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 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). 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	rUrArArUrUrUrCrUrArCrUrCrUrUrGrUrArGrArUrUrArArUrGrCrCrCrUrGrUrArGrUrCrUrCrUrCrUrG	SEQ ID NO. 1
HPRT-38228-S	rUrArArUrUrUrCrUrArCrUrCrUrUrGrUrArGrArUrUrArArUrUrArArCrArGrCrUrUrGrCrUrGrGrUrGrA	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
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AAAACCCCGATCCCGGATACACTGTATCAAGAACTGTATGATTATGTGAACCATCGTCTGAGCCATGATCTGA
GTGATGAAGCACGTGCCCTGCTGCCGAATGTTATTACCAAAGAAGTTAGCCACGAGATCATTAAAGATCGTCG
TTTTACCAGCGACAAATTCTTTTTTCATGTGCCGATTACCCTGAATTATCAGGCAGCAAATAGCCCGAGCAAAT
TTAACCAGCGTGTTAATGCATATCTGAAAGAACATCCAGAAACGCCGATTATTGGTATTGATCGTGGTGAACG
TAACCTGATTTATATCACCGTTATTGATAGCACCGGCAAAATCCTGGAACAGCGTAGCCTGAATACCATTCAGC
AGTTTGATTACCAGAAAAAACTGGATAATCGCGAGAAAGAACGTGTTGCAGCACGTCAGGCATGGTCAGTTG
TTGGTACAATTAAAGACCTGAAACAGGGTTATCTGAGCCAGGTTATTCATGAAATTGTGGATCTGATGATTCA
CTATCAGGCCGTTGTTGTGCTGGAAAACCTGAATTTTGGCTTTAAAAGCAAACGTACCGGCATTGCAGAAAAA
GCAGTTTATCAGCAGTTCGAGAAAATGCTGATTGACAAACTGAATTGCCTGGTGCTGAAAGATTATCCGGCTG
AAAAAGTTGGTGGTGTTCTGAATCCGTATCAGCTGACCGATCAGTTTACCAGCTTTGCAAAAATGGGCACCCA
GAGCGGATTTCTGTTTTATGTTCCGGCACCGTATACGAGCAAAATTGATCCGCTGACCGGTTTTGTTGATCCGT
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GTTAAAACGGGTGATTTCATCCTGCACTTTAAAATGAATCGCAATCTGAGTTTTCAGCGTGGCCTGCCTGGTTT
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GGTAAACGTATTGTTCCGGTGATTGAAAATCATCGTTTCACCGGTCGTTATCGCGATCTGTATCCGGCAAATG
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AAATGATGATAGCCATGCAATTGATACCATGGTTGCACTGATTCGTAGCGTTCTGCAGATGCGTAATAGCAAT
GCAGCAACCGGTGAAGATTACATTAATAGTCCGGTTCGTGATCTGAATGGTGTTTGTTTTGATAGCCGTTTTCA
GAATCCGGAATGGCCGATGGATGCAGATGCAAATGGTGCATATCATATTGCACTGAAAGGACAGCTGCTGCT
GAACCACCTGAAAGAAAGCAAAGATCTGAAACTGCAAAACGGCATTAGCAATCAGGATTGGCTGGCATATAT
CCAAGAACTGCGTAACCCTAAAAAAAAACGCAAAGTGAAGCTTGCGGCCGCACTCGAGCACCACCACCACCA
CCACTGA

[0097] SEQ ID NO.: 6

[0098] ATGGGCAGCAGCAGCAGCGGCCTGGTGCCGCGCGGCAGCCATATGGCTAGCATGACTGGT
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ACCCAGTTTGAAGGTTTCACCAATCTGTATCAGGTTAGCAAAACCCTGCGTTTTGAACTGATTCCGCAGGGTAA
AACCCTGAAACATATTCAAGAACAGGGCTTCATCGAAGAGGATAAAGCACGTAACGATCACTACAAAGAACT
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CACCGAAAAAATCAAAGGTCTGAATGAAGTGCTGAATCTGGCCATTCAGAAAAATGATGAAACCGCACATATT

