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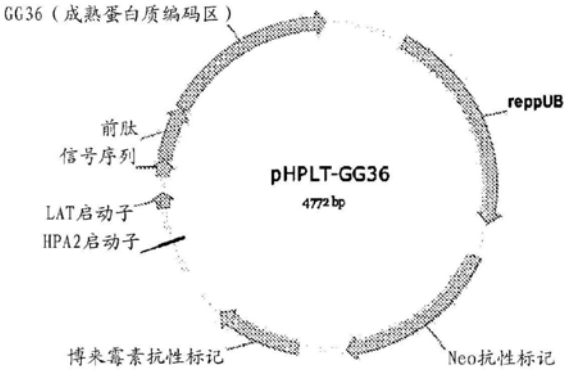
(54)发明名称

包含枯草杆菌蛋白酶变体的组合物和方法

(57)摘要

本发明提供由丝氨酸蛋白酶制备的丝氨酸蛋白酶变体。具体地讲，本发明提供与参照丝氨酸蛋白酶相比具有一个或多个置换的丝氨酸蛋白酶变体。此外，本发明提供包含这些丝氨酸蛋白酶变体的组合物。在一些实施例中，本发明提供包含这些丝氨酸蛋白酶变体中的至少一种的清洁组合物。



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1.一种分离的枯草杆菌蛋白酶变体,其中所述枯草杆菌蛋白酶变体为具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:N043R-N076D-S101A-S103A-V104I-A158E-S188D-L217E-A232V-Q245R-N248D-H249R-E271F,N043R-N076D-S101A-S103A-V104I-A158E-S188D-A232V-Q245R-N248D-H249R-E271F,N062E-A158E-S188D-H249R-E271F,N062E-R186H-S188D-H249R-E271F,N062E-S101A-S188D-H249R-E271F,N062E-V104L-A158E-S188D-H249R-E271F,S101A-S103A-V104I-A158E-S188D-A232V-Q245R-N248D-H249R-E271F-E271F,S128N-A158E-R186H-S188D-E271F,S128N-A158E-S188D-E271F,S128N-A158E-S188D-Y209E-E271F,A016S-N062E-V104L-R186H-S188D-E271F,A158E-R186H-S188D-H249R-E271F,N043R-N076D-S101A-S103A-V104I-A158E-S166D-S188D-A232V-Q245R-N248D-H249R-E271F,N062E-S101A-R186H-S188D-E271F,N062E-S101A-V104L-R186H-S188D-E271F,N076D-S101A-S103A-V104I-A158E-S166D-S188D-A232V-Q245R-N248D-H249R-E271F,N076D-S101A-S103A-V104I-A158E-S188D-A232V-Q245R-N248D-H249R-E271F,N076D-S101G-S103A-V104I-A114V-A158E-S188D-A232V-Q245R-N248D-H249R-E271F,S024R-N076D-S101A-S103A-V104I-A158E-S166D-S188D-A232V-Q245R-N248D-H249R-E271F,S101A-S103A-V104I-A158E-S166D-S188D-A232V-Q245R-N248D-H249R-E271F,S101A-S103A-V104I-A158E-S188D-A232V-Q245R-N248D-H249R-E271F,S101A-S103A-V104I-A158E-S188D-L217E-A232V-Q245R-N248D-H249R-E271F,S101A-S128N-A158E-S188D-Y209E-E271F,S101A-V104L-A158E-R186H-S188D-E271F,S101G-S103A-V104I-A158E-S166D-S188D-A232V-Q245R-N248D-H249R-E271F,V104L-A158E-R186H-S188D-H249R-E271F,V104L-A158E-S188D-H249R-E271F,和V104L-S128N-A158E-R186H-S188D-E271F,并且其中所述变体的总净电荷相对于如SEQ ID NO:2所示迟缓芽孢杆菌(Bacillus lentus)枯草杆菌蛋白酶GG36蛋白酶的总净电荷为0、+1、+2、+3、+4、+5、-1、-2、-3、-4或-5,并且其中所述总净电荷是通过一种或多种选自以下的置换来获得的:N43D,R45T,N62E,N76D,S101D,P129E,A158E,G159D,G159E,S166D,S188D,A230E,N18R,G20K,G20R,T22R,S24R,N43R,G118R,Q245R,H249R,N269R,E271F,和E271L,并且其中所述蛋白酶变体的氨基酸位置根据SEQ ID NO:1所示解淀粉芽孢杆菌(Bacillus amyloliquefaciens)枯草杆菌蛋白酶BPN'的氨基酸序列中对应的氨基酸位置的编号方式来进行编号。

2.权利要求1的一种分离的枯草杆菌蛋白酶变体,其中所述枯草杆菌蛋白酶变体为具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:N076D-S101A-S103A-V104I-A158E-S188D-L217E-A232V-Q245R-N248D-H249R-E271F,N076D-S101G-S103A-V104I-A158E-S166D-S188D-A232V-Q245R-N248D-H249R-E271F,S024R-N076D-S101G-S103A-V104I-A158E-S188D-A232V-Q245R-N248D-H249R-E271F,N076D-S101G-S103A-V104I-S128L-A158E-S188D-A232V-Q245R-N248D-H249R-E271F,和N043R-N076D-S101G-S103A-V104I-A158E-S166D-S188D-A232V-Q245R-N248D-H249R-E271F,并且其中所述变体的总净电荷相对于迟缓芽孢杆菌(Bacillus lentus)枯草杆菌蛋白酶GG36蛋白酶的总净电荷为0、+1、+2、+3、+4、+5、-1、-2、-3、-4或-5,并且其中所述总净电荷是通过一种或多种选自以下的置换来获得的:N43D,R45T,N62E,N76D,S101D,P129E,A158E,G159D,G159E,S166D,S188D,A230E,N18R,G20K,G20R,T22R,S24R,N43R,G118R,

Q245R,H249R,N269R,E271F,和E271L,并且其中所述蛋白酶变体的氨基酸位置根据SEQ ID NO:1所示解淀粉芽孢杆菌(Bacillus amyloliquefaciens)枯草杆菌蛋白酶BPN'的氨基酸序列中对应的氨基酸位置的编号方式来进行编号。

3.权利要求1或2的分离的枯草杆菌蛋白酶变体,所述枯草杆菌蛋白酶变体具有蛋白水解活性并包含具有选自以下的氨基酸置换的组合的氨基酸序列:N062E-A158E-S188D-H249R-E271F,S128N-A158E-S188D-Y209E-E271F,N062E-V104L-A158E-S188D-H249R-E271F,S128N-A158E-S188D-E271F,N062E-R186H-S188D-H249R-E271F,S128N-A158E-R186H-S188D-E271F,N062E-S101A-S188D-H249R-E271F,V104L-S128N-A158E-R186H-S188D-E271F,A016S-N062E-V104L-R186H-S188D-E271F,S101A-S128N-A158E-S188D-Y209E-E271F,N062E-S101A-R186H-S188D-E271F,N062E-S101A-V104L-R186H-S188D-E271F,A158E-R186H-S188D-H249R-E271F,V104L-A158E-R186H-S188D-H249R-E271F,S101A-V104L-A158E-R186H-S188D-E271F,和V104L-A158E-S188D-H249R-E271F,其中所述枯草杆菌蛋白酶变体的氨基酸位置通过与如SEQ ID NO:1所示解淀粉芽孢杆菌(B.amyloliquefaciens)枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

4.权利要求1或2的分离的枯草杆菌蛋白酶变体,所述枯草杆菌蛋白酶变体具有蛋白水解活性并包含具有选自以下的氨基酸置换的组合的氨基酸序列:N043R-N076D-S101A-S103A-V104I-A158E-S188D-A232V-Q245R-N248D-H249R-E271F,S101A-S103A-V104I-A158E-S188D-A232V-Q245R-N248D-H249R-E271F-E271F,S101A-S103A-V104I-A158E-S188D-L217E-A232V-Q245R-N248D-H249R-E271F,N076D-S101G-S103A-V104I-A114V-A158E-S188D-A232V-Q245R-N248D-H249R-E271F,S024R-N076D-S101G-S103A-V104I-A158E-S188D-A232V-Q245R-N248D-H249R-E271F,N076D-S101G-S103A-V104I-S128L-A158E-S188D-A232V-Q245R-N248D-H249R-E271F,N043R-N076D-S101G-S103A-V104I-A158E-S166D-S188D-A232V-Q245R-N248D-H249R-E271F,N043R-N076D-S101A-S103A-V104I-A158E-S188D-L217E-A232V-Q245R-N248D-H249R-E271F,N076D-S101A-S103A-V104I-A158E-S188D-A232V-Q245R-N248D-H249R-E271F,S024R-N076D-S101A-S103A-V104I-A158E-S166D-S188D-A232V-Q245R-N248D-H249R-E271F,S101A-S103A-V104I-A158E-S166D-S188D-A232V-Q245R-N248D-H249R-E271F,N043R-N076D-S101A-S103A-V104I-A158E-S166D-S188D-A232V-Q245R-N248D-H249R-E271F,S101G-S103A-V104I-A158E-S166D-S188D-A232V-Q245R-N248D-H249R-E271F,S101A-S103A-V104I-A158E-S188D-A232V-Q245R-N248D-H249R-E271F,N076D-S101A-S103A-V104I-A158E-S166D-S188D-A232V-Q245R-N248D-H249R-E271F,N076D-S101G-S103A-V104I-A158E-S166D-S188D-A232V-Q245R-N248D-H249R-E271F,和N076D-S101A-S103A-V104I-A158E-S188D-L217E-A232V-Q245R-N248D-H249R-E271F,其中所述枯草杆菌蛋白酶变体的氨基酸位置通过与如SEQ ID NO:1所示解淀粉芽孢杆菌(B.amyloliquefaciens)枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

5.根据权利要求1或2所述的蛋白酶变体,其中所述蛋白酶变体包含不同于SEQ ID NO:2的氨基酸序列的氨基酸序列,并且其中所述蛋白酶变体的总净电荷相对于迟缓芽孢杆菌(Bacillus lentus)枯草杆菌蛋白酶GG36蛋白酶的总净电荷为0、+1、+2、+3、+4、5、-1、-2、-3、-4或-5,其中亲本蛋白酶为GG36,并且其中所述蛋白酶变体的氨基酸位置根据SEQ ID

NO:1所示解淀粉芽孢杆菌(Bacillus amyloliquefaciens)枯草杆菌蛋白酶BPN'的氨基酸序列中的对应氨基酸位置的编号方式来进行编号,这是通过所述蛋白酶变体氨基酸序列与所述解淀粉芽孢杆菌(Bacillus amyloliquefaciens)枯草杆菌蛋白酶BPN'氨基酸序列的比对来确定的。

6.根据权利要求1或2所述的蛋白酶变体,其中所述蛋白酶变体具有以下特性中的一者或多者:a)测试方法2性能指数为至少1.1;b)测试方法3性能指数为至少1.1;c)测试方法4性能指数为至少1.0;和/或d)测试方法6性能指数为至少1.0,其中测试方法2包括:将衣物洗涤剂溶解于硬度为12gpg且调节至温度为16℃的水中,添加目的蛋白酶变体酶。然后按照所描述的BMI微样本测定法测定蛋白酶变体酶的性能。通过将蛋白酶变体酶的性能与具有SEQ ID NO:2的氨基酸序列的迟缓芽孢杆菌GG36枯草杆菌蛋白酶的性能相比较来确定性能指数;测试方法3包括:将衣物洗涤剂溶解于硬度为6gpg且调节至温度为16℃的水中,添加目的GG36蛋白酶变体酶,然后按照所描述的BMI微样本测定法测定GG36蛋白酶变体酶的性能,其中通过将GG36蛋白酶变体酶的性能与具有SEQ ID NO:2的氨基酸序列的迟缓芽孢杆菌GG36枯草杆菌蛋白酶的性能相比较来确定性能指数;测试方法4包括:将衣物洗涤剂溶解于硬度为6gpg且调节至温度为16℃的水中,添加目的GG36蛋白酶变体酶,然后按照所描述的BMI微样本测定法测定GG36蛋白酶变体酶的性能,其中通过将GG36蛋白酶变体酶的性能与参考酶GG36-A158E的性能相比较来确定性能指数,所述GG36-A158E参考酶由在位置158处具有丙氨酸置换为谷氨酸的单一置换的SEQ ID NO:2的迟缓芽孢杆菌枯草杆菌蛋白酶GG36蛋白酶氨基酸序列组成;测试方法6包括:将洗涤剂溶解于具有如表1-2中指定的硬度且调节至温度为16℃的水中,按照所描述的BMI微样本测定法测定变体酶的性能,其中通过将变体的性能与具有SEQ ID NO:2的酶的性能相比较来确定性能指数。

7.一种分离的核酸,其包含编码权利要求1-6中任一项提供的枯草杆菌蛋白酶变体的多核苷酸序列。

8.一种表达载体,其包含根据权利要求7所述的核酸。

9.一种宿主细胞,其包含根据权利要求8所述的表达载体。

10.一种包含至少一种根据权利要求1-6中任一项所述的枯草杆菌蛋白酶变体的组合物,其中所述组合物不是织物和家庭护理产品。

11.根据权利要求10所述的组合物,其中所述组合物为清洁组合物。

12.一种清洁方法,包括用包含至少一种根据权利要求1-6中任一项所述的枯草杆菌蛋白酶变体的清洁组合物来接触表面或物品。

13.一种清洁方法,包括用权利要求11示出的清洁组合物来接触表面或物品。

包含枯草杆菌蛋白酶变体的组合物和方法

[0001] 本申请是申请日为2011年5月5日、发明名称为“包含枯草杆菌蛋白酶变体的组合物和方法”的中国专利申请201180022692.4(国际申请号PCT/US2011/035389)的分案申请。

[0002] 相关专利申请的交叉引用

[0003] 本专利申请要求以下美国临时申请的权利:于2010年5月6日提交的No.61/332,151;于2010年5月6日提交的No.61/332,006;于2010年10月12日提交的No.61/392,364以及于2010年10月12日提交的No.61/392,188,所有这些临时申请全文均以引用方式并入本文。

技术领域

[0004] 本发明提供丝氨酸蛋白酶变体。具体地讲,本发明提供与参照丝氨酸蛋白酶相比具有一个或多个置换的丝氨酸蛋白酶变体。此外,本发明提供包含这些丝氨酸蛋白酶变体的组合物。在一些实施例中,本发明提供清洁组合物,其包含这些丝氨酸蛋白酶变体中的至少一种。

[0005] 发明背景

[0006] 尽管丝氨酸蛋白酶在工业酶领域中已久为人所知,但对于适于特定条件和用途的工程化蛋白酶仍存在需要。

发明内容

[0007] 本发明提供丝氨酸蛋白酶变体。具体地讲,本发明提供与参照丝氨酸蛋白酶相比具有一个或多个置换的丝氨酸蛋白酶变体。此外,本发明提供包含这些丝氨酸蛋白酶变体的组合物。在一些实施例中,本发明提供清洁组合物,其包含这些丝氨酸蛋白酶变体中的至少一种。

[0008] 本发明提供分离的枯草杆菌蛋白酶变体,其中该枯草杆菌蛋白酶变体为具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:X1R,X2W,X2M,X2R,X2A,X2S,X3R,X4R,X4C,X4S,X8A,X9F,X9W,X9A,X10S,X10M,X10H,X10A,X12R,X12F,X14K,X14F,X14Q,X15R,X15F,X16S,X17R,X17M,X17F,X18R,X18K,X20F,X20R,X20K,X22Y,X22A,X22R,X22V,X22Q,X22W,X22L,X23F,X23S,X23A,X24W,X24R,X24H,X24F,X24Q,X24L,X25V,X25F,X25R,X26F,X27V,X27F,X27L,X27R,X28N,X28E,X28A,X29T,X30E,X31F,X33D,X33G,X33S,X34P,X35M,X36F,X36R,X36T,X38L,X38F,X38R,X40L,X40W,X40N,X40R,X40T,X40H,X42I,X43D,X43I,X43R,X43M,X43F,X43W,X43S,X43A,X45T,X46R,X48R,X50C,X51H,X51W,X51F,X52F,X52E,X52N,X55Y,X57R,X59R,X59A,X59F,X60A,X60Q,X60P,X62E,X62Q,X63I,X63V,X63T,X63P,X63D,X63M,X63H,X63Q,X63E,X63A,X63S,X64F,X64T,X68C,X68A,X69N,X69P,X69W,X69T,X71G,X72C,X74C,X75F,X75A,X75R,X75E,X76D,X78I,X78R,X78N,X79W,X79Q,X81R,X82V,X82T,X82F,X82M,X82R,X85M,X86L,X86I,X86W,X89P,X89T,X89V,X89G,X89W,X89H,X89F,X89L,X89I,X91N,X91F,X92F,X94N,X99G,X99F,X99M,X99T,X99P,X100I,X100S,X100N,X100Q,X101N,X101A,X101G,X101P,X101F,X101E,X101T,X101D,X102H,X102N,X102E,X102T,X102A,X103G,X103D,X103N,X104D,X104E,X104I,X104L,

X105Q,X105E,X105T,X106F,X106V,X106G,X106E,X106T,X106D,X106A,X107F,X107M,X108G,X108I,X109M,X111V,X111I,X112V,X112L,X112Q,X114G,X115K,X115R,X116A,X116K,X116L,X117F,X118I,X118R,X119C,X120F,X120A,X120R,X121E,X121F,X123G,X123E,X124S,X128F,X128H,X128I,X128L,X128Q,X128N,X128M,X128D,X129E,X132E,X132A,X138G,X144R,X147L,X148I,X158E,X158E,X159E,X159C,X160D,X166D,X166E,X167W,X175V,X177C,X181A,X182R,X183F,X183I,X183D,X183R,X183M,X185E,X185I,X185V,X186H,X186K,X188R,X188E,X188D,X192H,X192W,X194V,X194F,X194E,X197F,X198L,X198F,X203E,X203C,X208S,X209N,X209F,X209E,X209S,X209H,X209G,X209T,X209L,X210R,X210V,X210L,X211R,X211Q,X212I,X212M,X212F,X213A,X214F,X215F,X215N,X215D,X215H,X215E,X216F,X216A,X217N,X217E,X217D,X218P,X218D,X218E,X224A,X224G,X227I,X230E,X231I,X231C,X233C,X234F,X235F,X236F,X236N,X238L,X238K,X238R,X239K,X239S,X239T,X239G,X239H,X239R,X239N,X239F,X240R,X241R,X242L,X242R,X243R,X243F,X244R,X246S,X248I,X248V,X248R,X249R,X249T,X250I,X251S,X251R,X252I,X252F,X252H,X252R,X253F,X253I,X253R,X254C,X256N,X258R,X260V,X260I,X262H,X262D,X263F,X265F,X267N,X267V,X267M,X269I,X269R,X270C,X271F,X271V,X271I,X271P,X271H,X271M,X271T,X271L,X271A,X272F,X272R,X272F,X273I,X273F,和X274G,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与如SEQ ID NO:1所示解淀粉芽孢杆菌(B.amyloliquefaciens)枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0009] 本发明还提供分离的枯草杆菌蛋白酶变体,其中该枯草杆菌蛋白酶变体为具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:X16S,X18R,X20R,X22A,X24R,X43R/D,X45T,X76D,X101A,X103G,X104L,X111V,X128N,X148I,X230E,X242R,和X249R,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与如SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0010] 本发明还提供分离的枯草杆菌蛋白酶变体,其中该枯草杆菌蛋白酶变体为具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:X1R,X230E,X271L,X115R,X20R,X249R,X235F,X27V/F/L,X75E,X82R,X18R,X269R,X43D,X43R,X76D,X45T,X212F,X242R,X24R,X78R,X9A,X22R,X121E,X244R,X28E,X30E,X4R,和X241R,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与如SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0011] 本发明还提供分离的枯草杆菌蛋白酶变体,其中该枯草杆菌蛋白酶变体为具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:X062E-X158E,X103G-X158E,X128N-X158E,X016S-X158E,X104L-X158E,X089P-X158E,X111V-X158E,X022A-X158E,X101A-X158E,X148I-X158E,X129E-X158E,X022A-X089P,X016S-X089P,X062E-X089P,X062E-X271F,X158E-X271F,X186H-X271F,X129E-X271F,X111V-X271F,X209E-X271F,X016S-X271F,X188D-X271F,X022A-X271F,X159E-X271F,X104L-X271F,X101A-X271F,X089P-X271F,X128N-X271F,X103G-X271F,X148I-X271F,X249R-X271F,X062E-X159E,X016S-X159E,X128N-X159E,X148I-X159E,X111V-X159E,X089P-X159E,X022A-X159E,X129E-X159E,X103G-X159E,X104L-X159E,X158E-X159E,X101A-

X159E,X158E-X249R,X111V-X249R,X129E-X249R,X062E-X249R,X016S-X249R,X186H-X249R,X148I-X249R,X159E-X249R,X101A-X249R,X188D-X249R,X104L-X249R,X209E-X249R,X022A-X249R,X128N-X249R,X103G-X249R,X089P-X249R,X022A-X111V,X101A-X111V,X016S-X111V,X104L-X111V,X062E-X111V,X103G-X111V,X089P-X111V,X016S-X148I,X062E-X148I,X022A-X148I,X129E-X148I,X104L-X148I,X103G-X148I,X128N-X148I,X101A-X148I,X089P-X148I,X111V-X148I,X016S-X062E,X022A-X062E,X062E-X129E,X022A-X129E,X128N-X129E,X016S-X129E,X101A-X129E,X104L-X129E,X089P-X129E,X103G-X129E,X111V-X129E,X062E-X186H,X128N-X186H,X101A-X186H,X022A-X186H,X016S-X186H,X158E-X186H,X089P-X186H,X129E-X186H,X159E-X186H,X103G-X186H,X104L-X186H,X111V-X186H,X148I-X186H,X062E-X101A,X022A-X101A,X016S-X101A,X089P-X101A,X062E-X103G,X022A-X103G,X016S-X103G,X101A-X103G,X089P-X103G,X062E-X128N,X016S-X128N,X022A-X128N,X101A-X128N,X104L-X128N,X089P-X128N,X103G-X128N,X111V-X128N,X111V-X188D,X062E-X188D,X016S-X188D,X148I-X188D,X022A-X188D,X128N-X188D,X101A-X188D,X104L-X188D,X089P-X188D,X129E-X188D,X159E-X188D,X186H-X188D,X103G-X188D,X158E-X188D,X016S-X022A,X016S-X104L,X022A-X104L,X101A-X104L,X062E-X104L,X103G-X104L,X089P-X104L,X159E-X209E,X111V-X209E,X101A-X209E,X016S-X209E,X128N-X209E,X148I-X209E,X129E-X209E,X062E-X209E,X022A-X209E,X103G-X209E,X158E-X209E,X188D-X209E,X104L-X209E,X089P-X209E,和X186H-X209E,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与如SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0012] 本发明还提供分离的枯草杆菌蛋白酶变体,其中该枯草杆菌蛋白酶变体为具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:X018R-X241R,X020R-X241R,X024R-X241R,X009A-X241R,X020R-X241R,X004R-X241R,X043R-X241R,X078R-X241R,X022R-X241R,X115R-X241R,X001R-X241R,X212F-X241R,X082R-X241R,X018R-X244R,X024R-X244R,X078R-X244R,X020R-X244R,X212F-X244R,X009A-X244R,X082R-X244R,X001R-X244R,X043R-X244R,X022R-X244R,X004R-X244R,X115R-X244R,X241R-X244R,X242R-X244R,X001R-X004R,X009A-X022R,X018R-X022R,X020R-X022R,X004R-X022R,X001R-X022R,X024R-X242R,X018R-X242R,X004R-X242R,X020R-X242R,X212F-X242R,X082R-X242R,X078R-X242R,X001R-X242R,X009A-X242R,X022R-X242R,X115R-X242R,X043R-X242R,X241R-X242R,X018R-X212F,X022R-X212F,X004R-X212F,X024R-X212F,X001R-X212F,X115R-X212F,X020R-X212F,X009A-X212F,X043R-X212F,X078R-X212F,X082R-X212F,X009A-X078R,X020R-X078R,X024R-X078R,X022R-X078R,X018R-X078R,X004R-X078R,X001R-X078R,X043R-X078R,X022R-X024R,X020R-X024R,X018R-X024R,X001R-X024R,X004R-X024R,X009A-X024R,X004R-X009A,X001R-X009A,X242R-X269R,X024R-X269R,X020R-X269R,X022R-X269R,X249R-X269R,X212F-X269R,X043R-X269R,X244R-X269R,X001R-X269R,X018R-X269R,X078R-X269R,X009A-X269R,X115R-X269R,X241R-X269R,X004R-X269R,X082R-X269R,X018R-X043R,X020R-X043R,X004R-X043R,X022R-X043R,X009A-X043R,X001R-X043R,X024R-X043R,X009A-

X018R,X004R-X018R,X001R-X018R,X024R-X082R,X009A-X082R,X018R-X082R,X001R-X082R,X078R-X082R,X020R-X082R,X022R-X082R,X004R-X082R,X043R-X082R,X043R-X249R,X020R-X249R,X004R-X249R,X018R-X249R,X009A-X249R,X212F-X249R,X022R-X249R,X024R-X249R,X115R-X249R,X001R-X249R,X082R-X249R,X242R-X249R,X241R-X249R,X244R-X249R,X078R-X249R,X018R-X115R,X020R-X115R,X022R-X115R,X078R-X115R,X009A-X115R,X004R-X115R,X001R-X115R,X082R-X115R,X043R-X115R,X024R-X115R,X009A-X020R,X018R-X020R,X004R-X020R,X001R-X020R,X009A-X271L,X020R-X271L,X024R-X271L,X244R-X271L,X241R-X271L,X043R-X271L,X022R-X271L,X249R-X271L,X212F-X271L,X115R-X271L,X242R-X271L,X078R-X271L,X004R-X271L,X269R-X271L,X001R-X271L,X018R-X271L,和X082R-X271L,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与如SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0013] 本发明还提供分离的枯草杆菌蛋白酶变体,其中该枯草杆菌蛋白酶变体为具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:X020R-X043R,X020K-X062E,X024F-X116L,X020K-X024F,X024R-X174T,X024R-X118R,X024R-X235F,X024R-X086R,X024R-X086W,X078R-X118R,X033S-X118R,X033S-X235F,X209A-X241R,X020R-X076D,X018R-X245R,X024R-X045T,X232V-X245R,X118R-X172V,X118R-X194T,X008T-X024R,X235F-X243F,X018R-X103A,X018R-X104I,X086W-X118R,X086W-X243F,X086W-X209A,X024C-X033S,X024R-X232V,X024R-X243F,X024R-X239Q,X024R-X101G,X024R-X141G,X024R-X033S,X024R-X274I,X024R-X209A,X078R-X086W,X101G-X232V,X033S-X148F,X033S-X086W,X033S-X201S,X033S-X078R,X033S-X241R,X033S-X209A,X230E-X249R,X232V-X249R,X118R-X235F,X076D-X245R,X086W-X235F,X024R-X247H,X024R-X104A,X078R-X235F,X101G-X249R,X103A-X232V,X033S-X048T,X033S-X239T,X033S-X253A,X143A-X209A,X209A-X235F,X018R-X045T,X209A-X243F,X024R-X272P,X024R-X269C,X101G-X104I,X104I-X232V,X076D-X249R,和X024R-X076D,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与如SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0014] 本发明还提供分离的枯草杆菌蛋白酶变体,其中该枯草杆菌蛋白酶变体为具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:X020R-X076D,X024R-X045T,X230E-X249R,X018R-X045T,X018R-X245R,X101G-X232V,X024R-X232V,X232V-X245R,X024R-X101G,X018R-X104I,X018R-X103A,X101G-X249R,X232V-X249R,X103A-X232V,X076D-X245R,X101G-X104I,X104I-X232V,X076D-X249R,X024R-X076D,X024F-X116L,X020K-X024F,X020K-X062E,X033S-X118R,X024R-X086W,X024R-X118R,X024R-X086R,X209A-X241R,X024R-X241R,X024R-X235F,X118R-X209A,X078R-X118R,X033S-X235F,X024R-X174T,X086W-X209A,X008T-X024R,X086W-X118R,X033S-X241R,X024R-X243F,X024R-X209A,X033S-X086W,X024R-X033S,X086W-X243F,X033S-X201S,X024R-X239Q,X078R-X086W,X235F-X243F,X118R-X172V,X033S-X148F,X033S-X078R,X033S-X243F,X024C-X033S,X118R-X194T,X033S-X209A,X024R-X141G,X024R-X274I,X086W-X235F,X015T-X033S,X209A-X235F,X024R-X247H,X078R-X235F,X024R-

X104A,X033S-X048T,X118R-X235F,X033S-X253A,X143A-X209A,X033S-X239T,X209A-X243F,X024R-X272P,和X024R-X269C,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与如SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0015] 本发明还提供分离的枯草杆菌蛋白酶变体,其中该枯草杆菌蛋白酶变体为具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:X004R-X009A-X020R-X242R,X020R-X043R-X241R,X020R-X242R-X269R,X004R-X009A-X020R-X043R,X004R-X020R-X249R,X018R-X024R-X244R,X009A-X022R-X212F-X241R,X020R-X043R-X269R,X018R-X024R-X242R,X004R-X009A-X043R-X241R,X020R-X043R-X244R,X020R-X022R-X242R,X004R-X020R-X043R,X004R-X009A-X020R-X043R-X242R,X020R-X043R-X242R,X020R-X043R-X242R-X249R,X020R-X212F-X249R,X004R-X009A-X241R,X001R-X009A-X043R,X020R-X043R-X249R,X009A-X020R-X043R-X241R,X020R-X022R-X043R,X020R-X249R-X269R,X020R-X022R-X241R,X004R-X009A-X024R-X043R-X241R,X009A-X043R-X078R,X004R-X020R-X024R-X244R,X020R-X022R-X078R-X242R,X020R-X024R-X242R-X249R,X004R-X009A-X078R-X241R,X009A-X043R-X078R-X242R,X004R-X020R-X024R,X009A-X043R-X212F,X020R-X043R-X212F,X024R-X078R-X212F,X009A-X020R-X024R-X043R,X009A-X022R-X043R-X078R,X020R-X022R-X212F-X241R,X020R-X043R-X212F-X241R,X009A-X043R-X241R,X020R-X043R-X271L,X020R-X022R-X078R-X241R,X020R-X024R-X043R-X242R,X020R-X022R-X043R-X241R,X009A-X020R-X043R-X212F,X004R-X009A-X020R-X024R-X242R,X020R-X043R-X249R-X271L,X020R-X022R-X024R-X242R,X009A-X022R-X078R-X212F,X020R-X043R-X242R-X271L,X009A-X022R-X078R-X212F-X241R,X004R-X020R-X024R-X249R,X020R-X022R-X271L,X020R-X022R-X043R-X212F,X004R-X020R-X024R-X043R-X242R,X004R-X020R-X024R-X043R,X004R-X009A-X022R-X078R-X212F,X020R-X022R-X078R-X212F-X241R,和X020R-X022R-X269R,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与如SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0016] 本发明还提供分离的枯草杆菌蛋白酶变体,其中该枯草杆菌蛋白酶变体为具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:X018R-X020R-X043D-X045T-X230E,X018R-X043R-X045T-X242R-X249R,X024R-X043D-X249R,X018R-X020R-X045T,X020R-X024R-X076D-X249R,X024R-X043R-X230E-X242R,X018R-X024R-X043D-X230E,X020R-X076D,X018R-X024R-X043D-X076D-X249R,X024R-X043R-X076D-X249R,X018R-X024R-X045T-X242R,X020R-X043D-X076D-X230E-X249R,X020R-X043R-X045T-X242R,X018R-X024R-X076D-X249R,X018R-X020R-X024R-X043D-X045T-X233I-X242R,X024R-X043R-X230E,X018R-X020R-X043D,X043R-X242R-X249R,X020R-X043R-X045T-X230E,X043R-X076D-X242R-X249R,X020R-X024R-X045T-X230E-X242R,X024R-X045T-X076D-X230E-X242R-X249R,X024R-X045T,X024R-X043R-X045T-X076D-X230E-X249R,X018R-X024R-X043D-X045T-X249R,X018R-X043R-X045T-X249R,X024R-X043R-X242R,X018R-X020R-X043R-X076D-X249R,X020R-X024R-X043D-X249R,X020R-X043R-X230E-X242R,X020R-X043R-X242R,X018R-X043R-X076D-X230E,X020R-X024R-

X043D-X242R,X020R-X043R-X230E,X018R-X020R-X043R-X076D-X242R-X249R,X043D-X045T-X076D-X249R,X018R-X043R-X242R-X249R,X018R-X020R-X043R-X045T-X242R,X018R-X020R-X043D-X230E-X242R,X020R-X024R-X043R-X045T-X249R,X024R-X043R-X249R,X020R-X024R-X27E-X043R-X076D-X230E,X024R-X043R-X045T-X242R,X018R-X020R-X024R-X043R-X045T-X076D-X230E,X020R-X043R-X076D-X230E-X249R,X018R-X043R-X045T-X242R,X020R-X242R-X249R,X018R-X043R-X076D-X230E-X242R-X249R,X018R-X024R-X076D,X020R-X024R-X27R-X043D-X242R-X249R,X018R-X020R-X024R-X043D-X076D-X242R,X018R-X043R-X076D-X242R-X249R,X018R-X024R-X043D-X230E-X249R,X018R-X020R-X043D-X249R,X018R-X020R-X043D-X045T-X076D-X242R,X024R-X043R-X076D-X230E-X242R,X020R-X024R-X38I-X043R-X045T-X076D-X242R-X249R,X018R-X020R-X043R,X018R-X024R-X045T-X230E-X242R,X018R-X020R-X249R,X024R-X043R-X076D,X018R-X020R-X024R-X043R-X045T-X076D-X249R,X018R-X043D-X045T-X076D-X242R-X249R,X024R-X043D-X242R-X249R,X018R-X020R-X024R-X043D-X045T-X242R,X020R-X024R-X043R-X076D,X018R-X020R-X043D-X045T-X230E-X242R,X020R-X024R-X043R-X045T-X076D-X242R-X249R,X018R-X043R-X045T-X076D-X242R,X018R-X020R-X043R-X076D-X230E-X242R,X018R-X024R-X043D-X249R,X018R-X024R-X043R-X045T-X230E-X249R,X018R-X020R-X043R-X045T-X076D-X249R,X018R-X024R-X242R,X018R-X043R-X045T-X076D-X230E-X242R,X045T-X242R-X249R,X018R-X024R-X043D-X242R,X018R-X020R-X043D-X045T-X240P,X024R-X043R-X045T-X242R-X249R,X018R-X024R-X30S-X31S-X32I-X33Q-X34V-X35F,X018R-X020R-X043R-X076D,X020R-X043D-X045T-X076D-X242R-X249R,X018R-X024R-X043D-X230E-X242R,X018R-X024R-X043D-X242R-X249R,X024R-X043D-X045T-X242R-X249R,X043R-X230E-X249R,X024R-X043R-X076D-X230E-X249R,X020R-X024R-X043D-X076D-X249R,X024R-X045T-X242R-X273V,X020R-X024R-X045T-X076D-X242R-X249R,X018R-X024R-X043D-X076D-X242R,X018R-X043R-X076D-X230E-X249R,X018R-X020R-X043R-X045T-X249R,X018R-X043R-X045T-X230E-X242R,X020R-X024R-X043D-X045T-X230E-X242R,X018R-X043D-X230E-X249R,X018R-X043R-X076D-X242R,X018R-X020R-X076D,X018R-X020R-X043D-X076D-X242R-X249R,X020R-X024R-X043D-X076D-X242R-X249R,X043D-X242R-X249R,X018R-X020R-X024R-X043R-X076D,X018R-X020R-X043D-X045T-X076D-X249R,X018R-X020R-X043R-X045T-X076D-X230E-X249R,X018R-X076D-X242R,X020R-X043R-X249R,X018R-X076D-X242R-X249R,X018R-X024R-X045T-X230E-X249R,X230E-X249R,X018R-X045T-X249R,X020R-X043R-X076D,X043R-X045T-X249R,X018R-X043D-X076D-X242R-X249R,X043R-X076D-X249R,X018R-X045T,X020R-X076D-X230E-X242R,X020R-X024R-X043D-X045T,X024R-X043D-X076D-X242R-X249R,X020R-X045T-X249R,X043R-X076D-X153A-X249R,X043R-X076D-X230E-X249R,X018R-X043D-X076D-X249R,和X020R-X043R-X076D-X227I,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与如SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0017] 本发明还提供分离的枯草杆菌蛋白酶变体,其中该枯草杆菌蛋白酶变体为具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:X101G-

X103A-X104I-X232V-X236H-X245R-X252K,X101G-X103A-X104I-X232V-X245R-X248R,X101G-X103A-X104I-X159R-X232V-X245R-X248D,X101G-X103A-X104I-X159D-X232V-X245R-X248R,X101G-X103A-X104I-X232V-X245R,X101G-X103A-X104I-X159D-X232V-X245R和X101G-X103A-X104I-X232V-X245R-X248D,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与如SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0018] 本发明还提供分离的枯草杆菌蛋白酶变体,其中该枯草杆菌蛋白酶变体为具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:X101G-X103A-X104I-X129E-X188D-X232V-X238R-X245R-X248D,X024R-X101G-X103A-X104I-X129E-X158E-X188D-X232V-X245R-X248D-X249R,X022A-X101G-X103A-X104I-X129E-X158E-X188D-X232V-X245R-X248D-X249R,X022A-X024R-X101G-X103A-X104I-X129E-X158E-X188D-X232V-X245R-X248D-X249R,X024R-X101G-X103A-X104I-X129E-X188D-X232V-X245R-X248D-X249R,X024R-X101G-X103A-X104I-X129E-X159E-X188D-X232V-X245R-X248D-X249R,X024R-X101G-X103A-X104I-X128N-X129E-X158E-X232V-X245R-X248D-X249R,X024R-X101G-X103A-X104I-X148I-X158E-X188D-X232V-X245R-X248D,X022A-X024R-X101G-X103A-X104I-X129E-X159E-X188D-X232V-X245R-X248D-X249R,X024R-X101G-X103A-X104I-X128N-X129E-X232V-X245R-X248D,X101G-X103A-X104I-X129E-X188D-X232V-X245R-X248D-X249R,X024R-X101G-X103A-X104I-X129E-X158E-X232V-X245R-X248D-X249R,X022A-X024R-X101G-X103A-X104I-X158E-X159E-X188D-X232V-X245R-X248D-X249R,X022A-X024R-X101G-X103A-X104I-X129E-X158E-X159E-X188D-X232V-X238R-X245R-X248D,X024R-X101G-X103A-X104I-X129E-X148I-X158E-X232V-X245R-X248D,X016S-X024R-X101G-X103A-X104I-X158E-X188D-X232V-X245R-X248D-X249R,X101G-X103A-X104I-X158E-X159E-X232V-X245R-X248D-X249R,X022A-X101G-X103A-X104I-X129E-X158E-X159E-X232V-X238R-X245R-X248D,X022A-X024R-X101G-X103A-X104I-X129E-X158E-X159E-X232V-X245R-X248D-X249R,X022A-X024R-X101G-X103A-X104I-X128N-X158E-X188D-X232V-X245R-X248D,X024R-X101G-X103A-X104I-X129E-X188D-X232V-X245R-X248D,X022A-X024R-X101G-X103A-X104I-X129E-X158E-X232V-X245R-X248D,X022A-X024R-X101G-X103A-X104I-X129E-X232V-X245R-X248D,X022A-X024R-X101G-X103A-X104I-X129E-X188D-X232V-X245R-X248D,X024R-X101G-X103A-X104I-X158E-X188D-X232V-X238R-X245R-X248D,X022A-X101G-X103A-X104I-X128N-X129E-X188D-X232V-X238R-X245R-X248D,X024R-X101G-X103A-X104I-X129E-X188D-X232V-X238R-X245R-X248D,X024R-X101G-X103A-X104I-X158E-X159E-X188D-X232V-X245R-X248D,X022A-X024R-X101G-X103A-X104I-X128N-X188D-X232V-X245R-X248D,X024R-X101G-X103A-X104I-X129E-X158E-X188D-X232V-X245R-X248D,X022A-X024R-X101G-X103A-X104I-X128N-X129E-X158E-X232V-X245R-X248D,X024R-X101G-X103A-X104I-X159E-X188D-X232V-X245R-X248D,X022A-X101G-X103A-X104I-X128N-X129E-X232V-X238R-X245R-X248D,X024R-X101G-X103A-X104I-X129E-X159E-X232V-X245R-X248D,X022A-X024R-X101G-X103A-X104I-X129E-X158E-X188D-X232V-X238R-X245R-X248D,X022A-X024R-X101G-X103A-X104I-X158E-X159E-X188D-X232V-

