VARIANTES DE ALFA-AMILASA Y POLINUCLEÓTIDOS QUE CODIFICAN LAS MISMAS

Referencia a un listado de secuencias

Esta solicitud contiene un Listado de Secuencias en forma legible por ordenador, que se incorpora en esta memoria como referencia.

ANTECEDENTES DE LA INVENCIÓN

Campo de la invención

La presente invención se refiere a variantes de alfa amilasa, a polinucleótidos que codifican las variantes, a métodos para producir las variantes y a métodos de uso de las variantes.

Descripción de la técnica relacionada

Las alfa-amilasas se han usado durante muchos años en el lavado de ropa, donde es de sobra conocido que las alfa-amilasas tienen un efecto beneficioso en la retirada de manchas que contienen o a base de almidón.

El documento WO95/26397 divulga amilasas alcalinas de *Bacillus* que tienen un buen rendimiento de lavado medido a temperaturas en el intervalo de 30-60°C.

Los documentos WO00/60060 y WO00/60058 divulgan alfa-amilasas bacterianas adicionales que tienen un buen rendimiento de lavado.

En los últimos años se ha deseado reducir la temperatura del lavado de ropa para reducir el consumo de energía. Una reducción de la temperatura de lavado normalmente tiene como consecuencia una reducción en el rendimiento de la composición detergente y de la enzima y por lo tanto, se obtiene un menor rendimiento de lavado a baja temperatura. Por lo tanto, se desea encontrar nuevas alfa-amilasas que tengan buen rendimiento de lavado a baja temperatura. Por consiguiente, un objeto de la presente invención es proporcionar alfa-amilasas que tengan buen

rendimiento de lavado a baja temperatura, tal como a 15°C. Por lo tanto, la presente invención proporciona dichas variantes de alfa-amilasa mejoradas adicionalmente con propiedades mejoradas en comparación con las parentales.

COMPENDIO DE LA INVENCIÓN

La presente invención se refiere a una variante de alfa-amilasa de un polipéptido parental que tiene actividad alfa-amilasa, en donde la variante es un polipéptido de fusión que tiene un rendimiento de lavado mejorado a baja temperatura y en donde dicha variante tiene actividad alfa-amilasa.

La presente invención también se refiere a polinucleótidos que codifican las variantes; a construcciones de ácido nucleico, vectores y células hospedadoras que comprenden los polinucleótidos; y a métodos para producir las variantes.

La presente invención también se refiere a métodos para mejorar el rendimiento de lavado de una alfa-amilasa parental.

Convenciones para designar las variantes

A efectos de la presente invención, el polipéptido maduro que se describe en la SEQ ID NO: 7 se utiliza para determinar el resto de aminoácido correspondiente en otra alfa-amilasa. Como alternativa, el polipéptido maduro divulgado en las SEQ ID NO: 13 y 14 puede usarse para determinar el resto de aminoácido correspondiente en otra alfa-amilasa. La secuencia de aminoácidos de otra alfa-amilasa se alinea con el polipéptido maduro que se describe en la SEQ ID NO: 7 y basándose en el alineamiento, el número de posición de aminoácido correspondiente a cualquier resto de aminoácido en el polipéptido maduro divulgado en cualquiera de las SEQ ID NO: 13 y 14 se determina utilizando el algoritmo de Needleman-Wunsch

(Needleman y Wunsch, 1970, *J. Mol. Biol.* 48: 443-453) según se implementa en el programa Needle del paquete EMBOSS (EMBOSS: The European Molecular Biology Open Software Suite, Rice *et al.*, 2000, *Trends Genet.* 16: 276-277), preferentemente la versión 5.0.0 o versiones posteriores. Los parámetros usados son penalización por apertura de hueco de 10, penalización por extensión de hueco de 0.5, y la matriz de sustitución EBLOSUM62 (versión EMBOSS de BLOSUM62).

La identificación del resto de aminoácido correspondiente en otra alfa-amilasa puede determinarse mediante una alineación de múltiples secuencias de polipéptidos utilizando varios programas informáticos incluido, a modo no taxativo, MUSCLE (comparación de múltiples secuencias por expectativa logarítmica; versión 3.5 o versiones posteriores; Edgar, 2004, *Nucleic Acids Research* 32: 1792-1797), MAFFT (versión 6.857 o versiones posteriores; Katoh y Kuma, 2002, *Nucleic Acids Research* 30: 3059-3066; Katoh *et al.*, 2005, *Nucleic Acids Research* 33: 511-518; Katoh y Toh, 2007, *Bioinformatics* 23: 372-374; Katoh *et al.*, 2009, *Methods in Molecular Biology* 537: 39-64; Katoh y Toh, 2010, *Bioinformatics* 26: 1899-1900) y EMBOSS EMMA empleando ClustalW (1.83 o posterior; Thompson *et al.*, 1994, *Nucleic Acids Research* 22: 4673-4680), utilizando sus parámetros predeterminados respectivos.

Cuando la otra enzima difiere del polipéptido maduro de la SEQ ID NO: 7 de manera que la comparación tradicional basada en la secuencia fracasa en detectar su relación (Lindahl y Elofsson, 2000, *J. Mol. Biol.* 295: 613-615), se pueden utilizar otros algoritmos de comparación de secuencias por pares. Puede obtenerse una mayor sensibilidad en la búsqueda basada en secuencias utilizando programas de búsqueda que empleen representaciones

probabilísticas de familias de polipéptidos (perfiles) para realizar búsquedas en bases de datos. Por ejemplo, el programa PSI-BLAST genera perfiles a través de un proceso de búsqueda de base de datos iterativo y es capaz de detectar homólogos remotos (Atschul *et al.*, 1997, *Nucleic Acids Res.* 25: 3389-3402). Puede obtenerse una sensibilidad incluso mayor si la familia o superfamilia para el polipéptido tiene uno o más representantes en las bases de datos de estructuras proteicas. Algunos programas tales como GenTHREADER (Jones, 1999, *J. Mol. Biol.* 287: 797-815; McGuffin y Jones, 2003, *Bioinformatics* 19: 874-881) utilizan información de varias fuentes (PSI-BLAST, predicción de estructura secundaria, perfiles de alineación estructurales y potenciales de solvatación) como entrada para una red neural que predice el plegamiento estructural para una secuencia problema. De manera similar, el método de Gough *et al.*, 2000, *J. Mol. Biol.* 313: 903-919 se puede utilizar para alinear una secuencia de estructura desconocida con los modelos de superfamilias presentes en la base de datos SCOP. A su vez, pueden utilizarse estos alineamientos para generar modelos de homología para el polipéptido y pueden evaluarse dichos modelos para determinar su precisión usando una diversidad de herramientas desarrolladas para ese fin.

Para proteínas de estructura conocida, se dispone de varias herramientas y recursos para recuperar y generar alineaciones estructurales. Por ejemplo, las superfamilias SCOP de proteínas se han alineadas estructuralmente, y estas alineaciones son accesibles y pueden descargarse. Dos o más estructuras proteicas pueden alinearse utilizando una variedad de algoritmos tales como la matriz de alineación de distancias (Holm y Sander, 1998, *Proteins* 33: 88-96) o la extensión combinatoria (Shindyalov y Bourne, 1998,

Protein Engineering 11: 739-747), y se puede utilizar adicionalmente la implementación de estos algoritmos para consultar bases de datos de estructuras con una estructura de interés con el fin de descubrir posibles homólogos estructurales (por ejemplo, Holm y Park, 2000, *Bioinformatics* 16: 566-567).

A la hora de describir las variantes de la presente invención, la nomenclatura que se describe a continuación se adapta para facilitar su referencia. Se emplea la abreviación de los aminoácidos de tres letras o de una única letra aceptada por la IUPAC.

Sustituciones: Para la sustitución de un aminoácido, se utiliza la siguiente nomenclatura: aminoácido original, posición, aminoácido sustituido. Por lo tanto, la sustitución de la treonina en la posición 226 con alanina se designa como "Thr226Ala" o "T226A". Las múltiples mutaciones están separadas por el signo de suma ("+"), por ejemplo, "Gly205Arg + Ser411Phe" o "G205R + S411F", que representan sustituciones en posiciones 205 y 411 de glicina (G), con arginina (R) y serina (S) con fenilalanina (F), respectivamente.

Eliminaciones: Para la eliminación de un aminoácido, se utiliza la siguiente nomenclatura: aminoácido original, posición, *. Por lo tanto, la eliminación de glicina en la posición 195 se designa como "Gly195*" o "G195*". Las múltiples eliminaciones se separan por el símbolo de suma ("+"), por ejemplo, "Gly195* + Ser411*" o "G195* + S411*".

Múltiples modificaciones: Las variantes que comprenden múltiples modificaciones están separadas por el signo de suma ("+"), por ejemplo, "Arg170Tyr+Gly195Glu" o "R170Y+G195E" representando una sustitución de arginina y glicina en posiciones 170 y 195 con tirosina y ácido glutámico, respectivamente.

Diferentes modificaciones: En los casos en los que pueden introducirse diferentes modificaciones en una posición, las diferentes alteraciones están separadas por una coma, por ejemplo, "Arg170Tyr,Glu" representando una sustitución de arginina en la posición 170 con tirosina y ácido glutámico. Por lo tanto, "Tyr167Gly,Ala+Arg170Gly,Ala" designa las siguientes variantes:

"Tyr167Gly+Arg170Gly", "Tyr167Gly+Arg170Ala", "Tyr167Ala+Arg170Gly", y "Tyr167Ala+Arg170Ala".

DESCRIPCIÓN DETALLADA DE LA INVENCIÓN

La presente invención se refiere a un conjunto de secuencias. Por comodidad, estas se listan a continuación;

SEQ ID NO: 1 es la secuencia de nucleótidos de una alfa-amilasa (AAI10)

SEQ ID NO: 2 es la secuencia de nucleótidos de una alfa-amilasa cuyo origen es de *Alicyclobacillus sp.*

SEQ ID NO: 3 es la secuencia de nucleótidos de una alfa-amilasa cuyo origen es de *Bacillus amyloliquefaciens.*

SEQ ID NO: 4 es la secuencia de aminoácidos de AAI10, que incluye el péptido de señal.

SEQ ID NO: 5 es la secuencia de aminoácidos de *Alicyclobacillus sp.*, que incluye el péptido de señal.

SEQ ID NO: 6 es la secuencia de aminoácidos de *Bacillus amyloliquefaciens*, que incluye el péptido de señal.

SEQ ID NO: 7 es la secuencia de aminoácidos de la AAI10 madura

SEQ ID NO: 8 es la secuencia de aminoácidos madura de *Alicyclobacillus sp*.

SEQ ID NO: 9 es la secuencia de aminoácidos madura de *Bacillus amyloliquefaciens*

SEQ ID NO: 10 es la secuencia de aminoácidos correspondiente a los dominios A y B de AAI10.

SEQ ID NO: 11 es la secuencia de aminoácidos correspondiente al dominio C de *Alicyclobacillus sp*.

SEQ ID NO: 12 es la secuencia de aminoácidos correspondiente al dominio C de *Bacillus amyloliquefaciens*

SEQ ID NO: 13 es la secuencia de aminoácidos del polipéptido de fusión que consiste en el dominio A y B de AAI10 y el dominio C de *Alicyclobacillus sp.*

SEQ ID NO: 14 es la secuencia de aminoácidos del polipéptido de fusión que consiste en los dominios A y B de AAI10 y el dominio C de *Bacillus amyloliquefaciens*

SEQ ID NO: 15 es la secuencia de aminoácidos de la alfa-amilasa AAI10 madura que comprende una doble eliminación en las posiciones correspondientes a las posiciones 182 y 183 de SEQ ID NO: 7

Variantes de la invención

En un aspecto, la presente invención se refiere a variantes de un polipéptido parental que tiene actividad alfa-amilasa. Por lo tanto, en un aspecto particular, la presente invención se refiere a una variante de un polipéptido parental que tiene actividad alfa-amilasa, en donde dicha variante es un polipéptido de fusión que tiene un rendimiento de lavado mejorado a baja temperatura y en donde dicha variante tiene actividad alfa-amilasa.

Se ha demostrado que las variantes de acuerdo con la presente invención tienen un rendimiento mejorado, tal como rendimiento de lavado, a baja temperatura, en particular a 15°C, en composiciones de detergente líquidas.

El término "variante", tal como se usa en el presente documento, se refiere a un polipéptido que tiene actividad alfa-amilasa que comprende una alteración, es decir, una sustitución, inserción y/o eliminación en una o más

posiciones (por ejemplo, varias). Una sustitución significa un reemplazo del aminoácido que ocupa una posición por un aminoácido diferente; una eliminación significa la retirada del aminoácido que ocupa una posición; y una inserción significa añadir un aminoácido adyacente a e inmediatamente después del aminoácido que ocupa una posición, todos como se han definido anteriormente. Las variantes de la presente invención tienen al menos un 20%, por ejemplo, al menos un 40%, al menos un 50%, al menos un 60%, al menos un 70%, al menos un 80%, al menos un 90%, al menos un 95% o al menos un 100% de la actividad alfa-amilasa del polipéptido de las SEQ ID NO: 7, 13, 14, 15 o el polipéptido maduro de SEQ ID NO: 4. Las variantes de la presente invención tienen al menos un 65%, tal como al menos un 70%, tal como al menos un 75%, tal como al menos un 80%, tal como al menos un 85%, tal como al menos un 90%, tal como al menos un 95%, tal como al menos un 97%, tal como al menos un 99% pero menos de un 100% de identidad de secuencia con una cualquiera de las SEQ ID NO: 4, 7, 13, 14 o 15

La expresión "polipéptido parental", tal como se usa en el presente documento, se refiere a un polipéptido en el que se efectúa una alteración para producir variantes de enzimas. El polipéptido que tiene cualquiera de las SEQ ID NO: 4, 7, 13, 14 y 15 puede ser, por ejemplo, un progenitor para las variantes de la presente invención. Cualquier polipéptido que tenga al menos un 65%, tal como al menos un 70%, tal como al menos un 75%, tal como al menos un 80%, tal como al menos un 85%, tal como al menos un 90%, tal como al menos un 95%, tal como al menos un 97%, tal como al menos un 99% de identidad de secuencia con una cualquiera de las SEQ ID NO: 4, 7, 13, 14 o 15 también puede ser un polipéptido parental para las variantes de la presente invención.

El polipéptido parental puede ser un polipéptido de fusión o un polipéptido de fusión escindible. Dicho polipéptido de fusión puede consistir en una subsecuencia de un polipéptido parental y una subsecuencia de un segundo polipéptido parental. En particular, un polipéptido de fusión puede consistir en un dominio A y B de una especie de alfa-amilasa y un dominio C de otra especie de alfa-amilasa y de este modo, proporciona un polipéptido parental para generar una variante de la presente invención. Las técnicas para producir polipéptidos de fusión son de uso común en la técnica e incluyen ligar las secuencias codificantes que codifican los polipéptidos de modo que estén en fase y que la expresión del polipéptido de fusión esté controlada por el mismo promotor o promotores y el mismo terminador. Los polipéptidos de fusión también se pueden construir utilizando la tecnología de inteínas en la cual los polipéptidos de fusión se crean después de la traducción (Cooper *et al.*, 1993, *EMBO J.* 12: 2575-2583; Dawson *et al.*, 1994, *Science* 266: 776-779).

Un polipéptido de fusión puede comprender además un sitio de escisión entre los dos polipéptidos. Al secretar la proteína de fusión, el sitio se escinde y se liberan los dos polipéptidos. Los ejemplos de sitios de escisión incluyen, sin carácter limitante, los sitios descritos en Martin *et al.*, 2003, *J. Ind. Microbiol. Biotechnol.* 3: 568-576; Svetina *et al.*, 2000, *J. Biotechnol.* 76: 245-251; Rasmussen-Wilson *et al.*, 1997, *Appl. Environ. Microbiol.* 63: 3488-3493; Ward *et al.*, 1995, *Biotechnology* 13: 498-503; Contreras *et al.*, 1991, *Biotechnology* 9: 378-381; Eaton *et al.*, 1986, *Biochemistry* 25: 505-512; Collins-Racie *et al.*, 1995, *Biotechnology* 13: 982-987; Carter *et al.*, 1989, *Proteins: Structure, Function, and Genetics* 6: 240-248; y Stevens, 2003, *Drug Discovery World* 4: 35-48.

El polipéptido parental puede obtenerse de microorganismos de cualquier género. Para los fines de la presente invención, la expresión "obtenido de", tal como se usa en el presente documento en conexión con una fuente dada significará que el polipéptido parental codificado por un polinucleótido se produce por la fuente o por una cepa en la que se ha insertado el polinucleótido de la fuente.

En algunos aspectos de la presente invención, el polipéptido parental es alfa-amilasa de *Bacillus* sp., por ejemplo, la alfa-amilasa de la SEQ ID NO: 4, el polipéptido maduro del mismo, es decir, la SEQ ID NO: 7. En aspectos particulares, el polipéptido parental es una proteína de fusión y tiene como origen tanto *Bacillus* sp como *Alicyclobacillus* sp., por ejemplo, la alfa-amilasa de SEQ ID NO: 13. En otros aspectos, el polipéptido parental es una proteína de fusión y se origina a partir de dos especies de *Bacillus* diferentes, dando como resultado, por ejemplo, la alfa-amilasa de SEQ ID NO: 14.

Se entenderá que para las especies mencionadas anteriormente, la invención abarca tanto los estados perfectos como los imperfectos y otros equivalentes taxonómicos, por ejemplo, anamorfos, independientemente del nombre de la especie con el que se los conoce. Los expertos en la técnica reconocerán fácilmente la identidad de los equivalentes apropiados.

Las cepas de estas especies son fácilmente accesibles para el público en una serie de colecciones de cultivos, tales como la *American Type Culture Collection* (ATCC), *Deutsche Sammlung von Mikroorganismen und Zellkulturen GmbH* (DSMZ), *Centraalbureau Voor Schimmelcultures* (CBS) y *Agricultural Research Service Patent Culture Collection, Northern Regional Research Center* (NRRL).

El polipéptido parental puede identificarse y obtenerse a partir de otras fuentes, que incluyen microorganismos aislados de la naturaleza (por ejemplo, suelo, compost, agua, etc.) o muestras de ADN obtenidas directamente a partir de materiales naturales (por ejemplo, suelo, compost, agua, etc.) utilizando las sondas mencionadas anteriormente. Se conocen bien en la técnica las técnicas para aislar microorganismos y ADN directamente a partir de hábitats naturales. A continuación, puede obtenerse un polinucleótido que codifica un polipéptido parental explorando de manera similar una biblioteca de ADN genómico o de ADNc de otro microorganismo o muestra de ADN mixto. Una vez que se ha detectado un polinucleótido que codifica un polipéptido parental con la(s) sonda(s), el polinucleótido puede aislarse o clonarse utilizando técnicas que se conocen por los expertos habituales en la técnica (véase, por ejemplo, Sambrook *et al.*, 1989, mencionado anteriormente).

En una realización, el polipéptido parental comprende o consiste en la secuencia de aminoácidos expuesta en las SEQ ID NO: 7, 13 o 15. En otra realización, el polipéptido parental comprende o consiste en el polipéptido maduro de la SEQ ID NO: 4. En particular, el polipéptido parental puede comprender o consistir en los aminoácidos 1 a 485 de la SEQ ID NO: 4.

En otra realización, el polipéptido parental es un fragmento del polipéptido maduro de la SEQ ID NO: 4 que contiene al menos 350, tal como al menos 390 restos de aminoácido, por ejemplo, al menos 395 y al menos 397 restos de aminoácido de la SEQ ID NO: 4.

En otra realización, el polipéptido parental es una variante alélica del polipéptido maduro de la SEQ ID NO: 4.

La expresión "identidad de secuencia", tal como se usa en el presente documento, se refiere al grado de relación entre dos secuencias de aminoácidos o entre dos secuencias de nucleótidos. Para los fines de la presente invención, la identidad de secuencia entre dos secuencias de aminoácidos se determina usando el algoritmo de Neddleman-Wunsch (Needleman y Wunsch, 1970, *J. Mol. Biol.* 48: 443-453) según se implementa en el programa Needle del paquete EMBOSS (EMBOSS: The European Molecular Biology Open Software Suite, Rice *et al.*, 2000, *Trends Genet.* 16: 276-277), preferentemente la versión 5.0.0 o versiones posteriores. Los parámetros usados son penalización por apertura de hueco de 10, penalización por extensión de hueco de 0.5, y la matriz de sustitución EBLOSUM62 (versión EMBOSS de BLOSUM62). El resultado de Needle marcado como “identidad más larga” (obtenido usando la opción –no corto) se usa como el porcentaje de identidad y se calcula del siguiente modo:

(Restos idénticos x 100)/(Longitud de la alineación - Número total de huecos en la alineación)

A efectos de la presente invención, la identidad de secuencia entre dos secuencias de desoxirribonucleótidos se determina utilizando el algoritmo de Needleman-Wunsch (Needleman y Wunsch, 1970, *supra*) según se implementa en el programa Needle del paquete EMBOSS (EMBOSS: The European Molecular Biology Open Software Suite”, Rice *et al.*, 2000, *supra*), preferentemente la versión 5.0.0 o versiones posteriores. Los parámetros utilizados son una penalización por la apertura de un hueco de 10, una penalización por la extensión del hueco de 0.5 y la matriz de sustitución EDNAFULL (versión EMBOSS de NCBI NUC4.4). El resultado de Needle marcado como “identidad más larga” (obtenido usando

la opción –no corto) se usa como el porcentaje de identidad y se calcula del siguiente modo:

(Desoxirribonucleótidos idénticos x 100)/(Longitud de la alineación - Número total de huecos en la alineación)

La expresión "actividad alfa-amilasa", tal como se usa en el presente documento, se refiere a la actividad de alfa-1,4-glucan-4-glucanohidrolasas, E.C. 3.2.1.1, las cuales constituyen un grupo de enzimas que catalizan la hidrólisis de almidón y otros oligo- y polisacáridos 1,4-glucosídicos lineales y ramificados. Por lo tanto, el término "alfa-amilasa", tal como se usa en el presente documento, se refiere a una enzima que tiene actividad alfa-amilasa (clase de enzima; EC 3.2.1.1) que hidroliza los enlaces alfa de polisacáridos grandes enlazados en alfa, tales como almidón y glucógeno, proporcionando glucosa y maltosa. Los términos "alfa-amilasa" y "amilasa" pueden usarse de manera indistinta y tienen el mismo significado y propósito dentro del alcance de la presente invención. A efectos de la presente invención, la actividad alfa-amilasa se determina de acuerdo con el procedimiento descrito en los ejemplos. En una realización, las variantes de la presente invención tienen al menos un 20%, por ejemplo, al menos un 40%, al menos un 50%, al menos un 60%, al menos un 70%, al menos un 80%, al menos un 90%, al menos un 95% o al menos un 100% de la actividad alfa-amilasa del polipéptido de las SEQ ID NO: 7, 13, 14 o 15; o el polipéptido maduro de SEQ ID NO: 4.

La expresión "polipéptido de fusión, tal como se usa en el presente documento, se refiere a un polipéptido que comprende secuencias de aminoácidos que tienen como origen más de una, tal como dos, tres o cuatro especies. Dicho polipéptido de fusión puede haberse generado mediante técnicas moleculares bien conocidas por un experto. Un

polipéptido de fusión de la presente invención tiene actividad alfa-amilasa. En particular, un polipéptido de fusión de la presente invención comprende, por ejemplo, un dominio A y B de una alfa-amilasa y un dominio C de otra alfa-amilasa.

La expresión "rendimiento de lavado", tal como se usa en el presente documento, se refiere a la capacidad de una enzima para eliminar almidón o manchas que contienen almidón presentes sobre el objeto que se vaya a limpiar durante, por ejemplo, el lavado de ropa o el lavado de superficies duras, tales como el lavado de vajilla. La expresión "rendimiento de lavado" incluye limpieza en general, por ejemplo, limpieza de superficies duras, tal como el lavado de vajilla, pero también rendimiento de lavado en artículos textiles, tales como lavado de ropa y también en limpieza industrial e institucional. El rendimiento de lavado puede cuantificarse calculando el denominado valor de intensidad y los resultados pueden presentarse como "factor de mejora" (IF). El rendimiento de lavado puede determinarse como se describe en los ejemplos del presente documento.

La expresión "valor de intensidad", tal como se usa en el presente documento, se refiere al rendimiento de lavado medido en forma de brillo expresado como la luz reflejada por la muestra cuando se ilumina con luz blanca. Cuando la muestra está manchada, la intensidad de la luz reflejada es menor que la de la muestra limpia. Por lo tanto, puede usarse la intensidad de la luz reflejada para medir el rendimiento de lavado, en donde un mayor valor de intensidad se correlaciona con un mayor rendimiento de lavado.

Las mediciones de color se efectúan con un escáner plano profesional (Kodak iQsmart, Kodak) usado para capturar una imagen del artículo textil lavado.

Con el fin de extraer un valor para la intensidad de la luz a partir de las imágenes escaneadas, los valores en píxeles de 24 bits de la imagen se convierten en valores para rojo, verde y azul (RBG, por sus siglas en inglés). El valor de la intensidad (Int) se calcula sumando los valores RBG como vectores y tomando a continuación la longitud del vector resultante:

$$Int = \sqrt{r^2 + g^2 + b^2}$$

La expresión "rendimiento de lavado mejorado", tal como se usa en el presente documento, se refiere a una mejora del rendimiento de lavado de una alfa-amilasa de la presente invención en relación con el rendimiento de lavado del polipéptido parental. El rendimiento de lavado mejorado puede medirse comparando el denominado valor de intensidad y calculando el valor de mejora (IF). El rendimiento de lavado mejorado se determina según se establece en la sección "Rendimiento de lavado de alfa-amilasas usando el ensayo de estrés mecánico automático" y usando el modelo de detergente J a 15°C, 30°C o 40°C. Pueden usarse otros modelos de detergente, tales como el detergente modelo A.

Por lo tanto, en una realización, el rendimiento de lavado mejorado se determina mediante un método que comprende las etapas de;

a) lavar un tejido manchado con almidón con una variante de alfa-amilasa y una muestra de polipéptido parental añadida, respectivamente, a una composición de detergente modelo, tal como el modelo A o el modelo J;

b) medir la intensidad de luz reflejada por la muestra cuando se ilumina con luz blanca; y

c) opcionalmente, calcular el factor de mejora (IF) como la relación de intensidad delta de la muestra de alfa-amilasa frente a la intensidad delta de la muestra de polipéptido parental.

En una realización, el rendimiento de lavado mejorado se determina mediante un método que comprende las etapas de;

a) lavar un tejido manchado con almidón con una variante de alfa-amilasa y una muestra de polipéptido parental añadida, respectivamente, a una composición de detergente modelo, tal como el modelo A o el modelo J durante 20 minutos a 15°C, 30°C y 40°C;

b) medir la intensidad de luz reflejada por la muestra cuando se ilumina con luz blanca; y

c) opcionalmente, calcular el factor de mejora (IF) como la relación de intensidad delta de la muestra de alfa-amilasa frente a la intensidad delta de la muestra de polipéptido parental.

La expresión "baja temperatura", tal como se usa en el presente documento, se refiere a una temperatura de entre 5-40°C, tal como de 5-35°C, preferentemente de 5-30°C, más preferentemente de 5-25°C, más preferentemente de 5-20°C, lo más preferentemente de 5-15°C y en particular, de 5-10°C. En una realización preferida, "baja temperatura" es una temperatura de 10-35°C, preferentemente de 10-30°C, más preferentemente de 10-25°C, lo más preferentemente de 10-20°C y en particular de 10-15°C. De manera más preferida, baja temperatura significa 15°C.

Por lo tanto, en una realización, la baja temperatura es de 5°C a 40°C, preferentemente de 10°C a 30°, aún más preferentemente, de 15°C a 20°C.

En una realización, el rendimiento de lavado mejorado tiene un factor de mejora (IF) de $\geq$1 cuando se compara con dicho polipéptido parental que tiene actividad alfa-amilasa.

La expresión "factor de mejora", tal como se usa en el presente documento, se refiere a una forma cuantitativa de calcular la mejora de una propiedad concreta de una variante de acuerdo con la presente invención. La determinación del factor de mejora puede ser de acuerdo con la siguiente fórmula:

$$\frac{\text{Valor de intensidad de la variante} - \text{Valor de intensidad del blanco}}{\text{Valor de intensidad del progenitor} - \text{Valor de intensidad del blanco}}$$

Pueden usarse otras fórmulas para determinar el factor de mejora. Los expertos en la materia conocen la fórmula presentada en el presente documento así como formas alternativas para calcular el factor de mejora.

De acuerdo con la presente invención, un valor de 1.0 corresponde al rendimiento observado para el polipéptido parental. Un valor por encima de 1.0 indica una mejora del rendimiento de la variante ensayada en comparación con el polipéptido parental. Por consiguiente, cualquier valor $\geq$ 1.0 indica mejora de una propiedad de la variante, tal como rendimiento, en comparación con el polipéptido parental.

De acuerdo con la presente invención, una variante que muestra mejora de una propiedad en al menos una condición ensayada se considera una variante que tiene una propiedad mejorada en comparación con el polipéptido parental.

En una realización, dicho polipéptido parental comprende un dominio A y B que comprende la secuencia de aminoácidos de la SEQ ID NO: 10 o un dominio A y B que

tiene al menos un 80%, tal como un 85%, tal como un 90%, tal como un 95%, tal como un 97% de identidad de secuencia con l SEQ ID NO: 10 y un dominio C de una alfa-amilasa de baja temperatura.

Las expresiones "dominio A", "dominio B" y "dominio C", tal como se usan en el presente documento, se refieren a tres dominios distintos, A, B y C que forman parte de la estructura de la alfa-amilasa, véase, por ejemplo, Machius *et al.*, 1995, *J. Mol. Biol.* 246: 545-559. Por lo tanto, una alfa-amilasa, tal como un polipéptido parental y uno variante de acuerdo con la invención, pueden comprender un dominio A, B y C. El término "dominio" significa una región de un polipéptido que forma por sí misma una subestructura distinta e independiente de la molécula completa. Las alfa-amilasas constan de -8 barriles beta/alfa que portan los restos del sitio activo, que se denominan dominio A, un bucle relativamente largo entre la beta-lámina 3 y la alfa-hélice 3, que denomina dominio B (conjuntamente; "dominio A y B") y un dominio C y en algunos casos también un sito de unión a carbohidratos (véase, por ejemplo, el documento WO 2005/001064; Machius *et al.*, citado anteriormente).

Pueden determinarse los dominios de una alfa-amilasa mediante análisis estructural, tal como mediante el uso de técnicas cristalográficas. Un método alternativo para determinar los dominios de una alfa-amilasa es mediante alineamiento de secuencias de la secuencia de aminoácidos de la alfa-amilasa con otra alfa-amilasa para la que se han determinado los dominios. La secuencia que se alinea con, por ejemplo, la secuencia del dominio C en la alfa-amilasa para la que se ha determinado el dominio C puede considerarse el dominio C para la alfa-amilasa dada.

La expresión "dominio A y B", tal como se usa en el presente documento, se refiere a dos dominios de una alfa-

amilasa tomados como una unidad, mientras que el dominio C es otra unidad de las alfa amilasas. Por lo tanto, la secuencia de aminoácidos del "dominio A y B" se entiende como una secuencia o como una parte de una secuencia de una alfa amilasa que comprende un "dominio A y B" y otros dominios (tal como el dominio C). Por lo tanto, la expresión "el dominio A y B tiene al menos un 65% de identidad de secuencia con la SEQ ID NO: 10" significa que la secuencia de aminoácidos que forma el dominio A y B tiene al menos un 65% de identidad de secuencia con la SEQ ID NO: 10. Tal como se usa en el presente documento, el "dominio A y B" de un polipéptido parental corresponde a los aminoácidos 1 a 399 de la SEQ ID NO: 7 o a los aminoácidos 1 a 397 de la SEQ ID NO: 15. El dominio A y B de un polipéptido parental puede tener la secuencia de aminoácidos de SEQ ID NO: 10.

La expresión "dominio C", tal como se usa en el presente documento, se refiere a un dominio de una alfa-amilasa como una unidad. El "dominio C" de una alfa-amilasa corresponde a los aminoácidos 400 a 485 de la SEQ ID NO: 7 o a los aminoácidos 398 a 483 de la SEQ ID NO: 15. Por lo tanto, puede hallarse el dominio C de una alfa-amilasa mediante el alineamiento de dicha alfa-amilasa con el polipéptido de SEQ ID NO: 7 o 15. La parte de dicha alfa-amilasa que se alinea con los aminoácidos 400 a 485 de la SEQ ID NO: 7 o con los aminoácidos 398 a 483 de la SEQ ID NO: 15 es, según la presente invención, el "dominio C" de la alfa-amilasa. El dominio C de un polipéptido parental puede tener la secuencia de aminoácidos de las SEQ ID NO: 11 o 12.

La expresión "dominio C de una alfa-amilasa de baja temperatura", tal como se usa en el presente documento, se refiere al dominio C de una alfa-amilasa que muestra

propiedades concretas a bajas temperaturas. Los ejemplos no limitantes de dichas alfa-amilasas de baja temperatura son aquellas que se originan a partir de *Alicyclobacillus* sp., así como a partir de *Bacillus amyloliquefaciens* (BAN).

En una realización, el polipéptido parental comprende un dominio C que comprende la secuencia de aminoácidos de las SEQ ID NO: 11 o 12 o un dominio C que tiene al menos un 80%, tal como un 85%, tal como un 90%, tal como un 95%, tal como un 97% de identidad de secuencia con las SEQ ID NO: 11 o 12.

En una realización, el polipéptido parental comprende la secuencia de aminoácidos de las SEQ ID NO: 13 o 14 o una secuencia que tiene al menos un 80%, tal como un 85%, tal como un 90%, tal como un 95%, tal como un 97% de identidad de secuencia con las SEQ ID NO: 13 o 14.

Tal como se indica en otras partes del presente documento, el polipéptido parental puede ser cualquier polipéptido que tenga actividad alfa-amilasa y al menos un 65% de identidad de secuencia con una cualquiera de las secuencias de aminoácidos expuestas en las SEQ ID NO: 13 y 14. En determinadas realizaciones, el polipéptido parental comprende las secuencias de aminoácidos expuestas en las SEQ ID NO: 10, 11 y 12.

En una realización, el polipéptido parental tiene una identidad de secuencia respecto de la secuencia de aminoácidos expuesta en las SEQ ID NO: 13 o 14 de al menos un 60%, por ejemplo, al menos un 65%, al menos un 70%, al menos un 75%, al menos un 80%, al menos un 85%, al menos un 90%, al menos un 91%, al menos un 92%, al menos un 93%, al menos un 94%, al menos un 95%, al menos un 96%, al menos un 97%, al menos un 98%, al menos un 99% o un 100%, y dicho polipéptido parental tiene actividad alfa-amilasa. En una realización, la secuencia de aminoácidos del polipéptido

parental difiere en hasta 10 aminoácidos, por ejemplo, en 1, 2, 3, 4, 5, 6, 7, 8, 9 o 10, respecto de las secuencias de aminoácidos expuestas en las SEQ ID NO: 7, 13 y 14.

La presente invención proporciona variantes de dichos polipéptidos parentales.

Las variantes de acuerdo con la presente invención pueden comprender, ventajosamente, alteraciones en posiciones específicas del dominio A y B. Por lo tanto, en una realización particular, la variante comprende alteraciones de aminoácidos en posiciones de aminoácidos correspondientes a la secuencia de aminoácidos expuesta en la SEQ ID NO: 10 o una secuencia que tenga al menos un 65% de identidad de secuencia respecto de la secuencia de aminoácidos expuesta en la SEQ ID NO: 10.

En particular, la presente invención se refiere, en una realización, en la que los dominios A y B comprenden una modificación en una o más de las siguientes posiciones correspondientes a las posiciones; H1, T5, G7, Q11, N16, V17, Q32, A37, T40, P45, W48, G50, T51, N54, V56, A60, K72, R87, Q98, M105, G109, F113, R116, Q118, Q125, G133, T134, W140, G142, G149, T165, W167, Q169, R171, Q172, L173, A174, G184, A186, E190, T193, N195, G196, A204, V206, P211, I214, V215, L217, L219, A225, L228, L235, V238, K242, S244, M246, M248, L250, G255, Q256, N260, A263, V264, A265, Y267, K269, N270, G273, S280, W284, T285, M286, F289, V291, N295, Q299, S304, R320, H321, S323, H324, V326, F328, T334, D337, Q345, G346, G348, T355, S376, D377, D379, Y382, S383, Q385, K391, K393 y Q395 de las SEQ ID NO: 7 o 10.

Se ha demostrado que dichas variantes tienen un rendimiento de lavado mejorado en al menos un ensayo, en donde la temperatura a la que se han probado las variantes era una temperatura baja, tal como 15°C, 30°C y 40°C.

Pueden verse las condiciones específicas en los ejemplos del presente documento.

El término "modificación", tal como se usa en el presente documento, se refiere tanto a sustituciones como a eliminaciones de aminoácidos dentro de la secuencia de aminoácidos de un polipéptido. Los términos "alteración" y "modificación" pueden usarse de manera indistinta en el presente documento. Esto no debe interpretarse como una limitación y por lo tanto, los términos tienen el mismo significado y propósito, a menos que se indique explícitamente lo contrario.

La expresión "correspondiente a", tal como se usa en el presente documento, se refiere a una forma de determinar el aminoácido específico de una secuencia, en donde se hace referencia a una secuencia de aminoácidos específica. Por ejemplo, a efectos de la presente invención, cuando se hace referencia a posiciones de aminoácidos específicas, el experto en la materia será capaz de alinear otra secuencia de aminoácidos con dicha secuencia de aminoácidos a la que se hace referencia para determinar qué aminoácido específico puede ser de interés en dicha otra secuencia de aminoácidos. El alineamiento de otra secuencia de aminoácidos con, por ejemplo, la secuencia expuesta en las SEQ ID NO: 4, 7 o cualquier otra secuencia listada en el presente documento, se ha descrito en otras partes del presente documento. Pueden usarse métodos de alineamiento alternativos y son de sobra conocidos por los expertos en la materia.

En una realización particular, la variante comprende una alteración en dos, tres, cuatro, cinco, seis, siete, ocho, nueve, diez, once, doce, trece, catorce, quince o dieciséis posiciones correspondientes a las siguientes posiciones; H1, T5, G7, Q11, N16, V17, Q32, A37, T40, P45,

W48, G50, T51, N54, V56, A60, K72, R87, Q98, M105, G109, F113, R116, Q118, Q125, G133, T134, W140, G142, G149, T165, W167, Q169, R171, Q172, L173, A174, G184, A186, E190, T193, N195, G196, A204, V206, P211, I214, V215, L217, L219, A225, L228, L235, V238, K242, S244, M246, M248, L250, G255, Q256, N260, A263, V264, A265, Y267, K269, N270, G273, S280, W284, T285, M286, F289, V291, Y295, Q299, S304, R320, H321, S323, H324, V326, F328, T334, D337, Q345, G346, G348, T355, S376, D377, D379, Y382, S383, Q385, K391, K393 y Q395 de las SEQ ID NO: 7 o 10.

En una realización particular, la variante comprende una alteración en las siguientes posiciones;

H1+T5	T40+L217	N54+T285	Q125+G255	G184+P211	M248+Q299
H1+G7	T40+L219	N54+M286	Q125+Q256	G184+I214	M248+S304
H1+Q11	T40+L228	N54+F289	Q125+A263	G184+V215	M248+R320
H1+N16	T40+L235	N54+V291	Q125+V264	G184+L217	M248+H321
H1+V17	T40+V238	N54+Q299	Q125+A265	G184+L219	M248+S323
H1+Q32	T40+M246	N54+S304	Q125+Y267	G184+L228	M248+H324
H1+A37	T40+M248	N54+R320	Q125+N270	G184+L235	M248+F328
H1+T40	T40+L250	N54+H321	Q125+G273	G184+V238	M248+T334
H1+P45	T40+G255	N54+S323	Q125+S280	G184+M246	M248+D337
H1+W48	T40+Q256	N54+H324	Q125+T285	G184+M248	M248+Q345
H1+G50	T40+A263	N54+F328	Q125+M286	G184+L250	M248+G346
H1+T51	T40+V264	N54+T334	Q125+F289	G184+G255	M248+G348
H1+N54	T40+A265	N54+D337	Q125+V291	G184+Q256	M248+T355
H1+V56	T40+Y267	N54+Q345	Q125+Q299	G184+A263	M248+S376
H1+A60	T40+N270	N54+G346	Q125+S304	G184+V264	M248+D377
H1+K72	T40+G273	N54+G348	Q125+R320	G184+A265	M248+D379
H1+R87	T40+S280	N54+T355	Q125+H321	G184+Y267	M248+Y382
H1+Q98	T40+T285	N54+S376	Q125+S323	G184+N270	M248+S383
H1+M105	T40+M286	N54+D377	Q125+H324	G184+G273	M248+Q385
H1+G109	T40+F289	N54+D379	Q125+F328	G184+S280	M248+K391

H1+F113	T40+V291	N54+Y382	Q125+T334	G184+T285	M248+K393
H1+R116	T40+Q299	N54+S383	Q125+D337	G184+M286	M248+Q395
H1+Q118	T40+S304	N54+Q385	Q125+Q345	G184+F289	L250+G255
H1+Q125	T40+R320	N54+K391	Q125+G346	G184+V291	L250+Q256
H1+G133	T40+H321	N54+K393	Q125+G348	G184+Q299	L250+A263
H1+T134	T40+S323	N54+Q395	Q125+T355	G184+S304	L250+V264
H1+W140	T40+H324	V56+A60	Q125+S376	G184+R320	L250+A265
H1+G142	T40+F328	V56+K72	Q125+D377	G184+H321	L250+Y267
H1+G149	T40+T334	V56+R87	Q125+D379	G184+S323	L250+N270
H1+T165	T40+D337	V56+Q98	Q125+Y382	G184+H324	L250+G273
H1+W167	T40+Q345	V56+M105	Q125+S383	G184+F328	L250+S280
H1+R171	T40+G346	V56+G109	Q125+Q385	G184+T334	L250+T285
H1+Q172	T40+G348	V56+F113	Q125+K391	G184+D337	L250+M286
H1+L173	T40+T355	V56+R116	Q125+K393	G184+Q345	L250+F289
H1+A174	T40+S376	V56+Q118	Q125+Q395	G184+G346	L250+V291
H1+G184	T40+D377	V56+Q125	G133+T134	G184+G348	L250+Q299
H1+T193	T40+D379	V56+G133	G133+W140	G184+T355	L250+S304
H1+N195	T40+Y382	V56+T134	G133+G142	G184+S376	L250+R320
H1+G196	T40+S383	V56+W140	G133+G149	G184+D377	L250+H321
H1+A204	T40+Q385	V56+G142	G133+T165	G184+D379	L250+S323
H1+V206	T40+K391	V56+G149	G133+W167	G184+Y382	L250+H324
H1+P211	T40+K393	V56+T165	G133+R171	G184+S383	L250+F328
H1+I214	T40+Q395	V56+W167	G133+Q172	G184+Q385	L250+T334
H1+V215	P45+W48	V56+R171	G133+L173	G184+K391	L250+D337
H1+L217	P45+G50	V56+Q172	G133+A174	G184+K393	L250+Q345
H1+L219	P45+T51	V56+L173	G133+G184	G184+Q395	L250+G346
H1+L228	P45+N54	V56+A174	G133+T193	T193+N195	L250+G348
H1+L235	P45+V56	V56+G184	G133+N195	T193+G196	L250+T355
H1+V238	P45+A60	V56+T193	G133+G196	T193+A204	L250+S376
H1+M246	P45+K72	V56+N195	G133+A204	T193+V206	L250+D377
H1+M248	P45+R87	V56+G196	G133+V206	T193+P211	L250+D379
H1+L250	P45+Q98	V56+A204	G133+P211	T193+I214	L250+Y382

H1+G255	P45+M105	V56+V206	G133+I214	T193+V215	L250+S383
H1+Q256	P45+G109	V56+P211	G133+V215	T193+L217	L250+Q385
H1+A263	P45+F113	V56+I214	G133+L217	T193+L219	L250+K391
H1+V264	P45+R116	V56+V215	G133+L219	T193+L228	L250+K393
H1+A265	P45+Q118	V56+L217	G133+L228	T193+L235	L250+Q395
H1+Y267	P45+Q125	V56+L219	G133+L235	T193+V238	G255+Q256
H1+N270	P45+G133	V56+L228	G133+V238	T193+M246	G255+A263
H1+G273	P45+T134	V56+L235	G133+M246	T193+M248	G255+V264
H1+S280	P45+W140	V56+V238	G133+M248	T193+L250	G255+A265
H1+T285	P45+G142	V56+M246	G133+L250	T193+G255	G255+Y267
H1+M286	P45+G149	V56+M248	G133+G255	T193+Q256	G255+N270
H1+F289	P45+T165	V56+L250	G133+Q256	T193+A263	G255+G273
H1+V291	P45+W167	V56+G255	G133+A263	T193+V264	G255+S280
H1+Q299	P45+R171	V56+Q256	G133+V264	T193+A265	G255+T285
H1+S304	P45+Q172	V56+A263	G133+A265	T193+Y267	G255+M286
H1+R320	P45+L173	V56+V264	G133+Y267	T193+N270	G255+F289
H1+H321	P45+A174	V56+A265	G133+N270	T193+G273	G255+V291
H1+S323	P45+G184	V56+Y267	G133+G273	T193+S280	G255+Q299
H1+H324	P45+T193	V56+N270	G133+S280	T193+T285	G255+S304
H1+F328	P45+N195	V56+G273	G133+T285	T193+M286	G255+R320
H1+T334	P45+G196	V56+S280	G133+M286	T193+F289	G255+H321
H1+D337	P45+A204	V56+T285	G133+F289	T193+V291	G255+S323
H1+Q345	P45+V206	V56+M286	G133+V291	T193+Q299	G255+H324
H1+G346	P45+P211	V56+F289	G133+Q299	T193+S304	G255+F328
H1+G348	P45+I214	V56+V291	G133+S304	T193+R320	G255+T334
H1+T355	P45+V215	V56+Q299	G133+R320	T193+H321	G255+D337
H1+S376	P45+L217	V56+S304	G133+H321	T193+S323	G255+Q345
H1+D377	P45+L219	V56+R320	G133+S323	T193+H324	G255+G346
H1+D379	P45+L228	V56+H321	G133+H324	T193+F328	G255+G348
H1+Y382	P45+L235	V56+S323	G133+F328	T193+T334	G255+T355
H1+S383	P45+V238	V56+H324	G133+T334	T193+D337	G255+S376
H1+Q385	P45+M246	V56+F328	G133+D337	T193+Q345	G255+D377

H1+K391	P45+M248	V56+T334	G133+Q345	T193+G346	G255+D379
H1+K393	P45+L250	V56+D337	G133+G346	T193+G348	G255+Y382
H1+Q395	P45+G255	V56+Q345	G133+G348	T193+T355	G255+S383
T5 +G7	P45+Q256	V56+G346	G133+T355	T193+S376	G255+Q385
T5 +Q11	P45+A263	V56+G348	G133+S376	T193+D377	G255+K391
T5 +N16	P45+V264	V56+T355	G133+D377	T193+D379	G255+K393
T5 +V17	P45+A265	V56+S376	G133+D379	T193+Y382	G255+Q395
T5 +Q32	P45+Y267	V56+D377	G133+Y382	T193+S383	Q256+A263
T5 +A37	P45+N270	V56+D379	G133+S383	T193+Q385	Q256+V264
T5 +T40	P45+G273	V56+Y382	G133+Q385	T193+K391	Q256+A265
T5 +P45	P45+S280	V56+S383	G133+K391	T193+K393	Q256+Y267
T5 +W48	P45+T285	V56+Q385	G133+K393	T193+Q395	Q256+N270
T5 +G50	P45+M286	V56+K391	G133+Q395	N195+G196	Q256+G273
T5 +T51	P45+F289	V56+K393	T134+W140	N195+A204	Q256+S280
T5 +N54	P45+V291	V56+Q395	T134+G142	N195+V206	Q256+T285
T5 +V56	P45+Q299	A60+K72	T134+G149	N195+P211	Q256+M286
T5 +A60	P45+S304	A60+R87	T134+T165	N195+I214	Q256+F289
T5 +K72	P45+R320	A60+Q98	T134+W167	N195+V215	Q256+V291
T5 +R87	P45+H321	A60+M105	T134+R171	N195+L217	Q256+Q299
T5 +Q98	P45+S323	A60+G109	T134+Q172	N195+L219	Q256+S304
T5	P45+H324	A60+F113	T134+L173	N195+L228	Q256+R320
+M105	P45+F328	A60+R116	T134+A174	N195+L235	Q256+H321
T5	P45+T334	A60+Q118	T134+G184	N195+V238	Q256+S323
+G109	P45+D337	A60+Q125	T134+T193	N195+M246	Q256+H324
T5	P45+Q345	A60+G133	T134+N195	N195+M248	Q256+F328
+F113	P45+G346	A60+T134	T134+G196	N195+L250	Q256+T334
T5	P45+G348	A60+W140	T134+A204	N195+G255	Q256+D337
+R116	P45+T355	A60+G142	T134+V206	N195+Q256	Q256+Q345
T5	P45+S376	A60+G149	T134+P211	N195+A263	Q256+G346
+Q118	P45+D377	A60+T165	T134+I214	N195+V264	Q256+G348
T5	P45+D379	A60+W167	T134+V215	N195+A265	Q256+T355
+Q125	P45+Y382	A60+R171	T134+L217	N195+Y267	Q256+S376

T5	P45+S383	A60+Q172	T134+L219	N195+N270	Q256+D377
+G133	P45+Q385	A60+L173	T134+L228	N195+G273	Q256+D379
T5	P45+K391	A60+A174	T134+L235	N195+S280	Q256+Y382
+T134	P45+K393	A60+G184	T134+V238	N195+T285	Q256+S383
T5	P45+Q395	A60+T193	T134+M246	N195+M286	Q256+Q385
+W140	W48+G50	A60+N195	T134+M248	N195+F289	Q256+K391
T5	W48+T51	A60+G196	T134+L250	N195+V291	Q256+K393
+G142	W48+N54	A60+A204	T134+G255	N195+Q299	Q256+Q395
T5	W48+V56	A60+V206	T134+Q256	N195+S304	A263+V264
+G149	W48+A60	A60+P211	T134+A263	N195+R320	A263+A265
T5	W48+K72	A60+I214	T134+V264	N195+H321	A263+Y267
+T165	W48+R87	A60+V215	T134+A265	N195+S323	A263+N270
T5	W48+Q98	A60+L217	T134+Y267	N195+H324	A263+G273
+W167	W48+M105	A60+L219	T134+N270	N195+F328	A263+S280
T5	W48+G109	A60+L228	T134+G273	N195+T334	A263+T285
+R171	W48+F113	A60+L235	T134+S280	N195+D337	A263+M286
T5	W48+R116	A60+V238	T134+T285	N195+Q345	A263+F289
+Q172	W48+Q118	A60+M246	T134+M286	N195+G346	A263+V291
T5	W48+Q125	A60+M248	T134+F289	N195+G348	A263+Q299
+L173	W48+G133	A60+L250	T134+V291	N195+T355	A263+S304
T5	W48+T134	A60+G255	T134+Q299	N195+S376	A263+R320
+A174	W48+W140	A60+Q256	T134+S304	N195+D377	A263+H321
T5	W48+G142	A60+A263	T134+R320	N195+D379	A263+S323
+G184	W48+G149	A60+V264	T134+H321	N195+Y382	A263+H324
T5	W48+T165	A60+A265	T134+S323	N195+S383	A263+F328
+T193	W48+W167	A60+Y267	T134+H324	N195+Q385	A263+T334
T5	W48+R171	A60+N270	T134+F328	N195+K391	A263+D337
+N195	W48+Q172	A60+G273	T134+T334	N195+K393	A263+Q345
T5	W48+L173	A60+S280	T134+D337	N195+Q395	A263+G346
+G196	W48+A174	A60+T285	T134+Q345	G196+A204	A263+G348
T5	W48+G184	A60+M286	T134+G346	G196+V206	A263+T355
+A204	W48+T193	A60+F289	T134+G348	G196+P211	A263+S376

T5	W48+N195	A60+V291	T134+T355	G196+I214	A263+D377
+V206	W48+G196	A60+Q299	T134+S376	G196+V215	A263+D379
T5	W48+A204	A60+S304	T134+D377	G196+L217	A263+Y382
+P211	W48+V206	A60+R320	T134+D379	G196+L219	A263+S383
T5	W48+P211	A60+H321	T134+Y382	G196+L228	A263+Q385
+I214	W48+I214	A60+S323	T134+S383	G196+L235	A263+K391
T5	W48+V215	A60+H324	T134+Q385	G196+V238	A263+K393
+V215	W48+L217	A60+F328	T134+K391	G196+M246	A263+Q395
T5	W48+L219	A60+T334	T134+K393	G196+M248	V264+A265
+L217	W48+L228	A60+D337	T134+Q395	G196+L250	V264+Y267
T5	W48+L235	A60+Q345	W140+G142	G196+G255	V264+N270
+L219	W48+V238	A60+G346	W140+G149	G196+Q256	V264+G273
T5	W48+M246	A60+G348	W140+T165	G196+A263	V264+S280
+L228	W48+M248	A60+T355	W140+W167	G196+V264	V264+T285
T5	W48+L250	A60+S376	W140+R171	G196+A265	V264+M286
+L235	W48+G255	A60+D377	W140+Q172	G196+Y267	V264+F289
T5	W48+Q256	A60+D379	W140+L173	G196+N270	V264+V291
+V238	W48+A263	A60+Y382	W140+A174	G196+G273	V264+Q299
T5	W48+V264	A60+S383	W140+G184	G196+S280	V264+S304
+M246	W48+A265	A60+Q385	W140+T193	G196+T285	V264+R320
T5	W48+Y267	A60+K391	W140+N195	G196+M286	V264+H321
+M248	W48+N270	A60+K393	W140+G196	G196+F289	V264+S323
T5	W48+G273	A60+Q395	W140+A204	G196+V291	V264+H324
+L250	W48+S280	K72+R87	W140+V206	G196+Q299	V264+F328
T5	W48+T285	K72+Q98	W140+P211	G196+S304	V264+T334
+G255	W48+M286	K72+M105	W140+I214	G196+R320	V264+D337
T5	W48+F289	K72+G109	W140+V215	G196+H321	V264+Q345
+Q256	W48+V291	K72+F113	W140+L217	G196+S323	V264+G346
T5	W48+Q299	K72+R116	W140+L219	G196+H324	V264+G348
+A263	W48+S304	K72+Q118	W140+L228	G196+F328	V264+T355
T5	W48+R320	K72+Q125	W140+L235	G196+T334	V264+S376
+V264	W48+H321	K72+G133	W140+V238	G196+D337	V264+D377

T5	W48+S323	K72+T134	W140+M246	G196+Q345	V264+D379
+A265	W48+H324	K72+W140	W140+M248	G196+G346	V264+Y382
T5	W48+F328	K72+G142	W140+L250	G196+G348	V264+S383
+Y267	W48+T334	K72+G149	W140+G255	G196+T355	V264+Q385
T5	W48+D337	K72+T165	W140+Q256	G196+S376	V264+K391
+N270	W48+Q345	K72+W167	W140+A263	G196+D377	V264+K393
T5	W48+G346	K72+R171	W140+V264	G196+D379	V264+Q395
+G273	W48+G348	K72+Q172	W140+A265	G196+Y382	A265+Y267
T5	W48+T355	K72+L173	W140+Y267	G196+S383	A265+N270
+S280	W48+S376	K72+A174	W140+N270	G196+Q385	A265+G273
T5	W48+D377	K72+G184	W140+G273	G196+K391	A265+S280
+T285	W48+D379	K72+T193	W140+S280	G196+K393	A265+T285
T5	W48+Y382	K72+N195	W140+T285	G196+Q395	A265+M286
+M286	W48+S383	K72+G196	W140+M286	A204+V206	A265+F289
T5	W48+Q385	K72+A204	W140+F289	A204+P211	A265+V291
+F289	W48+K391	K72+V206	W140+V291	A204+I214	A265+Q299
T5	W48+K393	K72+P211	W140+Q299	A204+V215	A265+S304
+V291	W48+Q395	K72+I214	W140+S304	A204+L217	A265+R320
T5	G50+T51	K72+V215	W140+R320	A204+L219	A265+H321
+Q299	G50+N54	K72+L217	W140+H321	A204+L228	A265+S323
T5	G50+V56	K72+L219	W140+S323	A204+L235	A265+H324
+S304	G50+A60	K72+L228	W140+H324	A204+V238	A265+F328
T5	G50+K72	K72+L235	W140+F328	A204+M246	A265+T334
+R320	G50+R87	K72+V238	W140+T334	A204+M248	A265+D337
T5	G50+Q98	K72+M246	W140+D337	A204+L250	A265+Q345
+H321	G50+M105	K72+M248	W140+Q345	A204+G255	A265+G346
T5	G50+G109	K72+L250	W140+G346	A204+Q256	A265+G348
+S323	G50+F113	K72+G255	W140+G348	A204+A263	A265+T355
T5	G50+R116	K72+Q256	W140+T355	A204+V264	A265+S376
+H324	G50+Q118	K72+A263	W140+S376	A204+A265	A265+D377
T5	G50+Q125	K72+V264	W140+D377	A204+Y267	A265+D379
+F328	G50+G133	K72+A265	W140+D379	A204+N270	A265+Y382

T5	G50+T134	K72+Y267	W140+Y382	A204+G273	A265+S383
+T334	G50+W140	K72+N270	W140+S383	A204+S280	A265+Q385
T5	G50+G142	K72+G273	W140+Q385	A204+T285	A265+K391
+D337	G50+G149	K72+S280	W140+K391	A204+M286	A265+K393
T5	G50+T165	K72+T285	W140+K393	A204+F289	A265+Q395
+Q345	G50+W167	K72+M286	W140+Q395	A204+V291	Y267+N270
T5	G50+R171	K72+F289	G142+G149	A204+Q299	Y267+G273
+G346	G50+Q172	K72+V291	G142+T165	A204+S304	Y267+S280
T5	G50+L173	K72+Q299	G142+W167	A204+R320	Y267+T285
+G348	G50+A174	K72+S304	G142+R171	A204+H321	Y267+M286
T5	G50+G184	K72+R320	G142+Q172	A204+S323	Y267+F289
+T355	G50+T193	K72+H321	G142+L173	A204+H324	Y267+V291
T5	G50+N195	K72+S323	G142+A174	A204+F328	Y267+Q299
+S376	G50+G196	K72+H324	G142+G184	A204+T334	Y267+S304
T5	G50+A204	K72+F328	G142+T193	A204+D337	Y267+R320
+D377	G50+V206	K72+T334	G142+N195	A204+Q345	Y267+H321
T5	G50+P211	K72+D337	G142+G196	A204+G346	Y267+S323
+D379	G50+I214	K72+Q345	G142+A204	A204+G348	Y267+H324
T5	G50+V215	K72+G346	G142+V206	A204+T355	Y267+F328
+Y382	G50+L217	K72+G348	G142+P211	A204+S376	Y267+T334
T5	G50+L219	K72+T355	G142+I214	A204+D377	Y267+D337
+S383	G50+L228	K72+S376	G142+V215	A204+D379	Y267+Q345
T5	G50+L235	K72+D377	G142+L217	A204+Y382	Y267+G346
+Q385	G50+V238	K72+D379	G142+L219	A204+S383	Y267+G348
T5	G50+M246	K72+Y382	G142+L228	A204+Q385	Y267+T355
+K391	G50+M248	K72+S383	G142+L235	A204+K391	Y267+S376
T5	G50+L250	K72+Q385	G142+V238	A204+K393	Y267+D377
+K393	G50+G255	K72+K391	G142+M246	A204+Q395	Y267+D379
T5	G50+Q256	K72+K393	G142+M248	V206+P211	Y267+Y382
+Q395	G50+A263	K72+Q395	G142+L250	V206+I214	Y267+S383
G7+Q11	G50+V264	R87+Q98	G142+G255	V206+V215	Y267+Q385
G7+N16	G50+A265	R87+M105	G142+Q256	V206+L217	Y267+K391

G7+V17	G50+Y267	R87+G109	G142+A263	V206+L219	Y267+K393
G7+Q32	G50+N270	R87+F113	G142+V264	V206+L228	Y267+Q395
G7+A37	G50+G273	R87+R116	G142+A265	V206+L235	N270+G273
G7+T40	G50+S280	R87+Q118	G142+Y267	V206+V238	N270+S280
G7+P45	G50+T285	R87+Q125	G142+N270	V206+M246	N270+T285
G7+W48	G50+M286	R87+G133	G142+G273	V206+M248	N270+M286
G7+G50	G50+F289	R87+T134	G142+S280	V206+L250	N270+F289
G7+T51	G50+V291	R87+W140	G142+T285	V206+G255	N270+V291
G7+N54	G50+Q299	R87+G142	G142+M286	V206+Q256	N270+Q299
G7+V56	G50+S304	R87+G149	G142+F289	V206+A263	N270+S304
G7+A60	G50+R320	R87+T165	G142+V291	V206+V264	N270+R320
G7+K72	G50+H321	R87+W167	G142+Q299	V206+A265	N270+H321
G7+R87	G50+S323	R87+R171	G142+S304	V206+Y267	N270+S323
G7+Q98	G50+H324	R87+Q172	G142+R320	V206+N270	N270+H324
G7+M105	G50+F328	R87+L173	G142+H321	V206+G273	N270+F328
G7+G109	G50+T334	R87+A174	G142+S323	V206+S280	N270+T334
G7+F113	G50+D337	R87+G184	G142+H324	V206+T285	N270+D337
G7+R116	G50+Q345	R87+T193	G142+F328	V206+M286	N270+Q345
G7+Q118	G50+G346	R87+N195	G142+T334	V206+F289	N270+G346
G7+Q125	G50+G348	R87+G196	G142+D337	V206+V291	N270+G348
G7+G133	G50+T355	R87+A204	G142+Q345	V206+Q299	N270+T355
G7+T134	G50+S376	R87+V206	G142+G346	V206+S304	N270+S376
G7+W140	G50+D377	R87+P211	G142+G348	V206+R320	N270+D377
G7+G142	G50+D379	R87+I214	G142+T355	V206+H321	N270+D379
G7+G149	G50+Y382	R87+V215	G142+S376	V206+S323	N270+Y382
G7+T165	G50+S383	R87+L217	G142+D377	V206+H324	N270+S383
G7+W167	G50+Q385	R87+L219	G142+D379	V206+F328	N270+Q385
G7+R171	G50+K391	R87+L228	G142+Y382	V206+T334	N270+K391
G7+Q172	G50+K393	R87+L235	G142+S383	V206+D337	N270+K393
G7+L173	G50+Q395	R87+V238	G142+Q385	V206+Q345	N270+Q395
G7+A174	T51+N54	R87+M246	G142+K391	V206+G346	G273+S280
G7+G184	T51+V56	R87+M248	G142+K393	V206+G348	G273+T285

G7+T193	T51+A60	R87+L250	G142+Q395	V206+T355	G273+M286
G7+N195	T51+K72	R87+G255	G149+T165	V206+S376	G273+F289
G7+G196	T51+R87	R87+Q256	G149+W167	V206+D377	G273+V291
G7+A204	T51+Q98	R87+A263	G149+R171	V206+D379	G273+Q299
G7+V206	T51+M105	R87+V264	G149+Q172	V206+Y382	G273+S304
G7+P211	T51+G109	R87+A265	G149+L173	V206+S383	G273+R320
G7+I214	T51+F113	R87+Y267	G149+A174	V206+Q385	G273+H321
G7+V215	T51+R116	R87+N270	G149+G184	V206+K391	G273+S323
G7+L217	T51+Q118	R87+G273	G149+T193	V206+K393	G273+H324
G7+L219	T51+Q125	R87+S280	G149+N195	V206+Q395	G273+F328
G7+L228	T51+G133	R87+T285	G149+G196	P211+I214	G273+T334
G7+L235	T51+T134	R87+M286	G149+A204	P211+V215	G273+D337
G7+V238	T51+W140	R87+F289	G149+V206	P211+L217	G273+Q345
G7+M246	T51+G142	R87+V291	G149+P211	P211+L219	G273+G346
G7+M248	T51+G149	R87+Q299	G149+I214	P211+L228	G273+G348
G7+L250	T51+T165	R87+S304	G149+V215	P211+L235	G273+T355
G7+G255	T51+W167	R87+R320	G149+L217	P211+V238	G273+S376
G7+Q256	T51+R171	R87+H321	G149+L219	P211+M246	G273+D377
G7+A263	T51+Q172	R87+S323	G149+L228	P211+M248	G273+D379
G7+V264	T51+L173	R87+H324	G149+L235	P211+L250	G273+Y382
G7+A265	T51+A174	R87+F328	G149+V238	P211+G255	G273+S383
G7+Y267	T51+G184	R87+T334	G149+M246	P211+Q256	G273+Q385
G7+N270	T51+T193	R87+D337	G149+M248	P211+A263	G273+K391
G7+G273	T51+N195	R87+Q345	G149+L250	P211+V264	G273+K393
G7+S280	T51+G196	R87+G346	G149+G255	P211+A265	G273+Q395
G7+T285	T51+A204	R87+G348	G149+Q256	P211+Y267	S280+T285
G7+M286	T51+V206	R87+T355	G149+A263	P211+N270	S280+M286
G7+F289	T51+P211	R87+S376	G149+V264	P211+G273	S280+F289
G7+V291	T51+I214	R87+D377	G149+A265	P211+S280	S280+V291
G7+Q299	T51+V215	R87+D379	G149+Y267	P211+T285	S280+Q299
G7+S304	T51+L217	R87+Y382	G149+N270	P211+M286	S280+S304
G7+R320	T51+L219	R87+S383	G149+G273	P211+F289	S280+R320

G7+H321	T51+L228	R87+Q385	G149+S280	P211+V291	S280+H321
G7+S323	T51+L235	R87+K391	G149+T285	P211+Q299	S280+S323
G7+H324	T51+V238	R87+K393	G149+M286	P211+S304	S280+H324
G7+F328	T51+M246	R87+Q395	G149+F289	P211+R320	S280+F328
G7+T334	T51+M248	Q98+M105	G149+V291	P211+H321	S280+T334
G7+D337	T51+L250	Q98+G109	G149+Q299	P211+S323	S280+D337
G7+Q345	T51+G255	Q98+F113	G149+S304	P211+H324	S280+Q345
G7+G346	T51+Q256	Q98+R116	G149+R320	P211+F328	S280+G346
G7+G348	T51+A263	Q98+Q118	G149+H321	P211+T334	S280+G348
G7+T355	T51+V264	Q98+Q125	G149+S323	P211+D337	S280+T355
G7+S376	T51+A265	Q98+G133	G149+H324	P211+Q345	S280+S376
G7+D377	T51+Y267	Q98+T134	G149+F328	P211+G346	S280+D377
G7+D379	T51+N270	Q98+W140	G149+T334	P211+G348	S280+D379
G7+Y382	T51+G273	Q98+G142	G149+D337	P211+T355	S280+Y382
G7+S383	T51+S280	Q98+G149	G149+Q345	P211+S376	S280+S383
G7+Q385	T51+T285	Q98+T165	G149+G346	P211+D377	S280+Q385
G7+K391	T51+M286	Q98+W167	G149+G348	P211+D379	S280+K391
G7+K393	T51+F289	Q98+R171	G149+T355	P211+Y382	S280+K393
G7+Q395	T51+V291	Q98+Q172	G149+S376	P211+S383	S280+Q395
Q11+N16	T51+Q299	Q98+L173	G149+D377	P211+Q385	T285+M286
Q11+V17	T51+S304	Q98+A174	G149+D379	P211+K391	T285+F289
Q11+Q32	T51+R320	Q98+G184	G149+Y382	P211+K393	T285+V291
Q11+A37	T51+H321	Q98+T193	G149+S383	P211+Q395	T285+Q299
Q11+T40	T51+S323	Q98+N195	G149+Q385	I214+V215	T285+S304
Q11+P45	T51+H324	Q98+G196	G149+K391	I214+L217	T285+R320
Q11+W48	T51+F328	Q98+A204	G149+K393	I214+L219	T285+H321
Q11+G50	T51+T334	Q98+V206	G149+Q395	I214+L228	T285+S323
Q11+T51	T51+D337	Q98+P211	T165+W167	I214+L235	T285+H324
Q11+N54	T51+Q345	Q98+I214	T165+R171	I214+V238	T285+F328
Q11+V56	T51+G346	Q98+V215	T165+Q172	I214+M246	T285+T334
Q11+A60	T51+G348	Q98+L217	T165+L173	I214+M248	T285+D337
Q11+K72	T51+T355	Q98+L219	T165+A174	I214+L250	T285+Q345

Q11+R87	T51+S376	Q98+L228	T165+G184	I214+G255	T285+G346
Q11+Q98	T51+D377	Q98+L235	T165+T193	I214+Q256	T285+G348
Q11+M10	T51+D379	Q98+V238	T165+N195	I214+A263	T285+T355
5	T51+Y382	Q98+M246	T165+G196	I214+V264	T285+S376
Q11+G10	T51+S383	Q98+M248	T165+A204	I214+A265	T285+D377
9	T51+Q385	Q98+L250	T165+V206	I214+Y267	T285+D379
Q11+F11	T51+K391	Q98+G255	T165+P211	I214+N270	T285+Y382
3	T51+K393	Q98+Q256	T165+I214	I214+G273	T285+S383
Q11+R11	T51+Q395	Q98+A263	T165+V215	I214+S280	T285+Q385
6	N54+V56	Q98+V264	T165+L217	I214+T285	T285+K391
Q11+Q11	N54+A60	Q98+A265	T165+L219	I214+M286	T285+K393
8	N54+K72	Q98+Y267	T165+L228	I214+F289	T285+Q395
Q11+Q12	N54+R87	Q98+N270	T165+L235	I214+V291	M286+F289
5	N54+Q98	Q98+G273	T165+V238	I214+Q299	M286+V291
Q11+G13	N54+M105	Q98+S280	T165+M246	I214+S304	M286+Q299
3	N54+G109	Q98+T285	T165+M248	I214+R320	M286+S304
Q11+T13	N54+F113	Q98+M286	T165+L250	I214+H321	M286+R320
4	N54+R116	Q98+F289	T165+G255	I214+S323	M286+H321
Q11+W14	N54+Q118	Q98+V291	T165+Q256	I214+H324	M286+S323
0	N54+Q125	Q98+Q299	T165+A263	I214+F328	M286+H324
Q11+G14	N54+G133	Q98+S304	T165+V264	I214+T334	M286+F328
2	N54+T134	Q98+R320	T165+A265	I214+D337	M286+T334
Q11+G14	N54+W140	Q98+H321	T165+Y267	I214+Q345	M286+D337
9	N54+G142	Q98+S323	T165+N270	I214+G346	M286+Q345
Q11+T16	N54+G149	Q98+H324	T165+G273	I214+G348	M286+G346
5	N54+T165	Q98+F328	T165+S280	I214+T355	M286+G348
Q11+W16	N54+W167	Q98+T334	T165+T285	I214+S376	M286+T355
7	N54+R171	Q98+D337	T165+M286	I214+D377	M286+S376
Q11+R17	N54+Q172	Q98+Q345	T165+F289	I214+D379	M286+D377
1	N54+L173	Q98+G346	T165+V291	I214+Y382	M286+D379
Q11+Q17	N54+A174	Q98+G348	T165+Q299	I214+S383	M286+Y382
2	N54+G184	Q98+T355	T165+S304	I214+Q385	M286+S383

