# NOVEL MUTATIONS THAT ENHANCE THE DNA CLEAVAGE ACTIVITY OF ACIDAMINOCOCCUS SP. CPF1

## CROSS-REFERENCE TO RELATED APPLICATIONS

**[0001]** This application claims benefit of priority under 35 U.S.C. 119 to U.S. Provisional Patent Application Serial Number 62/870,268, filed July 3, 2019 and entitled "OPTIMIZED CAS12A (CPF1) PROTEINS FOR EFFICIENT GENOME EDITING IN EUKARYOTIC CELLS," U.S. Provisional Patent Application Serial Number 62/749,607, filed October 23, 2018 and entitled "DEEP-SCANNING MUTAGENESIS UNCOVERS NOVEL MUTATIONS THAT ENHANCE THE DNA CLEAVAGE ACTIVITY OF ACIDAMINOCOCCUS SP. CAS12A/CAS12A AT NON-CANONICAL TTTT PAM SITES" and U.S. Provisional Patent Application Serial Number 62/716,138, filed August 8, 2018 and entitled "NOVEL MUTATIONS THAT ENHANCE THE DNA CLEAVAGE ACTIVITY OF ACIDAMINOCOCCUS SP. CPF1," the contents of each application are herein incorporated by reference in its entirety.

## FIELD OF THE INVENTION

**[0002]** This invention pertains to the ability to cleave double-stranded DNA of living organisms at precise positions with the CRISPR/Cas12a (Cpf1) nuclease system. In particular, a series of recombinant Cas12a proteins are described that are useful in a eukaryotic cell context.

## SEQUENCE LISTING

**[0003]** The instant application contains a Sequence Listing that has been submitted in ASCII format via EFS-Web and is hereby incorporated by reference in its entirety. The ASCII copy, created on _____, is named _____, and is _____ bytes in size.

## BACKGROUND OF THE INVENTION

**[0004]** Cas12a is an RNA-guided endonuclease found in bacterial species including *Acidaminococcus sp.* and is part of the Clustered Regularly Interspaced Short Palindromic Repeat (CRISPR) adaptive immune system. Cas12a is guided to a 21~24-nt DNA target

sequence, or commonly referred as protospacer, by a target site-specific 21~24-nt complementary RNA. The Cas12a-gRNA ribonucleoprotein (RNP) complex mediates double-stranded DNA breaks (DSBs), which are then repaired by either the non-homologous end joining (NHEJ, typically introduces mutations or indels at the cut site), or the homology directed repair (HDR) system for precise editing if a suitable template nucleic acid is present.

**[0005]** Critical to the recognition of correct DNA target for Cas12a includes both crRNA and the canonical "TTTV" protospacer adjacent motif (PAM), which is a 4-bp sequence immediately upstream of the protospacer. Compared to the 2-bp NGG PAM of Cas9 from *Streptococcus pyogenes*, Cas12a expanded the targetable loci in genome editing, particularly over the AT-rich sites that are inaccessible to the Cas9 system. However, due to its relatively low enzymatic activity, the likelihood that efficient genome editing can be achieved for a given site is much lower than that of the Cas9 system, which restricts its broader application. As the consequence, the Cas12a system is frequently considered as an alternative approach only when the genomic site is not targetable by Cas9.

**[0006]** Protein engineering by mutagenesis can alter the preference of PAM sequence of CRISPR system. Through a structural-guided mutagenic screening of residues in proximity of PAM sequence, previous study has identified two AsCpf1 variants that are compatible with TYCV and TATV PAMs, respectively. Although these variants collectively expanded the targetable sites of Cpf1 system over the coding region of the human genome by 3-fold, the utility of each individual variant is still limited, due to their mutually exclusive requirement of PAM sequences (TYCV vs TATV vs TTTV). Identifying Cpf1 variants with shorter PAM and greater sequence flexibility without sacrificing the activity at canonical PAM sites is highly desirable.

**[0007]** Thus, there is a need to enhance the utility of Cas12a. One aspect of the present application is to enhance the utility of Cpf1 by broadening its PAM compatibility. In this regard, certain novel *AsCas12a* variants with enhanced activity have been discovered. Another desired objective is to maximize delivery of the bacterial protein to the eukaryotic nucleus while simultaneously avoiding disruption of basic Cas12a function. Since the Cas12a is a bacterial protein, certain molecular genetic obstacles must first be overcome before one can achieve successful delivery of the protein to eukaryotic cells. This invention provides unique solutions to achieving these objectives.

## BRIEF SUMMARY OF THE INVENTION

**[0008]** In a first aspect, A CRISPR-associated protein comprising a polypeptide encoding a variant of AsCpf1 is provided. The variant of AsCpf1 is selected from the group consisting of M537R (SEQ ID NO.: 472), F870L (SEQ ID NO.: 473), and M537R/F870L (SEQ ID NO.: 465).

**[0009]** In a second aspect, a CRISPR ribonucleoprotein complex is provided. The CRISPR ribonucleoprotein complex includes a guide RNA and a CRISPR-associated protein. The CRISPR-associated protein including a polypeptide encoding a variant of AsCpf1. The variant of AsCpf1 is selected from the group consisting of M537R (SEQ ID NO.: 472), F870L (SEQ ID NO.: 473), and M537R/F870L (SEQ ID NO.: 465).

**[0010]** In a third aspect, a method of increasing efficiency of gene editing at TTT**N** PAM sites in a cell with a CRISPR ribonucleoprotein complex is provided. The method includes the step of contacting a cell with the CRISPR ribonucleoprotein complex. The CRISPR ribonucleoprotein complex includes a guide RNA and a CRISPR-associated protein. The CRISPR-associated protein including a polypeptide encoding a variant of AsCpf1. The variant of AsCpf1 is selected from the group consisting of M537R (SEQ ID NO.: 472), F870L (SEQ ID NO.: 473), and M537R/F870L (SEQ ID NO.: 465).

**[0011]** In a fourth aspect, a kit comprising a guide RNA and a CRISPR-associated protein is provided. The CRISPR-associated protein includes a polypeptide encoding a variant of AsCpf1.

**[0012]** In a fifth aspect, CRISPR-associated protein comprising a polypeptide encoding a variant of AsCas12a, wherein the variant of AsCas12a is selected from the group consisting of at least one variant amino acid selected from amino acid positions 499-640 and 840-913, provided that the variant AsCas12a provides an improvement in CRISPR/AsCas12a-associated nuclease activity at non-canonical TTTT PAM sites.

**[0013]** In a sixth aspect, a CRISPR ribonucleoprotein complex is provided. The CRISPR ribonucleoprotein complex includes a guide RNA and a CRISPR-associated protein. The CRISPR-associated protein includes a polypeptide encoding a variant of AsCas12a, wherein the variant of AsCas12a is selected from the group consisting of at least one variant amino acid selected from amino acid positions 499-640 and 840-913, provided that the variant AsCas12a provides an improvement in CRISPR/AsCas12a-associated nuclease activity at non-canonical TTTT PAM sites.

**[0014]** In a seventh aspect, a method of increasing efficiency of gene editing at non-canonical TTTT PAM sites in a cell with a CRISPR ribonucleoprotein complex is provided. The method includes a step of contacting a cell with the CRISPR ribonucleoprotein complex that includes a guide RNA and a CRISPR-associated protein. The CRISPR-associated protein includes a polypeptide encoding a variant of AsCas12a, wherein the variant of AsCas12a is selected from the group consisting of at least one variant amino acid selected from amino acid positions 499-640 and 840-913, provided that the variant AsCas12a provides an improvement in CRISPR/AsCas12a-associated nuclease activity at non-canonical TTTT PAM sites.

**[0015]** In an eighth aspect, a kit including a guide RNA and a CRISPR-associated protein comprising a polypeptide encoding a variant of AsCas12a is provided. The variant of AsCas12a is selected from the group consisting of at least one variant amino acid selected from amino acid positions 499-640 and 840-913, provided that the variant AsCas12a provides an improvement in CRISPR/AsCas12a-associated nuclease activity at non-canonical TTTT PAM sites.

**[0016]** In a ninth aspect, a nucleic acid encoding a CRISPR-associated protein comprising a polypeptide encoding a variant of AsCas12a is provided. The variant of AsCas12a is selected from the group consisting of at least one variant amino acid selected from amino acid positions 499-640 and 840-913, provided that the variant AsCas12a provides an improvement in CRISPR/AsCas12a-associated nuclease activity at non-canonical TTTT PAM sites.

**[0017]** In a tenth aspect, a polynucleotide sequence encoding a Cas12a polypeptide is provided. The polynucleotide sequence includes one member selected from the group consisting of SEQ ID NOs.: 5-17.

**[0018]** In an eleventh aspect, an amino acid sequence encoding a Cas12a polypeptide is provided. The amino acid sequence includes one member selected from the group consisting of SEQ ID NOs.: 18-30.

**[0019]** In a twelfth aspect, a CAS endonuclease system comprising an expression cassette encoding a polynucleotide sequence encoding a Cas12a polypeptide is provided. The includes one member selected from the group consisting of SEQ ID NOs.: 5-17.

**[0020]** In a thirteenth aspect, CAS endonuclease system comprising an amino acid sequence encoding a Cas12a polypeptide is provided The amino acid sequence includes one member selected from the group consisting of SEQ ID NOs.: 18-30.

**[0021]** In a fourteenth aspect, a method of performing genome editing in a eukaryotic cells is provided. The method includes the step of introducing an CAS endonuclease system into the eukaryotic cell, said CAS endonuclease system comprising an expression cassette encoding a polynucleotide sequence encoding a Cas12a polypeptide, comprising one member selected from the group consisting of SEQ ID NOs.: 5-17.

**[0022]** In a fifteenth aspect, a method of performing genome editing in a eukaryotic cell is provided. The method includes the step of introducing an CAS endonuclease system into the eukaryotic cell, said CAS endonuclease system comprising an amino acid sequence encoding a Cas12a polypeptide comprising one member selected from the group consisting of SEQ ID NOs.: 18-30.

**[0023]** In a sixteenth aspect, an CRISPR-associated protein comprising a fusion polypeptide is provided. The fusion polypeptide includes an AsCas12a open reading frame, a nuclear localization signal, optionally an amino acid linker and optionally an affinity tag.

**[0024]** In a seventeenth aspect, a method of performing genome editing in a eukaryotic cell is provided. The method includes the step of introducing an CAS endonuclease system into the eukaryotic cell, said CAS endonuclease system comprising a CRISPR-associated protein of according to the sixteenth aspect.

## BRIEF DESCRIPTION OF THE DRAWINGS

**[0025]** **FIG. 1** depicts multiple recombinant forms of Cas12a yields a spectrum of editing efficiencies. A series of recombinant Cas12a proteins with differing composition and arrangement of NLS sequences, purification tags, and linkers (A-M; corresponding to SEQ ID NOs.:18-30) were cloned and purified to homogeneity. The resulting purified Cas12a derivatives were delivered into HEK293 cells by electroporation complexed to RNA guides that target the *HPRT*-38186 (SEQ ID NO.:1) and *HPRT*-38228 loci (SEQ ID NO.:2). DNA was isolated from genome editing experiments 48 hr later, and editing efficiencies were determined by PCR amplification of edited loci using *HPRT*-FWD (SEQ ID NO.:3) and *HPRT*-REV (SEQ ID NO.:4) primers and the Alt-R Genome Editing Detection Kit (Integrated DNA Technologies). The following abbreviations apply for the illustrated constructs: V5 refers to V5 epitope tag (SEQ ID NO.: 485); SV40 refers to a nuclear

localization signal from simian virus SV40 large tumor antigen (SEQ ID NO.: 475); Cas12a refers to a Cas12a coding sequence; HIS refers to a hexahistidine tag (SEQ ID NO.: 487); OpT refers to an optimized nuclear localization signal (SEQ ID NO.: 477); aNLS refers to an alternative nuclear localization signal(SEQ ID NO.: 479); BIP1 refers to a first bipartite nuclear localization signal (SEQ ID NO.: 481); and BIP2 refers to a second bipartite nuclear localization signal (SEQ ID NO.: 483). The arrows provided in the constructs depict transcriptional start sites for mRNA transcripts originating from the DNA.

**[0026]** **FIG. 2** shows exemplary results of M537R and F870L mutations with enhanced the cleavage activity of Cpf1 in a bacterial-based activity assay. The screening *E.coli* strains were transformed with Cpf1 expression vectors and the crRNA targeting HPRT-38346 site on the toxin expression plasmid. The apparent activity of Cpf1 for TTTT or TTTC PAM can be estimated by the number of survived colonies under arabinose selection when equivalent amount of plasmids is delivered. Clearly, both mutations increased the survival rate at TTTC and TTTT PAM sites, indicating an improved cleavage activity over the WT-Cpf1.

**[0027]** **FIG. 3A** shows an exemplary SDS-PAGE analysis of AsCpf1 variants used in the *in vitro* cleavage assay and subsequent genome editing in human cell lines. Indicated quantity of protein was loaded, and no difference was observed comparing to the WT-Cpf1. These results demonstrate M537R and F870L mutations can increase the *in vitro* cleavage activity of Cpf1 at non-conical TTTT PAM site while maintaining high activity at canonical TTTV site.

**[0028]** **FIG. 3B** shows exemplary DNA cleavage activities of Cpf1 variants at HPRT-38346 site with TTTC or TTTT PAM. Both variants resulted in a higher percentage of DNA cleavage at TTTT PAM site than WT-Cpf1. These results demonstrate M537R and F870L mutations can increase the *in vitro* cleavage activity of Cpf1 at non-conical TTTT PAM site while maintaining high activity at canonical TTTV site.

**[0029]** **FIG. 4** shows a summary of results showing exemplary results of M537R and F870L mutations having broadly enhanced the genomic targeting efficiency of AsCpf1 at TTTN PAM sites in human cell line. The genomic targeting efficiencies of Cpf1 variants were tested in a human cell line model using T7 endonuclease I assay (T7EI). Twenty-four crRNAs targeting the *CTNNB1* gene with TTTN PAMs were synthesized, assembled with Cpf1 variants as RNP complex, and delivered by nucleofection (Lonza). The genomic DNA was collected 48 hours post-delivery to assess the formation of indels by T7EI. Not only

enabled DNA cleavage at all TTTT PAM sites that many were not targetable by WT-Cpf1, the reported variants, particularly the double-mutant (M537R/F870L), broadly enhanced the targeting efficiency of Cpf1 at 22 of 24 tested sites regardless of PAM sequence.

**[0030]** **FIG. 5A** shows exemplary correlation of relative survival rate of M537R/F870L-AsCas12a under condition 1 (X-axis) vs. relative survival rate of M537R/F870L-*AsCas12a* condition 2 (Y-axis). Consistent phenotype measurement was obtained ($\rho \sim 0.7$).

**[0031]** **FIG. 5B** shows exemplary correlation of relative survival rate of M537R/F870L-AsCas12a under condition 1 (X-axis) vs. relative survival rate of WT-AsCas12a under condition 3 (Y-axis). Consistent phenotype measurement was obtained ($\rho \sim 0.7$).

**[0032]** **FIG. 5C** shows exemplary correlation of relative survival rate of M537R/F870L-AsCas12a under condition 2 (X-axis) vs. relative survival rate of WT-AsCas12a under condition 2 (Y-axis). Consistent phenotype measurement was obtained ($\rho \sim 0.7$).

**[0033]** **FIG. 5D** shows exemplary variant scores of phenotype (relative survival rate) of single point mutations of a selected number of AsCas12a at positions 537 and 870 under conditions 1 and 2.

**[0034]** **FIG. 5E** shows exemplary variant scores of phenotype (relative survival rate) of single point mutations of a selected number of AsCas12a at positions 537 and 870 under conditions 1 and 2. **FIGs. 5D** and **5E** show that M537R and F870L are the optimal substitutions at respective positions, which is consistent with the result of our previous screening and mutant characterization.

**[0035]** **FIG. 5F** shows exemplary variant scores of phenotype (relative survival rate) of single point mutations of a selected number of AsCas12a at positions 505, 510, 569 and 599 under conditions 1, 2 and 3.

**[0036]** **FIG. 6A** shows survival rate of *E. coli* resulting from DNA cleavage activity of WT-AsCas12a at TTTT PAM. The cleavage activity of AsCas12a variants at TTTT PAM site was measured by bacterial-based activity assay. The petri dish plated with the initial bacterial plating is shown on the left, while the petri dish having the surviving bacterial colonies is shown on the right. The survival of *E. coli* under selection is dependent on the success cleavage of a toxin-expressing plasmid containing a TTTT PAM site.

**[0037]** **FIG. 6B** shows survival rate of *E. coli* resulting from DNA cleavage activity of L505K-AsCas12a variant at TTTT PAM. The presentation of petri dishes and experimental details are as set forth in **FIG. 6A**.

**[0038]** **FIG. 6C** shows survival rate of *E. coli* resulting from DNA cleavage activity of S510L-AsCas12a variant at TTTT PAM. The presentation of petri dishes and experimental details are as set forth in **FIG. 6A**.

**[0039]** **FIG. 6D** shows survival rate of *E. coli* resulting from DNA cleavage activity of M537R-AsCas12a variant at TTTT PAM. The presentation of petri dishes and experimental details are as set forth in **FIG. 6A**.

**[0040]** **FIG. 6E** shows survival rate of *E. coli* resulting from DNA cleavage activity of P569D-AsCas12a variant at TTTT PAM. The presentation of petri dishes and experimental details are as set forth in **FIG. 6A**.

**[0041]** **FIG. 6F** shows survival rate of *E. coli* resulting from DNA cleavage activity of P599G-AsCas12a variant at TTTT PAM. The presentation of petri dishes and experimental details are as set forth in **FIG. 6A**.

**[0042]** **FIG. 7A** shows survival rate of *E. coli* resulting from DNA cleavage activity of M537R/F870L-AsCas12a at TTTT PAM. The cleavage activity of M537R/F870L-AsCas12a variants at TTTT PAM site was measured by bacterial-based activity assay. The petri dish plated with the initial bacterial plating is shown on the left, while the petri dish having the surviving bacterial colonies is shown on the right. The survival of *E. coli* under selection is dependent on the success cleavage of a toxin-expressing plasmid containing a TTTT PAM site.

**[0043]** **FIG. 7B** shows survival rate of *E. coli* resulting from DNA cleavage activity of L505K/M537R/F870L-AsCas12a variant at TTTT PAM. The presentation of petri dishes and experimental details are as set forth in **FIG. 7A**.

**[0044]** **FIG. 7C** shows survival rate of *E. coli* resulting from DNA cleavage activity of M537R/F870L-AsCas12a variant at TTTT PAM. The presentation of petri dishes and experimental details are as set forth in **FIG. 7A**.

**[0045]** **FIG. 7D** shows survival rate of *E. coli* resulting from DNA cleavage activity of P569D/M537R/F870L-AsCas12a variant at TTTT PAM. The presentation of petri dishes and experimental details are as set forth in **FIG. 7A**.

**[0046]** **FIG. 7E** shows survival rate of *E. coli* resulting from DNA cleavage activity of P599G/M537R/F870L-AsCas12a variant at TTTT PAM. The presentation of petri dishes and experimental details are as set forth in **FIG. 7A**.

**[0047]** **FIG. 7F** shows survival rate of *E. coli* resulting from DNA cleavage activity of S510L/M537R/F870L-AsCas12a variant at TTTT PAM. The presentation of petri dishes and experimental details are as set forth in **FIG. 7A**.

DETAILED DESCRIPTION

**[0048]** The present invention concerns compositions of Cas12a variants and methods to enhance the utility of Cas12a and variants thereof for expression in eukaryotic cells.

Definitions

**[0049]** When introducing elements of aspects of the disclosure or particular embodiments, the articles "a," "an," "the," and "said" are intended to mean that there are one or more of the elements. The terms "comprising," "including," and "having" are intended to be inclusive and mean that there may be additional elements other than the listed elements. The term "or" means any one member of a particular list and also includes any combination of members of that list, unless otherwise specified.

**[0050]** As intended herein, the terms "substantially," "approximately," and "about" and similar terms are intended to have a broad meaning in harmony with the common and accepted usage in the art to which the subject matter of this disclosure pertains. It should be understood by those of skill in the art who review this disclosure that these terms are intended to allow a description of certain features described and claimed without restricting the scope of these features to precise numerical ranges provided. Accordingly, these terms should be interpreted as indicating that insubstantial or inconsequential modifications or alterations of the subject matter described and claimed are considered to be within the scope of the invention as recited in the appended claims.

**[0051]** Definitions pertaining to certain terms and phrases applicable herein may be found in related US patents and publications, such as U.S. Patent Application Serial Nos. 14/975,709, 15/299,549, 15/299,590, 15/299,593, 15/881,684, 15/729,491, 15/821,736, 15/964,041, 15/839,817, 15/839,820, 62/716,138, and U.S. Patent No. 9,840,702.

**[0052]** The term "substantially purified," as applied to a composition, refers to a composition having at least 90% purity or greater, including 90% purity, 95% purity, 99% purity and greater than 99% purity.

**[0053]** The adjective "isolated," when modifying a composition, such as a polynucleotide, a polypeptide or a ribonucleoprotein complex refers to a substantially purified composition, or in the case of a ribonucleoprotein complex, at least one component

being a substantially purified component. In further respect to an isolated ribonucleoprotein complex, preferably all components are substantially purified.

**[0054]** The terms "nucleic acid" and "polynucleotide" are interchangeable have the same meaning.

**[0055]** The terms "amino acid sequence," "polypeptide," and "protein" are interchangeable have the same meaning.

**[0056]** The term "affinity tag" refers to a ligand that permits detection and/or selection of an oligonucleotide sequence to which the ligand is attached. For the purposes of this disclosure, a bait may include an affinity tag. In particular, the affinity tag is positioned typically at either or both the N'-terminus and/or C'-terminus of a polypeptide through the use of conventional chemical coupling technology or recombinant DNA technology. Exemplary affinity tags include biotin, digoxigenin, streptavidin, polyhistine (for example, $(His_6)$,), glutathione-S-transferase (GST), HaloTag®, AviTag, Calmodulin-tag, polyglutamate tag, FLAG-tag, HA-tag, Myc-tag, S-tag, SBP-tag, Softag 3, V5 tag, Xpress tag, a hapten, among others.

**[0057]** The term "eukaryotic cell," includes those cells of or derived from a particular organism, such as a plant or a mammal, including but not limited to human, or non-human eukaryote or animal or mammal as herein discussed, e.g., mouse, rat, rabbit, dog, livestock, or non-human mammal or primate. In some embodiments, processes for modifying the germ line genetic identity of human beings and/or processes for modifying the genetic identity of animals which are likely to cause them suffering without any substantial medical benefit to man or animal, and also animals resulting from such processes, may be excluded. Preferred human cells include cells derived from somatic cells and germ line cells. Exemplary somatic cells include cells from every major organ and tissue system, including the immune system and hematopoietic system.

**[0058]** As set forth herein, the Conditions 1, 2 and 3 refer to different combinations of background strain and the amounts of gRNA introduced in the background strain before selection of the variants. Condition 1 is a M537R/F870L background that includes an introduced amount of gRNA (100 pmol per 10 microliter transformation/plating experiment) in which variants were selected. Condition 2 is a M537R/F870L background that includes an introduced amount of gRNA (50 pmol per 10 microliter transformation/plating experiment) in which variants were selected. Condition 3 is a Wild-type AsCpf1 background that includes

an introduced amount of gRNA (200 pmol per 10 microliter transformation/plating experiment) in which variants were selected.

*Cas12a polypeptides having eukaryotic nuclear localization signals*

**[0059]** Since Cas12a is a bacterial protein, it has no native targeting mechanism to reach the eukaryotic nucleus, where the target DNA resides.

**[0060]** To more efficiently target proteins to the eukaryotic nucleus, short protein sequences called nuclear localization signals (NLS) are commonly added to the amino- or carboxy-terminal ends of a given open reading frame. NLSs are recognized by import proteins on the eukaryotic nuclear envelope that first bind to the nuclear membrane, and subsequently permit pore translocation into the nucleus by an energy-dependent process. While recombinant protein tags like an NLS can greatly improve localization, any addition of exogenous amino acid sequences stands a reasonable chance of perturbing protein function. As such, discovering a recombinant Cas12a protein sequence that facilitates the highest amount of nuclear delivery without negatively affecting its activity will ultimately result in the most potent Cas12a genome editing solution, which is non-trivial and highly desirable.

**[0061]** To improve nuclear delivery of Cas12a without perturbing its function, several different recombinant versions of Cas12a were constructed in which the identity, location, and number of protein tags (NLS, hexahistidine tag (an exemplary affinity tag)) were varied. Whereas hexahistidine and V5 tags were added to Cas12a constructs to aid in protein purification and/or detection, the NLS tags were added to assist in delivery to the eukaryotic nucleus. Domain-breaking linker sequences were also varied in composition and location to empirically determine the best arrangement and context of tagged sequences. All constructs were first expressed in *E. coli*, and recombinant Cas12a proteins were purified with immobilized metal affinity chromatography (IMAC) followed by ion exchange chromatography as described previously.

*AsCpf1 polypeptide variants having novel cleavage activities*

**[0062]** Amino acid substitutions in AsCpf1 that enhance the cleavage activity at both canonical (TTTV) and non-canonical (TTTT) PAM sites using a bacterial screening approach are described. This screen contained two components: i) a toxin plasmid encoding an arabinose-inducible cell proliferation toxin and a CRISPR/Cpf1 on-target cleavage site (HPRT-38346) with TTTT PAM, and ii) a chloramphenicol resistance plasmid containing a randomly-mutagenized region within the *AsCpf1* sequence (~5 mutations per kb). The screen

was performed as follows: *E.coli* BW25141(λDE3) was transformed with the toxin plasmid containing the HPRT-38346 target site in the absence of arabinose, where the toxin is not produced and cell survival is permitted. Cells with stably replicating toxin plasmid are then transformed with the AsCpf1 expression plasmid and crRNA targeting HPRT-38346, and then cells were plated on media containing both chloramphenicol and arabinose. Bacteria that grew were those that i) successfully transformed with the AsCpf1 expression plasmid, ii) expressed sufficient AsCpf1 variant to cleave the toxin plasmid at HPRT-38346 site using TTTT PAM. The AsCpf1 expression plasmids within the survived cells were recovered and used in the subsequent round of selection. After multiple rounds of selection, the identities of enriched AsCpf1 variants were determined by DNA sequencing, and carried forward for analysis in mammalian cells.

**[0063]** The disclosure provides following two novel point mutations and the combination in the *AsCpf1* gene that enhances the cleavage activity: M537R and F870L. The cleavage activity of individual mutant was first tested in a bacterial-based activity assay. Next, purified proteins were further tested *in vitro* and in human cell lines. In summary, both substitutions significantly enhanced the DNA cleavage activity of Cpf1 at TTTT PAM sites in all assays. Further, the combination of M537R and F870L broadly enhanced the targeting efficiency of AsCpf1 in human cell line. Overall, the present invention identifies novel amino-acid positions in the *AsCpf1* gene that can be mutated to improve its cleavage activity at all TTT**N** (N = A/G/C/T) PAM sites.

**[0064]** As explained in the Background section, the prior art consists of using wild-type Cpf1 protein or two variants that are compatible with TYCV and TATV PAMs. As stated previously, these variants have limited utility due to the complex and mutually exclusive requirement of PAM sequence. Further, none of the variants showed any improved cleavage activity at TTT**T** PAM, which is unfortunately more frequent than other TTT**V** PAM sites (**V** = G/A/C) throughout the human genome. In contrast, not only enabling efficient cleavage at TTTT PAM, the mutations reported in this invention (M537R and F870L) broadly enhanced the cleavage activity of Cpf1 at canonical TTTV sites tested in human cell line. Together, the enhanced activity and broadened PAM flexibility (TTTN) of this invention makes it a superior CRISPR enzyme, which could directly replace the current wild-type Cpf1 in the application genomic editing.

*High-Throughput generation of AsCas12a variants having cleavage activity towards a TTTT PAM-containing target site.*

**[0065]** The phenotype of all point mutations in the following regions of *AsCas12a*: 499-640 and 840-913 in the bacterial screening measuring the DNA cleavage activity at non-canonical TTTT PAM is described. Three sets of screening were performed to measure the phenotype of each point mutation, in the background of both WT-AsCas12a and M537R/F870L-AsCas12a. Cross-comparison of three datasets revealed consistent phenotype measurements, which enabled us to isolate novel AsCas12a variants with enhanced activity beyond M537R and F870L.

**[0066]** The high-throughput characterization of Cas12a activity at a TTTT PAM site provided the functional consequence of every possible single amino acid change within targeted region. The unbiased strategy of the present invention enables one to identify a large collection of mutants to further enhance the cleavage activity of AsCas12a over our previous invention (M537R/F870L).

**[0067]** To improve the coverage and efficiency of the screening, we generated an *AsCas12a* deep-scanning mutagenesis library containing all possible point mutations on the protein level in the targeted regions (490-640 and 840-913), with most clones contain only one mutation. This type of library allowed us to directly evaluate the phenotype of each point mutation, by measuring their relative survival rates over the reference protein in the bacterial screen. Briefly, the screening strain harboring the toxin plasmid was transformed with *AsCas12a* library with TTTT PAM-containing target site on the toxin plasmid. After transformation, cells were plated on selective media. *AsCas12a* expression plasmids carried by the survived *E. coli* cells were extracted and purified. Both input and selected plasmid libraries were PCR amplified, and sequenced on Illumina MiSeq with 1~2 million reads per library. The frequencies of each *AsCas12a* variant in both libraries were determined using Enrich 2, and normalized to the reference protein (WT or M537R/F870L). The relative survival rate of each point mutation over reference was calculated as the ratio of normalized frequency between selected and input library. Since the degree of cell survival is indicative of the DNA cleavage activity of each *AsCas12a* variant, any variants with higher survival rate than the reference protein would be those with enhanced activity at TTTT PAM.

**[0068]** As presented herein, codon-optimized Cas12a polypeptides are provided, including codon-optimized Cas12a polypeptides for CRISPR ribonucleoprotein complexes.

An example of a codon-optimized sequence, is in this instance a sequence optimized for expression in eukaryotes, *e.g.*, humans (*i.e.*, being optimized for expression in humans), or for another eukaryote, animal or mammal as herein discussed. Whilst this is preferred, it will be appreciated that other examples are possible and codon optimization for a host species other than human, or for codon optimization for specific organs is known. In some embodiments, an enzyme coding sequence encoding a CRISPR Cas12a polypeptide is a codon optimized for expression in particular cells, such as eukaryotic cells. The eukaryotic cells may be those of or derived from a particular organism, such as a plant or a mammal, including but not limited to human, or non-human eukaryote or animal or mammal as herein discussed, e.g., mouse, rat, rabbit, dog, livestock, or non-human mammal or primate. In some embodiments, processes for modifying the germ line genetic identity of human beings and/or processes for modifying the genetic identity of animals which are likely to cause them suffering without any substantial medical benefit to man or animal, and also animals resulting from such processes, may be excluded.

**[0069]** Preferred human cells include cells derived from somatic cells and germ line cells. Exemplary somatic cells include cells from every major organ and tissue system, including the immune system and hematopoietic system.

**[0070]** In general, codon optimization refers to a process of modifying a nucleic acid sequence for enhanced expression in the host cells of interest by replacing at least one codon (e.g. about or more than about 1, 2, 3, 4, 5, 10, 15, 20, 25, 50, or more codons) of the native sequence with codons that are more frequently or most frequently used in the genes of that host cell while maintaining the native amino acid sequence. Various species exhibit particular bias for certain codons of a particular amino acid. Codon bias (differences in codon usage between organisms) often correlates with the efficiency of translation of messenger RNA (mRNA), which is in turn believed to be dependent on, among other things, the properties of the codons being translated and the availability of particular transfer RNA (tRNA) molecules. The predominance of selected tRNAs in a cell is generally a reflection of the codons used most frequently in peptide synthesis. Accordingly, genes can be tailored for optimal gene expression in a given organism based on codon optimization. Codon usage tables are readily available. See Nakamura, Y., et al. "Codon usage tabulated from the international DNA sequence databases: status for the year 2000" Nucl. Acids Res. 28:292 (2000). Computer algorithms for codon optimizing a particular sequence for expression in a particular host cell

are also available, such as Gene Forge (Aptagen; Jacobus, Pa.), are also available. In some embodiments, one or more codons (e.g. 1, 2, 3, 4, 5, 10, 15, 20, 25, 50, or more, or all codons) in a sequence encoding a Cas12a correspond to the most frequently used codon for a particular amino acid.

**[0071]** Additionally, codon-optimized Cas12a polypeptides are provided, including codon-optimized Cas12a polypeptides for CRISPR ribonucleoprotein complexes, wherein the Cas12a polypeptide sequence optimized for expression in prokaryotes, such as bacteria (*e.g.*, *E. coli).*

*Applications*

**[0072]** This invention is useful for either basic research or therapeutic fields for any CRISPR/Cas12a DNA cleavage and/or gene editing experiments or treatments. The superior activity of these recombinant variants could be applied to Cas12a from any species or potentially any CRISPR enzyme.

**[0073]** In a first aspect, A CRISPR-associated protein comprising a polypeptide encoding a variant of AsCpf1 is provided. The variant of AsCpf1 is selected from the group consisting of M537R (SEQ ID NO.: 472), F870L (SEQ ID NO.: 473), and M537R/F870L (SEQ ID NO.: 465). In a first respect, the CRISPR-associated protein corresponds to a variant of AsCpf1 is M537R. In a second respect, the CRISPR-associated protein corresponds to a variant of AsCpf1 is F870L (SEQ ID NO.: 473). In a third respect, the CRISPR-associated protein corresponds to a variant of AsCpf1 is M537R/F870L (SEQ ID NO.: 465).

**[0074]** In a second aspect, a CRISPR ribonucleoprotein complex is provided. The CRISPR ribonucleoprotein complex includes a guide RNA and a CRISPR-associated protein. The CRISPR-associated protein including a polypeptide encoding a variant of AsCpf1. The variant of AsCpf1 is selected from the group consisting of M537R (SEQ ID NO.: 472), F870L (SEQ ID NO.: 473), and M537R/F870L (SEQ ID NO.: 465). In a first respect, the CRISPR ribonucleoprotein complex includes the variant of AsCpf1 being M537R. In a second respect, the CRISPR ribonucleoprotein complex includes the variant of AsCpf1 being F870L (SEQ ID NO.: 473). In a third respect, the CRISPR ribonucleoprotein complex includes the variant of AsCpf1 being M537R/F870L (SEQ ID NO.: 465).

**[0075]** In a third aspect, a method of increasing efficiency of gene editing at TTTN PAM sites in a cell with a CRISPR ribonucleoprotein complex is provided. The method includes the step of contacting a cell with the CRISPR ribonucleoprotein complex. The CRISPR

ribonucleoprotein complex includes a guide RNA and a CRISPR-associated protein. The CRISPR-associated protein including a polypeptide encoding a variant of AsCpf1. The variant of AsCpf1 is selected from the group consisting of M537R (SEQ ID NO.: 472), F870L (SEQ ID NO.: 473) and M537R/F870L (SEQ ID NO.: 465). In a first respect, the TTTN PAM sites consists of one selected form the group of TTTA, TTTT and TTTC PAM sites.

**[0076]** In a fourth aspect, a kit includes a guide RNA and a CRISPR-associated protein is provided. The CRISPR-associated protein includes a polypeptide encoding a variant of AsCpf1. The variant of AsCpf1 is selected from the group consisting of M537R (SEQ ID NO.: 472), F870L (SEQ ID NO.: 473), and M537R/F870L (SEQ ID NO.: 465). In a first respect, the variant of AsCpf1 is M537R. In a second respect, the variant of AsCpf1 is F870L (SEQ ID NO.: 473). In a third respect, the variant of AsCpf1 is M537R/F870L (SEQ ID NO.: 465).

**[0077]** In a fifth aspect, a CRISPR-associated protein comprising a polypeptide encoding a variant of AsCas12a, wherein the variant of AsCas12a is selected from the group consisting of at least one variant amino acid selected from amino acid positions 499-640 and 840-913, provided that the variant AsCas12a provides an improvement in CRISPR/AsCas12a-associated nuclease activity at non-canonical TTTT PAM sites. In a first respect, the variant of AsCas12a is selected from the group consisting of SEQ ID NOs.: 59-245. In a second respect, the variant of AsCas12a, as described in the first aspect or the foregoing first respect of the first aspect, further comprises mutations of M537R/F870L (SEQ ID NO.: 465).

**[0078]** In a sixth aspect, a CRISPR ribonucleoprotein complex is provided. The CRISPR ribonucleoprotein complex includes a guide RNA and a CRISPR-associated protein. The CRISPR-associated protein includes a polypeptide encoding a variant of AsCas12a, wherein the variant of AsCas12a is selected from the group consisting of at least one variant amino acid selected from amino acid positions 499-640 and 840-913, provided that the variant AsCas12a provides an improvement in CRISPR/AsCas12a-associated nuclease activity at non-canonical TTTT PAM sites. In a first respect, the variant of AsCas12a is selected from the group consisting of SEQ ID NOs.: 59-245. In a second respect, the variant of AsCas12a, as described in the second aspect or the foregoing first respect of the second aspect, further comprises mutations of M537R/F870L (SEQ ID NO.: 465).

**[0079]** In a seventh aspect, a method of increasing efficiency of gene editing at non-canonical TTTT PAM sites in a cell with a CRISPR ribonucleoprotein complex is provided. The method includes a step of contacting a cell with the CRISPR ribonucleoprotein complex that includes a guide RNA and a CRISPR-associated protein. The CRISPR-associated protein includes a polypeptide encoding a variant of AsCas12a, wherein the variant of AsCas12a is selected from the group consisting of at least one variant amino acid selected from amino acid positions 499-640 and 840-913, provided that the variant AsCas12a provides an improvement in CRISPR/AsCas12a-associated nuclease activity at non-canonical TTTT PAM sites. In a first respect, the variant of AsCas12a is selected from the group consisting of SEQ ID NOs.: 59-245. In a second respect, the variant of AsCas12a, as described in the third aspect or the foregoing first respect of the third aspect, further comprises mutations of M537R/F870L (SEQ ID NO.: 465).

**[0080]** In an eighth aspect, a kit including a guide RNA and a CRISPR-associated protein comprising a polypeptide encoding a variant of AsCas12a is provided. The variant of AsCas12a is selected from the group consisting of at least one variant amino acid selected from amino acid positions 499-640 and 840-913, provided that the variant AsCas12a provides an improvement in CRISPR/AsCas12a-associated nuclease activity at non-canonical TTTT PAM sites. In a first respect, the variant of AsCas12a is selected from the group consisting of SEQ ID NOs.: 59-245. In a second respect, the variant of AsCas12a, as described in the fourth aspect or the foregoing first respect of the fourth aspect, further comprises mutations of M537R/F870L (SEQ ID NO.: 465).

**[0081]** In a ninth aspect, a nucleic acid encoding a CRISPR-associated protein comprising a polypeptide encoding a variant of AsCas12a is provided. The variant of AsCas12a is selected from the group consisting of at least one variant amino acid selected from amino acid positions 499-640 and 840-913, provided that the variant AsCas12a provides an improvement in CRISPR/AsCas12a-associated nuclease activity at non-canonical TTTT PAM sites. Highly preferred nucleic acids encoding a CRISPR-associated protein include isolated nucleic acids encoding a CRISPR-associated protein. In a first respect, the variant of AsCas12a is selected from the group consisting of SEQ ID NOs.: 59-245. In a second respect, the variant of AsCas12a further includes mutations of M537R/F870L (SEQ ID NO.: 465). In a third respect, the nucleic acid is operably linked to suitable transcription elements to express the nucleic acid. In a fourth respect, the nucleic acid is DNA or RNA.

**[0082]** In a tenth aspect, a polynucleotide sequence encoding a Cas12a polypeptide is provided. The polynucleotide sequence includes one member selected from the group consisting of SEQ ID NOs.: 5-17.

**[0083]** In an eleventh aspect, an amino acid sequence encoding a Cas12a polypeptide is provided. The amino acid sequence includes one member selected from the group consisting of SEQ ID NOs.: 18-30.

**[0084]** In a twelfth aspect, a CAS endonuclease system comprising an expression cassette encoding a polynucleotide sequence encoding a Cas12a polypeptide is provided. The includes one member selected from the group consisting of SEQ ID NOs.: 5-17.

**[0085]** In a thirteenth aspect, CAS endonuclease system comprising an amino acid sequence encoding a Cas12a polypeptide is provided The amino acid sequence includes one member selected from the group consisting of SEQ ID NOs.: 18-30.

**[0086]** In a fourteenth aspect, a method of performing genome editing in a eukaryotic cells is provided. The method includes the step of introducing an CAS endonuclease system into the eukaryotic cell, said CAS endonuclease system comprising an expression cassette encoding a polynucleotide sequence encoding a Cas12a polypeptide, comprising one member selected from the group consisting of SEQ ID NOs.: 5-17.

**[0087]** In a fifteenth aspect, a method of performing genome editing in a eukaryotic cell is provided. The method includes the step of introducing an CAS endonuclease system into the eukaryotic cell, said CAS endonuclease system comprising an amino acid sequence encoding a Cas12a polypeptide comprising one member selected from the group consisting of SEQ ID NOs.: 18-30.

**[0088]** In a sixteenth aspect, an CRISPR-associated protein comprising a fusion polypeptide is provided. The fusion polypeptide includes an AsCas12a open reading frame, a nuclear localization signal, optionally an amino acid linker and optionally an affinity tag. Highly preferred CRISPR-associated proteins include isolated CRISPR-associated proteins. In a first respect, the AsCas12a open reading frame is selected from the group consisting of SEQ ID NOs.: 59-245. In a second respect, the nuclear localization signal is selected from SEQ ID NOs.: 475, 477, 479, 481 and 483. In a third respect, the CRISPR-associated protein is encoded by SEQ ID NOs.: 488-491. In a fourth respect, the CRISPR-associated protein is selected from SEQ ID NOs.: 492 and 493.

**[0089]** In a seventeenth aspect, a method of performing genome editing in a eukaryotic cell is provided. The method includes the step of introducing an CAS endonuclease system into the eukaryotic cell, said CAS endonuclease system comprising an CRISPR-associated protein of according to the sixteenth aspect. Highly preferred CRISPR-associated proteins include isolated CRISPR-associated proteins.

## EXAMPLES

### Example 1. Recombinant Cas12a proteins with varying tags/linker sequences yield a spectrum of editing efficiencies

**[0090]** The following Example demonstrates that recombinant Cas12a proteins with only modest changes in tag sequences at the amino- and carboxy-termini results in proteins that demonstrate a wide range of editing efficiencies in human cells (**FIG. 1**).

**[0091]** Briefly, the method of site directed mutagenesis (SDM) was employed to create the expression constructs having As Cas12a coding sequences with different nuclear localization signals (NLS's). Site directed mutagenesis was performed by designing complimentary primers that encompass the desired nucleotide base change(s), along with flanking plasmid vector sequence, wherein each flanking region has a melting temperature ($T_m$) of at least 60°C. A polymerase chain reaction (PCR) run was then performed using standard cycling conditions for a total of 16 cycles. The restriction enzyme, DPN I, was added to digest away the starting plasmid vector material so only the new product containing the base changes remain. After DPN I treatment, a small amount of the PCR product was transformed into competent *E. coli* cells, recovered in SOC media and plated onto kanamycin resistance Luria Broth (LB) agar plates. Colonies were screened using the Sanger sequencing method to verify correct base changes in selected clones.

**[0092]** The results indicate that the ideal sequence and placement of NLS sequences on Cas12a is not obvious, and that a highly efficient Cas12a genome editing solution must be empirically determined as was done in this study. Proteins were tested using guides that target the *HPRT-38186* (SEQ ID NO.:1) and *HPRT-38228* (SEQ ID NO.:2) loci in human cells. SEQ ID NOs.: 1-4 are depicted in **Table 1**.

**[0093] Table 1. Sequence of oligonucleotides used as crRNAs or PCR primers.**

| Name | Sequence | SEQ ID NO. |
|---|---|---|
| *HPRT*-38186-S | rUrArArUrUrUrCrUrArCrUrCrUrUrGrUrArGrArUrUrArArUrGrCrCr CrUrGrUrArGrUrCrUrCrUrCrUrG | SEQ ID NO. 1 |
| *HPRT*-38228-S | rUrArArUrUrUrCrUrArCrUrCrUrUrGrUrArGrArUrUrArArUrUrArAr CrArGrCrUrUrGrCrUrGrGrUrGrA | SEQ ID NO. 2 |
| *HPRT*-FWD | AAGAATGTTGTGATAAAAGGTGATGCT | SEQ ID NO. 3 |
| *HPRT*-REV | GAGGCAGAAGTCCCATGGATGTGT | SEQ ID NO. 4 |

**[0094]** The following nucleotide sequences that encode preferred Cas12a polypeptides of this Example are depicted below:

**[0095]** SEQ ID NO.: 5

**[0096]** ATGGGCAGCAGCAGCAGCGGCCTGGTGCCGCGCGGCAGCCATATGGCTAGCATGACTGGT
GGACAGCAAATGGGTCGGGATCCAGGTAAACCGATTCCGAATCCGCTGCTGGGTCTGGATAGCACCGCACCG
AAAAAAAAACGTAAAGTTGGTATTCATGGTGTTCCGGCAGCAACCCAGTTTGAAGGTTTCACCAATCTGTATC
AGGTTAGCAAAACCCTGCGTTTTGAACTGATTCCGCAGGGTAAAACCCTGAAACATATTCAAGAACAGGGCTT
CATCGAAGAGGATAAAGCACGTAACGATCACTACAAAGAACTGAAACCGATTATCGACCGCATCTATAAAACC
TATGCAGATCAGTGTCTGCAGCTGGTTCAGCTGGATTGGGAAAATCTGAGCGCAGCAATTGATAGTTATCGCA
AAGAAAAAACCGAAGAAACCCGTAATGCACTGATTGAAGAACAGGCAACCTATCGTAATGCCATCCATGATT
ATTTCATTGGTCGTACCGATAATCTGACCGATGCAATTAACAAACGTCACGCCGAAATCTATAAAGGCCTGTTT
AAAGCCGAACTGTTTAATGGCAAAGTTCTGAAACAGCTGGGCACCGTTACCACCACCGAACATGAAAATGCAC
TGCTGCGTAGCTTTGATAAATTCACCACCTATTTCAGCGGCTTTTATGAGAATCGCAAAAACGTGTTTAGCGCA
GAAGATATTAGCACCGCAATTCCGCATCGTATTGTGCAGGATAATTTCCCGAAATTCAAAGAGAACTGCCACA
TTTTTACCCGTCTGATTACCGCAGTTCCGAGCCTGCGTGAACATTTTGAAAACGTTAAAAAAGCCATCGGCATC
TTTGTTAGCACCAGCATTGAAGAAGTTTTTAGCTTCCCGTTTTACAATCAGCTGCTGACCCAGACCCAGATTGA
TCTGTATAACCAACTGCTGGGTGGTATTAGCCGTGAAGCAGGCACCGAAAAAATCAAAGGTCTGAATGAAGT
GCTGAATCTGGCCATTCAGAAAAATGATGAAACCGCACATATTATTGCAAGCCTGCCGCATCGTTTTATTCCGC
TGTTCAAACAAATTCTGAGCGATCGTAATACCCTGAGCTTTATTCTGGAAGAATTCAAATCCGATGAAGAGGT
GATTCAGAGCTTTTGCAAATACAAAACGCTGCTGCGCAATGAAAATGTTCTGGAAACTGCCGAAGCACTGTTT
AACGAACTGAATAGCATTGATCTGACCCACATCTTTATCAGCCACAAAAAACTGGAAACCATTTCAAGCGCACT
GTGTGATCATTGGGATACCCTGCGTAATGCCCTGTATGAACGTCGTATTAGCGAACTGACCGGTAAAATTACC
AAAAGCGCGAAAGAAAAAGTTCAGCGCAGTCTGAAACATGAGGATATTAATCTGCAAGAGATTATTAGCGCA
GCCGGTAAAGAACTGTCAGAAGCATTTAAACAGAAAACCAGCGAAATTCTGTCACATGCACATGCAGCACTG
GATCAGCCGCTGCCGACCACCCTGAAAAAACAAGAAGAAAAAGAAATCCTGAAAAGCCAGCTGGATAGCCTG
CTGGGTCTGTATCATCTGCTGGACTGGTTTGCAGTTGATGAAAGCAATGAAGTTGATCCGGAATTTAGCGCAC
GTCTGACCGGCATTAAACTGGAAATGGAACCGAGCCTGAGCTTTTATAACAAAGCCCGTAATTATGCCACCAA
AAAACCGTATAGCGTCGAAAAATTCAAACTGAACTTTCAGATGCCGACCCTGGCAAGCGGTTGGGATGTTAAT
AAAGAAAAAAACAACGGTGCCATCCTGTTCGTGAAAAATGGCCTGTATTATCTGGGTATTATGCCGAAACAGA
AAGGTCGTTATAAAGCGCTGAGCTTTGAACCGACGGAAAAAACCAGTGAAGGTTTTGATAAAATGTACTACG
ACTATTTTCCGGATGCAGCCAAAATGATTCCGAAATGTAGCACCCAGCTGAAAGCAGTTACCGCACATTTTCA
GACCCATACCACCCCGATTCTGCTGAGCAATAACTTTATTGAACCGCTGGAAATCACCAAAGAGATCTACGAT
CTGAATAACCCGGAAAAAGAGCCGAAAAAATTCCAGACCGCATATGCAAAAAAAACCGGTGATCAGAAAGGT
TATCGTGAAGCGCTGTGTAAATGGATTGATTTCACCCGTGATTTTCTGAGCAAATACACCAAAACCACCAGTAT

CGATCTGAGCAGCCTGCGTCCGAGCAGCCAGTATAAAGATCTGGGCGAATATTATGCAGAACTGAATCCGCT
GCTGTATCATATTAGCTTTCAGCGTATTGCCGAGAAAGAAATCATGGACGCAGTTGAAACCGGTAAACTGTAC
CTGTTCCAGATCTACAATAAAGATTTTGCCAAAGGCCATCATGGCAAACCGAATCTGCATACCCTGTATTGGAC
CGGTCTGTTTAGCCCTGAAAATCTGGCAAAAACCTCGATTAAACTGAATGGTCAGGCGGAACTGTTTTATCGT
CCGAAAAGCCGTATGAAACGTATGGCACATCGTCTGGGTGAAAAAATGCTGAACAAAAAACTGAAAGACCAG
AAAACCCCGATCCCGGATACACTGTATCAAGAACTGTATGATTATGTGAACCATCGTCTGAGCCATGATCTGA
GTGATGAAGCACGTGCCCTGCTGCCGAATGTTATTACCAAAGAAGTTAGCCACGAGATCATTAAAGATCGTCG
TTTTACCAGCGACAAATTCTTTTTTCATGTGCCGATTACCCTGAATTATCAGGCAGCAAATAGCCCGAGCAAAT
TTAACCAGCGTGTTAATGCATATCTGAAAGAACATCCAGAAACGCCGATTATTGGTATTGATCGTGGTGAACG
TAACCTGATTTATATCACCGTTATTGATAGCACCGGCAAAATCCTGGAACAGCGTAGCCTGAATACCATTCAGC
AGTTTGATTACCAGAAAAAACTGGATAATCGCGAGAAAGAACGTGTTGCAGCACGTCAGGCATGGTCAGTTG
TTGGTACAATTAAAGACCTGAAACAGGGTTATCTGAGCCAGGTTATTCATGAAATTGTGGATCTGATGATTCA
CTATCAGGCCGTTGTTGTGCTGGAAAACCTGAATTTTGGCTTTAAAAGCAAACGTACCGGCATTGCAGAAAAA
GCAGTTTATCAGCAGTTCGAGAAAATGCTGATTGACAAACTGAATTGCCTGGTGCTGAAAGATTATCCGGCTG
AAAAAGTTGGTGGTGTTCTGAATCCGTATCAGCTGACCGATCAGTTTACCAGCTTTGCAAAAATGGGCACCCA
GAGCGGATTTCTGTTTTATGTTCCGGCACCGTATACGAGCAAAATTGATCCGCTGACCGGTTTTGTTGATCCGT
TTGTTTGGAAAACCATCAAAAACCATGAAAGCCGCAAACATTTTCTGGAAGGTTTCGATTTTCTGCATTACGAC
GTTAAAACGGGTGATTTCATCCTGCACTTTAAAATGAATCGCAATCTGAGTTTTCAGCGTGGCCTGCCTGGTTT
TATGCCTGCATGGGATATTGTGTTTGAGAAAAACGAAACACAGTTCGATGCAAAAGGCACCCCGTTTATTGCA
GGTAAACGTATTGTTCCGGTGATTGAAAATCATCGTTTCACCGGTCGTTATCGCGATCTGTATCCGGCAAATG
AACTGATCGCACTGCTGGAAGAGAAAGGTATTGTTTTTCGTGATGGCTCAAACATTCTGCCGAAACTGCTGGA
AAATGATGATAGCCATGCAATTGATACCATGGTTGCACTGATTCGTAGCGTTCTGCAGATGCGTAATAGCAAT
GCAGCAACCGGTGAAGATTACATTAATAGTCCGGTTCGTGATCTGAATGGTGTTTGTTTTGATAGCCGTTTTCA
GAATCCGGAATGGCCGATGGATGCAGATGCAAATGGTGCATATCATATTGCACTGAAAGGACAGCTGCTGCT
GAACCACCTGAAAGAAAGCAAAGATCTGAAACTGCAAAACGGCATTAGCAATCAGGATTGGCTGGCATATAT
CCAAGAACTGCGTAACCCTAAAAAAAAAACGCAAAGTGAAGCTTGCGGCCGCACTCGAGCACCACCACCACCA
CCACTGA

**[0097]** SEQ ID NO.: 6

**[0098]** ATGGGCAGCAGCAGCAGCGGCCTGGTGCCGCGCGGCAGCCATATGGCTAGCATGACTGGT
GGACAGCAAATGGGTCGGGATCCAGCACCGAAAAAAAAACGTAAAGTTGGTATTCATGGTGTTCCGGCAGCA
ACCCAGTTTGAAGGTTTCACCAATCTGTATCAGGTTAGCAAAACCCTGCGTTTTGAACTGATTCCGCAGGGTAA
AACCCTGAAACATATTCAAGAACAGGGCTTCATCGAAGAGGATAAAGCACGTAACGATCACTACAAAGAACT
GAAACCGATTATCGACCGCATCTATAAAACCTATGCAGATCAGTGTCTGCAGCTGGTTCAGCTGGATTGGGAA
AATCTGAGCGCAGCAATTGATAGTTATCGCAAAGAAAAAACCGAAGAAACCCGTAATGCACTGATTGAAGAA
CAGGCAACCTATCGTAATGCCATCCATGATTATTTCATTGGTCGTACCGATAATCTGACCGATGCAATTAACAA
ACGTCACGCCGAAATCTATAAAGGCCTGTTTAAAGCCGAACTGTTTAATGGCAAAGTTCTGAAACAGCTGGGC
ACCGTTACCACCACCGAACATGAAAATGCACTGCTGCGTAGCTTTGATAAATTCACCACCTATTTCAGCGGCTT
TTATGAGAATCGCAAAAACGTGTTTAGCGCAGAAGATATTAGCACCGCAATTCCGCATCGTATTGTGCAGGAT
AATTTCCCGAAATTCAAAGAGAACTGCCACATTTTTACCCGTCTGATTACCGCAGTTCCGAGCCTGCGTGAACA
TTTTGAAAACGTTAAAAAAGCCATCGGCATCTTTGTTAGCACCAGCATTGAAGAAGTTTTTAGCTTCCCGTTTT
ACAATCAGCTGCTGACCCAGACCCAGATTGATCTGTATAACCAACTGCTGGGTGGTATTAGCCGTGAAGCAGG
CACCGAAAAAATCAAAGGTCTGAATGAAGTGCTGAATCTGGCCATTCAGAAAAATGATGAAACCGCACATATT

ATTGCAAGCCTGCCGCATCGTTTTATTCCGCTGTTCAAACAAATTCTGAGCGATCGTAATACCCTGAGCTTTATT
CTGGAAGAATTCAAATCCGATGAAGAGGTGATTCAGAGCTTTTGCAAATACAAAACGCTGCTGCGCAATGAA
AATGTTCTGGAAACTGCCGAAGCACTGTTTAACGAACTGAATAGCATTGATCTGACCCACATCTTTATCAGCCA
CAAAAAACTGGAAACCATTTCAAGCGCACTGTGTGATCATTGGGATACCCTGCGTAATGCCCTGTATGAACGT
CGTATTAGCGAACTGACCGGTAAAATTACCAAAAGCGCGAAAGAAAAAGTTCAGCGCAGTCTGAAACATGAG
GATATTAATCTGCAAGAGATTATTAGCGCAGCCGGTAAAGAACTGTCAGAAGCATTTAAACAGAAAACCAGC
GAAATTCTGTCACATGCACATGCAGCACTGGATCAGCCGCTGCCGACCACCCTGAAAAAACAAGAAGAAAAA
GAAATCCTGAAAAGCCAGCTGGATAGCCTGCTGGGTCTGTATCATCTGCTGGACTGGTTTGCAGTTGATGAAA
GCAATGAAGTTGATCCGGAATTTAGCGCACGTCTGACCGGCATTAAACTGGAAATGGAACCGAGCCTGAGCT
TTTATAACAAAGCCCGTAATTATGCCACCAAAAAACCGTATAGCGTCGAAAAATTCAAACTGAACTTTCAGATG
CCGACCCTGGCAAGCGGTTGGGATGTTAATAAAGAAAAAAACAACGGTGCCATCCTGTTCGTGAAAAATGGC
CTGTATTATCTGGGTATTATGCCGAAACAGAAAGGTCGTTATAAAGCGCTGAGCTTTGAACCGACGGAAAAA
ACCAGTGAAGGTTTTGATAAAATGTACTACGACTATTTTCCGGATGCAGCCAAAATGATTCCGAAATGTAGCA
CCCAGCTGAAAGCAGTTACCGCACATTTTCAGACCCATACCACCCCGATTCTGCTGAGCAATAACTTTATTGAA
CCGCTGGAAATCACCAAAGAGATCTACGATCTGAATAACCCGGAAAAAGAGCCGAAAAAATTCCAGACCGCA
TATGCAAAAAAAACCGGTGATCAGAAAGGTTATCGTGAAGCGCTGTGTAAATGGATTGATTTCACCCGTGATT
TTCTGAGCAAATACACCAAAACCACCAGTATCGATCTGAGCAGCCTGCGTCCGAGCAGCCAGTATAAAGATCT
GGGCGAATATTATGCAGAACTGAATCCGCTGCTGTATCATATTAGCTTTCAGCGTATTGCCGAGAAAGAAATC
ATGGACGCAGTTGAAACCGGTAAACTGTACCTGTTCCAGATCTACAATAAAGATTTTGCCAAAGGCCATCATG
GCAAACCGAATCTGCATACCCTGTATTGGACCGGTCTGTTTAGCCCTGAAAATCTGGCAAAAACCTCGATTAA
ACTGAATGGTCAGGCGGAACTGTTTTATCGTCCGAAAAGCCGTATGAAACGTATGGCACATCGTCTGGGTGA
AAAAATGCTGAACAAAAAACTGAAAGACCAGAAAACCCCGATCCCGGATACACTGTATCAAGAACTGTATGA
TTATGTGAACCATCGTCTGAGCCATGATCTGAGTGATGAAGCACGTGCCCTGCTGCCGAATGTTATTACCAAA
GAAGTTAGCCACGAGATCATTAAAGATCGTCGTTTTACCAGCGACAAATTCTTTTTTCATGTGCCGATTACCCT
GAATTATCAGGCAGCAAATAGCCCGAGCAAATTTAACCAGCGTGTTAATGCATATCTGAAAGAACATCCAGAA
ACGCCGATTATTGGTATTGATCGTGGTGAACGTAACCTGATTTATATCACCGTTATTGATAGCACCGGCAAAAT
CCTGGAACAGCGTAGCCTGAATACCATTCAGCAGTTTGATTACCAGAAAAAACTGGATAATCGCGAGAAAGA
ACGTGTTGCAGCACGTCAGGCATGGTCAGTTGTTGGTACAATTAAAGACCTGAAACAGGGTTATCTGAGCCA
GGTTATTCATGAAATTGTGGATCTGATGATTCACTATCAGGCCGTTGTTGTGCTGGAAAACCTGAATTTTGGCT
TTAAAAGCAAACGTACCGGCATTGCAGAAAAAGCAGTTTATCAGCAGTTCGAGAAAATGCTGATTGACAAACT
GAATTGCCTGGTGCTGAAAGATTATCCGGCTGAAAAAGTTGGTGGTGTTCTGAATCCGTATCAGCTGACCGAT
CAGTTTACCAGCTTTGCAAAAATGGGCACCCAGAGCGGATTTCTGTTTTATGTTCCGGCACCGTATACGAGCA
AAATTGATCCGCTGACCGGTTTTGTTGATCCGTTTGTTTGGAAAACCATCAAAAACCATGAAAGCCGCAAACA
TTTTCTGGAAGGTTTCGATTTTCTGCATTACGACGTTAAAACGGGTGATTTCATCCTGCACTTTAAAATGAATC
GCAATCTGAGTTTTCAGCGTGGCCTGCCTGGTTTTATGCCTGCATGGGATATTGTGTTTGAGAAAAACGAAAC
ACAGTTCGATGCAAAAGGCACCCCGTTTATTGCAGGTAAACGTATTGTTCCGGTGATTGAAAATCATCGTTTCA
CCGGTCGTTATCGCGATCTGTATCCGGCAAATGAACTGATCGCACTGCTGGAAGAGAAAGGTATTGTTTTTCG
TGATGGCTCAAACATTCTGCCGAAACTGCTGGAAAATGATGATAGCCATGCAATTGATACCATGGTTGCACTG
ATTCGTAGCGTTCTGCAGATGCGTAATAGCAATGCAGCAACCGGTGAAGATTACATTAATAGTCCGGTTCGTG
ATCTGAATGGTGTTTGTTTTGATAGCCGTTTTCAGAATCCGGAATGGCCGATGGATGCAGATGCAAATGGTGC
ATATCATATTGCACTGAAAGGACAGCTGCTGCTGAACCACCTGAAAGAAAGCAAAGATCTGAAACTGCAAAA
CGGCATTAGCAATCAGGATTGGCTGGCATATATCCAAGAACTGCGTAACCCTAAAAAAAAACGCAAAGTGAA
GCTTGCGGCCGCACTCGAGCACCACCACCACCACCACTGA

**[0099]** SEQ ID NO.: 7

**[0100]** ATGCCGAAAAAAAAACGCAAAGTGGGTATTCATGGTGTTCCGGCAGCAACCCAGTTTGAA
GGTTTCACCAATCTGTATCAGGTTAGCAAAACCCTGCGTTTTGAACTGATTCCGCAGGGTAAAACCCTGAAAC
ATATTCAAGAACAGGGCTTCATCGAAGAGGATAAAGCACGTAACGATCACTACAAAGAACTGAAACCGATTA
TCGACCGCATCTATAAAACCTATGCAGATCAGTGTCTGCAGCTGGTTCAGCTGGATTGGGAAAATCTGAGCGC
AGCAATTGATAGTTATCGCAAAGAAAAAACCGAAGAAACCCGTAATGCACTGATTGAAGAACAGGCAACCTA
TCGTAATGCCATCCATGATTATTTCATTGGTCGTACCGATAATCTGACCGATGCAATTAACAAACGTCACGCCG
AAATCTATAAAGGCCTGTTTAAAGCCGAACTGTTTAATGGCAAAGTTCTGAAACAGCTGGGCACCGTTACCAC
CACCGAACATGAAAATGCACTGCTGCGTAGCTTTGATAAATTCACCACCTATTTCAGCGGCTTTTATGAGAATC
GCAAAAACGTGTTTAGCGCAGAAGATATTAGCACCGCAATTCCGCATCGTATTGTGCAGGATAATTTCCCGAA
ATTCAAAGAGAACTGCCACATTTTTACCCGTCTGATTACCGCAGTTCCGAGCCTGCGTGAACATTTTGAAAACG
TTAAAAAAGCCATCGGCATCTTTGTTAGCACCAGCATTGAAGAAGTTTTTAGCTTCCCGTTTTACAATCAGCTG
CTGACCCAGACCCAGATTGATCTGTATAACCAACTGCTGGGTGGTATTAGCCGTGAAGCAGGCACCGAAAAA
ATCAAAGGTCTGAATGAAGTGCTGAATCTGGCCATTCAGAAAAATGATGAAACCGCACATATTATTGCAAGCC
TGCCGCATCGTTTTATTCCGCTGTTCAAACAAATTCTGAGCGATCGTAATACCCTGAGCTTTATTCTGGAAGAA
TTCAAATCCGATGAAGAGGTGATTCAGAGCTTTTGCAAATACAAAACGCTGCTGCGCAATGAAAATGTTCTGG
AAACTGCCGAAGCACTGTTTAACGAACTGAATAGCATTGATCTGACCCACATCTTTATCAGCCACAAAAAACT
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GAACTGACCGGTAAAATTACCAAAAGCGCGAAAGAAAAAGTTCAGCGCAGTCTGAAACATGAGGATATTAAT
CTGCAAGAGATTATTAGCGCAGCCGGTAAAGAACTGTCAGAAGCATTTAAACAGAAAACCAGCGAAATTCTG
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GGCAAGCGGTTGGGATGTTAATAAAGAAAAAAACAACGGTGCCATCCTGTTCGTGAAAAATGGCCTGTATTA
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GCAATCAGGATTGGCTGGCATATATCCAAGAACTGCGTAACCCGAAAAAAAAACGCAAAGTGCTCGAGCACC
ACCACCACCACCACTGA

**[0101]** SEQ ID NO.: 8

**[0102]** ATGACCCAGTTTGAAGGTTTCACCAATCTGTATCAGGTTAGCAAAACCCTGCGTTTTGAACT
GATTCCGCAGGGTAAAACCCTGAAACATATTCAAGAACAGGGCTTCATCGAAGAGGATAAAGCACGTAACGA
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CAGCTGGATTGGGAAAATCTGAGCGCAGCAATTGATAGTTATCGCAAAGAAAAAACCGAAGAAACCCGTAAT
GCACTGATTGAAGAACAGGCAACCTATCGTAATGCCATCCATGATTATTTCATTGGTCGTACCGATAATCTGAC
CGATGCAATTAACAAACGTCACGCCGAAATCTATAAAGGCCTGTTTAAAGCCGAACTGTTTAATGGCAAAGTT
CTGAAACAGCTGGGCACCGTTACCACCACCGAACATGAAAATGCACTGCTGCGTAGCTTTGATAAATTCACCA
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TTGCCGAGAAAGAAATCATGGACGCAGTTGAAACCGGTAAACTGTACCTGTTCCAGATCTACAATAAAGATTT
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GATCTGAAACTGCAAAACGGCATTAGCAATCAGGATTGGCTGGCATATATCCAAGAACTGCGTAACCCGAAA
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**[0103]** SEQ ID NO.: 9

**[0104]** ATGGGCAGCAGCCATCATCATCATCACAGCAGCGGCCTGGTGCCGCGCGGCAGCCATA
TGGCTAGCATGACTGGTGGACAGCAAATGGGTCGGGATCCAACCCAGTTTGAAGGTTTCACCAATCTGTATCA
GGTTAGCAAAACCCTGCGTTTTGAACTGATTCCGCAGGGTAAAACCCTGAAACATATTCAAGAACAGGGCTTC
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ATGCAGATCAGTGTCTGCAGCTGGTTCAGCTGGATTGGGAAAATCTGAGCGCAGCAATTGATAGTTATCGCA
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TGCTGCGTAGCTTTGATAAATTCACCACCTATTTCAGCGGCTTTTATGAGAATCGCAAAAACGTGTTTAGCGCA
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GAACCACCTGAAAGAAAGCAAAGATCTGAAACTGCAAAACGGCATTAGCAATCAGGATTGGCTGGCATATAT

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AAAGAAACGTAAAGTTGGTGGTAGCGGTGGTTCAGGTGGTAGTGGCGGTAGTGGTGGCTCAGGGGGTTCTG
GTGGCTCTGGTGGTAGCCTCGAGCACCACCACCACCACCACTGA

**[0105]** SEQ ID NO.: 10

**[0106]** ATGACCCAGTTTGAAGGTTTCACCAATCTGTATCAGGTTAGCAAAACCCTGCGTTTTGAACT
GATTCCGCAGGGTAAAACCCTGAAACATATTCAAGAACAGGGCTTCATCGAAGAGGATAAAGCACGTAACGA
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CCTATTTCAGCGGCTTTTATGAGAATCGCAAAAACGTGTTTAGCGCAGAAGATATTAGCACCGCAATTCCGCA
TCGTATTGTGCAGGATAATTTCCCGAAATTCAAAGAGAACTGCCACATTTTTACCCGTCTGATTACCGCAGTTC
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GATAGCACCGGCAAAATCCTGGAACAGCGTAGCCTGAATACCATTCAGCAGTTTGATTACCAGAAAAAACTG
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TAGCGGTGGTTCAGGTGGTAGTGGCGGTAGTGGTGGCTCAGGGGGTTCTGGTGGCTCTGGTGGTAGCCTCG
AGCACCACCACCACCACCACTGA

**[0107]** SEQ ID NO.: 11

**[0108]** ATGGGCAGCAGCAGCAGCGGCCTGGTGCCGCGCGGCAGCCATATGGCTAGCATGACTGGT
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AAAGTTCAGCGCAGTCTGAAACATGAGGATATTAATCTGCAAGAGATTATTAGCGCAGCCGGTAAAGAACTG
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ACTGGAAATGGAACCGAGCCTGAGCTTTTATAACAAAGCCCGTAATTATGCCACCAAAAAACCGTATAGCGTC
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**[0109]** SEQ ID NO.: 12

**[0110]** ATGCCGCCTCCGAAACGTCCGCGTCTGGATGGTATCCACGGAGTCCCAGCAGCCACCCAGT
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**[0111]** SEQ ID NO.: 13

**[0112]** ATGAGCAGTGATGATGAAGCAACCGCAGATAGCCAGCATGCAGCACCGCCTAAAAAGAAA
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**[0113]** SEQ ID NO.: 14

**[0114]** ATGACCCAGTTTGAAGGTTTCACCAATCTGTATCAGGTTAGCAAAACCCTGCGTTTTGAACT
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GCACTGATTGAAGAACAGGCAACCTATCGTAATGCCATCCATGATTATTTCATTGGTCGTACCGATAATCTGAC
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ACTGA

**[0115]** SEQ ID NO.: 15

**[0116]** ATGACCCAGTTTGAAGGTTTCACCAATCTGTATCAGGTTAGCAAAACCCTGCGTTTTGAACT
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GCACTGATTGAAGAACAGGCAACCTATCGTAATGCCATCCATGATTATTTCATTGGTCGTACCGATAATCTGAC
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AATACCCTGAGCTTTATTCTGGAAGAATTCAAATCCGATGAAGAGGTGATTCAGAGCTTTTGCAAATACAAAA
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CCACATCTTTATCAGCCACAAAAAACTGGAAACCATTTCAAGCGCACTGTGTGATCATTGGGATACCCTGCGTA
ATGCCCTGTATGAACGTCGTATTAGCGAACTGACCGGTAAAATTACCAAAAGCGCGAAAGAAAAAGTTCAGC
GCAGTCTGAAACATGAGGATATTAATCTGCAAGAGATTATTAGCGCAGCCGGTAAAGAACTGTCAGAAGCAT
TTAAACAGAAAACCAGCGAAATTCTGTCACATGCACATGCAGCACTGGATCAGCCGCTGCCGACCACCCTGAA
AAAACAAGAAGAAAAAGAAATCCTGAAAAGCCAGCTGGATAGCCTGCTGGGTCTGTATCATCTGCTGGACTG
GTTTGCAGTTGATGAAAGCAATGAAGTTGATCCGGAATTTAGCGCACGTCTGACCGGCATTAAACTGGAAAT
GGAACCGAGCCTGAGCTTTTATAACAAAGCCCGTAATTATGCCACCAAAAAACCGTATAGCGTCGAAAAATTC
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TTGAACCGACGGAAAAAACCAGTGAAGGTTTTGATAAAATGTACTACGACTATTTTCCGGATGCAGCCAAAAT
GATTCCGAAATGTAGCACCCAGCTGAAAGCAGTTACCGCACATTTTCAGACCCATACCACCCCGATTCTGCTGA
GCAATAACTTTATTGAACCGCTGGAAATCACCAAAGAGATCTACGATCTGAATAACCCGGAAAAAGAGCCGA
AAAAATTCCAGACCGCATATGCAAAAAAAACCGGTGATCAGAAAGGTTATCGTGAAGCGCTGTGTAAATGGA
TTGATTTCACCCGTGATTTTCTGAGCAAATACACCAAAACCACCAGTATCGATCTGAGCAGCCTGCGTCCGAGC
AGCCAGTATAAAGATCTGGGCGAATATTATGCAGAACTGAATCCGCTGCTGTATCATATTAGCTTTCAGCGTA
TTGCCGAGAAAGAAATCATGGACGCAGTTGAAACCGGTAAACTGTACCTGTTCCAGATCTACAATAAAGATTT
TGCCAAAGGCCATCATGGCAAACCGAATCTGCATACCCTGTATTGGACCGGTCTGTTTAGCCCTGAAAATCTG
GCAAAAACCTCGATTAAACTGAATGGTCAGGCGGAACTGTTTTATCGTCCGAAAAGCCGTATGAAACGTATG
GCACATCGTCTGGGTGAAAAAATGCTGAACAAAAAACTGAAAGACCAGAAAACCCCGATCCCGGATACACTG
TATCAAGAACTGTATGATTATGTGAACCATCGTCTGAGCCATGATCTGAGTGATGAAGCACGTGCCCTGCTGC
CGAATGTTATTACCAAAGAAGTTAGCCACGAGATCATTAAAGATCGTCGTTTTACCAGCGACAAATTCTTTTTT
CATGTGCCGATTACCCTGAATTATCAGGCAGCAAATAGCCCGAGCAAATTTAACCAGCGTGTTAATGCATATC
TGAAAGAACATCCAGAAACGCCGATTATTGGTATTGATCGTGGTGAACGTAACCTGATTTATATCACCGTTATT
GATAGCACCGGCAAAATCCTGGAACAGCGTAGCCTGAATACCATTCAGCAGTTTGATTACCAGAAAAAACTG
GATAATCGCGAGAAAGAACGTGTTGCAGCACGTCAGGCATGGTCAGTTGTTGGTACAATTAAAGACCTGAAA
CAGGGTTATCTGAGCCAGGTTATTCATGAAATTGTGGATCTGATGATTCACTATCAGGCCGTTGTTGTGCTGG
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AATGCTGATTGACAAACTGAATTGCCTGGTGCTGAAAGATTATCCGGCTGAAAAAGTTGGTGGTGTTCTGAAT
CCGTATCAGCTGACCGATCAGTTTACCAGCTTTGCAAAAATGGGCACCCAGAGCGGATTTCTGTTTTATGTTCC
GGCACCGTATACGAGCAAAATTGATCCGCTGACCGGTTTTGTTGATCCGTTTGTTTGGAAAACCATCAAAAAC
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GCACTTTAAAATGAATCGCAATCTGAGTTTTCAGCGTGGCCTGCCTGGTTTTATGCCTGCATGGGATATTGTGT
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AAAGGTATTGTTTTTCGTGATGGCTCAAACATTCTGCCGAAACTGCTGGAAAATGATGATAGCCATGCAATTG
ATACCATGGTTGCACTGATTCGTAGCGTTCTGCAGATGCGTAATAGCAATGCAGCAACCGGTGAAGATTACAT
TAATAGTCCGGTTCGTGATCTGAATGGTGTTTGTTTTGATAGCCGTTTTCAGAATCCGGAATGGCCGATGGAT

GCAGATGCAAATGGTGCATATCATATTGCACTGAAAGGACAGCTGCTGCTGAACCACCTGAAAGAAAGCAAA
GATCTGAAACTGCAAAACGGCATTAGCAATCAGGATTGGCTGGCATATATCCAAGAACTGCGTAACGGTCGT
AAACGTACCGCAGATGGTAGCGAATTTGAAAGCCCGAAAAAAAAGCGTAAGGTGGAAGGTGGTAGCGGTGG
TTCAGGTGGTAGTGGCGGTAGTGGTGGCTCAGGGGGTTCTGGTGGCTCTGGTGGTAGCCTCGAGCACCACCA
CCACCACCACTGA

**[0117]** SEQ ID NO.: 16

**[0118]** ATGACCCAGTTTGAAGGTTTCACCAATCTGTATCAGGTTAGCAAAACCCTGCGTTTTGAACT
GATTCCGCAGGGTAAAACCCTGAAACATATTCAAGAACAGGGCTTCATCGAAGAGGATAAAGCACGTAACGA
TCACTACAAAGAACTGAAACCGATTATCGACCGCATCTATAAAACCTATGCAGATCAGTGTCTGCAGCTGGTT
CAGCTGGATTGGGAAAATCTGAGCGCAGCAATTGATAGTTATCGCAAAGAAAAAACCGAAGAAACCCGTAAT
GCACTGATTGAAGAACAGGCAACCTATCGTAATGCCATCCATGATTATTTCATTGGTCGTACCGATAATCTGAC
CGATGCAATTAACAAACGTCACGCCGAAATCTATAAAGGCCTGTTTAAAGCCGAACTGTTTAATGGCAAAGTT
CTGAAACAGCTGGGCACCGTTACCACCACCGAACATGAAAATGCACTGCTGCGTAGCTTTGATAAATTCACCA
CCTATTTCAGCGGCTTTTATGAGAATCGCAAAAACGTGTTTAGCGCAGAAGATATTAGCACCGCAATTCCGCA
TCGTATTGTGCAGGATAATTTCCCGAAATTCAAAGAGAACTGCCACATTTTTACCCGTCTGATTACCGCAGTTC
CGAGCCTGCGTGAACATTTTGAAAACGTTAAAAAAGCCATCGGCATCTTTGTTAGCACCAGCATTGAAGAAGT
TTTTAGCTTCCCGTTTTACAATCAGCTGCTGACCCAGACCCAGATTGATCTGTATAACCAACTGCTGGGTGGTA
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AATACCCTGAGCTTTATTCTGGAAGAATTCAAATCCGATGAAGAGGTGATTCAGAGCTTTTGCAAATACAAAA
CGCTGCTGCGCAATGAAAATGTTCTGGAAACTGCCGAAGCACTGTTTAACGAACTGAATAGCATTGATCTGAC
CCACATCTTTATCAGCCACAAAAAACTGGAAACCATTTCAAGCGCACTGTGTGATCATTGGGATACCCTGCGTA
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TTAAACAGAAAACCAGCGAAATTCTGTCACATGCACATGCAGCACTGGATCAGCCGCTGCCGACCACCCTGAA
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AAACTGAACTTTCAGATGCCGACCCTGGCAAGCGGTTGGGATGTTAATAAAGAAAAAAACAACGGTGCCATC
CTGTTCGTGAAAAATGGCCTGTATTATCTGGGTATTATGCCGAAACAGAAAGGTCGTTATAAAGCGCTGAGCT
TTGAACCGACGGAAAAAACCAGTGAAGGTTTTGATAAAATGTACTACGACTATTTTCCGGATGCAGCCAAAAT
GATTCCGAAATGTAGCACCCAGCTGAAAGCAGTTACCGCACATTTTCAGACCCATACCACCCCGATTCTGCTGA
GCAATAACTTTATTGAACCGCTGGAAATCACCAAAGAGATCTACGATCTGAATAACCCGGAAAAAGAGCCGA
AAAAATTCCAGACCGCATATGCAAAAAAAACCGGTGATCAGAAAGGTTATCGTGAAGCGCTGTGTAAATGGA
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TTGCCGAGAAAGAAATCATGGACGCAGTTGAAACCGGTAAACTGTACCTGTTCCAGATCTACAATAAAGATTT
TGCCAAAGGCCATCATGGCAAACCGAATCTGCATACCCTGTATTGGACCGGTCTGTTTAGCCCTGAAAATCTG
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GCACATCGTCTGGGTGAAAAAATGCTGAACAAAAAACTGAAAGACCAGAAAACCCCGATCCCGGATACACTG
TATCAAGAACTGTATGATTATGTGAACCATCGTCTGAGCCATGATCTGAGTGATGAAGCACGTGCCCTGCTGC
CGAATGTTATTACCAAAGAAGTTAGCCACGAGATCATTAAAGATCGTCGTTTTACCAGCGACAAATTCTTTTTT
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TGAAAGAACATCCAGAAACGCCGATTATTGGTATTGATCGTGGTGAACGTAACCTGATTTATATCACCGTTATT
GATAGCACCGGCAAAATCCTGGAACAGCGTAGCCTGAATACCATTCAGCAGTTTGATTACCAGAAAAAACTG
GATAATCGCGAGAAAGAACGTGTTGCAGCACGTCAGGCATGGTCAGTTGTTGGTACAATTAAAGACCTGAAA
CAGGGTTATCTGAGCCAGGTTATTCATGAAATTGTGGATCTGATGATTCACTATCAGGCCGTTGTTGTGCTGG
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CCGTATCAGCTGACCGATCAGTTTACCAGCTTTGCAAAAATGGGCACCCAGAGCGGATTTCTGTTTTATGTTCC
GGCACCGTATACGAGCAAAATTGATCCGCTGACCGGTTTTGTTGATCCGTTTGTTTGGAAAACCATCAAAAAC
CATGAAAGCCGCAAACATTTTCTGGAAGGTTTCGATTTTCTGCATTACGACGTTAAAACGGGTGATTTCATCCT
GCACTTTAAAATGAATCGCAATCTGAGTTTTCAGCGTGGCCTGCCTGGTTTTATGCCTGCATGGGATATTGTGT
TTGAGAAAAACGAAACACAGTTCGATGCAAAAGGCACCCCGTTTATTGCAGGTAAACGTATTGTTCCGGTGAT
TGAAAATCATCGTTTCACCGGTCGTTATCGCGATCTGTATCCGGCAAATGAACTGATCGCACTGCTGGAAGAG
AAAGGTATTGTTTTTCGTGATGGCTCAAACATTCTGCCGAAACTGCTGGAAAATGATGATAGCCATGCAATTG
ATACCATGGTTGCACTGATTCGTAGCGTTCTGCAGATGCGTAATAGCAATGCAGCAACCGGTGAAGATTACAT
TAATAGTCCGGTTCGTGATCTGAATGGTGTTTGTTTTGATAGCCGTTTTCAGAATCCGGAATGGCCGATGGAT
GCAGATGCAAATGGTGCATATCATATTGCACTGAAAGGACAGCTGCTGCTGAACCACCTGAAAGAAAGCAAA
GATCTGAAACTGCAAAACGGCATTAGCAATCAGGATTGGCTGGCATATATCCAAGAACTGCGTAACGGTCGT
AGCAGTGATGATGAAGCAACCGCAGATAGCCAGCATGCAGCACCGCCTAAAAAGAAACGTAAAGTTGGTGG
TAGCGGCGGTAGTAAACGTACCGCAGATGGTAGCGAATTTGAAAGCCCGAAAAAAAAGCGTAAGGTGGAAG
GTGGTAGCGGTGGTTCAGGTGGTAGTGGCGGTAGTGGTGGCTCAGGGGGTTCTGGTGGCTCTGGTGGTAGC
CTCGAGCACCACCACCACCACCACTGA

**[0119]** SEQ ID NO.: 17

**[0120]** ATGACCCAGTTTGAAGGTTTCACCAATCTGTATCAGGTTAGCAAAACCCTGCGTTTTGAACT
GATTCCGCAGGGTAAAACCCTGAAACATATTCAAGAACAGGGCTTCATCGAAGAGGATAAAGCACGTAACGA
TCACTACAAAGAACTGAAACCGATTATCGACCGCATCTATAAAACCTATGCAGATCAGTGTCTGCAGCTGGTT
CAGCTGGATTGGGAAAATCTGAGCGCAGCAATTGATAGTTATCGCAAAGAAAAAACCGAAGAAACCCGTAAT
GCACTGATTGAAGAACAGGCAACCTATCGTAATGCCATCCATGATTATTTCATTGGTCGTACCGATAATCTGAC
CGATGCAATTAACAAACGTCACGCCGAAATCTATAAAGGCCTGTTTAAAGCCGAACTGTTTAATGGCAAAGTT
CTGAAACAGCTGGGCACCGTTACCACCACCGAACATGAAAATGCACTGCTGCGTAGCTTTGATAAATTCACCA
CCTATTTCAGCGGCTTTTATGAGAATCGCAAAAACGTGTTTAGCGCAGAAGATATTAGCACCGCAATTCCGCA
TCGTATTGTGCAGGATAATTTCCCGAAATTCAAAGAGAACTGCCACATTTTTACCCGTCTGATTACCGCAGTTC
CGAGCCTGCGTGAACATTTTGAAAACGTTAAAAAAGCCATCGGCATCTTTGTTAGCACCAGCATTGAAGAAGT
TTTTAGCTTCCCGTTTTACAATCAGCTGCTGACCCAGACCCAGATTGATCTGTATAACCAACTGCTGGGTGGTA
TTAGCCGTGAAGCAGGCACCGAAAAAATCAAAGGTCTGAATGAAGTGCTGAATCTGGCCATTCAGAAAAATG
ATGAAACCGCACATATTATTGCAAGCCTGCCGCATCGTTTTATTCCGCTGTTCAAACAAATTCTGAGCGATCGT
AATACCCTGAGCTTTATTCTGGAAGAATTCAAATCCGATGAAGAGGTGATTCAGAGCTTTTGCAAATACAAAA
CGCTGCTGCGCAATGAAAATGTTCTGGAAACTGCCGAAGCACTGTTTAACGAACTGAATAGCATTGATCTGAC
CCACATCTTTATCAGCCACAAAAAACTGGAAACCATTTCAAGCGCACTGTGTGATCATTGGGATACCCTGCGTA
ATGCCCTGTATGAACGTCGTATTAGCGAACTGACCGGTAAAATTACCAAAAGCGCGAAAGAAAAAGTTCAGC
GCAGTCTGAAACATGAGGATATTAATCTGCAAGAGATTATTAGCGCAGCCGGTAAAGAACTGTCAGAAGCAT
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AAAACAAGAAGAAAAAGAAATCCTGAAAAGCCAGCTGGATAGCCTGCTGGGTCTGTATCATCTGCTGGACTG
GTTTGCAGTTGATGAAAGCAATGAAGTTGATCCGGAATTTAGCGCACGTCTGACCGGCATTAAACTGGAAAT