X245R-X248D,XO24R-X101G-X103A-X104I-X159E-X188D-X232V-X245R-X248D-X249R,XO22A-X101G-X103A-X104I-X129E-X158E-X232V-X238R-X245R-X248D,XO22A-XO24R-X101G-X103A-X104I-X129E-X158E-X232V-X245R-X248D-X249R,XO24R-X101G-X103A-X104I-X148I-X158E-X232V-X245R-X248D,XO22A-X101G-X103A-X104I-X158E-X159E-X188D-X232V-X245R-X248D-X249R,XO22A-X101G-X103A-X104I-X158E-X188D-X232V-X245R-X248D,XO22A-X101G-X103A-X104I-X129E-X188D-X232V-X238R-X245R-X248D,XO24R-X101G-X103A-X104I-X129E-X158E-X159E-X188D-X232V-X245R-X248D-X249R,XO22A-XO24R-X101G-X103A-X104I-X158E-X159E-X188D-X232V-X238R-X245R-X248D,X101G-X103A-X104I-X129E-X158E-X188D-X232V-X245R-X248D-X249R,XO24R-X101G-X103A-X104I-X128N-X158E-X232V-X245R-X248D,XO22A-XO24R-X101G-X103A-X104I-X128N-X129E-X188D-X232V-X245R-X248D,XO22A-X101G-X103A-X104I-X129E-X159E-X232V-X238R-X245R-X248D,X101G-X103A-X104I-X129E-X159E-X232V-X245R-X248D-X249R,XO22A-X101G-X103A-X104I-X129E-X158E-X232V-X245R-X248D-X249R,XO24R-X101G-X103A-X104I-X129E-X148I-X158E-X188D-X232V-X245R-X248D,XO22A-X101G-X103A-X104I-X129E-X159E-X232V-X245R-X248D-X249R,XO24R-X101G-X103A-X104I-X159E-X188D-X232V-X238R-X245R-X248D,XO24R-X101G-X103A-X104I-X129E-X158E-X159E-X232V-X245R-X248D-X249R,XO24R-X101G-X103A-X104I-X129E-X159E-X232V-X238R-X245R-X248D,XO24R-X101G-X103A-X104I-X128N-X159E-X188D-X232V-X245R-X248D,XO22A-X101G-X103A-X104I-X159E-X188D-X232V-X245R-X248D-X249R,XO24R-X101G-X103A-X104I-X129E-X159E-X188D-X232V-X238R-X245R-X248D,X101G-X103A-X104I-X158E-X232V-X238R-X245R-X248D,XO22A-X101G-X103A-X104I-X129E-X159E-X188D-X232V-X245R-X248D-X249R,XO24R-X101G-X103A-X104I-X129E-X148I-X188D-X232V-X245R-X248D,XO24R-X101G-X103A-X104I-X158E-X232V-X245R-X248D-X249R,XO22A-X101G-X103A-X104I-X158E-X159E-X232V-X238R-X245R-X248D,XO24R-X101G-X103A-X104I-X158E-X159E-X232V-X238R-X245R-X248D,XO22A-X101G-X103A-X104I-X129E-X158E-X159E-X232V-X245R-X248D-X249R,X101G-X103A-X104I-X129E-X158E-X188D-X232V-X238R-X245R-X248D,XO22A-XO24R-X101G-X103A-X104I-X129E-X158E-X159E-X232V-X245R-X248D,X101G-X103A-X104I-X188D-X232V-X238R-X245R-X248D,XO22A-XO24R-X101G-X103A-X104I-X158E-X232V-X245R-X248D-X249R,XO22A-XO24R-X101G-X103A-X104I-X148I-X158E-X232V-X245R-X248D,X101G-X103A-X104I-X129E-X158E-X159E-X232V-X238R-X245R-X248D,XO22A-X101G-X103A-X104I-X159E-X188D-X232V-X238R-X245R-X248D,XO22A-XO24R-X101G-X103A-X104I-X129E-X158E-X159E-X188D-X232V-X245R-X248D-X249R,XO22A-X101G-X103A-X104I-X129E-X232V-X238R-X245R-X248D,XO22A-XO24R-X101G-X103A-X104I-X188D-X232V-X245R-X248D-X249R,X101G-X103A-X104I-X129E-X158E-X159E-X232V-X245R-X248D-X249R,XO22A-X101G-X103A-X104I-X158E-X159E-X232V-X245R-X248D-X249R,X101G-X103A-X104I-X129E-X188D-X232V-X245R-X248D,XO24R-X101G-X103A-X104I-X129E-X159E-X232V-X238R-X245R-X248D,X101G-X103A-X104I-X128N-X129E-X232V-X245R-X248D,X101G-X103A-X104I-X158E-X188D-X232V-X245R-X248D,XO22A-XO24R-X101G-X103A-X104I-

X129E-X232V-X245R-X248D-X249R,X101G-X103A-X104I-X129E-X159E-X232V-X238R-X245R-X248D,X101G-X103A-X104I-X158E-X159E-X188D-X232V-X238R-X245R-X248D,XO24R-X101G-X103A-X104I-X232V-X245R-X248D-X249R,XO22A-XO24R-X101G-X103A-X104I-X129E-X148I-X232V-X245R-X248D,XO22A-XO24R-X101G-X103A-X104I-X158E-X232V-X238R-X245R-X248D,X101G-X103A-X104I-X128N-X129E-X232V-X238R-X245R-X248D,XO22A-X101G-X103A-X104I-X128N-X159E-X232V-X245R-X248D,XO22A-X101G-X103A-X104I-X128N-X129E-X158E-X232V-X238R-X245R-X248D,X101G-X103A-X104I-X128N-X129E-X188D-X232V-X245R-X248D-X249R,XO22A-XO24R-X101G-X103A-X104I-X128N-X129E-X158E-X188D-X232V-X245R-X248D-X249R,XO24R-X101G-X103A-X104I-X128N-X158E-X159E-X188D-X232V-X245R-X248D,XO22A-XO24K-X101G-X103A-X104I-X128N-X158E-X159E-X232V-X245R-X248D,X101G-X103A-X104I-X129E-X148I-X188D-X232V-X245R-X248D,XO24R-X101G-X103A-X104I-X148I-X232V-X245R-X248D,XO22A-X101G-X103A-X104I-X148I-X188D-X232V-X245R-X248D,XO24R-X101G-X103A-X104I-X128N-X129E-X188D-X232V-X245R-X248D,X101G-X103A-X104I-X128N-X129E-X158E-X232V-X238R-X245R-X248D,XO22A-XO24R-X101G-X103A-X104I-X129E-X148I-X158E-X188D-X232V-X245R-X248D,XO22A-XO24R-X101G-X103A-X104I-X148I-X158E-X188D-X232V-X245R-X248D,X101G-X103A-X104I-X148I-X159E-X232V-X245R-X248D,XO22A-XO24R-X101G-X103A-X104I-X158E-X188D-X232V-X245R-X248D,和X101G-X103A-X104I-X128N-X129E-X158E-X232V-X245R-X248D-X249R,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与如SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0019] 本发明还提供分离的枯草杆菌蛋白酶变体,其中该枯草杆菌蛋白酶变体为具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:XO22A-XO24R-X101G-X103A-X104I-X158E-X232V-X245R-X248D-X249R,XO22A-XO24R-X101G-X103A-X104I-X129E-X232V-X245R-X248D-X249R,XO24R-X101G-X103A-X104I-X158E-X159E-X232V-X238R-X245R-X248D,XO24R-X101G-X103A-X104I-X232V-X245R-X248D-X249R,X101G-X103A-X104I-X158E-X232V-X245R-X248D-X249R,X101G-X103A-X104I-X188D-X232V-X245R-X248D-X249R,XO24R-X101G-X103A-X104I-X159E-X188D-X232V-X245R-X248D-X249R,XO22A-XO24R-X101G-X103A-X104I-X158E-X232V-X238R-X245R-X248D,XO24R-X101G-X103A-X104I-X159E-X188D-X232V-X238R-X245R-X248D,XO22A-XO24R-X101G-X103A-X104I-X129E-X232V-X245R-X248D,XO24R-X101G-X103A-X104I-X148I-X232V-X245R-X248D,XO24R-X101G-X103A-X104I-X129E-X158E-X232V-X245R-X248D-X249R,XO24R-X101G-X103A-X104I-X148I-X158E-X232V-X245R-X248D,XO22A-XO24R-X101G-X103A-X104I-X129E-X158E-X232V-X245R-X248D-X249R,XO16S-XO24R-X101G-X103A-X104I-X158E-X188D-X232V-X245R-X248D-X249R,XO24R-X101G-X103A-X104I-X129E-X159E-X232V-X238R-X245R-X248D,XO24R-X101G-X103A-X104I-X129E-X188D-X232V-X245R-X248D-X249R,XO22A-X101G-X103A-X104I-X129E-X232V-X238R-X245R-X248D,XO22A-XO24R-X101G-X103A-X104I-X148I-X158E-X232V-X245R-X248D,XO24R-X101G-X103A-X104I-X129E-X188D-X232V-X238R-X245R-X248D,XO22A-XO24R-

X101G-X103A-X104I-X158E-X159E-X188D-X232V-X238R-X245R-X248D,X022A-X101G-X103A-X104I-X158E-X159E-X232V-X238R-X245R-X248D,X022A-X024R-X101G-X103A-X104I-X129E-X158E-X232V-X245R-X248D,X101G-X103A-X104I-X158E-X188D-X232V-X245R-X248D-X249R,X022A-X101G-X103A-X104I-X158E-X159E-X232V-X245R-X248D-X249R,和X024R-X101G-X103A-X104I-X158E-X159E-X232V-X245R-X248D,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与如SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0020] 本发明还提供分离的枯草杆菌蛋白酶变体,其中该枯草杆菌蛋白酶变体为具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:X104L-X128N-X158E-X186H-X249R,X128N-X158E-X188D-X249R,X062E-X128N-X158E-X159E-X271F,X062E-X158E-X188D-X249R-X271F,X062E-X158E-X186H-X249R-X271F,X128N-X158E-X188D-X209E-X271F,X062E-X159E-X188D-X249R,X016S-X062E-X158E-X186H-X249R,X062E-X158E-X159E-X249R,X101A-X128N-X158E-X209E-X249R,X128N-X158E-X186H-X271F,X062E-X158E-X188D-X249R,X062E-X158E-X186H-X271F,X062E-X158E-X186H-X249R,X062E-X101A-X186H-X249R,X062E-X101A-X158E-X186H-X271F,X062E-X104L-X158E-X188D-X249R-X271F,X062E-X159E-X186H-X249R,X062E-X159E-X249R,X128N-X158E-X186H-X249R,X128N-X158E-X188D-X271F,X062E-X158E-X249R,X062E-X186H-X188D-X249R-X271F,X128N-X158E-X209E-,X062E-X101A-X158E-X249R,X104L-X128N-X158E-X186H-X271F,X062E-X101A-X158E-X186H-X249R-X271F,X016S-X062E-X158E-X249R,X062E-X101A-X159E-X249R,X128N-X158E-X186H-X188D-X271F,X101A-X128N-X158E-X186H-X271F,X062E-X101A-X188D-X249R,X101A-X104L-X158E-X186H-X188D-X249R,X062E-X159E-X249R-X271F,X128N-X158E-X159E-X271F,X016S-X062E-X104L-X158E-X186H-X271F,X022A-X128N-X158E-X249R,X128N-X158E-X249R,X062E-X101A-X104L-X158E-X186H-X271F,X016S-X062E-X158E-X186H-X271F,X104L-X128N-X158E-X249R,X104L-X128N-X158E-X188D-X249R,X022A-X062E-X158E,X062E-X101A-X188D-X249R-X271F,X062E-X158E-X249R-X271F,X104L-X128N-X158E-X186H-X188D-X271F,X062E-X101A-X186H-X271F,X062E-X104L-X159E-X249R,X062E-X186H-X249R,X062E-X101A-X186H-X249R-X271F,X101A-X158E-X186H-X188D-X249R,X062E-X101A-X186H,X101A-X128N-X129E-X186H-X249R,X101A-X103G-X158E-X186H-X249R,X016S-X062E-X104L-X186H-X188D-X271F,X104L-X158E-X186H-X249R,X101A-X128N-X158E-X188D-X209E-X271F,X062E-X101A-X186H-X188D-X271F,X016S-X062E-X158E-X249R-X271F,X062E-X128N-X158E,X062E-X128N-X159E-X249R,X062E-X101A-X158E-X188D-X249R,X101A-X128N-X158E-X249R,X062E-X158E-X186H-X188D-X249R,X016S-X104L-X158E-X186H-X271F,X062E-X148I-X159E,X062E-X101A-X158E-X186H-X249R,X062E-X101A-X186H-X188D-X249R,X104L-X158E-X186H-X188D-X249R,X062E-X101A-X104L-X186H-X188D-X271F,X022A-X101A-X158E-X186H-X249R,X101A-X128N-X158E-X209E,X158E-X186H-X188D-X249R-X271F,X104L-X158E-X186H-X188D-X249R-X271F,X101A-X104L-X158E-X186H-X249R,X104L-X158E-X249R,X101A-X104L-X128N-X158E-X186H-X271F,X016S-X104L-X188D-X249R,X101A-X104L-X158E-X186H-X188D-X271F,X104L-

X128N-X159E-X271F,X104L-X158E-X186H-X249R-X271F,X158E-X186H-X249R,X101A-X158E-X186H-X249R,X104L-X158E-X188D-X249R-X271F,X016S-X128N-X158E-X186H,X104L-X128N-X186H-X188D-X249R,X016S-X101A-X128N-X186H,X016S-X062E-X128N-X186H-X271F,X016S-X128N-X186H-X271F,X128N-X129E-X186H,X158E-X186H-X249R-X271F,X016S-X158E-X249R,X016S-X158E-X186H-X249R,X016S-X022A-X158E-X186H-X271F,X089P-X101A-X129E-X186H,X022A-X128N-X158E-X186H,X101A-X104L-X128N-X158E-X186H,X022A-X128N-X186H-X188D-,X062E-X104L-X158E-X186H-X188D-X249R,X022A-X158E-X186H-X249R-X271F,X022A-X104L-X158E-X249R,X101A-X111V-X129E,X016S-X158E-X249R-X271F,X016S-X111V-X188D-,X022A-X104L-X186H-X188D-X249R,和X104L-X148I-X188D-X249R,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与如SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0021] 本发明还提供分离的枯草杆菌蛋白酶变体,其中该枯草杆菌蛋白酶变体为具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:X001R-X101G-X103A-X104I-X232V-X245R,X004R-X101G-X103A-X104I-X232V-X245R,X043R-X101G-X103A-X104I-X232V-X245R-X271L,X078R-X101G-X103A-X104I-X232V-X245R,X004R-X043R-X101G-X103A-X104I-X232V-X245R,X018R-X043R-X101G-X103A-X104I-X232V-X245R,X020R-X101G-X103A-X104I-X232V-X245R,X101G-X103A-X104I-X232V-X245R-X271L,X020R-X043R-X101G-X103A-X104I-X232V-X245R,X024R-X043R-X101G-X103A-X104I-X232V-X245R,X020R-X025R-X116A-X167W,X018R-X101G-X103A-X104I-X232V-X245R,X022R-X101G-X103A-X104I-X232V-X245R,X078R-X103N-X106G-X167W-X236N,X018R-X043D-X101G-X103A-X104I-X232V-X245R-X269R,X043R-X101G-X103A-X104I-X232V-X245R-X269R,X024R-X101A-X120F-X194F-X249R,X020R-X043D-X101G-X103A-X104I-X232V-X245R-X269R,X101G-X103A-X104I-X212F-X232V-X245R,X020R-X144R-X185I-X233C-X236N,X023A-X078R-X216F-X236N-X249R,X101G-X103A-X104I-X232V-X245R-X269R,X101G-X103A-X104I-X115R-X232V-X245R,X052N-X078R-X103N-X148I-X213A,X018R-X043D-X101G-X103A-X104I-X232V-X245R-X249R,X024R-X043D-X101G-X103A-X104I-X232V-X245R-X249R,X024R-X043D-X101G-X103A-X104I-X232V-X245R-X269R,X025R-X089I-X116A-X239S-X270C,X024R-X101G-X103A-X104I-X232V-X245R,X148I-X213A-X252R,X024R-X025R-X183D-X192W-X239S,X046R-X194F-X212M,X104L-X217E-X224A-X249R-X252R,X023A-X091F-X121F-X192W-X236N,X101G-X103A-X104I-X232V-X244R-X245R,X099F-X144R-X167W-X252R,X101G-X103A-X104I-X232V-X245R-X249R,X043R-X101G-X103A-X104I-X232V-X245R,X022W-X078R-X167W-X212M-X270C,X121F-X252R-X270C,X020R-X103N-X216F-X236N-X252R,X043R-X101G-X103A-X104I-X232V-X245R-X249R,X023A-X052N-X192W-X198L-X252R,X025R-X046R-X121F,X024R-X078R-X104L-X116A-X183D,X046R-X059A-X103N-X211Q-X212M,X020R-X052N-X062Q-X091F-X192W,X023A-X052N-X144R-X192W-X216F,X101G-X103A-X104I-X232V-X242R-X245R,X052N-X103N-X116A-X148I-X192W,X089I-X116A-X117F-X224A-X249R,X144R-X211Q-X238L-X239S-X249R,X043A-X062Q-X194F-X211Q,X020R-X024R-X052N-X059A-X216F,X024R-X167W-X224A-X249R,X057R-X167W-X249R,X025R-X103N-X186K-

X194F-X224A,X105T-X128N-X144R-X148I-X212M,X020R-X059A-X144R-X192W-X224A,X024R-X043A-X117F-X194F-X211Q,X117F-X194F-X213A-X270C,X078R-X091F-X121F-X233C-X252R,X057R-X099F-X105T-X198L-X213A,X023A-X091F-X101A-X198L-X252R,X062Q-X103N-X121F-X144R-X249R,X043R-X101G-X103A-X104I-X232V-X242R-X245R,X023A-X024R-X117F-X212M-X216F,X104L-X213A-X216F,X194F-X211Q-X236N,X062Q-X103N-X117F-X194F,X024R-X062Q-X104L-X106G-X249R,X057R-X089I-X198L,X046R-X059A-X106G-X217E-X249R,X117F-X213A-X215F,X101A-X120F-X192W-X215F-X224A,X043A-X057R-X117F-X144R-X183D,X046R-X183D-X238L,X025R-X043A-X089I-X117F,X078R-X104L-X213A-X215F-X224A,X091F-X099F-X101A-X105T-X167W,X106G-X117F-X238L,X046R-X089I-X091F-X101A-X116A,X020R-X062Q-X089I-X186K-X212M,X057R-X099F-X121F-X185I-X192W,X046R-X089I-X192W-X233C-X270C,X089I-X117F-X185I-X215F-X233C,X052N-X104L-X183D-X216F-X249R,X078R-X099F-X116A-X186K-X224A,X025R-X105T-X128N-X144R-X270C,X105T-X211Q-X216F,X024R-X046R-X091F-X121F,X106G-X185I-X216F-X236N,X062Q-X101A-X236N-X252R-X270C,X025R-X043A-X091F-X198L-X270C,X020R-X023A-X104L-X192W-X233C,X024R-X043A-X105T-X106G-X198L,X020R-X089I-X217E,X024R-X091F-X198L-X215F-X239S,X046R-X089I-X099F-X186K-X212M,X104L-X120F-X186K-X216F-X252R,X022W-X194F-X213A-X233C-X238L,X099F-X105T-X106G-X194F-X212M,X089I-X105T-X116A-X215F-X216F,X025R-X116A-X120F-X224A-X270C,X043A-X059A-X101A-X216F-X224A,X057R-X183D-X236N,X025R-X062Q-X128N-X144R-X185I,X103N-X120F-X167W-X198L-X233C,X022W-X089I-X216F,X024R-X106G-X116A-X212M-X224A,X020R-X052N-X101A-X198L-X233C,X089I-X091F-X185I-X211Q-X270C,X111I-X215F-X239S,X024R-X116A-X186K-X233C-X236N,和X023A-X103N-X106G-X212M-X215F,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与如SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0022] 本发明还提供分离的枯草杆菌蛋白酶变体,其中该枯草杆菌蛋白酶变体为具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:X020R-X022W-X078R-X101A-X103A-X104I-X116S-X213A-X215F-X232V-X245R,X018R-X078R-X101G-X103A-X104I-X232V-X245R,X024R-X045T-X101G-X103A-X104I-X232V-X245R-X269R,X020R-X022W-X078R-X101G-X103A-X104I-X116A-X232V-X245R,X020R-X22W-X101G-X103A-X104I-X232V-X245R,X018R-X043R-X101G-X103A-X104I-X232V-X245R,X018R-X022W-X024R-X076D-X101A-X116A-X232V-X245R,X018R-X104I-X232V-X249R,X018R-X024R-X076D-X101A-X116A-X211Q-X249R,X018R-X043D-X078R-X101G-X103A-X104I-X217E-X232V-X245R,X018R-X043R-X101G-X103A-X104I-X232V-X245R-X269R,X018R-X045T-X076D-X101G-X103A-X104I-X232V-X245R-X269R,X076D-X078R-X101G-X103A-X104I-X232V-X245R-X269R,X020R-X043D-X078R-X101G-X103A-X104I-X232V-X245R,X018R-X043D-X076D-X101G-X103A-X104I-X232V-X245R-X269R,X024R-X045T-X076D-X078R-X101G-X103A-X104I-X232V-X245R-X269R,X018R-X103A-X232V-X249R,X018R-X101G-X104I-X232V-X245R,X020R-X024R-X101G-X103A-X104I-X217E-X232V-X245R-X249R,X018R-X22K-X043D-X101G-X103A-X104I-X232V-X245R,X043R-X045T-X101G-X103A-

X104I-X232V-X245R-X269R,X020R-X22W-X101G-X103A-X104I-X211Q-X232V-X245R,X024R-X076D-X078R-X101G-X103A-X104I-X232V-X245R-X269R,X020R-X22W-X078R-X101A-X103A-X104I-X116A-X183D-X232V,X018R-X024R-X076D-X116A-X215F-X249R,X018R-X043R-X045T-X101G-X103A-X104I-X232V-X245R,X024R-X043R-X076D-X101G-X103A-X104I-X232V-X245R,X020R-X022W-X101G-X103A-X104I-X232V-X245R,X020R-X022W-X101G-X103A-X104I-X211Q-X232V-X245R,X020R-X022W-X078R-X101G-X103A-X104I-X116A-X213A-X215F-X232V-X245R,X043D-X076D-X078R-X101G-X103A-X104I-X232V-X245R-X269R,X018R-X024R-X076D-X101A-X116A-X213A-X249R,X018R-X024R-X076D-X116A-X211Q-X249R,X043R-X045T-X076D-X078R-X101G-X103A-X104I-X232V-X245R,X018R-X101G-X245R,X020R-X22W-X101A-X103A-X104I-X211Q-X213A-X232V-X245R,X020R-X024R-X043D-X076D-X078R-X101G-X103A-X104I-X232V-X245R,X018R-X045T-X076D-X078R-X101G-X103A-X104I-X232V-X245R,X020R-X078R-X101G-X103A-X104I-X211Q-X213A-X215F-X232V-X245R,X045T-X078R-X101G-X103A-X104I-X232V-X245R-X269R,X024R-X043D-X101G-X103A-X104I-X232V-X245R-X269R,X018R-X101G-X103A-X249R,X018R-X22W-X024R-X076D-X101A-X116A-X232V-X245R,X018R-X101G-X104I-X232V-X249R,X020R-X22W-X101A-X103A-X104I-X215F-X232V-X245R,X018R-X024R-X076D-X211Q-X213A-X249R,X018R-X022W-X024R-X076D-X101A-X198L-X249R,X024R-X101G-X103A-X104I-X232V-X245R,X020R-X076D-X101G-X103A-X104I-X232V-X245R-X269R,X020R-X101G-X103A-X104I-X232V-X245R-X269R,X043D-X078R-X101G-X103A-X104I-X232V-X245R,X020R-X101G-X104I-X213A-X215F-X232V-X245R,X020R-X101G-X103A-X104I-X116A-X215F-X232V-X245R,X024R-X103A-X104I-X249R,X018R-X076D-X078R-X101G-X103A-X104I-X232V-X245R,X045T-X076D-X078R-X101G-X103A-X104I-X232V-X245R-X269R,X024R-X101G-X104I-X245R,X020R-X101G-X103A-X104I-X211Q-X213A-X215F-X232V-X245R,X024R-X103A-X104I-X232V-X249R,X018R-X024R-X076D-X116A-X211Q-X215F-X249R,X018R-X245R,X024R-X103A-X245R,X024R-X103A-X104I-X245R,X020R-X078R-X101G-X232V-X245R,X018R-X024R-X076D-X104I-X249R,X018R-X024R-X104I-X249R,X024R-X101G-X103A-X104I-X232V-X245R,X018R-X024R-X076D-X211Q-X215F-X249R,X019H-X020R-X022W-X078R-X101G-X103A-X104I-X211Q-X232V-X245R,X018R-X024R-X076D-X101A-X198L-X211Q-X213A-X249R,X018R-X024R-X043D-X101G-X103A-X104I-X232V-X245R,X020R-X22W-X103A-X104I-X232V-X245R,X018R-X103A-X104I-X249R,X018R-X022W-X024R-X076D-X101A-X198L-X215F-X249R,X018R-X024R-X101G-X104I-X232V,X078R-X101G-X103A-X104I-X232V-X245R-X269R,X024R-X043R-X076D-X078R-X101G-X103A-X104I-X232V-X245R,X018R-X020R-X043D-X076D-X101G-X103A-X104I-X232V-X245R,X018R-X22W-X024R-X076D-X116A-X213A-X249R,X018R-X024R-X101G-X104I,X020R-X101A-X103A-X104I-X215F-X232V-X245R,X018R-X045T-X078R-X101G-X103A-X104I-X232V-X245R,X018R-X101G-X103A-X245R,X043R-X076D-X078R-X101G-X103A-X104I-X232V-X245R,X020R-X022W-X101A-X103A-X104I-X211Q-X215F-X232V-X245R,X020R-X22W-X078R-X101G-X103A-X104I-X116A-X213A-X215F-X232V-X245R,X020R-X078R-X101G-X103A-X104I-X215F-X232V-X245R,X020R-X022W-X078R-X101G-X103A-X104I-X116A-X183D-

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X183D-X249R,X018R-X022W-X024R-X076D-X101A-X183D-X198L-X215F-X249R,X018R-X020R-X043D-X045T-X076D-X101G-X103A-X104I-X232V-X245R,X020R-X022W-X101A-X103A-X104I-X183D-X198L-X215F-X232V-X245R,X076D-X101G-X103A-X104I-X249R,X018R-X020R-X024R-X076D-X183D-X198L-X215F-X249R,X018R-X020R-X022W-X024R-X076D-X101A-X183D-X215F-X249R,X018R-X020R-X024R-X076D-X211Q-X213A-X249R,X018R-X024R-X076D-X116A-X183D-X211Q-X213A-X249R,X018R-X024R-X076D-X116A-X183D-X198L-X249R,X018R-X020R-X024R-X076D-X211Q-X243D-X249R,X018R-X020R-X045T-X076D-X101G-X103A-X104I-X232V-X245R-X249R,X018R-X022W-X024R-X076D-X183D-X198L-X211Q-X213A-X249R,X018R-X024R-X076D-X101A-X116A-X183D-X198L-X211Q-X213A-X249R,X018R-X022W-X024R-X076D-X116A-X198L-X211Q-X213A-X215F-X249R,X024R-X076D-X101G,X018R-X020R-X024R-X076D-X101A-X198L-X213A-X215F-X249R,X018R-X022W-X024R-X076D-X116A-X183D-X211Q-X213A-X249R,X018R-X020R-X024R-X076D-X183D-X215F-X249R,X018R-X043D-X076D-X078R-X101G-X103A-X104I-X232V-X245R-X249R,X018R-X022W-X024R-X076D-X116A-X183D-X211Q-X213A-X245R,X020R-X024R-X076D-X078R-X101G-X103A-X104I-X232V-X245R-X249R,X018R-X020R-X045T-X101G-X103A-X104I-X232V-X245R-X249R,X018R-X024R-X076D-X101A-X183D-X198L-X211Q-X249R,X018R-X022W-X024R-X076D-X183D-X211Q-X213A-X249R,X018R-X020R-X024R-X076D-X116A-X198L-X211Q-X215F-X249R-X269S,X018R-X020R-X022W-X024R-X076D-X101A-X116A-X183D-X198L-X211Q-X215F-X249R,X020R-X022W-X101A-X103A-X104I-X183D-X213A-X215F-X232V-X245R,X018R-X024R-X076D-X086V-X101A-X183D-X198L-X211Q-X249R,X018R-X076D-X101G-X198T-X232V,X018R-X020R-X024R-X076D-X101A-X116A-X183D-X198L-X211Q-X215F-X249R,X018R-X022W-X024R-X076D-X101A-X116A-X183D-X213A-X215F-X249R,X018R-X022W-X024R-X076D-X101A-X183D-X211Q-X213A-X215F-X249R,X018R-X024R-X076D-X183D-X249R-X248T,X018R-X076D-X104I-X245R-X249R,X018R-X022W-X024R-X076D-X101A-X116A-X183D-X198L-X215F-X249R,X018R-X022W-X024R-X076D-X116A-X183D-X213A-X215F-X249R,X018R-X020R-X022W-X024R-X076D-X116A-X183D-X211Q-X213A-X215F-X249R,X018R-X020R-X024R-X076D-X101A-X249R,X018R-X020R-X024R-X076D-X101A-X116A-X213A-X215F-X249R,X018R-X022W-X024R-X076D-X116A-X183D-X211Q-X215F-X249R,X018R-X022W-X024R-X076D-X116A-X183D-X198L-X211Q-X213A-X249R,X043R-X045T-X078R-X101G-X103A-X104I-X217E-X232V-X245R,X043R-X045T-X101G-X103A-X104I-X232V-X245R-X249R,X018R-X076D-X101G-X104I,X020R-X045T-X076D-X078R-X101G-X103A-X104I-X232V-X245R-X249R,X043D-X076D-X101G-X103A-X104I-X232V-X245R,X018R-X020R-X022W-X024R-X076D-X101A-X116A-X183D-X198L-X249R,X018R-X076D-X104I,X018R-X020R-X043D-X101G-X103A-X104I-X232V-X245R-X249R,X018R-X020R-X022W-X024R-X076D-X183D-X211Q-X249R,X018R-X024R-X076D-X101A-X183D-X198L-X211Q-X215F-X249R,X101G-X104I,X018R-X022W-X024R-X076D-X116A-X183D-X198L-X211Q-X213A-X215F-X249R,X018R-X020R-X024R-X076D-X101A-X183D-X211Q-X213A-X215F-X249R,X018R-X020R-X024R-X076D-X116A-X183D-X215F-X249R-X263D,X018R-X022W-X024R-X076D-

X101A-X183D-X249R,X018R-X024R-X076D-X101A-X116A-X183D-X198L-X215F-X249R,X018R-X022W-X024R-X076D-X116A-X198L-X215F-X249R-X269H,X018R-X043D-X045T-X076D-X078R-X101G-X103A-X104I-X232V-X245R,X018R-X024R-X045T-X076D-X078R-X101G-X103A-X104I-X232V-X245R-X269R,X078R-X101G-X103A-X104I-X217E-X232V-X245R,X018R-X020R-X022W-X024R-X076D-X101A-X183D-X198L-X213A-X215F-X249R,X018R-X020R-X024R-X076D-X183D-X198L-X213A-X249R,X018R-X020R-X022W-X024R-X076D-X116A-X198L-X211Q-X215F-X249R,X018R-X020R-X022W-X024R-X076D-X116A-X183D-X211Q-X249R,X018R-X020R-X022W-X024R-X076D-X101A-X198L-X211Q-X213A-X249R,X018R-X020R-X022W-X024R-X076D-X249R,X020R-X022W-X101G-X103A-X104I-X116A-X183D-X198L-X211Q-X213A-X215F-X232V-X245R,X104I-X232V,X018R-X020R-X022W-X024R-X076D-X101A-X116A-X183D-X211Q-X215F-X249R,X018R-X020R-X022W-X024R-X076D-X101A-X116A-X183D-X198L-X211Q-X213A-X215F-X249R,X018R-X020R-X022W-X024R-X076D-X101A-X183D-X213A-X215F-X249R,X018R-X022W-X024R-X076D-X101A-X183D-X198L-X211Q-X213A-X249R,X018R-X022W-X024R-X076D-X101A-X183D-X198L-X249R,X043D-X045T-X101G-X103A-X104I-X232V-X245R-X269R,X018R-X020R-X024R-X076D-X101A-X183D-X198L-X211Q-X249R,X018R-X020R-X043R-X101G-X103A-X104I-X217E-X232V-X245R,X024R-X043R-X076D-X078R-X101G-X103A-X104I-X232V-X245R-X269R,X043R-X045T-X076D-X078R-X101G-X103A-X104I-X166F-X176P-X179V-X184T-X187P-X194P,X018R-X022W-X024R-X041E-X076D-X101A-X160T-X183D-X211Q-X213A-X249R,X018R-X020R-X022W-X024R-X076D-X116A-X183D-X198L-X211Q-X215F-X249R,X018R-X020R-X022W-X024R-X076D-X101A-X116A-X198L-X213A-X249R,X018R-X022W-X024R-X076D-X101A-X116A-X183D-X198L-X211Q-X213A-X249R,X018R-X020R-X024R-X076D-X198L-X213A-X249R,X018R-X020R-X022W-X024R-X076D-X116A-X183D-X198L-X211Q-X249R,X018R-X020R-X024R-X076D-X183D-X211Q-X215F-X249R,X024R-X076D-X104I,X018R-X076D-X101G-X232V,X018R-X024R-X076D-X101A-X116A-X183D-X198L-X211Q-X213A-X215F-X249R,X018R-X020R-X022W-X024R-X076D-X116A-X183D-X215F-X249R,X018R-X024R-X031F-X076D-X116A-X183D-X211Q-X213A-X215F-X249R,X018R-X024R-X076D-X101A-X116A-X183D-X198L-X213A-X249R-X269S,X018R-X020R-X024R-X076D-X101A-X116A-X198L-X215F-X249R,X018R-X043R-X076D-X078R-X101G-X103A-X104I-X232V-X245R-X269R,X018R-X020R-X024R-X076D-X101A-X114T-X198L-X211Q-X215F-X249R,X024R-X043R-X078R-X101G-X103A-X104I-X217E-X232V-X245R,X024R-X076D-X103A-X104I-X232V,X018R-X020R-X022W-X024R-X076D-X101A-X198L-X211Q-X215F-X249R,X101G-X104I-X232V,X018R-X022W-X024R-X076D-X183D-X198L-X213A-X215F-X249R,X018R-X022W-X024R-X076D-X183D-X198L-X211Q-X249R,X018R-X020R-X024R-X076D-X183D-X213A-X249R,X018R-X024R-X076D-X101A-X183D-X211Q-X215F-X249R,X018R-X020R-X022W-X024R-X076D-X116A-X211Q-X213A-X249R,X018R-X078R-X101G-X103A-X104I-X232V-X245R-X269R,X018R-X022W-X024R-X076D-X101A-X116A-X183D-X211Q-X215F-X249R-X260A,X076D-X249R,X018R-X022W-X024R-X076D-X183D-X211Q-X215F-X249R,X018R-X020R-X024R-X076D-X116A-X211Q-X215F-X249R,

X018R-X020R-X024R-X076D-X213A-X249R,X018R-X020R-X022W-X024R-X076D-X116A-X183D-X198L-X249R,X018R-X020R-X022W-X024R-X076D-X101A-X183D-X249R,X076D-X104I-X249R,X020R-X022W-X101A-X103A-X104I-X116A-X183D-X211Q-X213A-X215F-X232V-X245R,X024R-X043R-X045T-X078R-X101G-X103A-X104I-X217E-X232V-X245R,X018R-X020R-X022W-X024R-X076D-X183D-X198L-X215F-X249R,X018R-X076D-X101G-X103A,X020R-X024R-X101G-X103A-X104I-X232V-X245R-X269R,X018R-X020R-X024R-X076D-X101A-X116A-X183D-X211Q-X249R,X101G-X103A-X232V,X024R-X076D-X101G-X232V,X018R-X022W-X024R-X076D-X101A-X183D-X198L-X211Q-X249R,X018R-X020R-X024R-X076D-X101A-X183D-X198L-X211Q-X215F-X249R,X018R-X020R-X024R-X076D-X183D-X198L-X249R,X018R-X022W-X024R-X076D-X101A-X116A-X183D-X198L-X211Q-X249R,X018R-X020R-X024R-X076D-X116A-X156V-X183D-X211Q-X215F-X249R-X269S,X045T-X076D-X101G-X103A-X104I-X232V-X245R-X249R,X018R-X020R-X024R-X076D-X101A-X183D-X198L-X249R,X018R-X020R-X022W-X024R-X076D-X198L-X211Q-X215F-X249R,X018R-X020R-X022W-X024R-X076D-X101A-X116A-X198L-X211Q-X215F-X249R,X018R-X020R-X022W-X024R-X076D-X116A-X249R,X018R-X076D-X101G,X018R-X024R-X076D-X116A-X183D-X198L-X213A-X215F-X249R,X018R-X020R-X022W-X024R-X076D-X101A-X116A-X198L-X213A-X215F-X249R,X018R-X024R-X076D-X101A-X116A-X183D-X198L-X211Q-X249R,X018R-X076D-X232V,X018R-X020R-X024R-X076D-X101A-X232V-X245R,X018R-X043D-X045T-X076D-X101G-X103A-X104I-X232V-X245R,X018R-X022W-X024R-X076D-X183D-X213A-X215F-X249R,X018R-X024R-X076D-X101A-X116A-X211Q-X213A-X237D-X249R,X018R-X020R-X024R-X076D-X101A-X116A-X183D-X211Q-X249R-X275S,X018R-X022W-X024R-X076D-X101A-X116A-X183D-X198L-X211Q-X213A-X215F-X249R,X024R-X076D,X018R-X024R-X076D-X183D-X211Q-X215F-X249R,X018R-X022W-X024R-X076D-X116A-X183D-X198L-X213A-X215F-X249R,X076D-X104I-X232V-X249R,X018R-X076D-X103A-X232V,X018R-X020R-X024R-X076D-X101A-X116A-X183D-X198L-X211Q-X213A-X249R,X018R-X020R-X024R-X076D-X101A-X183D-X213A-X249R,X018R-X020R-X024R-X076D-X101A-X175E-X183D-X211Q-X215F-X249R,X018R-X020R-X043D-X078R-X101G-X103A-X104I-X217E-X232V-X245R-X273E,X020R-X024R-X043D-X045T-X076D-X101G-X103A-X104I-X232V-X245R,X005S-X101G-X103A-X104I-X232V-X245R-X249R,X103A-X104I-X232V,X018R-X020R-X024R-X068A-X076D-X101A-X116A-X213A-X215F-X249R,X018R-X022W-X024R-X076D-X101A-X198L-X215F-X249R-X275S,X018R-X024R-X076D-X183D-X198L-X211Q-X213A-X249R,和X043D-X045T-X101G-X103A-X104I-X232V-X245R,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与如SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0023] 本发明还提供分离的枯草杆菌蛋白酶变体,其中该枯草杆菌蛋白酶变体为具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:X018R-X024R-X043R-X076D-X249R-X269R,X018R-X022R-X024R-X043R-X076D-X249R,X018R-X043D-X101G-X103A-X104I-X232V-X245R,X020R-X043D-X101G-X103A-X104I-X232V-X245R,X043D-X101G-X103A-X104I-X232V-X245R-X269R,X043D-X078R-X101G-X103A-

X104I-X232V-X245R,X043R-X076D-X101G-X103A-X104I-X232V-X245R,X022R-X043R-X101G-X103A-X104I-X232V-X245R,X043R-X078R-X101G-X103A-X104I-X232V-X245R,X020R-X076D-X101G-X103A-X104I-X232V-X245R,X043R-X076D-X101G-X103A-X104I-X232V-X245R,X022R-X076D-X101G-X103A-X104I-X232V-X245R,X076D-X078R-X101G-X103A-X104I-X232V-X245R,X018R-X024R-X043R-X076D-X249R,X018R-X024R-X076D-X242R-X249R,X018R-X024R-X076D-X249R-X269R,X018R-X022R-X024R-X076D-X249R,X018R-X024R-X076D-X078R-X249R,X018R-X024R-X043D-X076D-X249R-X269R,X018R-X022R-X024R-X043D-X076D-X249R,X018R-X024R-X043D-X076D-X078R-X249R,X020R-X101G-X103G-X104I-X232V-X245R,X020R-X101G-X103A-X104L-X232V-X245R,X020R-X101G-X103A-X104V-X232V-X245R,X020R-X101G-X103S-X104I-X232V-X245R,X020R-X101G-X103S-X104L-X232V-X245R,X020R-X101S-X103S-X104I-X232V-X245R,X020R-X101S-X103S-X104L-X232V-X245R,X020R-X101A-X103A-X104L-X232V-X245R,X020R-X101S-X103S-X104V-X232V-X245R,X020R-X101S-X103A-X104I-X232V-X245R,X020R-X101S-X103A-X104V-X232V-X245R,X020R-X101S-X103G-X104I-X232V-X245R,X020R-X101S-X103G-X104V-X232V-X245R,X020R-X101A-X103A-X104V-X232V-X245R,X020R-X101A-X103S-X104I-X232V-X245R,X020R-X101A-X103S-X104V-X232V-X245R,X018R-X024R-X043R-X076D-X078R-X249R,X024R-X043D-X101G-X103A-X104I-X232V-X245R,X043D-X101G-X103A-X104I-X232V-X245R-X249R,X024R-X076D-X101G-X103A-X104I-X232V-X245R,X076D-X101G-X103A-X104I-X232V-X242R-X245R,X018R-X020R-X024R-X076D-X217E-X249R,X018R-X024R-X043R-X076D-X217E-X249R,X018R-X024R-X043D-X076D-X242R-X249R,X018R-X020R-X024R-X043R-X076D-X249R,X020R-X101A-X103G-X104V-X232V-X245R,X043D-X101G-X103A-X104I-X232V-X245R,X018R-X024R-X076D-X217E-X249R-X269R,和X018R-X024R-X076D-X217E-X242R-X249R,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与如SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0024] 本发明还提供分离的枯草杆菌蛋白酶变体,其中该枯草杆菌蛋白酶变体为具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:X020R-X101A-X103A-X104I-X118R-X232V-X245R,X020R-X024R-X116A-X213A,X043R-X101A-X116A-X215F-X269R,X024R-X043R-X101A-X116A,X024R-X043R-X101A-X116A-X215F-X269R,X020R-X101G-X103A-X104I-X215F-X232V-X245R,X043R-X101A-X269R,X024R-X043R-X116A-X213A-X269R,X020R-X024R-X043R-X045T-X101A-X213A,X024R-X043R-X116A-X215F-X269R,X020R-X024R-X213A-X215F,X020R-X116A-X269R,X024R-X116A-X213A-X269R,X043R-X101A-X116A-X269R,X101G-X103A-X104I-X116A-X213A-X232V-X245R-X269R,X024R-X043R-X045T-X101A-X116A-X215F-X269R,X020R-X043R-X101A-X269R,X101A-X103A-X104I-X213A-X232V-X245R-X269R,X024R-X215F-X269R,X043R-X101A-X116A-X213A-X215F-X269R,X043R-X101A-X213A-X269R,X020R-X024R-X043R-X045T-X116A-X213A,X101G-X103A-X104I-X232V-X245R-X269R,X024R-X043R-X045T-X101A-X116A-X213A-X269R,X024R-X043R-X045T-X269R,X020R-X043R-X045T-X101A-X269R,X024R-X043R-X116A-X269R,X020R-X024R-X043R-X045T,X043R-X116A-X269R,