Q11+L173	N54+T193	Q98+S376	T165+R320	I214+K391	M286+Q385
Q11+A174	N54+N195	Q98+D377	T165+H321	I214+K393	M286+K391
Q11+G184	N54+G196	Q98+D379	T165+S323	I214+Q395	M286+K393
Q11+T193	N54+A204	Q98+Y382	T165+H324	V215+L217	M286+Q395
Q11+N195	N54+V206	Q98+S383	T165+F328	V215+L219	F289+V291
Q11+G196	N54+P211	Q98+Q385	T165+T334	V215+L228	F289+Q299
Q11+T193	N54+I214	Q98+K391	T165+D337	V215+L235	F289+S304
Q11+N195	N54+V215	Q98+K393	T165+Q345	V215+V238	F289+R320
Q11+N195	N54+L217	Q98+Q395	T165+G346	V215+M246	F289+H321
Q11+G196	N54+L219	M105+G109	T165+G348	V215+M248	F289+S323
Q11+G196	N54+L228	M105+F113	T165+T355	V215+L250	F289+H324
Q11+A204	N54+L235	M105+R116	T165+S376	V215+G255	F289+F328
Q11+A204	N54+V238	M105+Q118	T165+D377	V215+Q256	F289+T334
Q11+V206	N54+M246	M105+Q125	T165+D379	V215+A263	F289+D337
Q11+V206	N54+M248	M105+G133	T165+Y382	V215+V264	F289+Q345
Q11+P211	N54+L250	M105+T134	T165+S383	V215+A265	F289+G346
Q11+P211	N54+G255	M105+W140	T165+Q385	V215+Y267	F289+G348
Q11+I214	N54+Q256	M105+G142	T165+K391	V215+N270	F289+T355
Q11+I214	N54+A263	M105+G149	T165+K393	V215+G273	F289+S376
Q11+V215	N54+V264	M105+T165	T165+Q395	V215+S280	F289+D377
Q11+V215	N54+A265	M105+W167	W167+R171	V215+T285	F289+D379
Q11+L217	N54+Y267	M105+R171	W167+Q172	V215+M286	F289+Y382
Q11+L217	N54+N270	M105+Q172	W167+L173	V215+F289	F289+S383
Q11+L219	N54+G273	M105+L173	W167+A174	V215+V291	F289+Q385
Q11+L219	N54+S280	M105+A174	W167+G184	V215+Q299	F289+K391
Q11+L228	Q118+V215	M105+G184	W167+T193	V215+S304	F289+K393
Q11+L228	Q118+L217	M105+T193	W167+N195	V215+R320	F289+Q395
Q11+L235	Q118+L219	M105+N195	W167+G196	V215+H321	V291+Q299
Q11+L235	Q118+L228	M105+G196	W167+A204	V215+S323	V291+S304
Q11+V238	Q118+L235	M105+A204	W167+V206	V215+H324	V291+R320
Q11+V238	Q118+V238	M105+V206	W167+P211	V215+F328	V291+H321
Q11+M246	Q118+M246	M105+P211	W167+I214	V215+T334	V291+S323

Q11+M24	Q118+M248	M105+I214	W167+V215	V215+D337	V291+H324
6	Q118+L250	M105+V215	W167+L217	V215+Q345	V291+F328
Q11+M24	Q118+G255	M105+L217	W167+L219	V215+G346	V291+T334
8	Q118+Q256	M105+L219	W167+L228	V215+G348	V291+D337
Q11+L25	Q118+A263	M105+L228	W167+L235	V215+T355	V291+Q345
0	Q118+V264	M105+L235	W167+V238	V215+S376	V291+G346
Q11+G25	Q118+A265	M105+V238	W167+M246	V215+D377	V291+G348
5	Q118+Y267	M105+M246	W167+M248	V215+D379	V291+T355
Q11+Q25	Q118+N270	M105+M248	W167+L250	V215+Y382	V291+S376
6	Q118+G273	M105+L250	W167+G255	V215+S383	V291+D377
Q11+A26	Q118+S280	M105+G255	W167+Q256	V215+Q385	V291+D379
3	Q118+T285	M105+Q256	W167+A263	V215+K391	V291+Y382
Q11+V26	Q118+M286	M105+A263	W167+V264	V215+K393	V291+S383
4	Q118+F289	M105+V264	W167+A265	V215+Q395	V291+Q385
Q11+A26	Q118+V291	M105+A265	W167+Y267	L217+L219	V291+K391
5	Q118+Q299	M105+Y267	W167+N270	L217+L228	V291+K393
Q11+Y26	Q118+S304	M105+N270	W167+G273	L217+L235	V291+Q395
7	Q118+R320	M105+G273	W167+S280	L217+V238	Q299+S304
Q11+N27	Q118+H321	M105+S280	W167+T285	L217+M246	Q299+R320
0	Q118+S323	M105+T285	W167+M286	L217+M248	Q299+H321
Q11+G27	Q118+H324	M105+M286	W167+F289	L217+L250	Q299+S323
3	Q118+F328	M105+F289	W167+V291	L217+G255	Q299+H324
Q11+S28	Q118+T334	M105+V291	W167+Q299	L217+Q256	Q299+F328
0	Q118+D337	M105+Q299	W167+S304	L217+A263	Q299+T334
Q11+T28	Q118+Q345	M105+S304	W167+R320	L217+V264	Q299+D337
5	Q118+G346	M105+R320	W167+H321	L217+A265	Q299+Q345
Q11+M28	Q118+G348	M105+H321	W167+S323	L217+Y267	Q299+G346
6	Q118+T355	M105+S323	W167+H324	L217+N270	Q299+G348
Q11+F28	Q118+S376	M105+H324	W167+F328	L217+G273	Q299+T355
9	Q118+D377	M105+F328	W167+T334	L217+S280	Q299+S376
Q11+V29	Q118+D379	M105+T334	W167+D337	L217+T285	Q299+D377
1	Q118+Y382	M105+D337	W167+Q345	L217+M286	Q299+D379

Q11+Q29	Q118+S383	M105+Q345	W167+G346	L217+F289	Q299+Y382
9	Q118+Q385	M105+G346	W167+G348	L217+V291	Q299+S383
Q11+S30	Q118+K391	M105+G348	W167+T355	L217+Q299	Q299+Q385
4	Q118+K393	M105+T355	W167+S376	L217+S304	Q299+K391
Q11+R32	Q118+Q395	M105+S376	W167+D377	L217+R320	Q299+K393
0	Q125+G133	M105+D377	W167+D379	L217+H321	Q299+Q395
Q11+H32	Q125+T134	M105+D379	W167+Y382	L217+S323	S304+R320
1	Q125+W140	M105+Y382	W167+S383	L217+H324	S304+H321
Q11+S32	Q125+G142	M105+S383	W167+Q385	L217+F328	S304+S323
3	Q125+G149	M105+Q385	W167+K391	L217+T334	S304+H324
Q11+H32	Q125+T165	M105+K391	W167+K393	L217+D337	S304+F328
4	Q125+W167	M105+K393	W167+Q395	L217+Q345	S304+T334
Q11+F32	Q125+R171	M105+Q395	R171+Q172	L217+G346	S304+D337
8	Q125+Q172	G109+F113	R171+L173	L217+G348	S304+Q345
Q11+T33	Q125+L173	G109+R116	R171+A174	L217+T355	S304+G346
4	Q125+A174	G109+Q118	R171+G184	L217+S376	S304+G348
Q11+D33	Q125+G184	G109+Q125	R171+T193	L217+D377	S304+T355
7	Q125+T193	G109+G133	R171+N195	L217+D379	S304+S376
Q11+Q34	Q125+N195	G109+T134	R171+G196	L217+Y382	S304+D377
5	Q125+G196	G109+W140	R171+A204	L217+S383	S304+D379
Q11+G34	Q125+A204	G109+G142	R171+V206	L217+Q385	S304+Y382
6	Q125+V206	G109+G149	R171+P211	L217+K391	S304+S383
Q11+G34	Q125+P211	G109+T165	R171+I214	L217+K393	S304+Q385
8	Q125+I214	G109+W167	R171+V215	L217+Q395	S304+K391
Q11+T35	Q125+V215	G109+R171	R171+L217	L219+L228	S304+K393
5	Q125+L217	G109+Q172	R171+L219	L219+L235	S304+Q395
Q11+S37	Q125+L219	G109+L173	R171+L228	L219+V238	R320+H321
6	Q125+L228	G109+A174	R171+L235	L219+M246	R320+S323
Q11+D37	Q125+L235	G109+G184	R171+V238	L219+M248	R320+H324
7	Q125+V238	G109+T193	R171+M246	L219+L250	R320+F328
Q11+D37	Q125+M246	G109+N195	R171+M248	L219+G255	R320+T334
9	Q125+M248	G109+G196	R171+L250	L219+Q256	R320+D337

Q11+Y38	Q125+L250	G109+A204	R171+G255	L219+A263	R320+Q345
2	A37+Q395	G109+V206	R171+Q256	L219+V264	R320+G346
Q11+S38	T40+P45	G109+P211	R171+A263	L219+A265	R320+G348
3	T40+W48	G109+I214	R171+V264	L219+Y267	R320+T355
Q11+Q38	T40+G50	G109+V215	R171+A265	L219+N270	R320+S376
5	T40+T51	G109+L217	R171+Y267	L219+G273	R320+D377
Q11+K39	T40+N54	G109+L219	R171+N270	L219+S280	R320+D379
1	T40+V56	G109+L228	R171+G273	L219+T285	R320+Y382
Q11+K39	T40+A60	G109+L235	R171+S280	L219+M286	R320+S383
3	T40+K72	G109+V238	R171+T285	L219+F289	R320+Q385
Q11+Q39	T40+R87	G109+M246	R171+M286	L219+V291	R320+K391
5	T40+Q98	G109+M248	R171+F289	L219+Q299	R320+K393
N16+V17	T40+M105	G109+L250	R171+V291	L219+S304	R320+Q395
N16+Q32	T40+G109	G109+G255	R171+Q299	L219+R320	H321+S323
N16+A37	T40+F113	G109+Q256	R171+S304	L219+H321	H321+H324
N16+T40	T40+R116	G109+A263	R171+R320	L219+S323	H321+F328
N16+P45	T40+Q118	G109+V264	R171+H321	L219+H324	H321+T334
N16+W48	T40+Q125	G109+A265	R171+S323	L219+F328	H321+D337
N16+G50	T40+G133	G109+Y267	R171+H324	L219+T334	H321+Q345
N16+T51	T40+T134	G109+N270	R171+F328	L219+D337	H321+G346
N16+N54	T40+W140	G109+G273	R171+T334	L219+Q345	H321+G348
N16+V56	T40+G142	G109+S280	R171+D337	L219+G346	H321+T355
N16+A60	T40+G149	G109+T285	R171+Q345	L219+G348	H321+S376
N16+K72	T40+T165	G109+M286	R171+G346	L219+T355	H321+D377
N16+R87	T40+W167	G109+F289	R171+G348	L219+S376	H321+D379
N16+Q98	T40+R171	G109+V291	R171+T355	L219+D377	H321+Y382
N16+M10	T40+Q172	G109+Q299	R171+S376	L219+D379	H321+S383
5	T40+L173	G109+S304	R171+D377	L219+Y382	H321+Q385
N16+G10	T40+A174	G109+R320	R171+D379	L219+S383	H321+K391
9	T40+G184	G109+H321	R171+Y382	L219+Q385	H321+K393
N16+F11	T40+T193	G109+S323	R171+S383	L219+K391	H321+Q395
3	T40+N195	G109+H324	R171+Q385	L219+K393	S323+H324

N16+R11	T40+G196	G109+F328	R171+K391	L219+Q395	S323+F328
6	T40+A204	G109+T334	R171+K393	L228+L235	S323+T334
N16+Q11	T40+V206	G109+D337	R171+Q395	L228+V238	S323+D337
8	T40+P211	G109+Q345	Q172+L173	L228+M246	S323+Q345
N16+Q12	T40+I214	G109+G346	Q172+A174	L228+M248	S323+G346
5	T40+V215	G109+G348	Q172+G184	L228+L250	S323+G348
N16+G13	H1+Q169	G109+T355	Q172+T193	L228+G255	S323+T355
3	H1+A186	G109+S376	Q172+N195	L228+Q256	S323+S376
N16+T13	H1+E190	G109+D377	Q172+G196	L228+A263	S323+D377
4	H1+A225	G109+D379	Q172+A204	L228+V264	S323+D379
N16+W14	H1+K242	G109+Y382	Q172+V206	L228+A265	S323+Y382
0	H1+S244	G109+S383	Q172+P211	L228+Y267	S323+S383
N16+G14	H1+N260	G109+Q385	Q172+I214	L228+N270	S323+Q385
2	H1+K269	G109+K391	Q172+V215	L228+G273	S323+K391
N16+G14	H1+W284	G109+K393	Q172+L217	L228+S280	S323+K393
9	H1+Y295	G109+Q395	Q172+L219	L228+T285	S323+Q395
N16+T16	H1+V326	F113+R116	Q172+L228	L228+M286	H324+F328
5	T5+Q169	F113+Q118	Q172+L235	L228+F289	H324+T334
N16+W16	T5+A186	F113+Q125	Q172+V238	L228+V291	H324+D337
7	T5+E190	F113+G133	Q172+M246	L228+Q299	H324+Q345
N16+R17	T5+A225	F113+T134	Q172+M248	L228+S304	H324+G346
1	T5+K242	F113+W140	Q172+L250	L228+R320	H324+G348
N16+Q17	T5+S244	F113+G142	Q172+G255	L228+H321	H324+T355
2	T5+N260	F113+G149	Q172+Q256	L228+S323	H324+S376
N16+L17	T5+K269	F113+T165	Q172+A263	L228+H324	H324+D377
3	T5+W284	F113+W167	Q172+V264	L228+F328	H324+D379
N16+A17	T5+Y295	F113+R171	Q172+A265	L228+T334	H324+Y382
4	T5+V326	F113+Q172	Q172+Y267	L228+D337	H324+S383
N16+G18	G7+Q169	F113+L173	Q172+N270	L228+Q345	H324+Q385
4	G7+A186	F113+A174	Q172+G273	L228+G346	H324+K391
N16+T19	G7+E190	F113+G184	Q172+S280	L228+G348	H324+K393
3	G7+A225	F113+T193	Q172+T285	L228+T355	H324+Q395

N16+N19	G7+K242	F113+N195	Q172+M286	L228+S376	F328+T334
5	G7+S244	F113+G196	Q172+F289	L228+D377	F328+D337
N16+G19	G7+N260	F113+A204	Q172+V291	L228+D379	F328+Q345
6	G7+K269	F113+V206	Q172+Q299	L228+Y382	F328+G346
N16+A20	G7+W284	F113+P211	Q172+S304	L228+S383	F328+G348
4	G7+Y295	F113+I214	Q172+R320	L228+Q385	F328+T355
N16+V20	G7+V326	F113+V215	Q172+H321	L228+K391	F328+S376
6	Q11+Q169	F113+L217	Q172+S323	L228+K393	F328+D377
N16+P21	Q11+A186	F113+L219	Q172+H324	L228+Q395	F328+D379
1	Q11+E190	F113+L228	Q172+F328	L235+V238	F328+Y382
N16+I21	Q11+A225	F113+L235	Q172+T334	L235+M246	F328+S383
4	Q11+K242	F113+V238	Q172+D337	L235+M248	F328+Q385
N16+V21	Q11+S244	F113+M246	Q172+Q345	L235+L250	F328+K391
5	Q11+N260	F113+M248	Q172+G346	L235+G255	F328+K393
N16+L21	Q11+K269	F113+L250	Q172+G348	L235+Q256	F328+Q395
7	Q11+W284	F113+G255	Q172+T355	L235+A263	T334+D337
N16+L21	Q11+Y295	F113+Q256	Q172+S376	L235+V264	T334+Q345
9	Q11+V326	F113+A263	Q172+D377	L235+A265	T334+G346
N16+L22	N16+Q169	F113+V264	Q172+D379	L235+Y267	T334+G348
8	N16+A186	F113+A265	Q172+Y382	L235+N270	T334+T355
N16+L23	N16+E190	F113+Y267	Q172+S383	L235+G273	T334+S376
5	N16+A225	F113+N270	Q172+Q385	L235+S280	T334+D377
N16+V23	N16+K242	F113+G273	Q172+K391	L235+T285	T334+D379
8	N16+S244	F113+S280	Q172+K393	L235+M286	T334+Y382
N16+M24	N16+N260	F113+T285	Q172+Q395	L235+F289	T334+S383
6	N16+K269	F113+M286	L173+A174	L235+V291	T334+Q385
N16+M24	N16+W284	F113+F289	L173+G184	L235+Q299	T334+K391
8	N16+Y295	F113+V291	L173+T193	L235+S304	T334+K393
N16+L25	N16+V326	F113+Q299	L173+N195	L235+R320	T334+Q395
0	V17+Q169	F113+S304	L173+G196	L235+H321	D337+Q345
N16+G25	V17+A186	F113+R320	L173+A204	L235+S323	D337+G346
5	V17+E190	F113+H321	L173+V206	L235+H324	D337+G348

N16+Q25	V17+A225	F113+S323	L173+P211	L235+F328	D337+T355
6	V17+K242	F113+H324	L173+I214	L235+T334	D337+S376
N16+A26	V17+S244	F113+F328	L173+V215	L235+D337	D337+D377
3	V17+N260	F113+T334	L173+L217	L235+Q345	D337+D379
N16+V26	V17+K269	F113+D337	L173+L219	L235+G346	D337+Y382
4	V17+W284	F113+Q345	L173+L228	L235+G348	D337+S383
N16+A26	V17+Y295	F113+G346	L173+L235	L235+T355	D337+Q385
5	V17+V326	F113+G348	L173+V238	L235+S376	D337+K391
N16+Y26	Q32+Q169	F113+T355	L173+M246	L235+D377	D337+K393
7	Q32+A186	F113+S376	L173+M248	L235+D379	D337+Q395
N16+N27	Q32+E190	F113+D377	L173+L250	L235+Y382	Q345+G346
0	Q32+A225	F113+D379	L173+G255	L235+S383	Q345+G348
N16+G27	Q32+K242	F113+Y382	L173+Q256	L235+Q385	Q345+T355
3	Q32+S244	F113+S383	L173+A263	L235+K391	Q345+S376
N16+S28	Q32+N260	F113+Q385	L173+V264	L235+K393	Q345+D377
0	Q32+K269	F113+K391	L173+A265	L235+Q395	Q345+D379
N16+T28	Q32+W284	F113+K393	L173+Y267	V238+M246	Q345+Y382
5	Q32+Y295	F113+Q395	L173+N270	V238+M248	Q345+S383
N16+M28	Q32+V326	R116+Q118	L173+G273	V238+L250	Q345+Q385
6	A37+Q169	R116+Q125	L173+S280	V238+G255	Q345+K391
N16+F28	A37+A186	R116+G133	L173+T285	V238+Q256	Q345+K393
9	A37+E190	R116+T134	L173+M286	V238+A263	Q345+Q395
N16+V29	A37+A225	R116+W140	L173+F289	V238+V264	G346+G348
1	A37+K242	R116+G142	L173+V291	V238+A265	G346+T355
N16+Q29	A37+S244	R116+G149	L173+Q299	V238+Y267	G346+S376
9	A37+N260	R116+T165	L173+S304	V238+N270	G346+D377
N16+S30	A37+K269	R116+W167	L173+R320	V238+G273	G346+D379
4	A37+W284	R116+R171	L173+H321	V238+S280	G346+Y382
N16+R32	A37+Y295	R116+Q172	L173+S323	V238+T285	G346+S383
0	A37+V326	R116+L173	L173+H324	V238+M286	G346+Q385
N16+H32	T40+Q169	R116+A174	L173+F328	V238+F289	G346+K391
1	T40+A186	R116+G184	L173+T334	V238+V291	G346+K393

N16+S32	T40+E190	R116+T193	L173+D337	V238+Q299	G346+Q395
3	T40+A225	R116+N195	L173+Q345	V238+S304	G348+T355
N16+H32	T40+K242	R116+G196	L173+G346	V238+R320	G348+S376
4	T40+S244	R116+A204	L173+G348	V238+H321	G348+D377
N16+F32	T40+N260	R116+V206	L173+T355	V238+S323	G348+D379
8	T40+K269	R116+P211	L173+S376	V238+H324	G348+Y382
N16+T33	T40+W284	R116+I214	L173+D377	V238+F328	G348+S383
4	T40+Y295	R116+V215	L173+D379	V238+T334	G348+Q385
N16+D33	T40+V326	R116+L217	L173+Y382	V238+D337	G348+K391
7	P45+Q169	R116+L219	L173+S383	V238+Q345	G348+K393
N16+Q34	P45+A186	R116+L228	L173+Q385	V238+G346	G348+Q395
5	P45+E190	R116+L235	L173+K391	V238+G348	T355+S376
N16+G34	P45+A225	R116+V238	L173+K393	V238+T355	T355+D377
6	P45+K242	R116+M246	L173+Q395	V238+S376	T355+D379
N16+G34	P45+S244	R116+M248	A174+G184	V238+D377	T355+Y382
8	P45+N260	R116+L250	A174+T193	V238+D379	T355+S383
N16+T35	P45+K269	R116+G255	A174+N195	V238+Y382	T355+Q385
5	P45+W284	R116+Q256	A174+G196	V238+S383	T355+K391
N16+S37	P45+Y295	R116+A263	A174+A204	V238+Q385	T355+K393
6	P45+V326	R116+V264	A174+V206	V238+K391	T355+Q395
N16+D37	W48+Q169	R116+A265	A174+P211	V238+K393	S376+D377
7	W48+A186	R116+Y267	A174+I214	V238+Q395	S376+D379
N16+D37	W48+E190	R116+N270	A174+V215	M246+M248	S376+Y382
9	W48+A225	R116+G273	A174+L217	M246+L250	S376+S383
N16+Y38	W48+K242	R116+S280	A174+L219	M246+G255	S376+Q385
2	W48+S244	R116+T285	A174+L228	M246+Q256	S376+K391
N16+S38	W48+N260	R116+M286	A174+L235	M246+A263	S376+K393
3	W48+K269	R116+F289	A174+V238	M246+V264	S376+Q395
N16+Q38	W48+W284	R116+V291	A174+M246	M246+A265	D377+D379
5	W48+Y295	R116+Q299	A174+M248	M246+Y267	D377+Y382
N16+K39	W48+V326	R116+S304	A174+L250	M246+N270	D377+S383
1	G50+Q169	R116+R320	A174+G255	M246+G273	D377+Q385

N16+K39	G50+A186	R116+H321	A174+Q256	M246+S280	D377+K391
3	G50+E190	R116+S323	A174+A263	M246+T285	D377+K393
N16+Q39	G50+A225	R116+H324	A174+V264	M246+M286	D377+Q395
5	G50+K242	R116+F328	A174+A265	M246+F289	D379+Y382
V17+Q32	G50+S244	R116+T334	A174+Y267	M246+V291	D379+S383
V17+A37	G50+N260	R116+D337	A174+N270	M246+Q299	D379+Q385
V17+T40	G50+K269	R116+Q345	A174+G273	M246+S304	D379+K391
V17+P45	G50+W284	R116+G346	A174+S280	M246+R320	D379+K393
V17+W48	G50+Y295	R116+G348	A174+T285	M246+H321	D379+Q395
V17+G50	G50+V326	R116+T355	A174+M286	M246+S323	Y382+S383
V17+T51	T51+Q169	R116+S376	A174+F289	M246+H324	Y382+Q385
V17+N54	T51+A186	R116+D377	A174+V291	M246+F328	Y382+K391
V17+V56	T51+E190	R116+D379	A174+Q299	M246+T334	Y382+K393
V17+A60	T51+A225	R116+Y382	A174+S304	M246+D337	Y382+Q395
V17+K72	T51+K242	R116+S383	A174+R320	M246+Q345	S383+Q385
V17+R87	T51+S244	R116+Q385	A174+H321	M246+G346	S383+K391
V17+Q98	T51+N260	R116+K391	A174+S323	M246+G348	S383+K393
V17+M10	T51+K269	R116+K393	A174+H324	M246+T355	S383+Q395
5	T51+W284	R116+Q395	A174+F328	M246+S376	Q385+K391
V17+G10	T51+Y295	Q118+Q125	A174+T334	M246+D377	Q385+K393
9	T51+V326	Q118+G133	A174+D337	M246+D379	Q385+Q395
V17+F11	N54+Q169	Q118+T134	A174+Q345	M246+Y382	K391+K393
3	N54+A186	Q118+W140	A174+G346	M246+S383	K391+Q395
V17+R11	N54+E190	Q118+G142	A174+G348	M246+Q385	K393+Q395
6	N54+A225	Q118+G149	A174+T355	M246+K391	M248+F289
V17+Q11	N54+K242	Q118+T165	A174+S376	M246+K393	M248+V291
8	N54+S244	Q118+W167	A174+D377	M246+Q395	G109+Q169
V17+Q12	N54+N260	Q118+R171	A174+D379	M248+L250	G109+A186
5	N54+K269	Q118+Q172	A174+Y382	M248+G255	G109+E190
V17+G13	N54+W284	Q118+L173	A174+S383	M248+Q256	G109+A225
3	N54+Y295	Q118+A174	A174+Q385	M248+A263	G109+K242
V17+T13	N54+V326	Q118+G184	A174+K391	M248+V264	G109+S244

4	V56+Q169	Q118+T193	A174+K393	M248+A265	G109+N260
V17+W14	V56+A186	Q118+N195	A174+Q395	M248+Y267	G109+K269
0	V56+E190	Q118+G196	G184+T193	M248+N270	G109+W284
V17+G14	V56+A225	Q118+A204	G184+N195	M248+G273	G109+Y295
2	V56+K242	Q118+V206	G184+G196	M248+S280	G109+V326
V17+G14	V56+S244	Q118+P211	G184+A204	M248+T285	F113+Q169
9	V56+N260	Q118+I214	G184+V206	M248+M286	F113+A186
V17+T16	V56+K269	G133+Q169	W167+Q169	R171+A186	F113+A225
5	V56+W284	G133+A186	W167+A186	R171+E190	F113+E190
V17+W16	V56+Y295	G133+E190	W167+E190	R171+A225	F113+K242
7	V56+V326	G133+A225	W167+A225	R171+K242	F113+S244
V17+R17	G184+A186	G133+K242	W167+K242	R171+S244	F113+N260
1	G184+E190	G133+S244	W167+S244	R171+N260	F113+K269
V17+Q17	G184+A225	G133+N260	W167+N260	R171+K269	F113+W284
2	G184+K242	G133+K269	W167+K269	R171+W284	F113+Y295
V17+L17	G184+S244	G133+W284	W167+W284	R171+Y295	F113+V326
3	G184+N260	G133+Y295	W167+Y295	R171+V326	R116+Q169
V17+A17	G184+K269	G133+V326	W167+V326	Q172+A186	R116+A186
4	G184+W284	T134+Q169	Q169+A186	Q172+E190	R116+E190
V17+G18	G184+Y295	T134+A186	Q169+E190	Q172+A225	R116+A225
4	G184+V326	T134+E190	Q169+L173	Q172+K242	R116+K242
V17+T19	A186+E190	T134+A225	Q169+A174	Q172+S244	R116+S244
3	A186+T193	T134+K242	Q169+G184	Q172+N260	R116+N260
V17+N19	A186+N195	T134+S244	Q169+T193	Q172+K269	R116+K269
5	A186+G196	T134+N260	Q169+N195	Q172+W284	R116+W284
V17+G19	A186+A204	T134+K269	Q169+G196	Q172+Y295	R116+Y295
6	A186+V206	T134+W284	Q169+A204	Q172+V326	R116+V326
V17+A20	A186+P211	T134+Y295	Q169+V206	L173+A186	Q118+Q169
4	A186+I214	T134+V326	Q169+P211	L173+E190	Q118+A186
V17+V20	A186+V215	W140+Q169	Q169+I214	L173+A225	Q118+A225
6	A186+L217	W140+A186	Q169+V215	L173+K242	Q118+K242
V17+P21	A186+L219	W140+E190	Q169+L217	L173+S244	Q118+S244

1	A186+A225	W140+A225	Q169+L219	L173+N260	Q118+N260
V17+I21	A186+L228	W140+K242	Q169+A225	L173+K269	Q118+K269
4	A186+L235	W140+S244	Q169+L228	L173+W284	Q118+W284
V17+V21	A186+V238	W140+N260	Q169+L235	L173+Y295	Q118+Y295
5	A186+K242	W140+K269	Q169+V238	L173+V326	Q118+V326
V17+L21	A186+S244	W140+W284	Q169+K242	A174+A186	Q125+Q169
7	A186+M246	W140+Y295	Q169+S244	A174+E190	Q125+A186
V17+L21	A186+M248	W140+V326	Q169+M246	A174+A225	Q125+E190
9	A186+L250	G142+Q169	Q169+M248	A174+K242	Q125+A225
V17+L22	A186+G255	G142+A186	Q169+L250	A174+S244	Q125+K242
8	A186+Q256	G142+E190	Q169+G255	A174+N260	Q125+S244
V17+L23	A186+N260	G142+A225	Q169+Q256	A174+K269	Q125+N260
5	A186+A263	G142+K242	Q169+N260	A174+W284	Q125+K269
V17+V23	A186+V264	G142+S244	Q169+A263	A174+Y295	Q125+W284
8	A186+A265	G142+N260	Q169+V264	A174+V326	Q125+Y295
V17+M24	A186+Y267	G142+K269	Q169+A265	T193+A225	Q125+V326
6	A186+K269	G142+W284	Q169+Y267	T193+K242	V215+A225
V17+M24	A186+N270	G142+Y295	Q169+K269	T193+S244	V215+K242
8	A186+G273	G142+V326	Q169+N270	T193+N260	V215+S244
V17+L25	A186+S280	G149+Q169	Q169+G273	T193+K269	V215+N260
0	A186+W284	G149+A186	Q169+S280	T193+W284	V215+K269
V17+G25	A186+T285	G149+E190	Q169+W284	T193+Y295	V215+W284V
5	A186+M286	G149+A225	Q169+T285	T193+V326	215+Y295
V17+Q25	A186+F289	G149+K242	Q169+M286	N195+A225	V215+V326
6	A186+V291	G149+S244	Q169+F289	N195+K242	L217+A225
V17+A26	A186+Y295	G149+N260	Q169+V291	N195+S244	L217+K242
3	A186+Q299	G149+K269	Q169+Y295	N195+N260	L217+S244
V17+V26	A186+S304	G149+W284	Q169+Q299	N195+K269	L217+N260
4	A186+R320	G149+Y295	Q169+S304	N195+W284	L217+K269
V17+A26	A186+H321	G149+V326	Q169+R320	N195+Y295	L217+W284
5	A186+S323	T165+Q169	Q169+H321	N195+V326	L217+Y295
V17+Y26	A186+H324	T165+A186	Q169+S323	G196+A225	L217+V326

7	A186+V326	T165+E190	Q169+H324	G196+K242	L219+A225
V17+N27	A186+F328	T165+A225	Q169+V326	G196+K242	L219+K242
0	A186+T334	T165+K242	Q169+F328	G196+S244	L219+S244
V17+G27	A186+D337	T165+S244	Q169+T334	G196+N260	L219+N260
3	A186+Q345	T165+N260	Q169+D337	G196+K269	L219+K269
V17+S28	A186+G346	T165+K269	Q169+Q345	G196+W284	L219+W284
0	A186+G348	T165+W284	Q169+G346	G196+Y295	L219+Y295
V17+T28	A186+T355	T165+Y295	Q169+G348	G196+V326	L219+V326
5	A186+S376	T165+V326	Q169+T355	A204+A225	M246+N260
V17+M28	A186+D377	L228+K242	Q169+S376	A204+K242	M246+K269M
6	A186+D379	L228+S244	Q169+D377	A204+S244	246+W284
V17+F28	A186+Y382	L228+N260	Q169+D379	A204+N260	M246+Y295
9	A186+S383	L228+K269	Q169+Y382	A204+K269	M246+V326M
V17+V29	A186+Q385	L228+W284	Q169+S383	A204+W284	248+N260
1	A186+K391	L228+Y295	Q169+Q385	A204+Y295	M248+K269M
V17+Q29	A186+K393	L228+V326	Q169+K391	A204+V326	248+W284
9	A186+Q395	L235+K242	Q169+K393	V206+A225	M248+Y295M
V17+S30	E190+T193	L235+S244	Q169+Q395	A206+K242	248+V326L2
4	E190+N195	L235+N260	Q256+N260	A206+S244	50+N260
V17+R32	E190+G196	L235+K269	G256+K269	A206+N260	L250+K269
0	E190+A204	L235+W284	Q256+W284	A206+K269	L250+W284
V17+H32	E190+V206	L235+Y295	Q256+Y295	A206+W284	L250+Y295
1	E190+P211	L235+V326	Q256+V326	A206+Y295	L250+V326
V17+S32	E190+I214	V238+K242	N260+A263	A206+V326	G255+N260
3	E190+V215	V238+S244	N260+V264	P211+A225	G255+K269G
V17+H32	E190+L217	V238+N260	N260+A265	P211+K242	255+W284
4	E190+L219	V238+K269	N260+Y267	P211+S244	G255+Y295
V17+F32	E190+A225	V238+W284	N260+K269	P211+N206	G255+V326
8	E190+L228	V238+Y295	N260+N270	P211+K269	N270+W284
V17+T33	E190+L235	V238+V326	N260+G273	P211+W284	N270+Y295
4	E190+V238	K242+S244	N260+S280	P211+Y295	N270+V326G
V17+D33	E190+K242	K242+M246	N260+W284	P211+V326	273+W284

7	E190+S244	K242+M248	N260+T285	I214+A225	G273+Y295
V17+Q34	E190+M246	K242+L250	N260+M286	I214+K242	G273+V326
5	E190+M248	K242+G255	N260+F289	I214+S244	S280+W284S
V17+G34	E190+L250	K242+Q256	N260+V291	I214+N260	280+Y295
6	E190+G255	K242+N260	N260+Y295	I214+K269	S280+V326
V17+G34	E190+Q256	K242+A263	N260+Q299	I214+W284	W284+T285W
8	E190+N260	K242+V264	N260+S304	I214+Y295	284+M286
V17+T35	E190+A263	K242+A265	N260+R320	I214+V326	W284+F289
5	E190+V264	K242+Y267	N260+H321	K269+N270	W284+V291
V17+S37	E190+A265	K242+K269	N260+S323	K269+G273	W284+Y295
6	E190+Y267	K242+N270	N260+H324	K269+S280	W284+Q299
V17+D37	E190+K269	K242+G273	N260+V326	K269+W284	W284+S304
7	E190+N270	K242+S280	N260+F328	K269+T285	W284+R320
V17+D37	E190+G273	K242+W284	N260+T334	K269+M286	W284+H321
9	E190+S280	K242+T285	N260+D337	K269+F289	W284+S323
V17+Y38	E190+W284	K242+M286	N260+Q345	K269+V291	W284+H324
2	E190+T285	K242+F289	N260+G346	K269+Y295	W284+V326
V17+S38	E190+M286	K242+V291	N260+G348	K269+Q299	W284+F328
3	E190+F289	K242+Y295	N260+T355	K269+S304	W284+T334
V17+Q38	E190+V291	K242+Q299	N260+S376	K269+R320	W284+D337
5	E190+Y295	K242+S304	N260+D377	K269+H321	W284+Q345
V17+K39	E190+Q299	K242+R320	N260+D379	K269+S323	W284+G346
1	E190+S304	K242+H321	N260+Y382	K269+H324	W284+G348
V17+K39	E190+R320	K242+S323	N260+S383	K269+V326	W284+T355
3	E190+H321	K242+H324	N260+Q385	K269+F328	W284+S376
V17+Q39	E190+S323	K242+V326	N260+K391	K269+T334	W284+D377
5	E190+H324	K242+F328	N260+K393	K269+D337	W284+D379
Q32+A37	E190+V326	K242+T334	N260+Q395	K269+Q345	W284+Y382
Q32+T40	E190+F328	K242+D337	Y295+S376	K269+G346	W284+S383
Q32+P45	E190+T334	K242+Q345	V326+S376	K269+G348	W284+Q385
Q32+W48	E190+D337	K242+G346	V326+D377	K269+T355	W284+K391
Q32+G50	E190+Q345	K242+G348	V326+D379	K269+S376	W284+K393

Q32+T51	E190+G346	K242+T355	V326+Y382	K269+D377	W284+Q395T
Q32+N54	E190+G348	K242+S376	V326+S383	K269+D379	285+Y295
Q32+V56	E190+T355	K242+D377	V326+Q385	K269+Y382	T285+V326M
Q32+A60	E190+S376	K242+D379	V326+K391	K269+S383	286+Y295M2
Q32+K72	E190+D377	K242+Y382	V326+K393	K269+Q385	86+V326
Q32+R87	E190+D379	K242+S383	V326+Q395	K269+K391	F289+Y295
Q32+Q98	E190+Y382	K242+Q385	S244+K393	K269+K393	F289+V326
Q32+M10	E190+S383	K242+K391	S244+Q395	K269+Q395	V291+Y295
5	E190+Q385	K242+K393	S244+Y267	S244+R320	V294+V326
Q32+G10	E190+K391	K242+Q395	S244+K269	S244+H321	Y295+Q299Y
9	E190+K393	S244+M246	S244+N270	S244+S323	295+S304
Q32+F11	E190+Q395	S244+M248	S244+G273	S244+H324	Y295+R320
3	S244+F289	S244+L250	S244+S280	S244+V326	Y295+H321Y
Q32+R11	S244+V291	S244+G255	S244+W284	S244+F328	295+S323
6	S244+Y295	S244+Q256	S244+T285	S244+T334	Y295+H324
Q32+Q11	S244+Q299	S244+N260	S244+S376	S244+D337	Y295+V326
8	S244+S304	S244+A263	S244+D377	S244+Q345	Y295+F328
Q32+Q12	S244+K391	S244+V264	S244+D379	S244+G346	Y295+T334
5	S244+M286	S244+A265	S244+Y382	S244+G348	Y295+F328
Q32+G13	Y295+Q345		S244+S383	S244+T355	Y295+T334
3	Y295+G346		S244+Q385		Y295+D337
Q32+T13					
4					
Q32+W14					
0					
Q32+G14					
2					
Q32+G14					
9					
Q32+T16					
5					
Q32+W16					

7 Q32+R171 Q32+Q172 Q32+L173 Q32+A174 Q32+G184 Q32+T193 Q32+N195 Q32+G196 Q32+A204 Q32+V206 Q32+P211 Q32+I214 Q32+V215 Q32+L217 Q32+L219 Q32+L22					

8 Q32+L235 Q32+V238 Q32+M246 Q32+M248 Q32+L250 Q32+G255 Q32+Q256 Q32+A263 Q32+V264 Q32+A265 Q32+Y267 Q32+N270 Q32+G273 Q32+S280 Q32+T285 Q32+M28					

6 Q32+F28 9 Q32+V29 1 Q32+Q29 9 Q32+S30 4 Q32+R32 0 Q32+H32 1 Q32+S32 3 Q32+H32 4 Q32+F32 8 Q32+T33 4 Q32+D33 7 Q32+Q34 5 Q32+G34 6 Q32+G34 8 Q32+T35 5 Q32+S37					

6 Q32+D377 Q32+D379 Q32+Y382 Q32+S383 Q32+Q385 Q32+K391 Q32+K393 Q32+Q395 A37+T40 A37+P45 A37+W48 A37+G50 A37+T51 A37+N54 A37+V56 A37+A60 A37+K72 A37+R87 A37+Q98 A37+M105 A37+G109					

A37+F113 A37+R116 A37+Q118 A37+Q125 A37+G133 A37+T134 A37+W140 A37+G142 A37+G149 A37+T165 A37+W167 A37+R171 A37+Q172 A37+L173 A37+A174 A37+G184					

A37+T193 A37+N195 A37+G196 A37+A204 A37+V206 A37+P211 A37+I214 A37+V215 A37+L217 A37+L219 A37+L228 A37+L235 A37+V238 A37+M246 A37+M248 A37+L250					

A37+G255 A37+Q256 A37+A263 A37+V264 A37+A265 A37+Y267 A37+N270 A37+G273 A37+S280 A37+T285 A37+M286 A37+F289 A37+V291 A37+Q299 A37+S304 A37+R320					

A37+H321 A37+S323 A37+H324 A37+F328 A37+T334 A37+D337 A37+Q345 A37+G346 A37+G348 A37+T355 A37+S376 A37+D377 A37+D379 A37+Y382 A37+S383 A37+Q385					

A37+K391 A37+K393 A60+Q169 A60+A186 A60+E190 A60+A225 A60+K242 A60+S244 A60+N260 A60+K269 A60+W284 A60+Y295 A60+V326 K72+Q169 K72+A186 K72+E190					

K72+A225 K72+K242 K72+S244 K72+N260 K72+K269 K72+W284 K72+Y295 K72+V326 R87+Q169 R87+A186 R87+E190 R87+A225 R87+K242 R87+S244 R87+N260 R87+K269					

R87+W284 R87+Y295 R87+V326 Q98+Q169 Q98+A186 Q98+E190 Q98+A225 Q98+K242 Q98+S244 Q98+N260 Q98+K269 Q98+W284 Q98+Y295 Q98+V326 M105+Q169 M105+A186					

M105+E190 M105+A225 M105+K242 M105+S244 M105+N260 M105+K269 M105+W284 M105+Y295 M105+V326 A225+L228 A225+L235 A225+V238 A225+K242 A225+S244 A225+M246 A225+M248					

A225+L250 A225+G255 A225+Q256 A225+N260 A225+A263 A225+V264 A225+A265 A225+Y267 A225+K269 A225+N270 A225+G273 A225+S280 A225+W284 A225+T285 A225+M286 A225+F289					

A225+V291 A225+Y295 A225+Q299 A225+S304 A225+R320 A225+H321 A225+S323 A225+H324 A225+V326 A225+F328 A225+T334 A225+D337 A225+Q345 A225+G346 A225+G348 A225+T355					

A225+S376 A225+D377 A225+D379 A225+Y382 A225+S383 A225+Q385 A225+K391 A225+K393 A225+Q395 A263+K269 A263+W284 A263+Y295 A263+V326 V264+K269 V264+W284 V264+Y295					

V264+V326 A265+K269 A265+W284 A265+Y295 A265+V326 A265+K269 A265+W284 A265+Y295 A265+V326 Y295+D377 Y295+D379 Y295+Y382 Y295+S383 Y295+Q385 Y295+K391 Y295+K393					

Y295+Q3 95 Q299+V3 26 S304+V3 26 R320+V3 26 H321+V3 26 S323+V3 26 H324+V3 26 V326+F3 28 V326+T3 34 V326+D3 37 V326+Q3 45 V326+G3 46 V326+G3 48 V326+T3 55 Y295+G3 48 Y295+T3 55					

En una realización particular, las modificaciones en una o más posiciones corresponden a las siguientes; H1*, T5K, G7K, G7A, Q11H, N16S, N16H, V17L, Q32S, A37H, A37M, A37V, A37S, A37Y, A37R, A37L, T40D, T40G, T40K, P45A, W48G, W48Y, W48F, G50A, T51K, T51E, T51G, T51A, T51S, T51G, T51D, N54S, V56T, A60V,K72R, K72H, K72S, K72Q, K72E, K72N, K72A, K72M, R87S, Q98S, Q98A, M105F, M105I, M105V, M105L, G109A, G109S, F113W, F113S, F113N, F113Y, F113R, F113L, F113Q, R116Q, R116V, R116K, R116W, R116L, R116A, R116H, R116M, R116E, R116S, R116I, R116G, Q118N, Q118K, Q118G, Q118S, Q118F, Q118R, Q125P, Q125K, Q125A, Q125T, N125D, G133S, F133Q, T134E, W140Y, G142T, G149Q, T165S, T165G, T165V, W167I, W167G, W167F, W167R, W167S, W167H, W167L, W167M, W167Y, Q169E, R171H, Q172G, Q172R, Q172N, Q172D, Q172Y, Q172M, Q172S, Q172T, Q172K, Q172H, Q172E, L173V, L173G, L173H, L173A, L173I, L173P, L173T, L173F, L173M, A174S, A174D, A174P, A174M, A174T, A174H, A174K, A174G, A174Q, A174N, A174V, A174L, G184T, A186D, A186N, A186E, A186Q, A186H, E190P, T193K, N195F, G196R, A204T, A204V, A204S, A204G, V206L, V206S, V206Y, P211D, I214G, I214H, I214S, I214T, I214L, I214E, I214W, V215T, L217T, L217Q, L219V, L219H, A225V, L228I, L235V, L235A, V238A, V238T, V238G, K242Q, S244Q, M246L, M246A, M246I, M246F, M246V, M246S, M248T, L250I, L250V, L250T, L250A, L250F, L250M, G255N, G255A, G255A, Q256A, N260G, A263G, V264I, V264T, A265G, Y267I, Y267M, Y267H, Y267L, K269Q, N270G, N270T, G273R, S280W, S280L, S280T, S280A, S280K, S280Q, W284H, T285L, T285Q, M286F, M286L, A288L, A288V, F289I, F289L, V291G, V291A, V291T, Y295N, Y295F, Q299V, S304N, S304R, R320A, R320V, H321Y, S323N, H324L, V326L, F328L, F328M, F328V, F328I, T334S, D337H, Q345D, G346T, G346D, G346P, G348S, G348P, T355L, T355F, S376H, S376T, S376V, D377H, D377S, D377A, D377Q, D379S, D379G, D379R, D379A, Y382M, Y382I,

Y382L, Y382F, S383G, S383A, Q385L, K391A, K391Y, K391V, K391M, K391E, K391D, K391R, K391H, K391W, K391I, K391Q, K391L, K393Y, K393R, K393Q, K393S, y Q395P, en donde dichas posiciones corresponden a posiciones de las SEQ ID NO: 7 o 10.

Los inventores de la presente invención han identificado que estas alteraciones específicas dentro del dominio A y B (como se define por la SEQ ID NO: 10) de la secuencia de aminoácidos expuesta en las SEQ ID NO: 7 y 10 son particularmente relevantes para mejorar el rendimiento de una alfa-amilasa variante que tiene al menos un 65% de identidad de secuencia con el polipéptido parental.

En una realización, la variante comprende una alteración en dos, tres, cuatro, cinco, seis, siete, ocho, nueve, diez, once, doce, trece, catorce, quince, dieciséis o diecisiete posiciones correspondientes a las siguientes posiciones; H1*, T5K, G7K, G7A, Q11H, N16S, N16H, V17L, Q32S, A37H, A37M, A37V, A37S, A37Y, A37R, A37L, T40D, T40G, T40K, P45A, W48G, W48Y, W48F, G50A, T51K, T51E, T51G, T51A, T51S, T51G, T51D, N54S, V56T, A60V,K72R, K72H, K72S, K72Q, K72E, K72N, K72A, K72M, R87S, Q98S, Q98A, M105F, M105I, M105V, M105L, G109A, G109S, F113W, F113S, F113N, F113Y, F113R, F113L, F113Q, R116Q, R116V, R116K, R116W, R116L, R116A, R116H, R116M, R116E, R116S, R116I, R116G, Q118N, Q118K, Q118G, Q118S, Q118F, Q118R, Q125P, Q125K, Q125A, Q125T, N125D, G133S, F133Q, T134E, W140Y, G142T, G149Q, T165S, T165G, T165V, W167I, W167G, W167F, W167R, W167S, W167H, W167L, W167M, W167Y, Q169E, R171H, Q172G, Q172R, Q172N, Q172D, Q172Y, Q172M, Q172S, Q172T, Q172K, Q172H, Q172E, L173V, L173G, L173H, L173A, L173I, L173P, L173T, L173F, L173M, A174S, A174D, A174P, A174M, A174T, A174H, A174K, A174G, A174Q, A174N, A174V, A174L, G184T, A186D, A186N, A186E, A186Q, A186H, E190P, T193K, N195F, G196R,

A204T, A204V, A204S, A204G, V206L, V206S, V206Y, P211D, I214G, I214H, I214S, I214T, I214L, I214E, I214W, V215T, L217T, L217Q, L219V, L219H, A225V, L228I, L235V, L235A, V238A, V238T, V238G, K242Q, S244Q, M246L, M246A, M246I, M246F, M246V, M246S, M248T, L250I, L250V, L250T, L250A, L250F, L250M, G255N, G255A, G255S, Q256A, N260G, A263G, V264I, V264T, A265G, Y267I, Y267M, Y267H, Y267L, K269Q, N270G, N270T, G273R, S280W, S280L, S280T, S280A, S280K, S280Q, W284H, T285L, T285Q, M286F, M286L, A288L, A288V, F289I, F289L, V291G, V291A, V291T, Y295N, Y295F, Q299V, S304N, S304R, R320A, R320V, H321Y, S323N, H324L, V326L, F328L, F328M, F328V, F328I, T334S, D337H, Q345D, G346T, G346D, G346P, G348S, G348P, T355L, T355F, S376H, S376T, S376V, D377H, D377S, D377A, D377Q, D379S, D379G, D379R, D379A, Y382M, Y382I, Y382L, Y382F, S383G, S383A, Q385L, K391A, K391Y, K391V, K391M, K391E, K391D, K391R, K391H, K391W, K391I, K391Q, K391L, K393Y, K393R, K393Q, K393S, y Q395P, en donde dichas posiciones corresponden a posiciones de las SEQ ID NO: 7 o 10.

El dominio C de una variante de acuerdo con la presente invención también puede comprender alteraciones. Por lo tanto, en una realización, la variante comprende una alteración en una o más posiciones de aminoácidos correspondientes a las posiciones de aminoácidos de la secuencia de aminoácidos expuesta en las SEQ ID NO: 11 o 12 o una secuencia de aminoácidos que tenga al menos un 65% de identidad de secuencia con una secuencia de aminoácidos expuesta en las SEQ ID NO: 11 o 12.

En una realización particular, el dominio C comprende una alteración en una o más de las siguientes posiciones correspondientes a las posiciones; A420, G423, T444, A445, Q449, T459, P473, C474, G476, G477 y K484 de la SEQ ID NO:

13 o I405, A421, A422, A428, R439 G448, W467, D476 y G477 de la SEQ ID NO: 14.

En una realización, la variante comprende una alteración en dos, tres, cuatro, cinco, seis, siete u ocho posiciones correspondientes a las siguientes posiciones; A420, G423, T444, A445, Q449, T459, P473, C474, G476, G477 y K484 de la SEQ ID NO: 13 o I405, A421, A422, A428, R439 G448, W467, D476 y G477 de la SEQ ID NO: 14.

Los inventores de la presente invención han identificado que algunas sustituciones de aminoácidos específicas dentro del dominio C de un polipéptido parental tienen un efecto mejorado en el rendimiento de las variantes. Po lo tanto, en una realización particular, la alteración en una o más posiciones corresponde a las siguientes T400P, H402R, A420Q, A420S, A420K, A420L, G423H, T444Q, T444S, T444D, T444Y, T444H, T444V, T444R, T444A, A445Q, Q449T, T459N, P473R, P473A, P473G, P473T, P473K, C474V, G476K, G477A, G477Q, K484A, K484G, K484P, K484E, K484Q, y K484S, en donde dichas posiciones corresponden a posiciones de la SEQ ID NO: 13; o I405L, A421H, A422P, A428T, G448D, D476K, D476G, D476N, D476Y, G477S, G477A, G477T, y G477Q, en donde dichas posiciones corresponden a posiciones de la SEQ ID NO: 14.

En una realización particular, la variante comprende una modificación en las siguientes posiciones;

H1+T5	T40+A174	R87+N270	W140+K39	V206+V21	Y267+C47
H1+G7	T40+G184	R87+G273	3	5	4
H1+Q11	T40+T193	R87+S280	W140+Q39	V206+L21	Y267+G47
H1+N16	T40+N195	R87+T285	5	7	6
H1+V17	T40+A204	R87+M286	W140+A42	V206+L21	Y267+G47
H1+Q32	T40+V206	R87+F289	0	9	7
H1+A37	T40+P211	R87+V291	W140+G42	V206+L23	Y267+K48

H1+T40	T40+I214	R87+Q299	3	5	4
H1+P45	T40+V215	R87+R320	W140+T44	V206+V23	N270+G27
H1+W48	T40+L217	R87+H321	4	8	3
H1+G50	T40+L219	R87+S323	W140+A44	V206+M24	N270+S28
H1+T51	T40+L235	R87+H324	5	6	0
H1+N54	T40+V238	R87+F328	W140+Q44	V206+M24	N270+T28
H1+V56	T40+M246	R87+T334	9	8	5
H1+K72	T40+M248	R87+D337	W140+T45	V206+L25	N270+M28
H1+R87	T40+L250	R87+Q345	9	0	6
H1+Q98	T40+G255	R87+G346	W140+P47	V206+G25	N270+F28
H1+M105	T40+Q256	R87+G348	3	5	9
H1+G109	T40+A263	R87+T355	W140+C47	V206+Q25	N270+V29
H1+F113	T40+V264	R87+S376	4	6	1
H1+R116	T40+Y267	R87+D377	W140+G47	V206+A26	N270+Q29
H1+Q118	T40+N270	R87+D379	6	3	9
H1+Q125	T40+G273	R87+Y382	W140+G47	V206+V26	N270+R32
H1+G133	T40+S280	R87+S383	7	4	0
H1+T134	T40+T285	R87+Q385	W140+K48	V206+Y26	N270+H32
H1+W140	T40+M286	R87+K391	4	7	1
H1+G142	T40+F289	R87+K393	G142+G14	V206+N27	N270+S32
H1+G149	T40+V291	R87+Q395	9	0	3
H1+T165	T40+Q299	R87+A420	G142+T16	V206+G27	N270+H32
H1+W167	T40+R320	R87+G423	5	3	4
H1+R171	T40+H321	R87+T444	G142+W16	V206+S28	N270+F32
H1+Q172	T40+S323	R87+A445	7	0	8
H1+L173	T40+H324	R87+Q449	G142+R17	V206+T28	N270+T33
H1+A174	T40+F328	R87+T459	1	5	4
H1+G184	T40+T334	R87+P473	G142+Q17	V206+M28	N270+D33
H1+T193	T40+D337	R87+C474	2	6	7
H1+N195	T40+Q345	R87+G476	G142+L17	V206+F28	N270+Q34
H1+A204	T40+G346	R87+G477	3	9	5
H1+V206	T40+G348	R87+K484	G142+A17	V206+V29	N270+G34

H1+P211	T40+T355	Q98+M105	4	1	6
H1+I214	T40+S376	Q98+G109	G142+G18	V206+Q29	N270+G34
H1+V215	T40+D377	Q98+F113	4	9	8
H1+L217	T40+D379	Q98+R116	G142+T19	V206+R32	N270+T35
H1+L219	T40+Y382	Q98+Q118	3	0	5
H1+L235	T40+S383	Q98+Q125	G142+N19	V206+H32	N270+S37
H1+V238	T40+Q385	Q98+G133	5	1	6
H1+M246	T40+K391	Q98+T134	G142+A20	V206+S32	N270+D37
H1+M248	T40+K393	Q98+W140	4	3	7
H1+L250	T40+Q395	Q98+G142	G142+V20	V206+H32	N270+D37
H1+G255	T40+A420	Q98+G149	6	4	9
H1+Q256	T40+G423	Q98+T165	G142+P21	V206+F32	N270+Y38
H1+A263	T40+T444	Q98+W167	1	8	2
H1+V264	T40+A445	Q98+R171	G142+I21	V206+T33	N270+S38
H1+Y267	T40+Q449	Q98+Q172	4	4	3
H1+N270	T40+T459	Q98+L173	G142+V21	V206+D33	N270+Q38
H1+G273	T40+P473	Q98+A174	5	7	5
H1+S280	T40+C474	Q98+G184	G142+L21	V206+Q34	N270+K39
H1+T285	T40+G476	Q98+T193	7	5	1
H1+M286	T40+G477	Q98+N195	G142+L21	V206+G34	N270+K39
H1+F289	T40+K484	Q98+A204	9	6	3
H1+V291	P45+W48	Q98+V206	G142+L23	V206+G34	N270+Q39
H1+Q299	P45+G50	Q98+P211	5	8	5
H1+R320	P45+T51	Q98+I214	G142+V23	V206+T35	N270+A42
H1+H321	P45+N54	Q98+V215	8	5	0
H1+S323	P45+V56	Q98+L217	G142+M24	V206+S37	N270+G42
H1+H324	P45+K72	Q98+L219	6	6	3
H1+F328	P45+R87	Q98+L235	G142+M24	V206+D37	N270+T44
H1+T334	P45+Q98	Q98+V238	8	7	4
H1+D337	P45+M105	Q98+M246	G142+L25	V206+D37	N270+A44
H1+Q345	P45+G109	Q98+M248	0	9	5
H1+G346	P45+F113	Q98+L250	G142+G25	V206+Y38	N270+Q44

H1+G348	P45+R116	Q98+G255	5	2	9
H1+T355	P45+Q118	Q98+Q256	G142+Q25	V206+S38	N270+T45
H1+S376	P45+Q125	Q98+A263	6	3	9
H1+D377	P45+G133	Q98+V264	G142+A26	V206+Q38	N270+P47
H1+D379	P45+T134	Q98+Y267	3	5	3
H1+Y382	P45+W140	Q98+N270	G142+V26	V206+K39	N270+C47
H1+S383	P45+G142	Q98+G273	4	1	4
H1+Q385	P45+G149	Q98+S280	G142+Y26	V206+K39	N270+G47
H1+K391	P45+T165	Q98+T285	7	3	6
H1+K393	P45+W167	Q98+M286	G142+N27	V206+Q39	N270+G47
H1+Q395	P45+R171	Q98+F289	0	5	7
H1+A420	P45+Q172	Q98+V291	G142+G27	V206+A42	N270+K48
H1+G423	P45+L173	Q98+Q299	3	0	4
H1+T444	P45+A174	Q98+R320	G142+S28	V206+G42	G273+S28
H1+A445	P45+G184	Q98+H321	0	3	0
H1+Q449	P45+T193	Q98+S323	G142+T28	V206+T44	G273+T28
H1+T459	P45+N195	Q98+H324	5	4	5
H1+P473	P45+A204	Q98+F328	G142+M28	V206+A44	G273+M28
H1+C474	P45+V206	Q98+T334	6	5	6
H1+G476	P45+P211	Q98+D337	G142+F28	V206+Q44	G273+F28
H1+G477	P45+I214	Q98+Q345	9	9	9
H1+K484	P45+V215	Q98+G346	G142+V29	V206+T45	G273+V29
T5+G7	P45+L217	Q98+G348	1	9	1
T5+Q11	P45+L219	Q98+T355	G142+Q29	V206+P47	G273+Q29
T5+N16	P45+L235	Q98+S376	9	3	9
T5+V17	P45+V238	Q98+D377	G142+R32	V206+C47	G273+R32
T5+Q32	P45+M246	Q98+D379	0	4	0
T5+A37	P45+M248	Q98+Y382	G142+H32	V206+G47	G273+H32
T5+T40	P45+L250	Q98+S383	1	6	1
T5+P45	P45+G255	Q98+Q385	G142+S32	V206+G47	G273+S32
T5+W48	P45+Q256	Q98+K391	3	7	3
T5+G50	P45+A263	Q98+K393	G142+H32	V206+K48	G273+H32

T5+T51	P45+V264	Q98+Q395	4	4	4
T5+N54	P45+Y267	Q98+A420	G142+F32	P211+I21	G273+F32
T5+V56	P45+N270	Q98+G423	8	4	8
T5+K72	P45+G273	Q98+T444	G142+T33	P211+V21	G273+T33
T5+R87	P45+S280	Q98+A445	4	5	4
T5+Q98	P45+T285	Q98+Q449	G142+D33	P211+L21	G273+D33
T5+M105	P45+M286	Q98+T459	7	7	7
T5+G109	P45+F289	Q98+P473	G142+Q34	P211+L21	G273+Q34
T5+F113	P45+V291	Q98+C474	5	9	5
T5+R116	P45+Q299	Q98+G476	G142+G34	P211+L23	G273+G34
T5+Q118	P45+R320	Q98+G477	6	5	6
T5+Q125	P45+H321	Q98+K484	G142+G34	P211+V23	G273+G34
T5+G133	P45+S323	M105+G10	8	8	8
T5+T134	P45+H324	9	G142+T35	P211+M24	G273+T35
T5+W140	P45+F328	M105+F11	5	6	5
T5+G142	P45+T334	3	G142+S37	P211+M24	G273+S37
T5+G149	P45+D337	M105+R11	6	8	6
T5+T165	P45+Q345	6	G142+D37	P211+L25	G273+D37
T5+W167	P45+G346	M105+Q11	7	0	7
T5+R171	P45+G348	8	G142+D37	P211+G25	G273+D37
T5+Q172	P45+T355	M105+Q12	9	5	9
T5+L173	P45+S376	5	G142+Y38	P211+Q25	G273+Y38
T5+A174	P45+D377	M105+G13	2	6	2
T5+G184	P45+D379	3	G142+S38	P211+A26	G273+S38
T5+T193	P45+Y382	M105+T13	3	3	3
T5+N195	P45+S383	4	G142+Q38	P211+V26	G273+Q38
T5+A204	P45+Q385	M105+W14	5	4	5
T5+V206	P45+K391	0	G142+K39	P211+Y26	G273+K39
T5+P211	P45+K393	M105+G14	1	7	1
T5+I214	P45+Q395	2	G142+K39	P211+N27	G273+K39
T5+V215	P45+A420	M105+G14	3	0	3
T5+L217	P45+G423	9	G142+Q39	P211+G27	G273+Q39

T5+L219	P45+T444	M105+T16	5	3	5
T5+L235	P45+A445	5	G142+A42	P211+S28	G273+A42
T5+V238	P45+Q449	M105+W16	0	0	0
T5+M246	P45+T459	7	G142+G42	P211+T28	G273+G42
T5+M248	P45+P473	M105+R17	3	5	3
T5+L250	P45+C474	1	G142+T44	P211+M28	G273+T44
T5+G255	P45+G476	M105+Q17	4	6	4
T5+Q256	P45+G477	2	G142+A44	P211+F28	G273+A44
T5+A263	P45+K484	M105+L17	5	9	5
T5+V264	W48+G50	3	G142+Q44	P211+V29	G273+Q44
T5+Y267	W48+T51	M105+A17	9	1	9
T5+N270	W48+N54	4	G142+T45	P211+Q29	G273+T45
T5+G273	W48+V56	M105+G18	9	9	9
T5+S280	W48+K72	4	G142+P47	P211+R32	G273+P47
T5+T285	W48+R87	M105+T19	3	0	3
T5+M286	W48+Q98	3	G142+C47	P211+H32	G273+C47
T5+F289	W48+M105	M105+N19	4	1	4
T5+V291	W48+G109	5	G142+G47	P211+S32	G273+G47
T5+Q299	W48+F113	M105+A20	6	3	6
T5+R320	W48+R116	4	G142+G47	P211+H32	G273+G47
T5+H321	W48+Q118	M105+V20	7	4	7
T5+S323	W48+Q125	6	G142+K48	P211+F32	G273+K48
T5+H324	W48+G133	M105+P21	4	8	4
T5+F328	W48+T134	1	G149+T16	P211+T33	S280+T28
T5+T334	W48+W140	M105+I21	5	4	5
T5+D337	W48+G142	4	G149+W16	P211+D33	S280+M28
T5+Q345	W48+G149	M105+V21	7	7	6
T5+G346	W48+T165	5	G149+R17	P211+Q34	S280+F28
T5+G348	W48+W167	M105+L21	1	5	9
T5+T355	W48+R171	7	G149+Q17	P211+G34	S280+V29
T5+S376	W48+Q172	M105+L21	2	6	1
T5+D377	W48+L173	9	G149+L17	P211+G34	S280+Q29

T5+D379	W48+A174	M105+L23	3	8	9
T5+Y382	W48+G184	5	G149+A17	P211+T35	S280+R32
T5+S383	W48+T193	M105+V23	4	5	0
T5+Q385	W48+N195	8	G149+G18	P211+S37	S280+H32
T5+K391	W48+A204	M105+M24	4	6	1
T5+K393	W48+V206	6	G149+T19	P211+D37	S280+S32
T5+Q395	W48+P211	M105+M24	3	7	3
T5+A420	W48+I214	8	G149+N19	P211+D37	S280+H32
T5+G423	W48+V215	M105+L25	5	9	4
T5+T444	W48+L217	0	G149+A20	P211+Y38	S280+F32
T5+A445	W48+L219	M105+G25	4	2	8
T5+Q449	W48+L235	5	G149+V20	P211+S38	S280+T33
T5+T459	W48+V238	M105+Q25	6	3	4
T5+P473	W48+M246	6	G149+P21	P211+Q38	S280+D33
T5+C474	W48+M248	M105+A26	1	5	7
T5+G476	W48+L250	3	G149+I21	P211+K39	S280+Q34
T5+G477	W48+G255	M105+V26	4	1	5
T5+K484	W48+Q256	4	G149+V21	P211+K39	S280+G34
G7+Q11	W48+A263	M105+Y26	5	3	6
G7+N16	W48+V264	7	G149+L21	P211+Q39	S280+G34
G7+V17	W48+Y267	M105+N27	7	5	8
G7+Q32	W48+N270	0	G149+L21	P211+A42	S280+T35
G7+A37	W48+G273	M105+G27	9	0	5
G7+T40	W48+S280	3	G149+L23	P211+G42	S280+S37
G7+P45	W48+T285	M105+S28	5	3	6
G7+W48	W48+M286	0	G149+V23	P211+T44	S280+D37
G7+G50	W48+F289	M105+T28	8	4	7
G7+T51	W48+V291	5	G149+M24	P211+A44	S280+D37
G7+N54	W48+Q299	M105+M28	6	5	9
G7+V56	W48+R320	6	G149+M24	P211+Q44	S280+Y38
G7+K72	W48+H321	M105+F28	8	9	2
G7+R87	W48+S323	9	G149+L25	P211+T45	S280+S38

G7+Q98	W48+H324	M105+V29	0	9	3
G7+M105	W48+F328	1	G149+G25	P211+P47	S280+Q38
G7+G109	W48+T334	M105+Q29	5	3	5
G7+F113	W48+D337	9	G149+Q25	P211+C47	S280+K39
G7+R116	W48+Q345	M105+R32	6	4	1
G7+Q118	W48+G346	0	G149+A26	P211+G47	S280+K39
G7+Q125	W48+G348	M105+H32	3	6	3
G7+G133	W48+T355	1	G149+V26	P211+G47	S280+Q39
G7+T134	W48+S376	M105+S32	4	7	5
G7+W140	W48+D377	3	G149+Y26	P211+K48	S280+A42
G7+G142	W48+D379	M105+H32	7	4	0
G7+G149	W48+Y382	4	G149+N27	I214+V21	S280+G42
G7+T165	W48+S383	M105+F32	0	5	3
G7+W167	W48+Q385	8	G149+G27	I214+L21	S280+T44
G7+R171	W48+K391	M105+T33	3	7	4
G7+Q172	W48+K393	4	G149+S28	I214+L21	S280+A44
G7+L173	W48+Q395	M105+D33	0	9	5
G7+A174	W48+A420	7	G149+T28	I214+L23	S280+Q44
G7+G184	W48+G423	M105+Q34	5	5	9
G7+T193	W48+T444	5	G149+M28	I214+V23	S280+T45
G7+N195	W48+A445	M105+G34	6	8	9
G7+A204	W48+Q449	6	G149+F28	I214+M24	S280+P47
G7+V206	W48+T459	M105+G34	9	6	3
G7+P211	W48+P473	8	G149+V29	I214+M24	S280+C47
G7+I214	W48+C474	M105+T35	1	8	4
G7+V215	W48+G476	5	G149+Q29	I214+L25	S280+G47
G7+L217	W48+G477	M105+S37	9	0	6
G7+L219	W48+K484	6	G149+R32	I214+G25	S280+G47
G7+L235	G50+T51	M105+D37	0	5	7
G7+V238	G50+N54	7	G149+H32	I214+Q25	S280+K48
G7+M246	G50+V56	M105+D37	1	6	4
G7+M248	G50+K72	9	G149+S32	I214+A26	T285+M28

G7+L250	G50+R87	M105+Y38	3	3	6
G7+G255	G50+Q98	2	G149+H32	I214+V26	T285+F28
G7+Q256	G50+M105	M105+S38	4	4	9
G7+A263	G50+G109	3	G149+F32	I214+Y26	T285+V29
G7+V264	G50+F113	M105+Q38	8	7	1
G7+Y267	G50+R116	5	G149+T33	I214+N27	T285+Q29
G7+N270	G50+Q118	M105+K39	4	0	9
G7+G273	G50+Q125	1	G149+D33	I214+G27	T285+R32
G7+S280	G50+G133	M105+K39	7	3	0
G7+T285	G50+T134	3	G149+Q34	I214+S28	T285+H32
G7+M286	G50+W140	M105+Q39	5	0	1
G7+F289	G50+G142	5	G149+G34	I214+T28	T285+S32
G7+V291	G50+G149	M105+A42	6	5	3
G7+Q299	G50+T165	0	G149+G34	I214+M28	T285+H32
G7+R320	G50+W167	M105+G42	8	6	4
G7+H321	G50+R171	3	G149+T35	I214+F28	T285+F32
G7+S323	G50+Q172	M105+T44	5	9	8
G7+H324	G50+L173	4	G149+S37	I214+V29	T285+T33
G7+F328	G50+A174	M105+A44	6	1	4
G7+T334	G50+G184	5	G149+D37	I214+Q29	T285+D33
G7+D337	G50+T193	M105+Q44	7	9	7
G7+Q345	G50+N195	9	G149+D37	I214+R32	T285+Q34
G7+G346	G50+A204	M105+T45	9	0	5
G7+G348	G50+V206	9	G149+Y38	I214+H32	T285+G34
G7+T355	G50+P211	M105+P47	2	1	6
G7+S376	G50+I214	3	G149+S38	I214+S32	T285+G34
G7+D377	G50+V215	M105+C47	3	3	8
G7+D379	G50+L217	4	G149+Q38	I214+H32	T285+T35
G7+Y382	G50+L219	M105+G47	5	4	5
G7+S383	G50+L235	6	G149+K39	I214+F32	T285+S37
G7+Q385	G50+V238	M105+G47	1	8	6
G7+K391	G50+M246	7	G149+K39	I214+T33	T285+D37

G7+K393	G50+M248	M105+K48	3	4	7
G7+Q395	G50+L250	4	G149+Q39	I214+D33	T285+D37
G7+A420	G50+G255	G109+F11	5	7	9
G7+G423	G50+Q256	3	G149+A42	I214+Q34	T285+Y38
G7+T444	G50+A263	G109+R11	0	5	2
G7+A445	G50+V264	6	G149+G42	I214+G34	T285+S38
G7+Q449	G50+Y267	G109+Q11	3	6	3
G7+T459	G50+N270	8	G149+T44	I214+G34	T285+Q38
G7+P473	G50+G273	G109+Q12	4	8	5
G7+C474	G50+S280	5	G149+A44	I214+T35	T285+K39
G7+G476	G50+T285	G109+G13	5	5	1
G7+G477	G50+M286	3	G149+Q44	I214+S37	T285+K39
G7+K484	G50+F289	G109+T13	9	6	3
Q11+N16	G50+V291	4	G149+T45	I214+D37	T285+Q39
Q11+V17	G50+Q299	G109+W14	9	7	5
Q11+Q32	G50+R320	0	G149+P47	I214+D37	T285+A42
Q11+A37	G50+H321	G109+G14	3	9	0
Q11+T40	G50+S323	2	G149+C47	I214+Y38	T285+G42
Q11+P45	G50+H324	G109+G14	4	2	3
Q11+W48	G50+F328	9	G149+G47	I214+S38	T285+T44
Q11+G50	G50+T334	G109+T16	6	3	4
Q11+T51	G50+D337	5	G149+G47	I214+Q38	T285+A44
Q11+N54	G50+Q345	G109+W16	7	5	5
Q11+V56	G50+G346	7	G149+K48	I214+K39	T285+Q44
Q11+K72	G50+G348	G109+R17	4	1	9
Q11+R87	G50+T355	1	T165+W16	I214+K39	T285+T45
Q11+Q98	G50+S376	G109+Q17	7	3	9
Q11+M105	G50+D377	2	T165+R17	I214+Q39	T285+P47
Q11+G109	G50+D379	G109+L17	1	5	3
Q11+F113	G50+Y382	3	T165+Q17	I214+A42	T285+C47
Q11+R116	G50+S383	G109+A17	2	0	4
Q11+Q118	G50+Q385	4	T165+L17	I214+G42	T285+G47