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CGTATTAGCGAACTGACCGGTAAAATTACCAAAAGCGCGAAAGAAAAAGTTCAGCGCAGTCTGAAACATGAG
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AAAAATGCTGAACAAAAAACTGAAAGACCAGAAAACCCCGATCCCGGATACACTGTATCAAGAACTGTATGA
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GCAATCTGAGTTTTCAGCGTGGCCTGCCTGGTTTTATGCCTGCATGGGATATTGTGTTTGAGAAAAACGAAAC
ACAGTTCGATGCAAAAGGCACCCCGTTTATTGCAGGTAAACGTATTGTTCCGGTGATTGAAAATCATCGTTTCA
CCGGTCGTTATCGCGATCTGTATCCGGCAAATGAACTGATCGCACTGCTGGAAGAGAAAGGTATTGTTTTTCG
TGATGGCTCAAACATTCTGCCGAAACTGCTGGAAAATGATGATAGCCATGCAATTGATACCATGGTTGCACTG
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ATCTGAATGGTGTTTGTTTTGATAGCCGTTTTCAGAATCCGGAATGGCCGATGGATGCAGATGCAAATGGTGC
ATATCATATTGCACTGAAAGGACAGCTGCTGCTGAACCACCTGAAAGAAAGCAAAGATCTGAAACTGCAAAA
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GCTTGCGGCCGCACTCGAGCACCACCACCACCACCACTGA

[0099] SEQ ID NO.: 7

[0100] ATGCCGAAAAAAAAACGCAAAGTGGGTATTCATGGTGTTCCGGCAGCAACCCAGTTTGAA
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TCGACCGCATCTATAAAACCTATGCAGATCAGTGTCTGCAGCTGGTTCAGCTGGATTGGGAAAATCTGAGCGC
AGCAATTGATAGTTATCGCAAAGAAAAAACCGAAGAAACCCGTAATGCACTGATTGAAGAACAGGCAACCTA
TCGTAATGCCATCCATGATTATTTCATTGGTCGTACCGATAATCTGACCGATGCAATTAACAAACGTCACGCCG
AAATCTATAAAGGCCTGTTTAAAGCCGAACTGTTTAATGGCAAAGTTCTGAAACAGCTGGGCACCGTTACCAC
CACCGAACATGAAAATGCACTGCTGCGTAGCTTTGATAAATTCACCACCTATTTCAGCGGCTTTTATGAGAATC
GCAAAAACGTGTTTAGCGCAGAAGATATTAGCACCGCAATTCCGCATCGTATTGTGCAGGATAATTTCCCGAA
ATTCAAAGAGAACTGCCACATTTTTACCCGTCTGATTACCGCAGTTCCGAGCCTGCGTGAACATTTTGAAAACG
TTAAAAAAGCCATCGGCATCTTTGTTAGCACCAGCATTGAAGAAGTTTTTAGCTTCCCGTTTTACAATCAGCTG
CTGACCCAGACCCAGATTGATCTGTATAACCAACTGCTGGGTGGTATTAGCCGTGAAGCAGGCACCGAAAAA
ATCAAAGGTCTGAATGAAGTGCTGAATCTGGCCATTCAGAAAAATGATGAAACCGCACATATTATTGCAAGCC
TGCCGCATCGTTTTATTCCGCTGTTCAAACAAATTCTGAGCGATCGTAATACCCTGAGCTTTATTCTGGAAGAA
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AAACTGCCGAAGCACTGTTTAACGAACTGAATAGCATTGATCTGACCCACATCTTTATCAGCCACAAAAAACT
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[0101] SEQ ID NO.: 8

[0102] ATGACCCAGTTTGAAGGTTTCACCAATCTGTATCAGGTTAGCAAAACCCTGCGTTTTGAACT
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[0103] SEQ ID NO.: 9