X024R-X043R-X101A-X215F-X269R,X024R-X043R-X045T-X213A-X215F-X269R,X020R-X024R-X045T-X269R,X020R-X043R-X101A-X116A-X213A-X215F,X020R-X101G-X103A-X104I-X213A-X215F-X232V-X245R,X020R-X024R-X045T-X116A-X269R,X020R-X101A-X116A-X269R,X024R-X043R-X215F,X020R-X024R-X213A,X024R-X043R-X101A-X215F,X020R-X024R-X043R-X045T-X116A,X020R-X024R-X043R-X045T-X101A-X269R,X020R-X024R-X101A-X215F,X020R-X024R-X116A-X213A-X215F,X020R-X024R-X116A,X020R-X024R-X101A-X116A,X043R-X213A-X215F-X269R,X024R-X101A-X269R,X024R-X043R-X116A-X215F,X020R-X038A-X043R-X101A,X020R-X024R-X116A-X215F,X024R-X043R-X101A-X213A,X014L-X020R-X024R-X043R-X045T-X101A-X215F,X020R-X024R-X215F,X020R-X116A-X215F-X269R,X020R-X045T-X116A-X269R,X020R-X024R-X043R-X045T-X215F,和X020R-X024R-X043R-X045T-X116A-X213A-X215F,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与如SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0025] 本发明还提供分离的枯草杆菌蛋白酶变体,其中该枯草杆菌蛋白酶变体为具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:X043R-X076D-X101A-X103A-X104I-X158E-X188D-X232V-X245R-X248D-X249R-X271F,X024R-X043R-X076D-X101A-X103A-X104I-X158E-X188D-X217E-X232V-X245R-X248D-X249R,X101A-X103A-X104I-X158E-X188D-X232V-X245R-X248D-X249R-X271F-X271F,X101A-X103A-X104I-X158E-X188D-X217E-X232V-X245R-X248D-X249R-X271F,X076D-X101G-X103A-X104I-X114V-X158E-X188D-X232V-X245R-X248D-X249R-X271F,X024R-X076D-X101G-X103A-X104I-X158E-X188D-X232V-X245R-X248D-X249R-X271F,X024R-X043R-X101A-X103A-X104I-X158E-X188D-X217E-X232V-X245R-X248D-X249R,X024R-X043R-X101A-X103A-X104I-X158E-X188D-X232V-X245R-X248D-X249R,X024R-X101A-X103A-X104I-X158E-X166D-X188D-X217E-X232V-X245R-X248D-X249R,X076D-X101G-X103A-X104I-X128L-X158E-X188D-X232V-X245R-X248D-X249R-X271F,和X043R-X076D-X101G-X103A-X104I-X158E-X166D-X188D-X232V-X245R-X248D-X249R-X271F,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与如SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0026] 本发明还提供分离的枯草杆菌蛋白酶变体,其中该枯草杆菌蛋白酶变体为具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:X022A-X101G-X103A-X104I-X159D-X217E-X232V-X245R-X248D-X271F,X022A-X043R-X101G-X103A-X104I-X159D-X188D-X217E-X232V-X245R-X248D-X271F,X022A-X101G-X103A-X104I-X159D-X188D-X232V-X245R-X248D-X271F,X043R-X101A-X103A-X104I-X158E-X188D-X217E-X232V-X245R-X248D-X249R,X043R-X076D-X101A-X103A-X104I-X158E-X188D-X217E-X232V-X245R-X248D-X249R-X271F,X024R-X101G-X103A-X104I-X158E-X188D-X217E-X232V-X245R-X248D-X249R,X024R-X101G-X103A-X104I-X158E-X188D-X232V-X245R-X248D-X249R,X101G-X103A-X104I-X158E-X188D-X232V-X245R-X248D-X249R,X024R-X101G-X103A-X104I-X158E-X183D-X188D-X232V-X245R-X248D-X249R,X022A-X076D-X101G-X103A-X104I-X159D-X188D-X232V-X245R-X248D-X271F,X022A-

X043R-X076D-X101G-X103A-X104I-X159D-X188D-X232V-X245R-X248D-X271F,X022A-X076D-X101G-X103A-X104I-X159D-X232V-X245R-X248D-X271F,X022A-X101G-X103A-X104I-X159D-X232V-X245R-X248D-X271F,X076D-X101A-X103A-X104I-X158E-X188D-X232V-X245R-X248D-X249R-X271F,X043R-X101A-X103A-X104I-X158E-X166D-X188D-X232V-X245R-X248D-X249R,X024R-X076D-X101A-X103A-X104I-X158E-X166D-X188D-X232V-X245R-X248D-X249R-X271F,X076D-X101A-X103A-X104I-X158E-X188D-X232V-X245R-X248D-X249R,X101A-X103A-X104I-X158E-X166D-X188D-X232V-X245R-X248D-X249R-X271F,X043R-X076D-X101A-X103A-X104I-X158E-X166D-X188D-X232V-X245R-X248D-X249R-X271F,X101G-X103A-X104I-X158E-X166D-X188D-X232V-X245R-X248D-X249R-X271F,X101A-X103A-X104I-X158E-X188D-X232V-X245R-X248D-X249R-X271F,X101A-X103A-X104I-X158E-X188D-X217E-X232V-X245R-X248D-X249R,X076D-X101A-X103A-X104I-X158E-X166D-X188D-X232V-X245R-X248D-X249R-X271F,X101G-X103A-X104I-X158E-X183D-X188D-X232V-X245R-X248D-X249R,X024R-X101G-X103A-X104I-X128L-X158E-X188D-X232V-X245R-X248D-X249R,X076D-X101G-X103A-X104I-X158E-X166D-X188D-X232V-X245R-X248D-X249R-X271F,X043R-X076D-X101A-X103A-X104I-X158E-X166D-X188D-X232V-X245R-X248D-X249R,和X076D-X101A-X103A-X104I-X158E-X188D-X217E-X232V-X245R-X248D-X249R-X271F,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与如SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0027] 本发明还提供分离的枯草杆菌蛋白酶变体,其中该枯草杆菌蛋白酶变体为具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:X017R-X022A-X076D-X101G-X103A-X104I-X159D-X188D-X232V-X245R-X248D-X271F,X022A-X043R-X101G-X103A-X104I-X159D-X232V-X245R-X248D-X271F,X022A-X101G-X103A-X104I-X159D-X188D-X232V-X245R-X248D-X249R-X271F,X017R-X022A-X076D-X101G-X103A-X104I-X159D-X232V-X245R-X248D-X271F,X022A-X076D-X101G-X103A-X104I-X159D-X232V-X245R-X248D-X249R-X271F,X022A-X101G-X102A-X103A-X104I-X159D-X188D-X232V-X245R-X248D-X271F,和X022A-X043R-X076D-X101G-X103A-X104I-X159D-X232V-X245R-X248D-X249R-X271F,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与如SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0028] 本发明还提供分离的枯草杆菌蛋白酶变体,其中该枯草杆菌蛋白酶变体为具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:X101S-X103A-X104I-X158E-X188D-X232V-X245R-X248D-X249R,X101S-X103G-X104V-X158E-X188D-X232V-X245R-X248D-X249R,X101G-X103S-X104I-X158E-X188D-X232V-X245R-X248D-X249R,X101A-X103A-X104I-X158E-X188D-X232V-X245R-X248D-X249R,X101A-X103A-X104L-X158E-X188D-X232V-X245R-X248D-X249R,X101G-X103G-X104I-X158E-X188D-X232V-X245R-X248D-X249R,X101S-X103G-X104I-X158E-X188D-X232V-X245R-X248D-X249R,X101S-X103S-X104I-X158E-X188D-X232V-X245R-X248D-X249R,X101S-X103S-X104V-X158E-X188D-X232V-X245R-X248D-X249R,X101A-X103S-X104I-X158E-X188D-X232V-X245R-X248D-X249R,X101A-X103S-X104I-X159E-X232V-X245R-X248D-

X249R,X101S-X103A-X104I-X159E-X232V-X245R-X248D-X249R,X101G-X103A-X104L-X158E-X188D-X232V-X245R-X248D-X249R,X101A-X103A-X104L-X159E-X232V-X245R-X248D-X249R,X101A-X103S-X104L-X159E-X232V-X245R-X248D-X249R,X101G-X103S-X104L-X159E-X232V-X245R-X248D-X249R,X101S-X103A-X104L-X159E-X232V-X245R-X248D-X249R,X101A-X103G-X104V-X159E-X232V-X245R-X248D-X249R,和X101S-X103A-X104V-X159E-X232V-X245R-X248D-X249R,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与如SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0029] 本发明还提供分离的枯草杆菌蛋白酶变体,其中该枯草杆菌蛋白酶变体为具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:X026F-X051W-X104L-X106E,X026F-X031F-X078N-X102A-X160D,X020K-X100S-X116L-X158E-X166D-X243F,X033S-X043W-X218D-X239G-X243F,X022L-X038F-X048R-X062E-X100S-X186K,X101D-X103N-X116L-X144R-X215D,X104L-X105T-X213A-X217E-X256N,X043W-X101D-X212M-X243F,X026F-X048R-X105T-X213A-X218D-X224A,X024F-X101D-X118R-X215D-X250I-X272F,X121F-X185E-X224A-X239G,X022L-X031F-X102A-X128D-X224A-X243F,X062E-X078N-X102A-X116L-X144R-X250I,X022L-X038F-X121F-X160D-X272F,X026F-X078N-X159C-X186K-X243F,X024F-X048R-X118R-X166D-X217E,X023A-X038F-X078N-X100S-X212M-X215D,X100S-X116L-X158E-X213A,X078N-X104L-X118R-X128D,X102A-X103N-X105T-X194E,X022L-X078N-X128D-X213A,X027R-X100S-X118R-X160D-X188D-X243F,X024F-X102A-X186K-X213A-X217E-X243F,X033S-X105T-X188D-X216F,X023A-X100S-X194E-X212M,X048R-X128D-X185E-X239G,X020K-X024F-X033S-X129E-X194E,X020K-X027R-X129E-X166D-X239G,X022L-X023A-X027R-X101D-X104L-X216F,X033S-X118R-X129E-X194E-X239G,X022L-X078N-X116L-X129E-X256N,X027R-X101D-X103N-X105T-X272F,X048R-X078N-X116L-X185E-X217E-X239G,X023A-X024F-X027R-X062E,X024F-X103N-X104L-X118R-X188D,X026F-X104L-X256N-X272F,X024F-X043W-X104L-X121F-X129E,X062E-X078N-X116L-X224A,X023A-X024F-X051W-X158E,X027R-X038F-X102A-X116L,X062E-X078N-X144R-X212M,X031F-X116L-X256N-X272F,X022L-X033S-X104L-X116L-X160D-X186K,X024F-X118R-X129E-X186K-X213A,X043W-X105T-X213A-X215D-X216F,X031F-X105T-X186K-X188D,X026F-X194E-X213A-X256N,和X103N-X160D-X250I-X256N,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与如SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0030] 本发明还提供分离的枯草杆菌蛋白酶变体,其中该枯草杆菌蛋白酶变体为具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:X022A-X024R-X101D-X103A-X104I-X118R-X159D-X188D-X232V-X248D-X271F,X022A-X024R-X103A-X104I-X129E-X159D-X188D-X232V-X248D-X271F,X022A-X024R-X103A-X104I-X118R-X159D-X188D-X217D-X232V-X248D,X022A-X024R-X101D-X103A-X104I-X118R-X129E-X159D-X188D-X232V-X245R-X248D,X022A-X024R-X101D-X103A-X104I-X159D-X188D-X232V-X245R-X248D,X022A-X043R-X103A-X104I-X118R-X129E-X159D-X188D-X232V-X245R-X248D,X022A-X043R-X103A-X104I-X118R-X128I-X129E-X159D-X188D-

X232V-X248D,X022A-X043R-X101D-X103A-X104I-X118R-X129E-X159D-X188D-X232V-X248D-X271F,X022A-X024R-X043R-X101D-X103A-X104I-X159D-X188D-X232V-X245R-X248D,X022A-X103A-X104I-X159D-X188D-X232V-X248D,X022A-X024R-X103A-X104I-X118R-X129E-X159D-X188D-X232V-X248D-X271F,X022A-X024R-X103A-X104I-X159D-X188D-X217D-X232V-X245R-X248D-X271F,X022A-X043R-X062E-X103A-X104I-X159D-X188D-X232V-X245R-X248D-X271F,X022A-X043R-X103A-X104I-X129E-X159D-X188D-X232V-X245R-X248D,X022A-X024R-X103A-X104I-X159D-X188D-X217D-X232V-X248D-X271F,X022A-X103A-X104I-X118R-X159D-X188D-X217D-X232V-X245R-X248D,X022A-X024R-X101D-X103A-X104I-X118R-X128I-X159D-X188D-X232V-X245R-X248D,X022A-X024R-X043R-X103A-X104I-X159D-X188D-X217D-X232V-X248D-X271F,X022A-X043R-X103A-X104I-X118R-X159D-X188D-X217D-X232V-X248D-X271F,X022A-X043R-X103A-X104I-X118R-X159D-X188D-X232V-X248D-X271F,X022A-X103A-X104I-X128I-X129E-X159D-X188D-X232V-X248D-X271F,X022A-X103A-X104I-X159D-X188D-X217D-X232V-X245R-X248D-X271F,X022A-X043R-X103A-X104I-X128I-X159D-X188D-X232V-X245R-X248D,X022A-X101D-X103A-X104I-X118R-X159D-X188D-X217D-X232V-X245R-X248D-X271F,X022A-X103A-X104I-X118R-X129E-X159D-X188D-X232V-X245R-X248D-X271F,X022A-X024R-X043R-X103A-X104I-X118R-X159D-X188D-X217D-X232V-X248D,X022A-X062E-X103A-X104I-X118R-X159D-X188D-X232V-X245R-X248D,X022A-X043R-X101D-X103A-X104I-X118R-X129E-X159D-X188D-X217D-X232V,X022A-X024R-X103A-X104I-X159D-X188D-X217D-X232V-X248D,X022A-X024R-X043R-X103A-X104I-X118R-X128I-X129E-X159D-X188D-X217D-X232V-X248D-X271F,和X022A-X103A-X104I-X118R-X159D-X188D-X217D-X232V-X245R-X248D-X271F,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与如SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0031] 本发明还提供分离的枯草杆菌蛋白酶变体,其中该枯草杆菌蛋白酶变体为具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:X02OK-X024F-X062E-X188D-X239G,X024F-X062E-X116L-X239G,X02OK-X023A-X062E-X188D,X02OK-X023A-X024F-X062E-X118R-X188D-X213A,X02OK-X043W-X062E-X116L-X188D-X213A-X239G,X023A-X062E-X116L-X118R,X023A-X024F-X062E-X116L-X118R,X024F-X116L,X024F-X062E-X188D-X213A,X023A-X062E-X116L-X118R-X188D-X239G,X02OK-X024F-X062E,X02OK-X043W-X062E-X116L-X239G,X024F-X062E-X116L-X213A-X239G,X02OK-X024F-X043W-X062E-X116L-X213A,X02OK-X023A-X024F-X062E-X116L-X188D-X213A,X024F-X062E-X188D-X239G,X023A-X043W-X062E-X116L-X118R-X213A,X062E-X188D-X239G,X02OK-X024F-X062E-X239G,X024F-X116L-X118R-X188D-X239G,X02OK-X023A-X062E-X116L-X118R-X213A,X02OK-X023A-X024F-X062E-X188D-X213A-X239G,X024F-X043W-X118R-X188D,X023A-X024F-X116L-X118R-X188D-X213A,X02OK-X023A-X043W-X116L-X188D-X213A-X239G,X023A-X024F-X116L-X188D-X239G,X023A-X043W-X116L-X118R-X188D,X023A-X024F-X118R-X188D-X239G,X023A-X024F-X043W-X062E-X116L-X118R,X02OK-X043W-X188D-X213A,X024F-X062E-X118R-X239G,X023A-X043W-

X188D-X213A,X020K-X024F-X043W-X062E-X116L-X118R-X188D-X239G,X020K-X116L-X188D-X239G,X020K-X043W-X062E-X118R,X020K-X043W-X116L-X188D-X213A,X020K-X024F,X023A-X043W-X116L-X239G,X023A-X024F-X043W-X116L-X118R-X188D-X239G,X020K-X023A-X043W-X213A,和X023A-X024F-X062E-X118R-X213A-X239G,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与如SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0032] 本发明还提供分离的枯草杆菌蛋白酶变体,其中该枯草杆菌蛋白酶变体为具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:X020K-X023A-X043W-X118R-X128I-X129E-X159D-X188D,X024F-X118R-X128I-X129E-X159D,X020K-X024F-X062E-X116L-X118R-X188D,X020K-X062E-X116L-X188D,X062E-X116L-X118R-X213A,X020K-X023A-X062E-X116L-X188D,X062E-X116L-X118R-X188D,X020K-X062E-X116L-X213A,X020K-X023A-X062E-X116L,X020K-X062E-X188D-X213A,X020K-X062E,X020K-X024F-X062E-X116L-X188D,X020K-X043W-X062E-X116L-X188D,X020K-X024F-X062E-X188D-X213A,X062E-X116L-X188D-X213A,X020K-X062E-X116L,X020K-X023A-X062E-X116L-X188D-X213A,X023A-X024F-X062E-X116L-X213A,X022A-X043R-X103A-X104I-X128I-X129E-X159D-X188D-X232V-X245R-X248D,X022A-X043R-X103A-X104I-X118R-X128I-X129E-X159D-X188D-X232V-X248D-X271F,X024F-X062E-X116L-X188D,X022A-X024R-X103A-X104I-X118R-X128I-X129E-X159D-X188D-X232V-X248D,X023A-X062E-X116L-X188D,X043W-X062E-X116L,X020K-X023A-X116L-X188D,X043W-X062E-X116L-X188D,X024F-X062E-X116L,X062E-X116L-X188D,和X022A-X024R-X103A-X104I-X128I-X159D-X188D-X232V-X248D,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与如SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0033] 本发明还提供分离的枯草杆菌蛋白酶变体,其中该枯草杆菌蛋白酶变体为具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:X087R-X101G-X103A-X104I-X109R-X212P-X232V-X245R-X271V,X101G-X103A-X104I-X109R-X232V-X245R,X101G-X103A-X104I-X109R-X212P-X232V-X245R-X271V,X101G-X103A-X104I-X109R-X212P-X232V-X245R,X076D-S87R-X103A-X104I-X212P-X271V,X076D-X103A-X104I-X109R,X076D-X103A-X104I-X212P-X271V,X076D-X103A-X104I-X109R-X245R,和X076D-X103A-X104I-X212P-X245L-X271V,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与如SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0034] 本发明还提供分离的枯草杆菌蛋白酶变体,其中该枯草杆菌蛋白酶变体为具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:X024R-X086W-X118R,X024R-X078R-X086W-X243F,X024R-X033S-X086S-X087N-X209A,X033S-X118R,X024R-X078R-X086W-X118R-X270T,X024R-X033S-X086W-X118R,X078R-X086W-X243F,X033S-X078R-X086W-X118R-X209A,X033S-X078R-X209A,X086W-X118R-X243F,X024R-X086W,X078R-X086W-X235F,X024R-X118R,X024R-X086R,X101G-X103A-X104I-X232V,X024R-X033S-X078R-X086W-X118R,X024R-X118R-X209A,X209A-X241R,X033S-

X086W-X243F,X033S-X172V-X209A,X118R-X209A-X243F,X024R-X086S-X141G,X024R-X118R-X209A-X243F,X024R-X033S-X086S-X085N-X235F,X024R-X033S-X133V,X024R-X033S-X078R-X086W,X024R-X086W-X209A,X024R-X241R,X033S-X118R-X243F,X024R-X235F,X024R-X078R-X086W,X024R-X118R-X209A-X235F,X024R-X209A-X241R,X033S-X118R-X241R,X086W-X118R-X209A,X033S-X118R-X159D-X209A,X033S-X078R-X086W,X024R-X086W-X243F,X118R-X209A,X024R-X086W-X118R-X203I,X078R-X209A-X235F,X024R-X033S-X241R,X078R-X118R,X033S-X118R-X209A-X243F,X021M-X024R-X033S,X024R-X033S-X086W,X033S-X235F,X078R-X086W-X209A,X024R-X033S-X209A-X235F,X033S-X086W-X118R,X024R-X033S-X078R-X209A,X033S-X086W-X118R-X209A-X243F,X086W-X209A-X243F,X005S-X078R-X118R-X241R,X024R-X174T,X033S-X209A-X243F,X086W-X118R-X133V,X024R-X033S-X118R,X024R-X086W-X209A-X235F,X086W-X209A,X008T-X024R,X086W-X118R,X033S-X241R,X005S-X024R-X033S-X243F,X024R-X209A-X242P,X024R-X033S-X078R-X118R,X024R-X033S-X194T,X024R-X243F,X024R-X209A,X024R-X033S-X118R-X209A,X033S-X086W,X024R-X033S,X024R-X033S-X078R-X243F,X086W-X243F,X033S-X118D-X138V-X209A,X033S-X209A-X235F,X024R-X086R-X118R,X033S-X201S,X024R-X239Q,X033S-X118R-X209A-,X078R-X086W,X235F-X243F,X024R-X209A-X235F,X118R-X172V,X017Y-X024R-X033S-X086W,X033S-X148F,X024R-X118R-X235F,X033S-X078R,X033S-X243F,X024C-X033S,X118R-X194T,X033S-X209A,X118R-X209A-X235F,X024R-X033S-X209A-X243F,X024R-X033S-X235F,X024R-X033S-X118R-X235F,X024R-X141G,X024R-X274I,X024R-X033S-X209A,X086W-X235F,X024R-X209A-X243F,X004E-X033S-X078R,X086W-X209A-X235F,X015T-X033S,X033S-X086W-X156L-X209A,X024R-X118R-X243F-X269H,X209A-X235F,X024R-X247H,X024R-X033S-X228T,X078R-X235F,X024R-X033S-X174V-X235F,X024R-X235F-X243F,X024R-X033S-X235F-X241R,X024R-X033S-X151V,X024R-X104A,X033S-X048T,X012H-X104A-X118R,X118R-X235F,X033S-X253A,X143A-X209A,X024R-X033S-X243F,X033S-X239T,X209A-X243F,X024R-X033S-X129H-X184D-X253M,X024R-X085V-X086W-X118R-X235F,X024R-X272P,和X024R-X269C,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与如SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0035] 本发明还提供分离的枯草杆菌蛋白酶变体,其中该枯草杆菌蛋白酶变体为具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:X020R-X087D-X101G-X103A-X104I-X232V-X245R,X020R-X101G-X103A-X104I-X150L-X232V-X245R,X018R-X020R-X024R-X076D-X087D-X249R,X018R-X020R-X024R-X076D-X150L-X249R,X018R-X024R-X043R-X076D-X087D-X249R,X018R-X024R-X043R-X076D-X150L-X249R,X018R-X024R-X076D-X078R-X087D-X249R,X018R-X024R-X076D-X078R-X150L-X249R,X018R-X024R-X076D-X087D-X249R-X269R,X018R-X024R-X076D-X087D-X242R-X249R,X018R-X024R-X076D-X087D-X150L-X249R,X018R-X024R-X076D-X150L-X249R,X018R-X087D-X101G-X103A-X104I-X232V-X245R,X018R-X101G-X103A-X104I-X150L-X232V-X245R,X018R-X022R-X024R-X076D-X087D-X249R,X018R-X022R-X024R-X076D-X150L-X249R,X043R-X087D-X101G-X103A-X104I-X232V-X245R-X269R,X043R-X101G-

X103A-X104I-X150L-X232V-X245R,X024R-X087D-X101G-X103A-X104I-X232V-X245R,X024R-X101G-X103A-X104I-X150L-X232V-X245R,X078R-X087D-X101G-X103A-X104I-X232V-X245R,X078R-X101G-X103A-X104I-X150L-X232V-X245R,X087D-X101G-X103A-X104I-X232V-X245R-X269R,X101G-X103A-X104I-X150L-X232V-X245R-X249R,X101G-X103A-X104I-X150L-X232V-X245R-X269R,X022R-X087D-X101G-X103A-X104I-X232V-X245R,X018R-X024R-X043D-X076D-X150L-X249R,X043R-X087D-X101G-X103A-X104I-X232V-X245R,X022R-X101G-X103A-X104I-X150L-X232V-X245R,X018R-X024R-X043D-X076D-X087D-X249R,X018R-X024R-X076D-X087D-X249R,X018R-X024R-X076D-X150L-X242R-X249R,X043R-X101G-X103A-X104I-X150L-X232V-X245R-X269R,X076D-X101G-X103A-X104I-X150L-X232V-X245R,X087D-X101G-X103A-X104I-X232V-X242R-X245R,X101G-X103A-X104I-X150L-X232V-X245R,X076D-X087D-X101G-X103A-X104I-X232V-X245R,X087D-X101G-X103A-X104I-X232V-X245R,和X101G-X103A-X104I-X150L-X232V-X242R-X245R,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与如SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0036] 本发明还提供分离的枯草杆菌蛋白酶变体,其中该枯草杆菌蛋白酶变体为具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:X024R-X101G-X103A-X104I-X129Q-X158E-X188D-X217E-X232V-X245R-X248D-X249R,X024R-X101G-X103A-X104I-X130A-X158E-X183D-X188D-X232V-X245R-X248D-X249R,X024R-X101G-X103A-X104I-X129Q-X158E-X183D-X188D-X232V-X245R-X248D-X249R,X101G-X103A-X104I-X130A-X158E-X188D-X232V-X245R-X248D-X249R,X024R-X101G-X103A-X104I-X129Q-X158E-X188D-X232V-X245R-X248D-X249R,X024R-X101G-X103A-X104I-X130A-X158E-X188D-X232V-X245R-X248D-X249R,X024R-X101G-X103A-X104I-X129Q-X130A-X158E-X183D-X188D-X232V-X245R-X248D-X249R,X024R-X101G-X103A-X104I-X128L-X129Q-X158E-X188D-X232V-X245R-X248D-X249R,X024R-X101G-X103A-X104I-X129Q-X130A-X158E-X188D-X232V-X245R-X248D-X249R,X101G-X103A-X104I-X129Q-X158E-X188D-X232V-X245R-X248D-X249R,X101G-X103A-X104I-X129Q-X130A-X158E-X188D-X232V-X245R-X248D-X249R,X024R-X101G-X103A-X104I-X128L-X129Q-X130A-X158E-X188D-X232V-X245R-X248D-X249R,X101G-X103A-X104I-X128L-X129Q-X158E-X188D-X232V-X245R-X248D-X249R,和X024R-X027R-X101G-X103A-X104I-X128L-X129Q-X130A-X158E-X188D-X232V-X245R-X248D-X249R,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与如SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0037] 本发明还提供分离的枯草杆菌蛋白酶变体,其中该枯草杆菌蛋白酶变体为具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:X101G-X103A-X104I-X232V-X222Q-X245R,X101G-X103A-X104I-X158E-X188D-X222S-X232V-X245R-X248D-X249R,X101G-X103A-X104I-X158E-X188D-X222Q-X232V-X245R-X248D-X249R,X076D-X101G-X103A-X104I-X232V-X222Q-X245R,X101G-X103A-X104I-X232V-X222S-X245R,X076D-X101G-X103A-X104I-X232V-X222S-X245R,和X076D-X101G-X103A-X104I-X158E-X188D-X222S-X232V-X245R-X248D-X249R,其中该枯草杆菌蛋白酶变体的氨

基酸位置通过与如SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0038] 本发明还提供分离的枯草杆菌蛋白酶变体,其中该枯草杆菌蛋白酶变体为具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:X024R-X101G-X103A-X104I-X128L-X129Q-X158E-X188D-X232V-X245R-X248D-X249R,X101G-X103A-X104I-X130A-X158E-X188D-X232V-X245R-X248D-X249R,X024R-X101G-X103A-X104I-X158E-X188D-X232V-X245R-X248D-X249R,X101G-X103A-X104I-X128L-X129Q-X158E-X188D-X232V-X245R-X248D-X249R,X101G-X103A-X104I-X129Q-X130A-X158E-X188D-X232V-X245R-X248D-X249R,X101G-X103A-X104I-X130A-X158E-X183D-X188D-X217E-X232V-X245R-X248D-X249R,X024R-X101G-X103A-X104I-X128L-X129Q-X130A-X158E-X188D-X232V-X245R-X248D-X249R,X024R-X101G-X103A-X104I-X129Q-X158E-X188D-X217E-X232V-X245R-X248D-X249R,X101G-X103A-X104I-X128L-X130A-X158E-X188D-X217E-X232V-X245R-X248D-X249R,X024R-X101G-X103A-X104I-X128L-X129Q-X158E-X183D-X188D-X232V-X245R-X248D-X249R,X024R-X101G-X103A-X104I-X128L-X129Q-X130A-X158E-X183D-X188D-X232V-X245R-X248D-X249R,X024R-X101G-X103A-X104I-X128L-X129Q-X158E-X188D-X232V-X245R-X248D-X249R-X271G,X101G-X103A-X104I-X129Q-X158E-X183D-X188D-X232V-X245R-X248D-X249R,X024R-X101G-X103A-X104I-X130A-X158E-X188D-X217E-X232V-X245R-X248D-X249R,X024R-X101G-X103A-X104I-X128L-X158E-X183D-X188D-X232V-X245R-X248D-X249R,X101G-X103A-X104I-X129Q-X158E-X188D-X217E-X232V-X245R-X248D-X249R,和X024R-X101G-X103A-X104I-X128L-X130A-X158E-X188D-X232V-X245R-X248D-X249R,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与如SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0039] 本发明还提供分离的枯草杆菌蛋白酶变体,其中该枯草杆菌蛋白酶变体为具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:X101G-X103A-X104I,X22A-X101A-X209E,S103G-L111V-G159E,X22A-X103G-X159E,X22A-X111V-X159E,X22A-X128N-X271F-X209E,X22A-X103G-X111V,X62E-X111V-X128N,X22A-X111V-X128N,X22A-X62E-X111V,X101A-X103G-X104L-X188D,X101G-X103A-X104I-X159D,X101A-X103G-X104L-X128N,X22A-X101A-X159E,X101A-X103G-X104L,X101A-X103G-X104L-X159E,X22A-X101A-X103G-X104L,X101A-X103G-X104L-X209E,X22A-X209E-X271F,X22A-X101A-X271F,和X101A-X209E-X271F,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与如SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0040] 本发明还提供分离的枯草杆菌蛋白酶变体,其中该枯草杆菌蛋白酶变体为具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:X103A-X104I-X159D-X232V-X236H-X245R-X248D-X252K,X101G-X104I-X159D-X232V-X236H-X245R-X248D-X252K,X101G-X103A-X159D-X232V-X236H-X245R-X248D-X252K,X101G-X103A-X104L-X232V-X236H-X245R-X248D-X252K,X101G-X103A-X104L-X159D-X236H-X245R-X248D-X252K,X101G-X103A-X104L-X159D-X232V-X245R-X248D-X252K,X101G-X103A-X104L-X159D-X232V-X236H-X248D-X252K,X101G-X103A-X104L-X159D-X232V-

X236H-X245R-X252K，和X101G-X103A-X104L-X159D-X232V-X236H-X245R-X248D，其中该枯草杆菌蛋白酶变体的氨基酸位置通过与如SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0041] 本发明还提供分离的枯草杆菌蛋白酶变体，其中该枯草杆菌蛋白酶变体为具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列：X101G-X103A-X104I-X159D-X232V-X245R-X248D，X101G-X103A-X104I-X159D-X232V-X245R-X248D-X271F，X101G-X103A-X104I-X159D-X232V-X245R-X248D-X238R，X101G-X103A-X104I-X159D-X232V-X245R-X248D-X248R，X101G-X103A-X104I-X159D-X232V-X245R-X248D-X253R，X101G-X103A-X104I-X159D-X232V-X245R-X248D-X24R，X101G-X103A-X104I-X159D-X232V-X245R-X248D-X76D，X101G-X103A-X104I-X159E-X232V-X245R-X248D-X249R，X101G-X103A-X104I-X159E-X232V-X245R-X248D-X271F，X101G-X103A-X104I-X158E-X232V-X245R-X248D-X249R，X101G-X103A-X104I-X158E-X232V-X245R-X248D-X271F，X22A-X101G-X103A-X104I-X159D-X232V-X245R-X248D-X249R，X22A-X101G-X103A-X104I-X159D-X232V-X245R-X248D-X271F，X62E-X101G-X103A-X104I-X159D-X232V-X245R-X248D-X249R，和X62E-X101G-X103A-X104I-X159D-X232V-X245R-X248D-X271F，其中该枯草杆菌蛋白酶变体的氨基酸位置通过与如SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0042] 本发明还提供分离的枯草杆菌蛋白酶变体，其中该枯草杆菌蛋白酶变体为具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列：X20R-X43R-X249R，X20R-X22R-X43R，X20R-X43R-X242R，X20R-X43R-X271L，X20R-X43R-X244R，X20R-X24R-X43R-X242R，X9A-X22R-X78R-X212F-X241R，X9A-X20R-X43R-X212F，X9A-X43R-X212F，X20R-X43R-X212F，X20R-X22R-X43R-X212F，X24R-X78R-X212F，X9A-X43R-X78R，X9A-X43R-X78R-X242R，X9A-X20R-X43R-X78R，X20R-X24R-X43R-X78R-X242R，X22R-X24R-X78R-X212F，X9A-X20R-X43R-X78R-X242R，X20R-X43R-X78R-X249R，X20R-X43R-X78R，X9A-X78R-X212F，X9A-X22R-X43R-X78R，X9A-X20R-X24R-X43R，X9A-X22R-X78R-X212F，X4R-X9A-X22R-X78R-X212F，X20R-X24R-X43R，X1R-X9A-X43R，X20R-X24R-X43R-X115R，X9A-X24R-X43R，X20R-X22R-X24R-X43R，X1R-X24R-X43R，X9A-X20R-X24R-X43R-X242R，X9A-X20R-X22R-X78R-X212F，X9A-X24R-X43R-X244R，X9A-X24R-X43R-X242R，X4R-X9A-X22R-X24R-X212F，和X22R-X24R-X43R，其中该枯草杆菌蛋白酶变体的氨基酸位置通过与如SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0043] 本发明还提供分离的枯草杆菌蛋白酶变体，其中该枯草杆菌蛋白酶变体为具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列：X101G-X103A-X104I-X232V-X245R-X248D，X101G-X103A-X104I-X159D-X232V-X245R，X101G-X103A-X104I-X159R-X232V-X245R-X248D，X101G-X103A-X104I-X159D-X232V-X245R-X248R，X101G-X103A-X104I-X232V-X245R，X101G-X103A-X104I-X232V-X245R-X248R，X101G-X103A-X104I-X159R-X232V-X245R-X248R，以及X101G，X103A，X104I，X232V，X236H，X245R，和X252K，其中该枯草杆菌蛋白酶变体的氨基酸位置通过与如SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0044] 本发明还提供分离的枯草杆菌蛋白酶变体，其中该枯草杆菌蛋白酶变体为具有蛋

白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:X16S,X22A,X24R,X62E,X76D,X89P,X101A/G,X103G/A,X104L/I,X111V,X128N,X129E,X232V,X148I,X158E,X159D/E,X166D,X186H,X188D,X209E,X236H,X238R,X245R,X248D/R,X249R,X252K/R,X253R,和X271F,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与如SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0045] 本发明还提供分离的枯草杆菌蛋白酶变体,其中该枯草杆菌蛋白酶变体为具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:N062E-A158E,S103G-A158E,S128N-A158E,A016S-A158E,V104L-A158E,E089P-A158E,L111V-A158E,T022A-A158E,S101A-A158E,L148I-A158E,P129E-A158E,T022A-E089P,A016S-E089P,N062E-E089P,N062E-E271F,A158E-E271F,R186H-E271F,P129E-E271F,L111V-E271F,Y209E-E271F,A016S-E271F,S188D-E271F,T022A-E271F,G159E-E271F,V104L-E271F,S101A-E271F,E089P-E271F,S128N-E271F,S103G-E271F,L148I-E271F,H249R-E271F,N062E-G159E,A016S-G159E,S128N-G159E,L148I-G159E,L111V-G159E,E089P-G159E,T022A-G159E,P129E-G159E,S103G-G159E,V104L-G159E,A158E-G159E,S101A-G159E,A158E-H249R,L111V-H249R,P129E-H249R,N062E-H249R,A016S-H249R,R186H-H249R,L148I-H249R,G159E-H249R,S101A-H249R,S188D-H249R,V104L-H249R,Y209E-H249R,T022A-H249R,S128N-H249R,S103G-H249R,E089P-H249R,T022A-L111V,S101A-L111V,A016S-L111V,V104L-L111V,N062E-L111V,S103G-L111V,E089P-L111V,A016S-L148I,N062E-L148I,T022A-L148I,P129E-L148I,V104L-L148I,S103G-L148I,S128N-L148I,S101A-L148I,E089P-L148I,L111V-L148I,A016S-N062E,T022A-N062E,N062E-P129E,T022A-P129E,S128N-P129E,A016S-P129E,S101A-P129E,V104L-P129E,E089P-P129E,S103G-P129E,L111V-P129E,N062E-R186H,S128N-R186H,S101A-R186H,T022A-R186H,A016S-R186H,A158E-R186H,E089P-R186H,P129E-R186H,G159E-R186H,S103G-R186H,V104L-R186H,L111V-R186H,L148I-R186H,N062E-S101A,T022A-S101A,A016S-S101A,E089P-S101A,N062E-S103G,T022A-S103G,A016S-S103G,S101A-S103G,E089P-S103G,N062E-S128N,A016S-S128N,T022A-S128N,S101A-S128N,V104L-S128N,E089P-S128N,S103G-S128N,L111V-S128N,L111V-S188D,N062E-S188D,A016S-S188D,L148I-S188D,T022A-S188D,S128N-S188D,S101A-S188D,V104L-S188D,E089P-S188D,P129E-S188D,G159E-S188D,R186H-S188D,S103G-S188D,A158E-S188D,A016S-T022A,A016S-V104L,T022A-V104L,S101A-V104L,N062E-V104L,S103G-V104L,E089P-V104L,G159E-Y209E,L111V-Y209E,S101A-Y209E,A016S-Y209E,S128N-Y209E,L148I-Y209E,P129E-Y209E,N062E-Y209E,T022A-Y209E,S103G-Y209E,A158E-Y209E,S188D-Y209E,V104L-Y209E,E089P-Y209E,和R186H-Y209E,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与如SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0046] 本发明还提供分离的枯草杆菌蛋白酶变体,其中该枯草杆菌蛋白酶变体为具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:N018R-W241R,G020R-W241R,S024R-W241R,S009A-W241R,G020R-W241R,V004R-W241R,N043R-W241R,S078R-W241R,T022R-W241R,G115R-W241R,A001R-W241R,S212F-W241R,L082R-

W241R,N018R-V244R,S024R-V244R,S078R-V244R,G020R-V244R,S212F-V244R,S009A-V244R,L082R-V244R,A001R-V244R,N043R-V244R,T022R-V244R,V004R-V244R,G115R-V244R,W241R-V244R,S242R-V244R,A001R-V004R,S009A-T022R,N018R-T022R,G020R-T022R,V004R-T022R,A001R-T022R,S024R-S242R,N018R-S242R,V004R-S242R,G020R-S242R,S212F-S242R,L082R-S242R,S078R-S242R,A001R-S242R,S009A-S242R,T022R-S242R,G115R-S242R,N043R-S242R,W241R-S242R,N018R-S212F,T022R-S212F,V004R-S212F,S024R-S212F,A001R-S212F,G115R-S212F,G020R-S212F,S009A-S212F,N043R-S212F,S078R-S212F,L082R-S212F,S009A-S078R,G020R-S078R,S024R-S078R,T022R-S078R,N018R-S078R,V004R-S078R,A001R-S078R,N043R-S078R,T022R-S024R,G020R-S024R,N018R-S024R,A001R-S024R,V004R-S024R,S009A-S024R,V004R-S009A,A001R-S009A,S242R-N269R,S024R-N269R,G020R-N269R,T022R-N269R,H249R-N269R,S212F-N269R,N043R-N269R,V244R-N269R,A001R-N269R,N018R-N269R,S078R-N269R,S009A-N269R,G115R-N269R,W241R-N269R,V004R-N269R,L082R-N269R,N018R-N043R,G020R-N043R,V004R-N043R,T022R-N043R,S009A-N043R,A001R-N043R,S024R-N043R,S009A-N018R,V004R-N018R,A001R-N018R,S024R-L082R,S009A-L082R,N018R-L082R,A001R-L082R,S078R-L082R,G020R-L082R,T022R-L082R,V004R-L082R,N043R-L082R,N043R-H249R,G020R-H249R,V004R-H249R,N018R-H249R,S009A-H249R,S212F-H249R,T022R-H249R,S024R-H249R,G115R-H249R,A001R-H249R,L082R-H249R,S242R-H249R,W241R-H249R,V244R-H249R,S078R-H249R,N018R-G115R,G020R-G115R,T022R-G115R,S078R-G115R,S009A-G115R,V004R-G115R,A001R-G115R,L082R-G115R,N043R-G115R,S024R-G115R,S009A-G020R,N018R-G020R,V004R-G020R,A001R-G020R,S009A-E271L,G020R-E271L,S024R-E271L,V244R-E271L,W241R-E271L,N043R-E271L,T022R-E271L,H249R-E271L,S212F-E271L,G115R-E271L,S242R-E271L,S078R-E271L,V004R-E271L,N269R-E271L,A001R-E271L,N018R-E271L,和L082R-E271L,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与如SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0047] 本发明还提供分离的枯草杆菌蛋白酶变体,其中所述枯草杆菌蛋白酶变体为具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:G020R-N043R,N062E-A158E,S103G-A158E,S128N-A158E,A016S-A158E,V104L-A158E,E089P-A158E,L111V-A158E,T022A-A158E,S101A-A158E,L148I-A158E,P129E-A158E,T022A-E089P,A016S-E089P,N062E-E089P,N062E-E271F,A158E-E271F,R186H-E271F,P129E-E271F,L111V-E271F,Y209E-E271F,A016S-E271F,S188D-E271F,T022A-E271F,G159E-E271F,V104L-E271F,S101A-E271F,E089P-E271F,S128N-E271F,S103G-E271F,L148I-E271F,H249R-E271F,N062E-G159E,A016S-G159E,S128N-G159E,L148I-G159E,L111V-G159E,E089P-G159E,T022A-G159E,P129E-G159E,S103G-G159E,V104L-G159E,A158E-G159E,S101A-G159E,A158E-H249R,L111V-H249R,P129E-H249R,N062E-H249R,A016S-H249R,R186H-H249R,L148I-H249R,G159E-H249R,S101A-H249R,S188D-H249R,V104L-H249R,Y209E-H249R,T022A-H249R,S128N-H249R,S103G-H249R,E089P-H249R,T022A-L111V,S101A-L111V,A016S-L111V,V104L-L111V,N062E-L111V,S103G-L111V,E089P-

