

HETERODIMERIC IGA FC CONSTRUCTS AND METHODS OF USE THEREOF

TECHNICAL FIELD

The present disclosure relates to the field of IgA-based immunotherapeutics and, in particular, to heterodimeric IgA Fc (IgA HetFc) constructs comprising one or more binding domain and the use of these constructs as therapeutics.

BACKGROUND

Typically, antibody-based therapeutics contain an IgG-derived framework. The Ig subtype is stable, binds to targets with high affinity, has favourable pharmacokinetic behaviour and has a well understood functional impact on target and effector cells as a result of decades of focused research. However, there are limits to IgG-based functionality with respect to the effector cells it is able to activate and the valencies that can be obtained.

Neutrophils are an integral part of the immune system and are the most prevalent leukocyte found in human blood (see Table 1). IgA is the only Ig isotype that interacts with FcαRI on neutrophils via residues in the Cα2/Cα3 (IgA CH2/CH3) interface of the Fc. Interaction of IgA with FcαRI on neutrophils elicits a variety of pro-inflammatory responses including the release of Neutrophil Extracellular Traps (NETs), degranulation and chemokine release (Heineke, 2017, *Eur J Clin Invest.*, 47(2):184-192). IgA also can mediate cytotoxicity *ex vivo*. Neutrophils activated by IgA have been shown to be capable of killing Her2⁺⁺⁺ BT474 cells (Borrok *et al.*, 2015, *MAbs* 7:743-751). IgA mediated tumor cell killing via Her2 and other targets has been shown by neutrophils *ex vivo* (Brandsma *et al.*, 2019, *Front Immunol*, 10:704). Moreover, IgA can mediate tumor growth inhibition *in vivo*. In particular, IgA has been shown to inhibit tumor growth *in vivo* in a FcαRI transgenic (Tg) mouse model (Boross *et al.*, 2013, *EMBO Mol Med*, 5:1213-1226).

Table 1: Immune Cells in Human Blood*

Cell type	Median Concentration in human blood [Cells x 10⁹ /L]	Median percentage of white blood cells
Neutrophils	3.65	53.0
Lymphocytes (incl. T cells, B cells and NK cells)	2.5	36.1
Eosinophils	0.15	3.2
Basophils	0.03	0.6
Monocytes	0.43	7.1

*Data collected from 291 adults (see Orfanakis, *et al.*, 1970, *Am J Clin Pathol*, 53:647-651)

Recruitment and activation of neutrophils via IgA affords new biological functions for antibody-based immunotherapies.

5 SUMMARY

Described herein are heterodimeric IgA Fc constructs and methods of use thereof. One aspect of the present disclosure relates to an IgA heterodimeric Fc (IgA HetFc) construct comprising a first Fc polypeptide and a second Fc polypeptide, the first Fc polypeptide comprising a first CH3 domain sequence and the second Fc polypeptide comprising an second CH3 domain sequence, the first and second CH3 domain sequences forming a modified CH3 domain, wherein the first and second CH3 domain sequences comprise amino acid mutations that promote formation of a heterodimeric Fc over a homodimeric Fc, wherein: the amino acid mutations in the first CH3 domain sequence comprise an amino acid substitution at position A6085Y selected from A6085YF, A6085YY, A6085YM, A6085YW and A6085YH, and an amino acid substitution at position T6086 selected from T6086Y, T6086F, T6086M, T6086W and T6086H, and the amino acid mutations in the second CH3 domain sequence comprise an amino acid substitution at position W6081 selected from W6081T, W6081L, W6081A, W6081V and W6081I, wherein the heterodimeric Fc is formed with a purity of 70% or higher, and wherein the numbering of amino acid positions is according to IMGT numbering.

Another aspect of the present disclosure relates to an IgA heterodimeric Fc (IgA HetFc) construct comprising a first Fc polypeptide and a second Fc polypeptide, the first Fc polypeptide comprising a first CH3 domain sequence and the second Fc polypeptide comprising an second CH3 domain sequence, the first and second CH3 domain sequences forming a modified CH3 domain, wherein the first and second CH3 domain sequences comprise amino acid mutations that promote formation of a heterodimeric Fc over a homodimeric Fc, wherein:

- (a) the amino acid mutations in the first CH3 domain sequence comprise the amino acid substitutions: A6085YY and T6086L, and the amino acid mutations in the second CH3 domain sequence comprise the amino acid substitutions: L6079T, W6081L and I6088L; or
- 10 (b) the amino acid mutations in the first CH3 domain sequence comprise the amino acid substitutions: A6085YY and T6086Y, and the amino acid mutations in the second CH3 domain sequence comprise the amino acid substitutions: L6079T, W6081L and I6088L; or
- (c) the amino acid mutations in the first CH3 domain sequence comprise the amino acid substitutions: A6085YF and T6086Y, and the amino acid mutations in the second CH3 domain sequence comprise the amino acid substitutions: L6079V, W6081L and I6088L; or
- 15 (d) the amino acid mutations in the first CH3 domain sequence comprise the amino acid substitutions: A6085YF and T6086Y, and the amino acid mutations in the second CH3 domain sequence comprise the amino acid substitutions: L6079V, W6081T and I6088L; or
- (e) the amino acid mutations in the first CH3 domain sequence comprise the amino acid substitutions: T6022V, A6085YF and T6086Y, and the amino acid mutations in the second CH3 domain sequence comprise the amino acid substitutions: L6079V, W6081T and I6088L; or
- 20 (f) the amino acid mutations in the first CH3 domain sequence comprise the amino acid substitutions: T6022L, A6085YF and T6086Y, and the amino acid mutations in the second CH3 domain sequence comprise the amino acid substitutions: L6079V, W6081T and I6088L; or
- 25 (g) the amino acid mutations in the first CH3 domain sequence comprise the amino acid substitutions: T6022I, A6085YF and T6086Y, and the amino acid mutations in the second CH3 domain sequence comprise the amino acid substitutions: L6079V, W6081T and I6088L; or

(h) the amino acid mutations in the first CH3 domain sequence comprise the amino acid substitutions: A6085YF and T6086Y, and the amino acid mutations in the second CH3 domain sequence comprise the amino acid substitutions: L6007F, L6079V, W6081T and I6088L

5 (i) the amino acid mutations in the first CH3 domain sequence comprise the amino acid substitutions: H6005Y, A6085YF and T6086Y, and the amino acid mutations in the second CH3 domain sequence comprise the amino acid substitutions: H6005Y, L6079V, W6081T and I6088L; or

10 (j) the amino acid mutations in the first CH3 domain sequence comprise the amino acid substitutions: H6005C, A6085YF and T6086Y, and the amino acid mutations in the second CH3 domain sequence comprise the amino acid substitutions: P6010C, L6079V, W6081T and I6088L; or

15 (k) the amino acid mutations in the first CH3 domain sequence comprise the amino acid substitutions: P6010C, A6085YF and T6086Y, and the amino acid mutations in the second CH3 domain sequence comprise the amino acid substitutions: H6005C, L6079V, W6081T and I6088L; or

(l) the amino acid mutations in the first CH3 domain sequence comprise the amino acid substitutions: H6005C, P6010C, A6085YF and T6086Y, and the amino acid mutations in the second CH3 domain sequence comprise the amino acid substitutions: H6005C, P6010C, L6079V, W6081T and I6088L,

20 wherein the heterodimeric Fc is formed with a purity of 70% or higher, and wherein the numbering of amino acid positions is according to IMGT numbering.

Another aspect of the present disclosure relates to a conjugate comprising an IgA HetFc construct as described herein and one or more therapeutic, diagnostic or labeling agents.

25 Another aspect of the present disclosure relates to an IgA HetFc multimer comprising two or more IgA HetFc constructs as described herein and a J chain, wherein two of the IgA HetFc constructs are joined by the J chain.

Another aspect of the present disclosure relates to a pharmaceutical composition comprising an IgA HetFc construct as described herein and a pharmaceutically acceptable carrier or diluent.

5 Another aspect of the present disclosure relates to a pharmaceutical composition comprising a conjugate comprising an IgA HetFc construct and one or more therapeutic, diagnostic or labeling agents as described herein, and a pharmaceutically acceptable carrier or diluent.

Another aspect of the present disclosure relates to a pharmaceutical composition comprising an IgA HetFc multimer comprising two or more IgA HetFc constructs and a J chain as described herein, and a pharmaceutically acceptable carrier or diluent.

10 Another aspect of the present disclosure relates to an isolated polynucleotide or set of polynucleotides encoding an IgA HetFc construct as described herein.

Another aspect of the present disclosure relates to a vector set or set of vectors comprising one or more polynucleotides encoding an IgA HetFc as described herein.

15 Another aspect of the present disclosure relates to a host cell comprising one or more polynucleotides encoding an IgA HetFc as described herein.

Another aspect of the present disclosure relates to a method of preparing an IgA HetFc construct as described herein comprising transfecting a host cell with one or more polynucleotides encoding the IgA HetFc construct, and culturing the host cell under conditions suitable for expression of the IgA HetFc construct.

20 Another aspect of the present disclosure relates to a method of preparing an IgA HetFc multimer as described herein, comprising transfecting a host cell with one or more polynucleotides encoding an IgA HetFc construct comprising an α -tailpiece and a polynucleotide encoding a J chain, and culturing the host cell under conditions suitable for expression of the IgA HetFc construct and the J chain.

BRIEF DESCRIPTION OF THE DRAWINGS

Fig. 1 presents a cartoon depicting negative and positive design concepts for mutations to drive heterodimerization of an IgA Fc.

Fig. 2 presents non-reducing CE-SDS profiles of IgA Fc one armed antibody (OAA) constructs after CaptureSelect™ IgA affinity purification: **(A)** IgA Fc OAA constructs comprising WT IgA CH3 (variant number 32595) or Steric Design 1, 2, 3, 4 or 6 (variant numbers 32516, 32517, 32518, 32519 and 32521, respectively), **(B)** IgA Fc OAA constructs comprising Steric Design 7, 8, 9, 10 or 11 (variant numbers 33330, 33331, 33332, 33333 and 33334, respectively).

Fig. 3 presents UPLC-SEC chromatograms of IgA Fc OAA constructs after CaptureSelect™ IgA affinity purification: **(A)** UPLC-SEC chromatogram of IgA Fc OAA construct comprising a WT IgA CH3 (variant number 32595); **(B-K)** UPLC-SEC chromatograms of IgA OAA constructs comprising Steric Design 1, 2, 3, 4, 6, 7, 8, 9, 10 or 11 (variant numbers 32516, 32517, 32518, 32519, 32521, 33330, 33331, 33332, 33333 and 33334, respectively).

Fig. 4 presents UPLC-SEC chromatograms of IgA Fc OAA constructs after purification by preparative SEC: **(A)** IgA OAA construct comprising WT IgA CH3 (variant number 32595), **(B-J)** IgA OAA constructs comprising Steric Design 1, 2, 3, 6, 7, 8, 9, 10 or 11 (variant numbers 32516, 32517, 32518, 32521, 33330, 33331, 33332, 33333 and 33334, respectively).

Fig. 5 presents non-reducing and reducing CE-SDS profiles of IgA Fc OAA constructs after purification by preparative SEC: **(A)** IgA OAA constructs comprising WT IgA CH3 (variant 32595) or Steric Design 1, 2, 3 or 6 (variant numbers 32516, 32517, 32518 and 32521, respectively), **(B)** IgA OAA constructs comprising Steric Design 7, 8, 9, 10 or 11 (variant numbers 33330, 33331, 33332, 33333 and 33334, respectively).

Fig. 6 presents an overlay of DSC thermograms for IgA Fc OAA constructs after purification by preparative SEC: **(A)** IgA Fc constructs comprising WT IgA CH3 (variant number 32595) or Steric Design 1, 2, 3 or 6 (variant numbers 32516, 32517, 32518 and 32521, respectively), **(B)** IgA Fc constructs comprising Steric Design 7-11 (variant numbers 33330 - 33334).

Fig. 7 depicts examples of components and configurations of IgA HetFc binding units: **(A)** the IgA HetFc scaffold to which binding domains are fused to form an IgA HetFc binding unit,

(B) illustrative IgA HetFc binding unit showing the IgA HetFc scaffold with two exemplary binding domains attached; (C-H) illustrative IgA HetFc binding units having from one to four binding domains fused to the IgA HetFc scaffold in different configurations. Binding domains are shown as Fabs for illustrative purposes but may be various other binding domains (e.g. scFv) and combinations of binding domains. The formats provided are for illustrative purposes and does not limit the disclosure in any way.

Fig. 8 depicts illustrative higher order IgA HetFc multimers comprising two, four and five IgA HetFc binding units joined by a J chain (stippled). The two chains of the IgA HetFc are shown in grey and striped. The tailpiece assembly in the centre of each structure is indicated. A single orientation is shown for each assembly but many orientations are possible. Since the J chain and Fc:Fc interactions are not selective for chain A or chain B, the orientation of the binding domains of each binding unit can be reversed. (A) a dimeric IgA HetFc multimer comprising two bispecific IgA HetFc binding units joined by a J chain, (B) a tetrameric IgA HetFc multimer comprising four bispecific IgA HetFc binding units joined by a J chain, and (C) a pentameric IgA HetFc multimer comprising five bispecific IgA HetFc binding units joined by a J chain.

Fig. 9 presents structural representations of IgA HetFc design (Steric 6) with chain A and chain B indicated. The protein backbone is depicted in cartoon representation and side chains are shown as line representation. Non-polar hydrogens are not shown. (A) shows the full IgA heterodimeric Fc, and (B) presents a magnified view of the mutated residues centered around the core positions A6085, T6086 (both chain A) and W6081 (chain B).

Fig. 10 presents an alignment of the amino acid sequences for the IgA1, IgA2m1 and IgA2m2 Fc regions.

Fig. 11 presents IgA OAA variants based on an IgA HetFc with mutations eliminating binding of Fc α R in one or both chains of the Fc.

Fig. 12 presents a modified IgA mAb based on an IgA HetFc that is capable of binding both Fc α R and FcRn.

DETAILED DESCRIPTION

The present disclosure relates to the engineering of IgA Fc regions to introduce amino acid mutations into the CH3 domain that promote formation of a heterodimeric IgA Fc (IgA HetFc).
5 The IgA HetFc allows for construction of IgA-based bispecific or multispecific binding proteins, as well as IgA-based multimeric binding proteins. In accordance with the present disclosure, the one or more amino acid mutations comprised by the IgA HetFc constructs allow for formation of a heterodimeric Fc having a purity of at least about 70%. The IgA HetFc constructs of the present disclosure are also thermostable. For example, in certain embodiments, the CH3 domain of the
10 IgA HetFc has a melting temperature (T_m) that is about 60°C or higher. In some embodiments, the CH3 domain of the IgA Het Fc has a T_m that is within 10°C ($\pm 10^\circ\text{C}$) of the T_m of a wild-type IgA CH3 domain.

The IgA HetFc constructs of the present disclosure include IgA HetFc scaffolds, which comprise an IgA Fc region together with a hinge region; IgA HetFc binding units, which comprise
15 an IgA scaffold and one or more binding domains; and IgA HetFc multimers, which comprise a plurality (*e.g.* two or more) IgA HetFc binding units.

The IgA HetFc constructs of the present disclosure introduce a multispecific potential to the IgA isotype with functionalities that are untapped by IgG. For example, in certain embodiments, the IgA HetFc facilitates the creation of multispecific and multimeric biologics
20 capable of recruitment of neutrophils via the Fc α RI. As neutrophils are an integral part of the immune system and are the most prevalent leukocyte found in human blood, recruitment and activation of neutrophils via IgA affords new biological functions for antibody-based immunotherapies. Certain embodiments of the present disclosure relate to methods of using IgA HetFc binding units and IgA HetFc multimers as therapeutics. Certain embodiments of the present
25 disclosure relate to methods of using IgA HetFc binding units and IgA HetFc multimers as diagnostics.

DEFINITIONS

Unless defined otherwise, all technical and scientific terms used herein have the same meaning as commonly understood by one of ordinary skill in the art.

As used herein, the term “about” refers to an approximately +/-10% variation from a given value, unless otherwise indicated. It is to be understood that such a variation is always included in any given value provided herein, whether or not it is specifically referred to.

The use of the word “a” or “an” when used herein in conjunction with the term “comprising” may mean “one,” but it is also consistent in certain embodiments with the meaning of “one or more,” “at least one” or “one or more than one.”

As used herein, the terms “comprising,” “having,” “including” and “containing,” and grammatical variations thereof, are inclusive or open-ended and do not exclude additional, unrecited elements and/or method steps. The term “consisting essentially of” when used herein in connection with a composition, use or method, denotes that additional elements and/or method steps may be present, but that these additions do not materially affect the manner in which the recited composition, method or use functions. The term “consisting of” when used herein in connection with a composition, use or method, excludes the presence of additional elements and/or method steps. A composition, use or method described herein as comprising certain elements and/or steps may also, in certain embodiments consist essentially of those elements and/or steps, and in other embodiments consist of those elements and/or steps, whether or not these embodiments are specifically referred to.

By “fused” is meant that the components of the multimers described herein (*e.g.* an antibody or antigen-binding fragment thereof and an Fc domain polypeptide) are linked by peptide bonds, either directly or via one or more peptide linkers.

As used herein, the term “single-chain” refers to a molecule comprising amino acid monomers linearly linked by peptide bonds. For example, an antigen-binding fragment of an antibody may comprise a single chain variable region (scFv).

As used herein an “IgA HetFc construct” is meant to include any of the IgA HetFc constructs described herein, including IgA HetFc scaffolds (heterodimeric IgA Fc), IgA HetFc binding units (heterodimeric IgA binding units) and IgA HetFc multimers.

5 The term “functional” in connection with a modified J chain means that the J chain retains the primary function of a native J chain, *e.g.*, a native human J chain, in particular, the ability to enable efficient polymerization (dimerization, tetramerization) of IgA and binding of such polymers (dimers, tetramers) to the secretory component (SC)/polymeric (p)Ig.

10 The term “isolated,” as used herein with reference to a material, means that the material is removed from its original environment (for example, the natural environment if it is naturally occurring). For example, a naturally occurring polynucleotide or polypeptide present in a living animal is not isolated, but the same polynucleotide or polypeptide separated from some or all of the co-existing materials in the natural system, is isolated. Such polynucleotides could be part of a vector and/or such polynucleotides or polypeptides could be part of a composition, and still be isolated in that such vector or composition is not part of its natural environment.

15 The term “conservatively modified variant” when used herein with reference to an amino acid sequence, such as a peptide, polypeptide or protein sequence, means that the amino acid sequence has been altered by substitution, addition or deletion of a single amino acid or a small percentage of amino acids without significantly impact the function of the sequence. For example, a conservatively modified variant may be an amino acid sequence that has been altered by one or
20 more conservative amino acid substitutions. Conservative substitution tables providing functionally similar amino acids are known to those of ordinary skill in the art. For example, the following eight groups each contain amino acids that are conservative substitutions for one another: 1) Alanine (A), Glycine (G); 2) Aspartic acid (D), Glutamic acid (E); 3) Asparagine (N), Glutamine (Q); 4) Arginine (R), Lysine (K); 5) Isoleucine (I), Leucine (L), Methionine (M), Valine
25 (V); 6) Phenylalanine (F), Tyrosine (Y), Tryptophan (W); 7) Serine (S), Threonine (T); and [0139] 8) Cysteine (C), Methionine (M) (see, for example, Creighton, *Proteins: Structures and Molecular Properties* (W H Freeman & Co.; 2nd edition (December 1993)). In certain embodiments, the IgA sequence used as a base sequence for the IgA HetFc constructs may be a conservatively modified variant.

The term “substantially identical” as used herein in relation to an amino acid sequence indicates that, when optimally aligned, for example using the methods described below, the sequence shares at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 96%, at least 97%, at least 98% or at least 99% sequence identity with a defined second amino acid sequence (or “reference sequence”). In certain embodiments, a substantially identical amino acid sequence has at least 95%, at least 96%, at least 97%, at least 98% or at least 99% sequence identity with the reference sequence. “Substantial identity” may be used to refer to various types and lengths of sequence, such as full-length sequence or a functional domain. Percent identity between two amino acid sequences can be determined in various ways well-known in the art, for example, using publicly available computer software such as Smith Waterman Alignment (Smith, T. F. and M. S. Waterman (1981) *J Mol Biol* 147:195-7); “BestFit” (Smith and Waterman, *Advances in Applied Mathematics*, 482-489 10 (1981)) as incorporated into GeneMatcher Plus™, Schwarz and Dayhof (1979) *Atlas of Protein Sequence and Structure*, Dayhof, M. O., Ed pp 353-358; BLAST program (Basic Local Alignment Search Tool (Altschul, S. F., W. Gish, *et al.* (1990) *J Mol Biol* 215: 403-10), and variations thereof including BLAST-2, BLAST-P, BLAST-N, BLAST-X, WU-BLAST-2, ALIGN, ALIGN-2, CLUSTAL, and Megalign (DNASTAR) software. In addition, those skilled in the art can determine appropriate parameters for measuring alignment, including algorithms needed to achieve maximal alignment over the length of the sequences being compared. In general, for amino acid sequences, the length of comparison sequences will be at least 10 amino acids. One skilled in the art will understand that the actual length will depend on the overall length of the sequences being compared and may be at least 20, at least 30, at least 40, at least 50, at least 60, at least 70, at least 80, at least 90, at least 100, at least 110, at least 120, at least 130, at least 140, at least 150, or at least 200 amino acids, or it may be the full-length of the amino acid sequence. In certain embodiments, an IgA HetFc construct comprises an amino acid sequence that is at least 90%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to a reference amino acid sequence or fragment thereof as set forth in the Table(s) herein.

The terms “derived from” and “based on” when used with reference to a recombinant amino acid sequence mean that the recombinant amino acid sequence is substantially identical to the sequence of the corresponding wild-type amino acid sequence. For example, an IgA Fc amino acid sequence that is derived from (or based on) a wild-type IgA Fc sequence is substantially

identical (*e.g.*, shares at least 90%, at least 95%, at least 96%, at least 97%, at least 98% or at least 99% sequence identity) with the wild-type IgA Fc sequence.

The term “subject,” as used herein, refers to an animal, in some embodiments a mammal, which is the object of treatment, observation or experiment. An animal may be a human, a non-
5 human primate, a companion animal (*e.g.*, a dog, cat, and the like), a farm animal (*e.g.*, a cow, sheep, pig, horse, and the like) or a laboratory animal (*e.g.*, a rat, mouse, guinea pig, and the like).

The term “mammal,” as used herein, includes but is not limited to humans, non-human primates, canines, felines, murines, bovines, equines and porcines.

The term “knock-out or knockout” as used herein, refers to a mutation or a set of mutations
10 within various locations in a variant resulting in eliminating or lessening binding to a binding target.

In the present description, any concentration range, percentage range, ratio range, or integer range is to be understood to include the value of any integer within the recited range and, when appropriate, fractions thereof (such as one tenth and one hundredth of an integer), unless otherwise
15 indicated.

It is contemplated that any embodiment discussed herein can be implemented with respect to any method, use or composition disclosed herein.

Particular features, structures and/or characteristics described in connection with an embodiment disclosed herein may be combined with features, structures and/or characteristics
20 described in connection with another embodiment disclosed herein in any suitable manner to provide one or more further embodiments.

It is also to be understood that the positive recitation of a feature in one embodiment, serves as a basis for excluding the feature in an alternative embodiment. For example, where a list of options is presented for a given embodiment or claim, it is to be understood that one or more option
25 may be deleted from the list and the shortened list may form an alternative embodiment, whether or not such an alternative embodiment is specifically referred to.

Terms understood by those in the art of antibody technology are each given the meaning acquired in the art, unless expressly defined differently herein. Antibodies are known to have variable regions, a hinge region, and constant domains. Immunoglobulin structure and function are

reviewed, for example, in Harlow *et al* (Eds.), *Antibodies: A Laboratory Manual*, Chapter 14 (Cold Spring Harbor Laboratory, Cold Spring Harbor, 1988).

Unless otherwise specified herein, numbering of amino acid residues in the IgA Fc region and IgA tailpiece is according to the IMGT numbering system (see Lefranc, *et al.*, 2003, *Dev Comp Immunol*, 27:55–77; Lefranc, *et al.*, 2005, *Dev Comp Immunol*, 29:185–203). Table 2 provides the IMGT numbering and amino acid sequence for the IgA2m1 Fc CH2 and CH3 domains, together with the equivalent EU numbering (by alignment). Numbering of other IgA Fc sequences can be readily determined by one skilled in the art by simple sequence alignment with the sequence shown in Table 2 using known techniques. Table 3 provides the IMGT numbering and amino acid sequence for the IgA tailpiece.

Table 2: IgA2m1* Fc CH2 and CH3 Domains Sequence, IMGT and EU Numbering

CH2 domain			CH3 domain		
IMGT No.	EU No.	Amino Acid	IMGT No.	EU No.	Amino Acid
5001	231	C	6001	341	G
5001A	232	C	6001A	342	N
5001Z	237	H	6001B	343	T
5002	238	P	6001Y	344	F
5003	239	R	6001Z	345	R
5004	240	L	6002	346	P
5005	241	S	6003	347	E
5006	242	L	6004	348	V
5007	243	H	6005	349	H
5008	244	R	6006	350	L
5009	245	P	6007	351	L
5010	246	A	6008	352	P
5011	247	L	6009	353	P
5012	248	E	6010	354	P
5013	249	D	6011	355	S
5014	250	L	6012	356	E
5015	251	L	6013	357	E
5015A	252	L	6014	358	L
5016	254	G	6015	359	A
5017	255	S	6015A	359A	L
5018	256	E	6016	360	N
5019	257	A	6017	361	E
5020	258	N	6018	362	L

CH2 domain			CH3 domain		
IMGT No.	EU No.	Amino Acid	IMGT No.	EU No.	Amino Acid
5021	259	L	6019	363	V
5022	260	T	6020	364	T
5023	261	C	6021	365	L
5024	262	T	6022	366	T
5025	263	L	6023	367	C
5026	264	T	6024	368	L
5027	265	G	6025	369	A
5028	266	L	6026	370	R
5029	267	R	6027	371	G
5030	268	D	6028	372	F
5031	269	A	6029	373	S
5035	271	S	6030	374	P
5036	272	G	6035	375	K
5037	273	A	6036	376	D
5038	274	T	6037	377	V
5039	275	F	6038	378	L
5040	276	T	6039	379	V
5041	277	W	6040	380	R
5042	278	T	6041	381	W
5043	279	P	6042	382	L
5044	280	S	6043	383	Q
5045	281	S	6044	384	G
5045A	282	G	6045	385	S
5045B	283	K	6045A	386	Q
5045Z	283A	S	6045B	387	E
5078	287	A	6045C	388	L
5079	288	V	6045X	389	P
5080	289	Q	6045Y	389A	R
5081	290	G	6045Z	389B	E
5082	291	P	6077	390	K
5083	292	P	6078	391	Y
5084	293	E	6079	392	L
5084A	294	R	6080	393	T
5084B	295	D	6081	394	W
5084C	296	L	6082	395	A
5084Y	297	C	6083	396	S
5084Z	298	G	6084	397	R
5085	299	C	6084A	398	Q

CH2 domain			CH3 domain		
IMGT No.	EU No.	Amino Acid	IMGT No.	EU No.	Amino Acid
5085A	300	Y	6084B	399	E
5085B	301	S	6084C	400	P
5085Z	302	V	6084X	401	S
5086	303	S	6084Y	401A	Q
5087	304	S	6084Z	401B	G
5088	305	V	6085	401C	T
5089	306	L	6085A	402	T
5090	307	P	6085B	403	T
5091	308	G	6085C	404	F
5092	309	C	6085Y	405	A
5093	310	A	6085Z	406	V
5094	311	Q	6086	407	T
5095	312	P	6087	408	S
5096	313	W	6088	409	I
5097	314	N	6089	410	L
5098	315	H	6090	411	R
5099	316	G	6091	412	V
5100	317	E	6092	413	A
5101	318	T	6093	414	A
5102	319	F	6094	415	E
5103	320	T	6095	416	D
5104	321	C	6096	417	W
5105	322	T	6097	418	K
5106	323	A	6098	419	K
5107	324	A	6099	420	G
5108	325	H	6100	421	D
5109	326	P	6101	422	T
5110	327	E	6102	423	F
5113	328	L	6103	424	S
5114	329	K	6104	425	C
5115	330	T	6105	426	M
5116	331	P	6106	427	V
5117	332	L	6107	428	G
5118	333	T	6108	429	H
5119	334	A	6109	430	E
5120	335	N	6110	431	A
5121	336	I	6112	432	L
5122	337	T	6113	433	P

CH2 domain			CH3 domain		
IMGT No.	EU No.	Amino Acid	IMGT No.	EU No.	Amino Acid
5123	338	K	6114	434	L
5124	339	S	6115	435	A
			6116	436	F
			6117	437	T
			6118	438	Q
			6119	439	K
			6120	440	T
			6121	441	I
			6122	442	D
			6123	443	R
			6124	444	L
			6125	445	A
			6129	446	G

* Chintalacharuvu, *et al.*, 1994, *J Immunol* 152:5299-5304

Table 3: IgA Tailpiece Sequence and IMGT Numbering

IMGT No.	Amino Acid
7001	K
7002	P
7003	T
7004	H
7005	V
7006	N
7007	V
7008	S
7009	V
7010	V
7011	M
7012	A
7013	E
7014	V
7015	D
7016	G
7017	T
7018	C
7019	Y

The section headings used herein are for organizational purposes only and are not to be construed as limiting the subject-matter described.

HETERODIMERIC IGA FC (IGA HETFC) CONSTRUCTS

The present disclosure relates to heterodimeric IgA Fc (IgA HetFc) constructs. The IgA
5 HetFc constructs comprise a heterodimer Fc region derived from an IgA Fc region. The
heterodimer Fc region comprises a modified CH3 domain that includes one or more asymmetric
amino acid mutations that promote heterodimer formation. In certain embodiments, the
heterodimer Fc region comprised by the IgA HetFc construct may act as a scaffold (an IgA HetFc
10 scaffold) to which one or more binding domains can be fused to provide an IgA HetFc binding
unit. In certain embodiments, multiple (*e.g.* two or more) IgA binding units may be fused together,
for example via a J-chain, to provide IgA HetFc multimers. Other agents (*e.g.*, therapeutic or
diagnostic agents) can optionally be conjugated to the IgA HetFc constructs in certain
embodiments.

IgA exists as two subtypes, IgA1 and IgA2, as well as various allotypic variants (IgA2m1,
15 IgA2m2, IgA2(n)). Of the two subtypes, IgA2 is more stable than IgA1 since its shorter hinge
region renders it resistant to certain bacterial proteases. This shorter hinge also results in a rigid
and non-planar structure which facilitates better multivalent binding of IgA2 to antigens on cell
surfaces. For the purposes of the present disclosure, the heterodimer Fc region of an IgA HetFc
construct may be derived from an IgA1 or IgA2 Fc region, including allotypic variants thereof. In
20 certain embodiments, the heterodimer Fc region of an IgA HetFc construct may be derived from
an IgA1 Fc region. In certain embodiments, the heterodimer Fc region of an IgA HetFc construct
may be derived from an IgA2 Fc region or an allotypic variant thereof. In some embodiments, the
heterodimer Fc region of an IgA HetFc construct may be derived from a human IgA Fc region. In
some embodiments, the heterodimer Fc region of an IgA HetFc construct may be derived from a
25 human IgA2 or IgA2m1 Fc region.

In some embodiments, the heterodimer Fc region of an IgA HetFc construct may be derived
from a human IgA2m1 Fc region. Table 4 provides the amino acid sequence of the wild-type
human IgA2m1 Fc sequence and of a modified form of IgA2m1 Fc sequence truncated to remove
the tailpiece and mutated to remove a free cysteine and a glycosylation site. The Fc sequences

correspond to IMGT numbering 5001-6129 of the human IgA2m1 heavy chain. The CH3 sequence of IgA2m1 (underlined) comprises amino acids 6097-6129 (IMGT numbering) of the full-length human IgA1 heavy chain (see *e.g.*, Chintalacharuvu, *et al.*, 1994, *J Immunol*, 152:5299-5304). The sequence of the IgA tailpiece is also shown. Amino acid sequences of the IgA1 and IgA2m2 Fc regions are provided in Sequence Table B as SEQ ID NOs:44 and 45. An alignment of the Fc sequences is provided in Fig. 10.

Table 4: IgA2m1 Fc Amino Acid Sequences

IgA2m1 wild type sequence ¹	CCHPRLSLHRPALEDLLLGSEANLTCTLTGLRDASGAT FTWTPSSGKSAVQGPPERDLCGCYSVSSVLPGCAQPW NHGETFTCTAAHPELKTPLTANITKSGNTFRPEVHLLP <u>PPSEELALNELVTLTCLARGFSPKDVLRWLQGSQELP</u> <u>REKYLTWASRQEPSQGTTTFAVTSILRVAAEDWKKGD</u> <u>TFSCMVGHEALPLAFTQKTIDRLAG</u> [SEQ ID NO:42]
Modified IgA2m1 sequence (C5092S/N5120T/I5121L /T5122S/ Δ α -tailpiece ²)	CCHPRLSLHRPALEDLLLGSEANLTCTLTGLRDASGAT FTWTPSSGKSAVQGPPERDLCGCYSVSSVLPGSAQPW NHGETFTCTAAHPELKTPLTATLKS ² SGNTFRPEVHLLP PPSEELALNELVTLTCLARGFSPKDVLRWLQGSQELP REKYLTWASRQEPSQGTTTFAVTSILRVAAEDWKKGD TFSCMVGHEALPLAFTQKTIDRLAG [SEQ ID NO:43]
IgA1/IgA2m1 Tailpiece	KPTHVNVSVVMAEVDGTCY [SEQ ID NO:46]

¹ Chintalacharuvu, *et al.*, 1994, *J Immunol*, 152:5299-5304

² Lohse *et al.*, 2016, *Cancer Res*, 76:403-417. Mutations shown in bold and underline.

The terms “Fc region,” “Fc domain” and “Fc,” are used interchangeably herein to define a C-terminal region of an immunoglobulin heavy chain. An Fc region typically comprises a CH2 domain and a CH3 domain. The Fc region may also be considered to encompass the hinge region in certain embodiments. An “Fc polypeptide” of a dimeric Fc as used herein refers to one of the two polypeptides forming the dimeric Fc domain, *i.e.*, a polypeptide comprising C-terminal constant regions of an immunoglobulin heavy chain, capable of stable self-association. For example, an Fc polypeptide of a dimeric IgA Fc comprises an IgA CH3 domain and may also comprise an IgA CH2 domain.

The Fc region of the IgA HetFc constructs is thus comprised of two Fc polypeptides: a first Fc polypeptide and a second Fc polypeptide, which may also be referred to herein as Chain A and Chain B. The terms first Fc polypeptide and second Fc polypeptide (or Chain A and Chain B) can be used interchangeably provided that each Fc region comprises one first Fc polypeptide and one
5 second Fc polypeptide (or one Chain A polypeptide and one Chain B polypeptide). The first and second Fc polypeptides meet at an “interface.” The “interface” comprises “contact” amino acid residues in the first Fc polypeptide that interact with one or more “contact” amino acid residues in the second Fc polypeptide.

The CH3 domain of an Fc region comprises two CH3 domain sequences, one from each of
10 the first and second Fc polypeptides of the dimeric Fc. The CH2 domain comprises two CH2 domain sequences, one from each of the first and second Fc polypeptides of the dimeric Fc.

The IgA HetFc constructs of the present disclosure comprise an IgA CH3 domain that has been asymmetrically modified to generate a heterodimer Fc region. Specifically, one or more amino acid mutations are introduced into the IgA CH3 domain in an asymmetric fashion resulting
15 in a heterodimer Fc. As used herein, an asymmetric amino acid mutation is a mutation resulting in an amino acid at a specific position in one Fc polypeptide being different from the amino acid in the second Fc polypeptide at the same position. This can be a result of mutation of only one of the two amino acids in the first and second Fc polypeptides or mutation of both amino acids to two different amino acids. The IgA HetFc constructs disclosed herein comprise one or more
20 asymmetric amino acid mutations in the CH3 domain.

The design of IgA HetFc regions from wild-type homodimers is illustrated by the concept of positive and negative design in the context of protein engineering by balancing stability vs. specificity, wherein mutations are introduced with the goal of driving heterodimer formation over homodimer formation when the polypeptides are expressed in cell culture conditions. These
25 general design concepts of positive and negative design are illustrated schematically in Fig. 1.

Negative design strategies maximize unfavorable interactions for the formation of homodimers, by either introducing bulky sidechains on one chain and small sidechains on the opposite, for example the knobs-into-holes strategy (Ridgway, *et al.*, 1996, *Protein Eng.*, 9(7):617-21; Atwell, *et al.*, 1997, *J Mol Biol.*, 270(1):26-35), or by electrostatic engineering that leads to

repulsion of homodimer formation, for example the electrostatic steering strategy developed by Gunasekaran, *et al.* 21010, *J Biol Chem.*, 285(25):19637-19646.

In positive design strategies, amino acid mutations are introduced into polypeptides to maximize favorable interactions within or between proteins. Such strategies assume that when
5 introducing multiple mutations that specifically stabilize the desired heterodimer while neglecting the effect on the homodimers, the net effect will be better specificity for the desired heterodimer interactions over the homodimers and hence a greater heterodimer specificity. It is understood in the context of protein engineering that positive design strategies optimize the stability of the desired protein interactions, but rarely achieve greater than 90% specificity (Havranek & Harbury,
10 2003, *Nat Struct Biol.*, 10(1):45-52; Bolon, *et al.*, 2005, *Proc Natl Acad Sci USA*, 102(36):12724-9; Huang, *et al.*, 2007, *Protein Sci.*, 16(12):2770-4).

Disclosed herein is a method for designing IgA Fc heterodimers that results in stable and highly specific heterodimer formation. This design method combines both negative and positive design strategies along with structural and computational modeling guided protein engineering
15 techniques (see Example 1 herein). The computational tools and structure-function analysis used in the method to generate the IgA HetFc constructs herein may include, for example, molecular dynamic analysis (MD), sidechain/backbone re-packing, Knowledge Base Potential (KBP), cavity (hydrophobic) packing analysis (LJ, AMBER, SASA, dSASA(carbon/all-atom)), electrostatic-GB calculations and coupling analysis. Computational methods for generating variant Fc regions are
20 also described in International Patent Publication Nos. WO 2012/058768, WO 2015/021540, WO 2014/201566, WO 2014/138994, WO 2014/026296, WO 2013/188984, WO 2013/138923, WO 2012/040833, WO 2012/037659 and WO 2011/063518.

In certain embodiments, the IgA HetFc constructs resulting from the implementation of this method have a purity of 70% or higher, and a stability (as measured by melting temperature
25 (T_m) of the CH3 domain) of 60°C or higher. In certain embodiments, the IgA HetFc constructs resulting from the implementation of this method have a purity of 70% or higher, and a stability CH3 domain T_m (stability) within 10°C of the CH3 domain T_m of the corresponding wild-type IgA Fc.

In accordance with the present disclosure, the amino acid mutations introduced into the
30 CH3 domain of the IgA Fc promote heterodimer formation as compared to homodimer formation.

This heterodimer formation as compared to homodimer formation is referred to herein interchangeably as “purity,” “specificity,” “heterodimer purity” or “heterodimer specificity.” It is understood that this heterodimer purity refers to the percentage of desired heterodimer formed as compared to homodimer species formed in solution under standard cell culture conditions.

5 Heterodimer purity is assessed prior to selective purification of the heterodimer species. In certain embodiments, purity may be assessed after an IgA affinity purification step that is not selective for homodimer/heterodimer purification (*e.g.*, after CaptureSelect™ IgA affinity purification). For instance, a heterodimer purity of 70% indicates that 70% of the Fc dimers isolated from cell culture after an IgA affinity purification step are the desired Fc heterodimer.

10 In certain embodiments, the IgA HetFc has a purity of greater than about 70%, for example, greater than about 71%, or greater than about 72%, or greater than about 73%, or greater than about 74%, or greater than about 75%, or greater than about 76%, or greater than about 77%, or greater than about 78%, or greater than about 79%. In some embodiments, the IgA HetFc has a purity of greater than about 80%, for example, greater than about 81%, or greater than about 82%,
15 or greater than about 83%, or greater than about 84%, or greater than about 85%, or greater than about 86%, or greater than about 87%, or greater than about 88%, or greater than about 89%. In some embodiments, the IgA HetFc has a purity of greater than about 90%, for example, greater than about 91%, or greater than about 92%, or greater than about 93%, or greater than about 94%, or greater than about 95%, or greater than about 96%, or greater than about 97%, or greater than
20 about 98%, or greater than about 99%.

In certain embodiments, the IgA HetFc has a purity of between about 70% and 100%. In some embodiments, the IgA HetFc has a purity of between about 70% and about 98%, or between about 70% and about 97%, or between about 70% and about 96%. In some embodiments, the IgA HetFc has a purity between about 72% and about 98%, or between about 74% and about 98%, or
25 between about 75% and about 98%.

The relative amounts of heterodimer and homodimer in a sample of IgA HetFc, and thus the purity of the IgA HetFc, may be determined using various techniques known in the art including, but not limited to, size-exclusion chromatography (SEC), non-reducing sodium dodecyl sulfate polyacrylamide gel electrophoresis (SDS-PAGE), non-reducing capillary electrophoresis
30 sodium dodecyl sulfate (CE-SDS) and liquid chromatography mass spectrometry (LC-MS).

In some embodiments, the IgA HetFc has a purity of greater than about 70% as determined by non-reducing CE-SDS. In some embodiments, the IgA HetFc has a purity of greater than about 70% as determined by non-reducing CE-SDS performed by running a High Throughput Protein Express assay using CE-SDS LabChip® GXII (Perkin Elmer, Waltham, MA). In some
5 embodiment, the IgA HetFc has a purity of greater than about 70% as determined by non-reducing CE-SDS performed as described in Example 4 herein.

In some embodiments, the IgA HetFc has a purity of greater than about 70% as determined by UPLC-SEC. In some embodiments, the IgA HetFc has a purity of greater than about 70% as determined by UPLC-SEC performed on an Agilent Technologies 1260 Infinity LC system using
10 an Agilent Technologies AdvanceBio SEC 300A column at 25°C. In some embodiments, the IgA HetFc has a purity of greater than about 70% as determined by UPLC-SEC performed as described in Example 4 herein.

The IgA HetFc constructs in accordance with the present disclosure are thermostable. In the context of the IgA HetFc constructs disclosed herein, “thermostable” means that the IgA HetFc
15 construct has a CH3 domain melting temperature (T_m) that is about 60°C or higher, or has a CH3 domain T_m that is within 10°C ($\pm 10^\circ\text{C}$) of the T_m of a corresponding wild-type IgA CH3 domain.

In certain embodiments, the IgA HetFc has a CH3 domain T_m of about 60°C or higher. In some embodiments, the IgA HetFc has a CH3 domain T_m of about 62°C or higher, for example, about 63°C or higher, or about 64°C or higher, or about 65°C or higher, or about 66°C or higher,
20 or about 67°C or higher, or about 68°C or higher, or about 69°C or higher. In some embodiments, the IgA HetFc has a CH3 domain T_m of about 70°C or higher, for example, about 71°C or higher, or about 72°C or higher, or about 73°C or higher.

In certain embodiments, the IgA HetFc has a CH3 domain T_m of between about 60°C and about 74°C. In some embodiments, the IgA HetFc has a CH3 domain T_m of between about 62°C
25 and about 74°C, or between about 63°C and about 74°C, or about 64°C and about 74°C, or between about 65°C and about 74°C.

In certain embodiments, the IgA HetFc construct has a CH3 domain T_m that is within 10°C ($\pm 10^\circ\text{C}$) of the T_m of a corresponding wild-type IgA CH3 domain. In some embodiments, the IgA HetFc construct has a CH3 domain T_m that is within 9°C ($\pm 9^\circ\text{C}$) of the T_m of a corresponding

wild-type IgA CH3 domain, for example, within 8°C ($\pm$ 8°C), or within 7°C ($\pm$ 7°C), or within 6°C ($\pm$ 6°C), or within 5°C ($\pm$ 5°C) of the T_m of a corresponding wild-type IgA CH3 domain.

In certain embodiments, the IgA HetFc construct has a CH3 domain T_m that is about 60°C or higher, or has a CH3 domain T_m that is within 10°C ($\pm$ 10°C) of the T_m of a corresponding wild-type IgA CH3 domain in the absence of any additional disulfide bonds in the CH3 domain. In certain embodiments, the IgA HetFc construct comprises one or more additional disulfide bonds in the CH3 domain as compared to wild-type IgA CH3 domain, but has a CH3 domain T_m that is about 60°C or higher, or has a CH3 domain T_m that is within 10°C ($\pm$ 10°C) of the T_m of a corresponding wild-type IgA CH3 domain in the absence of the one or more disulfide bonds.

Stability measured as T_m can be determined using techniques known in the art, such as by differential scanning calorimetry (DSC), differential scanning fluorimetry (DSF), circular dichroism spectroscopy (CD) and hydrogen exchange (HX). In certain embodiments, T_m is determined by DSC.

In certain embodiments, the IgA HetFc construct has a CH3 domain T_m that is about 60°C or higher, or has a CH3 domain T_m that is within 10°C ($\pm$ 10°C) of the T_m of a corresponding wild-type IgA CH3 domain, where the T_m is determined by DSC. In some embodiments, the IgA HetFc construct has a CH3 domain T_m that is about 60°C or higher, or has a CH3 domain T_m that is within 10°C ($\pm$ 10°C) of the T_m of a corresponding wild-type IgA CH3 domain, where the T_m is determined by DSC using a NanoDSC (TA Instruments, New Castle, DE, USA). In some embodiments, the IgA HetFc construct has a CH3 domain T_m that is about 60°C or higher, or has a CH3 domain T_m that is within 10°C ($\pm$ 10°C) of the T_m of a corresponding wild-type IgA CH3 domain, where the T_m is determined by DSC following the protocol described in Example 6 herein.

In certain embodiments, the IgA HetFc:

(i) has a purity of greater than about 70%, for example, greater than about 71%, or greater than about 72%, or greater than about 73%, or greater than about 74%, or greater than about 75%, or greater than about 76%, or greater than about 77%, or greater than about 78%, or greater than about 79%, or greater than about 80%, or greater than about 81%, or greater than about 82%, or greater than about 83%, or greater than about 84%, or greater than about 85%, or

greater than about 86%, or greater than about 87%, or greater than about 88%, or greater than about 89%, or greater than about 90%, or greater than about 91%, or greater than about 92%, or greater than about 93%, or greater than about 94%, or greater than about 95%, or greater than about 96%, or greater than about 97%, or greater than about 98%, or greater than about 99%, and

- 5 (ii) has a CH3 domain T_m that is between about 60°C and about 74°C, for example, between about 62°C and about 74°C, or between about 63°C and about 74°C, or about 64°C and about 74°C, or between about 65°C and about 74°C.

In certain embodiments, the IgA HetFc:

- 10 (i) has a purity of greater than about 70%, for example, greater than about 71%, or greater than about 72%, or greater than about 73%, or greater than about 74%, or greater than about 75%, or greater than about 76%, or greater than about 77%, or greater than about 78%, or greater than about 79%, or greater than about 80%, or greater than about 81%, or greater than about 82%, or greater than about 83%, or greater than about 84%, or greater than about 85%, or greater than about 86%, or greater than about 87%, or greater than about 88%, or greater than about 89%, or greater than about 90%, or greater than about 91%, or greater than about 92%, or greater than about 93%, or greater than about 94%, or greater than about 95%, or greater than about 96%, or greater than about 97%, or greater than about 98%, or greater than about 99%, and

- 15 (ii) has a CH3 domain T_m that is within 10°C ($\pm$ 10°C) of the T_m of a corresponding wild-type IgA CH3 domain, for example, within 9°C ($\pm$ 9°C), or within 8°C ($\pm$ 8°C), or within 7°C ($\pm$ 7°C), or within 6°C ($\pm$ 6°C), or within 5°C ($\pm$ 5°C) of the T_m of a corresponding wild-type IgA CH3 domain.

In certain embodiments, the IgA HetFc construct comprises one or more mutations to either eliminate binding to a binding target, or one or more mutations to introduce binding to the Neonatal Fc Receptor (FcRn), or both.

25 ***Modified CH3 Domains***

The IgA HetFc constructs described herein comprise a modified CH3 domain comprising asymmetric amino acid mutations. Specifically, the IgA HetFc constructs comprise two Fc polypeptides: a first Fc polypeptide that comprises a first CH3 domain sequence comprising one or more amino acid mutations and a second Fc polypeptide that comprises a second CH3 domain

sequence comprising one or more amino acid mutations, where at least one of the amino acid mutations in the first CH3 domain sequence is different to the amino acid mutations in the second CH3 domain sequence. The first and second CH3 domain sequences together form the modified CH3 domain. The amino acid mutations introduced asymmetrically into the first and second CH3 domain sequences result in formation of a heterodimeric Fc, rather than a homodimeric Fc, when the two CH3 domain sequences dimerize.

As noted above, an “asymmetric amino acid mutation” in this context refers to a mutation where an amino acid at a specific position in a first CH3 domain sequence is different from the amino acid in a second CH3 domain sequence at the same position. An asymmetric mutation can be a result of mutation of only one of the two amino acids at the same respective amino acid position in each CH3 domain sequence, or a different mutation of both amino acids at the same respective position on each of the first and second CH3 domain sequences. The CH3 domain sequences of an IgA HetFc can comprise one, or more than one, asymmetric amino acid mutation.

By employing the computational strategies disclosed herein, a core set of asymmetric mutations to the IgA CH3 domain were identified for providing the desired property of promoting formation of a heterodimer Fc. This core set of mutations is shown in Table 5.

Table 5: IgA HetFc Core Mutations

Chain	Position (IMGT)	Amino Acid Substitution
A	A6085Y	F, Y, M, W, H
	T6086	Y, F, M, W, H
B	W6081	T, L, A, V, I

In certain embodiments, the IgA HetFc construct comprises a modified CH3 domain in which the amino acid mutations in the first CH3 domain sequence comprise an amino acid substitution at position A6085Y selected from A6085YF, A6085YY, A6085YM, A6085YW and A6085YH, and an amino acid substitution at position T6086 selected from T6086Y, T6086F, T6086M, T6086W and T6086H; and the amino acid mutations in the second CH3 domain sequence comprise an amino acid substitution at position W6081 selected from W6081T, W6081L, W6081A, W6081V and W6081I.

In certain embodiments, the IgA HetFc construct comprises a modified CH3 domain comprising the amino acid mutations as set forth for any one of the designs shown in Table 7.

In some embodiments, the amino acid substitution at position A6085Y in the first CH3 domain sequence is A6085YF, A6085YY or A6085YW. In some embodiments, the amino acid substitution at position A6085Y in the first CH3 domain sequence is A6085YF or A6085YY.

In some embodiments, the amino acid substitution at position T6086 in the first CH3 domain sequence is T6086Y, T6086F or T6086W. In some embodiments, the amino acid substitution at position T6086 in the first CH3 domain sequence is T6086Y.

In some embodiments, the amino acid substitution at position W6081 in the second CH3 domain sequence is W6081T or W6081L.

In certain embodiments, the IgA HetFc construct comprises a modified CH3 domain in which the amino acid mutations in the first CH3 domain sequence comprise the amino acid substitutions A6085YF and T6086W, and the amino acid mutations in the second CH3 domain sequence comprise the amino acid substitution W6081T or W6081L.

In some embodiments, the IgA HetFc construct comprises a modified CH3 domain in which the amino acid mutations in the first CH3 domain sequence comprise the amino acid substitutions A6085YF and T6086W, and the amino acid mutations in the second CH3 domain sequence comprise the amino acid substitution W6081T.

In certain embodiments, the first CH3 domain sequence of the IgA HetFc construct may optionally further comprise one or more of:

(i) an amino acid substitution at position T6022 selected from T6022V, T6022I, T6022L and T6022A; and/or

(ii) an amino acid substitution at position H6005 selected from H6005Y, H6005F, H6005M and H6005W.

In certain embodiments, the second CH3 domain sequence of the IgA HetFc construct may optionally further comprise one or more of:

(i) an amino acid substitution at position H6005 selected from H6005Y, H6005F, H6005M and H6005W; and/or

(ii) an amino acid substitution at position L6079 selected from L6079V, L6079T, L6079A and L6079I; and/or

5 (iii) an amino acid substitution at position I6088 selected from I6088L, I6088A, I6088V and I6088T; and/or

(iv) an amino acid substitution at position L6007 selected from L6007F, L6007Y, L6007M, L6007W, L6007H and L6007I.