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[0105] SEQ ID NO.: 10

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[0107] SEQ ID NO.: 11

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[0109] SEQ ID NO.: 12

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[0111] SEQ ID NO.: 13

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[0113] SEQ ID NO.: 14

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[0115] SEQ ID NO.: 15

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GCAATAACTTTATTGAACCGCTGGAAATCACCAAAGAGATCTACGATCTGAATAACCCGGAAAAAGAGCCGA
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AGCCAGTATAAAGATCTGGGCGAATATTATGCAGAACTGAATCCGCTGCTGTATCATATTAGCTTTCAGCGTA
TTGCCGAGAAAGAAATCATGGACGCAGTTGAAACCGGTAAACTGTACCTGTTCCAGATCTACAATAAAGATTT
TGCCAAAGGCCATCATGGCAAACCGAATCTGCATACCCTGTATTGGACCGGTCTGTTTAGCCCTGAAAATCTG
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GCACATCGTCTGGGTGAAAAAATGCTGAACAAAAAACTGAAAGACCAGAAAACCCCGATCCCGGATACACTG
TATCAAGAACTGTATGATTATGTGAACCATCGTCTGAGCCATGATCTGAGTGATGAAGCACGTGCCCTGCTGC
CGAATGTTATTACCAAAGAAGTTAGCCACGAGATCATTAAAGATCGTCGTTTTACCAGCGACAAATTCTTTTTT
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TGAAAGAACATCCAGAAACGCCGATTATTGGTATTGATCGTGGTGAACGTAACCTGATTTATATCACCGTTATT
GATAGCACCGGCAAAATCCTGGAACAGCGTAGCCTGAATACCATTCAGCAGTTTGATTACCAGAAAAAACTG
GATAATCGCGAGAAAGAACGTGTTGCAGCACGTCAGGCATGGTCAGTTGTTGGTACAATTAAAGACCTGAAA
CAGGGTTATCTGAGCCAGGTTATTCATGAAATTGTGGATCTGATGATTCACTATCAGGCCGTTGTTGTGCTGG
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GCACTTTAAAATGAATCGCAATCTGAGTTTTCAGCGTGGCCTGCCTGGTTTTATGCCTGCATGGGATATTGTGT
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ATACCATGGTTGCACTGATTCGTAGCGTTCTGCAGATGCGTAATAGCAATGCAGCAACCGGTGAAGATTACAT
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GCAGATGCAAATGGTGCATATCATATTGCACTGAAAGGACAGCTGCTGCTGAACCACCTGAAAGAAAGCAAA
GATCTGAAACTGCAAAACGGCATTAGCAATCAGGATTGGCTGGCATATATCCAAGAACTGCGTAACGGTCGT
AAACGTACCGCAGATGGTAGCGAATTTGAAAGCCCGAAAAAAAAGCGTAAGGTGGAAGGTGGTAGCGGTGG
TTCAGGTGGTAGTGGCGGTAGTGGTGGCTCAGGGGGTTCTGGTGGCTCTGGTGGTAGCCTCGAGCACCACCA
CCACCACCACTGA

[0117] SEQ ID NO.: 16

[0118] ATGACCCAGTTTGAAGGTTTCACCAATCTGTATCAGGTTAGCAAAACCCTGCGTTTTGAACT
GATTCCGCAGGGTAAAACCCTGAAACATATTCAAGAACAGGGCTTCATCGAAGAGGATAAAGCACGTAACGA
TCACTACAAAGAACTGAAACCGATTATCGACCGCATCTATAAAACCTATGCAGATCAGTGTCTGCAGCTGGTT
CAGCTGGATTGGGAAAATCTGAGCGCAGCAATTGATAGTTATCGCAAAGAAAAAACCGAAGAAACCCGTAAT
GCACTGATTGAAGAACAGGCAACCTATCGTAATGCCATCCATGATTATTTCATTGGTCGTACCGATAATCTGAC
CGATGCAATTAACAAACGTCACGCCGAAATCTATAAAGGCCTGTTTAAAGCCGAACTGTTTAATGGCAAAGTT
CTGAAACAGCTGGGCACCGTTACCACCACCGAACATGAAAATGCACTGCTGCGTAGCTTTGATAAATTCACCA
CCTATTTCAGCGGCTTTTATGAGAATCGCAAAAACGTGTTTAGCGCAGAAGATATTAGCACCGCAATTCCGCA
TCGTATTGTGCAGGATAATTTCCCGAAATTCAAAGAGAACTGCCACATTTTTACCCGTCTGATTACCGCAGTTC
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TGAAAGAACATCCAGAAACGCCGATTATTGGTATTGATCGTGGTGAACGTAACCTGATTTATATCACCGTTATT
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AATGCTGATTGACAAACTGAATTGCCTGGTGCTGAAAGATTATCCGGCTGAAAAAGTTGGTGGTGTTCTGAAT
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CATGAAAGCCGCAAACATTTTCTGGAAGGTTTCGATTTTCTGCATTACGACGTTAAAACGGGTGATTTCATCCT
GCACTTTAAAATGAATCGCAATCTGAGTTTTCAGCGTGGCCTGCCTGGTTTTATGCCTGCATGGGATATTGTGT
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GATCTGAAACTGCAAAACGGCATTAGCAATCAGGATTGGCTGGCATATATCCAAGAACTGCGTAACGGTCGT
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TAGCGGCGGTAGTAAACGTACCGCAGATGGTAGCGAATTTGAAAGCCCGAAAAAAAAGCGTAAGGTGGAAG
GTGGTAGCGGTGGTTCAGGTGGTAGTGGCGGTAGTGGTGGCTCAGGGGGTTCTGGTGGCTCTGGTGGTAGC
CTCGAGCACCACCACCACCACCACTGA

