ ID NO:50; and

b) a LCDR 1 consisting of the amino acid sequence of SEQ ID NO:60, a LCDR2 consisting of the amino acid sequence of SEQ ID NO:67, and a LCDR3 consisting of the amino acid sequence of SEQ ID NO:71,

wherein the polypeptide is an antibody or an antigen-binding fragment thereof.

[00598] AB-2 CDR amino acid sequences as determined by Kabat numbering are:

[00599] HCDR1: TYGMH (SEQ ID NO:130)

[00600] HCDR2: VVWYDGSYTHYADSVKG (SEQ ID NO:131)

[00601] HCDR3: SPQWEEIFEAMDI (SEQ ID NO:132)

[00602] LCDR1: GGNNIGSKSVH (SEQ ID NO:133)

[00603] LCDR2: DDSDRPS (SEQ ID NO:134)

[00604] LCDR3: QIWDSSSSLVV (SEQ ID NO:71)

[00605] The disclosure also provides, among other things, a polypeptide comprising:

a) a HCDR 1 comprising the amino acid sequence of SEQ ID NO:130, a HCDR2 comprising the amino acid sequence of SEQ ID NO:131, and a HCDR3 comprising the amino acid sequence of SEQ ID NO:132; and

b) a LCDR 1 comprising the amino acid sequence of SEQ ID NO:133, a LCDR2 comprising the amino acid sequence of SEQ ID NO:134, and a LCDR3 comprising the amino acid sequence of SEQ ID NO:71,

wherein the polypeptide is an antibody or an antigen-binding fragment thereof.

[00606] The disclosure also provides, among other things, a polypeptide comprising:

a) a HCDR 1 consisting of the amino acid sequence of SEQ ID NO:130, a HCDR2 consisting of the amino acid sequence of SEQ ID NO:131, and a HCDR3 consisting of the amino acid sequence of SEQ ID NO:132; and

b) a LCDR 1 consisting of the amino acid sequence of SEQ ID NO:133, a LCDR2 consisting of the amino acid sequence of SEQ ID NO:134, and a LCDR3 consisting of the amino acid sequence of SEQ ID NO:71,

wherein the polypeptide is an antibody or an antigen-binding fragment thereof.

[00607] AB-2 CDR amino acid sequences as determined by Chothia numbering are:

[00608] HCDR1: GFTFRTY (SEQ ID NO:135)

[00609] HCDR2: WYDGSY (SEQ ID NO:136)

[00610] HCDR3: SPQWEEIFEAMDI (SEQ ID NO:132)

[00611] LCDR1: GGNNIGSKSVH (SEQ ID NO:133)

[00612] LCDR2: DDSDRPS (SEQ ID NO:134)

[00613] LCDR3: QIWDSSSSLVV (SEQ ID NO:71)

[00614] The disclosure also provides, among other things, a polypeptide comprising:

a) a HCDR 1 comprising the amino acid sequence of SEQ ID NO:135, a HCDR2 comprising the amino acid sequence of SEQ ID NO:136, and a HCDR3 comprising the amino acid sequence of SEQ ID NO:132; and

b) a LCDR 1 comprising the amino acid sequence of SEQ ID NO:133, a LCDR2 comprising the amino acid sequence of SEQ ID NO:134, and a LCDR3 comprising the amino acid sequence of SEQ ID NO:71,

wherein the polypeptide is an antibody or an antigen-binding fragment thereof.

[00615] The disclosure also provides, among other things, a polypeptide comprising:

a) a HCDR 1 consisting of the amino acid sequence of SEQ ID NO:135, a HCDR2 consisting of the amino acid sequence of SEQ ID NO:136, and a HCDR3 consisting of the amino acid sequence of SEQ ID NO:132; and

b) a LCDR 1 consisting of the amino acid sequence of SEQ ID NO:133, a LCDR2 consisting of the amino acid sequence of SEQ ID NO:134, and a LCDR3 consisting of the amino acid sequence of SEQ ID NO:71,

wherein the polypeptide is an antibody or an antigen-binding fragment thereof.

[00616] In some embodiments, a polypeptide comprises:

a) a V_H that is humanized, contains human framework regions, or a combination thereof;

b) a V_L that is humanized, contains human framework regions, or a combination thereof,

or both a) and b).

[00617] In some embodiments, a polypeptide comprises:

a) a V_H comprising the amino acid sequence of SEQ ID NO:5;

b) a V_L comprising the amino acid sequence of SEQ ID NO:21,

or both a) and b).

[00618] In some embodiments, an antigen-binding fragment comprises a single-chain fragment variable (scFv), a variable heavy domain of heavy chain (V_{HH}), a fragment antigen-binding (Fab), a Fab' or a $F(ab')_2$.

[00619] In some embodiments, a polypeptide comprises:

a) an antibody heavy chain constant domain;

b) an antibody light chain constant domain,

or both a) and b).

[00620] In some embodiments, an antibody heavy chain constant domain is an IgG1, IgG2, IgG3 or IgG4 constant domain. In some embodiments, an antibody heavy chain constant domain is an IgG1 or IgG2 constant domain. In some embodiments, an antibody heavy chain constant domain comprises one or more mutations which increase serum half-life of the antibody or antigen-binding fragment thereof in humans. In some embodiments, an antibody heavy chain constant domain comprises, relative to a wild-type human IgG constant domain, amino acid substitutions with tyrosine, threonine and glutamic acid at amino acid residues 252, 254 and 256, respectively, wherein the amino acid residues are numbered according to the EU index as in Kabat.

[00621] In some embodiments, a polypeptide comprises:

a) an antibody heavy chain (HC) comprising the amino acid sequence of SEQ ID NO:92;

b) an antibody light chain (LC) comprising the amino acid sequence of SEQ ID NO:120,

or both a) and b).

[00622] In some embodiments, a polypeptide comprises:

a) an antibody heavy chain (HC) comprising the amino acid sequence of SEQ ID NO:106;

b) an antibody light chain (LC) comprising the amino acid sequence of SEQ ID NO:120,

or both a) and b).

[00623] In some embodiments, a polypeptide specifically binds a TSLP.

[00624] The disclosure also provides, among other things, a composition comprising one or more polypeptides disclosed in the section entitled "AB-2", and one or more pharmaceutical excipients, diluents, or carriers.

[00625] In some embodiments, a composition further comprises one or more additional therapeutic agents. In some embodiments, one or more additional therapeutic agents comprise a corticosteroid, a beta-agonist, a muscarinic antagonist, an anti-inflammatory agent, an IL-4 and/or IL-13 antagonist (*e.g.*, an antibody or antigen-binding fragment thereof targeting IL-13, IL-4 or IL-4R), or a combination thereof.

[00626] The disclosure also provides, among other things, a method of treating a subject in need thereof, comprising administering an effective amount of a composition disclosed in the section entitled "AB-2".

[00627] In some embodiments, a subject has asthma, atopic dermatitis (AD), allergic conjunctivitis, chronic obstructive pulmonary disease (COPD), chronic spontaneous urticaria (CSU), rheumatoid arthritis (RA), rhinosinusitis (RS), eosinophilic esophagitis (EE), or a food-hypersensitivity reaction. In some embodiments, a subject has moderate asthma. In some embodiments, a subject has severe asthma. In some embodiments, a subject has COPD. In some embodiments, a subject has COPD and/or either moderate asthma or severe asthma.

[00628] In some embodiments, a method further comprises administering to the subject an effective amount of a corticosteroid, a beta-agonist, a muscarinic antagonist, an anti-inflammatory agent, an IL-4 and/or IL-13 antagonist (*e.g.*, an antibody or antigen-binding fragment thereof targeting IL-13, IL-4 or IL-4R), or a combination thereof.

[00629] The disclosure also provides, among other things, a method of reducing binding of TSLP to a TSLPR on a cell in a subject, comprising contacting the cell with an effective amount of the composition disclosed in the section entitled "AB-2".

[00630] The disclosure also provides, among other things, a fusion protein comprising a polypeptide disclosed in the section entitled "AB-2".

[00631] The disclosure also provides, among other things, a polynucleotide comprising a nucleotide sequence encoding a polypeptide disclosed in the section entitled "AB-2".

[00632] The disclosure also provides, among other things, a host cell comprising a polynucleotide disclosed in the section entitled "AB-2".

[00633] The disclosure also provides, among other things, a method of making a polypeptide disclosed in the section entitled "AB-2", comprising culturing a host cell comprising a nucleotide sequence encoding the polypeptide under conditions where the polypeptide is expressed in the host cell.

Computational definition and verification of sequences

[00634] Applicant, through computational design and experimental validation, has facilitated an understanding of structure and function interrelation of anti-TSLP antibodies and herein provides the skilled artisan the means to use such understanding. For example, the application provides Computer Program Listing Appendices (also referred to herein as Appendix A and Appendix B, respectively) that can be used to both evaluate (score) a given sequence or generate a sequence having a score that, when evaluated, is above a given threshold. These appendices include a Potts model (generalized Ising model) of polypeptides provided by the invention. In some embodiments, an implementation of a Potts model supposes that amino acids interact with their nearest neighbor but is able to determine relationship with distant (*e.g.*, more than one position away, therefore representing features of secondary and tertiary structure) amino acids as well.

[00635] The Potts model is a second order sequence model. In some embodiments, the Potts model is energy based. The model is designed to output an energy for a particular configuration. Given a sequence provided to an energy-based model, the model can be trained to produce a quantification of any measure. The Potts model is represented by a table of model weights. The table includes first- and second-order weights. In the first-order weights, the table includes position of a residue, the residue (*e.g.*, amino acid), and a score associated with the residue at that position. In the second-order weights, the table includes

two positions, two residues, and one score for the two residues at the respective positions. The scores are self-energies or energy scores.

[00636] The Computer Program Listing Appendices are referred to as Appendix A (claim.py) and Appendix B (fit_model.etab), which are available online at the respective addresses listed above and incorporated by reference in full into this application. A person having ordinary skill in the art can recognize that Appendix A can be executed in a python environment, compiler, or other equivalent environment that can run python scripts. A person having ordinary skill in the art can recognize that Appendix B can be loaded by the script of Appendix A. In embodiments, the table entries of Table 15 in Appendix D would be copied to an American Standard Code for Information Interchange (ASCII) document. In embodiments, a person of ordinary skill in the art can recognize that the script of Appendix C, "claim.py" is substantially similar to that of the file "claim.py", incorporated by reference in its entirety, of Appendix A. When running the claim.py file, two sequences (or one combined sequence) can be inputted. In embodiments, the below description further describes the source code and model of Appendices A/Appendix C and Appendix B/D.

[00637] FIG. 12A is a diagram 1000 illustrating zero-, first-, and second-order models. A zero-order model 1002 is a set of unordered amino acids. As the model is zero-order, there is no order or structure to the amino acids. In a physical metaphor, it can be thought of as a "bag" of amino acids because the amino acids placed in the bag would jumble around and have no order. Next, a first order model 1004 is a matrix which is represented as a quantification (*e.g.*, a peptide mass fingerprinting (PMF) of amino acids) at each residue of a protein sequence. Each row of the matrix is an amino acid sequence, and each column is configured to have a sum of the quantification of each residue in that column be 1. These first order energies can be referred to as an h-tensor, represented below as the "first hash table." A first order term in the model is said to be at a given position, and the model can assign a number of points for each particular position. With pair terms, the model can compare the scores given any two positions. The model can output an "energy," which is a number, and the lower the number the better, in embodiments.

[00638] A second-order sequence model 1006, or Potts model, represents energy for two residues being found together and energies associated with the first-order effects. The second-order energies of the two residues being found together are considered the j-tensor, while the energies associated with the first-order effects are referred to as the h-tensor. The second order energies, in other words, compare the energies between two positions of the

amino acid sequence. The second order sequences can therefore compare the energies between two positions of any amino acid sequence. A person of ordinary skill in the art can recognize that this can be repeated for multiple sequences, thereby rating many similar sequences all residue pairs of similar sequences.

[00639] FIG. 12B is a flow diagram 1050 illustrating an example of the process used by embodiments of this disclosure to determine claimed sequences. First, the process receives a given polypeptide sequence or pair of sequences (1052). The sequence pair, in different embodiments, can be separate polypeptide chains or, in some embodiments, a single polypeptide chain, *e.g.*, an scFV. A person of ordinary skill in the art can further recognize that model of Appendix B (or Appendix D), in embodiments, can be used to generate polypeptide sequences or pairs of sequences to test using the script of Appendix A (or Appendix C). The script of Appendix A (or Appendix C) scores the sequence using model weights provided in Appendix B (or Appendix D) (1054). The script then determines whether the score is above a predetermined threshold (although, a person of ordinary skill in the art can recognize that with different scoring regimes, the score may be below the threshold) (1056). If not, the polypeptide sequence or pair of sequences is not verified (1058). If it is, the polypeptide sequence or pair of sequences is verified (1060).

[00640] The Potts Model disclosed herein was generated from experimental validation of approximately 100 sequences to identify sequences with advantageous functions. The model coefficients are stored in the ASCII text file [fit_model.etab]. These sequences when assayed had acceptable polyspecific reactivity, self-aggregation propensity, and expression. Additionally, they all possessed biological function as determined by a SEAP reporter assay. The resulting model was verified to only claim sequences not reported in existing literature.

[00641] In some embodiments, a script is employed to determine whether a sequence pair (*e.g.*, V_H and V_L—although, for clarity, the sequence pair, in different embodiments, can be separate polypeptide chains or, in some embodiments, a single polypeptide chain, *e.g.*, an scFV) is claimed under the model, when scored, is above a threshold. The script is referred to as a computationally binding optimizing (CBO) script. Two hash tables are loaded from an existing file, and the script extracts first- and second-order index/position values, residue values, and corresponding scores for each. For the first-order table, the script extracts one position, one residue, and one score associated with the residue at the position. For the second-order table, the script extracts a first position, a second position, a first residue, a

second residue, and a score associated with the first residue at the first position and the second residue at the second position.

[00642] The two sequences, the V_H sequence and V_L sequence, are inputted to the script are then aligned. The alignment confirms that the V_H sequence and V_L sequence are the same length as reference sequence(s) and that given sections of both sequences are the same as the reference sequence(s). Once confirmed, residues from both of the inputted sequences at specified positions are extracted to form a trimmed and concatenated sequence. The positions used to extract the residues are positions where mutations were applied during training of the model. The positions used to confirm that the given sections of both sequences are the same as the reference sequence(s) are the positions where mutations were not applied during training of the model. Once trimmed to the positions used to train the model, the two input sequences are concatenated together. Then an energy score is calculated for the given concatenated sequence and the two hash tables. The following steps describe some embodiments of calculating the energy score.

[00643] First, let $\vec{\sigma}$ designate the sequence being scored with σ_i being its i-th amino acids. Further, let h represent the self-energy matrix (*e.g.*, first-order matrix) of the Potts model, such that $h_i(a)$ is the energy associated with amino acid a being at position i. Finally, let J represent the pair-energy matrix (*e.g.*, second-order matrix) of the model, such that $J_{ij}(a, b)$ is the pair energy associated with amino acids a and b being at positions i and j, respectively. With this notation, the total energy of sequence $\vec{\sigma}$ under the model is:

$$E(\vec{\sigma}) = \sum_{i=1}^{N} h_i(\sigma_i) + \sum_{i=1}^{N-1} \sum_{j=i+1}^{N} J_{ij}(\sigma_i, \sigma_j)$$

[00644] where N is the length of the sequence. Further, $\vec{\sigma}_{i \to a}$ can represent a sequence resulting in replacing the i-th amino acids of sequence $\vec{\sigma}$ with amino acid a. With this notation, a pseudo-likelihood of sequence $\vec{\sigma}$ under the model can be calculated as:

$$\rho(\vec{\sigma}) = \prod_{i=1}^{N} \frac{e^{-E(\vec{\sigma})}}{\sum_{a=1}^{\mu} e^{-E(\vec{\sigma}_{i \to a})}}$$

[00645] where μ is the total number of possible amino acids. In some embodiments, μ is 20 but a person of ordinary skill in the art can recognize that the value of μ can vary. Finally, the logarithm of the pseudo-likelihood of $\vec{\sigma}$ can be expressed as:

$$\log[\rho(\vec{\sigma})] = \sum_{i=1}^{N} \log\left[\frac{e^{-E(\vec{\sigma})}}{\sum_{a=1}^{\mu} e^{-E(\vec{\sigma}_{i\to a})}}\right] = -\sum_{i=1}^{N}\left(E(\vec{\sigma}) + \log\left[\sum_{a=1}^{\mu} e^{-E(\vec{\sigma}_{i\to a})}\right]\right)$$

[00646] The score_sequence function of the script of Appendix A (or Appendix C) calculates and returns the above value. The score_sequence function return represents a logarithmic probability that the sequence would occur given the weights of the Potts model that are inputted to the script. If the score is greater than the threshold, which in this embodiment is -7.7, then the sequences can meet the required parameters (*e.g.*, be confirmed/verified by the Potts model) and the function returns true. This score represents a logarithmic probability. Otherwise, the function returns false and the sequence pair is not confirmed the model. When the function returns true, this indicates that the sequence pair is suitable for the given purpose (*e.g.*, a purpose related to binding to human TSLP).

[00647] A person of ordinary skill in the art can recognize that other thresholds can be employed that represent a logarithmic probability that sequences can meet the required parameters. In some embodiments, an example range of thresholds calculated by the script can include about -7.7, -7.0, -6.5, -6.0, -5.5, -5.0, -4.5, -4.0, -3.5, -3.0, 2.9, -2.8, -2.7, -2.6, -2.5, -2.4, -2.3, -2.2, -2.1, -2.0, -1.9, -1.8, -1.7, -1.6, -1.5, -1.4, -1.3, -1.2, -1.1, -1.0, 0.9, -0.8, -0.7, -0.6, -0.5, -0.4, -0.3, -0.2, and -0.1. As the thresholds increase towards zero, the sequences spaces scored within those thresholds represent smaller sequence spaces that have higher levels of confidence. In some embodiments, the constants may be modified in script or the hash table, such as by multiplying all constants by a constant. In such an event, the threshold may be adjusted, as can be determined by a person of ordinary skill in the art. The threshold can further be calculated in a non-logarithmic manner, and represented as a confidence interval, or in a non-logarithmic range, or represented as another probabilistic threshold.

[00648] In some embodiments, the script of Appendix A defines a sequence scoring function (sequence_energy). This function calculates a sequence energy for the replacement of a residue (*e.g.*, an amino acid) with each other possible residue a group of positions in the sequence using a Potts model trained on replacing residues at those positions. As described above, the scoring checks each possible residue at each position requested. A person of ordinary skill in the art can recognize that the script can replace residues at each given position (as in the script of Appendix A). In some embodiments, a similar script could add residues into the sequence. Each score is calculated with a sequence_energy function, and is

added to an array of scores. For each position examined, sum of the scores in the array are summed and normalized with a softmax function. The scores are them logarithmically summed and returned.

[00649] In some embodiments, the sequence energy function inputs a sequence and the hash tables determined from the inputted etab file (or another format). The function iterates over all first order combinations, scoring them with a first hash table, and all second order combinations, scoring them with a second hash table. The sequence_energy function considers all replacement residues and their first and second order combinations, and sums those energies together.

[00650] In some embodiments, the etab file is read with a read_etab function. Each line in the file having three items is unpacked and converted into an entry in a first hash table for first order combinations. Each line in the file having five items is unpacked and converted into an entry of a second hash table for second order combinations. The two hash tables are returned.

[00651] The above steps and functions describe a "computationally binding optimized" (CBO) sequence, amino acid sequence, or polypeptide sequence. Such a sequence is a sequence that, when inputted into the above computationally binding optimizing script, returns a value of true. A person having ordinary skill in the art can recognize that the script can be implemented in other ways or with other series of steps. A person having ordinary skill in the art can also recognize that other functionally equivalent tables and constants can be used. However, the provided Python script, tables, and constants, when executed by a processor, are configured to output whether a given polypeptide sequence is a CBO sequence. Therefore, any sequence that, when run by the script, causes a Boolean "true" output is considered a CBO sequence. Any sequence that, when run by the script, causes a Boolean "false" output is considered excluded from the group of the CBO sequences. Thereby, in some embodiments, the script of Appendix A (or Appendix C) itself does not determine CBO sequences but is a tool to confirm whether a given sequence is a CBO sequence or not. When a CBO sequence is an amino acid sequence, the corresponding molecule having the amino acid sequence is referred to as a CBO polypeptide.

[00652] In some embodiments, a similar script is able to return the calculated scores of a given or multiple sequences in addition to or separate from a Boolean value representing a threshold.

[00653] In some embodiments, a similar script can return one or more generated sequences from the Potts model. To generate sequences, markov chain monte carlo [MCMC] sampling can be performed on the model. Then, the resulting samples can be reintegrated into the constant template. In some embodiments, a brute force method can be applied using the scoring functions.

[00654] In view of the above, Table 10 illustrates the trimmed sequences (vlt, vht) for proteins AB-1 through AB-14, the concatenated/combined sequences (vhvlt), and the resulting Potts model scores when the above script was applied to them. The sequences for AB-1 through AB-14 are illustrated in Tables 1 and 2. All of the proteins AB-1 through AB-14 were or would be verified by the script because their Potts model scores were above -7.7.

[00655] In view of Table 10, a person of ordinary skill in the art can recognize that equivalent Potts model scores, such as scores having a different scale or being multiplied by negative one, may result in scores being at or above or below a different threshold.

[00656] FIG. 13 illustrates a computer network or similar digital processing environment in which embodiments of the present invention may be implemented.

[00657] Client computer(s)/devices 50 and server computer(s) 60 provide processing, storage, and input/output devices executing application programs and the like. The client computer(s)/devices 50 can also be linked through communications network 70 to other computing devices, including other client devices/processes 50 and server computer(s) 60. The communications network 70 can be part of a remote access network, a global network (*e.g.*, the Internet), a worldwide collection of computers, local area or wide area networks, and gateways that currently use respective protocols (TCP/IP, Bluetooth®, etc.) to communicate with one another. Other electronic device/computer network architectures are suitable.

[00658] FIG. 14 is a diagram of an example internal structure of a computer (*e.g.*, client processor/device 50 or server computers 60) in the computer system of FIG. 13. Each computer 50, 60 contains a system bus 79, where a bus is a set of hardware lines used for data transfer among the components of a computer or processing system. The system bus 79 is essentially a shared conduit that connects different elements of a computer system (*e.g.*, processor, disk storage, memory, input/output ports, network ports, etc.) that enables the transfer of information between the elements. Attached to the system bus 79 is an I/O device interface 82 for connecting various input and output devices (*e.g.*, keyboard, mouse, displays, printers, speakers, etc.) to the computer 50, 60. A network interface 86 allows the computer

to connect to various other devices attached to a network (*e.g.*, network 70 of FIG. 13). Memory 90 provides volatile storage for computer software instructions 92 and data 94 used to implement some embodiments of the present invention (*e.g.*, CBO determination script, Potts model, model weights code detailed above and in Appendices A and B). Disk storage 95 provides non-volatile storage for computer software instructions 92 and data 94 used to implement some embodiments of the present invention. A central processor unit 84 is also attached to the system bus 79 and provides for the execution of computer instructions.

[00659] In one embodiment, the processor routines 92 and data 94 are a computer program product (generally referenced 92), including a non-transitory computer-readable medium (*e.g.*, a removable storage medium such as one or more DVD-ROM's, CD-ROM's, diskettes, tapes, etc.) that provides at least a portion of the software instructions for the invention system. The computer program product 92 can be installed by any suitable software installation procedure, as is well known in the art. In another embodiment, at least a portion of the software instructions may also be downloaded over a cable communication and/or wireless connection. In some embodiments, the invention programs are a computer program propagated signal product embodied on a propagated signal on a propagation medium (*e.g.*, a radio wave, an infrared wave, a laser wave, a sound wave, or an electrical wave propagated over a global network such as the Internet, or other network(s)). Such carrier medium or signals may be employed to provide at least a portion of the software instructions for the present invention routines/program 92.

[00660] In another aspect, the disclosure provides a polypeptide that specifically binds a TSLP (*e.g.*, a hTSLP): wherein a CBO model outputs a score that is above a predetermined threshold upon scoring an amino acid sequence of the polypeptide.

[00661] In another aspect, the disclosure provides a CBO polypeptide that specifically binds a TSLP (*e.g.*, a hTSLP): wherein a CBO model outputs a score that is above a predetermined threshold upon scoring an amino acid sequence representing the CBO polypeptide.

[00662] In another aspect, the disclosure provides a polypeptide that specifically binds a TSLP (*e.g.*, a hTSLP) and receives a score above a predetermined threshold from a CBO model upon scoring an amino acid sequence representing the polypeptide.

[00663] In another aspect, the disclosure provides a polypeptide that specifically binds a TSLP (*e.g.*, a hTSLP): wherein the polypeptide receives a score above a predetermined

threshold from a CBO model upon scoring an amino acid sequence representing the polypeptide.

[00664] In another aspect, the disclosure provides a computationally binding optimized (CBO) polypeptide, determined by a computationally binding optimized (CBO) model that specifically binds a TSLP (*e.g.*, a hTSLP).

[00665] In some embodiments, a CBO polypeptide comprises a paratope that is substantially similar to the paratope of an antibody comprising an amino acid sequence selected from:

SEQ ID NO:4 and SEQ ID NO:20 (AB-1);
SEQ ID NO:5 and SEQ ID NO:21 (AB-2);
SEQ ID NO:6 and SEQ ID NO:20 (AB-3);
SEQ ID NO:7 and SEQ ID NO:22 (AB-4);
SEQ ID NO:8 and SEQ ID NO:23 (AB-5);
SEQ ID NO:9 and SEQ ID NO:24 (AB-6);
SEQ ID NO:10 and SEQ ID NO:25 (AB-7);
SEQ ID NO:11 and SEQ ID NO:20 (AB-8);
SEQ ID NO:12 and SEQ ID NO:20 (AB-9);
SEQ ID NO:13 and SEQ ID NO:26 (AB-10);
SEQ ID NO:14 and SEQ ID NO:27 (AB-11);
SEQ ID NO:15 and SEQ ID NO:28 (AB-12);
SEQ ID NO:16 and SEQ ID NO:29 (AB-13); or
SEQ ID NO:17 and SEQ ID NO:30 (AB-14), or
a combination of the foregoing.

[00666] In some embodiments, the CBO polypeptide comprises a paratope that is substantially similar (*e.g.*, having at least about 90% sequence identity; having 100% sequence identity) to the paratope of a V_H/V_L combination selected from: SEQ ID NO:4/SEQ ID NO:20 (AB-1), SEQ ID NO:5/SEQ ID NO:21 (AB-2), SEQ ID NO:6/SEQ ID NO:20 (AB-3), SEQ ID NO:7/SEQ ID NO:22 (AB-4), SEQ ID NO:8/SEQ ID NO:23 (AB-5), SEQ ID NO:9/SEQ ID NO:24 (AB-6), SEQ ID NO:10/SEQ ID NO:25 (AB-7), SEQ ID NO:11/SEQ ID NO:20 (AB-8), SEQ ID NO:12/SEQ ID NO:20 (AB-9), SEQ ID NO:13/SEQ ID NO:26 (AB-10), SEQ ID NO:14/SEQ ID NO:27 (AB-11), SEQ ID NO:15/SEQ ID NO:28 (AB-12), SEQ ID NO:16/SEQ ID NO:29(AB-13) or SEQ ID NO:17/SEQ ID NO:30 (AB-14).

[00667] In some embodiments, the CBO polypeptide comprises a paratope that differs from the paratope of a V_H/V_L combination selected from: SEQ ID NO:4/SEQ ID NO:20 (AB-1), SEQ ID NO:5/SEQ ID NO:21 (AB-2), SEQ ID NO:6/SEQ ID NO:20 (AB-3), SEQ ID NO:7/SEQ ID NO:22 (AB-4), SEQ ID NO:8/SEQ ID NO:23 (AB-5), SEQ ID NO:9/SEQ ID NO:24 (AB-6), SEQ ID NO:10/SEQ ID NO:25 (AB-7), SEQ ID NO:11/SEQ ID NO:20 (AB-8), SEQ ID NO:12/SEQ ID NO:20 (AB-9), SEQ ID NO:13/SEQ ID NO:26 (AB-10), SEQ ID NO:14/SEQ ID NO:27 (AB-11), SEQ ID NO:15/SEQ ID NO:28 (AB-12), SEQ ID NO:16/SEQ ID NO:29(AB-13) or SEQ ID NO:17/SEQ ID NO:30 (AB-14), by substitution (*e.g.*, conservative such as highly conservative substitution) of from 1 to 3 (*e.g.*, 1, 2 or 3) residues.

[00668] In particular embodiments, the CBO polypeptide does not comprise a V_H and V_L pair selected from:

SEQ ID NO:4 and SEQ ID NO:20 (AB-1),
SEQ ID NO:5 and SEQ ID NO:21 (AB-2),
SEQ ID NO:6 and SEQ ID NO:20 (AB-3),
SEQ ID NO:7 and SEQ ID NO:22 (AB-4),
SEQ ID NO:8 and SEQ ID NO:23 (AB-5),
SEQ ID NO:9 and SEQ ID NO:24 (AB-6),
SEQ ID NO:10 and SEQ ID NO:25 (AB-7),
SEQ ID NO:11 and SEQ ID NO:20 (AB-8),
SEQ ID NO:12 and SEQ ID NO:20 (AB-9),
SEQ ID NO:13 and SEQ ID NO:26 (AB-10),
SEQ ID NO:14 and SEQ ID NO:27 (AB-11),
SEQ ID NO:15 and SEQ ID NO:28 (AB-12),
SEQ ID NO:16 and SEQ ID NO:29 (AB-13),
SEQ ID NO:17 and SEQ ID NO:30 (AB-14), and
combinations thereof.

[00669] In certain embodiments, a CBO polypeptide comprises a paratope that is substantially similar to the paratope of an antibody comprising an amino acid sequence selected from:

SEQ ID NO:4 and SEQ ID NO:20 (AB-1);
SEQ ID NO:5 and SEQ ID NO:21 (AB-2);
SEQ ID NO:6 and SEQ ID NO:20 (AB-3); or

SEQ ID NO:7 and SEQ ID NO:22 (AB-4), or

a combination of the foregoing.

[00670] In some embodiments, the CBO polypeptide comprises a paratope that is substantially similar (*e.g.*, having at least about 90% sequence identity; having 100% sequence identity) to the paratope of a V_H/V_L combination selected from: SEQ ID NO:4/SEQ ID NO:20 (AB-1), SEQ ID NO:5/SEQ ID NO:21 (AB-2), SEQ ID NO:6/SEQ ID NO:20 (AB-3) or SEQ ID NO:7/SEQ ID NO:22 (AB-4), by substitution (*e.g.*, conservative such as highly conservative substitution) of from 1 to 3 (*e.g.*, 1, 2 or 3) residues.

[00671] In some embodiments, the CBO polypeptide comprises a paratope that differs from the paratope of a V_H/V_L combination selected from: SEQ ID NO:4/SEQ ID NO:20 (AB-1), SEQ ID NO:5/SEQ ID NO:21 (AB-2), SEQ ID NO:6/SEQ ID NO:20 (AB-3) or SEQ ID NO:7/SEQ ID NO:22 (AB-4).

[00672] In particular embodiments, the CBO polypeptide does not comprise a V_H and V_L pair selected from:

SEQ ID NO:4 and SEQ ID NO:20 (AB-1),

SEQ ID NO:5 and SEQ ID NO:21 (AB-2),

SEQ ID NO:6 and SEQ ID NO:20 (AB-3),

SEQ ID NO:7 and SEQ ID NO:22 (AB-4), and

combinations thereof.

[00673] In some embodiments, a CBO polypeptide comprises:

a V_H amino acid sequence comprising a HCDR1, a HCDR2 and a HCDR3 that are substantially similar to a HCDR1, a HCDR2 and a HCDR3, respectively, of SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16 or SEQ ID NO:17; and

a V_L amino acid sequence comprising a LCDR1, a LCDR2 and a LCDR3 that are substantially similar to a LCDR1, a LCDR2 and a LCDR3, respectively, of SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29 or SEQ ID NO:30.

[00674] In some embodiments, the CBO polypeptide comprises a HCDR1, a HCDR2, a HCDR3, a LCDR1, a LCDR2 and a LCDR3 that substantially preserve one or more functional properties of a HCDR1, a HCDR2, a HCDR3, a LCDR1, a LCDR2 and a LCDR3

of AB-1, AB-2, AB-3, AB-4, AB-5, AB-6, AB-7, AB-8, AB-9, AB-10, AB-11, AB-12, AB-13 or AB-14.

[00675] In some embodiments, the CBO polypeptide comprises a HCDR1, a HCDR2, a HCDR3, a LCDR1, a LCDR2 and a LCDR3 comprising only one or more conservative substitutions (*e.g.*, only one or more highly conservative substitutions), relative a HCDR1, a HCDR2, a HCDR3, a LCDR1, a LCDR2 and a LCDR3 of AB-1, AB-2, AB-3, AB-4, AB-5, AB-6, AB-7, AB-8, AB-9, AB-10, AB-11, AB-12, AB-13 or AB-14.

[00676] In certain embodiments, the CBO polypeptide comprises a HCDR1, a HCDR2, a HCDR3, a LCDR1, a LCDR2 and a LCDR3 comprising up to 1, 2, or 3 conservative substitutions (*e.g.*, up to 1, 2, or 3 highly conservative substitutions), relative a HCDR1, a HCDR2, a HCDR3, a LCDR1, a LCDR2 and a LCDR3 of AB-1, AB-2, AB-3, AB-4, AB-5, AB-6, AB-7, AB-8, AB-9, AB-10, AB-11, AB-12, AB-13 or AB-14.

[00677] In particular embodiments, the CBO polypeptide comprises a HCDR1, a HCDR2, a HCDR3, a LCDR1, a LCDR2 and a LCDR3 having 100% sequence identity to a HCDR1, a HCDR2, a HCDR3, a LCDR1, a LCDR2 and a LCDR3 of AB-1, AB-2, AB-3, AB-4, AB-5, AB-6, AB-7, AB-8, AB-9, AB-10, AB-11, AB-12, AB-13 or AB-14.

[00678] In some embodiments, the CBO polypeptide comprises:

a) a HCDR1 comprising at least 1 amino acid substitution relative to the amino acid sequence of SEQ ID NO:31;

b) a HCDR2 comprising at least 1 amino acid substitution relative to at least one amino acid sequence set forth in SEQ ID NOs:33-46 (*e.g.*, at least one amino acid sequence set forth in SEQ ID NOs:34-46);

c) a HCDR3 comprising at least 1 amino acid substitution relative to at least one amino acid sequence set forth in SEQ ID NOs:48-57 (*e.g.*, at least one amino acid sequence set forth in SEQ ID NOs:49-57);

d) a LCDR1 comprising at least 1 amino acid substitution relative to the amino acid sequence set forth in SEQ ID NOs:59-66 (*e.g.*, at least one amino acid sequence set forth in SEQ ID NOs:60-66);

e) a LCDR2 comprising at least 1 amino acid substitution relative to the amino acid sequence of SEQ ID NO:67;

f) a LCDR3 comprising at least 1 amino acid substitution relative to at least one amino acid sequence set forth in SEQ ID NOs:69-80 (*e.g.*, at least one amino acid sequence set forth in SEQ ID NOs:70-80);

or a combination of the foregoing.

[00679] In some embodiments, the CBO polypeptide comprises:

a) a HCDR2 comprising at least 1 amino acid substitution relative to at least one amino acid sequence set forth in SEQ ID NOs:33-46 (*e.g.*, at least one amino acid sequence set forth in SEQ ID NOs:34-46);

b) a HCDR3 comprising at least 1 amino acid substitution relative to at least one amino acid sequence set forth in SEQ ID NOs:48-57 (*e.g.*, at least one amino acid sequence set forth in SEQ ID NOs:49-57);

c) a LCDR1 comprising at least 1 amino acid substitution relative to the amino acid sequence set forth in SEQ ID NOs:59-66 (*e.g.*, at least one amino acid sequence set forth in SEQ ID NOs:60-66);

d) a LCDR3 comprising at least 1 amino acid substitution relative to at least one amino acid sequence set forth in SEQ ID NOs:69-80 (*e.g.*, at least one amino acid sequence set forth in SEQ ID NOs:70-80);

or a combination of the foregoing.

[00680] In particular embodiments, the CBO polypeptide does not comprise a V_H and V_L pair selected from:

SEQ ID NO:4 and SEQ ID NO:20 (AB-1),
SEQ ID NO:5 and SEQ ID NO:21 (AB-2),
SEQ ID NO:6 and SEQ ID NO:20 (AB-3),
SEQ ID NO:7 and SEQ ID NO:22 (AB-4),
SEQ ID NO:8 and SEQ ID NO:23 (AB-5),
SEQ ID NO:9 and SEQ ID NO:24 (AB-6),
SEQ ID NO:10 and SEQ ID NO:25 (AB-7),
SEQ ID NO:11 and SEQ ID NO:20 (AB-8),
SEQ ID NO:12 and SEQ ID NO:20 (AB-9),
SEQ ID NO:13 and SEQ ID NO:26 (AB-10),
SEQ ID NO:14 and SEQ ID NO:27 (AB-11),
SEQ ID NO:15 and SEQ ID NO:28 (AB-12),
SEQ ID NO:16 and SEQ ID NO:29 (AB-13),
SEQ ID NO:17 and SEQ ID NO:30 (AB-14), and
combinations thereof.

[00681] In certain embodiments, a CBO polypeptide comprises:

a V_H amino acid sequence comprising a HCDR1, a HCDR2 and a HCDR3 that are substantially similar to a HCDR1, a HCDR2 and a HCDR3, respectively, of SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6 or SEQ ID NO:7; and

a V_L amino acid sequence comprising a LCDR1, a LCDR2 and a LCDR3 that are substantially similar to a LCDR1, a LCDR2 and a LCDR3, respectively, of SEQ ID NO:20, SEQ ID NO:21 or SEQ ID NO:22.

[00682] In some embodiments, the CBO polypeptide comprises a HCDR1, a HCDR2, a HCDR3, a LCDR1, a LCDR2 and a LCDR3 that substantially preserve one or more functional properties of a HCDR1, a HCDR2, a HCDR3, a LCDR1, a LCDR2 and a LCDR3 of AB-1, AB-2, AB-3 or AB-4.

[00683] In some embodiments, the CBO polypeptide comprises a HCDR1, a HCDR2, a HCDR3, a LCDR1, a LCDR2 and a LCDR3 comprising only one or more conservative substitutions (*e.g.*, only one or more highly conservative substitutions), relative a HCDR1, a HCDR2, a HCDR3, a LCDR1, a LCDR2 and a LCDR3 of AB-1, AB-2, AB-3 or AB-4.

[00684] In certain embodiments, the CBO polypeptide comprises a HCDR1, a HCDR2, a HCDR3, a LCDR1, a LCDR2 and a LCDR3 comprising up to 1, 2, or 3 conservative substitutions (*e.g.*, up to 1, 2, or 3 highly conservative substitutions), relative a HCDR1, a HCDR2, a HCDR3, a LCDR1, a LCDR2 and a LCDR3 of AB-1, AB-2, AB-3 or AB-4.

[00685] In particular embodiments, the CBO polypeptide comprises a HCDR1, a HCDR2, a HCDR3, a LCDR1, a LCDR2 and a LCDR3 having 100% sequence identity to a HCDR1, a HCDR2, a HCDR3, a LCDR1, a LCDR2 and a LCDR3 of AB-1, AB-2, AB-3 or AB-4.

[00686] In some embodiments, the CBO polypeptide comprises:

a) a HCDR1 comprising at least 1 amino acid substitution relative to the amino acid sequence of SEQ ID NO:31;

b) a HCDR2 comprising at least 1 amino acid substitution relative to at least one amino acid sequence set forth in SEQ ID NOs:33-37 (*e.g.*, at least one amino acid sequence set forth in SEQ ID NOs:34-37);

c) a HCDR3 comprising at least 1 amino acid substitution relative to at least one amino acid sequence set forth in SEQ ID NOs:48-52 (*e.g.*, at least one amino acid sequence set forth in SEQ ID NOs:49-52);

d) a LCDR1 comprising at least 1 amino acid substitution relative to the amino acid sequence set forth in SEQ ID NOs:59-61 (*e.g.*, at least one amino acid sequence set forth in SEQ ID NOs:60-61);

e) a LCDR2 comprising at least 1 amino acid substitution relative to the amino acid sequence of SEQ ID NO:67;

f) a LCDR3 comprising at least 1 amino acid substitution relative to at least one amino acid sequence set forth in SEQ ID NOs:69-72 (*e.g.*, at least one amino acid sequence set forth in SEQ ID NOs:70-72);

or a combination of the foregoing.

[00687] In some embodiments, the CBO polypeptide comprises:

a) a HCDR2 comprising at least 1 amino acid substitution relative to at least one amino acid sequence set forth in SEQ ID NOs:33-37 (*e.g.*, at least one amino acid sequence set forth in SEQ ID NOs:34-37);

b) a HCDR3 comprising at least 1 amino acid substitution relative to at least one amino acid sequence set forth in SEQ ID NOs:48-52 (*e.g.*, at least one amino acid sequence set forth in SEQ ID NOs:49-52);

c) a LCDR1 comprising at least 1 amino acid substitution relative to the amino acid sequence set forth in SEQ ID NOs:59-61 (*e.g.*, at least one amino acid sequence set forth in SEQ ID NOs:60-61);

d) a LCDR3 comprising at least 1 amino acid substitution relative to at least one amino acid sequence set forth in SEQ ID NOs:69-72 (*e.g.*, at least one amino acid sequence set forth in SEQ ID NOs:70-72);

or a combination of the foregoing.

[00688] In particular embodiments, the CBO polypeptide does not comprise a V_H and V_L pair selected from:

SEQ ID NO:4 and SEQ ID NO:20 (AB-1),
SEQ ID NO:5 and SEQ ID NO:21 (AB-2),
SEQ ID NO:6 and SEQ ID NO:20 (AB-3),
SEQ ID NO:7 and SEQ ID NO:22 (AB-4), and
combinations thereof.

[00689] In some embodiments, a CBO polypeptide comprises:

a) a V_H comprising an amino acid sequence that has at least 55% (*e.g.*, at least 60, 65, 70, 75, 80, 85, 90, 95, 98, or 99%) sequence identity to SEQ ID NO:3;

b) a V_L comprising an amino acid sequence that has at least 55% (*e.g.*, at least 60, 65, 70, 75, 80, 85, 90, 95, 98, or 99%) sequence identity to SEQ ID NO:19; or

both a) and b),

wherein the CBO polypeptide does not comprise all 6 CDRs of an antibody comprising a V_H amino acid sequence of SEQ ID NO:3 and a V_L amino acid sequence of SEQ ID NO:19.

[00690] In some embodiments, the CBO polypeptide comprises a V_H that has at least about 70% sequence identity to the amino acid sequence of SEQ ID NO:3. For example, the V_H can have at least about: 71%, 72%, 73%, 74%, 75%, 76%, 77%, 78%, 79%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% sequence identity to the amino acid sequence of SEQ ID NO:3. In some embodiments, the V_H has at least about 85% or at least about 90% sequence identity to the amino acid sequence of SEQ ID NO:3.

[00691] In some embodiments, the CBO polypeptide comprises a V_H that comprises at least 1 amino acid substitution relative to the amino acid sequence of SEQ ID NO:3. For example, the number of amino acid substitutions can be at least about: 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19 or 20, or about: 1-20, 1-19, 2-19, 2-18, 2-17, 3-17, 3-16, 4-16, 4-15, 5-15, 5-14, 6-14, 6-13, 7-13, 7-12, 8-12, 8-11 or 9-11. In some embodiments, the V_H comprises about 1-10 amino acid substitutions, relative to the amino acid sequence of SEQ ID NO:3. In certain embodiments, the at least 1 amino acid substitution replaces only a HCDR1, a HCDR2 and/or a HCDR3 residue, of SEQ ID NO:3. In particular embodiments, the at least 1 amino acid substitution replaces only a non-CDR residue (*e.g.*, within a framework region), of SEQ ID NO:3.

[00692] In some embodiments, the CBO polypeptide comprises a V_L that has at least about 70% sequence identity to the amino acid sequence of SEQ ID NO:19. For example, the V_L can be at least about: 71%, 72%, 73%, 74%, 75%, 76%, 77%, 78%, 79%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% sequence identity to the amino acid sequence of SEQ ID NO:19. In some embodiments, the V_L has at least about 85% or at least about 90% sequence identity to the amino acid sequence of SEQ ID NO:19.

[00693] In some embodiments, the CBO polypeptide comprises a V_L that comprises at least 1 amino acid substitution relative to the amino acid sequence of SEQ ID NO:19. For example, the number of amino acid substitutions can be at least about: 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19 or 20, or about: 1-20, 1-19, 2-19, 2-18, 2-17, 3-17, 3-16, 4-16, 4-15, 5-15, 5-14, 6-14, 6-13, 7-13, 7-12, 8-12, 8-11 or 9-11. In some embodiments, the V_L comprises about 1-10 amino acid substitutions, relative to the amino acid sequence of SEQ

ID NO:19. In certain embodiments, the at least 1 amino acid substitution replaces only a LCDR1, a LCDR2 and/or a LCDR3 residue, of SEQ ID NO:19. In particular embodiments, the at least 1 amino acid substitution replaces only a non-CDR residue (*e.g.*, within a framework region), of SEQ ID NO:19.

[00694] In some embodiments, the CBO polypeptide comprises a V_H that has at least about 70% sequence identity to the amino acid sequence of SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16 or SEQ ID NO:17, or a combination of the foregoing. For example, the V_H can have at least about: 71%, 72%, 73%, 74%, 75%, 76%, 77%, 78%, 79%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% sequence identity to the amino acid sequence of SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16 or SEQ ID NO:17, or a combination of the foregoing. In some embodiments, the V_H has at least about 85% or at least about 90% sequence identity to the amino acid sequence of SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16 or SEQ ID NO:17, or a combination of the foregoing.

[00695] In some embodiments, the CBO polypeptide comprises a V_H that comprises at least 1 amino acid substitution relative to the amino acid sequence of SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16 or SEQ ID NO:17, or a combination of the foregoing. For example, the number of amino acid substitutions can be at least about: 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19 or 20, or about: 1-20, 1-19, 2-19, 2-18, 2-17, 3-17, 3-16, 4-16, 4-15, 5-15, 5-14, 6-14, 6-13, 7-13, 7-12, 8-12, 8-11 or 9-11. In some embodiments, the V_H comprises about 1-10 amino acid substitutions, relative to the amino acid sequence of SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16 or SEQ ID NO:17, or a combination of the foregoing. In certain embodiments, the at least 1 amino acid substitution replaces only a HCDR1, a HCDR2 and/or a HCDR3 residue, of SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10,

SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16 or SEQ ID NO:17, or a combination of the foregoing. In particular embodiments, the at least 1 amino acid substitution replaces only a non-CDR residue (*e.g.*, within a framework region), of SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16 or SEQ ID NO:17, or a combination of the foregoing.

[00696] In some embodiments, the CBO polypeptide comprises a V_L that has at least about 70% sequence identity to the amino acid sequence of SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29 or SEQ ID NO:30, or a combination of the foregoing. For example, the V_L can be at least about: 71%, 72%, 73%, 74%, 75%, 76%, 77%, 78%, 79%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% sequence identity to the amino acid sequence of SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29 or SEQ ID NO:30, or a combination of the foregoing. In some embodiments, the V_L has at least about 85% or at least about 90% sequence identity to the amino acid sequence of SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29 or SEQ ID NO:30, or a combination of the foregoing.

[00697] In some embodiments, the CBO polypeptide comprises a V_L that comprises at least 1 amino acid substitution relative to the amino acid sequence of SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29 or SEQ ID NO:30, or a combination of the foregoing. For example, the number of amino acid substitutions can be at least about: 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19 or 20, or about: 1-20, 1-19, 2-19, 2-18, 2-17, 3-17, 3-16, 4-16, 4-15, 5-15, 5-14, 6-14, 6-13, 7-13, 7-12, 8-12, 8-11 or 9-11. In some embodiments, the V_L comprises about 1-10 amino acid substitutions, relative to the amino acid sequence of SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29 or SEQ ID NO:30, or a combination of the foregoing. In certain embodiments, the at least 1 amino acid substitution replaces only a LCDR1, a LCDR2 and/or a LCDR3 residue, of SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID

NO:25, SEQ ID NO:26, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29 or SEQ ID NO:30, or a combination of the foregoing. In particular embodiments, the at least 1 amino acid substitution replaces only a non-CDR residue (*e.g.*, within a framework region), of SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29 or SEQ ID NO:30, or a combination of the foregoing.

[00698] In particular embodiments, the CBO polypeptide does not comprise a V_H and V_L pair selected from:

SEQ ID NO:4 and SEQ ID NO:20 (AB-1),
SEQ ID NO:5 and SEQ ID NO:21 (AB-2),
SEQ ID NO:6 and SEQ ID NO:20 (AB-3),
SEQ ID NO:7 and SEQ ID NO:22 (AB-4),
SEQ ID NO:8 and SEQ ID NO:23 (AB-5),
SEQ ID NO:9 and SEQ ID NO:24 (AB-6),
SEQ ID NO:10 and SEQ ID NO:25 (AB-7),
SEQ ID NO:11 and SEQ ID NO:20 (AB-8),
SEQ ID NO:12 and SEQ ID NO:20 (AB-9),
SEQ ID NO:13 and SEQ ID NO:26 (AB-10),
SEQ ID NO:14 and SEQ ID NO:27 (AB-11),
SEQ ID NO:15 and SEQ ID NO:28 (AB-12),
SEQ ID NO:16 and SEQ ID NO:29 (AB-13),
SEQ ID NO:17 and SEQ ID NO:30 (AB-14), and
combinations thereof.

[00699] In some embodiments, a CBO polypeptide comprises a V_H that has at least about 70% sequence identity to the amino acid sequence of SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6 or SEQ ID NO:7, or a combination of the foregoing. For example, the V_H can have at least about: 71%, 72%, 73%, 74%, 75%, 76%, 77%, 78%, 79%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% sequence identity to the amino acid sequence of SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6 or SEQ ID NO:7, or a combination of the foregoing. In some embodiments, the V_H has at least about 85% or at least about 90% sequence identity to the amino acid sequence of SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6 or SEQ ID NO:7, or a combination of the foregoing.

[00700] In some embodiments, the CBO polypeptide comprises a V_H that comprises at least 1 amino acid substitution relative to the amino acid sequence of SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6 or SEQ ID NO:7, or a combination of the foregoing. For example, the number of amino acid substitutions can be at least about: 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19 or 20, or about: 1-20, 1-19, 2-19, 2-18, 2-17, 3-17, 3-16, 4-16, 4-15, 5-15, 5-14, 6-14, 6-13, 7-13, 7-12, 8-12, 8-11 or 9-11. In some embodiments, the V_H comprises about 1-10 amino acid substitutions, relative to the amino acid sequence of SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6 or SEQ ID NO:7, or a combination of the foregoing. In certain embodiments, the at least 1 amino acid substitution replaces only a HCDR1, a HCDR2 and/or a HCDR3 residue, of SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6 or SEQ ID NO:7, or a combination of the foregoing. In particular embodiments, the at least 1 amino acid substitution replaces only a non-CDR residue (*e.g.*, within a framework region), of SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6 or SEQ ID NO:7, or a combination of the foregoing.

[00701] In some embodiments, the CBO polypeptide comprises a V_L that has at least about 70% sequence identity to the amino acid sequence of SEQ ID NO:20, SEQ ID NO:21 or SEQ ID NO:22, or a combination of the foregoing. For example, the V_L can be at least about: 71%, 72%, 73%, 74%, 75%, 76%, 77%, 78%, 79%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% sequence identity to the amino acid sequence of SEQ ID NO:20, SEQ ID NO:21 or SEQ ID NO:22, or a combination of the foregoing. In some embodiments, the V_L has at least about 85% or at least about 90% sequence identity to the amino acid sequence of SEQ ID NO:20, SEQ ID NO:21 or SEQ ID NO:22, or a combination of the foregoing.

[00702] In some embodiments, the CBO polypeptide comprises a V_L that comprises at least 1 amino acid substitution relative to the amino acid sequence of SEQ ID NO:20, SEQ ID NO:21 or SEQ ID NO:22, or a combination of the foregoing. For example, the number of amino acid substitutions can be at least about: 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19 or 20, or about: 1-20, 1-19, 2-19, 2-18, 2-17, 3-17, 3-16, 4-16, 4-15, 5-15, 5-14, 6-14, 6-13, 7-13, 7-12, 8-12, 8-11 or 9-11. In some embodiments, the V_L comprises about 1-10 amino acid substitutions, relative to the amino acid sequence of SEQ ID NO:20, SEQ ID NO:21 or SEQ ID NO:22, or a combination of the foregoing. In certain embodiments, the at least 1 amino acid substitution replaces only a LCDR1, a LCDR2 and/or a LCDR3 residue, of SEQ ID NO:20, SEQ ID NO:21 or SEQ ID NO:22, or a combination of the foregoing. In particular embodiments, the at least 1 amino acid substitution replaces only a non-CDR

residue (*e.g.*, within a framework region), of SEQ ID NO:20, SEQ ID NO:21 or SEQ ID NO:22, or a combination of the foregoing.

[00703] In particular embodiments, the CBO polypeptide does not comprise a V_H and V_L pair selected from:

SEQ ID NO:4 and SEQ ID NO:20 (AB-1),

SEQ ID NO:5 and SEQ ID NO:21 (AB-2),

SEQ ID NO:6 and SEQ ID NO:20 (AB-3),

SEQ ID NO:7 and SEQ ID NO:22 (AB-4), and

combinations thereof.

[00704] In some embodiments, a CBO polypeptide comprises a V_H comprising SEQ ID NO:2, wherein:

X_1 is not I;

X_2 is not W;

X_3 is not D;

X_4 is not S;

X_5 is not N;

X_6 is not K;

X_7 is not A;

X_8 is not A;

X_9 is not L;

X_{10} is not V;

X_{11} is not H,

X_{12} is not A;

X_{13} is not F;

X_{14} is not I,

or any combination of the foregoing.

[00705] In some embodiments:

X_1 is I or V;

X_2 is W or S;

X_3 is D or S;

X_4 is S, T, Y or A;

X_5 is N, Y, D or T;

X_6 is K, T or I;

X_7 is A, S or T;

X_8 is A or S;

X_9 is L, D, E or S;

X_{10} is V or I;

X_{11} is H, F or Y;

X_{12} is A or S;

X_{13} is F, M or L;

X_{14} is I or V,

or any combination of the foregoing.

[00706] In some embodiments:

X_1 is V;

X_2 is S;

X_3 is S;

X_4 is T, Y or A;

X_5 is Y, D or T;

X_6 is T or I;

X_7 is S or T;

X_8 is S;

X_9 is D, E or S;

X_{10} is I;

X_{11} is F or Y;

X_{12} is S;

X_{13} is M or L;

X_{14} is V,

or any combination of the foregoing.

[00707] In some embodiments, the CBO polypeptide further comprises a V_L comprising SEQ ID NO:18, wherein:

X_{15} is not N;

X_{16} is not L;

X_{17} is not S;

X_{18} is not K;

X_{19} is not S;

X_{20} is not V;

X_{21} is not W;

X_{22} is not D;

X_{23} is not S;

X_{24} is not S;

X_{25} is not S;

X_{26} is not D;

X_{27} is not H,

or any combination of the foregoing.

[00708] In some embodiments:

X_{15} is N or Y;

X_{16} is L or I;

X_{17} is S or R;

X_{18} is K, F or Y;

X_{19} is S or N;

X_{20} is V or I;

X_{21} is W or Y;

X_{22} is D, V or S;

X_{23} is S, M or E;

X_{24} is S, A or T;

X_{25} is S, D or E;

X_{26} is D, S, R or F;

X_{27} is H, L, K or E,

or any combination of the foregoing.

[00709] In some embodiments:

X_{15} is Y;

X_{16} is I;

X_{17} is R;

X_{18} is F or Y;

X_{19} is N;

X_{20} is I;

X_{21} is Y;

X_{22} is V or S;

X_{23} is M or E;

X_{24} is A or T;

X_{25} is D or E;

X_{26} is S, R or F;

X_{27} is L, K or E,

or any combination of the foregoing.

[00710] In particular embodiments, the CBO polypeptide does not comprise a V_H and V_L pair selected from:

SEQ ID NO:4 and SEQ ID NO:20 (AB-1),

SEQ ID NO:5 and SEQ ID NO:21 (AB-2),

SEQ ID NO:6 and SEQ ID NO:20 (AB-3),

SEQ ID NO:7 and SEQ ID NO:22 (AB-4),

SEQ ID NO:8 and SEQ ID NO:23 (AB-5),

SEQ ID NO:9 and SEQ ID NO:24 (AB-6),

SEQ ID NO:10 and SEQ ID NO:25 (AB-7),

SEQ ID NO:11 and SEQ ID NO:20 (AB-8),

SEQ ID NO:12 and SEQ ID NO:20 (AB-9),

SEQ ID NO:13 and SEQ ID NO:26 (AB-10),

SEQ ID NO:14 and SEQ ID NO:27 (AB-11),

SEQ ID NO:15 and SEQ ID NO:28 (AB-12),

SEQ ID NO:16 and SEQ ID NO:29 (AB-13),

SEQ ID NO:17 and SEQ ID NO:30 (AB-14), and

combinations thereof.

[00711] In some embodiments:

X_1 is I or V;

X_2 is W;

X_3 is D or S;

X_4 is S or T;

X_5 is N, Y or D;

X_6 is K or T;

X_7 is A or S;

X_8 is A or S;

X_9 is L, D, E or S;

X_{10} is V or I;

X_{11} is H or F;

X_{12} is A or S;

X_{13} is F or M;

X_{14} is I or V,

or any combination of the foregoing.

[00712] In some embodiments:

X_1 is V;

X_2 is W;

X_3 is S;

X_4 is T;

X_5 is Y or D;

X_6 is T;

X_7 is S;

X_8 is S;

X_9 is D, E or S;

X_{10} is I;

X_{11} is F;

X_{12} is S;

X_{13} is M;

X_{14} is V,

or any combination of the foregoing.

[00713] In some embodiments:

X_{15} is N or Y;

X_{16} is L or I;

X_{17} is S;

X_{18} is K or F;

X_{19} is S;

X_{20} is V or I;

X_{21} is W or Y;

X_{22} is D or V;

X_{23} is S or M;

X_{24} is S or A;

X_{25} is S;

X_{26} is D, S or R;

X_{27} is H or L,

or any combination of the foregoing.

[00714] In some embodiments:

X_{15} is Y;

X_{16} is I;

X_{17} is S;

X_{18} is F;

X_{19} is S;

X_{20} is I;

X_{21} is Y;

X_{22} is V;

X_{23} is M;

X_{24} is A;

X_{25} is S;

X_{26} is S or R;

X_{27} is L,

or any combination of the foregoing.

[00715] In particular embodiments, the CBO polypeptide does not comprise a V_H and V_L pair selected from:

SEQ ID NO:4 and SEQ ID NO:20 (AB-1),

SEQ ID NO:5 and SEQ ID NO:21 (AB-2),

SEQ ID NO:6 and SEQ ID NO:20 (AB-3),

SEQ ID NO:7 and SEQ ID NO:22 (AB-4), and

combinations thereof.

[00716] In some embodiments, a computer-implemented method includes scoring a polypeptide comprising an amino acid sequence with a computationally binding optimized (CBO) model for a functional property relating to modulating the activity of a target molecule. The CBO model, for each amino acid position of the amino acid sequence of the polypeptide, calculates multiple energy scores, the multiple energy scores based on the amino acid at a given position in the amino acid sequence. The CBO model further adds each energy score calculated to an array. The CBO model further generates a normalized sum of the energy scores for each position. The CBO model further generates a score of the polypeptide

by summing each energy score calculated, the score representing a functional property of the polypeptide, the functional property relating to the polypeptide modulating the activity of the target molecule.

[00717] In some embodiments, the computer-implemented method includes calculating a logarithm of each energy score calculated.

[00718] In some embodiments, summing each energy score calculated is performed by summing the logarithms of each energy score calculated.

[00719] In some embodiments, the energy scores are further calculated based on having substituted the amino acid at the given position in the amino acid sequence with each of a plurality of different amino acids.

[00720] In some embodiments, the target molecule is a target polypeptide.

[00721] In some embodiments, the scoring the polypeptide using the CBO model is implemented by the script of Appendix A.

[00722] In some embodiments, the CBO model is substantially similar to the table of Appendix B. A substantially similar table to the Computer Programming Listing Appendix B is a table that scores polypeptides in line with the Computer Programming Listing Appendix B. In some embodiments, such a substantially similar table scores polypeptides so as to maintain their relative rank order. In certain embodiments, a substantially similar table returns scores within about: 30, 25, 20, 15, 10, 9, 8, 7, 6, 5, 4, 3, 2, or 1% of the score provided by the Computer Programming Listing Appendix B. In some embodiments, table substantially similar to the Computer Programming Listing Appendix B comprises substantially the same dimensions (rows and columns, *e.g.*, within about: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 12, 13, 14, 15%, or in some embodiments, the identical dimensions), wherein each entry in the table is substantially similar to a corresponding value in the Computer Programming Listing Appendix B, *e.g.*, within about: 30, 25, 20, 15, 10, 9, 8, 7, 6, 5, 4, 3, 2, 1%, or identical.

[00723] In some embodiments, scoring the polypeptide can further include extracting positions from the amino acid sequence, the extracted positions being positions where mutations were applied during training of the CBO model. Scoring the polypeptide can further include calculating the multiple energy scores is performed on the extracted positions.

[00724] In some embodiments, scoring the polypeptide further includes scoring a pair of amino acid sequences. Scoring the polypeptide can further include aligning a first amino acid sequence and second amino acid sequence of the pair of amino acid sequences such that (a)

the first amino acid sequence and second amino acid sequence are the same length and that (b) given sections of the first amino acid sequence and second amino acid sequence are the same.

[00725] In some embodiments, the multiple energy scores include a first-order energy score associated with each amino acid being at its position. The multiple energy scores further include, for each pair of amino acid positions of the amino acid sequence, a second-order energy score associated with the pair of amino acid positions. The first-order energy score and second-order energy score can be calculated based on corresponding entries of a trained first- and second- order energy score table of outputted weights of a model trained by a plurality of known amino acid sequences and corresponding properties of the known amino acid sequences.

[00726] In some embodiments, the computer-implemented method includes returning, based on the score, a flag indicating whether the sequence has the functional property associated with the polypeptide.

[00727] In some embodiments, the functional property is one or more of:

a) a binding affinity for a thymic stromal lymphopoietin (TSLP) polypeptide characterized by a K_D of 10 pM or less (optionally, as measured by KinExA);

b) a binding specificity for the AB-loop region and the C-terminal region of helix D of the TSLP;

c) a neutralizing activity against the TSLP (optionally, a full-length human TSLP); or

d) an inhibitory activity against TSLP-mediated signaling,

e) or a combination of the foregoing.

[00728] In some embodiments, a system includes a processor and a memory with computer code instructions stored thereon. The processor and the memory, with the computer code instructions, are configured to cause the system to score a polypeptide comprising an amino acid sequence with a CBO model for a functional property relating to modulating the activity of a target molecule. The CBO model, for each amino acid position of the amino acid sequence of the polypeptide, calculates multiple energy scores, the multiple energy scores based on the amino acid at a given position in the amino acid sequence. The CBO model further adds each energy score calculated to an array. The CBO model further generates a normalized sum of the energy scores for each position. The CBO model further generates a

score of the polypeptide by summing each energy score calculated, the score representing a functional property of the polypeptide.

[00729] In some embodiments, the instructions are further configured to cause the system to calculate a logarithm of each energy score calculated.

[00730] In some embodiments, summing each energy score calculated is performed by summing the logarithms of each energy score calculated.

[00731] In some embodiments, the energy scores are further calculated based on having substituted the amino acid at the given position in the amino acid sequence with each of a plurality of different amino acids.

[00732] In some embodiments, the target molecule is a target polypeptide.

[00733] In some embodiments, the scoring the polypeptide using the CBO model is implemented by the script of Appendix A.

[00734] In some embodiments, the CBO model is substantially similar to the table of Appendix B. A substantially similar table to the Computer Programming Listing Appendix B is a table that scores polypeptides in line with the Computer Programming Listing Appendix B. In some embodiments, such a substantially similar table scores polypeptides so as to maintain their relative rank order. In certain embodiments, a substantially similar table returns scores within about: 30, 25, 20, 15, 10, 9, 8, 7, 6, 5, 4, 3, 2, 1% of the score provided by the Computer Programming Listing Appendix B. In some embodiments, table substantially similar to the Computer Programming Listing Appendix B comprises substantially the same dimensions (rows and columns, *e.g.*, within about: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 12, 13, 14, 15%, in some embodiments, the identical dimensions), wherein each entry in the table is substantially similar to a corresponding value in the Computer Programming Listing Appendix B, *e.g.*, within about: 30, 25, 20, 15, 10, 9, 8, 7, 6, 5, 4, 3, 2, 1%.

[00735] In some embodiments, scoring the polypeptide further includes extracting positions from the amino acid sequence. The extracted positions can be positions where mutations were applied during training of the CBO model. Scoring the polypeptide further includes calculating the multiple energy scores is performed on the extracted positions.

[00736] In some embodiments, scoring the polypeptide further includes scoring a pair of amino acid sequences. Scoring the polypeptide further includes aligning a first amino acid sequence and second amino acid sequence of the pair of amino acid sequences such that (a) the first amino acid sequence and second amino acid sequence are the same length and that

(b) given sections of the first amino acid sequence and second amino acid sequence are the same.

[00737] In some embodiments, the multiple energy scores include a first-order energy score associated with each amino acid being at its position. The multiple energy scores further include, for each pair of amino acid positions of the amino acid sequence, a second-order energy score associated with the pair of amino acid positions. The first-order energy score and second-order energy score are calculated by respective entries from a trained first- and second- order energy score table of outputted weights of a model trained by a plurality of known amino acid sequences and corresponding properties of the known amino acid sequences.

[00738] In some embodiments, the processor further is configured to cause the system to return, based on the score, a flag indicating whether the sequence has the functional property associated with the polypeptide.

[00739] In some embodiments, the functional property is at least one of:

a) a binding affinity for the TSLP characterized by a K_D of 10 pM or less (*e.g.*, as measured by KinExA);

b) a binding specificity for the AB-loop region and the C-terminal region of helix D of the TSLP;

c) a neutralizing activity against the TSLP (*e.g.*, a full-length human TSLP); or

d) an inhibitory activity against TSLP-mediated signaling,

e) or a combination of the foregoing.

[00740] In some embodiments, the score being above the particular threshold represents that the functional property is met for the given polypeptide.

[00741] In some embodiments, a polypeptide that specifically binds a thymic stromal lymphopoietin (TSLP) comprises an amino acid sequence that is assigned a score above a predetermined threshold by a computationally binding optimized (CBO) model upon scoring the amino acid sequence of the polypeptide.

[00742] In some embodiments, the polypeptide is assigned the score by the CBO model that is calculated by a table substantially similar to that of Computer Program Listing Appendix B.

[00743] In some embodiments, the polypeptide is assigned the score that is calculated using the Computer Program Listing Appendix B.

[00744] In some embodiments, the polypeptide is assigned the score by a script substantially similar to Computer Program Listing Appendix A, the script employing the CBO model substantially similar to the table of Computer Program Listing Appendix B. In some embodiments, the polypeptide has a logarithmic score above or equivalent to being above at least one of -7.7, -7.0, -6.5, -6.0, -5.5, -5.0, -4.5, -4.0, -3.5, -3.0, 2.9, -2.8, -2.7, -2.6, -2.5, -2.4, -2.3, -2.2, -2.1, -2.0, -1.9, -1.8, -1.7, -1.6, -1.5, -1.4, -1.3, -1.2, -1.1, -1.0, 0.9, -0.8, -0.7, -0.6, -0.5, -0.4, -0.3, -0.2, and -0.1.

[00745] In some embodiments, the polypeptide is scorable by the script of Computer Program Listing Appendix A.

[00746] In some embodiments, the predetermined threshold is the logarithmic probability that the sequence inputted to the script would occur given the weights of the Potts model.

[00747] In some embodiments, a CBO script assigning the score to the polypeptide includes receiving a trained first- and second- order energy score table of outputted weights of a model trained by a plurality of known amino acid sequences and corresponding properties of the known amino acid sequences.

[00748] In some embodiments, the polypeptide comprises an immunoglobulin heavy chain variable domain (V_H) and an immunoglobulin light chain variable domain (V_L).

[00749] In some embodiments, the polypeptide has one or more properties selected from:

a) a binding affinity for the TSLP characterized by a K_D of 10 pM or less (*e.g.*, as measured by KinExA);

b) a binding specificity for the AB-loop region and the C-terminal region of helix D of the TSLP;

c) a neutralizing activity against the TSLP (*e.g.*, a full-length human TSLP); or

d) an inhibitory activity against TSLP-mediated signaling,

e) or a combination of the foregoing.

[00750] In some embodiments, the score being above the particular threshold represents that the functional property is met for the given polypeptide.

[00751] In some embodiments, the CBO model outputs a score that is equal to or above a score from the CBO model of one or more of a reference polypeptide that comprises a V_H and V_L pair selected from:

a) SEQ ID NO:4 and SEQ ID NO:20 (AB-1);

b) SEQ ID NO:5 and SEQ ID NO:21 (AB-2);

c) SEQ ID NO:6 and SEQ ID NO:20 (AB-3);

d) SEQ ID NO:7 and SEQ ID NO:22 (AB-4);

e) SEQ ID NO:8 and SEQ ID NO:23 (AB-5);

f) SEQ ID NO:9 and SEQ ID NO:24 (AB-6);

g) SEQ ID NO:10 and SEQ ID NO:25 (AB-7);

h) SEQ ID NO:11 and SEQ ID NO:20 (AB-8);

i) SEQ ID NO:12 and SEQ ID NO:20 (AB-9);

j) SEQ ID NO:13 and SEQ ID NO:26 (AB-10);

k) SEQ ID NO:14 and SEQ ID NO:27 (AB-11);

l) SEQ ID NO:15 and SEQ ID NO:28 (AB-12);

m) SEQ ID NO:16 and SEQ ID NO:29 (AB-13); or

n) SEQ ID NO:17 and SEQ ID NO:30 (AB-14).

[00752] In some embodiments, the polypeptide comprises a V_H and V_L pair selected from:

a) SEQ ID NO:4 and SEQ ID NO:20 (AB-1);

b) SEQ ID NO:5 and SEQ ID NO:21 (AB-2);

c) SEQ ID NO:6 and SEQ ID NO:20 (AB-3);

d) SEQ ID NO:7 and SEQ ID NO:22 (AB-4);

e) SEQ ID NO:8 and SEQ ID NO:23 (AB-5);

f) SEQ ID NO:9 and SEQ ID NO:24 (AB-6);

g) SEQ ID NO:10 and SEQ ID NO:25 (AB-7);

h) SEQ ID NO:11 and SEQ ID NO:20 (AB-8);

i) SEQ ID NO:12 and SEQ ID NO:20 (AB-9);

j) SEQ ID NO:13 and SEQ ID NO:26 (AB-10);

k) SEQ ID NO:14 and SEQ ID NO:27 (AB-11);

l) SEQ ID NO:15 and SEQ ID NO:28 (AB-12);

m) SEQ ID NO:16 and SEQ ID NO:29 (AB-13); or

n) SEQ ID NO:17 and SEQ ID NO:30 (AB-14).

[00753] In some embodiments, the polypeptide does not comprise a V_H and V_L pair selected from:

a) SEQ ID NO:4 and SEQ ID NO:20 (AB-1);

b) SEQ ID NO:5 and SEQ ID NO:21 (AB-2);

c) SEQ ID NO:6 and SEQ ID NO:20 (AB-3);

d) SEQ ID NO:7 and SEQ ID NO:22 (AB-4);

e) SEQ ID NO:8 and SEQ ID NO:23 (AB-5);

f) SEQ ID NO:9 and SEQ ID NO:24 (AB-6);

g) SEQ ID NO:10 and SEQ ID NO:25 (AB-7);

h) SEQ ID NO:11 and SEQ ID NO:20 (AB-8);

i) SEQ ID NO:12 and SEQ ID NO:20 (AB-9);

j) SEQ ID NO:13 and SEQ ID NO:26 (AB-10);

k) SEQ ID NO:14 and SEQ ID NO:27 (AB-11);

l) SEQ ID NO:15 and SEQ ID NO:28 (AB-12);

m) SEQ ID NO:16 and SEQ ID NO:29 (AB-13); or

n) SEQ ID NO:17 and SEQ ID NO:30 (AB-14).

[00754] In some embodiments, the polypeptide does not comprise a heavy chain comprising SEQ ID NO:81 and a light chain comprising SEQ ID NO:82.

[00755] In some embodiments, the polypeptide is an antibody or an antigen-binding fragment thereof.

[00756] In some embodiments, a polypeptide comprises an amino acid sequence that is assigned a score above a predetermined threshold by a computationally binding optimized (CBO) model upon scoring the amino acid sequence of the polypeptide.

[00757] In some embodiments, a polypeptide that binds human thymic stromal lymphopoietin (TSLP) is designed by a method comprising generating a polypeptide sequence with a CBO model. The polypeptide is further designed by verifying the generated polypeptide sequence using the CBO model by, for each amino acid position of the polypeptide sequence, calculating a plurality of energy scores. The energy scores can be based on having substituted the amino acid at a given position in the polypeptide sequence with each of a plurality of different amino acids. The polypeptide is further verified by adding each energy score calculated to an array. The polypeptide is further verified by generating a normalized sum of the energy scores for each position. The polypeptide is further verified by calculating a logarithm of each energy score calculated. The polypeptide is further verified by generating a score of the polypeptide sequence by summing the logarithms of each energy score calculated. The score represents a functional property of the polypeptide's ability to bind to human TSLP. In some embodiments, the polypeptide sequence is verified if the polypeptide scores above a particular threshold.

[00758] In some embodiments, the polypeptide is scored at least a score of one of more of -7.7, -7.0, -6.5, -6.0, -5.5, -5.0, -4.5, -4.0, -3.5, -3.0, 2.9, -2.8, -2.7, -2.6, -2.5, -2.4, -2.3, -2.2, -2.1, -2.0, -1.9, -1.8, -1.7, -1.6, -1.5, -1.4, -1.3, -1.2, -1.1, -1.0, 0.9, -0.8, -0.7, -0.6, -0.5, -0.4, -

0.3, -0.2, and -0.1 (*e.g.*, to be verified). In some embodiments, the polypeptide is an antibody or an antigen-binding fragment thereof.

[00759] In some embodiments, the polypeptide comprises a V_H and V_L pair comprising an amino acid sequence at least about: 60, 65, 70, 75, 80, 85, 86,87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, or 99 identical to a V_H and V_L pair selected from:

a) SEQ ID NO:4 and SEQ ID NO:20 (AB-1);
b) SEQ ID NO:5 and SEQ ID NO:21 (AB-2);
c) SEQ ID NO:6 and SEQ ID NO:20 (AB-3);
d) SEQ ID NO:7 and SEQ ID NO:22 (AB-4);
e) SEQ ID NO:8 and SEQ ID NO:23 (AB-5);
f) SEQ ID NO:9 and SEQ ID NO:24 (AB-6);
g) SEQ ID NO:10 and SEQ ID NO:25 (AB-7);
h) SEQ ID NO:11 and SEQ ID NO:20 (AB-8);
i) SEQ ID NO:12 and SEQ ID NO:20 (AB-9);
j) SEQ ID NO:13 and SEQ ID NO:26 (AB-10);
k) SEQ ID NO:14 and SEQ ID NO:27 (AB-11);
l) SEQ ID NO:15 and SEQ ID NO:28 (AB-12);
m) SEQ ID NO:16 and SEQ ID NO:29 (AB-13); or
n) SEQ ID NO:17 and SEQ ID NO:30 (AB-14)..

[00760] In some embodiments, the polypeptide comprises a V_H and V_L pair does not comprise an amino acid sequence 100% identical to a V_H and V_L pair selected from:

a) SEQ ID NO:4 and SEQ ID NO:20 (AB-1);
b) SEQ ID NO:5 and SEQ ID NO:21 (AB-2);
c) SEQ ID NO:6 and SEQ ID NO:20 (AB-3);
d) SEQ ID NO:7 and SEQ ID NO:22 (AB-4);
e) SEQ ID NO:8 and SEQ ID NO:23 (AB-5);
f) SEQ ID NO:9 and SEQ ID NO:24 (AB-6);
g) SEQ ID NO:10 and SEQ ID NO:25 (AB-7);
h) SEQ ID NO:11 and SEQ ID NO:20 (AB-8);
i) SEQ ID NO:12 and SEQ ID NO:20 (AB-9);
j) SEQ ID NO:13 and SEQ ID NO:26 (AB-10);
k) SEQ ID NO:14 and SEQ ID NO:27 (AB-11);

l) SEQ ID NO:15 and SEQ ID NO:28 (AB-12);

m) SEQ ID NO:16 and SEQ ID NO:29 (AB-13); or

n) SEQ ID NO:17 and SEQ ID NO:30 (AB-14)..

Embodiments of the Disclosure

1. A polypeptide that specifically binds a thymic stromal lymphopoietin (TSLP), wherein the polypeptide has one or more properties selected from:

a binding affinity for the TSLP characterized by a K_D of 10 pM or less (*e.g.*, as measured by KinExA);

a binding specificity for the AB-loop region and the C-terminal region of helix D of the TSLP;

a neutralizing activity against the TSLP (*e.g.*, a full-length human TSLP); or

an inhibitory activity against TSLP-mediated signaling,

or a combination of the foregoing.

2. A polypeptide that specifically binds a thymic stromal lymphopoietin (TSLP), comprising a paratope that is substantially similar to the paratope of an antibody comprising an amino acid sequence selected from:

SEQ ID NO:4 and SEQ ID NO:20 (AB-1);

SEQ ID NO:5 and SEQ ID NO:21 (AB-2);

SEQ ID NO:6 and SEQ ID NO:20 (AB-3);

SEQ ID NO:7 and SEQ ID NO:22 (AB-4);

SEQ ID NO:8 and SEQ ID NO:23 (AB-5);

SEQ ID NO:9 and SEQ ID NO:24 (AB-6);

SEQ ID NO:10 and SEQ ID NO:25 (AB-7);

SEQ ID NO:11 and SEQ ID NO:20 (AB-8);

SEQ ID NO:12 and SEQ ID NO:20 (AB-9);

SEQ ID NO:13 and SEQ ID NO:26 (AB-10);

SEQ ID NO:14 and SEQ ID NO:27 (AB-11);

SEQ ID NO:15 and SEQ ID NO:28 (AB-12);

SEQ ID NO:16 and SEQ ID NO:29 (AB-13); or

SEQ ID NO:17 and SEQ ID NO:30 (AB-14), or

a combination of the foregoing.

3. The polypeptide of Embodiment 1 or 2, comprising an immunoglobulin heavy chain variable domain (V_H) and an immunoglobulin light chain variable domain (V_L).

4. A polypeptide that specifically binds a thymic stromal lymphopoietin (TSLP), comprising:

a) an immunoglobulin heavy chain variable domain (V_H) amino acid sequence comprising a heavy chain complementarity determining region 1 (HCDR1), a heavy chain complementarity determining region 2 (HCDR2) and a heavy chain complementarity determining region 3 (HCDR3) that are substantially similar to a HCDR1, HCDR2 and HCDR3, respectively, of the amino acid sequence of SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16 or SEQ ID NO:17; and

b) an immunoglobulin light chain variable domain (V_L) amino acid sequence comprising a light chain complementarity determining region 1 (LCDR1), a light chain complementarity determining region 2 (LCDR2) and a light chain complementarity determining region 3 (LCDR3) that are substantially similar to a LCDR1, LCDR2 and LCDR3, respectively, of the amino acid sequence of SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29 or SEQ ID NO:30.

5. The polypeptide of any one of Embodiments 1-4, comprising the HCDR1, HCDR2 and HCDR3, and LCDR1, LCDR2 and LCDR3, of an antibody comprising an amino acid sequence selected from:

SEQ ID NO:4 and SEQ ID NO:20 (AB-1);
SEQ ID NO:5 and SEQ ID NO:21 (AB-2);
SEQ ID NO:6 and SEQ ID NO:20 (AB-3);
SEQ ID NO:7 and SEQ ID NO:22 (AB-4);
SEQ ID NO:8 and SEQ ID NO:23 (AB-5);
SEQ ID NO:9 and SEQ ID NO:24 (AB-6);
SEQ ID NO:10 and SEQ ID NO:25 (AB-7);
SEQ ID NO:11 and SEQ ID NO:20 (AB-8);

SEQ ID NO:12 and SEQ ID NO:20 (AB-9);
SEQ ID NO:13 and SEQ ID NO:26 (AB-10);
SEQ ID NO:14 and SEQ ID NO:27 (AB-11);
SEQ ID NO:15 and SEQ ID NO:28 (AB-12);
SEQ ID NO:16 and SEQ ID NO:29 (AB-13); or
SEQ ID NO:17 and SEQ ID NO:30 (AB-14).

6. The polypeptide of Embodiment 4 or 5, further comprising a paratope that is identical to the paratope of an antibody comprising an amino acid sequence selected from:
SEQ ID NO:4 and SEQ ID NO:20 (AB-1);
SEQ ID NO:5 and SEQ ID NO:21 (AB-2);
SEQ ID NO:6 and SEQ ID NO:20 (AB-3);
SEQ ID NO:7 and SEQ ID NO:22 (AB-4);
SEQ ID NO:8 and SEQ ID NO:23 (AB-5);
SEQ ID NO:9 and SEQ ID NO:24 (AB-6);
SEQ ID NO:10 and SEQ ID NO:25 (AB-7);
SEQ ID NO:11 and SEQ ID NO:20 (AB-8);
SEQ ID NO:12 and SEQ ID NO:20 (AB-9);
SEQ ID NO:13 and SEQ ID NO:26 (AB-10);
SEQ ID NO:14 and SEQ ID NO:27 (AB-11);
SEQ ID NO:15 and SEQ ID NO:28 (AB-12);
SEQ ID NO:16 and SEQ ID NO:29 (AB-13); or
SEQ ID NO:17 and SEQ ID NO:30 (AB-14).

7. A polypeptide that specifically binds a thymic stromal lymphopoietin (TSLP), comprising an immunoglobulin heavy chain variable domain (V_H) comprising the amino acid sequence of SEQ ID NO:2, wherein:
X_1 is not I;
X_2 is not W;
X_3 is not D;
X_4 is not S;
X_5 is not N;
X_6 is not K;
X_7 is not A;

X_8 is not A;

X_9 is not L;

X_{10} is not V;

X_{11} is not H;

X_{12} is not A;

X_{13} is not F;

X_{14} is not I,

or any combination of the foregoing.

8. The polypeptide of Embodiment 7, further comprising an immunoglobulin light chain variable domain (V_L) comprising the amino acid sequence of SEQ ID NO:18, wherein:

X_{15} is not N;

X_{16} is not L;

X_{17} is not S;

X_{18} is not K;

X_{19} is not S;

X_{20} is not V;

X_{21} is not W;

X_{22} is not D;

X_{23} is not S;

X_{24} is not S;

X_{25} is not S;

X_{26} is not D;

X_{27} is not H,

or any combination of the foregoing.

9. A polypeptide that specifically binds a thymic stromal lymphopoietin (TSLP), comprising an immunoglobulin heavy chain variable domain (V_H) comprising the amino acid sequence of SEQ ID NO:2, wherein:

X_1 is I or V;

X_2 is W or S;

X_3 is D or S;

X_4 is S, T, Y or A;

X_5 is N, Y, D or T;

X_6 is K, T or I;

X_7 is A, S or T;

X_8 is A or S;

X_9 is L, D, E or S;

X_{10} is V or I;

X_{11} is H, F or Y;

X_{12} is A or S;

X_{13} is F, M or L;

X_{14} is I or V,

or any combination of the foregoing.

10. A polypeptide that specifically binds a thymic stromal lymphopoietin (TSLP), comprising an immunoglobulin heavy chain variable domain (V_H) comprising the amino acid sequence of SEQ ID NO:2, wherein:

X_1 is V;

X_2 is S;

X_3 is S;

X_4 is T, Y or A;

X_5 is Y, D or T;

X_6 is T or I;

X_7 is S or T;

X_8 is S;

X_9 is D, E or S;

X_{10} is I;

X_{11} is F or Y,

X_{12} is S;

X_{13} is M or L;

X_{14} is V,

or any combination of the foregoing.

11. The polypeptide of Embodiment 9 or 10, further comprising an immunoglobulin light chain variable domain (V_L) comprising the amino acid sequence of SEQ ID NO:18, wherein:

X_{15} is N or Y;

X_{16} is L or I;

X_{17} is S or R;

X_{18} is K, F or Y;

X_{19} is S or N;

X_{20} is V or I;

X_{21} is W or Y;

X_{22} is D, V or S;

X_{23} is S, M or E;

X_{24} is S, A or T;

X_{25} is S, D or E;

X_{26} is D, S, R or F;

X_{27} is H, L, K or E,

or any combination of the foregoing.

12. The polypeptide of Embodiment 11, wherein:

X_{15} is Y;

X_{16} is I;

X_{17} is R;

X_{18} is F or Y;

X_{19} is N;

X_{20} is I;

X_{21} is Y;

X_{22} is V or S;

X_{23} is M or E;

X_{24} is A or T;

X_{25} is D or E;

X_{26} is S, R or F;

X_{27} is L, K or E,

or any combination of the foregoing.

13. The polypeptide of any one of Embodiments 1-4 and 6-12, wherein the V_H comprises a heavy chain complementarity determining region 1 (HCDR1), a heavy chain complementarity determining region 2 (HCDR2) and a heavy chain complementarity

determining region 3 (HCDR3) that are identical in amino acid sequence to the HCDR1, HCDR2 and HCDR3, respectively, of SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16 or SEQ ID NO:17.

14. The polypeptide of any one of Embodiments 1-4 and 6-13, wherein the V_L comprises a light chain complementarity determining region 1 (LCDR1), light chain complementarity determining region 2 (LCDR2) and light chain complementarity determining region 3 (LCDR3) that are identical in amino acid sequence to the LCDR1, LCDR2 and LCDR3, respectively, of SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29 or SEQ ID NO:30.

15. The polypeptide of any one of Embodiments 1-5 and 7-14, wherein the polypeptide comprises a paratope that is identical to the paratope of a V_H/V_L combination selected from the amino acid sequence of: SEQ ID NO:4/SEQ ID NO:20 (AB-1), SEQ ID NO:5/SEQ ID NO:21 (AB-2), SEQ ID NO:6/SEQ ID NO:20 (AB-3), SEQ ID NO:7/SEQ ID NO:22 (AB-4), SEQ ID NO:8/SEQ ID NO:23 (AB-5), SEQ ID NO:9/SEQ ID NO:24 (AB-6), SEQ ID NO:10/SEQ ID NO:25 (AB-7), SEQ ID NO:11/SEQ ID NO:20 (AB-8), SEQ ID NO:12/SEQ ID NO:20 (AB-9), SEQ ID NO:13/SEQ ID NO:26 (AB-10), SEQ ID NO:14/SEQ ID NO:27 (AB-11), SEQ ID NO:15/SEQ ID NO:28 (AB-12), SEQ ID NO:16/SEQ ID NO:29(AB-13) or SEQ ID NO:17/SEQ ID NO:30 (AB-14).

16. The polypeptide of any one of Embodiments 1-15, wherein the V_H has at least 85% sequence identity to the amino acid sequence of SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16 or SEQ ID NO:17, or a combination of the foregoing.

17. The polypeptide of any one of Embodiments 1-16, wherein the V_H comprises about 1-10 amino acid substitutions, relative to the amino acid sequence of SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID

NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16 or SEQ ID NO:17, or a combination of the foregoing.

18. The polypeptide of any one of Embodiments 1-17, wherein the V_L has at least 85% sequence identity to the amino acid sequence of SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29 or SEQ ID NO:30, or a combination of the foregoing.

19. The polypeptide of any one of Embodiments 1-18, wherein the V_L comprises about 1-10 amino acid substitutions, relative to the amino acid sequence of SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29 or SEQ ID NO:30, or a combination of the foregoing.

20. The polypeptide of Embodiment 17 or 19, wherein the amino acid substitutions are conservative substitutions.

21. The polypeptide of Embodiment 20, wherein the amino acid substitutions are highly conservative substitutions.

22. The polypeptide of any one of Embodiments 1-21, wherein:
    a) the V_H comprises the amino acid sequence of SEQ ID NO:4; and
    b) the V_L comprises the amino acid sequence of SEQ ID NO:20.

23. The polypeptide of any one of Embodiments 1-21, wherein:
    a) the V_H comprises the amino acid sequence of SEQ ID NO:5; and
    b) the V_L comprises the amino acid sequence of SEQ ID NO:21.

24. The polypeptide of any one of Embodiments 1-21, wherein:
    a) the V_H comprises the amino acid sequence of SEQ ID NO:6; and
    b) the V_L comprises the amino acid sequence of SEQ ID NO:20.

25. The polypeptide of any one of Embodiments 1-21, wherein:
    a) the V_H comprises the amino acid sequence of SEQ ID NO:7; and
    b) the V_L comprises the amino acid sequence of SEQ ID NO:22.

26. The polypeptide of any one of Embodiments 1-21, wherein:
    a) the V_H comprises the amino acid sequence of SEQ ID NO:8; and
    b) the V_L comprises the amino acid sequence of SEQ ID NO:23.

27. The polypeptide of any one of Embodiments 1-21, wherein:
    a) the V_H comprises the amino acid sequence of SEQ ID NO:9; and
    b) the V_L comprises the amino acid sequence of SEQ ID NO:24.

28. The polypeptide of any one of Embodiments 1-21, wherein:
    a) the V_H comprises the amino acid sequence of SEQ ID NO:10; and
    b) the V_L comprises the amino acid sequence of SEQ ID NO:25.

29. The polypeptide of any one of Embodiments 1-21, wherein:
    a) the V_H comprises the amino acid sequence of SEQ ID NO:11; and
    b) the V_L comprises the amino acid sequence of SEQ ID NO:20.

30. The polypeptide of any one of Embodiments 1-21, wherein:
    a) the V_H comprises the amino acid sequence of SEQ ID NO:12; and
    b) the V_L comprises the amino acid sequence of SEQ ID NO:20.

31. The polypeptide of any one of Embodiments 1-21, wherein:
    a) the V_H comprises the amino acid sequence of SEQ ID NO:13; and
    b) the V_L comprises the amino acid sequence of SEQ ID NO:26.

32. The polypeptide of any one of Embodiments 1-21, wherein:
    a) the V_H comprises the amino acid sequence of SEQ ID NO:14; and
    b) the V_L comprises the amino acid sequence of SEQ ID NO:27.

33. The polypeptide of any one of Embodiments 1-21, wherein:
    a) the V_H comprises the amino acid sequence of SEQ ID NO:15; and
    b) the V_L comprises the amino acid sequence of SEQ ID NO:28.

34. The polypeptide of any one of Embodiments 1-21, wherein:
    a) the V_H comprises the amino acid sequence of SEQ ID NO:16; and
    b) the V_L comprises the amino acid sequence of SEQ ID NO:29.

35. The polypeptide of any one of Embodiments 1-21, wherein:

a) the V_H comprises the amino acid sequence of SEQ ID NO:17; and

b) the V_L comprises the amino acid sequence of SEQ ID NO:30.

36. The polypeptide of any one of Embodiments 1-35, wherein the V_H and V_L are humanized, contain human framework regions, or a combination thereof.

37. The polypeptide of any one of Embodiments 1-36, wherein the polypeptide is an antibody or an antigen-binding fragment thereof, optionally comprising an Fc domain, in particular embodiments wherein the Fc domain comprises an effector function mutation (*see, e.g.*, Dumet *et al*. MABS 2019 (particularly Tables 1 and 2 therein), WO02060919), in more particular embodiments wherein the Fc domain comprises LS (M428L/N434S by Kabat) or YTE (M252Y/S254T/T256E by Kabat numbering).

38. The polypeptide of Embodiment 37, wherein the antigen binding fragment is selected from Fab, $F(ab')_2$, Fab', scFv, or Fv.

39. The polypeptide of Embodiment 37, further comprising an antibody heavy chain constant domain sequence, an antibody light chain constant domain sequence, or both an antibody heavy chain constant domain sequence and an antibody light chain constant domain sequence.

40. The polypeptide of Embodiment 39, wherein the antibody heavy chain constant domain is selected from the group consisting of an IgA constant domain, an IgD constant domain, an IgE constant domain, an IgG constant domain and an IgM constant domain.

41. The polypeptide of Embodiment 40, wherein the antibody heavy chain constant domain is an IgG2 heavy chain constant domain.

42. The polypeptide of any one of Embodiments 39-41, further comprising an antibody light chain constant domain selected from the group consisting of a κ constant domain or a λ constant domain.

43. The polypeptide of Embodiment 42, wherein the antibody light chain constant domain is a λ light chain constant domain.

44. The polypeptide of any one of Embodiments 1-43, wherein the polypeptide is conjugated to a heterologous moiety.

45. The polypeptide of Embodiment 44, wherein the heterologous moiety is a therapeutic agent, a diagnostic agent or a combination thereof

46. The polypeptide of Embodiment 44, wherein the heterologous moiety is selected from the group consisting of polyethylene glycol (PEG), hexadecanoic acid, a hydrogel, a lipid nanoparticle, a polymer nanoparticle, and a heterologous polypeptide sequence, or a combination thereof.

47. The polypeptide of Embodiment 46, wherein the polymer nanoparticle comprises poly(lactic-co-glycolic) acid (PLGA).

48. The polypeptide of Embodiment 44, wherein the heterologous polypeptide sequence comprises a carrier polypeptide.

49. The polypeptide of Embodiment 48, wherein the carrier polypeptide is albumin or an Fc polypeptide.

50. The polypeptide of any one of Embodiments 1-49, wherein the polypeptide:
    a) is capable of binding to an epitope in a TSLP protein (*e.g.*, a full-length human TSLP);
    b) binds a TSLP protein with a K_D of 1 μM or less;
    c) neutralizes an activity of a TSLP protein;
    d) reduces a TSLP-induced signal in a human cell,
    or any combination of the foregoing.

51. The polypeptide of Embodiment 50, wherein the polypeptide binds TSLP with a K_D of about 2 pM or less as measured by KinExA.

52. The polypeptide of Embodiment 50, wherein the polypeptide neutralizes an activity of TSLP with an IC_{50} of about 500 pM or less.

53. The polypeptide of Embodiment 50, wherein the polypeptide reduces a TSLP-induced signal in a human cell by at least about 30%.

54. A fusion protein comprising the polypeptide of any one of Embodiments 1-53.

55. A polynucleotide (*e.g.*, DNA or RNA; linear or circular; optionally containing one or more modified nucleotides) comprising a sequence encoding the polypeptide of any one of Embodiments 1-53 or the fusion protein of Embodiment 54.

56. A vector (*e.g.*, an expression vector, including a viral-delivery vector) comprising the polynucleotide of Embodiment 55.

57. A host cell comprising the polynucleotide of Embodiment 55 or the vector of Embodiment 56.

58. A composition comprising the polypeptide of any one of Embodiments 1-53 or the fusion protein of Embodiment 54 or the polynucleotide of Embodiment 55.

59. The composition of Embodiment 58, further comprising one or more pharmaceutical excipients, diluents, or carriers.

60. A method of treating a subject in need thereof, comprising administering an effective amount of the composition of Embodiment 58 or 59 to the subject.

61. A method of reducing binding of TSLP to TSLPR on a cell in a subject, comprising contacting the cell with an effective amount of the composition of Embodiment 58 or 59.

62. The method of Embodiment 60 or 61, wherein the subject has, or is suspected of having, a TSLP-associated disease or condition.

63. The method of Embodiment 60 or 61, wherein the subject is at risk of developing a TSLP-associated disease or condition.

64. The method of any one of Embodiments 60-63, wherein the subject is a human.

65. The method of any one of Embodiments 62 or 63, wherein the TSLP-associated disease or condition is selected from the group consisting of asthma, atopic dermatitis (AD), chronic obstructive pulmonary disease (COPD), chronic spontaneous urticaria

(CSU), rheumatoid arthritis (RA), rhinosinusitis (RS), cancer, a food-hypersensitivity reaction, and combinations thereof.

66. The method of any one of Embodiments 60-65, wherein the subject is 18 years or older.

67. The method of any one of Embodiments 60-66, further comprising administering a therapeutically effective amount of an additional therapeutic or prophylactic agent to the subject.

68. The method of any one of Embodiments 60-67, wherein the subject has asthma.

69. The method of any one of Embodiments 60-67, wherein the subject has AD.

70. A polypeptide that specifically binds human thymic stromal lymphopoietin (TSLP):

wherein a computationally binding optimized (CBO) model outputs a score that is above a predetermined threshold upon scoring an amino acid sequence of the polypeptide.

71. A computationally binding optimized (CBO) polypeptide that specifically binds a thymic stromal lymphopoietin (TSLP):

wherein a computationally binding optimized (CBO) model outputs a score that is above a predetermined threshold upon scoring an amino acid sequence representing the CBO polypeptide.

72. A polypeptide that specifically binds a thymic stromal lymphopoietin (TSLP) and receives a score above a predetermined threshold from a CBO model upon scoring an amino acid sequence representing the polypeptide.

73. A polypeptide that specifically binds a thymic stromal lymphopoietin (TSLP):

wherein the polypeptide being assigned a score above a predetermined threshold from a CBO model upon scoring an amino acid sequence representing the polypeptide.

74. A computationally binding optimized (CBO) polypeptide, determined by a computationally binding optimized (CBO) model that specifically binds a human thymic stromal lymphopoietin (TSLP).

75. The CBO polypeptide of any of Embodiments 70-74, wherein the CBO model is calculated by a table substantially similar to that of Computer Program Listing Appendix B.

76. The CBO polypeptide of any of Embodiments 70-75, wherein the CBO polypeptide is calculated using the Computer Program Listing Appendix B.

77. The CBO polypeptide of any of Embodiments 70-76, wherein the CBO polypeptide is scored by a script substantially similar to Computer Program Listing Appendix A, the script employing the CBO model substantially similar to the table of Computer Program Listing Appendix B, wherein the CBO polypeptide has a logarithmic score above -7.7.

78. The CBO polypeptide of any of Embodiments 70-77, wherein the CBO polypeptide is scorable by the script of Computer Program Listing Appendix A.

79. The polypeptide of any of Embodiments 70-78, wherein the predetermined threshold is the logarithmic probability that the sequence inputted to the script would occur given the weights of the Potts model.

80. The polypeptide of any of Embodiments 70-79, wherein a CBO script scoring the polypeptide receives a trained first- and second- order energy score table of outputted weights of a model trained by a plurality of known amino acid sequences and corresponding properties of the known amino acid sequences.

81. The polypeptide of any of Embodiments 70-80, wherein the polypeptide comprises an immunoglobulin heavy chain variable domain (V_H) and an immunoglobulin light chain variable domain (V_L).

82. The polypeptide of any of Embodiments 70-81, wherein the polypeptide has one or more properties selected from:

a binding affinity for the TSLP characterized by a K_D of 10 pM or less (*e.g.*, as measured by KinExA);

a binding specificity for the AB-loop region and the C-terminal region of helix D of the TSLP;

a neutralizing activity against the TSLP (*e.g.*, a full-length human TSLP); or

an inhibitory activity against TSLP-mediated signaling,
or a combination of the foregoing.

83. The polypeptide of any of Embodiments 70-82, wherein the polypeptide comprises a V_H and V_L pair selected from:
SEQ ID NO:4 and SEQ ID NO:20 (AB-1);
SEQ ID NO:5 and SEQ ID NO:21 (AB-2);
SEQ ID NO:6 and SEQ ID NO:20 (AB-3);
SEQ ID NO:7 and SEQ ID NO:22 (AB-4);
SEQ ID NO:8 and SEQ ID NO:23 (AB-5);
SEQ ID NO:9 and SEQ ID NO:24 (AB-6);
SEQ ID NO:10 and SEQ ID NO:25 (AB-7);
SEQ ID NO:11 and SEQ ID NO:20 (AB-8);
SEQ ID NO:12 and SEQ ID NO:20 (AB-9);
SEQ ID NO:13 and SEQ ID NO:26 (AB-10);
SEQ ID NO:14 and SEQ ID NO:27 (AB-11);
SEQ ID NO:15 and SEQ ID NO:28 (AB-12);
SEQ ID NO:16 and SEQ ID NO:29 (AB-13); or
SEQ ID NO:17 and SEQ ID NO:30 (AB-14).

84. The polypeptide of any of Embodiments 70-83, wherein the polypeptide does not comprise a V_H and V_L pair selected from:
SEQ ID NO:4 and SEQ ID NO:20 (AB-1);
SEQ ID NO:5 and SEQ ID NO:21 (AB-2);
SEQ ID NO:6 and SEQ ID NO:20 (AB-3);
SEQ ID NO:7 and SEQ ID NO:22 (AB-4);
SEQ ID NO:8 and SEQ ID NO:23 (AB-5);
SEQ ID NO:9 and SEQ ID NO:24 (AB-6);
SEQ ID NO:10 and SEQ ID NO:25 (AB-7);
SEQ ID NO:11 and SEQ ID NO:20 (AB-8);
SEQ ID NO:12 and SEQ ID NO:20 (AB-9);
SEQ ID NO:13 and SEQ ID NO:26 (AB-10);
SEQ ID NO:14 and SEQ ID NO:27 (AB-11);
SEQ ID NO:15 and SEQ ID NO:28 (AB-12);

SEQ ID NO:16 and SEQ ID NO:29 (AB-13); or

SEQ ID NO:17 and SEQ ID NO:30 (AB-14).

85. A computer-implemented method comprising:

scoring a polypeptide sequence with a computationally binding optimized (CBO) model, the CBO model:

for each amino acid position of the polypeptide sequence, calculating a plurality of energy scores, the energy scores based on having substituted the amino acid at a given position in the polypeptide sequence with each of a plurality of different amino acids,

adding each energy score calculated to an array,

generating a normalized sum of the energy scores for each position,

calculating a logarithm of each energy score calculated, and

generating a score of the polypeptide sequence by summing the logarithms of each energy score calculated, the score representing a functional property of the polypeptide.

86. A system comprising:

a processor; and

a memory with computer code instructions stored thereon, the processor and the memory, with the computer code instructions, being configured to cause the system to:

score a polypeptide sequence with a CBO model, the CBO model:

for each amino acid position of the polypeptide sequence, calculating a plurality of energy scores, the energy scores based on having substituted the amino acid at a given position in the polypeptide sequence with each of a plurality of different amino acids,

adding each energy score calculated to an array,

generating a normalized sum of the energy scores for each position,

calculating a logarithm of each energy score calculated, and

generating a score of the polypeptide sequence by summing the logarithms of each energy score calculated, the score representing a functional property of the polypeptide.

87. A computer-implemented method comprising:

scoring a polypeptide comprising an amino acid sequence with a computationally binding optimized (CBO) model for a functional property relating to modulating the activity of a target molecule, the CBO model:

for each amino acid position of the amino acid sequence of the polypeptide, calculating a plurality of energy scores, the energy scores based on the amino acid at a given position in the amino acid sequence,

adding each energy score calculated to an array,

generating a normalized sum of the energy scores for each position, and

generating a score of the polypeptide by summing each energy score calculated, the score representing the functional property of the polypeptide, the functional property relating to the polypeptide modulating the activity of the target molecule.

88. The computer-implemented method of Claim 87, further comprising:

calculating a logarithm of each energy score calculated.

89. The computer-implemented method of Claim 87 or 88, wherein summing each energy score calculated is performed by summing the logarithms of each energy score calculated.

90. The computer-implemented method of any of Claims 87-89, wherein the energy scores are further calculated based on having substituted the amino acid at the given position in the amino acid sequence with each of a plurality of different amino acids.

91. The computer-implemented method of any of Claims 87-90, wherein the target molecule is a target polypeptide.

92. The computer-implemented method of any of Claims 87-91, wherein scoring the polypeptide using the CBO model is implementable by the script of Appendix A.

93. The computer-implemented method of any of Claims 87-92, wherein the CBO model is substantially similar to the table of Appendix B.

94. The computer-implemented method of any of Claims 87-93, wherein scoring the polypeptide further includes:

extracting a plurality of positions from the amino acid sequence, the plurality of positions being positions where mutations were applied during training of the CBO model;

wherein calculating the plurality of energy scores is performed on the extracted plurality of positions.

95. The computer-implemented method of any of Claims 87-94, wherein scoring the polypeptide further includes scoring a pair of amino acid sequences, and scoring the polypeptide further comprises:

aligning a first amino acid sequence and second amino acid sequence of the pair of amino acid sequences such that the first amino acid sequence and second amino acid sequence are the same length and that given sections of the first amino acid sequence and second amino acid sequence are the same.

96. The computer-implemented method of any of Claims 87-95, wherein the plurality of energy scores includes a first-order energy score associated with each amino acid being at its position and, for each pair of amino acid positions of the amino acid sequence, a second-order energy score associated with the pair of amino acid positions, the first-order energy score and second-order energy score calculated based on corresponding entries of a trained first- and second- order energy score table of outputted weights of a model trained by a plurality of known amino acid sequences and corresponding properties of the known amino acid sequences.

97. The computer-implemented method of any of Claims 87-96, further comprising:

returning, based on the score, a flag indicating whether the sequence has the functional property associated with the polypeptide.