10 In certain embodiments, the IgA HetFc construct comprises a modified CH3 domain in which the amino acid mutations in the first CH3 domain sequence comprise an amino acid substitution at position A6085Y selected from A6085YF, A6085YY, A6085YM, A6085YW and A6085YH, and an amino acid substitution at position T6086 selected from T6086Y, T6086F, T6086M, T6086W and T6086H; and the amino acid mutations in the second CH3 domain sequence comprise an amino acid substitution at position W6081 selected from W6081T,
15 W6081L, W6081A, W6081V and W6081I; and

(i) the amino acid mutations in the first CH3 domain sequence further comprise an amino acid substitution at position T6022 selected from T6022V, T6022I, T6022L and T6022A; and/or

(ii) the amino acid mutations in the first CH3 domain sequence further comprise an amino acid substitution at position H6005 selected from H6005Y, H6005F, H6005M and H6005W;
20 and/or

(iii) the amino acid mutations in the second CH3 domain sequence further comprise an amino acid substitution at position H6005 selected from H6005Y, H6005F, H6005M and H6005W; and/or

(iv) the amino acid mutations in the first CH3 domain sequence further comprise an amino
25 acid substitution at position H6005 selected from H6005Y, H6005F, H6005M and H6005W, and the amino acid mutations in the second CH3 domain sequence further comprise an amino acid substitution at position H6005 selected from H6005Y, H6005F, H6005M and H6005W; and/or

(v) the amino acid mutations in the second CH3 domain sequence further comprise an amino acid substitution at position L6079 selected from L6079V, L6079T, L6079A and L6079I; and/or

(vi) the amino acid mutations in the second CH3 domain sequence further comprise an amino acid substitution at position I6088 selected from I6088L, I6088A, I6088V and I6088T; and/or

(vii) the amino acid mutations in the second CH3 domain sequence further comprise an amino acid substitution at position L6007 selected from L6007F, L6007Y, L6007M, L6007W, L6007H and L6007I.

10 In some embodiments, the amino acid mutation at position T6022 in the first CH3 domain sequence is selected from T6022V, T6022I and T6022L.

In some embodiments, the amino acid mutation at position H6005 in the first CH3 domain sequence is H6005Y.

15 In some embodiments, the amino acid mutation at position H6005 in the second CH3 domain sequence is H6005Y.

In some embodiments, the amino acid mutation at position L6079 in the second CH3 domain sequence is L6079V or L6079T.

In some embodiments, the amino acid mutation at position I6088 in the second CH3 domain sequence is I6088L.

20 In some embodiments, the amino acid mutation at position L6007 in the second CH3 domain sequence is L6007F.

In certain embodiments, the modified CH3 domain of the IgA HetFc construct further comprises amino acid substitutions to introduce cysteine residues capable of forming a disulfide bond. In some embodiments, the modified CH3 domain of the IgA HetFc construct further comprises two cysteine substitutions that introduce one disulfide bond into the CH3 domain. In some embodiments, the modified CH3 domain of the IgA HetFc construct further comprises four

cysteine substitutions that introduce two disulfide bonds into the CH3 domain. In some embodiments, the cysteine substitutions comprise the mutation H6005C in one CH3 domain sequence and the mutation P6010C in the other CH3 domain sequence. In some embodiments, the cysteine substitutions comprise the mutations H6005C and P6010C in one CH3 domain sequence
 5 and the mutations P6010C and H6005C in the other CH3 domain sequence.

Accordingly, in certain embodiments, the IgA HetFc construct comprises a modified CH3 domain comprising either one or two introduced (*i.e.* non-natural) disulfide bonds in which:

- (i) one CH3 domain sequence comprises the mutation H6005C and the other CH3 domain sequence comprises the mutation P6010C; or
- 10 (ii) one CH3 domain sequence comprises the mutations H6005C and P6010C, and the other CH3 domain sequence comprises the mutations P6010C and H6005C.

In certain embodiments, the IgA HetFc construct comprises a modified CH3 domain in which the amino acid mutations in the first CH3 domain sequence comprise an amino acid substitution at position A6085Y selected from A6085YF, A6085YY, A6085YM, A6085YW and
 15 A6085YH, and an amino acid substitution at position T6086 selected from T6086Y, T6086F, T6086M, T6086W and T6086H; and the amino acid mutations in the second CH3 domain sequence comprise an amino acid substitution at position W6081 selected from W6081T, W6081L, W6081A, W6081V and W6081I; where

(i) the first CH3 domain of the IgA HetFc construct may optionally further comprise an
 20 amino acid substitution at position T6022 selected from T6022V, T6022I, T6022L and T6022A; and

(ii) the second CH3 domain of the IgA HetFc construct may optionally further comprise one or more of: an amino acid substitution at position L6079 selected from L6079V, L6079T, L6079A and L6079I; and/or an amino acid substitution at position I6088 selected from I6088L,
 25 I6088A, I6088V and I6088T; and/or an amino acid substitution at position L6007 selected from L6007F, L6007Y, L6007M, L6007W, L6007H and L6007I, and

(iii) the modified CH3 domain comprises either one or two introduced (*i.e.*, non-natural) disulfide bonds as described above.

In certain embodiments, the IgA HetFc construct comprises a modified CH3 domain in which the amino acid mutations in the first CH3 domain sequence comprise an amino acid substitution at positions A6085Y and T6086, and the amino acid mutations in the second CH3 domain sequence comprise an amino acid substitution at position W6081 and optionally an amino acid mutation at one or both of positions L6079 and I6088, where

the amino acid substitution at position A6085 is selected from A6085YF, A6085YY, A6085YM, A6085YW and A6085YH;

the amino acid substitution at position T6086 is selected from T6086Y, T6086F, T6086M, T6086W and T6086H;

the amino acid substitution at position W6081 is selected from W6081T, W6081L, W6081A, W6081V and W6081I;

the optional amino acid substitution at position L6079 is selected from L6079V, L6079T, L6079A and L6079I; and

the optional amino acid substitution at position I6088 is selected from I6088L, I6088A, I6088V and I6088T.

In certain embodiments, the IgA HetFc construct comprises a modified CH3 domain comprising the amino acid mutations as set forth for any one of the designs shown in Table 8. In certain embodiments, the IgA HetFc construct comprises a modified CH3 domain comprising the amino acid mutations as set forth for any one of the designs shown in Table 9. In certain embodiments, the IgA HetFc construct comprises a modified CH3 domain comprising the amino acid mutations as set forth for any one of the designs shown in Table 10.

In some embodiments, the amino acid substitution at position A6085Y is A6085YF, A6085YY or A6085YW. In some embodiments, the amino acid substitution at position A6085Y is A6085YF or A6085YY. In some embodiments, the amino acid substitution at position T6086 is T6086Y, T6086F or T6086W. In some embodiments, the amino acid substitution at position

T6086 is T6086Y. In some embodiments, the amino acid substitution at position W6081 is W6081T or W6081L. In some embodiments, the optional amino acid substitution at position L6079 is L6079V or L6079T. In some embodiments, the optional amino acid substitution at position I6088 is I6088L.

5 In some embodiments, the the IgA HetFc construct comprises a modified CH3 domain in which the amino acid mutations in the first CH3 domain sequence comprise an amino acid substitution at positions A6085Y and T6086, and the amino acid mutations in the second CH3 domain sequence comprise an amino acid substitution at position W6081 and optionally at one or both of positions L6079 and I6088, as described in any one of the embodiments above, and either
10 the first CH3 domain sequence or the second CH3 domain sequence or both the first and second CH3 domain sequences further comprise an amino acid substitution at position H6005 selected from H6005Y, H6005F, H6005M and H6005W. In some embodiments, either the first CH3 domain sequence or the second CH3 domain sequence or both the first and second CH3 domain sequences further comprise the amino acid substitution H6005Y.

15 In certain embodiments, the IgA HetFc construct comprises a modified CH3 domain in which the amino acid mutations in the first CH3 domain sequence comprise an amino acid substitution at positions A6085Y and T6086, and the amino acid mutations in the second CH3 domain sequence comprise an amino acid substitution at position W6081 and optionally at one or more of positions L6007, L6079 and I6088, where

20 the amino acid substitution at position A6085 is selected from A6085YF, A6085YY, A6085YM, A6085YW and A6085YH;

 the amino acid substitution at position T6086 is selected from T6086Y, T6086F, T6086M, T6086W and T6086H;

 the amino acid substitution at position W6081 is selected from W6081T, W6081L,
25 W6081A, W6081V and W6081I;

 the optional amino acid substitution at position L6007 is selected from L6007F, L6007Y, L6007M, L6007W, L6007H and L6007I;

the optional amino acid substitution at position L6079 is selected from L6079V, L6079T, L6079A and L6079I; and

the optional amino acid substitution at position I6088 is selected from I6088L, I6088A, I6088V and I6088T.

5 In some embodiments, the amino acid substitution at position A6085Y is A6085YF, A6085YY or A6085YW. In some embodiments, the amino acid substitution at position A6085Y is A6085YF or A6085YY. In some embodiments, the amino acid substitution at position T6086 is T6086Y, T6086F or T6086W. In some embodiments, the amino acid substitution at position T6086 is T6086Y. In some embodiments, the amino acid substitution at position W6081 is W6081T or W6081L. In some embodiments, the amino acid substitution at position L6007 is L6007F. In some embodiments, the amino acid substitution at position L6079 is L6079V or L6079T. In some embodiments, the amino acid substitution at position I6088 is I6088L.

15 In some embodiments, the the IgA HetFc construct comprises a modified CH3 domain in which the amino acid mutations in the first CH3 domain sequence comprise an amino acid substitution at positions A6085Y and T6086, and the amino acid mutations in the second CH3 domain sequence comprise an amino acid substitution at position W6081 and optionally at one or more of positions L6007, L6079 and I6088, as described in any one of the embodiments above, and either the first CH3 domain sequence or the second CH3 domain sequence or both the first and second CH3 domain sequences further comprise an amino acid substitution at position H6005 selected from H6005Y, H6005F, H6005M and H6005W. In some embodiments, either the first CH3 domain sequence or the second CH3 domain sequence or both the first and second CH3 domain sequences further comprise the amino acid substitution H6005Y.

25 In certain embodiments, the IgA HetFc construct comprises a modified CH3 domain in which the amino acid mutations are the amino acid substitutions listed in Table 6 for any one of variants v32516, v32517, v32518, v32521, v33330, v33331, v33332, v33333, v33334, v34688, v34689 or v34690. In some embodiments, the IgA HetFc construct comprises a modified CH3 domain in which the amino acid mutations are the amino acid substitutions listed in Table 6 for any one of variants v32521, v33333 or v33334.

Table 6: Illustrative IgA HetFc Variants

Variant	Design	CH3 Domain Sequence Mutations	
		Chain A	Chain B
32516	Steric 1	A6085YY_T6086L	L6079T_W6081L_I6088L
32517	Steric 2	A6085YY_T6086Y	L6079T_W6081L_I6088L
32518	Steric 3	A6085YF_T6086Y	L6079V_W6081L_I6088L
32521	Steric 6	A6085YF_T6086Y	L6079V_W6081T_I6088L
33330	Steric 7	T6022V_A6085YF_T6086Y	L6079V_W6081T_I6088L
33331	Steric 8	T6022L_A6085YF_T6086Y	L6079V_W6081T_I6088L
33332	Steric 9	T6022I_A6085YF_T6086Y	L6079V_W6081T_I6088L
33333	Steric 10	A6085YF_T6086Y	L6007F_L6079V_W6081T_I6088L
33334	Steric 11	H6005Y_A6085YF_T6086Y	H6005Y_L6079V_W6081T_I6088L
34688	Steric 6 + Disulfide	H6005C_A6085YF_T6086Y	P6010C_L6079V_W6081T_I6088L
34689	Steric 6 + Disulfide	P6010C_A6085YF_T6086Y	H6005C_L6079V_W6081T_I6088L
34690	Steric 6 + 2x Disulfide	H6005C_P6010C_A6085YF_ T6086Y	H6005C_P6010C_L6079V_W6081T_ I6088L

In certain embodiments, the IgA HetFc construct of the present disclosure comprises a modified CH3 domain having an amino acid sequence as set forth in the CH3 domain sequence comprised by SEQ ID NOs. 15 and 20; SEQ ID NOs. 16 and 20; SEQ ID NOs. 17 and 21; SEQ ID NOs. 17 and 23; SEQ ID NOs. 24 and 23; SEQ ID NOs. 25 and 23; SEQ ID NOs. 26 and 23; SEQ ID NOs. 17 and 27; SEQ ID NOs. 28 and 29; SEQ ID NOs. 30 and 31; SEQ ID NOs. 32 and 33; or SEQ ID NOs. 34 and 35. IgA CH2 and CH3 domains can readily be identified within the noted SEQ ID NOs by comparison with the IgA sequences provided in Tables 2 and 4 herein.

Modified CH2 Domains

In certain embodiments, the IgA HetFc construct further comprises a modified CH2 domain comprising one or more amino acid mutations, for example, mutations that alter one or more functions of the CH2 domain. Illustrative mutations include, but are not limited to, mutations at position C5092 (which attaches to the secretory compartment in WT IgA) and mutations at the glycosylation site at position N5120.

In certain embodiments, the modified CH2 comprises a mutation at position C5092. In some embodiments, the mutation at position C5092 is an amino acid substitution selected from C5092S, C5092A, C5092T, C5092N and C5092Q. In some embodiments, the mutation at position C5092 is C5092S. In certain embodiments, the modified CH2 domain comprises a mutation at the glycosylation site at position N5120, where the mutation prevents glycosylation. In some embodiments, the mutation at position N5120 is the amino acid substitution N5120T.

In certain embodiments, the HetFc IgA construct comprises a modified CH2 domain that comprises a mutation at one or more of positions C5092, N5120, I5121 and T5122. In some embodiments, the HetFc IgA construct comprises a modified CH2 domain that comprises one or more amino acid substitutions selected from C5092S, N5120T, I5121L and T5122S. In some embodiments, the HetFc IgA construct comprises a modified CH2 domain that comprises the amino acid substitutions C5092S, N5120T, I5121L and T5122S.

In some embodiments, the modified CH2 domain comprises asymmetric amino acid substitutions in the first and/or second Fc polypeptide chain. In some embodiments, the modified CH2 domain comprises asymmetric amino acid substitutions that allow one chain of the CH2 domain to selectively bind an Fc receptor. In certain embodiments, the modified CH2 domain comprises asymmetric amino acid mutations that promote selective binding to Fc α receptors.

One skilled in the art will understand that the IgA HetFc constructs of the present disclosure may have altered ligand (*e.g.* Fc α RI) binding properties (examples of binding properties include but are not limited to, binding specificity, equilibrium dissociation constant (K_D), dissociation and association rates (k_{off} and k_{on} respectively), binding affinity and/or avidity) and that certain alterations may be more or less desirable depending on the end use of the IgA HetFc construct. It is well known in the art that the equilibrium dissociation constant (K_D) is defined as k_{off}/k_{on} . For

certain applications, it is generally understood that an IgA HetFc construct with a low K_D may be preferable to an IgA HetFc construct with a high K_D . However, in some instances the value of the k_{on} or k_{off} may be more relevant than the value of the K_D . One skilled in the art can determine which kinetic parameter is most important for a given IgA HetFc construct application.

5 In certain embodiments, the IgA HetFc comprises substitutions that reduce or eliminate binding to the Fc α receptors (see for example, Carayannopoulos, 1996, *JEM*, 183:1579-1586; Bakema, 2006, *J Immunol*, 176:3603-3610, <https://www.pnas.org/content/115/38/E8882>). IgA HetFc constructs with reduced or eliminated binding to the Fc α receptors can be useful, for example, in a setting in which activation of neutrophils is not desired, such as in a setting of
10 cytokine release syndrome where the IgA HetFc construct can bind and clear cytokines in a subject in need thereof while avoiding activation of neutrophils. An IgA HetFc with only one Fc α RI binding site can be useful to investigate the dependency of IgA-dependent neutrophil activation on the valency of Fc α RI engagement.

 An IgA HetFc can be useful to create a molecule capable of binding to Fc α RI as well as
15 the Neonatal Fc Receptor (FcRn) in a single Fc. Since binding sites for Fc α RI and FcRn are located in structurally equivalent regions of IgA and IgG, respectively (Kelton, W. *et al.*, 2014, *Chem Biol* **21**:1603-1609, <https://www.sciencedirect.com/science/article/pii/S1074552114004098?via%3Dihub>), their
introduction on a chain in an Fc is mutually exclusive and a heterodimeric Fc is needed. An IgA
20 HetFc with an FcRn binding site grafted onto one chain is useful as it is able to activate neutrophils via the Fc α RI as well as having an increased half-life due to the introduction of the interaction with FcRn, thus addressing the known half-life limitation when using IgA for the therapeutic benefit.

 An IgA HetFc can further be useful to create a molecule capable of binding to receptors or
25 purification resins or detection molecules in a monovalent fashion. Likewise, it can be useful to create IgA HetFc-based molecules with combinations of receptor binding sites, purification or detection sites that would otherwise lie in mutually exclusive regions of the Fc. One such example would be to equip previously described IgG/A hybrid molecules (Kelton, W. *et al.*, 2014, *Chem Biol* **21**:1603-1609, Borrok, M. J. *et al.*, 2015, *mAbs*, **7**:4, 743-751, DOI:

10.1080/19420862.2015.1047570) with differing Fc γ receptor binding sites on the two chains of the Fc to create an Fc γ receptor binding profile that has a unique biological activity. Receptor binding sites include Fc α R, FcRn, Fc γ receptors, C1q, Secretory Component, SSL7, Streptococcal IgA binding protein, *N. meningitidis* type 2 IgA1 protease, *H. influenzae* type 2 IgA1 protease.

5 Purification and detection sites include protein A, polyhistidine tags, FLAG tags and Myc tags. Introducing a protein A binding site, for example, can be used to purify the IgA HetFc based molecule using techniques established and widely used for IgG based therapeutics that are unsuitable for a WT IgA Fc due to the lack of protein A binding.

10 **Target Binding Domains**

The IgA HetFc described herein may function as a heterodimeric scaffold to which a variety of different binding domains or other moieties can be fused. In certain embodiments, the present disclosure relates to IgA HetFc constructs which are IgA HetFc binding units comprising one or more target binding domains fused to the IgA HetFc. Target binding domains for use in

15 the IgA HetFc binding units include various proteinaceous moieties that specifically bind to a target of interest. "Specifically binds," in this context, means that the binding is selective for the desired target and can be distinguished from unwanted or non-specific interactions. The ability of a binding domain to specifically bind to a target can be measured by various techniques familiar to one of skill in the art, *e.g.* enzyme-linked immunosorbent assay (ELISA), surface plasmon resonance (SPR) technique (*e.g.* analyzed on a BIAcore™ instrument) (Liljeblad, *et al.*, 2000, *Glyco J.*, 17:323-329) or traditional binding assays (Heeley, 2002, *Endocr Res.*, 28:217-229).

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Examples of target binding domains include, but are not limited to, receptors, receptor fragments (such as extracellular portions), ligands, cytokines and antigen-binding fragments of antibodies. In certain embodiments, the IgA HetFc binding unit comprises one or more binding

25 domains that are antigen-binding domains, for example, receptor or antibody fragments.

In certain embodiments, the IgA HetFc binding unit comprises one or more target binding domains that are antigen-binding antibody fragments. Such antigen-binding antibody fragments may be derived from IgA or from other antibody isotypes such as IgG, IgM, IgD, or IgE. In some embodiments, the antigen-binding antibody fragments may be synthetic, chimeric or humanized.

Antigen-binding antibody fragments include, but are not limited to, variable or hypervariable regions of light and/or heavy chains of an antibody (V_L , V_H), variable fragments (Fv), Fab' fragments, F(ab')₂ fragments, Fab fragments, single chain antibodies (scAb), single chain variable regions (scFv), VHH, complementarity determining regions (CDRs), domain antibodies (dAbs),
5 single domain heavy chain immunoglobulins and single domain light chain immunoglobulins. Antigen-binding sites of an antibody typically contain six CDRs which contribute in varying degrees to the affinity of the binding site for antigen. There are three heavy chain variable domain CDRs (CDRH1, CDRH2 and CDRH3) and three light chain variable domain CDRs (CDRL1, CDRL2 and CDRL3). The extent of CDR and framework regions (FRs) is determined by
10 comparison to a compiled database of amino acid sequences in which those regions have been defined according to variability among the sequences and/or structural information from antibody /antigen complexes. Also included within the scope of this disclosure are functional antigen-binding sites comprised of fewer CDRs (*i.e.* where binding specificity is determined by three, four or five CDRs). Less than a complete set of 6 CDRs may be sufficient for binding to some binding
15 targets. Thus, in some instances, the CDRs of a V_H or a V_L domain alone will be sufficient for specific binding. Furthermore, certain antibodies might have non-CDR-associated binding sites for an antigen. Such binding sites are specifically contemplated herein. Antigen-binding antibody fragments may be from a single species or may be chimeric or humanized.

In certain embodiments, the binding domain comprises an antigen-binding receptor
20 fragment, for example, an MHC-peptide complex-binding fragment of a T cell receptor (TCR). TCR fragments for use in the IgA HetFc constructs herein may comprise antigen-binding fragments of $\alpha\beta$ TCR or $\gamma\delta$ TCR heterodimers. In some embodiments, IgA HetFc constructs herein may comprise an antigen-binding fragment of a $\alpha\beta$ TCR heterodimer that comprises at least a TCR α chain variable domain and a TCR β chain variable domain such that the $\alpha\beta$ TCR fragment is able
25 to bind to its cognate MHC/peptide. In some embodiments, the antigen-binding TCR fragment is a single-chain TCR (scTCR) or a soluble TCR domain (see, for example, International Patent Publication Nos. WO 1999/018129 and WO 2009/117117). Other TCR antigen-binding fragments are known in the art and are described, for example, in Wilson & Garcia, 1997, *Curr. Opin. Struct. Biol.* 7:839–848; van Boxel, *et al.*, 2009, *J. Immunol. Methods*, 350:14–21; Stone, *et al.*, 2012,
30 *Methods Enzymol.*, 503:189–222 and Li, *et al.*, 2005, *Nat. Biotechnol.*, 23:349–354).

Other target binding domains include immunomodulatory Ig domains, non-Ig viral receptor decoys, non-immunoglobulin proteins that mimic antibody binding and structures such as anticalins, affilins, affibody molecules, affimers, affitins, alphabodies, avimers, DARPin, fynomers, kunitz domain peptides, monobodies, and binding domains based on other engineered scaffolds such as SpA, GroEL, fibronectin, lipocalin and CTLA4 scaffolds. Further examples of target binding domains include a ligand for a desired receptor, a ligand-binding portion of a receptor, a lectin and peptides that specifically bind to one or more target antigens.

In certain embodiments, the IgA HetFc binding unit comprises a binding domain that comprises an antigen-binding fragment of a therapeutic or diagnostic antibody. In some embodiments, a target binding domain comprised by the IgA HetFc binding unit specifically binds to a cell surface molecule, such as a protein, lipid or polysaccharide. In some embodiments, a binding domain comprised by the IgA HetFc binding unit specifically binds a target antigen expressed on a tumor cell, virally infected cell, bacterially infected cell, damaged red blood cell, arterial plaque cell, inflamed tissue cell or fibrotic tissue cell.

In certain embodiments, the target binding domain comprised by the IgA HetFc binding unit is an immune response modulator. In certain embodiments, the target binding domain comprised by the IgA HetFc binding unit specifically binds a cytokine receptor. In certain embodiments, the target binding domain comprised by the IgA HetFc binding unit specifically binds to a tumor antigen. In certain embodiments, the target binding domain comprised by the IgA HetFc binding unit is, or specifically binds to, an immune checkpoint protein.

As a result of the heterodimeric nature of the IgA HetFc, different binding domains can be fused to one or both chains of the Fc heterodimer to generate a wide range of functional multispecific IgA HetFc binding units. Non-limiting illustrative examples of such multispecific IgA HetFc binding units are shown in Fig. 7. In addition, higher order IgA HetFc multimers may be generated by joining multiple IgA HetFc binding units together, for example, by joining with a J chain. Multimeric IgA structures typically comprise an IgA dimer in a tail-to-tail configuration linked by a J chain and tailpiece-to-tailpiece interactions, with additional IgA monomers linked to the dimer just via tailpiece-to-tailpiece mediated disulfide bonds and no direct contacts to the J chain in the complex (see, for example, Kumar, *et al.*, 2020, *Science*, 10.1126/science.aaz5807). Non-limiting illustrative examples of such IgA HetFc multimers are shown in Fig. 8.

The IgA HetFc binding units according to the present disclosure may be monospecific, bispecific, trispecific, tetraspecific or have greater multispecificity. Multispecific IgA HetFc binding units may specifically bind to different epitopes of a desired target molecule or may specifically bind to different target molecules or may bind a target molecule as well as a
5 heterologous epitope, such as a heterologous polypeptide or solid support material.

In some embodiments, the IgA HetFc binding unit comprises two or more target binding domains each having a different binding specificity. In this regard, the binding domains may bind the same target but bind to different epitopes on the same target or they may each bind to a different target.

10 In certain embodiments, the IgA Fc binding unit comprises a target binding domain fused to one Fc polypeptide (*e.g.*, Chain A) and either no target binding domain or a different target binding domain fused to the other Fc polypeptide (*e.g.*, Chain B). Thus, Chain A and Chain B of the IgA HetFc differ in their Fc regions (as described above, having mutations in the CH3 domain to drive heterodimer formation) and may also differ in their binding specificities.

15 The term IgA HetFc binding unit is used herein to refer to an IgA HetFc construct having a heterodimer Fc as described herein (*e.g.*, a pair of IgA Fc polypeptides each comprising at least an IgA CH3 domain), where at least one IgA Fc polypeptide is fused to a target binding domain. In certain embodiments, both Fc polypeptides of the IgA HetFc construct are each independently fused to a target binding domain. As shown in Fig. 7, an IgA HetFc binding unit may comprise
20 from one to four target binding domains fused to the HetFc in a variety of different configurations. In certain embodiments, additional target binding domains may be included in the IgA HetFc binding unit by fusing one or more additional target binding domains to a target binding domain fused to the IgA HetFc.

25 IgA HetFc binding units in accordance with the present disclosure may be derived from a single species, or may be chimeric or humanized. For example, the IgA Fc polypeptides may be human and the target binding domains may be derived from another species, such as another mammal (*e.g.*, mouse, rat, rabbit, non-human primate, or the like).

Fig. 7 is a diagram showing illustrative configurations of IgA HetFc constructs comprising target binding domains (IgA HetFc binding units). In certain embodiments, an IgA HetFc binding

unit comprises one, two, three or four target binding domains fused the IgA HetFc. In some embodiments, an IgA HetFc binding unit has a one-armed format in that one Fc polypeptide is fused to a target binding domain and the other Fc polypeptide is not.

In some embodiments, the IgA HetFc binding unit comprises one target binding domain fused to the N-terminal end of one Fc polypeptide (*e.g.*, Chain A) and one target binding domain fused to the N-terminal end of the other Fc polypeptide (*e.g.*, Chain B) (see, for example, Fig. 7B, Fig. 7C). In some embodiments, the IgA HetFc binding unit comprises one target binding domain fused to the N-terminal end of one Fc polypeptide (*e.g.* Chain A) and one target binding domain fused to the C-terminal end of the other Fc polypeptide (*e.g.*, Chain B) (see, for example, Fig. 7F). In some embodiments, the IgA HetFc binding unit comprises one target binding domain fused to the C-terminal end of one Fc polypeptide (*e.g.*, Chain A) and one target binding domain fused to the C-terminal end of the other Fc polypeptide (*e.g.* Chain B) (see, for example, Fig. 7D). In some embodiments, the IgA HetFc binding unit comprises target binding domains fused to both ends of one Fc polypeptide (*e.g.* to the N-terminal end and to the C-terminal end of Chain A) (see, for example, Fig. 7E). In some embodiments, the IgA HetFc binding unit comprises target binding domains fused to both ends of one Fc polypeptide (*e.g.* to the N-terminal end and to the C-terminal end of Chain A), and a target binding domain fused to one end (either the N-terminal or C-terminal end) of the other Fc polypeptide (*e.g.* Chain B) (see, for example, Fig. 7G). In some embodiments, the IgA HetFc binding unit comprises target binding domains fused to both ends of one Fc polypeptide (*e.g.* to the N-terminal end and to the C-terminal end of Chain A), and target binding domains fused to both ends of the other Fc polypeptide (*e.g.* to the N-terminal end and to the C-terminal end of Chain B) (see, for example, Fig. 7H). Other configurations including additional target binding units fused in tandem are also contemplated.

In some embodiments, the IgA HetFc binding unit is bispecific, *i.e.* comprises two target binding domains, each having a different specificity. In some embodiments, the IgA HetFc binding unit is trispecific, *i.e.* comprises three target binding domains, each having a different specificity. In some embodiments, the IgA HetFc binding unit is tetraspecific, *i.e.* comprises four target binding domains, each having a different specificity. Greater specificities may be achievable by including some target binding domains in tandem. In some embodiments, at least some of the target binding domains in bispecific, trispecific or tetraspecific IgA HetFc binding units bind to

the same target but different epitopes on the target. In some embodiments, at least some of the target binding domains in bispecific, trispecific or tetraspecific IgA HetFc binding units bind to different target molecules.

It should be noted that the specificity of an IgA HetFc binding unit does not necessarily correlate to the number of target binding domains it contains, for example, an IgA HetFc binding unit may comprise two target binding domains but still be monospecific if both target binding domains bind the same target.

In certain embodiments, the present disclosure provides for higher order IgA HetFc multimers that comprise two or more IgA HetFc binding units. In certain embodiments, higher order IgA HetFc multimers of the present disclosure comprise two, four or five IgA HetFc binding units. In certain embodiments, at least two of the IgA HetFc binding units comprised by an IgA HetFc multimer are connected through their tailpieces by a J chain. In the IgA HetFc multimers disclosed herein, the J chain may be a full-length native J chain, but may also contain amino acid alterations, such as substitutions, insertions, deletions, truncations, specifically including J chain fragments, as long as the J chain remains functional. In certain embodiments, the J chain comprised by an IgA HetFc multimer is a modified J chain as described in International Patent Publication No. WO 2015/153912. In certain embodiments, the J chain has the amino acid sequence set forth in SEQ ID NO:48.

As noted above, the IgA HetFc binding units described herein allow for the assembly of IgA HetFc multimers, which are multimeric and multispecific. IgA HetFc multimers have the potential for fine-tuning avidity effects that can increase the apparent affinity of low-affinity target binding domains and increase clustering and specificity and the associated functionality associated with increased valency. Fig. 8 is a diagram showing illustrative configurations of IgA HetFc multimers.

In some embodiments, an IgA HetFc multimer may be “dimeric” in that it comprises two IgA HetFc binding units joined by a J chain. The IgA HetFc binding units may be monospecific, or they may be bispecific (see, for example, Fig. 8A), or a combination thereof. In some embodiments, a dimeric IgA HetFc multimer of the present disclosure comprises two bispecific IgA HetFc binding units, each binding unit having the same binding specificity (AB, AB). In some embodiments, a dimeric IgA HetFc multimer of the present disclosure comprises two bispecific

IgA HetFc binding units, where at least one of the two binding units has a different binding specificity (e.g. AB, BC or AC, BC or AB, CD). Thus, in certain embodiments, each of the two binding units has two specificities, which may be the same (AB, AB) or different (AB, CD or AB, AC, for example).

5 In some embodiments, the IgA HetFc multimer may be “tetrameric” in that it comprises four IgA HetFc binding units, at least two of which are joined by a J chain. The IgA HetFc binding units may be monospecific, or they may be bispecific (see, for example, Fig. 8B), or combinations thereof. In some embodiments, a tetrameric IgA HetFc multimer of the present disclosure comprises four bispecific binding units, each binding unit having the same binding specificity (AB,
10 AB, AB, AB). Tetrameric IgA HetFc multimers comprising IgA HetFc binding units that are either monospecific or bispecific and have different binding specificities are also contemplated in some embodiments.

In some embodiments, the IgA HetFc multimer may be “pentameric” in that it comprises five IgA HetFc binding units, at least two of which are joined by a J chain. The IgA HetFc binding
15 units may be monospecific, or they may be bispecific (see, for example, Fig. 8C), or combinations thereof. In some embodiments, a pentameric IgA HetFc multimer of the present disclosure comprises five bispecific binding units, each binding unit having the same binding specificity (AB, AB, AB, AB, AB). Pentameric IgA HetFc multimers comprising IgA HetFc binding units that are either monospecific or bispecific and have different binding specificities are also contemplated in
20 some embodiments.

The term “valent,” as used herein, denotes the presence of a specified number of binding sites in the IgA HetFc constructs. For example, the terms “bivalent,” “tetravalent,” “hexavalent,” “octavalent” and “decavalent” denote the presence of two binding sites, four binding sites, six binding sites, eight binding sites and ten binding sites, respectively. Thus, in reference to Fig. 8
25 herein, the dimeric IgA HetFc multimer shown in Fig. 8A, comprising two bispecific binding units, is tetravalent; the tetrameric IgA HetFc multimer shown in Fig. 8B is octavalent (*i.e.* comprises four bispecific binding units), and the pentameric IgA HetFc multimer shown in Fig. 8C is decavalent (*i.e.* comprises five bispecific binding units). Similarly, in reference to Fig. 7, the IgA HetFc binding units shown in Fig. 7B, C, D, E and F are bivalent, the IgA HetFc binding unit
30 shown in Fig. 7G is trivalent, and the IgA HetFc binding unit shown in Fig. 7H is tetravalent.

In the IgA HetFc binding units and multimers, different components or domains may be fused directly to one another (*i.e.* without a linker) or one or more of the components or domains may be fused to an adjoining component or domain indirectly via a peptide linker. Peptide linkers suitable for linking components of multi-component proteins are well-known in the art and are selected to allow arrangement of the components such that each may still carry out its intended function.

Peptide linkers are typically between about 2 and about 150 amino acids in length. Useful linkers include glycine-serine (GlySer) linkers, which are well-known in the art and comprise glycine and serine units combined in various orders. Examples include, but are not limited to, (GS)_n, (GSGGS)_n, (GGGS)_n and (GGGGS)_n, where n is an integer of at least one, typically an integer between 1 and about 10, for example, between 1 and about 8, between 1 and about 6, or between 1 and about 5; (Gly₃Ser)_n(Gly₄Ser)₁, (Gly₃Ser)₁(Gly₄Ser)_n, (Gly₃Ser)_n(Gly₄Ser)_n, or (Gly₄Ser)_n, wherein n is an integer of 1 to 5. Other useful linkers include sequences derived from immunoglobulin hinge sequences. The linker may comprise all or part of a hinge sequence from any one of the four IgG classes or from a TCR and may optionally include additional sequences. For example, the linker may include a portion of an immunoglobulin hinge sequence and a glycine-serine sequence. A non-limiting example is a linker that includes approximately the first 15 residues of the IgG1 hinge followed by a GlySer linker sequence, such as those described above, that is about 10 amino acids in length.

Conjugates

Certain embodiments of the present disclosure relate to conjugates comprising an IgA HetFc construct as described herein (*e.g.* an IgA HetFc scaffold, IgA HetFc binding unit or IgA HetFc multimer) conjugated to one or more active agents, such as therapeutic, diagnostic or labeling agents.

Examples of therapeutic agents include, but are not limited to, antimetabolites, alkylating agents, anthracyclines, antibiotics, anti-mitotic agents, toxins, apoptotic agents, thrombotic agents, anti-angiogenic agents, biological response modifiers, growth factors, radioactive materials and macrocyclic chelators useful for conjugating radiometal ions. Examples of diagnostic agents include, but are not limited to, various imaging agents such as fluorescent materials, luminescent materials and radioactive materials. Examples of labeling agents include, but are not limited to,

enzymes, prosthetic groups, fluorescent materials, luminescent materials and radioactive materials.

Conjugation of the selected active agent to an IgA HetFc construct can be accomplished in a variety of ways and may be direct or via a linker. Linkers for conjugation of active agents are bifunctional or multifunctional moieties capable of linking one or more active agents to an IgA HetFc construct. A bifunctional (or monovalent) linker links a single active agent to a single site on the construct, whereas a multifunctional (or polyvalent) linker links more than one active agent to a single site on the construct. Linkers capable of linking one active agent to more than one site on the IgA HetFc construct may also be considered to be multifunctional.

Conjugation may be achieved, for example, through surface lysines on the IgA HetFc construct, reductive-coupling to oxidized carbohydrates on the IgA HetFc construct, or through cysteine residues on the IgA HetFc construct liberated by reducing interchain disulfide linkages. Alternatively, conjugation may be achieved by modification of the IgA HetFc construct to include additional cysteine residues (see, for example, U.S. Patent Nos. 7,521,541; 8,455,622 and 9,000,130) or non-natural amino acids that provide reactive handles, such as selenomethionine, p-acetylphenylalanine, formylglycine or p-azidomethyl-L-phenylalanine (see, for example, Hofer *et al.*, 2009, *Biochemistry*, 48:12047-12057; Axup *et al.*, 2012, *PNAS*, 109:16101-16106; Wu *et al.*, 2009, *PNAS*, 106:3000-3005; Zimmerman *et al.*, 2014, *Bioconj. Chem.*, 25:351-361) to allow for site-specific conjugation.

Methods for conjugating various agents to proteins, including immunoglobulins, are known in the art (see, for example, in *Bioconjugate Techniques* (G.T. Hermanson, 2013, Academic Press)).

POLYNUCLEOTIDES AND METHODS OF PREPARING IGA HETFC CONSTRUCTS

The IgA HetFc constructs described herein may be prepared using standard recombinant methods. Recombinant production of an IgA HetFc construct generally involves synthesizing one or more polynucleotides encoding the IgA HetFc construct, cloning the one or more polynucleotides into an appropriate vector or vectors, and introducing the vector(s) into a suitable host cell for expression of the IgA HetFc construct. Recombinant production of proteins is well-known in the art and may be achieved using standard techniques as described, for example, in

Sambrook *et al.*, *Molecular Cloning: A Laboratory Manual*, 3rd ed., Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY (2001); Ausubel *et al.*, *Current Protocols in Molecular Biology*, (1987 & updates), John Wiley & Sons, New York, NY; and Harlow and Lane, *Antibodies: A Laboratory Manual*, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY (1990).

5 Certain embodiments of the present disclosure thus relate to an isolated polynucleotide or set of polynucleotides encoding an IgA HetFc construct as described herein. A polynucleotide in this context may encode all or part of an IgA HetFc construct.

 The terms “nucleic acid,” “nucleic acid molecule” and “polynucleotide” are used interchangeably herein and refer to a polymeric form of nucleotides of any length, either
10 deoxyribonucleotides or ribonucleotides, or analogues thereof. The polynucleotide may be of genomic, cDNA, RNA, semisynthetic or synthetic origin, or any combination thereof.

 A polynucleotide that “encodes” an IgA HetFc construct is a polynucleotide that is transcribed (in the case of DNA) and translated (in the case of mRNA) into a polypeptide *in vivo* when placed under the control of appropriate regulatory sequences. The boundaries of the coding
15 sequence are determined by a start codon at the 5' (amino) terminus and a translation stop codon at the 3' (carboxy) terminus. A transcription termination sequence may be located 3' to the coding sequence.

 The one or more polynucleotides encoding the IgA HetFc construct may be inserted into a suitable expression vector or vectors, either directly or after one or more subcloning steps, using
20 standard ligation techniques. Examples of suitable vectors include, but are not limited to, plasmids, phagemids, cosmids, bacteriophage, baculoviruses, retroviruses or DNA viruses. The vector is typically selected to be functional in the particular host cell that will be employed, *i.e.* the vector is compatible with the host cell machinery, permitting amplification and/or expression of the polynucleotide(s). Selection of appropriate vector and host cell combinations in this regard is well
25 within the ordinary skills of a worker in the art.

 Certain embodiments of the present disclosure thus relate to vectors (such as expression vectors) comprising one or more polynucleotides encoding an IgA HetFc construct. The polynucleotide(s) may be comprised by a single vector or by more than one vector. In some embodiments, the polynucleotides are comprised by a multicistronic vector.

Typically, expression vectors will contain one or more regulatory elements for plasmid maintenance and for cloning and expression of exogenous polynucleotide sequences. Examples of such regulatory elements include promoters, enhancer sequences, origins of replication, transcriptional termination sequences, donor and acceptor splice sites, leader sequences for polypeptide secretion, ribosome binding sites, polyadenylation sequences, polylinker regions for inserting the polynucleotide encoding the polypeptide to be expressed, and selectable markers.

Regulatory elements may be homologous (*i.e.* from the same species and/or strain as the host cell), heterologous (*i.e.* from a species other than the host cell species or strain), hybrid (*i.e.* a combination of regulatory elements from more than one source) or synthetic. As such, the source of a regulatory element may be any prokaryotic or eukaryotic organism provided that the flanking sequence is functional in, and can be activated by, the machinery of the host cell being employed.

Optionally, the vector may also contain a “tag”-encoding sequence. A tag-encoding sequence is a nucleic acid sequence located at the 5' or 3' end of the coding sequence that encodes a heterologous peptide sequence, such as a polyHis (for example, 6xHis), FLAG[®], HA (hemagglutinin influenza virus), myc, metal-affinity, avidin/streptavidin, glutathione-S-transferase (GST) or biotin tag. This tag typically remains fused to the expressed polypeptide and can serve as a means for affinity purification or detection of the polypeptide. Optionally, the tag can subsequently be removed from the purified polypeptide by various means such as using certain peptidases for cleavage.

Various expression vectors are readily available from commercial sources. Alternatively, when a commercial vector containing all the desired regulatory elements is not available, an expression vector may be constructed using a commercially available vector as a starting vector. Where one or more of the desired regulatory elements are not already present in the vector, they may be individually obtained and ligated into the vector. Methods and sources for obtaining various regulatory elements are well known to one skilled in the art.

Following construction of the expression vector(s) including the polynucleotide(s) encoding the IgA HetFc construct, the vector(s) may be inserted into a suitable host cell for amplification and/or protein expression. The transformation of an expression vector into a selected host cell may be accomplished by well-known methods including transfection, infection, calcium phosphate co-precipitation, electroporation, microinjection, lipofection, DEAE-dextran mediated

transfection, and other known techniques. The method selected will in part be a function of the type of host cell to be used. These methods and other suitable methods are well known to the skilled person (see, for example, Sambrook, *et al.*, *ibid.*).

5 A host cell, when cultured under appropriate conditions, expresses the polypeptide encoded by the vector and the polypeptide can subsequently be collected from the culture medium (if the host cell secretes the polypeptide) or directly from the host cell producing it (if the polypeptide is not secreted). The host cell may be prokaryotic (for example, a bacterial cell) or eukaryotic (for example, a yeast, fungi, plant or mammalian cell). The selection of an appropriate host cell can be readily made by the skilled person taking into account various factors, such as desired expression
10 levels, polypeptide modifications that are desirable or necessary for activity (such as glycosylation or phosphorylation) and ease of folding into a biologically active molecule.

Certain embodiments of the present disclosure thus relate to host cells comprising polynucleotide(s) encoding the IgA HetFc construct, or one or more vectors comprising the polynucleotide(s). In certain embodiments, the host cell is a eukaryotic cell.

15 For example, eukaryotic microbes such as filamentous fungi or yeast may be employed as host cells, including fungi and yeast strains whose glycosylation pathways have been “humanized” (see, for example, Gerngross, 2004, *Nat. Biotech.*, 22:1409-1414, and Li *et al.*, 2006, *Nat. Biotech.*, 24:210-215). Plant cells may also be utilized as host cells (see, for example, U.S. Patent Nos. 5,959,177; 6,040,498; 6,420,548; 7,125,978 and 6,417,429, describing PLANTIBODIES™
20 technology).

In some embodiments, the eukaryotic host cell is a mammalian cell. Various mammalian cell lines may be used as host cells. Examples of useful mammalian host cell lines include, but are not limited to, monkey kidney CV1 line transformed by SV40 (COS-7), human embryonic kidney line 293 (HEK293 cells as described, for example, in Graham, *et al.*, 1977, *J. Gen Virol.*, 36:59),
25 baby hamster kidney cells (BHK), mouse sertoli cells (TM4 cells as described, for example, in Mather, 1980, *Biol. Reprod.*, 23:243-251), monkey kidney cells (CV1), African green monkey kidney cells (VERO-76), human cervical carcinoma cells (HeLa), canine kidney cells (MDCK), buffalo rat liver cells (BRL 3A), human lung cells (W138), human liver cells (Hep G2), mouse mammary tumour cells (MMT 060562), TRI cells (as described, for example, in Mather, *et al.*, 1982, *Annals N.Y. Acad. Sci.*, 383:44-68), MRC 5 cells, FS4 cells, Chinese hamster ovary
30

(CHO) cells (including DHFR⁻ CHO cells as described in Urlaub, *et al.*, 1980, *Proc. Natl. Acad. Sci. USA*, 77:4216) and myeloma cell lines (such as Y0, NS0 and Sp2/0). See also, Yazaki and Wu, 2003, *Methods in Molecular Biology*, Vol. 248, pp. 255-268 (B.K.C. Lo, ed., Humana Press, Totowa, N.J.).

5 Certain embodiments of the present disclosure relate to methods of preparing an IgA HetFc construct described herein, comprising transfecting a host cell with one or more polynucleotides encoding the IgA HetFc construct, for example in the form of one or more vectors comprising the polynucleotide(s), and culturing the host cell under conditions suitable for expression of the encoded IgA HetFc construct.

10 Typically, the IgA HetFc construct is isolated from the host cell after expression and may optionally be purified. Methods for isolating and purifying expressed proteins are well-known in the art. Standard purification methods include, for example, chromatographic techniques, such ion exchange, hydrophobic interaction, affinity, sizing, gel filtration or reversed-phase, which may be carried out at atmospheric pressure or at medium or high pressure using systems such as FPLC,
15 MPLC and HPLC. Other purification methods include electrophoretic, immunological, precipitation, dialysis and chromatofocusing techniques. Ultrafiltration and diafiltration techniques, in conjunction with protein concentration, may also be useful.

 A variety of natural proteins are known in the art to bind Fc regions of antibodies, and these proteins can therefore be used in the purification of Fc-containing proteins. For example, the
20 bacterial proteins A and G bind to the Fc region. Purification can often be enabled by a particular fusion partner or affinity tag as described above. For example, antibodies may be purified using glutathione resin if a GST fusion is employed, Ni⁺² affinity chromatography if a His-tag is employed, or immobilized anti-flag antibody if a flag-tag is used. Examples of useful purification techniques are described in Harlow and Lane, *Antibodies: A Laboratory Manual*, Cold Spring
25 Harbor Laboratory Press, Cold Spring Harbor, NY (1990), and *Protein Purification: Principles and Practice*, 3rd Ed., Scopes, Springer-Verlag, NY (1994). The degree of purification necessary will vary depending on the use of the IgA HetFc construct. In some instances, no purification may be necessary.

 In certain embodiments, the IgA HetFc constructs herein are purified using one or more
30 purification methods known in the art, including but not limited to, affinity chromatography,

affinity chromatography by non-reducing CE-SDS, affinity purification (protein A purification columns, CaptureSelect™ IgA affinity purification) and size exclusion chromatography, *e.g.* UPLC-SEC (see also Examples 1-6).

POST-TRANSLATIONAL MODIFICATIONS

5 In certain embodiments, the IgA HetFc constructs described herein may be post-translationally modified.

 The term “post-translationally modified” and grammatical variations thereof such as “post-translational modification,” refers to a modification of a natural or non-natural amino acid that occurs to such an amino acid after it has been incorporated into a polypeptide chain. The term
10 encompasses, by way of example only, co-translational *in vivo* modifications, co-translational *in vitro* modifications (such as in a cell-free translation system), post-translational *in vivo* modifications and post-translational *in vitro* modifications.

 Specific examples of post-translational modifications include, but are not limited to, glycosylation, acetylation, phosphorylation, amidation, derivatization by known
15 protecting/blocking groups, proteolytic cleavage, or a combination thereof. Other examples include chemical modification by known techniques including, but not limited to, specific chemical cleavage by cyanogen bromide, trypsin, chymotrypsin, papain, V8 protease or NaBH₄; acetylation; formylation; oxidation; reduction or metabolic synthesis in the presence of tunicamycin.

20 Additional post-translational modifications include attachment of chemical moieties to the amino acid backbone, chemical modifications of N-linked or O-linked carbohydrate chains, and addition or deletion of an N-terminal methionine residue as a result of prokaryotic host cell expression.

 In certain embodiments, IgA HetFc constructs described herein may optionally be modified
25 with a detectable label, such as an enzymatic, fluorescent, isotopic or affinity label to allow for detection and isolation of the protein. Examples of suitable enzyme labels include horseradish peroxidase, alkaline phosphatase, beta-galactosidase and acetylcholinesterase; examples of suitable prosthetic group complexes include streptavidin/biotin and avidin/biotin; examples of suitable fluorescent materials include umbelliferone, fluorescein, fluorescein isothiocyanate,

rhodamine, dichlorotriazinylamine fluorescein, dansyl chloride and phycoerythrin; an example of a luminescent material includes luminol; examples of bioluminescent materials include luciferase, luciferin and aequorin; and examples of suitable radioactive materials include radioactive isotopes of iodine, carbon, sulfur, tritium, indium, technetium, thallium, gallium, palladium, molybdenum, 5 xenon and fluorine.

In some embodiments, the IgA HetFc constructs described herein may optionally be attached to macrocyclic chelators that associate with radiometal ions.

In those embodiments in which the IgA HetFc constructs are modified, either by natural processes, such as post-translational processing, or by chemical modification techniques, the same 10 type of modification may optionally be present in the same or varying degrees at several sites in a given polypeptide.

In certain embodiments, the IgA HetFc constructs may be attached to a solid support, which may be particularly useful for immunoassays or purification of polypeptides that are bound by, or bind to, or associate with proteins described herein. Such solid supports include, but are not limited to, 15 glass, cellulose, polyacrylamide, nylon, polystyrene, polyvinyl chloride and polypropylene.

CHARACTERIZATION OF IGA HETFC CONSTRUCTS

IgA HetFc constructs as described herein may be characterized in a variety of ways. For example, purity of the IgA HetFc constructs may be assessed using techniques well known in the art including, but not limited to, SDS-PAGE gels, western blots, densitometry, mass spectrometry, 20 size-exclusion chromatography (SEC) or non-reducing capillary electrophoresis sodium dodecyl sulfate (CE-SDS). In certain embodiments, purity of the IgA HetFc constructs is assessed by SEC or CE-SDS.

Protein stability may also be characterized using an array of art-known techniques including, but not limited to, size exclusion chromatography (SEC); UV, visible or CD 25 spectroscopy; mass spectroscopy; differential light scattering (DLS); bench top stability assay; freeze thawing coupled with other characterization techniques; differential scanning calorimetry (DSC); differential scanning fluorimetry (DSF); hydrophobic interaction chromatography (HIC); isoelectric focusing; receptor binding assays or relative protein expression levels. In certain embodiments, stability of the IgA HetFc constructs is assessed by measuring CH3 domain melting

temperature (T_m), as compared to wild-type CH3 domain T_m, using techniques well known in the art such as DSC or DSF.

Where appropriate, IgA HetFc constructs of the present disclosure may also be assayed for the ability to specifically bind to a ligand, receptor or target antigen (*e.g.* to Fc α RI, or to a target antigen of a binding domain comprised by the IgA HetFc construct). Various immunoassays known in the art may be employed to analyze specific binding and cross-reactivity including, but are not limited to, competitive and non-competitive assay systems using techniques such as western blots, radioimmunoassays, ELISA (enzyme-linked immunosorbent assay), “sandwich” immunoassays, immunoprecipitation assays, precipitin reactions, gel diffusion precipitin reactions, immunodiffusion assays, agglutination assays, complement-fixation assays, immunoradiometric assays, fluorescent immunoassays and protein A immunoassays. Such assays are routine and well known in the art (see, for example, Ausubel, *et al.*, eds, 1994, *Current Protocols in Molecular Biology*, John Wiley and Sons, Inc., New York).