[0119] SEQ ID NO.: 17

[0120] ATGACCCAGTTTGAAGGTTTCACCAATCTGTATCAGGTTAGCAAAACCCTGCGTTTTGAACT
GATTCCGCAGGGTAAAACCCTGAAACATATTCAAGAACAGGGCTTCATCGAAGAGGATAAAGCACGTAACGA
TCACTACAAAGAACTGAAACCGATTATCGACCGCATCTATAAAACCTATGCAGATCAGTGTCTGCAGCTGGTT
CAGCTGGATTGGGAAAATCTGAGCGCAGCAATTGATAGTTATCGCAAAGAAAAAACCGAAGAAACCCGTAAT
GCACTGATTGAAGAACAGGCAACCTATCGTAATGCCATCCATGATTATTTCATTGGTCGTACCGATAATCTGAC
CGATGCAATTAACAAACGTCACGCCGAAATCTATAAAGGCCTGTTTAAAGCCGAACTGTTTAATGGCAAAGTT
CTGAAACAGCTGGGCACCGTTACCACCACCGAACATGAAAATGCACTGCTGCGTAGCTTTGATAAATTCACCA
CCTATTTCAGCGGCTTTTATGAGAATCGCAAAAACGTGTTTAGCGCAGAAGATATTAGCACCGCAATTCCGCA
TCGTATTGTGCAGGATAATTTCCCGAAATTCAAAGAGAACTGCCACATTTTTACCCGTCTGATTACCGCAGTTC
CGAGCCTGCGTGAACATTTTGAAAACGTTAAAAAAGCCATCGGCATCTTTGTTAGCACCAGCATTGAAGAAGT
TTTTAGCTTCCCGTTTTACAATCAGCTGCTGACCCAGACCCAGATTGATCTGTATAACCAACTGCTGGGTGGTA
TTAGCCGTGAAGCAGGCACCGAAAAAATCAAAGGTCTGAATGAAGTGCTGAATCTGGCCATTCAGAAAAATG
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AATACCCTGAGCTTTATTCTGGAAGAATTCAAATCCGATGAAGAGGTGATTCAGAGCTTTTGCAAATACAAAA
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CCACATCTTTATCAGCCACAAAAAACTGGAAACCATTTCAAGCGCACTGTGTGATCATTGGGATACCCTGCGTA
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GCAATAACTTTATTGAACCGCTGGAAATCACCAAAGAGATCTACGATCTGAATAACCCGGAAAAAGAGCCGA
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CGAATGTTATTACCAAAGAAGTTAGCCACGAGATCATTAAAGATCGTCGTTTTACCAGCGACAAATTCTTTTTT
CATGTGCCGATTACCCTGAATTATCAGGCAGCAAATAGCCCGAGCAAATTTAACCAGCGTGTTAATGCATATC
TGAAAGAACATCCAGAAACGCCGATTATTGGTATTGATCGTGGTGAACGTAACCTGATTTATATCACCGTTATT
GATAGCACCGGCAAAATCCTGGAACAGCGTAGCCTGAATACCATTCAGCAGTTTGATTACCAGAAAAAACTG
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CAGGGTTATCTGAGCCAGGTTATTCATGAAATTGTGGATCTGATGATTCACTATCAGGCCGTTGTTGTGCTGG
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GCACTTTAAAATGAATCGCAATCTGAGTTTTCAGCGTGGCCTGCCTGGTTTTATGCCTGCATGGGATATTGTGT
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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 ºC. 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**	tacagcgtggaaaagtttaagNNKaacttccagatgcccaccctg
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**	catgcctaagcagaagggcNNKtacaaggccctgtcctttg
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**	ctgtcctttgagcccaccNNKaagaccagcgagggcttt
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**	gtactacgattacttccccNNKgccgccaagatgatcccca
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**	gaccgcccactttcagNNKcacaccacccccatcc
369	**622_NNK_HsCas12a_H622**	cgcccactttcagaccNNKaccacccccatcctgc
370	**623_NNK_HsCas12a_T623**	cccactttcagacccacNNKaccccatcctgctgag
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**	cctgctgagcaacaacttcNNKgagcccctggaaatcacca
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