L111V,A016S-L148I,N062E-L148I,T022A-L148I,P129E-L148I,V104L-L148I,S103G-L148I,S128N-L148I,S101A-L148I,E089P-L148I,L111V-L148I,A016S-N062E,T022A-N062E,N062E-P129E,T022A-P129E,S128N-P129E,A016S-P129E,S101A-P129E,V104L-P129E,E089P-P129E,S103G-P129E,L111V-P129E,N062E-R186H,S128N-R186H,S101A-R186H,T022A-R186H,A016S-R186H,A158E-R186H,E089P-R186H,P129E-R186H,G159E-R186H,S103G-R186H,V104L-R186H,L111V-R186H,L148I-R186H,N062E-S101A,T022A-S101A,A016S-S101A,E089P-S101A,N062E-S103G,T022A-S103G,A016S-S103G,S101A-S103G,E089P-S103G,N062E-S128N,A016S-S128N,T022A-S128N,S101A-S128N,V104L-S128N,E089P-S128N,S103G-S128N,L111V-S128N,L111V-S188D,N062E-S188D,A016S-S188D,L148I-S188D,T022A-S188D,S128N-S188D,S101A-S188D,V104L-S188D,E089P-S188D,P129E-S188D,G159E-S188D,R186H-S188D,S103G-S188D,A158E-S188D,A016S-T022A,A016S-V104L,T022A-V104L,S101A-V104L,N062E-V104L,S103G-V104L,E089P-V104L,G159E-Y209E,L111V-Y209E,S101A-Y209E,A016S-Y209E,S128N-Y209E,L148I-Y209E,P129E-Y209E,N062E-Y209E,T022A-Y209E,S103G-Y209E,A158E-Y209E,S188D-Y209E,V104L-Y209E,E089P-Y209E,R186H-Y209E,N018R-W241R,G020R-W241R,S024R-W241R,S009A-W241R,G020R-W241R,V004R-W241R,N043R-W241R,S078R-W241R,T022R-W241R,G115R-W241R,A001R-W241R,S212F-W241R,L082R-W241R,N018R-V244R,S024R-V244R,S078R-V244R,G020R-V244R,S212F-V244R,S009A-V244R,L082R-V244R,A001R-V244R,N043R-V244R,T022R-V244R,V004R-V244R,G115R-V244R,W241R-V244R,S242R-V244R,A001R-V004R,S009A-T022R,N018R-T022R,G020R-T022R,V004R-T022R,A001R-T022R,S024R-S242R,N018R-S242R,V004R-S242R,G020R-S242R,S212F-S242R,L082R-S242R,S078R-S242R,A001R-S242R,S009A-S242R,T022R-S242R,G115R-S242R,N043R-S242R,W241R-S242R,N018R-S212F,T022R-S212F,V004R-S212F,S024R-S212F,A001R-S212F,G115R-S212F,G020R-S212F,S009A-S212F,N043R-S212F,S078R-S212F,L082R-S212F,S009A-S078R,G020R-S078R,S024R-S078R,T022R-S078R,N018R-S078R,V004R-S078R,A001R-S078R,N043R-S078R,T022R-S024R,G020R-S024R,N018R-S024R,A001R-S024R,V004R-S024R,S009A-S024R,V004R-S009A,A001R-S009A,S242R-N269R,S024R-N269R,G020R-N269R,T022R-N269R,H249R-N269R,S212F-N269R,N043R-N269R,V244R-N269R,A001R-N269R,N018R-N269R,S078R-N269R,S009A-N269R,G115R-N269R,W241R-N269R,V004R-N269R,L082R-N269R,N018R-N043R,G020R-N043R,V004R-N043R,T022R-N043R,S009A-N043R,A001R-N043R,S024R-N043R,S009A-N018R,V004R-N018R,A001R-N018R,S024R-L082R,S009A-L082R,N018R-L082R,A001R-L082R,S078R-L082R,G020R-L082R,T022R-L082R,V004R-L082R,N043R-L082R,N043R-H249R,G020R-H249R,V004R-H249R,N018R-H249R,S009A-H249R,S212F-H249R,T022R-H249R,S024R-H249R,G115R-H249R,A001R-H249R,L082R-H249R,S242R-H249R,W241R-H249R,V244R-H249R,S078R-H249R,N018R-G115R,G020R-G115R,T022R-G115R,S078R-G115R,S009A-G115R,V004R-G115R,A001R-G115R,L082R-G115R,N043R-G115R,S024R-G115R,S009A-G020R,N018R-G020R,V004R-G020R,A001R-G020R,S009A-E271L,G020R-E271L,S024R-E271L,V244R-E271L,W241R-E271L,N043R-E271L,T022R-E271L,H249R-E271L,S212F-E271L,G115R-

E271L,S242R-E271L,S078R-E271L,V004R-E271L,N269R-E271L,A001R-E271L,N018R-E271L,和L082R-E271L,并且其中该变体的总净电荷相对于迟缓芽孢杆菌(Bacillus lentus)枯草杆菌蛋白酶GG36蛋白酶的总净电荷为0、+1、+2、+3、+4、+5、-1、-2、-3、-4或-5,而且其中该总净电荷是通过一种或多种选自以下的置换来获得的:N43D,R45T,N62E,N76D,S101D,P129E,A158E,G159D,G159E,S166D,S188D,A230E,N18R,G20K,G20R,T22R,S24R,N43R,G118R,Q245R,H249R,N269R,E271F,和E271L,并且其中该蛋白酶变体的氨基酸位置根据SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列中对应的氨基酸位置的编号方式来进行编号。

[0048] 在一个方面,所述蛋白酶变体包含:

[0049] a)以下突变中的两个或多个:X1R,X2S,V4R,V4S,X9A,X10S,X14K,X16S,X22A,X22R,X24R,X25V,X26F,X42I,X52F,X52E,X52N,X62E,X62Q,X68A,X68C,X71G,X72C,X74C,X75A,X75F,X78R,X89P,X89T,X89G,X89H,X89W,X91N,X94N,X100S,X101A,X101N,X101G,X101D,X103G,X103N,X104L,X104I,X108I,X111V,X112V,X115K,X117F,X121F,X128D,X128F,X128L,X128N,X129E,X148I,X158E,X159E,X160D,X166D,X185E,X186H,X188E,X188D,X203E,X209S,X209N,X209F,X209T,X209E,X209H,X209G,X210R,X212I,X212F,X214F,X215N,X215D,X215E,X217E,X217N,X224A,X230E,X231I,X236F,X238R,X238K,X239K,X239G,X239R,X248V,X249R,X250I,X262D,X263F,X265F,X267V,X267N,X269I,X269R,X271F,X271I,X271H和X272F;和/或

[0050] b)以下突变组中的一个或多个:X062E-X129E,X062E-X159E,X016S-X148I,X158E-X249R,X016S-X062E,X111V-X188D,X022A-X062E,X062E-X148I,X022A-X129E,X062E-X271F,X062E-X158E,X016S-X159E,X062E-X186H,X128N-X159E,X062E-X188D,X062E-X128N,X148I-X159E,X103G-X158E,X111V-X159E,X158E-X271F,X016S-X188D,X022A-X111V,X128N-X158E,X016S-X158E,X104L-X158E,X128N-X186H,X159E-X209E,X062E-X101A,X111V-X209E,X148I-X188D,X101A-X209E,X022A-X188D,X016S-X022A,X128N-X129E,X016S-X209E,X016S-X128N,X022A-X089P,X128N-X209E,X089P-X158E,X062E-X103G,X186H-X271F,X016S-X129E,X089P-X159E,X111V-X249R,X101A-X129E,X148I-X209E,X022A-X159E,X129E-X249R,X129E-X209E,X104L-X129E,X128N-X188D,X111V-X158E,X022A-X158E,X062E-X209E,X062E-X249R,X101A-X186H,X089P-X129E,X129E-X271F,X22A-X111V-X159E,X101A-X103G-X104L-X209E,X101A-X103G-X104L-X159E,X101A-X103G-X104L-X188D,X101G-X103A-X104I-X159D,X22A-X103G-X159E,X22A-X128N-X271F-X209E,X22A-X209E-X271F,X22A-X101A-X209E,X101A-X209E-X271F,X22A-X111V-X128N,X22A-X101A-X159E,X101A-X103G-X104L,X22A-X101A-X103G-X104L,X101A-X103G-X104L,X101G-X103A-X104I,X101A-X103G-X104L-X128N,X103A-X104I-X159D-X232V-X236H-X245R-X248D-X252K,X101G-X104I-X159D-X232V-X236H-X245R-X248D-X252K,X101G-X103A-X159D-X232V-X236H-X245R-X248D-X252K,X101G-X103A-X104L-X232V-X236H-X245R-X248D-X252K,X101G-X103A-X104L-X159D-X236H-X245R-X248D-X252K,X101G-X103A-X104L-X159D-X232V-X245R-X248D-X252K,X101G-X103A-X104L-X159D-X232V-X236H-X248D-X252K,X101G-X103A-X104L-X159D-X232V-X236H-X245R-X252K,X101G-X103A-X104L-X159D-X232V-X236H-X245R-X248D,X62E-X101G-X103A-X104I-X159D-X232V-

X245R-X248D-X271F,X62E-X101G-X103A-X104I-X159D-X232V-X245R-X248D-X249R,X22A-X101G-X103A-X104I-X159D-X232V-X245R-X248D-X249R,X101G-X103A-X104I-X159D-X232V-X245R-X248D-X24R,X101G-X103A-X104I-X159D-X232V-X245R-X248D-X253R,X101G-X103A-X104I-X158E-X232V-X245R-X248D-X249R,X22A-X101G-X103A-X104I-X159D-X232V-X245R-X248D-X271F,X101G-X103A-X104I-X159E-X232V-X245R-X248D-X249R,X101G-X103A-X104I-X159D-X232V-X245R-X248D-X238R,X101G-X103A-X104I-X158E-X232V-X245R-X248D-X271F,X101G-X103A-X104I-X159D-X232V-X245R-X248D,X101G-X103A-X104I-X159D-X232V-X245R-X248D-X271F,X101G-X103A-X104I-X159D-X232V-X245R-X248D-X76D和X101G-X103A-X104I-X159E-X232V-X245R-X248D-X271F;所述变体相对于具有SEQ ID NO:1氨基酸序列的迟缓芽孢杆菌枯草杆菌蛋白酶GG36蛋白酶有0、-1、-2、-3、-4或-5的总净电荷,优选地为0、-1、-2或-3。这些蛋白酶变体在低离子强度或低洗涤剂浓度的含水洗涤液中可特别优选。

[0051] 在一个方面,所述蛋白酶变体包含:

[0052] a)以下突变中的两个或多个:X4R,X17R,X18R,X20R,X22R,X24R,X24W,X25R,X43R,X43A,X46R,X52F,X52N,X57R,X59A,X62Q,X71G,X75R,X76D,X78R,X82R,X86W,X89P,X89W,X89T,X89I,X89H,X89V,X104L,X106V,X106G,X115R,X118I,X121F,X144R,X185I,X197F,X209N,X209S,X217E,X231I,X239R,X239S,X241R,X242R,X242L,X243R,X244R,X248I,X249R,X252R,X253R,X271T,X271V,X271L,X271H,X271F,X271P,X1R,X9A,X212F和X269R;和/或

[0053] b)以下突变组中的一个或多个:X022R-X024R,X009A-X271L,X018R-X241R,X018R-X115R,X043R-X249R,X020R-X249R,X004R-X249R,X020R-X024R,X018R-X249R,X009A-X020R,X020R-X241R,X009A-X078R,X020R-X115R,X018R-X024R,X024R-X242R,X022R-X115R,X018R-X043R,X020R-X043R,X018R-X242R,X242R-X269R,X018R-X244R,X024R-X269R,X020R-X271L,X024R-X271L,X004R-X009A,X020R-X269R,X001R-X024R,X244R-X271L,X009A-X018R,X241R-X271L,X004R-X024R,X009A-X249R,X009A-X022R,X101G-X103A-X104I-X159D-X232V-X245R-X248D-X271F,X101G-X103A-X104I-X158E-X232V-X245R-X248D-X271F,X101G-X103A-X104I-X158E-X232V-X245R-X248D-X249R,X101G-X103A-X104I-X159D-X232V-X245R-X248D-X24R,X101G-X103A-X104L-X159D-X232V-X236H-X245R-X252K,X101G-X103A-X104L-X232V-X236H-X245R-X248D-X252K;所述蛋白酶变体相对于具有SEQ ID NO:1氨基酸序列的迟缓芽孢杆菌枯草杆菌蛋白酶GG36蛋白酶具有0、+1、+2、+3、+4或+5的总净电荷,优选地具有正的总净电荷,最优选地为+1、+2或+3。这些蛋白酶变体在高离子强度或高洗涤剂浓度的含水洗涤液中可特别优选。

[0054] 本发明还提供分离的枯草杆菌蛋白酶变体,其中该枯草杆菌蛋白酶变体为具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:G020R-N043R,G020K-N062E,S024F-N116L,G020K-S024F,S024R-A174T,S024R-G118R,S024R-K235F,S024R-P086R,S024R-P086W,S078R-G118R,T033S-G118R,T033S-K235F,Y209A-W241R,G020R-N076D,N018R-Q245R,S024R-R045T,A232V-Q245R,G118R-A172V,G118R-A194T,I008T-S024R,K235F-N243F,N018R-S103A,N018R-V104I,P086W-G118R,P086W-N243F,P086W-Y209A,S024C-T033S,S024R-A232V,S024R-N243F,S024R-P239Q,S024R-

S101G,S024R-S141G,S024R-T033S,S024R-T274I,S024R-Y209A,S078R-P086W,S101G-A232V,T033S-L148F,T033S-P086W,T033S-P201S,T033S-S078R,T033S-W241R,T033S-Y209A,A230E-H249R,A232V-H249R,G118R-K235F,N076D-Q245R,P086W-K235F,S024R-R247H,S024R-V104A,S078R-K235F,S101G-H249R,S103A-A232V,T033S-A048T,T033S-P239T,T033S-T253A,T143A-Y209A,Y209A-K235F,N018R-R045T,Y209A-N243F,S024R-A272P,S024R-R269C,S101G-V104I,V104I-A232V,N076D-H249R,和S024R-N076D,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与如SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0055] 本发明还提供分离的枯草杆菌蛋白酶变体,其中该枯草杆菌蛋白酶变体为具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:G020R-N076D,S024R-R045T,A230E-H249R,N018R-R045T,N018R-Q245R,S101G-A232V,S024R-A232V,A232V-Q245R,S024R-S101G,N018R-V104I,N018R-S103A,S101G-H249R,A232V-H249R,S103A-A232V,N076D-Q245R,S101G-V104I,V104I-A232V,N076D-H249R,S024R-N076D,S024F-N116L,G020K-S024F,G020K-N062E,T033S-G118R,S024R-P086W,S024R-G118R,S024R-P086R,Y209A-W241R,S024R-W241R,S024R-K235F,G118R-Y209A,S078R-G118R,T033S-K235F,S024R-A174T,P086W-Y209A,I008T-S024R,P086W-G118R,T033S-W241R,S024R-N243F,S024R-Y209A,T033S-P086W,S024R-T033S,P086W-N243F,T033S-P201S,S024R-P239Q,S078R-P086W,K235F-N243F,G118R-A172V,T033S-L148F,T033S-S078R,T033S-N243F,S024C-T033S,G118R-A194T,T033S-Y209A,S024R-S141G,S024R-T274I,P086W-K235F,A015T-T033S,Y209A-K235F,S024R-R247H,S078R-K235F,S024R-V104A,T033S-A048T,G118R-K235F,T033S-T253A,T143A-Y209A,T033S-P239T,Y209A-N243F,S024R-A272P,和S024R-R269C,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与如SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0056] 本发明还提供分离的枯草杆菌蛋白酶变体,其中该枯草杆菌蛋白酶变体为具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:V004R-S009A-G020R-S242R,G020R-N043R-W241R,G020R-S242R-N269R,V004R-S009A-G020R-N043R,V004R-G020R-H249R,N018R-S024R-V244R,S009A-T022R-S212F-W241R,G020R-N043R-N269R,N018R-S024R-S242R,V004R-S009A-N043R-W241R,G020R-N043R-V244R,G020R-T022R-S242R,V004R-G020R-N043R,V004R-S009A-G020R-N043R-S242R,G020R-N043R-S242R,G020R-N043R-S242R-H249R,G020R-S212F-H249R,V004R-S009A-W241R,A001R-S009A-N043R,G020R-N043R-H249R,S009A-G020R-N043R-W241R,G020R-T022R-N043R,G020R-H249R-N269R,G020R-T022R-W241R,V004R-S009A-S024R-N043R-W241R,S009A-N043R-S078R,V004R-G020R-S024R-V244R,G020R-T022R-S078R-S242R,G020R-S024R-S242R-H249R,V004R-S009A-S078R-W241R,S009A-N043R-S078R-S242R,V004R-G020R-S024R,S009A-N043R-S212F,G020R-N043R-S212F,S024R-S078R-S212F,S009A-G020R-S024R-N043R,S009A-T022R-N043R-S078R,G020R-T022R-S212F-W241R,G020R-N043R-S212F-W241R,S009A-N043R-W241R,G020R-N043R-E271L,G020R-T022R-S078R-W241R,G020R-S024R-N043R-S242R,G020R-T022R-N043R-W241R,S009A-G020R-N043R-

S212F,V004R-S009A-G020R-S024R-S242R,G020R-N043R-H249R-E271L,G020R-T022R-S024R-S242R,S009A-T022R-S078R-S212F,G020R-N043R-S242R-E271L,S009A-T022R-S078R-S212F-W241R,V004R-G020R-S024R-H249R,G020R-T022R-E271L,G020R-T022R-N043R-S212F,V004R-G020R-S024R-N043R-S242R,V004R-G020R-S024R-N043R,V004R-S009A-T022R-S078R-S212F,G020R-T022R-S078R-S212F-W241R,和G020R-T022R-N269R,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与如SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0057] 本发明还提供分离的枯草杆菌蛋白酶变体,其中该枯草杆菌蛋白酶变体为具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:N018R-G020R-N043D-R045T-A230E,N018R-N043R-R045T-S242R-H249R,S024R-N043D-H249R,N018R-G020R-R045T,G020R-S024R-N076D-H249R,S024R-N043R-A230E-S242R,N018R-S024R-N043D-A230E,G020R-N076D,N018R-S024R-N043D-N076D-H249R,S024R-N043R-N076D-H249R,N018R-S024R-R045T-S242R,G020R-N043D-N076D-A230E-H249R,G020R-N043R-R045T-S242R,N018R-S024R-N076D-H249R,N018R-G020R-S024R-N043D-R045T-L233I-S242R,S024R-N043R-A230E,N018R-G020R-N043D,N043R-S242R-H249R,G020R-N043R-R045T-A230E,N043R-N076D-S242R-H249R,G020R-S024R-R045T-A230E-S242R,S024R-R045T-N076D-A230E-S242R-H249R,S024R-R045T,S024R-N043R-R045T-N076D-A230E-H249R,N018R-S024R-N043D-R045T-H249R,N018R-N043R-R045T-H249R,S024R-N043R-S242R,N018R-G020R-N043R-N076D-H249R,G020R-S024R-N043D-H249R,G020R-N043R-A230E-S242R,G020R-N043R-S242R,N018R-N043R-N076D-A230E,G020R-S024R-N043D-S242R,G020R-N043R-A230E,N018R-G020R-N043R-N076D-S242R-H249R,N043D-R045T-N076D-H249R,N018R-N043R-S242R-H249R,N018R-G020R-N043R-R045T-S242R,N018R-G020R-N043D-A230E-S242R,G020R-S024R-N043R-R045T-H249R,S024R-N043R-H249R,G020R-S024R-K27E-N043R-N076D-A230E,S024R-N043R-R045T-S242R,N018R-G020R-S024R-N043R-R045T-N076D-A230E,G020R-N043R-N076D-A230E-H249R,N018R-N043R-R045T-S242R,G020R-S242R-H249R,N018R-N043R-N076D-A230E-S242R-H249R,N018R-S024R-N076D,G020R-S024R-K27R-N043D-S242R-H249R,N018R-G020R-S024R-N043D-N076D-S242R,N018R-N043R-N076D-S242R-H249R,N018R-S024R-N043D-A230E-H249R,N018R-G020R-N043D-H249R,N018R-G020R-N043D-R045T-N076D-S242R,S024R-N043R-N076D-A230E-S242R,G020R-S024R-T38I-N043R-R045T-N076D-S242R-H249R,N018R-G020R-N043R,N018R-S024R-R045T-A230E-S242R,N018R-G020R-H249R,S024R-N043R-N076D,N018R-G020R-S024R-N043R-R045T-N076D-H249R,N018R-N043D-R045T-N076D-S242R-H249R,S024R-N043D-S242R-H249R,N018R-G020R-S024R-N043D-R045T-S242R,G020R-S024R-N043R-N076D,N018R-G020R-N043D-R045T-A230E-S242R,G020R-S024R-N043R-R045T-N076D-S242R-H249R,N018R-N043R-R045T-N076D-S242R,N018R-G020R-N043R-N076D-A230E-S242R,N018R-S024R-N043D-H249R,N018R-S024R-N043R-R045T-A230E-H249R,N018R-G020R-N043R-R045T-N076D-H249R,N018R-S024R-S242R,N018R-N043R-R045T-N076D-A230E-S242R,R045T-S242R-H249R,N018R-S024R-N043D-S242R,N018R-G020R-N043D-R045T-S240P,S024R-N043R-R045T-S242R-H249R,N018R-S024R-V30S-L31S-D32I-

T33Q-G34V-I35F,N018R-G020R-N043R-N076D,G020R-N043D-R045T-N076D-S242R-H249R,N018R-S024R-N043D-A230E-S242R,N018R-S024R-N043D-S242R-H249R,S024R-N043D-R045T-S242R-H249R,N043R-A230E-H249R,S024R-N043R-N076D-A230E-H249R,G020R-S024R-N043D-N076D-H249R,S024R-R045T-S242R-A273V,G020R-S024R-R045T-N076D-S242R-H249R,N018R-S024R-N043D-N076D-S242R,N018R-N043R-N076D-A230E-H249R,N018R-G020R-N043R-R045T-H249R,N018R-N043R-R045T-A230E-S242R,G020R-S024R-N043D-R045T-A230E-S242R,N018R-N043D-A230E-H249R,N018R-N043R-N076D-S242R,N018R-G020R-N076D,N018R-G020R-N043D-N076D-S242R-H249R,G020R-S024R-N043D-N076D-S242R-H249R,N043D-S242R-H249R,N018R-G020R-S024R-N043R-N076D,N018R-G020R-N043D-R045T-N076D-H249R,N018R-G020R-N043R-R045T-N076D-A230E-H249R,N018R-N076D-S242R,G020R-N043R-H249R,N018R-N076D-S242R-H249R,N018R-S024R-R045T-A230E-H249R,A230E-H249R,N018R-R045T-H249R,G020R-N043R-N076D,N043R-R045T-H249R,N018R-N043D-N076D-S242R-H249R,N043R-N076D-H249R,N018R-R045T,G020R-N076D-A230E-S242R,G020R-S024R-N043D-R045T,S024R-N043D-N076D-S242R-H249R,G020R-R045T-H249R,N043R-N076D-S153A-H249R,N043R-N076D-A230E-H249R,N018R-N043D-N076D-H249R,和G020R-N043R-N076D-V227I,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与如SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0058] 本发明还提供分离的枯草杆菌蛋白酶变体,其中该枯草杆菌蛋白酶变体为具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:S101G-S103A-V104I-A232V-Q236H-Q245R-N252K,S101G-S103A-V104I-A232V-Q245R-N248R,S101G-S103A-V104I-G159R-A232V-Q245R-N248D,S101G-S103A-V104I-G159D-A232V-Q245R-N248R,S101G-S103A-V104I-A232V-Q245R,S101G-S103A-V104I-G159D-A232V-Q245R和S101G-S103A-V104I-A232V-Q245R-N248D,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与如SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0059] 本发明还提供分离的枯草杆菌蛋白酶变体,其中该枯草杆菌蛋白酶变体为具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:S101G-S103A-V104I-P129E-S188D-A232V-N238R-Q245R-N248D,S024R-S101G-S103A-V104I-P129E-A158E-S188D-A232V-Q245R-N248D-H249R,T022A-S101G-S103A-V104I-P129E-A158E-S188D-A232V-Q245R-N248D-H249R,T022A-S024R-S101G-S103A-V104I-P129E-A158E-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-P129E-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-P129E-G159E-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-S128N-P129E-A158E-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-L148I-A158E-S188D-A232V-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-P129E-G159E-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-S128N-P129E-A232V-Q245R-N248D,S101G-S103A-V104I-P129E-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-P129E-A158E-A232V-Q245R-N248D-H249R,T022A-S024R-S101G-S103A-V104I-A158E-G159E-S188D-

A232V-Q245R-N248D-H249R,T022A-S024R-S101G-S103A-V104I-P129E-A158E-G159E-S188D-A232V-N238R-Q245R-N248D,S024R-S101G-S103A-V104I-P129E-L148I-A158E-A232V-Q245R-N248D,A016S-S024R-S101G-S103A-V104I-A158E-S188D-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-A158E-G159E-A232V-Q245R-N248D-H249R,T022A-S101G-S103A-V104I-P129E-A158E-G159E-A232V-N238R-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-P129E-A158E-G159E-A232V-Q245R-N248D-H249R,T022A-S024R-S101G-S103A-V104I-S128N-A158E-S188D-A232V-Q245R-N248D,S024R-S101G-S103A-V104I-P129E-S188D-A232V-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-P129E-A158E-A232V-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-P129E-A232V-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-P129E-S188D-A232V-Q245R-N248D,S024R-S101G-S103A-V104I-A158E-S188D-A232V-N238R-Q245R-N248D,T022A-S101G-S103A-V104I-S128N-P129E-S188D-A232V-N238R-Q245R-N248D,S024R-S101G-S103A-V104I-P129E-S188D-A232V-N238R-Q245R-N248D,S024R-S101G-S103A-V104I-A158E-G159E-S188D-A232V-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-S128N-S188D-A232V-Q245R-N248D,S024R-S101G-S103A-V104I-P129E-A158E-S188D-A232V-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-S128N-P129E-A158E-A232V-Q245R-N248D,S024R-S101G-S103A-V104I-G159E-S188D-A232V-Q245R-N248D,T022A-S101G-S103A-V104I-S128N-P129E-A232V-N238R-Q245R-N248D,S024R-S101G-S103A-V104I-P129E-G159E-A232V-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-P129E-A158E-S188D-A232V-N238R-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-A158E-G159E-S188D-A232V-Q245R-N248D,S024R-S101G-S103A-V104I-G159E-S188D-A232V-Q245R-N248D-H249R,T022A-S101G-S103A-V104I-P129E-A158E-A232V-N238R-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-P129E-A158E-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-L148I-A158E-A232V-Q245R-N248D,T022A-S101G-S103A-V104I-A158E-G159E-S188D-A232V-Q245R-N248D-H249R,T022A-S101G-S103A-V104I-A158E-S188D-A232V-Q245R-N248D,T022A-S101G-S103A-V104I-P129E-S188D-A232V-N238R-Q245R-N248D,S024R-S101G-S103A-V104I-P129E-A158E-G159E-S188D-A232V-Q245R-N248D-H249R,T022A-S024R-S101G-S103A-V104I-A158E-G159E-S188D-A232V-N238R-Q245R-N248D,S101G-S103A-V104I-P129E-A158E-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-S128N-A158E-A232V-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-S128N-P129E-S188D-A232V-Q245R-N248D,T022A-S101G-S103A-V104I-P129E-G159E-A232V-N238R-Q245R-N248D,S101G-S103A-V104I-P129E-G159E-A232V-Q245R-N248D-H249R,T022A-S101G-S103A-V104I-P129E-A158E-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-P129E-L148I-A158E-S188D-A232V-Q245R-N248D,T022A-S101G-S103A-V104I-P129E-G159E-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-G159E-S188D-A232V-N238R-Q245R-N248D,S024R-S101G-S103A-V104I-P129E-A158E-G159E-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-P129E-A158E-G159E-A232V-N238R-Q245R-N248D,S024R-S101G-S103A-V104I-S128N-G159E-S188D-A232V-Q245R-N248D,T022A-S101G-S103A-V104I-G159E-S188D-A232V-Q245R-N248D-H249R,

S024R-S101G-S103A-V104I-P129E-G159E-S188D-A232V-N238R-Q245R-N248D,S101G-S103A-V104I-A158E-A232V-N238R-Q245R-N248D,T022A-S101G-S103A-V104I-P129E-G159E-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-P129E-L148I-S188D-A232V-Q245R-N248D,S024R-S101G-S103A-V104I-A158E-A232V-Q245R-N248D-H249R,T022A-S101G-S103A-V104I-A158E-G159E-A232V-N238R-Q245R-N248D,S024R-S101G-S103A-V104I-A158E-G159E-A232V-N238R-Q245R-N248D,T022A-S101G-S103A-V104I-P129E-A158E-G159E-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-P129E-A158E-S188D-A232V-N238R-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-P129E-A158E-G159E-A232V-Q245R-N248D,S101G-S103A-V104I-S188D-A232V-N238R-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-A158E-A232V-Q245R-N248D-H249R,T022A-S024R-S101G-S103A-V104I-L148I-A158E-A232V-Q245R-N248D,S101G-S103A-V104I-P129E-A158E-G159E-A232V-N238R-Q245R-N248D,T022A-S101G-S103A-V104I-G159E-S188D-A232V-N238R-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-P129E-A158E-G159E-S188D-A232V-Q245R-N248D-H249R,T022A-S101G-S103A-V104I-P129E-A232V-N238R-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-S188D-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-P129E-A158E-G159E-A232V-Q245R-N248D-H249R,T022A-S101G-S103A-V104I-A158E-G159E-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-P129E-S188D-A232V-Q245R-N248D,S024R-S101G-S103A-V104I-P129E-G159E-A232V-N238R-Q245R-N248D,S101G-S103A-V104I-S128N-P129E-A232V-Q245R-N248D,S101G-S103A-V104I-A158E-S188D-A232V-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-P129E-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-P129E-G159E-A232V-N238R-Q245R-N248D,S101G-S103A-V104I-A158E-G159E-S188D-A232V-N238R-Q245R-N248D,S024R-S101G-S103A-V104I-A232V-Q245R-N248D-H249R,T022A-S024R-S101G-S103A-V104I-P129E-L148I-A232V-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-A158E-A232V-N238R-Q245R-N248D,S101G-S103A-V104I-S128N-P129E-A232V-N238R-Q245R-N248D,T022A-S101G-S103A-V104I-S128N-G159E-A232V-Q245R-N248D,T022A-S101G-S103A-V104I-S128N-P129E-A158E-A232V-N238R-Q245R-N248D,S101G-S103A-V104I-S128N-P129E-S188D-A232V-Q245R-N248D-H249R,T022A-S024R-S101G-S103A-V104I-S128N-P129E-A158E-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-S128N-A158E-G159E-S188D-A232V-Q245R-N248D,T022A-S024K-S101G-S103A-V104I-S128N-A158E-G159E-A232V-Q245R-N248D,S101G-S103A-V104I-P129E-L148I-S188D-A232V-Q245R-N248D,S024R-S101G-S103A-V104I-L148I-A232V-Q245R-N248D,T022A-S101G-S103A-V104I-L148I-S188D-A232V-Q245R-N248D,S024R-S101G-S103A-V104I-S128N-P129E-S188D-A232V-Q245R-N248D,S101G-S103A-V104I-S128N-P129E-A158E-A232V-N238R-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-P129E-L148I-A158E-S188D-A232V-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-L148I-A158E-S188D-A232V-Q245R-N248D,S101G-S103A-V104I-L148I-G159E-A232V-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-A158E-S188D-A232V-Q245R-N248D,和S101G-S103A-V104I-S128N-P129E-A158E-A232V-Q245R-N248D-H249R,其中该枯草杆菌蛋白酶变体的氨基酸位

置通过与如SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0060] 本发明还提供分离的枯草杆菌蛋白酶变体,其中该枯草杆菌蛋白酶变体为具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:T022A-S024R-S101G-S103A-V104I-A158E-A232V-Q245R-N248D-H249R,T022A-S024R-S101G-S103A-V104I-P129E-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-A158E-G159E-A232V-N238R-Q245R-N248D,S024R-S101G-S103A-V104I-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-A158E-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-G159E-S188D-A232V-Q245R-N248D-H249R,T022A-S024R-S101G-S103A-V104I-A158E-A232V-N238R-Q245R-N248D,S024R-S101G-S103A-V104I-G159E-S188D-A232V-N238R-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-P129E-A232V-Q245R-N248D,S024R-S101G-S103A-V104I-L148I-A232V-Q245R-N248D,S024R-S101G-S103A-V104I-P129E-A158E-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-L148I-A158E-A232V-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-P129E-A158E-A232V-Q245R-N248D-H249R,A016S-S024R-S101G-S103A-V104I-A158E-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-P129E-G159E-A232V-N238R-Q245R-N248D,S024R-S101G-S103A-V104I-P129E-S188D-A232V-Q245R-N248D-H249R,T022A-S101G-S103A-V104I-P129E-A232V-N238R-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-L148I-A158E-A232V-Q245R-N248D,S024R-S101G-S103A-V104I-P129E-S188D-A232V-N238R-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-A158E-G159E-S188D-A232V-N238R-Q245R-N248D,T022A-S101G-S103A-V104I-A158E-G159E-A232V-N238R-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-P129E-A158E-A232V-Q245R-N248D,S101G-S103A-V104I-A158E-S188D-A232V-Q245R-N248D-H249R,T022A-S101G-S103A-V104I-A158E-G159E-A232V-Q245R-N248D-H249R,和S024R-S101G-S103A-V104I-A158E-G159E-A232V-Q245R-N248D,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与如SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0061] 本发明还提供分离的枯草杆菌蛋白酶变体,其中该枯草杆菌蛋白酶变体为具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:V104L-S128N-A158E-R186H-H249R,S128N-A158E-S188D-H249R,N062E-S128N-A158E-G159E-E271F,N062E-A158E-S188D-H249R-E271F,N062E-A158E-R186H-H249R-E271F,S128N-A158E-S188D-Y209E-E271F,N062E-G159E-S188D-H249R,A016S-N062E-A158E-R186H-H249R,N062E-A158E-G159E-H249R,S101A-S128N-A158E-Y209E-H249R,S128N-A158E-R186H-E271F,N062E-A158E-S188D-H249R,N062E-A158E-R186H-E271F,N062E-A158E-R186H-H249R,N062E-S101A-R186H-H249R,N062E-S101A-A158E-R186H-E271F,N062E-V104L-A158E-S188D-H249R-E271F,N062E-G159E-R186H-H249R,N062E-G159E-H249R,S128N-A158E-R186H-H249R,S128N-A158E-S188D-E271F,N062E-A158E-H249R,N062E-R186H-S188D-H249R-E271F,S128N-A158E-Y209E-,N062E-S101A-A158E-H249R,V104L-S128N-A158E-R186H-E271F,N062E-S101A-A158E-R186H-H249R-E271F,A016S-N062E-

A158E-H249R,N062E-S101A-G159E-H249R,S128N-A158E-R186H-S188D-E271F,S101A-S128N-A158E-R186H-E271F,N062E-S101A-S188D-H249R,S101A-V104L-A158E-R186H-S188D-H249R,N062E-G159E-H249R-E271F,S128N-A158E-G159E-E271F,A016S-N062E-V104L-A158E-R186H-E271F,T022A-S128N-A158E-H249R,S128N-A158E-H249R,N062E-S101A-V104L-A158E-R186H-E271F,A016S-N062E-A158E-R186H-E271F,V104L-S128N-A158E-H249R,V104L-S128N-A158E-S188D-H249R,T022A-N062E-A158E,N062E-S101A-S188D-H249R-E271F,N062E-A158E-H249R-E271F,V104L-S128N-A158E-R186H-S188D-E271F,N062E-S101A-R186H-E271F,N062E-V104L-G159E-H249R,N062E-R186H-H249R,N062E-S101A-R186H-H249R-E271F,S101A-A158E-R186H-S188D-H249R,N062E-S101A-R186H,S101A-S128N-P129E-R186H-H249R,S101A-S103G-A158E-R186H-H249R,A016S-N062E-V104L-R186H-S188D-E271F,V104L-A158E-R186H-H249R,S101A-S128N-A158E-S188D-Y209E-E271F,N062E-S101A-R186H-S188D-E271F,A016S-N062E-A158E-H249R-E271F,N062E-S128N-A158E,N062E-S128N-G159E-H249R,N062E-S101A-A158E-S188D-H249R,S101A-S128N-A158E-H249R,N062E-A158E-R186H-S188D-H249R,A016S-V104L-A158E-R186H-E271F,N062E-L148I-G159E,N062E-S101A-A158E-R186H-H249R,N062E-S101A-R186H-S188D-H249R,V104L-A158E-R186H-S188D-H249R,N062E-S101A-V104L-R186H-S188D-E271F,T022A-S101A-A158E-R186H-H249R,S101A-S128N-A158E-Y209E,A158E-R186H-S188D-H249R-E271F,V104L-A158E-R186H-S188D-H249R-E271F,S101A-V104L-A158E-R186H-H249R,V104L-A158E-H249R,S101A-V104L-S128N-A158E-R186H-E271F,A016S-V104L-S188D-H249R,S101A-V104L-A158E-R186H-S188D-E271F,V104L-S128N-G159E-E271F,V104L-A158E-R186H-H249R-E271F,A158E-R186H-H249R,S101A-A158E-R186H-H249R,V104L-A158E-S188D-H249R-E271F,A016S-S128N-A158E-R186H,V104L-S128N-R186H-S188D-H249R,A016S-S101A-S128N-R186H,A016S-N062E-S128N-R186H-E271F,A016S-S128N-R186H-E271F,S128N-P129E-R186H,A158E-R186H-H249R-E271F,A016S-A158E-H249R,A016S-A158E-R186H-H249R,A016S-T022A-A158E-R186H-E271F,E089P-S101A-P129E-R186H,T022A-S128N-A158E-R186H,S101A-V104L-S128N-A158E-R186H,T022A-S128N-R186H-S188D-,N062E-V104L-A158E-R186H-S188D-H249R,T022A-A158E-R186H-H249R-E271F,T022A-V104L-A158E-H249R,S101A-L111V-P129E,A016S-A158E-H249R-E271F,A016S-L111V-S188D-,T022A-V104L-R186H-S188D-H249R,和V104L-L148I-S188D-H249R,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与如SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0062] 本发明还提供分离的枯草杆菌蛋白酶变体,其中该枯草杆菌蛋白酶变体为具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:A001R-S101G-S103A-V104I-A232V-Q245R,V004R-S101G-S103A-V104I-A232V-Q245R,N043R-S101G-S103A-V104I-A232V-Q245R-E271L,S078R-S101G-S103A-V104I-A232V-Q245R,V004R-N043R-S101G-S103A-V104I-A232V-Q245R,N018R-N043R-S101G-S103A-V104I-A232V-Q245R,G020R-S101G-S103A-V104I-A232V-Q245R,S101G-S103A-V104I-A232V-Q245R-E271L,G020R-N043R-S101G-S103A-V104I-A232V-Q245R,S024R-N043R-S101G-S103A-V104I-A232V-Q245R,G020R-G025R-N116A-Y167W,N018R-S101G-S103A-V104I-