IgA HetFc constructs that are confirmed to specifically bind to the target ligand, receptor or antigen may optionally also be assayed for their affinity for the ligand, receptor or antigen. Binding affinity and parameters such as the on-rate and the off-rate of the interaction can be determined, for example, by competitive binding assays. The kinetic parameters of an IgA HetFc construct may also be determined using surface plasmon resonance (SPR) based assays known in the art, such as BIAcore™ kinetic analysis. Various SPR-based assays are known in the art (see, for example, Mullet, *et al.*, 2000, *Methods*, 22:77-91; Dong, *et al.*, 2002, *Rev. Mol. Biotech.*, 82:303-23; Fivash, *et al.*, 1998, *Curr Opinion in Biotechnology*, 9:97-101; Rich, *et al.*, 2000, *Curr Opinion in Biotechnology*, 11:54-61, and U.S. Patent Nos. 6,373,577; 6,289,286; 5,322,798; 5,341,215 and 6,268,125). Fluorescence activated cell sorting (FACS), using techniques known to those skilled in the art, may also be used for characterizing the binding of an IgA HetFc construct to a molecule expressed on the cell surface (*e.g.* an Fc receptor or a cell surface antigen). Flow cytometers for sorting and examining biological cells are well known in the art (see, for example, U.S. Patent Nos. 4,347,935; 5,464,581; 5,483,469; 5,602,039; 5,643,796 and 6,211,477). Other known flow cytometers are the FACS Vantage™ system manufactured by Becton Dickinson and Company (Franklin Lakes, NJ) and the COPAS™ system manufactured by Union Biometrica (Holliston, MA). A detailed description of binding affinities and kinetics can be found in Paul, W.

E., *ed.*, 1999, *Fundamental Immunology*, 4th Ed., Lippincott-Raven, Philadelphia, which focuses on antibody-immunogen interactions.

Binding properties of the IgA HetFc constructs may also be characterized by *in vitro* functional assays for determining one or more Fc α RI downstream functions (see, for example, Bakema, 2006, *J Immunol*, 176:3603-3610).

METHODS OF USE

Certain embodiments of the present disclosure relate to the use of the IgA HetFc constructs described herein in therapeutic or diagnostic methods. For example, IgA constructs may be used in methods of engaging neutrophils via Fc α RI, and methods of activating neutrophils via Fc α RI.

IgA HetFc constructs comprising one or more binding domains and IgA HetFc constructs conjugated to a therapeutic agent may be used in methods of treatment, for example, treating a subject with cancer, autoimmune disease, immune or inflammatory disorders or an infectious disease. Similarly, IgA constructs comprising one or more binding domains and IgA HetFc constructs conjugated to a labeling or diagnostic agent may be used in methods of diagnosis, for example, diagnosing a subject with cancer, autoimmune disease, immune or inflammatory disorders or an infectious disease.

When used in methods of treatment, the IgA HetFc constructs are administered to the subject in a therapeutically effective amount. The term “therapeutically effective amount” as used herein refers to an amount of an IgA HetFc construct described herein or a composition comprising an IgA HetFc construct described herein being administered that will accomplish the goal of the recited method, for example, relieve to some extent one or more of the symptoms of the disease or disorder being treated. The amount of the composition described herein which will be effective in the treatment of the disease or disorder in question can be determined by standard clinical techniques. In addition, *in vitro* assays may optionally be employed to help identify optimal dosage ranges. The precise dose to be employed in the formulation will also depend on the route of administration, and the seriousness of the disease or disorder, and should be decided according to the judgment of the practitioner and each patient’s circumstances.

In some embodiments in which the IgA HetFc construct is used in a method of treatment, the IgA HetFc construct may be administered in combination with a therapeutically effective

amount of one or more additional therapeutic agents known to those skilled in the art for the treatment of the disease or disorder in question.

Desirable effects of treatment include, but are not limited to, one or more of alleviation of symptoms, diminishment of any direct or indirect pathological consequences of the disease or disorder, preventing metastasis, decreasing the rate of disease progression, amelioration or
5 palliation of the disease state, improved survival, remission, improved prognosis or delaying the recurrence of disease.

PHARMACEUTICAL COMPOSITIONS

For therapeutic or diagnostic use, the IgA HetFc constructs may be provided in the form
10 of compositions which comprise the IgA HetFc construct and a pharmaceutically acceptable carrier or diluent. The compositions may be prepared by known procedures using well-known and readily available ingredients and may be formulated for administration to a subject by, for example, oral (including, for example, buccal or sublingual), topical, parenteral, rectal or vaginal routes, or by inhalation or spray. The term “parenteral” as used herein includes injection or infusion
15 by subcutaneous, intradermal, intra-articular, intravenous, intramuscular, intravascular, intrasternal or intrathecal routes.

The composition will typically be formulated in a format suitable for administration to a subject by the chosen route, for example, as a syrup, elixir, tablet, troche, lozenge, hard or soft capsule, pill, suppository, oily or aqueous suspension, dispersible powder or granule, emulsion,
20 injectable or solution. Compositions may be provided as unit dosage formulations.

Pharmaceutically acceptable carriers are generally non-toxic to recipients at the dosages and concentrations employed. Examples of such carriers include, but are not limited to, buffers such as phosphate, citrate, and other organic acids; antioxidants such as ascorbic acid and methionine; preservatives such as octadecyldimethylbenzyl ammonium chloride, hexamethonium
25 chloride, benzalkonium chloride, benzethonium chloride, phenol, butyl alcohol, benzyl alcohol, alkyl parabens (such as methyl or propyl paraben), catechol, resorcinol, cyclohexanol, 3-pentanol and m-cresol; low molecular weight (less than about 10 amino acids) polypeptides; proteins such as serum albumin or gelatin; hydrophilic polymers such as polyvinylpyrrolidone; amino acids such as glycine, glutamine, asparagine, histidine, arginine or lysine; monosaccharides, disaccharides,

and other carbohydrates such as glucose, mannose or dextrans; chelating agents such as EDTA; sugars such as sucrose, mannitol, trehalose or sorbitol; salt-forming counter-ions such as sodium; metal complexes such as Zn-protein complexes, and non-ionic surfactants such as polyethylene glycol (PEG).

5 In certain embodiments, the compositions may be in the form of a sterile injectable aqueous or oleaginous solution or suspension. Such solutions or suspensions may be formulated using suitable dispersing or wetting agents and/or suspending agents that are known in the art. The sterile injectable solution or suspension may comprise the IgA HetFc constructs in a non-toxic parentally acceptable diluent or solvent. Acceptable diluents and solvents that may be employed include, for
10 example, 1,3-butanediol, water, Ringer's solution or isotonic sodium chloride solution. In addition, sterile, fixed oils may be employed as a solvent or suspending medium. For this purpose, various bland fixed oils may be employed, including synthetic mono- or diglycerides. In addition, fatty acids such as oleic acid find use in the preparation of injectables. Adjuvants such as local anaesthetics, preservatives and/or buffering agents as known in the art may also be included in the
15 injectable solution or suspension.

Other pharmaceutical compositions and methods of preparing pharmaceutical compositions are known in the art and are described, for example, in "*Remington: The Science and Practice of Pharmacy*" (formerly "*Remingtons Pharmaceutical Sciences*"); Gennaro, A., Lippincott, Williams & Wilkins, Philadelphia, PA (2000).

20 ***KITS AND ARTICLES OF MANUFACTURE***

Certain embodiments of the present disclosure relate to kits comprising one or more IgA HetFc constructs described herein. Individual components of the kit would be packaged in separate containers and, associated with such containers, can be a notice in the form prescribed by a governmental agency regulating the manufacture, use or sale of pharmaceuticals or biological
25 products, which notice reflects approval by the agency of manufacture, use or sale. The kit may optionally contain instructions or directions outlining the method of use or administration regimen for the IgA HetFc constructs.

When one or more components of the kit are provided as solutions, for example an aqueous solution, or a sterile aqueous solution, the container means may itself be an inhalant, syringe,

pipette, eye dropper, or other such like apparatus, from which the solution may be administered to a subject or applied to and mixed with the other components of the kit.

The components of the kit may also be provided in dried or lyophilized form and the kit can additionally contain a suitable solvent for reconstitution of the lyophilized components.

- 5 Irrespective of the number or type of containers, the kits described herein also may comprise an instrument for assisting with the administration of the composition to a patient. Such an instrument may be an inhalant, nasal spray device, syringe, pipette, forceps, measured spoon, eye dropper or similar medically approved delivery vehicle.

Certain embodiments relate to an article of manufacture containing materials useful for
10 treatment of a patient as described herein. The article of manufacture comprises a container and a label or package insert on or associated with the container. Suitable containers include, for example, bottles, vials, syringes, intravenous solution bags, and the like. The containers may be formed from a variety of materials such as glass or plastic. The container holds a composition comprising the IgA HetFc construct which is by itself or combined with another composition
15 effective for treating the patient and may have a sterile access port (for example the container may be an intravenous solution bag or a vial having a stopper pierceable by a hypodermic injection needle). The label or package insert indicates that the composition is used for treating the condition of choice. The article of manufacture may further comprise a second container comprising a pharmaceutically acceptable buffer, such as bacteriostatic water for injection (BWFI), phosphate-buffered saline, Ringer's solution or dextrose solution. The article of manufacture may optionally
20 further include other materials desirable from a commercial and user standpoint, including other buffers, diluents, filters, needles, and syringes.

The following Examples are provided for illustrative purposes and are not intended to limit the scope of the invention in any way.

25

Table 7: IgA HetFc Designs Comprising Core Mutations

No.	CH3 Domain Mutations	
	Chain A	Chain B
D1	A6085YF_T6086Y	W6081T
D2	A6085YY_T6086Y	W6081T
D3	A6085YM_T6086Y	W6081T

No.	CH3 Domain Mutations	
	Chain A	Chain B
D64	A6085YW_T6086M	W6081A
D65	A6085YH_T6086M	W6081A
D66	A6085YF_T6086W	W6081A

D4	A6085YW_T6086Y	W6081T
D5	A6085YH_T6086Y	W6081T
D6	A6085YF_T6086F	W6081T
D7	A6085YY_T6086F	W6081T
D8	A6085YM_T6086F	W6081T
D9	A6085YW_T6086F	W6081T
D10	A6085YH_T6086F	W6081T
D11	A6085YF_T6086M	W6081T
D12	A6085YY_T6086M	W6081T
D13	A6085YM_T6086M	W6081T
D14	A6085YW_T6086M	W6081T
D15	A6085YH_T6086M	W6081T
D16	A6085YF_T6086W	W6081T
D17	A6085YY_T6086W	W6081T
D18	A6085YM_T6086W	W6081T
D19	A6085YW_T6086W	W6081T
D20	A6085YH_T6086W	W6081T
D21	A6085YF_T6086H	W6081T
D22	A6085YY_T6086H	W6081T
D23	A6085YM_T6086H	W6081T
D24	A6085YW_T6086H	W6081T
D25	A6085YH_T6086H	W6081T
D26	A6085YF_T6086Y	W6081L
D27	A6085YY_T6086Y	W6081L
D28	A6085YM_T6086Y	W6081L
D29	A6085YW_T6086Y	W6081L
D30	A6085YH_T6086Y	W6081L
D31	A6085YF_T6086F	W6081L
D32	A6085YY_T6086F	W6081L
D33	A6085YM_T6086F	W6081L
D34	A6085YW_T6086F	W6081L

D67	A6085YY_T6086W	W6081A
D68	A6085YM_T6086W	W6081A
D69	A6085YW_T6086W	W6081A
D70	A6085YH_T6086W	W6081A
D71	A6085YF_T6086H	W6081A
D72	A6085YY_T6086H	W6081A
D73	A6085YM_T6086H	W6081A
D74	A6085YW_T6086H	W6081A
D75	A6085YH_T6086H	W6081A
D76	A6085YF_T6086Y	W6081V
D77	A6085YY_T6086Y	W6081V
D78	A6085YM_T6086Y	W6081V
D79	A6085YW_T6086Y	W6081V
D80	A6085YH_T6086Y	W6081V
D81	A6085YF_T6086F	W6081V
D82	A6085YY_T6086F	W6081V
D83	A6085YM_T6086F	W6081V
D84	A6085YW_T6086F	W6081V
D85	A6085YH_T6086F	W6081V
D86	A6085YF_T6086M	W6081V
D87	A6085YY_T6086M	W6081V
D88	A6085YM_T6086M	W6081V
D89	A6085YW_T6086M	W6081V
D90	A6085YH_T6086M	W6081V
D91	A6085YF_T6086W	W6081V
D92	A6085YY_T6086W	W6081V
D93	A6085YM_T6086W	W6081V
D94	A6085YW_T6086W	W6081V
D95	A6085YH_T6086W	W6081V
D96	A6085YF_T6086H	W6081V
D97	A6085YY_T6086H	W6081V

D35	A6085YH_T6086F	W6081L
D36	A6085YF_T6086M	W6081L
D37	A6085YY_T6086M	W6081L
D38	A6085YM_T6086M	W6081L
D39	A6085YW_T6086M	W6081L
D40	A6085YH_T6086M	W6081L
D41	A6085YF_T6086W	W6081L
D42	A6085YY_T6086W	W6081L
D43	A6085YM_T6086W	W6081L
D44	A6085YW_T6086W	W6081L
D45	A6085YH_T6086W	W6081L
D46	A6085YF_T6086H	W6081L
D47	A6085YY_T6086H	W6081L
D48	A6085YM_T6086H	W6081L
D49	A6085YW_T6086H	W6081L
D50	A6085YH_T6086H	W6081L
D51	A6085YF_T6086Y	W6081A
D52	A6085YY_T6086Y	W6081A
D53	A6085YM_T6086Y	W6081A
D54	A6085YW_T6086Y	W6081A
D55	A6085YH_T6086Y	W6081A
D56	A6085YF_T6086F	W6081A
D57	A6085YY_T6086F	W6081A
D58	A6085YM_T6086F	W6081A
D59	A6085YW_T6086F	W6081A
D60	A6085YH_T6086F	W6081A
D61	A6085YF_T6086M	W6081A
D62	A6085YY_T6086M	W6081A
D63	A6085YM_T6086M	W6081A

D98	A6085YM_T6086H	W6081V
D99	A6085YW_T6086H	W6081V
D100	A6085YH_T6086H	W6081V
D101	A6085YF_T6086Y	W6081I
D102	A6085YY_T6086Y	W6081I
D103	A6085YM_T6086Y	W6081I
D104	A6085YW_T6086Y	W6081I
D105	A6085YH_T6086Y	W6081I
D106	A6085YF_T6086F	W6081I
D107	A6085YY_T6086F	W6081I
D108	A6085YM_T6086F	W6081I
D109	A6085YW_T6086F	W6081I
D110	A6085YH_T6086F	W6081I
D111	A6085YF_T6086M	W6081I
D112	A6085YY_T6086M	W6081I
D113	A6085YM_T6086M	W6081I
D114	A6085YW_T6086M	W6081I
D115	A6085YH_T6086M	W6081I
D116	A6085YF_T6086W	W6081I
D117	A6085YY_T6086W	W6081I
D118	A6085YM_T6086W	W6081I
D119	A6085YW_T6086W	W6081I
D120	A6085YH_T6086W	W6081I
D121	A6085YF_T6086H	W6081I
D122	A6085YY_T6086H	W6081I
D123	A6085YM_T6086H	W6081I
D124	A6085YW_T6086H	W6081I
D125	A6085YH_T6086H	W6081I

Table 8: IgA HetFc Designs comprising Core Mutations in Combination with Mutation at Position 6079 in Chain B

No.	CH3 Domain Mutations	
	Chain A	Chain B
D126	A6085YF_T6086Y	L6079V_W6081T
D127	A6085YY_T6086Y	L6079V_W6081T
D128	A6085YM_T6086Y	L6079V_W6081T
D129	A6085YW_T6086Y	L6079V_W6081T
D130	A6085YH_T6086Y	L6079V_W6081T
D131	A6085YF_T6086F	L6079V_W6081T
D132	A6085YY_T6086F	L6079V_W6081T
D133	A6085YM_T6086F	L6079V_W6081T
D134	A6085YW_T6086F	L6079V_W6081T
D135	A6085YH_T6086F	L6079V_W6081T
D136	A6085YF_T6086M	L6079V_W6081T
D137	A6085YY_T6086M	L6079V_W6081T
D138	A6085YM_T6086M	L6079V_W6081T
D139	A6085YW_T6086M	L6079V_W6081T
D140	A6085YH_T6086M	L6079V_W6081T
D141	A6085YF_T6086W	L6079V_W6081T
D142	A6085YY_T6086W	L6079V_W6081T
D143	A6085YM_T6086W	L6079V_W6081T
D144	A6085YW_T6086W	L6079V_W6081T
D145	A6085YH_T6086W	L6079V_W6081T
D146	A6085YF_T6086H	L6079V_W6081T
D147	A6085YY_T6086H	L6079V_W6081T
D148	A6085YM_T6086H	L6079V_W6081T
D149	A6085YW_T6086H	L6079V_W6081T
D150	A6085YH_T6086H	L6079V_W6081T
D151	A6085YF_T6086Y	L6079V_W6081L
D152	A6085YY_T6086Y	L6079V_W6081L
D153	A6085YM_T6086Y	L6079V_W6081L
D154	A6085YW_T6086Y	L6079V_W6081L

No.	CH3 Domain Mutations	
	Chain A	Chain B
D376	A6085YF_T6086Y	L6079A_W6081T
D377	A6085YY_T6086Y	L6079A_W6081T
D378	A6085YM_T6086Y	L6079A_W6081T
D379	A6085YW_T6086Y	L6079A_W6081T
D380	A6085YH_T6086Y	L6079A_W6081T
D381	A6085YF_T6086F	L6079A_W6081T
D382	A6085YY_T6086F	L6079A_W6081T
D383	A6085YM_T6086F	L6079A_W6081T
D384	A6085YW_T6086F	L6079A_W6081T
D385	A6085YH_T6086F	L6079A_W6081T
D386	A6085YF_T6086M	L6079A_W6081T
D387	A6085YY_T6086M	L6079A_W6081T
D388	A6085YM_T6086M	L6079A_W6081T
D389	A6085YW_T6086M	L6079A_W6081T
D390	A6085YH_T6086M	L6079A_W6081T
D391	A6085YF_T6086W	L6079A_W6081T
D392	A6085YY_T6086W	L6079A_W6081T
D393	A6085YM_T6086W	L6079A_W6081T
D394	A6085YW_T6086W	L6079A_W6081T
D395	A6085YH_T6086W	L6079A_W6081T
D396	A6085YF_T6086H	L6079A_W6081T
D397	A6085YY_T6086H	L6079A_W6081T
D398	A6085YM_T6086H	L6079A_W6081T
D399	A6085YW_T6086H	L6079A_W6081T
D400	A6085YH_T6086H	L6079A_W6081T
D401	A6085YF_T6086Y	L6079A_W6081L
D402	A6085YY_T6086Y	L6079A_W6081L
D403	A6085YM_T6086Y	L6079A_W6081L
D404	A6085YW_T6086Y	L6079A_W6081L

No.	CH3 Domain Mutations	
	Chain A	Chain B
D155	A6085YH_T6086Y	L6079V_W6081L
D156	A6085YF_T6086F	L6079V_W6081L
D157	A6085YY_T6086F	L6079V_W6081L
D158	A6085YM_T6086F	L6079V_W6081L
D159	A6085YW_T6086F	L6079V_W6081L
D160	A6085YH_T6086F	L6079V_W6081L
D161	A6085YF_T6086M	L6079V_W6081L
D162	A6085YY_T6086M	L6079V_W6081L
D163	A6085YM_T6086M	L6079V_W6081L
D164	A6085YW_T6086M	L6079V_W6081L
D165	A6085YH_T6086M	L6079V_W6081L
D166	A6085YF_T6086W	L6079V_W6081L
D167	A6085YY_T6086W	L6079V_W6081L
D168	A6085YM_T6086W	L6079V_W6081L
D169	A6085YW_T6086W	L6079V_W6081L
D170	A6085YH_T6086W	L6079V_W6081L
D171	A6085YF_T6086H	L6079V_W6081L
D172	A6085YY_T6086H	L6079V_W6081L
D173	A6085YM_T6086H	L6079V_W6081L
D174	A6085YW_T6086H	L6079V_W6081L
D175	A6085YH_T6086H	L6079V_W6081L
D176	A6085YF_T6086Y	L6079V_W6081A
D177	A6085YY_T6086Y	L6079V_W6081A
D178	A6085YM_T6086Y	L6079V_W6081A
D179	A6085YW_T6086Y	L6079V_W6081A
D180	A6085YH_T6086Y	L6079V_W6081A
D181	A6085YF_T6086F	L6079V_W6081A
D182	A6085YY_T6086F	L6079V_W6081A
D183	A6085YM_T6086F	L6079V_W6081A
D184	A6085YW_T6086F	L6079V_W6081A
D185	A6085YH_T6086F	L6079V_W6081A

No.	CH3 Domain Mutations	
	Chain A	Chain B
D405	A6085YH_T6086Y	L6079A_W6081L
D406	A6085YF_T6086F	L6079A_W6081L
D407	A6085YY_T6086F	L6079A_W6081L
D408	A6085YM_T6086F	L6079A_W6081L
D409	A6085YW_T6086F	L6079A_W6081L
D410	A6085YH_T6086F	L6079A_W6081L
D411	A6085YF_T6086M	L6079A_W6081L
D412	A6085YY_T6086M	L6079A_W6081L
D413	A6085YM_T6086M	L6079A_W6081L
D414	A6085YW_T6086M	L6079A_W6081L
D415	A6085YH_T6086M	L6079A_W6081L
D416	A6085YF_T6086W	L6079A_W6081L
D417	A6085YY_T6086W	L6079A_W6081L
D418	A6085YM_T6086W	L6079A_W6081L
D419	A6085YW_T6086W	L6079A_W6081L
D420	A6085YH_T6086W	L6079A_W6081L
D421	A6085YF_T6086H	L6079A_W6081L
D422	A6085YY_T6086H	L6079A_W6081L
D423	A6085YM_T6086H	L6079A_W6081L
D424	A6085YW_T6086H	L6079A_W6081L
D425	A6085YH_T6086H	L6079A_W6081L
D426	A6085YF_T6086Y	L6079A_W6081A
D427	A6085YY_T6086Y	L6079A_W6081A
D428	A6085YM_T6086Y	L6079A_W6081A
D429	A6085YW_T6086Y	L6079A_W6081A
D430	A6085YH_T6086Y	L6079A_W6081A
D431	A6085YF_T6086F	L6079A_W6081A
D432	A6085YY_T6086F	L6079A_W6081A
D433	A6085YM_T6086F	L6079A_W6081A
D434	A6085YW_T6086F	L6079A_W6081A
D435	A6085YH_T6086F	L6079A_W6081A

No.	CH3 Domain Mutations	
	Chain A	Chain B
D186	A6085YF_T6086M	L6079V_W6081A
D187	A6085YY_T6086M	L6079V_W6081A
D188	A6085YM_T6086M	L6079V_W6081A
D189	A6085YW_T6086M	L6079V_W6081A
D190	A6085YH_T6086M	L6079V_W6081A
D191	A6085YF_T6086W	L6079V_W6081A
D192	A6085YY_T6086W	L6079V_W6081A
D193	A6085YM_T6086W	L6079V_W6081A
D194	A6085YW_T6086W	L6079V_W6081A
D195	A6085YH_T6086W	L6079V_W6081A
D196	A6085YF_T6086H	L6079V_W6081A
D197	A6085YY_T6086H	L6079V_W6081A
D198	A6085YM_T6086H	L6079V_W6081A
D199	A6085YW_T6086H	L6079V_W6081A
D200	A6085YH_T6086H	L6079V_W6081A
D201	A6085YF_T6086Y	L6079V_W6081V
D202	A6085YY_T6086Y	L6079V_W6081V
D203	A6085YM_T6086Y	L6079V_W6081V
D204	A6085YW_T6086Y	L6079V_W6081V
D205	A6085YH_T6086Y	L6079V_W6081V
D206	A6085YF_T6086F	L6079V_W6081V
D207	A6085YY_T6086F	L6079V_W6081V
D208	A6085YM_T6086F	L6079V_W6081V
D209	A6085YW_T6086F	L6079V_W6081V
D210	A6085YH_T6086F	L6079V_W6081V
D211	A6085YF_T6086M	L6079V_W6081V
D212	A6085YY_T6086M	L6079V_W6081V
D213	A6085YM_T6086M	L6079V_W6081V
D214	A6085YW_T6086M	L6079V_W6081V
D215	A6085YH_T6086M	L6079V_W6081V
D216	A6085YF_T6086W	L6079V_W6081V

No.	CH3 Domain Mutations	
	Chain A	Chain B
D436	A6085YF_T6086M	L6079A_W6081A
D437	A6085YY_T6086M	L6079A_W6081A
D438	A6085YM_T6086M	L6079A_W6081A
D439	A6085YW_T6086M	L6079A_W6081A
D440	A6085YH_T6086M	L6079A_W6081A
D441	A6085YF_T6086W	L6079A_W6081A
D442	A6085YY_T6086W	L6079A_W6081A
D443	A6085YM_T6086W	L6079A_W6081A
D444	A6085YW_T6086W	L6079A_W6081A
D445	A6085YH_T6086W	L6079A_W6081A
D446	A6085YF_T6086H	L6079A_W6081A
D447	A6085YY_T6086H	L6079A_W6081A
D448	A6085YM_T6086H	L6079A_W6081A
D449	A6085YW_T6086H	L6079A_W6081A
D450	A6085YH_T6086H	L6079A_W6081A
D451	A6085YF_T6086Y	L6079A_W6081V
D452	A6085YY_T6086Y	L6079A_W6081V
D453	A6085YM_T6086Y	L6079A_W6081V
D454	A6085YW_T6086Y	L6079A_W6081V
D455	A6085YH_T6086Y	L6079A_W6081V
D456	A6085YF_T6086F	L6079A_W6081V
D457	A6085YY_T6086F	L6079A_W6081V
D458	A6085YM_T6086F	L6079A_W6081V
D459	A6085YW_T6086F	L6079A_W6081V
D460	A6085YH_T6086F	L6079A_W6081V
D461	A6085YF_T6086M	L6079A_W6081V
D462	A6085YY_T6086M	L6079A_W6081V
D463	A6085YM_T6086M	L6079A_W6081V
D464	A6085YW_T6086M	L6079A_W6081V
D465	A6085YH_T6086M	L6079A_W6081V
D466	A6085YF_T6086W	L6079A_W6081V

No.	CH3 Domain Mutations	
	Chain A	Chain B
D217	A6085YY_T6086W	L6079V_W6081V
D218	A6085YM_T6086W	L6079V_W6081V
D219	A6085YW_T6086W	L6079V_W6081V
D220	A6085YH_T6086W	L6079V_W6081V
D221	A6085YF_T6086H	L6079V_W6081V
D222	A6085YY_T6086H	L6079V_W6081V
D223	A6085YM_T6086H	L6079V_W6081V
D224	A6085YW_T6086H	L6079V_W6081V
D225	A6085YH_T6086H	L6079V_W6081V
D226	A6085YF_T6086Y	L6079V_W6081I
D227	A6085YY_T6086Y	L6079V_W6081I
D228	A6085YM_T6086Y	L6079V_W6081I
D229	A6085YW_T6086Y	L6079V_W6081I
D230	A6085YH_T6086Y	L6079V_W6081I
D231	A6085YF_T6086F	L6079V_W6081I
D232	A6085YY_T6086F	L6079V_W6081I
D233	A6085YM_T6086F	L6079V_W6081I
D234	A6085YW_T6086F	L6079V_W6081I
D235	A6085YH_T6086F	L6079V_W6081I
D236	A6085YF_T6086M	L6079V_W6081I
D237	A6085YY_T6086M	L6079V_W6081I
D238	A6085YM_T6086M	L6079V_W6081I
D239	A6085YW_T6086M	L6079V_W6081I
D240	A6085YH_T6086M	L6079V_W6081I
D241	A6085YF_T6086W	L6079V_W6081I
D242	A6085YY_T6086W	L6079V_W6081I
D243	A6085YM_T6086W	L6079V_W6081I
D244	A6085YW_T6086W	L6079V_W6081I
D245	A6085YH_T6086W	L6079V_W6081I
D246	A6085YF_T6086H	L6079V_W6081I
D247	A6085YY_T6086H	L6079V_W6081I

No.	CH3 Domain Mutations	
	Chain A	Chain B
D467	A6085YY_T6086W	L6079A_W6081V
D468	A6085YM_T6086W	L6079A_W6081V
D469	A6085YW_T6086W	L6079A_W6081V
D470	A6085YH_T6086W	L6079A_W6081V
D471	A6085YF_T6086H	L6079A_W6081V
D472	A6085YY_T6086H	L6079A_W6081V
D473	A6085YM_T6086H	L6079A_W6081V
D474	A6085YW_T6086H	L6079A_W6081V
D475	A6085YH_T6086H	L6079A_W6081V
D476	A6085YF_T6086Y	L6079A_W6081I
D477	A6085YY_T6086Y	L6079A_W6081I
D478	A6085YM_T6086Y	L6079A_W6081I
D479	A6085YW_T6086Y	L6079A_W6081I
D480	A6085YH_T6086Y	L6079A_W6081I
D481	A6085YF_T6086F	L6079A_W6081I
D482	A6085YY_T6086F	L6079A_W6081I
D483	A6085YM_T6086F	L6079A_W6081I
D484	A6085YW_T6086F	L6079A_W6081I
D485	A6085YH_T6086F	L6079A_W6081I
D486	A6085YF_T6086M	L6079A_W6081I
D487	A6085YY_T6086M	L6079A_W6081I
D488	A6085YM_T6086M	L6079A_W6081I
D489	A6085YW_T6086M	L6079A_W6081I
D490	A6085YH_T6086M	L6079A_W6081I
D491	A6085YF_T6086W	L6079A_W6081I
D492	A6085YY_T6086W	L6079A_W6081I
D493	A6085YM_T6086W	L6079A_W6081I
D494	A6085YW_T6086W	L6079A_W6081I
D495	A6085YH_T6086W	L6079A_W6081I
D496	A6085YF_T6086H	L6079A_W6081I
D497	A6085YY_T6086H	L6079A_W6081I

No.	CH3 Domain Mutations	
	Chain A	Chain B
D248	A6085YM_T6086H	L6079V_W6081I
D249	A6085YW_T6086H	L6079V_W6081I
D250	A6085YH_T6086H	L6079V_W6081I
D251	A6085YF_T6086Y	L6079T_W6081T
D252	A6085YY_T6086Y	L6079T_W6081T
D253	A6085YM_T6086Y	L6079T_W6081T
D254	A6085YW_T6086Y	L6079T_W6081T
D255	A6085YH_T6086Y	L6079T_W6081T
D256	A6085YF_T6086F	L6079T_W6081T
D257	A6085YY_T6086F	L6079T_W6081T
D258	A6085YM_T6086F	L6079T_W6081T
D259	A6085YW_T6086F	L6079T_W6081T
D260	A6085YH_T6086F	L6079T_W6081T
D261	A6085YF_T6086M	L6079T_W6081T
D262	A6085YY_T6086M	L6079T_W6081T
D263	A6085YM_T6086M	L6079T_W6081T
D264	A6085YW_T6086M	L6079T_W6081T
D265	A6085YH_T6086M	L6079T_W6081T
D266	A6085YF_T6086W	L6079T_W6081T
D267	A6085YY_T6086W	L6079T_W6081T
D268	A6085YM_T6086W	L6079T_W6081T
D269	A6085YW_T6086W	L6079T_W6081T
D270	A6085YH_T6086W	L6079T_W6081T
D271	A6085YF_T6086H	L6079T_W6081T
D272	A6085YY_T6086H	L6079T_W6081T
D273	A6085YM_T6086H	L6079T_W6081T
D274	A6085YW_T6086H	L6079T_W6081T
D275	A6085YH_T6086H	L6079T_W6081T
D276	A6085YF_T6086Y	L6079T_W6081L
D277	A6085YY_T6086Y	L6079T_W6081L
D278	A6085YM_T6086Y	L6079T_W6081L

No.	CH3 Domain Mutations	
	Chain A	Chain B
D498	A6085YM_T6086H	L6079A_W6081I
D499	A6085YW_T6086H	L6079A_W6081I
D500	A6085YH_T6086H	L6079A_W6081I
D501	A6085YF_T6086Y	L6079I_W6081T
D502	A6085YY_T6086Y	L6079I_W6081T
D503	A6085YM_T6086Y	L6079I_W6081T
D504	A6085YW_T6086Y	L6079I_W6081T
D505	A6085YH_T6086Y	L6079I_W6081T
D506	A6085YF_T6086F	L6079I_W6081T
D507	A6085YY_T6086F	L6079I_W6081T
D508	A6085YM_T6086F	L6079I_W6081T
D509	A6085YW_T6086F	L6079I_W6081T
D510	A6085YH_T6086F	L6079I_W6081T
D511	A6085YF_T6086M	L6079I_W6081T
D512	A6085YY_T6086M	L6079I_W6081T
D513	A6085YM_T6086M	L6079I_W6081T
D514	A6085YW_T6086M	L6079I_W6081T
D515	A6085YH_T6086M	L6079I_W6081T
D516	A6085YF_T6086W	L6079I_W6081T
D517	A6085YY_T6086W	L6079I_W6081T
D518	A6085YM_T6086W	L6079I_W6081T
D519	A6085YW_T6086W	L6079I_W6081T
D520	A6085YH_T6086W	L6079I_W6081T
D521	A6085YF_T6086H	L6079I_W6081T
D522	A6085YY_T6086H	L6079I_W6081T
D523	A6085YM_T6086H	L6079I_W6081T
D524	A6085YW_T6086H	L6079I_W6081T
D525	A6085YH_T6086H	L6079I_W6081T
D526	A6085YF_T6086Y	L6079I_W6081L
D527	A6085YY_T6086Y	L6079I_W6081L
D528	A6085YM_T6086Y	L6079I_W6081L

No.	CH3 Domain Mutations	
	Chain A	Chain B
D279	A6085YW_T6086Y	L6079T_W6081L
D280	A6085YH_T6086Y	L6079T_W6081L
D281	A6085YF_T6086F	L6079T_W6081L
D282	A6085YY_T6086F	L6079T_W6081L
D283	A6085YM_T6086F	L6079T_W6081L
D284	A6085YW_T6086F	L6079T_W6081L
D285	A6085YH_T6086F	L6079T_W6081L
D286	A6085YF_T6086M	L6079T_W6081L
D287	A6085YY_T6086M	L6079T_W6081L
D288	A6085YM_T6086M	L6079T_W6081L
D289	A6085YW_T6086M	L6079T_W6081L
D290	A6085YH_T6086M	L6079T_W6081L
D291	A6085YF_T6086W	L6079T_W6081L
D292	A6085YY_T6086W	L6079T_W6081L
D293	A6085YM_T6086W	L6079T_W6081L
D294	A6085YW_T6086W	L6079T_W6081L
D295	A6085YH_T6086W	L6079T_W6081L
D296	A6085YF_T6086H	L6079T_W6081L
D297	A6085YY_T6086H	L6079T_W6081L
D298	A6085YM_T6086H	L6079T_W6081L
D299	A6085YW_T6086H	L6079T_W6081L
D300	A6085YH_T6086H	L6079T_W6081L
D301	A6085YF_T6086Y	L6079T_W6081A
D302	A6085YY_T6086Y	L6079T_W6081A
D303	A6085YM_T6086Y	L6079T_W6081A
D304	A6085YW_T6086Y	L6079T_W6081A
D305	A6085YH_T6086Y	L6079T_W6081A
D306	A6085YF_T6086F	L6079T_W6081A
D307	A6085YY_T6086F	L6079T_W6081A
D308	A6085YM_T6086F	L6079T_W6081A
D309	A6085YW_T6086F	L6079T_W6081A

No.	CH3 Domain Mutations	
	Chain A	Chain B
D529	A6085YW_T6086Y	L6079I_W6081L
D530	A6085YH_T6086Y	L6079I_W6081L
D531	A6085YF_T6086F	L6079I_W6081L
D532	A6085YY_T6086F	L6079I_W6081L
D533	A6085YM_T6086F	L6079I_W6081L
D534	A6085YW_T6086F	L6079I_W6081L
D535	A6085YH_T6086F	L6079I_W6081L
D536	A6085YF_T6086M	L6079I_W6081L
D537	A6085YY_T6086M	L6079I_W6081L
D538	A6085YM_T6086M	L6079I_W6081L
D539	A6085YW_T6086M	L6079I_W6081L
D540	A6085YH_T6086M	L6079I_W6081L
D541	A6085YF_T6086W	L6079I_W6081L
D542	A6085YY_T6086W	L6079I_W6081L
D543	A6085YM_T6086W	L6079I_W6081L
D544	A6085YW_T6086W	L6079I_W6081L
D545	A6085YH_T6086W	L6079I_W6081L
D546	A6085YF_T6086H	L6079I_W6081L
D547	A6085YY_T6086H	L6079I_W6081L
D548	A6085YM_T6086H	L6079I_W6081L
D549	A6085YW_T6086H	L6079I_W6081L
D550	A6085YH_T6086H	L6079I_W6081L
D551	A6085YF_T6086Y	L6079I_W6081A
D552	A6085YY_T6086Y	L6079I_W6081A
D553	A6085YM_T6086Y	L6079I_W6081A
D554	A6085YW_T6086Y	L6079I_W6081A
D555	A6085YH_T6086Y	L6079I_W6081A
D556	A6085YF_T6086F	L6079I_W6081A
D557	A6085YY_T6086F	L6079I_W6081A
D558	A6085YM_T6086F	L6079I_W6081A
D559	A6085YW_T6086F	L6079I_W6081A

No.	CH3 Domain Mutations	
	Chain A	Chain B
D310	A6085YH_T6086F	L6079T_W6081A
D311	A6085YF_T6086M	L6079T_W6081A
D312	A6085YY_T6086M	L6079T_W6081A
D313	A6085YM_T6086M	L6079T_W6081A
D314	A6085YW_T6086M	L6079T_W6081A
D315	A6085YH_T6086M	L6079T_W6081A
D316	A6085YF_T6086W	L6079T_W6081A
D317	A6085YY_T6086W	L6079T_W6081A
D318	A6085YM_T6086W	L6079T_W6081A
D319	A6085YW_T6086W	L6079T_W6081A
D320	A6085YH_T6086W	L6079T_W6081A
D321	A6085YF_T6086H	L6079T_W6081A
D322	A6085YY_T6086H	L6079T_W6081A
D323	A6085YM_T6086H	L6079T_W6081A
D324	A6085YW_T6086H	L6079T_W6081A
D325	A6085YH_T6086H	L6079T_W6081A
D326	A6085YF_T6086Y	L6079T_W6081V
D327	A6085YY_T6086Y	L6079T_W6081V
D328	A6085YM_T6086Y	L6079T_W6081V
D329	A6085YW_T6086Y	L6079T_W6081V
D330	A6085YH_T6086Y	L6079T_W6081V
D331	A6085YF_T6086F	L6079T_W6081V
D332	A6085YY_T6086F	L6079T_W6081V
D333	A6085YM_T6086F	L6079T_W6081V
D334	A6085YW_T6086F	L6079T_W6081V
D335	A6085YH_T6086F	L6079T_W6081V
D336	A6085YF_T6086M	L6079T_W6081V
D337	A6085YY_T6086M	L6079T_W6081V
D338	A6085YM_T6086M	L6079T_W6081V
D339	A6085YW_T6086M	L6079T_W6081V
D340	A6085YH_T6086M	L6079T_W6081V

No.	CH3 Domain Mutations	
	Chain A	Chain B
D560	A6085YH_T6086F	L6079I_W6081A
D561	A6085YF_T6086M	L6079I_W6081A
D562	A6085YY_T6086M	L6079I_W6081A
D563	A6085YM_T6086M	L6079I_W6081A
D564	A6085YW_T6086M	L6079I_W6081A
D565	A6085YH_T6086M	L6079I_W6081A
D566	A6085YF_T6086W	L6079I_W6081A
D567	A6085YY_T6086W	L6079I_W6081A
D568	A6085YM_T6086W	L6079I_W6081A
D569	A6085YW_T6086W	L6079I_W6081A
D570	A6085YH_T6086W	L6079I_W6081A
D571	A6085YF_T6086H	L6079I_W6081A
D572	A6085YY_T6086H	L6079I_W6081A
D573	A6085YM_T6086H	L6079I_W6081A
D574	A6085YW_T6086H	L6079I_W6081A
D575	A6085YH_T6086H	L6079I_W6081A
D576	A6085YF_T6086Y	L6079I_W6081V
D577	A6085YY_T6086Y	L6079I_W6081V
D578	A6085YM_T6086Y	L6079I_W6081V
D579	A6085YW_T6086Y	L6079I_W6081V
D580	A6085YH_T6086Y	L6079I_W6081V
D581	A6085YF_T6086F	L6079I_W6081V
D582	A6085YY_T6086F	L6079I_W6081V
D583	A6085YM_T6086F	L6079I_W6081V
D584	A6085YW_T6086F	L6079I_W6081V
D585	A6085YH_T6086F	L6079I_W6081V
D586	A6085YF_T6086M	L6079I_W6081V
D587	A6085YY_T6086M	L6079I_W6081V
D588	A6085YM_T6086M	L6079I_W6081V
D589	A6085YW_T6086M	L6079I_W6081V
D590	A6085YH_T6086M	L6079I_W6081V

No.	CH3 Domain Mutations	
	Chain A	Chain B
D341	A6085YF_T6086W	L6079T_W6081V
D342	A6085YY_T6086W	L6079T_W6081V
D343	A6085YM_T6086W	L6079T_W6081V
D344	A6085YW_T6086W	L6079T_W6081V
D345	A6085YH_T6086W	L6079T_W6081V
D346	A6085YF_T6086H	L6079T_W6081V
D347	A6085YY_T6086H	L6079T_W6081V
D348	A6085YM_T6086H	L6079T_W6081V
D349	A6085YW_T6086H	L6079T_W6081V
D350	A6085YH_T6086H	L6079T_W6081V
D351	A6085YF_T6086Y	L6079T_W6081I
D352	A6085YY_T6086Y	L6079T_W6081I
D353	A6085YM_T6086Y	L6079T_W6081I
D354	A6085YW_T6086Y	L6079T_W6081I
D355	A6085YH_T6086Y	L6079T_W6081I
D356	A6085YF_T6086F	L6079T_W6081I
D357	A6085YY_T6086F	L6079T_W6081I
D358	A6085YM_T6086F	L6079T_W6081I
D359	A6085YW_T6086F	L6079T_W6081I
D360	A6085YH_T6086F	L6079T_W6081I
D361	A6085YF_T6086M	L6079T_W6081I
D362	A6085YY_T6086M	L6079T_W6081I
D363	A6085YM_T6086M	L6079T_W6081I
D364	A6085YW_T6086M	L6079T_W6081I
D365	A6085YH_T6086M	L6079T_W6081I
D366	A6085YF_T6086W	L6079T_W6081I
D367	A6085YY_T6086W	L6079T_W6081I
D368	A6085YM_T6086W	L6079T_W6081I
D369	A6085YW_T6086W	L6079T_W6081I
D370	A6085YH_T6086W	L6079T_W6081I
D371	A6085YF_T6086H	L6079T_W6081I

No.	CH3 Domain Mutations	
	Chain A	Chain B
D591	A6085YF_T6086W	L6079I_W6081V
D592	A6085YY_T6086W	L6079I_W6081V
D593	A6085YM_T6086W	L6079I_W6081V
D594	A6085YW_T6086W	L6079I_W6081V
D595	A6085YH_T6086W	L6079I_W6081V
D596	A6085YF_T6086H	L6079I_W6081V
D597	A6085YY_T6086H	L6079I_W6081V
D598	A6085YM_T6086H	L6079I_W6081V
D599	A6085YW_T6086H	L6079I_W6081V
D600	A6085YH_T6086H	L6079I_W6081V
D601	A6085YF_T6086Y	L6079I_W6081I
D602	A6085YY_T6086Y	L6079I_W6081I
D603	A6085YM_T6086Y	L6079I_W6081I
D604	A6085YW_T6086Y	L6079I_W6081I
D605	A6085YH_T6086Y	L6079I_W6081I
D606	A6085YF_T6086F	L6079I_W6081I
D607	A6085YY_T6086F	L6079I_W6081I
D608	A6085YM_T6086F	L6079I_W6081I
D609	A6085YW_T6086F	L6079I_W6081I
D610	A6085YH_T6086F	L6079I_W6081I
D611	A6085YF_T6086M	L6079I_W6081I
D612	A6085YY_T6086M	L6079I_W6081I
D613	A6085YM_T6086M	L6079I_W6081I
D614	A6085YW_T6086M	L6079I_W6081I
D615	A6085YH_T6086M	L6079I_W6081I
D616	A6085YF_T6086W	L6079I_W6081I
D617	A6085YY_T6086W	L6079I_W6081I
D618	A6085YM_T6086W	L6079I_W6081I
D619	A6085YW_T6086W	L6079I_W6081I
D620	A6085YH_T6086W	L6079I_W6081I
D621	A6085YF_T6086H	L6079I_W6081I

No.	CH3 Domain Mutations	
	Chain A	Chain B
D372	A6085YY_T6086H	L6079T_W6081I
D373	A6085YM_T6086H	L6079T_W6081I
D374	A6085YW_T6086H	L6079T_W6081I
D375	A6085YH_T6086H	L6079T_W6081I

No.	CH3 Domain Mutations	
	Chain A	Chain B
D622	A6085YY_T6086H	L6079I_W6081I
D623	A6085YM_T6086H	L6079I_W6081I
D624	A6085YW_T6086H	L6079I_W6081I
D625	A6085YH_T6086H	L6079I_W6081I

Table 9: IgA HetFc Designs comprising Core Mutations in Combination with Mutation at Position 6088 in Chain B

No.	CH3 Domain Mutations	
	Chain A	Chain B
D626	A6085YF_T6086Y	W6081T_I6088L
D627	A6085YY_T6086Y	W6081T_I6088L
D628	A6085YM_T6086Y	W6081T_I6088L
D629	A6085YW_T6086Y	W6081T_I6088L
D630	A6085YH_T6086Y	W6081T_I6088L
D631	A6085YF_T6086F	W6081T_I6088L
D632	A6085YY_T6086F	W6081T_I6088L
D633	A6085YM_T6086F	W6081T_I6088L
D634	A6085YW_T6086F	W6081T_I6088L
D635	A6085YH_T6086F	W6081T_I6088L
D636	A6085YF_T6086M	W6081T_I6088L
D637	A6085YY_T6086M	W6081T_I6088L
D638	A6085YM_T6086M	W6081T_I6088L
D639	A6085YW_T6086M	W6081T_I6088L
D640	A6085YH_T6086M	W6081T_I6088L
D641	A6085YF_T6086W	W6081T_I6088L
D642	A6085YY_T6086W	W6081T_I6088L
D643	A6085YM_T6086W	W6081T_I6088L
D644	A6085YW_T6086W	W6081T_I6088L
D645	A6085YH_T6086W	W6081T_I6088L
D646	A6085YF_T6086H	W6081T_I6088L
D647	A6085YY_T6086H	W6081T_I6088L

No.	CH3 Domain Mutations	
	Chain A	Chain B
D876	A6085YF_T6086Y	W6081T_I6088V
D877	A6085YY_T6086Y	W6081T_I6088V
D878	A6085YM_T6086Y	W6081T_I6088V
D879	A6085YW_T6086Y	W6081T_I6088V
D880	A6085YH_T6086Y	W6081T_I6088V
D881	A6085YF_T6086F	W6081T_I6088V
D882	A6085YY_T6086F	W6081T_I6088V
D883	A6085YM_T6086F	W6081T_I6088V
D884	A6085YW_T6086F	W6081T_I6088V
D885	A6085YH_T6086F	W6081T_I6088V
D886	A6085YF_T6086M	W6081T_I6088V
D887	A6085YY_T6086M	W6081T_I6088V
D888	A6085YM_T6086M	W6081T_I6088V
D889	A6085YW_T6086M	W6081T_I6088V
D890	A6085YH_T6086M	W6081T_I6088V
D891	A6085YF_T6086W	W6081T_I6088V
D892	A6085YY_T6086W	W6081T_I6088V
D893	A6085YM_T6086W	W6081T_I6088V
D894	A6085YW_T6086W	W6081T_I6088V
D895	A6085YH_T6086W	W6081T_I6088V
D896	A6085YF_T6086H	W6081T_I6088V
D897	A6085YY_T6086H	W6081T_I6088V

No.	CH3 Domain Mutations	
	Chain A	Chain B
D648	A6085YM_T6086H	W6081T_I6088L
D649	A6085YW_T6086H	W6081T_I6088L
D650	A6085YH_T6086H	W6081T_I6088L
D651	A6085YF_T6086Y	W6081L_I6088L
D652	A6085YY_T6086Y	W6081L_I6088L
D653	A6085YM_T6086Y	W6081L_I6088L
D654	A6085YW_T6086Y	W6081L_I6088L
D655	A6085YH_T6086Y	W6081L_I6088L
D656	A6085YF_T6086F	W6081L_I6088L
D657	A6085YY_T6086F	W6081L_I6088L
D658	A6085YM_T6086F	W6081L_I6088L
D659	A6085YW_T6086F	W6081L_I6088L
D660	A6085YH_T6086F	W6081L_I6088L
D661	A6085YF_T6086M	W6081L_I6088L
D662	A6085YY_T6086M	W6081L_I6088L
D663	A6085YM_T6086M	W6081L_I6088L
D664	A6085YW_T6086M	W6081L_I6088L
D665	A6085YH_T6086M	W6081L_I6088L
D666	A6085YF_T6086W	W6081L_I6088L
D667	A6085YY_T6086W	W6081L_I6088L
D668	A6085YM_T6086W	W6081L_I6088L
D669	A6085YW_T6086W	W6081L_I6088L
D670	A6085YH_T6086W	W6081L_I6088L
D671	A6085YF_T6086H	W6081L_I6088L
D672	A6085YY_T6086H	W6081L_I6088L
D673	A6085YM_T6086H	W6081L_I6088L
D674	A6085YW_T6086H	W6081L_I6088L
D675	A6085YH_T6086H	W6081L_I6088L
D676	A6085YF_T6086Y	W6081A_I6088L
D677	A6085YY_T6086Y	W6081A_I6088L
D678	A6085YM_T6086Y	W6081A_I6088L

No.	CH3 Domain Mutations	
	Chain A	Chain B
D898	A6085YM_T6086H	W6081T_I6088V
D899	A6085YW_T6086H	W6081T_I6088V
D900	A6085YH_T6086H	W6081T_I6088V
D901	A6085YF_T6086Y	W6081L_I6088V
D902	A6085YY_T6086Y	W6081L_I6088V
D903	A6085YM_T6086Y	W6081L_I6088V
D904	A6085YW_T6086Y	W6081L_I6088V
D905	A6085YH_T6086Y	W6081L_I6088V
D906	A6085YF_T6086F	W6081L_I6088V
D907	A6085YY_T6086F	W6081L_I6088V
D908	A6085YM_T6086F	W6081L_I6088V
D909	A6085YW_T6086F	W6081L_I6088V
D910	A6085YH_T6086F	W6081L_I6088V
D911	A6085YF_T6086M	W6081L_I6088V
D912	A6085YY_T6086M	W6081L_I6088V
D913	A6085YM_T6086M	W6081L_I6088V
D914	A6085YW_T6086M	W6081L_I6088V
D915	A6085YH_T6086M	W6081L_I6088V
D916	A6085YF_T6086W	W6081L_I6088V
D917	A6085YY_T6086W	W6081L_I6088V
D918	A6085YM_T6086W	W6081L_I6088V
D919	A6085YW_T6086W	W6081L_I6088V
D920	A6085YH_T6086W	W6081L_I6088V
D921	A6085YF_T6086H	W6081L_I6088V
D922	A6085YY_T6086H	W6081L_I6088V
D923	A6085YM_T6086H	W6081L_I6088V
D924	A6085YW_T6086H	W6081L_I6088V
D925	A6085YH_T6086H	W6081L_I6088V
D926	A6085YF_T6086Y	W6081A_I6088V
D927	A6085YY_T6086Y	W6081A_I6088V
D928	A6085YM_T6086Y	W6081A_I6088V

No.	CH3 Domain Mutations	
	Chain A	Chain B
D679	A6085YW_T6086Y	W6081A_I6088L
D680	A6085YH_T6086Y	W6081A_I6088L
D681	A6085YF_T6086F	W6081A_I6088L
D682	A6085YY_T6086F	W6081A_I6088L
D683	A6085YM_T6086F	W6081A_I6088L
D684	A6085YW_T6086F	W6081A_I6088L
D685	A6085YH_T6086F	W6081A_I6088L
D686	A6085YF_T6086M	W6081A_I6088L
D687	A6085YY_T6086M	W6081A_I6088L
D688	A6085YM_T6086M	W6081A_I6088L
D689	A6085YW_T6086M	W6081A_I6088L
D690	A6085YH_T6086M	W6081A_I6088L
D691	A6085YF_T6086W	W6081A_I6088L
D692	A6085YY_T6086W	W6081A_I6088L
D693	A6085YM_T6086W	W6081A_I6088L
D694	A6085YW_T6086W	W6081A_I6088L
D695	A6085YH_T6086W	W6081A_I6088L
D696	A6085YF_T6086H	W6081A_I6088L
D697	A6085YY_T6086H	W6081A_I6088L
D698	A6085YM_T6086H	W6081A_I6088L
D699	A6085YW_T6086H	W6081A_I6088L
D700	A6085YH_T6086H	W6081A_I6088L
D701	A6085YF_T6086Y	W6081V_I6088L
D702	A6085YY_T6086Y	W6081V_I6088L
D703	A6085YM_T6086Y	W6081V_I6088L
D704	A6085YW_T6086Y	W6081V_I6088L
D705	A6085YH_T6086Y	W6081V_I6088L
D706	A6085YF_T6086F	W6081V_I6088L
D707	A6085YY_T6086F	W6081V_I6088L
D708	A6085YM_T6086F	W6081V_I6088L
D709	A6085YW_T6086F	W6081V_I6088L