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AACATCCAGAAACGCCGATTATTGGTATTGATCGTGGTGAACGTAACCTGATTTATATCACCGTTATTGATAGC

ACCGGCAAAATCCTGGAACAGCGTAGCCTGAATACCATTCAGCAGTTTGATTACCAGAAAAAACTGGATAATC

GCGAGAAAGAACGTGTTGCAGCACGTCAGGCATGGTCAGTTGTTGGTACAATTAAAGACCTGAAACAGGGTT

ATCTGAGCCAGGTTATTCATGAAATTGTGGATCTGATGATTCACTATCAGGCCGTTGTTGTGCTGGAAAACCT

GAATTTTGGCTTTAAAAGCAAACGTACCGGCATTGCAGAAAAAGCAGTTTATCAGCAGTTCGAGAAAATGCTG

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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

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TTCACCCGTGATTTTCTGAGCAAATACACCAAAACCACCAGTATCGATCTGAGCAGCCTGCGTCCGAGCAGCC

AGTATAAAGATCTGGGCGAATATTATGCAGAACTGAATCCGCTGCTGTATCATATTAGCTTTCAGCGTATTGCC

GAGAAAGAAATCATGGACGCAGTTGAAACCGGTAAACTGTACCTGTTCCAGATCTACAATAAAGATTTTGCCA

AAGGCCATCATGGCAAACCGAATCTGCATACCCTGTATTGGACCGGTCTGTTTAGCCCTGAAAATCTGGCAAA

AACCTCGATTAAACTGAATGGTCAGGCGGAACTGTTTTATCGTCCGAAAAGCCGTATGAAACGTATGGCACAT

CGTCTGGGTGAAAAAATGCTGAACAAAAAACTGAAAGACCAGAAAACCCCGATCCCGGATACACTGTATCAA

GAACTGTATGATTATGTGAACCATCGTCTGAGCCATGATCTGAGTGATGAAGCACGTGCCCTGCTGCCGAATG

TTATTACCAAAGAAGTTAGCCACGAGATCATTAAAGATCGTCGTTTTACCAGCGACAAATTCCTGTTTCATGTG

CCGATTACCCTGAATTATCAGGCAGCAAATAGCCCGAGCAAATTTAACCAGCGTGTTAATGCATATCTGAAAG

AACATCCAGAAACGCCGATTATTGGTATTGATCGTGGTGAACGTAACCTGATTTATATCACCGTTATTGATAGC

ACCGGCAAAATCCTGGAACAGCGTAGCCTGAATACCATTCAGCAGTTTGATTACCAGAAAAAACTGGATAATC

GCGAGAAAGAACGTGTTGCAGCACGTCAGGCATGGTCAGTTGTTGGTACAATTAAAGACCTGAAACAGGGTT

ATCTGAGCCAGGTTATTCATGAAATTGTGGATCTGATGATTCACTATCAGGCCGTTGTTGTGCTGGAAAACCT

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AGCTGACCGATCAGTTTACCAGCTTTGCAAAAATGGGCACCCAGAGCGGATTTCTGTTTTATGTTCCGGCACC