98. The computer-implemented method of any of Claims 87-97, wherein the functional property is at least one of:

a binding affinity for a thymic stromal lymphopoietin (TSLP) polypeptide characterized by a K_D of 10 pM or less; (optionally, as measured by KinExA);

a binding specificity for the AB-loop region and the C-terminal region of helix D of the TSLP polypeptide;

a neutralizing activity against the TSLP polypeptide (optionally, a full-length human TSLP); or

an inhibitory activity against TSLP-mediated signaling,

or a combination of the foregoing.

99. A system comprising:

a processor; and

a memory with computer code instructions stored thereon, the processor and the memory, with the computer code instructions, being configured to cause the system to:

score a polypeptide comprising an amino acid sequence with a CBO model for a functional property relating to modulating the activity of a target molecule, the CBO model:

for each amino acid position of the amino acid sequence of the polypeptide, calculating a plurality of energy scores, the energy scores based on the amino acid at a given position in the amino acid sequence,

add each energy score calculated to an array,

generate a normalized sum of the energy scores for each position, and

generate a score of the amino acid sequence by summing each energy score calculated, the score representing a functional property of the polypeptide, the functional property relating to the polypeptide modulating the activity of the target molecules.

100. The system of Claim 99, wherein the instructions are further configured to cause the system to calculate a logarithm of each energy score calculated.

101. The system of Claim 99 or 100, wherein summing each energy score calculated is performed by summing the logarithms of each energy score calculated.

102. The system of any of Claims 99-101, wherein the energy scores are further calculated based on having substituted the amino acid at the given position in the amino acid sequence with each of a plurality of different amino acids.

103. The system of any of Claims 99-102 , wherein the target molecule is a target polypeptide.

104. The system of any of Claims 99-103, wherein scoring the polypeptide using the CBO model is implemented by the script of Appendix A.

105. The system of any of Claims 99-104, wherein the CBO model is substantially similar to the table of Appendix B.

106. The system of any of Claims 99-105, wherein scoring the polypeptide further includes:

extracting a plurality of positions from the amino acid sequence, the plurality of positions being positions where mutations were applied during training of the CBO model;

wherein calculating the plurality of energy scores is performed on the extracted plurality of positions.

107. The system of any of Claims 99-106, wherein scoring the polypeptide further includes scoring a pair of amino acid sequences, and scoring the polypeptide further comprises:

aligning a first amino acid sequence and second amino acid sequence of the pair of amino acid sequences such that the first amino acid sequence and second amino acid sequence are the same length and that given sections of the first amino acid sequence and second amino acid sequence are the same.

108. The system of any of Claims 99-107, wherein the plurality of energy scores includes a first-order energy score associated with each amino acid being at its position and, for each pair of amino acid positions of the amino acid sequence, a second-order energy score associated with the pair of amino acid positions, the first-order energy score and second-order energy score being calculated by respective entries from a trained first- and second- order energy score table of outputted weights of a model trained by a plurality of known amino acid sequences and corresponding properties of the known amino acid sequences.

109. The system of any of Claims 99-108, further comprising:

returning, based on the score, a flag indicating whether the sequence has the functional property associated with the polypeptide.

110. The system of any of Claims 99-109, wherein the functional property is at least one of:

a binding affinity for a thymic stromal lymphopoietin (TSLP) polypeptide characterized by a K_D of 10 pM or less; (optionally, as measured by KinExA);

a binding specificity for the AB-loop region and the C-terminal region of helix D of the TSLP polypeptide;

a neutralizing activity against the TSLP polypeptide (optionally, a full-length human TSLP); or

an inhibitory activity against TSLP-mediated signaling,

or a combination of the foregoing.

111. A polypeptide that specifically binds a thymic stromal lymphopoietin (TSLP):

wherein the polypeptide comprises an amino acid sequence that is assigned a score above a predetermined threshold by a computationally binding optimized (CBO) model upon scoring the amino acid sequence of the polypeptide.

112. The polypeptide of Claim 111, wherein the CBO model is calculated by a table substantially similar to that of Computer Program Listing Appendix B.

113. The polypeptide of Claim 111-112, wherein the polypeptide is assigned the score that is calculated using the Computer Program Listing Appendix B.

114. The polypeptide of any of Claims 111-113, wherein the polypeptide is assigned the score by a script substantially similar to Computer Program Listing Appendix A, the script employing the CBO model substantially similar to the table of Computer Program Listing Appendix B, wherein the polypeptide has a logarithmic score of about: -7.7, -7.0, -6.5, -6.0, -5.5, -5.0, -4.5, -4.0, -3.5, -3.0, 2.9, -2.8, -2.7, -2.6, -2.5, -2.4, -2.3, -2.2, -2.1, -2.0, -1.9, -1.8, -1.7, -1.6, -1.5, -1.4, -1.3, -1.2, -1.1, -1.0, 0.9, -0.8, -0.7, -0.6, -0.5, -0.4, -0.3, -0.2, and -0.1.

115. The polypeptide of any of Claims 111-114, wherein the polypeptide is scorable by the script of Computer Program Listing Appendix A.

116. The polypeptide of any of Claims 111-115, wherein the predetermined threshold is the logarithmic probability that the sequence inputted to the script would occur given the weights of the Potts model.

117. The polypeptide of any of Claims 111-116, wherein a CBO script assigning the score to the polypeptide includes receiving a trained first- and second- order energy score table of outputted weights of a model trained by a plurality of known amino acid sequences and corresponding properties of the known amino acid sequences.

118. The polypeptide of any of Claims 111-117, wherein the polypeptide comprises an immunoglobulin heavy chain variable domain (V_H) and an immunoglobulin light chain variable domain (V_L).

119. The polypeptide of any of Claims 111-118, wherein the polypeptide has one or more properties selected from:

a binding affinity for a thymic stromal lymphopoietin (TSLP) polypeptide characterized by a K_D of 10 pM or less; (optionally, as measured by KinExA);

a binding specificity for the AB-loop region and the C-terminal region of helix D of the TSLP polypeptide;

a neutralizing activity against the TSLP polypeptide (optionally, a full-length human TSLP); or

an inhibitory activity against TSLP-mediated signaling,

or a combination of the foregoing.

120. The polypeptide of any of Claims 111-119, wherein the CBO model outputs a score that is equal to or above a score from the CBO model of one or more of a reference polypeptide that comprises a V_H and V_L pair selected from:

SEQ ID NO:4 and SEQ ID NO:20 (AB-1);

SEQ ID NO:5 and SEQ ID NO:21 (AB-2);

SEQ ID NO:6 and SEQ ID NO:20 (AB-3);

SEQ ID NO:7 and SEQ ID NO:22 (AB-4);

SEQ ID NO:8 and SEQ ID NO:23 (AB-5);

SEQ ID NO:9 and SEQ ID NO:24 (AB-6);

SEQ ID NO:10 and SEQ ID NO:25 (AB-7);

SEQ ID NO:11 and SEQ ID NO:20 (AB-8);
SEQ ID NO:12 and SEQ ID NO:20 (AB-9);
SEQ ID NO:13 and SEQ ID NO:26 (AB-10);
SEQ ID NO:14 and SEQ ID NO:27 (AB-11);
SEQ ID NO:15 and SEQ ID NO:28 (AB-12);
SEQ ID NO:16 and SEQ ID NO:29 (AB-13); or
SEQ ID NO:17 and SEQ ID NO:30 (AB-14).

121. The polypeptide of any of Claims 111-120, wherein the polypeptide comprises a V_H and V_L pair selected from:

SEQ ID NO:4 and SEQ ID NO:20 (AB-1);
SEQ ID NO:5 and SEQ ID NO:21 (AB-2);
SEQ ID NO:6 and SEQ ID NO:20 (AB-3);
SEQ ID NO:7 and SEQ ID NO:22 (AB-4);
SEQ ID NO:8 and SEQ ID NO:23 (AB-5);
SEQ ID NO:9 and SEQ ID NO:24 (AB-6);
SEQ ID NO:10 and SEQ ID NO:25 (AB-7);
SEQ ID NO:11 and SEQ ID NO:20 (AB-8);
SEQ ID NO:12 and SEQ ID NO:20 (AB-9);
SEQ ID NO:13 and SEQ ID NO:26 (AB-10);
SEQ ID NO:14 and SEQ ID NO:27 (AB-11);
SEQ ID NO:15 and SEQ ID NO:28 (AB-12);
SEQ ID NO:16 and SEQ ID NO:29 (AB-13); or
SEQ ID NO:17 and SEQ ID NO:30 (AB-14).

122. The polypeptide of any of Claims 111-121, wherein the polypeptide does not comprise a V_H and V_L pair selected from:

SEQ ID NO:4 and SEQ ID NO:20 (AB-1);
SEQ ID NO:5 and SEQ ID NO:21 (AB-2);
SEQ ID NO:6 and SEQ ID NO:20 (AB-3);
SEQ ID NO:7 and SEQ ID NO:22 (AB-4);
SEQ ID NO:8 and SEQ ID NO:23 (AB-5);
SEQ ID NO:9 and SEQ ID NO:24 (AB-6);
SEQ ID NO:10 and SEQ ID NO:25 (AB-7);

SEQ ID NO:11 and SEQ ID NO:20 (AB-8);
SEQ ID NO:12 and SEQ ID NO:20 (AB-9);
SEQ ID NO:13 and SEQ ID NO:26 (AB-10);
SEQ ID NO:14 and SEQ ID NO:27 (AB-11);
SEQ ID NO:15 and SEQ ID NO:28 (AB-12);
SEQ ID NO:16 and SEQ ID NO:29 (AB-13); or
SEQ ID NO:17 and SEQ ID NO:30 (AB-14).

123. The polypeptide of any of Claims 111-122, wherein the polypeptide does not comprise a heavy chain comprising SEQ ID NO:81 and a light chain comprising SEQ ID NO:82.

124. A polypeptide:
wherein the polypeptide comprises an amino acid sequence that is assigned a score above a predetermined threshold by a computationally binding optimized (CBO) model upon scoring the amino acid sequence of the polypeptide.

125. A polypeptide that binds human thymic stromal lymphopoietin (TSLP), wherein the polypeptide is designed by a method comprising:
generating a polypeptide sequence with a CBO model;
verifying the generated polypeptide sequence using the CBO model by:
for each amino acid position of the polypeptide sequence, calculating a plurality of energy scores, the energy scores based on having substituted the amino acid at a given position in the polypeptide sequence with each of a plurality of different amino acids,
adding each energy score calculated to an array,
generating a normalized sum of the energy scores for each position,
calculating a logarithm of each energy score calculated, and
generating a score of the polypeptide sequence by summing the logarithms of each energy score calculated, the score representing a functional property of the polypeptide's ability to bind to human TSLP.

126. The polypeptide of Claim 125, wherein the polypeptide is scored at least a score of about: -7.7, -7.0, -6.5, -6.0, -5.5, -5.0, -4.5, -4.0, -3.5, -3.0, 2.9, -2.8, -2.7, -2.6, -2.5, -

2.4, -2.3, -2.2, -2.1, -2.0, -1.9, -1.8, -1.7, -1.6, -1.5, -1.4, -1.3, -1.2, -1.1, -1.0, 0.9, -0.8, -0.7, -0.6, -0.5, -0.4, -0.3, -0.2, and -0.1.

127. A polypeptide that specifically binds human thymic stromal lymphopoietin (TSLP):

wherein a computationally binding optimized (CBO) model outputs a score that is equal to or above a score from the CBO model of one or more of a reference polypeptide that comprises a V_H and V_L pair selected from:

SEQ ID NO:4 and SEQ ID NO:20 (AB-1);
SEQ ID NO:5 and SEQ ID NO:21 (AB-2);
SEQ ID NO:6 and SEQ ID NO:20 (AB-3);
SEQ ID NO:7 and SEQ ID NO:22 (AB-4);
SEQ ID NO:8 and SEQ ID NO:23 (AB-5);
SEQ ID NO:9 and SEQ ID NO:24 (AB-6);
SEQ ID NO:10 and SEQ ID NO:25 (AB-7);
SEQ ID NO:11 and SEQ ID NO:20 (AB-8);
SEQ ID NO:12 and SEQ ID NO:20 (AB-9);
SEQ ID NO:13 and SEQ ID NO:26 (AB-10);
SEQ ID NO:14 and SEQ ID NO:27 (AB-11);
SEQ ID NO:15 and SEQ ID NO:28 (AB-12);
SEQ ID NO:16 and SEQ ID NO:29 (AB-13); or
SEQ ID NO:17 and SEQ ID NO:30 (AB-14).

128. The polypeptide of any of Claims 111-127, wherein the polypeptide is an antibody or an antigen-binding fragment thereof.

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[00761] Headings used in this application are for convenience only and do not affect the interpretation of this application.

[00762] Preferred features of each of the aspects provided by the invention are applicable to all of the other aspects of the invention *mutatis mutandis* and, without limitation, are exemplified by the dependent claims and also encompass combinations and permutations of individual features (*e.g.*, elements, including numerical ranges and exemplary embodiments)

of particular embodiments and aspects of the invention, including the working examples. For example, particular experimental parameters exemplified in the working examples can be adapted for use in the claimed invention piecemeal without departing from the invention. For example, for materials that are disclosed, while specific reference of each of the various individual and collective combinations and permutations of these compounds may not be explicitly disclosed, each is specifically contemplated and described herein. Thus, if a class of elements A, B, and C are disclosed as well as a class of elements D, E, and F and an example of a combination of elements A-D is disclosed, then, even if each is not individually recited, each is individually and collectively contemplated. Thus, in this example, each of the combinations A-E, A-F, B-D, B-E, B-F, C-D, C-E, and C-F are specifically contemplated and should be considered disclosed from disclosure of A, B, and C; D, E, and F; and the example combination A-D. Likewise, any subset or combination of these is also specifically contemplated and disclosed. Thus, for example, the sub-groups of A-E, B-F, and C-E are specifically contemplated and should be considered disclosed from disclosure of A, B, and C; D, E, and F; and the example combination A-D. This concept applies to all aspects of this application, including elements of a composition of matter and steps of method of making or using the compositions.

[00763] The forgoing aspects of the invention, as recognized by the person having ordinary skill in the art following the teachings of the specification, can be claimed in any combination or permutation to the extent that they are novel and non-obvious over the prior art—thus, to the extent an element is described in one or more references known to the person having ordinary skill in the art, they may be excluded from the claimed invention by, *inter alia*, a negative proviso or disclaimer of the feature or combination of features.

Exemplification

Example 1. Production of Full-Length IgG Molecules

[00764] Variable heavy (V_H) chain and variable light (V_L) chain sequences were synthesized and cloned into mammalian expression vectors containing nucleotide sequences encoding corresponding constant regions using conventional methods to be expressed as full-length human immunoglobulin 1 (IgG1) antibodies. The antibodies were generated using one expression plasmid per chain, containing a CMV promoter to drive expression and a signal peptide to promote secretion of the fully folded IgG into the supernatant. Mammalian

expression host systems (such as the Chinese hamster ovary - CHO S cell line) were employed for protein expression using cationic lipid-based transient transfection methodologies with fed-batch production procedures. The expressed, soluble full-length IgG molecules were purified using an affinity capture-based purification method using Protein A-affinity resin (such as the MabSelect SuRe™ resin, Cytiva, Marlborough, MA) and aqueous buffers. Elution was performed under acidic conditions with low pH (such as pH 3.5) and then neutralized to pH 7.5 using 2M Tris base. The purified antibodies were further stabilized in aqueous buffers (such as Histidine-based buffers containing NaCl) for long-term storage/freezing.

Example 2. Polyspecific Reactivity of Candidate TSLP Binders

[00765] Non-specific interaction, or poly-specific reactivity (PSR), measures the potential for an antibody to bind non-specifically to things other than its desired target, in this case, TSLP. PSR was measured with using a low-stringency ELISA-based method (Tiller *et al.*, J Immunol Methods. 329:112-24 (2008)). Briefly, a 384-well assay plate was coated with 10 µg/mL salmon sperm DNA (Rockland Immunochemicals, Inc., Gilbertsville, PA) and incubated overnight at 4°C. All antigens were diluted in Tris-buffered saline (TBS). The assay plate was washed 3 times with 100 µL TBS-Tween-20 (TBS-T) on an automated plate washer and blocked with 100 µL of TBS-T with 5% bovine serum albumin (BSA) for one hour at 37°C. The assay plate was washed 3 times as before. The purified full-length IgG molecules described in Example 1 were normalized to 100 nM in TBS-T and distributed in duplicate. The plate was incubated for 1 hour at 37°C and again washed 3 times as before. DELFIA® (dissociation-enhanced lanthanide fluorescence immunoassay) Eu-N1 anti-human IgG secondary (PerkinElmer Inc., Waltham, MA) was diluted to 100 ng/mL in TBS-T plus 5% BSA, and 25 µL was distributed into each well. The plate was incubated for 1 hour at 37°C then washed 3 time as before. 25 µL of DELFIA® Enhancement Solution (PerkinElmer Inc.) was added to each well and incubated in the dark for 15 minutes. Time Resolved Fluorescence (TRF) was measured for each well. Polyspecific binding to DNA was quantified by dividing the raw signal over signal from buffer-only wells. Representative data are shown in Table 6.

Example 3. Self-Association of Candidate TSLP Binders

[00766] Self-interaction properties of the antibody candidates were measured by Affinity Capture Self-Interaction Nanoparticle Spectroscopy (AC-SINS) (Liu *et. al.*, mAbs. 6:483-92

(2014)). AC-SINS leverages the ability of gold nanoparticles to absorb light at signature wavelengths and generate surface plasmons. There is an observable shift in the nanoparticle absorption spectra when inter-nanoparticle distance changes. This shift occurs when gold nanoparticles pre-coated with anti-human Fc antibodies are incubated with antibody candidates that self-interact. More self-interaction between the antibody candidates causes an increased maximum absorbance wavelength in the nanoparticle absorption spectra, compared to spectra of nanoparticles alone ($\Delta\lambda_{MAX}$). Polyclonal goat anti-human IgG Fcγ antibodies (Jackson ImmunoResearch Laboratories, Inc., West Grove, PA, #109-005-098) and non-specific goat antibodies (Jackson ImmunoResearch Laboratories, Inc., Catalog #005-000-003) were used to pre-coat the gold nanoparticle (Ted Pella Inc., Redding, CA, Catalog #15705). Coating solution was prepared at a 4:1 (v/v) ratio between capture and non-capture antibodies (0.4 mg/mL total antibodies). A 9:1 (v/v) ratio solution with gold nanoparticles and coating solution was prepared before incubation at RT and blocking of the empty gold nanoparticle sites with 0.1 μM thiolated PEG (Sigma-Aldrich, St. Louis, MO, Catalog #729140-1G). This was then filtered through 0.22 μm PVDF membrane (Millex-GV Syringe Filter Unit, 13 mm, MilliporeSigma, Burlington, MA). The particles retained on top were eluted with 1 x PBS. This coating solution was incubated with the antibody candidates at RT for 2 hours in a polypropylene plate before being transferred on to a polystyrene UV transparent plate. Absorption spectra is measured at this point from 510 to 570 nm at in increment of 2 nm. These data were analyzed to determine the wavelength shifts that are indicative of self-interaction in the antibody candidates. Representative AC-SINS data is shown in Table 6.

Example 4. TSLP Binding Enzyme-Linked Immunosorbent Assay (ELISA)

[00767] Human TSLP (hTSLP) Binding ELISA

[00768] Binding affinity of anti-TSLP monoclonal antibodies (mAbs) to human TSLP was assessed using an indirect ELISA assay. A 96 well half area plate was coated with 2 μg/mL of recombinant human TSLP (BioLegend, San Diego, CA) overnight. The next day, the plate was washed three times with ELISA Wash Buffer (PBS-Tween 0.5%), blocked with 1x ELISA assay diluent (BioLegend) for one hour. Plates were then washed three times with ELISA Wash Buffer, followed by addition of the anti-TSLP antibodies at the indicated concentrations and incubation at 37°C for one hour. The plate was washed three times with ELISA Wash Buffer, and horseradish peroxidase (HRP)-conjugated anti-human IgG Fc

secondary antibody (Promega, Madison, WI) at 1:2000 dilution in 1x ELISA assay diluent was added to detect binding of the primary antibody to the antigen. The plate was incubated for 30 minutes at 37°C with the secondary detection antibody, then the plate was washed and developed with tetramethyl benzidine (TMB) substrate solution (Thermo Fisher Scientific, Waltham, MA). The HRP enzymatic reaction was stopped after about 1 minute with acidic stop solution (Thermo Fisher Scientific), and the absorbance at 450 nm was determined using a standard plate reader. The EC_{50} values were calculated by fitting a four-parameter non-linear regression line to the average of two technical replicates per concentration.

[00769] To determine the binding profile of anti-TSLP antibodies, a binding ELISA against recombinant human TSLP was completed. ELISA assay plates were coated with human TSLP cytokine, and subsequently serial dilutions of anti-TSLP antibodies were plated. After one hour of incubation, the plates were washed and the binding of anti-TSLP antibodies to hTSLP was detected with anti-human IgG Fc conjugated to HRP and developed with TMB substrate. FIGs. 4A-4B demonstrate the binding profile of anti-TSLP mAbs to hTSLP. The EC_{50} values were determined by curve fitting (non-linear regression) (Table 7).

[00770] Cynomolgus Monkey TSLP Binding ELISA

[00771] The human indirect TSLP binding ELISA assay protocol as described above was used to determine species cross-reactivity of anti-TSLP antibodies to cynomolgus monkey TSLP (ACROBiosystems, Newark, DE). EC_{50} values for primary antibodies binding cynomolgus monkey TSLP and human TSLP were compared.

[00772] To determine the binding profile of anti-TSLP antibodies, a binding ELISA against recombinant cynomolgus TSLP was completed. ELISA assay plates were coated with cynomolgus TSLP cytokine and subsequently serial dilutions of anti-TSLP antibodies were plated. After one hour of incubation, the plates were washed and the binding of anti-TSLP antibodies to cynoTSLP was detected with anti-human IgG Fc conjugated to HRP and developed with TMB substrate. FIGs. 5A-5B demonstrate the binding profile of anti-TSLP mAbs to cynoTSLP The EC_{50} values were determined by curve fitting (non-linear regression) (Table 7).

Example 5. TSLP Blocking ELISA

[00773] Human TSLP Blocking ELISA

[00774] A 96 well half area flat bottom plate was coated with 50 µL of recombinant heterodimeric human TSLPR and human IL-7Rα Fc tagged fusion protein (2 µg/mL) in

ELISA coating buffer. The plate was incubated overnight at 4°C and was washed thrice with 150 µL ELISA Wash Buffer (1X PBS-Tween 0.5%) the next day. The plate was blocked with 50 µL of ELISA assay diluent for one hour at 37°C and was washed three times with 150 µL of ELISA wash buffer. Serial dilutions of primary antibodies were pre-incubated with hTSLP-biotin cytokine in 50 µl of ELISA assay diluent for 30 minutes at 37°C, followed by addition to the ELISA plate. The ELISA plate was incubated for 1 hour at 37°C followed by washing three times with ELISA wash buffer. HRP-Streptavidin (Thermo Fisher Scientific) was diluted 1:2000 in ELISA assay diluent 50 µl was added to each well and incubated for 30 minutes at 37°C followed by washing three times with ELISA wash buffer. The ELISA was developed by addition of 50 µL of TMB substrate (Thermo Fisher Scientific) and incubation for 2-3 minutes at room temperature (protected from light). The reaction was stopped with acidic stop solution (Thermo Fisher Scientific), and the absorbance was read at 450 nm wavelength using a standard plate reader. Percent inhibition of signal and IC_{50} values were determined.

[00775] FIGs. 6A-6B demonstrate the ability of anti-TSLP antibodies to block hTSLP from binding its receptor (TSLPR). A blocking ELISA was performed by coating an ELISA plate with hTSLPR overnight. The next day, serial dilutions of primary antibodies were pre-incubated with hTSLP-biotin cytokine for 30 minutes at 37°C, followed by addition to the ELISA plate. The ELISA plate was incubated for 1 hour at 37°C, followed by washing of the plate. To detect blocking of hTSLP cytokines from binding to the receptors, a detection HRP-Streptavidin was added to the plate and incubated for 30 minutes at 37°C, followed by washing of the plate. The ELISA was developed with TMB substrate, and the HRP enzymatic reaction was stopped with sulfuric acid solution. Percent inhibition of signal and IC_{50} values were determined (Table 8).

[00776] Cynomolgus Monkey TSLP Blocking ELISA

[00777] The human TSLP blocking ELISA assay protocol as described previously was used to determine the ability of primary antibodies to block cynomolgus TSLP cytokine from binding cynomolgus TSLPR. IC_{50} values for primary antibodies ability to block cynomolgus monkey TSLP and human TSLP from binding the TSLPR were compared.

[00778] FIGs. 7A-7B demonstrate the ability of anti-TSLP antibodies to block cynoTSLP from binding its receptor (TSLPR). A blocking ELISA was performed by coating an ELISA plate with hTSLPR overnight. The next day, serial dilutions of primary antibodies were pre-

incubated with cynoTSLP-biotin cytokine for 30 minutes at 37°C, followed by addition to the ELISA plate. The ELISA plate was incubated for 1 hour at 37°C, followed by washing of the plate. To detect blocking of cynoTSLP cytokines from binding to the receptors, a detection HRP-Streptavidin was added to the plate and incubated for 30 minutes at 37°C, followed by washing of the plate. The ELISA was developed with TMB substrate, and the HRP enzymatic reaction was stopped with sulfuric acid solution. Percent inhibition of signal and IC_{50} values were determined (Table 8).

Example 6. Kinetic Exclusion Assay (KinExA)

[00779] The solution equilibrium binding experiments were performed using KinExA 3200 instrument equipped with an autosampler (Sapidyne Instruments, Boise, ID, USA). All analyses were performed at 25°C, and all samples were prepared in 1x phosphate-buffered saline (PBS) filtered buffer supplemented with 1 mg/mL bovine serum albumin (BSA) and 0.02% sodium azide. Human TSLP and cyno TSLP were covalently immobilized onto azlactone beads. To a 50 mg aliquot of azlactone beads, 20 µg of human TSLP or 20 µg of cyno TSLP diluted in 1 mL of coating solution (50 mM sodium carbonate, 0.5 M sodium citrate, pH 9.0) was added to the azlactone beads and rocked for 2 hours. The beads were washed with blocking buffer (1 M Tris supplemented with 10 mg/mL BSA, pH 8.0) and rocked for 1 hour.

[00780] The sample injection volumes and flow rates were varied depending upon the antibody tested. Fixed concentrations of antibody (referred to as the constant binding partner or CBP) were incubated with two-fold serial dilutions of human TSLP or cyno TSLP (referred to as the titrant) to generate two equilibrium titration curves. The samples containing human TSLP or cyno TSLP were equilibrated for at least 36 hours under constant rocking before measuring the unbound antibody on KinExA 3200. The antibody bound to human TSLP or cyno TSLP coated azlactone beads was detected using Alexa Fluor647 AffiniPure goat anti-human IgG (H+L) secondary antibody. The concentration, volume and flow rate of the secondary antibody were varied to achieve a signal at less than 1.0 V.

[00781] For each antibody-TSLP interaction, multiple curves from independent experiments were analyzed using the N-curve analysis tool to obtain K_D values and CBP activities with 95% confidence intervals from K_D-controlled and concentration-controlled curves, respectively. A 1:1 binding equilibrium model was used with the titrant selected as the reference concentration. The drift correction option was used where appropriate.

[00782] The k_a of each antibody-TSLP interaction was measured using the direct method. Fixed concentrations of antibody were mixed with the human TSLP or cyno TSLP concentration that bound approximately 80% of the CBP in the solution equilibrium binding experiments, and the concentration of free CBP present in the sample was repeatedly measured over time using the human TSLP or cyno TSLP coated azlactone beads. The resulting exponential curve of unbound antibody as a function of time was fitted to calculate the k_a of the antibody-TSLP interaction. The k_d was determined by multiplying the ka value measured from the direct method by the K_D value obtained from the solution equilibrium binding experiment (Table 9).

Example 7. Inhibition of STAT5-Luciferase Signal

[00783] Generation of the Ba/F3-STAT5-Luciferase-hTSLPR/hIL-7R Cell Line

[00784] Human TSLP Receptor (CRLF2) forms a heterodimeric complex with the IL-7Rα (CD127) after binding of TSLP. A hIL-7Rα-P2A-hTSLPR construct was synthesized and cloned into a pcDNA3.1(+)/Hygro plasmid. The plasmid was transfected into the Ba/F3-STAT5-Luc cell line, which contains a STS5-inducible Luciferase reporter, to create a stable cell line expressing hTSLPR and hIL-7Rα. Ba/F3-STAT5-Luc cells expressing hTSLPR/hIL-7R were maintained in RPMI-1640 with Glutamax medium containing 10% fetal bovine serum (FBS), 1% penicillin-streptomycin, 10 ng/mL hTSLP, and 400 µg/mL hygromycin selection antibiotic. The hTSLPR/hIL-7R-expressing Ba/F3-STAT5-Luc cells had a dose dependent response to hTSLP with an EC_{50} of 0.03 nM (FIG. 8A).

[00785] Ba/F3-STAT5-Luc Assay

[00786] In a 96-well maxi-sorp (Thermo Fisher Scientific) plate, serial dilutions of anti-TSLP antibodies in 25 µl of Assay Media (RPMI-1640 + 10% FBS) were pre-incubated with 25 µl of 4 ng/mL hTSLP cytokine (BioLegend) at 37°C for 30 minutes. After incubation, 20,000 Ba/F3-STAT5-hTSLPR/hIL-7R-Luc cells in 50 µl of cell media were plated and incubated with antibodies and TSLP cytokine for four hours. After four hours, 100 µl of luciferase reagent (BPS Bioscience Inc., San Diego, CA) was added to each well of the plate and rocked gently for 15 minutes at room temperature, protected from light. Luminescence was measured with a luminometer within one hour of luciferase reagent addition.

[00787] FIGs. 8B-8C show effects of the anti-TSLP antibodies on STAT5-dependent luciferase expression. The results demonstrate that the anti-TSLP antibodies block binding of hTSLP to TSLPR and in turn, inhibit STAT5 signaling. The luminescence signal values were

baseline corrected and transformed to percent inhibition using the STAT5-luciferase signal of unstimulated cells. The IC_{50} values were obtained by a non-linear curve fit (Table 10). The tested anti-TSLP antibodies can block TSLP from binding the TSLPR on cells.

Example 8. Inhibition of STAT5-Luciferase Signal

[00788] Myeloid Dendritic Cell (mDC) TSLP Stimulation Assay

[00789] Peripheral Blood Mononuclear Cells (PBMCs) were isolated from fresh whole blood by Ficoll-Paque density centrifugation from 5 independent donors and cryopreserved in medium containing 90% fetal bovine serum and 10% DMSO. PBMCs were thawed into PBS containing 5 mM EDTA and 2% FBS, counted and myeloid dendritic cells (mDCs) were isolated using StemCell Technologies EasySep Human Myeloid DC Enrichment Kit. In a 96-well maxi-sorp (Thermo Fisher Scientific) plate serial dilutions of anti-TSLP antibodies in 25 µl of Assay Media (RPMI-1640 + 10% FBS) are pre-incubated with 25 µl of 1 ng/ml hTSLP cytokine (BioLegend) at 37°C for 30 minutes. After incubation 1E5 mDCs were plated and incubated with the antibodies and TSLP cytokine for forty-eight hours at 37°C. Media were collected, and the concentrations of CCL17 (TARC) were measured on an MSD instrument.

[00790] FIGs. 9B-9C show effects of the anti-TSLP antibodies on TSLP-induced CCL17 expression by mDCs from one representative donor. The results demonstrate that the anti-TSLP antibodies block binding of hTSLP to TSLPR and in turn, inhibit CCL17 secretion by mDCs. The IC_{50} values were obtained by a non-linear curve fit (Table 11). The tested anti-TSLP antibodies can block TSLP from binding the human mDCs from peripheral blood.

Example 9. Human TSLP Binding Enzyme-Linked Immunosorbent Assay (ELISA)

[00791] The binding affinity of anti-TSLP monoclonal antibodies (mAbs) to human TSLP, cyno TSLP, mouse TSLP, and human IL-7 was assessed using an indirect ELISA assay. A 96 well half area plate was coated with 2 µg/mL of recombinant protein (human TSLP, cyno TSLP, mouse TSLP, human IL-7) overnight at 4°C. The next day, the plates were washed three times with ELISA wash buffer and blocked with ELISA assay diluent B (BioLegend) for one hour at room temperature (RT). Plates were then washed three times with ELISA wash buffer, afterwards anti-TSLP antibodies (AB-2a, AB-2b, the Reference Antibody, IgG1 and IgG2 isotype controls) were added at the indicated concentrations and incubated at RT for one hour. Antibody binding was assessed using an 8-point titration curve in triplicates (1:3 serial dilution starting at 10 µg/mL). The plate was washed three times with ELISA wash buffer, and HRP-conjugated anti-human IgG-HRP secondary antibody (Jackson

ImmunoResearch Laboratories, Inc.) was added to wells at a 1:5000 dilution in 1x ELISA assay diluent. Secondary antibody was added to detect binding of the primary antibody to the antigen. The plate was incubated for 30 minutes at room temperature with the secondary detection antibody, then the plates were washed three times with ELISA wash buffer and developed with TMB substrate solution (Invitrogen, Waltham, MA). The HRP enzymatic reaction was stopped after about 1 minute with acidic stop solution (Invitrogen), and the absorbance at 450 nm on a Biotek plate reader.

[00792] The EC_{50} values were calculated using Graphpad Prism 9.2.0 by fitting a four-parameter non-linear regression curve to the average absorbance values of three technical replicates per concentration with three independent experiments. Curve fitting was set up as reported in Graphpad Prism 9.2.0 software documentation. Results for human TSLP are displayed as EC_{50}, EC_{80}, EC_{90} (μg/mL) with 95% confidence intervals (Table 12, FIG. 10A). N=4 independent experiments with 3 technical replicates. Results for cyno TSLP are displayed as EC_{50}, EC_{80}, EC_{90} (μg/mL) with 95% confidence intervals (Table 12, FIG. 10B). N=3 independent experiments with 3 technical replicates.

[00793] Results for mouse TSLP and human IL-7 are displayed in FIG. 10C and FIG.10D, respectively. N=3 independent experiments with 3 technical replicates. Results are displayed as mean with SEM. N=3 independent experiments with 3 technical replicates. The ELISA results of AB-2a, AB-2b and the Reference Antibody demonstrate a lack of binding to mouse TSLP cytokine and human IL-7.

Example 10. Human (TSLPR/IL-7Rα) Ba/F3 Assay

[00794] Materials

[00795] Antibodies: (1) AB-2a (Lot# REQ0000500); (2) AB-2b (lot#1098-260922-02, production#GFA-002); (3) the Reference Antibody (lot# 1143666, SN:100000005714, GTIN: 00355513112017); (4) IgG1 isotype (BioLegend, Cat#403502, Lot# B372653); (5) IgG2 isotype (BioLegend, Cat#400264, Lot# B341585).

[00796] Antigens: (1) Human TSLP (AGN-000143, ACRO Biosystems, Newark, DE); (2) Human TSLP, His Tag (Cat# TSP-H52Hb, Lot# 2671b-2158F1-12T).

[00797] Cell line: BA/F3 cell line with STAT5 Reporter (Luc) (BPS Bioscience Inc., Cat No: 79772 Lot No: 200504#18), transfected with hTSLPR/hIL-7Rα expression vector from GenScript Biotech (Piscataway, New Jersey).

[00798] Assay plates: Cell culture microplate, 96-well, PS, F-bottom, white, CELLSTAR® with lid (Greiner bio-one, Kremsmünster, Austria, Cat no: 655083, Lot no: E211036T).

[00799] Assay Medium: RPMI+ GlutaMAX (1x) (RPMI Medium 1640, Gibco, Billings, Montana, Cat no: 61870-036, Lot No: 2472360) +10% FBS (R&D Systems, Minneapolis, MN, Cat no: S12495H Lot no: A21012) + 1% Penicillin-Streptomycin (Gibco, Cat no:15140-122, Lot no: 2441835).

[00800] Luciferase reagent: One-step Luciferase Assay system (BPS Bioscience Inc., Cat No: 78262, Lot No:230201).

[00801] To assess functional potency of anti-TSLP mAbs *in vitro*, a Ba/F3 reporter cell line expressing human TSLP receptor and IL-7Rα with a luciferase readout was created. Human TSLP receptor (TSLPR) forms a heterodimeric complex with the IL-7Rα (CD127) and signals through STAT5 after binding of TSLP. A hIL-7Rα-P2A-hTSLPR construct was synthesized and cloned into a pcDNA3.1(+)/Hygro plasmid. The plasmid was transfected into the Ba/F3-STAT5-Luc cell line, which contains a STAT5-inducible luciferase reporter, to create a stable cell line expressing hTSLPR and hIL-7Rα. Ba/F3-STAT5-Luciferase cells stably expressing hTSLPR/hIL-7R were maintained in RPMI-1640 with Glutamax medium containing 10% fetal bovine serum (FBS), 1% penicillin-streptomycin, 10 ng/mL hTSLP, and 400 µg/mL hygromycin selection antibiotic, cells were deprived of hTSLP for 24 hours prior to use in the assay. The Ba/F3-STAT5-hTSLPR/hIL-7R-Luc cells had a dose dependent response to hTSLP, 1 ng/mL hTSLP was used as a final concentration for this assay.

[00802] In a 96-well cell culture microplate, serial dilutions of 4X anti-TSLP antibodies in 25 µl of assay media (RPMI-1640 + 10% FBS + 1%P/S) were pre-incubated with 25 µl of 4 ng/mL (4X) hTSLP cytokine at 37°C for 30 minutes. The cytokines used in this assay were purchased from a single source commercial vendor and reconstituted based on vendor instructions. Afterwards 20,000 Ba/F3-STAT5-hTSLPR/hIL-7R-Luc cells in 50 µl of cell media were plated and incubated with 4X antibodies (each of AB-2a, AB-2b, the Reference Antibody, IgG1 isotype control, and IgG2 isotype control was added at 4X concentration) and TSLP cytokine for four hours. After four hours, 100 µl of luciferase reagent was added to each well of the plate and rocked gently for 15 minutes at room temperature (RT), protected from light. Luminescence was measured with a luminometer (Envision) within one hour of luciferase reagent addition.

[00803] Graphpad Prism 9.2.0 was used to analyze data. Average luminescence values of three technical replicates per concentration from three independent experiments were baseline

corrected and transformed to percent inhibition of signal. IC_{50} values were obtained by non-linear regression curve fitting, set up as reported in Graphpad Prism 9.2.0 software documentation. N=3 independent experiments with 3 technical replicates. Functional potency in blocking receptor binding to hTSLP cytokine are displayed as IC_{50} (µg/mL) with 95% confidence intervals. As shown in FIG. 11A and Table 13, AB-2b has improved functional potency compared to the Reference Antibody.

Example 11. Cyno (TSLPR/IL-7Rα) Ba/F3 Assay

[00804] Materials

[00805] Antibodies: (1) AB-2a (Lot# REQ0000500); (2) AB-2b (lot#1098-260922-02, production#GFA-002); (3) the Reference Antibody (lot# 1143666, SN:100000005714, GTIN: 00355513112017); (4) IgG1 isotype (BioLegend, Cat#403502, Lot# B372653); (5) IgG2 isotype (BioLegend, Cat#400264, Lot# B341585).

[00806] Antigens: (1) Cyno TSLP (AGN-000144, ACRO Biosystems); (2) Cyno TSLP His Tag (Cat# TSP-C52H8, Lot# 3509-2182F1-12T).

[00807] Cell line: BA/F3 cell line with STAT5 Reporter (Luc) (BPS Bioscience Inc., Cat No: 79772 Lot No: 200504#18), transfected with cyno TSLPR/cyno IL-7Rα expression vector from GenScript Biotech.

[00808] Assay plates: Cell culture microplate, 96-well, PS, F-bottom, white, CELLSTAR® with lid (Greiner bio-one, Kremsmünster, Austria, Cat no: 655083, Lot no: E211036T).

[00809] Assay Medium: RPMI+ GlutaMAX (1x) (RPMI Medium 1640, Gibco, Billings, Montana, Cat no: 61870-036, Lot No: 2472360) +10% FBS (R&D Systems, Minneapolis, MN, Cat no: S12495H Lot no: A21012) + 1% Penicillin-Streptomycin (Gibco, Cat no:15140-122, Lot no: 2441835).

[00810] Luciferase reagent: One-step Luciferase Assay system (BPS Bioscience Inc., Cat No: 78262, Lot No:230201).

[00811] To assess functional potency of anti-TSLP mAbs in vitro a Ba/F3 reporter cell line expressing cynomolgus monkey TSLP receptor and IL-7Rα with a luciferase readout was created. TSLP receptor (TSLPR) forms a heterodimeric complex with the IL-7Rα (CD127) and signals through STAT5 after binding of TSLP. A cynoIL-7Rα-P2A-cynoTSLPR construct was synthesized and cloned into a pcDNA3.1(+)/Hygro plasmid. The plasmid was transfected into the Ba/F3-STAT5-Luc cell line, which contains a STS5-inducible luciferase reporter, to create a stable cell line expressing cynomolgus TSLPR and cynoIL-7Rα. Ba/F3-

STAT5-Luciferase cells expressing cynoTSLPR/cynoIL-7R were maintained in RPMI-1640 with Glutamax medium containing 10% fetal bovine serum (FBS), 1% penicillin-streptomycin, 10 ng/mL cynoTSLP, 10 ng/mL hIL-7, and 200 µg/mL hygromycin selection antibiotic, cells were deprived of cynoTSLP for 24 hours prior to use in the assay. The Ba/F3-STAT5-cynoTSLPR/cynoIL-7R-Luc cells had a dose dependent response to cynoTSLP, 1 ng/mL cynoTSLP was used as a final concentration for this assay.

[00812] In a 96-well cell culture microplate, serial dilutions of 4X anti-TSLP antibodies in 25 µl of assay media (RPMI-1640 + 10% FBS + 1% penicillin-streptomycin) were pre-incubated with 25 µl of 4 ng/mL (4X) cynoTSLP cytokine at 37°C for 30 minutes. Afterwards 20,000 Ba/F3-STAT5-cynoTSLPR/cynoIL-7R-Luc cells in 50 µl of cell media were plated and incubated with antibodies and cynoTSLP cytokine for four hours. After four hours, 100 µl of luciferase reagent was added to each well of the plate and rocked gently for 15 minutes at room temperature (RT), protected from light. Luminescence was measured with a luminometer (Envision) within one hour of luciferase reagent addition.

[00813] Graphpad Prism 9.2.0 was used to analyze data. Average luminescence values of three technical replicates per concentration with three independent experiments were baseline corrected and transformed to percent inhibition of signal. IC_{50} values were obtained by non-linear regression curve fitting, set up as reported in Graphpad Prism 9.2.0 software documentation. Functional potency in blocking receptor binding to cynoTSLP cytokine are displayed as IC_{50} (µg/mL) with 95% confidence intervals. As shown in FIG. 11B and Table 13, AB-2b can block cynoTSLP and prevent signaling through the TSLPR/IL-7Rα complex. AB-2b has improved functional potency compared to the Reference Antibody.

Table 1. V_H Amino Acid Sequences

Name	SEQ ID	Amino Acid Sequence
Consensus	NO:2	QMQLVESGGGVVQPGRSLRLSCAASGFTFRTYGMHWVRQAPGKGLEWVAVX_1X_2Y X_3G$X_4X_5X_6$HYADSVKGRFTITRDNSKNTLNLQMNSLRAEDTAVYYCX_7RX_8PQWE $X_9X_{10}X_{11}$E$X_{12}X_{13}$DX_{14}WGQGTMVTVSS
Reference	NO:3	QMQLVESGGGVVQPGRSLRLSCAASGFTFRTYGMHWVRQAPGKGLEWVAVIWYD GSNKHYADSVKGRFTITRDNSKNTLNLQMNSLRAEDTAVYYCARAPQWELVHEA FDIWGQGTMVTVSS
AB-1	NO:4	QMQLVESGGGVVQPGRSLRLSCAASGFTFRTYGMHWVRQAPGKGLEWVAVVWYS GSYTHYADSVKGRFTITRDNSKNTLNLQMNSLRAEDTAVYYCSRSPQWEDIFEA MDIWGQGTMVTVSS
AB-2	NO:5	QMQLVESGGGVVQPGRSLRLSCAASGFTFRTYGMHWVRQAPGKGLEWVAVVWYD GSYTHYADSVKGRFTITRDNSKNTLNLQMNSLRAEDTAVYYCARSPQWEEIFEA MDIWGQGTMVTVSS
AB-3	NO:6	QMQLVESGGGVVQPGRSLRLSCAASGFTFRTYGMHWVRQAPGKGLEWVAVIWYD GTYTHYADSVKGRFTITRDNSKNTLNLQMNSLRAEDTAVYYCARSPQWESIFEA FDIWGQGTMVTVSS
AB-4	NO:7	QMQLVESGGGVVQPGRSLRLSCAASGFTFRTYGMHWVRQAPGKGLEWVAVIWYS GSDTHYADSVKGRFTITRDNSKNTLNLQMNSLRAEDTAVYYCARSPQWEDIFES MDVWGQGTMVTVSS
AB-5	NO:8	QMQLVESGGGVVQPGRSLRLSCAASGFTFRTYGMHWVRQAPGKGLEWVAVVWYD GYDTHYADSVKGRFTITRDNSKNTLNLQMNSLRAEDTAVYYCSRSPQWEDIFES MDIWGQGTMVTVSS
AB-6	NO:9	QMQLVESGGGVVQPGRSLRLSCAASGFTFRTYGMHWVRQAPGKGLEWVAVVWYD GSDIHYADSVKGRFTITRDNSKNTLNLQMNSLRAEDTAVYYCSRSPQWEDIFES MDIWGQGTMVTVSS
AB-7	NO:10	QMQLVESGGGVVQPGRSLRLSCAASGFTFRTYGMHWVRQAPGKGLEWVAVIWYS GAYIHYADSVKGRFTITRDNSKNTLNLQMNSLRAEDTAVYYCSRSPQWEDIFEA MDIWGQGTMVTVSS
AB-8	NO:11	QMQLVESGGGVVQPGRSLRLSCAASGFTFRTYGMHWVRQAPGKGLEWVAVIWYD GSYTHYADSVKGRFTITRDNSKNTLNLQMNSLRAEDTAVYYCARSPQWEDIFEA FDIWGQGTMVTVSS
AB-9	NO:12	QMQLVESGGGVVQPGRSLRLSCAASGFTFRTYGMHWVRQAPGKGLEWVAVIWYD GSYTHYADSVKGRFTITRDNSKNTLNLQMNSLRAEDTAVYYCARSPQWESIFEA FDIWGQGTMVTVSS
AB-10	NO:13	QMQLVESGGGVVQPGRSLRLSCAASGFTFRTYGMHWVRQAPGKGLEWVAVIWYS GTTTHYADSVKGRFTITRDNSKNTLNLQMNSLRAEDTAVYYCSRSPQWEDIFES MDIWGQGTMVTVSS
AB-11	NO:14	QMQLVESGGGVVQPGRSLRLSCAASGFTFRTYGMHWVRQAPGKGLEWVAVISYS GSYIHYADSVKGRFTITRDNSKNTLNLQMNSLRAEDTAVYYCTRSPQWEEVYEA LDIWGQGTMVTVSS
AB-12	NO:15	QMQLVESGGGVVQPGRSLRLSCAASGFTFRTYGMHWVRQAPGKGLEWVAVVWYD GSNTHYADSVKGRFTITRDNSKNTLNLQMNSLRAEDTAVYYCARAPQWESVHEA FDIWGQGTMVTVSS
AB-13	NO:16	QMQLVESGGGVVQPGRSLRLSCAASGFTFRTYGMHWVRQAPGKGLEWVAVISYD GSTKHYADSVKGRFTITRDNSKNTLNLQMNSLRAEDTAVYYCARAPQWESVYEA FDIWGQGTMVTVSS
AB-14	NO:17	QMQLVESGGGVVQPGRSLRLSCAASGFTFRTYGMHWVRQAPGKGLEWVAVIWYD GSTKHYADSVKGRFTITRDNSKNTLNLQMNSLRAEDTAVYYCARAPQWELVHEA FDIWGQGTMVTVSS

Table 2. V_L Amino Acid Sequences

Name	SEQ ID	Amino Acid Sequence
Consensus	NO:18	SYVLTQPPSVSVAPGQTARITCGGNX$_{15}$X$_{16}$GX$_{17}$X$_{18}$X$_{19}$VHWYQQKPGQAPVLVVYD DSDRPSWIPERFSGSNSGNTATLTISRGEAGDEADYYCQX$_{20}$X$_{21}$X$_{22}$X$_{23}$X$_{24}$X$_{25}$X$_{26}$ X$_{27}$VVFGGGTKLTVL
Reference	NO:19	SYVLTQPPSVSVAPGQTARITCGGNNLGSKSVHWYQQKPGQAPVLVVYDDSDRPS WIPERFSGSNSGNTATLTISRGEAGDEADYYCQVWDSSSDHVVFGGGTKLTVL
AB-1, 3, 8, 9	NO:20	SYVLTQPPSVSVAPGQTARITCGGNNIGSKSVHWYQQKPGQAPVLVVYDDSDRPS WIPERFSGSNSGNTATLTISRGEAGDEADYYCQVWDSSSSLVVFGGGTKLTVL
AB-2	NO:21	SYVLTQPPSVSVAPGQTARITCGGNNIGSKSVHWYQQKPGQAPVLVVYDDSDRPS WIPERFSGSNSGNTATLTISRGEAGDEADYYCQIWDSSSSLVVFGGGTKLTVL
AB-4	NO:22	SYVLTQPPSVSVAPGQTARITCGGNYIGSFSVHWYQQKPGQAPVLVVYDDSDRPS WIPERFSGSNSGNTATLTISRGEAGDEADYYCQIYVSASRLVVFGGGTKLTVL
AB-5	NO:23	SYVLTQPPSVSVAPGQTARITCGGNNLGSKSVHWYQQKPGQAPVLVVYDDSDRPS WIPERFSGSNSGNTATLTISRGEAGDEADYYCQVWDMSSDLVVFGGGTKLTVL
AB-6	NO:24	SYVLTQPPSVSVAPGQTARITCGGNNIGSKSVHWYQQKPGQAPVLVVYDDSDRPS WIPERFSGSNSGNTATLTISRGEAGDEADYYCQIWDSSSDHVVFGGGTKLTVL
AB-7	NO:25	SYVLTQPPSVSVAPGQTARITCGGNNLGSYSVHWYQQKPGQAPVLVVYDDSDRPS WIPERFSGSNSGNTATLTISRGEAGDEADYYCQVWDMSSSLVVFGGGTKLTVL
AB-10	NO:26	SYVLTQPPSVSVAPGQTARITCGGNNIGSKNVHWYQQKPGQAPVLVVYDDSDRPS WIPERFSGSNSGNTATLTISRGEAGDEADYYCQVWDSSDFLVVFGGGTKLTVL
AB-11	NO:27	SYVLTQPPSVSVAPGQTARITCGGNNIGSFSVHWYQQKPGQAPVLVVYDDSDRPS WIPERFSGSNSGNTATLTISRGEAGDEADYYCQVWSSTSRHVVFGGGTKLTVL
AB-12	NO:28	SYVLTQPPSVSVAPGQTARITCGGNNIGRFSVHWYQQKPGQAPVLVVYDDSDRPS WIPERFSGSNSGNTATLTISRGEAGDEADYYCQVWVSTSDKVVFGGGTKLTVL
AB-13	NO:29	SYVLTQPPSVSVAPGQTARITCGGNNLGSFSVHWYQQKPGQAPVLVVYDDSDRPS WIPERFSGSNSGNTATLTISRGEAGDEADYYCQVWDSSEDLVVFGGGTKLTVL
AB-14	NO:30	SYVLTQPPSVSVAPGQTARITCGGNNIGSKNVHWYQQKPGQAPVLVVYDDSDRPS WIPERFSGSNSGNTATLTISRGEAGDEADYYCQVWDESSDEVVFGGGTKLTVL

Table 3. CDR Amino Acid Sequences as Determined by ImMunoGeneTics (IMGT) Numbering

Name	SEQ ID	Amino Acid Sequence
HCDR1		
Consensus, Reference, AB-1-14	NO:31	GFTFRTYG
HCDR2		
Consensus	NO:32	X$_1$X$_2$YX$_3$GX$_4$X$_5$X$_6$
Reference	NO:33	IWYDGSNK
AB-1	NO:34	VWYSGSYT
AB-2	NO:35	VWYDGSYT
AB-3	NO:36	IWYDGTYT
AB-4	NO:37	IWYSGSDT
AB-5	NO:38	VWYDGYDT
AB-6	NO:39	VWYDGSDI
AB-7	NO:40	IWYSGAYI
AB-8, 9	NO:41	IWYDGSYT
AB-10	NO:42	IWYSGTTT
AB-11	NO:43	ISYSGSYI

AB-12	NO:44	VWYDGSNT
AB-13	NO:45	ISYDGSTK
AB-14	NO:46	IWYDGSTK
HCDR3		
Consensus	NO:47	$X_7RX_8PQWEX_9X_{10}X_{11}EX_{12}X_{13}DX_{14}$
Reference, AB-14	NO:48	ARAPQWELVHEAFDI
AB-1, 7	NO:49	SRSPQWEDIFEAMDI
AB-2	NO:50	ARSPQWEEIFEAMDI
AB-3, 9	NO:51	ARSPQWESIFEAFDI
AB-4	NO:52	ARSPQWEDIFESMDV
AB-5, 6, 10	NO:53	SRSPQWEDIFESMDI
AB-8	NO:54	ARSPQWEDIFEAFDI
AB-11	NO:55	TRSPQWEEVYEALDI
AB-12	NO:56	ARAPQWESVHEAFDI
AB-13	NO:57	ARAPQWESVYEAFDI
LCDR1		
Consensus	NO:58	$X_{15}X_{16}GX_{17}X_{18}X_{19}$
Reference, AB-5	NO:59	NLGSKS
AB-1-3, 6, 8, 9	NO:60	NIGSKS
AB-4	NO:61	YIGSFS
AB-7	NO:62	NLGSYS
AB-10, 14	NO:63	NIGSKN
AB-11	NO:64	NIGSFS
AB-12	NO:65	NIGRFS
AB-13	NO:66	NLGSFS
LCDR2		
Consensus, Reference, AB-1-14	NO:67	DDS
LCDR3		
Consensus	NO:68	$QX_{20}X_{21}X_{22}X_{23}X_{24}X_{25}X_{26}X_{27}VV$
Reference	NO:69	QVWDSSSDHVV
AB-1, 3, 8, 9	NO:70	QVWDSSSSLVV
AB-2	NO:71	QIWDSSSSLVV
AB-4	NO:72	QIYVSASRLVV
AB-5	NO:73	QVWDMSSDLVV
AB-6	NO:74	QIWDSSSDHVV
AB-7	NO:75	QVWDMSSSLVV
AB-10	NO:76	QVWDSSDFLVV
AB-11	NO:77	QVWSSTSRHVV
AB-12	NO:78	QVWVSTSDKVV
AB-13	NO:79	QVWDSSEDLVV
AB-14	NO:80	QVWDESSDEVV

Table 4. Heavy Chain Amino Acid Sequences

Name	SEQ ID	Amino Acid Sequence
Reference	NO:81	QMQLVESGGGVVQPGRSLRLSCAASGFTFRTYGMHWVRQAPGKGLEWVAVIWYD GSNKHYADSVKGRFTITRDNSKNTLNLQMNSLRAEDTAVYYCARAPQWELVHEA FDIWGQGTMVTVSSASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVS

Name	SEQ ID	Amino Acid Sequence
		WNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSNFGTQTYTCNVDHKPSNTKV DKTVERKCCVECPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHE DPEVQFNWYVDGVEVHNAKTKPREEQFNSTFRVVSVLTVVHQDWLNGKEYKCKV SNKGLPAPIEKTISKTKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDI AVEWESNGQPENNYKTTPPMLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEA LHNHYTQKSLSLSPGK
AB-1a	NO:91	QMQLVESGGGVVQPGRSLRLSCAASGFTFRTYGMHWVRQAPGKGLEWVAVVWYS GSYTHYADSVKGRFTITRDNSKNTLNLQMNSLRAEDTAVYYCSRSPQWEDIFEA MDIWGQGTMVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVS WNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKV DKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVD VSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEY KCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFY PSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSV MHEALHNHYTQKSLSLSPGK
AB-2a	NO:92	QMQLVESGGGVVQPGRSLRLSCAASGFTFRTYGMHWVRQAPGKGLEWVAVVWYD GSYTHYADSVKGRFTITRDNSKNTLNLQMNSLRAEDTAVYYCARSPQWEEIFEA MDIWGQGTMVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVS WNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKV DKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVD VSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEY KCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFY PSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSV MHEALHNHYTQKSLSLSPGK
AB-3a	NO:93	QMQLVESGGGVVQPGRSLRLSCAASGFTFRTYGMHWVRQAPGKGLEWVAVIWYD GTYTHYADSVKGRFTITRDNSKNTLNLQMNSLRAEDTAVYYCARSPQWESIFEA FDIWGQGTMVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVS WNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKV DKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVD VSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEY KCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFY PSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSV MHEALHNHYTQKSLSLSPGK
AB-4a	NO:94	QMQLVESGGGVVQPGRSLRLSCAASGFTFRTYGMHWVRQAPGKGLEWVAVIWYS GSDTHYADSVKGRFTITRDNSKNTLNLQMNSLRAEDTAVYYCARSPQWEDIFES MDVWGQGTMVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVS WNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKV DKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVD VSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEY KCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFY PSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSV MHEALHNHYTQKSLSLSPGK
AB-5a	NO:95	QMQLVESGGGVVQPGRSLRLSCAASGFTFRTYGMHWVRQAPGKGLEWVAVVWYD GYDTHYADSVKGRFTITRDNSKNTLNLQMNSLRAEDTAVYYCSRSPQWEDIFES MDIWGQGTMVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVS WNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKV DKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVD VSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEY KCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFY PSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSV MHEALHNHYTQKSLSLSPGK

Name	SEQ ID	Amino Acid Sequence
AB-6a	NO:96	QMQLVESGGGVVQPGRSLRLSCAASGFTFRTYGMHWVRQAPGKGLEWVAVVWYD GSDIHYADSVKGRFTITRDNSKNTLNLQMNSLRAEDTAVYYCSRSPQWEDIFES MDIWGQGTMVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVS WNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKV DKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVD VSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEY KCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFY PSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSV MHEALHNHYTQKSLSLSPGK
AB-7a	NO:97	QMQLVESGGGVVQPGRSLRLSCAASGFTFRTYGMHWVRQAPGKGLEWVAVIWYS GAYIHYADSVKGRFTITRDNSKNTLNLQMNSLRAEDTAVYYCSRSPQWEDIFEA MDIWGQGTMVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVS WNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKV DKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVD VSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEY KCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFY PSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSV MHEALHNHYTQKSLSLSPGK
AB-8a	NO:98	QMQLVESGGGVVQPGRSLRLSCAASGFTFRTYGMHWVRQAPGKGLEWVAVIWYD GSYTHYADSVKGRFTITRDNSKNTLNLQMNSLRAEDTAVYYCARSPQWEDIFEA FDIWGQGTMVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVS WNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKV DKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVD VSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEY KCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFY PSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSV MHEALHNHYTQKSLSLSPGK
AB-9a	NO:99	QMQLVESGGGVVQPGRSLRLSCAASGFTFRTYGMHWVRQAPGKGLEWVAVIWYD GSYTHYADSVKGRFTITRDNSKNTLNLQMNSLRAEDTAVYYCARSPQWESIFEA FDIWGQGTMVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVS WNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKV DKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVD VSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEY KCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFY PSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSV MHEALHNHYTQKSLSLSPGK
AB-10a	NO:100	QMQLVESGGGVVQPGRSLRLSCAASGFTFRTYGMHWVRQAPGKGLEWVAVIWYS GTTTHYADSVKGRFTITRDNSKNTLNLQMNSLRAEDTAVYYCSRSPQWEDIFES MDIWGQGTMVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVS WNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKV DKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVD VSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEY KCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFY PSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSV MHEALHNHYTQKSLSLSPGK
AB-11a	NO:101	QMQLVESGGGVVQPGRSLRLSCAASGFTFRTYGMHWVRQAPGKGLEWVAVISYS GSYIHYADSVKGRFTITRDNSKNTLNLQMNSLRAEDTAVYYCTRSPQWEEVYEA LDIWGQGTMVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVS WNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKV DKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVD VSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEY KCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFY PSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSV MHEALHNHYTQKSLSLSPGK

Name	SEQ ID	Amino Acid Sequence
AB-12a	NO:102	QMQLVESGGGVVQPGRSLRLSCAASGFTFRTYGMHWVRQAPGKGLEWVAVVWYD GSNTHYADSVKGRFTITRDNSKNTLNLQMNSLRAEDTAVYYCARAPQWESVHEA FDIWGQGTMVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVS WNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKV DKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVD VSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEY KCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFY PSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSV MHEALHNHYTQKSLSLSPGK
AB-13a	NO:103	QMQLVESGGGVVQPGRSLRLSCAASGFTFRTYGMHWVRQAPGKGLEWVAVISYD GSTKHYADSVKGRFTITRDNSKNTLNLQMNSLRAEDTAVYYCARAPQWESVYEA FDIWGQGTMVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVS WNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKV DKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVD VSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEY KCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFY PSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSV MHEALHNHYTQKSLSLSPGK
AB-14a	NO:104	QMQLVESGGGVVQPGRSLRLSCAASGFTFRTYGMHWVRQAPGKGLEWVAVIWYD GSTKHYADSVKGRFTITRDNSKNTLNLQMNSLRAEDTAVYYCARAPQWELVHEA FDIWGQGTMVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVS WNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKV DKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVD VSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEY KCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFY PSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSV MHEALHNHYTQKSLSLSPGK
AB-1b	NO:105	QMQLVESGGGVVQPGRSLRLSCAASGFTFRTYGMHWVRQAPGKGLEWVAVVWYS GSYTHYADSVKGRFTITRDNSKNTLNLQMNSLRAEDTAVYYCSRSPQWEDIFEA MDIWGQGTMVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVS WNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKV DKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLYITREPEVTCVVVD VSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEY KCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFY PSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSV MHEALHNHYTQKSLSLSPGK
AB-2b	NO:106	QMQLVESGGGVVQPGRSLRLSCAASGFTFRTYGMHWVRQAPGKGLEWVAVVWYD GSYTHYADSVKGRFTITRDNSKNTLNLQMNSLRAEDTAVYYCARSPQWEEIFEA MDIWGQGTMVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVS WNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKV DKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLYITREPEVTCVVVD VSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEY KCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFY PSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSV MHEALHNHYTQKSLSLSPGK
AB-3b	NO:107	QMQLVESGGGVVQPGRSLRLSCAASGFTFRTYGMHWVRQAPGKGLEWVAVIWYD GTYTHYADSVKGRFTITRDNSKNTLNLQMNSLRAEDTAVYYCARSPQWESIFEA FDIWGQGTMVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVS WNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKV DKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLYITREPEVTCVVVD VSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEY KCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFY PSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSV MHEALHNHYTQKSLSLSPGK

Name	SEQ ID	Amino Acid Sequence
AB-4b	NO:108	QMQLVESGGGVVQPGRSLRLSCAASGFTFRTYGMHWVRQAPGKGLEWVAVIWYS GSDTHYADSVKGRFTITRDNSKNTLNLQMNSLRAEDTAVYYCARSPQWEDIFES MDVWGQGTMVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVS WNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKV DKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLYITREPEVTCVVVD VSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEY KCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFY PSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSV MHEALHNHYTQKSLSLSPGK
AB-5b	NO:109	QMQLVESGGGVVQPGRSLRLSCAASGFTFRTYGMHWVRQAPGKGLEWVAVVWYD GYDTHYADSVKGRFTITRDNSKNTLNLQMNSLRAEDTAVYYCSRSPQWEDIFES MDIWGQGTMVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVS WNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKV DKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLYITREPEVTCVVVD VSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEY KCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFY PSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSV MHEALHNHYTQKSLSLSPGK
AB-6b	NO:110	QMQLVESGGGVVQPGRSLRLSCAASGFTFRTYGMHWVRQAPGKGLEWVAVVWYD GSDIHYADSVKGRFTITRDNSKNTLNLQMNSLRAEDTAVYYCSRSPQWEDIFES MDIWGQGTMVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVS WNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKV DKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLYITREPEVTCVVVD VSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEY KCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFY PSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSV MHEALHNHYTQKSLSLSPGK
AB-7b	NO:111	QMQLVESGGGVVQPGRSLRLSCAASGFTFRTYGMHWVRQAPGKGLEWVAVIWYS GAYIHYADSVKGRFTITRDNSKNTLNLQMNSLRAEDTAVYYCSRSPQWEDIFEA MDIWGQGTMVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVS WNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKV DKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLYITREPEVTCVVVD VSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEY KCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFY PSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSV MHEALHNHYTQKSLSLSPGK
AB-8b	NO:112	QMQLVESGGGVVQPGRSLRLSCAASGFTFRTYGMHWVRQAPGKGLEWVAVIWYD GSYTHYADSVKGRFTITRDNSKNTLNLQMNSLRAEDTAVYYCARSPQWEDIFEA FDIWGQGTMVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVS WNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKV DKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLYITREPEVTCVVVD VSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEY KCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFY PSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSV MHEALHNHYTQKSLSLSPGK
AB-9b	NO:113	QMQLVESGGGVVQPGRSLRLSCAASGFTFRTYGMHWVRQAPGKGLEWVAVIWYD GSYTHYADSVKGRFTITRDNSKNTLNLQMNSLRAEDTAVYYCARSPQWESIFEA FDIWGQGTMVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVS WNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKV DKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLYITREPEVTCVVVD VSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEY KCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFY PSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSV MHEALHNHYTQKSLSLSPGK

Name	SEQ ID	Amino Acid Sequence
AB-10b	NO:114	QMQLVESGGGVVQPGRSLRLSCAASGFTFRTYGMHWVRQAPGKGLEWVAVIWYS GTTTHYADSVKGRFTITRDNSKNTLNLQMNSLRAEDTAVYYCSRSPQWEDIFES MDIWGQGTMVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVS WNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKV DKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLYITREPEVTCVVVD VSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEY KCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFY PSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSV MHEALHNHYTQKSLSLSPGK
AB-11b	NO:115	QMQLVESGGGVVQPGRSLRLSCAASGFTFRTYGMHWVRQAPGKGLEWVAVISYS GSYIHYADSVKGRFTITRDNSKNTLNLQMNSLRAEDTAVYYCTRSPQWEEVYEA LDIWGQGTMVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVS WNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKV DKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLYITREPEVTCVVVD VSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEY KCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFY PSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSV MHEALHNHYTQKSLSLSPGK
AB-12b	NO:116	QMQLVESGGGVVQPGRSLRLSCAASGFTFRTYGMHWVRQAPGKGLEWVAVVWYD GSNTHYADSVKGRFTITRDNSKNTLNLQMNSLRAEDTAVYYCARAPQWESVHEA FDIWGQGTMVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVS WNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKV DKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLYITREPEVTCVVVD VSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEY KCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFY PSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSV MHEALHNHYTQKSLSLSPGK
AB-13b	NO:117	QMQLVESGGGVVQPGRSLRLSCAASGFTFRTYGMHWVRQAPGKGLEWVAVISYD GSTKHYADSVKGRFTITRDNSKNTLNLQMNSLRAEDTAVYYCARAPQWESVYEA FDIWGQGTMVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVS WNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKV DKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLYITREPEVTCVVVD VSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEY KCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFY PSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSV MHEALHNHYTQKSLSLSPGK
AB-14b	NO:118	QMQLVESGGGVVQPGRSLRLSCAASGFTFRTYGMHWVRQAPGKGLEWVAVIWYD GSTKHYADSVKGRFTITRDNSKNTLNLQMNSLRAEDTAVYYCARAPQWELVHEA FDIWGQGTMVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVS WNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKV DKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLYITREPEVTCVVVD VSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEY KCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFY PSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSV MHEALHNHYTQKSLSLSPGK

Table 5. Light Chain Amino Acid Sequences

Name	SEQ ID	Amino Acid Sequence
Reference	NO:82	SYVLTQPPSVSVAPGQTARITCGGNNLGSKSVHWYQQKPGQAPVLVVYDDSDRPS WIPERFSGSNSGNTATLTISRGEAGDEADYYCQVWDSSSDHVVFGGGTKLTVLGQ PKAAPSVTLFPPSSEELQANKATLVCLISDFYPGAVTVAWKADSSPVKAGVETTT PSKQSNNKYAASSYLSLTPEQWKSHRSYSCQVTHEGSTVEKTVAPTECS
AB-1, 3, 8, 9	NO:119	SYVLTQPPSVSVAPGQTARITCGGNNIGSKSVHWYQQKPGQAPVLVVYDDSDRPS WIPERFSGSNSGNTATLTISRGEAGDEADYYCQVWDSSSSLVVFGGGTKLTVLGQ

Name	SEQ ID	Amino Acid Sequence
		PKAAPSVTLFPPSSEELQANKATLVCLISDFYPGAVTVAWKADSSPVKAGVETTT PSKQSNNKYAASSYLSLTPEQWKSHRSYSCQVTHEGSTVEKTVAPTECS
AB-2	NO:120	SYVLTQPPSVSVAPGQTARITCGGNNIGSKSVHWYQQKPGQAPVLVVYDDSDRPS WIPERFSGSNSGNTATLTISRGEAGDEADYYCQIWDSSSSLVVFGGGTKLTVLGQ PKAAPSVTLFPPSSEELQANKATLVCLISDFYPGAVTVAWKADSSPVKAGVETTT PSKQSNNKYAASSYLSLTPEQWKSHRSYSCQVTHEGSTVEKTVAPTECS
AB-4	NO:121	SYVLTQPPSVSVAPGQTARITCGGNYIGSFSVHWYQQKPGQAPVLVVYDDSDRPS WIPERFSGSNSGNTATLTISRGEAGDEADYYCQIYVSASRLVVFGGGTKLTVLGQ PKAAPSVTLFPPSSEELQANKATLVCLISDFYPGAVTVAWKADSSPVKAGVETTT PSKQSNNKYAASSYLSLTPEQWKSHRSYSCQVTHEGSTVEKTVAPTECS
AB-5	NO:122	SYVLTQPPSVSVAPGQTARITCGGNNLGSKSVHWYQQKPGQAPVLVVYDDSDRPS WIPERFSGSNSGNTATLTISRGEAGDEADYYCQVWDMSSDLVVFGGGTKLTVLGQ PKAAPSVTLFPPSSEELQANKATLVCLISDFYPGAVTVAWKADSSPVKAGVETTT PSKQSNNKYAASSYLSLTPEQWKSHRSYSCQVTHEGSTVEKTVAPTECS
AB-6	NO:123	SYVLTQPPSVSVAPGQTARITCGGNNIGSKSVHWYQQKPGQAPVLVVYDDSDRPS WIPERFSGSNSGNTATLTISRGEAGDEADYYCQIWDSSSDHVVFGGGTKLTVLGQ PKAAPSVTLFPPSSEELQANKATLVCLISDFYPGAVTVAWKADSSPVKAGVETTT PSKQSNNKYAASSYLSLTPEQWKSHRSYSCQVTHEGSTVEKTVAPTECS
AB-7	NO:124	SYVLTQPPSVSVAPGQTARITCGGNNLGSYSVHWYQQKPGQAPVLVVYDDSDRPS WIPERFSGSNSGNTATLTISRGEAGDEADYYCQVWDMSSSLVVFGGGTKLTVLGQ PKAAPSVTLFPPSSEELQANKATLVCLISDFYPGAVTVAWKADSSPVKAGVETTT PSKQSNNKYAASSYLSLTPEQWKSHRSYSCQVTHEGSTVEKTVAPTECS
AB-10	NO:125	SYVLTQPPSVSVAPGQTARITCGGNNIGSKNVHWYQQKPGQAPVLVVYDDSDRPS WIPERFSGSNSGNTATLTISRGEAGDEADYYCQVWDSSDFLVVFGGGTKLTVLGQ PKAAPSVTLFPPSSEELQANKATLVCLISDFYPGAVTVAWKADSSPVKAGVETTT PSKQSNNKYAASSYLSLTPEQWKSHRSYSCQVTHEGSTVEKTVAPTECS
AB-11	NO:126	SYVLTQPPSVSVAPGQTARITCGGNNIGSFSVHWYQQKPGQAPVLVVYDDSDRPS WIPERFSGSNSGNTATLTISRGEAGDEADYYCQVWSSTSRHVVFGGGTKLTVLGQ PKAAPSVTLFPPSSEELQANKATLVCLISDFYPGAVTVAWKADSSPVKAGVETTT PSKQSNNKYAASSYLSLTPEQWKSHRSYSCQVTHEGSTVEKTVAPTECS
AB-12	NO:127	SYVLTQPPSVSVAPGQTARITCGGNNIGRFSVHWYQQKPGQAPVLVVYDDSDRPS WIPERFSGSNSGNTATLTISRGEAGDEADYYCQVWVSTSDKVVFGGGTKLTVLGQ PKAAPSVTLFPPSSEELQANKATLVCLISDFYPGAVTVAWKADSSPVKAGVETTT PSKQSNNKYAASSYLSLTPEQWKSHRSYSCQVTHEGSTVEKTVAPTECS
AB-13	NO:128	SYVLTQPPSVSVAPGQTARITCGGNNLGSFSVHWYQQKPGQAPVLVVYDDSDRPS WIPERFSGSNSGNTATLTISRGEAGDEADYYCQVWDSSEDLVVFGGGTKLTVLGQ PKAAPSVTLFPPSSEELQANKATLVCLISDFYPGAVTVAWKADSSPVKAGVETTT PSKQSNNKYAASSYLSLTPEQWKSHRSYSCQVTHEGSTVEKTVAPTECS
AB-14	NO:129	SYVLTQPPSVSVAPGQTARITCGGNNIGSKNVHWYQQKPGQAPVLVVYDDSDRPS WIPERFSGSNSGNTATLTISRGEAGDEADYYCQVWDESSDEVVFGGGTKLTVLGQ PKAAPSVTLFPPSSEELQANKATLVCLISDFYPGAVTVAWKADSSPVKAGVETTT PSKQSNNKYAASSYLSLTPEQWKSHRSYSCQVTHEGSTVEKTVAPTECS

Table 6. Self-association Properties

clone	AC-SINS Score	PSR Score
AB-1	7	4
AB-2	4	4
AB-3	6	4
AB-4	6	4
AB-5	7	3
AB-6	7	3
AB-7	4	4
AB-8	5	4
AB-9	6	4
AB-10	6	2
AB-11	4	4
AB-12	6	4
AB-13	5	3
AB-14	5	4
Reference	5	2

Table 7. TSLP Binding ELISA

clone	hTSLP EC_{50} (nM)	cynoTSLP EC_{50} (nM)
AB-1	0.2651	0.4464
AB-2	0.2037	0.4019
AB-3	0.2369	0.5755
AB-4	0.2595	0.3314
AB-5	0.2635	0.3152
AB-6	0.3967	0.4243
AB-7	0.2898	0.6176
AB-8	0.2484	0.4624
AB-9	0.3881	0.4803
AB-10	0.2856	0.4352
AB-11	0.1734	0.336
AB-12	0.2912	0.4571
AB-13	0.2303	0.448
AB-14	0.264	0.3674
Reference	0.2387	0.5242

Table 8. TSLP Blocking ELISA

clone	hTSLP IC_{50} (nM)	cynoTSLP IC_{50} (nM)
AB-1	0.1693	0.1782
AB-2	0.29	0.3181
AB-3	0.2318	0.2574
AB-4	0.1704	0.2017
AB-5	0.2457	0.2045
AB-6	0.2224	0.2492
AB-7	0.1624	0.2051
AB-8	0.1995	0.2041
AB-9	0.2265	0.2597
AB-10	0.2505	0.2379
AB-11	0.2427	0.287
AB-12	0.29	0.2538
AB-13	0.2232	0.2449
AB-14	0.1865	0.2293
Reference	0.2939	0.2796

Table 9. KinExA Binding Affinities

clone	hTSLP Binding			cynoTSLP Binding		
	K_D (pM)	k_a (1/Ms)	k_d (1/s)	K_D (pM)	k_a (1/Ms)	k_d (1/s)
AB-1	0.208	2.66E+07	5.53E-06	3.28	1.34E+07	4.41E-05
AB-2	0.123	2.38E+07	2.93E-06	1.25	5.25E+07	6.56E-05
AB-3	0.302	1.65E+07	4.99E-06	1.72	1.98E+07	3.40E-06
AB-4	0.208	2.72E+07	5.66E-06	0.929	3.06E+07	2.84E-05
AB-5	0.14	5.83E+07	8.17E-06	2.01	2.58E+07	6.37E-05
AB-6	0.133	2.01E+08	2.65E-05	1.97	1.97E+07	3.83E-05
AB-7	0.184	2.21E+07	4.06E-06	0.754	2.71E+07	2.05E-05
AB-8	0.335	2.45E+07	5.62E-06	1.56	1.91E+07	2.97E-05
AB-9	0.496	1.73E+07	8.57E-06	2.17	3.47E+07	7.52E-05
AB-10	0.395	2.40E+07	9.48E-06			
AB-11	0.754	2.23E+07	1.68E-05			
AB-12	1.020	2.29E+07	2.33E-05			
AB-13						
AB-14	0.877	2.63E+07	2.31E-05			
Reference	2.15	1.54E+07	3.30E-05	9.05	9.80E+06	8.87E-05

Table 10. Inhibition of TSLP binding

clone	IC_{50} (nM)
AB-1	0.6233
AB-2	0.5868
AB-3	0.4106
AB-4	1.106
AB-5	2.329
AB-6	0.5309
AB-7	0.7316
AB-8	0.667
AB-9	0.2872
AB-10	1.993
AB-11	1.164
AB-12	2.784
AB-13	3.333
AB-14	3.942
Reference	1.931

Table 11. Inhibition of TSLP-Mediated STAT5 Signaling

clone	IC_{50} (nM)				
	Donor 1	Donor 2	Donor 3	Donor 4	Donor 5
AB-1	0.1675	0.6433	0.4553	0.1368	0.4494
AB-2	0.2402	0.349	0.1774	0.1427	0.3544
AB-3	0.1051	0.3053	0.1471	0.1326	0.1888
AB-4	0.1909	0.6764	0.1842	0.1994	0.4266
AB-5	0.1891	1.152	0.3254	0.4966	0.6762
AB-6	0.2321	0.7187	0.3392	0.2735	0.4777
AB-7	0.3685	1.31	0.6447	0.4997	0.7363
AB-8	0.1487	0.579	0.2684	0.2153	0.3164
AB-9	0.1958	0.7094	0.3161	0.1567	0.4098
Reference	1.158	1.402	1.132	1.044	1.774

Table 12. TSLP Binding ELISA

EC (95% confidence intervals) (μg/mL)	AB-2a	AB-2b	Reference Antibody	Human Isotype	
				IgG1	IgG2
Human TSLP					
EC_{50}	0.03 (0.03 to 0.04)	0.03 (0.02 to 0.05)	0.06 (0.06 to 0.07)	N/A	N/A
EC_{80}	0.09 (0.06 to 0.13)	0.10 (0.06 to 0.19)	0.14 (0.11 to 0.18)	N/A	N/A
EC_{90}	0.15 (0.08 to 0.27)	0.18 (0.09 to 0.45)	0.23 (0.16 to 0.31)	N/A	N/A
Cyno TSLP					
EC_{50}	0.04 (0.03 to 0.04)	0.04 (0.03 to 0.04)	0.06 (0.05 to 0.07)	N/A	N/A
EC_{80}	0.10 (0.07 to 0.13)	0.10 (0.08 to 0.14)	0.18 (0.13 to 0.24)	N/A	N/A
EC_{90}	0.17 (0.11 to 0.26)	0.19 (0.13 to 0.29)	0.33 (0.22 to 0.50)	N/A	N/A

Table 13. TSLPR/IL-7Rα BAF/3 Assay

IC (95% confidence intervals) (μg/mL)	AB-2a	AB-2b	Reference Antibody	Human Isotype	
				IgG1	IgG2
Human TSLPR/IL-7Rα					
IC_{50}	0.02 (0.004 to 0.12)	0.03 (0.006 to 0.18)	0.17 (0.05 to 0.65)	N/A	N/A
Cyno TSLPR/IL-7Rα					
IC_{50}	0.03 (0.01 to 0.07)	0.04 (0.02 to 0.07)	0.14 (0.05 to 0.40)	N/A	N/A

Table 14: Example Sequences and Potts Model Scores

protein	vht	vlt	vhvlt	potts_model_score
AB-2	GTRYVWDSYTASQWEEIFEAMI (SEQ ID NO:137)	NIGSKSDSQIWDSSSSLVV (SEQ ID NO:138)	GTRYVWDSYTASQWEEIFEAMINIGSKSDSQIWDSSSSLVV (SEQ ID NO:139)	-4.8525944
AB-1	GTRYVWSSYTSSQWEDIFEAMI (SEQ ID NO:140)	NIGSKSDSQVWDSSSSLVV(SEQ ID NO:141)	GTRYVWSSYTSSQWEDIFEAMINIGSKSDSQVWDSSSSLVV (SEQ ID NO:142)	-2.9628694
AB-8	GTRYIWDSYTASQWEDIFEAFI (SEQ ID NO:143)	NIGSKSDSQVWDSSSSLVV (SEQ ID NO:141)	GTRYIWDSYTASQWEDIFEAFINIGSKSDSQVWDSSSSLVV (SEQ ID NO:144)	-2.9442153
AB-6	GTRYVWDSDISSQWEDIFESMI (SEQ ID NO:145)	NIGSKSDSQIWDSSSDHVV (SEQ ID NO:146)	GTRYVWDSDISSQWEDIFESMINIGSKSDSQIWDSSSDHVV (SEQ ID NO:147)	-2.3772101
AB-3	GTRYIWDTYTASQWESIFEAFI (SEQ ID NO:148)	NIGSKSDSQVWDSSSSLVV (SEQ ID NO:141)	GTRYIWDTYTASQWESIFEAFINIGSKSDSQVWDSSSSLVV (SEQ ID NO:149)	-2.1100748
AB-5	GTRYVWDYDTSSQWEDIFESMI (SEQ ID NO:150)	NLGSKSDSQVWDMSSDLVV (SEQ ID NO:151)	GTRYVWDYDTSSQWEDIFESMINLGSKSDSQVWDMSSDLVV (SEQ ID NO:152)	-1.8960481
AB-7	GTRYIWSAYISSQWEDIFEAMI (SEQ ID NO:153)	NLGSYSDSQVWDMSSSLVV (SEQ ID NO:154)	GTRYIWSAYISSQWEDIFEAMINLGSYSDSQVWDMSSSLVV (SEQ ID NO:155)	-1.6204025
AB-10	GTRYIWSTTTSSQWEDIFESMI (SEQ ID NO:156)	NIGSKNDSQVWDSSDFLVV (SEQ ID NO:157)	GTRYIWSTTTSSQWEDIFESMINIGSKNDSQVWDSSDFLVV (SEQ ID NO:158)	-1.4744515
AB-13	GTRYISDSTKAAQWESVYEAFI (SEQ ID NO:159)	NLGSFSDSQVWDSSEDLVV (SEQ ID NO:160)	GTRYISDSTKAAQWESVYEAFINLGSFSDSQVWDSSEDLVV (SEQ ID NO:161)	-1.3488145
AB-14	GTRYIWDSTKAAQWELVHEAFI (SEQ ID NO:162)	NIGSKNDSQVWDESSDEVV (SEQ ID NO:163)	GTRYIWDSTKAAQWELVHEAFINIGSKNDSQVWDESSDEVV (SEQ ID NO:164)	-1.1853998
AB-12	GTRYVWDSNTAAQWESVHEAFI (SEQ ID NO:165)	NIGRFSDSQVWVSTSDKVV (SEQ ID NO:166)	GTRYVWDSNTAAQWESVHEAFINIGRFSDSQVWVSTSDKVV (SEQ ID NO:167)	-0.6803217
AB-11	GTRYISSSYITSQWEEVYEALI (SEQ ID NO:168)	NIGSFSDSQVWSSTSRHVV (SEQ ID NO:169)	GTRYISSSYITSQWEEVYEALINIGSFSDSQVWSSTSRHVV (SEQ ID NO:170)	-0.6461612
AB-4	GTRYIWSSDTASQWEDIFESMV (SEQ ID NO:171)	YIGSFSDSQIYVSASRLVV (SEQ ID NO:172)	GTRYIWSSDTASQWEDIFESMVYIGSFSDSQIYVSASRLVV (SEQ ID NO:173)	-0.62289006

[00815] The teachings of all patents, published applications and references cited herein are incorporated by reference in their entirety.

[00816] While example embodiments have been particularly shown and described, it will be understood by those skilled in the art that various changes in form and details may be made therein without departing from the scope of the embodiments encompassed by the appended claims.

Appendix C - claim.py

```
import itertools

import argparse

import numpy as np


#MAGIC NUMBERS

THRESHOLD = -7.7

VH_NATIVE =
'QMQLVESGGGVVQPGRSLRLSCAASGFTFRTYGMHWVRQAPGKGLEWVAVIWYD
GSNKHYADSVKGRFTITRDNSKNTLNLQMNSLRAEDTAVYYCARAPQWELVHEAF
DIWGQGTMVTVSS'

VL_NATIVE =
'SYVLTQPPSVSVAPGQTARITCGGNNLGSKSVHWYQQKPGQAPVLVVYDDSDRPS
WIPERFSGSNSGNTATLTISRGEAGDEADYYCQVWDSSSDHVVFGGGTKLTVL'

VH_POSITIONS = [25, 27, 29, 31, 50, 51, 53, 55, 56, 57, 96, 98, 100, 101, 102, 103, 104,
105, 106, 107, 108, 110]

VL_POSITIONS = [25, 26, 27, 28, 29, 30, 48, 50, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97]

ETAB_FILE = 'fit_model.etab'


tripleToSingle = {  'ALA': 'A',
                    'CYS': 'C',
                    'ASP': 'D',
                    'GLU': 'E',
                    'PHE': 'F',
                    'GLY': 'G',
                    'HIS': 'H',
                    'ILE': 'I',
                    'LYS': 'K',
                    'LEU': 'L',
                    'MET': 'M',
                    'ASN': 'N',
                    'PRO': 'P',
```

```
            'GLN': 'Q',
            'ARG': 'R',
            'SER': 'S',
            'THR': 'T',
            'VAL': 'V',
            'TRP': 'W',
            'TYR': 'Y',
            '---': '-'}

def read_etab(etab_file:str) -> (dict,dict):
    '''load an etab file and produce two hash tables'''
    h = dict()
    j = dict()
    with open(etab_file,'r') as file:
        for line in file:
            items = line.replace('\n','').split(' ')
            if len(items) == 3:
                #Unpack
                i1, r1, v = items

                #Transform
                i1 = int(i1[1:])
                r1 = tripleToSingle[r1]
                v = float(v)

                #Create New Entry in the hash table
                h[(i1,r1)] = v

            elif len(items) == 5:
                #Unpack
```

```
            i1, i2, r1, r2, v = items

            #Transform
            i1 = int(i1[1:])
            i2 = int(i2[1:])
            r1 = tripleToSingle[r1]
            r2 =  tripleToSingle[r2]
            v=float(v)

            #Create New Entry in the hash table
            j[(i1,i2,r1,r2)] = v
    return h,j


def trim_sequence(sequence, positions, native):
    if len(sequence) != len(native):
        return None
    else:
        return ''.join([sequence[p] for p in positions])


def sequence_energy(h:dict, j:dict, sequence:str, tokens='ACDEFGHIKLMNPQRSTVWY-')
-> float:
    score = 0
    #Score First Order Contributions
    for i,s in enumerate(sequence):
        try:
            score += h[(i,s)]
        except KeyError:
            pass

    #Score Second Order Contributions
    for c1, c2 in itertools.combinations(enumerate(sequence),2):
```

```
        assert c1[0] <= c2[0], 'first element of sequence should come before the second!'
        try:
            score += j[(c1[0],c2[0],c1[1],c2[1])]
        except KeyError:
            pass

    return score

def score_sequence(h:dict, j:dict, sequence:str, tokens='ACDEFGHIKLMNPQRSTVWY-') -
> float:
    logits = []
    native_logit = []

    for position in range(len(sequence)):

        scores = []
        for residue in tokens:

            #Construct new native sequence
            p_seq = sequence[:position] + residue + sequence[position+1:]

            score = sequence_energy(h,j,p_seq)

            #Add Score to Array
            es = np.exp(-score)
            scores.append(es)
            if residue == sequence[position]:
                native_logit.append(es)

        logits.append(sum(scores))
```

```
    #Convert Score into Log P...
    score = [np.log(n/s) for n,s in zip(native_logit,logits)]
    score = sum(score)
    return score

def claim_sequence(vh:str, vl:str) -> bool:
    '''take in a vh and vl sequence and return a boolean
    value either claiming or not claiming a sequence'''

    h,j = read_etab(ETAB_FILE)

    # Module for Sequence Alignment:
    tvh = trim_sequence(vh,VH_POSITIONS, VH_NATIVE)
    if tvh is None: return False

    tvl = trim_sequence(vl,VL_POSITIONS, VL_NATIVE)
    if tvl is None: return False

    sequence = tvh+tvl

    #Score Aligned Sequence & Claim
    score = score_sequence(h,j,sequence)
    if score > THRESHOLD:
        return True
    else:
        return False

if __name__ == "__main__":
    parser = argparse.ArgumentParser()
    parser.add_argument("vh", type=str, help="a vh sequence to check if it is claimed")
```

```
parser.add_argument("vl", type=str, help="a vl sequence to check if it is claimed")
args = parser.parse_args()
print(claim_sequence(args.vh,args.vl))
```

Appendix D – Table 15 “fit_model.etab”

S0 ALA 0.0348695
S0 CYS 0.0348695
S0 ASP 0.0348695
S0 GLU 0.0348695
S0 PHE 0.0348695
S0 GLY -0.415857
S0 HIS 0.0348695
S0 ILE 0.0348695
S0 LYS 0.0348695
S0 LEU 0.0348695
S0 MET 0.0348695
S0 ASN 0.0348695
S0 PRO 0.0348695
S0 GLN 0.0348695
S0 ARG 0.0348695
S0 SER -0.246663
S0 THR 0.0348695
S0 VAL 0.0348695
S0 TRP 0.0348695
S0 TYR 0.0348695
S0 --- 0.0348695
S1 ALA 0.0438896
S1 CYS 0.0438896
S1 ASP 0.0438896
S1 GLU 0.0438896
S1 PHE -0.152003
S1 GLY 0.0438896
S1 HIS 0.0438896
S1 ILE 0.0438896
S1 LYS 0.0438896
S1 LEU 0.0438896
S1 MET 0.0438896
S1 ASN 0.0438896
S1 PRO 0.0438896
S1 GLN 0.0438896
S1 ARG 0.0438896
S1 SER 0.0438896
S1 THR -0.418689
S1 VAL -0.219321
S1 TRP 0.0438896
S1 TYR 0.0438896
S1 --- 0.0438896
S2 ALA 0.037009
S2 CYS 0.037009
S2 ASP 0.037009
S2 GLU 0.037009
S2 PHE 0.037009
S2 GLY 0.037009
S2 HIS 0.037009
S2 ILE 0.037009
S2 LYS 0.037009
S2 LEU 0.037009
S2 MET 0.037009
S2 ASN 0.037009
S2 PRO 0.037009
S2 GLN 0.037009
S2 ARG -0.500026
S2 SER -0.203145
S2 THR 0.037009
S2 VAL 0.037009
S2 TRP 0.037009

S2 TYR 0.037009
S2 --- 0.037009
S3 ALA 0.0386357
S3 CYS 0.0386357
S3 ASP 0.0386357
S3 GLU 0.0386357
S3 PHE -0.154688
S3 GLY 0.0386357
S3 HIS 0.0386357
S3 ILE 0.0386357
S3 LYS 0.0386357
S3 LEU 0.0386357
S3 MET 0.0386357
S3 ASN 0.0386357
S3 PRO 0.0386357
S3 GLN 0.0386357
S3 ARG 0.0386357
S3 SER 0.0386357
S3 THR 0.0386357
S3 VAL 0.0386357
S3 TRP 0.0386357
S3 TYR -0.579389
S3 --- 0.0386357
S4 ALA 0.0504379
S4 CYS 0.0504379
S4 ASP 0.0504379
S4 GLU 0.0504379
S4 PHE 0.0504379
S4 GLY 0.0504379
S4 HIS 0.0504379
S4 ILE -0.773931
S4 LYS 0.0504379
S4 LEU 0.0504379
S4 MET 0.0504379
S4 ASN 0.0504379
S4 PRO 0.0504379
S4 GLN 0.0504379
S4 ARG 0.0504379
S4 SER 0.0504379
S4 THR 0.0504379
S4 VAL -0.184389
S4 TRP 0.0504379
S4 TYR 0.0504379
S4 --- 0.0504379
S5 ALA 0.0663807
S5 CYS 0.0663807
S5 ASP 0.0663807
S5 GLU 0.0663807
S5 PHE -0.201004
S5 GLY 0.0663807
S5 HIS 0.0663807
S5 ILE 0.0663807
S5 LYS 0.0663807
S5 LEU 0.0663807
S5 MET 0.0663807
S5 ASN 0.0663807
S5 PRO 0.0663807
S5 GLN 0.0663807
S5 ARG 0.0663807
S5 SER -0.419329
S5 THR -0.170842
S5 VAL 0.0663807
S5 TRP -0.337296

S5 TYR 0.0663807
S5 --- 0.0663807
S6 ALA 0.0502004
S6 CYS 0.0502004
S6 ASP -0.206001
S6 GLU 0.0502004
S6 PHE 0.0502004
S6 GLY 0.0502004
S6 HIS 0.0502004
S6 ILE 0.0502004
S6 LYS 0.0502004
S6 LEU 0.0502004
S6 MET 0.0502004
S6 ASN 0.0502004
S6 PRO 0.0502004
S6 GLN 0.0502004
S6 ARG 0.0502004
S6 SER -0.747806
S6 THR 0.0502004
S6 VAL 0.0502004
S6 TRP 0.0502004
S6 TYR 0.0502004
S6 --- 0.0502004
S7 ALA -0.301731
S7 CYS 0.071303
S7 ASP 0.071303
S7 GLU 0.071303
S7 PHE 0.071303
S7 GLY 0.071303
S7 HIS 0.071303
S7 ILE 0.071303
S7 LYS 0.071303
S7 LEU 0.071303
S7 MET 0.071303
S7 ASN 0.071303
S7 PRO 0.071303
S7 GLN 0.071303
S7 ARG 0.071303
S7 SER -0.306664
S7 THR -0.356833
S7 VAL 0.071303
S7 TRP 0.071303
S7 TYR -0.246923
S7 --- 0.071303
S8 ALA 0.0942919
S8 CYS 0.0942919
S8 ASP -0.275002
S8 GLU 0.0942919
S8 PHE 0.0942919
S8 GLY 0.0942919
S8 HIS -0.114226
S8 ILE 0.0942919
S8 LYS 0.0942919
S8 LEU 0.0942919
S8 MET 0.0942919
S8 ASN -0.375358
S8 PRO 0.0942919
S8 GLN 0.0942919
S8 ARG 0.0942919
S8 SER -0.16992
S8 THR -0.103591
S8 VAL 0.0942919
S8 TRP 0.0942919

S8 TYR -0.376282
S8 --- 0.0942919
S9 ALA 0.0737346
S9 CYS 0.0737346
S9 ASP 0.0737346
S9 GLU 0.0737346
S9 PHE 0.0737346
S9 GLY 0.0737346
S9 HIS 0.0737346
S9 ILE -0.20883
S9 LYS -0.388784
S9 LEU 0.0737346
S9 MET 0.0737346
S9 ASN 0.0737346
S9 PRO 0.0737346
S9 GLN 0.0737346
S9 ARG -0.159077
S9 SER 0.0737346
S9 THR -0.496796
S9 VAL 0.0737346
S9 TRP 0.0737346
S9 TYR 0.0737346
S9 --- 0.0737346
S10 ALA -0.525108
S10 CYS 0.0711782
S10 ASP 0.0711782
S10 GLU 0.0711782
S10 PHE 0.0711782
S10 GLY -0.198612
S10 HIS 0.0711782
S10 ILE 0.0711782
S10 LYS 0.0711782
S10 LEU 0.0711782
S10 MET 0.0711782
S10 ASN 0.0711782
S10 PRO 0.0711782
S10 GLN 0.0711782
S10 ARG 0.0711782
S10 SER -0.133623
S10 THR -0.352688
S10 VAL 0.0711782
S10 TRP 0.0711782
S10 TYR 0.0711782
S10 --- 0.0711782
S11 ALA -0.393326
S11 CYS 0.046279
S11 ASP 0.046279
S11 GLU 0.046279
S11 PHE 0.046279
S11 GLY 0.046279
S11 HIS 0.046279
S11 ILE 0.046279
S11 LYS 0.046279
S11 LEU 0.046279
S11 MET 0.046279
S11 ASN 0.046279
S11 PRO 0.046279
S11 GLN 0.046279
S11 ARG 0.046279
S11 SER -0.485976
S11 THR 0.046279
S11 VAL 0.046279
S11 TRP 0.046279

S11 TYR 0.046279
S11 --- 0.046279
S12 ALA 0.0425634
S12 CYS 0.0425634
S12 ASP 0.0425634
S12 GLU -0.12718
S12 PHE 0.0425634
S12 GLY 0.0425634
S12 HIS 0.0425634
S12 ILE 0.0425634
S12 LYS 0.0425634
S12 LEU 0.0425634
S12 MET 0.0425634
S12 ASN 0.0425634
S12 PRO 0.0425634
S12 GLN -0.681525
S12 ARG 0.0425634
S12 SER 0.0425634
S12 THR 0.0425634
S12 VAL 0.0425634
S12 TRP 0.0425634
S12 TYR 0.0425634
S12 --- 0.0425634
S13 ALA 0.0350693
S13 CYS 0.0350693
S13 ASP 0.0350693
S13 GLU 0.0350693
S13 PHE -0.225906
S13 GLY 0.0350693
S13 HIS 0.0350693
S13 ILE 0.0350693
S13 LYS 0.0350693
S13 LEU 0.0350693
S13 MET 0.0350693
S13 ASN 0.0350693
S13 PRO 0.0350693
S13 GLN 0.0350693
S13 ARG 0.0350693
S13 SER 0.0350693
S13 THR 0.0350693
S13 VAL 0.0350693
S13 TRP -0.440411
S13 TYR 0.0350693
S13 --- 0.0350694
S14 ALA 0.0614099
S14 CYS 0.0614099
S14 ASP -0.429779
S14 GLU -0.324399
S14 PHE 0.0614099
S14 GLY 0.0614099
S14 HIS 0.0614099
S14 ILE 0.0614099
S14 LYS 0.0614099
S14 LEU 0.0614099
S14 MET 0.0614099
S14 ASN 0.0614099
S14 PRO 0.0614099
S14 GLN 0.0614099
S14 ARG 0.0614099
S14 SER -0.202013
S14 THR -0.087777
S14 VAL 0.0614099
S14 TRP 0.0614099

S14 TYR 0.0614099
S14 --- 0.0614099
S15 ALA 0.0874824
S15 CYS 0.0874824
S15 ASP -0.705624
S15 GLU -0.113105
S15 PHE 0.0874824
S15 GLY 0.0874824
S15 HIS 0.0874824
S15 ILE 0.0874824
S15 LYS 0.0874824
S15 LEU -0.18486
S15 MET 0.0874824
S15 ASN 0.0874824
S15 PRO 0.0874824
S15 GLN -0.142708
S15 ARG 0.0874824
S15 SER -0.253421
S15 THR 0.0874824
S15 VAL 0.0874824
S15 TRP 0.0874824
S15 TYR 0.0874824
S15 --- 0.0874824
S16 ALA -0.198734
S16 CYS 0.0733211
S16 ASP 0.0733211
S16 GLU 0.0733211
S16 PHE 0.0733211
S16 GLY 0.0733211
S16 HIS 0.0733211
S16 ILE -0.402373
S16 LYS 0.0733211
S16 LEU -0.088552
S16 MET 0.0733211
S16 ASN 0.0733211
S16 PRO 0.0733211
S16 GLN 0.0733211
S16 ARG 0.0733211
S16 SER 0.0733211
S16 THR -0.110182
S16 VAL -0.373298
S16 TRP 0.0733211
S16 TYR 0.0733211
S16 --- 0.0733211
S17 ALA 0.0744083
S17 CYS 0.0744083
S17 ASP 0.0744083
S17 GLU 0.0744083
S17 PHE -0.340266
S17 GLY 0.0744083
S17 HIS -0.342293
S17 ILE -0.242542
S17 LYS 0.0744083
S17 LEU 0.0744083
S17 MET 0.0744083
S17 ASN 0.0744083
S17 PRO 0.0744083
S17 GLN 0.0744083
S17 ARG 0.0744083
S17 SER 0.0744083
S17 THR 0.0744083
S17 VAL 0.0744083
S17 TRP -0.0636423

S17 TYR -0.201789
S17 --- 0.0744083
S18 ALA 0.0385848
S18 CYS 0.0385848
S18 ASP 0.0385848
S18 GLU -0.404611
S18 PHE 0.0385848
S18 GLY 0.0385848
S18 HIS -0.328499
S18 ILE 0.0385848
S18 LYS 0.0385848
S18 LEU 0.0385848
S18 MET 0.0385848
S18 ASN 0.0385848
S18 PRO 0.0385848
S18 GLN 0.0385848
S18 ARG 0.0385848
S18 SER 0.0385848
S18 THR 0.0385848
S18 VAL 0.0385848
S18 TRP 0.0385848
S18 TYR 0.0385848
S18 --- 0.0385848
S19 ALA -0.530663
S19 CYS 0.0562474
S19 ASP 0.0562474
S19 GLU 0.0562474
S19 PHE 0.0562474
S19 GLY 0.0562474
S19 HIS 0.0562474
S19 ILE 0.0562474
S19 LYS 0.0562474
S19 LEU 0.0562474
S19 MET 0.0562474
S19 ASN 0.0562474
S19 PRO 0.0562474
S19 GLN 0.0562474
S19 ARG 0.0562474
S19 SER -0.298078
S19 THR 0.0562474
S19 VAL 0.0562474
S19 TRP 0.0562474
S19 TYR -0.183713
S19 --- 0.0562474
S20 ALA 0.0730277
S20 CYS 0.0730277
S20 ASP 0.0730277
S20 GLU 0.0730277
S20 PHE -0.0685541
S20 GLY 0.0730277
S20 HIS 0.0730277
S20 ILE 0.0730277
S20 LYS 0.0730277
S20 LEU -0.108393
S20 MET -0.868035
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S20 ARG 0.0730277
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S20 TRP 0.0730277

S20 TYR 0.0730277
S20 --- 0.0730277
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S21 GLU 0.0695988
S21 PHE -0.511315
S21 GLY 0.0695988
S21 HIS 0.0695988
S21 ILE -0.247771
S21 LYS 0.0695988
S21 LEU 0.0695988
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S21 SER 0.0695988
S21 THR 0.0695988
S21 VAL -0.217625
S21 TRP 0.0695988
S21 TYR -0.206468
S21 --- 0.0695988
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S22 CYS 0.0648231
S22 ASP -0.210811
S22 GLU -0.0736552
S22 PHE 0.0648231
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S22 ILE 0.0648231
S22 LYS 0.0648231
S22 LEU 0.0648231
S22 MET 0.0648231
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S22 PRO 0.0648231
S22 GLN 0.0648231
S22 ARG 0.0648231
S22 SER 0.0648231
S22 THR 0.0648231
S22 VAL 0.0648231
S22 TRP 0.0648231
S22 TYR -0.158449
S22 --- 0.0648231
S23 ALA 0.047353
S23 CYS 0.047353
S23 ASP 0.047353
S23 GLU 0.047353
S23 PHE 0.047353
S23 GLY 0.047353
S23 HIS 0.047353
S23 ILE -0.555556
S23 LYS 0.047353
S23 LEU -0.344152
S23 MET 0.047353
S23 ASN 0.047353
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S23 GLN 0.047353
S23 ARG 0.047353
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S23 THR 0.047353
S23 VAL 0.047353
S23 TRP 0.047353

S23 TYR 0.047353
S23 --- 0.047353
S24 ALA 0.0348695
S24 CYS 0.0348695
S24 ASP 0.0348695
S24 GLU 0.0348695
S24 PHE 0.0348695
S24 GLY -0.415858
S24 HIS 0.0348695
S24 ILE 0.0348695
S24 LYS 0.0348695
S24 LEU 0.0348695
S24 MET 0.0348695
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S24 GLN 0.0348695
S24 ARG 0.0348695
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S24 THR 0.0348695
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S24 TRP 0.0348695
S24 TYR 0.0348695
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S25 CYS 0.0792247
S25 ASP -0.0525735
S25 GLU -0.0995867
S25 PHE 0.0792247
S25 GLY 0.0792247
S25 HIS 0.0792247
S25 ILE 0.0792247
S25 LYS -0.152192
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S25 GLN 0.0792247
S25 ARG -0.272719
S25 SER -0.578296
S25 THR -0.0330032
S25 VAL 0.0792247
S25 TRP 0.0792247
S25 TYR 0.0792247
S25 --- 0.0792247
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S26 GLY 0.0631933
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S26 LYS -0.565442
S26 LEU 0.0631933
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S26 TRP 0.0631933