No.	CH3 Domain Mutations	
	Chain A	Chain B
D929	A6085YW_T6086Y	W6081A_I6088V
D930	A6085YH_T6086Y	W6081A_I6088V
D931	A6085YF_T6086F	W6081A_I6088V
D932	A6085YY_T6086F	W6081A_I6088V
D933	A6085YM_T6086F	W6081A_I6088V
D934	A6085YW_T6086F	W6081A_I6088V
D935	A6085YH_T6086F	W6081A_I6088V
D936	A6085YF_T6086M	W6081A_I6088V
D937	A6085YY_T6086M	W6081A_I6088V
D938	A6085YM_T6086M	W6081A_I6088V
D939	A6085YW_T6086M	W6081A_I6088V
D940	A6085YH_T6086M	W6081A_I6088V
D941	A6085YF_T6086W	W6081A_I6088V
D942	A6085YY_T6086W	W6081A_I6088V
D943	A6085YM_T6086W	W6081A_I6088V
D944	A6085YW_T6086W	W6081A_I6088V
D945	A6085YH_T6086W	W6081A_I6088V
D946	A6085YF_T6086H	W6081A_I6088V
D947	A6085YY_T6086H	W6081A_I6088V
D948	A6085YM_T6086H	W6081A_I6088V
D949	A6085YW_T6086H	W6081A_I6088V
D950	A6085YH_T6086H	W6081A_I6088V
D951	A6085YF_T6086Y	W6081V_I6088V
D952	A6085YY_T6086Y	W6081V_I6088V
D953	A6085YM_T6086Y	W6081V_I6088V
D954	A6085YW_T6086Y	W6081V_I6088V
D955	A6085YH_T6086Y	W6081V_I6088V
D956	A6085YF_T6086F	W6081V_I6088V
D957	A6085YY_T6086F	W6081V_I6088V
D958	A6085YM_T6086F	W6081V_I6088V
D959	A6085YW_T6086F	W6081V_I6088V

No.	CH3 Domain Mutations	
	Chain A	Chain B
D710	A6085YH_T6086F	W6081V_I6088L
D711	A6085YF_T6086M	W6081V_I6088L
D712	A6085YY_T6086M	W6081V_I6088L
D713	A6085YM_T6086M	W6081V_I6088L
D714	A6085YW_T6086M	W6081V_I6088L
D715	A6085YH_T6086M	W6081V_I6088L
D716	A6085YF_T6086W	W6081V_I6088L
D717	A6085YY_T6086W	W6081V_I6088L
D718	A6085YM_T6086W	W6081V_I6088L
D719	A6085YW_T6086W	W6081V_I6088L
D720	A6085YH_T6086W	W6081V_I6088L
D721	A6085YF_T6086H	W6081V_I6088L
D722	A6085YY_T6086H	W6081V_I6088L
D723	A6085YM_T6086H	W6081V_I6088L
D724	A6085YW_T6086H	W6081V_I6088L
D725	A6085YH_T6086H	W6081V_I6088L
D726	A6085YF_T6086Y	W6081I_I6088L
D727	A6085YY_T6086Y	W6081I_I6088L
D728	A6085YM_T6086Y	W6081I_I6088L
D729	A6085YW_T6086Y	W6081I_I6088L
D730	A6085YH_T6086Y	W6081I_I6088L
D731	A6085YF_T6086F	W6081I_I6088L
D732	A6085YY_T6086F	W6081I_I6088L
D733	A6085YM_T6086F	W6081I_I6088L
D734	A6085YW_T6086F	W6081I_I6088L
D735	A6085YH_T6086F	W6081I_I6088L
D736	A6085YF_T6086M	W6081I_I6088L
D737	A6085YY_T6086M	W6081I_I6088L
D738	A6085YM_T6086M	W6081I_I6088L
D739	A6085YW_T6086M	W6081I_I6088L
D740	A6085YH_T6086M	W6081I_I6088L

No.	CH3 Domain Mutations	
	Chain A	Chain B
D960	A6085YH_T6086F	W6081V_I6088V
D961	A6085YF_T6086M	W6081V_I6088V
D962	A6085YY_T6086M	W6081V_I6088V
D963	A6085YM_T6086M	W6081V_I6088V
D964	A6085YW_T6086M	W6081V_I6088V
D965	A6085YH_T6086M	W6081V_I6088V
D966	A6085YF_T6086W	W6081V_I6088V
D967	A6085YY_T6086W	W6081V_I6088V
D968	A6085YM_T6086W	W6081V_I6088V
D969	A6085YW_T6086W	W6081V_I6088V
D970	A6085YH_T6086W	W6081V_I6088V
D971	A6085YF_T6086H	W6081V_I6088V
D972	A6085YY_T6086H	W6081V_I6088V
D973	A6085YM_T6086H	W6081V_I6088V
D974	A6085YW_T6086H	W6081V_I6088V
D975	A6085YH_T6086H	W6081V_I6088V
D976	A6085YF_T6086Y	W6081I_I6088V
D977	A6085YY_T6086Y	W6081I_I6088V
D978	A6085YM_T6086Y	W6081I_I6088V
D979	A6085YW_T6086Y	W6081I_I6088V
D980	A6085YH_T6086Y	W6081I_I6088V
D981	A6085YF_T6086F	W6081I_I6088V
D982	A6085YY_T6086F	W6081I_I6088V
D983	A6085YM_T6086F	W6081I_I6088V
D984	A6085YW_T6086F	W6081I_I6088V
D985	A6085YH_T6086F	W6081I_I6088V
D986	A6085YF_T6086M	W6081I_I6088V
D987	A6085YY_T6086M	W6081I_I6088V
D988	A6085YM_T6086M	W6081I_I6088V
D989	A6085YW_T6086M	W6081I_I6088V
D990	A6085YH_T6086M	W6081I_I6088V

No.	CH3 Domain Mutations	
	Chain A	Chain B
D741	A6085YF_T6086W	W6081I_I6088L
D742	A6085YY_T6086W	W6081I_I6088L
D743	A6085YM_T6086W	W6081I_I6088L
D744	A6085YW_T6086W	W6081I_I6088L
D745	A6085YH_T6086W	W6081I_I6088L
D746	A6085YF_T6086H	W6081I_I6088L
D747	A6085YY_T6086H	W6081I_I6088L
D748	A6085YM_T6086H	W6081I_I6088L
D749	A6085YW_T6086H	W6081I_I6088L
D750	A6085YH_T6086H	W6081I_I6088L
D751	A6085YF_T6086Y	W6081T_I6088A
D752	A6085YY_T6086Y	W6081T_I6088A
D753	A6085YM_T6086Y	W6081T_I6088A
D754	A6085YW_T6086Y	W6081T_I6088A
D755	A6085YH_T6086Y	W6081T_I6088A
D756	A6085YF_T6086F	W6081T_I6088A
D757	A6085YY_T6086F	W6081T_I6088A
D758	A6085YM_T6086F	W6081T_I6088A
D759	A6085YW_T6086F	W6081T_I6088A
D760	A6085YH_T6086F	W6081T_I6088A
D761	A6085YF_T6086M	W6081T_I6088A
D762	A6085YY_T6086M	W6081T_I6088A
D763	A6085YM_T6086M	W6081T_I6088A
D764	A6085YW_T6086M	W6081T_I6088A
D765	A6085YH_T6086M	W6081T_I6088A
D766	A6085YF_T6086W	W6081T_I6088A
D767	A6085YY_T6086W	W6081T_I6088A
D768	A6085YM_T6086W	W6081T_I6088A
D769	A6085YW_T6086W	W6081T_I6088A
D770	A6085YH_T6086W	W6081T_I6088A
D771	A6085YF_T6086H	W6081T_I6088A

No.	CH3 Domain Mutations	
	Chain A	Chain B
D991	A6085YF_T6086W	W6081I_I6088V
D992	A6085YY_T6086W	W6081I_I6088V
D993	A6085YM_T6086W	W6081I_I6088V
D994	A6085YW_T6086W	W6081I_I6088V
D995	A6085YH_T6086W	W6081I_I6088V
D996	A6085YF_T6086H	W6081I_I6088V
D997	A6085YY_T6086H	W6081I_I6088V
D998	A6085YM_T6086H	W6081I_I6088V
D999	A6085YW_T6086H	W6081I_I6088V
D1000	A6085YH_T6086H	W6081I_I6088V
D1001	A6085YF_T6086Y	W6081T_I6088T
D1002	A6085YY_T6086Y	W6081T_I6088T
D1003	A6085YM_T6086Y	W6081T_I6088T
D1004	A6085YW_T6086Y	W6081T_I6088T
D1005	A6085YH_T6086Y	W6081T_I6088T
D1006	A6085YF_T6086F	W6081T_I6088T
D1007	A6085YY_T6086F	W6081T_I6088T
D1008	A6085YM_T6086F	W6081T_I6088T
D1009	A6085YW_T6086F	W6081T_I6088T
D1010	A6085YH_T6086F	W6081T_I6088T
D1011	A6085YF_T6086M	W6081T_I6088T
D1012	A6085YY_T6086M	W6081T_I6088T
D1013	A6085YM_T6086M	W6081T_I6088T
D1014	A6085YW_T6086M	W6081T_I6088T
D1015	A6085YH_T6086M	W6081T_I6088T
D1016	A6085YF_T6086W	W6081T_I6088T
D1017	A6085YY_T6086W	W6081T_I6088T
D1018	A6085YM_T6086W	W6081T_I6088T
D1019	A6085YW_T6086W	W6081T_I6088T
D1020	A6085YH_T6086W	W6081T_I6088T
D1021	A6085YF_T6086H	W6081T_I6088T

No.	CH3 Domain Mutations	
	Chain A	Chain B
D772	A6085YY_T6086H	W6081T_I6088A
D773	A6085YM_T6086H	W6081T_I6088A
D774	A6085YW_T6086H	W6081T_I6088A
D775	A6085YH_T6086H	W6081T_I6088A
D776	A6085YF_T6086Y	W6081L_I6088A
D777	A6085YY_T6086Y	W6081L_I6088A
D778	A6085YM_T6086Y	W6081L_I6088A
D779	A6085YW_T6086Y	W6081L_I6088A
D780	A6085YH_T6086Y	W6081L_I6088A
D781	A6085YF_T6086F	W6081L_I6088A
D782	A6085YY_T6086F	W6081L_I6088A
D783	A6085YM_T6086F	W6081L_I6088A
D784	A6085YW_T6086F	W6081L_I6088A
D785	A6085YH_T6086F	W6081L_I6088A
D786	A6085YF_T6086M	W6081L_I6088A
D787	A6085YY_T6086M	W6081L_I6088A
D788	A6085YM_T6086M	W6081L_I6088A
D789	A6085YW_T6086M	W6081L_I6088A
D790	A6085YH_T6086M	W6081L_I6088A
D791	A6085YF_T6086W	W6081L_I6088A
D792	A6085YY_T6086W	W6081L_I6088A
D793	A6085YM_T6086W	W6081L_I6088A
D794	A6085YW_T6086W	W6081L_I6088A
D795	A6085YH_T6086W	W6081L_I6088A
D796	A6085YF_T6086H	W6081L_I6088A
D797	A6085YY_T6086H	W6081L_I6088A
D798	A6085YM_T6086H	W6081L_I6088A
D799	A6085YW_T6086H	W6081L_I6088A
D800	A6085YH_T6086H	W6081L_I6088A
D801	A6085YF_T6086Y	W6081A_I6088A
D802	A6085YY_T6086Y	W6081A_I6088A

No.	CH3 Domain Mutations	
	Chain A	Chain B
D1022	A6085YY_T6086H	W6081T_I6088T
D1023	A6085YM_T6086H	W6081T_I6088T
D1024	A6085YW_T6086H	W6081T_I6088T
D1025	A6085YH_T6086H	W6081T_I6088T
D1026	A6085YF_T6086Y	W6081L_I6088T
D1027	A6085YY_T6086Y	W6081L_I6088T
D1028	A6085YM_T6086Y	W6081L_I6088T
D1029	A6085YW_T6086Y	W6081L_I6088T
D1030	A6085YH_T6086Y	W6081L_I6088T
D1031	A6085YF_T6086F	W6081L_I6088T
D1032	A6085YY_T6086F	W6081L_I6088T
D1033	A6085YM_T6086F	W6081L_I6088T
D1034	A6085YW_T6086F	W6081L_I6088T
D1035	A6085YH_T6086F	W6081L_I6088T
D1036	A6085YF_T6086M	W6081L_I6088T
D1037	A6085YY_T6086M	W6081L_I6088T
D1038	A6085YM_T6086M	W6081L_I6088T
D1039	A6085YW_T6086M	W6081L_I6088T
D1040	A6085YH_T6086M	W6081L_I6088T
D1041	A6085YF_T6086W	W6081L_I6088T
D1042	A6085YY_T6086W	W6081L_I6088T
D1043	A6085YM_T6086W	W6081L_I6088T
D1044	A6085YW_T6086W	W6081L_I6088T
D1045	A6085YH_T6086W	W6081L_I6088T
D1046	A6085YF_T6086H	W6081L_I6088T
D1047	A6085YY_T6086H	W6081L_I6088T
D1048	A6085YM_T6086H	W6081L_I6088T
D1049	A6085YW_T6086H	W6081L_I6088T
D1050	A6085YH_T6086H	W6081L_I6088T
D1051	A6085YF_T6086Y	W6081A_I6088T
D1052	A6085YY_T6086Y	W6081A_I6088T

No.	CH3 Domain Mutations	
	Chain A	Chain B
D803	A6085YM_T6086Y	W6081A_I6088A
D804	A6085YW_T6086Y	W6081A_I6088A
D805	A6085YH_T6086Y	W6081A_I6088A
D806	A6085YF_T6086F	W6081A_I6088A
D807	A6085YY_T6086F	W6081A_I6088A
D808	A6085YM_T6086F	W6081A_I6088A
D809	A6085YW_T6086F	W6081A_I6088A
D810	A6085YH_T6086F	W6081A_I6088A
D811	A6085YF_T6086M	W6081A_I6088A
D812	A6085YY_T6086M	W6081A_I6088A
D813	A6085YM_T6086M	W6081A_I6088A
D814	A6085YW_T6086M	W6081A_I6088A
D815	A6085YH_T6086M	W6081A_I6088A
D816	A6085YF_T6086W	W6081A_I6088A
D817	A6085YY_T6086W	W6081A_I6088A
D818	A6085YM_T6086W	W6081A_I6088A
D819	A6085YW_T6086W	W6081A_I6088A
D820	A6085YH_T6086W	W6081A_I6088A
D821	A6085YF_T6086H	W6081A_I6088A
D822	A6085YY_T6086H	W6081A_I6088A
D823	A6085YM_T6086H	W6081A_I6088A
D824	A6085YW_T6086H	W6081A_I6088A
D825	A6085YH_T6086H	W6081A_I6088A
D826	A6085YF_T6086Y	W6081V_I6088A
D827	A6085YY_T6086Y	W6081V_I6088A
D828	A6085YM_T6086Y	W6081V_I6088A
D829	A6085YW_T6086Y	W6081V_I6088A
D830	A6085YH_T6086Y	W6081V_I6088A
D831	A6085YF_T6086F	W6081V_I6088A
D832	A6085YY_T6086F	W6081V_I6088A
D833	A6085YM_T6086F	W6081V_I6088A

No.	CH3 Domain Mutations	
	Chain A	Chain B
D1053	A6085YM_T6086Y	W6081A_I6088T
D1054	A6085YW_T6086Y	W6081A_I6088T
D1055	A6085YH_T6086Y	W6081A_I6088T
D1056	A6085YF_T6086F	W6081A_I6088T
D1057	A6085YY_T6086F	W6081A_I6088T
D1058	A6085YM_T6086F	W6081A_I6088T
D1059	A6085YW_T6086F	W6081A_I6088T
D1060	A6085YH_T6086F	W6081A_I6088T
D1061	A6085YF_T6086M	W6081A_I6088T
D1062	A6085YY_T6086M	W6081A_I6088T
D1063	A6085YM_T6086M	W6081A_I6088T
D1064	A6085YW_T6086M	W6081A_I6088T
D1065	A6085YH_T6086M	W6081A_I6088T
D1066	A6085YF_T6086W	W6081A_I6088T
D1067	A6085YY_T6086W	W6081A_I6088T
D1068	A6085YM_T6086W	W6081A_I6088T
D1069	A6085YW_T6086W	W6081A_I6088T
D1070	A6085YH_T6086W	W6081A_I6088T
D1071	A6085YF_T6086H	W6081A_I6088T
D1072	A6085YY_T6086H	W6081A_I6088T
D1073	A6085YM_T6086H	W6081A_I6088T
D1074	A6085YW_T6086H	W6081A_I6088T
D1075	A6085YH_T6086H	W6081A_I6088T
D1076	A6085YF_T6086Y	W6081V_I6088T
D1077	A6085YY_T6086Y	W6081V_I6088T
D1078	A6085YM_T6086Y	W6081V_I6088T
D1079	A6085YW_T6086Y	W6081V_I6088T
D1080	A6085YH_T6086Y	W6081V_I6088T
D1081	A6085YF_T6086F	W6081V_I6088T
D1082	A6085YY_T6086F	W6081V_I6088T
D1083	A6085YM_T6086F	W6081V_I6088T

No.	CH3 Domain Mutations	
	Chain A	Chain B
D834	A6085YW_T6086F	W6081V_I6088A
D835	A6085YH_T6086F	W6081V_I6088A
D836	A6085YF_T6086M	W6081V_I6088A
D837	A6085YY_T6086M	W6081V_I6088A
D838	A6085YM_T6086M	W6081V_I6088A
D839	A6085YW_T6086M	W6081V_I6088A
D840	A6085YH_T6086M	W6081V_I6088A
D841	A6085YF_T6086W	W6081V_I6088A
D842	A6085YY_T6086W	W6081V_I6088A
D843	A6085YM_T6086W	W6081V_I6088A
D844	A6085YW_T6086W	W6081V_I6088A
D845	A6085YH_T6086W	W6081V_I6088A
D846	A6085YF_T6086H	W6081V_I6088A
D847	A6085YY_T6086H	W6081V_I6088A
D848	A6085YM_T6086H	W6081V_I6088A
D849	A6085YW_T6086H	W6081V_I6088A
D850	A6085YH_T6086H	W6081V_I6088A
D851	A6085YF_T6086Y	W6081I_I6088A
D852	A6085YY_T6086Y	W6081I_I6088A
D853	A6085YM_T6086Y	W6081I_I6088A
D854	A6085YW_T6086Y	W6081I_I6088A
D855	A6085YH_T6086Y	W6081I_I6088A
D856	A6085YF_T6086F	W6081I_I6088A
D857	A6085YY_T6086F	W6081I_I6088A
D858	A6085YM_T6086F	W6081I_I6088A
D859	A6085YW_T6086F	W6081I_I6088A
D860	A6085YH_T6086F	W6081I_I6088A
D861	A6085YF_T6086M	W6081I_I6088A
D862	A6085YY_T6086M	W6081I_I6088A
D863	A6085YM_T6086M	W6081I_I6088A
D864	A6085YW_T6086M	W6081I_I6088A

No.	CH3 Domain Mutations	
	Chain A	Chain B
D1084	A6085YW_T6086F	W6081V_I6088T
D1085	A6085YH_T6086F	W6081V_I6088T
D1086	A6085YF_T6086M	W6081V_I6088T
D1087	A6085YY_T6086M	W6081V_I6088T
D1088	A6085YM_T6086M	W6081V_I6088T
D1089	A6085YW_T6086M	W6081V_I6088T
D1090	A6085YH_T6086M	W6081V_I6088T
D1091	A6085YF_T6086W	W6081V_I6088T
D1092	A6085YY_T6086W	W6081V_I6088T
D1093	A6085YM_T6086W	W6081V_I6088T
D1094	A6085YW_T6086W	W6081V_I6088T
D1095	A6085YH_T6086W	W6081V_I6088T
D1096	A6085YF_T6086H	W6081V_I6088T
D1097	A6085YY_T6086H	W6081V_I6088T
D1098	A6085YM_T6086H	W6081V_I6088T
D1099	A6085YW_T6086H	W6081V_I6088T
D1100	A6085YH_T6086H	W6081V_I6088T
D1101	A6085YF_T6086Y	W6081I_I6088T
D1102	A6085YY_T6086Y	W6081I_I6088T
D1103	A6085YM_T6086Y	W6081I_I6088T
D1104	A6085YW_T6086Y	W6081I_I6088T
D1105	A6085YH_T6086Y	W6081I_I6088T
D1106	A6085YF_T6086F	W6081I_I6088T
D1107	A6085YY_T6086F	W6081I_I6088T
D1108	A6085YM_T6086F	W6081I_I6088T
D1109	A6085YW_T6086F	W6081I_I6088T
D1110	A6085YH_T6086F	W6081I_I6088T
D1111	A6085YF_T6086M	W6081I_I6088T
D1112	A6085YY_T6086M	W6081I_I6088T
D1113	A6085YM_T6086M	W6081I_I6088T
D1114	A6085YW_T6086M	W6081I_I6088T

No.	CH3 Domain Mutations	
	Chain A	Chain B
D865	A6085YH_T6086M	W6081I_I6088A
D866	A6085YF_T6086W	W6081I_I6088A
D867	A6085YY_T6086W	W6081I_I6088A
D868	A6085YM_T6086W	W6081I_I6088A
D869	A6085YW_T6086W	W6081I_I6088A
D870	A6085YH_T6086W	W6081I_I6088A
D871	A6085YF_T6086H	W6081I_I6088A
D872	A6085YY_T6086H	W6081I_I6088A
D873	A6085YM_T6086H	W6081I_I6088A
D874	A6085YW_T6086H	W6081I_I6088A
D875	A6085YH_T6086H	W6081I_I6088A

No.	CH3 Domain Mutations	
	Chain A	Chain B
D1115	A6085YH_T6086M	W6081I_I6088T
D1116	A6085YF_T6086W	W6081I_I6088T
D1117	A6085YY_T6086W	W6081I_I6088T
D1118	A6085YM_T6086W	W6081I_I6088T
D1119	A6085YW_T6086W	W6081I_I6088T
D1120	A6085YH_T6086W	W6081I_I6088T
D1121	A6085YF_T6086H	W6081I_I6088T
D1122	A6085YY_T6086H	W6081I_I6088T
D1123	A6085YM_T6086H	W6081I_I6088T
D1124	A6085YW_T6086H	W6081I_I6088T
D1125	A6085YH_T6086H	W6081I_I6088T

Table 10: IgA HetFc Designs comprising Core Mutations in Combination with Mutations at Positions 6079 and 6088 in Chain B

No.	CH3 Domain Mutations	
	Chain A	Chain B
D1126	A6085YF_T6086Y	L6079V_W6081T_I6088L
D1127	A6085YY_T6086Y	L6079V_W6081T_I6088L
D1128	A6085YM_T6086Y	L6079V_W6081T_I6088L
D1129	A6085YW_T6086Y	L6079V_W6081T_I6088L
D1130	A6085YH_T6086Y	L6079V_W6081T_I6088L
D1131	A6085YF_T6086F	L6079V_W6081T_I6088L
D1132	A6085YY_T6086F	L6079V_W6081T_I6088L
D1133	A6085YM_T6086F	L6079V_W6081T_I6088L
D1134	A6085YW_T6086F	L6079V_W6081T_I6088L
D1135	A6085YH_T6086F	L6079V_W6081T_I6088L
D1136	A6085YF_T6086M	L6079V_W6081T_I6088L
D1137	A6085YY_T6086M	L6079V_W6081T_I6088L
D1138	A6085YM_T6086M	L6079V_W6081T_I6088L
D1139	A6085YW_T6086M	L6079V_W6081T_I6088L

No.	CH3 Domain Mutations	
	Chain A	Chain B
D1140	A6085YH_T6086M	L6079V_W6081T_I6088L
D1141	A6085YF_T6086W	L6079V_W6081T_I6088L
D1142	A6085YY_T6086W	L6079V_W6081T_I6088L
D1143	A6085YM_T6086W	L6079V_W6081T_I6088L
D1144	A6085YW_T6086W	L6079V_W6081T_I6088L
D1145	A6085YH_T6086W	L6079V_W6081T_I6088L
D1146	A6085YF_T6086H	L6079V_W6081T_I6088L
D1147	A6085YY_T6086H	L6079V_W6081T_I6088L
D1148	A6085YM_T6086H	L6079V_W6081T_I6088L
D1149	A6085YW_T6086H	L6079V_W6081T_I6088L
D1150	A6085YH_T6086H	L6079V_W6081T_I6088L
D1151	A6085YF_T6086Y	L6079V_W6081L_I6088L
D1152	A6085YY_T6086Y	L6079V_W6081L_I6088L
D1153	A6085YM_T6086Y	L6079V_W6081L_I6088L
D1154	A6085YW_T6086Y	L6079V_W6081L_I6088L
D1155	A6085YH_T6086Y	L6079V_W6081L_I6088L
D1156	A6085YF_T6086F	L6079V_W6081L_I6088L
D1157	A6085YY_T6086F	L6079V_W6081L_I6088L
D1158	A6085YM_T6086F	L6079V_W6081L_I6088L
D1159	A6085YW_T6086F	L6079V_W6081L_I6088L
D1160	A6085YH_T6086F	L6079V_W6081L_I6088L
D1161	A6085YF_T6086M	L6079V_W6081L_I6088L
D1162	A6085YY_T6086M	L6079V_W6081L_I6088L
D1163	A6085YM_T6086M	L6079V_W6081L_I6088L
D1164	A6085YW_T6086M	L6079V_W6081L_I6088L
D1165	A6085YH_T6086M	L6079V_W6081L_I6088L
D1166	A6085YF_T6086W	L6079V_W6081L_I6088L
D1167	A6085YY_T6086W	L6079V_W6081L_I6088L
D1168	A6085YM_T6086W	L6079V_W6081L_I6088L

No.	CH3 Domain Mutations	
	Chain A	Chain B
D1169	A6085YW_T6086W	L6079V_W6081L_I6088L
D1170	A6085YH_T6086W	L6079V_W6081L_I6088L
D1171	A6085YF_T6086H	L6079V_W6081L_I6088L
D1172	A6085YY_T6086H	L6079V_W6081L_I6088L
D1173	A6085YM_T6086H	L6079V_W6081L_I6088L
D1174	A6085YW_T6086H	L6079V_W6081L_I6088L
D1175	A6085YH_T6086H	L6079V_W6081L_I6088L
D1176	A6085YF_T6086Y	L6079V_W6081A_I6088L
D1177	A6085YY_T6086Y	L6079V_W6081A_I6088L
D1178	A6085YM_T6086Y	L6079V_W6081A_I6088L
D1179	A6085YW_T6086Y	L6079V_W6081A_I6088L
D1180	A6085YH_T6086Y	L6079V_W6081A_I6088L
D1181	A6085YF_T6086F	L6079V_W6081A_I6088L
D1182	A6085YY_T6086F	L6079V_W6081A_I6088L
D1183	A6085YM_T6086F	L6079V_W6081A_I6088L
D1184	A6085YW_T6086F	L6079V_W6081A_I6088L
D1185	A6085YH_T6086F	L6079V_W6081A_I6088L
D1186	A6085YF_T6086M	L6079V_W6081A_I6088L
D1187	A6085YY_T6086M	L6079V_W6081A_I6088L
D1188	A6085YM_T6086M	L6079V_W6081A_I6088L
D1189	A6085YW_T6086M	L6079V_W6081A_I6088L
D1190	A6085YH_T6086M	L6079V_W6081A_I6088L
D1191	A6085YF_T6086W	L6079V_W6081A_I6088L
D1192	A6085YY_T6086W	L6079V_W6081A_I6088L
D1193	A6085YM_T6086W	L6079V_W6081A_I6088L
D1194	A6085YW_T6086W	L6079V_W6081A_I6088L
D1195	A6085YH_T6086W	L6079V_W6081A_I6088L
D1196	A6085YF_T6086H	L6079V_W6081A_I6088L
D1197	A6085YY_T6086H	L6079V_W6081A_I6088L

No.	CH3 Domain Mutations	
	Chain A	Chain B
D1198	A6085YM_T6086H	L6079V_W6081A_I6088L
D1199	A6085YW_T6086H	L6079V_W6081A_I6088L
D1200	A6085YH_T6086H	L6079V_W6081A_I6088L
D1201	A6085YF_T6086Y	L6079V_W6081V_I6088L
D1202	A6085YY_T6086Y	L6079V_W6081V_I6088L
D1203	A6085YM_T6086Y	L6079V_W6081V_I6088L
D1204	A6085YW_T6086Y	L6079V_W6081V_I6088L
D1205	A6085YH_T6086Y	L6079V_W6081V_I6088L
D1206	A6085YF_T6086F	L6079V_W6081V_I6088L
D1207	A6085YY_T6086F	L6079V_W6081V_I6088L
D1208	A6085YM_T6086F	L6079V_W6081V_I6088L
D1209	A6085YW_T6086F	L6079V_W6081V_I6088L
D1210	A6085YH_T6086F	L6079V_W6081V_I6088L
D1211	A6085YF_T6086M	L6079V_W6081V_I6088L
D1212	A6085YY_T6086M	L6079V_W6081V_I6088L
D1213	A6085YM_T6086M	L6079V_W6081V_I6088L
D1214	A6085YW_T6086M	L6079V_W6081V_I6088L
D1215	A6085YH_T6086M	L6079V_W6081V_I6088L
D1216	A6085YF_T6086W	L6079V_W6081V_I6088L
D1217	A6085YY_T6086W	L6079V_W6081V_I6088L
D1218	A6085YM_T6086W	L6079V_W6081V_I6088L
D1219	A6085YW_T6086W	L6079V_W6081V_I6088L
D1220	A6085YH_T6086W	L6079V_W6081V_I6088L
D1221	A6085YF_T6086H	L6079V_W6081V_I6088L
D1222	A6085YY_T6086H	L6079V_W6081V_I6088L
D1223	A6085YM_T6086H	L6079V_W6081V_I6088L
D1224	A6085YW_T6086H	L6079V_W6081V_I6088L
D1225	A6085YH_T6086H	L6079V_W6081V_I6088L
D1226	A6085YF_T6086Y	L6079V_W6081I_I6088L

No.	CH3 Domain Mutations	
	Chain A	Chain B
D1227	A6085YY_T6086Y	L6079V_W6081I_I6088L
D1228	A6085YM_T6086Y	L6079V_W6081I_I6088L
D1229	A6085YW_T6086Y	L6079V_W6081I_I6088L
D1230	A6085YH_T6086Y	L6079V_W6081I_I6088L
D1231	A6085YF_T6086F	L6079V_W6081I_I6088L
D1232	A6085YY_T6086F	L6079V_W6081I_I6088L
D1233	A6085YM_T6086F	L6079V_W6081I_I6088L
D1234	A6085YW_T6086F	L6079V_W6081I_I6088L
D1235	A6085YH_T6086F	L6079V_W6081I_I6088L
D1236	A6085YF_T6086M	L6079V_W6081I_I6088L
D1237	A6085YY_T6086M	L6079V_W6081I_I6088L
D1238	A6085YM_T6086M	L6079V_W6081I_I6088L
D1239	A6085YW_T6086M	L6079V_W6081I_I6088L
D1240	A6085YH_T6086M	L6079V_W6081I_I6088L
D1241	A6085YF_T6086W	L6079V_W6081I_I6088L
D1242	A6085YY_T6086W	L6079V_W6081I_I6088L
D1243	A6085YM_T6086W	L6079V_W6081I_I6088L
D1244	A6085YW_T6086W	L6079V_W6081I_I6088L
D1245	A6085YH_T6086W	L6079V_W6081I_I6088L
D1246	A6085YF_T6086H	L6079V_W6081I_I6088L
D1247	A6085YY_T6086H	L6079V_W6081I_I6088L
D1248	A6085YM_T6086H	L6079V_W6081I_I6088L
D1249	A6085YW_T6086H	L6079V_W6081I_I6088L
D1250	A6085YH_T6086H	L6079V_W6081I_I6088L
D1251	A6085YF_T6086Y	L6079T_W6081T_I6088L
D1252	A6085YY_T6086Y	L6079T_W6081T_I6088L
D1253	A6085YM_T6086Y	L6079T_W6081T_I6088L
D1254	A6085YW_T6086Y	L6079T_W6081T_I6088L
D1255	A6085YH_T6086Y	L6079T_W6081T_I6088L

No.	CH3 Domain Mutations	
	Chain A	Chain B
D1256	A6085YF_T6086F	L6079T_W6081T_I6088L
D1257	A6085YY_T6086F	L6079T_W6081T_I6088L
D1258	A6085YM_T6086F	L6079T_W6081T_I6088L
D1259	A6085YW_T6086F	L6079T_W6081T_I6088L
D1260	A6085YH_T6086F	L6079T_W6081T_I6088L
D1261	A6085YF_T6086M	L6079T_W6081T_I6088L
D1262	A6085YY_T6086M	L6079T_W6081T_I6088L
D1263	A6085YM_T6086M	L6079T_W6081T_I6088L
D1264	A6085YW_T6086M	L6079T_W6081T_I6088L
D1265	A6085YH_T6086M	L6079T_W6081T_I6088L
D1266	A6085YF_T6086W	L6079T_W6081T_I6088L
D1267	A6085YY_T6086W	L6079T_W6081T_I6088L
D1268	A6085YM_T6086W	L6079T_W6081T_I6088L
D1269	A6085YW_T6086W	L6079T_W6081T_I6088L
D1270	A6085YH_T6086W	L6079T_W6081T_I6088L
D1271	A6085YF_T6086H	L6079T_W6081T_I6088L
D1272	A6085YY_T6086H	L6079T_W6081T_I6088L
D1273	A6085YM_T6086H	L6079T_W6081T_I6088L
D1274	A6085YW_T6086H	L6079T_W6081T_I6088L
D1275	A6085YH_T6086H	L6079T_W6081T_I6088L
D1276	A6085YF_T6086Y	L6079T_W6081L_I6088L
D1277	A6085YY_T6086Y	L6079T_W6081L_I6088L
D1278	A6085YM_T6086Y	L6079T_W6081L_I6088L
D1279	A6085YW_T6086Y	L6079T_W6081L_I6088L
D1280	A6085YH_T6086Y	L6079T_W6081L_I6088L
D1281	A6085YF_T6086F	L6079T_W6081L_I6088L
D1282	A6085YY_T6086F	L6079T_W6081L_I6088L
D1283	A6085YM_T6086F	L6079T_W6081L_I6088L
D1284	A6085YW_T6086F	L6079T_W6081L_I6088L

No.	CH3 Domain Mutations	
	Chain A	Chain B
D1285	A6085YH_T6086F	L6079T_W6081L_I6088L
D1286	A6085YF_T6086M	L6079T_W6081L_I6088L
D1287	A6085YY_T6086M	L6079T_W6081L_I6088L
D1288	A6085YM_T6086M	L6079T_W6081L_I6088L
D1289	A6085YW_T6086M	L6079T_W6081L_I6088L
D1290	A6085YH_T6086M	L6079T_W6081L_I6088L
D1291	A6085YF_T6086W	L6079T_W6081L_I6088L
D1292	A6085YY_T6086W	L6079T_W6081L_I6088L
D1293	A6085YM_T6086W	L6079T_W6081L_I6088L
D1294	A6085YW_T6086W	L6079T_W6081L_I6088L
D1295	A6085YH_T6086W	L6079T_W6081L_I6088L
D1296	A6085YF_T6086H	L6079T_W6081L_I6088L
D1297	A6085YY_T6086H	L6079T_W6081L_I6088L
D1298	A6085YM_T6086H	L6079T_W6081L_I6088L
D1299	A6085YW_T6086H	L6079T_W6081L_I6088L
D1300	A6085YH_T6086H	L6079T_W6081L_I6088L
D1301	A6085YF_T6086Y	L6079T_W6081A_I6088L
D1302	A6085YY_T6086Y	L6079T_W6081A_I6088L
D1303	A6085YM_T6086Y	L6079T_W6081A_I6088L
D1304	A6085YW_T6086Y	L6079T_W6081A_I6088L
D1305	A6085YH_T6086Y	L6079T_W6081A_I6088L
D1306	A6085YF_T6086F	L6079T_W6081A_I6088L
D1307	A6085YY_T6086F	L6079T_W6081A_I6088L
D1308	A6085YM_T6086F	L6079T_W6081A_I6088L
D1309	A6085YW_T6086F	L6079T_W6081A_I6088L
D1310	A6085YH_T6086F	L6079T_W6081A_I6088L
D1311	A6085YF_T6086M	L6079T_W6081A_I6088L
D1312	A6085YY_T6086M	L6079T_W6081A_I6088L
D1313	A6085YM_T6086M	L6079T_W6081A_I6088L

No.	CH3 Domain Mutations	
	Chain A	Chain B
D1314	A6085YW_T6086M	L6079T_W6081A_I6088L
D1315	A6085YH_T6086M	L6079T_W6081A_I6088L
D1316	A6085YF_T6086W	L6079T_W6081A_I6088L
D1317	A6085YY_T6086W	L6079T_W6081A_I6088L
D1318	A6085YM_T6086W	L6079T_W6081A_I6088L
D1319	A6085YW_T6086W	L6079T_W6081A_I6088L
D1320	A6085YH_T6086W	L6079T_W6081A_I6088L
D1321	A6085YF_T6086H	L6079T_W6081A_I6088L
D1322	A6085YY_T6086H	L6079T_W6081A_I6088L
D1323	A6085YM_T6086H	L6079T_W6081A_I6088L
D1324	A6085YW_T6086H	L6079T_W6081A_I6088L
D1325	A6085YH_T6086H	L6079T_W6081A_I6088L
D1326	A6085YF_T6086Y	L6079T_W6081V_I6088L
D1327	A6085YY_T6086Y	L6079T_W6081V_I6088L
D1328	A6085YM_T6086Y	L6079T_W6081V_I6088L
D1329	A6085YW_T6086Y	L6079T_W6081V_I6088L
D1330	A6085YH_T6086Y	L6079T_W6081V_I6088L
D1331	A6085YF_T6086F	L6079T_W6081V_I6088L
D1332	A6085YY_T6086F	L6079T_W6081V_I6088L
D1333	A6085YM_T6086F	L6079T_W6081V_I6088L
D1334	A6085YW_T6086F	L6079T_W6081V_I6088L
D1335	A6085YH_T6086F	L6079T_W6081V_I6088L
D1336	A6085YF_T6086M	L6079T_W6081V_I6088L
D1337	A6085YY_T6086M	L6079T_W6081V_I6088L
D1338	A6085YM_T6086M	L6079T_W6081V_I6088L
D1339	A6085YW_T6086M	L6079T_W6081V_I6088L
D1340	A6085YH_T6086M	L6079T_W6081V_I6088L
D1341	A6085YF_T6086W	L6079T_W6081V_I6088L
D1342	A6085YY_T6086W	L6079T_W6081V_I6088L

No.	CH3 Domain Mutations	
	Chain A	Chain B
D1343	A6085YM_T6086W	L6079T_W6081V_I6088L
D1344	A6085YW_T6086W	L6079T_W6081V_I6088L
D1345	A6085YH_T6086W	L6079T_W6081V_I6088L
D1346	A6085YF_T6086H	L6079T_W6081V_I6088L
D1347	A6085YY_T6086H	L6079T_W6081V_I6088L
D1348	A6085YM_T6086H	L6079T_W6081V_I6088L
D1349	A6085YW_T6086H	L6079T_W6081V_I6088L
D1350	A6085YH_T6086H	L6079T_W6081V_I6088L
D1351	A6085YF_T6086Y	L6079T_W6081I_I6088L
D1352	A6085YY_T6086Y	L6079T_W6081I_I6088L
D1353	A6085YM_T6086Y	L6079T_W6081I_I6088L
D1354	A6085YW_T6086Y	L6079T_W6081I_I6088L
D1355	A6085YH_T6086Y	L6079T_W6081I_I6088L
D1356	A6085YF_T6086F	L6079T_W6081I_I6088L
D1357	A6085YY_T6086F	L6079T_W6081I_I6088L
D1358	A6085YM_T6086F	L6079T_W6081I_I6088L
D1359	A6085YW_T6086F	L6079T_W6081I_I6088L
D1360	A6085YH_T6086F	L6079T_W6081I_I6088L
D1361	A6085YF_T6086M	L6079T_W6081I_I6088L
D1362	A6085YY_T6086M	L6079T_W6081I_I6088L
D1363	A6085YM_T6086M	L6079T_W6081I_I6088L
D1364	A6085YW_T6086M	L6079T_W6081I_I6088L
D1365	A6085YH_T6086M	L6079T_W6081I_I6088L
D1366	A6085YF_T6086W	L6079T_W6081I_I6088L
D1367	A6085YY_T6086W	L6079T_W6081I_I6088L
D1368	A6085YM_T6086W	L6079T_W6081I_I6088L
D1369	A6085YW_T6086W	L6079T_W6081I_I6088L
D1370	A6085YH_T6086W	L6079T_W6081I_I6088L
D1371	A6085YF_T6086H	L6079T_W6081I_I6088L

No.	CH3 Domain Mutations	
	Chain A	Chain B
D1372	A6085YY_T6086H	L6079T_W6081I_I6088L
D1373	A6085YM_T6086H	L6079T_W6081I_I6088L
D1374	A6085YW_T6086H	L6079T_W6081I_I6088L
D1375	A6085YH_T6086H	L6079T_W6081I_I6088L
D1376	A6085YF_T6086Y	L6079A_W6081T_I6088L
D1377	A6085YY_T6086Y	L6079A_W6081T_I6088L
D1378	A6085YM_T6086Y	L6079A_W6081T_I6088L
D1379	A6085YW_T6086Y	L6079A_W6081T_I6088L
D1380	A6085YH_T6086Y	L6079A_W6081T_I6088L
D1381	A6085YF_T6086F	L6079A_W6081T_I6088L
D1382	A6085YY_T6086F	L6079A_W6081T_I6088L
D1383	A6085YM_T6086F	L6079A_W6081T_I6088L
D1384	A6085YW_T6086F	L6079A_W6081T_I6088L
D1385	A6085YH_T6086F	L6079A_W6081T_I6088L
D1386	A6085YF_T6086M	L6079A_W6081T_I6088L
D1387	A6085YY_T6086M	L6079A_W6081T_I6088L
D1388	A6085YM_T6086M	L6079A_W6081T_I6088L
D1389	A6085YW_T6086M	L6079A_W6081T_I6088L
D1390	A6085YH_T6086M	L6079A_W6081T_I6088L
D1391	A6085YF_T6086W	L6079A_W6081T_I6088L
D1392	A6085YY_T6086W	L6079A_W6081T_I6088L
D1393	A6085YM_T6086W	L6079A_W6081T_I6088L
D1394	A6085YW_T6086W	L6079A_W6081T_I6088L
D1395	A6085YH_T6086W	L6079A_W6081T_I6088L
D1396	A6085YF_T6086H	L6079A_W6081T_I6088L
D1397	A6085YY_T6086H	L6079A_W6081T_I6088L
D1398	A6085YM_T6086H	L6079A_W6081T_I6088L
D1399	A6085YW_T6086H	L6079A_W6081T_I6088L
D1400	A6085YH_T6086H	L6079A_W6081T_I6088L

No.	CH3 Domain Mutations	
	Chain A	Chain B
D1401	A6085YF_T6086Y	L6079A_W6081L_I6088L
D1402	A6085YY_T6086Y	L6079A_W6081L_I6088L
D1403	A6085YM_T6086Y	L6079A_W6081L_I6088L
D1404	A6085YW_T6086Y	L6079A_W6081L_I6088L
D1405	A6085YH_T6086Y	L6079A_W6081L_I6088L
D1406	A6085YF_T6086F	L6079A_W6081L_I6088L
D1407	A6085YY_T6086F	L6079A_W6081L_I6088L
D1408	A6085YM_T6086F	L6079A_W6081L_I6088L
D1409	A6085YW_T6086F	L6079A_W6081L_I6088L
D1410	A6085YH_T6086F	L6079A_W6081L_I6088L
D1411	A6085YF_T6086M	L6079A_W6081L_I6088L
D1412	A6085YY_T6086M	L6079A_W6081L_I6088L
D1413	A6085YM_T6086M	L6079A_W6081L_I6088L
D1414	A6085YW_T6086M	L6079A_W6081L_I6088L
D1415	A6085YH_T6086M	L6079A_W6081L_I6088L
D1416	A6085YF_T6086W	L6079A_W6081L_I6088L
D1417	A6085YY_T6086W	L6079A_W6081L_I6088L
D1418	A6085YM_T6086W	L6079A_W6081L_I6088L
D1419	A6085YW_T6086W	L6079A_W6081L_I6088L
D1420	A6085YH_T6086W	L6079A_W6081L_I6088L
D1421	A6085YF_T6086H	L6079A_W6081L_I6088L
D1422	A6085YY_T6086H	L6079A_W6081L_I6088L
D1423	A6085YM_T6086H	L6079A_W6081L_I6088L
D1424	A6085YW_T6086H	L6079A_W6081L_I6088L
D1425	A6085YH_T6086H	L6079A_W6081L_I6088L
D1426	A6085YF_T6086Y	L6079A_W6081A_I6088L
D1427	A6085YY_T6086Y	L6079A_W6081A_I6088L
D1428	A6085YM_T6086Y	L6079A_W6081A_I6088L
D1429	A6085YW_T6086Y	L6079A_W6081A_I6088L

No.	CH3 Domain Mutations	
	Chain A	Chain B
D1430	A6085YH_T6086Y	L6079A_W6081A_I6088L
D1431	A6085YF_T6086F	L6079A_W6081A_I6088L
D1432	A6085YY_T6086F	L6079A_W6081A_I6088L
D1433	A6085YM_T6086F	L6079A_W6081A_I6088L
D1434	A6085YW_T6086F	L6079A_W6081A_I6088L
D1435	A6085YH_T6086F	L6079A_W6081A_I6088L
D1436	A6085YF_T6086M	L6079A_W6081A_I6088L
D1437	A6085YY_T6086M	L6079A_W6081A_I6088L
D1438	A6085YM_T6086M	L6079A_W6081A_I6088L
D1439	A6085YW_T6086M	L6079A_W6081A_I6088L
D1440	A6085YH_T6086M	L6079A_W6081A_I6088L
D1441	A6085YF_T6086W	L6079A_W6081A_I6088L
D1442	A6085YY_T6086W	L6079A_W6081A_I6088L
D1443	A6085YM_T6086W	L6079A_W6081A_I6088L
D1444	A6085YW_T6086W	L6079A_W6081A_I6088L
D1445	A6085YH_T6086W	L6079A_W6081A_I6088L
D1446	A6085YF_T6086H	L6079A_W6081A_I6088L
D1447	A6085YY_T6086H	L6079A_W6081A_I6088L
D1448	A6085YM_T6086H	L6079A_W6081A_I6088L
D1449	A6085YW_T6086H	L6079A_W6081A_I6088L
D1450	A6085YH_T6086H	L6079A_W6081A_I6088L
D1451	A6085YF_T6086Y	L6079A_W6081V_I6088L
D1452	A6085YY_T6086Y	L6079A_W6081V_I6088L
D1453	A6085YM_T6086Y	L6079A_W6081V_I6088L
D1454	A6085YW_T6086Y	L6079A_W6081V_I6088L
D1455	A6085YH_T6086Y	L6079A_W6081V_I6088L
D1456	A6085YF_T6086F	L6079A_W6081V_I6088L
D1457	A6085YY_T6086F	L6079A_W6081V_I6088L
D1458	A6085YM_T6086F	L6079A_W6081V_I6088L

No.	CH3 Domain Mutations	
	Chain A	Chain B
D1459	A6085YW_T6086F	L6079A_W6081V_I6088L
D1460	A6085YH_T6086F	L6079A_W6081V_I6088L
D1461	A6085YF_T6086M	L6079A_W6081V_I6088L
D1462	A6085YY_T6086M	L6079A_W6081V_I6088L
D1463	A6085YM_T6086M	L6079A_W6081V_I6088L
D1464	A6085YW_T6086M	L6079A_W6081V_I6088L
D1465	A6085YH_T6086M	L6079A_W6081V_I6088L
D1466	A6085YF_T6086W	L6079A_W6081V_I6088L
D1467	A6085YY_T6086W	L6079A_W6081V_I6088L
D1468	A6085YM_T6086W	L6079A_W6081V_I6088L
D1469	A6085YW_T6086W	L6079A_W6081V_I6088L
D1470	A6085YH_T6086W	L6079A_W6081V_I6088L
D1471	A6085YF_T6086H	L6079A_W6081V_I6088L
D1472	A6085YY_T6086H	L6079A_W6081V_I6088L
D1473	A6085YM_T6086H	L6079A_W6081V_I6088L
D1474	A6085YW_T6086H	L6079A_W6081V_I6088L
D1475	A6085YH_T6086H	L6079A_W6081V_I6088L
D1476	A6085YF_T6086Y	L6079A_W6081I_I6088L
D1477	A6085YY_T6086Y	L6079A_W6081I_I6088L
D1478	A6085YM_T6086Y	L6079A_W6081I_I6088L
D1479	A6085YW_T6086Y	L6079A_W6081I_I6088L
D1480	A6085YH_T6086Y	L6079A_W6081I_I6088L
D1481	A6085YF_T6086F	L6079A_W6081I_I6088L
D1482	A6085YY_T6086F	L6079A_W6081I_I6088L
D1483	A6085YM_T6086F	L6079A_W6081I_I6088L
D1484	A6085YW_T6086F	L6079A_W6081I_I6088L
D1485	A6085YH_T6086F	L6079A_W6081I_I6088L
D1486	A6085YF_T6086M	L6079A_W6081I_I6088L
D1487	A6085YY_T6086M	L6079A_W6081I_I6088L

No.	CH3 Domain Mutations	
	Chain A	Chain B
D1488	A6085YM_T6086M	L6079A_W6081I_I6088L
D1489	A6085YW_T6086M	L6079A_W6081I_I6088L
D1490	A6085YH_T6086M	L6079A_W6081I_I6088L
D1491	A6085YF_T6086W	L6079A_W6081I_I6088L
D1492	A6085YY_T6086W	L6079A_W6081I_I6088L
D1493	A6085YM_T6086W	L6079A_W6081I_I6088L
D1494	A6085YW_T6086W	L6079A_W6081I_I6088L
D1495	A6085YH_T6086W	L6079A_W6081I_I6088L
D1496	A6085YF_T6086H	L6079A_W6081I_I6088L
D1497	A6085YY_T6086H	L6079A_W6081I_I6088L
D1498	A6085YM_T6086H	L6079A_W6081I_I6088L
D1499	A6085YW_T6086H	L6079A_W6081I_I6088L
D1500	A6085YH_T6086H	L6079A_W6081I_I6088L
D1501	A6085YF_T6086Y	L6079I_W6081T_I6088L
D1502	A6085YY_T6086Y	L6079I_W6081T_I6088L
D1503	A6085YM_T6086Y	L6079I_W6081T_I6088L
D1504	A6085YW_T6086Y	L6079I_W6081T_I6088L
D1505	A6085YH_T6086Y	L6079I_W6081T_I6088L
D1506	A6085YF_T6086F	L6079I_W6081T_I6088L
D1507	A6085YY_T6086F	L6079I_W6081T_I6088L
D1508	A6085YM_T6086F	L6079I_W6081T_I6088L
D1509	A6085YW_T6086F	L6079I_W6081T_I6088L
D1510	A6085YH_T6086F	L6079I_W6081T_I6088L
D1511	A6085YF_T6086M	L6079I_W6081T_I6088L
D1512	A6085YY_T6086M	L6079I_W6081T_I6088L
D1513	A6085YM_T6086M	L6079I_W6081T_I6088L
D1514	A6085YW_T6086M	L6079I_W6081T_I6088L
D1515	A6085YH_T6086M	L6079I_W6081T_I6088L
D1516	A6085YF_T6086W	L6079I_W6081T_I6088L