GGAACCGAGCCTGAGCTTTTATAACAAAGCCCGTAATTATGCCACCAAAAAACCGTATAGCGTCGAAAAATTC
AAACTGAACTTTCAGATGCCGACCCTGGCAAGCGGTTGGGATGTTAATAAAGAAAAAAACAACGGTGCCATC
CTGTTCGTGAAAAATGGCCTGTATTATCTGGGTATTATGCCGAAACAGAAAGGTCGTTATAAAGCGCTGAGCT
TTGAACCGACGGAAAAAACCAGTGAAGGTTTTGATAAAATGTACTACGACTATTTTCCGGATGCAGCCAAAAT
GATTCCGAAATGTAGCACCCAGCTGAAAGCAGTTACCGCACATTTTCAGACCCATACCACCCCGATTCTGCTGA
GCAATAACTTTATTGAACCGCTGGAAATCACCAAAGAGATCTACGATCTGAATAACCCGGAAAAAGAGCCGA
AAAAATTCCAGACCGCATATGCAAAAAAAACCGGTGATCAGAAAGGTTATCGTGAAGCGCTGTGTAAATGGA
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TTGCCGAGAAAGAAATCATGGACGCAGTTGAAACCGGTAAACTGTACCTGTTCCAGATCTACAATAAAGATTT
TGCCAAAGGCCATCATGGCAAACCGAATCTGCATACCCTGTATTGGACCGGTCTGTTTAGCCCTGAAAATCTG
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GCACATCGTCTGGGTGAAAAAATGCTGAACAAAAAACTGAAAGACCAGAAAACCCCGATCCCGGATACACTG
TATCAAGAACTGTATGATTATGTGAACCATCGTCTGAGCCATGATCTGAGTGATGAAGCACGTGCCCTGCTGC
CGAATGTTATTACCAAAGAAGTTAGCCACGAGATCATTAAAGATCGTCGTTTTACCAGCGACAAATTCTTTTTT
CATGTGCCGATTACCCTGAATTATCAGGCAGCAAATAGCCCGAGCAAATTTAACCAGCGTGTTAATGCATATC
TGAAAGAACATCCAGAAACGCCGATTATTGGTATTGATCGTGGTGAACGTAACCTGATTTATATCACCGTTATT
GATAGCACCGGCAAAATCCTGGAACAGCGTAGCCTGAATACCATTCAGCAGTTTGATTACCAGAAAAAACTG
GATAATCGCGAGAAAGAACGTGTTGCAGCACGTCAGGCATGGTCAGTTGTTGGTACAATTAAAGACCTGAAA
CAGGGTTATCTGAGCCAGGTTATTCATGAAATTGTGGATCTGATGATTCACTATCAGGCCGTTGTTGTGCTGG
AAAACCTGAATTTTGGCTTTAAAAGCAAACGTACCGGCATTGCAGAAAAAGCAGTTTATCAGCAGTTCGAGAA
AATGCTGATTGACAAACTGAATTGCCTGGTGCTGAAAGATTATCCGGCTGAAAAAGTTGGTGGTGTTCTGAAT
CCGTATCAGCTGACCGATCAGTTTACCAGCTTTGCAAAAATGGGCACCCAGAGCGGATTTCTGTTTTATGTTCC
GGCACCGTATACGAGCAAAATTGATCCGCTGACCGGTTTTGTTGATCCGTTTGTTTGGAAAACCATCAAAAAC
CATGAAAGCCGCAAACATTTTCTGGAAGGTTTCGATTTTCTGCATTACGACGTTAAAACGGGTGATTTCATCCT
GCACTTTAAAATGAATCGCAATCTGAGTTTTCAGCGTGGCCTGCCTGGTTTTATGCCTGCATGGGATATTGTGT
TTGAGAAAAACGAAACACAGTTCGATGCAAAAGGCACCCCGTTTATTGCAGGTAAACGTATTGTTCCGGTGAT
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AAAGGTATTGTTTTTCGTGATGGCTCAAACATTCTGCCGAAACTGCTGGAAAATGATGATAGCCATGCAATTG
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TAATAGTCCGGTTCGTGATCTGAATGGTGTTTGTTTTGATAGCCGTTTTCAGAATCCGGAATGGCCGATGGAT
GCAGATGCAAATGGTGCATATCATATTGCACTGAAAGGACAGCTGCTGCTGAACCACCTGAAAGAAAGCAAA
GATCTGAAACTGCAAAACGGCATTAGCAATCAGGATTGGCTGGCATATATCCAAGAACTGCGTAACGGTCGT
AAACGTCCGGCAGCAACCAAAAAAGCAGGTCAGGCAAAAAAGAAAAAAGGTGGTAGCGGCGGTAGTAAAC
GTACCGCAGATGGTAGCGAATTTGAAAGCCCGAAAAAAAAGCGTAAGGTGGAAGGTGGTAGCGGTGGTTCA
GGTGGTAGTGGCGGTAGTGGTGGCTCAGGGGGTTCTGGTGGCTCTGGTGGTAGCCTCGAGCACCACCACCA
CCACCACTGA

**[0121]** The following amino acid sequences of preferred Cas12a polypeptides are depicted below.

**[0122]** SEQ ID NO.:18

**[0123]** MGSSSSGLVPRGSHMASMTGGQQMGRDPGKPIPNPLLGLDSTAPKKKRKVGIHGVPAATQF
EGFTNLYQVSKTLRFELIPQGKTLKHIQEQGFIEEDKARNDHYKELKPIIDRIYKTYADQCLQLVQLDWENLSAAIDSY

RKEKTEETRNALIEEQATYRNAIHDYFIGRTDNLTDAINKRHAEIYKGLFKAELFNGKVLKQLGTVTTTEHENALLRSF
DKFTTYFSGFYENRKNVFSAEDISTAIPHRIVQDNFPKFKENCHIFTRLITAVPSLREHFENVKKAIGIFVSTSIEEVFSFP
FYNQLLTQTQIDLYNQLLGGISREAGTEKIKGLNEVLNLAIQKNDETAHIIASLPHRFIPLFKQILSDRNTLSFILEEFKSD
EEVIQSFCKYKTLLRNENVLETAEALFNELNSIDLTHIFISHKKLETISSALCDHWDTLRNALYERRISELTGKITKSAKEK
VQRSLKHEDINLQEIISAAGKELSEAFKQKTSEILSHAHAALDQPLPTTLKKQEEKEILKSQLDSLLGLYHLLDWFAVDE
SNEVDPEFSARLTGIKLEMEPSLSFYNKARNYATKKPYSVEKFKLNFQMPTLASGWDVNKEKNNGAILFVKNGLYYL
GIMPKQKGRYKALSFEPTEKTSEGFDKMYYDYFPDAAKMIPKCSTQLKAVTAHFQTHTTPILLSNNFIEPLEITKEIYD
LNNPEKEPKKFQTAYAKKTGDQKGYREALCKWIDFTRDFLSKYTKTTSIDLSSLRPSSQYKDLGEYYAELNPLLYHISF
QRIAEKEIMDAVETGKLYLFQIYNKDFAKGHHGKPNLHTLYWTGLFSPENLAKTSIKLNGQAELFYRPKSRMKRMA
HRLGEKMLNKKLKDQKTPIPDTLYQELYDYVNHRLSHDLSDEARALLPNVITKEVSHEIIKDRRFTSDKFFFHVPITLN
YQAANSPSKFNQRVNAYLKEHPETPIIGIDRGERNLIYITVIDSTGKILEQRSLNTIQQFDYQKKLDNREKERVAARQA
WSVVGTIKDLKQGYLSQVIHEIVDLMIHYQAVVVLENLNFGFKSKRTGIAEKAVYQQFEKMLIDKLNCLVLKDYPAE
KVGGVLNPYQLTDQFTSFAKMGTQSGFLFYVPAPYTSKIDPLTGFVDPFVWKTIKNHESRKHFLEGFDFLHYDVKT
GDFILHFKMNRNLSFQRGLPGFMPAWDIVFEKNETQFDAKGTPFIAGKRIVPVIENHRFTGRYRDLYPANELIALLE
EKGIVFRDGSNILPKLLENDDSHAIDTMVALIRSVLQMRNSNAATGEDYINSPVRDLNGVCFDSRFQNPEWPMDA
DANGAYHIALKGQLLLNHLKESKDLKLQNGISNQDWLAYIQELRNPKKKRKVKLAAALEHHHHHH

**[0124]** SEQ ID NO.:19

**[0125]** MGSSSSGLVPRGSHMASMTGGQQMGRDPAPKKKRKVGIHGVPAATQFEGFTNLYQVSKTLR
FELIPQGKTLKHIQEQGFIEEDKARNDHYKELKPIIDRIYKTYADQCLQLVQLDWENLSAAIDSYRKEKTEETRNALIEE
QATYRNAIHDYFIGRTDNLTDAINKRHAEIYKGLFKAELFNGKVLKQLGTVTTTEHENALLRSFDKFTTYFSGFYENR
KNVFSAEDISTAIPHRIVQDNFPKFKENCHIFTRLITAVPSLREHFENVKKAIGIFVSTSIEEVFSFPFYNQLLTQTQIDLY
NQLLGGISREAGTEKIKGLNEVLNLAIQKNDETAHIIASLPHRFIPLFKQILSDRNTLSFILEEFKSDEEVIQSFCKYKTLL
RNENVLETAEALFNELNSIDLTHIFISHKKLETISSALCDHWDTLRNALYERRISELTGKITKSAKEKVQRSLKHEDINLQ
EIISAAGKELSEAFKQKTSEILSHAHAALDQPLPTTLKKQEEKEILKSQLDSLLGLYHLLDWFAVDESNEVDPEFSARLT
GIKLEMEPSLSFYNKARNYATKKPYSVEKFKLNFQMPTLASGWDVNKEKNNGAILFVKNGLYYLGIMPKQKGRYKA
LSFEPTEKTSEGFDKMYYDYFPDAAKMIPKCSTQLKAVTAHFQTHTTPILLSNNFIEPLEITKEIYDLNNPEKEPKKFQ
TAYAKKTGDQKGYREALCKWIDFTRDFLSKYTKTTSIDLSSLRPSSQYKDLGEYYAELNPLLYHISFQRIAEKEIMDAV
ETGKLYLFQIYNKDFAKGHHGKPNLHTLYWTGLFSPENLAKTSIKLNGQAELFYRPKSRMKRMAHRLGEKMLNKKL
KDQKTPIPDTLYQELYDYVNHRLSHDLSDEARALLPNVITKEVSHEIIKDRRFTSDKFFFHVPITLNYQAANSPSKFNQ
RVNAYLKEHPETPIIGIDRGERNLIYITVIDSTGKILEQRSLNTIQQFDYQKKLDNREKERVAARQAWSVVGTIKDLKQ
GYLSQVIHEIVDLMIHYQAVVVLENLNFGFKSKRTGIAEKAVYQQFEKMLIDKLNCLVLKDYPAEKVGGVLNPYQLT
DQFTSFAKMGTQSGFLFYVPAPYTSKIDPLTGFVDPFVWKTIKNHESRKHFLEGFDFLHYDVKTGDFILHFKMNRNL
SFQRGLPGFMPAWDIVFEKNETQFDAKGTPFIAGKRIVPVIENHRFTGRYRDLYPANELIALLEEKGIVFRDGSNILP
KLLENDDSHAIDTMVALIRSVLQMRNSNAATGEDYINSPVRDLNGVCFDSRFQNPEWPMDADANGAYHIALKG
QLLLNHLKESKDLKLQNGISNQDWLAYIQELRNPKKKRKVKLAAALEHHHHHH

**[0126]** SEQ ID NO.:20

**[0127]** MPKKKRKVGIHGVPAATQFEGFTNLYQVSKTLRFELIPQGKTLKHIQEQGFIEEDKARNDHYKEL
KPIIDRIYKTYADQCLQLVQLDWENLSAAIDSYRKEKTEETRNALIEEQATYRNAIHDYFIGRTDNLTDAINKRHAEIY
KGLFKAELFNGKVLKQLGTVTTTEHENALLRSFDKFTTYFSGFYENRKNVFSAEDISTAIPHRIVQDNFPKFKENCHIF
TRLITAVPSLREHFENVKKAIGIFVSTSIEEVFSFPFYNQLLTQTQIDLYNQLLGGISREAGTEKIKGLNEVLNLAIQKND
ETAHIIASLPHRFIPLFKQILSDRNTLSFILEEFKSDEEVIQSFCKYKTLLRNENVLETAEALFNELNSIDLTHIFISHKKLETI

SSALCDHWDTLRNALYERRISELTGKITKSAKEKVQRSLKHEDINLQEIISAAGKELSEAFKQKTSEILSHAHAALDQPL
PTTLKKQEEKEILKSQLDSLLGLYHLLDWFAVDESNEVDPEFSARLTGIKLEMEPSLSFYNKARNYATKKPYSVEKFKL
NFQMPTLASGWDVNKEKNNGAILFVKNGLYYLGIMPKQKGRYKALSFEPTEKTSEGFDKMYYDYFPDAAKMIPKC
STQLKAVTAHFQTHTTPILLSNNFIEPLEITKEIYDLNNPEKEPKKFQTAYAKKTGDQKGYREALCKWIDFTRDFLSKY
TKTTSIDLSSLRPSSQYKDLGEYYAELNPLLYHISFQRIAEKEIMDAVETGKLYLFQIYNKDFAKGHHGKPNLHTLYWT
GLFSPENLAKTSIKLNGQAELFYRPKSRMKRMAHRLGEKMLNKKLKDQKTPIPDTLYQELYDYVNHRLSHDLSDEA
RALLPNVITKEVSHEIIKDRRFTSDKFFFHVPITLNYQAANSPSKFNQRVNAYLKEHPETPIIGIDRGERNLIYITVIDST
GKILEQRSLNTIQQFDYQKKLDNREKERVAARQAWSVVGTIKDLKQGYLSQVIHEIVDLMIHYQAVVVLENLNFGF
KSKRTGIAEKAVYQQFEKMLIDKLNCLVLKDYPAEKVGGVLNPYQLTDQFTSFAKMGTQSGFLFYVPAPYTSKIDPL
TGFVDPFVWKTIKNHESRKHFLEGFDFLHYDVKTGDFILHFKMNRNLSFQRGLPGFMPAWDIVFEKNETQFDAKG
TPFIAGKRIVPVIENHRFTGRYRDLYPANELIALLEEKGIVFRDGSNILPKLLENDDSHAIDTMVALIRSVLQMRNSNA
ATGEDYINSPVRDLNGVCFDSRFQNPEWPMDADANGAYHIALKGQLLLNHLKESKDLKLQNGISNQDWLAYIQEL
RNPKKKRKVLEHHHHHH

**[0128]** SEQ ID NO.:21

**[0129]** MTQFEGFTNLYQVSKTLRFELIPQGKTLKHIQEQGFIEEDKARNDHYKELKPIIDRIYKTYADQCL
QLVQLDWENLSAAIDSYRKEKTEETRNALIEEQATYRNAIHDYFIGRTDNLTDAINKRHAEIYKGLFKAELFNGKVLK
QLGTVTTTEHENALLRSFDKFTTYFSGFYENRKNVFSAEDISTAIPHRIVQDNFPKFKENCHIFTRLITAVPSLREHFEN
VKKAIGIFVSTSIEEVFSFPFYNQLLTQTQIDLYNQLLGGISREAGTEKIKGLNEVLNLAIQKNDETAHIIASLPHRFIPLF
KQILSDRNTLSFILEEFKSDEEVIQSFCKYKTLLRNENVLETAEALFNELNSIDLTHIFISHKKLETISSALCDHWDTLRNA
LYERRISELTGKITKSAKEKVQRSLKHEDINLQEIISAAGKELSEAFKQKTSEILSHAHAALDQPLPTTLKKQEEKEILKSQ
LDSLLGLYHLLDWFAVDESNEVDPEFSARLTGIKLEMEPSLSFYNKARNYATKKPYSVEKFKLNFQMPTLASGWDV
NKEKNNGAILFVKNGLYYLGIMPKQKGRYKALSFEPTEKTSEGFDKMYYDYFPDAAKMIPKCSTQLKAVTAHFQTH
TTPILLSNNFIEPLEITKEIYDLNNPEKEPKKFQTAYAKKTGDQKGYREALCKWIDFTRDFLSKYTKTTSIDLSSLRPSSQ
YKDLGEYYAELNPLLYHISFQRIAEKEIMDAVETGKLYLFQIYNKDFAKGHHGKPNLHTLYWTGLFSPENLAKTSIKLN
GQAELFYRPKSRMKRMAHRLGEKMLNKKLKDQKTPIPDTLYQELYDYVNHRLSHDLSDEARALLPNVITKEVSHEII
KDRRFTSDKFFFHVPITLNYQAANSPSKFNQRVNAYLKEHPETPIIGIDRGERNLIYITVIDSTGKILEQRSLNTIQQFD
YQKKLDNREKERVAARQAWSVVGTIKDLKQGYLSQVIHEIVDLMIHYQAVVVLENLNFGFKSKRTGIAEKAVYQQF
EKMLIDKLNCLVLKDYPAEKVGGVLNPYQLTDQFTSFAKMGTQSGFLFYVPAPYTSKIDPLTGFVDPFVWKTIKNHE
SRKHFLEGFDFLHYDVKTGDFILHFKMNRNLSFQRGLPGFMPAWDIVFEKNETQFDAKGTPFIAGKRIVPVIENHR
FTGRYRDLYPANELIALLEEKGIVFRDGSNILPKLLENDDSHAIDTMVALIRSVLQMRNSNAATGEDYINSPVRDLNG
VCFDSRFQNPEWPMDADANGAYHIALKGQLLLNHLKESKDLKLQNGISNQDWLAYIQELRNPKKKRKVLEHHHH
HH

**[0130]** SEQ ID NO.:22

**[0131]** MGSSHHHHHHSSGLVPRGSHMASMTGGQQMGRDPTQFEGFTNLYQVSKTLRFELIPQGKTL
KHIQEQGFIEEDKARNDHYKELKPIIDRIYKTYADQCLQLVQLDWENLSAAIDSYRKEKTEETRNALIEEQATYRNAIH
DYFIGRTDNLTDAINKRHAEIYKGLFKAELFNGKVLKQLGTVTTTEHENALLRSFDKFTTYFSGFYENRKNVFSAEDIS
TAIPHRIVQDNFPKFKENCHIFTRLITAVPSLREHFENVKKAIGIFVSTSIEEVFSFPFYNQLLTQTQIDLYNQLLGGISR
EAGTEKIKGLNEVLNLAIQKNDETAHIIASLPHRFIPLFKQILSDRNTLSFILEEFKSDEEVIQSFCKYKTLLRNENVLETA
EALFNELNSIDLTHIFISHKKLETISSALCDHWDTLRNALYERRISELTGKITKSAKEKVQRSLKHEDINLQEIISAAGKEL
SEAFKQKTSEILSHAHAALDQPLPTTLKKQEEKEILKSQLDSLLGLYHLLDWFAVDESNEVDPEFSARLTGIKLEMEPS
LSFYNKARNYATKKPYSVEKFKLNFQMPTLASGWDVNKEKNNGAILFVKNGLYYLGIMPKQKGRYKALSFEPTEKT

SEGFDKMYYDYFPDAAKMIPKCSTQLKAVTAHFQTHTTPILLSNNFIEPLEITKEIYDLNNPEKEPKKFQTAYAKKTG
DQKGYREALCKWIDFTRDFLSKYTKTTSIDLSSLRPSSQYKDLGEYYAELNPLLYHISFQRIAEKEIMDAVETGKLYLFQ
IYNKDFAKGHHGKPNLHTLYWTGLFSPENLAKTSIKLNGQAELFYRPKSRMKRMAHRLGEKMLNKKLKDQKTPIP
DTLYQELYDYVNHRLSHDLSDEARALLPNVITKEVSHEIIKDRRFTSDKFFFHVPITLNYQAANSPSKFNQRVNAYLKE
HPETPIIGIDRGERNLIYITVIDSTGKILEQRSLNTIQQFDYQKKLDNREKERVAARQAWSVVGTIKDLKQGYLSQVIH
EIVDLMIHYQAVVVLENLNFGFKSKRTGIAEKAVYQQFEKMLIDKLNCLVLKDYPAEKVGGVLNPYQLTDQFTSFAK
MGTQSGFLFYVPAPYTSKIDPLTGFVDPFVWKTIKNHESRKHFLEGFDFLHYDVKTGDFILHFKMNRNLSFQRGLP
GFMPAWDIVFEKNETQFDAKGTPFIAGKRIVPVIENHRFTGRYRDLYPANELIALLEEKGIVFRDGSNILPKLLENDD
SHAIDTMVALIRSVLQMRNSNAATGEDYINSPVRDLNGVCFDSRFQNPEWPMDADANGAYHIALKGQLLLNHLK
ESKDLKLQNGISNQDWLAYIQELRNGRSSDDEATADSQHAAPPKKKRKVGGSGGSGGSGGSGGSGGSGGSGGSL
EHHHHHH

**[0132]** SEQ ID NO.:23

**[0133]** MTQFEGFTNLYQVSKTLRFELIPQGKTLKHIQEQGFIEEDKARNDHYKELKPIIDRIYKTYADQCL
QLVQLDWENLSAAIDSYRKEKTEETRNALIEEQATYRNAIHDYFIGRTDNLTDAINKRHAEIYKGLFKAELFNGKVLK
QLGTVTTTEHENALLRSFDKFTTYFSGFYENRKNVFSAEDISTAIPHRIVQDNFPKFKENCHIFTRLITAVPSLREHFEN
VKKAIGIFVSTSIEEVFSFPFYNQLLTQTQIDLYNQLLGGISREAGTEKIKGLNEVLNLAIQKNDETAHIIASLPHRFIPLF
KQILSDRNTLSFILEEFKSDEEVIQSFCKYKTLLRNENVLETAEALFNELNSIDLTHIFISHKKLETISSALCDHWDTLRNA
LYERRISELTGKITKSAKEKVQRSLKHEDINLQEIISAAGKELSEAFKQKTSEILSHAHAALDQPLPTTLKKQEEKEILKSQ
LDSLLGLYHLLDWFAVDESNEVDPEFSARLTGIKLEMEPSLSFYNKARNYATKKPYSVEKFKLNFQMPTLASGWDV
NKEKNNGAILFVKNGLYYLGIMPKQKGRYKALSFEPTEKTSEGFDKMYYDYFPDAAKMIPKCSTQLKAVTAHFQTH
TTPILLSNNFIEPLEITKEIYDLNNPEKEPKKFQTAYAKKTGDQKGYREALCKWIDFTRDFLSKYTKTTSIDLSSLRPSSQ
YKDLGEYYAELNPLLYHISFQRIAEKEIMDAVETGKLYLFQIYNKDFAKGHHGKPNLHTLYWTGLFSPENLAKTSIKLN
GQAELFYRPKSRMKRMAHRLGEKMLNKKLKDQKTPIPDTLYQELYDYVNHRLSHDLSDEARALLPNVITKEVSHEII
KDRRFTSDKFFFHVPITLNYQAANSPSKFNQRVNAYLKEHPETPIIGIDRGERNLIYITVIDSTGKILEQRSLNTIQQFD
YQKKLDNREKERVAARQAWSVVGTIKDLKQGYLSQVIHEIVDLMIHYQAVVVLENLNFGFKSKRTGIAEKAVYQQF
EKMLIDKLNCLVLKDYPAEKVGGVLNPYQLTDQFTSFAKMGTQSGFLFYVPAPYTSKIDPLTGFVDPFVWKTIKNHE
SRKHFLEGFDFLHYDVKTGDFILHFKMNRNLSFQRGLPGFMPAWDIVFEKNETQFDAKGTPFIAGKRIVPVIENHR
FTGRYRDLYPANELIALLEEKGIVFRDGSNILPKLLENDDSHAIDTMVALIRSVLQMRNSNAATGEDYINSPVRDLNG
VCFDSRFQNPEWPMDADANGAYHIALKGQLLLNHLKESKDLKLQNGISNQDWLAYIQELRNGRSSDDEATADSQ
HAAPPKKKRKVGGSGGSGGSGGSGGSGGSGGSGGSLEHHHHHH

**[0134]** SEQ ID NO.:24

**[0135]** MGSSSSGLVPRGSHMASMTGGQQMGRDPTQFEGFTNLYQVSKTLRFELIPQGKTLKHIQEQG
FIEEDKARNDHYKELKPIIDRIYKTYADQCLQLVQLDWENLSAAIDSYRKEKTEETRNALIEEQATYRNAIHDYFIGRT
DNLTDAINKRHAEIYKGLFKAELFNGKVLKQLGTVTTTEHENALLRSFDKFTTYFSGFYENRKNVFSAEDISTAIPHRI
VQDNFPKFKENCHIFTRLITAVPSLREHFENVKKAIGIFVSTSIEEVFSFPFYNQLLTQTQIDLYNQLLGGISREAGTEKI
KGLNEVLNLAIQKNDETAHIIASLPHRFIPLFKQILSDRNTLSFILEEFKSDEEVIQSFCKYKTLLRNENVLETAEALFNEL
NSIDLTHIFISHKKLETISSALCDHWDTLRNALYERRISELTGKITKSAKEKVQRSLKHEDINLQEIISAAGKELSEAFKQK
TSEILSHAHAALDQPLPTTLKKQEEKEILKSQLDSLLGLYHLLDWFAVDESNEVDPEFSARLTGIKLEMEPSLSFYNKA
RNYATKKPYSVEKFKLNFQMPTLASGWDVNKEKNNGAILFVKNGLYYLGIMPKQKGRYKALSFEPTEKTSEGFDK
MYYDYFPDAAKMIPKCSTQLKAVTAHFQTHTTPILLSNNFIEPLEITKEIYDLNNPEKEPKKFQTAYAKKTGDQKGYR
EALCKWIDFTRDFLSKYTKTTSIDLSSLRPSSQYKDLGEYYAELNPLLYHISFQRIAEKEIMDAVETGKLYLFQIYNKDFA

KGHHGKPNLHTLYWTGLFSPENLAKTSIKLNGQAELFYRPKSRMKRMAHRLGEKMLNKKLKDQKTPIPDTLYQELY
DYVNHRLSHDLSDEARALLPNVITKEVSHEIIKDRRFTSDKFFFHVPITLNYQAANSPSKFNQRVNAYLKEHPETPIIGI
DRGERNLIYITVIDSTGKILEQRSLNTIQQFDYQKKLDNREKERVAARQAWSVVGTIKDLKQGYLSQVIHEIVDLMIH
YQAVVVLENLNFGFKSKRTGIAEKAVYQQFEKMLIDKLNCLVLKDYPAEKVGGVLNPYQLTDQFTSFAKMGTQSGF
LFYVPAPYTSKIDPLTGFVDPFVWKTIKNHESRKHFLEGFDFLHYDVKTGDFILHFKMNRNLSFQRGLPGFMPAWD
IVFEKNETQFDAKGTPFIAGKRIVPVIENHRFTGRYRDLYPANELIALLEEKGIVFRDGSNILPKLLENDDSHAIDTMV
ALIRSVLQMRNSNAATGEDYINSPVRDLNGVCFDSRFQNPEWPMDADANGAYHIALKGQLLLNHLKESKDLKLQ
NGISNQDWLAYIQELRNGRSSDDEATADSQHAAPPKKKRKVGGSGGSGGSGGSGGSGGSGGSGGSLEHHHHHH

**[0136]** SEQ ID NO.:25

**[0137]** MPPPKRPRLDGIHGVPAATQFEGFTNLYQVSKTLRFELIPQGKTLKHIQEQGFIEEDKARNDHYK
ELKPIIDRIYKTYADQCLQLVQLDWENLSAAIDSYRKEKTEETRNALIEEQATYRNAIHDYFIGRTDNLTDAINKRHAEI
YKGLFKAELFNGKVLKQLGTVTTTEHENALLRSFDKFTTYFSGFYENRKNVFSAEDISTAIPHRIVQDNFPKFKENCHI
FTRLITAVPSLREHFENVKKAIGIFVSTSIEEVFSFPFYNQLLTQTQIDLYNQLLGGISREAGTEKIKGLNEVLNLAIQKN
DETAHIIASLPHRFIPLFKQILSDRNTLSFILEEFKSDEEVIQSFCKYKTLLRNENVLETAEALFNELNSIDLTHIFISHKKLE
TISSALCDHWDTLRNALYERRISELTGKITKSAKEKVQRSLKHEDINLQEIISAAGKELSEAFKQKTSEILSHAHAALDQ
PLPTTLKKQEEKEILKSQLDSLLGLYHLLDWFAVDESNEVDPEFSARLTGIKLEMEPSLSFYNKARNYATKKPYSVEKF
KLNFQMPTLASGWDVNKEKNNGAILFVKNGLYYLGIMPKQKGRYKALSFEPTEKTSEGFDKMYYDYFPDAAKMIP
KCSTQLKAVTAHFQTHTTPILLSNNFIEPLEITKEIYDLNNPEKEPKKFQTAYAKKTGDQKGYREALCKWIDFTRDFLS
KYTKTTSIDLSSLRPSSQYKDLGEYYAELNPLLYHISFQRIAEKEIMDAVETGKLYLFQIYNKDFAKGHHGKPNLHTLY
WTGLFSPENLAKTSIKLNGQAELFYRPKSRMKRMAHRLGEKMLNKKLKDQKTPIPDTLYQELYDYVNHRLSHDLSD
EARALLPNVITKEVSHEIIKDRRFTSDKFFFHVPITLNYQAANSPSKFNQRVNAYLKEHPETPIIGIDRGERNLIYITVID
STGKILEQRSLNTIQQFDYQKKLDNREKERVAARQAWSVVGTIKDLKQGYLSQVIHEIVDLMIHYQAVVVLENLNF
GFKSKRTGIAEKAVYQQFEKMLIDKLNCLVLKDYPAEKVGGVLNPYQLTDQFTSFAKMGTQSGFLFYVPAPYTSKID
PLTGFVDPFVWKTIKNHESRKHFLEGFDFLHYDVKTGDFILHFKMNRNLSFQRGLPGFMPAWDIVFEKNETQFDA
KGTPFIAGKRIVPVIENHRFTGRYRDLYPANELIALLEEKGIVFRDGSNILPKLLENDDSHAIDTMVALIRSVLQMRNS
NAATGEDYINSPVRDLNGVCFDSRFQNPEWPMDADANGAYHIALKGQLLLNHLKESKDLKLQNGISNQDWLAYI
QELRNGRSSDDEATADSQHAAPPKKKRKVGGSGGSGGSGGSGGSGGSGGSGGSLEHHHHHH

**[0138]** SEQ ID NO.:26

**[0139]** MSSDDEATADSQHAAPPKKKRKVGIHGVPAATQFEGFTNLYQVSKTLRFELIPQGKTLKHIQEQ
GFIEEDKARNDHYKELKPIIDRIYKTYADQCLQLVQLDWENLSAAIDSYRKEKTEETRNALIEEQATYRNAIHDYFIGR
TDNLTDAINKRHAEIYKGLFKAELFNGKVLKQLGTVTTTEHENALLRSFDKFTTYFSGFYENRKNVFSAEDISTAIPHRI
VQDNFPKFKENCHIFTRLITAVPSLREHFENVKKAIGIFVSTSIEEVFSFPFYNQLLTQTQIDLYNQLLGGISREAGTEKI
KGLNEVLNLAIQKNDETAHIIASLPHRFIPLFKQILSDRNTLSFILEEFKSDEEVIQSFCKYKTLLRNENVLETAEALFNEL
NSIDLTHIFISHKKLETISSALCDHWDTLRNALYERRISELTGKITKSAKEKVQRSLKHEDINLQEIISAAGKELSEAFKQK
TSEILSHAHAALDQPLPTTLKKQEEKEILKSQLDSLLGLYHLLDWFAVDESNEVDPEFSARLTGIKLEMEPSLSFYNKA
RNYATKKPYSVEKFKLNFQMPTLASGWDVNKEKNNGAILFVKNGLYYLGIMPKQKGRYKALSFEPTEKTSEGFDK
MYYDYFPDAAKMIPKCSTQLKAVTAHFQTHTTPILLSNNFIEPLEITKEIYDLNNPEKEPKKFQTAYAKKTGDQKGYR
EALCKWIDFTRDFLSKYTKTTSIDLSSLRPSSQYKDLGEYYAELNPLLYHISFQRIAEKEIMDAVETGKLYLFQIYNKDFA
KGHHGKPNLHTLYWTGLFSPENLAKTSIKLNGQAELFYRPKSRMKRMAHRLGEKMLNKKLKDQKTPIPDTLYQELY
DYVNHRLSHDLSDEARALLPNVITKEVSHEIIKDRRFTSDKFFFHVPITLNYQAANSPSKFNQRVNAYLKEHPETPIIGI
DRGERNLIYITVIDSTGKILEQRSLNTIQQFDYQKKLDNREKERVAARQAWSVVGTIKDLKQGYLSQVIHEIVDLMIH

YQAVVVLENLNFGFKSKRTGIAEKAVYQQFEKMLIDKLNCLVLKDYPAEKVGGVLNPYQLTDQFTSFAKMGTQSGF
LFYVPAPYTSKIDPLTGFVDPFVWKTIKNHESRKHFLEGFDFLHYDVKTGDFILHFKMNRNLSFQRGLPGFMPAWD
IVFEKNETQFDAKGTPFIAGKRIVPVIENHRFTGRYRDLYPANELIALLEEKGIVFRDGSNILPKLLENDDSHAIDTMV
ALIRSVLQMRNSNAATGEDYINSPVRDLNGVCFDSRFQNPEWPMDADANGAYHIALKGQLLLNHLKESKDLKLQ
NGISNQDWLAYIQELRNGRSSDDEATADSQHAAPPKKKRKVGGSGGSGGSGGSGGSGGSGGSGGSLEHHHHHH

**[0140]** SEQ ID NO.:27

**[0141]** MTQFEGFTNLYQVSKTLRFELIPQGKTLKHIQEQGFIEEDKARNDHYKELKPIIDRIYKTYADQCL
QLVQLDWENLSAAIDSYRKEKTEETRNALIEEQATYRNAIHDYFIGRTDNLTDAINKRHAEIYKGLFKAELFNGKVLK
QLGTVTTTEHENALLRSFDKFTTYFSGFYENRKNVFSAEDISTAIPHRIVQDNFPKFKENCHIFTRLITAVPSLREHFEN
VKKAIGIFVSTSIEEVFSFPFYNQLLTQTQIDLYNQLLGGISREAGTEKIKGLNEVLNLAIQKNDETAHIIASLPHRFIPLF
KQILSDRNTLSFILEEFKSDEEVIQSFCKYKTLLRNENVLETAEALFNELNSIDLTHIFISHKKLETISSALCDHWDTLRNA
LYERRISELTGKITKSAKEKVQRSLKHEDINLQEIISAAGKELSEAFKQKTSEILSHAHAALDQPLPTTLKKQEEKEILKSQ
LDSLLGLYHLLDWFAVDESNEVDPEFSARLTGIKLEMEPSLSFYNKARNYATKKPYSVEKFKLNFQMPTLASGWDV
NKEKNNGAILFVKNGLYYLGIMPKQKGRYKALSFEPTEKTSEGFDKMYYDYFPDAAKMIPKCSTQLKAVTAHFQTH
TTPILLSNNFIEPLEITKEIYDLNNPEKEPKKFQTAYAKKTGDQKGYREALCKWIDFTRDFLSKYTKTTSIDLSSLRPSSQ
YKDLGEYYAELNPLLYHISFQRIAEKEIMDAVETGKLYLFQIYNKDFAKGHHGKPNLHTLYWTGLFSPENLAKTSIKLN
GQAELFYRPKSRMKRMAHRLGEKMLNKKLKDQKTPIPDTLYQELYDYVNHRLSHDLSDEARALLPNVITKEVSHEII
KDRRFTSDKFFFHVPITLNYQAANSPSKFNQRVNAYLKEHPETPIIGIDRGERNLIYITVIDSTGKILEQRSLNTIQQFD
YQKKLDNREKERVAARQAWSVVGTIKDLKQGYLSQVIHEIVDLMIHYQAVVVLENLNFGFKSKRTGIAEKAVYQQF
EKMLIDKLNCLVLKDYPAEKVGGVLNPYQLTDQFTSFAKMGTQSGFLFYVPAPYTSKIDPLTGFVDPFVWKTIKNHE
SRKHFLEGFDFLHYDVKTGDFILHFKMNRNLSFQRGLPGFMPAWDIVFEKNETQFDAKGTPFIAGKRIVPVIENHR
FTGRYRDLYPANELIALLEEKGIVFRDGSNILPKLLENDDSHAIDTMVALIRSVLQMRNSNAATGEDYINSPVRDLNG
VCFDSRFQNPEWPMDADANGAYHIALKGQLLLNHLKESKDLKLQNGISNQDWLAYIQELRNGRKRPAATKKAGQ
AKKKKGGSGGSGGSGGSGGSGGSGGSGGSLEHHHHHH

**[0142]** SEQ ID NO.:28

**[0143]** MTQFEGFTNLYQVSKTLRFELIPQGKTLKHIQEQGFIEEDKARNDHYKELKPIIDRIYKTYADQCL
QLVQLDWENLSAAIDSYRKEKTEETRNALIEEQATYRNAIHDYFIGRTDNLTDAINKRHAEIYKGLFKAELFNGKVLK
QLGTVTTTEHENALLRSFDKFTTYFSGFYENRKNVFSAEDISTAIPHRIVQDNFPKFKENCHIFTRLITAVPSLREHFEN
VKKAIGIFVSTSIEEVFSFPFYNQLLTQTQIDLYNQLLGGISREAGTEKIKGLNEVLNLAIQKNDETAHIIASLPHRFIPLF
KQILSDRNTLSFILEEFKSDEEVIQSFCKYKTLLRNENVLETAEALFNELNSIDLTHIFISHKKLETISSALCDHWDTLRNA
LYERRISELTGKITKSAKEKVQRSLKHEDINLQEIISAAGKELSEAFKQKTSEILSHAHAALDQPLPTTLKKQEEKEILKSQ
LDSLLGLYHLLDWFAVDESNEVDPEFSARLTGIKLEMEPSLSFYNKARNYATKKPYSVEKFKLNFQMPTLASGWDV
NKEKNNGAILFVKNGLYYLGIMPKQKGRYKALSFEPTEKTSEGFDKMYYDYFPDAAKMIPKCSTQLKAVTAHFQTH
TTPILLSNNFIEPLEITKEIYDLNNPEKEPKKFQTAYAKKTGDQKGYREALCKWIDFTRDFLSKYTKTTSIDLSSLRPSSQ
YKDLGEYYAELNPLLYHISFQRIAEKEIMDAVETGKLYLFQIYNKDFAKGHHGKPNLHTLYWTGLFSPENLAKTSIKLN
GQAELFYRPKSRMKRMAHRLGEKMLNKKLKDQKTPIPDTLYQELYDYVNHRLSHDLSDEARALLPNVITKEVSHEII
KDRRFTSDKFFFHVPITLNYQAANSPSKFNQRVNAYLKEHPETPIIGIDRGERNLIYITVIDSTGKILEQRSLNTIQQFD
YQKKLDNREKERVAARQAWSVVGTIKDLKQGYLSQVIHEIVDLMIHYQAVVVLENLNFGFKSKRTGIAEKAVYQQF
EKMLIDKLNCLVLKDYPAEKVGGVLNPYQLTDQFTSFAKMGTQSGFLFYVPAPYTSKIDPLTGFVDPFVWKTIKNHE
SRKHFLEGFDFLHYDVKTGDFILHFKMNRNLSFQRGLPGFMPAWDIVFEKNETQFDAKGTPFIAGKRIVPVIENHR
FTGRYRDLYPANELIALLEEKGIVFRDGSNILPKLLENDDSHAIDTMVALIRSVLQMRNSNAATGEDYINSPVRDLNG

VCFDSRFQNPEWPMDADANGAYHIALKGQLLLNHLKESKDLKLQNGISNQDWLAYIQELRNGRKRTADGSEFES
PKKKRKVEGGSGGSGGSGGSGGSGGSGGSGGSLEHHHHHH

**[0144]** SEQ ID NO.:29

**[0145]** MTQFEGFTNLYQVSKTLRFELIPQGKTLKHIQEQGFIEEDKARNDHYKELKPIIDRIYKTYADQCL
QLVQLDWENLSAAIDSYRKEKTEETRNALIEEQATYRNAIHDYFIGRTDNLTDAINKRHAEIYKGLFKAELFNGKVLK
QLGTVTTTEHENALLRSFDKFTTYFSGFYENRKNVFSAEDISTAIPHRIVQDNFPKFKENCHIFTRLITAVPSLREHFEN
VKKAIGIFVSTSIEEVFSFPFYNQLLTQTQIDLYNQLLGGISREAGTEKIKGLNEVLNLAIQKNDETAHIIASLPHRFIPLF
KQILSDRNTLSFILEEFKSDEEVIQSFCKYKTLLRNENVLETAEALFNELNSIDLTHIFISHKKLETISSALCDHWDTLRNA
LYERRISELTGKITKSAKEKVQRSLKHEDINLQEIISAAGKELSEAFKQKTSEILSHAHAALDQPLPTTLKKQEEKEILKSQ
LDSLLGLYHLLDWFAVDESNEVDPEFSARLTGIKLEMEPSLSFYNKARNYATKKPYSVEKFKLNFQMPTLASGWDV
NKEKNNGAILFVKNGLYYLGIMPKQKGRYKALSFEPTEKTSEGFDKMYYDYFPDAAKMIPKCSTQLKAVTAHFQTH
TTPILLSNNFIEPLEITKEIYDLNNPEKEPKKFQTAYAKKTGDQKGYREALCKWIDFTRDFLSKYTKTTSIDLSSLRPSSQ
YKDLGEYYAELNPLLYHISFQRIAEKEIMDAVETGKLYLFQIYNKDFAKGHHGKPNLHTLYWTGLFSPENLAKTSIKLN
GQAELFYRPKSRMKRMAHRLGEKMLNKKLKDQKTPIPDTLYQELYDYVNHRLSHDLSDEARALLPNVITKEVSHEII
KDRRFTSDKFFFHVPITLNYQAANSPSKFNQRVNAYLKEHPETPIIGIDRGERNLIYITVIDSTGKILEQRSLNTIQQFD
YQKKLDNREKERVAARQAWSVVGTIKDLKQGYLSQVIHEIVDLMIHYQAVVVLENLNFGFKSKRTGIAEKAVYQQF
EKMLIDKLNCLVLKDYPAEKVGGVLNPYQLTDQFTSFAKMGTQSGFLFYVPAPYTSKIDPLTGFVDPFVWKTIKNHE
SRKHFLEGFDFLHYDVKTGDFILHFKMNRNLSFQRGLPGFMPAWDIVFEKNETQFDAKGTPFIAGKRIVPVIENHR
FTGRYRDLYPANELIALLEEKGIVFRDGSNILPKLLENDDSHAIDTMVALIRSVLQMRNSNAATGEDYINSPVRDLNG
VCFDSRFQNPEWPMDADANGAYHIALKGQLLLNHLKESKDLKLQNGISNQDWLAYIQELRNGRSSDDEATADSQ
HAAPPKKKRKVGGSGGSKRTADGSEFESPKKKRKVEGGSGGSGGSGGSGGSGGSGGSGGSLEHHHHHH

**[0146]** SEQ ID NO.:30

**[0147]** MTQFEGFTNLYQVSKTLRFELIPQGKTLKHIQEQGFIEEDKARNDHYKELKPIIDRIYKTYADQCL
QLVQLDWENLSAAIDSYRKEKTEETRNALIEEQATYRNAIHDYFIGRTDNLTDAINKRHAEIYKGLFKAELFNGKVLK
QLGTVTTTEHENALLRSFDKFTTYFSGFYENRKNVFSAEDISTAIPHRIVQDNFPKFKENCHIFTRLITAVPSLREHFEN
VKKAIGIFVSTSIEEVFSFPFYNQLLTQTQIDLYNQLLGGISREAGTEKIKGLNEVLNLAIQKNDETAHIIASLPHRFIPLF
KQILSDRNTLSFILEEFKSDEEVIQSFCKYKTLLRNENVLETAEALFNELNSIDLTHIFISHKKLETISSALCDHWDTLRNA
LYERRISELTGKITKSAKEKVQRSLKHEDINLQEIISAAGKELSEAFKQKTSEILSHAHAALDQPLPTTLKKQEEKEILKSQ
LDSLLGLYHLLDWFAVDESNEVDPEFSARLTGIKLEMEPSLSFYNKARNYATKKPYSVEKFKLNFQMPTLASGWDV
NKEKNNGAILFVKNGLYYLGIMPKQKGRYKALSFEPTEKTSEGFDKMYYDYFPDAAKMIPKCSTQLKAVTAHFQTH
TTPILLSNNFIEPLEITKEIYDLNNPEKEPKKFQTAYAKKTGDQKGYREALCKWIDFTRDFLSKYTKTTSIDLSSLRPSSQ
YKDLGEYYAELNPLLYHISFQRIAEKEIMDAVETGKLYLFQIYNKDFAKGHHGKPNLHTLYWTGLFSPENLAKTSIKLN
GQAELFYRPKSRMKRMAHRLGEKMLNKKLKDQKTPIPDTLYQELYDYVNHRLSHDLSDEARALLPNVITKEVSHEII
KDRRFTSDKFFFHVPITLNYQAANSPSKFNQRVNAYLKEHPETPIIGIDRGERNLIYITVIDSTGKILEQRSLNTIQQFD
YQKKLDNREKERVAARQAWSVVGTIKDLKQGYLSQVIHEIVDLMIHYQAVVVLENLNFGFKSKRTGIAEKAVYQQF
EKMLIDKLNCLVLKDYPAEKVGGVLNPYQLTDQFTSFAKMGTQSGFLFYVPAPYTSKIDPLTGFVDPFVWKTIKNHE
SRKHFLEGFDFLHYDVKTGDFILHFKMNRNLSFQRGLPGFMPAWDIVFEKNETQFDAKGTPFIAGKRIVPVIENHR
FTGRYRDLYPANELIALLEEKGIVFRDGSNILPKLLENDDSHAIDTMVALIRSVLQMRNSNAATGEDYINSPVRDLNG
VCFDSRFQNPEWPMDADANGAYHIALKGQLLLNHLKESKDLKLQNGISNQDWLAYIQELRNGRKRPAATKKAGQ
AKKKKGGSGGSKRTADGSEFESPKKKRKVEGGSGGSGGSGGSGGSGGSGGSGGSLEHHHHHH

**Example 2. Novel Cpf1 mutants enhance the DNA cleavage activity at TTTT PAM site in the bacterial-based activity assay.**

**[0148]** The following Example demonstrates the enhanced activity of the invention at both TTTT and TTTC PAM sites in a bacterial-based activity assay (**FIG. 2**). The screening strains harboring the toxin plasmid were transformed with WT, M537R or F870L AsCpf1 expression plasmid. After recovery and IPTG induction, cells were plated on LB-Chloramphenicol media with or without arabinose. The degree of cell survival under the arabinose selection compared to the transformation input control (without arabinose) is indicative of the cleavage activity of Cpf1 variants at the HPRT-38346 protospacer on the toxin plasmid, in the context of TTTT or TTTC PAM.

**[0149]** For WT-Cpf1, the survival rate of transformed *E.coli* at TTTC is significantly higher than the TTTT PAM, which is in good agreement with the prior knowledge that the TTTT is a low activity PAM site [6]. In contrast, both M537R and F870L increased the survival rate at TTTT PAM, indicating these mutants broadened the PAM compatibility of AsCpf1 at this alternative PAM site. More importantly, the survival rate of both mutants at the canonical TTTC PAM is even higher than the WT-Cpf1, suggesting these mutants generally enhanced the performance of AsCpf1 protein at other TTTV sites as well. Given these positive results, individual AsCpf1 variant and the double mutant (M537R/F870L) were expressed and purified to determine their intrinsic cleavage activities *in vitro*.

**Example 3. Novel Cpf1 mutants enhances the intrinsic DNA cleavage activity at TTTT PAM sites in vitro**

**[0150]** The intrinsic DNA cleavage activities of AsCpf1 variants (M537R, F870L and M537R/F870L) were compared to the wild type protein using *in vitro* cleavage assay. Briefly, the Cpf1-crRNA ribonucleoprotein (RNP) complex was first assembled by incubating the purified proteins (**FIG. 3A**) with HPRT-38346 crRNA in 1X cleavage buffer (20 mM HEPES, pH 7.5, 150 mM KCl, 5 mM $MgCl_2$, 10% Glycerol, and 1 mM DTT) for 15 minutes at 37 ˚C. The cleavage reactions were initiated by titrating RNP complex (8~500 nM) in 10 nM dsDNA substrate containing the HPRT-38346 protospacer, in the context of TTTC or TTTT PAM. Cleavage reactions at various time points were sampled and quenched by 50 mM EDTA. After removing the AsCpf1 protein by Proteanise K treatment (56˚C, 30 minutes), reactions were resolved using capillary electrophoresis (Fragment Analyzer,

AATI). The relative concentration of cleavage products and uncleaved dsDNA were quantified to calculate the percentage of DNA cleavage.

**[0151]** The intrinsic DNA cleavage activities of WT and Cpf1 variants at the TTTT and TTTC PAM sites were compared in **FIG. 3B**. Only a single RNP concentration (31 nM) at 20 seconds time-point was shown for simplicity. As expected, the single-nucleotide change of PAM sequence from TTT**C** to TTT**T** reduced the cleavage activity of WT-Cpf1 from ~95% to ~40%. Consistent with the observations in the bacterial-based activity assay, both mutants significantly increased the DNA cleavage at TTTT PAM, while maintaining high activity at TTTC PAM **(FIG. 3B)**. The double-mutant (M537R/F870L) has similar activities to the M537R in this assay. However, it is worth to note that this is likely due to the limited resolution of this particular assay, to resolve further differences among those high-activity variants. Overall, these results demonstrated that the reported mutations improved the activity of Cpf1 by enhancing the intrinsic DNA cleavage. Therefore, we anticipate that the observed benefits of these mutants will be broadly applicable and independent of the delivery methods and/or cellular contexts of the specific experiment.

**Example 4. Novel mutants broadly enhance the targeting efficiency of TTTN PAM sites in human cell line.**

**[0152]** The following Example demonstrates the ability of the invention to increase the efficiency of gene editing at TTT**N** PAM sites when the Cpf1-crRNA complex is delivered into cells as an RNP.

**[0153]** CRISPR/Cpf1 cellular editing experiments were performed by first forming 4 mM RNP complex with purified Cpf1 protein and the Alt-R™ crRNAs in Opti-MEM for 5 min at 25 ℃. The targeted protospacers and PAM sequences in CTNNB1 loci are shown in **Table 2**. RNP complexes were then transfected into HEK293 cells by Lonza nucleofection. Experiments were performed in biological triplicate. After 48 hr at 37° C with 5% $CO_2$, adherent cells were washed with 0.1 ml PBS and lysed with 0.05 ml QuickExtract™ DNA extraction solution. Cell lysates were incubated at 65° C for 15 min followed by heat-inactivation at 98° C for 3 min. Crude DNA samples were then diluted 3-fold with 0.1 ml $ddH_2O$ and used as PCR templates. PCR primers are indicated in **Table 2**. PCR was used to amplify 1 kb fragments of the CTNNB1 loci using the KAPA HiFi DNA Polymerase and the following cycling parameters: $95^{5:00}$, ($98^{0:20}$, $64^{0:15}$, $72^{0:30}$) repeated 29 times, $72^{2:00}$.

Heteroduplexes were formed using the following cycling parameters: $95^{10:00}$ cooled to 85 over 1 min, $85^{1:00}$ cooled to 75 over 1 min, $75^{1:00}$ cooled to 65 over 1 min, $65^{1:00}$ cooled to 55 over 1 min, $55^{1:00}$ cooled to 45 over 1 min, $45^{1:00}$ cooled to 35 over 1 min, $35^{1:00}$ cooled to 25 over 1 min, $25^{1:00}$. Heteroduplexes were cleaved by the addition of 2U T7 Endonuclease I (New England Biolabs) for 1 hr at 37 C, and cut products were analyzed by capillary electrophoresis (Fragment Analyzer, Advanced Analytical).

**[0154] Table 2. Sequence of DNA target sites and primer used for PCR amplification (SEQ ID NOs.: 31-58).**

| Name | Sequence (5'-3') | SEQ ID NO.: |
|---|---|---|
| **HPRT38346 TTTT PAM** | TTTTACATAAAACTCTTTTAGGTTA | SEQ ID NO.: 31 |
| **HPRT38346 TTTC PAM** | TTTCACATAAAACTCTTTTAGGTTA | SEQ ID NO.: 32 |
| **CTNNB1 111-S** | TTTTCCCCTCCCTGGCTTTTATTAT | SEQ ID NO.: 33 |
| **CTNNB1 112-S** | TTTCCCCTCCCTGGCTTTTATTATT | SEQ ID NO.: 34 |
| **CTNNB1 127-S** | TTTTATTATTACAACTCTGTGCTTT | SEQ ID NO.: 35 |
| **CTNNB1 128-S** | TTTATTATTACAACTCTGTGCTTTT | SEQ ID NO.: 36 |
| **CTNNB1 149-S** | TTTTTCATCACCATCCTGAATATCT | SEQ ID NO.: 37 |
| **CTNNB1 150-S** | TTTTCATCACCATCCTGAATATCTA | SEQ ID NO.: 38 |
| **CTNNB1 151-S** | TTTCATCACCATCCTGAATATCTAT | SEQ ID NO.: 39 |
| **CTNNB1 184-S** | TTTATACTATTAATAAAAAGACATT | SEQ ID NO.: 40 |
| **CTNNB1 193-AS** | TTTATTAATAGTATAAATATTAATT | SEQ ID NO.: 41 |
| **CTNNB1 194-AS** | TTTTATTAATAGTATAAATATTAAT | SEQ ID NO.: 42 |
| **CTNNB1 195-AS** | TTTTTATTAATAGTATAAATATTAA | SEQ ID NO.: 43 |
| **CTNNB1 207-S** | TTTTTGGTAAGGAGGAGTTTTCACT | SEQ ID NO.: 44 |
| **CTNNB1 208-S** | TTTTGGTAAGGAGGAGTTTTCACTG | SEQ ID NO.: 45 |
| **CTNNB1 209-S** | TTTGGTAAGGAGGAGTTTTCACTGA | SEQ ID NO.: 46 |
| **CTNNB1 224-S** | TTTTCACTGAAGTTCAGCAGTGATG | SEQ ID NO.: 47 |
| **CTNNB1 225-S** | TTTCACTGAAGTTCAGCAGTGATGG | SEQ ID NO.: 48 |
| **CTNNB1 291-S** | TTTCACTAACCTGGTAAAAGAGGAT | SEQ ID NO.: 49 |
| **CTNNB1 301-AS** | TTTACCAGGTTAGTGAAACGCAGAC | SEQ ID NO.: 50 |
| **CTNNB1 302-AS** | TTTTACCAGGTTAGTGAAACGCAGA | SEQ ID NO.: 51 |
| **CTNNB1 321-S** | TTTTTTTTGTGGGTGTAATAGTGAC | SEQ ID NO.: 52 |
| **CTNNB1 322-S** | TTTTTTTGTGGGTGTAATAGTGACA | SEQ ID NO.: 53 |
| **CTNNB1 323-S** | TTTTTTGTGGGTGTAATAGTGACAT | SEQ ID NO.: 54 |
| **CTNNB1 324-S** | TTTTTGTGGGTGTAATAGTGACATT | SEQ ID NO.: 55 |
| **CTNNB1 325-S** | TTTTGTGGGTGTAATAGTGACATTT | SEQ ID NO.: 56 |
| **CTNNB1_FWD** | TCCCACTGTACCTCTGTTATCCA | SEQ ID NO.: 57 |
| **CTNNB1_REV** | TGGTCCTCGTCATTTAGCAGTTT | SEQ ID NO.: 58 |

**[0155]** Referring to **FIG. 4**, T7EI assay revealed significant improvement of the targeting efficiency by M537R and F870L mutations. First, M537R, F870L or the double-mutant (M537R/F870L) enabled efficient cleavage at all 15 sites with TTTT PAM, where 11 of 15 have no detectable cleavage by WT-Cpf1. For other sites with canonical TTTV PAM, these variants maintained or improved the targeting efficiency. The benefit is particularly significant at those low-activity sites, such as CTNNB1 111-s (3-fold improvement over WT). Among these variants, the double-mutant (M537R/F870) has the most consistent improvement of targeting efficiency across all tested sites, where the singly mutants

exhibited more site-dependent variations, such as F870L at 323-S (no activity, same as WT). Overall, the described invention exhibits vastly superior on-target potency than the WT-Cpf1.

**Example 5. High-throughput measurement of the DNA cleavage activity of AsCas12a variants at TTTT PAM site in *E. coli.***

**[0156]** The following Example demonstrates the robustness of our novel high-throughput screening strategy to directly measure the cleavage activity of thousands *AsCas12a* variants at TTTT PAM site in the bacterial-based activity assay (**FIG. 5**). **FIG. 5A-F** shows exemplary high-throughput phenotype measurement of *AsCas12a* point mutations by deep-scanning mutagenesis. A library encompassing every possible single point mutation of *AsCas12a* in the targeted region (499-640 and 840-913) was generated in the context of WT-*AsCas12a* or M537R/F870L-*AsCas12a*. The relative survival rate of each variant over the reference protein in an *E. coli*-based activity assay was determined by deep-sequencing. The phenotype of individual point mutations was measured under multiple selection stringencies in the context of M537R/F870L (condition 1 and 2), and a third condition in the WT-*AsCas12a* background (condition 3). As shown in **FIG. 5A-C**, the phenotype scores (i.e. natural logarithm of relative survival rate) of variants are positively correlated under different conditions ($\rho \sim 0.7$), demonstrating the consistency and reproducibility of this approach. As the positive control, only the M537R and F870L/I, but not any other substitutions at these positions, survived more than the WT-*AsCas12a* (**FIG. 5D**). Conversely, mutating R537 or L870 on the M537R/F870L-*AsCas12a* ubiquitously reduced the survival rate (**FIG. 5E**). These results demonstrated that the phenotype score measured by the bacterial screening reflects the DNA cleavage activity of previously characterized *AsCas12a* variants at TTTT PAM.

**[0157]** To further validate the result of our bacterial screen, we studied four point mutations of *AsCas12a* with greater survival rate than the reference under all three conditions (L505K, S510L, P569D and P599G**, FIG. 5F**), Of note, P599G has been shown to enhance the cleavage activity of *AsCas12a* at TTCC PAM. The other three point mutations have not been characterized by any published studies so far. We therefore measured the survival rate of *E. coli* cells transformed with plasmids expressing individual *AsCas12a* variant under selection. Compared to WT-*AsCas12a*, all selected point mutations increased the survival rate when targeting a TTTT-PAM site (**FIG. 6**). Unexpectedly, the benefits of these point

mutations held true even in the context of M537R/F870L-*AsCas12a*, where the survival rate was further elevated (**FIG. 7**). Collectively, these results demonstrated that our high-throughput screening can accurately predict the phenotype of uncharacterized *AsCas12a* variants.

**[0158]** The phenotype scores of 3,194 *AsCas12a* variants with single point mutation covered by the screening with sufficient sequencing count are listed in **Table 3**. Overall, ~60% exhibited some benefits (i.e. phenotype score > 0) in one of the three condition.

**[0159] Table 3. Summary of selected variants in different background conditions.**[1]

| Mutant | Enrich. Score (1) | Stand. Error (1) | Enrich. Score (2) | Stand. Error (2) | Enrich. Score (3) | Stand. Error (3) | Any positive enrichment? | Consistent positive enrichment? |
|---|---|---|---|---|---|---|---|---|
| R499C | 0.14 | 0.08 | 0.60 | 0.07 | 0.06 | 0.10 | Yes | Yes |
| R499L | 0.08 | 0.05 | 0.05 | 0.06 | 0.09 | 0.15 | Yes | Yes |
| R499K | 0.54 | 0.06 | 0.23 | 0.06 | 0.38 | 0.10 | Yes | Yes |
| R499A | -0.29 | 0.05 | 0.27 | 0.04 | 0.22 | 0.07 | Yes | No |
| R499N | 0.39 | 0.11 | -0.49 | 0.15 | -0.13 | 0.29 | Yes | No |
| R499D | 0.03 | 0.09 | -1.01 | 0.12 | -0.51 | 0.44 | Yes | No |
| R499Q | -0.10 | 0.08 | 0.42 | 0.07 | 0.19 | 0.20 | Yes | No |
| R499E | -0.23 | 0.06 | 0.50 | 0.05 | -0.10 | 0.10 | Yes | No |
| R499G | -0.11 | 0.03 | 0.12 | 0.03 | 0.14 | 0.06 | Yes | No |
| R499H | -0.45 | 0.11 | 0.50 | 0.09 | NA | NA | Yes | No |
| R499I | -0.14 | 0.10 | 0.09 | 0.09 | -0.18 | 0.13 | Yes | No |
| R499M | -0.44 | 0.09 | 0.50 | 0.07 | 0.27 | 0.21 | Yes | No |
| R499F | 0.01 | 0.15 | -0.31 | 0.17 | NA | NA | Yes | No |
| R499P | -0.56 | 0.08 | -0.06 | 0.07 | -0.70 | 0.26 | No | No |
| R499S | -0.14 | 0.05 | 0.02 | 0.05 | -0.04 | 0.06 | Yes | No |
| R499* | -0.76 | 0.10 | -0.61 | 0.10 | -1.06 | 0.18 | No | No |
| R499T | -0.01 | 0.07 | 0.56 | 0.06 | 0.23 | 0.16 | Yes | No |
| R499W | -0.27 | 0.05 | 0.11 | 0.05 | -0.53 | 0.11 | Yes | No |
| R499V | 0.09 | 0.05 | 0.09 | 0.05 | -0.10 | 0.14 | Yes | No |
| L500M | 0.01 | 0.05 | 0.30 | 0.05 | 0.28 | 0.12 | Yes | Yes |
| L500A | -0.27 | 0.04 | 0.21 | 0.03 | -0.15 | 0.07 | Yes | No |
| L500R | -0.35 | 0.03 | -0.40 | 0.03 | -0.47 | 0.05 | No | No |
| L500N | -1.11 | 0.14 | -0.60 | 0.12 | -0.50 | 0.16 | No | No |
| L500D | -1.03 | 0.08 | -1.98 | 0.13 | -1.26 | 0.19 | No | No |
| L500C | -0.19 | 0.05 | 0.26 | 0.05 | 0.00 | 0.10 | Yes | No |
| L500Q | -0.67 | 0.06 | -0.63 | 0.06 | -0.13 | 0.07 | No | No |
| L500E | -1.00 | 0.06 | -1.22 | 0.07 | -1.29 | 0.07 | No | No |
| L500G | -0.72 | 0.03 | -0.79 | 0.03 | -0.84 | 0.03 | No | No |
| L500H | -0.30 | 0.09 | 0.01 | 0.08 | 0.01 | 0.22 | Yes | No |

| Mutant | Enrich. Score (1) | Stand. Error (1) | Enrich. Score (2) | Stand. Error (2) | Enrich. Score (3) | Stand. Error (3) | Any positive enrichment? | Consistent positive enrichment? |
|---|---|---|---|---|---|---|---|---|
| L500I | -0.31 | 0.09 | 0.07 | 0.08 | 0.26 | 0.15 | Yes | No |
| L500K | -1.21 | 0.09 | -0.32 | 0.07 | -0.28 | 0.07 | No | No |
| L500F | -0.19 | 0.08 | -0.33 | 0.09 | 0.09 | 0.21 | Yes | No |
| L500P | -0.79 | 0.05 | -0.80 | 0.05 | -0.91 | 0.07 | No | No |
| L500S | -0.84 | 0.04 | -0.43 | 0.04 | -0.37 | 0.07 | No | No |
| L500* | -1.39 | 0.09 | -1.60 | 0.11 | -1.66 | 0.16 | No | No |
| L500T | -0.19 | 0.05 | -0.37 | 0.06 | -0.17 | 0.06 | No | No |
| L500W | -0.25 | 0.04 | -0.29 | 0.04 | 0.01 | 0.11 | Yes | No |
| L500Y | -0.01 | 0.09 | 0.04 | 0.09 | 0.05 | 0.22 | Yes | No |
| L500V | -0.13 | 0.03 | 0.11 | 0.03 | -0.03 | 0.06 | Yes | No |
| T501L | 0.18 | 0.04 | 0.32 | 0.04 | 0.12 | 0.07 | Yes | Yes |
| T501M | 0.32 | 0.07 | 0.35 | 0.07 | 0.17 | 0.29 | Yes | Yes |
| T501V | 0.22 | 0.06 | 0.29 | 0.06 | 0.13 | 0.20 | Yes | Yes |
| T501A | -0.06 | 0.03 | -0.13 | 0.03 | -0.07 | 0.10 | No | No |
| T501R | 0.01 | 0.03 | -0.16 | 0.03 | 0.54 | 0.07 | Yes | No |
| T501N | 0.69 | 0.14 | 0.16 | 0.15 | NA | NA | Yes | No |
| T501D | 0.12 | 0.12 | -0.12 | 0.13 | NA | NA | Yes | No |
| T501C | 0.52 | 0.09 | -0.40 | 0.11 | 0.31 | 0.26 | Yes | No |
| T501Q | -0.19 | 0.10 | -0.04 | 0.10 | -0.24 | 0.31 | No | No |
| T501E | -0.39 | 0.09 | 0.05 | 0.08 | -0.34 | 0.26 | Yes | No |
| T501G | 0.12 | 0.04 | 0.44 | 0.04 | -0.03 | 0.09 | Yes | No |
| T501I | 0.13 | 0.07 | 0.05 | 0.07 | -0.19 | 0.11 | Yes | No |
| T501K | -0.30 | 0.09 | 0.21 | 0.08 | 0.55 | 0.24 | Yes | No |
| T501F | 0.08 | 0.08 | -0.12 | 0.08 | -0.12 | 0.14 | Yes | No |
| T501P | -0.29 | 0.07 | 0.14 | 0.06 | -0.39 | 0.13 | Yes | No |
| T501S | 0.06 | 0.05 | 0.14 | 0.05 | -0.10 | 0.09 | Yes | No |
| T501* | -1.18 | 0.12 | -0.58 | 0.10 | -0.85 | 0.21 | No | No |
| T501W | -0.02 | 0.07 | 0.26 | 0.06 | -0.30 | 0.09 | Yes | No |
| T501Y | -0.08 | 0.12 | 0.11 | 0.12 | -0.29 | 0.29 | Yes | No |
| G502R | 0.14 | 0.05 | 0.28 | 0.05 | 0.98 | 0.07 | Yes | Yes |
| G502E | 0.42 | 0.08 | 0.17 | 0.08 | 0.19 | 0.30 | Yes | Yes |
| G502L | 0.45 | 0.07 | 0.10 | 0.07 | 0.00 | 0.11 | Yes | Yes |
| G502S | 0.08 | 0.06 | 0.23 | 0.06 | 0.16 | 0.12 | Yes | Yes |
| G502W | 0.14 | 0.07 | 0.65 | 0.06 | 0.36 | 0.14 | Yes | Yes |
| G502V | 0.21 | 0.05 | 0.21 | 0.05 | 0.13 | 0.07 | Yes | Yes |
| G502A | -0.05 | 0.05 | -0.34 | 0.05 | 0.08 | 0.07 | Yes | No |
| G502D | -0.14 | 0.08 | 0.37 | 0.07 | 0.10 | 0.15 | Yes | No |
| G502C | -0.17 | 0.08 | 0.23 | 0.08 | -0.04 | 0.13 | Yes | No |
| G502Q | 0.78 | 0.11 | 0.02 | 0.13 | -0.06 | 0.55 | Yes | No |
| G502H | 0.61 | 0.15 | 0.01 | 0.17 | NA | NA | Yes | No |
| G502M | -0.34 | 0.13 | 0.35 | 0.11 | NA | NA | Yes | No |
| G502F | NA | NA | NA | NA | 0.08 | 0.37 | Yes | No |

| Mutant | Enrich. Score (1) | Stand. Error (1) | Enrich. Score (2) | Stand. Error (2) | Enrich. Score (3) | Stand. Error (3) | Any positive enrichment? | Consistent positive enrichment? |
|---|---|---|---|---|---|---|---|---|
| G502P | -0.41 | 0.14 | 0.01 | 0.13 | NA | NA | Yes | No |
| G502* | -1.16 | 0.15 | -0.82 | 0.13 | NA | NA | Yes | No |
| G502T | 0.69 | 0.10 | -0.23 | 0.13 | 0.24 | 0.35 | Yes | No |
| I503A | -0.76 | 0.09 | 0.32 | 0.07 | -0.16 | 0.21 | Yes | No |
| I503R | -0.86 | 0.07 | -0.67 | 0.07 | -0.51 | 0.17 | No | No |
| I503N | -0.03 | 0.09 | -0.30 | 0.10 | -0.26 | 0.17 | No | No |
| I503D | -0.50 | 0.13 | -0.57 | 0.13 | NA | NA | Yes | No |
| I503C | -0.24 | 0.11 | 0.84 | 0.09 | 0.00 | 0.33 | Yes | No |
| I503E | NA | NA | NA | NA | -0.71 | 0.36 | Yes | No |
| I503G | -0.69 | 0.06 | -0.30 | 0.05 | -0.53 | 0.15 | No | No |
| I503L | 0.13 | 0.06 | -0.46 | 0.07 | -0.31 | 0.15 | Yes | No |
| I503K | 0.03 | 0.12 | -0.51 | 0.15 | NA | NA | Yes | No |
| I503M | -0.08 | 0.10 | -0.17 | 0.10 | -0.13 | 0.27 | No | No |
| I503F | -0.17 | 0.09 | -0.17 | 0.09 | -0.25 | 0.19 | No | No |
| I503S | -0.45 | 0.07 | -0.27 | 0.07 | -0.23 | 0.19 | No | No |
| I503T | -0.23 | 0.08 | 0.33 | 0.07 | 0.20 | 0.14 | Yes | No |
| I503W | -1.21 | 0.11 | -0.88 | 0.10 | -0.61 | 0.28 | No | No |
| I503V | -0.09 | 0.05 | 0.34 | 0.04 | -0.03 | 0.09 | Yes | No |
| K504A | -0.15 | 0.07 | -0.33 | 0.07 | -0.30 | 0.20 | No | No |
| K504R | -0.05 | 0.03 | 0.04 | 0.03 | -0.08 | 0.06 | Yes | No |
| K504N | 0.01 | 0.03 | -0.54 | 0.04 | -0.50 | 0.04 | Yes | No |
| K504C | -0.46 | 0.13 | 0.02 | 0.12 | NA | NA | Yes | No |
| K504Q | -0.16 | 0.05 | -0.25 | 0.05 | -0.22 | 0.07 | No | No |
| K504E | -0.03 | 0.05 | -0.32 | 0.06 | -0.65 | 0.11 | No | No |
| K504G | -0.84 | 0.05 | -0.46 | 0.05 | -0.52 | 0.15 | No | No |
| K504H | -0.59 | 0.13 | -0.01 | 0.11 | -0.51 | 0.16 | No | No |
| K504I | -0.07 | 0.08 | 0.12 | 0.07 | -0.31 | 0.14 | Yes | No |
| K504L | -0.39 | 0.05 | -0.05 | 0.05 | -0.10 | 0.14 | No | No |
| K504M | -0.32 | 0.08 | -0.06 | 0.08 | -0.06 | 0.10 | No | No |
| K504F | -0.71 | 0.14 | -0.24 | 0.12 | NA | NA | Yes | No |
| K504S | -0.50 | 0.08 | -0.45 | 0.08 | -0.19 | 0.23 | No | No |
| K504* | -0.43 | 0.09 | -0.59 | 0.10 | -0.76 | 0.15 | No | No |
| K504T | -0.22 | 0.08 | 0.08 | 0.07 | -0.15 | 0.14 | Yes | No |
| K504W | -0.48 | 0.08 | 0.09 | 0.07 | -0.53 | 0.24 | Yes | No |
| K504V | -0.48 | 0.05 | -0.27 | 0.05 | -0.36 | 0.12 | No | No |
| L505A | 0.61 | 0.05 | 0.50 | 0.05 | 0.47 | 0.13 | Yes | Yes |
| L505R | 0.40 | 0.03 | 0.56 | 0.03 | 0.81 | 0.05 | Yes | Yes |
| L505Q | 0.30 | 0.07 | 0.82 | 0.07 | 0.16 | 0.11 | Yes | Yes |
| L505E | 0.18 | 0.06 | 0.03 | 0.07 | 0.14 | 0.21 | Yes | Yes |
| L505G | 0.18 | 0.03 | 0.72 | 0.03 | 0.40 | 0.05 | Yes | Yes |
| L505H | 0.33 | 0.11 | 0.83 | 0.10 | 0.34 | 0.32 | Yes | Yes |
| L505K | 0.02 | 0.10 | 1.00 | 0.08 | 1.00 | 0.13 | Yes | Yes |

| Mutant | Enrich. Score (1) | Stand. Error (1) | Enrich. Score (2) | Stand. Error (2) | Enrich. Score (3) | Stand. Error (3) | Any positive enrichment? | Consistent positive enrichment? |
|---|---|---|---|---|---|---|---|---|
| L505S | 0.13 | 0.06 | 0.32 | 0.06 | 0.60 | 0.07 | Yes | Yes |
| L505N | -0.53 | 0.17 | 0.27 | 0.14 | NA | NA | Yes | No |
| L505D | -0.28 | 0.11 | 0.59 | 0.10 | 0.10 | 0.49 | Yes | No |
| L505C | 0.26 | 0.07 | -0.14 | 0.08 | 0.47 | 0.27 | Yes | No |
| L505M | -0.05 | 0.09 | -0.06 | 0.09 | -0.18 | 0.18 | No | No |
| L505F | -0.97 | 0.15 | 0.28 | 0.11 | -0.33 | 0.41 | Yes | No |
| L505P | -0.55 | 0.07 | -0.09 | 0.06 | -0.09 | 0.11 | No | No |
| L505T | -0.23 | 0.09 | 0.44 | 0.08 | 0.59 | 0.17 | Yes | No |
| L505W | -0.03 | 0.06 | 0.28 | 0.05 | -0.19 | 0.17 | Yes | No |
| L505V | -0.03 | 0.04 | 0.15 | 0.04 | 0.45 | 0.11 | Yes | No |
| E506A | 0.33 | 0.03 | 0.47 | 0.03 | 0.70 | 0.05 | Yes | Yes |
| E506R | 0.46 | 0.03 | 0.81 | 0.03 | 1.20 | 0.04 | Yes | Yes |
| E506N | 0.24 | 0.09 | 0.53 | 0.09 | 0.50 | 0.29 | Yes | Yes |
| E506C | 0.20 | 0.06 | 0.29 | 0.06 | 0.49 | 0.19 | Yes | Yes |
| E506Q | 0.09 | 0.07 | 0.74 | 0.06 | 0.33 | 0.15 | Yes | Yes |
| E506G | 0.24 | 0.02 | 0.39 | 0.02 | 0.53 | 0.03 | Yes | Yes |
| E506H | 0.35 | 0.09 | 0.10 | 0.10 | 0.98 | 0.31 | Yes | Yes |
| E506I | 0.47 | 0.09 | 0.45 | 0.09 | 0.69 | 0.13 | Yes | Yes |
| E506L | 0.30 | 0.04 | 0.61 | 0.04 | 0.56 | 0.07 | Yes | Yes |
| E506K | 0.18 | 0.06 | 0.59 | 0.05 | 1.08 | 0.08 | Yes | Yes |
| E506M | 0.53 | 0.06 | 0.28 | 0.07 | 0.47 | 0.17 | Yes | Yes |
| E506S | 0.01 | 0.05 | 0.47 | 0.04 | 0.50 | 0.06 | Yes | Yes |
| E506T | 0.39 | 0.06 | 0.12 | 0.07 | 0.90 | 0.23 | Yes | Yes |
| E506Y | 0.16 | 0.09 | 0.29 | 0.09 | 0.43 | 0.25 | Yes | Yes |
| E506V | 0.45 | 0.03 | 0.51 | 0.03 | 0.75 | 0.05 | Yes | Yes |
| E506D | 0.19 | 0.04 | -0.30 | 0.05 | -0.08 | 0.08 | Yes | No |
| E506F | -0.21 | 0.10 | 0.47 | 0.08 | 0.20 | 0.25 | Yes | No |
| E506P | -0.07 | 0.08 | 0.37 | 0.07 | 0.52 | 0.26 | Yes | No |
| E506* | -0.79 | 0.08 | -0.79 | 0.08 | -1.11 | 0.07 | No | No |
| E506W | 0.43 | 0.04 | 0.10 | 0.04 | -0.07 | 0.05 | Yes | No |
| M507A | -0.47 | 0.06 | -0.34 | 0.06 | -0.32 | 0.19 | No | No |
| M507R | -0.42 | 0.02 | -0.58 | 0.03 | -0.64 | 0.04 | No | No |
| M507C | -0.41 | 0.09 | -0.31 | 0.09 | 0.15 | 0.28 | Yes | No |
| M507Q | -0.68 | 0.07 | -0.56 | 0.07 | -0.44 | 0.17 | No | No |
| M507E | NA | NA | NA | NA | -1.23 | 0.19 | Yes | No |
| M507G | -0.98 | 0.05 | -0.71 | 0.05 | -1.24 | 0.12 | No | No |
| M507H | -0.65 | 0.12 | 0.68 | 0.09 | -0.86 | 0.28 | Yes | No |
| M507I | -0.06 | 0.04 | -0.12 | 0.04 | 0.01 | 0.07 | Yes | No |
| M507L | -0.20 | 0.03 | -0.35 | 0.03 | -0.16 | 0.03 | No | No |
| M507K | -1.42 | 0.13 | -0.06 | 0.09 | -1.00 | 0.19 | No | No |
| M507F | 0.05 | 0.09 | -0.78 | 0.12 | -0.05 | 0.36 | Yes | No |
| M507P | -2.08 | 0.12 | -2.19 | 0.13 | -1.58 | 0.18 | No | No |

| Mutant | Enrich. Score (1) | Stand. Error (1) | Enrich. Score (2) | Stand. Error (2) | Enrich. Score (3) | Stand. Error (3) | Any positive enrichment? | Consistent positive enrichment? |
|---|---|---|---|---|---|---|---|---|
| M507S | -1.03 | 0.09 | -0.34 | 0.07 | -0.46 | 0.18 | No | No |
| M507* | -1.68 | 0.15 | -0.72 | 0.11 | NA | NA | Yes | No |
| M507T | -0.11 | 0.06 | -0.30 | 0.07 | -0.03 | 0.13 | No | No |
| M507W | -0.94 | 0.08 | -0.59 | 0.07 | -0.82 | 0.18 | No | No |
| M507V | -0.17 | 0.03 | 0.06 | 0.03 | -0.28 | 0.06 | Yes | No |
| E508A | 0.36 | 0.03 | 0.20 | 0.03 | 0.18 | 0.06 | Yes | Yes |
| E508R | 0.54 | 0.03 | 0.80 | 0.03 | 0.82 | 0.06 | Yes | Yes |
| E508Q | 0.25 | 0.06 | 0.11 | 0.07 | 0.51 | 0.13 | Yes | Yes |
| E508G | 0.16 | 0.02 | 0.17 | 0.02 | 0.22 | 0.04 | Yes | Yes |
| E508L | 0.03 | 0.04 | 0.10 | 0.04 | 0.26 | 0.11 | Yes | Yes |
| E508K | 0.20 | 0.06 | 0.49 | 0.06 | 0.66 | 0.08 | Yes | Yes |
| E508M | 0.25 | 0.07 | 0.57 | 0.06 | 0.54 | 0.11 | Yes | Yes |
| E508F | 0.27 | 0.08 | 0.19 | 0.08 | 0.39 | 0.29 | Yes | Yes |
| E508S | 0.31 | 0.05 | 0.62 | 0.04 | 0.34 | 0.06 | Yes | Yes |
| E508T | 0.19 | 0.06 | 0.73 | 0.06 | 0.55 | 0.10 | Yes | Yes |
| E508Y | 0.35 | 0.09 | 0.19 | 0.10 | 0.21 | 0.27 | Yes | Yes |
| E508V | 0.16 | 0.03 | 0.22 | 0.03 | 0.34 | 0.05 | Yes | Yes |
| E508N | -0.08 | 0.11 | -0.10 | 0.11 | 0.55 | 0.20 | Yes | No |
| E508D | 0.09 | 0.04 | -0.15 | 0.04 | -0.16 | 0.06 | Yes | No |
| E508C | -0.15 | 0.08 | 0.18 | 0.07 | 0.02 | 0.24 | Yes | No |
| E508H | -0.25 | 0.11 | 0.57 | 0.09 | 0.65 | 0.24 | Yes | No |
| E508I | 0.29 | 0.09 | -0.12 | 0.10 | 0.54 | 0.15 | Yes | No |
| E508P | -0.52 | 0.08 | -0.67 | 0.08 | -0.63 | 0.20 | No | No |
| E508* | -0.63 | 0.06 | -0.82 | 0.07 | -0.79 | 0.09 | No | No |
| E508W | -0.29 | 0.05 | 0.45 | 0.05 | 0.07 | 0.09 | Yes | No |
| P509R | 0.23 | 0.03 | 0.27 | 0.03 | 1.04 | 0.05 | Yes | Yes |
| P509K | 0.01 | 0.07 | 0.12 | 0.07 | 1.29 | 0.13 | Yes | Yes |
| P509M | 0.34 | 0.07 | 0.34 | 0.07 | 0.10 | 0.22 | Yes | Yes |
| P509S | 0.10 | 0.04 | 0.14 | 0.04 | 0.14 | 0.10 | Yes | Yes |
| P509W | 0.04 | 0.05 | 0.33 | 0.05 | 0.61 | 0.18 | Yes | Yes |
| P509Y | 0.18 | 0.09 | 0.20 | 0.09 | 0.53 | 0.30 | Yes | Yes |
| P509A | 0.45 | 0.04 | -0.19 | 0.04 | -0.04 | 0.05 | Yes | No |
| P509N | 0.18 | 0.09 | -0.33 | 0.11 | 0.63 | 0.29 | Yes | No |
| P509D | -0.12 | 0.08 | -0.12 | 0.08 | -0.01 | 0.21 | No | No |
| P509C | 0.00 | 0.06 | -0.37 | 0.07 | 0.05 | 0.20 | Yes | No |
| P509Q | 0.08 | 0.05 | -0.10 | 0.06 | 0.36 | 0.08 | Yes | No |
| P509E | -0.27 | 0.06 | 0.33 | 0.05 | 0.38 | 0.17 | Yes | No |
| P509G | -0.06 | 0.03 | 0.19 | 0.03 | 0.00 | 0.05 | Yes | No |
| P509H | 0.09 | 0.03 | -0.31 | 0.03 | -0.19 | 0.05 | Yes | No |
| P509I | -0.10 | 0.09 | -0.34 | 0.10 | -0.56 | 0.28 | No | No |
| P509L | 0.11 | 0.04 | 0.17 | 0.04 | -0.17 | 0.05 | Yes | No |
| P509F | -0.12 | 0.09 | 0.24 | 0.08 | 0.52 | 0.11 | Yes | No |

| Mutant | Enrich. Score (1) | Stand. Error (1) | Enrich. Score (2) | Stand. Error (2) | Enrich. Score (3) | Stand. Error (3) | Any positive enrichment? | Consistent positive enrichment? |
|---|---|---|---|---|---|---|---|---|
| P509* | -2.22 | 0.15 | -0.93 | 0.09 | NA | NA | Yes | No |
| P509T | 0.10 | 0.06 | 0.58 | 0.05 | -0.04 | 0.11 | Yes | No |
| P509V | 0.09 | 0.04 | 0.07 | 0.04 | -0.45 | 0.08 | Yes | No |
| S510G | 0.18 | 0.03 | 0.49 | 0.03 | 0.21 | 0.06 | Yes | Yes |
| S510L | 0.57 | 0.06 | 0.72 | 0.06 | 0.74 | 0.09 | Yes | Yes |
| S510A | 0.29 | 0.06 | -0.25 | 0.07 | 0.04 | 0.22 | Yes | No |
| S510R | -0.38 | 0.03 | -0.43 | 0.03 | -0.53 | 0.04 | No | No |
| S510N | -0.36 | 0.09 | -0.11 | 0.09 | 0.06 | 0.17 | Yes | No |
| S510D | -1.40 | 0.15 | -1.36 | 0.15 | NA | NA | Yes | No |
| S510C | -0.14 | 0.06 | 0.03 | 0.06 | 0.28 | 0.14 | Yes | No |
| S510E | -0.71 | 0.09 | -1.10 | 0.11 | -1.07 | 0.25 | No | No |
| S510I | 0.02 | 0.05 | -0.39 | 0.06 | -0.76 | 0.03 | Yes | No |
| S510M | -1.15 | 0.14 | -0.15 | 0.10 | 0.36 | 0.23 | Yes | No |
| S510F | -0.15 | 0.12 | 0.48 | 0.11 | NA | NA | Yes | No |
| S510* | -1.11 | 0.13 | -1.36 | 0.15 | NA | NA | Yes | No |
| S510T | 0.18 | 0.08 | 0.64 | 0.08 | -0.17 | 0.16 | Yes | No |
| S510W | -0.06 | 0.06 | -0.94 | 0.08 | -0.37 | 0.17 | No | No |
| S510V | -0.05 | 0.05 | 0.44 | 0.05 | 0.44 | 0.18 | Yes | No |
| L511A | 0.07 | 0.10 | -0.06 | 0.11 | -0.31 | 0.15 | Yes | No |
| L511R | 0.00 | 0.03 | -0.21 | 0.04 | 0.09 | 0.06 | Yes | No |
| L511Q | -0.72 | 0.15 | 0.45 | 0.11 | NA | NA | Yes | No |
| L511E | -0.31 | 0.12 | -0.25 | 0.13 | -0.81 | 0.34 | No | No |
| L511G | -0.42 | 0.07 | 0.08 | 0.06 | -0.02 | 0.27 | Yes | No |
| L511K | 0.26 | 0.13 | 0.44 | 0.12 | NA | NA | Yes | No |
| L511M | -0.67 | 0.11 | 0.33 | 0.08 | 0.25 | 0.20 | Yes | No |
| L511P | 0.04 | 0.08 | 0.00 | 0.09 | 0.26 | 0.13 | Yes | No |
| L511S | -0.12 | 0.12 | -0.37 | 0.13 | 0.02 | 0.33 | Yes | No |
| L511W | 0.61 | 0.08 | 0.02 | 0.09 | -0.40 | 0.38 | Yes | No |
| L511V | -0.26 | 0.06 | 0.38 | 0.06 | -0.02 | 0.16 | Yes | No |
| S512R | 0.07 | 0.07 | 0.34 | 0.07 | 0.07 | 0.19 | Yes | Yes |
| S512A | 0.11 | 0.05 | -0.15 | 0.06 | -0.16 | 0.06 | Yes | No |
| S512N | -0.12 | 0.19 | 0.58 | 0.16 | NA | NA | Yes | No |
| S512D | -0.14 | 0.12 | -0.33 | 0.13 | 0.47 | 0.39 | Yes | No |
| S512C | 0.06 | 0.08 | 0.61 | 0.08 | -0.18 | 0.19 | Yes | No |
| S512E | 0.44 | 0.10 | -0.11 | 0.12 | 0.21 | 0.36 | Yes | No |
| S512G | -0.15 | 0.05 | -0.15 | 0.05 | 0.10 | 0.12 | Yes | No |
| S512L | -0.16 | 0.10 | 0.53 | 0.09 | -0.21 | 0.20 | Yes | No |
| S512K | 0.65 | 0.15 | 0.57 | 0.15 | NA | NA | Yes | No |
| S512M | 0.28 | 0.14 | 0.24 | 0.15 | NA | NA | Yes | No |
| S512F | -0.28 | 0.08 | -0.16 | 0.08 | -0.32 | 0.13 | No | No |
| S512P | -0.22 | 0.08 | -0.09 | 0.08 | -0.16 | 0.13 | No | No |
| S512T | -0.17 | 0.09 | 0.05 | 0.08 | -0.07 | 0.15 | Yes | No |