S26 TYR -0.0942078
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S27 MET 0.0457017
S27 ASN -0.201565
S27 PRO 0.0457017
S27 GLN 0.0457017
S27 ARG 0.0457017
S27 SER -0.666768
S27 THR 0.0457017
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S28 GLU -0.168379
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S28 TYR 0.0428323
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S29 CYS 0.0535839
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S29 MET 0.0535839
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S29 TRP 0.0535839

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S30 TRP 0.0374425
S30 TYR 0.0374425
S30 --- 0.0374425
S31 ALA 0.0558533
S31 CYS 0.0558533
S31 ASP -0.304866
S31 GLU 0.0558533
S31 PHE 0.0558533
S31 GLY 0.0558533
S31 HIS 0.0558533
S31 ILE -0.182195
S31 LYS 0.0558533
S31 LEU 0.0558533
S31 MET 0.0558533
S31 ASN 0.0558533
S31 PRO 0.0558533
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S31 ARG 0.0558533
S31 SER 0.0558533
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S31 VAL -0.518299
S31 TRP 0.0558533
S31 TYR 0.0558533
S31 --- 0.0558533
S32 ALA 0.0747264
S32 CYS 0.0747264
S32 ASP 0.0747264
S32 GLU 0.0747264
S32 PHE 0.00925722
S32 GLY 0.0747264
S32 HIS -0.292244
S32 ILE 0.0747264
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S32 MET 0.0747264
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S32 SER 0.0747264
S32 THR 0.0747264
S32 VAL 0.0747264
S32 TRP -0.763152

S32 TYR -0.22421
S32 --- 0.0747264
S33 ALA 0.0739303
S33 CYS 0.0739303
S33 ASP -0.766069
S33 GLU 0.0739303
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S33 LYS -0.0694441
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S33 ARG 0.0739303
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S33 THR 0.0739303
S33 VAL -0.082849
S33 TRP 0.0739303
S33 TYR 0.0739303
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S34 ALA 0.0744114
S34 CYS 0.0744114
S34 ASP 0.0744114
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S34 PHE 0.0744114
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S34 LEU 0.0744114
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S34 GLN 0.0744114
S34 ARG -0.176137
S34 SER -0.564181
S34 THR -0.275204
S34 VAL 0.0744114
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S34 TYR 0.0744114
S34 --- 0.0744114
S35 ALA -0.42276
S35 CYS 0.0651425
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S35 THR -0.321945
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S35 TRP 0.0651425

S35 TYR 0.0651425
S35 --- 0.0651425
S36 ALA 0.0727566
S36 CYS 0.0727566
S36 ASP -0.1544
S36 GLU -0.278801
S36 PHE 0.0727566
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S36 THR -0.0628059
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S36 TYR 0.0727566
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S37 CYS 0.087549
S37 ASP -0.140104
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S37 VAL 0.087549
S37 TRP 0.087549
S37 TYR 0.087549
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S38 CYS 0.0941538
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S38 PHE 0.0941538
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S38 TRP 0.0941538

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S38 --- 0.0941538
S39 ALA 0.0563575
S39 CYS 0.0563575
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S39 VAL -0.507753
S39 TRP -0.116358
S39 TYR 0.0563575
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S1 S14 VAL THR 0.00310419
S1 S14 VAL VAL 0.00082059
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S1 S14 VAL TYR 0.00082059
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S1 S14 TRP SER 0.0012436
S1 S14 TRP THR 0.000210894
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S1 S15 ALA LEU 0.000899769
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S1 S15 PHE HIS 4.34414e-05
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S1 S15 PHE LYS 4.34414e-05
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S1 S15 PHE TYR 4.34414e-05
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S1 S15 GLY LEU 0.000899769
S1 S15 GLY GLN 0.000121694
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S1 S15 HIS LEU 0.000899769
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S1 S15 ILE LEU 0.000899769
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S1 S16 ILE LEU 1.38418e-05

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S1 S16 VAL PHE 8.97161e-05
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S1 S16 VAL LYS 8.97161e-05
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S1 S18 ASP GLU 0.0140559
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S1 S18 VAL GLY 7.66213e-05
S1 S18 VAL HIS 0.00708297
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S1 S18 VAL LYS 7.66213e-05
S1 S18 VAL LEU 7.66213e-05
S1 S18 VAL MET 7.66213e-05
S1 S18 VAL ASN 7.66213e-05
S1 S18 VAL PRO 7.66213e-05
S1 S18 VAL GLN 7.66213e-05
S1 S18 VAL ARG 7.66213e-05
S1 S18 VAL SER 7.66213e-05
S1 S18 VAL THR 7.66213e-05
S1 S18 VAL VAL 7.66213e-05
S1 S18 VAL TRP 7.66213e-05
S1 S18 VAL TYR 7.66213e-05
S1 S18 VAL --- 7.66213e-05
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S1 S18 TRP HIS 0.000550185
S1 S18 TYR GLU 0.0140559
S1 S18 TYR HIS 0.000550185
S1 S18 --- GLU 0.0140559
S1 S18 --- HIS 0.000550185
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S1 S19 ALA TYR 0.000682089
S1 S19 CYS ALA 0.00747885
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S1 S19 ASP TYR 0.000682089
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S1 S19 GLU TYR 0.000682089
S1 S19 PHE ALA 0.144556
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S1 S19 PHE GLU 0.000568566
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S1 S19 PHE MET 0.000568566
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S1 S19 PHE PRO 0.000568566
S1 S19 PHE GLN 0.000568566
S1 S19 PHE ARG 0.000568566

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S1 S19 PHE TYR 0.0190843
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S1 S19 HIS TYR 0.000682089
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S1 S22 PHE CYS 0.000448993

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S1 S22 THR PHE 0.0208172
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S1 S23 CYS ILE 0.0110513
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S1 S23 GLU ILE 0.0110513
S1 S23 GLU LEU 0.00355482
S1 S23 PHE ALA 0.000275106

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S1 S23 THR TYR 0.0152576
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S1 S23 TYR LEU 0.00355482
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S1 S23 --- LEU 0.00355482
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S1 S25 ASP THR 0.000159317
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S1 S25 GLY SER 0.0122305
S1 S25 GLY THR 0.000159317
S1 S25 HIS ASP 5.0827e-05
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S1 S25 HIS SER 0.0122305
S1 S25 HIS THR 0.000159317
S1 S25 ILE ASP 5.0827e-05
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S1 S25 ILE ARG 0.00127899
S1 S25 ILE SER 0.0122305
S1 S25 ILE THR 0.000159317

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S1 S25 LYS THR 0.000159317
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S1 S25 TYR THR 0.000159317
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S1 S27 VAL HIS 7.49142e-05
S1 S27 VAL ILE 7.49142e-05
S1 S27 VAL LYS 7.49142e-05
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S1 S27 VAL GLN 7.49142e-05
S1 S27 VAL ARG 7.49142e-05
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S1 S27 VAL VAL 7.49142e-05

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S1 S27 VAL TYR 7.49142e-05
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S1 S40 THR --- 0.0151607
S1 S40 VAL ALA 0.000239127
S1 S40 VAL CYS 0.000239127
S1 S40 VAL ASP 0.000239127
S1 S40 VAL GLU 0.000239127
S1 S40 VAL PHE 0.000239127
S1 S40 VAL GLY 0.000239127
S1 S40 VAL HIS 0.000239127
S1 S40 VAL ILE 0.01348
S1 S40 VAL LYS 0.000239127
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S1 S40 VAL MET 0.000239127
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S1 S40 VAL PRO 0.000239127
S1 S40 VAL GLN 0.000239127
S1 S40 VAL ARG 0.000239127
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S1 S40 VAL THR 0.000239127
S1 S40 VAL VAL -0.11702
S1 S40 VAL TRP 0.000239127
S1 S40 VAL TYR 0.000239127
S1 S40 VAL --- 0.000239127

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S1 S40 TRP LEU 0.00167038
S1 S40 TRP VAL 0.0113845
S1 S40 TYR ILE 0.00155124
S1 S40 TYR LEU 0.00167038
S1 S40 TYR VAL 0.0113845
S1 S40 --- ILE 0.00155124
S1 S40 --- LEU 0.00167038
S1 S40 --- VAL 0.0113845
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S2 S3 ALA TYR 0.0121925
S2 S3 CYS PHE 0.000126492
S2 S3 CYS TYR 0.0121925
S2 S3 ASP PHE 0.000126492
S2 S3 ASP TYR 0.0121925
S2 S3 GLU PHE 0.000126492
S2 S3 GLU TYR 0.0121925
S2 S3 PHE PHE 0.000126492
S2 S3 PHE TYR 0.0121925
S2 S3 GLY PHE 0.000126492
S2 S3 GLY TYR 0.0121925
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S2 S3 HIS TYR 0.0121925
S2 S3 ILE PHE 0.000126492
S2 S3 ILE TYR 0.0121925
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S2 S3 LYS TYR 0.0121925
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S2 S3 MET TYR 0.0121925
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S2 S3 ASN TYR 0.0121925
S2 S3 PRO PHE 0.000126492
S2 S3 PRO TYR 0.0121925
S2 S3 GLN PHE 0.000126492
S2 S3 GLN TYR 0.0121925
S2 S3 ARG ALA 0.01235
S2 S3 ARG CYS 0.01235
S2 S3 ARG ASP 0.01235
S2 S3 ARG GLU 0.01235
S2 S3 ARG PHE -0.0614851
S2 S3 ARG GLY 0.01235
S2 S3 ARG HIS 0.01235
S2 S3 ARG ILE 0.01235
S2 S3 ARG LYS 0.01235
S2 S3 ARG LEU 0.01235
S2 S3 ARG MET 0.01235
S2 S3 ARG ASN 0.01235
S2 S3 ARG PRO 0.01235
S2 S3 ARG GLN 0.01235
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S2 S3 ARG SER 0.01235
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S2 S3 ARG TRP 0.01235
S2 S3 ARG TYR -0.339863
S2 S3 ARG --- 0.01235
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S2 S3 SER CYS 0.000503535
S2 S3 SER ASP 0.000503535
S2 S3 SER GLU 0.000503535
S2 S3 SER PHE 0.0077266

S2 S3 SER GLY 0.000503535
S2 S3 SER HIS 0.000503535
S2 S3 SER ILE 0.000503535
S2 S3 SER LYS 0.000503535
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S2 S3 SER MET 0.000503535
S2 S3 SER ASN 0.000503535
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S2 S3 TRP TYR 0.0121925
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S2 S3 --- TYR 0.0121925
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S2 S18 SER GLY 0.000672779

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S2 S38 SER TYR 0.00105921
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S2 S38 THR HIS 0.00337985
S2 S38 THR LYS 0.00326727
S2 S38 THR LEU 0.00423158
S2 S38 THR ARG 0.000657639
S2 S38 VAL GLU 0.000782617
S2 S38 VAL HIS 0.00337985
S2 S38 VAL LYS 0.00326727
S2 S38 VAL LEU 0.00423158
S2 S38 VAL ARG 0.000657639
S2 S38 TRP GLU 0.000782617
S2 S38 TRP HIS 0.00337985
S2 S38 TRP LYS 0.00326727
S2 S38 TRP LEU 0.00423158
S2 S38 TRP ARG 0.000657639
S2 S38 TYR GLU 0.000782617
S2 S38 TYR HIS 0.00337985
S2 S38 TYR LYS 0.00326727
S2 S38 TYR LEU 0.00423158
S2 S38 TYR ARG 0.000657639
S2 S38 --- GLU 0.000782617
S2 S38 --- HIS 0.00337985
S2 S38 --- LYS 0.00326727
S2 S38 --- LEU 0.00423158
S2 S38 --- ARG 0.000657639
S2 S39 ALA ILE 0.0014879
S2 S39 ALA LEU 0.00127534
S2 S39 ALA VAL 0.00880183
S2 S39 ALA TRP 0.000753895
S2 S39 CYS ILE 0.0014879
S2 S39 CYS LEU 0.00127534
S2 S39 CYS VAL 0.00880183
S2 S39 CYS TRP 0.000753895
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S2 S39 ASP VAL 0.00880183
S2 S39 ASP TRP 0.000753895
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S2 S39 GLU VAL 0.00880183
S2 S39 GLU TRP 0.000753895
S2 S39 PHE ILE 0.0014879
S2 S39 PHE LEU 0.00127534
S2 S39 PHE VAL 0.00880183
S2 S39 PHE TRP 0.000753895
S2 S39 GLY ILE 0.0014879
S2 S39 GLY LEU 0.00127534
S2 S39 GLY VAL 0.00880183
S2 S39 GLY TRP 0.000753895
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S2 S39 HIS LEU 0.00127534
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S2 S39 HIS TRP 0.000753895
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S2 S39 ILE TRP 0.000753895
S2 S39 LYS ILE 0.0014879
S2 S39 LYS LEU 0.00127534
S2 S39 LYS VAL 0.00880183

S2 S39 LYS TRP 0.000753895
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S2 S39 LEU LEU 0.00127534
S2 S39 LEU VAL 0.00880183
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S2 S39 SER GLY 0.00322504
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S2 S39 SER PRO 0.00322504
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S2 S39 SER THR 0.00322504
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S2 S39 SER TRP -0.475241
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S2 S39 SER --- 0.00322504

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S2 S39 VAL TRP 0.000753895
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S2 S39 TRP LEU 0.00127534
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S2 S39 --- TRP 0.000753895
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S2 S40 VAL LEU 0.000558096
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S2 S40 TRP LEU 0.000558096
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S2 S40 TYR LEU 0.000558096
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S2 S40 --- VAL 0.0105966
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S3 S4 CYS ILE 0.00885846
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S3 S4 PHE PHE 0.000964133
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S3 S4 PHE LYS 0.000964133
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S3 S4 PHE MET 0.000964133
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S3 S4 TYR GLN 0.0157955
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S3 S4 TYR TYR 0.0157955
S3 S4 TYR --- 0.0157955
S3 S4 --- ILE 0.00885846
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S3 S5 CYS TRP 0.00901188
S3 S5 ASP PHE 0.000448164
S3 S5 ASP SER 0.00328911
S3 S5 ASP THR 0.000104341
S3 S5 ASP TRP 0.00901188
S3 S5 GLU PHE 0.000448164
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S3 S5 GLU TRP 0.00901188
S3 S5 PHE ALA 0.00016153
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S3 S5 PHE ILE 0.00016153
S3 S5 PHE LYS 0.00016153
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S3 S5 HIS TRP 0.00901188
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S3 S5 LYS THR 0.000104341
S3 S5 LYS TRP 0.00901188

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S3 S5 MET TRP 0.00901188
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S3 S5 VAL TRP 0.00901188
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S3 S5 TYR LYS 0.0218922
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S3 S6 PHE LYS 0.000429326
S3 S6 PHE LEU 0.000429326
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S3 S6 PHE ASN 0.000429326
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S3 S6 TYR LEU 0.0162559
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S3 S6 TYR TYR 0.0162559
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S3 S6 --- ASP 0.00862245
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S3 S7 HIS THR 0.0018666

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S3 S22 GLU ASP 0.00124368
S3 S22 GLU GLU 0.000153008
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S3 S22 GLU TYR 0.00157254
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S3 S27 TYR PRO 0.0147831
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S3 S27 --- SER 0.0107276
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S3 S28 ALA GLU 0.00166789
S3 S28 CYS ASP 0.0111856
S3 S28 CYS GLU 0.00166789
S3 S28 ASP ASP 0.0111856

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S3 S28 GLU GLU 0.00166789
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S3 S28 PHE CYS 0.000272728
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S3 S28 PHE GLU 0.129531
S3 S28 PHE PHE 0.000272728
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S3 S30 ALA GLN 0.0124894
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S3 S33 GLY VAL 0.00167926
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S3 S33 HIS VAL 0.00167926
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S3 S38 ALA LYS 0.00173518
S3 S38 ALA LEU 0.00475807
S3 S38 ALA ARG 0.00110797
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S3 S38 CYS HIS 0.00442119
S3 S38 CYS LYS 0.00173518
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S3 S38 ASP HIS 0.00442119
S3 S38 ASP LYS 0.00173518
S3 S38 ASP LEU 0.00475807
S3 S38 ASP ARG 0.00110797
S3 S38 GLU GLU 0.000831087

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S3 S38 GLU LEU 0.00475807
S3 S38 GLU ARG 0.00110797
S3 S38 PHE ALA 0.000649326
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S3 S38 PHE LYS 0.0569212
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S3 S38 PHE MET 0.000649326
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S3 S38 PHE SER 0.000649326
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S3 S38 GLY LYS 0.00173518
S3 S38 GLY LEU 0.00475807
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S3 S38 LYS LYS 0.00173518
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S3 S39 ALA TRP 0.0001057
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S4 S5 ASP SER 0.00551463
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S4 S11 ILE MET 0.0103883

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S4 S11 LEU SER 0.0100463
S4 S11 MET ALA 0.00671327
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S4 S12 GLU GLU 0.00177113
S4 S12 GLU GLN 0.0149885

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S4 S12 PHE GLN 0.0149885
S4 S12 GLY GLU 0.00177113
S4 S12 GLY GLN 0.0149885
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S4 S12 LYS GLN 0.0149885
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S4 S12 MET GLN 0.0149885
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S4 S14 ALA THR 0.000430296
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S4 S14 CYS SER 0.000186149
S4 S14 CYS THR 0.000430296
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S4 S14 ASP GLU 0.0143444
S4 S14 ASP SER 0.000186149
S4 S14 ASP THR 0.000430296
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S4 S14 ILE LYS 0.0131217

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S4 S15 ILE LYS 0.0207373
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S4 S15 LYS LEU 0.000990189
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S4 S16 SER LEU 5.07394e-05
S4 S16 SER THR 0.000259231
S4 S16 SER VAL 0.00607713
S4 S16 THR ALA 0.000181739

S4 S16 THR ILE 0.0101908
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S4 S16 THR THR 0.000259231
S4 S16 THR VAL 0.00607713
S4 S16 VAL ALA 0.147618
S4 S16 VAL CYS 0.004714
S4 S16 VAL ASP 0.004714
S4 S16 VAL GLU 0.004714
S4 S16 VAL PHE 0.004714
S4 S16 VAL GLY 0.004714
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S4 S16 VAL LYS 0.004714
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S4 S16 VAL TYR 0.004714
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S4 S16 TRP ALA 0.000181739
S4 S16 TRP ILE 0.0101908
S4 S16 TRP LEU 5.07394e-05
S4 S16 TRP THR 0.000259231
S4 S16 TRP VAL 0.00607713
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S4 S16 TYR ILE 0.0101908
S4 S16 TYR LEU 5.07394e-05
S4 S16 TYR THR 0.000259231
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S4 S16 --- ILE 0.0101908
S4 S16 --- LEU 5.07394e-05
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S4 S16 --- VAL 0.00607713
S4 S17 ALA PHE 0.00797025
S4 S17 ALA HIS 0.00550108
S4 S17 ALA ILE 0.00119162
S4 S17 ALA TRP 4.43689e-05
S4 S17 ALA TYR 0.00205229
S4 S17 CYS PHE 0.00797025
S4 S17 CYS HIS 0.00550108
S4 S17 CYS ILE 0.00119162
S4 S17 CYS TRP 4.43689e-05
S4 S17 CYS TYR 0.00205229
S4 S17 ASP PHE 0.00797025
S4 S17 ASP HIS 0.00550108
S4 S17 ASP ILE 0.00119162
S4 S17 ASP TRP 4.43689e-05
S4 S17 ASP TYR 0.00205229
S4 S17 GLU PHE 0.00797025
S4 S17 GLU HIS 0.00550108
S4 S17 GLU ILE 0.00119162
S4 S17 GLU TRP 4.43689e-05
S4 S17 GLU TYR 0.00205229
S4 S17 PHE PHE 0.00797025
S4 S17 PHE HIS 0.00550108
S4 S17 PHE ILE 0.00119162

S4 S17 PHE TRP 4.43689e-05
S4 S17 PHE TYR 0.00205229
S4 S17 GLY PHE 0.00797025
S4 S17 GLY HIS 0.00550108
S4 S17 GLY ILE 0.00119162
S4 S17 GLY TRP 4.43689e-05
S4 S17 GLY TYR 0.00205229
S4 S17 HIS PHE 0.00797025
S4 S17 HIS HIS 0.00550108
S4 S17 HIS ILE 0.00119162
S4 S17 HIS TRP 4.43689e-05
S4 S17 HIS TYR 0.00205229
S4 S17 ILE ALA 0.0180557
S4 S17 ILE CYS 0.0180557
S4 S17 ILE ASP 0.0180557
S4 S17 ILE GLU 0.0180557
S4 S17 ILE PHE -0.599395
S4 S17 ILE GLY 0.0180557
S4 S17 ILE HIS 0.176934
S4 S17 ILE ILE -0.256058
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S4 S17 ILE GLN 0.0180557
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S4 S17 ILE TYR 0.209531
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S4 S17 LYS PHE 0.00797025
S4 S17 LYS HIS 0.00550108
S4 S17 LYS ILE 0.00119162
S4 S17 LYS TRP 4.43689e-05
S4 S17 LYS TYR 0.00205229
S4 S17 LEU PHE 0.00797025
S4 S17 LEU HIS 0.00550108
S4 S17 LEU ILE 0.00119162
S4 S17 LEU TRP 4.43689e-05
S4 S17 LEU TYR 0.00205229
S4 S17 MET PHE 0.00797025
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S4 S17 MET ILE 0.00119162
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S4 S17 MET TYR 0.00205229
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S4 S17 PRO ILE 0.00119162
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S4 S17 PRO TYR 0.00205229
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S4 S17 GLN HIS 0.00550108
S4 S17 GLN ILE 0.00119162
S4 S17 GLN TRP 4.43689e-05
S4 S17 GLN TYR 0.00205229

S4 S17 ARG PHE 0.00797025
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S4 S17 THR HIS 0.00550108
S4 S17 THR ILE 0.00119162
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S4 S17 VAL ALA 0.00666346
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S4 S17 VAL LEU 0.00666346
S4 S17 VAL MET 0.00666346
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S4 S17 VAL PRO 0.00666346
S4 S17 VAL GLN 0.00666346
S4 S17 VAL ARG 0.00666346
S4 S17 VAL SER 0.00666346
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S4 S17 VAL --- 0.00666346
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S4 S17 TRP HIS 0.00550108
S4 S17 TRP ILE 0.00119162
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S4 S17 TRP TYR 0.00205229
S4 S17 TYR PHE 0.00797025
S4 S17 TYR HIS 0.00550108
S4 S17 TYR ILE 0.00119162
S4 S17 TYR TRP 4.43689e-05
S4 S17 TYR TYR 0.00205229
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S4 S17 --- HIS 0.00550108
S4 S17 --- ILE 0.00119162
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S4 S17 --- TYR 0.00205229
S4 S18 ALA GLU 0.0161708
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S4 S18 GLU GLU 0.0161708
S4 S18 GLU HIS 0.000588765
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S4 S18 PHE HIS 0.000588765
S4 S18 GLY GLU 0.0161708
S4 S18 GLY HIS 0.000588765

S4 S18 HIS GLU 0.0161708
S4 S18 HIS HIS 0.000588765
S4 S18 ILE ALA 0.00972416
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S4 S18 ILE GLU -0.0638768
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S4 S18 GLN GLU 0.0161708
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S4 S18 VAL TYR 0.00311607
S4 S18 VAL --- 0.00311607
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S4 S18 TYR HIS 0.000588765
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S4 S18 --- HIS 0.000588765
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S4 S19 CYS TYR 0.000569605
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S4 S19 ASP SER 0.00687577
S4 S19 ASP TYR 0.000569605
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S4 S19 GLU SER 0.00687577
S4 S19 GLU TYR 0.000569605
S4 S19 PHE ALA 0.00931424
S4 S19 PHE SER 0.00687577
S4 S19 PHE TYR 0.000569605
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S4 S19 ILE ALA -0.551384
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S4 S19 ILE GLY 0.0115092
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S4 S19 ILE ILE 0.0115092
S4 S19 ILE LYS 0.0115092
S4 S19 ILE LEU 0.0115092
S4 S19 ILE MET 0.0115092
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S4 S19 PRO TYR 0.000569605
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S4 S20 CYS LEU 0.000922062
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S4 S20 CYS VAL 0.000326645
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S4 S20 ASP LEU 0.000922062
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S4 S20 GLU VAL 0.000326645
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S4 S20 PHE LEU 0.000922062
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S4 S20 PHE VAL 0.000326645
S4 S20 GLY PHE 0.00943882
S4 S20 GLY LEU 0.000922062

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S4 S20 GLY VAL 0.000326645
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S4 S20 HIS LEU 0.000922062
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S4 S20 HIS VAL 0.000326645
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S4 S20 ILE CYS 0.0163607
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S4 S20 ILE PHE -0.0177586
S4 S20 ILE GLY 0.0163607
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S4 S20 TYR PHE 0.00943882
S4 S20 TYR LEU 0.000922062
S4 S20 TYR MET 0.00607209
S4 S20 TYR VAL 0.000326645
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S4 S20 --- MET 0.00607209
S4 S20 --- VAL 0.000326645
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S4 S21 ALA ILE 0.0120761
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S4 S21 ALA TYR 0.000796338
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S4 S21 CYS ILE 0.0120761
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S4 S21 CYS TYR 0.000796338
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S4 S21 ASP ILE 0.0120761
S4 S21 ASP VAL 0.00243496
S4 S21 ASP TYR 0.000796338
S4 S21 GLU PHE 0.0014522
S4 S21 GLU ILE 0.0120761
S4 S21 GLU VAL 0.00243496
S4 S21 GLU TYR 0.000796338
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S4 S21 ILE CYS 0.0193555

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S4 S21 ILE MET 0.0193555
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S4 S21 LYS TYR 0.000796338
S4 S21 LEU PHE 0.0014522
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S4 S21 THR VAL 0.00243496
S4 S21 THR TYR 0.000796338
S4 S21 VAL ALA 0.00377031
S4 S21 VAL CYS 0.00377031
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S4 S21 VAL HIS 0.00377031
S4 S21 VAL ILE -0.706058

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S4 S21 VAL GLN 0.00377031
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S4 S21 TRP ILE 0.0120761
S4 S21 TRP VAL 0.00243496
S4 S21 TRP TYR 0.000796338
S4 S21 TYR PHE 0.0014522
S4 S21 TYR ILE 0.0120761
S4 S21 TYR VAL 0.00243496
S4 S21 TYR TYR 0.000796338
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S4 S21 --- ILE 0.0120761
S4 S21 --- VAL 0.00243496
S4 S21 --- TYR 0.000796338
S4 S22 ALA ASP 0.00195769
S4 S22 ALA GLU 0.0009078
S4 S22 ALA ASN 0.0125576
S4 S22 ALA TYR 0.00133651
S4 S22 CYS ASP 0.00195769
S4 S22 CYS GLU 0.0009078
S4 S22 CYS ASN 0.0125576
S4 S22 CYS TYR 0.00133651
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S4 S22 ASP GLU 0.0009078
S4 S22 ASP ASN 0.0125576
S4 S22 ASP TYR 0.00133651
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S4 S22 GLU ASN 0.0125576
S4 S22 GLU TYR 0.00133651
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S4 S22 PHE ASN 0.0125576
S4 S22 PHE TYR 0.00133651
S4 S22 GLY ASP 0.00195769
S4 S22 GLY GLU 0.0009078
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S4 S22 GLY TYR 0.00133651
S4 S22 HIS ASP 0.00195769
S4 S22 HIS GLU 0.0009078
S4 S22 HIS ASN 0.0125576
S4 S22 HIS TYR 0.00133651
S4 S22 ILE ALA 0.0120408
S4 S22 ILE CYS 0.0120408
S4 S22 ILE ASP 0.274541
S4 S22 ILE GLU 0.531699
S4 S22 ILE PHE 0.0120408
S4 S22 ILE GLY 0.0120408
S4 S22 ILE HIS 0.0120408
S4 S22 ILE ILE 0.0120408
S4 S22 ILE LYS 0.0120408
S4 S22 ILE LEU 0.0120408

S4 S22 ILE MET 0.0120408
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S4 S22 ILE ARG 0.0120408
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S4 S22 ILE THR 0.0120408
S4 S22 ILE VAL 0.0120408
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S4 S22 ILE TYR -0.676347
S4 S22 ILE --- 0.0120408
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S4 S22 LYS GLU 0.0009078
S4 S22 LYS ASN 0.0125576
S4 S22 LYS TYR 0.00133651
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S4 S22 LEU TYR 0.00133651
S4 S22 MET ASP 0.00195769
S4 S22 MET GLU 0.0009078
S4 S22 MET ASN 0.0125576
S4 S22 MET TYR 0.00133651
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S4 S22 ASN GLU 0.0009078
S4 S22 ASN ASN 0.0125576
S4 S22 ASN TYR 0.00133651
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S4 S22 PRO ASN 0.0125576
S4 S22 PRO TYR 0.00133651
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S4 S22 GLN GLU 0.0009078
S4 S22 GLN ASN 0.0125576
S4 S22 GLN TYR 0.00133651
S4 S22 ARG ASP 0.00195769
S4 S22 ARG GLU 0.0009078
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S4 S22 ARG TYR 0.00133651
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S4 S22 SER GLU 0.0009078
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S4 S22 SER TYR 0.00133651
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S4 S22 VAL HIS 0.00949315
S4 S22 VAL ILE 0.00949315
S4 S22 VAL LYS 0.00949315
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S4 S22 VAL GLN 0.00949315
S4 S22 VAL ARG 0.00949315
S4 S22 VAL SER 0.00949315

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S4 S22 VAL TRP 0.00949315
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S4 S22 --- TYR 0.00133651
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S4 S23 CYS ILE 0.012377
S4 S23 CYS LEU 0.00438266
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S4 S23 ASP LEU 0.00438266
S4 S23 GLU ILE 0.012377
S4 S23 GLU LEU 0.00438266
S4 S23 PHE ILE 0.012377
S4 S23 PHE LEU 0.00438266
S4 S23 GLY ILE 0.012377
S4 S23 GLY LEU 0.00438266
S4 S23 HIS ILE 0.012377
S4 S23 HIS LEU 0.00438266
S4 S23 ILE ALA 0.0118095
S4 S23 ILE CYS 0.0118095
S4 S23 ILE ASP 0.0118095
S4 S23 ILE GLU 0.0118095
S4 S23 ILE PHE 0.0118095
S4 S23 ILE GLY 0.0118095
S4 S23 ILE HIS 0.0118095
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S4 S23 ILE LYS 0.0118095
S4 S23 ILE LEU -0.00939919
S4 S23 ILE MET 0.0118095
S4 S23 ILE ASN 0.0118095
S4 S23 ILE PRO 0.0118095
S4 S23 ILE GLN 0.0118095
S4 S23 ILE ARG 0.0118095
S4 S23 ILE SER 0.0118095
S4 S23 ILE THR 0.0118095
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S4 S23 PRO ILE 0.012377
S4 S23 PRO LEU 0.00438266
S4 S23 GLN ILE 0.012377

S4 S23 GLN LEU 0.00438266
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S4 S23 SER LEU 0.00438266
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S4 S23 VAL GLU 0.00393284
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S4 S23 VAL PRO 0.00393284
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S4 S23 VAL ARG 0.00393284
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S4 S23 VAL --- 0.00393284
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S4 S23 TYR ILE 0.012377
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S4 S24 ALA GLY 0.0165735
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S4 S24 CYS SER 0.000186149
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S4 S24 ASP SER 0.000186149
S4 S24 GLU GLY 0.0165735
S4 S24 GLU SER 0.000186149
S4 S24 PHE GLY 0.0165735
S4 S24 PHE SER 0.000186149
S4 S24 GLY GLY 0.0165735
S4 S24 GLY SER 0.000186149
S4 S24 HIS GLY 0.0165735
S4 S24 HIS SER 0.000186149
S4 S24 ILE ALA 0.00690828
S4 S24 ILE CYS 0.00690828
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S4 S24 ILE GLU 0.00690828
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S4 S24 ILE GLY -0.568562
S4 S24 ILE HIS 0.00690828
S4 S24 ILE ILE 0.00690828
S4 S24 ILE LYS 0.00690828
S4 S24 ILE LEU 0.00690828
S4 S24 ILE MET 0.00690828
S4 S24 ILE ASN 0.00690828
S4 S24 ILE PRO 0.00690828
S4 S24 ILE GLN 0.00690828
S4 S24 ILE ARG 0.00690828

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S4 S24 ILE TRP 0.00690828
S4 S24 ILE TYR 0.00690828
S4 S24 ILE --- 0.00690828
S4 S24 LYS GLY 0.0165735
S4 S24 LYS SER 0.000186149
S4 S24 LEU GLY 0.0165735
S4 S24 LEU SER 0.000186149
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S4 S24 MET SER 0.000186149
S4 S24 ASN GLY 0.0165735
S4 S24 ASN SER 0.000186149
S4 S24 PRO GLY 0.0165735
S4 S24 PRO SER 0.000186149
S4 S24 GLN GLY 0.0165735
S4 S24 GLN SER 0.000186149
S4 S24 ARG GLY 0.0165735
S4 S24 ARG SER 0.000186149
S4 S24 SER GLY 0.0165735
S4 S24 SER SER 0.000186149
S4 S24 THR GLY 0.0165735
S4 S24 THR SER 0.000186149
S4 S24 VAL ALA 0.00470991
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S4 S24 VAL ASP 0.00470991
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S4 S24 VAL ILE 0.00470991
S4 S24 VAL LYS 0.00470991
S4 S24 VAL LEU 0.00470991
S4 S24 VAL MET 0.00470991
S4 S24 VAL ASN 0.00470991
S4 S24 VAL PRO 0.00470991
S4 S24 VAL GLN 0.00470991
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S4 S24 VAL VAL 0.00470991
S4 S24 VAL TRP 0.00470991
S4 S24 VAL TYR 0.00470991
S4 S24 VAL --- 0.00470991
S4 S24 TRP GLY 0.0165735
S4 S24 TRP SER 0.000186149
S4 S24 TYR GLY 0.0165735
S4 S24 TYR SER 0.000186149
S4 S24 --- GLY 0.0165735
S4 S24 --- SER 0.000186149
S4 S25 ALA ASP 9.82682e-05
S4 S25 ALA GLU 0.00019669
S4 S25 ALA LYS 0.0003714
S4 S25 ALA ARG 0.00289879
S4 S25 ALA SER 0.0124513
S4 S25 ALA THR 0.000743203
S4 S25 CYS ASP 9.82682e-05
S4 S25 CYS GLU 0.00019669
S4 S25 CYS LYS 0.0003714
S4 S25 CYS ARG 0.00289879
S4 S25 CYS SER 0.0124513
S4 S25 CYS THR 0.000743203

S4 S25 ASP ASP 9.82682e-05
S4 S25 ASP GLU 0.00019669
S4 S25 ASP LYS 0.0003714
S4 S25 ASP ARG 0.00289879
S4 S25 ASP SER 0.0124513
S4 S25 ASP THR 0.000743203
S4 S25 GLU ASP 9.82682e-05
S4 S25 GLU GLU 0.00019669
S4 S25 GLU LYS 0.0003714
S4 S25 GLU ARG 0.00289879
S4 S25 GLU SER 0.0124513
S4 S25 GLU THR 0.000743203
S4 S25 PHE ASP 9.82682e-05
S4 S25 PHE GLU 0.00019669
S4 S25 PHE LYS 0.0003714
S4 S25 PHE ARG 0.00289879
S4 S25 PHE SER 0.0124513
S4 S25 PHE THR 0.000743203
S4 S25 GLY ASP 9.82682e-05
S4 S25 GLY GLU 0.00019669
S4 S25 GLY LYS 0.0003714
S4 S25 GLY ARG 0.00289879
S4 S25 GLY SER 0.0124513
S4 S25 GLY THR 0.000743203
S4 S25 HIS ASP 9.82682e-05
S4 S25 HIS GLU 0.00019669
S4 S25 HIS LYS 0.0003714
S4 S25 HIS ARG 0.00289879
S4 S25 HIS SER 0.0124513
S4 S25 HIS THR 0.000743203
S4 S25 ILE ALA 0.017277
S4 S25 ILE CYS 0.017277
S4 S25 ILE ASP 0.2503
S4 S25 ILE GLU -0.289907
S4 S25 ILE PHE 0.017277
S4 S25 ILE GLY 0.017277
S4 S25 ILE HIS 0.017277
S4 S25 ILE ILE 0.017277
S4 S25 ILE LYS -0.203832
S4 S25 ILE LEU 0.017277
S4 S25 ILE MET 0.017277
S4 S25 ILE ASN 0.017277
S4 S25 ILE PRO 0.017277
S4 S25 ILE GLN 0.017277
S4 S25 ILE ARG 0.819104
S4 S25 ILE SER -0.235526
S4 S25 ILE THR -0.855623
S4 S25 ILE VAL 0.017277
S4 S25 ILE TRP 0.017277
S4 S25 ILE TYR 0.017277
S4 S25 ILE --- 0.017277
S4 S25 LYS ASP 9.82682e-05
S4 S25 LYS GLU 0.00019669
S4 S25 LYS LYS 0.0003714
S4 S25 LYS ARG 0.00289879
S4 S25 LYS SER 0.0124513
S4 S25 LYS THR 0.000743203
S4 S25 LEU ASP 9.82682e-05
S4 S25 LEU GLU 0.00019669
S4 S25 LEU LYS 0.0003714
S4 S25 LEU ARG 0.00289879
S4 S25 LEU SER 0.0124513
S4 S25 LEU THR 0.000743203

S4 S25 MET ASP 9.82682e-05
S4 S25 MET GLU 0.00019669
S4 S25 MET LYS 0.0003714
S4 S25 MET ARG 0.00289879
S4 S25 MET SER 0.0124513
S4 S25 MET THR 0.000743203
S4 S25 ASN ASP 9.82682e-05
S4 S25 ASN GLU 0.00019669
S4 S25 ASN LYS 0.0003714
S4 S25 ASN ARG 0.00289879
S4 S25 ASN SER 0.0124513
S4 S25 ASN THR 0.000743203
S4 S25 PRO ASP 9.82682e-05
S4 S25 PRO GLU 0.00019669
S4 S25 PRO LYS 0.0003714
S4 S25 PRO ARG 0.00289879
S4 S25 PRO SER 0.0124513
S4 S25 PRO THR 0.000743203
S4 S25 GLN ASP 9.82682e-05
S4 S25 GLN GLU 0.00019669
S4 S25 GLN LYS 0.0003714
S4 S25 GLN ARG 0.00289879
S4 S25 GLN SER 0.0124513
S4 S25 GLN THR 0.000743203
S4 S25 ARG ASP 9.82682e-05
S4 S25 ARG GLU 0.00019669
S4 S25 ARG LYS 0.0003714
S4 S25 ARG ARG 0.00289879
S4 S25 ARG SER 0.0124513
S4 S25 ARG THR 0.000743203
S4 S25 SER ASP 9.82682e-05
S4 S25 SER GLU 0.00019669
S4 S25 SER LYS 0.0003714
S4 S25 SER ARG 0.00289879
S4 S25 SER SER 0.0124513
S4 S25 SER THR 0.000743203
S4 S25 THR ASP 9.82682e-05
S4 S25 THR GLU 0.00019669
S4 S25 THR LYS 0.0003714
S4 S25 THR ARG 0.00289879
S4 S25 THR SER 0.0124513
S4 S25 THR THR 0.000743203
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S4 S25 VAL CYS 0.00904099
S4 S25 VAL ASP -0.269689
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S4 S25 VAL PHE 0.00904099
S4 S25 VAL GLY 0.00904099
S4 S25 VAL HIS 0.00904099
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S4 S25 VAL LEU 0.00904099
S4 S25 VAL MET 0.00904099
S4 S25 VAL ASN 0.00904099
S4 S25 VAL PRO 0.00904099
S4 S25 VAL GLN 0.00904099
S4 S25 VAL ARG -0.964809
S4 S25 VAL SER -0.193066
S4 S25 VAL THR 0.83044
S4 S25 VAL VAL 0.00904099
S4 S25 VAL TRP 0.00904099
S4 S25 VAL TYR 0.00904099
S4 S25 VAL --- 0.00904099

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S4 S25 TRP GLU 0.00019669
S4 S25 TRP LYS 0.0003714
S4 S25 TRP ARG 0.00289879
S4 S25 TRP SER 0.0124513
S4 S25 TRP THR 0.000743203
S4 S25 TYR ASP 9.82682e-05
S4 S25 TYR GLU 0.00019669
S4 S25 TYR LYS 0.0003714
S4 S25 TYR ARG 0.00289879
S4 S25 TYR SER 0.0124513
S4 S25 TYR THR 0.000743203
S4 S25 --- ASP 9.82682e-05
S4 S25 --- GLU 0.00019669
S4 S25 --- LYS 0.0003714
S4 S25 --- ARG 0.00289879
S4 S25 --- SER 0.0124513
S4 S25 --- THR 0.000743203
S4 S26 ALA PHE 0.00685845
S4 S26 ALA LYS 0.00922733
S4 S26 ALA TYR 0.000673824
S4 S26 CYS PHE 0.00685845
S4 S26 CYS LYS 0.00922733
S4 S26 CYS TYR 0.000673824
S4 S26 ASP PHE 0.00685845
S4 S26 ASP LYS 0.00922733
S4 S26 ASP TYR 0.000673824
S4 S26 GLU PHE 0.00685845
S4 S26 GLU LYS 0.00922733
S4 S26 GLU TYR 0.000673824
S4 S26 PHE PHE 0.00685845
S4 S26 PHE LYS 0.00922733
S4 S26 PHE TYR 0.000673824
S4 S26 GLY PHE 0.00685845
S4 S26 GLY LYS 0.00922733
S4 S26 GLY TYR 0.000673824
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S4 S26 HIS LYS 0.00922733
S4 S26 HIS TYR 0.000673824
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S4 S26 ILE CYS 0.0152685
S4 S26 ILE ASP 0.0152685
S4 S26 ILE GLU 0.0152685
S4 S26 ILE PHE 0.279557
S4 S26 ILE GLY 0.0152685
S4 S26 ILE HIS 0.0152685
S4 S26 ILE ILE 0.0152685
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S4 S26 ILE LEU 0.0152685
S4 S26 ILE MET 0.0152685
S4 S26 ILE ASN 0.0152685
S4 S26 ILE PRO 0.0152685
S4 S26 ILE GLN 0.0152685
S4 S26 ILE ARG 0.0152685
S4 S26 ILE SER 0.0152685
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S4 S26 ILE VAL 0.0152685
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S4 S26 LYS LYS 0.00922733
S4 S26 LYS TYR 0.000673824

S4 S26 LEU PHE 0.00685845
S4 S26 LEU LYS 0.00922733
S4 S26 LEU TYR 0.000673824
S4 S26 MET PHE 0.00685845
S4 S26 MET LYS 0.00922733
S4 S26 MET TYR 0.000673824
S4 S26 ASN PHE 0.00685845
S4 S26 ASN LYS 0.00922733
S4 S26 ASN TYR 0.000673824
S4 S26 PRO PHE 0.00685845
S4 S26 PRO LYS 0.00922733
S4 S26 PRO TYR 0.000673824
S4 S26 GLN PHE 0.00685845
S4 S26 GLN LYS 0.00922733
S4 S26 GLN TYR 0.000673824
S4 S26 ARG PHE 0.00685845
S4 S26 ARG LYS 0.00922733
S4 S26 ARG TYR 0.000673824
S4 S26 SER PHE 0.00685845
S4 S26 SER LYS 0.00922733
S4 S26 SER TYR 0.000673824
S4 S26 THR PHE 0.00685845
S4 S26 THR LYS 0.00922733
S4 S26 THR TYR 0.000673824
S4 S26 VAL ALA 0.00572116
S4 S26 VAL CYS 0.00572116
S4 S26 VAL ASP 0.00572116
S4 S26 VAL GLU 0.00572116
S4 S26 VAL PHE -0.568471
S4 S26 VAL GLY 0.00572116
S4 S26 VAL HIS 0.00572116
S4 S26 VAL ILE 0.00572116
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S4 S26 VAL MET 0.00572116
S4 S26 VAL ASN 0.00572116
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S4 S26 VAL SER 0.00572116
S4 S26 VAL THR 0.00572116
S4 S26 VAL VAL 0.00572116
S4 S26 VAL TRP 0.00572116
S4 S26 VAL TYR 0.901714
S4 S26 VAL --- 0.00572116
S4 S26 TRP PHE 0.00685845
S4 S26 TRP LYS 0.00922733
S4 S26 TRP TYR 0.000673824
S4 S26 TYR PHE 0.00685845
S4 S26 TYR LYS 0.00922733
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S4 S26 --- PHE 0.00685845
S4 S26 --- LYS 0.00922733
S4 S26 --- TYR 0.000673824
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S4 S27 CYS SER 0.0149343
S4 S27 ASP ASN 0.00182532
S4 S27 ASP SER 0.0149343
S4 S27 GLU ASN 0.00182532
S4 S27 GLU SER 0.0149343
S4 S27 PHE ASN 0.00182532

S4 S27 PHE SER 0.0149343
S4 S27 GLY ASN 0.00182532
S4 S27 GLY SER 0.0149343
S4 S27 HIS ASN 0.00182532
S4 S27 HIS SER 0.0149343
S4 S27 ILE ALA 0.010696
S4 S27 ILE CYS 0.010696
S4 S27 ILE ASP 0.010696
S4 S27 ILE GLU 0.010696
S4 S27 ILE PHE 0.010696
S4 S27 ILE GLY 0.010696
S4 S27 ILE HIS 0.010696
S4 S27 ILE ILE 0.010696
S4 S27 ILE LYS 0.010696
S4 S27 ILE LEU 0.010696
S4 S27 ILE MET 0.010696
S4 S27 ILE ASN -0.189486
S4 S27 ILE PRO 0.010696
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S4 S27 ILE SER -0.270067
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S4 S27 LYS SER 0.0149343
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S4 S27 LEU SER 0.0149343
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S4 S27 VAL GLY 0.00450006
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S4 S27 VAL ILE 0.00450006
S4 S27 VAL LYS 0.00450006
S4 S27 VAL LEU 0.00450006
S4 S27 VAL MET 0.00450006
S4 S27 VAL ASN 0.0874998
S4 S27 VAL PRO 0.00450006
S4 S27 VAL GLN 0.00450006
S4 S27 VAL ARG 0.00450006
S4 S27 VAL SER -0.235105
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S4 S27 VAL TRP 0.00450006

S4 S27 VAL TYR 0.00450006
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S4 S27 --- SER 0.0149343
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S4 S28 ASP ASP 0.0147234
S4 S28 ASP GLU 0.0020362
S4 S28 GLU ASP 0.0147234
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S4 S28 PHE GLU 0.0020362
S4 S28 GLY ASP 0.0147234
S4 S28 GLY GLU 0.0020362
S4 S28 HIS ASP 0.0147234
S4 S28 HIS GLU 0.0020362
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S4 S28 ILE CYS 0.00995388
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S4 S28 ILE GLU -0.00315503
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S4 S32 TYR TYR 0.00218519
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S4 S32 --- HIS 0.00146178
S4 S32 --- TRP 0.0125174
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S4 S33 ILE PHE 0.0183099
S4 S33 ILE GLY 0.0183099
S4 S33 ILE HIS 0.0183099
S4 S33 ILE ILE 0.0183099
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S4 S37 PRO PHE 0.00101826
S4 S37 PRO ASN 0.000432172
S4 S37 PRO ARG 0.00171108
S4 S37 PRO SER 0.00660557
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S4 S37 GLN PHE 0.00101826

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S4 S37 VAL TYR 0.00735093
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S4 S38 ALA HIS 0.00465853
S4 S38 ALA LYS 0.0039589

S4 S38 ALA LEU 0.005692
S4 S38 ALA ARG 0.00173524
S4 S38 CYS GLU 0.00071494
S4 S38 CYS HIS 0.00465853
S4 S38 CYS LYS 0.0039589
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S4 S38 CYS ARG 0.00173524
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S4 S38 ASP HIS 0.00465853
S4 S38 ASP LYS 0.0039589
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S4 S38 GLU LYS 0.0039589
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S4 S38 GLU ARG 0.00173524
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S4 S38 PHE LYS 0.0039589
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S4 S38 HIS ARG 0.00173524
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S4 S38 LEU HIS 0.00465853
S4 S38 LEU LYS 0.0039589
S4 S38 LEU LEU 0.005692
S4 S38 LEU ARG 0.00173524

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S4 S39 --- LEU 0.000842092
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S5 S15 ALA LEU 0.00181293
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S5 S15 GLU SER 0.00907235
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S5 S15 HIS SER 0.00907235
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S5 S15 ILE SER 0.00907235
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S5 S15 LYS LEU 0.00181293
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S5 S15 TRP LYS 0.0202087

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S5 S16 ASP ILE 0.0111878
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S5 S16 HIS ILE 0.0111878
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S5 S16 HIS THR 0.000758675
S5 S16 HIS VAL 0.00898403
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S5 S16 ILE ILE 0.0111878
S5 S16 ILE LEU 0.000155273
S5 S16 ILE THR 0.000758675
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S5 S17 ALA TYR 0.00269902
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S5 S18 SER LYS 0.00458017
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S5 S18 SER TRP 0.00458017
S5 S18 SER TYR 0.00458017
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S5 S18 THR MET 0.000646727

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S5 S18 THR TYR 0.000646727
S5 S18 THR --- 0.000646727
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S5 S18 VAL HIS 0.00225252
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S5 S18 TRP ASP 0.00622947
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S5 S18 TRP HIS 0.467679
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S5 S18 TRP LEU 0.00622947
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S5 S19 ALA TYR 0.000672559
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S5 S19 CYS TYR 0.000672559
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S5 S19 ASP SER 0.00881701
S5 S19 ASP TYR 0.000672559
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S5 S19 GLU TYR 0.000672559
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S5 S19 PHE MET 0.000317762
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S5 S19 PHE GLN 0.000317762

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S5 S19 HIS TYR 0.000672559
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S5 S19 THR GLU 9.39832e-05
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S5 S19 THR LEU 9.39832e-05
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S5 S19 THR ASN 9.39832e-05
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S5 S19 THR GLN 9.39832e-05
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S5 S25 ALA THR 0.000126941
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S5 S25 CYS THR 0.000126941
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S5 S25 ASP SER 0.0194354
S5 S25 ASP THR 0.000126941

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S5 S25 HIS ARG 0.00228088
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S5 S25 HIS THR 0.000126941
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S5 S25 ILE THR 0.000126941
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S5 S25 PRO THR 0.000126941
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S5 S27 THR PHE 7.93633e-05

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S5 S27 THR LYS 7.93633e-05
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S5 S28 THR GLN 4.71235e-05
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S5 S31 ASP VAL 0.0186134
S5 S31 GLU ASP 0.00156969

S5 S31 GLU ILE 0.00187071
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S5 S31 PHE CYS 0.000691529
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S5 S31 PHE PHE 0.000691529
S5 S31 PHE GLY 0.000691529
S5 S31 PHE HIS 0.000691529
S5 S31 PHE ILE 0.017724
S5 S31 PHE LYS 0.000691529
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S5 S31 --- VAL 0.0186134
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S6 S38 THR ARG 0.00182485
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S6 S38 VAL LYS 0.00251022
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S6 S38 VAL ARG 0.00182485
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S7 S9 TYR GLN 0.00265784
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S7 S9 TYR TYR 0.00265784
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S7 S9 --- LYS 0.00547508
S7 S9 --- ARG 0.000471266
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S7 S17 THR ALA 0.00379119
S7 S17 THR CYS 0.00379119
S7 S17 THR ASP 0.00379119
S7 S17 THR GLU 0.00379119
S7 S17 THR PHE -0.23367
S7 S17 THR GLY 0.00379119
S7 S17 THR HIS 0.108828
S7 S17 THR ILE 0.122084
S7 S17 THR LYS 0.00379119
S7 S17 THR LEU 0.00379119
S7 S17 THR MET 0.00379119
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S7 S17 THR PRO 0.00379119
S7 S17 THR GLN 0.00379119
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S7 S17 THR VAL 0.00379119
S7 S17 THR TRP 0.0190941
S7 S17 THR TYR -0.195185
S7 S17 THR --- 0.00379119
S7 S17 VAL PHE 0.0143789
S7 S17 VAL HIS 0.00536159
S7 S17 VAL ILE 0.00105336
S7 S17 VAL TRP 2.42173e-05
S7 S17 VAL TYR 0.00287149
S7 S17 TRP PHE 0.0143789
S7 S17 TRP HIS 0.00536159
S7 S17 TRP ILE 0.00105336
S7 S17 TRP TRP 2.42173e-05
S7 S17 TRP TYR 0.00287149
S7 S17 TYR ALA 0.00374039
S7 S17 TYR CYS 0.00374039
S7 S17 TYR ASP 0.00374039
S7 S17 TYR GLU 0.00374039
S7 S17 TYR PHE 0.228354
S7 S17 TYR GLY 0.00374039
S7 S17 TYR HIS -0.157228
S7 S17 TYR ILE -0.437271
S7 S17 TYR LYS 0.00374039
S7 S17 TYR LEU 0.00374039
S7 S17 TYR MET 0.00374039
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S7 S17 TYR SER 0.00374039

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S7 S17 TYR TYR 0.196948
S7 S17 TYR --- 0.00374039
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S7 S17 --- HIS 0.00536159
S7 S17 --- ILE 0.00105336
S7 S17 --- TRP 2.42173e-05
S7 S17 --- TYR 0.00287149
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S7 S18 ALA CYS 0.00152735
S7 S18 ALA ASP 0.00152735
S7 S18 ALA GLU 0.359031
S7 S18 ALA PHE 0.00152735
S7 S18 ALA GLY 0.00152735
S7 S18 ALA HIS -0.487988
S7 S18 ALA ILE 0.00152735
S7 S18 ALA LYS 0.00152735
S7 S18 ALA LEU 0.00152735
S7 S18 ALA MET 0.00152735
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S7 S18 ALA VAL 0.00152735
S7 S18 ALA TRP 0.00152735
S7 S18 ALA TYR 0.00152735
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S7 S18 CYS GLU 0.0223571
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S7 S18 ASP GLU 0.0223571
S7 S18 ASP HIS 0.00133251
S7 S18 GLU GLU 0.0223571
S7 S18 GLU HIS 0.00133251
S7 S18 PHE GLU 0.0223571
S7 S18 PHE HIS 0.00133251
S7 S18 GLY GLU 0.0223571
S7 S18 GLY HIS 0.00133251
S7 S18 HIS GLU 0.0223571
S7 S18 HIS HIS 0.00133251
S7 S18 ILE GLU 0.0223571
S7 S18 ILE HIS 0.00133251
S7 S18 LYS GLU 0.0223571
S7 S18 LYS HIS 0.00133251
S7 S18 LEU GLU 0.0223571
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S7 S18 GLN GLU 0.0223571
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S7 S18 ARG HIS 0.00133251
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S7 S18 SER CYS 0.00720774
S7 S18 SER ASP 0.00720774
S7 S18 SER GLU -0.899085

S7 S18 SER PHE 0.00720774
S7 S18 SER GLY 0.00720774
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S7 S18 SER ILE 0.00720774
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S7 S18 SER TRP 0.00720774
S7 S18 SER TYR 0.00720774
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S7 S18 THR ASP 0.00279208
S7 S18 THR GLU 0.187788
S7 S18 THR PHE 0.00279208
S7 S18 THR GLY 0.00279208
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S7 S18 THR LYS 0.00279208
S7 S18 THR LEU 0.00279208
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S7 S18 THR TYR 0.00279208
S7 S18 THR --- 0.00279208
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S7 S18 TRP GLU 0.0223571
S7 S18 TRP HIS 0.00133251
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S7 S18 TYR CYS 0.00131306
S7 S18 TYR ASP 0.00131306
S7 S18 TYR GLU -0.163161
S7 S18 TYR PHE 0.00131306
S7 S18 TYR GLY 0.00131306
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S7 S18 TYR LYS 0.00131306
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S7 S19 ALA ALA -0.56491
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S7 S19 ALA ASP 0.000495508
S7 S19 ALA GLU 0.000495508
S7 S19 ALA PHE 0.000495508
S7 S19 ALA GLY 0.000495508
S7 S19 ALA HIS 0.000495508
S7 S19 ALA ILE 0.000495508
S7 S19 ALA LYS 0.000495508
S7 S19 ALA LEU 0.000495508
S7 S19 ALA MET 0.000495508
S7 S19 ALA ASN 0.000495508
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S7 S19 ALA TRP 0.000495508
S7 S19 ALA TYR 0.0174699
S7 S19 ALA --- 0.000495508
S7 S19 CYS ALA 0.0157532
S7 S19 CYS SER 0.00762131
S7 S19 CYS TYR 0.000315053
S7 S19 ASP ALA 0.0157532
S7 S19 ASP SER 0.00762131
S7 S19 ASP TYR 0.000315053
S7 S19 GLU ALA 0.0157532
S7 S19 GLU SER 0.00762131
S7 S19 GLU TYR 0.000315053
S7 S19 PHE ALA 0.0157532
S7 S19 PHE SER 0.00762131
S7 S19 PHE TYR 0.000315053
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S7 S19 ILE TYR 0.000315053
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S7 S19 PRO TYR 0.000315053
S7 S19 GLN ALA 0.0157532
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S7 S19 GLN TYR 0.000315053
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S7 S19 SER ASP 0.012029
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S7 S19 SER TRP 0.012029
S7 S19 SER TYR 0.0924922
S7 S19 SER --- 0.012029
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S7 S19 THR GLU 0.0027584
S7 S19 THR PHE 0.0027584
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S7 S19 THR HIS 0.0027584
S7 S19 THR ILE 0.0027584
S7 S19 THR LYS 0.0027584
S7 S19 THR LEU 0.0027584
S7 S19 THR MET 0.0027584
S7 S19 THR ASN 0.0027584
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S7 S19 THR TRP 0.0027584
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S7 S19 THR --- 0.0027584
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S7 S19 VAL TYR 0.000315053
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S7 S19 TRP TYR 0.000315053
S7 S19 TYR ALA 0.732248
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S7 S19 TYR LYS 0.00341057
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S7 S19 TYR MET 0.00341057
S7 S19 TYR ASN 0.00341057
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S7 S20 ALA ALA 0.000699846
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S7 S20 ALA GLU 0.000699846
S7 S20 ALA PHE -0.27564
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S7 S20 ALA HIS 0.000699846
S7 S20 ALA ILE 0.000699846
S7 S20 ALA LYS 0.000699846
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S7 S20 HIS LEU 0.00179003
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S7 S20 LYS LEU 0.00179003
S7 S20 LYS MET 0.0100607

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S7 S20 SER GLY 0.0150539
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S7 S20 SER LEU 0.805981
S7 S20 SER MET -0.809203
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S7 S20 THR ILE 0.00294626
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S7 S20 THR THR 0.00294626

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S7 S21 ALA GLY 0.000816638
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S7 S21 ALA TRP 0.000816638
S7 S21 ALA TYR -0.443303
S7 S21 ALA --- 0.000816638
S7 S21 CYS PHE 0.00113991
S7 S21 CYS ILE 0.0196493
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S7 S21 CYS TYR 0.00162265
S7 S21 ASP PHE 0.00113991

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S7 S21 ASP TYR 0.00162265
S7 S21 GLU PHE 0.00113991
S7 S21 GLU ILE 0.0196493
S7 S21 GLU VAL 0.0012777
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S7 S21 PHE PHE 0.00113991
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S7 S21 MET ILE 0.0196493
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S7 S21 PRO PHE 0.00113991
S7 S21 PRO ILE 0.0196493
S7 S21 PRO VAL 0.0012777
S7 S21 PRO TYR 0.00162265
S7 S21 GLN PHE 0.00113991
S7 S21 GLN ILE 0.0196493
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S7 S21 ARG PHE 0.00113991
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S7 S21 SER HIS 0.0179856
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S7 S21 SER LYS 0.0179856
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S7 S21 SER MET 0.0179856
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S7 S21 SER TRP 0.0179856
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S7 S21 THR GLU 0.00223792
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S7 S21 THR GLY 0.00223792
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S7 S21 THR LYS 0.00223792
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S7 S21 THR TRP 0.00223792
S7 S21 THR TYR 0.129634
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S7 S21 VAL ILE 0.0196493
S7 S21 VAL VAL 0.0012777
S7 S21 VAL TYR 0.00162265
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S7 S21 TRP ILE 0.0196493
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S7 S21 TYR CYS 0.00208566
S7 S21 TYR ASP 0.00208566
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S7 S21 --- ILE 0.0196493
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S7 S21 --- TYR 0.00162265

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S7 S22 ALA PHE 0.000596692
S7 S22 ALA GLY 0.000596692
S7 S22 ALA HIS 0.000596692
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S7 S22 ALA LYS 0.000596692
S7 S22 ALA LEU 0.000596692
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S7 S22 ASP TYR 0.001133
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S7 S22 GLU TYR 0.001133
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S7 S22 GLY TYR 0.001133
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S7 S22 HIS TYR 0.001133
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S7 S25 THR PHE 0.00351305
S7 S25 THR GLY 0.00351305
S7 S25 THR HIS 0.00351305
S7 S25 THR ILE 0.00351305
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S7 S25 THR GLN 0.00351305
S7 S25 THR ARG 0.61119
S7 S25 THR SER -0.413379
S7 S25 THR THR 0.0713733
S7 S25 THR VAL 0.00351305
S7 S25 THR TRP 0.00351305
S7 S25 THR TYR 0.00351305
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S7 S25 VAL GLU 0.000731658
S7 S25 VAL LYS 0.000819613
S7 S25 VAL ARG 0.002898
S7 S25 VAL SER 0.0184802
S7 S25 VAL THR 0.000673737
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S7 S25 TRP LYS 0.000819613
S7 S25 TRP ARG 0.002898
S7 S25 TRP SER 0.0184802
S7 S25 TRP THR 0.000673737
S7 S25 TYR ALA 0.00463619
S7 S25 TYR CYS 0.00463619
S7 S25 TYR ASP 0.0838122
S7 S25 TYR GLU 0.0564244
S7 S25 TYR PHE 0.00463619
S7 S25 TYR GLY 0.00463619
S7 S25 TYR HIS 0.00463619
S7 S25 TYR ILE 0.00463619
S7 S25 TYR LYS 0.10938
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S7 S25 TYR SER -0.440345
S7 S25 TYR THR -0.34727
S7 S25 TYR VAL 0.00463619
S7 S25 TYR TRP 0.00463619
S7 S25 TYR TYR 0.00463619

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S7 S25 --- LYS 0.000819613
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S7 S26 ALA ASP 0.00261111
S7 S26 ALA GLU 0.00261111
S7 S26 ALA PHE -0.104355
S7 S26 ALA GLY 0.00261111
S7 S26 ALA HIS 0.00261111
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S7 S26 ALA LYS -0.141115
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S7 S26 ALA TRP 0.00261111
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S7 S26 ASP LYS 0.0132647
S7 S26 ASP TYR 0.00311297
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S7 S26 GLU LYS 0.0132647
S7 S26 GLU TYR 0.00311297
S7 S26 PHE PHE 0.00731196
S7 S26 PHE LYS 0.0132647
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S7 S26 HIS LYS 0.0132647
S7 S26 HIS TYR 0.00311297
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S7 S26 PRO LYS 0.0132647

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S7 S26 VAL TYR 0.00311297
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S7 S26 TRP LYS 0.0132647
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S7 S26 TYR ILE 0.00226105

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S7 S27 GLN SER 0.021112

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S7 S28 TYR --- 0.000650904
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S7 S28 --- GLU 0.00262095

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S7 S29 TYR GLY 0.00340137
S7 S29 TYR HIS 0.00340137
S7 S29 TYR ILE 0.00340137
S7 S29 TYR LYS 0.0355198
S7 S29 TYR LEU 0.0267758
S7 S29 TYR MET 0.00340137
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S7 S29 TYR PRO 0.00340137
S7 S29 TYR GLN 0.00340137
S7 S29 TYR ARG 0.00340137
S7 S29 TYR SER 0.00634942
S7 S29 TYR THR 0.00340137
S7 S29 TYR VAL 0.00340137
S7 S29 TYR TRP 0.00340137
S7 S29 TYR TYR 0.00340137
S7 S29 TYR --- 0.00340137
S7 S29 --- LYS 0.000292536
S7 S29 --- LEU 0.000471266
S7 S29 --- ASN 8.43695e-05
S7 S29 --- SER 0.0228414
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S7 S30 ALA CYS 0.00111252
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S7 S30 ALA PHE 0.00111252
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S7 S30 CYS SER 0.000824404
S7 S30 ASP GLN 0.0228652
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S7 S30 HIS GLN 0.0228652
S7 S30 HIS SER 0.000824404
S7 S30 ILE GLN 0.0228652
S7 S30 ILE SER 0.000824404
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S7 S30 LYS SER 0.000824404

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S7 S30 LEU SER 0.000824404
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S7 S30 SER CYS 0.00750935
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S7 S30 SER PHE 0.00750935
S7 S30 SER GLY 0.00750935
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S7 S30 SER MET 0.00750935
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S7 S30 SER TYR 0.00750935
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S7 S30 THR ASP 0.00298561
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S7 S30 THR PHE 0.00298561
S7 S30 THR GLY 0.00298561
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S7 S30 THR LYS 0.00298561
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S7 S30 THR ASN 0.00298561
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S7 S30 TYR PHE 0.000858762

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S7 S31 ALA ILE 0.172007
S7 S31 ALA LYS 0.0017046
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S7 S31 GLU ILE 0.00189333
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S7 S31 LYS VAL 0.0206483

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S7 S31 TYR LYS 0.00168665
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S7 S32 ALA LYS 0.000833295
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S7 S37 PRO ASN 0.000285824
S7 S37 PRO ARG 0.000903194
S7 S37 PRO SER 0.0115523
S7 S37 GLN ALA 0.00117259
S7 S37 GLN ASP 0.00840476

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S7 S38 GLU LYS 0.00229795
S7 S38 GLU LEU 0.013767

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S7 S38 GLY LYS 0.00229795
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S7 S38 GLY ARG 0.0013693
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S7 S38 ARG LYS 0.00229795
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S7 S38 SER ASP 0.0199157
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S7 S38 SER LEU 0.27434
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S8 S15 SER LEU 0.160801
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S8 S15 THR TRP 0.00469457
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S8 S15 VAL LEU 0.00555373
S8 S15 VAL GLN 0.00106959
S8 S15 VAL SER 0.0144183
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S8 S15 TRP GLU 0.00197294
S8 S15 TRP LEU 0.00555373
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S8 S15 TYR LEU 0.506186
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S8 S15 TYR TYR 0.0119328
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S8 S16 CYS ILE 0.017021
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S8 S16 PHE THR 0.00166595
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S8 S16 HIS VAL 0.169124
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S8 S16 LYS ILE 0.017021
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S8 S16 ASN --- 0.00293069
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S8 S16 PRO LEU 0.000272087
S8 S16 PRO THR 0.00166595
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S8 S16 GLN ALA 0.000449719
S8 S16 GLN ILE 0.017021
S8 S16 GLN LEU 0.000272087

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S8 S16 SER LEU 0.0145786
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S8 S16 THR LYS 0.00489689
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S8 S18 TYR GLU -0.0623408
S8 S18 TYR PHE 0.00477037
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S8 S18 TYR HIS -0.152864
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S8 S18 --- GLU 0.0301487

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S8 S19 ALA TYR 0.000112734
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S8 S19 CYS TYR 0.000112734
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S8 S19 ASP CYS 0.00612016
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S8 S19 PHE TYR 0.000112734
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S8 S21 VAL ILE 0.0228639
S8 S21 VAL VAL 0.00523533
S8 S21 VAL TYR 0.00208395
S8 S21 TRP PHE 0.0011222
S8 S21 TRP ILE 0.0228639
S8 S21 TRP VAL 0.00523533
S8 S21 TRP TYR 0.00208395
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S8 S21 TYR CYS 0.00699218
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S8 S21 TYR GLU 0.00699218
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S8 S21 TYR GLY 0.00699218
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S8 S21 TYR TYR 0.754914
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S8 S22 ALA TYR 0.00118639
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S8 S22 CYS ASN 0.0253581
S8 S22 CYS TYR 0.00118639
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S8 S22 ASP CYS 0.00580612
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S8 S22 ASP GLU 0.102673
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S8 S26 GLU TYR 0.00200305
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S8 S26 PHE TYR 0.00200305
S8 S26 GLY PHE 0.00891677
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S8 S26 GLY TYR 0.00200305
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S8 S31 TRP ASP 0.0010731
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S8 S31 TRP VAL 0.0261543
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S8 S31 TYR ASP 0.219267
S8 S31 TYR GLU 0.00546725
S8 S31 TYR PHE 0.00546725
S8 S31 TYR GLY 0.00546725
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S8 S31 TYR ILE -0.0896938
S8 S31 TYR LYS 0.00546725
S8 S31 TYR LEU 0.00546725
S8 S31 TYR MET 0.00546725
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S8 S31 TYR TYR 0.00546725
S8 S31 TYR --- 0.00546725
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S8 S32 CYS TRP 0.0237336
S8 S32 CYS TYR 0.00366227
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S8 S32 ASP CYS 0.00550775
S8 S32 ASP ASP 0.00550775
S8 S32 ASP GLU 0.00550775
S8 S32 ASP PHE 0.0253523
S8 S32 ASP GLY 0.00550775

S8 S32 ASP HIS 0.249352
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S8 S32 THR ILE 0.00168837

S8 S32 THR LYS 0.00168837
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S8 S37 THR ARG 0.0693317
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S8 S37 THR TYR 0.00420486
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S8 S37 VAL PHE 0.00133735
S8 S37 VAL ASN 0.000432551
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S8 S37 TYR ASP 0.643052
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S8 S37 TYR PHE 0.340476
S8 S37 TYR GLY 0.00943607
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S8 S37 TYR LYS 0.00943607
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S8 S37 TYR --- 0.00943607
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S8 S38 ALA HIS 0.00730189

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S8 S38 ALA LEU 0.0132925
S8 S38 ALA ARG 0.00115767
S8 S38 CYS GLU 0.00507122
S8 S38 CYS HIS 0.00730189
S8 S38 CYS LYS 0.00448206
S8 S38 CYS LEU 0.0132925
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S8 S38 ASP LYS 0.0435612
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S8 S38 SER LEU 0.0547188
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S8 S40 THR TYR 0.00242474
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S8 S40 VAL ILE 0.00231469
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S8 S40 TYR LYS 0.0083999
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S9 S11 ARG GLY 4.8871e-05
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S9 S11 ARG ILE 4.8871e-05
S9 S11 ARG LYS 4.8871e-05
S9 S11 ARG LEU 4.8871e-05
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S9 S14 ASP ASP 0.0026273

S9 S14 ASP GLU 0.0210852
S9 S14 ASP SER 6.89279e-05
S9 S14 ASP THR 0.000703656
S9 S14 GLU ASP 0.0026273
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S9 S14 ILE CYS 0.00340909
S9 S14 ILE ASP 0.560293
S9 S14 ILE GLU -1.06363
S9 S14 ILE PHE 0.00340909
S9 S14 ILE GLY 0.00340909
S9 S14 ILE HIS 0.00340909
S9 S14 ILE ILE 0.00340909
S9 S14 ILE LYS 0.00340909
S9 S14 ILE LEU 0.00340909
S9 S14 ILE MET 0.00340909
S9 S14 ILE ASN 0.00340909
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S9 S14 ILE GLN 0.00340909
S9 S14 ILE ARG 0.00340909
S9 S14 ILE SER 0.0388723
S9 S14 ILE THR 0.336925
S9 S14 ILE VAL 0.00340909
S9 S14 ILE TRP 0.00340909
S9 S14 ILE TYR 0.00340909
S9 S14 ILE --- 0.00340909
S9 S14 LYS ALA 0.00676555
S9 S14 LYS CYS 0.00676555
S9 S14 LYS ASP -1.02047
S9 S14 LYS GLU 0.55356
S9 S14 LYS PHE 0.00676555
S9 S14 LYS GLY 0.00676555
S9 S14 LYS HIS 0.00676555
S9 S14 LYS ILE 0.00676555
S9 S14 LYS LYS 0.00676555
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S9 S14 LYS MET 0.00676555
S9 S14 LYS ASN 0.00676555
S9 S14 LYS PRO 0.00676555
S9 S14 LYS GLN 0.00676555
S9 S14 LYS ARG 0.00676555
S9 S14 LYS SER 0.0444044
S9 S14 LYS THR 0.178334
S9 S14 LYS VAL 0.00676555
S9 S14 LYS TRP 0.00676555
S9 S14 LYS TYR 0.00676555
S9 S14 LYS --- 0.00676555
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S9 S14 LEU GLU 0.0210852

S9 S14 LEU SER 6.89279e-05
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S9 S14 MET GLU 0.0210852
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S9 S14 MET THR 0.000703656
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S9 S14 ASN GLU 0.0210852
S9 S14 ASN SER 6.89279e-05
S9 S14 ASN THR 0.000703656
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S9 S14 PRO GLU 0.0210852
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S9 S14 PRO THR 0.000703656
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S9 S14 ARG CYS 0.000198995
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S9 S14 ARG GLU -0.113931
S9 S14 ARG PHE 0.000198995
S9 S14 ARG GLY 0.000198995
S9 S14 ARG HIS 0.000198995
S9 S14 ARG ILE 0.000198995
S9 S14 ARG LYS 0.000198995
S9 S14 ARG LEU 0.000198995
S9 S14 ARG MET 0.000198995
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S9 S14 THR ARG 0.0100357
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S9 S14 THR TRP 0.0100357
S9 S14 THR TYR 0.0100357

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S9 S14 VAL THR 0.000703656
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S9 S14 TRP SER 6.89279e-05
S9 S14 TRP THR 0.000703656
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S9 S14 TYR GLU 0.0210852
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S9 S14 TYR THR 0.000703656
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S9 S15 ALA GLN 0.00013537
S9 S15 ALA SER 0.00740582
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S9 S15 CYS LEU 0.00242238
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S9 S15 ASP GLU 0.00164345
S9 S15 ASP LEU 0.00242238
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S9 S15 GLU ASP 0.0128781
S9 S15 GLU GLU 0.00164345
S9 S15 GLU LEU 0.00242238
S9 S15 GLU GLN 0.00013537
S9 S15 GLU SER 0.00740582
S9 S15 PHE ASP 0.0128781
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S9 S15 PHE LEU 0.00242238
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S9 S15 PHE SER 0.00740582
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S9 S15 GLY LEU 0.00242238
S9 S15 GLY GLN 0.00013537
S9 S15 GLY SER 0.00740582
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S9 S15 HIS GLU 0.00164345
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S9 S15 ILE GLU -0.305656
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S9 S15 ILE ILE 0.0036717
S9 S15 ILE LYS 0.0036717
S9 S15 ILE LEU -0.127035
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S9 S15 ILE THR 0.0036717
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S9 S15 ILE TYR 0.0036717
S9 S15 ILE --- 0.0036717
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S9 S15 LYS CYS 0.010891
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S9 S15 LYS GLU 0.393617
S9 S15 LYS PHE 0.010891
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S9 S15 LYS ILE 0.010891
S9 S15 LYS LYS 0.010891
S9 S15 LYS LEU -0.700693
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S9 S15 ARG GLY 0.000455694
S9 S15 ARG HIS 0.000455694

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S9 S15 THR LYS 0.0140207
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S9 S15 TYR LEU 0.00242238
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S9 S15 --- LEU 0.00242238
S9 S15 --- GLN 0.00013537
S9 S15 --- SER 0.00740582
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S9 S16 ALA ILE 0.0155362
S9 S16 ALA LEU 0.000373991

S9 S16 ALA THR 0.000542849
S9 S16 ALA VAL 0.00791535
S9 S16 CYS ALA 0.00011673
S9 S16 CYS ILE 0.0155362
S9 S16 CYS LEU 0.000373991
S9 S16 CYS THR 0.000542849
S9 S16 CYS VAL 0.00791535
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S9 S16 ASP ILE 0.0155362
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S9 S16 GLU ILE 0.0155362
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S9 S16 PHE ILE 0.0155362
S9 S16 PHE LEU 0.000373991
S9 S16 PHE THR 0.000542849
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S9 S16 GLY ILE 0.0155362
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S9 S16 HIS ILE 0.0155362
S9 S16 HIS LEU 0.000373991
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S9 S16 ILE GLY 0.00401358
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S9 S16 ILE LYS 0.00401358
S9 S16 ILE LEU -0.567419
S9 S16 ILE MET 0.00401358
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S9 S16 ILE TYR 0.00401358
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S9 S16 LYS GLU 0.00922215
S9 S16 LYS PHE 0.00922215
S9 S16 LYS GLY 0.00922215
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S9 S16 LYS TYR 0.00922215
S9 S16 LYS --- 0.00922215
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S9 S16 LEU ILE 0.0155362
S9 S16 LEU LEU 0.000373991
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S9 S16 PRO ILE 0.0155362
S9 S16 PRO LEU 0.000373991
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S9 S16 ARG CYS 0.000592144
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S9 S16 ARG LYS 0.000592144
S9 S16 ARG LEU 0.00946835
S9 S16 ARG MET 0.000592144
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S9 S16 ARG PRO 0.000592144
S9 S16 ARG GLN 0.000592144
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S9 S16 ARG TYR 0.000592144
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S9 S16 SER ILE 0.0155362
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S9 S16 THR ASN 0.010531
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S9 S16 THR TYR 0.010531
S9 S16 THR --- 0.010531
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S9 S16 TRP ILE 0.0155362
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S9 S16 TRP VAL 0.00791535
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S9 S16 TYR ILE 0.0155362
S9 S16 TYR LEU 0.000373991
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S9 S16 --- ILE 0.0155362
S9 S16 --- LEU 0.000373991
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S9 S16 --- VAL 0.00791535
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S9 S17 ALA ILE 0.00130439
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S9 S17 ALA TYR 0.00330785
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S9 S17 ASP PHE 0.0132407
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S9 S17 GLU HIS 0.00658154
S9 S17 GLU ILE 0.00130439
S9 S17 GLU TRP 5.05955e-05
S9 S17 GLU TYR 0.00330785
S9 S17 PHE PHE 0.0132407
S9 S17 PHE HIS 0.00658154
S9 S17 PHE ILE 0.00130439

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S9 S17 GLY TYR 0.00330785
S9 S17 HIS PHE 0.0132407
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S9 S17 HIS TYR 0.00330785
S9 S17 ILE ALA 0.0033171
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S9 S17 ILE PHE 0.184364
S9 S17 ILE GLY 0.0033171
S9 S17 ILE HIS -0.0259299
S9 S17 ILE ILE -0.274797
S9 S17 ILE LYS 0.0033171
S9 S17 ILE LEU 0.0033171
S9 S17 ILE MET 0.0033171
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S9 S17 ILE THR 0.0033171
S9 S17 ILE VAL 0.0033171
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S9 S17 ILE TYR -0.048776
S9 S17 ILE --- 0.0033171
S9 S17 LYS ALA 0.0110119
S9 S17 LYS CYS 0.0110119
S9 S17 LYS ASP 0.0110119
S9 S17 LYS GLU 0.0110119
S9 S17 LYS PHE 0.296051
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S9 S17 LYS ILE -0.203535
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S9 S17 LYS MET 0.0110119
S9 S17 LYS ASN 0.0110119
S9 S17 LYS PRO 0.0110119
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S9 S17 LYS TYR 0.0511874
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S9 S17 LEU PHE 0.0132407
S9 S17 LEU HIS 0.00658154
S9 S17 LEU ILE 0.00130439
S9 S17 LEU TRP 5.05955e-05
S9 S17 LEU TYR 0.00330785
S9 S17 MET PHE 0.0132407
S9 S17 MET HIS 0.00658154
S9 S17 MET ILE 0.00130439
S9 S17 MET TRP 5.05955e-05

S9 S17 MET TYR 0.00330785
S9 S17 ASN PHE 0.0132407
S9 S17 ASN HIS 0.00658154
S9 S17 ASN ILE 0.00130439
S9 S17 ASN TRP 5.05955e-05
S9 S17 ASN TYR 0.00330785
S9 S17 PRO PHE 0.0132407
S9 S17 PRO HIS 0.00658154
S9 S17 PRO ILE 0.00130439
S9 S17 PRO TRP 5.05955e-05
S9 S17 PRO TYR 0.00330785
S9 S17 GLN PHE 0.0132407
S9 S17 GLN HIS 0.00658154
S9 S17 GLN ILE 0.00130439
S9 S17 GLN TRP 5.05955e-05
S9 S17 GLN TYR 0.00330785
S9 S17 ARG ALA 9.39191e-05
S9 S17 ARG CYS 9.39191e-05
S9 S17 ARG ASP 9.39191e-05
S9 S17 ARG GLU 9.39191e-05
S9 S17 ARG PHE -0.124322
S9 S17 ARG GLY 9.39191e-05
S9 S17 ARG HIS 0.0324642
S9 S17 ARG ILE 0.00535415
S9 S17 ARG LYS 9.39191e-05
S9 S17 ARG LEU 9.39191e-05
S9 S17 ARG MET 9.39191e-05
S9 S17 ARG ASN 9.39191e-05
S9 S17 ARG PRO 9.39191e-05
S9 S17 ARG GLN 9.39191e-05
S9 S17 ARG ARG 9.39191e-05
S9 S17 ARG SER 9.39191e-05
S9 S17 ARG THR 9.39191e-05
S9 S17 ARG VAL 9.39191e-05
S9 S17 ARG TRP 0.000941007
S9 S17 ARG TYR 0.031276
S9 S17 ARG --- 9.39191e-05
S9 S17 SER PHE 0.0132407
S9 S17 SER HIS 0.00658154
S9 S17 SER ILE 0.00130439
S9 S17 SER TRP 5.05955e-05
S9 S17 SER TYR 0.00330785
S9 S17 THR ALA 0.0102963
S9 S17 THR CYS 0.0102963
S9 S17 THR ASP 0.0102963
S9 S17 THR GLU 0.0102963
S9 S17 THR PHE -0.694257
S9 S17 THR GLY 0.0102963
S9 S17 THR HIS 0.0814782
S9 S17 THR ILE 0.370348
S9 S17 THR LYS 0.0102963
S9 S17 THR LEU 0.0102963
S9 S17 THR MET 0.0102963
S9 S17 THR ASN 0.0102963
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S9 S17 THR GLN 0.0102963
S9 S17 THR ARG 0.0102963
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S9 S17 THR TYR -0.156925
S9 S17 THR --- 0.0102963

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S9 S17 VAL HIS 0.00658154
S9 S17 VAL ILE 0.00130439
S9 S17 VAL TRP 5.05955e-05
S9 S17 VAL TYR 0.00330785
S9 S17 TRP PHE 0.0132407
S9 S17 TRP HIS 0.00658154
S9 S17 TRP ILE 0.00130439
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S9 S17 TYR HIS 0.00658154
S9 S17 TYR ILE 0.00130439
S9 S17 TYR TRP 5.05955e-05
S9 S17 TYR TYR 0.00330785
S9 S17 --- PHE 0.0132407
S9 S17 --- HIS 0.00658154
S9 S17 --- ILE 0.00130439
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S9 S17 --- TYR 0.00330785
S9 S18 ALA GLU 0.0238087
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S9 S18 CYS GLU 0.0238087
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S9 S18 ASP GLU 0.0238087
S9 S18 ASP HIS 0.000676398
S9 S18 GLU GLU 0.0238087
S9 S18 GLU HIS 0.000676398
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S9 S18 PHE HIS 0.000676398
S9 S18 GLY GLU 0.0238087
S9 S18 GLY HIS 0.000676398
S9 S18 HIS GLU 0.0238087
S9 S18 HIS HIS 0.000676398
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S9 S18 ILE ASP 0.00259494
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S9 S18 ILE PHE 0.00259494
S9 S18 ILE GLY 0.00259494
S9 S18 ILE HIS -0.356142
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S9 S18 ILE LYS 0.00259494
S9 S18 ILE LEU 0.00259494
S9 S18 ILE MET 0.00259494
S9 S18 ILE ASN 0.00259494
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S9 S18 ILE GLN 0.00259494
S9 S18 ILE ARG 0.00259494
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S9 S18 ILE VAL 0.00259494
S9 S18 ILE TRP 0.00259494
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S9 S18 LYS ILE 0.00433594

S9 S18 LYS LYS 0.00433594
S9 S18 LYS LEU 0.00433594
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S9 S18 LYS ASN 0.00433594
S9 S18 LYS PRO 0.00433594
S9 S18 LYS GLN 0.00433594
S9 S18 LYS ARG 0.00433594
S9 S18 LYS SER 0.00433594
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S9 S18 LYS TRP 0.00433594
S9 S18 LYS TYR 0.00433594
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S9 S18 GLN GLU 0.0238087
S9 S18 GLN HIS 0.000676398
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S9 S18 ARG CYS 0.000315475
S9 S18 ARG ASP 0.000315475
S9 S18 ARG GLU -0.0801235
S9 S18 ARG PHE 0.000315475
S9 S18 ARG GLY 0.000315475
S9 S18 ARG HIS 0.0213459
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S9 S18 ARG LEU 0.000315475
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S9 S19 CYS TYR 0.000633533
S9 S19 ASP ALA 0.0155336
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S9 S19 ASP TYR 0.000633533
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S9 S19 GLU SER 0.00831795
S9 S19 GLU TYR 0.000633533
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S9 S19 PHE TYR 0.000633533
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S9 S19 GLY TYR 0.000633533
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S9 S19 HIS TYR 0.000633533
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S9 S19 LYS PHE 0.00657669
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S9 S19 LYS HIS 0.00657669
S9 S19 LYS ILE 0.00657669
S9 S19 LYS LYS 0.00657669

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S9 S19 LYS MET 0.00657669
S9 S19 LYS ASN 0.00657669
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S9 S19 MET TYR 0.000633533
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S9 S19 ARG LYS 0.000275621
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S9 S19 THR ILE 0.00844924
S9 S19 THR LYS 0.00844924
S9 S19 THR LEU 0.00844924
S9 S19 THR MET 0.00844924
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S9 S20 ILE PHE 0.0407514
S9 S20 ILE GLY 0.00486689
S9 S20 ILE HIS 0.00486689
S9 S20 ILE ILE 0.00486689
S9 S20 ILE LYS 0.00486689
S9 S20 ILE LEU -0.842673
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S9 S20 LYS ALA 0.00794318
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S9 S21 GLU TYR 0.00189846

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S9 S21 PHE TYR 0.00189846
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S9 S21 LYS TRP 0.0107023
S9 S21 LYS TYR 0.0447163
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S9 S21 LEU ILE 0.0171965
S9 S21 LEU VAL 0.00367068
S9 S21 LEU TYR 0.00189846
S9 S21 MET PHE 0.00171946
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S9 S21 ASN PHE 0.00171946

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S9 S21 THR MET 0.00906922
S9 S21 THR ASN 0.00906922
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S9 S22 GLY TYR 0.00229496
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S9 S22 ILE GLU 0.0442658
S9 S22 ILE PHE 0.0032882
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S9 S22 ILE MET 0.0032882
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S9 S22 PRO ASN 0.0181697
S9 S22 PRO TYR 0.00229496
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S9 S23 PHE ILE 0.0165376
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S9 S23 ILE PRO 0.00279443

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S9 S25 LEU LYS 0.000540462
S9 S25 LEU ARG 0.0043058
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S9 S25 LEU THR 0.000301173
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S9 S25 MET LYS 0.000540462
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S9 S32 ARG LYS 8.35682e-05
S9 S32 ARG LEU 8.35682e-05
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S9 S33 ASN LYS 0.000470815
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S9 S33 PRO LYS 0.000470815
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S9 S33 GLN LYS 0.000470815
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S9 S33 ARG PHE 5.43316e-05
S9 S33 ARG GLY 5.43316e-05
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S9 S33 ARG ASN 5.43316e-05
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S9 S33 ARG THR 5.43316e-05
S9 S33 ARG VAL 0.0337105
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S9 S33 ARG TYR 5.43316e-05
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S9 S33 SER LYS 0.000470815
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S9 S33 SER VAL 0.00337124
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S9 S33 THR CYS 0.0115417
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S9 S33 THR GLY 0.0115417
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S9 S34 ILE CYS 0.0067163

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S9 S34 ILE GLY 0.0067163
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S9 S34 ILE LYS 0.0067163
S9 S34 ILE LEU 0.0067163
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S9 S34 ILE ASN 0.0067163
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S9 S34 ILE GLN 0.0067163
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S9 S34 ILE THR -0.0146866
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S9 S34 ILE TYR 0.0067163
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S9 S34 LYS CYS 0.00547883
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S9 S34 LYS GLY 0.00547883
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S9 S34 LYS PRO 0.00547883
S9 S34 LYS GLN 0.00547883
S9 S34 LYS ARG 0.0484987
S9 S34 LYS SER -0.719191
S9 S34 LYS THR 0.281295
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S9 S34 LYS TRP 0.00547883
S9 S34 LYS TYR 0.00547883
S9 S34 LYS --- 0.00547883
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S9 S34 ARG ASP 0.000387089
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S9 S34 ARG GLY 0.000387089
S9 S34 ARG HIS 0.000387089
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S9 S35 ASP THR 0.00361433
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S9 S35 GLU THR 0.00361433
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S9 S35 PHE THR 0.00361433
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S9 S35 GLY THR 0.00361433
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S9 S35 HIS THR 0.00361433
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S9 S35 MET THR 0.00361433
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S9 S35 ARG TYR 4.60602e-05
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S9 S35 SER THR 0.00361433
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S9 S35 THR TYR 0.0118866
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S9 S36 ILE GLY 0.00528474
S9 S36 ILE HIS 0.00528474
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S9 S36 ARG LYS 0.000288439
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S9 S36 ARG THR 0.00606018
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S9 S36 ARG --- 0.000288439

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S9 S37 PHE ARG 0.00349509
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S9 S37 ILE ALA 0.0447431
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S9 S37 ILE GLU 0.00387472
S9 S37 ILE PHE 0.190547
S9 S37 ILE GLY 0.00387472
S9 S37 ILE HIS 0.00387472
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S9 S37 ILE ASN 0.09652
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S9 S37 ILE GLN 0.00387472
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S9 S37 LYS HIS 0.0124978
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S9 S37 LYS LYS 0.0124978
S9 S37 LYS LEU 0.0124978
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S9 S37 LYS PRO 0.0124978
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S9 S37 LYS SER 0.133058
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S9 S37 THR HIS 0.0123433

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S9 S37 THR LYS 0.0123433
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S9 S37 THR MET 0.0123433
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S9 S37 THR PRO 0.0123433
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S9 S37 THR TRP 0.0123433
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S9 S38 ALA LYS 0.00330821
S9 S38 ALA LEU 0.00919394
S9 S38 ALA ARG 0.00262312
S9 S38 CYS GLU 0.00111847
S9 S38 CYS HIS 0.00824134
S9 S38 CYS LYS 0.00330821
S9 S38 CYS LEU 0.00919394
S9 S38 CYS ARG 0.00262312
S9 S38 ASP GLU 0.00111847
S9 S38 ASP HIS 0.00824134
S9 S38 ASP LYS 0.00330821
S9 S38 ASP LEU 0.00919394
S9 S38 ASP ARG 0.00262312
S9 S38 GLU GLU 0.00111847
S9 S38 GLU HIS 0.00824134
S9 S38 GLU LYS 0.00330821
S9 S38 GLU LEU 0.00919394
S9 S38 GLU ARG 0.00262312
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S9 S38 PHE HIS 0.00824134
S9 S38 PHE LYS 0.00330821
S9 S38 PHE LEU 0.00919394
S9 S38 PHE ARG 0.00262312

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S9 S38 GLY LYS 0.00330821
S9 S38 GLY LEU 0.00919394
S9 S38 GLY ARG 0.00262312
S9 S38 HIS GLU 0.00111847
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S9 S38 ILE GLU 0.2599
S9 S38 ILE PHE 0.0046199
S9 S38 ILE GLY 0.0046199
S9 S38 ILE HIS -0.959404
S9 S38 ILE ILE 0.0046199
S9 S38 ILE LYS 0.616026
S9 S38 ILE LEU 1.05486
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S9 S38 ILE ARG -1.11488
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S9 S38 LYS --- 0.0133265
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S9 S38 LEU LYS 0.00330821
S9 S38 LEU LEU 0.00919394
S9 S38 LEU ARG 0.00262312
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S9 S38 MET LYS 0.00330821
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S9 S38 ASN GLU 0.00111847

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S9 S38 ASN LYS 0.00330821
S9 S38 ASN LEU 0.00919394
S9 S38 ASN ARG 0.00262312
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S9 S38 PRO LYS 0.00330821
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S10 S16 CYS THR 0.000754378
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S10 S16 ASP ALA 0.000324655
S10 S16 ASP ILE 0.0157749

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S10 S18 GLY GLN 7.66213e-05
S10 S18 GLY ARG 7.66213e-05
S10 S18 GLY SER 7.66213e-05
S10 S18 GLY THR 7.66213e-05
S10 S18 GLY VAL 7.66213e-05
S10 S18 GLY TRP 7.66213e-05
S10 S18 GLY TYR 7.66213e-05
S10 S18 GLY --- 7.66213e-05
S10 S18 HIS GLU 0.0232159
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S10 S18 ILE GLU 0.0232159
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S10 S18 LYS HIS 0.0004259
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S10 S18 PRO HIS 0.0004259
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S10 S18 SER GLY 0.00339857
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S10 S18 SER MET 0.00339857
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S10 S18 THR PHE 0.00151225
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S10 S18 THR HIS 0.0654233
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S10 S18 THR --- 0.00151225
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S10 S18 TRP GLU 0.0232159
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S10 S19 ALA HIS 0.00997879
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S10 S19 ALA LEU 0.00997879
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S10 S19 ALA ASN 0.00997879
S10 S19 ALA PRO 0.00997879

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S10 S19 ALA ARG 0.00997879
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S10 S19 ALA TRP 0.00997879
S10 S19 ALA TYR 0.141317
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S10 S19 CYS TYR 0.00047249
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S10 S19 ASP SER 0.0104098
S10 S19 ASP TYR 0.00047249
S10 S19 GLU ALA 0.0127596
S10 S19 GLU SER 0.0104098
S10 S19 GLU TYR 0.00047249
S10 S19 PHE ALA 0.0127596
S10 S19 PHE SER 0.0104098
S10 S19 PHE TYR 0.00047249
S10 S19 GLY ALA -0.154115
S10 S19 GLY CYS 0.000158348
S10 S19 GLY ASP 0.000158348
S10 S19 GLY GLU 0.000158348
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S10 S19 GLY TYR 0.0125938
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S10 S19 HIS TYR 0.00047249
S10 S19 ILE ALA 0.0127596
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S10 S19 ILE TYR 0.00047249
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S10 S19 LYS TYR 0.00047249
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S10 S19 LEU TYR 0.00047249
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S10 S19 PRO TYR 0.00047249
S10 S19 GLN ALA 0.0127596

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S10 S19 GLN TYR 0.00047249
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S10 S19 ARG TYR 0.00047249
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S10 S19 SER LYS 0.00581608
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S10 S20 GLU LEU 0.00139955
S10 S20 GLU MET 0.0131208
S10 S20 GLU VAL 0.00105978
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S10 S20 GLY PHE 0.154871
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S10 S20 GLY HIS 9.04256e-05
S10 S20 GLY ILE 9.04256e-05
S10 S20 GLY LYS 9.04256e-05
S10 S20 GLY LEU 0.00716664
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S10 S20 TYR LEU 0.00139955
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S10 S22 HIS ASN 0.0171574
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S10 S22 MET TYR 0.0023825

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S10 S30 TRP SER 0.00105734
S10 S30 TYR GLN 0.0225845

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S10 S31 ALA LYS 0.0126102
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S10 S31 ALA MET 0.0126102
S10 S31 ALA ASN 0.0126102
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S10 S31 CYS VAL 0.018532
S10 S31 ASP ASP 0.000425368
S10 S31 ASP ILE 0.00468447
S10 S31 ASP VAL 0.018532
S10 S31 GLU ASP 0.000425368
S10 S31 GLU ILE 0.00468447
S10 S31 GLU VAL 0.018532
S10 S31 PHE ASP 0.000425368
S10 S31 PHE ILE 0.00468447
S10 S31 PHE VAL 0.018532
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S10 S31 GLY CYS 0.000203021
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S10 S31 GLY GLU 0.000203021
S10 S31 GLY PHE 0.000203021
S10 S31 GLY GLY 0.000203021
S10 S31 GLY HIS 0.000203021
S10 S31 GLY ILE 0.130687
S10 S31 GLY LYS 0.000203021
S10 S31 GLY LEU 0.000203021
S10 S31 GLY MET 0.000203021
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S10 S31 GLY SER 0.000203021
S10 S31 GLY THR 0.000203021
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S10 S31 ILE VAL 0.018532

S10 S31 LYS ASP 0.000425368
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S10 S31 THR --- 0.00211841

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S10 S31 --- ASP 0.000425368
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S10 S32 ALA ILE 0.0186406
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S11 S13 PHE TRP 0.0153845
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S11 S13 --- TRP 0.0153845
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S11 S14 ALA PHE 0.0060582
S11 S14 ALA GLY 0.0060582
S11 S14 ALA HIS 0.0060582
S11 S14 ALA ILE 0.0060582
S11 S14 ALA LYS 0.0060582
S11 S14 ALA LEU 0.0060582
S11 S14 ALA MET 0.0060582
S11 S14 ALA ASN 0.0060582
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S11 S14 ALA THR 0.0922316
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S11 S14 ALA TYR 0.0060582
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S11 S14 CYS THR 0.000166807
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S11 S14 PHE THR 0.000166807
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S11 S15 ALA GLU 0.21972
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S11 S15 ALA GLY 0.0115669
S11 S15 ALA HIS 0.0115669
S11 S15 ALA ILE 0.0115669
S11 S15 ALA LYS 0.0115669

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S11 S15 ALA MET 0.0115669
S11 S15 ALA ASN 0.0115669
S11 S15 ALA PRO 0.0115669
S11 S15 ALA GLN -0.113676
S11 S15 ALA ARG 0.0115669
S11 S15 ALA SER -0.855676
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S11 S15 ALA TYR 0.0115669
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S11 S15 CYS LEU 0.00190442
S11 S15 CYS GLN 7.99265e-05
S11 S15 CYS SER 0.00733903
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S11 S15 ASP GLU 0.000619174
S11 S15 ASP LEU 0.00190442
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S11 S15 SER LEU 0.196246
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S11 S17 SER CYS 0.0127866
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S11 S17 TRP HIS 0.00545255
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S11 S18 SER HIS -0.00635819
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S11 S23 ALA GLY 0.00791668
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S11 S23 ALA LYS 0.00791668
S11 S23 ALA LEU -0.547761

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S11 S23 CYS LEU 0.00220077
S11 S23 ASP ILE 0.0131863
S11 S23 ASP LEU 0.00220077
S11 S23 GLU ILE 0.0131863
S11 S23 GLU LEU 0.00220077
S11 S23 PHE ILE 0.0131863
S11 S23 PHE LEU 0.00220077
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S11 S23 HIS LEU 0.00220077
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S11 S23 ILE LEU 0.00220077
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S11 S23 LYS LEU 0.00220077
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S11 S23 MET LEU 0.00220077
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S11 S23 ASN LEU 0.00220077
S11 S23 PRO ILE 0.0131863
S11 S23 PRO LEU 0.00220077
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S11 S23 GLN LEU 0.00220077
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S11 S23 SER ASP 0.00782563
S11 S23 SER GLU 0.00782563
S11 S23 SER PHE 0.00782563
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S11 S23 SER HIS 0.00782563
S11 S23 SER ILE -0.701663
S11 S23 SER LYS 0.00782563
S11 S23 SER LEU 0.391527
S11 S23 SER MET 0.00782563
S11 S23 SER ASN 0.00782563
S11 S23 SER PRO 0.00782563
S11 S23 SER GLN 0.00782563
S11 S23 SER ARG 0.00782563
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S11 S23 SER VAL 0.00782563
S11 S23 SER TRP 0.00782563
S11 S23 SER TYR 0.00782563
S11 S23 SER --- 0.00782563
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S11 S23 THR LEU 0.00220077
S11 S23 VAL ILE 0.0131863

S11 S23 VAL LEU 0.00220077
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S11 S23 TRP LEU 0.00220077
S11 S23 TYR ILE 0.0131863
S11 S23 TYR LEU 0.00220077
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S11 S23 --- LEU 0.00220077
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S11 S24 ALA GLU 0.00469266
S11 S24 ALA PHE 0.00469266
S11 S24 ALA GLY -0.255715
S11 S24 ALA HIS 0.00469266
S11 S24 ALA ILE 0.00469266
S11 S24 ALA LYS 0.00469266
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S11 S24 ALA MET 0.00469266
S11 S24 ALA ASN 0.00469266
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S11 S24 ALA ARG 0.00469266
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S11 S24 ALA VAL 0.00469266
S11 S24 ALA TRP 0.00469266
S11 S24 ALA TYR 0.00469266
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S11 S24 ASP GLY 0.015366
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S11 S24 GLU GLY 0.015366
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S11 S24 PHE GLY 0.015366
S11 S24 PHE SER 2.10307e-05
S11 S24 GLY GLY 0.015366
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S11 S24 SER LYS 0.00692553
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S11 S24 SER ARG 0.00692553
S11 S24 SER SER -0.117776
S11 S24 SER THR 0.00692553
S11 S24 SER VAL 0.00692553
S11 S24 SER TRP 0.00692553
S11 S24 SER TYR 0.00692553
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S11 S25 ALA GLY 0.00743691
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S11 S25 ALA ILE 0.00743691
S11 S25 ALA LYS -0.627911
S11 S25 ALA LEU 0.00743691
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S11 S25 ALA ASN 0.00743691
S11 S25 ALA PRO 0.00743691
S11 S25 ALA GLN 0.00743691
S11 S25 ALA ARG -0.237956
S11 S25 ALA SER 0.457346
S11 S25 ALA THR 0.0698141
S11 S25 ALA VAL 0.00743691
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S11 S25 ALA TYR 0.00743691
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S11 S25 CYS THR 0.00022852
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S11 S25 GLY THR 0.00022852
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S11 S25 HIS GLU 5.83786e-06
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S11 S25 HIS ARG 0.00368066
S11 S25 HIS SER 0.00963051
S11 S25 HIS THR 0.00022852
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S11 S25 ILE GLU 5.83786e-06
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S11 S25 SER LYS 0.543746
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S11 S25 SER THR -0.085218
S11 S25 SER VAL 0.0188811
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S11 S26 ALA HIS 0.00748766
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S11 S28 ALA THR 0.00468564
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S11 S28 SER GLY 0.00955898
S11 S28 SER HIS 0.00955898
S11 S28 SER ILE 0.00955898
S11 S28 SER LYS 0.00955898
S11 S28 SER LEU 0.00955898
S11 S28 SER MET 0.00955898
S11 S28 SER ASN 0.00955898
S11 S28 SER PRO 0.00955898
S11 S28 SER GLN 0.00955898
S11 S28 SER ARG 0.00955898
S11 S28 SER SER 0.00955898
S11 S28 SER THR 0.00955898
S11 S28 SER VAL 0.00955898
S11 S28 SER TRP 0.00955898
S11 S28 SER TYR 0.00955898
S11 S28 SER --- 0.00955898
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S11 S28 THR GLU 0.00270849
S11 S28 VAL ASP 0.0126786
S11 S28 VAL GLU 0.00270849
S11 S28 TRP ASP 0.0126786
S11 S28 TRP GLU 0.00270849
S11 S28 TYR ASP 0.0126786
S11 S28 TYR GLU 0.00270849
S11 S28 --- ASP 0.0126786
S11 S28 --- GLU 0.00270849
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S11 S29 ALA CYS 0.0069745

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S11 S29 ALA PHE 0.0069745
S11 S29 ALA GLY 0.0069745
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S11 S29 ALA ILE 0.0069745
S11 S29 ALA LYS -0.142776
S11 S29 ALA LEU 0.0453437
S11 S29 ALA MET 0.0069745
S11 S29 ALA ASN 0.0647493
S11 S29 ALA PRO 0.0069745
S11 S29 ALA GLN 0.0069745
S11 S29 ALA ARG 0.0069745
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S11 S29 ALA TRP 0.0069745
S11 S29 ALA TYR 0.0069745
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S11 S29 CYS LEU 4.8871e-05
S11 S29 CYS ASN 0.000115263
S11 S29 CYS SER 0.0151376
S11 S29 ASP LYS 8.53077e-05
S11 S29 ASP LEU 4.8871e-05
S11 S29 ASP ASN 0.000115263
S11 S29 ASP SER 0.0151376
S11 S29 GLU LYS 8.53077e-05
S11 S29 GLU LEU 4.8871e-05
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S11 S29 PHE LEU 4.8871e-05
S11 S29 PHE ASN 0.000115263
S11 S29 PHE SER 0.0151376
S11 S29 GLY LYS 8.53077e-05
S11 S29 GLY LEU 4.8871e-05
S11 S29 GLY ASN 0.000115263
S11 S29 GLY SER 0.0151376
S11 S29 HIS LYS 8.53077e-05
S11 S29 HIS LEU 4.8871e-05
S11 S29 HIS ASN 0.000115263
S11 S29 HIS SER 0.0151376
S11 S29 ILE LYS 8.53077e-05
S11 S29 ILE LEU 4.8871e-05
S11 S29 ILE ASN 0.000115263
S11 S29 ILE SER 0.0151376
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S11 S29 LYS LEU 4.8871e-05
S11 S29 LYS ASN 0.000115263
S11 S29 LYS SER 0.0151376
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S11 S29 ASN LEU 4.8871e-05
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S11 S29 ASN SER 0.0151376