Q11+Q125	G50+K391	G109+G183		3	6
Q11+G133	G50+K393		T165+A174	I214+T444	T285+G477
Q11+T134	G50+Q395	G109+T193			
Q11+W140	G50+A420		T165+G184	I214+A445	T285+K484
Q11+G142	G50+G423	G109+N195			
Q11+G149	G50+T444		T165+T193	I214+Q449	M286+F289
Q11+T165	G50+A445	G109+A204			
Q11+W167	G50+Q449		T165+N195	I214+T459	M286+V291
Q11+R171	G50+T459	G109+V206			
Q11+Q172	G50+P473		T165+A204	I214+P473	M286+Q299
Q11+L173	G50+C474	G109+P211			
Q11+A174	G50+G476		T165+V206	I214+C474	M286+R320
Q11+G184	G50+G477	G109+I214			
Q11+T193	G50+K484		T165+P211	I214+G476	M286+H321
Q11+N195	T51+N54	G109+V215			
Q11+A204	T51+V56		T165+I214	I214+G477	M286+S323
Q11+V206	T51+K72	G109+L217			
Q11+P211	T51+R87		T165+V215	I214+K484	M286+H324
Q11+I214	T51+Q98	G109+L219			
Q11+V215	T51+M105		T165+L217	V215+L217	M286+F328
Q11+L217	T51+G109	G109+L235			
Q11+L219	T51+F113		T165+L219	V215+L219	M286+T334
Q11+L235	T51+R116	G109+V238			
Q11+V238	T51+Q118		T165+L235	V215+L235	M286+D337
Q11+M246	T51+Q125	G109+M246			
Q11+M248	T51+G133		T165+V238	V215+V238	M286+Q345
Q11+L250	T51+T134	G109+M248			
Q11+G255	T51+W140		T165+M246	V215+M246	M286+G346
Q11+Q256	T51+G142	G109+L250			
Q11+A263	T51+G149		T165+M248	V215+M248	M286+G348
Q11+V264	T51+T165	G109+G255			
Q11+Y267	T51+W167		T165+L250	V215+L250	M286+T350

Q11+N270	T51+R171	G109+Q25	0	0	5
Q11+G273	T51+Q172	6	T165+G25	V215+G25	M286+S37
Q11+S280	T51+L173	G109+A26	5	5	6
Q11+T285	T51+A174	3	T165+Q25	V215+Q25	M286+D37
Q11+M286	T51+G184	G109+V26	6	6	7
Q11+F289	T51+T193	4	T165+A26	V215+A26	M286+D37
Q11+V291	T51+N195	G109+Y26	3	3	9
Q11+Q299	T51+A204	7	T165+V26	V215+V26	M286+Y38
Q11+R320	T51+V206	G109+N27	4	4	2
Q11+H321	T51+P211	0	T165+Y26	V215+Y26	M286+S38
Q11+S323	T51+I214	G109+G27	7	7	3
Q11+H324	T51+V215	3	T165+N27	V215+N27	M286+Q38
Q11+F328	T51+L217	G109+S28	0	0	5
Q11+T334	T51+L219	0	T165+G27	V215+G27	M286+K39
Q11+D337	T51+L235	G109+T28	3	3	1
Q11+Q345	T51+V238	5	T165+S28	V215+S28	M286+K39
Q11+G346	T51+M246	G109+M28	0	0	3
Q11+G348	T51+M248	6	T165+T28	V215+T28	M286+Q39
Q11+T355	T51+L250	G109+F28	5	5	5
Q11+S376	T51+G255	9	T165+M28	V215+M28	M286+A42
Q11+D377	T51+Q256	G109+V29	6	6	0
Q11+D379	T51+A263	1	T165+F28	V215+F28	M286+G42
Q11+Y382	T51+V264	G109+Q29	9	9	3
Q11+S383	T51+Y267	9	T165+V29	V215+V29	M286+T44
Q11+Q385	T51+N270	G109+R32	1	1	4
Q11+K391	T51+G273	0	T165+Q29	V215+Q29	M286+A44
Q11+K393	T51+S280	G109+H32	9	9	5
Q11+Q395	T51+T285	1	T165+R32	V215+R32	M286+Q44
Q11+A420	T51+M286	G109+S32	0	0	9
Q11+G423	T51+F289	3	T165+H32	V215+H32	M286+T45
Q11+T444	T51+V291	G109+H32	1	1	9
Q11+A445	T51+Q299	4	T165+S32	V215+S32	M286+P47

Q11+Q449	T51+R320	G109+F32	3	3	3
Q11+T459	T51+H321	8	T165+H32	V215+H32	M286+C47
Q11+P473	T51+S323	G109+T33	4	4	4
Q11+C474	T51+H324	4	T165+F32	V215+F32	M286+G47
Q11+G476	T51+F328	G109+D33	8	8	6
Q11+G477	T51+T334	7	T165+T33	V215+T33	M286+G47
Q11+K484	T51+D337	G109+Q34	4	4	7
N16+V17	T51+Q345	5	T165+D33	V215+D33	M286+K48
N16+Q32	T51+G346	G109+G34	7	7	4
N16+A37	T51+G348	6	T165+Q34	V215+Q34	F289+V29
N16+T40	T51+T355	G109+G34	5	5	1
N16+P45	T51+S376	8	T165+G34	V215+G34	F289+Q29
N16+W48	T51+D377	G109+T35	6	6	9
N16+G50	T51+D379	5	T165+G34	V215+G34	F289+R32
N16+T51	T51+Y382	G109+S37	8	8	0
N16+N54	T51+S383	6	T165+T35	V215+T35	F289+H32
N16+V56	T51+Q385	G109+D37	5	5	1
N16+K72	T51+K391	7	T165+S37	V215+S37	F289+S32
N16+R87	T51+K393	G109+D37	6	6	3
N16+Q98	T51+Q395	9	T165+D37	V215+D37	F289+H32
N16+M105	T51+A420	G109+Y38	7	7	4
N16+G109	T51+G423	2	T165+D37	V215+D37	F289+F32
N16+F113	T51+T444	G109+S38	9	9	8
N16+R116	T51+A445	3	T165+Y38	V215+Y38	F289+T33
N16+Q118	T51+Q449	G109+Q38	2	2	4
N16+Q125	T51+T459	5	T165+S38	V215+S38	F289+D33
N16+G133	T51+P473	G109+K39	3	3	7
N16+T134	T51+C474	1	T165+Q38	V215+Q38	F289+Q34
N16+W140	T51+G476	G109+K39	5	5	5
N16+G142	T51+G477	3	T165+K39	V215+K39	F289+G34
N16+G149	T51+K484	G109+Q39	1	1	6
N16+T165	N54+V56	5	T165+K39	V215+K39	F289+G34

N16+W167	N54+K72	G109+A42	3	3	8
N16+R171	N54+R87	0	T165+Q39	V215+Q39	F289+T35
N16+Q172	N54+Q98	G109+G42	5	5	5
N16+L173	N54+M105	3	T165+A42	V215+A42	F289+S37
N16+A174	N54+G109	G109+T44	0	0	6
N16+G184	N54+F113	4	T165+G42	V215+G42	F289+D37
N16+T193	N54+R116	G109+A44	3	3	7
N16+N195	N54+Q118	5	T165+T44	V215+T44	F289+D37
N16+A204	N54+Q125	G109+Q44	4	4	9
N16+V206	N54+G133	9	T165+A44	V215+A44	F289+Y38
N16+P211	N54+T134	G109+T45	5	5	2
N16+I214	N54+W140	9	T165+Q44	V215+Q44	F289+S38
N16+V215	N54+G142	G109+P47	9	9	3
N16+L217	N54+G149	3	T165+T45	V215+T45	F289+Q38
N16+L219	N54+T165	G109+C47	9	9	5
N16+L235	N54+W167	4	T165+P47	V215+P47	F289+K39
N16+V238	N54+R171	G109+G47	3	3	1
N16+M246	N54+Q172	6	T165+C47	V215+C47	F289+K39
N16+M248	N54+L173	G109+G47	4	4	3
N16+L250	N54+A174	7	T165+G47	V215+G47	F289+Q39
N16+G255	N54+G184	G109+K48	6	6	5
N16+Q256	N54+T193	4	T165+G47	V215+G47	F289+A42
N16+A263	N54+N195	F113+R11	7	7	0
N16+V264	N54+A204	6	T165+K48	V215+K48	F289+G42
N16+Y267	N54+V206	F113+Q11	4	4	3
N16+N270	N54+P211	8	W167+R17	L217+L21	F289+T44
N16+G273	N54+I214	F113+Q12	1	9	4
N16+S280	N54+V215	5	W167+Q17	L217+L23	F289+A44
N16+T285	N54+L217	F113+G13	2	5	5
N16+M286	N54+L219	3	W167+L17	L217+V23	F289+Q44
N16+F289	N54+L235	F113+T13	3	8	9
N16+V291	N54+V238	4	W167+A17	L217+M24	F289+T45

N16+Q299	N54+M246	F113+W14	4	6	9
N16+R320	N54+M248	0	W167+G18	L217+M24	F289+P47
N16+H321	N54+L250	F113+G14	4	8	3
N16+S323	N54+G255	2	W167+T19	L217+L25	F289+C47
N16+H324	N54+Q256	F113+G14	3	0	4
N16+F328	N54+A263	9	W167+N19	L217+G25	F289+G47
N16+T334	N54+V264	F113+T16	5	5	6
N16+D337	N54+Y267	5	W167+A20	L217+Q25	F289+G47
N16+Q345	N54+N270	F113+W16	4	6	7
N16+G346	N54+G273	7	W167+V20	L217+A26	F289+K48
N16+G348	N54+S280	F113+R17	6	3	4
N16+T355	N54+T285	1	W167+P21	L217+V26	V291+Q29
N16+S376	N54+M286	F113+Q17	1	4	9
N16+D377	N54+F289	2	W167+I21	L217+Y26	V291+R32
N16+D379	N54+V291	F113+L17	4	7	0
N16+Y382	N54+Q299	3	W167+V21	L217+N27	V291+H32
N16+S383	N54+R320	F113+A17	5	0	1
N16+Q385	N54+H321	4	W167+L21	L217+G27	V291+S32
N16+K391	N54+S323	F113+G18	7	3	3
N16+K393	N54+H324	4	W167+L21	L217+S28	V291+H32
N16+Q395	N54+F328	F113+T19	9	0	4
N16+A420	N54+T334	3	W167+L23	L217+T28	V291+F32
N16+G423	N54+D337	F113+N19	5	5	8
N16+T444	N54+Q345	5	W167+V23	L217+M28	V291+T33
N16+A445	N54+G346	F113+A20	8	6	4
N16+Q449	N54+G348	4	W167+M24	L217+F28	V291+D33
N16+T459	N54+T355	F113+V20	6	9	7
N16+P473	N54+S376	6	W167+M24	L217+V29	V291+Q34
N16+C474	N54+D377	F113+P21	8	1	5
N16+G476	N54+D379	1	W167+L25	L217+Q29	V291+G34
N16+G477	N54+Y382	F113+I21	0	9	6
N16+K484	N54+S383	4	W167+G25	L217+R32	V291+G34

V17+Q32	N54+Q385	F113+V21	5	0	8
V17+A37	N54+K391	5	W167+Q25	L217+H32	V291+T35
V17+T40	N54+K393	F113+L21	6	1	5
V17+P45	N54+Q395	7	W167+A26	L217+S32	V291+S37
V17+W48	N54+A420	F113+L21	3	3	6
V17+G50	N54+G423	9	W167+V26	L217+H32	V291+D37
V17+T51	N54+T444	F113+L23	4	4	7
V17+N54	N54+A445	5	W167+Y26	L217+F32	V291+D37
V17+V56	N54+Q449	F113+V23	7	8	9
V17+K72	N54+T459	8	W167+N27	L217+T33	V291+Y38
V17+R87	N54+P473	F113+M24	0	4	2
V17+Q98	N54+C474	6	W167+G27	L217+D33	V291+S38
V17+M105	N54+G476	F113+M24	3	7	3
V17+G109	N54+G477	8	W167+S28	L217+Q34	V291+Q38
V17+F113	N54+K484	F113+L25	0	5	5
V17+R116	V56+K72	0	W167+T28	L217+G34	V291+K39
V17+Q118	V56+R87	F113+G25	5	6	1
V17+Q125	V56+Q98	5	W167+M28	L217+G34	V291+K39
V17+G133	V56+M105	F113+Q25	6	8	3
V17+T134	V56+G109	6	W167+F28	L217+T35	V291+Q39
V17+W140	V56+F113	F113+A26	9	5	5
V17+G142	V56+R116	3	W167+V29	L217+S37	V291+A42
V17+G149	V56+Q118	F113+V26	1	6	0
V17+T165	V56+Q125	4	W167+Q29	L217+D37	V291+G42
V17+W167	V56+G133	F113+Y26	9	7	3
V17+R171	V56+T134	7	W167+R32	L217+D37	V291+T44
V17+Q172	V56+W140	F113+N27	0	9	4
V17+L173	V56+G142	0	W167+H32	L217+Y38	V291+A44
V17+A174	V56+G149	F113+G27	1	2	5
V17+G184	V56+T165	3	W167+S32	L217+S38	V291+Q44
V17+T193	V56+W167	F113+S28	3	3	9
V17+N195	V56+R171	0	W167+H32	L217+Q38	V291+T45

V17+A204	V56+Q172	F113+T28	4	5	9
V17+V206	V56+L173	5	W167+F32	L217+K39	V291+P47
V17+P211	V56+A174	F113+M28	8	1	3
V17+I214	V56+G184	6	W167+T33	L217+K39	V291+C47
V17+V215	V56+T193	F113+F28	4	3	4
V17+L217	V56+N195	9	W167+D33	L217+Q39	V291+G47
V17+L219	V56+A204	F113+V29	7	5	6
V17+L235	V56+V206	1	W167+Q34	L217+A42	V291+G47
V17+V238	V56+P211	F113+Q29	5	0	7
V17+M246	V56+I214	9	W167+G34	L217+G42	V291+K48
V17+M248	V56+V215	F113+R32	6	3	4
V17+L250	V56+L217	0	W167+G34	L217+T44	Q299+R32
V17+G255	V56+L219	F113+H32	8	4	0
V17+Q256	V56+L235	1	W167+T35	L217+A44	Q299+H32
V17+A263	V56+V238	F113+S32	5	5	1
V17+V264	V56+M246	3	W167+S37	L217+Q44	Q299+S32
V17+Y267	V56+M248	F113+H32	6	9	3
V17+N270	V56+L250	4	W167+D37	L217+T45	Q299+H32
V17+G273	V56+G255	F113+F32	7	9	4
V17+S280	V56+Q256	8	W167+D37	L217+P47	Q299+F32
V17+T285	V56+A263	F113+T33	9	3	8
V17+M286	V56+V264	4	W167+Y38	L217+C47	Q299+T33
V17+F289	V56+Y267	F113+D33	2	4	4
V17+V291	V56+N270	7	W167+S38	L217+G47	Q299+D33
V17+Q299	V56+G273	F113+Q34	3	6	7
V17+R320	V56+S280	5	W167+Q38	L217+G47	Q299+Q34
V17+H321	V56+T285	F113+G34	5	7	5
V17+S323	V56+M286	6	W167+K39	L217+K48	Q299+G34
V17+H324	V56+F289	F113+G34	1	4	6
V17+F328	V56+V291	8	W167+K39	L219+L23	Q299+G34
V17+T334	V56+Q299	F113+T35	3	5	8
V17+D337	V56+R320	5	W167+Q39	L219+V23	Q299+T35

V17+Q345	V56+H321	F113+S37	5	8	5
V17+G346	V56+S323	6	W167+A42	L219+M24	Q299+S37
V17+G348	V56+H324	F113+D37	0	6	6
V17+T355	V56+F328	7	W167+G42	L219+M24	Q299+D37
V17+S376	V56+T334	F113+D37	3	8	7
V17+D377	V56+D337	9	W167+T44	L219+L25	Q299+D37
V17+D379	V56+Q345	F113+Y38	4	0	9
V17+Y382	V56+G346	2	W167+A44	L219+G25	Q299+Y38
V17+S383	V56+G348	F113+S38	5	5	2
V17+Q385	V56+T355	3	W167+Q44	L219+Q25	Q299+S38
V17+K391	V56+S376	F113+Q38	9	6	3
V17+K393	V56+D377	5	W167+T45	L219+A26	Q299+Q38
V17+Q395	V56+D379	F113+K39	9	3	5
V17+A420	V56+Y382	1	W167+P47	L219+V26	Q299+K39
V17+G423	V56+S383	F113+K39	3	4	1
V17+T444	V56+Q385	3	W167+C47	L219+Y26	Q299+K39
V17+A445	V56+K391	F113+Q39	4	7	3
V17+Q449	V56+K393	5	W167+G47	L219+N27	Q299+Q39
V17+T459	V56+Q395	F113+A42	6	0	5
V17+P473	V56+A420	0	W167+G47	L219+G27	Q299+A42
V17+C474	V56+G423	F113+G42	7	3	0
V17+G476	V56+T444	3	W167+K48	L219+S28	Q299+G42
V17+G477	V56+A445	F113+T44	4	0	3
V17+K484	V56+Q449	4	R171+Q17	L219+T28	Q299+T44
Q32+A37	V56+T459	F113+A44	2	5	4
Q32+T40	V56+P473	5	R171+L17	L219+M28	Q299+A44
Q32+P45	V56+C474	F113+Q44	3	6	5
Q32+W48	V56+G476	9	R171+A17	L219+F28	Q299+Q44
Q32+G50	V56+G477	F113+T45	4	9	9
Q32+T51	V56+K484	9	R171+G18	L219+V29	Q299+T45
Q32+N54	K72+R87	F113+P47	4	1	9
Q32+V56	K72+Q98	3	R171+T19	L219+Q29	Q299+P47

Q32+K72	K72+M105	F113+C47	3	9	3
Q32+R87	K72+G109	4	R171+N19	L219+R32	Q299+C47
Q32+Q98	K72+F113	F113+G47	5	0	4
Q32+M105	K72+R116	6	R171+A20	L219+H32	Q299+G47
Q32+G109	K72+Q118	F113+G47	4	1	6
Q32+F113	K72+Q125	7	R171+V20	L219+S32	Q299+G47
Q32+R116	K72+G133	F113+K48	6	3	7
Q32+Q118	K72+T134	4	R171+P21	L219+H32	Q299+K48
Q32+Q125	K72+W140	R116+Q11	1	4	4
Q32+G133	K72+G142	8	R171+I21	L219+F32	R320+H32
Q32+T134	K72+G149	R116+Q12	4	8	1
Q32+W140	K72+T165	5	R171+V21	L219+T33	R320+S32
Q32+G142	K72+W167	R116+G13	5	4	3
Q32+G149	K72+R171	3	R171+L21	L219+D33	R320+H32
Q32+T165	K72+Q172	R116+T13	7	7	4
Q32+W167	K72+L173	4	R171+L21	L219+Q34	R320+F32
Q32+R171	K72+A174	R116+W14	9	5	8
Q32+Q172	K72+G184	0	R171+L23	L219+G34	R320+T33
Q32+L173	K72+T193	R116+G14	5	6	4
Q32+A174	K72+N195	2	R171+V23	L219+G34	R320+D33
Q32+G184	K72+A204	R116+G14	8	8	7
Q32+T193	K72+V206	9	R171+M24	L219+T35	R320+Q34
Q32+N195	K72+P211	R116+T16	6	5	5
Q32+A204	K72+I214	5	R171+M24	L219+S37	R320+G34
Q32+V206	K72+V215	R116+W16	8	6	6
Q32+P211	K72+L217	7	R171+L25	L219+D37	R320+G34
Q32+I214	K72+L219	R116+R17	0	7	8
Q32+V215	K72+L235	1	R171+G25	L219+D37	R320+T35
Q32+L217	K72+V238	R116+Q17	5	9	5
Q32+L219	K72+M246	2	R171+Q25	L219+Y38	R320+S37
Q32+L235	K72+M248	R116+L17	6	2	6
Q32+V238	K72+L250	3	R171+A26	L219+S38	R320+D37

Q32+M246	K72+G255	R116+A17	3	3	7
Q32+M248	K72+Q256	4	R171+V26	L219+Q38	R320+D37
Q32+L250	K72+A263	R116+G18	4	5	9
Q32+G255	K72+V264	4	R171+Y26	L219+K39	R320+Y38
Q32+Q256	K72+Y267	R116+T19	7	1	2
Q32+A263	K72+N270	3	R171+N27	L219+K39	R320+S38
Q32+V264	K72+G273	R116+N19	0	3	3
Q32+Y267	K72+S280	5	R171+G27	L219+Q39	R320+Q38
Q32+N270	K72+T285	R116+A20	3	5	5
Q32+G273	K72+M286	4	R171+S28	L219+A42	R320+K39
Q32+S280	K72+F289	R116+V20	0	0	1
Q32+T285	K72+V291	6	R171+T28	L219+G42	R320+K39
Q32+M286	K72+Q299	R116+P21	5	3	3
Q32+F289	K72+R320	1	R171+M28	L219+T44	R320+Q39
Q32+V291	K72+H321	R116+I21	6	4	5
Q32+Q299	K72+S323	4	R171+F28	L219+A44	R320+A42
Q32+R320	K72+H324	R116+V21	9	5	0
Q32+H321	K72+F328	5	R171+V29	L219+Q44	R320+G42
Q32+S323	K72+T334	R116+L21	1	9	3
Q32+H324	K72+D337	7	R171+Q29	L219+T45	R320+T44
Q32+F328	K72+Q345	R116+L21	9	9	4
Q32+T334	K72+G346	9	R171+R32	L219+P47	R320+A44
Q32+D337	K72+G348	R116+L23	0	3	5
Q32+Q345	K72+T355	5	R171+H32	L219+C47	R320+Q44
Q32+G346	K72+S376	R116+V23	1	4	9
Q32+G348	K72+D377	8	R171+S32	L219+G47	R320+T45
Q32+T355	K72+D379	R116+M24	3	6	9
Q32+S376	K72+Y382	6	R171+H32	L219+G47	R320+P47
Q32+D377	K72+S383	R116+M24	4	7	3
Q32+D379	K72+Q385	8	R171+F32	L219+K48	R320+C47
Q32+Y382	K72+K391	R116+L25	8	4	4
Q32+S383	K72+K393	0	R171+T33	L235+V23	R320+G47

Q32+Q385	K72+Q395	R116+G25	4	8	6
Q32+K391	K72+A420	5	R171+D33	L235+M24	R320+G47
Q32+K393	K72+G423	R116+Q25	7	6	7
Q32+Q395	K72+T444	6	R171+Q34	L235+M24	R320+K48
Q32+A420	K72+A445	R116+A26	5	8	4
Q32+G423	K72+Q449	3	R171+G34	L235+L25	H321+S32
Q32+T444	K72+T459	R116+V26	6	0	3
Q32+A445	K72+P473	4	R171+G34	L235+G25	H321+H32
Q32+Q449	K72+C474	R116+Y26	8	5	4
Q32+T459	K72+G476	7	R171+T35	L235+Q25	H321+F32
Q32+P473	K72+G477	R116+N27	5	6	8
Q32+C474	K72+K484	0	R171+S37	L235+A26	H321+T33
Q32+G476	R87+Q98	R116+G27	6	3	4
Q32+G477	R87+M105	3	R171+D37	L235+V26	H321+D33
Q32+K484	R87+G109	R116+S28	7	4	7
A37+T40	R87+F113	0	R171+D37	L235+Y26	H321+Q34
A37+P45	R87+R116	R116+T28	9	7	5
A37+W48	R87+Q118	5	R171+Y38	L235+N27	H321+G34
A37+G50	R87+Q125	R116+M28	2	0	6
A37+T51	R87+G133	6	R171+S38	L235+G27	H321+G34
A37+N54	R87+T134	R116+F28	3	3	8
A37+V56	R87+W140	9	R171+Q38	L235+S28	H321+T35
A37+K72	R87+G142	R116+V29	5	0	5
A37+R87	R87+G149	1	R171+K39	L235+T28	H321+S37
A37+Q98	R87+T165	R116+Q29	1	5	6
A37+M105	R87+W167	9	R171+K39	L235+M28	H321+D37
A37+G109	R87+R171	R116+R32	3	6	7
A37+F113	R87+Q172	0	R171+Q39	L235+F28	H321+D37
A37+R116	R87+L173	R116+H32	5	9	9
A37+Q118	R87+A174	1	R171+A42	L235+V29	H321+Y38
A37+Q125	R87+G184	R116+S32	0	1	2
A37+G133	R87+T193	3	R171+G42	L235+Q29	H321+S38

A37+T134	R87+N195	R116+H32	3	9	3
A37+W140	R87+A204	4	R171+T44	L235+R32	H321+Q38
A37+G142	R87+V206	R116+F32	4	0	5
A37+G149	R87+P211	8	R171+A44	L235+H32	H321+K39
A37+T165	R87+I214	R116+T33	5	1	1
A37+W167	R87+V215	4	R171+Q44	L235+S32	H321+K39
A37+R171	R87+L217	R116+D33	9	3	3
A37+Q172	R87+L219	7	R171+T45	L235+H32	H321+Q39
A37+L173	R87+L235	R116+Q34	9	4	5
A37+A174	R87+V238	5	R171+P47	L235+F32	H321+A42
A37+G184	R87+M246	R116+G34	3	8	0
A37+T193	R87+M248	6	R171+C47	L235+T33	H321+G42
A37+N195	R87+L250	R116+G34	4	4	3
A37+A204	R87+G255	8	R171+G47	L235+D33	H321+T44
A37+V206	R87+Q256	R116+T35	6	7	4
A37+P211	R87+A263	5	R171+G47	L235+Q34	H321+A44
A37+I214	R87+V264	R116+S37	7	5	5
A37+V215	R87+Y267	6	R171+K48	L235+G34	H321+Q44
A37+L217	H1+Q169	R116+D37	4	6	9
A37+L219	H1+A186	7	Q172+L17	L235+G34	H321+T45
A37+L235	H1+E190	R116+D37	3	8	9
A37+V238	H1+A225	9	Q172+A17	L235+T35	H321+P47
A37+M246	H1+K242	R116+Y38	4	5	3
A37+M248	H1+S244	2	Q172+G18	L235+S37	H321+C47
A37+L250	H1+G258	R116+S38	4	6	4
A37+G255	H1+N260	3	Q172+T19	L235+D37	H321+G47
A37+Q256	H1+K269	R116+Q38	3	7	6
A37+A263	H1+W284	5	Q172+N19	L235+D37	H321+G47
A37+V264	H1+Y295	R116+K39	5	9	7
A37+Y267	H1+S304	1	Q172+A20	L235+Y38	H321+K48
A37+N270	H1+V326	R116+K39	4	2	4
A37+G273	T5+Q169	3	Q172+V20	L235+S38	S323+H32

A37+S280	T5+A186	R116+Q39	6	3	4
A37+T285	T5+E190	5	Q172+P21	L235+Q38	S323+F32
A37+M286	T5+A225	R116+A42	1	5	8
A37+F289	T5+K242	0	Q172+I21	L235+K39	S323+T33
A37+V291	T5+S244	R116+G42	4	1	4
A37+Q299	T5+G258	3	Q172+V21	L235+K39	S323+D33
A37+R320	T5+N260	R116+T44	5	3	7
A37+H321	T5+K269	4	Q172+L21	L235+Q39	S323+Q34
A37+S323	T5+W284	R116+A44	7	5	5
A37+H324	T5+Y295	5	Q172+L21	L235+A42	S323+G34
A37+F328	T5+S304	R116+Q44	9	0	6
A37+T334	T5+V326	9	Q172+L23	L235+G42	S323+G34
A37+D337	G7+Q169	R116+T45	5	3	8
A37+Q345	G7+A186	9	Q172+V23	L235+T44	S323+T35
A37+G346	G7+E190	R116+P47	8	4	5
A37+G348	G7+A225	3	Q172+M24	L235+A44	S323+S37
A37+T355	G7+K242	R116+C47	6	5	6
A37+S376	G7+S244	4	Q172+M24	L235+Q44	S323+D37
A37+D377	G7+G258	R116+G47	8	9	7
A37+D379	G7+N260	6	Q172+L25	L235+T45	S323+D37
A37+Y382	G7+A265	R116+G47	0	9	9
A37+S383	G7+K269	7	Q172+G25	L235+P47	S323+Y38
A37+Q385	G7+W284	R116+K48	5	3	2
A37+K391	G7+Y295	4	Q172+Q25	L235+C47	S323+S38
A37+K393	G7+S304	Q118+Q12	6	4	3
A37+Q395	G7+V326	5	Q172+A26	L235+G47	S323+Q38
A37+A420	Q11+Q169	Q118+G13	3	6	5
A37+G423	Q11+A186	3	Q172+V26	L235+G47	S323+K39
A37+T444	Q11+E190	Q118+T13	4	7	1
A37+A445	Q11+A225	4	Q172+Y26	L235+K48	S323+K39
A37+Q449	Q11+K242	Q118+W14	7	4	3
A37+T459	Q11+S244	0	Q172+N27	V238+M24	S323+Q39

A37+P473	Q11+G258	Q118+G14	0	6	5
A37+C474	Q11+N260	2	Q172+G27	V238+M24	S323+A42
A37+G476	Q11+K269	Q118+G14	3	8	0
A37+G477	Q11+W284	9	Q172+S28	V238+L25	S323+G42
A37+K484	Q11+Y295	Q118+T16	0	0	3
T40+P45	Q11+S304	5	Q172+T28	V238+G25	S323+T44
T40+W48	Q11+V326	Q118+W16	5	5	4
T40+G50	N16+Q169	7	Q172+M28	V238+Q25	S323+A44
T40+T51	N16+A186	Q118+R17	6	6	5
T40+N54	N16+E190	1	Q172+F28	V238+A26	S323+Q44
T40+V56	N16+A225	Q118+Q17	9	3	9
T40+K72	N16+K242	2	Q172+V29	V238+V26	S323+T45
T40+R87	N16+S244	Q118+L17	1	4	9
T40+Q98	N16+G258	3	Q172+Q29	V238+Y26	S323+P47
T40+M105	N16+N260	Q118+A17	9	7	3
T40+G109	N16+K269	4	Q172+R32	V238+N27	S323+C47
T40+F113	N16+W284	Q118+G18	0	0	4
T40+R116	N16+Y295	4	Q172+H32	V238+G27	S323+G47
T40+Q118	N16+S304	Q118+T19	1	3	6
T40+Q125	N16+V326	3	Q172+S32	V238+S28	S323+G47
T40+G133	V17+Q169	Q118+N19	3	0	7
T40+T134	V17+A186	5	Q172+H32	V238+T28	S323+K48
T40+W140	V17+E190	Q118+A20	4	5	4
T40+G142	V17+A225	4	Q172+F32	V238+M28	H324+F32
T40+G149	V17+K242	Q118+V20	8	6	8
T40+T165	V17+S244	6	Q172+T33	V238+F28	H324+T33
T40+W167	V17+G258	Q118+P21	4	9	4
T40+R171	V17+N260	1	Q172+D33	V238+V29	H324+D33
T40+Q172	V17+K269	Q118+I21	7	1	7
T40+L173	V17+W284	4	Q172+Q34	V238+Q29	H324+Q34
T40+Q169	V17+Y295	Q118+V21	5	9	5
T40+A186	V17+S304	5	Q172+G34	V238+R32	H324+G34

T40+E190	V17+V326	Q118+L21	6	0	6
T40+A225	Q32+Q169	7	Q172+G34	V238+H32	H324+G34
T40+K242	Q32+A186	Q118+L21	8	1	8
T40+S244	Q32+E190	9	Q172+T35	V238+S32	H324+T35
T40+G258	Q32+A225	Q118+L23	5	3	5
T40+N260	Q32+K242	5	Q172+S37	V238+H32	H324+S37
T40+K269	Q32+S244	Q118+V23	6	4	6
T40+W284	Q32+G258	8	Q172+D37	V238+F32	H324+D37
T40+Y295	Q32+N260	Q118+M24	7	8	7
T40+S304	Q32+K269	6	Q172+D37	V238+T33	H324+D37
T40+V326	Q32+W284	Q118+M24	9	4	9
P45+Q169	Q32+Y295	8	Q172+Y38	V238+D33	H324+Y38
P45+A186	Q32+S304	Q118+L25	2	7	2
P45+E190	Q32+V326	0	Q172+S38	V238+Q34	H324+S38
P45+A225	A37+Q169	Q118+G25	3	5	3
P45+K242	A37+A186	5	Q172+Q38	V238+G34	H324+Q38
P45+S244	A37+E190	Q118+Q25	5	6	5
P45+G258	A37+A225	6	Q172+K39	V238+G34	H324+K39
P45+N260	A37+K242	Q118+A26	1	8	1
P45+K269	A37+S244	3	Q172+K39	V238+T35	H324+K39
P45+W284	A37+G258	Q118+V26	3	5	3
P45+Y295	A37+N260	4	Q172+Q39	V238+S37	H324+Q39
P45+S304	A37+K269	Q118+Y26	5	6	5
P45+V326	A37+W284	7	Q172+A42	V238+D37	H324+A42
W48+Q169	A37+Y295	Q118+N27	0	7	0
W48+A186	A37+S304	0	Q172+G42	V238+D37	H324+G42
W48+E190	A37+V326	Q118+G27	3	9	3
W48+A225	G142+Q16	3	Q172+T44	V238+Y38	H324+T44
W48+K242	9	Q118+S28	4	2	4
W48+S244	G142+A18	0	Q172+A44	V238+S38	H324+A44
W48+G258	6	Q118+T28	5	3	5
W48+N260	G142+E19	5	Q172+Q44	V238+Q38	H324+Q44

W48+K269	0	Q118+M28	9	5	9
W48+W284	G142+A22	6	Q172+T45	V238+K39	H324+T45
W48+Y295	5	Q118+F28	9	1	9
W48+S304	G142+K24	9	Q172+P47	V238+K39	H324+P47
W48+V326	2	Q118+V29	3	3	3
G50+Q169	G142+S24	1	Q172+C47	V238+Q39	H324+C47
G50+A186	4	Q118+Q29	4	5	4
G50+E190	G142+G25	9	Q172+G47	V238+A42	H324+G47
G50+A225	8	Q118+R32	6	0	6
G50+K242	G142+N26	0	Q172+G47	V238+G42	H324+G47
G50+S244	0	Q118+H32	7	3	7
G50+G258	G142+K26	1	Q172+K48	V238+T44	H324+K48
G50+N260	9	Q118+S32	4	4	4
G50+K269	G142+W28	3	L173+A17	V238+A44	F328+T33
G50+W284	4	Q118+H32	4	5	4
G50+Y295	G142+Y29	4	L173+G18	V238+Q44	F328+D33
G50+S304	5	Q118+F32	4	9	7
G50+V326	G142+S30	8	L173+T19	V238+T45	F328+Q34
T51+Q169	4	Q118+T33	3	9	5
T51+A186	G142+V32	4	L173+N19	V238+P47	F328+G34
T51+E190	6	Q118+D33	5	3	6
T51+A225	G149+Q16	7	L173+A20	V238+C47	F328+G34
T51+K242	9	Q118+Q34	4	4	8
T51+S244	G149+A18	5	L173+V20	V238+G47	F328+T35
T51+G258	6	Q118+G34	6	6	5
T51+N260	G149+E19	6	L173+P21	V238+G47	F328+S37
T51+K269	0	Q118+G34	1	7	6
T51+W284	G149+A22	8	L173+I21	V238+K48	F328+D37
T51+Y295	5	Q118+T35	4	4	7
T51+S304	G149+K24	5	L173+V21	M246+M24	F328+D37
T51+V326	2	Q118+S37	5	8	9
A186+E19	G149+S24	6	L173+L21	M246+L25	F328+Y38

0	4	Q118+D377	7	0	2
A186+T193	G149+G258	Q118+D379	L173+L219	M246+G255	F328+S383
A186+N195	G149+N260	Q118+Y382	L173+L235	M246+Q256	F328+Q385
A186+A204	G149+K269	Q118+S383	L173+V238	M246+A263	F328+K391
A186+V206	G149+W284	Q118+Q385	L173+M246	M246+V264	F328+K393
A186+P211	G149+Y295	Q118+K391	L173+M248	M246+Y267	F328+Q395
A186+I214	G149+S304	Q118+K393	L173+L250	M246+N270	F328+A420
A186+V215	G149+V326	Q118+Q395	L173+G255	M246+G273	F328+G423
A186+L217	T165+Q169	Q118+A420	L173+Q256	M246+S280	F328+T444
A186+L219	T165+A186	Q118+G423	L173+A263	M246+T285	F328+A445
A186+A225	T165+E190	Q118+T444	L173+V264	M246+M286	F328+Q449
A186+L235	T165+A225	Q118+A445	L173+Y267	M246+F289	F328+T459
A186+V238	T165+K242	Q118+Q449	L173+N270	M246+V291	F328+P473
A186+K242	T165+S244	Q118+T459	L173+G273	M246+Q299	F328+C474
A186+S244	T165+G258	Q118+P473	L173+S280	M246+R320	F328+G476
A186+M246	T165+N260	Q118+C474	L173+T285	M246+H321	F328+G477
A186+M24	T165+K26		L173+M28	M246+S32	F328+K48

8	9	Q118+G476	6	3	4
A186+L250	T165+W284	Q118+G477	L173+F289	M246+H324	T334+D337
A186+G255	T165+Y295	Q118+K484	L173+V291	M246+F328	T334+Q345
A186+Q256	T165+S304	Q125+G133	L173+Q299	M246+T334	T334+G346
A186+G258	T165+V326	Q125+T134	L173+R320	M246+D337	T334+G348
A186+N260	W167+Q169	Q125+W140	L173+H321	M246+Q345	T334+T355
A186+A263	W167+A186	Q125+G142	L173+S323	M246+G346	T334+S376
A186+V264	W167+E190	Q125+G149	L173+H324	M246+G348	T334+D377
A186+Y267	W167+A225	Q125+T165	L173+F328	M246+T355	T334+D379
A186+K269	W167+K242	Q125+W167	L173+T334	M246+S376	T334+Y382
A186+N270	W167+S244	Q125+R171	L173+D337	M246+D377	T334+S383
A186+G273	W167+G258	Q125+Q172	L173+Q345	M246+D379	T334+Q385
A186+S280	W167+N260	Q125+L173	L173+G346	M246+Y382	T334+K391
A186+W284	W167+K269	Q125+A174	L173+G348	M246+S383	T334+K393
A186+T285	W167+W284	Q125+G184	L173+T355	M246+Q385	T334+Q395
A186+M286	W167+Y295	Q125+T193	L173+S376	M246+K391	T334+A420
A186+F28	W167+S30		L173+D37	M246+K39	T334+G42

9	4	Q125+N19	7	3	3
A186+V29	W167+V32	5	L173+D37	M246+Q39	T334+T44
1	6	Q125+A20	9	5	4
A186+Y29	E190+T19	4	L173+Y38	M246+A42	T334+A44
5	3	Q125+V20	2	0	5
A186+Q29	E190+N19	6	L173+S38	M246+G42	T334+Q44
9	5	Q125+P21	3	3	9
A186+S30	E190+A20	1	L173+Q38	M246+T44	T334+T45
4	4	Q125+I21	5	4	9
A186+R32	E190+V20	4	L173+K39	M246+A44	T334+P47
0	6	Q125+V21	1	5	3
A186+H32	E190+P21	5	L173+K39	M246+Q44	T334+C47
1	1	Q125+L21	3	9	4
A186+S32	E190+I21	7	L173+Q39	M246+T45	T334+G47
3	4	Q125+L21	5	9	6
A186+H32	E190+V21	9	L173+A42	M246+P47	T334+G47
4	5	Q125+L23	0	3	7
A186+V32	E190+L21	5	L173+G42	M246+C47	T334+K48
6	7	Q125+V23	3	4	4
A186+F32	E190+L21	8	L173+T44	M246+G47	D337+Q34
8	9	Q125+M24	4	6	5
A186+T33	E190+A22	6	L173+A44	M246+G47	D337+G34
4	5	Q125+M24	5	7	6
A186+D33	E190+L23	8	L173+Q44	M246+K48	D337+G34
7	5	Q125+L25	9	4	8
A186+Q34	E190+V23	0	L173+T45	M248+L25	D337+T35
5	8	Q125+G25	9	0	5
A186+G34	E190+K24	5	L173+P47	M248+G25	D337+S37
6	2	Q125+Q25	3	5	6
A186+G34	E190+S24	6	L173+C47	M248+Q25	D337+D37
8	4	Q125+A26	4	6	7
A186+T35	E190+M24	3	L173+G47	M248+A26	D337+D37

5	6	Q125+V26	6	3	9
A186+S37	E190+M24	4	L173+G47	M248+V26	D337+Y38
6	8	Q125+Y26	7	4	2
A186+D37	E190+L25	7	L173+K48	M248+Y26	D337+S38
7	0	Q125+N27	4	7	3
A186+D37	E190+G25	0	A174+G18	M248+N27	D337+Q38
9	5	Q125+G27	4	0	5
A186+Y38	E190+Q25	3	A174+T19	M248+G27	D337+K39
2	6	Q125+S28	3	3	1
A186+S38	E190+G25	0	A174+N19	M248+S28	D337+K39
3	8	Q125+T28	5	0	3
A186+Q38	E190+N26	5	A174+A20	M248+T28	D337+Q39
5	0	Q125+M28	4	5	5
A186+K39	E190+A26	6	A174+V20	M248+M28	D337+A42
1	3	Q125+F28	6	6	0
A186+K39	E190+V26	9	A174+P21	M248+F28	D337+G42
3	4	Q125+V29	1	9	3
A186+Q39	E190+Y26	1	A174+I21	M248+V29	D337+T44
5	7	Q125+Q29	4	1	4
A186+A42	E190+K26	9	A174+V21	M248+Q29	D337+A44
0	9	Q125+R32	5	9	5
A186+G42	E190+N27	0	A174+L21	M248+R32	D337+Q44
3	0	Q125+H32	7	0	9
A186+T44	E190+G27	1	A174+L21	M248+H32	D337+T45
4	3	Q125+S32	9	1	9
A186+A44	E190+S28	3	A174+L23	M248+S32	D337+P47
5	0	Q125+H32	5	3	3
A186+Q44	E190+W28	4	A174+V23	M248+H32	D337+C47
9	4	Q125+F32	8	4	4
A186+T45	E190+T28	8	A174+M24	M248+F32	D337+G47
9	5	Q125+T33	6	8	6
A186+P47	E190+M28	4	A174+M24	M248+T33	D337+G47

3	6	Q125+D33	8	4	7
A186+C47	E190+F28	7	A174+L25	M248+D33	D337+K48
4	9	Q125+Q34	0	7	4
A186+G47	E190+V29	5	A174+G25	M248+Q34	Q345+G34
6	1	Q125+G34	5	5	6
A186+G47	E190+Y29	6	A174+Q25	M248+G34	Q345+G34
7	5	Q125+G34	6	6	8
A186+K48	E190+Q29	8	A174+A26	M248+G34	Q345+T35
4	9	Q125+T35	3	8	5
I214+A22	E190+S30	5	A174+V26	M248+T35	Q345+S37
5	4	Q125+S37	4	5	6
I214+K24	E190+R32	6	A174+Y26	M248+S37	Q345+D37
2	0	Q125+D37	7	6	7
I214+S24	E190+H32	7	A174+N27	M248+D37	Q345+D37
4	1	Q125+D37	0	7	9
I214+G25	E190+S32	9	A174+G27	M248+D37	Q345+Y38
8	3	Q125+Y38	3	9	2
I214+N26	E190+H32	2	A174+S28	M248+Y38	Q345+S38
0	4	Q125+S38	0	2	3
I214+K26	E190+V32	3	A174+T28	M248+S38	Q345+Q38
9	6	Q125+Q38	5	3	5
I214+W28	E190+F32	5	A174+M28	M248+Q38	Q345+K39
4	8	Q125+K39	6	5	1
I214+Y29	E190+T33	1	A174+F28	M248+K39	Q345+K39
5	4	Q125+K39	9	1	3
I214+S30	E190+D33	3	A174+V29	M248+K39	Q345+Q39
4	7	Q125+Q39	1	3	5
I214+V32	E190+Q34	5	A174+Q29	M248+Q39	Q345+A42
6	5	Q125+A42	9	5	0
V215+A22	E190+G34	0	A174+R32	M248+A42	Q345+G42
5	6	Q125+G42	0	0	3
V215+K24	E190+G34	3	A174+H32	M248+G42	Q345+T44

2	8	Q125+T444	1	3	4
V215+S244	E190+T355	Q125+A445	A174+S323	M248+T444	Q345+A445
V215+G258	E190+S376	Q125+Q449	A174+H324	M248+A445	Q345+Q449
V215+N260	E190+D377	Q125+T459	A174+F328	M248+Q449	Q345+T459
V215+K269	E190+D379	Q125+P473	A174+T334	M248+T459	Q345+P473
V215+W284	E190+Y382	Q125+C474	A174+D337	M248+P473	Q345+C474
V215+Y295	E190+S383	Q125+G476	A174+Q345	M248+C474	Q345+G476
V215+S304	E190+Q385	Q125+G477	A174+G346	M248+G476	Q345+G477
V215+V326	E190+K391	Q125+K484	A174+G348	M248+G477	Q345+K484
N270+W284	E190+K393	G133+T134	A174+T355	M248+K484	G346+G348
N270+Y295	E190+Q395	G133+W140	A174+S376	L250+G255	G346+T355
N270+S304	E190+A420	G133+G142	A174+D377	L250+Q256	G346+S376
N270+V326	E190+G423	G133+G149	A174+D379	L250+A263	G346+D377
G273+W284	E190+T444	G133+T165	A174+Y382	L250+V264	G346+D379
G273+Y295	E190+A445	G133+W167	A174+S383	L250+Y267	G346+Y382
G273+S304	E190+Q449	G133+R171	A174+Q385	L250+N270	G346+S383
G273+V326	E190+T45		A174+K39	L250+G27	G346+Q38

6	9	G133+Q17	1	3	5
S280+W28	E190+P47	2	A174+K39	L250+S28	G346+K39
4	3	G133+L17	3	0	1
S280+Y29	E190+C47	3	A174+Q39	L250+T28	G346+K39
5	4	G133+A17	5	5	3
S280+S30	E190+G47	4	A174+A42	L250+M28	G346+Q39
4	6	G133+G18	0	6	5
S280+V32	E190+G47	4	A174+G42	L250+F28	G346+A42
6	7	G133+T19	3	9	0
T285+Y29	E190+K48	3	A174+T44	L250+V29	G346+G42
5	4	G133+N19	4	1	3
T285+S30	G258+N26	5	A174+A44	L250+Q29	G346+T44
4	0	G133+A20	5	9	4
T285+V32	G258+A26	4	A174+Q44	L250+R32	G346+A44
6	3	G133+V20	9	0	5
M286+Y29	G258+V26	6	A174+T45	L250+H32	G346+Q44
5	4	G133+P21	9	1	9
M286+S30	G258+Y26	1	A174+P47	L250+S32	G346+T45
4	7	G133+I21	3	3	9
M286+V32	G258+K26	4	A174+C47	L250+H32	G346+P47
6	9	G133+V21	4	4	3
F289+Y29	G258+N27	5	A174+G47	L250+F32	G346+C47
5	0	G133+L21	6	8	4
F289+S30	G258+G27	7	A174+G47	L250+T33	G346+G47
4	3	G133+L21	7	4	6
F289+V32	G258+S28	9	A174+K48	L250+D33	G346+G47
6	0	G133+L23	4	7	7
V291+Y29	G258+W28	5	G184+T19	L250+Q34	G346+K48
5	4	G133+V23	3	5	4
V291+S30	G258+T28	8	G184+N19	L250+G34	G348+T35
4	5	G133+M24	5	6	5
V291+V32	G258+M28	6	G184+A20	L250+G34	G348+S37

6	6	G133+M24	4	8	6
Y295+Q29	G258+F28	8	G184+V20	L250+T35	G348+D37
9	9	G133+L25	6	5	7
Y295+S30	G258+V29	0	G184+P21	L250+S37	G348+D37
4	1	G133+G25	1	6	9
Y295+R32	G258+Y29	5	G184+I21	L250+D37	G348+Y38
0	5	G133+Q25	4	7	2
Y295+H32	G258+Q29	6	G184+V21	L250+D37	G348+S38
1	9	G133+A26	5	9	3
Y295+S32	G258+S30	3	G184+L21	L250+Y38	G348+Q38
3	4	G133+V26	7	2	5
Y295+H32	G258+R32	4	G184+L21	L250+S38	G348+K39
4	0	G133+Y26	9	3	1
Y295+V32	G258+H32	7	G184+L23	L250+Q38	G348+K39
6	1	G133+N27	5	5	3
Y295+F32	G258+S32	0	G184+V23	L250+K39	G348+Q39
8	3	G133+G27	8	1	5
Y295+T33	G258+H32	3	G184+M24	L250+K39	G348+A42
4	4	G133+S28	6	3	0
Y295+D33	G258+V32	0	G184+M24	L250+Q39	G348+G42
7	6	G133+T28	8	5	3
Y295+Q34	G258+F32	5	G184+L25	L250+A42	G348+T44
5	8	G133+M28	0	0	4
Y295+G34	G258+T33	6	G184+G25	L250+G42	G348+A44
6	4	G133+F28	5	3	5
Y295+G34	G258+D33	9	G184+Q25	L250+T44	G348+Q44
8	7	G133+V29	6	4	9
Y295+T35	G258+Q34	1	G184+A26	L250+A44	G348+T45
5	5	G133+Q29	3	5	9
Y295+S37	G258+G34	9	G184+V26	L250+Q44	G348+P47
6	6	G133+R32	4	9	3
Y295+D37	G258+G34	0	G184+Y26	L250+T45	G348+C47

7	8	G133+H32	7	9	4
Y295+D37	G258+T35	1	G184+N27	L250+P47	G348+G47
9	5	G133+S32	0	3	6
Y295+Y38	G258+S37	3	G184+G27	L250+C47	G348+G47
2	6	G133+H32	3	4	7
Y295+S38	G258+D37	4	G184+S28	L250+G47	G348+K48
3	7	G133+F32	0	6	4
Y295+Q38	G258+D37	8	G184+T28	L250+G47	T355+S37
5	9	G133+T33	5	7	6
Y295+K39	G258+Y38	4	G184+M28	L250+K48	T355+D37
1	2	G133+D33	6	4	7
Y295+K39	G258+S38	7	G184+F28	G255+Q25	T355+D37
3	3	G133+Q34	9	6	9
Y295+Q39	G258+Q38	5	G184+V29	G255+A26	T355+Y38
5	5	G133+G34	1	3	2
Y295+A42	G258+K39	6	G184+Q29	G255+V26	T355+S38
0	1	G133+G34	9	4	3
Y295+G42	G258+K39	8	G184+R32	G255+Y26	T355+Q38
3	3	G133+T35	0	7	5
Y295+T44	G258+Q39	5	G184+H32	G255+N27	T355+K39
4	5	G133+S37	1	0	1
Y295+A44	G258+A42	6	G184+S32	G255+G27	T355+K39
5	0	G133+D37	3	3	3
Y295+Q44	G258+G42	7	G184+H32	G255+S28	T355+Q39
9	3	G133+D37	4	0	5
Y295+T45	G258+T44	9	G184+F32	G255+T28	T355+A42
9	4	G133+Y38	8	5	0
	G258+A44	2	G184+T33	G255+M28	T355+G42
	5	G133+S38	4	6	3
	G258+Q44	3	G184+D33	G255+F28	T355+T44
	9	G133+Q38	7	9	4
	G258+T45	5	G184+Q34	G255+V29	T355+A44

	9 G258+P473 G258+C474 G258+G476 G258+G477 G258+K484 Q299+S304 Q299+V326 R320+V326 H321+V326 S323+V326 H324+V326 Y295+P473 Y295+C474 Y295+G476 Y295+G477	G133+K391 G133+K393 G133+Q395 G133+A420 G133+G423 G133+T444 G133+A445 G133+Q449 G133+T459 G133+P473 G133+C474 G133+G476 G133+G477 G133+K484 T134+W140 T134+G142	5 G184+G346 G184+G348 G184+T355 G184+S376 G184+D377 G184+D379 G184+Y382 G184+S383 G184+Q385 G184+K391 G184+K393 G184+Q395 G184+A420 G184+G423 G184+T444 G184+A445	1 G255+Q299 G255+R320 G255+H321 G255+S323 G255+H324 G255+F328 G255+T334 G255+D337 G255+Q345 G255+G346 G255+G348 G255+T355 G255+S376 G255+D377 G255+D379 G255+Y382	5 T355+Q449 T355+T459 T355+P473 T355+C474 T355+G476 T355+G477 T355+K484 S376+D377 S376+D379 S376+Y382 S376+S383 S376+Q385 S376+K391 S376+K393 S376+Q395 S376+A420

		T134+G149 T134+T165 T134+W167 T134+R171 T134+Q172 T134+L173 T134+A174 T134+G184 T134+T193 T134+N195 T134+A204 T134+V206 T134+P211 T134+I214 T134+V215 T134+L217	5 G184+Q449 G184+T459 G184+P473 G184+C474 G184+G476 G184+G477 G184+K484 T193+N195 T193+A204 T193+V206 T193+P211 T193+I214 T193+V215 T193+L217 T193+L219 T193+L23	2 G255+S383 G255+Q385 G255+K391 G255+K393 G255+Q395 G255+A420 G255+G423 G255+T444 G255+A445 G255+Q449 G255+T459 G255+P473 G255+C474 G255+G476 G255+G477 G255+K48	0 S376+G423 S376+T444 S376+A445 S376+Q449 S376+T459 S376+P473 S376+C474 S376+G476 S376+G477 S376+K484 D377+D379 D377+Y382 D377+S383 D377+Q385 D377+K391 D377+K39

		T134+L219 T134+L235 T134+V238 T134+M246 T134+M248 T134+L250 T134+G255 T134+Q256 T134+A263 T134+V264 T134+Y267 T134+N270 T134+G273 T134+S280 T134+T285 T134+M286	5 T193+V238 T193+M246 T193+M248 T193+L250 T193+G255 T193+Q256 T193+A263 T193+V264 T193+Y267 T193+N270 T193+G273 T193+S280 T193+T285 T193+M286 T193+F289 T193+V29	4 Q256+A263 Q256+V264 Q256+Y267 Q256+N270 Q256+G273 Q256+S280 Q256+T285 Q256+M286 Q256+F289 Q256+V291 Q256+Q299 Q256+R320 Q256+H321 Q256+S323 Q256+H324 Q256+F32	3 D377+Q395 D377+A420 D377+G423 D377+T444 D377+A445 D377+Q449 D377+T459 D377+P473 D377+C474 D377+G476 D377+G477 D377+K484 D379+Y382 D379+S383 D379+Q385 D379+K39

		T134+F289 T134+V291 T134+Q299 T134+R320 T134+H321 T134+S323 T134+H324 T134+F328 T134+T334 T134+D337 T134+Q345 T134+G346 T134+G348 T134+T355 T134+S376 T134+D377	1 T193+Q299 T193+R320 T193+H321 T193+S323 T193+H324 T193+F328 T193+T334 T193+D337 T193+Q345 T193+G346 T193+G348 T193+T355 T193+S376 T193+D377 T193+D379 T193+Y38	8 Q256+T334 Q256+D337 Q256+Q345 Q256+G346 Q256+G348 Q256+T355 Q256+S376 Q256+D377 Q256+D379 Q256+Y382 Q256+S383 Q256+Q385 Q256+K391 Q256+K393 Q256+Q395 Q256+A42	1 D379+K393 D379+Q395 D379+A420 D379+G423 D379+T444 D379+A445 D379+Q449 D379+T459 D379+P473 D379+C474 D379+G476 D379+G477 D379+K484 Y382+S383 Y382+Q385 Y382+K39

		T134+D379 T134+Y382 T134+S383 T134+Q385 T134+K391 T134+K393 T134+Q395 T134+A420 T134+G423 T134+T444 T134+A445 T134+Q449 T134+T459 T134+P473 T134+C474 T134+G476	2 T193+S383 T193+Q385 T193+K391 T193+K393 T193+Q395 T193+A420 T193+G423 T193+T444 T193+A445 T193+Q449 T193+T459 T193+P473 T193+C474 T193+G476 T193+G477 T193+K484	0 Q256+G423 Q256+T444 Q256+A445 Q256+Q449 Q256+T459 Q256+P473 Q256+C474 Q256+G476 Q256+G477 Q256+K484 A263+V264 A263+Y267 A263+N270 A263+G273 A263+S280 A263+T281	1 Y382+K393 Y382+Q395 Y382+A420 Y382+G423 Y382+T444 Y382+A445 Y382+Q449 Y382+T459 Y382+P473 Y382+C474 Y382+G476 Y382+G477 Y382+K484 S383+Q385 S383+K391 S383+K393

		T134+G477 T134+K484 W140+G142 W140+G149 W140+T165 W140+W167 W140+R171 W140+Q172 W140+L173 W140+A174 W140+G184 W140+T193 W140+N195 W140+A204 W140+V206 W140+P211	4 N195+A204 N195+V206 N195+P211 N195+I214 N195+V215 N195+L217 N195+L219 N195+L235 N195+V238 N195+M246 N195+M248 N195+L250 N195+G255 N195+Q256 N195+A263 N195+V26	5 A263+M286 A263+F289 A263+V291 A263+Q299 A263+R320 A263+H321 A263+S323 A263+H324 A263+F328 A263+T334 A263+D337 A263+Q345 A263+G346 A263+G348 A263+T355 A263+S37	3 S383+Q395 S383+A420 S383+G423 S383+T444 S383+A445 S383+Q449 S383+T459 S383+P473 S383+C474 S383+G476 S383+G477 S383+K484 Q385+K391 Q385+K393 Q385+Q395 Q385+A42

		W140+I214 W140+V215 W140+L217 W140+L219 W140+L235 W140+V238 W140+M246 W140+M248 W140+L250 W140+G255 W140+Q256 W140+A263 W140+V264 W140+Y267 W140+N270 W140+G273	4 N195+Y267 7 N195+N270 0 N195+G273 3 N195+S280 0 N195+T285 5 N195+M286 6 N195+F289 9 N195+V291 1 N195+Q299 9 N195+R320 0 N195+H321 1 N195+S323 3 N195+H324 4 N195+F328 8 N195+T334 4 N195+D33	6 A263+D377 7 A263+D379 9 A263+Y382 2 A263+S383 3 A263+Q385 5 A263+K391 1 A263+K393 3 A263+Q395 5 A263+A420 0 A263+G423 3 A263+T444 4 A263+A445 5 A263+Q449 9 A263+T459 9 A263+P473 3 A263+C47	0 Q385+G423 3 Q385+T444 4 Q385+A445 5 Q385+Q449 9 Q385+T459 9 Q385+P473 3 Q385+C474 4 Q385+G476 6 Q385+G477 7 Q385+K484 4 K391+K393 3 K391+Q395 5 K391+A420 0 K391+G423 3 K391+T444 4 K391+A44

		W140+S280 W140+T285 W140+M286 W140+F289 W140+V291 W140+Q299 W140+R320 W140+H321 W140+S323 W140+H324 W140+F328 W140+T334 W140+D337 W140+Q345 W140+G346 W140+G348	7 N195+Q345 N195+G346 N195+G348 N195+T355 N195+S376 N195+D377 N195+D379 N195+Y382 N195+S383 N195+Q385 N195+K391 N195+K393 N195+Q395 N195+A420 N195+G423 N195+T44	4 A263+G476 A263+G477 A263+K484 V264+Y267 V264+N270 V264+G273 V264+S280 V264+T285 V264+M286 V264+F289 V264+V291 V264+Q299 V264+R320 V264+H321 V264+S323 V264+H32	5 K391+Q449 K391+T459 K391+P473 K391+C474 K391+G476 K391+G477 K391+K484 K393+Q395 K393+A420 K393+G423 K393+T444 K393+A445 K393+Q449 K393+T459 K393+P473 K393+C47

		W140+T355 W140+S376 W140+D377 W140+D379 W140+Y382 W140+S383 W140+Q385 W140+K391 N54+Q169 N54+A186 N54+E190 N54+A225 N54+K242 N54+S244 N54+G258 N54+N260 N54+K269 N54+W284 N54+Y295 N54+S304 N54+V326 V56+Q169 V56+A186 V56+E190	4 N195+A445 N195+Q449 N195+T459 N195+P473 N195+C474 N195+G476 N195+G477 N195+K484 A204+V206 A204+P211 A204+I214 A204+V215 A204+L217 A204+L219 A204+L235 A204+V23	4 V264+F328 V264+T334 V264+D337 V264+Q345 V264+G346 V264+G348 V264+T355 V264+S376 V264+D377 V264+D379 V264+Y382 V264+S383 V264+Q385 V264+K391 V264+K393 V264+Q39	4 K393+G476 K393+G477 K393+K484 Q395+A420 Q395+G423 Q395+T444 Q395+A445 Q395+Q449 Q395+T459 Q395+P473 Q395+C474 Q395+G476 Q395+G477 Q395+K484 A420+G423 A420+T44

		V56+A225 V56+K242 V56+S244 V56+G258 V56+N260 V56+K269 V56+W284 V56+Y295 V56+S304 V56+V326 Q169+R171 Q169+Q172 Q169+L173 Q169+A174 Q169+G184 Q169+A186 Q169+E190 Q169+T193 Q169+N195 Q169+A204 Q169+V206	8 A204+M246 A204+M248 A204+L250 A204+G255 A204+Q256 A204+A263 A204+V264 A204+Y267 A204+N270 A204+G273 A204+S280 A204+T285 A204+M286 A204+F289 A204+V291 A204+Q29	5 V264+A420 V264+G423 V264+T444 V264+A445 V264+Q449 V264+T459 V264+P473 V264+C474 V264+G476 V264+G477 V264+K484 Y267+N270 Y267+G273 Y267+S280 Y267+T285 Y267+M28	4 A420+A445 A420+Q449 A420+T459 A420+P473 A420+C474 A420+G476 A420+G477 A420+K484 G423+T444 G423+A445 G423+Q449 G423+T459 G423+P473 G423+C474 G423+G476 G423+G47

		Q169+P211 Q169+I214 Q169+V215 Q169+L217 Q169+L219 Q169+A225 Q169+L235 Q169+V238 Q169+K242 Q169+S244 Q169+M246 Q169+M248 Q169+L250 Q169+G255 Q169+Q256 Q169+G258	9 A204+R320 A204+H321 A204+S323 A204+H324 A204+F328 A204+T334 A204+D337 A204+Q345 A204+G346 A204+G348 A204+T355 A204+S376 A204+D377 A204+D379 A204+Y382 A204+S38	6 Y267+F289 Y267+V291 Y267+Q299 Y267+R320 Y267+H321 Y267+S323 Y267+H324 Y267+F328 Y267+T334 Y267+D337 Y267+Q345 Y267+G346 Y267+G348 Y267+T355 Y267+S376 Y267+D37	7 G423+K484 T444+A445 T444+Q449 T444+T459 T444+P473 T444+C474 T444+G476 T444+G477 T444+K484 A445+Q449 A445+T459 A445+P473 A445+C474 A445+G476 A445+G477 A445+K48

		Q169+N260 Q169+A263 Q169+V264 Q169+Y267 Q169+K269 Q169+N270 Q169+G273 Q169+S280 Q169+W284 Q169+T285 Q169+M286 Q169+F289 Q169+V291 Q169+Y295 Q169+Q299 Q169+S304	3 A204+Q385 A204+K391 A204+K393 A204+Q395 A204+A420 A204+G423 A204+T444 A204+A445 A204+Q449 A204+T459 A204+P473 A204+C474 A204+G476 A204+G477 A204+K484 V206+P21	7 Y267+D379 Y267+Y382 Y267+S383 Y267+Q385 Y267+K391 Y267+K393 Y267+Q395 Y267+A420 Y267+G423 Y267+T444 Y267+A445 Y267+Q449 Y267+T459 Y267+P473 G109+Q169 G109+A18	4 Q449+T459 Q449+P473 Q449+C474 Q449+G476 Q449+G477 Q449+K484 T459+P473 T459+C474 T459+G476 T459+G477 T459+K484 P473+C474 P473+G476 P473+G477 P473+K484 C474+G47

		Q169+R320 Q169+H321 Q169+S323 Q169+H324 Q169+V326 Q169+F328 Q169+T334 Q169+D337 Q169+Q345 Q169+G346 Q169+G348 Q169+T355 Q169+S376 Q169+D377 Q169+D379 Q169+Y382	1 V206+I214 K72+Q169 K72+A186 K72+E190 K72+A225 K72+K242 K72+S244 K72+G258 K72+N260 K72+K269 K72+W284 K72+Y295 K72+S304 K72+V326 R87+Q169 R87+A186 R87+E190 R87+A225 R87+K242 R87+S244 R87+G258 R87+N260 R87+K269 R87+W284 R87+Y295 R87+S304 R87+V326 Q98+Q169 Q98+A186 Q98+E190	6 G109+E190 G109+A225 G109+K242 G109+S244 G109+G258 G109+N260 G109+K269 G109+W284 G109+Y295 G109+S304 G109+V326 F113+Q169 F113+A186 F113+E190 F113+A225 F113+K242	6 C474+G477 C474+K484 G476+G477 G476+K484 G477+K484 G133+Q169 G133+A186 G133+E190 G133+A225 G133+K242 G133+S244 G133+G258 G133+N260 G133+K269 G133+W284 G133+Y29

		Q169+S383 Q169+Q385 Q169+K391 Q169+K393 Q169+Q395 Q169+A420 Q169+G423 Q169+T444 Q169+A445 Q169+Q449 Q169+T459 Q169+P473 Q169+C474 Q169+G476 Q169+G477 Q169+K484	Q98+A225 Q98+K242 Q98+S244 Q98+G258 Q98+N260 Q98+K269 Q98+W284 Q98+Y295 Q98+S304 Q98+V326 M105+Q169 M105+A186 M105+E190 M105+A225 M105+K242 M105+S244 M105+G258 M105+N260 M105+K269 M105+W284 M105+Y295	2 F113+S244 F113+G258 F113+N260 F113+K269 F113+W284 F113+Y295 F113+S304 F113+V326 R116+Q169 R116+A186 R116+E190 R116+A225 R116+K242 R116+S244 R116+G258 R116+N26	5 G133+S304 G133+V326 T134+Q169 T134+A186 T134+E190 T134+A225 T134+K242 T134+S244 T134+G258 T134+N260 T134+K269 T134+W284 T134+Y295 T134+S304 T134+V326 W140+Q16

		T193+A225 T193+K242 T193+S244 T193+G258 T193+N260 T193+K269 T193+W284 T193+Y295 T193+S304 T193+V326 N195+A225 N195+K242 N195+S244 N195+G258 N195+N260 N195+K269	M105+S304 M105+V326 R171+A186 R171+E190 R171+A225 R171+K242 R171+S244 R171+G258 R171+N260 R171+K269 R171+W284 R171+Y295 R171+S304 R171+V326 Q172+A186 Q172+E190	0 R116+K269 R116+W284 R116+Y295 R116+S304 R116+V326 Q118+Q169 Q118+A186 Q118+E190 Q118+A225 Q118+K242 Q118+S244 Q118+G258 Q118+N260 Q118+K269 Q118+W284 Q118+Y29	9 W140+A186 W140+E190 W140+A225 W140+K242 W140+S244 W140+G258 W140+N260 W140+K269 W140+W284 W140+Y295 W140+S304 W140+V326 E190+L235 A225+V238 A225+K242 A225+S24

		N195+W284 N195+Y295 N195+S304 N195+V326 A204+A225 A204+K242 A204+S244 A204+G258 A204+N260 A204+K269 A204+W284 A204+Y295 A204+S304 A204+V326 V206+A225 V206+K242	Q172+A225 Q172+K242 Q172+S244 Q172+G258 Q172+N260 Q172+K269 Q172+W284 Q172+Y295 Q172+S304 Q172+V326 L173+A186 L173+E190 L173+A225 L173+K242 L173+S244 L173+G258	5 Q118+S304 Q118+V326 Q125+Q169 Q125+A186 Q125+E190 Q125+A225 Q125+K242 Q125+S244 Q125+G258 Q125+N260 Q125+K269 Q125+W284 Q125+Y295 Q125+S304 Q125+V326 G184+A18	4 A225+M246 A225+M248 A225+L250 A225+G255 A225+Q256 A225+G258 A225+N260 A225+A263 A225+V264 A225+Y267 A225+K269 A225+N270 A225+G273 A225+S280 A225+W284 A225+T28

		V206+S244 V206+G258 V206+N260 V206+K269 V206+W284 V206+Y295 V206+S304 V206+V326 P211+A225 P211+K242 P211+S244 P211+G258 P211+N260 P211+K269 P211+W284 P211+Y295	L173+N260 L173+K269 L173+W284 L173+Y295 L173+S304 L173+V326 A174+A186 A174+E190 A174+A225 A174+K242 A174+S244 A174+G258 A174+N260 A174+K269 A174+W284 A174+Y295	6 G184+E190 G184+A225 G184+K242 G184+S244 G184+G258 G184+N260 G184+K269 G184+W284 G184+Y295 G184+S304 G184+V326 L235+K242 L235+S244 L235+G258 L235+N260 L235+K26	5 A225+M286 A225+F289 A225+V291 A225+Y295 A225+Q299 A225+S304 A225+R320 A225+H321 A225+S323 A225+H324 A225+V326 A225+F328 A225+T334 A225+D337 A225+Q345 A225+G34

		P211+S304 P211+V326 A236+K269 A236+W284 A236+Y295 A236+S304 A236+V326 V264+K269 V264+W284 V264+Y295 V264+S304 V267+V326 Y267+K269 Y267+W284 Y267+Y295 Y267+S304	A174+S304 A174+V326 L217+A225 L217+K242 L217+S244 L217+G258 L217+N260 L217+K269 L217+W284 L217+Y295 L217+S304 L217+V326 L219+A225 L219+K242 L219+S244 L219+G258	9 L235+W284 L235+Y295 L235+S304 L235+V326 V238+K242 V238+S244 V238+G258 V238+N260 V238+K269 V238+W284 V238+Y295 V238+S304 V238+V326 K242+S244 K242+M246 K242+M24	6 A225+G348 A225+T355 A225+S376 A225+D377 A225+D379 A225+Y382 A225+S383 A225+Q385 A225+K391 A225+K393 A225+Q395 A225+A420 A225+G423 A225+T444 A225+A445 A225+Q44

		Y267+V326 A288+F289 A288+V291 A288+Y295 A288+Q299 A288+S304 A288+R320 A288+H321 A288+S323 A288+H324 A288+V326 A288+F328 A288+T334 A288+D337 A288+Q345 A288+G346	L219+N260 L219+K269 L219+W284 L219+Y295 L219+S304 L219+V326 M246+G258 M246+N260 M246+K269 M246+W284 M246+Y295 M246+S304 M246+V326 M248+G258 M248+N260 M248+K269	8 K242+L250 K242+G255 K242+Q256 K242+G258 K242+N260 K242+A263 K242+V264 K242+Y267 K242+K269 K242+N270 K242+G273 K242+S280 K242+W284 K242+T285 K242+M286 K242+F28	9 A225+T459 A225+P473 A225+C474 A225+G476 A225+G477 A225+K484 S244+M248 S244+L250 S244+G255 S244+Q256 S244+G258 S244+N260 S244+A263 S244+V264 S244+Y267 S244+K26

		A288+G348 A288+T355 A288+S376 A288+D377 A288+D379 A288+Y382 A288+S383 A288+Q385 A288+K391 A288+K393 A288+Q395 A288+A420 A288+G423 A288+T444 A288+A445 A288+Q449	M248+W284 M248+Y295 M248+S304 M248+V326 L250+G258 L250+N260 L250+K269 L250+W284 L250+Y295 L250+S304 L250+V326 G255+G258 G255+N260 G255+K269 G255+W284 G255+Y295	9 K242+V291 K242+Y295 K242+Q299 K242+S304 K242+R320 K242+H321 K242+S323 K242+H324 K242+V326 K242+F328 K242+T334 K242+D337 K242+Q345 K242+G346 K242+G348 K242+T35	9 S244+N270 S244+G273 S244+S280 S244+W284 S244+T285 S244+M286 S244+F289 S244+V291 S244+Y295 S244+Q299 S244+S304 S244+R320 S244+H321 S244+S323 S244+H324 S244+V32

		A288+T459 A288+P473 A288+C474 A288+G476 A288+G477 A288+K484 S304+Q345 S304+G346 S304+G348 Y295+K484	G255+S304 G255+V326 Q256+G258 Q256+N260 Q256+K269 Q256+W284 Q256+Y295 Q256+S304 Q256+V326 W284+T285 W284+M286 W284+F289 W284+V291 W284+Y295 W284+Q299 W284+S304	5 K242+S376 K242+D377 K242+D379 K242+Y382 K242+S383 K242+Q385 K242+K391 K242+K393 K242+Q395 K242+A420 K242+G423 K242+T444 K242+A445 K242+Q449 K242+T459 K242+P47	6 S244+F328 S244+T334 S244+D337 S244+Q345 S244+G346 S244+G348 S244+T355 S244+S376 S244+D377 S244+D379 S244+Y382 S244+S383 S244+Q385 S244+K391 S244+K393 S244+Q39