A232V-Q245R,T022R-S101G-S103A-V104I-A232V-Q245R,S078R-S103N-S106G-Y167W-Q236N,N018R-N043D-S101G-S103A-V104I-A232V-Q245R-N269R,N043R-S101G-S103A-V104I-A232V-Q245R-N269R,S024R-S101A-H120F-A194F-H249R,G020R-N043D-S101G-S103A-V104I-A232V-Q245R-N269R,S101G-S103A-V104I-S212F-A232V-Q245R,G020R-S144R-N185I-L233C-Q236N,G023A-S078R-S216F-Q236N-H249R,S101G-S103A-V104I-A232V-Q245R-N269R,S101G-S103A-V104I-G115R-A232V-Q245R,P052N-S078R-S103N-L148I-T213A,N018R-N043D-S101G-S103A-V104I-A232V-Q245R-H249R,S024R-N043D-S101G-S103A-V104I-A232V-Q245R-H249R,S024R-N043D-S101G-S103A-V104I-A232V-Q245R-N269R,G025R-E089I-N116A-P239S-A270C,S024R-S101G-S103A-V104I-A232V-Q245R,L148I-T213A-N252R,S024R-G025R-N183D-Y192W-P239S,G046R-A194F-S212M,V104L-L217E-T224A-H249R-N252R,G023A-Y091F-V121F-Y192W-Q236N,S101G-S103A-V104I-A232V-V244R-Q245R,S099F-S144R-Y167W-N252R,S101G-S103A-V104I-A232V-Q245R-H249R,N043R-S101G-S103A-V104I-A232V-Q245R,T022W-S078R-Y167W-S212M-A270C,V121F-N252R-A270C,G020R-S103N-S216F-Q236N-N252R,N043R-S101G-S103A-V104I-A232V-Q245R-H249R,G023A-P052N-Y192W-I198L-N252R,G025R-G046R-V121F,S024R-S078R-V104L-N116A-N183D,G046R-Q059A-S103N-G211Q-S212M,G020R-P052N-N062Q-Y091F-Y192W,G023A-P052N-S144R-Y192W-S216F,S101G-S103A-V104I-A232V-S242R-Q245R,P052N-S103N-N116A-L148I-Y192W,E089I-N116A-N117F-T224A-H249R,S144R-G211Q-N238L-P239S-H249R,N043A-N062Q-A194F-G211Q,G020R-S024R-P052N-Q059A-S216F,S024R-Y167W-T224A-H249R,T057R-Y167W-H249R,G025R-S103N-R186K-A194F-T224A,S105T-S128N-S144R-L148I-S212M,G020R-Q059A-S144R-Y192W-T224A,S024R-N043A-N117F-A194F-G211Q,N117F-A194F-T213A-A270C,S078R-Y091F-V121F-L233C-N252R,T057R-S099F-S105T-I198L-T213A,G023A-Y091F-S101A-I198L-N252R,N062Q-S103N-V121F-S144R-H249R,N043R-S101G-S103A-V104I-A232V-S242R-Q245R,G023A-S024R-N117F-S212M-S216F,V104L-T213A-S216F,A194F-G211Q-Q236N,N062Q-S103N-N117F-A194F,S024R-N062Q-V104L-S106G-H249R,T057R-E089I-I198L,G046R-Q059A-S106G-L217E-H249R,N117F-T213A-A215F,S101A-H120F-Y192W-A215F-T224A,N043A-T057R-N117F-S144R-N183D,G046R-N183D-N238L,G025R-N043A-E089I-N117F,S078R-V104L-T213A-A215F-T224A,Y091F-S099F-S101A-S105T-Y167W,S106G-N117F-N238L,G046R-E089I-Y091F-S101A-N116A,G020R-N062Q-E089I-R186K-S212M,T057R-S099F-V121F-N185I-Y192W,G046R-E089I-Y192W-L233C-A270C,E089I-N117F-N185I-A215F-L233C,P052N-V104L-N183D-S216F-H249R,S078R-S099F-N116A-R186K-T224A,G025R-S105T-S128N-S144R-A270C,S105T-G211Q-S216F,S024R-G046R-Y091F-V121F,S106G-N185I-S216F-Q236N,N062Q-S101A-Q236N-N252R-A270C,G025R-N043A-Y091F-I198L-A270C,G020R-G023A-V104L-Y192W-L233C,S024R-N043A-S105T-S106G-I198L,G020R-E089I-L217E,S024R-Y091F-I198L-A215F-P239S,G046R-E089I-S099F-R186K-S212M,V104L-H120F-R186K-S216F-N252R,T022W-A194F-T213A-L233C-N238L,S099F-S105T-S106G-A194F-S212M,E089I-S105T-N116A-A215F-S216F,G025R-N116A-H120F-T224A-A270C,N043A-Q059A-S101A-S216F-T224A,T057R-N183D-Q236N,G025R-N062Q-

S128N-S144R-N185I,S103N-H120F-Y167W-I198L-L233C,T022W-E089I-S216F,S024R-S106G-N116A-S212M-T224A,G020R-P052N-S101A-I198L-L233C,E089I-Y091F-N185I-G211Q-A270C,L111I-A215F-P239S,S024R-N116A-R186K-L233C-Q236N,和G023A-S103N-S106G-S212M-A215F,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与如SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0063] 本发明还提供分离的枯草杆菌蛋白酶变体,其中该枯草杆菌蛋白酶变体为具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:G020R-T022W-S078R-S101A-S103A-V104I-N116S-T213A-A215F-A232V-Q245R,N018R-S078R-S101G-S103A-V104I-A232V-Q245R,S024R-R045T-S101G-S103A-V104I-A232V-Q245R-N269R,G020R-T022W-S078R-S101G-S103A-V104I-N116A-A232V-Q245R,G020R-T22W-S101G-S103A-V104I-A232V-Q245R,N018R-N043R-S101G-S103A-V104I-A232V-Q245R,N018R-T022W-S024R-N076D-S101A-N116A-A232V-Q245R,N018R-V104I-A232V-H249R,N018R-S024R-N076D-S101A-N116A-G211Q-H249R,N018R-N043D-S078R-S101G-S103A-V104I-L217E-A232V-Q245R,N018R-N043R-S101G-S103A-V104I-A232V-Q245R-N269R,N018R-R045T-N076D-S101G-S103A-V104I-A232V-Q245R-N269R,N076D-S078R-S101G-S103A-V104I-A232V-Q245R-N269R,G020R-N043D-S078R-S101G-S103A-V104I-A232V-Q245R,N018R-N043D-N076D-S101G-S103A-V104I-A232V-Q245R-N269R,S024R-R045T-N076D-S078R-S101G-S103A-V104I-A232V-Q245R-N269R,N018R-S103A-A232V-H249R,N018R-S101G-V104I-A232V-Q245R,G020R-S024R-S101G-S103A-V104I-L217E-A232V-Q245R-H249R,N018R-T22K-N043D-S101G-S103A-V104I-A232V-Q245R,N043R-R045T-S101G-S103A-V104I-A232V-Q245R-N269R,G020R-T22W-S101G-S103A-V104I-G211Q-A232V-Q245R,S024R-N076D-S078R-S101G-S103A-V104I-A232V-Q245R-N269R,G020R-T22W-S078R-S101A-S103A-V104I-N116A-N183D-A232V,N018R-S024R-N076D-N116A-A215F-H249R,N018R-N043R-R045T-S101G-S103A-V104I-A232V-Q245R,S024R-N043R-N076D-S101G-S103A-V104I-A232V-Q245R,G020R-T022W-S101G-S103A-V104I-A232V-Q245R,G020R-T022W-S101G-S103A-V104I-G211Q-A232V-Q245R,G020R-T022W-S078R-S101G-S103A-V104I-N116A-T213A-A215F-A232V-Q245R,N043D-N076D-S078R-S101G-S103A-V104I-A232V-Q245R-N269R,N018R-S024R-N076D-S101A-N116A-T213A-H249R,N018R-S024R-N076D-N116A-G211Q-H249R,N043R-R045T-N076D-S078R-S101G-S103A-V104I-A232V-Q245R,N018R-S101G-Q245R,G020R-T22W-S101A-S103A-V104I-G211Q-T213A-A232V-Q245R,G020R-S024R-N043D-N076D-S078R-S101G-S103A-V104I-A232V-Q245R,N018R-R045T-N076D-S078R-S101G-S103A-V104I-A232V-Q245R,G020R-S078R-S101G-S103A-V104I-G211Q-T213A-A215F-A232V-Q245R,R045T-S078R-S101G-S103A-V104I-A232V-Q245R-N269R,S024R-N043D-S101G-S103A-V104I-A232V-Q245R-N269R,N018R-S101G-S103A-H249R,N018R-T22W-S024R-N076D-S101A-N116A-A232V-Q245R,N018R-S101G-V104I-A232V-H249R,G020R-T22W-S101A-S103A-V104I-A215F-A232V-Q245R,N018R-S024R-N076D-G211Q-T213A-H249R,N018R-T022W-S024R-N076D-S101A-I198L-H249R,S024R-S101G-S103A-V104I-A232V-Q245R,G020R-N076D-S101G-S103A-V104I-A232V-Q245R-N269R,G020R-S101G-S103A-V104I-A232V-Q245R-N269R,N043D-S078R-S101G-S103A-V104I-A232V-Q245R,G020R-

S101G-V104I-T213A-A215F-A232V-Q245R,G020R-S101G-S103A-V104I-N116A-A215F-A232V-Q245R,S024R-S103A-V104I-H249R,N018R-N076D-S078R-S101G-S103A-V104I-A232V-Q245R,R045T-N076D-S078R-S101G-S103A-V104I-A232V-Q245R-N269R,S024R-S101G-V104I-Q245R,G020R-S101G-S103A-V104I-G211Q-T213A-A215F-A232V-Q245R,S024R-S103A-V104I-A232V-H249R,N018R-S024R-N076D-N116A-G211Q-A215F-H249R,N018R-Q245R,S024R-S103A-Q245R,S024R-S103A-V104I-Q245R,G020R-S078R-S101G-A232V-Q245R,N018R-S024R-N076D-V104I-H249R,N018R-S024R-V104I-H249R,S024R-S101G-S103A-V104I-A232V-Q245R,N018R-S024R-N076D-G211Q-A215F-H249R,R019H-G020R-T022W-S078R-S101G-S103A-V104I-G211Q-A232V-Q245R,N018R-S024R-N076D-S101A-I198L-G211Q-T213A-H249R,N018R-S024R-N043D-S101G-S103A-V104I-A232V-Q245R,G020R-T22W-S103A-V104I-A232V-Q245R,N018R-S103A-V104I-H249R,N018R-T022W-S024R-N076D-S101A-I198L-A215F-H249R,N018R-S024R-S101G-V104I-A232V,S078R-S101G-S103A-V104I-A232V-Q245R-N269R,S024R-N043R-N076D-S078R-S101G-S103A-V104I-A232V-Q245R,N018R-G020R-N043D-N076D-S101G-S103A-V104I-A232V-Q245R,N018R-T22W-S024R-N076D-N116A-T213A-H249R,N018R-S024R-S101G-V104I,G020R-S101A-S103A-V104I-A215F-A232V-Q245R,N018R-R045T-S078R-S101G-S103A-V104I-A232V-Q245R,N018R-S101G-S103A-Q245R,N043R-N076D-S078R-S101G-S103A-V104I-A232V-Q245R,G020R-T022W-S101A-S103A-V104I-G211Q-A215F-A232V-Q245R,G020R-T22W-S078R-S101G-S103A-V104I-N116A-T213A-A215F-A232V-Q245R,G020R-S078R-S101G-S103A-V104I-A215F-A232V-Q245R,G020R-T022W-S078R-S101G-S103A-V104I-N116A-N183D-A232V-Q245R,N076D-S101G-S103A-V104I-A232V-Q245R,N076D-S101G-S103A-V104I-A232V-Q245R-N269R,G020R-T22W-S101A-S103A-V104I-A232V-Q245R,G020R-S101G-S103A-A232V-Q245R,G020R-T022W-S078R-S101A-S103A-V104I-N116A-N183D-A232V-Q245R,N018R-G020R-S024R-R045T-N076D-S101G-S103A-V104I-A232V-Q245R-N269R,N043R-R045T-S078R-S101G-S103A-V104I-A232V-Q245R,N018R-S101G-V104I-H249R,G020R-T22W-S078R-S101G-S103A-V104I-N116A-N183D-A232V-Q245R,G020R-T022W-S101G-S103A-V104I-I198L-G211Q-T213A-A232V-Q245R,G020R-S078R-S101A-S103A-V104I-N116A-N183D-T213A-A232V-Q245R,S024R-N076D-V104I-A232V-Q245R,N018R-G020R-N076D-S101G-S103A-V104I-A232V-Q245R,N018R-S024R-N076D-S101G-V104I-A232V-H249R,N018R-N043D-S078R-S101G-S103A-V104I-A232V-Q245R,A001T-N018R-S024R-N076D-N116A-T213A-H249R,N076D-S078R-S101G-S103A-V104I-A232V-Q245R,G020R-S078R-S101G-S103A-V104I-N116A-A232V-Q245R,N043R-N076D-S101G-S103A-V104I-A232V-Q245R,N018R-R045T-S101G-S103A-V104I-A232V-Q245R,N018R-N076D-S101G-V104I-A232V-Q245R,G020R-S078R-S101G-S103A-V104I-N116A-N183D-A232V-Q245R,N018R-S024R-N076D-S101A-G211Q-T213A-A215F-H249R,R045T-S078R-S101G-S103A-V104I-A232V-Q245R,N043R-N076D-S101G-S103A-V104I-A232V-Q245R-N269R,G020R-T022W-S078R-S101G-S103A-V104I-N116A-N183D-T213A-A232V-Q245R,G020R-T022W-S101G-S103A-V104I-N116A-N183D-T213A-A232V-Q245R,G020R-S101G-I198L-A215F-A232V-Q245R,N018R-S024R-N076D-T213A-A215F-H249R,G020R-S078R-S101G-S103A-V104I-

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S103A-V104I-N183D-T213A-A215F-A232V-Q245R,N018R-S024R-N076D-A086V-S101A-N183D-I198L-G211Q-H249R,N018R-N076D-S101G-I198T-A232V,N018R-G020R-S024R-N076D-S101A-N116A-N183D-I198L-G211Q-A215F-H249R,N018R-T022W-S024R-N076D-S101A-N116A-N183D-T213A-A215F-H249R,N018R-T022W-S024R-N076D-S101A-N183D-G211Q-T213A-A215F-H249R,N018R-S024R-N076D-N183D-H249R-A248T,N018R-N076D-V104I-Q245R-H249R,N018R-T022W-S024R-N076D-S101A-N116A-N183D-I198L-A215F-H249R,N018R-T022W-S024R-N076D-N116A-N183D-T213A-A215F-H249R,N018R-G020R-T022W-S024R-N076D-N116A-N183D-G211Q-T213A-A215F-H249R,N018R-G020R-S024R-N076D-S101A-H249R,N018R-G020R-S024R-N076D-S101A-N116A-T213A-A215F-H249R,N018R-T022W-S024R-N076D-N116A-N183D-G211Q-A215F-H249R,N018R-T022W-S024R-N076D-N116A-N183D-I198L-G211Q-T213A-H249R,N043R-R045T-S078R-S101G-S103A-V104I-L217E-A232V-Q245R,N043R-R045T-S101G-S103A-V104I-A232V-Q245R-H249R,N018R-N076D-S101G-V104I,G020R-R045T-N076D-S078R-S101G-S103A-V104I-A232V-Q245R-H249R,N043D-N076D-S101G-S103A-V104I-A232V-Q245R,N018R-G020R-T022W-S024R-N076D-S101A-N116A-N183D-I198L-H249R,N018R-N076D-V104I,N018R-G020R-N043D-S101G-S103A-V104I-A232V-Q245R-H249R,N018R-G020R-T022W-S024R-N076D-N183D-G211Q-H249R,N018R-S024R-N076D-S101A-N183D-I198L-G211Q-A215F-H249R,S101G-V104I,N018R-T022W-S024R-N076D-N116A-N183D-I198L-G211Q-T213A-A215F-H249R,N018R-G020R-S024R-N076D-S101A-N183D-G211Q-T213A-A215F-H249R,N018R-G020R-S024R-N076D-N116A-N183D-A215F-H249R-N263D,N018R-T022W-S024R-N076D-S101A-N183D-H249R,N018R-S024R-N076D-S101A-N116A-N183D-I198L-A215F-H249R,N018R-T022W-S024R-N076D-N116A-I198L-A215F-H249R-R269H,N018R-N043D-R045T-N076D-S078R-S101G-S103A-V104I-A232V-Q245R,N018R-S024R-R045T-N076D-S078R-S101G-S103A-V104I-A232V-Q245R-N269R,S078R-S101G-S103A-V104I-L217E-A232V-Q245R,N018R-G020R-T022W-S024R-N076D-S101A-N183D-I198L-T213A-A215F-H249R,N018R-G020R-S024R-N076D-N183D-I198L-T213A-H249R,N018R-G020R-T022W-S024R-N076D-N116A-I198L-G211Q-A215F-H249R,N018R-G020R-T022W-S024R-N076D-N116A-N183D-G211Q-H249R,N018R-G020R-T022W-S024R-N076D-S101A-I198L-G211Q-T213A-H249R,N018R-G020R-T022W-S024R-N076D-H249R,G020R-T022W-S101G-S103A-V104I-N116A-N183D-I198L-G211Q-T213A-A215F-A232V-Q245R,V104I-A232V,N018R-G020R-T022W-S024R-N076D-S101A-N116A-N183D-G211Q-A215F-H249R,N018R-G020R-T022W-S024R-N076D-S101A-N116A-N183D-I198L-G211Q-T213A-A215F-H249R,N018R-G020R-T022W-S024R-N076D-S101A-N183D-T213A-A215F-H249R,N018R-T022W-S024R-N076D-S101A-N183D-I198L-G211Q-T213A-H249R,N018R-T022W-S024R-N076D-S101A-N183D-I198L-H249R,N043D-R045T-S101G-S103A-V104I-A232V-Q245R-N269R,N018R-G020R-S024R-N076D-S101A-N183D-I198L-G211Q-H249R,N018R-G020R-N043R-S101G-S103A-V104I-L217E-A232V-Q245R,S024R-N043R-N076D-S078R-S101G-S103A-V104I-A232V-Q245R-N269R,N043R-R045T-N076D-S078R-S101G-S103A-V104I-Y166F-A176P-A179V-N184T-A187P-A194P,N018R-T022W-S024R-D041E-N076D-S101A-S160T-N183D-G211Q-

T213A-H249R,N018R-G020R-T022W-S024R-N076D-N116A-N183D-I198L-G211Q-A215F-H249R,N018R-G020R-T022W-S024R-N076D-S101A-N116A-I198L-T213A-H249R,N018R-T022W-S024R-N076D-S101A-N116A-N183D-I198L-G211Q-T213A-H249R,N018R-G020R-S024R-N076D-I198L-T213A-H249R,N018R-G020R-T022W-S024R-N076D-N116A-N183D-I198L-G211Q-H249R,N018R-G020R-S024R-N076D-N183D-G211Q-A215F-H249R,S024R-N076D-V104I,N018R-N076D-S101G-A232V,N018R-S024R-N076D-S101A-N116A-N183D-I198L-G211Q-T213A-A215F-H249R,N018R-G020R-T022W-S024R-N076D-N116A-N183D-A215F-H249R,N018R-S024R-L031F-N076D-N116A-N183D-G211Q-T213A-A215F-H249R,N018R-S024R-N076D-S101A-N116A-N183D-I198L-T213A-H249R-N269S,N018R-G020R-S024R-N076D-S101A-N116A-I198L-A215F-H249R,N018R-N043R-N076D-S078R-S101G-S103A-V104I-A232V-Q245R-N269R,N018R-G020R-S024R-N076D-S101A-N114T-I198L-G211Q-A215F-H249R,S024R-N043R-S078R-S101G-S103A-V104I-L217E-A232V-Q245R,S024R-N076D-S103A-V104I-A232V,N018R-G020R-T022W-S024R-N076D-S101A-I198L-G211Q-A215F-H249R,S101G-V104I-A232V,N018R-T022W-S024R-N076D-N183D-I198L-T213A-A215F-H249R,N018R-T022W-S024R-N076D-N183D-I198L-G211Q-H249R,N018R-G020R-S024R-N076D-N183D-T213A-H249R,N018R-S024R-N076D-S101A-N183D-G211Q-A215F-H249R,N018R-G020R-T022W-S024R-N076D-N116A-G211Q-T213A-H249R,N018R-S078R-S101G-S103A-V104I-A232V-Q245R-N269R,N018R-T022W-S024R-N076D-S101A-N116A-N183D-G211Q-A215F-H249R-T260A,N076D-H249R,N018R-T022W-S024R-N076D-N183D-G211Q-A215F-H249R,N018R-G020R-S024R-N076D-N116A-G211Q-A215F-H249R,N018R-G020R-S024R-N076D-T213A-H249R,N018R-G020R-T022W-S024R-N076D-N116A-N183D-I198L-H249R,N018R-G020R-T022W-S024R-N076D-S101A-N183D-H249R,N076D-V104I-H249R,G020R-T022W-S101A-S103A-V104I-N116A-N183D-G211Q-T213A-A215F-A232V-Q245R,S024R-N043R-R045T-S078R-S101G-S103A-V104I-L217E-A232V-Q245R,N018R-G020R-T022W-S024R-N076D-N183D-I198L-A215F-H249R,N018R-N076D-S101G-S103A,G020R-S024R-S101G-S103A-V104I-A232V-Q245R-N269R,N018R-G020R-S024R-N076D-S101A-N116A-N183D-G211Q-H249R,S101G-S103A-A232V,S024R-N076D-S101G-A232V,N018R-T022W-S024R-N076D-S101A-N183D-I198L-G211Q-H249R,N018R-G020R-S024R-N076D-S101A-N183D-I198L-G211Q-A215F-H249R,N018R-G020R-S024R-N076D-N183D-I198L-H249R,N018R-T022W-S024R-N076D-S101A-N116A-N183D-I198L-G211Q-H249R,N018R-G020R-S024R-N076D-N116A-A156V-N183D-G211Q-A215F-H249R-N269S,R045T-N076D-S101G-S103A-V104I-A232V-Q245R-H249R,N018R-G020R-S024R-N076D-S101A-N183D-I198L-H249R,N018R-G020R-T022W-S024R-N076D-I198L-G211Q-A215F-H249R,N018R-G020R-T022W-S024R-N076D-S101A-N116A-I198L-G211Q-A215F-H249R,N018R-G020R-T022W-S024R-N076D-N116A-H249R,N018R-N076D-S101G,N018R-S024R-N076D-N116A-N183D-I198L-T213A-A215F-H249R,N018R-G020R-T022W-S024R-N076D-S101A-N116A-I198L-T213A-A215F-H249R,N018R-S024R-N076D-S101A-N116A-N183D-I198L-G211Q-H249R,N018R-N076D-A232V,N018R-G020R-S024R-N076D-S101A-A232V-Q245R,N018R-N043D-R045T-N076D-S101G-S103A-V104I-A232V-Q245R,N018R-T022W-

S024R-N076D-N183D-T213A-A215F-H249R,N018R-S024R-N076D-S101A-N116A-G211Q-T213A-N237D-H249R,N018R-G020R-S024R-N076D-S101A-N116A-N183D-G211Q-H249R-R275S,N018R-T022W-S024R-N076D-S101A-N116A-N183D-I198L-G211Q-T213A-A215F-H249R,S024R-N076D,N018R-S024R-N076D-N183D-G211Q-A215F-H249R,N018R-T022W-S024R-N076D-N116A-N183D-I198L-T213A-A215F-H249R,N076D-V104I-A232V-H249R,N018R-N076D-S103A-A232V,N018R-G020R-S024R-N076D-S101A-N116A-N183D-I198L-G211Q-T213A-H249R,N018R-G020R-S024R-N076D-S101A-N183D-T213A-H249R,N018R-G020R-S024R-N076D-S101A-D175E-N183D-G211Q-A215F-H249R,N018R-G020R-N043D-S078R-S101G-S103A-V104I-L217E-A232V-Q245R-A273E,G020R-S024R-N043D-R045T-N076D-S101G-S103A-V104I-A232V-Q245R,P005S-S101G-S103A-V104I-A232V-Q245R-H249R,S103A-V104I-A232V,N018R-G020R-S024R-V068A-N076D-S101A-N116A-T213A-A215F-H249R,N018R-T022W-S024R-N076D-S101A-I198L-A215F-H249R-R275S,N018R-S024R-N076D-N183D-I198L-G211Q-T213A-H249R,和N043D-R045T-S101G-S103A-V104I-A232V-Q245R,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与如SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0064] 本发明还提供分离的枯草杆菌蛋白酶变体,其中该枯草杆菌蛋白酶变体为具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:N018R-S024R-N043R-N076D-H249R-N269R,N018R-T022R-S024R-N043R-N076D-H249R,N018R-N043D-S101G-S103A-V104I-A232V-Q245R,G020R-N043D-S101G-S103A-V104I-A232V-Q245R,N043D-S101G-S103A-V104I-A232V-Q245R-N269R,N043D-S078R-S101G-S103A-V104I-A232V-Q245R,N043R-N076D-S101G-S103A-V104I-A232V-Q245R,T022R-N043R-S101G-S103A-V104I-A232V-Q245R,N043R-S078R-S101G-S103A-V104I-A232V-Q245R,G020R-N076D-S101G-S103A-V104I-A232V-Q245R,N043R-N076D-S101G-S103A-V104I-A232V-Q245R,T022R-N076D-S101G-S103A-V104I-A232V-Q245R,N076D-S078R-S101G-S103A-V104I-A232V-Q245R,N018R-S024R-N043R-N076D-H249R,N018R-S024R-N076D-S242R-H249R,N018R-S024R-N076D-H249R-N269R,N018R-T022R-S024R-N076D-H249R,N018R-S024R-N076D-S078R-H249R,N018R-S024R-N043D-N076D-H249R-N269R,N018R-T022R-S024R-N043D-N076D-H249R,N018R-S024R-N043D-N076D-S078R-H249R,G020R-S101G-S103G-V104I-A232V-Q245R,G020R-S101G-S103A-V104L-A232V-Q245R,G020R-S101G-S103A-V104V-A232V-Q245R,G020R-S101G-S103S-V104I-A232V-Q245R,G020R-S101G-S103S-V104L-A232V-Q245R,G020R-S101S-S103S-V104I-A232V-Q245R,G020R-S101S-S103S-V104L-A232V-Q245R,G020R-S101A-S103A-V104L-A232V-Q245R,G020R-S101S-S103S-V104V-A232V-Q245R,G020R-S101S-S103A-V104I-A232V-Q245R,G020R-S101S-S103A-V104V-A232V-Q245R,G020R-S101S-S103G-V104I-A232V-Q245R,G020R-S101S-S103G-V104V-A232V-Q245R,G020R-S101A-S103A-V104V-A232V-Q245R,G020R-S101A-S103S-V104I-A232V-Q245R,G020R-S101A-S103S-V104V-A232V-Q245R,N018R-S024R-N043R-N076D-S078R-H249R,S024R-N043D-S101G-S103A-V104I-A232V-Q245R,N043D-S101G-S103A-V104I-A232V-Q245R-H249R,S024R-N076D-S101G-S103A-V104I-A232V-Q245R,N076D-S101G-S103A-V104I-A232V-S242R-Q245R,N018R-G020R-S024R-

N076D-L217E-H249R,N018R-S024R-N043R-N076D-L217E-H249R,N018R-S024R-N043D-N076D-S242R-H249R,N018R-G020R-S024R-N043R-N076D-H249R,G020R-S101A-S103G-V104V-A232V-Q245R,N043D-S101G-S103A-V104I-A232V-Q245R,N018R-S024R-N076D-L217E-H249R-N269R,和N018R-S024R-N076D-L217E-S242R-H249R,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与如SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0065] 本发明还提供分离的枯草杆菌蛋白酶变体,其中该枯草杆菌蛋白酶变体为具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:G020R-S101A-S103A-V104I-G118R-A232V-Q245R,G020R-S024R-N116A-T213A,N043R-S101A-N116A-A215F-N269R,S024R-N043R-S101A-N116A,S024R-N043R-S101A-N116A-A215F-N269R,G020R-S101G-S103A-V104I-A215F-A232V-Q245R,N043R-S101A-N269R,S024R-N043R-N116A-T213A-N269R,G020R-S024R-N043R-R045T-S101A-T213A,S024R-N043R-N116A-A215F-N269R,G020R-S024R-T213A-A215F,G020R-N116A-N269R,S024R-N116A-T213A-N269R,N043R-S101A-N116A-N269R,S101G-S103A-V104I-N116A-T213A-A232V-Q245R-N269R,S024R-N043R-R045T-S101A-N116A-A215F-N269R,G020R-N043R-S101A-N269R,S101A-S103A-V104I-T213A-A232V-Q245R-N269R,S024R-A215F-N269R,N043R-S101A-N116A-T213A-A215F-N269R,N043R-S101A-T213A-N269R,G020R-S024R-N043R-R045T-N116A-T213A,S101G-S103A-V104I-A232V-Q245R-N269R,S024R-N043R-R045T-S101A-N116A-T213A-N269R,S024R-N043R-R045T-N269R,G020R-N043R-R045T-S101A-N269R,S024R-N043R-N116A-N269R,G020R-S024R-N043R-R045T,N043R-N116A-N269R,S024R-N043R-S101A-A215F-N269R,S024R-N043R-R045T-T213A-A215F-N269R,G020R-S024R-R045T-N269R,G020R-N043R-S101A-N116A-T213A-A215F,G020R-S101G-S103A-V104I-T213A-A215F-A232V-Q245R,G020R-S024R-R045T-N116A-N269R,G020R-S101A-N116A-N269R,S024R-N043R-A215F,G020R-S024R-T213A,S024R-N043R-S101A-A215F,G020R-S024R-N043R-R045T-N116A,G020R-S024R-N043R-R045T-S101A-N269R,G020R-S024R-S101A-A215F,G020R-S024R-N116A-T213A-A215F,G020R-S024R-N116A,G020R-S024R-S101A-N116A,N043R-T213A-A215F-N269R,S024R-S101A-N269R,S024R-N043R-N116A-A215F,G020R-T038A-N043R-S101A,G020R-S024R-N116A-A215F,S024R-N043R-S101A-T213A,P014L-G020R-S024R-N043R-R045T-S101A-A215F,G020R-S024R-A215F,G020R-N116A-A215F-N269R,G020R-R045T-N116A-N269R,G020R-S024R-N043R-R045T-A215F,和G020R-S024R-N043R-R045T-N116A-T213A-A215F,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与如SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0066] 本发明还提供分离的枯草杆菌蛋白酶变体,其中该枯草杆菌蛋白酶变体为具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:N043R-N076D-S101A-S103A-V104I-A158E-S188D-A232V-Q245R-N248D-H249R-E271F,S024R-N043R-N076D-S101A-S103A-V104I-A158E-S188D-L217E-A232V-Q245R-N248D-H249R,S101A-S103A-V104I-A158E-S188D-A232V-Q245R-N248D-H249R-E271F-E271F,S101A-S103A-V104I-A158E-S188D-L217E-A232V-Q245R-N248D-H249R-E271F,N076D-S101G-

S103A-V104I-A114V-A158E-S188D-A232V-Q245R-N248D-H249R-E271F,SO24R-NO76D-S101G-S103A-V104I-A158E-S188D-A232V-Q245R-N248D-H249R-E271F,SO24R-NO43R-S101A-S103A-V104I-A158E-S188D-L217E-A232V-Q245R-N248D-H249R,SO24R-NO43R-S101A-S103A-V104I-A158E-S188D-A232V-Q245R-N248D-H249R,SO24R-S101A-S103A-V104I-A158E-S166D-S188D-L217E-A232V-Q245R-N248D-H249R,NO76D-S101G-S103A-V104I-S128L-A158E-S188D-A232V-Q245R-N248D-H249R-E271F,和NO43R-NO76D-S101G-S103A-V104I-A158E-S166D-S188D-A232V-Q245R-N248D-H249R-E271F,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与如SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0067] 本发明还提供分离的枯草杆菌蛋白酶变体,其中该枯草杆菌蛋白酶变体为具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:TO22A-S101G-S103A-V104I-G159D-L217E-A232V-Q245R-N248D-E271F,TO22A-NO43R-S101G-S103A-V104I-G159D-S188D-L217E-A232V-Q245R-N248D-E271F,TO22A-S101G-S103A-V104I-G159D-S188D-A232V-Q245R-N248D-E271F,NO43R-S101A-S103A-V104I-A158E-S188D-L217E-A232V-Q245R-N248D-H249R,NO43R-NO76D-S101A-S103A-V104I-A158E-S188D-L217E-A232V-Q245R-N248D-H249R-E271F,SO24R-S101G-S103A-V104I-A158E-S188D-L217E-A232V-Q245R-N248D-H249R,SO24R-S101G-S103A-V104I-A158E-S188D-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-A158E-S188D-A232V-Q245R-N248D-H249R,SO24R-S101G-S103A-V104I-A158E-N183D-S188D-A232V-Q245R-N248D-H249R,TO22A-NO76D-S101G-S103A-V104I-G159D-S188D-A232V-Q245R-N248D-E271F,TO22A-NO43R-NO76D-S101G-S103A-V104I-G159D-S188D-A232V-Q245R-N248D-E271F,TO22A-NO76D-S101G-S103A-V104I-G159D-A232V-Q245R-N248D-E271F,TO22A-S101G-S103A-V104I-G159D-A232V-Q245R-N248D-E271F,NO76D-S101A-S103A-V104I-A158E-S188D-A232V-Q245R-N248D-H249R-E271F,NO43R-S101A-S103A-V104I-A158E-S166D-S188D-A232V-Q245R-N248D-H249R,SO24R-NO76D-S101A-S103A-V104I-A158E-S166D-S188D-A232V-Q245R-N248D-H249R-E271F,NO76D-S101A-S103A-V104I-A158E-S188D-A232V-Q245R-N248D-H249R,S101A-S103A-V104I-A158E-S166D-S188D-A232V-Q245R-N248D-H249R-E271F,NO43R-NO76D-S101A-S103A-V104I-A158E-S166D-S188D-A232V-Q245R-N248D-H249R-E271F,S101G-S103A-V104I-A158E-S166D-S188D-A232V-Q245R-N248D-H249R-E271F,S101A-S103A-V104I-A158E-S188D-A232V-Q245R-N248D-H249R-E271F,S101A-S103A-V104I-A158E-S188D-L217E-A232V-Q245R-N248D-H249R,NO76D-S101A-S103A-V104I-A158E-S166D-S188D-A232V-Q245R-N248D-H249R-E271F,S101G-S103A-V104I-A158E-N183D-S188D-A232V-Q245R-N248D-H249R,SO24R-S101G-S103A-V104I-S128L-A158E-S188D-A232V-Q245R-N248D-H249R,NO76D-S101G-S103A-V104I-A158E-S166D-S188D-A232V-Q245R-N248D-H249R-E271F,NO43R-NO76D-S101A-S103A-V104I-A158E-S166D-S188D-A232V-Q245R-N248D-H249R,和NO76D-S101A-S103A-V104I-A158E-S188D-L217E-A232V-Q245R-N248D-H249R-E271F,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与如SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0068] 本发明还提供分离的枯草杆菌蛋白酶变体，其中该枯草杆菌蛋白酶变体为具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列：H017R-T022A-N076D-S101G-S103A-V104I-G159D-S188D-A232V-Q245R-N248D-E271F，T022A-N043R-S101G-S103A-V104I-G159D-A232V-Q245R-N248D-E271F，T022A-S101G-S103A-V104I-G159D-S188D-A232V-Q245R-N248D-H249R-E271F，H017R-T022A-N076D-S101G-S103A-V104I-G159D-A232V-Q245R-N248D-E271F，T022A-N076D-S101G-S103A-V104I-G159D-A232V-Q245R-N248D-H249R-E271F，T022A-S101G-G102A-S103A-V104I-G159D-S188D-A232V-Q245R-N248D-E271F，和T022A-N043R-N076D-S101G-S103A-V104I-G159D-A232V-Q245R-N248D-H249R-E271F，其中该枯草杆菌蛋白酶变体的氨基酸位置通过与如SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0069] 本发明还提供分离的枯草杆菌蛋白酶变体，其中该枯草杆菌蛋白酶变体为具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列：S101S-S103A-V104I-A158E-S188D-A232V-Q245R-N248D-H249R，S101S-S103G-V104V-A158E-S188D-A232V-Q245R-N248D-H249R，S101G-S103S-V104I-A158E-S188D-A232V-Q245R-N248D-H249R，S101A-S103A-V104I-A158E-S188D-A232V-Q245R-N248D-H249R，S101A-S103A-V104L-A158E-S188D-A232V-Q245R-N248D-H249R，S101G-S103G-V104I-A158E-S188D-A232V-Q245R-N248D-H249R，S101S-S103G-V104I-A158E-S188D-A232V-Q245R-N248D-H249R，S101S-S103S-V104I-A158E-S188D-A232V-Q245R-N248D-H249R，S101S-S103S-V104V-A158E-S188D-A232V-Q245R-N248D-H249R，S101A-S103S-V104I-A158E-S188D-A232V-Q245R-N248D-H249R，S101A-S103S-V104I-G159E-A232V-Q245R-N248D-H249R，S101S-S103A-V104I-G159E-A232V-Q245R-N248D-H249R，S101G-S103A-V104L-A158E-S188D-A232V-Q245R-N248D-H249R，S101A-S103A-V104L-G159E-A232V-Q245R-N248D-H249R，S101A-S103S-V104L-G159E-A232V-Q245R-N248D-H249R，S101G-S103S-V104L-G159E-A232V-Q245R-N248D-H249R，S101S-S103A-V104L-G159E-A232V-Q245R-N248D-H249R，S101A-S103G-V104V-G159E-A232V-Q245R-N248D-H249R，和S101S-S103A-V104V-G159E-A232V-Q245R-N248D-H249R，其中该枯草杆菌蛋白酶变体的氨基酸位置通过与如SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0070] 本发明还提供分离的枯草杆菌蛋白酶变体，其中该枯草杆菌蛋白酶变体为具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列：V026F-V051W-V104L-S106E，V026F-L031F-S078N-G102A-S160D，G020K-G100S-N116L-A158E-S166D-N243F，T033S-N043W-N218D-P239G-N243F，T022L-T038F-A048R-N062E-G100S-R186K，S101D-S103N-N116L-S144R-A215D，V104L-S105T-T213A-L217E-S256N，N043W-S101D-S212M-N243F，V026F-A048R-S105T-T213A-N218D-T224A，S024F-S101D-G118R-A215D-L250I-A272F，V121F-N185E-T224A-P239G，T022L-L031F-G102A-S128D-T224A-N243F，N062E-S078N-G102A-N116L-S144R-L250I，T022L-T038F-V121F-S160D-A272F，V026F-S078N-G159C-R186K-N243F，S024F-A048R-G118R-S166D-L217E，G023A-T038F-S078N-G100S-S212M-A215D，G100S-N116L-A158E-T213A，S078N-V104L-G118R-S128D，G102A-S103N-S105T-A194E，T022L-S078N-S128D-T213A，K027R-G100S-G118R-S160D-

S188D-N243F,S024F-G102A-R186K-T213A-L217E-N243F,T033S-S105T-S188D-S216F,G023A-G100S-A194E-S212M,A048R-S128D-N185E-P239G,G020K-S024F-T033S-P129E-A194E,G020K-K027R-P129E-S166D-P239G,T022L-G023A-K027R-S101D-V104L-S216F,T033S-G118R-P129E-A194E-P239G,T022L-S078N-N116L-P129E-S256N,K027R-S101D-S103N-S105T-A272F,A048R-S078N-N116L-N185E-L217E-P239G,G023A-S024F-K027R-N062E,S024F-S103N-V104L-G118R-S188D,V026F-V104L-S256N-A272F,S024F-N043W-V104L-V121F-P129E,N062E-S078N-N116L-T224A,G023A-S024F-V051W-A158E,K027R-T038F-G102A-N116L,N062E-S078N-S144R-S212M,L031F-N116L-S256N-A272F,T022L-T033S-V104L-N116L-S160D-R186K,S024F-G118R-P129E-R186K-T213A,N043W-S105T-T213A-A215D-S216F,L031F-S105T-R186K-S188D,V026F-A194E-T213A-S256N,和S103N-S160D-L250I-S256N,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与如SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0071] 本发明还提供分离的枯草杆菌蛋白酶变体,其中该枯草杆菌蛋白酶变体为具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:T022A-S024R-S101D-S103A-V104I-G118R-G159D-S188D-A232V-N248D-E271F,T022A-S024R-S103A-V104I-P129E-G159D-S188D-A232V-N248D-E271F,T022A-S024R-S103A-V104I-G118R-G159D-S188D-L217D-A232V-N248D,T022A-S024R-S101D-S103A-V104I-G118R-P129E-G159D-S188D-A232V-Q245R-N248D,T022A-S024R-S101D-S103A-V104I-G159D-S188D-A232V-Q245R-N248D,T022A-N043R-S103A-V104I-G118R-P129E-G159D-S188D-A232V-Q245R-N248D,T022A-N043R-S103A-V104I-G118R-S128I-P129E-G159D-S188D-A232V-N248D,T022A-N043R-S101D-S103A-V104I-G118R-P129E-G159D-S188D-A232V-N248D-E271F,T022A-S024R-N043R-S101D-S103A-V104I-G159D-S188D-A232V-Q245R-N248D,T022A-S103A-V104I-G159D-S188D-A232V-N248D,T022A-S024R-S103A-V104I-G118R-P129E-G159D-S188D-A232V-N248D-E271F,T022A-S024R-S103A-V104I-G159D-S188D-L217D-A232V-Q245R-N248D-E271F,T022A-N043R-N062E-S103A-V104I-G159D-S188D-A232V-Q245R-N248D-E271F,T022A-N043R-S103A-V104I-P129E-G159D-S188D-A232V-Q245R-N248D,T022A-S024R-S103A-V104I-G159D-S188D-L217D-A232V-N248D-E271F,T022A-S103A-V104I-G118R-G159D-S188D-L217D-A232V-Q245R-N248D,T022A-S024R-S101D-S103A-V104I-G118R-S128I-G159D-S188D-A232V-Q245R-N248D,T022A-S024R-N043R-S103A-V104I-G159D-S188D-L217D-A232V-N248D-E271F,T022A-N043R-S103A-V104I-G118R-G159D-S188D-L217D-A232V-N248D-E271F,T022A-N043R-S103A-V104I-G118R-G159D-S188D-A232V-N248D-E271F,T022A-S103A-V104I-S128I-P129E-G159D-S188D-A232V-N248D-E271F,T022A-S103A-V104I-G159D-S188D-L217D-A232V-Q245R-N248D-E271F,T022A-N043R-S103A-V104I-S128I-G159D-S188D-A232V-Q245R-N248D,T022A-S101D-S103A-V104I-G118R-G159D-S188D-L217D-A232V-Q245R-N248D-E271F,T022A-S103A-V104I-G118R-P129E-G159D-S188D-A232V-Q245R-N248D-E271F,T022A-S024R-N043R-S103A-V104I-G118R-G159D-S188D-L217D-A232V-N248D,T022A-N062E-S103A-V104I-G118R-G159D-S188D-A232V-Q245R-N248D,T022A-N043R-S101D-S103A-V104I-G118R-P129E-G159D-S188D-L217D-A232V,T022A-S024R-S103A-V104I-