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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
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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
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AGCTGGATTGGGAAAATCTGAGCGCAGCAATTGATAGTTATCGCAAAGAAAAAACCGAAGAAACCCGTAATG
CACTGATTGAAGAACAGGCAACCTATCGTAATGCCATCCATGATTATTTCATTGGTCGTACCGATAATCTGACC
GATGCAATTAACAAACGTCACGCCGAAATCTATAAAGGCCTGTTTAAAGCCGAACTGTTTAATGGCAAAGTTC
TGAAACAGCTGGGCACCGTTACCACCACCGAACATGAAAATGCACTGCTGCGTAGCTTTGATAAATTCACCAC
CTATTTCAGCGGCTTTTATGAGAATCGCAAAAACGTGTTTAGCGCAGAAGATATTAGCACCGCAATTCCGCAT
CGTATTGTGCAGGATAATTTCCCGAAATTCAAAGAGAACTGCCACATTTTTACCCGTCTGATTACCGCAGTTCC
GAGCCTGCGTGAACATTTTGAAAACGTTAAAAAAGCCATCGGCATCTTTGTTAGCACCAGCATTGAAGAAGTT
TTTAGCTTCCCGTTTTACAATCAGCTGCTGACCCAGACCCAGATTGATCTGTATAACCAACTGCTGGGTGGTAT
TAGCCGTGAAGCAGGCACCGAAAAAATCAAAGGTCTGAATGAAGTGCTGAATCTGGCCATTCAGAAAAATGA
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ATACCCTGAGCTTTATTCTGGAAGAATTCAAATCCGATGAAGAGGTGATTCAGAGCTTTTGCAAATACAAAAC
GCTGCTGCGCAATGAAAATGTTCTGGAAACTGCCGAAGCACTGTTTAACGAACTGAATAGCATTGATCTGACC
CACATCTTTATCAGCCACAAAAAACTGGAAACCATTTCAAGCGCACTGTGTGATCATTGGGATACCCTGCGTA
ATGCCCTGTATGAACGTCGTATTAGCGAACTGACCGGTAAAATTACCAAAAGCGCGAAAGAAAAAGTTCAGC
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TTAAACAGAAAACCAGCGAAATTCTGTCACATGCACATGCAGCACTGGATCAGCCGCTGCCGACCACCCTGAA
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GGAACCGAGCCTGAGCTTTTATAACAAAGCCCGTAATTATGCCACCAAAAAACCGTATAGCGTCGAAAAATTC
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CTGTTCGTGAAAAATGGCCTGTATTATCTGGGTATTATGCCGAAACAGAAAGGTCGTTATAAAGCGCTGAGCT
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GATTCCGAAATGTAGCACCCAGCTGAAAGCAGTTACCGCACATTTTCAGACCCATACCACCCCGATTCTGCTGA
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TGCCAAAGGCCATCATGGCAAACCGAATCTGCATACCCTGTATTGGACCGGTCTGTTTAGCCCTGAAAATCTG
GCAAAAACCTCGATTAAACTGAATGGTCAGGCGGAACTGTTTTATCGTCCGAAAAGCCGTATGAAACGTATG
GCACATCGTCTGGGTGAAAAAATGCTGAACAAAAAACTGAAAGACCAGAAAACCCCGATCCCGGATACACTG
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CGAATGTTATTACCAAAGAAGTTAGCCACGAGATCATTAAAGATCGTCGTTTTACCAGCGACAAATTCCTGTTT
CATGTGCCGATTACCCTGAATTATCAGGCAGCAAATAGCCCGAGCAAATTTAACCAGCGTGTTAATGCATATC
TGAAAGAACATCCAGAAACGCCGATTATTGGTATTGATCGTGGTGAACGTAACCTGATTTATATCACCGTTATT
GATAGCACCGGCAAAATCCTGGAACAGCGTAGCCTGAATACCATTCAGCAGTTTGATTACCAGAAAAAACTG
GATAATCGCGAGAAAGAACGTGTTGCAGCACGTCAGGCATGGTCAGTTGTTGGTACAATTAAAGACCTGAAA
CAGGGTTATCTGAGCCAGGTTATTCATGAAATTGTGGATCTGATGATTCACTATCAGGCCGTTGTTGTGCTGG
AAAACCTGAATTTTGGCTTTAAAAGCAAACGTACCGGCATTGCAGAAAAAGCAGTTTATCAGCAGTTCGAGAA
AATGCTGATTGACAAACTGAATTGCCTGGTGCTGAAAGATTATCCGGCTGAAAAAGTTGGTGGTGTTCTGAAT
CCGTATCAGCTGACCGATCAGTTTACCAGCTTTGCAAAAATGGGCACCCAGAGCGGATTTCTGTTTTATGTTCC
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CATGAAAGCCGCAAACATTTTCTGGAAGGTTTCGATTTTCTGCATTACGACGTTAAAACGGGTGATTTCATCCT
GCACTTTAAAATGAATCGCAATCTGAGTTTTCAGCGTGGCCTGCCTGGTTTTATGCCTGCATGGGATATTGTGT
TTGAGAAAAACGAAACACAGTTCGATGCAAAAGGCACCCCGTTTATTGCAGGTAAACGTATTGTTCCGGTGAT
TGAAAATCATCGTTTCACCGGTCGTTATCGCGATCTGTATCCGGCAAATGAACTGATCGCACTGCTGGAAGAG
AAAGGTATTGTTTTTCGTGATGGCTCAAACATTCTGCCGAAACTGCTGGAAAATGATGATAGCCATGCAATTG
ATACCATGGTTGCACTGATTCGTAGCGTTCTGCAGATGCGTAATAGCAATGCAGCAACCGGTGAAGATTACAT
TAATAGTCCGGTTCGTGATCTGAATGGTGTTTGTTTTGATAGCCGTTTTCAGAATCCGGAATGGCCGATGGAT
GCAGATGCAAATGGTGCATATCATATTGCACTGAAAGGACAGCTGCTGCTGAACCACCTGAAAGAAAGCAAA
GATCTGAAACTGCAAAACGGCATTAGCAATCAGGATTGGCTGGCATATATCCAAGAACTGCGTAAC