			W284+R320 W284+H321 W284+S323 W284+H324 W284+V326 W284+F328 W284+T334 W284+D337 W284+Q345 W284+G346 W284+G348 W284+T355 W284+S376 W284+D377 W284+D379 W284+Y382	3 K242+C474 K242+G476 K242+G477 K242+K484 N260+A263 N260+V264 N260+Y267 N260+K269 N260+N270 N260+G273 N260+S280 N260+W284 N260+T285 N260+M286 N260+F289 N260+V29	5 S244+A420 S244+G423 S244+T444 S244+A445 S244+Q449 S244+T459 S244+P473 S244+C474 S244+G476 S244+G477 S244+K484 K269+N270 K269+G273 K269+S280 K269+W284 K269+T28

			W284+S383 W284+Q385 W284+K391 W284+K393 W284+Q395 W284+A420 W284+G423 W284+T444 W284+A445 W284+Q449 W284+T459 W284+P473 W284+C474 W284+G476 W284+G477 W284+K484	1 N260+Y295 N260+Q299 N260+S304 N260+R320 N260+H321 N260+S323 N260+H324 N260+V326 N260+F328 N260+T334 N260+D337 N260+Q345 N260+G346 N260+G348 N260+T355 N260+S37	5 K269+M286 K269+F289 K269+V291 K269+Y295 K269+Q299 K269+S304 K269+R320 K269+H321 K269+S323 K269+H324 K269+V326 K269+F328 K269+T334 K269+D337 K269+Q345 K269+G34

			S304+V326 S304+Y295 S304+S304 S304+V326 S304+Q299 S304+S304 S304+R320 S304+H321 S304+S323 S304+H324 S304+V326 S304+F328 S304+T334	6 N260+D377 N260+D379 N260+Y382 N260+S383 N260+Q385 N260+K391 N260+K393 N260+Q395 N260+A420 N260+G423 N260+T444 N260+A445 N260+Q449 N260+T459 N260+P473 N260+C47	6 K269+G348 K269+T355 K269+S376 K269+D377 K269+D379 K269+Y382 K269+S383 K269+Q385 K269+K391 K269+K393 K269+Q395 K269+A420 K269+G423 K269+T444 K269+A445 K269+Q44

				4 N260+G476 N260+G477 N260+K484 S304+K393 S304+Q395 S304+A420 S304+G423 S304+T444 S304+A445 S304+Q449 S304+T459 S304+P473 S304+C474 S304+G476 S304+G477 S304+K48	9 K269+T459 K269+P473 K269+C474 K269+G476 K269+G477 K269+K484 S304+T355 S304+S376 S304+D377 S304+D379 S304+Y382 S304+S383 S304+Q385 S304+K391 S304+D337

				4	

en donde la numeración es acorde con la SEQ ID NO: 13;

o

H1+A37	N54+F113	K72+G109	R116+A17	T165+A17	N195+V20
H1+T40	N54+R116	K72+F113	4	4	6
H1+N54	N54+N125	K72+R116	R116+G18	T165+G18	N195+L22
H1+V56	N54+F133	K72+N125	4	4	8
H1+A60	N54+T134	K72+F133	R116+N19	T165+N19	N195+G25
H1+K72	N54+T165	K72+T134	5	5	5
H1+G109	N54+Q172	K72+T165	R116+G19	T165+G19	N195+A26
H1+F113	N54+L173	K72+Q172	6	6	5
H1+R116	N54+A174	K72+L173	R116+A20	T165+A20	N195+S28
H1+N125	N54+G184	K72+A174	4	4	0
H1+F133	N54+N195	K72+G184	R116+V20	T165+V20	N195+S30
H1+T134	N54+G196	K72+N195	6	6	4
H1+T165	N54+A204	K72+G196	R116+L22	T165+L22	N195+R32
H1+Q172	N54+V206	K72+A204	8	8	0
H1+L173	N54+L228	K72+V206	R116+G25	T165+G25	N195+H32
H1+A174	N54+G255	K72+L228	5	5	1
H1+G184	N54+A265	K72+G255	R116+A26	T165+A26	N195+S32
H1+N195	N54+S280	K72+A265	5	5	3
H1+G196	N54+S304	K72+S280	R116+S28	T165+S28	N195+K39
H1+A204	N54+R320	K72+S304	0	0	1
H1+V206	N54+H321	K72+R320	R116+S30	T165+S30	G196+A20
H1+L228	N54+S323	K72+H321	4	4	4
H1+G255	N54+K391	K72+S323	R116+R32	T165+R32	G196+V20
H1+A265	V56+A60	K72+K391	0	0	6
H1+S280	V56+K72	G109+F11	R116+H32	T165+H32	G196+L22
H1+S304	V56+G109	3	1	1	8
H1+R320	V56+F113	G109+R11	R116+S32	T165+S32	G196+G25
H1+H321	V56+R116	6	3	3	5
H1+S323	V56+N125	G109+N12	R116+K39	T165+K39	G196+A26

H1+K391	V56+F133	5	1	1	5
A37+T40	V56+T134	G109+F13	N125+F13	Q172+L17	G196+S28
A37+N54	V56+T165	3	3	3	0
A37+V56	V56+Q172	G109+T13	N125+T13	Q172+A17	G196+S30
A37+A60	V56+L173	4	4	4	4
A37+K72	V56+A174	G109+T16	N125+T16	Q172+G18	G196+R32
A37+G109	V56+G184	5	5	4	0
A37+F113	V56+N195	G109+Q17	N125+Q17	Q172+N19	G196+H32
A37+R116	V56+G196	2	2	5	1
A37+N125	V56+A204	G109+L17	N125+L17	Q172+G19	G196+S32
A37+F133	V56+V206	3	3	6	3
A37+T134	V56+L228	G109+A17	N125+A17	Q172+A20	G196+K39
A37+T165	V56+G255	4	4	4	1
A37+Q172	V56+A265	G109+G18	N125+G18	Q172+V20	A204+V20
A37+L173	V56+S280	4	4	6	6
A37+A174	V56+S304	G109+N19	N125+N19	Q172+L22	A204+L22
A37+G184	V56+R320	5	5	8	8
A37+N195	V56+H321	G109+G19	N125+G19	Q172+G25	A204+G25
A37+G196	V56+S323	6	6	5	5
A37+A204	V56+K391	G109+A20	N125+A20	Q172+A26	A204+A26
A37+V206	A60+K72	4	4	5	5
A37+L228	A60+G109	G109+V20	N125+V20	Q172+S28	A204+S28
A37+G255	A60+F113	6	6	0	0
A37+A265	A60+R116	G109+L22	N125+L22	Q172+S30	A204+S30
A37+S280	A60+N125	8	8	4	4
A37+S304	A60+F133	G109+G25	N125+G25	Q172+R32	A204+R32
A37+R320	A60+T134	5	5	0	0
A37+H321	A60+T165	G109+A26	N125+A26	Q172+H32	A204+H32
A37+S323	A60+Q172	5	5	1	1
A37+K391	A60+L173	G109+S28	N125+S28	Q172+S32	A204+S32
T40+N54	A60+A174	0	0	3	3
T40+V56	A60+G184	G109+S30	N125+S30	Q172+K39	A204+K39

T40+A60	A60+N195	4	4	1	1
T40+K72	A60+G196	G109+R32	N125+R32	L173+A17	V206+L22
T40+G109	A60+A204	0	0	4	8
T40+F113	A60+V206	G109+H32	N125+H32	L173+G18	V206+G25
T40+R116	A60+L228	1	1	4	5
T40+N125	A60+G255	G109+S32	N125+S32	L173+N19	V206+A26
T40+F133	A60+A265	3	3	5	5
T40+T134	A60+S280	G109+K39	N125+K39	L173+G19	V206+S28
T40+T165	A60+S304	1	1	6	0
T40+Q172	A60+R320	F113+R11	F133+T13	L173+A20	V206+S30
T40+L173	A60+H321	6	4	4	4
T40+A174	A60+S323	F113+N12	F133+T16	L173+V20	V206+R32
T40+G184	A60+K391	5	5	6	0
T40+N195	T40+S323	F113+F13	F133+Q17	L173+L22	V206+H32
T40+G196	T40+K391	3	2	8	1
T40+A204	N54+V56	F113+T13	F133+L17	L173+G25	V206+S32
T40+V206	N54+A60	4	3	5	3
T40+L228	N54+K72	F113+T16	F133+A17	L173+A26	V206+K39
T40+G255	N54+G109	5	4	5	1
T40+Q169	R116+Q16	F113+Q17	F133+G18	L173+S28	L228+G25
T40+A186	9	2	4	0	5
T40+E190	R116+A18	F113+L17	F133+N19	L173+S30	L228+A26
T40+A225	6	3	5	4	5
T40+K242	R116+E19	F113+A17	F133+G19	L173+R32	L228+S28
T40+S244	0	4	6	0	0
T40+G258	R116+A22	F113+G18	F133+A20	L173+H32	L228+S30
T40+N260	5	4	4	1	4
T40+K269	R116+K24	F113+N19	F133+V20	L173+S32	L228+R32
T40+W284	2	5	6	3	0
T40+Y295	R116+S24	F113+G19	F133+L22	L173+K39	L228+H32
T40+S304	4	6	8	1	1
T40+V326	R116+G25	F113+A20	F133+G25	A174+G18	L228+S32

N54+Q169	8	4	5	4	3
N54+A186	R116+N26	F113+V20	F133+A26	A174+N19	L228+K39
N54+E190	0	6	5	5	1
N54+A225	R116+K26	F113+L22	F133+S28	A174+G19	G255+A26
N54+K242	9	8	0	6	5
N54+S244	R116+W28	F113+G25	F133+S30	A174+A20	G255+S28
N54+G258	4	5	4	4	0
N54+N260	R116+Y29	F113+A26	F133+R32	A174+V20	G255+S30
N54+K269	5	5	0	6	4
N54+W284	R116+S30	F113+S28	F133+H32	A174+L22	G255+R32
N54+Y295	4	0	1	8	0
N54+S304	N125+Q16	F113+S30	F133+S32	A174+G25	G255+H32
N54+V326	9	4	3	5	1
V56+Q169	N125+A18	F113+R32	F133+K39	A174+A26	G255+S32
V56+A186	6	0	1	5	3
V56+E190	N125+E19	F113+H32	T134+T16	A174+S28	G255+K39
V56+A225	0	1	5	0	1
V56+K242	N125+A22	F113+S32	T134+Q17	A174+S30	A265+S28
V56+S244	5	3	2	4	0
V56+G258	N125+K24	F113+K39	T134+L17	A174+R32	A265+S30
V56+N260	2	1	3	0	4
V56+K269	N125+S24	R116+N12	T134+A17	A174+H32	A265+R32
V56+W284	4	5	4	1	0
V56+Y295	N125+G25	R116+F13	T134+G18	A174+S32	A265+H32
V56+S304	8	3	4	3	1
V56+V326	N125+N26	R116+T13	T134+N19	A174+K39	A265+S32
A60+Q169	0	4	5	1	3
A60+A186	N125+K26	R116+T16	T134+G19	G184+N19	A265+K39
A60+E190	9	5	6	5	1
A60+A225	N125+W28	R116+Q17	T134+A20	G184+G19	S280+S30
A60+K242	4	2	4	6	4
A60+S244	N125+Y29	R116+L17	T134+V20	G184+A20	S280+R32

A60+G258	5	3	6	4	0
A60+N260	N125+S30	T40+A265	T134+L22	G184+V20	S280+H32
A60+K269	4	T40+S280	8	6	1
A60+W284	F133+Q16	T40+S304	T134+G25	G184+L22	S280+S32
A60+Y295	9	T40+R320	5	8	3
A60+S304	F133+A18	T40+H321	T134+A26	G184+G25	S280+K39
A60+V326	6	A204+A22	5	5	1
K72+Q169	F133+E19	5	T134+S28	G184+A26	S304+R32
K72+A186	0	A204+K24	0	5	0
K72+E190	F133+A22	2	T134+S30	G184+S28	S304+H32
K72+A225	5	A204+S24	4	0	1
K72+K242	F133+K24	4	T134+R32	G184+S30	S304+S32
K72+S244	2	A204+G25	0	4	3
K72+G258	F133+S24	8	T134+H32	G184+R32	S304+K39
K72+N260	4	A204+N26	1	0	1
K72+K269	F133+G25	0	T134+S32	G184+H32	R320+H32
K72+W284	8	A204+K26	3	1	1
K72+Y295	F133+N26	9	T134+K39	G184+S32	R320+S32
K72+S304	0	A204+W28	1	3	3
G109+Q16	F133+K26	4	T165+Q17	G184+K39	R320+K39
9	9	A204+Y29	2	1	1
G109+A18	F133+W28	5	T165+L17	N195+G19	H321+S32
6	4	A204+S30	3	6	3
G109+E19	F133+Y29	4	H1+Q169	N195+A20	H321+K39
0	5	V206+A22	H1+A186	4	1
G109+A22	F133+S30	5	H1+E190	S244+G25	S323+K39
5	4	V206+K24	H1+A225	5	1
G109+K24	T134+Q16	2	H1+K242	S244+G25	A265+K26
2	9	V206+S24	H1+S244	8	9
G109+S24	T134+A18	4	H1+G258	S244+N26	A265+W28
4	6	V206+G25	H1+N260	0	4
G109+G25	T134+E19	8	H1+K269	S244+A26	A265+Y29

8	0	V206+N26	H1+W284	5	5
G109+N26	T134+A22	0	H1+Y295	S244+K26	A265+S30
0	5	V206+K26	H1+S304	9	4
G109+K26	T134+K24	9	H1+V326	S244+S28	A265+V32
9	2	V206+W28	A37+Q169	0	6
G109+W28	T134+S24	4	A37+A186	S244+W28	K269+S28
4	4	V206+Y29	A37+E190	4	0
G109+Y29	T134+G25	5	A37+A225	S244+Y29	K269+W28
5	8	V206+S30	A37+K242	5	4
G109+S30	T134+N26	4	A37+S244	S244+S30	K269+Y29
4	0	V206+V32	A37+G258	4	5
G109+V32	T134+K26	6	A37+N260	S244+R32	K269+S30
6	9	A225+L22	A37+K269	0	4
F113+Q16	T134+W28	8	A37+W284	S244+H32	K269+R32
9	4	A225+K24	A37+Y295	1	0
F113+A18	T134+Y29	2	A37+S304	S244+S32	K269+H32
6	5	A225+S24	A37+V326	3	1
F113+E19	T134+S30	4	Q172+A18	S244+V32	K269+S32
0	4	A225+G25	6	6	3
F113+A22	T134+V32	5	Q172+E19	S244+K39	K269+V32
5	6	A225+G25	0	1	6
F113+K24	T165+Q16	8	Q172+A22	S244+I40	K269+K39
2	9	A225+N26	5	5	1
F113+S24	T165+A18	0	Q172+K24	S244+A42	K269+I40
4	6	A225+A26	2	1	5
F113+G25	T165+E19	5	Q172+S24	S244+A42	K269+A42
8	0	A225+K26	4	2	1
F113+N26	T165+N19	9	Q172+G25	S244+A42	K269+A42
0	5	A225+S28	8	8	2
F113+K26	T165+A22	0	Q172+N26	S244+G44	K269+A42
9	5	A225+W28	0	8	8
F113+W28	T165+K24	4	Q172+K26	S244+D47	K269+G44

4 F113+Y295 F113+S304 F113+V326	2 T165+S244 T165+G258 T165+N260 T165+K269 T165+W284 T165+Y295 T165+S304 Q169+Q172 Q169+L173 Q169+A174 Q169+G184 Q169+A186 Q169+E190 Q169+N195 Q169+G196 Q169+A20	A225+Y295 A225+S304 A225+R320 A225+H321 A225+S323 A225+V326 A225+K391 A225+I405 A225+A421 A225+A422 A225+A428 A225+G448 A225+D476 A225+G477 L228+K242 L228+S244	9 Q172+W284 Q172+Y295 Q172+S304 L173+A186 L173+E190 L173+A225 L173+K242 L173+S244 L173+G258 L173+N260 L173+K269 L173+W284 L173+Y295 L173+S304 A174+A186 A174+E19	6 S244+G477 G255+G258 G255+N260 G255+K269 G255+W284 G255+Y295 G255+S304 G255+V326 G258+N260 G258+A265 G258+K269 G258+S280 G258+W284 G258+Y295 G258+S304 G258+R32	8 K269+D476 K269+G477 S280+W284 S280+Y295 S280+S304 S280+V326 W284+Y295 W284+S304 W284+R320 W284+H321 W284+S323 W284+V326 W284+K391 W284+I405 W284+A421 W284+A42

	4 Q169+V206 Q169+A225 Q169+L228 Q169+K242 Q169+S244 Q169+G255 Q169+G258 Q169+N260 Q169+A265 Q169+K269 Q169+S280 Q169+W284 Q169+Y295 Q169+S304 Q169+R320 Q169+H32	L228+G258 L228+N260 L228+K269 L228+W284 L228+Y295 L228+S304 L228+V326 K242+S244 K242+G255 K242+G258 K242+N260 K242+A265 K242+K269 K242+S280 K242+W284 K242+Y295	0 A174+A225 A174+K242 A174+S244 A174+G258 A174+N260 A174+K269 A174+W284 A174+Y295 A174+S304 G184+A186 G184+E190 G184+A225 G184+K242 G184+S244 G184+G258 G184+N26	0 G258+H321 G258+S323 G258+V326 G258+K391 G258+I405 G258+A421 G258+A422 G258+A428 G258+G448 G258+D476 G258+G477 N260+A265 N260+K269 N260+S280 N260+W284 N260+Y29	2 W284+A428 W284+G448 W284+D476 W284+G477 Y295+S304 Y295+R320 Y295+H321 Y295+S323 Y295+V326 Y295+K391 Y295+I405 Y295+A421 Y295+A422 Y295+A428 Y295+G448 Y295+D47

	1 Q169+S323 Q169+V326 Q169+K391	K242+S304 K242+R320 K242+H321 K242+S323 K242+V326 K242+K391 K242+I405 K242+A421 K242+A422 K242+A428 K242+G448 K242+D476 K242+G477 E190+A204 E190+V206 E190+A225	0 G184+K269 G184+W284 G184+Y295 G184+S304 A186+E190 A186+N195 A186+G196 A186+A204 A186+V206 A186+A225 A186+L228 A186+K242 A186+S244 A186+G255 A186+G258 A186+N26	5 N260+S304 N260+R320 N260+H321 N260+S323 N260+V326 N260+K391 N260+I405 N260+A421 N260+A422 N260+A428 N260+G448 N260+D476 N260+G477 N195+A225 N195+K242 N195+S24	6 Y295+G477 S304+R320 S304+H321 S304+S323 S304+V326 S304+K391 S304+I405 S304+A421 S304+A422 S304+A428 S304+G448 S304+D476 S304+G477 R320+H321 R320+V326 H321+V32

		E190+L228 E190+K242 E190+S244 E190+G255 E190+G258 E190+N260 E190+A265 E190+K269 E190+S280 E190+W284 Q169+I405 Q169+A421	0 A186+A265 A186+K269 A186+S280 A186+W284 A186+Y295 A186+S304 A186+R320 A186+H321 A186+S323 A186+V326 A186+K391 A186+I405 A186+A421	4 N195+G258 N195+N260 N195+K269 N195+W284 N195+Y295 N195+S304 N195+V326 G196+A225 G196+K242 G196+S244 G196+G258 G196+N260 G196+K269 G196+W284 G196+Y295 G196+S30	6 S323+V326 V326+K391 V326+I405 V326+A421 V326+A422 V326+A428 V326+G448 V326+D476 V326+G477 E190+Y295 E190+S304 E190+R320 E190+H321 E190+S323 E190+V326 E190+K39

				4 G196+V326 A186+G448 A186+D476 A186+G477 E190+N195 E190+G196 Q169+A422 Q169+A428 Q169+G448 Q169+D476 Q169+G477	1 E190+I405 E190+A421 E190+A422 E190+A428 E190+G448 E190+D476 E190+G477 A186+A422 A186+A428

en donde la numeración es acorde con la SEQ ID NO: 14.

Puede mejorarse la estabilidad de un polipéptido parental introduciendo una eliminación emparejada dentro del dominio B de un polipéptido parental. Por lo tanto, en una realización, dicha variante comprende

a) una eliminación y/o una sustitución en dos o más posiciones correspondientes a las posiciones R181, G182, D183 y G184 de la secuencia de aminoácidos expuesta en las SEQ ID NO: 7 o 10 y

b) una alteración en una o más posiciones correspondientes a las posiciones H1, T5, G7, Q11, N16, V17, Q32, A37, T40, P45, W48, G50, T51, N54, V56, K72, R87, Q98, M105, G109, F113, R116, Q118, Q125, G133, T134, W140, G142, G149, T165, W167, Q169, R171, Q172, L173, A174, G184, A186, E190, T193, N195, A204, V206, P211, I214, V215, L217, L219, A225, L235, V238, K242, S244, M246, M248, L250, G255, Q256, N260, A263, V264, Y267, K269, N270, G273, S280, W284, T285, M286, F289, V291, Y295, Q299, R320, H321, S323, H324, V326, F328, T334, D337, Q345, G346, G348, T355, S376, D377, D379, Y382, S383, Q385, K391, K393, Q395, A420, G423, T444, A445, Q449, T459, P473, C474, G476, G477, y K484 de la SEQ ID NO: 13; o H1, A37, T40, N54, V56, A60, K72, G109, F113, R116, N125, F133, T134, T165, Q172, L173, A174, G184, N195, G196, A204, V206, L228, G255, A265, S280, S304, R320, H321, S323, K391, I405, A421, A422, A428, R439, G448, W467, D476, y G477 de la SEQ ID NO: 14.

La expresión "eliminación emparejada", tal como se usa en el presente documento, se refiere a una eliminación de un aminoácido en dos posiciones. Dichas dos posiciones pueden ser adyacentes entre sí, pero también pueden estar separadas por uno, dos, tres, cuatro o cinco aminoácidos.

En una realización particular, la eliminación a) se selecciona entre el grupo que consiste en R181+G182, R181+D183, R181+G184, G182+D183, G182+G184 o D183+G184.

En una realización, la variante comprende una o más de las siguientes alteraciones; H1*, T5K, G7K, G7A, Q11H, N16S, N16H, V17L, Q32S, A37H, A37M, A37V, A37S, A37Y, A37R, A37L, T40G, T40K, P45A, W48G, W48Y, W48F, G50A, T51K, T51E, T51G, T51A, T51S, T51G, T51D, N54S, V56T, K72R, K72H, K72S, K72Q, K72E, K72N, K72A, K72M, R87S, Q98S, Q98A, M105F, M105I, M105V, M105L, G109A, G109S, F113W, F113S, F113N, F113Y, F113R, F113L, F113Q, R116Q, R116V, R116K, R116W,

R116L, R116A, R116H, R116M, R116E, R116S, R116I, R116G, Q118N, Q118K, Q118G, Q118S, Q118F, Q118R, Q125P, Q125K, Q125A, Q125T, G133S, T134E, W140Y, G142T, G149Q, T165S, T165G, T165V, W167I, W167G, W167F, W167R, W167S, W167H, W167L, W167M, W167Y, Q169E, R171H, Q172G, Q172R, Q172N, Q172D, Q172Y, Q172M, Q172S, Q172T, Q172K, Q172H, Q172E, L173V, L173G, L173H, L173A, L173I, L173P, L173T, L173F, L173M, A174S, A174D, A174P, A174M, A174T, A174H, A174K, A174G, A174Q, A174N, A174V, A174L, G184T, A186D, A186N, A186E, A186Q, A186H, E190P, T193K, N195F, A204T, A204V, A204S, A204G, V206L, V206S, V206Y, P211D, I214G, I214H, I214S, I214T, I214L, I214E, I214W, V215T, L217T, L217Q, L219V, L219H, A225V, L235V, L235A, V238A, V238T, V238G, K242Q, S244Q, M246L, M246A, M246I, M246F, M246V, M246S, M248T, L250I, L250V, L250T, L250A, L250F, L250M, G255N, G255A, G255S, Q256A, N260G, A263G, V264I, V264T, Y267I, Y267M, Y267H, Y267L, K269Q, N270G, N270T, G273R, S280W, S280L, S280T, S280A, S280K, S280Q, W284H, T285L, T285Q, M286F, M286L, A288L, A288V, F289I, F289L, V291G, V291A, V291T, Y295F, Y295N, Q299V, S304R, S304N, R320A, R320V, H321Y, S323N, H324L, V326L, F328L, F328M, F328V, F328I, T334S, D337H, Q345D, G346T, G346D, G346P, G348S, G348P, T355L, T355F, S376H, S376T, S376V, D377H, D377S, D377A, D377Q, D379S, D379G, D379R, D379A, Y382M, Y382I, Y382L, Y382F, S383G, S383A, Q385L, K391A, K391Y, K391V, K391M, K391E, K391D, K391R, K391H, K391W, K391I, K391Q, K391L, K393Y, K393R, K393Q, K393S, Q395P, T400P, H402R, A420Q, A420S, A420K, A420L, G423H, T444Q, T444S, T444D, T444Y, T444H, T444V, T444R, T444A, A445Q, Q449T, T459N, P473R, P473A, P473G, P473T, P473K, C474V, G476K, G477A, G477Q, K484A, K484G, K484P, K484E, K484Q, y K484S de la SEQ ID NO: 13; o H1*, G7A, A37H, T40D, W48Y, W48F, N54S, V56T, A60V, K72R, Q98A, G109A, F113Q, R116H, R116V, R116Q, N125D,

F133Q, T134E, T165G, Q169E, Q172D, Q172G, Q172N, L173V, A174S, G184T, A186D, A186N, A186E, A186Q, A186H, E190P, N195F, G196R, A204G, V206L, V206Y, A225V, L228I, K242Q, S244Q, G255A, G255S, N260G, A265G, K269Q, N270T, S280Q, W284H, A288L, A288V, F289L, Y295F, Y295N, S304N, S304R, S304N, R320A, H321Y, S323N, V326L, K391A, I405L, A421H, A422P, A428T, G448D, D476K, D476G, D476N, D476Y, G477S, G477A, G477T, y G477Q de la SEQ ID NO: 14.

En una realización particular, la variante tiene un IF de >1 cuando se compara con dicho polipéptido parental y en donde dicha variante se selecciona entre

G182*+D183*+N195F

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K

H1*+N54S+V56T+R87S+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K

H1*+T40G+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K

H1*+T51K+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K

H1*+N54S+V56T+K72R+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K

H1*+N54S+V56T+K72H+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K

H1*+A37H+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K

H1*+A37M+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K

H1*+A37V+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K

H1*+A37S+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K

H1*+A37Y+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K

H1*+A37R+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K

H1*+N54S+V56T+G109A+F113W+A174S+G182*+D183*+N195F+V206L+K391A+G476K

H1*+N54S+V56T+G109A+F113S+A174S+G182*+D183*+N195F+V206L+K391A+G476K

H1*+N54S+V56T+G109A+F113N+A174S+G182*+D183*+N195F+V206L+K391A+G476K

H1*+N54S+V56T+G109A+F113Y+A174S+G182*+D183*+N195F+V206L+K391A+G476K

H1*+N54S+V56T+G109A+F113R+A174S+G182*+D183*+N195F+V206L+K391A+G476K

H1*+N54S+V56T+G109A+Q118N+A174S+G182*+D183*+N195F+V206L+K391A+G476K

H1*+N54S+V56T+G109A+R116Q+A174S+G182*+D183*+N195F+V206L+K391A+G476K

H1*+N54S+V56T+G109A+R116V+A174S+G182*+D183*+N195F+V206L+K391A+G476K

H1*+N54S+V56T+G109A+R116K+A174S+G182*+D183*+N195F+V206L+K391A+G476K

H1*+N54S+V56T+G109A+R116W+A174S+G182*+D183*+N195F+V206L+K391A+G476K

H1*+N54S+V56T+G109A+R116L+A174S+G182*+D183*+N195F+V206L+K391A+G476K

H1*+N54S+V56T+G109A+G142T+A174S+G182*+D183*+N195F+V206L+K391A+G476K

H1*+N54S+V56T+G109A+Q125P+A174S+G182*+D183*+N195F+V206L+K391A+G476K

H1*+N54S+V56T+G109A+Q125K+A174S+G182*+D183*+N195F+V206L+K391A+G476K

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+S381G+K391A+G476K

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+M246T+K391A+G476K

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+V213T+K391A+G476K

H1*+A37L+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K

H1*+N54S+V56T+G109A+Q118K+A174S+G182*+D183*+N195F+V206L+K391A+G476K

H1*+N54S+V56T+G109A+R116A+A174S+G182*+D183*+N195F+V206L+K391A+G476K

H1*+N54S+V56T+G109A+R116H+A174S+G182*+D183*+N195F+V206L+K391A+G476K

H1*+N54S+V56T+G109A+Q125A+A174S+G182*+D183*+N195F+V206L+K391A+G476K

H1*+N54S+V56T+G109A+Q172G+A174S+G182*+D183*+N195F+V206L+K391A+G476K

H1*+N54S+V56T+G109A+Q172R+A174S+G182*+D183*+N195F+V206L+K391A+G476K

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+D377S+K391A+G476K

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+D377G+K391A+G476K

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+D377R+K391A+G476K

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+D377A+K391A+G476K

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+I214G+K391A+G476K

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+S381A+K391A+G476K

H1*+N54S+V56T+G109A+W167I+A174S+G182*+D183*+N195F+V206L+K391A+G476K

H1*+N54S+V56T+G109A+W167G+A174S+G182*+D183*+N195F+V206L+K391A+G476K

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+G346S+K391A+G476K

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+G346P+K391A+G476K

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+I214H+K391A+G476K

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+I214S+K391A+G476K

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+I214T+K391A+G476K

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+A420Q+G476K

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+A420S+G476K

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+A420K+G476K

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+A420L+G476K

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+K391Y+G476K

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+K391R+G476K

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+P473R+G476K

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+P473A+G476K

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+P473G+G476K

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+P473T+G476K

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+Q395P+G476K

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+T444Q+G476K

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+T444S+G476K

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+T444D+G476K

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+T444Y+G476K

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+S280W+K391A+G476K

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+S280L+K391A+G476K

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+S280T+K391A+G476K

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G476K

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G476K

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G476K

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G476K

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G476K

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G476K

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K391A+G476K

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K391A+T444Q+G476K

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K391A+G476K
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G476K
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P473R+G476K

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T444Q+P473R+G476K

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P473R+G476K

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K391A+G476K,

H1*+N54S+V56T+G109A+F113Q+R116H+A174S+G182*+D183*+N195F+V206L+K391A+

G476K,

H1*+N54S+V56T+G109A+Q172G+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+A174S+A186D+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+A225V+

K391A+G476K,

H1*+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+G255S+
K391A+G476K,
H1*+N54S+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+K269Q+
K391A+G476K,
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+G255S+K391A+G476K,
H1*+N54S+V56T+G109A+Q169E+Q172K+A174S+G182*+D183*+N195F+V206L+K391A+
G476K,
G182*+D183*+N195F,
H1*+N54S+V56T+G109A+Q169E+A174S+G182*+D183*+N195F+V206L+K391A+G476K,
H1*+N54S+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+W284H+
K391A+G476K,
H1*+N54S+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K,
H1*+N54S+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+S304R+
K391A+G476K,
H1*+N54S+V56T+K72R+G109A+F113Q+R116Q+W167F+Q172G+A174S+G182*+D183*+
G184T+N195F+V206L+K391A+P473R,
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+M246V+K391A+G476K,
H1*+N54S+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+K391A,
H1*+N54S+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+N270G+
K391A+G476K,

H1*+N54S+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+Y295F+
K391A+G476K,
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+R320A+K391A+G476K,
H1*+N54S+V56T+G109A+Q169E+Q172K+A174T+G182*+D183*+N195F+V206L+K391A+
G476K,
H1*+N54S+V56T+G109A+Q169E+Q172K+G182*+D183*+N195F+V206L+K391A+G476K,
H1*+N54S+V56T+G109A+W140Y+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+
K391A+G476K,
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A,
H1*+N54S+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+F328L+
K391A+G476K,
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+G476K,
F113Q+R116H+D183*+G182*+N195F,
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+A288L+K391A+G476K,
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+N270G+K391A+G476K,
Q169E+Q172K+A174*+D183*+G182*+N195F,
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K269Q+K391A+G476K,
H1*+W48F+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K,
F113Q+R116Q+D183*+G182*+N195F,
N54S+V56T+D183*+G182*+N195F,

H1*+N54S+V56T+G109A+A174T+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+R116W+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

Q169E+Q172K+G182*+D183*+N195F,

G182*+D183*+A186D,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+V238A+K391A+G476K,

G182*+D183*+A186N,

H1*+N54S+V56T+G109A+A174S+V206L+G182*+D183*+K391A+G476K,

H1*+N54S+V56T+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206F+K391A+G476K,

H1*+N54S+V56T+G109A+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+Q172K+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+Q172K+A174*+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+A174N+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+A174S+A186N+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+F289L+K391A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+Y295F+K391A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+V291A+K391A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+S244Q+K391A+G476K,

G182*+D183*+F328L,

G182*+D183*+N195F+A288V,

G182*+D183*+A186N+N195F,

G182*+D183*+E190P+N195F,

W140Y+G182*+D183*+N195F,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+A225V+K391A+G476K,

G182*+D183*+A186D+N195F,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+P473R+G476K,

H1*+W48Y+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+K391A+

G476K,

G182*+D183*+N195F+V238A,

G182*+D183*+Y295N,

Q172G+G182*+D183*,

F113Q+G182*+D183*+N195F,

H1*+N54S+V56T+Q98A+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

G182*+D183*+N195F+Y295F,

G182*+D183*+A186E,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206Y+K391A+G476K,

G182*+D183*+N195F+W284H,

G182*+D183*+A186Q+N195F,

K72R+G182*+D183*,

D183*+G182*+N195F+V326L,

D183*+G182*+A186E+N195F,

Q169E+G182*+D183*+N195F,

D183*+G182*+N195F+K242Q,

G7A+G182*+D183*+N195F,

D183*+G182*+N195F+N260G,

D183*+G182*+R321A+S323N,

D183*+G182*+W284H,

H1*+D183*+G182*,

D183*+G182*+A186H+N195F,

D183*+G182*+F289V,

D183*+G182*+K391A,

D183*+G182*+S304R,

W167F+G182*+D183*+N195F,

F113Q+R116H+D183*+G182*,

D183*+G182*+N270G,

D183*+G182*+S244Q,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+G184T+N195F+V206L+K391A+G476K,

D183*+G182*+N195F+Y295N,

W48F+D183*+G182*,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+G255A+K391A+G476K,

D183*+G182*+A186Q,

W140Y+D183*+G182*,

D183*+G182*+K242Q,

D183*+G182*+V206L,

D183*+G182*+N195F+V206F,

Q169E+D183*+G182*,

D183*+G182*+N195F+R320A,

G182*+D183*+G184T+N195F,

D183*+G182*+G184T,

N54S+V56T+D183*+G182*,

D183*+G182*+P473R,

W48Y+D183*+G182*,

D183*+G182*+R323A,

G7A+D183*+G182*,

G109A+D183*+G182*,

W167F+D183*+G182*,

H1*+N54S+V56T+G109A+Q169E+Q172K+A174S+G182*+D183*+N195F+V206L+K391A+

G476K,

A174S+D183*+G182*,

R116Q+D183*+G182*,

D183*+G182*+N195F+V291A,

Q172K+D183*+G182*,

N54S+D183*+G182*,

D183*+G182*+N195F+S323N,

D183*+G182*+N195F+M246V,

W48Y+D183*+G182*+N195F,

D183*+G182*+N195F+S304R,

V56T+D183*+G182*, en donde la numeración es acorde con la SEQ ID NO: 13; y

N54S+G182*+D183*+N195F,

G109A+G182*+D183*+N195F,

G182*+D183*+N195F+K391A,

G182*+D183*+N195F+G476K,

H1*+G182*+D183*+N195F,

N54S+G182*+D183*+N195F,

V56T+G182*+D183*+N195F,

G182*+D183*+N195F+I405L,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+I405L+A421H+A422P+

A428T+D476K,

A174S+G182*+D183*+N195F,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+I405L+A421H+A422P+

A428T,

H1*+N54S+V56T+G109A+A174S+D183*+N195F+V206L+K391A+I405L+A421H+A422P+

A428T,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+I405L+A421H+
A422P+A428T+D476K,
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+I405L+A421H+
A422P+A428T+D476G,
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+I405L+A421H+
A422P+A428T+D476K+G477S,
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+I405L+A421H+
A422P+A428T+D476K,
H1*+N54S+V56T+K72R+G109A+W167F+A174S+G182*+D183*+N195F+V206L+I405L+A421+A422P+A428T,
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+S304N+I405L+A421H+
A422P+A428T+D476K,
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+I405L+A421H+
A422P+A428T+D476K+G477A,
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+I405L+A421H+
A422P+A428T+D476G+G477T,
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+I405L+A421H+
A422P+A428T+G477Q,
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+I405L+A421H+
A422P+A428T+G477A,
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+I405L+A421H+
A422P+A428T+D476K+G477Q,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+I405L+A421H+
A422P+A428T+D476N,
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+I405L+A421H+
A422P+A428T+D476Y,
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206I+I405L+A421H+A422P+A428T,
H1*+N54S+V56T+G109A+Q172D+A174S+G182*+D183*+N195F+A204G+V206L+I405L+
A421H+A422P+A428T,
H1*+N54S+V56T+K72R+G109A+T134E+A174S+G182*+D183*+N195F+A204G+V206L+
G255A+I405L+A421H+A422P+A428T,
H1*+N54S+V56T+G109A+F113Q+R116H+T165G+Q172G+A174S+G182*+D183*+N195F+
V206L+I405L+A421H+A422P+A428T,
H1*+N54S+V56T+G109A+F113Q+Q172N+A174S+G182*+D183*+N195F+V206L+I405L+
A421H+A422P+A428T,
H1*+N54S+V56T+K72R+G109A+T134E+A174S+G182*+D183*+N195F+G196R+V206L+
G255A+I405L+A421H+A422P+A428T+N475S,
H1*+N54S+V56T+G109A+T134E+A174S+G182*+D183*+N195F+V206L+I405L+A421H+
A422P+A428T,
H1*+T40D+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+I405L+A421H+A422P+A428T,
H1*+N54S+V56T+G109A+F113Q+N125D+A174S+G182*+D183*+N195F+V206L+I405L+
A421H+A422P+A428T,
H1*+N54S+V56T+A60V+G109A+R116Q+A174S+G182*+D183*+N195F+V206L+I405L+A421H+A422P+A428T,

H1*+N54S+V56T+G109A+R116V+A174S+G182*+D183*+N195F+V206L+I405L+A421H+

A422P+A428T,

H1*+N54S+V56T+G109A+R116Q+G133Q+T165G+Q172G+A174S+G182*+D183*+N195F+

V206L+I405L+A421H+A422P+A428T,

H1*+N54S+V56T+G109A+F113Q+R116H+Q172G+A174S+G182*+D183*+N195F+V206L+

I405L+A421H+A422P+A428T,

H1*+N54S+V56T+G109A+F113Q+R116Q+Q172G+A174S+G182*+D183*+N195F+V206L+

I405L+A421H+A422P+A428T+G448D,

H1*+N54S+V56T+G109A+F113Q+R116H+Q172N+A174S+G182*+D183*+N195F+V206L+

I405L+A421H+A422P+A428T,

H1*+N54S+V56T+K72R+G109A+T134E+W167F+Q172N+A174S+G182*+D183*+N195F+

V206L+G255A+A265G+I405L+A421H+A422P+A428T,

H1*+N54S+V56T+K72R+G109A+R116Q+W167F+Q172R+L173V+A174S+G182*+D183*+

N195F+V206L+A265G+I405L+A421H+A422P+A428T,

H1*+N54S+V56T+K72R+G109A+R116Q+W167F+Q172R+A174S+G182*+D183*+N195F+

V206L+I405L+A421H+A422P+A428T,

H1*+N54S+V56T+K72R+G109A+F113Q+T134E+W167F+Q172G+A174S+G182*+D183*+

N195F+V206L+G255A+I405L+A421H+A422P+A428T,

H1*+N54S+V56T+K72R+G109A+F113Q+R116H+W167F+Q172G+L173V+A174S+G182*+

D183*+G184T+N195F+V206L+I405L+A421H+A422P+A428T,

H1*+N54S+V56T+G109A+F113Q+W167F+Q172G+A174S+G182*+D183*+N195F+V206L+

I405L+A421H+A422P+A428T,

H1*+N54S+V56T+K72R+G109A+A174S+G182*+D183*+N195F+V206L+G255A+I405L+A421H+A422P+A428T,

H1*+N54S+V56T+G109A+F113Q+R116Q+A174S+G182*+D183*+N195F+V206L+I405L+

A421H+A422P+A428T,

H1*+N54S+V56T+K72R+G109A+F113Q+F116H+W167F+Q172G+L173V+A174S+G182*+

D183*+N195F+V206L+I405L+A421H+A422P+A428T,

H1*+N54S+V56T+K72R+G109A+F113Q+R116Q+W167F+Q172G+A174S+G182*+D183*+

G184T+N195F+V206L+I405L+A421H+A422P+A428T,

H1*+N54S+V56T+G109A+F113Q+R116Q+W167F+Q172G+A174S+G182*+D183*+N195F+

A204G+V206L+I405L+A421H+A422P+A428T,

H1*+N54S+V56T+G109A+F113Q+R116H+W167F+Q172G+A174S+G182*+D183*+N195F+

V206L+A265G+I405L+A421H+A422P+A428T,

H1*+N54S+V56T+G109A+R116Q+A174S+G182*+D183*+N195F+V206L+I405L+A421H+

A422P+A428T,

H1*+N54S+V56T+A60V+G109A+R116Q+W167F+Q172N+L173V+A174S+G182*+D183*+

N195F+V206L+I405L+A421H+A422P+A428T,

H1*+A37H+N54S+V56T+A60V+G109A+R116Q+T165G+A174S+G182*+D183*+N195F+V206L+I405L+A421H+A422P+A428T,

H1*+N54S+V56T+G109A+A174S+M105F+G182*+D183*+N195F+V206L+L228I+R320A+

S323N+I405L+A421H+A422P+A428T,

H1*+N54S+V56T+K72R+G109A+F113Q+T134E+A174S+G182*+D183*+N195F+V206L+

G255A+I405L+A421H+A422P+A428T,

H1*+N54S+V56T+K72R+G109A+R116Q+V120L+A174S+G182*+D183*+G184T+N195F+

V206L+I405L+A421H+A422P+A428T,

H1*+N54S+V56T+G109A+F113Q+R116H+W167F+Q172G+L173V+A174S+G182*+D183*+

N195F+V206L+I405L+A421H+A422P+A428T,

H1*+N54S+V56T+G109A+F113Q+R116Q+Q172N+A174S+G182*+D183*+N195F+V206L+

A265G+I405L+A421H+A422P+A428T,

H1*+A37H+N54S+V56T+A60V+G109A+R116Q+W167F+Q172R+A174S+G182*+D183*+

N195F+V206L+I405L+A421H+A422P+A428T, en donde la numeración es acorde con la SEQ ID NO: 14.

Tal como puede observarse de los datos obtenidos en los ejemplos 3 y 4, todas las variantes probadas tienen un factor de mejora (IF) de al menos 1.0, es decir, al menos a la par con un polipéptido parental que tenga la SEQ ID NO: 15, cuando se prueba en (i) un detergente de modelo A a 15°C y una concentración de enzima de 0.05mg/L, (ii) un detergente modelo A a 15°C y una concentración de enzima de 0.2mg/L, (iii) un detergente modelo J a 15°C y una concentración de enzima de 0.05mg/L o (iv) un detergente modelo J a 15°C y una concentración de enzima de 0.2mg/L. Por lo tanto, las variantes de la presente invención tienen incluso en diferentes composiciones de modelo de detergente, a una baja temperatura así como a bajas concentraciones, un rendimiento de lavado al menos igual al del polipéptido parental que tiene la SEQ ID NO: 15. Las especificaciones de los detergentes modelo y las condiciones de ensayo específicas para el AMSA pueden verse en los ejemplos 3 y 4.

En otra realización, la variante se selecciona entre el grupo que consiste en;

G182*+D183*+N195F+V206F+N260P+L312I+L313I+R320A+T355L+L389I+T400P,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+G50A+T51A+V56T+G109A+A174S+G182*+D183*+N195F+V206L+G476K,

H1*+N54S+V56T+M105F+G109A+A174S+G182*+D183*+N195F+V206L+R320A+S323N+K391A+G476K,

H1*+T40K+N54S+V56T+G109A+G149H+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+K72R+G109A+A174S+G182*+D183*+N195F+V206L+G255A+K391A+G476K,

H1*+N16H+V17L+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+Q22N+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+Q32S+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+H28N+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N29S+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+H28N+N29S+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+A174S+R176K+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+Q169E+Q172K+A174*+R176K+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+A174S+N175G+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+V291A+Y295N+Q299T+
K391A+G476K,
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K269S+A274K+K391A+
G476K,
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+L235I+K391A+G476K,
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+L235V+V238A+K391A+
G476K,
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+Q365S+K391A+G476K,
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+H402R+G476K,
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+R320S+H321N+K391A+
G476K,
H1*+N54S+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+K391A+
G476K,
H1*+N54S+V56T+G109A+Q125S+A174S+G182*+D183*+N195F+V206L+K391A+G476K,
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+L235V+K391A+G476K,
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+A265G+K391A+G476K,
H1*+T51Q+N54S+V56T+G109A+A174S+G182*+D183*+N195F+Y203F+V206L+K391A+
G476K,
H1*+N54S+V56T+G109A+Q169E+Q172K+A174*+N175Q+G182*+D183*+N195F+V206L+
K391A+G476K,

H1*+H28N+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+T134E+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+D377H+K391A+G476K,

H1*+G50A+T51A+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+G7K+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+M202V+V206L+K391A+G476K,

H1*+N54S+V56T+M105F+G109A+A174S+G182*+D183*+N195F+V206L+M246F+K391A+

G476K,

H1*+N16H+V17L+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+D377H+K391A+G476K,

H1*+T51G+N54S+V56T+G109A+A174S+G182*+D183*+N195F+Y203G+V206L+K391A+

G476K,

H1*+T51G+N54S+V56T+G109A+G110N+A174S+G182*+D183*+N195F+V206L+K391A+

G476K,

H1*+N54S+V56T+G109A+Q125S+A174S+N175G+G182*+D183*+N195F+V206L+K391A+

G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+A265G+V291A+F328L+

K391A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+M246F+A265G+V291A+

F328L+Q365S+K391A+G476K,

H1*+N16Y+N54S+V56T+G109A+R116H+A174S+G182*+D183*+N195F+V206L+G337E+

D377H+K391A+G476K,

H1*+I9L+N54S+V56T+G109A+Q125S+V131T+A174*+G182*+D183*+V206L+Y267F+F289H+Q361E+K391A+G476K,

H1*+N54S+V56T+G109A+R116H+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+

K391A+G476K,

H1*+N54S+V56T+G109A+A174*+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+K72R+G109A+F113Q+R116Q+W167F+Q172G+A174S+G182*+D183*+G184T+N195F+

V206L+K391A+P473R+G476K,

H1*+N54S+V56T+K72R+G109A+F113Q+R116Q+W167F+Q172G+A174S+G182*+D183*+

G184T+N195F+V206L+P473R+G476K,

H1*+N54S+V56T+G109A+Q169E+Q172G+A174*+G182*+D183*+N195F+V206L+K391A+

G476K,

H1*+N54S+V56T+K72R+G109A+F113Q+R116Q+W167F+Q172G+A174S+G182*+D183*+

G184T+N195F+K391A+P473R+G476K,

H1*+N54S+V56T+G109A+R116W+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+

K391A+G476K,

H1*+N54S+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206F+K391A+

G476K,

H1*+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+N260G+K391A+G476K,

H1*+N54S+V56T+K72R+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+G184T+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+Y295N+K391A+G476K,

H1*+N54S+V56T+G109A+W167F+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+A186N+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+A288V+K391A+G476K,

H1*+N54S+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+G255A+K391A+G476K,

H1*+N54S+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+W48F+N54S+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+V291A+K391A+G476K,

H1*+N54S+V56T+G109A+F113Q+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+R320A+S323N+K391A+G476K,

H1*+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+K72R+G109A+F113Q+R116H+W167F+Q172G+A174S+G182*+D183*+

G184T+N195F+V206L+K391A+P473R+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+N270T+K391A+G476K,

H1*+N54S+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+G476K,

H1*+N54S+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+N260G+

K391A+G476K,

H1*+N54S+V56T+G109A+F113Q+R116H+A174S+G182*+D183*+N195F+V206L+K391A+

G476K,

H1*+N54S+V56T+G109A+Q172G+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+A174S+A186D+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+A225V+

K391A+G476K,

H1*+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+G255S+

K391A+G476K,

H1*+N54S+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+K269Q+

K391A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+G255S+K391A+G476K,

H1*+N54S+V56T+G109A+Q169E+Q172K+A174S+G182*+D183*+N195F+V206L+K391A+

G476K,

G182*+D183*+N195F,

H1*+N54S+V56T+G109A+Q169E+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+W284H+

K391A+G476K,

H1*+N54S+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+S304R+

K391A+G476K,

H1*+N54S+V56T+K72R+G109A+F113Q+R116Q+W167F+Q172G+A174S+G182*+D183*+

G184T+N195F+V206L+K391A+P473R,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+M246V+K391A+G476K,

H1*+N54S+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+K391A,

H1*+N54S+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+N270G+K391A+G476K,

H1*+N54S+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+Y295F+K391A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+R320A+K391A+G476K,

H1*+N54S+V56T+G109A+Q169E+Q172K+A174T+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+Q169E+Q172K+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+W140Y+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A,

H1*+N54S+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+F328L+K391A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+G476K,

F113Q+R116H+D183*+G182*+N195F,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+A288L+K391A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+N270G+K391A+G476K,

Q169E+Q172K+A174*+D183*+G182*+N195F,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K269Q+K391A+G476K,

H1*+W48F+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

F113Q+R116Q+D183*+G182*+N195F,

N54S+V56T+D183*+G182*+N195F,

H1*+N54S+V56T+G109A+A174T+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+R116W+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

Q169E+Q172K+G182*+D183*+N195F,

G182*+D183*+A186D,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+V238A+K391A+G476K,

G182*+D183*+A186N,

H1*+N54S+V56T+G109A+A174S+V206L+G182*+D183*+K391A+G476K,

H1*+N54S+V56T+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206F+K391A+G476K,

H1*+N54S+V56T+G109A+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+Q172K+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+Q172K+A174*+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+A174N+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+A174S+A186N+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+F289L+K391A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+Y295F+K391A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+V291A+K391A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+S244Q+K391A+G476K,

G182*+D183*+F328L,

G182*+D183*+N195F+A288V,

G182*+D183*+A186N+N195F,

G182*+D183*+E190P+N195F,

W140Y+G182*+D183*+N195F,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+A225V+K391A+G476K,

G182*+D183*+A186D+N195F,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+P473R+G476K,

H1*+W48Y+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+K391A+

G476K,

G182*+D183*+N195F+V238A,

G182*+D183*+Y295N,

Q172G+G182*+D183*,

F113Q+G182*+D183*+N195F,

H1*+N54S+V56T+Q98A+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

G182*+D183*+N195F+Y295F,

G182*+D183*+A186E,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206Y+K391A+G476K,

G182*+D183*+N195F+W284H,

G182*+D183*+A186Q+N195F,

K72R+G182*+D183*,

D183*+G182*+N195F+V326L,

D183*+G182*+A186E+N195F,

Q169E+G182*+D183*+N195F,

D183*+G182*+N195F+K242Q,

G7A+G182*+D183*+N195F,

D183*+G182*+N195F+N260G,

D183*+G182*+R321A+S323N,

D183*+G182*+W284H,

H1*+D183*+G182*,

D183*+G182*+A186H+N195F,

D183*+G182*+F289V,

D183*+G182*+K391A,

D183*+G182*+S304R,

W167F+G182*+D183*+N195F,

F113Q+R116H+D183*+G182*,

D183*+G182*+N270G,

D183*+G182*+S244Q,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+G184T+N195F+V206L+K391A+G476K,

D183*+G182*+N195F+Y295N,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+G255A+K391A+G476K,

D183*+G182*+A186Q,

D183*+G182*+N195F+V206F,

D183*+G182*+N195F+R320A,

G182*+D183*+G184T+N195F,

N54S+V56T+D183*+G182*,

W48Y+D183*+G182*,

A174S+D183*+G182*,

G7A+D183*+G182*,

N54S+D183*+G182*,

D183*+G182*+N195F+M246V,

W48Y+D183*+G182*+N195F,

D183*+G182*+N195F+S304R,

en donde la numeración es acorde con la SEQ ID NO: 13 y en donde el IF se determina mediante el uso del detergente modelo A.

En una realización, el IF se determina mediante el uso del detergente modelo A a una temperatura de 15°C. En una realización particular, las variantes tienen un IF de >1 en comparación con el polipéptido parental, en donde el IF se determina mediante el uso del detergente modelo A a una temperatura de 15°C y una concentración de 0.05mg/L. A partir de las tablas en los ejemplos divulgados en el presente documento puede observarse cuáles pueden ser estas variantes.

En otra realización, la variante tiene un IF de al menos 1.0 cuando se compara con el polipéptido parental cuando se ensaya en detergente modelo J y en donde la variante se selecciona entre el grupo que consiste en:

G182*+D183*+N195F,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+R87S+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+T40G+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+T51K+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+K72R+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+K72H+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+A37H+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+A37M+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+A37V+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+A37S+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+A37Y+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+A37R+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+F113W+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+F113S+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+F113N+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+F113Y+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+F113R+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+Q118N+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+R116Q+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+R116V+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+R116K+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+R116W+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+R116L+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+G142T+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+Q125P+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+Q125K+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+S381G+K391A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+M246T+K391A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+V213T+K391A+G476K,

H1*+A37L+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+Q118K+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+R116A+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+R116H+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+Q125A+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+Q172G+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

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G476K,

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G476K,

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G476K,

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K391A+G476K,

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G476K,

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A+G476K,

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+K391A+G476K,

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G476K,

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K391A+G476K,

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G476K,

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K391A+G476K,

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K391A+G476K,

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G476K,

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G476K,

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P473R+G476K,

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G255A+K391A+P473R+G476K,

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K391A+G476K,

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K391A+P473R+G476K,

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C474V+G476K,

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K391A+C474V+G476K,

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K391A+G476K,

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K391A+G476K,

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+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

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G476K,

H1*+N54S+V56T+G109A+W167Y+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+W167H+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+T165V+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+A174N+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+A174Q+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N16H+V17L+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+Y382F+K391A+G476K,

H1*+Q32S+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+Q385L+K391A+

G476K,

H1*+N54S+V56T+R87S+G109A+R171H+A174S+G182*+D183*+N195F+V206L+K391A+

G476K,

N54S+G182*+D183*+N195F,

G109A+G182*+D183*+N195F,

A174S+G182*+D183*+N195F,

G182*+D183*+N195F+K391A,

G182*+D183*+N195F+G476K,

H1*+N54S+V56T+G109A+R116H+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+

K391A+G476K,

H1*+N54S+V56T+G109A+A174*+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+K72R+G109A+F113Q+R116Q+W167F+Q172G+A174S+G182*+D183*+G184T+N195F+
V206L+K391A+P473R+G476K,
H1*+N54S+V56T+K72R+G109A+F113Q+R116Q+W167F+Q172G+A174S+G182*+D183*+
G184T+N195F+V206L+P473R+G476K,
H1*+N54S+V56T+G109A+Q169E+Q172G+A174*+G182*+D183*+N195F+V206L+K391A+
G476K,
H1*+N54S+V56T+K72R+G109A+F113Q+R116Q+W167F+Q172G+A174S+G182*+D183*+
G184T+N195F+K391A+P473R+G476K,
H1*+N54S+V56T+G109A+R116W+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+
K391A+G476K,
H1*+N54S+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206F+K391A+
G476K,
H1*+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K,
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+N260G+K391A+G476K,
H1*+N54S+V56T+K72R+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K,
H1*+N54S+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+G184T+N195F+V206L+
K391A+G476K,
H1*+N54S+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+Y295N+
K391A+G476K,
H1*+N54S+V56T+G109A+W167F+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+A186N+N195F+V206L+
K391A+G476K,
H1*+N54S+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+A288V+
K391A+G476K,
H1*+N54S+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+G255A+
K391A+G476K,
H1*+N54S+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+K391A+G476K,
H1*+W48F+N54S+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+
K391A+G476K,
H1*+N54S+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+V291A+
K391A+G476K,
H1*+N54S+V56T+G109A+F113Q+A174S+G182*+D183*+N195F+V206L+K391A+G476K,
H1*+N54S+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+R320A+
S323N+K391A+G476K,
H1*+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+K391A+G476K,
H1*+N54S+V56T+K72R+G109A+F113Q+R116H+W167F+Q172G+A174S+G182*+D183*+
G184T+N195F+V206L+K391A+P473R+G476K,
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H1*+N54S+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+N260G+

K391A+G476K,

H1*+N54S+V56T+G109A+F113Q+R116H+A174S+G182*+D183*+N195F+V206L+K391A+

G476K,

H1*+N54S+V56T+G109A+Q172G+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+A174S+A186D+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+A225V+

K391A+G476K,

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H1*+N54S+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+G255S+

K391A+G476K,

H1*+N54S+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+K269Q+

K391A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+G255S+K391A+G476K,

H1*+N54S+V56T+G109A+Q169E+Q172K+A174S+G182*+D183*+N195F+V206L+K391A+

G476K,

G182*+D183*+N195F,

H1*+N54S+V56T+G109A+Q169E+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+W284H+

K391A+G476K,

H1*+N54S+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

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K391A+G476K,
H1*+N54S+V56T+K72R+G109A+F113Q+R116Q+W167F+Q172G+A174S+G182*+D183*+
G184T+N195F+V206L+K391A+P473R,
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K391A+G476K,
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K391A+G476K,
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G476K,
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K391A+G476K,
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H1*+N54S+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+F328L+
K391A+G476K,
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+G476K,

F113Q+R116H+D183*+G182*+N195F,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+A288L+K391A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+N270G+K391A+G476K,

Q169E+Q172K+A174*+D183*+G182*+N195F,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K269Q+K391A+G476K,

H1*+W48F+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

F113Q+R116Q+D183*+G182*+N195F,

N54S+V56T+D183*+G182*+N195F,

H1*+N54S+V56T+G109A+A174T+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+R116W+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

Q169E+Q172K+G182*+D183*+N195F,

G182*+D183*+A186D,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+V238A+K391A+G476K,

G182*+D183*+A186N,

H1*+N54S+V56T+G109A+A174S+V206L+G182*+D183*+K391A+G476K,

H1*+N54S+V56T+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+K391A+G476K,

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G182*+D183*+N195F+A288V,

G182*+D183*+A186N+N195F,

G182*+D183*+E190P+N195F,

W140Y+G182*+D183*+N195F,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+A225V+K391A+G476K,

G182*+D183*+A186D+N195F,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+P473R+G476K,

H1*+W48Y+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+K391A+

G476K,

G182*+D183*+N195F+V238A,

G182*+D183*+Y295N,

Q172G+G182*+D183*,

F113Q+G182*+D183*+N195F,

H1*+N54S+V56T+Q98A+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

G182*+D183*+N195F+Y295F,

G182*+D183*+A186E,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206Y+K391A+G476K,

G182*+D183*+N195F+W284H,

G182*+D183*+A186Q+N195F,

K72R+G182*+D183*,

D183*+G182*+N195F+V326L,

D183*+G182*+A186E+N195F,

Q169E+G182*+D183*+N195F,

D183*+G182*+N195F+K242Q,

G7A+G182*+D183*+N195F,

D183*+G182*+N195F+N260G,

D183*+G182*+R321A+S323N,

D183*+G182*+W284H,

H1*+D183*+G182*,

D183*+G182*+A186H+N195F,

D183*+G182*+F289V,

D183*+G182*+K391A,

D183*+G182*+S304R,

W167F+G182*+D183*+N195F,

F113Q+R116H+D183*+G182*,

D183*+G182*+N270G,

D183*+G182*+S244Q,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+G184T+N195F+V206L+K391A+G476K,

D183*+G182*+N195F+Y295N,

W48F+D183*+G182*,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+G255A+K391A+G476K,

D183*+G182*+A186Q,

W140Y+D183*+G182*,

D183*+G182*+K242Q,

D183*+G182*+V206L,

D183*+G182*+N195F+V206F,

Q169E+D183*+G182*,

D183*+G182*+N195F+R320A,

G182*+D183*+G184T+N195F,

D183*+G182*+G184T,

D183*+G182*+P473R,

W48Y+D183*+G182*,

D183*+G182*+R323A,

G7A+D183*+G182*,

H1*+N54S+V56T+G109A+Q169E+Q172K+A174S+G182*+D183*+N195F+V206L+K391A+

G476K,

A174S+D183*+G182*,

D183*+G182*+N195F+S323N,

D183*+G182*+N195F+M246V,

W48Y+D183*+G182*+N195F,

V56T+D183*+G182*,

en donde la numeración es acorde con la SEQ ID NO: 13,

G182*+D183*+N195F+A428T,

G182*+D183*+N195F,

H1*+G182*+D183*+N195F,

N54S+G182*+D183*+N195F,

V56T+G182*+D183*+N195F,

G182*+D183*+N195F+I405L,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+I405L+A421H+A422P+

A428T+D476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+I405L+A421H+A422P+

A428T,

H1*+N54S+V56T+G109A+A174S+D183*+N195F+V206L+K391A+I405L+A421H+A422P+

A428T,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+I405L+A421H+

A422P+A428T+D476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+I405L+A421H+

A422P+A428T+D476G,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+I405L+A421H+

A422P+A428T+D476K+G477S,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+I405L+A421H+

A422P+A428T+D476K,

H1*+N54S+V56T+K72R+G109A+W167F+A174S+G182*+D183*+N195F+V206L+I405L+A421H+A422P+A428T,

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A421H+A422P+A428T,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+S304N+I405L+A421H+

A422P+A428T+D476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+I405L+A421H+

A422P+A428T+D476K+G477A,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+I405L+A421H+

A422P+A428T+D476G+G477T,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+I405L+A421H+

A422P+A428T+G477Q,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+I405L+A421H+A422P+A428T+G477A,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+I405L+A421H+
A422P+A428T+D476K+G477Q,
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+I405L+A421H+
A422P+A428T+D476N,
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+I405L+A421H+
A422P+A428T+D476Y,
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206I+I405L+A421H+A422P+A428T,
H1*+N54S+V56T+G109A+Q172D+A174S+G182*+D183*+N195F+A204G+V206L+I405L+
A421H+A422P+A428T,
H1*+N54S+V56T+K72R+G109A+T134E+A174S+G182*+D183*+N195F+A204G+V206L+
G255A+I405L+A421H+A422P+A428T,
H1*+N54S+V56T+G109A+F113Q+R116H+T165G+Q172G+A174S+G182*+D183*+N195F+
V206L+I405L+A421H+A422P+A428T,
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A421H+A422P+A428T,
H1*+N54S+V56T+K72R+G109A+T134E+A174S+G182*+D183*+N195F+G196R+V206L+
G255A+I405L+A421H+A422P+A428T+N475S,
H1*+N54S+V56T+G109A+T134E+A174S+G182*+D183*+N195F+V206L+I405L+A421H+
A422P+A428T,
H1*+T40D+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+I405L+A421H+A422P+A428T,
H1*+N54S+V56T+G109A+F113Q+N125D+A174S+G182*+D183*+N195F+V206L+I405L+

A421H+A422P+A428T,

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H1*+N54S+V56T+G109A+F113Q+R116Q+Q172G+A174S+G182*+D183*+N195F+V206L+I405L+A421H+A422P+A428T+G448D,

H1*+N54S+V56T+G109A+F113Q+R116H+Q172N+A174S+G182*+D183*+N195F+V206L+I405L+A421H+A422P+A428T,

H1*+N54S+V56T+K72R+G109A+T134E+W167F+Q172N+A174S+G182*+D183*+N195F+V206L+G255A+A265G+I405L+A421H+A422P+A428T,

H1*+N54S+V56T+K72R+G109A+R116Q+W167F+Q172R+L173V+A174S+G182*+D183*+N195F+V206L+A265G+I405L+A421H+A422P+A428T,

H1*+N54S+V56T+K72R+G109A+R116Q+W167F+Q172R+A174S+G182*+D183*+N195F+V206L+I405L+A421H+A422P+A428T,

H1*+N54S+V56T+K72R+G109A+F113Q+T134E+W167F+Q172G+A174S+G182*+D183*+N195F+V206L+G255A+I405L+A421H+A422P+A428T,

H1*+N54S+V56T+K72R+G109A+F113Q+R116H+W167F+Q172G+L173V+A174S+G182*+D183*+G184T+N195F+V206L+I405L+A421H+A422P+A428T,

H1*+N54S+V56T+G109A+F113Q+W167F+Q172G+A174S+G182*+D183*+N195F+V206L+

I405L+A421H+A422P+A428T,

H1*+N54S+V56T+K72R+G109A+A174S+G182*+D183*+N195F+V206L+G255A+I405L+A421H+A422P+A428T,

H1*+N54S+V56T+G109A+F113Q+R116Q+A174S+G182*+D183*+N195F+V206L+I405L+

A421H+A422P+A428T,

H1*+N54S+V56T+K72R+G109A+F113Q+R116Q+W167F+Q172G+A174S+G182*+D183*+

G184T+N195F+V206L+I405L+A421H+A422P+A428T,

H1*+N54S+V56T+G109A+F113Q+R116Q+W167F+Q172G+A174S+G182*+D183*+N195F+

A204G+V206L+I405L+A421H+A422P+A428T,

H1*+N54S+V56T+G109A+F113Q+R116H+W167F+Q172G+A174S+G182*+D183*+N195F+

V206L+A265G+I405L+A421H+A422P+A428T,

H1*+N54S+V56T+G109A+R116Q+A174S+G182*+D183*+N195F+V206L+I405L+A421H+

A422P+A428T,

H1*+N54S+V56T+A60V+G109A+R116Q+W167F+Q172N+L173V+A174S+G182*+D183*+

N195F+V206L+I405L+A421H+A422P+A428T,

H1*+A37H+N54S+V56T+A60V+G109A+R116Q+T165G+A174S+G182*+D183*+N195F+V206L+I405L+A421H+A422P+A428T,

H1*+N54S+V56T+G109A+A174S+M105F+G182*+D183*+N195F+V206L+L228I+R320A+

S323N+I405L+A421H+A422P+A428T,

H1*+N54S+V56T+K72R+G109A+F113Q+T134E+A174S+G182*+D183*+N195F+V206L+

G255A+I405L+A421H+A422P+A428T,

H1*+N54S+V56T+K72R+G109A+R116Q+V120L+A174S+G182*+D183*+G184T+N195F+

V206L+I405L+A421H+A422P+A428T,

H1*+N54S+V56T+G109A+F113Q+R116H+W167F+Q172G+L173V+A174S+G182*+D183*+

N195F+V206L+I405L+A421H+A422P+A428T,

H1*+N54S+V56T+G109A+F113Q+R116Q+Q172N+A174S+G182*+D183*+N195F+V206L+

A265G+I405L+A421H+A422P+A428T,

H1*+A37H+N54S+V56T+A60V+G109A+R116Q+W167F+Q172R+A174S+G182*+D183*+

N195F+V206L+I405L+A421H+A422P+A428T, en donde la numeración es acorde con la SEQ ID NO: 14.

En una realización, el IF se determina mediante el uso del detergente modelo J a una temperatura de 15°C. En una realización particular, las variantes tienen un IF de >1 en comparación con el polipéptido parental, en donde el IF se determina mediante el uso del detergente modelo J a una temperatura de 15°C y una concentración de 0.05mg/L. A partir de las tablas en los ejemplos divulgados en el presente documento puede observarse cuáles pueden ser estas variantes.