No.	CH3 Domain Mutations	
	Chain A	Chain B
D1517	A6085YY_T6086W	L6079I_W6081T_I6088L
D1518	A6085YM_T6086W	L6079I_W6081T_I6088L
D1519	A6085YW_T6086W	L6079I_W6081T_I6088L
D1520	A6085YH_T6086W	L6079I_W6081T_I6088L
D1521	A6085YF_T6086H	L6079I_W6081T_I6088L
D1522	A6085YY_T6086H	L6079I_W6081T_I6088L
D1523	A6085YM_T6086H	L6079I_W6081T_I6088L
D1524	A6085YW_T6086H	L6079I_W6081T_I6088L
D1525	A6085YH_T6086H	L6079I_W6081T_I6088L
D1526	A6085YF_T6086Y	L6079I_W6081L_I6088L
D1527	A6085YY_T6086Y	L6079I_W6081L_I6088L
D1528	A6085YM_T6086Y	L6079I_W6081L_I6088L
D1529	A6085YW_T6086Y	L6079I_W6081L_I6088L
D1530	A6085YH_T6086Y	L6079I_W6081L_I6088L
D1531	A6085YF_T6086F	L6079I_W6081L_I6088L
D1532	A6085YY_T6086F	L6079I_W6081L_I6088L
D1533	A6085YM_T6086F	L6079I_W6081L_I6088L
D1534	A6085YW_T6086F	L6079I_W6081L_I6088L
D1535	A6085YH_T6086F	L6079I_W6081L_I6088L
D1536	A6085YF_T6086M	L6079I_W6081L_I6088L
D1537	A6085YY_T6086M	L6079I_W6081L_I6088L
D1538	A6085YM_T6086M	L6079I_W6081L_I6088L
D1539	A6085YW_T6086M	L6079I_W6081L_I6088L
D1540	A6085YH_T6086M	L6079I_W6081L_I6088L
D1541	A6085YF_T6086W	L6079I_W6081L_I6088L
D1542	A6085YY_T6086W	L6079I_W6081L_I6088L
D1543	A6085YM_T6086W	L6079I_W6081L_I6088L
D1544	A6085YW_T6086W	L6079I_W6081L_I6088L
D1545	A6085YH_T6086W	L6079I_W6081L_I6088L

No.	CH3 Domain Mutations	
	Chain A	Chain B
D1546	A6085YF_T6086H	L6079I_W6081L_I6088L
D1547	A6085YY_T6086H	L6079I_W6081L_I6088L
D1548	A6085YM_T6086H	L6079I_W6081L_I6088L
D1549	A6085YW_T6086H	L6079I_W6081L_I6088L
D1550	A6085YH_T6086H	L6079I_W6081L_I6088L
D1551	A6085YF_T6086Y	L6079I_W6081A_I6088L
D1552	A6085YY_T6086Y	L6079I_W6081A_I6088L
D1553	A6085YM_T6086Y	L6079I_W6081A_I6088L
D1554	A6085YW_T6086Y	L6079I_W6081A_I6088L
D1555	A6085YH_T6086Y	L6079I_W6081A_I6088L
D1556	A6085YF_T6086F	L6079I_W6081A_I6088L
D1557	A6085YY_T6086F	L6079I_W6081A_I6088L
D1558	A6085YM_T6086F	L6079I_W6081A_I6088L
D1559	A6085YW_T6086F	L6079I_W6081A_I6088L
D1560	A6085YH_T6086F	L6079I_W6081A_I6088L
D1561	A6085YF_T6086M	L6079I_W6081A_I6088L
D1562	A6085YY_T6086M	L6079I_W6081A_I6088L
D1563	A6085YM_T6086M	L6079I_W6081A_I6088L
D1564	A6085YW_T6086M	L6079I_W6081A_I6088L
D1565	A6085YH_T6086M	L6079I_W6081A_I6088L
D1566	A6085YF_T6086W	L6079I_W6081A_I6088L
D1567	A6085YY_T6086W	L6079I_W6081A_I6088L
D1568	A6085YM_T6086W	L6079I_W6081A_I6088L
D1569	A6085YW_T6086W	L6079I_W6081A_I6088L
D1570	A6085YH_T6086W	L6079I_W6081A_I6088L
D1571	A6085YF_T6086H	L6079I_W6081A_I6088L
D1572	A6085YY_T6086H	L6079I_W6081A_I6088L
D1573	A6085YM_T6086H	L6079I_W6081A_I6088L
D1574	A6085YW_T6086H	L6079I_W6081A_I6088L

No.	CH3 Domain Mutations	
	Chain A	Chain B
D1575	A6085YH_T6086H	L6079I_W6081A_I6088L
D1576	A6085YF_T6086Y	L6079I_W6081V_I6088L
D1577	A6085YY_T6086Y	L6079I_W6081V_I6088L
D1578	A6085YM_T6086Y	L6079I_W6081V_I6088L
D1579	A6085YW_T6086Y	L6079I_W6081V_I6088L
D1580	A6085YH_T6086Y	L6079I_W6081V_I6088L
D1581	A6085YF_T6086F	L6079I_W6081V_I6088L
D1582	A6085YY_T6086F	L6079I_W6081V_I6088L
D1583	A6085YM_T6086F	L6079I_W6081V_I6088L
D1584	A6085YW_T6086F	L6079I_W6081V_I6088L
D1585	A6085YH_T6086F	L6079I_W6081V_I6088L
D1586	A6085YF_T6086M	L6079I_W6081V_I6088L
D1587	A6085YY_T6086M	L6079I_W6081V_I6088L
D1588	A6085YM_T6086M	L6079I_W6081V_I6088L
D1589	A6085YW_T6086M	L6079I_W6081V_I6088L
D1590	A6085YH_T6086M	L6079I_W6081V_I6088L
D1591	A6085YF_T6086W	L6079I_W6081V_I6088L
D1592	A6085YY_T6086W	L6079I_W6081V_I6088L
D1593	A6085YM_T6086W	L6079I_W6081V_I6088L
D1594	A6085YW_T6086W	L6079I_W6081V_I6088L
D1595	A6085YH_T6086W	L6079I_W6081V_I6088L
D1596	A6085YF_T6086H	L6079I_W6081V_I6088L
D1597	A6085YY_T6086H	L6079I_W6081V_I6088L
D1598	A6085YM_T6086H	L6079I_W6081V_I6088L
D1599	A6085YW_T6086H	L6079I_W6081V_I6088L
D1600	A6085YH_T6086H	L6079I_W6081V_I6088L
D1601	A6085YF_T6086Y	L6079I_W6081I_I6088L
D1602	A6085YY_T6086Y	L6079I_W6081I_I6088L
D1603	A6085YM_T6086Y	L6079I_W6081I_I6088L

No.	CH3 Domain Mutations	
	Chain A	Chain B
D1604	A6085YW_T6086Y	L6079I_W6081I_I6088L
D1605	A6085YH_T6086Y	L6079I_W6081I_I6088L
D1606	A6085YF_T6086F	L6079I_W6081I_I6088L
D1607	A6085YY_T6086F	L6079I_W6081I_I6088L
D1608	A6085YM_T6086F	L6079I_W6081I_I6088L
D1609	A6085YW_T6086F	L6079I_W6081I_I6088L
D1610	A6085YH_T6086F	L6079I_W6081I_I6088L
D1611	A6085YF_T6086M	L6079I_W6081I_I6088L
D1612	A6085YY_T6086M	L6079I_W6081I_I6088L
D1613	A6085YM_T6086M	L6079I_W6081I_I6088L
D1614	A6085YW_T6086M	L6079I_W6081I_I6088L
D1615	A6085YH_T6086M	L6079I_W6081I_I6088L
D1616	A6085YF_T6086W	L6079I_W6081I_I6088L
D1617	A6085YY_T6086W	L6079I_W6081I_I6088L
D1618	A6085YM_T6086W	L6079I_W6081I_I6088L
D1619	A6085YW_T6086W	L6079I_W6081I_I6088L
D1620	A6085YH_T6086W	L6079I_W6081I_I6088L
D1621	A6085YF_T6086H	L6079I_W6081I_I6088L
D1622	A6085YY_T6086H	L6079I_W6081I_I6088L
D1623	A6085YM_T6086H	L6079I_W6081I_I6088L
D1624	A6085YW_T6086H	L6079I_W6081I_I6088L
D1625	A6085YH_T6086H	L6079I_W6081I_I6088L
D1626	A6085YF_T6086Y	L6079V_W6081T_I6088A
D1627	A6085YY_T6086Y	L6079V_W6081T_I6088A
D1628	A6085YM_T6086Y	L6079V_W6081T_I6088A
D1629	A6085YW_T6086Y	L6079V_W6081T_I6088A
D1630	A6085YH_T6086Y	L6079V_W6081T_I6088A
D1631	A6085YF_T6086F	L6079V_W6081T_I6088A
D1632	A6085YY_T6086F	L6079V_W6081T_I6088A

No.	CH3 Domain Mutations	
	Chain A	Chain B
D1633	A6085YM_T6086F	L6079V_W6081T_I6088A
D1634	A6085YW_T6086F	L6079V_W6081T_I6088A
D1635	A6085YH_T6086F	L6079V_W6081T_I6088A
D1636	A6085YF_T6086M	L6079V_W6081T_I6088A
D1637	A6085YY_T6086M	L6079V_W6081T_I6088A
D1638	A6085YM_T6086M	L6079V_W6081T_I6088A
D1639	A6085YW_T6086M	L6079V_W6081T_I6088A
D1640	A6085YH_T6086M	L6079V_W6081T_I6088A
D1641	A6085YF_T6086W	L6079V_W6081T_I6088A
D1642	A6085YY_T6086W	L6079V_W6081T_I6088A
D1643	A6085YM_T6086W	L6079V_W6081T_I6088A
D1644	A6085YW_T6086W	L6079V_W6081T_I6088A
D1645	A6085YH_T6086W	L6079V_W6081T_I6088A
D1646	A6085YF_T6086H	L6079V_W6081T_I6088A
D1647	A6085YY_T6086H	L6079V_W6081T_I6088A
D1648	A6085YM_T6086H	L6079V_W6081T_I6088A
D1649	A6085YW_T6086H	L6079V_W6081T_I6088A
D1650	A6085YH_T6086H	L6079V_W6081T_I6088A
D1651	A6085YF_T6086Y	L6079V_W6081L_I6088A
D1652	A6085YY_T6086Y	L6079V_W6081L_I6088A
D1653	A6085YM_T6086Y	L6079V_W6081L_I6088A
D1654	A6085YW_T6086Y	L6079V_W6081L_I6088A
D1655	A6085YH_T6086Y	L6079V_W6081L_I6088A
D1656	A6085YF_T6086F	L6079V_W6081L_I6088A
D1657	A6085YY_T6086F	L6079V_W6081L_I6088A
D1658	A6085YM_T6086F	L6079V_W6081L_I6088A
D1659	A6085YW_T6086F	L6079V_W6081L_I6088A
D1660	A6085YH_T6086F	L6079V_W6081L_I6088A
D1661	A6085YF_T6086M	L6079V_W6081L_I6088A

No.	CH3 Domain Mutations	
	Chain A	Chain B
D1662	A6085YY_T6086M	L6079V_W6081L_I6088A
D1663	A6085YM_T6086M	L6079V_W6081L_I6088A
D1664	A6085YW_T6086M	L6079V_W6081L_I6088A
D1665	A6085YH_T6086M	L6079V_W6081L_I6088A
D1666	A6085YF_T6086W	L6079V_W6081L_I6088A
D1667	A6085YY_T6086W	L6079V_W6081L_I6088A
D1668	A6085YM_T6086W	L6079V_W6081L_I6088A
D1669	A6085YW_T6086W	L6079V_W6081L_I6088A
D1670	A6085YH_T6086W	L6079V_W6081L_I6088A
D1671	A6085YF_T6086H	L6079V_W6081L_I6088A
D1672	A6085YY_T6086H	L6079V_W6081L_I6088A
D1673	A6085YM_T6086H	L6079V_W6081L_I6088A
D1674	A6085YW_T6086H	L6079V_W6081L_I6088A
D1675	A6085YH_T6086H	L6079V_W6081L_I6088A
D1676	A6085YF_T6086Y	L6079V_W6081A_I6088A
D1677	A6085YY_T6086Y	L6079V_W6081A_I6088A
D1678	A6085YM_T6086Y	L6079V_W6081A_I6088A
D1679	A6085YW_T6086Y	L6079V_W6081A_I6088A
D1680	A6085YH_T6086Y	L6079V_W6081A_I6088A
D1681	A6085YF_T6086F	L6079V_W6081A_I6088A
D1682	A6085YY_T6086F	L6079V_W6081A_I6088A
D1683	A6085YM_T6086F	L6079V_W6081A_I6088A
D1684	A6085YW_T6086F	L6079V_W6081A_I6088A
D1685	A6085YH_T6086F	L6079V_W6081A_I6088A
D1686	A6085YF_T6086M	L6079V_W6081A_I6088A
D1687	A6085YY_T6086M	L6079V_W6081A_I6088A
D1688	A6085YM_T6086M	L6079V_W6081A_I6088A
D1689	A6085YW_T6086M	L6079V_W6081A_I6088A
D1690	A6085YH_T6086M	L6079V_W6081A_I6088A

No.	CH3 Domain Mutations	
	Chain A	Chain B
D1691	A6085YF_T6086W	L6079V_W6081A_I6088A
D1692	A6085YY_T6086W	L6079V_W6081A_I6088A
D1693	A6085YM_T6086W	L6079V_W6081A_I6088A
D1694	A6085YW_T6086W	L6079V_W6081A_I6088A
D1695	A6085YH_T6086W	L6079V_W6081A_I6088A
D1696	A6085YF_T6086H	L6079V_W6081A_I6088A
D1697	A6085YY_T6086H	L6079V_W6081A_I6088A
D1698	A6085YM_T6086H	L6079V_W6081A_I6088A
D1699	A6085YW_T6086H	L6079V_W6081A_I6088A
D1700	A6085YH_T6086H	L6079V_W6081A_I6088A
D1701	A6085YF_T6086Y	L6079V_W6081V_I6088A
D1702	A6085YY_T6086Y	L6079V_W6081V_I6088A
D1703	A6085YM_T6086Y	L6079V_W6081V_I6088A
D1704	A6085YW_T6086Y	L6079V_W6081V_I6088A
D1705	A6085YH_T6086Y	L6079V_W6081V_I6088A
D1706	A6085YF_T6086F	L6079V_W6081V_I6088A
D1707	A6085YY_T6086F	L6079V_W6081V_I6088A
D1708	A6085YM_T6086F	L6079V_W6081V_I6088A
D1709	A6085YW_T6086F	L6079V_W6081V_I6088A
D1710	A6085YH_T6086F	L6079V_W6081V_I6088A
D1711	A6085YF_T6086M	L6079V_W6081V_I6088A
D1712	A6085YY_T6086M	L6079V_W6081V_I6088A
D1713	A6085YM_T6086M	L6079V_W6081V_I6088A
D1714	A6085YW_T6086M	L6079V_W6081V_I6088A
D1715	A6085YH_T6086M	L6079V_W6081V_I6088A
D1716	A6085YF_T6086W	L6079V_W6081V_I6088A
D1717	A6085YY_T6086W	L6079V_W6081V_I6088A
D1718	A6085YM_T6086W	L6079V_W6081V_I6088A
D1719	A6085YW_T6086W	L6079V_W6081V_I6088A

No.	CH3 Domain Mutations	
	Chain A	Chain B
D1720	A6085YH_T6086W	L6079V_W6081V_I6088A
D1721	A6085YF_T6086H	L6079V_W6081V_I6088A
D1722	A6085YY_T6086H	L6079V_W6081V_I6088A
D1723	A6085YM_T6086H	L6079V_W6081V_I6088A
D1724	A6085YW_T6086H	L6079V_W6081V_I6088A
D1725	A6085YH_T6086H	L6079V_W6081V_I6088A
D1726	A6085YF_T6086Y	L6079V_W6081I_I6088A
D1727	A6085YY_T6086Y	L6079V_W6081I_I6088A
D1728	A6085YM_T6086Y	L6079V_W6081I_I6088A
D1729	A6085YW_T6086Y	L6079V_W6081I_I6088A
D1730	A6085YH_T6086Y	L6079V_W6081I_I6088A
D1731	A6085YF_T6086F	L6079V_W6081I_I6088A
D1732	A6085YY_T6086F	L6079V_W6081I_I6088A
D1733	A6085YM_T6086F	L6079V_W6081I_I6088A
D1734	A6085YW_T6086F	L6079V_W6081I_I6088A
D1735	A6085YH_T6086F	L6079V_W6081I_I6088A
D1736	A6085YF_T6086M	L6079V_W6081I_I6088A
D1737	A6085YY_T6086M	L6079V_W6081I_I6088A
D1738	A6085YM_T6086M	L6079V_W6081I_I6088A
D1739	A6085YW_T6086M	L6079V_W6081I_I6088A
D1740	A6085YH_T6086M	L6079V_W6081I_I6088A
D1741	A6085YF_T6086W	L6079V_W6081I_I6088A
D1742	A6085YY_T6086W	L6079V_W6081I_I6088A
D1743	A6085YM_T6086W	L6079V_W6081I_I6088A
D1744	A6085YW_T6086W	L6079V_W6081I_I6088A
D1745	A6085YH_T6086W	L6079V_W6081I_I6088A
D1746	A6085YF_T6086H	L6079V_W6081I_I6088A
D1747	A6085YY_T6086H	L6079V_W6081I_I6088A
D1748	A6085YM_T6086H	L6079V_W6081I_I6088A

No.	CH3 Domain Mutations	
	Chain A	Chain B
D1749	A6085YW_T6086H	L6079V_W6081I_I6088A
D1750	A6085YH_T6086H	L6079V_W6081I_I6088A
D1751	A6085YF_T6086Y	L6079T_W6081T_I6088A
D1752	A6085YY_T6086Y	L6079T_W6081T_I6088A
D1753	A6085YM_T6086Y	L6079T_W6081T_I6088A
D1754	A6085YW_T6086Y	L6079T_W6081T_I6088A
D1755	A6085YH_T6086Y	L6079T_W6081T_I6088A
D1756	A6085YF_T6086F	L6079T_W6081T_I6088A
D1757	A6085YY_T6086F	L6079T_W6081T_I6088A
D1758	A6085YM_T6086F	L6079T_W6081T_I6088A
D1759	A6085YW_T6086F	L6079T_W6081T_I6088A
D1760	A6085YH_T6086F	L6079T_W6081T_I6088A
D1761	A6085YF_T6086M	L6079T_W6081T_I6088A
D1762	A6085YY_T6086M	L6079T_W6081T_I6088A
D1763	A6085YM_T6086M	L6079T_W6081T_I6088A
D1764	A6085YW_T6086M	L6079T_W6081T_I6088A
D1765	A6085YH_T6086M	L6079T_W6081T_I6088A
D1766	A6085YF_T6086W	L6079T_W6081T_I6088A
D1767	A6085YY_T6086W	L6079T_W6081T_I6088A
D1768	A6085YM_T6086W	L6079T_W6081T_I6088A
D1769	A6085YW_T6086W	L6079T_W6081T_I6088A
D1770	A6085YH_T6086W	L6079T_W6081T_I6088A
D1771	A6085YF_T6086H	L6079T_W6081T_I6088A
D1772	A6085YY_T6086H	L6079T_W6081T_I6088A
D1773	A6085YM_T6086H	L6079T_W6081T_I6088A
D1774	A6085YW_T6086H	L6079T_W6081T_I6088A
D1775	A6085YH_T6086H	L6079T_W6081T_I6088A
D1776	A6085YF_T6086Y	L6079T_W6081L_I6088A
D1777	A6085YY_T6086Y	L6079T_W6081L_I6088A

No.	CH3 Domain Mutations	
	Chain A	Chain B
D1778	A6085YM_T6086Y	L6079T_W6081L_I6088A
D1779	A6085YW_T6086Y	L6079T_W6081L_I6088A
D1780	A6085YH_T6086Y	L6079T_W6081L_I6088A
D1781	A6085YF_T6086F	L6079T_W6081L_I6088A
D1782	A6085YY_T6086F	L6079T_W6081L_I6088A
D1783	A6085YM_T6086F	L6079T_W6081L_I6088A
D1784	A6085YW_T6086F	L6079T_W6081L_I6088A
D1785	A6085YH_T6086F	L6079T_W6081L_I6088A
D1786	A6085YF_T6086M	L6079T_W6081L_I6088A
D1787	A6085YY_T6086M	L6079T_W6081L_I6088A
D1788	A6085YM_T6086M	L6079T_W6081L_I6088A
D1789	A6085YW_T6086M	L6079T_W6081L_I6088A
D1790	A6085YH_T6086M	L6079T_W6081L_I6088A
D1791	A6085YF_T6086W	L6079T_W6081L_I6088A
D1792	A6085YY_T6086W	L6079T_W6081L_I6088A
D1793	A6085YM_T6086W	L6079T_W6081L_I6088A
D1794	A6085YW_T6086W	L6079T_W6081L_I6088A
D1795	A6085YH_T6086W	L6079T_W6081L_I6088A
D1796	A6085YF_T6086H	L6079T_W6081L_I6088A
D1797	A6085YY_T6086H	L6079T_W6081L_I6088A
D1798	A6085YM_T6086H	L6079T_W6081L_I6088A
D1799	A6085YW_T6086H	L6079T_W6081L_I6088A
D1800	A6085YH_T6086H	L6079T_W6081L_I6088A
D1801	A6085YF_T6086Y	L6079T_W6081A_I6088A
D1802	A6085YY_T6086Y	L6079T_W6081A_I6088A
D1803	A6085YM_T6086Y	L6079T_W6081A_I6088A
D1804	A6085YW_T6086Y	L6079T_W6081A_I6088A
D1805	A6085YH_T6086Y	L6079T_W6081A_I6088A
D1806	A6085YF_T6086F	L6079T_W6081A_I6088A

No.	CH3 Domain Mutations	
	Chain A	Chain B
D1807	A6085YY_T6086F	L6079T_W6081A_I6088A
D1808	A6085YM_T6086F	L6079T_W6081A_I6088A
D1809	A6085YW_T6086F	L6079T_W6081A_I6088A
D1810	A6085YH_T6086F	L6079T_W6081A_I6088A
D1811	A6085YF_T6086M	L6079T_W6081A_I6088A
D1812	A6085YY_T6086M	L6079T_W6081A_I6088A
D1813	A6085YM_T6086M	L6079T_W6081A_I6088A
D1814	A6085YW_T6086M	L6079T_W6081A_I6088A
D1815	A6085YH_T6086M	L6079T_W6081A_I6088A
D1816	A6085YF_T6086W	L6079T_W6081A_I6088A
D1817	A6085YY_T6086W	L6079T_W6081A_I6088A
D1818	A6085YM_T6086W	L6079T_W6081A_I6088A
D1819	A6085YW_T6086W	L6079T_W6081A_I6088A
D1820	A6085YH_T6086W	L6079T_W6081A_I6088A
D1821	A6085YF_T6086H	L6079T_W6081A_I6088A
D1822	A6085YY_T6086H	L6079T_W6081A_I6088A
D1823	A6085YM_T6086H	L6079T_W6081A_I6088A
D1824	A6085YW_T6086H	L6079T_W6081A_I6088A
D1825	A6085YH_T6086H	L6079T_W6081A_I6088A
D1826	A6085YF_T6086Y	L6079T_W6081V_I6088A
D1827	A6085YY_T6086Y	L6079T_W6081V_I6088A
D1828	A6085YM_T6086Y	L6079T_W6081V_I6088A
D1829	A6085YW_T6086Y	L6079T_W6081V_I6088A
D1830	A6085YH_T6086Y	L6079T_W6081V_I6088A
D1831	A6085YF_T6086F	L6079T_W6081V_I6088A
D1832	A6085YY_T6086F	L6079T_W6081V_I6088A
D1833	A6085YM_T6086F	L6079T_W6081V_I6088A
D1834	A6085YW_T6086F	L6079T_W6081V_I6088A
D1835	A6085YH_T6086F	L6079T_W6081V_I6088A

No.	CH3 Domain Mutations	
	Chain A	Chain B
D1836	A6085YF_T6086M	L6079T_W6081V_I6088A
D1837	A6085YY_T6086M	L6079T_W6081V_I6088A
D1838	A6085YM_T6086M	L6079T_W6081V_I6088A
D1839	A6085YW_T6086M	L6079T_W6081V_I6088A
D1840	A6085YH_T6086M	L6079T_W6081V_I6088A
D1841	A6085YF_T6086W	L6079T_W6081V_I6088A
D1842	A6085YY_T6086W	L6079T_W6081V_I6088A
D1843	A6085YM_T6086W	L6079T_W6081V_I6088A
D1844	A6085YW_T6086W	L6079T_W6081V_I6088A
D1845	A6085YH_T6086W	L6079T_W6081V_I6088A
D1846	A6085YF_T6086H	L6079T_W6081V_I6088A
D1847	A6085YY_T6086H	L6079T_W6081V_I6088A
D1848	A6085YM_T6086H	L6079T_W6081V_I6088A
D1849	A6085YW_T6086H	L6079T_W6081V_I6088A
D1850	A6085YH_T6086H	L6079T_W6081V_I6088A
D1851	A6085YF_T6086Y	L6079T_W6081I_I6088A
D1852	A6085YY_T6086Y	L6079T_W6081I_I6088A
D1853	A6085YM_T6086Y	L6079T_W6081I_I6088A
D1854	A6085YW_T6086Y	L6079T_W6081I_I6088A
D1855	A6085YH_T6086Y	L6079T_W6081I_I6088A
D1856	A6085YF_T6086F	L6079T_W6081I_I6088A
D1857	A6085YY_T6086F	L6079T_W6081I_I6088A
D1858	A6085YM_T6086F	L6079T_W6081I_I6088A
D1859	A6085YW_T6086F	L6079T_W6081I_I6088A
D1860	A6085YH_T6086F	L6079T_W6081I_I6088A
D1861	A6085YF_T6086M	L6079T_W6081I_I6088A
D1862	A6085YY_T6086M	L6079T_W6081I_I6088A
D1863	A6085YM_T6086M	L6079T_W6081I_I6088A
D1864	A6085YW_T6086M	L6079T_W6081I_I6088A

No.	CH3 Domain Mutations	
	Chain A	Chain B
D1865	A6085YH_T6086M	L6079T_W6081I_I6088A
D1866	A6085YF_T6086W	L6079T_W6081I_I6088A
D1867	A6085YY_T6086W	L6079T_W6081I_I6088A
D1868	A6085YM_T6086W	L6079T_W6081I_I6088A
D1869	A6085YW_T6086W	L6079T_W6081I_I6088A
D1870	A6085YH_T6086W	L6079T_W6081I_I6088A
D1871	A6085YF_T6086H	L6079T_W6081I_I6088A
D1872	A6085YY_T6086H	L6079T_W6081I_I6088A
D1873	A6085YM_T6086H	L6079T_W6081I_I6088A
D1874	A6085YW_T6086H	L6079T_W6081I_I6088A
D1875	A6085YH_T6086H	L6079T_W6081I_I6088A
D1876	A6085YF_T6086Y	L6079A_W6081T_I6088A
D1877	A6085YY_T6086Y	L6079A_W6081T_I6088A
D1878	A6085YM_T6086Y	L6079A_W6081T_I6088A
D1879	A6085YW_T6086Y	L6079A_W6081T_I6088A
D1880	A6085YH_T6086Y	L6079A_W6081T_I6088A
D1881	A6085YF_T6086F	L6079A_W6081T_I6088A
D1882	A6085YY_T6086F	L6079A_W6081T_I6088A
D1883	A6085YM_T6086F	L6079A_W6081T_I6088A
D1884	A6085YW_T6086F	L6079A_W6081T_I6088A
D1885	A6085YH_T6086F	L6079A_W6081T_I6088A
D1886	A6085YF_T6086M	L6079A_W6081T_I6088A
D1887	A6085YY_T6086M	L6079A_W6081T_I6088A
D1888	A6085YM_T6086M	L6079A_W6081T_I6088A
D1889	A6085YW_T6086M	L6079A_W6081T_I6088A
D1890	A6085YH_T6086M	L6079A_W6081T_I6088A
D1891	A6085YF_T6086W	L6079A_W6081T_I6088A
D1892	A6085YY_T6086W	L6079A_W6081T_I6088A
D1893	A6085YM_T6086W	L6079A_W6081T_I6088A

No.	CH3 Domain Mutations	
	Chain A	Chain B
D1894	A6085YW_T6086W	L6079A_W6081T_I6088A
D1895	A6085YH_T6086W	L6079A_W6081T_I6088A
D1896	A6085YF_T6086H	L6079A_W6081T_I6088A
D1897	A6085YY_T6086H	L6079A_W6081T_I6088A
D1898	A6085YM_T6086H	L6079A_W6081T_I6088A
D1899	A6085YW_T6086H	L6079A_W6081T_I6088A
D1900	A6085YH_T6086H	L6079A_W6081T_I6088A
D1901	A6085YF_T6086Y	L6079A_W6081L_I6088A
D1902	A6085YY_T6086Y	L6079A_W6081L_I6088A
D1903	A6085YM_T6086Y	L6079A_W6081L_I6088A
D1904	A6085YW_T6086Y	L6079A_W6081L_I6088A
D1905	A6085YH_T6086Y	L6079A_W6081L_I6088A
D1906	A6085YF_T6086F	L6079A_W6081L_I6088A
D1907	A6085YY_T6086F	L6079A_W6081L_I6088A
D1908	A6085YM_T6086F	L6079A_W6081L_I6088A
D1909	A6085YW_T6086F	L6079A_W6081L_I6088A
D1910	A6085YH_T6086F	L6079A_W6081L_I6088A
D1911	A6085YF_T6086M	L6079A_W6081L_I6088A
D1912	A6085YY_T6086M	L6079A_W6081L_I6088A
D1913	A6085YM_T6086M	L6079A_W6081L_I6088A
D1914	A6085YW_T6086M	L6079A_W6081L_I6088A
D1915	A6085YH_T6086M	L6079A_W6081L_I6088A
D1916	A6085YF_T6086W	L6079A_W6081L_I6088A
D1917	A6085YY_T6086W	L6079A_W6081L_I6088A
D1918	A6085YM_T6086W	L6079A_W6081L_I6088A
D1919	A6085YW_T6086W	L6079A_W6081L_I6088A
D1920	A6085YH_T6086W	L6079A_W6081L_I6088A
D1921	A6085YF_T6086H	L6079A_W6081L_I6088A
D1922	A6085YY_T6086H	L6079A_W6081L_I6088A

No.	CH3 Domain Mutations	
	Chain A	Chain B
D1923	A6085YM_T6086H	L6079A_W6081L_I6088A
D1924	A6085YW_T6086H	L6079A_W6081L_I6088A
D1925	A6085YH_T6086H	L6079A_W6081L_I6088A
D1926	A6085YF_T6086Y	L6079A_W6081A_I6088A
D1927	A6085YY_T6086Y	L6079A_W6081A_I6088A
D1928	A6085YM_T6086Y	L6079A_W6081A_I6088A
D1929	A6085YW_T6086Y	L6079A_W6081A_I6088A
D1930	A6085YH_T6086Y	L6079A_W6081A_I6088A
D1931	A6085YF_T6086F	L6079A_W6081A_I6088A
D1932	A6085YY_T6086F	L6079A_W6081A_I6088A
D1933	A6085YM_T6086F	L6079A_W6081A_I6088A
D1934	A6085YW_T6086F	L6079A_W6081A_I6088A
D1935	A6085YH_T6086F	L6079A_W6081A_I6088A
D1936	A6085YF_T6086M	L6079A_W6081A_I6088A
D1937	A6085YY_T6086M	L6079A_W6081A_I6088A
D1938	A6085YM_T6086M	L6079A_W6081A_I6088A
D1939	A6085YW_T6086M	L6079A_W6081A_I6088A
D1940	A6085YH_T6086M	L6079A_W6081A_I6088A
D1941	A6085YF_T6086W	L6079A_W6081A_I6088A
D1942	A6085YY_T6086W	L6079A_W6081A_I6088A
D1943	A6085YM_T6086W	L6079A_W6081A_I6088A
D1944	A6085YW_T6086W	L6079A_W6081A_I6088A
D1945	A6085YH_T6086W	L6079A_W6081A_I6088A
D1946	A6085YF_T6086H	L6079A_W6081A_I6088A
D1947	A6085YY_T6086H	L6079A_W6081A_I6088A
D1948	A6085YM_T6086H	L6079A_W6081A_I6088A
D1949	A6085YW_T6086H	L6079A_W6081A_I6088A
D1950	A6085YH_T6086H	L6079A_W6081A_I6088A
D1951	A6085YF_T6086Y	L6079A_W6081V_I6088A

No.	CH3 Domain Mutations	
	Chain A	Chain B
D1952	A6085YY_T6086Y	L6079A_W6081V_I6088A
D1953	A6085YM_T6086Y	L6079A_W6081V_I6088A
D1954	A6085YW_T6086Y	L6079A_W6081V_I6088A
D1955	A6085YH_T6086Y	L6079A_W6081V_I6088A
D1956	A6085YF_T6086F	L6079A_W6081V_I6088A
D1957	A6085YY_T6086F	L6079A_W6081V_I6088A
D1958	A6085YM_T6086F	L6079A_W6081V_I6088A
D1959	A6085YW_T6086F	L6079A_W6081V_I6088A
D1960	A6085YH_T6086F	L6079A_W6081V_I6088A
D1961	A6085YF_T6086M	L6079A_W6081V_I6088A
D1962	A6085YY_T6086M	L6079A_W6081V_I6088A
D1963	A6085YM_T6086M	L6079A_W6081V_I6088A
D1964	A6085YW_T6086M	L6079A_W6081V_I6088A
D1965	A6085YH_T6086M	L6079A_W6081V_I6088A
D1966	A6085YF_T6086W	L6079A_W6081V_I6088A
D1967	A6085YY_T6086W	L6079A_W6081V_I6088A
D1968	A6085YM_T6086W	L6079A_W6081V_I6088A
D1969	A6085YW_T6086W	L6079A_W6081V_I6088A
D1970	A6085YH_T6086W	L6079A_W6081V_I6088A
D1971	A6085YF_T6086H	L6079A_W6081V_I6088A
D1972	A6085YY_T6086H	L6079A_W6081V_I6088A
D1973	A6085YM_T6086H	L6079A_W6081V_I6088A
D1974	A6085YW_T6086H	L6079A_W6081V_I6088A
D1975	A6085YH_T6086H	L6079A_W6081V_I6088A
D1976	A6085YF_T6086Y	L6079A_W6081I_I6088A
D1977	A6085YY_T6086Y	L6079A_W6081I_I6088A
D1978	A6085YM_T6086Y	L6079A_W6081I_I6088A
D1979	A6085YW_T6086Y	L6079A_W6081I_I6088A
D1980	A6085YH_T6086Y	L6079A_W6081I_I6088A

No.	CH3 Domain Mutations	
	Chain A	Chain B
D1981	A6085YF_T6086F	L6079A_W6081I_I6088A
D1982	A6085YY_T6086F	L6079A_W6081I_I6088A
D1983	A6085YM_T6086F	L6079A_W6081I_I6088A
D1984	A6085YW_T6086F	L6079A_W6081I_I6088A
D1985	A6085YH_T6086F	L6079A_W6081I_I6088A
D1986	A6085YF_T6086M	L6079A_W6081I_I6088A
D1987	A6085YY_T6086M	L6079A_W6081I_I6088A
D1988	A6085YM_T6086M	L6079A_W6081I_I6088A
D1989	A6085YW_T6086M	L6079A_W6081I_I6088A
D1990	A6085YH_T6086M	L6079A_W6081I_I6088A
D1991	A6085YF_T6086W	L6079A_W6081I_I6088A
D1992	A6085YY_T6086W	L6079A_W6081I_I6088A
D1993	A6085YM_T6086W	L6079A_W6081I_I6088A
D1994	A6085YW_T6086W	L6079A_W6081I_I6088A
D1995	A6085YH_T6086W	L6079A_W6081I_I6088A
D1996	A6085YF_T6086H	L6079A_W6081I_I6088A
D1997	A6085YY_T6086H	L6079A_W6081I_I6088A
D1998	A6085YM_T6086H	L6079A_W6081I_I6088A
D1999	A6085YW_T6086H	L6079A_W6081I_I6088A
D2000	A6085YH_T6086H	L6079A_W6081I_I6088A
D2001	A6085YF_T6086Y	L6079I_W6081T_I6088A
D2002	A6085YY_T6086Y	L6079I_W6081T_I6088A
D2003	A6085YM_T6086Y	L6079I_W6081T_I6088A
D2004	A6085YW_T6086Y	L6079I_W6081T_I6088A
D2005	A6085YH_T6086Y	L6079I_W6081T_I6088A
D2006	A6085YF_T6086F	L6079I_W6081T_I6088A
D2007	A6085YY_T6086F	L6079I_W6081T_I6088A
D2008	A6085YM_T6086F	L6079I_W6081T_I6088A
D2009	A6085YW_T6086F	L6079I_W6081T_I6088A

No.	CH3 Domain Mutations	
	Chain A	Chain B
D2010	A6085YH_T6086F	L6079I_W6081T_I6088A
D2011	A6085YF_T6086M	L6079I_W6081T_I6088A
D2012	A6085YY_T6086M	L6079I_W6081T_I6088A
D2013	A6085YM_T6086M	L6079I_W6081T_I6088A
D2014	A6085YW_T6086M	L6079I_W6081T_I6088A
D2015	A6085YH_T6086M	L6079I_W6081T_I6088A
D2016	A6085YF_T6086W	L6079I_W6081T_I6088A
D2017	A6085YY_T6086W	L6079I_W6081T_I6088A
D2018	A6085YM_T6086W	L6079I_W6081T_I6088A
D2019	A6085YW_T6086W	L6079I_W6081T_I6088A
D2020	A6085YH_T6086W	L6079I_W6081T_I6088A
D2021	A6085YF_T6086H	L6079I_W6081T_I6088A
D2022	A6085YY_T6086H	L6079I_W6081T_I6088A
D2023	A6085YM_T6086H	L6079I_W6081T_I6088A
D2024	A6085YW_T6086H	L6079I_W6081T_I6088A
D2025	A6085YH_T6086H	L6079I_W6081T_I6088A
D2026	A6085YF_T6086Y	L6079I_W6081L_I6088A
D2027	A6085YY_T6086Y	L6079I_W6081L_I6088A
D2028	A6085YM_T6086Y	L6079I_W6081L_I6088A
D2029	A6085YW_T6086Y	L6079I_W6081L_I6088A
D2030	A6085YH_T6086Y	L6079I_W6081L_I6088A
D2031	A6085YF_T6086F	L6079I_W6081L_I6088A
D2032	A6085YY_T6086F	L6079I_W6081L_I6088A
D2033	A6085YM_T6086F	L6079I_W6081L_I6088A
D2034	A6085YW_T6086F	L6079I_W6081L_I6088A
D2035	A6085YH_T6086F	L6079I_W6081L_I6088A
D2036	A6085YF_T6086M	L6079I_W6081L_I6088A
D2037	A6085YY_T6086M	L6079I_W6081L_I6088A
D2038	A6085YM_T6086M	L6079I_W6081L_I6088A

No.	CH3 Domain Mutations	
	Chain A	Chain B
D2039	A6085YW_T6086M	L6079I_W6081L_I6088A
D2040	A6085YH_T6086M	L6079I_W6081L_I6088A
D2041	A6085YF_T6086W	L6079I_W6081L_I6088A
D2042	A6085YY_T6086W	L6079I_W6081L_I6088A
D2043	A6085YM_T6086W	L6079I_W6081L_I6088A
D2044	A6085YW_T6086W	L6079I_W6081L_I6088A
D2045	A6085YH_T6086W	L6079I_W6081L_I6088A
D2046	A6085YF_T6086H	L6079I_W6081L_I6088A
D2047	A6085YY_T6086H	L6079I_W6081L_I6088A
D2048	A6085YM_T6086H	L6079I_W6081L_I6088A
D2049	A6085YW_T6086H	L6079I_W6081L_I6088A
D2050	A6085YH_T6086H	L6079I_W6081L_I6088A
D2051	A6085YF_T6086Y	L6079I_W6081A_I6088A
D2052	A6085YY_T6086Y	L6079I_W6081A_I6088A
D2053	A6085YM_T6086Y	L6079I_W6081A_I6088A
D2054	A6085YW_T6086Y	L6079I_W6081A_I6088A
D2055	A6085YH_T6086Y	L6079I_W6081A_I6088A
D2056	A6085YF_T6086F	L6079I_W6081A_I6088A
D2057	A6085YY_T6086F	L6079I_W6081A_I6088A
D2058	A6085YM_T6086F	L6079I_W6081A_I6088A
D2059	A6085YW_T6086F	L6079I_W6081A_I6088A
D2060	A6085YH_T6086F	L6079I_W6081A_I6088A
D2061	A6085YF_T6086M	L6079I_W6081A_I6088A
D2062	A6085YY_T6086M	L6079I_W6081A_I6088A
D2063	A6085YM_T6086M	L6079I_W6081A_I6088A
D2064	A6085YW_T6086M	L6079I_W6081A_I6088A
D2065	A6085YH_T6086M	L6079I_W6081A_I6088A
D2066	A6085YF_T6086W	L6079I_W6081A_I6088A
D2067	A6085YY_T6086W	L6079I_W6081A_I6088A

No.	CH3 Domain Mutations	
	Chain A	Chain B
D2068	A6085YM_T6086W	L6079I_W6081A_I6088A
D2069	A6085YW_T6086W	L6079I_W6081A_I6088A
D2070	A6085YH_T6086W	L6079I_W6081A_I6088A
D2071	A6085YF_T6086H	L6079I_W6081A_I6088A
D2072	A6085YY_T6086H	L6079I_W6081A_I6088A
D2073	A6085YM_T6086H	L6079I_W6081A_I6088A
D2074	A6085YW_T6086H	L6079I_W6081A_I6088A
D2075	A6085YH_T6086H	L6079I_W6081A_I6088A
D2076	A6085YF_T6086Y	L6079I_W6081V_I6088A
D2077	A6085YY_T6086Y	L6079I_W6081V_I6088A
D2078	A6085YM_T6086Y	L6079I_W6081V_I6088A
D2079	A6085YW_T6086Y	L6079I_W6081V_I6088A
D2080	A6085YH_T6086Y	L6079I_W6081V_I6088A
D2081	A6085YF_T6086F	L6079I_W6081V_I6088A
D2082	A6085YY_T6086F	L6079I_W6081V_I6088A
D2083	A6085YM_T6086F	L6079I_W6081V_I6088A
D2084	A6085YW_T6086F	L6079I_W6081V_I6088A
D2085	A6085YH_T6086F	L6079I_W6081V_I6088A
D2086	A6085YF_T6086M	L6079I_W6081V_I6088A
D2087	A6085YY_T6086M	L6079I_W6081V_I6088A
D2088	A6085YM_T6086M	L6079I_W6081V_I6088A
D2089	A6085YW_T6086M	L6079I_W6081V_I6088A
D2090	A6085YH_T6086M	L6079I_W6081V_I6088A
D2091	A6085YF_T6086W	L6079I_W6081V_I6088A
D2092	A6085YY_T6086W	L6079I_W6081V_I6088A
D2093	A6085YM_T6086W	L6079I_W6081V_I6088A
D2094	A6085YW_T6086W	L6079I_W6081V_I6088A
D2095	A6085YH_T6086W	L6079I_W6081V_I6088A
D2096	A6085YF_T6086H	L6079I_W6081V_I6088A

No.	CH3 Domain Mutations	
	Chain A	Chain B
D2097	A6085YY_T6086H	L6079I_W6081V_I6088A
D2098	A6085YM_T6086H	L6079I_W6081V_I6088A
D2099	A6085YW_T6086H	L6079I_W6081V_I6088A
D2100	A6085YH_T6086H	L6079I_W6081V_I6088A
D2101	A6085YF_T6086Y	L6079I_W6081I_I6088A
D2102	A6085YY_T6086Y	L6079I_W6081I_I6088A
D2103	A6085YM_T6086Y	L6079I_W6081I_I6088A
D2104	A6085YW_T6086Y	L6079I_W6081I_I6088A
D2105	A6085YH_T6086Y	L6079I_W6081I_I6088A
D2106	A6085YF_T6086F	L6079I_W6081I_I6088A
D2107	A6085YY_T6086F	L6079I_W6081I_I6088A
D2108	A6085YM_T6086F	L6079I_W6081I_I6088A
D2109	A6085YW_T6086F	L6079I_W6081I_I6088A
D2110	A6085YH_T6086F	L6079I_W6081I_I6088A
D2111	A6085YF_T6086M	L6079I_W6081I_I6088A
D2112	A6085YY_T6086M	L6079I_W6081I_I6088A
D2113	A6085YM_T6086M	L6079I_W6081I_I6088A
D2114	A6085YW_T6086M	L6079I_W6081I_I6088A
D2115	A6085YH_T6086M	L6079I_W6081I_I6088A
D2116	A6085YF_T6086W	L6079I_W6081I_I6088A
D2117	A6085YY_T6086W	L6079I_W6081I_I6088A
D2118	A6085YM_T6086W	L6079I_W6081I_I6088A
D2119	A6085YW_T6086W	L6079I_W6081I_I6088A
D2120	A6085YH_T6086W	L6079I_W6081I_I6088A
D2121	A6085YF_T6086H	L6079I_W6081I_I6088A
D2122	A6085YY_T6086H	L6079I_W6081I_I6088A
D2123	A6085YM_T6086H	L6079I_W6081I_I6088A
D2124	A6085YW_T6086H	L6079I_W6081I_I6088A
D2125	A6085YH_T6086H	L6079I_W6081I_I6088A

No.	CH3 Domain Mutations	
	Chain A	Chain B
D2126	A6085YF_T6086Y	L6079V_W6081T_I6088V
D2127	A6085YY_T6086Y	L6079V_W6081T_I6088V
D2128	A6085YM_T6086Y	L6079V_W6081T_I6088V
D2129	A6085YW_T6086Y	L6079V_W6081T_I6088V
D2130	A6085YH_T6086Y	L6079V_W6081T_I6088V
D2131	A6085YF_T6086F	L6079V_W6081T_I6088V
D2132	A6085YY_T6086F	L6079V_W6081T_I6088V
D2133	A6085YM_T6086F	L6079V_W6081T_I6088V
D2134	A6085YW_T6086F	L6079V_W6081T_I6088V
D2135	A6085YH_T6086F	L6079V_W6081T_I6088V
D2136	A6085YF_T6086M	L6079V_W6081T_I6088V
D2137	A6085YY_T6086M	L6079V_W6081T_I6088V
D2138	A6085YM_T6086M	L6079V_W6081T_I6088V
D2139	A6085YW_T6086M	L6079V_W6081T_I6088V
D2140	A6085YH_T6086M	L6079V_W6081T_I6088V
D2141	A6085YF_T6086W	L6079V_W6081T_I6088V
D2142	A6085YY_T6086W	L6079V_W6081T_I6088V
D2143	A6085YM_T6086W	L6079V_W6081T_I6088V
D2144	A6085YW_T6086W	L6079V_W6081T_I6088V
D2145	A6085YH_T6086W	L6079V_W6081T_I6088V
D2146	A6085YF_T6086H	L6079V_W6081T_I6088V
D2147	A6085YY_T6086H	L6079V_W6081T_I6088V
D2148	A6085YM_T6086H	L6079V_W6081T_I6088V
D2149	A6085YW_T6086H	L6079V_W6081T_I6088V
D2150	A6085YH_T6086H	L6079V_W6081T_I6088V
D2151	A6085YF_T6086Y	L6079V_W6081L_I6088V
D2152	A6085YY_T6086Y	L6079V_W6081L_I6088V
D2153	A6085YM_T6086Y	L6079V_W6081L_I6088V
D2154	A6085YW_T6086Y	L6079V_W6081L_I6088V

No.	CH3 Domain Mutations	
	Chain A	Chain B
D2155	A6085YH_T6086Y	L6079V_W6081L_I6088V
D2156	A6085YF_T6086F	L6079V_W6081L_I6088V
D2157	A6085YY_T6086F	L6079V_W6081L_I6088V
D2158	A6085YM_T6086F	L6079V_W6081L_I6088V
D2159	A6085YW_T6086F	L6079V_W6081L_I6088V
D2160	A6085YH_T6086F	L6079V_W6081L_I6088V
D2161	A6085YF_T6086M	L6079V_W6081L_I6088V
D2162	A6085YY_T6086M	L6079V_W6081L_I6088V
D2163	A6085YM_T6086M	L6079V_W6081L_I6088V
D2164	A6085YW_T6086M	L6079V_W6081L_I6088V
D2165	A6085YH_T6086M	L6079V_W6081L_I6088V
D2166	A6085YF_T6086W	L6079V_W6081L_I6088V
D2167	A6085YY_T6086W	L6079V_W6081L_I6088V
D2168	A6085YM_T6086W	L6079V_W6081L_I6088V
D2169	A6085YW_T6086W	L6079V_W6081L_I6088V
D2170	A6085YH_T6086W	L6079V_W6081L_I6088V
D2171	A6085YF_T6086H	L6079V_W6081L_I6088V
D2172	A6085YY_T6086H	L6079V_W6081L_I6088V
D2173	A6085YM_T6086H	L6079V_W6081L_I6088V
D2174	A6085YW_T6086H	L6079V_W6081L_I6088V
D2175	A6085YH_T6086H	L6079V_W6081L_I6088V
D2176	A6085YF_T6086Y	L6079V_W6081A_I6088V
D2177	A6085YY_T6086Y	L6079V_W6081A_I6088V
D2178	A6085YM_T6086Y	L6079V_W6081A_I6088V
D2179	A6085YW_T6086Y	L6079V_W6081A_I6088V
D2180	A6085YH_T6086Y	L6079V_W6081A_I6088V
D2181	A6085YF_T6086F	L6079V_W6081A_I6088V
D2182	A6085YY_T6086F	L6079V_W6081A_I6088V
D2183	A6085YM_T6086F	L6079V_W6081A_I6088V

No.	CH3 Domain Mutations	
	Chain A	Chain B
D2184	A6085YW_T6086F	L6079V_W6081A_I6088V
D2185	A6085YH_T6086F	L6079V_W6081A_I6088V
D2186	A6085YF_T6086M	L6079V_W6081A_I6088V
D2187	A6085YY_T6086M	L6079V_W6081A_I6088V
D2188	A6085YM_T6086M	L6079V_W6081A_I6088V
D2189	A6085YW_T6086M	L6079V_W6081A_I6088V
D2190	A6085YH_T6086M	L6079V_W6081A_I6088V
D2191	A6085YF_T6086W	L6079V_W6081A_I6088V
D2192	A6085YY_T6086W	L6079V_W6081A_I6088V
D2193	A6085YM_T6086W	L6079V_W6081A_I6088V
D2194	A6085YW_T6086W	L6079V_W6081A_I6088V
D2195	A6085YH_T6086W	L6079V_W6081A_I6088V
D2196	A6085YF_T6086H	L6079V_W6081A_I6088V
D2197	A6085YY_T6086H	L6079V_W6081A_I6088V
D2198	A6085YM_T6086H	L6079V_W6081A_I6088V
D2199	A6085YW_T6086H	L6079V_W6081A_I6088V
D2200	A6085YH_T6086H	L6079V_W6081A_I6088V
D2201	A6085YF_T6086Y	L6079V_W6081V_I6088V
D2202	A6085YY_T6086Y	L6079V_W6081V_I6088V
D2203	A6085YM_T6086Y	L6079V_W6081V_I6088V
D2204	A6085YW_T6086Y	L6079V_W6081V_I6088V
D2205	A6085YH_T6086Y	L6079V_W6081V_I6088V
D2206	A6085YF_T6086F	L6079V_W6081V_I6088V
D2207	A6085YY_T6086F	L6079V_W6081V_I6088V
D2208	A6085YM_T6086F	L6079V_W6081V_I6088V
D2209	A6085YW_T6086F	L6079V_W6081V_I6088V
D2210	A6085YH_T6086F	L6079V_W6081V_I6088V
D2211	A6085YF_T6086M	L6079V_W6081V_I6088V
D2212	A6085YY_T6086M	L6079V_W6081V_I6088V