| Mutant | Enrich. Score (1) | Stand. Error (1) | Enrich. Score (2) | Stand. Error (2) | Enrich. Score (3) | Stand. Error (3) | Any positive enrichment? | Consistent positive enrichment? |
|---|---|---|---|---|---|---|---|---|
| S512W | -0.13 | 0.10 | 0.13 | 0.10 | NA | NA | Yes | No |
| S512Y | -0.26 | 0.13 | -0.68 | 0.15 | NA | NA | Yes | No |
| S512V | -0.38 | 0.08 | -0.54 | 0.09 | -0.64 | 0.19 | No | No |
| F513L | 0.53 | 0.04 | 0.63 | 0.04 | 0.41 | 0.07 | Yes | Yes |
| F513W | 0.04 | 0.06 | 0.35 | 0.06 | 0.28 | 0.13 | Yes | Yes |
| F513A | -1.58 | 0.11 | 0.20 | 0.06 | -0.49 | 0.25 | Yes | No |
| F513R | -1.56 | 0.09 | -1.47 | 0.09 | -0.89 | 0.06 | No | No |
| F513D | -1.02 | 0.15 | 0.12 | 0.11 | NA | NA | Yes | No |
| F513C | -0.83 | 0.10 | -0.27 | 0.09 | -0.27 | 0.14 | No | No |
| F513Q | 0.00 | 0.13 | 0.58 | 0.12 | NA | NA | Yes | No |
| F513E | -0.37 | 0.09 | 0.33 | 0.08 | -0.38 | 0.38 | Yes | No |
| F513G | -1.33 | 0.06 | -0.80 | 0.05 | -1.00 | 0.13 | No | No |
| F513I | 0.78 | 0.10 | 0.21 | 0.11 | NA | NA | Yes | No |
| F513M | -0.36 | 0.12 | 0.73 | 0.10 | 0.49 | 0.23 | Yes | No |
| F513S | -0.59 | 0.07 | -0.47 | 0.07 | -0.61 | 0.10 | No | No |
| F513T | NA | NA | NA | NA | -0.35 | 0.19 | Yes | No |
| F513Y | -0.10 | 0.10 | 0.26 | 0.09 | 0.44 | 0.12 | Yes | No |
| F513V | -0.53 | 0.06 | -0.27 | 0.06 | 0.06 | 0.19 | Yes | No |
| Y514A | -0.28 | 0.05 | -0.43 | 0.05 | -0.73 | 0.13 | No | No |
| Y514R | -0.23 | 0.04 | -0.47 | 0.05 | -0.86 | 0.14 | No | No |
| Y514N | -0.17 | 0.09 | 0.07 | 0.08 | -0.53 | 0.17 | Yes | No |
| Y514D | -1.11 | 0.10 | -1.20 | 0.11 | -1.22 | 0.16 | No | No |
| Y514C | -0.39 | 0.05 | -0.35 | 0.05 | -0.55 | 0.09 | No | No |
| Y514Q | -1.35 | 0.13 | -0.62 | 0.10 | -1.01 | 0.29 | No | No |
| Y514E | -1.08 | 0.08 | -0.93 | 0.08 | -1.50 | 0.19 | No | No |
| Y514G | -0.76 | 0.04 | -0.49 | 0.04 | -1.06 | 0.11 | No | No |
| Y514H | 0.39 | 0.06 | 0.29 | 0.06 | -0.31 | 0.12 | Yes | No |
| Y514I | -0.14 | 0.09 | -0.84 | 0.11 | NA | NA | Yes | No |
| Y514L | -0.37 | 0.05 | -0.57 | 0.05 | -0.73 | 0.10 | No | No |
| Y514K | -0.52 | 0.09 | -1.28 | 0.12 | NA | NA | Yes | No |
| Y514M | -0.50 | 0.07 | -0.38 | 0.07 | -0.59 | 0.19 | No | No |
| Y514F | -0.29 | 0.07 | 0.14 | 0.06 | -0.35 | 0.11 | Yes | No |
| Y514S | -0.33 | 0.05 | -0.32 | 0.05 | -0.86 | 0.11 | No | No |
| Y514* | -0.91 | 0.08 | -1.20 | 0.10 | -1.18 | 0.13 | No | No |
| Y514T | -1.01 | 0.09 | -1.31 | 0.10 | -0.98 | 0.18 | No | No |
| Y514W | 0.17 | 0.05 | 0.46 | 0.05 | -0.09 | 0.23 | Yes | No |
| Y514V | -0.45 | 0.04 | -0.41 | 0.04 | -0.92 | 0.06 | No | No |
| N515A | 0.60 | 0.06 | 0.82 | 0.06 | 0.12 | 0.11 | Yes | Yes |
| N515R | 0.63 | 0.06 | 0.82 | 0.05 | 0.19 | 0.11 | Yes | Yes |
| N515I | 0.23 | 0.07 | 0.30 | 0.07 | 0.16 | 0.14 | Yes | Yes |
| N515L | 0.33 | 0.06 | 0.53 | 0.06 | 0.07 | 0.20 | Yes | Yes |
| N515T | 0.41 | 0.08 | 0.14 | 0.08 | 0.29 | 0.16 | Yes | Yes |

| Mutant | Enrich. Score (1) | Stand. Error (1) | Enrich. Score (2) | Stand. Error (2) | Enrich. Score (3) | Stand. Error (3) | Any positive enrichment? | Consistent positive enrichment? |
|---|---|---|---|---|---|---|---|---|
| N515V | 0.50 | 0.05 | 0.49 | 0.05 | 0.45 | 0.09 | Yes | Yes |
| N515D | 0.05 | 0.06 | -0.17 | 0.06 | -0.30 | 0.10 | Yes | No |
| N515C | 0.59 | 0.12 | 0.62 | 0.12 | -0.02 | 0.30 | Yes | No |
| N515Q | 0.46 | 0.11 | 0.69 | 0.11 | NA | NA | Yes | No |
| N515E | 0.47 | 0.07 | 0.56 | 0.07 | -0.14 | 0.19 | Yes | No |
| N515G | -0.10 | 0.05 | 0.37 | 0.04 | -0.13 | 0.07 | Yes | No |
| N515H | 0.09 | 0.10 | -0.59 | 0.13 | -0.25 | 0.21 | Yes | No |
| N515K | 0.07 | 0.08 | 0.16 | 0.08 | -0.13 | 0.16 | Yes | No |
| N515M | 0.73 | 0.09 | 0.45 | 0.10 | -0.01 | 0.12 | Yes | No |
| N515F | 0.49 | 0.12 | 0.48 | 0.12 | NA | NA | Yes | No |
| N515P | -1.10 | 0.16 | -0.13 | 0.12 | -0.32 | 0.38 | No | No |
| N515S | 0.08 | 0.05 | -0.15 | 0.05 | 0.19 | 0.08 | Yes | No |
| N515W | 0.79 | 0.08 | 0.42 | 0.09 | -0.60 | 0.31 | Yes | No |
| N515Y | -0.30 | 0.12 | -0.55 | 0.13 | 0.03 | 0.22 | Yes | No |
| K516R | 0.01 | 0.03 | 0.26 | 0.03 | 0.40 | 0.06 | Yes | Yes |
| K516A | 0.25 | 0.05 | 0.13 | 0.06 | -0.33 | 0.21 | Yes | No |
| K516N | 0.37 | 0.09 | 0.01 | 0.11 | -0.01 | 0.16 | Yes | No |
| K516D | NA | NA | NA | NA | -0.48 | 0.31 | Yes | No |
| K516C | -1.37 | 0.13 | 0.14 | 0.08 | -0.36 | 0.16 | Yes | No |
| K516Q | 0.08 | 0.07 | -0.76 | 0.10 | -0.08 | 0.16 | Yes | No |
| K516E | -0.23 | 0.04 | -0.32 | 0.05 | -0.33 | 0.09 | No | No |
| K516G | -0.34 | 0.03 | -0.01 | 0.03 | -0.34 | 0.05 | No | No |
| K516I | -0.29 | 0.14 | -0.03 | 0.14 | NA | NA | Yes | No |
| K516L | -0.29 | 0.06 | -0.06 | 0.06 | -0.56 | 0.18 | No | No |
| K516M | -0.29 | 0.08 | -0.21 | 0.08 | -0.31 | 0.17 | No | No |
| K516P | -0.37 | 0.10 | -0.96 | 0.12 | NA | NA | Yes | No |
| K516S | -0.34 | 0.06 | 0.23 | 0.06 | -0.22 | 0.21 | Yes | No |
| K516* | -0.66 | 0.09 | -0.86 | 0.10 | -1.08 | 0.19 | No | No |
| K516T | -0.18 | 0.04 | -0.43 | 0.04 | -0.09 | 0.06 | No | No |
| K516W | -0.42 | 0.06 | -0.55 | 0.07 | -1.18 | 0.16 | No | No |
| K516V | -0.47 | 0.05 | -0.20 | 0.05 | -1.04 | 0.11 | No | No |
| A517R | -2.02 | 0.07 | -1.56 | 0.06 | -1.46 | 0.07 | No | No |
| A517D | -1.35 | 0.11 | -0.85 | 0.09 | -1.19 | 0.18 | No | No |
| A517C | -0.35 | 0.08 | 0.68 | 0.07 | 0.14 | 0.17 | Yes | No |
| A517E | -1.34 | 0.09 | -1.16 | 0.09 | -1.86 | 0.16 | No | No |
| A517G | -0.69 | 0.03 | -0.65 | 0.03 | -0.77 | 0.04 | No | No |
| A517I | 0.77 | 0.10 | -0.42 | 0.13 | NA | NA | Yes | No |
| A517L | -0.30 | 0.06 | -0.44 | 0.06 | -1.22 | 0.17 | No | No |
| A517M | -0.50 | 0.10 | -0.24 | 0.10 | -0.57 | 0.30 | No | No |
| A517F | -0.50 | 0.12 | -0.90 | 0.14 | NA | NA | Yes | No |
| A517P | -0.75 | 0.08 | -1.06 | 0.09 | -0.86 | 0.12 | No | No |
| A517S | -0.28 | 0.05 | -0.24 | 0.05 | -0.65 | 0.14 | No | No |

| Mutant | Enrich. Score (1) | Stand. Error (1) | Enrich. Score (2) | Stand. Error (2) | Enrich. Score (3) | Stand. Error (3) | Any positive enrichment? | Consistent positive enrichment? |
|---|---|---|---|---|---|---|---|---|
| A517T | -0.34 | 0.06 | 0.06 | 0.06 | -0.42 | 0.11 | Yes | No |
| A517W | -1.22 | 0.07 | -0.27 | 0.05 | -1.43 | 0.16 | No | No |
| A517Y | 0.02 | 0.13 | 0.04 | 0.13 | NA | NA | Yes | No |
| A517V | -0.33 | 0.04 | -0.14 | 0.04 | -0.44 | 0.07 | No | No |
| R518K | 0.20 | 0.09 | 0.72 | 0.08 | 0.05 | 0.17 | Yes | Yes |
| R518A | -0.12 | 0.07 | -0.28 | 0.07 | -0.87 | 0.24 | No | No |
| R518C | -1.13 | 0.12 | -0.21 | 0.09 | NA | NA | Yes | No |
| R518E | -0.72 | 0.10 | -1.08 | 0.12 | NA | NA | Yes | No |
| R518G | -1.34 | 0.05 | -0.78 | 0.04 | -0.87 | 0.08 | No | No |
| R518L | -1.49 | 0.12 | -1.84 | 0.15 | NA | NA | Yes | No |
| R518F | -0.96 | 0.16 | 0.45 | 0.11 | NA | NA | Yes | No |
| R518S | -0.74 | 0.08 | -1.20 | 0.09 | -0.73 | 0.12 | No | No |
| R518* | -0.33 | 0.08 | -0.34 | 0.08 | -0.69 | 0.13 | No | No |
| R518T | -0.50 | 0.10 | -0.37 | 0.10 | -0.40 | 0.15 | No | No |
| R518W | -1.01 | 0.09 | -1.13 | 0.10 | -1.22 | 0.19 | No | No |
| R518V | -0.44 | 0.06 | -1.39 | 0.09 | -1.43 | 0.09 | No | No |
| N519A | 0.64 | 0.06 | 1.07 | 0.06 | -0.06 | 0.25 | Yes | No |
| N519R | 0.47 | 0.05 | 0.46 | 0.05 | -0.02 | 0.08 | Yes | No |
| N519D | 0.10 | 0.05 | -0.13 | 0.05 | -0.29 | 0.07 | Yes | No |
| N519C | 0.21 | 0.11 | 0.23 | 0.11 | NA | NA | Yes | No |
| N519Q | 0.14 | 0.12 | 0.71 | 0.11 | NA | NA | Yes | No |
| N519E | -0.66 | 0.10 | -0.38 | 0.09 | -0.89 | 0.23 | No | No |
| N519G | 0.21 | 0.04 | 0.10 | 0.04 | -0.54 | 0.08 | Yes | No |
| N519H | 0.10 | 0.09 | -0.67 | 0.11 | NA | NA | Yes | No |
| N519I | 0.29 | 0.09 | 0.18 | 0.09 | -0.02 | 0.15 | Yes | No |
| N519L | 0.28 | 0.06 | 0.47 | 0.06 | -0.37 | 0.08 | Yes | No |
| N519K | -0.17 | 0.09 | -0.35 | 0.10 | -0.46 | 0.19 | No | No |
| N519M | -0.19 | 0.10 | 0.36 | 0.09 | -0.05 | 0.13 | Yes | No |
| N519F | 0.38 | 0.14 | 0.21 | 0.15 | NA | NA | Yes | No |
| N519P | -0.72 | 0.13 | -0.23 | 0.11 | NA | NA | Yes | No |
| N519S | 0.08 | 0.05 | -0.03 | 0.05 | 0.02 | 0.12 | Yes | No |
| N519T | 0.24 | 0.08 | 0.01 | 0.09 | -0.37 | 0.16 | Yes | No |
| N519W | -0.02 | 0.08 | 0.38 | 0.08 | -0.12 | 0.31 | Yes | No |
| N519Y | 0.10 | 0.12 | 0.65 | 0.11 | -0.09 | 0.22 | Yes | No |
| N519V | 0.12 | 0.05 | 0.14 | 0.05 | -0.39 | 0.06 | Yes | No |
| Y520A | -1.19 | 0.12 | -0.30 | 0.09 | NA | NA | Yes | No |
| Y520R | -0.37 | 0.08 | -1.30 | 0.11 | -1.04 | 0.24 | No | No |
| Y520N | -0.05 | 0.09 | -0.45 | 0.10 | -0.62 | 0.14 | No | No |
| Y520D | -0.50 | 0.12 | -0.04 | 0.10 | NA | NA | Yes | No |
| Y520C | -0.23 | 0.07 | -0.24 | 0.07 | -0.52 | 0.12 | No | No |
| Y520E | -0.61 | 0.13 | -0.85 | 0.15 | NA | NA | Yes | No |
| Y520G | -1.91 | 0.10 | -1.08 | 0.08 | -1.47 | 0.09 | No | No |

| Mutant | Enrich. Score (1) | Stand. Error (1) | Enrich. Score (2) | Stand. Error (2) | Enrich. Score (3) | Stand. Error (3) | Any positive enrichment? | Consistent positive enrichment? |
|---|---|---|---|---|---|---|---|---|
| Y520H | 0.12 | 0.07 | -0.14 | 0.07 | -0.34 | 0.10 | Yes | No |
| Y520F | 0.19 | 0.13 | -0.21 | 0.15 | NA | NA | Yes | No |
| Y520S | -0.73 | 0.11 | -0.66 | 0.11 | -1.13 | 0.18 | No | No |
| Y520* | -0.19 | 0.07 | -0.42 | 0.08 | -0.48 | 0.15 | No | No |
| Y520W | -0.38 | 0.10 | 0.06 | 0.09 | -0.03 | 0.16 | Yes | No |
| Y520V | -1.45 | 0.13 | -1.16 | 0.12 | NA | NA | Yes | No |
| A521D | -0.72 | 0.13 | -0.50 | 0.13 | NA | NA | Yes | No |
| A521C | 0.90 | 0.16 | 1.29 | 0.16 | NA | NA | Yes | No |
| A521G | -0.52 | 0.05 | -0.73 | 0.06 | -0.98 | 0.12 | No | No |
| A521L | -0.61 | 0.10 | -0.13 | 0.09 | -0.98 | 0.12 | No | No |
| A521P | -0.19 | 0.11 | -0.78 | 0.14 | NA | NA | Yes | No |
| A521S | 0.00 | 0.09 | 0.04 | 0.10 | -0.51 | 0.27 | Yes | No |
| A521T | -0.23 | 0.07 | 0.10 | 0.06 | -0.33 | 0.11 | Yes | No |
| A521V | -0.40 | 0.06 | -0.88 | 0.07 | -0.60 | 0.13 | No | No |
| T522L | 1.10 | 0.05 | 0.92 | 0.05 | 0.28 | 0.10 | Yes | Yes |
| T522M | 0.92 | 0.07 | 0.81 | 0.08 | 0.53 | 0.21 | Yes | Yes |
| T522V | 0.16 | 0.05 | 0.28 | 0.05 | 0.04 | 0.07 | Yes | Yes |
| T522A | -0.01 | 0.05 | -0.37 | 0.06 | -0.55 | 0.08 | No | No |
| T522R | -0.17 | 0.04 | 0.31 | 0.04 | -0.40 | 0.12 | Yes | No |
| T522N | 0.11 | 0.07 | -1.14 | 0.11 | -0.50 | 0.13 | Yes | No |
| T522C | 0.09 | 0.08 | 0.38 | 0.08 | -0.41 | 0.38 | Yes | No |
| T522Q | 0.71 | 0.09 | 0.47 | 0.10 | -0.51 | 0.36 | Yes | No |
| T522E | -0.22 | 0.08 | -1.54 | 0.13 | -0.72 | 0.27 | No | No |
| T522G | -0.37 | 0.04 | -0.18 | 0.04 | -0.85 | 0.08 | No | No |
| T522I | 0.23 | 0.07 | -0.06 | 0.08 | -0.11 | 0.17 | Yes | No |
| T522K | -0.16 | 0.11 | -0.23 | 0.11 | -0.67 | 0.26 | No | No |
| T522F | 0.08 | 0.13 | 0.34 | 0.12 | NA | NA | Yes | No |
| T522P | -1.16 | 0.11 | -1.52 | 0.14 | -1.14 | 0.16 | No | No |
| T522S | 0.23 | 0.05 | -0.20 | 0.05 | -0.38 | 0.10 | Yes | No |
| T522W | -0.26 | 0.07 | -0.35 | 0.07 | -0.90 | 0.13 | No | No |
| K523R | 0.17 | 0.02 | 0.37 | 0.02 | 0.00 | 0.03 | Yes | Yes |
| K523A | -0.19 | 0.03 | 0.15 | 0.03 | -0.48 | 0.09 | Yes | No |
| K523N | -0.31 | 0.07 | -0.48 | 0.07 | -1.00 | 0.08 | No | No |
| K523D | -1.14 | 0.07 | -1.35 | 0.08 | -1.21 | 0.09 | No | No |
| K523C | -0.22 | 0.05 | 0.07 | 0.04 | -0.81 | 0.12 | Yes | No |
| K523Q | -0.12 | 0.04 | -0.22 | 0.04 | 0.01 | 0.06 | Yes | No |
| K523E | -0.57 | 0.04 | -0.56 | 0.04 | -0.86 | 0.06 | No | No |
| K523G | -0.16 | 0.02 | 0.09 | 0.02 | -0.56 | 0.03 | Yes | No |
| K523H | -1.08 | 0.11 | -0.05 | 0.08 | -1.04 | 0.28 | No | No |
| K523I | -0.20 | 0.07 | 0.41 | 0.06 | -1.23 | 0.21 | Yes | No |
| K523L | -0.78 | 0.04 | -0.30 | 0.03 | -0.70 | 0.07 | No | No |
| K523M | -0.19 | 0.04 | -0.18 | 0.04 | -0.52 | 0.06 | No | No |

| Mutant | Enrich. Score (1) | Stand. Error (1) | Enrich. Score (2) | Stand. Error (2) | Enrich. Score (3) | Stand. Error (3) | Any positive enrichment? | Consistent positive enrichment? |
|---|---|---|---|---|---|---|---|---|
| K523F | -1.08 | 0.08 | -0.93 | 0.08 | -1.27 | 0.09 | No | No |
| K523P | -1.41 | 0.08 | -0.39 | 0.06 | -1.21 | 0.15 | No | No |
| K523S | 0.13 | 0.03 | 0.10 | 0.03 | -0.36 | 0.07 | Yes | No |
| K523* | -1.40 | 0.07 | -1.46 | 0.08 | -1.19 | 0.12 | No | No |
| K523T | -0.19 | 0.04 | -0.19 | 0.04 | -0.49 | 0.08 | No | No |
| K523W | -0.97 | 0.04 | -0.87 | 0.04 | -1.41 | 0.09 | No | No |
| K523Y | -1.25 | 0.10 | -0.43 | 0.08 | -1.36 | 0.19 | No | No |
| K523V | -0.57 | 0.03 | -0.57 | 0.03 | -1.12 | 0.08 | No | No |
| K524A | -0.88 | 0.09 | -0.32 | 0.08 | -0.50 | 0.24 | No | No |
| K524R | -0.32 | 0.04 | 0.15 | 0.04 | -0.28 | 0.09 | Yes | No |
| K524N | 0.04 | 0.04 | -0.48 | 0.05 | -0.19 | 0.09 | Yes | No |
| K524C | 0.06 | 0.10 | 0.03 | 0.10 | NA | NA | Yes | No |
| K524Q | -0.42 | 0.09 | -0.54 | 0.10 | -0.47 | 0.14 | No | No |
| K524E | -0.53 | 0.06 | -0.11 | 0.06 | -0.49 | 0.10 | No | No |
| K524G | -0.43 | 0.04 | -0.19 | 0.04 | -0.80 | 0.06 | No | No |
| K524L | -0.25 | 0.07 | 0.32 | 0.06 | -0.81 | 0.21 | Yes | No |
| K524M | -1.28 | 0.15 | -0.75 | 0.13 | -0.69 | 0.15 | No | No |
| K524P | -0.70 | 0.12 | -0.10 | 0.10 | 0.02 | 0.29 | Yes | No |
| K524S | -0.67 | 0.08 | -0.04 | 0.07 | -0.73 | 0.12 | No | No |
| K524* | -0.92 | 0.11 | -0.75 | 0.11 | -0.76 | 0.13 | No | No |
| K524T | -0.10 | 0.04 | -0.26 | 0.04 | -0.15 | 0.06 | No | No |
| K524W | -0.58 | 0.08 | -1.54 | 0.12 | -1.19 | 0.22 | No | No |
| K524V | -0.71 | 0.07 | -0.01 | 0.06 | -0.68 | 0.22 | No | No |
| P525A | -0.21 | 0.03 | 0.06 | 0.03 | -0.29 | 0.07 | Yes | No |
| P525R | -0.30 | 0.02 | -0.10 | 0.02 | -0.62 | 0.05 | No | No |
| P525N | -0.38 | 0.09 | -0.35 | 0.10 | -0.10 | 0.19 | No | No |
| P525D | 0.42 | 0.05 | -0.02 | 0.05 | -0.30 | 0.08 | Yes | No |
| P525C | -0.28 | 0.05 | -0.12 | 0.05 | -0.48 | 0.14 | No | No |
| P525Q | -0.21 | 0.06 | -0.19 | 0.06 | -0.35 | 0.13 | No | No |
| P525E | -0.22 | 0.04 | 0.24 | 0.04 | -0.30 | 0.05 | Yes | No |
| P525G | -0.24 | 0.02 | -0.17 | 0.02 | -0.51 | 0.05 | No | No |
| P525H | 0.17 | 0.06 | 0.18 | 0.07 | -0.24 | 0.12 | Yes | No |
| P525I | -0.48 | 0.09 | 0.06 | 0.08 | 0.19 | 0.22 | Yes | No |
| P525L | -0.37 | 0.03 | 0.25 | 0.03 | -0.61 | 0.06 | Yes | No |
| P525K | -0.90 | 0.08 | -1.00 | 0.09 | -0.57 | 0.17 | No | No |
| P525M | -0.55 | 0.06 | -0.18 | 0.06 | -0.54 | 0.13 | No | No |
| P525F | -0.17 | 0.07 | -0.61 | 0.08 | -0.70 | 0.16 | No | No |
| P525S | -0.06 | 0.03 | 0.04 | 0.03 | -0.42 | 0.08 | Yes | No |
| P525* | -1.61 | 0.09 | -1.54 | 0.09 | -1.56 | 0.08 | No | No |
| P525T | -0.25 | 0.05 | -0.31 | 0.05 | -0.45 | 0.11 | No | No |
| P525W | -0.25 | 0.04 | -0.04 | 0.03 | -0.59 | 0.11 | No | No |
| P525Y | -1.08 | 0.10 | -1.08 | 0.10 | -0.77 | 0.08 | No | No |

| Mutant | Enrich. Score (1) | Stand. Error (1) | Enrich. Score (2) | Stand. Error (2) | Enrich. Score (3) | Stand. Error (3) | Any positive enrichment? | Consistent positive enrichment? |
|---|---|---|---|---|---|---|---|---|
| P525V | -0.31 | 0.03 | -0.08 | 0.03 | -0.39 | 0.08 | No | No |
| Y526A | -0.28 | 0.07 | 0.17 | 0.06 | -0.89 | 0.19 | Yes | No |
| Y526R | -0.71 | 0.07 | -0.17 | 0.06 | -1.09 | 0.19 | No | No |
| Y526N | -0.64 | 0.11 | -0.15 | 0.09 | -0.25 | 0.17 | No | No |
| Y526D | -0.44 | 0.09 | 0.07 | 0.08 | -0.69 | 0.15 | Yes | No |
| Y526C | 0.04 | 0.06 | -0.03 | 0.06 | -0.26 | 0.12 | Yes | No |
| Y526Q | -0.10 | 0.11 | -0.64 | 0.13 | NA | NA | Yes | No |
| Y526E | -0.46 | 0.08 | -0.87 | 0.10 | -0.84 | 0.21 | No | No |
| Y526G | -0.22 | 0.05 | -0.17 | 0.05 | -0.65 | 0.16 | No | No |
| Y526H | -0.32 | 0.08 | -0.25 | 0.08 | -0.19 | 0.12 | No | No |
| Y526I | -0.40 | 0.13 | -0.52 | 0.14 | NA | NA | Yes | No |
| Y526L | -0.53 | 0.06 | -0.18 | 0.05 | -0.73 | 0.12 | No | No |
| Y526M | -0.47 | 0.10 | -0.40 | 0.10 | -1.12 | 0.27 | No | No |
| Y526F | -0.02 | 0.07 | -0.01 | 0.07 | -0.44 | 0.13 | No | No |
| Y526P | -0.19 | 0.10 | -0.88 | 0.13 | NA | NA | Yes | No |
| Y526S | -0.57 | 0.06 | -0.68 | 0.07 | -0.68 | 0.12 | No | No |
| Y526* | -0.42 | 0.05 | -0.44 | 0.06 | -0.61 | 0.09 | No | No |
| Y526T | -0.01 | 0.09 | -0.22 | 0.10 | -0.69 | 0.21 | No | No |
| Y526W | -1.02 | 0.10 | -0.19 | 0.08 | -0.32 | 0.13 | No | No |
| Y526V | -0.61 | 0.05 | -0.14 | 0.05 | -0.86 | 0.14 | No | No |
| S527D | 0.13 | 0.11 | 0.01 | 0.11 | 0.34 | 0.41 | Yes | Yes |
| S527A | 0.00 | 0.06 | -0.37 | 0.07 | -0.07 | 0.20 | Yes | No |
| S527R | -0.14 | 0.04 | -0.73 | 0.05 | -0.70 | 0.07 | No | No |
| S527N | -0.10 | 0.10 | -0.43 | 0.11 | 0.01 | 0.19 | Yes | No |
| S527C | -0.21 | 0.09 | -0.35 | 0.09 | -0.10 | 0.22 | No | No |
| S527Q | 0.09 | 0.12 | -0.39 | 0.14 | NA | NA | Yes | No |
| S527E | -0.49 | 0.10 | 0.57 | 0.08 | 0.03 | 0.16 | Yes | No |
| S527G | -0.43 | 0.04 | -0.21 | 0.04 | -0.53 | 0.09 | No | No |
| S527H | 0.47 | 0.15 | 0.10 | 0.17 | NA | NA | Yes | No |
| S527I | -1.06 | 0.16 | -0.43 | 0.14 | NA | NA | Yes | No |
| S527L | -0.12 | 0.07 | -0.24 | 0.07 | -0.44 | 0.27 | No | No |
| S527K | -0.09 | 0.11 | -0.57 | 0.13 | NA | NA | Yes | No |
| S527P | 0.07 | 0.10 | -0.33 | 0.11 | -0.47 | 0.36 | Yes | No |
| S527T | 0.01 | 0.09 | -0.30 | 0.10 | -0.22 | 0.18 | Yes | No |
| S527W | 0.03 | 0.07 | 0.15 | 0.07 | -0.50 | 0.23 | Yes | No |
| S527Y | 0.31 | 0.17 | 0.05 | 0.18 | NA | NA | Yes | No |
| S527V | -0.54 | 0.07 | -0.52 | 0.07 | -0.52 | 0.10 | No | No |
| V528D | 0.01 | 0.07 | 0.27 | 0.07 | 0.12 | 0.12 | Yes | Yes |
| V528L | 0.55 | 0.03 | 0.59 | 0.03 | 0.31 | 0.07 | Yes | Yes |
| V528M | 0.19 | 0.05 | 0.02 | 0.05 | 0.13 | 0.10 | Yes | Yes |
| V528A | -0.09 | 0.04 | 0.29 | 0.04 | -0.13 | 0.06 | Yes | No |
| V528R | -0.04 | 0.04 | 0.07 | 0.04 | -0.03 | 0.07 | Yes | No |

| Mutant | Enrich. Score (1) | Stand. Error (1) | Enrich. Score (2) | Stand. Error (2) | Enrich. Score (3) | Stand. Error (3) | Any positive enrichment? | Consistent positive enrichment? |
|---|---|---|---|---|---|---|---|---|
| V528N | 0.01 | 0.11 | -0.47 | 0.14 | 0.31 | 0.42 | Yes | No |
| V528C | 0.16 | 0.07 | 0.20 | 0.07 | -0.06 | 0.24 | Yes | No |
| V528Q | -0.44 | 0.09 | -0.29 | 0.09 | 0.07 | 0.11 | Yes | No |
| V528E | -0.66 | 0.06 | 0.16 | 0.05 | 0.00 | 0.11 | Yes | No |
| V528G | -0.14 | 0.02 | -0.19 | 0.02 | -0.19 | 0.03 | No | No |
| V528H | -0.62 | 0.15 | 1.01 | 0.11 | NA | NA | Yes | No |
| V528I | 0.16 | 0.08 | -0.09 | 0.09 | 0.07 | 0.11 | Yes | No |
| V528K | -0.14 | 0.08 | 0.36 | 0.08 | 0.13 | 0.14 | Yes | No |
| V528F | -0.10 | 0.09 | 0.39 | 0.08 | -0.59 | 0.21 | Yes | No |
| V528P | -0.10 | 0.08 | -0.66 | 0.10 | 0.10 | 0.11 | Yes | No |
| V528S | -0.12 | 0.05 | 0.26 | 0.05 | 0.11 | 0.06 | Yes | No |
| V528* | -1.66 | 0.13 | -1.20 | 0.12 | NA | NA | Yes | No |
| V528T | 0.29 | 0.07 | 0.00 | 0.07 | 0.18 | 0.17 | Yes | No |
| V528W | -1.31 | 0.07 | -1.47 | 0.08 | -0.99 | 0.14 | No | No |
| V528Y | -0.77 | 0.13 | -0.50 | 0.12 | 0.24 | 0.12 | Yes | No |
| E529A | -0.38 | 0.08 | -0.18 | 0.08 | 0.04 | 0.15 | Yes | No |
| E529R | NA | NA | NA | NA | -0.70 | 0.34 | Yes | No |
| E529D | 0.02 | 0.07 | -0.61 | 0.08 | 0.10 | 0.15 | Yes | No |
| E529Q | -0.43 | 0.14 | -0.49 | 0.15 | NA | NA | Yes | No |
| E529G | -0.25 | 0.05 | -0.16 | 0.05 | -0.61 | 0.11 | No | No |
| E529L | -0.45 | 0.11 | -0.56 | 0.11 | NA | NA | Yes | No |
| E529K | 0.21 | 0.10 | -0.28 | 0.11 | -0.65 | 0.19 | Yes | No |
| E529P | 0.08 | 0.15 | -0.30 | 0.17 | NA | NA | Yes | No |
| E529S | -0.18 | 0.11 | -0.08 | 0.11 | -0.20 | 0.45 | No | No |
| E529* | -0.22 | 0.11 | -0.69 | 0.14 | -0.58 | 0.17 | No | No |
| E529W | -0.19 | 0.13 | -0.11 | 0.13 | NA | NA | Yes | No |
| E529V | -0.35 | 0.06 | 0.08 | 0.06 | -0.48 | 0.10 | Yes | No |
| K530A | -0.96 | 0.10 | -0.76 | 0.10 | -0.90 | 0.14 | No | No |
| K530R | -0.56 | 0.04 | -0.32 | 0.04 | -0.59 | 0.08 | No | No |
| K530N | -0.78 | 0.15 | -0.73 | 0.16 | NA | NA | Yes | No |
| K530C | -0.10 | 0.10 | -0.43 | 0.11 | NA | NA | Yes | No |
| K530Q | -0.22 | 0.05 | -0.56 | 0.05 | -0.60 | 0.10 | No | No |
| K530E | -0.48 | 0.05 | -0.35 | 0.05 | -0.85 | 0.09 | No | No |
| K530G | -1.18 | 0.07 | -1.09 | 0.07 | -1.15 | 0.14 | No | No |
| K530L | -1.74 | 0.09 | -1.04 | 0.07 | -1.40 | 0.14 | No | No |
| K530M | -0.72 | 0.07 | -0.42 | 0.07 | -0.83 | 0.13 | No | No |
| K530F | -1.17 | 0.15 | -0.40 | 0.12 | NA | NA | Yes | No |
| K530S | -1.15 | 0.09 | -0.65 | 0.08 | -1.15 | 0.13 | No | No |
| K530* | -0.63 | 0.07 | -0.43 | 0.07 | -0.68 | 0.09 | No | No |
| K530T | -0.51 | 0.07 | -0.72 | 0.07 | -0.68 | 0.10 | No | No |
| K530W | -1.73 | 0.12 | -0.35 | 0.08 | -1.35 | 0.20 | No | No |
| K530V | -0.98 | 0.08 | -1.46 | 0.10 | -1.55 | 0.23 | No | No |

| Mutant | Enrich. Score (1) | Stand. Error (1) | Enrich. Score (2) | Stand. Error (2) | Enrich. Score (3) | Stand. Error (3) | Any positive enrichment? | Consistent positive enrichment? |
|---|---|---|---|---|---|---|---|---|
| F531A | -1.39 | 0.13 | -1.72 | 0.15 | NA | NA | Yes | No |
| F531R | -1.90 | 0.12 | -1.41 | 0.10 | -1.75 | 0.23 | No | No |
| F531C | -0.40 | 0.05 | -0.81 | 0.06 | -0.85 | 0.09 | No | No |
| F531G | -1.68 | 0.08 | -1.22 | 0.07 | -1.58 | 0.14 | No | No |
| F531I | -0.43 | 0.09 | -0.86 | 0.11 | -0.62 | 0.11 | No | No |
| F531L | -0.35 | 0.05 | -0.40 | 0.05 | -0.55 | 0.07 | No | No |
| F531S | -0.56 | 0.07 | -0.79 | 0.08 | -0.98 | 0.11 | No | No |
| F531W | -1.68 | 0.13 | -0.86 | 0.10 | -0.27 | 0.21 | No | No |
| F531Y | -0.99 | 0.16 | -0.55 | 0.14 | NA | NA | Yes | No |
| F531V | -0.22 | 0.02 | -0.64 | 0.03 | -0.74 | 0.05 | No | No |
| K532A | NA | NA | NA | NA | -0.93 | 0.19 | Yes | No |
| K532R | -0.63 | 0.05 | -0.63 | 0.05 | -0.56 | 0.10 | No | No |
| K532N | -0.39 | 0.11 | -0.71 | 0.13 | -0.45 | 0.12 | No | No |
| K532Q | -0.42 | 0.08 | -0.74 | 0.10 | -0.96 | 0.11 | No | No |
| K532E | -0.49 | 0.05 | -0.38 | 0.05 | -0.64 | 0.12 | No | No |
| K532G | -1.74 | 0.08 | -1.15 | 0.07 | -1.35 | 0.11 | No | No |
| K532L | -1.28 | 0.11 | -1.26 | 0.11 | -1.36 | 0.21 | No | No |
| K532M | -0.48 | 0.09 | -0.58 | 0.10 | -0.65 | 0.09 | No | No |
| K532S | NA | NA | NA | NA | -0.93 | 0.25 | Yes | No |
| K532* | -0.42 | 0.06 | -0.27 | 0.06 | -0.65 | 0.12 | No | No |
| K532T | -0.37 | 0.06 | -1.05 | 0.07 | -0.52 | 0.10 | No | No |
| K532V | -1.99 | 0.11 | -1.32 | 0.09 | -1.19 | 0.12 | No | No |
| L533R | -0.17 | 0.04 | -0.41 | 0.04 | -0.57 | 0.08 | No | No |
| L533G | -1.82 | 0.14 | -1.54 | 0.13 | NA | NA | Yes | No |
| L533M | -0.36 | 0.12 | -0.29 | 0.12 | -0.12 | 0.17 | No | No |
| L533P | -0.18 | 0.07 | -0.06 | 0.07 | -0.28 | 0.12 | No | No |
| L533V | -1.49 | 0.12 | -0.64 | 0.09 | -0.58 | 0.19 | No | No |
| N534A | -1.49 | 0.08 | -1.30 | 0.08 | -0.31 | 0.09 | No | No |
| N534R | -1.13 | 0.05 | -1.37 | 0.06 | -0.52 | 0.04 | No | No |
| N534D | -1.07 | 0.08 | -0.72 | 0.07 | -0.75 | 0.11 | No | No |
| N534C | -1.50 | 0.13 | -1.27 | 0.12 | 0.19 | 0.20 | Yes | No |
| N534Q | NA | NA | NA | NA | -0.67 | 0.24 | Yes | No |
| N534E | -2.05 | 0.10 | -1.48 | 0.08 | -1.32 | 0.13 | No | No |
| N534G | -1.43 | 0.04 | -0.96 | 0.04 | -1.10 | 0.04 | No | No |
| N534H | -0.18 | 0.03 | -0.50 | 0.04 | -0.20 | 0.06 | No | No |
| N534I | -0.54 | 0.08 | 0.00 | 0.07 | -0.60 | 0.18 | Yes | No |
| N534L | -1.92 | 0.11 | -1.79 | 0.11 | -0.26 | 0.07 | No | No |
| N534K | -1.00 | 0.07 | -0.74 | 0.07 | -0.01 | 0.10 | No | No |
| N534M | -1.72 | 0.12 | -0.90 | 0.09 | 0.88 | 0.19 | Yes | No |
| N534F | 0.11 | 0.10 | -1.16 | 0.16 | 0.16 | 0.30 | Yes | No |
| N534P | -0.33 | 0.07 | -0.26 | 0.07 | -1.27 | 0.16 | No | No |
| N534S | -1.00 | 0.06 | -0.72 | 0.06 | 0.22 | 0.05 | Yes | No |

| Mutant | Enrich. Score (1) | Stand. Error (1) | Enrich. Score (2) | Stand. Error (2) | Enrich. Score (3) | Stand. Error (3) | Any positive enrichment? | Consistent positive enrichment? |
|---|---|---|---|---|---|---|---|---|
| N534* | -1.20 | 0.09 | -2.22 | 0.15 | -1.84 | 0.10 | No | No |
| N534T | -0.38 | 0.04 | -0.40 | 0.04 | 0.49 | 0.06 | Yes | No |
| N534W | -1.54 | 0.08 | -0.69 | 0.06 | -0.29 | 0.07 | No | No |
| N534Y | -0.97 | 0.12 | -0.47 | 0.10 | -0.57 | 0.17 | No | No |
| N534V | -1.35 | 0.07 | -1.17 | 0.06 | -0.59 | 0.06 | No | No |
| N534A | NA | NA | NA | NA | -0.33 | 0.09 | Yes | No |
| N534R | NA | NA | NA | NA | -0.55 | 0.04 | Yes | No |
| N534D | -0.11 | 0.09 | -0.10 | 0.09 | -0.69 | 0.10 | No | No |
| N534C | NA | NA | NA | NA | 0.16 | 0.19 | Yes | No |
| N534Q | NA | NA | NA | NA | -0.72 | 0.24 | Yes | No |
| N534E | NA | NA | NA | NA | -1.34 | 0.13 | Yes | No |
| N534G | NA | NA | NA | NA | -1.11 | 0.04 | Yes | No |
| N534H | NA | NA | NA | NA | -0.19 | 0.24 | Yes | No |
| N534I | -0.14 | 0.19 | -0.05 | 0.19 | -0.61 | 0.19 | No | No |
| N534L | NA | NA | NA | NA | -0.22 | 0.07 | Yes | No |
| N534K | -0.47 | 0.14 | -0.26 | 0.13 | -0.06 | 0.09 | No | No |
| N534M | NA | NA | NA | NA | 0.83 | 0.18 | Yes | No |
| N534F | NA | NA | NA | NA | 0.26 | 0.30 | Yes | No |
| N534S | -0.15 | 0.07 | -0.03 | 0.07 | 0.20 | 0.05 | Yes | No |
| N534* | NA | NA | NA | NA | -1.73 | 0.10 | Yes | No |
| N534T | NA | NA | NA | NA | 0.91 | 0.15 | Yes | No |
| N534W | NA | NA | NA | NA | -0.32 | 0.07 | Yes | No |
| N534Y | -0.01 | 0.13 | 0.04 | 0.13 | -0.53 | 0.16 | Yes | No |
| N534V | NA | NA | NA | NA | -0.57 | 0.06 | Yes | No |
| F535A | -1.29 | 0.08 | -1.38 | 0.09 | -1.53 | 0.15 | No | No |
| F535R | -2.11 | 0.10 | -1.42 | 0.08 | -1.73 | 0.13 | No | No |
| F535C | -0.48 | 0.06 | -0.52 | 0.06 | -0.79 | 0.05 | No | No |
| F535E | -2.40 | 0.14 | -1.29 | 0.09 | -1.54 | 0.09 | No | No |
| F535G | -1.68 | 0.06 | -1.41 | 0.05 | -1.60 | 0.04 | No | No |
| F535I | -0.99 | 0.13 | -0.63 | 0.12 | NA | NA | Yes | No |
| F535L | -0.97 | 0.06 | -0.52 | 0.05 | -0.92 | 0.05 | No | No |
| F535M | -0.78 | 0.11 | -0.99 | 0.13 | -0.68 | 0.24 | No | No |
| F535S | -0.91 | 0.06 | -0.54 | 0.06 | -1.11 | 0.09 | No | No |
| F535W | -2.13 | 0.11 | -1.41 | 0.09 | -1.73 | 0.15 | No | No |
| F535Y | -0.65 | 0.10 | -0.50 | 0.10 | -0.62 | 0.16 | No | No |
| F535V | -0.87 | 0.04 | -1.00 | 0.05 | -0.98 | 0.04 | No | No |
| F535A | NA | NA | NA | NA | -1.47 | 0.15 | Yes | No |
| F535R | NA | NA | NA | NA | -1.74 | 0.12 | Yes | No |
| F535C | -0.09 | 0.06 | 0.09 | 0.05 | -0.54 | 0.06 | Yes | No |
| F535E | NA | NA | NA | NA | -1.65 | 0.09 | Yes | No |
| F535G | NA | NA | NA | NA | -1.93 | 0.04 | Yes | No |
| F535L | -0.04 | 0.06 | 0.03 | 0.06 | -0.69 | 0.05 | Yes | No |

| Mutant | Enrich. Score (1) | Stand. Error (1) | Enrich. Score (2) | Stand. Error (2) | Enrich. Score (3) | Stand. Error (3) | Any positive enrichment? | Consistent positive enrichment? |
|---|---|---|---|---|---|---|---|---|
| F535M | NA | NA | NA | NA | -0.67 | 0.21 | Yes | No |
| F535S | -0.14 | 0.08 | 0.00 | 0.08 | -1.14 | 0.09 | No | No |
| F535W | NA | NA | NA | NA | -1.68 | 0.14 | Yes | No |
| F535Y | -0.19 | 0.12 | -0.06 | 0.12 | -0.53 | 0.17 | No | No |
| F535V | -0.05 | 0.05 | -0.01 | 0.05 | -0.76 | 0.06 | No | No |
| Q536A | NA | NA | NA | NA | -0.02 | 0.19 | Yes | No |
| Q536R | 0.02 | 0.08 | -0.02 | 0.09 | 0.08 | 0.05 | Yes | No |
| Q536D | NA | NA | NA | NA | 0.23 | 0.28 | Yes | No |
| Q536C | NA | NA | NA | NA | -1.02 | 0.28 | Yes | No |
| Q536E | 0.00 | 0.16 | 0.02 | 0.16 | -0.66 | 0.08 | Yes | No |
| Q536G | NA | NA | NA | NA | 1.22 | 0.05 | Yes | No |
| Q536H | -0.05 | 0.19 | -0.05 | 0.19 | -0.34 | 0.22 | No | No |
| Q536L | -0.10 | 0.15 | -0.11 | 0.15 | -1.09 | 0.14 | No | No |
| Q536K | 0.56 | 0.09 | -0.36 | 0.11 | -0.09 | 0.13 | Yes | No |
| Q536S | NA | NA | NA | NA | 0.60 | 0.09 | Yes | No |
| Q536* | 0.15 | 0.09 | 0.03 | 0.10 | -0.74 | 0.10 | Yes | No |
| Q536V | NA | NA | NA | NA | -1.88 | 0.09 | Yes | No |
| R537A | -1.11 | 0.10 | -1.99 | 0.15 | NA | NA | Yes | No |
| R537Q | -0.56 | 0.13 | -1.08 | 0.16 | NA | NA | Yes | No |
| R537E | -1.40 | 0.13 | -1.33 | 0.13 | NA | NA | Yes | No |
| R537G | -1.10 | 0.05 | -1.07 | 0.05 | NA | NA | Yes | No |
| R537L | -1.50 | 0.13 | -1.38 | 0.12 | NA | NA | Yes | No |
| R537K | -0.58 | 0.09 | -0.81 | 0.10 | NA | NA | Yes | No |
| R537M | -1.57 | 0.02 | -1.19 | 0.02 | NA | NA | Yes | No |
| R537S | -1.30 | 0.11 | -0.65 | 0.08 | NA | NA | Yes | No |
| R537W | -1.42 | 0.10 | -1.60 | 0.11 | NA | NA | Yes | No |
| R537V | -1.52 | 0.11 | -1.85 | 0.12 | NA | NA | Yes | No |
| M537A | NA | NA | NA | NA | -1.52 | 0.24 | Yes | No |
| M537R | NA | NA | NA | NA | 1.70 | 0.04 | Yes | No |
| M537G | NA | NA | NA | NA | -1.55 | 0.08 | Yes | No |
| M537I | NA | NA | NA | NA | -0.01 | 0.15 | Yes | No |
| M537L | NA | NA | NA | NA | -0.09 | 0.13 | Yes | No |
| M537K | NA | NA | NA | NA | 0.19 | 0.14 | Yes | No |
| M537T | NA | NA | NA | NA | -0.29 | 0.13 | Yes | No |
| M537W | NA | NA | NA | NA | -1.30 | 0.19 | Yes | No |
| M537V | NA | NA | NA | NA | -0.62 | 0.10 | Yes | No |
| P538A | NA | NA | NA | NA | -1.19 | 0.06 | Yes | No |
| P538R | NA | NA | NA | NA | -1.72 | 0.08 | Yes | No |
| P538Q | NA | NA | NA | NA | -1.46 | 0.11 | Yes | No |
| P538E | NA | NA | NA | NA | -1.79 | 0.22 | Yes | No |
| P538G | NA | NA | NA | NA | -1.67 | 0.09 | Yes | No |
| P538H | -0.20 | 0.17 | -0.19 | 0.17 | NA | NA | Yes | No |

| Mutant | Enrich. Score (1) | Stand. Error (1) | Enrich. Score (2) | Stand. Error (2) | Enrich. Score (3) | Stand. Error (3) | Any positive enrichment? | Consistent positive enrichment? |
|---|---|---|---|---|---|---|---|---|
| P538L | -0.23 | 0.12 | -0.09 | 0.11 | -1.49 | 0.05 | No | No |
| P538S | 0.19 | 0.12 | 0.18 | 0.12 | -1.47 | 0.11 | Yes | No |
| P538T | -0.08 | 0.06 | 0.13 | 0.06 | -0.38 | 0.06 | Yes | No |
| P538W | NA | NA | NA | NA | -1.82 | 0.17 | Yes | No |
| P538V | NA | NA | NA | NA | -0.71 | 0.14 | Yes | No |
| T539A | 0.08 | 0.07 | -0.03 | 0.08 | -1.10 | 0.06 | Yes | No |
| T539R | NA | NA | NA | NA | -1.51 | 0.10 | Yes | No |
| T539N | 0.16 | 0.14 | 0.06 | 0.15 | -1.00 | 0.17 | Yes | No |
| T539C | NA | NA | NA | NA | -1.11 | 0.14 | Yes | No |
| T539Q | NA | NA | NA | NA | -1.19 | 0.20 | Yes | No |
| T539E | NA | NA | NA | NA | -1.61 | 0.12 | Yes | No |
| T539G | NA | NA | NA | NA | -1.63 | 0.05 | Yes | No |
| T539I | -0.20 | 0.13 | 0.00 | 0.13 | -1.04 | 0.16 | No | No |
| T539L | NA | NA | NA | NA | -2.07 | 0.13 | Yes | No |
| T539K | NA | NA | NA | NA | -1.23 | 0.26 | Yes | No |
| T539M | NA | NA | NA | NA | -1.64 | 0.18 | Yes | No |
| T539P | -0.33 | 0.14 | -0.40 | 0.14 | -1.51 | 0.14 | No | No |
| T539S | -0.03 | 0.05 | -0.17 | 0.05 | -0.14 | 0.04 | No | No |
| T539V | NA | NA | NA | NA | -1.65 | 0.11 | Yes | No |
| L540R | -0.17 | 0.15 | -0.30 | 0.15 | -1.27 | 0.14 | No | No |
| L540Q | 0.12 | 0.08 | 0.13 | 0.08 | -0.05 | 0.08 | Yes | No |
| L540G | NA | NA | NA | NA | -1.83 | 0.13 | Yes | No |
| L540M | 0.04 | 0.08 | -0.02 | 0.09 | -0.13 | 0.07 | Yes | No |
| L540P | 0.05 | 0.09 | 0.09 | 0.09 | -0.40 | 0.13 | Yes | No |
| L540V | NA | NA | NA | NA | -1.58 | 0.24 | Yes | No |
| A541R | NA | NA | NA | NA | -1.71 | 0.09 | Yes | No |
| A541D | 0.11 | 0.12 | 0.35 | 0.11 | -0.22 | 0.06 | Yes | No |
| A541C | NA | NA | NA | NA | 0.02 | 0.39 | Yes | No |
| A541G | 0.38 | 0.07 | 0.36 | 0.07 | -0.06 | 0.12 | Yes | No |
| A541L | NA | NA | NA | NA | 0.32 | 0.23 | Yes | No |
| A541S | -0.11 | 0.15 | -0.14 | 0.15 | -1.66 | 0.14 | No | No |
| A541T | -0.11 | 0.05 | -0.11 | 0.05 | -0.50 | 0.12 | No | No |
| A541V | -0.06 | 0.09 | 0.00 | 0.09 | -0.77 | 0.12 | No | No |
| S542N | 0.24 | 0.09 | 0.02 | 0.09 | 0.29 | 0.07 | Yes | Yes |
| S542C | 0.03 | 0.17 | 0.15 | 0.17 | 0.42 | 0.16 | Yes | Yes |
| S542A | NA | NA | NA | NA | 0.79 | 0.05 | Yes | No |
| S542R | -0.37 | 0.10 | -0.13 | 0.10 | 1.34 | 0.04 | Yes | No |
| S542D | NA | NA | NA | NA | -0.70 | 0.14 | Yes | No |
| S542Q | NA | NA | NA | NA | 0.04 | 0.23 | Yes | No |
| S542E | NA | NA | NA | NA | -1.68 | 0.07 | Yes | No |
| S542G | 0.23 | 0.07 | -0.10 | 0.08 | -0.79 | 0.06 | Yes | No |
| S542H | NA | NA | NA | NA | 0.08 | 0.35 | Yes | No |

| Mutant | Enrich. Score (1) | Stand. Error (1) | Enrich. Score (2) | Stand. Error (2) | Enrich. Score (3) | Stand. Error (3) | Any positive enrichment? | Consistent positive enrichment? |
|---|---|---|---|---|---|---|---|---|
| S542I | NA | NA | NA | NA | -0.13 | 0.32 | Yes | No |
| S542L | NA | NA | NA | NA | 0.67 | 0.10 | Yes | No |
| S542K | NA | NA | NA | NA | 1.36 | 0.09 | Yes | No |
| S542M | NA | NA | NA | NA | 1.10 | 0.11 | Yes | No |
| S542P | NA | NA | NA | NA | -0.85 | 0.27 | Yes | No |
| S542T | 0.68 | 0.17 | 0.24 | 0.19 | -0.08 | 0.10 | Yes | No |
| S542W | NA | NA | NA | NA | -0.34 | 0.06 | Yes | No |
| S542V | NA | NA | NA | NA | 0.38 | 0.08 | Yes | No |
| G543A | -2.33 | 0.07 | -1.64 | 0.05 | -2.12 | 0.10 | No | No |
| G543R | -1.78 | 0.05 | -1.75 | 0.05 | -1.89 | 0.07 | No | No |
| G543D | -1.02 | 0.07 | -1.88 | 0.09 | NA | NA | Yes | No |
| G543C | -0.32 | 0.04 | -0.29 | 0.04 | -0.07 | 0.06 | No | No |
| G543E | -2.56 | 0.11 | -1.80 | 0.08 | -2.09 | 0.18 | No | No |
| G543I | -1.30 | 0.14 | -1.24 | 0.13 | NA | NA | Yes | No |
| G543L | -1.74 | 0.08 | -1.17 | 0.06 | -1.85 | 0.22 | No | No |
| G543F | -0.91 | 0.09 | -0.77 | 0.08 | -0.93 | 0.14 | No | No |
| G543P | -1.28 | 0.08 | -1.18 | 0.08 | -1.40 | 0.22 | No | No |
| G543S | -1.21 | 0.05 | -1.22 | 0.05 | -1.63 | 0.08 | No | No |
| G543* | -1.66 | 0.13 | -1.93 | 0.14 | NA | NA | Yes | No |
| G543W | -1.55 | 0.08 | -1.49 | 0.07 | NA | NA | Yes | No |
| G543V | -0.80 | 0.03 | -0.81 | 0.03 | -0.80 | 0.06 | No | No |
| W544A | -1.17 | 0.05 | -1.90 | 0.06 | -1.67 | 0.09 | No | No |
| W544R | -1.30 | 0.03 | -1.40 | 0.03 | -1.35 | 0.04 | No | No |
| W544N | -1.11 | 0.10 | -1.78 | 0.13 | NA | NA | Yes | No |
| W544D | -1.61 | 0.09 | -1.58 | 0.09 | -1.51 | 0.14 | No | No |
| W544C | -0.88 | 0.06 | -1.34 | 0.07 | -1.21 | 0.10 | No | No |
| W544Q | -1.24 | 0.08 | -1.17 | 0.08 | NA | NA | Yes | No |
| W544E | -1.14 | 0.05 | -1.44 | 0.05 | -1.54 | 0.06 | No | No |
| W544G | -1.68 | 0.03 | -1.47 | 0.03 | -1.55 | 0.04 | No | No |
| W544H | -0.01 | 0.08 | -1.46 | 0.13 | NA | NA | Yes | No |
| W544L | -1.76 | 0.06 | -1.40 | 0.05 | -1.41 | 0.04 | No | No |
| W544K | -2.26 | 0.11 | -1.33 | 0.07 | -1.39 | 0.08 | No | No |
| W544M | -2.09 | 0.11 | -1.42 | 0.08 | -1.45 | 0.15 | No | No |
| W544F | -0.96 | 0.09 | -1.72 | 0.12 | NA | NA | Yes | No |
| W544P | -1.84 | 0.09 | -1.34 | 0.08 | -1.51 | 0.09 | No | No |
| W544S | -0.66 | 0.03 | -0.59 | 0.03 | -0.57 | 0.03 | No | No |
| W544* | -0.85 | 0.05 | -1.05 | 0.05 | -1.09 | 0.07 | No | No |
| W544T | -1.81 | 0.09 | -1.08 | 0.07 | -1.83 | 0.17 | No | No |
| W544V | -1.60 | 0.05 | -1.52 | 0.05 | -1.52 | 0.09 | No | No |
| D545A | -1.34 | 0.06 | -1.18 | 0.06 | -1.75 | 0.13 | No | No |
| D545R | -2.22 | 0.08 | -1.82 | 0.06 | -1.53 | 0.12 | No | No |
| D545N | -1.00 | 0.10 | -0.89 | 0.09 | -1.05 | 0.15 | No | No |

| Mutant | Enrich. Score (1) | Stand. Error (1) | Enrich. Score (2) | Stand. Error (2) | Enrich. Score (3) | Stand. Error (3) | Any positive enrichment? | Consistent positive enrichment? |
|---|---|---|---|---|---|---|---|---|
| D545C | -2.14 | 0.13 | -1.41 | 0.10 | NA | NA | Yes | No |
| D545E | -1.54 | 0.07 | -2.07 | 0.09 | -1.66 | 0.14 | No | No |
| D545G | -1.30 | 0.04 | -1.13 | 0.04 | -1.44 | 0.07 | No | No |
| D545H | -1.20 | 0.14 | -0.72 | 0.12 | NA | NA | Yes | No |
| D545L | -1.77 | 0.08 | -1.23 | 0.06 | -1.75 | 0.21 | No | No |
| D545K | -1.83 | 0.15 | -1.54 | 0.14 | NA | NA | Yes | No |
| D545M | -1.30 | 0.11 | -0.90 | 0.10 | NA | NA | Yes | No |
| D545P | -1.73 | 0.12 | -1.07 | 0.09 | NA | NA | Yes | No |
| D545S | -0.99 | 0.06 | -0.97 | 0.06 | -1.65 | 0.18 | No | No |
| D545T | -2.02 | 0.14 | -1.36 | 0.10 | -1.24 | 0.25 | No | No |
| D545W | -2.52 | 0.12 | -2.44 | 0.12 | -1.79 | 0.16 | No | No |
| D545Y | -1.34 | 0.12 | -1.40 | 0.12 | NA | NA | Yes | No |
| D545V | -1.90 | 0.07 | -1.31 | 0.05 | -1.58 | 0.10 | No | No |
| V546A | 0.05 | 0.04 | -0.28 | 0.04 | -1.03 | 0.08 | Yes | No |
| V546R | -0.34 | 0.04 | -0.10 | 0.04 | -0.24 | 0.05 | No | No |
| V546D | -1.89 | 0.14 | -0.98 | 0.10 | -1.80 | 0.23 | No | No |
| V546C | -0.63 | 0.08 | 0.12 | 0.06 | -1.17 | 0.18 | Yes | No |
| V546Q | -0.14 | 0.09 | -0.04 | 0.08 | -0.37 | 0.22 | No | No |
| V546E | -0.85 | 0.06 | -0.72 | 0.06 | -1.16 | 0.10 | No | No |
| V546G | -0.89 | 0.03 | -0.75 | 0.03 | -1.38 | 0.06 | No | No |
| V546I | 0.17 | 0.09 | -0.21 | 0.10 | -0.01 | 0.36 | Yes | No |
| V546L | -0.09 | 0.04 | -0.03 | 0.04 | -0.77 | 0.12 | No | No |
| V546K | -0.23 | 0.09 | -0.07 | 0.09 | -0.28 | 0.09 | No | No |
| V546M | -0.48 | 0.06 | -0.39 | 0.06 | -0.14 | 0.11 | No | No |
| V546F | -0.58 | 0.10 | -1.20 | 0.13 | NA | NA | Yes | No |
| V546S | -0.24 | 0.05 | -0.75 | 0.06 | -1.19 | 0.07 | No | No |
| V546* | -1.55 | 0.12 | -1.19 | 0.10 | -1.56 | 0.23 | No | No |
| V546T | 0.15 | 0.07 | -0.59 | 0.09 | -0.82 | 0.09 | Yes | No |
| V546W | -1.75 | 0.08 | -1.06 | 0.06 | -1.43 | 0.15 | No | No |
| V546Y | 0.40 | 0.10 | -0.50 | 0.13 | -0.45 | 0.39 | Yes | No |
| N547A | -0.97 | 0.06 | -0.81 | 0.06 | -1.74 | 0.12 | No | No |
| N547R | -0.75 | 0.04 | -0.98 | 0.05 | -1.25 | 0.05 | No | No |
| N547D | -1.06 | 0.08 | -0.98 | 0.08 | -1.08 | 0.12 | No | No |
| N547E | -1.13 | 0.07 | -1.64 | 0.09 | NA | NA | Yes | No |
| N547G | -0.99 | 0.04 | -1.38 | 0.05 | -1.68 | 0.04 | No | No |
| N547I | -0.57 | 0.10 | -0.69 | 0.10 | -0.97 | 0.15 | No | No |
| N547L | -2.14 | 0.12 | -1.01 | 0.07 | -1.56 | 0.18 | No | No |
| N547K | -0.72 | 0.08 | -0.48 | 0.07 | -0.83 | 0.12 | No | No |
| N547S | -0.69 | 0.06 | -0.98 | 0.06 | -1.07 | 0.09 | No | No |
| N547T | -2.13 | 0.13 | -1.62 | 0.11 | NA | NA | Yes | No |
| N547W | -1.69 | 0.09 | -1.84 | 0.10 | NA | NA | Yes | No |
| N547Y | -0.39 | 0.10 | -0.94 | 0.12 | -1.04 | 0.21 | No | No |

| Mutant | Enrich. Score (1) | Stand. Error (1) | Enrich. Score (2) | Stand. Error (2) | Enrich. Score (3) | Stand. Error (3) | Any positive enrichment? | Consistent positive enrichment? |
|---|---|---|---|---|---|---|---|---|
| N547V | -1.63 | 0.07 | -1.46 | 0.07 | -1.86 | 0.15 | No | No |
| K548A | -1.24 | 0.04 | -1.12 | 0.04 | -1.74 | 0.03 | No | No |
| K548R | -0.59 | 0.02 | -0.51 | 0.02 | -0.18 | 0.03 | No | No |
| K548N | -0.98 | 0.07 | -1.11 | 0.08 | -1.10 | 0.09 | No | No |
| K548D | -2.69 | 0.13 | -1.63 | 0.08 | -2.01 | 0.14 | No | No |
| K548C | -0.97 | 0.06 | -0.64 | 0.05 | -1.44 | 0.14 | No | No |
| K548Q | -0.31 | 0.04 | -0.24 | 0.04 | -0.41 | 0.06 | No | No |
| K548E | -1.54 | 0.05 | -1.45 | 0.05 | -1.51 | 0.04 | No | No |
| K548G | -1.14 | 0.02 | -0.95 | 0.02 | -1.61 | 0.02 | No | No |
| K548H | -1.58 | 0.14 | -1.58 | 0.14 | NA | NA | Yes | No |
| K548I | -1.05 | 0.07 | -1.27 | 0.08 | -0.98 | 0.06 | No | No |
| K548L | -1.72 | 0.06 | -1.56 | 0.05 | -1.96 | 0.08 | No | No |
| K548M | -0.27 | 0.04 | -0.19 | 0.04 | -1.10 | 0.10 | No | No |
| K548F | -2.01 | 0.12 | -1.60 | 0.10 | NA | NA | Yes | No |
| K548P | -1.78 | 0.09 | -1.04 | 0.07 | -1.86 | 0.16 | No | No |
| K548S | -0.97 | 0.04 | -0.55 | 0.03 | -1.40 | 0.08 | No | No |
| K548* | -1.65 | 0.08 | -0.85 | 0.06 | -1.40 | 0.13 | No | No |
| K548T | -0.12 | 0.04 | -0.74 | 0.05 | -1.19 | 0.07 | No | No |
| K548W | -2.13 | 0.07 | -1.65 | 0.05 | -1.44 | 0.07 | No | No |
| K548Y | -1.07 | 0.09 | -1.63 | 0.11 | NA | NA | Yes | No |
| K548V | -0.72 | 0.03 | -0.39 | 0.03 | -0.97 | 0.05 | No | No |
| E549A | -1.80 | 0.06 | -1.49 | 0.05 | -1.69 | 0.07 | No | No |
| E549R | -1.64 | 0.05 | -1.69 | 0.05 | -1.80 | 0.09 | No | No |
| E549D | -1.63 | 0.09 | -1.13 | 0.07 | -1.53 | 0.14 | No | No |
| E549C | -2.08 | 0.12 | -1.84 | 0.11 | -1.56 | 0.18 | No | No |
| E549Q | -0.41 | 0.05 | -0.41 | 0.05 | -0.80 | 0.10 | No | No |
| E549G | -1.50 | 0.03 | -1.53 | 0.03 | -1.60 | 0.04 | No | No |
| E549I | -1.07 | 0.12 | -1.12 | 0.13 | NA | NA | Yes | No |
| E549L | -1.62 | 0.07 | -1.31 | 0.06 | -1.65 | 0.13 | No | No |
| E549K | -0.91 | 0.07 | -0.89 | 0.07 | -0.99 | 0.08 | No | No |
| E549M | -2.06 | 0.12 | -1.66 | 0.10 | -1.57 | 0.17 | No | No |
| E549F | -1.59 | 0.14 | -1.27 | 0.13 | NA | NA | Yes | No |
| E549S | -2.21 | 0.08 | -1.69 | 0.07 | -1.91 | 0.05 | No | No |
| E549* | -1.66 | 0.09 | -1.47 | 0.09 | -1.59 | 0.14 | No | No |
| E549T | NA | NA | NA | NA | -1.39 | 0.10 | Yes | No |
| E549W | -0.99 | 0.05 | -1.72 | 0.07 | -1.85 | 0.11 | No | No |
| E549V | -1.01 | 0.04 | -0.79 | 0.04 | -1.37 | 0.04 | No | No |
| K550R | 0.05 | 0.03 | 0.18 | 0.03 | 0.17 | 0.07 | Yes | Yes |
| K550A | -0.24 | 0.04 | -0.06 | 0.04 | -0.91 | 0.13 | No | No |
| K550N | 0.11 | 0.07 | -0.13 | 0.07 | -0.46 | 0.13 | Yes | No |
| K550D | -0.86 | 0.09 | 0.22 | 0.07 | -1.48 | 0.23 | Yes | No |
| K550C | -0.08 | 0.07 | -0.18 | 0.07 | -0.84 | 0.21 | No | No |

| Mutant | Enrich. Score (1) | Stand. Error (1) | Enrich. Score (2) | Stand. Error (2) | Enrich. Score (3) | Stand. Error (3) | Any positive enrichment? | Consistent positive enrichment? |
|---|---|---|---|---|---|---|---|---|
| K550Q | -0.18 | 0.07 | 0.45 | 0.07 | -0.64 | 0.18 | Yes | No |
| K550E | -0.86 | 0.06 | -0.45 | 0.05 | -1.11 | 0.09 | No | No |
| K550G | -0.25 | 0.02 | -0.16 | 0.02 | -1.14 | 0.04 | No | No |
| K550H | -0.22 | 0.15 | -0.42 | 0.16 | NA | NA | Yes | No |
| K550I | -0.51 | 0.12 | 0.79 | 0.09 | NA | NA | Yes | No |
| K550L | 0.01 | 0.05 | -0.17 | 0.05 | -0.95 | 0.06 | Yes | No |
| K550M | -0.71 | 0.08 | -0.17 | 0.07 | -0.72 | 0.15 | No | No |
| K550F | -0.14 | 0.10 | -0.39 | 0.11 | NA | NA | Yes | No |
| K550P | -0.02 | 0.08 | -0.78 | 0.10 | -0.95 | 0.27 | No | No |
| K550S | -0.07 | 0.05 | -0.22 | 0.05 | -1.05 | 0.08 | No | No |
| K550* | -0.98 | 0.08 | -1.14 | 0.09 | -1.19 | 0.10 | No | No |
| K550T | -0.13 | 0.06 | -0.44 | 0.07 | -0.87 | 0.14 | No | No |
| K550W | 0.18 | 0.04 | 0.20 | 0.04 | -0.66 | 0.07 | Yes | No |
| K550Y | -0.12 | 0.11 | -0.58 | 0.12 | NA | NA | Yes | No |
| K550V | -0.12 | 0.04 | -0.70 | 0.05 | -1.02 | 0.13 | No | No |
| N551D | 0.14 | 0.04 | 0.15 | 0.04 | 0.67 | 0.07 | Yes | Yes |
| N551A | -0.29 | 0.04 | -0.42 | 0.04 | -0.37 | 0.05 | No | No |
| N551R | -0.92 | 0.04 | -1.40 | 0.05 | -1.64 | 0.09 | No | No |
| N551C | -0.52 | 0.08 | -0.26 | 0.08 | -0.39 | 0.28 | No | No |
| N551Q | -0.77 | 0.09 | -0.58 | 0.08 | -0.76 | 0.10 | No | No |
| N551E | -1.32 | 0.06 | -0.66 | 0.05 | -1.51 | 0.10 | No | No |
| N551G | -0.95 | 0.03 | -0.96 | 0.03 | -1.10 | 0.04 | No | No |
| N551H | 0.51 | 0.09 | -1.02 | 0.14 | 0.55 | 0.13 | Yes | No |
| N551I | -0.01 | 0.05 | 0.20 | 0.05 | -0.18 | 0.11 | Yes | No |
| N551L | -0.07 | 0.05 | -0.83 | 0.06 | -1.35 | 0.11 | No | No |
| N551K | -1.43 | 0.07 | -1.28 | 0.07 | -1.22 | 0.08 | No | No |
| N551M | -1.01 | 0.09 | -0.58 | 0.08 | -0.94 | 0.18 | No | No |
| N551F | -0.65 | 0.11 | -0.19 | 0.09 | -0.04 | 0.24 | No | No |
| N551P | -1.24 | 0.10 | -0.91 | 0.09 | -1.21 | 0.12 | No | No |
| N551S | -0.06 | 0.03 | 0.02 | 0.03 | -0.23 | 0.05 | Yes | No |
| N551* | -1.09 | 0.10 | -1.44 | 0.11 | -1.45 | 0.20 | No | No |
| N551T | 0.21 | 0.05 | -0.29 | 0.06 | 0.07 | 0.11 | Yes | No |
| N551W | -0.36 | 0.06 | -0.69 | 0.06 | -0.63 | 0.13 | No | No |
| N551Y | -0.28 | 0.07 | 0.04 | 0.06 | 0.95 | 0.10 | Yes | No |
| N551V | -0.31 | 0.04 | -0.21 | 0.04 | 0.03 | 0.05 | Yes | No |
| N552A | -1.33 | 0.07 | -1.21 | 0.07 | -1.32 | 0.08 | No | No |
| N552R | -1.19 | 0.04 | -1.37 | 0.05 | -1.47 | 0.04 | No | No |
| N552D | -1.18 | 0.07 | -1.04 | 0.06 | -1.24 | 0.06 | No | No |
| N552C | -1.59 | 0.10 | -1.44 | 0.09 | -1.65 | 0.17 | No | No |
| N552Q | -1.21 | 0.11 | -0.81 | 0.10 | NA | NA | Yes | No |
| N552E | -1.93 | 0.09 | -0.57 | 0.05 | -1.89 | 0.06 | No | No |
| N552G | -1.80 | 0.05 | -1.17 | 0.04 | -2.06 | 0.03 | No | No |

| Mutant | Enrich. Score (1) | Stand. Error (1) | Enrich. Score (2) | Stand. Error (2) | Enrich. Score (3) | Stand. Error (3) | Any positive enrichment? | Consistent positive enrichment? |
|---|---|---|---|---|---|---|---|---|
| N552H | -0.25 | 0.10 | -0.21 | 0.10 | NA | NA | Yes | No |
| N552I | -0.34 | 0.05 | -0.02 | 0.05 | -0.50 | 0.09 | No | No |
| N552L | -1.13 | 0.07 | -1.91 | 0.10 | -1.73 | 0.12 | No | No |
| N552K | -1.34 | 0.08 | -1.25 | 0.08 | -1.07 | 0.10 | No | No |
| N552M | -1.92 | 0.12 | -1.44 | 0.10 | -1.67 | 0.11 | No | No |
| N552P | -1.69 | 0.12 | -0.81 | 0.09 | NA | NA | Yes | No |
| N552S | -0.11 | 0.03 | -0.20 | 0.03 | -0.58 | 0.05 | No | No |
| N552* | NA | NA | NA | NA | -1.37 | 0.20 | Yes | No |
| N552T | -0.16 | 0.03 | 0.00 | 0.03 | -1.04 | 0.10 | No | No |
| N552W | -1.97 | 0.10 | -1.69 | 0.08 | -1.53 | 0.15 | No | No |
| N552Y | -0.89 | 0.10 | -0.99 | 0.10 | -1.08 | 0.18 | No | No |
| N552V | -1.60 | 0.07 | -1.17 | 0.06 | -1.56 | 0.05 | No | No |
| G553A | -0.56 | 0.05 | -0.61 | 0.05 | -1.53 | 0.11 | No | No |
| G553R | -1.58 | 0.06 | -1.17 | 0.05 | -0.39 | 0.07 | No | No |
| G553D | -0.48 | 0.08 | -0.91 | 0.09 | -0.94 | 0.19 | No | No |
| G553Q | -1.38 | 0.15 | -1.10 | 0.14 | NA | NA | Yes | No |
| G553E | -2.07 | 0.11 | -1.79 | 0.10 | -1.67 | 0.17 | No | No |
| G553S | -0.78 | 0.06 | -0.54 | 0.06 | -0.72 | 0.09 | No | No |
| G553* | -1.04 | 0.12 | -1.39 | 0.14 | NA | NA | Yes | No |
| G553W | -1.11 | 0.07 | -1.87 | 0.09 | -1.59 | 0.16 | No | No |
| G553V | -0.34 | 0.03 | -0.24 | 0.03 | -0.30 | 0.05 | No | No |
| A554I | 0.15 | 0.09 | 0.71 | 0.08 | 0.39 | 0.34 | Yes | Yes |
| A554T | 0.45 | 0.04 | 0.32 | 0.05 | 0.93 | 0.07 | Yes | Yes |
| A554V | 0.57 | 0.03 | 0.48 | 0.03 | 0.54 | 0.04 | Yes | Yes |
| A554R | -1.28 | 0.05 | -1.12 | 0.05 | -2.05 | 0.11 | No | No |
| A554N | 0.04 | 0.09 | -0.71 | 0.11 | -0.12 | 0.13 | Yes | No |
| A554D | -1.96 | 0.10 | -0.95 | 0.07 | -0.83 | 0.04 | No | No |
| A554C | -0.05 | 0.07 | 0.32 | 0.06 | 1.05 | 0.09 | Yes | No |
| A554Q | -0.47 | 0.10 | -0.57 | 0.10 | -1.06 | 0.28 | No | No |
| A554E | -1.85 | 0.09 | -0.79 | 0.06 | -1.86 | 0.11 | No | No |
| A554G | -0.43 | 0.03 | -0.54 | 0.03 | -0.70 | 0.04 | No | No |
| A554L | -0.23 | 0.05 | -0.11 | 0.05 | -0.32 | 0.17 | No | No |
| A554M | 0.27 | 0.07 | -0.26 | 0.08 | -0.72 | 0.23 | Yes | No |
| A554P | -1.28 | 0.09 | -1.84 | 0.12 | NA | NA | Yes | No |
| A554S | 0.14 | 0.03 | 0.15 | 0.03 | -0.07 | 0.05 | Yes | No |
| A554* | -1.77 | 0.14 | -1.03 | 0.11 | NA | NA | Yes | No |
| A554W | -1.54 | 0.09 | -2.63 | 0.14 | NA | NA | Yes | No |
| I555V | 0.41 | 0.03 | 0.13 | 0.03 | 0.14 | 0.06 | Yes | Yes |
| I555A | -0.39 | 0.05 | -0.48 | 0.05 | -0.79 | 0.14 | No | No |
| I555R | -0.47 | 0.04 | -1.21 | 0.05 | -0.58 | 0.09 | No | No |
| I555N | -0.51 | 0.08 | -0.76 | 0.08 | -0.76 | 0.13 | No | No |
| I555D | -1.00 | 0.09 | -1.17 | 0.10 | NA | NA | Yes | No |

| Mutant | Enrich. Score (1) | Stand. Error (1) | Enrich. Score (2) | Stand. Error (2) | Enrich. Score (3) | Stand. Error (3) | Any positive enrichment? | Consistent positive enrichment? |
|---|---|---|---|---|---|---|---|---|
| I555C | -1.00 | 0.12 | -0.93 | 0.12 | -0.75 | 0.10 | No | No |
| I555Q | -0.79 | 0.11 | -0.92 | 0.11 | -0.84 | 0.21 | No | No |
| I555E | -2.31 | 0.12 | -0.09 | 0.05 | -1.79 | 0.15 | No | No |
| I555G | -1.15 | 0.04 | -1.07 | 0.04 | -1.57 | 0.03 | No | No |
| I555L | 0.18 | 0.05 | -0.03 | 0.05 | -0.30 | 0.14 | Yes | No |
| I555K | -0.71 | 0.09 | -0.03 | 0.07 | -1.33 | 0.11 | No | No |
| I555M | -0.04 | 0.05 | -0.01 | 0.05 | -0.27 | 0.08 | No | No |
| I555F | -0.18 | 0.09 | -0.17 | 0.09 | -0.32 | 0.13 | No | No |
| I555P | -1.29 | 0.11 | -1.66 | 0.13 | -1.11 | 0.36 | No | No |
| I555S | -0.16 | 0.03 | -0.12 | 0.03 | -0.31 | 0.05 | No | No |
| I555T | -0.01 | 0.05 | -0.09 | 0.05 | -0.45 | 0.11 | No | No |
| I555W | -1.78 | 0.11 | -1.29 | 0.09 | -1.81 | 0.15 | No | No |
| I555Y | -1.05 | 0.14 | -1.16 | 0.15 | NA | NA | Yes | No |
| L556M | 0.08 | 0.08 | 0.10 | 0.08 | 0.11 | 0.21 | Yes | Yes |
| L556A | -0.52 | 0.07 | -1.77 | 0.12 | -1.33 | 0.24 | No | No |
| L556R | -1.06 | 0.06 | -0.91 | 0.06 | -1.39 | 0.10 | No | No |
| L556C | -1.31 | 0.13 | -0.58 | 0.10 | NA | NA | Yes | No |
| L556Q | -0.06 | 0.06 | -0.34 | 0.07 | -0.36 | 0.11 | No | No |
| L556G | -1.55 | 0.07 | -1.49 | 0.07 | -1.60 | 0.06 | No | No |
| L556I | 0.58 | 0.12 | 0.07 | 0.14 | NA | NA | Yes | No |
| L556P | -0.19 | 0.07 | -0.54 | 0.08 | -0.91 | 0.13 | No | No |
| L556S | -1.56 | 0.11 | -1.28 | 0.10 | NA | NA | Yes | No |
| L556T | -0.95 | 0.12 | -0.69 | 0.11 | NA | NA | Yes | No |
| L556W | -1.77 | 0.12 | -1.41 | 0.11 | NA | NA | Yes | No |
| L556V | -0.45 | 0.06 | -0.17 | 0.05 | -0.76 | 0.14 | No | No |
| F557A | -0.39 | 0.05 | -0.06 | 0.05 | -0.75 | 0.07 | No | No |
| F557R | -1.79 | 0.06 | -1.05 | 0.05 | -1.57 | 0.08 | No | No |
| F557N | NA | NA | NA | NA | -0.90 | 0.11 | Yes | No |
| F557C | -0.63 | 0.06 | -0.55 | 0.06 | -0.32 | 0.13 | No | No |
| F557Q | -1.87 | 0.15 | -0.40 | 0.09 | -0.98 | 0.25 | No | No |
| F557E | -1.90 | 0.10 | -1.64 | 0.09 | -1.50 | 0.16 | No | No |
| F557G | -1.17 | 0.04 | -1.02 | 0.04 | -0.98 | 0.06 | No | No |
| F557I | -0.32 | 0.05 | -0.07 | 0.04 | -0.05 | 0.08 | No | No |
| F557L | -0.04 | 0.04 | -0.08 | 0.04 | 0.14 | 0.08 | Yes | No |
| F557K | -1.25 | 0.10 | -0.84 | 0.09 | -0.79 | 0.30 | No | No |
| F557M | 0.33 | 0.07 | -0.19 | 0.08 | -0.15 | 0.18 | Yes | No |
| F557P | -1.14 | 0.10 | -1.38 | 0.11 | -1.69 | 0.21 | No | No |
| F557S | -0.87 | 0.05 | -0.74 | 0.05 | -0.48 | 0.09 | No | No |
| F557* | -1.30 | 0.10 | -2.32 | 0.15 | NA | NA | Yes | No |
| F557T | -1.21 | 0.09 | -0.72 | 0.08 | -0.44 | 0.25 | No | No |
| F557W | -0.87 | 0.06 | -0.37 | 0.05 | -1.24 | 0.11 | No | No |
| F557Y | -0.74 | 0.08 | -0.15 | 0.07 | -0.87 | 0.13 | No | No |

| Mutant | Enrich. Score (1) | Stand. Error (1) | Enrich. Score (2) | Stand. Error (2) | Enrich. Score (3) | Stand. Error (3) | Any positive enrichment? | Consistent positive enrichment? |
|---|---|---|---|---|---|---|---|---|
| F557V | -0.50 | 0.04 | -0.91 | 0.05 | -0.42 | 0.04 | No | No |
| V558M | 0.24 | 0.06 | 0.15 | 0.06 | 0.10 | 0.12 | Yes | Yes |
| V558A | -0.11 | 0.04 | -0.13 | 0.04 | 0.26 | 0.09 | Yes | No |
| V558R | -0.63 | 0.06 | -0.46 | 0.05 | -0.26 | 0.14 | No | No |
| V558D | 0.64 | 0.09 | 0.05 | 0.10 | -0.46 | 0.14 | Yes | No |
| V558C | -0.01 | 0.12 | 0.01 | 0.12 | -0.28 | 0.55 | Yes | No |
| V558Q | 0.40 | 0.11 | -0.65 | 0.14 | -0.21 | 0.55 | Yes | No |
| V558E | 0.15 | 0.04 | -0.31 | 0.05 | -0.12 | 0.07 | Yes | No |
| V558G | -0.07 | 0.03 | -0.48 | 0.04 | -0.36 | 0.10 | No | No |
| V558L | 0.16 | 0.04 | 0.03 | 0.04 | -0.16 | 0.09 | Yes | No |
| V558K | 0.05 | 0.10 | -0.15 | 0.11 | -0.02 | 0.48 | Yes | No |
| V558F | -0.21 | 0.13 | -0.36 | 0.13 | NA | NA | Yes | No |
| V558S | -0.36 | 0.09 | -0.49 | 0.09 | -0.10 | 0.27 | No | No |
| V558T | -0.19 | 0.12 | -0.28 | 0.12 | 0.15 | 0.41 | Yes | No |
| V558W | -0.76 | 0.10 | -0.75 | 0.10 | -0.93 | 0.30 | No | No |
| K559A | 0.17 | 0.04 | 0.08 | 0.04 | 0.13 | 0.08 | Yes | Yes |
| K559R | 0.14 | 0.03 | -0.02 | 0.03 | 0.11 | 0.06 | Yes | No |
| K559N | 0.05 | 0.03 | 0.05 | 0.03 | -0.04 | 0.05 | Yes | No |
| K559D | 0.25 | 0.08 | -0.33 | 0.09 | -0.39 | 0.25 | Yes | No |
| K559C | 0.31 | 0.08 | -0.20 | 0.09 | -0.05 | 0.22 | Yes | No |
| K559Q | -0.23 | 0.07 | 0.03 | 0.07 | 0.00 | 0.21 | Yes | No |
| K559E | -0.20 | 0.04 | -0.52 | 0.04 | -0.40 | 0.06 | No | No |
| K559G | -0.35 | 0.03 | -0.41 | 0.03 | -0.16 | 0.03 | No | No |
| K559H | 0.53 | 0.14 | -0.21 | 0.16 | NA | NA | Yes | No |
| K559I | -0.62 | 0.12 | 0.01 | 0.10 | NA | NA | Yes | No |
| K559L | -0.39 | 0.06 | -0.29 | 0.06 | -0.71 | 0.13 | No | No |
| K559M | -0.27 | 0.06 | -0.65 | 0.07 | 0.01 | 0.12 | Yes | No |
| K559F | -0.45 | 0.13 | 0.13 | 0.11 | NA | NA | Yes | No |
| K559S | -0.28 | 0.06 | -0.32 | 0.06 | 0.22 | 0.20 | Yes | No |
| K559* | -0.63 | 0.07 | -0.48 | 0.07 | -1.15 | 0.09 | No | No |
| K559T | 0.30 | 0.06 | 0.52 | 0.06 | -0.20 | 0.15 | Yes | No |
| K559W | -0.64 | 0.06 | -0.34 | 0.06 | -0.32 | 0.18 | No | No |
| K559Y | -0.13 | 0.11 | -0.01 | 0.11 | NA | NA | Yes | No |
| K559V | -0.53 | 0.05 | -0.50 | 0.05 | -0.27 | 0.13 | No | No |
| N560A | 0.34 | 0.05 | 0.18 | 0.05 | 0.18 | 0.08 | Yes | Yes |
| N560D | 0.16 | 0.04 | 0.18 | 0.04 | 0.16 | 0.08 | Yes | Yes |
| N560E | 0.48 | 0.06 | 0.28 | 0.06 | 0.11 | 0.25 | Yes | Yes |
| N560M | 0.16 | 0.09 | 0.31 | 0.09 | 0.18 | 0.13 | Yes | Yes |
| N560R | 0.10 | 0.04 | 0.04 | 0.04 | -0.07 | 0.06 | Yes | No |
| N560C | -0.11 | 0.08 | -0.20 | 0.08 | -0.15 | 0.09 | No | No |
| N560Q | 0.55 | 0.09 | -1.07 | 0.14 | -0.09 | 0.38 | Yes | No |
| N560G | 0.01 | 0.04 | 0.03 | 0.04 | -0.02 | 0.09 | Yes | No |

| Mutant | Enrich. Score (1) | Stand. Error (1) | Enrich. Score (2) | Stand. Error (2) | Enrich. Score (3) | Stand. Error (3) | Any positive enrichment? | Consistent positive enrichment? |
|---|---|---|---|---|---|---|---|---|
| N560H | -0.35 | 0.13 | -0.17 | 0.13 | NA | NA | Yes | No |
| N560I | 0.22 | 0.05 | 0.28 | 0.05 | -0.13 | 0.10 | Yes | No |
| N560L | -0.64 | 0.08 | -0.16 | 0.07 | -0.12 | 0.11 | No | No |
| N560K | 0.11 | 0.06 | -0.29 | 0.07 | 0.14 | 0.14 | Yes | No |
| N560F | 0.14 | 0.12 | -0.03 | 0.13 | NA | NA | Yes | No |
| N560P | 0.19 | 0.09 | -0.69 | 0.11 | -0.13 | 0.29 | Yes | No |
| N560S | 0.03 | 0.03 | 0.18 | 0.03 | -0.01 | 0.05 | Yes | No |
| N560* | -1.15 | 0.11 | -1.78 | 0.15 | NA | NA | Yes | No |
| N560T | -0.40 | 0.08 | 0.00 | 0.07 | 0.01 | 0.14 | Yes | No |
| N560W | -0.36 | 0.07 | -0.72 | 0.08 | -0.27 | 0.16 | No | No |
| N560Y | -0.24 | 0.09 | 0.04 | 0.08 | 0.07 | 0.12 | Yes | No |
| N560V | 0.13 | 0.06 | -0.15 | 0.06 | -0.11 | 0.16 | Yes | No |
| G561A | -0.10 | 0.05 | -0.36 | 0.06 | -0.05 | 0.07 | No | No |
| G561R | -0.20 | 0.04 | 0.00 | 0.04 | -0.16 | 0.05 | No | No |
| G561N | 0.20 | 0.16 | 1.09 | 0.14 | NA | NA | Yes | No |
| G561D | -0.43 | 0.11 | 0.54 | 0.08 | -0.03 | 0.27 | Yes | No |
| G561C | -0.19 | 0.08 | 0.03 | 0.08 | -0.26 | 0.27 | Yes | No |
| G561Q | -0.15 | 0.12 | 0.67 | 0.10 | -0.08 | 0.26 | Yes | No |
| G561E | 0.14 | 0.06 | -0.19 | 0.06 | -0.05 | 0.14 | Yes | No |
| G561H | 0.74 | 0.14 | 1.07 | 0.14 | NA | NA | Yes | No |
| G561L | -0.57 | 0.09 | -0.30 | 0.09 | -0.60 | 0.09 | No | No |
| G561K | 0.24 | 0.12 | 0.17 | 0.12 | NA | NA | Yes | No |
| G561M | -0.33 | 0.14 | 0.12 | 0.12 | NA | NA | Yes | No |
| G561P | -0.84 | 0.12 | -0.45 | 0.11 | 0.02 | 0.17 | Yes | No |
| G561S | 0.00 | 0.06 | 0.54 | 0.05 | -0.09 | 0.18 | Yes | No |
| G561* | -0.53 | 0.11 | -0.01 | 0.09 | NA | NA | Yes | No |
| G561T | 0.10 | 0.09 | -0.87 | 0.13 | -0.23 | 0.34 | Yes | No |
| G561W | -0.47 | 0.06 | -0.34 | 0.06 | -0.51 | 0.17 | No | No |
| G561V | -0.02 | 0.02 | -0.04 | 0.02 | 0.08 | 0.06 | Yes | No |
| L562A | -0.46 | 0.07 | -0.26 | 0.07 | -0.17 | 0.22 | No | No |
| L562R | -0.38 | 0.05 | 0.08 | 0.04 | -0.17 | 0.08 | Yes | No |
| L562D | -0.37 | 0.13 | -0.90 | 0.15 | -0.46 | 0.35 | No | No |
| L562C | 0.18 | 0.10 | -0.63 | 0.12 | 0.13 | 0.29 | Yes | No |
| L562Q | -0.43 | 0.09 | -0.20 | 0.08 | -0.07 | 0.17 | No | No |
| L562E | -0.32 | 0.07 | -0.62 | 0.08 | -0.29 | 0.18 | No | No |
| L562G | -0.75 | 0.05 | -0.60 | 0.05 | -0.36 | 0.08 | No | No |
| L562H | 0.23 | 0.12 | -0.50 | 0.15 | NA | NA | Yes | No |
| L562K | -0.69 | 0.12 | 0.32 | 0.09 | -0.53 | 0.29 | Yes | No |
| L562M | 0.19 | 0.06 | -0.26 | 0.07 | -0.04 | 0.12 | Yes | No |
| L562F | 0.48 | 0.14 | 0.79 | 0.13 | NA | NA | Yes | No |
| L562P | -0.10 | 0.06 | -0.05 | 0.06 | -0.26 | 0.09 | No | No |
| L562S | -0.65 | 0.10 | -0.27 | 0.09 | -0.04 | 0.26 | No | No |