G159D-S188D-L217D-A232V-N248D,T022A-S024R-N043R-S103A-V104I-G118R-S128I-P129E-G159D-S188D-L217D-A232V-N248D-E271F,和T022A-S103A-V104I-G118R-G159D-S188D-L217D-A232V-Q245R-N248D-E271F,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与如SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0072] 本发明还提供分离的枯草杆菌蛋白酶变体,其中该枯草杆菌蛋白酶变体为具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:G020K-S024F-N062E-S188D-P239G,S024F-N062E-N116L-P239G,G020K-G023A-N062E-S188D,G020K-G023A-S024F-N062E-G118R-S188D-T213A,G020K-N043W-N062E-N116L-S188D-T213A-P239G,G023A-N062E-N116L-G118R,G023A-S024F-N062E-N116L-G118R,S024F-N116L,S024F-N062E-S188D-T213A,G023A-N062E-N116L-G118R-S188D-P239G,G020K-S024F-N062E,G020K-N043W-N062E-N116L-P239G,S024F-N062E-N116L-T213A-P239G,G020K-S024F-N043W-N062E-N116L-T213A,G020K-G023A-S024F-N062E-N116L-S188D-T213A,S024F-N062E-S188D-P239G,G023A-N043W-N062E-N116L-G118R-T213A,N062E-S188D-P239G,G020K-S024F-N062E-P239G,S024F-N116L-G118R-S188D-P239G,G020K-G023A-N062E-N116L-G118R-T213A,G020K-G023A-S024F-N062E-S188D-T213A-P239G,S024F-N043W-G118R-S188D,G023A-S024F-N116L-G118R-S188D-T213A,G020K-G023A-N043W-N116L-S188D-T213A-P239G,G023A-S024F-N116L-S188D-P239G,G023A-N043W-N116L-G118R-S188D,G023A-S024F-G118R-S188D-P239G,G023A-S024F-N043W-N062E-N116L-G118R,G020K-N043W-S188D-T213A,S024F-N062E-G118R-P239G,G023A-N043W-S188D-T213A,G020K-S024F-N043W-N062E-N116L-G118R-S188D-P239G,G020K-N116L-S188D-P239G,G020K-N043W-N062E-G118R,G020K-N043W-N116L-S188D-T213A,G020K-S024F,G023A-N043W-N116L-P239G,G023A-S024F-N043W-N116L-G118R-S188D-P239G,G020K-G023A-N043W-T213A,和G023A-S024F-N062E-G118R-T213A-P239G,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与如SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0073] 本发明还提供分离的枯草杆菌蛋白酶变体,其中该枯草杆菌蛋白酶变体为具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:G020K-G023A-N043W-G118R-S128I-P129E-G159D-S188D,S024F-G118R-S128I-P129E-G159D,G020K-S024F-N062E-N116L-G118R-S188D,G020K-N062E-N116L-S188D,N062E-N116L-G118R-T213A,G020K-G023A-N062E-N116L-S188D,N062E-N116L-G118R-S188D,G020K-N062E-N116L-T213A,G020K-G023A-N062E-N116L,G020K-N062E-S188D-T213A,G020K-N062E,G020K-S024F-N062E-N116L-S188D,G020K-N043W-N062E-N116L-S188D,G020K-S024F-N062E-S188D-T213A,N062E-N116L-S188D-T213A,G020K-N062E-N116L,G020K-G023A-N062E-N116L-S188D-T213A,G023A-S024F-N062E-N116L-T213A,T022A-N043R-S103A-V104I-S128I-P129E-G159D-S188D-A232V-Q245R-N248D,T022A-N043R-S103A-V104I-G118R-S128I-P129E-G159D-S188D-A232V-N248D-E271F,S024F-N062E-N116L-S188D,T022A-S024R-S103A-V104I-G118R-S128I-P129E-G159D-S188D-A232V-N248D,G023A-N062E-N116L-S188D,N043W-N062E-N116L,G020K-G023A-N116L-S188D,N043W-

N062E-N116L-S188D,S024F-N062E-N116L,N062E-N116L-S188D,和T022A-S024R-S103A-V104I-S128I-G159D-S188D-A232V-N248D,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与如SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0074] 本发明还提供分离的枯草杆菌蛋白酶变体,其中该枯草杆菌蛋白酶变体为具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:S087R-S101G-S103A-V104I-Q109R-S212P-A232V-Q245R-E271V,S101G-S103A-V104I-Q109R-A232V-Q245R,S101G-S103A-V104I-Q109R-S212P-A232V-Q245R-E271V,S101G-S103A-V104I-Q109R-S212P-A232V-Q245R,N076D-S87R-S103A-V104I-S212P-E271V,N076D-S103A-V104I-Q109R,N076D-S103A-V104I-S212P-E271V,N076D-S103A-V104I-Q109R-Q245R,和N076D-S103A-V104I-S212P-Q245L-E271V,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与如SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0075] 本发明还提供分离的枯草杆菌蛋白酶变体,其中该枯草杆菌蛋白酶变体为具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:S024R-P086W-G118R,S024R-S078R-P086W-N243F,S024R-T033S-P086S-S087N-Y209A,T033S-G118R,S024R-S078R-P086W-G118R-A270T,S024R-T033S-P086W-G118R,S078R-P086W-N243F,T033S-S078R-P086W-G118R-Y209A,T033S-S078R-Y209A,P086W-G118R-N243F,S024R-P086W,S078R-P086W-K235F,S024R-G118R,S024R-P086R,S101G-S103A-V104I-A232V,S024R-T033S-S078R-P086W-G118R,S024R-G118R-Y209A,Y209A-W241R,T033S-P086W-N243F,T033S-A172V-Y209A,G118R-Y209A-N243F,S024R-P086S-S141G,S024R-G118R-Y209A-N243F,S024R-T033S-P086S-S085N-K235F,S024R-T033S-A133V,S024R-T033S-S078R-P086W,S024R-P086W-Y209A,S024R-W241R,T033S-G118R-N243F,S024R-K235F,S024R-S078R-P086W,S024R-G118R-Y209A-K235F,S024R-Y209A-W241R,T033S-G118R-W241R,P086W-G118R-Y209A,T033S-G118R-G159D-Y209A,T033S-S078R-P086W,S024R-P086W-N243F,G118R-Y209A,S024R-P086W-G118R-V203I,S078R-Y209A-K235F,S024R-T033S-W241R,S078R-G118R,T033S-G118R-Y209A-N243F,L021M-S024R-T033S,S024R-T033S-P086W,T033S-K235F,S078R-P086W-Y209A,S024R-T033S-Y209A-K235F,T033S-P086W-G118R,S024R-T033S-S078R-Y209A,T033S-P086W-G118R-Y209A-N243F,P086W-Y209A-N243F,P005S-S078R-G118R-W241R,S024R-A174T,T033S-Y209A-N243F,P086W-G118R-A133V,S024R-T033S-G118R,S024R-P086W-Y209A-K235F,P086W-Y209A,I008T-S024R,P086W-G118R,T033S-W241R,P005S-S024R-T033S-N243F,S024R-Y209A-S242P,S024R-T033S-S078R-G118R,S024R-T033S-A194T,S024R-N243F,S024R-Y209A,S024R-T033S-G118R-Y209A,T033S-P086W,S024R-T033S,S024R-T033S-S078R-N243F,P086W-N243F,T033S-G118D-A138V-Y209A,T033S-Y209A-K235F,S024R-P086R-G118R,T033S-P201S,S024R-P239Q,T033S-G118R-Y209A-,S078R-P086W,K235F-N243F,S024R-Y209A-K235F,G118R-A172V,H017Y-S024R-T033S-P086W,T033S-L148F,S024R-G118R-K235F,T033S-S078R,T033S-N243F,S024C-T033S,G118R-A194T,T033S-Y209A,G118R-Y209A-K235F,S024R-T033S-Y209A-N243F,S024R-T033S-K235F,S024R-T033S-G118R-

K235F,S024R-S141G,S024R-T274I,S024R-T033S-Y209A,P086W-K235F,S024R-Y209A-N243F,V004E-T033S-S078R,P086W-Y209A-K235F,A015T-T033S,T033S-P086W-S156L-Y209A,S024R-G118R-N243F-R269H,Y209A-K235F,S024R-R247H,S024R-T033S-A228T,S078R-K235F,S024R-T033S-A174V-K235F,S024R-K235F-N243F,S024R-T033S-K235F-W241R,S024R-T033S-A151V,S024R-V104A,T033S-A048T,Q012H-V104A-G118R,G118R-K235F,T033S-T253A,T143A-Y209A,S024R-T033S-N243F,T033S-P239T,Y209A-N243F,S024R-T033S-P129H-N184D-T253M,S024R-A085V-P086W-G118R-K235F,S024R-A272P,和S024R-R269C,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与如SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0076] 本发明还提供分离的枯草杆菌蛋白酶变体,其中该枯草杆菌蛋白酶变体为具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:G020R-S087D-S101G-S103A-V104I-A232V-Q245R,G020R-S101G-S103A-V104I-V150L-A232V-Q245R,N018R-G020R-S024R-N076D-S087D-H249R,N018R-G020R-S024R-N076D-V150L-H249R,N018R-S024R-N043R-N076D-S087D-H249R,N018R-S024R-N043R-N076D-V150L-H249R,N018R-S024R-N076D-S078R-S087D-H249R,N018R-S024R-N076D-S078R-V150L-H249R,N018R-S024R-N076D-S087D-H249R-N269R,N018R-S024R-N076D-S087D-S242R-H249R,N018R-S024R-N076D-S087D-V150L-H249R,N018R-S024R-N076D-V150L-H249R,N018R-S087D-S101G-S103A-V104I-A232V-Q245R,N018R-S101G-S103A-V104I-V150L-A232V-Q245R,N018R-T022R-S024R-N076D-S087D-H249R,N018R-T022R-S024R-N076D-V150L-H249R,N043R-S087D-S101G-S103A-V104I-A232V-Q245R-N269R,N043R-S101G-S103A-V104I-V150L-A232V-Q245R,S024R-S087D-S101G-S103A-V104I-A232V-Q245R,S024R-S101G-S103A-V104I-V150L-A232V-Q245R,S078R-S087D-S101G-S103A-V104I-A232V-Q245R,S078R-S101G-S103A-V104I-V150L-A232V-Q245R,S087D-S101G-S103A-V104I-A232V-Q245R-N269R,S101G-S103A-V104I-V150L-A232V-Q245R-H249R,S101G-S103A-V104I-V150L-A232V-Q245R-N269R,T022R-S087D-S101G-S103A-V104I-A232V-Q245R,N018R-S024R-N043D-N076D-V150L-H249R,N043R-S087D-S101G-S103A-V104I-A232V-Q245R,T022R-S101G-S103A-V104I-V150L-A232V-Q245R,N018R-S024R-N043D-N076D-S087D-H249R,N018R-S024R-N076D-S087D-H249R,N018R-S024R-N076D-V150L-S242R-H249R,N043R-S101G-S103A-V104I-V150L-A232V-Q245R-N269R,N076D-S101G-S103A-V104I-V150L-A232V-Q245R,S087D-S101G-S103A-V104I-A232V-S242R-Q245R,S101G-S103A-V104I-V150L-A232V-Q245R,N076D-S087D-S101G-S103A-V104I-A232V-Q245R,S087D-S101G-S103A-V104I-A232V-Q245R,和S101G-S103A-V104I-V150L-A232V-S242R-Q245R,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与如SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0077] 本发明还提供分离的枯草杆菌蛋白酶变体,其中该枯草杆菌蛋白酶变体为具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:S024R-S101G-S103A-V104I-P129Q-A158E-S188D-L217E-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-S130A-A158E-N183D-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-P129Q-A158E-N183D-S188D-A232V-Q245R-N248D-H249R,S101G-

S103A-V104I-S130A-A158E-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-P129Q-A158E-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-S130A-A158E-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-P129Q-S130A-A158E-N183D-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-S128L-P129Q-A158E-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-P129Q-S130A-A158E-S188D-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-P129Q-A158E-S188D-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-P129Q-S130A-A158E-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-S128L-P129Q-S130A-A158E-S188D-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-S128L-P129Q-A158E-S188D-A232V-Q245R-N248D-H249R,和S024R-K027R-S101G-S103A-V104I-S128L-P129Q-S130A-A158E-S188D-A232V-Q245R-N248D-H249R,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与如SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0078] 本发明还提供分离的枯草杆菌蛋白酶变体,其中该枯草杆菌蛋白酶变体为具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:S101G-S103A-V104I-A232V-M222Q-Q245R,S101G-S103A-V104I-A158E-S188D-M222S-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-A158E-S188D-M222Q-A232V-Q245R-N248D-H249R,N076D-S101G-S103A-V104I-A232V-M222Q-Q245R,S101G-S103A-V104I-A232V-M222S-Q245R,N076D-S101G-S103A-V104I-A232V-M222S-Q245R,和N076D-S101G-S103A-V104I-A158E-S188D-M222S-A232V-Q245R-N248D-H249R,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与如SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0079] 本发明还提供分离的枯草杆菌蛋白酶变体,其中该枯草杆菌蛋白酶变体为具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:S024R-S101G-S103A-V104I-S128L-P129Q-A158E-S188D-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-S130A-A158E-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-A158E-S188D-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-S128L-P129Q-A158E-S188D-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-P129Q-S130A-A158E-S188D-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-S130A-A158E-N183D-S188D-L217E-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-S128L-P129Q-S130A-A158E-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-P129Q-A158E-S188D-L217E-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-S128L-S130A-A158E-S188D-L217E-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-S128L-P129Q-A158E-N183D-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-S128L-P129Q-S130A-A158E-N183D-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-S128L-P129Q-A158E-S188D-A232V-Q245R-N248D-H249R-E271G,S101G-S103A-V104I-P129Q-A158E-N183D-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-S130A-A158E-S188D-L217E-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-S128L-A158E-N183D-S188D-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-

P129Q-A158E-S188D-L217E-A232V-Q245R-N248D-H249R，和S024R-S101G-S103A-V104I-S128L-S130A-A158E-S188D-A232V-Q245R-N248D-H249R，其中该枯草杆菌蛋白酶变体的氨基酸位置通过与如SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0080] 本发明还提供分离的枯草杆菌蛋白酶变体，其中该枯草杆菌蛋白酶变体为具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:S101G-S103A-V104I,T22A-S101A-Y209E,S103G-L111V-G159E,T22A-S103G-G159E,T22A-L111V-G159E,T22A-S128N-E271F-Y209E,T22A-S103G-L111V,N62E-L111V-S128N,T22A-L111V-S128N,T22A-N62E-L111V,S101A-S103G-V104L-S188D,S101G-S103A-V104I-G159D,S101A-S103G-V104L-S128N,T22A-S101A-G159E,S101A-S103G-V104L,S101A-S103G-V104L-G159E,T22A-S101A-S103G-V104L,S101A-S103G-V104L-Y209E,T22A-Y209E-E271F,T22A-S101A-E271F，和S101A-Y209E-E271F，其中该枯草杆菌蛋白酶变体的氨基酸位置通过与如SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0081] 本发明还提供分离的枯草杆菌蛋白酶变体，其中该枯草杆菌蛋白酶变体为具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:S103A-V104I-G159D-A232V-Q236H-Q245R-N248D-N252K,S101G-V104I-G159D-A232V-Q236H-Q245R-N248D-N252K,S101G-S103A-G159D-A232V-Q236H-Q245R-N248D-N252K,S101G-S103A-V104L-A232V-Q236H-Q245R-N248D-N252K,S101G-S103A-V104L-G159D-Q236H-Q245R-N248D-N252K,S101G-S103A-V104L-G159D-A232V-Q245R-N248D-N252K,S101G-S103A-V104L-G159D-A232V-Q236H-N248D-N252K,S101G-S103A-V104L-G159D-A232V-Q236H-Q245R-N252K，和S101G-S103A-V104L-G159D-A232V-Q236H-Q245R-N248D，其中该枯草杆菌蛋白酶变体的氨基酸位置通过与如SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0082] 本发明还提供分离的枯草杆菌蛋白酶变体，其中该枯草杆菌蛋白酶变体为具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:S101G-S103A-V104I-G159D-A232V-Q245R-N248D,S101G-S103A-V104I-G159D-A232V-Q245R-N248D-E271F,S101G-S103A-V104I-G159D-A232V-Q245R-N248D-N238R,S101G-S103A-V104I-G159D-A232V-Q245R-N248D-N248R,S101G-S103A-V104I-G159D-A232V-Q245R-N248D-T253R,S101G-S103A-V104I-G159D-A232V-Q245R-N248D-S24R,S101G-S103A-V104I-G159D-A232V-Q245R-N248D-N76D,S101G-S103A-V104I-G159E-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-G159E-A232V-Q245R-N248D-E271F,S101G-S103A-V104I-A158E-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-A158E-A232V-Q245R-N248D-E271F,T22A-S101G-S103A-V104I-G159D-A232V-Q245R-N248D-H249R,T22A-S101G-S103A-V104I-G159D-A232V-Q245R-N248D-E271F,N62E-S101G-S103A-V104I-G159D-A232V-Q245R-N248D-H249R，和N62E-S101G-S103A-V104I-G159D-A232V-Q245R-N248D-E271F，其中该枯草杆菌蛋白酶变体的氨基酸位置通过与如SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0083] 本发明还提供分离的枯草杆菌蛋白酶变体，其中该枯草杆菌蛋白酶变体为具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:A1R，

A230E,E271L,G115R,G20R,H249R,K235F,K27V/F/L,L75E,L82R,N18R,N269R,N43D,N43R,N76D,R45T,S212F,S242R,S24R,S78R,S9A,T22R,V121E,V244R,V28E,V30E,V4R,W241R,G20R-N43R-H249R,G20R-T22R-N43R,G20R-N43R-S242R,G20R-N43R-E271L,G20R-N43R-V244R,G20R-S24R-N43R-S242R,S9A-T22R-S78R-S212F-W241R,S9A-G20R-N43R-S212F,S9A-N43R-S212F,G20R-N43R-S212F,G20R-T22R-N43R-S212F,S24R-S78R-S212F,S9A-N43R-S78R,S9A-N43R-S78R-S242R,S9A-G20R-N43R-S78R,G20R-S24R-N43R-S78R-S242R,T22R-S24R-S78R-S212F,S9A-G20R-N43R-S78R-S242R,G20R-N43R-S78R-H249R,G20R-N43R-S78R,S9A-S78R-S212F,S9A-T22R-N43R-S78R,S9A-G20R-S24R-N43R,S9A-T22R-S78R-S212F,V4R-S9A-T22R-S78R-S212F,G20R-S24R-N43R,A1R-S9A-N43R,G20R-S24R-N43R-G115R,S9A-S24R-N43R,G20R-T22R-S24R-N43R,A1R-S24R-N43R,S9A-G20R-S24R-N43R-S242R,S9A-G20R-T22R-S78R-S212F,S9A-S24R-N43R-V244R,S9A-S24R-N43R-S242R,V4R-S9A-T22R-S24R-S212F,和T22R-S24R-N43R,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与如SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0084] 本发明还提供分离的枯草杆菌蛋白酶变体,其中该枯草杆菌蛋白酶变体为具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:S101G-S103A-V104I-A232V-Q245R-N248D,S101G-S103A-V104I-G159D-A232V-Q245R,S101G-S103A-V104I-G159R-A232V-Q245R-N248D,S101G-S103A-V104I-G159D-A232V-Q245R-N248R,S101G-S103A-V104I-A232V-Q245R,S101G-S103A-V104I-A232V-Q245R-N248R,S101G-S103A-V104I-G159R-A232V-Q245R-N248R,S101G,S103A,V104I,A232V,Q236H,和Q245R,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与如SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0085] 本发明还提供分离的枯草杆菌蛋白酶变体,其中该枯草杆菌蛋白酶变体为具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:A16S,T22A,S24R,N62E,N76D,E89P,S101A/G,S103G/A,V104L/I,L111V,S128N,P129E,A232V,L148I,A158E,G159D/E,R186H,S188D,Y209E,Q236H,Q245R,N248D/R,H249R,N252K/R,T253R,和E271F,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与如SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0086] 本发明还提供分离的枯草杆菌蛋白酶变体,其中该枯草杆菌蛋白酶变体为具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:A1R,Q2S,Q2M,Q2A,Q2R,Q2W,S3R,V4R,V4S,V4C,I8A,S9A,S9F,S9W,R10S,R10A,R10H,R10M,Q12F,Q12R,P14K,P14F,P14Q,A15R,A15F,A16S,H17R,H17M,H17F,N18R,N18K,G20F,G20K,G20R,T22A,T22R,T22Y,T22V,T22Q,T22L,T22W,G23A,G23S,G23F,S24R,S24F,S24W,S24Q,S24H,S24L,G25V,G25F,G25R,V26F,K27L,K27F,K27R,K27V,V28A,V28N,V28E,A29T,V30E,L31F,T33S,T33G,T33D,G34P,I35M,S36T,S36F,S36R,T38L,T38F,T38R,P40N,P40L,P40T,P40W,P40H,P40R,L42I,N43A,N43F,N43I,N43S,N43R,N43M,N43W,N43D,R45T,G46R,A48R,F50C,V51W,V51F,V51H,P52F,P52E,P52N,P55Y,T57R,Q59A,Q59F,Q59R,D60P,D60Q,D60A,N62E,N62Q,G63V,G63M,G63T,G63I,G63A,G63S,G63H,G63Q,G63D,G63E,G63P,H64F,H64T,V68A,V68C,A69N,A69T,A69P,A69W,T71G,T71G,I72C,A74C,L75A,L75F,L75E,L75R,N76D,S78R,S78N,S78I,S78R,I79W,I79Q,V81R,L82F,L82T,L82V,L82R,L82M,A85M,P86W,P86L,P86I,

E89P,E89T,E89G,E89H,E89W,E89L,E89V,E89W,E89F,E89I,Y91N,Y91F,A92F,K94N,S99F,S99T,S99P,S99G,S99M,G100S,G100N,G100Q,G100I,S101A,S101N,S101G,S101D,S101T,S101D,S101E,S101P,S101F,G102A,G102T,G102N,G102H,G102E,S103G,S103N,S103D,S103A,V104L,V104I,V104E,V104D,S105T,S105E,S105Q,S106G,S106T,S106E,S106D,S106A,S106V,S106F,I107M,I107F,A108I,A108G,Q109M,L111V,L111I,E112V,E112L,E112Q,A114G,G115K,G115R,N116K,N116A,N116L,N117F,G118R,G118I,M119C,H120A,H120F,H120R,V121F,V121F,V121E,N123G,N123E,L124S,S128D,S128F,S128L,S128N,S128H,S128M,S128I,S128Q,P129E,S132A,S132E,A138G,S144R,V147L,L148I,A158E,G159D,G159E,G159C,S160D,S166D,S166E,Y167W,M175V,V177C,D181A,Q182R,N183I,N183D,N183M,N183R,N183F,N183R,N185E,N185V,N185I,R186H,R186K,S188E,S188D,S188R,Y192H,Y192W,A194E,A194V,A194F,D197F,D197F,I198L,I198F,V203E,V203C,T208S,Y209S,Y209N,Y209F,Y209T,Y209E,Y209H,Y209G,Y209L,P210R,P210V,P210L,G211Q,G211R,S212I,S212M,S212F,T213A,Y214F,A215N,A215D,A215E,A215H,A215F,S216F,S216A,L217E,L217N,L217D,N218D,N218P,N218E,T224A,T224G,V227I,A230E,A231I,A231C,A232V,L233C,V234F,K235F,Q236F,Q236N,Q236H,N238R,N238K,N238L,P239K,P239G,P239R,P239R,P239H,P239T,P239N,P239S,P239F,S240R,W241R,S242L,S242R,N243F,N243R,V244R,Q245R,I246S,N248D,N248V,N248I,N248R,H249R,H249T,L250I,K251R,K251S,N252I,N252F,N252R,N252K,N252H,T253I,T253R,T253F,A254C,S256N,G258R,T260V,T260I,L262D,L262H,Y263F,S265F,L267V,L267N,L267M,N269I,N269R,A270C,E271I,E271H,E271V,E271H,E271M,E271L,E271P,E271A,E271F,E271T,A272F,A272F,A272R,A273F,A273I,和T274G,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与如SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0087] 本发明还提供迟缓芽孢杆菌枯草杆菌蛋白酶GG36蛋白酶的蛋白酶变体,其中该迟缓芽孢杆菌枯草杆菌蛋白酶GG36蛋白酶包含SEQ ID NO:2所示氨基酸序列,其中该蛋白酶变体包含与SEQ ID NO:2的氨基酸序列相差不超过2、3、4、5、6、7、8、9、10、11、12、13、14、15、16、17、18、19、20、21、22、23、24或25个突变的氨基酸序列,所述突变处于选自氨基酸1、2、3、4、8、9、10、12、14、15、16、17、18、20、22、23、24、25、26、27、28、29、30、31、33、34、35、36、38、40、42、43、45、46、48、50、51、52、55、57、59、60、62、63、64、68、69、71、72、74、75、76、78、79、81、82、85、86、89、91、92、94、99、100、101、102、103、104、105、106、107、108、109、111、112、114、115、116、117、118、119、120、121、123、124、128、129、132、138、44、147、148、158、159、160、166、167、175、177、181、182、183、185、186、188、192、194、197、198、203、208、209、210、211、212、213、214、215、216、217、218、224、227、230、231、233、234、235、236、236、238、238、239、240、241、242、243、244、246、248、249、250、251、252、253、254、256、258、260、262、263、265、267、269、270、271、272、273和274的氨基酸位置,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号,其中该蛋白酶变体的氨基酸位置根据SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列中对应的氨基酸位置的编号方式来进行编号,这是通过该变体蛋白酶氨基酸序列与解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'氨基酸序列的比对来确定的。

[0088] 本发明还提供迟缓芽孢杆菌枯草杆菌蛋白酶GG36蛋白酶的蛋白酶变体，其中该迟缓芽孢杆菌枯草杆菌蛋白酶GG36蛋白酶包含SEQ ID NO:2所示氨基酸序列，其中该蛋白酶变体包含与SEQ ID NO:2的氨基酸序列相差不超过2、3、4、5、6、7、8、9、10、11、12、13、14、15、16、17、18、19、20、21、22、23、24或25个突变的氨基酸序列，所述突变选自A1R,Q2S,Q2M,Q2A,Q2R,Q2W,S3R,V4R,V4S,V4C,I8A,S9A,S9F,S9W,R10S,R10A,R10H,R10M,Q12F,Q12R,P14K,P14F,P14Q,A15R,A15F,A16S,H17R,H17M,H17F,N18R,N18K,G20F,G20K,G20R,T22A,T22R,T22Y,T22V,T22Q,T22L,T22W,G23A,G23S,G23F,S24R,S24F,S24W,S24Q,S24H,S24L,G25V,G25F,G25R,V26F,K27L,K27F,K27R,K27V,V28A,V28N,V28E,A29T,V30E,L31F,T33S,T33G,T33D,G34P,I35M,S36T,S36F,S36R,T38L,T38F,T38R,P40N,P40L,P40T,P40W,P40H,P40R,L42I,N43A,N43F,N43I,N43S,N43R,N43M,N43W,N43D,R45T,G46R,A48R,F50C,V51W,V51F,V51H,P52F,P52E,P52N,P55Y,T57R,Q59A,Q59F,Q59R,D60P,D60Q,D60A,N62E,N62Q,G63V,G63M,G63T,G63I,G63A,G63S,G63H,G63Q,G63D,G63E,G63P,H64F,H64T,V68A,V68C,A69N,A69T,A69P,A69W,T71G,T71G,I72C,A74C,L75A,L75F,L75E,L75R,N76D,S78R,S78N,S78I,S78R,I79W,I79Q,V81R,L82F,L82T,L82V,L82R,L82M,A85M,P86W,P86L,P86I,E89P,E89T,E89G,E89H,E89W,E89L,E89V,E89W,E89F,E89I,Y91N,Y91F,A92F,K94N,S99F,S99T,S99P,S99G,S99M,G100S,G100N,G100Q,G100I,S101A,S101N,S101G,S101D,S101T,S101D,S101E,S101P,S101F,G102A,G102T,G102N,G102H,G102E,S103G,S103N,S103D,S103A,V104L,V104I,V104E,V104D,S105T,S105E,S105Q,S106G,S106T,S106E,S106D,S106A,S106V,S106F,I107M,I107F,A108I,A108G,Q109M,L111V,L111I,E112V,E112L,E112Q,A114G,G115K,G115R,N116K,N116A,N116L,N117F,G118R,G118I,M119C,H120A,H120F,H120R,V121F,V121F,V121E,N123G,N123E,L124S,S128D,S128F,S128L,S128N,S128H,S128M,S128I,S128Q,P129E,S132A,S132E,A138G,S144R,V147L,L148I,A158E,G159D,G159E,G159C,S160D,S166D,S166E,Y167W,M175V,V177C,D181A,Q182R,N183I,N183D,N183M,N183R,N183F,N183R,N185E,N185V,N185I,R186H,R186K,S188E,S188D,S188R,Y192H,Y192W,A194E,A194V,A194F,D197F,D197F,I198L,I198F,V203E,V203C,T208S,Y209S,Y209N,Y209F,Y209T,Y209E,Y209H,Y209G,Y209L,P210R,P210V,P210L,G211Q,G211R,S212I,S212M,S212F,T213A,Y214F,A215N,A215D,A215E,A215H,A215F,S216F,S216A,L217E,L217N,L217D,N218D,N218P,N218E,T224A,T224G,V227I,A230E,A231I,A231C,A232V,L233C,V234F,K235F,Q236F,Q236N,Q236H,N238R,N238K,N238L,P239K,P239G,P239R,P239R,P239H,P239T,P239N,P239S,P239F,S240R,W241R,S242L,S242R,N243F,N243R,V244R,Q245R,I246S,N248D,N248V,N248I,N248R,H249R,H249T,L250I,K251R,K251S,N252I,N252F,N252R,N252K,N252H,T253I,T253R,T253F,A254C,S256N,G258R,T260V,T260I,L262D,L262H,Y263F,S265F,L267V,L267N,L267M,N269I,N269R,A270C,E271I,E271H,E271V,E271H,E271M,E271L,E271P,E271A,E271F,E271T,A272F,A272F,A272R,A273F,A273I,和T274G，其中该蛋白酶变体的氨基酸位置根据SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列中对应的氨基酸位置的编号方式来进行编号，这是通过该蛋白酶变体氨基酸序列与解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'氨基酸序列的比对来确定的。

[0089] 本发明还提供迟缓芽孢杆菌枯草杆菌蛋白酶GG36蛋白酶的蛋白酶变体，其中该迟

缓芽孢杆菌枯草杆菌蛋白酶GG36蛋白酶包含SEQ ID NO:2所示氨基酸序列，其中该蛋白酶变体包含与SEQ ID NO:2的氨基酸序列相差不超过2、3、4、5、6、7、8、9、10、11、12、13、14、15、16、17、18、19、20、21、22、23、24或25个突变的氨基酸序列，所述突变选自A1R,Q2S,V4R,V4S,S9A,R10S,P14K,A16S,H17R,N18R,G20R,T22A,T22R,S24R,S24W,G25R,G25V,V26F,L42I,N43R,N43A,G46R,P52F,P52E,P52N,T57R,Q59A,N62E,N62Q,V68A,V68C,T71G,I72C,A74C.L75A,L75F,L75R,N76D,S78R,L82R,P86W,E89P,E89T,E89G,E89H,E89I,E89V,E89W,Y91N,K94N,G100S,S101A,S101N,S101G,S101D,S103G,S103N,V104L,V104I,S106V,S106G,A108I,L111V,E112V,G115K,G115R,N117F,G118I,V121F,S128D,S128F,S128L,S128N,P129E,S144R,L148I,A158E,G159E,S160D,S166D,N185E,N185I,R186H,S188E,S188D,D197F,V203E,Y209S,Y209N,Y209F,Y209T,Y209E,Y209H,Y209G,P210R,S212I,S212F,Y214F,A215N,A215D,A215E,L217E,L217N,T224A,A230E,A231I,Q236F,N238R,N238K,P239K,P239G,P239R,P239S,W241R,S242R,S242L,N243R,V244R,N248I,N248V,H249R,L250I,N252R,T253R,L262D,Y263F,S265F,L267V,L267N.N269I,N269R,E271F,E271I,E271H,E271P,E271T,E271V,E271L和A272F，并且该蛋白酶变体任选地包含至少一个选自S103A,G159D,Q236H,Q245R,N248D和N252K的突变，其中该蛋白酶变体的氨基酸位置根据SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列中对应的氨基酸位置的编号方式来进行编号，这是通过该蛋白酶变体氨基酸序列与解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'氨基酸序列的比对来确定的。

[0090] 本发明还提供迟缓芽孢杆菌枯草杆菌蛋白酶GG36蛋白酶的蛋白酶变体，其中该迟缓芽孢杆菌枯草杆菌蛋白酶GG36蛋白酶包含SEQ ID NO:2所示氨基酸序列，其中该蛋白酶变体包含与SEQ ID NO:2的氨基酸序列相差不超过2、3、4、5、6、7、8、9、10、11、12、13、14、15、16、17、18、19、20、21、22、23、24或25个突变的氨基酸序列，所述突变选自A16S,T22A,S24R,N62E,N76D,E89P,S101A/G,S103G/A,V104L/I,L111V,S128N,P129E,A232V,L148I,A158E,G159D/E,R186H,S188D,Y209E,Q236H,Q245R,N248D/R,H249R,N252K/R,T253R，和E271F，其中该蛋白酶变体的氨基酸位置根据SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列中对应的氨基酸位置的编号方式来进行编号，这是通过该蛋白酶变体氨基酸序列与解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'氨基酸序列的比对来确定的。

[0091] 本发明还提供迟缓芽孢杆菌枯草杆菌蛋白酶GG36蛋白酶的蛋白酶变体，其中该迟缓芽孢杆菌枯草杆菌蛋白酶GG36蛋白酶包含SEQ ID NO:2所示氨基酸序列，其中该蛋白酶变体包含与SEQ ID NO:2的氨基酸序列相差不超过2、3、4、5、6、7、8、9、10、11、12、13、14、15、16、17、18、19、20、21、22、23、24或25个突变的氨基酸序列，所述突变选自G20K,G20R,G23A,S24F,S24R,N43R,N43W,R45T,N62E,N76D,S101A,N116A,N116L,G118R,S128I,P129E,S166D,S188D,T213A,A215F,L217E,P239G，和N269R，其中该蛋白酶变体的氨基酸位置根据SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列中对应的氨基酸位置的编号方式来进行编号，这是通过该蛋白酶变体氨基酸序列与解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'氨基酸序列的比对来确定的。

[0092] 本发明还提供迟缓芽孢杆菌枯草杆菌蛋白酶GG36蛋白酶的蛋白酶变体，其中该迟缓芽孢杆菌枯草杆菌蛋白酶GG36蛋白酶包含SEQ ID NO:2所示氨基酸序列，其中该蛋白酶变体包含与SEQ ID NO:2的氨基酸序列相差不超过2、3、4、5、6、7、8、9、10、11、12、13、14、15、

16、17、18、19、20、21、22、23、24或25个突变的氨基酸序列，所述突变选自A1R,A230E,E271L,G115R,G20R,H249R,K235F,K27V/F/L,L75E,L82R,N18R,N269R,N43D,N43R,N76D,R45T,S212F,S242R,S24R,S78R,S9A,T22R,V121E,V244R,V28E,V30E,V4R，和W241R，其中该蛋白酶变体的氨基酸位置根据SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列中对应的氨基酸位置的编号方式来进行编号，这是通过该蛋白酶变体氨基酸序列与解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'氨基酸序列的比对来确定的。

[0093] 本发明还提供迟缓芽孢杆菌枯草杆菌蛋白酶GG36蛋白酶的蛋白酶变体，其中该迟缓芽孢杆菌枯草杆菌蛋白酶GG36蛋白酶包含SEQ ID NO:2所示氨基酸序列，其中该蛋白酶变体包含与SEQ ID NO:2的氨基酸序列相差不超过2、3、4、5、6、7、8、9、10、11、12、13、14、15、16、17、18、19、20、21、22、23、24或25个突变的氨基酸序列，所述突变选自A1R,A230E,E271L,G115R,G20R,H249R,K235F,K27V/F/L,L75E,L82R,N18R,N269R,N43D,N43R,N76D,R45T,S212F,S242R,S24R,S78R,S9A,T22R,V121E,V244R,V28E,V30E,V4R，和W241R，并且任选地包含至少一个选自S103A,G159D,Q236H,Q245R,N248D和N252K,的突变，其中该蛋白酶变体的氨基酸位置根据SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列中对应的氨基酸位置的编号方式来进行编号，这是通过该蛋白酶变体氨基酸序列与解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'氨基酸序列的比对来确定的。

[0094] 本发明还提供包含与SEQ ID NO:2的氨基酸序列不同的氨基酸序列的蛋白酶变体，并且其中该蛋白酶变体的总净电荷相对于迟缓芽孢杆菌枯草杆菌蛋白酶GG36蛋白酶的总净电荷为0、+1、+2、+3、+4、+5、-1、-2、-3、-4或-5，并且其中该蛋白酶变体的氨基酸位置根据SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列中的对应氨基酸位置的编号方式来进行编号，这是通过该蛋白酶变体氨基酸序列与解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'氨基酸序列的比对来确定的。在某些情况下，该蛋白酶变体的总净电荷相对于迟缓芽孢杆菌枯草杆菌蛋白酶GG36蛋白酶的总净电荷为0。在某些情况下，该蛋白酶变体的总净电荷相对于迟缓芽孢杆菌枯草杆菌蛋白酶GG36蛋白酶的总净电荷为-5。在某些情况下，该蛋白酶变体的总净电荷相对于迟缓芽孢杆菌枯草杆菌蛋白酶GG36蛋白酶的总净电荷为-4。在某些情况下，该蛋白酶变体的总净电荷相对于迟缓芽孢杆菌枯草杆菌蛋白酶GG36蛋白酶的总净电荷为-3。在某些情况下，该蛋白酶变体的总净电荷相对于迟缓芽孢杆菌枯草杆菌蛋白酶GG36蛋白酶的总净电荷为-2。在某些情况下，该蛋白酶变体的总净电荷相对于迟缓芽孢杆菌枯草杆菌蛋白酶GG36蛋白酶的总净电荷为-1。在某些情况下，该蛋白酶变体的总净电荷相对于迟缓芽孢杆菌枯草杆菌蛋白酶GG36蛋白酶的总净电荷为+1。在某些情况下，该蛋白酶变体的总净电荷相对于迟缓芽孢杆菌枯草杆菌蛋白酶GG36蛋白酶的总净电荷为+2。在某些情况下，该蛋白酶变体的总净电荷相对于迟缓芽孢杆菌枯草杆菌蛋白酶GG36蛋白酶的总净电荷为+3。在某些情况下，该蛋白酶变体的总净电荷相对于迟缓芽孢杆菌枯草杆菌蛋白酶GG36蛋白酶的总净电荷为+4。在某些情况下，该蛋白酶变体的总净电荷相对于迟缓芽孢杆菌枯草杆菌蛋白酶GG36蛋白酶的总净电荷为+5。在某些情况下，蛋白酶变体的总净电荷不同于0(即该蛋白酶的总净电荷不是中性的)。

[0095] 本发明还提供具有以下特性中的一者或多者的蛋白酶变体：a)测试方法2性能指数为至少1.1、至少1.2、至少1.3、至少1.4、至少1.5、至少1.6、至少1.7、至少1.8、至少1.9、至少2、1.1至约10、1.1至约8或甚至1.1至约5；b)测试方法3性能指数为至少1.1、至少1.2、

至少1.3、至少1.4、至少1.5、至少1.6、至少1.7、至少1.8、至少1.9、至少2、1.1至约10、1.1至约8或甚至1.1至约5;c)测试方法4性能指数为至少1.0、至少1.1、至少1.2、至少1.3、至少1.4、至少1.5、至少1.6、至少1.7、至少1.8、至少1.9、至少2、1.0至约10、1.0至约8或甚至1.0至约5;和/或d)测试方法6性能指数为至少1.0、至少1.1、至少1.2、至少1.3、至少1.4、至少1.5、至少1.6、至少1.7、至少1.8、至少1.9、至少2、1.0至约10、1.0至约8或甚至1.0至约5。

[0096] 本发明还提供包含编码本文提供的枯草杆菌蛋白酶变体的多核苷酸序列的分离核酸。本发明还提供包含编码本文提供的枯草杆菌蛋白酶变体的核酸序列的表达载体。在另一些实施例中,表达载体中的核酸与启动子有效连接。本发明还提供包含本文提供的表达载体的宿主细胞。在一些实施例中,宿主细胞为芽孢杆菌属(Bacillus)宿主细胞。在另一些实施例中,宿主细胞为枯草芽孢杆菌(B.subtilis)宿主细胞。

[0097] 本发明还提供制备至少一种枯草杆菌蛋白酶变体的方法,所述方法包括:用包含至少一种编码至少一种本文提供的枯草杆菌蛋白酶变体的核酸的表达载体来转化宿主细胞,以制备转化的宿主细胞;以及在适于制备至少一种枯草杆菌蛋白酶变体的条件下培养该转化的宿主细胞,以制备至少一种枯草杆菌蛋白酶变体。在一些实施例中,所述方法还包括收获制备的枯草杆菌蛋白酶变体。在另一些实施例中,表达载体中的核酸与启动子有效连接。在另一些实施例中,表达载体中的核酸与启动子有效连接。本发明还提供包含本文提供的表达载体的宿主细胞。在一些实施例中,宿主细胞为芽孢杆菌属宿主细胞。在另一些实施例中,宿主细胞为枯草芽孢杆菌宿主细胞。

[0098] 本发明的蛋白酶变体还可用于包含至少一种本文提供的枯草杆菌蛋白酶变体的织物和家庭护理产品。在一些实施例中,该织物和家庭护理产品为清洁组合物。在另一些实施例中,该清洁组合物为颗粒、粉末、固体、条棒、液体、片剂、凝胶或糊剂组合物。在一些另外的实施例中,该清洁组合物为洗涤剂组合物。在一些另外的实施例中,该清洁组合物为冷水洗涤剂组合物、低pH洗涤剂组合物或致密型洗涤剂组合物。在一些另外的实施例中,该清洁组合物为衣物洗涤剂组合物、盘碟洗涤剂组合物和/或硬质表面清洁组合物。在一些实施例中,该盘碟洗涤剂组合物为手洗盘碟洗涤剂组合物或自动盘碟洗涤剂组合物。在一些另外的实施例中,该织物和家庭护理产品还包含至少一种漂白剂。在一些另外的实施例中,该清洁组合物不含磷酸盐,而在其他实施例中,该清洁组合物包含磷酸盐。在另一些实施例中,该织物和家庭护理产品还包含至少一种另外的酶。在还有一些另外的实施例中,该至少一种另外的酶选自半纤维素酶、纤维素酶、过氧化物酶、蛋白酶、金属蛋白酶、木聚糖酶、脂肪酶、磷脂酶、酯酶、过水解酶、角质酶、果胶酶、果胶酸裂解酶、甘露聚糖酶、角蛋白酶、还原酶、氧化酶、酚氧化酶、脂加氧酶、木质素酶、支链淀粉酶、鞣酸酶、戊聚糖酶、malanase、β-葡聚糖酶、阿拉伯糖苷酶、透明质酸酶、软骨素酶、漆酶和淀粉酶或它们的任何组合。在一些实施例中,该织物和家庭护理产品包含至少一种非冷水蛋白酶的枯草杆菌蛋白酶变体。