En otra realización, la variante tiene un IF de al menos >1.5 cuando se compara con dicho polipéptido parental y en donde dicha variante se selecciona entre

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+R87S+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+T40G+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+T51K+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+K72R+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+K72H+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+A37H+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+A37M+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+A37V+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+A37S+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+A37Y+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+A37R+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+F113W+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+F113S+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+F113N+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+F113Y+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+Q118N+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+R116Q+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+R116V+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+R116K+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+R116W+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+R116L+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+G142T+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+Q125P+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+Q125K+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+S381G+K391A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+M246T+K391A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+V213T+K391A+G476K,

H1*+A37L+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+Q118K+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+R116A+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+R116H+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+Q125A+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+Q172G+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+Q172R+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+D377S+K391A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+D377G+K391A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+D377R+K391A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+D377A+K391A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+I214G+K391A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+S381A+K391A+G476K,

H1*+N54S+V56T+G109A+W167I+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+W167G+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+G346S+K391A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+G346P+K391A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+I214H+K391A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+I214S+K391A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+I214T+K391A+G476K,

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H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+A420S+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+A420K+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+A420L+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+K391Y+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+K391R+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+P473R+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+P473A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+P473G+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+P473T+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+Q395P+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+T444Q+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+T444S+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+T444D+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+T444Y+G476K,

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H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+S280L+K391A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+S280T+K391A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+S280A+K391A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+G255N+K391A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+T285L+K391A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+T285Q+K391A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+Q449T+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+P473K+G476K,

H1*+N54S+V56T+K72S+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+T40K+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+G346T+K391A+

G476K,

H1*+G50A+N54S+V56T+G109A++Q172N+A174S+G182*+D183*+N195F+V206L+K391A+

G476K,

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H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K+K484G,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K+K484P,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K+K484E,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K+K484Q,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K+K484S,

H1*K+G50A+N54S+V56T+G109A+W167F+A174S+G182*+D183*+N195F+V206L+K391A+

G476K,

H1*+N54S+V56T+G109A+L173V+A174S+G182*+D183*+N195F+A204T+V206L+K391A+

G476K,

H1*+N54S+V56T+G109A+W140Y+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+Q98S+G109A+A174S+G182*+D183*+N195F+V206L+R320A+K391A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+H324L+K391A+G476K,

H1*+N54S+V56T+G109A+G149Q+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+G346T+K391A+G476K+G477A,

H1*+N54S+V56T+G109AG255A++A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+G50A+N54S+V56T+G109A+F113L+R116L+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+W167F+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+L173V+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

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H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+Q345D+K391A+G476K+G477Q,

H1*+G50A+N54S+V56T+G109A+Q172D+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+V264I+K391A+G423H+

G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+R320V+K391A+G476Y,

H1*+T5K+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+R116M+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+Q172Y+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+I214L+K391A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+L217V+K391A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+L217H+K391A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+P211D+K391A+G476K,

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H1*+G50A+N54S+V56T+G109A+L173V+A174S+G182*+D183*+N195F+A204V+V206L+

K391A+G476K,

H1*+G50A+N54S+V56T+G109A+F113L+W167F+A174S+G182*+D183*+N195F+V206L+

K391A+G476K,

H1*+G7K+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+R320A+K391A+G476K,

H1*+N54S+V56T+G109A+Q118G+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+S280K+K391A+G476K,

H1*+N54S+V56T+G109A+Q172D+A174S+G182*+D183*+N195F+V206L+G346T+K391A+

G476K+G477A,

H1*+N54S+V56T+G109A+Q118S+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+R320A+K391A+G476K,

H1*+N54S+V56T+G109A+T134E+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

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G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+Y382M+K391A+G476K,

H1*+N54S+V56T+K72R+G109A+A174S+G182*+D183*+N195F+V206L+G255A+D377H+

K391A+G476K,

H1*+N54S+V56T+K72R+G109A+T134E+A174S+G182*+D183*+N195F+V206L+G255A+

K391A+G476K,

H1*+N54S+V56T+K72R+M105F+G109A+A174S+G182*+D183*+N195F+V206L+G255A+

K391A+G476K,

H1*+N54S+V56T+M105F+G109A+T134E+A174S+G182*+D183*+N195F+V206L+K391A+

G476K,

H1*+N54S+V56T+M105F+G109A+Q118F+T134E+A174S+G182*+D183*+N195F+V206L+

K391A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+R320A+S323N+D377H+

K391A+G476K,

H1*+T51E+N54S+V56T+G109A+A174H+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+L173A+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+Q299V+K391A+G476K,

H1*+N54S+V56T+G109A+L173G+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+T355L+K391A+G476K,

H1*+G50A+N54S+V56T+G109A+A174S+G182*+D183*+N195F+A204T+V206L+K391A+

G476K,

H1*+G50A+N54S+V56T+G109A+A174E+G182*+D183*+N195F+A204T+V206L+K391A+

G476K,

H1*+N54S+V56T+K72R+G109A+A174S+G182*+D183*+N195F+V206L+R320A+S323N+

K391A+G476K,

H1*+N54S+V56T+M105I+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+M246L+K391A+G476K,

H1*+T51G+N54S+V56T+G109A+A174N+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+A174D+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+T51S+N54S+V56T+G109A+A174P+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+K72A+G109A+W167S+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

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H1*+Q11H+N54S+V56T+G109A+Q118R+T134E+A174S+G184T+G182*+D183*+N195F+V206L+D377H+K391A+G476K,

H1*+N54S+V56T+K72R+G109A+T134E+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+K72R+G109A+T134E+A174S+G182*+D183*+N195F+V206L+D377H+K391A+G476K,

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H1*+N54S+V56T+G109A+Q118R+T134E+A174S+G182*+D183*+N195F+V206L+G255A+K391A+G476K,

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K391A+G476K,

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G476K,

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G476K,

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+G184T+N195F+
V206L+K391A+T444Q+G476K,
H1*+N54S+V56T+G109S+F113Q+A174S+G182*+D183*+N195F+V206
L+K391A+T444Q+
G476K,
H1*+N54S+V56T+G109A+F113Q+R116H+W167F+Q172G+L173V+A174
S+G182*+D183*+
N195F+V206L+K391A+P473R+G476K,
H1*+N54S+V56T+G109A+F113Q+R116Q+Q172N+A174S+G182*+D183
*+N195F+V206L+
A265G+K391A+P473R+G476K,
H1*+N54S+V56T+G109A+F113Q+W167F+Q172N+A174S+G182*+D183
*+N195F+A204G+
V206L+K391A+P473R+G476K,
H1*+N54S+V56T+G109A+F113Q+R116H+W167F+Q172R+A174S+G182
+D183+N195F+
A204G+V206L+K391A+P473R+G476K,
H1*+N54S+V56T+G109A+R116A+A174S+G182*+D183*+N195F+V206
L+K391A+T444Q+
P473R+G476K,
H1*+N54S+V56T+G109A+R116H+Q172R+A174S+G182*+D183*+N195
F+A204G+V206L+
K391A+P473R+G476K,

H1*+A37V+N54S+V56T+G109A+R116Q+T165G+A174S+G182*+D183*+N195F+V206L+

K391A+G476K,

H1*+A37H+N54S+V56T+G109A+R116H+T165G+A174S+G182*+D183*+N195F+V206L+

M246F+K391A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+K391A+G476K,

H1*+G109A+G182*+D183*+N195F+V206L+K391A+G476K,

G109A+G182*+D183*+N195F+V206L+G476K,

H1*+G109A+G182*+D183*+N195F+K391A,

H1*+N54S+V56T+G109A+G133S+A174S+G182*+D183*+N195F+K391A+G476H,

H1*+N54S+V56T+G109A+R116A+Q172N+L173V+A174S+G182*+D183*+N195F+V206L+

K391A+G476K,

H1*+A37V+N54S+V56T+G109A+R116H+T165G+A174S+G182*+D183*+N195F+V206L+

K391A+G476K,

H1*+P45A+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+C474V+

G476K,

H1*+N54S+V56T+G109A+P124A+A174S+G182*+D183*+N195F+V206L+K391A+C474V+

G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+P364A+K391A+C474V+

G476K,

H1*+N54S+V56T+G109A+Q118R+T134E+A174S+G182*+D183*+N195F+V206L+K391A+

G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+G184T+N195F+V206L+K391A+G476K,

H1*+G50A+T51A+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+V264F+K391A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+Y382L+K391A+G476K,

H1*+G7K
+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+G255A+Q256A+K391A+
G476K,

H1*+N54S+V56T+G109A+W167Y+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+W167H
+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+T165V+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+A174N+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+A174Q+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N16H+V17L+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+Y382F+K391A+G476K,

H1*+Q32S+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+Q385L+K391A+
G476K,

H1*+N54S+V56T+R87S+G109A+R171H+A174S+G182*+D183*+N195F+V206L+K391A+
G476K,

G109A+G182*+D183*+N195F,

G182*+D183*+N195F+K391A,

H1*+N54S+V56T+G109A+R116H+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+
K391A+G476K,
H1*+N54S+V56T+G109A+A174*+G182*+D183*+N195F+V206L+K391A+G476K,
H1*+K72R+G109A+F113Q+R116Q+W167F+Q172G+A174S+G182*+D183*+G184T+N195F+
V206L+K391A+P473R+G476K,
H1*+N54S+V56T+K72R+G109A+F113Q+R116Q+W167F+Q172G+A174S+G182*+D183*+
G184T+N195F+V206L+P473R+G476K,
H1*+N54S+V56T+G109A+Q169E+Q172G+A174*+G182*+D183*+N195F+V206L+K391A+
G476K,
H1*+N54S+V56T+K72R+G109A+F113Q+R116Q+W167F+Q172G+A174S+G182*+D183*+
G184T+N195F+K391A+P473R+G476K,
H1*+N54S+V56T+G109A+R116W+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+
K391A+G476K,
H1*+N54S+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206F+K391A+
G476K,
H1*+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K,
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+N260G+K391A+G476K,
H1*+N54S+V56T+K72R+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K,
H1*+N54S+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+G184T+N195F+V206L+
K391A+G476K,

H1*+N54S+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+Y295N+
K391A+G476K,
H1*+N54S+V56T+G109A+W167F+A174S+G182*+D183*+N195F+V206L+K391A+G476K,
H1*+N54S+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+A186N+N195F+V206L+
K391A+G476K,
H1*+N54S+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+A288V+
K391A+G476K,
H1*+N54S+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+G255A+
K391A+G476K,
H1*+N54S+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+K391A+G476K,
H1*+W48F+N54S+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+
K391A+G476K,
H1*+N54S+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+V291A+
K391A+G476K,
H1*+N54S+V56T+G109A+F113Q+A174S+G182*+D183*+N195F+V206L+K391A+G476K,
H1*+N54S+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+R320A+
S323N+K391A+G476K,
H1*+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+K391A+G476K,
H1*+N54S+V56T+K72R+G109A+F113Q+R116H+W167F+Q172G+A174S+G182*+D183*+
G184T+N195F+V206L+K391A+P473R+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+N270T+K391A+G476K,

H1*+N54S+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+G476K,

H1*+N54S+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+N260G+
K391A+G476K,

H1*+N54S+V56T+G109A+F113Q+R116H+A174S+G182*+D183*+N195F+V206L+K391A+
G476K,

H1*+N54S+V56T+G109A+Q172G+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+A174S+A186D+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+A225V+
K391A+G476K,

H1*+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+G255S+
K391A+G476K,

H1*+N54S+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+K269Q+
K391A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+G255S+K391A+G476K,

H1*+N54S+V56T+G109A+Q169E+Q172K+A174S+G182*+D183*+N195F+V206L+K391A+
G476K,

G182*+D183*+N195F,

H1*+N54S+V56T+G109A+Q169E+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+W284H+
K391A+G476K,
H1*+N54S+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K,
H1*+N54S+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+S304R+
K391A+G476K,
H1*+N54S+V56T+K72R+G109A+F113Q+R116Q+W167F+Q172G+A174S+G182*+D183*+
G184T+N195F+V206L+K391A+P473R,
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+M246V+K391A+G476K,
H1*+N54S+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+K391A,
H1*+N54S+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+N270G+
K391A+G476K,
H1*+N54S+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+Y295F+
K391A+G476K,
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+R320A+K391A+G476K,
H1*+N54S+V56T+G109A+Q169E+Q172K+A174T+G182*+D183*+N195F+V206L+K391A+
G476K,
H1*+N54S+V56T+G109A+Q169E+Q172K+G182*+D183*+N195F+V206L+K391A+G476K,
H1*+N54S+V56T+G109A+W140Y+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+
K391A+G476K,
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A,

H1*+N54S+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+F328L+

K391A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+G476K,

F113Q+R116H+D183*+G182*+N195F,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+A288L+K391A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+N270G+K391A+G476K,

Q169E+Q172K+A174*+D183*+G182*+N195F,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K269Q+K391A+G476K,

H1*+W48F+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

F113Q+R116Q+D183*+G182*+N195F,

N54S+V56T+D183*+G182*+N195F,

H1*+N54S+V56T+G109A+A174T+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+R116W+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

Q169E+Q172K+G182*+D183*+N195F,

G182*+D183*+A186D,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+V238A+K391A+G476K,

G182*+D183*+A186N,

H1*+N54S+V56T+G109A+A174S+V206L+G182*+D183*+K391A+G476K,

H1*+N54S+V56T+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206F+K391A+G476K,

H1*+N54S+V56T+G109A+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+Q172K+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+Q172K+A174*+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+A174N+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+A174S+A186N+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+F289L+K391A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+Y295F+K391A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+V291A+K391A+G476K,

G182*+D183*+A186N+N195F,

G182*+D183*+A186D+N195F,

G182*+D183*+N195F+W284H,

D183*+G182*+N195F+V326L,

en donde la numeración es acorde con la SEQ ID NO: 13, y

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+I405L+A421H+

A422P+A428T+D476G+G477T,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+I405L+A421H+

A422P+A428T+G477Q,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+I405L+A421H+

A422P+A428T+G477A,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+I405L+A421H+

A422P+A428T+D476N,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+I405L+A421H+

A422P+A428T+D476Y,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206I+I405L+A421H+A422P+A428T,

H1*+N54S+V56T+G109A+T134E+A174S+G182*+D183*+N195F+V206L+I405L+A421H+

A422P+A428T,

H1*+T40D+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+I405L+A421H+

A422P+A428T,

H1*+N54S+V56T+G109A+F113Q+N125D+A174S+G182*+D183*+N195F+V206L+I405L+

A421H+A422P+A428T,

H1*+N54S+V56T+A60V+G109A+R116Q+A174S+G182*+D183*+N195F+V206L+I405L+A421H+A422P+A428T,

H1*+N54S+V56T+G109A+F113Q+R116H+Q172G+A174S+G182*+D183*+N195F+V206L+

I405L+A421H+A422P+A428T,

H1*+N54S+V56T+G109A+F113Q+R116H+Q172N+A174S+G182*+D183*+N195F+V206L+

I405L+A421H+A422P+A428T,

H1*+N54S+V56T+K72R+G109A+T134E+W167F+Q172N+A174S+G182*+D183*+N195F+

V206L+G255A+A265G+I405L+A421H+A422P+A428T,

H1*+N54S+V56T+K72R+G109A+R116Q+W167F+Q172R+L173V+A174S+G182*+D183*+

N195F+V206L+A265G+I405L+A421H+A422P+A428T,

H1*+N54S+V56T+K72R+G109A+R116Q+W167F+Q172R+A174S+G182*+D183*+N195F+

V206L+I405L+A421H+A422P+A428T,

H1*+N54S+V56T+K72R+G109A+F113Q+T134E+W167F+Q172G+A174S+G182*+D183*+
N195F+V206L+G255A+I405L+A421H+A422P+A428T,
H1*+N54S+V56T+K72R+G109A+F113Q+R116H+W167F+Q172G+L173V+A174S+G182*+
D183*+G184T+N195F+V206L+I405L+A421H+A422P+A428T,
H1*+N54S+V56T+K72R+G109A+A174S+G182*+D183*+N195F+V206L+G255A+I405L+A421H+A422P+A428T,
H1*+N54S+V56T+G109A+F113Q+R116Q+A174S+G182*+D183*+N195F+V206L+I405L+
A421H+A422P+A428T,
H1*+N54S+V56T+K72R+G109A+F113Q+F116H+W167F+Q172G+L173V+A174S+G182*+
D183*+N195F+V206L+I405L+A421H+A422P+A428T,
H1*+N54S+V56T+K72R+G109A+F113Q+R116Q+W167F+Q172G+A174S+G182*+D183*+
G184T+N195F+V206L+I405L+A421H+A422P+A428T,
H1*+N54S+V56T+G109A+F113Q+R116Q+W167F+Q172G+A174S+G182*+D183*+N195F+
A204G+V206L+I405L+A421H+A422P+A428T,
H1*+N54S+V56T+G109A+F113Q+R116H+W167F+Q172G+A174S+G182*+D183*+N195F+
V206L+A265G+I405L+A421H+A422P+A428T,
H1*+N54S+V56T+G109A+R116Q+A174S+G182*+D183*+N195F+V206L+I405L+A421H+
A422P+A428T,
H1*+A37H+N54S+V56T+A60V+G109A+R116Q+T165G+A174S+G182*+D183*+N195F+V206L+I405L+A421H+A422P+A428T,
H1*+N54S+V56T+K72R+G109A+F113Q+T134E+A174S+G182*+D183*+N195F+V206L+
G255A+I405L+A421H+A422P+A428T,
H1*+N54S+V56T+K72R+G109A+R116Q+V120L+A174S+G182*+D183*+G184T+N195F+

V206L+I405L+A421H+A422P+A428T,

H1*+N54S+V56T+G109A+F113Q+R116H+W167F+Q172G+L173V+A174S+G182*+D183*+

N195F+V206L+I405L+A421H+A422P+A428T,

H1*+N54S+V56T+G109A+F113Q+R116Q+Q172N+A174S+G182*+D183*+N195F+V206L+

A265G+I405L+A421H+A422P+A428T,

H1*+A37H+N54S+V56T+A60V+G109A+R116Q+W167F+Q172R+A174S+G182*+D183*+

N195F+V206L+I405L+A421H+A422P+A428T, en donde la numeración es acorde con la SEQ ID NO: 14 y en donde el IF se determina mediante el uso del detergente modelo A.

En una realización, el IF se determina mediante el uso del detergente modelo A a una temperatura de 15°C. En una realización particular, las variantes tienen un IF de >1.5 en comparación con el polipéptido parental, en donde el IF se determina mediante el uso del detergente modelo A a una temperatura de 15°C y una concentración de 0.05mg/L. A partir de las tablas en los ejemplos divulgados en el presente documento puede observarse cuáles pueden ser estas variantes.

En otra realización, la variante tiene un IF de al menos 1.5 en comparación con el polipéptido parental y cuando se determina mediante el uso del detergente modelo J, en donde la variante se selecciona entre el grupo que consiste en:

G182*+D183*+N195F,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+R87S+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+T40G+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+T51K+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+K72R+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+K72H+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+A37H+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

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H1*+G50A+T51A+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+V264F+K391A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+Y382L+K391A+G476K,

H1*+G7K
+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+G255A+Q256A+K391A+ G476K,

H1*+N54S+V56T+G109A+W167Y+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+W167H
+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+T165V+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+A174N+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+A174Q+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N16H+V17L+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+Y382F+K391A+G476K,

H1*+Q32S+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+Q385L+K391A+ G476K,

H1*+N54S+V56T+R87S+G109A+R171H+A174S+G182*+D183*+N195F+V206L+K391A+ G476K,

N54S+G182*+D183*+N195F,

G109A+G182*+D183*+N195F,

G182*+D183*+N195F+G476K,

H1*+N54S+V56T+G109A+R116H+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+

K391A+G476K,

H1*+N54S+V56T+G109A+A174*+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+K72R+G109A+F113Q+R116Q+W167F+Q172G+A174S+G182*+D183*+G184T+N195F+

V206L+K391A+P473R+G476K,

H1*+N54S+V56T+K72R+G109A+F113Q+R116Q+W167F+Q172G+A174S+G182*+D183*+

G184T+N195F+V206L+P473R+G476K,

H1*+N54S+V56T+G109A+Q169E+Q172G+A174*+G182*+D183*+N195F+V206L+K391A+

G476K,

H1*+N54S+V56T+K72R+G109A+F113Q+R116Q+W167F+Q172G+A174S+G182*+D183*+

G184T+N195F+K391A+P473R+G476K,

H1*+N54S+V56T+G109A+R116W+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+

K391A+G476K,

H1*+N54S+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206F+K391A+

G476K,

H1*+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+N260G+K391A+G476K,

H1*+N54S+V56T+K72R+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+G184T+N195F+V206L+

K391A+G476K,

H1*+N54S+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+Y295N+

K391A+G476K,

H1*+N54S+V56T+G109A+W167F+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+A186N+N195F+V206L+

K391A+G476K,

H1*+N54S+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+A288V+

K391A+G476K,

H1*+N54S+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+G255A+

K391A+G476K,

H1*+N54S+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+W48F+N54S+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+

K391A+G476K,

H1*+N54S+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+V291A+

K391A+G476K,

H1*+N54S+V56T+G109A+F113Q+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+R320A+

S323N+K391A+G476K,

H1*+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+K72R+G109A+F113Q+R116H+W167F+Q172G+A174S+G182*+D183*+

G184T+N195F+V206L+K391A+P473R+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+N270T+K391A+G476K,

H1*+N54S+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+G476K,

H1*+N54S+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+N260G+

K391A+G476K,

H1*+N54S+V56T+G109A+F113Q+R116H+A174S+G182*+D183*+N195F+V206L+K391A+

G476K,

H1*+N54S+V56T+G109A+Q172G+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+A174S+A186D+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+A225V+

K391A+G476K,

H1*+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+G255S+
K391A+G476K,

H1*+N54S+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+K269Q+
K391A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+G255S+K391A+G476K,

H1*+N54S+V56T+G109A+Q169E+Q172K+A174S+G182*+D183*+N195F+V206L+K391A+
G476K,

G182*+D183*+N195F,

H1*+N54S+V56T+G109A+Q169E+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+W284H+
K391A+G476K,

H1*+N54S+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+S304R+
K391A+G476K,

H1*+N54S+V56T+K72R+G109A+F113Q+R116Q+W167F+Q172G+A174S+G182*+D183*+
G184T+N195F+V206L+K391A+P473R,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+M246V+K391A+G476K,

H1*+N54S+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+K391A,

H1*+N54S+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+N270G+

K391A+G476K,

H1*+N54S+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+Y295F+

K391A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+R320A+K391A+G476K,

H1*+N54S+V56T+G109A+Q169E+Q172K+A174T+G182*+D183*+N195F+V206L+K391A+

G476K,

H1*+N54S+V56T+G109A+Q169E+Q172K+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+W140Y+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+

K391A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A,

H1*+N54S+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+F328L+

K391A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+G476K,

F113Q+R116H+D183*+G182*+N195F,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+A288L+K391A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+N270G+K391A+G476K,

Q169E+Q172K+A174*+D183*+G182*+N195F,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K269Q+K391A+G476K,

H1*+W48F+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

F113Q+R116Q+D183*+G182*+N195F,

N54S+V56T+D183*+G182*+N195F,

H1*+N54S+V56T+G109A+A174T+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+R116W+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

Q169E+Q172K+G182*+D183*+N195F,

G182*+D183*+A186D,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+V238A+K391A+G476K,

G182*+D183*+A186N,

H1*+N54S+V56T+G109A+A174S+V206L+G182*+D183*+K391A+G476K,

H1*+N54S+V56T+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206F+K391A+G476K,

H1*+N54S+V56T+G109A+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+Q172K+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+Q172K+A174*+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+A174N+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+A174S+A186N+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+F289L+K391A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+Y295F+K391A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+V291A+K391A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+S244Q+K391A+G476K,

G182*+D183*+F328L,

G182*+D183*+N195F+A288V,

G182*+D183*+A186N+N195F,

G182*+D183*+E190P+N195F,

W140Y+G182*+D183*+N195F,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+A225V+K391A+G476K,

G182*+D183*+A186D+N195F,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+P473R+G476K,

H1*+W48Y+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+K391A+

G476K,

G182*+D183*+N195F+V238A,

G182*+D183*+Y295N,

Q172G+G182*+D183*,

F113Q+G182*+D183*+N195F,

H1*+N54S+V56T+Q98A+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

G182*+D183*+N195F+Y295F,

G182*+D183*+A186E,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206Y+K391A+G476K,

G182*+D183*+N195F+W284H,

G182*+D183*+A186Q+N195F,

K72R+G182*+D183*,

D183*+G182*+N195F+V326L,

D183*+G182*+A186E+N195F,

Q169E+G182*+D183*+N195F,

D183*+G182*+N195F+K242Q,

G7A+G182*+D183*+N195F,

D183*+G182*+N195F+N260G,

D183*+G182*+R321A+S323N,

D183*+G182*+W284H,

D183*+G182*+A186H+N195F,

D183*+G182*+K391A,

en donde la numeración es acorde con la SEQ ID NO: 13,

V56T+G182*+D183*+N195F,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+I405L+A421H+A422P+ A428T,

H1*+N54S+V56T+G109A+A174S+D183*+N195F+V206L+K391A+I405L+A421H+A422P+ A428T,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+I405L+A421H+ A422P+A428T+D476K+G477S,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+I405L+A421H+ A422P+A428T+D476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+I405L+A421H+ A422P+A428T+D476G+G477T,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+I405L+A421H+ A422P+A428T+G477Q,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+I405L+A421H+ A422P+A428T+G477A,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+I405L+A421H+ A422P+A428T+D476K+G477Q,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+I405L+A421H+ A422P+A428T+D476N,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+I405L+A421H+ A422P+A428T+D476Y,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206I+I405L+A421H+A422P+ A428T,

H1*+N54S+V56T+G109A+Q172D+A174S+G182*+D183*+N195F+A204G+V206L+I405L+ A421H+A422P+A428T,

H1*+N54S+V56T+K72R+G109A+T134E+A174S+G182*+D183*+N195F+A204G+V206L+ G255A+I405L+A421H+A422P+A428T,

H1*+N54S+V56T+G109A+F113Q+R116H+T165G+Q172G+A174S+G182*+D183*+N195F+ V206L+I405L+A421H+A422P+A428T,

H1*+N54S+V56T+G109A+F113Q+Q172N+A174S+G182*+D183*+N195F+V206L+I405L+ A421H+A422P+A428T,

H1*+N54S+V56T+K72R+G109A+T134E+A174S+G182*+D183*+N195F+G196R+V206L+ G255A+I405L+A421H+A422P+A428T+N475S,

H1*+N54S+V56T+G109A+T134E+A174S+G182*+D183*+N195F+V206L+I405L+A421H+ A422P+A428T,

H1*+T40D+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+I405L+A421H+A422P+A428T,

H1*+N54S+V56T+G109A+F113Q+N125D+A174S+G182*+D183*+N195F+V206L+I405L+ A421H+A422P+A428T,

H1*+N54S+V56T+A60V+G109A+R116Q+A174S+G182*+D183*+N195F+V206L+I405L+A421H+A422P+A428T,

H1*+N54S+V56T+G109A+R116V+A174S+G182*+D183*+N195F+V206L+I405L+A421H+ A422P+A428T,

H1*+N54S+V56T+G109A+R116Q+G133Q+T165G+Q172G+A174S+G182*+D183*+N195F+ V206L+I405L+A421H+A422P+A428T,

H1*+N54S+V56T+G109A+F113Q+R116H+Q172G+A174S+G182*+D183*+N195F+V206L+ I405L+A421H+A422P+A428T,

H1*+N54S+V56T+G109A+F113Q+R116Q+Q172G+A174S+G182*+D183*+N195F+V206L+ I405L+A421H+A422P+A428T+G448D,

H1*+N54S+V56T+G109A+F113Q+R116H+Q172N+A174S+G182*+D183*+N195F+V206L+ I405L+A421H+A422P+A428T,

H1*+N54S+V56T+K72R+G109A+T134E+W167F+Q172N+A174S+G182*+D183*+N195F+ V206L+G255A+A265G+I405L+A421H+A422P+A428T,

H1*+N54S+V56T+K72R+G109A+R116Q+W167F+Q172R+L173V+A174S+G182*+D183*+ N195F+V206L+A265G+I405L+A421H+A422P+A428T,

H1*+N54S+V56T+K72R+G109A+R116Q+W167F+Q172R+A174S+G182*+D183*+N195F+ V206L+I405L+A421H+A422P+A428T,

H1*+N54S+V56T+K72R+G109A+F113Q+T134E+W167F+Q172G+A174S+G182*+D183*+ N195F+V206L+G255A+I405L+A421H+A422P+A428T,

H1*+N54S+V56T+K72R+G109A+F113Q+R116H+W167F+Q172G+L173V+A174S+G182*+
D183*+G184T+N195F+V206L+I405L+A421H+A422P+A428T,

H1*+N54S+V56T+G109A+F113Q+W167F+Q172G+A174S+G182*+D183*+N195F+V206L+ I405L+A421H+A422P+A428T,

H1*+N54S+V56T+K72R+G109A+A174S+G182*+D183*+N195F+V206L+G255A+I405L+A421H+A422P+A428T,

H1*+N54S+V56T+K72R+G109A+F113Q+R116Q+W167F+Q172G+A174S+G182*+D183*+ G184T+N195F+V206L+I405L+A421H+A422P+A428T,

H1*+N54S+V56T+G109A+F113Q+R116Q+W167F+Q172G+A174S+G182*+D183*+N195F+ A204G+V206L+I405L+A421H+A422P+A428T,

H1*+N54S+V56T+G109A+R116Q+A174S+G182*+D183*+N195F+V206L+I405L+A421H+ A422P+A428T,

H1*+A37H+N54S+V56T+A60V+G109A+R116Q+T165G+A174S+G182*+D183*+N195F+V206L+I405L+A421H+A422P+A428T,

H1*+N54S+V56T+G109A+A174S+M105F+G182*+D183*+N195F+V206L+L228I+R320A+ S323N+I405L+A421H+A422P+A428T,

H1*+N54S+V56T+K72R+G109A+F113Q+T134E+A174S+G182*+D183*+N195F+V206L+ G255A+I405L+A421H+A422P+A428T,

H1*+N54S+V56T+K72R+G109A+R116Q+V120L+A174S+G182*+D183*+G184T+N195F+ V206L+I405L+A421H+A422P+A428T,

H1*+N54S+V56T+G109A+F113Q+R116H+W167F+Q172G+L173V+A174S+G182*+D183*+ N195F+V206L+I405L+A421H+A422P+A428T,

H1*+N54S+V56T+G109A+F113Q+R116Q+Q172N+A174S+G182*+D183*+N195F+V206L+ A265G+I405L+A421H+A422P+A428T,

H1*+A37H+N54S+V56T+A60V+G109A+R116Q+W167F+Q172R+A174S+G182*+D183*+ N195F+V206L+I405L+A421H+A422P+A428T, en donde la numeración es acorde con la SEQ ID NO: 14.

En una realización, el IF se determina mediante el uso del detergente modelo J a una temperatura de 15°C. En una realización particular, las variantes tienen un IF de >1.5 en comparación con el polipéptido parental, en donde el IF se determina mediante el uso del detergente

modelo J a una temperatura de 15°C y una concentración de 0.05mg/L. A partir de las tablas en los ejemplos divulgados en el presente documento puede observarse cuáles pueden ser estas variantes.

Algunas variantes de acuerdo con la presente invención tienen un rendimiento de lavado aún más mejorado indicado por un IF de al menos 2.0 cuando se compara con el polipéptido parental que tiene una secuencia de aminoácidos expuesta en la SEQ ID NO: 15 y en donde el IF se determina mediante el uso de detergente modelo A a una temperatura de 15°C.

Por lo tanto, en una realización, la variante tiene un IF de al menos >2.0 cuando se compara con dicho polipéptido parental y en donde dicha variante se selecciona entre

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+R87S+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+T40G+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+T51K+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+K72R+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+K72H+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+A37H+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+A37M+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+A37V+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+A37S+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+A37Y+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+A37R+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+F113W+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+F113S+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+F113N+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+R116Q+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+R116V+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+R116K+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+Q125P+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+S381G+K391A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+M246T+K391A+G476K,

H1*+A37L+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+R116A+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+R116H+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+Q125A+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+Q172G+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+Q172R+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+D377S+K391A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+D377A+K391A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+S381A+K391A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+G346P+K391A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+I214H+K391A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+I214S+K391A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+A420Q+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+A420S+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+A420K+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+A420L+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+K391Y+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+P473R+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+P473A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+P473G+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+T444D+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+T444Y+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+S280W+K391A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+S280L+K391A+G476K,

H1*+N54S+V56T+K72S+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+T40K+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+G346T+K391A+

G476K,

H1*+G50A+N54S+V56T+G109A++Q172N+A174S+G182*+D183*+N195F+V206L+K391A+

G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K+K484S,

H1*K+G50A+N54S+V56T+G109A+W167F+A174S+G182*+D183*+N195F+V206L+K391A+

G476K,

H1*+N54S+V56T+G109A+L173V+A174S+G182*+D183*+N195F+A204T+V206L+K391A+

G476K,

H1*+N54S+V56T+G109A+W140Y+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+G346T+K391A+G476K+

G477A,

H1*+N54S+V56T+G109AG255A++A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+G50A+N54S+V56T+G109A+F113L+R116L+A174S+G182*+D183*+N195F+V206L+

K391A+G476K,

H1*+N54S+V56T+G109A+W167F+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+K72R+G109A+W167F+A174S+G182*+D183*+N195F+V206L+K391A+

G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+R320V+K391A+G476Y,

H1*+N54S+V56T+G109A+R116M+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+Q172Y+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+I214L+K391A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+L217V+K391A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+L217H+K391A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+P211D+K391A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+K391Q+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+T444H+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+T444V+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+T444R+G476K,

H1*+G50A+N54S+V56T+G109A+L173V+A174S+G182*+D183*+N195F+A204V+V206L+

K391A+G476K,

H1*+G7K+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+R320A+K391A+G476K,

H1*+N54S+V56T+G109A+Q172D+A174S+G182*+D183*+N195F+V206L+G346T+K391A+
G476K+G477A,
H1*+N54S+V56T+G109A+Q118S+A174S+G182*+D183*+N195F+V206L+K391A+G476K,
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+R320A+K391A+G476K,
H1*+N54S+V56T+G109A+T134E+A174S+G182*+D183*+N195F+V206L+K391A+G476K,
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+Y382M+K391A+G476K,
H1*+N54S+V56T+K72R+G109A+T134E+A174S+G182*+D183*+N195F+V206L+G255A+
K391A+G476K,
H1*+N54S+V56T+K72R+M105F+G109A+A174S+G182*+D183*+N195F+V206L+G255A+
K391A+G476K,
H1*+N54S+V56T+M105F+G109A+T134E+A174S+G182*+D183*+N195F+V206L+K391A+
G476K,
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+R320A+S323N+D377H+
K391A+G476K,
H1*+T51E+N54S+V56T+G109A+A174H+G182*+D183*+N195F+V206L+K391A+G476K,
H1*+N54S+V56T+G109A+L173A+A174S+G182*+D183*+N195F+V206L+K391A+G476K,
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+Q299V+K391A+G476K,
H1*+N54S+V56T+G109A+L173G+A174S+G182*+D183*+N195F+V206L+K391A+G476K,
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+T355L+K391A+G476K,

H1*+G50A+N54S+V56T+G109A+A174S+G182*+D183*+N195F+A204T
+V206L+K391A+
G476K,
H1*+N54S+V56T+K72R+G109A+A174S+G182*+D183*+N195F+V206L
+R320A+S323N+
K391A+G476K,
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+M246
L+K391A+G476K,
H1*+N54S+V56T+K72Q+G109A+W167H+A174S+G182*+D183*+N195F
+V206L+K391A+
G476K,
H1*+N54S+V56T+K72R+G109A+T134E+A174S+G182*+D183*+N195F
+V206L+K391A+
G476K,
H1*+N54S+V56T+K72R+G109A+T134E+A174S+G182*+D183*+N195F
+V206L+D377H+
K391A+G476K,
H1*+N54S+V56T+K72R+G109A+T134E+A174S+G182*+D183*+G184T
+N195F+V206L+
K391A+G476K,
H1*+N54S+V56T+G109A+Q118R+T134E+A174S+G182*+D183*+N195
F+V206L+G255A+
K391A+G476K,
H1*+N54S+V56T+G109A+Q118R+A174S+G182*+D183*+N195F+V206
L+D377H+K391A+
G476K,
H1*+N54S+V56T+G109A+T134E+A174S+G182*+D183*+G184T+N195
F+V206L+D377H+
K391A+G476K,
H1*+N54S+V56T+G109A+Q172D+A174Q+G182*+D183*+N195F+V206
L+K391A+G476K+
G477A,

H1*+N54S+V56T+K72R+G109A+A174S+G182*+D183*+G184T+N195F+V206L+G255A+
K391A+G476K,
H1*+N54S+V56T+G109A+A174S+G182*+D183*+G184T+N195F+V206L+D377H+K391A+
G476K,
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+G255A+D377H+K391A+
G476K,
H1*+N54S+V56T+G109A+T134E+A174S+G182*+D183*+G184T+N195F+V206L+K391A+
G476K,
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+V238T+D377H+K391A+
G476K,
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+V291A+D377H+K391A+
G476K,
H1*+N54S+V56T+K72R+G109A+T134E+A174S+G182*+D183*+G184T+N195F+V206L+
G255A+K391A+G476K,
H1*+N54S+V56T+G109A+L173H+A174S+G182*+D183*+N195F+V206L+K391A+G476K,
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H1*+N54S+V56T+K72N+G109A+W167L+A174S+G182*+D183*+N195F+V206L+K391A+
G476K,
H1*+N54S+V56T+G109A+Q118R+T134E+A174S+G182*+D183*+N195F+V206L+G255A+
D377H+K391A+G476K,
H1*+N54S+V56T+K72R+G109A+A174S+G182*+D183*+N195F+G184T+V206L+K391A+

G476K,

H1*+N54S+V56T+K72R+G109A+Q118R+A174S+G182*+D183*+N195F+V206L+G255A+

D377H+K391A+G476K,H1*+N54S+V56T+G109A+G182*+D183*+N195F+V206L+D377H+K391A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+D377H+K391A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+D377H+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+D377H+K391A,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+D377S+K391A+G476K,

H1*+N54S+V56T+G109A+R116E+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+T134E+A174S+G182*+D183*+N195F+V206L+D377H+K391A+

G476K,

H1*+N54S+V56T+G109A+R116S+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+R116I+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+R116G+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+T51A+N54S+V56T+G109A+Q172S+A174S+G182*+D183*+N195F+V206L+K391A+

G476K,

H1*+T51E+N54S+V56T+G109A+Q172T+A174S+G182*+D183*+N195F+V206L+K391A+

G476K,

H1*+T51S+N54S+V56T+G109A+Q172N+A174S+G182*+D183*+N195F+V206L+K391A+

G476K,

H1*+T51E+N54S+V56T+G109A+Q172L+A174S+G182*+D183*+N195F+V206L+K391A+

G476K,

H1*+T51E+N54S+V56T+G109A+Q172R+A174S+G182*+D183*+N195F+V206L+K391A+

G476K,

H1*+N54S+V56T+G109A+Q172K+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+K72R+G109A+Q172S+A174S+G182*+D183*+N195F+V206L+K391A+

G476K,

H1*+N54S+V56T+K72H+G109A+Q172T+A174S+G182*+D183*+N195F+V206L+K391A+

G476K,

H1*+N54S+V56T+K72Q+G109A+Q172R+A174S+G182*+D183*+N195F+V206L+K391A+

G476K,

H1*+N54S+V56T+K72R+G109A+Q172T+A174S+G182*+D183*+N195F+V206L+K391A+

G476K,

H1*+N54S+V56T+K72M+G109A+Q172S+A174S+G182*+D183*+N195F+V206L+K391A+

G476K,

H1*+N54S+V56T+K72Q+G109A+Q172M+A174S+G182*+D183*+N195F+V206L+K391A+

G476K,

H1*+N54S+V56T+K72S+G109A+A174H+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+K72Q+G109A+A174D+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+K72R+G109A+A174D+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+K72Q+G109A+A174K+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+A174G+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+K72R+G109A+A174Q+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+K72Q+G109A+A174G+G182*+D183*+N195F+V206L+K391A+G476K,

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H1*+N54S+V56T+K72R+G109A+A174H+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+G50A+N54S+V56T+G109A+A174E+G182*+D183*+N195F+A204T+V206L+S323N+

K391A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+A204G+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+Y382I+K391A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+I214W+K391A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+A204S+V206L+D377H+K391A+

G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+T334S+D377H+K391A+

G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+A263G+D377H+K391A+

G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+M286F+D377H+K391A+

G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+L235V+D377H+K391A+
G476K,
H1*+N54S+V56T+M105L+G109A+A174S+G182*+D183*+N195F+V206L+D377H+K391A+
G476K,
H1*+N54S+V56T+M105I+G109A+A174S+G182*+D183*+N195F+V206L+D377H+K391A+
G476K,
H1*+N54S+V56T+M105V+G109A+A174S+G182*+D183*+N195F+V206L+D377H+K391A+
G476K,
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+M246I+D377H+K391A+
G476K,
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+L250I+D377H+K391A+
G476K,
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+L250V+D377H+K391A+
G476K,
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391Y+G476K,
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391V+G476K,
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391M+G476K,
H1*+N54S+V56T+G109A+T165G+A174S+G182*+D183*+N195F+V206L+D377H+K391A+
G476K,
H1*+N54S+V56T+G109S+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+A174V+G182*+D183*+N195F+V206L+K391A+G476K,

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H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+M246V+D377H+K391A+G476K,

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G476K,

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K391A+G476K,

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H1*+N54S+V56T+G109A+F113Q+W167F+Q172N+A174S+G182*+D183*+N195F+A204G+

V206L+K391A+P473R+G476K,

H1*+N54S+V56T+G109A+F113Q+R116H+W167F+Q172R+A174S+G182*+D183*+N195F+

A204G+V206L+K391A+P473R+G476K,

H1*+N54S+V56T+G109A+R116A+A174S+G182*+D183*+N195F+V206L+K391A+T444Q+

P473R+G476K,

H1*+N54S+V56T+G109A+R116H+Q172R+A174S+G182*+D183*+N195F+A204G+V206L+

K391A+P473R+G476K,

H1*+A37V+N54S+V56T+G109A+R116Q+T165G+A174S+G182*+D183*+N195F+V206L+

K391A+G476K,

H1*+A37H+N54S+V56T+G109A+R116H+T165G+A174S+G182*+D183*+N195F+V206L+

M246F+K391A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+K391A+G476K,

H1*+N54S+V56T+G109A+G133S+A174S+G182*+D183*+N195F+K391A+G476H,

H1*+N54S+V56T+G109A+R116A+Q172N+L173V+A174S+G182*+D183*+N195F+V206L+

K391A+G476K,

H1*+A37V+N54S+V56T+G109A+R116H+T165G+A174S+G182*+D183*+N195F+V206L+

K391A+G476K,

H1*+P45A+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+C474V+

G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+P364A+K391A+C474V+

G476K,

H1*+N54S+V56T+G109A+Q118R+T134E+A174S+G182*+D183*+N195F+V206L+K391A+

G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+G184T+N195F+V206L+K391A+G476K,

H1*+G50A+T51A+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+V264F+K391A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+Y382L+K391A+G476K,

H1*+G7K

+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+G255A+Q256A+K391A+

G476K,

H1*+N54S+V56T+G109A+W167Y+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+W167H+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+T165V+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+A174N+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+A174Q+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N16H+V17L+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+Y382F+K391A+G476K,

H1*+Q32S+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+Q385L+K391A+

G476K,

H1*+N54S+V56T+R87S+G109A+R171H+A174S+G182*+D183*+N195F+V206L+K391A+

G476K,

H1*+N54S+V56T+G109A+R116H+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+

K391A+G476K,

H1*+N54S+V56T+G109A+A174*+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+K72R+G109A+F113Q+R116Q+W167F+Q172G+A174S+G182*+D183*+G184T+N195F+

V206L+K391A+P473R+G476K,

H1*+N54S+V56T+K72R+G109A+F113Q+R116Q+W167F+Q172G+A174S+G182*+D183*+

G184T+N195F+V206L+P473R+G476K,

H1*+N54S+V56T+G109A+Q169E+Q172G+A174*+G182*+D183*+N195F+V206L+K391A+

G476K,

H1*+N54S+V56T+K72R+G109A+F113Q+R116Q+W167F+Q172G+A174S+G182*+D183*+

G184T+N195F+K391A+P473R+G476K,

H1*+N54S+V56T+G109A+R116W+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+

K391A+G476K,

H1*+N54S+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206F+K391A+

G476K,

H1*+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+N260G+K391A+G476K,

H1*+N54S+V56T+K72R+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+G184T+N195F+V206L+
K391A+G476K,
H1*+N54S+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+Y295N+
K391A+G476K,
H1*+N54S+V56T+G109A+W167F+A174S+G182*+D183*+N195F+V206L+K391A+G476K,
H1*+N54S+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+A186N+N195F+V206L+
K391A+G476K,
H1*+N54S+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+A288V+
K391A+G476K,
H1*+N54S+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+G255A+
K391A+G476K,
H1*+N54S+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+K391A+G476K,
H1*+W48F+N54S+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+
K391A+G476K,
H1*+N54S+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+V291A+
K391A+G476K,
H1*+N54S+V56T+G109A+F113Q+A174S+G182*+D183*+N195F+V206L+K391A+G476K,
H1*+N54S+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+R320A+
S323N+K391A+G476K,
H1*+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+K72R+G109A+F113Q+R116H+W167F+Q172G+A174S+G182*+D183*+

G184T+N195F+V206L+K391A+P473R+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+N270T+K391A+G476K,

H1*+N54S+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+G476K,

H1*+N54S+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+N260G+

K391A+G476K,

H1*+N54S+V56T+G109A+F113Q+R116H+A174S+G182*+D183*+N195F+V206L+K391A+

G476K,

H1*+N54S+V56T+G109A+Q172G+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+A174S+A186D+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+A225V+

K391A+G476K,

H1*+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+G255S+

K391A+G476K,

H1*+N54S+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+K269Q+

K391A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+G255S+K391A+G476K,

H1*+N54S+V56T+G109A+Q169E+Q172K+A174S+G182*+D183*+N195F+V206L+K391A+

G476K,

en donde la numeración es acorde con la SEQ ID NO: 13 y

H1*+T40D+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+I405L+A421H+A422P+A428T

H1*+N54S+V56T+G109A+F113Q+N125D+A174S+G182*+D183*+N195F+V206L+I405L+
A421H+A422P+A428T

H1*+N54S+V56T+G109A+F113Q+R116H+Q172N+A174S+G182*+D183*+N195F+V206L+
I405L+A421H+A422P+A428T

H1*+N54S+V56T+K72R+G109A+T134E+W167F+Q172N+A174S+G182*+D183*+N195F+
V206L+G255A+A265G+I405L+A421H+A422P+A428T

H1*+N54S+V56T+K72R+G109A+R116Q+W167F+Q172R+L173V+A174S+G182*+D183*+
N195F+V206L+A265G+I405L+A421H+A422P+A428T

H1*+N54S+V56T+K72R+G109A+R116Q+W167F+Q172R+A174S+G182*+D183*+N195F+
V206L+I405L+A421H+A422P+A428T

H1*+N54S+V56T+K72R+G109A+F113Q+T134E+W167F+Q172G+A174S+G182*+D183*+
N195F+V206L+G255A+I405L+A421H+A422P+A428T

H1*+N54S+V56T+G109A+F113Q+R116Q+W167F+Q172G+A174S+G182*+D183*+N195F+
A204G+V206L+I405L+A421H+A422P+A428T

H1*+N54S+V56T+K72R+G109A+R116Q+V120L+A174S+G182*+D183*+G184T+N195F+
V206L+I405L+A421H+A422P+A428T

H1*+N54S+V56T+G109A+F113Q+R116H+W167F+Q172G+L173V+A174S+G182*+D183*+
N195F+V206L+I405L+A421H+A422P+A428T

H1*+N54S+V56T+G109A+F113Q+R116Q+Q172N+A174S+G182*+D183*+N195F+V206L+

A265G+I405L+A421H+A422P+A428T

H1*+A37H+N54S+V56T+A60V+G109A+R116Q+W167F+Q172R+A174S+G182*+D183*+

N195F+V206L+I405L+A421H+A422P+A428T, en donde la numeración es acorde con la SEQ ID NO: 14 y en donde el IF se determina mediante el uso del detergente modelo A.

En una realización, la variante tiene un IF de al menos 2.0 cuando se compara con el polipéptido parental, en donde el IF se determina mediante el uso de detergente modelo A a una temperatura de 15°C y una concentración de 0.05 mg de enzima/L.

En una realización, la variante tiene un IF de al menos 2.0 en comparación con el polipéptido parental y cuando se determina mediante el uso del detergente modelo J y en donde la variante se selecciona entre el grupo que consiste en:

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+R87S+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+T40G+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+T51K+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+K72R+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+K72H+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+A37H+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+A37M+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+A37V+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+A37S+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+A37Y+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+A37R+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+F113W+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+F113S+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+F113N+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+F113Y+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+F113R+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+Q118N+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+R116Q+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+R116V+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+R116K+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+Q125P+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+Q125K+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+S381G+K391A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+M246T+K391A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+V213T+K391A+G476K,

H1*+A37L+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+R116A+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+R116H+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+Q125A+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+Q172G+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+Q172R+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+D377S+K391A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+D377G+K391A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+D377R+K391A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+D377A+K391A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+I214G+K391A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+S381A+K391A+G476K,

H1*+N54S+V56T+G109A+W167I+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+W167G+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+G346S+K391A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+G346P+K391A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+I214H+K391A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+I214S+K391A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+I214T+K391A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+A420S+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+A420K+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+A420L+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+K391Y+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+K391R+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+P473R+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+P473A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+P473G+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+P473T+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+Q395P+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+T444Q+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+T444S+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+T444D+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+T444Y+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+S280W+K391A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+S280L+K391A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+S280T+K391A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+S280A+K391A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+G255N+K391A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+T285L+K391A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+T285Q+K391A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+P473K+G476K,

H1*+N54S+V56T+K72S+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+T40K+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+G346T+K391A+

G476K,

H1*+G50A+N54S+V56T+G109A++Q172N+A174S+G182*+D183*+N195F+V206L+K391A+

G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K+K484A,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K+K484G,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K+K484P,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K+K484E,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K+K484Q,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K+K484S,

H1*K+G50A+N54S+V56T+G109A+W167F+A174S+G182*+D183*+N195F+V206L+K391A+

G476K,

H1*+N54S+V56T+G109A+L173V+A174S+G182*+D183*+N195F+A204T+V206L+K391A+

G476K,

H1*+N54S+V56T+G109A+W140Y+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+Q98S+G109A+A174S+G182*+D183*+N195F+V206L+R320A+K391A+

G476K,

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G477A,

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H1*+G50A+N54S+V56T+G109A+F113L+R116L+A174S+G182*+D183*+N195F+V206L+

K391A+G476K,

H1*+N54S+V56T+G109A+W167F+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+L173V+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+K72R+G109A+W167F+A174S+G182*+D183*+N195F+V206L+K391A+

G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K+G477Q,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+Q345D+K391A+G476K+

G477Q,

H1*+G50A+N54S+V56T+G109A+Q172D+A174S+G182*+D183*+N195F+V206L+K391A+

G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+V264I+K391A+G423H+

G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+R320V+K391A+G476Y,

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K391A+G476K,
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K391A+G476K,

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G476K,

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G476K,

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G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+L250M+D377H+K391A+

G476K,

H1*+N54S+V56T+G109A+Q172H+L173A+A174P+G182*+D183*+N195F+V206L+K391A+

G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+G184T+N195F+V206L+G255A+K391A+

G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+G184T+N195F+V206L+G255A+D377H+

K391A+G476K,

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H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+S376V+K391A+G476K,

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G476K,

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G476K,

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G476K,

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G476K,

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K391A+G476K,

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K391A+G476K,

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G476K,

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G476K,

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K391A+G476K,

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K391A+G476K,

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G476K,

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K391A+G476K,

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K391A+P473R+G476K,

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P473R+G476K,

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C474V+G476K,

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N54S+V56T+G109A+A174S+G182*+D183*+N195F+K391A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+K391A,

H1*+N54S+V56T+G109A+F113Q+Q172M+A174S+G182*+D183*+N195F+V206L+K391A+

G476K,

H1*+N54S+V56T+K72R+G109A+F113Q+T134E+A174S+G182*+D183*
+N195F+V206L+
G255A+K391A+G476K,
H1*+N54S+V56T+K72R+G109A+F113Q+T134E+A174S+G182*+D183*
+N195F+V206L+
G255A+K391A+P473R+G476K,
H1*+N54S+V56T+K72R+G109A+R116Q+A174S+G182*+D183*+G184T
+N195F+V206L+
K391A+G476K,
H1*+A37V+N54S+V56T+G109A+R116A+T165G+A174S+G182*+D183*
+N195F+V206L+
K391A+G476K,
H1*+A37V+N54S+V56T+G109A+R116Q+T165G+A174S+G182*+D183*
+N195F+V206L+
M246F+K391A+G476K,
H1*+V56A+G109A+A174S+G182*+D183*+N195F+V206L+G476K,
H1*+N54S+V56T+G109A+G182*+D183*+N195F+V206L+K391A,
H1*+N54S+V56T+K72R+G109A+F113Q+R116H+A174S+G182*+D183*
+G184T+N195F+
V206L+K391A+T444Q+G476K,
H1*+N54S+V56T+G109S+F113Q+A174S+G182*+D183*+N195F+V206
L+K391A+T444Q+
G476K,
H1*+N54S+V56T+G109A+F113Q+R116H+W167F+Q172G+L173V+A174
S+G182*+D183*+
N195F+V206L+K391A+P473R+G476K,
H1*+N54S+V56T+G109A+F113Q+R116Q+Q172N+A174S+G182*+D183
*+N195F+V206L+
A265G+K391A+P473R+G476K,
H1*+N54S+V56T+G109A+F113Q+W167F+Q172N+A174S+G182*+D183
*+N195F+A204G+
V206L+K391A+P473R+G476K,

H1*+N54S+V56T+G109A+F113Q+R116H+W167F+Q172R+A174S+G182*+D183*+N195F+

A204G+V206L+K391A+P473R+G476K,

H1*+N54S+V56T+G109A+R116A+A174S+G182*+D183*+N195F+V206L+K391A+T444Q+

P473R+G476K,

H1*+N54S+V56T+G109A+R116H+Q172R+A174S+G182*+D183*+N195F+A204G+V206L+

K391A+P473R+G476K,

H1*+A37V+N54S+V56T+G109A+R116Q+T165G+A174S+G182*+D183*+N195F+V206L+

K391A+G476K,

H1*+A37H+N54S+V56T+G109A+R116H+T165G+A174S+G182*+D183*+N195F+V206L+

M246F+K391A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+K391A+G476K,

G109A+G182*+D183*+N195F+V206L+G476K,

H1*+N54S+V56T+G109A+G133S+A174S+G182*+D183*+N195F+K391A+G476H,

H1*+N54S+V56T+G109A+R116A+Q172N+L173V+A174S+G182*+D183*+N195F+V206L+

K391A+G476K,

H1*+A37V+N54S+V56T+G109A+R116H+T165G+A174S+G182*+D183*+N195F+V206L+

K391A+G476K,

H1*+P45A+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+C474V+

G476K,

H1*+N54S+V56T+G109A+P124A+A174S+G182*+D183*+N195F+V206L+K391A+C474V+

G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+P364A+K391A+C474V+

G476K,

H1*+N54S+V56T+G109A+Q118R+T134E+A174S+G182*+D183*+N195F+V206L+K391A+

G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+G184T+N195F+V206L+K391A+G476K,

H1*+G50A+T51A+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+V264F+K391A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+Y382L+K391A+G476K,

H1*+G7K

+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+G255A+Q256A+K391A+

G476K,

H1*+N54S+V56T+G109A+W167Y+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+W167H

+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+T165V+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+A174N+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+A174Q+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N16H+V17L+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+Y382F+K391A+G476K,

H1*+Q32S+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+Q385L+K391A+

G476K,

H1*+N54S+V56T+R87S+G109A+R171H+A174S+G182*+D183*+N195F+V206L+K391A+

G476K,

H1*+N54S+V56T+G109A+R116H+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+

K391A+G476K,

H1*+N54S+V56T+G109A+A174*+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+K72R+G109A+F113Q+R116Q+W167F+Q172G+A174S+G182*+D183*+G184T+N195F+

V206L+K391A+P473R+G476K,

H1*+N54S+V56T+K72R+G109A+F113Q+R116Q+W167F+Q172G+A174S+G182*+D183*+

G184T+N195F+V206L+P473R+G476K,

H1*+N54S+V56T+G109A+Q169E+Q172G+A174*+G182*+D183*+N195F+V206L+K391A+

G476K,

H1*+N54S+V56T+K72R+G109A+F113Q+R116Q+W167F+Q172G+A174S+G182*+D183*+

G184T+N195F+K391A+P473R+G476K,

H1*+N54S+V56T+G109A+R116W+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+

K391A+G476K,

H1*+N54S+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206F+K391A+

G476K,

H1*+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+N260G+K391A+G476K,

H1*+N54S+V56T+K72R+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+G184T+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+Y295N+K391A+G476K,

H1*+N54S+V56T+G109A+W167F+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+A186N+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+A288V+K391A+G476K,

H1*+N54S+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+G255A+K391A+G476K,

H1*+N54S+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+W48F+N54S+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+V291A+K391A+G476K,

H1*+N54S+V56T+G109A+F113Q+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+R320A+S323N+K391A+G476K,

H1*+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+K72R+G109A+F113Q+R116H+W167F+Q172G+A174S+G182*+D183*+

G184T+N195F+V206L+K391A+P473R+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+N270T+K391A+G476K,

H1*+N54S+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+G476K,

H1*+N54S+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+N260G+

K391A+G476K,

H1*+N54S+V56T+G109A+F113Q+R116H+A174S+G182*+D183*+N195F+V206L+K391A+

G476K,

H1*+N54S+V56T+G109A+Q172G+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+A174S+A186D+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+A225V+

K391A+G476K,

H1*+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+G255S+

K391A+G476K,

H1*+N54S+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+K269Q+

K391A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+G255S+K391A+G476K,

H1*+N54S+V56T+G109A+Q169E+Q172K+A174S+G182*+D183*+N195F+V206L+K391A+

G476K,

G182*+D183*+N195F,

H1*+N54S+V56T+G109A+Q169E+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+W284H+

K391A+G476K,

H1*+N54S+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+S304R+

K391A+G476K,

H1*+N54S+V56T+K72R+G109A+F113Q+R116Q+W167F+Q172G+A174S+G182*+D183*+

G184T+N195F+V206L+K391A+P473R,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+M246V+K391A+G476K,

H1*+N54S+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+K391A,

H1*+N54S+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+N270G+

K391A+G476K,

H1*+N54S+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+Y295F+

K391A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+R320A+K391A+G476K,

H1*+N54S+V56T+G109A+Q169E+Q172K+A174T+G182*+D183*+N195F+V206L+K391A+

G476K,

H1*+N54S+V56T+G109A+Q169E+Q172K+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+W140Y+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+

K391A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A,

H1*+N54S+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+F328L+

K391A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+G476K,

F113Q+R116H+D183*+G182*+N195F,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+A288L+K391A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+N270G+K391A+G476K,

Q169E+Q172K+A174*+D183*+G182*+N195F,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K269Q+K391A+G476K,

H1*+W48F+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

F113Q+R116Q+D183*+G182*+N195F,

N54S+V56T+D183*+G182*+N195F,

H1*+N54S+V56T+G109A+A174T+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+R116W+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

Q169E+Q172K+G182*+D183*+N195F,

G182*+D183*+A186D,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+V238A+K391A+G476K,

G182*+D183*+A186N,

en donde la numeración es acorde con la SEQ ID NO: 13,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206I+I405L+A421H+A422P+A428T,

H1*+N54S+V56T+G109A+Q172D+A174S+G182*+D183*+N195F+A204G+V206L+I405L+
A421H+A422P+A428T,

H1*+N54S+V56T+K72R+G109A+T134E+A174S+G182*+D183*+N195F+A204G+V206L+
G255A+I405L+A421H+A422P+A428T,

H1*+N54S+V56T+G109A+F113Q+R116H+T165G+Q172G+A174S+G182*+D183*+N195F+
V206L+I405L+A421H+A422P+A428T,

H1*+N54S+V56T+K72R+G109A+T134E+A174S+G182*+D183*+N195F+G196R+V206L+
G255A+I405L+A421H+A422P+A428T+N475S,

H1*+N54S+V56T+G109A+T134E+A174S+G182*+D183*+N195F+V206L+I405L+A421H+
A422P+A428T,

H1*+N54S+V56T+G109A+F113Q+N125D+A174S+G182*+D183*+N195F+V206L+I405L+
A421H+A422P+A428T,

H1*+N54S+V56T+G109A+R116V+A174S+G182*+D183*+N195F+V206L+I405L+A421H+
A422P+A428T,

H1*+N54S+V56T+G109A+R116Q+G133Q+T165G+Q172G+A174S+G182*+D183*+N195F+
V206L+I405L+A421H+A422P+A428T,

H1*+N54S+V56T+G109A+F113Q+R116H+Q172G+A174S+G182*+D183*+N195F+V206L+
I405L+A421H+A422P+A428T,

H1*+N54S+V56T+G109A+F113Q+R116Q+Q172G+A174S+G182*+D183*+N195F+V206L+
I405L+A421H+A422P+A428T+G448D,

H1*+N54S+V56T+G109A+F113Q+R116H+Q172N+A174S+G182*+D183*+N195F+V206L+
I405L+A421H+A422P+A428T,
H1*+N54S+V56T+K72R+G109A+T134E+W167F+Q172N+A174S+G182*+D183*+N195F+
V206L+G255A+A265G+I405L+A421H+A422P+A428T,
H1*+N54S+V56T+K72R+G109A+R116Q+W167F+Q172R+L173V+A174S+G182*+D183*+
N195F+V206L+A265G+I405L+A421H+A422P+A428T,
H1*+N54S+V56T+K72R+G109A+R116Q+W167F+Q172R+A174S+G182*+D183*+N195F+
V206L+I405L+A421H+A422P+A428T,
H1*+N54S+V56T+K72R+G109A+F113Q+T134E+W167F+Q172G+A174S+G182*+D183*+
N195F+V206L+G255A+I405L+A421H+A422P+A428T,
H1*+N54S+V56T+G109A+F113Q+W167F+Q172G+A174S+G182*+D183*+N195F+V206L+
I405L+A421H+A422P+A428T,
H1*+N54S+V56T+K72R+G109A+A174S+G182*+D183*+N195F+V206L+G255A+I405L+A421H+A422P+A428T,
H1*+N54S+V56T+K72R+G109A+R116Q+V120L+A174S+G182*+D183*+G184T+N195F+
V206L+I405L+A421H+A422P+A428T,
H1*+N54S+V56T+G109A+F113Q+R116H+W167F+Q172G+L173V+A174S+G182*+D183*+
N195F+V206L+I405L+A421H+A422P+A428T,
H1*+N54S+V56T+G109A+F113Q+R116Q+Q172N+A174S+G182*+D183*+N195F+V206L+A265G+I405L+A421H+A422P+A428T,
H1*+A37H+N54S+V56T+A60V+G109A+R116Q+W167F+Q172R+A174S+G182*+D183*+N195F+V206L+I405L+A421H+A422P+A428T, en donde la numeración es acorde con la SEQ ID NO: 14.

En una realización, la variante tiene un IF de al menos 2.0 cuando se compara con el polipéptido parental, en

donde el IF se determina mediante el uso de detergente modelo A a una temperatura de 15°C y una concentración de enzima de 0.05 mg/L.

Otras variantes de acuerdo con la invención tienen un IF de al menos 3.0, lo que indica que al menos estas variantes tienen un rendimiento de lavado significativamente mejorado en comparación con el polipéptido parental que tiene una secuencia de aminoácidos expuesta en la SEQ ID NO: 15.

En una realización particular, la variante se selecciona entre un grupo que consiste en:

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+Q169E+Q172K+A174*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+R116H+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+K72R+G109A+F113Q+R116Q+W167F+Q172G+A174S+G182*+D183*+

G184T+N195F+V206L+K391A+P473R+G476K,

H1*+N54S+V56T+G109A+R116Q+W167F+A174S+G182*+D183*+G184T+N195F+V206L+ K391A+G476K,

-

H1*+N54S+V56T+K72R+G109A+F113Q+R116Q+W167F+Q172G+A174S+G182*+D183*+ N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+F113Q+R116Q+Q172N+A174S+G182*+D183*+N195F+V206L+

A265G+K391A+P473R+G476K,

H1*+N54S+V56T+K72R+G109A+G133Q+W167F+Q172R+A174S+G182*+D183*+N195F+

V206L+K391A+G476K,

H1*+N54S+V56T+K72R+G109A+R116H+T134E+W167F+Q172G+L173V+A174S+G182*+

D183*+N195F+V206L+G255A+K391A+G476K, y

H1*+N54S+V56T+K72R+G109A+R116H+T134E+W167F+Q172G+L173V+A174S+G182*+

D183*+N195F+V206L+G255A+K391A+Q395P+T444Q+P473R+G476K,

en donde la numeración es acorde con la SEQ ID NO: 13.

En otra realización, la variante tiene un IF de al menos 3.0 en comparación con el polipéptido parental y se determina mediante el uso del detergente modelo J y en donde la variante se selecciona entre el grupo que consiste en:

H1*+T51K+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+A37V+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+F113Y+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+R116Q+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+Q125A+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+P473R+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+P473A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+T444D+G476K,

H1*+N54S+V56T+K72S+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+G50A+N54S+V56T+G109A+L173V+A174S+G182*+D183*+N195F+A204V+V206L+

K391A+G476K,

H1*+N54S+V56T+G109A+Q172D+A174S+G182*+D183*+N195F+V206L+G346T+K391A+

G476K+G477A,

H1*+N54S+V56T+K72R+G109A+T134E+A174S+G182*+D183*+N195F+V206L+G255A+

K391A+G476K,

H1*+N54S+V56T+K72R+G109A+T134E+A174S+G182*+D183*+N195F+V206L+K391A+

G476K,

H1*+N54S+V56T+K72R+G109A+T134E+A174S+G182*+D183*+N195F+V206L+D377H+

K391A+G476K,

H1*+N54S+V56T+K72R+G109A+T134E+A174S+G182*+D183*+G184T+N195F+V206L+

K391A+G476K,

H1*+N54S+V56T+G109A+T134E+A174S+G182*+D183*+G184T+N195F+V206L+D377H+

K391A+G476K,

H1*+N54S+V56T+G109A+Q172D+A174Q+G182*+D183*+N195F+V206L+K391A+G476K+

G477A,

H1*+N54S+V56T+G109A+T134E+A174S+G182*+D183*+G184T+N195F+V206L+K391A+

G476K,

H1*+N54S+V56T+K72R+G109A+A174S+G182*+D183*+N195F+G184T+V206L+K391A+

G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+V238G +K391A+G476K,

H1*+N54S+V56T+G109A+W167F+Q172E+L173P+A174K+G182*+D183*+N195F+V206L+

K391A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+L250M+K391A+G476K,

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K391A+G476K,
H1*+N54S+V56T+G109S+F113Q+R116Q+A174S+G182*+D183*+N195F+V206L+K391A+
G476K,
H1*+N54S+V56T+G109A+Q172D+A174S+G182*+D183*+N195F+A204G+V206L+K391A+
P473R+G476K,
H1*+N54S+V56T+K72R+G109A+T134E+A174S+G182*+D183*+N195F+A204G+V206L+
G255A+K391A+P473R+G476K,
H1*+N54S+V56T+K72R+G109A+W167F+A174S+G182*+D183*+N195F+A204G+V206L+
K391A+G476K,
H1*+N54S+V56T+M105F+G109A+A174S+G182*+D183*+N195F+V206L+R320A+S323N+
K391A+C474V+G476K,
H1*+N54S+V56T+K72R+G109A+A174S+G182*+D183*+N195F+V206L+G255A+K391A+
C474V+G476K,
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G476K,
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+D377H+K391A+C474V+
G476K,
H1*+N54S+V56T+K72R+G109A+A174S+G182*+D183*+N195F+V206L+K391A+C474V+
G476K,
H1*+N54S+V56T+G109A+R116Q+Q172D+A174S+G182*+D183*+N195F+V206L+G346T+
K391A+T444Q+G477A+G476K,

H1*+N54S+V56T+G109S+R116Q+W167F+Q172N+A174S+G182*+D183*+N195F+V206L+
K391A+G476K,
H1*+N54S+V56T+G109S+W167F+Q172G+A174S+G182*+D183*+N195F+V206L+K391A+
G476K,
H1*+N54S+V56T+G109A+F113Q+Q172G+A174S+G182*+D183*+N195F+V206L+K391A+
T444Q+G476K,
H1*+N54S+V56T+G109A+F113Q+R116H+Q172G+A174S+G182*+D183*+N195F+V206L+
K391A+T444Q+G476K,
H1*+N54S+V56T+G109A+F113Q+A174S+G182*+D183*+N195F+V206L+K391A+C474V+
G476K,
H1*+N54S+V56T+G109A+Q172N+A174S+G182*+D183*+N195F+V206L+V264I+K391A+
C474V+G476K,
H1*+N54S+V56T+K72R+G109A+T134E+A174S+G182*+D183*+N195F+V206L+G255A+
K391A+C474V+G476K,
H1*+N54S+V56T+G109A+F113Q+R116H+Q172G+A174S+G182*+D183*+N195F+V206L+
K391A+T444Q+P473R+G476K,
H1*+N54S+V56T+G109A+F113Q+R116Q+Q172G+A174S+G182*+D183*+N195F+V206L+
K391A+T444Q+G476K,
H1*+N54S+V56T+G109A+F113Q+R116H+T165G+Q172G+A174S+G182*+D183*+N195F+
V206L+K391A+T444Q+G476K,
H1*+N54S+V56T+G109A+F113Q+R116Q+T165G+Q172G+A174S+G182*+D183*+N195F+
V206L+K391A+T444Q+G476K,

H1*+N54S+V56T+G109A+F113Q+Q172N+A174S+G182*+D183*+N195F+V206L+K391A+

T444Q+G476K,

H1*+N54S+V56T+G109A+F113Q+R116H+Q172N+A174S+G182*+D183*+N195F+V206L+

K391A+G476K,

H1*+N54S+V56T+G109A+F113Q+R116H+Q172M+A174S+G182*+D183*+N195F+V206L+

K391A+G476K,

H1*+N54S+V56T+K72R+G109A+T134E+T165G+A174S+G182*+D183*+N195F+V206L+

G255A+K391A+G476K,

H1*+N54S+V56T+G109A+F113Q+R116H+Q172N+A174S+G182*+D183*+N195F+V206L+

K391A+G476K,

H1*+N54S+V56T+G109A+R116Q+W167F+Q172N+L173V+A174S+G182*+D183*+N195F+

V206L+K391A+T444Q+G476K,

H1*+N54S+V56T+G109A+G133Q+W167F+Q172N+A174S+G182*+D183*+N195F+V206L+

Q395P+K391A+G476K,

H1*+A37V+N54S+V56T+K72R+G109A+R116H+W167F+Q172R+A174S+G182*+D183*+

G184T+N195F+V206L+K391A+P473R+G476K,

H1*+N54S+V56T+K72R+G109A+F113Q+R116H+W167F+Q172G+L173V+A174S+G182*+

D183*+G184T+N195F+V206L+K391A+T444Q+P473R+G476K,

H1*+N54S+V56T+G109S+R116Q+W167F+Q172R+A174S+G182*+D183*+N195F+V206L+

K391A+G476K,

H1*+N54S+V56T+G109S+R116Q+W167F+Q172G+A174S+G182*+D183*+N195F+V206L+

K391A+P473R+G476K,

H1*+N54S+V56T+G109S+F113Q+W167F+Q172N+A174S+G182*+D183*+N195F+V206L+

K391A+G476K,

H1*+A37V+N54S+V56T+G109S+F113Q+W167F+Q172R+A174S+G182*+D183*+N195F+

V206L+K391A+G476K,

H1*+N54S+V56T+K72R+G109A+R116H+T134E+W167F+Q172G+L173V+A174S+G182*+

D183*+N195F+V206L+G255A+K391A+Q395P+T444Q+P473R+G476K,

H1*+N54S+V56T+K72R+G109A+F113Q+R116Q+W167F+Q172G+A174S+G182*+D183*+

G184T+N195F+V206L+K391A+P473R+G476K,

H1*+N54S+V56T+K72R+G109A+F113Q+R116Q+T134E+W167F+Q172R+A174S+G182*+

D183*+N195F+V206L+G255A+K391A+T444Q+P473R+G476K,

H1*+N54S+V56T+K72R+G109A+T134E+W167F+Q172N+A174S+G182*+D183*+N195F+

V206L+G255A+A265G+K391A+T444Q+P473R+G476K,

H1*+N54S+V56T+K72R+G109A+G133Q+W167F+Q172R+A174S+G182*+D183*+N195F+

V206L+K391A+G476K,

H1*+N54S+V56T+K72R+G109A+F113Q+R116Q+W167F+Q172G+A174S+G182*+D183*+

N195F+A204G+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+F113Q+R116Q+A174S+G182*+D183*+N195F+V206L+K391A+

P473R+G476K,

H1*+N54S+V56T+A60V+G109A+R116Q+W167F+Q172N+A174S+G182*+D183*+N195F+

V206L+K391A+G476K,

H1*+N54S+V56T+A60V+G109A+R116H+Q172R+L173V+A174S+G182*+D183*+N195F+

V206L+K391A+G476K,

H1*+A37H+N54S+V56T+A60V+G109A+R116Q+T165G+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+A60V+G109A+R116Q+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+A37H+N54S+V56T+A60V+G109A+R116Q+W167F+Q172R+A174S+G182*+D183*+

N195F+V206L+K391A+G476K,

H1*+A37H+N54S+V56T+A60V+G109A+R116Q+W167F+Q172N+A174S+G182*+D183*+

N195F+V206L+K391A+G476K,

H1*+N54S+V56T+A60V+G109A+R116Q+T165G+A174S+G182*+D183*+N195F+V206L+

K391A+T444Q+P473R+G476K,

H1*+N54S+V56T+A60V+G109A+R116Q+W167F+Q172N+L173V+A174S+G182*+D183*+

N195F+V206L+K391A+G476K,

H1*+N54S+V56T+A60V+G109A+R116Q+W167F+Q172R+A174S+G182*+D183*+N195F+

V206L+K391A+G476K,

H1*+N54S+V56T+G109A+R116A+A174S+G182*+D183*+N195F+A204G+V206L+K391A+

P473R+G476K,

H1*+N54S+V56T+K72R+G109A+F113Q+T134E+A174S+G182*+D183*+N195F+V206L+

G255A+K391A+P473R+G476K,

H1*+N54S+V56T+K72R+G109A+R116Q+A174S+G182*+D183*+G184T+N195F+V206L+

K391A+G476K,

H1*+A37V+N54S+V56T+G109A+R116A+T165G+A174S+G182*+D183*+N195F+V206L+

K391A+G476K,

H1*+A37V+N54S+V56T+G109A+R116Q+T165G+A174S+G182*+D183*+N195F+V206L+

M246F+K391A+G476K,

H1*+N54S+V56T+K72R+G109A+F113Q+R116H+A174S+G182*+D183*+G184T+N195F+

V206L+K391A+T444Q+G476K,

H1*+N54S+V56T+G109S+F113Q+A174S+G182*+D183*+N195F+V206L+K391A+T444Q+

G476K,

H1*+N54S+V56T+G109A+F113Q+R116H+W167F+Q172G+L173V+A174S+G182*+D183*+

N195F+V206L+K391A+P473R+G476K,

H1*+N54S+V56T+G109A+F113Q+R116Q+Q172N+A174S+G182*+D183*+N195F+V206L+

A265G+K391A+P473R+G476K,

H1*+A37V+N54S+V56T+G109A+R116Q+T165G+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+A37H+N54S+V56T+G109A+R116H+T165G+A174S+G182*+D183*+N195F+V206L+

M246F+K391A+G476K,

H1*+N54S+V56T+G109A+R116A+Q172N+L173V+A174S+G182*+D183*+N195F+V206L+

K391A+G476K,

H1*+P45A+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+C474V+

G476K,

H1*+N54S+V56T+G109A+Q118R+T134E+A174S+G182*+D183*+N195F+V206L+K391A+

G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+G184T+N195F+V206L+K391A+G476K,

H1*+G50A+T51A+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+V264F+K391A+G476K,

H1*+G7K
+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K,
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+G255A+Q256A+K391A+
G476K,
H1*+N54S+V56T+G109A+W167Y+A174S+G182*+D183*+N195F+V206L+K391A+G476K,
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K,
H1*+N16H+V17L+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+Y382F+K391A+G476K,
H1*+Q32S+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+Q385L+K391A+
G476K,
H1*+N54S+V56T+R87S+G109A+R171H+A174S+G182*+D183*+N195F+V206L+K391A+
G476K,
H1*+N54S+V56T+G109A+R116H+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+
K391A+G476K,
H1*+N54S+V56T+G109A+A174*+G182*+D183*+N195F+V206L+K391A+G476K,
H1*+K72R+G109A+F113Q+R116Q+W167F+Q172G+A174S+G182*+D183*+G184T+N195F+
V206L+K391A+P473R+G476K,
H1*+N54S+V56T+K72R+G109A+F113Q+R116Q+W167F+Q172G+A174S+G182*+D183*+
G184T+N195F+V206L+P473R+G476K,
H1*+N54S+V56T+G109A+Q169E+Q172G+A174*+G182*+D183*+N195F+V206L+K391A+
G476K,
H1*+N54S+V56T+K72R+G109A+F113Q+R116Q+W167F+Q172G+A174S+G182*+D183*+

G184T+N195F+K391A+P473R+G476K,

H1*+N54S+V56T+G109A+R116W+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+

K391A+G476K,

H1*+N54S+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206F+K391A+

G476K,

H1*+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+N260G+K391A+G476K,

H1*+N54S+V56T+K72R+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+G184T+N195F+V206L+

K391A+G476K,

H1*+N54S+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+Y295N+

K391A+G476K,

H1*+N54S+V56T+G109A+W167F+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+A186N+N195F+V206L+

K391A+G476K,

H1*+N54S+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+A288V+

K391A+G476K,

H1*+N54S+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+G255A+

K391A+G476K,

H1*+N54S+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+W48F+N54S+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+

K391A+G476K,

H1*+N54S+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+V291A+

K391A+G476K,

H1*+N54S+V56T+G109A+F113Q+A174S+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+R320A+

S323N+K391A+G476K,

H1*+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+K391A+G476K,

H1*+N54S+V56T+K72R+G109A+F113Q+R116H+W167F+Q172G+A174S+G182*+D183*+

G184T+N195F+V206L+K391A+P473R+G476K,

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+N270T+K391A+G476K,

H1*+N54S+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+G476K,

H1*+N54S+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+N260G+

K391A+G476K,

H1*+N54S+V56T+G109A+F113Q+R116H+A174S+G182*+D183*+N195F+V206L+K391A+

G476K,

en donde la numeración es acorde con la SEQ ID NO: 13,

H1*+N54S+V56T+G109A+F113Q+R116H+Q172G+A174S+G182*+D183*+N195F+V206L+

I405L+A421H+A422P+A428T,

H1*+N54S+V56T+G109A+F113Q+R116Q+Q172N+A174S+G182*+D183*+N195F+V206L+

A265G+I405L+A421H+A422P+A428T, en donde la numeración es acorde con la SEQ ID NO: 14.