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S11 S29 PRO LEU 4.8871e-05
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S11 S29 PRO SER 0.0151376
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S11 S29 GLN LEU 4.8871e-05
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S11 S29 GLN SER 0.0151376
S11 S29 ARG LYS 8.53077e-05
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S11 S29 SER GLY 0.0108537
S11 S29 SER HIS 0.0108537
S11 S29 SER ILE 0.0108537
S11 S29 SER LYS 0.096814
S11 S29 SER LEU -0.107159
S11 S29 SER MET 0.0108537
S11 S29 SER ASN -0.131185
S11 S29 SER PRO 0.0108537
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S11 S29 SER SER -0.204431
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S11 S29 SER VAL 0.0108537
S11 S29 SER TRP 0.0108537
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S11 S30 ALA PHE 0.00365416
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S11 S30 ALA GLN -0.298499
S11 S30 ALA ARG 0.00365416
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S11 S30 PHE SER 2.97575e-05
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S11 S30 ILE GLN 0.0153573
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S11 S30 SER ASN 0.00881208
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S11 S30 SER GLN -0.150216
S11 S30 SER ARG 0.00881208
S11 S30 SER SER -0.178662
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S11 S30 --- SER 2.97575e-05
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S11 S31 ALA ILE 0.293423
S11 S31 ALA LYS 0.00765908
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S11 S31 ALA MET 0.00765908
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S11 S31 CYS ILE 0.00272005
S11 S31 CYS VAL 0.0122785
S11 S31 ASP ASP 0.000388519
S11 S31 ASP ILE 0.00272005
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S11 S31 GLU ASP 0.000388519
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S11 S31 PHE ILE 0.00272005
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S11 S31 GLY VAL 0.0122785
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S11 S31 ILE ASP 0.000388519
S11 S31 ILE ILE 0.00272005
S11 S31 ILE VAL 0.0122785
S11 S31 LYS ASP 0.000388519
S11 S31 LYS ILE 0.00272005
S11 S31 LYS VAL 0.0122785
S11 S31 LEU ASP 0.000388519
S11 S31 LEU ILE 0.00272005
S11 S31 LEU VAL 0.0122785
S11 S31 MET ASP 0.000388519
S11 S31 MET ILE 0.00272005
S11 S31 MET VAL 0.0122785
S11 S31 ASN ASP 0.000388519
S11 S31 ASN ILE 0.00272005
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S11 S31 PRO ASP 0.000388519
S11 S31 PRO ILE 0.00272005

S11 S31 PRO VAL 0.0122785
S11 S31 GLN ASP 0.000388519
S11 S31 GLN ILE 0.00272005
S11 S31 GLN VAL 0.0122785
S11 S31 ARG ASP 0.000388519
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S11 S31 ARG VAL 0.0122785
S11 S31 SER ALA 0.0109019
S11 S31 SER CYS 0.0109019
S11 S31 SER ASP 0.0324788
S11 S31 SER GLU 0.0109019
S11 S31 SER PHE 0.0109019
S11 S31 SER GLY 0.0109019
S11 S31 SER HIS 0.0109019
S11 S31 SER ILE -0.405893
S11 S31 SER LYS 0.0109019
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S11 S31 SER MET 0.0109019
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S11 S31 SER PRO 0.0109019
S11 S31 SER GLN 0.0109019
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S11 S31 SER THR 0.0109019
S11 S31 SER VAL 0.0157314
S11 S31 SER TRP 0.0109019
S11 S31 SER TYR 0.0109019
S11 S31 SER --- 0.0109019
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S11 S31 THR ILE 0.00272005
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S11 S31 VAL ILE 0.00272005
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S11 S31 TRP ASP 0.000388519
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S11 S31 TRP VAL 0.0122785
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S11 S31 TYR ILE 0.00272005
S11 S31 TYR VAL 0.0122785
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S11 S31 --- ILE 0.00272005
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S11 S32 ALA PHE -0.0260593
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S11 S32 ALA TYR -0.542863

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S11 S38 LEU HIS 0.00354602
S11 S38 LEU LYS 0.00344328
S11 S38 LEU LEU 0.00561883
S11 S38 LEU ARG 0.00154869
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S11 S38 MET LYS 0.00344328
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S11 S38 MET ARG 0.00154869
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S11 S38 ASN LYS 0.00344328
S11 S38 ASN LEU 0.00561883
S11 S38 ASN ARG 0.00154869
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S11 S38 ARG LYS 0.00344328
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S11 S38 SER CYS 0.0145128

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S11 S38 SER GLY 0.0145128
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S11 S38 SER TYR 0.0145128
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S11 S39 GLU TRP 0.000259154
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S11 S39 SER LEU 0.0517089
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S11 S40 ASP VAL 0.0125458

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S12 S25 MET THR 0.000305353
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S12 S25 TRP THR 0.000305353
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S12 S31 GLU THR 0.00225402
S12 S31 GLU VAL 0.0802333
S12 S31 GLU TRP 0.00225402
S12 S31 GLU TYR 0.00225402

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S12 S31 PHE ILE 0.00180774
S12 S31 PHE VAL 0.0118282
S12 S31 GLY ASP 0.000523872
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S12 S31 GLY VAL 0.0118282
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S12 S31 HIS ILE 0.00180774
S12 S31 HIS VAL 0.0118282
S12 S31 ILE ASP 0.000523872
S12 S31 ILE ILE 0.00180774
S12 S31 ILE VAL 0.0118282
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S12 S31 LYS VAL 0.0118282
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S12 S31 GLN LYS 0.0163069
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S12 S31 GLN MET 0.0163069
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S12 S31 GLN TYR 0.0163069
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S12 S31 SER VAL 0.0118282
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S12 S31 THR VAL 0.0118282
S12 S31 VAL ASP 0.000523872
S12 S31 VAL ILE 0.00180774
S12 S31 VAL VAL 0.0118282
S12 S31 TRP ASP 0.000523872
S12 S31 TRP ILE 0.00180774

S12 S31 TRP VAL 0.0118282
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S12 S31 TYR VAL 0.0118282
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S12 S31 --- VAL 0.0118282
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S12 S32 ALA HIS 0.00196938
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S12 S32 ALA TYR 0.00174315
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S12 S32 CYS HIS 0.00196938
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S12 S32 CYS TYR 0.00174315
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S12 S32 ASP TYR 0.00174315
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S12 S32 GLU CYS 0.00363689
S12 S32 GLU ASP 0.00363689
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S12 S32 VAL TYR 0.00174315
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S12 S33 CYS VAL 0.00228902
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S12 S34 CYS MET 0.000343286
S12 S34 CYS ARG 7.62148e-05
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S12 S34 GLY THR 0.00119115
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S12 S34 HIS MET 0.000343286
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S12 S34 HIS THR 0.00119115
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S12 S34 ILE MET 0.000343286
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S12 S34 ILE THR 0.00119115
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S12 S34 THR MET 0.000343286
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S12 S34 TYR MET 0.000343286
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S12 S34 TYR THR 0.00119115
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S12 S34 --- MET 0.000343286
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S12 S35 CYS THR 0.00241288
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S12 S35 ASP THR 0.00241288
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S12 S36 HIS THR 0.000938202
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S12 S36 ILE THR 0.000938202
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S12 S37 GLU ARG 0.129655

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S12 S38 ALA LYS 0.00282805

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S12 S38 CYS GLU 0.00193853
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S12 S38 CYS LYS 0.00282805
S12 S38 CYS LEU 0.00418045
S12 S38 CYS ARG 0.00205159
S12 S38 ASP GLU 0.00193853
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S12 S38 ASP LYS 0.00282805
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S12 S38 ASP ARG 0.00205159
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S12 S40 GLN LYS 0.0138191
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S12 S40 GLN THR 0.0138191
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S12 S40 VAL VAL 0.0120946
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S13 S14 ALA SER 0.000175636
S13 S14 ALA THR 0.000154843
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S13 S14 CYS SER 0.000175636
S13 S14 CYS THR 0.000154843
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S13 S14 ASP SER 0.000175636
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S13 S14 GLU SER 0.000175636
S13 S14 GLU THR 0.000154843
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S13 S14 PHE CYS 0.000787784
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S13 S14 PHE GLU 0.324019
S13 S14 PHE PHE 0.000787784
S13 S14 PHE GLY 0.000787784
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S13 S14 PHE ILE 0.000787784
S13 S14 PHE LYS 0.000787784
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S13 S14 PHE THR 0.0120532
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S13 S16 LYS VAL 0.00442577
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S13 S16 LEU ILE 0.00621431
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S13 S24 PHE CYS 0.000114309
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S13 S24 PHE LYS 0.000114309
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S13 S25 ALA GLU 0.00019314

S13 S25 ALA LYS 0.000593305
S13 S25 ALA ARG 0.00137389
S13 S25 ALA SER 0.00927799
S13 S25 ALA THR 0.000214898
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S13 S25 CYS GLU 0.00019314
S13 S25 CYS LYS 0.000593305
S13 S25 CYS ARG 0.00137389
S13 S25 CYS SER 0.00927799
S13 S25 CYS THR 0.000214898
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S13 S25 ASP THR 0.000214898
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S13 S25 GLU LYS 0.000593305
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S13 S25 PHE TYR 0.000142497
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S13 S25 GLY SER 0.00927799
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S13 S25 HIS LYS 0.000593305
S13 S25 HIS ARG 0.00137389
S13 S25 HIS SER 0.00927799
S13 S25 HIS THR 0.000214898
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S13 S25 ILE LYS 0.000593305
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S13 S25 ILE SER 0.00927799
S13 S25 ILE THR 0.000214898
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S13 S25 TYR GLU 0.00019314
S13 S25 TYR LYS 0.000593305
S13 S25 TYR ARG 0.00137389
S13 S25 TYR SER 0.00927799
S13 S25 TYR THR 0.000214898
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S13 S26 ASP TYR 0.000997277
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S13 S28 TRP HIS 0.0141975
S13 S28 TRP ILE 0.0141975
S13 S28 TRP LYS 0.0141975
S13 S28 TRP LEU 0.0141975
S13 S28 TRP MET 0.0141975
S13 S28 TRP ASN 0.0141975
S13 S28 TRP PRO 0.0141975
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S13 S28 TRP THR 0.0141975
S13 S28 TRP VAL 0.0141975
S13 S28 TRP TRP 0.0141975
S13 S28 TRP TYR 0.0141975
S13 S28 TRP --- 0.0141975
S13 S28 TYR ASP 0.010571
S13 S28 TYR GLU 0.00110813
S13 S28 --- ASP 0.010571
S13 S28 --- GLU 0.00110813
S13 S29 ALA LYS 0.000205274
S13 S29 ALA LEU 0.000208984
S13 S29 ALA ASN 0.000244991
S13 S29 ALA SER 0.0110199
S13 S29 CYS LYS 0.000205274
S13 S29 CYS LEU 0.000208984
S13 S29 CYS ASN 0.000244991
S13 S29 CYS SER 0.0110199
S13 S29 ASP LYS 0.000205274
S13 S29 ASP LEU 0.000208984
S13 S29 ASP ASN 0.000244991
S13 S29 ASP SER 0.0110199
S13 S29 GLU LYS 0.000205274
S13 S29 GLU LEU 0.000208984
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S13 S29 PHE PHE 0.000148301
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S13 S29 PHE ILE 0.000148301
S13 S29 PHE LYS 0.0017619
S13 S29 PHE LEU 0.00655467
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S13 S29 PHE ASN 0.00611352

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S13 S29 PHE VAL 0.000148301
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S13 S29 PHE TYR 0.000148301
S13 S29 PHE --- 0.000148301
S13 S29 GLY LYS 0.000205274
S13 S29 GLY LEU 0.000208984
S13 S29 GLY ASN 0.000244991
S13 S29 GLY SER 0.0110199
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S13 S29 HIS LEU 0.000208984
S13 S29 HIS ASN 0.000244991
S13 S29 HIS SER 0.0110199
S13 S29 ILE LYS 0.000205274
S13 S29 ILE LEU 0.000208984
S13 S29 ILE ASN 0.000244991
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S13 S31 ALA ILE 0.00133888
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S13 S31 PHE CYS 0.000119984
S13 S31 PHE ASP 0.0149409
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S13 S31 PHE GLY 0.000119984
S13 S31 PHE HIS 0.000119984

S13 S31 PHE ILE 0.0125013
S13 S31 PHE LYS 0.000119984
S13 S31 PHE LEU 0.000119984
S13 S31 PHE MET 0.000119984
S13 S31 PHE ASN 0.000119984
S13 S31 PHE PRO 0.000119984
S13 S31 PHE GLN 0.000119984
S13 S31 PHE ARG 0.000119984
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S13 S31 PHE THR 0.000119984
S13 S31 PHE VAL -0.104451
S13 S31 PHE TRP 0.000119984
S13 S31 PHE TYR 0.000119984
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S13 S31 GLY ILE 0.00133888
S13 S31 GLY VAL 0.00970053
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S13 S31 HIS ILE 0.00133888
S13 S31 HIS VAL 0.00970053
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S13 S31 ILE ILE 0.00133888
S13 S31 ILE VAL 0.00970053
S13 S31 LYS ASP 0.000639762
S13 S31 LYS ILE 0.00133888
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S13 S31 LEU ILE 0.00133888
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S13 S31 GLN ILE 0.00133888
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S13 S31 VAL ILE 0.00133888
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S13 S32 CYS HIS 0.000992052
S13 S32 CYS TRP 0.00899655
S13 S32 CYS TYR 0.00127573
S13 S32 ASP PHE 0.000414835
S13 S32 ASP HIS 0.000992052
S13 S32 ASP TRP 0.00899655
S13 S32 ASP TYR 0.00127573
S13 S32 GLU PHE 0.000414835
S13 S32 GLU HIS 0.000992052
S13 S32 GLU TRP 0.00899655
S13 S32 GLU TYR 0.00127573
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S13 S32 LYS TYR 0.00127573
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S13 S38 LYS LYS 0.00227468
S13 S38 LYS LEU 0.0046064
S13 S38 LYS ARG 0.00110867
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S13 S38 LEU HIS 0.00265294
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S13 S38 MET ARG 0.00110867
S13 S38 ASN GLU 0.00103648
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S14 S16 GLN ILE 0.0136158
S14 S16 GLN LEU 3.44014e-06

S14 S16 GLN THR 0.000101818
S14 S16 GLN VAL 0.00590051
S14 S16 ARG ALA 0.000787784
S14 S16 ARG ILE 0.0136158
S14 S16 ARG LEU 3.44014e-06
S14 S16 ARG THR 0.000101818
S14 S16 ARG VAL 0.00590051
S14 S16 SER ALA 0.0132866
S14 S16 SER CYS 8.97161e-05
S14 S16 SER ASP 8.97161e-05
S14 S16 SER GLU 8.97161e-05
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S14 S16 SER GLY 8.97161e-05
S14 S16 SER HIS 8.97161e-05
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S14 S16 SER LYS 8.97161e-05
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S14 S16 SER MET 8.97161e-05
S14 S16 SER ASN 8.97161e-05
S14 S16 SER PRO 8.97161e-05
S14 S16 SER GLN 8.97161e-05
S14 S16 SER ARG 8.97161e-05
S14 S16 SER SER 8.97161e-05
S14 S16 SER THR 0.00238979
S14 S16 SER VAL 0.0261473
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S14 S16 SER TYR 8.97161e-05
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S14 S16 THR GLU 0.000181184
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S14 S16 THR HIS 0.000181184
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S14 S16 THR TRP 0.000181184
S14 S16 THR TYR 0.000181184
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S14 S16 VAL ALA 0.000787784
S14 S16 VAL ILE 0.0136158
S14 S16 VAL LEU 3.44014e-06
S14 S16 VAL THR 0.000101818
S14 S16 VAL VAL 0.00590051
S14 S16 TRP ALA 0.000787784
S14 S16 TRP ILE 0.0136158
S14 S16 TRP LEU 3.44014e-06
S14 S16 TRP THR 0.000101818
S14 S16 TRP VAL 0.00590051
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S14 S16 TYR ILE 0.0136158
S14 S16 TYR LEU 3.44014e-06
S14 S16 TYR THR 0.000101818

S14 S16 TYR VAL 0.00590051
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S14 S16 --- ILE 0.0136158
S14 S16 --- LEU 3.44014e-06
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S14 S16 --- VAL 0.00590051
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S14 S17 ALA TRP 0.000123122
S14 S17 ALA TYR 0.00296731
S14 S17 CYS PHE 0.0130878
S14 S17 CYS HIS 0.00330939
S14 S17 CYS ILE 0.000921746
S14 S17 CYS TRP 0.000123122
S14 S17 CYS TYR 0.00296731
S14 S17 ASP ALA 0.00239585
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S14 S17 GLU PHE 0.290352
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S14 S17 PHE ILE 0.000921746
S14 S17 PHE TRP 0.000123122
S14 S17 PHE TYR 0.00296731

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S14 S17 GLY ILE 0.000921746
S14 S17 GLY TRP 0.000123122
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S14 S17 HIS ILE 0.000921746
S14 S17 HIS TRP 0.000123122
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S14 S17 ILE TRP 0.000123122
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S14 S17 LYS PHE 0.0130878
S14 S17 LYS HIS 0.00330939
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S14 S17 LYS TRP 0.000123122
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S14 S17 LEU PHE 0.0130878
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S14 S17 MET TRP 0.000123122
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S14 S17 PRO TRP 0.000123122
S14 S17 PRO TYR 0.00296731
S14 S17 GLN PHE 0.0130878
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S14 S17 GLN TRP 0.000123122
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S14 S17 SER GLU 0.000155978
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S14 S17 SER HIS 0.0255932
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S14 S18 CYS HIS 0.000994843
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S14 S18 ASP CYS 0.00218629
S14 S18 ASP ASP 0.00218629
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S14 S19 GLU ILE 0.0154887
S14 S19 GLU LYS 0.0154887
S14 S19 GLU LEU 0.0154887
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S14 S19 PHE SER 0.00737266
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S14 S19 HIS TYR 0.00161921
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S14 S19 THR ILE 0.000134878
S14 S19 THR LYS 0.000134878
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S14 S19 VAL SER 0.00737266
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S14 S20 LYS LEU 0.000828313
S14 S20 LYS MET 0.00950727
S14 S20 LYS VAL 0.00186378
S14 S20 LEU PHE 0.00820997
S14 S20 LEU LEU 0.000828313
S14 S20 LEU MET 0.00950727
S14 S20 LEU VAL 0.00186378
S14 S20 MET PHE 0.00820997
S14 S20 MET LEU 0.000828313

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S14 S20 MET VAL 0.00186378
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S14 S20 SER PRO 9.04256e-05
S14 S20 SER GLN 9.04256e-05
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S14 S20 SER THR 9.04256e-05
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S14 S20 SER TYR 9.04256e-05
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S14 S20 VAL PHE 0.00820997
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S14 S20 VAL MET 0.00950727

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S14 S20 TRP LEU 0.000828313
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S14 S21 ALA VAL 0.00216145
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S14 S21 CYS ILE 0.0135625
S14 S21 CYS VAL 0.00216145
S14 S21 CYS TYR 0.00065284
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S14 S21 GLU TRP 0.0199178
S14 S21 GLU TYR -0.222564
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S14 S21 GLY VAL 0.00216145
S14 S21 GLY TYR 0.00065284
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S14 S21 HIS VAL 0.00216145
S14 S21 HIS TYR 0.00065284
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S14 S21 LYS ILE 0.0135625
S14 S21 LYS VAL 0.00216145
S14 S21 LYS TYR 0.00065284
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S14 S22 CYS TYR 0.000627727
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S14 S22 ASP CYS 0.00158851
S14 S22 ASP ASP -0.300078
S14 S22 ASP GLU 0.011362
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S14 S22 HIS TYR 0.000627727
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S14 S24 ASN SER 0.00082059
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S14 S24 GLN SER 0.00082059
S14 S24 ARG GLY 0.0195887
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S14 S24 SER GLY 0.363066
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S14 S24 THR ASP 9.95126e-05
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S14 S24 THR TRP 9.95126e-05
S14 S24 THR TYR 9.95126e-05
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S14 S24 TYR SER 0.00082059
S14 S24 --- GLY 0.0195887
S14 S24 --- SER 0.00082059
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S14 S25 ALA LYS 0.000847392
S14 S25 ALA ARG 0.00280561
S14 S25 ALA SER 0.0161422
S14 S25 ALA THR 0.000241431
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S14 S25 CYS LYS 0.000847392
S14 S25 CYS ARG 0.00280561
S14 S25 CYS SER 0.0161422
S14 S25 CYS THR 0.000241431
S14 S25 ASP ALA 0.00151162
S14 S25 ASP CYS 0.00151162

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S14 S25 PHE THR 0.000241431
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S14 S25 GLY ARG 0.00280561
S14 S25 GLY SER 0.0161422
S14 S25 GLY THR 0.000241431
S14 S25 HIS ASP 8.61499e-05
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S14 S25 HIS LYS 0.000847392
S14 S25 HIS ARG 0.00280561
S14 S25 HIS SER 0.0161422
S14 S25 HIS THR 0.000241431
S14 S25 ILE ASP 8.61499e-05
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S14 S25 ILE LYS 0.000847392
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S14 S25 ILE SER 0.0161422

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S14 S25 LYS THR 0.000241431
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S14 S25 LEU THR 0.000241431
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S14 S25 THR TYR 0.00117245
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S14 S27 THR GLU 2.39268e-05
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S14 S29 GLU PHE 0.0145212
S14 S29 GLU GLY 0.0145212
S14 S29 GLU HIS 0.0145212
S14 S29 GLU ILE 0.0145212
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S14 S29 GLU LEU -0.135341
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S14 S29 GLU PRO 0.0145212
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S14 S32 GLN PHE 0.000530671
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S14 S33 ASP CYS 0.00134184
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S14 S33 GLU PHE 0.0229756

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S14 S33 GLU ILE 0.0229756
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S14 S34 ASP ASN 0.00310769
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S14 S34 ASP SER -0.334232
S14 S34 ASP THR 0.0593612
S14 S34 ASP VAL 0.00310769
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S14 S39 TRP LEU 0.000869876

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S14 S39 TRP TRP 0.000101713
S14 S39 TYR ILE 0.00091874
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S14 S39 TYR VAL 0.018519
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S14 S40 ALA VAL 0.0174064
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S14 S40 GLU LYS 0.0136971
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S14 S40 GLY LEU 0.00154386

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S15 S16 VAL LEU 0.000128721
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S15 S16 VAL VAL 0.0103133

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S15 S18 CYS HIS 0.000674128
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S15 S18 ASP CYS 0.00525703
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S15 S18 ASP GLY 0.00525703
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S15 S21 GLN GLY 9.00638e-05
S15 S21 GLN HIS 9.00638e-05
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S15 S21 GLN LYS 9.00638e-05
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S15 S21 GLN GLN 9.00638e-05
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S15 S21 GLN THR 9.00638e-05
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S15 S22 ALA TYR 0.00153849
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S15 S22 GLN ARG 0.000473127
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S15 S25 GLY LYS 0.00147344
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S15 S25 GLY THR 0.000741223
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S15 S25 HIS SER 0.0207303
S15 S25 HIS THR 0.000741223
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S15 S25 ILE THR 0.000741223
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S15 S25 ASN LYS 0.00147344
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S15 S28 TRP ASP 0.0243566
S15 S28 TRP GLU 0.00468243
S15 S28 TYR ASP 0.0243566
S15 S28 TYR GLU 0.00468243
S15 S28 --- ASP 0.0243566
S15 S28 --- GLU 0.00468243
S15 S29 ALA LYS 0.000775864
S15 S29 ALA LEU 0.000455694
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S15 S29 ALA SER 0.0277184
S15 S29 CYS LYS 0.000775864
S15 S29 CYS LEU 0.000455694
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S15 S29 CYS SER 0.0277184
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S15 S29 ASP CYS 0.00891189
S15 S29 ASP ASP 0.00891189
S15 S29 ASP GLU 0.00891189
S15 S29 ASP PHE 0.00891189
S15 S29 ASP GLY 0.00891189
S15 S29 ASP HIS 0.00891189
S15 S29 ASP ILE 0.00891189
S15 S29 ASP LYS 0.106947
S15 S29 ASP LEU -0.261193
S15 S29 ASP MET 0.00891189
S15 S29 ASP ASN -0.163315
S15 S29 ASP PRO 0.00891189
S15 S29 ASP GLN 0.00891189
S15 S29 ASP ARG 0.00891189
S15 S29 ASP SER -0.0673175
S15 S29 ASP THR 0.00891189
S15 S29 ASP VAL 0.00891189
S15 S29 ASP TRP 0.00891189
S15 S29 ASP TYR 0.00891189
S15 S29 ASP --- 0.00891189
S15 S29 GLU ALA 0.000529642
S15 S29 GLU CYS 0.000529642
S15 S29 GLU ASP 0.000529642
S15 S29 GLU GLU 0.000529642
S15 S29 GLU PHE 0.000529642
S15 S29 GLU GLY 0.000529642
S15 S29 GLU HIS 0.000529642
S15 S29 GLU ILE 0.000529642
S15 S29 GLU LYS 0.00902341
S15 S29 GLU LEU 0.0126085
S15 S29 GLU MET 0.000529642
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S15 S29 GLU PRO 0.000529642
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S15 S29 GLU TRP 0.000529642
S15 S29 GLU TYR 0.000529642
S15 S29 GLU --- 0.000529642
S15 S29 PHE LYS 0.000775864
S15 S29 PHE LEU 0.000455694
S15 S29 PHE ASN 8.90895e-05
S15 S29 PHE SER 0.0277184

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S15 S29 HIS LEU 0.000455694
S15 S29 HIS ASN 8.90895e-05
S15 S29 HIS SER 0.0277184
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S15 S29 ILE LEU 0.000455694
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S15 S29 ILE SER 0.0277184
S15 S29 LYS LYS 0.000775864
S15 S29 LYS LEU 0.000455694
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S15 S29 LEU CYS 0.00276932
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S15 S29 LEU GLU 0.00276932
S15 S29 LEU PHE 0.00276932
S15 S29 LEU GLY 0.00276932
S15 S29 LEU HIS 0.00276932
S15 S29 LEU ILE 0.00276932
S15 S29 LEU LYS -0.339637
S15 S29 LEU LEU 0.0658077
S15 S29 LEU MET 0.00276932
S15 S29 LEU ASN 0.0196474
S15 S29 LEU PRO 0.00276932
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S15 S29 MET LYS 0.000775864
S15 S29 MET LEU 0.000455694
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S15 S29 MET SER 0.0277184
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S15 S29 ASN LEU 0.000455694
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S15 S29 PRO LYS 0.000775864
S15 S29 PRO LEU 0.000455694
S15 S29 PRO ASN 8.90895e-05
S15 S29 PRO SER 0.0277184
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S15 S29 GLN CYS 5.64594e-05
S15 S29 GLN ASP 5.64594e-05
S15 S29 GLN GLU 5.64594e-05
S15 S29 GLN PHE 5.64594e-05
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S15 S29 GLN LEU 0.0029022
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S15 S29 GLN ASN 0.000592987
S15 S29 GLN PRO 5.64594e-05
S15 S29 GLN GLN 5.64594e-05

S15 S29 GLN ARG 5.64594e-05
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S15 S29 GLN TRP 5.64594e-05
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S15 S29 SER PHE 0.00556088
S15 S29 SER GLY 0.00556088
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S15 S29 SER LYS 0.135018
S15 S29 SER LEU 0.111697
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S15 S29 VAL LEU 0.000455694
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S15 S29 TYR LEU 0.000455694
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S15 S29 --- LEU 0.000455694
S15 S29 --- ASN 8.90895e-05
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S15 S30 CYS GLN 0.0288091
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S15 S30 ASP ALA 0.0073371
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S15 S30 ASP ASP 0.0073371
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S15 S30 ASP PHE 0.0073371
S15 S30 ASP GLY 0.0073371
S15 S30 ASP HIS 0.0073371

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S15 S30 ASP LYS 0.0073371
S15 S30 ASP LEU 0.0073371
S15 S30 ASP MET 0.0073371
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S15 S30 ASP PRO 0.0073371
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S15 S30 ASP ARG 0.0073371
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S15 S30 ASP TRP 0.0073371
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S15 S30 GLU CYS 0.000636035
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S15 S30 LEU CYS 0.00174879
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S15 S30 LEU PHE 0.00174879
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S15 S30 LEU ILE 0.00174879
S15 S30 LEU LYS 0.00174879
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S15 S30 LEU ARG 0.00174879
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S15 S30 LEU VAL 0.00174879

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S15 S30 LEU TYR 0.00174879
S15 S30 LEU --- 0.00174879
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S15 S30 ASN GLN 0.0288091
S15 S30 ASN SER 0.000229954
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S15 S30 PRO SER 0.000229954
S15 S30 GLN ALA 0.000193642
S15 S30 GLN CYS 0.000193642
S15 S30 GLN ASP 0.000193642
S15 S30 GLN GLU 0.000193642
S15 S30 GLN PHE 0.000193642
S15 S30 GLN GLY 0.000193642
S15 S30 GLN HIS 0.000193642
S15 S30 GLN ILE 0.000193642
S15 S30 GLN LYS 0.000193642
S15 S30 GLN LEU 0.000193642
S15 S30 GLN MET 0.000193642
S15 S30 GLN ASN 0.000193642
S15 S30 GLN PRO 0.000193642
S15 S30 GLN GLN -0.0658808
S15 S30 GLN ARG 0.000193642
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S15 S30 GLN TRP 0.000193642
S15 S30 GLN TYR 0.000193642
S15 S30 GLN --- 0.000193642
S15 S30 ARG GLN 0.0288091
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S15 S30 SER ALA 0.00255067
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S15 S30 SER PHE 0.00255067
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S15 S30 SER ILE 0.00255067
S15 S30 SER LYS 0.00255067
S15 S30 SER LEU 0.00255067
S15 S30 SER MET 0.00255067
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S15 S30 SER ARG 0.00255067
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S15 S30 TYR SER 0.000229954
S15 S30 --- GLN 0.0288091
S15 S30 --- SER 0.000229954

S15 S31 ALA ASP 0.00076715
S15 S31 ALA ILE 0.00436751
S15 S31 ALA VAL 0.0239044
S15 S31 CYS ASP 0.00076715
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S15 S31 CYS VAL 0.0239044
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S15 S31 ASP CYS 0.00776383
S15 S31 ASP ASP -0.180728
S15 S31 ASP GLU 0.00776383
S15 S31 ASP PHE 0.00776383
S15 S31 ASP GLY 0.00776383
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S15 S31 ASP ILE 0.433058
S15 S31 ASP LYS 0.00776383
S15 S31 ASP LEU 0.00776383
S15 S31 ASP MET 0.00776383
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S15 S31 ASP TRP 0.00776383
S15 S31 ASP TYR 0.00776383
S15 S31 ASP --- 0.00776383
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S15 S31 GLU CYS 0.000993098
S15 S31 GLU ASP 0.0193506
S15 S31 GLU GLU 0.000993098
S15 S31 GLU PHE 0.000993098
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S15 S31 GLU LYS 0.000993098
S15 S31 GLU LEU 0.000993098
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S15 S31 GLU ASN 0.000993098
S15 S31 GLU PRO 0.000993098
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S15 S31 GLU --- 0.000993098
S15 S31 PHE ASP 0.00076715
S15 S31 PHE ILE 0.00436751
S15 S31 PHE VAL 0.0239044
S15 S31 GLY ASP 0.00076715
S15 S31 GLY ILE 0.00436751
S15 S31 GLY VAL 0.0239044
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S15 S31 HIS ILE 0.00436751
S15 S31 HIS VAL 0.0239044
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S15 S31 LYS ILE 0.00436751
S15 S31 LYS VAL 0.0239044

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S15 S31 LEU CYS 0.00210431
S15 S31 LEU ASP 0.109892
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S15 S31 LEU PHE 0.00210431
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S15 S31 LEU ILE 0.483525
S15 S31 LEU LYS 0.00210431
S15 S31 LEU LEU 0.00210431
S15 S31 LEU MET 0.00210431
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S15 S31 ASN VAL 0.0239044
S15 S31 PRO ASP 0.00076715
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S15 S31 GLN LYS 0.000150219
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S15 S31 SER LYS 0.0075495

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S15 S31 VAL ILE 0.00436751
S15 S31 VAL VAL 0.0239044
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S15 S32 CYS TYR 0.00220774
S15 S32 ASP ALA 0.00912949
S15 S32 ASP CYS 0.00912949
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S15 S32 ASP GLU 0.00912949
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S15 S32 ASP TYR 0.0946713
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S15 S32 GLU LYS 0.000445511
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S15 S32 PHE TYR 0.00220774
S15 S32 GLY PHE 0.00088616
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S15 S32 GLY TYR 0.00220774
S15 S32 HIS PHE 0.00088616
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S15 S32 HIS TYR 0.00220774
S15 S32 ILE PHE 0.00088616
S15 S32 ILE HIS 0.00275885
S15 S32 ILE TRP 0.0231863
S15 S32 ILE TYR 0.00220774
S15 S32 LYS PHE 0.00088616
S15 S32 LYS HIS 0.00275885
S15 S32 LYS TRP 0.0231863
S15 S32 LYS TYR 0.00220774
S15 S32 LEU ALA 0.00180238
S15 S32 LEU CYS 0.00180238
S15 S32 LEU ASP 0.00180238
S15 S32 LEU GLU 0.00180238
S15 S32 LEU PHE 0.351141
S15 S32 LEU GLY 0.00180238
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S15 S32 LEU ILE 0.00180238
S15 S32 LEU LYS 0.00180238
S15 S32 LEU LEU 0.00180238
S15 S32 LEU MET 0.00180238
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S15 S32 LEU TYR 0.101642
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S15 S32 ASN HIS 0.00275885
S15 S32 ASN TRP 0.0231863
S15 S32 ASN TYR 0.00220774

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S15 S32 PRO HIS 0.00275885
S15 S32 PRO TRP 0.0231863
S15 S32 PRO TYR 0.00220774
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S15 S32 GLN GLU 0.000224572
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S15 S32 GLN HIS 0.096876
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S15 S32 THR TYR 0.00220774
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S15 S32 VAL TYR 0.00220774
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S15 S32 TRP TYR 0.00220774
S15 S32 TYR PHE 0.00088616

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S15 S33 ASP CYS 0.00713196
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S15 S33 HIS VAL 0.00407757
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S15 S39 ALA LEU 0.00145767

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S15 S39 CYS ILE 0.00150732
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S15 S39 ASP ALA 0.00371734
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S15 S39 ASP VAL -0.544129
S15 S39 ASP TRP 0.0320252
S15 S39 ASP TYR 0.00371734
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S15 S39 GLU ALA 0.00103677
S15 S39 GLU CYS 0.00103677
S15 S39 GLU ASP 0.00103677
S15 S39 GLU GLU 0.00103677
S15 S39 GLU PHE 0.00103677
S15 S39 GLU GLY 0.00103677
S15 S39 GLU HIS 0.00103677
S15 S39 GLU ILE 0.0546977
S15 S39 GLU LYS 0.00103677
S15 S39 GLU LEU 0.0337954
S15 S39 GLU MET 0.00103677
S15 S39 GLU ASN 0.00103677
S15 S39 GLU PRO 0.00103677
S15 S39 GLU GLN 0.00103677
S15 S39 GLU ARG 0.00103677
S15 S39 GLU SER 0.00103677
S15 S39 GLU THR 0.00103677
S15 S39 GLU VAL -0.1545
S15 S39 GLU TRP 0.0107866
S15 S39 GLU TYR 0.00103677
S15 S39 GLU --- 0.00103677
S15 S39 PHE ILE 0.00150732
S15 S39 PHE LEU 0.00145767
S15 S39 PHE VAL 0.026064
S15 S39 PHE TRP 1.01086e-05
S15 S39 GLY ILE 0.00150732
S15 S39 GLY LEU 0.00145767
S15 S39 GLY VAL 0.026064
S15 S39 GLY TRP 1.01086e-05
S15 S39 HIS ILE 0.00150732
S15 S39 HIS LEU 0.00145767
S15 S39 HIS VAL 0.026064
S15 S39 HIS TRP 1.01086e-05
S15 S39 ILE ILE 0.00150732
S15 S39 ILE LEU 0.00145767
S15 S39 ILE VAL 0.026064

S15 S39 ILE TRP 1.01086e-05
S15 S39 LYS ILE 0.00150732
S15 S39 LYS LEU 0.00145767
S15 S39 LYS VAL 0.026064
S15 S39 LYS TRP 1.01086e-05
S15 S39 LEU ALA 0.00140979
S15 S39 LEU CYS 0.00140979
S15 S39 LEU ASP 0.00140979
S15 S39 LEU GLU 0.00140979
S15 S39 LEU PHE 0.00140979
S15 S39 LEU GLY 0.00140979
S15 S39 LEU HIS 0.00140979
S15 S39 LEU ILE 0.190869
S15 S39 LEU LYS 0.00140979
S15 S39 LEU LEU 0.0374761
S15 S39 LEU MET 0.00140979
S15 S39 LEU ASN 0.00140979
S15 S39 LEU PRO 0.00140979
S15 S39 LEU GLN 0.00140979
S15 S39 LEU ARG 0.00140979
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S15 S39 LEU THR 0.00140979
S15 S39 LEU VAL -0.322179
S15 S39 LEU TRP 0.0083421
S15 S39 LEU TYR 0.00140979
S15 S39 LEU --- 0.00140979
S15 S39 MET ILE 0.00150732
S15 S39 MET LEU 0.00145767
S15 S39 MET VAL 0.026064
S15 S39 MET TRP 1.01086e-05
S15 S39 ASN ILE 0.00150732
S15 S39 ASN LEU 0.00145767
S15 S39 ASN VAL 0.026064
S15 S39 ASN TRP 1.01086e-05
S15 S39 PRO ILE 0.00150732
S15 S39 PRO LEU 0.00145767
S15 S39 PRO VAL 0.026064
S15 S39 PRO TRP 1.01086e-05
S15 S39 GLN ALA 0.000186649
S15 S39 GLN CYS 0.000186649
S15 S39 GLN ASP 0.000186649
S15 S39 GLN GLU 0.000186649
S15 S39 GLN PHE 0.000186649
S15 S39 GLN GLY 0.000186649
S15 S39 GLN HIS 0.000186649
S15 S39 GLN ILE 0.0337663
S15 S39 GLN LYS 0.000186649
S15 S39 GLN LEU 0.0399336
S15 S39 GLN MET 0.000186649
S15 S39 GLN ASN 0.000186649
S15 S39 GLN PRO 0.000186649
S15 S39 GLN GLN 0.000186649
S15 S39 GLN ARG 0.000186649
S15 S39 GLN SER 0.000186649
S15 S39 GLN THR 0.000186649
S15 S39 GLN VAL -0.12625
S15 S39 GLN TRP 0.00193613
S15 S39 GLN TYR 0.000186649
S15 S39 GLN --- 0.000186649
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S15 S39 ARG LEU 0.00145767
S15 S39 ARG VAL 0.026064
S15 S39 ARG TRP 1.01086e-05

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S15 S39 SER GLU 0.0123877
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S15 S39 SER GLY 0.0123877
S15 S39 SER HIS 0.0123877
S15 S39 SER ILE -0.493226
S15 S39 SER LYS 0.0123877
S15 S39 SER LEU -0.271151
S15 S39 SER MET 0.0123877
S15 S39 SER ASN 0.0123877
S15 S39 SER PRO 0.0123877
S15 S39 SER GLN 0.0123877
S15 S39 SER ARG 0.0123877
S15 S39 SER SER 0.0123877
S15 S39 SER THR 0.0123877
S15 S39 SER VAL 0.560956
S15 S39 SER TRP -0.0918568
S15 S39 SER TYR 0.0123877
S15 S39 SER --- 0.0123877
S15 S39 THR ILE 0.00150732
S15 S39 THR LEU 0.00145767
S15 S39 THR VAL 0.026064
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S15 S39 VAL ILE 0.00150732
S15 S39 VAL LEU 0.00145767
S15 S39 VAL VAL 0.026064
S15 S39 VAL TRP 1.01086e-05
S15 S39 TRP ILE 0.00150732
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S15 S39 TRP VAL 0.026064
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S15 S40 ALA ILE 0.00296102
S15 S40 ALA LEU 4.34414e-05
S15 S40 ALA VAL 0.0260346
S15 S40 CYS ILE 0.00296102
S15 S40 CYS LEU 4.34414e-05
S15 S40 CYS VAL 0.0260346
S15 S40 ASP ALA 0.00767256
S15 S40 ASP CYS 0.00767256
S15 S40 ASP ASP 0.00767256
S15 S40 ASP GLU 0.00767256
S15 S40 ASP PHE 0.00767256
S15 S40 ASP GLY 0.00767256
S15 S40 ASP HIS 0.00767256
S15 S40 ASP ILE -0.34275
S15 S40 ASP LYS 0.00767256
S15 S40 ASP LEU -0.128164
S15 S40 ASP MET 0.00767256
S15 S40 ASP ASN 0.00767256
S15 S40 ASP PRO 0.00767256
S15 S40 ASP GLN 0.00767256
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S15 S40 ASP SER 0.00767256

S15 S40 ASP THR 0.00767256
S15 S40 ASP VAL 0.0994309
S15 S40 ASP TRP 0.00767256
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S15 S40 ASP --- 0.00767256
S15 S40 GLU ALA 0.00177612
S15 S40 GLU CYS 0.00177612
S15 S40 GLU ASP 0.00177612
S15 S40 GLU GLU 0.00177612
S15 S40 GLU PHE 0.00177612
S15 S40 GLU GLY 0.00177612
S15 S40 GLU HIS 0.00177612
S15 S40 GLU ILE -0.2674
S15 S40 GLU LYS 0.00177612
S15 S40 GLU LEU 0.00579452
S15 S40 GLU MET 0.00177612
S15 S40 GLU ASN 0.00177612
S15 S40 GLU PRO 0.00177612
S15 S40 GLU GLN 0.00177612
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S15 S40 GLU VAL 0.192041
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S15 S40 GLU --- 0.00177612
S15 S40 PHE ILE 0.00296102
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S15 S40 HIS VAL 0.0260346
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S15 S40 LEU THR 0.000730541
S15 S40 LEU VAL -0.13639
S15 S40 LEU TRP 0.000730541
S15 S40 LEU TYR 0.000730541
S15 S40 LEU --- 0.000730541
S15 S40 MET ILE 0.00296102

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S15 S40 MET VAL 0.0260346
S15 S40 ASN ILE 0.00296102
S15 S40 ASN LEU 4.34414e-05
S15 S40 ASN VAL 0.0260346
S15 S40 PRO ILE 0.00296102
S15 S40 PRO LEU 4.34414e-05
S15 S40 PRO VAL 0.0260346
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S15 S40 GLN CYS 0.000334828
S15 S40 GLN ASP 0.000334828
S15 S40 GLN GLU 0.000334828
S15 S40 GLN PHE 0.000334828
S15 S40 GLN GLY 0.000334828
S15 S40 GLN HIS 0.000334828
S15 S40 GLN ILE 0.141464
S15 S40 GLN LYS 0.000334828
S15 S40 GLN LEU 0.00257153
S15 S40 GLN MET 0.000334828
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S15 S40 GLN VAL -0.197504
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S15 S40 GLN TYR 0.000334828
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S15 S40 SER CYS 0.00589505
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S15 S40 SER PHE 0.00589505
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S15 S40 SER LYS 0.00589505
S15 S40 SER LEU 0.0594117
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S15 S40 SER GLN 0.00589505
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S15 S40 SER SER 0.00589505
S15 S40 SER THR 0.00589505
S15 S40 SER VAL -0.542455
S15 S40 SER TRP 0.00589505
S15 S40 SER TYR 0.00589505
S15 S40 SER --- 0.00589505
S15 S40 THR ILE 0.00296102
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S15 S40 VAL LEU 4.34414e-05
S15 S40 VAL VAL 0.0260346
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S15 S40 TRP LEU 4.34414e-05
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S15 S40 TYR ILE 0.00296102

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S15 S40 TYR VAL 0.0260346
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S16 S17 ALA GLY 0.000292269
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S16 S17 CYS HIS 0.0106823
S16 S17 CYS ILE 0.00200922
S16 S17 CYS TRP 0.000651505
S16 S17 CYS TYR 0.00387592
S16 S17 ASP PHE 0.00714001
S16 S17 ASP HIS 0.0106823
S16 S17 ASP ILE 0.00200922
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S16 S17 ASP TYR 0.00387592
S16 S17 GLU PHE 0.00714001
S16 S17 GLU HIS 0.0106823
S16 S17 GLU ILE 0.00200922
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S16 S17 GLU TYR 0.00387592
S16 S17 PHE PHE 0.00714001
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S16 S17 PHE ILE 0.00200922
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S16 S17 GLY PHE 0.00714001
S16 S17 GLY HIS 0.0106823
S16 S17 GLY ILE 0.00200922
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S16 S17 GLY TYR 0.00387592
S16 S17 HIS PHE 0.00714001
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S16 S17 ILE ASP 0.0140222
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S16 S17 MET ILE 0.00200922
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S16 S17 MET TYR 0.00387592
S16 S17 ASN PHE 0.00714001
S16 S17 ASN HIS 0.0106823
S16 S17 ASN ILE 0.00200922
S16 S17 ASN TRP 0.000651505
S16 S17 ASN TYR 0.00387592
S16 S17 PRO PHE 0.00714001
S16 S17 PRO HIS 0.0106823
S16 S17 PRO ILE 0.00200922
S16 S17 PRO TRP 0.000651505
S16 S17 PRO TYR 0.00387592
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S16 S17 GLN HIS 0.0106823
S16 S17 GLN ILE 0.00200922
S16 S17 GLN TRP 0.000651505
S16 S17 GLN TYR 0.00387592
S16 S17 ARG PHE 0.00714001
S16 S17 ARG HIS 0.0106823
S16 S17 ARG ILE 0.00200922

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S16 S17 THR PRO 0.000647921
S16 S17 THR GLN 0.000647921
S16 S17 THR ARG 0.000647921
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S16 S17 THR TYR 0.10339
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S16 S17 VAL ALA 0.00960672
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S16 S17 VAL ASP 0.00960672
S16 S17 VAL GLU 0.00960672
S16 S17 VAL PHE 0.0207306
S16 S17 VAL GLY 0.00960672
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S16 S17 VAL ILE 0.260023
S16 S17 VAL LYS 0.00960672
S16 S17 VAL LEU 0.00960672
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S16 S17 TRP ILE 0.00200922
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S16 S18 ALA ASN 0.000646727
S16 S18 ALA PRO 0.000646727
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S16 S18 ALA SER 0.000646727
S16 S18 ALA THR 0.000646727
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S16 S18 CYS GLU 0.0237445
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S16 S18 ASP GLU 0.0237445
S16 S18 ASP HIS 0.00061441
S16 S18 GLU GLU 0.0237445
S16 S18 GLU HIS 0.00061441
S16 S18 PHE GLU 0.0237445
S16 S18 PHE HIS 0.00061441
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S16 S18 ILE ALA 0.00541978
S16 S18 ILE CYS 0.00541978
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S16 S18 ILE GLY 0.00541978
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S16 S18 ILE LYS 0.00541978
S16 S18 ILE LEU 0.00541978
S16 S18 ILE MET 0.00541978
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S16 S18 ILE PRO 0.00541978
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S16 S18 ILE ARG 0.00541978
S16 S18 ILE SER 0.00541978
S16 S18 ILE THR 0.00541978
S16 S18 ILE VAL 0.00541978
S16 S18 ILE TRP 0.00541978
S16 S18 ILE TYR 0.00541978
S16 S18 ILE --- 0.00541978
S16 S18 LYS GLU 0.0237445
S16 S18 LYS HIS 0.00061441
S16 S18 LEU ALA 3.96923e-05
S16 S18 LEU CYS 3.96923e-05
S16 S18 LEU ASP 3.96923e-05
S16 S18 LEU GLU -0.0379384
S16 S18 LEU PHE 3.96923e-05
S16 S18 LEU GLY 3.96923e-05

S16 S18 LEU HIS 0.00776707
S16 S18 LEU ILE 3.96923e-05
S16 S18 LEU LYS 3.96923e-05
S16 S18 LEU LEU 3.96923e-05
S16 S18 LEU MET 3.96923e-05
S16 S18 LEU ASN 3.96923e-05
S16 S18 LEU PRO 3.96923e-05
S16 S18 LEU GLN 3.96923e-05
S16 S18 LEU ARG 3.96923e-05
S16 S18 LEU SER 3.96923e-05
S16 S18 LEU THR 3.96923e-05
S16 S18 LEU VAL 3.96923e-05
S16 S18 LEU TRP 3.96923e-05
S16 S18 LEU TYR 3.96923e-05
S16 S18 LEU --- 3.96923e-05
S16 S18 MET GLU 0.0237445
S16 S18 MET HIS 0.00061441
S16 S18 ASN GLU 0.0237445
S16 S18 ASN HIS 0.00061441
S16 S18 PRO GLU 0.0237445
S16 S18 PRO HIS 0.00061441
S16 S18 GLN GLU 0.0237445
S16 S18 GLN HIS 0.00061441
S16 S18 ARG GLU 0.0237445
S16 S18 ARG HIS 0.00061441
S16 S18 SER GLU 0.0237445
S16 S18 SER HIS 0.00061441
S16 S18 THR ALA 0.000180612
S16 S18 THR CYS 0.000180612
S16 S18 THR ASP 0.000180612
S16 S18 THR GLU -0.0483921
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S16 S18 THR GLY 0.000180612
S16 S18 THR HIS 0.00834322
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S16 S18 THR LYS 0.000180612
S16 S18 THR LEU 0.000180612
S16 S18 THR MET 0.000180612
S16 S18 THR ASN 0.000180612
S16 S18 THR PRO 0.000180612
S16 S18 THR GLN 0.000180612
S16 S18 THR ARG 0.000180612
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S16 S18 THR THR 0.000180612
S16 S18 THR VAL 0.000180612
S16 S18 THR TRP 0.000180612
S16 S18 THR TYR 0.000180612
S16 S18 THR --- 0.000180612
S16 S18 VAL ALA 0.00655342
S16 S18 VAL CYS 0.00655342
S16 S18 VAL ASP 0.00655342
S16 S18 VAL GLU -0.179002
S16 S18 VAL PHE 0.00655342
S16 S18 VAL GLY 0.00655342
S16 S18 VAL HIS -0.0696797
S16 S18 VAL ILE 0.00655342
S16 S18 VAL LYS 0.00655342
S16 S18 VAL LEU 0.00655342
S16 S18 VAL MET 0.00655342
S16 S18 VAL ASN 0.00655342
S16 S18 VAL PRO 0.00655342
S16 S18 VAL GLN 0.00655342
S16 S18 VAL ARG 0.00655342

S16 S18 VAL SER 0.00655342
S16 S18 VAL THR 0.00655342
S16 S18 VAL VAL 0.00655342
S16 S18 VAL TRP 0.00655342
S16 S18 VAL TYR 0.00655342
S16 S18 VAL --- 0.00655342
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S16 S18 TRP HIS 0.00061441
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S16 S18 TYR HIS 0.00061441
S16 S18 --- GLU 0.0237445
S16 S18 --- HIS 0.00061441
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S16 S19 ALA ASP 9.39832e-05
S16 S19 ALA GLU 9.39832e-05
S16 S19 ALA PHE 9.39832e-05
S16 S19 ALA GLY 9.39832e-05
S16 S19 ALA HIS 9.39832e-05
S16 S19 ALA ILE 9.39832e-05
S16 S19 ALA LYS 9.39832e-05
S16 S19 ALA LEU 9.39832e-05
S16 S19 ALA MET 9.39832e-05
S16 S19 ALA ASN 9.39832e-05
S16 S19 ALA PRO 9.39832e-05
S16 S19 ALA GLN 9.39832e-05
S16 S19 ALA ARG 9.39832e-05
S16 S19 ALA SER 0.0826653
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S16 S19 ALA VAL 9.39832e-05
S16 S19 ALA TRP 9.39832e-05
S16 S19 ALA TYR 0.00448575
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S16 S19 ASP TYR 0.000427186
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S16 S19 GLU SER 0.00728655
S16 S19 GLU TYR 0.000427186
S16 S19 PHE ALA 0.0166452
S16 S19 PHE SER 0.00728655
S16 S19 PHE TYR 0.000427186
S16 S19 GLY ALA 0.0166452
S16 S19 GLY SER 0.00728655
S16 S19 GLY TYR 0.000427186
S16 S19 HIS ALA 0.0166452
S16 S19 HIS SER 0.00728655
S16 S19 HIS TYR 0.000427186
S16 S19 ILE ALA 0.242162
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S16 S19 ILE ASP 0.0112251
S16 S19 ILE GLU 0.0112251
S16 S19 ILE PHE 0.0112251
S16 S19 ILE GLY 0.0112251
S16 S19 ILE HIS 0.0112251
S16 S19 ILE ILE 0.0112251
S16 S19 ILE LYS 0.0112251
S16 S19 ILE LEU 0.0112251
S16 S19 ILE MET 0.0112251
S16 S19 ILE ASN 0.0112251

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S16 S19 ILE TYR -0.132398
S16 S19 ILE --- 0.0112251
S16 S19 LYS ALA 0.0166452
S16 S19 LYS SER 0.00728655
S16 S19 LYS TYR 0.000427186
S16 S19 LEU ALA -0.125146
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S16 S19 LEU ASP 5.91361e-05
S16 S19 LEU GLU 5.91361e-05
S16 S19 LEU PHE 5.91361e-05
S16 S19 LEU GLY 5.91361e-05
S16 S19 LEU HIS 5.91361e-05
S16 S19 LEU ILE 5.91361e-05
S16 S19 LEU LYS 5.91361e-05
S16 S19 LEU LEU 5.91361e-05
S16 S19 LEU MET 5.91361e-05
S16 S19 LEU ASN 5.91361e-05
S16 S19 LEU PRO 5.91361e-05
S16 S19 LEU GLN 5.91361e-05
S16 S19 LEU ARG 5.91361e-05
S16 S19 LEU SER 0.0904305
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S16 S19 LEU VAL 5.91361e-05
S16 S19 LEU TRP 5.91361e-05
S16 S19 LEU TYR 0.00423389
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S16 S19 MET TYR 0.000427186
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S16 S19 ASN TYR 0.000427186
S16 S19 PRO ALA 0.0166452
S16 S19 PRO SER 0.00728655
S16 S19 PRO TYR 0.000427186
S16 S19 GLN ALA 0.0166452
S16 S19 GLN SER 0.00728655
S16 S19 GLN TYR 0.000427186
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S16 S19 ARG SER 0.00728655
S16 S19 ARG TYR 0.000427186
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S16 S19 SER TYR 0.000427186
S16 S19 THR ALA 0.423337
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S16 S19 THR ASP 0.000568935
S16 S19 THR GLU 0.000568935
S16 S19 THR PHE 0.000568935
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S16 S19 THR ILE 0.000568935
S16 S19 THR LYS 0.000568935
S16 S19 THR LEU 0.000568935
S16 S19 THR MET 0.000568935
S16 S19 THR ASN 0.000568935

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S16 S19 THR GLN 0.000568935
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S16 S19 THR THR 0.000568935
S16 S19 THR VAL 0.000568935
S16 S19 THR TRP 0.000568935
S16 S19 THR TYR 0.0036962
S16 S19 THR --- 0.000568935
S16 S19 VAL ALA -0.828187
S16 S19 VAL CYS 0.00674629
S16 S19 VAL ASP 0.00674629
S16 S19 VAL GLU 0.00674629
S16 S19 VAL PHE 0.00674629
S16 S19 VAL GLY 0.00674629
S16 S19 VAL HIS 0.00674629
S16 S19 VAL ILE 0.00674629
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S16 S19 VAL LEU 0.00674629
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S16 S19 VAL THR 0.00674629
S16 S19 VAL VAL 0.00674629
S16 S19 VAL TRP 0.00674629
S16 S19 VAL TYR 0.0521672
S16 S19 VAL --- 0.00674629
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S16 S19 TRP SER 0.00728655
S16 S19 TRP TYR 0.000427186
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S16 S19 TYR SER 0.00728655
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S16 S19 --- TYR 0.000427186
S16 S20 ALA ALA 0.0003547
S16 S20 ALA CYS 0.0003547
S16 S20 ALA ASP 0.0003547
S16 S20 ALA GLU 0.0003547
S16 S20 ALA PHE 0.106728
S16 S20 ALA GLY 0.0003547
S16 S20 ALA HIS 0.0003547
S16 S20 ALA ILE 0.0003547
S16 S20 ALA LYS 0.0003547
S16 S20 ALA LEU 0.0575663
S16 S20 ALA MET -0.250223
S16 S20 ALA ASN 0.0003547
S16 S20 ALA PRO 0.0003547
S16 S20 ALA GLN 0.0003547
S16 S20 ALA ARG 0.0003547
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S16 S20 ALA VAL 0.0141241
S16 S20 ALA TRP 0.0003547
S16 S20 ALA TYR 0.0003547
S16 S20 ALA --- 0.0003547
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S16 S20 CYS LEU 0.00360594
S16 S20 CYS MET 0.00724829

S16 S20 CYS VAL 0.000460061
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S16 S20 ASP LEU 0.00360594
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S16 S20 GLU PHE 0.0130446
S16 S20 GLU LEU 0.00360594
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S16 S20 GLU VAL 0.000460061
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S16 S20 PHE LEU 0.00360594
S16 S20 PHE MET 0.00724829
S16 S20 PHE VAL 0.000460061
S16 S20 GLY PHE 0.0130446
S16 S20 GLY LEU 0.00360594
S16 S20 GLY MET 0.00724829
S16 S20 GLY VAL 0.000460061
S16 S20 HIS PHE 0.0130446
S16 S20 HIS LEU 0.00360594
S16 S20 HIS MET 0.00724829
S16 S20 HIS VAL 0.000460061
S16 S20 ILE ALA 0.0127908
S16 S20 ILE CYS 0.0127908
S16 S20 ILE ASP 0.0127908
S16 S20 ILE GLU 0.0127908
S16 S20 ILE PHE -0.483064
S16 S20 ILE GLY 0.0127908
S16 S20 ILE HIS 0.0127908
S16 S20 ILE ILE 0.0127908
S16 S20 ILE LYS 0.0127908
S16 S20 ILE LEU 0.781163
S16 S20 ILE MET -0.752347
S16 S20 ILE ASN 0.0127908
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S16 S20 ILE GLN 0.0127908
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S16 S20 ILE VAL 0.103039
S16 S20 ILE TRP 0.0127908
S16 S20 ILE TYR 0.0127908
S16 S20 ILE --- 0.0127908
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S16 S20 LYS LEU 0.00360594
S16 S20 LYS MET 0.00724829
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S16 S20 LEU ALA 3.49324e-05
S16 S20 LEU CYS 3.49324e-05
S16 S20 LEU ASP 3.49324e-05
S16 S20 LEU GLU 3.49324e-05
S16 S20 LEU PHE -0.125301
S16 S20 LEU GLY 3.49324e-05
S16 S20 LEU HIS 3.49324e-05
S16 S20 LEU ILE 3.49324e-05
S16 S20 LEU LYS 3.49324e-05
S16 S20 LEU LEU 0.0297246
S16 S20 LEU MET 0.0615187
S16 S20 LEU ASN 3.49324e-05
S16 S20 LEU PRO 3.49324e-05
S16 S20 LEU GLN 3.49324e-05
S16 S20 LEU ARG 3.49324e-05
S16 S20 LEU SER 3.49324e-05
S16 S20 LEU THR 3.49324e-05

S16 S20 LEU VAL 0.00404689
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S16 S20 LEU TYR 3.49324e-05
S16 S20 LEU --- 3.49324e-05
S16 S20 MET PHE 0.0130446
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S16 S20 MET MET 0.00724829
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S16 S20 ASN LEU 0.00360594
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S16 S20 PRO LEU 0.00360594
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S16 S20 GLN LEU 0.00360594
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S16 S20 GLN VAL 0.000460061
S16 S20 ARG PHE 0.0130446
S16 S20 ARG LEU 0.00360594
S16 S20 ARG MET 0.00724829
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S16 S20 SER MET 0.00724829
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S16 S20 THR GLY 0.00106876
S16 S20 THR HIS 0.00106876
S16 S20 THR ILE 0.00106876
S16 S20 THR LYS 0.00106876
S16 S20 THR LEU 0.0725124
S16 S20 THR MET -0.406404
S16 S20 THR ASN 0.00106876
S16 S20 THR PRO 0.00106876
S16 S20 THR GLN 0.00106876
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S16 S20 THR TRP 0.00106876
S16 S20 THR TYR 0.00106876
S16 S20 THR --- 0.00106876
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S16 S20 VAL CYS 0.0100006
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S16 S20 VAL GLY 0.0100006
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S16 S20 VAL --- 0.0100006
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S16 S20 TRP LEU 0.00360594
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S16 S20 TYR LEU 0.00360594
S16 S20 TYR MET 0.00724829
S16 S20 TYR VAL 0.000460061
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S16 S21 ALA GLY 0.000586723
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S16 S21 ALA ILE -0.210844
S16 S21 ALA LYS 0.000586723
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S16 S21 ALA GLN 0.000586723
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S16 S21 CYS PHE 0.000677228
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S16 S21 GLU PHE 0.000677228
S16 S21 GLU ILE 0.0194848
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S16 S21 GLU TYR 0.00165257
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S16 S21 PHE ILE 0.0194848
S16 S21 PHE VAL 0.0025443
S16 S21 PHE TYR 0.00165257
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S16 S21 GLY VAL 0.0025443
S16 S21 GLY TYR 0.00165257
S16 S21 HIS PHE 0.000677228
S16 S21 HIS ILE 0.0194848
S16 S21 HIS VAL 0.0025443

S16 S21 HIS TYR 0.00165257
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S16 S21 ILE MET 0.0135606
S16 S21 ILE ASN 0.0135606
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S16 S21 ILE GLN 0.0135606
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S16 S21 ILE TYR 0.291121
S16 S21 ILE --- 0.0135606
S16 S21 LYS PHE 0.000677228
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S16 S21 LYS VAL 0.0025443
S16 S21 LYS TYR 0.00165257
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S16 S21 LEU CYS 0.000310309
S16 S21 LEU ASP 0.000310309
S16 S21 LEU GLU 0.000310309
S16 S21 LEU PHE 0.0081991
S16 S21 LEU GLY 0.000310309
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S16 S21 LEU LYS 0.000310309
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S16 S21 LEU MET 0.000310309
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S16 S21 LEU TYR 0.0628966
S16 S21 LEU --- 0.000310309
S16 S21 MET PHE 0.000677228
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S16 S21 ASN PHE 0.000677228
S16 S21 ASN ILE 0.0194848
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S16 S21 ASN TYR 0.00165257
S16 S21 PRO PHE 0.000677228
S16 S21 PRO ILE 0.0194848
S16 S21 PRO VAL 0.0025443
S16 S21 PRO TYR 0.00165257
S16 S21 GLN PHE 0.000677228
S16 S21 GLN ILE 0.0194848
S16 S21 GLN VAL 0.0025443
S16 S21 GLN TYR 0.00165257

S16 S21 ARG PHE 0.000677228
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S16 S21 SER PHE 0.000677228
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S16 S21 THR ALA 0.000410499
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S16 S21 THR ASN 0.000410499
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S16 S21 THR --- 0.000410499
S16 S21 VAL ALA 0.00825775
S16 S21 VAL CYS 0.00825775
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S16 S21 VAL GLY 0.00825775
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S16 S21 VAL ILE 0.27132
S16 S21 VAL LYS 0.00825775
S16 S21 VAL LEU 0.00825775
S16 S21 VAL MET 0.00825775
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S16 S21 VAL PRO 0.00825775
S16 S21 VAL GLN 0.00825775
S16 S21 VAL ARG 0.00825775
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S16 S21 VAL THR 0.00825775
S16 S21 VAL VAL -0.0713185
S16 S21 VAL TRP 0.00825775
S16 S21 VAL TYR -0.591153
S16 S21 VAL --- 0.00825775
S16 S21 TRP PHE 0.000677228
S16 S21 TRP ILE 0.0194848
S16 S21 TRP VAL 0.0025443
S16 S21 TRP TYR 0.00165257
S16 S21 TYR PHE 0.000677228
S16 S21 TYR ILE 0.0194848
S16 S21 TYR VAL 0.0025443
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S16 S21 --- PHE 0.000677228
S16 S21 --- ILE 0.0194848
S16 S21 --- VAL 0.0025443
S16 S21 --- TYR 0.00165257
S16 S22 ALA ALA 5.43345e-05

S16 S22 ALA CYS 5.43345e-05
S16 S22 ALA ASP 0.025058
S16 S22 ALA GLU 0.00577728
S16 S22 ALA PHE 5.43345e-05
S16 S22 ALA GLY 5.43345e-05
S16 S22 ALA HIS 5.43345e-05
S16 S22 ALA ILE 5.43345e-05
S16 S22 ALA LYS 5.43345e-05
S16 S22 ALA LEU 5.43345e-05
S16 S22 ALA MET 5.43345e-05
S16 S22 ALA ASN -0.099428
S16 S22 ALA PRO 5.43345e-05
S16 S22 ALA GLN 5.43345e-05
S16 S22 ALA ARG 5.43345e-05
S16 S22 ALA SER 5.43345e-05
S16 S22 ALA THR 5.43345e-05
S16 S22 ALA VAL 5.43345e-05
S16 S22 ALA TRP 5.43345e-05
S16 S22 ALA TYR 0.00189423
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S16 S22 CYS ASP 0.00215305
S16 S22 CYS GLU 0.00131175
S16 S22 CYS ASN 0.020648
S16 S22 CYS TYR 0.000246115
S16 S22 ASP ASP 0.00215305
S16 S22 ASP GLU 0.00131175
S16 S22 ASP ASN 0.020648
S16 S22 ASP TYR 0.000246115
S16 S22 GLU ASP 0.00215305
S16 S22 GLU GLU 0.00131175
S16 S22 GLU ASN 0.020648
S16 S22 GLU TYR 0.000246115
S16 S22 PHE ASP 0.00215305
S16 S22 PHE GLU 0.00131175
S16 S22 PHE ASN 0.020648
S16 S22 PHE TYR 0.000246115
S16 S22 GLY ASP 0.00215305
S16 S22 GLY GLU 0.00131175
S16 S22 GLY ASN 0.020648
S16 S22 GLY TYR 0.000246115
S16 S22 HIS ASP 0.00215305
S16 S22 HIS GLU 0.00131175
S16 S22 HIS ASN 0.020648
S16 S22 HIS TYR 0.000246115
S16 S22 ILE ALA 0.0120758
S16 S22 ILE CYS 0.0120758
S16 S22 ILE ASP -0.492079
S16 S22 ILE GLU 0.320773
S16 S22 ILE PHE 0.0120758
S16 S22 ILE GLY 0.0120758
S16 S22 ILE HIS 0.0120758
S16 S22 ILE ILE 0.0120758
S16 S22 ILE LYS 0.0120758
S16 S22 ILE LEU 0.0120758
S16 S22 ILE MET 0.0120758
S16 S22 ILE ASN -0.00544335
S16 S22 ILE PRO 0.0120758
S16 S22 ILE GLN 0.0120758
S16 S22 ILE ARG 0.0120758
S16 S22 ILE SER 0.0120758
S16 S22 ILE THR 0.0120758
S16 S22 ILE VAL 0.0120758
S16 S22 ILE TRP 0.0120758

S16 S22 ILE TYR -0.162306
S16 S22 ILE --- 0.0120758
S16 S22 LYS ASP 0.00215305
S16 S22 LYS GLU 0.00131175
S16 S22 LYS ASN 0.020648
S16 S22 LYS TYR 0.000246115
S16 S22 LEU ALA 7.84583e-06
S16 S22 LEU CYS 7.84583e-06
S16 S22 LEU ASP 0.0113017
S16 S22 LEU GLU 0.00485104
S16 S22 LEU PHE 7.84583e-06
S16 S22 LEU GLY 7.84583e-06
S16 S22 LEU HIS 7.84583e-06
S16 S22 LEU ILE 7.84583e-06
S16 S22 LEU LYS 7.84583e-06
S16 S22 LEU LEU 7.84583e-06
S16 S22 LEU MET 7.84583e-06
S16 S22 LEU ASN -0.047249
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S16 S22 LEU GLN 7.84583e-06
S16 S22 LEU ARG 7.84583e-06
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S16 S22 LEU THR 7.84583e-06
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S16 S22 LEU TYR 0.00154562
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S16 S22 MET TYR 0.000246115
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S16 S22 ASN GLU 0.00131175
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S16 S22 ASN TYR 0.000246115
S16 S22 PRO ASP 0.00215305
S16 S22 PRO GLU 0.00131175
S16 S22 PRO ASN 0.020648
S16 S22 PRO TYR 0.000246115
S16 S22 GLN ASP 0.00215305
S16 S22 GLN GLU 0.00131175
S16 S22 GLN ASN 0.020648
S16 S22 GLN TYR 0.000246115
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S16 S22 ARG TYR 0.000246115
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S16 S22 THR GLU 0.0410255
S16 S22 THR PHE 0.000203508
S16 S22 THR GLY 0.000203508
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S16 S22 THR ILE 0.000203508
S16 S22 THR LYS 0.000203508
S16 S22 THR LEU 0.000203508
S16 S22 THR MET 0.000203508
S16 S22 THR ASN -0.108582

S16 S22 THR PRO 0.000203508
S16 S22 THR GLN 0.000203508
S16 S22 THR ARG 0.000203508
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S16 S22 THR THR 0.000203508
S16 S22 THR VAL 0.000203508
S16 S22 THR TRP 0.000203508
S16 S22 THR TYR 0.00604368
S16 S22 THR --- 0.000203508
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S16 S22 VAL CYS 0.00919248
S16 S22 VAL ASP 0.329663
S16 S22 VAL GLU -0.417996
S16 S22 VAL PHE 0.00919248
S16 S22 VAL GLY 0.00919248
S16 S22 VAL HIS 0.00919248
S16 S22 VAL ILE 0.00919248
S16 S22 VAL LYS 0.00919248
S16 S22 VAL LEU 0.00919248
S16 S22 VAL MET 0.00919248
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S16 S22 VAL SER 0.00919248
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S16 S22 VAL TRP 0.00919248
S16 S22 VAL TYR 0.0961621
S16 S22 VAL --- 0.00919248
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S16 S22 TRP GLU 0.00131175
S16 S22 TRP ASN 0.020648
S16 S22 TRP TYR 0.000246115
S16 S22 TYR ASP 0.00215305
S16 S22 TYR GLU 0.00131175
S16 S22 TYR ASN 0.020648
S16 S22 TYR TYR 0.000246115
S16 S22 --- ASP 0.00215305
S16 S22 --- GLU 0.00131175
S16 S22 --- ASN 0.020648
S16 S22 --- TYR 0.000246115
S16 S23 ALA ALA 0.000216996
S16 S23 ALA CYS 0.000216996
S16 S23 ALA ASP 0.000216996
S16 S23 ALA GLU 0.000216996
S16 S23 ALA PHE 0.000216996
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S16 S23 ALA HIS 0.000216996
S16 S23 ALA ILE -0.23408
S16 S23 ALA LYS 0.000216996
S16 S23 ALA LEU 0.164182
S16 S23 ALA MET 0.000216996
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S16 S23 ALA PRO 0.000216996
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S16 S23 ALA TRP 0.000216996
S16 S23 ALA TYR 0.000216996
S16 S23 ALA --- 0.000216996

S16 S23 CYS ILE 0.0156177
S16 S23 CYS LEU 0.0087412
S16 S23 ASP ILE 0.0156177
S16 S23 ASP LEU 0.0087412
S16 S23 GLU ILE 0.0156177
S16 S23 GLU LEU 0.0087412
S16 S23 PHE ILE 0.0156177
S16 S23 PHE LEU 0.0087412
S16 S23 GLY ILE 0.0156177
S16 S23 GLY LEU 0.0087412
S16 S23 HIS ILE 0.0156177
S16 S23 HIS LEU 0.0087412
S16 S23 ILE ALA 0.00822318
S16 S23 ILE CYS 0.00822318
S16 S23 ILE ASP 0.00822318
S16 S23 ILE GLU 0.00822318
S16 S23 ILE PHE 0.00822318
S16 S23 ILE GLY 0.00822318
S16 S23 ILE HIS 0.00822318
S16 S23 ILE ILE -0.254066
S16 S23 ILE LYS 0.00822318
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S16 S23 ILE TYR 0.00822318
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S16 S23 LYS LEU 0.0087412
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S16 S23 LEU CYS 0.000119733
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S16 S23 LEU GLU 0.000119733
S16 S23 LEU PHE 0.000119733
S16 S23 LEU GLY 0.000119733
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S16 S23 LEU ILE 0.358342
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S16 S23 LEU LEU -0.390034
S16 S23 LEU MET 0.000119733
S16 S23 LEU ASN 0.000119733
S16 S23 LEU PRO 0.000119733
S16 S23 LEU GLN 0.000119733
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S16 S23 MET ILE 0.0156177
S16 S23 MET LEU 0.0087412
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S16 S23 PRO LEU 0.0087412
S16 S23 GLN ILE 0.0156177

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S16 S23 THR ASP 0.00041173
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S16 S23 THR LYS 0.00041173
S16 S23 THR LEU -0.0628843
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S16 S23 THR TYR 0.00041173
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S16 S23 VAL GLU 0.00677068
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S16 S23 VAL GLY 0.00677068
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S16 S23 VAL LYS 0.00677068
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S16 S23 VAL MET 0.00677068
S16 S23 VAL ASN 0.00677068
S16 S23 VAL PRO 0.00677068
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S16 S23 VAL --- 0.00677068
S16 S23 TRP ILE 0.0156177
S16 S23 TRP LEU 0.0087412
S16 S23 TYR ILE 0.0156177
S16 S23 TYR LEU 0.0087412
S16 S23 --- ILE 0.0156177
S16 S23 --- LEU 0.0087412
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S16 S24 ALA THR 0.000114309
S16 S24 ALA VAL 0.000114309
S16 S24 ALA TRP 0.000114309
S16 S24 ALA TYR 0.000114309
S16 S24 ALA --- 0.000114309
S16 S24 CYS GLY 0.0242692
S16 S24 CYS SER 8.97161e-05
S16 S24 ASP GLY 0.0242692
S16 S24 ASP SER 8.97161e-05
S16 S24 GLU GLY 0.0242692
S16 S24 GLU SER 8.97161e-05
S16 S24 PHE GLY 0.0242692
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S16 S24 GLY GLY 0.0242692
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S16 S24 HIS GLY 0.0242692
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S16 S24 ILE ALA 0.00731069
S16 S24 ILE CYS 0.00731069
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S16 S24 ILE GLU 0.00731069
S16 S24 ILE PHE 0.00731069
S16 S24 ILE GLY -0.152508
S16 S24 ILE HIS 0.00731069
S16 S24 ILE ILE 0.00731069
S16 S24 ILE LYS 0.00731069
S16 S24 ILE LEU 0.00731069
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S16 S24 ILE TRP 0.00731069
S16 S24 ILE TYR 0.00731069
S16 S24 ILE --- 0.00731069
S16 S24 LYS GLY 0.0242692
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S16 S24 LEU ALA 2.62678e-05
S16 S24 LEU CYS 2.62678e-05
S16 S24 LEU ASP 2.62678e-05
S16 S24 LEU GLU 2.62678e-05
S16 S24 LEU PHE 2.62678e-05
S16 S24 LEU GLY -0.0309344
S16 S24 LEU HIS 2.62678e-05
S16 S24 LEU ILE 2.62678e-05
S16 S24 LEU LYS 2.62678e-05
S16 S24 LEU LEU 2.62678e-05
S16 S24 LEU MET 2.62678e-05
S16 S24 LEU ASN 2.62678e-05
S16 S24 LEU PRO 2.62678e-05
S16 S24 LEU GLN 2.62678e-05
S16 S24 LEU ARG 2.62678e-05
S16 S24 LEU SER 0.00101811
S16 S24 LEU THR 2.62678e-05

S16 S24 LEU VAL 2.62678e-05
S16 S24 LEU TRP 2.62678e-05
S16 S24 LEU TYR 2.62678e-05
S16 S24 LEU --- 2.62678e-05
S16 S24 MET GLY 0.0242692
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S16 S24 ASN GLY 0.0242692
S16 S24 ASN SER 8.97161e-05
S16 S24 PRO GLY 0.0242692
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S16 S24 GLN GLY 0.0242692
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S16 S24 ARG GLY 0.0242692
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S16 S24 THR GLU 0.000335033
S16 S24 THR PHE 0.000335033
S16 S24 THR GLY -0.0475581
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S16 S24 THR ILE 0.000335033
S16 S24 THR LYS 0.000335033
S16 S24 THR LEU 0.000335033
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S16 S24 VAL ALA 0.00383189
S16 S24 VAL CYS 0.00383189
S16 S24 VAL ASP 0.00383189
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S16 S24 VAL PHE 0.00383189
S16 S24 VAL GLY -0.22319
S16 S24 VAL HIS 0.00383189
S16 S24 VAL ILE 0.00383189
S16 S24 VAL LYS 0.00383189
S16 S24 VAL LEU 0.00383189
S16 S24 VAL MET 0.00383189
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S16 S24 VAL TRP 0.00383189
S16 S24 VAL TYR 0.00383189
S16 S24 VAL --- 0.00383189
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S16 S24 TYR GLY 0.0242692
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S16 S24 --- GLY 0.0242692

S16 S24 --- SER 8.97161e-05
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S16 S25 ALA GLU 0.0104732
S16 S25 ALA PHE 0.000142497
S16 S25 ALA GLY 0.000142497
S16 S25 ALA HIS 0.000142497
S16 S25 ALA ILE 0.000142497
S16 S25 ALA LYS 0.0135403
S16 S25 ALA LEU 0.000142497
S16 S25 ALA MET 0.000142497
S16 S25 ALA ASN 0.000142497
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S16 S25 ALA ARG 0.00865602
S16 S25 ALA SER -0.10234
S16 S25 ALA THR 0.00139256
S16 S25 ALA VAL 0.000142497
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S16 S25 ALA TYR 0.000142497
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S16 S25 CYS LYS 0.000572043
S16 S25 CYS ARG 0.00128052
S16 S25 CYS SER 0.0223818
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S16 S25 ASP ARG 0.00128052
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S16 S25 GLU ARG 0.00128052
S16 S25 GLU SER 0.0223818
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S16 S25 PHE GLU 7.38973e-05
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S16 S25 PHE ARG 0.00128052
S16 S25 PHE SER 0.0223818
S16 S25 PHE THR 3.68095e-05
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S16 S25 GLY LYS 0.000572043
S16 S25 GLY ARG 0.00128052
S16 S25 GLY SER 0.0223818
S16 S25 GLY THR 3.68095e-05
S16 S25 HIS ASP 1.38702e-05
S16 S25 HIS GLU 7.38973e-05
S16 S25 HIS LYS 0.000572043
S16 S25 HIS ARG 0.00128052
S16 S25 HIS SER 0.0223818
S16 S25 HIS THR 3.68095e-05
S16 S25 ILE ALA 0.0206928
S16 S25 ILE CYS 0.0206928
S16 S25 ILE ASP -0.0681063
S16 S25 ILE GLU -0.0632418
S16 S25 ILE PHE 0.0206928

S16 S25 ILE GLY 0.0206928
S16 S25 ILE HIS 0.0206928
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S16 S25 ILE LYS -0.180935
S16 S25 ILE LEU 0.0206928
S16 S25 ILE MET 0.0206928
S16 S25 ILE ASN 0.0206928
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S16 S25 LYS GLU 7.38973e-05
S16 S25 LYS LYS 0.000572043
S16 S25 LYS ARG 0.00128052
S16 S25 LYS SER 0.0223818
S16 S25 LYS THR 3.68095e-05
S16 S25 LEU ALA 1.05338e-05
S16 S25 LEU CYS 1.05338e-05
S16 S25 LEU ASP 5.2096e-05
S16 S25 LEU GLU 0.00042646
S16 S25 LEU PHE 1.05338e-05
S16 S25 LEU GLY 1.05338e-05
S16 S25 LEU HIS 1.05338e-05
S16 S25 LEU ILE 1.05338e-05
S16 S25 LEU LYS 0.00209936
S16 S25 LEU LEU 1.05338e-05
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S16 S25 LEU GLN 1.05338e-05
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S16 S25 LEU SER -0.0439521
S16 S25 LEU THR 0.000298555
S16 S25 LEU VAL 1.05338e-05
S16 S25 LEU TRP 1.05338e-05
S16 S25 LEU TYR 1.05338e-05
S16 S25 LEU --- 1.05338e-05
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S16 S25 GLN GLU 7.38973e-05

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S16 S25 THR TYR 0.000498226
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S16 S26 GLU TYR 0.0032653
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S16 S26 PHE TYR 0.0032653
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S16 S26 VAL ILE 0.00705581
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S16 S27 ILE CYS 0.0102235
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S16 S27 ILE GLY 0.0102235
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S16 S27 ILE LYS 0.0102235
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S16 S28 VAL --- 0.00374033
S16 S28 TRP ASP 0.0234354
S16 S28 TRP GLU 0.000923477
S16 S28 TYR ASP 0.0234354
S16 S28 TYR GLU 0.000923477
S16 S28 --- ASP 0.0234354
S16 S28 --- GLU 0.000923477
S16 S29 ALA ALA 0.000148301

S16 S29 ALA CYS 0.000148301
S16 S29 ALA ASP 0.000148301
S16 S29 ALA GLU 0.000148301
S16 S29 ALA PHE 0.000148301
S16 S29 ALA GLY 0.000148301
S16 S29 ALA HIS 0.000148301
S16 S29 ALA ILE 0.000148301
S16 S29 ALA LYS 0.00301451
S16 S29 ALA LEU 0.0137987
S16 S29 ALA MET 0.000148301
S16 S29 ALA ASN 0.00499232
S16 S29 ALA PRO 0.000148301
S16 S29 ALA GLN 0.000148301
S16 S29 ALA ARG 0.000148301
S16 S29 ALA SER -0.0901014
S16 S29 ALA THR 0.000148301
S16 S29 ALA VAL 0.000148301
S16 S29 ALA TRP 0.000148301
S16 S29 ALA TYR 0.000148301
S16 S29 ALA --- 0.000148301
S16 S29 CYS LYS 0.000812094
S16 S29 CYS LEU 0.000592144
S16 S29 CYS ASN 0.000138611
S16 S29 CYS SER 0.0228161
S16 S29 ASP LYS 0.000812094
S16 S29 ASP LEU 0.000592144
S16 S29 ASP ASN 0.000138611
S16 S29 ASP SER 0.0228161
S16 S29 GLU LYS 0.000812094
S16 S29 GLU LEU 0.000592144
S16 S29 GLU ASN 0.000138611
S16 S29 GLU SER 0.0228161
S16 S29 PHE LYS 0.000812094
S16 S29 PHE LEU 0.000592144
S16 S29 PHE ASN 0.000138611
S16 S29 PHE SER 0.0228161
S16 S29 GLY LYS 0.000812094
S16 S29 GLY LEU 0.000592144
S16 S29 GLY ASN 0.000138611
S16 S29 GLY SER 0.0228161
S16 S29 HIS LYS 0.000812094
S16 S29 HIS LEU 0.000592144
S16 S29 HIS ASN 0.000138611
S16 S29 HIS SER 0.0228161
S16 S29 ILE ALA 0.0104749
S16 S29 ILE CYS 0.0104749
S16 S29 ILE ASP 0.0104749
S16 S29 ILE GLU 0.0104749
S16 S29 ILE PHE 0.0104749
S16 S29 ILE GLY 0.0104749
S16 S29 ILE HIS 0.0104749
S16 S29 ILE ILE 0.0104749
S16 S29 ILE LYS 0.246542
S16 S29 ILE LEU -0.194776
S16 S29 ILE MET 0.0104749
S16 S29 ILE ASN -0.135595
S16 S29 ILE PRO 0.0104749
S16 S29 ILE GLN 0.0104749
S16 S29 ILE ARG 0.0104749
S16 S29 ILE SER -0.228011
S16 S29 ILE THR 0.0104749
S16 S29 ILE VAL 0.0104749
S16 S29 ILE TRP 0.0104749

S16 S29 ILE TYR 0.0104749
S16 S29 ILE --- 0.0104749
S16 S29 LYS LYS 0.000812094
S16 S29 LYS LEU 0.000592144
S16 S29 LYS ASN 0.000138611
S16 S29 LYS SER 0.0228161
S16 S29 LEU ALA 2.56431e-05
S16 S29 LEU CYS 2.56431e-05
S16 S29 LEU ASP 2.56431e-05
S16 S29 LEU GLU 2.56431e-05
S16 S29 LEU PHE 2.56431e-05
S16 S29 LEU GLY 2.56431e-05
S16 S29 LEU HIS 2.56431e-05
S16 S29 LEU ILE 2.56431e-05
S16 S29 LEU LYS 0.00689376
S16 S29 LEU LEU 0.00679721
S16 S29 LEU MET 2.56431e-05
S16 S29 LEU ASN 0.00043945
S16 S29 LEU PRO 2.56431e-05
S16 S29 LEU GLN 2.56431e-05
S16 S29 LEU ARG 2.56431e-05
S16 S29 LEU SER -0.0439836
S16 S29 LEU THR 2.56431e-05
S16 S29 LEU VAL 2.56431e-05
S16 S29 LEU TRP 2.56431e-05
S16 S29 LEU TYR 2.56431e-05
S16 S29 LEU --- 2.56431e-05
S16 S29 MET LYS 0.000812094
S16 S29 MET LEU 0.000592144
S16 S29 MET ASN 0.000138611
S16 S29 MET SER 0.0228161
S16 S29 ASN LYS 0.000812094
S16 S29 ASN LEU 0.000592144
S16 S29 ASN ASN 0.000138611
S16 S29 ASN SER 0.0228161
S16 S29 PRO LYS 0.000812094
S16 S29 PRO LEU 0.000592144
S16 S29 PRO ASN 0.000138611
S16 S29 PRO SER 0.0228161
S16 S29 GLN LYS 0.000812094
S16 S29 GLN LEU 0.000592144
S16 S29 GLN ASN 0.000138611
S16 S29 GLN SER 0.0228161
S16 S29 ARG LYS 0.000812094
S16 S29 ARG LEU 0.000592144
S16 S29 ARG ASN 0.000138611
S16 S29 ARG SER 0.0228161
S16 S29 SER LYS 0.000812094
S16 S29 SER LEU 0.000592144
S16 S29 SER ASN 0.000138611
S16 S29 SER SER 0.0228161
S16 S29 THR ALA 0.000750756
S16 S29 THR CYS 0.000750756
S16 S29 THR ASP 0.000750756
S16 S29 THR GLU 0.000750756
S16 S29 THR PHE 0.000750756
S16 S29 THR GLY 0.000750756
S16 S29 THR HIS 0.000750756
S16 S29 THR ILE 0.000750756
S16 S29 THR LYS -0.409328
S16 S29 THR LEU 0.00562105
S16 S29 THR MET 0.000750756
S16 S29 THR ASN 0.00412984

S16 S29 THR PRO 0.000750756
S16 S29 THR GLN 0.000750756
S16 S29 THR ARG 0.000750756
S16 S29 THR SER 0.350197
S16 S29 THR THR 0.000750756
S16 S29 THR VAL 0.000750756
S16 S29 THR TRP 0.000750756
S16 S29 THR TYR 0.000750756
S16 S29 THR --- 0.000750756
S16 S29 VAL ALA 0.00642855
S16 S29 VAL CYS 0.00642855
S16 S29 VAL ASP 0.00642855
S16 S29 VAL GLU 0.00642855
S16 S29 VAL PHE 0.00642855
S16 S29 VAL GLY 0.00642855
S16 S29 VAL HIS 0.00642855
S16 S29 VAL ILE 0.00642855
S16 S29 VAL LYS 0.095543
S16 S29 VAL LEU 0.0981977
S16 S29 VAL MET 0.00642855
S16 S29 VAL ASN 0.0595701
S16 S29 VAL PRO 0.00642855
S16 S29 VAL GLN 0.00642855
S16 S29 VAL ARG 0.00642855
S16 S29 VAL SER -0.486763
S16 S29 VAL THR 0.00642855
S16 S29 VAL VAL 0.00642855
S16 S29 VAL TRP 0.00642855
S16 S29 VAL TYR 0.00642855
S16 S29 VAL --- 0.00642855
S16 S29 TRP LYS 0.000812094
S16 S29 TRP LEU 0.000592144
S16 S29 TRP ASN 0.000138611
S16 S29 TRP SER 0.0228161
S16 S29 TYR LYS 0.000812094
S16 S29 TYR LEU 0.000592144
S16 S29 TYR ASN 0.000138611
S16 S29 TYR SER 0.0228161
S16 S29 --- LYS 0.000812094
S16 S29 --- LEU 0.000592144
S16 S29 --- ASN 0.000138611
S16 S29 --- SER 0.0228161
S16 S30 ALA ALA 0.000144181
S16 S30 ALA CYS 0.000144181
S16 S30 ALA ASP 0.000144181
S16 S30 ALA GLU 0.000144181
S16 S30 ALA PHE 0.000144181
S16 S30 ALA GLY 0.000144181
S16 S30 ALA HIS 0.000144181
S16 S30 ALA ILE 0.000144181
S16 S30 ALA LYS 0.000144181
S16 S30 ALA LEU 0.000144181
S16 S30 ALA MET 0.000144181
S16 S30 ALA ASN 0.000144181
S16 S30 ALA PRO 0.000144181
S16 S30 ALA GLN -0.0798405
S16 S30 ALA ARG 0.000144181
S16 S30 ALA SER 0.0113263
S16 S30 ALA THR 0.000144181
S16 S30 ALA VAL 0.000144181
S16 S30 ALA TRP 0.000144181
S16 S30 ALA TYR 0.000144181
S16 S30 ALA --- 0.000144181

S16 S30 CYS GLN 0.0242722
S16 S30 CYS SER 8.67498e-05
S16 S30 ASP GLN 0.0242722
S16 S30 ASP SER 8.67498e-05
S16 S30 GLU GLN 0.0242722
S16 S30 GLU SER 8.67498e-05
S16 S30 PHE GLN 0.0242722
S16 S30 PHE SER 8.67498e-05
S16 S30 GLY GLN 0.0242722
S16 S30 GLY SER 8.67498e-05
S16 S30 HIS GLN 0.0242722
S16 S30 HIS SER 8.67498e-05
S16 S30 ILE ALA 0.00898112
S16 S30 ILE CYS 0.00898112
S16 S30 ILE ASP 0.00898112
S16 S30 ILE GLU 0.00898112
S16 S30 ILE PHE 0.00898112
S16 S30 ILE GLY 0.00898112
S16 S30 ILE HIS 0.00898112
S16 S30 ILE ILE 0.00898112
S16 S30 ILE LYS 0.00898112
S16 S30 ILE LEU 0.00898112
S16 S30 ILE MET 0.00898112
S16 S30 ILE ASN 0.00898112
S16 S30 ILE PRO 0.00898112
S16 S30 ILE GLN -0.155988
S16 S30 ILE ARG 0.00898112
S16 S30 ILE SER -0.14842
S16 S30 ILE THR 0.00898112
S16 S30 ILE VAL 0.00898112
S16 S30 ILE TRP 0.00898112
S16 S30 ILE TYR 0.00898112
S16 S30 ILE --- 0.00898112
S16 S30 LYS GLN 0.0242722
S16 S30 LYS SER 8.67498e-05
S16 S30 LEU ALA 6.46374e-06
S16 S30 LEU CYS 6.46374e-06
S16 S30 LEU ASP 6.46374e-06
S16 S30 LEU GLU 6.46374e-06
S16 S30 LEU PHE 6.46374e-06
S16 S30 LEU GLY 6.46374e-06
S16 S30 LEU HIS 6.46374e-06
S16 S30 LEU ILE 6.46374e-06
S16 S30 LEU LYS 6.46374e-06
S16 S30 LEU LEU 6.46374e-06
S16 S30 LEU MET 6.46374e-06
S16 S30 LEU ASN 6.46374e-06
S16 S30 LEU PRO 6.46374e-06
S16 S30 LEU GLN -0.0300016
S16 S30 LEU ARG 6.46374e-06
S16 S30 LEU SER 0.000461611
S16 S30 LEU THR 6.46374e-06
S16 S30 LEU VAL 6.46374e-06
S16 S30 LEU TRP 6.46374e-06
S16 S30 LEU TYR 6.46374e-06
S16 S30 LEU --- 6.46374e-06
S16 S30 MET GLN 0.0242722
S16 S30 MET SER 8.67498e-05
S16 S30 ASN GLN 0.0242722
S16 S30 ASN SER 8.67498e-05
S16 S30 PRO GLN 0.0242722
S16 S30 PRO SER 8.67498e-05
S16 S30 GLN GLN 0.0242722

S16 S30 GLN SER 8.67498e-05
S16 S30 ARG GLN 0.0242722
S16 S30 ARG SER 8.67498e-05
S16 S30 SER GLN 0.0242722
S16 S30 SER SER 8.67498e-05
S16 S30 THR ALA 0.000412394
S16 S30 THR CYS 0.000412394
S16 S30 THR ASP 0.000412394
S16 S30 THR GLU 0.000412394
S16 S30 THR PHE 0.000412394
S16 S30 THR GLY 0.000412394
S16 S30 THR HIS 0.000412394
S16 S30 THR ILE 0.000412394
S16 S30 THR LYS 0.000412394
S16 S30 THR LEU 0.000412394
S16 S30 THR MET 0.000412394
S16 S30 THR ASN 0.000412394
S16 S30 THR PRO 0.000412394
S16 S30 THR GLN -0.0526382
S16 S30 THR ARG 0.000412394
S16 S30 THR SER 0.00818539
S16 S30 THR THR 0.000412394
S16 S30 THR VAL 0.000412394
S16 S30 THR TRP 0.000412394
S16 S30 THR TYR 0.000412394
S16 S30 THR --- 0.000412394
S16 S30 VAL ALA 0.00292208
S16 S30 VAL CYS 0.00292208
S16 S30 VAL ASP 0.00292208
S16 S30 VAL GLU 0.00292208
S16 S30 VAL PHE 0.00292208
S16 S30 VAL GLY 0.00292208
S16 S30 VAL HIS 0.00292208
S16 S30 VAL ILE 0.00292208
S16 S30 VAL LYS 0.00292208
S16 S30 VAL LEU 0.00292208
S16 S30 VAL MET 0.00292208
S16 S30 VAL ASN 0.00292208
S16 S30 VAL PRO 0.00292208
S16 S30 VAL GLN -0.226812
S16 S30 VAL ARG 0.00292208
S16 S30 VAL SER 0.047126
S16 S30 VAL THR 0.00292208
S16 S30 VAL VAL 0.00292208
S16 S30 VAL TRP 0.00292208
S16 S30 VAL TYR 0.00292208
S16 S30 VAL --- 0.00292208
S16 S30 TRP GLN 0.0242722
S16 S30 TRP SER 8.67498e-05
S16 S30 TYR GLN 0.0242722
S16 S30 TYR SER 8.67498e-05
S16 S30 --- GLN 0.0242722
S16 S30 --- SER 8.67498e-05
S16 S31 ALA ALA 0.000119984
S16 S31 ALA CYS 0.000119984
S16 S31 ALA ASP 0.0193839
S16 S31 ALA GLU 0.000119984
S16 S31 ALA PHE 0.000119984
S16 S31 ALA GLY 0.000119984
S16 S31 ALA HIS 0.000119984
S16 S31 ALA ILE 0.00816805
S16 S31 ALA LYS 0.000119984
S16 S31 ALA LEU 0.000119984

S16 S31 ALA MET 0.000119984
S16 S31 ALA ASN 0.000119984
S16 S31 ALA PRO 0.000119984
S16 S31 ALA GLN 0.000119984
S16 S31 ALA ARG 0.000119984
S16 S31 ALA SER 0.000119984
S16 S31 ALA THR 0.000119984
S16 S31 ALA VAL -0.0954864
S16 S31 ALA TRP 0.000119984
S16 S31 ALA TYR 0.000119984
S16 S31 ALA --- 0.000119984
S16 S31 CYS ASP 0.000920638
S16 S31 CYS ILE 0.000907023
S16 S31 CYS VAL 0.0225312
S16 S31 ASP ASP 0.000920638
S16 S31 ASP ILE 0.000907023
S16 S31 ASP VAL 0.0225312
S16 S31 GLU ASP 0.000920638
S16 S31 GLU ILE 0.000907023
S16 S31 GLU VAL 0.0225312
S16 S31 PHE ASP 0.000920638
S16 S31 PHE ILE 0.000907023
S16 S31 PHE VAL 0.0225312
S16 S31 GLY ASP 0.000920638
S16 S31 GLY ILE 0.000907023
S16 S31 GLY VAL 0.0225312
S16 S31 HIS ASP 0.000920638
S16 S31 HIS ILE 0.000907023
S16 S31 HIS VAL 0.0225312
S16 S31 ILE ALA 0.011244
S16 S31 ILE CYS 0.011244
S16 S31 ILE ASP -0.0850606
S16 S31 ILE GLU 0.011244
S16 S31 ILE PHE 0.011244
S16 S31 ILE GLY 0.011244
S16 S31 ILE HIS 0.011244
S16 S31 ILE ILE -0.608455
S16 S31 ILE LYS 0.011244
S16 S31 ILE LEU 0.011244
S16 S31 ILE MET 0.011244
S16 S31 ILE ASN 0.011244
S16 S31 ILE PRO 0.011244
S16 S31 ILE GLN 0.011244
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S16 S31 ILE SER 0.011244
S16 S31 ILE THR 0.011244
S16 S31 ILE VAL 0.357356
S16 S31 ILE TRP 0.011244
S16 S31 ILE TYR 0.011244
S16 S31 ILE --- 0.011244
S16 S31 LYS ASP 0.000920638
S16 S31 LYS ILE 0.000907023
S16 S31 LYS VAL 0.0225312
S16 S31 LEU ALA 1.15287e-05
S16 S31 LEU CYS 1.15287e-05
S16 S31 LEU ASP 0.0112305
S16 S31 LEU GLU 1.15287e-05
S16 S31 LEU PHE 1.15287e-05
S16 S31 LEU GLY 1.15287e-05
S16 S31 LEU HIS 1.15287e-05
S16 S31 LEU ILE 0.00732264
S16 S31 LEU LYS 1.15287e-05
S16 S31 LEU LEU 1.15287e-05

S16 S31 LEU MET 1.15287e-05
S16 S31 LEU ASN 1.15287e-05
S16 S31 LEU PRO 1.15287e-05
S16 S31 LEU GLN 1.15287e-05
S16 S31 LEU ARG 1.15287e-05
S16 S31 LEU SER 1.15287e-05
S16 S31 LEU THR 1.15287e-05
S16 S31 LEU VAL -0.0481779
S16 S31 LEU TRP 1.15287e-05
S16 S31 LEU TYR 1.15287e-05
S16 S31 LEU --- 1.15287e-05
S16 S31 MET ASP 0.000920638
S16 S31 MET ILE 0.000907023
S16 S31 MET VAL 0.0225312
S16 S31 ASN ASP 0.000920638
S16 S31 ASN ILE 0.000907023
S16 S31 ASN VAL 0.0225312
S16 S31 PRO ASP 0.000920638
S16 S31 PRO ILE 0.000907023
S16 S31 PRO VAL 0.0225312
S16 S31 GLN ASP 0.000920638
S16 S31 GLN ILE 0.000907023
S16 S31 GLN VAL 0.0225312
S16 S31 ARG ASP 0.000920638
S16 S31 ARG ILE 0.000907023
S16 S31 ARG VAL 0.0225312
S16 S31 SER ASP 0.000920638
S16 S31 SER ILE 0.000907023
S16 S31 SER VAL 0.0225312
S16 S31 THR ALA 0.000414817
S16 S31 THR CYS 0.000414817
S16 S31 THR ASP 0.0090811
S16 S31 THR GLU 0.000414817
S16 S31 THR PHE 0.000414817
S16 S31 THR GLY 0.000414817
S16 S31 THR HIS 0.000414817
S16 S31 THR ILE 0.049422
S16 S31 THR LYS 0.000414817
S16 S31 THR LEU 0.000414817
S16 S31 THR MET 0.000414817
S16 S31 THR ASN 0.000414817
S16 S31 THR PRO 0.000414817
S16 S31 THR GLN 0.000414817
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S16 S31 THR SER 0.000414817
S16 S31 THR THR 0.000414817
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S16 S31 THR TRP 0.000414817
S16 S31 THR TYR 0.000414817
S16 S31 THR --- 0.000414817
S16 S31 VAL ALA 0.00677063
S16 S31 VAL CYS 0.00677063
S16 S31 VAL ASP -0.0703475
S16 S31 VAL GLU 0.00677063
S16 S31 VAL PHE 0.00677063
S16 S31 VAL GLY 0.00677063
S16 S31 VAL HIS 0.00677063
S16 S31 VAL ILE 0.468241
S16 S31 VAL LYS 0.00677063
S16 S31 VAL LEU 0.00677063
S16 S31 VAL MET 0.00677063
S16 S31 VAL ASN 0.00677063
S16 S31 VAL PRO 0.00677063

S16 S31 VAL GLN 0.00677063
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S16 S31 VAL THR 0.00677063
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S16 S31 VAL TRP 0.00677063
S16 S31 VAL TYR 0.00677063
S16 S31 VAL --- 0.00677063
S16 S31 TRP ASP 0.000920638
S16 S31 TRP ILE 0.000907023
S16 S31 TRP VAL 0.0225312
S16 S31 TYR ASP 0.000920638
S16 S31 TYR ILE 0.000907023
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S16 S31 --- ASP 0.000920638
S16 S31 --- ILE 0.000907023
S16 S31 --- VAL 0.0225312
S16 S32 ALA ALA 8.0449e-05
S16 S32 ALA CYS 8.0449e-05
S16 S32 ALA ASP 8.0449e-05
S16 S32 ALA GLU 8.0449e-05
S16 S32 ALA PHE 0.0172042
S16 S32 ALA GLY 8.0449e-05
S16 S32 ALA HIS 0.0198371
S16 S32 ALA ILE 8.0449e-05
S16 S32 ALA LYS 8.0449e-05
S16 S32 ALA LEU 8.0449e-05
S16 S32 ALA MET 8.0449e-05
S16 S32 ALA ASN 8.0449e-05
S16 S32 ALA PRO 8.0449e-05
S16 S32 ALA GLN 8.0449e-05
S16 S32 ALA ARG 8.0449e-05
S16 S32 ALA SER 8.0449e-05
S16 S32 ALA THR 8.0449e-05
S16 S32 ALA VAL 8.0449e-05
S16 S32 ALA TRP -0.116869
S16 S32 ALA TYR 0.012685
S16 S32 ALA --- 8.0449e-05
S16 S32 CYS PHE 0.00212781
S16 S32 CYS HIS 0.00295693
S16 S32 CYS TRP 0.0179763
S16 S32 CYS TYR 0.00129791
S16 S32 ASP PHE 0.00212781
S16 S32 ASP HIS 0.00295693
S16 S32 ASP TRP 0.0179763
S16 S32 ASP TYR 0.00129791
S16 S32 GLU PHE 0.00212781
S16 S32 GLU HIS 0.00295693
S16 S32 GLU TRP 0.0179763
S16 S32 GLU TYR 0.00129791
S16 S32 PHE PHE 0.00212781
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S16 S32 PHE TRP 0.0179763
S16 S32 PHE TYR 0.00129791
S16 S32 GLY PHE 0.00212781
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S16 S32 GLY TRP 0.0179763
S16 S32 GLY TYR 0.00129791
S16 S32 HIS PHE 0.00212781
S16 S32 HIS HIS 0.00295693
S16 S32 HIS TRP 0.0179763
S16 S32 HIS TYR 0.00129791
S16 S32 ILE ALA 0.0113034