[0099] 本发明还提供包含至少一种枯草杆菌蛋白酶变体的清洁组合物。在一些实施例中,该清洁组合物为颗粒、粉末、固体、条棒、液体、片剂、凝胶或糊剂组合物。在另一些实施例中,该清洁组合物为洗涤剂组合物。在一些另外的实施例中,该清洁组合物为冷水洗涤剂组合物、低pH洗涤剂组合物和/或致密型洗涤剂组合物。在一些另外的实施例中,该清洁组合物为衣物洗涤剂组合物、盘碟洗涤剂组合物和/或硬质表面清洁组合物。在另一些实施例中,该盘碟洗涤剂为手洗盘碟洗涤剂组合物或自动盘碟洗涤剂组合物。在一些另外的实施

例中，该清洁组合物为衣物洗涤剂组合物。在另一些实施例中，该清洁组合物还包含至少一种漂白剂。在一些另外的实施例中，该清洁组合物不含磷酸盐，而在其他的实施例中该清洁组合物含有磷酸盐。在另一些实施例中，该清洁组合物还包含至少一种另外的酶。在还有一些另外的实施例中，该清洁组合物的至少一种另外的酶选自半纤维素酶、纤维素酶、过氧化物酶、蛋白酶、金属蛋白酶、木聚糖酶、脂肪酶、磷脂酶、酯酶、过水解酶、角质酶、果胶酶、果胶酸裂解酶、甘露聚糖酶、角蛋白酶、还原酶、氧化酶、酚氧化酶、脂加氧酶、木质素酶、支链淀粉酶、鞣酸酶、戊聚糖酶、malanase、β-葡聚糖酶、阿拉伯糖苷酶、透明质酸酶、软骨素酶、漆酶和淀粉酶或它们的任何组合。在一些实施例中，该清洁组合物包含至少一种非冷水蛋白酶的枯草杆菌蛋白酶变体。这种组合物可以是织物和家庭护理产品，或者这种组合物可以不是织物和家庭护理产品。

[0100] 本发明还提供清洁方法，所述方法包括用包含至少一种本文提供的枯草杆菌蛋白酶变体的清洁组合物来接触表面或物品。在一些实施例中，所述清洁方法包括用至少一种本文提供的清洁组合物来接触表面或物品。在一些实施例中，所述方法还包括在用清洁组合物分别接触该表面或物品之后漂洗该表面或物品。在一些实施例中，该物品为盘碟，而在其他实施例中，该物品为织物。在一些实施例中，所述方法还包括在用清洁组合物接触表面或物品之后漂洗该表面或物品的步骤。在一些另外的实施例中，所述方法还包括在漂洗该表面或物品之后干燥该表面或物品的步骤。在一些实施例中，该清洁组合物包含至少一种非冷水蛋白酶的枯草杆菌蛋白酶变体。

[0101] 本发明提供清洁表面或物品的方法，所述包括：提供本文提供的清洁组合物和需要清洁的表面或物品；以及在适于清洗该需要清洁的表面或物品的表面的条件下使该清洁组合物接触该表面或物品，以得到洁净的表面或物品。在一些实施例中，本发明的方法还包括漂洗该洁净的表面或物品以得到漂洗过的表面或物品的步骤。在另一些实施例中，所述方法还包括干燥该漂洗过的表面或物品的步骤。在一些实施例中，该清洁组合物包含至少一种非冷水蛋白酶的枯草杆菌蛋白酶变体。

附图说明

[0102] 图1提供了包括BPN'(SEQ ID NO:1)和GG36(SEQ ID NO:2)的成熟参照蛋白酶的比对。本文所述的每种蛋白酶变体(包括每种冷水蛋白酶变体)的每个氨基酸位置根据解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'(SEQ ID NO:1)的氨基酸序列中对应的氨基酸位置的编号方式(如图1中所示)进行编号，这是通过该蛋白酶变体氨基酸序列与解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'氨基酸序列的比对来确定的。因而，除非本文另外指明，否则置换位置是以与BPN'的关系给出。

[0103] 图2提供了pHPLT-GG36的图谱。

[0104] 图3提供了pRA68的图谱。

[0105] 图4提供了pRA96的图谱。

具体实施方式

[0106] 本发明提供丝氨酸蛋白酶变体。具体地讲，本发明提供与参照丝氨酸蛋白酶相比具有一个或多个置换的丝氨酸蛋白酶变体。此外，本发明提供包含这些丝氨酸蛋白酶变体

的组合物。在一些实施例中，本发明提供清洁组合物，其包含这些丝氨酸蛋白酶变体中的至少一种。

[0107] 定义

[0108] 除非另外指明，否则本发明的实施涉及处于本领域技术范围内的常用于分子生物学、蛋白质工程、微生物学和重组DNA的常规技术。这类技术是本领域技术人员已知的并描述于本领域技术人员众所周知的许多文章和参考著作中。藉此将本文提及的所有专利、专利申请、文章和出版物(包括上文中和下文中的)，都明确以引用的方式并入本文。

[0109] 除非另外定义，否则本文所用的所有技术和科学术语均具有与本发明所属领域普通技术人员所一般理解的含义相同的含义。许多技术词典是本领域技术人员已知的。尽管与本文描述的方法和材料相似或等同的任何方法和材料均可用于本发明的实施，但在本文中描述了一些合适的方法和材料。因此，下文就要定义的术语通过整体参考本说明书可得到更完全的描述。另外，如本文所用，除非上下文明确指明，否则单数术语“一”、“一个”和“所述”包括复数含义。数值范围包括限定该范围的数值。除非另外说明，否则分别是核酸以5’至3’的取向从左向右书写，而氨基酸序列以氨基至羧基取向从左向右书写。应当理解，本发明不限于所描述的具体方法学、方案和试剂，因为这些方面可根据本领域技术人员使用它们的背景而有所变化。

[0110] 除非另外指明，否则本发明的实施可采用蛋白质纯化、分子生物学、微生物学、重组DNA技术以及蛋白质测序的常规技术，所有这些均在本领域技术人员的技能之内。

[0111] 此外，本文提供的标题并不是对本发明的各个方面或实施例的限制，这些方面或实施例都可以通过整体参考本说明书而获得。因此，下文就要定义的术语通过整体参考本说明书可得到更完全的限定。尽管如此，为了便于理解本发明，将多个术语定义以下。

[0112] 本文所用的术语“蛋白酶”和“肽酶”是指具有分解其他蛋白质的能力的酶蛋白。蛋白酶具有进行“蛋白水解”的能力，其通过水解在形成该蛋白质的肽或多肽链中将氨基酸连接在一起的肽键而开始蛋白质分解代谢。蛋白酶作为蛋白质消化酶的这个活性称为“蛋白水解活性”。存在多个熟知的用于测量蛋白水解活性的程序(参见例如，Kalisz，“Microbial Proteinases，”In:Fiechter(ed.)，Advances in Biochemical Engineering/Biotechnology，(1988)(Kalisz，“微生物蛋白酶”，载于Fiechter编辑，《生物化学工程/生物技术进展》，1988年))。例如，蛋白水解活性可通过可分析分别的蛋白酶水解商业底物的能力的比较测定法来确定。可用于蛋白酶或蛋白水解活性的分析的示例性底物包括但不限于：二甲基酪蛋白(Sigma C-9801)、牛胶原(Sigma C-9879)、牛弹性蛋白(Sigma E-1625)和牛角蛋白(ICN Biomedical 902111)。利用这些底物的比色测定法为本领域所熟知(例如参见，WO 99/34011和美国专利No.6,376,450，将这两个专利以引用的方式并入本文)。pNA测定法(参见例如Del Mar et al.，Anal.Biochem.99:316-320[1979](Del Mar等人，《分析生物化学》，第99卷，第316-320页，1979年))也可以用于测定在梯度洗脱过程中收集的级分的活性酶浓度。这个测定法测量当该酶水解可溶性的合成底物即琥珀酰-丙氨酸-丙氨酸-脯氨酸-苯丙氨酸-对硝基苯胺(suc-AAPF-pNA)时对硝基苯胺释放的速率。用分光光度计在410nm处测量从该水解反应产生黄色的速率，该速率与活性酶浓度成比例。此外，280纳米(nm)处的吸光度测量可用于测定总蛋白质浓度。活性酶/总蛋白质比率给出了酶纯度。

[0113] 本文所用的术语“枯草杆菌蛋白酶”是指如在MEROPS-肽酶数据库中所述的S8丝氨

酸蛋白酶家族的任何成员(参见Rawlings et al.,MEROPS:the peptidase database,Nucl Acids Res,34Database issue,D270-272[2006](Rawlings等人,“MEROPS:肽酶数据库”,《核酸研究》,第34卷,数据库专刊,第D270-272页,2006年))。如其中所述,肽酶家族S8含有丝氨酸内肽酶枯草杆菌蛋白酶及其同源物(Rawlings and Barrett,Biochem J.,290:205-218,[1993](Rawlings和Barrett,《生物化学杂志》,第290卷,第205-218页,1993年))。S8家族也称为枯草杆菌酶(subtilase)家族,是丝氨酸肽酶的第二大家族。现在已经测定了S8家族若干成员的三级结构。典型的S8蛋白质结构由三个层组成,一个七股β片层夹在两层螺旋之间。枯草杆菌蛋白酶(S08.001)是异种集团(clan)SB(SB)的典型结构。尽管结构不同,但枯草杆菌蛋白酶和胰凝乳蛋白酶(S01.001)的活性位点可叠合,这表明该相似性是趋同进化而不是趋异进化的结果。

[0114] 本文所用的术语“蛋白酶变体”、“变体蛋白酶”、“变体丝氨酸蛋白酶”、“丝氨酸蛋白酶变体”、“枯草杆菌蛋白酶变体”、“突变蛋白酶”用于指与参照蛋白酶(可以为野生型枯草杆菌蛋白酶)相似的蛋白酶(尤其是在其功能上),但在其氨基酸序列中有使得它们在序列上与衍生该变体蛋白酶的野生型蛋白酶或任何起始参照蛋白酶(即“亲本”蛋白酶)不同的突变。在一些实施例中,本发明提供“GG36变体”(或“GG36枯草杆菌蛋白酶变体”),其中突变存在于SEQ ID NO:2所示的成熟GG36序列中。然而,无意于将参照蛋白酶限于任何特定的氨基酸序列。此外,意在使该术语涵盖亲本蛋白酶的变体,其中该亲本蛋白酶的序列与SEQ ID NO:2的氨基酸序列至少90%、至少95%、至少96%、至少97%、至少98%、至少99%或100%相同。

[0115] 本文所用的术语“冷水蛋白酶变体”意指亲本蛋白酶的蛋白酶变体,其中迟缓芽孢杆菌枯草杆菌蛋白酶GG36蛋白酶具有SEQ ID NO:2的氨基酸序列,其中所述蛋白酶变体具有以下特性中的一者或多者:a)测试方法2性能指数为至少1.1、至少1.2、至少1.3、至少1.4、至少1.5、至少1.6、至少1.7、至少1.8、至少1.9、至少2、1.1至约10、1.1至约8或甚至1.1至约5;b)测试方法3性能指数为至少1.1、至少1.2、至少1.3、至少1.4、至少1.5、至少1.6、至少1.7、至少1.8、至少1.9、至少2、1.1至约10、1.1至约8或甚至1.1至约5;c)测试方法4性能指数为至少1.0、至少1.1、至少1.2、至少1.3、至少1.4、至少1.5、至少1.6、至少1.7、至少1.8、至少1.9、至少2、1.0至约10、1.0至约8或甚至1.0至约5;和/或d)测试方法6性能指数为至少1.1、至少1.2、至少1.3、至少1.4、至少1.5、至少1.6、至少1.7、至少1.8、至少1.9、至少2、1.0至约10、1.0至约8或甚至1.0至约5。测试方法2、测试方法3、测试方法4和测试方法6在下文的实例1题为“测试方法”的章节中明确地进行了描述。此外,意在使该术语涵盖亲本蛋白酶的变体,其中该亲本蛋白酶的序列与SEQ ID NO:2的氨基酸序列至少90%、至少95%、至少96%、至少97%、至少98%、至少99%或100%相同。

[0116] 在本发明的一些实施例中,亲本蛋白酶(即“参照”或“起始”蛋白酶)为市售蛋白酶,包括但不限于以以下商品名销售的蛋白酶:SAVINASE®、POLARZYME®、KANNASE®、LIQUINASE®、LIQUINASE ULTRA®、SAVINASE ULTRA®、OVOZYME®(由诺维信公司(Novozymes A/S)生产);

MAXACAL®、PROPERASE®、PURAFECT®、FN3®、FN4®和PURAFECT OXP®、PURAFAST™、PURAFECT® PRIME、PURAMAX®(由丹尼斯克美国公司杰能科

分公司(Danisco US,Genencor Division)生产);以及可得自汉高/凯米拉(Henkel/Kemira)的那些,即BLAP(US 5,352,604的图29中所示的具有以下突变的序列:S99D+S101R+S103A+V104I+G159S,以下简称为BLAP)和BLAP X(具有S3T+V4I+V205I的BLAP)。

[0117] 本文所用的术语"变体多肽"是指包含与亲本或参照多肽(包括但不限于野生型多肽)的氨基酸序列相差至少一个氨基酸残基的氨基酸序列的多肽。

[0118] 如本文所用,"芽孢杆菌属"包括本领域技术人员已知的"芽孢杆菌属"内的所有种,包括但不限于例如枯草芽孢杆菌、地衣芽孢杆菌(B.licheniformis)、迟缓芽孢杆菌、短芽孢杆菌(B.brevis)、嗜热脂肪芽孢杆菌(B.stearothermophilus)、嗜碱芽孢杆菌(B.alkalophilus)、解淀粉芽孢杆菌、克劳氏芽孢杆菌(B.clausii)、耐盐芽孢杆菌(B.halodurans)、巨大芽孢杆菌(B.megaterium)、凝结芽孢杆菌(B.coagulans)、环状芽孢杆菌(B.circulans)、灿烂芽孢杆菌(B.lautus)和苏云金芽孢杆菌(B.thuringiensis)。应该认识到,还在继续对芽孢杆菌属进行分类学整理。因此,意在使该属包括已经重新分类的种,包括但不限于诸如现在命名为"嗜热脂肪地芽孢杆菌(Geobacillus stearothermophilus)"的嗜热脂肪芽孢杆菌之类的生物体。在存在氧气的情况下抗性内生孢子的产生被视为芽孢杆菌属的定义性特征,但该特性还适用于最近命名的脂环酸芽孢杆菌属(Alicyclobacillus)、双芽孢杆菌属(Amphibacillus)、解硫胺素芽孢杆菌属(Aneurinibacillus)、厌氧芽孢杆菌属(Anoxybacillus)、短芽孢杆菌属(Brevibacillus)、线芽孢杆菌属(Filobacillus)、薄壁芽孢杆菌属(Gracilibacillus)、嗜盐芽孢杆菌属(Halobacillus)、类芽孢杆菌属(Paenibacillus)、盐芽孢杆菌属(Salibacillus)、热芽孢杆菌属(Thermobacillus)、脲芽孢杆菌属(Ureibacillus)和枝芽孢杆菌属(Virgibacillus)。

[0119] 术语"多核苷酸"和"核酸"在本文中可互换使用,指由在链中共价键合的核苷酸单体组成的任何长度的聚合物。DNA(脱氧核糖核酸)(包含脱氧核糖核苷酸的多核苷酸)和RNA(核糖核酸)(核糖核苷酸的聚合物)是具有独特生物学功能的多核苷酸或核酸的例子。多核苷酸或核酸包括但不限于:单链、双链或三链DNA、基因组DNA、cDNA、RNA、DNA-RNA杂交体,或包含嘌呤和嘧啶碱基的聚合物,或其他天然的、经化学修饰的、经生物化学修饰的、非天然的或衍生化的核苷酸碱基。以下是多核苷酸的非限制性实例:基因、基因片段、染色体片段、表达序列标签(EST)、外显子、内含子、信使RNA(mRNA)、转运RNA(tRNA)、核糖体RNA(rRNA)、核酶、互补DNA(cDNA)、重组多核苷酸、分支多核苷酸、质粒、载体、任何序列的分离的DNA、任何序列的分离的RNA、核酸探针和引物。在一些实施例中,多核苷酸包括经修饰的核苷酸,例如甲基化的核苷酸和核苷酸类似物、尿嘧啶(uracyl)、其他糖和连接基如氟代核糖和硫代酸酯,以及核苷酸支链。在一个具体实施例中,核苷酸的序列间夹有非核苷酸组分。

[0120] 本文所用的术语"突变"指在起始氨基酸或核酸序列中作出的变化。意在使该术语涵盖置换、插入和缺失。

[0121] 本文所用的术语"载体"指用于将核酸或多核苷酸引入或转移进靶细胞或组织中的核酸构建体或多核苷酸构建体。载体通常用于将外来DNA引入另一细胞或组织中。载体通常包含作为转基因的DNA序列和充当该载体"骨架"的较大的多核苷酸序列。载体通常起到转移遗传信息(如插入的转基因)至靶细胞或组织的作用,以便在该靶细胞或组织中分离、增殖或表达该插入物。载体包括质粒、克隆载体、噬菌体、病毒(如病毒载体)、黏粒、表达载

体、穿梭载体、表达盒(cassette)等等。载体通常包含复制起点、多克隆位点和选择性标记。将载体插入靶细胞中的过程通常称为转染。用病毒载体进行的细胞转染通常称为转导。在一些实施例中,本发明包括载体,该载体包含编码变体蛋白酶(如前体或成熟变体蛋白酶)的DNA序列,该DNA序列与能够实现其在合适宿主中表达的合适前序列(如分泌序列、信号肽序列等)有效连接。

[0122] 本文所用的术语"表达盒"、"表达质粒"或"表达载体"指以重组方式或以合成方式产生的、用于目的核酸(如外来核酸或转基因)在靶细胞中的表达的核酸构建体或载体。目的核酸通常表达目的蛋白质。表达载体或表达盒通常包含驱动或促进外来核酸的表达的启动子核苷酸序列。表达载体或盒还通常包含任何其他允许特定核酸在靶细胞中的转录的指定核酸元件。重组表达盒可掺入质粒、染色体、线粒体DNA、质体DNA、病毒或核酸片段中。某些表达载体具有使异源DNA片段掺入宿主细胞中并使其在宿主细胞中表达的能力。许多原核和真核表达载体是可商购获得的。适宜的表达载体的选择在本领域技术人员的知识范围内。用于从掺入到表达载体中的核酸序列表达蛋白质的适当表达载体的选择在本领域技术人员的知识范围内。

[0123] DNA构建体是可被引入到靶细胞或组织中的人工构建的核酸区段。DNA构建体通常包含已被亚克隆进载体中的DNA插入物,该DNA插入物包含编码目的蛋白质的核苷酸序列。载体可含有用于在细菌中生长的细菌抗性基因和用于目的蛋白质在生物体中的表达的启动子。DNA可通过PCR或本领域技术人员已知的任何其他合适的技术体外产生。在一些实施例中,DNA构建体包含目的核酸序列。在一些实施例中,该序列与另外的元件如控制元件(例如启动子等)有效连接。DNA构建体可还包含选择性标记并且可还包含侧接有同源盒(homology box)的输入序列(incoming sequence)。构建体可包含添加至末端的其他非同源序列(如填充序列(stuffer sequence)或旁侧序列(flank))。在一些实施例中,序列的末端是闭合的,使得DNA构建体形成闭环。用本领域熟知的技术掺入到DNA构建体中的目的核酸序列可以是野生型的、突变的或经修饰的核酸。在一些实施例中,DNA构建体包含一条或多条与宿主细胞染色体同源的核酸序列。在其他实施例中,DNA构建体包含一条或多条非同源核苷酸序列。一旦体外装配了DNA构建体,则可将其用于例如:1)将异源序列插入宿主细胞的所需靶序列中;和/或2)诱变宿主细胞染色体的区域(即用异源序列置换内源序列);3)使靶基因缺失;和/或4)将复制型质粒引入宿主中。在本文中"DNA构建体"可与"表达盒"互换使用。

[0124] 如本文所用,"质粒"指染色体外DNA分子,其能够独立于染色体DNA进行复制。质粒是双链的(ds)并且可以是环状的,通常用作克隆载体。

[0125] 如本文在将核酸序列引入细胞中的语境中所用,术语"引入"指任何适于将核酸序列转移进细胞中的方法。这类引入方法包括但不限于:原生质体融合、转染、转化、电穿孔、接合和转导(参见例如Ferrari et al.,"Genetics,"in Hardwood et al.(eds.),Bacillus,Plenum Publishing Corp.,pp.57-72[1989](Ferrari等人,"遗传学",载于Hardwood等人编辑,《芽孢杆菌》,普莱南出版公司,第57-72页,1989年))。

[0126] 转化指因遗传物质(如DNA)的吸收、基因组掺入和表达所致的细胞的遗传变更。

[0127] 如本文所用,当某核酸被设置成与另一核酸序列处于功能关系中时,其与另一核酸序列"有效连接"。例如,如果启动子或增强子影响核苷酸编码序列的转录,则该启动子与

该编码序列有效连接。如果核糖体结合位点被设置成有利于编码序列的翻译，则该核糖体结合位点可与该编码序列有效连接。通常，“有效连接的”DNA序列是连续的。然而，增强子不必是连续的。连接是通过在便利的限制性位点处的连接来实现。如果这类位点不存在，则可根据常规操作使用合成的寡核苷酸衔接子或接头。

[0128] 本文所用的术语“基因”是指这样的多核苷酸(如DNA片段)，其编码多肽并且包括编码区之前和之后的区域以及位于各个编码片段(外显子)之间的间插序列(内含子)。

[0129] 如本文所用，“重组的”在用于指细胞时，通常表示该细胞已通过引入异源核酸序列进行了修饰或表示该细胞衍自经过如此修饰的细胞。例如，重组细胞可包含这样的基因，其不以相同的形式存在于天然(非重组)形式的细胞内，或者重组细胞可包含(存在于天然形式的细胞中的)天然基因，但该基因已经过修饰并被再次引入该细胞中。重组细胞可包含细胞内源性核酸，该核酸在未将其从该细胞移除的情况下进行了修饰；这种修饰包括通过基因置换、定点突变以及本领域一般技术人员已知的相关技术获得的那些修饰。重组DNA技术包括体外产生重组DNA以及将该重组DNA转移进细胞中的技术，在所述细胞中该重组DNA可被表达和增殖，从而产生重组多肽。多核苷酸或核酸的“重组”和“被重组”一般是指两条或更多条核酸或多核苷酸链或片段的组装或组合，以产生新的多核苷酸或核酸。重组多核苷酸或核酸有时称为嵌合体。当核酸或多肽为人工的或工程化改造的，或衍生自人工的或工程化改造的蛋白质或核酸时，则该核酸或多肽是“重组的”。

[0130] 本文所用的术语核酸或基因“扩增”是指这样的一种过程，通过该过程特定DNA序列以不成比例的方式复制，使得被扩增的核酸或基因以高于基因组中最初存在的拷贝数的拷贝数存在。在一些实施例中，通过在药物(如可抑制的酶的抑制剂)的存在下进行生长来选择细胞，可导致编码在该药物存在下的生长所需的基因产物的内源基因的扩增，或者导致编码这个核酸或基因产物的外源(即输入)序列的扩增，或者导致这两种扩增。

[0131] “扩增”是涉及模板特异性的核酸复制的特例。要将它与非特异性模板复制(即依赖于模板，但不依赖于特定模板的复制)区分开来。在这里，模板特异性与复制保真性(即正确多核苷酸序列的合成)和核苷酸(核糖核苷酸或脱氧核糖核苷酸)特异性有区别。模板特异性在很多情况下以“靶”特异性来描述。在要设法将靶序列从其他核酸挑选出来的意义上，靶序列是“靶”。已经设计出主要用于这个挑选的扩增技术。

[0132] 本文所用的术语“引物”指这样的寡核苷酸(核苷酸残基的聚合物)，无论是如在纯化的限制酶切消化物中天然存在的还是以合成方式产生的，其当被置于其中与某核酸链互补的引物延伸产物的合成得以诱导的条件下(即在核苷酸、诱导剂如DNA聚合酶的存在下以及在合适的温度和pH下)时能够充当合成起始点。为了使扩增效率最高，引物优选为单链的，但作为另一种选择其也可以是双链的。如果是双链，则首先对引物进行处理以分离其链，然后再用于制备延伸产物。在一些实施例中，引物为寡脱氧核糖核苷酸。引物必须足够长以在诱导剂的存在下引发延伸产物的合成。引物的确切长度取决于多种因素，包括温度、引物来源以及该方法的使用。

[0133] 本文所用的术语“探针”指这样的寡核苷酸，无论是如在纯化的限制酶切消化物中的天然存在的还是以合成方式、重组方式或通过PCR扩增产生的，其通常能够与目的的另一寡核苷酸杂交。探针可以是单链的或双链的。探针可用于特定基因序列的检测、鉴别和分离。设想到，本发明中所用的任何探针将用任何“报告分子”进行标记，从而其可在任何检测

系统中检测，所述检测系统包括但不限于酶系统(如ELISA，以及基于酶的组织化学测定法)、荧光系统、放射性系统和发光系统。无意于将本发明限制于任何具体的检测系统或标记。

[0134] 本文所用的术语“靶”当用于指涉聚合酶链反应时，是指用于聚合酶链反应的引物所结合的核酸区域。因此，“靶”被设法从其他核酸序列中挑选出来。核苷酸“区段”是在靶核酸序列内的核酸区域。

[0135] 本文所用的术语“聚合酶链反应”(PCR)指美国专利No.4,683,195、No.4,683,202和No.4,965,188的方法(这些专利以引用方式并入本文)，其包括在不进行克隆或纯化的情况下增加靶序列的某个区段在基因组DNA的混合物中的浓度的方法。这个扩增靶序列的方法是本领域众所周知的。

[0136] 本文所用的术语“扩增试剂”指进行扩增所需的除引物、核酸模板以及扩增酶以外的那些试剂(如脱氧核糖核苷三磷酸、缓冲剂等)。通常，将扩增试剂连同其他反应组分放置和装于反应容器(试管、微孔等)中。

[0137] 本文所用的术语“限制性内切核酸酶”或“限制酶”指能够在称为限制位点的特定核苷酸序列处或附近切开双链或单链DNA的酶(如细菌酶)。包含限制位点的核苷酸序列为给定的限制性内切核酸酶或限制酶所识别和切割并且常常是DNA片段的插入位点。可将限制位点工程引入到表达载体或DNA构建体中。

[0138] “同源重组”是指两个DNA分子或成对染色体之间在相同或几乎相同的核苷酸序列位点处进行的DNA片段交换。在一些实施例中，染色体整合是同源重组。

[0139] 如果核酸或多核苷酸在其天然状态下或在通过本领域的技术人员已知的方法操纵时，可转录和/或翻译产生多肽或其片段，则称该核酸或多核苷酸“编码”多肽。也称这种核酸的反义链编码该序列。

[0140] 如本领域已知的，DNA序列可被RNA聚合酶转录而产生RNA序列，但RNA序列可被逆转录酶逆转录而产生DNA序列。

[0141] “宿主菌株”或“宿主细胞”指对于包含目的DNA序列的表达载体适合的宿主。目的DNA序列可在宿主菌株或宿主细胞中表达目的蛋白质。

[0142] “蛋白质”或“多肽”包含氨基酸残基的聚合序列。在本文中，术语“蛋白质”与“多肽”可互换使用。遵照国际纯化学及应用化学联合会-国际生物化学联合会的生物化学命名委员会(IUPAC-IUB Joint Commission on Biochemical Nomenclature,JCBN))定义的氨基酸单字母和三字母代码在整个本公开中使用。单字母X指二十种氨基酸中的任一种。还应理解，由于遗传密码的简并性，多肽可由不止一种核苷酸序列编码。突变按以下方式命名：亲本氨基酸的单字母代码，后跟三位数或两位数的位置编号，然后是变体氨基酸的单字母代码。例如，位置87处的甘氨酸(G)突变为丝氨酸(S)表示为“G087S”或“G87S”。多点突变通过在各突变之间插入“-”表示。位置87和90处的突变表示为“G087S-A090Y”或“G87S-A90Y”或“G87S+A90Y”或“G087S+A090Y”。对于缺失，使用单字母代码“Z”。对于相对于亲本序列的插入，单字母代码“Z”位于该位置编号的左侧。对于缺失，单字母代码“Z”位于该位置编号的右侧。对于插入，位置编号是在插入的氨基酸的前面的位置编号，每个氨基酸加0.01。例如，在位置87和88之间丙氨酸(A)、丝氨酸(S)和酪氨酸(Y)三个氨基酸的插入表示为“Z087.01A-Z087.02S-Z087.03Y”。因此，在位置100处组合上述所有突变再加上缺失为：

“G087S-Z087.01A-Z087.02S-Z087.03Y-A090Y-A100Z”。

[0143] “前序列”或“前肽序列”指蛋白酶分泌所必要的处于信号肽序列和成熟蛋白酶序列之间的氨基酸序列。前序列或前肽序列的切除会得到成熟的活性蛋白酶。

[0144] 术语“信号序列”或“信号肽”指可参与成熟或前体形式的蛋白质的分泌或直接转运的氨基酸残基序列。信号序列通常位于该前体或成熟蛋白质序列的N端。信号序列可以是内源性的或外源性的。一种示例性的外源性信号序列包含来自枯草芽孢杆菌(Bacillus subtilis)枯草杆菌蛋白酶的信号序列的前七个氨基酸残基和这七个氨基酸残基所融合到的来自迟缓芽孢杆菌(Bacillus lentus,ATCC 21536)枯草杆菌蛋白酶的信号序列的其余部分。通常,成熟蛋白质缺少信号序列。在转运该蛋白质后,通常由信号肽酶从该蛋白质切除信号序列。

[0145] 术语“杂合信号序列”指与待表达的基因的信号序列融合的信号序列,其中该序列的一部分从表达宿主获得。在一些实施例中,利用合成的序列。

[0146] 术语蛋白质、多肽或肽的“成熟”形式指无信号肽序列和前肽序列的该蛋白质、多肽或肽功能形式。

[0147] 术语蛋白质或肽的“前体”形式指具有与该蛋白质的氨基或羰基末端有效连接的前序列的该蛋白质成熟形式。前体还可具有与前序列的氨基末端有效连接的“信号”序列。前体还可以具有涉及翻译后活性的另外的多核苷酸(例如这样的多核苷酸,从前体上将其切除会留下蛋白质或肽的成熟形式)。

[0148] 指涉氨基酸序列或核酸序列的术语“野生型”表示该氨基酸序列或核酸序列是天然的或天然存在的序列。本文所用的术语“天然存在的”指自然界中存在的(即还未借助重组方法进行过操纵的)任何东西(如蛋白质、氨基酸或核酸序列)。

[0149] 本文所用的术语“非天然存在的”指自然界中不存在的任何东西(如实验室中产生的重组核酸)。

[0150] 如本文所用,对于氨基酸残基位置,“与……相对应”或“对应于”或“对应”是指在蛋白质或肽中的列举位置处的氨基酸残基,或与蛋白质或肽中列举的残基类似、同源或等同的氨基酸残基。如本文所用,“对应区域”一般是指沿着相关蛋白质或参照蛋白质的类似位置。

[0151] 术语“衍生自”和“得自”不仅指由所考虑的生物菌株产生或可产生的蛋白酶,还指由从这种菌株分离的DNA序列编码并在包含这种DNA序列的宿主生物中产生的蛋白酶。另外,该术语指由合成来源的和/或cDNA来源的DNA序列编码的,并且具有所考虑的蛋白酶的鉴别特性的蛋白酶。例如,“衍生自芽孢杆菌属的蛋白酶”是指那些由芽孢杆菌天然产生的具有蛋白水解活性的酶,以及指与由芽孢杆菌来源产生的那些蛋白酶类似的丝氨酸蛋白酶,但这些丝氨酸蛋白酶是使用基因工程技术通过编码丝氨酸蛋白酶的核酸转化的非芽孢杆菌生物产生的。

[0152] 在两条核酸或多肽序列的语境中,术语“相同”是指当进行比对以达到最大对应程度时两条序列中相同的残基,这是使用以下序列比较或分析算法中的一种测量的。

[0153] 如本文所用,“同源基因”是指来自不同但通常相关的物种的一对基因,这对基因彼此对应并且彼此相同或非常类似。该术语涵盖因物种形成(即新物种的发展)而分开的基因(如垂直同源基因),以及因遗传复制而分开的基因(如平行同源基因)。

[0154] 如本文所用,“同源性”指序列相似性或同一性,其中同一性是优选的。同源性可以使用本领域已知的标准技术测定(参见例如Smith and Waterman,Adv.Appl.Math.2:482[1981](Smith和Waterman,《应用数学进展》,第2卷,第482页,1981年);Needleman and Wunsch,J.Mol.Biol.48:443[1970](Needleman和Wunsch,《分子生物学杂志》,第48卷,第443页,1970年);Pearson and Lipman,Proc.Natl.Acad.Sci.USA 85:2444[1988](Pearson和Lipman,《美国国家科学院院刊》,第85卷,第2444页,1988年);软件程序,例如在威斯康星遗传学软件包(Wisconsin Genetics Software Package,得自威斯康星州麦迪逊市遗传学计算机小组(Genetics Computer Group,Madison,WI))中的GAP、BESTFIT、FASTA和TFASTA;以及Devereux et al.,Nucl.Acid Res.12:387-395[1984](Devereux等人,《核酸研究》,第12卷,第387-395页,1984年))。可用的算法的一个实例是PILEUP。PILEUP使用渐进式逐对比对从一组相关序列产生多个序列对比。它还能够绘制显示聚类关系(用于产生比对)的树形图。PILEUP使用Feng和Doolittle的渐进式比对方法(参见Feng and Doolittle,J.Mol.Evol.35:351-360[1987](Feng和Doolittle,《分子进化杂志》,第35卷,第351-360页,1987年))的简化版。该方法与Higgins和Sharp描述的方法类似(参见Higgins and Sharp,CABIOS 5:151-153[1989](Higgins和Sharp,《计算机在生物科学中的应用》,第5卷,第151-153页,1989年))。可用的PILEUP参数包括:默认间隙权重3.00、默认间隙长度权重0.10,以及加权末端间隙。可用的算法的另一个例子是Altschul等人描述的BLAST算法(参见Altschul et al.,J.Mol.Biol.215:403-410[1990](Altschul等人,《分子生物学杂志》,第215卷,第403-410页,1990年);以及Karlin and Altschul,Proc.Natl.Acad.Sci.USA 90:5873-5787[1993](Karlin和Altschul,《美国国家科学院院刊》,第90卷,第5873-5787页,1993年))。特别有用的BLAST程序为WU-BLAST-2程序(参见Altschul et al.,Meth.Enzymol.266:460-480[1996](Altschul等人,《酶学方法》,第266卷,第460-480页,1996年))。WU-BLAST-2使用几种搜索参数,大部分参数设定为默认值。可调参数用以下值设定:重叠跨度(overlap span)=1,重叠分数(overlap fraction)=0.125,字串阈值(word threshold)(T)=11。HSP S和HSP S2参数是动态值,由程序自身根据特定序列的组成和被用来搜索目的序列的特定数据库的组成来确定。然而,可以调整所述值来增加灵敏度。

[0155] 参照序列和目的测试序列之间的序列同一性百分数可由本领域技术人员容易地测定。多核苷酸或多肽序列共有的同一性百分数通过分子之间序列信息的直接比较来确定,所述比较通过比对序列并用本领域已知的方法确定同一性来进行。适用于确定序列相似性的算法的例子是BLAST算法(参见Altschul,et al.,J.Mol.Biol.,215:403-410[1990](Altschul等人,《分子生物学杂志》,第215卷,第403-410页,1990年))。进行BLAST分析的软件可通过美国国家生物技术信息中心(National Center for Biotechnology Information)公开获得。该算法涉及首先通过在查询序列中鉴定长度为W的短字串来鉴定高打分序列对(high scoring sequence pair,HSP),该短字串当与数据库序列中相同长度的字串比对时匹配或满足某取正值的阈值分数T。这些最初的邻近命中字串充当起点来寻找含有它们的更长的HSP。使命中字串沿进行比较的两条序列的每一条朝两个方向扩展至累积比对分数不能增加为止。命中字串的延伸在以下情况时停止:累积比对分数从最大获得值下降达数量X;累积分数达到零或零以下;或者到达任一序列的末端。BLAST算法参数W、T和X决定该算法的灵敏度和速度。BLAST程序使用的默认值是字长(W)为11、BLOSUM62打分

矩阵(参见Henikoff and Henikoff,Proc.Natl.Acad.Sci.USA 89:10915[1992](Henikoff和Henikoff,《美国国家科学院院刊》,第89卷,第10915页,1992年))比对(B)为50,期望值(E)为10,M'5,N'-4,以及对两条链的比较。

[0156] BLAST算法然后对两条序列之间的相似性进行统计分析(参见例如Karlin和Altschul,出处同上)。BLAST算法提供的一种相似性量度是最小合计概率(smallest sum probability,P(N)),其指示两条核苷酸或氨基酸序列之间的匹配会偶然发生的概率。例如,如果在测试核酸与丝氨酸蛋白酶核酸的比较中最小合计概率低于约0.1,更优选低于约0.01,最优选低于约0.001,则该核酸可视为与本发明的丝氨酸蛋白酶核酸相似。在测试核酸编码丝氨酸蛋白酶多肽的情况中,如果比较得到低于约0.5,更优选低于约0.2的最小合计概率,则其视为与指定的丝氨酸蛋白酶核酸相似。

[0157] 在两条或更多条核酸或多肽序列的语境中,"相同"或"同一性"百分数是指,当进行比较和比对以达到最大相似性时,两条或更多条序列是相同的或分别具有指定百分比的相同核酸残基或氨基酸残基,这是使用序列比较算法或通过目测确定的。主题氨基酸序列与参照(即查询)氨基酸序列的"序列同一性百分数"或"同一性%"或"序列同一性%"或"氨基酸序列同一性%"意指当将序列进行最佳比对时,在比较长度上主题氨基酸序列与查询氨基酸序列相同(即以氨基酸比氨基酸计)达指定的百分数。因此,就两条氨基酸序列而言,80%氨基酸序列同一性或80%同一性意指两条最佳比对的氨基酸序列中80%氨基酸残基是相同的。

[0158] 主题核酸序列与参照(即查询)核酸序列的"序列同一性百分数"或"同一性%"或"序列同一性%"或"核苷酸序列同一性%"意指当将序列进行最佳比对时,在比较长度上主题核酸序列与查询序列相同(即以多核苷酸序列的核苷酸比核苷酸计)达指定的百分数。因此,就两条核酸序列而言,80%核苷酸序列同一性或80%同一性意指两条最佳比对的核酸序列中80%核苷酸残基是相同的。

[0159] 在一些实施例中,主题序列与查询序列的"序列同一性百分数"或"序列同一性%"或"同一性%"可通过将两条序列进行最佳比对并在比较长度上比较两条最佳比对的序列来计算。确定在最佳比对中相同的残基出现在两条序列中的位置数目,从而提供匹配位置的数目,然后将匹配位置的数目除以比较长度(除非另外指明,否则其为查询序列的长度)的位置总数。所得的数目乘以100而得到主题序列与查询序列的序列同一性百分数。

[0160] "最佳比对"或"最佳比对的"指两条(或更多条)序列的给出最高同一性百分比分数的比对。例如,可通过将两条蛋白质序列进行手动比对使得每条序列中最大数目的相同氨基酸残基被一起比对,或通过使用本文描述的或本领域已知的软件程序或方法,来实现两条蛋白质序列的最佳比对。可通过将两条核酸序列进行手动比对使得每条序列中最大数目的相同核苷酸残基被一起比对,或通过使用本文描述的或本领域已知的软件程序或方法,来实现两条核酸序列的最佳比对。

[0161] 在一些实施例中,当用限定的参数,例如限定的氨基酸置换矩阵、空位存在罚分(也称为空位开放罚分)和空位延伸罚分来比对两条多肽序列,以实现该对序列可能的最高相似性分数时,这两条多肽序列被认为是"最佳比对的"。在多肽序列比对算法(如BLASTP)中,BLOSUM62打分矩阵(参见Henikoff和Henikoff,出处同上)通常用作默认的打分置换矩阵。施加空位存在罚分以在被比对的序列之一者中引入单个氨基酸空位,并为该空位中的

每一个残基位置施加空位延伸罚分。所采用的示例性比对参数是:BLOSUM62打分矩阵,空位存在罚分=11,空位延伸罚分=1。比对分数由每条序列的该对比开始和结束的氨基酸位置(如比对窗口),以及任选由一条或两条序列中一个空位或多个空位的插入来限定,以实现可能的最高相似性分数。

[0162] 两条或更多条序列之间的最佳比对可通过目测手动来确定,或通过使用计算机,例如但不限于如BLASTP程序(用于氨基酸序列)和BLASTN程序(用于核酸序列)(参见例如Altschul et al.,Nucleic Acids Res.25(17):3389-3402(1997)(Altschul等人,《核酸研究》,第25卷,第17期,第3389-3402页,1997年);还可参见美国国家生物技术信息中心(National Center for Biotechnology Information(NCBI)网站)来确定。

[0163] 如果目的多肽包含与参照多肽的氨基酸序列具有至少约70%、至少约75%、至少约80%、至少约85%、至少约90%、至少约91%、至少约92%、至少约93%、至少约94%、至少约95%、至少约96%、至少约97%、至少约98%、至少约99%或至少约99.5%序列同一性的氨基酸序列,则可称目的多肽与参照多肽"基本上相同"。两条这类多肽之间的同一性百分数可通过检查两条经最佳比对的多肽序列来手动确定,或通过使用软件程序或算法(如BLAST、ALIGN、CLUSTAL)采用标准参数来确定。两条多肽基本上相同的一个指示是第一多肽与第二多肽是免疫交叉反应性的。通常,因保守氨基酸置换而不同的多肽是免疫交叉反应性的。因而,例如在某条多肽与第二多肽仅因保守氨基酸置换或一个或多个保守氨基酸置换而不同的情况中,这两条多肽是基本上相同的。