No.	CH3 Domain Mutations	
	Chain A	Chain B
D2213	A6085YM_T6086M	L6079V_W6081V_I6088V
D2214	A6085YW_T6086M	L6079V_W6081V_I6088V
D2215	A6085YH_T6086M	L6079V_W6081V_I6088V
D2216	A6085YF_T6086W	L6079V_W6081V_I6088V
D2217	A6085YY_T6086W	L6079V_W6081V_I6088V
D2218	A6085YM_T6086W	L6079V_W6081V_I6088V
D2219	A6085YW_T6086W	L6079V_W6081V_I6088V
D2220	A6085YH_T6086W	L6079V_W6081V_I6088V
D2221	A6085YF_T6086H	L6079V_W6081V_I6088V
D2222	A6085YY_T6086H	L6079V_W6081V_I6088V
D2223	A6085YM_T6086H	L6079V_W6081V_I6088V
D2224	A6085YW_T6086H	L6079V_W6081V_I6088V
D2225	A6085YH_T6086H	L6079V_W6081V_I6088V
D2226	A6085YF_T6086Y	L6079V_W6081I_I6088V
D2227	A6085YY_T6086Y	L6079V_W6081I_I6088V
D2228	A6085YM_T6086Y	L6079V_W6081I_I6088V
D2229	A6085YW_T6086Y	L6079V_W6081I_I6088V
D2230	A6085YH_T6086Y	L6079V_W6081I_I6088V
D2231	A6085YF_T6086F	L6079V_W6081I_I6088V
D2232	A6085YY_T6086F	L6079V_W6081I_I6088V
D2233	A6085YM_T6086F	L6079V_W6081I_I6088V
D2234	A6085YW_T6086F	L6079V_W6081I_I6088V
D2235	A6085YH_T6086F	L6079V_W6081I_I6088V
D2236	A6085YF_T6086M	L6079V_W6081I_I6088V
D2237	A6085YY_T6086M	L6079V_W6081I_I6088V
D2238	A6085YM_T6086M	L6079V_W6081I_I6088V
D2239	A6085YW_T6086M	L6079V_W6081I_I6088V
D2240	A6085YH_T6086M	L6079V_W6081I_I6088V
D2241	A6085YF_T6086W	L6079V_W6081I_I6088V

No.	CH3 Domain Mutations	
	Chain A	Chain B
D2242	A6085YY_T6086W	L6079V_W6081I_I6088V
D2243	A6085YM_T6086W	L6079V_W6081I_I6088V
D2244	A6085YW_T6086W	L6079V_W6081I_I6088V
D2245	A6085YH_T6086W	L6079V_W6081I_I6088V
D2246	A6085YF_T6086H	L6079V_W6081I_I6088V
D2247	A6085YY_T6086H	L6079V_W6081I_I6088V
D2248	A6085YM_T6086H	L6079V_W6081I_I6088V
D2249	A6085YW_T6086H	L6079V_W6081I_I6088V
D2250	A6085YH_T6086H	L6079V_W6081I_I6088V
D2251	A6085YF_T6086Y	L6079T_W6081T_I6088V
D2252	A6085YY_T6086Y	L6079T_W6081T_I6088V
D2253	A6085YM_T6086Y	L6079T_W6081T_I6088V
D2254	A6085YW_T6086Y	L6079T_W6081T_I6088V
D2255	A6085YH_T6086Y	L6079T_W6081T_I6088V
D2256	A6085YF_T6086F	L6079T_W6081T_I6088V
D2257	A6085YY_T6086F	L6079T_W6081T_I6088V
D2258	A6085YM_T6086F	L6079T_W6081T_I6088V
D2259	A6085YW_T6086F	L6079T_W6081T_I6088V
D2260	A6085YH_T6086F	L6079T_W6081T_I6088V
D2261	A6085YF_T6086M	L6079T_W6081T_I6088V
D2262	A6085YY_T6086M	L6079T_W6081T_I6088V
D2263	A6085YM_T6086M	L6079T_W6081T_I6088V
D2264	A6085YW_T6086M	L6079T_W6081T_I6088V
D2265	A6085YH_T6086M	L6079T_W6081T_I6088V
D2266	A6085YF_T6086W	L6079T_W6081T_I6088V
D2267	A6085YY_T6086W	L6079T_W6081T_I6088V
D2268	A6085YM_T6086W	L6079T_W6081T_I6088V
D2269	A6085YW_T6086W	L6079T_W6081T_I6088V
D2270	A6085YH_T6086W	L6079T_W6081T_I6088V

No.	CH3 Domain Mutations	
	Chain A	Chain B
D2271	A6085YF_T6086H	L6079T_W6081T_I6088V
D2272	A6085YY_T6086H	L6079T_W6081T_I6088V
D2273	A6085YM_T6086H	L6079T_W6081T_I6088V
D2274	A6085YW_T6086H	L6079T_W6081T_I6088V
D2275	A6085YH_T6086H	L6079T_W6081T_I6088V
D2276	A6085YF_T6086Y	L6079T_W6081L_I6088V
D2277	A6085YY_T6086Y	L6079T_W6081L_I6088V
D2278	A6085YM_T6086Y	L6079T_W6081L_I6088V
D2279	A6085YW_T6086Y	L6079T_W6081L_I6088V
D2280	A6085YH_T6086Y	L6079T_W6081L_I6088V
D2281	A6085YF_T6086F	L6079T_W6081L_I6088V
D2282	A6085YY_T6086F	L6079T_W6081L_I6088V
D2283	A6085YM_T6086F	L6079T_W6081L_I6088V
D2284	A6085YW_T6086F	L6079T_W6081L_I6088V
D2285	A6085YH_T6086F	L6079T_W6081L_I6088V
D2286	A6085YF_T6086M	L6079T_W6081L_I6088V
D2287	A6085YY_T6086M	L6079T_W6081L_I6088V
D2288	A6085YM_T6086M	L6079T_W6081L_I6088V
D2289	A6085YW_T6086M	L6079T_W6081L_I6088V
D2290	A6085YH_T6086M	L6079T_W6081L_I6088V
D2291	A6085YF_T6086W	L6079T_W6081L_I6088V
D2292	A6085YY_T6086W	L6079T_W6081L_I6088V
D2293	A6085YM_T6086W	L6079T_W6081L_I6088V
D2294	A6085YW_T6086W	L6079T_W6081L_I6088V
D2295	A6085YH_T6086W	L6079T_W6081L_I6088V
D2296	A6085YF_T6086H	L6079T_W6081L_I6088V
D2297	A6085YY_T6086H	L6079T_W6081L_I6088V
D2298	A6085YM_T6086H	L6079T_W6081L_I6088V
D2299	A6085YW_T6086H	L6079T_W6081L_I6088V

No.	CH3 Domain Mutations	
	Chain A	Chain B
D2300	A6085YH_T6086H	L6079T_W6081L_I6088V
D2301	A6085YF_T6086Y	L6079T_W6081A_I6088V
D2302	A6085YY_T6086Y	L6079T_W6081A_I6088V
D2303	A6085YM_T6086Y	L6079T_W6081A_I6088V
D2304	A6085YW_T6086Y	L6079T_W6081A_I6088V
D2305	A6085YH_T6086Y	L6079T_W6081A_I6088V
D2306	A6085YF_T6086F	L6079T_W6081A_I6088V
D2307	A6085YY_T6086F	L6079T_W6081A_I6088V
D2308	A6085YM_T6086F	L6079T_W6081A_I6088V
D2309	A6085YW_T6086F	L6079T_W6081A_I6088V
D2310	A6085YH_T6086F	L6079T_W6081A_I6088V
D2311	A6085YF_T6086M	L6079T_W6081A_I6088V
D2312	A6085YY_T6086M	L6079T_W6081A_I6088V
D2313	A6085YM_T6086M	L6079T_W6081A_I6088V
D2314	A6085YW_T6086M	L6079T_W6081A_I6088V
D2315	A6085YH_T6086M	L6079T_W6081A_I6088V
D2316	A6085YF_T6086W	L6079T_W6081A_I6088V
D2317	A6085YY_T6086W	L6079T_W6081A_I6088V
D2318	A6085YM_T6086W	L6079T_W6081A_I6088V
D2319	A6085YW_T6086W	L6079T_W6081A_I6088V
D2320	A6085YH_T6086W	L6079T_W6081A_I6088V
D2321	A6085YF_T6086H	L6079T_W6081A_I6088V
D2322	A6085YY_T6086H	L6079T_W6081A_I6088V
D2323	A6085YM_T6086H	L6079T_W6081A_I6088V
D2324	A6085YW_T6086H	L6079T_W6081A_I6088V
D2325	A6085YH_T6086H	L6079T_W6081A_I6088V
D2326	A6085YF_T6086Y	L6079T_W6081V_I6088V
D2327	A6085YY_T6086Y	L6079T_W6081V_I6088V
D2328	A6085YM_T6086Y	L6079T_W6081V_I6088V

No.	CH3 Domain Mutations	
	Chain A	Chain B
D2329	A6085YW_T6086Y	L6079T_W6081V_I6088V
D2330	A6085YH_T6086Y	L6079T_W6081V_I6088V
D2331	A6085YF_T6086F	L6079T_W6081V_I6088V
D2332	A6085YY_T6086F	L6079T_W6081V_I6088V
D2333	A6085YM_T6086F	L6079T_W6081V_I6088V
D2334	A6085YW_T6086F	L6079T_W6081V_I6088V
D2335	A6085YH_T6086F	L6079T_W6081V_I6088V
D2336	A6085YF_T6086M	L6079T_W6081V_I6088V
D2337	A6085YY_T6086M	L6079T_W6081V_I6088V
D2338	A6085YM_T6086M	L6079T_W6081V_I6088V
D2339	A6085YW_T6086M	L6079T_W6081V_I6088V
D2340	A6085YH_T6086M	L6079T_W6081V_I6088V
D2341	A6085YF_T6086W	L6079T_W6081V_I6088V
D2342	A6085YY_T6086W	L6079T_W6081V_I6088V
D2343	A6085YM_T6086W	L6079T_W6081V_I6088V
D2344	A6085YW_T6086W	L6079T_W6081V_I6088V
D2345	A6085YH_T6086W	L6079T_W6081V_I6088V
D2346	A6085YF_T6086H	L6079T_W6081V_I6088V
D2347	A6085YY_T6086H	L6079T_W6081V_I6088V
D2348	A6085YM_T6086H	L6079T_W6081V_I6088V
D2349	A6085YW_T6086H	L6079T_W6081V_I6088V
D2350	A6085YH_T6086H	L6079T_W6081V_I6088V
D2351	A6085YF_T6086Y	L6079T_W6081I_I6088V
D2352	A6085YY_T6086Y	L6079T_W6081I_I6088V
D2353	A6085YM_T6086Y	L6079T_W6081I_I6088V
D2354	A6085YW_T6086Y	L6079T_W6081I_I6088V
D2355	A6085YH_T6086Y	L6079T_W6081I_I6088V
D2356	A6085YF_T6086F	L6079T_W6081I_I6088V
D2357	A6085YY_T6086F	L6079T_W6081I_I6088V

No.	CH3 Domain Mutations	
	Chain A	Chain B
D2358	A6085YM_T6086F	L6079T_W6081I_I6088V
D2359	A6085YW_T6086F	L6079T_W6081I_I6088V
D2360	A6085YH_T6086F	L6079T_W6081I_I6088V
D2361	A6085YF_T6086M	L6079T_W6081I_I6088V
D2362	A6085YY_T6086M	L6079T_W6081I_I6088V
D2363	A6085YM_T6086M	L6079T_W6081I_I6088V
D2364	A6085YW_T6086M	L6079T_W6081I_I6088V
D2365	A6085YH_T6086M	L6079T_W6081I_I6088V
D2366	A6085YF_T6086W	L6079T_W6081I_I6088V
D2367	A6085YY_T6086W	L6079T_W6081I_I6088V
D2368	A6085YM_T6086W	L6079T_W6081I_I6088V
D2369	A6085YW_T6086W	L6079T_W6081I_I6088V
D2370	A6085YH_T6086W	L6079T_W6081I_I6088V
D2371	A6085YF_T6086H	L6079T_W6081I_I6088V
D2372	A6085YY_T6086H	L6079T_W6081I_I6088V
D2373	A6085YM_T6086H	L6079T_W6081I_I6088V
D2374	A6085YW_T6086H	L6079T_W6081I_I6088V
D2375	A6085YH_T6086H	L6079T_W6081I_I6088V
D2376	A6085YF_T6086Y	L6079A_W6081T_I6088V
D2377	A6085YY_T6086Y	L6079A_W6081T_I6088V
D2378	A6085YM_T6086Y	L6079A_W6081T_I6088V
D2379	A6085YW_T6086Y	L6079A_W6081T_I6088V
D2380	A6085YH_T6086Y	L6079A_W6081T_I6088V
D2381	A6085YF_T6086F	L6079A_W6081T_I6088V
D2382	A6085YY_T6086F	L6079A_W6081T_I6088V
D2383	A6085YM_T6086F	L6079A_W6081T_I6088V
D2384	A6085YW_T6086F	L6079A_W6081T_I6088V
D2385	A6085YH_T6086F	L6079A_W6081T_I6088V
D2386	A6085YF_T6086M	L6079A_W6081T_I6088V

No.	CH3 Domain Mutations	
	Chain A	Chain B
D2387	A6085YY_T6086M	L6079A_W6081T_I6088V
D2388	A6085YM_T6086M	L6079A_W6081T_I6088V
D2389	A6085YW_T6086M	L6079A_W6081T_I6088V
D2390	A6085YH_T6086M	L6079A_W6081T_I6088V
D2391	A6085YF_T6086W	L6079A_W6081T_I6088V
D2392	A6085YY_T6086W	L6079A_W6081T_I6088V
D2393	A6085YM_T6086W	L6079A_W6081T_I6088V
D2394	A6085YW_T6086W	L6079A_W6081T_I6088V
D2395	A6085YH_T6086W	L6079A_W6081T_I6088V
D2396	A6085YF_T6086H	L6079A_W6081T_I6088V
D2397	A6085YY_T6086H	L6079A_W6081T_I6088V
D2398	A6085YM_T6086H	L6079A_W6081T_I6088V
D2399	A6085YW_T6086H	L6079A_W6081T_I6088V
D2400	A6085YH_T6086H	L6079A_W6081T_I6088V
D2401	A6085YF_T6086Y	L6079A_W6081L_I6088V
D2402	A6085YY_T6086Y	L6079A_W6081L_I6088V
D2403	A6085YM_T6086Y	L6079A_W6081L_I6088V
D2404	A6085YW_T6086Y	L6079A_W6081L_I6088V
D2405	A6085YH_T6086Y	L6079A_W6081L_I6088V
D2406	A6085YF_T6086F	L6079A_W6081L_I6088V
D2407	A6085YY_T6086F	L6079A_W6081L_I6088V
D2408	A6085YM_T6086F	L6079A_W6081L_I6088V
D2409	A6085YW_T6086F	L6079A_W6081L_I6088V
D2410	A6085YH_T6086F	L6079A_W6081L_I6088V
D2411	A6085YF_T6086M	L6079A_W6081L_I6088V
D2412	A6085YY_T6086M	L6079A_W6081L_I6088V
D2413	A6085YM_T6086M	L6079A_W6081L_I6088V
D2414	A6085YW_T6086M	L6079A_W6081L_I6088V
D2415	A6085YH_T6086M	L6079A_W6081L_I6088V

No.	CH3 Domain Mutations	
	Chain A	Chain B
D2416	A6085YF_T6086W	L6079A_W6081L_I6088V
D2417	A6085YY_T6086W	L6079A_W6081L_I6088V
D2418	A6085YM_T6086W	L6079A_W6081L_I6088V
D2419	A6085YW_T6086W	L6079A_W6081L_I6088V
D2420	A6085YH_T6086W	L6079A_W6081L_I6088V
D2421	A6085YF_T6086H	L6079A_W6081L_I6088V
D2422	A6085YY_T6086H	L6079A_W6081L_I6088V
D2423	A6085YM_T6086H	L6079A_W6081L_I6088V
D2424	A6085YW_T6086H	L6079A_W6081L_I6088V
D2425	A6085YH_T6086H	L6079A_W6081L_I6088V
D2426	A6085YF_T6086Y	L6079A_W6081A_I6088V
D2427	A6085YY_T6086Y	L6079A_W6081A_I6088V
D2428	A6085YM_T6086Y	L6079A_W6081A_I6088V
D2429	A6085YW_T6086Y	L6079A_W6081A_I6088V
D2430	A6085YH_T6086Y	L6079A_W6081A_I6088V
D2431	A6085YF_T6086F	L6079A_W6081A_I6088V
D2432	A6085YY_T6086F	L6079A_W6081A_I6088V
D2433	A6085YM_T6086F	L6079A_W6081A_I6088V
D2434	A6085YW_T6086F	L6079A_W6081A_I6088V
D2435	A6085YH_T6086F	L6079A_W6081A_I6088V
D2436	A6085YF_T6086M	L6079A_W6081A_I6088V
D2437	A6085YY_T6086M	L6079A_W6081A_I6088V
D2438	A6085YM_T6086M	L6079A_W6081A_I6088V
D2439	A6085YW_T6086M	L6079A_W6081A_I6088V
D2440	A6085YH_T6086M	L6079A_W6081A_I6088V
D2441	A6085YF_T6086W	L6079A_W6081A_I6088V
D2442	A6085YY_T6086W	L6079A_W6081A_I6088V
D2443	A6085YM_T6086W	L6079A_W6081A_I6088V
D2444	A6085YW_T6086W	L6079A_W6081A_I6088V

No.	CH3 Domain Mutations	
	Chain A	Chain B
D2445	A6085YH_T6086W	L6079A_W6081A_I6088V
D2446	A6085YF_T6086H	L6079A_W6081A_I6088V
D2447	A6085YY_T6086H	L6079A_W6081A_I6088V
D2448	A6085YM_T6086H	L6079A_W6081A_I6088V
D2449	A6085YW_T6086H	L6079A_W6081A_I6088V
D2450	A6085YH_T6086H	L6079A_W6081A_I6088V
D2451	A6085YF_T6086Y	L6079A_W6081V_I6088V
D2452	A6085YY_T6086Y	L6079A_W6081V_I6088V
D2453	A6085YM_T6086Y	L6079A_W6081V_I6088V
D2454	A6085YW_T6086Y	L6079A_W6081V_I6088V
D2455	A6085YH_T6086Y	L6079A_W6081V_I6088V
D2456	A6085YF_T6086F	L6079A_W6081V_I6088V
D2457	A6085YY_T6086F	L6079A_W6081V_I6088V
D2458	A6085YM_T6086F	L6079A_W6081V_I6088V
D2459	A6085YW_T6086F	L6079A_W6081V_I6088V
D2460	A6085YH_T6086F	L6079A_W6081V_I6088V
D2461	A6085YF_T6086M	L6079A_W6081V_I6088V
D2462	A6085YY_T6086M	L6079A_W6081V_I6088V
D2463	A6085YM_T6086M	L6079A_W6081V_I6088V
D2464	A6085YW_T6086M	L6079A_W6081V_I6088V
D2465	A6085YH_T6086M	L6079A_W6081V_I6088V
D2466	A6085YF_T6086W	L6079A_W6081V_I6088V
D2467	A6085YY_T6086W	L6079A_W6081V_I6088V
D2468	A6085YM_T6086W	L6079A_W6081V_I6088V
D2469	A6085YW_T6086W	L6079A_W6081V_I6088V
D2470	A6085YH_T6086W	L6079A_W6081V_I6088V
D2471	A6085YF_T6086H	L6079A_W6081V_I6088V
D2472	A6085YY_T6086H	L6079A_W6081V_I6088V
D2473	A6085YM_T6086H	L6079A_W6081V_I6088V

No.	CH3 Domain Mutations	
	Chain A	Chain B
D2474	A6085YW_T6086H	L6079A_W6081V_I6088V
D2475	A6085YH_T6086H	L6079A_W6081V_I6088V
D2476	A6085YF_T6086Y	L6079A_W6081I_I6088V
D2477	A6085YY_T6086Y	L6079A_W6081I_I6088V
D2478	A6085YM_T6086Y	L6079A_W6081I_I6088V
D2479	A6085YW_T6086Y	L6079A_W6081I_I6088V
D2480	A6085YH_T6086Y	L6079A_W6081I_I6088V
D2481	A6085YF_T6086F	L6079A_W6081I_I6088V
D2482	A6085YY_T6086F	L6079A_W6081I_I6088V
D2483	A6085YM_T6086F	L6079A_W6081I_I6088V
D2484	A6085YW_T6086F	L6079A_W6081I_I6088V
D2485	A6085YH_T6086F	L6079A_W6081I_I6088V
D2486	A6085YF_T6086M	L6079A_W6081I_I6088V
D2487	A6085YY_T6086M	L6079A_W6081I_I6088V
D2488	A6085YM_T6086M	L6079A_W6081I_I6088V
D2489	A6085YW_T6086M	L6079A_W6081I_I6088V
D2490	A6085YH_T6086M	L6079A_W6081I_I6088V
D2491	A6085YF_T6086W	L6079A_W6081I_I6088V
D2492	A6085YY_T6086W	L6079A_W6081I_I6088V
D2493	A6085YM_T6086W	L6079A_W6081I_I6088V
D2494	A6085YW_T6086W	L6079A_W6081I_I6088V
D2495	A6085YH_T6086W	L6079A_W6081I_I6088V
D2496	A6085YF_T6086H	L6079A_W6081I_I6088V
D2497	A6085YY_T6086H	L6079A_W6081I_I6088V
D2498	A6085YM_T6086H	L6079A_W6081I_I6088V
D2499	A6085YW_T6086H	L6079A_W6081I_I6088V
D2500	A6085YH_T6086H	L6079A_W6081I_I6088V
D2501	A6085YF_T6086Y	L6079I_W6081T_I6088V
D2502	A6085YY_T6086Y	L6079I_W6081T_I6088V

No.	CH3 Domain Mutations	
	Chain A	Chain B
D2503	A6085YM_T6086Y	L6079I_W6081T_I6088V
D2504	A6085YW_T6086Y	L6079I_W6081T_I6088V
D2505	A6085YH_T6086Y	L6079I_W6081T_I6088V
D2506	A6085YF_T6086F	L6079I_W6081T_I6088V
D2507	A6085YY_T6086F	L6079I_W6081T_I6088V
D2508	A6085YM_T6086F	L6079I_W6081T_I6088V
D2509	A6085YW_T6086F	L6079I_W6081T_I6088V
D2510	A6085YH_T6086F	L6079I_W6081T_I6088V
D2511	A6085YF_T6086M	L6079I_W6081T_I6088V
D2512	A6085YY_T6086M	L6079I_W6081T_I6088V
D2513	A6085YM_T6086M	L6079I_W6081T_I6088V
D2514	A6085YW_T6086M	L6079I_W6081T_I6088V
D2515	A6085YH_T6086M	L6079I_W6081T_I6088V
D2516	A6085YF_T6086W	L6079I_W6081T_I6088V
D2517	A6085YY_T6086W	L6079I_W6081T_I6088V
D2518	A6085YM_T6086W	L6079I_W6081T_I6088V
D2519	A6085YW_T6086W	L6079I_W6081T_I6088V
D2520	A6085YH_T6086W	L6079I_W6081T_I6088V
D2521	A6085YF_T6086H	L6079I_W6081T_I6088V
D2522	A6085YY_T6086H	L6079I_W6081T_I6088V
D2523	A6085YM_T6086H	L6079I_W6081T_I6088V
D2524	A6085YW_T6086H	L6079I_W6081T_I6088V
D2525	A6085YH_T6086H	L6079I_W6081T_I6088V
D2526	A6085YF_T6086Y	L6079I_W6081L_I6088V
D2527	A6085YY_T6086Y	L6079I_W6081L_I6088V
D2528	A6085YM_T6086Y	L6079I_W6081L_I6088V
D2529	A6085YW_T6086Y	L6079I_W6081L_I6088V
D2530	A6085YH_T6086Y	L6079I_W6081L_I6088V
D2531	A6085YF_T6086F	L6079I_W6081L_I6088V

No.	CH3 Domain Mutations	
	Chain A	Chain B
D2532	A6085YY_T6086F	L6079I_W6081L_I6088V
D2533	A6085YM_T6086F	L6079I_W6081L_I6088V
D2534	A6085YW_T6086F	L6079I_W6081L_I6088V
D2535	A6085YH_T6086F	L6079I_W6081L_I6088V
D2536	A6085YF_T6086M	L6079I_W6081L_I6088V
D2537	A6085YY_T6086M	L6079I_W6081L_I6088V
D2538	A6085YM_T6086M	L6079I_W6081L_I6088V
D2539	A6085YW_T6086M	L6079I_W6081L_I6088V
D2540	A6085YH_T6086M	L6079I_W6081L_I6088V
D2541	A6085YF_T6086W	L6079I_W6081L_I6088V
D2542	A6085YY_T6086W	L6079I_W6081L_I6088V
D2543	A6085YM_T6086W	L6079I_W6081L_I6088V
D2544	A6085YW_T6086W	L6079I_W6081L_I6088V
D2545	A6085YH_T6086W	L6079I_W6081L_I6088V
D2546	A6085YF_T6086H	L6079I_W6081L_I6088V
D2547	A6085YY_T6086H	L6079I_W6081L_I6088V
D2548	A6085YM_T6086H	L6079I_W6081L_I6088V
D2549	A6085YW_T6086H	L6079I_W6081L_I6088V
D2550	A6085YH_T6086H	L6079I_W6081L_I6088V
D2551	A6085YF_T6086Y	L6079I_W6081A_I6088V
D2552	A6085YY_T6086Y	L6079I_W6081A_I6088V
D2553	A6085YM_T6086Y	L6079I_W6081A_I6088V
D2554	A6085YW_T6086Y	L6079I_W6081A_I6088V
D2555	A6085YH_T6086Y	L6079I_W6081A_I6088V
D2556	A6085YF_T6086F	L6079I_W6081A_I6088V
D2557	A6085YY_T6086F	L6079I_W6081A_I6088V
D2558	A6085YM_T6086F	L6079I_W6081A_I6088V
D2559	A6085YW_T6086F	L6079I_W6081A_I6088V
D2560	A6085YH_T6086F	L6079I_W6081A_I6088V

No.	CH3 Domain Mutations	
	Chain A	Chain B
D2561	A6085YF_T6086M	L6079I_W6081A_I6088V
D2562	A6085YY_T6086M	L6079I_W6081A_I6088V
D2563	A6085YM_T6086M	L6079I_W6081A_I6088V
D2564	A6085YW_T6086M	L6079I_W6081A_I6088V
D2565	A6085YH_T6086M	L6079I_W6081A_I6088V
D2566	A6085YF_T6086W	L6079I_W6081A_I6088V
D2567	A6085YY_T6086W	L6079I_W6081A_I6088V
D2568	A6085YM_T6086W	L6079I_W6081A_I6088V
D2569	A6085YW_T6086W	L6079I_W6081A_I6088V
D2570	A6085YH_T6086W	L6079I_W6081A_I6088V
D2571	A6085YF_T6086H	L6079I_W6081A_I6088V
D2572	A6085YY_T6086H	L6079I_W6081A_I6088V
D2573	A6085YM_T6086H	L6079I_W6081A_I6088V
D2574	A6085YW_T6086H	L6079I_W6081A_I6088V
D2575	A6085YH_T6086H	L6079I_W6081A_I6088V
D2576	A6085YF_T6086Y	L6079I_W6081V_I6088V
D2577	A6085YY_T6086Y	L6079I_W6081V_I6088V
D2578	A6085YM_T6086Y	L6079I_W6081V_I6088V
D2579	A6085YW_T6086Y	L6079I_W6081V_I6088V
D2580	A6085YH_T6086Y	L6079I_W6081V_I6088V
D2581	A6085YF_T6086F	L6079I_W6081V_I6088V
D2582	A6085YY_T6086F	L6079I_W6081V_I6088V
D2583	A6085YM_T6086F	L6079I_W6081V_I6088V
D2584	A6085YW_T6086F	L6079I_W6081V_I6088V
D2585	A6085YH_T6086F	L6079I_W6081V_I6088V
D2586	A6085YF_T6086M	L6079I_W6081V_I6088V
D2587	A6085YY_T6086M	L6079I_W6081V_I6088V
D2588	A6085YM_T6086M	L6079I_W6081V_I6088V
D2589	A6085YW_T6086M	L6079I_W6081V_I6088V

No.	CH3 Domain Mutations	
	Chain A	Chain B
D2590	A6085YH_T6086M	L6079I_W6081V_I6088V
D2591	A6085YF_T6086W	L6079I_W6081V_I6088V
D2592	A6085YY_T6086W	L6079I_W6081V_I6088V
D2593	A6085YM_T6086W	L6079I_W6081V_I6088V
D2594	A6085YW_T6086W	L6079I_W6081V_I6088V
D2595	A6085YH_T6086W	L6079I_W6081V_I6088V
D2596	A6085YF_T6086H	L6079I_W6081V_I6088V
D2597	A6085YY_T6086H	L6079I_W6081V_I6088V
D2598	A6085YM_T6086H	L6079I_W6081V_I6088V
D2599	A6085YW_T6086H	L6079I_W6081V_I6088V
D2600	A6085YH_T6086H	L6079I_W6081V_I6088V
D2601	A6085YF_T6086Y	L6079I_W6081I_I6088V
D2602	A6085YY_T6086Y	L6079I_W6081I_I6088V
D2603	A6085YM_T6086Y	L6079I_W6081I_I6088V
D2604	A6085YW_T6086Y	L6079I_W6081I_I6088V
D2605	A6085YH_T6086Y	L6079I_W6081I_I6088V
D2606	A6085YF_T6086F	L6079I_W6081I_I6088V
D2607	A6085YY_T6086F	L6079I_W6081I_I6088V
D2608	A6085YM_T6086F	L6079I_W6081I_I6088V
D2609	A6085YW_T6086F	L6079I_W6081I_I6088V
D2610	A6085YH_T6086F	L6079I_W6081I_I6088V
D2611	A6085YF_T6086M	L6079I_W6081I_I6088V
D2612	A6085YY_T6086M	L6079I_W6081I_I6088V
D2613	A6085YM_T6086M	L6079I_W6081I_I6088V
D2614	A6085YW_T6086M	L6079I_W6081I_I6088V
D2615	A6085YH_T6086M	L6079I_W6081I_I6088V
D2616	A6085YF_T6086W	L6079I_W6081I_I6088V
D2617	A6085YY_T6086W	L6079I_W6081I_I6088V
D2618	A6085YM_T6086W	L6079I_W6081I_I6088V

No.	CH3 Domain Mutations	
	Chain A	Chain B
D2619	A6085YW_T6086W	L6079I_W6081I_I6088V
D2620	A6085YH_T6086W	L6079I_W6081I_I6088V
D2621	A6085YF_T6086H	L6079I_W6081I_I6088V
D2622	A6085YY_T6086H	L6079I_W6081I_I6088V
D2623	A6085YM_T6086H	L6079I_W6081I_I6088V
D2624	A6085YW_T6086H	L6079I_W6081I_I6088V
D2625	A6085YH_T6086H	L6079I_W6081I_I6088V
D2626	A6085YF_T6086Y	L6079V_W6081T_I6088T
D2627	A6085YY_T6086Y	L6079V_W6081T_I6088T
D2628	A6085YM_T6086Y	L6079V_W6081T_I6088T
D2629	A6085YW_T6086Y	L6079V_W6081T_I6088T
D2630	A6085YH_T6086Y	L6079V_W6081T_I6088T
D2631	A6085YF_T6086F	L6079V_W6081T_I6088T
D2632	A6085YY_T6086F	L6079V_W6081T_I6088T
D2633	A6085YM_T6086F	L6079V_W6081T_I6088T
D2634	A6085YW_T6086F	L6079V_W6081T_I6088T
D2635	A6085YH_T6086F	L6079V_W6081T_I6088T
D2636	A6085YF_T6086M	L6079V_W6081T_I6088T
D2637	A6085YY_T6086M	L6079V_W6081T_I6088T
D2638	A6085YM_T6086M	L6079V_W6081T_I6088T
D2639	A6085YW_T6086M	L6079V_W6081T_I6088T
D2640	A6085YH_T6086M	L6079V_W6081T_I6088T
D2641	A6085YF_T6086W	L6079V_W6081T_I6088T
D2642	A6085YY_T6086W	L6079V_W6081T_I6088T
D2643	A6085YM_T6086W	L6079V_W6081T_I6088T
D2644	A6085YW_T6086W	L6079V_W6081T_I6088T
D2645	A6085YH_T6086W	L6079V_W6081T_I6088T
D2646	A6085YF_T6086H	L6079V_W6081T_I6088T
D2647	A6085YY_T6086H	L6079V_W6081T_I6088T

No.	CH3 Domain Mutations	
	Chain A	Chain B
D2648	A6085YM_T6086H	L6079V_W6081T_I6088T
D2649	A6085YW_T6086H	L6079V_W6081T_I6088T
D2650	A6085YH_T6086H	L6079V_W6081T_I6088T
D2651	A6085YF_T6086Y	L6079V_W6081L_I6088T
D2652	A6085YY_T6086Y	L6079V_W6081L_I6088T
D2653	A6085YM_T6086Y	L6079V_W6081L_I6088T
D2654	A6085YW_T6086Y	L6079V_W6081L_I6088T
D2655	A6085YH_T6086Y	L6079V_W6081L_I6088T
D2656	A6085YF_T6086F	L6079V_W6081L_I6088T
D2657	A6085YY_T6086F	L6079V_W6081L_I6088T
D2658	A6085YM_T6086F	L6079V_W6081L_I6088T
D2659	A6085YW_T6086F	L6079V_W6081L_I6088T
D2660	A6085YH_T6086F	L6079V_W6081L_I6088T
D2661	A6085YF_T6086M	L6079V_W6081L_I6088T
D2662	A6085YY_T6086M	L6079V_W6081L_I6088T
D2663	A6085YM_T6086M	L6079V_W6081L_I6088T
D2664	A6085YW_T6086M	L6079V_W6081L_I6088T
D2665	A6085YH_T6086M	L6079V_W6081L_I6088T
D2666	A6085YF_T6086W	L6079V_W6081L_I6088T
D2667	A6085YY_T6086W	L6079V_W6081L_I6088T
D2668	A6085YM_T6086W	L6079V_W6081L_I6088T
D2669	A6085YW_T6086W	L6079V_W6081L_I6088T
D2670	A6085YH_T6086W	L6079V_W6081L_I6088T
D2671	A6085YF_T6086H	L6079V_W6081L_I6088T
D2672	A6085YY_T6086H	L6079V_W6081L_I6088T
D2673	A6085YM_T6086H	L6079V_W6081L_I6088T
D2674	A6085YW_T6086H	L6079V_W6081L_I6088T
D2675	A6085YH_T6086H	L6079V_W6081L_I6088T
D2676	A6085YF_T6086Y	L6079V_W6081A_I6088T

No.	CH3 Domain Mutations	
	Chain A	Chain B
D2677	A6085YY_T6086Y	L6079V_W6081A_I6088T
D2678	A6085YM_T6086Y	L6079V_W6081A_I6088T
D2679	A6085YW_T6086Y	L6079V_W6081A_I6088T
D2680	A6085YH_T6086Y	L6079V_W6081A_I6088T
D2681	A6085YF_T6086F	L6079V_W6081A_I6088T
D2682	A6085YY_T6086F	L6079V_W6081A_I6088T
D2683	A6085YM_T6086F	L6079V_W6081A_I6088T
D2684	A6085YW_T6086F	L6079V_W6081A_I6088T
D2685	A6085YH_T6086F	L6079V_W6081A_I6088T
D2686	A6085YF_T6086M	L6079V_W6081A_I6088T
D2687	A6085YY_T6086M	L6079V_W6081A_I6088T
D2688	A6085YM_T6086M	L6079V_W6081A_I6088T
D2689	A6085YW_T6086M	L6079V_W6081A_I6088T
D2690	A6085YH_T6086M	L6079V_W6081A_I6088T
D2691	A6085YF_T6086W	L6079V_W6081A_I6088T
D2692	A6085YY_T6086W	L6079V_W6081A_I6088T
D2693	A6085YM_T6086W	L6079V_W6081A_I6088T
D2694	A6085YW_T6086W	L6079V_W6081A_I6088T
D2695	A6085YH_T6086W	L6079V_W6081A_I6088T
D2696	A6085YF_T6086H	L6079V_W6081A_I6088T
D2697	A6085YY_T6086H	L6079V_W6081A_I6088T
D2698	A6085YM_T6086H	L6079V_W6081A_I6088T
D2699	A6085YW_T6086H	L6079V_W6081A_I6088T
D2700	A6085YH_T6086H	L6079V_W6081A_I6088T
D2701	A6085YF_T6086Y	L6079V_W6081V_I6088T
D2702	A6085YY_T6086Y	L6079V_W6081V_I6088T
D2703	A6085YM_T6086Y	L6079V_W6081V_I6088T
D2704	A6085YW_T6086Y	L6079V_W6081V_I6088T
D2705	A6085YH_T6086Y	L6079V_W6081V_I6088T

No.	CH3 Domain Mutations	
	Chain A	Chain B
D2706	A6085YF_T6086F	L6079V_W6081V_I6088T
D2707	A6085YY_T6086F	L6079V_W6081V_I6088T
D2708	A6085YM_T6086F	L6079V_W6081V_I6088T
D2709	A6085YW_T6086F	L6079V_W6081V_I6088T
D2710	A6085YH_T6086F	L6079V_W6081V_I6088T
D2711	A6085YF_T6086M	L6079V_W6081V_I6088T
D2712	A6085YY_T6086M	L6079V_W6081V_I6088T
D2713	A6085YM_T6086M	L6079V_W6081V_I6088T
D2714	A6085YW_T6086M	L6079V_W6081V_I6088T
D2715	A6085YH_T6086M	L6079V_W6081V_I6088T
D2716	A6085YF_T6086W	L6079V_W6081V_I6088T
D2717	A6085YY_T6086W	L6079V_W6081V_I6088T
D2718	A6085YM_T6086W	L6079V_W6081V_I6088T
D2719	A6085YW_T6086W	L6079V_W6081V_I6088T
D2720	A6085YH_T6086W	L6079V_W6081V_I6088T
D2721	A6085YF_T6086H	L6079V_W6081V_I6088T
D2722	A6085YY_T6086H	L6079V_W6081V_I6088T
D2723	A6085YM_T6086H	L6079V_W6081V_I6088T
D2724	A6085YW_T6086H	L6079V_W6081V_I6088T
D2725	A6085YH_T6086H	L6079V_W6081V_I6088T
D2726	A6085YF_T6086Y	L6079V_W6081I_I6088T
D2727	A6085YY_T6086Y	L6079V_W6081I_I6088T
D2728	A6085YM_T6086Y	L6079V_W6081I_I6088T
D2729	A6085YW_T6086Y	L6079V_W6081I_I6088T
D2730	A6085YH_T6086Y	L6079V_W6081I_I6088T
D2731	A6085YF_T6086F	L6079V_W6081I_I6088T
D2732	A6085YY_T6086F	L6079V_W6081I_I6088T
D2733	A6085YM_T6086F	L6079V_W6081I_I6088T
D2734	A6085YW_T6086F	L6079V_W6081I_I6088T

No.	CH3 Domain Mutations	
	Chain A	Chain B
D2735	A6085YH_T6086F	L6079V_W6081I_I6088T
D2736	A6085YF_T6086M	L6079V_W6081I_I6088T
D2737	A6085YY_T6086M	L6079V_W6081I_I6088T
D2738	A6085YM_T6086M	L6079V_W6081I_I6088T
D2739	A6085YW_T6086M	L6079V_W6081I_I6088T
D2740	A6085YH_T6086M	L6079V_W6081I_I6088T
D2741	A6085YF_T6086W	L6079V_W6081I_I6088T
D2742	A6085YY_T6086W	L6079V_W6081I_I6088T
D2743	A6085YM_T6086W	L6079V_W6081I_I6088T
D2744	A6085YW_T6086W	L6079V_W6081I_I6088T
D2745	A6085YH_T6086W	L6079V_W6081I_I6088T
D2746	A6085YF_T6086H	L6079V_W6081I_I6088T
D2747	A6085YY_T6086H	L6079V_W6081I_I6088T
D2748	A6085YM_T6086H	L6079V_W6081I_I6088T
D2749	A6085YW_T6086H	L6079V_W6081I_I6088T
D2750	A6085YH_T6086H	L6079V_W6081I_I6088T
D2751	A6085YF_T6086Y	L6079T_W6081T_I6088T
D2752	A6085YY_T6086Y	L6079T_W6081T_I6088T
D2753	A6085YM_T6086Y	L6079T_W6081T_I6088T
D2754	A6085YW_T6086Y	L6079T_W6081T_I6088T
D2755	A6085YH_T6086Y	L6079T_W6081T_I6088T
D2756	A6085YF_T6086F	L6079T_W6081T_I6088T
D2757	A6085YY_T6086F	L6079T_W6081T_I6088T
D2758	A6085YM_T6086F	L6079T_W6081T_I6088T
D2759	A6085YW_T6086F	L6079T_W6081T_I6088T
D2760	A6085YH_T6086F	L6079T_W6081T_I6088T
D2761	A6085YF_T6086M	L6079T_W6081T_I6088T
D2762	A6085YY_T6086M	L6079T_W6081T_I6088T
D2763	A6085YM_T6086M	L6079T_W6081T_I6088T

No.	CH3 Domain Mutations	
	Chain A	Chain B
D2764	A6085YW_T6086M	L6079T_W6081T_I6088T
D2765	A6085YH_T6086M	L6079T_W6081T_I6088T
D2766	A6085YF_T6086W	L6079T_W6081T_I6088T
D2767	A6085YY_T6086W	L6079T_W6081T_I6088T
D2768	A6085YM_T6086W	L6079T_W6081T_I6088T
D2769	A6085YW_T6086W	L6079T_W6081T_I6088T
D2770	A6085YH_T6086W	L6079T_W6081T_I6088T
D2771	A6085YF_T6086H	L6079T_W6081T_I6088T
D2772	A6085YY_T6086H	L6079T_W6081T_I6088T
D2773	A6085YM_T6086H	L6079T_W6081T_I6088T
D2774	A6085YW_T6086H	L6079T_W6081T_I6088T
D2775	A6085YH_T6086H	L6079T_W6081T_I6088T
D2776	A6085YF_T6086Y	L6079T_W6081L_I6088T
D2777	A6085YY_T6086Y	L6079T_W6081L_I6088T
D2778	A6085YM_T6086Y	L6079T_W6081L_I6088T
D2779	A6085YW_T6086Y	L6079T_W6081L_I6088T
D2780	A6085YH_T6086Y	L6079T_W6081L_I6088T
D2781	A6085YF_T6086F	L6079T_W6081L_I6088T
D2782	A6085YY_T6086F	L6079T_W6081L_I6088T
D2783	A6085YM_T6086F	L6079T_W6081L_I6088T
D2784	A6085YW_T6086F	L6079T_W6081L_I6088T
D2785	A6085YH_T6086F	L6079T_W6081L_I6088T
D2786	A6085YF_T6086M	L6079T_W6081L_I6088T
D2787	A6085YY_T6086M	L6079T_W6081L_I6088T
D2788	A6085YM_T6086M	L6079T_W6081L_I6088T
D2789	A6085YW_T6086M	L6079T_W6081L_I6088T
D2790	A6085YH_T6086M	L6079T_W6081L_I6088T
D2791	A6085YF_T6086W	L6079T_W6081L_I6088T
D2792	A6085YY_T6086W	L6079T_W6081L_I6088T

No.	CH3 Domain Mutations	
	Chain A	Chain B
D2793	A6085YM_T6086W	L6079T_W6081L_I6088T
D2794	A6085YW_T6086W	L6079T_W6081L_I6088T
D2795	A6085YH_T6086W	L6079T_W6081L_I6088T
D2796	A6085YF_T6086H	L6079T_W6081L_I6088T
D2797	A6085YY_T6086H	L6079T_W6081L_I6088T
D2798	A6085YM_T6086H	L6079T_W6081L_I6088T
D2799	A6085YW_T6086H	L6079T_W6081L_I6088T
D2800	A6085YH_T6086H	L6079T_W6081L_I6088T
D2801	A6085YF_T6086Y	L6079T_W6081A_I6088T
D2802	A6085YY_T6086Y	L6079T_W6081A_I6088T
D2803	A6085YM_T6086Y	L6079T_W6081A_I6088T
D2804	A6085YW_T6086Y	L6079T_W6081A_I6088T
D2805	A6085YH_T6086Y	L6079T_W6081A_I6088T
D2806	A6085YF_T6086F	L6079T_W6081A_I6088T
D2807	A6085YY_T6086F	L6079T_W6081A_I6088T
D2808	A6085YM_T6086F	L6079T_W6081A_I6088T
D2809	A6085YW_T6086F	L6079T_W6081A_I6088T
D2810	A6085YH_T6086F	L6079T_W6081A_I6088T
D2811	A6085YF_T6086M	L6079T_W6081A_I6088T
D2812	A6085YY_T6086M	L6079T_W6081A_I6088T
D2813	A6085YM_T6086M	L6079T_W6081A_I6088T
D2814	A6085YW_T6086M	L6079T_W6081A_I6088T
D2815	A6085YH_T6086M	L6079T_W6081A_I6088T
D2816	A6085YF_T6086W	L6079T_W6081A_I6088T
D2817	A6085YY_T6086W	L6079T_W6081A_I6088T
D2818	A6085YM_T6086W	L6079T_W6081A_I6088T
D2819	A6085YW_T6086W	L6079T_W6081A_I6088T
D2820	A6085YH_T6086W	L6079T_W6081A_I6088T
D2821	A6085YF_T6086H	L6079T_W6081A_I6088T

No.	CH3 Domain Mutations	
	Chain A	Chain B
D2822	A6085YY_T6086H	L6079T_W6081A_I6088T
D2823	A6085YM_T6086H	L6079T_W6081A_I6088T
D2824	A6085YW_T6086H	L6079T_W6081A_I6088T
D2825	A6085YH_T6086H	L6079T_W6081A_I6088T
D2826	A6085YF_T6086Y	L6079T_W6081V_I6088T
D2827	A6085YY_T6086Y	L6079T_W6081V_I6088T
D2828	A6085YM_T6086Y	L6079T_W6081V_I6088T
D2829	A6085YW_T6086Y	L6079T_W6081V_I6088T
D2830	A6085YH_T6086Y	L6079T_W6081V_I6088T
D2831	A6085YF_T6086F	L6079T_W6081V_I6088T
D2832	A6085YY_T6086F	L6079T_W6081V_I6088T
D2833	A6085YM_T6086F	L6079T_W6081V_I6088T
D2834	A6085YW_T6086F	L6079T_W6081V_I6088T
D2835	A6085YH_T6086F	L6079T_W6081V_I6088T
D2836	A6085YF_T6086M	L6079T_W6081V_I6088T
D2837	A6085YY_T6086M	L6079T_W6081V_I6088T
D2838	A6085YM_T6086M	L6079T_W6081V_I6088T
D2839	A6085YW_T6086M	L6079T_W6081V_I6088T
D2840	A6085YH_T6086M	L6079T_W6081V_I6088T
D2841	A6085YF_T6086W	L6079T_W6081V_I6088T
D2842	A6085YY_T6086W	L6079T_W6081V_I6088T
D2843	A6085YM_T6086W	L6079T_W6081V_I6088T
D2844	A6085YW_T6086W	L6079T_W6081V_I6088T
D2845	A6085YH_T6086W	L6079T_W6081V_I6088T
D2846	A6085YF_T6086H	L6079T_W6081V_I6088T
D2847	A6085YY_T6086H	L6079T_W6081V_I6088T
D2848	A6085YM_T6086H	L6079T_W6081V_I6088T
D2849	A6085YW_T6086H	L6079T_W6081V_I6088T
D2850	A6085YH_T6086H	L6079T_W6081V_I6088T

No.	CH3 Domain Mutations	
	Chain A	Chain B
D2851	A6085YF_T6086Y	L6079T_W6081I_I6088T
D2852	A6085YY_T6086Y	L6079T_W6081I_I6088T
D2853	A6085YM_T6086Y	L6079T_W6081I_I6088T
D2854	A6085YW_T6086Y	L6079T_W6081I_I6088T
D2855	A6085YH_T6086Y	L6079T_W6081I_I6088T
D2856	A6085YF_T6086F	L6079T_W6081I_I6088T
D2857	A6085YY_T6086F	L6079T_W6081I_I6088T
D2858	A6085YM_T6086F	L6079T_W6081I_I6088T
D2859	A6085YW_T6086F	L6079T_W6081I_I6088T
D2860	A6085YH_T6086F	L6079T_W6081I_I6088T
D2861	A6085YF_T6086M	L6079T_W6081I_I6088T
D2862	A6085YY_T6086M	L6079T_W6081I_I6088T
D2863	A6085YM_T6086M	L6079T_W6081I_I6088T
D2864	A6085YW_T6086M	L6079T_W6081I_I6088T
D2865	A6085YH_T6086M	L6079T_W6081I_I6088T
D2866	A6085YF_T6086W	L6079T_W6081I_I6088T
D2867	A6085YY_T6086W	L6079T_W6081I_I6088T
D2868	A6085YM_T6086W	L6079T_W6081I_I6088T
D2869	A6085YW_T6086W	L6079T_W6081I_I6088T
D2870	A6085YH_T6086W	L6079T_W6081I_I6088T
D2871	A6085YF_T6086H	L6079T_W6081I_I6088T
D2872	A6085YY_T6086H	L6079T_W6081I_I6088T
D2873	A6085YM_T6086H	L6079T_W6081I_I6088T
D2874	A6085YW_T6086H	L6079T_W6081I_I6088T
D2875	A6085YH_T6086H	L6079T_W6081I_I6088T
D2876	A6085YF_T6086Y	L6079A_W6081T_I6088T
D2877	A6085YY_T6086Y	L6079A_W6081T_I6088T
D2878	A6085YM_T6086Y	L6079A_W6081T_I6088T
D2879	A6085YW_T6086Y	L6079A_W6081T_I6088T

No.	CH3 Domain Mutations	
	Chain A	Chain B
D2880	A6085YH_T6086Y	L6079A_W6081T_I6088T
D2881	A6085YF_T6086F	L6079A_W6081T_I6088T
D2882	A6085YY_T6086F	L6079A_W6081T_I6088T
D2883	A6085YM_T6086F	L6079A_W6081T_I6088T
D2884	A6085YW_T6086F	L6079A_W6081T_I6088T
D2885	A6085YH_T6086F	L6079A_W6081T_I6088T
D2886	A6085YF_T6086M	L6079A_W6081T_I6088T
D2887	A6085YY_T6086M	L6079A_W6081T_I6088T
D2888	A6085YM_T6086M	L6079A_W6081T_I6088T
D2889	A6085YW_T6086M	L6079A_W6081T_I6088T
D2890	A6085YH_T6086M	L6079A_W6081T_I6088T
D2891	A6085YF_T6086W	L6079A_W6081T_I6088T
D2892	A6085YY_T6086W	L6079A_W6081T_I6088T
D2893	A6085YM_T6086W	L6079A_W6081T_I6088T
D2894	A6085YW_T6086W	L6079A_W6081T_I6088T
D2895	A6085YH_T6086W	L6079A_W6081T_I6088T
D2896	A6085YF_T6086H	L6079A_W6081T_I6088T
D2897	A6085YY_T6086H	L6079A_W6081T_I6088T
D2898	A6085YM_T6086H	L6079A_W6081T_I6088T
D2899	A6085YW_T6086H	L6079A_W6081T_I6088T
D2900	A6085YH_T6086H	L6079A_W6081T_I6088T
D2901	A6085YF_T6086Y	L6079A_W6081L_I6088T
D2902	A6085YY_T6086Y	L6079A_W6081L_I6088T
D2903	A6085YM_T6086Y	L6079A_W6081L_I6088T
D2904	A6085YW_T6086Y	L6079A_W6081L_I6088T
D2905	A6085YH_T6086Y	L6079A_W6081L_I6088T
D2906	A6085YF_T6086F	L6079A_W6081L_I6088T
D2907	A6085YY_T6086F	L6079A_W6081L_I6088T
D2908	A6085YM_T6086F	L6079A_W6081L_I6088T