S16 S32 ILE CYS 0.0113034
S16 S32 ILE ASP 0.0113034
S16 S32 ILE GLU 0.0113034
S16 S32 ILE PHE -0.154296
S16 S32 ILE GLY 0.0113034
S16 S32 ILE HIS 0.484907
S16 S32 ILE ILE 0.0113034
S16 S32 ILE LYS 0.0113034
S16 S32 ILE LEU 0.0113034
S16 S32 ILE MET 0.0113034
S16 S32 ILE ASN 0.0113034
S16 S32 ILE PRO 0.0113034
S16 S32 ILE GLN 0.0113034
S16 S32 ILE ARG 0.0113034
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S16 S32 ILE THR 0.0113034
S16 S32 ILE VAL 0.0113034
S16 S32 ILE TRP -0.582159
S16 S32 ILE TYR -0.0743779
S16 S32 ILE --- 0.0113034
S16 S32 LYS PHE 0.00212781
S16 S32 LYS HIS 0.00295693
S16 S32 LYS TRP 0.0179763
S16 S32 LYS TYR 0.00129791
S16 S32 LEU ALA 0.000464724
S16 S32 LEU CYS 0.000464724
S16 S32 LEU ASP 0.000464724
S16 S32 LEU GLU 0.000464724
S16 S32 LEU PHE 0.092979
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S16 S32 LEU HIS -0.687228
S16 S32 LEU ILE 0.000464724
S16 S32 LEU LYS 0.000464724
S16 S32 LEU LEU 0.000464724
S16 S32 LEU MET 0.000464724
S16 S32 LEU ASN 0.000464724
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S16 S32 LEU THR 0.000464724
S16 S32 LEU VAL 0.000464724
S16 S32 LEU TRP 0.524089
S16 S32 LEU TYR 0.0328419
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S16 S32 MET HIS 0.00295693
S16 S32 MET TRP 0.0179763
S16 S32 MET TYR 0.00129791
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S16 S32 PRO HIS 0.00295693
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S16 S32 PRO TYR 0.00129791
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S16 S32 GLN HIS 0.00295693
S16 S32 GLN TRP 0.0179763
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S16 S32 ARG TYR 0.00129791
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S16 S32 SER TYR 0.00129791
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S16 S32 THR ASP 0.000559742
S16 S32 THR GLU 0.000559742
S16 S32 THR PHE 0.148006
S16 S32 THR GLY 0.000559742
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S16 S32 THR LYS 0.000559742
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S16 S32 THR TYR 0.0201073
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S16 S32 VAL ALA 0.0124021
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S16 S32 VAL GLU 0.0124021
S16 S32 VAL PHE -0.135397
S16 S32 VAL GLY 0.0124021
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S16 S32 TYR TYR 0.00129791
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S16 S33 ALA TYR 0.000126989
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S16 S33 CYS LYS 0.00122974
S16 S33 CYS SER 0.00474147
S16 S33 CYS VAL 0.00213181
S16 S33 ASP ASP 0.0162559
S16 S33 ASP LYS 0.00122974
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S16 S33 GLU ASP 0.0162559
S16 S33 GLU LYS 0.00122974
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S16 S33 PHE LYS 0.00122974
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S16 S33 PHE VAL 0.00213181
S16 S33 GLY ASP 0.0162559
S16 S33 GLY LYS 0.00122974
S16 S33 GLY SER 0.00474147
S16 S33 GLY VAL 0.00213181
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S16 S33 HIS LYS 0.00122974
S16 S33 HIS SER 0.00474147
S16 S33 HIS VAL 0.00213181
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S16 S33 ILE CYS 0.0129492
S16 S33 ILE ASP 0.162817
S16 S33 ILE GLU 0.0129492
S16 S33 ILE PHE 0.0129492
S16 S33 ILE GLY 0.0129492
S16 S33 ILE HIS 0.0129492
S16 S33 ILE ILE 0.0129492
S16 S33 ILE LYS -0.551853
S16 S33 ILE LEU 0.0129492
S16 S33 ILE MET 0.0129492
S16 S33 ILE ASN 0.0129492
S16 S33 ILE PRO 0.0129492
S16 S33 ILE GLN 0.0129492
S16 S33 ILE ARG 0.0129492
S16 S33 ILE SER 0.441094
S16 S33 ILE THR 0.0129492
S16 S33 ILE VAL -0.405961
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S16 S33 ILE TYR 0.0129492
S16 S33 ILE --- 0.0129492

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S16 S33 LYS SER 0.00474147
S16 S33 LYS VAL 0.00213181
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S16 S33 LEU CYS 9.00357e-06
S16 S33 LEU ASP -0.0767184
S16 S33 LEU GLU 9.00357e-06
S16 S33 LEU PHE 9.00357e-06
S16 S33 LEU GLY 9.00357e-06
S16 S33 LEU HIS 9.00357e-06
S16 S33 LEU ILE 9.00357e-06
S16 S33 LEU LYS 0.0127248
S16 S33 LEU LEU 9.00357e-06
S16 S33 LEU MET 9.00357e-06
S16 S33 LEU ASN 9.00357e-06
S16 S33 LEU PRO 9.00357e-06
S16 S33 LEU GLN 9.00357e-06
S16 S33 LEU ARG 9.00357e-06
S16 S33 LEU SER 0.0218749
S16 S33 LEU THR 9.00357e-06
S16 S33 LEU VAL 0.0125485
S16 S33 LEU TRP 9.00357e-06
S16 S33 LEU TYR 9.00357e-06
S16 S33 LEU --- 9.00357e-06
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S16 S33 ASN LYS 0.00122974
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S16 S33 PRO LYS 0.00122974
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S16 S33 GLN LYS 0.00122974
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S16 S33 ARG VAL 0.00213181
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S16 S33 SER SER 0.00474147
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S16 S33 THR ALA 0.00141991
S16 S33 THR CYS 0.00141991
S16 S33 THR ASP 0.279736
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S16 S33 THR GLY 0.00141991
S16 S33 THR HIS 0.00141991
S16 S33 THR ILE 0.00141991
S16 S33 THR LYS 0.111029
S16 S33 THR LEU 0.00141991
S16 S33 THR MET 0.00141991
S16 S33 THR ASN 0.00141991
S16 S33 THR PRO 0.00141991
S16 S33 THR GLN 0.00141991

S16 S33 THR ARG 0.00141991
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S16 S33 THR THR 0.00141991
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S16 S33 THR TRP 0.00141991
S16 S33 THR TYR 0.00141991
S16 S33 THR --- 0.00141991
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S16 S33 VAL ASP -0.739517
S16 S33 VAL GLU 0.0100479
S16 S33 VAL PHE 0.0100479
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S16 S33 VAL HIS 0.0100479
S16 S33 VAL ILE 0.0100479
S16 S33 VAL LYS 0.377528
S16 S33 VAL LEU 0.0100479
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S16 S33 VAL ASN 0.0100479
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S16 S33 VAL GLN 0.0100479
S16 S33 VAL ARG 0.0100479
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S16 S33 VAL THR 0.0100479
S16 S33 VAL VAL 0.233132
S16 S33 VAL TRP 0.0100479
S16 S33 VAL TYR 0.0100479
S16 S33 VAL --- 0.0100479
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S16 S33 TRP VAL 0.00213181
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S16 S33 TYR LYS 0.00122974
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S16 S33 TYR VAL 0.00213181
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S16 S33 --- VAL 0.00213181
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S16 S34 ALA PHE 0.000370007
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S16 S34 ALA ASN 0.000370007
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S16 S34 ALA THR 0.0380833
S16 S34 ALA VAL 0.000370007
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S16 S34 GLU SER 0.0181483
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S16 S34 PHE GLU 0.00172273
S16 S34 PHE MET 0.00199283
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S16 S34 ILE SER -0.623528
S16 S34 ILE THR -0.187646
S16 S34 ILE VAL 0.0143142
S16 S34 ILE TRP 0.0143142
S16 S34 ILE TYR 0.0143142
S16 S34 ILE --- 0.0143142
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S16 S34 LEU GLY 0.000217568
S16 S34 LEU HIS 0.000217568
S16 S34 LEU ILE 0.000217568
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S16 S34 LEU TYR 0.000217568
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S16 S34 ARG SER 0.0181483
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S16 S34 VAL CYS 0.00950783
S16 S34 VAL ASP 0.00950783
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S16 S34 VAL PHE 0.00950783
S16 S34 VAL GLY 0.00950783
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S16 S35 THR TRP 0.000832314
S16 S35 THR TYR 0.000832314
S16 S35 THR --- 0.000832314
S16 S35 VAL ALA -0.118749
S16 S35 VAL CYS 0.00796499
S16 S35 VAL ASP 0.00796499
S16 S35 VAL GLU 0.00796499
S16 S35 VAL PHE 0.00796499
S16 S35 VAL GLY 0.00796499
S16 S35 VAL HIS 0.00796499
S16 S35 VAL ILE 0.00796499
S16 S35 VAL LYS 0.00796499
S16 S35 VAL LEU 0.00796499
S16 S35 VAL MET 0.00796499
S16 S35 VAL ASN 0.00796499
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S16 S35 VAL ARG 0.00796499
S16 S35 VAL SER 0.406718
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S16 S35 VAL VAL 0.00796499
S16 S35 VAL TRP 0.00796499
S16 S35 VAL TYR 0.00796499
S16 S35 VAL --- 0.00796499
S16 S35 TRP ALA 0.00185508
S16 S35 TRP SER 0.0175784
S16 S35 TRP THR 0.00492547
S16 S35 TYR ALA 0.00185508
S16 S35 TYR SER 0.0175784
S16 S35 TYR THR 0.00492547
S16 S35 --- ALA 0.00185508
S16 S35 --- SER 0.0175784
S16 S35 --- THR 0.00492547

S16 S36 ALA ALA 0.000781526
S16 S36 ALA CYS 0.000781526
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S16 S36 ALA GLU 0.0499774
S16 S36 ALA PHE 0.000781526
S16 S36 ALA GLY 0.000781526
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S16 S36 ALA THR 0.0523945
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S16 S36 ALA TYR 0.000781526
S16 S36 ALA --- 0.000781526
S16 S36 CYS ASP 0.00303575
S16 S36 CYS GLU 0.00358472
S16 S36 CYS SER 0.0162524
S16 S36 CYS THR 0.00148603
S16 S36 ASP ASP 0.00303575
S16 S36 ASP GLU 0.00358472
S16 S36 ASP SER 0.0162524
S16 S36 ASP THR 0.00148603
S16 S36 GLU ASP 0.00303575
S16 S36 GLU GLU 0.00358472
S16 S36 GLU SER 0.0162524
S16 S36 GLU THR 0.00148603
S16 S36 PHE ASP 0.00303575
S16 S36 PHE GLU 0.00358472
S16 S36 PHE SER 0.0162524
S16 S36 PHE THR 0.00148603
S16 S36 GLY ASP 0.00303575
S16 S36 GLY GLU 0.00358472
S16 S36 GLY SER 0.0162524
S16 S36 GLY THR 0.00148603
S16 S36 HIS ASP 0.00303575
S16 S36 HIS GLU 0.00358472
S16 S36 HIS SER 0.0162524
S16 S36 HIS THR 0.00148603
S16 S36 ILE ALA 0.0112714
S16 S36 ILE CYS 0.0112714
S16 S36 ILE ASP -0.0325884
S16 S36 ILE GLU 0.667966
S16 S36 ILE PHE 0.0112714
S16 S36 ILE GLY 0.0112714
S16 S36 ILE HIS 0.0112714
S16 S36 ILE ILE 0.0112714
S16 S36 ILE LYS 0.0112714
S16 S36 ILE LEU 0.0112714
S16 S36 ILE MET 0.0112714
S16 S36 ILE ASN 0.0112714
S16 S36 ILE PRO 0.0112714
S16 S36 ILE GLN 0.0112714
S16 S36 ILE ARG 0.0112714
S16 S36 ILE SER -0.957882
S16 S36 ILE THR -0.00287562
S16 S36 ILE VAL 0.0112714

S16 S36 ILE TRP 0.0112714
S16 S36 ILE TYR 0.0112714
S16 S36 ILE --- 0.0112714
S16 S36 LYS ASP 0.00303575
S16 S36 LYS GLU 0.00358472
S16 S36 LYS SER 0.0162524
S16 S36 LYS THR 0.00148603
S16 S36 LEU ALA 0.000175265
S16 S36 LEU CYS 0.000175265
S16 S36 LEU ASP 0.0354316
S16 S36 LEU GLU 0.061424
S16 S36 LEU PHE 0.000175265
S16 S36 LEU GLY 0.000175265
S16 S36 LEU HIS 0.000175265
S16 S36 LEU ILE 0.000175265
S16 S36 LEU LYS 0.000175265
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S16 S36 LEU ASN 0.000175265
S16 S36 LEU PRO 0.000175265
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S16 S36 LEU THR 0.0120578
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S16 S36 LEU TYR 0.000175265
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S16 S36 PRO THR 0.00148603
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S16 S36 GLN THR 0.00148603
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S16 S36 ARG THR 0.00148603
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S16 S36 SER THR 0.00148603
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S16 S36 THR CYS 0.000530522
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S16 S36 THR GLU 0.0999488
S16 S36 THR PHE 0.000530522
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S16 S36 THR HIS 0.000530522
S16 S36 THR ILE 0.000530522
S16 S36 THR LYS 0.000530522
S16 S36 THR LEU 0.000530522
S16 S36 THR MET 0.000530522

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S16 S36 THR PRO 0.000530522
S16 S36 THR GLN 0.000530522
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S16 S36 THR TYR 0.000530522
S16 S36 THR --- 0.000530522
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S16 S36 VAL CYS 0.0114001
S16 S36 VAL ASP -0.00799805
S16 S36 VAL GLU -1.02928
S16 S36 VAL PHE 0.0114001
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S16 S36 VAL HIS 0.0114001
S16 S36 VAL ILE 0.0114001
S16 S36 VAL LYS 0.0114001
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S16 S36 VAL THR -0.166464
S16 S36 VAL VAL 0.0114001
S16 S36 VAL TRP 0.0114001
S16 S36 VAL TYR 0.0114001
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S16 S36 TRP SER 0.0162524
S16 S36 TRP THR 0.00148603
S16 S36 TYR ASP 0.00303575
S16 S36 TYR GLU 0.00358472
S16 S36 TYR SER 0.0162524
S16 S36 TYR THR 0.00148603
S16 S36 --- ASP 0.00303575
S16 S36 --- GLU 0.00358472
S16 S36 --- SER 0.0162524
S16 S36 --- THR 0.00148603
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S16 S37 ALA CYS 0.000218118
S16 S37 ALA ASP 0.0697346
S16 S37 ALA GLU 0.000218118
S16 S37 ALA PHE 0.0724101
S16 S37 ALA GLY 0.000218118
S16 S37 ALA HIS 0.000218118
S16 S37 ALA ILE 0.000218118
S16 S37 ALA LYS 0.000218118
S16 S37 ALA LEU 0.000218118
S16 S37 ALA MET 0.000218118
S16 S37 ALA ASN 0.00223002
S16 S37 ALA PRO 0.000218118
S16 S37 ALA GLN 0.000218118
S16 S37 ALA ARG 0.0169807
S16 S37 ALA SER -0.236787
S16 S37 ALA THR 0.000218118
S16 S37 ALA VAL 0.000218118
S16 S37 ALA TRP 0.000218118
S16 S37 ALA TYR 0.000218118

S16 S37 ALA --- 0.000218118
S16 S37 CYS ALA 0.00137312
S16 S37 CYS ASP 0.00766062
S16 S37 CYS PHE 0.00102043
S16 S37 CYS ASN 0.000671808
S16 S37 CYS ARG 0.00169318
S16 S37 CYS SER 0.0119398
S16 S37 ASP ALA 0.00137312
S16 S37 ASP ASP 0.00766062
S16 S37 ASP PHE 0.00102043
S16 S37 ASP ASN 0.000671808
S16 S37 ASP ARG 0.00169318
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S16 S37 GLU ASP 0.00766062
S16 S37 GLU PHE 0.00102043
S16 S37 GLU ASN 0.000671808
S16 S37 GLU ARG 0.00169318
S16 S37 GLU SER 0.0119398
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S16 S37 PHE ASP 0.00766062
S16 S37 PHE PHE 0.00102043
S16 S37 PHE ASN 0.000671808
S16 S37 PHE ARG 0.00169318
S16 S37 PHE SER 0.0119398
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S16 S37 GLY ASP 0.00766062
S16 S37 GLY PHE 0.00102043
S16 S37 GLY ASN 0.000671808
S16 S37 GLY ARG 0.00169318
S16 S37 GLY SER 0.0119398
S16 S37 HIS ALA 0.00137312
S16 S37 HIS ASP 0.00766062
S16 S37 HIS PHE 0.00102043
S16 S37 HIS ASN 0.000671808
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S16 S37 HIS SER 0.0119398
S16 S37 ILE ALA 0.213294
S16 S37 ILE CYS 0.0161309
S16 S37 ILE ASP 0.0142042
S16 S37 ILE GLU 0.0161309
S16 S37 ILE PHE -0.323183
S16 S37 ILE GLY 0.0161309
S16 S37 ILE HIS 0.0161309
S16 S37 ILE ILE 0.0161309
S16 S37 ILE LYS 0.0161309
S16 S37 ILE LEU 0.0161309
S16 S37 ILE MET 0.0161309
S16 S37 ILE ASN 0.238976
S16 S37 ILE PRO 0.0161309
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S16 S37 ILE ARG -0.153796
S16 S37 ILE SER -0.365225
S16 S37 ILE THR 0.0161309
S16 S37 ILE VAL 0.0161309
S16 S37 ILE TRP 0.0161309
S16 S37 ILE TYR 0.0161309
S16 S37 ILE --- 0.0161309
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S16 S37 LYS ASP 0.00766062
S16 S37 LYS PHE 0.00102043
S16 S37 LYS ASN 0.000671808
S16 S37 LYS ARG 0.00169318

S16 S37 LYS SER 0.0119398
S16 S37 LEU ALA 0.00512493
S16 S37 LEU CYS 3.84458e-06
S16 S37 LEU ASP 0.0611836
S16 S37 LEU GLU 3.84458e-06
S16 S37 LEU PHE 0.00769432
S16 S37 LEU GLY 3.84458e-06
S16 S37 LEU HIS 3.84458e-06
S16 S37 LEU ILE 3.84458e-06
S16 S37 LEU LYS 3.84458e-06
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S16 S37 LEU ASN 0.00508819
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S16 S37 LEU GLN 3.84458e-06
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S16 S37 LEU THR 3.84458e-06
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S16 S37 LEU TRP 3.84458e-06
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S16 S37 PRO ARG 0.00169318
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S16 S37 GLN ARG 0.00169318
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S16 S37 SER ASP 0.00766062
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S16 S37 THR ALA 0.075646
S16 S37 THR CYS 0.00199909
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S16 S37 THR GLU 0.00199909
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S16 S37 THR GLY 0.00199909
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S16 S37 THR LYS 0.00199909
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S16 S38 ALA ILE 0.00019896

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S16 S38 ILE TYR 0.0169928

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S16 S38 ASN LYS 0.00501305
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S16 S38 VAL HIS -0.591187
S16 S38 VAL ILE 0.0125355
S16 S38 VAL LYS -0.306547
S16 S38 VAL LEU 0.736982
S16 S38 VAL MET 0.0125355
S16 S38 VAL ASN 0.0125355
S16 S38 VAL PRO 0.0125355
S16 S38 VAL GLN 0.0125355
S16 S38 VAL ARG -0.493609
S16 S38 VAL SER 0.0125355
S16 S38 VAL THR 0.0125355
S16 S38 VAL VAL 0.0125355
S16 S38 VAL TRP 0.0125355
S16 S38 VAL TYR 0.0125355
S16 S38 VAL --- 0.0125355
S16 S38 TRP GLU 0.00374291
S16 S38 TRP HIS 0.00469618
S16 S38 TRP LYS 0.00501305
S16 S38 TRP LEU 0.00807831
S16 S38 TRP ARG 0.00282846
S16 S38 TYR GLU 0.00374291
S16 S38 TYR HIS 0.00469618
S16 S38 TYR LYS 0.00501305
S16 S38 TYR LEU 0.00807831
S16 S38 TYR ARG 0.00282846
S16 S38 --- GLU 0.00374291
S16 S38 --- HIS 0.00469618
S16 S38 --- LYS 0.00501305
S16 S38 --- LEU 0.00807831
S16 S38 --- ARG 0.00282846
S16 S39 ALA ALA 0.000254657
S16 S39 ALA CYS 0.000254657
S16 S39 ALA ASP 0.000254657
S16 S39 ALA GLU 0.000254657
S16 S39 ALA PHE 0.000254657
S16 S39 ALA GLY 0.000254657
S16 S39 ALA HIS 0.000254657
S16 S39 ALA ILE 0.0171962
S16 S39 ALA LYS 0.000254657
S16 S39 ALA LEU 0.00802585
S16 S39 ALA MET 0.000254657
S16 S39 ALA ASN 0.000254657

S16 S39 ALA PRO 0.000254657
S16 S39 ALA GLN 0.000254657
S16 S39 ALA ARG 0.000254657
S16 S39 ALA SER 0.000254657
S16 S39 ALA THR 0.000254657
S16 S39 ALA VAL -0.10724
S16 S39 ALA TRP 0.0119142
S16 S39 ALA TYR 0.000254657
S16 S39 ALA --- 0.000254657
S16 S39 CYS ILE 0.00155786
S16 S39 CYS LEU 0.00147688
S16 S39 CYS VAL 0.0206377
S16 S39 CYS TRP 0.000686493
S16 S39 ASP ILE 0.00155786
S16 S39 ASP LEU 0.00147688
S16 S39 ASP VAL 0.0206377
S16 S39 ASP TRP 0.000686493
S16 S39 GLU ILE 0.00155786
S16 S39 GLU LEU 0.00147688
S16 S39 GLU VAL 0.0206377
S16 S39 GLU TRP 0.000686493
S16 S39 PHE ILE 0.00155786
S16 S39 PHE LEU 0.00147688
S16 S39 PHE VAL 0.0206377
S16 S39 PHE TRP 0.000686493
S16 S39 GLY ILE 0.00155786
S16 S39 GLY LEU 0.00147688
S16 S39 GLY VAL 0.0206377
S16 S39 GLY TRP 0.000686493
S16 S39 HIS ILE 0.00155786
S16 S39 HIS LEU 0.00147688
S16 S39 HIS VAL 0.0206377
S16 S39 HIS TRP 0.000686493
S16 S39 ILE ALA 0.00601161
S16 S39 ILE CYS 0.00601161
S16 S39 ILE ASP 0.00601161
S16 S39 ILE GLU 0.00601161
S16 S39 ILE PHE 0.00601161
S16 S39 ILE GLY 0.00601161
S16 S39 ILE HIS 0.00601161
S16 S39 ILE ILE 0.0789104
S16 S39 ILE LYS 0.00601161
S16 S39 ILE LEU 0.0913591
S16 S39 ILE MET 0.00601161
S16 S39 ILE ASN 0.00601161
S16 S39 ILE PRO 0.00601161
S16 S39 ILE GLN 0.00601161
S16 S39 ILE ARG 0.00601161
S16 S39 ILE SER 0.00601161
S16 S39 ILE THR 0.00601161
S16 S39 ILE VAL -0.537017
S16 S39 ILE TRP 0.130784
S16 S39 ILE TYR 0.00601161
S16 S39 ILE --- 0.00601161
S16 S39 LYS ILE 0.00155786
S16 S39 LYS LEU 0.00147688
S16 S39 LYS VAL 0.0206377
S16 S39 LYS TRP 0.000686493
S16 S39 LEU ALA 5.6253e-05
S16 S39 LEU CYS 5.6253e-05
S16 S39 LEU ASP 5.6253e-05
S16 S39 LEU GLU 5.6253e-05
S16 S39 LEU PHE 5.6253e-05

S16 S39 LEU GLY 5.6253e-05
S16 S39 LEU HIS 5.6253e-05
S16 S39 LEU ILE 0.0199643
S16 S39 LEU LYS 5.6253e-05
S16 S39 LEU LEU 0.0154632
S16 S39 LEU MET 5.6253e-05
S16 S39 LEU ASN 5.6253e-05
S16 S39 LEU PRO 5.6253e-05
S16 S39 LEU GLN 5.6253e-05
S16 S39 LEU ARG 5.6253e-05
S16 S39 LEU SER 5.6253e-05
S16 S39 LEU THR 5.6253e-05
S16 S39 LEU VAL -0.0743382
S16 S39 LEU TRP 0.00853725
S16 S39 LEU TYR 5.6253e-05
S16 S39 LEU --- 5.6253e-05
S16 S39 MET ILE 0.00155786
S16 S39 MET LEU 0.00147688
S16 S39 MET VAL 0.0206377
S16 S39 MET TRP 0.000686493
S16 S39 ASN ILE 0.00155786
S16 S39 ASN LEU 0.00147688
S16 S39 ASN VAL 0.0206377
S16 S39 ASN TRP 0.000686493
S16 S39 PRO ILE 0.00155786
S16 S39 PRO LEU 0.00147688
S16 S39 PRO VAL 0.0206377
S16 S39 PRO TRP 0.000686493
S16 S39 GLN ILE 0.00155786
S16 S39 GLN LEU 0.00147688
S16 S39 GLN VAL 0.0206377
S16 S39 GLN TRP 0.000686493
S16 S39 ARG ILE 0.00155786
S16 S39 ARG LEU 0.00147688
S16 S39 ARG VAL 0.0206377
S16 S39 ARG TRP 0.000686493
S16 S39 SER ILE 0.00155786
S16 S39 SER LEU 0.00147688
S16 S39 SER VAL 0.0206377
S16 S39 SER TRP 0.000686493
S16 S39 THR ALA 0.00105994
S16 S39 THR CYS 0.00105994
S16 S39 THR ASP 0.00105994
S16 S39 THR GLU 0.00105994
S16 S39 THR PHE 0.00105994
S16 S39 THR GLY 0.00105994
S16 S39 THR HIS 0.00105994
S16 S39 THR ILE 0.110842
S16 S39 THR LYS 0.00105994
S16 S39 THR LEU 0.0546519
S16 S39 THR MET 0.00105994
S16 S39 THR ASN 0.00105994
S16 S39 THR PRO 0.00105994
S16 S39 THR GLN 0.00105994
S16 S39 THR ARG 0.00105994
S16 S39 THR SER 0.00105994
S16 S39 THR THR 0.00105994
S16 S39 THR VAL -0.244493
S16 S39 THR TRP 0.0243621
S16 S39 THR TYR 0.00105994
S16 S39 THR --- 0.00105994
S16 S39 VAL ALA 0.0113558
S16 S39 VAL CYS 0.0113558

S16 S39 VAL ASP 0.0113558
S16 S39 VAL GLU 0.0113558
S16 S39 VAL PHE 0.0113558
S16 S39 VAL GLY 0.0113558
S16 S39 VAL HIS 0.0113558
S16 S39 VAL ILE -0.314349
S16 S39 VAL LYS 0.0113558
S16 S39 VAL LEU -0.241487
S16 S39 VAL MET 0.0113558
S16 S39 VAL ASN 0.0113558
S16 S39 VAL PRO 0.0113558
S16 S39 VAL GLN 0.0113558
S16 S39 VAL ARG 0.0113558
S16 S39 VAL SER 0.0113558
S16 S39 VAL THR 0.0113558
S16 S39 VAL VAL 0.463807
S16 S39 VAL TRP -0.225186
S16 S39 VAL TYR 0.0113558
S16 S39 VAL --- 0.0113558
S16 S39 TRP ILE 0.00155786
S16 S39 TRP LEU 0.00147688
S16 S39 TRP VAL 0.0206377
S16 S39 TRP TRP 0.000686493
S16 S39 TYR ILE 0.00155786
S16 S39 TYR LEU 0.00147688
S16 S39 TYR VAL 0.0206377
S16 S39 TYR TRP 0.000686493
S16 S39 --- ILE 0.00155786
S16 S39 --- LEU 0.00147688
S16 S39 --- VAL 0.0206377
S16 S39 --- TRP 0.000686493
S16 S40 ALA ALA 0.000151929
S16 S40 ALA CYS 0.000151929
S16 S40 ALA ASP 0.000151929
S16 S40 ALA GLU 0.000151929
S16 S40 ALA PHE 0.000151929
S16 S40 ALA GLY 0.000151929
S16 S40 ALA HIS 0.000151929
S16 S40 ALA ILE 0.0161677
S16 S40 ALA LYS 0.000151929
S16 S40 ALA LEU 0.0176943
S16 S40 ALA MET 0.000151929
S16 S40 ALA ASN 0.000151929
S16 S40 ALA PRO 0.000151929
S16 S40 ALA GLN 0.000151929
S16 S40 ALA ARG 0.000151929
S16 S40 ALA SER 0.000151929
S16 S40 ALA THR 0.000151929
S16 S40 ALA VAL -0.102372
S16 S40 ALA TRP 0.000151929
S16 S40 ALA TYR 0.000151929
S16 S40 ALA --- 0.000151929
S16 S40 CYS ILE 0.00210153
S16 S40 CYS LEU 0.000147473
S16 S40 CYS VAL 0.0221099
S16 S40 ASP ILE 0.00210153
S16 S40 ASP LEU 0.000147473
S16 S40 ASP VAL 0.0221099
S16 S40 GLU ILE 0.00210153
S16 S40 GLU LEU 0.000147473
S16 S40 GLU VAL 0.0221099
S16 S40 PHE ILE 0.00210153
S16 S40 PHE LEU 0.000147473

S16 S40 PHE VAL 0.0221099
S16 S40 GLY ILE 0.00210153
S16 S40 GLY LEU 0.000147473
S16 S40 GLY VAL 0.0221099
S16 S40 HIS ILE 0.00210153
S16 S40 HIS LEU 0.000147473
S16 S40 HIS VAL 0.0221099
S16 S40 ILE ALA 0.00815063
S16 S40 ILE CYS 0.00815063
S16 S40 ILE ASP 0.00815063
S16 S40 ILE GLU 0.00815063
S16 S40 ILE PHE 0.00815063
S16 S40 ILE GLY 0.00815063
S16 S40 ILE HIS 0.00815063
S16 S40 ILE ILE -0.0394867
S16 S40 ILE LYS 0.00815063
S16 S40 ILE LEU -0.136094
S16 S40 ILE MET 0.00815063
S16 S40 ILE ASN 0.00815063
S16 S40 ILE PRO 0.00815063
S16 S40 ILE GLN 0.00815063
S16 S40 ILE ARG 0.00815063
S16 S40 ILE SER 0.00815063
S16 S40 ILE THR 0.00815063
S16 S40 ILE VAL -0.104897
S16 S40 ILE TRP 0.00815063
S16 S40 ILE TYR 0.00815063
S16 S40 ILE --- 0.00815063
S16 S40 LYS ILE 0.00210153
S16 S40 LYS LEU 0.000147473
S16 S40 LYS VAL 0.0221099
S16 S40 LEU ALA 1.18254e-06
S16 S40 LEU CYS 1.18254e-06
S16 S40 LEU ASP 1.18254e-06
S16 S40 LEU GLU 1.18254e-06
S16 S40 LEU PHE 1.18254e-06
S16 S40 LEU GLY 1.18254e-06
S16 S40 LEU HIS 1.18254e-06
S16 S40 LEU ILE 0.00741819
S16 S40 LEU LYS 1.18254e-06
S16 S40 LEU LEU 0.00021061
S16 S40 LEU MET 1.18254e-06
S16 S40 LEU ASN 1.18254e-06
S16 S40 LEU PRO 1.18254e-06
S16 S40 LEU GLN 1.18254e-06
S16 S40 LEU ARG 1.18254e-06
S16 S40 LEU SER 1.18254e-06
S16 S40 LEU THR 1.18254e-06
S16 S40 LEU VAL -0.0370673
S16 S40 LEU TRP 1.18254e-06
S16 S40 LEU TYR 1.18254e-06
S16 S40 LEU --- 1.18254e-06
S16 S40 MET ILE 0.00210153
S16 S40 MET LEU 0.000147473
S16 S40 MET VAL 0.0221099
S16 S40 ASN ILE 0.00210153
S16 S40 ASN LEU 0.000147473
S16 S40 ASN VAL 0.0221099
S16 S40 PRO ILE 0.00210153
S16 S40 PRO LEU 0.000147473
S16 S40 PRO VAL 0.0221099
S16 S40 GLN ILE 0.00210153
S16 S40 GLN LEU 0.000147473

S16 S40 GLN VAL 0.0221099
S16 S40 ARG ILE 0.00210153
S16 S40 ARG LEU 0.000147473
S16 S40 ARG VAL 0.0221099
S16 S40 SER ILE 0.00210153
S16 S40 SER LEU 0.000147473
S16 S40 SER VAL 0.0221099
S16 S40 THR ALA 2.25303e-05
S16 S40 THR CYS 2.25303e-05
S16 S40 THR ASP 2.25303e-05
S16 S40 THR GLU 2.25303e-05
S16 S40 THR PHE 2.25303e-05
S16 S40 THR GLY 2.25303e-05
S16 S40 THR HIS 2.25303e-05
S16 S40 THR ILE 0.0087004
S16 S40 THR LYS 2.25303e-05
S16 S40 THR LEU 0.00123276
S16 S40 THR MET 2.25303e-05
S16 S40 THR ASN 2.25303e-05
S16 S40 THR PRO 2.25303e-05
S16 S40 THR GLN 2.25303e-05
S16 S40 THR ARG 2.25303e-05
S16 S40 THR SER 2.25303e-05
S16 S40 THR THR 2.25303e-05
S16 S40 THR VAL -0.046956
S16 S40 THR TRP 2.25303e-05
S16 S40 THR TYR 2.25303e-05
S16 S40 THR --- 2.25303e-05
S16 S40 VAL ALA 0.00808283
S16 S40 VAL CYS 0.00808283
S16 S40 VAL ASP 0.00808283
S16 S40 VAL GLU 0.00808283
S16 S40 VAL PHE 0.00808283
S16 S40 VAL GLY 0.00808283
S16 S40 VAL HIS 0.00808283
S16 S40 VAL ILE -0.0985403
S16 S40 VAL LYS 0.00808283
S16 S40 VAL LEU 0.0596728
S16 S40 VAL MET 0.00808283
S16 S40 VAL ASN 0.00808283
S16 S40 VAL PRO 0.00808283
S16 S40 VAL GLN 0.00808283
S16 S40 VAL ARG 0.00808283
S16 S40 VAL SER 0.00808283
S16 S40 VAL THR 0.00808283
S16 S40 VAL VAL -0.23079
S16 S40 VAL TRP 0.00808283
S16 S40 VAL TYR 0.00808283
S16 S40 VAL --- 0.00808283
S16 S40 TRP ILE 0.00210153
S16 S40 TRP LEU 0.000147473
S16 S40 TRP VAL 0.0221099
S16 S40 TYR ILE 0.00210153
S16 S40 TYR LEU 0.000147473
S16 S40 TYR VAL 0.0221099
S16 S40 --- ILE 0.00210153
S16 S40 --- LEU 0.000147473
S16 S40 --- VAL 0.0221099
S17 S18 ALA GLU 0.0236257
S17 S18 ALA HIS 0.00109344
S17 S18 CYS GLU 0.0236257
S17 S18 CYS HIS 0.00109344
S17 S18 ASP GLU 0.0236257

S17 S18 ASP HIS 0.00109344
S17 S18 GLU GLU 0.0236257
S17 S18 GLU HIS 0.00109344
S17 S18 PHE ALA 0.00532494
S17 S18 PHE CYS 0.00532494
S17 S18 PHE ASP 0.00532494
S17 S18 PHE GLU -0.150793
S17 S18 PHE PHE 0.00532494
S17 S18 PHE GLY 0.00532494
S17 S18 PHE HIS -0.0634527
S17 S18 PHE ILE 0.00532494
S17 S18 PHE LYS 0.00532494
S17 S18 PHE LEU 0.00532494
S17 S18 PHE MET 0.00532494
S17 S18 PHE ASN 0.00532494
S17 S18 PHE PRO 0.00532494
S17 S18 PHE GLN 0.00532494
S17 S18 PHE ARG 0.00532494
S17 S18 PHE SER 0.00532494
S17 S18 PHE THR 0.00532494
S17 S18 PHE VAL 0.00532494
S17 S18 PHE TRP 0.00532494
S17 S18 PHE TYR 0.00532494
S17 S18 PHE --- 0.00532494
S17 S18 GLY GLU 0.0236257
S17 S18 GLY HIS 0.00109344
S17 S18 HIS ALA 0.00493137
S17 S18 HIS CYS 0.00493137
S17 S18 HIS ASP 0.00493137
S17 S18 HIS GLU -0.00692213
S17 S18 HIS PHE 0.00493137
S17 S18 HIS GLY 0.00493137
S17 S18 HIS HIS -0.200644
S17 S18 HIS ILE 0.00493137
S17 S18 HIS LYS 0.00493137
S17 S18 HIS LEU 0.00493137
S17 S18 HIS MET 0.00493137
S17 S18 HIS ASN 0.00493137
S17 S18 HIS PRO 0.00493137
S17 S18 HIS GLN 0.00493137
S17 S18 HIS ARG 0.00493137
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S17 S18 HIS THR 0.00493137
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S17 S18 HIS TRP 0.00493137
S17 S18 HIS TYR 0.00493137
S17 S18 HIS --- 0.00493137
S17 S18 ILE ALA 0.000668427
S17 S18 ILE CYS 0.000668427
S17 S18 ILE ASP 0.000668427
S17 S18 ILE GLU -0.108754
S17 S18 ILE PHE 0.000668427
S17 S18 ILE GLY 0.000668427
S17 S18 ILE HIS 0.0155977
S17 S18 ILE ILE 0.000668427
S17 S18 ILE LYS 0.000668427
S17 S18 ILE LEU 0.000668427
S17 S18 ILE MET 0.000668427
S17 S18 ILE ASN 0.000668427
S17 S18 ILE PRO 0.000668427
S17 S18 ILE GLN 0.000668427
S17 S18 ILE ARG 0.000668427
S17 S18 ILE SER 0.000668427

S17 S18 ILE THR 0.000668427
S17 S18 ILE VAL 0.000668427
S17 S18 ILE TRP 0.000668427
S17 S18 ILE TYR 0.000668427
S17 S18 ILE --- 0.000668427
S17 S18 LYS GLU 0.0236257
S17 S18 LYS HIS 0.00109344
S17 S18 LEU GLU 0.0236257
S17 S18 LEU HIS 0.00109344
S17 S18 MET GLU 0.0236257
S17 S18 MET HIS 0.00109344
S17 S18 ASN GLU 0.0236257
S17 S18 ASN HIS 0.00109344
S17 S18 PRO GLU 0.0236257
S17 S18 PRO HIS 0.00109344
S17 S18 GLN GLU 0.0236257
S17 S18 GLN HIS 0.00109344
S17 S18 ARG GLU 0.0236257
S17 S18 ARG HIS 0.00109344
S17 S18 SER GLU 0.0236257
S17 S18 SER HIS 0.00109344
S17 S18 THR GLU 0.0236257
S17 S18 THR HIS 0.00109344
S17 S18 VAL GLU 0.0236257
S17 S18 VAL HIS 0.00109344
S17 S18 TRP ALA 7.05917e-05
S17 S18 TRP CYS 7.05917e-05
S17 S18 TRP ASP 7.05917e-05
S17 S18 TRP GLU -0.0436625
S17 S18 TRP PHE 7.05917e-05
S17 S18 TRP GLY 7.05917e-05
S17 S18 TRP HIS 0.0212156
S17 S18 TRP ILE 7.05917e-05
S17 S18 TRP LYS 7.05917e-05
S17 S18 TRP LEU 7.05917e-05
S17 S18 TRP MET 7.05917e-05
S17 S18 TRP ASN 7.05917e-05
S17 S18 TRP PRO 7.05917e-05
S17 S18 TRP GLN 7.05917e-05
S17 S18 TRP ARG 7.05917e-05
S17 S18 TRP SER 7.05917e-05
S17 S18 TRP THR 7.05917e-05
S17 S18 TRP VAL 7.05917e-05
S17 S18 TRP TRP 7.05917e-05
S17 S18 TRP TYR 7.05917e-05
S17 S18 TRP --- 7.05917e-05
S17 S18 TYR ALA 0.00184489
S17 S18 TYR CYS 0.00184489
S17 S18 TYR ASP 0.00184489
S17 S18 TYR GLU -0.203237
S17 S18 TYR PHE 0.00184489
S17 S18 TYR GLY 0.00184489
S17 S18 TYR HIS 0.101181
S17 S18 TYR ILE 0.00184489
S17 S18 TYR LYS 0.00184489
S17 S18 TYR LEU 0.00184489
S17 S18 TYR MET 0.00184489
S17 S18 TYR ASN 0.00184489
S17 S18 TYR PRO 0.00184489
S17 S18 TYR GLN 0.00184489
S17 S18 TYR ARG 0.00184489
S17 S18 TYR SER 0.00184489
S17 S18 TYR THR 0.00184489

S17 S18 TYR VAL 0.00184489
S17 S18 TYR TRP 0.00184489
S17 S18 TYR TYR 0.00184489
S17 S18 TYR --- 0.00184489
S17 S18 --- GLU 0.0236258
S17 S18 --- HIS 0.00109344
S17 S19 ALA ALA 0.0177055
S17 S19 ALA SER 0.00663819
S17 S19 ALA TYR 0.000375478
S17 S19 CYS ALA 0.0177055
S17 S19 CYS SER 0.00663819
S17 S19 CYS TYR 0.000375478
S17 S19 ASP ALA 0.0177055
S17 S19 ASP SER 0.00663819
S17 S19 ASP TYR 0.000375478
S17 S19 GLU ALA 0.0177055
S17 S19 GLU SER 0.00663819
S17 S19 GLU TYR 0.000375478
S17 S19 PHE ALA -0.176475
S17 S19 PHE CYS 0.00889479
S17 S19 PHE ASP 0.00889479
S17 S19 PHE GLU 0.00889479
S17 S19 PHE PHE 0.00889479
S17 S19 PHE GLY 0.00889479
S17 S19 PHE HIS 0.00889479
S17 S19 PHE ILE 0.00889479
S17 S19 PHE LYS 0.00889479
S17 S19 PHE LEU 0.00889479
S17 S19 PHE MET 0.00889479
S17 S19 PHE ASN 0.00889479
S17 S19 PHE PRO 0.00889479
S17 S19 PHE GLN 0.00889479
S17 S19 PHE ARG 0.00889479
S17 S19 PHE SER 0.0455162
S17 S19 PHE THR 0.00889479
S17 S19 PHE VAL 0.00889479
S17 S19 PHE TRP 0.00889479
S17 S19 PHE TYR -0.142219
S17 S19 PHE --- 0.00889479
S17 S19 GLY ALA 0.0177055
S17 S19 GLY SER 0.00663819
S17 S19 GLY TYR 0.000375478
S17 S19 HIS ALA -0.354428
S17 S19 HIS CYS 0.00621669
S17 S19 HIS ASP 0.00621669
S17 S19 HIS GLU 0.00621669
S17 S19 HIS PHE 0.00621669
S17 S19 HIS GLY 0.00621669
S17 S19 HIS HIS 0.00621669
S17 S19 HIS ILE 0.00621669
S17 S19 HIS LYS 0.00621669
S17 S19 HIS LEU 0.00621669
S17 S19 HIS MET 0.00621669
S17 S19 HIS ASN 0.00621669
S17 S19 HIS PRO 0.00621669
S17 S19 HIS GLN 0.00621669
S17 S19 HIS ARG 0.00621669
S17 S19 HIS SER 0.0958558
S17 S19 HIS THR 0.00621669
S17 S19 HIS VAL 0.00621669
S17 S19 HIS TRP 0.00621669
S17 S19 HIS TYR 0.032801
S17 S19 HIS --- 0.00621669

S17 S19 ILE ALA 0.309586
S17 S19 ILE CYS 0.00076988
S17 S19 ILE ASP 0.00076988
S17 S19 ILE GLU 0.00076988
S17 S19 ILE PHE 0.00076988
S17 S19 ILE GLY 0.00076988
S17 S19 ILE HIS 0.00076988
S17 S19 ILE ILE 0.00076988
S17 S19 ILE LYS 0.00076988
S17 S19 ILE LEU 0.00076988
S17 S19 ILE MET 0.00076988
S17 S19 ILE ASN 0.00076988
S17 S19 ILE PRO 0.00076988
S17 S19 ILE GLN 0.00076988
S17 S19 ILE ARG 0.00076988
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S17 S19 ILE THR 0.00076988
S17 S19 ILE VAL 0.00076988
S17 S19 ILE TRP 0.00076988
S17 S19 ILE TYR 0.0113241
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S17 S19 LYS SER 0.00663819
S17 S19 LYS TYR 0.000375478
S17 S19 LEU ALA 0.0177055
S17 S19 LEU SER 0.00663819
S17 S19 LEU TYR 0.000375478
S17 S19 MET ALA 0.0177055
S17 S19 MET SER 0.00663819
S17 S19 MET TYR 0.000375478
S17 S19 ASN ALA 0.0177055
S17 S19 ASN SER 0.00663819
S17 S19 ASN TYR 0.000375478
S17 S19 PRO ALA 0.0177055
S17 S19 PRO SER 0.00663819
S17 S19 PRO TYR 0.000375478
S17 S19 GLN ALA 0.0177055
S17 S19 GLN SER 0.00663819
S17 S19 GLN TYR 0.000375478
S17 S19 ARG ALA 0.0177055
S17 S19 ARG SER 0.00663819
S17 S19 ARG TYR 0.000375478
S17 S19 SER ALA 0.0177055
S17 S19 SER SER 0.00663819
S17 S19 SER TYR 0.000375478
S17 S19 THR ALA 0.0177055
S17 S19 THR SER 0.00663819
S17 S19 THR TYR 0.000375478
S17 S19 VAL ALA 0.0177055
S17 S19 VAL SER 0.00663819
S17 S19 VAL TYR 0.000375478
S17 S19 TRP ALA -0.0968355
S17 S19 TRP CYS 6.09635e-05
S17 S19 TRP ASP 6.09635e-05
S17 S19 TRP GLU 6.09635e-05
S17 S19 TRP PHE 6.09635e-05
S17 S19 TRP GLY 6.09635e-05
S17 S19 TRP HIS 6.09635e-05
S17 S19 TRP ILE 6.09635e-05
S17 S19 TRP LYS 6.09635e-05
S17 S19 TRP LEU 6.09635e-05
S17 S19 TRP MET 6.09635e-05
S17 S19 TRP ASN 6.09635e-05

S17 S19 TRP PRO 6.09635e-05
S17 S19 TRP GLN 6.09635e-05
S17 S19 TRP ARG 6.09635e-05
S17 S19 TRP SER 0.0707743
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S17 S19 TRP VAL 6.09635e-05
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S17 S19 TRP TYR 0.00385819
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S17 S19 TYR ALA -0.141264
S17 S19 TYR CYS 0.00275115
S17 S19 TYR ASP 0.00275115
S17 S19 TYR GLU 0.00275115
S17 S19 TYR PHE 0.00275115
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S17 S19 TYR LYS 0.00275115
S17 S19 TYR LEU 0.00275115
S17 S19 TYR MET 0.00275115
S17 S19 TYR ASN 0.00275115
S17 S19 TYR PRO 0.00275115
S17 S19 TYR GLN 0.00275115
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S17 S19 TYR THR 0.00275115
S17 S19 TYR VAL 0.00275115
S17 S19 TYR TRP 0.00275115
S17 S19 TYR TYR 0.0272485
S17 S19 TYR --- 0.00275115
S17 S19 --- ALA 0.0177055
S17 S19 --- SER 0.00663819
S17 S19 --- TYR 0.000375478
S17 S20 ALA PHE 0.0148255
S17 S20 ALA LEU 0.00218488
S17 S20 ALA MET 0.00636975
S17 S20 ALA VAL 0.00133906
S17 S20 CYS PHE 0.0148255
S17 S20 CYS LEU 0.00218488
S17 S20 CYS MET 0.00636975
S17 S20 CYS VAL 0.00133906
S17 S20 ASP PHE 0.0148255
S17 S20 ASP LEU 0.00218488
S17 S20 ASP MET 0.00636975
S17 S20 ASP VAL 0.00133906
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S17 S20 GLU LEU 0.00218488
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S17 S20 GLU VAL 0.00133906
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S17 S20 PHE ASP 0.0109135
S17 S20 PHE GLU 0.0109135
S17 S20 PHE PHE 0.145545
S17 S20 PHE GLY 0.0109135
S17 S20 PHE HIS 0.0109135
S17 S20 PHE ILE 0.0109135
S17 S20 PHE LYS 0.0109135
S17 S20 PHE LEU -0.0531957
S17 S20 PHE MET -0.431627
S17 S20 PHE ASN 0.0109135
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S17 S20 PHE GLN 0.0109135

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S17 S20 PHE SER 0.0109135
S17 S20 PHE THR 0.0109135
S17 S20 PHE VAL 0.0406763
S17 S20 PHE TRP 0.0109135
S17 S20 PHE TYR 0.0109135
S17 S20 PHE --- 0.0109135
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S17 S20 GLY VAL 0.00133906
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S17 S20 HIS CYS 0.00787784
S17 S20 HIS ASP 0.00787784
S17 S20 HIS GLU 0.00787784
S17 S20 HIS PHE -0.110333
S17 S20 HIS GLY 0.00787784
S17 S20 HIS HIS 0.00787784
S17 S20 HIS ILE 0.00787784
S17 S20 HIS LYS 0.00787784
S17 S20 HIS LEU 0.561522
S17 S20 HIS MET -0.91859
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S17 S20 ILE ALA 0.000929718
S17 S20 ILE CYS 0.000929718
S17 S20 ILE ASP 0.000929718
S17 S20 ILE GLU 0.000929718
S17 S20 ILE PHE 0.226982
S17 S20 ILE GLY 0.000929718
S17 S20 ILE HIS 0.000929718
S17 S20 ILE ILE 0.000929718
S17 S20 ILE LYS 0.000929718
S17 S20 ILE LEU -0.498876
S17 S20 ILE MET 0.16139
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S17 S20 ILE PRO 0.000929718
S17 S20 ILE GLN 0.000929718
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S17 S20 ILE TYR 0.000929718
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S17 S20 LEU PHE 0.0148255
S17 S20 LEU LEU 0.00218488
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S17 S20 LEU VAL 0.00133906
S17 S20 MET PHE 0.0148255
S17 S20 MET LEU 0.00218488

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S17 S20 MET VAL 0.00133906
S17 S20 ASN PHE 0.0148255
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S17 S20 PRO PHE 0.0148255
S17 S20 PRO LEU 0.00218488
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S17 S20 PRO VAL 0.00133906
S17 S20 GLN PHE 0.0148255
S17 S20 GLN LEU 0.00218488
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S17 S20 TRP CYS 2.4499e-05
S17 S20 TRP ASP 2.4499e-05
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S17 S20 TRP PHE -0.0858659
S17 S20 TRP GLY 2.4499e-05
S17 S20 TRP HIS 2.4499e-05
S17 S20 TRP ILE 2.4499e-05
S17 S20 TRP LYS 2.4499e-05
S17 S20 TRP LEU 0.0131413
S17 S20 TRP MET 0.0285929
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S17 S20 TYR ASP 0.00450417
S17 S20 TYR GLU 0.00450417
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S17 S20 TYR GLY 0.00450417
S17 S20 TYR HIS 0.00450417
S17 S20 TYR ILE 0.00450417
S17 S20 TYR LYS 0.00450417
S17 S20 TYR LEU -0.0937449
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S17 S20 TYR ASN 0.00450417

S17 S20 TYR PRO 0.00450417
S17 S20 TYR GLN 0.00450417
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S17 S20 --- VAL 0.00133906
S17 S21 ALA PHE 0.000763334
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S17 S21 ALA VAL 0.0054356
S17 S21 ALA TYR 0.00225093
S17 S21 CYS PHE 0.000763334
S17 S21 CYS ILE 0.0162693
S17 S21 CYS VAL 0.0054356
S17 S21 CYS TYR 0.00225093
S17 S21 ASP PHE 0.000763334
S17 S21 ASP ILE 0.0162693
S17 S21 ASP VAL 0.0054356
S17 S21 ASP TYR 0.00225093
S17 S21 GLU PHE 0.000763334
S17 S21 GLU ILE 0.0162693
S17 S21 GLU VAL 0.0054356
S17 S21 GLU TYR 0.00225093
S17 S21 PHE ALA 0.0109664
S17 S21 PHE CYS 0.0109664
S17 S21 PHE ASP 0.0109664
S17 S21 PHE GLU 0.0109664
S17 S21 PHE PHE -0.459233
S17 S21 PHE GLY 0.0109664
S17 S21 PHE HIS 0.0109664
S17 S21 PHE ILE -0.0112025
S17 S21 PHE LYS 0.0109664
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S17 S21 PHE ASN 0.0109664
S17 S21 PHE PRO 0.0109664
S17 S21 PHE GLN 0.0109664
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S17 S21 PHE SER 0.0109664
S17 S21 PHE THR 0.0109664
S17 S21 PHE VAL 0.0964439
S17 S21 PHE TRP 0.0109664
S17 S21 PHE TYR 0.0744914
S17 S21 PHE --- 0.0109664
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S17 S21 GLY VAL 0.0054356
S17 S21 GLY TYR 0.00225093
S17 S21 HIS ALA 0.00636453
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S17 S21 HIS ASP 0.00636453
S17 S21 HIS GLU 0.00636453
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S17 S21 HIS HIS 0.00636453
S17 S21 HIS ILE -0.379711
S17 S21 HIS LYS 0.00636453

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S17 S21 HIS MET 0.00636453
S17 S21 HIS ASN 0.00636453
S17 S21 HIS PRO 0.00636453
S17 S21 HIS GLN 0.00636453
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S17 S21 HIS TYR -0.424889
S17 S21 HIS --- 0.00636453
S17 S21 ILE ALA 0.00147544
S17 S21 ILE CYS 0.00147544
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S17 S21 ILE GLY 0.00147544
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S17 S21 ILE ILE -0.0344767
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S17 S21 ILE TYR 0.105261
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S17 S21 LYS TYR 0.00225093
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S17 S21 PRO TYR 0.00225093
S17 S21 GLN PHE 0.000763334
S17 S21 GLN ILE 0.0162693
S17 S21 GLN VAL 0.0054356
S17 S21 GLN TYR 0.00225093
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S17 S21 TYR CYS 0.00401095
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S17 S21 TYR LYS 0.00401095
S17 S21 TYR LEU 0.00401095
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S17 S21 TYR TRP 0.00401095
S17 S21 TYR TYR 0.102806
S17 S21 TYR --- 0.00401095
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S17 S22 CYS ASN 0.0208491

S17 S22 CYS TYR 0.000972962
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S17 S22 ASP GLU 0.000415228
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S17 S22 ASP TYR 0.000972962
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S17 S22 HIS ALA 0.00732705
S17 S22 HIS CYS 0.00732705
S17 S22 HIS ASP 0.13495
S17 S22 HIS GLU -0.308001
S17 S22 HIS PHE 0.00732705
S17 S22 HIS GLY 0.00732705
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S17 S22 HIS LYS 0.00732705
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S17 S22 HIS --- 0.00732705
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S17 S22 ILE CYS 0.0023263
S17 S22 ILE ASP -0.729963
S17 S22 ILE GLU 0.0501211
S17 S22 ILE PHE 0.0023263
S17 S22 ILE GLY 0.0023263
S17 S22 ILE HIS 0.0023263
S17 S22 ILE ILE 0.0023263

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S17 S22 ILE LEU 0.0023263
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S17 S22 TRP HIS 9.91797e-05
S17 S22 TRP ILE 9.91797e-05
S17 S22 TRP LYS 9.91797e-05
S17 S22 TRP LEU 9.91797e-05

S17 S22 TRP MET 9.91797e-05
S17 S22 TRP ASN -0.0488365
S17 S22 TRP PRO 9.91797e-05
S17 S22 TRP GLN 9.91797e-05
S17 S22 TRP ARG 9.91797e-05
S17 S22 TRP SER 9.91797e-05
S17 S22 TRP THR 9.91797e-05
S17 S22 TRP VAL 9.91797e-05
S17 S22 TRP TRP 9.91797e-05
S17 S22 TRP TYR 0.00680342
S17 S22 TRP --- 9.91798e-05
S17 S22 TYR ALA 0.00337275
S17 S22 TYR CYS 0.00337275
S17 S22 TYR ASP 0.0764042
S17 S22 TYR GLU 0.195591
S17 S22 TYR PHE 0.00337275
S17 S22 TYR GLY 0.00337275
S17 S22 TYR HIS 0.00337275
S17 S22 TYR ILE 0.00337275
S17 S22 TYR LYS 0.00337275
S17 S22 TYR LEU 0.00337275
S17 S22 TYR MET 0.00337275
S17 S22 TYR ASN -0.469823
S17 S22 TYR PRO 0.00337275
S17 S22 TYR GLN 0.00337275
S17 S22 TYR ARG 0.00337275
S17 S22 TYR SER 0.00337275
S17 S22 TYR THR 0.00337275
S17 S22 TYR VAL 0.00337275
S17 S22 TYR TRP 0.00337275
S17 S22 TYR TYR 0.0734879
S17 S22 TYR --- 0.00337274
S17 S22 --- ASP 0.00248193
S17 S22 --- GLU 0.000415228
S17 S22 --- ASN 0.0208491
S17 S22 --- TYR 0.000972962
S17 S23 ALA ILE 0.0177338
S17 S23 ALA LEU 0.00698542
S17 S23 CYS ILE 0.0177338
S17 S23 CYS LEU 0.00698542
S17 S23 ASP ILE 0.0177338
S17 S23 ASP LEU 0.00698542
S17 S23 GLU ILE 0.0177338
S17 S23 GLU LEU 0.00698542
S17 S23 PHE ALA 0.00633788
S17 S23 PHE CYS 0.00633788
S17 S23 PHE ASP 0.00633788
S17 S23 PHE GLU 0.00633788
S17 S23 PHE PHE 0.00633788
S17 S23 PHE GLY 0.00633788
S17 S23 PHE HIS 0.00633788
S17 S23 PHE ILE 0.187575
S17 S23 PHE LYS 0.00633788
S17 S23 PHE LEU -0.421067
S17 S23 PHE MET 0.00633788
S17 S23 PHE ASN 0.00633788
S17 S23 PHE PRO 0.00633788
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S17 S23 PHE THR 0.00633788
S17 S23 PHE VAL 0.00633788
S17 S23 PHE TRP 0.00633788

S17 S23 PHE TYR 0.00633788
S17 S23 PHE --- 0.00633788
S17 S23 GLY ILE 0.0177338
S17 S23 GLY LEU 0.00698542
S17 S23 HIS ALA 0.00484813
S17 S23 HIS CYS 0.00484813
S17 S23 HIS ASP 0.00484813
S17 S23 HIS GLU 0.00484813
S17 S23 HIS PHE 0.00484813
S17 S23 HIS GLY 0.00484813
S17 S23 HIS HIS 0.00484813
S17 S23 HIS ILE -0.179022
S17 S23 HIS LYS 0.00484813
S17 S23 HIS LEU -0.0269627
S17 S23 HIS MET 0.00484813
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S17 S23 HIS TRP 0.00484813
S17 S23 HIS TYR 0.00484813
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S17 S23 ILE CYS 0.00169658
S17 S23 ILE ASP 0.00169658
S17 S23 ILE GLU 0.00169658
S17 S23 ILE PHE 0.00169658
S17 S23 ILE GLY 0.00169658
S17 S23 ILE HIS 0.00169658
S17 S23 ILE ILE -0.928563
S17 S23 ILE LYS 0.00169658
S17 S23 ILE LEU 0.815872
S17 S23 ILE MET 0.00169658
S17 S23 ILE ASN 0.00169658
S17 S23 ILE PRO 0.00169658
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S17 S23 ILE TRP 0.00169658
S17 S23 ILE TYR 0.00169658
S17 S23 ILE --- 0.00169658
S17 S23 LYS ILE 0.0177338
S17 S23 LYS LEU 0.00698542
S17 S23 LEU ILE 0.0177338
S17 S23 LEU LEU 0.00698542
S17 S23 MET ILE 0.0177338
S17 S23 MET LEU 0.00698542
S17 S23 ASN ILE 0.0177338
S17 S23 ASN LEU 0.00698542
S17 S23 PRO ILE 0.0177338
S17 S23 PRO LEU 0.00698542
S17 S23 GLN ILE 0.0177338
S17 S23 GLN LEU 0.00698542
S17 S23 ARG ILE 0.0177338
S17 S23 ARG LEU 0.00698542
S17 S23 SER ILE 0.0177338
S17 S23 SER LEU 0.00698542
S17 S23 THR ILE 0.0177338

S17 S23 THR LEU 0.00698542
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S17 S23 VAL LEU 0.00698542
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S17 S23 TRP CYS 0.000254897
S17 S23 TRP ASP 0.000254897
S17 S23 TRP GLU 0.000254897
S17 S23 TRP PHE 0.000254897
S17 S23 TRP GLY 0.000254897
S17 S23 TRP HIS 0.000254897
S17 S23 TRP ILE 0.61661
S17 S23 TRP LYS 0.000254897
S17 S23 TRP LEU -0.642559
S17 S23 TRP MET 0.000254897
S17 S23 TRP ASN 0.000254897
S17 S23 TRP PRO 0.000254897
S17 S23 TRP GLN 0.000254897
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S17 S23 TYR GLU 0.00260483
S17 S23 TYR PHE 0.00260483
S17 S23 TYR GLY 0.00260483
S17 S23 TYR HIS 0.00260483
S17 S23 TYR ILE -0.165026
S17 S23 TYR LYS 0.00260483
S17 S23 TYR LEU 0.0485305
S17 S23 TYR MET 0.00260483
S17 S23 TYR ASN 0.00260483
S17 S23 TYR PRO 0.00260483
S17 S23 TYR GLN 0.00260483
S17 S23 TYR ARG 0.00260483
S17 S23 TYR SER 0.00260483
S17 S23 TYR THR 0.00260483
S17 S23 TYR VAL 0.00260483
S17 S23 TYR TRP 0.00260483
S17 S23 TYR TYR 0.00260483
S17 S23 TYR --- 0.00260483
S17 S23 --- ILE 0.0177338
S17 S23 --- LEU 0.00698542
S17 S24 ALA GLY 0.0245632
S17 S24 ALA SER 0.000155978
S17 S24 CYS GLY 0.0245632
S17 S24 CYS SER 0.000155978
S17 S24 ASP GLY 0.0245632
S17 S24 ASP SER 0.000155978
S17 S24 GLU GLY 0.0245632
S17 S24 GLU SER 0.000155978
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S17 S24 PHE CYS 0.00585894
S17 S24 PHE ASP 0.00585894
S17 S24 PHE GLU 0.00585894
S17 S24 PHE PHE 0.00585894
S17 S24 PHE GLY -0.0773601
S17 S24 PHE HIS 0.00585894
S17 S24 PHE ILE 0.00585894

S17 S24 PHE LYS 0.00585894
S17 S24 PHE LEU 0.00585894
S17 S24 PHE MET 0.00585894
S17 S24 PHE ASN 0.00585894
S17 S24 PHE PRO 0.00585894
S17 S24 PHE GLN 0.00585894
S17 S24 PHE ARG 0.00585894
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S17 S24 PHE VAL 0.00585894
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S17 S24 PHE TYR 0.00585894
S17 S24 PHE --- 0.00585894
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S17 S24 HIS CYS 0.00325249
S17 S24 HIS ASP 0.00325249
S17 S24 HIS GLU 0.00325249
S17 S24 HIS PHE 0.00325249
S17 S24 HIS GLY -0.210926
S17 S24 HIS HIS 0.00325249
S17 S24 HIS ILE 0.00325249
S17 S24 HIS LYS 0.00325249
S17 S24 HIS LEU 0.00325249
S17 S24 HIS MET 0.00325249
S17 S24 HIS ASN 0.00325249
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S17 S24 HIS ARG 0.00325249
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S17 S24 HIS TYR 0.00325249
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S17 S24 ILE CYS 0.00104741
S17 S24 ILE ASP 0.00104741
S17 S24 ILE GLU 0.00104741
S17 S24 ILE PHE 0.00104741
S17 S24 ILE GLY -0.11385
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S17 S24 ILE ILE 0.00104741
S17 S24 ILE LYS 0.00104741
S17 S24 ILE LEU 0.00104741
S17 S24 ILE MET 0.00104741
S17 S24 ILE ASN 0.00104741
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S17 S24 ILE ARG 0.00104741
S17 S24 ILE SER 0.0134939
S17 S24 ILE THR 0.00104741
S17 S24 ILE VAL 0.00104741
S17 S24 ILE TRP 0.00104741
S17 S24 ILE TYR 0.00104741
S17 S24 ILE --- 0.00104741
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S17 S24 LYS SER 0.000155978
S17 S24 LEU GLY 0.0245632
S17 S24 LEU SER 0.000155978
S17 S24 MET GLY 0.0245632
S17 S24 MET SER 0.000155978

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S17 S24 ASN SER 0.000155978
S17 S24 PRO GLY 0.0245632
S17 S24 PRO SER 0.000155978
S17 S24 GLN GLY 0.0245632
S17 S24 GLN SER 0.000155978
S17 S24 ARG GLY 0.0245632
S17 S24 ARG SER 0.000155978
S17 S24 SER GLY 0.0245632
S17 S24 SER SER 0.000155978
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S17 S24 THR SER 0.000155978
S17 S24 VAL GLY 0.0245632
S17 S24 VAL SER 0.000155978
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S17 S24 TRP CYS 5.18864e-05
S17 S24 TRP ASP 5.18864e-05
S17 S24 TRP GLU 5.18864e-05
S17 S24 TRP PHE 5.18864e-05
S17 S24 TRP GLY -0.0237937
S17 S24 TRP HIS 5.18864e-05
S17 S24 TRP ILE 5.18864e-05
S17 S24 TRP LYS 5.18864e-05
S17 S24 TRP LEU 5.18864e-05
S17 S24 TRP MET 5.18864e-05
S17 S24 TRP ASN 5.18864e-05
S17 S24 TRP PRO 5.18864e-05
S17 S24 TRP GLN 5.18864e-05
S17 S24 TRP ARG 5.18864e-05
S17 S24 TRP SER 0.00170217
S17 S24 TRP THR 5.18864e-05
S17 S24 TRP VAL 5.18864e-05
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S17 S24 TRP TYR 5.18864e-05
S17 S24 TRP --- 5.18864e-05
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S17 S24 TYR CYS 0.00140746
S17 S24 TYR ASP 0.00140746
S17 S24 TYR GLU 0.00140746
S17 S24 TYR PHE 0.00140746
S17 S24 TYR GLY -0.1061
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S17 S24 TYR ILE 0.00140746
S17 S24 TYR LYS 0.00140746
S17 S24 TYR LEU 0.00140746
S17 S24 TYR MET 0.00140746
S17 S24 TYR ASN 0.00140746
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S17 S24 TYR GLN 0.00140746
S17 S24 TYR ARG 0.00140746
S17 S24 TYR SER 0.0123546
S17 S24 TYR THR 0.00140746
S17 S24 TYR VAL 0.00140746
S17 S24 TYR TRP 0.00140746
S17 S24 TYR TYR 0.00140746
S17 S24 TYR --- 0.00140746
S17 S24 --- GLY 0.0245632
S17 S24 --- SER 0.000155978
S17 S25 ALA ASP 1.25508e-05
S17 S25 ALA GLU 9.8106e-05
S17 S25 ALA LYS 0.000622521
S17 S25 ALA ARG 0.00332611
S17 S25 ALA SER 0.0205521

S17 S25 ALA THR 0.000107759
S17 S25 CYS ASP 1.25508e-05
S17 S25 CYS GLU 9.8106e-05
S17 S25 CYS LYS 0.000622521
S17 S25 CYS ARG 0.00332611
S17 S25 CYS SER 0.0205521
S17 S25 CYS THR 0.000107759
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S17 S25 ASP GLU 9.8106e-05
S17 S25 ASP LYS 0.000622521
S17 S25 ASP ARG 0.00332611
S17 S25 ASP SER 0.0205521
S17 S25 ASP THR 0.000107759
S17 S25 GLU ASP 1.25508e-05
S17 S25 GLU GLU 9.8106e-05
S17 S25 GLU LYS 0.000622521
S17 S25 GLU ARG 0.00332611
S17 S25 GLU SER 0.0205521
S17 S25 GLU THR 0.000107759
S17 S25 PHE ALA 0.0182076
S17 S25 PHE CYS 0.0182076
S17 S25 PHE ASP -0.0871013
S17 S25 PHE GLU -0.0793895
S17 S25 PHE PHE 0.0182076
S17 S25 PHE GLY 0.0182076
S17 S25 PHE HIS 0.0182076
S17 S25 PHE ILE 0.0182076
S17 S25 PHE LYS -0.233971
S17 S25 PHE LEU 0.0182076
S17 S25 PHE MET 0.0182076
S17 S25 PHE ASN 0.0182076
S17 S25 PHE PRO 0.0182076
S17 S25 PHE GLN 0.0182076
S17 S25 PHE ARG -0.0294505
S17 S25 PHE SER 0.12051
S17 S25 PHE THR -0.0767835
S17 S25 PHE VAL 0.0182076
S17 S25 PHE TRP 0.0182076
S17 S25 PHE TYR 0.0182076
S17 S25 PHE --- 0.0182076
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S17 S25 GLY GLU 9.8106e-05
S17 S25 GLY LYS 0.000622521
S17 S25 GLY ARG 0.00332611
S17 S25 GLY SER 0.0205521
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S17 S25 HIS ALA 0.00538415
S17 S25 HIS CYS 0.00538415
S17 S25 HIS ASP 0.0489326
S17 S25 HIS GLU 0.0167225
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S17 S25 HIS LYS 0.140762
S17 S25 HIS LEU 0.00538415
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S17 S25 HIS ASN 0.00538415
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S17 S25 HIS THR 0.0242906

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S17 S25 HIS TYR 0.00538415
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S17 S25 ILE ALA 0.00140773
S17 S25 ILE CYS 0.00140773
S17 S25 ILE ASP 0.00621014
S17 S25 ILE GLU 0.0101432
S17 S25 ILE PHE 0.00140773
S17 S25 ILE GLY 0.00140773
S17 S25 ILE HIS 0.00140773
S17 S25 ILE ILE 0.00140773
S17 S25 ILE LYS 0.0161324
S17 S25 ILE LEU 0.00140773
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S17 S25 ILE ASN 0.00140773
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S17 S25 ILE GLN 0.00140773
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S17 S25 ILE SER 0.558053
S17 S25 ILE THR 0.030794
S17 S25 ILE VAL 0.00140773
S17 S25 ILE TRP 0.00140773
S17 S25 ILE TYR 0.00140773
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S17 S25 LYS GLU 9.8106e-05
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S17 S25 LYS ARG 0.00332611
S17 S25 LYS SER 0.0205521
S17 S25 LYS THR 0.000107759
S17 S25 LEU ASP 1.25508e-05
S17 S25 LEU GLU 9.8106e-05
S17 S25 LEU LYS 0.000622521
S17 S25 LEU ARG 0.00332611
S17 S25 LEU SER 0.0205521
S17 S25 LEU THR 0.000107759
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S17 S25 MET GLU 9.8106e-05
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S17 S25 MET THR 0.000107759
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S17 S25 ASN SER 0.0205521
S17 S25 ASN THR 0.000107759
S17 S25 PRO ASP 1.25508e-05
S17 S25 PRO GLU 9.8106e-05
S17 S25 PRO LYS 0.000622521
S17 S25 PRO ARG 0.00332611
S17 S25 PRO SER 0.0205521
S17 S25 PRO THR 0.000107759
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S17 S25 GLN GLU 9.8106e-05
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S17 S25 GLN ARG 0.00332611
S17 S25 GLN SER 0.0205521
S17 S25 GLN THR 0.000107759
S17 S25 ARG ASP 1.25508e-05
S17 S25 ARG GLU 9.8106e-05

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S17 S25 SER ARG 0.00332611
S17 S25 SER SER 0.0205521
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S17 S25 THR GLU 9.8106e-05
S17 S25 THR LYS 0.000622521
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S17 S25 THR THR 0.000107759
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S17 S25 VAL SER 0.0205521
S17 S25 VAL THR 0.000107759
S17 S25 TRP ALA 2.5233e-05
S17 S25 TRP CYS 2.5233e-05
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S17 S25 TYR GLU 0.0175819
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S17 S25 TYR TYR 0.00129329

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S17 S26 ALA PHE 0.00697412
S17 S26 ALA LYS 0.0162785
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S17 S26 CYS PHE 0.00697412
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S17 S26 CYS TYR 0.00146658
S17 S26 ASP PHE 0.00697412
S17 S26 ASP LYS 0.0162785
S17 S26 ASP TYR 0.00146658
S17 S26 GLU PHE 0.00697412
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S17 S26 PHE ALA 0.0119678
S17 S26 PHE CYS 0.0119678
S17 S26 PHE ASP 0.0119678
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S17 S26 PHE TYR -0.583441
S17 S26 PHE --- 0.0119678
S17 S26 GLY PHE 0.00697412
S17 S26 GLY LYS 0.0162785
S17 S26 GLY TYR 0.00146658
S17 S26 HIS ALA 0.00499232
S17 S26 HIS CYS 0.00499232
S17 S26 HIS ASP 0.00499232
S17 S26 HIS GLU 0.00499232
S17 S26 HIS PHE 0.613352
S17 S26 HIS GLY 0.00499232
S17 S26 HIS HIS 0.00499232
S17 S26 HIS ILE 0.00499232
S17 S26 HIS LYS -1.12751
S17 S26 HIS LEU 0.00499232
S17 S26 HIS MET 0.00499232
S17 S26 HIS ASN 0.00499232
S17 S26 HIS PRO 0.00499232
S17 S26 HIS GLN 0.00499232
S17 S26 HIS ARG 0.00499232
S17 S26 HIS SER 0.00499232
S17 S26 HIS THR 0.00499232
S17 S26 HIS VAL 0.00499232
S17 S26 HIS TRP 0.00499232
S17 S26 HIS TYR 0.310429

S17 S26 HIS --- 0.00499232
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S17 S26 ILE CYS 0.00103884
S17 S26 ILE ASP 0.00103884
S17 S26 ILE GLU 0.00103884
S17 S26 ILE PHE 0.45593
S17 S26 ILE GLY 0.00103884
S17 S26 ILE HIS 0.00103884
S17 S26 ILE ILE 0.00103884
S17 S26 ILE LYS -0.612177
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S17 S26 ILE TYR 0.0570918
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S17 S26 LYS PHE 0.00697412
S17 S26 LYS LYS 0.0162785
S17 S26 LYS TYR 0.00146658
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S17 S26 LEU LYS 0.0162785
S17 S26 LEU TYR 0.00146658
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S17 S26 MET LYS 0.0162785
S17 S26 MET TYR 0.00146658
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S17 S26 ASN LYS 0.0162785
S17 S26 ASN TYR 0.00146658
S17 S26 PRO PHE 0.00697412
S17 S26 PRO LYS 0.0162785
S17 S26 PRO TYR 0.00146658
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S17 S26 GLN LYS 0.0162785
S17 S26 GLN TYR 0.00146658
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S17 S26 ARG LYS 0.0162785
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S17 S26 SER LYS 0.0162785
S17 S26 SER TYR 0.00146658
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S17 S26 THR LYS 0.0162785
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S17 S26 VAL PHE 0.00697412
S17 S26 VAL LYS 0.0162785
S17 S26 VAL TYR 0.00146658
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S17 S26 TRP CYS 3.86991e-05
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S17 S26 TRP GLU 3.86991e-05
S17 S26 TRP PHE 0.0414635
S17 S26 TRP GLY 3.86991e-05
S17 S26 TRP HIS 3.86991e-05
S17 S26 TRP ILE 3.86991e-05
S17 S26 TRP LYS -0.0802735
S17 S26 TRP LEU 3.86991e-05
S17 S26 TRP MET 3.86991e-05

S17 S26 TRP ASN 3.86991e-05
S17 S26 TRP PRO 3.86991e-05
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S17 S26 TRP ARG 3.86991e-05
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S17 S26 TRP TYR 0.0170078
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S17 S26 TYR HIS 0.00295202
S17 S26 TYR ILE 0.00295202
S17 S26 TYR LYS 0.822662
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S17 S26 TYR ASN 0.00295202
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S17 S27 PHE ILE 0.00918412
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S17 S27 HIS ARG 0.00429937
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S17 S27 HIS TYR 0.00429937
S17 S27 HIS --- 0.00429937
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S17 S27 ILE CYS 0.000693549
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S17 S27 ILE GLU 0.000693549
S17 S27 ILE PHE 0.000693549
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S17 S27 ILE ILE 0.000693549
S17 S27 ILE LYS 0.000693549
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S17 S28 PHE ASP 0.0784942
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S17 S28 PHE GLY 0.00867904
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S17 S29 TYR ARG 0.00193589
S17 S29 TYR SER -0.178909
S17 S29 TYR THR 0.00193589
S17 S29 TYR VAL 0.00193589
S17 S29 TYR TRP 0.00193589
S17 S29 TYR TYR 0.00193589
S17 S29 TYR --- 0.00193589
S17 S29 --- LYS 0.000218675
S17 S29 --- LEU 9.39191e-05
S17 S29 --- ASN 0.000558285
S17 S29 --- SER 0.0238483
S17 S30 ALA GLN 0.0245832
S17 S30 ALA SER 0.000135959
S17 S30 CYS GLN 0.0245832
S17 S30 CYS SER 0.000135959
S17 S30 ASP GLN 0.0245832
S17 S30 ASP SER 0.000135959
S17 S30 GLU GLN 0.0245832
S17 S30 GLU SER 0.000135959
S17 S30 PHE ALA 0.00830439
S17 S30 PHE CYS 0.00830439
S17 S30 PHE ASP 0.00830439
S17 S30 PHE GLU 0.00830439
S17 S30 PHE PHE 0.00830439
S17 S30 PHE GLY 0.00830439
S17 S30 PHE HIS 0.00830439
S17 S30 PHE ILE 0.00830439
S17 S30 PHE LYS 0.00830439
S17 S30 PHE LEU 0.00830439
S17 S30 PHE MET 0.00830439
S17 S30 PHE ASN 0.00830439
S17 S30 PHE PRO 0.00830439
S17 S30 PHE GLN -0.12655
S17 S30 PHE ARG 0.00830439
S17 S30 PHE SER -0.144305
S17 S30 PHE THR 0.00830439
S17 S30 PHE VAL 0.00830439
S17 S30 PHE TRP 0.00830439

S17 S30 PHE TYR 0.00830439
S17 S30 PHE --- 0.00830439
S17 S30 GLY GLN 0.0245832
S17 S30 GLY SER 0.000135959
S17 S30 HIS ALA 0.00216564
S17 S30 HIS CYS 0.00216564
S17 S30 HIS ASP 0.00216564
S17 S30 HIS GLU 0.00216564
S17 S30 HIS PHE 0.00216564
S17 S30 HIS GLY 0.00216564
S17 S30 HIS HIS 0.00216564
S17 S30 HIS ILE 0.00216564
S17 S30 HIS LYS 0.00216564
S17 S30 HIS LEU 0.00216564
S17 S30 HIS MET 0.00216564
S17 S30 HIS ASN 0.00216564
S17 S30 HIS PRO 0.00216564
S17 S30 HIS GLN -0.183047
S17 S30 HIS ARG 0.00216564
S17 S30 HIS SER 0.0280292
S17 S30 HIS THR 0.00216564
S17 S30 HIS VAL 0.00216564
S17 S30 HIS TRP 0.00216564
S17 S30 HIS TYR 0.00216564
S17 S30 HIS --- 0.00216564
S17 S30 ILE ALA 0.00076377
S17 S30 ILE CYS 0.00076377
S17 S30 ILE ASP 0.00076377
S17 S30 ILE GLU 0.00076377
S17 S30 ILE PHE 0.00076377
S17 S30 ILE GLY 0.00076377
S17 S30 ILE HIS 0.00076377
S17 S30 ILE ILE 0.00076377
S17 S30 ILE LYS 0.00076377
S17 S30 ILE LEU 0.00076377
S17 S30 ILE MET 0.00076377
S17 S30 ILE ASN 0.00076377
S17 S30 ILE PRO 0.00076377
S17 S30 ILE GLN -0.106851
S17 S30 ILE ARG 0.00076377
S17 S30 ILE SER 0.0118841
S17 S30 ILE THR 0.00076377
S17 S30 ILE VAL 0.00076377
S17 S30 ILE TRP 0.00076377
S17 S30 ILE TYR 0.00076377
S17 S30 ILE --- 0.00076377
S17 S30 LYS GLN 0.0245832
S17 S30 LYS SER 0.000135959
S17 S30 LEU GLN 0.0245832
S17 S30 LEU SER 0.000135959
S17 S30 MET GLN 0.0245832
S17 S30 MET SER 0.000135959
S17 S30 ASN GLN 0.0245832
S17 S30 ASN SER 0.000135959
S17 S30 PRO GLN 0.0245832
S17 S30 PRO SER 0.000135959
S17 S30 GLN GLN 0.0245832
S17 S30 GLN SER 0.000135959
S17 S30 ARG GLN 0.0245832
S17 S30 ARG SER 0.000135959
S17 S30 SER GLN 0.0245832
S17 S30 SER SER 0.000135959
S17 S30 THR GLN 0.0245832

S17 S30 THR SER 0.000135959
S17 S30 VAL GLN 0.0245832
S17 S30 VAL SER 0.000135959
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S17 S30 TRP CYS 1.10159e-05
S17 S30 TRP ASP 1.10159e-05
S17 S30 TRP GLU 1.10159e-05
S17 S30 TRP PHE 1.10159e-05
S17 S30 TRP GLY 1.10159e-05
S17 S30 TRP HIS 1.10159e-05
S17 S30 TRP ILE 1.10159e-05
S17 S30 TRP LYS 1.10159e-05
S17 S30 TRP LEU 1.10159e-05
S17 S30 TRP MET 1.10159e-05
S17 S30 TRP ASN 1.10159e-05
S17 S30 TRP PRO 1.10159e-05
S17 S30 TRP GLN -0.0217653
S17 S30 TRP ARG 1.10159e-05
S17 S30 TRP SER 0.000450319
S17 S30 TRP THR 1.10159e-05
S17 S30 TRP VAL 1.10159e-05
S17 S30 TRP TRP 1.10159e-05
S17 S30 TRP TYR 1.10159e-05
S17 S30 TRP --- 1.10159e-05
S17 S30 TYR ALA 0.00122143
S17 S30 TYR CYS 0.00122143
S17 S30 TYR ASP 0.00122143
S17 S30 TYR GLU 0.00122143
S17 S30 TYR PHE 0.00122143
S17 S30 TYR GLY 0.00122143
S17 S30 TYR HIS 0.00122143
S17 S30 TYR ILE 0.00122143
S17 S30 TYR LYS 0.00122143
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S17 S30 TYR MET 0.00122143
S17 S30 TYR ASN 0.00122143
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S17 S30 TYR GLN -0.112045
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S17 S30 TYR THR 0.00122143
S17 S30 TYR VAL 0.00122143
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S17 S30 TYR TYR 0.00122143
S17 S30 TYR --- 0.00122143
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S17 S30 --- SER 0.000135959
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S17 S31 ALA ILE 0.00322629
S17 S31 ALA VAL 0.0205978
S17 S31 CYS ASP 0.000895091
S17 S31 CYS ILE 0.00322629
S17 S31 CYS VAL 0.0205978
S17 S31 ASP ASP 0.000895091
S17 S31 ASP ILE 0.00322629
S17 S31 ASP VAL 0.0205978
S17 S31 GLU ASP 0.000895091
S17 S31 GLU ILE 0.00322629
S17 S31 GLU VAL 0.0205978
S17 S31 PHE ALA 0.009201
S17 S31 PHE CYS 0.009201
S17 S31 PHE ASP 0.0248874
S17 S31 PHE GLU 0.009201

S17 S31 PHE PHE 0.009201
S17 S31 PHE GLY 0.009201
S17 S31 PHE HIS 0.009201
S17 S31 PHE ILE -0.573303
S17 S31 PHE LYS 0.009201
S17 S31 PHE LEU 0.009201
S17 S31 PHE MET 0.009201
S17 S31 PHE ASN 0.009201
S17 S31 PHE PRO 0.009201
S17 S31 PHE GLN 0.009201
S17 S31 PHE ARG 0.009201
S17 S31 PHE SER 0.009201
S17 S31 PHE THR 0.009201
S17 S31 PHE VAL 0.269726
S17 S31 PHE TRP 0.009201
S17 S31 PHE TYR 0.009201
S17 S31 PHE --- 0.009201
S17 S31 GLY ASP 0.000895091
S17 S31 GLY ILE 0.00322629
S17 S31 GLY VAL 0.0205978
S17 S31 HIS ALA 0.00451583
S17 S31 HIS CYS 0.00451583
S17 S31 HIS ASP -0.298815
S17 S31 HIS GLU 0.00451583
S17 S31 HIS PHE 0.00451583
S17 S31 HIS GLY 0.00451583
S17 S31 HIS HIS 0.00451583
S17 S31 HIS ILE 0.388167
S17 S31 HIS LYS 0.00451583
S17 S31 HIS LEU 0.00451583
S17 S31 HIS MET 0.00451583
S17 S31 HIS ASN 0.00451583
S17 S31 HIS PRO 0.00451583
S17 S31 HIS GLN 0.00451583
S17 S31 HIS ARG 0.00451583
S17 S31 HIS SER 0.00451583
S17 S31 HIS THR 0.00451583
S17 S31 HIS VAL -0.284508
S17 S31 HIS TRP 0.00451583
S17 S31 HIS TYR 0.00451583
S17 S31 HIS --- 0.00451583
S17 S31 ILE ALA 0.00147034
S17 S31 ILE CYS 0.00147034
S17 S31 ILE ASP 0.00879145
S17 S31 ILE GLU 0.00147034
S17 S31 ILE PHE 0.00147034
S17 S31 ILE GLY 0.00147034
S17 S31 ILE HIS 0.00147034
S17 S31 ILE ILE -0.292184
S17 S31 ILE LYS 0.00147034
S17 S31 ILE LEU 0.00147034
S17 S31 ILE MET 0.00147034
S17 S31 ILE ASN 0.00147034
S17 S31 ILE PRO 0.00147034
S17 S31 ILE GLN 0.00147034
S17 S31 ILE ARG 0.00147034
S17 S31 ILE SER 0.00147034
S17 S31 ILE THR 0.00147034
S17 S31 ILE VAL 0.17647
S17 S31 ILE TRP 0.00147034
S17 S31 ILE TYR 0.00147034
S17 S31 ILE --- 0.00147034
S17 S31 LYS ASP 0.000895091

S17 S31 LYS ILE 0.00322629
S17 S31 LYS VAL 0.0205978
S17 S31 LEU ASP 0.000895091
S17 S31 LEU ILE 0.00322629
S17 S31 LEU VAL 0.0205978
S17 S31 MET ASP 0.000895091
S17 S31 MET ILE 0.00322629
S17 S31 MET VAL 0.0205978
S17 S31 ASN ASP 0.000895091
S17 S31 ASN ILE 0.00322629
S17 S31 ASN VAL 0.0205978
S17 S31 PRO ASP 0.000895091
S17 S31 PRO ILE 0.00322629
S17 S31 PRO VAL 0.0205978
S17 S31 GLN ASP 0.000895091
S17 S31 GLN ILE 0.00322629
S17 S31 GLN VAL 0.0205978
S17 S31 ARG ASP 0.000895091
S17 S31 ARG ILE 0.00322629
S17 S31 ARG VAL 0.0205978
S17 S31 SER ASP 0.000895091
S17 S31 SER ILE 0.00322629
S17 S31 SER VAL 0.0205978
S17 S31 THR ASP 0.000895091
S17 S31 THR ILE 0.00322629
S17 S31 THR VAL 0.0205978
S17 S31 VAL ASP 0.000895091
S17 S31 VAL ILE 0.00322629
S17 S31 VAL VAL 0.0205978
S17 S31 TRP ALA 0.000136662
S17 S31 TRP CYS 0.000136662
S17 S31 TRP ASP 0.0275084
S17 S31 TRP GLU 0.000136662
S17 S31 TRP PHE 0.000136662
S17 S31 TRP GLY 0.000136662
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S17 S31 TRP ILE 0.0328595
S17 S31 TRP LYS 0.000136662
S17 S31 TRP LEU 0.000136662
S17 S31 TRP MET 0.000136662
S17 S31 TRP ASN 0.000136662
S17 S31 TRP PRO 0.000136662
S17 S31 TRP GLN 0.000136662
S17 S31 TRP ARG 0.000136662
S17 S31 TRP SER 0.000136662
S17 S31 TRP THR 0.000136662
S17 S31 TRP VAL -0.0839336
S17 S31 TRP TRP 0.000136662
S17 S31 TRP TYR 0.000136662
S17 S31 TRP --- 0.000136662
S17 S31 TYR ALA 0.00323713
S17 S31 TYR CYS 0.00323713
S17 S31 TYR ASP 0.122323
S17 S31 TYR GLU 0.00323713
S17 S31 TYR PHE 0.00323713
S17 S31 TYR GLY 0.00323713
S17 S31 TYR HIS 0.00323713
S17 S31 TYR ILE 0.33205
S17 S31 TYR LYS 0.00323713
S17 S31 TYR LEU 0.00323713
S17 S31 TYR MET 0.00323713
S17 S31 TYR ASN 0.00323713
S17 S31 TYR PRO 0.00323713

S17 S31 TYR GLN 0.00323713
S17 S31 TYR ARG 0.00323713
S17 S31 TYR SER 0.00323713
S17 S31 TYR THR 0.00323713
S17 S31 TYR VAL -0.579646
S17 S31 TYR TRP 0.00323713
S17 S31 TYR TYR 0.00323713
S17 S31 TYR --- 0.00323713
S17 S31 --- ASP 0.000895091
S17 S31 --- ILE 0.00322629
S17 S31 --- VAL 0.0205978
S17 S32 ALA PHE 0.00184902
S17 S32 ALA HIS 0.00218642
S17 S32 ALA TRP 0.0175493
S17 S32 ALA TYR 0.00313441
S17 S32 CYS PHE 0.00184902
S17 S32 CYS HIS 0.00218642
S17 S32 CYS TRP 0.0175493
S17 S32 CYS TYR 0.00313441
S17 S32 ASP PHE 0.00184902
S17 S32 ASP HIS 0.00218642
S17 S32 ASP TRP 0.0175493
S17 S32 ASP TYR 0.00313441
S17 S32 GLU PHE 0.00184902
S17 S32 GLU HIS 0.00218642
S17 S32 GLU TRP 0.0175493
S17 S32 GLU TYR 0.00313441
S17 S32 PHE ALA 0.00763081
S17 S32 PHE CYS 0.00763081
S17 S32 PHE ASP 0.00763081
S17 S32 PHE GLU 0.00763081
S17 S32 PHE PHE 0.298633
S17 S32 PHE GLY 0.00763081
S17 S32 PHE HIS 0.355212
S17 S32 PHE ILE 0.00763081
S17 S32 PHE LYS 0.00763081
S17 S32 PHE LEU 0.00763081
S17 S32 PHE MET 0.00763081
S17 S32 PHE ASN 0.00763081
S17 S32 PHE PRO 0.00763081
S17 S32 PHE GLN 0.00763081
S17 S32 PHE ARG 0.00763081
S17 S32 PHE SER 0.00763081
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S17 S32 PHE VAL 0.00763081
S17 S32 PHE TRP -1.09713
S17 S32 PHE TYR 0.200487
S17 S32 PHE --- 0.00763081
S17 S32 GLY PHE 0.00184902
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S17 S32 GLY TRP 0.0175493
S17 S32 GLY TYR 0.00313441
S17 S32 HIS ALA 0.0105988
S17 S32 HIS CYS 0.0105988
S17 S32 HIS ASP 0.0105988
S17 S32 HIS GLU 0.0105988
S17 S32 HIS PHE -0.384198
S17 S32 HIS GLY 0.0105988
S17 S32 HIS HIS 0.0142779
S17 S32 HIS ILE 0.0105988
S17 S32 HIS LYS 0.0105988
S17 S32 HIS LEU 0.0105988
S17 S32 HIS MET 0.0105988

S17 S32 HIS ASN 0.0105988
S17 S32 HIS PRO 0.0105988
S17 S32 HIS GLN 0.0105988
S17 S32 HIS ARG 0.0105988
S17 S32 HIS SER 0.0105988
S17 S32 HIS THR 0.0105988
S17 S32 HIS VAL 0.0105988
S17 S32 HIS TRP 0.309745
S17 S32 HIS TYR -0.233875
S17 S32 HIS --- 0.0105988
S17 S32 ILE ALA 0.00230893
S17 S32 ILE CYS 0.00230893
S17 S32 ILE ASP 0.00230893
S17 S32 ILE GLU 0.00230893
S17 S32 ILE PHE -0.420331
S17 S32 ILE GLY 0.00230893
S17 S32 ILE HIS 0.136874
S17 S32 ILE ILE 0.00230893
S17 S32 ILE LYS 0.00230893
S17 S32 ILE LEU 0.00230893
S17 S32 ILE MET 0.00230893
S17 S32 ILE ASN 0.00230893
S17 S32 ILE PRO 0.00230893
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S17 S32 ILE ARG 0.00230893
S17 S32 ILE SER 0.00230893
S17 S32 ILE THR 0.00230893
S17 S32 ILE VAL 0.00230893
S17 S32 ILE TRP 0.488975
S17 S32 ILE TYR -0.325225
S17 S32 ILE --- 0.00230893
S17 S32 LYS PHE 0.00184902
S17 S32 LYS HIS 0.00218642
S17 S32 LYS TRP 0.0175493
S17 S32 LYS TYR 0.00313441
S17 S32 LEU PHE 0.00184902
S17 S32 LEU HIS 0.00218642
S17 S32 LEU TRP 0.0175493
S17 S32 LEU TYR 0.00313441
S17 S32 MET PHE 0.00184902
S17 S32 MET HIS 0.00218642
S17 S32 MET TRP 0.0175493
S17 S32 MET TYR 0.00313441
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S17 S32 ASN HIS 0.00218642
S17 S32 ASN TRP 0.0175493
S17 S32 ASN TYR 0.00313441
S17 S32 PRO PHE 0.00184902
S17 S32 PRO HIS 0.00218642
S17 S32 PRO TRP 0.0175493
S17 S32 PRO TYR 0.00313441
S17 S32 GLN PHE 0.00184902
S17 S32 GLN HIS 0.00218642
S17 S32 GLN TRP 0.0175493
S17 S32 GLN TYR 0.00313441
S17 S32 ARG PHE 0.00184902
S17 S32 ARG HIS 0.00218642
S17 S32 ARG TRP 0.0175493
S17 S32 ARG TYR 0.00313441
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S17 S32 SER HIS 0.00218642
S17 S32 SER TRP 0.0175493
S17 S32 SER TYR 0.00313441

S17 S32 THR PHE 0.00184902
S17 S32 THR HIS 0.00218642
S17 S32 THR TRP 0.0175493
S17 S32 THR TYR 0.00313441
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S17 S32 VAL HIS 0.00218642
S17 S32 VAL TRP 0.0175493
S17 S32 VAL TYR 0.00313441
S17 S32 TRP ALA 0.000160894
S17 S32 TRP CYS 0.000160894
S17 S32 TRP ASP 0.000160894
S17 S32 TRP GLU 0.000160894
S17 S32 TRP PHE 0.0183108
S17 S32 TRP GLY 0.000160894
S17 S32 TRP HIS 0.0378336
S17 S32 TRP ILE 0.000160894
S17 S32 TRP LYS 0.000160894
S17 S32 TRP LEU 0.000160894
S17 S32 TRP MET 0.000160894
S17 S32 TRP ASN 0.000160894
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S17 S32 TRP TYR 0.0334765
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S17 S32 TYR ALA 0.004111
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S17 S32 TYR ASP 0.004111
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S17 S32 TYR PHE 0.460542
S17 S32 TYR GLY 0.004111
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S17 S32 TYR ILE 0.004111
S17 S32 TYR LYS 0.004111
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S17 S32 TYR MET 0.004111
S17 S32 TYR ASN 0.004111
S17 S32 TYR PRO 0.004111
S17 S32 TYR GLN 0.004111
S17 S32 TYR ARG 0.004111
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S17 S32 TYR --- 0.004111
S17 S32 --- PHE 0.00184902
S17 S32 --- HIS 0.00218642
S17 S32 --- TRP 0.0175493
S17 S32 --- TYR 0.00313441
S17 S33 ALA ASP 0.0181715
S17 S33 ALA LYS 0.00024512
S17 S33 ALA SER 0.0033473
S17 S33 ALA VAL 0.00295528
S17 S33 CYS ASP 0.0181715
S17 S33 CYS LYS 0.00024512
S17 S33 CYS SER 0.0033473
S17 S33 CYS VAL 0.00295528
S17 S33 ASP ASP 0.0181715

S17 S33 ASP LYS 0.00024512
S17 S33 ASP SER 0.0033473
S17 S33 ASP VAL 0.00295528
S17 S33 GLU ASP 0.0181715
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S17 S33 PHE LYS 0.135161
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S17 S33 GLY ASP 0.0181715
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S17 S33 GLY SER 0.0033473
S17 S33 GLY VAL 0.00295528
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S17 S33 HIS CYS 0.0105799
S17 S33 HIS ASP 0.360801
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S17 S33 HIS PHE 0.0105799
S17 S33 HIS GLY 0.0105799
S17 S33 HIS HIS 0.0105799
S17 S33 HIS ILE 0.0105799
S17 S33 HIS LYS -0.20996
S17 S33 HIS LEU 0.0105799
S17 S33 HIS MET 0.0105799
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S17 S33 HIS THR 0.0105799
S17 S33 HIS VAL -0.754231
S17 S33 HIS TRP 0.0105799
S17 S33 HIS TYR 0.0105799
S17 S33 HIS --- 0.0105799
S17 S33 ILE ALA 0.00125401
S17 S33 ILE CYS 0.00125401
S17 S33 ILE ASP -0.357531
S17 S33 ILE GLU 0.00125401
S17 S33 ILE PHE 0.00125401
S17 S33 ILE GLY 0.00125401
S17 S33 ILE HIS 0.00125401
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S17 S33 ILE LEU 0.00125401

S17 S33 ILE MET 0.00125401
S17 S33 ILE ASN 0.00125401
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S17 S33 ILE TYR 0.00125401
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S17 S33 LYS ASP 0.0181715
S17 S33 LYS LYS 0.00024512
S17 S33 LYS SER 0.0033473
S17 S33 LYS VAL 0.00295528
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S17 S33 ASN LYS 0.00024512
S17 S33 ASN SER 0.0033473
S17 S33 ASN VAL 0.00295528
S17 S33 PRO ASP 0.0181715
S17 S33 PRO LYS 0.00024512
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S17 S33 PRO VAL 0.00295528
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S17 S33 GLN LYS 0.00024512
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S17 S33 GLN VAL 0.00295528
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S17 S33 ARG LYS 0.00024512
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S17 S33 ARG VAL 0.00295528
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S17 S33 SER LYS 0.00024512
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S17 S33 THR LYS 0.00024512
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S17 S33 VAL LYS 0.00024512
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S17 S33 TRP ASN 0.000280895

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S17 S33 TYR CYS 0.00266101
S17 S33 TYR ASP 0.045917
S17 S33 TYR GLU 0.00266101
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S17 S34 CYS ARG 0.000558285
S17 S34 CYS SER 0.0207433
S17 S34 CYS THR 0.00109176
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S17 S34 ASP MET 0.000672651
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S17 S34 PHE GLN 0.0120639
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S17 S34 PHE THR 0.323648
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S17 S34 ILE ARG 0.0304999
S17 S34 ILE SER 0.395752
S17 S34 ILE THR -0.682049
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S17 S34 TYR ASP 0.00151776
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S17 S34 TYR GLN 0.00151776
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S17 S34 TYR SER -0.350919
S17 S34 TYR THR 0.063306
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S17 S35 CYS THR 0.002047
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S17 S35 GLU SER 0.0197849
S17 S35 GLU THR 0.002047
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S17 S35 PHE CYS 0.0106429
S17 S35 PHE ASP 0.0106429
S17 S35 PHE GLU 0.0106429
S17 S35 PHE PHE 0.0106429
S17 S35 PHE GLY 0.0106429
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S17 S35 PHE ILE 0.0106429
S17 S35 PHE LYS 0.0106429
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S17 S35 PHE THR 0.298347
S17 S35 PHE VAL 0.0106429
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S17 S35 PHE TYR 0.0106429
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S17 S35 GLY SER 0.0197849
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S17 S35 HIS ALA -0.439129
S17 S35 HIS CYS 0.00713423
S17 S35 HIS ASP 0.00713423
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S17 S35 HIS THR -0.475149
S17 S35 HIS VAL 0.00713423
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S17 S35 ILE ALA 0.454933
S17 S35 ILE CYS 0.00130349
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S17 S35 GLN THR 0.002047

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S17 S36 TYR LEU 0.00332272
S17 S36 TYR MET 0.00332272
S17 S36 TYR ASN 0.00332272
S17 S36 TYR PRO 0.00332272
S17 S36 TYR GLN 0.00332272
S17 S36 TYR ARG 0.00332272
S17 S36 TYR SER -0.525172
S17 S36 TYR THR 0.449208
S17 S36 TYR VAL 0.00332272
S17 S36 TYR TRP 0.00332272
S17 S36 TYR TYR 0.00332272
S17 S36 TYR --- 0.00332272
S17 S36 --- ASP 0.00146045
S17 S36 --- GLU 0.00342023
S17 S36 --- SER 0.018129
S17 S36 --- THR 0.00170951
S17 S37 ALA ALA 0.000456641
S17 S37 ALA ASP 0.00985136
S17 S37 ALA PHE 0.000808883
S17 S37 ALA ASN 0.0014036
S17 S37 ALA ARG 0.00170273
S17 S37 ALA SER 0.010496
S17 S37 CYS ALA 0.000456641
S17 S37 CYS ASP 0.00985136
S17 S37 CYS PHE 0.000808883
S17 S37 CYS ASN 0.0014036
S17 S37 CYS ARG 0.00170273
S17 S37 CYS SER 0.010496
S17 S37 ASP ALA 0.000456641
S17 S37 ASP ASP 0.00985136
S17 S37 ASP PHE 0.000808883
S17 S37 ASP ASN 0.0014036
S17 S37 ASP ARG 0.00170273
S17 S37 ASP SER 0.010496
S17 S37 GLU ALA 0.000456641
S17 S37 GLU ASP 0.00985136
S17 S37 GLU PHE 0.000808883
S17 S37 GLU ASN 0.0014036
S17 S37 GLU ARG 0.00170273
S17 S37 GLU SER 0.010496
S17 S37 PHE ALA -0.101617
S17 S37 PHE CYS 0.0113419

S17 S37 PHE ASP 0.0835026
S17 S37 PHE GLU 0.0113419
S17 S37 PHE PHE -0.414687
S17 S37 PHE GLY 0.0113419
S17 S37 PHE HIS 0.0113419
S17 S37 PHE ILE 0.0113419
S17 S37 PHE LYS 0.0113419
S17 S37 PHE LEU 0.0113419
S17 S37 PHE MET 0.0113419
S17 S37 PHE ASN 0.0484544
S17 S37 PHE PRO 0.0113419
S17 S37 PHE GLN 0.0113419
S17 S37 PHE ARG 0.0431936
S17 S37 PHE SER 0.0579533
S17 S37 PHE THR 0.0113419
S17 S37 PHE VAL 0.0113419
S17 S37 PHE TRP 0.0113419
S17 S37 PHE TYR 0.0113419
S17 S37 PHE --- 0.0113419
S17 S37 GLY ALA 0.000456641
S17 S37 GLY ASP 0.00985136
S17 S37 GLY PHE 0.000808883
S17 S37 GLY ASN 0.0014036
S17 S37 GLY ARG 0.00170273
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S17 S37 HIS ALA -0.223345
S17 S37 HIS CYS 0.0106895
S17 S37 HIS ASP -0.254726
S17 S37 HIS GLU 0.0106895
S17 S37 HIS PHE 0.216555
S17 S37 HIS GLY 0.0106895
S17 S37 HIS HIS 0.0106895
S17 S37 HIS ILE 0.0106895
S17 S37 HIS LYS 0.0106895
S17 S37 HIS LEU 0.0106895
S17 S37 HIS MET 0.0106895
S17 S37 HIS ASN 0.318013
S17 S37 HIS PRO 0.0106895
S17 S37 HIS GLN 0.0106895
S17 S37 HIS ARG 0.217938
S17 S37 HIS SER -0.548647
S17 S37 HIS THR 0.0106895
S17 S37 HIS VAL 0.0106895
S17 S37 HIS TRP 0.0106895
S17 S37 HIS TYR 0.0106895
S17 S37 HIS --- 0.0106895
S17 S37 ILE ALA 0.0470531
S17 S37 ILE CYS 0.00176605
S17 S37 ILE ASP 0.661659
S17 S37 ILE GLU 0.00176605
S17 S37 ILE PHE 0.0349325
S17 S37 ILE GLY 0.00176605
S17 S37 ILE HIS 0.00176605
S17 S37 ILE ILE 0.00176605
S17 S37 ILE LYS 0.00176605
S17 S37 ILE LEU 0.00176605
S17 S37 ILE MET 0.00176605
S17 S37 ILE ASN 0.0577859
S17 S37 ILE PRO 0.00176605
S17 S37 ILE GLN 0.00176605
S17 S37 ILE ARG 0.0355447
S17 S37 ILE SER -0.943922
S17 S37 ILE THR 0.00176605

S17 S37 ILE VAL 0.00176605
S17 S37 ILE TRP 0.00176605
S17 S37 ILE TYR 0.00176605
S17 S37 ILE --- 0.00176605
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S17 S37 LYS PHE 0.000808883
S17 S37 LYS ASN 0.0014036
S17 S37 LYS ARG 0.00170273
S17 S37 LYS SER 0.010496
S17 S37 LEU ALA 0.000456641
S17 S37 LEU ASP 0.00985136
S17 S37 LEU PHE 0.000808883
S17 S37 LEU ASN 0.0014036
S17 S37 LEU ARG 0.00170273
S17 S37 LEU SER 0.010496
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S17 S37 PRO ASP 0.00985136
S17 S37 PRO PHE 0.000808883
S17 S37 PRO ASN 0.0014036
S17 S37 PRO ARG 0.00170273
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S17 S37 GLN ALA 0.000456641
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S17 S37 GLN PHE 0.000808883
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S17 S37 ARG ALA 0.000456641
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S17 S37 ARG PHE 0.000808883
S17 S37 ARG ASN 0.0014036
S17 S37 ARG ARG 0.00170273
S17 S37 ARG SER 0.010496
S17 S37 SER ALA 0.000456641
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S17 S37 SER PHE 0.000808883
S17 S37 SER ASN 0.0014036
S17 S37 SER ARG 0.00170273
S17 S37 SER SER 0.010496
S17 S37 THR ALA 0.000456641
S17 S37 THR ASP 0.00985136
S17 S37 THR PHE 0.000808883
S17 S37 THR ASN 0.0014036
S17 S37 THR ARG 0.00170273
S17 S37 THR SER 0.010496
S17 S37 VAL ALA 0.000456641
S17 S37 VAL ASP 0.00985136
S17 S37 VAL PHE 0.000808883
S17 S37 VAL ASN 0.0014036
S17 S37 VAL ARG 0.00170273