Las variantes de acuerdo con la presente invención pueden comprender además una o más alteraciones adicionales distintas de aquellas descritas anteriormente en una o más (por ejemplo, varias) posiciones diferentes.

Los cambios de los aminoácidos pueden ser poco relevantes, es decir, inserciones o sustituciones conservadoras de aminoácidos que no afectan significativamente al plegamiento y/o la actividad de la proteína; eliminaciones pequeñas, normalmente de 1-30 aminoácidos; extensiones pequeñas en el extremo amino o en el extremo carboxilo, tales como un resto de metionina en el extremo amino; un péptido conector pequeño de hasta 20-25 restos; o una extensión pequeña que facilita la purificación al cambiar la carga neta u otra función, tal como una región de polihistidina, un epítopo antigénico o un dominio de unión.

Algunos ejemplos de sustituciones conservadoras son las sustituciones dentro de los grupos de aminoácidos básicos (arginina, lisina e histidina), aminoácidos ácidos (ácido glutámico y ácido aspártico), aminoácidos polares (glutamina y asparagina), aminoácidos hidrófobos (leucina, isoleucina y valina), aminoácidos aromáticos (fenilalanina, triptófano y tirosina) y aminoácidos de bajo peso molecular (glicina, alanina, serina, treonina y metionina). Las sustituciones de aminoácidos que no alteran generalmente la actividad específica son conocidas en la técnica y están descritas, por ejemplo, por H. Neurath y R.L. Hill, 1979, *In*, *The Proteins*, Academic Press, Nueva York. Algunas sustituciones comunes son Ala/Ser, Val/Ile, Asp/Glu, Thr/Ser, Ala/Gly, Ala/Thr, Ser/Asn, Ala/Val, Ser/Gly,

Tyr/Phe, Ala/Pro, Lys/Arg, Asp/Asn, Leu/Ile, Leu/Val, Ala/Glu y Asp/Gly.

De forma alternativa, los cambios de los aminoácidos son de tal naturaleza que las propiedades fisicoquímicas de los polipéptidos están alteradas. Por ejemplo, los cambios de los aminoácidos pueden mejorar la estabilidad térmica del polipéptido, alterar la especificidad por el sustrato, cambiar el pH óptimo y efectos similares.

Los aminoácidos esenciales de un polipéptido se pueden identificar según procedimientos de uso común en la técnica tales como la mutagénesis dirigida o la mutagénesis de barrido de alanina (Cunningham y Wells, 1989, *Science* 244: 1081-1085). En la última técnica, se introducen mutaciones únicas de alanina en cada resto de la molécula y las moléculas mutadas resultantes se evalúan para determinar su actividad alfa-amilasa y para identificar los restos de aminoácido que son cruciales para la actividad de la molécula. Véase también, Hilton *et al.*, 1996, *J. Biol. Chem.* 271: 4699-4708. El sitio activo de la enzima u otra interacción biológica también puede determinarse mediante el análisis físico de la estructura, tal como se determina mediante técnicas tales como la resonancia magnética nuclear, cristalografía, difracción de electrones o marcaje por fotoafinidad, junto con la mutación de posibles aminoácidos del sitio de contacto. Véase, por ejemplo, de Vos *et al.*, 1992, *Science* 255: 306-312; Smith *et al.*, 1992, *J. Mol. Biol.* 224: 899-904; Wlodaver *et al.*, 1992, *FEBS Lett.* 309: 59-64. La identidad de los aminoácidos esenciales también puede deducirse a partir de una alineación con un polipéptido relacionado.

Las variantes de acuerdo con la presente invención pueden constar de 400 a 485 aminoácidos, por ejemplo, de 410 a 485, de 425 a 485 y de 440 a 485 aminoácidos.

Polinucleótidos

La presente invención también se refiere a polinucleótidos que codifican una variante de la presente invención. Por lo tanto, en particular, la presente invención se refiere a un polipéptido que codifica una variante que comprende una alteración en una o más posiciones correspondientes a las H1, T5, G7, Q11, N16, V17, Q32, A37, T40, P45, W48, G50, T51, N54, V56, K72, R87, Q98, M105, G109, F113, R116, Q118, Q125, G133, T134, W140, G142, G149, T165, W167, Q169, R171, Q172, L173, A174, G184, A186, E190, T193, N195, A204, V206, P211, I214, V215, L217, L219, A225, L235, V238, K242, S244, M246, M248, L250, G255, Q256, N260, A263, V264, Y267, K269, N270, G273, S280, W284, T285, M286, F289, V291, Y295, Q299, R320, H321, S323, H324, V326, F328, T334, D337, Q345, G346, G348, T355, S376, D377, D379, Y382, S383, Q385, K391, K393, Q395, A420, G423, T444, A445, Q449, T459, P473, C474, G476, G477, y K484 de la SEQ ID NO: 13; o H1, A37, T40, N54, V56, A60, K72, G109, F113, R116, N125, F133, T134, T165, Q169, Q172, L173, A174, G184, A186, E190, N195, G196, A204, V206, A225, L228, K242, S244, G255, N260, A265, K269, S280, W284, S304, R320, H321, S323, V326, K391, I405, A421, A422, A428, G448, D476, y G477 de la SEQ ID NO: 14.

La expresión "polinucleótido que codifica", tal como se usa en el presente documento, se refiere a un polinucleótido que codifica un polipéptido maduro que tiene actividad alfa-amilasa. En un aspecto, la secuencia codificante del polipéptido es la secuencia de nucleótidos expuesta en las SEQ ID NO: 1, 2 o 3.

En una realización, el polinucleótido que codifica una variante de acuerdo con la presente invención tiene al menos un 60%, tal como al menos un 65%, tal como al menos un 70%, tal como al menos un 75%, tal como al menos un 80%,

tal como al menos un 85%, tal como al menos un 90%, tal como al menos un 95%, tal como al menos un 96%, tal como al menos un 97%, tal como al menos un 98%, tal como al menos un 99% pero menos de un 100% de identidad de secuencia con el polinucleótido de las SEQ ID NO: 1, 2 y 3.

Construcciones de ácido nucleico

La presente invención también se refiere a construcciones de ácido nucleico que comprenden un polinucleótido que codifica una variante de la presente invención unido operativamente a una o más secuencias de control que dirigen la expresión de la secuencia codificante en una célula hospedadora adecuada en condiciones compatibles con las secuencias de control. Por lo tanto, en particular, la presente invención se refiere a una construcción de ácido nucleico que comprende un polinucleótido que codifica una variante que comprende una alteración en una o más posiciones correspondientes a las posiciones H1, T5, G7, Q11, N16, V17, Q32, A37, T40, P45, W48, G50, T51, N54, V56, K72, R87, Q98, M105, G109, F113, R116, Q118, Q125, G133, T134, W140, G142, G149, T165, W167, Q169, R171, Q172, L173, A174, G184, A186, E190, T193, N195, A204, V206, P211, I214, V215, L217, L219, A225, L235, V238, K242, S244, M246, M248, L250, G255, Q256, N260, A263, V264, Y267, K269, N270, G273, S280, W284, T285, M286, F289, V291, Y295, Q299, R320, H321, S323, H324, V326, F328, T334, D337, Q345, G346, G348, T355, S376, D377, D379, Y382, S383, Q385, K391, K393, Q395, A420, G423, T444, A445, Q449, T459, P473, C474, G476, G477, y K484 de la SEQ ID NO: 13; o H1, A37, T40, N54, V56, A60, K72, G109, F113, R116, N125, F133, T134, T165, Q169, Q172, L173, A174, G184, A186, N195, G196, A204, V206, A225, L228, K242, S244, G255, N260, A265, K269, S280, W284, Y295, S304, R320, H321, S323, V326, K391, I405, A421, A422, A428, R439, G448, W467, D476, y G477 de la SEQ

ID NO: 14, en donde el polinucleótido está unido operativamente a una o más secuencias de control.

La expresión "construcción de ácido nucleico", tal como se usa en el presente documento, se refiere a una molécula de ácido nucleico, ya sea mono- o bicatenaria, que se aísla a partir de un gen presente de manera natural o se modifica para que contenga segmentos de ácidos nucleicos de un modo que de otra manera no existiría en la naturaleza o que es sintético, que comprende una o más secuencias de control.

La expresión "unido operativamente", tal como se usa en el presente documento, se refiere a una configuración en la que una secuencia de control se coloca en una posición adecuada con respecto a la secuencia codificante de un polinucleótido de modo que la secuencia de control dirige la expresión de la secuencia codificante.

Los polinucleótidos pueden manipularse de una variedad de maneras para proporcionar la expresión de una variante. La manipulación del polinucleótido antes de su inserción en un vector puede ser deseable o necesaria dependiendo del vector de expresión. Las técnicas para modificar polinucleótidos que utilizan métodos de ADN recombinante son de uso común en la materia.

La secuencia de control puede ser un promotor, un polinucleótido que se reconoce por una célula hospedadora para la expresión del polinucleótido. El promotor comprende secuencias de control de la transcripción que regulan la expresión de la variante. El promotor puede ser cualquier polinucleótido que muestre actividad transcripcional en la célula hospedadora, incluyendo promotores mutantes, truncados e híbridos y puede obtenerse a partir de genes que codifican polipéptidos extracelulares o intracelulares, ya sean homólogos o heterólogos para la célula hospedadora.

Vectores de expresión

La presente invención también se refiere a vectores de expresión recombinantes que comprenden un polinucleótido que codifica una variante de la presente invención, un promotor y señales de terminación de la transcripción y la traducción. Por lo tanto, la presente invención se refiere a un vector de expresión, opcionalmente recombinante, que comprende un polinucleótido que codifica una variante que comprende una alteración en una o más posiciones correspondientes a las posiciones H1, T5, G7, Q11, N16, V17, Q32, A37, T40, P45, W48, G50, T51, N54, V56, K72, R87, Q98, M105, G109, F113, R116, Q118, Q125, G133, T134, W140, G142, G149, T165, W167, Q169, R171, Q172, L173, A174, G184, A186, E190, T193, N195, A204, V206, P211, I214, V215, L217, L219, A225, L235, V238, K242, S244, M246, M248, L250, G255, Q256, N260, A263, V264, Y267, K269, N270, G273, S280, W284, T285, M286, F289, V291, Y295, Q299, R320, H321, S323, H324, V326, F328, T334, D337, Q345, G346, G348, T355, S376, D377, D379, Y382, S383, Q385, K391, K393, Q395, A420, G423, T444, A445, Q449, T459, P473, C474, G476, G477, y K484 de la SEQ ID NO: 13; o H1, A37, T40, N54, V56, A60, K72, G109, F113, R116, N125, F133, T134, T165, Q169, Q172, L173, A174, G184, A186, N195, G196, A204, V206, A225, L228, K242, S244, G255, N260, A265, K269, S280, W284, Y295, S304, R320, H321, S323, V326, K391, I405, A421, A422, A428, R439, G448, W467, D476, y G477 de la SEQ ID NO: 14, un promotor y señales de parada transcripcional y traduccional.

La expresión "vector de expresión", tal como se usa en el presente documento, se refiere a una molécula de ADN lineal o circular que comprende un polinucleótido que codifica una variante y está unida operativamente a secuencias de control que posibilitan su expresión.

Los diferentes nucleótidos y secuencias de control pueden unirse entre sí para producir un vector de expresión recombinante que puede incluir uno o más sitios de restricción convenientes para permitir la inserción o sustitución del polinucleótido que codifica la variante en sitios de este tipo. Como alternativa, el polinucleótido puede expresarse insertando el polinucleótido o una construcción de ácido nucleico que comprenda el polinucleótido en un vector apropiado para la expresión. Cuando se crea el vector de expresión, la secuencia codificante se sitúa en el vector de modo que la secuencia codificante esté ligada operativamente a las secuencias de control adecuadas para la expresión.

El vector de expresión recombinante puede ser cualquier vector (por ejemplo, un plásmido o un virus) que se pueda someter convenientemente a procedimientos de ADN recombinante y que pueda propiciar la expresión del polinucleótido. La elección del vector dependerá normalmente de la compatibilidad del vector con la célula hospedadora en la que se va a introducir el vector. El vector puede ser un plásmido lineal o circular cerrado.

El vector puede ser un vector de replicación autónoma, es decir, un vector que existe como una entidad extracromosómica, cuya replicación es independiente de la replicación cromosómica, por ejemplo, un plásmido, un elemento extracromosómico, un minicromosoma o un cromosoma artificial. El vector puede contener cualquier medio para garantizar la autorreplicación. Como alternativa, el vector puede ser uno que, cuando se introduce en la célula hospedadora, se integra en el genoma y se replica junto con el o los cromosomas en los que ha sido integrado. Además, puede utilizarse un único vector o plásmido o dos o más vectores o plásmidos que contengan de forma conjunta el ADN

total que se va a introducir en el genoma de la célula hospedadora o puede utilizarse un transposón.

El vector contiene preferiblemente uno o más marcadores de selección que permiten una selección sencilla de las células transformadas, transfectadas, transducidas o similares. Un marcador de selección es un gen cuyo producto proporciona resistencia a virus o biocidas, resistencia a metales pesados, prototrofia a los auxótrofos y similares.

El experto en la materia sabrá qué vector de expresión es el más adecuado para sistemas de expresión específicos. Por lo tanto, la presente invención no está limitada a cualquier vector de expresión específico, sino que se considera como parte de la presente invención cualquier vector de expresión que comprenda el polinucleótido que codifica una variante de acuerdo con la invención.

Células hospedadoras

La presente invención también se refiere a células hospedadoras recombinantes, que comprenden un polinucleótido que codifica una variante de la presente invención unido operativamente a una o más secuencias de control que dirigen la producción de una variante de la presente invención. Por lo tanto, la presente invención se refiere a una célula hospedadora, opcionalmente una célula hospedadora recombinante, que comprende un polinucleótido que codifica una variante que comprende una alteración en una o más posiciones correspondientes a las posiciones H1, T5, G7, Q11, N16, V17, Q32, A37, T40, P45, W48, G50, T51, N54, V56, K72, R87, Q98, M105, G109, F113, R116, Q118, Q125, G133, T134, W140, G142, G149, T165, W167, Q169, R171, Q172, L173, A174, G184, A186, E190, T193, N195, A204, V206, P211, I214, V215, L217, L219, A225, L235, V238, K242, S244, M246, M248, L250, G255, Q256, N260, A263, V264, Y267, K269, N270, G273, S280, W284, T285, M286, F289, V291, Y295, Q299,

R320, H321, S323, H324, V326, F328, T334, D337, Q345, G346, G348, T355, S376, D377, D379, Y382, S383, Q385, K391, K393, Q395, A420, G423, T444, A445, Q449, T459, P473, C474, G476, G477, y K484 de SEQ ID NO: 13; o H1, A37, T40, N54, V56, A60, K72, G109, F113, R116, N125, F133, T134, T165, Q169, Q172, L173, A174, G184, A186, E190, N195, G196, A204, V206, A225, L228, K242, S244, G255, N260, A265, K269, S280, W284, Y295, S304, R320, H321, S323, V326, K391, I405, A421, A422, A428, R439, G448, W467, D476, y G477 de SEQ ID NO: 14, unido operativamente a una o más secuencias de control que dirigen la producción de la variante.

La expresión "célula hospedadora", tal como se usa en el presente documento, se refiere a cualquier tipo de célula que sea susceptible a la transformación, transfección, transducción o similares con una construcción de ácido nucleico o un vector de expresión que comprenda un polinucleótido de la presente invención. La expresión "célula hospedadora" abarca cualquier descendencia de una célula progenitora que no sea idéntica a la célula progenitora debido a mutaciones que puedan producirse durante la replicación.

Se introduce una construcción o vector que comprende un polinucleótido en una célula hospedadora, de tal forma que la construcción o vector se mantiene en forma de un integrante cromosómico o como un vector extracromosómico autorreplicante, tal como se ha descrito anteriormente. La elección de una célula hospedadora dependerá en gran medida del gen que codifica la variante y su fuente.

La célula hospedadora puede ser cualquier célula útil en la producción recombinante de una variante, por ejemplo, una célula procariota o eucariota.

La célula hospedadora procariota puede ser cualquier bacteria grampositiva o gramnegativa. Las bacterias

grampositivas incluyen, sin carácter limitante, *Bacillus*, *Clostridium*, *Enterococcus*, *Geobacillus*, *Lactobacillus*, *Lactococcus*, *Oceanobacillus*, *Staphylococcus*, *Streptococcus*, y *Streptomyces*. Las bacterias Gram-negativas incluyen, sin limitación, *Campylobacter*, *E. coli*, *Flavobacterium*, *Fusobacterium*, *Helicobacter*, *Ilyobacter*, *Neisseria*, *Pseudomonas*, *Salmonella* y *Ureaplasma*.

Métodos de acuerdo con la invención

La presente invención también se refiere a métodos para producir una variante, que comprenden: (a) cultivar una célula hospedadora de la presente invención en condiciones adecuadas para la expresión de la variante; y (b) recuperar la variante. Por lo tanto, la presente invención se refiere a un método para producir una variante que comprende una alteración en una o más posiciones correspondientes a las posiciones H1, T5, G7, Q11, N16, V17, Q32, A37, T40, P45, W48, G50, T51, N54, V56, K72, R87, Q98, M105, G109, F113, R116, Q118, Q125, G133, T134, W140, G142, G149, T165, W167, Q169, R171, Q172, L173, A174, G184, A186, E190, T193, N195, A204, V206, P211, I214, V215, L217, L219, A225, L235, V238, K242, S244, M246, M248, L250, G255, Q256, N260, A263, V264, Y267, K269, N270, G273, S280, W284, T285, M286, F289, V291, Y295, Q299, R320, H321, S323, H324, V326, F328, T334, D337, Q345, G346, G348, T355, S376, D377, D379, Y382, S383, Q385, K391, K393, Q395, A420, G423, T444, A445, Q449, T459, P473, C474, G476, G477, y K484 de la SEQ ID NO: 13; o H1, A37, T40, N54, V56, A60, K72, G109, F113, R116, N125, F133, T134, T165, Q169, Q172, L173, A174, G184, A186, E190, N195, G196, A204, V206, A225, L228, K242, S244, G255, N260, A265, K269, S280, W284, Y295, S304, R320, H321, S323, V326, K391, I405, A421, A422, A428, R439, G448, W467, D476, y G477 de la SEQ ID NO: 14, en donde le método comprende las etapas de a) cultivar una célula hospedadora

de acuerdo con la invención en condiciones adecuadas para la expresión de la variante y b) recuperar la variante.

Las células hospedadoras se cultivan en un medio nutritivo adecuado para la producción de la variante utilizando métodos conocidos en la técnica. Por ejemplo, la célula puede cultivarse mediante el cultivo en un matraz agitado o la fermentación a pequeña escala o gran escala (incluyendo fermentaciones continua, discontinua, semicontinua o de estado sólido) en fermentadores de laboratorio o industriales, llevada a cabo en un medio adecuado y en condiciones que permitan que la variante se exprese y/o se aísle. El cultivo tiene lugar en un medio nutritivo adecuado que comprende fuentes de carbono y nitrógeno y sales inorgánicas, utilizando procedimientos conocidos en la técnica. Los medios adecuados pueden adquirirse de proveedores comerciales o pueden prepararse según las composiciones publicadas (por ejemplo, en los catálogos de la *American Type Culture Collection*). Si la variante se secreta al medio nutritivo, la variante puede recuperarse directamente del medio. Si la variante no se secreta, puede recuperarse a partir de los lisados celulares.

La variante puede detectarse usando métodos conocidos en la técnica que son específicos para los polipéptidos que tienen actividad alfa-amilasa. Estos métodos de detección incluyen, sin carácter limitante, el uso de anticuerpos específicos, la formación de un producto enzimático o la desaparición de un sustrato enzimático. Por ejemplo, puede utilizarse un ensayo enzimático para determinar la actividad de la variante.

La variante puede recuperarse utilizando métodos conocidos en la técnica. Por ejemplo, la variante puede recuperarse del medio nutritivo mediante procedimientos

convencionales que incluyen, sin limitación, recolección, centrifugación, filtración, extracción, secado por pulverización, evaporación o precipitación.

La variante puede purificarse mediante varios procedimientos conocidos en la técnica que incluyen, sin limitación, cromatografía (por ejemplo, de intercambio iónico, afinidad, hidrófoba, cromatoenfoque y de exclusión molecular), procedimientos electroforéticos (por ejemplo, isoelectroenfoque preparativo), solubilidad diferencial (por ejemplo, precipitación con sulfato de amonio), SDS-PAGE o extracción (véase, por ejemplo, *Protein Purification*, Janson y Ryden, editores, VCH Publishers, Nueva York, 1989) para obtener variantes sustancialmente puras.

En un aspecto alternativo, la variante no se recupera, sino que en su lugar se utiliza una célula hospedadora de la presente invención que expresa la variante como fuente de la variante.

Además, la presente invención se refiere a métodos para obtener una variante que comprenden introducir en una alta-amilasa parental que tiene al menos un 80% de identidad de secuencia con el polipéptido de la SEQ ID NO: 4

(a) una sustitución y/o eliminación de dos o más posiciones en la alfa amilasa parental, correspondiendo dichas posiciones a las posiciones 181, 182, 183 y 184 del polipéptido maduro de SEQ ID NO: 4; y

(b) una alteración en una o más posiciones correspondientes a las posiciones H1, T5, G7, Q11, N16, V17, Q32, A37, T40, P45, W48, G50, T51, N54, V56, K72, R87, Q98, M105, G109, F113, R116, Q118, Q125, G133, T134, W140, G142, G149, T165, W167, Q169, R171, Q172, L173, A174, G184, A186, E190, T193, N195, A204, V206, P211, I214, V215, L217,

L219, A225, L235, V238, K242, S244, M246, M248, L250, G255, Q256, N260, A263, V264, Y267, K269, N270, G273, S280, W284, T285, M286, F289, V291, Y295, Q299, R320, H321, S323, H324, V326, F328, T334, D337, Q345, G346, G348, T355, S376, D377, D379, Y382, S383, Q385, K391, K393, Q395, A420, G423, T444, A445, Q449, T459, P473, C474, G476, G477, y K484 de la SEQ ID NO: 13; o H1, A37, T40, N54, V56, A60, K72, G109, F113, R116, N125, F133, T134, T165, Q169, Q172, L173, A174, G184, A186, E190, N195, G196, A204, V206, A225, L228, K242, S244, G255, N260, A265, K269, S280, W284, Y295, S304, R320, H321, S323, V326, K391, I405, A421, A422, A428, R439, G448, W467, D476, y G477 de la SEQ ID NO: 14,

en donde la variante resultante tiene al menos un 80%, tal como al menos un 85%, tal como al menos un 90%, tal como al menos un 95%, tal como al menos un 97% pero menos de un 100% de identidad de secuencia con el polipéptido maduro de la SEQ ID NO: 4, en donde dicha variante tiene actividad alfa-amilasa;

(c) recuperar dicha variante.

Las variantes pueden prepararse utilizando cualquier procedimiento de mutagénesis conocido en la técnica tal como la mutagénesis dirigida, la construcción de genes sintéticos, la construcción de genes semisintéticos, la mutagénesis aleatoria, el intercambio, etc.

La mutagénesis dirigida es una técnica en la que se introducen una o más (por ejemplo, varias) mutaciones en uno o más sitios definidos de un polinucleótido que codifica el progenitor.

La mutagénesis dirigida puede llevarse a cabo *in vitro* mediante PCR que implica el uso de cebadores oligonucleotídicos que contienen la mutación deseada. También puede efectuarse mutagénesis de sitio dirigido *in vitro* mediante mutagénesis por inserción de casete que

implica la escisión mediante una enzima de restricción en un sitio en el plásmido que comprende un polinucleótido que codifica el polipéptido parental y la posterior ligadura de un oligonucleótido que contiene la mutación en el polinucleótido. Normalmente, la enzima de restricción que digiere el plásmido y el oligonucleótido es la misma, lo que permite que los extremos adhesivos del plásmido y la inserción se liguen entre sí. Véanse, por ejemplo, Scherer y Davis, 1979, *Proc. Natl. Acad. Sci. USA* 76: 4949-4955; y Barton *et al.*, 1990, *Nucleic Acids Res.* 18: 7349-4966.

La mutagénesis dirigida también puede llevarse a cabo *in vivo* utilizando métodos conocidos en la técnica. Véanse, por ejemplo, la publicación de solicitud de patente de los Estados Unidos n.º 2004/0171154; Storici *et al.*, 2001, *Nature Biotechnol.* 19: 773-776; Kren *et al.*, 1998, *Nat. Med.* 4: 285-290; y Calissano y Macino, 1996, *Fungal Genet. Newslett.* 43: 15-16.

Puede usarse en la presente invención cualquier procedimiento de mutagénesis de sitio dirigido. Existen muchos kits comerciales disponibles que pueden utilizarse para preparar las variantes. El experto en la materia será conocedor de dichos kits comerciales y de cómo usarlos.

La construcción de genes sintéticos implica la síntesis *in vitro* de una molécula de polinucleótido diseñada para que codifique un polipéptido de interés. La síntesis de genes puede llevarse a cabo utilizando una serie de técnicas tales como la tecnología basada en microchips multiplex descrita por Tian *et al.* (2004, *Nature* 432: 1050-1054) y tecnologías similares en las que se sintetizan oligonucleótidos y se ensamblan sobre chips microfluídicos programables.

Las sustituciones, eliminaciones y/o inserciones de un único aminoácido o de múltiples aminoácidos se pueden

realizar y evaluar utilizando métodos conocidos de mutagénesis, recombinación y/o reordenamiento, seguidos de un procedimiento de cribado relevante, como los descritos por Reidhaar-Olson y Sauer, 1988, *Science* 241: 53-57; Bowie y Sauer, 1989, *Proc. Natl. Acad. Sci. USA* 86: 2152-2156; WO 95/17413 o WO 95/22625. Otros métodos que pueden usarse incluyen PCR propensa a errores, presentación en fagos (por ejemplo, Lowman *et al.*, 1991, *Biochemistry* 30: 10832-10837; Patente de EE. UU. N.º 5.223.409; WO 92/06204) y la mutagénesis dirigida a una región (Derbyshire *et al.*, 1986, *Gene* 46: 145; Ner *et al.*, 1988, *ADN* 7: 127).

Los métodos de mutagénesis/reordenamiento pueden combinarse con métodos de cribado automatizados ultrarrápidos para detectar la actividad de polipéptidos mutados clonados expresados por las células hospedadoras (Ness *et al.*, 1999, *Nature Biotechnology* 17: 893-896). Las moléculas de ADN mutadas que codifican polipéptidos activos pueden recuperarse a partir de las células hospedadoras y secuenciarse rápidamente utilizando métodos convencionales en la técnica. Estos métodos permiten determinar rápidamente la importancia de restos de aminoácido individuales en un polipéptido.

La construcción de genes semi-sintéticos se consigue combinando aspectos de la construcción de genes sintéticos, y/o mutagénesis dirigida al sitio, y/o mutagénesis aleatoria y/o mediante intercambio. La construcción semi-sintética está tipificada por un procedimiento que utiliza fragmentos de polinucleótidos que se sintetizan en combinación con técnicas de PCR. De este modo, las regiones definidas de los genes pueden sintetizarse *de novo*, mientras que otras regiones pueden amplificarse utilizando cebadores mutagénicos específicos para un sitio, mientras que aún otras regiones pueden someterse a amplificación por

PCR propensa a error o por PCR no propensa a error. A continuación, pueden permutarse al azar las subsecuencias de polinucleótidos.

La presente invención también se refiere a un método para mejorar el rendimiento de lavado de un polipéptido parental que tiene la secuencia de aminoácidos de SEQ ID NO: 13 o 14 o que tiene al menos un 80% de identidad de secuencia con los mismos, comprendiendo dicho método las etapas de:

a) una sustitución y/o eliminación de dos, tres o cuatro posiciones en la alfa-amilasa parental, correspondiendo dichas posiciones a las posiciones 181, G182, D183 y G184 del polipéptido maduro de SEQ ID NO: 4; y

b) una alteración en una o más posiciones correspondientes a las posiciones H1, T5, G7, Q11, N16, V17, Q32, A37, T40, P45, W48, G50, T51, N54, V56, K72, R87, Q98, M105, G109, F113, R116, Q118, Q125, G133, T134, W140, G142, G149, T165, W167, Q169, R171, Q172, L173, A174, G184, A186, E190, T193, N195, A204, V206, P211, I214, V215, L217, L219, A225, L235, V238, K242, S244, M246, M248, L250, G255, Q256, N260, A263, V264, Y267, K269, N270, G273, S280, W284, T285, M286, F289, V291, Y295, Q299, R320, H321, S323, H324, V326, F328, T334, D337, Q345, G346, G348, T355, S376, D377, D379, Y382, S383, Q385, K391, K393, Q395, A420, G423, T444, A445, Q449, T459, P473, C474, G476, G477, y K484 de la SEQ ID NO: 13; o H1, A37, T40, N54, V56, A60, K72, G109, F113, R116, N125, F133, T134, T165, Q169, Q172, L173, A174, G184, A186, E190, N195, G196, A204, V206, A225, L228, K242, S244, G255, N260, A265, K269, S280, W284, Y295, S304, R320, H321, S323, V326, K391, I405, A421, A422, A428, R439, G448, W467, D476, y G477 de la SEQ ID NO: 14,

en donde la variante tiene al menos un 80%, al menos un 85%, al menos un 90%, al menos un 95%, al menos un 97%,

al menos un 98%, al menos un 99% pero menos de un 100% de identidad de secuencia con el polipéptido de SEQ ID NO: 4 o 7 y en donde la variante tiene actividad alfa-amilasa y un rendimiento de lavado mejorado en comparación con el polipéptido parental.

En una realización, la variante tiene al menos un 50%, tal como al menos un 60%, o al menos un 70%, o al menos un 80%, o al menos un 90%, o al menos un 100% de la actividad del polipéptido parental que tiene la secuencia de aminoácidos de SEQ ID NO: 7.

En una realización, la actividad se determina de acuerdo con un ensayo de Phadebas.

La actividad alfa-amilasa puede determinarse mediante un método que utiliza un sustrato de Phadebas (de, por ejemplo, Magle Life Sciences, Lund, Suecia). Un comprimido de Phadebas incluye polímeros de almidón interligados que se encuentran en forma de microesferas globulares que son insolubles en agua. Un tinte azul se une covalentemente a estas microesferas. Los polímeros de almidón interligados en la microesfera se degradan a una velocidad que es proporcional a la actividad alfa-amilasa. Cuando la alfa-amilasa se degrada de los polímeros de almidón, el tinte azul liberado es soluble en agua y la concentración del tinte puede determinarse al medir la absorbancia a 620nm. La concentración de azul es proporcional a la actividad alfa-amilasa en la muestra.

La muestra de variante que se va a analizar se diluye en tampón de actividad con el pH deseado. Se suspenden dos comprimidos de sustrato en 5mL de tampón de actividad y se mezclan en un agitador magnético. Durante el mezclado del sustrato, se transfieren 150µl a la placa de microtitulación (MTP) o PCR-MTP. Se añaden 30µl de la muestra de amilasa diluida a 150µl de sustrato y se mezcla.

Se incuba durante 15 minutos a 37°C. La reacción se detiene mediante la adición de 30µl de NaOH 1M y se mezcla. Se centrifuga la MTP durante 5 minutos a 4000xg. Se transfieren 100µl a una MTP nueva y se mide la absorbancia a 620nm.

La muestra de alfa-amilasa debe diluirse de tal forma que la absorbancia a 620nm es de entre 0 y 2.2 y se encuentra dentro del intervalo lineal del ensayo de actividad.

Por lo tanto, en una realización, la actividad se determina mediante un método que comprende las etapas de;

a) incubar una variante de alfa-amilasa de acuerdo con la invención con un sustrato de amilosa teñido durante 15 minutos a 37°C; y
b) medir la absorción a una DO de 620 nm.

En una realización adicional, la actividad se determina mediante un método que comprende las etapas de;

a) incubar una variante de alfa-amilasa de acuerdo con la invención con un sustrato de amilosa teñido durante 15 minutos a 37°C; y
b) centrifugar la muestra;
c) transferir el sobrenadante a una placa lectora y medir la absorción a una DO de 620 nm.

Formulaciones de caldo de fermentación o composiciones celulares

La presente invención también se refiere a una formulación de un caldo de fermentación o una composición celular que comprende un polipéptido de la presente invención. Por lo tanto, en una realización, la formulación del caldo de fermentación o la composición celular comprende un polinucleótido que codifica una variante que comprende una alteración en una o más posiciones correspondientes a las posiciones H1, T5, G7, Q11, N16,

V17, Q32, A37, T40, P45, W48, G50, T51, N54, V56, K72, R87, Q98, M105, G109, F113, R116, Q118, Q125, G133, T134, W140, G142, G149, T165, W167, Q169, R171, Q172, L173, A174, G184, A186, E190, T193, N195, A204, V206, P211, I214, V215, L217, L219, A225, L235, V238, K242, S244, M246, M248, L250, G255, Q256, N260, A263, V264, Y267, K269, N270, G273, S280, W284, T285, M286, F289, V291, Y295, Q299, R320, H321, S323, H324, V326, F328, T334, D337, Q345, G346, G348, T355, S376, D377, D379, Y382, S383, Q385, K391, K393, Q395, A420, G423, T444, A445, Q449, T459, P473, C474, G476, G477, y K484 de SEQ ID NO: 13; o H1, A37, T40, N54, V56, A60, K72, G109, F113, R116, N125, F133, T134, T165, Q169, Q172, L173, A174, G184, A186, E190, N195, G196, A204, V206, A225, L228, K242, S244, G255, N260, A265, K269, S280, W284, Y295, S304, R320, H321, S323, V326, K391, I405, A421, A422, A428, R439, G448, W467, D476, y G477 de SEQ ID NO: 14, una construcción de ácido nucleico que codifica una variante que comprende una alteración en una o más posiciones correspondientes a las posiciones H1, T5, G7, Q11, N16, V17, Q32, A37, T40, P45, W48, G50, T51, N54, V56, K72, R87, Q98, M105, G109, F113, R116, Q118, Q125, G133, T134, W140, G142, G149, T165, W167, Q169, R171, Q172, L173, A174, G184, A186, E190, T193, N195, A204, V206, P211, I214, V215, L217, L219, A225, L235, V238, K242, S244, M246, M248, L250, G255, Q256, N260, A263, V264, Y267, K269, N270, G273, S280, W284, T285, M286, F289, V291, Y295, Q299, R320, H321, S323, H324, V326, F328, T334, D337, Q345, G346, G348, T355, S376, D377, D379, Y382, S383, Q385, K391, K393, Q395, A420, G423, T444, A445, Q449, T459, P473, C474, G476, G477, y K484 de SEQ ID NO: 13; o H1, A37, T40, N54, V56, A60, K72, G109, F113, R116, N125, F133, T134, T165, Q169, Q172, L173, A174, G184, A186, E190, N195, G196, A204, V206, A225, L228, K242, S244, G255, N260, A265, K269, S280, W284, Y295, S304, R320, H321, S323, V326, K391, I405,

A421, A422, A428, R439, G448, W467, D476, y G477 de SEQ ID NO: 14 o un vector de expresión que codifica una variante que comprende una alteración en una o más posiciones correspondientes a las posiciones H1, T5, G7, Q11, N16, V17, Q32, A37, T40, P45, W48, G50, T51, N54, V56, K72, R87, Q98, M105, G109, F113, R116, Q118, Q125, G133, T134, W140, G142, G149, T165, W167, Q269, R171, Q172, L173, A174, G184, A186, E190, T193, N195, A204, V206, P211, I214, V215, L217, L219, A225, L235, V238, K242, S244, M246, M248, L250, G255, Q256, N260, A263, V264, Y267, K269, N270, G273, S280, W284, T285, M286, F289, V291, Y295, Q299, R320, H321, S323, H324, V326, F328, T334, D337, Q345, G346, G348, T355, S376, D377, D379, Y382, S383, Q385, K391, K393, Q395, A420, G423, T444, A445, Q449, T459, P473, C474, G476, G477, y K484 de SEQ ID NO: 13; o H1, A37, T40, N54, V56, A60, K72, G109, F113, R116, N125, F133, T134, T165, Q169, Q172, L173, A174, G184, A186, E190, N195, G196, A204, V206, A225, L228, K242, S244, G255, N260, A265, K269, S280, W284, Y295, S304, R320, H321, S323, V326, K391, I405, A421, A422, A428, R439, G448, W467, D476, y G477 de SEQ ID NO: 14. El producto de caldo de fermentación puede comprender además componentes adicionales utilizados en el proceso de fermentación tales como, por ejemplo, células (que incluyen, las células hospedadoras que contienen el gen que codifica el polipéptido de la presente invención que se utilizan para producir el polipéptido de interés), desechos celulares, biomasa, medio de fermentación y/o productos de fermentación. En algunas realizaciones, la composición es un caldo entero de células muertas que contiene uno o más ácidos orgánicos, células muertas y/o desechos celulares, y medio de cultivo.

La expresión "caldo de fermentación", tal como se utiliza en el presente documento, se refiere a un preparado

producido mediante fermentación celular que se somete a una recuperación y/o purificación mínima o nula. Por ejemplo, los caldos de fermentación se producen cuando se cultivan cultivos microbianos hasta la saturación y se incuban en condiciones de carbono limitado para permitir la síntesis de proteínas (por ejemplo, la expresión de enzimas por parte de las células hospedadoras) y la secreción al medio de cultivo celular. El caldo de fermentación puede contener contenidos fraccionados o no fraccionados de los materiales de fermentación obtenidos al final de la fermentación. Normalmente, el caldo de fermentación no está fraccionado y comprende el medio de cultivo gastado y los desechos celulares presentes después de que se hayan eliminado las células microbianas (por ejemplo, células fúngicas filamentosas), por ejemplo, mediante centrifugación. En algunas realizaciones, el caldo de fermentación contiene medio de cultivo celular gastado, enzimas extracelulares y células microbianas viables y/o no viables.

En una realización, la formulación del caldo de fermentación y las composiciones celulares comprenden un primer componente de tipo ácido orgánico que comprende al menos un ácido orgánico de 1-5 carbonos y/o una sal de este y un segundo componente de tipo ácido orgánico que comprende al menos un ácido orgánico de 6 o más carbonos y/o una sal del mismo. En una realización particular, el primer componente de tipo ácido orgánico es ácido acético, ácido fórmico, ácido propiónico, una sal de estos o una mezcla de dos o más de los anteriores y el segundo componente de tipo ácido orgánico es ácido benzoico, ácido ciclohexanocarboxílico, ácido 4-metilvalérico, ácido fenilacético, una sal de estos o una mezcla de dos o más de los anteriores.

En una realización, la composición contiene uno o más ácidos orgánicos y opcionalmente contiene además células muertas y/o desechos celulares. En una realización, las células muertas y/o desechos celulares se eliminan de un caldo completo de células muertas para proporcionar una composición que esté libre de estos componentes.

Las formulaciones del caldo de fermentación o composiciones celulares pueden comprender además un agente conservante y/o antimicrobiano (por ejemplo, bacteriostático), que incluye, sin carácter limitante, sorbitol, cloruro de sodio, sorbato de potasio y otros conocidos en la técnica.

El caldo entero de células muertas o la composición pueden comprender los contenidos no fraccionados de los materiales de fermentación obtenidos al final de la fermentación. Normalmente, el caldo entero de células muertas o la composición comprende el medio de cultivo gastado y los desechos celulares presentes después de que las células microbianas (por ejemplo, células fúngicas filamentosas) se hayan cultivado hasta la saturación e incubado en condiciones de carbono limitado para permitir la síntesis de proteínas. En algunas realizaciones, el caldo entero de células muertas o la composición comprende el medio de cultivo celular gastado, enzimas extracelulares y células fúngicas filamentosas muertas. En algunas realizaciones, las células microbianas presentes en el caldo entero de células muertas o la composición se pueden permeabilizar y/o lisar utilizando métodos conocidos en la técnica.

Un caldo entero o una composición celular según se describe en el presente documento es normalmente líquido, pero puede comprender componentes insolubles tales como células muertas, desechos celulares, componentes de medios

de cultivo y/o una o más enzimas insolubles. En algunas realizaciones, se pueden eliminar los componentes insolubles para proporcionar una composición líquida clarificada.

Las formulaciones de caldo completo y las composiciones celulares de la presente invención pueden producirse mediante un método descrito en el documento WO 90/15861 o WO 2010/096673.

Composiciones enzimáticas

La presente invención también se refiere a composiciones que comprenden una variante de acuerdo con la invención. Por lo tanto, la invención se refiere a una composición que comprende una variante que comprende una alteración en una o más posiciones correspondientes a las posiciones H1, T5, G7, Q11, N16, V17, Q32, A37, T40, P45, W48, G50, T51, N54, V56, K72, R87, Q98, M105, G109, F113, R116, Q118, Q125, G133, T134, W140, G142, G149, T165, W167, Q169, R171, Q172, L173, A174, G184, A186, E190, T193, N195, A204, V206, P211, I214, V215, L217, L219, A225, L235, V238, K242, S244, M246, M248, L250, G255, Q256, N260, A263, V264, Y267, K269, N270, G273, S280, W284, T285, M286, F289, V291, Y295, Q299, R320, H321, S323, H324, V326, F328, T334, D337, Q345, G346, G348, T355, S376, D377, D379, Y382, S383, Q385, K391, K393, Q395, A420, G423, T444, A445, Q449, T459, P473, C474, G476, G477, y K484 de la SEQ ID NO: 13; o H1, A37, T40, N54, V56, A60, K72, G109, F113, R116, N125, F133, T134, T165, Q169, Q172, L173, A174, G184, A186, E190, N195, G196, A204, V206, A225, L228, K242, S244, G255, N260, A265, K269, S280, W284, Y295, S304, R320, H321, S323, V326, K391, I405, A421, A422, A428, R439, G448, W467, D476, y G477 de SEQ ID NO: 14.

En una realización, la composición comprende una variante que comprende

a) una eliminación y/o una sustitución en dos o más posiciones correspondientes a las posiciones R181, G182, D183 y G184 de la secuencia de aminoácidos expuesta en las SEQ ID NO: 7 o 10 y

b) una alteración en una o más posiciones correspondientes a las posiciones H1, T5, G7, Q11, N16, V17, Q32, A37, T40, P45, W48, G50, T51, N54, V56, K72,R87, Q98, M105, G109, F113, R116, Q118, Q125, G133, T134, W140, G142, G149, T165, W167, Q169, R171, Q172, T173, A174, A186, E190, T193, N195, A204, V206, P211, V213, I214, L217, A225, L235, V238, K242, S244, M246, L250, G255, Q256, N260, A263, V264, Y267, K269, N270, G273, S280, W284, T285, M286, F289, V291, Y295, Q299, R320, H321, S323, H324, V326, F328, T334, G337, Q345, G346, T355, S376, D377, S381, Y382, Q385, K391, K393, Q395, A420, G423, T444, A445, Q449, T459, P473, C474, G476, G477, y K484 de la SEQ ID NO: 13; o H1, A37, T40, N54, V56, A60, K72, G109, F113, R116, N125, F133, T134, T165, Q169, Q172, L173, A174, G184, A186, E190, N195, G196, A204, V206, A225, L228, K242, S244, G255, N260, A265, K269, S280, W284, Y295, S304, R320, H321, S323, V326, K391, I405, A421, A422, A428, R439, G448, W467, D476, y G477 de la SEQ ID NO: 14. Preferentemente, las composiciones están enriquecidas en una variante de este tipo. El término "enriquecido", tal como se usa en el presente documento, se refiere a que se ha aumentado la actividad alfa-amilasa de la composición, por ejemplo, con un factor de enriquecimiento de al menos 1.1.

Las composiciones pueden comprender una variante de la presente invención como el componente enzimático principal, por ejemplo, una composición monocomponente. En otra realización, la composición comprende además un componente activo adicional.

La expresión "componente activo", tal como se usa en el presente documento, se refiere a cualquier molécula biológica o no biológica que sea activa por sí misma. Por ejemplo, un componente activo es una enzima.

Por lo tanto, en una realización, el componente activo adicional es una enzima, tal como una proteasa, lipasa, celulosa, pectato liasa y mananasa. Por lo tanto, las composiciones pueden comprender múltiples actividades enzimáticas tales como una o más (por ejemplo, varias) enzimas seleccionadas a partir del grupo constituido por una hidrolasa, isomerasa, ligasa, liasa, oxidorreductasa o transferasa, por ejemplo, una alfa-galactosidasa, alfa-glucosidasa, aminopeptidasa, amilasa, beta-galactosidasa, beta-glucosidasa, beta-xilosidasa, carbohidrasa, carboxipeptidasa, catalasa, celobiohidrolasa, celulasa, quitinasa, cutinasa, ciclodextrina glucosiltransferasa, desoxirribonucleasa, endoglucanasa, esterasa, glucoamilasa, invertasa, lacasa, lipasa, manosidasa, mutanasa, oxidasa, enzima pectinolítica, peroxidasa, fitasa, polifenoloxidasa, enzima proteolítica, ribonucleasa, transglutaminasa o xilanasa.

En una realización, la composición es una composición líquida para el lavado de ropa o para el lavado de vajilla, tal como una composición de detergente líquido para lavavajillas automático (ADW) o un detergente en polvo para ropa, tal como una pastilla de jabón o una composición de lavavajillas en polvo, tal como una composición de detergente en dosis unitaria para ADW y tal como una composición de detergente para el lavado a mano de vajilla (HDW).

La elección de componentes adicionales se encuentra dentro de las competencias del experto en la materia e incluye ingredientes adicionales, que incluyen los

componentes ejemplares no limitantes expuestos más adelante. La elección de los componentes puede incluir, para el cuidado de telas, tener en cuenta el tipo de tela que se ha de limpiar, el tipo y/o grado de suciedad, la temperatura a la cual va a tener lugar la limpieza y la formulación del producto detergente. Aunque los componentes que se mencionan a continuación están clasificados según un título general según una funcionalidad particular, esto no debe interpretarse como una limitación, ya que un componente puede comprender funcionalidades adicionales que podrá apreciar el experto en la técnica.

En una realización de la presente invención, la variante de la presente invención puede añadirse a una composición detergente en una cantidad correspondiente a 0.001-100 mg de proteína, tal como 0.01-100 mg de proteína, preferentemente 0.005-50 mg de proteína, más preferentemente 0.01-25 mg de proteína, aún más preferentemente 0.05-10 mg de proteína, más preferentemente 0.05-5 mg de proteína e incluso más preferentemente 0.01-1 mg de proteína por litro de solución de lavado. Se contempla que el término "proteína", en este contexto, se sobreentienda como inclusivo de una variante de acuerdo con la presente invención.

Una composición para su uso en un lavavajillas automático (ADW) puede incluir, por ejemplo, un 0.0001%-50%, tal como un 0.001%-20%, tal como un 0.01%-10%, tal como un 0.05%-5% de proteína enzimática en peso de la composición.

Una composición para su uso en un detergente granulado para lavar la ropa puede incluir, por ejemplo, un 0.0001%-50%, tal como un 0.001%-20%, tal como un 0.01%-10%, tal como un 0.05%-5% de proteína enzimática en peso de la composición.

Una composición para uso en un detergente líquido para lavar la ropa puede incluir por ejemplo, un 0.0001%-10%, tal como un 0.001%-7%, tal como un 0.1%-5% de proteína enzimática en peso de la composición.

Las variantes de la invención, así como los componentes activos adicionales, tales como enzimas adicionales, pueden estabilizarse usando agentes estabilizantes convencionales, por ejemplo, un poliol, tal como propilenglicol o glicerol, un azúcar o alcohol de azúcar, ácido láctico, ácido bórico o un derivado del ácido bórico, por ejemplo, un éster aromático de borato o un derivado del ácido fenilborónico, tal como ácido 4-formilfenil borónico y la composición puede formularse tal como se describe, por ejemplo, en los documentos WO92/19709 y WO92/19708.

En algunos mercados, se utilizan diferentes condiciones de lavado, y por ende, diferentes tipos de detergentes. Esto se divulga, por ejemplo, en el documento EP 1 025 240. Por ejemplo, en Asia (Japón), se utiliza un sistema de concentración baja de detergente, mientras que en Estados Unidos, se utiliza un sistema de concentración media y en Europa se utiliza un sistema de concentración alta de detergente.

Un sistema de concentración baja de detergente incluye detergentes donde menos de aproximadamente 800 ppm de componentes detergentes están presentes en el agua de lavado. Los detergentes japoneses se consideran normalmente un sistema de concentración baja de detergente dado que tienen aproximadamente 667 ppm de componentes detergentes presentes en el agua de lavado.

Una concentración media de detergente incluye detergentes donde entre aproximadamente 800 ppm y aproximadamente 2000ppm de componentes detergentes están

presentes en el agua de lavado. Los detergentes norteamericanos se consideran normalmente sistemas de concentración media de detergente dado que tienen aproximadamente 975 ppm de componentes detergentes presentes en el agua de lavado.

Un sistema de concentración alta de detergente incluye detergentes donde más de aproximadamente 2000 ppm de componentes detergentes están presentes en el agua de lavado. Los detergentes europeos se consideran generalmente sistemas de concentración alta de detergente dado que tienen aproximadamente 4500-5000 ppm de componentes detergentes en el agua de lavado.

Los detergentes latinoamericanos son generalmente detergentes con adyuvantes de tipo fosfato potenciadores la espuma en un grado elevado y puede considerarse que la gama de detergentes utilizados en América Latina tienen tanto concentraciones de detergente medias como elevadas ya que están comprendidas entre 1500 ppm y 6000 ppm de componentes detergentes en el agua de lavado. Este tipo de composiciones detergentes abarcan todas las realizaciones de la invención.

Una variante de la presente invención también puede incorporarse en las formulaciones de detergente descritas en el documento WO97/07202, que se incorpora a la presente por referencia.

En el presente documento se proporcionan ejemplos de usos preferidos de las composiciones de la presente invención. La dosis de la composición y otras condiciones en las cuales se utiliza la composición se pueden determinar basándose en métodos conocidos en la técnica.

En particular, una composición de acuerdo con la presente invención comprende además un quelante.

El término "quelante", tal como se usa en el presente documento, se refiere a agentes químicos que forman moléculas con determinados iones metálicos, inactivando los iones de tal forma que no pueden reaccionar con otros elementos. Por lo tanto, un quelante puede definirse como un agente de unión que suprime la actividad química formando quelatos. La quelación es la formación o presencia de dos o más ligantes separados entre un ligando y un único átomo central. El ligando puede ser cualquier compuesto orgánico, un silicato o un fosfato. En este contexto, la expresión "agentes quelantes" comprende quelantes, agente quelante, agentes quelantes, agentes de formación de complejos o agentes secuestrantes que forman complejos solubles en agua con iones metálicos, tales como calcio y magnesio. El efecto del quelato describe la afinidad mejorada de los ligandos quelantes por un ion metálico comparada con la afinidad de una colección de ligandos no quelantes similares para el mismo metal. Los agentes quelantes que tienen la capacidad de unirse a metales iónicos, en particular iones de calcio (Ca^{2+}), se han utilizado ampliamente en detergentes y composiciones para el lavado en general, tales como lavado de ropa o de vajilla. Se ha demostrado, sin embargo, que los agentes quelantes inhiben la actividad enzimática. La expresión "agente quelante" se utiliza en la presente solicitud indistintamente con "agente de formación de complejos" o "agente quelante" o "quelante".

Debido a que la mayoría de las alfa-amilasas son sensibles al calcio, la presencia de agentes quelantes puede inhibir la actividad enzimática. La sensibilidad al calcio de las alfa-amilasas se puede determinar mediante la incubación de una alfa-amilasa dada en presencia de un agente quelante fuerte y el análisis del impacto de esta

incubación en la actividad de la alfa-amilasa en cuestión. Una alfa-amilasa sensible al calcio perderá una parte significativa de toda su actividad durante la incubación. El agente quelante puede estar presente en la composición en una cantidad del 0.0001% en peso al 20% en peso, preferentemente del 0.01 al 10% en peso, más preferentemente del 0.1 al 5% en peso.

Los ejemplos no limitantes de agentes quelantes son; EDTA, DTMPA, HEDP y citrato. Por lo tanto, en una realización, la composición comprende una variante de acuerdo con la invención y un agente quelante, tal como EDTA, DTMPA, HEDP o citrato.

El término "EDTA", tal como se usa en el presente documento, se refiere a ácido etilendiaminotetraacético, que se encuentra dentro de la definición de "agentes quelantes fuertes".

El término "DTMPA", tal como se usa en el presente documento, se refiere a ácido dietilentriamina penta(metilen fosfónico). El DTMPA puede inhibir la escalada de formación de carbonato, sulfato y fosfato.

El término "HEDP", tal como se usa en el presente documento, se refiere a ácido hidroxietano disfosfónico, que se encuentra dentro de la definición de "agentes quelantes fuertes".

El efecto del quelato o el efecto quelante describe la afinidad mejorada de los ligandos quelantes por un ion metálico comparada con la afinidad de una colección de ligandos no quelantes similares para el mismo metal. Sin embargo, la fuerza de este efecto del quelante puede determinarse mediante diversos tipos de ensayos o métodos de medida, diferenciando o clasificando de este modo a los agentes quelantes según su efecto (o fuerza) quelante.

En un ensayo, los agentes quelantes pueden caracterizarse por su capacidad para reducir la concentración de iones de calcio libres (Ca2+) de 2.0 mM a 0.10 mM o menos a pH 8.0, por ejemplo, usando una prueba basada en el método descrito por M.K. Nagarajan et al., JAOCS, Vol. 61, n.º 9 (septiembre de 1984), págs. 1475-1478.

Por referencia, se dice que un quelante que tenga la misma capacidad para reducir la concentración de iones de calcio libres (Ca2+) de 2.0 mM a 0.10 mM a este pH que el EDTA a concentraciones iguales del quelante es un quelante fuerte.

La composición de la presente invención se puede encontrar en cualquier forma conveniente, por ejemplo, una barra, un comprimido homogéneo, un comprimido que tiene dos o más capas, una bolsita que tiene uno o más compartimentos, un polvo regular o compacto, un gránulo, una pasta, un gel o un líquido regular, compacto o concentrado. Existen varias formas de formulación detergente tales como capas (fases idénticas o diferentes), bolsas, así como también para unidades dosificadoras para máquinas.

Las bolsas pueden configurarse con un único compartimento o con múltiples compartimentos. Puede tener cualquier forma, diseño y material que sea adecuado para guardar la composición, por ejemplo, sin permitir la liberación de la composición desde la bolsita antes de entrar en contacto con el agua. La bolsita está hecha de una película hidrosoluble que encierra un volumen interno. Dicho volumen interno puede dividirse en compartimientos de la bolsita. Las películas preferidas son materiales poliméricos, preferiblemente polímeros que se forman en una hoja o película. Los polímeros, copolímeros o derivados de

los mismos preferidos son poliacrilatos seleccionados y copolímeros de acrilato hidrosolubles, metilcelulosa, carboximetilcelulosa, dextrina de sodio, etilcelulosa, hidroxietilcelulosa, hidroxipropilmetilcelulosa, maltodextrina, polimetacrilatos, más preferiblemente copolímeros de poli(alcohol vinílico) e hidroxipropilmetilcelulosa (HPMC). Preferiblemente, el nivel de polímero en la película, por ejemplo, PVA es de al menos aproximadamente el 60%. El peso molecular promedio preferido generalmente será de aproximadamente 20,000 a aproximadamente 150,000. Las películas también pueden estar constituidas por composiciones mezcladas que comprenden mezclas de polímeros hidrosolubles y degradables hidrolíticamente tales como ácido poliláctico y poli(alcohol vinílico) (conocidos con la referencia comercial M8630 y comercializados por Chris Craft In. Prod. Of Gary, Ind., EE. UU.), además de plastificantes tales como glicerol, etilenglicerol, propilenglicol, sorbitol y mezclas de estos. Las bolsitas pueden comprender una composición o componentes parciales de limpieza para la ropa sólidos y/o una composición o componentes parciales de limpieza líquidos separados por la película hidrosoluble. El compartimiento para los componentes líquidos puede tener una composición diferente que los compartimentos que contienen los sólidos. Ref: (US2009/0011970 A1).

Los componentes del detergente se pueden separar físicamente unos de otros mediante compartimentos en bolsas que se disuelven en agua o en diferentes capas de comprimidos. De este modo, pueden evitarse interacciones negativas entre los componentes durante el almacenamiento. Los diferentes perfiles de disolución de cada uno de los compartimentos también pueden dar lugar a una disolución

más tardía de los componentes seleccionados en la disolución de lavado.

Un detergente líquido o en gel, que no se dosifica por unidad, puede ser acuoso, generalmente que contiene al menos un 20% en peso y hasta un 95% de agua, como hasta aproximadamente un 70% de agua, hasta aproximadamente un 65% de agua, hasta aproximadamente un 55% de agua, hasta aproximadamente un 45% de agua, hasta aproximadamente un 35% de agua. Se pueden incluir otros tipos de líquidos, que incluyen, sin carácter limitante, alcanoles, aminas, dioles, éteres y polioles, en un líquido o gel acuoso. Un detergente en gel o líquido acuoso puede contener desde el 0-30% de un disolvente orgánico. Un detergente en gel o líquido puede ser no acuoso.

Otra forma de composición se encuentra en forma de una pastilla de jabón, tal como una pastilla de jabón para lavado de ropa y puede usarse para el lavado a mano de ropa, tejidos y/o artículos textiles. La expresión "pastilla de jabón", tal como se usa en el presente documento, incluye pastillas para el lavado de ropa, pastillas de jabón, pastillas combinadas, pastillas Syndet y pastillas de detergente. Normalmente, los tipos de pastilla difieren en el tipo de tensioactivo que contienen, y la expresión "pastilla de jabón para lavar la ropa" incluye aquellas que contienen jabones de ácidos grasos y/o jabones sintéticos. La pastilla de jabón para lavar la ropa tiene una forma física que es sólida y no es un líquido, gel ni polvo a temperatura ambiente. El término "sólido", tal como se usa en el presente documento, se refiere a una forma física que no cambia significativamente con el transcurso del tiempo, es decir, si un objeto sólido (por ejemplo, una pastilla de jabón para lavar la ropa) se coloca en un recipiente, el objeto sólido no cambia para

llenar el recipiente en el que se coloca. La pastilla es un sólido normalmente en forma de barra pero puede adoptar otras formas sólidas tales como redonda u ovalada.

La pastilla de jabón también puede comprender agentes de complejación como EDTA y HEDP, perfumes y/o diferentes tipos de rellenos, tensioactivos, por ejemplo, tensioactivos sintéticos aniónicos, adyuvantes, agentes poliméricos para liberar la suciedad, quelantes detergentes, agentes estabilizantes, rellenos, tintes, colorantes, inhibidores de la transferencia de tintes, policarbonatos alcoxilados, supresores de la espuma de jabones, estructurantes, aglutinantes, agentes de lixiviación, agentes activadores de la decoloración, agentes que eliminan la suciedad de arcillas, agentes contra la redeposición, agentes dispersantes poliméricos, abrillantadores, suavizantes para tejidos, perfumes y/u otros compuestos conocidos en la técnica.

La pastilla de jabón se puede procesar en un equipo convencional de producción de pastillas de jabón para lavar la ropa tal como, sin carácter limitante: mezcladoras, compresoras, por ejemplo, una compresora de vacío de dos etapas, extrusoras, cortadoras, estampadoras de logos, túneles de enfriamiento y empaquetadoras. La invención no se limita a preparar las pastillas de jabón mediante cualquier método único. La premezcla de la invención se puede añadir al jabón en diferentes etapas del procedimiento. Por ejemplo, la premezcla que comprende un jabón, una enzima, opcionalmente una o más enzimas adicionales, un inhibidor de proteasas y una sal de un catión monovalente y un anión orgánico se puede preparar y posteriormente puede extruirse la mezcla. La enzima y las enzimas opcionales adicionales pueden añadirse en el mismo momento que el inhibidor enzimático, por ejemplo, un

inhibidor de proteasas, por ejemplo, en forma líquida. Además de la etapa de mezclar y la etapa de comprimir, el procedimiento puede comprender además las etapas de moler, extrudir, cortar, estampar, enfriar y/o envolver.

Usos

La presente invención se refiere además al uso de una variante de acuerdo con la presente invención en un proceso de limpieza, tal como de lavado de ropa o de limpieza de superficies duras, incluyendo el lavado de vajillas automático y la limpieza industrial. La suciedad y las manchas que son importantes para limpiar están compuestas de muchas sustancias diferentes, y se ha desarrollado una gama de diferentes enzimas, todas con especificidades de sustratos diferentes para su uso en detergentes tanto en relación con el lavado de la ropa como con la limpieza de superficies duras, tal como el lavado de la vajilla. Se considera que estas enzimas proporcionan un beneficio de detergencia enzimática, ya que mejoran específicamente la eliminación de manchas en el proceso de lavado en el que se usan en comparación con el mismo proceso sin enzimas. Las enzimas para la eliminación de manchas que se conocen en la técnica incluyen enzimas tales como proteasas, amilasas, lipasas, cutinasas, celulasas, endoglucanasas, xiloglucanasas, pectinasas, pectina liasas, xantanasas, peroxidasas, haloperoxigenasas, catalasas y mananasas.

En una realización, la invención se refiere al uso de variantes de la presente invención en composiciones de detergente, para su uso en la limpieza de superficies duras, tal como el lavado de vajillas o en lavandería o para la eliminación de manchas. En otra realización, la invención se refiere al uso de una variante de alfa-amilasa de acuerdo con la invención en un proceso de lavado, tal como lavado de ropa o limpieza de superficies duras que

incluye, pero sin limitación, el lavado de vajilla y la limpieza industrial. Por lo tanto, en una realización, la invención se refiere al uso de una variante que comprende una alteración en una o más posiciones correspondientes a las posiciones H1, T5, G7, Q11, N16, V17, Q32, A37, T40, P45, W48, G50, T51, N54, V56, K72, R87, Q98, M105, G109, F113, R116, Q118, Q125, G133, T134, W140, G142, G149, T165, W167, Q169, R171, Q172, L173, A174, G184, A186, E190, T193, N195, A204, V206, P211, I214, V215, L217, L219, A225, L235, V238, K242, S244, M246, M248, L250, G255, Q256, N260, A263, V264, Y267, K269, N270, G273, S280, W284, T285, M286, F289, V291, Y295, Q299, R320, H321, S323, H324, V326, F328, T334, D337, Q345, G346, G348, T355, S376, D377, D379, Y382, S383, Q385, K391, K393, Q395, A420, G423, T444, A445, Q449, T459, P473, C474, G476, G477, y K484 de la SEQ ID NO: 13; o H1, A37, T40, N54, V56, A60, K72, G109, F113, R116, N125, F133, T134, T165, Q169, Q172, L173, A174, G184, A186, E190, N195, G196, A204, V206, A225, L228, K242, S244, G255, N260, A265, K269, S280, W284, Y295, S304, R320, H321, S323, V326, K391, I405, A421, A422, A428, R439, G448, W467, D476, y G477 de la SEQ ID NO: 14 en un proceso de lavado, tal como lavado de ropa o limpieza de superficies duras, incluyendo lavado de vajilla y limpieza industrial.

En una realización particular, la invención se refiere al uso de una variante que comprende a) una sustitución y/o eliminación de dos, tres o cuatro posiciones en la alfa-amilasa parental, correspondiendo dichas posiciones a las posiciones 181, G182, D183 y G184 del polipéptido maduro de SEQ ID NO: 4; y

b) una alteración en una o más posiciones correspondientes a las posiciones H1, T5, G7, Q11, N16, V17, Q32, A37, T40, P45, W48, G50, T51, N54, V56, K72, R87, Q98, M105, G109, F113, R116, Q118, Q125, G133, T134, W140,

G142, G149, T165, W167, Q169, R171, Q172, L173, A174, G184, A186, E190, T193, N195, A204, V206, P211, I214, V215, L217, L219, A225, L235, V238, K242, S244, M246, M248, L250, G255, Q256, N260, A263, V264, Y267, K269, N270, G273, S280, W284, T285, M286, F289, V291, Y295, Q299, R320, H321, S323, H324, V326, F328, T334, D337, Q345, G346, G348, T355, S376, D377, D379, Y382, S383, Q385, K391, K393, Q395, A420, G423, T444, A445, Q449, T459, P473, C474, G476, G477, y K484 de la SEQ ID NO: 13; o H1, A37, T40, N54, V56, A60, K72, G109, F113, R116, N125, F133, T134, T165, Q169, Q172, L173, A174, G184, A186, E190, N195, G196, A204, V206, A225, L228, K242, S244, G255, N260, A265, K269, S280, W284, Y295, S304, R320, H321, S323, V326, K391, I405, A421, A422, A428, R439, G448, W467, D476, y G477 de la SEQ ID NO: 14, en un proceso de lavado, tal como lavado de ropa o limpieza de superficies duras, incluyendo lavado de vajilla y limpieza industrial.

En una realización, la invención se refiere al uso de una composición de acuerdo con la invención que comprende una variante de la presente invención junto con uno o más tensioactvos y opcionalmente uno o más componentes detergentes, seleccionados de la lista que comprende hidrotropos, adyuvantes y coadyuvantes, sistemas blanqueantes, polímeros, agentes de matizado de tejidos y materiales adjuntos o una mezcla de los mismos en composiciones detergentes y en aplicaciones de detergente.

Una realización adicional es el uso de la composición de acuerdo con la invención que comprende una variante de la presente invención junto con uno o más tensioactivos y una o más enzimas adicionales seleccionadas dentro del grupo que comprende proteasas, lipasas, cutinasas, celulasas, endoglucanasas, xiloglucanasas, pectinasas, pectina liasas, xantanasas, peroxidasas, haloperoxigenasas, catalasas y mananasas o cualquier mezcla de las mismas en

composiciones de detergente y en aplicaciones de detergente.

En otro aspecto, la invención se refiere a un proceso de lavado de ropa que puede ser para lavandería doméstica así como lavandería industrial. Además, la invención se refiere a un proceso para el lavado de artículos textiles (por ejemplo, telas, prendas de vestir, tejidos, etc.) donde el proceso comprende tratar el artículo textil con una solución de lavado que contiene una composición de detergente y una alfa-amilasa de la presente invención. El lavado de ropa puede llevarse a cabo, por ejemplo, usado una máquina de lavado doméstica o industrial o llevarse a cabo manualmente usando una composición de detergente que contiene una glucoamilasa de la invención.

En otro aspecto, la invención se refiere a un proceso para el lavado de vajilla que pude ser para lavado de vajilla doméstico así como lavado de vajilla industrial. El término "lavado de vajilla", tal como se usa en el presente documento, se refiere tanto al lavado manual de vajilla como al lavado de vajilla automatizado. Además, la invención se refiere a un proceso para el lavado de superficies duras (por ejemplo, cubertería, tal como cuchillos, tenedores, cucharas; vajilla, tal como platos, vasos, boles; y ollas) donde el proceso comprende tratar la superficie dura con una solución de lavado que contiene una composición de detergente y una variante de alfa-amilasa de la presente invención. El lavado de superficies duras puede llevarse a cabo, por ejemplo, usando un lavavajillas doméstico o industrial o llevarse a cabo a mano usando una composición de detergente que contiene una alfa-amilasa de la invención, opcionalmente junto con una o más enzimas adicionales, seleccionadas entre el grupo que comprende proteasas, amilasas, lipasas, cutinasas, celulasas,

endoglucanasas, xiloglucanasas, pectinasas, pectina liasas, xantanasas, peroxidasas, haloperoxigenasas, catalasas, mananasas o cualquier mezcla de los mismos.

En un aspecto adicional, la invención se refiere a un método para eliminar una mancha de una superficie que comprende poner en contacto la superficie con una composición que comprende una alfa-amilasa de la presente invención junto con uno o más tensioactvos y opcionalmente uno o más componentes detergentes, seleccionados de la lista que comprende hidrotropos, adyuvantes y coadyuvantes, sistemas blanqueantes, polímeros, agentes de matizado de tejidos y materiales adjuntos o una mezcla de los mismos en composiciones detergentes y en aplicaciones de detergente. Un aspecto adicional es un método para eliminar una mancha de una superficie que comprende poner en contacto la superficie con una composición que comprende una variante de alfa-amilasa de la presente invención junto con uno o más tensioactivos, una o más enzimas adicionales seleccionadas dentro del grupo que comprende proteasas, lipasas, cutinasas, celulasas, endoglucanasas, xiloglucanasas, pectinasas, pectina liasas, xantanasas, peroxidasas, haloperoxigenasas, catalasas y mananasas o cualquier mezcla de las mismas en composiciones de detergente y en aplicaciones de detergente.

La presente invención se describe adicionalmente mediante los siguientes ejemplos que no deben considerarse limitantes del alcance de la invención.

EJEMPLOS

Ejemplo 1a: Construcción del polipéptido parental como se expone en la SEQ ID NO: 13

Construcción de un híbrido entre el dominio A y B de un polipéptido que tiene la secuencia de aminoácidos expuesta en la SEQ ID NO: 10 (el primer polipéptido

parental) y el dominio C de un polipéptido que tiene la secuencia de aminoácidos expuesta en la SEQ ID NO: 11 (el segundo polipéptido parental).

Basándose en el alineamiento estructural en 3D de las dos amilasas, del aminoácido n.º 1 al aminoácido n.º 397 del primer polipéptido parental se definen como dominio A y B y del aminoácido n.º 398 al aminoácido n.º 485 del segundo polipéptido parental se definen como el dominio C. Se diseñaron fragmentos de ADN sintético que codifican parte del dominio A del primer polipéptido parental y el dominio C del segundo polipéptido parental y se adquirieron de un proveedor externo. Además de combinar fragmentos de las dos amilasas diferentes, se diseñaron las siguientes sustituciones estabilizantes en el gen de amilasa sintético: G182* y D183*.