| Mutant | Enrich. Score (1) | Stand. Error (1) | Enrich. Score (2) | Stand. Error (2) | Enrich. Score (3) | Stand. Error (3) | Any positive enrichment? | Consistent positive enrichment? |
|---|---|---|---|---|---|---|---|---|
| L562* | -1.29 | 0.14 | -1.10 | 0.13 | NA | NA | Yes | No |
| L562T | -1.14 | 0.15 | -1.09 | 0.15 | NA | NA | Yes | No |
| L562W | -0.37 | 0.07 | -0.38 | 0.07 | -0.45 | 0.18 | No | No |
| L562Y | -0.63 | 0.16 | -0.49 | 0.16 | NA | NA | Yes | No |
| L562V | -0.20 | 0.05 | -0.49 | 0.06 | -0.71 | 0.11 | No | No |
| Y563A | -1.58 | 0.09 | -1.18 | 0.08 | -1.03 | 0.07 | No | No |
| Y563R | -1.46 | 0.06 | -1.08 | 0.05 | -1.59 | 0.11 | No | No |
| Y563N | -0.16 | 0.08 | 0.04 | 0.07 | -0.30 | 0.16 | Yes | No |
| Y563D | -0.56 | 0.07 | -0.65 | 0.07 | -0.73 | 0.07 | No | No |
| Y563C | -0.49 | 0.06 | -0.50 | 0.06 | -0.32 | 0.09 | No | No |
| Y563Q | -0.48 | 0.10 | -0.52 | 0.10 | -0.93 | 0.25 | No | No |
| Y563E | -1.21 | 0.08 | 0.07 | 0.06 | -1.73 | 0.14 | Yes | No |
| Y563G | -1.13 | 0.04 | -1.64 | 0.05 | -1.26 | 0.03 | No | No |
| Y563H | -0.25 | 0.08 | -0.14 | 0.08 | -0.06 | 0.15 | No | No |
| Y563L | -1.95 | 0.12 | -1.69 | 0.11 | -1.15 | 0.19 | No | No |
| Y563F | 0.13 | 0.07 | 0.06 | 0.07 | -0.06 | 0.11 | Yes | No |
| Y563S | -0.91 | 0.07 | -0.95 | 0.07 | -0.96 | 0.08 | No | No |
| Y563* | -0.54 | 0.08 | -0.93 | 0.09 | -1.33 | 0.14 | No | No |
| Y563T | -1.67 | 0.15 | 0.09 | 0.08 | -0.51 | 0.22 | Yes | No |
| Y563W | -0.84 | 0.06 | -0.78 | 0.05 | -1.12 | 0.11 | No | No |
| Y563V | -1.32 | 0.08 | -1.12 | 0.07 | -1.13 | 0.17 | No | No |
| Y564A | -1.20 | 0.15 | -0.93 | 0.14 | NA | NA | Yes | No |
| Y564R | -1.37 | 0.10 | -1.99 | 0.13 | -1.19 | 0.19 | No | No |
| Y564N | -0.18 | 0.12 | 0.08 | 0.11 | -0.14 | 0.21 | Yes | No |
| Y564D | -0.05 | 0.06 | -0.60 | 0.07 | -0.25 | 0.10 | No | No |
| Y564C | 0.09 | 0.05 | -0.22 | 0.05 | -0.08 | 0.10 | Yes | No |
| Y564G | -1.96 | 0.11 | -1.74 | 0.10 | -1.32 | 0.19 | No | No |
| Y564H | -0.05 | 0.08 | -0.10 | 0.08 | 0.04 | 0.13 | Yes | No |
| Y564L | -0.24 | 0.10 | -1.01 | 0.13 | NA | NA | Yes | No |
| Y564F | -0.04 | 0.11 | 0.35 | 0.10 | NA | NA | Yes | No |
| Y564S | -0.47 | 0.09 | -0.36 | 0.08 | -0.35 | 0.20 | No | No |
| Y564* | -0.43 | 0.11 | -0.68 | 0.12 | NA | NA | Yes | No |
| Y564W | -0.37 | 0.10 | 0.03 | 0.09 | -0.52 | 0.29 | Yes | No |
| Y564V | -1.90 | 0.15 | -0.72 | 0.10 | NA | NA | Yes | No |
| L565A | -0.65 | 0.07 | -0.47 | 0.06 | -1.27 | 0.23 | No | No |
| L565R | -0.27 | 0.03 | -0.79 | 0.03 | -0.12 | 0.05 | No | No |
| L565C | -1.21 | 0.13 | -0.10 | 0.09 | -0.66 | 0.24 | No | No |
| L565Q | -0.36 | 0.08 | -0.84 | 0.09 | -0.76 | 0.15 | No | No |
| L565E | -1.93 | 0.12 | -1.02 | 0.09 | -1.55 | 0.19 | No | No |
| L565G | -2.36 | 0.08 | -1.62 | 0.06 | -1.50 | 0.10 | No | No |
| L565I | -0.07 | 0.13 | -0.42 | 0.14 | NA | NA | Yes | No |
| L565M | -0.20 | 0.07 | -0.26 | 0.07 | 0.03 | 0.10 | Yes | No |

| Mutant | Enrich. Score (1) | Stand. Error (1) | Enrich. Score (2) | Stand. Error (2) | Enrich. Score (3) | Stand. Error (3) | Any positive enrichment? | Consistent positive enrichment? |
|---|---|---|---|---|---|---|---|---|
| L565P | -0.60 | 0.07 | -0.92 | 0.08 | -0.67 | 0.13 | No | No |
| L565S | -1.07 | 0.09 | -0.75 | 0.08 | -1.13 | 0.08 | No | No |
| L565W | -1.64 | 0.10 | -2.31 | 0.13 | NA | NA | Yes | No |
| L565V | -0.57 | 0.06 | -0.48 | 0.05 | -1.19 | 0.13 | No | No |
| G566A | -0.36 | 0.08 | -0.39 | 0.08 | -0.57 | 0.21 | No | No |
| G566R | -1.37 | 0.09 | -1.97 | 0.12 | -1.83 | 0.11 | No | No |
| G566D | -0.67 | 0.11 | -1.03 | 0.12 | -0.62 | 0.18 | No | No |
| G566C | -0.08 | 0.11 | -0.83 | 0.13 | NA | NA | Yes | No |
| G566S | -0.14 | 0.06 | -0.40 | 0.07 | -0.18 | 0.11 | No | No |
| G566V | -0.52 | 0.07 | -0.99 | 0.08 | -0.68 | 0.10 | No | No |
| I567A | -1.35 | 0.11 | -1.01 | 0.09 | -1.13 | 0.07 | No | No |
| I567R | -1.78 | 0.09 | -0.11 | 0.05 | -1.44 | 0.11 | No | No |
| I567N | -0.05 | 0.07 | -0.10 | 0.07 | 0.15 | 0.10 | Yes | No |
| I567E | -1.64 | 0.12 | -1.70 | 0.13 | NA | NA | Yes | No |
| I567G | -1.23 | 0.06 | -1.14 | 0.06 | -1.70 | 0.09 | No | No |
| I567L | -0.67 | 0.08 | 0.29 | 0.06 | -0.48 | 0.13 | Yes | No |
| I567M | -0.51 | 0.09 | -0.82 | 0.10 | -0.88 | 0.10 | No | No |
| I567F | -0.43 | 0.12 | 0.00 | 0.11 | -0.48 | 0.19 | No | No |
| I567S | -0.56 | 0.07 | -0.67 | 0.07 | -0.82 | 0.12 | No | No |
| I567T | -0.15 | 0.05 | -0.27 | 0.06 | 0.13 | 0.09 | Yes | No |
| I567W | -1.85 | 0.12 | -2.17 | 0.14 | -1.22 | 0.13 | No | No |
| I567V | -0.54 | 0.05 | -0.26 | 0.05 | -0.68 | 0.08 | No | No |
| M568A | -0.52 | 0.06 | -0.34 | 0.06 | -0.04 | 0.11 | No | No |
| M568R | -0.30 | 0.04 | -0.82 | 0.05 | -0.20 | 0.07 | No | No |
| M568C | -0.33 | 0.10 | -0.78 | 0.11 | -0.18 | 0.28 | No | No |
| M568Q | -0.61 | 0.12 | -0.40 | 0.12 | NA | NA | Yes | No |
| M568E | -1.29 | 0.09 | -0.86 | 0.08 | -1.65 | 0.22 | No | No |
| M568G | -1.32 | 0.05 | -0.45 | 0.04 | -0.80 | 0.04 | No | No |
| M568H | 0.40 | 0.14 | -0.11 | 0.15 | NA | NA | Yes | No |
| M568I | 0.16 | 0.05 | -0.01 | 0.06 | 0.15 | 0.11 | Yes | No |
| M568L | -0.42 | 0.06 | -0.23 | 0.05 | -0.27 | 0.09 | No | No |
| M568K | -0.19 | 0.08 | -0.20 | 0.08 | -0.17 | 0.16 | No | No |
| M568P | -1.11 | 0.13 | -0.81 | 0.12 | NA | NA | Yes | No |
| M568S | 0.29 | 0.06 | -0.47 | 0.07 | -0.54 | 0.22 | Yes | No |
| M568T | -0.13 | 0.06 | -0.25 | 0.06 | -0.07 | 0.12 | No | No |
| M568W | -0.20 | 0.06 | 0.14 | 0.05 | -0.93 | 0.18 | Yes | No |
| M568V | -0.26 | 0.04 | -0.28 | 0.04 | 0.06 | 0.08 | Yes | No |
| P569D | 0.60 | 0.08 | 0.33 | 0.08 | 1.25 | 0.11 | Yes | Yes |
| P569A | -0.12 | 0.05 | -0.39 | 0.05 | 0.23 | 0.08 | Yes | No |
| P569R | -0.60 | 0.04 | -0.52 | 0.04 | -0.13 | 0.05 | No | No |
| P569N | -0.14 | 0.14 | -0.71 | 0.16 | NA | NA | Yes | No |
| P569C | -1.16 | 0.09 | -0.36 | 0.07 | 0.07 | 0.19 | Yes | No |

| Mutant | Enrich. Score (1) | Stand. Error (1) | Enrich. Score (2) | Stand. Error (2) | Enrich. Score (3) | Stand. Error (3) | Any positive enrichment? | Consistent positive enrichment? |
|---|---|---|---|---|---|---|---|---|
| P569Q | -0.26 | 0.09 | -0.13 | 0.09 | 0.40 | 0.21 | Yes | No |
| P569E | -0.07 | 0.07 | -0.16 | 0.07 | -0.11 | 0.22 | No | No |
| P569G | -0.54 | 0.03 | -0.49 | 0.03 | -0.65 | 0.07 | No | No |
| P569H | 0.12 | 0.09 | -0.25 | 0.10 | 0.16 | 0.17 | Yes | No |
| P569I | 0.03 | 0.13 | -0.32 | 0.14 | 0.10 | 0.31 | Yes | No |
| P569L | -0.47 | 0.05 | -0.21 | 0.04 | -0.30 | 0.11 | No | No |
| P569K | -0.35 | 0.12 | 0.36 | 0.10 | 0.23 | 0.31 | Yes | No |
| P569M | -0.98 | 0.11 | -0.54 | 0.10 | -0.28 | 0.12 | No | No |
| P569F | NA | NA | NA | NA | -0.67 | 0.31 | Yes | No |
| P569S | -0.07 | 0.05 | -0.24 | 0.05 | 0.02 | 0.11 | Yes | No |
| P569T | -0.38 | 0.07 | -0.20 | 0.07 | -0.06 | 0.15 | No | No |
| P569W | -0.74 | 0.06 | -1.07 | 0.07 | -1.18 | 0.14 | No | No |
| P569V | -0.34 | 0.04 | -0.82 | 0.05 | 0.15 | 0.14 | Yes | No |
| K570A | -0.95 | 0.06 | -0.28 | 0.05 | -1.70 | 0.16 | No | No |
| K570R | -0.47 | 0.03 | -0.56 | 0.04 | -0.39 | 0.05 | No | No |
| K570N | -0.30 | 0.11 | -0.73 | 0.12 | NA | NA | Yes | No |
| K570D | -1.38 | 0.12 | -1.42 | 0.13 | NA | NA | Yes | No |
| K570C | -1.71 | 0.11 | -1.70 | 0.11 | NA | NA | Yes | No |
| K570Q | -0.90 | 0.09 | -0.32 | 0.08 | -1.25 | 0.18 | No | No |
| K570E | -1.37 | 0.07 | -0.71 | 0.05 | -1.40 | 0.10 | No | No |
| K570G | -0.62 | 0.03 | -0.33 | 0.03 | -1.61 | 0.09 | No | No |
| K570L | -1.83 | 0.08 | -1.48 | 0.07 | -1.35 | 0.14 | No | No |
| K570M | -1.02 | 0.09 | -0.76 | 0.09 | -1.52 | 0.18 | No | No |
| K570P | -1.15 | 0.12 | -0.12 | 0.09 | NA | NA | Yes | No |
| K570S | -1.28 | 0.09 | -0.51 | 0.07 | -1.52 | 0.14 | No | No |
| K570* | -1.31 | 0.10 | -1.26 | 0.10 | -1.24 | 0.15 | No | No |
| K570T | -0.02 | 0.03 | 0.11 | 0.03 | -0.05 | 0.03 | Yes | No |
| K570W | -2.06 | 0.09 | -2.64 | 0.12 | -1.61 | 0.14 | No | No |
| K570V | -1.33 | 0.06 | -0.81 | 0.05 | -1.85 | 0.11 | No | No |
| Q571A | 0.64 | 0.07 | 0.39 | 0.08 | 1.09 | 0.23 | Yes | Yes |
| Q571P | 0.17 | 0.07 | 0.61 | 0.07 | 0.13 | 0.14 | Yes | Yes |
| Q571S | 0.25 | 0.09 | 0.20 | 0.09 | 0.89 | 0.23 | Yes | Yes |
| Q571T | 0.22 | 0.13 | 0.19 | 0.13 | 0.87 | 0.41 | Yes | Yes |
| Q571R | -0.03 | 0.04 | -0.43 | 0.05 | 0.19 | 0.10 | Yes | No |
| Q571C | -0.60 | 0.16 | 0.23 | 0.12 | -0.33 | 0.24 | Yes | No |
| Q571E | -0.22 | 0.05 | -0.40 | 0.06 | -0.17 | 0.05 | No | No |
| Q571G | 0.00 | 0.06 | -0.25 | 0.06 | -0.41 | 0.18 | No | No |
| Q571H | -0.23 | 0.11 | -0.65 | 0.12 | 0.06 | 0.24 | Yes | No |
| Q571L | -0.41 | 0.07 | -0.45 | 0.07 | -0.66 | 0.11 | No | No |
| Q571K | -0.47 | 0.16 | -0.33 | 0.15 | 0.08 | 0.31 | Yes | No |
| Q571* | -0.59 | 0.11 | -0.27 | 0.10 | -0.67 | 0.17 | No | No |
| Q571W | -0.09 | 0.08 | -0.80 | 0.09 | -0.51 | 0.24 | No | No |

| Mutant | Enrich. Score (1) | Stand. Error (1) | Enrich. Score (2) | Stand. Error (2) | Enrich. Score (3) | Stand. Error (3) | Any positive enrichment? | Consistent positive enrichment? |
|---|---|---|---|---|---|---|---|---|
| Q571V | -0.36 | 0.11 | -0.20 | 0.10 | -0.44 | 0.32 | No | No |
| K572E | 0.11 | 0.04 | 0.25 | 0.04 | 0.42 | 0.08 | Yes | Yes |
| K572A | -0.24 | 0.04 | 0.33 | 0.04 | -0.11 | 0.11 | Yes | No |
| K572R | -0.08 | 0.03 | -0.05 | 0.03 | 0.03 | 0.03 | Yes | No |
| K572N | -0.17 | 0.07 | 0.17 | 0.06 | 0.02 | 0.11 | Yes | No |
| K572D | -0.09 | 0.09 | 0.03 | 0.08 | 0.45 | 0.19 | Yes | No |
| K572C | 0.23 | 0.07 | -0.87 | 0.09 | -0.19 | 0.25 | Yes | No |
| K572Q | -0.21 | 0.06 | 0.11 | 0.06 | 0.37 | 0.16 | Yes | No |
| K572G | -0.17 | 0.03 | -0.08 | 0.03 | 0.42 | 0.03 | Yes | No |
| K572H | NA | NA | NA | NA | 0.11 | 0.33 | Yes | No |
| K572L | -0.11 | 0.05 | 0.16 | 0.05 | -0.32 | 0.15 | Yes | No |
| K572M | -0.71 | 0.08 | 0.02 | 0.06 | 0.21 | 0.06 | Yes | No |
| K572P | 0.09 | 0.06 | 0.91 | 0.06 | -0.88 | 0.23 | Yes | No |
| K572S | 0.30 | 0.05 | 0.01 | 0.05 | -0.29 | 0.15 | Yes | No |
| K572* | -1.34 | 0.08 | -0.86 | 0.07 | -0.86 | 0.08 | No | No |
| K572T | -0.04 | 0.04 | -0.09 | 0.04 | -0.24 | 0.07 | No | No |
| K572W | -0.46 | 0.05 | -0.47 | 0.05 | -0.68 | 0.14 | No | No |
| K572Y | -1.04 | 0.16 | -1.01 | 0.15 | NA | NA | Yes | No |
| K572V | -0.08 | 0.04 | -0.31 | 0.04 | -0.71 | 0.04 | No | No |
| G573A | 0.04 | 0.04 | -0.11 | 0.04 | -0.99 | 0.09 | Yes | No |
| G573R | -0.04 | 0.03 | -0.31 | 0.04 | -0.66 | 0.08 | No | No |
| G573N | 0.45 | 0.12 | -0.94 | 0.17 | -0.29 | 0.41 | Yes | No |
| G573D | -0.05 | 0.06 | -0.41 | 0.07 | -0.95 | 0.13 | No | No |
| G573C | -0.22 | 0.06 | -0.35 | 0.06 | -0.42 | 0.11 | No | No |
| G573Q | 0.40 | 0.07 | -0.29 | 0.08 | -0.43 | 0.26 | Yes | No |
| G573E | -0.09 | 0.05 | 0.36 | 0.05 | -0.50 | 0.08 | Yes | No |
| G573H | -0.77 | 0.12 | 0.37 | 0.09 | -0.51 | 0.30 | Yes | No |
| G573L | -0.04 | 0.05 | 0.07 | 0.05 | -0.43 | 0.05 | Yes | No |
| G573K | -1.43 | 0.13 | -0.29 | 0.09 | -0.32 | 0.25 | No | No |
| G573M | -0.32 | 0.10 | -0.32 | 0.09 | -0.28 | 0.26 | No | No |
| G573F | -0.45 | 0.14 | -0.19 | 0.12 | NA | NA | Yes | No |
| G573P | 0.16 | 0.06 | -0.38 | 0.06 | -0.10 | 0.21 | Yes | No |
| G573S | 0.11 | 0.04 | -0.42 | 0.05 | -0.55 | 0.10 | Yes | No |
| G573* | -1.18 | 0.12 | -1.27 | 0.12 | -0.75 | 0.28 | No | No |
| G573T | 0.02 | 0.08 | -0.53 | 0.09 | -0.62 | 0.08 | Yes | No |
| G573W | -0.08 | 0.05 | -0.60 | 0.05 | -0.67 | 0.09 | No | No |
| G573Y | 0.13 | 0.11 | -0.81 | 0.14 | -0.48 | 0.30 | Yes | No |
| G573V | -0.06 | 0.04 | -0.40 | 0.04 | -0.71 | 0.06 | No | No |
| R574A | -0.83 | 0.07 | -0.54 | 0.06 | -0.64 | 0.10 | No | No |
| R574N | -0.85 | 0.17 | -0.69 | 0.16 | NA | NA | Yes | No |
| R574D | -0.32 | 0.10 | -1.05 | 0.13 | NA | NA | Yes | No |
| R574C | 0.58 | 0.07 | 0.15 | 0.07 | -1.16 | 0.22 | Yes | No |

| Mutant | Enrich. Score (1) | Stand. Error (1) | Enrich. Score (2) | Stand. Error (2) | Enrich. Score (3) | Stand. Error (3) | Any positive enrichment? | Consistent positive enrichment? |
|---|---|---|---|---|---|---|---|---|
| R574Q | NA | NA | NA | NA | -1.08 | 0.26 | Yes | No |
| R574E | -0.53 | 0.08 | -0.38 | 0.07 | -1.34 | 0.15 | No | No |
| R574G | -0.21 | 0.03 | -0.27 | 0.03 | -0.60 | 0.07 | No | No |
| R574I | -0.50 | 0.11 | -0.47 | 0.11 | NA | NA | Yes | No |
| R574L | -0.36 | 0.07 | -0.25 | 0.07 | -0.78 | 0.18 | No | No |
| R574K | -0.33 | 0.08 | 0.42 | 0.06 | -0.33 | 0.17 | Yes | No |
| R574M | 0.51 | 0.07 | -0.36 | 0.08 | -0.64 | 0.07 | Yes | No |
| R574F | 0.06 | 0.12 | -0.99 | 0.16 | NA | NA | Yes | No |
| R574P | -0.38 | 0.13 | 0.11 | 0.11 | -0.72 | 0.23 | Yes | No |
| R574S | 0.12 | 0.04 | 0.02 | 0.04 | -1.04 | 0.03 | Yes | No |
| R574* | -0.34 | 0.07 | -0.51 | 0.07 | -0.84 | 0.09 | No | No |
| R574T | -0.65 | 0.09 | 0.35 | 0.07 | -0.83 | 0.16 | Yes | No |
| R574W | -0.10 | 0.05 | -0.10 | 0.05 | -0.73 | 0.06 | No | No |
| R574Y | -0.25 | 0.12 | 0.13 | 0.11 | NA | NA | Yes | No |
| R574V | 0.59 | 0.05 | -0.27 | 0.05 | -1.08 | 0.14 | Yes | No |
| Y575G | 0.53 | 0.04 | 0.21 | 0.04 | 0.32 | 0.07 | Yes | Yes |
| Y575M | 0.89 | 0.11 | 0.27 | 0.12 | 0.31 | 0.41 | Yes | Yes |
| Y575A | 0.55 | 0.05 | 0.01 | 0.06 | -0.07 | 0.18 | Yes | No |
| Y575R | 0.15 | 0.05 | -0.04 | 0.06 | -0.56 | 0.10 | Yes | No |
| Y575N | -0.07 | 0.10 | 0.34 | 0.09 | -0.21 | 0.10 | Yes | No |
| Y575D | -0.07 | 0.09 | 0.15 | 0.09 | -0.45 | 0.25 | Yes | No |
| Y575C | 0.20 | 0.06 | 0.17 | 0.06 | -0.26 | 0.09 | Yes | No |
| Y575Q | -0.22 | 0.13 | -0.32 | 0.13 | -0.16 | 0.30 | No | No |
| Y575E | 0.03 | 0.08 | -0.32 | 0.09 | -0.41 | 0.35 | Yes | No |
| Y575H | -0.24 | 0.08 | -0.29 | 0.08 | 0.23 | 0.13 | Yes | No |
| Y575I | 0.04 | 0.14 | -0.37 | 0.15 | NA | NA | Yes | No |
| Y575L | -0.05 | 0.07 | -0.43 | 0.08 | -0.22 | 0.23 | No | No |
| Y575K | 0.95 | 0.11 | 0.22 | 0.12 | NA | NA | Yes | No |
| Y575F | 0.14 | 0.08 | -0.45 | 0.09 | -0.16 | 0.12 | Yes | No |
| Y575P | -0.06 | 0.09 | -0.22 | 0.09 | -0.14 | 0.31 | No | No |
| Y575S | 0.02 | 0.06 | 0.01 | 0.06 | -0.07 | 0.09 | Yes | No |
| Y575* | -0.20 | 0.07 | -0.46 | 0.08 | -0.51 | 0.12 | No | No |
| Y575T | -0.55 | 0.10 | -0.40 | 0.09 | -0.14 | 0.30 | No | No |
| Y575W | -0.44 | 0.09 | 0.31 | 0.07 | -0.36 | 0.16 | Yes | No |
| Y575V | -0.10 | 0.07 | -0.35 | 0.07 | -0.29 | 0.24 | No | No |
| K576C | 0.27 | 0.07 | 0.25 | 0.07 | 0.10 | 0.26 | Yes | Yes |
| K576A | -0.05 | 0.05 | 0.16 | 0.05 | 0.27 | 0.06 | Yes | No |
| K576R | -0.31 | 0.03 | -0.11 | 0.03 | 0.05 | 0.07 | Yes | No |
| K576N | -0.28 | 0.08 | -0.47 | 0.08 | -0.11 | 0.15 | No | No |
| K576D | -0.01 | 0.08 | -0.22 | 0.09 | -1.04 | 0.26 | No | No |
| K576Q | -0.06 | 0.06 | 0.02 | 0.05 | 0.57 | 0.08 | Yes | No |
| K576E | -0.63 | 0.05 | -0.38 | 0.05 | -0.27 | 0.09 | No | No |

| Mutant | Enrich. Score (1) | Stand. Error (1) | Enrich. Score (2) | Stand. Error (2) | Enrich. Score (3) | Stand. Error (3) | Any positive enrichment? | Consistent positive enrichment? |
|---|---|---|---|---|---|---|---|---|
| K576G | -0.03 | 0.03 | -0.13 | 0.03 | 0.28 | 0.04 | Yes | No |
| K576H | -0.26 | 0.14 | -0.46 | 0.14 | NA | NA | Yes | No |
| K576I | 0.10 | 0.11 | -0.10 | 0.12 | 0.37 | 0.16 | Yes | No |
| K576L | -0.04 | 0.05 | 0.01 | 0.04 | 0.24 | 0.05 | Yes | No |
| K576M | 0.21 | 0.05 | -0.14 | 0.06 | 0.07 | 0.09 | Yes | No |
| K576F | -0.41 | 0.13 | -1.12 | 0.15 | 0.20 | 0.34 | Yes | No |
| K576P | -0.07 | 0.09 | -1.70 | 0.14 | -0.15 | 0.17 | No | No |
| K576S | -0.20 | 0.05 | -0.43 | 0.06 | 0.64 | 0.15 | Yes | No |
| K576* | -1.75 | 0.10 | -1.41 | 0.08 | -0.09 | 0.15 | No | No |
| K576T | -0.05 | 0.06 | 0.30 | 0.05 | 0.20 | 0.08 | Yes | No |
| K576W | -0.33 | 0.05 | -0.65 | 0.05 | -0.56 | 0.13 | No | No |
| K576Y | -1.23 | 0.16 | -0.48 | 0.12 | NA | NA | Yes | No |
| K576V | -0.36 | 0.04 | -0.69 | 0.05 | 0.38 | 0.07 | Yes | No |
| A577R | -0.12 | 0.03 | -0.60 | 0.04 | 0.88 | 0.06 | Yes | No |
| A577N | 0.11 | 0.09 | -0.85 | 0.11 | 0.34 | 0.13 | Yes | No |
| A577D | -0.06 | 0.05 | -0.11 | 0.05 | -0.37 | 0.13 | No | No |
| A577C | -0.24 | 0.06 | -0.02 | 0.06 | -0.39 | 0.20 | No | No |
| A577Q | -0.37 | 0.07 | 0.63 | 0.06 | 0.10 | 0.23 | Yes | No |
| A577E | -0.66 | 0.05 | -2.12 | 0.09 | -0.27 | 0.14 | No | No |
| A577G | 0.22 | 0.02 | -0.05 | 0.03 | 0.49 | 0.05 | Yes | No |
| A577H | 0.02 | 0.08 | -0.59 | 0.10 | 0.25 | 0.22 | Yes | No |
| A577I | -0.94 | 0.12 | -0.35 | 0.10 | NA | NA | Yes | No |
| A577L | -0.90 | 0.06 | -0.37 | 0.05 | -0.15 | 0.06 | No | No |
| A577K | -0.40 | 0.08 | -0.80 | 0.09 | 1.09 | 0.07 | Yes | No |
| A577M | -0.40 | 0.08 | -0.20 | 0.07 | -0.28 | 0.20 | No | No |
| A577F | -0.79 | 0.11 | -0.99 | 0.12 | -0.78 | 0.19 | No | No |
| A577P | -0.25 | 0.06 | -0.11 | 0.05 | -0.29 | 0.11 | No | No |
| A577S | -0.31 | 0.04 | -0.26 | 0.04 | 0.08 | 0.10 | Yes | No |
| A577* | -1.65 | 0.11 | -1.75 | 0.11 | NA | NA | Yes | No |
| A577T | -0.09 | 0.05 | -0.38 | 0.05 | -0.02 | 0.08 | No | No |
| A577W | -0.63 | 0.05 | -0.66 | 0.05 | -0.66 | 0.08 | No | No |
| A577Y | -0.22 | 0.09 | -0.20 | 0.09 | 0.05 | 0.32 | Yes | No |
| A577V | -0.06 | 0.03 | -0.28 | 0.04 | -0.42 | 0.09 | No | No |
| L578A | -0.22 | 0.03 | -0.43 | 0.03 | -0.20 | 0.07 | No | No |
| L578R | -0.11 | 0.02 | -0.49 | 0.02 | 0.04 | 0.03 | Yes | No |
| L578N | -0.35 | 0.11 | -0.09 | 0.10 | -0.47 | 0.23 | No | No |
| L578D | -0.09 | 0.06 | -0.41 | 0.06 | -0.92 | 0.07 | No | No |
| L578C | 0.05 | 0.04 | -0.34 | 0.05 | -0.03 | 0.10 | Yes | No |
| L578Q | 0.11 | 0.04 | -0.12 | 0.05 | 0.00 | 0.10 | Yes | No |
| L578E | -0.33 | 0.04 | -0.53 | 0.04 | -0.77 | 0.12 | No | No |
| L578G | -0.26 | 0.02 | -0.45 | 0.02 | -0.29 | 0.02 | No | No |
| L578H | -0.27 | 0.07 | 0.10 | 0.06 | 0.03 | 0.14 | Yes | No |

| Mutant | Enrich. Score (1) | Stand. Error (1) | Enrich. Score (2) | Stand. Error (2) | Enrich. Score (3) | Stand. Error (3) | Any positive enrichment? | Consistent positive enrichment? |
|---|---|---|---|---|---|---|---|---|
| L578I | -0.28 | 0.09 | 0.32 | 0.08 | 0.22 | 0.23 | Yes | No |
| L578K | -0.62 | 0.07 | -1.21 | 0.09 | 0.50 | 0.20 | Yes | No |
| L578M | -0.12 | 0.03 | -0.21 | 0.03 | -0.03 | 0.05 | No | No |
| L578F | 0.36 | 0.06 | 0.21 | 0.06 | -0.12 | 0.14 | Yes | No |
| L578P | -0.62 | 0.05 | 0.03 | 0.04 | -0.31 | 0.06 | Yes | No |
| L578S | -0.37 | 0.04 | -0.33 | 0.04 | -0.08 | 0.09 | No | No |
| L578* | -1.90 | 0.09 | -1.28 | 0.07 | -1.24 | 0.09 | No | No |
| L578T | -0.29 | 0.06 | -0.06 | 0.05 | 0.26 | 0.06 | Yes | No |
| L578W | -0.37 | 0.03 | -0.41 | 0.03 | -0.08 | 0.04 | No | No |
| L578Y | 0.36 | 0.07 | -0.21 | 0.07 | -0.24 | 0.07 | Yes | No |
| L578V | -0.19 | 0.03 | -0.28 | 0.03 | 0.01 | 0.04 | Yes | No |
| S579T | 0.17 | 0.04 | 0.33 | 0.04 | 0.01 | 0.06 | Yes | Yes |
| S579V | 0.04 | 0.03 | 0.02 | 0.03 | 0.05 | 0.07 | Yes | Yes |
| S579A | -0.06 | 0.03 | 0.06 | 0.02 | 0.08 | 0.03 | Yes | No |
| S579R | 0.04 | 0.03 | -0.11 | 0.03 | -0.15 | 0.05 | Yes | No |
| S579N | -0.19 | 0.07 | -0.45 | 0.08 | -0.39 | 0.23 | No | No |
| S579D | -0.39 | 0.06 | -0.43 | 0.06 | 0.03 | 0.06 | Yes | No |
| S579C | 0.02 | 0.03 | 0.07 | 0.03 | -0.02 | 0.05 | Yes | No |
| S579Q | -0.19 | 0.07 | -0.66 | 0.08 | 0.30 | 0.20 | Yes | No |
| S579E | -0.10 | 0.04 | -0.54 | 0.05 | -0.15 | 0.05 | No | No |
| S579G | -0.25 | 0.03 | -0.12 | 0.02 | 0.11 | 0.05 | Yes | No |
| S579H | 0.09 | 0.08 | -0.15 | 0.08 | -0.18 | 0.12 | Yes | No |
| S579I | -0.05 | 0.06 | 0.25 | 0.06 | 0.04 | 0.15 | Yes | No |
| S579L | -0.65 | 0.04 | -0.32 | 0.04 | 0.11 | 0.05 | Yes | No |
| S579K | -0.15 | 0.06 | -0.55 | 0.07 | 0.13 | 0.22 | Yes | No |
| S579M | -0.18 | 0.06 | 0.05 | 0.05 | 0.28 | 0.19 | Yes | No |
| S579F | 0.27 | 0.04 | 0.16 | 0.04 | -0.08 | 0.07 | Yes | No |
| S579P | -0.19 | 0.05 | -0.75 | 0.05 | -0.05 | 0.10 | No | No |
| S579* | -1.34 | 0.08 | -1.06 | 0.07 | -1.30 | 0.11 | No | No |
| S579W | -0.09 | 0.04 | -0.35 | 0.04 | -0.37 | 0.06 | No | No |
| S579Y | -0.06 | 0.05 | -0.21 | 0.05 | -0.36 | 0.04 | No | No |
| F580A | -0.80 | 0.08 | -0.25 | 0.07 | -1.44 | 0.19 | No | No |
| F580R | -1.58 | 0.09 | -1.48 | 0.08 | -1.26 | 0.19 | No | No |
| F580C | -0.22 | 0.09 | -0.47 | 0.10 | -0.11 | 0.18 | No | No |
| F580E | -0.96 | 0.12 | -0.21 | 0.09 | NA | NA | Yes | No |
| F580G | -0.91 | 0.05 | -1.05 | 0.05 | -1.21 | 0.04 | No | No |
| F580I | -0.14 | 0.09 | -0.06 | 0.09 | -0.17 | 0.28 | No | No |
| F580L | -0.11 | 0.05 | -0.28 | 0.05 | 0.01 | 0.09 | Yes | No |
| F580M | 0.31 | 0.12 | -0.37 | 0.14 | NA | NA | Yes | No |
| F580P | NA | NA | NA | NA | -0.75 | 0.28 | Yes | No |
| F580S | -0.22 | 0.07 | -0.70 | 0.07 | -0.67 | 0.10 | No | No |
| F580W | -1.14 | 0.10 | 0.30 | 0.07 | 0.67 | 0.24 | Yes | No |

| Mutant | Enrich. Score (1) | Stand. Error (1) | Enrich. Score (2) | Stand. Error (2) | Enrich. Score (3) | Stand. Error (3) | Any positive enrichment? | Consistent positive enrichment? |
|---|---|---|---|---|---|---|---|---|
| F580Y | 0.39 | 0.11 | -0.45 | 0.14 | -0.09 | 0.23 | Yes | No |
| F580V | 0.18 | 0.06 | -0.33 | 0.06 | -0.52 | 0.13 | Yes | No |
| E581A | -0.08 | 0.03 | 0.16 | 0.03 | -0.13 | 0.06 | Yes | No |
| E581R | -0.31 | 0.03 | -0.14 | 0.03 | -0.36 | 0.04 | No | No |
| E581N | -0.14 | 0.15 | 0.56 | 0.13 | NA | NA | Yes | No |
| E581D | 0.04 | 0.06 | 0.25 | 0.06 | -0.21 | 0.09 | Yes | No |
| E581C | 0.12 | 0.07 | 0.54 | 0.06 | -0.12 | 0.15 | Yes | No |
| E581Q | 0.01 | 0.04 | 0.09 | 0.04 | -0.12 | 0.06 | Yes | No |
| E581G | -0.15 | 0.02 | -0.05 | 0.02 | -0.03 | 0.03 | No | No |
| E581H | -0.31 | 0.12 | 1.00 | 0.10 | -0.67 | 0.35 | Yes | No |
| E581I | -0.12 | 0.14 | 0.03 | 0.13 | 0.40 | 0.44 | Yes | No |
| E581L | 0.09 | 0.04 | -0.12 | 0.04 | 0.29 | 0.12 | Yes | No |
| E581K | -0.10 | 0.05 | -0.02 | 0.05 | -0.33 | 0.07 | No | No |
| E581M | -0.05 | 0.08 | -0.79 | 0.09 | 0.12 | 0.13 | Yes | No |
| E581F | -0.32 | 0.11 | -0.09 | 0.10 | -0.40 | 0.30 | No | No |
| E581P | -0.49 | 0.07 | -0.09 | 0.06 | -0.25 | 0.13 | No | No |
| E581S | 0.00 | 0.05 | -1.01 | 0.06 | -0.11 | 0.06 | Yes | No |
| E581* | -1.00 | 0.07 | -0.93 | 0.07 | -0.92 | 0.13 | No | No |
| E581T | -0.23 | 0.07 | -0.29 | 0.07 | 0.06 | 0.09 | Yes | No |
| E581W | 0.25 | 0.04 | -0.31 | 0.04 | 0.04 | 0.05 | Yes | No |
| E581Y | NA | NA | NA | NA | 0.25 | 0.28 | Yes | No |
| E581V | -0.18 | 0.04 | 0.31 | 0.03 | 0.26 | 0.10 | Yes | No |
| P582A | -0.46 | 0.07 | -0.64 | 0.07 | -0.60 | 0.13 | No | No |
| P582R | 0.24 | 0.05 | -0.24 | 0.06 | -0.48 | 0.17 | Yes | No |
| P582N | -0.02 | 0.05 | -0.24 | 0.05 | -0.22 | 0.11 | No | No |
| P582D | -0.41 | 0.18 | -0.64 | 0.18 | NA | NA | Yes | No |
| P582C | 0.14 | 0.11 | -0.07 | 0.12 | 0.17 | 0.64 | Yes | No |
| P582Q | -0.74 | 0.13 | -0.13 | 0.11 | -0.07 | 0.25 | No | No |
| P582G | -0.10 | 0.06 | -0.80 | 0.07 | -0.50 | 0.18 | No | No |
| P582H | -0.03 | 0.02 | -0.15 | 0.02 | -0.12 | 0.04 | No | No |
| P582L | -0.14 | 0.07 | -0.96 | 0.08 | -0.26 | 0.13 | No | No |
| P582K | -0.33 | 0.19 | 0.97 | 0.15 | NA | NA | Yes | No |
| P582F | NA | NA | NA | NA | 0.02 | 0.55 | Yes | No |
| P582S | 0.19 | 0.06 | 0.48 | 0.05 | -1.33 | 0.16 | Yes | No |
| P582T | -0.13 | 0.03 | -0.19 | 0.03 | -0.48 | 0.06 | No | No |
| P582W | -1.46 | 0.15 | -0.73 | 0.11 | -0.12 | 0.35 | No | No |
| P582V | -0.90 | 0.10 | -0.27 | 0.08 | -0.81 | 0.09 | No | No |
| T583I | 0.04 | 0.08 | 0.11 | 0.07 | 0.07 | 0.17 | Yes | Yes |
| T583A | 0.02 | 0.04 | -0.22 | 0.04 | -0.17 | 0.08 | Yes | No |
| T583R | 0.12 | 0.05 | -0.31 | 0.05 | -0.04 | 0.09 | Yes | No |
| T583N | 0.00 | 0.06 | 0.01 | 0.06 | -0.20 | 0.09 | Yes | No |
| T583D | 0.23 | 0.12 | -0.96 | 0.16 | NA | NA | Yes | No |

| Mutant | Enrich. Score (1) | Stand. Error (1) | Enrich. Score (2) | Stand. Error (2) | Enrich. Score (3) | Stand. Error (3) | Any positive enrichment? | Consistent positive enrichment? |
|---|---|---|---|---|---|---|---|---|
| T583C | 0.67 | 0.09 | -0.82 | 0.12 | -0.67 | 0.27 | Yes | No |
| T583Q | NA | NA | NA | NA | -0.28 | 0.36 | Yes | No |
| T583E | -0.62 | 0.10 | 0.01 | 0.09 | -0.72 | 0.28 | Yes | No |
| T583G | -0.17 | 0.05 | -0.35 | 0.05 | 0.16 | 0.06 | Yes | No |
| T583L | -0.09 | 0.06 | -0.72 | 0.07 | -0.24 | 0.22 | No | No |
| T583K | NA | NA | NA | NA | -0.15 | 0.44 | Yes | No |
| T583M | -0.72 | 0.13 | -0.89 | 0.14 | -0.12 | 0.32 | No | No |
| T583F | -0.41 | 0.13 | -0.83 | 0.15 | -0.13 | 0.36 | No | No |
| T583P | -0.14 | 0.08 | -0.64 | 0.08 | -0.37 | 0.14 | No | No |
| T583S | 0.18 | 0.05 | 0.11 | 0.05 | -0.34 | 0.07 | Yes | No |
| T583W | -0.31 | 0.07 | -0.54 | 0.08 | -0.09 | 0.08 | No | No |
| T583V | 0.01 | 0.06 | -0.05 | 0.06 | 0.15 | 0.22 | Yes | No |
| E584H | 0.09 | 0.07 | 0.22 | 0.07 | 0.17 | 0.14 | Yes | Yes |
| E584V | 0.10 | 0.03 | 0.06 | 0.03 | 0.12 | 0.04 | Yes | Yes |
| E584A | -0.01 | 0.03 | 0.09 | 0.03 | 0.10 | 0.06 | Yes | No |
| E584R | -0.23 | 0.03 | -0.12 | 0.03 | -0.10 | 0.05 | No | No |
| E584N | -0.50 | 0.09 | -0.38 | 0.08 | -0.11 | 0.20 | No | No |
| E584D | 0.46 | 0.04 | 0.51 | 0.04 | -0.02 | 0.08 | Yes | No |
| E584C | -0.03 | 0.05 | 0.09 | 0.05 | 0.13 | 0.07 | Yes | No |
| E584Q | 0.09 | 0.07 | -0.88 | 0.08 | -0.09 | 0.10 | Yes | No |
| E584G | -0.02 | 0.02 | 0.06 | 0.02 | 0.16 | 0.04 | Yes | No |
| E584I | 0.32 | 0.07 | -0.34 | 0.08 | -0.03 | 0.20 | Yes | No |
| E584L | -0.27 | 0.04 | 0.00 | 0.04 | -0.06 | 0.10 | No | No |
| E584K | -0.29 | 0.06 | -0.78 | 0.07 | 0.39 | 0.09 | Yes | No |
| E584M | -0.17 | 0.07 | -0.68 | 0.08 | 0.34 | 0.13 | Yes | No |
| E584F | -0.11 | 0.08 | -0.41 | 0.09 | 0.27 | 0.19 | Yes | No |
| E584P | 0.12 | 0.05 | -0.13 | 0.06 | -0.24 | 0.17 | Yes | No |
| E584S | -0.44 | 0.04 | 0.09 | 0.04 | 0.26 | 0.09 | Yes | No |
| E584* | -1.22 | 0.09 | -1.26 | 0.08 | -1.15 | 0.13 | No | No |
| E584T | -0.03 | 0.05 | -0.03 | 0.05 | 0.17 | 0.15 | Yes | No |
| E584W | -0.73 | 0.06 | -0.52 | 0.05 | -0.32 | 0.07 | No | No |
| E584Y | -0.13 | 0.07 | 0.55 | 0.06 | 0.05 | 0.25 | Yes | No |
| K585R | 0.07 | 0.03 | 0.32 | 0.03 | 0.06 | 0.05 | Yes | Yes |
| K585F | 0.51 | 0.09 | 0.04 | 0.09 | 0.61 | 0.36 | Yes | Yes |
| K585A | 0.21 | 0.04 | -0.23 | 0.05 | 0.16 | 0.13 | Yes | No |
| K585N | -0.13 | 0.09 | 0.18 | 0.08 | -0.67 | 0.12 | Yes | No |
| K585D | -0.05 | 0.07 | -0.08 | 0.07 | -0.05 | 0.23 | No | No |
| K585C | -0.25 | 0.07 | -0.61 | 0.08 | -0.11 | 0.29 | No | No |
| K585Q | 0.07 | 0.06 | 0.41 | 0.06 | -0.09 | 0.08 | Yes | No |
| K585E | -0.33 | 0.05 | -0.44 | 0.05 | 0.10 | 0.12 | Yes | No |
| K585G | -0.18 | 0.03 | -0.04 | 0.03 | 0.16 | 0.04 | Yes | No |
| K585H | 0.12 | 0.11 | -0.60 | 0.13 | 0.28 | 0.14 | Yes | No |

| Mutant | Enrich. Score (1) | Stand. Error (1) | Enrich. Score (2) | Stand. Error (2) | Enrich. Score (3) | Stand. Error (3) | Any positive enrichment? | Consistent positive enrichment? |
|---|---|---|---|---|---|---|---|---|
| K585I | -1.45 | 0.14 | 0.35 | 0.08 | 0.11 | 0.25 | Yes | No |
| K585L | -0.10 | 0.04 | -0.06 | 0.04 | 0.27 | 0.13 | Yes | No |
| K585M | -0.25 | 0.07 | -0.05 | 0.06 | 0.21 | 0.17 | Yes | No |
| K585P | 0.20 | 0.06 | -0.04 | 0.07 | 0.15 | 0.21 | Yes | No |
| K585S | -0.17 | 0.05 | 0.24 | 0.04 | 0.20 | 0.11 | Yes | No |
| K585* | -0.91 | 0.07 | -0.60 | 0.06 | -0.61 | 0.11 | No | No |
| K585T | 0.08 | 0.05 | -0.30 | 0.05 | 0.05 | 0.07 | Yes | No |
| K585W | -0.21 | 0.05 | -0.15 | 0.05 | 0.18 | 0.16 | Yes | No |
| K585Y | 0.18 | 0.10 | -0.92 | 0.13 | 0.07 | 0.40 | Yes | No |
| K585V | -0.16 | 0.04 | -0.68 | 0.04 | 0.37 | 0.06 | Yes | No |
| T586A | -0.30 | 0.05 | -0.02 | 0.04 | -0.01 | 0.11 | No | No |
| T586R | -0.56 | 0.05 | -0.06 | 0.04 | -0.20 | 0.14 | No | No |
| T586N | -0.07 | 0.05 | 0.15 | 0.05 | -0.02 | 0.07 | Yes | No |
| T586D | -0.41 | 0.12 | 1.10 | 0.09 | 0.41 | 0.30 | Yes | No |
| T586C | -0.60 | 0.11 | -0.45 | 0.10 | 0.10 | 0.29 | Yes | No |
| T586Q | -0.65 | 0.14 | 0.28 | 0.11 | NA | NA | Yes | No |
| T586E | -0.29 | 0.09 | 0.04 | 0.08 | 0.16 | 0.37 | Yes | No |
| T586G | -0.21 | 0.04 | 0.22 | 0.03 | -0.07 | 0.09 | Yes | No |
| T586I | -0.77 | 0.11 | 0.90 | 0.07 | -0.48 | 0.19 | Yes | No |
| T586L | -0.06 | 0.06 | -0.85 | 0.07 | 0.01 | 0.18 | Yes | No |
| T586K | -0.06 | 0.12 | 0.80 | 0.10 | -0.12 | 0.13 | Yes | No |
| T586M | -0.62 | 0.11 | -1.06 | 0.13 | 0.22 | 0.34 | Yes | No |
| T586F | 0.21 | 0.13 | -0.21 | 0.14 | 0.02 | 0.54 | Yes | No |
| T586P | 0.38 | 0.06 | -0.09 | 0.06 | 0.22 | 0.12 | Yes | No |
| T586S | -0.22 | 0.05 | -0.08 | 0.05 | 0.01 | 0.08 | Yes | No |
| T586W | -0.48 | 0.07 | -0.61 | 0.07 | -0.29 | 0.24 | No | No |
| T586Y | NA | NA | NA | NA | 0.24 | 0.26 | Yes | No |
| T586V | -0.97 | 0.07 | -0.13 | 0.05 | 0.13 | 0.17 | Yes | No |
| S587A | NA | NA | NA | NA | 0.45 | 0.32 | Yes | No |
| S587R | 0.15 | 0.08 | -0.61 | 0.09 | -0.34 | 0.15 | Yes | No |
| S587N | -0.30 | 0.13 | -0.31 | 0.13 | -0.26 | 0.18 | No | No |
| S587C | 0.01 | 0.15 | 0.00 | 0.14 | NA | NA | Yes | No |
| S587E | 0.33 | 0.16 | -0.40 | 0.19 | NA | NA | Yes | No |
| S587G | -0.32 | 0.06 | -0.81 | 0.07 | -0.21 | 0.06 | No | No |
| S587L | 0.21 | 0.14 | 0.27 | 0.13 | NA | NA | Yes | No |
| S587T | 0.80 | 0.11 | -0.41 | 0.14 | -0.13 | 0.23 | Yes | No |
| S587V | 0.20 | 0.11 | -0.25 | 0.12 | -0.04 | 0.12 | Yes | No |
| E588A | -0.01 | 0.05 | 0.25 | 0.05 | 0.17 | 0.10 | Yes | No |
| E588R | -0.39 | 0.05 | -0.61 | 0.05 | -0.31 | 0.07 | No | No |
| E588D | 0.00 | 0.08 | -0.12 | 0.08 | -0.55 | 0.13 | Yes | No |
| E588C | -0.64 | 0.11 | -0.35 | 0.10 | 0.00 | 0.10 | No | No |
| E588Q | 0.11 | 0.09 | -0.25 | 0.09 | -0.08 | 0.13 | Yes | No |

| Mutant | Enrich. Score (1) | Stand. Error (1) | Enrich. Score (2) | Stand. Error (2) | Enrich. Score (3) | Stand. Error (3) | Any positive enrichment? | Consistent positive enrichment? |
|---|---|---|---|---|---|---|---|---|
| E588G | -0.16 | 0.04 | -0.19 | 0.04 | -0.34 | 0.04 | No | No |
| E588H | -0.35 | 0.17 | -0.26 | 0.16 | NA | NA | Yes | No |
| E588L | -0.31 | 0.07 | -0.29 | 0.07 | 0.41 | 0.12 | Yes | No |
| E588K | 0.18 | 0.07 | 0.13 | 0.07 | -0.25 | 0.15 | Yes | No |
| E588M | -0.50 | 0.12 | -0.10 | 0.11 | 0.54 | 0.12 | Yes | No |
| E588F | -0.23 | 0.15 | 0.13 | 0.14 | NA | NA | Yes | No |
| E588P | -0.04 | 0.10 | 0.06 | 0.09 | 0.52 | 0.19 | Yes | No |
| E588S | -0.03 | 0.07 | -0.34 | 0.08 | -0.47 | 0.08 | No | No |
| E588* | -1.05 | 0.11 | -1.06 | 0.11 | -1.02 | 0.15 | No | No |
| E588T | 0.32 | 0.09 | -1.53 | 0.15 | NA | NA | Yes | No |
| E588W | -0.02 | 0.07 | 0.03 | 0.07 | -0.01 | 0.19 | Yes | No |
| E588Y | -0.11 | 0.17 | 0.93 | 0.14 | NA | NA | Yes | No |
| E588V | -0.70 | 0.06 | -0.19 | 0.05 | 0.07 | 0.08 | Yes | No |
| G589A | -0.44 | 0.05 | -0.09 | 0.04 | -0.52 | 0.14 | No | No |
| G589R | -0.21 | 0.04 | -0.73 | 0.04 | -0.69 | 0.07 | No | No |
| G589D | -0.29 | 0.08 | -0.88 | 0.10 | -0.70 | 0.17 | No | No |
| G589C | -0.14 | 0.04 | -0.12 | 0.04 | -0.59 | 0.07 | No | No |
| G589Q | NA | NA | NA | NA | -0.13 | 0.27 | Yes | No |
| G589E | -0.39 | 0.06 | -1.47 | 0.08 | -0.59 | 0.24 | No | No |
| G589L | 0.07 | 0.06 | -1.02 | 0.08 | -1.07 | 0.20 | Yes | No |
| G589M | -0.45 | 0.12 | -1.01 | 0.14 | NA | NA | Yes | No |
| G589P | -0.34 | 0.08 | -2.17 | 0.15 | -1.08 | 0.12 | No | No |
| G589S | -0.13 | 0.04 | -0.30 | 0.04 | -0.54 | 0.10 | No | No |
| G589T | -0.52 | 0.11 | -0.51 | 0.10 | -1.12 | 0.28 | No | No |
| G589W | -0.62 | 0.06 | -0.77 | 0.07 | -0.26 | 0.13 | No | No |
| G589Y | NA | NA | NA | NA | -0.01 | 0.41 | Yes | No |
| G589V | -0.65 | 0.05 | -0.97 | 0.06 | -0.22 | 0.13 | No | No |
| F590A | -0.43 | 0.05 | -1.38 | 0.07 | -1.07 | 0.15 | No | No |
| F590R | -0.22 | 0.05 | -0.83 | 0.05 | -0.62 | 0.15 | No | No |
| F590N | -0.95 | 0.17 | -0.65 | 0.15 | NA | NA | Yes | No |
| F590C | -0.49 | 0.08 | -0.73 | 0.08 | -1.06 | 0.20 | No | No |
| F590E | -1.00 | 0.09 | -1.26 | 0.10 | -0.44 | 0.26 | No | No |
| F590G | -1.05 | 0.04 | -1.44 | 0.05 | -1.47 | 0.09 | No | No |
| F590I | 0.01 | 0.09 | 0.10 | 0.08 | NA | NA | Yes | No |
| F590L | -0.02 | 0.04 | -0.21 | 0.04 | -0.51 | 0.06 | No | No |
| F590M | -0.27 | 0.12 | -0.41 | 0.12 | NA | NA | Yes | No |
| F590P | -1.08 | 0.10 | -1.31 | 0.10 | -1.37 | 0.17 | No | No |
| F590S | -0.03 | 0.05 | -0.29 | 0.05 | -0.61 | 0.07 | No | No |
| F590T | -1.50 | 0.15 | -1.08 | 0.12 | NA | NA | Yes | No |
| F590W | 0.04 | 0.07 | -0.11 | 0.07 | -0.87 | 0.26 | Yes | No |
| F590Y | 0.07 | 0.06 | -0.18 | 0.07 | -0.19 | 0.17 | Yes | No |
| F590V | -1.03 | 0.06 | -0.97 | 0.06 | -0.98 | 0.14 | No | No |

| Mutant | Enrich. Score (1) | Stand. Error (1) | Enrich. Score (2) | Stand. Error (2) | Enrich. Score (3) | Stand. Error (3) | Any positive enrichment? | Consistent positive enrichment? |
|---|---|---|---|---|---|---|---|---|
| D591A | 0.20 | 0.04 | 0.07 | 0.04 | -0.54 | 0.05 | Yes | No |
| D591R | -0.94 | 0.05 | -1.06 | 0.05 | -0.45 | 0.13 | No | No |
| D591N | -0.49 | 0.10 | -0.61 | 0.10 | -0.54 | 0.14 | No | No |
| D591C | -0.66 | 0.10 | -0.68 | 0.09 | -0.47 | 0.23 | No | No |
| D591Q | -0.34 | 0.10 | 0.11 | 0.09 | -0.15 | 0.38 | Yes | No |
| D591E | -0.43 | 0.05 | -0.39 | 0.05 | -0.84 | 0.14 | No | No |
| D591G | -0.62 | 0.03 | -0.81 | 0.03 | -0.59 | 0.03 | No | No |
| D591H | -1.19 | 0.16 | -0.84 | 0.14 | NA | NA | Yes | No |
| D591L | -0.17 | 0.06 | -0.59 | 0.07 | -0.99 | 0.20 | No | No |
| D591K | -0.51 | 0.12 | -0.27 | 0.11 | NA | NA | Yes | No |
| D591M | -0.90 | 0.12 | -0.93 | 0.12 | -0.36 | 0.27 | No | No |
| D591S | -0.69 | 0.07 | -1.41 | 0.09 | -0.67 | 0.17 | No | No |
| D591T | -0.15 | 0.08 | -0.93 | 0.10 | -1.04 | 0.23 | No | No |
| D591W | -1.02 | 0.08 | -0.91 | 0.07 | -0.42 | 0.16 | No | No |
| D591Y | 0.08 | 0.10 | -0.62 | 0.12 | -0.50 | 0.17 | Yes | No |
| D591V | -0.76 | 0.05 | -1.11 | 0.05 | -1.12 | 0.11 | No | No |
| K592A | -1.60 | 0.09 | -0.60 | 0.06 | -1.42 | 0.15 | No | No |
| K592R | -0.98 | 0.05 | -0.77 | 0.04 | -1.03 | 0.05 | No | No |
| K592N | -0.12 | 0.10 | 0.07 | 0.10 | -0.91 | 0.19 | Yes | No |
| K592Q | -0.52 | 0.07 | -0.77 | 0.08 | -0.30 | 0.10 | No | No |
| K592E | -0.52 | 0.07 | -0.76 | 0.07 | -1.22 | 0.10 | No | No |
| K592G | -1.76 | 0.06 | -1.45 | 0.05 | -1.64 | 0.08 | No | No |
| K592L | -1.72 | 0.08 | -1.52 | 0.08 | -1.24 | 0.13 | No | No |
| K592M | -0.70 | 0.07 | -0.58 | 0.07 | -0.68 | 0.07 | No | No |
| K592P | -1.70 | 0.14 | -1.63 | 0.13 | NA | NA | Yes | No |
| K592S | -1.67 | 0.10 | -1.56 | 0.10 | NA | NA | Yes | No |
| K592* | 0.00 | 0.08 | -1.63 | 0.13 | -0.91 | 0.18 | Yes | No |
| K592T | -1.38 | 0.11 | -0.98 | 0.09 | NA | NA | Yes | No |
| K592W | -1.60 | 0.10 | -1.14 | 0.08 | -0.21 | 0.20 | No | No |
| K592V | -1.60 | 0.06 | -1.14 | 0.05 | -1.90 | 0.08 | No | No |
| M593A | -1.94 | 0.07 | -1.00 | 0.05 | -1.73 | 0.06 | No | No |
| M593R | -0.79 | 0.03 | -0.81 | 0.03 | -0.81 | 0.03 | No | No |
| M593N | -1.58 | 0.13 | -1.89 | 0.15 | NA | NA | Yes | No |
| M593D | -2.12 | 0.13 | -1.32 | 0.09 | -1.77 | 0.18 | No | No |
| M593C | -0.95 | 0.07 | -0.04 | 0.06 | -1.27 | 0.10 | No | No |
| M593Q | NA | NA | NA | NA | -0.83 | 0.19 | Yes | No |
| M593E | -2.30 | 0.10 | -2.14 | 0.09 | -1.55 | 0.14 | No | No |
| M593G | -1.83 | 0.04 | -1.88 | 0.04 | -1.09 | 0.07 | No | No |
| M593I | -0.83 | 0.07 | -1.05 | 0.08 | -1.17 | 0.12 | No | No |
| M593L | -0.10 | 0.03 | -0.33 | 0.03 | -0.52 | 0.06 | No | No |
| M593K | -1.64 | 0.09 | -1.56 | 0.08 | -1.09 | 0.05 | No | No |
| M593F | -1.98 | 0.12 | -0.83 | 0.08 | -1.61 | 0.12 | No | No |

| Mutant | Enrich. Score (1) | Stand. Error (1) | Enrich. Score (2) | Stand. Error (2) | Enrich. Score (3) | Stand. Error (3) | Any positive enrichment? | Consistent positive enrichment? |
|---|---|---|---|---|---|---|---|---|
| M593P | -1.56 | 0.10 | -2.23 | 0.12 | -0.38 | 0.12 | No | No |
| M593S | -1.58 | 0.06 | -1.88 | 0.07 | -1.33 | 0.11 | No | No |
| M593* | -2.27 | 0.12 | -2.28 | 0.12 | -1.55 | 0.18 | No | No |
| M593T | -1.01 | 0.06 | -0.79 | 0.05 | -0.64 | 0.10 | No | No |
| M593W | -0.92 | 0.05 | -1.57 | 0.07 | -2.41 | 0.16 | No | No |
| M593V | -0.56 | 0.03 | -1.41 | 0.04 | -1.07 | 0.07 | No | No |
| Y594A | -0.40 | 0.04 | -1.29 | 0.05 | -1.34 | 0.10 | No | No |
| Y594R | -0.02 | 0.03 | -0.18 | 0.03 | -1.14 | 0.08 | No | No |
| Y594N | -1.08 | 0.10 | -0.80 | 0.08 | -0.62 | 0.15 | No | No |
| Y594D | -1.17 | 0.07 | -1.36 | 0.07 | -1.43 | 0.13 | No | No |
| Y594C | -0.47 | 0.06 | -0.08 | 0.06 | -1.45 | 0.10 | No | No |
| Y594Q | -1.06 | 0.08 | -0.26 | 0.06 | -1.14 | 0.12 | No | No |
| Y594E | -0.42 | 0.04 | -0.82 | 0.05 | -2.58 | 0.11 | No | No |
| Y594G | -1.21 | 0.03 | -1.58 | 0.03 | -1.51 | 0.04 | No | No |
| Y594H | 0.04 | 0.07 | -0.11 | 0.07 | -0.42 | 0.12 | Yes | No |
| Y594I | -0.73 | 0.10 | -0.78 | 0.10 | -0.74 | 0.27 | No | No |
| Y594L | -0.88 | 0.05 | -0.67 | 0.04 | -1.45 | 0.10 | No | No |
| Y594K | -0.40 | 0.06 | -0.88 | 0.07 | -1.41 | 0.17 | No | No |
| Y594M | 0.05 | 0.06 | -0.76 | 0.07 | -1.47 | 0.18 | Yes | No |
| Y594F | -0.18 | 0.07 | -0.07 | 0.06 | -0.45 | 0.14 | No | No |
| Y594S | -1.00 | 0.05 | -0.88 | 0.05 | -1.40 | 0.06 | No | No |
| Y594* | -1.41 | 0.08 | -0.73 | 0.06 | -1.67 | 0.13 | No | No |
| Y594T | -1.66 | 0.09 | -1.71 | 0.09 | -1.37 | 0.15 | No | No |
| Y594W | -0.33 | 0.04 | -0.93 | 0.05 | -1.06 | 0.10 | No | No |
| Y594V | -0.40 | 0.04 | -0.47 | 0.04 | -0.96 | 0.08 | No | No |
| Y595A | -1.63 | 0.05 | -1.08 | 0.04 | -2.32 | 0.10 | No | No |
| Y595R | -1.29 | 0.04 | -1.66 | 0.05 | -2.00 | 0.06 | No | No |
| Y595N | -1.61 | 0.14 | -0.78 | 0.10 | -0.80 | 0.19 | No | No |
| Y595D | -1.27 | 0.09 | -1.50 | 0.09 | -1.84 | 0.06 | No | No |
| Y595C | -0.14 | 0.05 | -0.50 | 0.05 | -1.06 | 0.11 | No | No |
| Y595Q | -1.71 | 0.10 | -1.18 | 0.08 | -1.13 | 0.22 | No | No |
| Y595E | -2.05 | 0.08 | -2.21 | 0.08 | -2.32 | 0.03 | No | No |
| Y595G | -1.67 | 0.03 | -1.31 | 0.03 | -1.77 | 0.03 | No | No |
| Y595H | -0.86 | 0.09 | -0.57 | 0.08 | -0.77 | 0.13 | No | No |
| Y595I | -1.20 | 0.14 | -1.49 | 0.15 | NA | NA | Yes | No |
| Y595L | -0.09 | 0.04 | 0.08 | 0.04 | -0.83 | 0.12 | Yes | No |
| Y595K | -1.17 | 0.09 | -1.74 | 0.11 | NA | NA | Yes | No |
| Y595M | 0.24 | 0.06 | -0.10 | 0.07 | -0.34 | 0.19 | Yes | No |
| Y595F | -1.21 | 0.09 | -0.70 | 0.08 | -1.09 | 0.14 | No | No |
| Y595S | -1.31 | 0.05 | -1.19 | 0.05 | -1.64 | 0.09 | No | No |
| Y595* | -1.32 | 0.07 | -1.52 | 0.08 | -1.60 | 0.09 | No | No |
| Y595T | -0.27 | 0.05 | -0.81 | 0.06 | NA | NA | Yes | No |

| Mutant | Enrich. Score (1) | Stand. Error (1) | Enrich. Score (2) | Stand. Error (2) | Enrich. Score (3) | Stand. Error (3) | Any positive enrichment? | Consistent positive enrichment? |
|---|---|---|---|---|---|---|---|---|
| Y595W | -1.72 | 0.06 | -1.71 | 0.06 | -1.97 | 0.10 | No | No |
| Y595V | -0.32 | 0.03 | -0.74 | 0.04 | -2.00 | 0.06 | No | No |
| D596E | 0.04 | 0.04 | 0.24 | 0.04 | 0.69 | 0.05 | Yes | Yes |
| D596A | 0.07 | 0.03 | -0.18 | 0.04 | -0.99 | 0.09 | Yes | No |
| D596R | 0.01 | 0.03 | 0.07 | 0.03 | -0.20 | 0.04 | Yes | No |
| D596N | -0.12 | 0.08 | 0.29 | 0.08 | 0.39 | 0.15 | Yes | No |
| D596C | -0.01 | 0.07 | -0.24 | 0.07 | -0.55 | 0.06 | No | No |
| D596Q | -0.04 | 0.09 | 0.42 | 0.08 | 0.46 | 0.31 | Yes | No |
| D596G | -0.23 | 0.02 | -0.22 | 0.02 | -1.16 | 0.05 | No | No |
| D596H | 0.24 | 0.10 | -0.18 | 0.11 | 0.16 | 0.26 | Yes | No |
| D596L | -0.92 | 0.07 | -0.10 | 0.05 | -0.75 | 0.18 | No | No |
| D596K | 0.01 | 0.08 | 0.36 | 0.07 | -0.07 | 0.19 | Yes | No |
| D596M | 0.26 | 0.08 | 0.29 | 0.07 | -0.27 | 0.28 | Yes | No |
| D596F | 0.03 | 0.11 | -0.55 | 0.13 | 0.09 | 0.13 | Yes | No |
| D596P | NA | NA | NA | NA | -0.56 | 0.24 | Yes | No |
| D596S | -0.58 | 0.06 | -0.29 | 0.05 | 0.37 | 0.07 | Yes | No |
| D596* | -0.99 | 0.11 | -1.29 | 0.12 | NA | NA | Yes | No |
| D596T | -1.56 | 0.12 | 0.65 | 0.06 | -1.10 | 0.23 | Yes | No |
| D596W | -0.19 | 0.05 | 0.12 | 0.05 | -1.34 | 0.11 | Yes | No |
| D596Y | -0.55 | 0.09 | -0.32 | 0.08 | -0.27 | 0.16 | No | No |
| D596V | -0.06 | 0.03 | -0.22 | 0.03 | -1.39 | 0.08 | No | No |
| Y597A | -2.00 | 0.06 | -1.33 | 0.05 | -2.10 | 0.12 | No | No |
| Y597R | -2.18 | 0.05 | -2.13 | 0.05 | -2.18 | 0.04 | No | No |
| Y597N | -1.28 | 0.11 | -0.66 | 0.09 | -1.35 | 0.13 | No | No |
| Y597D | -0.30 | 0.03 | -0.28 | 0.03 | -0.34 | 0.04 | No | No |
| Y597C | -0.79 | 0.06 | -1.14 | 0.07 | -1.47 | 0.05 | No | No |
| Y597E | -2.33 | 0.09 | -2.41 | 0.09 | NA | NA | Yes | No |
| Y597G | -1.89 | 0.04 | -2.15 | 0.04 | -1.96 | 0.05 | No | No |
| Y597H | -0.45 | 0.07 | -0.25 | 0.06 | -0.71 | 0.10 | No | No |
| Y597I | -0.51 | 0.11 | -1.26 | 0.13 | NA | NA | Yes | No |
| Y597L | 0.24 | 0.04 | 0.32 | 0.04 | -0.31 | 0.09 | Yes | No |
| Y597M | -0.11 | 0.07 | -1.15 | 0.10 | NA | NA | Yes | No |
| Y597F | -0.08 | 0.07 | -0.16 | 0.07 | 0.56 | 0.06 | Yes | No |
| Y597P | -2.03 | 0.11 | -2.30 | 0.11 | NA | NA | Yes | No |
| Y597S | -1.25 | 0.05 | -1.04 | 0.05 | -2.00 | 0.09 | No | No |
| Y597* | -0.94 | 0.06 | -0.96 | 0.06 | -2.02 | 0.13 | No | No |
| Y597T | -1.78 | 0.09 | -2.62 | 0.12 | -1.94 | 0.04 | No | No |
| Y597W | -1.16 | 0.05 | -1.33 | 0.05 | -2.30 | 0.08 | No | No |
| Y597V | -1.95 | 0.07 | -1.63 | 0.06 | -2.69 | 0.08 | No | No |
| F598A | -1.68 | 0.07 | -1.98 | 0.08 | -2.09 | 0.12 | No | No |
| F598R | -1.81 | 0.06 | -2.21 | 0.07 | -1.57 | 0.11 | No | No |
| F598C | -1.96 | 0.12 | -2.25 | 0.13 | -1.21 | 0.15 | No | No |

| Mutant | Enrich. Score (1) | Stand. Error (1) | Enrich. Score (2) | Stand. Error (2) | Enrich. Score (3) | Stand. Error (3) | Any positive enrichment? | Consistent positive enrichment? |
|---|---|---|---|---|---|---|---|---|
| F598G | -2.06 | 0.05 | -1.79 | 0.04 | -0.96 | 0.03 | No | No |
| F598I | -0.32 | 0.09 | -0.44 | 0.09 | -0.75 | 0.12 | No | No |
| F598L | -0.25 | 0.04 | -0.09 | 0.04 | -0.65 | 0.04 | No | No |
| F598M | -0.35 | 0.09 | -0.55 | 0.09 | -0.87 | 0.27 | No | No |
| F598P | NA | NA | NA | NA | -1.93 | 0.07 | Yes | No |
| F598S | -1.12 | 0.06 | -1.33 | 0.06 | -1.35 | 0.08 | No | No |
| F598W | -1.23 | 0.06 | -0.34 | 0.05 | -1.74 | 0.12 | No | No |
| F598Y | -0.52 | 0.09 | -0.44 | 0.09 | -0.60 | 0.15 | No | No |
| F598V | -1.37 | 0.06 | -1.39 | 0.05 | -2.25 | 0.09 | No | No |
| P599G | 0.84 | 0.04 | 0.83 | 0.04 | 1.01 | 0.05 | Yes | Yes |
| P599A | -1.03 | 0.07 | -0.85 | 0.06 | -1.42 | 0.11 | No | No |
| P599R | -1.89 | 0.09 | -1.20 | 0.06 | -2.08 | 0.14 | No | No |
| P599N | -0.66 | 0.16 | -0.33 | 0.14 | NA | NA | Yes | No |
| P599E | -2.04 | 0.15 | -2.07 | 0.15 | NA | NA | Yes | No |
| P599H | -1.01 | 0.14 | -0.99 | 0.14 | NA | NA | Yes | No |
| P599L | -1.56 | 0.09 | -1.36 | 0.08 | -1.46 | 0.11 | No | No |
| P599S | -0.09 | 0.03 | -0.10 | 0.03 | -0.56 | 0.04 | No | No |
| P599* | -1.14 | 0.13 | -1.42 | 0.14 | NA | NA | Yes | No |
| P599T | -0.42 | 0.07 | -0.95 | 0.08 | -1.37 | 0.14 | No | No |
| P599V | -1.88 | 0.12 | -1.85 | 0.11 | -1.81 | 0.14 | No | No |
| D600A | 0.43 | 0.06 | -0.31 | 0.07 | 0.68 | 0.14 | Yes | No |
| D600R | -0.88 | 0.07 | -0.40 | 0.06 | -1.67 | 0.19 | No | No |
| D600N | -0.03 | 0.07 | -0.16 | 0.07 | 0.67 | 0.14 | Yes | No |
| D600C | NA | NA | NA | NA | -0.32 | 0.48 | Yes | No |
| D600Q | -0.37 | 0.15 | -0.01 | 0.13 | NA | NA | Yes | No |
| D600E | -0.44 | 0.07 | -0.46 | 0.07 | -0.95 | 0.22 | No | No |
| D600G | -0.19 | 0.04 | -0.33 | 0.04 | 1.07 | 0.05 | Yes | No |
| D600H | -0.08 | 0.13 | -0.54 | 0.14 | NA | NA | Yes | No |
| D600L | -1.26 | 0.13 | -1.19 | 0.12 | -0.50 | 0.29 | No | No |
| D600P | -0.14 | 0.11 | -1.46 | 0.16 | 0.47 | 0.45 | Yes | No |
| D600S | 0.86 | 0.07 | -0.03 | 0.08 | 0.74 | 0.14 | Yes | No |
| D600T | -1.42 | 0.15 | -0.70 | 0.12 | 0.43 | 0.29 | Yes | No |
| D600W | -0.67 | 0.11 | -0.51 | 0.10 | NA | NA | Yes | No |
| D600Y | -0.29 | 0.13 | -0.19 | 0.12 | NA | NA | Yes | No |
| D600V | -0.05 | 0.06 | -0.23 | 0.06 | -0.56 | 0.13 | No | No |
| A601R | -1.65 | 0.07 | -1.62 | 0.07 | NA | NA | Yes | No |
| A601D | -1.38 | 0.13 | -1.10 | 0.11 | NA | NA | Yes | No |
| A601C | 0.26 | 0.08 | 0.26 | 0.08 | -0.25 | 0.24 | Yes | No |
| A601G | -1.05 | 0.04 | -0.63 | 0.04 | -1.44 | 0.04 | No | No |
| A601L | -2.16 | 0.13 | -1.44 | 0.09 | NA | NA | Yes | No |
| A601P | -1.40 | 0.13 | -1.20 | 0.11 | NA | NA | Yes | No |
| A601S | -0.60 | 0.06 | 0.23 | 0.04 | -0.52 | 0.08 | Yes | No |

| Mutant | Enrich. Score (1) | Stand. Error (1) | Enrich. Score (2) | Stand. Error (2) | Enrich. Score (3) | Stand. Error (3) | Any positive enrichment? | Consistent positive enrichment? |
|---|---|---|---|---|---|---|---|---|
| A601T | -0.84 | 0.08 | -0.53 | 0.07 | -0.99 | 0.12 | No | No |
| A601W | -1.89 | 0.12 | -1.84 | 0.11 | NA | NA | Yes | No |
| A601V | -0.48 | 0.05 | -0.23 | 0.04 | -0.77 | 0.06 | No | No |
| A602C | 0.64 | 0.09 | 0.61 | 0.09 | 0.73 | 0.28 | Yes | Yes |
| A602R | -0.59 | 0.07 | -0.97 | 0.08 | NA | NA | Yes | No |
| A602D | 0.04 | 0.04 | -0.09 | 0.04 | -0.40 | 0.05 | Yes | No |
| A602G | -0.52 | 0.05 | -0.56 | 0.05 | -1.62 | 0.06 | No | No |
| A602H | NA | NA | NA | NA | 0.37 | 0.35 | Yes | No |
| A602L | -1.97 | 0.14 | -1.06 | 0.10 | NA | NA | Yes | No |
| A602P | -0.80 | 0.09 | -0.42 | 0.08 | -0.71 | 0.15 | No | No |
| A602S | -0.38 | 0.07 | -0.14 | 0.06 | -0.73 | 0.16 | No | No |
| A602T | -0.28 | 0.06 | -0.03 | 0.06 | -0.51 | 0.11 | No | No |
| A602W | NA | NA | NA | NA | -0.89 | 0.37 | Yes | No |
| A602V | -0.77 | 0.06 | -0.66 | 0.05 | -1.41 | 0.10 | No | No |
| K603A | -1.34 | 0.07 | -1.59 | 0.07 | -1.76 | 0.05 | No | No |
| K603R | -0.56 | 0.04 | -0.37 | 0.03 | -0.46 | 0.04 | No | No |
| K603N | -1.59 | 0.16 | -1.11 | 0.13 | NA | NA | Yes | No |
| K603C | -1.03 | 0.10 | -1.23 | 0.10 | NA | NA | Yes | No |
| K603Q | -1.30 | 0.11 | -1.57 | 0.12 | NA | NA | Yes | No |
| K603E | -1.40 | 0.07 | -0.68 | 0.05 | -1.60 | 0.10 | No | No |
| K603G | -1.88 | 0.05 | -1.70 | 0.04 | -1.97 | 0.08 | No | No |
| K603H | NA | NA | NA | NA | -0.51 | 0.41 | Yes | No |
| K603L | -0.77 | 0.06 | -0.60 | 0.06 | -1.63 | 0.14 | No | No |
| K603M | 0.00 | 0.06 | -0.57 | 0.07 | -1.02 | 0.11 | No | No |
| K603P | -1.70 | 0.12 | -1.06 | 0.09 | NA | NA | Yes | No |
| K603S | NA | NA | NA | NA | -2.06 | 0.05 | Yes | No |
| K603* | -1.20 | 0.09 | -1.66 | 0.11 | -1.37 | 0.16 | No | No |
| K603T | -1.11 | 0.08 | -1.15 | 0.08 | -1.13 | 0.13 | No | No |
| K603W | -2.79 | 0.14 | -1.74 | 0.09 | -1.45 | 0.14 | No | No |
| K603V | -1.72 | 0.07 | -1.54 | 0.06 | -2.40 | 0.07 | No | No |
| M604A | -2.19 | 0.15 | -1.92 | 0.13 | NA | NA | Yes | No |
| M604R | -0.96 | 0.06 | -1.76 | 0.08 | -2.02 | 0.13 | No | No |
| M604G | -2.12 | 0.08 | -0.82 | 0.05 | -1.81 | 0.12 | No | No |
| M604I | -0.58 | 0.10 | -0.71 | 0.10 | -0.51 | 0.15 | No | No |
| M604L | -0.74 | 0.06 | -0.50 | 0.06 | -0.25 | 0.06 | No | No |
| M604K | -1.08 | 0.15 | -0.78 | 0.13 | NA | NA | Yes | No |
| M604T | -0.14 | 0.06 | 0.01 | 0.06 | -0.44 | 0.09 | Yes | No |
| M604W | -1.97 | 0.14 | -2.03 | 0.14 | NA | NA | Yes | No |
| M604V | -1.38 | 0.08 | -1.32 | 0.07 | -1.38 | 0.09 | No | No |
| I605A | -1.32 | 0.09 | -1.04 | 0.08 | NA | NA | Yes | No |
| I605R | -2.07 | 0.09 | -2.36 | 0.10 | -2.12 | 0.15 | No | No |
| I605N | -0.93 | 0.10 | -0.19 | 0.08 | -0.76 | 0.16 | No | No |

| Mutant | Enrich. Score (1) | Stand. Error (1) | Enrich. Score (2) | Stand. Error (2) | Enrich. Score (3) | Stand. Error (3) | Any positive enrichment? | Consistent positive enrichment? |
|---|---|---|---|---|---|---|---|---|
| I605C | 0.20 | 0.09 | -0.98 | 0.13 | NA | NA | Yes | No |
| I605G | -1.69 | 0.07 | -1.41 | 0.06 | -2.04 | 0.14 | No | No |
| I605L | -0.93 | 0.07 | -0.25 | 0.06 | -1.49 | 0.14 | No | No |
| I605M | -1.09 | 0.09 | -0.86 | 0.08 | -1.44 | 0.15 | No | No |
| I605F | -0.50 | 0.11 | -0.52 | 0.10 | NA | NA | Yes | No |
| I605S | -1.91 | 0.11 | -1.82 | 0.10 | -1.55 | 0.10 | No | No |
| I605T | -0.45 | 0.07 | -0.67 | 0.07 | -1.09 | 0.12 | No | No |
| I605V | 0.13 | 0.05 | -0.04 | 0.05 | -0.33 | 0.11 | Yes | No |
| I605A | -1.42 | 0.10 | -0.82 | 0.08 | NA | NA | Yes | No |
| I605R | -2.12 | 0.09 | -2.15 | 0.10 | -1.82 | 0.16 | No | No |
| I605N | 0.04 | 0.06 | 0.36 | 0.06 | -0.41 | 0.09 | Yes | No |
| I605D | -1.00 | 0.09 | -0.60 | 0.08 | -0.72 | 0.14 | No | No |
| I605C | 0.10 | 0.10 | -0.82 | 0.13 | NA | NA | Yes | No |
| I605G | -1.69 | 0.07 | -1.23 | 0.06 | -1.96 | 0.13 | No | No |
| I605L | -0.10 | 0.03 | 0.14 | 0.03 | -1.00 | 0.08 | Yes | No |
| I605M | -0.89 | 0.09 | -0.63 | 0.08 | -1.25 | 0.21 | No | No |
| I605F | -0.55 | 0.10 | -0.33 | 0.09 | NA | NA | Yes | No |
| I605S | -0.22 | 0.04 | 0.10 | 0.04 | -1.29 | 0.08 | Yes | No |
| I605T | -0.02 | 0.04 | 0.21 | 0.04 | -0.53 | 0.07 | Yes | No |
| I605V | 0.19 | 0.05 | 0.25 | 0.05 | -0.06 | 0.10 | Yes | No |
| P606A | -1.59 | 0.10 | -2.27 | 0.12 | -1.25 | 0.17 | No | No |
| P606R | -1.77 | 0.08 | -2.62 | 0.12 | -1.94 | 0.15 | No | No |
| P606G | -1.63 | 0.07 | -2.12 | 0.08 | -1.89 | 0.14 | No | No |
| P606H | -0.89 | 0.13 | -0.93 | 0.13 | NA | NA | Yes | No |
| P606L | -0.77 | 0.07 | -1.12 | 0.08 | -1.30 | 0.15 | No | No |
| P606S | -1.42 | 0.10 | -1.22 | 0.09 | -1.16 | 0.14 | No | No |
| P606T | -0.06 | 0.06 | -0.63 | 0.07 | -0.40 | 0.08 | No | No |
| P606W | -0.88 | 0.11 | -1.05 | 0.11 | NA | NA | Yes | No |
| P606V | NA | NA | NA | NA | -1.59 | 0.24 | Yes | No |
| P606A | -1.59 | 0.10 | -2.27 | 0.14 | -1.33 | 0.19 | No | No |
| P606R | -1.77 | 0.09 | -1.59 | 0.08 | -1.76 | 0.15 | No | No |
| P606Q | NA | NA | NA | NA | -0.43 | 0.12 | Yes | No |
| P606G | -1.73 | 0.08 | -2.00 | 0.09 | -1.79 | 0.16 | No | No |
| P606H | 0.13 | 0.07 | 0.17 | 0.07 | -0.14 | 0.04 | Yes | No |
| P606L | -0.98 | 0.08 | -1.23 | 0.09 | -1.00 | 0.16 | No | No |
| P606S | -1.64 | 0.12 | -1.35 | 0.11 | -1.37 | 0.17 | No | No |
| P606T | -0.10 | 0.07 | -0.63 | 0.08 | -0.65 | 0.11 | No | No |
| P606W | -1.06 | 0.12 | -0.93 | 0.11 | NA | NA | Yes | No |
| P606V | NA | NA | NA | NA | -1.33 | 0.27 | Yes | No |
| K607A | -1.61 | 0.05 | -1.70 | 0.06 | -2.05 | 0.10 | No | No |
| K607R | -1.65 | 0.04 | -1.32 | 0.03 | -2.05 | 0.03 | No | No |
| K607N | -0.51 | 0.07 | -0.19 | 0.07 | NA | NA | Yes | No |

| Mutant | Enrich. Score (1) | Stand. Error (1) | Enrich. Score (2) | Stand. Error (2) | Enrich. Score (3) | Stand. Error (3) | Any positive enrichment? | Consistent positive enrichment? |
|---|---|---|---|---|---|---|---|---|
| K607D | -2.48 | 0.14 | -1.83 | 0.11 | NA | NA | Yes | No |
| K607C | -1.09 | 0.07 | -1.20 | 0.08 | NA | NA | Yes | No |
| K607Q | -1.77 | 0.09 | -1.64 | 0.09 | -1.87 | 0.13 | No | No |
| K607E | -1.93 | 0.06 | -1.40 | 0.05 | -1.61 | 0.07 | No | No |
| K607G | -1.81 | 0.03 | -1.60 | 0.03 | -1.79 | 0.03 | No | No |
| K607H | -1.16 | 0.12 | -0.39 | 0.10 | NA | NA | Yes | No |
| K607L | -1.08 | 0.05 | -1.66 | 0.06 | -1.63 | 0.08 | No | No |
| K607M | -0.42 | 0.06 | -1.47 | 0.08 | -0.97 | 0.05 | No | No |
| K607F | -1.55 | 0.12 | -1.20 | 0.11 | NA | NA | Yes | No |
| K607P | NA | NA | NA | NA | -1.84 | 0.14 | Yes | No |
| K607S | -1.89 | 0.06 | -1.43 | 0.06 | -1.53 | 0.04 | No | No |
| K607* | -1.44 | 0.07 | -0.97 | 0.06 | -1.20 | 0.14 | No | No |
| K607T | -2.23 | 0.09 | -1.26 | 0.06 | -1.98 | 0.11 | No | No |
| K607W | -1.92 | 0.06 | -1.88 | 0.06 | -1.81 | 0.10 | No | No |
| K607V | -1.80 | 0.05 | -1.85 | 0.06 | -1.86 | 0.03 | No | No |
| C608A | -1.60 | 0.09 | -1.32 | 0.08 | -1.81 | 0.15 | No | No |
| C608R | -0.90 | 0.04 | -0.72 | 0.04 | -1.23 | 0.09 | No | No |
| C608E | -1.06 | 0.09 | -1.27 | 0.10 | NA | NA | Yes | No |
| C608G | -1.44 | 0.05 | -0.58 | 0.04 | -1.66 | 0.09 | No | No |
| C608L | -1.11 | 0.08 | -0.49 | 0.07 | NA | NA | Yes | No |
| C608F | -1.13 | 0.12 | -0.91 | 0.12 | NA | NA | Yes | No |
| C608P | -1.62 | 0.14 | -1.13 | 0.12 | NA | NA | Yes | No |
| C608S | -0.62 | 0.05 | -0.49 | 0.05 | -1.56 | 0.12 | No | No |
| C608* | -1.61 | 0.13 | -0.66 | 0.10 | NA | NA | Yes | No |
| C608W | -1.58 | 0.09 | -1.31 | 0.08 | NA | NA | Yes | No |
| C608Y | -0.27 | 0.06 | -0.09 | 0.06 | -0.65 | 0.15 | No | No |
| C608V | -1.32 | 0.07 | -2.23 | 0.11 | NA | NA | Yes | No |
| S609A | 0.10 | 0.07 | 0.21 | 0.07 | -0.16 | 0.22 | Yes | No |
| S609R | -0.60 | 0.05 | -0.45 | 0.05 | -1.32 | 0.06 | No | No |
| S609N | -1.18 | 0.12 | -0.49 | 0.10 | NA | NA | Yes | No |
| S609C | -0.69 | 0.12 | 0.21 | 0.09 | -0.27 | 0.25 | Yes | No |
| S609G | 0.00 | 0.04 | -0.27 | 0.04 | -0.17 | 0.10 | No | No |
| S609I | -0.16 | 0.12 | 0.43 | 0.11 | NA | NA | Yes | No |
| S609T | -0.76 | 0.12 | 0.55 | 0.09 | NA | NA | Yes | No |
| S609W | -1.36 | 0.13 | -0.51 | 0.10 | NA | NA | Yes | No |
| T610A | -0.40 | 0.05 | -0.40 | 0.05 | -0.93 | 0.09 | No | No |
| T610R | -1.61 | 0.07 | -0.98 | 0.06 | -1.76 | 0.15 | No | No |
| T610N | -0.27 | 0.10 | -0.20 | 0.10 | -0.58 | 0.12 | No | No |
| T610C | -0.26 | 0.09 | -0.31 | 0.09 | NA | NA | Yes | No |
| T610Q | NA | NA | NA | NA | -0.53 | 0.36 | Yes | No |
| T610G | -1.36 | 0.05 | -1.25 | 0.05 | -1.62 | 0.12 | No | No |
| T610I | -0.82 | 0.11 | -0.98 | 0.12 | NA | NA | Yes | No |