S17 S37 VAL SER 0.010496
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S17 S37 TRP CYS 0.000228791
S17 S37 TRP ASP -0.54017
S17 S37 TRP GLU 0.000228791
S17 S37 TRP PHE 0.00277872
S17 S37 TRP GLY 0.000228791
S17 S37 TRP HIS 0.000228791
S17 S37 TRP ILE 0.000228791
S17 S37 TRP LYS 0.000228791
S17 S37 TRP LEU 0.000228791
S17 S37 TRP MET 0.000228791
S17 S37 TRP ASN 0.0172196
S17 S37 TRP PRO 0.000228791
S17 S37 TRP GLN 0.000228791
S17 S37 TRP ARG 0.0111663
S17 S37 TRP SER 0.480768
S17 S37 TRP THR 0.000228791
S17 S37 TRP VAL 0.000228791
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S17 S37 TRP TYR 0.000228791
S17 S37 TRP --- 0.000228791
S17 S37 TYR ALA 0.217312
S17 S37 TYR CYS 0.00504532
S17 S37 TYR ASP -0.1553
S17 S37 TYR GLU 0.00504532
S17 S37 TYR PHE 0.100334
S17 S37 TYR GLY 0.00504532
S17 S37 TYR HIS 0.00504532
S17 S37 TYR ILE 0.00504532
S17 S37 TYR LYS 0.00504532
S17 S37 TYR LEU 0.00504532
S17 S37 TYR MET 0.00504532
S17 S37 TYR ASN -0.487231
S17 S37 TYR PRO 0.00504532
S17 S37 TYR GLN 0.00504532
S17 S37 TYR ARG -0.396773
S17 S37 TYR SER 0.578974
S17 S37 TYR THR 0.00504532
S17 S37 TYR VAL 0.00504532
S17 S37 TYR TRP 0.00504532
S17 S37 TYR TYR 0.00504532
S17 S37 TYR --- 0.00504532
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S17 S37 --- ASP 0.00985136
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S17 S38 ALA GLU 0.00327506
S17 S38 ALA HIS 0.00617046
S17 S38 ALA LYS 0.00242501
S17 S38 ALA LEU 0.0107614
S17 S38 ALA ARG 0.00208722
S17 S38 CYS GLU 0.00327506
S17 S38 CYS HIS 0.00617046
S17 S38 CYS LYS 0.00242501
S17 S38 CYS LEU 0.0107614
S17 S38 CYS ARG 0.00208722
S17 S38 ASP GLU 0.00327506
S17 S38 ASP HIS 0.00617046
S17 S38 ASP LYS 0.00242501
S17 S38 ASP LEU 0.0107614

S17 S38 ASP ARG 0.00208722
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S17 S38 GLU ARG 0.00208722
S17 S38 PHE ALA 0.0117481
S17 S38 PHE CYS 0.0117481
S17 S38 PHE ASP 0.0117481
S17 S38 PHE GLU -0.0167217
S17 S38 PHE PHE 0.0117481
S17 S38 PHE GLY 0.0117481
S17 S38 PHE HIS -0.305617
S17 S38 PHE ILE 0.0117481
S17 S38 PHE LYS -0.315812
S17 S38 PHE LEU -0.101434
S17 S38 PHE MET 0.0117481
S17 S38 PHE ASN 0.0117481
S17 S38 PHE PRO 0.0117481
S17 S38 PHE GLN 0.0117481
S17 S38 PHE ARG 0.438543
S17 S38 PHE SER 0.0117481
S17 S38 PHE THR 0.0117481
S17 S38 PHE VAL 0.0117481
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S17 S38 PHE TYR 0.0117481
S17 S38 PHE --- 0.0117481
S17 S38 GLY GLU 0.00327506
S17 S38 GLY HIS 0.00617046
S17 S38 GLY LYS 0.00242501
S17 S38 GLY LEU 0.0107614
S17 S38 GLY ARG 0.00208722
S17 S38 HIS ALA 0.0114914
S17 S38 HIS CYS 0.0114914
S17 S38 HIS ASP 0.0114914
S17 S38 HIS GLU 0.473473
S17 S38 HIS PHE 0.0114914
S17 S38 HIS GLY 0.0114914
S17 S38 HIS HIS 0.0902549
S17 S38 HIS ILE 0.0114914
S17 S38 HIS LYS -0.950807
S17 S38 HIS LEU 0.540232
S17 S38 HIS MET 0.0114914
S17 S38 HIS ASN 0.0114914
S17 S38 HIS PRO 0.0114914
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S17 S38 HIS ARG -0.450886
S17 S38 HIS SER 0.0114914
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S17 S38 HIS TRP 0.0114914
S17 S38 HIS TYR 0.0114914
S17 S38 HIS --- 0.0114914
S17 S38 ILE ALA 0.00292801
S17 S38 ILE CYS 0.00292801
S17 S38 ILE ASP 0.00292801
S17 S38 ILE GLU 0.208851
S17 S38 ILE PHE 0.00292801
S17 S38 ILE GLY 0.00292801
S17 S38 ILE HIS 0.438972
S17 S38 ILE ILE 0.00292801
S17 S38 ILE LYS 0.251964
S17 S38 ILE LEU -0.597152

S17 S38 ILE MET 0.00292801
S17 S38 ILE ASN 0.00292801
S17 S38 ILE PRO 0.00292801
S17 S38 ILE GLN 0.00292801
S17 S38 ILE ARG -0.429938
S17 S38 ILE SER 0.00292801
S17 S38 ILE THR 0.00292801
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S17 S38 ILE TYR 0.00292801
S17 S38 ILE --- 0.00292801
S17 S38 LYS GLU 0.00327506
S17 S38 LYS HIS 0.00617046
S17 S38 LYS LYS 0.00242501
S17 S38 LYS LEU 0.0107614
S17 S38 LYS ARG 0.00208722
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S17 S38 LEU HIS 0.00617046
S17 S38 LEU LYS 0.00242501
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S17 S38 LEU ARG 0.00208722
S17 S38 MET GLU 0.00327506
S17 S38 MET HIS 0.00617046
S17 S38 MET LYS 0.00242501
S17 S38 MET LEU 0.0107614
S17 S38 MET ARG 0.00208722
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S17 S38 ASN HIS 0.00617046
S17 S38 ASN LYS 0.00242501
S17 S38 ASN LEU 0.0107614
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S17 S38 PRO GLU 0.00327506
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S17 S38 PRO LYS 0.00242501
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S17 S38 GLN LYS 0.00242501
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S17 S38 ARG LEU 0.0107614
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S17 S38 SER LEU 0.0107614
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S17 S38 THR LYS 0.00242501
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S17 S38 VAL LYS 0.00242501
S17 S38 VAL LEU 0.0107614
S17 S38 VAL ARG 0.00208722
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S17 S38 TRP CYS 0.000345263

S17 S38 TRP ASP 0.000345263
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S17 S38 TRP PHE 0.000345263
S17 S38 TRP GLY 0.000345263
S17 S38 TRP HIS 0.128684
S17 S38 TRP ILE 0.000345263
S17 S38 TRP LYS 0.023508
S17 S38 TRP LEU 0.420019
S17 S38 TRP MET 0.000345263
S17 S38 TRP ASN 0.000345263
S17 S38 TRP PRO 0.000345263
S17 S38 TRP GLN 0.000345263
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S17 S38 TRP SER 0.000345263
S17 S38 TRP THR 0.000345263
S17 S38 TRP VAL 0.000345263
S17 S38 TRP TRP 0.000345263
S17 S38 TRP TYR 0.000345263
S17 S38 TRP --- 0.000345263
S17 S38 TYR ALA 0.00473822
S17 S38 TYR CYS 0.00473822
S17 S38 TYR ASP 0.00473822
S17 S38 TYR GLU -0.130619
S17 S38 TYR PHE 0.00473822
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S17 S38 TYR LEU -0.521057
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S17 S39 CYS TRP 0.000608631
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S17 S39 ASP LEU 0.000248905
S17 S39 ASP VAL 0.0215618
S17 S39 ASP TRP 0.000608631
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S17 S39 PHE CYS 0.00411783

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S17 S39 PHE GLU 0.00411783
S17 S39 PHE PHE 0.00411783
S17 S39 PHE GLY 0.00411783
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S17 S39 PHE ILE -0.304554
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S17 S39 PHE MET 0.00411783
S17 S39 PHE ASN 0.00411783
S17 S39 PHE PRO 0.00411783
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S17 S39 PHE TRP 0.0520941
S17 S39 PHE TYR 0.00411783
S17 S39 PHE --- 0.00411783
S17 S39 GLY ILE 0.00229987
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S17 S39 GLY VAL 0.0215618
S17 S39 GLY TRP 0.000608631
S17 S39 HIS ALA 0.00895092
S17 S39 HIS CYS 0.00895092
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S17 S39 HIS GLU 0.00895092
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S17 S39 HIS GLY 0.00895092
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S17 S39 HIS LYS 0.00895092
S17 S39 HIS LEU -0.19618
S17 S39 HIS MET 0.00895092
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S17 S39 HIS GLN 0.00895092
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S17 S39 HIS TYR 0.00895092
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S17 S39 ILE CYS 0.00128291
S17 S39 ILE ASP 0.00128291
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S17 S39 ILE PHE 0.00128291
S17 S39 ILE GLY 0.00128291
S17 S39 ILE HIS 0.00128291
S17 S39 ILE ILE 0.120107
S17 S39 ILE LYS 0.00128291
S17 S39 ILE LEU 0.00494881
S17 S39 ILE MET 0.00128291
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S17 S39 ILE PRO 0.00128291
S17 S39 ILE GLN 0.00128291
S17 S39 ILE ARG 0.00128291
S17 S39 ILE SER 0.00128291
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S17 S39 ILE TRP 0.0128409

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S17 S39 ASN LEU 0.000248905
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S17 S39 PRO ILE 0.00229987
S17 S39 PRO LEU 0.000248905
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S17 S39 GLN ILE 0.00229987
S17 S39 GLN LEU 0.000248905
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S17 S39 SER LEU 0.000248905
S17 S39 SER VAL 0.0215618
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S17 S39 THR LEU 0.000248905
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S17 S39 VAL LEU 0.000248905
S17 S39 VAL VAL 0.0215618
S17 S39 VAL TRP 0.000608631
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S17 S39 TRP CYS 3.99042e-05
S17 S39 TRP ASP 3.99042e-05
S17 S39 TRP GLU 3.99042e-05
S17 S39 TRP PHE 3.99042e-05
S17 S39 TRP GLY 3.99042e-05
S17 S39 TRP HIS 3.99042e-05
S17 S39 TRP ILE 0.0207659
S17 S39 TRP LYS 3.99042e-05
S17 S39 TRP LEU 0.000782134
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S17 S39 TRP GLN 3.99042e-05
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S17 S39 TRP TYR 3.99042e-05
S17 S39 TRP --- 3.99042e-05

S17 S39 TYR ALA 0.0043467
S17 S39 TYR CYS 0.0043467
S17 S39 TYR ASP 0.0043467
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S17 S39 TYR PHE 0.0043467
S17 S39 TYR GLY 0.0043467
S17 S39 TYR HIS 0.0043467
S17 S39 TYR ILE -0.336116
S17 S39 TYR LYS 0.0043467
S17 S39 TYR LEU 0.110754
S17 S39 TYR MET 0.0043467
S17 S39 TYR ASN 0.0043467
S17 S39 TYR PRO 0.0043467
S17 S39 TYR GLN 0.0043467
S17 S39 TYR ARG 0.0043467
S17 S39 TYR SER 0.0043467
S17 S39 TYR THR 0.0043467
S17 S39 TYR VAL 0.553496
S17 S39 TYR TRP -0.469031
S17 S39 TYR TYR 0.0043467
S17 S39 TYR --- 0.0043467
S17 S39 --- ILE 0.00229987
S17 S39 --- LEU 0.000248905
S17 S39 --- VAL 0.0215618
S17 S39 --- TRP 0.000608631
S17 S40 ALA ILE 0.00218818
S17 S40 ALA LEU 0.000194025
S17 S40 ALA VAL 0.022337
S17 S40 CYS ILE 0.00218818
S17 S40 CYS LEU 0.000194025
S17 S40 CYS VAL 0.022337
S17 S40 ASP ILE 0.00218818
S17 S40 ASP LEU 0.000194025
S17 S40 ASP VAL 0.022337
S17 S40 GLU ILE 0.00218818
S17 S40 GLU LEU 0.000194025
S17 S40 GLU VAL 0.022337
S17 S40 PHE ALA 0.00612696
S17 S40 PHE CYS 0.00612696
S17 S40 PHE ASP 0.00612696
S17 S40 PHE GLU 0.00612696
S17 S40 PHE PHE 0.00612696
S17 S40 PHE GLY 0.00612696
S17 S40 PHE HIS 0.00612696
S17 S40 PHE ILE 0.234442
S17 S40 PHE LYS 0.00612696
S17 S40 PHE LEU -0.14768
S17 S40 PHE MET 0.00612696
S17 S40 PHE ASN 0.00612696
S17 S40 PHE PRO 0.00612696
S17 S40 PHE GLN 0.00612696
S17 S40 PHE ARG 0.00612696
S17 S40 PHE SER 0.00612696
S17 S40 PHE THR 0.00612696
S17 S40 PHE VAL -0.310119
S17 S40 PHE TRP 0.00612696
S17 S40 PHE TYR 0.00612696
S17 S40 PHE --- 0.00612696
S17 S40 GLY ILE 0.00218818
S17 S40 GLY LEU 0.000194025
S17 S40 GLY VAL 0.022337
S17 S40 HIS ALA 0.00679827
S17 S40 HIS CYS 0.00679827

S17 S40 HIS ASP 0.00679827
S17 S40 HIS GLU 0.00679827
S17 S40 HIS PHE 0.00679827
S17 S40 HIS GLY 0.00679827
S17 S40 HIS HIS 0.00679827
S17 S40 HIS ILE -0.307396
S17 S40 HIS LYS 0.00679827
S17 S40 HIS LEU 0.0626224
S17 S40 HIS MET 0.00679827
S17 S40 HIS ASN 0.00679827
S17 S40 HIS PRO 0.00679827
S17 S40 HIS GLN 0.00679827
S17 S40 HIS ARG 0.00679827
S17 S40 HIS SER 0.00679827
S17 S40 HIS THR 0.00679827
S17 S40 HIS VAL 0.00853437
S17 S40 HIS TRP 0.00679827
S17 S40 HIS TYR 0.00679827
S17 S40 HIS --- 0.00679827
S17 S40 ILE ALA 0.000307956
S17 S40 ILE CYS 0.000307956
S17 S40 ILE ASP 0.000307956
S17 S40 ILE GLU 0.000307956
S17 S40 ILE PHE 0.000307956
S17 S40 ILE GLY 0.000307956
S17 S40 ILE HIS 0.000307956
S17 S40 ILE ILE 0.0227219
S17 S40 ILE LYS 0.000307956
S17 S40 ILE LEU 0.00489202
S17 S40 ILE MET 0.000307956
S17 S40 ILE ASN 0.000307956
S17 S40 ILE PRO 0.000307956
S17 S40 ILE GLN 0.000307956
S17 S40 ILE ARG 0.000307956
S17 S40 ILE SER 0.000307956
S17 S40 ILE THR 0.000307956
S17 S40 ILE VAL -0.113613
S17 S40 ILE TRP 0.000307956
S17 S40 ILE TYR 0.000307956
S17 S40 ILE --- 0.000307956
S17 S40 LYS ILE 0.00218818
S17 S40 LYS LEU 0.000194025
S17 S40 LYS VAL 0.022337
S17 S40 LEU ILE 0.00218818
S17 S40 LEU LEU 0.000194025
S17 S40 LEU VAL 0.022337
S17 S40 MET ILE 0.00218818
S17 S40 MET LEU 0.000194025
S17 S40 MET VAL 0.022337
S17 S40 ASN ILE 0.00218818
S17 S40 ASN LEU 0.000194025
S17 S40 ASN VAL 0.022337
S17 S40 PRO ILE 0.00218818
S17 S40 PRO LEU 0.000194025
S17 S40 PRO VAL 0.022337
S17 S40 GLN ILE 0.00218818
S17 S40 GLN LEU 0.000194025
S17 S40 GLN VAL 0.022337
S17 S40 ARG ILE 0.00218818
S17 S40 ARG LEU 0.000194025
S17 S40 ARG VAL 0.022337
S17 S40 SER ILE 0.00218818
S17 S40 SER LEU 0.000194025

S17 S40 SER VAL 0.022337
S17 S40 THR ILE 0.00218818
S17 S40 THR LEU 0.000194025
S17 S40 THR VAL 0.022337
S17 S40 VAL ILE 0.00218818
S17 S40 VAL LEU 0.000194025
S17 S40 VAL VAL 0.022337
S17 S40 TRP ALA 0.000123149
S17 S40 TRP CYS 0.000123149
S17 S40 TRP ASP 0.000123149
S17 S40 TRP GLU 0.000123149
S17 S40 TRP PHE 0.000123149
S17 S40 TRP GLY 0.000123149
S17 S40 TRP HIS 0.000123149
S17 S40 TRP ILE 0.0352408
S17 S40 TRP LYS 0.000123149
S17 S40 TRP LEU 0.00160178
S17 S40 TRP MET 0.000123149
S17 S40 TRP ASN 0.000123149
S17 S40 TRP PRO 0.000123149
S17 S40 TRP GLN 0.000123149
S17 S40 TRP ARG 0.000123149
S17 S40 TRP SER 0.000123149
S17 S40 TRP THR 0.000123149
S17 S40 TRP VAL -0.060165
S17 S40 TRP TRP 0.000123149
S17 S40 TRP TYR 0.000123149
S17 S40 TRP --- 0.000123149
S17 S40 TYR ALA 0.00305277
S17 S40 TYR CYS 0.00305277
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S17 S40 TYR GLU 0.00305277
S17 S40 TYR PHE 0.00305277
S17 S40 TYR GLY 0.00305277
S17 S40 TYR HIS 0.00305277
S17 S40 TYR ILE -0.0921352
S17 S40 TYR LYS 0.00305277
S17 S40 TYR LEU 0.020535
S17 S40 TYR MET 0.00305277
S17 S40 TYR ASN 0.00305277
S17 S40 TYR PRO 0.00305277
S17 S40 TYR GLN 0.00305277
S17 S40 TYR ARG 0.00305277
S17 S40 TYR SER 0.00305277
S17 S40 TYR THR 0.00305277
S17 S40 TYR VAL -0.0503531
S17 S40 TYR TRP 0.00305277
S17 S40 TYR TYR 0.00305277
S17 S40 TYR --- 0.00305277
S17 S40 --- ILE 0.00218818
S17 S40 --- LEU 0.000194025
S17 S40 --- VAL 0.022337
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S18 S19 ALA SER 0.00367814
S18 S19 ALA TYR 0.000143265
S18 S19 CYS ALA 0.00901882
S18 S19 CYS SER 0.00367814
S18 S19 CYS TYR 0.000143265
S18 S19 ASP ALA 0.00901882
S18 S19 ASP SER 0.00367814
S18 S19 ASP TYR 0.000143265
S18 S19 GLU ALA -0.0916106
S18 S19 GLU CYS 0.0184166

S18 S19 GLU ASP 0.0184166
S18 S19 GLU GLU 0.0184166
S18 S19 GLU PHE 0.0184166
S18 S19 GLU GLY 0.0184166
S18 S19 GLU HIS 0.0184166
S18 S19 GLU ILE 0.0184166
S18 S19 GLU LYS 0.0184166
S18 S19 GLU LEU 0.0184166
S18 S19 GLU MET 0.0184166
S18 S19 GLU ASN 0.0184166
S18 S19 GLU PRO 0.0184166
S18 S19 GLU GLN 0.0184166
S18 S19 GLU ARG 0.0184166
S18 S19 GLU SER -0.308405
S18 S19 GLU THR 0.0184166
S18 S19 GLU VAL 0.0184166
S18 S19 GLU TRP 0.0184166
S18 S19 GLU TYR -0.0668403
S18 S19 GLU --- 0.0184166
S18 S19 PHE ALA 0.00901882
S18 S19 PHE SER 0.00367814
S18 S19 PHE TYR 0.000143265
S18 S19 GLY ALA 0.00901882
S18 S19 GLY SER 0.00367814
S18 S19 GLY TYR 0.000143265
S18 S19 HIS ALA -0.255875
S18 S19 HIS CYS 0.000276868
S18 S19 HIS ASP 0.000276868
S18 S19 HIS GLU 0.000276868
S18 S19 HIS PHE 0.000276868
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S18 S19 HIS ILE 0.000276868
S18 S19 HIS LYS 0.000276868
S18 S19 HIS LEU 0.000276868
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S18 S19 HIS ASN 0.000276868
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S18 S19 HIS GLN 0.000276868
S18 S19 HIS ARG 0.000276868
S18 S19 HIS SER 0.139145
S18 S19 HIS THR 0.000276868
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S18 S19 HIS TRP 0.000276868
S18 S19 HIS TYR 0.00313845
S18 S19 HIS --- 0.000276868
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S18 S19 ILE TYR 0.000143265
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S18 S19 LYS SER 0.00367814
S18 S19 LYS TYR 0.000143265
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S18 S19 LEU SER 0.00367814
S18 S19 LEU TYR 0.000143265
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S18 S19 MET SER 0.00367814
S18 S19 MET TYR 0.000143265
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S18 S19 ASN SER 0.00367814
S18 S19 ASN TYR 0.000143265
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S18 S19 PRO SER 0.00367814

S18 S19 PRO TYR 0.000143265
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S18 S19 GLN SER 0.00367814
S18 S19 GLN TYR 0.000143265
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S18 S19 ARG SER 0.00367814
S18 S19 ARG TYR 0.000143265
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S18 S19 SER SER 0.00367814
S18 S19 SER TYR 0.000143265
S18 S19 THR ALA 0.00901882
S18 S19 THR SER 0.00367814
S18 S19 THR TYR 0.000143265
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S18 S19 VAL SER 0.00367814
S18 S19 VAL TYR 0.000143265
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S18 S19 TRP SER 0.00367814
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S18 S19 TYR SER 0.00367814
S18 S19 TYR TYR 0.000143265
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S18 S19 --- SER 0.00367814
S18 S19 --- TYR 0.000143265
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S18 S20 CYS PHE 0.00714391
S18 S20 CYS LEU 0.0010424
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S18 S20 ASP PHE 0.00714391
S18 S20 ASP LEU 0.0010424
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S18 S20 ASP VAL 0.000614942
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S18 S20 GLU CYS 0.0237944
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S18 S20 GLU HIS 0.0237944
S18 S20 GLU ILE 0.0237944
S18 S20 GLU LYS 0.0237944
S18 S20 GLU LEU -0.12483
S18 S20 GLU MET -0.176923
S18 S20 GLU ASN 0.0237944
S18 S20 GLU PRO 0.0237944
S18 S20 GLU GLN 0.0237944
S18 S20 GLU ARG 0.0237944
S18 S20 GLU SER 0.0237944
S18 S20 GLU THR 0.0237944
S18 S20 GLU VAL -0.110962
S18 S20 GLU TRP 0.0237944
S18 S20 GLU TYR 0.0237944
S18 S20 GLU --- 0.0237944
S18 S20 PHE PHE 0.00714391
S18 S20 PHE LEU 0.0010424
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S18 S20 HIS GLU 0.000455341
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S18 S20 HIS GLY 0.000455341
S18 S20 HIS HIS 0.000455341
S18 S20 HIS ILE 0.000455341
S18 S20 HIS LYS 0.000455341
S18 S20 HIS LEU 0.0688291
S18 S20 HIS MET -0.186581
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S18 S20 HIS VAL 0.0340811
S18 S20 HIS TRP 0.000455341
S18 S20 HIS TYR 0.000455341
S18 S20 HIS --- 0.000455341
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S18 S20 LYS LEU 0.0010424
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S18 S20 ASN LEU 0.0010424
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S18 S20 GLN LEU 0.0010424
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S18 S20 THR MET 0.00403897

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S18 S20 --- VAL 0.000614942
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S18 S21 ALA ILE 0.00803763
S18 S21 ALA VAL 0.00208685
S18 S21 ALA TYR 0.00183703
S18 S21 CYS PHE 0.000878709
S18 S21 CYS ILE 0.00803763
S18 S21 CYS VAL 0.00208685
S18 S21 CYS TYR 0.00183703
S18 S21 ASP PHE 0.000878709
S18 S21 ASP ILE 0.00803763
S18 S21 ASP VAL 0.00208685
S18 S21 ASP TYR 0.00183703
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S18 S21 GLU CYS 0.022116
S18 S21 GLU ASP 0.022116
S18 S21 GLU GLU 0.022116
S18 S21 GLU PHE -0.283944
S18 S21 GLU GLY 0.022116
S18 S21 GLU HIS 0.022116
S18 S21 GLU ILE -0.282796
S18 S21 GLU LYS 0.022116
S18 S21 GLU LEU 0.022116
S18 S21 GLU MET 0.022116
S18 S21 GLU ASN 0.022116
S18 S21 GLU PRO 0.022116
S18 S21 GLU GLN 0.022116
S18 S21 GLU ARG 0.022116
S18 S21 GLU SER 0.022116
S18 S21 GLU THR 0.022116
S18 S21 GLU VAL -0.189887
S18 S21 GLU TRP 0.022116
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S18 S21 GLU --- 0.022116
S18 S21 PHE PHE 0.000878709
S18 S21 PHE ILE 0.00803763
S18 S21 PHE VAL 0.00208685
S18 S21 PHE TYR 0.00183703
S18 S21 GLY PHE 0.000878709
S18 S21 GLY ILE 0.00803763
S18 S21 GLY VAL 0.00208685
S18 S21 GLY TYR 0.00183703
S18 S21 HIS ALA 0.00100986
S18 S21 HIS CYS 0.00100986
S18 S21 HIS ASP 0.00100986
S18 S21 HIS GLU 0.00100986
S18 S21 HIS PHE 0.0980965

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S18 S21 HIS HIS 0.00100986
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S18 S21 HIS LYS 0.00100986
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S18 S21 HIS MET 0.00100986
S18 S21 HIS ASN 0.00100986
S18 S21 HIS PRO 0.00100986
S18 S21 HIS GLN 0.00100986
S18 S21 HIS ARG 0.00100986
S18 S21 HIS SER 0.00100986
S18 S21 HIS THR 0.00100986
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S18 S21 HIS TRP 0.00100986
S18 S21 HIS TYR -0.348659
S18 S21 HIS --- 0.00100986
S18 S21 ILE PHE 0.000878709
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S18 S21 ILE VAL 0.00208685
S18 S21 ILE TYR 0.00183703
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S18 S21 LYS VAL 0.00208685
S18 S21 LYS TYR 0.00183703
S18 S21 LEU PHE 0.000878709
S18 S21 LEU ILE 0.00803763
S18 S21 LEU VAL 0.00208685
S18 S21 LEU TYR 0.00183703
S18 S21 MET PHE 0.000878709
S18 S21 MET ILE 0.00803763
S18 S21 MET VAL 0.00208685
S18 S21 MET TYR 0.00183703
S18 S21 ASN PHE 0.000878709
S18 S21 ASN ILE 0.00803763
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S18 S21 PRO PHE 0.000878709
S18 S21 PRO ILE 0.00803763
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S18 S21 PRO TYR 0.00183703
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S18 S21 GLN ILE 0.00803763
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S18 S21 GLN TYR 0.00183703
S18 S21 ARG PHE 0.000878709
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S18 S21 --- VAL 0.00208685
S18 S21 --- TYR 0.00183703
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S18 S22 ALA GLU 0.00042566
S18 S22 ALA ASN 0.0107857
S18 S22 ALA TYR 0.000271345
S18 S22 CYS ASP 0.00135752
S18 S22 CYS GLU 0.00042566
S18 S22 CYS ASN 0.0107857
S18 S22 CYS TYR 0.000271345
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S18 S22 ASP GLU 0.00042566
S18 S22 ASP ASN 0.0107857
S18 S22 ASP TYR 0.000271345
S18 S22 GLU ALA 0.0213778
S18 S22 GLU CYS 0.0213778
S18 S22 GLU ASP -0.133817
S18 S22 GLU GLU -0.0399073
S18 S22 GLU PHE 0.0213778
S18 S22 GLU GLY 0.0213778
S18 S22 GLU HIS 0.0213778
S18 S22 GLU ILE 0.0213778
S18 S22 GLU LYS 0.0213778
S18 S22 GLU LEU 0.0213778
S18 S22 GLU MET 0.0213778
S18 S22 GLU ASN -0.264887
S18 S22 GLU PRO 0.0213778
S18 S22 GLU GLN 0.0213778
S18 S22 GLU ARG 0.0213778
S18 S22 GLU SER 0.0213778
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S18 S22 GLU VAL 0.0213778
S18 S22 GLU TRP 0.0213778
S18 S22 GLU TYR -0.0601674
S18 S22 GLU --- 0.0213778
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S18 S22 PHE GLU 0.00042566
S18 S22 PHE ASN 0.0107857
S18 S22 PHE TYR 0.000271345
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S18 S22 GLY GLU 0.00042566
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S18 S22 HIS ASP 0.0378526
S18 S22 HIS GLU 0.00723781
S18 S22 HIS PHE 0.000156183
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S18 S22 HIS ILE 0.000156183
S18 S22 HIS LYS 0.000156183
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S18 S22 HIS MET 0.000156183
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S18 S22 HIS PRO 0.000156183

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S18 S22 ILE TYR 0.000271345
S18 S22 LYS ASP 0.00135752
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S18 S23 CYS LEU 0.00422293
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S18 S23 ASP LEU 0.00422293
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S18 S23 GLU CYS 0.0152397
S18 S23 GLU ASP 0.0152397
S18 S23 GLU GLU 0.0152397
S18 S23 GLU PHE 0.0152397
S18 S23 GLU GLY 0.0152397
S18 S23 GLU HIS 0.0152397
S18 S23 GLU ILE -0.283854
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S18 S23 PHE LEU 0.00422293
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S18 S23 HIS GLU 0.000502656
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S18 S23 --- LEU 0.00422293
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S18 S24 GLU GLU 0.0113335
S18 S24 GLU PHE 0.0113335
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S18 S24 GLU ILE 0.0113335
S18 S24 GLU LYS 0.0113335
S18 S24 GLU LEU 0.0113335
S18 S24 GLU MET 0.0113335
S18 S24 GLU ASN 0.0113335
S18 S24 GLU PRO 0.0113335
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S18 S24 GLU ARG 0.0113335
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S18 S24 HIS PHE 0.00028466
S18 S24 HIS GLY -0.118405
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S18 S24 HIS LYS 0.00028466
S18 S24 HIS LEU 0.00028466
S18 S24 HIS MET 0.00028466
S18 S24 HIS ASN 0.00028466
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S18 S24 HIS GLN 0.00028466

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S18 S24 HIS TRP 0.00028466
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S18 S25 GLU TYR 0.0257699
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S18 S25 TYR THR 0.000259874
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S18 S25 --- SER 0.0107373
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S18 S26 ASP TYR 0.00109295
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S18 S27 GLU LYS 0.0149657
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S18 S27 THR ASN 0.00171601
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S18 S27 --- SER 0.0111242
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S18 S28 CYS ASP 0.0119185
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S18 S28 ASP GLU 0.000921771
S18 S28 GLU ALA 0.0141132
S18 S28 GLU CYS 0.0141132

S18 S28 GLU ASP -0.314913
S18 S28 GLU GLU -0.0885951
S18 S28 GLU PHE 0.0141132
S18 S28 GLU GLY 0.0141132
S18 S28 GLU HIS 0.0141132
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S18 S28 GLU LYS 0.0141132
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S18 S28 GLU TYR 0.0141132
S18 S28 GLU --- 0.0141132
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S18 S28 PHE GLU 0.000921771
S18 S28 GLY ASP 0.0119185
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S18 S28 HIS ALA 0.000131384
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S18 S28 HIS ASP -0.125896
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S18 S28 LYS ASP 0.0119185
S18 S28 LYS GLU 0.000921771
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S18 S28 MET ASP 0.0119185
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S18 S28 PRO GLU 0.000921771
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S18 S28 SER GLU 0.000921771
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S18 S28 TYR GLU 0.000921771
S18 S28 --- ASP 0.0119185
S18 S28 --- GLU 0.000921771
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S18 S29 CYS LEU 0.000315475
S18 S29 CYS ASN 0.000313644
S18 S29 CYS SER 0.01206
S18 S29 ASP LYS 0.000151063
S18 S29 ASP LEU 0.000315475
S18 S29 ASP ASN 0.000313644
S18 S29 ASP SER 0.01206
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S18 S29 GLU ASP 0.0172942
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S18 S29 GLU PHE 0.0172942
S18 S29 GLU GLY 0.0172942
S18 S29 GLU HIS 0.0172942
S18 S29 GLU ILE 0.0172942
S18 S29 GLU LYS -0.0506403
S18 S29 GLU LEU -0.0894288
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S18 S29 HIS PRO 0.000533971

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S18 S30 HIS TYR 0.000205176
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S18 S31 GLU ALA 0.0177831
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S18 S31 GLU PHE 0.0177831
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S18 S31 GLU LYS 0.0177831
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S18 S31 GLU ASN 0.0177831
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S18 S31 HIS LYS 0.000777819

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S18 S31 HIS PRO 0.000777819
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S18 S32 ASP TYR 0.00137964
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S18 S33 ALA SER 0.00179041
S18 S33 ALA VAL 0.00142132
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S18 S38 GLU PHE 0.0301464
S18 S38 GLU GLY 0.0301464
S18 S38 GLU HIS 0.215586
S18 S38 GLU ILE 0.0301464
S18 S38 GLU LYS -0.349774
S18 S38 GLU LEU -0.141667
S18 S38 GLU MET 0.0301464
S18 S38 GLU ASN 0.0301464
S18 S38 GLU PRO 0.0301464
S18 S38 GLU GLN 0.0301464
S18 S38 GLU ARG -0.229829
S18 S38 GLU SER 0.0301464
S18 S38 GLU THR 0.0301464
S18 S38 GLU VAL 0.0301464
S18 S38 GLU TRP 0.0301464
S18 S38 GLU TYR 0.0301464
S18 S38 GLU --- 0.0301464
S18 S38 PHE GLU 0.000985071
S18 S38 PHE HIS 0.00437088
S18 S38 PHE LYS 0.00231212
S18 S38 PHE LEU 0.0039738
S18 S38 PHE ARG 0.00119836
S18 S38 GLY GLU 0.000985071
S18 S38 GLY HIS 0.00437088
S18 S38 GLY LYS 0.00231212
S18 S38 GLY LEU 0.0039738
S18 S38 GLY ARG 0.00119836
S18 S38 HIS ALA 0.00110455
S18 S38 HIS CYS 0.00110455
S18 S38 HIS ASP 0.00110455
S18 S38 HIS GLU 0.0434523
S18 S38 HIS PHE 0.00110455
S18 S38 HIS GLY 0.00110455
S18 S38 HIS HIS -0.424568
S18 S38 HIS ILE 0.00110455
S18 S38 HIS LYS 0.11995
S18 S38 HIS LEU -0.0210438
S18 S38 HIS MET 0.00110455
S18 S38 HIS ASN 0.00110455
S18 S38 HIS PRO 0.00110455
S18 S38 HIS GLN 0.00110455
S18 S38 HIS ARG 0.155928
S18 S38 HIS SER 0.00110455
S18 S38 HIS THR 0.00110455
S18 S38 HIS VAL 0.00110455
S18 S38 HIS TRP 0.00110455
S18 S38 HIS TYR 0.00110455
S18 S38 HIS --- 0.00110455
S18 S38 ILE GLU 0.000985071
S18 S38 ILE HIS 0.00437088
S18 S38 ILE LYS 0.00231212
S18 S38 ILE LEU 0.0039738
S18 S38 ILE ARG 0.00119836
S18 S38 LYS GLU 0.000985071
S18 S38 LYS HIS 0.00437088
S18 S38 LYS LYS 0.00231212
S18 S38 LYS LEU 0.0039738
S18 S38 LYS ARG 0.00119836
S18 S38 LEU GLU 0.000985071
S18 S38 LEU HIS 0.00437088
S18 S38 LEU LYS 0.00231212
S18 S38 LEU LEU 0.0039738
S18 S38 LEU ARG 0.00119836

S18 S38 MET GLU 0.000985071
S18 S38 MET HIS 0.00437088
S18 S38 MET LYS 0.00231212
S18 S38 MET LEU 0.0039738
S18 S38 MET ARG 0.00119836
S18 S38 ASN GLU 0.000985071
S18 S38 ASN HIS 0.00437088
S18 S38 ASN LYS 0.00231212
S18 S38 ASN LEU 0.0039738
S18 S38 ASN ARG 0.00119836
S18 S38 PRO GLU 0.000985071
S18 S38 PRO HIS 0.00437088
S18 S38 PRO LYS 0.00231212
S18 S38 PRO LEU 0.0039738
S18 S38 PRO ARG 0.00119836
S18 S38 GLN GLU 0.000985071
S18 S38 GLN HIS 0.00437088
S18 S38 GLN LYS 0.00231212
S18 S38 GLN LEU 0.0039738
S18 S38 GLN ARG 0.00119836
S18 S38 ARG GLU 0.000985071
S18 S38 ARG HIS 0.00437088
S18 S38 ARG LYS 0.00231212
S18 S38 ARG LEU 0.0039738
S18 S38 ARG ARG 0.00119836
S18 S38 SER GLU 0.000985071
S18 S38 SER HIS 0.00437088
S18 S38 SER LYS 0.00231212
S18 S38 SER LEU 0.0039738
S18 S38 SER ARG 0.00119836
S18 S38 THR GLU 0.000985071
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S18 S38 THR LYS 0.00231212
S18 S38 THR LEU 0.0039738
S18 S38 THR ARG 0.00119836
S18 S38 VAL GLU 0.000985071
S18 S38 VAL HIS 0.00437088
S18 S38 VAL LYS 0.00231212
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S18 S38 VAL ARG 0.00119836
S18 S38 TRP GLU 0.000985071
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S18 S38 TRP ARG 0.00119836
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S18 S38 TYR LYS 0.00231212
S18 S38 TYR LEU 0.0039738
S18 S38 TYR ARG 0.00119836
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S18 S38 --- HIS 0.00437088
S18 S38 --- LYS 0.00231212
S18 S38 --- LEU 0.0039738
S18 S38 --- ARG 0.00119836
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S18 S39 ALA VAL 0.0112692
S18 S39 ALA TRP 0.000299846
S18 S39 CYS ILE 0.000898287
S18 S39 CYS LEU 0.000372933
S18 S39 CYS VAL 0.0112692
S18 S39 CYS TRP 0.000299846

S18 S39 ASP ILE 0.000898287
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S18 S39 ASP VAL 0.0112692
S18 S39 ASP TRP 0.000299846
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S18 S39 GLU CYS 0.0179092
S18 S39 GLU ASP 0.0179092
S18 S39 GLU GLU 0.0179092
S18 S39 GLU PHE 0.0179092
S18 S39 GLU GLY 0.0179092
S18 S39 GLU HIS 0.0179092
S18 S39 GLU ILE -0.111295
S18 S39 GLU LYS 0.0179092
S18 S39 GLU LEU -0.0625046
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S18 S39 GLU ASN 0.0179092
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S18 S39 GLU GLN 0.0179092
S18 S39 GLU ARG 0.0179092
S18 S39 GLU SER 0.0179092
S18 S39 GLU THR 0.0179092
S18 S39 GLU VAL -0.174314
S18 S39 GLU TRP -0.0917
S18 S39 GLU TYR 0.0179092
S18 S39 GLU --- 0.0179092
S18 S39 PHE ILE 0.000898287
S18 S39 PHE LEU 0.000372933
S18 S39 PHE VAL 0.0112692
S18 S39 PHE TRP 0.000299846
S18 S39 GLY ILE 0.000898287
S18 S39 GLY LEU 0.000372933
S18 S39 GLY VAL 0.0112692
S18 S39 GLY TRP 0.000299846
S18 S39 HIS ALA 0.000829018
S18 S39 HIS CYS 0.000829018
S18 S39 HIS ASP 0.000829018
S18 S39 HIS GLU 0.000829018
S18 S39 HIS PHE 0.000829018
S18 S39 HIS GLY 0.000829018
S18 S39 HIS HIS 0.000829018
S18 S39 HIS ILE 0.0317174
S18 S39 HIS LYS 0.000829018
S18 S39 HIS LEU 0.00706199
S18 S39 HIS MET 0.000829018
S18 S39 HIS ASN 0.000829018
S18 S39 HIS PRO 0.000829018
S18 S39 HIS GLN 0.000829018
S18 S39 HIS ARG 0.000829018
S18 S39 HIS SER 0.000829018
S18 S39 HIS THR 0.000829018
S18 S39 HIS VAL -0.208879
S18 S39 HIS TRP 0.047398
S18 S39 HIS TYR 0.000829018
S18 S39 HIS --- 0.000829018
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S18 S39 ILE LEU 0.000372933
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S18 S39 LYS LEU 0.000372933
S18 S39 LYS VAL 0.0112692
S18 S39 LYS TRP 0.000299846
S18 S39 LEU ILE 0.000898287

S18 S39 LEU LEU 0.000372933
S18 S39 LEU VAL 0.0112692
S18 S39 LEU TRP 0.000299846
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S18 S39 PRO LEU 0.000372933
S18 S39 PRO VAL 0.0112692
S18 S39 PRO TRP 0.000299846
S18 S39 GLN ILE 0.000898287
S18 S39 GLN LEU 0.000372933
S18 S39 GLN VAL 0.0112692
S18 S39 GLN TRP 0.000299846
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S18 S39 ARG LEU 0.000372933
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S18 S39 ARG TRP 0.000299846
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S18 S39 SER LEU 0.000372933
S18 S39 SER VAL 0.0112692
S18 S39 SER TRP 0.000299846
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S18 S39 THR LEU 0.000372933
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S18 S39 THR TRP 0.000299846
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S18 S39 VAL LEU 0.000372933
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S18 S39 TYR TRP 0.000299846
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S18 S40 ALA VAL 0.0105458
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S18 S40 CYS VAL 0.0105458
S18 S40 ASP ILE 0.00166791
S18 S40 ASP LEU 0.00062648
S18 S40 ASP VAL 0.0105458
S18 S40 GLU ALA 0.0160482
S18 S40 GLU CYS 0.0160482
S18 S40 GLU ASP 0.0160482
S18 S40 GLU GLU 0.0160482
S18 S40 GLU PHE 0.0160482
S18 S40 GLU GLY 0.0160482
S18 S40 GLU HIS 0.0160482

S18 S40 GLU ILE -0.148215
S18 S40 GLU LYS 0.0160482
S18 S40 GLU LEU -0.107151
S18 S40 GLU MET 0.0160482
S18 S40 GLU ASN 0.0160482
S18 S40 GLU PRO 0.0160482
S18 S40 GLU GLN 0.0160482
S18 S40 GLU ARG 0.0160482
S18 S40 GLU SER 0.0160482
S18 S40 GLU THR 0.0160482
S18 S40 GLU VAL -0.168859
S18 S40 GLU TRP 0.0160482
S18 S40 GLU TYR 0.0160482
S18 S40 GLU --- 0.0160482
S18 S40 PHE ILE 0.00166791
S18 S40 PHE LEU 0.00062648
S18 S40 PHE VAL 0.0105458
S18 S40 GLY ILE 0.00166791
S18 S40 GLY LEU 0.00062648
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S18 S40 HIS ALA 0.000360878
S18 S40 HIS CYS 0.000360878
S18 S40 HIS ASP 0.000360878
S18 S40 HIS GLU 0.000360878
S18 S40 HIS PHE 0.000360878
S18 S40 HIS GLY 0.000360878
S18 S40 HIS HIS 0.000360878
S18 S40 HIS ILE 0.0444087
S18 S40 HIS LYS 0.000360878
S18 S40 HIS LEU 0.0403234
S18 S40 HIS MET 0.000360878
S18 S40 HIS ASN 0.000360878
S18 S40 HIS PRO 0.000360878
S18 S40 HIS GLN 0.000360878
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S18 S40 HIS SER 0.000360878
S18 S40 HIS THR 0.000360878
S18 S40 HIS VAL -0.199836
S18 S40 HIS TRP 0.000360878
S18 S40 HIS TYR 0.000360878
S18 S40 HIS --- 0.000360878
S18 S40 ILE ILE 0.00166791
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S18 S40 LYS LEU 0.00062648
S18 S40 LYS VAL 0.0105458
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S18 S40 LEU LEU 0.00062648
S18 S40 LEU VAL 0.0105458
S18 S40 MET ILE 0.00166791
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S18 S40 ASN ILE 0.00166791
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S18 S40 PRO ILE 0.00166791
S18 S40 PRO LEU 0.00062648
S18 S40 PRO VAL 0.0105458
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S18 S40 GLN LEU 0.00062648
S18 S40 GLN VAL 0.0105458
S18 S40 ARG ILE 0.00166791

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S18 S40 SER LEU 0.00062648
S18 S40 SER VAL 0.0105458
S18 S40 THR ILE 0.00166791
S18 S40 THR LEU 0.00062648
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S18 S40 VAL LEU 0.00062648
S18 S40 VAL VAL 0.0105458
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S19 S20 ALA GLU 0.0125207
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S19 S20 ALA GLY 0.0125207
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S19 S20 ALA ILE 0.0125207
S19 S20 ALA LYS 0.0125207
S19 S20 ALA LEU 0.127289
S19 S20 ALA MET -0.512167
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S19 S20 CYS PHE 0.00935332
S19 S20 CYS LEU 0.000674988
S19 S20 CYS MET 0.00748651
S19 S20 CYS VAL 0.00117866
S19 S20 ASP PHE 0.00935332
S19 S20 ASP LEU 0.000674988
S19 S20 ASP MET 0.00748651
S19 S20 ASP VAL 0.00117866
S19 S20 GLU PHE 0.00935332
S19 S20 GLU LEU 0.000674988
S19 S20 GLU MET 0.00748651
S19 S20 GLU VAL 0.00117866
S19 S20 PHE PHE 0.00935332
S19 S20 PHE LEU 0.000674988
S19 S20 PHE MET 0.00748651
S19 S20 PHE VAL 0.00117866
S19 S20 GLY PHE 0.00935332
S19 S20 GLY LEU 0.000674988
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S19 S20 GLY VAL 0.00117866
S19 S20 HIS PHE 0.00935332
S19 S20 HIS LEU 0.000674988

S19 S20 HIS MET 0.00748651
S19 S20 HIS VAL 0.00117866
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S19 S20 LEU VAL 0.00117866
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S19 S20 ARG PHE 0.00935332
S19 S20 ARG LEU 0.000674988
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S19 S20 SER ALA 0.0103527
S19 S20 SER CYS 0.0103527
S19 S20 SER ASP 0.0103527
S19 S20 SER GLU 0.0103527
S19 S20 SER PHE 0.109116
S19 S20 SER GLY 0.0103527
S19 S20 SER HIS 0.0103527
S19 S20 SER ILE 0.0103527
S19 S20 SER LYS 0.0103527
S19 S20 SER LEU -0.217838
S19 S20 SER MET -0.157018
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S19 S20 SER THR 0.0103527
S19 S20 SER VAL -0.00963195
S19 S20 SER TRP 0.0103527
S19 S20 SER TYR 0.0103527
S19 S20 SER --- 0.0103527
S19 S20 THR PHE 0.00935332
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S19 S20 THR VAL 0.00117866
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S19 S20 VAL LEU 0.000674988
S19 S20 VAL MET 0.00748651
S19 S20 VAL VAL 0.00117866

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S19 S20 TRP LEU 0.000674988
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S19 S20 TYR ASP 0.00137632
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S19 S20 TYR PHE -0.473281
S19 S20 TYR GLY 0.00137632
S19 S20 TYR HIS 0.00137632
S19 S20 TYR ILE 0.00137632
S19 S20 TYR LYS 0.00137632
S19 S20 TYR LEU 0.0422039
S19 S20 TYR MET 0.247664
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S19 S20 TYR VAL 0.0990359
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S19 S20 TYR TYR 0.00137632
S19 S20 TYR --- 0.00137632
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S19 S20 --- LEU 0.000674988
S19 S20 --- MET 0.00748651
S19 S20 --- VAL 0.00117866
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S19 S21 ALA ASP 0.013095
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S19 S21 ALA PHE 0.37382
S19 S21 ALA GLY 0.013095
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S19 S21 ALA ILE -0.0393959
S19 S21 ALA LYS 0.013095
S19 S21 ALA LEU 0.013095
S19 S21 ALA MET 0.013095
S19 S21 ALA ASN 0.013095
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S19 S21 ALA GLN 0.013095
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S19 S21 ALA VAL -0.653976
S19 S21 ALA TRP 0.013095
S19 S21 ALA TYR -0.0791911
S19 S21 ALA --- 0.013095
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S19 S21 CYS ILE 0.0139898
S19 S21 CYS VAL 0.00205646
S19 S21 CYS TYR 0.00115324
S19 S21 ASP PHE 0.00149394
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S19 S21 GLU PHE 0.00149394
S19 S21 GLU ILE 0.0139898
S19 S21 GLU VAL 0.00205646
S19 S21 GLU TYR 0.00115324
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S19 S21 PHE ILE 0.0139898
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S19 S21 PHE TYR 0.00115324
S19 S21 GLY PHE 0.00149394
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S19 S21 ILE VAL 0.00205646
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S19 S21 LYS ILE 0.0139898
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S19 S21 LYS TYR 0.00115324
S19 S21 LEU PHE 0.00149394
S19 S21 LEU ILE 0.0139898
S19 S21 LEU VAL 0.00205646
S19 S21 LEU TYR 0.00115324
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S19 S21 GLN PHE 0.00149394
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S19 S21 SER ALA 0.00980583
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S19 S21 SER HIS 0.00980583
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S19 S21 SER LYS 0.00980583
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S19 S21 SER MET 0.00980583
S19 S21 SER ASN 0.00980583
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S19 S21 SER TRP 0.00980583
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S19 S21 THR ILE 0.0139898
S19 S21 THR VAL 0.00205646
S19 S21 THR TYR 0.00115324
S19 S21 VAL PHE 0.00149394
S19 S21 VAL ILE 0.0139898
S19 S21 VAL VAL 0.00205646
S19 S21 VAL TYR 0.00115324
S19 S21 TRP PHE 0.00149394
S19 S21 TRP ILE 0.0139898
S19 S21 TRP VAL 0.00205646
S19 S21 TRP TYR 0.00115324
S19 S21 TYR ALA 0.000224974
S19 S21 TYR CYS 0.000224974
S19 S21 TYR ASP 0.000224974
S19 S21 TYR GLU 0.000224974
S19 S21 TYR PHE -0.540041
S19 S21 TYR GLY 0.000224974
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S19 S21 TYR ILE 0.461233
S19 S21 TYR LYS 0.000224974
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S19 S21 TYR VAL 0.00655799
S19 S21 TYR TRP 0.000224974
S19 S21 TYR TYR 0.00744496
S19 S21 TYR --- 0.000224974
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S19 S21 --- TYR 0.00115324
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S19 S22 ALA CYS 0.0137166
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S19 S22 ALA GLU 0.423523
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S19 S22 ALA GLY 0.0137166
S19 S22 ALA HIS 0.0137166
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S19 S22 ALA LYS 0.0137166
S19 S22 ALA LEU 0.0137166
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S19 S22 CYS ASN 0.014808
S19 S22 CYS TYR 0.00112963

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S19 S22 ASP ASN 0.014808
S19 S22 ASP TYR 0.00112963
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S19 S22 GLU TYR 0.00112963
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S19 S22 PHE TYR 0.00112963
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S19 S22 HIS GLU 0.000826154
S19 S22 HIS ASN 0.014808
S19 S22 HIS TYR 0.00112963
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S19 S22 SER LEU 0.00775138
S19 S22 SER MET 0.00775138

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S19 S22 TYR GLU 0.00316309
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S19 S22 TYR GLY 6.5937e-05
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S19 S24 ASN SER 0.000158348

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S19 S26 ALA TYR -0.551326
S19 S26 ALA --- 0.01405
S19 S26 CYS PHE 0.00736922
S19 S26 CYS LYS 0.0108141
S19 S26 CYS TYR 0.000510164
S19 S26 ASP PHE 0.00736922

S19 S26 ASP LYS 0.0108141
S19 S26 ASP TYR 0.000510164
S19 S26 GLU PHE 0.00736922
S19 S26 GLU LYS 0.0108141
S19 S26 GLU TYR 0.000510164
S19 S26 PHE PHE 0.00736922
S19 S26 PHE LYS 0.0108141
S19 S26 PHE TYR 0.000510164
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S19 S26 GLY LYS 0.0108141
S19 S26 GLY TYR 0.000510164
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S19 S26 HIS LYS 0.0108141
S19 S26 HIS TYR 0.000510164
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S19 S26 ILE TYR 0.000510164
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S19 S26 LYS TYR 0.000510164
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S19 S26 MET LYS 0.0108141
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S19 S26 ASN LYS 0.0108141
S19 S26 ASN TYR 0.000510164
S19 S26 PRO PHE 0.00736922
S19 S26 PRO LYS 0.0108141
S19 S26 PRO TYR 0.000510164
S19 S26 GLN PHE 0.00736922
S19 S26 GLN LYS 0.0108141
S19 S26 GLN TYR 0.000510164
S19 S26 ARG PHE 0.00736922
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S19 S26 SER ASP 0.00674077
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S19 S26 SER PHE -0.165181
S19 S26 SER GLY 0.00674077
S19 S26 SER HIS 0.00674077
S19 S26 SER ILE 0.00674077
S19 S26 SER LYS -0.563883
S19 S26 SER LEU 0.00674077
S19 S26 SER MET 0.00674077
S19 S26 SER ASN 0.00674077
S19 S26 SER PRO 0.00674077
S19 S26 SER GLN 0.00674077
S19 S26 SER ARG 0.00674077
S19 S26 SER SER 0.00674077
S19 S26 SER THR 0.00674077
S19 S26 SER VAL 0.00674077
S19 S26 SER TRP 0.00674077
S19 S26 SER TYR 0.508355
S19 S26 SER --- 0.00674077
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S19 S26 THR LYS 0.0108141
S19 S26 THR TYR 0.000510164
S19 S26 VAL PHE 0.00736922

S19 S26 VAL LYS 0.0108141
S19 S26 VAL TYR 0.000510164
S19 S26 TRP PHE 0.00736922
S19 S26 TRP LYS 0.0108141
S19 S26 TRP TYR 0.000510164
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S19 S26 TYR GLU 0.000198944
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S19 S26 TYR GLY 0.000198944
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S19 S26 TYR ILE 0.000198944
S19 S26 TYR LYS 0.282197
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S19 S26 TYR TYR 0.00216016
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S19 S26 --- LYS 0.0108141
S19 S26 --- TYR 0.000510164
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S19 S27 ALA LYS 0.00971883
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S19 S27 PHE SER 0.0160124
S19 S27 GLY ASN 0.00268112
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S19 S27 HIS SER 0.0160124
S19 S27 ILE ASN 0.00268112

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S19 S27 SER LEU 0.00546134
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S19 S27 TYR CYS 1.5885e-05
S19 S27 TYR ASP 1.5885e-05
S19 S27 TYR GLU 1.5885e-05
S19 S27 TYR PHE 1.5885e-05
S19 S27 TYR GLY 1.5885e-05
S19 S27 TYR HIS 1.5885e-05
S19 S27 TYR ILE 1.5885e-05
S19 S27 TYR LYS 1.5885e-05
S19 S27 TYR LEU 1.5885e-05
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S19 S27 TYR PRO 1.5885e-05
S19 S27 TYR GLN 1.5885e-05
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S19 S27 TYR VAL 1.5885e-05
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S19 S27 TYR --- 1.5885e-05

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S19 S27 --- SER 0.0160124
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S19 S28 TYR GLU 0.00571655
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S19 S28 TYR LYS 4.83767e-05
S19 S28 TYR LEU 4.83767e-05
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S19 S28 TYR PRO 4.83767e-05
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S19 S30 SER TRP 0.00505708
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S19 S31 ASP ILE 0.00271219
S19 S31 ASP VAL 0.0155228
S19 S31 GLU ASP 0.000458505
S19 S31 GLU ILE 0.00271219
S19 S31 GLU VAL 0.0155228
S19 S31 PHE ASP 0.000458505
S19 S31 PHE ILE 0.00271219
S19 S31 PHE VAL 0.0155228
S19 S31 GLY ASP 0.000458505
S19 S31 GLY ILE 0.00271219
S19 S31 GLY VAL 0.0155228
S19 S31 HIS ASP 0.000458505
S19 S31 HIS ILE 0.00271219
S19 S31 HIS VAL 0.0155228
S19 S31 ILE ASP 0.000458505
S19 S31 ILE ILE 0.00271219
S19 S31 ILE VAL 0.0155228
S19 S31 LYS ASP 0.000458505

S19 S31 LYS ILE 0.00271219
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S19 S31 LEU ILE 0.00271219
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S19 S31 PRO ILE 0.00271219
S19 S31 PRO VAL 0.0155228
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S19 S31 GLN ILE 0.00271219
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S19 S31 SER CYS 0.0051945
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S19 S31 SER LYS 0.0051945
S19 S31 SER LEU 0.0051945
S19 S31 SER MET 0.0051945
S19 S31 SER ASN 0.0051945
S19 S31 SER PRO 0.0051945
S19 S31 SER GLN 0.0051945
S19 S31 SER ARG 0.0051945
S19 S31 SER SER 0.0051945
S19 S31 SER THR 0.0051945
S19 S31 SER VAL -0.187332
S19 S31 SER TRP 0.0051945
S19 S31 SER TYR 0.0051945
S19 S31 SER --- 0.0051945
S19 S31 THR ASP 0.000458505
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S19 S31 THR VAL 0.0155228
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S19 S31 TYR ASP 0.0026541
S19 S31 TYR GLU 0.000194962
S19 S31 TYR PHE 0.000194962
S19 S31 TYR GLY 0.000194962
S19 S31 TYR HIS 0.000194962
S19 S31 TYR ILE 0.0428775
S19 S31 TYR LYS 0.000194962
S19 S31 TYR LEU 0.000194962
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S19 S31 TYR PRO 0.000194962

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S19 S31 TYR THR 0.000194962
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S19 S31 TYR TRP 0.000194962
S19 S31 TYR TYR 0.000194962
S19 S31 TYR --- 0.000194962
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S19 S32 ALA HIS 0.18678
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S19 S32 ALA TYR -0.000854823
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S19 S32 ASP TYR 0.00112067
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S19 S32 GLU TRP 0.0140719
S19 S32 GLU TYR 0.00112067
S19 S32 PHE PHE 0.00179618
S19 S32 PHE HIS 0.00170474
S19 S32 PHE TRP 0.0140719
S19 S32 PHE TYR 0.00112067
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S19 S32 GLY HIS 0.00170474
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S19 S32 GLY TYR 0.00112067
S19 S32 HIS PHE 0.00179618
S19 S32 HIS HIS 0.00170474
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S19 S32 LYS TRP 0.0140719

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S19 S32 SER LEU 0.00960117
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S19 S32 TRP TYR 0.00112067
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S19 S32 TYR CYS 4.05581e-05
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S19 S32 TYR GLU 4.05581e-05
S19 S32 TYR PHE 0.016734

S19 S32 TYR GLY 4.05581e-05
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S19 S32 TYR LYS 4.05581e-05
S19 S32 TYR LEU 4.05581e-05
S19 S32 TYR MET 4.05581e-05
S19 S32 TYR ASN 4.05581e-05
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S19 S32 TYR GLN 4.05581e-05
S19 S32 TYR ARG 4.05581e-05
S19 S32 TYR SER 4.05581e-05
S19 S32 TYR THR 4.05581e-05
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S19 S33 ALA PHE 0.0159951
S19 S33 ALA GLY 0.0159951
S19 S33 ALA HIS 0.0159951
S19 S33 ALA ILE 0.0159951
S19 S33 ALA LYS -0.720452
S19 S33 ALA LEU 0.0159951
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S19 S33 ALA ASN 0.0159951
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S19 S33 HIS LYS 0.000470534

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S19 S33 SER GLY 0.00853649
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S19 S33 SER LYS 0.686825
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S19 S33 SER THR 0.00853649
S19 S33 SER VAL -0.0887188
S19 S33 SER TRP 0.00853649
S19 S33 SER TYR 0.00853649
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S19 S33 VAL LYS 0.000470534
S19 S33 VAL SER 0.00258812
S19 S33 VAL VAL 0.0023874

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S19 S33 TRP VAL 0.0023874
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S19 S33 TYR ASP -0.0824881
S19 S33 TYR GLU 2.14594e-05
S19 S33 TYR PHE 2.14594e-05
S19 S33 TYR GLY 2.14594e-05
S19 S33 TYR HIS 2.14594e-05
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S19 S33 TYR LYS 0.00199769
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S19 S33 TYR ASN 2.14594e-05
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S19 S36 ASP THR 0.00112755
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S19 S39 TYR PRO 2.09961e-05
S19 S39 TYR GLN 2.09961e-05

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S19 S40 ALA GLY 0.00975026
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S19 S40 ALA ILE -0.544546
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S19 S40 ALA LEU 0.147721
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S20 S22 CYS TYR 0.000698645
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S20 S27 LEU PRO 0.000995379
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S20 S27 PRO ASN 0.00386444

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S20 S27 VAL CYS 3.43173e-05
S20 S27 VAL ASP 3.43173e-05
S20 S27 VAL GLU 3.43173e-05
S20 S27 VAL PHE 3.43173e-05
S20 S27 VAL GLY 3.43173e-05
S20 S27 VAL HIS 3.43173e-05
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S20 S27 VAL LYS 3.43173e-05
S20 S27 VAL LEU 3.43173e-05
S20 S27 VAL MET 3.43173e-05
S20 S27 VAL ASN 0.0418824
S20 S27 VAL PRO 3.43173e-05
S20 S27 VAL GLN 3.43173e-05
S20 S27 VAL ARG 3.43173e-05
S20 S27 VAL SER -0.107732
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S20 S27 VAL VAL 3.43173e-05
S20 S27 VAL TRP 3.43173e-05
S20 S27 VAL TYR 3.43173e-05
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S20 S27 TYR ASN 0.00386444
S20 S27 TYR SER 0.0203853
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S20 S27 --- SER 0.0203853
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S20 S28 CYS GLU 0.00207037
S20 S28 ASP ASP 0.0221794
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S20 S28 GLU ASP 0.0221794
S20 S28 GLU GLU 0.00207037
S20 S28 PHE ALA 0.00746427
S20 S28 PHE CYS 0.00746427
S20 S28 PHE ASP 0.173305
S20 S28 PHE GLU -0.339216
S20 S28 PHE PHE 0.00746427
S20 S28 PHE GLY 0.00746427
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S20 S28 PHE ILE 0.00746427
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S20 S28 PHE TRP 0.00746427

S20 S28 PHE TYR 0.00746427
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S20 S28 ILE ASP 0.0221794
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S20 S28 VAL GLU 0.0318035
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S20 S31 VAL PHE 0.000737281
S20 S31 VAL GLY 0.000737281
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S20 S31 VAL LYS 0.000737281
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S20 S31 VAL TYR 0.000737281
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S20 S31 TRP ILE 0.00213648
S20 S31 TRP VAL 0.0218077
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S20 S31 TYR ILE 0.00213648
S20 S31 TYR VAL 0.0218077
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S20 S31 --- ILE 0.00213648
S20 S31 --- VAL 0.0218077
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S20 S32 ALA HIS 0.00339763
S20 S32 ALA TRP 0.0180836
S20 S32 ALA TYR 0.00177479
S20 S32 CYS PHE 0.000993731
S20 S32 CYS HIS 0.00339763
S20 S32 CYS TRP 0.0180836
S20 S32 CYS TYR 0.00177479

S20 S32 ASP PHE 0.000993731
S20 S32 ASP HIS 0.00339763
S20 S32 ASP TRP 0.0180836
S20 S32 ASP TYR 0.00177479
S20 S32 GLU PHE 0.000993731
S20 S32 GLU HIS 0.00339763
S20 S32 GLU TRP 0.0180836
S20 S32 GLU TYR 0.00177479
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S20 S32 PHE CYS 0.0152815
S20 S32 PHE ASP 0.0152815
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S20 S32 PHE GLY 0.0152815
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S20 S38 TYR LEU 0.00594068
S20 S38 TYR ARG 0.00259674
S20 S38 --- GLU 0.00316238
S20 S38 --- HIS 0.00692479
S20 S38 --- LYS 0.00562515
S20 S38 --- LEU 0.00594068
S20 S38 --- ARG 0.00259674
S20 S39 ALA ILE 0.00175691
S20 S39 ALA LEU 0.0020953
S20 S39 ALA VAL 0.0197469
S20 S39 ALA TRP 0.00065066
S20 S39 CYS ILE 0.00175691
S20 S39 CYS LEU 0.0020953
S20 S39 CYS VAL 0.0197469
S20 S39 CYS TRP 0.00065066
S20 S39 ASP ILE 0.00175691
S20 S39 ASP LEU 0.0020953
S20 S39 ASP VAL 0.0197469
S20 S39 ASP TRP 0.00065066
S20 S39 GLU ILE 0.00175691
S20 S39 GLU LEU 0.0020953
S20 S39 GLU VAL 0.0197469
S20 S39 GLU TRP 0.00065066
S20 S39 PHE ALA 0.00988599
S20 S39 PHE CYS 0.00988599
S20 S39 PHE ASP 0.00988599
S20 S39 PHE GLU 0.00988599
S20 S39 PHE PHE 0.00988599
S20 S39 PHE GLY 0.00988599
S20 S39 PHE HIS 0.00988599
S20 S39 PHE ILE -0.00293383
S20 S39 PHE LYS 0.00988599
S20 S39 PHE LEU 0.526355
S20 S39 PHE MET 0.00988599

S20 S39 PHE ASN 0.00988599
S20 S39 PHE PRO 0.00988599
S20 S39 PHE GLN 0.00988599
S20 S39 PHE ARG 0.00988599
S20 S39 PHE SER 0.00988599
S20 S39 PHE THR 0.00988599
S20 S39 PHE VAL -0.450623
S20 S39 PHE TRP -0.26495
S20 S39 PHE TYR 0.00988599
S20 S39 PHE --- 0.00988599
S20 S39 GLY ILE 0.00175691
S20 S39 GLY LEU 0.0020953
S20 S39 GLY VAL 0.0197469
S20 S39 GLY TRP 0.00065066
S20 S39 HIS ILE 0.00175691
S20 S39 HIS LEU 0.0020953
S20 S39 HIS VAL 0.0197469
S20 S39 HIS TRP 0.00065066
S20 S39 ILE ILE 0.00175691
S20 S39 ILE LEU 0.0020953
S20 S39 ILE VAL 0.0197469
S20 S39 ILE TRP 0.00065066
S20 S39 LYS ILE 0.00175691
S20 S39 LYS LEU 0.0020953
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S20 S39 LYS TRP 0.00065066
S20 S39 LEU ALA 0.00124534
S20 S39 LEU CYS 0.00124534
S20 S39 LEU ASP 0.00124534
S20 S39 LEU GLU 0.00124534
S20 S39 LEU PHE 0.00124534
S20 S39 LEU GLY 0.00124534
S20 S39 LEU HIS 0.00124534
S20 S39 LEU ILE 0.155116
S20 S39 LEU LYS 0.00124534
S20 S39 LEU LEU 0.0657165
S20 S39 LEU MET 0.00124534
S20 S39 LEU ASN 0.00124534
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S20 S39 LEU THR 0.00124534
S20 S39 LEU VAL -0.311624
S20 S39 LEU TRP 0.0334254
S20 S39 LEU TYR 0.00124534
S20 S39 LEU --- 0.00124534
S20 S39 MET ALA 0.00696643
S20 S39 MET CYS 0.00696643
S20 S39 MET ASP 0.00696643
S20 S39 MET GLU 0.00696643
S20 S39 MET PHE 0.00696643
S20 S39 MET GLY 0.00696643
S20 S39 MET HIS 0.00696643
S20 S39 MET ILE -0.290033
S20 S39 MET LYS 0.00696643
S20 S39 MET LEU -0.69975
S20 S39 MET MET 0.00696643
S20 S39 MET ASN 0.00696643
S20 S39 MET PRO 0.00696643
S20 S39 MET GLN 0.00696643
S20 S39 MET ARG 0.00696643
S20 S39 MET SER 0.00696643

S20 S39 MET THR 0.00696643
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S20 S39 MET TRP 0.139147
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S20 S39 ASN TRP 0.00065066
S20 S39 PRO ILE 0.00175691
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S20 S39 PRO TRP 0.00065066
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S20 S39 VAL TRP 0.0427111
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S20 S39 TRP ILE 0.00175691
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S20 S39 TYR ILE 0.00175691
S20 S39 TYR LEU 0.0020953
S20 S39 TYR VAL 0.0197469
S20 S39 TYR TRP 0.00065066
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S20 S39 --- LEU 0.0020953
S20 S39 --- VAL 0.0197469
S20 S39 --- TRP 0.00065066
S20 S40 ALA ILE 0.00246294

S20 S40 ALA LEU 0.000389353
S20 S40 ALA VAL 0.0213974
S20 S40 CYS ILE 0.00246294
S20 S40 CYS LEU 0.000389353
S20 S40 CYS VAL 0.0213974
S20 S40 ASP ILE 0.00246294
S20 S40 ASP LEU 0.000389353
S20 S40 ASP VAL 0.0213974
S20 S40 GLU ILE 0.00246294
S20 S40 GLU LEU 0.000389353
S20 S40 GLU VAL 0.0213974
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S20 S40 PHE CYS 0.00827114
S20 S40 PHE ASP 0.00827114
S20 S40 PHE GLU 0.00827114
S20 S40 PHE PHE 0.00827114
S20 S40 PHE GLY 0.00827114
S20 S40 PHE HIS 0.00827114
S20 S40 PHE ILE -0.440195
S20 S40 PHE LYS 0.00827114
S20 S40 PHE LEU 0.0969193
S20 S40 PHE MET 0.00827114
S20 S40 PHE ASN 0.00827114
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S20 S40 PHE TYR 0.00827114
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S20 S40 GLY VAL 0.0213974
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S20 S40 HIS LEU 0.000389353
S20 S40 HIS VAL 0.0213974
S20 S40 ILE ILE 0.00246294
S20 S40 ILE LEU 0.000389353
S20 S40 ILE VAL 0.0213974
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S20 S40 LEU CYS 0.00105379
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S20 S40 LEU GLY 0.00105379
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S20 S40 LEU LYS 0.00105379
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S20 S40 LEU VAL -0.345613
S20 S40 LEU TRP 0.00105379

S20 S40 LEU TYR 0.00105379
S20 S40 LEU --- 0.00105379
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S20 S40 MET CYS 0.0066769
S20 S40 MET ASP 0.0066769
S20 S40 MET GLU 0.0066769
S20 S40 MET PHE 0.0066769
S20 S40 MET GLY 0.0066769
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S20 S40 MET ILE 0.0280362
S20 S40 MET LYS 0.0066769
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S20 S40 MET VAL -0.246345
S20 S40 MET TRP 0.0066769
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S20 S40 ASN ILE 0.00246294
S20 S40 ASN LEU 0.000389353
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S20 S40 PRO LEU 0.000389353
S20 S40 PRO VAL 0.0213974
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S20 S40 THR ILE 0.00246294
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S20 S40 VAL ALA 0.000407276
S20 S40 VAL CYS 0.000407276
S20 S40 VAL ASP 0.000407276
S20 S40 VAL GLU 0.000407276
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S20 S40 VAL ILE 0.0232615
S20 S40 VAL LYS 0.000407276
S20 S40 VAL LEU 0.0146381
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S20 S40 VAL VAL -0.110428
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S20 S40 VAL --- 0.000407276
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S20 S40 TRP LEU 0.000389353
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S20 S40 --- VAL 0.0213974
S21 S22 ALA ASP 0.000920323
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S21 S22 ALA ASN 0.0159853
S21 S22 ALA TYR 0.00542098
S21 S22 CYS ASP 0.000920323
S21 S22 CYS GLU 0.000799261
S21 S22 CYS ASN 0.0159853
S21 S22 CYS TYR 0.00542098
S21 S22 ASP ASP 0.000920323
S21 S22 ASP GLU 0.000799261
S21 S22 ASP ASN 0.0159853
S21 S22 ASP TYR 0.00542098
S21 S22 GLU ASP 0.000920323
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S21 S22 GLU ASN 0.0159853
S21 S22 GLU TYR 0.00542098
S21 S22 PHE ALA 0.000875629
S21 S22 PHE CYS 0.000875629
S21 S22 PHE ASP 0.140286
S21 S22 PHE GLU 0.0180325
S21 S22 PHE PHE 0.000875629
S21 S22 PHE GLY 0.000875629
S21 S22 PHE HIS 0.000875629
S21 S22 PHE ILE 0.000875629
S21 S22 PHE LYS 0.000875629
S21 S22 PHE LEU 0.000875629
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S21 S22 PHE PRO 0.000875629
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S21 S22 GLY TYR 0.00542098
S21 S22 HIS ASP 0.000920323
S21 S22 HIS GLU 0.000799261
S21 S22 HIS ASN 0.0159853
S21 S22 HIS TYR 0.00542098
S21 S22 ILE ALA 0.0169628
S21 S22 ILE CYS 0.0169628
S21 S22 ILE ASP -0.360886
S21 S22 ILE GLU -0.158791
S21 S22 ILE PHE 0.0169628
S21 S22 ILE GLY 0.0169628
S21 S22 ILE HIS 0.0169628
S21 S22 ILE ILE 0.0169628
S21 S22 ILE LYS 0.0169628
S21 S22 ILE LEU 0.0169628

S21 S22 ILE MET 0.0169628
S21 S22 ILE ASN -0.350777
S21 S22 ILE PRO 0.0169628
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S21 S22 ILE TYR 0.498939
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S21 S22 LYS GLU 0.000799261
S21 S22 LYS ASN 0.0159853
S21 S22 LYS TYR 0.00542098
S21 S22 LEU ASP 0.000920323
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S21 S22 LEU ASN 0.0159853
S21 S22 LEU TYR 0.00542098
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S21 S22 MET GLU 0.000799261
S21 S22 MET ASN 0.0159853
S21 S22 MET TYR 0.00542098
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S21 S22 ASN TYR 0.00542098
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S21 S22 PRO GLU 0.000799261
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S21 S22 PRO TYR 0.00542098
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S21 S22 GLN GLU 0.000799261
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S21 S22 GLN TYR 0.00542098
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S21 S22 ARG TYR 0.00542098
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S21 S22 SER GLU 0.000799261
S21 S22 SER ASN 0.0159853
S21 S22 SER TYR 0.00542098
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S21 S22 VAL ALA 0.00325056
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S21 S22 VAL ILE 0.00325056
S21 S22 VAL LYS 0.00325056
S21 S22 VAL LEU 0.00325056
S21 S22 VAL MET 0.00325056
S21 S22 VAL ASN -0.115189
S21 S22 VAL PRO 0.00325056
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S21 S22 VAL SER 0.00325056

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S21 S22 VAL TRP 0.00325056
S21 S22 VAL TYR -0.212289
S21 S22 VAL --- 0.00325056
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S21 S22 TRP ASN 0.0159853
S21 S22 TRP TYR 0.00542098
S21 S22 TYR ALA 0.000444929
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S21 S22 TYR ASP 0.0208843
S21 S22 TYR GLU 0.0166541
S21 S22 TYR PHE 0.000444929
S21 S22 TYR GLY 0.000444929
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S21 S22 TYR ILE 0.000444929
S21 S22 TYR LYS 0.000444929
S21 S22 TYR LEU 0.000444929
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S21 S22 --- ASN 0.0159853
S21 S22 --- TYR 0.00542098
S21 S23 ALA ILE 0.0164133
S21 S23 ALA LEU 0.00671252
S21 S23 CYS ILE 0.0164133
S21 S23 CYS LEU 0.00671252
S21 S23 ASP ILE 0.0164133
S21 S23 ASP LEU 0.00671252
S21 S23 GLU ILE 0.0164133
S21 S23 GLU LEU 0.00671252
S21 S23 PHE ALA 0.000619848
S21 S23 PHE CYS 0.000619848
S21 S23 PHE ASP 0.000619848
S21 S23 PHE GLU 0.000619848
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S21 S23 PHE GLY 0.000619848
S21 S23 PHE HIS 0.000619848
S21 S23 PHE ILE -0.206072
S21 S23 PHE LYS 0.000619848
S21 S23 PHE LEU 0.0251432
S21 S23 PHE MET 0.000619848
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S21 S23 PHE --- 0.000619848

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S21 S23 GLY LEU 0.00671252
S21 S23 HIS ILE 0.0164133
S21 S23 HIS LEU 0.00671252
S21 S23 ILE ALA 0.0114124
S21 S23 ILE CYS 0.0114124
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S21 S23 ILE GLU 0.0114124
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S21 S23 ILE GLY 0.0114124
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S21 S23 ILE LYS 0.0114124
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S21 S23 ILE TRP 0.0114124
S21 S23 ILE TYR 0.0114124
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S21 S23 PRO LEU 0.00671252
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S21 S23 GLN LEU 0.00671252
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S21 S23 SER LEU 0.00671252
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S21 S23 VAL ALA 0.00262026
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S21 S23 VAL ASP 0.00262026
S21 S23 VAL GLU 0.00262026
S21 S23 VAL PHE 0.00262026
S21 S23 VAL GLY 0.00262026
S21 S23 VAL HIS 0.00262026
S21 S23 VAL ILE -0.107879
S21 S23 VAL LYS 0.00262026
S21 S23 VAL LEU -0.0142914
S21 S23 VAL MET 0.00262026
S21 S23 VAL ASN 0.00262026
S21 S23 VAL PRO 0.00262026
S21 S23 VAL GLN 0.00262026
S21 S23 VAL ARG 0.00262026
S21 S23 VAL SER 0.00262026
S21 S23 VAL THR 0.00262026
S21 S23 VAL VAL 0.00262026
S21 S23 VAL TRP 0.00262026
S21 S23 VAL TYR 0.00262026

S21 S23 VAL --- 0.00262026
S21 S23 TRP ILE 0.0164133
S21 S23 TRP LEU 0.00671252
S21 S23 TYR ALA 0.00108983
S21 S23 TYR CYS 0.00108983
S21 S23 TYR ASP 0.00108983
S21 S23 TYR GLU 0.00108983
S21 S23 TYR PHE 0.00108983
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S21 S23 TYR HIS 0.00108983
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S21 S23 TYR LYS 0.00108983
S21 S23 TYR LEU -0.37245
S21 S23 TYR MET 0.00108983
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S21 S23 TYR PRO 0.00108983
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S21 S23 --- LEU 0.00671252
S21 S24 ALA GLY 0.0229246
S21 S24 ALA SER 0.000201263
S21 S24 CYS GLY 0.0229246
S21 S24 CYS SER 0.000201263
S21 S24 ASP GLY 0.0229246
S21 S24 ASP SER 0.000201263
S21 S24 GLU GLY 0.0229246
S21 S24 GLU SER 0.000201263
S21 S24 PHE ALA 0.00188316
S21 S24 PHE CYS 0.00188316
S21 S24 PHE ASP 0.00188316
S21 S24 PHE GLU 0.00188316
S21 S24 PHE PHE 0.00188316
S21 S24 PHE GLY 0.180071
S21 S24 PHE HIS 0.00188316
S21 S24 PHE ILE 0.00188316
S21 S24 PHE LYS 0.00188316
S21 S24 PHE LEU 0.00188316
S21 S24 PHE MET 0.00188316
S21 S24 PHE ASN 0.00188316
S21 S24 PHE PRO 0.00188316
S21 S24 PHE GLN 0.00188316
S21 S24 PHE ARG 0.00188316
S21 S24 PHE SER -0.385003
S21 S24 PHE THR 0.00188316
S21 S24 PHE VAL 0.00188316
S21 S24 PHE TRP 0.00188316
S21 S24 PHE TYR 0.00188316
S21 S24 PHE --- 0.00188316
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S21 S24 GLY SER 0.000201263
S21 S24 HIS GLY 0.0229246
S21 S24 HIS SER 0.000201263
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S21 S24 ILE CYS 0.0073099
S21 S24 ILE ASP 0.0073099
S21 S24 ILE GLU 0.0073099

S21 S24 ILE PHE 0.0073099
S21 S24 ILE GLY -0.500941
S21 S24 ILE HIS 0.0073099
S21 S24 ILE ILE 0.0073099
S21 S24 ILE LYS 0.0073099
S21 S24 ILE LEU 0.0073099
S21 S24 ILE MET 0.0073099
S21 S24 ILE ASN 0.0073099
S21 S24 ILE PRO 0.0073099
S21 S24 ILE GLN 0.0073099
S21 S24 ILE ARG 0.0073099
S21 S24 ILE SER 0.278906
S21 S24 ILE THR 0.0073099
S21 S24 ILE VAL 0.0073099
S21 S24 ILE TRP 0.0073099
S21 S24 ILE TYR 0.0073099
S21 S24 ILE --- 0.0073099
S21 S24 LYS GLY 0.0229246
S21 S24 LYS SER 0.000201263
S21 S24 LEU GLY 0.0229246
S21 S24 LEU SER 0.000201263
S21 S24 MET GLY 0.0229246
S21 S24 MET SER 0.000201263
S21 S24 ASN GLY 0.0229246
S21 S24 ASN SER 0.000201263
S21 S24 PRO GLY 0.0229246
S21 S24 PRO SER 0.000201263
S21 S24 GLN GLY 0.0229246
S21 S24 GLN SER 0.000201263
S21 S24 ARG GLY 0.0229246
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S21 S24 SER GLY 0.0229246
S21 S24 SER SER 0.000201263
S21 S24 THR GLY 0.0229246
S21 S24 THR SER 0.000201263
S21 S24 VAL ALA 0.00192981
S21 S24 VAL CYS 0.00192981
S21 S24 VAL ASP 0.00192981
S21 S24 VAL GLU 0.00192981
S21 S24 VAL PHE 0.00192981
S21 S24 VAL GLY -0.125174
S21 S24 VAL HIS 0.00192981
S21 S24 VAL ILE 0.00192981
S21 S24 VAL LYS 0.00192981
S21 S24 VAL LEU 0.00192981
S21 S24 VAL MET 0.00192981
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S21 S24 VAL PRO 0.00192981
S21 S24 VAL GLN 0.00192981
S21 S24 VAL ARG 0.00192981
S21 S24 VAL SER 0.0161227
S21 S24 VAL THR 0.00192981
S21 S24 VAL VAL 0.00192981
S21 S24 VAL TRP 0.00192981
S21 S24 VAL TYR 0.00192981
S21 S24 VAL --- 0.00192981
S21 S24 TRP GLY 0.0229246
S21 S24 TRP SER 0.000201263
S21 S24 TYR ALA 0.000495324
S21 S24 TYR CYS 0.000495324
S21 S24 TYR ASP 0.000495324
S21 S24 TYR GLU 0.000495324
S21 S24 TYR PHE 0.000495324

S21 S24 TYR GLY -0.0826929
S21 S24 TYR HIS 0.000495324
S21 S24 TYR ILE 0.000495324
S21 S24 TYR LYS 0.000495324
S21 S24 TYR LEU 0.000495324
S21 S24 TYR MET 0.000495324
S21 S24 TYR ASN 0.000495324
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S21 S24 TYR GLN 0.000495324
S21 S24 TYR ARG 0.000495324
S21 S24 TYR SER 0.00482593
S21 S24 TYR THR 0.000495324
S21 S24 TYR VAL 0.000495324
S21 S24 TYR TRP 0.000495324
S21 S24 TYR TYR 0.000495324
S21 S24 TYR --- 0.000495324
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S21 S24 --- SER 0.000201263
S21 S25 ALA ASP 0.000109699
S21 S25 ALA GLU 7.72451e-05
S21 S25 ALA LYS 8.99467e-05
S21 S25 ALA ARG 0.00378424
S21 S25 ALA SER 0.0188213
S21 S25 ALA THR 0.000243374
S21 S25 CYS ASP 0.000109699
S21 S25 CYS GLU 7.72451e-05
S21 S25 CYS LYS 8.99467e-05
S21 S25 CYS ARG 0.00378424
S21 S25 CYS SER 0.0188213
S21 S25 CYS THR 0.000243374
S21 S25 ASP ASP 0.000109699
S21 S25 ASP GLU 7.72451e-05
S21 S25 ASP LYS 8.99467e-05
S21 S25 ASP ARG 0.00378424
S21 S25 ASP SER 0.0188213
S21 S25 ASP THR 0.000243374
S21 S25 GLU ASP 0.000109699
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S21 S25 GLU LYS 8.99467e-05
S21 S25 GLU ARG 0.00378424
S21 S25 GLU SER 0.0188213
S21 S25 GLU THR 0.000243374
S21 S25 PHE ALA 0.00127668
S21 S25 PHE CYS 0.00127668
S21 S25 PHE ASP 0.0301195
S21 S25 PHE GLU 0.0205115
S21 S25 PHE PHE 0.00127668
S21 S25 PHE GLY 0.00127668
S21 S25 PHE HIS 0.00127668
S21 S25 PHE ILE 0.00127668
S21 S25 PHE LYS 0.0391939
S21 S25 PHE LEU 0.00127668
S21 S25 PHE MET 0.00127668
S21 S25 PHE ASN 0.00127668
S21 S25 PHE PRO 0.00127668
S21 S25 PHE GLN 0.00127668
S21 S25 PHE ARG 0.273123
S21 S25 PHE SER -0.583021
S21 S25 PHE THR 0.0317708
S21 S25 PHE VAL 0.00127668
S21 S25 PHE TRP 0.00127668
S21 S25 PHE TYR 0.00127668
S21 S25 PHE --- 0.00127668

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S21 S25 GLY GLU 7.72451e-05
S21 S25 GLY LYS 8.99467e-05
S21 S25 GLY ARG 0.00378424
S21 S25 GLY SER 0.0188213
S21 S25 GLY THR 0.000243374
S21 S25 HIS ASP 0.000109699
S21 S25 HIS GLU 7.72451e-05
S21 S25 HIS LYS 8.99467e-05
S21 S25 HIS ARG 0.00378424
S21 S25 HIS SER 0.0188213
S21 S25 HIS THR 0.000243374
S21 S25 ILE ALA 0.019771
S21 S25 ILE CYS 0.019771
S21 S25 ILE ASP -0.143549
S21 S25 ILE GLU -0.0839256
S21 S25 ILE PHE 0.019771
S21 S25 ILE GLY 0.019771
S21 S25 ILE HIS 0.019771
S21 S25 ILE ILE 0.019771
S21 S25 ILE LYS -0.1434
S21 S25 ILE LEU 0.019771
S21 S25 ILE MET 0.019771
S21 S25 ILE ASN 0.019771
S21 S25 ILE PRO 0.019771
S21 S25 ILE GLN 0.019771
S21 S25 ILE ARG 0.0119446
S21 S25 ILE SER 0.125394
S21 S25 ILE THR -0.146175
S21 S25 ILE VAL 0.019771
S21 S25 ILE TRP 0.019771
S21 S25 ILE TYR 0.019771
S21 S25 ILE --- 0.019771
S21 S25 LYS ASP 0.000109699
S21 S25 LYS GLU 7.72451e-05
S21 S25 LYS LYS 8.99467e-05
S21 S25 LYS ARG 0.00378424
S21 S25 LYS SER 0.0188213
S21 S25 LYS THR 0.000243374
S21 S25 LEU ASP 0.000109699
S21 S25 LEU GLU 7.72451e-05
S21 S25 LEU LYS 8.99467e-05
S21 S25 LEU ARG 0.00378424
S21 S25 LEU SER 0.0188213
S21 S25 LEU THR 0.000243374
S21 S25 MET ASP 0.000109699
S21 S25 MET GLU 7.72451e-05
S21 S25 MET LYS 8.99467e-05
S21 S25 MET ARG 0.00378424
S21 S25 MET SER 0.0188213
S21 S25 MET THR 0.000243374
S21 S25 ASN ASP 0.000109699
S21 S25 ASN GLU 7.72451e-05
S21 S25 ASN LYS 8.99467e-05
S21 S25 ASN ARG 0.00378424
S21 S25 ASN SER 0.0188213
S21 S25 ASN THR 0.000243374
S21 S25 PRO ASP 0.000109699
S21 S25 PRO GLU 7.72451e-05
S21 S25 PRO LYS 8.99467e-05
S21 S25 PRO ARG 0.00378424
S21 S25 PRO SER 0.0188213
S21 S25 PRO THR 0.000243374

S21 S25 GLN ASP 0.000109699
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S21 S25 GLN LYS 8.99467e-05
S21 S25 GLN ARG 0.00378424
S21 S25 GLN SER 0.0188213
S21 S25 GLN THR 0.000243374
S21 S25 ARG ASP 0.000109699
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S21 S25 ARG LYS 8.99467e-05
S21 S25 ARG ARG 0.00378424
S21 S25 ARG SER 0.0188213
S21 S25 ARG THR 0.000243374
S21 S25 SER ASP 0.000109699
S21 S25 SER GLU 7.72451e-05
S21 S25 SER LYS 8.99467e-05
S21 S25 SER ARG 0.00378424
S21 S25 SER SER 0.0188213
S21 S25 SER THR 0.000243374
S21 S25 THR ASP 0.000109699
S21 S25 THR GLU 7.72451e-05
S21 S25 THR LYS 8.99467e-05
S21 S25 THR ARG 0.00378424
S21 S25 THR SER 0.0188213
S21 S25 THR THR 0.000243374
S21 S25 VAL ALA 0.00287731
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S21 S25 VAL GLU 0.0163757
S21 S25 VAL PHE 0.00287731
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S21 S25 VAL LYS 0.0169242
S21 S25 VAL LEU 0.00287731
S21 S25 VAL MET 0.00287731
S21 S25 VAL ASN 0.00287731
S21 S25 VAL PRO 0.00287731
S21 S25 VAL GLN 0.00287731
S21 S25 VAL ARG 0.0451296
S21 S25 VAL SER -0.266665
S21 S25 VAL THR 0.018888
S21 S25 VAL VAL 0.00287731
S21 S25 VAL TRP 0.00287731
S21 S25 VAL TYR 0.00287731
S21 S25 VAL --- 0.00287731
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S21 S25 TRP LYS 8.99467e-05
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S21 S25 TRP SER 0.0188213
S21 S25 TRP THR 0.000243374
S21 S25 TYR ALA 0.00239297
S21 S25 TYR CYS 0.00239297
S21 S25 TYR ASP 0.0402403
S21 S25 TYR GLU 0.0127192
S21 S25 TYR PHE 0.00239297
S21 S25 TYR GLY 0.00239297
S21 S25 TYR HIS 0.00239297
S21 S25 TYR ILE 0.00239297
S21 S25 TYR LYS 0.0352195
S21 S25 TYR LEU 0.00239297
S21 S25 TYR MET 0.00239297
S21 S25 TYR ASN 0.00239297

S21 S25 TYR PRO 0.00239297
S21 S25 TYR GLN 0.00239297
S21 S25 TYR ARG -0.485158
S21 S25 TYR SER 0.212311
S21 S25 TYR THR 0.0803171
S21 S25 TYR VAL 0.00239297
S21 S25 TYR TRP 0.00239297
S21 S25 TYR TYR 0.00239297
S21 S25 TYR --- 0.00239297
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S21 S25 --- GLU 7.72451e-05
S21 S25 --- LYS 8.99466e-05
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S21 S25 --- SER 0.0188213
S21 S25 --- THR 0.000243374
S21 S26 ALA PHE 0.010444
S21 S26 ALA LYS 0.0117514
S21 S26 ALA TYR 0.000930426
S21 S26 CYS PHE 0.010444
S21 S26 CYS LYS 0.0117514
S21 S26 CYS TYR 0.000930426
S21 S26 ASP PHE 0.010444
S21 S26 ASP LYS 0.0117514
S21 S26 ASP TYR 0.000930426
S21 S26 GLU PHE 0.010444
S21 S26 GLU LYS 0.0117514
S21 S26 GLU TYR 0.000930426
S21 S26 PHE ALA 0.00120353
S21 S26 PHE CYS 0.00120353
S21 S26 PHE ASP 0.00120353
S21 S26 PHE GLU 0.00120353
S21 S26 PHE PHE -0.0430792
S21 S26 PHE GLY 0.00120353
S21 S26 PHE HIS 0.00120353
S21 S26 PHE ILE 0.00120353
S21 S26 PHE LYS -0.233556
S21 S26 PHE LEU 0.00120353
S21 S26 PHE MET 0.00120353
S21 S26 PHE ASN 0.00120353
S21 S26 PHE PRO 0.00120353
S21 S26 PHE GLN 0.00120353
S21 S26 PHE ARG 0.00120353
S21 S26 PHE SER 0.00120353
S21 S26 PHE THR 0.00120353
S21 S26 PHE VAL 0.00120353
S21 S26 PHE TRP 0.00120353
S21 S26 PHE TYR 0.08582
S21 S26 PHE --- 0.00120353
S21 S26 GLY PHE 0.010444
S21 S26 GLY LYS 0.0117514
S21 S26 GLY TYR 0.000930426
S21 S26 HIS PHE 0.010444
S21 S26 HIS LYS 0.0117514
S21 S26 HIS TYR 0.000930426
S21 S26 ILE ALA 0.0163167
S21 S26 ILE CYS 0.0163167
S21 S26 ILE ASP 0.0163167
S21 S26 ILE GLU 0.0163167
S21 S26 ILE PHE -0.244881
S21 S26 ILE GLY 0.0163167
S21 S26 ILE HIS 0.0163167
S21 S26 ILE ILE 0.0163167
S21 S26 ILE LYS 0.137871

S21 S26 ILE LEU 0.0163167
S21 S26 ILE MET 0.0163167
S21 S26 ILE ASN 0.0163167
S21 S26 ILE PRO 0.0163167
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S21 S26 ILE ARG 0.0163167
S21 S26 ILE SER 0.0163167
S21 S26 ILE THR 0.0163167
S21 S26 ILE VAL 0.0163167
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S21 S26 ILE TYR -0.269838
S21 S26 ILE --- 0.0163167
S21 S26 LYS PHE 0.010444
S21 S26 LYS LYS 0.0117514
S21 S26 LYS TYR 0.000930426
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S21 S26 LEU LYS 0.0117514
S21 S26 LEU TYR 0.000930426
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S21 S26 MET LYS 0.0117514
S21 S26 MET TYR 0.000930426
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S21 S26 SER TYR 0.000930426
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S21 S26 VAL ALA 0.00188554
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S21 S26 VAL ILE 0.00188554
S21 S26 VAL LYS -0.43742
S21 S26 VAL LEU 0.00188554
S21 S26 VAL MET 0.00188554
S21 S26 VAL ASN 0.00188554
S21 S26 VAL PRO 0.00188554
S21 S26 VAL GLN 0.00188554
S21 S26 VAL ARG 0.00188554
S21 S26 VAL SER 0.00188554
S21 S26 VAL THR 0.00188554
S21 S26 VAL VAL 0.00188554
S21 S26 VAL TRP 0.00188554
S21 S26 VAL TYR 0.0621376
S21 S26 VAL --- 0.00188554
S21 S26 TRP PHE 0.010444
S21 S26 TRP LYS 0.0117514
S21 S26 TRP TYR 0.000930426

S21 S26 TYR ALA 0.00158389
S21 S26 TYR CYS 0.00158389
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S21 S26 TYR GLY 0.00158389
S21 S26 TYR HIS 0.00158389
S21 S26 TYR ILE 0.00158389
S21 S26 TYR LYS 0.145747
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S21 S26 TYR ARG 0.00158389
S21 S26 TYR SER 0.00158389
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S21 S26 TYR VAL 0.00158389
S21 S26 TYR TRP 0.00158389
S21 S26 TYR TYR 0.0744359
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S21 S26 --- LYS 0.0117514
S21 S26 --- TYR 0.000930426
S21 S27 ALA ASN 0.00281808
S21 S27 ALA SER 0.0203078
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S21 S27 ASP SER 0.0203078
S21 S27 GLU ASN 0.00281808
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S21 S27 PHE ILE 0.0016357
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S21 S27 GLY ASN 0.00281808
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S21 S27 HIS ASN 0.00281808
S21 S27 HIS SER 0.0203078
S21 S27 ILE ALA 0.0115184
S21 S27 ILE CYS 0.0115184
S21 S27 ILE ASP 0.0115184
S21 S27 ILE GLU 0.0115184
S21 S27 ILE PHE 0.0115184
S21 S27 ILE GLY 0.0115184

S21 S27 ILE HIS 0.0115184
S21 S27 ILE ILE 0.0115184
S21 S27 ILE LYS 0.0115184
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S21 S27 ILE MET 0.0115184
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S21 S27 ILE PRO 0.0115184
S21 S27 ILE GLN 0.0115184
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S21 S27 ILE THR 0.0115184
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S21 S27 ILE TRP 0.0115184
S21 S27 ILE TYR 0.0115184
S21 S27 ILE --- 0.0115184
S21 S27 LYS ASN 0.00281808
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S21 S27 LEU ASN 0.00281808
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S21 S27 PRO SER 0.0203078
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S21 S27 THR SER 0.0203078
S21 S27 VAL ALA 0.00175651
S21 S27 VAL CYS 0.00175651
S21 S27 VAL ASP 0.00175651
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S21 S27 VAL ILE 0.00175651
S21 S27 VAL LYS 0.00175651
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S21 S27 VAL THR 0.00175651
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S21 S27 VAL --- 0.00175651
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S21 S27 TRP SER 0.0203078
S21 S27 TYR ALA 0.000285428
S21 S27 TYR CYS 0.000285428
S21 S27 TYR ASP 0.000285428
S21 S27 TYR GLU 0.000285428
S21 S27 TYR PHE 0.000285428
S21 S27 TYR GLY 0.000285428
S21 S27 TYR HIS 0.000285428

S21 S27 TYR ILE 0.000285428
S21 S27 TYR LYS 0.000285428
S21 S27 TYR LEU 0.000285428
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S21 S27 TYR PRO 0.000285428
S21 S27 TYR GLN 0.000285428
S21 S27 TYR ARG 0.000285428
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S21 S27 TYR THR 0.000285428
S21 S27 TYR VAL 0.000285428
S21 S27 TYR TRP 0.000285428
S21 S27 TYR TYR 0.000285428
S21 S27 TYR --- 0.000285428
S21 S27 --- ASN 0.00281808
S21 S27 --- SER 0.0203078
S21 S28 ALA ASP 0.0204003
S21 S28 ALA GLU 0.00272556
S21 S28 CYS ASP 0.0204003
S21 S28 CYS GLU 0.00272556
S21 S28 ASP ASP 0.0204003
S21 S28 ASP GLU 0.00272556
S21 S28 GLU ASP 0.0204003
S21 S28 GLU GLU 0.00272556
S21 S28 PHE ALA 0.000627163
S21 S28 PHE CYS 0.000627163
S21 S28 PHE ASP -0.391907
S21 S28 PHE GLU 0.210839
S21 S28 PHE PHE 0.000627163
S21 S28 PHE GLY 0.000627163
S21 S28 PHE HIS 0.000627163
S21 S28 PHE ILE 0.000627163
S21 S28 PHE LYS 0.000627163
S21 S28 PHE LEU 0.000627163
S21 S28 PHE MET 0.000627163
S21 S28 PHE ASN 0.000627163
S21 S28 PHE PRO 0.000627163
S21 S28 PHE GLN 0.000627163
S21 S28 PHE ARG 0.000627163
S21 S28 PHE SER 0.000627163
S21 S28 PHE THR 0.000627163
S21 S28 PHE VAL 0.000627163
S21 S28 PHE TRP 0.000627163
S21 S28 PHE TYR 0.000627163
S21 S28 PHE --- 0.000627163
S21 S28 GLY ASP 0.0204003
S21 S28 GLY GLU 0.00272556
S21 S28 HIS ASP 0.0204003
S21 S28 HIS GLU 0.00272556
S21 S28 ILE ALA 0.00906029
S21 S28 ILE CYS 0.00906029
S21 S28 ILE ASP -0.0962542
S21 S28 ILE GLU -0.159038
S21 S28 ILE PHE 0.00906029
S21 S28 ILE GLY 0.00906029
S21 S28 ILE HIS 0.00906029
S21 S28 ILE ILE 0.00906029
S21 S28 ILE LYS 0.00906029
S21 S28 ILE LEU 0.00906029
S21 S28 ILE MET 0.00906029
S21 S28 ILE ASN 0.00906029
S21 S28 ILE PRO 0.00906029
S21 S28 ILE GLN 0.00906029

S21 S28 ILE ARG 0.00906029
S21 S28 ILE SER 0.00906029
S21 S28 ILE THR 0.00906029
S21 S28 ILE VAL 0.00906029
S21 S28 ILE TRP 0.00906029
S21 S28 ILE TYR 0.00906029
S21 S28 ILE --- 0.00906029
S21 S28 LYS ASP 0.0204003
S21 S28 LYS GLU 0.00272556
S21 S28 LEU ASP 0.0204003
S21 S28 LEU GLU 0.00272556
S21 S28 MET ASP 0.0204003
S21 S28 MET GLU 0.00272556
S21 S28 ASN ASP 0.0204003
S21 S28 ASN GLU 0.00272556
S21 S28 PRO ASP 0.0204003
S21 S28 PRO GLU 0.00272556
S21 S28 GLN ASP 0.0204003
S21 S28 GLN GLU 0.00272556
S21 S28 ARG ASP 0.0204003
S21 S28 ARG GLU 0.00272556
S21 S28 SER ASP 0.0204003
S21 S28 SER GLU 0.00272556
S21 S28 THR ASP 0.0204003
S21 S28 THR GLU 0.00272556
S21 S28 VAL ALA 0.00380032
S21 S28 VAL CYS 0.00380032
S21 S28 VAL ASP 0.386693
S21 S28 VAL GLU -0.531284
S21 S28 VAL PHE 0.00380032
S21 S28 VAL GLY 0.00380032
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S21 S28 VAL TRP 0.00380032
S21 S28 VAL TYR 0.00380032
S21 S28 VAL --- 0.00380032
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S21 S28 TRP GLU 0.00272556
S21 S28 TYR ALA 0.000756854
S21 S28 TYR CYS 0.000756854
S21 S28 TYR ASP -0.459696
S21 S28 TYR GLU 0.37686
S21 S28 TYR PHE 0.000756854
S21 S28 TYR GLY 0.000756854
S21 S28 TYR HIS 0.000756854
S21 S28 TYR ILE 0.000756854
S21 S28 TYR LYS 0.000756854
S21 S28 TYR LEU 0.000756854
S21 S28 TYR MET 0.000756854
S21 S28 TYR ASN 0.000756854
S21 S28 TYR PRO 0.000756854
S21 S28 TYR GLN 0.000756854
S21 S28 TYR ARG 0.000756854

S21 S28 TYR SER 0.000756854
S21 S28 TYR THR 0.000756854
S21 S28 TYR VAL 0.000756854
S21 S28 TYR TRP 0.000756854
S21 S28 TYR TYR 0.000756854
S21 S28 TYR --- 0.000756854
S21 S28 --- ASP 0.0204003
S21 S28 --- GLU 0.00272556
S21 S29 ALA LYS 0.000288812
S21 S29 ALA LEU 0.00065323
S21 S29 ALA ASN 4.60034e-05
S21 S29 ALA SER 0.0221378
S21 S29 CYS LYS 0.000288812
S21 S29 CYS LEU 0.00065323
S21 S29 CYS ASN 4.60034e-05
S21 S29 CYS SER 0.0221378
S21 S29 ASP LYS 0.000288812
S21 S29 ASP LEU 0.00065323
S21 S29 ASP ASN 4.60034e-05
S21 S29 ASP SER 0.0221378
S21 S29 GLU LYS 0.000288812
S21 S29 GLU LEU 0.00065323
S21 S29 GLU ASN 4.60034e-05
S21 S29 GLU SER 0.0221378
S21 S29 PHE ALA 0.00175355
S21 S29 PHE CYS 0.00175355
S21 S29 PHE ASP 0.00175355
S21 S29 PHE GLU 0.00175355
S21 S29 PHE PHE 0.00175355
S21 S29 PHE GLY 0.00175355
S21 S29 PHE HIS 0.00175355
S21 S29 PHE ILE 0.00175355
S21 S29 PHE LYS 0.0297068
S21 S29 PHE LEU 0.0627293
S21 S29 PHE MET 0.00175355
S21 S29 PHE ASN 0.0376418
S21 S29 PHE PRO 0.00175355
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S21 S29 PHE ARG 0.00175355
S21 S29 PHE SER -0.32904
S21 S29 PHE THR 0.00175355
S21 S29 PHE VAL 0.00175355
S21 S29 PHE TRP 0.00175355
S21 S29 PHE TYR 0.00175355
S21 S29 PHE --- 0.00175355
S21 S29 GLY LYS 0.000288812
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S21 S29 GLY ASN 4.60034e-05
S21 S29 GLY SER 0.0221378
S21 S29 HIS LYS 0.000288812
S21 S29 HIS LEU 0.00065323
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S21 S29 HIS SER 0.0221378
S21 S29 ILE ALA 0.0137514
S21 S29 ILE CYS 0.0137514
S21 S29 ILE ASP 0.0137514
S21 S29 ILE GLU 0.0137514
S21 S29 ILE PHE 0.0137514
S21 S29 ILE GLY 0.0137514
S21 S29 ILE HIS 0.0137514
S21 S29 ILE ILE 0.0137514
S21 S29 ILE LYS -0.10319
S21 S29 ILE LEU -0.199919