El nuevo gen que consistía en un fragmento génico que codifica el dominio A y B del primer polipéptido parental y el dominio C del segundo polipéptido parental codificado por los fragmentos génicos sintéticos se construyó mediante el método de PCR de triple SOE (corte y empalme por extensión de solapamiento). Los dos fragmentos se ensamblaron mediante reacción en cadena de la polimerasa de corte y empalme por extensión de solapamiento y se transformaron en un hospedador competente de *B. subtilis* para su sobreexpresión. La amilasa resultante que consistía en el dominio A y B del primer polipéptido parental y el dominio C del segundo polipéptido parental y que tiene las eliminaciones G182* y D183* es el polipéptido expuesto en la SEQ ID NO: 13.

Ejemplo 1b: Construcción del polipéptido parental como se expone en la SEQ ID NO: 14

Construcción de un híbrido entre el dominio A y B de un polipéptido que tiene la secuencia de aminoácidos

expuesta en la SEQ ID NO: 10 (el primer polipéptido parental) y el dominio C de un polipéptido que tiene la secuencia de aminoácidos expuesta en la SEQ ID NO: 12 (el tercer polipéptido parental).

Basándose en el alineamiento estructural en 3D de las dos amilasas, del aminoácido n.º 1 al aminoácido n.º 397 del primer polipéptido parental se definen como dominio A y B y del aminoácido n.º 398 al aminoácido n.º 485 del tercer polipéptido parental se definen como el dominio C. Se diseñaron fragmentos de ADN sintético que codifican parte del dominio A del primer polipéptido parental y el dominio C del segundo polipéptido parental y se adquirieron de un proveedor externo. Además de combinar fragmentos de las dos amilasas diferentes, se diseñaron las siguientes sustituciones estabilizantes en el gen de amilasa sintético: G182* y D183*.

El nuevo gen que consistía en un fragmento génico que codifica el dominio A y B del primer polipéptido parental y el dominio C del segundo polipéptido parental codificado por los fragmentos génicos sintéticos se construyó mediante el método de PCR de triple SOE (corte y empalme por extensión de solapamiento). Se amplificó un fragmento de ADN a partir de un clon de expresión de la primera amilasa. Los fragmentos se ensamblaron finalmente mediante triple SOE y el fragmento obtenido de la PCR se transformó en un hospedador de *B. subtilis* adecuado y se integró el gen en el cromosoma de *B. subtilis* mediante recombinación de homólogos en el locus de la pectato liasa (pel). El gen que codificaba la cloranfenicol-acetiltransferasa se utilizó como marcador (como se describe en (Diderichsen et al., 1993, Plasmid 30: 312-315). Los clones resistentes al cloranfenicol se analizaron secuenciando el ADN para verificar la secuencia de ADN correcta de la construcción.

La amilasa resultante que consistía en el dominio A y B del primer polipéptido parental y el dominio C del segundo polipéptido parental y que tiene las eliminaciones G182* y D183* es el polipéptido expuesto en la SEQ ID NO: 14.

Ejemplo 2: Generación de variantes de acuerdo con la invención

Las variantes de la presente invención se han generado mediante mutagénesis de sitio dirigido.

Se usó ADN genómico preparado a partir del organismo que contiene el gen de amilasa y el locus de pel como molde para generar los mutantes de sitio dirigido.

El cebador directo mutagénico y PnMi4490 (CAATCCAAGAGAACCCTGATACGGATG – SEQ ID NO: 16), el cebador inverso, se usaron para generar un fragmento de ~3.8 kb. Este fragmento se usó como un mega-cebador junto con PnMi4491 (CGGAACGCCTGGCTGACAACACG – SEQ ID NO: 17), el cebador directo, para obtener un casete de inserción de 6 kb. Para permitir la integración en el locus de Pel mediante doble sobrecruzamiento tras la transformación, junto con los genes de amilasa y cat, el casete contenía secuencias de Pel cadena arriba y cadena abajo en los extremos. La selección se efectuó en LB Agar que contenía cloranfenicol y se confirmó la mutación mediante secuenciación de ADN del gen de amilasa.

Se generó una biblioteca de variantes donde se efectuaron combinaciones de alteraciones en las siguientes posiciones: H1, T5, G7, Q11, N16, V17, Q32, A37, T40, P45, W48, G50, T51, N54, V56, A60, K72, R87, Q98, M105, G109, F113, R116, Q118, Q125, G133, T134, W140, G142, G149, T165, W167, Q169, R171, Q172, L173, A174, G184, A186, E190, T193, N195, G196, A204, V206, P211, V213, I214, L217, A225, L228, L235, V238, K242, S244, M246, L2502, G255, N260, A263, V264, A265, Y267, K269, N270, G273, S280, W284, T285, M286,

F289, V291, Y295, Q299, S304, R320, H321, S323, H324, V326, F328, T334, G337, Q345, G346, T355, S376, D377, D381, Y382, Q385, K391, y Q395 de las SEQ ID NO: 7 o 10; A420, G423, T444, A445, Q449, T459, P473, C474, G476, G477, y K484 de la SEQ ID NO: 13; e I405, A421, A422, A428, G448, D476 y G477 de la SEQ ID NO: 14.

Las variantes generadas se listan en los ejemplos siguientes.

Ejemplo 3: Rendimiento de lavado de las variantes generadas usando el ensayo de estrés mecánico automático (AMSA)

Para evaluar el rendimiento de lavado de las variantes de la presente invención en una composición base de detergente, pueden llevarse a cabo experimentos usando el ensayo de estrés mecánico automático (AMSA). Con el ensayo AMSA, se puede examinar el rendimiento de lavado de una gran cantidad de soluciones detergentes enzimáticas de volumen pequeño. La placa AMSA tiene una serie de ranuras para las soluciones de ensayo y una tapa que aprieta con firmeza la muestra del artículo textil que se ha de lavar contra todos los orificios de las ranuras. Durante el tiempo de lavado, la placa, las soluciones de ensayo, el artículo textil y la tapa se agitaron enérgicamente para que la solución de ensayo entrara en contacto con el artículo textil y para aplicar un estrés mecánico de modo regular, periódico y oscilante. Para consultar una descripción más detallada, remítase a WO 02/42740, especialmente el párrafo "Realizaciones especiales del método" en las páginas 23-24.

Descripción general del rendimiento de lavado

Se prepara una solución de ensayo que comprende agua (6°dH), 0.79 g/L de detergente, por ejemplo, detergente de modelo J como se describe más adelante y la enzima de la

invención a una concentración de 0, 0.05 o 0.2 mg de proteína enzimática/L. Se añadieron las telas manchadas con almidón (CS-28 del Center For Testmaterials BV, P.O. Box 120, 3133 KT, Vlaardingen, Países Bajos) y se lavaron durante 20 minutos a 15°C y 30°C o como alternativa, 20 minutos a 15°C y 40°C como se especifica más adelante. Después de un aclarado exhaustivo con agua del grifo y secado en la oscuridad, se midieron los valores de intensidad lumínica de los tejidos teñidos como una medida del rendimiento de lavado. Como blanco, se usó la prueba con 0 mg de proteína enzimática/l y correspondió a la contribución por parte del detergente. Preferentemente, se aplica una acción mecánica durante el paso de lavado, por ejemplo, en forma de vibración, rotación o agitación de la solución de lavado con las telas. Los experimentos de rendimiento de lavado AMSA se llevaron a cabo en las condiciones experimentales que se especifican a continuación:

Tabla A: Condiciones experimentales

Detergente	Detergente líquido modelo J (véase la tabla B)
Dosis del detergente	0.79 g/l
Volumen de la solución de ensayo	160 µL
pH	Tal como es
Tiempo de lavado	20 minutos
Temperatura	15 °C o 30 °C
Dureza del agua	6°dH
Concentración de la enzima en el ensayo	0.2 mg de proteína enzimática/L y 0.05 mg de proteína enzimática/L
Material de ensayo	CS-28 (algodón con almidón de arroz)

Tabla B: Detergente modelo J

Compuesto	**Contenido de compuesto (% p/p)**	**% de componente activo (% p/p)**
LAS sulfonatos de alquilbenceno lineales	5.15	5.00
AS sulfonatos de alquilbenceno	5.00	4.50
AEOS alquil etoxi sulfato	14.18	10.00
Ácido graso de coco	1.00	1.00
AEO etoxilato de alquilo	5.00	5.00
MEA monoetanolamina	0.30	0.30
MPG monopropilenglicol	3.00	3.00
Etanol	1.50	1.35
DTPA (en forma de sal de Na5) ácido pentasodio dietilentriaminapentaacético	0.25	0.10
Citrato de sodio	4.00	4.00
Formiato de sodio	1.00	1.00
Hidróxido de sodio	0.66	0.66
H_2O, sometida a intercambio de iones	58.95	58.95

La dureza del agua se ajustó a 6°dH mediante la adición de CaCl2, MgCl2 y NaHCO3 (Ca^{2+}:Mg^{2+}:$HCO3^-$ = 2:1:4.5) al sistema de ensayo. Tras el lavado, los artículos textiles se enjuagaron con agua del grifo y se secaron.

Tabla C: Condiciones experimentales

Detergente	Detergente líquido modelo A (véase la tabla D)
Dosis del detergente	3.33 g/l
Volumen de la solución de ensayo	160 µL
pH	Tal como es
Tiempo de lavado	20 minutos
Temperatura	15 °C o 40 °C
Dureza del agua	15°dH
Concentración de la enzima en el ensayo	0.2 mg de proteína enzimática/L, 0.05 mg de proteína enzimática/L
Material de ensayo	CS-28 (algodón con almidón de arroz)

Tabla D: Detergente modelo A

Compuesto	**Contenido de compuesto (% p/p)**	**% de componente activo (% p/p)**
LAS (sulfonatos de alquilbenceno lineales)	12.00	11.60
AEOS (alquil etoxi sulfato), SLES (lauril éter sulfato de sodio)	17.63	4.90
Ácido graso de soja	2.75	2.48
Ácido graso de coco	2.75	2.80
AEO (etoxilato de alquilo)	11.00	11.00
Hidróxido de sodio	1.75	1.80
Etanol / Propan-2-ol	3.00	2.70/0.30
MPG monopropilenglicol	6.00	6.00

Glicerol	1.71	1.70
TEA (trietanolamina)	3.33	3.30
Formiato de sodio	1.00	1.00
Citrato de sodio	2.00	2.00
DTMPA (ácido dietilentriaminapentaacético)	0.48	0.20
PCA polímero de tipo ácido policarboxílico	0.46	0.18
Fenoxietanol	0.50	0.50
H_2O, sometida a intercambio de iones	33.64	33.64

La dureza del agua se ajustó a 15°dH mediante la adición de CaCl2, MgCl2 y NaHCO3 (Ca^{2+}:Mg^{2+}:$HCO3^-$ = 4:1:7.5) al sistema de ensayo. Después del lavado, los materiales textiles se enjuagaron en agua del grifo y se secaron.

El rendimiento de lavado se midió como le brillo expresado como la intensidad de la luz reflejada por la muestra cuando se ilumina con luz blanca. Cuando la muestra estuvo manchada, la intensidad de la luz reflejada fue menor que la de la muestra limpia. Por lo tanto, la intensidad de la luz reflejada se puede utilizar para medir el rendimiento de lavado.

Las mediciones del color se efectuaron con un escáner plano profesional (EPSON Expression 10000XL, EPSON) usado para capturar una imagen del artículo textil lavado.

Con el fin de extraer un valor para la intensidad de la luz a partir de las imágenes escaneadas, los valores en píxeles de 48→24 bits de color de la imagen se convirtieron en valores para rojo, verde y azul (RBG, por sus siglas en inglés). El valor de la intensidad (Int) se

calcula sumando los valores RBG como vectores y tomando a continuación la longitud del vector resultante:

$$Int = \sqrt{r^2 + g^2 + b^2}$$

La expresión "rendimiento de lavado mejorado" del presente experimento se define como muestra de una alteración del rendimiento de lavado de una variante de la presente invención en relación con el rendimiento de lavado del polipéptido que tiene una secuencia de aminoácidos como se expone en la SEQ ID NO: 15. La alteración puede verse, por ejemplo, con un aumento en la eliminación de manchas. El rendimiento de lavado mejorado se determinó como se ha descrito anteriormente. Se consideró que el rendimiento de lavado estaba mejorado en caso de que el factor de mejora (IF) fuese de al menos 1.0, preferentemente de al menos 1.05 en una o más de las condiciones listadas anteriormente; es decir, en el detergente modelo A a 15°C o 40°C, donde la concentración de la variante era de 0.05 o 0.2 mg/l o en el detergente modelo J a 15°C o 30°C, donde la concentración de la variante era de 0.05 o 0.2 mg/L. Las condiciones de lavado fueron como se han descrito anteriormente en las tablas A y C.

Las expresiones "intensidad delta" o "valor de intensidad delta", tal como se usan ene l presente documento, se refieren al resultado de una medición de intensidad de un material de ensayo, por ejemplo, una muestra de CS-28 (Center For Testmaterals BV, P.O. Box 120, 3133 KT Vlaardingen, Países Bajos). La muestra se midió con una porción de la muestra lavada en condiciones idénticas, como fondo. La intensidad delta es el valor de intensidad del material de ensayo lavado con amilasa restando el valor de intensidad del material de ensayo lavado sin amilasa.

Los rendimientos de lavado de las variantes de acuerdo con la invención obtenidas mediante AMSA son los siguientes;

Modificaciones en la SEQ ID NO: 13	A-15-0.05mg/L	A-15-0.2mg/L	A-40-0.05mg/L	A-40-0.2mg/L	J-15-0.05mg/L	J-15-0.2mg/L	J-30-0.05mg/L	J-30-0.2mg/L
Referencia	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0
G182*+D183*+N195F	1.0	1.3	1.1	1.0	1.5	1.3	1.0	1.0
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K	2.1	1.9	1.2	1.2	2.6	2.0	1.5	1.3
H1*+N54S+V56T+R87S+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K	2.8	2.2	1.3	1.1	2.6	2.4	1.9	1.5
H1*+T40G+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K	2.2	1.7	1.3	1.1	2.5	2.2	1.9	1.6
H1*+T51K+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K	2.7	2.1	1.3	1.1	3.2	2.3	2.0	1.5
H1*+N54S+V56T+K72R+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K	2.6	2.2	1.2	1.0	2.6	2.5	1.7	1.5
H1*+N54S+V56T+K72H+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K	2.5	2.4	1.4	1.1	2.6	2.3	1.7	1.6
H1*+A37H+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K	2.8	2.7	1.4	1.2	2.8	2.8	1.9	1.6

H1*+A37M+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K	2.0	2.3	1.4	1.2	2.7	2.5	2.1	1.6
H1*+A37V+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K	3.0	2.6	1.4	1.2	3.1	2.5	2.2	1.7
H1*+A37S+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K	2.9	2.5	1.2	1.2	2.9	2.3	1.5	1.3
H1*+A37Y+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K	2.6	2.0	1.3	1.2	2.5	2.1	1.5	1.3
H1*+A37R+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K	2.2	1.9	1.3	1.2	2.5	2.1	1.4	1.3
H1*+N54S+V56T+G109A+F113W+A174S+G182*+D183*+N195F+V206L+K391A+G476K	2.8	2.2	1.3	1.2	2.7	2.1	1.5	1.2
H1*+N54S+V56T+G109A+F113S+A174S+G182*+D183*+N195F+V206L+K391A+G476K	2.3	1.9	1.3	1.1	2.4	1.7	1.3	1.2
H1*+N54S+V56T+G109A+F113N+A174S+G182*+D183*+N195F+V206L+K391A+G476K	2.0	1.9	1.2	1.2	2.3	2.1	1.4	1.2
H1*+N54S+V56T+G109A+F113Y+A174S+G182*+D183*+N195F+V206L+K391A+G476K	1.9	2.1	1.2	1.2	3.1	2.3	1.5	1.3
H1*+N54S+V56T+G109A+F113R+A174S+G182*+D183*+N195F+V206L+K391A+G476K	1.0	1.4	1.2	1.2	2.0	1.8	1.4	1.3

H1*+N54S+V56T+G109A+Q118N+A174S+G182*+D183*+N195F+V206L+K391A+G476K	1.9	1.8	1.3	1.2	2.9	2.3	1.5	1.3
H1*+N54S+V56T+G109A+R116Q+A174S+G182*+D183*+N195F+V206L+K391A+G476K	2.6	2.0	1.2	1.2	3.5	2.6	1.7	1.4
H1*+N54S+V56T+G109A+R116V+A174S+G182*+D183*+N195F+V206L+K391A+G476K	2.1	2.0	1.1	1.1	2.7	2.3	1.6	1.3
H1*+N54S+V56T+G109A+R116K+A174S+G182*+D183*+N195F+V206L+K391A+G476K	2.2	2.1	1.2	1.1	2.4	2.2	1.4	1.3
H1*+N54S+V56T+G109A+R116W+A174S+G182*+D183*+N195F+V206L+K391A+G476K	1.8	2.0	0.7	0.9	1.1	1.9	1.0	1.2
H1*+N54S+V56T+G109A+R116L+A174S+G182*+D183*+N195F+V206L+K391A+G476K	1.8	1.8	1.2	1.1	1.9	2.0	1.3	1.2
H1*+N54S+V56T+G109A+G142T+A174S+G182*+D183*+N195F+V206L+K391A+G476K	1.6	1.7	1.2	1.1	1.9	2.0	1.3	1.1
H1*+N54S+V56T+G109A+Q125P+A174S+G182*+D183*+N195F+V206L+K391A+G476K	2.1	2.1	1.2	1.1	2.4	2.0	1.4	1.3
H1*+N54S+V56T+G109A+Q125K+A174S+G182*+D183*+N195F+V206L+K391A+G476K	1.9	1.8	1.3	1.1	2.6	1.9	1.5	1.2
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+S381G+K391A+G476K	2.3	2.1	1.0	1.0	2.5	2.2	1.4	1.2

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+M246T+K391A+G476K	2.0	1.9	1.1	1.0	2.6	1.8	1.5	1.2
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+V213T+K391A+G476K	1.9	1.9	1.1	1.1	2.8	2.1	1.5	1.3
H1*+A37L+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K	2.5	2.2	1.2	1.1	2.5	2.2	1.8	1.4
H1*+N54S+V56T+G109A+Q118K+A174S+G182*+D183*+N195F+V206L+K391A+G476K	1.8	2.0	1.2	1.1	1.5	1.6	1.4	1.2
H1*+N54S+V56T+G109A+R116A+A174S+G182*+D183*+N195F+V206L+K391A+G476K	2.7	2.3	1.2	1.1	2.4	2.1	1.6	1.3
H1*+N54S+V56T+G109A+R116H+A174S+G182*+D183*+N195F+V206L+K391A+G476K	2.9	2.4	1.3	1.2	2.4	2.3	1.9	1.5
H1*+N54S+V56T+G109A+Q125A+A174S+G182*+D183*+N195F+V206L+K391A+G476K	2.1	2.0	1.1	1.2	3.1	2.1	1.5	1.2
H1*+N54S+V56T+G109A+Q172G+A174S+G182*+D183*+N195F+V206L+K391A+G476K	2.6	2.1	1.4	1.2	2.7	2.2	2.1	1.5
H1*+N54S+V56T+G109A+Q172R+A174S+G182*+D183*+N195F+V206L+K391A+G476K	2.6	2.2	1.4	1.2	2.7	2.4	2.0	1.5
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+D377S+K391A+G476K	2.4	1.7	1.3	1.2	2.8	1.8	1.7	1.3

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+D377G+K391A+G476K	1.7	1.7	1.2	1.1	2.3	1.5	1.7	1.3
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+D377R+K391A+G476K	1.9	1.5	1.1	1.1	2.6	1.6	1.4	1.2
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+D377A+K391A+G476K	2.0	1.9	1.2	1.0	2.8	1.9	1.5	1.2
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+I214G+K391A+G476K	1.6	1.6	1.3	1.1	2.9	1.7	1.5	1.1
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+S381A+K391A+G476K	2.3	1.6	1.4	1.2	2.8	1.9	1.6	1.4
H1*+N54S+V56T+G109A+W167I+A174S+G182*+D183*+N195F+V206L+K391A+G476K	1.7	1.9	1.3	1.2	2.8	1.8	1.6	1.3
H1*+N54S+V56T+G109A+W167G+A174S+G182*+D183*+N195F+V206L+K391A+G476K	1.5	1.8	1.2	1.1	2.5	1.8	1.5	1.3
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+G346S+K391A+G476K	1.7	1.8	1.3	1.2	2.8	2.0	1.6	1.3
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+G346P+K391A+G476K	2.1	1.9	1.3	1.1	2.9	2.1	1.6	1.3
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+I214H+K391A+G476K	2.2	1.7	1.3	1.1	2.2	2.1	1.7	1.3

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+I214S+K391A+G476K	2.3	1.8	1.3	1.1	2.9	2.0	1.5	1.3
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+I214T+K391A+G476K	1.9	1.7	1.3	1.2	2.4	1.7	1.6	1.3
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+A420Q+G476K	2.0	1.7	1.2	1.1	1.9	1.7	1.3	1.1
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+A420S+G476K	2.0	1.8	1.2	1.1	2.6	1.8	1.5	1.3
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+A420K+G476K	2.2	1.9	1.3	1.2	2.3	1.8	1.7	1.4
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+A420L+G476K	2.2	2.0	1.3	1.2	2.4	1.9	1.2	1.3
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+K391Y+G476K	2.0	1.9	1.3	1.2	2.9	1.9	1.1	1.3
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+K391R+G476K	1.9	1.9	1.3	1.2	2.5	1.7	1.4	1.4
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+P473R+G476K	2.2	1.9	1.2	1.2	3.4	2.0	2.1	1.3
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+P473A+G476K	2.5	1.8	1.5	1.1	3.4	1.9	1.9	1.4

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+P473G+G476K	2.5	1.9	1.3	1.2	2.8	1.9	1.5	1.3
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+P473T+G476K	1.9	1.7	1.3	1.2	2.5	1.9	1.5	1.2
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+Q395P+G476K	1.8	1.6	1.3	1.1	2.3	1.8	1.8	1.4
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+T444Q+G476K	1.7	1.8	1.3	1.2	2.8	2.0	1.4	1.3
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+T444S+G476K	1.7	1.8	1.3	1.2	2.8	2.0	1.5	1.4
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+T444D+G476K	2.3	1.8	1.3	1.3	3.0	2.3	1.7	1.4
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+T444Y+G476K	2.0	1.7	1.5	1.2	2.0	2.1	1.8	1.5
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+S280W+K391A+G476K	2.3	1.7	1.3	1.1	2.5	2.0	1.5	1.3
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+S280L+K391A+G476K	2.1	1.7	1.2	1.1	2.5	1.8	1.4	1.3
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+S280T+K391A+G476K	1.7	1.6	1.1	1.1	2.4	1.6	1.3	1.2

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+S280A+K391A+G476K	1.9	1.4	1.2	1.0	2.3	1.8	1.3	1.1
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+G255N+K391A+G476K	1.9	1.7	1.2	1.2	2.6	2.1	1.5	1.4
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+T285L+K391A+G476K	1.9	1.8	1.3	1.2	2.3	2.2	1.5	1.3
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+T285Q+K391A+G476K	1.6	1.7	1.2	1.2	2.2	2.1	1.6	1.3
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+Q449T+G476K	1.8	1.6	1.1	1.1	1.8	1.6	1.2	1.2
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+P473K+G476K	1.8	1.7	1.3	1.1	2.2	2.0	1.3	1.2
H1*+N54S+V56T+K72S+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K	2.5	2.3	1.2	1.1	3.7	2.2	1.5	1.4
H1*+T40K+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+G346T+K391A+G476K	2.3	2.1	1.2	1.1	2.0	1.7	1.5	1.3
H1*+G50A+N54S+V56T+G109A++Q172N+A174S+G182*+D183*+N195F+V206L+K391A+G476K	2.4	2.1	1.2	1.2	2.0	1.9	1.4	1.3
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K+K484A	1.9	1.7	1.3	1.0	2.4	1.6	1.5	1.3

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K+K484G	1.8	1.8	1.2	1.0	2.2	1.8	1.4	1.2
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K+K484P	1.8	1.7	1.1	1.0	2.4	2.0	1.4	1.3
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K+K484E	1.9	1.4	1.2	1.1	2.5	1.7	1.3	1.2
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K+K484Q	1.7	1.5	1.1	1.0	2.0	1.3	1.3	1.2
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K+K484S	2.3	2.0	1.2	1.2	2.7	1.7	1.6	1.4
H1*K+G50A+N54S+V56T+G109A+W167F+A174S+G182*+D183*+N195F+V206L+K391A+G476K	2.1	1.9	1.1	1.1	2.2	1.7	1.3	1.2
H1*+N54S+V56T+G109A+L173V+A174S+G182*+D183*+N195F+A204T+V206L+K391A+G476K	2.2	1.8	1.1	1.1	2.2	1.7	1.1	1.1
H1*+N54S+V56T+G109A+W140Y+A174S+G182*+D183*+N195F+V206L+K391A+G476K	2.2	1.9	1.2	1.1	2.5	1.9	1.3	1.3
H1*+N54S+V56T+Q98S+G109A+A174S+G182*+D183*+N195F+V206L+R320A+K391A+G476K	1.9	1.8	1.2	1.1	2.1	1.8	1.1	1.1
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+H324L+K391A+G476K	1.9	1.7	1.1	1.1	2.1	1.5	1.2	1.1

H1*+N54S+V56T+G109A+G149Q+A174S+G182*+D183*+N195F+V206L+K391A+G476K	1.7	1.9	1.2	1.2	1.6	1.4	1.0	1.2
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+G346T+K391A+G476K+G477A	2.1	2.0	1.2	1.2	2.3	1.7	1.2	1.2
H1*+N54S+V56T+G109AG255A++A174S+G182*+D183*+N195F+V206L+K391A+G476K	2.1	2.0	1.2	1.2	2.3	1.8	1.2	1.2
H1*+G50A+N54S+V56T+G109A+F113L+R116L+A174S+G182*+D183*+N195F+V206L+K391A+G476K	2.3	2.2	1.2	1.1	2.6	2.2	1.3	1.2
H1*+N54S+V56T+G109A+W167F+A174S+G182*+D183*+N195F+V206L+K391A+G476K	2.0	1.9	1.1	1.0	2.3	2.0	1.4	1.2
H1*+N54S+V56T+G109A+L173V+A174S+G182*+D183*+N195F+V206L+K391A+G476K	1.8	1.9	1.0	1.0	2.2	1.8	1.4	1.3
H1*+N54S+V56T+K72R+G109A+W167F+A174S+G182*+D183*+N195F+V206L+K391A+G476K	2.1	1.7	1.1	1.1	2.9	2.0	1.4	1.3
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K+G477Q	1.8	1.4	1.0	1.1	2.4	1.9	1.4	1.3
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+Q345D+K391A+G476K+G477Q	1.6	1.5	1.0	1.0	2.2	1.7	1.3	1.2
H1*+G50A+N54S+V56T+G109A+Q172D+A174S+G182*+D183*+N195F+V206L+K391A+G476K	1.9	1.9	0.9	1.1	2.1	1.9	1.6	1.3

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+V264I+K391A+G423H+G476K	1.9	1.9	0.7	1.0	2.2	2.0	1.4	1.3
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+R320V+K391A+G476Y	2.1	2.0	0.8	1.0	2.1	2.1	1.5	1.3
H1*+T5K+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K	1.7	1.8	0.9	1.0	1.8	1.7	1.4	1.2
H1*+N54S+V56T+G109A+R116M+A174S+G182*+D183*+N195F+V206L+K391A+G476K	2.9	2.2	1.2	1.1	2.8	2.1	1.2	1.1
H1*+N54S+V56T+G109A+Q172Y+A174S+G182*+D183*+N195F+V206L+K391A+G476K	2.1	1.8	1.1	1.1	1.9	1.8	1.4	1.1
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+I214L+K391A+G476K	2.0	1.7	1.1	1.1	1.9	1.7	1.3	1.2
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+L217V+K391A+G476K	2.2	1.9	1.2	1.2	2.2	2.2	1.3	1.2
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+L217H+K391A+G476K	2.2	1.7	1.2	1.2	2.3	2.1	1.4	1.2
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+P211D+K391A+G476K	2.1	2.0	1.1	1.1	2.3	2.1	1.2	1.2
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+K391Q+G476K	2.1	1.9	1.1	1.2	2.3	1.9	1.3	1.3

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+T444H+G476K	2.0	1.9	1.1	1.1	2.3	1.9	1.4	1.2
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+T444V+G476K	2.2	1.7	1.1	1.0	2.3	1.8	1.2	1.2
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+T444R+G476K	2.0	1.6	1.2	1.1	1.9	1.8	1.3	1.2
H1*+G50A+N54S+V56T+G109A+L173V+A174S+G182*+D183*+N195F+A204V+V206L+K391A+G476K	2.4	2.1	1.2	1.2	3.2	2.2	1.6	1.4
H1*+G50A+N54S+V56T+G109A+F113L+W167F+A174S+G182*+D183*+N195F+V206L+K391A+G476K	1.9	1.7	1.0	1.1	2.1	1.8	1.2	1.2
H1*+G7K+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+R320A+K391A+G476K	2.0	1.8	1.1	1.1	2.7	2.1	1.6	1.2
H1*+N54S+V56T+G109A+Q118G+A174S+G182*+D183*+N195F+V206L+K391A+G476K	1.7	1.8	1.1	1.1	2.4	1.6	1.5	1.2
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+S280K+K391A+G476K	1.6	1.6	1.0	1.1	1.6	1.6	1.3	1.2
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+N270G+K391A+G476K	1.4	1.6	1.1	1.1	1.8	1.6	1.4	1.2

H1*+N54S+V56T+G109A+Q172D+A174S+G182*+D183*+N195F+V206L+G346T+K391A+G476K+G477A	2.1	1.9	1.2	1.1	3.1	2.3	1.6	1.4
H1*+N54S+V56T+G109A+Q118S+A174S+G182*+D183*+N195F+V206L+K391A+G476K	2.1	1.9	1.1	1.1	1.8	1.5	1.4	1.2
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+R320A+K391A+G476K	2.0	1.9	1.2	1.2	2.3	1.7	1.5	1.3
H1*+N54S+V56T+G109A+T134E+A174S+G182*+D183*+N195F+V206L+K391A+G476K	2.4	2.1	1.2	1.1	2.8	2.4	1.4	1.4
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+G337H+Q385L+K391A+G476K	1.7	1.8	1.0	1.0	1.8	1.8	1.2	1.2
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+Y382M+K391A+G476K	2.0	1.8	1.1	1.1	2.2	1.9	1.3	1.2
H1*+N54S+V56T+K72R+G109A+A174S+G182*+D183*+N195F+V206L+G255A+D377H+K391A+G476K	1.9	1.9	1.1	1.1	2.7	2.2	1.4	1.3
H1*+N54S+V56T+K72R+G109A+T134E+A174S+G182*+D183*+N195F+V206L+G255A+K391A+G476K	2.4	2.0	1.2	1.1	3.0	2.3	1.4	1.3
H1*+N54S+V56T+K72R+M105F+G109A+A174S+G182*+D183	2.0	1.7	1.2	1.1	2.5	2.0	1.4	1.2

*+N195F+V206L+G255A+K391A+ G476K								
H1*+N54S+V56T+M105F+G109A+T134E+A174S+G182*+D183*+N195F+V206L+K391A+G476K	2.0	1.9	1.0	1.0	2.3	2.1	1.2	1.1
H1*+N54S+V56T+M105F+G109A+Q118F+T134E+A174S+G182*+D183*+N195F+V206L+K391A+ G476K	1.9	1.7	1.1	1.1	1.7	1.9	1.3	1.2
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+R320A+S323N+D377H+K391A+ G476K	2.0	1.9	1.1	1.0	2.3	2.0	1.4	1.3
H1*+T51E+N54S+V56T+G109A+A174H+G182*+D183*+N195F+V206L+K391A+G476K	2.3	1.9	1.2	1.1	2.6	2.2	1.6	1.4
H1*+N54S+V56T+G109A+L173A+A174S+G182*+D183*+N195F+V206L+K391A+G476K	2.4	2.0	1.3	1.2	2.4	2.0	1.6	1.4
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+Q299V+K391A+G476K	2.5	2.0	1.3	1.2	2.4	1.6	1.6	1.4
H1*+N54S+V56T+G109A+L173G+A174S+G182*+D183*+N195F+V206L+K391A+G476K	2.2	2.0	1.3	1.2	2.3	1.9	1.7	1.4
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+T355L+K391A+G476K	2.1	2.0	1.3	1.2	2.4	2.0	1.5	1.3

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+T355F+K391A+G476K	1.3	1.7	1.0	1.0	1.9	1.6	1.2	1.1
H1*+G50A+N54S+V56T+G109A+A174S+G182*+D183*+N195F+A204T+V206L+K391A+G476K	2.3	2.0	1.2	1.1	2.1	1.8	1.4	1.3
H1*+G50A+N54S+V56T+G109A+A174E+G182*+D183*+N195F+A204T+V206L+K391A+G476K	1.8	1.6	1.1	1.1	2.1	1.8	1.2	1.2
H1*+N54S+V56T+K72R+G109A+A174S+G182*+D183*+N195F+V206L+R320A+S323N+K391A+G476K	2.2	1.8	1.2	1.1	2.7	2.1	1.4	1.2
H1*+N54S+V56T+M105I+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K	1.8	1.8	1.1	1.1	1.5	1.5	1.3	1.2
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+M246L+K391A+G476K	2.0	1.8	1.1	1.0	1.8	1.6	1.3	1.2
H1*+T51G+N54S+V56T+G109A+A174N+G182*+D183*+N195F+V206L+K391A+G476K	1.6	1.5	1.0	1.0	2.1	1.7	1.3	1.1
H1*+T51A+N54S+V56T+G109A+A174G+G182*+D183*+N195F+V206L+K391A+G476K	1.4	1.5	0.9	0.9	1.6	1.5	1.3	1.0
H1*+N54S+V56T+G109A+A174D+G182*+D183*+N195F+V206L+K391A+G476K	1.9	1.5	1.0	1.0	1.5	1.5	1.1	1.0
H1*+T51S+N54S+V56T+G109A+A174P+G182*+D183*+N195	1.7	1.7	0.9	1.0	1.1	1.2	0.8	0.9

F+V206L+K391A+G476K								
H1*+T51G+N54S+V56T+G109A+A174M+G182*+D183*+N195F+V206L+K391A+G476K	1.3	1.5	1.0	1.0	1.6	1.5	0.9	1.1
H1*+N54S+V56T+G109A+K72A+W167R+A174S+G182*+D183*+N195F+V206L+K391A+G476K	0.9	1.2	0.5	0.7	0.7	0.8	0.4	0.7
H1*+N54S+V56T+K72A+G109A+W167S+A174S+G182*+D183*+N195F+V206L+K391A+G476K	1.6	1.8	0.4	0.8	0.7	1.2	0.6	0.8
H1*+N54S+V56T+K72R+G109A+W167R+A174S+G182*+D183*+N195F+V206L+K391A+G476K	1.1	1.1	0.8	0.8	0.7	0.8	0.7	0.7
H1*+N54S+V56T+K72Q+G109A+W167H+A174S+G182*+D183*+N195F+V206L+K391A+G476K	2.4	2.2	0.9	1.0	1.8	1.7	1.0	1.1
H1*+N54S+V56T+G109A+Q118R+T134E+A174S+G182*+D183*+N195F+V206L+D377H+K391A+G476K	1.8	1.7	1.1	1.0	2.1	1.7	1.2	1.1
H1*+Q11H+N54S+V56T+G109A+Q118R+T134E+A174S+G184T+G182*+D183*+N195F+V206L+D377H+K391A+G476K	1.9	1.6	1.1	1.0	2.2	1.6	1.3	1.3
H1*+N54S+V56T+K72R+G109A+T134E+A174S+G182*+D183*+N195F+V206L+K391A+G476K	2.3	2.1	1.2	1.1	3.2	1.9	1.3	1.3
H1*+N54S+V56T+K72R+G109A+T134E+A174S+G182*+D183	2.2	2.0	1.1	1.0	3.8	1.9	1.3	1.2

*+N195F+V206L+D377H+K391A+ G476K								
H1*+N54S+V56T+K72R+G109A+T134E+A174S+G182*+D183 *+G184T+N195F+V206L+K391A+ G476K	2.2	2.0	1.2	1.1	3.9	2.4	1.4	1.3
H1*+N54S+V56T+G109A+Q118R+T134E+A174S+G182*+D18 3*+N195F+V206L+G255A+K391A+ G476K	2.0	1.9	1.0	1.2	2.5	2.0	1.2	1.1
H1*+N54S+V56T+G109A+Q118R+A174S+G182*+D183*+N19 5F+V206L+D377H+K391A+G476K	2.2	1.9	1.1	1.1	2.8	1.8	1.2	1.2
H1*+N54S+V56T+G109A+T134E+A174S+G182*+D183*+G18 4T+N195F+V206L+D377H+K391A+ G476K	2.1	2.1	1.0	1.1	3.4	2.3	1.3	1.3
H1*+N54S+V56T+G109A+Q172D+A174Q+G182*+D183*+N19 5F+V206L+K391A+G476K+G477A	2.0	1.9	1.2	1.1	3.0	2.2	1.1	1.2
H1*+N54S+V56T+K72A+G109A+W167F+A174S+G182*+D183 *+N195F+V206L+K391A+G476K	1.1	1.4	0.6	0.8	1.5	1.3	1.0	0.8
H1*+N54S+V56T+G109A+W167S+G182*+D183*+N195F+A17 4S+V206L+K391A+G476K	1.4	1.3	0.8	1.0	1.5	1.6	1.3	1.1
H1*+N54S+V56T+K72H+G109A+W167S+A174S+G182*+D183	1.4	1.4	0.5	1.0	1.0	1.4	0.8	1.1

*+N195F+V206L+K391A+G476K								
H1*+N54S+V56T+K72R+G109A+W167T+A174S+G182*+D183*+N195F+V206L+K391A+G476K	1.3	1.2	0.8	0.8	1.2	1.0	1.1	1.0
H1*+N54S+V56T+K72E+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K	1.3	1.4	0.8	0.9	1.4	1.3	0.9	0.9
H1*+N54S+V56T+K72R+G109A+W167L+A174S+G182*+D183*+N195F+V206L+K391A+G476K	1.6	1.6	1.1	1.1	2.0	1.5	1.4	1.2
H1*+N54S+V56T+K72R+G109A+W167M+A174S+G182*+D183*+N195F+V206L+K391A+G476K	1.5	1.6	0.8	1.0	1.5	1.3	1.2	1.2
H1*+N54S+V56T+K72R+G109A+W167H+A174S+G182*+D183*+N195F+V206L+K391A+G476K	1.3	1.4	0.6	1.0	1.6	1.3	0.9	1.1
H1*+N54S+V56T+K72R+G109A+A174S+G182*+D183*+G184T+N195F+V206L+G255A+K391A+G476K	2.0	1.9	1.2	1.1	2.5	2.0	1.4	1.3
H1*+N54S+V56T+G109A+A174S+G182*+D183*+G184T+N195F+V206L+D377H+K391A+G476K	2.2	1.9	1.1	1.1	2.3	1.9	1.5	1.4
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+G255A+D377H+K391A+G476K	2.1	2.0	1.2	1.0	2.1	1.7	1.3	1.3
H1*+N54S+V56T+G109A+Q118R+A174S+G182*+D183*+N195F+V206L+G255A+D377H+K391A+G476K	1.2	1.5	1.0	1.0	1.8	1.2	1.0	1.0

H1*+N54S+V56T+G109A+A174S+G182*+D183*+G184A+T193K+N195F+V206L+K391A+G476K	1.2	1.3	0.9	1.0	1.3	1.3	1.0	1.0
H1*+N54S+V56T+M105F+G109A+A174S+G182*+D183*+G184T+N195F+V206L+K391A+G476K	1.9	2.0	1.1	1.2	2.1	1.9	1.4	1.3
H1*+N54S+V56T+G109A+T134E+A174S+G182*+D183*+N195F+V206L+R320A+S323N+K391A+ G476K	1.7	2.1	1.1	1.1	2.1	2.0	1.3	1.3
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+V291G+D377H+K391A+G476K	1.7	1.8	1.2	1.1	2.1	1.9	1.4	1.3
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+V291A+F328L+D377H+K391A+ G476K	1.7	1.9	1.1	1.1	2.1	1.9	1.3	1.3
H1*+V56T+G109A+A174S+G182*+D183*+N195F+V206L+D377H+K391A+G476K	1.3	1.8	1.1	1.1	1.5	1.5	1.3	1.2
H1*+N54S+V56T+G109A+T134E+A174S+G182*+D183*+G184T +N195F+V206L+K391A+G476K	2.4	2.2	1.1	1.1	3.0	2.4	1.5	1.3
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+V238A+D377H+K391A+G476K	1.7	1.8	1.2	1.1	2.1	1.9	1.4	1.2
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+V238T+D377H+K391A+G476K	2.0	1.8	1.1	1.1	2.5	1.9	1.3	1.2

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+V238G+D377H+K391A+G476K	1.9	1.6	1.1	1.1	2.3	1.8	1.2	1.2
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+F328M+D377H+K391A+G476K	1.6	1.8	1.0	1.0	2.1	1.8	1.2	1.2
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+F328L+D377H+K391A+G476K	1.6	1.7	0.9	1.0	1.7	1.5	1.0	1.1
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+F328V+D377H+K391A+G476K	1.6	1.6	0.8	1.0	1.8	1.7	1.0	1.1
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+F328I+D377H+K391A+G476K	1.6	1.6	0.9	1.1	2.0	1.6	1.1	1.0
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+V291T+D377H+K391A+G476K	1.9	1.8	1.2	1.1	2.4	1.9	1.3	1.2
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+V291A+D377H+K391A+G476K	2.4	1.9	1.2	1.2	2.9	2.1	1.5	1.3
H1*+N54S+V56T+K72R+G109A+T134E+A174S+G182*+D183*+G184T+N195F+V206L+G255A+K391A+G476K	2.1	1.9	1.0	1.1	2.1	2.0	1.4	1.2
H1*+N54S+V56T+G109A+L173H+A174S+G182*+D183*+N195F+V206L+K391A+G476K	2.0	1.8	1.2	1.1	2.6	2.0	1.4	1.2
H1*+N54S+V56T+G109A+Q125T+A174S+G182*+D183*+N19	1.4	1.7	0.9	1.0	2.0	1.8	1.2	1.0

5F+V206L+K391A+G476K								
H1*+N16S+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K	1.9	1.6	1.0	1.0	2.1	1.9	1.3	1.2
H1*+N54S+V56T+K72N+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K	2.1	1.6	1.0	1.0	2.1	2.2	1.3	1.3
H1*+N54S+V56T+K72N+G109A+W167L+A174S+G182*+D183*+N195F+V206L+K391A+G476K	2.2	1.9	0.9	1.2	1.9	2.1	1.2	1.2
H1*+N54S+V56T+K72A+G109A+W167Y+A174S+G182*+D183*+N195F+V206L+K391A+G476K	1.7	1.8	0.8	1.1	1.6	2.0	1.1	1.2
H1*+N54S+V56T+G109A+Q118R+T134E+A174S+G182*+D183*+N195F+V206L+G255A+D377H+K391A+G476K	2.0	1.9	1.0	1.1	2.0	2.0	1.2	1.2
H1*+N54S+V56T+K72R+G109A+A174S+G182*+D183*+N195F+G184T+V206L+K391A+G476K	2.2	2.1	1.1	1.1	3.3	2.5	1.5	1.3
H1*+N54S+V56T+K72R+G109A+Q118R+A174S+G182*+D183*+G184T+N195F+V206L+D377H+K391A+G476K	0.9	1.3	0.8	0.9	1.3	1.5	1.0	1.1
H1*+N54S+V56T+K72R+G109A+Q118R+A174S+G182*+D183*+N195F+V206L+G255A+D377H+K391A+G476K	2.4	2.1	1.2	1.2	2.8	2.2	1.5	1.3

H1*+N54S+V56T+G109A+A174S+G182*+D183*+G184T+N195F+V206L+R320A+S323N+K391A+G476K	1.9	1.8	1.2	1.1	2.5	2.0	1.5	1.4
H1*+N54S+G109A+A174S+G182*+D183*+N195F+V206L+D377H+K391A+G476K	1.5	1.7	1.1	1.1	2.3	1.8	1.4	1.3
H1*+N54S+V56T+A174S+G182*+D183*+N195F+V206L+D377H+K391A+G476K	1.8	1.7	1.1	0.9	2.1	1.7	1.4	1.2
H1*+N54S+V56T+G109A+G182*+D183*+N195F+V206L+D377H+K391A+G476K	2.0	1.8	1.2	1.2	2.6	1.7	1.3	1.2
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+D377H+K391A+G476K	1.6	1.6	1.3	1.1	2.8	2.1	1.5	1.2
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+D377H+K391A+G476K	2.0	1.6	1.1	1.1	2.6	2.0	1.3	1.1
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+D377H+G476K	2.2	2.0	1.2	1.1	2.6	1.9	1.5	1.4
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+D377H+K391A	2.0	1.9	1.2	1.1	2.5	1.8	1.6	1.4
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+D377R+K391A+G476K	1.4	1.6	1.1	1.0	1.5	1.7	1.3	1.0
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V20	1.5	1.7	1.1	1.0	2.3	1.2	1.4	1.2

6L+L217T+K391A+G476K								
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+D377S+K391A+G476K	2.0	1.8	1.3	1.2	2.4	1.8	1.5	1.4
H1*+N54S+V56T+G109A+R116E+A174S+G182*+D183*+N195F+V206L+K391A+G476K	2.0	1.9	1.2	1.1	2.3	2.0	1.5	1.3
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+L217Q+K391A+G476K	1.5	1.7	1.0	1.1	1.7	1.4	1.2	1.2
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+G346D+K391A+G476K	1.3	1.5	1.0	1.0	1.7	1.6	1.2	1.2
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+D377A+K391A+G476K	1.9	1.7	1.1	1.2	2.5	1.7	1.4	1.3
H1*+N54S+V56T+G109A+T134E+A174S+G182*+D183*+N195F+V206L+D377H+K391A+G476K	2.2	2.1	1.2	1.1	2.3	2.1	1.1	1.2
H1*+N54S+V56T+G109A+Q118R+T134E+A174S+G182*+D183*+G184T+N195F+V206L+K391A+G476K	1.9	1.7	1.3	1.2	2.0	1.7	1.2	1.2
H1*+N54S+V56T+K72R+G109A+Q118R+T134E+A174S+G182*+D183*+N195F+V206L+K391A+G476K	1.9	1.7	1.1	1.1	2.1	1.9	1.0	1.1
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V20	1.7	1.6	1.2	1.1	2.3	1.9	1.2	1.1

6L+G346P+K391A+G476K								
H1*+N54S+V56T+G109A+R116S+A174S+G182*+D183*+N195F+V206L+K391A+G476K	2.0	1.8	1.2	1.1	2.1	1.9	1.1	1.2
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+D377Q+K391A+G476K	1.7	1.8	1.2	1.1	2.0	2.0	1.2	1.2
H1*+N54S+V56T+G109A+R116I+A174S+G182*+D183*+N195F+V206L+K391A+G476K	2.2	1.8	1.2	1.1	2.1	2.0	1.3	1.3
H1*+N54S+V56T+G109A+A174F+G182*+D183*+N195F+V206L+K391A+G476K	1.7	1.5	1.1	1.0	1.5	1.6	1.3	1.2
H1*+N54S+V56T+G109A+R116G+A174S+G182*+D183*+N195F+V206L+K391A+G476K	2.0	1.9	1.2	1.2	2.1	2.0	1.0	1.2
H1*+N54S+V56T+G109A+A174T+G182*+D183*+N195F+V206L+K391A+G476K	1.9	1.8	1.2	1.2	1.9	2.0	1.1	1.2
H1*+N54S+V56T+G109A+Q118R+T134E+A174S+G182*+D183*+G184T+N195F+V206L+G255A+ K391A+G476K	1.5	1.8	1.1	1.0	1.9	1.9	1.4	1.2
H1*+N54S+V56T+K72R+G109A+Q118R+T134E+A174S+G182*+D183*+N195F+V206L+G255A+ K391A+G476K	1.7	1.8	1.1	1.0	2.2	1.8	1.5	1.2
H1*+T51G+N54S+V56T+G109A+Q172R+A174S+G182*+D183	1.2	1.6	1.0	1.0	1.6	1.4	1.3	1.1

*+N195F+V206L+K391A+G476K								
H1*+T51A+N54S+V56T+G109A+Q172D+A174S+G182*+D183 *+N195F+V206L+K391A+G476K	1.5	1.7	1.0	1.0	2.3	1.9	1.4	1.2
H1*+T51S+N54S+V56T+G109A+Q172M+A174S+G182*+D183 *+N195F+V206L+K391A+G476K	1.7	1.6	1.0	1.0	2.0	1.8	1.2	1.2
H1*+T51A+N54S+V56T+G109A+Q172S+A174S+G182*+D183 *+N195F+V206L+K391A+G476K	2.4	1.8	1.3	1.1	2.8	2.1	1.7	1.3
H1*+T51E+N54S+V56T+G109A+Q172T+A174S+G182*+D183 *+N195F+V206L+K391A+G476K	2.0	1.8	0.9	1.0	2.6	1.9	1.6	1.3
H1*+T51A+N54S+V56T+G109A+Q172A+A174S+G182*+D183 *+N195F+V206L+K391A+G476K	1.9	1.8	1.0	1.1	2.3	1.9	1.6	1.3
H1*+T51S+N54S+V56T+G109A+Q172N+A174S+G182*+D183 *+N195F+V206L+K391A+G476K	2.2	1.9	1.1	1.1	2.4	1.9	1.5	1.3
H1*+T51G+N54S+V56T+G109A+Q172K+A174S+G182*+D183 *+N195F+V206L+K391A+G476K	1.4	1.3	1.0	0.9	1.7	1.5	1.2	1.1
H1*+T51A+N54S+V56T+G109A+Q172G+A174S+G182*+D183 *+N195F+V206L+K391A+G476K	1.7	1.7	1.2	1.0	2.2	1.9	1.4	1.2
H1*+T51E+N54S+V56T+G109A+Q172L+A174S+G182*+D183 *+N195F+V206L+K391A+G476K	2.0	1.9	1.0	1.1	2.2	1.8	1.2	1.1
H1*+T51E+N54S+V56T+G109A+Q172R+A174S+G182*+D183	2.0	1.9	1.1	1.1	1.8	1.7	1.4	1.1

*+N195F+V206L+K391A+G476K								
H1*+N54S+V56T+G109A+Q172K+A174S+G182*+D183*+N195F+V206L+K391A+G476K	2.1	1.8	1.0	1.1	2.0	1.6	1.3	1.2
H1*+T51D+N54S+V56T+G109A+Q172N+A174S+G182*+D183*+N195F+V206L+K391A+G476K	1.8	1.7	1.0	1.0	1.9	1.6	1.3	1.1
H1*+T51A+N54S+V56T+G109A+Q172K+A174S+G182*+D183*+N195F+V206L+K391A+G476K	1.7	1.7	1.2	1.1	1.8	1.4	1.3	1.2
H1*+N54S+V56T+K72R+G109A+Q172S+A174S+G182*+D183*+N195F+V206L+K391A+G476K	2.0	1.8	1.3	1.1	2.6	1.8	1.4	1.3
H1*+N54S+V56T+K72H+G109A+Q172T+A174S+G182*+D183*+N195F+V206L+K391A+G476K	2.0	1.8	1.2	1.1	2.0	1.9	1.3	1.2
H1*+N54S+V56T+K72R+G109A+Q172R+A174S+K179E+G182*+D183*+N195F+V206L+K391A+ G476K	1.8	1.6	1.1	1.1	1.4	1.5	1.1	1.1
H1*+N54S+V56T+K72R+G109A+Q172M+A174S+G182*+D183*+N195F+V206L+Y295N+K391A+ G476K	1.9	1.8	1.2	1.1	2.1	1.7	1.3	1.2
H1*+N54S+V56T+K72R+G109A+Q172R+A174S+G182*+D183*+N195F+V206L+K391A+G476K	1.4	1.4	1.0	1.0	1.5	1.4	1.2	0.9
H1*+N54S+V56T+K72Q+G109A+Q172R	2.0	2.0	1.0	1.0	2.6	2.1	1.3	1.2

+A174S+G182*+D183*+N195F+V206L+K391A+G476K								
H1*+N54S+V56T+K72R+G109A+Q172T+A174S+G182*+D183*+N195F+V206L+K391A+G476K	2.1	2.1	1.3	1.1	2.3	2.0	1.4	1.2
H1*+N54S+V56T+K72M+G109A+Q172S+A174S+G182*+D183*+N195F+V206L+K391A+G476K	2.3	1.9	1.2	1.1	2.4	2.0	1.2	1.2
H1*+N54S+V56T+K72Q+G109A+Q172M+A174S+G182*+D183*+N195F+V206L+K391A+G476K	2.1	2.1	1.3	1.1	2.8	2.2	1.5	1.3
H1*+N54S+V56T+G109A+Q172M+A174S+G182*+D183*+N195F+V206L+K391A+G476K	1.9	2.0	1.2	1.1	2.4	1.7	1.4	1.3
H1*+N54S+V56T+K72S+G109A+A174H+G182*+D183*+N195F+V206L+K391A+G476K	2.3	2.0	1.2	1.1	2.2	2.1	1.4	1.4
H1*+N54S+V56T+K72Q+G109A+A174D+G182*+D183*+N195F+V206L+K391A+G476K	2.3	2.1	1.1	1.1	2.2	1.9	1.4	1.3
H1*+N54S+V56T+K72R+G109A+A174D+G182*+D183*+N195F+V206L+K391A+G476K	2.5	2.0	1.1	1.1	2.3	2.1	1.4	1.3
H1*+N54S+V56T+K72Q+G109A+A174K+G182*+D183*+N195F+V206L+K391A+G476K	2.2	1.9	1.2	1.1	2.6	2.0	1.5	1.3
H1*+N54S+V56T+G109A+A174G+G182*+D183*+N195F+V206L+K391A+G476K	2.3	1.9	1.2	1.1	2.6	2.2	1.5	1.4
H1*+N54S+V56T+K72R+G109A+A174Q+G182*+D183*+N195	2.5	2.1	1.2	1.2	2.3	2.1	1.5	1.4

F+V206L+K391A+G476K								
H1*+N54S+V56T+K72Q+G109A+A174G+G182*+D183*+N195F+V206L+K391A+G476K	2.3	2.1	1.1	1.1	2.6	2.2	1.4	1.4
H1*+N54S+V56T+K72S+G109A+A174N+G182*+D183*+N195F+V206L+K391A+G476K	2.6	2.1	1.3	1.1	2.6	2.3	1.5	1.4
H1*+N54S+V56T+K72R+G109A+A174H+G182*+D183*+N195F+V206L+K391A+G476K	2.1	1.9	1.3	1.2	2.5	2.2	1.5	1.4
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+K391S+G476K	1.7	1.7	1.1	1.1	1.9	1.6	1.4	1.2
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+T444A+G476K	1.7	1.6	1.2	1.1	2.2	1.6	1.4	1.2
H1*+N54S+V56T+G109A+F113L+W167F+A174S+G182*+D183*+N195F+V206L+K391A+G476K	1.7	1.6	1.0	1.0	2.1	1.7	1.2	1.2
H1*+G50A+N54S+V56T+G109A+A174E+G182*+D183*+N195F+A204T+V206L+S323N+K391A+G476K	2.0	1.8	1.0	1.1	1.5	1.7	1.3	1.2
H1*+N54S+V56T+K72R+G109A+Q118R+A174S+G182*+D183*+G184T+N195F+V206L+G255A+K391A+G476K	1.6	1.6	1.1	1.0	1.2	1.3	1.2	1.2
H1*+N54S+V56T+M105F+G109A+A174S+G182*+D183*+N19	1.8	1.9	1.2	1.1	2.6	1.9	1.5	1.3

5F+V206L+D377H+K391A+G476K								
H1*+N54S+V56T+K72R+G109A+Q118R+A174S+G182*+D183*+N195F+V206L+D377H+K391A+G476K	1.5	1.6	1.1	1.1	1.4	1.3	1.3	1.2
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+A204G+V206L+K391A+G476K	2.7	2.1	1.2	1.2	2.9	2.6	1.6	1.4
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+A225F+K391A+G476K	1.8	1.8	1.0	0.9	1.8	1.7	1.4	1.2
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+M246A+K391A+G476K	1.8	1.6	0.9	0.9	1.7	1.8	1.2	1.2
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+Y382I+K391A+G476K	2.1	1.7	0.9	0.9	1.8	1.5	1.3	1.1
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+S376H+K391A+G476K	1.8	1.7	1.1	0.9	2.1	2.0	1.3	1.1
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+I214E+K391A+G476K	1.7	1.5	1.1	0.9	2.1	2.1	1.2	1.3
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+I214W+K391A+G476K	2.2	1.9	1.1	1.1	2.4	2.0	1.4	1.3
H1*+N54S+V56T+K72R+G109A+Q172K+A174S+G182*+D183*+N195F+V206L+K391A+G476K	1.7	1.4	0.9	1.0	2.1	1.7	1.2	1.1

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+A204T+V206L+D377H+K391A+G476K	1.9	1.9	1.1	1.1	2.7	2.1	1.5	1.3
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+A204S+V206L+D377H+K391A+G476K	2.1	1.6	1.2	1.1	2.2	1.8	1.3	1.3
H1*+N54S+V56T+G109A+T165S+A174S+G182*+D183*+N195F+V206L+D377H+K391A+G476K	1.9	1.8	1.1	1.1	2.3	2.0	1.4	1.2
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+T334S+D377H+K391A+G476K	2.0	1.6	1.0	1.0	2.3	1.7	1.5	1.3
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+A263G+D377H+K391A+G476K	2.0	1.6	1.0	1.0	2.1	1.6	1.4	1.1
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+M286F+D377H+K391A+G476K	2.0	1.6	1.1	1.0	2.3	1.7	1.3	1.1
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+Y267I+D377H+K391A+G476K	1.9	1.6	1.0	1.0	1.8	1.7	1.3	1.2
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+L235V+D377H+K391A+G476K	2.1	1.8	1.1	1.0	2.5	2.1	1.5	1.3
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+L235A+D377H+K391A+G476K	1.6	1.6	0.8	0.9	2.3	1.9	1.3	1.2
H1*+N54S+V56T+M105L+G109A+A174S+G182*+D183*+N195F+V206L+D377H+K391A+G476K	2.1	1.9	1.1	1.1	2.9	2.1	1.5	1.3

H1*+N54S+V56T+M105I+G109A+A174S+G182*+D183*+N195F+V206L+D377H+K391A+G476K	2.2	2.0	1.1	1.1	2.3	2.0	1.6	1.4
H1*+N54S+V56T+M105V+G109A+A174S+G182*+D183*+N195F+V206L+D377H+K391A+G476K	2.3	2.1	1.2	1.1	2.6	2.1	1.5	1.4
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+M246I+D377H+K391A+G476K	2.2	1.9	1.3	1.1	2.6	2.0	1.7	1.3
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+L250I+D377H+K391A+G476K	2.3	2.0	1.3	1.1	2.3	1.9	1.6	1.3
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+L250V+D377H+K391A+G476K	2.2	1.9	1.3	1.2	2.5	2.0	1.6	1.3
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391Y+G476K	2.2	1.9	1.2	1.1	2.1	1.9	1.6	1.4
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391V+G476K	2.1	1.9	1.0	1.0	2.1	1.8	1.4	1.3
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391M+G476K	2.2	1.8	1.3	1.1	2.6	2.1	1.5	1.3
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391E+G476K	1.8	1.6	1.2	1.0	2.1	1.9	1.3	1.1
H1*+N54S+V56T+G109A+T165G+A174S+G182*+D183*+N195F+V206L+D377H+K391A+G476K	2.3	2.0	1.3	1.1	2.9	2.0	1.7	1.3

H1*+N54R+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K	1.3	1.4	1.1	1.1	1.1	1.1	1.1	0.8
H1*+N54L+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K	1.6	1.4	1.1	1.0	1.3	1.6	1.3	1.2
H1*+N54S+V56T+G109S+A174S+G182*+D183*+N195F+V206L+K391A+G476K	2.4	2.4	1.4	1.2	2.3	2.0	1.4	1.3
H1*+N54S+V56T+G109A+A174V+G182*+D183*+N195F+V206L+K391A+G476K	2.2	2.2	1.3	1.3	2.3	2.0	1.5	1.4
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+M246F+D377H+K391A+G476K	2.6	2.3	1.3	1.1	2.5	2.0	1.6	1.2
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+M246V+D377H+K391A+G476K	2.2	1.8	1.3	1.2	1.9	1.8	1.4	1.3
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+M246S+D377H+K391A+G476K	2.3	1.9	1.2	1.2	1.8	1.6	1.4	1.1
H1*+N54S+V56T+G109A+A174R+G182*+D183*+N195F+V206L+K391A+G476K	1.7	1.6	1.2	1.1	1.7	1.6	1.4	1.2
H1*+N54S+V56T+G109A+A174L+G182*+D183*+N195F+V206L+K391A+G476K	1.9	1.7	1.2	1.2	2.2	1.7	1.3	1.2
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206S+K391A+G476K	1.8	1.6	1.0	1.1	2.0	1.7	1.3	1.3

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391D+G476K	1.9	2.0	1.3	1.2	2.2	2.0	1.5	1.4
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391R+G476K	2.3	1.8	1.3	1.2	2.5	1.9	1.4	1.3
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391H+G476K	2.2	1.9	1.2	1.2	2.3	2.0	1.5	1.3
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391W+G476K	2.2	1.6	1.3	1.2	2.5	2.0	1.4	1.3
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391I+G476K	2.1	1.8	1.2	1.2	2.0	1.8	1.3	1.3
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+L250T+D377H+K391A+G476K	2.0	1.6	1.1	1.1	2.6	2.0	1.4	1.3
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+L250A+D377H+K391A+G476K	2.1	1.8	1.0	1.0	2.6	2.0	1.5	1.3
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+L250F+D377H+K391A+G476K	2.2	1.7	1.1	1.1	2.4	2.0	1.6	1.2
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+L250M+D377H+K391A+G476K	2.2	1.7	1.1	1.1	2.0	1.9	1.4	1.3
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391Q+G476K	1.8	1.4	1.1	1.0	1.5	1.7	1.2	1.2

H1*+N54S+V56T+G109A+Q172H+L173A+A174P+G182*+D183*+N195F+V206L+K391A+G476K	2.5	1.8	1.3	1.2	2.3	2.1	1.6	1.4
H1*+N54S+V56T+G109A+Q172E+L173A+A174R+G182*+D183*+N195F+V206L+K391A+G476K	1.1	1.4	0.7	1.0	1.8	1.7	1.2	1.2
H1*+N54S+V56T+K72Q+G109A+W167R+A174S+G182*+D183*+N195F+V206L+K391A+G476K	1.9	1.7	1.2	1.1	1.6	1.6	1.0	1.1
H1*+N54S+V56T+G109A+A174S+G182*+D183*+G184T+N195F+V206L+G255A+K391A+G476K	1.8	1.7	1.1	1.0	2.0	1.7	1.3	1.2
H1*+N54S+V56T+K72R+G109A+A174S+G182*+D183*+G184T+N195F+V206L+D377H+K391A+G476K	1.7	1.6	1.1	1.1	1.9	1.6	1.1	1.0
H1*+N54S+V56T+G109A+A174S+G182*+D183*+G184T+N195F+V206L+G255A+D377H+K391A+G476K	2.4	2.1	1.3	1.2	2.3	2.0	1.4	1.2
H1*+N54S+V56T+G109A+Q118R+A174S+G182*+D183*+N195F+V206L+K391A+G476K	1.6	1.5	1.1	1.2	0.7	1.1	0.8	1.0
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+S376T+K391A+G476K	2.2	2.0	1.3	1.2	2.3	1.8	1.3	1.3
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+S376V+K391A+G476K	2.0	1.8	1.2	1.2	2.1	1.8	1.4	1.3

H1*+N54S+V56T+G109A+Q172E+L173I+A174N+G182*+D183*+N195F+V206L+K391A+G476K	2.3	1.9	1.1	1.1	2.1	1.9	1.1	1.2
H1*+N54S+V56T+G109A+Q172D+L173A+A174T+G182*+D183*+N195F+V206L+K391A+G476K	2.3	2.0	1.1	1.1	2.2	2.0	1.1	1.2
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+Y267M+D377H+K391A+G476K	2.1	2.0	1.2	1.2	2.6	2.0	1.5	1.3
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+Y267H+D377H+K391A+G476K	1.7	1.6	1.1	1.0	2.5	1.9	1.2	1.2
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+V238A+K391A+G476K	1.6	1.5	1.1	1.0	2.3	1.7	1.2	1.1
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+V238T+K391A+G476K	1.5	1.3	1.1	0.9	1.7	1.5	1.2	1.1
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+V238G +K391A+G476K	2.3	1.7	1.2	1.1	3.0	2.1	1.4	1.3
H1*+N54S+V56T+M105V+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K	2.0	1.7	1.2	1.1	2.3	2.1	1.5	1.4
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+V264T+K391A+G476K	2.2	2.1	1.2	1.0	2.9	1.9	1.4	1.3
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+V264I+K391A+G476K	2.4	1.8	1.3	1.1	2.9	2.3	1.5	1.4

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+L235V +K391A+G476K	1.9	1.7	1.1	1.0	2.4	1.9	1.3	1.3
H1*+N54S+V56T+G109A+W167H+Q172N+L173A+A174S+G182*+D183*+N195F+V206L+K391A+G476K	2.0	1.7	1.2	1.1	2.9	2.1	1.4	1.3
H1*+N54S+V56T+G109A+W167F+Q172E+L173P+A174K+G182*+D183*+N195F+V206L+K391A+ G476K	1.7	1.9	1.2	1.1	3.3	2.2	1.5	1.3
H1*+N54S+V56T+G109A+Q172N+L173T+A174S+G182*+D183*+N195F+V206L+K391A+G476K	2.0	1.7	1.2	1.1	2.8	2.0	1.4	1.4
H1*+N54S+V56T+G109A+Q172K+L173V+A174T+G182*+D183*+N195F+V206L+K391A+G476K	1.6	1.4	1.0	1.1	1.6	1.6	1.0	1.0
H1*+N54S+V56T+G109A+Q172E+L173F+A174R+G182*+D183*+N195F+V206L+K391A+G476K	1.9	1.6	1.1	1.0	2.0	1.9	1.3	1.1
H1*+N54S+V56T+G109A+Q172E+L173T+A174R+G182*+D183*+N195F+V206L+K391A+G476K	1.9	1.8	1.2	1.2	2.5	2.1	0.9	1.3
H1*+N54S+V56T+G109A+Q172N+L173V+A174R+G182*+D183*+N195F+V206L+K391A+G476K	1.9	1.7	1.3	1.2	2.2	1.8	0.9	1.2
H1*+N54S+V56T+G109A+L173V+A174R+G182*+D183*+N195F+V206L+K391A+G476K	1.7	1.8	1.3	1.2	1.7	1.6	0.8	1.1
H1*+N54S+V56T+G109A+Q172E+L173M+A174H+G182*+D18	2.1	2.1	1.3	1.2	2.8	2.1	1.3	1.3

3*+N195F+V206L+K391A+G476K								
H1*+N54S+V56T+G109A+Q172E+L173F+A174P+G182*+D183*+N195F+V206L+K391A+G476K	1.9	1.9	1.2	1.2	2.7	2.3	0.8	1.3
H1*+N54S+V56T+G109A+W167Y+Q172E+L173V+A174H+G182*+D183*+N195F+V206L+K391A+G476K	2.0	1.8	1.1	1.0	2.8	2.0	1.4	1.3
H1*+N54S+V56T+G109A+L173A+A174T+G182*+D183*+N195F+V206L+K391A+G476K	2.0	1.8	1.0	1.0	2.4	1.8	1.4	1.3
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+V291A+F328L +K391A+G476K	2.0	1.6	1.1	1.0	2.9	1.7	1.4	1.2
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+M246L+K391A+G476K	2.2	1.7	1.0	1.0	2.8	1.7	1.2	1.2
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+M246S +K391A+G476K	1.8	1.8	1.2	1.1	2.9	2.0	1.5	1.4
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+L250V +K391A+G476K	2.0	1.9	1.3	1.2	2.8	2.0	1.6	1.4
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+L250F +K391A+G476K	2.0	1.8	1.1	1.0	2.9	2.1	1.5	1.3
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+L250M+K391A+G476K	2.3	1.7	1.2	1.1	3.0	2.1	1.5	1.4
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V20	1.9	1.8	1.3	1.0	2.8	2.0	1.3	1.3

6L+K391A+C474V+G476K								
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+A204S+V206L+K391A+G476K	1.7	1.6	1.0	1.0	1.7	1.8	1.4	1.3
H1*+N54S+V56T+G109A+T165G+A174S+G182*+D183*+N195F+V206L+K391A+G476K	2.3	1.9	1.2	1.1	2.9	2.2	1.3	1.3
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+T334S +K391A+G476K	1.9	1.7	1.0	1.0	2.6	2.0	1.4	1.3
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+A263G+M286F+K391A+G476K	1.1	1.3	1.0	0.9	1.4	1.3	1.1	1.1
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+A263G+M286L+K391A+G476K	1.7	1.5	1.1	1.0	2.2	1.9	1.3	1.1
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+Y267H +K391A+G476K	1.9	1.9	1.2	1.2	2.7	2.2	1.5	1.4
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+Y267L+K391A+G476K	1.9	1.8	1.0	1.1	2.4	2.2	1.5	1.4
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+Y267I +K391A+G476K	1.2	1.5	0.7	0.9	1.7	1.9	1.3	1.3
H1*+T51A+N54S+V56T+G109A+Q172R+A174S+G182*+D183*+N195F+V206L+K391A+G476K	2.1	1.5	1.1	1.0	1.5	1.6	1.4	1.1
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V20	2.4	1.9	1.1	1.1	2.5	1.9	1.4	1.2

6L+K391L+G476K								
H1*+N54S+V56T+G109A+F113Q+R116H+Q172G+A174S+G182*+D183*+N195F+V206L+K391A+G476K	2.6	2.1	1.1	1.0	3.1	2.1	1.4	1.2
H1*+N54S+V56T+G109A+F113Q+Q172G+A174S+G182*+D183*+N195F+V206L+K391A+G476K	1.9	1.8	0.9	0.9	2.7	1.9	1.2	1.1
H1*+N54S+V56T+G109S+F113Q+R116Q+A174S+G182*+D183*+N195F+V206L+K391A+G476K	2.9	2.2	1.2	1.1	3.3	2.6	1.5	1.3
H1*+N54S+V56T+G109A+Q172D+A174S+G182*+D183*+N195F+A204G+V206L+K391A+P473R+ G476K	2.7	2.2	1.2	1.1	3.1	2.1	1.5	1.3
H1*+N54S+V56T+K72R+G109A+T134E+A174S+G182*+D183*+N195F+A204G+V206L+G255A+ K391A+P473R+G476K	2.8	2.3	1.2	1.1	3.4	2.4	1.7	1.3
H1*+N54S+V56T+K72R+G109A+W167F+A174S+G182*+D183*+N195F+A204G+V206L+K391A+ G476K	2.7	2.2	1.2	1.1	3.1	2.2	1.6	1.3
H1*+N54S+V56T+K72R+G109A+A174S+G182*+D183*+G184T+N195F+A204G+V206L+K391A+ P473R+G476K	2.3	2.1	1.2	1.1	2.7	2.0	1.4	1.3
H1*+N54S+V56T+G109A+W167F+Q172N+A174S+G182*+D18	2.5	1.8	1.3	1.2	2.6	1.8	1.6	1.2