| Mutant | Enrich. Score (1) | Stand. Error (1) | Enrich. Score (2) | Stand. Error (2) | Enrich. Score (3) | Stand. Error (3) | Any positive enrichment? | Consistent positive enrichment? |
|---|---|---|---|---|---|---|---|---|
| T610L | -1.78 | 0.11 | -2.29 | 0.14 | NA | NA | Yes | No |
| T610P | 0.07 | 0.04 | 0.33 | 0.04 | -0.62 | 0.08 | Yes | No |
| T610S | -0.35 | 0.06 | -0.62 | 0.06 | -0.53 | 0.07 | No | No |
| T610V | 0.26 | 0.05 | -1.14 | 0.08 | -1.58 | 0.17 | Yes | No |
| Q611A | -2.61 | 0.13 | -1.23 | 0.08 | -1.40 | 0.13 | No | No |
| Q611R | -0.68 | 0.04 | -0.69 | 0.04 | -1.33 | 0.04 | No | No |
| Q611E | -1.22 | 0.07 | -0.58 | 0.06 | -1.18 | 0.11 | No | No |
| Q611G | -1.38 | 0.05 | -1.84 | 0.06 | -1.82 | 0.08 | No | No |
| Q611H | 0.04 | 0.07 | -0.20 | 0.07 | -0.91 | 0.13 | Yes | No |
| Q611L | -1.21 | 0.08 | -1.74 | 0.10 | -1.67 | 0.16 | No | No |
| Q611K | -0.93 | 0.09 | -0.83 | 0.09 | -1.38 | 0.16 | No | No |
| Q611P | 0.13 | 0.06 | -0.14 | 0.06 | -0.81 | 0.08 | Yes | No |
| Q611S | -2.07 | 0.11 | -0.89 | 0.07 | NA | NA | Yes | No |
| Q611* | -0.75 | 0.09 | -1.11 | 0.10 | -1.17 | 0.16 | No | No |
| Q611W | -1.28 | 0.08 | -0.88 | 0.07 | NA | NA | Yes | No |
| Q611V | -1.42 | 0.07 | -1.15 | 0.07 | NA | NA | Yes | No |
| L612M | 0.70 | 0.07 | 0.70 | 0.07 | 0.01 | 0.03 | Yes | Yes |
| L612A | -1.32 | 0.11 | -1.11 | 0.11 | -0.98 | 0.22 | No | No |
| L612R | 0.03 | 0.05 | 0.16 | 0.05 | -0.58 | 0.11 | Yes | No |
| L612Q | -0.94 | 0.10 | -0.43 | 0.09 | NA | NA | Yes | No |
| L612E | -1.18 | 0.11 | -1.65 | 0.13 | NA | NA | Yes | No |
| L612G | -0.97 | 0.07 | -2.15 | 0.11 | -1.70 | 0.17 | No | No |
| L612I | -0.18 | 0.13 | 0.66 | 0.11 | -0.24 | 0.15 | Yes | No |
| L612K | -1.41 | 0.16 | -0.48 | 0.12 | NA | NA | Yes | No |
| L612P | -0.34 | 0.06 | -0.33 | 0.06 | -0.72 | 0.11 | No | No |
| L612* | -1.69 | 0.15 | -0.55 | 0.10 | NA | NA | Yes | No |
| L612T | -0.27 | 0.09 | -1.35 | 0.13 | NA | NA | Yes | No |
| L612V | -1.05 | 0.08 | -0.90 | 0.08 | -1.51 | 0.05 | No | No |
| K613R | -0.22 | 0.06 | -0.18 | 0.06 | -0.40 | 0.05 | No | No |
| K613N | 0.04 | 0.10 | 0.16 | 0.10 | NA | NA | Yes | No |
| K613Q | 0.14 | 0.04 | 0.38 | 0.04 | NA | NA | Yes | No |
| K613E | -0.75 | 0.08 | 0.06 | 0.07 | NA | NA | Yes | No |
| K613G | -1.17 | 0.08 | -1.36 | 0.09 | NA | NA | Yes | No |
| K613L | 0.12 | 0.09 | 0.49 | 0.09 | -0.52 | 0.26 | Yes | No |
| K613M | -0.26 | 0.11 | 0.73 | 0.09 | NA | NA | Yes | No |
| K613* | -0.72 | 0.11 | -0.72 | 0.11 | NA | NA | Yes | No |
| K613T | 0.26 | 0.05 | 0.46 | 0.05 | -0.65 | 0.08 | Yes | No |
| K613W | -1.27 | 0.12 | -1.60 | 0.14 | NA | NA | Yes | No |
| K613V | -0.89 | 0.10 | -0.25 | 0.08 | NA | NA | Yes | No |
| A614R | 0.28 | 0.04 | 0.07 | 0.05 | 0.16 | 0.05 | Yes | Yes |
| A614I | 0.52 | 0.11 | 0.59 | 0.11 | 0.41 | 0.22 | Yes | Yes |
| A614D | -0.02 | 0.08 | -0.34 | 0.09 | NA | NA | Yes | No |

| Mutant | Enrich. Score (1) | Stand. Error (1) | Enrich. Score (2) | Stand. Error (2) | Enrich. Score (3) | Stand. Error (3) | Any positive enrichment? | Consistent positive enrichment? |
|---|---|---|---|---|---|---|---|---|
| A614C | -0.54 | 0.09 | -0.12 | 0.08 | 0.02 | 0.22 | Yes | No |
| A614Q | 0.50 | 0.10 | 0.17 | 0.11 | NA | NA | Yes | No |
| A614E | -0.71 | 0.08 | -0.80 | 0.09 | NA | NA | Yes | No |
| A614G | -0.16 | 0.03 | 0.09 | 0.03 | -0.21 | 0.08 | Yes | No |
| A614L | 0.09 | 0.06 | -0.21 | 0.06 | 0.02 | 0.12 | Yes | No |
| A614K | NA | NA | NA | NA | 0.28 | 0.38 | Yes | No |
| A614M | -0.39 | 0.13 | 1.39 | 0.09 | NA | NA | Yes | No |
| A614F | -0.66 | 0.14 | -0.11 | 0.12 | NA | NA | Yes | No |
| A614P | -0.22 | 0.09 | -0.09 | 0.09 | -0.68 | 0.25 | No | No |
| A614S | -0.46 | 0.07 | 0.19 | 0.06 | -0.55 | 0.15 | Yes | No |
| A614* | NA | NA | NA | NA | -0.35 | 0.32 | Yes | No |
| A614T | 0.03 | 0.06 | 0.37 | 0.06 | -0.49 | 0.14 | Yes | No |
| A614W | -0.74 | 0.07 | -0.88 | 0.08 | -0.97 | 0.14 | No | No |
| A614V | 0.17 | 0.04 | 0.29 | 0.04 | -0.03 | 0.11 | Yes | No |
| V615A | -0.05 | 0.03 | 0.09 | 0.03 | -0.35 | 0.04 | Yes | No |
| V615R | -1.73 | 0.05 | -1.23 | 0.04 | -1.21 | 0.07 | No | No |
| V615N | -0.21 | 0.08 | -1.01 | 0.11 | -0.72 | 0.15 | No | No |
| V615D | -0.95 | 0.07 | -0.97 | 0.07 | -1.54 | 0.13 | No | No |
| V615C | -0.18 | 0.06 | -0.18 | 0.06 | -0.01 | 0.19 | No | No |
| V615Q | -1.87 | 0.10 | -1.41 | 0.09 | NA | NA | Yes | No |
| V615E | -0.82 | 0.04 | -0.59 | 0.04 | -1.03 | 0.05 | No | No |
| V615G | -0.57 | 0.03 | -0.88 | 0.03 | -1.19 | 0.04 | No | No |
| V615I | -0.51 | 0.09 | -0.73 | 0.10 | -0.67 | 0.23 | No | No |
| V615L | -0.07 | 0.03 | 0.05 | 0.03 | -0.88 | 0.05 | Yes | No |
| V615K | -1.22 | 0.08 | -1.81 | 0.10 | -1.56 | 0.07 | No | No |
| V615M | -0.52 | 0.06 | -0.54 | 0.06 | -0.54 | 0.12 | No | No |
| V615F | -1.88 | 0.14 | -1.30 | 0.12 | NA | NA | Yes | No |
| V615P | -1.53 | 0.10 | -1.82 | 0.11 | -1.42 | 0.06 | No | No |
| V615S | 0.17 | 0.04 | -0.23 | 0.04 | -0.63 | 0.05 | Yes | No |
| V615* | -1.04 | 0.07 | -0.78 | 0.07 | -1.35 | 0.16 | No | No |
| V615T | 0.19 | 0.05 | -0.12 | 0.06 | -0.07 | 0.17 | Yes | No |
| V615W | -1.19 | 0.06 | -1.55 | 0.07 | -1.90 | 0.05 | No | No |
| T616A | 0.32 | 0.03 | 0.24 | 0.04 | 0.09 | 0.05 | Yes | Yes |
| T616R | 0.19 | 0.03 | 0.12 | 0.03 | 0.62 | 0.04 | Yes | Yes |
| T616Q | 0.35 | 0.07 | 0.38 | 0.07 | 0.78 | 0.20 | Yes | Yes |
| T616G | 0.22 | 0.03 | 0.01 | 0.03 | 0.16 | 0.06 | Yes | Yes |
| T616Y | 0.54 | 0.09 | 0.64 | 0.09 | 0.05 | 0.38 | Yes | Yes |
| T616N | -0.11 | 0.08 | 0.20 | 0.08 | 0.16 | 0.07 | Yes | No |
| T616D | -0.66 | 0.08 | 0.14 | 0.07 | -0.18 | 0.26 | Yes | No |
| T616C | 0.54 | 0.06 | 0.27 | 0.06 | -0.24 | 0.11 | Yes | No |
| T616E | -0.28 | 0.06 | -0.38 | 0.06 | -0.17 | 0.07 | No | No |
| T616H | 0.62 | 0.08 | -0.13 | 0.10 | 1.21 | 0.25 | Yes | No |

| Mutant | Enrich. Score (1) | Stand. Error (1) | Enrich. Score (2) | Stand. Error (2) | Enrich. Score (3) | Stand. Error (3) | Any positive enrichment? | Consistent positive enrichment? |
|---|---|---|---|---|---|---|---|---|
| T616I | -0.33 | 0.08 | 0.30 | 0.07 | 0.19 | 0.18 | Yes | No |
| T616L | -0.27 | 0.05 | -0.43 | 0.05 | -0.19 | 0.13 | No | No |
| T616K | -0.36 | 0.08 | 0.23 | 0.07 | 0.66 | 0.09 | Yes | No |
| T616M | -0.49 | 0.08 | -0.40 | 0.08 | -0.44 | 0.25 | No | No |
| T616F | -0.58 | 0.11 | 0.07 | 0.09 | 0.10 | 0.36 | Yes | No |
| T616P | -0.89 | 0.07 | -0.68 | 0.07 | -0.80 | 0.06 | No | No |
| T616S | -0.02 | 0.04 | 0.12 | 0.04 | 0.13 | 0.07 | Yes | No |
| T616* | NA | NA | NA | NA | -1.14 | 0.24 | Yes | No |
| T616W | -0.28 | 0.05 | 0.25 | 0.04 | -0.22 | 0.19 | Yes | No |
| T616V | -0.07 | 0.04 | -0.09 | 0.04 | 0.21 | 0.07 | Yes | No |
| A617G | 0.03 | 0.03 | 0.05 | 0.03 | 0.24 | 0.06 | Yes | Yes |
| A617R | -0.10 | 0.04 | 0.07 | 0.04 | -0.32 | 0.11 | Yes | No |
| A617N | NA | NA | NA | NA | 0.12 | 0.42 | Yes | No |
| A617D | -0.76 | 0.09 | -0.05 | 0.07 | NA | NA | Yes | No |
| A617C | -0.73 | 0.09 | 0.26 | 0.07 | 0.13 | 0.18 | Yes | No |
| A617Q | 0.25 | 0.08 | 0.07 | 0.09 | -0.48 | 0.30 | Yes | No |
| A617E | -0.12 | 0.06 | 0.08 | 0.06 | -0.40 | 0.20 | Yes | No |
| A617H | -0.11 | 0.11 | -0.46 | 0.12 | NA | NA | Yes | No |
| A617I | -0.26 | 0.11 | 0.09 | 0.10 | -0.52 | 0.38 | Yes | No |
| A617L | -0.11 | 0.05 | 0.18 | 0.05 | -0.18 | 0.16 | Yes | No |
| A617K | NA | NA | NA | NA | -0.08 | 0.28 | Yes | No |
| A617M | 0.32 | 0.07 | 0.30 | 0.07 | -0.34 | 0.27 | Yes | No |
| A617F | -0.17 | 0.10 | -0.39 | 0.11 | -0.42 | 0.36 | No | No |
| A617P | -0.48 | 0.08 | -0.88 | 0.09 | 0.05 | 0.18 | Yes | No |
| A617S | -0.13 | 0.05 | 0.25 | 0.05 | -0.58 | 0.06 | Yes | No |
| A617* | -0.96 | 0.11 | -1.57 | 0.14 | NA | NA | Yes | No |
| A617T | -0.23 | 0.05 | 0.26 | 0.05 | -0.30 | 0.10 | Yes | No |
| A617W | 0.17 | 0.05 | -0.93 | 0.07 | -0.69 | 0.15 | Yes | No |
| A617V | -0.03 | 0.04 | -0.09 | 0.04 | -0.42 | 0.12 | No | No |
| H618A | -0.73 | 0.14 | -0.80 | 0.15 | 0.36 | 0.36 | Yes | No |
| H618R | -0.08 | 0.05 | 0.24 | 0.05 | -0.46 | 0.06 | Yes | No |
| H618N | -0.37 | 0.17 | -0.24 | 0.16 | NA | NA | Yes | No |
| H618D | 0.48 | 0.13 | 0.89 | 0.12 | NA | NA | Yes | No |
| H618Q | -0.62 | 0.14 | 0.01 | 0.12 | NA | NA | Yes | No |
| H618G | -0.56 | 0.07 | -0.91 | 0.09 | -0.91 | 0.19 | No | No |
| H618L | 0.02 | 0.06 | 0.10 | 0.06 | -0.47 | 0.07 | Yes | No |
| H618P | 0.32 | 0.08 | 0.47 | 0.08 | -0.51 | 0.08 | Yes | No |
| H618S | -0.50 | 0.14 | -0.26 | 0.13 | NA | NA | Yes | No |
| H618W | NA | NA | NA | NA | 0.44 | 0.31 | Yes | No |
| H618Y | 0.23 | 0.10 | -0.28 | 0.11 | -0.26 | 0.19 | Yes | No |
| F619M | 0.12 | 0.07 | 0.55 | 0.07 | 0.22 | 0.25 | Yes | Yes |
| F619A | -0.57 | 0.05 | -1.25 | 0.06 | -0.78 | 0.05 | No | No |

| Mutant | Enrich. Score (1) | Stand. Error (1) | Enrich. Score (2) | Stand. Error (2) | Enrich. Score (3) | Stand. Error (3) | Any positive enrichment? | Consistent positive enrichment? |
|---|---|---|---|---|---|---|---|---|
| F619R | -1.24 | 0.05 | -1.94 | 0.07 | -0.66 | 0.07 | No | No |
| F619N | -0.61 | 0.13 | -0.15 | 0.12 | NA | NA | Yes | No |
| F619D | -1.39 | 0.12 | -0.62 | 0.09 | NA | NA | Yes | No |
| F619C | 0.07 | 0.03 | 0.08 | 0.03 | -0.37 | 0.04 | Yes | No |
| F619Q | -1.13 | 0.12 | -1.57 | 0.15 | NA | NA | Yes | No |
| F619E | -1.58 | 0.08 | -2.40 | 0.12 | -1.54 | 0.08 | No | No |
| F619G | -1.29 | 0.03 | -1.03 | 0.03 | -1.57 | 0.05 | No | No |
| F619H | NA | NA | NA | NA | -0.31 | 0.34 | Yes | No |
| F619I | -0.69 | 0.12 | -0.28 | 0.11 | -0.42 | 0.22 | No | No |
| F619L | 0.17 | 0.03 | 0.12 | 0.03 | -0.48 | 0.05 | Yes | No |
| F619P | -1.00 | 0.09 | -1.22 | 0.10 | NA | NA | Yes | No |
| F619S | -0.26 | 0.04 | -0.95 | 0.06 | -0.56 | 0.06 | No | No |
| F619* | -1.91 | 0.14 | -0.92 | 0.10 | NA | NA | Yes | No |
| F619T | NA | NA | NA | NA | -1.08 | 0.24 | Yes | No |
| F619W | -0.08 | 0.04 | -0.81 | 0.05 | 0.00 | 0.07 | Yes | No |
| F619Y | 0.06 | 0.08 | -0.79 | 0.11 | 0.28 | 0.11 | Yes | No |
| F619V | -0.51 | 0.04 | -0.49 | 0.04 | -0.64 | 0.04 | No | No |
| Q620A | 0.22 | 0.04 | 0.00 | 0.05 | 0.18 | 0.09 | Yes | Yes |
| Q620R | 0.25 | 0.03 | 0.18 | 0.03 | 0.17 | 0.04 | Yes | Yes |
| Q620N | 0.26 | 0.14 | 0.28 | 0.14 | 0.36 | 0.21 | Yes | Yes |
| Q620L | 0.14 | 0.04 | 0.45 | 0.04 | 0.40 | 0.16 | Yes | Yes |
| Q620K | 0.10 | 0.07 | 0.24 | 0.07 | 0.04 | 0.10 | Yes | Yes |
| Q620D | -0.16 | 0.07 | -0.25 | 0.08 | 0.24 | 0.23 | Yes | No |
| Q620C | -0.22 | 0.07 | -0.95 | 0.10 | 0.03 | 0.23 | Yes | No |
| Q620E | 0.21 | 0.05 | 0.13 | 0.05 | -0.09 | 0.10 | Yes | No |
| Q620G | -0.14 | 0.02 | 0.02 | 0.02 | 0.19 | 0.04 | Yes | No |
| Q620H | -0.08 | 0.08 | 0.16 | 0.08 | -0.05 | 0.20 | Yes | No |
| Q620I | 0.27 | 0.11 | -0.38 | 0.14 | NA | NA | Yes | No |
| Q620M | 0.70 | 0.07 | -0.03 | 0.08 | 0.20 | 0.26 | Yes | No |
| Q620F | 0.37 | 0.11 | 1.00 | 0.10 | -0.47 | 0.44 | Yes | No |
| Q620P | -0.04 | 0.06 | 0.12 | 0.06 | -0.26 | 0.10 | Yes | No |
| Q620S | 0.17 | 0.05 | -0.15 | 0.06 | 0.16 | 0.17 | Yes | No |
| Q620* | -0.82 | 0.08 | -0.58 | 0.07 | -0.64 | 0.15 | No | No |
| Q620T | -0.20 | 0.09 | 0.41 | 0.08 | 0.17 | 0.12 | Yes | No |
| Q620W | -0.12 | 0.04 | 0.09 | 0.04 | 0.08 | 0.11 | Yes | No |
| Q620Y | -0.74 | 0.14 | 0.21 | 0.11 | -0.19 | 0.38 | Yes | No |
| Q620V | 0.29 | 0.03 | -0.11 | 0.04 | 0.26 | 0.07 | Yes | No |
| T621A | 0.18 | 0.04 | 0.13 | 0.04 | 0.17 | 0.10 | Yes | Yes |
| T621R | -0.04 | 0.04 | -0.45 | 0.05 | -0.06 | 0.15 | No | No |
| T621N | -0.39 | 0.12 | -0.09 | 0.11 | 0.02 | 0.21 | Yes | No |
| T621D | 0.12 | 0.12 | 0.26 | 0.12 | -0.11 | 0.44 | Yes | No |
| T621C | 0.07 | 0.09 | -0.29 | 0.10 | NA | NA | Yes | No |

| Mutant | Enrich. Score (1) | Stand. Error (1) | Enrich. Score (2) | Stand. Error (2) | Enrich. Score (3) | Stand. Error (3) | Any positive enrichment? | Consistent positive enrichment? |
|---|---|---|---|---|---|---|---|---|
| T621Q | -0.90 | 0.12 | 0.06 | 0.10 | 0.44 | 0.38 | Yes | No |
| T621E | -0.29 | 0.07 | 0.13 | 0.06 | -0.05 | 0.24 | Yes | No |
| T621G | -0.02 | 0.03 | -0.21 | 0.04 | 0.48 | 0.04 | Yes | No |
| T621H | 0.33 | 0.15 | 0.72 | 0.14 | NA | NA | Yes | No |
| T621I | 0.36 | 0.08 | -0.09 | 0.10 | 0.21 | 0.20 | Yes | No |
| T621L | 0.16 | 0.06 | -0.40 | 0.07 | -0.30 | 0.10 | Yes | No |
| T621K | -0.02 | 0.09 | -0.09 | 0.09 | -0.08 | 0.37 | No | No |
| T621M | 0.21 | 0.07 | -0.15 | 0.08 | 1.17 | 0.09 | Yes | No |
| T621F | -0.61 | 0.16 | -0.16 | 0.14 | NA | NA | Yes | No |
| T621P | 0.04 | 0.04 | 0.18 | 0.04 | -0.38 | 0.06 | Yes | No |
| T621S | -0.06 | 0.06 | -0.08 | 0.06 | 0.28 | 0.09 | Yes | No |
| T621W | -0.21 | 0.06 | 0.08 | 0.06 | 0.12 | 0.17 | Yes | No |
| T621Y | -0.23 | 0.16 | 0.36 | 0.14 | NA | NA | Yes | No |
| T621V | -0.28 | 0.05 | 0.32 | 0.05 | 0.32 | 0.19 | Yes | No |
| H622G | 0.05 | 0.03 | 0.18 | 0.03 | 0.07 | 0.06 | Yes | Yes |
| H622S | 0.16 | 0.06 | 0.59 | 0.06 | 0.08 | 0.10 | Yes | Yes |
| H622T | 0.01 | 0.09 | 0.84 | 0.08 | 0.31 | 0.34 | Yes | Yes |
| H622V | 0.18 | 0.05 | 0.15 | 0.05 | 0.31 | 0.12 | Yes | Yes |
| H622A | -0.17 | 0.06 | 0.16 | 0.06 | 0.41 | 0.08 | Yes | No |
| H622R | -0.19 | 0.04 | 0.12 | 0.04 | 0.05 | 0.04 | Yes | No |
| H622N | -0.05 | 0.07 | 0.30 | 0.07 | -0.11 | 0.12 | Yes | No |
| H622D | -0.84 | 0.11 | 0.63 | 0.07 | 0.48 | 0.10 | Yes | No |
| H622C | -0.50 | 0.09 | -0.10 | 0.08 | 0.11 | 0.11 | Yes | No |
| H622Q | -0.06 | 0.08 | 0.29 | 0.07 | -0.14 | 0.05 | Yes | No |
| H622E | -0.11 | 0.07 | 0.15 | 0.06 | 0.23 | 0.10 | Yes | No |
| H622I | -0.05 | 0.14 | 0.45 | 0.13 | 0.36 | 0.49 | Yes | No |
| H622L | -0.49 | 0.06 | 0.06 | 0.05 | -0.14 | 0.11 | Yes | No |
| H622K | 0.29 | 0.10 | 1.39 | 0.08 | 0.00 | 0.28 | Yes | No |
| H622M | -0.07 | 0.11 | -0.07 | 0.11 | 0.05 | 0.34 | Yes | No |
| H622F | 0.14 | 0.11 | -0.61 | 0.14 | 0.07 | 0.13 | Yes | No |
| H622P | 0.14 | 0.03 | 0.25 | 0.03 | -0.44 | 0.04 | Yes | No |
| H622* | -1.50 | 0.13 | -1.18 | 0.12 | -0.74 | 0.16 | No | No |
| H622W | 0.08 | 0.05 | 0.21 | 0.05 | -0.08 | 0.19 | Yes | No |
| H622Y | 0.07 | 0.09 | 0.14 | 0.09 | -0.08 | 0.18 | Yes | No |
| T623E | 0.32 | 0.05 | 0.23 | 0.05 | 0.02 | 0.05 | Yes | Yes |
| T623H | 0.60 | 0.10 | 0.01 | 0.11 | 0.58 | 0.55 | Yes | Yes |
| T623L | 0.33 | 0.05 | 0.18 | 0.05 | 0.17 | 0.16 | Yes | Yes |
| T623M | 0.21 | 0.07 | 0.28 | 0.07 | 0.59 | 0.22 | Yes | Yes |
| T623F | 0.80 | 0.10 | 0.61 | 0.10 | 0.47 | 0.32 | Yes | Yes |
| T623A | -0.14 | 0.04 | 0.35 | 0.03 | -0.04 | 0.07 | Yes | No |
| T623R | -0.16 | 0.03 | -0.40 | 0.04 | 0.15 | 0.09 | Yes | No |
| T623N | 0.02 | 0.09 | 0.19 | 0.09 | -0.28 | 0.16 | Yes | No |

| Mutant | Enrich. Score (1) | Stand. Error (1) | Enrich. Score (2) | Stand. Error (2) | Enrich. Score (3) | Stand. Error (3) | Any positive enrichment? | Consistent positive enrichment? |
|---|---|---|---|---|---|---|---|---|
| T623D | -0.69 | 0.09 | 0.41 | 0.07 | -0.34 | 0.14 | Yes | No |
| T623C | -0.39 | 0.08 | 0.01 | 0.08 | 0.40 | 0.28 | Yes | No |
| T623Q | 0.23 | 0.07 | 0.38 | 0.07 | -0.01 | 0.32 | Yes | No |
| T623G | -0.40 | 0.03 | -0.09 | 0.03 | -0.05 | 0.03 | No | No |
| T623I | -0.59 | 0.10 | 0.11 | 0.08 | -0.13 | 0.13 | Yes | No |
| T623K | 1.10 | 0.07 | -0.02 | 0.08 | 0.53 | 0.17 | Yes | No |
| T623P | -0.16 | 0.06 | -0.29 | 0.07 | -0.11 | 0.17 | No | No |
| T623S | 0.67 | 0.04 | 0.21 | 0.04 | -0.06 | 0.07 | Yes | No |
| T623W | -0.01 | 0.05 | -0.29 | 0.06 | -0.27 | 0.10 | No | No |
| T623Y | NA | NA | NA | NA | -0.11 | 0.29 | Yes | No |
| T623V | -0.26 | 0.04 | -0.20 | 0.04 | 0.41 | 0.05 | Yes | No |
| T624P | 0.92 | 0.02 | 0.92 | 0.02 | 0.04 | 0.03 | Yes | Yes |
| T624A | 0.65 | 0.02 | 0.76 | 0.02 | -0.07 | 0.03 | Yes | No |
| T624R | 0.41 | 0.07 | 0.34 | 0.07 | -0.55 | 0.23 | Yes | No |
| T624N | 0.15 | 0.10 | 0.20 | 0.10 | NA | NA | Yes | No |
| T624C | -0.20 | 0.15 | 0.21 | 0.14 | NA | NA | Yes | No |
| T624E | 0.38 | 0.09 | -0.63 | 0.12 | -0.11 | 0.55 | Yes | No |
| T624G | -0.21 | 0.06 | 0.12 | 0.06 | 0.15 | 0.21 | Yes | No |
| T624I | 0.58 | 0.11 | 0.35 | 0.11 | NA | NA | Yes | No |
| T624L | 0.41 | 0.09 | -0.84 | 0.13 | 0.96 | 0.48 | Yes | No |
| T624S | 1.15 | 0.04 | 1.20 | 0.04 | -0.13 | 0.04 | Yes | No |
| T624W | 0.56 | 0.10 | -0.20 | 0.12 | 0.10 | 0.16 | Yes | No |
| T624V | -0.12 | 0.08 | -0.52 | 0.10 | 0.18 | 0.23 | Yes | No |
| P625A | -0.27 | 0.11 | 0.30 | 0.10 | 0.31 | 0.10 | Yes | No |
| P625R | 0.06 | 0.07 | -1.01 | 0.10 | -0.04 | 0.22 | Yes | No |
| P625C | 0.56 | 0.14 | -0.17 | 0.16 | -0.02 | 0.82 | Yes | No |
| P625E | -0.24 | 0.13 | -0.22 | 0.13 | -0.41 | 0.64 | No | No |
| P625G | -0.41 | 0.08 | 0.40 | 0.06 | 0.04 | 0.24 | Yes | No |
| P625H | -0.25 | 0.15 | -0.02 | 0.15 | NA | NA | Yes | No |
| P625L | -0.48 | 0.09 | -0.82 | 0.11 | -0.56 | 0.17 | No | No |
| P625S | -0.38 | 0.08 | -0.55 | 0.09 | 0.03 | 0.20 | Yes | No |
| P625T | 0.30 | 0.08 | 0.23 | 0.08 | -0.06 | 0.10 | Yes | No |
| P625W | -0.60 | 0.13 | -0.64 | 0.13 | NA | NA | Yes | No |
| P625V | -0.17 | 0.09 | -0.63 | 0.11 | NA | NA | Yes | No |
| I626A | 0.16 | 0.12 | 0.80 | 0.11 | NA | NA | Yes | No |
| I626R | -0.89 | 0.12 | 0.14 | 0.09 | -0.09 | 0.31 | Yes | No |
| I626N | 0.42 | 0.04 | 0.61 | 0.04 | -0.37 | 0.06 | Yes | No |
| I626E | NA | NA | NA | NA | -0.15 | 0.55 | Yes | No |
| I626G | -1.04 | 0.10 | -1.35 | 0.12 | -0.48 | 0.27 | No | No |
| I626L | 0.61 | 0.11 | -0.85 | 0.16 | NA | NA | Yes | No |
| I626S | 0.36 | 0.04 | 0.60 | 0.04 | -0.65 | 0.07 | Yes | No |
| I626T | 0.17 | 0.02 | 0.34 | 0.02 | -0.37 | 0.03 | Yes | No |

| Mutant | Enrich. Score (1) | Stand. Error (1) | Enrich. Score (2) | Stand. Error (2) | Enrich. Score (3) | Stand. Error (3) | Any positive enrichment? | Consistent positive enrichment? |
|---|---|---|---|---|---|---|---|---|
| I626W | -0.74 | 0.16 | 0.22 | 0.13 | NA | NA | Yes | No |
| I626V | -0.51 | 0.10 | 0.05 | 0.09 | 0.10 | 0.18 | Yes | No |
| L627C | 0.14 | 0.13 | 0.84 | 0.11 | 0.57 | 0.48 | Yes | Yes |
| L627A | 0.00 | 0.08 | 0.24 | 0.08 | 1.31 | 0.29 | Yes | No |
| L627R | 0.29 | 0.04 | 0.03 | 0.04 | -0.10 | 0.05 | Yes | No |
| L627N | 0.71 | 0.15 | 1.09 | 0.15 | NA | NA | Yes | No |
| L627D | 0.32 | 0.10 | -1.12 | 0.16 | 1.13 | 0.55 | Yes | No |
| L627Q | 0.23 | 0.07 | 0.39 | 0.07 | -0.27 | 0.11 | Yes | No |
| L627E | 0.29 | 0.07 | -0.06 | 0.08 | 0.17 | 0.11 | Yes | No |
| L627G | -0.04 | 0.04 | -0.01 | 0.04 | 0.23 | 0.10 | Yes | No |
| L627K | 0.57 | 0.11 | 0.27 | 0.12 | NA | NA | Yes | No |
| L627M | -0.57 | 0.12 | 0.33 | 0.10 | -0.09 | 0.22 | Yes | No |
| L627P | 0.10 | 0.05 | 0.31 | 0.05 | -0.25 | 0.08 | Yes | No |
| L627S | 0.34 | 0.08 | 0.18 | 0.08 | -0.29 | 0.27 | Yes | No |
| L627* | 0.52 | 0.10 | -0.87 | 0.15 | NA | NA | Yes | No |
| L627T | 0.60 | 0.09 | -0.76 | 0.14 | NA | NA | Yes | No |
| L627W | -0.71 | 0.09 | 0.85 | 0.07 | 0.27 | 0.32 | Yes | No |
| L627V | -0.89 | 0.08 | 0.48 | 0.06 | -0.23 | 0.19 | Yes | No |
| L628C | 0.31 | 0.09 | 0.10 | 0.10 | 0.29 | 0.31 | Yes | Yes |
| L628W | 0.25 | 0.06 | 0.01 | 0.07 | 0.67 | 0.15 | Yes | Yes |
| L628A | -0.22 | 0.06 | -0.58 | 0.07 | -0.36 | 0.11 | No | No |
| L628R | -0.13 | 0.04 | -0.50 | 0.05 | 0.53 | 0.06 | Yes | No |
| L628Q | -0.10 | 0.10 | -0.04 | 0.10 | -0.36 | 0.23 | No | No |
| L628E | -0.73 | 0.10 | -1.59 | 0.14 | NA | NA | Yes | No |
| L628G | -0.65 | 0.04 | -1.57 | 0.06 | -0.96 | 0.14 | No | No |
| L628I | -0.47 | 0.17 | -0.57 | 0.17 | NA | NA | Yes | No |
| L628K | 0.75 | 0.11 | -0.44 | 0.15 | -0.21 | 0.31 | Yes | No |
| L628M | -0.49 | 0.09 | -0.37 | 0.09 | -0.21 | 0.12 | No | No |
| L628P | -0.27 | 0.08 | -0.45 | 0.08 | -0.39 | 0.14 | No | No |
| L628S | -0.78 | 0.08 | -1.36 | 0.10 | -0.83 | 0.21 | No | No |
| L628T | -0.16 | 0.10 | -0.52 | 0.12 | -0.60 | 0.27 | No | No |
| L628V | -0.13 | 0.05 | 0.34 | 0.05 | -0.31 | 0.09 | Yes | No |
| S629A | -0.99 | 0.12 | 0.49 | 0.08 | -0.09 | 0.29 | Yes | No |
| S629R | 0.10 | 0.02 | 0.29 | 0.02 | -0.37 | 0.03 | Yes | No |
| S629N | 0.40 | 0.05 | 0.36 | 0.05 | -0.32 | 0.08 | Yes | No |
| S629D | -0.54 | 0.18 | -0.23 | 0.17 | NA | NA | Yes | No |
| S629C | 0.30 | 0.10 | 0.10 | 0.11 | -0.08 | 0.21 | Yes | No |
| S629Q | 0.76 | 0.17 | 0.40 | 0.18 | NA | NA | Yes | No |
| S629E | 0.84 | 0.10 | 0.61 | 0.11 | -0.08 | 0.48 | Yes | No |
| S629G | -0.30 | 0.05 | 0.40 | 0.05 | 0.09 | 0.08 | Yes | No |
| S629I | 0.05 | 0.14 | 0.42 | 0.13 | NA | NA | Yes | No |
| S629L | NA | NA | NA | NA | 0.03 | 0.36 | Yes | No |

| Mutant | Enrich. Score (1) | Stand. Error (1) | Enrich. Score (2) | Stand. Error (2) | Enrich. Score (3) | Stand. Error (3) | Any positive enrichment? | Consistent positive enrichment? |
|---|---|---|---|---|---|---|---|---|
| S629K | 0.37 | 0.13 | 0.80 | 0.12 | NA | NA | Yes | No |
| S629P | -0.03 | 0.15 | -0.34 | 0.17 | NA | NA | Yes | No |
| S629T | -0.60 | 0.13 | 0.01 | 0.11 | 0.22 | 0.32 | Yes | No |
| S629W | -0.03 | 0.11 | -0.66 | 0.13 | 0.42 | 0.54 | Yes | No |
| S629V | -0.87 | 0.11 | -0.82 | 0.11 | 0.05 | 0.14 | Yes | No |
| N630R | 0.53 | 0.05 | 0.06 | 0.06 | 0.94 | 0.08 | Yes | Yes |
| N630A | -0.53 | 0.09 | 0.62 | 0.07 | -0.06 | 0.23 | Yes | No |
| N630D | -0.33 | 0.09 | 0.49 | 0.07 | -0.22 | 0.14 | Yes | No |
| N630C | 0.42 | 0.10 | -0.12 | 0.12 | NA | NA | Yes | No |
| N630E | -0.67 | 0.09 | 0.69 | 0.07 | -0.30 | 0.26 | Yes | No |
| N630G | 0.32 | 0.04 | -0.11 | 0.04 | 0.22 | 0.10 | Yes | No |
| N630H | 0.06 | 0.10 | 0.51 | 0.09 | -0.29 | 0.13 | Yes | No |
| N630I | -0.45 | 0.12 | 0.44 | 0.10 | -0.27 | 0.18 | Yes | No |
| N630L | -0.24 | 0.09 | 0.55 | 0.08 | -0.78 | 0.15 | Yes | No |
| N630K | 0.37 | 0.10 | 0.93 | 0.09 | -0.25 | 0.18 | Yes | No |
| N630F | -0.58 | 0.18 | -0.11 | 0.16 | NA | NA | Yes | No |
| N630S | 0.34 | 0.06 | -0.21 | 0.07 | 0.16 | 0.13 | Yes | No |
| N630T | 0.16 | 0.03 | 0.38 | 0.02 | -0.53 | 0.04 | Yes | No |
| N630W | -0.11 | 0.09 | -1.04 | 0.12 | NA | NA | Yes | No |
| N630Y | -0.24 | 0.12 | 0.59 | 0.10 | 0.14 | 0.19 | Yes | No |
| N630V | -0.20 | 0.06 | -0.90 | 0.08 | -0.26 | 0.18 | No | No |
| N631A | -0.03 | 0.07 | 0.06 | 0.07 | -0.70 | 0.25 | Yes | No |
| N631R | -0.11 | 0.06 | 0.27 | 0.05 | 1.20 | 0.07 | Yes | No |
| N631D | -0.56 | 0.10 | -0.38 | 0.09 | -0.77 | 0.13 | No | No |
| N631C | -0.71 | 0.15 | -0.64 | 0.15 | NA | NA | Yes | No |
| N631E | NA | NA | NA | NA | -0.95 | 0.23 | Yes | No |
| N631G | -0.67 | 0.05 | -0.39 | 0.05 | -1.02 | 0.07 | No | No |
| N631I | 0.31 | 0.10 | -0.62 | 0.13 | NA | NA | Yes | No |
| N631L | -1.12 | 0.10 | -0.57 | 0.08 | NA | NA | Yes | No |
| N631K | -0.05 | 0.08 | -0.20 | 0.09 | 0.70 | 0.11 | Yes | No |
| N631M | -0.10 | 0.10 | 0.36 | 0.09 | -0.27 | 0.30 | Yes | No |
| N631P | 0.06 | 0.12 | 0.30 | 0.12 | NA | NA | Yes | No |
| N631S | 0.15 | 0.06 | 0.06 | 0.06 | -0.36 | 0.13 | Yes | No |
| N631T | 0.07 | 0.04 | 0.24 | 0.04 | -0.37 | 0.05 | Yes | No |
| N631Y | -0.48 | 0.12 | -0.03 | 0.11 | NA | NA | Yes | No |
| N631V | -0.66 | 0.07 | -1.17 | 0.08 | -0.78 | 0.23 | No | No |
| F632A | -0.79 | 0.07 | -1.34 | 0.09 | -1.29 | 0.12 | No | No |
| F632R | -0.76 | 0.05 | -0.40 | 0.05 | -0.13 | 0.05 | No | No |
| F632D | -1.62 | 0.15 | -1.61 | 0.15 | NA | NA | Yes | No |
| F632C | 0.66 | 0.02 | 0.78 | 0.02 | -0.06 | 0.02 | Yes | No |
| F632Q | NA | NA | NA | NA | -0.18 | 0.55 | Yes | No |
| F632E | -1.35 | 0.10 | -0.87 | 0.09 | NA | NA | Yes | No |

| Mutant | Enrich. Score (1) | Stand. Error (1) | Enrich. Score (2) | Stand. Error (2) | Enrich. Score (3) | Stand. Error (3) | Any positive enrichment? | Consistent positive enrichment? |
|---|---|---|---|---|---|---|---|---|
| F632G | -0.01 | 0.03 | 0.12 | 0.03 | -0.03 | 0.02 | Yes | No |
| F632H | -0.31 | 0.16 | 0.08 | 0.15 | NA | NA | Yes | No |
| F632I | -0.33 | 0.10 | -0.01 | 0.10 | -0.87 | 0.13 | No | No |
| F632L | -0.28 | 0.05 | 0.22 | 0.05 | -0.26 | 0.07 | Yes | No |
| F632K | -0.49 | 0.13 | 0.74 | 0.10 | NA | NA | Yes | No |
| F632M | 0.00 | 0.10 | 0.16 | 0.10 | NA | NA | Yes | No |
| F632S | -0.75 | 0.06 | -0.56 | 0.06 | -0.83 | 0.06 | No | No |
| F632* | -0.69 | 0.12 | -0.55 | 0.12 | NA | NA | Yes | No |
| F632T | -0.09 | 0.09 | -0.80 | 0.12 | NA | NA | Yes | No |
| F632W | 0.17 | 0.06 | -0.14 | 0.06 | -0.44 | 0.19 | Yes | No |
| F632Y | -0.15 | 0.08 | 0.38 | 0.07 | -0.07 | 0.10 | Yes | No |
| F632V | 0.38 | 0.02 | 0.41 | 0.02 | -0.07 | 0.02 | Yes | No |
| I633N | 0.16 | 0.06 | 0.65 | 0.06 | 0.15 | 0.10 | Yes | Yes |
| I633M | 0.17 | 0.07 | 0.28 | 0.07 | 0.10 | 0.19 | Yes | Yes |
| I633S | 0.02 | 0.04 | 0.35 | 0.04 | 0.22 | 0.08 | Yes | Yes |
| I633A | 0.15 | 0.05 | -0.24 | 0.06 | 0.42 | 0.13 | Yes | No |
| I633R | -0.42 | 0.04 | 0.41 | 0.04 | 0.22 | 0.06 | Yes | No |
| I633D | -0.62 | 0.09 | -0.01 | 0.08 | -0.12 | 0.10 | No | No |
| I633C | 0.15 | 0.07 | -0.34 | 0.08 | -0.04 | 0.14 | Yes | No |
| I633Q | -0.26 | 0.10 | 1.05 | 0.08 | -0.37 | 0.22 | Yes | No |
| I633E | -0.98 | 0.07 | -0.34 | 0.06 | 0.30 | 0.11 | Yes | No |
| I633G | -0.09 | 0.03 | 0.10 | 0.03 | 0.05 | 0.06 | Yes | No |
| I633H | -0.71 | 0.14 | -0.16 | 0.13 | NA | NA | Yes | No |
| I633L | -0.10 | 0.05 | 0.00 | 0.05 | 0.25 | 0.06 | Yes | No |
| I633K | -0.29 | 0.09 | 0.17 | 0.08 | 0.63 | 0.29 | Yes | No |
| I633F | -0.11 | 0.09 | 0.24 | 0.09 | 0.51 | 0.22 | Yes | No |
| I633P | 0.23 | 0.08 | -0.90 | 0.12 | 0.19 | 0.31 | Yes | No |
| I633* | -1.45 | 0.12 | -1.53 | 0.13 | NA | NA | Yes | No |
| I633T | 0.13 | 0.04 | 0.40 | 0.04 | -0.17 | 0.06 | Yes | No |
| I633W | -0.35 | 0.05 | 0.14 | 0.05 | -0.07 | 0.09 | Yes | No |
| I633Y | NA | NA | NA | NA | -0.09 | 0.34 | Yes | No |
| I633V | 0.09 | 0.04 | -0.06 | 0.04 | 0.39 | 0.06 | Yes | No |
| E634N | 0.52 | 0.12 | 0.46 | 0.12 | 0.00 | 0.36 | Yes | Yes |
| E634A | 0.20 | 0.02 | 0.38 | 0.02 | -0.36 | 0.03 | Yes | No |
| E634R | -0.06 | 0.04 | 0.30 | 0.04 | 0.33 | 0.08 | Yes | No |
| E634D | -0.10 | 0.06 | 0.30 | 0.06 | 0.01 | 0.10 | Yes | No |
| E634C | -0.12 | 0.08 | -0.30 | 0.09 | 0.42 | 0.13 | Yes | No |
| E634Q | -0.28 | 0.09 | 0.79 | 0.07 | 0.35 | 0.10 | Yes | No |
| E634G | -0.12 | 0.03 | 0.10 | 0.02 | 0.33 | 0.03 | Yes | No |
| E634I | 0.43 | 0.13 | -0.05 | 0.15 | NA | NA | Yes | No |
| E634L | 0.12 | 0.05 | -0.46 | 0.06 | 0.47 | 0.19 | Yes | No |
| E634K | 0.14 | 0.06 | -0.04 | 0.07 | 0.16 | 0.13 | Yes | No |

| Mutant | Enrich. Score (1) | Stand. Error (1) | Enrich. Score (2) | Stand. Error (2) | Enrich. Score (3) | Stand. Error (3) | Any positive enrichment? | Consistent positive enrichment? |
|---|---|---|---|---|---|---|---|---|
| E634M | -0.14 | 0.08 | -0.22 | 0.08 | 0.42 | 0.27 | Yes | No |
| E634F | 0.25 | 0.14 | 0.08 | 0.15 | NA | NA | Yes | No |
| E634P | -0.23 | 0.10 | -0.95 | 0.13 | NA | NA | Yes | No |
| E634S | -0.22 | 0.06 | 0.07 | 0.05 | 0.30 | 0.07 | Yes | No |
| E634* | 0.11 | 0.03 | 0.29 | 0.03 | -0.34 | 0.05 | Yes | No |
| E634T | 0.01 | 0.09 | 0.30 | 0.08 | -0.51 | 0.28 | Yes | No |
| E634W | -0.46 | 0.06 | 0.16 | 0.05 | 0.45 | 0.17 | Yes | No |
| E634V | -0.20 | 0.04 | 0.26 | 0.04 | 0.33 | 0.08 | Yes | No |
| P635A | 0.04 | 0.05 | 0.29 | 0.05 | 0.59 | 0.07 | Yes | Yes |
| P635D | 0.14 | 0.09 | 0.49 | 0.09 | 0.52 | 0.14 | Yes | Yes |
| P635E | 0.51 | 0.06 | 0.49 | 0.06 | 0.70 | 0.16 | Yes | Yes |
| P635T | 0.36 | 0.06 | 0.06 | 0.06 | 0.01 | 0.08 | Yes | Yes |
| P635R | -0.51 | 0.04 | -0.39 | 0.04 | 0.24 | 0.08 | Yes | No |
| P635N | 0.13 | 0.14 | -0.31 | 0.16 | NA | NA | Yes | No |
| P635C | -0.65 | 0.10 | -0.70 | 0.11 | 0.26 | 0.25 | Yes | No |
| P635Q | -0.86 | 0.12 | -0.40 | 0.11 | 0.43 | 0.38 | Yes | No |
| P635G | -0.01 | 0.03 | -0.02 | 0.03 | 0.15 | 0.06 | Yes | No |
| P635H | -0.05 | 0.10 | 0.20 | 0.09 | 0.22 | 0.07 | Yes | No |
| P635I | NA | NA | NA | NA | 0.13 | 0.37 | Yes | No |
| P635L | -0.02 | 0.05 | -0.33 | 0.06 | 0.22 | 0.10 | Yes | No |
| P635K | NA | NA | NA | NA | 0.18 | 0.41 | Yes | No |
| P635M | 0.96 | 0.08 | -0.61 | 0.12 | 0.06 | 0.31 | Yes | No |
| P635F | 1.00 | 0.11 | 0.14 | 0.13 | NA | NA | Yes | No |
| P635S | -0.22 | 0.06 | 0.35 | 0.05 | 0.02 | 0.12 | Yes | No |
| P635W | -0.24 | 0.06 | 0.25 | 0.06 | -0.12 | 0.20 | Yes | No |
| P635Y | -0.31 | 0.15 | -0.01 | 0.14 | NA | NA | Yes | No |
| P635V | -0.06 | 0.05 | -0.29 | 0.05 | 0.44 | 0.20 | Yes | No |
| L636A | -0.52 | 0.05 | -1.17 | 0.06 | 0.08 | 0.11 | Yes | No |
| L636R | -1.28 | 0.04 | -1.29 | 0.04 | -1.27 | 0.08 | No | No |
| L636C | -0.14 | 0.07 | -0.19 | 0.07 | -0.07 | 0.17 | No | No |
| L636Q | -0.25 | 0.05 | -0.09 | 0.05 | -0.16 | 0.09 | No | No |
| L636E | -1.02 | 0.07 | -0.96 | 0.07 | -1.27 | 0.21 | No | No |
| L636G | -1.44 | 0.04 | -1.31 | 0.04 | -1.36 | 0.06 | No | No |
| L636I | -0.87 | 0.13 | -0.24 | 0.11 | NA | NA | Yes | No |
| L636K | -0.17 | 0.08 | -0.33 | 0.09 | -1.00 | 0.28 | No | No |
| L636M | -0.40 | 0.07 | -0.08 | 0.06 | 0.16 | 0.16 | Yes | No |
| L636F | -0.45 | 0.10 | 0.29 | 0.09 | NA | NA | Yes | No |
| L636P | 0.24 | 0.05 | -0.84 | 0.06 | -0.88 | 0.11 | Yes | No |
| L636S | -1.62 | 0.07 | -1.47 | 0.07 | -0.73 | 0.15 | No | No |
| L636* | -1.09 | 0.10 | -1.51 | 0.12 | NA | NA | Yes | No |
| L636T | 0.12 | 0.06 | -2.04 | 0.13 | -0.41 | 0.09 | Yes | No |
| L636W | -0.55 | 0.05 | -1.36 | 0.06 | -0.68 | 0.11 | No | No |

| Mutant | Enrich. Score (1) | Stand. Error (1) | Enrich. Score (2) | Stand. Error (2) | Enrich. Score (3) | Stand. Error (3) | Any positive enrichment? | Consistent positive enrichment? |
|---|---|---|---|---|---|---|---|---|
| L636V | -0.35 | 0.04 | -0.05 | 0.03 | -0.65 | 0.08 | No | No |
| E637A | 0.15 | 0.04 | 0.23 | 0.04 | -0.25 | 0.07 | Yes | No |
| E637R | -0.23 | 0.07 | 1.02 | 0.06 | 0.18 | 0.32 | Yes | No |
| E637D | -0.88 | 0.14 | -0.01 | 0.11 | NA | NA | Yes | No |
| E637Q | 0.83 | 0.14 | 0.47 | 0.15 | NA | NA | Yes | No |
| E637G | -0.05 | 0.04 | 0.22 | 0.04 | 0.06 | 0.05 | Yes | No |
| E637L | NA | NA | NA | NA | 0.35 | 0.32 | Yes | No |
| E637K | -0.33 | 0.12 | -0.66 | 0.13 | NA | NA | Yes | No |
| E637M | 0.60 | 0.15 | 1.04 | 0.14 | NA | NA | Yes | No |
| E637S | 0.23 | 0.10 | -0.55 | 0.12 | 0.66 | 0.39 | Yes | No |
| E637* | -0.03 | 0.09 | 0.24 | 0.08 | NA | NA | Yes | No |
| E637W | -0.18 | 0.10 | -0.73 | 0.12 | -0.20 | 0.34 | No | No |
| E637V | -0.15 | 0.07 | -0.36 | 0.07 | -0.45 | 0.10 | No | No |
| I638R | -1.56 | 0.13 | -0.55 | 0.10 | NA | NA | Yes | No |
| I638N | 0.35 | 0.16 | 0.42 | 0.16 | -0.63 | 0.15 | Yes | No |
| I638C | 1.11 | 0.14 | -0.05 | 0.17 | NA | NA | Yes | No |
| I638L | NA | NA | NA | NA | -0.24 | 0.30 | Yes | No |
| I638S | 0.04 | 0.05 | 0.05 | 0.05 | -0.18 | 0.05 | Yes | No |
| I638T | -0.43 | 0.12 | -0.42 | 0.12 | -0.14 | 0.18 | No | No |
| I638V | 0.39 | 0.07 | -0.45 | 0.08 | -0.04 | 0.13 | Yes | No |
| T639G | 0.52 | 0.06 | 0.44 | 0.06 | 0.06 | 0.23 | Yes | Yes |
| T639A | 0.25 | 0.05 | 0.47 | 0.05 | -0.34 | 0.06 | Yes | No |
| T639R | -0.48 | 0.10 | -0.68 | 0.11 | -0.16 | 0.35 | No | No |
| T639N | 0.03 | 0.16 | -0.02 | 0.17 | NA | NA | Yes | No |
| T639D | 0.61 | 0.17 | 0.43 | 0.18 | NA | NA | Yes | No |
| T639E | 0.71 | 0.12 | 0.82 | 0.12 | NA | NA | Yes | No |
| T639I | 0.17 | 0.13 | -0.19 | 0.14 | NA | NA | Yes | No |
| T639L | -0.28 | 0.15 | -0.39 | 0.16 | NA | NA | Yes | No |
| T639P | -0.10 | 0.12 | 0.08 | 0.12 | -0.21 | 0.22 | Yes | No |
| T639S | 0.07 | 0.07 | 0.09 | 0.07 | -0.53 | 0.12 | Yes | No |
| T639V | 0.75 | 0.09 | -1.09 | 0.14 | 0.78 | 0.28 | Yes | No |
| K640A | -0.31 | 0.07 | -0.59 | 0.07 | 0.20 | 0.26 | Yes | No |
| K640R | -0.15 | 0.04 | 0.07 | 0.04 | 0.01 | 0.11 | Yes | No |
| K640N | 0.07 | 0.03 | 0.32 | 0.03 | -0.43 | 0.05 | Yes | No |
| K640D | -0.14 | 0.09 | -0.73 | 0.11 | -0.52 | 0.30 | No | No |
| K640C | 0.06 | 0.08 | 0.34 | 0.08 | -0.51 | 0.27 | Yes | No |
| K640Q | -0.86 | 0.12 | 0.36 | 0.09 | 0.29 | 0.31 | Yes | No |
| K640E | -0.30 | 0.06 | 0.08 | 0.06 | -0.03 | 0.15 | Yes | No |
| K640G | -0.26 | 0.04 | -0.59 | 0.04 | -0.48 | 0.12 | No | No |
| K640H | 0.81 | 0.12 | -0.26 | 0.15 | NA | NA | Yes | No |
| K640I | -0.10 | 0.12 | -0.11 | 0.12 | NA | NA | Yes | No |
| K640L | 0.21 | 0.06 | 0.05 | 0.06 | -0.31 | 0.20 | Yes | No |

| Mutant | Enrich. Score (1) | Stand. Error (1) | Enrich. Score (2) | Stand. Error (2) | Enrich. Score (3) | Stand. Error (3) | Any positive enrichment? | Consistent positive enrichment? |
|---|---|---|---|---|---|---|---|---|
| K640M | -1.04 | 0.15 | 0.36 | 0.10 | -0.12 | 0.31 | Yes | No |
| K640F | 0.24 | 0.12 | -0.13 | 0.13 | NA | NA | Yes | No |
| K640P | 0.40 | 0.09 | 0.14 | 0.10 | -0.03 | 0.55 | Yes | No |
| K640S | -0.60 | 0.07 | 0.52 | 0.06 | -0.11 | 0.22 | Yes | No |
| K640* | -0.85 | 0.10 | -0.19 | 0.09 | -0.96 | 0.21 | No | No |
| K640T | 0.10 | 0.03 | 0.35 | 0.03 | -0.52 | 0.06 | Yes | No |
| K640W | -0.53 | 0.07 | 0.41 | 0.06 | 0.12 | 0.25 | Yes | No |
| K640Y | -0.76 | 0.15 | -0.28 | 0.14 | 0.36 | 0.37 | Yes | No |
| K640V | -0.26 | 0.05 | -0.56 | 0.05 | 0.05 | 0.11 | Yes | No |
| D840S | 0.37 | 0.08 | 0.33 | 0.08 | 0.10 | 0.16 | Yes | Yes |
| D840A | -0.07 | 0.07 | 0.40 | 0.06 | 0.18 | 0.13 | Yes | No |
| D840R | -0.03 | 0.05 | 0.09 | 0.05 | 0.10 | 0.33 | Yes | No |
| D840N | -0.64 | 0.12 | -0.31 | 0.11 | -0.04 | 0.16 | No | No |
| D840C | 0.62 | 0.12 | -1.20 | 0.16 | 0.07 | 0.48 | Yes | No |
| D840Q | -0.22 | 0.14 | -0.03 | 0.13 | 0.34 | NA | Yes | No |
| D840E | 0.32 | 0.07 | -0.07 | 0.07 | 0.08 | 0.06 | Yes | No |
| D840G | 0.21 | 0.04 | -0.26 | 0.04 | 0.02 | 0.05 | Yes | No |
| D840L | -0.64 | 0.10 | -0.25 | 0.09 | -0.27 | 0.82 | No | No |
| D840K | 0.13 | 0.13 | 0.33 | 0.12 | -0.03 | 0.82 | Yes | No |
| D840M | NA | NA | NA | NA | -0.30 | 0.13 | Yes | No |
| D840P | -0.09 | 0.12 | -0.12 | 0.12 | 0.11 | 0.82 | Yes | No |
| D840T | -1.14 | 0.14 | 0.11 | 0.10 | 0.29 | 0.15 | Yes | No |
| D840W | -0.33 | 0.09 | 0.05 | 0.08 | -0.39 | 0.19 | Yes | No |
| D840Y | 0.13 | 0.08 | 0.11 | 0.08 | -0.18 | 0.11 | Yes | No |
| D840V | 0.16 | 0.06 | -0.03 | 0.06 | -0.10 | 0.07 | Yes | No |
| E841A | -0.26 | 0.06 | -0.54 | 0.06 | 0.08 | 0.08 | Yes | No |
| E841R | -0.66 | 0.06 | -0.57 | 0.05 | -0.18 | 0.10 | No | No |
| E841N | 0.04 | 0.14 | -0.53 | 0.15 | -0.14 | 0.48 | Yes | No |
| E841D | -0.33 | 0.09 | -0.04 | 0.08 | 0.12 | 0.15 | Yes | No |
| E841C | -0.43 | 0.13 | -0.39 | 0.12 | -0.46 | 0.16 | No | No |
| E841Q | -0.64 | 0.12 | -0.41 | 0.11 | 0.21 | 0.14 | Yes | No |
| E841G | 0.21 | 0.04 | -0.11 | 0.04 | -0.04 | 0.04 | Yes | No |
| E841H | -0.71 | 0.18 | -0.82 | 0.18 | NA | NA | Yes | No |
| E841L | -1.39 | 0.10 | -0.35 | 0.07 | -0.41 | 0.06 | No | No |
| E841K | -0.55 | 0.09 | -0.26 | 0.09 | -0.34 | 0.17 | No | No |
| E841M | -1.21 | 0.14 | -0.41 | 0.11 | -0.24 | 0.54 | No | No |
| E841P | -0.22 | 0.11 | -0.23 | 0.11 | 0.00 | 0.08 | No | No |
| E841S | -0.16 | 0.07 | -0.22 | 0.07 | 0.04 | 0.10 | Yes | No |
| E841* | -0.19 | 0.06 | -0.19 | 0.06 | 0.07 | 0.03 | Yes | No |
| E841T | 0.40 | 0.09 | -0.59 | 0.10 | -0.27 | 0.19 | Yes | No |
| E841W | -1.06 | 0.09 | -1.15 | 0.09 | -1.11 | 0.33 | No | No |
| E841V | -0.99 | 0.07 | -0.68 | 0.06 | -0.53 | 0.08 | No | No |

| Mutant | Enrich. Score (1) | Stand. Error (1) | Enrich. Score (2) | Stand. Error (2) | Enrich. Score (3) | Stand. Error (3) | Any positive enrichment? | Consistent positive enrichment? |
|---|---|---|---|---|---|---|---|---|
| A842S | 0.36 | 0.06 | 0.08 | 0.06 | 0.04 | 0.10 | Yes | Yes |
| A842R | -2.56 | 0.11 | -1.06 | 0.06 | -1.25 | 0.15 | No | No |
| A842D | -0.37 | 0.11 | -1.49 | 0.15 | -1.07 | 0.19 | No | No |
| A842C | 0.15 | 0.10 | -0.39 | 0.11 | -0.26 | 0.13 | Yes | No |
| A842E | NA | NA | NA | NA | -1.19 | 0.12 | Yes | No |
| A842G | -0.18 | 0.04 | -0.18 | 0.04 | -0.09 | 0.04 | No | No |
| A842L | -1.71 | 0.11 | -1.29 | 0.09 | -1.19 | 0.33 | No | No |
| A842K | -0.53 | 0.13 | -1.41 | 0.16 | NA | NA | Yes | No |
| A842P | -0.87 | 0.10 | -0.94 | 0.10 | NA | NA | Yes | No |
| A842T | -1.47 | 0.11 | -0.57 | 0.08 | -1.03 | 0.10 | No | No |
| A842W | -1.87 | 0.12 | -1.92 | 0.12 | -1.46 | 0.40 | No | No |
| A842V | -1.40 | 0.08 | -0.77 | 0.06 | -1.17 | 0.20 | No | No |
| R843A | -0.28 | 0.10 | 0.30 | 0.09 | 0.15 | 0.11 | Yes | No |
| R843E | -1.03 | 0.17 | -1.31 | 0.17 | 0.09 | 0.64 | Yes | No |
| R843G | 0.18 | 0.05 | -0.37 | 0.06 | -0.43 | 0.07 | Yes | No |
| R843L | -0.31 | 0.13 | -0.08 | 0.12 | -0.05 | 0.30 | No | No |
| R843K | -0.16 | 0.13 | 0.01 | 0.12 | 0.45 | 0.16 | Yes | No |
| R843M | NA | NA | NA | NA | 0.26 | 0.83 | Yes | No |
| R843S | -0.08 | 0.07 | 0.08 | 0.07 | -0.08 | 0.10 | Yes | No |
| R843* | -0.64 | 0.17 | -0.23 | 0.15 | NA | NA | Yes | No |
| R843T | NA | NA | NA | NA | -0.19 | 0.30 | Yes | No |
| R843W | -0.99 | 0.15 | 0.22 | 0.12 | -0.55 | 0.14 | Yes | No |
| R843V | -0.09 | 0.10 | -0.23 | 0.10 | 0.04 | 0.17 | Yes | No |
| A844E | 0.38 | 0.10 | 0.06 | 0.10 | 0.13 | 0.21 | Yes | Yes |
| A844R | 0.45 | 0.07 | -0.04 | 0.07 | 0.03 | 0.37 | Yes | No |
| A844D | NA | NA | NA | NA | 0.36 | 0.11 | Yes | No |
| A844C | NA | NA | NA | NA | 0.02 | 0.19 | Yes | No |
| A844Q | -0.26 | 0.18 | 0.84 | 0.15 | -0.11 | 0.44 | Yes | No |
| A844G | -0.48 | 0.06 | -0.26 | 0.05 | -0.01 | 0.06 | No | No |
| A844L | 0.54 | 0.10 | -0.25 | 0.11 | 0.18 | 0.14 | Yes | No |
| A844K | NA | NA | NA | NA | 0.14 | 0.27 | Yes | No |
| A844M | NA | NA | NA | NA | 0.23 | 0.41 | Yes | No |
| A844P | 0.28 | 0.11 | -1.04 | 0.14 | -0.72 | 0.25 | Yes | No |
| A844S | -0.22 | 0.08 | -0.06 | 0.07 | 0.17 | 0.10 | Yes | No |
| A844T | -0.37 | 0.11 | -0.05 | 0.10 | 0.22 | 0.21 | Yes | No |
| A844W | -1.01 | 0.13 | -0.64 | 0.11 | -0.10 | NA | No | No |
| A844V | -0.19 | 0.08 | 0.12 | 0.07 | 0.06 | 0.08 | Yes | No |
| L845A | -0.70 | 0.08 | -0.23 | 0.07 | -0.59 | 0.11 | No | No |
| L845R | -2.01 | 0.10 | -1.83 | 0.09 | -1.29 | 0.05 | No | No |
| L845C | -0.27 | 0.14 | -0.84 | 0.15 | -0.37 | 0.82 | No | No |
| L845Q | NA | NA | NA | NA | -0.49 | 0.25 | Yes | No |
| L845E | -0.93 | 0.12 | -1.26 | 0.13 | -0.79 | 0.48 | No | No |

| Mutant | Enrich. Score (1) | Stand. Error (1) | Enrich. Score (2) | Stand. Error (2) | Enrich. Score (3) | Stand. Error (3) | Any positive enrichment? | Consistent positive enrichment? |
|---|---|---|---|---|---|---|---|---|
| L845G | -1.31 | 0.06 | -1.09 | 0.06 | -1.46 | 0.20 | No | No |
| L845K | -0.17 | 0.18 | 0.03 | 0.17 | NA | NA | Yes | No |
| L845M | -0.15 | 0.12 | -0.17 | 0.12 | -0.20 | 0.25 | No | No |
| L845P | -0.64 | 0.10 | -0.71 | 0.10 | -0.61 | 0.11 | No | No |
| L845S | -1.48 | 0.13 | -0.91 | 0.10 | -0.82 | 0.35 | No | No |
| L845T | -0.85 | 0.14 | 0.43 | 0.11 | NA | NA | Yes | No |
| L845W | -0.12 | 0.08 | -1.89 | 0.13 | -0.47 | 0.33 | No | No |
| L845V | -0.31 | 0.06 | -0.80 | 0.07 | -0.20 | 0.10 | No | No |
| L846A | -1.10 | 0.08 | -0.78 | 0.07 | -0.78 | 0.82 | No | No |
| L846R | -0.86 | 0.06 | -0.85 | 0.05 | -1.09 | 0.11 | No | No |
| L846C | -1.57 | 0.15 | -1.32 | 0.13 | -0.93 | 0.14 | No | No |
| L846Q | -1.21 | 0.15 | -0.87 | 0.13 | -0.99 | 0.27 | No | No |
| L846E | -0.34 | 0.08 | -0.41 | 0.08 | -0.71 | 0.17 | No | No |
| L846G | -1.11 | 0.05 | -0.81 | 0.05 | -1.29 | 0.15 | No | No |
| L846I | NA | NA | NA | NA | 0.11 | 0.49 | Yes | No |
| L846M | -0.29 | 0.09 | 0.19 | 0.08 | -0.28 | 0.13 | Yes | No |
| L846F | -0.48 | 0.14 | -0.27 | 0.13 | NA | NA | Yes | No |
| L846P | -1.04 | 0.10 | -0.74 | 0.09 | -0.74 | 0.13 | No | No |
| L846S | -0.77 | 0.09 | -0.24 | 0.08 | -1.23 | 0.37 | No | No |
| L846T | -0.74 | 0.12 | -1.37 | 0.14 | -0.56 | 0.12 | No | No |
| L846W | -1.13 | 0.09 | -0.51 | 0.08 | -0.35 | 0.06 | No | No |
| L846Y | -0.02 | 0.16 | -0.98 | 0.19 | NA | NA | Yes | No |
| L846V | -1.23 | 0.07 | -0.61 | 0.06 | -0.40 | 0.06 | No | No |
| P847A | 0.24 | 0.11 | -1.48 | 0.16 | NA | NA | Yes | No |
| P847R | -0.47 | 0.09 | -0.88 | 0.10 | -1.09 | 0.26 | No | No |
| P847G | -0.32 | 0.07 | -1.12 | 0.08 | -0.48 | 0.43 | No | No |
| P847H | -0.24 | 0.18 | -0.19 | 0.17 | -0.10 | 0.18 | No | No |
| P847L | -1.09 | 0.12 | -0.92 | 0.11 | -0.76 | 0.15 | No | No |
| P847S | -0.42 | 0.11 | -0.55 | 0.11 | -0.76 | 0.23 | No | No |
| P847T | -0.69 | 0.19 | -0.89 | 0.19 | NA | NA | Yes | No |
| P847V | -0.31 | 0.12 | -1.08 | 0.14 | NA | NA | Yes | No |
| N848A | -0.53 | 0.11 | 0.02 | 0.10 | 0.14 | 0.43 | Yes | No |
| N848R | -0.30 | 0.07 | -0.60 | 0.07 | -0.35 | 0.10 | No | No |
| N848D | 0.06 | 0.11 | -0.08 | 0.11 | -0.13 | 0.15 | Yes | No |
| N848C | -0.16 | 0.14 | -0.15 | 0.14 | -0.31 | NA | No | No |
| N848Q | -0.31 | 0.18 | -0.55 | 0.19 | NA | NA | Yes | No |
| N848E | -0.64 | 0.11 | 0.35 | 0.09 | 0.48 | 0.09 | Yes | No |
| N848G | -0.87 | 0.07 | -0.40 | 0.06 | -0.33 | 0.11 | No | No |
| N848H | -0.07 | 0.05 | 0.05 | 0.05 | -0.06 | 0.05 | Yes | No |
| N848I | 0.00 | 0.17 | -0.09 | 0.17 | NA | NA | Yes | No |
| N848L | 0.08 | 0.10 | -1.50 | 0.14 | -0.10 | NA | Yes | No |
| N848K | -0.25 | 0.14 | -0.45 | 0.14 | -0.20 | 0.19 | No | No |

| Mutant | Enrich. Score (1) | Stand. Error (1) | Enrich. Score (2) | Stand. Error (2) | Enrich. Score (3) | Stand. Error (3) | Any positive enrichment? | Consistent positive enrichment? |
|---|---|---|---|---|---|---|---|---|
| N848M | NA | NA | NA | NA | 0.10 | 0.64 | Yes | No |
| N848S | -0.89 | 0.10 | -0.37 | 0.08 | -0.30 | 0.16 | No | No |
| N848T | 0.37 | 0.12 | -0.11 | 0.12 | -0.17 | 0.11 | Yes | No |
| N848W | -0.76 | 0.12 | -0.04 | 0.10 | 0.22 | 0.40 | Yes | No |
| N848Y | -0.61 | 0.18 | 0.16 | 0.16 | -0.20 | 0.24 | Yes | No |
| N848V | -0.51 | 0.09 | -0.84 | 0.10 | -0.29 | 0.64 | No | No |
| V849A | -0.93 | 0.12 | 0.41 | 0.09 | -0.39 | 0.18 | Yes | No |
| V849R | -1.79 | 0.16 | -1.96 | 0.16 | -1.01 | 0.29 | No | No |
| V849G | -1.07 | 0.08 | -1.40 | 0.08 | -1.48 | 0.05 | No | No |
| V849L | 0.90 | 0.09 | -0.43 | 0.11 | -0.12 | 0.13 | Yes | No |
| V849M | -0.12 | 0.12 | -0.31 | 0.12 | -0.19 | 0.19 | No | No |
| I850A | 0.25 | 0.05 | -0.76 | 0.06 | -0.17 | 0.06 | Yes | No |
| I850R | -0.32 | 0.04 | -0.27 | 0.04 | -0.21 | 0.06 | No | No |
| I850N | -0.38 | 0.13 | -0.44 | 0.13 | -0.50 | 0.10 | No | No |
| I850D | -1.19 | 0.12 | -0.73 | 0.10 | -0.71 | 0.54 | No | No |
| I850C | -0.30 | 0.08 | 0.19 | 0.08 | 0.13 | 0.14 | Yes | No |
| I850Q | -0.08 | 0.11 | -0.31 | 0.11 | 0.00 | 0.43 | No | No |
| I850E | -0.24 | 0.07 | -0.45 | 0.07 | -0.35 | 0.25 | No | No |
| I850G | -0.90 | 0.04 | -0.86 | 0.04 | -0.96 | 0.06 | No | No |
| I850H | 0.45 | 0.12 | -0.44 | 0.13 | -0.29 | 0.54 | Yes | No |
| I850L | -0.15 | 0.04 | -0.17 | 0.04 | -0.26 | 0.05 | No | No |
| I850K | -1.20 | 0.13 | -0.19 | 0.10 | -0.01 | 0.82 | No | No |
| I850M | -0.83 | 0.09 | -0.82 | 0.09 | -0.28 | 0.18 | No | No |
| I850F | -0.83 | 0.11 | -0.97 | 0.11 | -0.61 | 0.17 | No | No |
| I850P | -0.43 | 0.09 | -1.72 | 0.12 | -1.01 | 0.12 | No | No |
| I850S | -0.42 | 0.06 | -0.18 | 0.05 | -0.52 | 0.06 | No | No |
| I850T | 0.00 | 0.07 | -0.22 | 0.07 | 0.06 | 0.07 | Yes | No |
| I850W | -1.02 | 0.07 | -1.26 | 0.08 | -0.97 | 0.10 | No | No |
| I850V | -0.03 | 0.04 | 0.12 | 0.04 | 0.22 | 0.05 | Yes | No |
| T851A | 0.41 | 0.06 | 0.14 | 0.06 | 0.08 | 0.10 | Yes | Yes |
| T851V | 0.32 | 0.06 | 0.13 | 0.06 | 0.54 | 0.07 | Yes | Yes |
| T851R | -0.18 | 0.06 | -0.82 | 0.06 | -0.93 | 0.17 | No | No |
| T851C | 0.00 | 0.14 | -0.03 | 0.14 | -0.11 | 0.82 | No | No |
| T851Q | NA | NA | NA | NA | -0.17 | 0.29 | Yes | No |
| T851E | -0.44 | 0.09 | -0.88 | 0.10 | -0.08 | 0.08 | No | No |
| T851G | -1.22 | 0.06 | -0.82 | 0.05 | -0.95 | 0.19 | No | No |
| T851I | 0.21 | 0.13 | -0.17 | 0.13 | 0.20 | 0.20 | Yes | No |
| T851L | 0.35 | 0.08 | 0.01 | 0.09 | -0.05 | 0.37 | Yes | No |
| T851K | -0.23 | 0.14 | -0.49 | 0.14 | NA | NA | Yes | No |
| T851M | 0.52 | 0.11 | -0.71 | 0.14 | -0.02 | 0.23 | Yes | No |
| T851F | -0.32 | 0.18 | 0.44 | 0.16 | 0.28 | NA | Yes | No |
| T851P | -0.06 | 0.04 | 0.04 | 0.04 | 0.03 | 0.05 | Yes | No |

| Mutant | Enrich. Score (1) | Stand. Error (1) | Enrich. Score (2) | Stand. Error (2) | Enrich. Score (3) | Stand. Error (3) | Any positive enrichment? | Consistent positive enrichment? |
|---|---|---|---|---|---|---|---|---|
| T851S | -0.01 | 0.07 | -0.04 | 0.07 | -0.08 | 0.13 | No | No |
| T851W | 0.07 | 0.09 | -0.34 | 0.09 | -0.01 | 0.48 | Yes | No |
| K852A | -1.49 | 0.14 | -1.41 | 0.13 | NA | NA | Yes | No |
| K852R | -0.07 | 0.06 | -0.48 | 0.07 | -0.37 | 0.10 | No | No |
| K852N | 0.12 | 0.10 | -0.39 | 0.11 | 0.01 | 0.08 | Yes | No |
| K852Q | -0.04 | 0.05 | 0.10 | 0.04 | 0.14 | 0.06 | Yes | No |
| K852E | -0.99 | 0.12 | -0.80 | 0.11 | -1.03 | 0.07 | No | No |
| K852G | -1.42 | 0.09 | -2.60 | 0.13 | -1.20 | 0.18 | No | No |
| K852P | -0.25 | 0.07 | -0.24 | 0.07 | -0.22 | 0.08 | No | No |
| K852S | -1.14 | 0.13 | -0.56 | 0.10 | -0.56 | 0.48 | No | No |
| K852* | -0.98 | 0.15 | -1.24 | 0.16 | NA | NA | Yes | No |
| K852T | -0.16 | 0.03 | -0.02 | 0.03 | 0.16 | 0.04 | Yes | No |
| K852V | -0.65 | 0.09 | -0.18 | 0.08 | -0.78 | 0.48 | No | No |
| E853V | 0.14 | 0.07 | 0.10 | 0.07 | 0.38 | 0.09 | Yes | Yes |
| E853A | -0.49 | 0.08 | -0.35 | 0.08 | -0.05 | 0.09 | No | No |
| E853R | 0.23 | 0.06 | -0.13 | 0.06 | -0.20 | 0.31 | Yes | No |
| E853D | -0.30 | 0.10 | -0.26 | 0.10 | 0.42 | 0.18 | Yes | No |
| E853C | 0.07 | 0.11 | 0.12 | 0.11 | -0.24 | 0.13 | Yes | No |
| E853Q | -0.55 | 0.17 | 0.09 | 0.14 | 0.17 | 0.31 | Yes | No |
| E853G | -0.18 | 0.04 | -0.41 | 0.05 | -0.47 | 0.07 | No | No |
| E853L | -0.85 | 0.10 | 0.03 | 0.08 | 0.08 | 0.08 | Yes | No |
| E853K | 0.05 | 0.12 | -0.95 | 0.15 | 0.21 | 0.20 | Yes | No |
| E853M | -0.08 | 0.15 | -0.94 | 0.17 | 0.01 | 0.11 | Yes | No |
| E853P | 0.46 | 0.13 | -0.02 | 0.14 | 0.28 | 0.40 | Yes | No |
| E853S | -0.30 | 0.09 | -0.41 | 0.09 | 0.07 | 0.15 | Yes | No |
| E853* | -0.52 | 0.09 | -0.38 | 0.09 | -0.25 | 0.08 | No | No |
| E853T | -0.33 | 0.15 | -0.61 | 0.15 | 0.57 | 0.25 | Yes | No |
| E853W | 0.25 | 0.08 | -1.68 | 0.12 | -0.52 | 0.14 | Yes | No |
| V854A | -0.95 | 0.08 | -0.31 | 0.06 | -0.94 | 0.15 | No | No |
| V854R | -1.42 | 0.07 | -1.14 | 0.06 | -1.31 | 0.13 | No | No |
| V854D | -0.58 | 0.13 | -1.22 | 0.15 | NA | NA | Yes | No |
| V854C | -0.91 | 0.13 | -0.17 | 0.11 | -0.54 | 0.35 | No | No |
| V854E | -1.32 | 0.11 | -1.01 | 0.09 | -1.15 | 0.18 | No | No |
| V854G | -1.40 | 0.06 | -1.44 | 0.06 | -1.28 | 0.09 | No | No |
| V854L | -1.49 | 0.10 | -0.60 | 0.07 | -1.28 | 0.13 | No | No |
| V854M | -1.32 | 0.13 | -1.02 | 0.11 | -0.94 | 0.16 | No | No |
| V854P | -1.29 | 0.16 | -1.22 | 0.15 | NA | NA | Yes | No |
| V854S | -1.58 | 0.12 | -0.89 | 0.09 | -1.26 | 0.21 | No | No |
| V854W | -1.48 | 0.10 | -0.37 | 0.07 | -1.34 | 0.06 | No | No |
| S855A | 0.70 | 0.10 | -0.77 | 0.12 | 0.01 | 0.40 | Yes | No |
| S855R | 0.40 | 0.10 | -0.66 | 0.11 | 0.61 | 0.12 | Yes | No |
| S855C | -0.24 | 0.17 | 0.37 | 0.15 | NA | NA | Yes | No |

| Mutant | Enrich. Score (1) | Stand. Error (1) | Enrich. Score (2) | Stand. Error (2) | Enrich. Score (3) | Stand. Error (3) | Any positive enrichment? | Consistent positive enrichment? |
|---|---|---|---|---|---|---|---|---|
| S855G | 0.01 | 0.07 | -0.69 | 0.08 | -0.49 | 0.48 | Yes | No |
| S855L | NA | NA | NA | NA | -0.20 | 0.82 | Yes | No |
| S855F | -0.02 | 0.17 | 0.31 | 0.16 | NA | NA | Yes | No |
| S855P | -0.31 | 0.12 | 0.14 | 0.10 | -0.08 | 0.16 | Yes | No |
| S855T | 0.53 | 0.13 | -0.42 | 0.15 | 0.41 | 0.24 | Yes | No |
| S855Y | NA | NA | NA | NA | 0.21 | 0.29 | Yes | No |
| S855V | 0.17 | 0.13 | 0.00 | 0.14 | 0.24 | 0.82 | Yes | No |
| H856R | -0.04 | 0.07 | -0.29 | 0.07 | -0.62 | 0.16 | No | No |
| H856N | -1.01 | 0.17 | -0.62 | 0.15 | NA | NA | Yes | No |
| H856E | -0.49 | 0.12 | -0.23 | 0.11 | NA | NA | Yes | No |
| H856G | -0.96 | 0.07 | -1.35 | 0.07 | -1.43 | 0.08 | No | No |
| H856L | -0.83 | 0.12 | -0.29 | 0.10 | -0.42 | 0.20 | No | No |
| H856P | -0.26 | 0.09 | 0.07 | 0.09 | -0.29 | 0.09 | Yes | No |
| H856S | -1.39 | 0.17 | -0.13 | 0.12 | NA | NA | Yes | No |
| H856W | NA | NA | NA | NA | -0.62 | 0.17 | Yes | No |
| H856Y | -0.65 | 0.16 | -0.05 | 0.13 | 0.50 | 0.20 | Yes | No |
| H856V | NA | NA | NA | NA | -0.60 | 0.21 | Yes | No |
| E857A | -0.23 | 0.05 | -0.30 | 0.05 | -0.51 | 0.06 | No | No |
| E857R | -0.92 | 0.06 | -1.30 | 0.06 | -1.05 | 0.13 | No | No |
| E857D | 0.50 | 0.09 | -0.31 | 0.10 | -1.09 | 0.21 | Yes | No |
| E857C | -0.44 | 0.13 | -1.14 | 0.15 | -0.59 | 0.40 | No | No |
| E857Q | -0.89 | 0.14 | -1.04 | 0.14 | -0.73 | 0.29 | No | No |
| E857G | -0.98 | 0.04 | -0.90 | 0.04 | -1.19 | 0.03 | No | No |
| E857L | -0.09 | 0.08 | -0.75 | 0.09 | -0.99 | 0.22 | No | No |
| E857K | 0.23 | 0.09 | -0.93 | 0.11 | -0.76 | 0.14 | Yes | No |
| E857M | -0.36 | 0.13 | -0.31 | 0.12 | NA | NA | Yes | No |
| E857P | -0.10 | 0.11 | -0.53 | 0.12 | -0.58 | 0.54 | No | No |
| E857S | -0.17 | 0.08 | -0.67 | 0.08 | -0.71 | 0.16 | No | No |
| E857* | -1.28 | 0.15 | -0.53 | 0.12 | NA | NA | Yes | No |
| E857T | -1.10 | 0.14 | 0.08 | 0.10 | -0.09 | 0.54 | Yes | No |
| E857W | -0.75 | 0.08 | -1.02 | 0.08 | -1.03 | 0.15 | No | No |
| E857V | -0.10 | 0.05 | -0.43 | 0.05 | -0.29 | 0.08 | No | No |
| I858R | -1.30 | 0.11 | -1.37 | 0.10 | -1.32 | 0.24 | No | No |
| I858G | -2.03 | 0.11 | -0.89 | 0.07 | -1.33 | 0.09 | No | No |
| I858L | -0.32 | 0.08 | -0.64 | 0.08 | -0.25 | 0.08 | No | No |
| I858F | -0.53 | 0.17 | -0.64 | 0.17 | NA | NA | Yes | No |
| I858S | -1.55 | 0.16 | -0.66 | 0.12 | NA | NA | Yes | No |
| I858T | -0.49 | 0.13 | -0.72 | 0.13 | -0.26 | 0.20 | No | No |
| I858V | -0.43 | 0.08 | -0.43 | 0.08 | -0.69 | 0.11 | No | No |
| I859A | -2.25 | 0.14 | -1.44 | 0.10 | -0.96 | 0.35 | No | No |
| I859R | -1.46 | 0.08 | -1.27 | 0.07 | -1.13 | 0.07 | No | No |
| I859N | -0.63 | 0.17 | -0.59 | 0.16 | -0.31 | 0.21 | No | No |

| Mutant | Enrich. Score (1) | Stand. Error (1) | Enrich. Score (2) | Stand. Error (2) | Enrich. Score (3) | Stand. Error (3) | Any positive enrichment? | Consistent positive enrichment? |
|---|---|---|---|---|---|---|---|---|
| I859D | -1.17 | 0.15 | -1.53 | 0.16 | NA | NA | Yes | No |
| I859Q | -0.35 | 0.17 | 0.41 | 0.15 | NA | NA | Yes | No |
| I859E | -0.25 | 0.09 | -0.09 | 0.08 | -0.48 | 0.11 | No | No |
| I859G | -1.65 | 0.07 | -1.30 | 0.06 | -1.32 | 0.22 | No | No |
| I859L | -0.20 | 0.04 | -0.01 | 0.04 | -0.26 | 0.04 | No | No |
| I859M | -0.66 | 0.12 | 0.38 | 0.10 | -0.64 | 0.11 | Yes | No |
| I859F | -0.18 | 0.12 | -0.15 | 0.12 | -0.59 | 0.12 | No | No |
| I859S | -0.34 | 0.08 | -1.05 | 0.09 | -1.12 | 0.17 | No | No |
| I859T | -0.26 | 0.09 | -0.27 | 0.09 | -0.35 | 0.15 | No | No |
| I859W | -1.84 | 0.15 | -0.31 | 0.09 | -0.74 | 0.64 | No | No |
| I859V | 0.30 | 0.04 | -0.13 | 0.05 | 0.24 | 0.05 | Yes | No |
| K860A | -0.50 | 0.06 | -0.35 | 0.06 | -1.06 | 0.07 | No | No |
| K860R | -0.39 | 0.05 | -0.83 | 0.05 | -0.83 | 0.10 | No | No |
| K860N | -0.63 | 0.12 | -1.47 | 0.14 | -0.88 | 0.16 | No | No |
| K860C | -0.36 | 0.10 | -0.81 | 0.11 | NA | NA | Yes | No |
| K860Q | -0.18 | 0.04 | -0.19 | 0.04 | -0.15 | 0.06 | No | No |
| K860E | -0.89 | 0.06 | -1.15 | 0.07 | -1.08 | 0.05 | No | No |
| K860G | -1.23 | 0.05 | -1.22 | 0.05 | -1.28 | 0.06 | No | No |
| K860L | -0.68 | 0.07 | -1.58 | 0.09 | -1.19 | 0.11 | No | No |
| K860M | -0.24 | 0.09 | -0.56 | 0.09 | -1.00 | 0.15 | No | No |
| K860P | -0.21 | 0.07 | -0.49 | 0.07 | -0.50 | 0.09 | No | No |
| K860S | -1.38 | 0.08 | -1.80 | 0.09 | -1.30 | 0.07 | No | No |
| K860* | -1.43 | 0.12 | -1.23 | 0.11 | -1.17 | 0.16 | No | No |
| K860T | -0.15 | 0.04 | -0.15 | 0.04 | -0.07 | 0.06 | No | No |
| K860W | -1.18 | 0.08 | -1.46 | 0.09 | -1.24 | 0.09 | No | No |
| K860V | -0.88 | 0.06 | -1.87 | 0.08 | -1.03 | 0.04 | No | No |
| D861A | -0.47 | 0.05 | -0.76 | 0.06 | -1.12 | 0.11 | No | No |
| D861R | -1.43 | 0.06 | -1.83 | 0.06 | -1.24 | 0.09 | No | No |
| D861N | -0.46 | 0.10 | -0.59 | 0.10 | -0.60 | 0.17 | No | No |
| D861C | -0.40 | 0.08 | -0.50 | 0.08 | -0.69 | 0.08 | No | No |
| D861Q | -0.65 | 0.11 | 0.09 | 0.09 | NA | NA | Yes | No |
| D861E | -0.97 | 0.07 | -0.89 | 0.06 | -0.50 | 0.12 | No | No |
| D861G | -0.85 | 0.03 | -1.00 | 0.03 | -1.03 | 0.03 | No | No |
| D861H | 0.92 | 0.12 | -0.60 | 0.15 | -0.36 | 0.21 | Yes | No |
| D861L | -0.37 | 0.07 | 0.09 | 0.06 | -0.18 | 0.27 | Yes | No |
| D861K | 0.55 | 0.09 | -1.49 | 0.13 | -1.22 | 0.43 | Yes | No |
| D861M | -0.29 | 0.10 | -0.57 | 0.10 | -0.68 | 0.40 | No | No |
| D861F | -1.05 | 0.15 | -0.55 | 0.13 | -0.22 | 0.12 | No | No |
| D861S | -1.43 | 0.09 | -1.60 | 0.09 | -1.45 | 0.28 | No | No |
| D861W | -0.88 | 0.07 | -0.84 | 0.07 | -0.15 | 0.08 | No | No |
| D861Y | -0.18 | 0.17 | 0.14 | 0.16 | -0.35 | 0.14 | Yes | No |
| D861V | -1.18 | 0.06 | -0.99 | 0.05 | -1.28 | 0.12 | No | No |