S21 S29 ILE MET 0.0137514
S21 S29 ILE ASN -0.116003
S21 S29 ILE PRO 0.0137514
S21 S29 ILE GLN 0.0137514
S21 S29 ILE ARG 0.0137514
S21 S29 ILE SER 0.102191
S21 S29 ILE THR 0.0137514
S21 S29 ILE VAL 0.0137514
S21 S29 ILE TRP 0.0137514
S21 S29 ILE TYR 0.0137514
S21 S29 ILE --- 0.0137514
S21 S29 LYS LYS 0.000288812
S21 S29 LYS LEU 0.00065323
S21 S29 LYS ASN 4.60034e-05
S21 S29 LYS SER 0.0221378
S21 S29 LEU LYS 0.000288812
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S21 S29 PRO LEU 0.00065323
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S21 S29 GLN LYS 0.000288812
S21 S29 GLN LEU 0.00065323
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S21 S29 VAL ALA 0.00152962
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S21 S29 VAL PHE 0.00152962
S21 S29 VAL GLY 0.00152962
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S21 S29 VAL ILE 0.00152962
S21 S29 VAL LYS 0.0123737
S21 S29 VAL LEU 0.0330845
S21 S29 VAL MET 0.00152962
S21 S29 VAL ASN 0.00817908
S21 S29 VAL PRO 0.00152962
S21 S29 VAL GLN 0.00152962
S21 S29 VAL ARG 0.00152962
S21 S29 VAL SER -0.152026

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S21 S29 VAL VAL 0.00152962
S21 S29 VAL TRP 0.00152962
S21 S29 VAL TYR 0.00152962
S21 S29 VAL --- 0.00152962
S21 S29 TRP LYS 0.000288812
S21 S29 TRP LEU 0.00065323
S21 S29 TRP ASN 4.60034e-05
S21 S29 TRP SER 0.0221378
S21 S29 TYR ALA 0.000793629
S21 S29 TYR CYS 0.000793629
S21 S29 TYR ASP 0.000793629
S21 S29 TYR GLU 0.000793629
S21 S29 TYR PHE 0.000793629
S21 S29 TYR GLY 0.000793629
S21 S29 TYR HIS 0.000793629
S21 S29 TYR ILE 0.000793629
S21 S29 TYR LYS 0.0118578
S21 S29 TYR LEU 0.0321133
S21 S29 TYR MET 0.000793629
S21 S29 TYR ASN 0.00515366
S21 S29 TYR PRO 0.000793629
S21 S29 TYR GLN 0.000793629
S21 S29 TYR ARG 0.000793629
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S21 S29 TYR THR 0.000793629
S21 S29 TYR VAL 0.000793629
S21 S29 TYR TRP 0.000793629
S21 S29 TYR TYR 0.000793629
S21 S29 TYR --- 0.000793629
S21 S29 --- LYS 0.000288812
S21 S29 --- LEU 0.00065323
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S21 S29 --- SER 0.0221378
S21 S30 ALA GLN 0.021564
S21 S30 ALA SER 0.00156184
S21 S30 CYS GLN 0.021564
S21 S30 CYS SER 0.00156184
S21 S30 ASP GLN 0.021564
S21 S30 ASP SER 0.00156184
S21 S30 GLU GLN 0.021564
S21 S30 GLU SER 0.00156184
S21 S30 PHE ALA 0.00121482
S21 S30 PHE CYS 0.00121482
S21 S30 PHE ASP 0.00121482
S21 S30 PHE GLU 0.00121482
S21 S30 PHE PHE 0.00121482
S21 S30 PHE GLY 0.00121482
S21 S30 PHE HIS 0.00121482
S21 S30 PHE ILE 0.00121482
S21 S30 PHE LYS 0.00121482
S21 S30 PHE LEU 0.00121482
S21 S30 PHE MET 0.00121482
S21 S30 PHE ASN 0.00121482
S21 S30 PHE PRO 0.00121482
S21 S30 PHE GLN 0.42358
S21 S30 PHE ARG 0.00121482
S21 S30 PHE SER -0.615814
S21 S30 PHE THR 0.00121482
S21 S30 PHE VAL 0.00121482
S21 S30 PHE TRP 0.00121482
S21 S30 PHE TYR 0.00121482
S21 S30 PHE --- 0.00121482

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S21 S30 GLY SER 0.00156184
S21 S30 HIS GLN 0.021564
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S21 S30 ILE CYS 0.00828389
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S21 S30 ILE GLU 0.00828389
S21 S30 ILE PHE 0.00828389
S21 S30 ILE GLY 0.00828389
S21 S30 ILE HIS 0.00828389
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S21 S30 LYS SER 0.00156184
S21 S30 LEU GLN 0.021564
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S21 S30 PRO SER 0.00156184
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S21 S30 VAL LYS 0.0025139
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S21 S30 VAL ARG 0.0025139
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S21 S30 VAL TRP 0.0025139
S21 S30 VAL TYR 0.0025139

S21 S30 VAL --- 0.0025139
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S21 S30 TRP SER 0.00156184
S21 S30 TYR ALA 0.000453631
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S21 S30 TYR ASP 0.000453631
S21 S30 TYR GLU 0.000453631
S21 S30 TYR PHE 0.000453631
S21 S30 TYR GLY 0.000453631
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S21 S30 TYR ILE 0.000453631
S21 S30 TYR LYS 0.000453631
S21 S30 TYR LEU 0.000453631
S21 S30 TYR MET 0.000453631
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S21 S30 TYR PRO 0.000453631
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S21 S30 TYR ARG 0.000453631
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S21 S30 TYR TRP 0.000453631
S21 S30 TYR TYR 0.000453631
S21 S30 TYR --- 0.000453631
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S21 S30 --- SER 0.00156184
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S21 S31 ALA VAL 0.0168323
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S21 S31 CYS ILE 0.00521723
S21 S31 CYS VAL 0.0168323
S21 S31 ASP ASP 0.00107636
S21 S31 ASP ILE 0.00521723
S21 S31 ASP VAL 0.0168323
S21 S31 GLU ASP 0.00107636
S21 S31 GLU ILE 0.00521723
S21 S31 GLU VAL 0.0168323
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S21 S31 PHE CYS 0.000982354
S21 S31 PHE ASP 0.0517512
S21 S31 PHE GLU 0.000982354
S21 S31 PHE PHE 0.000982354
S21 S31 PHE GLY 0.000982354
S21 S31 PHE HIS 0.000982354
S21 S31 PHE ILE 0.00356285
S21 S31 PHE LYS 0.000982354
S21 S31 PHE LEU 0.000982354
S21 S31 PHE MET 0.000982354
S21 S31 PHE ASN 0.000982354
S21 S31 PHE PRO 0.000982354
S21 S31 PHE GLN 0.000982354
S21 S31 PHE ARG 0.000982354
S21 S31 PHE SER 0.000982354
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S21 S31 PHE TRP 0.000982354
S21 S31 PHE TYR 0.000982354
S21 S31 PHE --- 0.000982354
S21 S31 GLY ASP 0.00107636
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S21 S31 GLY VAL 0.0168323
S21 S31 HIS ASP 0.00107636

S21 S31 HIS ILE 0.00521723
S21 S31 HIS VAL 0.0168323
S21 S31 ILE ALA 0.012592
S21 S31 ILE CYS 0.012592
S21 S31 ILE ASP 0.138805
S21 S31 ILE GLU 0.012592
S21 S31 ILE PHE 0.012592
S21 S31 ILE GLY 0.012592
S21 S31 ILE HIS 0.012592
S21 S31 ILE ILE 0.37088
S21 S31 ILE LYS 0.012592
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S21 S31 ILE MET 0.012592
S21 S31 ILE ASN 0.012592
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S21 S31 ILE TRP 0.012592
S21 S31 ILE TYR 0.012592
S21 S31 ILE --- 0.012592
S21 S31 LYS ASP 0.00107636
S21 S31 LYS ILE 0.00521723
S21 S31 LYS VAL 0.0168323
S21 S31 LEU ASP 0.00107636
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S21 S31 LEU VAL 0.0168323
S21 S31 MET ASP 0.00107636
S21 S31 MET ILE 0.00521723
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S21 S31 THR VAL 0.0168323
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S21 S31 VAL CYS 0.00341951
S21 S31 VAL ASP 0.0830452
S21 S31 VAL GLU 0.00341951
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S21 S31 VAL ILE -0.834304
S21 S31 VAL LYS 0.00341951
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S21 S31 VAL GLN 0.00341951
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S21 S31 VAL THR 0.00341951
S21 S31 VAL VAL 0.617322
S21 S31 VAL TRP 0.00341951
S21 S31 VAL TYR 0.00341951
S21 S31 VAL --- 0.00341951
S21 S31 TRP ASP 0.00107636
S21 S31 TRP ILE 0.00521723
S21 S31 TRP VAL 0.0168323
S21 S31 TYR ALA 0.00156714
S21 S31 TYR CYS 0.00156714
S21 S31 TYR ASP -0.392882
S21 S31 TYR GLU 0.00156714
S21 S31 TYR PHE 0.00156714
S21 S31 TYR GLY 0.00156714
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S21 S31 TYR ILE 0.31038
S21 S31 TYR LYS 0.00156714
S21 S31 TYR LEU 0.00156714
S21 S31 TYR MET 0.00156714
S21 S31 TYR ASN 0.00156714
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S21 S31 TYR GLN 0.00156714
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S21 S31 TYR SER 0.00156714
S21 S31 TYR THR 0.00156714
S21 S31 TYR VAL -0.0141623
S21 S31 TYR TRP 0.00156714
S21 S31 TYR TYR 0.00156714
S21 S31 TYR --- 0.00156714
S21 S31 --- ASP 0.00107636
S21 S31 --- ILE 0.00521723
S21 S31 --- VAL 0.0168323
S21 S32 ALA PHE 0.00227621
S21 S32 ALA HIS 0.0015521
S21 S32 ALA TRP 0.0164016
S21 S32 ALA TYR 0.00289599
S21 S32 CYS PHE 0.00227621
S21 S32 CYS HIS 0.0015521
S21 S32 CYS TRP 0.0164016
S21 S32 CYS TYR 0.00289599
S21 S32 ASP PHE 0.00227621
S21 S32 ASP HIS 0.0015521
S21 S32 ASP TRP 0.0164016
S21 S32 ASP TYR 0.00289599
S21 S32 GLU PHE 0.00227621
S21 S32 GLU HIS 0.0015521
S21 S32 GLU TRP 0.0164016
S21 S32 GLU TYR 0.00289599
S21 S32 PHE ALA 0.000827737
S21 S32 PHE CYS 0.000827737
S21 S32 PHE ASP 0.000827737
S21 S32 PHE GLU 0.000827737
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S21 S32 PHE GLY 0.000827737
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S21 S32 PHE ILE 0.000827737
S21 S32 PHE LYS 0.000827737
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S21 S32 PHE ASN 0.000827737

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S21 S32 PHE GLN 0.000827737
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S21 S32 HIS TRP 0.0164016
S21 S32 HIS TYR 0.00289599
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S21 S32 ILE CYS 0.0147313
S21 S32 ILE ASP 0.0147313
S21 S32 ILE GLU 0.0147313
S21 S32 ILE PHE 0.0173982
S21 S32 ILE GLY 0.0147313
S21 S32 ILE HIS 0.00712969
S21 S32 ILE ILE 0.0147313
S21 S32 ILE LYS 0.0147313
S21 S32 ILE LEU 0.0147313
S21 S32 ILE MET 0.0147313
S21 S32 ILE ASN 0.0147313
S21 S32 ILE PRO 0.0147313
S21 S32 ILE GLN 0.0147313
S21 S32 ILE ARG 0.0147313
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S21 S32 ILE THR 0.0147313
S21 S32 ILE VAL 0.0147313
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S21 S32 ILE TYR 0.445277
S21 S32 ILE --- 0.0147313
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S21 S32 LYS HIS 0.0015521
S21 S32 LYS TRP 0.0164016
S21 S32 LYS TYR 0.00289599
S21 S32 LEU PHE 0.00227621
S21 S32 LEU HIS 0.0015521
S21 S32 LEU TRP 0.0164016
S21 S32 LEU TYR 0.00289599
S21 S32 MET PHE 0.00227621
S21 S32 MET HIS 0.0015521
S21 S32 MET TRP 0.0164016
S21 S32 MET TYR 0.00289599
S21 S32 ASN PHE 0.00227621
S21 S32 ASN HIS 0.0015521
S21 S32 ASN TRP 0.0164016
S21 S32 ASN TYR 0.00289599
S21 S32 PRO PHE 0.00227621
S21 S32 PRO HIS 0.0015521
S21 S32 PRO TRP 0.0164016
S21 S32 PRO TYR 0.00289599
S21 S32 GLN PHE 0.00227621
S21 S32 GLN HIS 0.0015521
S21 S32 GLN TRP 0.0164016
S21 S32 GLN TYR 0.00289599
S21 S32 ARG PHE 0.00227621

S21 S32 ARG HIS 0.0015521
S21 S32 ARG TRP 0.0164016
S21 S32 ARG TYR 0.00289599
S21 S32 SER PHE 0.00227621
S21 S32 SER HIS 0.0015521
S21 S32 SER TRP 0.0164016
S21 S32 SER TYR 0.00289599
S21 S32 THR PHE 0.00227621
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S21 S32 THR TRP 0.0164016
S21 S32 THR TYR 0.00289599
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S21 S32 VAL CYS 0.00620378
S21 S32 VAL ASP 0.00620378
S21 S32 VAL GLU 0.00620378
S21 S32 VAL PHE 0.469899
S21 S32 VAL GLY 0.00620378
S21 S32 VAL HIS -0.616965
S21 S32 VAL ILE 0.00620378
S21 S32 VAL LYS 0.00620378
S21 S32 VAL LEU 0.00620378
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S21 S32 VAL ARG 0.00620378
S21 S32 VAL SER 0.00620378
S21 S32 VAL THR 0.00620378
S21 S32 VAL VAL 0.00620378
S21 S32 VAL TRP 1.05068
S21 S32 VAL TYR -1.08146
S21 S32 VAL --- 0.00620378
S21 S32 TRP PHE 0.00227621
S21 S32 TRP HIS 0.0015521
S21 S32 TRP TRP 0.0164016
S21 S32 TRP TYR 0.00289599
S21 S32 TYR ALA 0.0030476
S21 S32 TYR CYS 0.0030476
S21 S32 TYR ASP 0.0030476
S21 S32 TYR GLU 0.0030476
S21 S32 TYR PHE -0.635651
S21 S32 TYR GLY 0.0030476
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S21 S32 TYR ILE 0.0030476
S21 S32 TYR LYS 0.0030476
S21 S32 TYR LEU 0.0030476
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S21 S32 TYR ASN 0.0030476
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S21 S32 TYR SER 0.0030476
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S21 S32 TYR VAL 0.0030476
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S21 S32 TYR TYR 0.313295
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S21 S33 ALA LYS 0.000127485

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S21 S33 ALA VAL 0.006572
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S21 S33 CYS LYS 0.000127485
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S21 S33 CYS VAL 0.006572
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S21 S33 ASP LYS 0.000127485
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S21 S33 GLU LYS 0.000127485
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S21 S33 GLU VAL 0.006572
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S21 S33 PHE CYS 0.00128166
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S21 S33 PHE GLU 0.00128166
S21 S33 PHE PHE 0.00128166
S21 S33 PHE GLY 0.00128166
S21 S33 PHE HIS 0.00128166
S21 S33 PHE ILE 0.00128166
S21 S33 PHE LYS 0.0348725
S21 S33 PHE LEU 0.00128166
S21 S33 PHE MET 0.00128166
S21 S33 PHE ASN 0.00128166
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S21 S33 PHE GLN 0.00128166
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S21 S33 PHE TYR 0.00128166
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S21 S33 GLY VAL 0.006572
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S21 S33 HIS LYS 0.000127485
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S21 S33 ILE CYS 0.0186762
S21 S33 ILE ASP -0.619826
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S21 S33 ILE PHE 0.0186762
S21 S33 ILE GLY 0.0186762
S21 S33 ILE HIS 0.0186762
S21 S33 ILE ILE 0.0186762
S21 S33 ILE LYS -0.104239
S21 S33 ILE LEU 0.0186762
S21 S33 ILE MET 0.0186762
S21 S33 ILE ASN 0.0186762
S21 S33 ILE PRO 0.0186762
S21 S33 ILE GLN 0.0186762
S21 S33 ILE ARG 0.0186762
S21 S33 ILE SER -0.252777
S21 S33 ILE THR 0.0186762
S21 S33 ILE VAL 0.576198
S21 S33 ILE TRP 0.0186762
S21 S33 ILE TYR 0.0186762

S21 S33 ILE --- 0.0186762
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S21 S33 LYS LYS 0.000127485
S21 S33 LYS SER 0.0025576
S21 S33 LYS VAL 0.006572
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S21 S33 LEU LYS 0.000127485
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S21 S33 MET ASP 0.0138688
S21 S33 MET LYS 0.000127485
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S21 S33 PRO VAL 0.006572
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S21 S33 GLN LYS 0.000127485
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S21 S33 GLN VAL 0.006572
S21 S33 ARG ASP 0.0138688
S21 S33 ARG LYS 0.000127485
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S21 S33 SER LYS 0.000127485
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S21 S33 THR ASP 0.0138688
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S21 S33 VAL CYS 0.00359454
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S21 S33 VAL GLY 0.00359454
S21 S33 VAL HIS 0.00359454
S21 S33 VAL ILE 0.00359454
S21 S33 VAL LYS 0.0357777
S21 S33 VAL LEU 0.00359454
S21 S33 VAL MET 0.00359454
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S21 S33 VAL GLN 0.00359454
S21 S33 VAL ARG 0.00359454
S21 S33 VAL SER -0.156634
S21 S33 VAL THR 0.00359454
S21 S33 VAL VAL -0.718586
S21 S33 VAL TRP 0.00359454
S21 S33 VAL TYR 0.00359454
S21 S33 VAL --- 0.00359454
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S21 S33 TYR CYS 0.0010006
S21 S33 TYR ASP -0.302551
S21 S33 TYR GLU 0.0010006
S21 S33 TYR PHE 0.0010006
S21 S33 TYR GLY 0.0010006
S21 S33 TYR HIS 0.0010006
S21 S33 TYR ILE 0.0010006
S21 S33 TYR LYS 0.00826116
S21 S33 TYR LEU 0.0010006
S21 S33 TYR MET 0.0010006
S21 S33 TYR ASN 0.0010006
S21 S33 TYR PRO 0.0010006
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S21 S33 TYR SER 0.163349
S21 S33 TYR THR 0.0010006
S21 S33 TYR VAL 0.0454742
S21 S33 TYR TRP 0.0010006
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S21 S33 TYR --- 0.0010006
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S21 S34 CYS GLU 0.000119664
S21 S34 CYS MET 0.00120864
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S21 S34 CYS SER 0.0205091
S21 S34 CYS THR 0.00124241
S21 S34 ASP GLU 0.000119664
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S21 S34 PHE CYS 0.00102844
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S21 S34 PHE HIS 0.00102844
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S21 S34 PHE LYS 0.00102844
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S21 S34 PHE GLN 0.00102844
S21 S34 PHE ARG 0.0264616
S21 S34 PHE SER -0.41032
S21 S34 PHE THR 0.0802831
S21 S34 PHE VAL 0.00102844
S21 S34 PHE TRP 0.00102844

S21 S34 PHE TYR 0.00102844
S21 S34 PHE --- 0.00102844
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S21 S34 GLY MET 0.00120864
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S21 S34 GLY THR 0.00124241
S21 S34 HIS GLU 0.000119664
S21 S34 HIS MET 0.00120864
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S21 S34 HIS SER 0.0205091
S21 S34 HIS THR 0.00124241
S21 S34 ILE ALA 0.0204189
S21 S34 ILE CYS 0.0204189
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S21 S34 ILE GLU -0.100097
S21 S34 ILE PHE 0.0204189
S21 S34 ILE GLY 0.0204189
S21 S34 ILE HIS 0.0204189
S21 S34 ILE ILE 0.0204189
S21 S34 ILE LYS 0.0204189
S21 S34 ILE LEU 0.0204189
S21 S34 ILE MET -0.48297
S21 S34 ILE ASN 0.0204189
S21 S34 ILE PRO 0.0204189
S21 S34 ILE GLN 0.0204189
S21 S34 ILE ARG -0.102501
S21 S34 ILE SER 0.69714
S21 S34 ILE THR -0.421422
S21 S34 ILE VAL 0.0204189
S21 S34 ILE TRP 0.0204189
S21 S34 ILE TYR 0.0204189
S21 S34 ILE --- 0.0204189
S21 S34 LYS GLU 0.000119664
S21 S34 LYS MET 0.00120864
S21 S34 LYS ARG 4.60034e-05
S21 S34 LYS SER 0.0205091
S21 S34 LYS THR 0.00124241
S21 S34 LEU GLU 0.000119664
S21 S34 LEU MET 0.00120864
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S21 S34 MET GLU 0.000119664
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S21 S34 MET THR 0.00124241
S21 S34 ASN GLU 0.000119664
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S21 S34 PRO THR 0.00124241
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S21 S34 GLN SER 0.0205091
S21 S34 GLN THR 0.00124241

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S21 S34 SER THR 0.00124241
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S21 S34 VAL LYS 0.00161826
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S21 S34 VAL SER -0.382982
S21 S34 VAL THR 0.146048
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S21 S34 VAL TYR 0.00161826
S21 S34 VAL --- 0.00161826
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S21 S34 TYR CYS 0.00164742
S21 S34 TYR ASP 0.00164742
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S21 S34 TYR GLN 0.00164742
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S21 S34 TYR SER -0.43978
S21 S34 TYR THR 0.0827015
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S21 S34 TYR TYR 0.00164742
S21 S34 TYR --- 0.00164742
S21 S34 --- GLU 0.000119664

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S21 S35 ILE TYR 0.0161941

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S21 S35 LYS SER 0.0145497
S21 S35 LYS THR 0.00191451
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S21 S35 LEU THR 0.00191451
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S21 S35 TRP THR 0.00191451
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S21 S35 TYR CYS 0.0015553
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S21 S35 TYR GLY 0.0015553
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S21 S35 TYR LYS 0.0015553
S21 S35 TYR LEU 0.0015553
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S21 S35 TYR VAL 0.0015553
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S21 S35 TYR TYR 0.0015553
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S21 S36 ALA ASP 0.000921793
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S21 S36 CYS SER 0.0168347
S21 S36 CYS THR 0.000873086
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S21 S36 ASP THR 0.000873086
S21 S36 GLU ASP 0.000921793
S21 S36 GLU GLU 0.00449631
S21 S36 GLU SER 0.0168347
S21 S36 GLU THR 0.000873086
S21 S36 PHE ALA 0.00215742
S21 S36 PHE CYS 0.00215742
S21 S36 PHE ASP -0.298025
S21 S36 PHE GLU -0.39103
S21 S36 PHE PHE 0.00215742
S21 S36 PHE GLY 0.00215742
S21 S36 PHE HIS 0.00215742
S21 S36 PHE ILE 0.00215742
S21 S36 PHE LYS 0.00215742
S21 S36 PHE LEU 0.00215742
S21 S36 PHE MET 0.00215742
S21 S36 PHE ASN 0.00215742
S21 S36 PHE PRO 0.00215742
S21 S36 PHE GLN 0.00215742
S21 S36 PHE ARG 0.00215742
S21 S36 PHE SER 0.262331
S21 S36 PHE THR 0.220895
S21 S36 PHE VAL 0.00215742
S21 S36 PHE TRP 0.00215742
S21 S36 PHE TYR 0.00215742
S21 S36 PHE --- 0.00215742
S21 S36 GLY ASP 0.000921793
S21 S36 GLY GLU 0.00449631
S21 S36 GLY SER 0.0168347
S21 S36 GLY THR 0.000873086
S21 S36 HIS ASP 0.000921793
S21 S36 HIS GLU 0.00449631
S21 S36 HIS SER 0.0168347
S21 S36 HIS THR 0.000873086
S21 S36 ILE ALA 0.0179841
S21 S36 ILE CYS 0.0179841
S21 S36 ILE ASP 0.0559062
S21 S36 ILE GLU -0.234248
S21 S36 ILE PHE 0.0179841

S21 S36 ILE GLY 0.0179841
S21 S36 ILE HIS 0.0179841
S21 S36 ILE ILE 0.0179841
S21 S36 ILE LYS 0.0179841
S21 S36 ILE LEU 0.0179841
S21 S36 ILE MET 0.0179841
S21 S36 ILE ASN 0.0179841
S21 S36 ILE PRO 0.0179841
S21 S36 ILE GLN 0.0179841
S21 S36 ILE ARG 0.0179841
S21 S36 ILE SER 0.161477
S21 S36 ILE THR -0.372011
S21 S36 ILE VAL 0.0179841
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S21 S36 ILE TYR 0.0179841
S21 S36 ILE --- 0.0179841
S21 S36 LYS ASP 0.000921793
S21 S36 LYS GLU 0.00449631
S21 S36 LYS SER 0.0168347
S21 S36 LYS THR 0.000873086
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S21 S36 LEU GLU 0.00449631
S21 S36 LEU SER 0.0168347
S21 S36 LEU THR 0.000873086
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S21 S36 MET GLU 0.00449631
S21 S36 MET SER 0.0168347
S21 S36 MET THR 0.000873086
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S21 S36 ASN GLU 0.00449631
S21 S36 ASN SER 0.0168347
S21 S36 ASN THR 0.000873086
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S21 S36 PRO GLU 0.00449631
S21 S36 PRO SER 0.0168347
S21 S36 PRO THR 0.000873086
S21 S36 GLN ASP 0.000921793
S21 S36 GLN GLU 0.00449631
S21 S36 GLN SER 0.0168347
S21 S36 GLN THR 0.000873086
S21 S36 ARG ASP 0.000921793
S21 S36 ARG GLU 0.00449631
S21 S36 ARG SER 0.0168347
S21 S36 ARG THR 0.000873086
S21 S36 SER ASP 0.000921793
S21 S36 SER GLU 0.00449631
S21 S36 SER SER 0.0168347
S21 S36 SER THR 0.000873086
S21 S36 THR ASP 0.000921793
S21 S36 THR GLU 0.00449631
S21 S36 THR SER 0.0168347
S21 S36 THR THR 0.000873086
S21 S36 VAL ALA 0.002189
S21 S36 VAL CYS 0.002189
S21 S36 VAL ASP 0.0925909
S21 S36 VAL GLU -0.312165
S21 S36 VAL PHE 0.002189
S21 S36 VAL GLY 0.002189
S21 S36 VAL HIS 0.002189
S21 S36 VAL ILE 0.002189
S21 S36 VAL LYS 0.002189
S21 S36 VAL LEU 0.002189
S21 S36 VAL MET 0.002189

S21 S36 VAL ASN 0.002189
S21 S36 VAL PRO 0.002189
S21 S36 VAL GLN 0.002189
S21 S36 VAL ARG 0.002189
S21 S36 VAL SER 0.0534322
S21 S36 VAL THR 0.0565435
S21 S36 VAL VAL 0.002189
S21 S36 VAL TRP 0.002189
S21 S36 VAL TYR 0.002189
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S21 S36 TRP SER 0.0168347
S21 S36 TRP THR 0.000873086
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S21 S36 TYR CYS 0.00182831
S21 S36 TYR ASP 0.0823001
S21 S36 TYR GLU 0.768398
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S21 S36 TYR GLY 0.00182831
S21 S36 TYR HIS 0.00182831
S21 S36 TYR ILE 0.00182831
S21 S36 TYR LYS 0.00182831
S21 S36 TYR LEU 0.00182831
S21 S36 TYR MET 0.00182831
S21 S36 TYR ASN 0.00182831
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S21 S36 TYR GLN 0.00182831
S21 S36 TYR ARG 0.00182831
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S21 S36 TYR THR 0.0585277
S21 S36 TYR VAL 0.00182831
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S21 S36 TYR TYR 0.00182831
S21 S36 TYR --- 0.00182831
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S21 S37 ALA PHE 0.00100563
S21 S37 ALA ASN 0.000799906
S21 S37 ALA ARG 0.00404292
S21 S37 ALA SER 0.00764345
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S21 S37 CYS ARG 0.00404292
S21 S37 CYS SER 0.00764345
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S21 S37 ASP ASP 0.00792157
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S21 S37 GLU ASP 0.00792157
S21 S37 GLU PHE 0.00100563
S21 S37 GLU ASN 0.000799906
S21 S37 GLU ARG 0.00404292
S21 S37 GLU SER 0.00764345

S21 S37 PHE ALA 0.0615991
S21 S37 PHE CYS 0.000949457
S21 S37 PHE ASP 0.433729
S21 S37 PHE GLU 0.000949457
S21 S37 PHE PHE -0.290692
S21 S37 PHE GLY 0.000949457
S21 S37 PHE HIS 0.000949457
S21 S37 PHE ILE 0.000949457
S21 S37 PHE LYS 0.000949457
S21 S37 PHE LEU 0.000949457
S21 S37 PHE MET 0.000949457
S21 S37 PHE ASN 0.00250614
S21 S37 PHE PRO 0.000949457
S21 S37 PHE GLN 0.000949457
S21 S37 PHE ARG -0.199455
S21 S37 PHE SER -0.191082
S21 S37 PHE THR 0.000949457
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S21 S37 PHE TRP 0.000949457
S21 S37 PHE TYR 0.000949457
S21 S37 PHE --- 0.000949457
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S21 S37 GLY PHE 0.00100563
S21 S37 GLY ASN 0.000799906
S21 S37 GLY ARG 0.00404292
S21 S37 GLY SER 0.00764345
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S21 S37 HIS PHE 0.00100563
S21 S37 HIS ASN 0.000799906
S21 S37 HIS ARG 0.00404292
S21 S37 HIS SER 0.00764345
S21 S37 ILE ALA 0.347479
S21 S37 ILE CYS 0.0201296
S21 S37 ILE ASP -0.770964
S21 S37 ILE GLU 0.0201296
S21 S37 ILE PHE 0.126392
S21 S37 ILE GLY 0.0201296
S21 S37 ILE HIS 0.0201296
S21 S37 ILE ILE 0.0201296
S21 S37 ILE LYS 0.0201296
S21 S37 ILE LEU 0.0201296
S21 S37 ILE MET 0.0201296
S21 S37 ILE ASN 0.360116
S21 S37 ILE PRO 0.0201296
S21 S37 ILE GLN 0.0201296
S21 S37 ILE ARG 0.235617
S21 S37 ILE SER -0.683729
S21 S37 ILE THR 0.0201296
S21 S37 ILE VAL 0.0201296
S21 S37 ILE TRP 0.0201296
S21 S37 ILE TYR 0.0201296
S21 S37 ILE --- 0.0201296
S21 S37 LYS ALA 0.00171237
S21 S37 LYS ASP 0.00792157
S21 S37 LYS PHE 0.00100563
S21 S37 LYS ASN 0.000799906
S21 S37 LYS ARG 0.00404292
S21 S37 LYS SER 0.00764345
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S21 S37 LEU ASP 0.00792157
S21 S37 LEU PHE 0.00100563

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S21 S37 LEU ARG 0.00404292
S21 S37 LEU SER 0.00764345
S21 S37 MET ALA 0.00171237
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S21 S37 PRO ASN 0.000799906
S21 S37 PRO ARG 0.00404292
S21 S37 PRO SER 0.00764345
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S21 S37 GLN ASP 0.00792157
S21 S37 GLN PHE 0.00100563
S21 S37 GLN ASN 0.000799906
S21 S37 GLN ARG 0.00404292
S21 S37 GLN SER 0.00764345
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S21 S37 ARG ASP 0.00792157
S21 S37 ARG PHE 0.00100563
S21 S37 ARG ASN 0.000799906
S21 S37 ARG ARG 0.00404292
S21 S37 ARG SER 0.00764345
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S21 S37 SER PHE 0.00100563
S21 S37 SER ASN 0.000799906
S21 S37 SER ARG 0.00404292
S21 S37 SER SER 0.00764345
S21 S37 THR ALA 0.00171237
S21 S37 THR ASP 0.00792157
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S21 S37 VAL ALA 0.168899
S21 S37 VAL CYS 0.00488507
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S21 S37 VAL GLU 0.00488507
S21 S37 VAL PHE 0.0461172
S21 S37 VAL GLY 0.00488507
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S21 S37 VAL ILE 0.00488507
S21 S37 VAL LYS 0.00488507
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S21 S37 VAL MET 0.00488507
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S21 S37 VAL PRO 0.00488507
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S21 S37 VAL VAL 0.00488507

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S21 S37 VAL --- 0.00488507
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S21 S37 TRP PHE 0.00100563
S21 S37 TRP ASN 0.000799906
S21 S37 TRP ARG 0.00404292
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S21 S37 TYR ALA -0.656679
S21 S37 TYR CYS 0.00310747
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S21 S37 TYR GLU 0.00310747
S21 S37 TYR PHE 0.0539423
S21 S37 TYR GLY 0.00310747
S21 S37 TYR HIS 0.00310747
S21 S37 TYR ILE 0.00310747
S21 S37 TYR LYS 0.00310747
S21 S37 TYR LEU 0.00310747
S21 S37 TYR MET 0.00310747
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S21 S37 TYR PRO 0.00310747
S21 S37 TYR GLN 0.00310747
S21 S37 TYR ARG 0.212884
S21 S37 TYR SER -0.198043
S21 S37 TYR THR 0.00310747
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S21 S37 TYR TYR 0.00310747
S21 S37 TYR --- 0.00310747
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S21 S37 --- SER 0.00764345
S21 S38 ALA GLU 0.00162105
S21 S38 ALA HIS 0.00407535
S21 S38 ALA LYS 0.0029387
S21 S38 ALA LEU 0.0121969
S21 S38 ALA ARG 0.00229386
S21 S38 CYS GLU 0.00162105
S21 S38 CYS HIS 0.00407535
S21 S38 CYS LYS 0.0029387
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S21 S38 ASP LEU 0.0121969
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S21 S38 GLU LYS 0.0029387
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S21 S38 PHE CYS 0.00215335
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S21 S38 PHE HIS 0.505809

S21 S38 PHE ILE 0.00215335
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S21 S38 PHE LEU -0.0236376
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S21 S38 PHE TRP 0.00215335
S21 S38 PHE TYR 0.00215335
S21 S38 PHE --- 0.00215335
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S21 S38 GLY LYS 0.0029387
S21 S38 GLY LEU 0.0121969
S21 S38 GLY ARG 0.00229386
S21 S38 HIS GLU 0.00162105
S21 S38 HIS HIS 0.00407535
S21 S38 HIS LYS 0.0029387
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S21 S38 HIS ARG 0.00229386
S21 S38 ILE ALA 0.0220645
S21 S38 ILE CYS 0.0220645
S21 S38 ILE ASP 0.0220645
S21 S38 ILE GLU -0.0126673
S21 S38 ILE PHE 0.0220645
S21 S38 ILE GLY 0.0220645
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S21 S38 ILE LYS -0.486979
S21 S38 ILE LEU 0.224724
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S21 S38 LYS ARG 0.00229386
S21 S38 LEU GLU 0.00162105
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S21 S38 LEU LYS 0.0029387
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S21 S38 LEU ARG 0.00229386
S21 S38 MET GLU 0.00162105
S21 S38 MET HIS 0.00407535
S21 S38 MET LYS 0.0029387
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S21 S38 ASN LYS 0.0029387

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S21 S38 PRO LYS 0.0029387
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S21 S38 GLN LYS 0.0029387
S21 S38 GLN LEU 0.0121969
S21 S38 GLN ARG 0.00229386
S21 S38 ARG GLU 0.00162105
S21 S38 ARG HIS 0.00407535
S21 S38 ARG LYS 0.0029387
S21 S38 ARG LEU 0.0121969
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S21 S38 SER GLU 0.00162105
S21 S38 SER HIS 0.00407535
S21 S38 SER LYS 0.0029387
S21 S38 SER LEU 0.0121969
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S21 S38 THR GLU 0.00162105
S21 S38 THR HIS 0.00407535
S21 S38 THR LYS 0.0029387
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S21 S38 THR ARG 0.00229386
S21 S38 VAL ALA 0.00350657
S21 S38 VAL CYS 0.00350657
S21 S38 VAL ASP 0.00350657
S21 S38 VAL GLU -0.392514
S21 S38 VAL PHE 0.00350657
S21 S38 VAL GLY 0.00350657
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S21 S38 VAL ILE 0.00350657
S21 S38 VAL LYS 0.156327
S21 S38 VAL LEU 0.143259
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S21 S38 VAL TRP 0.00350657
S21 S38 VAL TYR 0.00350657
S21 S38 VAL --- 0.00350657
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S21 S38 TRP LYS 0.0029387
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S21 S38 TYR ALA 0.00352655
S21 S38 TYR CYS 0.00352655
S21 S38 TYR ASP 0.00352655
S21 S38 TYR GLU 0.17
S21 S38 TYR PHE 0.00352655
S21 S38 TYR GLY 0.00352655
S21 S38 TYR HIS 0.0854405
S21 S38 TYR ILE 0.00352655
S21 S38 TYR LYS 0.534763
S21 S38 TYR LEU -0.638902

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S21 S38 TYR ASN 0.00352655
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S21 S38 TYR VAL 0.00352655
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S21 S38 TYR TYR 0.00352655
S21 S38 TYR --- 0.00352655
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S21 S38 --- HIS 0.00407535
S21 S38 --- LYS 0.0029387
S21 S38 --- LEU 0.0121969
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S21 S39 ALA LEU 0.000420505
S21 S39 ALA VAL 0.0204196
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S21 S39 ASP LEU 0.000420505
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S21 S39 ASP TRP 0.000382461
S21 S39 GLU ILE 0.00190325
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S21 S39 PHE CYS 0.000873987
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S21 S39 PHE GLU 0.000873987
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S21 S39 PHE LYS 0.000873987
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S21 S39 PHE PRO 0.000873987
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S21 S39 GLY ILE 0.00190325
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S21 S39 GLY VAL 0.0204196
S21 S39 GLY TRP 0.000382461
S21 S39 HIS ILE 0.00190325
S21 S39 HIS LEU 0.000420505
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S21 S39 ILE CYS 0.0124671

S21 S39 ILE ASP 0.0124671
S21 S39 ILE GLU 0.0124671
S21 S39 ILE PHE 0.0124671
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S21 S39 ILE HIS 0.0124671
S21 S39 ILE ILE -0.109753
S21 S39 ILE LYS 0.0124671
S21 S39 ILE LEU -0.117201
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S21 S39 ILE GLN 0.0124671
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S21 S39 ILE TYR 0.0124671
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S21 S39 LYS ILE 0.00190325
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S21 S40 ASP VAL 0.021515
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S21 S40 PHE LYS 0.00171903

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S22 S26 GLU GLU 7.67267e-05

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S22 S30 ASP CYS 0.00088745
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S22 S30 ASP GLU 0.00088745
S22 S30 ASP PHE 0.00088745
S22 S30 ASP GLY 0.00088745
S22 S30 ASP HIS 0.00088745
S22 S30 ASP ILE 0.00088745

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S22 S31 ASP CYS 0.00235229
S22 S31 ASP ASP 0.0615647
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S22 S31 ASP PHE 0.00235229
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S22 S31 ASP GLN 0.00235229

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S22 S31 HIS VAL 0.0171391
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S22 S40 TYR THR 0.00124861
S22 S40 TYR VAL -0.189036
S22 S40 TYR TRP 0.00124861

S22 S40 TYR TYR 0.00124861
S22 S40 TYR --- 0.00124861
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S22 S40 --- LEU 0.000448993
S22 S40 --- VAL 0.0174188
S23 S24 ALA GLY 0.0155327
S23 S24 ALA SER 0.000209625
S23 S24 CYS GLY 0.0155327
S23 S24 CYS SER 0.000209625
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S23 S24 ASP SER 0.000209625
S23 S24 GLU GLY 0.0155327
S23 S24 GLU SER 0.000209625
S23 S24 PHE GLY 0.0155327
S23 S24 PHE SER 0.000209625
S23 S24 GLY GLY 0.0155327
S23 S24 GLY SER 0.000209625
S23 S24 HIS GLY 0.0155327
S23 S24 HIS SER 0.000209625
S23 S24 ILE ALA 0.00908393
S23 S24 ILE CYS 0.00908393
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S23 S24 ILE GLU 0.00908393
S23 S24 ILE PHE 0.00908393
S23 S24 ILE GLY -0.185211
S23 S24 ILE HIS 0.00908393
S23 S24 ILE ILE 0.00908393
S23 S24 ILE LYS 0.00908393
S23 S24 ILE LEU 0.00908393
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S23 S24 LEU CYS 0.00253426
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S23 S24 LEU PHE 0.00253426
S23 S24 LEU GLY -0.248929
S23 S24 LEU HIS 0.00253426
S23 S24 LEU ILE 0.00253426
S23 S24 LEU LYS 0.00253426
S23 S24 LEU LEU 0.00253426
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S23 S24 LEU ASN 0.00253426
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S23 S24 LEU VAL 0.00253426
S23 S24 LEU TRP 0.00253426
S23 S24 LEU TYR 0.00253426
S23 S24 LEU --- 0.00253426

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S23 S24 PRO SER 0.000209625
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S23 S24 GLN SER 0.000209625
S23 S24 ARG GLY 0.0155327
S23 S24 ARG SER 0.000209625
S23 S24 SER GLY 0.0155327
S23 S24 SER SER 0.000209625
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S23 S24 --- GLY 0.0155327
S23 S24 --- SER 0.000209625
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S23 S25 ALA GLU 0.000248062
S23 S25 ALA LYS 0.000176921
S23 S25 ALA ARG 0.00219906
S23 S25 ALA SER 0.0125102
S23 S25 ALA THR 0.000586762
S23 S25 CYS ASP 2.12823e-05
S23 S25 CYS GLU 0.000248062
S23 S25 CYS LYS 0.000176921
S23 S25 CYS ARG 0.00219906
S23 S25 CYS SER 0.0125102
S23 S25 CYS THR 0.000586762
S23 S25 ASP ASP 2.12823e-05
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S23 S25 ASP LYS 0.000176921
S23 S25 ASP ARG 0.00219906
S23 S25 ASP SER 0.0125102
S23 S25 ASP THR 0.000586762
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S23 S25 PHE LYS 0.000176921
S23 S25 PHE ARG 0.00219906
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S23 S25 GLY LYS 0.000176921
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S23 S25 GLY SER 0.0125102
S23 S25 GLY THR 0.000586762
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S23 S25 HIS LYS 0.000176921
S23 S25 HIS ARG 0.00219906
S23 S25 HIS SER 0.0125102

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S23 S25 ILE GLU -0.254019
S23 S25 ILE PHE 0.0213845
S23 S25 ILE GLY 0.0213845
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S23 S25 ASN THR 0.000586762
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S23 S25 TYR LYS 0.000176921
S23 S25 TYR ARG 0.00219906
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S23 S25 TYR THR 0.000586762
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S23 S26 ALA LYS 0.0102078
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S23 S26 CYS LYS 0.0102078
S23 S26 CYS TYR 0.00175804
S23 S26 ASP PHE 0.00377646
S23 S26 ASP LYS 0.0102078
S23 S26 ASP TYR 0.00175804
S23 S26 GLU PHE 0.00377646
S23 S26 GLU LYS 0.0102078

S23 S26 GLU TYR 0.00175804
S23 S26 PHE PHE 0.00377646
S23 S26 PHE LYS 0.0102078
S23 S26 PHE TYR 0.00175804
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S23 S26 LEU CYS 0.00679478
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S23 S26 PRO PHE 0.00377646
S23 S26 PRO LYS 0.0102078

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S23 S26 GLN LYS 0.0102078
S23 S26 GLN TYR 0.00175804
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S23 S27 LEU PHE 0.00158091
S23 S27 LEU GLY 0.00158091
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S23 S28 ILE HIS 0.0118515

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S23 S30 GLY SER 0.000250867

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S23 S31 LEU LYS 0.00472977
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S23 S39 ALA ILE 0.00180889
S23 S39 ALA LEU 0.000301793
S23 S39 ALA VAL 0.0134894
S23 S39 ALA TRP 0.00014227
S23 S39 CYS ILE 0.00180889
S23 S39 CYS LEU 0.000301793
S23 S39 CYS VAL 0.0134894
S23 S39 CYS TRP 0.00014227
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S23 S39 ASP LEU 0.000301793
S23 S39 ASP VAL 0.0134894
S23 S39 ASP TRP 0.00014227
S23 S39 GLU ILE 0.00180889
S23 S39 GLU LEU 0.000301793
S23 S39 GLU VAL 0.0134894
S23 S39 GLU TRP 0.00014227
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S23 S39 PHE LEU 0.000301793
S23 S39 PHE VAL 0.0134894
S23 S39 PHE TRP 0.00014227
S23 S39 GLY ILE 0.00180889

S23 S39 GLY LEU 0.000301793
S23 S39 GLY VAL 0.0134894
S23 S39 GLY TRP 0.00014227
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S23 S39 HIS LEU 0.000301793
S23 S39 HIS VAL 0.0134894
S23 S39 HIS TRP 0.00014227
S23 S39 ILE ALA 0.011098
S23 S39 ILE CYS 0.011098
S23 S39 ILE ASP 0.011098
S23 S39 ILE GLU 0.011098
S23 S39 ILE PHE 0.011098
S23 S39 ILE GLY 0.011098
S23 S39 ILE HIS 0.011098
S23 S39 ILE ILE 0.174017
S23 S39 ILE LYS 0.011098
S23 S39 ILE LEU 0.0815186
S23 S39 ILE MET 0.011098
S23 S39 ILE ASN 0.011098
S23 S39 ILE PRO 0.011098
S23 S39 ILE GLN 0.011098
S23 S39 ILE ARG 0.011098
S23 S39 ILE SER 0.011098
S23 S39 ILE THR 0.011098
S23 S39 ILE VAL -0.774655
S23 S39 ILE TRP 0.145769
S23 S39 ILE TYR 0.011098
S23 S39 ILE --- 0.011098
S23 S39 LYS ILE 0.00180889
S23 S39 LYS LEU 0.000301793
S23 S39 LYS VAL 0.0134894
S23 S39 LYS TRP 0.00014227
S23 S39 LEU ALA 0.00764031
S23 S39 LEU CYS 0.00764031
S23 S39 LEU ASP 0.00764031
S23 S39 LEU GLU 0.00764031
S23 S39 LEU PHE 0.00764031
S23 S39 LEU GLY 0.00764031
S23 S39 LEU HIS 0.00764031
S23 S39 LEU ILE -0.270896
S23 S39 LEU LYS 0.00764031
S23 S39 LEU LEU -0.13561
S23 S39 LEU MET 0.00764031
S23 S39 LEU ASN 0.00764031
S23 S39 LEU PRO 0.00764031
S23 S39 LEU GLN 0.00764031
S23 S39 LEU ARG 0.00764031
S23 S39 LEU SER 0.00764031
S23 S39 LEU THR 0.00764031
S23 S39 LEU VAL 0.349279
S23 S39 LEU TRP -0.187077
S23 S39 LEU TYR 0.00764031
S23 S39 LEU --- 0.00764031
S23 S39 MET ILE 0.00180889
S23 S39 MET LEU 0.000301793
S23 S39 MET VAL 0.0134894
S23 S39 MET TRP 0.00014227
S23 S39 ASN ILE 0.00180889
S23 S39 ASN LEU 0.000301793
S23 S39 ASN VAL 0.0134894
S23 S39 ASN TRP 0.00014227
S23 S39 PRO ILE 0.00180889
S23 S39 PRO LEU 0.000301793

S23 S39 PRO VAL 0.0134894
S23 S39 PRO TRP 0.00014227
S23 S39 GLN ILE 0.00180889
S23 S39 GLN LEU 0.000301793
S23 S39 GLN VAL 0.0134894
S23 S39 GLN TRP 0.00014227
S23 S39 ARG ILE 0.00180889
S23 S39 ARG LEU 0.000301793
S23 S39 ARG VAL 0.0134894
S23 S39 ARG TRP 0.00014227
S23 S39 SER ILE 0.00180889
S23 S39 SER LEU 0.000301793
S23 S39 SER VAL 0.0134894
S23 S39 SER TRP 0.00014227
S23 S39 THR ILE 0.00180889
S23 S39 THR LEU 0.000301793
S23 S39 THR VAL 0.0134894
S23 S39 THR TRP 0.00014227
S23 S39 VAL ILE 0.00180889
S23 S39 VAL LEU 0.000301793
S23 S39 VAL VAL 0.0134894
S23 S39 VAL TRP 0.00014227
S23 S39 TRP ILE 0.00180889
S23 S39 TRP LEU 0.000301793
S23 S39 TRP VAL 0.0134894
S23 S39 TRP TRP 0.00014227
S23 S39 TYR ILE 0.00180889
S23 S39 TYR LEU 0.000301793
S23 S39 TYR VAL 0.0134894
S23 S39 TYR TRP 0.00014227
S23 S39 --- ILE 0.00180889
S23 S39 --- LEU 0.000301793
S23 S39 --- VAL 0.0134894
S23 S39 --- TRP 0.00014227
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S23 S40 ALA LEU 0.000275106
S23 S40 ALA VAL 0.0146421
S23 S40 CYS ILE 0.000825141
S23 S40 CYS LEU 0.000275106
S23 S40 CYS VAL 0.0146421
S23 S40 ASP ILE 0.000825141
S23 S40 ASP LEU 0.000275106
S23 S40 ASP VAL 0.0146421
S23 S40 GLU ILE 0.000825141
S23 S40 GLU LEU 0.000275106
S23 S40 GLU VAL 0.0146421
S23 S40 PHE ILE 0.000825141
S23 S40 PHE LEU 0.000275106
S23 S40 PHE VAL 0.0146421
S23 S40 GLY ILE 0.000825141
S23 S40 GLY LEU 0.000275106
S23 S40 GLY VAL 0.0146421
S23 S40 HIS ILE 0.000825141
S23 S40 HIS LEU 0.000275106
S23 S40 HIS VAL 0.0146421
S23 S40 ILE ALA 0.0134112
S23 S40 ILE CYS 0.0134112
S23 S40 ILE ASP 0.0134112
S23 S40 ILE GLU 0.0134112
S23 S40 ILE PHE 0.0134112
S23 S40 ILE GLY 0.0134112
S23 S40 ILE HIS 0.0134112
S23 S40 ILE ILE -0.228523

S23 S40 ILE LYS 0.0134112
S23 S40 ILE LEU -0.135438
S23 S40 ILE MET 0.0134112
S23 S40 ILE ASN 0.0134112
S23 S40 ILE PRO 0.0134112
S23 S40 ILE GLN 0.0134112
S23 S40 ILE ARG 0.0134112
S23 S40 ILE SER 0.0134112
S23 S40 ILE THR 0.0134112
S23 S40 ILE VAL -0.0621271
S23 S40 ILE TRP 0.0134112
S23 S40 ILE TYR 0.0134112
S23 S40 ILE --- 0.0134112
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S23 S40 LYS LEU 0.000275106
S23 S40 LYS VAL 0.0146421
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S23 S40 LEU CYS 0.00299788
S23 S40 LEU ASP 0.00299788
S23 S40 LEU GLU 0.00299788
S23 S40 LEU PHE 0.00299788
S23 S40 LEU GLY 0.00299788
S23 S40 LEU HIS 0.00299788
S23 S40 LEU ILE 0.140729
S23 S40 LEU LYS 0.00299788
S23 S40 LEU LEU 0.0752866
S23 S40 LEU MET 0.00299788
S23 S40 LEU ASN 0.00299788
S23 S40 LEU PRO 0.00299788
S23 S40 LEU GLN 0.00299788
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S23 S40 LEU SER 0.00299788
S23 S40 LEU THR 0.00299788
S23 S40 LEU VAL -0.384396
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S23 S40 LEU TYR 0.00299788
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S23 S40 MET ILE 0.000825141
S23 S40 MET LEU 0.000275106
S23 S40 MET VAL 0.0146421
S23 S40 ASN ILE 0.000825141
S23 S40 ASN LEU 0.000275106
S23 S40 ASN VAL 0.0146421
S23 S40 PRO ILE 0.000825141
S23 S40 PRO LEU 0.000275106
S23 S40 PRO VAL 0.0146421
S23 S40 GLN ILE 0.000825141
S23 S40 GLN LEU 0.000275106
S23 S40 GLN VAL 0.0146421
S23 S40 ARG ILE 0.000825141
S23 S40 ARG LEU 0.000275106
S23 S40 ARG VAL 0.0146421
S23 S40 SER ILE 0.000825141
S23 S40 SER LEU 0.000275106
S23 S40 SER VAL 0.0146421
S23 S40 THR ILE 0.000825141
S23 S40 THR LEU 0.000275106
S23 S40 THR VAL 0.0146421
S23 S40 VAL ILE 0.000825141
S23 S40 VAL LEU 0.000275106
S23 S40 VAL VAL 0.0146421
S23 S40 TRP ILE 0.000825141
S23 S40 TRP LEU 0.000275106

S23 S40 TRP VAL 0.0146421
S23 S40 TYR ILE 0.000825141
S23 S40 TYR LEU 0.000275106
S23 S40 TYR VAL 0.0146421
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S23 S40 --- LEU 0.000275106
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S24 S25 ALA GLU 8.19954e-05
S24 S25 ALA LYS 0.000465837
S24 S25 ALA ARG 0.00196234
S24 S25 ALA SER 0.00890338
S24 S25 ALA THR 0.000139451
S24 S25 CYS ASP 6.5189e-05
S24 S25 CYS GLU 8.19954e-05
S24 S25 CYS LYS 0.000465837
S24 S25 CYS ARG 0.00196234
S24 S25 CYS SER 0.00890338
S24 S25 CYS THR 0.000139451
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S24 S25 ASP GLU 8.19954e-05
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S24 S25 ASP ARG 0.00196234
S24 S25 ASP SER 0.00890338
S24 S25 ASP THR 0.000139451
S24 S25 GLU ASP 6.5189e-05
S24 S25 GLU GLU 8.19954e-05
S24 S25 GLU LYS 0.000465837
S24 S25 GLU ARG 0.00196234
S24 S25 GLU SER 0.00890338
S24 S25 GLU THR 0.000139451
S24 S25 PHE ASP 6.5189e-05
S24 S25 PHE GLU 8.19954e-05
S24 S25 PHE LYS 0.000465837
S24 S25 PHE ARG 0.00196234
S24 S25 PHE SER 0.00890338
S24 S25 PHE THR 0.000139451
S24 S25 GLY ALA 0.0260819
S24 S25 GLY CYS 0.0260819
S24 S25 GLY ASP -0.0215035
S24 S25 GLY GLU -0.0383327
S24 S25 GLY PHE 0.0260819
S24 S25 GLY GLY 0.0260819
S24 S25 GLY HIS 0.0260819
S24 S25 GLY ILE 0.0260819
S24 S25 GLY LYS -0.0662964
S24 S25 GLY LEU 0.0260819
S24 S25 GLY MET 0.0260819
S24 S25 GLY ASN 0.0260819
S24 S25 GLY PRO 0.0260819
S24 S25 GLY GLN 0.0260819
S24 S25 GLY ARG -0.217768
S24 S25 GLY SER -0.171509
S24 S25 GLY THR -0.0148366
S24 S25 GLY VAL 0.0260819
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S24 S25 GLY TYR 0.0260819
S24 S25 GLY --- 0.0260819
S24 S25 HIS ASP 6.5189e-05
S24 S25 HIS GLU 8.19954e-05
S24 S25 HIS LYS 0.000465837
S24 S25 HIS ARG 0.00196234
S24 S25 HIS SER 0.00890338

S24 S25 HIS THR 0.000139451
S24 S25 ILE ASP 6.5189e-05
S24 S25 ILE GLU 8.19954e-05
S24 S25 ILE LYS 0.000465837
S24 S25 ILE ARG 0.00196234
S24 S25 ILE SER 0.00890338
S24 S25 ILE THR 0.000139451
S24 S25 LYS ASP 6.5189e-05
S24 S25 LYS GLU 8.19954e-05
S24 S25 LYS LYS 0.000465837
S24 S25 LYS ARG 0.00196234
S24 S25 LYS SER 0.00890338
S24 S25 LYS THR 0.000139451
S24 S25 LEU ASP 6.5189e-05
S24 S25 LEU GLU 8.19954e-05
S24 S25 LEU LYS 0.000465837
S24 S25 LEU ARG 0.00196234
S24 S25 LEU SER 0.00890338
S24 S25 LEU THR 0.000139451
S24 S25 MET ASP 6.5189e-05
S24 S25 MET GLU 8.19954e-05
S24 S25 MET LYS 0.000465837
S24 S25 MET ARG 0.00196234
S24 S25 MET SER 0.00890338
S24 S25 MET THR 0.000139451
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S24 S25 ASN GLU 8.19954e-05
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S24 S25 ASN ARG 0.00196234
S24 S25 ASN SER 0.00890338
S24 S25 ASN THR 0.000139451
S24 S25 PRO ASP 6.5189e-05
S24 S25 PRO GLU 8.19954e-05
S24 S25 PRO LYS 0.000465837
S24 S25 PRO ARG 0.00196234
S24 S25 PRO SER 0.00890338
S24 S25 PRO THR 0.000139451
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S24 S25 GLN ARG 0.00196234
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S24 S25 GLN THR 0.000139451
S24 S25 ARG ASP 6.5189e-05
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S24 S25 SER PHE 0.000236086
S24 S25 SER GLY 0.000236086
S24 S25 SER HIS 0.000236086
S24 S25 SER ILE 0.000236086
S24 S25 SER LYS 0.00691188
S24 S25 SER LEU 0.000236086
S24 S25 SER MET 0.000236086
S24 S25 SER ASN 0.000236086
S24 S25 SER PRO 0.000236086
S24 S25 SER GLN 0.000236086

S24 S25 SER ARG 0.0898555
S24 S25 SER SER -0.189673
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S24 S25 THR GLU 8.19954e-05
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S24 S25 THR ARG 0.00196234
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S24 S25 THR THR 0.000139451
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S24 S25 VAL GLU 8.19954e-05
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S24 S25 VAL ARG 0.00196234
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S24 S25 VAL THR 0.000139451
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S24 S25 TRP ARG 0.00196234
S24 S25 TRP SER 0.00890338
S24 S25 TRP THR 0.000139451
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S24 S25 TYR GLU 8.19954e-05
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S24 S25 TYR ARG 0.00196234
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S24 S25 TYR THR 0.000139451
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S24 S26 CYS LYS 0.00738669
S24 S26 CYS TYR 0.000756832
S24 S26 ASP PHE 0.00347467
S24 S26 ASP LYS 0.00738669
S24 S26 ASP TYR 0.000756832
S24 S26 GLU PHE 0.00347467
S24 S26 GLU LYS 0.00738669
S24 S26 GLU TYR 0.000756832
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S24 S26 GLY CYS 0.0208347
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S24 S26 GLY GLU 0.0208347
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S24 S26 GLY GLY 0.0208347
S24 S26 GLY HIS 0.0208347
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S24 S26 GLY LYS -0.157368
S24 S26 GLY LEU 0.0208347
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S24 S26 HIS LYS 0.00738669
S24 S26 HIS TYR 0.000756832
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S24 S26 ILE LYS 0.00738669
S24 S26 ILE TYR 0.000756832
S24 S26 LYS PHE 0.00347467
S24 S26 LYS LYS 0.00738669
S24 S26 LYS TYR 0.000756832
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S24 S26 LEU LYS 0.00738669
S24 S26 LEU TYR 0.000756832
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S24 S26 MET LYS 0.00738669
S24 S26 MET TYR 0.000756832
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S24 S26 ASN LYS 0.00738669
S24 S26 ASN TYR 0.000756832
S24 S26 PRO PHE 0.00347467
S24 S26 PRO LYS 0.00738669
S24 S26 PRO TYR 0.000756832
S24 S26 GLN PHE 0.00347467
S24 S26 GLN LYS 0.00738669
S24 S26 GLN TYR 0.000756832
S24 S26 ARG PHE 0.00347467
S24 S26 ARG LYS 0.00738669
S24 S26 ARG TYR 0.000756832
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S24 S26 SER CYS 0.00015502
S24 S26 SER ASP 0.00015502
S24 S26 SER GLU 0.00015502
S24 S26 SER PHE 0.0737312
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S24 S26 SER LYS -0.170563
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S24 S26 SER MET 0.00015502
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S24 S26 SER PRO 0.00015502
S24 S26 SER GLN 0.00015502
S24 S26 SER ARG 0.00015502
S24 S26 SER SER 0.00015502
S24 S26 SER THR 0.00015502
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S24 S26 SER TRP 0.00015502
S24 S26 SER TYR 0.0123141
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S24 S26 THR LYS 0.00738669
S24 S26 THR TYR 0.000756832
S24 S26 VAL PHE 0.00347467
S24 S26 VAL LYS 0.00738669

S24 S26 VAL TYR 0.000756832
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S24 S26 TRP LYS 0.00738669
S24 S26 TRP TYR 0.000756832
S24 S26 TYR PHE 0.00347467
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S24 S27 CYS ASN 0.00180768
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S24 S27 ASP SER 0.00981051
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S24 S27 PHE SER 0.00981051
S24 S27 GLY ALA 0.0151211
S24 S27 GLY CYS 0.0151211
S24 S27 GLY ASP 0.0151211
S24 S27 GLY GLU 0.0151211
S24 S27 GLY PHE 0.0151211
S24 S27 GLY GLY 0.0151211
S24 S27 GLY HIS 0.0151211
S24 S27 GLY ILE 0.0151211
S24 S27 GLY LYS 0.0151211
S24 S27 GLY LEU 0.0151211
S24 S27 GLY MET 0.0151211
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S24 S27 GLY TRP 0.0151211
S24 S27 GLY TYR 0.0151211
S24 S27 GLY --- 0.0151211
S24 S27 HIS ASN 0.00180768
S24 S27 HIS SER 0.00981051
S24 S27 ILE ASN 0.00180768
S24 S27 ILE SER 0.00981051
S24 S27 LYS ASN 0.00180768
S24 S27 LYS SER 0.00981051
S24 S27 LEU ASN 0.00180768
S24 S27 LEU SER 0.00981051
S24 S27 MET ASN 0.00180768
S24 S27 MET SER 0.00981051
S24 S27 ASN ASN 0.00180768
S24 S27 ASN SER 0.00981051
S24 S27 PRO ASN 0.00180768
S24 S27 PRO SER 0.00981051
S24 S27 GLN ASN 0.00180768
S24 S27 GLN SER 0.00981051
S24 S27 ARG ASN 0.00180768
S24 S27 ARG SER 0.00981051
S24 S27 SER ALA 7.49142e-05
S24 S27 SER CYS 7.49142e-05
S24 S27 SER ASP 7.49142e-05
S24 S27 SER GLU 7.49142e-05

S24 S27 SER PHE 7.49142e-05
S24 S27 SER GLY 7.49142e-05
S24 S27 SER HIS 7.49142e-05
S24 S27 SER ILE 7.49142e-05
S24 S27 SER LYS 7.49142e-05
S24 S27 SER LEU 7.49142e-05
S24 S27 SER MET 7.49142e-05
S24 S27 SER ASN 0.0220983
S24 S27 SER PRO 7.49142e-05
S24 S27 SER GLN 7.49142e-05
S24 S27 SER ARG 7.49142e-05
S24 S27 SER SER -0.105249
S24 S27 SER THR 7.49142e-05
S24 S27 SER VAL 7.49142e-05
S24 S27 SER TRP 7.49142e-05
S24 S27 SER TYR 7.49142e-05
S24 S27 SER --- 7.49142e-05
S24 S27 THR ASN 0.00180768
S24 S27 THR SER 0.00981051
S24 S27 VAL ASN 0.00180768
S24 S27 VAL SER 0.00981051
S24 S27 TRP ASN 0.00180768
S24 S27 TRP SER 0.00981051
S24 S27 TYR ASN 0.00180768
S24 S27 TYR SER 0.00981051
S24 S27 --- ASN 0.00180768
S24 S27 --- SER 0.00981051
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S24 S28 ALA GLU 0.0014866
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S24 S28 GLY GLU -0.108458
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S24 S38 ASP HIS 0.00292689
S24 S38 ASP LYS 0.00199593
S24 S38 ASP LEU 0.00464573
S24 S38 ASP ARG 0.00109373
S24 S38 GLU GLU 0.00095591
S24 S38 GLU HIS 0.00292689
S24 S38 GLU LYS 0.00199593
S24 S38 GLU LEU 0.00464573
S24 S38 GLU ARG 0.00109373
S24 S38 PHE GLU 0.00095591
S24 S38 PHE HIS 0.00292689
S24 S38 PHE LYS 0.00199593
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S24 S38 PHE ARG 0.00109373
S24 S38 GLY ALA 0.0308666
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S24 S38 GLY GLY 0.0308666
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S24 S38 GLY LEU 0.0596151
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S24 S38 GLY TYR 0.0308666
S24 S38 GLY --- 0.0308666
S24 S38 HIS GLU 0.00095591

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S24 S38 HIS LEU 0.00464573
S24 S38 HIS ARG 0.00109373
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S24 S38 ILE HIS 0.00292689
S24 S38 ILE LYS 0.00199593
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S24 S38 MET ARG 0.00109373
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S24 S38 ASN LYS 0.00199593
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S24 S38 ASN ARG 0.00109373
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S24 S38 PRO HIS 0.00292689
S24 S38 PRO LYS 0.00199593
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S24 S38 PRO ARG 0.00109373
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S24 S38 GLN ARG 0.00109373
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S24 S38 ARG HIS 0.00292689
S24 S38 ARG LYS 0.00199593
S24 S38 ARG LEU 0.00464573
S24 S38 ARG ARG 0.00109373
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S24 S38 SER ILE 0.000384437
S24 S38 SER LYS 0.037515
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S24 S38 SER GLN 0.000384437
S24 S38 SER ARG 0.0384876
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S24 S38 SER THR 0.000384437
S24 S38 SER VAL 0.000384437
S24 S38 SER TRP 0.000384437

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S24 S38 VAL LEU 0.00464573
S24 S38 VAL ARG 0.00109373
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S24 S38 TRP LYS 0.00199593
S24 S38 TRP LEU 0.00464573
S24 S38 TRP ARG 0.00109373
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S24 S38 TYR ARG 0.00109373
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S24 S38 --- LYS 0.00199593
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S24 S39 CYS TRP 9.70886e-05
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S24 S39 ASP TRP 9.70886e-05
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S24 S39 GLU TRP 9.70886e-05
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S24 S39 GLY PHE 0.0186077
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S24 S39 GLY SER 0.0186077

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S25 S26 ALA LYS 0.00979922
S25 S26 ALA TYR 0.00161372
S25 S26 CYS PHE 0.014905
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S25 S26 CYS TYR 0.00161372
S25 S26 ASP ALA 2.7766e-05
S25 S26 ASP CYS 2.7766e-05

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S25 S26 ASP GLU 2.7766e-05
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S25 S26 ASP LYS 0.102514
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S25 S26 HIS LYS 0.00979922
S25 S26 HIS TYR 0.00161372
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S25 S26 LYS ILE 0.00165165
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S25 S26 SER CYS 0.0153072
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S25 S26 SER LEU 0.0153072
S25 S26 SER MET 0.0153072
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S25 S26 SER PRO 0.0153072
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S25 S26 SER SER 0.0153072
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S25 S26 SER TYR -0.244943
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S25 S26 THR CYS 0.000114843
S25 S26 THR ASP 0.000114843
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S25 S26 THR ASN 0.000114843
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S25 S27 ASP GLN 0.000121915
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S25 S27 ASP TYR 0.000121915
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S25 S27 GLU ALA 0.000161428

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S25 S27 GLU GLU 0.000161428
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S25 S27 GLU LYS 0.000161428
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S25 S27 GLY SER 0.0227889
S25 S27 HIS ASN 0.00352905
S25 S27 HIS SER 0.0227889
S25 S27 ILE ASN 0.00352905
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S25 S28 GLY GLU 0.00401071
S25 S28 HIS ASP 0.0223072
S25 S28 HIS GLU 0.00401071
S25 S28 ILE ASP 0.0223072
S25 S28 ILE GLU 0.00401071
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S25 S28 LYS CYS 0.000840738
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S25 S28 LYS GLU 0.243359
S25 S28 LYS PHE 0.000840738

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S25 S28 LYS ILE 0.000840738
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S25 S30 SER CYS 0.00837501
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S25 S30 SER THR 0.00837501
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S25 S30 THR CYS 0.000275275
S25 S30 THR ASP 0.000275275
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S25 S30 THR HIS 0.000275275
S25 S30 THR ILE 0.000275275
S25 S30 THR LYS 0.000275275
S25 S30 THR LEU 0.000275275
S25 S30 THR MET 0.000275275
S25 S30 THR ASN 0.000275275
S25 S30 THR PRO 0.000275275
S25 S30 THR GLN -0.0351232
S25 S30 THR ARG 0.000275275
S25 S30 THR SER 0.0188309
S25 S30 THR THR 0.000275275
S25 S30 THR VAL 0.000275275
S25 S30 THR TRP 0.000275275
S25 S30 THR TYR 0.000275275
S25 S30 THR --- 0.000275275
S25 S30 VAL GLN 0.0251777
S25 S30 VAL SER 0.00114027
S25 S30 TRP GLN 0.0251777
S25 S30 TRP SER 0.00114027
S25 S30 TYR GLN 0.0251777
S25 S30 TYR SER 0.00114027
S25 S30 --- GLN 0.0251777
S25 S30 --- SER 0.00114027
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S25 S31 ALA ILE 0.00543787

S25 S31 ALA VAL 0.0204033
S25 S31 CYS ASP 0.000476815
S25 S31 CYS ILE 0.00543787
S25 S31 CYS VAL 0.0204033
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S25 S31 ASP CYS 0.000121991
S25 S31 ASP ASP 0.00424137
S25 S31 ASP GLU 0.000121991
S25 S31 ASP PHE 0.000121991
S25 S31 ASP GLY 0.000121991
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S25 S31 ASP TRP 0.000121991
S25 S31 ASP TYR 0.000121991
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S25 S31 GLU CYS 0.000184845
S25 S31 GLU ASP 0.0056281
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S25 S31 GLU GLY 0.000184845
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S25 S31 GLU ILE 0.0840872
S25 S31 GLU LYS 0.000184845
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S25 S31 PHE ILE 0.00543787
S25 S31 PHE VAL 0.0204033
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S25 S31 GLY ILE 0.00543787
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S25 S31 HIS ILE 0.00543787
S25 S31 HIS VAL 0.0204033
S25 S31 ILE ASP 0.000476815
S25 S31 ILE ILE 0.00543787
S25 S31 ILE VAL 0.0204033
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S25 S31 LYS CYS 0.000433994
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S25 S31 LYS PHE 0.000433994

S25 S31 LYS GLY 0.000433994
S25 S31 LYS HIS 0.000433994
S25 S31 LYS ILE 0.0703762
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S25 S31 LYS MET 0.000433994
S25 S31 LYS ASN 0.000433994
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S25 S31 LYS TYR 0.000433994
S25 S31 LYS --- 0.000433994
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S25 S31 LEU ILE 0.00543787
S25 S31 LEU VAL 0.0204033
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S25 S31 MET VAL 0.0204033
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S25 S31 PRO ILE 0.00543787
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S25 S31 ARG GLY 0.00383486
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S25 S31 ARG LYS 0.00383486
S25 S31 ARG LEU 0.00383486
S25 S31 ARG MET 0.00383486
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S25 S31 ARG VAL -0.028078
S25 S31 ARG TRP 0.00383486
S25 S31 ARG TYR 0.00383486
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S25 S31 SER CYS 0.0138563
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S25 S31 SER GLU 0.0138563
S25 S31 SER PHE 0.0138563
S25 S31 SER GLY 0.0138563
S25 S31 SER HIS 0.0138563
S25 S31 SER ILE 0.188118
S25 S31 SER LYS 0.0138563
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S25 S31 SER MET 0.0138563

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S25 S31 THR LYS 0.000128986
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S25 S31 THR ASN 0.000128986
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S25 S32 GLU GLN 5.34447e-05
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S25 S33 ARG CYS 0.00404648
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S25 S33 SER CYS 0.0183612
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S25 S33 SER PHE 0.0183612
S25 S33 SER GLY 0.0183612
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S25 S33 SER LYS -0.110254
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S25 S33 SER ARG 0.0183612
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S25 S33 SER THR 0.0183612
S25 S33 SER VAL -0.210992
S25 S33 SER TRP 0.0183612
S25 S33 SER TYR 0.0183612
S25 S33 SER --- 0.0183612

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S25 S33 THR ILE 0.000326168
S25 S33 THR LYS 0.00494815
S25 S33 THR LEU 0.000326168
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S25 S33 THR THR 0.000326168
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S25 S33 THR TRP 0.000326168
S25 S33 THR TYR 0.000326168
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S25 S33 VAL LYS 0.000303138
S25 S33 VAL SER 0.00244588
S25 S33 VAL VAL 0.00470818
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S25 S33 TRP LYS 0.000303138
S25 S33 TRP SER 0.00244588
S25 S33 TRP VAL 0.00470818
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S25 S33 TYR LYS 0.000303138
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S25 S33 TYR VAL 0.00470818
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S25 S33 --- SER 0.00244588
S25 S33 --- VAL 0.00470818
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S25 S34 ALA ARG 0.000158706
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S25 S34 CYS MET 0.00236548
S25 S34 CYS ARG 0.000158706
S25 S34 CYS SER 0.0208363
S25 S34 CYS THR 0.0024877
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S25 S34 ASP PHE 6.2064e-05
S25 S34 ASP GLY 6.2064e-05
S25 S34 ASP HIS 6.2064e-05
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S25 S34 ASP PRO 6.2064e-05
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S25 S34 ASP SER -0.0818777

S25 S34 ASP THR 0.0468881
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S25 S34 ASP TYR 6.2064e-05
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S25 S34 GLU CYS 0.00041461
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S25 S34 GLU LEU 0.00041461
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S25 S34 GLU PRO 0.00041461
S25 S34 GLU GLN 0.00041461
S25 S34 GLU ARG 0.00194888
S25 S34 GLU SER 0.39307
S25 S34 GLU THR 0.0654045
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S25 S34 GLU TRP 0.00041461
S25 S34 GLU TYR 0.00041461
S25 S34 GLU --- 0.00041461
S25 S34 PHE GLU 0.000469752
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S25 S34 LYS GLU 0.0224095
S25 S34 LYS PHE 0.00196371
S25 S34 LYS GLY 0.00196371
S25 S34 LYS HIS 0.00196371
S25 S34 LYS ILE 0.00196371
S25 S34 LYS LYS 0.00196371
S25 S34 LYS LEU 0.00196371
S25 S34 LYS MET 0.157972
S25 S34 LYS ASN 0.00196371
S25 S34 LYS PRO 0.00196371
S25 S34 LYS GLN 0.00196371
S25 S34 LYS ARG 0.00832865
S25 S34 LYS SER 0.231984
S25 S34 LYS THR -0.502647

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S25 S34 LYS TRP 0.00196371
S25 S34 LYS TYR 0.00196371
S25 S34 LYS --- 0.00196371
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S25 S34 LEU THR 0.0024877
S25 S34 MET GLU 0.000469752
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S25 S34 MET ARG 0.000158706
S25 S34 MET SER 0.0208363
S25 S34 MET THR 0.0024877
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S25 S34 ASN SER 0.0208363
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S25 S34 ARG ASP 0.00251629
S25 S34 ARG GLU 0.0570039
S25 S34 ARG PHE 0.00251629
S25 S34 ARG GLY 0.00251629
S25 S34 ARG HIS 0.00251629
S25 S34 ARG ILE 0.00251629
S25 S34 ARG LYS 0.00251629
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S25 S34 ARG PRO 0.00251629
S25 S34 ARG GLN 0.00251629
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S25 S34 ARG THR 0.414188
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S25 S34 ARG TYR 0.00251629
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S25 S34 SER CYS 0.0194461
S25 S34 SER ASP 0.0194461
S25 S34 SER GLU -0.117784
S25 S34 SER PHE 0.0194461
S25 S34 SER GLY 0.0194461
S25 S34 SER HIS 0.0194461
S25 S34 SER ILE 0.0194461
S25 S34 SER LYS 0.0194461
S25 S34 SER LEU 0.0194461
S25 S34 SER MET 0.313897
S25 S34 SER ASN 0.0194461
S25 S34 SER PRO 0.0194461

S25 S34 SER GLN 0.0194461
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S25 S34 SER SER -0.347092
S25 S34 SER THR -0.234813
S25 S34 SER VAL 0.0194461
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S25 S34 SER TYR 0.0194461
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S25 S34 THR PHE 0.00031025
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S25 S34 TRP THR 0.0024877
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S25 S35 ALA THR 0.00247706
S25 S35 CYS ALA 0.0116078
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S25 S35 CYS THR 0.00247706
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S25 S35 ASP CYS 9.97513e-05
S25 S35 ASP ASP 9.97513e-05
S25 S35 ASP GLU 9.97513e-05
S25 S35 ASP PHE 9.97513e-05
S25 S35 ASP GLY 9.97513e-05
S25 S35 ASP HIS 9.97513e-05
S25 S35 ASP ILE 9.97513e-05

S25 S35 ASP LYS 9.97513e-05
S25 S35 ASP LEU 9.97513e-05
S25 S35 ASP MET 9.97513e-05
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S25 S35 ASP TYR 9.97513e-05
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S25 S35 GLU ASP 0.000369203
S25 S35 GLU GLU 0.000369203
S25 S35 GLU PHE 0.000369203
S25 S35 GLU GLY 0.000369203
S25 S35 GLU HIS 0.000369203
S25 S35 GLU ILE 0.000369203
S25 S35 GLU LYS 0.000369203
S25 S35 GLU LEU 0.000369203
S25 S35 GLU MET 0.000369203
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S25 S35 HIS THR 0.00247706
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S25 S35 LYS PHE 0.00114095
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S25 S35 LYS ILE 0.00114095
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S25 S35 ARG VAL 0.00532532
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S25 S35 SER THR 0.0349594
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S25 S36 HIS SER 0.0207338
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S25 S36 MET GLU 0.00217415
S25 S36 MET SER 0.0207338
S25 S36 MET THR 0.00089938

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S25 S36 ARG CYS 0.00104778
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S25 S36 ARG GLU 0.170332
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S25 S36 ARG MET 0.00104778
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S25 S36 ARG THR 0.172658
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S25 S36 ARG TYR 0.00104778
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S25 S36 THR ILE 0.000998541
S25 S36 THR LYS 0.000998541

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S25 S36 THR THR 0.119055
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S25 S36 THR TYR 0.000998541
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S25 S36 VAL ASP 0.00251067
S25 S36 VAL GLU 0.00217415
S25 S36 VAL SER 0.0207338
S25 S36 VAL THR 0.00089938
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S25 S36 TRP GLU 0.00217415
S25 S36 TRP SER 0.0207338
S25 S36 TRP THR 0.00089938
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S25 S36 TYR GLU 0.00217415
S25 S36 TYR SER 0.0207338
S25 S36 TYR THR 0.00089938
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S25 S37 ALA SER 0.0113946
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S25 S37 CYS ASN 0.000169644
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S25 S37 ASP ALA 0.0566862
S25 S37 ASP CYS 0.000430605
S25 S37 ASP ASP 0.193986
S25 S37 ASP GLU 0.000430605
S25 S37 ASP PHE 0.0188132
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S25 S37 ASP LYS 0.000430605
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S25 S37 ASP TYR 0.000430605
S25 S37 ASP --- 0.000430605
S25 S37 GLU ALA 0.0099213
S25 S37 GLU CYS 0.000329815

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S25 S37 GLU GLU 0.000329815
S25 S37 GLU PHE 0.0483618
S25 S37 GLU GLY 0.000329815
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S25 S37 GLU ILE 0.000329815
S25 S37 GLU LYS 0.000329815
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S25 S37 LYS VAL 0.000407747
S25 S37 LYS TRP 0.000407747
S25 S37 LYS TYR 0.000407747

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S25 S37 ARG ILE 0.00421844
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S25 S37 SER PHE 0.0753619
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S25 S37 SER MET 0.0227501

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S25 S38 CYS LYS 0.00313875

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S25 S38 ILE LEU 0.0126636

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S25 S39 SER TRP -0.0823211
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S25 S39 THR HIS 7.51178e-05
S25 S39 THR ILE 0.00671295
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S25 S39 THR LEU 0.000749918
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S25 S39 THR TYR 7.51178e-05
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S25 S39 VAL VAL 0.0253892
S25 S39 VAL TRP 9.33777e-05
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S25 S39 --- VAL 0.0253892

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S25 S40 LYS LEU 0.0153577
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S26 S27 LEU SER 0.0169072
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S26 S29 VAL LEU 0.000140866
S26 S29 VAL ASN 0.000172676
S26 S29 VAL SER 0.0204821
S26 S29 TRP LYS 0.000194083
S26 S29 TRP LEU 0.000140866
S26 S29 TRP ASN 0.000172676
S26 S29 TRP SER 0.0204821
S26 S29 TYR ALA 0.00265326
S26 S29 TYR CYS 0.00265326
S26 S29 TYR ASP 0.00265326
S26 S29 TYR GLU 0.00265326
S26 S29 TYR PHE 0.00265326
S26 S29 TYR GLY 0.00265326
S26 S29 TYR HIS 0.00265326
S26 S29 TYR ILE 0.00265326
S26 S29 TYR LYS 0.0252117
S26 S29 TYR LEU -0.234888
S26 S29 TYR MET 0.00265326
S26 S29 TYR ASN 0.022401
S26 S29 TYR PRO 0.00265326
S26 S29 TYR GLN 0.00265326
S26 S29 TYR ARG 0.00265326
S26 S29 TYR SER 0.110543
S26 S29 TYR THR 0.00265326
S26 S29 TYR VAL 0.00265326
S26 S29 TYR TRP 0.00265326
S26 S29 TYR TYR 0.00265326
S26 S29 TYR --- 0.00265326
S26 S29 --- LYS 0.000194083
S26 S29 --- LEU 0.000140866
S26 S29 --- ASN 0.000172676

S26 S29 --- SER 0.0204821
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S26 S30 ALA SER 0.000772366
S26 S30 CYS GLN 0.0202173
S26 S30 CYS SER 0.000772366
S26 S30 ASP GLN 0.0202173
S26 S30 ASP SER 0.000772366
S26 S30 GLU GLN 0.0202173
S26 S30 GLU SER 0.000772366
S26 S30 PHE ALA 0.00669951
S26 S30 PHE CYS 0.00669951
S26 S30 PHE ASP 0.00669951
S26 S30 PHE GLU 0.00669951
S26 S30 PHE PHE 0.00669951
S26 S30 PHE GLY 0.00669951
S26 S30 PHE HIS 0.00669951
S26 S30 PHE ILE 0.00669951
S26 S30 PHE LYS 0.00669951
S26 S30 PHE LEU 0.00669951
S26 S30 PHE MET 0.00669951
S26 S30 PHE ASN 0.00669951
S26 S30 PHE PRO 0.00669951
S26 S30 PHE GLN 0.488122
S26 S30 PHE ARG 0.00669951
S26 S30 PHE SER -0.774017
S26 S30 PHE THR 0.00669951
S26 S30 PHE VAL 0.00669951
S26 S30 PHE TRP 0.00669951
S26 S30 PHE TYR 0.00669951
S26 S30 PHE --- 0.00669951
S26 S30 GLY GLN 0.0202173
S26 S30 GLY SER 0.000772366
S26 S30 HIS GLN 0.0202173
S26 S30 HIS SER 0.000772366
S26 S30 ILE GLN 0.0202173
S26 S30 ILE SER 0.000772366
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S26 S30 LYS CYS 0.00422025
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S26 S30 LYS LYS 0.00422025
S26 S30 LYS LEU 0.00422025
S26 S30 LYS MET 0.00422025
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S26 S30 LYS GLN -0.627588
S26 S30 LYS ARG 0.00422025
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S26 S30 LYS THR 0.00422025
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S26 S30 LYS TRP 0.00422025
S26 S30 LYS TYR 0.00422025
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S26 S30 LEU SER 0.000772366
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S26 S30 ASN SER 0.000772366

S26 S30 PRO GLN 0.0202173
S26 S30 PRO SER 0.000772366
S26 S30 GLN GLN 0.0202173
S26 S30 GLN SER 0.000772366
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S26 S30 TYR GLU 0.00154648
S26 S30 TYR PHE 0.00154648
S26 S30 TYR GLY 0.00154648
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S26 S30 TYR ASN 0.00154648
S26 S30 TYR PRO 0.00154648
S26 S30 TYR GLN -0.381373
S26 S30 TYR ARG 0.00154648
S26 S30 TYR SER 0.320362
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S26 S30 TYR VAL 0.00154648
S26 S30 TYR TRP 0.00154648
S26 S30 TYR TYR 0.00154648
S26 S30 TYR --- 0.00154648
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S26 S30 --- SER 0.000772366
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S26 S31 ALA ILE 0.00219287
S26 S31 ALA VAL 0.0179816
S26 S31 CYS ASP 0.000815177
S26 S31 CYS ILE 0.00219287
S26 S31 CYS VAL 0.0179816
S26 S31 ASP ASP 0.000815177
S26 S31 ASP ILE 0.00219287
S26 S31 ASP VAL 0.0179816
S26 S31 GLU ASP 0.000815177
S26 S31 GLU ILE 0.00219287
S26 S31 GLU VAL 0.0179816
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S26 S31 PHE CYS 0.00664009
S26 S31 PHE ASP 0.19309
S26 S31 PHE GLU 0.00664009
S26 S31 PHE PHE 0.00664009
S26 S31 PHE GLY 0.00664009
S26 S31 PHE HIS 0.00664009
S26 S31 PHE ILE -0.673145
S26 S31 PHE LYS 0.00664009
S26 S31 PHE LEU 0.00664009
S26 S31 PHE MET 0.00664009
S26 S31 PHE ASN 0.00664009
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S26 S31 PHE GLN 0.00664009

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S26 S31 PHE VAL 0.20193
S26 S31 PHE TRP 0.00664009
S26 S31 PHE TYR 0.00664009
S26 S31 PHE --- 0.00664009
S26 S31 GLY ASP 0.000815177
S26 S31 GLY ILE 0.00219287
S26 S31 GLY VAL 0.0179816
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S26 S31 HIS VAL 0.0179816
S26 S31 ILE ASP 0.000815177
S26 S31 ILE ILE 0.00219287
S26 S31 ILE VAL 0.0179816
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S26 S31 LYS CYS 0.00972321
S26 S31 LYS ASP -0.136038
S26 S31 LYS GLU 0.00972321
S26 S31 LYS PHE 0.00972321
S26 S31 LYS GLY 0.00972321
S26 S31 LYS HIS 0.00972321
S26 S31 LYS ILE 0.268673
S26 S31 LYS LYS 0.00972321
S26 S31 LYS LEU 0.00972321
S26 S31 LYS MET 0.00972321
S26 S31 LYS ASN 0.00972321
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S26 S31 LYS ARG 0.00972321
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S26 S31 LYS THR 0.00972321
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S26 S31 LYS TRP 0.00972321
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S26 S31 LEU VAL 0.0179816
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S26 S31 PRO ILE 0.00219287
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S26 S31 GLN ILE 0.00219287
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S26 S31 TRP ILE 0.00219287
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S26 S31 TYR CYS 0.00219766
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S26 S31 TYR GLU 0.00219766
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S26 S31 TYR MET 0.00219766
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S26 S31 TYR THR 0.00219766
S26 S31 TYR VAL -0.202689
S26 S31 TYR TRP 0.00219766
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S26 S32 CYS TYR 0.00103719
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S26 S32 ASP HIS 0.00128988
S26 S32 ASP TRP 0.0173788
S26 S32 ASP TYR 0.00103719
S26 S32 GLU PHE 0.00128386
S26 S32 GLU HIS 0.00128988
S26 S32 GLU TRP 0.0173788
S26 S32 GLU TYR 0.00103719
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S26 S32 PHE CYS 0.00721177
S26 S32 PHE ASP 0.00721177
S26 S32 PHE GLU 0.00721177
S26 S32 PHE PHE -0.57246
S26 S32 PHE GLY 0.00721177
S26 S32 PHE HIS 0.117926
S26 S32 PHE ILE 0.00721177
S26 S32 PHE LYS 0.00721177
S26 S32 PHE LEU 0.00721177
S26 S32 PHE MET 0.00721177
S26 S32 PHE ASN 0.00721177
S26 S32 PHE PRO 0.00721177
S26 S32 PHE GLN 0.00721177
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S26 S32 PHE SER 0.00721177
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S26 S32 PHE VAL 0.00721177
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S26 S32 GLY PHE 0.00128386
S26 S32 GLY HIS 0.00128988
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S26 S32 HIS TRP 0.0173788
S26 S32 HIS TYR 0.00103719
S26 S32 ILE PHE 0.00128386
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S26 S32 LYS ASP 0.0172463
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S26 S32 LYS PHE 0.425336
S26 S32 LYS GLY 0.0172463
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S26 S32 LYS ILE 0.0172463
S26 S32 LYS LYS 0.0172463
S26 S32 LYS LEU 0.0172463
S26 S32 LYS MET 0.0172463
S26 S32 LYS ASN 0.0172463
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S26 S32 TYR ILE 0.000352411
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S26 S32 TYR ASN 0.000352411
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S26 S33 PHE LEU 0.00794878

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S26 S33 LYS GLU 0.0151711
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S26 S33 LYS ILE 0.0151711
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S26 S34 ALA THR 0.00172374
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S26 S34 ASP THR 0.00172374
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S26 S34 GLU MET 0.00306185

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S26 S34 GLY THR 0.00172374
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S26 S37 ALA PHE 0.00254501
S26 S37 ALA ASN 0.000443966
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S26 S37 ALA SER 0.00782123
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S26 S37 HIS ASP 0.00852111

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S26 S38 ALA LYS 0.00269565
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S26 S38 CYS LYS 0.00269565

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S26 S38 PHE LYS -0.136354
S26 S38 PHE LEU -0.84013
S26 S38 PHE MET 0.00817043
S26 S38 PHE ASN 0.00817043
S26 S38 PHE PRO 0.00817043
S26 S38 PHE GLN 0.00817043
S26 S38 PHE ARG 0.0896294
S26 S38 PHE SER 0.00817043
S26 S38 PHE THR 0.00817043
S26 S38 PHE VAL 0.00817043
S26 S38 PHE TRP 0.00817043
S26 S38 PHE TYR 0.00817043
S26 S38 PHE --- 0.00817043
S26 S38 GLY GLU 0.00170483
S26 S38 GLY HIS 0.00500097
S26 S38 GLY LYS 0.00269565
S26 S38 GLY LEU 0.0100077
S26 S38 GLY ARG 0.00158049
S26 S38 HIS GLU 0.00170483
S26 S38 HIS HIS 0.00500097
S26 S38 HIS LYS 0.00269565
S26 S38 HIS LEU 0.0100077
S26 S38 HIS ARG 0.00158049
S26 S38 ILE GLU 0.00170483
S26 S38 ILE HIS 0.00500097
S26 S38 ILE LYS 0.00269565
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S26 S38 LYS CYS 0.0221551
S26 S38 LYS ASP 0.0221551
S26 S38 LYS GLU -0.305649
S26 S38 LYS PHE 0.0221551
S26 S38 LYS GLY 0.0221551
S26 S38 LYS HIS -0.357913
S26 S38 LYS ILE 0.0221551
S26 S38 LYS LYS -0.155725
S26 S38 LYS LEU 0.561253
S26 S38 LYS MET 0.0221551
S26 S38 LYS ASN 0.0221551
S26 S38 LYS PRO 0.0221551
S26 S38 LYS GLN 0.0221551
S26 S38 LYS ARG -0.284031

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S26 S38 LYS THR 0.0221551
S26 S38 LYS VAL 0.0221551
S26 S38 LYS TRP 0.0221551
S26 S38 LYS TYR 0.0221551
S26 S38 LYS --- 0.0221551
S26 S38 LEU GLU 0.00170483
S26 S38 LEU HIS 0.00500097
S26 S38 LEU LYS 0.00269565
S26 S38 LEU LEU 0.0100077
S26 S38 LEU ARG 0.00158049
S26 S38 MET GLU 0.00170483
S26 S38 MET HIS 0.00500097
S26 S38 MET LYS 0.00269565
S26 S38 MET LEU 0.0100077
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S26 S38 TRP LYS 0.00269565
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S26 S38 TRP ARG 0.00158049
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S26 S38 TYR CYS 0.000925496
S26 S38 TYR ASP 0.000925496
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S26 S38 TYR PHE 0.000925496
S26 S38 TYR GLY 0.000925496
S26 S38 TYR HIS 0.192211

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S26 S38 TYR LYS 0.0576635
S26 S38 TYR LEU 0.0115286
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S26 S38 TYR TYR 0.000925496
S26 S38 TYR --- 0.000925495
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S26 S38 --- HIS 0.00500097
S26 S38 --- LYS 0.00269565
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S26 S38 --- ARG 0.00158049
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S26 S39 ALA TRP 0.000175413
S26 S39 CYS ILE 0.0013629
S26 S39 CYS LEU 0.000749284
S26 S39 CYS VAL 0.0187021
S26 S39 CYS TRP 0.000175413
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S26 S39 ASP TRP 0.000175413
S26 S39 GLU ILE 0.0013629
S26 S39 GLU LEU 0.000749284
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S26 S39 GLU TRP 0.000175413
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S26 S39 PHE CYS 0.00287331
S26 S39 PHE ASP 0.00287331
S26 S39 PHE GLU 0.00287331
S26 S39 PHE PHE 0.00287331
S26 S39 PHE GLY 0.00287331
S26 S39 PHE HIS 0.00287331
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S26 S39 PHE LYS 0.00287331
S26 S39 PHE LEU 0.133713
S26 S39 PHE MET 0.00287331
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S26 S39 PHE PRO 0.00287331
S26 S39 PHE GLN 0.00287331
S26 S39 PHE ARG 0.00287331
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S26 S39 PHE THR 0.00287331
S26 S39 PHE VAL -1.07865
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S26 S39 PHE --- 0.00287331
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S26 S39 GLY VAL 0.0187021
S26 S39 GLY TRP 0.000175413
S26 S39 HIS ILE 0.0013629
S26 S39 HIS LEU 0.000749284
S26 S39 HIS VAL 0.0187021

S26 S39 HIS TRP 0.000175413
S26 S39 ILE ILE 0.0013629
S26 S39 ILE LEU 0.000749284
S26 S39 ILE VAL 0.0187021
S26 S39 ILE TRP 0.000175413
S26 S39 LYS ALA 0.0154168
S26 S39 LYS CYS 0.0154168
S26 S39 LYS ASP 0.0154168
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S26 S39 LYS GLY 0.0154168
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S26 S39 LYS LYS 0.0154168
S26 S39 LYS LEU -0.206496
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S26 S39 TYR LYS 0.000448149
S26 S39 TYR LEU 0.0109382
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S26 S39 TYR TRP 0.00705758
S26 S39 TYR TYR 0.000448149
S26 S39 TYR --- 0.000448149
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S26 S39 --- TRP 0.000175413
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S26 S40 CYS LEU 0.00082438
S26 S40 CYS VAL 0.0183704
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S26 S40 ASP LEU 0.00082438
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S26 S40 GLU LEU 0.00082438
S26 S40 GLU VAL 0.0183704
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S26 S40 PHE CYS 0.00503994
S26 S40 PHE ASP 0.00503994
S26 S40 PHE GLU 0.00503994
S26 S40 PHE PHE 0.00503994
S26 S40 PHE GLY 0.00503994
S26 S40 PHE HIS 0.00503994
S26 S40 PHE ILE -0.178845
S26 S40 PHE LYS 0.00503994
S26 S40 PHE LEU 0.281077
S26 S40 PHE MET 0.00503994
S26 S40 PHE ASN 0.00503994
S26 S40 PHE PRO 0.00503994
S26 S40 PHE GLN 0.00503994
S26 S40 PHE ARG 0.00503994
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S26 S40 PHE TYR 0.00503994
S26 S40 PHE --- 0.00503994
S26 S40 GLY ILE 0.00179492
S26 S40 GLY LEU 0.00082438

S26 S40 GLY VAL 0.0183704
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S26 S40 HIS LEU 0.00082438
S26 S40 HIS VAL 0.0183704
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S26 S40 ILE LEU 0.00082438
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S26 S40 LYS GLU 0.0103483
S26 S40 LYS PHE 0.0103483
S26 S40 LYS GLY 0.0103483
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S26 S40 LYS LEU -0.390709
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S26 S40 LYS PRO 0.0103483
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S26 S40 TYR PHE 0.00102086

S26 S40 TYR GLY 0.00102086
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S26 S40 TYR LYS 0.00102086
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S26 S40 TYR --- 0.00102086
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S27 S28 HIS GLU 0.00325831
S27 S28 ILE ASP 0.0119377
S27 S28 ILE GLU 0.00325831
S27 S28 LYS ASP 0.0119377
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S27 S28 ASN CYS 0.00321752
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S27 S28 ASN GLU -0.441805
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S27 S28 ASN GLY 0.00321752
S27 S28 ASN HIS 0.00321752
S27 S28 ASN ILE 0.00321752
S27 S28 ASN LYS 0.00321752
S27 S28 ASN LEU 0.00321752
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S27 S28 ASN ASN 0.00321752
S27 S28 ASN PRO 0.00321752
S27 S28 ASN GLN 0.00321752
S27 S28 ASN ARG 0.00321752
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S27 S28 ASN VAL 0.00321752
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S27 S28 ASN TYR 0.00321752
S27 S28 ASN --- 0.00321752
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S27 S28 PRO GLU 0.00325831
S27 S28 GLN ASP 0.0119377
S27 S28 GLN GLU 0.00325831
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S27 S28 SER GLU 0.323608
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S27 S29 HIS ASN 9.73504e-06

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S27 S29 ASN LYS -0.206904
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S27 S29 ASN TYR 0.00383961
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S27 S29 PRO LEU 0.00042018
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S27 S29 SER ASN -0.0853284
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S27 S29 SER SER -0.305549
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S27 S29 SER TYR 0.0139886
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S27 S29 TRP LEU 0.00042018
S27 S29 TRP ASN 9.73504e-06
S27 S29 TRP SER 0.014462
S27 S29 TYR LYS 0.000304132
S27 S29 TYR LEU 0.00042018
S27 S29 TYR ASN 9.73504e-06
S27 S29 TYR SER 0.014462
S27 S29 --- LYS 0.000304132
S27 S29 --- LEU 0.00042018
S27 S29 --- ASN 9.73504e-06
S27 S29 --- SER 0.014462
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S27 S30 ALA SER 0.000689201
S27 S30 CYS GLN 0.0145068
S27 S30 CYS SER 0.000689201
S27 S30 ASP GLN 0.0145068
S27 S30 ASP SER 0.000689201
S27 S30 GLU GLN 0.0145068
S27 S30 GLU SER 0.000689201
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S27 S30 PHE SER 0.000689201
S27 S30 GLY GLN 0.0145068
S27 S30 GLY SER 0.000689201
S27 S30 HIS GLN 0.0145068
S27 S30 HIS SER 0.000689201
S27 S30 ILE GLN 0.0145068
S27 S30 ILE SER 0.000689201
S27 S30 LYS GLN 0.0145068
S27 S30 LYS SER 0.000689201
S27 S30 LEU GLN 0.0145068
S27 S30 LEU SER 0.000689201
S27 S30 MET GLN 0.0145068
S27 S30 MET SER 0.000689201
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S27 S30 ASN CYS 0.00389715
S27 S30 ASN ASP 0.00389715
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S27 S30 ASN PHE 0.00389715
S27 S30 ASN GLY 0.00389715
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S27 S30 ASN ILE 0.00389715
S27 S30 ASN LYS 0.00389715
S27 S30 ASN LEU 0.00389715
S27 S30 ASN MET 0.00389715
S27 S30 ASN ASN 0.00389715
S27 S30 ASN PRO 0.00389715

S27 S30 ASN GLN 0.440514
S27 S30 ASN ARG 0.00389715
S27 S30 ASN SER -0.581865
S27 S30 ASN THR 0.00389715
S27 S30 ASN VAL 0.00389715
S27 S30 ASN TRP 0.00389715
S27 S30 ASN TYR 0.00389715
S27 S30 ASN --- 0.00389715
S27 S30 PRO GLN 0.0145068
S27 S30 PRO SER 0.000689201
S27 S30 GLN GLN 0.0145068
S27 S30 GLN SER 0.000689201
S27 S30 ARG GLN 0.0145068
S27 S30 ARG SER 0.000689201
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S27 S30 SER CYS 0.00856909
S27 S30 SER ASP 0.00856909
S27 S30 SER GLU 0.00856909
S27 S30 SER PHE 0.00856909
S27 S30 SER GLY 0.00856909
S27 S30 SER HIS 0.00856909
S27 S30 SER ILE 0.00856909
S27 S30 SER LYS 0.00856909
S27 S30 SER LEU 0.00856909
S27 S30 SER MET 0.00856909
S27 S30 SER ASN 0.00856909
S27 S30 SER PRO 0.00856909
S27 S30 SER GLN -0.873071
S27 S30 SER ARG 0.00856909
S27 S30 SER SER 0.488838
S27 S30 SER THR 0.00856909
S27 S30 SER VAL 0.00856909
S27 S30 SER TRP 0.00856909
S27 S30 SER TYR 0.00856909
S27 S30 SER --- 0.00856909
S27 S30 THR GLN 0.0145068
S27 S30 THR SER 0.000689201
S27 S30 VAL GLN 0.0145068
S27 S30 VAL SER 0.000689201
S27 S30 TRP GLN 0.0145068
S27 S30 TRP SER 0.000689201
S27 S30 TYR GLN 0.0145068
S27 S30 TYR SER 0.000689201
S27 S30 --- GLN 0.0145068
S27 S30 --- SER 0.000689201
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S27 S31 ALA ILE 0.00366776
S27 S31 ALA VAL 0.0109572
S27 S31 CYS ASP 0.000571128
S27 S31 CYS ILE 0.00366776
S27 S31 CYS VAL 0.0109572
S27 S31 ASP ASP 0.000571128
S27 S31 ASP ILE 0.00366776
S27 S31 ASP VAL 0.0109572
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S27 S31 PHE ILE 0.00366776
S27 S31 PHE VAL 0.0109572
S27 S31 GLY ASP 0.000571128
S27 S31 GLY ILE 0.00366776
S27 S31 GLY VAL 0.0109572

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S27 S31 HIS VAL 0.0109572
S27 S31 ILE ASP 0.000571128
S27 S31 ILE ILE 0.00366776
S27 S31 ILE VAL 0.0109572
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S27 S31 LYS ILE 0.00366776
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S27 S31 MET ILE 0.00366776
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S27 S31 ASN CYS 0.00315352
S27 S31 ASN ASP 0.171109
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S27 S31 ASN GLY 0.00315352
S27 S31 ASN HIS 0.00315352
S27 S31 ASN ILE -0.671247
S27 S31 ASN LYS 0.00315352
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S27 S31 ASN MET 0.00315352
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S27 S31 ASN VAL 0.37607
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S27 S31 ASN TYR 0.00315352
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S27 S31 PRO VAL 0.0109572
S27 S31 GLN ASP 0.000571128
S27 S31 GLN ILE 0.00366776
S27 S31 GLN VAL 0.0109572
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S27 S31 SER CYS 0.0154074
S27 S31 SER ASP -0.282943
S27 S31 SER GLU 0.0154074
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S27 S31 SER GLY 0.0154074
S27 S31 SER HIS 0.0154074
S27 S31 SER ILE 0.540771
S27 S31 SER LYS 0.0154074
S27 S31 SER LEU 0.0154074
S27 S31 SER MET 0.0154074
S27 S31 SER ASN 0.0154074
S27 S31 SER PRO 0.0154074
S27 S31 SER GLN 0.0154074
S27 S31 SER ARG 0.0154074
S27 S31 SER SER 0.0154074
S27 S31 SER THR 0.0154074
S27 S31 SER VAL -0.756583

S27 S31 SER TRP 0.0154074
S27 S31 SER TYR 0.0154074
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S27 S31 THR ILE 0.00366776
S27 S31 THR VAL 0.0109572
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S27 S31 VAL ILE 0.00366776
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S27 S31 TRP ILE 0.00366776
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S27 S31 TYR ILE 0.00366776
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S27 S31 --- ASP 0.000571128
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S27 S32 ASP TYR 0.00108404
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S27 S32 GLU TYR 0.00108404
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S27 S32 PHE TYR 0.00108404
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S27 S32 MET TRP 0.0133142
S27 S32 MET TYR 0.00108404
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S27 S32 ASN GLY 0.00206706
S27 S32 ASN HIS 0.122405
S27 S32 ASN ILE 0.00206706
S27 S32 ASN LYS 0.00206706
S27 S32 ASN LEU 0.00206706
S27 S32 ASN MET 0.00206706
S27 S32 ASN ASN 0.00206706
S27 S32 ASN PRO 0.00206706
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S27 S32 ASN SER 0.00206706
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S27 S32 ASN TYR 0.129207
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S27 S32 PRO PHE 0.000312003
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S27 S32 SER ILE 0.0227434
S27 S32 SER LYS 0.0227434
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S27 S32 SER SER 0.0227434
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S27 S32 VAL TRP 0.0133142
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S27 S33 ASN ILE 0.00707471
S27 S33 ASN LYS -0.174726