No.	CH3 Domain Mutations	
	Chain A	Chain B
D2909	A6085YW_T6086F	L6079A_W6081L_I6088T
D2910	A6085YH_T6086F	L6079A_W6081L_I6088T
D2911	A6085YF_T6086M	L6079A_W6081L_I6088T
D2912	A6085YY_T6086M	L6079A_W6081L_I6088T
D2913	A6085YM_T6086M	L6079A_W6081L_I6088T
D2914	A6085YW_T6086M	L6079A_W6081L_I6088T
D2915	A6085YH_T6086M	L6079A_W6081L_I6088T
D2916	A6085YF_T6086W	L6079A_W6081L_I6088T
D2917	A6085YY_T6086W	L6079A_W6081L_I6088T
D2918	A6085YM_T6086W	L6079A_W6081L_I6088T
D2919	A6085YW_T6086W	L6079A_W6081L_I6088T
D2920	A6085YH_T6086W	L6079A_W6081L_I6088T
D2921	A6085YF_T6086H	L6079A_W6081L_I6088T
D2922	A6085YY_T6086H	L6079A_W6081L_I6088T
D2923	A6085YM_T6086H	L6079A_W6081L_I6088T
D2924	A6085YW_T6086H	L6079A_W6081L_I6088T
D2925	A6085YH_T6086H	L6079A_W6081L_I6088T
D2926	A6085YF_T6086Y	L6079A_W6081A_I6088T
D2927	A6085YY_T6086Y	L6079A_W6081A_I6088T
D2928	A6085YM_T6086Y	L6079A_W6081A_I6088T
D2929	A6085YW_T6086Y	L6079A_W6081A_I6088T
D2930	A6085YH_T6086Y	L6079A_W6081A_I6088T
D2931	A6085YF_T6086F	L6079A_W6081A_I6088T
D2932	A6085YY_T6086F	L6079A_W6081A_I6088T
D2933	A6085YM_T6086F	L6079A_W6081A_I6088T
D2934	A6085YW_T6086F	L6079A_W6081A_I6088T
D2935	A6085YH_T6086F	L6079A_W6081A_I6088T
D2936	A6085YF_T6086M	L6079A_W6081A_I6088T
D2937	A6085YY_T6086M	L6079A_W6081A_I6088T

No.	CH3 Domain Mutations	
	Chain A	Chain B
D2938	A6085YM_T6086M	L6079A_W6081A_I6088T
D2939	A6085YW_T6086M	L6079A_W6081A_I6088T
D2940	A6085YH_T6086M	L6079A_W6081A_I6088T
D2941	A6085YF_T6086W	L6079A_W6081A_I6088T
D2942	A6085YY_T6086W	L6079A_W6081A_I6088T
D2943	A6085YM_T6086W	L6079A_W6081A_I6088T
D2944	A6085YW_T6086W	L6079A_W6081A_I6088T
D2945	A6085YH_T6086W	L6079A_W6081A_I6088T
D2946	A6085YF_T6086H	L6079A_W6081A_I6088T
D2947	A6085YY_T6086H	L6079A_W6081A_I6088T
D2948	A6085YM_T6086H	L6079A_W6081A_I6088T
D2949	A6085YW_T6086H	L6079A_W6081A_I6088T
D2950	A6085YH_T6086H	L6079A_W6081A_I6088T
D2951	A6085YF_T6086Y	L6079A_W6081V_I6088T
D2952	A6085YY_T6086Y	L6079A_W6081V_I6088T
D2953	A6085YM_T6086Y	L6079A_W6081V_I6088T
D2954	A6085YW_T6086Y	L6079A_W6081V_I6088T
D2955	A6085YH_T6086Y	L6079A_W6081V_I6088T
D2956	A6085YF_T6086F	L6079A_W6081V_I6088T
D2957	A6085YY_T6086F	L6079A_W6081V_I6088T
D2958	A6085YM_T6086F	L6079A_W6081V_I6088T
D2959	A6085YW_T6086F	L6079A_W6081V_I6088T
D2960	A6085YH_T6086F	L6079A_W6081V_I6088T
D2961	A6085YF_T6086M	L6079A_W6081V_I6088T
D2962	A6085YY_T6086M	L6079A_W6081V_I6088T
D2963	A6085YM_T6086M	L6079A_W6081V_I6088T
D2964	A6085YW_T6086M	L6079A_W6081V_I6088T
D2965	A6085YH_T6086M	L6079A_W6081V_I6088T
D2966	A6085YF_T6086W	L6079A_W6081V_I6088T

No.	CH3 Domain Mutations	
	Chain A	Chain B
D2967	A6085YY_T6086W	L6079A_W6081V_I6088T
D2968	A6085YM_T6086W	L6079A_W6081V_I6088T
D2969	A6085YW_T6086W	L6079A_W6081V_I6088T
D2970	A6085YH_T6086W	L6079A_W6081V_I6088T
D2971	A6085YF_T6086H	L6079A_W6081V_I6088T
D2972	A6085YY_T6086H	L6079A_W6081V_I6088T
D2973	A6085YM_T6086H	L6079A_W6081V_I6088T
D2974	A6085YW_T6086H	L6079A_W6081V_I6088T
D2975	A6085YH_T6086H	L6079A_W6081V_I6088T
D2976	A6085YF_T6086Y	L6079A_W6081I_I6088T
D2977	A6085YY_T6086Y	L6079A_W6081I_I6088T
D2978	A6085YM_T6086Y	L6079A_W6081I_I6088T
D2979	A6085YW_T6086Y	L6079A_W6081I_I6088T
D2980	A6085YH_T6086Y	L6079A_W6081I_I6088T
D2981	A6085YF_T6086F	L6079A_W6081I_I6088T
D2982	A6085YY_T6086F	L6079A_W6081I_I6088T
D2983	A6085YM_T6086F	L6079A_W6081I_I6088T
D2984	A6085YW_T6086F	L6079A_W6081I_I6088T
D2985	A6085YH_T6086F	L6079A_W6081I_I6088T
D2986	A6085YF_T6086M	L6079A_W6081I_I6088T
D2987	A6085YY_T6086M	L6079A_W6081I_I6088T
D2988	A6085YM_T6086M	L6079A_W6081I_I6088T
D2989	A6085YW_T6086M	L6079A_W6081I_I6088T
D2990	A6085YH_T6086M	L6079A_W6081I_I6088T
D2991	A6085YF_T6086W	L6079A_W6081I_I6088T
D2992	A6085YY_T6086W	L6079A_W6081I_I6088T
D2993	A6085YM_T6086W	L6079A_W6081I_I6088T
D2994	A6085YW_T6086W	L6079A_W6081I_I6088T
D2995	A6085YH_T6086W	L6079A_W6081I_I6088T

No.	CH3 Domain Mutations	
	Chain A	Chain B
D2996	A6085YF_T6086H	L6079A_W6081I_I6088T
D2997	A6085YY_T6086H	L6079A_W6081I_I6088T
D2998	A6085YM_T6086H	L6079A_W6081I_I6088T
D2999	A6085YW_T6086H	L6079A_W6081I_I6088T
D3000	A6085YH_T6086H	L6079A_W6081I_I6088T
D3001	A6085YF_T6086Y	L6079I_W6081T_I6088T
D3002	A6085YY_T6086Y	L6079I_W6081T_I6088T
D3003	A6085YM_T6086Y	L6079I_W6081T_I6088T
D3004	A6085YW_T6086Y	L6079I_W6081T_I6088T
D3005	A6085YH_T6086Y	L6079I_W6081T_I6088T
D3006	A6085YF_T6086F	L6079I_W6081T_I6088T
D3007	A6085YY_T6086F	L6079I_W6081T_I6088T
D3008	A6085YM_T6086F	L6079I_W6081T_I6088T
D3009	A6085YW_T6086F	L6079I_W6081T_I6088T
D3010	A6085YH_T6086F	L6079I_W6081T_I6088T
D3011	A6085YF_T6086M	L6079I_W6081T_I6088T
D3012	A6085YY_T6086M	L6079I_W6081T_I6088T
D3013	A6085YM_T6086M	L6079I_W6081T_I6088T
D3014	A6085YW_T6086M	L6079I_W6081T_I6088T
D3015	A6085YH_T6086M	L6079I_W6081T_I6088T
D3016	A6085YF_T6086W	L6079I_W6081T_I6088T
D3017	A6085YY_T6086W	L6079I_W6081T_I6088T
D3018	A6085YM_T6086W	L6079I_W6081T_I6088T
D3019	A6085YW_T6086W	L6079I_W6081T_I6088T
D3020	A6085YH_T6086W	L6079I_W6081T_I6088T
D3021	A6085YF_T6086H	L6079I_W6081T_I6088T
D3022	A6085YY_T6086H	L6079I_W6081T_I6088T
D3023	A6085YM_T6086H	L6079I_W6081T_I6088T
D3024	A6085YW_T6086H	L6079I_W6081T_I6088T

No.	CH3 Domain Mutations	
	Chain A	Chain B
D3025	A6085YH_T6086H	L6079I_W6081T_I6088T
D3026	A6085YF_T6086Y	L6079I_W6081L_I6088T
D3027	A6085YY_T6086Y	L6079I_W6081L_I6088T
D3028	A6085YM_T6086Y	L6079I_W6081L_I6088T
D3029	A6085YW_T6086Y	L6079I_W6081L_I6088T
D3030	A6085YH_T6086Y	L6079I_W6081L_I6088T
D3031	A6085YF_T6086F	L6079I_W6081L_I6088T
D3032	A6085YY_T6086F	L6079I_W6081L_I6088T
D3033	A6085YM_T6086F	L6079I_W6081L_I6088T
D3034	A6085YW_T6086F	L6079I_W6081L_I6088T
D3035	A6085YH_T6086F	L6079I_W6081L_I6088T
D3036	A6085YF_T6086M	L6079I_W6081L_I6088T
D3037	A6085YY_T6086M	L6079I_W6081L_I6088T
D3038	A6085YM_T6086M	L6079I_W6081L_I6088T
D3039	A6085YW_T6086M	L6079I_W6081L_I6088T
D3040	A6085YH_T6086M	L6079I_W6081L_I6088T
D3041	A6085YF_T6086W	L6079I_W6081L_I6088T
D3042	A6085YY_T6086W	L6079I_W6081L_I6088T
D3043	A6085YM_T6086W	L6079I_W6081L_I6088T
D3044	A6085YW_T6086W	L6079I_W6081L_I6088T
D3045	A6085YH_T6086W	L6079I_W6081L_I6088T
D3046	A6085YF_T6086H	L6079I_W6081L_I6088T
D3047	A6085YY_T6086H	L6079I_W6081L_I6088T
D3048	A6085YM_T6086H	L6079I_W6081L_I6088T
D3049	A6085YW_T6086H	L6079I_W6081L_I6088T
D3050	A6085YH_T6086H	L6079I_W6081L_I6088T
D3051	A6085YF_T6086Y	L6079I_W6081A_I6088T
D3052	A6085YY_T6086Y	L6079I_W6081A_I6088T
D3053	A6085YM_T6086Y	L6079I_W6081A_I6088T

No.	CH3 Domain Mutations	
	Chain A	Chain B
D3054	A6085YW_T6086Y	L6079I_W6081A_I6088T
D3055	A6085YH_T6086Y	L6079I_W6081A_I6088T
D3056	A6085YF_T6086F	L6079I_W6081A_I6088T
D3057	A6085YY_T6086F	L6079I_W6081A_I6088T
D3058	A6085YM_T6086F	L6079I_W6081A_I6088T
D3059	A6085YW_T6086F	L6079I_W6081A_I6088T
D3060	A6085YH_T6086F	L6079I_W6081A_I6088T
D3061	A6085YF_T6086M	L6079I_W6081A_I6088T
D3062	A6085YY_T6086M	L6079I_W6081A_I6088T
D3063	A6085YM_T6086M	L6079I_W6081A_I6088T
D3064	A6085YW_T6086M	L6079I_W6081A_I6088T
D3065	A6085YH_T6086M	L6079I_W6081A_I6088T
D3066	A6085YF_T6086W	L6079I_W6081A_I6088T
D3067	A6085YY_T6086W	L6079I_W6081A_I6088T
D3068	A6085YM_T6086W	L6079I_W6081A_I6088T
D3069	A6085YW_T6086W	L6079I_W6081A_I6088T
D3070	A6085YH_T6086W	L6079I_W6081A_I6088T
D3071	A6085YF_T6086H	L6079I_W6081A_I6088T
D3072	A6085YY_T6086H	L6079I_W6081A_I6088T
D3073	A6085YM_T6086H	L6079I_W6081A_I6088T
D3074	A6085YW_T6086H	L6079I_W6081A_I6088T
D3075	A6085YH_T6086H	L6079I_W6081A_I6088T
D3076	A6085YF_T6086Y	L6079I_W6081V_I6088T
D3077	A6085YY_T6086Y	L6079I_W6081V_I6088T
D3078	A6085YM_T6086Y	L6079I_W6081V_I6088T
D3079	A6085YW_T6086Y	L6079I_W6081V_I6088T
D3080	A6085YH_T6086Y	L6079I_W6081V_I6088T
D3081	A6085YF_T6086F	L6079I_W6081V_I6088T
D3082	A6085YY_T6086F	L6079I_W6081V_I6088T

No.	CH3 Domain Mutations	
	Chain A	Chain B
D3083	A6085YM_T6086F	L6079I_W6081V_I6088T
D3084	A6085YW_T6086F	L6079I_W6081V_I6088T
D3085	A6085YH_T6086F	L6079I_W6081V_I6088T
D3086	A6085YF_T6086M	L6079I_W6081V_I6088T
D3087	A6085YY_T6086M	L6079I_W6081V_I6088T
D3088	A6085YM_T6086M	L6079I_W6081V_I6088T
D3089	A6085YW_T6086M	L6079I_W6081V_I6088T
D3090	A6085YH_T6086M	L6079I_W6081V_I6088T
D3091	A6085YF_T6086W	L6079I_W6081V_I6088T
D3092	A6085YY_T6086W	L6079I_W6081V_I6088T
D3093	A6085YM_T6086W	L6079I_W6081V_I6088T
D3094	A6085YW_T6086W	L6079I_W6081V_I6088T
D3095	A6085YH_T6086W	L6079I_W6081V_I6088T
D3096	A6085YF_T6086H	L6079I_W6081V_I6088T
D3097	A6085YY_T6086H	L6079I_W6081V_I6088T
D3098	A6085YM_T6086H	L6079I_W6081V_I6088T
D3099	A6085YW_T6086H	L6079I_W6081V_I6088T
D3100	A6085YH_T6086H	L6079I_W6081V_I6088T
D3101	A6085YF_T6086Y	L6079I_W6081I_I6088T
D3102	A6085YY_T6086Y	L6079I_W6081I_I6088T
D3103	A6085YM_T6086Y	L6079I_W6081I_I6088T
D3104	A6085YW_T6086Y	L6079I_W6081I_I6088T
D3105	A6085YH_T6086Y	L6079I_W6081I_I6088T
D3106	A6085YF_T6086F	L6079I_W6081I_I6088T
D3107	A6085YY_T6086F	L6079I_W6081I_I6088T
D3108	A6085YM_T6086F	L6079I_W6081I_I6088T
D3109	A6085YW_T6086F	L6079I_W6081I_I6088T
D3110	A6085YH_T6086F	L6079I_W6081I_I6088T
D3111	A6085YF_T6086M	L6079I_W6081I_I6088T

No.	CH3 Domain Mutations	
	Chain A	Chain B
D3112	A6085YY_T6086M	L6079I_W6081I_I6088T
D3113	A6085YM_T6086M	L6079I_W6081I_I6088T
D3114	A6085YW_T6086M	L6079I_W6081I_I6088T
D3115	A6085YH_T6086M	L6079I_W6081I_I6088T
D3116	A6085YF_T6086W	L6079I_W6081I_I6088T
D3117	A6085YY_T6086W	L6079I_W6081I_I6088T
D3118	A6085YM_T6086W	L6079I_W6081I_I6088T
D3119	A6085YW_T6086W	L6079I_W6081I_I6088T
D3120	A6085YH_T6086W	L6079I_W6081I_I6088T
D3121	A6085YF_T6086H	L6079I_W6081I_I6088T
D3122	A6085YY_T6086H	L6079I_W6081I_I6088T
D3123	A6085YM_T6086H	L6079I_W6081I_I6088T
D3124	A6085YW_T6086H	L6079I_W6081I_I6088T
D3125	A6085YH_T6086H	L6079I_W6081I_I6088T

EXAMPLES

EXAMPLE 1: IN SILICO SELECTION OF LEAD IGA HETERODIMER DESIGNS

This example describes the *in silico* analysis and selection of potential IgA Fc Cα3 (CH3) mutations to drive heterodimerization over homodimerization of IgA Fc dimers.

Methods

In an extensive structural analysis of the CH3:CH3 interface of the IgA Fc (PDB ID: 2QEJ, Ramsland *et al.*, 2007, *Proc Natl Acad Sci USA* 104:15051-15056), residues in the interface were characterized according to their energetic contribution to dimerization. For this, proprietary tools for analysis of connectivity as well as energetics of the structure based on knowledge-based and physics-based potentials were used on a static structure as well as a 50 ns explicit molecular dynamics trajectory. Guided by results from this initial analysis and in a first “negative design” round, residues were selected for the introduction of mutations predicted to be disruptive to

dimerization. These mutations were chosen based on two main design concepts illustrated in Fig. 1. Negative electrostatic designs relied on the introduction of same-charge pairs and the associated repulsion across the interface while negative steric designs were based on the introduction of cavities or steric clashes in the interface. These negative designs were modelled and evaluated energetically using proprietary *in silico* tools. In a second “positive design” step, additional mutations were introduced with the goal of rescuing heterodimerization. The stabilization of the heterodimeric complex was either based on introduction of salt bridges via opposing charges across the interface or the accommodation of residues with large side chains by cavities on the opposite side of the interface. Designs with the largest energetic differences between homodimers and heterodimers were selected to be expressed and evaluated.

Results

The mutations of the lead designs based on the analyzed metrics are shown in Table 11. A select set of *in silico* metrics for models of homodimeric and heterodimeric lead designs are shown in Table 12. Energies are with respect to wild-type. Negative energies indicate a favourable interaction, positive energies indicate a disfavoured interaction.

Notably, the steric designs with the largest energetic differences between homo- and heterodimer were centered around mutations to large hydrophobic side chains at positions A6085Y and T6086 in Chain A and a swap of W6081 for a small residue on the opposing Chain B. An example of a lead design (Steric 6) is shown in Fig. 9 where large hydrophobic residues were introduced at positions 6085Y and 6086 in Chain A, while a cavity was created by swap of W6081 for threonine in Chain B. While Steric 6 includes two additional Chain B mutations, it is the substitution of tryptophan at position 6081 for a residue with a smaller side chain that is responsible for creating the cavity that accommodates the large hydrophobic residues introduced at positions 6085Y and 6086 in Chain A. Together these three mutations are considered to produce the predominant steric design favouring heterodimer formation. As such, mutations at these three positions (A: 6085Y & 6086, B:6081) are considered to constitute a minimal core set of mutations to promote IgA Fc heterodimer formation. Specifically, the core set of mutations is: substitution of each of A6085Y and T6086 in Chain A with residues containing larger and/or more hydrophobic side chains combined with substitution of W6081 in Chain B with a residue having a smaller side chain. Larger and/or more hydrophobic residues that are predicted by *in silico* analysis to be

suitable for introduction at positions 6085Y and 6086 include F, Y, M, W and H, and smaller residues predicted by *in silico* analysis to be suitable for introduction at position 6081 include T, L, A, V and I.

Table 11: Mutations in Lead Designs

Variant	Design	Chain A Mutations	Chain B Mutations
Electrostatic Designs			
32510	Electrost. 1	T6020D_L6024D_R6026D_I6088E	T6020R_L6024R
32511	Electrost. 2	T6020E_L6024E_R6026D_I6088D_R6090E	T6020R_L6024K
32512	Electrost. 3	T6020E_R6026D_I6088D_R6090D	T6020R_L6024K_I6088R
32513	Electrost. 4	T6020E_R6026D_I6088E_R6090E	T6020K_L6024K_R6026K_I6088R
32514	Electrost. 5	R6026D_E6084BD_I6088D_R6090E	L6024K_R6026K_E6084BR_I6088K
32515	Electrost. 6	R6026D_E6084BD_I6088D_R6090E	L6024K_R6026K_I6088K
Steric Designs			
32516	Steric 1	A6085YY_T6086L	L6079T_W6081L_I6088L
32517	Steric 2	A6085YY_T6086Y	L6079T_W6081L_I6088L
32518	Steric 3	A6085YF_T6086Y	L6079V_W6081L_I6088L
32519	Steric 4	L6024M_A6085YF_T6086W	W6081L
32520	Steric 5	A6085YY_T6086M	L6079V_W6081L_I6088L
32521	Steric 6	A6085YF_T6086Y	L6079V_W6081T_I6088L
33330	Steric 7	T6022V_A6085YF_T6086Y	L6079V_W6081T_I6088L
33331	Steric 8	T6022L_A6085YF_T6086Y	L6079V_W6081T_I6088L
33332	Steric 9	T6022I_A6085YF_T6086Y	L6079V_W6081T_I6088L
33333	Steric 10	A6085YF_T6086Y	L6007F_L6079V_W6081T_I6088L
33334	Steric 11	H6005Y_A6085YF_T6086Y	H6005Y_L6079V_W6081T_I6088L

5

Table 12: Exemplary Metrics Used for Lead Design Selection

Design	Chains ¹	Δ Physics-Based Affinity [kcal/mol] ^{2,3}	Δ Knowledge-Based Affinity [kcal/mol] ^{2,3}	Δ SASA [$\text{\AA}^2$] ^{2,4}	Largest Exceeded vdW Overlap [$\text{\AA}$] ⁵
Steric 1	A/A	2.3E+02	2.3E+02	-3.1E+01	5.1E-01

Design	Chains ¹	Δ Physics-Based Affinity [kcal/mol] ^{2,3}	Δ Knowledge-Based Affinity [kcal/mol] ^{2,3}	Δ SASA [$\text{\AA}^2$] ^{2,4}	Largest Exceeded vdW Overlap [$\text{\AA}$] ⁵
	B/B	6.1E+01	1.8E+02	1.1E+02	1.8E-01
	A/B	2.0E+01	-7.4E+01	3.3E+01	1.6E-01
	B/A	1.7E+01	-1.0E+02	1.0E+01	7.0E-02
Steric 2	A/A	2.5E+02	5.5E+02	-3.5E+01	6.2E-01
	B/B	6.1E+01	1.8E+02	1.1E+02	1.8E-01
	A/B	1.6E+01	-7.3E+01	5.0E+01	1.8E-01
	B/A	4.9E+00	-5.4E+01	-5.4E+00	1.6E-01
Steric 3	A/A	1.5E+02	7.8E+02	-3.2E+01	6.5E-01
	B/B	6.3E+01	1.3E+02	1.2E+02	2.2E-01
	A/B	2.5E+00	-1.7E+02	2.4E+01	1.0E-01
	B/A	5.1E-01	-1.7E+02	-3.6E+01	1.6E-01
Steric 4	A/A	7.9E+01	5.8E+02	-8.0E+01	5.1E-01
	B/B	5.5E+01	8.6E+01	1.4E+02	3.0E-02
	A/B	2.1E+01	3.4E+01	1.5E+00	4.2E-01
	B/A	8.5E+00	-1.3E+02	2.0E+01	2.6E-01
Steric 5	A/A	9.5E+01	2.1E+01	-2.9E+01	4.9E-01
	B/B	6.3E+01	1.3E+02	1.2E+02	2.2E-01
	A/B	1.6E+01	-7.7E+01	3.5E+01	1.3E-01
	B/A	1.2E+01	-5.8E+01	-9.8E+00	1.4E-01
Steric 6	A/A	1.0E+02	6.5E+02	-2.4E+01	6.2E-01
	B/B	7.2E+01	3.0E+02	1.4E+02	2.2E-01
	A/B	1.4E+01	-1.0E+02	7.1E+00	1.0E-01
	B/A	1.1E+01	-6.8E+01	-1.8E+01	1.8E-01
Steric 7	A/A	-1.2E+01	3.1E+02	-1.3E+00	3.5E-01
	B/B	7.4E+01	3.5E+02	1.4E+02	1.9E-01
	A/B	1.5E+01	-1.0E+02	-8.2E+00	2.6E-01
	B/A	1.1E+01	-1.0E+02	3.1E+01	2.1E-01
Steric 8	A/A	-2.6E+01	2.1E+02	-3.3E+01	3.4E-01
	B/B	7.4E+01	3.5E+02	1.4E+02	1.9E-01

Design	Chains ¹	Δ Physics-Based Affinity [kcal/mol] ^{2,3}	Δ Knowledge-Based Affinity [kcal/mol] ^{2,3}	Δ SASA [$\text{\AA}^2$] ^{2,4}	Largest Exceeded vdW Overlap [$\text{\AA}$] ⁵
	A/B	4.2E+00	-1.6E+02	-1.1E+01	1.6E-01
	B/A	1.9E+01	-9.5E+01	4.2E+00	2.9E-01
Steric 9	A/A	-1.6E+01	2.4E+02	-3.2E+01	2.6E-01
	B/B	7.4E+01	3.5E+02	1.4E+02	1.9E-01
	A/B	5.1E+00	-1.5E+02	-3.6E+00	1.5E-01
	B/A	1.2E+01	-1.4E+02	1.3E+01	1.8E-01
Steric 10	A/A	-1.2E+01	3.3E+02	6.4E+00	4.6E-01
	B/B	6.0E+01	3.2E+02	1.6E+02	1.8E-01
	A/B	-2.7E-01	-8.5E+01	-2.2E+01	1.6E-01
	B/A	6.6E+00	1.3E+02	6.7E+00	1.9E-01
Steric 11	A/A	-2.6E+01	3.1E+02	-4.0E+01	4.0E-01
	B/B	6.6E+01	2.0E+02	1.5E+02	1.9E-01
	A/B	4.8E-01	-2.0E+02	-6.4E+00	1.2E-01
	B/A	4.9E+00	-1.8E+02	1.2E+01	1.8E-01
Electrostatic 1	B/B	9.4E+01	1.8E+02	-3.0E+01	2.1E-01
	A/A	3.1E+01	4.4E+02	7.7E+01	1.0E-01
	B/A	-3.0E-02	1.4E+02	6.5E+00	1.4E-01
	A/B	-1.6E+00	1.3E+02	3.0E+01	1.9E-01
Electrostatic 2	B/B	1.2E+02	3.2E+02	-6.7E+00	2.7E-01
	A/A	5.8E+01	5.9E+02	7.5E+01	2.0E-01
	B/A	-5.2E+00	2.4E+02	5.2E+01	1.8E-01
	A/B	-1.0E+01	2.2E+02	9.1E+00	1.6E-01
Electrostatic 3	B/B	1.2E+02	3.1E+02	-7.0E+01	1.6E-01
	A/A	5.4E+01	5.7E+02	5.3E+01	1.7E-01
	B/A	6.4E+00	1.9E+02	2.3E+01	1.1E-01
	A/B	9.5E-01	1.9E+02	2.6E+01	1.7E-01
Electrostatic 4	B/B	8.9E+01	3.4E+02	-2.2E+01	3.4E-01
	A/A	5.1E+01	5.8E+02	8.8E+01	1.7E-01
	B/A	-2.8E+00	2.5E+02	4.1E+01	1.4E-01

Design	Chains ¹	Δ Physics-Based Affinity [kcal/mol] ^{2,3}	Δ Knowledge-Based Affinity [kcal/mol] ^{2,3}	Δ SASA [$\text{\AA}^2$] ^{2,4}	Largest Exceeded vdW Overlap [$\text{\AA}$] ⁵
	A/B	-3.0E+00	2.3E+02	8.7E+00	2.6E-01
Electrostatic 5	B/B	8.1E+01	4.1E+02	-5.5E+00	1.8E-01
	A/A	1.9E+01	3.6E+02	1.7E+02	1.0E-01
	B/A	-1.7E+01	2.6E+02	6.6E+01	5.0E-02
	A/B	-1.5E+01	2.5E+02	2.0E+01	5.0E-02
Electrostatic 6	B/B	5.5E+01	3.6E+02	-1.1E+01	1.9E-01
	A/A	1.9E+01	3.4E+02	1.6E+02	1.2E-01
	B/A	-2.2E+01	3.4E+02	7.7E+01	1.8E-01
	A/B	-2.0E+01	3.0E+02	6.6E+01	1.1E-01

¹ Refers to the chains used in the complex investigated as defined in Table 11. A/A and B/B are homodimers designed to be disfavoured, A/B and B/A refer to heterodimers designed to be the favoured complexes.

² Δ refers to difference in the reported metric compared to wild-type (WT) IgA CH3 homodimer.

5 ³ Metrics reporting on the energetics of the interactions of chain A and chain B compared to the WT complex. Negative values indicate a more favourable interaction compared to the WT complex, positive values indicate a less favourable interaction compared to the WT complex.

⁴ SASA = solvent accessible surface area. Negative values indicate a loss in SASA compared to the WT complex, generally associated with better packing and a more favourable interaction. Positive values indicate a gain in SASA, generally associated with poorer packing and a less favourable interaction compared to the WT complex.

10 ⁵ A metric reporting on the extent of the largest van der Waals (vdW) clash. High values are generally associated with poor structural model quality and are less likely to produce stable complexes while low values are associated with good model quality and high predictive power of the other metrics.

EXAMPLE 2: GENERATION OF ONE-ARMED ANTIBODY (OAA) CONSTRUCTS USING A HETERODIMERIC IGA FC

15 Mutations that were predicted to drive heterodimerization as described in Example 1 were introduced into one-armed antibody constructs containing an IgA Fc to assess their functionality.

Methods

20 In order to assess mutations designed to drive heterodimeric pairing of an IgA Fc for their effectiveness, an IgA one-armed antibody format with significant weight differences between its two halves was designed. One half-antibody consisted of an IgG1-based anti-Her2 Fab (heavy chain: SEQ ID NO:38, light chain: SEQ ID NO:39, Carter, *et al.*, 1992, *Proc Natl Acad Sci USA*, 89:4285-4289) that was fused in the heavy chain to an IgA Fc. A chimeric hinge comprising the

upper IgG1 hinge (SEQ ID NO: 40) N-terminally attached to an IgA2 hinge (SEQ ID NO:41) was used to connect the IgG1 Fab to the IgA2 Fc. The sequence of the IgA Fc resembled that of CH2 and CH3 domain of the IgA2m1 allotype (Chintalacharuvu, *et al.*, 1994, *J Immunol*, 152:5299-5304). Position C5092 (IMGT numbering as shown in Table 2), which attaches to the secretory compartment in WT IgA, and the N5120 glycosylation site were mutated and the α -tailpiece was removed, ending the construct with G6129 as described in Lohse *et al.*, 2016, *Cancer Res*, 76:403-417 (see SEQ ID NO:43 in Table 4).

The other half of the one-armed antibody format consisted of just an IgA2 hinge (SEQ ID NO:41) fused to an IgA2m1 CH2 and CH3 without a Fab. The same Fc-mutations as in the heavy chain above were also included. Mutations predicted to drive heterodimeric pairing in Example 1 and listed in Table 11 were introduced into the CH3 domains of the Fc of the one-armed antibody constructs and resulted in the variants described in Table 13. Chain A mutations were introduced in the heavy chain including VH and CH1 (H1) and Chain B mutations were introduced in the Fc-only heavy chain.

Table 13: Heterodimeric IgA Variants in OAA Format

Variant	Design	Clone No. H1	Clone No. L1	Clone No. H2
32595	WT IgA	21755	11150	21715
32510	Electrostatic 1	23773	11150	23767
32511	Electrostatic 2	23774	11150	23768
32512	Electrostatic 3	23775	11150	23769
32513	Electrostatic 4	23776	11150	23770
32514	Electrostatic 5	23777	11150	23771
32515	Electrostatic 6	23777	11150	23772
32516	Steric 1	23778	11150	23783
32517	Steric 2	23779	11150	23783
32518	Steric 3	23780	11150	23784
32519	Steric 4	23781	11150	23785
32520	Steric 5	23782	11150	23784
32521	Steric 6	23780	11150	23786
33330	Steric 7	24674	11150	23786

Variant	Design	Clone No. H1	Clone No. L1	Clone No. H2
33331	Steric 8	24675	11150	23786
33332	Steric 9	24676	11150	23786
33333	Steric 10	23780	11150	24677
33334	Steric 11	24678	11150	24679

EXAMPLE 3: PRODUCTION OF HETERODIMERIC IGA ONE ARMED ANTIBODIES

Sequences of heavy and light chains of modified IgA OAA variants designed in Examples 1 and 2 were cloned into expression vectors and expressed and purified as described below.

5 Methods

Vector inserts comprising a signal peptide (EFATMRPTWAWWLFLVLLALWAPARG [SEQ ID NO:49]) (Barash *et al.*, 2002, *Biochem and Biophys Res. Comm.*, 294:835–842) and the heavy and light chain sequences described in Example 2 were ligated into a pTT5 vector to produce heavy and light chain expression vectors. Vectors were sequenced to confirm correct reading frame and sequence of the coding DNA.

Heavy and light chains and the Fc-only chains of the modified IgA OAA variants were co-expressed in 25 mL cultures of Expi293FTM cells (Thermo Fisher, Waltham, MA). Expi293TM cells were cultured at 37°C in Expi293TM Expression Medium (Thermo Fisher, Waltham, MA) on an orbital shaker rotating at 125 rpm in a humidified atmosphere of 8% CO₂. A volume of 25 mL with a total cell count of 7.5×10^7 cells was transfected with a total of 25 µg DNA at a transfection ratio of 30:40:30 for H1:L1:H2. Prior to transfection the DNA was diluted in 1.5 mL Opti-MEMTM I Reduced Serum Medium (Thermo Fisher, Waltham, MA). In a volume of 1.42 mL Opti-MEMTM I Reduced Serum Medium, 80 µL of ExpiFectamineTM 293 reagent (Thermo Fisher, Waltham, MA) were diluted and, after incubation for five minutes, combined with the DNA transfection mix to a total volume of 3 mL. After 10 to 20 minutes the DNA-ExpiFectamineTM293 reagent mixture was added to the cell culture. After incubation at 37°C for 18-22 hours, 150 µL of ExpiFectamineTM 293 Enhancer 1 and 1.5 mL of ExpiFectamineTM 293 Enhancer 2 (Thermo Fisher, Waltham, MA) were added to each culture. Cells were incubated for five to seven days, and supernatants were harvested for protein purification.

Clarified supernatant samples were diluted 1:1 with PBS and applied to 2 mL of CaptureSelect™ IgA Affinity Matrix (ThermoFisher, Waltham, MA) packed in-house in a Millipore Vantage L x 250 column on AKTA™ Pure FPLC System (GE Life Sciences). The column was equilibrated in PBS. After loading, the column was washed with PBS and protein
5 eluted with 0.1 M glycine, pH 2.5. The eluted samples were pH adjusted by adding 10% (v/v) 1 M Tris, pH 9 to yield a final pH of 6-7. The variants were assessed for heterodimeric purity after affinity chromatography by non-reducing CE-SDS and UPLC-SEC as described in Example 4.

After concentration and to separate heterodimeric from homodimeric Fc species and other impurities, the material of variants with significant amounts of heterodimeric species was injected
10 into an AKTA™ Pure FPLC System (GE Life Sciences) and run on a Superdex 200 Increase 10/300 GL (GE Life Sciences) column pre-equilibrated with PBS pH 7.4. The protein was eluted from the column at a rate of 0.75 mL/min and collected in 0.5 mL fractions. Peak fractions with concentrations of > 0.5 mg/mL of target protein and a CE-SDS purity of > 95 % were pooled and concentrated using Vivaspın™ 20, 30 kDa MWCO polyethersulfone concentrators
15 (MilliporeSigma, Burlington, MA). After sterile filtering through 0.2 µm PALL Acrodisc™ Syringe Filters with Supor™ Membrane, proteins were quantitated based on A280 nm (Nanodrop), frozen and stored at -80 °C until further use.

Results

Inclusion of electrostatic design mutations did not result in variants with detectable
20 expression, pointing to a disruptive nature of these mutations. Conversely, all steric designs showed expression under the conditions tested and ten designs were purified and investigated further (Steric 1-4, Steric 6-11). While some samples of these variants showed highly pure, heterodimeric species after affinity chromatography, preparative SEC was required in order to obtain samples of high purity for most due to the presence of homodimeric Fc species as well as
25 other impurities such as half antibodies and aggregates (see Example 4). After preparative SEC was performed on Steric 1-3 and Steric 6-11 designs as well as the WT IgA Fc OAA, yields ranged from 30-200 mg/L of expression culture. The assessment of sample purity and stability is described in Example 4, Example 5 and Example 6.

EXAMPLE 4: ASSESSMENT OF HETERODIMERIC PURITY OF LEAD DESIGNS AFTER AFFINITY CHROMATOGRAPHY

OAA variants were assessed for heterodimeric purity and sample homogeneity by non-reducing CE-SDS and UPLC-SEC after CaptureSelect IgA affinity purification and before SEC
5 purification.

Methods

Following CaptureSelect IgA affinity purification, purity of samples was assessed by non-reducing and reducing High Throughput Protein Express assay using CE-SDS LabChip® GXII (Perkin Elmer, Waltham, MA). Procedures were carried out according to HT Protein Express
10 LabChip® User Guide version 2 with the following modifications. Antibody samples, at either 2ul or 5ul (concentration range 5-2000 ng/ul), were added to separate wells in 96 well plates (BioRad, Hercules, CA) along with 7ul of HT Protein Express Sample Buffer (Perkin Elmer # 760328). Samples were then denatured at 90°C for 5 mins and 35 µl of water was added to each sample well. The LabChip® instrument was operated using the HT Protein Express Chip (Perkin Elmer
15 #760499) and the HT Protein Express 200 assay setting (14 kDa-200 kDa).

UPLC-SEC was performed on an Agilent Technologies 1260 Infinity LC system using an Agilent Technologies AdvanceBio SEC 300A column at 25°C. Before injection, samples were centrifuged at 10000 g for 5 minutes, and 5 µL was injected into the column. Samples were run for 7 min at a flow rate of 1 mL/min in PBS, pH 7.4 and elution was monitored by UV absorbance
20 at 190-400 nm. Chromatograms were extracted at 280 nm. Peak integration was performed using the OpenLAB CDS ChemStation software.

Results

Analysis of non-reducing CE-SDS of the WT IgA OAA (v32595) showed a mix of homodimeric Full Sized Antibody (FSA) together with Fc and heterodimeric OAA species (Fig.
25 2). The heterodimeric species was the most prominent with less of each homodimeric species present. This is the expected distribution of species at equimolar expression of both Fc chains without any mutations promoting heterodimer formation present (Ridgway, *et al.*, 1996, *Protein Eng*, 9:617-621) and was also seen by UPLC-SEC (Fig. 3A).

15 Variants including mutations promoting heterodimer formation showed notably different distribution of species in both non-reducing CE-SDS (Fig. 2) and UPLC-SEC (Fig. 3) as compared to WT IgA OAA. While FSA homodimers were not present for any of the steric designs shown in Figs. 2 and 3, varying levels of Fc homodimers and half antibody species could be found in addition to OAA heterodimers. Most notably, Steric 3 (v32518; Fig. 3D) and Steric 6 (v32521; Fig. 3F) designs showed significantly increased purity of OAA heterodimeric species with Steric 6 reaching heterodimeric purity of > 95 % by both CE-SDS and UPLC-SEC. Conversely, Steric 4 (v32519; Fig. 3E) contained no OAA heterodimer or FSA homodimer species but only Fc homodimer and the corresponding half-antibody, pointing to a problem in the expression of the other heavy chain likely caused by the introduced mutations. The presence of small peaks at retention times < 3 min indicated the presence of small amounts of high molecular weight species such as oligomers and aggregates in all samples.

EXAMPLE 5: ASSESSMENT OF HETERODIMERIC PURITY OF LEAD DESIGNS AFTER SIZE EXCLUSION CHROMATOGRAPHY

15 After SEC purification of select designs, samples were assessed for homogeneity of the sample by non-reducing as well as reducing CE-SDS and UPLC-SEC as described below.

Methods

Non-reducing CE-SDS and UPLC-SEC were performed as described in Example 4. For electrophoretic analysis under reducing conditions, the CE-SDS protocol was modified by adding 3.5 µL of DTT(1M) to 100 µL of HT Protein Express Sample Buffer.

Results

25 UPLC-SEC traces and CE-SDS electrophoresis profiles (reducing and non-reducing) of heterodimeric OAA samples purified by SEC as described in Example 3 are shown in Fig. 4 and Fig. 5, respectively. Analysis of UPLC-SEC showed highly homogeneous samples that contained 90% - 100% of heterodimeric OAA species. The presence of a small peak at a low retention time and a shoulder at higher retention time compared to the main species indicates the presence of small amounts of homodimers in WT IgA (Fig. 4A), Steric 1 (Fig. 4B) and Steric 2 (Fig. 4C) designs. After SEC purification, non-reducing CE-SDS showed a single predominant species for

all variants investigated. Only bands corresponding to the three intact chains of all variants were observed by reducing CE-SDS. Notably, light chain as well as the Fc-only heavy chain have a similar molecular weight (23.4 kDa and 23.7 kDa) and appear as one band in the reducing CE-SDS profile.

5 **EXAMPLE 6: THERMAL STABILITY OF LEAD IGA HETERODIMER DESIGNS**

Purified samples of heterodimeric OAA variants after preparative SEC were assessed for thermal stability by Differential Scanning Calorimetry (DSC) as described below.

Methods

After preparative SEC as described in Example 3, samples of heterodimeric OAA designs
10 were diluted in PBS to 0.5-1 mg/ml. For DSC analysis using NanoDSC (TA Instruments, New
Castle, DE, USA), 950 μ l of sample and matching buffer (PBS) were added to sample and
reference 96 well plates, respectively. At the start of the DSC run, a buffer (PBS) blank injection
was performed to stabilize the baseline. Each sample was then injected and scanned from 25°C to
15 95°C at 1°C/min with 60 psi nitrogen pressure. Thermograms were analyzed using the
NanoAnalyze software. The matching buffer thermogram was subtracted from sample thermogram
and baseline fit using a sigmoidal curve. Data was then fit with a two-state scaled DSC model.

Results

The DSC thermogram of WT IgA OAA with an unmodified IgA CH3-CH3 interface
(v32595) showed two transitions at 74 °C and 81 °C (Fig. 6A). The more dominant transition at
20 81 °C was present for all investigated designs and was attributed to the unfolding of the Fab
overlapped with unfolding of the CH2 domain, neither of which was mutated in the designs.
Conversely, a transition was observed to change across designs and was attributed to the unfolding
of the CH3 domain (Fig. 6A-B). While the modified CH3 in Steric 2 (v32517) was significantly
destabilized compared to WT (T_m of 55 °C vs 74 °C), the designs with the highest heterodimeric
25 purity show CH3 stabilities close to WT. Transitions were observed at 65.9 °C and 71.9 °C for
Steric 3 (v32518) and Steric 6 (v32521), respectively. The two designs that showed the highest
thermal stability were Steric 10 (v33333) and Steric 11 (v33334) with CH3 unfolding transitions
observed at 72.0 °C and 73.6 °C, respectively. This higher thermal stability was observed while

the heterodimeric purity of these two designs as assessed by CE-SDS and UPLC-SEC in Example 4 was lower than that of Steric 3 and Steric 6.

5 In summary, combinations of mutations were identified in the IgA CH3 domain that significantly drove heterodimer formation of the IgA Fc. The thermal stability of the CH3 domain of heterodimeric variants bearing these mutations was within ~2 °C of the WT IgA CH3 for the Steric 6 (v32521), Steric 10 (v33333) and Steric 11 (v33334) designs. The properties of the Steric designs tested are summarized in Table 14.

Table 14: Summary of Properties of Steric Designs 1-3 and 6-11

Variant	Design	HetFc Mutations		Post CSIgA Purification			Post prepSEC Purification			T _m * (°C)
		Chain A	Chain B	UPLC-SEC purity (%)	CE-SDS purity (%)	Yield (mg/L culture)	UPLC-SEC purity (%)	CE-SDS purity (%)	Yield (mg/L culture)	
32595	WT IgA	--	--	52	49	324	91	92	76	74.2
32516	Steric 1	A6085YY_T6086L	L6079T_W6081L_I6088L	49	36	148	98	93	36	71.1
32517	Steric 2	A6085YY_T6086Y	L6079T_W6081L_I6088L	65	55	240	97	96	76	55
32518	Steric 3	A6085YF_T6086Y	L6079V_W6081L_I6088L	91	89	328	100	98	136	65.9
32519	Steric 4	L6024M_A6085YF_T6086W	W6081L	5	3.7	60	ND	ND	ND	ND
32521	Steric 6	A6085YF_T6086Y	L6079V_W6081T_I6088L	96	92	320	100	97	100	71.9
33330	Steric 7	T6022V_A6085YF_T6086Y	L6079V_W6081T_I6088L	82	31	130	100	99	52	69.2
33331	Steric 8	T6022L_A6085YF_T6086Y	L6079V_W6081T_I6088L	75	97	370	100	95	140	67.6
33332	Steric 9	T6022I_A6085YF_T6086Y	L6079V_W6081T_I6088L	87	97	390	100	95	210	69
33333	Steric 10	A6085YF_T6086Y	L6007F_L6079V_W6081T_I6088L	72	88	370	100	85	82	72
33334	Steric 11	H6005Y_A6085YF_T6086Y	H6005Y_L6079V_W6081T_I6088L	74	95	440	100	93	71	73.6

* CH3 domain T_m determined by DSC

EXAMPLE 7: FURTHER STABILIZATION OF IGA HETFC DESIGNS

To increase the thermal stability and heterodimeric purity of lead IgA HetFc designs via covalent disulfide bridges across the interface, cysteine mutations were introduced in the CH3 interface of the IgA Fc.

5 *Methods*

Residue pairs in the interface of the IgA Fc were selected based on C α and C β distances determined to be sufficient to accommodate the geometry of a disulfide bond. The selected residues were then substituted with cysteine residues and the resultant covalent disulfide bonds were modelled. The resulting structures were evaluated energetically using proprietary *in silico* tools.

10*Results*

Cysteine substitutions were introduced into the Steric 6 design and evaluated by proprietary *in silico* tools. Exemplary metrics for select designs are shown in Table 15. The cysteine substitutions were then introduced as single and double disulfide designs in an OAA format of Steric 6 as well as a single disulfide design in a WT OAA (Table 16).

15

The variants shown in Table 16 will be expressed and evaluated for heterodimeric purity and thermal stability. While the high heterodimeric purity of Steric 6 based designs (34688-34690) as assessed by UPLC-SEC and CE-SDS is expected to be preserved when compared to that of Steric 6 (> 90 % as assessed by UPLC-SEC and CE-SDS after CaptureSelect IgA purification, see example 6), the thermal stability of these designs, as measured by DSC, is predicted to be significantly increased when compared to that of Steric 6 (> 71 °C, see example 6) due to the addition of one or two covalent disulfide bonds in the interface. When introduced as a single disulfide design in an asymmetric manner in an otherwise unchanged WT IgA Fc (34691), heterodimeric purity as assessed by UPLC-SEC and CE-SDS is expected to be significantly improved compared to WT IgA (> 50 % as assessed by UPLC-SEC and CE-SDS after CaptureSelect IgA purification, see example 6) and thermal stability is predicted to be at or above WT (> 74 °C, see example 6).

20
25

The identified disulfide designs may also be combined with other lead HetFc designs identified in Examples 1-6, expressed in OAA format, purified and assessed for heterodimeric purity as well as thermal stability as described in Examples 2-6.

Table 15: Exemplary Metrics used for Disulfide Bond Design Selection

Chain A Cysteine Mutation	Chain B Cysteine Mutation	Δ Physics-Based Affinity [kcal/mol] ^{1,2}	Δ Knowledge-Based Affinity [kcal/mol] ^{1,2}	Disulfide Dihedral Angle Energy [kJ/mol] ³	Number of Clashes ⁴
H6005C	P6010C	2.5E+01	-5.6E+01	1.3E+01	0
P6010C	H6005C	1.4E+01	-5.7E+01	1.4E+01	0

5 ¹ Δ refers to difference in the reported metric compared to WT IgA CH3 homodimer.

² Metrics reporting on the non-covalent energetics of the interactions of Chain A and Chain B compared to the WT complex. Negative values indicate a more favourable interaction compared to the WT complex, positive values indicate a less favourable interaction compared to the WT complex. The energy difference afforded by the formation of the covalent disulfide bridge is not included.

10 ³ Metric reporting on the dihedral angle strain in the disulfide bond. Smaller values indicate less angle strain.

⁴ Clashes are flagged for distances between heavy atoms that fall below distance cut-offs defined for different types of interactions.

Table 16: Selected Heterodimeric IgA Variants Including a Disulfide Bond

Variant	Description	Clone No. H1	Clone No. L1	Clone No. H2
34688	IgA Het_Fc OAA Steric 6 A H6005C B P6010C	25880	11150	25881
34689	IgA Het_Fc OAA Steric 6 A P6010C B H6005C	25882	11150	25883
34690	IgA Het_Fc OAA Steric 6 A H6005C P6010C B H6005C P6010C	25884	11150	25885
34691	WT IgA OAA A H6005C B P6010C	25886	11150	25887

EXAMPLE 8: MULTIMERIC, MULTISPECIFIC FORMATS BASED ON IGA HETFC

Mutations driving heterodimeric pairing of the IgA Fc described in Example 1-7 can be used to construct multimeric, multispecific variants, which may then be tested for target binding and functionality.

5 *Methods*

The two chains of an IgA1, IgA2m1 or IgA2m2 Fc including a C-terminal tailpiece (SEQ ID NO:46 or 47) are equipped with mutations in the CH3 domain that drive heterodimer formation as described in Examples 1-6 and Table 11, to form the core IgA HetFc scaffold. A binding domain (e.g. Fab, scFv, VHH, Immunomodulatory Ig domain, non-Ig viral receptor decoy, and as described elsewhere herein) specific for one target is linked to the N-terminus of one of the IgA HetFc chains via an IgA1, IgA2 or IgG1/IgA2 chimeric hinge while the same hinges are used to link a second binding domain specific for another target to the N-terminus of the other chain of the IgA HetFc. The resulting two chains are then transiently expressed in a mammalian expression system together with a joining chain (J-chain) as well as any additional polypeptide chains needed to complete the IgA HetFc construct (e.g. other chains to complete Fabs used as targeting domains). Depending on the IgA allotype used for the Fc and the ratio of J chain to IgA Fc chains, this results in the formation of dimeric, tetrameric or pentameric molecules (Lombana *et al.*, 2019, *MAbs*, **11**:1122-1138, Kumar, *et al.*, 2020, *Science*, **367**:1008-1014) in which each IgA HetFc binding unit of the dimeric, tetrameric or pentameric IgA HetFc multimer possesses two binding domains (see Fig. 8). After purification by **CaptureSelect™ IgA affinity chromatography**, **samples are assessed for purity and homogeneity of particle sizes by one or more of non-reducing and reducing SDS-PAGE or CE-SDS, UPLC-SEC, multi-angle light scattering (MALS) or dynamic light scattering (DLS). If needed, samples are further purified by SEC as described in Example 3 and their sample quality assessed as described before. Samples are then tested for target binding by one or more of surface plasmon resonance (SPR), flow cytometry or functional assays specific to the target.**

Results

While IgA HetFc multimer variants based on an IgA1 and IgA2m1 HetFc will be predominately dimeric, those based on an IgA2m2 HetFc will show dimeric, tetrameric and

pentameric species that can be separated by SEC. In binding studies to the individual targets, an increased apparent affinity compared to monovalent binding is expected due to the avidity provided by the multimeric scaffold. This avidity effect on the apparent affinity is expected to be further enhanced when both targets are present in the binding assay. When compared to IgG-based, monomeric and bispecific antibodies, IgA HetFc multimers with increasing valency (monomer < dimer < tetramer < pentamer) should demonstrate a sequentially enhanced apparent affinity. Taken together, this avidity effect is expected to lead to high specificity and high efficacy for binding targets which is reflected in functional studies as seen previously (Slaga *et al.*, 2018, *Sci Transl Med*, 10(463):eaat5775; International Patent Publication Nos. WO 2016/141303 and WO 2016/118641). When used to target viral or bacterial pathogens, the high valency of IgA HetFc multimers is expected to lead to agglutination and clearance of the target(s), while multi-specificity limits mutational escape and assures a consistently high level of neutralization.

EXAMPLE 9: A HETERODIMERIC IGA FC INCLUDING A MUTATIONS TO ELIMINATE BINDING TO FC α RI

To assess the impact of valency of Fc α RI engagement via the IgA Fc on its functionality, a heterodimeric IgA Fc based on mutations described in Examples 1-7 was used to construct an IgA Fc with a single Fc α RI binding site.

Methods

A mutation that has been identified to disrupt the IgA Fc:Fc α RI interaction (F6116A, Posgai, M. T. *et al.*, 2018, *Proc Natl Acad Sci USA* 115:E8882-E8891) was introduced into either one or both heavy chains of OAA variants of the Steric 6 design (Table 17). These variants as well as a wild-type Steric 6 OAA (32521) were then expressed and purified as described in examples 3-6. Other constructs may include combinations of mutations achieving differing Fc α RI affinities on the two chains of a heterodimeric IgA Fc. Possible combinations are shown in Table 18. These variants can be evaluated for binding to Fc α RI and neutrophil activation. Schematics of the variants containing two, one or no Fc α RI binding sites are shown in Figure 11.