| Mutant | Enrich. Score (1) | Stand. Error (1) | Enrich. Score (2) | Stand. Error (2) | Enrich. Score (3) | Stand. Error (3) | Any positive enrichment? | Consistent positive enrichment? |
|---|---|---|---|---|---|---|---|---|
| R862K | 0.04 | 0.14 | 0.54 | 0.13 | 0.02 | 0.38 | Yes | Yes |
| R862A | -1.76 | 0.13 | -0.42 | 0.08 | -0.71 | 0.31 | No | No |
| R862C | -0.64 | 0.12 | -1.78 | 0.16 | -0.65 | 0.28 | No | No |
| R862Q | -0.27 | 0.10 | -0.07 | 0.09 | -0.28 | 0.13 | No | No |
| R862E | -0.64 | 0.12 | -1.63 | 0.15 | -0.76 | 0.09 | No | No |
| R862G | -0.72 | 0.05 | -0.83 | 0.05 | -0.85 | 0.07 | No | No |
| R862L | -0.90 | 0.08 | -0.16 | 0.07 | -0.39 | 0.09 | No | No |
| R862M | -1.06 | 0.17 | -0.69 | 0.15 | NA | NA | Yes | No |
| R862P | -1.33 | 0.17 | -1.10 | 0.15 | NA | NA | Yes | No |
| R862W | -1.35 | 0.11 | -0.91 | 0.09 | -1.10 | 0.14 | No | No |
| R862V | NA | NA | NA | NA | -1.61 | 0.43 | Yes | No |
| R863Q | -0.49 | 0.13 | -0.79 | 0.14 | NA | NA | Yes | No |
| R863G | -1.68 | 0.09 | -1.14 | 0.07 | -1.45 | 0.07 | No | No |
| R863L | -1.18 | 0.15 | -1.68 | 0.17 | -1.02 | 0.13 | No | No |
| R863W | -1.27 | 0.11 | -1.06 | 0.10 | -1.17 | 0.14 | No | No |
| F864I | -0.25 | 0.11 | -0.08 | 0.11 | -0.19 | 0.12 | No | No |
| F864L | 0.01 | 0.07 | -0.06 | 0.07 | 0.06 | 0.08 | Yes | No |
| F864S | -0.34 | 0.14 | -0.27 | 0.14 | -0.35 | 0.17 | No | No |
| F864W | -0.66 | 0.18 | -0.77 | 0.18 | NA | NA | Yes | No |
| F864V | -0.11 | 0.06 | -0.13 | 0.05 | 0.00 | 0.08 | No | No |
| T865A | -0.65 | 0.14 | -0.29 | 0.12 | -0.09 | 0.18 | No | No |
| T865N | 0.07 | 0.03 | -0.05 | 0.03 | -0.15 | 0.04 | Yes | No |
| T865I | -0.01 | 0.10 | 0.20 | 0.09 | 0.20 | 0.13 | Yes | No |
| T865L | NA | NA | NA | NA | 0.57 | 0.29 | Yes | No |
| T865P | -0.10 | 0.05 | -0.07 | 0.05 | -0.01 | 0.06 | No | No |
| T865S | -0.20 | 0.02 | -0.20 | 0.02 | 0.01 | 0.03 | Yes | No |
| T865Y | -0.16 | 0.06 | -0.17 | 0.05 | -0.16 | 0.10 | No | No |
| S866F | 0.00 | 0.13 | 0.06 | 0.12 | 0.10 | 0.14 | Yes | Yes |
| S866T | 0.05 | 0.13 | 0.02 | 0.13 | 0.40 | 0.15 | Yes | Yes |
| S866A | -0.10 | 0.09 | -0.40 | 0.10 | 0.05 | 0.07 | Yes | No |
| S866R | NA | NA | NA | NA | -0.33 | 0.09 | Yes | No |
| S866D | NA | NA | NA | NA | 0.02 | 0.24 | Yes | No |
| S866C | NA | NA | NA | NA | -0.05 | 0.43 | Yes | No |
| S866Q | NA | NA | NA | NA | -0.04 | 0.27 | Yes | No |
| S866E | NA | NA | NA | NA | 0.58 | 0.22 | Yes | No |
| S866G | NA | NA | NA | NA | -0.97 | 0.29 | Yes | No |
| S866L | NA | NA | NA | NA | 0.57 | 0.10 | Yes | No |
| S866M | NA | NA | NA | NA | 0.85 | 0.14 | Yes | No |
| S866P | 0.08 | 0.03 | -0.07 | 0.03 | 0.00 | 0.03 | Yes | No |
| S866W | NA | NA | NA | NA | -0.67 | 0.37 | Yes | No |
| S866Y | 0.13 | 0.16 | -0.17 | 0.17 | 0.03 | 0.11 | Yes | No |
| S866V | NA | NA | NA | NA | 1.00 | 0.08 | Yes | No |

| Mutant | Enrich. Score (1) | Stand. Error (1) | Enrich. Score (2) | Stand. Error (2) | Enrich. Score (3) | Stand. Error (3) | Any positive enrichment? | Consistent positive enrichment? |
|---|---|---|---|---|---|---|---|---|
| D867A | 0.05 | 0.02 | -0.05 | 0.02 | -0.05 | 0.02 | Yes | No |
| D867R | NA | NA | NA | NA | -1.39 | 0.06 | Yes | No |
| D867N | NA | NA | NA | NA | -0.17 | 0.14 | Yes | No |
| D867C | NA | NA | NA | NA | -0.98 | 0.17 | Yes | No |
| D867E | -0.16 | 0.11 | -0.21 | 0.11 | -0.99 | 0.09 | No | No |
| D867G | 0.06 | 0.02 | 0.00 | 0.02 | -0.11 | 0.02 | Yes | No |
| D867H | -0.04 | 0.09 | 0.11 | 0.08 | NA | NA | Yes | No |
| D867S | NA | NA | NA | NA | -0.98 | 0.09 | Yes | No |
| D867W | NA | NA | NA | NA | -1.25 | 0.13 | Yes | No |
| D867Y | NA | NA | NA | NA | -1.02 | 0.12 | Yes | No |
| D867V | -0.04 | 0.10 | -0.07 | 0.10 | -0.92 | 0.07 | No | No |
| K868A | NA | NA | NA | NA | -1.23 | 0.28 | Yes | No |
| K868R | -0.01 | 0.02 | 0.02 | 0.02 | -0.76 | 0.04 | Yes | No |
| K868N | NA | NA | NA | NA | -1.00 | 0.11 | Yes | No |
| K868Q | -0.14 | 0.09 | -0.02 | 0.09 | -0.11 | 0.08 | No | No |
| K868E | -0.43 | 0.19 | -0.52 | 0.19 | -1.33 | 0.19 | No | No |
| K868G | NA | NA | NA | NA | -1.49 | 0.08 | Yes | No |
| K868P | NA | NA | NA | NA | -1.00 | 0.09 | Yes | No |
| K868S | NA | NA | NA | NA | -1.32 | 0.15 | Yes | No |
| K868* | NA | NA | NA | NA | -1.02 | 0.18 | Yes | No |
| K868T | -0.15 | 0.03 | -0.12 | 0.03 | -0.14 | 0.07 | No | No |
| K868W | NA | NA | NA | NA | -1.50 | 0.15 | Yes | No |
| K868V | NA | NA | NA | NA | -1.12 | 0.16 | Yes | No |
| F869A | NA | NA | NA | NA | -1.10 | 0.15 | Yes | No |
| F869R | NA | NA | NA | NA | -1.47 | 0.27 | Yes | No |
| F869C | NA | NA | NA | NA | -1.20 | 0.15 | Yes | No |
| F869E | NA | NA | NA | NA | -1.41 | 0.09 | Yes | No |
| F869G | NA | NA | NA | NA | -1.40 | 0.04 | Yes | No |
| F869I | 0.06 | 0.10 | -0.10 | 0.10 | 0.04 | 0.09 | Yes | No |
| F869L | -0.16 | 0.03 | -0.17 | 0.03 | -0.01 | 0.06 | No | No |
| F869M | NA | NA | NA | NA | 0.14 | 0.09 | Yes | No |
| F869S | NA | NA | NA | NA | -1.16 | 0.09 | Yes | No |
| F869W | NA | NA | NA | NA | -1.32 | 0.12 | Yes | No |
| F869Y | NA | NA | NA | NA | -0.21 | 0.24 | Yes | No |
| F869V | -0.16 | 0.05 | -0.18 | 0.05 | -0.62 | 0.05 | No | No |
| L870A | -0.86 | 0.11 | -0.83 | 0.10 | NA | NA | Yes | No |
| L870R | -1.55 | 0.08 | -1.55 | 0.07 | NA | NA | Yes | No |
| L870E | -1.23 | 0.14 | -1.60 | 0.15 | NA | NA | Yes | No |
| L870G | -1.54 | 0.07 | -1.47 | 0.07 | NA | NA | Yes | No |
| L870M | -0.94 | 0.16 | -1.13 | 0.17 | NA | NA | Yes | No |
| L870F | -1.01 | 0.07 | -0.78 | 0.07 | NA | NA | Yes | No |
| L870P | -0.29 | 0.06 | -0.36 | 0.06 | NA | NA | Yes | No |

| Mutant | Enrich. Score (1) | Stand. Error (1) | Enrich. Score (2) | Stand. Error (2) | Enrich. Score (3) | Stand. Error (3) | Any positive enrichment? | Consistent positive enrichment? |
|---|---|---|---|---|---|---|---|---|
| L870V | -0.67 | 0.08 | -0.82 | 0.08 | NA | NA | Yes | No |
| F870A | NA | NA | NA | NA | -1.06 | 0.37 | Yes | No |
| F870R | NA | NA | NA | NA | -1.61 | 0.14 | Yes | No |
| F870C | NA | NA | NA | NA | -0.66 | 0.43 | Yes | No |
| F870G | NA | NA | NA | NA | -1.20 | 0.19 | Yes | No |
| F870I | NA | NA | NA | NA | 0.71 | 0.17 | Yes | No |
| F870L | NA | NA | NA | NA | 1.11 | 0.06 | Yes | No |
| F870M | NA | NA | NA | NA | -0.04 | 0.44 | Yes | No |
| F870S | NA | NA | NA | NA | -0.82 | 0.17 | Yes | No |
| F870V | NA | NA | NA | NA | 0.05 | 0.09 | Yes | No |
| F871R | NA | NA | NA | NA | -1.55 | 0.28 | Yes | No |
| F871C | -0.24 | 0.17 | -0.04 | 0.16 | NA | NA | Yes | No |
| F871G | NA | NA | NA | NA | -1.08 | 0.22 | Yes | No |
| F871L | -0.17 | 0.07 | -0.16 | 0.07 | -0.50 | 0.08 | No | No |
| F871S | NA | NA | NA | NA | -0.74 | 0.12 | Yes | No |
| F871V | 0.19 | 0.12 | -0.06 | 0.12 | -0.68 | 0.22 | Yes | No |
| H872R | -0.49 | 0.19 | -0.27 | 0.18 | -1.33 | 0.16 | No | No |
| H872Q | -0.40 | 0.10 | -0.32 | 0.10 | -0.60 | 0.11 | No | No |
| H872G | NA | NA | NA | NA | -1.61 | 0.11 | Yes | No |
| H872L | 0.00 | 0.08 | -0.15 | 0.08 | -0.43 | 0.08 | No | No |
| H872P | 0.04 | 0.02 | -0.01 | 0.02 | 0.34 | 0.02 | Yes | No |
| H872Y | NA | NA | NA | NA | 0.10 | 0.21 | Yes | No |
| H872V | NA | NA | NA | NA | -1.51 | 0.48 | Yes | No |
| V873A | 0.16 | 0.11 | 0.05 | 0.11 | 0.08 | 0.16 | Yes | Yes |
| V873E | -0.40 | 0.14 | -0.35 | 0.14 | NA | NA | Yes | No |
| V873G | -0.13 | 0.04 | -0.20 | 0.03 | -0.27 | 0.07 | No | No |
| V873L | -0.20 | 0.05 | 0.24 | 0.05 | -0.40 | 0.08 | Yes | No |
| V873M | -0.48 | 0.12 | -0.33 | 0.11 | -0.16 | 0.16 | No | No |
| P874A | -0.12 | 0.06 | 0.06 | 0.06 | 0.03 | 0.11 | Yes | No |
| P874G | NA | NA | NA | NA | -0.22 | 0.17 | Yes | No |
| P874S | -0.06 | 0.10 | -0.17 | 0.10 | 0.58 | 0.11 | Yes | No |
| P874T | -0.23 | 0.06 | -0.24 | 0.06 | -0.09 | 0.04 | No | No |
| I875R | -0.33 | 0.12 | -0.24 | 0.11 | -0.82 | 0.10 | No | No |
| I875N | -0.01 | 0.07 | -0.09 | 0.07 | 0.03 | 0.08 | Yes | No |
| I875G | NA | NA | NA | NA | -1.64 | 0.10 | Yes | No |
| I875H | 0.10 | 0.11 | -0.01 | 0.11 | -0.25 | 0.11 | Yes | No |
| I875L | 0.08 | 0.02 | 0.02 | 0.02 | -0.08 | 0.02 | Yes | No |
| I875M | -0.44 | 0.17 | -0.26 | 0.16 | 0.05 | 0.17 | Yes | No |
| I875F | -0.20 | 0.09 | -0.13 | 0.09 | -0.12 | 0.10 | No | No |
| I875S | -0.06 | 0.07 | -0.04 | 0.07 | -0.22 | 0.07 | No | No |
| I875T | -0.01 | 0.10 | -0.10 | 0.09 | -0.11 | 0.11 | No | No |
| I875V | -0.24 | 0.17 | -0.16 | 0.16 | -0.44 | 0.10 | No | No |

| Mutant | Enrich. Score (1) | Stand. Error (1) | Enrich. Score (2) | Stand. Error (2) | Enrich. Score (3) | Stand. Error (3) | Any positive enrichment? | Consistent positive enrichment? |
|---|---|---|---|---|---|---|---|---|
| T876A | NA | NA | NA | NA | -1.21 | 0.20 | Yes | No |
| T876R | NA | NA | NA | NA | -1.72 | 0.26 | Yes | No |
| T876N | -0.10 | 0.03 | -0.09 | 0.03 | -0.07 | 0.05 | No | No |
| T876G | NA | NA | NA | NA | -1.44 | 0.22 | Yes | No |
| T876P | -0.03 | 0.06 | -0.07 | 0.06 | -0.30 | 0.05 | No | No |
| T876S | NA | NA | NA | NA | -0.63 | 0.19 | Yes | No |
| T876V | NA | NA | NA | NA | -1.34 | 0.33 | Yes | No |
| L877A | 0.09 | 0.12 | -0.51 | 0.13 | NA | NA | Yes | No |
| L877R | -0.89 | 0.08 | -1.39 | 0.09 | -1.53 | 0.08 | No | No |
| L877C | -0.26 | 0.17 | -0.47 | 0.17 | NA | NA | Yes | No |
| L877Q | -0.43 | 0.11 | -0.45 | 0.11 | -0.39 | 0.13 | No | No |
| L877G | -1.42 | 0.09 | -2.38 | 0.13 | -1.74 | 0.35 | No | No |
| L877P | -0.08 | 0.07 | -0.22 | 0.07 | -0.40 | 0.12 | No | No |
| L877S | -1.11 | 0.16 | -0.99 | 0.15 | NA | NA | Yes | No |
| L877V | -1.25 | 0.14 | 0.04 | 0.10 | -0.96 | 0.08 | Yes | No |
| L877A | -0.03 | 0.10 | -0.76 | 0.11 | NA | NA | Yes | No |
| L877R | -0.15 | 0.04 | -0.31 | 0.04 | -0.02 | 0.04 | No | No |
| L877C | -0.29 | 0.15 | -0.65 | 0.15 | NA | NA | Yes | No |
| L877Q | -0.26 | 0.11 | -0.47 | 0.11 | NA | NA | Yes | No |
| L877E | NA | NA | NA | NA | -0.74 | 0.64 | Yes | No |
| L877G | -1.40 | 0.08 | -2.82 | 0.12 | -1.79 | 0.22 | No | No |
| L877M | -0.19 | 0.11 | 0.18 | 0.10 | 0.26 | 0.10 | Yes | No |
| L877P | -0.28 | 0.09 | -0.39 | 0.08 | -0.46 | 0.15 | No | No |
| L877S | -1.31 | 0.14 | -1.01 | 0.12 | NA | NA | Yes | No |
| L877V | -1.10 | 0.10 | -0.29 | 0.08 | -0.58 | 0.06 | No | No |
| N878D | 0.03 | 0.06 | 0.02 | 0.06 | 0.04 | 0.08 | Yes | Yes |
| N878A | 0.17 | 0.16 | -0.41 | 0.17 | -0.06 | 0.25 | Yes | No |
| N878Q | -0.22 | 0.17 | -0.53 | 0.17 | NA | NA | Yes | No |
| N878E | -0.73 | 0.15 | -0.44 | 0.13 | -0.84 | 0.13 | No | No |
| N878G | -0.57 | 0.10 | -0.98 | 0.11 | -0.70 | 0.06 | No | No |
| N878H | -0.01 | 0.05 | -0.10 | 0.05 | 0.03 | 0.05 | Yes | No |
| N878L | NA | NA | NA | NA | -0.13 | 0.64 | Yes | No |
| N878K | -0.01 | 0.02 | -0.05 | 0.02 | -0.06 | 0.02 | No | No |
| N878S | -1.08 | 0.15 | -0.43 | 0.12 | -0.38 | 0.10 | No | No |
| N878T | -0.16 | 0.06 | 0.09 | 0.06 | 0.15 | 0.07 | Yes | No |
| N878Y | -0.05 | 0.07 | 0.00 | 0.06 | 0.06 | 0.04 | Yes | No |
| N878V | -1.01 | 0.17 | -0.32 | 0.14 | -0.19 | 0.34 | No | No |
| N878A | 0.03 | 0.14 | -0.32 | 0.14 | -0.19 | 0.54 | Yes | No |
| N878D | -0.11 | 0.12 | -0.34 | 0.12 | -0.62 | 0.15 | No | No |
| N878C | NA | NA | NA | NA | 0.58 | 0.42 | Yes | No |
| N878G | -0.62 | 0.10 | -1.09 | 0.11 | -0.81 | 0.05 | No | No |
| N878I | -0.35 | 0.16 | -0.02 | 0.15 | -0.41 | 0.17 | No | No |

| Mutant | Enrich. Score (1) | Stand. Error (1) | Enrich. Score (2) | Stand. Error (2) | Enrich. Score (3) | Stand. Error (3) | Any positive enrichment? | Consistent positive enrichment? |
|---|---|---|---|---|---|---|---|---|
| N878L | NA | NA | NA | NA | -0.12 | 0.82 | Yes | No |
| N878K | -0.34 | 0.13 | -0.40 | 0.13 | -0.39 | 0.08 | No | No |
| N878M | NA | NA | NA | NA | 0.25 | 0.16 | Yes | No |
| N878S | -0.54 | 0.11 | -0.30 | 0.10 | -0.50 | 0.07 | No | No |
| N878T | -0.19 | 0.05 | -0.20 | 0.05 | -0.37 | 0.09 | No | No |
| N878Y | -0.34 | 0.18 | -0.28 | 0.17 | -0.12 | 0.21 | No | No |
| N878V | -0.98 | 0.15 | -0.37 | 0.12 | -0.51 | 0.32 | No | No |
| Y879A | -2.04 | 0.15 | -1.14 | 0.10 | NA | NA | Yes | No |
| Y879R | -0.78 | 0.08 | -1.40 | 0.08 | -1.48 | 0.11 | No | No |
| Y879D | 0.39 | 0.05 | -0.19 | 0.06 | -0.18 | 0.07 | Yes | No |
| Y879C | 0.50 | 0.06 | -0.02 | 0.07 | -0.50 | 0.09 | Yes | No |
| Y879Q | -0.72 | 0.19 | -0.38 | 0.17 | NA | NA | Yes | No |
| Y879E | -1.40 | 0.13 | -1.23 | 0.11 | NA | NA | Yes | No |
| Y879G | -0.58 | 0.05 | -1.93 | 0.07 | -1.84 | 0.23 | No | No |
| Y879H | 0.35 | 0.09 | 0.04 | 0.09 | -0.16 | 0.12 | Yes | No |
| Y879L | -1.45 | 0.13 | 0.26 | 0.08 | -1.39 | 0.33 | Yes | No |
| Y879K | 0.13 | 0.14 | -1.11 | 0.17 | NA | NA | Yes | No |
| Y879F | -0.05 | 0.12 | -0.01 | 0.11 | 0.01 | 0.17 | Yes | No |
| Y879S | 0.37 | 0.04 | -0.29 | 0.04 | -0.43 | 0.07 | Yes | No |
| Y879* | -0.20 | 0.11 | 0.92 | 0.09 | -0.81 | 0.15 | Yes | No |
| Y879W | -0.05 | 0.08 | -0.07 | 0.07 | 0.60 | 0.07 | Yes | No |
| Y879V | -0.53 | 0.08 | -0.97 | 0.08 | NA | NA | Yes | No |
| Q880R | 0.13 | 0.05 | 0.02 | 0.05 | 0.01 | 0.06 | Yes | Yes |
| Q880G | 0.25 | 0.04 | 0.19 | 0.04 | 0.64 | 0.05 | Yes | Yes |
| Q880A | -0.10 | 0.08 | 0.40 | 0.07 | -0.19 | 0.20 | Yes | No |
| Q880D | 0.81 | 0.14 | -1.10 | 0.18 | NA | NA | Yes | No |
| Q880C | -0.08 | 0.14 | -1.19 | 0.17 | 0.17 | 0.14 | Yes | No |
| Q880E | -0.73 | 0.10 | -1.06 | 0.10 | -0.58 | 0.08 | No | No |
| Q880H | 0.24 | 0.08 | -0.08 | 0.08 | -0.10 | 0.08 | Yes | No |
| Q880L | -0.80 | 0.08 | -0.59 | 0.07 | -1.39 | 0.07 | No | No |
| Q880K | -0.23 | 0.13 | -0.27 | 0.13 | -0.44 | 0.09 | No | No |
| Q880M | -0.93 | 0.16 | -0.77 | 0.14 | -0.49 | 0.17 | No | No |
| Q880P | -0.07 | 0.10 | -0.40 | 0.10 | 0.12 | 0.07 | Yes | No |
| Q880S | -0.31 | 0.09 | -0.76 | 0.10 | -0.09 | 0.07 | No | No |
| Q880* | -1.27 | 0.14 | -0.76 | 0.11 | -1.05 | 0.11 | No | No |
| Q880T | -0.52 | 0.14 | -0.18 | 0.12 | 0.07 | 0.29 | Yes | No |
| Q880W | -0.68 | 0.08 | -0.91 | 0.08 | -0.82 | 0.06 | No | No |
| Q880V | -1.77 | 0.10 | -0.81 | 0.07 | -0.63 | 0.07 | No | No |
| A881R | -0.95 | 0.07 | -1.75 | 0.08 | -1.43 | 0.18 | No | No |
| A881D | -0.36 | 0.11 | -0.32 | 0.10 | -0.48 | 0.19 | No | No |
| A881C | -0.35 | 0.14 | -0.78 | 0.15 | -0.49 | 0.10 | No | No |
| A881G | 0.14 | 0.04 | 0.32 | 0.04 | -0.41 | 0.04 | Yes | No |

| Mutant | Enrich. Score (1) | Stand. Error (1) | Enrich. Score (2) | Stand. Error (2) | Enrich. Score (3) | Stand. Error (3) | Any positive enrichment? | Consistent positive enrichment? |
|---|---|---|---|---|---|---|---|---|
| A881L | -1.36 | 0.11 | -2.39 | 0.15 | NA | NA | Yes | No |
| A881P | -1.05 | 0.16 | -0.99 | 0.14 | -0.80 | 0.18 | No | No |
| A881S | 0.13 | 0.05 | 0.13 | 0.05 | -0.13 | 0.06 | Yes | No |
| A881T | -0.73 | 0.10 | -0.95 | 0.10 | -0.44 | 0.14 | No | No |
| A881W | -1.25 | 0.12 | -1.48 | 0.12 | NA | NA | Yes | No |
| A881V | -1.66 | 0.09 | -1.28 | 0.07 | -0.91 | 0.08 | No | No |
| A882D | 0.32 | 0.05 | 0.22 | 0.05 | 0.10 | 0.07 | Yes | Yes |
| A882S | 0.11 | 0.12 | 0.14 | 0.11 | 0.23 | 0.22 | Yes | Yes |
| A882R | -0.10 | 0.10 | 0.54 | 0.09 | 0.51 | 0.35 | Yes | No |
| A882G | -0.43 | 0.07 | -0.32 | 0.06 | -0.14 | 0.06 | No | No |
| A882L | -1.02 | 0.19 | 0.32 | 0.14 | NA | NA | Yes | No |
| A882P | -0.12 | 0.14 | -0.11 | 0.13 | -0.12 | 0.24 | No | No |
| A882T | -0.14 | 0.09 | 0.05 | 0.09 | -0.09 | 0.13 | Yes | No |
| A882V | 0.39 | 0.08 | 0.04 | 0.08 | -0.17 | 0.15 | Yes | No |
| N883G | 0.42 | 0.08 | 0.37 | 0.08 | 0.03 | 0.11 | Yes | Yes |
| N883K | 0.12 | 0.16 | 0.23 | 0.16 | 0.16 | 0.10 | Yes | Yes |
| N883A | -0.26 | 0.15 | -1.10 | 0.17 | 0.05 | 0.55 | Yes | No |
| N883R | NA | NA | NA | NA | 0.84 | 0.11 | Yes | No |
| N883D | -0.02 | 0.13 | -0.37 | 0.14 | -0.36 | 0.18 | No | No |
| N883I | 0.00 | 0.16 | 0.08 | 0.15 | -0.37 | 0.12 | Yes | No |
| N883S | 0.08 | 0.10 | 0.04 | 0.10 | -0.13 | 0.09 | Yes | No |
| N883T | 0.27 | 0.11 | -0.02 | 0.11 | -0.21 | 0.12 | Yes | No |
| S884V | 0.05 | 0.11 | 0.61 | 0.10 | 0.03 | 0.14 | Yes | Yes |
| S884A | 0.07 | 0.13 | -0.01 | 0.12 | 0.02 | NA | Yes | No |
| S884R | -0.28 | 0.06 | -0.11 | 0.06 | 0.34 | 0.07 | Yes | No |
| S884N | 0.14 | 0.14 | 0.48 | 0.13 | -0.07 | 0.25 | Yes | No |
| S884C | NA | NA | NA | NA | 0.18 | 0.19 | Yes | No |
| S884E | -0.10 | 0.16 | -0.04 | 0.15 | NA | NA | Yes | No |
| S884G | -0.09 | 0.06 | -0.11 | 0.06 | 0.01 | 0.10 | Yes | No |
| S884L | NA | NA | NA | NA | 0.02 | 0.55 | Yes | No |
| S884T | -0.01 | 0.10 | 0.05 | 0.10 | NA | NA | Yes | No |
| S884W | -0.99 | 0.18 | -0.38 | 0.14 | 0.43 | 0.82 | Yes | No |
| P885A | -0.36 | 0.06 | -0.32 | 0.05 | -0.12 | 0.13 | No | No |
| P885R | -0.03 | 0.04 | -0.89 | 0.05 | 0.00 | 0.06 | Yes | No |
| P885N | -0.47 | 0.17 | -0.73 | 0.17 | NA | NA | Yes | No |
| P885D | -0.73 | 0.12 | -1.21 | 0.12 | -0.83 | 0.35 | No | No |
| P885C | -1.54 | 0.14 | -0.39 | 0.09 | -0.01 | 0.09 | No | No |
| P885Q | -1.26 | 0.18 | -0.04 | 0.13 | -0.65 | 0.33 | No | No |
| P885E | -0.08 | 0.08 | -1.01 | 0.09 | -0.98 | 0.16 | No | No |
| P885G | -1.22 | 0.05 | -0.98 | 0.04 | -0.39 | 0.04 | No | No |
| P885H | -0.06 | 0.13 | -0.41 | 0.13 | 0.09 | 0.12 | Yes | No |
| P885I | NA | NA | NA | NA | -0.01 | 0.44 | Yes | No |

| Mutant | Enrich. Score (1) | Stand. Error (1) | Enrich. Score (2) | Stand. Error (2) | Enrich. Score (3) | Stand. Error (3) | Any positive enrichment? | Consistent positive enrichment? |
|---|---|---|---|---|---|---|---|---|
| P885L | -0.66 | 0.07 | -0.90 | 0.07 | -0.60 | 0.05 | No | No |
| P885K | -0.12 | 0.12 | -0.28 | 0.12 | -0.32 | 0.22 | No | No |
| P885M | -1.32 | 0.15 | -1.01 | 0.13 | -0.52 | 0.13 | No | No |
| P885F | -0.98 | 0.16 | -0.49 | 0.14 | -0.31 | 0.10 | No | No |
| P885S | -0.88 | 0.07 | -0.65 | 0.06 | -0.11 | 0.12 | No | No |
| P885T | -0.35 | 0.04 | -0.29 | 0.04 | 0.03 | 0.05 | Yes | No |
| P885W | -0.76 | 0.07 | -1.20 | 0.08 | -0.94 | 0.23 | No | No |
| P885Y | -0.19 | 0.16 | 0.72 | 0.13 | 0.22 | 0.48 | Yes | No |
| P885V | -0.86 | 0.06 | -0.46 | 0.05 | 0.05 | 0.12 | Yes | No |
| S886L | 0.09 | 0.08 | 0.12 | 0.08 | 0.05 | 0.11 | Yes | Yes |
| S886M | 0.32 | 0.11 | 0.15 | 0.11 | 0.40 | 0.35 | Yes | Yes |
| S886W | 0.23 | 0.07 | 0.01 | 0.07 | 0.70 | 0.19 | Yes | Yes |
| S886A | -0.52 | 0.07 | -0.42 | 0.07 | -0.04 | 0.14 | No | No |
| S886R | 0.12 | 0.04 | -0.08 | 0.04 | 0.36 | 0.04 | Yes | No |
| S886N | 0.34 | 0.10 | -0.34 | 0.11 | -0.03 | 0.14 | Yes | No |
| S886D | 0.60 | 0.10 | -0.69 | 0.12 | NA | NA | Yes | No |
| S886C | 0.11 | 0.09 | -0.64 | 0.09 | 0.34 | 0.23 | Yes | No |
| S886Q | -0.33 | 0.14 | -0.65 | 0.14 | 0.19 | 0.64 | Yes | No |
| S886E | -0.60 | 0.10 | -0.56 | 0.10 | NA | NA | Yes | No |
| S886G | -0.20 | 0.04 | -0.18 | 0.04 | 0.10 | 0.05 | Yes | No |
| S886I | 0.89 | 0.13 | -0.13 | 0.14 | 0.07 | 0.29 | Yes | No |
| S886K | -0.70 | 0.14 | 0.01 | 0.12 | 0.56 | 0.12 | Yes | No |
| S886F | NA | NA | NA | NA | 0.75 | 0.44 | Yes | No |
| S886P | NA | NA | NA | NA | -0.28 | 0.14 | Yes | No |
| S886T | 0.07 | 0.07 | -0.05 | 0.07 | -0.29 | 0.10 | Yes | No |
| S886Y | NA | NA | NA | NA | 0.79 | 0.55 | Yes | No |
| S886V | -0.10 | 0.07 | -0.15 | 0.06 | 0.35 | 0.20 | Yes | No |
| K887A | 0.03 | 0.04 | -0.38 | 0.05 | -0.54 | 0.04 | Yes | No |
| K887R | -0.09 | 0.03 | -0.04 | 0.03 | 0.21 | 0.03 | Yes | No |
| K887N | 0.24 | 0.10 | 0.07 | 0.10 | -0.45 | 0.24 | Yes | No |
| K887D | -1.19 | 0.10 | -0.97 | 0.09 | -1.27 | 0.28 | No | No |
| K887C | -0.76 | 0.08 | 0.16 | 0.07 | -0.59 | 0.06 | Yes | No |
| K887Q | 0.10 | 0.08 | -0.05 | 0.07 | -0.25 | 0.11 | Yes | No |
| K887E | -0.33 | 0.05 | -0.39 | 0.05 | -0.97 | 0.06 | No | No |
| K887G | -0.14 | 0.03 | -0.22 | 0.02 | -0.42 | 0.03 | No | No |
| K887H | -0.04 | 0.12 | -1.21 | 0.15 | -0.21 | 0.40 | No | No |
| K887I | -0.31 | 0.12 | -0.04 | 0.11 | NA | NA | Yes | No |
| K887L | -0.88 | 0.06 | -0.67 | 0.05 | -0.68 | 0.07 | No | No |
| K887M | -0.12 | 0.07 | -0.23 | 0.07 | -0.44 | 0.16 | No | No |
| K887F | 0.22 | 0.11 | -0.22 | 0.11 | -0.74 | 0.25 | Yes | No |
| K887P | -0.29 | 0.08 | -0.61 | 0.08 | -0.32 | 0.18 | No | No |
| K887S | -0.03 | 0.05 | -0.50 | 0.05 | -0.66 | 0.08 | No | No |

| Mutant | Enrich. Score (1) | Stand. Error (1) | Enrich. Score (2) | Stand. Error (2) | Enrich. Score (3) | Stand. Error (3) | Any positive enrichment? | Consistent positive enrichment? |
|---|---|---|---|---|---|---|---|---|
| K887* | -0.88 | 0.08 | -1.30 | 0.08 | -1.22 | 0.10 | No | No |
| K887T | -0.79 | 0.08 | -0.22 | 0.07 | -0.74 | 0.11 | No | No |
| K887W | -0.59 | 0.05 | -0.69 | 0.05 | -0.65 | 0.07 | No | No |
| K887Y | 0.36 | 0.10 | -0.98 | 0.13 | -0.40 | 0.17 | Yes | No |
| K887V | 0.09 | 0.04 | -0.88 | 0.04 | -0.89 | 0.07 | Yes | No |
| F888A | -2.01 | 0.10 | -1.31 | 0.07 | -1.30 | 0.28 | No | No |
| F888R | -1.27 | 0.07 | -1.04 | 0.06 | -1.82 | 0.18 | No | No |
| F888D | -1.09 | 0.12 | -1.32 | 0.12 | NA | NA | Yes | No |
| F888C | 0.01 | 0.04 | -0.10 | 0.04 | 0.10 | 0.03 | Yes | No |
| F888Q | -0.58 | 0.13 | -1.37 | 0.15 | NA | NA | Yes | No |
| F888E | -0.89 | 0.08 | -2.09 | 0.11 | -1.77 | 0.12 | No | No |
| F888G | -1.75 | 0.05 | -1.53 | 0.05 | -1.57 | 0.03 | No | No |
| F888I | 0.09 | 0.11 | -0.24 | 0.11 | -0.50 | 0.15 | Yes | No |
| F888L | -0.13 | 0.04 | -0.06 | 0.03 | -0.23 | 0.05 | No | No |
| F888M | -0.65 | 0.12 | 0.31 | 0.10 | -0.04 | 0.10 | Yes | No |
| F888P | -0.69 | 0.12 | -1.56 | 0.15 | NA | NA | Yes | No |
| F888S | -1.42 | 0.08 | -1.17 | 0.07 | -1.14 | 0.12 | No | No |
| F888* | -1.06 | 0.13 | -0.77 | 0.11 | -1.31 | 0.08 | No | No |
| F888T | -0.62 | 0.11 | -1.69 | 0.13 | -1.19 | 0.64 | No | No |
| F888W | -1.15 | 0.08 | -2.14 | 0.11 | -1.37 | 0.05 | No | No |
| F888Y | -0.73 | 0.13 | -1.27 | 0.14 | -0.60 | 0.12 | No | No |
| F888V | 0.07 | 0.04 | 0.10 | 0.04 | -0.31 | 0.03 | Yes | No |
| N889A | NA | NA | NA | NA | -0.86 | 0.64 | Yes | No |
| N889R | -0.94 | 0.09 | -0.07 | 0.07 | -0.55 | 0.48 | No | No |
| N889D | -0.34 | 0.10 | -0.44 | 0.10 | -0.39 | 0.14 | No | No |
| N889G | -0.87 | 0.06 | -1.32 | 0.07 | -0.83 | 0.07 | No | No |
| N889I | -0.51 | 0.17 | -0.43 | 0.16 | NA | NA | Yes | No |
| N889K | -0.76 | 0.17 | -0.47 | 0.15 | -0.34 | 0.24 | No | No |
| N889S | -1.13 | 0.11 | 0.08 | 0.08 | -0.26 | 0.14 | Yes | No |
| N889T | -0.55 | 0.16 | -0.45 | 0.14 | -0.36 | 0.30 | No | No |
| N889V | -1.82 | 0.15 | -1.28 | 0.12 | -1.16 | 0.64 | No | No |
| Q890C | 0.03 | 0.11 | 0.64 | 0.10 | 0.08 | 0.54 | Yes | Yes |
| Q890H | 0.39 | 0.09 | 0.07 | 0.09 | 0.04 | 0.11 | Yes | Yes |
| Q890W | 0.03 | 0.08 | 0.23 | 0.07 | 0.03 | 0.08 | Yes | Yes |
| Q890A | 0.39 | 0.06 | 0.05 | 0.06 | -0.02 | 0.11 | Yes | No |
| Q890R | -0.10 | 0.05 | -0.24 | 0.05 | -0.05 | 0.10 | No | No |
| Q890N | -0.25 | 0.15 | -0.66 | 0.16 | 0.31 | NA | Yes | No |
| Q890D | 0.54 | 0.10 | -0.52 | 0.11 | -0.35 | 0.20 | Yes | No |
| Q890E | 0.17 | 0.06 | -0.62 | 0.07 | -0.33 | 0.06 | Yes | No |
| Q890G | -0.35 | 0.04 | -0.60 | 0.04 | -0.15 | 0.07 | No | No |
| Q890I | -0.26 | 0.16 | -0.94 | 0.18 | NA | NA | Yes | No |
| Q890L | 0.09 | 0.06 | -0.14 | 0.06 | 0.29 | 0.17 | Yes | No |

| Mutant | Enrich. Score (1) | Stand. Error (1) | Enrich. Score (2) | Stand. Error (2) | Enrich. Score (3) | Stand. Error (3) | Any positive enrichment? | Consistent positive enrichment? |
|---|---|---|---|---|---|---|---|---|
| Q890K | 0.23 | 0.10 | 0.25 | 0.10 | -0.22 | 0.16 | Yes | No |
| Q890M | 0.32 | 0.11 | -0.13 | 0.11 | -0.07 | 0.48 | Yes | No |
| Q890F | 0.25 | 0.15 | -0.11 | 0.15 | 0.09 | 0.82 | Yes | No |
| Q890P | -1.20 | 0.12 | -0.75 | 0.10 | -0.11 | 0.17 | No | No |
| Q890S | -0.58 | 0.08 | -0.01 | 0.07 | -0.19 | 0.08 | No | No |
| Q890* | -1.12 | 0.11 | -1.26 | 0.11 | -0.88 | 0.13 | No | No |
| Q890T | -0.36 | 0.10 | 0.11 | 0.09 | 0.08 | 0.09 | Yes | No |
| Q890Y | NA | NA | NA | NA | 0.03 | 0.13 | Yes | No |
| Q890V | -0.39 | 0.06 | -0.33 | 0.06 | 0.21 | 0.06 | Yes | No |
| R891A | -0.41 | 0.08 | -0.46 | 0.07 | -0.44 | 0.31 | No | No |
| R891D | -1.17 | 0.16 | -0.76 | 0.14 | -0.63 | 0.64 | No | No |
| R891C | -0.10 | 0.10 | -0.56 | 0.11 | -0.05 | 0.17 | No | No |
| R891Q | NA | NA | NA | NA | -0.08 | 0.64 | Yes | No |
| R891E | -1.06 | 0.11 | -0.65 | 0.09 | -0.59 | 0.64 | No | No |
| R891G | -0.70 | 0.04 | -0.40 | 0.04 | -0.11 | 0.04 | No | No |
| R891L | 0.07 | 0.08 | -0.02 | 0.08 | -0.25 | 0.33 | Yes | No |
| R891K | -0.04 | 0.11 | -0.37 | 0.11 | -0.03 | 0.26 | No | No |
| R891M | NA | NA | NA | NA | -0.14 | NA | Yes | No |
| R891S | -0.18 | 0.07 | -0.49 | 0.07 | -0.28 | 0.08 | No | No |
| R891* | -0.88 | 0.13 | -0.57 | 0.11 | -0.74 | 0.20 | No | No |
| R891T | -0.20 | 0.10 | -0.28 | 0.10 | -0.16 | 0.10 | No | No |
| R891W | -1.03 | 0.08 | -1.42 | 0.08 | -0.78 | 0.43 | No | No |
| R891V | -0.28 | 0.07 | -0.77 | 0.07 | -0.53 | 0.09 | No | No |
| V892A | -1.02 | 0.08 | -1.08 | 0.08 | -0.18 | 0.07 | No | No |
| V892R | -1.49 | 0.09 | -1.55 | 0.08 | -1.41 | 0.09 | No | No |
| V892C | -0.58 | 0.14 | -0.80 | 0.14 | -0.01 | 0.13 | No | No |
| V892E | -0.97 | 0.10 | -1.28 | 0.10 | -0.93 | 0.17 | No | No |
| V892G | -1.01 | 0.05 | -1.11 | 0.05 | -0.90 | 0.05 | No | No |
| V892L | -0.58 | 0.09 | -1.35 | 0.10 | -0.93 | 0.14 | No | No |
| V892M | -0.59 | 0.12 | -0.62 | 0.12 | NA | NA | Yes | No |
| V892S | -1.15 | 0.13 | -1.21 | 0.12 | NA | NA | Yes | No |
| V892T | -0.34 | 0.15 | 0.05 | 0.13 | 0.11 | 0.64 | Yes | No |
| V892W | -1.99 | 0.15 | -1.09 | 0.10 | NA | NA | Yes | No |
| N893A | -1.02 | 0.07 | -0.18 | 0.05 | -0.37 | 0.05 | No | No |
| N893R | -0.35 | 0.04 | -0.57 | 0.04 | -0.42 | 0.06 | No | No |
| N893D | -0.71 | 0.10 | -0.39 | 0.08 | -0.71 | 0.11 | No | No |
| N893C | -0.80 | 0.10 | -0.20 | 0.09 | -0.24 | 0.07 | No | No |
| N893Q | -1.58 | 0.15 | -0.86 | 0.11 | -0.57 | 0.20 | No | No |
| N893E | -0.89 | 0.07 | -1.03 | 0.07 | -1.10 | 0.10 | No | No |
| N893G | -0.30 | 0.03 | -0.68 | 0.03 | -0.34 | 0.04 | No | No |
| N893H | 0.02 | 0.13 | -0.74 | 0.14 | NA | NA | Yes | No |
| N893I | 0.33 | 0.11 | -0.24 | 0.12 | -0.68 | 0.11 | Yes | No |

| Mutant | Enrich. Score (1) | Stand. Error (1) | Enrich. Score (2) | Stand. Error (2) | Enrich. Score (3) | Stand. Error (3) | Any positive enrichment? | Consistent positive enrichment? |
|---|---|---|---|---|---|---|---|---|
| N893L | -1.03 | 0.08 | -0.46 | 0.07 | -0.86 | 0.17 | No | No |
| N893K | -0.39 | 0.07 | -0.07 | 0.06 | -0.27 | 0.07 | No | No |
| N893M | 0.26 | 0.08 | -0.81 | 0.10 | -1.04 | 0.33 | Yes | No |
| N893S | 0.64 | 0.05 | 0.08 | 0.05 | -0.47 | 0.06 | Yes | No |
| N893* | -1.54 | 0.12 | -1.43 | 0.11 | -1.26 | 0.17 | No | No |
| N893T | 1.09 | 0.06 | -0.04 | 0.06 | -0.62 | 0.08 | Yes | No |
| N893W | -0.63 | 0.06 | -0.48 | 0.06 | -0.78 | 0.10 | No | No |
| N893Y | -0.51 | 0.12 | -0.87 | 0.12 | -0.38 | 0.18 | No | No |
| N893V | -0.70 | 0.06 | -0.74 | 0.06 | -0.59 | 0.05 | No | No |
| A894R | 0.19 | 0.06 | 0.06 | 0.06 | 0.04 | 0.08 | Yes | Yes |
| A894D | 0.04 | 0.06 | 0.09 | 0.06 | 0.21 | 0.05 | Yes | Yes |
| A894C | -0.13 | 0.15 | -0.29 | 0.14 | NA | NA | Yes | No |
| A894Q | 0.87 | 0.14 | -0.47 | 0.16 | NA | NA | Yes | No |
| A894E | -0.35 | 0.10 | -0.85 | 0.10 | -0.45 | 0.20 | No | No |
| A894G | -0.47 | 0.05 | 0.09 | 0.05 | 0.21 | 0.06 | Yes | No |
| A894L | -0.45 | 0.11 | 0.57 | 0.09 | 0.08 | 0.12 | Yes | No |
| A894K | NA | NA | NA | NA | 0.27 | 0.15 | Yes | No |
| A894M | 0.14 | 0.13 | -0.17 | 0.13 | 0.25 | 0.18 | Yes | No |
| A894P | -0.67 | 0.14 | -1.05 | 0.15 | NA | NA | Yes | No |
| A894S | 0.57 | 0.08 | -0.97 | 0.10 | 0.12 | 0.23 | Yes | No |
| A894* | -0.76 | 0.19 | 0.06 | 0.16 | NA | NA | Yes | No |
| A894T | -0.68 | 0.10 | -0.49 | 0.09 | 0.21 | 0.15 | Yes | No |
| A894W | 0.67 | 0.09 | -0.44 | 0.10 | 0.02 | 0.54 | Yes | No |
| A894V | -0.22 | 0.07 | -0.05 | 0.06 | 0.12 | 0.18 | Yes | No |
| Y895D | 0.16 | 0.04 | 0.00 | 0.04 | 0.09 | 0.04 | Yes | Yes |
| Y895A | -1.08 | 0.12 | -0.85 | 0.11 | -0.53 | 0.37 | No | No |
| Y895R | NA | NA | NA | NA | -0.75 | 0.07 | Yes | No |
| Y895N | -0.12 | 0.11 | -0.43 | 0.11 | -0.07 | 0.23 | No | No |
| Y895C | 0.61 | 0.06 | 0.14 | 0.06 | -0.26 | 0.07 | Yes | No |
| Y895E | -0.53 | 0.11 | -0.74 | 0.10 | -0.62 | 0.13 | No | No |
| Y895G | -0.59 | 0.06 | -1.69 | 0.08 | -1.72 | 0.07 | No | No |
| Y895H | -0.21 | 0.10 | -0.10 | 0.10 | -0.25 | 0.16 | No | No |
| Y895F | 0.70 | 0.12 | -0.28 | 0.13 | -0.20 | 0.21 | Yes | No |
| Y895S | 0.18 | 0.05 | -0.17 | 0.05 | -0.12 | 0.06 | Yes | No |
| Y895* | -0.03 | 0.05 | -0.04 | 0.05 | 0.16 | 0.06 | Yes | No |
| Y895W | -0.08 | 0.11 | 0.17 | 0.10 | -0.18 | 0.31 | Yes | No |
| Y895V | -1.60 | 0.12 | -0.11 | 0.08 | -0.61 | 0.40 | No | No |
| L896A | -1.48 | 0.09 | -1.26 | 0.08 | -1.68 | 0.35 | No | No |
| L896R | 0.19 | 0.04 | -0.11 | 0.04 | -0.30 | 0.04 | Yes | No |
| L896Q | 0.42 | 0.04 | 0.08 | 0.04 | -0.17 | 0.05 | Yes | No |
| L896E | -1.31 | 0.11 | -1.65 | 0.12 | NA | NA | Yes | No |
| L896G | -2.17 | 0.07 | -1.66 | 0.05 | -1.77 | 0.05 | No | No |

| Mutant | Enrich. Score (1) | Stand. Error (1) | Enrich. Score (2) | Stand. Error (2) | Enrich. Score (3) | Stand. Error (3) | Any positive enrichment? | Consistent positive enrichment? |
|---|---|---|---|---|---|---|---|---|
| L896M | 0.31 | 0.11 | -0.22 | 0.11 | -0.74 | 0.17 | Yes | No |
| L896F | -0.69 | 0.18 | -0.97 | 0.18 | NA | NA | Yes | No |
| L896P | -0.37 | 0.08 | -0.52 | 0.08 | -0.53 | 0.10 | No | No |
| L896S | NA | NA | NA | NA | -1.38 | 0.48 | Yes | No |
| L896W | -1.69 | 0.12 | -1.64 | 0.11 | -0.97 | 0.54 | No | No |
| L896V | -0.04 | 0.06 | -0.69 | 0.06 | -0.81 | 0.07 | No | No |
| K897A | -0.76 | 0.08 | -0.22 | 0.07 | -0.07 | 0.15 | No | No |
| K897R | 0.03 | 0.04 | -0.01 | 0.04 | -0.05 | 0.05 | Yes | No |
| K897N | 0.58 | 0.11 | 0.26 | 0.11 | -0.06 | 0.09 | Yes | No |
| K897D | -1.39 | 0.13 | -0.61 | 0.10 | -0.10 | 0.25 | No | No |
| K897C | 0.02 | 0.09 | -0.54 | 0.10 | -0.11 | 0.08 | Yes | No |
| K897Q | -0.06 | 0.10 | 0.16 | 0.10 | -0.04 | 0.21 | Yes | No |
| K897E | 0.17 | 0.05 | -0.03 | 0.05 | -0.29 | 0.08 | Yes | No |
| K897G | 0.01 | 0.04 | -0.29 | 0.04 | -0.07 | 0.03 | Yes | No |
| K897H | -0.18 | 0.15 | 0.06 | 0.14 | 0.22 | 0.36 | Yes | No |
| K897I | -0.29 | 0.13 | -1.02 | 0.14 | -0.06 | 0.06 | No | No |
| K897L | -0.19 | 0.07 | -0.26 | 0.07 | 0.28 | 0.35 | Yes | No |
| K897M | -0.35 | 0.09 | -0.01 | 0.08 | 0.23 | 0.11 | Yes | No |
| K897F | -0.72 | 0.18 | 0.16 | 0.15 | -0.08 | 0.64 | Yes | No |
| K897P | -1.22 | 0.13 | -1.78 | 0.14 | NA | NA | Yes | No |
| K897S | -0.22 | 0.07 | -0.29 | 0.07 | -0.13 | 0.10 | No | No |
| K897* | -0.92 | 0.11 | -0.93 | 0.11 | -0.93 | 0.11 | No | No |
| K897T | 0.27 | 0.08 | -0.32 | 0.08 | -0.02 | 0.06 | Yes | No |
| K897W | -0.08 | 0.07 | -0.54 | 0.07 | 0.00 | 0.19 | No | No |
| K897Y | -0.95 | 0.19 | 0.19 | 0.14 | -0.23 | 0.13 | Yes | No |
| K897V | -0.30 | 0.05 | -0.29 | 0.05 | 0.19 | 0.07 | Yes | No |
| E898A | -0.19 | 0.06 | 0.08 | 0.06 | -0.25 | 0.07 | Yes | No |
| E898R | -0.44 | 0.07 | -0.49 | 0.07 | -0.10 | 0.31 | No | No |
| E898D | 0.42 | 0.10 | -0.32 | 0.11 | -0.12 | 0.16 | Yes | No |
| E898C | NA | NA | NA | NA | 0.23 | 0.15 | Yes | No |
| E898Q | -0.43 | 0.14 | -0.57 | 0.13 | 0.29 | 0.39 | Yes | No |
| E898G | -0.27 | 0.05 | -0.27 | 0.05 | 0.12 | 0.06 | Yes | No |
| E898L | 0.07 | 0.11 | -0.46 | 0.12 | 0.15 | 0.12 | Yes | No |
| E898K | -0.93 | 0.16 | -0.35 | 0.14 | 0.13 | 0.31 | Yes | No |
| E898P | -0.40 | 0.19 | -0.60 | 0.19 | NA | NA | Yes | No |
| E898S | 0.17 | 0.14 | -1.32 | 0.18 | 0.38 | 0.55 | Yes | No |
| E898W | -1.01 | 0.12 | -1.33 | 0.12 | -0.16 | 0.14 | No | No |
| E898V | -0.06 | 0.07 | 0.31 | 0.07 | 0.01 | 0.07 | Yes | No |
| H899A | 0.21 | 0.08 | 0.16 | 0.07 | 0.01 | 0.48 | Yes | Yes |
| H899N | 0.15 | 0.15 | 0.70 | 0.14 | 0.08 | 0.18 | Yes | Yes |
| H899R | -0.20 | 0.04 | -0.12 | 0.04 | -0.12 | 0.03 | No | No |
| H899D | -0.84 | 0.13 | -0.16 | 0.11 | -0.47 | 0.25 | No | No |

| Mutant | Enrich. Score (1) | Stand. Error (1) | Enrich. Score (2) | Stand. Error (2) | Enrich. Score (3) | Stand. Error (3) | Any positive enrichment? | Consistent positive enrichment? |
|---|---|---|---|---|---|---|---|---|
| H899C | -0.98 | 0.14 | -0.02 | 0.11 | -0.12 | 0.13 | No | No |
| H899Q | -0.15 | 0.05 | -0.20 | 0.05 | 0.00 | 0.03 | No | No |
| H899E | -0.85 | 0.10 | -0.64 | 0.09 | -0.36 | 0.27 | No | No |
| H899G | -0.79 | 0.05 | -0.96 | 0.05 | -0.65 | 0.05 | No | No |
| H899L | -0.27 | 0.08 | -0.41 | 0.08 | -0.50 | 0.14 | No | No |
| H899K | NA | NA | NA | NA | 0.05 | 0.49 | Yes | No |
| H899P | -0.07 | 0.07 | 0.01 | 0.07 | -0.33 | 0.10 | Yes | No |
| H899S | -0.31 | 0.10 | -0.33 | 0.09 | 0.07 | 0.32 | Yes | No |
| H899T | -0.37 | 0.15 | -0.14 | 0.14 | -0.03 | 0.48 | No | No |
| H899W | -0.32 | 0.08 | -0.24 | 0.07 | -0.25 | 0.48 | No | No |
| H899Y | -0.09 | 0.12 | -0.87 | 0.13 | 0.11 | 0.16 | Yes | No |
| H899V | -0.07 | 0.07 | -0.99 | 0.08 | 0.05 | 0.22 | Yes | No |
| P900A | -0.09 | 0.05 | 0.03 | 0.04 | 0.04 | 0.11 | Yes | No |
| P900R | -0.17 | 0.04 | -0.23 | 0.03 | 0.09 | 0.04 | Yes | No |
| P900N | -1.13 | 0.14 | 0.05 | 0.11 | 0.35 | 0.30 | Yes | No |
| P900D | -0.42 | 0.08 | -0.19 | 0.07 | 0.19 | 0.12 | Yes | No |
| P900C | -0.28 | 0.07 | 0.15 | 0.06 | 0.12 | 0.15 | Yes | No |
| P900Q | 0.28 | 0.08 | -0.19 | 0.09 | 0.23 | 0.30 | Yes | No |
| P900E | -0.19 | 0.06 | 0.18 | 0.05 | 0.29 | 0.08 | Yes | No |
| P900G | -0.03 | 0.03 | -0.15 | 0.03 | 0.11 | 0.03 | Yes | No |
| P900H | 0.07 | 0.08 | -0.18 | 0.08 | 0.25 | 0.12 | Yes | No |
| P900I | -0.83 | 0.12 | -0.36 | 0.10 | 0.33 | 0.33 | Yes | No |
| P900L | 0.03 | 0.04 | -0.20 | 0.04 | 0.07 | 0.04 | Yes | No |
| P900K | 0.16 | 0.08 | -0.61 | 0.08 | 0.05 | 0.13 | Yes | No |
| P900M | -1.26 | 0.10 | -0.21 | 0.07 | 0.06 | 0.12 | Yes | No |
| P900F | 0.33 | 0.10 | -0.07 | 0.10 | -0.19 | 0.09 | Yes | No |
| P900S | -0.10 | 0.05 | 0.15 | 0.04 | 0.14 | 0.04 | Yes | No |
| P900* | -0.32 | 0.08 | -1.30 | 0.10 | NA | NA | Yes | No |
| P900T | 0.24 | 0.06 | -0.22 | 0.06 | 0.19 | 0.09 | Yes | No |
| P900W | -0.16 | 0.05 | -0.48 | 0.06 | -0.04 | 0.06 | No | No |
| P900Y | -0.49 | 0.11 | -0.86 | 0.11 | -0.25 | 0.82 | No | No |
| P900V | 0.10 | 0.04 | -0.35 | 0.04 | 0.14 | 0.05 | Yes | No |
| E901D | 0.07 | 0.10 | 0.05 | 0.10 | 0.14 | 0.15 | Yes | Yes |
| E901A | -0.81 | 0.08 | 0.24 | 0.07 | 0.08 | 0.08 | Yes | No |
| E901R | -0.15 | 0.06 | -0.19 | 0.06 | -0.03 | 0.06 | No | No |
| E901C | -0.08 | 0.13 | -0.32 | 0.13 | 0.21 | 0.64 | Yes | No |
| E901Q | -0.69 | 0.16 | 0.04 | 0.13 | -0.16 | 0.40 | Yes | No |
| E901G | -0.44 | 0.04 | 0.07 | 0.04 | 0.10 | 0.06 | Yes | No |
| E901L | -0.12 | 0.08 | -0.80 | 0.09 | -0.13 | 0.20 | No | No |
| E901K | -0.11 | 0.10 | 0.20 | 0.10 | 0.08 | 0.13 | Yes | No |
| E901M | 0.16 | 0.12 | -0.14 | 0.12 | 0.03 | 0.82 | Yes | No |
| E901P | -0.99 | 0.19 | -1.23 | 0.19 | NA | NA | Yes | No |

| Mutant | Enrich. Score (1) | Stand. Error (1) | Enrich. Score (2) | Stand. Error (2) | Enrich. Score (3) | Stand. Error (3) | Any positive enrichment? | Consistent positive enrichment? |
|---|---|---|---|---|---|---|---|---|
| E901S | -1.40 | 0.13 | 0.16 | 0.08 | 0.05 | 0.11 | Yes | No |
| E901* | -0.29 | 0.13 | -1.11 | 0.15 | -0.63 | 0.14 | No | No |
| E901T | NA | NA | NA | NA | -0.05 | 0.44 | Yes | No |
| E901W | 0.02 | 0.08 | -0.49 | 0.09 | 0.21 | 0.08 | Yes | No |
| E901V | -1.13 | 0.07 | -0.49 | 0.06 | 0.11 | 0.06 | Yes | No |
| T902A | -0.07 | 0.05 | -0.35 | 0.05 | -0.20 | 0.09 | No | No |
| T902R | -0.60 | 0.06 | -1.09 | 0.07 | -0.48 | 0.12 | No | No |
| T902C | 0.17 | 0.11 | -0.55 | 0.12 | -0.25 | 0.82 | Yes | No |
| T902Q | -0.92 | 0.15 | -0.24 | 0.13 | NA | NA | Yes | No |
| T902E | -0.55 | 0.10 | -1.12 | 0.11 | NA | NA | Yes | No |
| T902G | -1.03 | 0.06 | -1.00 | 0.06 | -0.74 | 0.15 | No | No |
| T902I | -0.22 | 0.14 | 0.19 | 0.12 | -0.10 | 0.20 | Yes | No |
| T902L | -0.92 | 0.11 | -0.09 | 0.09 | -0.12 | 0.09 | No | No |
| T902K | -0.31 | 0.04 | -0.01 | 0.04 | 0.13 | 0.06 | Yes | No |
| T902M | NA | NA | NA | NA | 0.01 | 0.54 | Yes | No |
| T902P | -1.06 | 0.13 | -0.32 | 0.10 | -0.81 | 0.21 | No | No |
| T902S | -0.15 | 0.07 | -0.38 | 0.07 | -0.15 | 0.07 | No | No |
| T902W | NA | NA | NA | NA | -0.80 | 0.54 | Yes | No |
| T902V | -0.15 | 0.07 | 0.06 | 0.07 | -0.03 | 0.14 | Yes | No |
| P903T | 0.64 | 0.13 | 0.52 | 0.12 | 0.39 | 0.18 | Yes | Yes |
| P903A | -0.22 | 0.11 | -0.37 | 0.10 | -0.12 | 0.31 | No | No |
| P903R | -1.86 | 0.13 | -0.87 | 0.09 | -0.31 | 0.27 | No | No |
| P903C | 0.75 | 0.15 | -0.71 | 0.18 | NA | NA | Yes | No |
| P903E | NA | NA | NA | NA | 0.05 | 0.22 | Yes | No |
| P903G | -1.37 | 0.10 | -1.66 | 0.10 | -0.49 | 0.35 | No | No |
| P903H | NA | NA | NA | NA | 0.04 | 0.17 | Yes | No |
| P903L | -0.52 | 0.11 | -0.93 | 0.12 | 0.29 | 0.10 | Yes | No |
| P903S | -0.61 | 0.12 | 0.03 | 0.10 | 0.07 | 0.22 | Yes | No |
| P903V | -0.44 | 0.12 | -0.77 | 0.12 | 0.25 | 0.16 | Yes | No |
| I904A | 0.28 | 0.05 | 0.32 | 0.05 | -0.01 | 0.10 | Yes | No |
| I904R | -0.52 | 0.05 | -0.28 | 0.04 | -0.14 | 0.04 | No | No |
| I904N | -0.26 | 0.11 | 0.07 | 0.10 | -0.29 | 0.13 | Yes | No |
| I904D | NA | NA | NA | NA | -1.33 | 0.37 | Yes | No |
| I904C | -0.37 | 0.09 | -0.06 | 0.08 | 0.16 | 0.09 | Yes | No |
| I904Q | -0.28 | 0.11 | 0.17 | 0.10 | 0.03 | 0.37 | Yes | No |
| I904E | -1.15 | 0.08 | -1.73 | 0.09 | -0.77 | 0.30 | No | No |
| I904G | -1.05 | 0.04 | -0.45 | 0.04 | -0.39 | 0.03 | No | No |
| I904H | NA | NA | NA | NA | -0.20 | 0.48 | Yes | No |
| I904L | -0.35 | 0.07 | 0.47 | 0.06 | 0.12 | 0.09 | Yes | No |
| I904K | -1.71 | 0.15 | -0.48 | 0.10 | 0.05 | 0.09 | Yes | No |
| I904M | 0.19 | 0.08 | -0.04 | 0.08 | 0.03 | 0.05 | Yes | No |
| I904F | -0.71 | 0.13 | 0.38 | 0.11 | 0.15 | 0.20 | Yes | No |

| Mutant | Enrich. Score (1) | Stand. Error (1) | Enrich. Score (2) | Stand. Error (2) | Enrich. Score (3) | Stand. Error (3) | Any positive enrichment? | Consistent positive enrichment? |
|---|---|---|---|---|---|---|---|---|
| I904S | 0.20 | 0.04 | -0.09 | 0.04 | 0.07 | 0.03 | Yes | No |
| I904* | -1.37 | 0.12 | -1.64 | 0.13 | NA | NA | Yes | No |
| I904T | 0.33 | 0.07 | -0.20 | 0.07 | -0.13 | 0.08 | Yes | No |
| I904W | -0.01 | 0.06 | -0.07 | 0.06 | -0.35 | 0.24 | No | No |
| I904Y | 0.53 | 0.12 | -0.47 | 0.13 | 0.01 | 0.64 | Yes | No |
| I904V | -0.13 | 0.05 | 0.08 | 0.04 | 0.00 | 0.04 | Yes | No |
| I905A | -0.31 | 0.06 | -0.49 | 0.06 | -0.02 | 0.14 | No | No |
| I905R | -1.93 | 0.08 | -1.23 | 0.06 | -1.47 | 0.09 | No | No |
| I905N | -0.95 | 0.15 | -0.68 | 0.14 | NA | NA | Yes | No |
| I905D | -1.69 | 0.14 | -1.47 | 0.12 | NA | NA | Yes | No |
| I905C | -0.01 | 0.10 | 0.49 | 0.09 | -0.12 | 0.11 | Yes | No |
| I905E | -1.48 | 0.10 | -2.09 | 0.12 | -1.57 | 0.43 | No | No |
| I905G | -1.25 | 0.05 | -0.83 | 0.04 | -0.80 | 0.04 | No | No |
| I905L | -0.65 | 0.07 | -0.31 | 0.06 | -0.12 | 0.07 | No | No |
| I905M | 0.15 | 0.06 | -0.40 | 0.07 | -0.10 | 0.06 | Yes | No |
| I905F | -0.10 | 0.11 | -0.09 | 0.11 | -0.55 | 0.18 | No | No |
| I905S | -1.01 | 0.07 | -1.06 | 0.07 | -0.63 | 0.06 | No | No |
| I905T | -0.17 | 0.09 | -0.86 | 0.09 | -0.52 | 0.12 | No | No |
| I905W | -1.31 | 0.10 | -1.78 | 0.11 | -1.43 | 0.28 | No | No |
| I905V | -0.18 | 0.05 | -0.21 | 0.05 | 0.10 | 0.06 | Yes | No |
| G906A | 0.41 | 0.05 | 0.56 | 0.04 | 0.42 | 0.05 | Yes | Yes |
| G906S | 0.40 | 0.05 | 0.16 | 0.05 | 0.15 | 0.06 | Yes | Yes |
| G906R | -1.82 | 0.06 | -2.39 | 0.07 | -1.63 | 0.08 | No | No |
| G906D | -1.49 | 0.10 | -1.05 | 0.08 | -1.38 | 0.18 | No | No |
| G906C | -1.50 | 0.11 | -1.21 | 0.09 | -1.62 | 0.11 | No | No |
| G906E | -2.26 | 0.12 | -1.63 | 0.09 | -1.49 | 0.11 | No | No |
| G906L | -1.51 | 0.09 | -2.32 | 0.11 | -1.69 | 0.27 | No | No |
| G906P | -1.68 | 0.12 | -1.05 | 0.09 | -1.66 | 0.10 | No | No |
| G906* | NA | NA | NA | NA | -1.21 | 0.40 | Yes | No |
| G906T | -1.69 | 0.11 | -2.68 | 0.15 | NA | NA | Yes | No |
| G906W | -2.22 | 0.11 | -1.14 | 0.07 | -1.71 | 0.08 | No | No |
| G906V | -0.85 | 0.05 | -1.20 | 0.05 | -1.27 | 0.06 | No | No |
| I907A | 0.70 | 0.10 | 0.42 | 0.10 | 0.27 | 0.54 | Yes | Yes |
| I907V | 0.15 | 0.07 | 0.12 | 0.07 | 0.13 | 0.06 | Yes | Yes |
| I907R | -0.92 | 0.08 | -1.15 | 0.08 | -0.89 | 0.09 | No | No |
| I907D | -0.44 | 0.17 | -0.97 | 0.18 | NA | NA | Yes | No |
| I907C | -0.16 | 0.16 | 0.84 | 0.13 | 0.12 | 0.64 | Yes | No |
| I907E | -1.06 | 0.15 | -0.42 | 0.12 | NA | NA | Yes | No |
| I907G | -0.42 | 0.06 | -0.40 | 0.06 | -0.03 | 0.06 | No | No |
| I907L | 0.34 | 0.09 | 0.24 | 0.08 | -0.33 | 0.09 | Yes | No |
| I907M | NA | NA | NA | NA | 0.12 | 0.25 | Yes | No |
| I907F | -0.50 | 0.19 | -0.17 | 0.17 | NA | NA | Yes | No |

| Mutant | Enrich. Score (1) | Stand. Error (1) | Enrich. Score (2) | Stand. Error (2) | Enrich. Score (3) | Stand. Error (3) | Any positive enrichment? | Consistent positive enrichment? |
|---|---|---|---|---|---|---|---|---|
| I907S | -0.29 | 0.03 | -0.18 | 0.03 | 0.25 | 0.03 | Yes | No |
| I907T | -0.44 | 0.15 | 0.78 | 0.12 | 0.28 | 0.12 | Yes | No |
| D908A | -2.26 | 0.13 | -1.92 | 0.11 | -1.10 | 0.16 | No | No |
| D908R | NA | NA | NA | NA | -1.53 | 0.09 | Yes | No |
| D908N | -0.27 | 0.12 | -0.30 | 0.12 | -0.70 | 0.14 | No | No |
| D908E | -1.61 | 0.13 | -1.42 | 0.11 | -1.11 | 0.11 | No | No |
| D908G | -2.25 | 0.09 | -2.15 | 0.08 | -1.77 | 0.14 | No | No |
| D908S | -1.92 | 0.16 | -1.78 | 0.14 | NA | NA | Yes | No |
| D908W | -1.93 | 0.15 | -2.11 | 0.15 | NA | NA | Yes | No |
| D908Y | 0.26 | 0.11 | -0.07 | 0.12 | -0.15 | 0.12 | Yes | No |
| D908V | -1.74 | 0.10 | -1.76 | 0.10 | -1.52 | 0.09 | No | No |
| R909A | NA | NA | NA | NA | -1.45 | 0.37 | Yes | No |
| R909Q | -0.25 | 0.18 | -0.94 | 0.20 | NA | NA | Yes | No |
| R909G | -1.30 | 0.05 | -1.49 | 0.05 | -1.38 | 0.06 | No | No |
| R909K | -0.87 | 0.16 | -0.60 | 0.14 | NA | NA | Yes | No |
| R909S | -1.08 | 0.10 | -0.84 | 0.09 | -0.58 | 0.12 | No | No |
| R909T | -1.28 | 0.15 | -0.89 | 0.13 | NA | NA | Yes | No |
| R909W | -0.96 | 0.10 | -1.94 | 0.13 | NA | NA | Yes | No |
| R909V | -1.36 | 0.11 | -2.33 | 0.14 | -1.34 | 0.47 | No | No |
| G910R | -1.03 | 0.08 | -1.62 | 0.09 | -1.75 | 0.16 | No | No |
| G910D | NA | NA | NA | NA | -0.69 | 0.19 | Yes | No |
| G910C | -0.91 | 0.13 | -1.29 | 0.14 | NA | NA | Yes | No |
| G910S | -1.15 | 0.10 | -1.28 | 0.10 | -1.41 | 0.19 | No | No |
| G910W | -1.93 | 0.15 | -1.82 | 0.13 | NA | NA | Yes | No |
| G910V | -1.34 | 0.08 | -1.15 | 0.07 | -0.66 | 0.13 | No | No |
| E911A | -0.79 | 0.12 | -1.56 | 0.14 | -0.93 | 0.10 | No | No |
| E911R | -1.42 | 0.12 | -2.19 | 0.14 | NA | NA | Yes | No |
| E911D | -0.45 | 0.14 | -0.47 | 0.13 | -0.18 | 0.25 | No | No |
| E911G | -0.65 | 0.06 | -0.80 | 0.06 | -0.83 | 0.08 | No | No |
| E911L | NA | NA | NA | NA | -0.50 | 0.15 | Yes | No |
| E911K | -0.39 | 0.13 | -0.14 | 0.12 | -0.57 | 0.15 | No | No |
| E911* | -0.20 | 0.11 | 0.12 | 0.10 | -0.18 | 0.16 | Yes | No |
| E911V | -0.21 | 0.08 | -0.62 | 0.08 | -0.61 | 0.09 | No | No |
| R912A | 0.46 | 0.09 | 0.49 | 0.09 | 0.31 | 0.64 | Yes | Yes |
| R912L | 0.53 | 0.08 | 0.38 | 0.08 | 0.21 | 0.16 | Yes | Yes |
| R912S | 1.04 | 0.11 | 0.30 | 0.11 | 0.31 | 0.54 | Yes | Yes |
| R912V | 0.19 | 0.09 | 0.23 | 0.09 | 0.03 | 0.09 | Yes | Yes |
| R912C | 0.43 | 0.15 | 0.54 | 0.15 | -0.29 | 0.16 | Yes | No |
| R912Q | 0.22 | 0.05 | 0.15 | 0.05 | -0.05 | 0.09 | Yes | No |
| R912E | 0.53 | 0.12 | -0.67 | 0.14 | NA | NA | Yes | No |
| R912G | -0.21 | 0.05 | -1.04 | 0.06 | -0.56 | 0.05 | No | No |
| R912P | 0.53 | 0.09 | 0.79 | 0.09 | -0.40 | 0.14 | Yes | No |

| Mutant | Enrich. Score (1) | Stand. Error (1) | Enrich. Score (2) | Stand. Error (2) | Enrich. Score (3) | Stand. Error (3) | Any positive enrichment? | Consistent positive enrichment? |
|---|---|---|---|---|---|---|---|---|
| R912T | -0.54 | 0.17 | -0.07 | 0.15 | 0.52 | 0.65 | Yes | No |
| R912W | -0.09 | 0.07 | -0.14 | 0.07 | -0.43 | 0.10 | No | No |
| N913A | -1.19 | 0.13 | -0.97 | 0.11 | -0.87 | 0.33 | No | No |
| N913R | -2.49 | 0.14 | -0.64 | 0.07 | -1.67 | 0.40 | No | No |
| N913D | -0.62 | 0.13 | -0.44 | 0.12 | -0.75 | 0.10 | No | No |
| N913E | -0.91 | 0.12 | -1.92 | 0.16 | NA | NA | Yes | No |
| N913G | -1.34 | 0.07 | -0.91 | 0.06 | -1.56 | 0.30 | No | No |
| N913H | 0.12 | 0.07 | 0.13 | 0.07 | -0.20 | 0.12 | Yes | No |
| N913I | -0.16 | 0.09 | -0.18 | 0.09 | -0.18 | 0.12 | No | No |
| N913L | -0.39 | 0.11 | -0.72 | 0.11 | NA | NA | Yes | No |
| N913K | -0.37 | 0.05 | -0.29 | 0.04 | -0.27 | 0.08 | No | No |
| N913S | -0.29 | 0.08 | -0.06 | 0.07 | -0.20 | 0.12 | No | No |
| N913T | 0.09 | 0.11 | -0.67 | 0.12 | -0.35 | 0.24 | Yes | No |
| N913Y | -0.47 | 0.18 | -0.44 | 0.17 | NA | NA | Yes | No |
| N913V | -1.32 | 0.12 | -0.89 | 0.10 | -1.09 | 0.18 | No | No |

**[0160]** [1]Key to Header abbreviations: Mutants are defined by single letter amino acid (wild-type) at a given position in the wild-type AsCas12a polypeptide (e.g., amino acid position 500), followed by the variant amino acid change thereafter; "Enrich. Score (1)" refers to Enrichment score of the variant in a Condition 1 background; "Stand. Error (1) refers to the Standard error for experiments conducted for a given variant in a Condition 1 background; "Enrich. Score (2)" refers to Enrichment Score of the variant in a Condition 2 background; "Stand. Error (2) refers to the Standard Error for experiments conducted for a given variant in a Condition 2 background; "Enrich. Score (3)" refers to Enrichment Score of the variant in a Condition 3 background; "Stand. Error (3) refers to the Standard Error for experiments conducted for a given variant in a Condition 3 background; "Any Positive Enrichment?" refers to the occurrence of positive enrichment for a given variant under at least one experimental Condition background; "Consistent positive enrichment?" refers to the occurrence of positive enrichment for a given variant under all tested experimental Condition backgrounds.

**[0161]** One hundred eighty-seven (187) variants (~6% of total) consistently enhanced the survival rate under all conditions (**Table 4**). These variants, including the four validated individually, can be stacked on the WT- or M537R/F870L-*AsCas12a*, to boost its DNA cleavage activity at TTTT-PAM.

**[0162] Table 4. Point mutations consistently enriched over the reference proteins under all conditions.[1]**

| SEQ ID NO.: | Mutant | Position | Variant score (condition 1) | Variant score (condition 2) | Variant score (condition 3) |
|---|---|---|---|---|---|
| 59 | R499C | 499 | 0.14±0.08 | 0.6±0.07 | 0.06±0.1 |
| 60 | R499L | 499 | 0.08±0.05 | 0.05±0.06 | 0.09±0.15 |
| 61 | R499K | 499 | 0.54±0.06 | 0.23±0.06 | 0.38±0.1 |
| 62 | L500M | 500 | 0.01±0.05 | 0.3±0.05 | 0.28±0.12 |

| SEQ ID NO.: | Mutant | Position | Variant score (condition 1) | Variant score (condition 2) | Variant score (condition 3) |
|---|---|---|---|---|---|
| 63 | T501L | 501 | 0.18±0.04 | 0.32±0.04 | 0.12±0.07 |
| 64 | T501M | 501 | 0.32±0.07 | 0.35±0.07 | 0.17±0.29 |
| 65 | T501V | 501 | 0.22±0.06 | 0.29±0.06 | 0.13±0.2 |
| 66 | G502R | 502 | 0.14±0.05 | 0.28±0.05 | 0.98±0.07 |
| 67 | G502E | 502 | 0.42±0.08 | 0.17±0.08 | 0.19±0.3 |
| 68 | G502L | 502 | 0.45±0.07 | 0.1±0.07 | 0±0.11 |
| 69 | G502S | 502 | 0.08±0.06 | 0.23±0.06 | 0.16±0.12 |
| 70 | G502W | 502 | 0.14±0.07 | 0.65±0.06 | 0.36±0.14 |
| 71 | G502V | 502 | 0.21±0.05 | 0.21±0.05 | 0.13±0.07 |
| 72 | L505A | 505 | 0.61±0.05 | 0.5±0.05 | 0.47±0.13 |
| 73 | L505R | 505 | 0.4±0.03 | 0.56±0.03 | 0.81±0.05 |
| 74 | L505Q | 505 | 0.3±0.07 | 0.82±0.07 | 0.16±0.11 |
| 75 | L505E | 505 | 0.18±0.06 | 0.03±0.07 | 0.14±0.21 |
| 76 | L505G | 505 | 0.18±0.03 | 0.72±0.03 | 0.4±0.05 |
| 77 | L505H | 505 | 0.33±0.11 | 0.83±0.1 | 0.34±0.32 |
| 78 | L505K | 505 | 0.02±0.1 | 1±0.08 | 1±0.13 |
| 79 | L505S | 505 | 0.13±0.06 | 0.32±0.06 | 0.6±0.07 |
| 80 | E506A | 506 | 0.33±0.03 | 0.47±0.03 | 0.7±0.05 |
| 81 | E506R | 506 | 0.46±0.03 | 0.81±0.03 | 1.2±0.04 |
| 82 | E506N | 506 | 0.24±0.09 | 0.53±0.09 | 0.5±0.29 |
| 83 | E506C | 506 | 0.2±0.06 | 0.29±0.06 | 0.49±0.19 |
| 84 | E506Q | 506 | 0.09±0.07 | 0.74±0.06 | 0.33±0.15 |
| 85 | E506G | 506 | 0.24±0.02 | 0.39±0.02 | 0.53±0.03 |
| 86 | E506H | 506 | 0.35±0.09 | 0.1±0.1 | 0.98±0.31 |
| 87 | E506I | 506 | 0.47±0.09 | 0.45±0.09 | 0.69±0.13 |
| 88 | E506L | 506 | 0.3±0.04 | 0.61±0.04 | 0.56±0.07 |
| 89 | E506K | 506 | 0.18±0.06 | 0.59±0.05 | 1.08±0.08 |
| 90 | E506M | 506 | 0.53±0.06 | 0.28±0.07 | 0.47±0.17 |
| 91 | E506S | 506 | 0.01±0.05 | 0.47±0.04 | 0.5±0.06 |
| 92 | E506T | 506 | 0.39±0.06 | 0.12±0.07 | 0.9±0.23 |
| 93 | E506Y | 506 | 0.16±0.09 | 0.29±0.09 | 0.43±0.25 |
| 94 | E506V | 506 | 0.45±0.03 | 0.51±0.03 | 0.75±0.05 |
| 95 | E508A | 508 | 0.36±0.03 | 0.2±0.03 | 0.18±0.06 |
| 96 | E508R | 508 | 0.54±0.03 | 0.8±0.03 | 0.82±0.06 |
| 97 | E508Q | 508 | 0.25±0.06 | 0.11±0.07 | 0.51±0.13 |
| 98 | E508G | 508 | 0.16±0.02 | 0.17±0.02 | 0.22±0.04 |
| 99 | E508L | 508 | 0.03±0.04 | 0.1±0.04 | 0.26±0.11 |
| 100 | E508K | 508 | 0.2±0.06 | 0.49±0.06 | 0.66±0.08 |
| 101 | E508M | 508 | 0.25±0.07 | 0.57±0.06 | 0.54±0.11 |
| 102 | E508F | 508 | 0.27±0.08 | 0.19±0.08 | 0.39±0.29 |
| 103 | E508S | 508 | 0.31±0.05 | 0.62±0.04 | 0.34±0.06 |
| 104 | E508T | 508 | 0.19±0.06 | 0.73±0.06 | 0.55±0.1 |
| 105 | E508Y | 508 | 0.35±0.09 | 0.19±0.1 | 0.21±0.27 |
| 106 | E508V | 508 | 0.16±0.03 | 0.22±0.03 | 0.34±0.05 |
| 107 | P509R | 509 | 0.23±0.03 | 0.27±0.03 | 1.04±0.05 |
| 108 | P509K | 509 | 0.01±0.07 | 0.12±0.07 | 1.29±0.13 |
| 109 | P509M | 509 | 0.34±0.07 | 0.34±0.07 | 0.1±0.22 |
| 110 | P509S | 509 | 0.1±0.04 | 0.14±0.04 | 0.14±0.1 |
| 111 | P509W | 509 | 0.04±0.05 | 0.33±0.05 | 0.61±0.18 |
| 112 | P509Y | 509 | 0.18±0.09 | 0.2±0.09 | 0.53±0.3 |
| 113 | S510G | 510 | 0.18±0.03 | 0.49±0.03 | 0.21±0.06 |
| 114 | S510L | 510 | 0.57±0.06 | 0.72±0.06 | 0.74±0.09 |
| 115 | S512R | 512 | 0.07±0.07 | 0.34±0.07 | 0.07±0.19 |
| 116 | F513L | 513 | 0.53±0.04 | 0.63±0.04 | 0.41±0.07 |
| 117 | F513W | 513 | 0.04±0.06 | 0.35±0.06 | 0.28±0.13 |
| 118 | N515A | 515 | 0.6±0.06 | 0.82±0.06 | 0.12±0.11 |
| 119 | N515R | 515 | 0.63±0.06 | 0.82±0.05 | 0.19±0.11 |
| 120 | N515I | 515 | 0.23±0.07 | 0.3±0.07 | 0.16±0.14 |
| 121 | N515L | 515 | 0.33±0.06 | 0.53±0.06 | 0.07±0.2 |
| 122 | N515T | 515 | 0.41±0.08 | 0.14±0.08 | 0.29±0.16 |

| SEQ ID NO.: | Mutant | Position | Variant score (condition 1) | Variant score (condition 2) | Variant score (condition 3) |
|---|---|---|---|---|---|
| 123 | N515V | 515 | 0.5±0.05 | 0.49±0.05 | 0.45±0.09 |
| 124 | K516R | 516 | 0.01±0.03 | 0.26±0.03 | 0.4±0.06 |
| 125 | R518K | 518 | 0.2±0.09 | 0.72±0.08 | 0.05±0.17 |
| 126 | T522L | 522 | 1.1±0.05 | 0.92±0.05 | 0.28±0.1 |
| 127 | T522M | 522 | 0.92±0.07 | 0.81±0.08 | 0.53±0.21 |
| 128 | T522V | 522 | 0.16±0.05 | 0.28±0.05 | 0.04±0.07 |
| 129 | K523R | 523 | 0.17±0.02 | 0.37±0.02 | 0±0.03 |
| 130 | S527D | 527 | 0.13±0.11 | 0.01±0.11 | 0.34±0.41 |
| 131 | V528D | 528 | 0.01±0.07 | 0.27±0.07 | 0.12±0.12 |
| 132 | V528L | 528 | 0.55±0.03 | 0.59±0.03 | 0.31±0.07 |
| 133 | V528M | 528 | 0.19±0.05 | 0.02±0.05 | 0.13±0.1 |
| 134 | S542N | 542 | 0.24±0.09 | 0.02±0.09 | 0.29±0.07 |
| 135 | S542C | 542 | 0.03±0.17 | 0.15±0.17 | 0.42±0.16 |
| 136 | K550R | 550 | 0.05±0.03 | 0.18±0.03 | 0.17±0.07 |
| 137 | N551D | 551 | 0.14±0.04 | 0.15±0.04 | 0.67±0.07 |
| 138 | A554I | 554 | 0.15±0.09 | 0.71±0.08 | 0.39±0.34 |
| 139 | A554T | 554 | 0.45±0.04 | 0.32±0.05 | 0.93±0.07 |
| 140 | A554V | 554 | 0.57±0.03 | 0.48±0.03 | 0.54±0.04 |
| 141 | I555V | 555 | 0.41±0.03 | 0.13±0.03 | 0.14±0.06 |
| 142 | L556M | 556 | 0.08±0.08 | 0.1±0.08 | 0.11±0.21 |
| 143 | V558M | 558 | 0.24±0.06 | 0.15±0.06 | 0.1±0.12 |
| 144 | K559A | 559 | 0.17±0.04 | 0.08±0.04 | 0.13±0.08 |
| 145 | N560A | 560 | 0.34±0.05 | 0.18±0.05 | 0.18±0.08 |
| 146 | N560D | 560 | 0.16±0.04 | 0.18±0.04 | 0.16±0.08 |
| 147 | N560E | 560 | 0.48±0.06 | 0.28±0.06 | 0.11±0.25 |
| 148 | N560M | 560 | 0.16±0.09 | 0.31±0.09 | 0.18±0.13 |
| 149 | P569D | 569 | 0.6±0.08 | 0.33±0.08 | 1.25±0.11 |
| 150 | Q571A | 571 | 0.64±0.07 | 0.39±0.08 | 1.09±0.23 |
| 151 | Q571P | 571 | 0.17±0.07 | 0.61±0.07 | 0.13±0.14 |
| 152 | Q571S | 571 | 0.25±0.09 | 0.2±0.09 | 0.89±0.23 |
| 153 | Q571T | 571 | 0.22±0.13 | 0.19±0.13 | 0.87±0.41 |
| 154 | K572E | 572 | 0.11±0.04 | 0.25±0.04 | 0.42±0.08 |
| 155 | Y575G | 575 | 0.53±0.04 | 0.21±0.04 | 0.32±0.07 |
| 156 | Y575M | 575 | 0.89±0.11 | 0.27±0.12 | 0.31±0.41 |
| 157 | K576C | 576 | 0.27±0.07 | 0.25±0.07 | 0.1±0.26 |
| 158 | S579T | 579 | 0.17±0.04 | 0.33±0.04 | 0.01±0.06 |
| 159 | S579V | 579 | 0.04±0.03 | 0.02±0.03 | 0.05±0.07 |
| 160 | T583I | 583 | 0.04±0.08 | 0.11±0.07 | 0.07±0.17 |
| 161 | E584H | 584 | 0.09±0.07 | 0.22±0.07 | 0.17±0.14 |
| 162 | E584V | 584 | 0.1±0.03 | 0.06±0.03 | 0.12±0.04 |
| 163 | K585R | 585 | 0.07±0.03 | 0.32±0.03 | 0.06±0.05 |
| 164 | K585F | 585 | 0.51±0.09 | 0.04±0.09 | 0.61±0.36 |
| 165 | D596E | 596 | 0.04±0.04 | 0.24±0.04 | 0.69±0.05 |
| 166 | P599G | 599 | 0.84±0.04 | 0.83±0.04 | 1.01±0.05 |
| 167 | A602C | 602 | 0.64±0.09 | 0.61±0.09 | 0.73±0.28 |
| 168 | L612M | 612 | 0.7±0.07 | 0.7±0.07 | 0.01±0.03 |
| 169 | A614R | 614 | 0.28±0.04 | 0.07±0.05 | 0.16±0.05 |
| 170 | A614I | 614 | 0.52±0.11 | 0.59±0.11 | 0.41±0.22 |
| 171 | T616A | 616 | 0.32±0.03 | 0.24±0.04 | 0.09±0.05 |
| 172 | T616R | 616 | 0.19±0.03 | 0.12±0.03 | 0.62±0.04 |
| 173 | T616Q | 616 | 0.35±0.07 | 0.38±0.07 | 0.78±0.2 |
| 174 | T616G | 616 | 0.22±0.03 | 0.01±0.03 | 0.16±0.06 |
| 175 | T616Y | 616 | 0.54±0.09 | 0.64±0.09 | 0.05±0.38 |
| 176 | A617G | 617 | 0.03±0.03 | 0.05±0.03 | 0.24±0.06 |
| 177 | F619M | 619 | 0.12±0.07 | 0.55±0.07 | 0.22±0.25 |
| 178 | Q620A | 620 | 0.22±0.04 | 0±0.05 | 0.18±0.09 |
| 179 | Q620R | 620 | 0.25±0.03 | 0.18±0.03 | 0.17±0.04 |
| 180 | Q620N | 620 | 0.26±0.14 | 0.28±0.14 | 0.36±0.21 |
| 181 | Q620L | 620 | 0.14±0.04 | 0.45±0.04 | 0.4±0.16 |
| 182 | Q620K | 620 | 0.1±0.07 | 0.24±0.07 | 0.04±0.1 |

| SEQ ID NO.: | Mutant | Position | Variant score (condition 1) | Variant score (condition 2) | Variant score (condition 3) |
|---|---|---|---|---|---|
| 183 | T621A | 621 | 0.18±0.04 | 0.13±0.04 | 0.17±0.1 |
| 184 | H622G | 622 | 0.05±0.03 | 0.18±0.03 | 0.07±0.06 |
| 185 | H622S | 622 | 0.16±0.06 | 0.59±0.06 | 0.08±0.1 |
| 186 | H622T | 622 | 0.01±0.09 | 0.84±0.08 | 0.31±0.34 |
| 187 | H622V | 622 | 0.18±0.05 | 0.15±0.05 | 0.31±0.12 |
| 188 | T623E | 623 | 0.32±0.05 | 0.23±0.05 | 0.02±0.05 |
| 189 | T623H | 623 | 0.6±0.1 | 0.01±0.11 | 0.58±0.55 |
| 190 | T623L | 623 | 0.33±0.05 | 0.18±0.05 | 0.17±0.16 |
| 191 | T623M | 623 | 0.21±0.07 | 0.28±0.07 | 0.59±0.22 |
| 192 | T623F | 623 | 0.8±0.1 | 0.61±0.1 | 0.47±0.32 |
| 193 | T624P | 624 | 0.92±0.02 | 0.92±0.02 | 0.04±0.03 |
| 194 | L627C | 627 | 0.14±0.13 | 0.84±0.11 | 0.57±0.48 |
| 195 | L628C | 628 | 0.31±0.09 | 0.1±0.1 | 0.29±0.31 |
| 196 | L628W | 628 | 0.25±0.06 | 0.01±0.07 | 0.67±0.15 |
| 197 | N630R | 630 | 0.53±0.05 | 0.06±0.06 | 0.94±0.08 |
| 198 | I633N | 633 | 0.16±0.06 | 0.65±0.06 | 0.15±0.1 |
| 199 | I633M | 633 | 0.17±0.07 | 0.28±0.07 | 0.1±0.19 |
| 200 | I633S | 633 | 0.02±0.04 | 0.35±0.04 | 0.22±0.08 |
| 201 | E634N | 634 | 0.52±0.12 | 0.46±0.12 | 0±0.36 |
| 202 | P635A | 635 | 0.04±0.05 | 0.29±0.05 | 0.59±0.07 |
| 203 | P635D | 635 | 0.14±0.09 | 0.49±0.09 | 0.52±0.14 |
| 204 | P635E | 635 | 0.51±0.06 | 0.49±0.06 | 0.7±0.16 |
| 205 | P635T | 635 | 0.36±0.06 | 0.06±0.06 | 0.01±0.08 |
| 206 | T639G | 639 | 0.52±0.06 | 0.44±0.06 | 0.06±0.23 |
| 207 | D840S | 840 | 0.37±0.08 | 0.33±0.08 | 0.1±0.16 |
| 208 | A842S | 842 | 0.36±0.06 | 0.08±0.06 | 0.04±0.1 |
| 209 | A844E | 844 | 0.38±0.1 | 0.06±0.1 | 0.13±0.21 |
| 210 | T851A | 851 | 0.41±0.06 | 0.14±0.06 | 0.08±0.1 |
| 211 | T851V | 851 | 0.32±0.06 | 0.13±0.06 | 0.54±0.07 |
| 212 | E853V | 853 | 0.14±0.07 | 0.1±0.07 | 0.38±0.09 |
| 213 | R862K | 862 | 0.04±0.14 | 0.54±0.13 | 0.02±0.38 |
| 214 | S866F | 866 | 0±0.13 | 0.06±0.12 | 0.1±0.14 |
| 215 | S866T | 866 | 0.05±0.13 | 0.02±0.13 | 0.4±0.15 |
| 216 | V873A | 873 | 0.16±0.11 | 0.05±0.11 | 0.08±0.16 |
| 217 | N878D | 878 | 0.03±0.06 | 0.02±0.06 | 0.04±0.08 |
| 218 | Q880R | 880 | 0.13±0.05 | 0.02±0.05 | 0.01±0.06 |
| 219 | Q880G | 880 | 0.25±0.04 | 0.19±0.04 | 0.64±0.05 |
| 220 | A882D | 882 | 0.32±0.05 | 0.22±0.05 | 0.1±0.07 |
| 221 | A882S | 882 | 0.11±0.12 | 0.14±0.11 | 0.23±0.22 |
| 222 | N883G | 883 | 0.42±0.08 | 0.37±0.08 | 0.03±0.11 |
| 223 | N883K | 883 | 0.12±0.16 | 0.23±0.16 | 0.16±0.1 |
| 224 | S884V | 884 | 0.05±0.11 | 0.61±0.1 | 0.03±0.14 |
| 225 | S886L | 886 | 0.09±0.08 | 0.12±0.08 | 0.05±0.11 |
| 226 | S886M | 886 | 0.32±0.11 | 0.15±0.11 | 0.4±0.35 |
| 227 | S886W | 886 | 0.23±0.07 | 0.01±0.07 | 0.7±0.19 |
| 228 | Q890C | 890 | 0.03±0.11 | 0.64±0.1 | 0.08±0.54 |
| 229 | Q890H | 890 | 0.39±0.09 | 0.07±0.09 | 0.04±0.11 |
| 230 | Q890W | 890 | 0.03±0.08 | 0.23±0.07 | 0.03±0.08 |
| 231 | A894R | 894 | 0.19±0.06 | 0.06±0.06 | 0.04±0.08 |
| 232 | A894D | 894 | 0.04±0.06 | 0.09±0.06 | 0.21±0.05 |
| 233 | Y895D | 895 | 0.16±0.04 | 0±0.04 | 0.09±0.04 |
| 234 | H899A | 899 | 0.21±0.08 | 0.16±0.07 | 0.01±0.48 |
| 235 | H899N | 899 | 0.15±0.15 | 0.7±0.14 | 0.08±0.18 |
| 236 | E901D | 901 | 0.07±0.1 | 0.05±0.1 | 0.14±0.15 |
| 237 | P903T | 903 | 0.64±0.13 | 0.52±0.12 | 0.39±0.18 |
| 328 | G906A | 906 | 0.41±0.05 | 0.56±0.04 | 0.42±0.05 |
| 239 | G906S | 906 | 0.4±0.05 | 0.16±0.05 | 0.15±0.06 |
| 240 | I907A | 907 | 0.7±0.1 | 0.42±0.1 | 0.27±0.54 |
| 241 | I907V | 907 | 0.15±0.07 | 0.12±0.07 | 0.13±0.06 |
| 242 | R912A | 912 | 0.46±0.09 | 0.49±0.09 | 0.31±0.64 |

| SEQ ID NO.: | Mutant | Position | Variant score (condition 1) | Variant score (condition 2) | Variant score (condition 3) |
|---|---|---|---|---|---|
| 243 | R912L | 912 | 0.53±0.08 | 0.38±0.08 | 0.21±0.16 |
| 244 | R912S | 912 | 1.04±0.11 | 0.3±0.11 | 0.31±0.54 |
| 245 | R912V | 912 | 0.19±0.09 | 0.23±0.09 | 0.03±0.09 |

[1]The phenotype scores (i.e. natural logarithm of relative enrichment) of each point mutation are provided. The error bar estimates the precision of the measurement, which is dependent on the sequencing count of each variant in the libraries. Only variants with counts greater than 50 in all libraries were included in the analysis.