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S27 S33 ASN MET 0.00707471
S27 S33 ASN ASN 0.00707471
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S27 S33 ASN THR 0.00707471
S27 S33 ASN VAL -0.666695
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S27 S33 ASN TYR 0.00707471
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S27 S33 SER GLY 0.0174783
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S27 S33 SER ILE 0.0174783
S27 S33 SER LYS 0.149824
S27 S33 SER LEU 0.0174783
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S27 S33 SER ASN 0.0174783
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S27 S33 SER THR 0.0174783
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S27 S33 SER TRP 0.0174783
S27 S33 SER TYR 0.0174783
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S27 S33 VAL ASP 0.00919909
S27 S33 VAL LYS 9.16876e-05
S27 S33 VAL SER 0.00160857
S27 S33 VAL VAL 0.0042967
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S27 S33 TRP LYS 9.16876e-05
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S27 S34 ALA MET 0.000807617
S27 S34 ALA ARG 9.73504e-06
S27 S34 ALA SER 0.0127025
S27 S34 ALA THR 0.00075042
S27 S34 CYS GLU 0.000925794
S27 S34 CYS MET 0.000807617
S27 S34 CYS ARG 9.73504e-06
S27 S34 CYS SER 0.0127025
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S27 S34 ASP GLU 0.000925794
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S27 S34 GLU THR 0.00075042
S27 S34 PHE GLU 0.000925794
S27 S34 PHE MET 0.000807617
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S27 S34 PHE SER 0.0127025
S27 S34 PHE THR 0.00075042
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S27 S34 GLY SER 0.0127025
S27 S34 GLY THR 0.00075042
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S27 S34 HIS MET 0.000807617
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S27 S34 HIS SER 0.0127025
S27 S34 HIS THR 0.00075042
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S27 S34 ILE MET 0.000807617
S27 S34 ILE ARG 9.73504e-06
S27 S34 ILE SER 0.0127025
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S27 S34 LEU MET 0.000807617
S27 S34 LEU ARG 9.73504e-06
S27 S34 LEU SER 0.0127025
S27 S34 LEU THR 0.00075042
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S27 S34 MET MET 0.000807617
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S27 S34 MET THR 0.00075042
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S27 S34 ASN CYS 0.00392142
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S27 S34 ASN GLY 0.00392142

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S27 S34 PRO MET 0.000807617
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S27 S34 ARG ARG 9.73504e-06
S27 S34 ARG SER 0.0127025
S27 S34 ARG THR 0.00075042
S27 S34 SER ALA 0.0207916
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S27 S34 SER ASP 0.0207916
S27 S34 SER GLU 0.528109
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S27 S34 SER GLY 0.0207916
S27 S34 SER HIS 0.0207916
S27 S34 SER ILE 0.0207916
S27 S34 SER LYS 0.0207916
S27 S34 SER LEU 0.0207916
S27 S34 SER MET -0.464038
S27 S34 SER ASN 0.0207916
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S27 S34 SER GLN 0.0207916
S27 S34 SER ARG -0.0760526
S27 S34 SER SER -0.0713805
S27 S34 SER THR -0.470724
S27 S34 SER VAL 0.0207916
S27 S34 SER TRP 0.0207916
S27 S34 SER TYR 0.0207916
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S27 S34 THR MET 0.000807617
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S27 S34 TRP SER 0.0127025
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S27 S34 TYR MET 0.000807617
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S27 S34 TYR SER 0.0127025
S27 S34 TYR THR 0.00075042
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S27 S34 --- MET 0.000807617
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S27 S34 --- SER 0.0127025
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S27 S35 ALA ALA 0.00432323
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S27 S39 ASN TYR 0.00181979
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S27 S39 PRO LEU 0.000350537
S27 S39 PRO VAL 0.0140504
S27 S39 PRO TRP 1.5457e-05
S27 S39 GLN ILE 0.000779704
S27 S39 GLN LEU 0.000350537
S27 S39 GLN VAL 0.0140504
S27 S39 GLN TRP 1.5457e-05
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S27 S39 SER ALA 0.0169185
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S27 S39 SER ASP 0.0169185
S27 S39 SER GLU 0.0169185
S27 S39 SER PHE 0.0169185
S27 S39 SER GLY 0.0169185
S27 S39 SER HIS 0.0169185
S27 S39 SER ILE -0.431171
S27 S39 SER LYS 0.0169185
S27 S39 SER LEU -0.0756087
S27 S39 SER MET 0.0169185
S27 S39 SER ASN 0.0169185
S27 S39 SER PRO 0.0169185
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S27 S39 SER THR 0.0169185
S27 S39 SER VAL 0.0449964
S27 S39 SER TRP -0.0472513
S27 S39 SER TYR 0.0169185
S27 S39 SER --- 0.0169185
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S27 S39 THR LEU 0.000350537
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S27 S39 VAL TRP 1.5457e-05
S27 S39 TRP ILE 0.000779704

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S27 S39 TRP VAL 0.0140504
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S27 S39 TYR ILE 0.000779704
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S27 S39 TYR VAL 0.0140504
S27 S39 TYR TRP 1.5457e-05
S27 S39 --- ILE 0.000779704
S27 S39 --- LEU 0.000350537
S27 S39 --- VAL 0.0140504
S27 S39 --- TRP 1.5457e-05
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S27 S40 ALA VAL 0.013467
S27 S40 CYS ILE 0.000711944
S27 S40 CYS LEU 0.00101713
S27 S40 CYS VAL 0.013467
S27 S40 ASP ILE 0.000711944
S27 S40 ASP LEU 0.00101713
S27 S40 ASP VAL 0.013467
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S27 S40 GLU LEU 0.00101713
S27 S40 GLU VAL 0.013467
S27 S40 PHE ILE 0.000711944
S27 S40 PHE LEU 0.00101713
S27 S40 PHE VAL 0.013467
S27 S40 GLY ILE 0.000711944
S27 S40 GLY LEU 0.00101713
S27 S40 GLY VAL 0.013467
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S27 S40 HIS LEU 0.00101713
S27 S40 HIS VAL 0.013467
S27 S40 ILE ILE 0.000711944
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S27 S40 ILE VAL 0.013467
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S27 S40 LEU ILE 0.000711944
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S27 S40 LEU VAL 0.013467
S27 S40 MET ILE 0.000711944
S27 S40 MET LEU 0.00101713
S27 S40 MET VAL 0.013467
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S27 S40 ASN CYS 0.00136754
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S27 S40 ASN GLY 0.00136754
S27 S40 ASN HIS 0.00136754
S27 S40 ASN ILE 0.0931427
S27 S40 ASN LYS 0.00136754
S27 S40 ASN LEU 0.417348
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S27 S40 ASN TRP 0.00136754

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S28 S29 ALA SER 0.0137619
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S28 S29 CYS LEU 0.000302797
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S28 S29 CYS SER 0.0137619
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S28 S29 ASP CYS 0.0169953
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S28 S29 ASP PHE 0.0169953
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S28 S29 ASP ILE 0.0169953

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S28 S29 ASP LEU -0.10972
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S28 S29 ASP ASN -0.0753292
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S28 S32 SER HIS 0.000509875
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S28 S32 SER TYR 0.00247474
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S28 S32 VAL TYR 0.00247474
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S28 S32 --- TYR 0.00247474
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S28 S33 ASP CYS 0.0209719
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S28 S33 GLU CYS 0.00358118
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S28 S34 ALA THR 0.000813549
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S29 S31 CYS ASP 0.0010305
S29 S31 CYS ILE 0.00194129
S29 S31 CYS VAL 0.0148564
S29 S31 ASP ASP 0.0010305
S29 S31 ASP ILE 0.00194129
S29 S31 ASP VAL 0.0148564
S29 S31 GLU ASP 0.0010305
S29 S31 GLU ILE 0.00194129
S29 S31 GLU VAL 0.0148564
S29 S31 PHE ASP 0.0010305

S29 S31 PHE ILE 0.00194129
S29 S31 PHE VAL 0.0148564
S29 S31 GLY ASP 0.0010305
S29 S31 GLY ILE 0.00194129
S29 S31 GLY VAL 0.0148564
S29 S31 HIS ASP 0.0010305
S29 S31 HIS ILE 0.00194129
S29 S31 HIS VAL 0.0148564
S29 S31 ILE ASP 0.0010305
S29 S31 ILE ILE 0.00194129
S29 S31 ILE VAL 0.0148564
S29 S31 LYS ALA 0.00041307
S29 S31 LYS CYS 0.00041307
S29 S31 LYS ASP 0.00532596
S29 S31 LYS GLU 0.00041307
S29 S31 LYS PHE 0.00041307
S29 S31 LYS GLY 0.00041307
S29 S31 LYS HIS 0.00041307
S29 S31 LYS ILE 0.0624861
S29 S31 LYS LYS 0.00041307
S29 S31 LYS LEU 0.00041307
S29 S31 LYS MET 0.00041307
S29 S31 LYS ASN 0.00041307
S29 S31 LYS PRO 0.00041307
S29 S31 LYS GLN 0.00041307
S29 S31 LYS ARG 0.00041307
S29 S31 LYS SER 0.00041307
S29 S31 LYS THR 0.00041307
S29 S31 LYS VAL -0.119589
S29 S31 LYS TRP 0.00041307
S29 S31 LYS TYR 0.00041307
S29 S31 LYS --- 0.00041307
S29 S31 LEU ALA 0.000715524
S29 S31 LEU CYS 0.000715524
S29 S31 LEU ASP -0.504513
S29 S31 LEU GLU 0.000715524
S29 S31 LEU PHE 0.000715524
S29 S31 LEU GLY 0.000715524
S29 S31 LEU HIS 0.000715524
S29 S31 LEU ILE 0.0357925
S29 S31 LEU LYS 0.000715524
S29 S31 LEU LEU 0.000715524
S29 S31 LEU MET 0.000715524
S29 S31 LEU ASN 0.000715524
S29 S31 LEU PRO 0.000715524
S29 S31 LEU GLN 0.000715524
S29 S31 LEU ARG 0.000715524
S29 S31 LEU SER 0.000715524
S29 S31 LEU THR 0.000715524
S29 S31 LEU VAL 0.394954
S29 S31 LEU TRP 0.000715524
S29 S31 LEU TYR 0.000715524
S29 S31 LEU --- 0.000715524
S29 S31 MET ASP 0.0010305
S29 S31 MET ILE 0.00194129
S29 S31 MET VAL 0.0148564
S29 S31 ASN ALA 0.000163947
S29 S31 ASN CYS 0.000163947
S29 S31 ASN ASP 0.00795922
S29 S31 ASN GLU 0.000163947
S29 S31 ASN PHE 0.000163947
S29 S31 ASN GLY 0.000163947
S29 S31 ASN HIS 0.000163947

S29 S31 ASN ILE 0.0237792
S29 S31 ASN LYS 0.000163947
S29 S31 ASN LEU 0.000163947
S29 S31 ASN MET 0.000163947
S29 S31 ASN ASN 0.000163947
S29 S31 ASN PRO 0.000163947
S29 S31 ASN GLN 0.000163947
S29 S31 ASN ARG 0.000163947
S29 S31 ASN SER 0.000163947
S29 S31 ASN THR 0.000163947
S29 S31 ASN VAL -0.0989355
S29 S31 ASN TRP 0.000163947
S29 S31 ASN TYR 0.000163947
S29 S31 ASN --- 0.000163947
S29 S31 PRO ASP 0.0010305
S29 S31 PRO ILE 0.00194129
S29 S31 PRO VAL 0.0148564
S29 S31 GLN ASP 0.0010305
S29 S31 GLN ILE 0.00194129
S29 S31 GLN VAL 0.0148564
S29 S31 ARG ASP 0.0010305
S29 S31 ARG ILE 0.00194129
S29 S31 ARG VAL 0.0148564
S29 S31 SER ALA 0.0172684
S29 S31 SER CYS 0.0172684
S29 S31 SER ASP 0.372727
S29 S31 SER GLU 0.0172684
S29 S31 SER PHE 0.0172684
S29 S31 SER GLY 0.0172684
S29 S31 SER HIS 0.0172684
S29 S31 SER ILE -0.215849
S29 S31 SER LYS 0.0172684
S29 S31 SER LEU 0.0172684
S29 S31 SER MET 0.0172684
S29 S31 SER ASN 0.0172684
S29 S31 SER PRO 0.0172684
S29 S31 SER GLN 0.0172684
S29 S31 SER ARG 0.0172684
S29 S31 SER SER 0.0172684
S29 S31 SER THR 0.0172684
S29 S31 SER VAL -0.601315
S29 S31 SER TRP 0.0172684
S29 S31 SER TYR 0.0172684
S29 S31 SER --- 0.0172684
S29 S31 THR ASP 0.0010305
S29 S31 THR ILE 0.00194129
S29 S31 THR VAL 0.0148564
S29 S31 VAL ASP 0.0010305
S29 S31 VAL ILE 0.00194129
S29 S31 VAL VAL 0.0148564
S29 S31 TRP ASP 0.0010305
S29 S31 TRP ILE 0.00194129
S29 S31 TRP VAL 0.0148564
S29 S31 TYR ASP 0.0010305
S29 S31 TYR ILE 0.00194129
S29 S31 TYR VAL 0.0148564
S29 S31 --- ASP 0.0010305
S29 S31 --- ILE 0.00194129
S29 S31 --- VAL 0.0148564
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S29 S32 ALA TRP 0.0142591
S29 S32 ALA TYR 0.000836506

S29 S32 CYS PHE 0.00116429
S29 S32 CYS HIS 0.00156831
S29 S32 CYS TRP 0.0142591
S29 S32 CYS TYR 0.000836506
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S29 S32 ASP HIS 0.00156831
S29 S32 ASP TRP 0.0142591
S29 S32 ASP TYR 0.000836506
S29 S32 GLU PHE 0.00116429
S29 S32 GLU HIS 0.00156831
S29 S32 GLU TRP 0.0142591
S29 S32 GLU TYR 0.000836506
S29 S32 PHE PHE 0.00116429
S29 S32 PHE HIS 0.00156831
S29 S32 PHE TRP 0.0142591
S29 S32 PHE TYR 0.000836506
S29 S32 GLY PHE 0.00116429
S29 S32 GLY HIS 0.00156831
S29 S32 GLY TRP 0.0142591
S29 S32 GLY TYR 0.000836506
S29 S32 HIS PHE 0.00116429
S29 S32 HIS HIS 0.00156831
S29 S32 HIS TRP 0.0142591
S29 S32 HIS TYR 0.000836506
S29 S32 ILE PHE 0.00116429
S29 S32 ILE HIS 0.00156831
S29 S32 ILE TRP 0.0142591
S29 S32 ILE TYR 0.000836506
S29 S32 LYS ALA 0.000417347
S29 S32 LYS CYS 0.000417347
S29 S32 LYS ASP 0.000417347
S29 S32 LYS GLU 0.000417347
S29 S32 LYS PHE 0.126155
S29 S32 LYS GLY 0.000417347
S29 S32 LYS HIS 0.0455387
S29 S32 LYS ILE 0.000417347
S29 S32 LYS LYS 0.000417347
S29 S32 LYS LEU 0.000417347
S29 S32 LYS MET 0.000417347
S29 S32 LYS ASN 0.000417347
S29 S32 LYS PRO 0.000417347
S29 S32 LYS GLN 0.000417347
S29 S32 LYS ARG 0.000417347
S29 S32 LYS SER 0.000417347
S29 S32 LYS THR 0.000417347
S29 S32 LYS VAL 0.000417347
S29 S32 LYS TRP -0.229276
S29 S32 LYS TYR 0.00614641
S29 S32 LYS --- 0.000417347
S29 S32 LEU ALA 8.35682e-05
S29 S32 LEU CYS 8.35682e-05
S29 S32 LEU ASP 8.35682e-05
S29 S32 LEU GLU 8.35682e-05
S29 S32 LEU PHE 0.0112597
S29 S32 LEU GLY 8.35682e-05
S29 S32 LEU HIS 0.0100959
S29 S32 LEU ILE 8.35682e-05
S29 S32 LEU LYS 8.35682e-05
S29 S32 LEU LEU 8.35682e-05
S29 S32 LEU MET 8.35682e-05
S29 S32 LEU ASN 8.35682e-05
S29 S32 LEU PRO 8.35682e-05
S29 S32 LEU GLN 8.35682e-05

S29 S32 LEU ARG 8.35682e-05
S29 S32 LEU SER 8.35682e-05
S29 S32 LEU THR 8.35682e-05
S29 S32 LEU VAL 8.35682e-05
S29 S32 LEU TRP -0.0972601
S29 S32 LEU TYR 0.0135972
S29 S32 LEU --- 8.35682e-05
S29 S32 MET PHE 0.00116429
S29 S32 MET HIS 0.00156831
S29 S32 MET TRP 0.0142591
S29 S32 MET TYR 0.000836506
S29 S32 ASN ALA 2.19418e-05
S29 S32 ASN CYS 2.19418e-05
S29 S32 ASN ASP 2.19418e-05
S29 S32 ASN GLU 2.19418e-05
S29 S32 ASN PHE 0.0160181
S29 S32 ASN GLY 2.19418e-05
S29 S32 ASN HIS 0.011983
S29 S32 ASN ILE 2.19418e-05
S29 S32 ASN LYS 2.19418e-05
S29 S32 ASN LEU 2.19418e-05
S29 S32 ASN MET 2.19418e-05
S29 S32 ASN ASN 2.19418e-05
S29 S32 ASN PRO 2.19418e-05
S29 S32 ASN GLN 2.19418e-05
S29 S32 ASN ARG 2.19418e-05
S29 S32 ASN SER 2.19418e-05
S29 S32 ASN THR 2.19418e-05
S29 S32 ASN VAL 2.19418e-05
S29 S32 ASN TRP -0.0962063
S29 S32 ASN TYR 0.00358617
S29 S32 ASN --- 2.19418e-05
S29 S32 PRO PHE 0.00116429
S29 S32 PRO HIS 0.00156831
S29 S32 PRO TRP 0.0142591
S29 S32 PRO TYR 0.000836506
S29 S32 GLN PHE 0.00116429
S29 S32 GLN HIS 0.00156831
S29 S32 GLN TRP 0.0142591
S29 S32 GLN TYR 0.000836506
S29 S32 ARG PHE 0.00116429
S29 S32 ARG HIS 0.00156831
S29 S32 ARG TRP 0.0142591
S29 S32 ARG TYR 0.000836506
S29 S32 SER ALA 0.0242876
S29 S32 SER CYS 0.0242876
S29 S32 SER ASP 0.0242876
S29 S32 SER GLU 0.0242876
S29 S32 SER PHE -0.170684
S29 S32 SER GLY 0.0242876
S29 S32 SER HIS -0.191301
S29 S32 SER ILE 0.0242876
S29 S32 SER LYS 0.0242876
S29 S32 SER LEU 0.0242876
S29 S32 SER MET 0.0242876
S29 S32 SER ASN 0.0242876
S29 S32 SER PRO 0.0242876
S29 S32 SER GLN 0.0242876
S29 S32 SER ARG 0.0242876
S29 S32 SER SER 0.0242876
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S29 S32 SER VAL 0.0242876
S29 S32 SER TRP -0.0724347

S29 S32 SER TYR -0.112074
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S29 S32 THR PHE 0.00116429
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S29 S32 THR TRP 0.0142591
S29 S32 THR TYR 0.000836506
S29 S32 VAL PHE 0.00116429
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S29 S32 VAL TRP 0.0142591
S29 S32 VAL TYR 0.000836506
S29 S32 TRP PHE 0.00116429
S29 S32 TRP HIS 0.00156831
S29 S32 TRP TRP 0.0142591
S29 S32 TRP TYR 0.000836506
S29 S32 TYR PHE 0.00116429
S29 S32 TYR HIS 0.00156831
S29 S32 TYR TRP 0.0142591
S29 S32 TYR TYR 0.000836506
S29 S32 --- PHE 0.00116429
S29 S32 --- HIS 0.00156831
S29 S32 --- TRP 0.0142591
S29 S32 --- TYR 0.000836506
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S29 S33 ALA LYS 0.000277289
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S29 S33 ALA VAL 0.00147938
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S29 S33 CYS LYS 0.000277289
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S29 S33 CYS VAL 0.00147938
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S29 S33 ASP LYS 0.000277289
S29 S33 ASP SER 0.00299903
S29 S33 ASP VAL 0.00147938
S29 S33 GLU ASP 0.0130725
S29 S33 GLU LYS 0.000277289
S29 S33 GLU SER 0.00299903
S29 S33 GLU VAL 0.00147938
S29 S33 PHE ASP 0.0130725
S29 S33 PHE LYS 0.000277289
S29 S33 PHE SER 0.00299903
S29 S33 PHE VAL 0.00147938
S29 S33 GLY ASP 0.0130725
S29 S33 GLY LYS 0.000277289
S29 S33 GLY SER 0.00299903
S29 S33 GLY VAL 0.00147938
S29 S33 HIS ASP 0.0130725
S29 S33 HIS LYS 0.000277289
S29 S33 HIS SER 0.00299903
S29 S33 HIS VAL 0.00147938
S29 S33 ILE ASP 0.0130725
S29 S33 ILE LYS 0.000277289
S29 S33 ILE SER 0.00299903
S29 S33 ILE VAL 0.00147938
S29 S33 LYS ALA 0.00140384
S29 S33 LYS CYS 0.00140384
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S29 S33 LYS GLU 0.00140384
S29 S33 LYS PHE 0.00140384
S29 S33 LYS GLY 0.00140384
S29 S33 LYS HIS 0.00140384
S29 S33 LYS ILE 0.00140384
S29 S33 LYS LYS 0.0506919

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S29 S33 LYS THR 0.00140384
S29 S33 LYS VAL 0.0707137
S29 S33 LYS TRP 0.00140384
S29 S33 LYS TYR 0.00140384
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S29 S33 LEU CYS 5.43316e-05
S29 S33 LEU ASP -0.102501
S29 S33 LEU GLU 5.43316e-05
S29 S33 LEU PHE 5.43316e-05
S29 S33 LEU GLY 5.43316e-05
S29 S33 LEU HIS 5.43316e-05
S29 S33 LEU ILE 5.43316e-05
S29 S33 LEU LYS 0.00335529
S29 S33 LEU LEU 5.43316e-05
S29 S33 LEU MET 5.43316e-05
S29 S33 LEU ASN 5.43316e-05
S29 S33 LEU PRO 5.43316e-05
S29 S33 LEU GLN 5.43316e-05
S29 S33 LEU ARG 5.43316e-05
S29 S33 LEU SER 0.0132143
S29 S33 LEU THR 5.43316e-05
S29 S33 LEU VAL 0.0241215
S29 S33 LEU TRP 5.43316e-05
S29 S33 LEU TYR 5.43316e-05
S29 S33 LEU --- 5.43316e-05
S29 S33 MET ASP 0.0130725
S29 S33 MET LYS 0.000277289
S29 S33 MET SER 0.00299903
S29 S33 MET VAL 0.00147938
S29 S33 ASN ALA 2.27175e-05
S29 S33 ASN CYS 2.27175e-05
S29 S33 ASN ASP -0.0975491
S29 S33 ASN GLU 2.27175e-05
S29 S33 ASN PHE 2.27175e-05
S29 S33 ASN GLY 2.27175e-05
S29 S33 ASN HIS 2.27175e-05
S29 S33 ASN ILE 2.27175e-05
S29 S33 ASN LYS 0.000914219
S29 S33 ASN LEU 2.27175e-05
S29 S33 ASN MET 2.27175e-05
S29 S33 ASN ASN 2.27175e-05
S29 S33 ASN PRO 2.27175e-05
S29 S33 ASN GLN 2.27175e-05
S29 S33 ASN ARG 2.27175e-05
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S29 S33 ASN THR 2.27175e-05
S29 S33 ASN VAL 0.00676714
S29 S33 ASN TRP 2.27175e-05
S29 S33 ASN TYR 2.27175e-05
S29 S33 ASN --- 2.27175e-05
S29 S33 PRO ASP 0.0130725
S29 S33 PRO LYS 0.000277289
S29 S33 PRO SER 0.00299903
S29 S33 PRO VAL 0.00147938
S29 S33 GLN ASP 0.0130725

S29 S33 GLN LYS 0.000277289
S29 S33 GLN SER 0.00299903
S29 S33 GLN VAL 0.00147938
S29 S33 ARG ASP 0.0130725
S29 S33 ARG LYS 0.000277289
S29 S33 ARG SER 0.00299903
S29 S33 ARG VAL 0.00147938
S29 S33 SER ALA 0.0230722
S29 S33 SER CYS 0.0230722
S29 S33 SER ASP -0.679516
S29 S33 SER GLU 0.0230722
S29 S33 SER PHE 0.0230722
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S29 S33 SER HIS 0.0230722
S29 S33 SER ILE 0.0230722
S29 S33 SER LYS -0.0828354
S29 S33 SER LEU 0.0230722
S29 S33 SER MET 0.0230722
S29 S33 SER ASN 0.0230722
S29 S33 SER PRO 0.0230722
S29 S33 SER GLN 0.0230722
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S29 S33 SER SER 0.391346
S29 S33 SER THR 0.0230722
S29 S33 SER VAL -0.154826
S29 S33 SER TRP 0.0230722
S29 S33 SER TYR 0.0230722
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S29 S33 THR ASP 0.0130725
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S29 S33 THR SER 0.00299903
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S29 S33 VAL LYS 0.000277289
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S29 S33 VAL VAL 0.00147938
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S29 S33 TRP LYS 0.000277289
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S29 S33 TYR LYS 0.000277289
S29 S33 TYR SER 0.00299903
S29 S33 TYR VAL 0.00147938
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S29 S34 ALA SER 0.0122343
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S29 S34 CYS GLU 0.00152863
S29 S34 CYS MET 0.00224563
S29 S34 CYS ARG 0.000696228
S29 S34 CYS SER 0.0122343
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S29 S34 ASP GLU 0.00152863
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S29 S34 ASP ARG 0.000696228
S29 S34 ASP SER 0.0122343
S29 S34 ASP THR 0.00112337

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S29 S34 HIS MET 0.00224563
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S29 S34 HIS SER 0.0122343
S29 S34 HIS THR 0.00112337
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S29 S34 ILE ARG 0.000696228
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S29 S34 LYS ALA 0.000252434
S29 S34 LYS CYS 0.000252434
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S29 S34 LYS GLU 0.0364345
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S29 S34 LYS GLY 0.000252434
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S29 S34 LYS GLN 0.000252434
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S29 S34 LYS THR 0.024044
S29 S34 LYS VAL 0.000252434
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S29 S34 LYS TYR 0.000252434
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S29 S34 LEU ALA 0.000387089
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S29 S34 LEU ASP 0.000387089
S29 S34 LEU GLU 0.0307274
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S29 S34 LEU HIS 0.000387089
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S29 S38 ILE ARG 0.00152777
S29 S38 LYS ALA 0.00108098
S29 S38 LYS CYS 0.00108098
S29 S38 LYS ASP 0.00108098
S29 S38 LYS GLU -0.465744
S29 S38 LYS PHE 0.00108098
S29 S38 LYS GLY 0.00108098
S29 S38 LYS HIS 0.0834567
S29 S38 LYS ILE 0.00108098
S29 S38 LYS LYS 0.1703
S29 S38 LYS LEU 0.0940765
S29 S38 LYS MET 0.00108098
S29 S38 LYS ASN 0.00108098
S29 S38 LYS PRO 0.00108098
S29 S38 LYS GLN 0.00108098
S29 S38 LYS ARG 0.0562735
S29 S38 LYS SER 0.00108098
S29 S38 LYS THR 0.00108098
S29 S38 LYS VAL 0.00108098
S29 S38 LYS TRP 0.00108098
S29 S38 LYS TYR 0.00108098
S29 S38 LYS --- 0.00108098
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S29 S38 LEU CYS 4.77823e-05
S29 S38 LEU ASP 4.77823e-05
S29 S38 LEU GLU 0.0399716
S29 S38 LEU PHE 4.77823e-05

S29 S38 LEU GLY 4.77823e-05
S29 S38 LEU HIS 0.0183586
S29 S38 LEU ILE 4.77823e-05
S29 S38 LEU LYS 0.0414865
S29 S38 LEU LEU -0.174241
S29 S38 LEU MET 4.77823e-05
S29 S38 LEU ASN 4.77823e-05
S29 S38 LEU PRO 4.77823e-05
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S29 S38 LEU THR 4.77823e-05
S29 S38 LEU VAL 4.77823e-05
S29 S38 LEU TRP 4.77823e-05
S29 S38 LEU TYR 4.77823e-05
S29 S38 LEU --- 4.77823e-05
S29 S38 MET GLU 0.00276752
S29 S38 MET HIS 0.00257302
S29 S38 MET LYS 0.00525436
S29 S38 MET LEU 0.00570551
S29 S38 MET ARG 0.00152777
S29 S38 ASN ALA 0.000958711
S29 S38 ASN CYS 0.000958711
S29 S38 ASN ASP 0.000958711
S29 S38 ASN GLU 0.055887
S29 S38 ASN PHE 0.000958711
S29 S38 ASN GLY 0.000958711
S29 S38 ASN HIS 0.0707913
S29 S38 ASN ILE 0.000958711
S29 S38 ASN LYS -0.499888
S29 S38 ASN LEU 0.231163
S29 S38 ASN MET 0.000958711
S29 S38 ASN ASN 0.000958711
S29 S38 ASN PRO 0.000958711
S29 S38 ASN GLN 0.000958711
S29 S38 ASN ARG 0.0624609
S29 S38 ASN SER 0.000958711
S29 S38 ASN THR 0.000958711
S29 S38 ASN VAL 0.000958711
S29 S38 ASN TRP 0.000958711
S29 S38 ASN TYR 0.000958711
S29 S38 ASN --- 0.000958711
S29 S38 PRO GLU 0.00276752
S29 S38 PRO HIS 0.00257302
S29 S38 PRO LYS 0.00525436
S29 S38 PRO LEU 0.00570551
S29 S38 PRO ARG 0.00152777
S29 S38 GLN GLU 0.00276752
S29 S38 GLN HIS 0.00257302
S29 S38 GLN LYS 0.00525436
S29 S38 GLN LEU 0.00570551
S29 S38 GLN ARG 0.00152777
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S29 S38 ARG HIS 0.00257302
S29 S38 ARG LYS 0.00525436
S29 S38 ARG LEU 0.00570551
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S29 S38 SER CYS 0.0291635
S29 S38 SER ASP 0.0291635
S29 S38 SER GLU 0.272992
S29 S38 SER PHE 0.0291635
S29 S38 SER GLY 0.0291635

S29 S38 SER HIS -0.342283
S29 S38 SER ILE 0.0291635
S29 S38 SER LYS 0.0128828
S29 S38 SER LEU -0.335201
S29 S38 SER MET 0.0291635
S29 S38 SER ASN 0.0291635
S29 S38 SER PRO 0.0291635
S29 S38 SER GLN 0.0291635
S29 S38 SER ARG -0.208611
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S29 S38 SER THR 0.0291635
S29 S38 SER VAL 0.0291635
S29 S38 SER TRP 0.0291635
S29 S38 SER TYR 0.0291635
S29 S38 SER --- 0.0291635
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S29 S38 THR HIS 0.00257302
S29 S38 THR LYS 0.00525436
S29 S38 THR LEU 0.00570551
S29 S38 THR ARG 0.00152777
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S29 S38 VAL LYS 0.00525436
S29 S38 VAL LEU 0.00570551
S29 S38 VAL ARG 0.00152777
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S29 S38 TYR LYS 0.00525436
S29 S38 TYR LEU 0.00570551
S29 S38 TYR ARG 0.00152777
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S29 S38 --- HIS 0.00257302
S29 S38 --- LYS 0.00525436
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S29 S39 ALA LEU 0.00115865
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S29 S39 CYS LEU 0.00115865
S29 S39 CYS VAL 0.0158517
S29 S39 CYS TRP 0.000150275
S29 S39 ASP ILE 0.000667596
S29 S39 ASP LEU 0.00115865
S29 S39 ASP VAL 0.0158517
S29 S39 ASP TRP 0.000150275
S29 S39 GLU ILE 0.000667596
S29 S39 GLU LEU 0.00115865
S29 S39 GLU VAL 0.0158517
S29 S39 GLU TRP 0.000150275
S29 S39 PHE ILE 0.000667596
S29 S39 PHE LEU 0.00115865
S29 S39 PHE VAL 0.0158517
S29 S39 PHE TRP 0.000150275
S29 S39 GLY ILE 0.000667596
S29 S39 GLY LEU 0.00115865
S29 S39 GLY VAL 0.0158517

S29 S39 GLY TRP 0.000150275
S29 S39 HIS ILE 0.000667596
S29 S39 HIS LEU 0.00115865
S29 S39 HIS VAL 0.0158517
S29 S39 HIS TRP 0.000150275
S29 S39 ILE ILE 0.000667596
S29 S39 ILE LEU 0.00115865
S29 S39 ILE VAL 0.0158517
S29 S39 ILE TRP 0.000150275
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S29 S39 LYS ASP 0.00102425
S29 S39 LYS GLU 0.00102425
S29 S39 LYS PHE 0.00102425
S29 S39 LYS GLY 0.00102425
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S29 S39 LYS ILE 0.100879
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S29 S39 LYS TYR 0.00102425
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S29 S39 ASN GLN 4.72143e-05
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S29 S39 ASN TRP 0.000971738
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S29 S39 --- LEU 0.00115865
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S29 S40 ASP LEU 0.00122096
S29 S40 ASP VAL 0.0158681
S29 S40 GLU ILE 0.000739086
S29 S40 GLU LEU 0.00122096
S29 S40 GLU VAL 0.0158681
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S29 S40 PHE LEU 0.00122096
S29 S40 PHE VAL 0.0158681
S29 S40 GLY ILE 0.000739086
S29 S40 GLY LEU 0.00122096
S29 S40 GLY VAL 0.0158681
S29 S40 HIS ILE 0.000739086
S29 S40 HIS LEU 0.00122096
S29 S40 HIS VAL 0.0158681
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S29 S40 SER LYS 0.0159388
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S29 S40 SER ASN 0.0159388
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S30 S31 SER MET 0.000322985
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S30 S32 ASP PHE 0.000332731
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S30 S32 ASP TRP 0.0101098
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S30 S32 TRP TYR 0.00166835
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S30 S32 TYR TRP 0.0101098
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S30 S32 --- TYR 0.00166835
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S30 S33 ALA VAL 0.00332099
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S30 S37 GLU ASP 0.00349333
S30 S37 GLU PHE 0.00168488
S30 S37 GLU ASN 0.000154359
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S30 S37 PHE PHE 0.00168488
S30 S37 PHE ASN 0.000154359
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S30 S37 PHE SER 0.00412911
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S30 S37 GLY SER 0.00412911
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S30 S37 HIS PHE 0.00168488
S30 S37 HIS ASN 0.000154359
S30 S37 HIS ARG 0.00264398
S30 S37 HIS SER 0.00412911
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S30 S38 CYS LYS 0.00123944
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S30 S38 GLU LYS 0.00123944
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S30 S38 PHE LEU 0.00702548
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S30 S38 GLY LYS 0.00123944
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S30 S38 HIS ARG 0.000962327
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S30 S38 ILE HIS 0.001746
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S30 S38 LYS LEU 0.00702548
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S31 S33 ALA SER 0.00281504
S31 S33 ALA VAL 0.00285273
S31 S33 CYS ASP 0.012831
S31 S33 CYS LYS 6.21882e-05
S31 S33 CYS SER 0.00281504
S31 S33 CYS VAL 0.00285273
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S31 S33 ASP CYS 0.000260033
S31 S33 ASP ASP -0.202647
S31 S33 ASP GLU 0.000260033
S31 S33 ASP PHE 0.000260033
S31 S33 ASP GLY 0.000260033
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S31 S33 PHE VAL 0.00285273
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S31 S33 GLY LYS 6.21882e-05
S31 S33 GLY SER 0.00281504

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S31 S33 ILE PHE 0.00281425
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S31 S34 ALA THR 0.0014481
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S31 S36 TRP GLU 0.00164419
S31 S36 TRP SER 0.0148477
S31 S36 TRP THR 0.000422978
S31 S36 TYR ASP 0.00164609
S31 S36 TYR GLU 0.00164419
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S31 S36 TYR THR 0.000422978
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S31 S36 --- SER 0.0148477
S31 S36 --- THR 0.000422978
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S31 S37 ALA PHE 0.00175617
S31 S37 ALA ASN 0.00109372

S31 S37 ALA ARG 0.00192516
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S31 S37 CYS PHE 0.00175617
S31 S37 CYS ASN 0.00109372
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S31 S37 ASP CYS 0.00125931
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S31 S37 GLU ASP 0.00859369
S31 S37 GLU PHE 0.00175617
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S31 S37 GLU ARG 0.00192516
S31 S37 GLU SER 0.00487191
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S31 S37 PHE ASP 0.00859369
S31 S37 PHE PHE 0.00175617
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S31 S37 PHE ARG 0.00192516
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S31 S37 HIS PHE 0.00175617
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S31 S37 HIS SER 0.00487191
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S31 S37 ILE GLU 0.00386218
S31 S37 ILE PHE 0.129924
S31 S37 ILE GLY 0.00386218
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S31 S37 ILE LYS 0.00386218
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S31 S37 LYS PHE 0.00175617
S31 S37 LYS ASN 0.00109372
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S31 S37 LEU SER 0.00487191
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S31 S38 ALA HIS 0.00546439
S31 S38 ALA LYS 0.00204787
S31 S38 ALA LEU 0.00739219
S31 S38 ALA ARG 0.00145403
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S31 S38 CYS HIS 0.00546439
S31 S38 CYS LYS 0.00204787
S31 S38 CYS LEU 0.00739219
S31 S38 CYS ARG 0.00145403
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S31 S38 ASP CYS 0.000953372
S31 S38 ASP ASP 0.000953372
S31 S38 ASP GLU 0.0794664
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S31 S38 GLU LYS 0.00204787
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S31 S38 PHE LYS 0.00204787
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S31 S38 HIS GLU 0.00220248
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S31 S38 HIS LYS 0.00204787
S31 S38 HIS LEU 0.00739219
S31 S38 HIS ARG 0.00145403
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S31 S38 ILE CYS 0.00339974
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S31 S38 PRO LYS 0.00204787
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S31 S38 VAL VAL 0.0268979
S31 S38 VAL TRP 0.0268979
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S31 S38 VAL --- 0.0268979
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S31 S38 TYR LYS 0.00204787
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S31 S38 TYR ARG 0.00145403

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S31 S38 --- LYS 0.00204787
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S31 S39 ASP CYS 0.000705097
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S31 S39 ASP LYS 0.000705097
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S31 S40 ALA VAL 0.0159681
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S31 S40 GLN VAL 0.0159681
S31 S40 ARG ILE 0.00214664
S31 S40 ARG LEU 0.000446232
S31 S40 ARG VAL 0.0159681
S31 S40 SER ILE 0.00214664
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S31 S40 THR LEU 0.000446232
S31 S40 THR VAL 0.0159681
S31 S40 VAL ALA 0.0140164
S31 S40 VAL CYS 0.0140164
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S31 S40 VAL GLU 0.0140164
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S31 S40 VAL GLY 0.0140164
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S31 S40 VAL ILE -0.416357
S31 S40 VAL LYS 0.0140164
S31 S40 VAL LEU -0.109557
S31 S40 VAL MET 0.0140164
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S31 S40 VAL THR 0.0140164
S31 S40 VAL VAL 0.101292
S31 S40 VAL TRP 0.0140164
S31 S40 VAL TYR 0.0140164
S31 S40 VAL --- 0.0140164
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S31 S40 TRP LEU 0.000446232
S31 S40 TRP VAL 0.0159681
S31 S40 TYR ILE 0.00214664

S31 S40 TYR LEU 0.000446232
S31 S40 TYR VAL 0.0159681
S31 S40 --- ILE 0.00214664
S31 S40 --- LEU 0.000446232
S31 S40 --- VAL 0.0159681
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S32 S33 ALA LYS 8.71185e-05
S32 S33 ALA SER 0.00407712
S32 S33 ALA VAL 0.00477177
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S32 S33 CYS LYS 8.71185e-05
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S32 S33 CYS VAL 0.00477177
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S32 S33 ASP LYS 8.71185e-05
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S32 S33 ASP VAL 0.00477177
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S32 S33 GLU LYS 8.71185e-05
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S32 S33 GLU VAL 0.00477177
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S32 S33 PHE GLU 0.00124036
S32 S33 PHE PHE 0.00124036
S32 S33 PHE GLY 0.00124036
S32 S33 PHE HIS 0.00124036
S32 S33 PHE ILE 0.00124036
S32 S33 PHE LYS 0.0149455
S32 S33 PHE LEU 0.00124036
S32 S33 PHE MET 0.00124036
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S32 S33 PHE ARG 0.00124036
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S32 S33 PHE THR 0.00124036
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S32 S33 PHE --- 0.00124036
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S32 S33 GLY LYS 8.71185e-05
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S32 S33 GLY VAL 0.00477177
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S32 S33 HIS CYS 0.00213708
S32 S33 HIS ASP -0.11249
S32 S33 HIS GLU 0.00213708
S32 S33 HIS PHE 0.00213708
S32 S33 HIS GLY 0.00213708
S32 S33 HIS HIS 0.00213708
S32 S33 HIS ILE 0.00213708
S32 S33 HIS LYS 0.0262558
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S32 S33 HIS ASN 0.00213708
S32 S33 HIS PRO 0.00213708
S32 S33 HIS GLN 0.00213708
S32 S33 HIS ARG 0.00213708
S32 S33 HIS SER -0.27896
S32 S33 HIS THR 0.00213708

S32 S33 HIS VAL 0.231841
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S32 S33 HIS TYR 0.00213708
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S32 S33 ILE SER 0.00407712
S32 S33 ILE VAL 0.00477177
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S32 S33 LYS LYS 8.71185e-05
S32 S33 LYS SER 0.00407712
S32 S33 LYS VAL 0.00477177
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S32 S33 LEU SER 0.00407712
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S32 S33 PRO LYS 8.71185e-05
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S32 S33 PRO VAL 0.00477177
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S32 S33 GLN LYS 8.71185e-05
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S32 S33 ARG LYS 8.71185e-05
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S32 S33 THR ASP 0.0158744
S32 S33 THR LYS 8.71185e-05
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S32 S33 VAL ASP 0.0158744
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S32 S33 TRP GLU 0.0188564
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S32 S33 TRP GLY 0.0188564
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S32 S33 TRP ILE 0.0188564
S32 S33 TRP LYS -0.0867532
S32 S33 TRP LEU 0.0188564
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S32 S33 TRP ASN 0.0188564
S32 S33 TRP PRO 0.0188564
S32 S33 TRP GLN 0.0188564
S32 S33 TRP ARG 0.0188564

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S32 S33 TRP THR 0.0188564
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S32 S33 TRP TRP 0.0188564
S32 S33 TRP TYR 0.0188564
S32 S33 TRP --- 0.0188564
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S32 S33 TYR CYS 0.00231923
S32 S33 TYR ASP -0.356743
S32 S33 TYR GLU 0.00231923
S32 S33 TYR PHE 0.00231923
S32 S33 TYR GLY 0.00231923
S32 S33 TYR HIS 0.00231923
S32 S33 TYR ILE 0.00231923
S32 S33 TYR LYS 0.0209109
S32 S33 TYR LEU 0.00231923
S32 S33 TYR MET 0.00231923
S32 S33 TYR ASN 0.00231923
S32 S33 TYR PRO 0.00231923
S32 S33 TYR GLN 0.00231923
S32 S33 TYR ARG 0.00231923
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S32 S33 TYR VAL -0.170228
S32 S33 TYR TRP 0.00231923
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S32 S33 TYR --- 0.00231923
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S32 S34 ALA THR 0.00292074
S32 S34 CYS GLU 0.00025344
S32 S34 CYS MET 0.000505105
S32 S34 CYS ARG 2.19418e-05
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S32 S34 PHE GLU 0.0988719
S32 S34 PHE PHE 0.00264358
S32 S34 PHE GLY 0.00264358
S32 S34 PHE HIS 0.00264358
S32 S34 PHE ILE 0.00264358
S32 S34 PHE LYS 0.00264358
S32 S34 PHE LEU 0.00264358
S32 S34 PHE MET 0.17657
S32 S34 PHE ASN 0.00264358

S32 S34 PHE PRO 0.00264358
S32 S34 PHE GLN 0.00264358
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S32 S34 PHE THR -0.501226
S32 S34 PHE VAL 0.00264358
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S32 S34 PHE TYR 0.00264358
S32 S34 PHE --- 0.00264358
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S32 S34 HIS ALA 0.000835027
S32 S34 HIS CYS 0.000835027
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S32 S34 HIS GLY 0.000835027
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S32 S34 TYR GLN 0.00238095
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S32 S34 TYR --- 0.00238095
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S32 S34 --- MET 0.000505105
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S32 S35 CYS THR 0.00336061
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S32 S35 ASP THR 0.00336061
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S32 S35 PHE TYR 0.000618872
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S32 S35 LEU THR 0.00336061
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S32 S36 PHE TYR 0.00201534
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S32 S36 HIS CYS 0.00287563

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S32 S36 HIS LYS 0.00287563
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S32 S36 SER THR 0.00118898
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S32 S36 VAL THR 0.00118898

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S32 S36 TRP HIS 0.0180461
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S32 S36 TYR CYS 0.0012218
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S32 S37 HIS PRO 0.00274194
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S32 S37 HIS --- 0.00274194
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S32 S37 LYS ASP 0.00675293

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S32 S37 ASN PHE 0.000803688
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S32 S37 ASN ARG 0.00294235
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S32 S37 TYR GLU 0.00182078
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S32 S37 TYR --- 0.00182078
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S32 S38 ALA LYS 0.00358339
S32 S38 ALA LEU 0.0100425
S32 S38 ALA ARG 0.00258985
S32 S38 CYS GLU 0.0010859
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S32 S38 CYS LYS 0.00358339
S32 S38 CYS LEU 0.0100425
S32 S38 CYS ARG 0.00258985
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S32 S38 GLU LYS 0.00358339
S32 S38 GLU LEU 0.0100425
S32 S38 GLU ARG 0.00258985

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S32 S38 HIS LEU -0.138104
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S32 S38 LYS LYS 0.00358339
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S32 S38 LYS ARG 0.00258985
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S32 S38 LEU ARG 0.00258985
S32 S38 MET GLU 0.0010859

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S32 S38 MET LEU 0.0100425
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S32 S38 ASN LYS 0.00358339
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S32 S38 PRO LYS 0.00358339
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S32 S38 TYR --- 0.00336912
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S32 S39 TYR PHE 0.00200643
S32 S39 TYR GLY 0.00200643
S32 S39 TYR HIS 0.00200643
S32 S39 TYR ILE 0.195559
S32 S39 TYR LYS 0.00200643
S32 S39 TYR LEU 0.0312104
S32 S39 TYR MET 0.00200643
S32 S39 TYR ASN 0.00200643
S32 S39 TYR PRO 0.00200643
S32 S39 TYR GLN 0.00200643
S32 S39 TYR ARG 0.00200643
S32 S39 TYR SER 0.00200643
S32 S39 TYR THR 0.00200643
S32 S39 TYR VAL -0.396725
S32 S39 TYR TRP 0.0613225
S32 S39 TYR TYR 0.00200643
S32 S39 TYR --- 0.00200643
S32 S39 --- ILE 0.00314496
S32 S39 --- LEU 0.00148835
S32 S39 --- VAL 0.0192723
S32 S39 --- TRP 0.000904842
S32 S40 ALA ILE 0.00288968
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S32 S40 ALA VAL 0.0218583
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S32 S40 CYS VAL 0.0218583
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S32 S40 GLU VAL 0.0218583
S32 S40 PHE ALA 0.000339646
S32 S40 PHE CYS 0.000339646

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S32 S40 PHE PHE 0.000339646
S32 S40 PHE GLY 0.000339646
S32 S40 PHE HIS 0.000339646
S32 S40 PHE ILE 0.140661
S32 S40 PHE LYS 0.000339646
S32 S40 PHE LEU 0.00485218
S32 S40 PHE MET 0.000339646
S32 S40 PHE ASN 0.000339646
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S32 S40 PHE THR 0.000339646
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S32 S40 PHE TRP 0.000339646
S32 S40 PHE TYR 0.000339646
S32 S40 PHE --- 0.000339646
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S32 S40 HIS CYS 0.0011965
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S32 S40 HIS --- 0.0011965
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S32 S40 TRP PHE 0.012577
S32 S40 TRP GLY 0.012577
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S32 S40 TRP LYS 0.012577
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S32 S40 TYR LEU 0.014427
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S32 S40 TYR TYR 0.00229599
S32 S40 TYR --- 0.00229599
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S33 S34 ALA THR 0.00151482

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S33 S34 CYS THR 0.00151482
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S33 S34 ASP ASP 0.0209679
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S33 S34 ASP GLY 0.0209679
S33 S34 ASP HIS 0.0209679
S33 S34 ASP ILE 0.0209679
S33 S34 ASP LYS 0.0209679
S33 S34 ASP LEU 0.0209679
S33 S34 ASP MET -0.316945
S33 S34 ASP ASN 0.0209679
S33 S34 ASP PRO 0.0209679
S33 S34 ASP GLN 0.0209679
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S33 S34 ASP THR 0.017221
S33 S34 ASP VAL 0.0209679
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S33 S34 ASP TYR 0.0209679
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S33 S34 PHE GLU 0.00148688
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S33 S34 PHE THR 0.00151482
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S33 S34 HIS GLU 0.00148688
S33 S34 HIS MET 0.000460829
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S33 S34 HIS THR 0.00151482
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S33 S34 LYS CYS 8.38225e-05
S33 S34 LYS ASP 8.38225e-05
S33 S34 LYS GLU 0.0463784
S33 S34 LYS PHE 8.38225e-05
S33 S34 LYS GLY 8.38225e-05
S33 S34 LYS HIS 8.38225e-05
S33 S34 LYS ILE 8.38225e-05
S33 S34 LYS LYS 8.38225e-05
S33 S34 LYS LEU 8.38225e-05
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S33 S34 LYS PRO 8.38225e-05
S33 S34 LYS GLN 8.38225e-05
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S33 S34 LYS THR 0.0103652
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S33 S34 LEU THR 0.00151482
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S33 S35 PHE THR 0.00384921
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S33 S35 GLY THR 0.00384921
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S33 S35 HIS SER 0.0146198
S33 S35 HIS THR 0.00384921
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S33 S35 LYS GLU 7.44572e-05
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S33 S35 LYS ILE 7.44572e-05
S33 S35 LYS LYS 7.44572e-05
S33 S35 LYS LEU 7.44572e-05
S33 S35 LYS MET 7.44572e-05
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S33 S36 ASP ALA 0.0178362
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S33 S40 ASP SER 0.00871752
S33 S40 ASP THR 0.00871752
S33 S40 ASP VAL -0.180505
S33 S40 ASP TRP 0.00871752
S33 S40 ASP TYR 0.00871752
S33 S40 ASP --- 0.00871752
S33 S40 GLU ILE 0.00258297
S33 S40 GLU LEU 0.00103178
S33 S40 GLU VAL 0.0209383
S33 S40 PHE ILE 0.00258297
S33 S40 PHE LEU 0.00103178
S33 S40 PHE VAL 0.0209383
S33 S40 GLY ILE 0.00258297
S33 S40 GLY LEU 0.00103178
S33 S40 GLY VAL 0.0209383
S33 S40 HIS ILE 0.00258297
S33 S40 HIS LEU 0.00103178
S33 S40 HIS VAL 0.0209383
S33 S40 ILE ILE 0.00258297
S33 S40 ILE LEU 0.00103178
S33 S40 ILE VAL 0.0209383
S33 S40 LYS ALA 6.83679e-05
S33 S40 LYS CYS 6.83679e-05
S33 S40 LYS ASP 6.83679e-05
S33 S40 LYS GLU 6.83679e-05
S33 S40 LYS PHE 6.83679e-05
S33 S40 LYS GLY 6.83679e-05
S33 S40 LYS HIS 6.83679e-05
S33 S40 LYS ILE 0.00750251

S33 S40 LYS LYS 6.83679e-05
S33 S40 LYS LEU 0.0158132
S33 S40 LYS MET 6.83679e-05
S33 S40 LYS ASN 6.83679e-05
S33 S40 LYS PRO 6.83679e-05
S33 S40 LYS GLN 6.83679e-05
S33 S40 LYS ARG 6.83679e-05
S33 S40 LYS SER 6.83679e-05
S33 S40 LYS THR 6.83679e-05
S33 S40 LYS VAL -0.0477065
S33 S40 LYS TRP 6.83679e-05
S33 S40 LYS TYR 6.83679e-05
S33 S40 LYS --- 6.83679e-05
S33 S40 LEU ILE 0.00258297
S33 S40 LEU LEU 0.00103178
S33 S40 LEU VAL 0.0209383
S33 S40 MET ILE 0.00258297
S33 S40 MET LEU 0.00103178
S33 S40 MET VAL 0.0209383
S33 S40 ASN ILE 0.00258297
S33 S40 ASN LEU 0.00103178
S33 S40 ASN VAL 0.0209383
S33 S40 PRO ILE 0.00258297
S33 S40 PRO LEU 0.00103178
S33 S40 PRO VAL 0.0209383
S33 S40 GLN ILE 0.00258297
S33 S40 GLN LEU 0.00103178
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S33 S40 ARG LEU 0.00103178
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S33 S40 SER CYS 0.00420511
S33 S40 SER ASP 0.00420511
S33 S40 SER GLU 0.00420511
S33 S40 SER PHE 0.00420511
S33 S40 SER GLY 0.00420511
S33 S40 SER HIS 0.00420511
S33 S40 SER ILE -0.01029
S33 S40 SER LYS 0.00420511
S33 S40 SER LEU 0.0692351
S33 S40 SER MET 0.00420511
S33 S40 SER ASN 0.00420511
S33 S40 SER PRO 0.00420511
S33 S40 SER GLN 0.00420511
S33 S40 SER ARG 0.00420511
S33 S40 SER SER 0.00420511
S33 S40 SER THR 0.00420511
S33 S40 SER VAL -0.247072
S33 S40 SER TRP 0.00420511
S33 S40 SER TYR 0.00420511
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S33 S40 THR LEU 0.00103178
S33 S40 THR VAL 0.0209383
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S33 S40 VAL CYS 0.00341811
S33 S40 VAL ASP 0.00341811
S33 S40 VAL GLU 0.00341811
S33 S40 VAL PHE 0.00341811
S33 S40 VAL GLY 0.00341811
S33 S40 VAL HIS 0.00341811
S33 S40 VAL ILE -0.155944

S33 S40 VAL LYS 0.00341811
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S33 S40 VAL MET 0.00341811
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S33 S40 VAL SER 0.00341811
S33 S40 VAL THR 0.00341811
S33 S40 VAL VAL -0.0489907
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S33 S40 VAL --- 0.00341811
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S33 S40 TRP VAL 0.0209383
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S34 S35 CYS THR 0.00188071
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S34 S35 ASP THR 0.00188071
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S34 S35 GLU ASP 0.000800004
S34 S35 GLU GLU 0.000800004
S34 S35 GLU PHE 0.000800004
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S34 S35 GLU ILE 0.000800004
S34 S35 GLU LYS 0.000800004
S34 S35 GLU LEU 0.000800004
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S34 S35 GLU THR 0.0524479
S34 S35 GLU VAL 0.000800004
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S34 S35 GLU TYR 0.000800004
S34 S35 GLU --- 0.000800004
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S34 S35 PHE SER 0.0173909
S34 S35 PHE THR 0.00188071
S34 S35 GLY ALA 0.00544142
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S34 S35 GLY THR 0.00188071
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S34 S35 HIS SER 0.0173909
S34 S35 HIS THR 0.00188071
S34 S35 ILE ALA 0.00544142
S34 S35 ILE SER 0.0173909

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S34 S35 LYS SER 0.0173909
S34 S35 LYS THR 0.00188071
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S34 S35 LEU THR 0.00188071
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S34 S35 MET CYS 0.00162143
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S34 S35 MET ILE 0.00162143
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S34 S35 MET LEU 0.00162143
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S34 S35 MET SER -0.334725
S34 S35 MET THR -0.342246
S34 S35 MET VAL 0.00162143
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S34 S35 MET TYR 0.00162143
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S34 S35 SER THR -0.118062
S34 S35 SER VAL 0.0169977
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S34 S35 SER TYR 0.0169977
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S34 S36 CYS THR 0.00070052
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S34 S36 ASP THR 0.00070052
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S34 S36 GLU CYS 0.000612101

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S34 S36 GLU LYS 0.000612101
S34 S36 GLU LEU 0.000612101
S34 S36 GLU MET 0.000612101
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S34 S36 GLU ARG 0.000612101
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S34 S36 HIS THR 0.00070052
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S34 S36 LYS THR 0.00070052
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S34 S36 MET GLU 0.218111
S34 S36 MET PHE 0.00200758
S34 S36 MET GLY 0.00200758
S34 S36 MET HIS 0.00200758
S34 S36 MET ILE 0.00200758
S34 S36 MET LYS 0.00200758
S34 S36 MET LEU 0.00200758
S34 S36 MET MET 0.00200758
S34 S36 MET ASN 0.00200758
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S34 S36 MET GLN 0.00200758
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S34 S36 MET THR 0.140293
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S34 S36 MET TYR 0.00200758

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S34 S36 PRO GLU 0.00284042
S34 S36 PRO SER 0.0166103
S34 S36 PRO THR 0.00070052
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S34 S36 ARG TYR 0.000772248
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S34 S37 VAL ASN 0.000192683
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S34 S40 LEU VAL 0.0212134
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S35 S36 ALA ILE 0.00278017
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S35 S36 ALA TRP 0.00278017

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S35 S36 HIS THR 0.00138019
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S35 S39 SER TYR 0.012602
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S35 S39 THR ALA 0.00379699
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S35 S39 THR ILE 0.202233
S35 S39 THR LYS 0.00379699
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S35 S39 THR MET 0.00379699
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S35 S39 THR TRP 0.296544
S35 S39 THR TYR 0.00379699
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S35 S39 VAL LEU 0.000479899
S35 S39 VAL VAL 0.0193729
S35 S39 VAL TRP 0.000239345
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S35 S39 TRP VAL 0.0193729
S35 S39 TRP TRP 0.000239345

S35 S39 TYR ILE 0.00154136
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S35 S39 TYR VAL 0.0193729
S35 S39 TYR TRP 0.000239345
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S35 S39 --- LEU 0.000479899
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S35 S40 ALA PHE 0.00303747
S35 S40 ALA GLY 0.00303747
S35 S40 ALA HIS 0.00303747
S35 S40 ALA ILE -0.385191
S35 S40 ALA LYS 0.00303747
S35 S40 ALA LEU 0.0568452
S35 S40 ALA MET 0.00303747
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S35 S40 ALA GLN 0.00303747
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S35 S40 ALA THR 0.00303747
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S35 S40 ALA TRP 0.00303747
S35 S40 ALA TYR 0.00303747
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S35 S40 PHE ILE 0.00263033
S35 S40 PHE LEU 0.000144431
S35 S40 PHE VAL 0.0188588
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S35 S40 GLY VAL 0.0188588
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S35 S40 ILE ILE 0.00263033
S35 S40 ILE LEU 0.000144431
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S35 S40 TYR LEU 0.000144431
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S36 S37 CYS PHE 0.00144645
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S36 S37 CYS SER 0.0115239
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S36 S37 ASP CYS 0.00374945
S36 S37 ASP ASP 0.277182
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S36 S37 SER ILE 0.0184763
S36 S37 SER LYS 0.0184763
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S36 S38 ALA LYS 0.00524095
S36 S38 ALA LEU 0.00616286

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S36 S38 SER TYR 0.0200328
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S36 S39 CYS VAL 0.0201484
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S36 S39 ASP ASP 0.00291058
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S36 S39 ASP LYS 0.00291058
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S36 S39 GLU TYR 0.00466812
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S36 S39 PHE ILE 0.00249507
S36 S39 PHE LEU 0.00121739
S36 S39 PHE VAL 0.0201484
S36 S39 PHE TRP 0.000297924
S36 S39 GLY ILE 0.00249507
S36 S39 GLY LEU 0.00121739
S36 S39 GLY VAL 0.0201484
S36 S39 GLY TRP 0.000297924
S36 S39 HIS ILE 0.00249507
S36 S39 HIS LEU 0.00121739
S36 S39 HIS VAL 0.0201484
S36 S39 HIS TRP 0.000297924
S36 S39 ILE ILE 0.00249507
S36 S39 ILE LEU 0.00121739
S36 S39 ILE VAL 0.0201484
S36 S39 ILE TRP 0.000297924
S36 S39 LYS ILE 0.00249507
S36 S39 LYS LEU 0.00121739
S36 S39 LYS VAL 0.0201484
S36 S39 LYS TRP 0.000297924
S36 S39 LEU ILE 0.00249507
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S36 S39 LEU TRP 0.000297924
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S36 S39 MET VAL 0.0201484
S36 S39 MET TRP 0.000297924
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S36 S39 ASN VAL 0.0201484
S36 S39 ASN TRP 0.000297924
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S36 S39 PRO LEU 0.00121739
S36 S39 PRO VAL 0.0201484
S36 S39 PRO TRP 0.000297924
S36 S39 GLN ILE 0.00249507

S36 S39 GLN LEU 0.00121739
S36 S39 GLN VAL 0.0201484
S36 S39 GLN TRP 0.000297924
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S36 S39 SER ASP 0.00981551
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S36 S39 SER PHE 0.00981551
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S36 S39 SER HIS 0.00981551
S36 S39 SER ILE 0.230191
S36 S39 SER LYS 0.00981551
S36 S39 SER LEU 0.195522
S36 S39 SER MET 0.00981551
S36 S39 SER ASN 0.00981551
S36 S39 SER PRO 0.00981551
S36 S39 SER GLN 0.00981551
S36 S39 SER ARG 0.00981551
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S36 S39 SER VAL -0.61976
S36 S39 SER TRP -0.21815
S36 S39 SER TYR 0.00981551
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S36 S39 THR CYS 0.00134406
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S36 S39 THR GLY 0.00134406
S36 S39 THR HIS 0.00134406
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S36 S39 THR LYS 0.00134406
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S36 S39 VAL VAL 0.0201484
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S36 S39 TRP ILE 0.00249507
S36 S39 TRP LEU 0.00121739
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S36 S39 --- LEU 0.00121739

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S36 S40 ALA VAL 0.0212875
S36 S40 CYS ILE 0.00216727
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S36 S40 CYS VAL 0.0212875
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S36 S40 ASP CYS 0.00185258
S36 S40 ASP ASP 0.00185258
S36 S40 ASP GLU 0.00185258
S36 S40 ASP PHE 0.00185258
S36 S40 ASP GLY 0.00185258
S36 S40 ASP HIS 0.00185258
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S36 S40 ASP LYS 0.00185258
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S36 S40 ASP MET 0.00185258
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S36 S40 GLU PHE 0.00320656
S36 S40 GLU GLY 0.00320656
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S36 S40 GLU LYS 0.00320656
S36 S40 GLU LEU 0.098108
S36 S40 GLU MET 0.00320656
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S36 S40 GLU PRO 0.00320656
S36 S40 GLU GLN 0.00320656
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S36 S40 GLU VAL 0.499213
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S36 S40 GLU TYR 0.00320656
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S36 S40 GLY LEU 0.00070402
S36 S40 GLY VAL 0.0212875
S36 S40 HIS ILE 0.00216727
S36 S40 HIS LEU 0.00070402
S36 S40 HIS VAL 0.0212875
S36 S40 ILE ILE 0.00216727
S36 S40 ILE LEU 0.00070402
S36 S40 ILE VAL 0.0212875
S36 S40 LYS ILE 0.00216727

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S36 S40 THR LYS 0.00187114
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S37 S38 ALA PHE 0.00116016
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S37 S38 ALA LYS -0.354331
S37 S38 ALA LEU -0.166461
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S37 S38 CYS ARG 0.00303697
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S37 S38 GLU LYS 0.00524598
S37 S38 GLU LEU 0.0101926
S37 S38 GLU ARG 0.00303697

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S37 S38 HIS LYS 0.00524598
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S37 S38 PRO LYS 0.00524598
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S37 S39 ARG GLU 0.00130728
S37 S39 ARG PHE 0.00130728
S37 S39 ARG GLY 0.00130728
S37 S39 ARG HIS 0.00130728
S37 S39 ARG ILE 0.0368286
S37 S39 ARG LYS 0.00130728
S37 S39 ARG LEU 0.030119
S37 S39 ARG MET 0.00130728
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S37 S39 ARG GLN 0.00130728
S37 S39 ARG ARG 0.00130728
S37 S39 ARG SER 0.00130728
S37 S39 ARG THR 0.00130728
S37 S39 ARG VAL -0.16696
S37 S39 ARG TRP 0.0161013
S37 S39 ARG TYR 0.00130728
S37 S39 ARG --- 0.00130728
S37 S39 SER ALA 0.0101094
S37 S39 SER CYS 0.0101094
S37 S39 SER ASP 0.0101094
S37 S39 SER GLU 0.0101094
S37 S39 SER PHE 0.0101094
S37 S39 SER GLY 0.0101094
S37 S39 SER HIS 0.0101094
S37 S39 SER ILE -0.425786
S37 S39 SER LYS 0.0101094
S37 S39 SER LEU -0.22598
S37 S39 SER MET 0.0101094
S37 S39 SER ASN 0.0101094
S37 S39 SER PRO 0.0101094
S37 S39 SER GLN 0.0101094
S37 S39 SER ARG 0.0101094
S37 S39 SER SER 0.0101094
S37 S39 SER THR 0.0101094
S37 S39 SER VAL 0.5135
S37 S39 SER TRP -0.240531
S37 S39 SER TYR 0.0101094
S37 S39 SER --- 0.0101094

S37 S39 THR ILE 0.00154255
S37 S39 THR LEU 0.00136533
S37 S39 THR VAL 0.025529
S37 S39 THR TRP 0.000634693
S37 S39 VAL ILE 0.00154255
S37 S39 VAL LEU 0.00136533
S37 S39 VAL VAL 0.025529
S37 S39 VAL TRP 0.000634693
S37 S39 TRP ILE 0.00154255
S37 S39 TRP LEU 0.00136533
S37 S39 TRP VAL 0.025529
S37 S39 TRP TRP 0.000634693
S37 S39 TYR ILE 0.00154255
S37 S39 TYR LEU 0.00136533
S37 S39 TYR VAL 0.025529
S37 S39 TYR TRP 0.000634693
S37 S39 --- ILE 0.00154255
S37 S39 --- LEU 0.00136533
S37 S39 --- VAL 0.025529
S37 S39 --- TRP 0.000634693
S37 S40 ALA ALA 0.00173585
S37 S40 ALA CYS 0.00173585
S37 S40 ALA ASP 0.00173585
S37 S40 ALA GLU 0.00173585
S37 S40 ALA PHE 0.00173585
S37 S40 ALA GLY 0.00173585
S37 S40 ALA HIS 0.00173585
S37 S40 ALA ILE 0.23324
S37 S40 ALA LYS 0.00173585
S37 S40 ALA LEU 0.0168399
S37 S40 ALA MET 0.00173585
S37 S40 ALA ASN 0.00173585
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S37 S40 ALA GLN 0.00173585
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S37 S40 ALA SER 0.00173585
S37 S40 ALA THR 0.00173585
S37 S40 ALA VAL -0.330917
S37 S40 ALA TRP 0.00173585
S37 S40 ALA TYR 0.00173585
S37 S40 ALA --- 0.00173585
S37 S40 CYS ILE 0.0031677
S37 S40 CYS LEU 0.000267708
S37 S40 CYS VAL 0.0256362
S37 S40 ASP ALA 0.00680942
S37 S40 ASP CYS 0.00680942
S37 S40 ASP ASP 0.00680942
S37 S40 ASP GLU 0.00680942
S37 S40 ASP PHE 0.00680942
S37 S40 ASP GLY 0.00680942
S37 S40 ASP HIS 0.00680942
S37 S40 ASP ILE -0.767513
S37 S40 ASP LYS 0.00680942
S37 S40 ASP LEU 0.06041
S37 S40 ASP MET 0.00680942
S37 S40 ASP ASN 0.00680942
S37 S40 ASP PRO 0.00680942
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S37 S40 ASP SER 0.00680942
S37 S40 ASP THR 0.00680942
S37 S40 ASP VAL 0.537121
S37 S40 ASP TRP 0.00680942

S37 S40 ASP TYR 0.00680942
S37 S40 ASP --- 0.00680942
S37 S40 GLU ILE 0.0031677
S37 S40 GLU LEU 0.000267708
S37 S40 GLU VAL 0.0256362
S37 S40 PHE ALA 0.00140557
S37 S40 PHE CYS 0.00140557
S37 S40 PHE ASP 0.00140557
S37 S40 PHE GLU 0.00140557
S37 S40 PHE PHE 0.00140557
S37 S40 PHE GLY 0.00140557
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S37 S40 PHE ILE 0.0105066
S37 S40 PHE LYS 0.00140557
S37 S40 PHE LEU -0.299593
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S37 S40 PHE ASN 0.00140557
S37 S40 PHE PRO 0.00140557
S37 S40 PHE GLN 0.00140557
S37 S40 PHE ARG 0.00140557
S37 S40 PHE SER 0.00140557
S37 S40 PHE THR 0.00140557
S37 S40 PHE VAL 0.216641
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S37 S40 PHE TYR 0.00140557
S37 S40 PHE --- 0.00140557
S37 S40 GLY ILE 0.0031677
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S37 S40 GLY VAL 0.0256362
S37 S40 HIS ILE 0.0031677
S37 S40 HIS LEU 0.000267708
S37 S40 HIS VAL 0.0256362
S37 S40 ILE ILE 0.0031677
S37 S40 ILE LEU 0.000267708
S37 S40 ILE VAL 0.0256362
S37 S40 LYS ILE 0.0031677
S37 S40 LYS LEU 0.000267708
S37 S40 LYS VAL 0.0256362
S37 S40 LEU ILE 0.0031677
S37 S40 LEU LEU 0.000267708
S37 S40 LEU VAL 0.0256362
S37 S40 MET ILE 0.0031677
S37 S40 MET LEU 0.000267708
S37 S40 MET VAL 0.0256362
S37 S40 ASN ALA 0.000561488
S37 S40 ASN CYS 0.000561488
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S37 S40 ASN PHE 0.000561488
S37 S40 ASN GLY 0.000561488
S37 S40 ASN HIS 0.000561488
S37 S40 ASN ILE 0.0536803
S37 S40 ASN LYS 0.000561488
S37 S40 ASN LEU 0.00307196
S37 S40 ASN MET 0.000561488
S37 S40 ASN ASN 0.000561488
S37 S40 ASN PRO 0.000561488
S37 S40 ASN GLN 0.000561488
S37 S40 ASN ARG 0.000561488
S37 S40 ASN SER 0.000561488
S37 S40 ASN THR 0.000561488
S37 S40 ASN VAL -0.09016
S37 S40 ASN TRP 0.000561488

S37 S40 ASN TYR 0.000561488
S37 S40 ASN --- 0.000561488
S37 S40 PRO ILE 0.0031677
S37 S40 PRO LEU 0.000267708
S37 S40 PRO VAL 0.0256362
S37 S40 GLN ILE 0.0031677
S37 S40 GLN LEU 0.000267708
S37 S40 GLN VAL 0.0256362
S37 S40 ARG ALA 0.00293847
S37 S40 ARG CYS 0.00293847
S37 S40 ARG ASP 0.00293847
S37 S40 ARG GLU 0.00293847
S37 S40 ARG PHE 0.00293847
S37 S40 ARG GLY 0.00293847
S37 S40 ARG HIS 0.00293847
S37 S40 ARG ILE -0.219172
S37 S40 ARG LYS 0.00293847
S37 S40 ARG LEU 0.0195116
S37 S40 ARG MET 0.00293847
S37 S40 ARG ASN 0.00293847
S37 S40 ARG PRO 0.00293847
S37 S40 ARG GLN 0.00293847
S37 S40 ARG ARG 0.00293847
S37 S40 ARG SER 0.00293847
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S37 S40 ARG VAL 0.0850815
S37 S40 ARG TRP 0.00293847
S37 S40 ARG TYR 0.00293847
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S37 S40 SER CYS 0.0029583
S37 S40 SER ASP 0.0029583
S37 S40 SER GLU 0.0029583
S37 S40 SER PHE 0.0029583
S37 S40 SER GLY 0.0029583
S37 S40 SER HIS 0.0029583
S37 S40 SER ILE 0.569626
S37 S40 SER LYS 0.0029583
S37 S40 SER LEU 0.14082
S37 S40 SER MET 0.0029583
S37 S40 SER ASN 0.0029583
S37 S40 SER PRO 0.0029583
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S37 S40 SER ARG 0.0029583
S37 S40 SER SER 0.0029583
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S37 S40 SER VAL -0.970632
S37 S40 SER TRP 0.0029583
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S37 S40 THR ILE 0.0031677
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S37 S40 THR VAL 0.0256362
S37 S40 VAL ILE 0.0031677
S37 S40 VAL LEU 0.000267708
S37 S40 VAL VAL 0.0256362
S37 S40 TRP ILE 0.0031677
S37 S40 TRP LEU 0.000267708
S37 S40 TRP VAL 0.0256362
S37 S40 TYR ILE 0.0031677
S37 S40 TYR LEU 0.000267708
S37 S40 TYR VAL 0.0256362
S37 S40 --- ILE 0.0031677

S37 S40 --- LEU 0.000267708
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S38 S39 ALA ILE 0.00202576
S38 S39 ALA LEU 0.000568521
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S38 S39 CYS TRP 0.000490688
S38 S39 ASP ILE 0.00202576
S38 S39 ASP LEU 0.000568521
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S38 S39 ASP TRP 0.000490688
S38 S39 GLU ALA 0.0013284
S38 S39 GLU CYS 0.0013284
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S38 S39 GLU ILE 0.124622
S38 S39 GLU LYS 0.0013284
S38 S39 GLU LEU 0.0147271
S38 S39 GLU MET 0.0013284
S38 S39 GLU ASN 0.0013284
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S38 S39 GLU GLN 0.0013284
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S38 S39 GLU THR 0.0013284
S38 S39 GLU VAL -0.249861
S38 S39 GLU TRP 0.0380835
S38 S39 GLU TYR 0.0013284
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S38 S39 GLY TRP 0.000490688
S38 S39 HIS ALA 0.00592805
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S38 S39 HIS ASP 0.00592805
S38 S39 HIS GLU 0.00592805
S38 S39 HIS PHE 0.00592805
S38 S39 HIS GLY 0.00592805
S38 S39 HIS HIS 0.00592805
S38 S39 HIS ILE -1.06664
S38 S39 HIS LYS 0.00592805
S38 S39 HIS LEU 0.0973573
S38 S39 HIS MET 0.00592805
S38 S39 HIS ASN 0.00592805
S38 S39 HIS PRO 0.00592805
S38 S39 HIS GLN 0.00592805
S38 S39 HIS ARG 0.00592805
S38 S39 HIS SER 0.00592805
S38 S39 HIS THR 0.00592805
S38 S39 HIS VAL 0.668472
S38 S39 HIS TRP 0.0740961
S38 S39 HIS TYR 0.00592805

S38 S39 HIS --- 0.00592805
S38 S39 ILE ILE 0.00202576
S38 S39 ILE LEU 0.000568521
S38 S39 ILE VAL 0.028166
S38 S39 ILE TRP 0.000490688
S38 S39 LYS ALA 0.004416
S38 S39 LYS CYS 0.004416
S38 S39 LYS ASP 0.004416
S38 S39 LYS GLU 0.004416
S38 S39 LYS PHE 0.004416
S38 S39 LYS GLY 0.004416
S38 S39 LYS HIS 0.004416
S38 S39 LYS ILE 0.260169
S38 S39 LYS LYS 0.004416
S38 S39 LYS LEU -0.466436
S38 S39 LYS MET 0.004416
S38 S39 LYS ASN 0.004416
S38 S39 LYS PRO 0.004416
S38 S39 LYS GLN 0.004416
S38 S39 LYS ARG 0.004416
S38 S39 LYS SER 0.004416
S38 S39 LYS THR 0.004416
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S38 S39 LYS TRP 0.11534
S38 S39 LYS TYR 0.004416
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S38 S39 LEU ALA 0.00580175
S38 S39 LEU CYS 0.00580175
S38 S39 LEU ASP 0.00580175
S38 S39 LEU GLU 0.00580175
S38 S39 LEU PHE 0.00580175
S38 S39 LEU GLY 0.00580175
S38 S39 LEU HIS 0.00580175
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S38 S39 LEU LYS 0.00580175
S38 S39 LEU LEU 0.290609
S38 S39 LEU MET 0.00580175
S38 S39 LEU ASN 0.00580175
S38 S39 LEU PRO 0.00580175
S38 S39 LEU GLN 0.00580175
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S38 S39 LEU TRP -0.342629
S38 S39 LEU TYR 0.00580175
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S38 S39 MET ILE 0.00202576
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S38 S39 MET VAL 0.028166
S38 S39 MET TRP 0.000490688
S38 S39 ASN ILE 0.00202576
S38 S39 ASN LEU 0.000568521
S38 S39 ASN VAL 0.028166
S38 S39 ASN TRP 0.000490688
S38 S39 PRO ILE 0.00202576
S38 S39 PRO LEU 0.000568521
S38 S39 PRO VAL 0.028166
S38 S39 PRO TRP 0.000490688
S38 S39 GLN ILE 0.00202576
S38 S39 GLN LEU 0.000568521
S38 S39 GLN VAL 0.028166
S38 S39 GLN TRP 0.000490688

S38 S39 ARG ALA 0.00126407
S38 S39 ARG CYS 0.00126407
S38 S39 ARG ASP 0.00126407
S38 S39 ARG GLU 0.00126407
S38 S39 ARG PHE 0.00126407
S38 S39 ARG GLY 0.00126407
S38 S39 ARG HIS 0.00126407
S38 S39 ARG ILE 0.183225
S38 S39 ARG LYS 0.00126407
S38 S39 ARG LEU 0.00628925
S38 S39 ARG MET 0.00126407
S38 S39 ARG ASN 0.00126407
S38 S39 ARG PRO 0.00126407
S38 S39 ARG GLN 0.00126407
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S38 S39 ARG SER 0.00126407
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S38 S39 ARG TRP 0.0686528
S38 S39 ARG TYR 0.00126407
S38 S39 ARG --- 0.00126407
S38 S39 SER ILE 0.00202576
S38 S39 SER LEU 0.000568521
S38 S39 SER VAL 0.028166
S38 S39 SER TRP 0.000490688
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S38 S39 THR LEU 0.000568521
S38 S39 THR VAL 0.028166
S38 S39 THR TRP 0.000490688
S38 S39 VAL ILE 0.00202576
S38 S39 VAL LEU 0.000568521
S38 S39 VAL VAL 0.028166
S38 S39 VAL TRP 0.000490688
S38 S39 TRP ILE 0.00202576
S38 S39 TRP LEU 0.000568521
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S38 S39 TRP TRP 0.000490688
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S38 S39 TYR LEU 0.000568521
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S38 S39 --- LEU 0.000568521
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S38 S40 ALA LEU 0.000655811
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S38 S40 CYS LEU 0.000655811
S38 S40 CYS VAL 0.0281558
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S38 S40 GLU ALA 0.00108399
S38 S40 GLU CYS 0.00108399
S38 S40 GLU ASP 0.00108399
S38 S40 GLU GLU 0.00108399
S38 S40 GLU PHE 0.00108399
S38 S40 GLU GLY 0.00108399
S38 S40 GLU HIS 0.00108399
S38 S40 GLU ILE 0.141446
S38 S40 GLU LYS 0.00108399

S38 S40 GLU LEU 0.0370501
S38 S40 GLU MET 0.00108399
S38 S40 GLU ASN 0.00108399
S38 S40 GLU PRO 0.00108399
S38 S40 GLU GLN 0.00108399
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S38 S40 HIS ASN 0.00517598
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S38 S40 HIS TRP 0.00517598
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S38 S40 ILE ILE 0.0024394
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S38 S40 ILE VAL 0.0281558
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S38 S40 LYS ASN 0.00411829
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S38 S40 LYS GLN 0.00411829
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S38 S40 LEU HIS 0.00361867
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S38 S40 LEU LEU 0.405927
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S38 S40 LEU ASN 0.00361867
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S38 S40 LEU TRP 0.00361867
S38 S40 LEU TYR 0.00361867
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S38 S40 MET ILE 0.0024394
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S38 S40 SER ILE 0.0024394
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S38 S40 VAL VAL 0.0281558

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S38 S40 --- VAL 0.0281558
S39 S40 ALA ILE 0.00191981
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S39 S40 ALA VAL 0.0161141
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S39 S40 CYS LEU 0.000704404
S39 S40 CYS VAL 0.0161141
S39 S40 ASP ILE 0.00191981
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S39 S40 ASP VAL 0.0161141
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S39 S40 GLY ILE 0.00191981
S39 S40 GLY LEU 0.000704404
S39 S40 GLY VAL 0.0161141
S39 S40 HIS ILE 0.00191981
S39 S40 HIS LEU 0.000704404
S39 S40 HIS VAL 0.0161141
S39 S40 ILE ALA 0.00091104
S39 S40 ILE CYS 0.00091104
S39 S40 ILE ASP 0.00091104
S39 S40 ILE GLU 0.00091104
S39 S40 ILE PHE 0.00091104
S39 S40 ILE GLY 0.00091104
S39 S40 ILE HIS 0.00091104
S39 S40 ILE ILE 0.110178
S39 S40 ILE LYS 0.00091104
S39 S40 ILE LEU 0.0155448
S39 S40 ILE MET 0.00091104
S39 S40 ILE ASN 0.00091104
S39 S40 ILE PRO 0.00091104
S39 S40 ILE GLN 0.00091104
S39 S40 ILE ARG 0.00091104
S39 S40 ILE SER 0.00091104
S39 S40 ILE THR 0.00091104
S39 S40 ILE VAL -0.204632
S39 S40 ILE TRP 0.00091104
S39 S40 ILE TYR 0.00091104
S39 S40 ILE --- 0.00091104
S39 S40 LYS ILE 0.00191981
S39 S40 LYS LEU 0.000704404
S39 S40 LYS VAL 0.0161141
S39 S40 LEU ALA 0.000594115
S39 S40 LEU CYS 0.000594115
S39 S40 LEU ASP 0.000594115
S39 S40 LEU GLU 0.000594115
S39 S40 LEU PHE 0.000594115
S39 S40 LEU GLY 0.000594115
S39 S40 LEU HIS 0.000594115
S39 S40 LEU ILE 0.0134807
S39 S40 LEU LYS 0.000594115

S39 S40 LEU LEU 0.0191364
S39 S40 LEU MET 0.000594115
S39 S40 LEU ASN 0.000594115
S39 S40 LEU PRO 0.000594115
S39 S40 LEU GLN 0.000594115
S39 S40 LEU ARG 0.000594115
S39 S40 LEU SER 0.000594115
S39 S40 LEU THR 0.000594115
S39 S40 LEU VAL -0.0916681
S39 S40 LEU TRP 0.000594115
S39 S40 LEU TYR 0.000594115
S39 S40 LEU --- 0.000594115
S39 S40 MET ILE 0.00191981
S39 S40 MET LEU 0.000704404
S39 S40 MET VAL 0.0161141
S39 S40 ASN ILE 0.00191981
S39 S40 ASN LEU 0.000704404
S39 S40 ASN VAL 0.0161141
S39 S40 PRO ILE 0.00191981
S39 S40 PRO LEU 0.000704404
S39 S40 PRO VAL 0.0161141
S39 S40 GLN ILE 0.00191981
S39 S40 GLN LEU 0.000704404
S39 S40 GLN VAL 0.0161141
S39 S40 ARG ILE 0.00191981
S39 S40 ARG LEU 0.000704404
S39 S40 ARG VAL 0.0161141
S39 S40 SER ILE 0.00191981
S39 S40 SER LEU 0.000704404
S39 S40 SER VAL 0.0161141
S39 S40 THR ILE 0.00191981
S39 S40 THR LEU 0.000704404
S39 S40 THR VAL 0.0161141
S39 S40 VAL ALA 0.0148731
S39 S40 VAL CYS 0.0148731
S39 S40 VAL ASP 0.0148731
S39 S40 VAL GLU 0.0148731
S39 S40 VAL PHE 0.0148731
S39 S40 VAL GLY 0.0148731
S39 S40 VAL HIS 0.0148731
S39 S40 VAL ILE -0.24218
S39 S40 VAL LYS 0.0148731
S39 S40 VAL LEU -0.106537
S39 S40 VAL MET 0.0148731
S39 S40 VAL ASN 0.0148731
S39 S40 VAL PRO 0.0148731
S39 S40 VAL GLN 0.0148731
S39 S40 VAL ARG 0.0148731
S39 S40 VAL SER 0.0148731
S39 S40 VAL THR 0.0148731
S39 S40 VAL VAL -0.088077
S39 S40 VAL TRP 0.0148731
S39 S40 VAL TYR 0.0148731
S39 S40 VAL --- 0.0148731
S39 S40 TRP ALA 3.08846e-05
S39 S40 TRP CYS 3.08846e-05
S39 S40 TRP ASP 3.08846e-05
S39 S40 TRP GLU 3.08846e-05
S39 S40 TRP PHE 3.08846e-05
S39 S40 TRP GLY 3.08846e-05
S39 S40 TRP HIS 3.08846e-05
S39 S40 TRP ILE 0.0137681
S39 S40 TRP LYS 3.08846e-05

S39 S40 TRP LEU 0.00495701
S39 S40 TRP MET 3.08846e-05
S39 S40 TRP ASN 3.08846e-05
S39 S40 TRP PRO 3.08846e-05
S39 S40 TRP GLN 3.08846e-05
S39 S40 TRP ARG 3.08846e-05
S39 S40 TRP SER 3.08846e-05
S39 S40 TRP THR 3.08846e-05
S39 S40 TRP VAL -0.057886
S39 S40 TRP TRP 3.08846e-05
S39 S40 TRP TYR 3.08846e-05
S39 S40 TRP --- 3.08846e-05
S39 S40 TYR ILE 0.00191981
S39 S40 TYR LEU 0.000704404
S39 S40 TYR VAL 0.0161141
S39 S40 --- ILE 0.00191981
S39 S40 --- LEU 0.000704404
S39 S40 --- VAL 0.0161141

CLAIMS

What is claimed is:

1. A polypeptide comprising:

a) an immunoglobulin heavy chain variable domain (V_H) amino acid sequence comprising a heavy chain complementarity determining region 1 (HCDR1), a heavy chain complementarity determining region 2 (HCDR2) and a heavy chain complementarity determining region 3 (HCDR3) that are substantially similar to a HCDR1, HCDR2 and HCDR3, respectively, of the amino acid sequence of SEQ ID NO:5, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16 or SEQ ID NO:17; and

b) an immunoglobulin light chain variable domain (V_L) amino acid sequence comprising a light chain complementarity determining region 1 (LCDR1), a light chain complementarity determining region 2 (LCDR2) and a light chain complementarity determining region 3 (LCDR3) that are substantially similar to a LCDR1, LCDR2 and LCDR3, respectively, of the amino acid sequence of SEQ ID NO:21, SEQ ID NO:20, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29 or SEQ ID NO:30,

wherein the polypeptide is an antibody or an antigen-binding fragment thereof.

2. The polypeptide of Claim 1, comprising a HCDR1, HCDR2 and HCDR3, and LCDR1, LCDR2 and LCDR3, of an antibody comprising a V_H and V_L pair selected from:

SEQ ID NO:5 and SEQ ID NO:21 (AB-2);
SEQ ID NO:4 and SEQ ID NO:20 (AB-1);
SEQ ID NO:6 and SEQ ID NO:20 (AB-3);
SEQ ID NO:7 and SEQ ID NO:22 (AB-4);
SEQ ID NO:8 and SEQ ID NO:23 (AB-5);
SEQ ID NO:9 and SEQ ID NO:24 (AB-6);
SEQ ID NO:10 and SEQ ID NO:25 (AB-7);

SEQ ID NO:11 and SEQ ID NO:20 (AB-8);
SEQ ID NO:12 and SEQ ID NO:20 (AB-9);
SEQ ID NO:13 and SEQ ID NO:26 (AB-10);
SEQ ID NO:14 and SEQ ID NO:27 (AB-11);
SEQ ID NO:15 and SEQ ID NO:28 (AB-12);
SEQ ID NO:16 and SEQ ID NO:29 (AB-13); or
SEQ ID NO:17 and SEQ ID NO:30 (AB-14).

3. The polypeptide of Claim 1, comprising a V_H and V_L pair selected from:
SEQ ID NO:5 and SEQ ID NO:21 (AB-2);
SEQ ID NO:4 and SEQ ID NO:20 (AB-1);
SEQ ID NO:6 and SEQ ID NO:20 (AB-3);
SEQ ID NO:7 and SEQ ID NO:22 (AB-4);
SEQ ID NO:8 and SEQ ID NO:23 (AB-5);
SEQ ID NO:9 and SEQ ID NO:24 (AB-6);
SEQ ID NO:10 and SEQ ID NO:25 (AB-7);
SEQ ID NO:11 and SEQ ID NO:20 (AB-8);
SEQ ID NO:12 and SEQ ID NO:20 (AB-9);
SEQ ID NO:13 and SEQ ID NO:26 (AB-10);
SEQ ID NO:14 and SEQ ID NO:27 (AB-11);
SEQ ID NO:15 and SEQ ID NO:28 (AB-12);
SEQ ID NO:16 and SEQ ID NO:29 (AB-13); or
SEQ ID NO:17 and SEQ ID NO:30 (AB-14).

4. A polypeptide comprising:
a) an immunoglobulin heavy chain (HC) comprising the amino acid sequence of SEQ ID NO:92 or SEQ ID NO:106; and/or
b) an immunoglobulin light chain (LC) comprising the amino acid sequence of SEQ ID NO:120,
wherein the polypeptide is an antibody or an antigen-binding fragment thereof.

5. A polypeptide that comprises an immunoglobulin heavy chain variable domain (V_H) and an immunoglobulin light chain variable domain (V_L), comprising a paratope that

is substantially similar to the paratope of an antibody comprising an amino acid sequence selected from:

SEQ ID NO:5 and SEQ ID NO:21 (AB-2);
SEQ ID NO:4 and SEQ ID NO:20 (AB-1);
SEQ ID NO:6 and SEQ ID NO:20 (AB-3);
SEQ ID NO:7 and SEQ ID NO:22 (AB-4);
SEQ ID NO:8 and SEQ ID NO:23 (AB-5);
SEQ ID NO:9 and SEQ ID NO:24 (AB-6);
SEQ ID NO:10 and SEQ ID NO:25 (AB-7);
SEQ ID NO:11 and SEQ ID NO:20 (AB-8);
SEQ ID NO:12 and SEQ ID NO:20 (AB-9);
SEQ ID NO:13 and SEQ ID NO:26 (AB-10);
SEQ ID NO:14 and SEQ ID NO:27 (AB-11);
SEQ ID NO:15 and SEQ ID NO:28 (AB-12);
SEQ ID NO:16 and SEQ ID NO:29 (AB-13); or
SEQ ID NO:17 and SEQ ID NO:30 (AB-14), or
a combination of the foregoing,

wherein the polypeptide is an antibody or an antigen-binding fragment thereof.

6. A polypeptide comprising an immunoglobulin heavy chain variable domain (V_H), wherein the V_H comprises the amino acid sequence of SEQ ID NO:2, wherein:

X_1 is I or V;
X_2 is W or S;
X_3 is D or S;
X_4 is S, T, Y or A;
X_5 is N, Y, D or T;
X_6 is K, T or I;
X_7 is A, S or T;
X_8 is A or S;
X_9 is L, D, E or S;
X_{10} is V or I;
X_{11} is H, F or Y;
X_{12} is A or S;

X_{13} is F, M or L;

X_{14} is I or V,

or any combination of the foregoing,

and wherein the polypeptide is an antibody or an antigen-binding fragment thereof.

7. A polypeptide comprising an immunoglobulin heavy chain variable domain (V_H), wherein the V_H comprises the amino acid sequence of SEQ ID NO:2, wherein:

X_1 is V;

X_2 is S;

X_3 is S;

X_4 is T, Y or A;

X_5 is Y, D or T;

X_6 is T or I;

X_7 is S or T;

X_8 is S;

X_9 is D, E or S;

X_{10} is I;

X_{11} is F or Y,

X_{12} is S;

X_{13} is M or L;

X_{14} is V,

or any combination of the foregoing,

and wherein the polypeptide is an antibody or an antigen-binding fragment thereof.

8. The polypeptide of Claim 6 or 7, further comprising an immunoglobulin light chain variable domain (V_L), wherein the V_L comprises the amino acid sequence of SEQ ID NO:18, and wherein:

X_{15} is N or Y;

X_{16} is L or I;

X_{17} is S or R;

X_{18} is K, F or Y;

X_{19} is S or N;

X_{20} is V or I;

X_{21} is W or Y;

X_{22} is D, V or S;

X_{23} is S, M or E;

X_{24} is S, A or T;

X_{25} is S, D or E;

X_{26} is D, S, R or F;

X_{27} is H, L, K or E,

or any combination of the foregoing.

9. The polypeptide of Claim 8, wherein:

X_{15} is Y;

X_{16} is I;

X_{17} is R;

X_{18} is F or Y;

X_{19} is N;

X_{20} is I;

X_{21} is Y;

X_{22} is V or S;

X_{23} is M or E;

X_{24} is A or T;

X_{25} is D or E;

X_{26} is S, R or F;

X_{27} is L, K or E,

or any combination of the foregoing.

10. The polypeptide of any of the preceding claims, wherein the polypeptide specifically binds a thymic stromal lymphopoietin (TSLP).

11. The polypeptide of any one of Claims 1-3 and 5-10, wherein the antigen binding fragment comprises a single-chain fragment variable (scFv), a variable heavy domain of heavy chain (V_{HH}), a fragment antigen-binding (Fab), a Fab' or a $F(ab')_2$.

12. The polypeptide of any of the preceding claims, comprising an antibody heavy chain constant domain, an antibody light chain constant domain, or both an antibody heavy chain constant domain and an antibody light chain constant domain.

13. The polypeptide of Claim 12, wherein:
    a) the antibody heavy chain constant domain is an IgG1, IgG2, IgG3 or IgG4 constant domain;
    b) the antibody light chain constant domain is a κ constant domain or a λ constant domain, or

    both a) and b).

14. The polypeptide of Claim 12 or 13, wherein the antibody heavy chain constant domain comprises one or more mutations which increase serum half-life of the antibody or antigen-binding fragment thereof in humans, optionally, wherein the antibody heavy chain constant domain comprises, relative to a wild-type human IgG constant domain, amino acid substitutions with tyrosine, threonine and glutamic acid at amino acid residues 252, 254 and 256, respectively, wherein the amino acid residues are numbered according to the EU index as in Kabat.

15. The polypeptide of any one of Claims 12-14, wherein the antibody heavy chain constant domain comprises the amino acid sequence of SEQ ID NO:85.

16. A fusion protein comprising the polypeptide of any of the preceding claims.

17. A polynucleotide comprising a nucleotide sequence encoding the polypeptide of any of Claims 1-15, or the fusion protein of Claim 16.

18. A vector comprising the polynucleotide of Claim 17.

19. A host cell comprising the polynucleotide of Claim 17 or the vector of Claim 18.

20. A composition comprising the polypeptide of any one of Claims 1-15, the fusion protein of Claim 16, the polynucleotide of Claim 17, the vector of Claim 18, or the host cell of Claim 19.

21. The composition of Claim 20, further comprising one or more pharmaceutical excipients, diluents, or carriers.

22. The composition of Claim 20 or 21, further comprising one or more additional therapeutic agents.

23. The composition of Claim 22, wherein the one or more additional therapeutic agents comprise a corticosteroid, a beta-agonist, a muscarinic antagonist, or a combination thereof.

24. A method of treating a subject in need thereof, comprising administering an effective amount of the composition of any one of Claims 20-23 to the subject, optionally, wherein the subject is a human.

25. The method of Claim 24, further comprising administering a therapeutically effective amount of an additional therapeutic or prophylactic agent to the subject.

26. The method of claim 25, wherein the additional therapeutic or prophylactic agent comprises a corticosteroid, a beta-agonist, a muscarinic antagonist, or a combination thereof.

27. A method of reducing binding of thymic stromal lymphopoietin (TSLP) to a TSLP receptor (TSLPR) on a cell in a subject, comprising contacting the cell with an effective amount of the composition of any one of Claims 19-21, optionally, wherein the subject is a human.

28. The method of any one of Claims 24-27, wherein the subject is a pediatric patient, optionally, the subject is 12 years of age or older.

29. The method of any one of Claims 24-28, wherein the subject has asthma, atopic dermatitis (AD), allergic conjunctivitis, chronic obstructive pulmonary disease (COPD), chronic spontaneous urticaria (CSU), rheumatoid arthritis (RA), rhinosinusitis (RS), eosinophilic esophagitis (EE), or a food-hypersensitivity reaction, optionally, wherein the subject has COPD and/or either moderate asthma or severe asthma.

30. A method of making the polypeptide of any one of Claims 1-15, comprising culturing a host cell comprising a nucleotide sequence encoding the polypeptide under conditions where the polypeptide is expressed in the host cell.

31. A computer-implemented method comprising:

scoring a polypeptide comprising an amino acid sequence with a computationally binding optimized (CBO) model for a functional property relating to modulating the activity of a target molecule, the CBO model:

for each amino acid position of the amino acid sequence of the polypeptide, calculating a plurality of energy scores, the energy scores based on the amino acid at a given position in the amino acid sequence,

adding each energy score calculated to an array,

generating a normalized sum of the energy scores for each position, and

generating a score of the polypeptide by summing each energy score calculated, the score representing the functional property of the polypeptide, the functional property relating to the polypeptide modulating the activity of the target molecule.

32. The computer-implemented method of Claim 31, further comprising:

calculating a logarithm of each energy score calculated;

wherein summing each energy score calculated is performed by summing the logarithms of each energy score calculated;

wherein the energy scores are further calculated based on having substituted the amino acid at the given position in the amino acid sequence with each of a plurality of different amino acids.

33. The computer-implemented method of any of Claims 31-32, wherein scoring the polypeptide using the CBO model is implementable by the script of Appendix A, and the CBO model is substantially similar to the table of Appendix B.

34. The method of any of Claims 31-33, wherein the functional property is at least one of:

a binding affinity for a thymic stromal lymphopoietin (TSLP) polypeptide characterized by a K_D of 10 pM or less; (optionally, as measured by KinExA);

a binding specificity for the AB-loop region and the C-terminal region of helix D of the TSLP polypeptide;

a neutralizing activity against the TSLP polypeptide (optionally, a full-length human TSLP); or

an inhibitory activity against TSLP-mediated signaling,

or a combination of the foregoing.

35. The method of Claim 34, wherein the target molecule is thymic stromal lymphopoietin (TSLP), and the functional property of the relating to the polypeptide modulates the activity of the TSLP.

36. A system comprising:

a processor; and

a memory with computer code instructions stored thereon, the processor and the memory, with the computer code instructions, being configured to cause the system to:

score a polypeptide comprising an amino acid sequence with a CBO model for a functional property relating to modulating the activity of a target molecule, the CBO model:

for each amino acid position of the amino acid sequence of the polypeptide, calculating a plurality of energy scores, the energy scores based on the amino acid at a given position in the amino acid sequence,

add each energy score calculated to an array,

generate a normalized sum of the energy scores for each position, and

generate a score of the amino acid sequence by summing each energy score calculated, the score representing a functional property of the polypeptide, the functional property relating to the polypeptide modulating the activity of the target molecules.

37. The system of Claim 36, wherein the instructions are further configured to cause the system to calculate a logarithm of each energy score calculated;

wherein summing each energy score calculated is performed by summing the logarithms of each energy score calculated;

wherein the energy scores are further based on having substituted the amino acid at the given position in the amino acid sequence with each of a plurality of different amino acids.

38. The system of any of Claims 36-37, wherein scoring the polypeptide using the CBO model is implemented by the script of Appendix A and wherein the CBO model is substantially similar to the table of Appendix B.

39. The system of any of Claims 36-38 wherein the functional property is at least one of:

a binding affinity for a thymic stromal lymphopoietin (TSLP) polypeptide characterized by a K_D of 10 pM or less; (optionally, as measured by KinExA);

a binding specificity for the AB-loop region and the C-terminal region of helix D of the TSLP polypeptide;

a neutralizing activity against the TSLP polypeptide (optionally, a full-length human TSLP); or

an inhibitory activity against TSLP-mediated signaling,

or a combination of the foregoing.

40. The method of Claim 39, wherein the target molecule is thymic stromal lymphopoietin (TSLP), and the functional property of the relating to the polypeptide modulates the activity of the TSLP.

41. A polypeptide that specifically binds a thymic stromal lymphopoietin (TSLP):

wherein the polypeptide comprises an amino acid sequence that is assigned a score above a predetermined threshold by a computationally binding optimized (CBO) model upon scoring the amino acid sequence of the polypeptide.

42. The polypeptide of Claim 41, wherein the polypeptide is scorable by the script of Computer Program Listing Appendix A and wherein the CBO model is calculated by a table substantially similar to that of Computer Program Listing Appendix B and wherein the polypeptide is assigned the score that is calculated using the Computer Program Listing Appendix B;

wherein the polypeptide is assigned the score by a script substantially similar to Computer Program Listing Appendix A, the script employing the CBO model substantially similar to the table of Computer Program Listing Appendix B, wherein the polypeptide has a logarithmic score of at least about: -7.7, -7.0, -6.5, -6.0, -5.5, -5.0, -4.5, -4.0, -3.5, -3.0, 2.9, -2.8, -2.7, -2.6, -2.5, -2.4, -2.3, -2.2, -2.1, -2.0, -1.9, -1.8,

-1.7, -1.6, -1.5, -1.4, -1.3, -1.2, -1.1, -1.0, 0.9, -0.8, -0.7, -0.6, -0.5, -0.4, -0.3, -0.2, and -0.1.

43. The polypeptide of any of Claims 41-42, wherein the polypeptide has one or more properties selected from:

a binding affinity for a thymic stromal lymphopoietin (TSLP) polypeptide characterized by a K_D of 10 pM or less; (optionally, as measured by KinExA);

a binding specificity for the AB-loop region and the C-terminal region of helix D of the TSLP polypeptide;

a neutralizing activity against the TSLP polypeptide (optionally, a full-length human TSLP); or

an inhibitory activity against TSLP-mediated signaling,

or a combination of the foregoing.

44. The polypeptide of any of Claims 41-43, wherein the CBO model outputs a score that is equal to or above a score from the CBO model of one or more of a reference polypeptide that comprises a V_H and V_L pair selected from:

SEQ ID NO:4 and SEQ ID NO:20 (AB-1);
SEQ ID NO:5 and SEQ ID NO:21 (AB-2);
SEQ ID NO:6 and SEQ ID NO:20 (AB-3);
SEQ ID NO:7 and SEQ ID NO:22 (AB-4);
SEQ ID NO:8 and SEQ ID NO:23 (AB-5);
SEQ ID NO:9 and SEQ ID NO:24 (AB-6);
SEQ ID NO:10 and SEQ ID NO:25 (AB-7);
SEQ ID NO:11 and SEQ ID NO:20 (AB-8);
SEQ ID NO:12 and SEQ ID NO:20 (AB-9);
SEQ ID NO:13 and SEQ ID NO:26 (AB-10);
SEQ ID NO:14 and SEQ ID NO:27 (AB-11);
SEQ ID NO:15 and SEQ ID NO:28 (AB-12);
SEQ ID NO:16 and SEQ ID NO:29 (AB-13); or
SEQ ID NO:17 and SEQ ID NO:30 (AB-14).

45. The polypeptide of any of Claims 41-44, wherein the polypeptide does not comprise a heavy chain comprising SEQ ID NO:81 and a light chain comprising SEQ ID NO:82.

46. A polypeptide:

wherein the polypeptide comprises an amino acid sequence that is assigned a score above a predetermined threshold by a computationally binding optimized (CBO) model upon scoring the amino acid sequence of the polypeptide.

47. A polypeptide that binds human thymic stromal lymphopoietin (TSLP), wherein the polypeptide is designed by a method comprising:

generating a polypeptide sequence with a CBO model;

verifying the generated polypeptide sequence using the CBO model by:

for each amino acid position of the polypeptide sequence, calculating a plurality of energy scores, the energy scores based on having substituted the amino acid at a given position in the polypeptide sequence with each of a plurality of different amino acids,

adding each energy score calculated to an array,

generating a normalized sum of the energy scores for each position,

calculating a logarithm of each energy score calculated, and

generating a score of the polypeptide sequence by summing the logarithms of each energy score calculated, the score representing a functional property of the polypeptide's ability to bind to human TSLP.