3*+N195F+V206L+K391A+P473R+G476K								
H1*+N54S+V56T+G109A+W167F+Q172G+A174S+G182*+D183*+N195F+V206L+K391A+P473G+G476K	2.4	2.0	1.3	1.2	2.8	2.0	1.6	1.2
H1*+N54S+V56T+G109A+W167F+Q172G+A174S+G182*+D183*+N195F+V206L+K391A+P473R+G476K	2.1	1.8	1.3	1.1	2.3	1.8	1.5	1.2
H1*+N54S+V56T+K72R+G109A+W167F+Q172R+A174S+G182*+D183*+N195F+V206L+K391A+G476K	2.2	1.9	1.1	1.1	2.0	1.8	1.2	1.1
H1*+N54S+V56T+K72R+G109A+R116H+W167F+Q172R+A174S+G182*+D183*+N195F+V206L+K391A+G476K	2.4	1.8	1.2	1.1	2.4	1.9	1.5	1.2
H1*+N54S+V56T+M105F+G109A+A174S+G182*+D183*+N195F+V206L+R320A+S323N+K391A+C474V+G476K	2.6	2.2	1.3	1.3	3.4	2.4	1.5	1.4
H1*+N54S+V56T+K72R+G109A+A174S+G182*+D183*+N195F+V206L+G255A+K391A+C474V+G476K	2.4	2.1	1.4	1.3	3.2	2.2	1.7	1.3
H1*+N54S+V56T+G109A+T134E+A174S+G182*+D183*+N195F+V206L+K391A+C474V+G476K	2.8	2.3	1.3	1.2	3.7	2.3	1.6	1.4
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V20	2.6	2.0	1.3	1.2	3.0	2.1	1.5	1.3

6L+D377H+K391A+C474V+G476K								
H1*+N54S+V56T+K72R+G109A+A174S+G182*+D183*+N195F+V206L+K391A+C474V+G476K	2.8	2.1	1.3	1.2	3.3	2.4	1.5	1.4
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+A265G+K391A+T444Q+G476K+G477A	2.1	1.9	1.0	1.1	2.6	2.0	1.5	1.3
H1*+A37V+N54S+V56T+G109A+W167F+Q172G+A174S+G182*+D183*+N195F+V206L+K391A+G346T+G477A+G476K	2.3	2.0	1.2	1.2	2.8	2.2	1.5	1.3
H1*+N54S+V56T+G109A+R116Q+Q172D+A174S+G182*+D183*+N195F+V206L+G346T+K391A+T444Q+G477A+G476K	2.3	2.1	0.9	1.1	3.1	2.4	1.4	1.3
H1*+N54S+V56T+G109A+R116Q+W167F+Q172N+A174S+G182*+D183*+N195F+V206L+G346T+K391A+T444Q+G477A+G476K	2.2	2.2	1.1	1.2	2.7	2.4	1.3	1.3
H1*+N54S+V56T+G109S+W167F+Q172R+A174S+G182*+D183*+N195F+V206L+K391A+G476K	1.9	1.4	1.2	1.1	2.1	1.6	1.3	1.2
H1*+N54S+V56T+G109S+R116Q+W167F+Q172N+A174S+G182*+D183*+N195F+V206L+K391A+G476K	2.8	2.2	1.4	1.2	3.2	3.0	1.5	1.5
H1*+N54S+V56T+G109S+W167F+Q172G+A174S+G182*+D18	2.6	1.9	1.4	1.1	3.2	2.2	1.6	1.5

3*+N195F+V206L+K391A+G476K								
H1*+N54S+V56T+G109A+F113Q+Q172G+A174S+G182*+D183*+N195F+V206L+K391A+T444Q+G476K	2.5	2.0	1.5	1.2	3.2	2.2	1.5	1.4
H1*+N54S+V56T+G109A+F113Q+R116H+Q172G+A174S+G182*+D183*+N195F+V206L+K391A+T444Q+G476K	2.6	2.2	1.3	1.1	3.5	2.6	1.7	1.4
H1*+N54S+V56T+G109A+F113Q+A174S+G182*+D183*+N195F+V206L+K391A+C474V+G476K	2.5	2.0	1.3	1.1	3.1	2.6	1.6	1.5
H1*+N54S+V56T+G109A+Q172N+A174S+G182*+D183*+N195F+V206L+V264I+K391A+C474V+G476K	2.4	1.7	1.4	1.1	3.2	2.4	1.5	1.4
H1*+N54S+V56T+G109A+Q172N+A174S+G182*+D183*+N195F+V206L+K391A+C474V+G476K	2.5	1.7	1.3	1.1	2.0	2.1	1.3	1.3
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+S280Q+H321Y+K391A+C474V+G476K	2.1	1.8	1.2	1.1	2.9	2.1	1.5	1.4
H1*+N54S+V56T+K72R+G109A+T134E+A174S+G182*+D183*+N195F+V206L+G255A+K391A+C474V+G476K	2.1	1.8	1.2	1.0	3.3	2.3	1.6	1.4
H1*+N54S+V56T+G109A+F113Q+R116H+Q172G+A174S+G18	2.4	2.0	1.2	1.1	3.3	2.3	1.7	1.3

2*+D183*+N195F+V206L+K391A+ T444Q+P473R+G476K								
H1*+N54S+V56T+G109A+F113Q+R116Q+Q172G+A174S+G182*+D183*+N195F+V206L+K391A+ T444Q+G476K	2.8	2.1	1.3	1.1	3.1	2.3	1.5	1.3
H1*+N54S+V56T+G109A+R116H+W167F+Q172N+A174S+G182*+D183*+N195F+V206L+K391A+G476K	2.4	2.0	1.2	1.1	2.8	2.2	1.5	1.3
H1*+N54S+V56T+G109A+F113Q+R116H+T165G+Q172G+A174S+G182*+D183*+N195F+V206L+ K391A+T444Q+G476K	2.4	2.0	1.2	1.1	3.1	2.2	1.6	1.2
H1*+N54S+V56T+G109A+F113Q+R116Q+T165G+Q172G+A174S+G182*+D183*+N195F+V206L+ K391A+T444Q+G476K	2.5	2.1	1.3	1.2	3.4	2.3	1.7	1.4
H1*+N54S+V56T+G109A+F113Q+R116H+W167F+Q172R+A174S+G182*+D183*+N195F+V206L+F289I+K391A+G476K	2.3	1.8	1.2	1.1	2.6	2.0	1.4	1.3
H1*+N54S+V56T+G109A+F113Q+Q172N+A174S+G182*+D183*+N195F+V206L+K391A+T444Q+G476K	2.6	2.2	1.3	1.2	3.3	2.3	1.6	1.3
H1*+N54S+V56T+G109A+F113Q+R116H+Q172N+A174S+G182*+D183*+N195F+V206L+K391A+G476K	2.6	2.0	1.3	1.2	3.2	2.2	1.7	1.4
H1*+N54S+V56T+G109A+F113Q+R116Q+Q172M+A174S+G18	2.2	2.0	1.2	1.1	2.8	2.2	1.3	1.3

2*+D183*+N195F+V206L+K391A+T444Q+G476K								
H1*+N54S+V56T+G109A+F113Q+R116H+Q172M+A174S+G182*+D183*+N195F+V206L+K391A+G476K	2.2	1.9	1.2	1.0	3.0	2.4	1.5	1.3
H1*+N54S+V56T+G109A+R116H+Q172M+A174S+G182*+D183*+N195F+V206L+K391A+G476K	2.3	2.1	1.1	1.0	2.7	2.1	1.5	1.3
H1*+N54S+V56T+G109A+F113Q+R116H+T165G+Q172M+A174S+G182*+D183*+N195F+V206L+K391A+Q395P+G476K	1.9	1.7	1.2	1.1	2.6	1.8	1.5	1.3
H1*+N54S+V56T+G109A+F113Q+A174S+G182*+D183*+N195F+V206L+K391A+T444Q+P473R+G476K	1.7	1.3	0.9	1.0	1.9	1.6	0.9	1.0
H1*+N54S+V56T+G109A+R116Q+A174S+G182*+D183*+N195F+V206L+A265G+K391A+T444Q+P473R+G476K	2.4	2.2	1.3	1.2	2.7	2.4	1.5	1.4
H1*+N54S+V56T+G109A+R116Q+A174S+G182*+D183*+N195F+V206L+K391A+T444Q+P473R+G476K	2.4	2.1	1.3	1.1	2.9	2.3	1.3	1.3
H1*+N54S+V56T+K72R+G109A+T134E+T165G+A174S+G182*+D183*+N195F+V206L+G255A+K391A+G476K	2.5	2.1	1.2	1.1	3.0	2.3	1.4	1.3
H1*+N54S+V56T+G109A+F113Q+R116H+W167F+Q172R+A17	2.1	2.0	1.2	1.2	2.9	2.3	1.5	1.3

4S+G182*+D183*+N195F+V206L+K391A+G476K								
H1*+N54S+V56T+G109A+R116Q+W167F+Q172R+A174S+G182*+D183*+N195F+V206L+A265G+K391A+P473R+G476K	2.0	1.8	1.2	1.1	2.2	2.0	1.3	1.3
H1*+N54S+V56T+G109A+F113Q+A174S+G182*+D183*+N195F+V206L+K391A+G476K	2.1	1.9	1.0	1.0	2.6	2.0	1.4	1.2
H1*+N54S+V56T+G109A+Q172N+A174S+G182*+D183*+N195F+V206L+K391A+G476K	2.0	1.7	1.2	1.1	2.5	1.9	1.5	1.1
H1*+T51V+N54S+V56T+G109A+Q172D+A174S+G182*+D183*+N195F+V206L+K391A+G476K	2.4	1.9	1.2	1.1	2.6	1.9	1.6	1.2
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+S280Q+H321Y +K391A+G476K	2.3	1.9	1.2	1.1	2.5	1.8	1.5	1.2
H1*+N54S+V56T+G109A+F113Q+R116H+Q172N+A174S+G182*+D183*+N195F+V206L+K391A+G476K	2.6	2.3	1.3	1.2	3.1	2.4	1.7	1.4
H1*+N54S+V56T+G109A+F113Q+R116H+Q172G+L173V+A174S+G182*+D183*+N195F+V206L+ K391A+T444Q+P473R+G476K	2.3	2.0	1.3	1.2	2.9	2.3	1.6	1.3
H1*+N54S+V56T+G109A+R116Q+W167F+Q172N+L173V+A174S+G182*+D183*+N195F+V206L+K391A+T444Q+G476K	2.6	2.2	1.3	1.1	3.3	2.5	1.8	1.3
H1*+N54S+V56T+G109A+G133Q+W167F+Q172N+A174S+G182*+D183*+N195F+V206L+Q395P+K391A+G476K	2.5	2.3	1.3	1.2	3.3	2.4	1.8	1.4

H1*+N54S+V56T+G109A+F113Q+R116H+W167F+Q172N+L173V+A174S+G182*+D183*+N195F+V206L+K391A+G476K	2.3	2.0	1.2	1.2	2.8	2.3	1.6	1.3
H1*+A37V+N54S+V56T+K72R+G109A+R116H+W167F+Q172R+A174S+G182*+D183*+G184T+N195F+V206L+K391A+P473R+G476K	2.5	2.2	1.3	1.1	3.3	2.5	1.7	1.2
H1*+N54S+V56T+K72R+G109A+F113Q+R116H+W167F+Q172G+L173V+A174S+G182*+D183*+G184T+N195F+V206L+K391A+T444Q+P473R+G476K	2.2	2.2	1.2	1.1	3.1	2.4	1.7	1.3
H1*+N54S+V56T+G109S+R116Q+W167F+Q172R+A174S+G182*+D183*+N195F+V206L+K391A+G476K	2.5	2.2	1.2	1.0	3.1	2.5	1.6	1.3
H1*+N54S+V56T+G109S+R116Q+W167F+Q172G+A174S+G182*+D183*+N195F+V206L+K391A+P473R+G476K	2.5	2.1	1.2	1.1	3.0	2.3	1.6	1.2
H1*+N54S+V56T+G109S+F113Q+W167F+Q172N+A174S+G182*+D183*+N195F+V206L+K391A+G476K	2.7	2.4	1.4	1.3	3.1	2.5	1.7	1.4
H1*+A37V+N54S+V56T+G109S+F113Q+W167F+Q172R+A174S+G182*+D183*+N195F+V206L+K391A+G476K	2.8	2.4	1.3	1.2	3.5	2.5	1.7	1.3
H1*+N54S+V56T+K72R+G109A+R116H+T134E+W167F+Q172G+L173V+A174S+G182*+D183*+N195F+V206L+G255A+K391A+G476K	2.2	1.9	1.2	1.1	2.7	2.4	1.6	1.3

H1*+N54S+V56T+K72R+G109A+R116H+T134E+W167F+Q172G+L173V+A174S+G182*+D183*+N195F+V206L+G255A+K391A+Q395P+T444Q+P473R+G476K	2.5	2.0	1.2	1.1	3.5	2.5	1.6	1.3
H1*+N54S+V56T+K72R+G109A+F113Q+R116Q+W167F+Q172G+A174S+G182*+D183*+G184T+N195F+V206L+K391A+P473R+G476K	2.5	2.1	1.3	1.1	3.4	2.5	1.6	1.3
H1*+N54S+V56T+K72R+G109A+F113Q+R116Q+T134E+W167F+Q172R+A174S+G182*+D183*+N195F+V206L+G255A+K391A+T444Q+P473R+G476K	2.3	2.0	1.1	1.1	3.1	2.6	1.5	1.3
H1*+N54S+V56T+K72R+G109A+F113Q+T134E+W167F+Q172R+A174S+G182*+D183*+N195F+V206L+G255A+K391A+Q395P+A445Q+P473R+G476K	1.9	1.9	1.1	1.1	2.7	2.1	1.6	1.3
H1*+N54S+V56T+K72R+G109A+F113Q+R116H+T134E+W167F+Q172R+A174S+G182*+D183*+N195F+V206L+G255A+K391A+Q395P+G476K	2.1	2.2	1.3	1.2	2.9	2.4	1.6	1.4
H1*+N54S+V56T+K72R+G109A+T134E+W167F+Q172N+A174S+G182*+D183*+N195F+V206L+G255A+A265G+K391A+T444Q+P473R+G476K	2.6	2.4	1.3	1.2	3.2	2.5	1.7	1.4
H1*+N54S+V56T+K72R+G109A+G133Q+W167F+Q172R+A174S+G182*+D183*+N195F+V206L+	2.4	2.2	1.3	1.2	3.2	2.4	1.6	1.4

K391A+G476K								
H1*+N54S+V56T+K72R+G109A+F113Q+R116Q+W167F+Q172G+A174S+G182*+D183*+N195F+A204G+V206L+K391A+G476K	2.9	2.3	1.3	1.2	3.7	2.8	1.8	1.4
H1*+N54S+V56T+K72R+G109A+F113Q+R116Q+W167F+Q172N+L173V+A174S+G182*+D183*+G184T+N195F+V206L+K391A+T444Q+P473R+G476K	2.0	2.0	1.3	1.2	2.7	2.1	1.5	1.3
H1*+A37H+N54S+V56T+G109A+F113Q+W167F+Q172N+A174S+G182*+D183*+N195F+V206L+K391A+G476K	2.5	1.9	1.2	1.1	2.6	1.8	1.6	1.3
H1*+A37H+N54S+V56T+G109A+F113Q+A174S+G182*+D183*+N195F+V206L+K391A+G476K	1.9	1.7	1.3	1.2	2.8	2.0	1.3	1.3
H1*+N54S+V56T+G109A+F113Q+W167F+Q172N+A174S+G182*+D183*+N195F+V206L+K391A+T459N+G476K	2.3	1.6	1.3	1.2	2.8	1.8	1.5	1.2
H1*+N54S+V56T+G109A+F113Q+Q172R+L173V+A174S+G182*+D183*+N195F+V206L+K391A+T444Q+G476K	1.9	1.5	1.1	1.0	2.6	1.5	1.3	1.1
H1*+N54S+V56T+G109A+F113Q+R116Q+A174S+G182*+D183*+N195F+V206L+K391A+P473R+G476K	2.3	2.2	1.1	1.1	3.2	2.3	1.4	1.2

H1*+N54S+V56T+A60V+G109A+R116Q+W167F+Q172N+A174S+G182*+D183*+N195F+V206L+K391A+G476K	2.4	2.2	1.2	1.2	3.3	2.4	1.3	1.4
H1*+N54S+V56T+A60V+G109A+R116H+Q172R+L173V+A174S+G182*+D183*+N195F+V206L+K391A+G476K	2.7	2.0	1.4	1.2	3.2	2.5	1.3	1.4
H1*+A37V+N54S+V56T+A60V+G109A+R116Q+T165G+A174S+G182*+D183*+N195F+V206L+K391A+G476K	2.5	1.9	1.1	1.2	2.9	2.1	1.1	1.3
H1*+A37H+N54S+V56T+A60V+G109A+R116Q+T165G+A174S+G182*+D183*+N195F+V206L+K391A+G476K	2.7	2.2	1.2	1.2	3.6	2.5	1.7	1.4
H1*+N54S+V56T+A60V+G109A+R116Q+W167F+Q172G+L173V+A174S+G182*+D183*+N195F+V206L+K391A+G476K	2.3	2.3	1.0	1.2	2.5	2.3	1.2	1.3
H1*+N54S+V56T+A60V+G109A+R116Q+A174S+G182*+D183*+N195F+V206L+K391A+G476K	2.3	2.1	0.9	1.1	3.1	2.4	1.4	1.3
H1*+A37H+N54S+V56T+A60V+G109A+R116Q+W167F+Q172R+A174S+G182*+D183*+N195F+V206L+K391A+G476K	3.0	2.4	1.2	1.1	3.6	2.4	1.7	1.3

H1*+A37H+N54S+V56T+A60V+G109A+R116Q+W167F+Q172N+A174S+G182*+D183*+N195F+V206L+K391A+G476K	2.7	2.7	1.1	1.1	3.0	2.4	1.4	1.3
H1*+N54S+V56T+A60V+G109A+R116Q+T165G+A174S+G182*+D183*+N195F+V206L+K391A+T444Q+P473R+G476K	2.4	2.2	1.2	1.2	3.0	2.2	1.3	1.2
H1*+N54S+V56T+A60V+G109A+R116Q+A174S+G182*+D183*+N195F+V206L+K391A+T444Q+P473R+G476K	2.5	1.8	0.9	1.0	2.2	2.0	1.1	1.2
H1*+N54S+V56T+A60V+G109A+R116Q+W167F+Q172N+L173V+A174S+G182*+D183*+N195F+V206L+K391A+G476K	2.7	2.8	1.0	1.1	3.3	2.7	1.6	1.4
H1*+N54S+V56T+A60V+G109A+R116Q+W167F+Q172R+A174S+G182*+D183*+N195F+V206L+K391A+G476K	2.8	2.5	1.3	1.2	3.6	2.7	1.7	1.4
H1*+N54S+V56T+G109A+R116A+W167F+Q172R+A174S+G182*+D183*+N195F+A204G+V206L+K391A+P473R+G476K	2.3	2.0	1.1	1.1	2.5	2.0	1.6	1.3
H1*+N54S+V56T+G109A+R116A+A174S+G182*+D183*+N195F+A204G+V206L+K391A+P473R+G476K	2.8	2.5	1.3	1.2	3.4	2.3	1.6	1.5

H1*+N54S+V56T+G109A+R116A+T165G+A174S+G182*+D183*+N195F+V206L+K391A+T444Q+P473R+G476K	2.5	2.1	1.2	1.1	2.8	2.0	1.6	1.3
H1*+N54S+V56T+G109A+G182*+D183*+N195F+K391A+G476K	2.2	2.2	1.2	1.1	2.3	2.1	1.5	1.5
H1*+N54S+V56T+G109A+G182*+D183*+N195F+V206L	2.2	2.0	1.3	1.2	2.4	1.9	1.5	1.4
N54S+V56T+G109A+G182*+D183*+N195F	2.2	2.0	1.3	1.2	2.3	2.0	1.5	1.4
N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K	2.4	2.0	1.3	1.2	2.5	2.0	1.5	1.4
H1*+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K	1.9	1.9	1.3	1.2	2.4	2.0	1.5	1.3
H1*+N54S+V56T+G109A+G182*+D183*+N195F+V206L+K391A+G476K	2.2	1.9	1.2	1.1	2.5	1.7	1.3	1.3
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A	2.0	1.9	1.2	1.1	2.2	1.8	1.5	1.3
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+G476K	2.0	1.9	1.2	1.1	2.5	1.9	1.4	1.3
H1*+N54S+V56T+A174S+G182*+D183*+N195F+V206L+G273R+K391A+G476K	2.3	2.0	1.2	1.1	2.6	2.1	1.4	1.4
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V20	2.4	2.1	1.3	1.1	2.7	2.1	1.6	1.4

6L								
H1*+W48G+G109A+G182*+D183*+N195F+V206L+K391A+G476K	1.7	1.6	1.2	1.1	2.2	1.7	1.3	1.2
N54S+V56T+G109A+A174S+G182*+D183*+N195F+K391A+G476K	2.0	1.7	1.2	1.2	2.9	2.2	1.5	1.3
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+K391A	1.4	1.5	1.1	1.1	2.3	1.8	1.3	1.3
H1*+N54S+V56T+G109A+F113Q+Q172M+A174S+G182*+D183*+N195F+V206L+K391A+G476K	2.0	1.9	1.2	1.1	2.9	2.2	1.3	1.2
H1*+N54S+V56T+G109A+R116Q+A174S+G182*+D183*+N195F+A204G+V206L+K391A+G476K	1.8	1.6	0.9	1.0	1.7	1.8	1.0	1.1
H1*+N54S+V56T+K72R+G109A+F113Q+T134E+A174S+G182*+D183*+N195F+V206L+G255A+ K391A+G476K	2.5	2.2	1.2	1.2	2.9	2.5	1.4	1.4
H1*+N54S+V56T+K72R+G109A+F113Q+T134E+A174S+G182*+D183*+N195F+V206L+G255A+ K391A+P473R+G476K	2.7	2.3	1.3	1.2	3.3	2.5	1.7	1.4
H1*+N54S+V56T+K72R+G109A+R116Q+A174S+G182*+D183*+G184T+N195F+V206L+K391A+ G476K	2.7	2.2	1.2	1.2	3.4	2.4	1.6	1.3

H1*+A37V+N54S+V56T+G109A+R116A+T165G+A174S+G182*+D183*+N195F+V206L+K391A+G476K	2.4	2.2	1.2	1.2	3.1	2.5	1.5	1.3
H1*+A37V+N54S+V56T+G109A+R116Q+T165G+A174S+G182*+D183*+N195F+V206L+M246F+K391A+G476K	2.5	2.2	1.2	1.2	3.0	2.3	1.5	1.3
H1*+V56A+G109A+A174S+G182*+D183*+N195F+V206L+G476K	2.0	2.0	1.1	1.1	2.5	2.1	1.5	1.3
H1*+N54S+V56T+G109A+G182*+D183*+N195F+V206L+K391A	1.8	2.0	1.2	1.0	2.2	1.9	1.6	1.4
H1*+N54S+V56T+G109A+G182*+D183*+N195F+V206L+G476K	1.8	1.7	1.0	1.1	1.9	1.9	1.4	1.3
G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K	1.5	1.6	1.0	1.0	1.7	1.7	1.2	1.2
N54S+V56T+G109A+G182*+D183*+N195F+V206L+K391T+G476K	1.7	1.7	1.2	1.0	1.6	1.7	1.4	1.3
H1*+N54S+V56T+K72R+G109A+F113Q+R116H+A174S+G182*+D183*+G184T+N195F+V206L+K391A+T444Q+G476K	2.4	2.2	1.2	1.2	3.4	2.3	1.4	1.4
H1*+N54S+V56T+G109S+F113Q+A174S+G182*+D183*+N195F+V206L+K391A+T444Q+G476K	2.4	2.0	1.3	1.2	3.1	2.2	1.6	1.3

H1*+N54S+V56T+G109A+F113Q+R116H+W167F+Q172G+L173V+A174S+G182*+D183*+N195F+V206L+K391A+P473R+G476K	2.9	2.3	1.3	1.2	3.8	2.6	1.8	1.4
H1*+N54S+V56T+G109A+F113Q+R116Q+Q172N+A174S+G182*+D183*+N195F+V206L+A265G+K391A+P473R+G476K	2.8	2.3	1.2	1.2	3.5	2.6	1.7	1.5
H1*+N54S+V56T+G109A+F113Q+W167F+Q172N+A174S+G182*+D183*+N195F+A204G+V206L+K391A+P473R+G476K	2.5	2.0	1.2	1.2	2.9	2.2	1.7	1.4
H1*+N54S+V56T+G109A+F113Q+R116H+W167F+Q172R+A174S+G182*+D183*+N195F+A204G+V206L+K391A+P473R+G476K	2.1	1.9	1.2	1.1	2.3	1.8	1.3	1.3
H1*+N54S+V56T+G109A+R116A+A174S+G182*+D183*+N195F+V206L+K391A+T444Q+P473R+G476K	2.1	1.9	1.1	1.1	2.7	2.2	1.5	1.3
H1*+N54S+V56T+G109A+R116H+Q172R+A174S+G182*+D183*+N195F+A204G+V206L+K391A+P473R+G476K	2.2	1.6	1.2	1.1	2.5	1.8	1.5	1.2
H1*+A37V+N54S+V56T+G109A+R116Q+T165G+A174S+G182*+D183*+N195F+V206L+K391A+G476K	2.3	2.0	1.2	1.1	3.0	2.1	1.5	1.4
H1*+A37H+N54S+V56T+G109A+R116H+T165G+A174S+G182	2.3	2.0	1.3	1.1	3.2	2.2	1.5	1.4

+D183+N195F+V206L+M246F+ K391A+G476K								
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+K391A+G476K	2.0	1.9	1.1	1.1	2.1	1.9	1.2	1.2
H1*+G109A+G182*+D183*+N195F+V206L+K391A+G476K	1.7	1.6	1.1	1.1	1.8	1.5	1.3	1.2
G109A+G182*+D183*+N195F+V206L+G476K	1.9	1.7	1.2	1.1	2.1	1.5	1.2	1.1
H1*+G109A+G182*+D183*+N195F+K391A	1.9	1.9	1.2	1.2	1.6	1.7	1.3	1.3
H1*+N54S+V56T+G109A+G133S+A174S+G182*+D183*+N195F+K391A+G476H	2.2	1.9	1.2	1.1	2.4	2.0	1.3	1.3
H1*+N54S+V56T+G109A+R116A+Q172N+L173V+A174S+G182*+D183*+N195F+V206L+K391A+ G476K	2.5	2.3	1.2	1.2	3.2	2.5	1.6	1.4
H1*+A37V+N54S+V56T+G109A+R116H+T165G+A174S+G182*+D183*+N195F+V206L+K391A+ G476K	2.5	2.1	1.1	1.2	2.6	2.3	1.4	1.3
H1*+P45A+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+C474V+G476K	2.3	2.1	1.3	1.2	3.1	2.1	1.5	1.4
H1*+N54S+V56T+G109A+P124A+A174S+G182*+D183*+N195F+V206L+K391A+C474V+G476K	1.9	2.2	1.3	1.2	2.8	2.2	1.4	1.3
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V20	2.0	2.0	1.3	1.2	2.4	2.1	1.5	1.4

6L+P364A+K391A+C474V+G476K								
H1*+N54S+V56T+G109A+Q118R+T134E+A174S+G182*+D183*+N195F+V206L+K391A+G476K	3.7	2.5	1.6	1.2	3.2	2.6	1.5	1.6
H1*+N54S+V56T+G109A+A174S+G182*+D183*+G184T+N195F+V206L+K391A+G476K	3.4	2.4	1.6	1.3	3.9	2.7	1.6	1.7
H1*+G50A+T51A+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K	3.2	2.2	1.5	1.2	3.1	2.4	1.8	1.5
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+V264F+K391A+G476K	3.2	2.3	1.6	1.3	3.4	2.3	1.7	1.5
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+Y382L+K391A+G476K	3.0	2.2	1.6	1.2	2.9	2.4	1.4	1.4
H1*+G7K +N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K	3.7	2.2	1.5	1.1	3.7	2.6	1.7	1.3
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+G255A+Q256A+K391A+G476K	3.0	2.2	1.5	1.2	3.2	2.6	1.7	1.5
H1*+N54S+V56T+G109A+W167Y+A174S+G182*+D183*+N195F+V206L+K391A+G476K	3.4	2.3	1.4	1.3	3.0	2.4	1.8	1.5
H1*+N54S+V56T+G109A+W167H +A174S+G182*+D183*+N195F+V206L+K391A+G476K	2.9	2.0	1.4	1.1	2.5	2.1	1.8	1.5

H1*+N54S+V56T+G109A+T165V+A174S+G182*+D183*+N195F+V206L+K391A+G476K	2.6	2.0	1.4	1.2	2.5	2.2	1.6	1.5
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K	3.2	2.4	1.3	1.2	3.0	2.1	1.9	1.5
H1*+N54S+V56T+G109A+A174N+G182*+D183*+N195F+V206L+K391A+G476K	2.8	2.2	1.4	1.2	2.7	1.8	1.4	1.4
H1*+N54S+V56T+G109A+A174Q+G182*+D183*+N195F+V206L+K391A+G476K	3.5	2.0	1.6	1.2	2.4	2.1	1.8	1.5
H1*+N16H+V17L+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+Y382F+K391A+G476K	2.7	1.9	1.3	1.2	4.6	2.3	1.6	1.4
H1*+Q32S+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+Q385L+K391A+G476K	2.7	1.8	1.3	1.1	3.5	2.2	1.4	1.3
H1*+N54S+V56T+R87S+G109A+R171H+A174S+G182*+D183*+N195F+V206L+K391A+G476K	2.5	1.9	1.1	1.1	3.4	2.1	1.4	1.4
N54S+G182*+D183*+N195F	1.1	1.1	1.1	1.0	1.6	1.5	1.0	1.0
G109A+G182*+D183*+N195F	1.6	1.4	1.3	1.0	1.8	1.4	1.0	1.1
A174S+G182*+D183*+N195F	0.8	1.1	1.3	0.9	1.2	1.2	0.9	1.0
G182*+D183*+N195F+V206L	0.7	0.7	1.0	1.0	0.9	1.3	0.8	1.0
G182*+D183*+N195F+K391A	1.6	1.4	1.3	1.0	1.4	1.5	1.0	1.1

G182*+D183*+N195F+G476K	1.3	1.4	1.3	1.0	1.8	1.5	1.1	1.0
H1*+N54S+V56T+G109A+R116H+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+K391A+G476K	3.5	1.9	1.2	1.1	3.4	2.2	1.6	1.2
H1*+N54S+V56T+G109A+A174*+G182*+D183*+N195F+V206L+K391A+G476K	3.4	2.1	1.3	1.1	3.2	2.1	1.5	1.1
H1*+K72R+G109A+F113Q+R116Q+W167F+Q172G+A174S+G182*+D183*+G184T+N195F+V206L+K391A+P473R+G476K	3.1	2.0	1.1	1.0	3.0	2.1	1.7	1.4
H1*+N54S+V56T+K72R+G109A+F113Q+R116Q+W167F+Q172G+A174S+G182*+D183*+G184T+N195F+V206L+P473R+G476K	3.1	1.9	1.2	1.0	3.0	1.9	1.6	1.3
H1*+N54S+V56T+G109A+Q169E+Q172G+A174*+G182*+D183*+N195F+V206L+K391A+G476K	3.0	1.9	1.1	1.0	2.7	2.0	1.3	1.2
H1*+N54S+V56T+K72R+G109A+F113Q+R116Q+W167F+Q172G+A174S+G182*+D183*+G184T+N195F+K391A+P473R+G476K	2.9	1.8	1.1	1.0	2.9	1.9	1.4	1.1
H1*+N54S+V56T+G109A+R116W+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+K391A+G476K	2.8	1.9	1.1	1.0	3.2	2.1	1.5	1.1
H1*+N54S+V56T+G109A+Q169E+Q172K+A174*+G182*+D18	2.7	1.8	1.3	1.0	3.3	2.0	1.7	1.2

3*+N195F+V206F+K391A+G476K								
H1*+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K	2.6	1.6	1.2	1.1	2.4	1.6	1.4	1.1
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+N260G+K391A+G476K	2.6	1.7	1.2	1.0	3.4	2.2	1.4	1.1
H1*+N54S+V56T+K72R+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K	2.6	1.5	1.2	1.0	3.1	1.8	1.6	1.2
H1*+N54S+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+G184T+N195F+V206L+K391A+ G476K	2.5	1.8	1.2	1.0	2.2	1.7	1.6	1.2
H1*+N54S+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+Y295N+K391A+ G476K	2.4	1.6	1.1	1.0	2.6	1.9	1.5	1.2
H1*+N54S+V56T+G109A+W167F+A174S+G182*+D183*+N195F+V206L+K391A+G476K	2.4	1.7	1.2	1.0	2.5	1.9	1.7	1.3
H1*+N54S+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+A186N+N195F+V206L+K391A+G476K	2.4	1.6	1.4	1.0	4.9	1.8	1.8	1.2
H1*+N54S+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+A288V+K391A+ G476K	2.4	1.6	1.1	1.0	2.4	1.6	1.3	1.1

H1*+N54S+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+G255A+K391A+G476K	2.4	1.9	1.2	1.0	3.2	2.2	2.0	1.3
H1*+N54S+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+K391A+G476K	2.3	1.7	1.1	1.1	3.2	2.2	1.5	1.2
H1*+W48F+N54S+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+K391A+G476K	2.3	1.6	1.1	1.0	2.3	1.6	1.4	1.2
H1*+N54S+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+V291A+K391A+G476K	2.3	1.8	1.2	1.1	1.8	1.8	1.6	1.2
H1*+N54S+V56T+G109A+F113Q+A174S+G182*+D183*+N195F+V206L+K391A+G476K	2.3	1.7	1.3	1.0	2.3	2.0	1.7	1.3
H1*+N54S+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+R320A+S323N+K391A+G476K	2.3	1.6	1.2	1.0	3.3	2.0	1.6	1.2
H1*+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+K391A+G476K	2.3	1.6	1.2	0.9	2.0	1.7	1.6	1.1
H1*+N54S+V56T+K72R+G109A+F113Q+R116H+W167F+Q172G+A174S+G182*+D183*+G184T+N195F+V206L+K391A+P473R+G476K	2.3	1.7	1.1	1.0	2.0	1.7	1.7	1.2

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+N270T+K391A+G476K	2.2	1.7	1.1	1.0	2.6	2.1	1.8	1.4
H1*+N54S+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+G476K	2.2	1.6	1.2	1.1	2.4	1.6	1.3	1.2
H1*+N54S+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+N260G+K391A+G476K	2.2	1.6	1.1	1.0	3.2	2.0	1.7	1.2
H1*+N54S+V56T+G109A+F113Q+R116H+A174S+G182*+D183*+N195F+V206L+K391A+G476K	2.2	1.7	1.1	1.1	3.4	2.1	1.4	1.2
H1*+N54S+V56T+G109A+Q172G+A174S+G182*+D183*+N195F+V206L+K391A+G476K	2.2	1.8	1.2	1.1	2.3	1.9	1.6	1.3
H1*+N54S+V56T+G109A+A174S+A186D+G182*+D183*+N195F+V206L+K391A+G476K	2.1	1.7	1.2	1.0	2.2	1.7	1.5	1.2
H1*+N54S+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+A225V+K391A+ G476K	2.1	1.8	1.0	0.9	2.0	2.0	1.9	1.3
H1*+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+K391A+G476K	2.1	1.5	1.1	0.9	1.8	1.4	1.3	1.1
H1*+N54S+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+G255S+K391A+ G476K	2.1	1.6	1.2	1.0	3.3	2.1	1.6	1.2

H1*+N54S+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+K269Q+K391A+G476K	2.1	1.7	1.0	1.1	2.0	1.8	1.4	1.3
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+G255S+K391A+G476K	2.1	1.5	1.1	1.0	2.0	1.5	1.2	1.0
H1*+N54S+V56T+G109A+Q169E+Q172K+A174S+G182*+D183*+N195F+V206L+K391A+G476K	2.1	1.6	1.1	1.1	2.9	2.1	1.5	1.3
G182*+D183*+N195F	2.0	1.7	1.2	0.9	2.9	1.8	1.8	1.2
H1*+N54S+V56T+G109A+Q169E+A174S+G182*+D183*+N195F+V206L+K391A+G476K	2.0	1.6	1.1	1.1	2.0	1.8	1.6	1.3
H1*+N54S+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+W284H+K391A+G476K	2.0	1.5	1.1	1.0	2.8	1.9	1.4	1.2
H1*+N54S+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K	2.0	1.5	1.1	1.0	2.3	1.8	1.4	1.2
H1*+N54S+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+S304R+K391A+ G476K	2.0	1.5	1.4	1.0	5.8	1.7	1.9	1.3
H1*+N54S+V56T+K72R+G109A+F113Q+R116Q+W167F+Q172G+A174S+G182*+D183*+G184T+ N195F+V206L+K391A+P473R	2.0	1.6	1.2	1.1	2.0	1.6	1.3	1.1
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V20	2.0	1.7	1.2	1.1	1.9	1.9	1.5	1.3

6L+M246V+K391A+G476K								
H1*+N54S+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+K391A	1.9	1.4	1.2	1.1	2.7	2.0	1.4	1.2
H1*+N54S+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+N270G+K391A+G476K	1.9	1.5	1.1	1.0	2.2	1.7	1.4	1.1
H1*+N54S+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+Y295F+K391A+G476K	1.9	1.6	1.2	1.0	2.7	1.8	1.4	1.2
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+R320A+K391A+G476K	1.9	1.5	1.2	1.1	2.9	1.8	1.3	1.3
H1*+N54S+V56T+G109A+Q169E+Q172K+A174T+G182*+D183*+N195F+V206L+K391A+G476K	1.9	1.9	1.2	1.0	2.4	2.1	1.6	1.4
H1*+N54S+V56T+G109A+Q169E+Q172K+G182*+D183*+N195F+V206L+K391A+G476K	1.9	1.7	1.1	1.0	2.6	1.7	1.8	1.2
H1*+N54S+V56T+G109A+W140Y+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+K391A+G476K	1.9	1.4	1.1	1.0	2.1	1.8	1.5	1.4
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A	1.9	1.6	1.1	1.1	2.2	1.9	1.7	1.4
H1*+N54S+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+F328L+K391A+	1.8	1.6	1.1	1.0	1.7	1.4	1.5	1.1

G476K								
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+G476K	1.8	2.0	1.5	1.1	5.2	2.0	1.8	1.5
F113Q+R116H+D183*+G182*+N195F	1.8	1.7	1.1	1.0	1.9	1.9	1.7	1.3
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+A288L+K391A+G476K	1.8	1.3	1.1	1.0	2.6	1.8	1.5	1.2
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+N270G+K391A+G476K	1.8	1.6	1.2	1.1	1.9	1.8	1.6	1.2
Q169E+Q172K+A174*+D183*+G182*+N195F	1.8	1.2	1.2	1.0	3.3	1.4	1.5	1.3
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K269Q+K391A+G476K	1.8	1.0	1.1	0.9	1.8	1.4	1.5	1.1
H1*+W48F+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K	1.8	1.4	1.1	1.0	2.2	1.7	1.5	1.2
F113Q+R116Q+D183*+G182*+N195F	1.8	1.7	1.1	1.0	2.1	1.7	1.7	1.4
N54S+V56T+D183*+G182*+N195F	1.8	1.2	0.8	0.9	1.3	1.3	1.0	1.0
H1*+N54S+V56T+G109A+A174T+G182*+D183*+N195F+V206L+K391A+G476K	1.7	1.7	1.2	1.1	2.4	1.9	1.8	1.3
H1*+N54S+V56T+G109A+R116W+A174S+G182*+D183*+N195F+V206L+K391A+G476K	1.7	1.6	1.2	1.1	1.8	1.8	1.6	1.2
Q169E+Q172K+G182*+D183*+N195F	1.7	1.4	1.3	1.0	4.9	1.6	1.8	1.3

G182*+D183*+A186D	1.7	1.6	1.0	1.0	1.6	1.7	1.3	1.1
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+V238A+K391A+G476K	1.7	1.5	1.1	1.0	1.8	1.6	1.4	1.1
G182*+D183*+A186N	1.7	1.8	1.2	1.1	3.8	1.8	1.6	1.5
H1*+N54S+V56T+G109A+A174S+V206L+G182*+D183*+K391A+G476K	1.7	1.1	1.1	1.0	3.3	1.1	1.3	1.1
H1*+N54S+V56T+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+K391A+G476K	1.7	1.4	1.3	1.0	3.6	1.4	1.8	1.2
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206F+K391A+G476K	1.7	1.7	1.2	1.0	1.7	1.7	1.6	1.3
H1*+N54S+V56T+G109A+G182*+D183*+N195F+V206L+K391A+G476K	1.7	1.4	1.1	1.0	1.9	1.6	1.2	1.0
H1*+N54S+V56T+G109A+Q172K+A174S+G182*+D183*+N195F+V206L+K391A+G476K	1.7	1.5	1.1	1.1	3.6	1.6	1.5	1.3
H1*+N54S+V56T+G109A+Q172K+A174*+G182*+D183*+N195F+V206L+K391A+G476K	1.6	1.4	1.1	1.1	1.6	1.4	1.3	1.1
H1*+N54S+V56T+G109A+A174N+G182*+D183*+N195F+V206L+K391A+G476K	1.6	1.8	1.2	1.2	4.6	2.0	2.0	1.7
H1*+N54S+V56T+G109A+A174S+A186N+G182*+D183*+N195F+V206L+K391A+G476K	1.6	1.8	1.1	1.0	1.5	1.9	1.7	1.3

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+F289L+K391A+G476K	1.6	1.5	1.0	1.0	1.7	1.7	1.4	1.2
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+Y295F+K391A+G476K	1.6	1.2	1.0	0.8	1.2	1.2	1.3	1.1
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+V291A+K391A+G476K	1.6	1.2	1.1	1.0	1.2	1.0	1.2	1.0
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+S244Q+K391A+G476K	1.5	1.4	1.1	1.0	2.1	1.5	1.3	1.1
G182*+D183*+F328L	1.5	1.5	1.1	1.1	1.8	1.8	1.6	1.3
G182*+D183*+N195F+A288V	1.5	1.3	1.2	1.0	1.8	1.6	1.5	1.1
G182*+D183*+A186N+N195F	1.5	1.6	0.9	0.9	2.4	1.7	1.5	1.2
G182*+D183*+E190P+N195F	1.5	1.4	0.9	1.0	2.1	1.7	1.1	1.1
W140Y+G182*+D183*+N195F	1.5	1.4	1.1	1.1	1.4	1.7	1.5	1.3
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+A225V+K391A+G476K	1.5	1.0	1.1	0.9	1.5	1.0	1.5	1.0
G182*+D183*+A186D+N195F	1.5	1.7	1.4	1.1	3.3	2.0	1.8	1.6
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+P473R+G476K	1.5	1.2	1.1	1.0	1.5	1.2	1.3	1.2
H1*+W48Y+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K	1.5	1.3	1.0	1.1	1.2	1.4	1.3	1.2

H1*+N54S+V56T+G109A+Q169E+Q172K+A174*+G182*+D183*+N195F+V206L+K391A+G476K	1.5	1.3	1.4	1.1	3.8	1.4	1.5	1.3
G182*+D183*+N195F+V238A	1.5	1.5	1.0	1.1	1.9	1.4	1.1	1.0
G182*+D183*+Y295N	1.4	1.1	1.3	1.0	2.5	1.2	1.6	1.2
Q172G+G182*+D183*	1.4	1.4	1.1	1.0	1.4	1.3	1.5	1.3
F113Q+G182*+D183*+N195F	1.4	0.8	1.0	0.8	1.0	1.0	1.3	1.0
H1*+N54S+V56T+Q98A+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K	1.4	1.3	1.2	1.0	2.7	1.1	1.5	1.2
G182*+D183*+N195F+Y295F	1.3	1.3	1.2	1.1	1.3	1.2	1.4	1.1
G182*+D183*+A186E	1.3	1.2	1.2	1.0	2.0	1.4	1.4	1.2
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206Y+K391A+G476K	1.3	1.1	1.2	1.1	2.8	1.2	1.3	1.2
G182*+D183*+N195F+W284H	1.3	1.6	1.1	1.2	3.3	1.8	1.6	1.6
G182*+D183*+A186Q+N195F	1.3	1.2	1.1	1.0	2.0	1.7	1.5	1.1
K72R+G182*+D183*	1.3	1.3	1.0	1.0	1.4	1.5	1.3	1.1
D183*+G182*+N195F+V326L	1.3	1.6	1.2	1.2	3.5	1.8	1.5	1.6
D183*+G182*+A186E+N195F	1.3	1.3	1.1	1.0	1.7	1.4	1.5	1.2
Q169E+G182*+D183*+N195F	1.2	1.0	1.1	1.0	1.7	0.8	1.4	1.2
D183*+G182*+N195F+K242Q	1.2	0.8	0.9	0.9	2.0	1.2	0.9	1.0
G7A+G182*+D183*+N195F	1.2	1.2	1.1	1.0	1.5	1.6	1.4	1.1

D183*+G182*+N195F+N260G	1.2	1.4	1.0	0.9	1.6	1.2	1.3	1.1
D183*+G182*+R321A+S323N	1.2	1.3	1.1	1.1	1.2	1.1	1.5	1.2
D183*+G182*+W284H	1.2	0.9	1.2	1.0	0.9	1.0	1.1	1.1
H1*+D183*+G182*	1.2	1.5	1.0	1.0	3.6	1.7	1.6	1.3
D183*+G182*+A186H+N195F	1.1	1.3	1.1	1.0	2.0	1.2	1.4	1.0
D183*+G182*+F289V	1.1	1.3	1.0	1.0	2.2	1.3	1.7	1.4
D183*+G182*+K391A	1.1	0.7	1.0	0.8	0.7	0.7	1.0	0.8
D183*+G182*+S304R	1.1	1.2	0.9	0.9	0.6	0.9	1.0	1.0
W167F+G182*+D183*+N195F	1.1	1.0	1.0	0.9	3.3	1.1	1.3	1.1
F113Q+R116H+D183*+G182*	1.1	0.7	1.0	0.8	1.2	0.8	1.3	0.9
D183*+G182*+N270G	1.1	1.0	0.9	0.9	1.0	1.3	1.0	1.0
D183*+G182*+S244Q	1.0	1.1	1.1	0.9	1.8	1.6	1.5	1.0
H1*+N54S+V56T+G109A+A174S+G182*+D183*+G184T+N195F+V206L+K391A+G476K	1.0	1.0	1.1	1.0	0.6	0.6	0.9	0.9
D183*+G182*+N195F+Y295N	1.0	1.1	1.0	1.0	1.6	0.9	1.2	1.3
W48F+D183*+G182*	1.0	0.9	1.0	0.9	1.8	1.0	1.3	1.0
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+G255A+K391A+G476K	1.0	1.2	1.0	1.0	1.8	1.1	1.2	1.1
D183*+G182*+A186Q	1.0	0.7	1.1	0.9	0.4	0.5	1.0	0.9
W140Y+D183*+G182*	0.9	0.6	0.9	0.9	0.5	0.9	1.1	1.0

D183*+G182*+K242Q	0.9	0.8	1.0	0.9	0.8	0.9	1.0	1.1
D183*+G182*+V206L	0.9	0.8	0.9	0.9	1.1	0.9	0.9	0.9
D183*+G182*+N195F+V206F	0.9	0.9	0.9	1.1	0.5	0.8	1.1	1.0
Q169E+D183*+G182*	0.9	0.8	1.0	0.9	1.1	0.8	0.9	0.9
D183*+G182*+N195F+R320A	0.8	0.9	1.1	1.0	0.8	0.9	1.0	1.0
G182*+D183*+G184T+N195F	0.8	1.1	0.9	1.0	0.9	1.0	1.2	1.0
D183*+G182*+G184T	0.8	0.9	1.0	0.9	0.7	0.8	1.0	1.1
N54S+V56T+D183*+G182*	0.8	0.8	1.1	1.0	0.9	0.7	1.1	0.9
D183*+G182*+P473R	0.8	0.9	1.0	1.0	1.1	0.8	1.0	1.0
W48Y+D183*+G182*	0.8	0.9	1.1	1.1	1.0	0.6	1.0	0.9
D183*+G182*+R323A	0.8	0.8	0.9	1.0	1.1	0.8	1.1	0.8
G7A+D183*+G182*	0.8	0.8	1.1	0.9	1.3	1.1	1.2	1.0
G109A+D183*+G182*	0.8	0.8	0.8	0.8	0.0	0.6	1.0	1.1
W167F+D183*+G182*	0.7	0.7	1.0	0.9	1.4	0.9	1.1	1.0
H1*+N54S+V56T+G109A+Q169E+Q172K+A174S+G182*+D183*+N195F+V206L+K391A+G476K	0.7	0.7	0.8	0.9	1.1	0.5	0.8	0.8
A174S+D183*+G182*	0.7	1.2	0.8	0.9	2.2	0.9	1.1	1.3
R116Q+D183*+G182*	0.7	0.7	0.9	0.9	0.7	0.6	1.1	0.9
D183*+G182*+N195F+V291A	0.7	0.9	1.0	1.1	0.6	0.9	0.9	1.0
Q172K+D183*+G182*	0.7	0.9	0.9	1.0	0.4	0.5	1.1	0.9

N54S+D183*+G182*	0.7	1.2	1.0	1.1	1.7	1.1	1.0	1.3
D183*+G182*+N195F+S323N	0.7	0.9	0.8	0.9	1.8	1.0	1.0	1.0
D183*+G182*+N195F+M246V	0.7	0.8	1.1	1.0	0.6	0.5	0.9	0.9
W48Y+D183*+G182*+N195F	0.6	1.2	1.1	1.1	2.0	1.5	1.2	1.4
D183*+G182*+N195F+S304R	0.6	1.1	0.7	1.0	1.6	0.7	1.0	1.2
V56T+D183*+G182*	0.3	0.8	0.2	0.6	1.9	0.6	0.3	0.7

Modificaciones en la SEQ ID NO: 14	**A-15-0.05mg/L**	**A-15-0.2mg/L**	**A-40-0.05mg/L**	**A-40-0.2mg/L**	**J-15-0.05mg/L**	**J-15-0.2mg/L**	**J-30-0.05mg/L**	**J-30-0.2mg/L**
Referencia	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0
G182*+D183*+N195F	1.4	1.2	1.0	1.0	1.2	1.3	1.1	1.1
H1*+G182*+D183*+N195F	1.1	1.0	1.0	1.1	1.1	1.0	1.1	1.1
N54S+G182*+D183*+N195F	1.2	1.1	0.9	1.1	1.3	1.1	1.1	1.1
V56T+G182*+D183*+N195F	1.4	1.1	1.0	1.0	1.5	1.2	1.1	1.1
G182*+D183*+N195F+I405L	1.1	1.1	1.0	1.0	1.1	1.1	1.0	1.0
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F +V206L+I405L+A421H+A422P+A428T+ D476K	1.0	1.1	0.9	0.9	1.4	1.0	1.1	0.9

A174S+G182*+D183*+N195F	1.2	1.0	1.0	0.9	0.9	0.9	1.0	1.0
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F +V206L+I405L+A421H+A422P+A428T	1.4	1.3	1.1	1.0	1.6	1.3	1.3	1.1
H1*+N54S+V56T+G109A+A174S+D183*+N195F+V206L +K391A+I405L+A421H+A422P+A428T	1.2	1.3	1.0	1.0	1.6	1.3	1.2	1.1
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F +V206L+K391A+I405L+A421H+A422P+ A428T+D476K	1.3	1.3	1.1	1.0	1.4	1.3	1.1	1.0
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F +V206L+K391A+I405L+A421H+A422P+ A428T+D476G	1.2	1.1	1.1	1.0	1.4	1.2	1.2	1.1
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F +V206L+K391A+I405L+A421H+A422P+ A428T+D476K+G477S	1.3	1.3	1.0	1.0	1.5	1.2	1.1	1.0
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F +V206L+K391A+I405L+A421H+A422P+ A428T+D476K	1.3	1.2	1.0	1.0	1.5	1.2	1.2	1.0
H1*+N54S+V56T+K72R+G109A+W167F+A174S+G182*+ D183*+N195F+V206L+I405L+A421H+ A422P+A428T	1.1	1.2	1.0	1.1	1.4	1.4	1.3	1.1

H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F +V206L+S280Q+H321Y+I405L+A421H+ A422P+A428T	0.9	1.2	1.1	0.9	1.3	1.2	1.3	1.0
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F +V206L+S304N+I405L+A421H+A422P+ A428T+D476K	1.1	1.2	1.0	1.0	1.2	1.1	1.1	1.0
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F +V206L+K391A+I405L+A421H+A422P+ A428T+D476K+G477A	1.2	1.2	1.0	1.0	1.2	1.0	1.0	0.9
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F +V206L+K391A+I405L+A421H+A422P+ A428T+D476G+G477T	1.6	1.4	1.1	1.1	1.9	1.4	1.3	1.2
H1*+N54S+V56T+G109A+F113Q+R116Q+Q172N+A174S +G182*+D183*+N195F+V206L+I405L+ A421H+A422P+A428T	0.9	1.2	0.8	1.1	0.8	1.7	0.9	1.1
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F +V206L+K391A+I405L+A421H+A422P+ A428T+G477Q	1.7	1.3	1.1	1.0	1.9	1.4	1.3	1.1
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F +V206L+K391A+I405L+A421H+A422P+	1.5	1.4	1.1	1.0	1.9	1.4	1.3	1.1

A428T+G477A								
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F +V206L+K391A+I405L+A421H+A422P+ A428T+D476K+G477Q	1.3	1.3	1.0	1.0	1.7	1.2	1.1	1.0
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F +V206L+K391A+I405L+A421H+A422P+ A428T+D476N	1.5	1.3	1.1	1.1	1.7	1.4	1.3	1.2
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F +V206L+K391A+I405L+A421H+A422P+ A428T+D476Y	1.5	1.3	1.1	1.0	1.7	1.3	1.3	1.2
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F +V206I+I405L+A421H+A422P+A428T	1.5	1.2	1.1	1.1	2.2	1.4	1.4	1.1
H1*+N54S+V56T+G109A+Q172D+A174S+G182*+D183* +N195F+A204G+V206L+I405L+A421H+ A422P+A428T	1.4	1.3	1.1	1.0	2.8	2.0	1.4	1.2
H1*+N54S+V56T+K72R+G109A+T134E+A174S+G182*+ D183*+N195F+A204G+V206L+G255A+ I405L+A421H+A422P+A428T	1.3	1.1	1.0	1.0	2.1	2.1	1.3	1.0
H1*+N54S+V56T+G109A+F113Q+R116H+T165G+Q172G +A174S+G182*+D183*+N195F+V206L+	1.3	1.3	1.0	1.0	2.9	1.9	1.3	1.1

I405L+A421H+A422P+A428T								
H1*+N54S+V56T+G109A+F113Q+Q172N+A174S+G182*+D183*+N195F+V206L+I405L+A421H+A422P+A428T	1.3	1.3	1.1	1.1	1.9	2.2	1.5	1.3
H1*+N54S+V56T+K72R+G109A+T134E+A174S+G182*+D183*+N195F+G196R+V206L+G255A+I405L+A421H+A422P+A428T+N475S	1.4	1.3	1.1	1.1	2.5	2.3	1.5	1.3
H1*+N54S+V56T+G109A+T134E+A174S+G182*+D183*+N195F+V206L+I405L+A421H+A422P+A428T	1.8	1.5	1.2	1.0	2.3	1.8	1.5	1.2
H1*+T40D+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+I405L+A421H+A422P+A428T	2.0	1.5	1.2	1.1	1.8	1.6	1.5	1.3
H1*+N54S+V56T+G109A+F113Q+N125D+A174S+G182*+D183*+N195F+V206L+I405L+A421H+A422P+A428T	2.1	1.6	1.3	1.0	2.2	1.7	1.5	1.2
H1*+N54S+V56T+A60V+G109A+R116Q+A174S+G182*+D183*+N195F+V206L+I405L+A421H+A422P+A428T	1.6	1.6	1.1	1.0	1.9	1.6	1.4	1.2
H1*+N54S+V56T+G109A+R116V+A174S+G182*+D183*	1.4	1.4	1.0	1.0	2.1	1.4	1.4	1.2

+N195F+V206L+I405L+A421H+A422P+ A428T								
H1*+N54S+V56T+G109A+R116Q+G133Q+T165G+Q172G +A174S+G182*+D183*+N195F+V206L+ I405L+A421H+A422P+A428T	1.1	1.4	1.0	1.1	2.0	2.3	1.5	1.3
H1*+N54S+V56T+G109A+F113Q+R116H+Q172G+A174S +G182*+D183*+N195F+V206L+I405L+ A421H+A422P+A428T	1.7	1.6	1.2	1.1	3.0	1.9	1.5	1.2
H1*+N54S+V56T+G109A+F113Q+R116Q+Q172G+A174S +G182*+D183*+N195F+V206L+I405L+ A421H+A422P+A428T+G448D	1.4	1.5	1.1	1.1	2.1	1.8	1.3	1.2
H1*+N54S+V56T+G109A+F113Q+R116H+Q172N+A174S +G182*+D183*+N195F+V206L+I405L+ A421H+A422P+A428T	2.2	1.6	1.3	1.2	2.5	1.6	1.6	1.3
H1*+N54S+V56T+K72R+G109A+T134E+W167F+Q172N+ A174S+G182*+D183*+N195F+V206L+ G255A+A265G+I405L+A421H+A422P+A428T	2.2	1.6	1.3	1.2	2.4	1.6	1.7	1.2
H1*+N54S+V56T+K72R+G109A+R116Q+W167F+Q172R+ L173V+A174S+G182*+D183*+N195F+ V206L+A265G+I405L+A421H+A422P+A428T	2.0	1.6	1.2	1.2	2.3	1.6	1.7	1.2

H1*+N54S+V56T+K72R+G109A+R116Q+W167F+Q172R+ A174S+G182*+D183*+N195F+V206L+ I405L+A421H+A422P+A428T	2.1	1.4	1.3	1.2	2.3	1.6	1.7	1.2
H1*+N54S+V56T+K72R+G109A+F113Q+T134E+W167F+ Q172G+A174S+G182*+D183*+N195F+ V206L+G255A+I405L+A421H+A422P+A428T	2.0	1.5	1.1	1.1	2.6	1.9	1.4	1.2
H1*+N54S+V56T+K72R+G109A+F113Q+R116H+W167F+ Q172G+L173V+A174S+G182*+D183*+ G184T+N195F+V206L+I405L+A421H+A422P+A428T	1.7	1.6	1.0	0.9	1.8	1.5	1.1	1.1
H1*+N54S+V56T+G109A+F113Q+W167F+Q172G+A174S +G182*+D183*+N195F+V206L+I405L+ A421H+A422P+A428T	1.2	1.2	1.0	0.9	2.2	1.3	1.2	1.1
H1*+N54S+V56T+K72R+G109A+A174S+G182*+D183*+ N195F+V206L+G255A+I405L+A421H+ A422P+A428T	1.5	1.2	1.2	1.0	2.2	1.1	1.5	1.1
H1*+N54S+V56T+G109A+F113Q+R116Q+A174S+G182* +D183*+N195F+V206L+I405L+A421H+ A422P+A428T	1.6	1.3	1.1	1.0	1.4	1.2	1.3	1.1
H1*+N54S+V56T+K72R+G109A+F113Q+F116H+W167F+ Q172G+L173V+A174S+G182*+D183*+	1.8	1.6	1.0	1.0	0.9	1.4	0.9	1.1

N195F+V206L+I405L+A421H+A422P+A428T								
H1*+N54S+V56T+K72R+G109A+F113Q+R116Q+W167F+ Q172G+A174S+G182*+D183*+G184T+ N195F+V206L+I405L+A421H+A422P+A428T	1.8	1.5	1.1	1.0	1.9	1.5	1.3	1.1
H1*+N54S+V56T+G109A+F113Q+R116Q+W167F+Q172G +A174S+G182*+D183*+N195F+A204G+V206L+I405L+ A421H+A422P+A428T	2.0	1.5	1.0	1.0	1.8	1.5	1.2	1.0
H1*+N54S+V56T+G109A+F113Q+R116H+W167F+Q172G +A174S+G182*+D183*+N195F+V206L+A265G+I405L+ A421H+A422P+A428T	1.5	1.3	0.9	0.9	1.4	1.3	1.2	1.1
H1*+N54S+V56T+G109A+R116Q+A174S+G182*+D183* +N195F+V206L+I405L+A421H+A422P+ A428T	1.8	1.6	1.0	0.9	1.6	1.3	1.4	1.1
H1*+N54S+V56T+A60V+G109A+R116Q+W167F+Q172N+ L173V+A174S+G182*+D183*+N195F+ V206L+I405L+A421H+A422P+A428T	1.4	1.4	0.7	0.9	1.1	1.3	0.8	1.0
H1*+A37H+N54S+V56T+A60V+G109A+R116Q+T165G+A 174S+G182*+D183*+N195F+V206L+ I405L+A421H+A422P+A428T	1.9	1.6	1.1	1.1	1.7	1.6	1.4	1.2
H1*+N54S+V56T+G109A+A174S+M105F+G182*+D183*	1.4	1.2	1.0	1.0	1.5	1.2	1.2	1.0

+N195F+V206L+L228I+R320A+S323N+ I405L+A421H+A422P+A428T								
H1*+N54S+V56T+K72R+G109A+F113Q+T134E+A174S+ G182*+D183*+N195F+V206L+G255A+ I405L+A421H+A422P+A428T	1.8	1.5	1.1	1.0	1.7	2.1	1.4	1.2
H1*+N54S+V56T+K72R+G109A+R116Q+V120L+A174S+ G182*+D183*+G184T+N195F+V206L+ I405L+A421H+A422P+A428T	2.1	1.8	1.2	1.1	2.8	2.5	1.6	1.3
H1*+N54S+V56T+G109A+F113Q+R116H+W167F+Q172G +L173V+A174S+G182*+D183*+N195F+V206L+I405L+ A421H+A422P+A428T	2.6	1.9	1.2	1.1	2.8	2.6	1.6	1.3
H1*+N54S+V56T+G109A+F113Q+R116Q+Q172N+A174S +G182*+D183*+N195F+V206L+A265G+ I405L+A421H+A422P+A428T	2.3	1.6	1.1	1.1	3.0	2.1	1.5	1.3
H1*+A37H+N54S+V56T+A60V+G109A+R116Q+W167F+Q 172R+A174S+G182*+D183*+N195F+ V206L+I405L+A421H+A422P+A428T	2.1	1.7	1.2	1.1	2.5	2.1	1.5	1.2

Ejemplo 4: Rendimiento de lavado de un subconjunto de variantes de acuerdo con la invención (AMSA)

Se han probado las siguientes variantes, tal como se ha descrito anteriormente. Las mediciones de color se llevaron a cabo mediante el uso de un escáner plano profesional (Kodak iQsmart, Kodak) usado para capturar una imagen del artículo textil lavado y con un sistema para obtención de imágenes digitales controlado (DigiEye) para capturar una imagen de las placas de melamina lavadas.

Con el fin de extraer un valor para la intensidad de la luz a partir de las imágenes escaneadas, los valores en píxeles de 24 bits de la imagen se convierten en valores para rojo, verde y azul (RBG, por sus siglas en inglés). El valor de la intensidad (Int) se calcula sumando los valores RBG como vectores y tomando a continuación la longitud del vector resultante:

$$Int = \sqrt{r^2 + g^2 + b^2}$$

Los resultados obtenidos fueron los siguientes;

Modificaciones en la SEQ ID NO: 13	**A-15-0.05mg/L**	**A-15-0.2mg/L**	**A-40-0.05mg/L**	**A-40-0.2mg/L**	**J-15-0.05mg/L**	**J-15-0.2mg/L**	**J-30-0.05mg/L**	**J-30-0.2mg/L**
Referencia	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0
G182*+D183*+N195F + V206F + N260P + L312I + L313I + R320A + T355L + L389I + T400P	0.7	1.0	0.6	0.7	1.3	0.9	0.8	1.0
G182* + D183* + N195F	0.1	0.7	1.0	1.0	1.0	0.8	1.0	1.0
H1*+N54S+V56T+G109A+A174S+G182*+D183*+N195F+V206L+K391A+G476K	1.7	1.9	1.7	1.3	2.5	1.9	1.2	1.2
H1* + G50A + T51A + V56T + G109A + A174S + G182* + D183* + N195F + V206L + G476K	1.5	1.6	1.5	1.4	2.5	1.6	1.3	1.2
H1* + N54S + V56T + M105F + G109A + A174S + G182* + D183* + N195F + V206L + R320A + S323N + K391A + G476K	2.5	2.2	1.6	1.4	3.8	1.9	1.2	1.1
H1* + T40K + N54S + V56T + G109A + G149H + A174S + G182* + D183* + N195F + V206L + K391A + G476K	0.9	1.2	1.0	1.0	0.8	1.2	0.9	1.0
H1* + N54S + V56T + K72R + G109A + A174S + G182* + D183* + N195F + V206L + G255A + K391A + G476K	1.9	1.7	1.4	1.4	2.8	1.5	1.2	1.1
H1* + N16H + V17L + N54S + V56T + G109A + A174S + G182* + D183* + N195F + V206L + K391A + G476K	2.6	1.8	1.7	1.4	3.6	1.8	1.3	1.1

H1* + Q22N + N54S + V56T + G109A + A174S + G182* + D183* + N195F + V206L + K391A + G476K	2.5	1.9	1.8	1.4	3.8	2.1	1.3	1.1
H1* + Q32S + N54S + V56T + G109A + A174S + G182* + D183* + N195F + V206L + K391A + G476K	2.3	1.9	1.9	1.5	3.3	2.0	1.2	1.2
H1* + H28N + N54S + V56T + G109A + A174S + G182* + D183* + N195F + V206L + K391A + G476K	2.7	1.7	1.6	1.5	4.2	2.0	1.3	1.1
H1* + N29S + N54S + V56T + G109A + A174S + G182* + D183* + N195F + V206L + K391A + G476K	1.6	1.3	1.3	1.4	2.6	1.6	1.2	1.0
H1* + H28N + N29S + N54S + V56T + G109A + A174S + G182* + D183* + N195F + V206L + K391A + G476K	1.8	1.9	1.8	1.4	3.1	1.8	1.2	1.1
H1* + N54S + V56T + G109A + A174S + R176K + N195F + V206L + K391A + G476K	2.3	2.0	1.7	1.5	5.1	1.9	1.3	1.2
H1* + N54S + V56T + G109A + Q169E + Q172K + A174* + R176K + N195F + V206L + K391A + G476K	3.8	2.4	2.1	1.7	5.6	2.8	1.4	1.2
H1* + N54S + V56T + G109A + A174S + N175G + N195F + V206L + K391A + G476K	2.6	1.8	1.8	1.4	4.9	2.0	1.3	1.2
H1* + N54S + V56T + G109A + A174S + N195F + V206L + V291A + Y295N + Q299T + K391A + G476K	1.7	1.4	1.4	1.3	2.7	1.6	1.0	1.1
H1* + N54S + V56T + G109A + A174S + N195F + V206L + K269S + A274K + K391A + G476K	1.7	1.4	1.6	1.2	1.4	1.8	1.0	1.0

H1* + N54S + V56T + G109A +A174S + N195F +V206L + L235I + K391A + G476K	2.6	1.5	2.0	1.3	1.3	2.1	1.0	1.1
H1* + N54S + V56T + G109A + A174S + N195F + V206L + L235V + V238A + K391A + G476K	2.8	1.4	1.7	1.2	0.6	2.2	1.1	1.0
H1* + N54S + V56T + G109A + A174S + N195F + V206L + Q365S + K391A + G476K	1.9	1.5	1.9	1.3	2.0	1.7	1.2	1.0
H1* + N54S + V56T + G109A + A174S + N195F + V206L + K391A + H402R + G476K	2.2	1.4	2.0	1.2	0.6	1.2	1.1	1.1
H1* + N54S + V56T + G109A + A174S + N195F + V206L + R320S + H321N + K391A + G476K	5.6	2.7	2.5	1.6	4.2	2.9	1.2	1.2
H1* + N54S + V56T + G109A + Q169E + Q172K + A174* + N195F + V206L + K391A + G476K	3.8	2.6	3.0	1.7	3.6	2.8	1.3	1.2
H1* + N54S + V56T + G109A + Q125S + A174S + N195F + V206L + K391A + G476K	3.1	2.2	2.4	1.4	2.0	2.3	1.3	1.1
H1* + N54S + V56T + G109A + A174S + N195F + V206L + L235V + K391A + G476K	4.2	1.9	1.9	1.5	1.8	2.4	1.0	1.0
H1* + N54S + V56T + G109A + A174S + N195F + V206L + A265G + K391A + G476K	4.2	1.5	2.2	1.4	1.2	2.6	1.1	1.1
H1* + T51Q + N54S + V56T + G109A + A174S + N195F + Y203F + V206L + K391A + G476K	3.7	2.1	2.6	1.6	3.6	2.7	1.3	1.1

H1* + N54S + V56T + G109A + Q169E + Q172K + A174* + N175Q + N195F + V206L + K391A + G476K	4.0	2.0	2.7	1.5	3.3	2.8	1.2	1.2
H1* + H28N + N54S + V56T + G109A + A174S + G182* + D183* + N195F + V206L + K391A + G476K	4.5	2.3	2.5	1.6	3.1	2.7	1.2	1.1
H1* + N54S + V56T + G109A + T134E + A174S + G182* + D183* + N195F + V206L + K391A + G476K	3.9	2.1	2.6	1.6	3.3	3.0	1.4	1.1
H1* + N54S + V56T + G109A + A174S + G182* + D183* + N195F + V206L + D377H + K391A + G476K	5.3	2.9	3.0	1.7	3.8	2.9	1.3	1.2
H1* + G50A + T51A + N54S + V56T + G109A + A174S + G182* + D183* + N195F + V206L + K391A + G476K	4.4	2.1	2.3	1.4	2.6	2.3	1.3	1.2
H1* + G7K + N54S + V56T + G109A + A174S + G182* + D183* + N195F + V206L + K391A + G476K	4.1	2.3	2.7	1.6	2.4	2.5	1.3	1.2
H1* + N54S + V56T + G109A + A174S + G182* + D183* + N195F + M202V + V206L + K391A + G476K	2.7	1.9	1.4	1.4	1.9	2.2	0.9	1.0
H1* + N54S + V56T + M105F + G109A + A174S + N195F + V206L + M246F + K391A + G476K	3.7	2.1	2.4	1.5	2.7	2.5	1.2	1.1
H1* + N16H + V17L + N54S + V56T + G109A + A174S + G182* + D183* + N195F + V206L + D377H + K391A + G476K	4.5	2.7	1.8	1.4	4.3	2.2	1.5	1.3
H1* + N54S + V56T + G109A + A174S + N195F + V206L	1.1	1.9	1.3	1.1	3.0	1.9	1.3	1.1

H1* + T51G + N54S + V56T + G109A + A174S + N195F + Y203G + V206L + K391A + G476K	2.2	1.8	1.1	1.0	2.7	2.0	0.9	1.1
H1*+ T51G + N54S + V56T + G109A + G110N + A174S + N195F + V206L + K391A + G476K	1.6	2.1	1.0	1.1	1.9	1.9	1.1	1.1
H1* + N54S + V56T + G109A + Q125S + A174S + N175G + N195F + V206L + K391A + G476K	2.0	2.3	1.5	1.2	2.6	1.8	1.3	1.2
H1* + N54S + V56T + G109A + A174S + N195F + V206L + A265G + V291A + F328L + K391A + G476K	0.7	2.1	1.1	1.0	1.8	1.7	1.0	1.1
H1* + N54S + V56T + G109A + A174S + N195F + V206L + M246F + A265G + V291A + F328L + Q365S + K391A + G476K	3.9	2.6	1.9	1.4	4.0	2.1	1.5	1.2
H1* + N16Y + N54S + V56T + G109A + R116H + A174S + N195F + V206L + G337E + D377H + K391A + G476K	4.8	3.5	2.0	1.5	4.9	2.7	1.5	1.3
H1* + I9L + N54S + V56T + G109A + Q125S + V131T + A174* + V206L + Y267F + F289H + Q361E + K391A + G476K	3.1	2.9	1.4	1.2	2.5	2.0	1.2	1.1

La invención descrita y reivindicada en la presente no debe estar limitada en cuanto a su alcance por los aspectos específicos que se describen en la presente, ya que se pretende que estos aspectos sean ilustraciones de varios aspectos de la invención. Se pretende que cualesquiera aspectos equivalentes queden incluidos en el alcance de esta invención. De hecho, varias modificaciones de la invención, además de las mostradas y descritas en la presente, serán evidentes para los expertos en la técnica teniendo en cuenta la descripción anterior. También se pretende que tales modificaciones queden incluidas en el alcance de las reivindicaciones adjuntas. En caso de contradicción, prevalecerá la presente descripción, incluidas las definiciones.

Se hace constar que con relación a esta fecha, el mejor método conocido por la solicitante para llevar a la práctica la citada invención, es el que resulta claro de la presente descripción de la invención.