**[0163]** **Table 5** shows the sequences used as primers to generate the *AsCas12a* saturation mutagenesis library. Standard recombinant methods and techniques were used. The screening library was constructed using the method described in Wrenbeck *et al.* (2016).

**[0164]** **Table 5. Primer sequences to generate *AsCas12a* saturation mutagenesis library.**

| SEQ ID NO.: | Name | Sequence (5'-3')[a] |
|---|---|---|
| 246 | **499_NNK_HsCas12a_R499** | gaccccgagttctccgccNNKctgacaggcatcaaactg |
| 247 | **500_NNK_HsCas12a_L500** | ggaccccgagttctccgccagaNNKacaggcatcaaac |
| 248 | **501_NNK_HsCas12a_T501** | cgagttctccgccagactgNNKggcatcaaactggaaatgg |
| 249 | **502_NNK_HsCas12a_G502** | gagttctccgccagactgacaNNKatcaaactggaaatggaaccc |
| 250 | **503_NNK_HsCas12a_I503** | ctccgccagactgacaggcNNKaaactggaaatggaaccca |
| 251 | **504_NNK_HsCas12a_K504** | gccagactgacaggcatcNNKctggaaatggaacccagc |
| 252 | **505_NNK_HsCas12a_L505** | ccagactgacaggcatcaaaNNKgaaatggaacccagcctgtc |
| 253 | **506_NNK_HsCas12a_E506** | gactgacaggcatcaaactgNNKatggaacccagcctgtcctt |
| 254 | **507_NNK_HsCas12a_M507** | ctgacaggcatcaaactggaaNNKgaacccagcctgtccttctac |
| 255 | **508_NNK_HsCas12a_E508** | ctgacaggcatcaaactggaaatgNNKcccagcctgtccttc |
| 256 | **509_NNK_HsCas12a_P509** | gactgacaggcatcaaactggaaatggaaNNKagcctgtccttctac |
| 257 | **510_NNK_HsCas12a_S510** | atcaaactggaaatggaacccNNKctgtccttctacaacaaggcc |
| 258 | **511_NNK_HsCas12a_L511** | aaactggaaatggaacccagcNNKtccttctacaacaaggccaga |
| 259 | **512_NNK_HsCas12a_S512** | ctggaaatggaacccagcctgNNKttctacaacaaggccagaaac |
| 260 | **513_NNK_HsCas12a_F513** | gaaatggaacccagcctgtccNNKtacaacaaggccagaaactac |
| 261 | **514_NNK_HsCas12a_Y514** | ggaacccagcctgtccttcNNKaacaaggccagaaactacg |
| 262 | **515_NNK_HsCas12a_N515** | cccagcctgtccttctacNNKaaggccagaaactacgcc |
| 263 | **516_NNK_HsCas12a_K516** | cagcctgtccttctacaacNNKgccagaaactacgccacca |
| 264 | **517_NNK_HsCas12a_A517** | cagcctgtccttctacaacaagNNKagaaactacgccaccaagaaac |
| 265 | **518_NNK_HsCas12a_R518** | ctgtccttctacaacaaggccNNKaactacgccaccaagaaaccc |
| 266 | **519_NNK_HsCas12a_N519** | tccttctacaacaaggccagaNNKtacgccaccaagaaaccctac |
| 267 | **520_NNK_HsCas12a_Y520** | ttctacaacaaggccagaaacNNKgccaccaagaaaccctacagc |
| 268 | **521_NNK_HsCas12a_A521** | tacaacaaggccagaaactacNNKaccaagaaaccctacagcgtg |
| 269 | **522_NNK_HsCas12a_T522** | caaggccagaaactacgccNNKaagaaaccctacagcgtgg |
| 270 | **523_NNK_HsCas12a_K523** | ggccagaaactacgccaccNNKaaaccctacagcgtggaaa |
| 271 | **524_NNK_HsCas12a_K524** | ccagaaactacgccaccaagNNKccctacagcgtggaaaagtt |
| 272 | **525_NNK_HsCas12a_P525** | ggccagaaactacgccaccaagaaaNNKtacagcgtggaaaagtttaag |
| 273 | **526_NNK_HsCas12a_Y526** | aactacgccaccaagaaacccNNKagcgtggaaaagtttaagctg |
| 274 | **527_NNK_HsCas12a_S527** | ctacgccaccaagaaaccctacNNKgtggaaaagtttaagctgaactt |
| 275 | **528_NNK_HsCas12a_V528** | cgccaccaagaaaccctacagcNNKgaaaagtttaagctgaacttcc |
| 276 | **529_NNK_HsCas12a_E529** | caccaagaaaccctacagcgtgNNKaagtttaagctgaacttccaga |
| 277 | **530_NNK_HsCas12a_K530** | caagaaaccctacagcgtggaaNNKtttaagctgaacttccagatgc |
| 278 | **531_NNK_HsCas12a_F531** | aaaccctacagcgtggaaaagNNKaagctgaacttccagatgccc |
| 279 | **532_NNK_HsCas12a_K532** | ccctacagcgtggaaaagtttNNKctgaacttccagatgcccac |
| 280 | **533_NNK_HsCas12a_L533** | tacagcgtggaaaagtttaagNNKaacttccagatgcccacctg |
| 281 | **534_NNK_HsCas12a_N534** | gcgtggaaaagtttaagctgNNKttccagatgcccaccctggc |
| 282 | **535_NNK_HsCas12a_F535** | cgtggaaaagtttaagctgaacNNKcagatgcccaccctggccag |
| 283 | **536_NNK_HsCas12a_Q536** | ggaaaagtttaagctgaacttcNNKatgcccaccctggccagcg |
| 284 | **537_NNK_HsCas12a_M537** | ttaagctgaacttccagNNKcccaccctggccagcgg |
| 285 | **538_NNK_HsCas12a_P538** | aagctgaacttccagatgNNKaccctggccagcggct |

| SEQ ID NO.: | Name | Sequence (5'-3')[a] |
|---|---|---|
| 286 | 539_NNK_HsCas12a_T539 | gaacttccagatgcccNNKctggccagcggctggg |
| 287 | 540_NNK_HsCas12a_L540 | ttccagatgcccaccNNKgccagcggctgggac |
| 288 | 541_NNK_HsCas12a_A541 | cagatgcccaccctgNNKagcggctgggacgtg |
| 289 | 542_NNK_HsCas12a_S542 | atgcccaccctggccNNKggctgggacgtgaacaa |
| 290 | 543_NNK_HsCas12a_G543 | gcccaccctggccagcNNKtgggacgtgaacaaag |
| 291 | 544_NNK_HsCas12a_W544 | ccaccctggccagcggcNNKgacgtgaacaaagagaag |
| 292 | 545_NNK_HsCas12a_D545 | ccctggccagcggctggNNKgtgaacaaagagaagaac |
| 293 | 546_NNK_HsCas12a_V546 | ctggccagcggctgggacNNKaacaaagagaagaacaacg |
| 294 | 547_NNK_HsCas12a_N547 | ccagcggctgggacgtgNNKaaagagaagaacaacggc |
| 295 | 548_NNK_HsCas12a_K548 | gcggctgggacgtgaacNNKgagaagaacaacggcgc |
| 296 | 549_NNK_HsCas12a_E549 | cggctgggacgtgaacaaaNNKaagaacaacggcgccatc |
| 297 | 550_NNK_HsCas12a_K550 | ctgggacgtgaacaaagagNNKaacaacggcgccatcctgt |
| 298 | 551_NNK_HsCas12a_N551 | gggacgtgaacaaagagaagNNKaacggcgccatcctgttcg |
| 299 | 552_NNK_HsCas12a_N552 | gacgtgaacaaagagaagaacNNKggcgccatcctgttcgtgaa |
| 300 | 553_NNK_HsCas12a_G553 | cgtgaacaaagagaagaacaacNNKgccatcctgttcgtgaagaacg |
| 301 | 554_NNK_HsCas12a_A554 | gaacaaagagaagaacaacggcNNKatcctgttcgtgaagaacggac |
| 302 | 555_NNK_HsCas12a_I555 | agagaagaacaacggcgccNNKctgttcgtgaagaacggac |
| 303 | 556_NNK_HsCas12a_L556 | gagaagaacaacggcgccatcNNKttcgtgaagaacggactgtac |
| 304 | 557_NNK_HsCas12a_F557 | gaacaacggcgccatcctgNNKgtgaagaacggactgtact |
| 305 | 558_NNK_HsCas12a_V558 | caacggcgccatcctgttcNNKaagaacggactgtactacc |
| 306 | 559_NNK_HsCas12a_K559 | ggcgccatcctgttcgtgNNKaacggactgtactacctg |
| 307 | 560_NNK_HsCas12a_N560 | gccatcctgttcgtgaagNNKggactgtactacctgggc |
| 308 | 561_NNK_HsCas12a_G561 | gccatcctgttcgtgaagaacNNKctgtactacctgggcatcatg |
| 309 | 562_NNK_HsCas12a_L562 | tcctgttcgtgaagaacggaNNKtactacctgggcatcatgcc |
| 310 | 563_NNK_HsCas12a_Y563 | ctgttcgtgaagaacggactgNNKtacctgggcatcatgcctaag |
| 311 | 564_NNK_HsCas12a_Y564 | cgtgaagaacggactgtacNNKctgggcatcatgcctaagc |
| 312 | 565_NNK_HsCas12a_L565 | gtgaagaacggactgtactacNNKggcatcatgcctaagcagaag |
| 313 | 566_NNK_HsCas12a_G566 | aagaacggactgtactacctgNNKatcatgcctaagcagaagggc |
| 314 | 567_NNK_HsCas12a_I567 | ggactgtactacctgggcNNKatgcctaagcagaagggc |
| 315 | 568_NNK_HsCas12a_M568 | gactgtactacctgggcatcNNKcctaagcagaagggcagata |
| 316 | 569_NNK_HsCas12a_P569 | ctgtactacctgggcatcatgNNKaagcagaagggcagatacaag |
| 317 | 570_NNK_HsCas12a_K570 | ctacctgggcatcatgcctNNKcagaagggcagatacaagg |
| 318 | 571_NNK_HsCas12a_Q571 | cctgggcatcatgcctaagNNKaagggcagatacaaggccc |
| 319 | 572_NNK_HsCas12a_K572 | ggcatcatgcctaagcagNNKggcagatacaaggccctg |
| 320 | 573_NNK_HsCas12a_G573 | ggcatcatgcctaagcagaagNNKagatacaaggccctgtccttt |
| 321 | 574_NNK_HsCas12a_R574 | catgcctaagcagaagggcNNKtacaaggccctgtccttg |
| 322 | 575_NNK_HsCas12a_Y575 | gcctaagcagaagggcagaNNKaaggccctgtcctttgagc |
| 323 | 576_NNK_HsCas12a_K576 | aagcagaagggcagatacNNKgccctgtcctttgagccc |
| 324 | 577_NNK_HsCas12a_A577 | gcagaagggcagatacaagNNKctgtcctttgagcccaccg |
| 325 | 578_NNK_HsCas12a_L578 | gaagggcagatacaaggccNNKtcctttgagcccaccgaaa |
| 326 | 579_NNK_HsCas12a_S579 | gggcagatacaaggccctgNNKtttgagcccaccgaaaaga |
| 327 | 580_NNK_HsCas12a_F580 | agatacaaggccctgtccNNKgagcccaccgaaaagacc |
| 328 | 581_NNK_HsCas12a_E581 | ggcagatacaaggccctgtcctttNNKcccaccgaaaagac |
| 329 | 582_NNK_HsCas12a_P582 | caaggccctgtcctttgagNNKaccgaaaagaccagcgag |
| 330 | 584_NNK_HsCas12a_E584 | ctgtcctttgagcccaccNNKaagaccagcgagggctttt |
| 331 | 584_NNK_HsCas12a_T584 | ccctgtcctttgagcccNNKgaaaagaccagcgaggg |
| 332 | 585_NNK_HsCas12a_K585 | gtcctttgagcccaccgaaNNKaccagcgagggctttg |
| 333 | 586_NNK_HsCas12a_T586 | tgtcctttgagcccaccgaaaagNNKagcgagggctttgac |
| 334 | 587_NNK_HsCas12a_S587 | tttgagcccaccgaaaagaccNNKgagggctttgacaagatgtac |
| 335 | 588_NNK_HsCas12a_E588 | gagcccaccgaaaagaccagcNNKggctttgacaagatgtactac |
| 336 | 589_NNK_HsCas12a_G589 | cccaccgaaaagaccagcgagNNKtttgacaagatgtactacgat |
| 337 | 590_NNK_HsCas12a_F590 | accgaaaagaccagcgagggcNNKgacaagatgtactacgattact |
| 338 | 591_NNK_HsCas12a_D591 | ccgaaaagaccagcgagggctttNNKaagatgtactacgattacttcc |
| 339 | 592_NNK_HsCas12a_K592 | aagaccagcgagggctttgacNNKatgtactacgattacttcccc |
| 340 | 593_NNK_HsCas12a_M593 | ccagcgagggctttgacaagNNKtactacgattacttccccga |
| 341 | 594_NNK_HsCas12a_Y594 | gcgagggctttgacaagatgNNKtacgattacttccccgacgc |
| 342 | 595_NNK_HsCas12a_Y595 | gggctttgacaagatgtacNNKgattacttccccgacgccg |
| 343 | 596_NNK_HsCas12a_D596 | ggctttgacaagatgtactacNNKtacttccccgacgccgccaa |
| 344 | 597_NNK_HsCas12a_Y597 | agggctttgacaagatgtactacgatNNKttccccgacgccgc |
| 345 | 598_NNK_HsCas12a_F598 | gctttgacaagatgtactacgattacNNKcccgacgccgccaaga |
| 346 | 599_NNK_HsCas12a_P599 | tttgacaagatgtactacgattacttcNNKgacgccgccaagatgatc |
| 347 | 600_NNK_HsCas12a_D600 | gtactacgattacttccccNNKgccgccaagatgatccccca |
| 348 | 601_NNK_HsCas12a_A601 | actacgattacttccccgacNNKgccaagatgatccccaagtg |
| 349 | 602_NNK_HsCas12a_A602 | cgattacttccccgacgccNNKaagatgatccccaagtgca |
| 350 | 603_NNK_HsCas12a_K603 | cttccccgacgccgccNNKatgatccccaagtgca |
| 351 | 604_NNK_HsCas12a_M604 | cccgacgccgccaagNNKatccccaagtgcagc |
| 352 | 605_NNK_HsCas12a_I605 | cgacgccgccaagatgNNKcccaagtgcagcaccc |
| 353 | 606_NNK_HsCas12a_P606 | gacgccgccaagatgatcNNKaagtgcagcacccagctg |

| SEQ ID NO.: | Name | Sequence (5'-3')[a] |
|---|---|---|
| 354 | 607_NNK_HsCas12a_K607 | ccgccaagatgatccccNNKtgcagcacccagctgaa |
| 355 | 608_NNK_HsCas12a_C608 | gccaagatgatccccaagNNKagcacccagctgaaggcc |
| 356 | 609_NNK_HsCas12a_S609 | aagatgatccccaagtgcNNKacccagctgaaggccgtg |
| 357 | 610_NNK_HsCas12a_T610 | tgatccccaagtgcagcNNKcagctgaaggccgtgac |
| 358 | 611_NNK_HsCas12a_Q611 | ccccaagtgcagcaccNNKctgaaggccgtgaccg |
| 359 | 613_NNK_HsCas12a_K613 | tgcagcacccagctgNNKgccgtgaccgcccac |
| 360 | 613_NNK_HsCas12a_L613 | caagtgcagcacccagNNKaaggccgtgaccgccc |
| 361 | 614_NNK_HsCas12a_A614 | gcagcacccagctgaagNNKgtgaccgcccactttca |
| 362 | 615_NNK_HsCas12a_V615 | gcacccagctgaaggccNNKaccgcccactttcagac |
| 363 | 616_NNK_HsCas12a_T616 | ccagctgaaggccgtgNNKgcccactttcagaccc |
| 364 | 617_NNK_HsCas12a_A617 | cagctgaaggccgtgaccNNKcactttcagacccacacc |
| 365 | 618_NNK_HsCas12a_H618 | tgaaggccgtgaccgccNNKtttcagacccacaccac |
| 366 | 619_NNK_HsCas12a_F619 | gccgtgaccgcccacNNKcagacccacaccacc |
| 367 | 620_NNK_HsCas12a_Q620 | aaggccgtgaccgcccactttNNKacccacaccacc |
| 368 | 621_NNK_HsCas12a_T621 | gaccgcccactttcagNNKcacaccaccccatcc |
| 369 | 622_NNK_HsCas12a_H622 | cgcccactttcagaccNNKaccaccccatcctgc |
| 370 | 623_NNK_HsCas12a_T623 | cccactttcagacccacNNKacccccatcctgctgag |
| 371 | 624_NNK_HsCas12a_T624 | cactttcagacccacaccNNKcccatcctgctgagcaac |
| 372 | 625_NNK_HsCas12a_P625 | cactttcagacccacaccaccNNKatcctgctgagcaacaacttc |
| 373 | 626_NNK_HsCas12a_I626 | cagacccacaccacccccNNKctgctgagcaacaacttc |
| 374 | 627_NNK_HsCas12a_L627 | gacccacaccacccccatcNNKctgagcaacaacttcatcg |
| 375 | 628_NNK_HsCas12a_L628 | ccacaccacccccatcctgNNKagcaacaacttcatcgagc |
| 376 | 629_NNK_HsCas12a_S629 | accacccccatcctgctgNNKaacaacttcatcgagccc |
| 377 | 630_NNK_HsCas12a_N630 | cccccatcctgctgagcNNKaacttcatcgagcccct |
| 378 | 631_NNK_HsCas12a_N631 | cccatcctgctgagcaacNNKttcatcgagcccctggaa |
| 379 | 632_NNK_HsCas12a_F632 | ccatcctgctgagcaacaacNNKatcgagcccctggaaatcac |
| 380 | 633_NNK_HsCas12a_I633 | cctgctgagcaacaactttcNNKgagcccctggaaatcacca |
| 381 | 634_NNK_HsCas12a_E634 | cctgctgagcaacaacttcatcNNKcccctggaaatcaccaaagag |
| 382 | 635_NNK_HsCas12a_P635 | gctgagcaacaacttcatcgagNNKctggaaatcaccaaagagatct |
| 383 | 636_NNK_HsCas12a_L636 | gagcaacaacttcatcgagcccNNKgaaatcaccaaagagatctacg |
| 384 | 637_NNK_HsCas12a_E637 | aacaacttcatcgagcccctgNNKatcaccaaagagatctacgac |
| 385 | 638_NNK_HsCas12a_I638 | aacaacttcatcgagcccctggaaNNKaccaaagagatctacgacc |
| 386 | 639_NNK_HsCas12a_T639 | ttcatcgagcccctggaaatcNNKaaagagatctacgacctgaac |
| 387 | 640_NNK_HsCas12a_K640 | cgagcccctggaaatcaccNNKgagatctacgacctgaaca |
| 388 | 840_NNK_HsCas12a_D840 | ctgagccacgacctgtccNNKgaagctagagcactgctg |
| 389 | 841_NNK_HsCas12a_E841 | ccacgacctgtccgacNNKgctagagcactgctgc |
| 390 | 842_NNK_HsCas12a_A842 | ccacgacctgtccgacgaaNNKagagcactgctgccc |
| 391 | 843_NNK_HsCas12a_R843 | gacctgtccgacgaagctNNKgcactgctgcccaacg |
| 392 | 844_NNK_HsCas12a_A844 | ctgtccgacgaagctagaNNKctgctgcccaacgtgatc |
| 393 | 845_NNK_HsCas12a_L845 | gtccgacgaagctagagcaNNKctgcccaacgtgatcacaa |
| 394 | 846_NNK_HsCas12a_L846 | ccgacgaagctagagcactgNNKcccaacgtgatcacaaaaga |
| 395 | 847_NNK_HsCas12a_P847 | gacgaagctagagcactgctgNNKaacgtgatcacaaaagaggtg |
| 396 | 848_NNK_HsCas12a_N848 | aagctagagcactgctgcccNNKgtgatcacaaaagaggtgtc |
| 397 | 849_NNK_HsCas12a_V849 | ctagagcactgctgcccaacNNKatcacaaaagaggtgtccca |
| 398 | 850_NNK_HsCas12a_I850 | gcactgctgcccaacgtgNNKacaaaagaggtgtcccac |
| 399 | 851_NNK_HsCas12a_T851 | ctgctgcccaacgtgatcNNKaaagaggtgtcccacgag |
| 400 | 852_NNK_HsCas12a_K852 | ctgcccaacgtgatcacaNNKgaggtgtcccacgagatc |
| 401 | 853_NNK_HsCas12a_E853 | cactgctgcccaacgtgatcacaaaaNNKgtgtcccacgagat |
| 402 | 854_NNK_HsCas12a_V854 | gcccaacgtgatcacaaaagagNNKtcccacgagatcatcaaggac |
| 403 | 855_NNK_HsCas12a_S855 | aacgtgatcacaaaagaggtgNNKcacgagatcatcaaggaccgg |
| 404 | 856_NNK_HsCas12a_H856 | tgatcacaaaagaggtgtccNNKgagatcatcaaggaccggcg |
| 405 | 857_NNK_HsCas12a_E857 | cacaaaagaggtgtcccacNNKatcatcaaggaccggcggt |
| 406 | 858_NNK_HsCas12a_I858 | caaaagaggtgtcccacgagNNKatcaaggaccggcggtttac |
| 407 | 859_NNK_HsCas12a_I859 | gaggtgtcccacgagatcNNKaaggaccggcggtttacc |
| 408 | 860_NNK_HsCas12a_K860 | gtgtcccacgagatcatcNNKgaccggcggtttacctc |
| 409 | 861_NNK_HsCas12a_D861 | gtgtcccacgagatcatcaagNNKcggcggtttacctcc |
| 410 | 862_NNK_HsCas12a_R862 | tcccacgagatcatcaaggacNNKcggtttacctccgataagttc |
| 411 | 863_NNK_HsCas12a_R863 | cacgagatcatcaaggaccggNNKtttacctccgataagttcttc |
| 412 | 864_NNK_HsCas12a_F864 | gagatcatcaaggaccggcggNNKacctccgataagttcttcttc |
| 413 | 865_NNK_HsCas12a_T865 | cgagatcatcaaggaccggcggtttNNKtccgataagttcttcttc |
| 414 | 866_NNK_HsCas12a_S866 | atcaaggaccggcggtttaccNNKgataagttcttcttccacgtg |
| 415 | 867_NNK_HsCas12a_D867 | ggaccggcggtttacctccNNKaagttcttcttccacgtgc |
| 416 | 868_NNK_HsCas12a_K868 | ccggcggtttacctccgatNNKttcttcttccacgtgccc |
| 417 | 869_NNK_HsCas12a_F869 | ggcggtttacctccgataagNNKttcttccacgtgcccatcac |
| 418 | 870_NNK_HsCas12a_F870 | ggtttacctccgataagttcNNKttccacgtgcccatcaccct |
| 419 | 871_NNK_HsCas12a_F871 | tttacctccgataagttcttcNNKcacgtgcccatcaccctgaac |
| 420 | 872_NNK_HsCas12a_H872 | acctccgataagttcttcttcNNKgtgcccatcaccctgaactac |
| 421 | 873_NNK_HsCas12a_V873 | tccgataagttcttcttccacNNKcccatcaccctgaactaccag |

| SEQ ID NO.: | Name | Sequence (5'-3')[a] |
|---|---|---|
| 422 | 874_NNK_HsCas12a_P874 | gataagttcttcttccacgtgNNKatcaccctgaactaccaggcc |
| 423 | 875_NNK_HsCas12a_I875 | ttcttcttccacgtgcccNNKaccctgaactaccaggcc |
| 424 | 876_NNK_HsCas12a_T876 | tcttccacgtgcccatcNNKctgaactaccaggccgc |
| 425 | 877_NNK_HsCas12a_L877 | ccacgtgcccatcaccNNKaactaccaggccgcca |
| 426 | 878_NNK_HsCas12a_N878 | cgtgcccatcaccctgNNKtaccaggccgccaaca |
| 427 | 879_NNK_HsCas12a_Y879 | gcccatcaccctgaacNNKcaggccgccaacagcc |
| 428 | 880_NNK_HsCas12a_Q880 | ccatcaccctgaactacNNKgccgccaacagcccca |
| 429 | 881_NNK_HsCas12a_A881 | atcaccctgaactaccagNNKgccaacagccccagcaag |
| 430 | 882_NNK_HsCas12a_A882 | accctgaactaccaggccNNKaacagccccagcaagttc |
| 431 | 883_NNK_HsCas12a_N883 | ctgaactaccaggccgccNNKagccccagcaagttcaac |
| 432 | 884_NNK_HsCas12a_S884 | aactaccaggccgccaacNNKcccagcaagttcaaccag |
| 433 | 885_NNK_HsCas12a_P885 | ctaccaggccgccaacagcNNKagcaagttcaaccagagag |
| 434 | 886_NNK_HsCas12a_S886 | caggccgccaacagccccNNKaagttcaaccagagagtg |
| 435 | 887_NNK_HsCas12a_K887 | gccgccaacagccccagcNNKttcaaccagagagtgaac |
| 436 | 888_NNK_HsCas12a_F888 | gccaacagccccagcaagNNKaaccagagagtgaacgcc |
| 437 | 889_NNK_HsCas12a_N889 | caacagccccagcaagttcNNKcagagagtgaacgcctacc |
| 438 | 890_NNK_HsCas12a_Q890 | cagccccagcaagttcaacNNKagagtgaacgcctacctga |
| 439 | 891_NNK_HsCas12a_R891 | ccccagcaagttcaaccagNNKgtgaacgcctacctgaaag |
| 440 | 892_NNK_HsCas12a_V892 | cccagcaagttcaaccagagaNNKaacgcctacctgaaagagcac |
| 441 | 893_NNK_HsCas12a_N893 | gcaagttcaaccagagagtgNNKgcctacctgaaagagcaccc |
| 442 | 894_NNK_HsCas12a_A894 | aagttcaaccagagagtgaacNNKtacctgaaagagcaccccgag |
| 443 | 895_NNK_HsCas12a_Y895 | aaccagagagtgaacgccNNKctgaaagagcaccccgag |
| 444 | 896_NNK_HsCas12a_L896 | ccagagagtgaacgcctacNNKaaagagcaccccgagacac |
| 445 | 897_NNK_HsCas12a_K897 | gagtgaacgcctacctgNNKgagcaccccgagacacc |
| 446 | 898_NNK_HsCas12a_E898 | agagagtgaacgcctacctgaaaNNKcaccccgagacacc |
| 447 | 899_NNK_HsCas12a_H899 | gaacgcctacctgaaagagNNKcccgagacacccatcattg |
| 448 | 900_NNK_HsCas12a_P900 | cgcctacctgaaagagcacNNKgagacacccatcattggca |
| 449 | 901_NNK_HsCas12a_E901 | ctacctgaaagagcaccccNNKacacccatcattggcatcg |
| 450 | 902_NNK_HsCas12a_T902 | ctgaaagagcaccccgagNNKcccatcattggcatcgac |
| 451 | 903_NNK_HsCas12a_P903 | tgaaagagcaccccgagacaNNKatcattggcatcgacagagg |
| 452 | 904_NNK_HsCas12a_I904 | agcaccccgagacacccNNKattggcatcgacagagg |
| 453 | 905_NNK_HsCas12a_I905 | ccccgagacacccatcNNKggcatcgacagaggcg |
| 454 | 906_NNK_HsCas12a_G906 | gagcaccccgagacacccatcattNNKatcgacagaggcg |
| 455 | 907_NNK_HsCas12a_I907 | gagacacccatcattggcNNKgacagaggcgagcggaac |
| 456 | 908_NNK_HsCas12a_D908 | acacccatcattggcatcNNKagaggcgagcggaacctg |
| 457 | 909_NNK_HsCas12a_R909 | cccatcattggcatcgacNNKggcgagcggaacctgatc |
| 458 | 910_NNK_HsCas12a_G910 | cccatcattggcatcgacagaNNKgagcggaacctgatctacatc |
| 459 | 911_NNK_HsCas12a_E911 | tcattggcatcgacagaggcNNKcggaacctgatctacatcac |
| 460 | 912_NNK_HsCas12a_R912 | tggcatcgacagaggcgagNNKaacctgatctacatcaccg |
| 461 | 913_NNK_HsCas12a_N913 | atcgacagaggcgagcggNNKctgatctacatcaccgtg |

[a]For "NNK", N refers to A, C, T or G; K refers to G or T.

**[0165]** With respect to **Table 4**, the reference (*i.e.*, wild-type) polypeptide sequence is SEQ ID NO.: 462 upon which these mutants are based by comparison. Polynucleotides codon-optimized for expression in *E. coli* and human cells that encode SEQ ID NO.:462 are SEQ ID NOs.: 463 and 464, respectively. The same mutations were introduced as well into M537R/F870L-*AsCas12a* background. The corresponding reference polypeptide sequence for the M537R/F870L-Cas12a is SEQ ID NO.: 465 (the altered amino acids are underlined). Polynucleotides codon-optimized for expression in *E. coli* and human cells that encode SEQ ID NO.:465 are SEQ ID NOs.: 466 and 467, respectively (the altered codons are underlined).

**[0166]** SEQ ID NO.: 462

**[0167]** MTQFEGFTNLYQVSKTLRFELIPQGKTLKHIQEQGFIEEDKARNDHYKELKPIIDRIYKTYADQCLQLV
QLDWENLSAAIDSYRKEKTEETRNALIEEQATYRNAIHDYFIGRTDNLTDAINKRHAEIYKGLFKAELFNGKVLKQLG
TVTTTEHENALLRSFDKFTTYFSGFYENRKNVFSAEDISTAIPHRIVQDNFPKFKENCHIFTRLITAVPSLREHFENVKK
AIGIFVSTSIEEVFSFPFYNQLLTQTQIDLYNQLLGGISREAGTEKIKGLNEVLNLAIQKNDETAHIIASLPHRFIPLFKQI
LSDRNTLSFILEEFKSDEEVIQSFCKYKTLLRNENVLETAEALFNELNSIDLTHIFISHKKLETISSALCDHWDTLRNALYE
RRISELTGKITKSAKEKVQRSLKHEDINLQEIISAAGKELSEAFKQKTSEILSHAHAALDQPLPTTLKKQEEKEILKSQLD
SLLGLYHLLDWFAVDESNEVDPEFSARLTGIKLEMEPSLSFYNKARNYATKKPYSVEKFKLNFQMPTLASGWDVNK
EKNNGAILFVKNGLYYLGIMPKQKGRYKALSFEPTEKTSEGFDKMYYDYFPDAAKMIPKCSTQLKAVTAHFQTHTT
PILLSNNFIEPLEITKEIYDLNNPEKEPKKFQTAYAKKTGDQKGYREALCKWIDFTRDFLSKYTKTTSIDLSSLRPSSQYK
DLGEYYAELNPLLYHISFQRIAEKEIMDAVETGKLYLFQIYNKDFAKGHHGKPNLHTLYWTGLFSPENLAKTSIKLNG
QAELFYRPKSRMKRMAHRLGEKMLNKKLKDQKTPIPDTLYQELYDYVNHRLSHDLSDEARALLPNVITKEVSHEIIK
DRRFTSDKFFFHVPITLNYQAANSPSKFNQRVNAYLKEHPETPIIGIDRGERNLIYITVIDSTGKILEQRSLNTIQQFDY
QKKLDNREKERVAARQAWSVVGTIKDLKQGYLSQVIHEIVDLMIHYQAVVVLENLNFGFKSKRTGIAEKAVYQQFE
KMLIDKLNCLVLKDYPAEKVGGVLNPYQLTDQFTSFAKMGTQSGFLFYVPAPYTSKIDPLTGFVDPFVWKTIKNHES
RKHFLEGFDFLHYDVKTGDFILHFKMNRNLSFQRGLPGFMPAWDIVFEKNETQFDAKGTPFIAGKRIVPVIENHRF
TGRYRDLYPANELIALLEEKGIVFRDGSNILPKLLENDDSHAIDTMVALIRSVLQMRNSNAATGEDYINSPVRDLNG
VCFDSRFQNPEWPMDADANGAYHIALKGQLLLNHLKESKDLKLQNGISNQDWLAYIQELRN

**[0168]** SEQ ID NO.: 463

**[0169]** atgACCCAGTTTGAAGGTTTCACCAATCTGTATCAGGTTAGCAAAACCCTGCGTTTTGAACTGATT
CCGCAGGGTAAAACCCTGAAACATATTCAAGAACAGGGCTTCATCGAAGAGGATAAAGCACGTAACGATCAC
TACAAAGAACTGAAACCGATTATCGACCGCATCTATAAAACCTATGCAGATCAGTGTCTGCAGCTGGTTCAGC
TGGATTGGGAAAATCTGAGCGCAGCAATTGATAGTTATCGCAAAGAAAAAACCGAAGAAACCCGTAATGCAC
TGATTGAAGAACAGGCAACCTATCGTAATGCCATCCATGATTATTTCATTGGTCGTACCGATAATCTGACCGAT
GCAATTAACAAACGTCACGCCGAAATCTATAAAGGCCTGTTTAAAGCCGAACTGTTTAATGGCAAAGTTCTGA
AACAGCTGGGCACCGTTACCACCACCGAACATGAAAATGCACTGCTGCGTAGCTTTGATAAATTCACCACCTA
TTTCAGCGGCTTTTATGAGAATCGCAAAAACGTGTTTAGCGCAGAAGATATTAGCACCGCAATTCCGCATCGT
ATTGTGCAGGATAATTTCCCGAAATTCAAAGAGAACTGCCACATTTTTACCCGTCTGATTACCGCAGTTCCGAG
CCTGCGTGAACATTTTGAAAACGTTAAAAAAGCCATCGGCATCTTTGTTAGCACCAGCATTGAAGAAGTTTTTA
GCTTCCCGTTTTACAATCAGCTGCTGACCCAGACCCAGATTGATCTGTATAACCAACTGCTGGGTGGTATTAGC
CGTGAAGCAGGCACCGAAAAAATCAAAGGTCTGAATGAAGTGCTGAATCTGGCCATTCAGAAAAATGATGAA
ACCGCACATATTATTGCAAGCCTGCCGCATCGTTTTATTCCGCTGTTCAAACAAATTCTGAGCGATCGTAATAC

CCTGAGCTTTATTCTGGAAGAATTCAAATCCGATGAAGAGGTGATTCAGAGCTTTTGCAAATACAAAACGCTG
CTGCGCAATGAAAATGTTCTGGAAACTGCCGAAGCACTGTTTAACGAACTGAATAGCATTGATCTGACCCACA
TCTTTATCAGCCACAAAAAACTGGAAACCATTTCAAGCGCACTGTGTGATCATTGGGATACCCTGCGTAATGCC
CTGTATGAACGTCGTATTAGCGAACTGACCGGTAAAATTACCAAAAGCGCGAAAGAAAAAGTTCAGCGCAGT
CTGAAACATGAGGATATTAATCTGCAAGAGATTATTAGCGCAGCCGGTAAAGAACTGTCAGAAGCATTTAAA
CAGAAAACCAGCGAAATTCTGTCACATGCACATGCAGCACTGGATCAGCCGCTGCCGACCACCCTGAAAAAAC
AAGAAGAAAAAGAAATCCTGAAAAGCCAGCTGGATAGCCTGCTGGGTCTGTATCATCTGCTGGACTGGTTTG
CAGTTGATGAAAGCAATGAAGTTGATCCGGAATTTAGCGCACGTCTGACCGGCATTAAACTGGAAATGGAAC
CGAGCCTGAGCTTTTATAACAAAGCCCGTAATTATGCCACCAAAAAACCGTATAGCGTCGAAAAATTCAAACT
GAACTTTCAGATGCCGACCCTGGCAAGCGGTTGGGATGTTAATAAAGAAAAAAACAACGGTGCCATCCTGTT
CGTGAAAAATGGCCTGTATTATCTGGGTATTATGCCGAAACAGAAAGGTCGTTATAAAGCGCTGAGCTTTGAA
CCGACGGAAAAAACCAGTGAAGGTTTTGATAAAATGTACTACGACTATTTTCCGGATGCAGCCAAAATGATTC
CGAAATGTAGCACCCAGCTGAAAGCAGTTACCGCACATTTTCAGACCCATACCACCCCGATTCTGCTGAGCAA
TAACTTTATTGAACCGCTGGAAATCACCAAAGAGATCTACGATCTGAATAACCCGGAAAAAGAGCCGAAAAA
ATTCCAGACCGCATATGCAAAAAAAACCGGTGATCAGAAAGGTTATCGTGAAGCGCTGTGTAAATGGATTGA
TTTCACCCGTGATTTTCTGAGCAAATACACCAAAACCACCAGTATCGATCTGAGCAGCCTGCGTCCGAGCAGC
CAGTATAAAGATCTGGGCGAATATTATGCAGAACTGAATCCGCTGCTGTATCATATTAGCTTTCAGCGTATTGC
CGAGAAAGAAATCATGGACGCAGTTGAAACCGGTAAACTGTACCTGTTCCAGATCTACAATAAAGATTTTGCC
AAAGGCCATCATGGCAAACCGAATCTGCATACCCTGTATTGGACCGGTCTGTTTAGCCCTGAAAATCTGGCAA
AAACCTCGATTAAACTGAATGGTCAGGCGGAACTGTTTTATCGTCCGAAAAGCCGTATGAAACGTATGGCACA
TCGTCTGGGTGAAAAAATGCTGAACAAAAAACTGAAAGACCAGAAAACCCCGATCCCGGATACACTGTATCA
AGAACTGTATGATTATGTGAACCATCGTCTGAGCCATGATCTGAGTGATGAAGCACGTGCCCTGCTGCCGAAT
GTTATTACCAAAGAAGTTAGCCACGAGATCATTAAAGATCGTCGTTTTACCAGCGACAAATTCTTTTTTCATGT
GCCGATTACCCTGAATTATCAGGCAGCAAATAGCCCGAGCAAATTTAACCAGCGTGTTAATGCATATCTGAAA
GAACATCCAGAAACGCCGATTATTGGTATTGATCGTGGTGAACGTAACCTGATTTATATCACCGTTATTGATAG
CACCGGCAAAATCCTGGAACAGCGTAGCCTGAATACCATTCAGCAGTTTGATTACCAGAAAAAACTGGATAAT
CGCGAGAAAGAACGTGTTGCAGCACGTCAGGCATGGTCAGTTGTTGGTACAATTAAAGACCTGAAACAGGGT
TATCTGAGCCAGGTTATTCATGAAATTGTGGATCTGATGATTCACTATCAGGCCGTTGTTGTGCTGGAAAACCT
GAATTTTGGCTTTAAAAGCAAACGTACCGGCATTGCAGAAAAAGCAGTTTATCAGCAGTTCGAGAAAATGCTG
ATTGACAAACTGAATTGCCTGGTGCTGAAAGATTATCCGGCTGAAAAAGTTGGTGGTGTTCTGAATCCGTATC
AGCTGACCGATCAGTTTACCAGCTTTGCAAAAATGGGCACCCAGAGCGGATTTCTGTTTTATGTTCCGGCACC
GTATACGAGCAAAATTGATCCGCTGACCGGTTTTGTTGATCCGTTTGTTTGGAAAACCATCAAAAACCATGAA
AGCCGCAAACATTTTCTGGAAGGTTTCGATTTTCTGCATTACGACGTTAAAACGGGTGATTTCATCCTGCACTT

TAAAATGAATCGCAATCTGAGTTTTCAGCGTGGCCTGCCTGGTTTTATGCCTGCATGGGATATTGTGTTTGAGA
AAAACGAAACACAGTTCGATGCAAAAGGCACCCCGTTTATTGCAGGTAAACGTATTGTTCCGGTGATTGAAAA
TCATCGTTTCACCGGTCGTTATCGCGATCTGTATCCGGCAAATGAACTGATCGCACTGCTGGAAGAGAAAGGT
ATTGTTTTTCGTGATGGCTCAAACATTCTGCCGAAACTGCTGGAAAATGATGATAGCCATGCAATTGATACCAT
GGTTGCACTGATTCGTAGCGTTCTGCAGATGCGTAATAGCAATGCAGCAACCGGTGAAGATTACATTAATAGT
CCGGTTCGTGATCTGAATGGTGTTTGTTTTGATAGCCGTTTTCAGAATCCGGAATGGCCGATGGATGCAGATG
CAAATGGTGCATATCATATTGCACTGAAAGGACAGCTGCTGCTGAACCACCTGAAAGAAAGCAAAGATCTGA
AACTGCAAAACGGCATTAGCAATCAGGATTGGCTGGCATATATCCAAGAACTGCGTAAC

**[0170]** SEQ ID NO.: 464

**[0171]** atgACCCAGTTTGAAGGTTTCACCAATCTGTATCAGGTTAGCAAAACCCTGCGTTTTGAACTGATT
CCGCAGGGTAAAACCCTGAAACATATTCAAGAACAGGGCTTCATCGAAGAGGATAAAGCACGTAACGATCAC
TACAAAGAACTGAAACCGATTATCGACCGCATCTATAAAACCTATGCAGATCAGTGTCTGCAGCTGGTTCAGC
TGGATTGGGAAAATCTGAGCGCAGCAATTGATAGTTATCGCAAAGAAAAAACCGAAGAAACCCGTAATGCAC
TGATTGAAGAACAGGCAACCTATCGTAATGCCATCCATGATTATTTCATTGGTCGTACCGATAATCTGACCGAT
GCAATTAACAAACGTCACGCCGAAATCTATAAAGGCCTGTTTAAAGCCGAACTGTTTAATGGCAAAGTTCTGA
AACAGCTGGGCACCGTTACCACCACCGAACATGAAAATGCACTGCTGCGTAGCTTTGATAAATTCACCACCTA
TTTCAGCGGCTTTTATGAGAATCGCAAAAACGTGTTTAGCGCAGAAGATATTAGCACCGCAATTCCGCATCGT
ATTGTGCAGGATAATTTCCCGAAATTCAAAGAGAACTGCCACATTTTTACCCGTCTGATTACCGCAGTTCCGAG
CCTGCGTGAACATTTTGAAAACGTTAAAAAAGCCATCGGCATCTTTGTTAGCACCAGCATTGAAGAAGTTTTTA
GCTTCCCGTTTTACAATCAGCTGCTGACCCAGACCCAGATTGATCTGTATAACCAACTGCTGGGTGGTATTAGC
CGTGAAGCAGGCACCGAAAAAATCAAAGGTCTGAATGAAGTGCTGAATCTGGCCATTCAGAAAAATGATGAA
ACCGCACATATTATTGCAAGCCTGCCGCATCGTTTTATTCCGCTGTTCAAACAAATTCTGAGCGATCGTAATAC
CCTGAGCTTTATTCTGGAAGAATTCAAATCCGATGAAGAGGTGATTCAGAGCTTTTGCAAATACAAAACGCTG
CTGCGCAATGAAAATGTTCTGGAAACTGCCGAAGCACTGTTTAACGAACTGAATAGCATTGATCTGACCCACA
TCTTTATCAGCCACAAAAAACTGGAAACCATTTCAAGCGCACTGTGTGATCATTGGGATACCCTGCGTAATGCC
CTGTATGAACGTCGTATTAGCGAACTGACCGGTAAAATTACCAAAAGCGCGAAAGAAAAAGTTCAGCGCAGT
CTGAAACATGAGGATATTAATCTGCAAGAGATTATTAGCGCAGCCGGTAAAGAACTGTCAGAAGCATTTAAA
CAGAAAACCAGCGAAATTCTGTCACATGCACATGCAGCACTGGATCAGCCGCTGCCGACCACCCTGAAAAAAC
AAGAAGAAAAAGAAATCCTGAAAAGCCAGCTGGATAGCCTGCTGGGTCTGTATCATCTGCTGGACTGGTTTG
CAGTTGATGAAAGCAATGAAGTTGATCCGGAATTTAGCGCACGTCTGACCGGCATTAAACTGGAAATGGAAC
CGAGCCTGAGCTTTTATAACAAAGCCCGTAATTATGCCACCAAAAAACCGTATAGCGTCGAAAAATTCAAACT
GAACTTTCAGATGCCGACCCTGGCAAGCGGTTGGGATGTTAATAAAGAAAAAAACAACGGTGCCATCCTGTT

CGTGAAAAATGGCCTGTATTATCTGGGTATTATGCCGAAACAGAAAGGTCGTTATAAAGCGCTGAGCTTTGAA
CCGACGGAAAAAACCAGTGAAGGTTTTGATAAAATGTACTACGACTATTTTCCGGATGCAGCCAAAATGATTC
CGAAATGTAGCACCCAGCTGAAAGCAGTTACCGCACATTTTCAGACCCATACCACCCCGATTCTGCTGAGCAA
TAACTTTATTGAACCGCTGGAAATCACCAAAGAGATCTACGATCTGAATAACCCGGAAAAAGAGCCGAAAAA
ATTCCAGACCGCATATGCAAAAAAAACCGGTGATCAGAAAGGTTATCGTGAAGCGCTGTGTAAATGGATTGA
TTTCACCCGTGATTTTCTGAGCAAATACACCAAAACCACCAGTATCGATCTGAGCAGCCTGCGTCCGAGCAGC
CAGTATAAAGATCTGGGCGAATATTATGCAGAACTGAATCCGCTGCTGTATCATATTAGCTTTCAGCGTATTGC
CGAGAAAGAAATCATGGACGCAGTTGAAACCGGTAAACTGTACCTGTTCCAGATCTACAATAAAGATTTTGCC
AAAGGCCATCATGGCAAACCGAATCTGCATACCCTGTATTGGACCGGTCTGTTTAGCCCTGAAAATCTGGCAA
AAACCTCGATTAAACTGAATGGTCAGGCGGAACTGTTTTATCGTCCGAAAAGCCGTATGAAACGTATGGCACA
TCGTCTGGGTGAAAAAATGCTGAACAAAAAACTGAAAGACCAGAAAACCCCGATCCCGGATACACTGTATCA
AGAACTGTATGATTATGTGAACCATCGTCTGAGCCATGATCTGAGTGATGAAGCACGTGCCCTGCTGCCGAAT
GTTATTACCAAAGAAGTTAGCCACGAGATCATTAAAGATCGTCGTTTTACCAGCGACAAATTCTTTTTTCATGT
GCCGATTACCCTGAATTATCAGGCAGCAAATAGCCCGAGCAAATTTAACCAGCGTGTTAATGCATATCTGAAA
GAACATCCAGAAACGCCGATTATTGGTATTGATCGTGGTGAACGTAACCTGATTTATATCACCGTTATTGATAG
CACCGGCAAAATCCTGGAACAGCGTAGCCTGAATACCATTCAGCAGTTTGATTACCAGAAAAAACTGGATAAT
CGCGAGAAAGAACGTGTTGCAGCACGTCAGGCATGGTCAGTTGTTGGTACAATTAAAGACCTGAAACAGGGT
TATCTGAGCCAGGTTATTCATGAAATTGTGGATCTGATGATTCACTATCAGGCCGTTGTTGTGCTGGAAAACCT
GAATTTTGGCTTTAAAAGCAAACGTACCGGCATTGCAGAAAAAGCAGTTTATCAGCAGTTCGAGAAAATGCTG
ATTGACAAACTGAATTGCCTGGTGCTGAAAGATTATCCGGCTGAAAAAGTTGGTGGTGTTCTGAATCCGTATC
AGCTGACCGATCAGTTTACCAGCTTTGCAAAAATGGGCACCCAGAGCGGATTTCTGTTTTATGTTCCGGCACC
GTATACGAGCAAAATTGATCCGCTGACCGGTTTTGTTGATCCGTTTGTTTGGAAAACCATCAAAAACCATGAA
AGCCGCAAACATTTTCTGGAAGGTTTCGATTTTCTGCATTACGACGTTAAAACGGGTGATTTCATCCTGCACTT
TAAAATGAATCGCAATCTGAGTTTTCAGCGTGGCCTGCCTGGTTTTATGCCTGCATGGGATATTGTGTTTGAGA
AAAACGAAACACAGTTCGATGCAAAAGGCACCCCGTTTATTGCAGGTAAACGTATTGTTCCGGTGATTGAAAA
TCATCGTTTCACCGGTCGTTATCGCGATCTGTATCCGGCAAATGAACTGATCGCACTGCTGGAAGAGAAAGGT
ATTGTTTTTCGTGATGGCTCAAACATTCTGCCGAAACTGCTGGAAAATGATGATAGCCATGCAATTGATACCAT
GGTTGCACTGATTCGTAGCGTTCTGCAGATGCGTAATAGCAATGCAGCAACCGGTGAAGATTACATTAATAGT
CCGGTTCGTGATCTGAATGGTGTTTGTTTTGATAGCCGTTTTCAGAATCCGGAATGGCCGATGGATGCAGATG
CAAATGGTGCATATCATATTGCACTGAAAGGACAGCTGCTGCTGAACCACCTGAAAGAAAGCAAAGATCTGA
AACTGCAAAACGGCATTAGCAATCAGGATTGGCTGGCATATATCCAAGAACTGCGTAAC

**[0172]** SEQ ID NO.: 465

**[0173]** MTQFEGFTNLYQVSKTLRFELIPQGKTLKHIQEQGFIEEDKARNDHYKELKPIIDRIYKTYADQCLQLV
QLDWENLSAAIDSYRKEKTEETRNALIEEQATYRNAIHDYFIGRTDNLTDAINKRHAEIYKGLFKAELFNGKVLKQLG
TVTTTEHENALLRSFDKFTTYFSGFYENRKNVFSAEDISTAIPHRIVQDNFPKFKENCHIFTRLITAVPSLREHFENVKK
AIGIFVSTSIEEVFSFPFYNQLLTQTQIDLYNQLLGGISREAGTEKIKGLNEVLNLAIQKNDETAHIIASLPHRFIPLFKQI
LSDRNTLSFILEEFKSDEEVIQSFCKYKTLLRNENVLETAEALFNELNSIDLTHIFISHKKLETISSALCDHWDTLRNALYE
RRISELTGKITKSAKEKVQRSLKHEDINLQEIISAAGKELSEAFKQKTSEILSHAHAALDQPLPTTLKKQEEKEILKSQLD
SLLGLYHLLDWFAVDESNEVDPEFSARLTGIKLEMEPSLSFYNKARNYATKKPYSVEKFKLNFQRPTLASGWDVNKE
KNNGAILFVKNGLYYLGIMPKQKGRYKALSFEPTEKTSEGFDKMYYDYFPDAAKMIPKCSTQLKAVTAHFQTHTTPI
LLSNNFIEPLEITKEIYDLNNPEKEPKKFQTAYAKKTGDQKGYREALCKWIDFTRDFLSKYTKTTSIDLSSLRPSSQYKD
LGEYYAELNPLLYHISFQRIAEKEIMDAVETGKLYLFQIYNKDFAKGHHGKPNLHTLYWTGLFSPENLAKTSIKLNGQ
AELFYRPKSRMKRMAHRLGEKMLNKKLKDQKTPIPDTLYQELYDYVNHRLSHDLSDEARALLPNVITKEVSHEIIKD
RRFTSDKFLFHVPITLNYQAANSPSKFNQRVNAYLKEHPETPIIGIDRGERNLIYITVIDSTGKILEQRSLNTIQQFDYQ
KKLDNREKERVAARQAWSVVGTIKDLKQGYLSQVIHEIVDLMIHYQAVVVLENLNFGFKSKRTGIAEKAVYQQFEK
MLIDKLNCLVLKDYPAEKVGGVLNPYQLTDQFTSFAKMGTQSGFLFYVPAPYTSKIDPLTGFVDPFVWKTIKNHESR
KHFLEGFDFLHYDVKTGDFILHFKMNRNLSFQRGLPGFMPAWDIVFEKNETQFDAKGTPFIAGKRIVPVIENHRFT
GRYRDLYPANELIALLEEKGIVFRDGSNILPKLLENDDSHAIDTMVALIRSVLQMRNSNAATGEDYINSPVRDLNGV
CFDSRFQNPEWPMDADANGAYHIALKGQLLLNHLKESKDLKLQNGISNQDWLAYIQELRN

**[0174]** SEQ ID NO.: 466

**[0175]** atgACCCAGTTTGAAGGTTTCACCAATCTGTATCAGGTTAGCAAAACCCTGCGTTTTGAACTGATT
CCGCAGGGTAAAACCCTGAAACATATTCAAGAACAGGGCTTCATCGAAGAGGATAAAGCACGTAACGATCAC
TACAAAGAACTGAAACCGATTATCGACCGCATCTATAAAACCTATGCAGATCAGTGTCTGCAGCTGGTTCAGC
TGGATTGGGAAAATCTGAGCGCAGCAATTGATAGTTATCGCAAAGAAAAAACCGAAGAAACCCGTAATGCAC
TGATTGAAGAACAGGCAACCTATCGTAATGCCATCCATGATTATTTCATTGGTCGTACCGATAATCTGACCGAT
GCAATTAACAAACGTCACGCCGAAATCTATAAAGGCCTGTTTAAAGCCGAACTGTTTAATGGCAAAGTTCTGA
AACAGCTGGGCACCGTTACCACCACCGAACATGAAAATGCACTGCTGCGTAGCTTTGATAAATTCACCACCTA
TTTCAGCGGCTTTTATGAGAATCGCAAAAACGTGTTTAGCGCAGAAGATATTAGCACCGCAATTCCGCATCGT
ATTGTGCAGGATAATTTCCCGAAATTCAAAGAGAACTGCCACATTTTTACCCGTCTGATTACCGCAGTTCCGAG
CCTGCGTGAACATTTTGAAAACGTTAAAAAAGCCATCGGCATCTTTGTTAGCACCAGCATTGAAGAAGTTTTTA
GCTTCCCGTTTTACAATCAGCTGCTGACCCAGACCCAGATTGATCTGTATAACCAACTGCTGGGTGGTATTAGC
CGTGAAGCAGGCACCGAAAAAATCAAAGGTCTGAATGAAGTGCTGAATCTGGCCATTCAGAAAAATGATGAA
ACCGCACATATTATTGCAAGCCTGCCGCATCGTTTTATTCCGCTGTTCAAACAAATTCTGAGCGATCGTAATAC

CCTGAGCTTTATTCTGGAAGAATTCAAATCCGATGAAGAGGTGATTCAGAGCTTTTGCAAATACAAAACGCTG
CTGCGCAATGAAAATGTTCTGGAAACTGCCGAAGCACTGTTTAACGAACTGAATAGCATTGATCTGACCCACA
TCTTTATCAGCCACAAAAAACTGGAAACCATTTCAAGCGCACTGTGTGATCATTGGGATACCCTGCGTAATGCC
CTGTATGAACGTCGTATTAGCGAACTGACCGGTAAAATTACCAAAAGCGCGAAAGAAAAAGTTCAGCGCAGT
CTGAAACATGAGGATATTAATCTGCAAGAGATTATTAGCGCAGCCGGTAAAGAACTGTCAGAAGCATTTAAA
CAGAAAACCAGCGAAATTCTGTCACATGCACATGCAGCACTGGATCAGCCGCTGCCGACCACCCTGAAAAAAC
AAGAAGAAAAAGAAATCCTGAAAAGCCAGCTGGATAGCCTGCTGGGTCTGTATCATCTGCTGGACTGGTTTG
CAGTTGATGAAAGCAATGAAGTTGATCCGGAATTTAGCGCACGTCTGACCGGCATTAAACTGGAAATGGAAC
CGAGCCTGAGCTTTTATAACAAAGCCCGTAATTATGCCACCAAAAAACCGTATAGCGTCGAAAAATTCAAACT
GAACTTTCAGCGTCCGACCCTGGCAAGCGGTTGGGATGTTAATAAAGAAAAAAACAACGGTGCCATCCTGTTC
GTGAAAAATGGCCTGTATTATCTGGGTATTATGCCGAAACAGAAAGGTCGTTATAAAGCGCTGAGCTTTGAAC
CGACGGAAAAAACCAGTGAAGGTTTTGATAAAATGTACTACGACTATTTTCCGGATGCAGCCAAAATGATTCC
GAAATGTAGCACCCAGCTGAAAGCAGTTACCGCACATTTTCAGACCCATACCACCCCGATTCTGCTGAGCAAT
AACTTTATTGAACCGCTGGAAATCACCAAAGAGATCTACGATCTGAATAACCCGGAAAAAGAGCCGAAAAAA
TTCCAGACCGCATATGCAAAAAAAACCGGTGATCAGAAAGGTTATCGTGAAGCGCTGTGTAAATGGATTGAT
TTCACCCGTGATTTTCTGAGCAAATACACCAAAACCACCAGTATCGATCTGAGCAGCCTGCGTCCGAGCAGCC
AGTATAAAGATCTGGGCGAATATTATGCAGAACTGAATCCGCTGCTGTATCATATTAGCTTTCAGCGTATTGCC
GAGAAAGAAATCATGGACGCAGTTGAAACCGGTAAACTGTACCTGTTCCAGATCTACAATAAAGATTTTGCCA
AAGGCCATCATGGCAAACCGAATCTGCATACCCTGTATTGGACCGGTCTGTTTAGCCCTGAAAATCTGGCAAA
AACCTCGATTAAACTGAATGGTCAGGCGGAACTGTTTTATCGTCCGAAAAGCCGTATGAAACGTATGGCACAT
CGTCTGGGTGAAAAAATGCTGAACAAAAAACTGAAAGACCAGAAAACCCCGATCCCGGATACACTGTATCAA
GAACTGTATGATTATGTGAACCATCGTCTGAGCCATGATCTGAGTGATGAAGCACGTGCCCTGCTGCCGAATG
TTATTACCAAAGAAGTTAGCCACGAGATCATTAAAGATCGTCGTTTTACCAGCGACAAATTCCTGTTTCATGTG
CCGATTACCCTGAATTATCAGGCAGCAAATAGCCCGAGCAAATTTAACCAGCGTGTTAATGCATATCTGAAAG
AACATCCAGAAACGCCGATTATTGGTATTGATCGTGGTGAACGTAACCTGATTTATATCACCGTTATTGATAGC
ACCGGCAAAATCCTGGAACAGCGTAGCCTGAATACCATTCAGCAGTTTGATTACCAGAAAAAACTGGATAATC
GCGAGAAAGAACGTGTTGCAGCACGTCAGGCATGGTCAGTTGTTGGTACAATTAAAGACCTGAAACAGGGTT
ATCTGAGCCAGGTTATTCATGAAATTGTGGATCTGATGATTCACTATCAGGCCGTTGTTGTGCTGGAAAACCT
GAATTTTGGCTTTAAAAGCAAACGTACCGGCATTGCAGAAAAAGCAGTTTATCAGCAGTTCGAGAAAATGCTG
ATTGACAAACTGAATTGCCTGGTGCTGAAAGATTATCCGGCTGAAAAAGTTGGTGGTGTTCTGAATCCGTATC
AGCTGACCGATCAGTTTACCAGCTTTGCAAAAATGGGCACCCAGAGCGGATTTCTGTTTTATGTTCCGGCACC
GTATACGAGCAAAATTGATCCGCTGACCGGTTTTGTTGATCCGTTTGTTTGGAAAACCATCAAAAACCATGAA
AGCCGCAAACATTTTCTGGAAGGTTTCGATTTTCTGCATTACGACGTTAAAACGGGTGATTTCATCCTGCACTT

TAAAATGAATCGCAATCTGAGTTTTCAGCGTGGCCTGCCTGGTTTTATGCCTGCATGGGATATTGTGTTTGAGA
AAAACGAAACACAGTTCGATGCAAAAGGCACCCCGTTTATTGCAGGTAAACGTATTGTTCCGGTGATTGAAAA
TCATCGTTTCACCGGTCGTTATCGCGATCTGTATCCGGCAAATGAACTGATCGCACTGCTGGAAGAGAAAGGT
ATTGTTTTTCGTGATGGCTCAAACATTCTGCCGAAACTGCTGGAAAATGATGATAGCCATGCAATTGATACCAT
GGTTGCACTGATTCGTAGCGTTCTGCAGATGCGTAATAGCAATGCAGCAACCGGTGAAGATTACATTAATAGT
CCGGTTCGTGATCTGAATGGTGTTTGTTTTGATAGCCGTTTTCAGAATCCGGAATGGCCGATGGATGCAGATG
CAAATGGTGCATATCATATTGCACTGAAAGGACAGCTGCTGCTGAACCACCTGAAAGAAAGCAAAGATCTGA
AACTGCAAAACGGCATTAGCAATCAGGATTGGCTGGCATATATCCAAGAACTGCGTAAC

**[0176]** SEQ ID NO.: 467

**[0177]** atgACCCAGTTTGAAGGTTTCACCAATCTGTATCAGGTTAGCAAAACCCTGCGTTTTGAACTGATT
CCGCAGGGTAAAACCCTGAAACATATTCAAGAACAGGGCTTCATCGAAGAGGATAAAGCACGTAACGATCAC
TACAAAGAACTGAAACCGATTATCGACCGCATCTATAAAACCTATGCAGATCAGTGTCTGCAGCTGGTTCAGC
TGGATTGGGAAAATCTGAGCGCAGCAATTGATAGTTATCGCAAAGAAAAAACCGAAGAAACCCGTAATGCAC
TGATTGAAGAACAGGCAACCTATCGTAATGCCATCCATGATTATTTCATTGGTCGTACCGATAATCTGACCGAT
GCAATTAACAAACGTCACGCCGAAATCTATAAAGGCCTGTTTAAAGCCGAACTGTTTAATGGCAAAGTTCTGA
AACAGCTGGGCACCGTTACCACCACCGAACATGAAAATGCACTGCTGCGTAGCTTTGATAAATTCACCACCTA
TTTCAGCGGCTTTTATGAGAATCGCAAAAACGTGTTTAGCGCAGAAGATATTAGCACCGCAATTCCGCATCGT
ATTGTGCAGGATAATTTCCCGAAATTCAAAGAGAACTGCCACATTTTTACCCGTCTGATTACCGCAGTTCCGAG
CCTGCGTGAACATTTTGAAAACGTTAAAAAAGCCATCGGCATCTTTGTTAGCACCAGCATTGAAGAAGTTTTTA
GCTTCCCGTTTTACAATCAGCTGCTGACCCAGACCCAGATTGATCTGTATAACCAACTGCTGGGTGGTATTAGC
CGTGAAGCAGGCACCGAAAAAATCAAAGGTCTGAATGAAGTGCTGAATCTGGCCATTCAGAAAAATGATGAA
ACCGCACATATTATTGCAAGCCTGCCGCATCGTTTTATTCCGCTGTTCAAACAAATTCTGAGCGATCGTAATAC
CCTGAGCTTTATTCTGGAAGAATTCAAATCCGATGAAGAGGTGATTCAGAGCTTTTGCAAATACAAAACGCTG
CTGCGCAATGAAAATGTTCTGGAAACTGCCGAAGCACTGTTTAACGAACTGAATAGCATTGATCTGACCCACA
TCTTTATCAGCCACAAAAAACTGGAAACCATTTCAAGCGCACTGTGTGATCATTGGGATACCCTGCGTAATGCC
CTGTATGAACGTCGTATTAGCGAACTGACCGGTAAAATTACCAAAAGCGCGAAAGAAAAAGTTCAGCGCAGT
CTGAAACATGAGGATATTAATCTGCAAGAGATTATTAGCGCAGCCGGTAAAGAACTGTCAGAAGCATTTAAA
CAGAAAACCAGCGAAATTCTGTCACATGCACATGCAGCACTGGATCAGCCGCTGCCGACCACCCTGAAAAAAC
AAGAAGAAAAAGAAATCCTGAAAAGCCAGCTGGATAGCCTGCTGGGTCTGTATCATCTGCTGGACTGGTTTG
CAGTTGATGAAAGCAATGAAGTTGATCCGGAATTTAGCGCACGTCTGACCGGCATTAAACTGGAAATGGAAC
CGAGCCTGAGCTTTTATAACAAAGCCCGTAATTATGCCACCAAAAAACCGTATAGCGTCGAAAAATTCAAACT
GAACTTTCAGCGTCCGACCCTGGCAAGCGGTTGGGATGTTAATAAAGAAAAAAACAACGGTGCCATCCTGTTC

GTGAAAAATGGCCTGTATTATCTGGGTATTATGCCGAAACAGAAAGGTCGTTATAAAGCGCTGAGCTTTGAAC
CGACGGAAAAAACCAGTGAAGGTTTTGATAAAATGTACTACGACTATTTTCCGGATGCAGCCAAAATGATTCC
GAAATGTAGCACCCAGCTGAAAGCAGTTACCGCACATTTTCAGACCCATACCACCCCGATTCTGCTGAGCAAT
AACTTTATTGAACCGCTGGAAATCACCAAAGAGATCTACGATCTGAATAACCCGGAAAAAGAGCCGAAAAAA
TTCCAGACCGCATATGCAAAAAAAACCGGTGATCAGAAAGGTTATCGTGAAGCGCTGTGTAAATGGATTGAT
TTCACCCGTGATTTTCTGAGCAAATACACCAAAACCACCAGTATCGATCTGAGCAGCCTGCGTCCGAGCAGCC
AGTATAAAGATCTGGGCGAATATTATGCAGAACTGAATCCGCTGCTGTATCATATTAGCTTTCAGCGTATTGCC
GAGAAAGAAATCATGGACGCAGTTGAAACCGGTAAACTGTACCTGTTCCAGATCTACAATAAAGATTTTGCCA
AAGGCCATCATGGCAAACCGAATCTGCATACCCTGTATTGGACCGGTCTGTTTAGCCCTGAAAATCTGGCAAA
AACCTCGATTAAACTGAATGGTCAGGCGGAACTGTTTTATCGTCCGAAAAGCCGTATGAAACGTATGGCACAT
CGTCTGGGTGAAAAAATGCTGAACAAAAAACTGAAAGACCAGAAAACCCCGATCCCGGATACACTGTATCAA
GAACTGTATGATTATGTGAACCATCGTCTGAGCCATGATCTGAGTGATGAAGCACGTGCCCTGCTGCCGAATG
TTATTACCAAAGAAGTTAGCCACGAGATCATTAAAGATCGTCGTTTTACCAGCGACAAATTCCTGTTTCATGTG
CCGATTACCCTGAATTATCAGGCAGCAAATAGCCCGAGCAAATTTAACCAGCGTGTTAATGCATATCTGAAAG
AACATCCAGAAACGCCGATTATTGGTATTGATCGTGGTGAACGTAACCTGATTTATATCACCGTTATTGATAGC
ACCGGCAAAATCCTGGAACAGCGTAGCCTGAATACCATTCAGCAGTTTGATTACCAGAAAAAACTGGATAATC
GCGAGAAAGAACGTGTTGCAGCACGTCAGGCATGGTCAGTTGTTGGTACAATTAAAGACCTGAAACAGGGTT
ATCTGAGCCAGGTTATTCATGAAATTGTGGATCTGATGATTCACTATCAGGCCGTTGTTGTGCTGGAAAACCT
GAATTTTGGCTTTAAAAGCAAACGTACCGGCATTGCAGAAAAAGCAGTTTATCAGCAGTTCGAGAAAATGCTG
ATTGACAAACTGAATTGCCTGGTGCTGAAAGATTATCCGGCTGAAAAAGTTGGTGGTGTTCTGAATCCGTATC
AGCTGACCGATCAGTTTACCAGCTTTGCAAAAATGGGCACCCAGAGCGGATTTCTGTTTTATGTTCCGGCACC
GTATACGAGCAAAATTGATCCGCTGACCGGTTTTGTTGATCCGTTTGTTTGGAAAACCATCAAAAACCATGAA
AGCCGCAAACATTTTCTGGAAGGTTTCGATTTTCTGCATTACGACGTTAAAACGGGTGATTTCATCCTGCACTT
TAAAATGAATCGCAATCTGAGTTTTCAGCGTGGCCTGCCTGGTTTTATGCCTGCATGGGATATTGTGTTTGAGA
AAAACGAAACACAGTTCGATGCAAAAGGCACCCCGTTTATTGCAGGTAAACGTATTGTTCCGGTGATTGAAAA
TCATCGTTTCACCGGTCGTTATCGCGATCTGTATCCGGCAAATGAACTGATCGCACTGCTGGAAGAGAAAGGT
ATTGTTTTTCGTGATGGCTCAAACATTCTGCCGAAACTGCTGGAAAATGATGATAGCCATGCAATTGATACCAT
GGTTGCACTGATTCGTAGCGTTCTGCAGATGCGTAATAGCAATGCAGCAACCGGTGAAGATTACATTAATAGT
CCGGTTCGTGATCTGAATGGTGTTTGTTTTGATAGCCGTTTTCAGAATCCGGAATGGCCGATGGATGCAGATG
CAAATGGTGCATATCATATTGCACTGAAAGGACAGCTGCTGCTGAACCACCTGAAAGAAAGCAAAGATCTGA
AACTGCAAAACGGCATTAGCAATCAGGATTGGCTGGCATATATCCAAGAACTGCGTAAC

**[0178]** Additional polynucleotides and polypeptides relevant to this Example include Cas12a variants having single amino acid substitution at M537R and F870L, as shown below. The underlined codons or amino acids correspond to the changes relative to the corresponding WT Cas12a sequences.