Table 17: Heterodimeric IgA Variants based on Steric 6 OAA Including Mutations in Fc α R Binding Site

Variant	Additional mutations chain A	Additional mutations chain B	Clone No. H1	Clone No. L1	Clone No. H2
35060	F6116A	F6116A	26235	11150	26236
35061	F6116A		26235	11150	23786

Table 18: Possible Combinations of Fc α RI Affinities in IgA HetFc

Chain A Fc α RI affinity	Chain B Fc α R affinity
Increased compared to WT	Increased compared to WT
Increased compared to WT	WT
Increased compared to WT	Decreased compared to WT
Increased compared to WT	Eliminated
WT	Increased compared to WT
WT	WT
WT	Decreased compared to WT
WT	Eliminated
Decreased compared to WT	Increased compared to WT
Decreased compared to WT	WT
Decreased compared to WT	Decreased compared to WT
Decreased compared to WT	Eliminated
Eliminated	Increased compared to WT
Eliminated	WT
Eliminated	Decreased compared to WT
Eliminated	Eliminated

5

Results

Variants with modified Fc α RI binding sites aimed at increasing, lowering or eliminating binding are expected to show a range of affinities to Fc α RI and a range of activities in neutrophil activation

assays compared to a WT IgA Fc. While knockout mutations in both chains are expected to eliminate binding and neutrophil activation, mutations aimed at increasing Fc α RI binding in both chains are expected to increase binding and neutrophil activation and constitute the highest possible activity. All other combinations shown in Table 18 are expected show binding and
5 neutrophil activation at a level between these limits.

EXAMPLE 10: A HETERODIMERIC IGA FC INCLUDING FC α RI AND FCRN BINDING SITES

Mutations driving the assembly of a heterodimeric IgA Fc described in Examples 1-7 are used to
10 construct IgA-based variants capable of activating neutrophils via the Fc α RI as well as having an increased half-life due to the presence of a FcRn binding site.

Methods

Residues important for binding of an IgG Fc to the Neonatal Fc Receptor (FcRn) (Oganesyan, V. *et al.*, 2014, *J Biol Chem* 289:7812-7824) are grafted onto heterodimeric IgA variants to create
15 constructs capable engaging FcRn as well as Fc α RI. A heterodimeric Fc is necessary since Fc α RI and FcRn binding sites are located in structurally equivalent locations at the CH2/CH3 interfaces in IgA and IgG, respectively (Kelton, W. *et al.*, 2014, *Chem Biol* 21:1603-1609). Grafting of the FcRn binding site is achieved by an overlay of peptide backbone atoms of IgA and IgG Fc and identification of structurally equivalent residues in IgA to the IgG:FcRn binding patch. These are
20 then swapped for their IgG counterpart. Alternatively, mutations can be included that are known to modify FcRn affinity in IgG (Robbie, G. J. *et al.*, 2013, *Antimicrob Agents Chemother* 57:6147-6153, Yeung, Y. A. *et al.*, 2009, *J Immunol* 182:7663-7671, Hinton, P. R. *et al.*, 2006, *J Immunol* 176:346-356, Hinton, P. R. *et al.*, 2004, *J Biol Chem* 279:6213-6216, 1 Dall'Acqua, W. F., Kiener, P. A. & Wu, H., 2006, *J Biol Chem* 281:23514-23524). Multiple designs are evaluated
25 energetically using proprietary *in silico* tools. They are expressed, purified and then assessed for their binding to Fc α RI and FcRn as well as neutrophil activation *in vitro* and half-life *in vivo*. A schematic of such a variant is shown in Figure 12.

Results

Variants where binding to both Fc α RI and FcRn is achieved are expected to show activity in a neutrophil ADCC assay as well as significantly increased half-life in FcRn in *in vivo* models when compared to an IgA Fc without a FcRn binding site.

5

SEQUENCE TABLES

A brief description of the SEQ ID NOs for the clones described herein is provided in Table A. Amino acid sequences for each SEQ ID NO. are provided in Table B.

Table A: Brief Description of the Clones used to Prepare IgA HetFc Constructs (see also Table 13 and Table 16)

SEQ ID NO	Clone ID	Domain structure
1	11150	Tras* VL – IgKCL
2	21715	IgA2 hinge - IgA2m1 CH2 - IgA2m1 CH3
3	21755	Tras VH - IgG1 CH1 - IgG1/IgA2 hinge - IgA2m1 CH2 - IgA2m1 CH3
4	23767	IgA2 hinge - IgA2m1 CH2 - IgA2m1 CH3
5	23768	IgA2 hinge - IgA2m1 CH2 - IgA2m1 CH3
6	23769	IgA2 hinge - IgA2m1 CH2 - IgA2m1 CH3
7	23770	IgA2 hinge - IgA2m1 CH2 - IgA2m1 CH3
8	23771	IgA2 hinge - IgA2m1 CH2 - IgA2m1 CH3
9	23772	IgA2 hinge - IgA2m1 CH2 - IgA2m1 CH3
10	23773	Tras VH - IgG1 CH1 - IgG1/IgA2 hinge - IgA2m1 CH2 - IgA2m1 CH3
11	23774	Tras VH - IgG1 CH1 - IgG1/IgA2 hinge - IgA2m1 CH2 - IgA2m1 CH3
12	23775	Tras VH - IgG1 CH1 - IgG1/IgA2 hinge - IgA2m1 CH2 - IgA2m1 CH3
13	23776	Tras VH - IgG1 CH1 - IgG1/IgA2 hinge - IgA2m1 CH2 - IgA2m1 CH3
14	23777	Tras VH - IgG1 CH1 - IgG1/IgA2 hinge - IgA2m1 CH2 - IgA2m1 CH3
15	23778	Tras VH - IgG1 CH1 - IgG1/IgA2 hinge - IgA2m1 CH2 - IgA2m1 CH3
16	23779	Tras VH - IgG1 CH1 - IgG1/IgA2 hinge - IgA2m1 CH2 - IgA2m1 CH3
17	23780	Tras VH - IgG1 CH1 - IgG1/IgA2 hinge - IgA2m1 CH2 - IgA2m1 CH3
18	23781	Tras VH - IgG1 CH1 - IgG1/IgA2 hinge - IgA2m1 CH2 - IgA2m1 CH3
19	23782	Tras VH - IgG1 CH1 - IgG1/IgA2 hinge - IgA2m1 CH2 - IgA2m1 CH3

SEQ ID NO	Clone ID	Domain structure
20	23783	IgA2 hinge - IgA2m1 CH2 - IgA2m1 CH3
21	23784	IgA2 hinge - IgA2m1 CH2 - IgA2m1 CH3
22	23785	IgA2 hinge - IgA2m1 CH2 - IgA2m1 CH3
23	23786	IgA2 hinge - IgA2m1 CH2 - IgA2m1 CH3
24	24674	Tras VH - IgG1 CH1 - IgG1/IgA2 hinge - IgA2m1 CH2 - IgA2m1 CH3
25	24675	Tras VH - IgG1 CH1 - IgG1/IgA2 hinge - IgA2m1 CH2 - IgA2m1 CH3
26	24676	Tras VH - IgG1 CH1 - IgG1/IgA2 hinge - IgA2m1 CH2 - IgA2m1 CH3
27	24677	IgA2 hinge - IgA2m1 CH2 - IgA2m1 CH3
28	24678	Tras VH - IgG1 CH1 - IgG1/IgA2 hinge - IgA2m1 CH2 - IgA2m1 CH3
29	24679	IgA2 hinge - IgA2m1 CH2 - IgA2m1 CH3
30	25880	Tras VH - IgG1 CH1 - IgG1/IgA2 hinge - IgA2m1 CH2 - IgA2m1 CH3
31	25881	IgA2 hinge - IgA2m1 CH2 - IgA2m1 CH3
32	25882	Tras VH - IgG1 CH1 - IgG1/IgA2 hinge - IgA2m1 CH2 - IgA2m1 CH3
33	25883	IgA2 hinge - IgA2m1 CH2 - IgA2m1 CH3
34	25884	Tras VH - IgG1 CH1 - IgG1/IgA2 hinge - IgA2m1 CH2 - IgA2m1 CH3
35	25885	IgA2 hinge - IgA2m1 CH2 - IgA2m1 CH3
36	25886	Tras VH - IgG1 CH1 - IgG1/IgA2 hinge - IgA2m1 CH2 - IgA2m1 CH3
37	25887	IgA2 hinge - IgA2m1 CH2 - IgA2m1 CH3

*Tras - Trastuzumab

Table B: Amino Acid Sequences

SEQ ID NO	Clone No.	Description	Sequence
1	11150	Full	DIQMTQSPSSLSASVGDRVITICRASQDVNTAVAW YQQKPGKAPKLLIYSASFLYSGVPSRFSGRSGTDF TLTISSLQPEDFATYYCQQHYTTPPTFGQGTKVEIK RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPRE AKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSS TLTSLKADYEKHKVYACEVTHQGLSSPVTKSFNR GEC
2	21715	Full	RVPPPPPCCHPRLSLHRPALEDLLLGSEANLTCTLT GLRDASGATFTWTPSSGKSAVQGPPERDLCGCYS VSSVLPGSAQPWNHGETFTCTAAHPELKTPLTATL SKSGNTFRPEVHLLPPPSEELALNELVTLTCLARGF SPKDVLRWLQGSQELPREKYL TWASRQEPSQGT

SEQ ID NO	Clone No.	Description	Sequence
			TTFVAVTSILRVAAEDWKKGDTFSCMVGHEALPLA FTQKTIDRLAG
3	21755	Full	EVQLVESGGGLVQPGGSLRLSCAASGFINIKDTYIH WVRQAPGKGLEWVARIYPTNGYTRYADSVKGRF TISADTSKNTAYLQMNSLRAEDTAVYYCSRWGGD GFYAMDYWGQGTLLTVSSASTKGPSVFPLAPSSK STSGGTAALGCLVKDYFPEPVTVSWNSGALTSGV HTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVN HKPSNTKVDKKVEPKSCRVPPIPPPCCHPRLSLHRP ALEDLLLGSEANLTCTLTGLRDASGATFTWTPSSG KSAVQGPAPERDLCGCSYVSSVLPQSAQPNHGET FTCTAAHPELKTPLTATLSKSGNTFRPEVHLLPPPS EELALNELVTLTCLARGFSPKDVLRWLQGSQELP REKYLTVASRQEPSQGTTFVAVTSILRVAAEDWK KGDTFSCMVGHEALPLAFTQKTIDRLAG
4	23767	Full	RVPIPPPCCHPRLSLHRPALEDLLLGSEANLTCTLT GLRDASGATFTWTPSSGKSAVQGPAPERDLCGCSY VSSVLPQSAQPNHGETFTCTAAHPELKTPLTATL SKSGNTFRPEVHLLPPSEELALNELVRLTCRARGF SPKDVLRWLQGSQELPREKYLTVASRQEPSQGT TTFVAVTSILRVAAEDWKKGDTFSCMVGHEALPLA FTQKTIDRLAG
5	23768	Full	RVPIPPPCCHPRLSLHRPALEDLLLGSEANLTCTLT GLRDASGATFTWTPSSGKSAVQGPAPERDLCGCSY VSSVLPQSAQPNHGETFTCTAAHPELKTPLTATL SKSGNTFRPEVHLLPPSEELALNELVRLTCKARGF SPKDVLRWLQGSQELPREKYLTVASRQEPSQGT TTFVAVTSILRVAAEDWKKGDTFSCMVGHEALPLA FTQKTIDRLAG
6	23769	Full	RVPIPPPCCHPRLSLHRPALEDLLLGSEANLTCTLT GLRDASGATFTWTPSSGKSAVQGPAPERDLCGCSY VSSVLPQSAQPNHGETFTCTAAHPELKTPLTATL SKSGNTFRPEVHLLPPSEELALNELVRLTCKARGF SPKDVLRWLQGSQELPREKYLTVASRQEPSQGT TTFVAVTSRLRVAAEDWKKGDTFSCMVGHEALPLA FTQKTIDRLAG
7	23770	Full	RVPIPPPCCHPRLSLHRPALEDLLLGSEANLTCTLT GLRDASGATFTWTPSSGKSAVQGPAPERDLCGCSY VSSVLPQSAQPNHGETFTCTAAHPELKTPLTATL SKSGNTFRPEVHLLPPSEELALNELVRLTCKAKGF SPKDVLRWLQGSQELPREKYLTVASRQEPSQGT TTFVAVTSRLRVAAEDWKKGDTFSCMVGHEALPLA FTQKTIDRLAG

SEQ ID NO	Clone No.	Description	Sequence
8	23771	Full	RVPPPPPCCHPRLSLHRPALEDLLLGSEANLTCTLT GLRDASGATFTWTPSSGKSAVQGPPELDLCGCYS VSSVLPGSAQPWNHGETFTCTAAHPELKTPLTATL SKSGNTFRPEVHLLPPPSEELALNELVTLTCKAKGF SPKDVLRWLQGSQELPREKYLTWASRQPSQGT TTFAVTSKLRVAAEDWKKGDTFSCMVGHEALPLA FTQKTIDRLAG
9	23772	Full	RVPPPPPCCHPRLSLHRPALEDLLLGSEANLTCTLT GLRDASGATFTWTPSSGKSAVQGPPELDLCGCYS VSSVLPGSAQPWNHGETFTCTAAHPELKTPLTATL SKSGNTFRPEVHLLPPPSEELALNELVTLTCKAKGF SPKDVLRWLQGSQELPREKYLTWASRQEPSQGT TTFAVTSKLRVAAEDWKKGDTFSCMVGHEALPLA FTQKTIDRLAG
10	23773	Full	EVQLVESGGGLVQPGGSLRLSCAASGFNIKDTYIH WVRQAPGKGLEWVARIYPTNGYTRYADSVKGRF TISADTSKNTAYLQMNSLRAEDTAVYYCSRWGGD GFYAMDYWGQGLTVTVSSASTKGPSVFPLAPSSK STSGGTAALGCLVKDYFPEPVTVSWNSGALTSGV HTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVN HKPSNTKVDKKVEPKSCRVPVPPPPCCHPRLSLHRP ALEDLLLGSEANLTCTLTGLRDASGATFTWTPSSG KSAVQGPPELDLCGCYSVSSVLPGSAQPWNHGET FTCTAAHPELKTPLTATLSKSGNTFRPEVHLLPPPS EELALNELVDLTCDADGFSPKDVLRWLQGSQEL PREKYLTWASRQEPSQGTTFFAVTSELVAAEDW KKGDTFSCMVGHEALPLAFTQKTIDRLAG
11	23774	Full	EVQLVESGGGLVQPGGSLRLSCAASGFNIKDTYIH WVRQAPGKGLEWVARIYPTNGYTRYADSVKGRF TISADTSKNTAYLQMNSLRAEDTAVYYCSRWGGD GFYAMDYWGQGLTVTVSSASTKGPSVFPLAPSSK STSGGTAALGCLVKDYFPEPVTVSWNSGALTSGV HTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVN HKPSNTKVDKKVEPKSCRVPVPPPPCCHPRLSLHRP ALEDLLLGSEANLTCTLTGLRDASGATFTWTPSSG KSAVQGPPELDLCGCYSVSSVLPGSAQPWNHGET FTCTAAHPELKTPLTATLSKSGNTFRPEVHLLPPPS EELALNELVELTCEADGFSPKDVLRWLQGSQELP REKYLTWASRQEPSQGTTFFAVTSDELVAEDWK KGDTFSCMVGHEALPLAFTQKTIDRLAG
12	23775	Full	EVQLVESGGGLVQPGGSLRLSCAASGFNIKDTYIH WVRQAPGKGLEWVARIYPTNGYTRYADSVKGRF TISADTSKNTAYLQMNSLRAEDTAVYYCSRWGGD GFYAMDYWGQGLTVTVSSASTKGPSVFPLAPSSK

SEQ ID NO	Clone No.	Description	Sequence
			STSGGTAALGCLVKDYFPEPVTVSWNSGALTSGV HTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVN HKPSNTKVDKKVEPKSCRVP PPPPCCHPRLSLHRP ALEDLLLGSEANLTCTLTGLRDASGATFTWTPSSG KSAVQGPPERDLCGCYSVSSVLPGSAQPWNHGET FTCTAAHPELKTPLTATLSKSGNTFRPEVHLLPPPS EELALNELVELTCLADGFSPKDVLVRWLQGSQELP REKYLTWASRQEPSQGT TTF AVTSDLDVAAEDWK KGDTFSCMVGHEALPLAFTQKTIDRLAG
13	23776	Full	EVQLVESGGGLVQPGGSLRLSCAASGFNIKDTYIH WVRQAPGKGLEWVARIYPTNGYTRYADSVKGRF TISADTSKNTAYLQMNSLRAEDTAVYYCSRWGGD GFYAMDYWGQGT LTVSSASTKGPSVFPLAPSSK STSGGTAALGCLVKDYFPEPVTVSWNSGALTSGV HTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVN HKPSNTKVDKKVEPKSCRVP PPPPCCHPRLSLHRP ALEDLLLGSEANLTCTLTGLRDASGATFTWTPSSG KSAVQGPPERDLCGCYSVSSVLPGSAQPWNHGET FTCTAAHPELKTPLTATLSKSGNTFRPEVHLLPPPS EELALNELVELTCLADGFSPKDVLVRWLQGSQELP REKYLTWASRQEPSQGT TTF AVTSELEVAEDWK KGDTFSCMVGHEALPLAFTQKTIDRLAG
14	23777	Full	EVQLVESGGGLVQPGGSLRLSCAASGFNIKDTYIH WVRQAPGKGLEWVARIYPTNGYTRYADSVKGRF TISADTSKNTAYLQMNSLRAEDTAVYYCSRWGGD GFYAMDYWGQGT LTVSSASTKGPSVFPLAPSSK STSGGTAALGCLVKDYFPEPVTVSWNSGALTSGV HTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVN HKPSNTKVDKKVEPKSCRVP PPPPCCHPRLSLHRP ALEDLLLGSEANLTCTLTGLRDASGATFTWTPSSG KSAVQGPPERDLCGCYSVSSVLPGSAQPWNHGET FTCTAAHPELKTPLTATLSKSGNTFRPEVHLLPPPS EELALNELVTLTCLADGFSPKDVLVRWLQGSQELP REKYLTWASRQDPSQGT TTF AVTSDLEVAEDWK KGDTFSCMVGHEALPLAFTQKTIDRLAG
15	23778	Full	EVQLVESGGGLVQPGGSLRLSCAASGFNIKDTYIH WVRQAPGKGLEWVARIYPTNGYTRYADSVKGRF TISADTSKNTAYLQMNSLRAEDTAVYYCSRWGGD GFYAMDYWGQGT LTVSSASTKGPSVFPLAPSSK STSGGTAALGCLVKDYFPEPVTVSWNSGALTSGV HTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVN HKPSNTKVDKKVEPKSCRVP PPPPCCHPRLSLHRP ALEDLLLGSEANLTCTLTGLRDASGATFTWTPSSG KSAVQGPPERDLCGCYSVSSVLPGSAQPWNHGET

SEQ ID NO	Clone No.	Description	Sequence
			FTCTAAHPELKTPLTATLSKSGNTFRPEVHLLPPPS EELALNELVTLTCLARGFSPKDVLRWLQGSQELP REKYLTWASRQEPSQGTTFYVLSILRVAAEDWK KGDTFSCMVGHEALPLAFTQKTIDRLAG
16	23779	Full	EVQLVESGGGLVQPGGSLRLSCAASGFINIKDTYIH WVRQAPGKGLEWVARIYPTNGYTRYADSVKGRF TISADTSKNTAYLQMNSLRAEDTAVYYCSRWGGD GFYAMDYWGQGTLLTVSSASTKGPSVFPLAPSSK STSGGTAALGCLVKDYFPEPVTVSWNSGALTSGV HTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVN HKPSNTKVDKKVEPKSCRVPVPVPPPCCHPRLSLHRP ALEDLLGSEANLTCTLTGLRDASGATFTWTPSSG KSAVQGPPELDLCGCYSVSSVLPGSAQPWNHGET FTCTAAHPELKTPLTATLSKSGNTFRPEVHLLPPPS EELALNELVTLTCLARGFSPKDVLRWLQGSQELP REKYLTWASRQEPSQGTTFYVYSILRVAAEDWK KGDTFSCMVGHEALPLAFTQKTIDRLAG
17	23780	Full	EVQLVESGGGLVQPGGSLRLSCAASGFINIKDTYIH WVRQAPGKGLEWVARIYPTNGYTRYADSVKGRF TISADTSKNTAYLQMNSLRAEDTAVYYCSRWGGD GFYAMDYWGQGTLLTVSSASTKGPSVFPLAPSSK STSGGTAALGCLVKDYFPEPVTVSWNSGALTSGV HTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVN HKPSNTKVDKKVEPKSCRVPVPVPPPCCHPRLSLHRP ALEDLLGSEANLTCTLTGLRDASGATFTWTPSSG KSAVQGPPELDLCGCYSVSSVLPGSAQPWNHGET FTCTAAHPELKTPLTATLSKSGNTFRPEVHLLPPPS EELALNELVTLTCLARGFSPKDVLRWLQGSQELP REKYLTWASRQEPSQGTTFVYSILRVAAEDWK KGDTFSCMVGHEALPLAFTQKTIDRLAG
18	23781	Full	EVQLVESGGGLVQPGGSLRLSCAASGFINIKDTYIH WVRQAPGKGLEWVARIYPTNGYTRYADSVKGRF TISADTSKNTAYLQMNSLRAEDTAVYYCSRWGGD GFYAMDYWGQGTLLTVSSASTKGPSVFPLAPSSK STSGGTAALGCLVKDYFPEPVTVSWNSGALTSGV HTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVN HKPSNTKVDKKVEPKSCRVPVPVPPPCCHPRLSLHRP ALEDLLGSEANLTCTLTGLRDASGATFTWTPSSG KSAVQGPPELDLCGCYSVSSVLPGSAQPWNHGET FTCTAAHPELKTPLTATLSKSGNTFRPEVHLLPPPS EELALNELVTLTCMARGFSPKDVLRWLQGSQEL PREKYLTWASRQEPSQGTTFVWSILRVAAEDW KKGDTFSCMVGHEALPLAFTQKTIDRLAG

SEQ ID NO	Clone No.	Description	Sequence
19	23782	Full	EVQLVESGGGLVQPGGSLRLSCAASGFNIKDTYIH WVRQAPGKGLEWVARIYPTNGYTRYADSVKGRF TISADTSKNTAYLQMNSLRAEDTAVYYCSRWGGD GFYAMDYWGQGTLLTVSSASTKGPSVFPLAPSSK STSGGTAALGCLVKDYFPEPVTVSWNSGALTSGV HTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVN HKPSNTKVDKKVEPKSCRVP PPPPCCHPRLSLHRP ALEDLLLGSEANLTCTLTGLRDASGATFTWTPSSG KSAVQGPPERDLCGCYSVSSVLPGSAQPWNHGET FTCTAAHPELKTPLTATLSKSGNTFRPEVHLLPPPS EELALNELVTLTCLARGFSPKDVLRWLQGSQELP REKYL TWASRQEPSQGT TTFYVMSILRVA AEDWK KGDTFSCMVGHEALPLAFTQKTIDRLAG
20	23783	Full	RVPPPPPCCHPRLSLHRPALEDLLLGSEANLTCTLT GLRDASGATFTWTPSSGKSAVQGPPERDLCGCYS VSSVLPGSAQPWNHGETFTCTAAHPELKTPLTATL SKSGNTFRPEVHLLPPPSEELALNELVTLTCLARGF SPKDVLRWLQGSQELPREKYTTLASRQEPSQGT TFAVTSLLRVAAEDWKKGD TFSCMVGHEALPLAF TQKTIDRLAG
21	23784	Full	RVPPPPPCCHPRLSLHRPALEDLLLGSEANLTCTLT GLRDASGATFTWTPSSGKSAVQGPPERDLCGCYS VSSVLPGSAQPWNHGETFTCTAAHPELKTPLTATL SKSGNTFRPEVHLLPPPSEELALNELVTLTCLARGF SPKDVLRWLQGSQELPREKYVTLASRQEPSQGT TFAVTSLLRVAAEDWKKGD TFSCMVGHEALPLAF TQKTIDRLAG
22	23785	Full	RVPPPPPCCHPRLSLHRPALEDLLLGSEANLTCTLT GLRDASGATFTWTPSSGKSAVQGPPERDLCGCYS VSSVLPGSAQPWNHGETFTCTAAHPELKTPLTATL SKSGNTFRPEVHLLPPPSEELALNELVTLTCLARGF SPKDVLRWLQGSQELPREKYLTLASRQEPSQGT TFAVTSILRVAAEDWKKGD TFSCMVGHEALPLAF TQKTIDRLAG
23	23786	Full	RVPPPPPCCHPRLSLHRPALEDLLLGSEANLTCTLT GLRDASGATFTWTPSSGKSAVQGPPERDLCGCYS VSSVLPGSAQPWNHGETFTCTAAHPELKTPLTATL SKSGNTFRPEVHLLPPPSEELALNELVTLTCLARGF SPKDVLRWLQGSQELPREKYVTTASRQEPSQGT TFAVTSLLRVAAEDWKKGD TFSCMVGHEALPLAF TQKTIDRLAG
24	24674	Full	EVQLVESGGGLVQPGGSLRLSCAASGFNIKDTYIH WVRQAPGKGLEWVARIYPTNGYTRYADSVKGRF TISADTSKNTAYLQMNSLRAEDTAVYYCSRWGGD

SEQ ID NO	Clone No.	Description	Sequence
			GFYAMDYWGQGTLLTVSSASTKGPSVFPLAPSSK STSGGTAALGCLVKDYFPEPVTVSWNSGALTSGV HTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVN HKPSNTKVDKKVEPKSCRVP PPPPCCHPRLSLHRP ALEDLLLGSEANLTCTLTGLRDASGATFTWTPSSG KSAVQGPPERDLCGCYSVSSVLPGSAQPWNHGET FTCTAAHPELKTPLTATLSKSGNTFRPEVHLLPPPS EELALNELVTLVCLARGFSPKDVLRWLQGSQELP REKYLTWASRQEPSQGT TTTFFVYSILRVAEDWK KGDTFSCMVGHEALPLAFTQKTIDRLAG
25	24675	Full	EVQLVESGGGLVQPGGSLRLSCAASGFNIKDTYIH WVRQAPGKGLEWVARIYPTNGYTRYADSVKGRF TISADTSKNTAYLQMNSLRAEDTAVYYCSRWGGD GFYAMDYWGQGTLLTVSSASTKGPSVFPLAPSSK STSGGTAALGCLVKDYFPEPVTVSWNSGALTSGV HTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVN HKPSNTKVDKKVEPKSCRVP PPPPCCHPRLSLHRP ALEDLLLGSEANLTCTLTGLRDASGATFTWTPSSG KSAVQGPPERDLCGCYSVSSVLPGSAQPWNHGET FTCTAAHPELKTPLTATLSKSGNTFRPEVHLLPPPS EELALNELVTLLCLARGFSPKDVLRWLQGSQELP REKYLTWASRQEPSQGT TTTFFVYSILRVAEDWK KGDTFSCMVGHEALPLAFTQKTIDRLAG
26	24676	Full	EVQLVESGGGLVQPGGSLRLSCAASGFNIKDTYIH WVRQAPGKGLEWVARIYPTNGYTRYADSVKGRF TISADTSKNTAYLQMNSLRAEDTAVYYCSRWGGD GFYAMDYWGQGTLLTVSSASTKGPSVFPLAPSSK STSGGTAALGCLVKDYFPEPVTVSWNSGALTSGV HTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVN HKPSNTKVDKKVEPKSCRVP PPPPCCHPRLSLHRP ALEDLLLGSEANLTCTLTGLRDASGATFTWTPSSG KSAVQGPPERDLCGCYSVSSVLPGSAQPWNHGET FTCTAAHPELKTPLTATLSKSGNTFRPEVHLLPPPS EELALNELVTLICLARGFSPKDVLRWLQGSQELP REKYLTWASRQEPSQGT TTTFFVYSILRVAEDWK KGDTFSCMVGHEALPLAFTQKTIDRLAG
27	24677	Full	RVPPPPPCCHPRLSLHRPALEDLLLGSEANLTCTLT GLRDASGATFTWTPSSGKSAVQGPPERDLCGCYS VSSVLPGSAQPWNHGETFTCTAAHPELKTPLTATL SKSGNTFRPEVHLFPPPSEELALNELVTLTCLARGF SPKDVLRWLQGSQELPREKYVTTASRQEPSQGT TFAVTSLLRVAEDWKKGDTFSCMVGHEALPLAF TQKTIDRLAG

SEQ ID NO	Clone No.	Description	Sequence
28	24678	Full	EVQLVESGGGLVQPGGSLRLSCAASGFNIKDTYIH WVRQAPGKGLEWVARIYPTNGYTRYADSVKGRF TISADTSKNTAYLQMNSLRAEDTAVYYCSRWGGD GFYAMDYWGQGTLLTVSSASTKGPSVFPLAPSSK STSGGTAALGCLVKDYFPEPVTVSWNSGALTSGV HTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVN HKPSNTKVDKKVEPKSCRVP PPPPCCHPRLSLHRP ALEDLLLGSEANLTCTLTGLRDASGATFTWTPSSG KSAVQGPPERDLCGCYSVSSVLPGSAQPWNHGET FTCTAAHPELKTPLTATLSKSGNTFRPEVYLLPPPS EELALNELVTLTCLARGFSPKDVLVRWLQGSQELP REKYLTWASRQEPSQGT TTFVYSILRVA AEDWK KGDTFSCMVGHEALPLAFTQKTIDRLAG
29	24679	Full	RVPPPPPCCHPRLSLHRPALEDLLLGSEANLTCTLT GLRDASGATFTWTPSSGKSAVQGPPERDLCGCYS VSSVLPGSAQPWNHGETFTCTAAHPELKTPLTATL SKSGNTFRPEVYLLPPSEELALNELVTLTCLARGF SPKDVLVRWLQGSQELPREKYVTTASRQEPSQGT TFAVTSLLRVAAEDWKKGDTFSCMVGHEALPLAF TQKTIDRLAG
30	25880	Full	EVQLVESGGGLVQPGGSLRLSCAASGFNIKDTYIH WVRQAPGKGLEWVARIYPTNGYTRYADSVKGRF TISADTSKNTAYLQMNSLRAEDTAVYYCSRWGGD GFYAMDYWGQGTLLTVSSASTKGPSVFPLAPSSK STSGGTAALGCLVKDYFPEPVTVSWNSGALTSGV HTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVN HKPSNTKVDKKVEPKSCRVP PPPPCCHPRLSLHRP ALEDLLLGSEANLTCTLTGLRDASGATFTWTPSSG KSAVQGPPERDLCGCYSVSSVLPGSAQPWNHGET FTCTAAHPELKTPLTATLSKSGNTFRPEVCLPPPS EELALNELVTLTCLARGFSPKDVLVRWLQGSQELP REKYLTWASRQEPSQGT TTFVYSILRVA AEDWK KGDTFSCMVGHEALPLAFTQKTIDRLAG
31	25881	Full	RVPPPPPCCHPRLSLHRPALEDLLLGSEANLTCTLT GLRDASGATFTWTPSSGKSAVQGPPERDLCGCYS VSSVLPGSAQPWNHGETFTCTAAHPELKTPLTATL SKSGNTFRPEVHLLPPCSEELALNELVTLTCLARGF SPKDVLVRWLQGSQELPREKYVTTASRQEPSQGT TFAVTSLLRVAAEDWKKGDTFSCMVGHEALPLAF TQKTIDRLAG
32	25882	Full	EVQLVESGGGLVQPGGSLRLSCAASGFNIKDTYIH WVRQAPGKGLEWVARIYPTNGYTRYADSVKGRF TISADTSKNTAYLQMNSLRAEDTAVYYCSRWGGD GFYAMDYWGQGTLLTVSSASTKGPSVFPLAPSSK

SEQ ID NO	Clone No.	Description	Sequence
			STSGGTAALGCLVKDYFPEPVTVSWNSGALTSGV HTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVN HKPSNTKVDKKVEPKSCRVP PPPPCCHPRLSLHRP ALEDLLGSEANLTCTLTGLRDASGATFTWTPSSG KSAVQGPPERDLCGCYSVSSVLPGSAQPWNHGET FTCTAAHPELKTPLTATLSKSGNTFRPEVHLLPPCS EELALNELVTLTCLARGFSPKDVLRWLQGSQELP REKYL TWASRQEPSQGT TTFVYSILRVAAEDWK KGDTFSCMVGHEALPLAFTQKTIDRLAG
33	25883	Full	RVPPPPPCCHPRLSLHRPALEDLLGSEANLTCTLT GLRDASGATFTWTPSSGKSAVQGPPERDLCGCYS VSSVLPGSAQPWNHGETFTCTAAHPELKTPLTATL SKSGNTFRPEVCLLPPSEELALNELVTLTCLARGF SPKDVLRWLQGSQELPREKYVTTASRQEPSQGT TFAVTSLLRVAAEDWKKGDTFSCMVGHEALPLAF TQKTIDRLAG
34	25884	Full	EVQLVESGGGLVQPGGSLRLSCAASGFNIKDTYIH WVRQAPGKGLEWVARIYPTNGYTRYADSVKGRF TISADTSKNTAYLQMNSLRAEDTAVYYCSRWGGD GFYAMDYWGQGLTVTVSSASTKGPSVFPLAPSSK STSGGTAALGCLVKDYFPEPVTVSWNSGALTSGV HTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVN HKPSNTKVDKKVEPKSCRVP PPPPCCHPRLSLHRP ALEDLLGSEANLTCTLTGLRDASGATFTWTPSSG KSAVQGPPERDLCGCYSVSSVLPGSAQPWNHGET FTCTAAHPELKTPLTATLSKSGNTFRPEVCLLPPCS EELALNELVTLTCLARGFSPKDVLRWLQGSQELP REKYL TWASRQEPSQGT TTFVYSILRVAAEDWK KGDTFSCMVGHEALPLAFTQKTIDRLAG
35	25885	Full	RVPPPPPCCHPRLSLHRPALEDLLGSEANLTCTLT GLRDASGATFTWTPSSGKSAVQGPPERDLCGCYS VSSVLPGSAQPWNHGETFTCTAAHPELKTPLTATL SKSGNTFRPEVCLLPPCSEELALNELVTLTCLARGF SPKDVLRWLQGSQELPREKYVTTASRQEPSQGT TFAVTSLLRVAAEDWKKGDTFSCMVGHEALPLAF TQKTIDRLAG
36	25886	Full	EVQLVESGGGLVQPGGSLRLSCAASGFNIKDTYIH WVRQAPGKGLEWVARIYPTNGYTRYADSVKGRF TISADTSKNTAYLQMNSLRAEDTAVYYCSRWGGD GFYAMDYWGQGLTVTVSSASTKGPSVFPLAPSSK STSGGTAALGCLVKDYFPEPVTVSWNSGALTSGV HTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVN HKPSNTKVDKKVEPKSCRVP PPPPCCHPRLSLHRP ALEDLLGSEANLTCTLTGLRDASGATFTWTPSSG

SEQ ID NO	Clone No.	Description	Sequence
			KSAVQGPPELDLCGCYSVSSVLPGSAQPWNHGET FTCTAAHPELKTPLTATLSKSGNTFRPEVCLLPPPS EELALNELVTLTCLARGFSPKDVLRWLQGSQELP REKYLTWASRQEPSQGTTFFAVTSILRVAAEDWK KGDTFSCMVGHEALPLAFTQKTIDRLAG
37	25887	Full	RVPPPPPCCHPRLSLHRPALEDLLGSEANLTCTLT GLRDASGATFTWTPSSGKSAVQGPPELDLCGCYS VSSVLPGSAQPWNHGETFTCTAAHPELKTPLTATL SKSGNTFRPEVHLLPPCSEELALNELVTLTCLARGF SPKDVLRWLQGSQELPREKYLTWASRQEPSQGT TTFVTSILRVAAEDWKKGDTFSCMVGHEALPLA FTQKTIDRLAG
38	N/A	Anti-Her2 Fab HC	EVQLVESGGGLVQPGGSLRLSCAASGFNIKDTYIH WVRQAPGKGLEWVARIYPTNGYTRYADSVKGRF TISADTSKNTAYLQMNSLRADTA VYYCSRWGGD GFYAMDYWGQGLTVTVSSASTKGPSVFPLAPSSK STSGGTAALGCLVKDYFPEPVTVSWNSGALTSGV HTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVN HKPSNTKVDKKV
39	N/A	Anti-Her2 Fab LC	DIQMTQSPSSLSASVGDRVTITCRASQDVNTAVAW YQQKPGKAPKLLIYSASFLYSGVPSRFSGRSGTDF TLTISSLQPEDFATYYCQQHYTTPTFGQGTKVEIK RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPRE AKVQWKVDNALQSGNSQESVTEQDSKDYSLSS TLTSLKADYEKHKVYACEVTHQGLSSPVTKSFNR GEC
40	N/A	IgG1 upper hinge	EPKSC
41	N/A	IgA2 hinge	RVPPPPP
42	N/A	IgA2m1 wild type sequence	CCHPRLSLHRPALEDLLGSEANLTCTLTGLRDAS GATFTWTPSSGKSAVQGPPELDLCGCYSVSSVLP CAQPWNHGETFTCTAAHPELKTPLTANITKSGNTF RPEVHLLPPPSEELALNELVTLTCLARGFSPKDVLR RWLQGSQELPREKYLTWASRQEPSQGTTFFAVTSI LRVAAEDWKKGDTFSCMVGHEALPLAFTQKTIDR LAG
43	N/A	IgA2m1 C5092S/N5 120T/I5121 L/T5122S/ Δ α -tailpiece	CCHPRLSLHRPALEDLLGSEANLTCTLTGLRDAS GATFTWTPSSGKSAVQGPPELDLCGCYSVSSVLP SAQPWNHGETFTCTAAHPELKTPLTATLSKSGNTF RPEVHLLPPPSEELALNELVTLTCLARGFSPKDVLR RWLQGSQELPREKYLTWASRQEPSQGTTFFAVTSI LRVAAEDWKKGDTFSCMVGHEALPLAFTQKTIDR LAG

SEQ ID NO	Clone No.	Description	Sequence
44	N/A	IgA1 wild type	CCHPRLSLHRPALEDLLLGSEANLTCTLTGLRDAS GVFTFTWTPSSGKSAVQGPPERDLCGCYSVSSVLP CAEPWNHGKTFTCTAAYPESKTPLTATLSKSGNTF RPEVHLLPPPSEELALNELVTLTCLARGFSPKDV LVRWLQGSQELPREKYLTWASRQEPSQGTTF FAVTSILRVAAEDWKKGDTFSCMVGHEALPLAFTQKTIDRLAG
45	N/A	IgA2m2 wild type	CCHPRLSLHRPALEDLLLGSEANLTCTLTGLRDAS GATFTWTPSSGKSAVQGPPERDLCGCYSVSSVLP CAQPWNHGETFTCTAAHPELKTPLTANITKSGNTF RPEVHLLPPPSEELALNELVTLTCLARGFSPKDV LVRWLQGSQELPREKYLTWASRQEPSQGTTTYAVTSILRVAAEDWKKGETFSCMVGHEALPLAFTQKTIDRLAG
46	N/A	α -tailpiece IgA1 IgA2m1	KPTHVNVSVVMAEVDGTCY
47	N/A	α -tailpiece IgA2m2	KPTHINVSVMMAEADGTCY
48	N/A	J Chain	EFATMRPTWAWWLFLVLLLALWAPARGQEDERI VLVDNKCKCARITSRIIRSSDPNEDIVERNIRIIVPL NNRENISDPTSPLRTRFVYHLSDLCKKCDPTEVELD NQIVTATQSNICDEDSATETCYTYDRNKCYTAVVPL LVYGGGETKMVETALTPDACYPD
49	N/A	Signal peptide	EFATMRPTWAWWLFLVLLLALWAPARG

It is to be understood that the methods and compositions described herein are not limited to the particular methodology, protocols, cell lines, constructs, and reagents described herein and as such may vary. It is also to be understood that the terminology used herein is for the purpose of describing particular embodiments only and is not intended to limit the scope of the methods and compositions described herein, which will be limited only by the appended claims.

The disclosures of all patents, patent applications, publications and database entries referenced in this specification are hereby specifically incorporated by reference in their entirety to the same extent as if each such individual patent, patent application, publication and database entry were specifically and individually indicated to be incorporated by reference.

WE CLAIM:

1. An IgA heterodimeric Fc (IgA HetFc) construct comprising a first Fc polypeptide and a second Fc polypeptide, the first Fc polypeptide comprising a first CH3 domain sequence and the second Fc polypeptide comprising an second CH3 domain sequence, the first and second CH3 domain sequences forming a modified CH3 domain,

wherein the first and second CH3 domain sequences comprise amino acid mutations that promote formation of a heterodimeric Fc over a homodimeric Fc,

wherein:

the amino acid mutations in the first CH3 domain sequence comprise an amino acid substitution at position A6085Y selected from A6085YF, A6085YY, A6085YM, A6085YW and A6085YH, and an amino acid substitution at position T6086 selected from T6086Y, T6086F, T6086M, T6086W and T6086H, and

the amino acid mutations in the second CH3 domain sequence comprise an amino acid substitution at position W6081 selected from W6081T, W6081L, W6081A, W6081V and W6081I,

wherein the heterodimeric Fc is formed with a purity of 70% or higher,

and wherein the numbering of amino acid positions is according to IMGT numbering.

2. The IgA HetFc construct according to claim 1, wherein the modified CH3 domain has a melting temperature (T_m) that is 60°C or higher.

3. The IgA HetFc construct according to claim 1, wherein the modified CH3 domain has a melting temperature (T_m) that is $\pm 10^\circ\text{C}$ of the T_m of a corresponding wild-type IgA CH3 domain.

4. The IgA HetFc construct according to any one of claims 1 to 3, wherein the amino acid substitution at position A6085Y is A6085YF, A6085YY or A6085YW.

5. The IgA HetFc construct according to any one of claims 1 to 3, wherein the amino acid substitution at position A6085Y is A6085YF or A6085YY.

6. The IgA HetFc construct according to any one of claims 1 to 5, wherein the amino acid substitution at position T6086 is T6086Y, T6086F or T6086W.

7. The IgA HetFc construct according to any one of claims 1 to 5, wherein the amino acid substitution at position T6086 is T6086Y.

8. The IgA HetFc construct according to any one of claims 1 to 7, wherein the amino acid substitution at position W6081 is W6081T or W6081L.

9. The IgA HetFc construct according to any one of claims 1 to 3, wherein the amino acid mutations in the first CH3 domain sequence comprise the amino acid substitutions A6085YF, and T6086W, and the amino acid mutations in the second CH3 domain sequence comprise the amino acid substitution W6081T or W6081L.

10. The IgA HetFc construct according to claim 9, wherein the amino acid mutations in the second CH3 domain sequence comprise the amino acid substitution W6081T.

11. The IgA HetFc construct according to any one of claims 1 to 10, wherein the amino acid mutations in the second CH3 domain sequence further comprise an amino acid substitution at position L6079 selected from L6079V, L6079T, L6079A and L6079I.

12. The IgA HetFc construct according to any one of claims 1 to 10, wherein the amino acid mutations in the second CH3 domain sequence further comprise an amino acid substitution at position L6079 selected from L6079V and L6079T.

13. The IgA HetFc construct according to any one of claims 1 to 12, wherein the amino acid mutations in the second CH3 domain sequence further comprise an amino acid substitution at position I6088 selected from I6088L, I6088A, L6088V and L6088T.

14. The IgA HetFc construct according to any one of claims 1 to 12, wherein the amino acid mutations in the second CH3 domain sequence further comprise the amino acid substitution I6088L.

15. The IgA HetFc construct according to any one of claims 1 to 14, wherein the amino acid mutations in the first CH3 domain sequence further comprise an amino acid substitution at position T6022 selected from T6022V, T6022I, T6022L and T6022A.

16. The IgA HetFc construct according to any one of claims 1 to 14, wherein the amino acid mutations in the first CH3 domain sequence further comprise an amino acid substitution at position T6022 selected from T6022V, T6022I and T6022L.

17. The IgA HetFc construct according to any one of claims 1 to 16, wherein the amino acid mutations in the second CH3 domain sequence further comprise an amino acid substitution at position L6007 selected from L6007F, L6007Y, L6007M, L6007W, L6007H and L6007I.

18. The IgA HetFc construct according to any one of claims 1 to 16, wherein the amino acid mutations in the second CH3 domain sequence further comprise the amino acid substitution L6007F.

19. The IgA HetFc construct according to any one of claims 1 to 18, wherein the amino acid mutations in the first CH3 domain sequence further comprise an amino acid substitution at position H6005 selected from H6005Y, H6005F, H6005M and H6005W.

20. The IgA HetFc construct according to any one of claims 1 to 18, wherein the amino acid mutations in the first CH3 domain sequence further comprise the amino acid substitution H6005Y.

21. The IgA HetFc construct according to any one of claims 1 to 20, wherein the amino acid mutations in the second CH3 domain sequence further comprise an amino acid substitution at position H6005 selected from H6005Y, H6005F, H6005M and H6005W.

22. The IgA HetFc construct according to any one of claims 1 to 20, wherein the amino acid mutations in the second CH3 domain sequence further comprise the amino acid substitution H6005Y.

23. The IgA HetFc construct according to any one of claims 1 to 10, wherein the modified CH3 domain further comprises amino acid substitutions to introduce cysteine residues capable of forming a disulfide bond.

24. The IgA HetFc construct according to claim 23, wherein the modified CH3 domain comprises two amino acid substitutions to introduce cysteine residues that form one disulfide bond in the modified CH3 domain, or four amino acid substitutions to introduce cysteine residues that form two disulfide bonds in the modified CH3 domain.

25. The IgA Het Fc construct according to claim 23, wherein the amino acid substitutions to introduce cysteine residues comprise the mutation H6005C in one CH3 domain sequence and the mutation P6010C in the other CH3 domain sequence.

26. The IgA HetFc construct according to claim 23, wherein the amino acid substitutions to introduce cysteine residues comprise the mutations H6005C and P6010C in one CH3 domain sequence and the mutations P6010C and H6005C in the other CH3 domain sequence.

27. An IgA heterodimeric Fc (IgA HetFc) construct comprising a first Fc polypeptide and a second Fc polypeptide, the first Fc polypeptide comprising a first CH3 domain sequence and the second Fc polypeptide comprising an second CH3 domain sequence, the first and second CH3 domain sequences forming a modified CH3 domain,

wherein the first and second CH3 domain sequences comprise amino acid mutations that promote formation of a heterodimeric Fc over a homodimeric Fc,

wherein:

(a) the amino acid mutations in the first CH3 domain sequence comprise the amino acid substitutions: A6085YY and T6086L, and the amino acid mutations in the second CH3 domain sequence comprise the amino acid substitutions: L6079T, W6081L and I6088L; or

(b) the amino acid mutations in the first CH3 domain sequence comprise the amino acid substitutions: A6085YY and T6086Y, and the amino acid mutations in the second CH3 domain sequence comprise the amino acid substitutions: L6079T, W6081L and I6088L; or

(c) the amino acid mutations in the first CH3 domain sequence comprise the amino acid substitutions: A6085YF and T6086Y, and the amino acid mutations in the second CH3 domain sequence comprise the amino acid substitutions: L6079V, W6081L and I6088L; or

(d) the amino acid mutations in the first CH3 domain sequence comprise the amino acid substitutions: A6085YF and T6086Y, and the amino acid mutations in the second CH3 domain sequence comprise the amino acid substitutions: L6079V, W6081T and I6088L; or

(e) the amino acid mutations in the first CH3 domain sequence comprise the amino acid substitutions: T6022V, A6085YF and T6086Y, and the amino acid mutations in the second CH3 domain sequence comprise the amino acid substitutions: L6079V, W6081T and I6088L; or

(f) the amino acid mutations in the first CH3 domain sequence comprise the amino acid substitutions: T6022L, A6085YF and T6086Y, and the amino acid mutations in the second CH3 domain sequence comprise the amino acid substitutions: L6079V, W6081T and I6088L; or

(g) the amino acid mutations in the first CH3 domain sequence comprise the amino acid substitutions: T6022I, A6085YF and T6086Y, and the amino acid mutations in the second CH3 domain sequence comprise the amino acid substitutions: L6079V, W6081T and I6088L; or

(h) the amino acid mutations in the first CH3 domain sequence comprise the amino acid substitutions: A6085YF and T6086Y, and the amino acid mutations in the second CH3 domain sequence comprise the amino acid substitutions: L6007F, L6079V, W6081T and I6088L

(i) the amino acid mutations in the first CH3 domain sequence comprise the amino acid substitutions: H6005Y, A6085YF and T6086Y, and the amino acid mutations in the second CH3 domain sequence comprise the amino acid substitutions: H6005Y, L6079V, W6081T and I6088L; or

(j) the amino acid mutations in the first CH3 domain sequence comprise the amino acid substitutions: H6005C, A6085YF and T6086Y, and the amino acid mutations in the second CH3 domain sequence comprise the amino acid substitutions: P6010C, L6079V, W6081T and I6088L; or

(k) the amino acid mutations in the first CH3 domain sequence comprise the amino acid substitutions: P6010C, A6085YF and T6086Y, and the amino acid mutations in the second CH3 domain sequence comprise the amino acid substitutions: H6005C, L6079V, W6081T and I6088L; or

(l) the amino acid mutations in the first CH3 domain sequence comprise the amino acid substitutions: H6005C, P6010C, A6085YF and T6086Y, and the amino acid mutations in the

second CH3 domain sequence comprise the amino acid substitutions: H6005C, P6010C, L6079V, W6081T and I6088L,

wherein the heterodimeric Fc is formed with a purity of 70% or higher,

and wherein the numbering of amino acid positions is according to IMGT numbering.

28. The IgA HetFc construct according to claim 27, wherein the modified CH3 domain has a melting temperature (T_m) that is 60°C or higher.

29. The IgA HetFc construct according to claim 27, wherein the modified CH3 domain has a melting temperature (T_m) that is $\pm 10^\circ\text{C}$ of the T_m of a corresponding wild-type IgA CH3 domain.

30. The IgA HetFc construct according to any one of claims 1 to 29 further comprising one or more target binding domains.

31. The IgA HetFc construct according to claim 30, wherein the one or more target binding domains are antigen-binding antibody fragments.

32. The IgA HetFc construct according to claim 31, wherein each of the one or more antigen-binding antibody fragments are independently selected from a Fab and an scFv.

33. The IgA HetFc construct according to any one of claims 30 to 32, wherein the IgA HetFc construct comprises two target binding domains and is bispecific.

34. The IgA HetFc construct according to any one of claims 1 to 33, wherein the modified IgA CH3 domain comprises an α -tailpiece.

35. The IgA HetFc construct according to any one of claims 1 to 33, wherein the modified IgA CH3 domain lacks an α -tailpiece.

36. A conjugate comprising the IgA HetFc construct according to any one of claims 1 to 35 and one or more therapeutic, diagnostic or labeling agents.

37. An IgA HetFc multimer comprising two or more IgA HetFc constructs according to any one of claims 1 to 34 and a J chain, wherein two of the IgA HetFc constructs are joined by the J chain.
38. A pharmaceutical composition comprising the IgA HetFc construct according to any one of claims 1 to 35 and a pharmaceutically acceptable carrier or diluent.
39. A pharmaceutical composition comprising the conjugate according to claim 36 and a pharmaceutically acceptable carrier or diluent.
40. A pharmaceutical composition comprising the IgA HetFc multimer according to claim 37 and a pharmaceutically acceptable carrier or diluent.
41. An isolated polynucleotide or set of polynucleotides encoding the IgA HetFc construct according to any one of claims 1 to 35.
42. A vector set or set of vectors comprising one or more polynucleotides encoding the IgA HetFc according to any one of claims 1 to 35.
43. A host cell comprising one or more polynucleotides encoding the IgA HetFc according to any one of claims 1 to 35.
44. A method of preparing the IgA HetFc construct according to any one of claims 1 to 35 comprising transfecting a host cell with one or more polynucleotides encoding the IgA HetFc construct, and culturing the host cell under conditions suitable for expression of the IgA HetFc construct.
45. A method of preparing the IgA HetFc multimer according to claim 37 comprising transfecting a host cell with one or more polynucleotides encoding the IgA HetFc construct according to claim 34 and a polynucleotide encoding a J chain, and culturing the host cell under conditions suitable for expression of the IgA HetFc construct and the J chain.
46. An IgA HetFc construct of any one of claims 1 to 35, wherein the IgA HetFc includes one or more mutations to eliminate binding to a binding target.

47. An IgA HetFc construct of any one of claims 1 to 35, wherein the IgA HetFc includes one or more mutations to introduce binding to the Neonatal Fc Receptor (FcRn).