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

[0184] atgACCCAGTTTGAAGGTTTCACCAATCTGTATCAGGTTAGCAAAACCCTGCGTTTTGAACTG
ATTCCGCAGGGTAAAACCCTGAAACATATTCAAGAACAGGGCTTCATCGAAGAGGATAAAGCACGTAACGAT
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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
LDSLLGLYHLLDWFAVDESNEVDPEFSARLTGIKLEMEPSLSFYNKARNYATKKPYSVEKFKLNFQ<u>R</u>PTLASGWDVN
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
GATCTGAAACTGCAAAACGGCATTAGCAATCAGGATTGGCTGGCATATATCCAAGAACTGCGTAACGGTCGT
AGCAGTGATGATGAAGCAACCGCAGATAGCCAGCATGCAGCACCGCCTAAAAAGAAACGTAAAGTTGGTGG
TAGCGGTGGTTCAGGTGGTAGTGGCGGTAGTGGTGGCTCAGGGGGTTCTGGTGGCTCTGGTGGTAGCctcgag
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
GATCTGAAACTGCAAAACGGCATTAGCAATCAGGATTGGCTGGCATATATCCAAGAACTGCGTAACGGTCGT

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>GRS</u><u>SDDEATADSQ</u>
<u>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:**

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[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

1. A CRISPR-associated protein comprising a variant of a Cas12a, wherein the variant of the Cas12a comprises an amino acid sequence selected from the group consisting of SEQ ID NOs.: 472, 473 and 465.

2. The CRISPR-associated protein according to claim 1, wherein the varianSSt of Cas12a consists of SEQ ID NO.: 472.

3. The CRISPR-associated protein according to claim 1, wherein the variant of Cas12a consists of SEQ ID NO.: 473.

4. The CRISPR-associated protein according to claim 1, wherein the variant of Cas12a consists of SEQ ID NO.: 465.

5. A CRISPR ribonucleoprotein complex, comprising:
a guide RNA; and
a CRISPR-associated protein comprising a variant of a Cas12a, wherein the variant of the Cas12a comprises an amino acid sequence selected from the group consisting of SEQ ID NOs.: 472, 473 and 465.

6. The CRISPR ribonucleoprotein complex of claim 5, wherein the variant of the Cas12a consists of SEQ ID NO.: 472.

7. The CRISPR ribonucleoprotein complex of claim 5, wherein the variant of the Cas12a consists of SEQ ID NO.: 473.

8. The CRISPR ribonucleoprotein complex of claim 5, wherein the variant of the Cas12a consists of SEQ ID NO.: 465.

9. A CRISPR-associated protein comprising a variant of the Cas12a of SEQ ID NO: 462, wherein the variant of the Cas12a comprises an amino acid sequence selected from the group consisting of SEQ ID NOs.: 59-245.

10. A Cas12a polypeptide comprising an amino acid sequence selected from the group consisting of SEQ ID NO:18-22 and 24-30.

11. A CRISPR-associated protein comprising a fusion polypeptide comprising a Cas12a protein, a nuclear localization signal, optionally an amino acid linker and optionally an affinity tag, wherein the Cas12a protein comprises an amino acid sequence selected from the group consisting of SEQ ID NOs.: 59-245 and wherein the nuclear localization signal comprises an amino acid sequence selected from SEQ ID NOs.: 475, 477, 479, 481 and 483.

12. A CRISPR-associated protein, wherein the CRISPR-associated protein is encoded by a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 489 and 491.

13. A CRISPR-associated protein, wherein the CRISPR-associated protein comprises SEQ ID NO. 493.