**[0179]** SEQ ID NO.: 468 E. coli optimized DNA M537R

**[0180]** atgACCCAGTTTGAAGGTTTCACCAATCTGTATCAGGTTAGCAAAACCCTGCGTTTTGAACTG
ATTCCGCAGGGTAAAACCCTGAAACATATTCAAGAACAGGGCTTCATCGAAGAGGATAAAGCACGTAACGAT
CACTACAAAGAACTGAAACCGATTATCGACCGCATCTATAAAACCTATGCAGATCAGTGTCTGCAGCTGGTTC
AGCTGGATTGGGAAAATCTGAGCGCAGCAATTGATAGTTATCGCAAAGAAAAAACCGAAGAAACCCGTAATG
CACTGATTGAAGAACAGGCAACCTATCGTAATGCCATCCATGATTATTTCATTGGTCGTACCGATAATCTGACC
GATGCAATTAACAAACGTCACGCCGAAATCTATAAAGGCCTGTTTAAAGCCGAACTGTTTAATGGCAAAGTTC
TGAAACAGCTGGGCACCGTTACCACCACCGAACATGAAAATGCACTGCTGCGTAGCTTTGATAAATTCACCAC
CTATTTCAGCGGCTTTTATGAGAATCGCAAAAACGTGTTTAGCGCAGAAGATATTAGCACCGCAATTCCGCAT
CGTATTGTGCAGGATAATTTCCCGAAATTCAAAGAGAACTGCCACATTTTTACCCGTCTGATTACCGCAGTTCC
GAGCCTGCGTGAACATTTTGAAAACGTTAAAAAAGCCATCGGCATCTTTGTTAGCACCAGCATTGAAGAAGTT
TTTAGCTTCCCGTTTTACAATCAGCTGCTGACCCAGACCCAGATTGATCTGTATAACCAACTGCTGGGTGGTAT
TAGCCGTGAAGCAGGCACCGAAAAAATCAAAGGTCTGAATGAAGTGCTGAATCTGGCCATTCAGAAAAATGA
TGAAACCGCACATATTATTGCAAGCCTGCCGCATCGTTTTATTCCGCTGTTCAAACAAATTCTGAGCGATCGTA
ATACCCTGAGCTTTATTCTGGAAGAATTCAAATCCGATGAAGAGGTGATTCAGAGCTTTTGCAAATACAAAAC
GCTGCTGCGCAATGAAAATGTTCTGGAAACTGCCGAAGCACTGTTTAACGAACTGAATAGCATTGATCTGACC
CACATCTTTATCAGCCACAAAAAACTGGAAACCATTTCAAGCGCACTGTGTGATCATTGGGATACCCTGCGTA
ATGCCCTGTATGAACGTCGTATTAGCGAACTGACCGGTAAAATTACCAAAAGCGCGAAAGAAAAAGTTCAGC
GCAGTCTGAAACATGAGGATATTAATCTGCAAGAGATTATTAGCGCAGCCGGTAAAGAACTGTCAGAAGCAT
TTAAACAGAAAACCAGCGAAATTCTGTCACATGCACATGCAGCACTGGATCAGCCGCTGCCGACCACCCTGAA
AAAACAAGAAGAAAAAGAAATCCTGAAAAGCCAGCTGGATAGCCTGCTGGGTCTGTATCATCTGCTGGACTG
GTTTGCAGTTGATGAAAGCAATGAAGTTGATCCGGAATTTAGCGCACGTCTGACCGGCATTAAACTGGAAAT
GGAACCGAGCCTGAGCTTTTATAACAAAGCCCGTAATTATGCCACCAAAAAACCGTATAGCGTCGAAAAATTC
AAACTGAACTTTCAGCGTCCGACCCTGGCAAGCGGTTGGGATGTTAATAAAGAAAAAAACAACGGTGCCATC
CTGTTCGTGAAAAATGGCCTGTATTATCTGGGTATTATGCCGAAACAGAAAGGTCGTTATAAAGCGCTGAGCT
TTGAACCGACGGAAAAAACCAGTGAAGGTTTTGATAAAATGTACTACGACTATTTTCCGGATGCAGCCAAAAT
GATTCCGAAATGTAGCACCCAGCTGAAAGCAGTTACCGCACATTTTCAGACCCATACCACCCCGATTCTGCTGA
GCAATAACTTTATTGAACCGCTGGAAATCACCAAAGAGATCTACGATCTGAATAACCCGGAAAAAGAGCCGA
AAAAATTCCAGACCGCATATGCAAAAAAAACCGGTGATCAGAAAGGTTATCGTGAAGCGCTGTGTAAATGGA
TTGATTTCACCCGTGATTTTCTGAGCAAATACACCAAAACCACCAGTATCGATCTGAGCAGCCTGCGTCCGAGC
AGCCAGTATAAAGATCTGGGCGAATATTATGCAGAACTGAATCCGCTGCTGTATCATATTAGCTTTCAGCGTA
TTGCCGAGAAAGAAATCATGGACGCAGTTGAAACCGGTAAACTGTACCTGTTCCAGATCTACAATAAAGATTT
TGCCAAAGGCCATCATGGCAAACCGAATCTGCATACCCTGTATTGGACCGGTCTGTTTAGCCCTGAAAATCTG
GCAAAAACCTCGATTAAACTGAATGGTCAGGCGGAACTGTTTTATCGTCCGAAAAGCCGTATGAAACGTATG
GCACATCGTCTGGGTGAAAAAATGCTGAACAAAAAACTGAAAGACCAGAAAACCCCGATCCCGGATACACTG
TATCAAGAACTGTATGATTATGTGAACCATCGTCTGAGCCATGATCTGAGTGATGAAGCACGTGCCCTGCTGC
CGAATGTTATTACCAAAGAAGTTAGCCACGAGATCATTAAAGATCGTCGTTTTACCAGCGACAAATTCTTTTTT

CATGTGCCGATTACCCTGAATTATCAGGCAGCAAATAGCCCGAGCAAATTTAACCAGCGTGTTAATGCATATC
TGAAAGAACATCCAGAAACGCCGATTATTGGTATTGATCGTGGTGAACGTAACCTGATTTATATCACCGTTATT
GATAGCACCGGCAAAATCCTGGAACAGCGTAGCCTGAATACCATTCAGCAGTTTGATTACCAGAAAAAACTG
GATAATCGCGAGAAAGAACGTGTTGCAGCACGTCAGGCATGGTCAGTTGTTGGTACAATTAAAGACCTGAAA
CAGGGTTATCTGAGCCAGGTTATTCATGAAATTGTGGATCTGATGATTCACTATCAGGCCGTTGTTGTGCTGG
AAAACCTGAATTTTGGCTTTAAAAGCAAACGTACCGGCATTGCAGAAAAAGCAGTTTATCAGCAGTTCGAGAA
AATGCTGATTGACAAACTGAATTGCCTGGTGCTGAAAGATTATCCGGCTGAAAAAGTTGGTGGTGTTCTGAAT
CCGTATCAGCTGACCGATCAGTTTACCAGCTTTGCAAAAATGGGCACCCAGAGCGGATTTCTGTTTTATGTTCC
GGCACCGTATACGAGCAAAATTGATCCGCTGACCGGTTTTGTTGATCCGTTTGTTTGGAAAACCATCAAAAAC
CATGAAAGCCGCAAACATTTTCTGGAAGGTTTCGATTTTCTGCATTACGACGTTAAAACGGGTGATTTCATCCT
GCACTTTAAAATGAATCGCAATCTGAGTTTTCAGCGTGGCCTGCCTGGTTTTATGCCTGCATGGGATATTGTGT
TTGAGAAAAACGAAACACAGTTCGATGCAAAAGGCACCCCGTTTATTGCAGGTAAACGTATTGTTCCGGTGAT
TGAAAATCATCGTTTCACCGGTCGTTATCGCGATCTGTATCCGGCAAATGAACTGATCGCACTGCTGGAAGAG
AAAGGTATTGTTTTTCGTGATGGCTCAAACATTCTGCCGAAACTGCTGGAAAATGATGATAGCCATGCAATTG
ATACCATGGTTGCACTGATTCGTAGCGTTCTGCAGATGCGTAATAGCAATGCAGCAACCGGTGAAGATTACAT
TAATAGTCCGGTTCGTGATCTGAATGGTGTTTGTTTTGATAGCCGTTTTCAGAATCCGGAATGGCCGATGGAT
GCAGATGCAAATGGTGCATATCATATTGCACTGAAAGGACAGCTGCTGCTGAACCACCTGAAAGAAAGCAAA
GATCTGAAACTGCAAAACGGCATTAGCAATCAGGATTGGCTGGCATATATCCAAGAACTGCGTAAC

**[0181]** SEQ ID NO.: 469 E. coli optimized DNA F870L Cas12a

**[0182]** atgACCCAGTTTGAAGGTTTCACCAATCTGTATCAGGTTAGCAAAACCCTGCGTTTTGAACTG
ATTCCGCAGGGTAAAACCCTGAAACATATTCAAGAACAGGGCTTCATCGAAGAGGATAAAGCACGTAACGAT
CACTACAAAGAACTGAAACCGATTATCGACCGCATCTATAAAACCTATGCAGATCAGTGTCTGCAGCTGGTTC
AGCTGGATTGGGAAAATCTGAGCGCAGCAATTGATAGTTATCGCAAAGAAAAAACCGAAGAAACCCGTAATG
CACTGATTGAAGAACAGGCAACCTATCGTAATGCCATCCATGATTATTTCATTGGTCGTACCGATAATCTGACC
GATGCAATTAACAAACGTCACGCCGAAATCTATAAAGGCCTGTTTAAAGCCGAACTGTTTAATGGCAAAGTTC
TGAAACAGCTGGGCACCGTTACCACCACCGAACATGAAAATGCACTGCTGCGTAGCTTTGATAAATTCACCAC
CTATTTCAGCGGCTTTTATGAGAATCGCAAAAACGTGTTTAGCGCAGAAGATATTAGCACCGCAATTCCGCAT
CGTATTGTGCAGGATAATTTCCCGAAATTCAAAGAGAACTGCCACATTTTTACCCGTCTGATTACCGCAGTTCC
GAGCCTGCGTGAACATTTTGAAAACGTTAAAAAAGCCATCGGCATCTTTGTTAGCACCAGCATTGAAGAAGTT
TTTAGCTTCCCGTTTTACAATCAGCTGCTGACCCAGACCCAGATTGATCTGTATAACCAACTGCTGGGTGGTAT
TAGCCGTGAAGCAGGCACCGAAAAAATCAAAGGTCTGAATGAAGTGCTGAATCTGGCCATTCAGAAAAATGA
TGAAACCGCACATATTATTGCAAGCCTGCCGCATCGTTTTATTCCGCTGTTCAAACAAATTCTGAGCGATCGTA
ATACCCTGAGCTTTATTCTGGAAGAATTCAAATCCGATGAAGAGGTGATTCAGAGCTTTTGCAAATACAAAAC
GCTGCTGCGCAATGAAAATGTTCTGGAAACTGCCGAAGCACTGTTTAACGAACTGAATAGCATTGATCTGACC
CACATCTTTATCAGCCACAAAAAACTGGAAACCATTTCAAGCGCACTGTGTGATCATTGGGATACCCTGCGTA
ATGCCCTGTATGAACGTCGTATTAGCGAACTGACCGGTAAAATTACCAAAAGCGCGAAAGAAAAAGTTCAGC
GCAGTCTGAAACATGAGGATATTAATCTGCAAGAGATTATTAGCGCAGCCGGTAAAGAACTGTCAGAAGCAT
TTAAACAGAAAACCAGCGAAATTCTGTCACATGCACATGCAGCACTGGATCAGCCGCTGCCGACCACCCTGAA
AAAACAAGAAGAAAAAGAAATCCTGAAAAGCCAGCTGGATAGCCTGCTGGGTCTGTATCATCTGCTGGACTG
GTTTGCAGTTGATGAAAGCAATGAAGTTGATCCGGAATTTAGCGCACGTCTGACCGGCATTAAACTGGAAAT
GGAACCGAGCCTGAGCTTTTATAACAAAGCCCGTAATTATGCCACCAAAAAACCGTATAGCGTCGAAAAATTC
AAACTGAACTTTCAGATGCCGACCCTGGCAAGCGGTTGGGATGTTAATAAAGAAAAAAACAACGGTGCCATC

CTGTTCGTGAAAAATGGCCTGTATTATCTGGGTATTATGCCGAAACAGAAAGGTCGTTATAAAGCGCTGAGCT
TTGAACCGACGGAAAAAACCAGTGAAGGTTTTGATAAAATGTACTACGACTATTTTCCGGATGCAGCCAAAAT
GATTCCGAAATGTAGCACCCAGCTGAAAGCAGTTACCGCACATTTTCAGACCCATACCACCCCGATTCTGCTGA
GCAATAACTTTATTGAACCGCTGGAAATCACCAAAGAGATCTACGATCTGAATAACCCGGAAAAAGAGCCGA
AAAAATTCCAGACCGCATATGCAAAAAAAACCGGTGATCAGAAAGGTTATCGTGAAGCGCTGTGTAAATGGA
TTGATTTCACCCGTGATTTTCTGAGCAAATACACCAAAACCACCAGTATCGATCTGAGCAGCCTGCGTCCGAGC
AGCCAGTATAAAGATCTGGGCGAATATTATGCAGAACTGAATCCGCTGCTGTATCATATTAGCTTTCAGCGTA
TTGCCGAGAAAGAAATCATGGACGCAGTTGAAACCGGTAAACTGTACCTGTTCCAGATCTACAATAAAGATTT
TGCCAAAGGCCATCATGGCAAACCGAATCTGCATACCCTGTATTGGACCGGTCTGTTTAGCCCTGAAAATCTG
GCAAAAACCTCGATTAAACTGAATGGTCAGGCGGAACTGTTTTATCGTCCGAAAAGCCGTATGAAACGTATG
GCACATCGTCTGGGTGAAAAAATGCTGAACAAAAAACTGAAAGACCAGAAAACCCCGATCCCGGATACACTG
TATCAAGAACTGTATGATTATGTGAACCATCGTCTGAGCCATGATCTGAGTGATGAAGCACGTGCCCTGCTGC
CGAATGTTATTACCAAAGAAGTTAGCCACGAGATCATTAAAGATCGTCGTTTTACCAGCGACAAATTCCTGTTT
CATGTGCCGATTACCCTGAATTATCAGGCAGCAAATAGCCCGAGCAAATTTAACCAGCGTGTTAATGCATATC
TGAAAGAACATCCAGAAACGCCGATTATTGGTATTGATCGTGGTGAACGTAACCTGATTTATATCACCGTTATT
GATAGCACCGGCAAAATCCTGGAACAGCGTAGCCTGAATACCATTCAGCAGTTTGATTACCAGAAAAAACTG
GATAATCGCGAGAAAGAACGTGTTGCAGCACGTCAGGCATGGTCAGTTGTTGGTACAATTAAAGACCTGAAA
CAGGGTTATCTGAGCCAGGTTATTCATGAAATTGTGGATCTGATGATTCACTATCAGGCCGTTGTTGTGCTGG
AAAACCTGAATTTTGGCTTTAAAAGCAAACGTACCGGCATTGCAGAAAAAGCAGTTTATCAGCAGTTCGAGAA
AATGCTGATTGACAAACTGAATTGCCTGGTGCTGAAAGATTATCCGGCTGAAAAAGTTGGTGGTGTTCTGAAT
CCGTATCAGCTGACCGATCAGTTTACCAGCTTTGCAAAAATGGGCACCCAGAGCGGATTTCTGTTTTATGTTCC
GGCACCGTATACGAGCAAAATTGATCCGCTGACCGGTTTTGTTGATCCGTTTGTTTGGAAAACCATCAAAAAC
CATGAAAGCCGCAAACATTTTCTGGAAGGTTTCGATTTTCTGCATTACGACGTTAAAACGGGTGATTTCATCCT
GCACTTTAAAATGAATCGCAATCTGAGTTTTCAGCGTGGCCTGCCTGGTTTTATGCCTGCATGGGATATTGTGT
TTGAGAAAAACGAAACACAGTTCGATGCAAAAGGCACCCCGTTTATTGCAGGTAAACGTATTGTTCCGGTGAT
TGAAAATCATCGTTTCACCGGTCGTTATCGCGATCTGTATCCGGCAAATGAACTGATCGCACTGCTGGAAGAG
AAAGGTATTGTTTTTCGTGATGGCTCAAACATTCTGCCGAAACTGCTGGAAAATGATGATAGCCATGCAATTG
ATACCATGGTTGCACTGATTCGTAGCGTTCTGCAGATGCGTAATAGCAATGCAGCAACCGGTGAAGATTACAT
TAATAGTCCGGTTCGTGATCTGAATGGTGTTTGTTTTGATAGCCGTTTTCAGAATCCGGAATGGCCGATGGAT
GCAGATGCAAATGGTGCATATCATATTGCACTGAAAGGACAGCTGCTGCTGAACCACCTGAAAGAAAGCAAA
GATCTGAAACTGCAAAACGGCATTAGCAATCAGGATTGGCTGGCATATATCCAAGAACTGCGTAAC

**[0183]** SEQ ID NO.: 470 Human optimized DNA M537R Cas12a

**[0184]** atgACCCAGTTTGAAGGTTTCACCAATCTGTATCAGGTTAGCAAAACCCTGCGTTTTGAACTG
ATTCCGCAGGGTAAAACCCTGAAACATATTCAAGAACAGGGCTTCATCGAAGAGGATAAAGCACGTAACGAT
CACTACAAAGAACTGAAACCGATTATCGACCGCATCTATAAAACCTATGCAGATCAGTGTCTGCAGCTGGTTC
AGCTGGATTGGGAAAATCTGAGCGCAGCAATTGATAGTTATCGCAAAGAAAAAACCGAAGAAACCCGTAATG
CACTGATTGAAGAACAGGCAACCTATCGTAATGCCATCCATGATTATTTCATTGGTCGTACCGATAATCTGACC
GATGCAATTAACAAACGTCACGCCGAAATCTATAAAGGCCTGTTTAAAGCCGAACTGTTTAATGGCAAAGTTC
TGAAACAGCTGGGCACCGTTACCACCACCGAACATGAAAATGCACTGCTGCGTAGCTTTGATAAATTCACCAC
CTATTTCAGCGGCTTTTATGAGAATCGCAAAAACGTGTTTAGCGCAGAAGATATTAGCACCGCAATTCCGCAT
CGTATTGTGCAGGATAATTTCCCGAAATTCAAAGAGAACTGCCACATTTTTACCCGTCTGATTACCGCAGTTCC
GAGCCTGCGTGAACATTTTGAAAACGTTAAAAAAGCCATCGGCATCTTTGTTAGCACCAGCATTGAAGAAGTT

TTTAGCTTCCCGTTTTACAATCAGCTGCTGACCCAGACCCAGATTGATCTGTATAACCAACTGCTGGGTGGTAT
TAGCCGTGAAGCAGGCACCGAAAAAATCAAAGGTCTGAATGAAGTGCTGAATCTGGCCATTCAGAAAAATGA
TGAAACCGCACATATTATTGCAAGCCTGCCGCATCGTTTTATTCCGCTGTTCAAACAAATTCTGAGCGATCGTA
ATACCCTGAGCTTTATTCTGGAAGAATTCAAATCCGATGAAGAGGTGATTCAGAGCTTTTGCAAATACAAAAC
GCTGCTGCGCAATGAAAATGTTCTGGAAACTGCCGAAGCACTGTTTAACGAACTGAATAGCATTGATCTGACC
CACATCTTTATCAGCCACAAAAAACTGGAAACCATTTCAAGCGCACTGTGTGATCATTGGGATACCCTGCGTA
ATGCCCTGTATGAACGTCGTATTAGCGAACTGACCGGTAAAATTACCAAAAGCGCGAAAGAAAAAGTTCAGC
GCAGTCTGAAACATGAGGATATTAATCTGCAAGAGATTATTAGCGCAGCCGGTAAAGAACTGTCAGAAGCAT
TTAAACAGAAAACCAGCGAAATTCTGTCACATGCACATGCAGCACTGGATCAGCCGCTGCCGACCACCCTGAA
AAAACAAGAAGAAAAAGAAATCCTGAAAAGCCAGCTGGATAGCCTGCTGGGTCTGTATCATCTGCTGGACTG
GTTTGCAGTTGATGAAAGCAATGAAGTTGATCCGGAATTTAGCGCACGTCTGACCGGCATTAAACTGGAAAT
GGAACCGAGCCTGAGCTTTTATAACAAAGCCCGTAATTATGCCACCAAAAAACCGTATAGCGTCGAAAAATTC
AAACTGAACTTTCAGCGTCCGACCCTGGCAAGCGGTTGGGATGTTAATAAAGAAAAAAACAACGGTGCCATC
CTGTTCGTGAAAAATGGCCTGTATTATCTGGGTATTATGCCGAAACAGAAAGGTCGTTATAAAGCGCTGAGCT
TTGAACCGACGGAAAAAACCAGTGAAGGTTTTGATAAAATGTACTACGACTATTTTCCGGATGCAGCCAAAAT
GATTCCGAAATGTAGCACCCAGCTGAAAGCAGTTACCGCACATTTTCAGACCCATACCACCCCGATTCTGCTGA
GCAATAACTTTATTGAACCGCTGGAAATCACCAAAGAGATCTACGATCTGAATAACCCGGAAAAAGAGCCGA
AAAAATTCCAGACCGCATATGCAAAAAAAACCGGTGATCAGAAAGGTTATCGTGAAGCGCTGTGTAAATGGA
TTGATTTCACCCGTGATTTTCTGAGCAAATACACCAAAACCACCAGTATCGATCTGAGCAGCCTGCGTCCGAGC
AGCCAGTATAAAGATCTGGGCGAATATTATGCAGAACTGAATCCGCTGCTGTATCATATTAGCTTTCAGCGTA
TTGCCGAGAAAGAAATCATGGACGCAGTTGAAACCGGTAAACTGTACCTGTTCCAGATCTACAATAAAGATTT
TGCCAAAGGCCATCATGGCAAACCGAATCTGCATACCCTGTATTGGACCGGTCTGTTTAGCCCTGAAAATCTG
GCAAAAACCTCGATTAAACTGAATGGTCAGGCGGAACTGTTTTATCGTCCGAAAAGCCGTATGAAACGTATG
GCACATCGTCTGGGTGAAAAAATGCTGAACAAAAAACTGAAAGACCAGAAAACCCCGATCCCGGATACACTG
TATCAAGAACTGTATGATTATGTGAACCATCGTCTGAGCCATGATCTGAGTGATGAAGCACGTGCCCTGCTGC
CGAATGTTATTACCAAAGAAGTTAGCCACGAGATCATTAAAGATCGTCGTTTTACCAGCGACAAATTCTTTTTT
CATGTGCCGATTACCCTGAATTATCAGGCAGCAAATAGCCCGAGCAAATTTAACCAGCGTGTTAATGCATATC
TGAAAGAACATCCAGAAACGCCGATTATTGGTATTGATCGTGGTGAACGTAACCTGATTTATATCACCGTTATT
GATAGCACCGGCAAAATCCTGGAACAGCGTAGCCTGAATACCATTCAGCAGTTTGATTACCAGAAAAAACTG
GATAATCGCGAGAAAGAACGTGTTGCAGCACGTCAGGCATGGTCAGTTGTTGGTACAATTAAAGACCTGAAA
CAGGGTTATCTGAGCCAGGTTATTCATGAAATTGTGGATCTGATGATTCACTATCAGGCCGTTGTTGTGCTGG
AAAACCTGAATTTTGGCTTTAAAAGCAAACGTACCGGCATTGCAGAAAAAGCAGTTTATCAGCAGTTCGAGAA
AATGCTGATTGACAAACTGAATTGCCTGGTGCTGAAAGATTATCCGGCTGAAAAAGTTGGTGGTGTTCTGAAT
CCGTATCAGCTGACCGATCAGTTTACCAGCTTTGCAAAAATGGGCACCCAGAGCGGATTTCTGTTTTATGTTCC
GGCACCGTATACGAGCAAAATTGATCCGCTGACCGGTTTTGTTGATCCGTTTGTTTGGAAAACCATCAAAAAC
CATGAAAGCCGCAAACATTTTCTGGAAGGTTTCGATTTTCTGCATTACGACGTTAAAACGGGTGATTTCATCCT
GCACTTTAAAATGAATCGCAATCTGAGTTTTCAGCGTGGCCTGCCTGGTTTTATGCCTGCATGGGATATTGTGT
TTGAGAAAAACGAAACACAGTTCGATGCAAAAGGCACCCCGTTTATTGCAGGTAAACGTATTGTTCCGGTGAT
TGAAAATCATCGTTTCACCGGTCGTTATCGCGATCTGTATCCGGCAAATGAACTGATCGCACTGCTGGAAGAG
AAAGGTATTGTTTTTCGTGATGGCTCAAACATTCTGCCGAAACTGCTGGAAAATGATGATAGCCATGCAATTG
ATACCATGGTTGCACTGATTCGTAGCGTTCTGCAGATGCGTAATAGCAATGCAGCAACCGGTGAAGATTACAT
TAATAGTCCGGTTCGTGATCTGAATGGTGTTTGTTTTGATAGCCGTTTTCAGAATCCGGAATGGCCGATGGAT

GCAGATGCAAATGGTGCATATCATATTGCACTGAAAGGACAGCTGCTGCTGAACCACCTGAAAGAAAGCAAA
GATCTGAAACTGCAAAACGGCATTAGCAATCAGGATTGGCTGGCATATATCCAAGAACTGCGTAAC

**[0185]** SEQ ID NO.: 471 Human optimized DNA F870L Cas12a

**[0186]** atgACCCAGTTTGAAGGTTTCACCAATCTGTATCAGGTTAGCAAAACCCTGCGTTTTGAACTG
ATTCCGCAGGGTAAAACCCTGAAACATATTCAAGAACAGGGCTTCATCGAAGAGGATAAAGCACGTAACGAT
CACTACAAAGAACTGAAACCGATTATCGACCGCATCTATAAAACCTATGCAGATCAGTGTCTGCAGCTGGTTC
AGCTGGATTGGGAAAATCTGAGCGCAGCAATTGATAGTTATCGCAAAGAAAAAACCGAAGAAACCCGTAATG
CACTGATTGAAGAACAGGCAACCTATCGTAATGCCATCCATGATTATTTCATTGGTCGTACCGATAATCTGACC
GATGCAATTAACAAACGTCACGCCGAAATCTATAAAGGCCTGTTTAAAGCCGAACTGTTTAATGGCAAAGTTC
TGAAACAGCTGGGCACCGTTACCACCACCGAACATGAAAATGCACTGCTGCGTAGCTTTGATAAATTCACCAC
CTATTTCAGCGGCTTTTATGAGAATCGCAAAAACGTGTTTAGCGCAGAAGATATTAGCACCGCAATTCCGCAT
CGTATTGTGCAGGATAATTTCCCGAAATTCAAAGAGAACTGCCACATTTTTACCCGTCTGATTACCGCAGTTCC
GAGCCTGCGTGAACATTTTGAAAACGTTAAAAAAGCCATCGGCATCTTTGTTAGCACCAGCATTGAAGAAGTT
TTTAGCTTCCCGTTTTACAATCAGCTGCTGACCCAGACCCAGATTGATCTGTATAACCAACTGCTGGGTGGTAT
TAGCCGTGAAGCAGGCACCGAAAAAATCAAAGGTCTGAATGAAGTGCTGAATCTGGCCATTCAGAAAAATGA
TGAAACCGCACATATTATTGCAAGCCTGCCGCATCGTTTTATTCCGCTGTTCAAACAAATTCTGAGCGATCGTA
ATACCCTGAGCTTTATTCTGGAAGAATTCAAATCCGATGAAGAGGTGATTCAGAGCTTTTGCAAATACAAAAC
GCTGCTGCGCAATGAAAATGTTCTGGAAACTGCCGAAGCACTGTTTAACGAACTGAATAGCATTGATCTGACC
CACATCTTTATCAGCCACAAAAAACTGGAAACCATTTCAAGCGCACTGTGTGATCATTGGGATACCCTGCGTA
ATGCCCTGTATGAACGTCGTATTAGCGAACTGACCGGTAAAATTACCAAAAGCGCGAAAGAAAAAGTTCAGC
GCAGTCTGAAACATGAGGATATTAATCTGCAAGAGATTATTAGCGCAGCCGGTAAAGAACTGTCAGAAGCAT
TTAAACAGAAAACCAGCGAAATTCTGTCACATGCACATGCAGCACTGGATCAGCCGCTGCCGACCACCCTGAA
AAAACAAGAAGAAAAAGAAATCCTGAAAAGCCAGCTGGATAGCCTGCTGGGTCTGTATCATCTGCTGGACTG
GTTTGCAGTTGATGAAAGCAATGAAGTTGATCCGGAATTTAGCGCACGTCTGACCGGCATTAAACTGGAAAT
GGAACCGAGCCTGAGCTTTTATAACAAAGCCCGTAATTATGCCACCAAAAAACCGTATAGCGTCGAAAAATTC
AAACTGAACTTTCAGATGCCGACCCTGGCAAGCGGTTGGGATGTTAATAAAGAAAAAAACAACGGTGCCATC
CTGTTCGTGAAAAATGGCCTGTATTATCTGGGTATTATGCCGAAACAGAAAGGTCGTTATAAAGCGCTGAGCT
TTGAACCGACGGAAAAAACCAGTGAAGGTTTTGATAAAATGTACTACGACTATTTTCCGGATGCAGCCAAAAT
GATTCCGAAATGTAGCACCCAGCTGAAAGCAGTTACCGCACATTTTCAGACCCATACCACCCCGATTCTGCTGA
GCAATAACTTTATTGAACCGCTGGAAATCACCAAAGAGATCTACGATCTGAATAACCCGGAAAAAGAGCCGA
AAAAATTCCAGACCGCATATGCAAAAAAAACCGGTGATCAGAAAGGTTATCGTGAAGCGCTGTGTAAATGGA
TTGATTTCACCCGTGATTTTCTGAGCAAATACACCAAAACCACCAGTATCGATCTGAGCAGCCTGCGTCCGAGC
AGCCAGTATAAAGATCTGGGCGAATATTATGCAGAACTGAATCCGCTGCTGTATCATATTAGCTTTCAGCGTA
TTGCCGAGAAAGAAATCATGGACGCAGTTGAAACCGGTAAACTGTACCTGTTCCAGATCTACAATAAAGATTT
TGCCAAAGGCCATCATGGCAAACCGAATCTGCATACCCTGTATTGGACCGGTCTGTTTAGCCCTGAAAATCTG
GCAAAAACCTCGATTAAACTGAATGGTCAGGCGGAACTGTTTTATCGTCCGAAAAGCCGTATGAAACGTATG
GCACATCGTCTGGGTGAAAAAATGCTGAACAAAAAACTGAAAGACCAGAAAACCCCGATCCCGGATACACTG
TATCAAGAACTGTATGATTATGTGAACCATCGTCTGAGCCATGATCTGAGTGATGAAGCACGTGCCCTGCTGC
CGAATGTTATTACCAAAGAAGTTAGCCACGAGATCATTAAAGATCGTCGTTTTACCAGCGACAAATTCCTGTTT
CATGTGCCGATTACCCTGAATTATCAGGCAGCAAATAGCCCGAGCAAATTTAACCAGCGTGTTAATGCATATC
TGAAAGAACATCCAGAAACGCCGATTATTGGTATTGATCGTGGTGAACGTAACCTGATTTATATCACCGTTATT
GATAGCACCGGCAAAATCCTGGAACAGCGTAGCCTGAATACCATTCAGCAGTTTGATTACCAGAAAAAACTG

GATAATCGCGAGAAAGAACGTGTTGCAGCACGTCAGGCATGGTCAGTTGTTGGTACAATTAAAGACCTGAAA
CAGGGTTATCTGAGCCAGGTTATTCATGAAATTGTGGATCTGATGATTCACTATCAGGCCGTTGTTGTGCTGG
AAAACCTGAATTTTGGCTTTAAAAGCAAACGTACCGGCATTGCAGAAAAAGCAGTTTATCAGCAGTTCGAGAA
AATGCTGATTGACAAACTGAATTGCCTGGTGCTGAAAGATTATCCGGCTGAAAAAGTTGGTGGTGTTCTGAAT
CCGTATCAGCTGACCGATCAGTTTACCAGCTTTGCAAAAATGGGCACCCAGAGCGGATTTCTGTTTTATGTTCC
GGCACCGTATACGAGCAAAATTGATCCGCTGACCGGTTTTGTTGATCCGTTTGTTTGGAAAACCATCAAAAAC
CATGAAAGCCGCAAACATTTTCTGGAAGGTTTCGATTTTCTGCATTACGACGTTAAAACGGGTGATTTCATCCT
GCACTTTAAAATGAATCGCAATCTGAGTTTTCAGCGTGGCCTGCCTGGTTTTATGCCTGCATGGGATATTGTGT
TTGAGAAAAACGAAACACAGTTCGATGCAAAAGGCACCCCGTTTATTGCAGGTAAACGTATTGTTCCGGTGAT
TGAAAATCATCGTTTCACCGGTCGTTATCGCGATCTGTATCCGGCAAATGAACTGATCGCACTGCTGGAAGAG
AAAGGTATTGTTTTTCGTGATGGCTCAAACATTCTGCCGAAACTGCTGGAAAATGATGATAGCCATGCAATTG
ATACCATGGTTGCACTGATTCGTAGCGTTCTGCAGATGCGTAATAGCAATGCAGCAACCGGTGAAGATTACAT
TAATAGTCCGGTTCGTGATCTGAATGGTGTTTGTTTTGATAGCCGTTTTCAGAATCCGGAATGGCCGATGGAT
GCAGATGCAAATGGTGCATATCATATTGCACTGAAAGGACAGCTGCTGCTGAACCACCTGAAAGAAAGCAAA
GATCTGAAACTGCAAAACGGCATTAGCAATCAGGATTGGCTGGCATATATCCAAGAACTGCGTAAC

**[0187]** SEQ ID NO.: 472 M537R Cas12a AA

**[0188]** MTQFEGFTNLYQVSKTLRFELIPQGKTLKHIQEQGFIEEDKARNDHYKELKPIIDRIYKTYADQCL
QLVQLDWENLSAAIDSYRKEKTEETRNALIEEQATYRNAIHDYFIGRTDNLTDAINKRHAEIYKGLFKAELFNGKVLK
QLGTVTTTEHENALLRSFDKFTTYFSGFYENRKNVFSAEDISTAIPHRIVQDNFPKFKENCHIFTRLITAVPSLREHFEN
VKKAIGIFVSTSIEEVFSFPFYNQLLTQTQIDLYNQLLGGISREAGTEKIKGLNEVLNLAIQKNDETAHIIASLPHRFIPLF
KQILSDRNTLSFILEEFKSDEEVIQSFCKYKTLLRNENVLETAEALFNELNSIDLTHIFISHKKLETISSALCDHWDTLRNA
LYERRISELTGKITKSAKEKVQRSLKHEDINLQEIISAAGKELSEAFKQKTSEILSHAHAALDQPLPTTLKKQEEKEILKSQ
LDSLLGLYHLLDWFAVDESNEVDPEFSARLTGIKLEMEPSLSFYNKARNYATKKPYSVEKFKLNFQRPTLASGWDVN
KEKNNGAILFVKNGLYYLGIMPKQKGRYKALSFEPTEKTSEGFDKMYYDYFPDAAKMIPKCSTQLKAVTAHFQTHT
TPILLSNNFIEPLEITKEIYDLNNPEKEPKKFQTAYAKKTGDQKGYREALCKWIDFTRDFLSKYTKTTSIDLSSLRPSSQY
KDLGEYYAELNPLLYHISFQRIAEKEIMDAVETGKLYLFQIYNKDFAKGHHGKPNLHTLYWTGLFSPENLAKTSIKLN
GQAELFYRPKSRMKRMAHRLGEKMLNKKLKDQKTPIPDTLYQELYDYVNHRLSHDLSDEARALLPNVITKEVSHEII
KDRRFTSDKFFFHVPITLNYQAANSPSKFNQRVNAYLKEHPETPIIGIDRGERNLIYITVIDSTGKILEQRSLNTIQQFD
YQKKLDNREKERVAARQAWSVVGTIKDLKQGYLSQVIHEIVDLMIHYQAVVVLENLNFGFKSKRTGIAEKAVYQQF
EKMLIDKLNCLVLKDYPAEKVGGVLNPYQLTDQFTSFAKMGTQSGFLFYVPAPYTSKIDPLTGFVDPFVWKTIKNHE
SRKHFLEGFDFLHYDVKTGDFILHFKMNRNLSFQRGLPGFMPAWDIVFEKNETQFDAKGTPFIAGKRIVPVIENHR
FTGRYRDLYPANELIALLEEKGIVFRDGSNILPKLLENDDSHAIDTMVALIRSVLQMRNSNAATGEDYINSPVRDLNG
VCFDSRFQNPEWPMDADANGAYHIALKGQLLLNHLKESKDLKLQNGISNQDWLAYIQELRN

**[0189]** SEQ ID NO.: 473 F870L Cas12a AA

**[0190]** MTQFEGFTNLYQVSKTLRFELIPQGKTLKHIQEQGFIEEDKARNDHYKELKPIIDRIYKTYADQCL
QLVQLDWENLSAAIDSYRKEKTEETRNALIEEQATYRNAIHDYFIGRTDNLTDAINKRHAEIYKGLFKAELFNGKVLK
QLGTVTTTEHENALLRSFDKFTTYFSGFYENRKNVFSAEDISTAIPHRIVQDNFPKFKENCHIFTRLITAVPSLREHFEN
VKKAIGIFVSTSIEEVFSFPFYNQLLTQTQIDLYNQLLGGISREAGTEKIKGLNEVLNLAIQKNDETAHIIASLPHRFIPLF
KQILSDRNTLSFILEEFKSDEEVIQSFCKYKTLLRNENVLETAEALFNELNSIDLTHIFISHKKLETISSALCDHWDTLRNA
LYERRISELTGKITKSAKEKVQRSLKHEDINLQEIISAAGKELSEAFKQKTSEILSHAHAALDQPLPTTLKKQEEKEILKSQ
LDSLLGLYHLLDWFAVDESNEVDPEFSARLTGIKLEMEPSLSFYNKARNYATKKPYSVEKFKLNFQMPTLASGWDV

NKEKNNGAILFVKNGLYYLGIMPKQKGRYKALSFEPTEKTSEGFDKMYYDYFPDAAKMIPKCSTQLKAVTAHFQTH
TTPILLSNNFIEPLEITKEIYDLNNPEKEPKKFQTAYAKKTGDQKGYREALCKWIDFTRDFLSKYTKTTSIDLSSLRPSSQ
YKDLGEYYAELNPLLYHISFQRIAEKEIMDAVETGKLYLFQIYNKDFAKGHHGKPNLHTLYWTGLFSPENLAKTSIKLN
GQAELFYRPKSRMKRMAHRLGEKMLNKKLKDQKTPIPDTLYQELYDYVNHRLSHDLSDEARALLPNVITKEVSHEII
KDRRFTSDKFLFHVPITLNYQAANSPSKFNQRVNAYLKEHPETPIIGIDRGERNLIYITVIDSTGKILEQRSLNTIQQFD
YQKKLDNREKERVAARQAWSVVGTIKDLKQGYLSQVIHEIVDLMIHYQAVVVLENLNFGFKSKRTGIAEKAVYQQF
EKMLIDKLNCLVLKDYPAEKVGGVLNPYQLTDQFTSFAKMGTQSGFLFYVPAPYTSKIDPLTGFVDPFVWKTIKNHE
SRKHFLEGFDFLHYDVKTGDFILHFKMNRNLSFQRGLPGFMPAWDIVFEKNETQFDAKGTPFIAGKRIVPVIENHR
FTGRYRDLYPANELIALLEEKGIVFRDGSNILPKLLENDDSHAIDTMVALIRSVLQMRNSNAATGEDYINSPVRDLNG
VCFDSRFQNPEWPMDADANGAYHIALKGQLLLNHLKESKDLKLQNGISNQDWLAYIQELRN

**Example 6. Rational Design of Fusion Cas12a polypeptides**

**[0191]** Fusion Cas12/a polypeptides having additional motifs enabling nuclear localization into eukaryotic cells (collectively, "NLS" or "NLS sequences"), and/or purification and label detection motifs (collectively, "affinity tags") fall within the scope of the present invention. Exemplary nuclear localization signals ("NLS" or "NLS sequences") are well known in the art and include those listed identified by polynucleotide and amino acid sequences depicted in **Table 6**.

**[0192] Table 6. Exemplary NLS sequences**

| SEQ ID NO.: | NLS Name | Sequence (5'→3' or N→C) |
|---|---|---|
| 474 | SV40 | CCGAAAAAAAAAACGTAAAGTTGG |
| 475 | SV40 | PKKKRKV |
| 476 | OpT | AGCAGTGATGATGAAGCAACCGCAGATAGCCAGCATGCAGCACCGCC TAAAAAGAAACGTAAAGTT |
| 477 | OpT | SSDDEATADSQHAAPPKKKRKV |
| 478 | aNLS | CCGCCTCCGAAACGTCCGCGTCTGGAT |
| 479 | aNLS | PPPKRPRLD |
| 480 | BIP1 | AAACGTCCGGCAGCAACCAAAAAAGCAGGTCAGGCAAAAAAGAAAAA A |
| 481 | BIP1 | KRPAATKKAGQAKKKK |
| 482 | BIP2 | AAACGTACCGCAGATGGTAGCGAATTTGAAAGCCCGAAAAAAAAGCG TAAGGTGGAA |
| 483 | BIP2 | KRTADGSEFESPKKKRKVE |

**[0193]** Exemplary purification and/or label detection motifs include affinity tags that are also well known in the art. Often, additional amino acid linkers inserted before or after the additional motifs can provide improvements in expression and/or stability of the expressed fusion Cas12/a polypeptide. Two examples of affinity tags are defined by polynucleotide and amino acid sequences depicted below in **Table 7**.

**[0194]** **Table 7. Exemplary affinity tags**

| SEQ ID NO.: | Affinity Tag Name | Sequence (5'→3' or N→C) |
|---|---|---|
| 484 | V5 | GGTAAACCGATTCCGAATCCGCTGCTGGGTCTGGATAGCACC |
| 485 | V5 | GKPIPNPLLGLDST |
| 486 | HIS | CACCACCACCACCACCAC |
| 487 | HIS | HHHHHH |

**[0195]** Fusion Cas12a polypeptides that include a nuclear localization signal, linker amino acids and/or affinity tags can be readily constructed using chemical polypeptide methods or expressed from engineered polynucleotides encoding in-frame polypeptides created with recombinant DNA technology. Such technologies are well known and within the purview of one skilled in the art. Working examples of such polynucleotides and polypeptides are illustrated by SEQ ID NOs.: 5-30. Fusion Cas12a polypeptide variants that encode the open reading frames of SEQ ID NOs.: 59-245 having nuclear localization sequences and/or affinity tags and optionally amino acid linkers as needed fall within the scope of this disclosure. Exemplary Cas12a variants having nuclear localization signals are presented below.

**[0196]** Briefly, the method of site directed mutagenesis (SDM) was employed to create the expression constructs having As Cas12a coding sequences with different nuclear localization signals (NLS's). Site directed mutagenesis was performed by designing complimentary primers that encompass the desired nucleotide base change(s), along with flanking plasmid vector sequence, wherein each flanking region has a melting temperature ($T_m$) of at least 60°C. A polymerase chain reaction (PCR) run was then performed using standard cycling conditions for a total of 16 cycles. The restriction enzyme, DPN I, was added to digest away the starting plasmid vector material so only the new product containing the base changes remain. After DPN I treatment, a small amount of the PCR product was

transformed into competent *E. coli* cells, recovered in SOC media and plated onto kanamycin resistance Luria Broth (LB) agar plates. Colonies were screened using the Sanger sequencing method to verify correct base changes in selected clones.

**[0197]** SEQ ID NO.: 488 *E. coli* optimized DNA WT Cas12a with NLS linkers

**[0198]** atgACCCAGTTTGAAGGTTTCACCAATCTGTATCAGGTTAGCAAAACCCTGCGTTTTGAACTG
ATTCCGCAGGGTAAAACCCTGAAACATATTCAAGAACAGGGCTTCATCGAAGAGGATAAAGCACGTAACGAT
CACTACAAAGAACTGAAACCGATTATCGACCGCATCTATAAAACCTATGCAGATCAGTGTCTGCAGCTGGTTC
AGCTGGATTGGGAAAATCTGAGCGCAGCAATTGATAGTTATCGCAAAGAAAAAACCGAAGAAACCCGTAATG
CACTGATTGAAGAACAGGCAACCTATCGTAATGCCATCCATGATTATTTCATTGGTCGTACCGATAATCTGACC
GATGCAATTAACAAACGTCACGCCGAAATCTATAAAGGCCTGTTTAAAGCCGAACTGTTTAATGGCAAAGTTC
TGAAACAGCTGGGCACCGTTACCACCACCGAACATGAAAATGCACTGCTGCGTAGCTTTGATAAATTCACCAC
CTATTTCAGCGGCTTTTATGAGAATCGCAAAAACGTGTTTAGCGCAGAAGATATTAGCACCGCAATTCCGCAT
CGTATTGTGCAGGATAATTTCCCGAAATTCAAAGAGAACTGCCACATTTTTACCCGTCTGATTACCGCAGTTCC
GAGCCTGCGTGAACATTTTGAAAACGTTAAAAAAGCCATCGGCATCTTTGTTAGCACCAGCATTGAAGAAGTT
TTTAGCTTCCCGTTTTACAATCAGCTGCTGACCCAGACCCAGATTGATCTGTATAACCAACTGCTGGGTGGTAT
TAGCCGTGAAGCAGGCACCGAAAAAATCAAAGGTCTGAATGAAGTGCTGAATCTGGCCATTCAGAAAAATGA
TGAAACCGCACATATTATTGCAAGCCTGCCGCATCGTTTTATTCCGCTGTTCAAACAAATTCTGAGCGATCGTA
ATACCCTGAGCTTTATTCTGGAAGAATTCAAATCCGATGAAGAGGTGATTCAGAGCTTTTGCAAATACAAAAC
GCTGCTGCGCAATGAAAATGTTCTGGAAACTGCCGAAGCACTGTTTAACGAACTGAATAGCATTGATCTGACC
CACATCTTTATCAGCCACAAAAAACTGGAAACCATTTCAAGCGCACTGTGTGATCATTGGGATACCCTGCGTA
ATGCCCTGTATGAACGTCGTATTAGCGAACTGACCGGTAAAATTACCAAAAGCGCGAAAGAAAAAGTTCAGC
GCAGTCTGAAACATGAGGATATTAATCTGCAAGAGATTATTAGCGCAGCCGGTAAAGAACTGTCAGAAGCAT
TTAAACAGAAAACCAGCGAAATTCTGTCACATGCACATGCAGCACTGGATCAGCCGCTGCCGACCACCCTGAA
AAAACAAGAAGAAAAAGAAATCCTGAAAAGCCAGCTGGATAGCCTGCTGGGTCTGTATCATCTGCTGGACTG
GTTTGCAGTTGATGAAAGCAATGAAGTTGATCCGGAATTTAGCGCACGTCTGACCGGCATTAAACTGGAAAT
GGAACCGAGCCTGAGCTTTTATAACAAAGCCCGTAATTATGCCACCAAAAAACCGTATAGCGTCGAAAAATTC
AAACTGAACTTTCAGATGCCGACCCTGGCAAGCGGTTGGGATGTTAATAAAGAAAAAAACAACGGTGCCATC
CTGTTCGTGAAAAATGGCCTGTATTATCTGGGTATTATGCCGAAACAGAAAGGTCGTTATAAAGCGCTGAGCT
TTGAACCGACGGAAAAAACCAGTGAAGGTTTTGATAAAATGTACTACGACTATTTTCCGGATGCAGCCAAAAT
GATTCCGAAATGTAGCACCCAGCTGAAAGCAGTTACCGCACATTTTCAGACCCATACCACCCCGATTCTGCTGA
GCAATAACTTTATTGAACCGCTGGAAATCACCAAAGAGATCTACGATCTGAATAACCCGGAAAAAGAGCCGA
AAAAATTCCAGACCGCATATGCAAAAAAAACCGGTGATCAGAAAGGTTATCGTGAAGCGCTGTGTAAATGGA
TTGATTTCACCCGTGATTTTCTGAGCAAATACACCAAAACCACCAGTATCGATCTGAGCAGCCTGCGTCCGAGC
AGCCAGTATAAAGATCTGGGCGAATATTATGCAGAACTGAATCCGCTGCTGTATCATATTAGCTTTCAGCGTA
TTGCCGAGAAAGAAATCATGGACGCAGTTGAAACCGGTAAACTGTACCTGTTCCAGATCTACAATAAAGATTT
TGCCAAAGGCCATCATGGCAAACCGAATCTGCATACCCTGTATTGGACCGGTCTGTTTAGCCCTGAAAATCTG
GCAAAAACCTCGATTAAACTGAATGGTCAGGCGGAACTGTTTTATCGTCCGAAAAGCCGTATGAAACGTATG
GCACATCGTCTGGGTGAAAAAATGCTGAACAAAAAACTGAAAGACCAGAAAACCCCGATCCCGGATACACTG
TATCAAGAACTGTATGATTATGTGAACCATCGTCTGAGCCATGATCTGAGTGATGAAGCACGTGCCCTGCTGC
CGAATGTTATTACCAAAGAAGTTAGCCACGAGATCATTAAAGATCGTCGTTTTACCAGCGACAAATTCTTTTTT
CATGTGCCGATTACCCTGAATTATCAGGCAGCAAATAGCCCGAGCAAATTTAACCAGCGTGTTAATGCATATC

TGAAAGAACATCCAGAAACGCCGATTATTGGTATTGATCGTGGTGAACGTAACCTGATTTATATCACCGTTATT
GATAGCACCGGCAAAATCCTGGAACAGCGTAGCCTGAATACCATTCAGCAGTTTGATTACCAGAAAAAACTG
GATAATCGCGAGAAAGAACGTGTTGCAGCACGTCAGGCATGGTCAGTTGTTGGTACAATTAAAGACCTGAAA
CAGGGTTATCTGAGCCAGGTTATTCATGAAATTGTGGATCTGATGATTCACTATCAGGCCGTTGTTGTGCTGG
AAAACCTGAATTTTGGCTTTAAAAGCAAACGTACCGGCATTGCAGAAAAAGCAGTTTATCAGCAGTTCGAGAA
AATGCTGATTGACAAACTGAATTGCCTGGTGCTGAAAGATTATCCGGCTGAAAAAGTTGGTGGTGTTCTGAAT
CCGTATCAGCTGACCGATCAGTTTACCAGCTTTGCAAAAATGGGCACCCAGAGCGGATTTCTGTTTTATGTTCC
GGCACCGTATACGAGCAAAATTGATCCGCTGACCGGTTTTGTTGATCCGTTTGTTTGGAAAACCATCAAAAAC
CATGAAAGCCGCAAACATTTTCTGGAAGGTTTCGATTTTCTGCATTACGACGTTAAAACGGGTGATTTCATCCT
GCACTTTAAAATGAATCGCAATCTGAGTTTTCAGCGTGGCCTGCCTGGTTTTATGCCTGCATGGGATATTGTGT
TTGAGAAAAACGAAACACAGTTCGATGCAAAAGGCACCCCGTTTATTGCAGGTAAACGTATTGTTCCGGTGAT
TGAAAATCATCGTTTCACCGGTCGTTATCGCGATCTGTATCCGGCAAATGAACTGATCGCACTGCTGGAAGAG
AAAGGTATTGTTTTTCGTGATGGCTCAAACATTCTGCCGAAACTGCTGGAAAATGATGATAGCCATGCAATTG
ATACCATGGTTGCACTGATTCGTAGCGTTCTGCAGATGCGTAATAGCAATGCAGCAACCGGTGAAGATTACAT
TAATAGTCCGGTTCGTGATCTGAATGGTGTTTGTTTTGATAGCCGTTTTCAGAATCCGGAATGGCCGATGGAT
GCAGATGCAAATGGTGCATATCATATTGCACTGAAAGGACAGCTGCTGCTGAACCACCTGAAAGAAAGCAAA
GATCTGAAACTGCAAAACGGCATTAGCAATCAGGATTGGCTGGCATATATCCAAGAACTGCGTAACGGTCGT
AGCAGTGATGATGAAGCAACCGCAGATAGCCAGCATGCAGCACCGCCTAAAAAGAAACGTAAAGTTGGTGG
TAGCGGTGGTTCAGGTGGTAGTGGCGGTAGTGGTGGCTCAGGGGGTTCTGGTGGCTCTGGTGGTAGCctcgag
*caccaccaccaccaccac*

**[0199]** The underlined sequences refer to nucleotides encoding amino acid linker sequences. The double-underlined sequences refer to nucleotides encoding nuclear localization sequences (NLS linker). The italicized sequences refer to nucleotides encoding amino acid affinity tag sequences ($(HIS)_6$).

**[0200]** SEQ ID NO. 489 E. coli optimized DNA M537R F870L Cas12a with NLS linkers

**[0201]** atgACCCAGTTTGAAGGTTTCACCAATCTGTATCAGGTTAGCAAAACCCTGCGTTTTGAACTG
ATTCCGCAGGGTAAAACCCTGAAACATATTCAAGAACAGGGCTTCATCGAAGAGGATAAAGCACGTAACGAT
CACTACAAAGAACTGAAACCGATTATCGACCGCATCTATAAAACCTATGCAGATCAGTGTCTGCAGCTGGTTC
AGCTGGATTGGGAAAATCTGAGCGCAGCAATTGATAGTTATCGCAAAGAAAAAACCGAAGAAACCCGTAATG
CACTGATTGAAGAACAGGCAACCTATCGTAATGCCATCCATGATTATTTCATTGGTCGTACCGATAATCTGACC
GATGCAATTAACAAACGTCACGCCGAAATCTATAAAGGCCTGTTTAAAGCCGAACTGTTTAATGGCAAAGTTC
TGAAACAGCTGGGCACCGTTACCACCACCGAACATGAAAATGCACTGCTGCGTAGCTTTGATAAATTCACCAC
CTATTTCAGCGGCTTTTATGAGAATCGCAAAAACGTGTTTAGCGCAGAAGATATTAGCACCGCAATTCCGCAT
CGTATTGTGCAGGATAATTTCCCGAAATTCAAAGAGAACTGCCACATTTTTACCCGTCTGATTACCGCAGTTCC
GAGCCTGCGTGAACATTTTGAAAACGTTAAAAAAGCCATCGGCATCTTTGTTAGCACCAGCATTGAAGAAGTT
TTTAGCTTCCCGTTTTACAATCAGCTGCTGACCCAGACCCAGATTGATCTGTATAACCAACTGCTGGGTGGTAT
TAGCCGTGAAGCAGGCACCGAAAAAATCAAAGGTCTGAATGAAGTGCTGAATCTGGCCATTCAGAAAAATGA
TGAAACCGCACATATTATTGCAAGCCTGCCGCATCGTTTTATTCCGCTGTTCAAACAAATTCTGAGCGATCGTA
ATACCCTGAGCTTTATTCTGGAAGAATTCAAATCCGATGAAGAGGTGATTCAGAGCTTTTGCAAATACAAAAC

GCTGCTGCGCAATGAAAATGTTCTGGAAACTGCCGAAGCACTGTTTAACGAACTGAATAGCATTGATCTGACC
CACATCTTTATCAGCCACAAAAAACTGGAAACCATTTCAAGCGCACTGTGTGATCATTGGGATACCCTGCGTA
ATGCCCTGTATGAACGTCGTATTAGCGAACTGACCGGTAAAATTACCAAAAGCGCGAAAGAAAAAGTTCAGC
GCAGTCTGAAACATGAGGATATTAATCTGCAAGAGATTATTAGCGCAGCCGGTAAAGAACTGTCAGAAGCAT
TTAAACAGAAAACCAGCGAAATTCTGTCACATGCACATGCAGCACTGGATCAGCCGCTGCCGACCACCCTGAA
AAAACAAGAAGAAAAAGAAATCCTGAAAAGCCAGCTGGATAGCCTGCTGGGTCTGTATCATCTGCTGGACTG
GTTTGCAGTTGATGAAAGCAATGAAGTTGATCCGGAATTTAGCGCACGTCTGACCGGCATTAAACTGGAAAT
GGAACCGAGCCTGAGCTTTTATAACAAAGCCCGTAATTATGCCACCAAAAAACCGTATAGCGTCGAAAAATTC
AAACTGAACTTTCAG**CGT**CCGACCCTGGCAAGCGGTTGGGATGTTAATAAAGAAAAAAACAACGGTGCCATC
CTGTTCGTGAAAAATGGCCTGTATTATCTGGGTATTATGCCGAAACAGAAAGGTCGTTATAAAGCGCTGAGCT
TTGAACCGACGGAAAAAACCAGTGAAGGTTTTGATAAAATGTACTACGACTATTTTCCGGATGCAGCCAAAAT
GATTCCGAAATGTAGCACCCAGCTGAAAGCAGTTACCGCACATTTTCAGACCCATACCACCCCGATTCTGCTGA
GCAATAACTTTATTGAACCGCTGGAAATCACCAAAGAGATCTACGATCTGAATAACCCGGAAAAAGAGCCGA
AAAAATTCCAGACCGCATATGCAAAAAAAACCGGTGATCAGAAAGGTTATCGTGAAGCGCTGTGTAAATGGA
TTGATTTCACCCGTGATTTTCTGAGCAAATACACCAAAACCACCAGTATCGATCTGAGCAGCCTGCGTCCGAGC
AGCCAGTATAAAGATCTGGGCGAATATTATGCAGAACTGAATCCGCTGCTGTATCATATTAGCTTTCAGCGTA
TTGCCGAGAAAGAAATCATGGACGCAGTTGAAACCGGTAAACTGTACCTGTTCCAGATCTACAATAAAGATTT
TGCCAAAGGCCATCATGGCAAACCGAATCTGCATACCCTGTATTGGACCGGTCTGTTTAGCCCTGAAAATCTG
GCAAAAACCTCGATTAAACTGAATGGTCAGGCGGAACTGTTTTATCGTCCGAAAAGCCGTATGAAACGTATG
GCACATCGTCTGGGTGAAAAAATGCTGAACAAAAAACTGAAAGACCAGAAAACCCCGATCCCGGATACACTG
TATCAAGAACTGTATGATTATGTGAACCATCGTCTGAGCCATGATCTGAGTGATGAAGCACGTGCCCTGCTGC
CGAATGTTATTACCAAAGAAGTTAGCCACGAGATCATTAAAGATCGTCGTTTTACCAGCGACAAATTC**CTG**TTT
CATGTGCCGATTACCCTGAATTATCAGGCAGCAAATAGCCCGAGCAAATTTAACCAGCGTGTTAATGCATATC
TGAAAGAACATCCAGAAACGCCGATTATTGGTATTGATCGTGGTGAACGTAACCTGATTTATATCACCGTTATT
GATAGCACCGGCAAAATCCTGGAACAGCGTAGCCTGAATACCATTCAGCAGTTTGATTACCAGAAAAAACTG
GATAATCGCGAGAAAGAACGTGTTGCAGCACGTCAGGCATGGTCAGTTGTTGGTACAATTAAAGACCTGAAA
CAGGGTTATCTGAGCCAGGTTATTCATGAAATTGTGGATCTGATGATTCACTATCAGGCCGTTGTTGTGCTGG
AAAACCTGAATTTTGGCTTTAAAAGCAAACGTACCGGCATTGCAGAAAAAGCAGTTTATCAGCAGTTCGAGAA
AATGCTGATTGACAAACTGAATTGCCTGGTGCTGAAAGATTATCCGGCTGAAAAAGTTGGTGGTGTTCTGAAT
CCGTATCAGCTGACCGATCAGTTTACCAGCTTTGCAAAAATGGGCACCCAGAGCGGATTTCTGTTTTATGTTCC
GGCACCGTATACGAGCAAAATTGATCCGCTGACCGGTTTTGTTGATCCGTTTGTTTGGAAAACCATCAAAAAC
CATGAAAGCCGCAAACATTTTCTGGAAGGTTTCGATTTTCTGCATTACGACGTTAAAACGGGTGATTTCATCCT
GCACTTTAAAATGAATCGCAATCTGAGTTTTCAGCGTGGCCTGCCTGGTTTTATGCCTGCATGGGATATTGTGT
TTGAGAAAAACGAAACACAGTTCGATGCAAAAGGCACCCCGTTTATTGCAGGTAAACGTATTGTTCCGGTGAT
TGAAAATCATCGTTTCACCGGTCGTTATCGCGATCTGTATCCGGCAAATGAACTGATCGCACTGCTGGAAGAG
AAAGGTATTGTTTTTCGTGATGGCTCAAACATTCTGCCGAAACTGCTGGAAAATGATGATAGCCATGCAATTG
ATACCATGGTTGCACTGATTCGTAGCGTTCTGCAGATGCGTAATAGCAATGCAGCAACCGGTGAAGATTACAT
TAATAGTCCGGTTCGTGATCTGAATGGTGTTTGTTTTGATAGCCGTTTTCAGAATCCGGAATGGCCGATGGAT
GCAGATGCAAATGGTGCATATCATATTGCACTGAAAGGACAGCTGCTGCTGAACCACCTGAAAGAAAGCAAA
GATCTGAAACTGCAAAACGGCATTAGCAATCAGGATTGGCTGGCATATATCCAAGAACTGCGTAAC<u>GGTCGT
AGCAGTGATGATGAAGCAACCGCAGATAGCCAGCATGCAGCACCGCCTAAAAAGAAACGTAAAGTT</u>GGTGG
<u>TAGCGGTGGTTCAGGTGGTAGTGGCGGTAGTGGTGGCTCAGGGGGTTCTGGTGGCTCTGGTGGTAGCctcgag</u>
*caccaccaccaccaccac*

**[0202]** The bolded and underlined sequences refer to mutant codons introduced into the Cas12a open reading frame. The underlined sequences refer to nucleotides encoding amino acid linker sequences. The double-underlined sequences refer to nucleotides encoding nuclear localization sequences (NLS linker). The italicized sequences refer to nucleotides encoding amino acid affinity tag sequences ($(HIS)_6$).

**[0203]** SEQ ID NO.: 490 Human optimized DNA WT Cas12a with NLS linkers

**[0204]** atgACCCAGTTTGAAGGTTTCACCAATCTGTATCAGGTTAGCAAAACCCTGCGTTTTGAACTG
ATTCCGCAGGGTAAAACCCTGAAACATATTCAAGAACAGGGCTTCATCGAAGAGGATAAAGCACGTAACGAT
CACTACAAAGAACTGAAACCGATTATCGACCGCATCTATAAAACCTATGCAGATCAGTGTCTGCAGCTGGTTC
AGCTGGATTGGGAAAATCTGAGCGCAGCAATTGATAGTTATCGCAAAGAAAAAACCGAAGAAACCCGTAATG
CACTGATTGAAGAACAGGCAACCTATCGTAATGCCATCCATGATTATTTCATTGGTCGTACCGATAATCTGACC
GATGCAATTAACAAACGTCACGCCGAAATCTATAAAGGCCTGTTTAAAGCCGAACTGTTTAATGGCAAAGTTC
TGAAACAGCTGGGCACCGTTACCACCACCGAACATGAAAATGCACTGCTGCGTAGCTTTGATAAATTCACCAC
CTATTTCAGCGGCTTTTATGAGAATCGCAAAAACGTGTTTAGCGCAGAAGATATTAGCACCGCAATTCCGCAT
CGTATTGTGCAGGATAATTTCCCGAAATTCAAAGAGAACTGCCACATTTTTACCCGTCTGATTACCGCAGTTCC
GAGCCTGCGTGAACATTTTGAAAACGTTAAAAAAGCCATCGGCATCTTTGTTAGCACCAGCATTGAAGAAGTT
TTTAGCTTCCCGTTTTACAATCAGCTGCTGACCCAGACCCAGATTGATCTGTATAACCAACTGCTGGGTGGTAT
TAGCCGTGAAGCAGGCACCGAAAAAATCAAAGGTCTGAATGAAGTGCTGAATCTGGCCATTCAGAAAAATGA
TGAAACCGCACATATTATTGCAAGCCTGCCGCATCGTTTTATTCCGCTGTTCAAACAAATTCTGAGCGATCGTA
ATACCCTGAGCTTTATTCTGGAAGAATTCAAATCCGATGAAGAGGTGATTCAGAGCTTTTGCAAATACAAAAC
GCTGCTGCGCAATGAAAATGTTCTGGAAACTGCCGAAGCACTGTTTAACGAACTGAATAGCATTGATCTGACC
CACATCTTTATCAGCCACAAAAAACTGGAAACCATTTCAAGCGCACTGTGTGATCATTGGGATACCCTGCGTA
ATGCCCTGTATGAACGTCGTATTAGCGAACTGACCGGTAAAATTACCAAAAGCGCGAAAGAAAAAGTTCAGC
GCAGTCTGAAACATGAGGATATTAATCTGCAAGAGATTATTAGCGCAGCCGGTAAAGAACTGTCAGAAGCAT
TTAAACAGAAAACCAGCGAAATTCTGTCACATGCACATGCAGCACTGGATCAGCCGCTGCCGACCACCCTGAA
AAAACAAGAAGAAAAAGAAATCCTGAAAAGCCAGCTGGATAGCCTGCTGGGTCTGTATCATCTGCTGGACTG
GTTTGCAGTTGATGAAAGCAATGAAGTTGATCCGGAATTTAGCGCACGTCTGACCGGCATTAAACTGGAAAT
GGAACCGAGCCTGAGCTTTTATAACAAAGCCCGTAATTATGCCACCAAAAAACCGTATAGCGTCGAAAAATTC
AAACTGAACTTTCAGATGCCGACCCTGGCAAGCGGTTGGGATGTTAATAAAGAAAAAAACAACGGTGCCATC
CTGTTCGTGAAAAATGGCCTGTATTATCTGGGTATTATGCCGAAACAGAAAGGTCGTTATAAAGCGCTGAGCT
TTGAACCGACGGAAAAAACCAGTGAAGGTTTTGATAAAATGTACTACGACTATTTTCCGGATGCAGCCAAAAT
GATTCCGAAATGTAGCACCCAGCTGAAAGCAGTTACCGCACATTTTCAGACCCATACCACCCCGATTCTGCTGA
GCAATAACTTTATTGAACCGCTGGAAATCACCAAAGAGATCTACGATCTGAATAACCCGGAAAAAGAGCCGA
AAAAATTCCAGACCGCATATGCAAAAAAAACCGGTGATCAGAAAGGTTATCGTGAAGCGCTGTGTAAATGGA
TTGATTTCACCCGTGATTTTCTGAGCAAATACACCAAAACCACCAGTATCGATCTGAGCAGCCTGCGTCCGAGC
AGCCAGTATAAAGATCTGGGCGAATATTATGCAGAACTGAATCCGCTGCTGTATCATATTAGCTTTCAGCGTA
TTGCCGAGAAAGAAATCATGGACGCAGTTGAAACCGGTAAACTGTACCTGTTCCAGATCTACAATAAAGATTT
TGCCAAAGGCCATCATGGCAAACCGAATCTGCATACCCTGTATTGGACCGGTCTGTTTAGCCCTGAAAATCTG
GCAAAAACCTCGATTAAACTGAATGGTCAGGCGGAACTGTTTTATCGTCCGAAAAGCCGTATGAAACGTATG
GCACATCGTCTGGGTGAAAAAATGCTGAACAAAAAACTGAAAGACCAGAAAACCCCGATCCCGGATACACTG

TATCAAGAACTGTATGATTATGTGAACCATCGTCTGAGCCATGATCTGAGTGATGAAGCACGTGCCCTGCTGC
CGAATGTTATTACCAAAGAAGTTAGCCACGAGATCATTAAAGATCGTCGTTTTACCAGCGACAAATTCTTTTTT
CATGTGCCGATTACCCTGAATTATCAGGCAGCAAATAGCCCGAGCAAATTTAACCAGCGTGTTAATGCATATC
TGAAAGAACATCCAGAAACGCCGATTATTGGTATTGATCGTGGTGAACGTAACCTGATTTATATCACCGTTATT
GATAGCACCGGCAAAATCCTGGAACAGCGTAGCCTGAATACCATTCAGCAGTTTGATTACCAGAAAAAACTG
GATAATCGCGAGAAAGAACGTGTTGCAGCACGTCAGGCATGGTCAGTTGTTGGTACAATTAAAGACCTGAAA
CAGGGTTATCTGAGCCAGGTTATTCATGAAATTGTGGATCTGATGATTCACTATCAGGCCGTTGTTGTGCTGG
AAAACCTGAATTTTGGCTTTAAAAGCAAACGTACCGGCATTGCAGAAAAAGCAGTTTATCAGCAGTTCGAGAA
AATGCTGATTGACAAACTGAATTGCCTGGTGCTGAAAGATTATCCGGCTGAAAAAGTTGGTGGTGTTCTGAAT
CCGTATCAGCTGACCGATCAGTTTACCAGCTTTGCAAAAATGGGCACCCAGAGCGGATTTCTGTTTTATGTTCC
GGCACCGTATACGAGCAAAATTGATCCGCTGACCGGTTTTGTTGATCCGTTTGTTTGGAAAACCATCAAAAAC
CATGAAAGCCGCAAACATTTTCTGGAAGGTTTCGATTTTCTGCATTACGACGTTAAAACGGGTGATTTCATCCT
GCACTTTAAAATGAATCGCAATCTGAGTTTTCAGCGTGGCCTGCCTGGTTTTATGCCTGCATGGGATATTGTGT
TTGAGAAAAACGAAACACAGTTCGATGCAAAAGGCACCCCGTTTATTGCAGGTAAACGTATTGTTCCGGTGAT
TGAAAATCATCGTTTCACCGGTCGTTATCGCGATCTGTATCCGGCAAATGAACTGATCGCACTGCTGGAAGAG
AAAGGTATTGTTTTTCGTGATGGCTCAAACATTCTGCCGAAACTGCTGGAAAATGATGATAGCCATGCAATTG
ATACCATGGTTGCACTGATTCGTAGCGTTCTGCAGATGCGTAATAGCAATGCAGCAACCGGTGAAGATTACAT
TAATAGTCCGGTTCGTGATCTGAATGGTGTTTGTTTTGATAGCCGTTTTCAGAATCCGGAATGGCCGATGGAT
GCAGATGCAAATGGTGCATATCATATTGCACTGAAAGGACAGCTGCTGCTGAACCACCTGAAAGAAAGCAAA
GATCTGAAACTGCAAAACGGCATTAGCAATCAGGATTGGCTGGCATATATCCAAGAACTGCGTAACGGTCGT
AGCAGTGATGATGAAGCAACCGCAGATAGCCAGCATGCAGCACCGCCTAAAAAGAAACGTAAAGTTGGTGG
TAGCGGTGGTTCAGGTGGTAGTGGCGGTAGTGGTGGCTCAGGGGGTTCTGGTGGCTCTGGTGGTAGCctcgag
*caccaccaccaccaccac*

**[0205]** The underlined sequences refer to nucleotides encoding amino acid linker sequences. The double-underlined sequences refer to nucleotides encoding nuclear localization sequences (NLS linker). The italicized sequences refer to nucleotides encoding amino acid affinity tag sequences ($(HIS)_6$).

**[0206]** SEQ ID NO.: 491 Human optimized DNA M537R F870L Cas12a with NLS linkers

**[0207]** atgACCCAGTTTGAAGGTTTCACCAATCTGTATCAGGTTAGCAAAACCCTGCGTTTTGAACTG
ATTCCGCAGGGTAAAACCCTGAAACATATTCAAGAACAGGGCTTCATCGAAGAGGATAAAGCACGTAACGAT
CACTACAAAGAACTGAAACCGATTATCGACCGCATCTATAAAACCTATGCAGATCAGTGTCTGCAGCTGGTTC
AGCTGGATTGGGAAAATCTGAGCGCAGCAATTGATAGTTATCGCAAAGAAAAAACCGAAGAAACCCGTAATG
CACTGATTGAAGAACAGGCAACCTATCGTAATGCCATCCATGATTATTTCATTGGTCGTACCGATAATCTGACC
GATGCAATTAACAAACGTCACGCCGAAATCTATAAAGGCCTGTTTAAAGCCGAACTGTTTAATGGCAAAGTTC
TGAAACAGCTGGGCACCGTTACCACCACCGAACATGAAAATGCACTGCTGCGTAGCTTTGATAAATTCACCAC
CTATTTCAGCGGCTTTTATGAGAATCGCAAAAACGTGTTTAGCGCAGAAGATATTAGCACCGCAATTCCGCAT
CGTATTGTGCAGGATAATTTCCCGAAATTCAAAGAGAACTGCCACATTTTTACCCGTCTGATTACCGCAGTTCC
GAGCCTGCGTGAACATTTTGAAAACGTTAAAAAAGCCATCGGCATCTTTGTTAGCACCAGCATTGAAGAAGTT
TTTAGCTTCCCGTTTTACAATCAGCTGCTGACCCAGACCCAGATTGATCTGTATAACCAACTGCTGGGTGGTAT

TAGCCGTGAAGCAGGCACCGAAAAAATCAAAGGTCTGAATGAAGTGCTGAATCTGGCCATTCAGAAAAATGA
TGAAACCGCACATATTATTGCAAGCCTGCCGCATCGTTTTATTCCGCTGTTCAAACAAATTCTGAGCGATCGTA
ATACCCTGAGCTTTATTCTGGAAGAATTCAAATCCGATGAAGAGGTGATTCAGAGCTTTTGCAAATACAAAAC
GCTGCTGCGCAATGAAAATGTTCTGGAAACTGCCGAAGCACTGTTTAACGAACTGAATAGCATTGATCTGACC
CACATCTTTATCAGCCACAAAAAACTGGAAACCATTTCAAGCGCACTGTGTGATCATTGGGATACCCTGCGTA
ATGCCCTGTATGAACGTCGTATTAGCGAACTGACCGGTAAAATTACCAAAAGCGCGAAAGAAAAAGTTCAGC
GCAGTCTGAAACATGAGGATATTAATCTGCAAGAGATTATTAGCGCAGCCGGTAAAGAACTGTCAGAAGCAT
TTAAACAGAAAACCAGCGAAATTCTGTCACATGCACATGCAGCACTGGATCAGCCGCTGCCGACCACCCTGAA
AAAACAAGAAGAAAAAGAAATCCTGAAAAGCCAGCTGGATAGCCTGCTGGGTCTGTATCATCTGCTGGACTG
GTTTGCAGTTGATGAAAGCAATGAAGTTGATCCGGAATTTAGCGCACGTCTGACCGGCATTAAACTGGAAAT
GGAACCGAGCCTGAGCTTTTATAACAAAGCCCGTAATTATGCCACCAAAAAACCGTATAGCGTCGAAAAATTC
AAACTGAACTTTCAG**CGT**CCGACCCTGGCAAGCGGTTGGGATGTTAATAAAGAAAAAAACAACGGTGCCATC
CTGTTCGTGAAAAATGGCCTGTATTATCTGGGTATTATGCCGAAACAGAAAGGTCGTTATAAAGCGCTGAGCT
TTGAACCGACGGAAAAAACCAGTGAAGGTTTTGATAAAATGTACTACGACTATTTTCCGGATGCAGCCAAAAT
GATTCCGAAATGTAGCACCCAGCTGAAAGCAGTTACCGCACATTTTCAGACCCATACCACCCCGATTCTGCTGA
GCAATAACTTTATTGAACCGCTGGAAATCACCAAAGAGATCTACGATCTGAATAACCCGGAAAAAGAGCCGA
AAAAATTCCAGACCGCATATGCAAAAAAAACCGGTGATCAGAAAGGTTATCGTGAAGCGCTGTGTAAATGGA
TTGATTTCACCCGTGATTTTCTGAGCAAATACACCAAAACCACCAGTATCGATCTGAGCAGCCTGCGTCCGAGC
AGCCAGTATAAAGATCTGGGCGAATATTATGCAGAACTGAATCCGCTGCTGTATCATATTAGCTTTCAGCGTA
TTGCCGAGAAAGAAATCATGGACGCAGTTGAAACCGGTAAACTGTACCTGTTCCAGATCTACAATAAAGATTT
TGCCAAAGGCCATCATGGCAAACCGAATCTGCATACCCTGTATTGGACCGGTCTGTTTAGCCCTGAAAATCTG
GCAAAAACCTCGATTAAACTGAATGGTCAGGCGGAACTGTTTTATCGTCCGAAAAGCCGTATGAAACGTATG
GCACATCGTCTGGGTGAAAAAATGCTGAACAAAAAACTGAAAGACCAGAAAACCCCGATCCCGGATACACTG
TATCAAGAACTGTATGATTATGTGAACCATCGTCTGAGCCATGATCTGAGTGATGAAGCACGTGCCCTGCTGC
CGAATGTTATTACCAAAGAAGTTAGCCACGAGATCATTAAAGATCGTCGTTTTACCAGCGACAAATTC**CTG**TTT
CATGTGCCGATTACCCTGAATTATCAGGCAGCAAATAGCCCGAGCAAATTTAACCAGCGTGTTAATGCATATC
TGAAAGAACATCCAGAAACGCCGATTATTGGTATTGATCGTGGTGAACGTAACCTGATTTATATCACCGTTATT
GATAGCACCGGCAAAATCCTGGAACAGCGTAGCCTGAATACCATTCAGCAGTTTGATTACCAGAAAAAACTG
GATAATCGCGAGAAAGAACGTGTTGCAGCACGTCAGGCATGGTCAGTTGTTGGTACAATTAAAGACCTGAAA
CAGGGTTATCTGAGCCAGGTTATTCATGAAATTGTGGATCTGATGATTCACTATCAGGCCGTTGTTGTGCTGG
AAAACCTGAATTTTGGCTTTAAAAGCAAACGTACCGGCATTGCAGAAAAAGCAGTTTATCAGCAGTTCGAGAA
AATGCTGATTGACAAACTGAATTGCCTGGTGCTGAAAGATTATCCGGCTGAAAAAGTTGGTGGTGTTCTGAAT
CCGTATCAGCTGACCGATCAGTTTACCAGCTTTGCAAAAATGGGCACCCAGAGCGGATTTCTGTTTTATGTTCC
GGCACCGTATACGAGCAAAATTGATCCGCTGACCGGTTTTGTTGATCCGTTTGTTTGGAAAACCATCAAAAAC
CATGAAAGCCGCAAACATTTTCTGGAAGGTTTCGATTTTCTGCATTACGACGTTAAAACGGGTGATTTCATCCT
GCACTTTAAAATGAATCGCAATCTGAGTTTTCAGCGTGGCCTGCCTGGTTTTATGCCTGCATGGGATATTGTGT
TTGAGAAAAACGAAACACAGTTCGATGCAAAAGGCACCCCGTTTATTGCAGGTAAACGTATTGTTCCGGTGAT
TGAAAATCATCGTTTCACCGGTCGTTATCGCGATCTGTATCCGGCAAATGAACTGATCGCACTGCTGGAAGAG
AAAGGTATTGTTTTTCGTGATGGCTCAAACATTCTGCCGAAACTGCTGGAAAATGATGATAGCCATGCAATTG
ATACCATGGTTGCACTGATTCGTAGCGTTCTGCAGATGCGTAATAGCAATGCAGCAACCGGTGAAGATTACAT
TAATAGTCCGGTTCGTGATCTGAATGGTGTTTGTTTTGATAGCCGTTTTCAGAATCCGGAATGGCCGATGGAT
GCAGATGCAAATGGTGCATATCATATTGCACTGAAAGGACAGCTGCTGCTGAACCACCTGAAAGAAAGCAAA
GATCTGAAACTGCAAAACGGCATTAGCAATCAGGATTGGCTGGCATATATCCAAGAACTGCGTAAC<u>GGTCGT</u>

AGCAGTGATGATGAAGCAACCGCAGATAGCCAGCATGCAGCACCGCCTAAAAAGAAACGTAAAGTTGGTGG
TAGCGGTGGTTCAGGTGGTAGTGGCGGTAGTGGTGGCTCAGGGGGTTCTGGTGGCTCTGGTGGTAGCctcgag
*caccaccaccaccaccac*

**[0208]** The bolded and underlined sequences refer to mutant codons introduced into the Cas12a open reading frame. The underlined sequences refer to nucleotides encoding amino acid linker sequences. The double-underlined sequences refer to nucleotides encoding nuclear localization sequences (NLS linker). The italicized sequences refer to nucleotides encoding amino acid affinity tag sequences ($(HIS)_6$).

**[0209]** SEQ ID NO.: 492 WT Cas12a AA with NLS linkers

**[0210]** MTQFEGFTNLYQVSKTLRFELIPQGKTLKHIQEQGFIEEDKARNDHYKELKPIIDRIYKTYADQCL
QLVQLDWENLSAAIDSYRKEKTEETRNALIEEQATYRNAIHDYFIGRTDNLTDAINKRHAEIYKGLFKAELFNGKVLK
QLGTVTTTEHENALLRSFDKFTTYFSGFYENRKNVFSAEDISTAIPHRIVQDNFPKFKENCHIFTRLITAVPSLREHFEN
VKKAIGIFVSTSIEEVFSFPFYNQLLTQTQIDLYNQLLGGISREAGTEKIKGLNEVLNLAIQKNDETAHIIASLPHRFIPLF
KQILSDRNTLSFILEEFKSDEEVIQSFCKYKTLLRNENVLETAEALFNELNSIDLTHIFISHKKLETISSALCDHWDTLRNA
LYERRISELTGKITKSAKEKVQRSLKHEDINLQEIISAAGKELSEAFKQKTSEILSHAHAALDQPLPTTLKKQEEKEILKSQ
LDSLLGLYHLLDWFAVDESNEVDPEFSARLTGIKLEMEPSLSFYNKARNYATKKPYSVEKFKLNFQMPTLASGWDV
NKEKNNGAILFVKNGLYYLGIMPKQKGRYKALSFEPTEKTSEGFDKMYYDYFPDAAKMIPKCSTQLKAVTAHFQTH
TTPILLSNNFIEPLEITKEIYDLNNPEKEPKKFQTAYAKKTGDQKGYREALCKWIDFTRDFLSKYTKTTSIDLSSLRPSSQ
YKDLGEYYAELNPLLYHISFQRIAEKEIMDAVETGKLYLFQIYNKDFAKGHHGKPNLHTLYWTGLFSPENLAKTSIKLN
GQAELFYRPKSRMKRMAHRLGEKMLNKKLKDQKTPIPDTLYQELYDYVNHRLSHDLSDEARALLPNVITKEVSHEII
KDRRFTSDKFFFHVPITLNYQAANSPSKFNQRVNAYLKEHPETPIIGIDRGERNLIYITVIDSTGKILEQRSLNTIQQFD
YQKKLDNREKERVAARQAWSVVGTIKDLKQGYLSQVIHEIVDLMIHYQAVVVLENLNFGFKSKRTGIAEKAVYQQF
EKMLIDKLNCLVLKDYPAEKVGGVLNPYQLTDQFTSFAKMGTQSGFLFYVPAPYTSKIDPLTGFVDPFVWKTIKNHE
SRKHFLEGFDFLHYDVKTGDFILHFKMNRNLSFQRGLPGFMPAWDIVFEKNETQFDAKGTPFIAGKRIVPVIENHR
FTGRYRDLYPANELIALLEEKGIVFRDGSNILPKLLENDDSHAIDTMVALIRSVLQMRNSNAATGEDYINSPVRDLNG
VCFDSRFQNPEWPMDADANGAYHIALKGQLLLNHLKESKDLKLQNGISNQDWLAYIQELRNGRSSDDEATADSQ
HAAPPKKKRKVGGSGGSGGSGGSGGSGGSGGSGGSLE*HHHHHH*

**[0211]** The underlined sequences refer to amino acid sequences encoding amino acid linker sequences. The double-underlined sequences refer to amino acid sequences encoding nuclear localization sequences (NLS linker). The italicized sequences refer to amino acid sequences encoding amino acid affinity tag sequences ($(HIS)_6$).

**[0212]** SEQ ID NO.: 493 M537R F870L Cas12a AA with NLS linkers

**[0213]** MTQFEGFTNLYQVSKTLRFELIPQGKTLKHIQEQGFIEEDKARNDHYKELKPIIDRIYKTYADQCL
QLVQLDWENLSAAIDSYRKEKTEETRNALIEEQATYRNAIHDYFIGRTDNLTDAINKRHAEIYKGLFKAELFNGKVLK
QLGTVTTTEHENALLRSFDKFTTYFSGFYENRKNVFSAEDISTAIPHRIVQDNFPKFKENCHIFTRLITAVPSLREHFEN
VKKAIGIFVSTSIEEVFSFPFYNQLLTQTQIDLYNQLLGGISREAGTEKIKGLNEVLNLAIQKNDETAHIIASLPHRFIPLF

KQILSDRNTLSFILEEFKSDEEVIQSFCKYKTLLRNENVLETAEALFNELNSIDLTHIFISHKKLETISSALCDHWDTLRNA
LYERRISELTGKITKSAKEKVQRSLKHEDINLQEIISAAGKELSEAFKQKTSEILSHAHAALDQPLPTTLKKQEEKEILKSQ
LDSLLGLYHLLDWFAVDESNEVDPEFSARLTGIKLEMEPSLSFYNKARNYATKKPYSVEKFKLNFQ**R**PTLASGWDVN
KEKNNGAILFVKNGLYYLGIMPKQKGRYKALSFEPTEKTSEGFDKMYYDYFPDAAKMIPKCSTQLKAVTAHFQTHT
TPILLSNNFIEPLEITKEIYDLNNPEKEPKKFQTAYAKKTGDQKGYREALCKWIDFTRDFLSKYTKTTSIDLSSLRPSSQY
KDLGEYYAELNPLLYHISFQRIAEKEIMDAVETGKLYLFQIYNKDFAKGHHGKPNLHTLYWTGLFSPENLAKTSIKLN
GQAELFYRPKSRMKRMAHRLGEKMLNKKLKDQKTPIPDTLYQELYDYVNHRLSHDLSDEARALLPNVITKEVSHEII
KDRRFTSDKF**L**FHVPITLNYQAANSPSKFNQRVNAYLKEHPETPIIGIDRGERNLIYITVIDSTGKILEQRSLNTIQQFD
YQKKLDNREKERVAARQAWSVVGTIKDLKQGYLSQVIHEIVDLMIHYQAVVVLENLNFGFKSKRTGIAEKAVYQQF
EKMLIDKLNCLVLKDYPAEKVGGVLNPYQLTDQFTSFAKMGTQSGFLFYVPAPYTSKIDPLTGFVDPFVWKTIKNHE
SRKHFLEGFDFLHYDVKTGDFILHFKMNRNLSFQRGLPGFMPAWDIVFEKNETQFDAKGTPFIAGKRIVPVIENHR
FTGRYRDLYPANELIALLEEKGIVFRDGSNILPKLLENDDSHAIDTMVALIRSVLQMRNSNAATGEDYINSPVRDLNG
VCFDSRFQNPEWPMDADANGAYHIALKGQLLLNHLKESKDLKLQNGISNQDWLAYIQELRN<u>GRSSDDEATADSQ
HAAPPKKKRKV</u>GGSGGSGGSGGSGGSGGSGGSGGSLE*HHHHHH*

**[0214]** The bolded and underlined sequences refer to mutant amino acids introduced into the Cas12a polypeptide variant. The underlined sequences refer to amino acid sequences encoding amino acid linker sequences. The double-underlined sequences refer to amino acid sequences encoding nuclear localization sequences (NLS linker). The italicized sequences refer to amino acid sequences encoding amino acid affinity tag sequences ($(HIS)_6$).

**[0215]** **References:**

**[0216]** Chen, J.S., et al., *Enhanced proofreading governs CRISPR-Cas9 targeting accuracy.* Nature, 2017. **550**(7676): p. 407-410.

**[0217]** Gao, L., et al., *Engineered Cpf1 variants with altered PAM specificities increase genome targeting range*. Nat Biotechnol. 2017; **35**(8): 789–792.

**[0218]** Jinek M, et al. *A programmable dual-RNA–guided DNA endonuclease in adaptive bacterial immunity*. Science. 2012;337:816–821. doi: 10.1126/science.1225829.

**[0219]** Kleinstiver, B.P., et al., *High-fidelity CRISPR-Cas9 nucleases with no detectable genome-wide off-target effects.* Nature, 2016. **529**(7587): p. 490-5.

**[0220]** Slaymaker, I.M., et al., *Rationally engineered Cas9 nucleases with improved specificity.* Science, 2016. **351**(6268): p. 84-8.

**[0221]** Sun, Y., et al., *Factors influencing the nuclear targeting ability of nuclear localization signals.* J Drug Target, 2016. **24**(10): p. 927-933.

**[0222]** Wrenbeck EE, Klesmith JR, Stapleton JA, Adeniran A, Tyo KE, Whitehead TA. Plasmid-based one-pot saturation mutagenesis. *Nat Methods*. 2016;13(11):928–930. doi:10.1038/nmeth.4029

**[0223]** Zetsche, B., et al., *Cpf1 Is a Single RNA-Guided Endonuclease of a Class 2 CRISPR-Cas System*. Cell. 2015;163:759–771. doi: 10.1016/j.cell.2015.09.038.

**[0224]** Incorporation by Reference

**[0225]** All of the patents, patent applications, patent application publications, and other publications cited herein are hereby incorporated by reference as if set forth in their entirety.

**[0226]** Preferred embodiments

**[0227]** The present invention has been described in connection with what are presently considered to be the most practical and preferred embodiments. However, the invention has been presented by way of illustration and is not intended to be limited to the disclosed embodiments. Accordingly, one of skill in the art will realize that the invention is intended to encompass all modifications and alternative arrangements within the spirit and scope of the invention as set forth in the appended claims.

CLAIMS

What is claimed is:

1. A CRISPR-associated protein comprising a polypeptide encoding a variant of AsCpf1, wherein the variant of AsCpf1 is selected from the group consisting of M537R (SEQ ID NO.: 472), F870L (SEQ ID NO.: 473), and M537R/F870L (SEQ ID NO.: 465).

2. The CRISPR-associated protein according to claim 1, wherein the variant of AsCpf1 is M537R (SEQ ID NO.: 472).

3. The CRISPR-associated protein according to claim 1, wherein the variant of AsCpf1 is F870L (SEQ ID NO.: 473).

4. The CRISPR-associated protein according to claim 1, wherein the variant of AsCpf1 is M537R/F870L (SEQ ID NO.: 465).

5. A CRISPR ribonucleoprotein complex, comprising:

a guide RNA; and

a CRISPR-associated protein comprising a polypeptide encoding a variant of AsCpf1, wherein the variant of AsCpf1 is selected from the group consisting of M537R (SEQ ID NO.: 472), F870L (SEQ ID NO.: 473), and M537R/F870L (SEQ ID NO.: 465).

6. The CRISPR ribonucleoprotein complex of claim 5, wherein the variant of AsCpf1 is M537R (SEQ ID NO.: 472).

7. The CRISPR ribonucleoprotein complex of claim 5, wherein the variant of AsCpf1 is F870L (SEQ ID NO.: 473)

8. The CRISPR ribonucleoprotein complex of claim 5, wherein the variant of AsCpf1 is M537R/F870L (SEQ ID NO.: 465).

9. A method of increasing efficiency of gene editing at TTTN PAM sites in a cell with a CRISPR ribonucleoprotein complex, comprising:

contacting a cell with the CRISPR ribonucleoprotein complex according to any of claims 5-8.

10. The method according to claim 9, wherein the TTTN PAM sites consists of one selected form the group of TTTA, TTTT and TTTC PAM sites.

11. A kit comprising a guide RNA and a CRISPR-associated protein comprising a polypeptide encoding a variant of AsCpf1, wherein the variant of AsCpf1 is selected from the group consisting of M537R (SEQ ID NO.: 472), F870L (SEQ ID NO.: 473), and M537R/F870L (SEQ ID NO.: 465).

12. The kit according to claim 11, wherein the variant of AsCpf1 is M537R (SEQ ID NO.: 472).

13. The kit according to claim 11, wherein the variant of AsCpf1 is F870L (SEQ ID NO.: 473).

14. The kit according to claim 11, wherein the variant of AsCpf1 is M537R/F870L (SEQ ID NO.: 465).

15. A CRISPR-associated protein comprising a polypeptide encoding a variant of AsCas12a, wherein the variant of AsCas12a is selected from the group consisting of at least one variant amino acid selected from amino acid positions 499-640 and 840-913, provided that the variant AsCas12a provides an improvement in CRISPR/AsCas12a-associated nuclease activity at non-canonical TTTT PAM sites.

16. The CRISPR-associated protein according to claim 15, wherein the variant of AsCas12a is selected from the group consisting of SEQ ID NOs.: 59-245.

17. The CRISPR-associated protein according to claims 15 or 16, wherein the variant of AsCas12a further comprises mutations of M537R/F870L (SEQ ID NO.: 465).

18. A CRISPR ribonucleoprotein complex, comprising:

a guide RNA; and

a CRISPR-associated protein comprising a polypeptide encoding a variant of AsCas12a, wherein the variant of AsCas12a is selected from the group consisting of at least one variant amino acid selected from amino acid positions 499-640 and 840-913, provided that the variant AsCas12a provides an improvement in CRISPR/AsCas12a-associated nuclease activity at non-canonical TTTT PAM sites.

19. The CRISPR ribonucleoprotein complex of claim 18, wherein the variant of AsCas12a is selected from the group consisting of SEQ ID NOs.: 59-245.

20. The CRISPR ribonucleoprotein complex of claims 18 or 19, wherein the variant of AsCas12a further comprises mutations of M537R/F870L (SEQ ID NO.: 465).

21. A method of increasing efficiency of gene editing at non-canonical TTTT PAM sites in a cell with a CRISPR ribonucleoprotein complex, comprising:

contacting a cell with the CRISPR ribonucleoprotein complex according to any of claims 18-20.

22. A kit comprising a guide RNA and a CRISPR-associated protein comprising a polypeptide encoding a variant of AsCas12a, wherein the variant of AsCas12a is selected from the group consisting of at least one variant amino acid selected from amino acid positions 499-640 and 840-913, provided that the variant AsCas12a provides an improvement in CRISPR/AsCas12a-associated nuclease activity at non-canonical TTTT PAM sites.

23. The kit according to claim 22, wherein the variant of AsCas12a is selected from the group consisting of SEQ ID NOs.: 59-245.

24. The kit according to claims 22 or 23, wherein the variant of AsCas12a further comprises mutations of M537R/F870L (SEQ ID NO.: 465).

25. A nucleic acid encoding a CRISPR-associated protein comprising a polypeptide encoding a variant of AsCas12a, wherein the variant of AsCas12a is selected from the group consisting of at least one variant amino acid selected from amino acid positions 499-640 and 840-913, provided that the variant AsCas12a provides an improvement in CRISPR/AsCas12a-associated nuclease activity at non-canonical TTTT PAM sites.

26. The nucleic acid of claim 25, wherein the variant of AsCas12a is selected from the group consisting of SEQ ID NOs.: 59-245.

27. The nucleic acid of claims 25 or 26, wherein the variant of AsCas12a further comprises mutations of M537R/F870L (SEQ ID NO.: 465).

28. The nucleic acid of claims 25-27, wherein the nucleic acid is operably linked to suitable transcription elements to express the nucleic acid.

29. The nucleic acid of claims 25-28, wherein the nucleic acid is DNA or RNA.

30. A polynucleotide sequence encoding a Cas12a polypeptide, comprising one member selected from the group consisting of SEQ ID NOs.: 5-17.

31. An amino acid sequence encoding a Cas12a polypeptide, comprising one member selected from the group consisting of SEQ ID NOs.: 18-30.

32. A CAS endonuclease system comprising an expression cassette encoding a polynucleotide sequence encoding a Cas12a polypeptide, comprising one member selected from the group consisting of SEQ ID NOs.: 5-17.

33. A CAS endonuclease system comprising an amino acid sequence encoding a Cas12a polypeptide, comprising one member selected from the group consisting of SEQ ID NOs.: 18-30.

34. A method of performing genome editing in a eukaryotic cell, comprising:

introducing an CAS endonuclease system into the eukaryotic cell, said CAS endonuclease system comprising an expression cassette encoding a polynucleotide sequence encoding a Cas12a polypeptide, comprising one member selected from the group consisting of SEQ ID NOs.: 5-17.

35. A method of performing genome editing in a eukaryotic cell, comprising:

introducing an CAS endonuclease system into the eukaryotic cell, said CAS endonuclease system comprising an amino acid sequence encoding a Cas12a polypeptide comprising one member selected from the group consisting of SEQ ID NOs.: 18-30.

36. A CRISPR-associated protein comprising a fusion polypeptide encoding an AsCas12a open reading frame, a nuclear localization signal, optionally an amino acid linker and optionally an affinity tag.

37. The CRISPR-associated protein of claim 36, wherein the AsCas12a open reading frame is selected from the group consisting of SEQ ID NOs.: 59-245.

38. The CRISPR-associated protein of claim 36, wherein the nuclear localization signal is selected from SEQ ID NOs.: 475, 477, 479, 481 and 483.

39. The CRISPR-associated protein of claim 36, wherein the CRISPR-associated protein is encoded by SEQ ID NOs.: 488-491.

40. The CRISPR-associated protein of claim 36, wherein the CRISPR-associated protein is selected from SEQ ID NOs.: 492 and 493.

41. A method of performing genome editing in a eukaryotic cell, comprising:

introducing an CAS endonuclease system into the eukaryotic cell, said CAS endonuclease system comprising a CRISPR-associated protein of claims 36-40.