[0164] 如果目的核酸包含与参照核酸的核苷酸序列具有至少约70%、至少约75%、至少约80%、至少约85%、至少约90%、至少约91%、至少约92%、至少约93%、至少约94%、至少约95%、至少约96%、至少约97%、至少约98%、至少约99%或至少约99.5%序列同一性的核苷酸序列,则可称目的核酸与参照核酸"基本上相同"。两条这类核酸之间的同一性百分数可通过检查两条经最佳比对的核酸序列来手动确定,或通过使用软件程序或算法(如BLAST、ALIGN、CLUSTAL)采用标准参数来确定。两条核酸序列基本上相同的一个指示是这两条核酸分子在严格条件(例如,在中等严格性至高严格性的范围内)下彼此杂交。

[0165] 当核酸或多核苷酸从其他组分(包括但不限于例如其他蛋白质、核酸、细胞等)部分地或完全地分离时,该核酸或多核苷酸是"分离的"。相似地,当多肽、蛋白质或肽从其他组分(包括但不限于例如其他蛋白质、核酸、细胞等)部分地或完全地分离时,该多肽、蛋白质或肽是"分离的"。以摩尔浓度计,在组合物中,分离的物质的丰度比其他物质更高。例如,分离的物质可以占所有存在的大分子物质的至少约50%、约70%、约80%、约85%、约90%、约91%、约92%、约93%、约94%、约95%、约96%、约97%、约98%、约99%或约100%(以摩尔浓度计)。优选地,目的物质纯化为基本上均一的(即通过常规检测方法在组合物中检测不到污染物)。纯度和均一性可以使用本领域熟知的多种技术测定,例如对蛋白质或核酸样品进行琼脂糖或聚丙烯酰胺凝胶电泳,然后染色显示。如果需要,可采用高分辨率技术,例如高效液相色谱法(HPLC)或类似的方法来纯化材料。

[0166] 应用于核酸或多肽的术语"纯化的"一般表示经本领域熟知的分析技术测定,核酸或多肽基本上不含其他组分(例如,纯化的多肽或多核苷酸在电泳凝胶、色谱洗脱物和/或经密度梯度离心的介质中形成离散的条带)。例如,在电泳凝胶中产生基本上一个条带的核酸或多肽是"纯化的"。纯化的核酸或多肽的纯度为至少约50%,通常纯度为至少约75%、约

80％、约85％、约90％、约91％、约92％、约93％、约94％、约95％、约96％、约97％、约98％、约99％、约99.5％、约99.6％、约99.7％、约99.8％或更大(例如以摩尔浓度计的重量％)。在相关的意义上,本发明提供对组合物富集一种或多种本发明的分子,如一种或多种本发明的多肽或多核苷酸的方法。在应用纯化或富集技术后某分子的浓度有实质性增加时,则对组合物富集了该分子。基本上纯的本发明的多肽或多核苷酸(如,分别为基本上纯的本发明变体蛋白酶或编码本发明变体蛋白酶的多核苷酸)通常将占特定组合物中的所有大分子物质重量(以摩尔浓度计)的至少约55％、约60％、约70％、约80％、约85％、约90％、约91％、约92％、约93％、约94％、约95％、约96％、约97％、约98、约99％、约99.5％或更高。

[0167] 在相关的意义上,本发明提供对组合物富集一种或多种本发明的分子,如一种或多种本发明的多肽(例如一种或多种本发明的变体蛋白酶)或一种或多种本发明的核酸(例如一种或多种编码一种或多种本发明变体蛋白酶的核酸)的方法。在应用纯化或富集技术后某分子的浓度有实质性增加时,则对组合物富集了该分子。基本上纯的多肽或多核苷酸通常将占特定组合物中的所有大分子物质重量(以摩尔浓度计)的至少约55％、约60％、约70％、约80％、约85％、约90％、约91％、约92％、约93％、约94％、约95％、约96％、约97％、约98、约99％、约99.5％或更高。

[0168] 本文所用的术语“组合诱变”或“组合”指产生参照核酸序列的核酸变体的文库的方法。在这些文库中,变体含有一个或数个选自一组预定突变的突变。这类方法还提供引入随机突变的手段,这些随机突变不是该预定突变组的成员。一些此类方法包括在美国专利No.6,582,914中示出的那些方法,该专利以引用的方式并入本文。一些此类组合诱变方法包括和/或涵盖在市售试剂盒(例如QUIKCHANGE®多定点诱变试剂盒(Stratagene公司),PCR融合/延伸PCR)中体现的方法。

[0169] 如本文所用,结合变体蛋白酶使用的“具有改善的特性”是指相对于对应的参照蛋白酶(例如野生型或天然存在的蛋白酶)而言,变体蛋白酶具有改善的或增强的洗涤或清洁性能,和/或具有改善的或增强的稳定性并任选地保持了洗涤或清洁性能。变体蛋白酶的改善的特性可以包括改善的洗涤或清洁性能和/或改善的稳定性。在一些实施例中,本发明提供表现出以下特性中的一者或多者的本发明变体蛋白酶:相对于参照蛋白酶(例如,野生型蛋白酶,如野生型枯草杆菌蛋白酶)而言改善的手动洗涤性能、改善的手动或人工盘碟洗涤性能、改善的自动盘碟洗涤性能、改善的衣物洗涤性能和/或改善的稳定性。

[0170] 本文所用的术语“功能测定法”指提供蛋白质活性的指示的测定法。在一些实施例中,该术语是指其中针对蛋白质以其惯常的本领发挥作用的能力对该蛋白质进行分析的测定系统。例如,就酶而言,功能测定法涉及测定该酶催化反应的有效性。

[0171] 本文所用的术语“靶性质”是指要改变的起始基因的性质。无意于将本发明局限于任何特定的靶性质。然而,在一些实施例中,靶性质是基因产物的稳定性(如,对变性、蛋白水解或其他降解因素的抵抗),而在其他实施例中,在生产宿主中的生产水平被改变。

[0172] 如本文所用,在核酸的语境中,术语“性质”或其语法等同形式是指可选择或检测的核酸的任何特性或属性。这些性质包括但不限于影响与多肽的结合的性质、被赋予到包含特定核酸的细胞上的性质、影响基因转录的性质(如,启动子强度、启动子识别、启动子调控、增强子功能)、影响RNA加工的性质(如,RNA剪接、RNA稳定性、RNA构象和转录后修饰)、影响翻译的性质(如mRNA的水平、调控、与核糖体蛋白的结合、翻译后修饰)。例如,可以改变核

酸的转录因子、聚合酶、调节因子等的结合位点以产生所需的特性或鉴别不期望的特性。

[0173] 如本文所用，在多肽(包括蛋白质)的语境中，术语“性质”或其语法等同形式是指可选择或检测的多肽的任何特性或属性。这些性质包括但不限于氧化稳定性、底物特异性、催化活性、酶活性、热稳定性、碱稳定性、pH活性分布、对蛋白降解的抗性、K_M、k_{cat}、k_{cat}/k_M比率、蛋白质折叠、诱导免疫应答、与配体结合的能力、与受体结合的能力、被分泌的能力、在细胞表面上展示的能力、低聚化的能力、信号传导的能力、刺激细胞增殖的能力、抑制细胞增殖的能力、诱导细胞凋亡的能力、被磷酸化或糖基化作用修饰的能力和/或治疗疾病的能力等。

[0174] 本文所用的术语“筛选”具有其在本领域中的通常含义。在一个示例性筛选方法中，提供了突变体核酸或由其编码的变体多肽，并且分别评估或测定了该突变体核酸或变体多肽的性质。可将突变体核酸或变体多肽的测定性质分别与对应的前体(亲本)核酸的性质或对应的亲本多肽的性质比较。

[0175] 对技术人员而言将显而易见的是，获得具有改变的性质的核酸或蛋白质的筛选程序取决于原料性质，突变体核酸的产生旨在促进对原料性质的修饰。因此，技术人员将认识到，本发明不限于要筛选的任何具体性质，并且以下性质描述仅列举了示例性的例子。筛选任何特定性质的方法通常在本领域中有所描述。例如，可在突变之前和之后测量结合性、pH、特异性等，其中的变化表明发生了变更。优选地，筛选以高通量方式进行，包括同时筛选多个样品，包括但不限于利用芯片、噬菌体展示以及多种底物和/或指示剂的测定法。

[0176] 如本文所用，在一些实施例中，筛选方法涵盖一个或多个选择步骤，以从一群变体中富集目的变体。这些实施例的例子包括对赋予宿主生物生长优势的变体的选择，以及噬菌体展示或任何其他展示方法，其中变体可根据其结合或催化性质从一群变体捕集。在一些实施例中，将变体库暴露于胁迫(如热、变性等)，随后对仍然完整的变体在筛选中进行鉴定或通过选择进行富集。意在使该术语涵盖任何合适的选择手段。实际上，无意于将本发明限制于任何特定的筛选方法。

[0177] 术语“经修饰的核酸序列”和“经修饰的基因”在本文中可互换使用，是指包含天然存在的(即野生型)核酸序列的缺失、插入或中断的核酸序列。在一些实施例中，经修饰的核酸序列的表达产物是截短的蛋白质(例如，如果该修饰为序列的缺失或中断的话)。在一些实施例中，截短的蛋白质保持生物活性。在另选的实施例中，经修饰的核酸序列的表达产物是延长的蛋白质(例如，修饰包括向核酸序列中的插入)。在一些实施例中，核苷酸插入核酸序列中会导致截短的蛋白质(例如，当插入导致形成终止密码子时)。因此，插入可以产生截短的蛋白质或延长的蛋白质作为表达产物。

[0178] “突变型”核酸序列通常指这样的核酸序列，其在宿主细胞的野生型序列中存在的至少一个密码子中具有改变，使得该突变型核酸序列的表达产物是相对于野生型蛋白质而言具有改变的氨基酸序列的蛋白质。表达产物可具有改变的功能本领(例如增强的酶活性)。

[0179] 如本文所用，词语“底物特异性的改变”是指酶的底物特异性的变化。在一些实施例中，底物特异性的变化被定义为由于酶的突变或反应条件的改变而导致的特定底物的k_{cat}和/或K_m的变化。通过比较酶表现出的对不同底物的催化效率，来确定酶的底物特异性。这些测定尤其可用于评估突变酶的效率，因为通常期望产生对目的底物表现出更大k_{cat}/K_m

比率的变体酶。然而，无意于将本发明限制于任何特定的底物组合物或底物特异性。

[0180] 如本文所用，“表面性质”用于指静电荷，以及蛋白质的表面所展现的诸如疏水性和亲水性之类的性质。

[0181] 本文所用的术语“净电荷”被定义为分子中存在的所有电荷的总和。可对亲本蛋白质分子作出“净电荷改变”，以提供具有与该亲本分子的净电荷不同的净电荷的变体(即该变体具有的净电荷与亲本分子的净电荷不相同)。例如，用带负电的氨基酸置换中性氨基酸或用中性氨基酸置换带正电的氨基酸，会导致相对于亲本分子而言净电荷为-1。用带负电的氨基酸置换带正电的氨基酸，会导致相对于亲本而言净电荷为-2。用带正电的氨基酸置换中性氨基酸或用中性氨基酸置换带负电的氨基酸，会导致相对于亲本而言净电荷为+1。用带正电的氨基酸置换带负电的氨基酸，会导致相对于亲本而言净电荷为+2。亲本蛋白质的净电荷还可通过缺失和/或插入带电的氨基酸来改变。

[0182] 术语“热稳定的”和“热稳定”和“热稳定性”是指蛋白酶在本发明的蛋白水解、水解、清洁或其他处理期间的主要条件下(同时暴露于改变的温度)，暴露于指定的温度达给定时间段后仍保持指定量的酶活性。“改变的温度”涵盖增加的或降低的温度。在一些实施例中，蛋白酶在暴露于改变的温度达给定时间段(例如至少约60分钟、约120分钟、约180分钟、约240分钟、约300分钟等)后保持至少约50％、约60％、约70％、约75％、约80％、约85％、约90％、约92％、约95％、约96％、约97％、约98％或约99％的蛋白水解活性。

[0183] 在氧化、螯合剂、热和/或pH稳定性蛋白酶的语境中，术语“增强的稳定性”是指与其他蛋白酶(例如枯草杆菌蛋白酶)和/或野生型酶相比，随时间推移保持了更高的蛋白水解活性。

[0184] 在氧化、螯合剂、热和/或pH稳定性蛋白酶的语境中，术语“降低的稳定性”是指与其他蛋白酶(例如枯草杆菌蛋白酶)和/或野生型酶相比，随时间推移保持了更低的蛋白水解活性。

[0185] 术语“清洁活性”是指在本发明的蛋白水解、水解、清洁或其他处理期间的主要条件下，变体蛋白酶或参照蛋白酶实现的清洁性能。在一些实施例中，变体蛋白酶或参照蛋白酶的清洁性能可以使用用于清洁物品或表面上的一种或多种不同的酶敏感性污渍(例如来自食物、草、血、墨、奶、油和/或卵蛋白的污渍)的各种测定法来测定。变体或参照蛋白酶的清洁性能可通过使物品或表面上的污渍经受标准洗涤条件，并且使用各种色谱方法、分光光度方法或其他定量方法评估污渍被移除的程度来测定。示例性的清洁测定法和方法是本领域已知的，包括但不限于WO 99/34011和美国专利6,605,458(这二个专利均以引用方式并入本文)中描述的那些方法以及下文提供的实例中包括的那些清洁测定法和方法。

[0186] 术语变体蛋白酶或参照蛋白酶的“清洁有效量”是指在特定清洁组合物中实现所需水平的酶活性的蛋白酶的量。这种有效量可由本领域一般技术人员容易地确定并且基于多种因素，如所用的特定蛋白酶、清洁应用、清洁组合物的具体组成，以及是需要液体组合物还是干燥(例如颗粒状、片状、条棒状)组合物等等。

[0187] 术语“清洁辅助材料”是指清洁组合物中包含的除本发明变体蛋白酶之外的任何液体、固体或气体材料。在一些实施例中，本发明的清洁组合物包括一种或多种清洁辅助材料。每种清洁辅助材料通常根据清洁组合物的具体类型和形式(例如液体、颗粒、粉末、条、糊、喷雾、片、凝胶、泡沫或其他组合物)来选择。优选地，每种清洁辅助材料与组合物中所用

的蛋白酶相容。

[0188] 在清洁活性的语境中术语“增强的性能”是指酶对某些酶敏感性污渍如蛋、奶、草、墨、油和/或血的增加的或更高的清洁活性，这种活性是在标准的洗涤循环和/或多个洗涤循环后通过常用的评价法来测定的。

[0189] 在清洁活性的语境中术语“降低的性能”是指酶对某些酶敏感性污渍如蛋、奶、草或血的降低的或较小的清洁活性，这种活性是在标准的洗涤循环后通过常用的评价法来测定的。

[0190] 在本发明变体蛋白酶的清洁活性语境中，术语“相当的性能”是指比较或参照蛋白酶(如市售蛋白酶)的清洁活性的至少约60％、至少约70％、至少约75％、至少约80％、至少约85％、至少约90％、至少约91％、至少约92％、至少约93％、至少约94％、至少约95％、至少约96％、至少约97％、至少约98％、至少约99％、至少约99.5％，所述比较或参照蛋白酶包括但不限于例如OPTIMASE™蛋白酶(杰能科公司(Genencor))、PURAFECT™蛋白酶产品(杰能科公司(Genencor))、SAVINASE™蛋白酶(诺维信公司(Novozymes))、BPN’-变体(参见例如美国专利No.Re 34,606)、RELASE™、DURAZYME™、EVERLASE™、KANNASE™蛋白酶(诺维信公司(Novozymes))、MAXACAL™、MAXAPEM™、PROPERASE™蛋白酶(杰能科公司(Genencor)；还可参见美国专利No.Re 34,606和美国专利No.5,700,676、No.5,955,340、No.6,312,936和No.6,482,628)和迟缓芽孢杆菌变体蛋白酶产品(例如WO 92/21760、WO 95/23221和/或WO 97/07770中描述的那些)。可如下测定清洁性能：在涉及酶敏感性污渍(例如草、血、墨、油和/或奶)的各种清洁测定法中，将本发明变体蛋白酶与参照枯草杆菌蛋白酶进行比较，如在标准洗涤循环条件后通过常用的分光光度测定或分析法来测定。

[0191] 本文所用的术语“消费品”意指织物和家庭护理产品。本文所用的术语“织物和家庭护理产品”或“织物和家居护理产品”包括通常旨在以其销售形式使用或消耗并且用于处理织物、硬质表面和任何其他表面的产品，及所有用于无生命表面的护理和清洁的清洁系统，以及织物调理剂产品和其他特别设计用于织物的护理和维护的产品，以及空气护理产品，包括：空气护理(包括空气清新剂和气味传送系统)、汽车护理、宠物护理、牲畜护理、个人护理、珠宝护理、盘碟洗涤、织物调理(包括软化和/或清新)、衣物去垢、衣物洗涤和漂洗添加剂和/或护理剂、预处理清洁组合物、硬质表面清洁和/或处理，所述硬质表面清洁和/或处理包括地板和抽水马桶清洁剂、玻璃清洁剂和/或处理剂、瓷砖清洁剂和/或处理剂、陶瓷清洁剂和/或处理剂以及其他消费或公共场所用途的清洁剂。在一些实施例中，织物和家庭护理产品适用于伤口和/或皮肤。“织物和家庭护理产品”包括消费和公共场所产品。

[0192] 本文所用的术语“非织物和家庭护理产品”是指这样的组合物，其被添加至其他组合物中以产生可以为织物和家庭护理产品的最终产品。

[0193] 本文所用的术语“公共场所用清洁组合物”是指适用于公共场所的产品，公共场所包括但不限于学校、医院、工厂、商场、公司、建筑物、餐馆、办公楼和商厦、加工和/或制造车间、兽医院、工厂化农场、工厂化牧场等)。

[0194] 本文所用的术语“清洁和/或处理组合物”是指织物和家庭护理产品的这样的子集，除非另外指明，该子集包括适用于清洁和/或处理物品的组合物。此类产品包括但不限于用于处理织物和家庭护理领域中的织物、硬质表面和任何其他表面的产品，包括：空气护理(包括空气清新剂和气味传送系统)、汽车护理、盘碟洗涤、织物调理(包括软化和/或清

新)、衣物去垢、衣物洗涤和漂洗添加剂和/或护理剂、硬质表面清洁和/或处理,所述硬质表面清洁和/或处理包括地板和抽水马桶清洁剂、颗粒状或粉末形式的多功能或“重垢型”洗涤剂,尤其是清洁洗涤剂;液体、凝胶或糊剂形式多功能洗涤剂,尤其是所谓的重垢型液体类型;液体精细织物洗涤剂;手动盘碟洗涤剂或轻垢型盘碟洗涤剂,尤其是那些高泡类型;机器盘碟洗涤剂,包括用于家居和公共场所用途的各种片剂、颗粒、液体和漂洗助剂类型:汽车或地毯清洗剂、浴室清洁剂(包括抽水马桶清洁剂);以及清洁辅剂例如漂白添加剂和“去污棒”或预处理类型,填充有基质的产品例如添加有干燥剂的片材。

[0195] 实际上,如本文所用,本发明的“清洁组合物”或“清洁制剂”是指任何可用于从待清洁的物体、物品或表面移除或除去化合物(如不需要的化合物)的本发明组合物,所述待清洁的物体、物品或表面包括但不限于,例如织物、织物物品、盘碟物品、餐具物品、玻璃器具物品、接触镜、其他固体基材、毛发(洗发剂)(包括人或动物毛发)、皮肤(肥皂或/和霜剂)、牙齿(漱口水、牙膏)、物品或物体的表面(如硬质表面,例如桌子的硬质表面、桌面、墙壁、家具物品、地板、天花板、非盘碟物品、非餐具物品等)、过滤器、膜(如过滤膜,包括但不限于超滤膜)等。该术语涵盖为所需清洁组合物的特定类型和产品的形式(如液体、凝胶、颗粒、喷雾或其他组合物)选择的任何材料和/或添加的化合物,只要该组合物与用于组合物的蛋白酶和其他酶相容即可。易于通过考虑待清洁的表面、物体、物品或织物以及对使用期间的清洁条件理想的组合物形式,来具体选择清洁组合物材料。

[0196] 清洁组合物和清洁制剂包括任何适于对任何物体、物品和/或表面进行清洁、漂白、消毒和/或灭菌的组合物。此类组合物和制剂包括但不限于例如液体和/或固体组合物,包括清洁或洗涤剂组合物(如液体、片剂、凝胶、条棒、颗粒和/或固体衣物清洁或洗涤剂组合物和精细织物洗涤剂组合物;硬质表面清洁组合物和制剂,例如用于玻璃、木材、陶瓷和金属台面和窗户;地毯清洁剂;烘箱清洁剂;织物清新剂;织物软化剂;以及纺织物、衣物助洗剂清洁或洗涤剂组合物、衣物洗涤添加剂清洁组合物和衣物预洗剂清洁组合物;盘碟洗涤组合物,包括手动或人工盘碟洗涤组合物(如“手动”或“人工”盘碟洗涤剂)和自动盘碟洗涤组合物(如“自动盘碟洗涤剂”)。

[0197] 如本文所用,除非另外指明,否则清洁组合物或清洁制剂包括颗粒或粉末形式的通用或重垢型洗涤剂,尤其是清洁洗涤剂;液体、颗粒、凝胶、固体、片剂或糊剂形式的通用洗涤剂,尤其是所谓的重垢型液体(HDL)洗涤剂或重垢型粉末洗涤剂(HDD)类型;液体精细织物洗涤剂;手动或人工盘碟洗涤剂,包括那些高泡类型;手动或人工盘碟洗涤、自动盘碟洗涤、或盘碟或餐具洗涤剂,包括用于家居和公共场所用途的各种片剂、粉末、固体、颗粒、液体、凝胶和漂洗助剂类型;液体清洁和消毒剂,包括抗菌手动洗涤类型、清洁条棒、漱口水、假牙清洁剂、汽车清洗剂、地毯清洗剂、浴室清洁剂;人和其他动物的洗发剂和/或毛发清洗剂;沐浴凝胶和泡沫浴和金属清洁剂;以及清洁辅剂,例如漂白添加剂和“去污棒”或预处理类型。在一些实施例中,颗粒状组合物为“致密”形式;在一些实施例中,液体组合物为“浓缩”形式。

[0198] 如本文所用,“织物清洁组合物”包括手洗和机洗衣物洗涤剂组合物,包括洗衣添加剂组合物和适用于染污织物(如衣物、亚麻布和其他纺织材料)的浸洗和/或预处理的组合物在内。

[0199] 如本文所用,“非织物清洁组合物”包括非纺织物(即非织物)表面清洁组合物,包

括但不限于例如手动或人工或自动盘碟洗涤剂组合物、口腔清洁组合物、假牙清洁组合物和个人清洁组合物。

[0200] 本文所用的术语“织物和/或硬质表面清洁和/或处理组合物”是清洁和处理组合物的子集，除非另外指明，否则其包括颗粒或粉末形式的通用或“重垢型”洗涤剂，尤其是清洁洗涤剂；液体、凝胶或糊剂形式的通用洗涤剂，尤其是所谓的重垢型液体类型；液体精细织物洗涤剂；手动盘碟洗涤剂或轻垢型盘碟洗涤剂，尤其是那些高泡类型；机器盘碟洗涤剂，包括用于家居和公共场所用途的各种片剂、颗粒、液体和漂洗助剂类型：液体清洁和消毒剂、汽车或地毯清洗剂、浴室清洁剂(包括抽水马桶清洁剂)；织物调理产品，包括可为液体、固体和/或干燥剂片材形式的软化和/或清新产品；以及清洁辅剂例如漂白添加剂和“去污棒”或预处理类型，填充有基质的产品例如添加有干燥剂的片材。所有此类适用的产品可以是标准、浓缩或甚至高浓缩形式，甚至浓缩到使此类产品在某些方面为非水性的程度。

[0201] 本文所用的术语“洗涤剂组合物”或“洗涤剂制剂”用于指旨在用于洗涤介质中用来清洁染污的或脏的物体(包括特定的织物和/或非织物物体或物品)的组合物。本发明的这类组合物不限于任何特定的洗涤剂组合物或制剂。实际上，在一些实施例中，本发明的洗涤剂包含至少一种本发明的变体蛋白酶，此外还包含一种或多种表面活性剂、转移酶、水解酶、氧化还原酶、助洗剂(例如助洗剂盐)、漂白剂、漂白活化剂、上蓝剂、荧光染料、结块抑制剂、掩蔽剂、酶激活剂、抗氧化剂和/或增溶剂。在某些情况下，助洗剂盐为硅酸盐和磷酸盐的混合物，优选硅酸盐(如偏硅酸钠)比磷酸盐(如三聚磷酸钠)多。本发明的一些组合物(例如但不限于清洁组合物或洗涤剂组合物)不含有任何磷酸盐(如磷酸盐或磷酸盐助洗剂)。

[0202] 本文所用的术语“漂白”是指以足够的时长和/或在合适的pH和/或温度条件下处理材料(如织物、衣物、纸浆等)或表面以实现该材料的增亮(增白)和/或清洁。适用于漂白的化学品的例子包括但不限于例如ClO_2、H_2O_2、过酸、NO_2等。

[0203] 如本文所用，蛋白酶(如本发明的变体蛋白酶)的“洗涤性能”是指变体蛋白酶对洗涤的贡献，与未向组合物中添加该变体蛋白酶的洗涤剂相比该贡献为洗涤剂提供额外的清洁性能。洗涤性能是在相关的洗涤条件下进行比较。在一些测试系统中，其他相关因素(如洗涤剂组成、泡沫浓度、水硬度、洗涤力学、时间、pH和/或温度)可以以使得某些细分市场中的家居应用(手动或人工盘碟洗涤、自动盘碟洗涤、盘碟清洁、餐具清洁、织物清洁等)的典型条件得以模拟的方式进行控制。

[0204] 术语“相关洗涤条件”在本文中用于表示在手动盘碟洗涤、自动盘碟洗涤或衣物洗涤剂细分市场中在家庭中实际上使用的条件，特别是洗涤温度、时间、洗涤力学、泡沫浓度、洗涤剂类型和水硬度。

[0205] 术语“改善的洗涤性能”用于表示在相关洗涤条件下在去污方面获得更好的最终结果，或以重量计，相对于相应的野生型或起始亲本蛋白酶，需要较少的变体蛋白酶来获得相同的最终结果。

[0206] 本文所用的术语“消毒”是指从表面除去污染物，以及抑制或杀死物品表面上的微生物。无意于将本发明限制于任何特定表面、物品或待移除的污染物或微生物。

[0207] 本文的清洁组合物的“致密”形式最好由密度反映，就组成来说，由无机填料盐的量反映。无机填料盐是呈粉末形式的洗涤剂组合物的常规成分。在常规洗涤剂组合物中，填料盐是大量存在，通常占总组合物的约17重量％至约35重量％。相比之下，在致密型组合物

中，填料盐以不超过总组合物的约15％的量存在。在一些实施例中，填料盐以不超过组合物的约10重量％，或更优选不超过约5重量％的量存在。在一些实施例中，无机填料盐选自碱金属和碱土金属硫酸盐和氯化物。在一些实施例中，填料盐为硫酸钠。

[0208] 在本文中，给定氨基酸序列中氨基酸残基的位置通常利用SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'氨基酸序列的对应氨基酸残基的位置的编号方式进行编号。SEQ ID NO:1的解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'氨基酸序列因而充当参照序列。可利用本文所述的比对算法将给定氨基酸序列(例如本文描述的变体蛋白酶氨基酸序列)与BPN'序列(SEQ ID NO:1)比对，该给定氨基酸序列中与BPN'序列中的氨基酸残基比对(优选最佳比对)的氨基酸残基可通过参照该枯草杆菌蛋白酶BPN'序列中的对应氨基酸残基便利地进行编号。或者，如果枯草杆菌蛋白酶变体蛋白酶序列的氨基酸残基位置利用GG36氨基酸序列(SEQ ID NO:2)中的氨基酸残基位置的实际编号方式进行编号，并且在比对时不参照BPN'序列中的对应氨基酸位置，则枯草杆菌蛋白酶变体蛋白酶可描述为SEQ ID NO:2所示的GG36蛋白酶的变体蛋白酶。

[0209] 一般来讲，本文所用的命名以及下文描述的细胞培养、分子遗传学、分子生物学、核酸化学和蛋白质化学中的实验室方法中的许多方法是众所周知的，并常常为本领域一般技术人员所采用。重组核酸的产生和操纵的方法、核酸合成的方法、细胞培养方法以及转基因掺入(如转染、电穿孔)是本领域技术人员已知的并在许多标准文献中有描述。寡核苷酸合成和纯化步骤通常根据说明书来进行。技术和程序通常根据本领域众所周知的常规方法以及本文通篇中提供的各种一般文献来进行。其中的程序据信是本领域普通技术人员所熟知的，并为了阅读者的便利而提供。

[0210] 本发明的多肽

[0211] 本发明提供新型多肽，这些多肽可统称为“本发明的多肽”。本发明的多肽包括分离的、重组的、基本上纯的或非天然存在的变体蛋白酶多肽，包括例如具有酶活性(如蛋白水解活性)的变体枯草杆菌蛋白酶多肽。在一些实施例中，本发明的多肽可用于清洁应用，并且可掺入可在清洁需要进行清洁的物品或表面(如物品的表面)的方法中使用的清洁组合物中。

[0212] 在一些实施例中，本发明的变体蛋白酶包括“变体枯草杆菌蛋白酶”。在一些实施例中，本发明提供“芽孢杆菌变体蛋白酶”。在一些实施例中，本发明提供“芽孢杆菌变体枯草杆菌蛋白酶”。

[0213] 在一些实施例中，本发明包括分离的、重组的、基本上纯的或非天然存在的具有蛋白水解活性的变体蛋白酶，该蛋白酶多肽包含与编码本文提供的变体蛋白酶的氨基酸序列具有至少约85％、至少约86％、至少约87％、至少约88％、至少约89％、至少约90％、至少约91％、至少约92％、至少约93％、至少约94％、至少约95％、至少约96％、至少约97％、至少约98％、至少约99％、至少约99.5％或100％序列同一性的多肽序列。

[0214] 如上所述，本发明的变体蛋白酶多肽具有酶活性(如蛋白水解活性)并且因而可用于清洁应用，包括但不限于用于清洁盘碟物品、餐具物品、织物和具有硬质表面的物品(如桌子、桌面、墙壁、家具物品、地板、天花板等的硬质表面)的方法。包含一种或多种本发明的变体蛋白酶多肽的示例性清洁组合物在下文中进行描述。本发明的变体蛋白酶多肽的酶活性(如蛋白酶活性)可使用本领域普通技术人员熟知的程序容易地测定。下文给出的实例部

分描述了用于评价酶活性、清洁性能和/或洗涤性能的方法。本发明的变体蛋白酶在移除污渍(例如蛋白质性质的污渍)、清洁硬质表面或清洁衣物、盘碟或餐具物品方面的性能可用本领域所熟知的程序和/或通过使用实例部分中示出的程序容易地测定。

[0215] 可对本发明的多肽作出各种变化,如一个或多个氨基酸的插入、缺失和/或置换(保守的或非保守的置换),包括其中这类变化不会实质上改变该多肽的酶活性的情况。类似地,也可对本发明的核酸作出各种变化,如在一个或多个密码子中对一个或多个核酸进行一种或多种置换使得特定的密码子编码相同或不同的氨基酸,从而导致沉默变异(如,核苷酸序列中的突变可导致氨基酸序列中的沉默突变,例如当所编码的氨基酸未因该核酸突变而改变时)或非沉默变异;序列中一个或多个核酸(或密码子)的一种或多种缺失;序列中一个或多个核酸(密码子)的一种或多种添加或插入;和/或序列中一个或多个核酸(密码子)的切除或序列中一个或多个核酸(密码子)的一种或多种截短。与原始核酸序列编码的变体蛋白酶相比,核酸序列中的许多此类变化可能不会实质上改变所得的编码的变体蛋白酶的酶活性。还可对本发明的核酸进行修饰以包括一个或多个使得能在表达系统(如细菌表达系统)中进行最佳表达的密码子,同时如果需要,所述一个或多个密码子仍编码相同氨基酸。

[0216] 在一些实施例中,本发明提供这样一类多肽,其包括具有所需酶活性(如蛋白酶活性或清洁性能活性)的变体蛋白酶多肽,所述变体蛋白酶多肽包含具有本文所述的氨基酸置换的序列并且还包含一个或多个另外的氨基酸置换,例如保守和非保守置换,其中多肽表现出、维持或大致维持所需的酶活性(如蛋白酶活性或枯草杆菌蛋白酶活性,如该变体蛋白酶的清洁活性或性能所反映的)。根据本发明的氨基酸置换可包括但不限于一个或多个非保守置换和/或一个或多个保守氨基酸置换。保守氨基酸残基置换通常涉及将一个功能类别的氨基酸残基中的成员替换为属于同一功能类别的残基(在计算功能同源性百分数时相同氨基酸残基被视为在功能上是同源的或保守的)。保守氨基酸置换通常涉及用功能相似的氨基酸置换氨基酸序列中的氨基酸。例如,丙氨酸、甘氨酸、丝氨酸和苏氨酸是功能相似的,因而可充当彼此的保守氨基酸置换。天冬氨酸和谷氨酸可充当彼此的保守置换。天冬酰胺和谷氨酰胺可充当彼此的保守置换。精氨酸、赖氨酸和组氨酸可充当彼此的保守置换。异亮氨酸、亮氨酸、甲硫氨酸和缬氨酸可充当彼此的保守置换。苯丙氨酸、酪氨酸和色氨酸可充当彼此的保守置换。

[0217] 可以设想其他的保守氨基酸置换组。例如,可通过相似的功能或化学结构或组成对氨基酸进行分组(如酸性、碱性、脂族、芳族、含硫氨基酸)。例如,脂族分组可以包括:甘氨酸(G)、丙氨酸(A)、缬氨酸(V)、亮氨酸(L)、异亮氨酸(I)。包含被视为彼此的保守置换的氨基酸的其他分组包括:芳族:苯丙氨酸(F)、酪氨酸(Y)、色氨酸(W);含硫:甲硫氨酸(M)、半胱氨酸(C);碱性:精氨酸(R)、赖氨酸(K)、组氨酸(H);酸性:天冬氨酸(D)、谷氨酸(E);非极性不带电残基:半胱氨酸(C)、甲硫氨酸(M)和脯氨酸(P);亲水性不带电残基:丝氨酸(S)、苏氨酸(T)、天冬酰胺(N)和谷氨酰胺(Q)。另外的氨基酸分组是本领域技术人员所熟知的并在各种标准教科书中有描述。本文的多肽序列的列表,结合上文的置换组,提供了所有保守置换的多肽序列的明确列表。

[0218] 在上文描述的氨基酸残基类别中存在更保守的置换,其也可以是合适的或者其作为另一种选择可以是合适的。更保守置换的保守组包括:缬氨酸-亮氨酸-异亮氨酸、苯丙氨

酸-酪氨酸、赖氨酸-精氨酸、丙氨酸-缬氨酸和天冬酰胺-谷氨酰胺。因此，例如在一些实施例中，本发明提供分离或重组的具有蛋白水解活性的变体蛋白酶多肽(如变体枯草杆菌蛋白酶)，所述变体蛋白酶多肽包含与SEQ ID NO:2的氨基酸序列具有至少约90％、约95％、约96％、约97％、约98％、约99％或约99.5％序列同一性的氨基酸序列。本发明的变体蛋白酶中一个氨基酸保守置换另一个氨基酸预计不会显著改变该变体蛋白酶的酶活性或清洁性能活性。所得的蛋白酶的酶活性或清洁性能活性可容易地用标准测定法和本文所述的测定法进行测定。

[0219] 本发明的多肽序列(例如本发明的变体蛋白酶)的保守置换变异包括用相同保守置换组的保守选择氨基酸来置换该多肽序列的少部分的，有时低于约25％、约20％、约15％、约14％、约13％、约12％、约11％、约10％、约9％、约8％、约7％或约6％的氨基酸，或该多肽序列的低于约5％、约4％、约3％、约2％或约1％的氨基酸。

[0220] 如本文其他地方更详细描述的以及本文提供的实例部分中描述的，本发明的多肽可具有可与已知蛋白酶(包括已知枯草杆菌蛋白酶)相当的清洁能力。示例性的已知枯草杆菌蛋白酶包括但不限于例如迟缓芽孢杆菌枯草杆菌蛋白酶GG36、解淀粉芽孢杆菌枯草杆菌蛋白酶BPN’、解淀粉芽孢杆菌枯草杆菌蛋白酶BPN’-Y217L，和克劳氏芽孢杆菌PB92。成熟迟缓芽孢杆菌枯草杆菌蛋白酶GG36蛋白的氨基酸序列为：

[0221] AQSVPWGISRVQAPAAHNRGLTGSGVKVAVLDTGISTHPDLNIRGGASFVPGEPSTQDGNGHGTHVAGTIAALNNSIGVLGVAPSAELYAVKVLGASGSGSVSSIAQGLEWAGNNGMHVANLSLGSPSPSATLEQAVNSATSRGVLVVAASGNSGAGSISYPARYANAMAVGATDQNNNRASFSQYGAGLDIVAPGVNVQSTYPGSTYASLNGTSMATPHVAGAAALVKQKNPSWSNVQIRNHLKNTATSLGSTNLYGSGLVNAEAATR(SEQ ID NO:2)

[0222] 成熟解淀粉芽孢杆菌枯草杆菌蛋白酶BPN’蛋白的氨基酸序列为：

[0223] AQSVPYGVSQIKAPALHSQGYTGSNVKVAVIDSGIDSSHPDLKVAGGASMVPSETNPFQDNNSHGTHVAGTVAALNNSIGVLGVAPSASLYAVKVLGADGSGQYSWIINGIEWAIANNMDVINMSLGGPSGSAALKAAVDKAVASGVVVVAAAGNEGTSGSSSTVGYPGKYPSVIAVGAVDSSNQRASFSSVGPELDVMAPGVSIQSTLPGNKYGAYNGTSMASPHVAGAAALILSKHPNWTNTQVRSSLENTTTKLGDSFYYGKGLINVQAAAQ(SEQ ID NO:1)

[0224] 本发明提供包含芽孢杆菌属枯草杆菌蛋白酶的枯草杆菌蛋白酶变体的多肽，其中该枯草杆菌蛋白酶变体是具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:X1R,X2W,X2M,X2R,X2A,X2S,X3R,X4R,X4C,X4S,X8A,X9F,X9W,X9A,X10S,X10M,X10H,X10A,X12R,X12F,X14K,X14F,X14Q,X15R,X15F,X16S,X17R,X17M,X17F,X18R,X18K,X20F,X20R,X20K,X22Y,X22A,X22R,X22V,X22Q,X22W,X22L,X23F,X23S,X23A,X24W,X24R,X24H,X24F,X24Q,X24L,X25V,X25F,X25R,X26F,X27V,X27F,X27L,X27R,X28N,X28E,X28A,X29T,X30E,X31F,X33D,X33G,X33S,X34P,X35M,X36F,X36R,X36T,X38L,X38F,X38R,X40L,X40W,X40N,X40R,X40T,X40H,X42I,X43D,X43I,X43R,X43M,X43F,X43W,X43S,X43A,X45T,X46R,X48R,X50C,X51H,X51W,X51F,X52F,X52E,X52N,X55Y,X57R,X59R,X59A,X59F,X60A,X60Q,X60P,X62E,X62Q,X63I,X63V,X63T,X63P,X63D,X63M,X63H,X63Q,X63E,X63A,X63S,X64F,X64T,X68C,X68A,X69N,X69P,X69W,X69T,X71G,X72C,X74C,X75F,X75A,X75R,X75E,X76D,X78I,X78R,X78N,X79W,X79Q,X81R,X82V,X82T,X82F,X82M,X82R,X85M,X86L,X86I,X86W,X89P,X89T,X89V,X89G,X89W,X89H,X89F,X89L,X89I,X91N,X91F,X92F,X94N,X99G,X99F,X99M,X99T,X99P,X100I,X100S,X100N,X100Q,X101N,X101A,X101G,

X101P,X101F,X101E,X101T,X101D,X102H,X102N,X102E,X102T,X102A,X103G,X103D,X103N,X104D,X104E,X104I,X104L,X105Q,X105E,X105T,X106F,X106V,X106G,X106E,X106T,X106D,X106A,X107F,X107M,X108G,X108I,X109M,X111V,X111I,X112V,X112L,X112Q,X114G,X115K,X115R,X116A,X116K,X116L,X117F,X118I,X118R,X119C,X120F,X120A,X120R,X121E,X121F,X123G,X123E,X124S,X128F,X128H,X128I,X128L,X128Q,X128N,X128M,X128D,X129E,X132E,X132A,X138G,X144R,X147L,X148I,X158E,X158E,X159E,X159C,X160D,X166D,X166E,X167W,X175V,X177C,X181A,X182R,X183F,X183I,X183D,X183R,X183M,X185E,X185I,X185V,X186H,X186K,X188R,X188E,X188D,X192H,X192W,X194V,X194F,X194E,X197F,X198L,X198F,X203E,X203C,X208S,X209N,X209F,X209E,X209S,X209H,X209G,X209T,X209L,X210R,X210V,X210L,X211R,X211Q,X212I,X212M,X212F,X213A,X214F,X215F,X215N,X215D,X215H,X215E,X216F,X216A,X217N,X217E,X217D,X218P,X218D,X218E,X224A,X224G,X227I,X230E,X231I,X231C,X233C,X234F,X235F,X236F,X236N,X238L,X238K,X238R,X239K,X239S,X239T,X239G,X239H,X239R,X239N,X239F,X240R,X241R,X242L,X242R,X243R,X243F,X244R,X246S,X248I,X248V,X248R,X249R,X249T,X250I,X251S,X251R,X252I,X252F,X252H,X252R,X253F,X253I,X253R,X254C,X256N,X258R,X260V,X260I,X262H,X262D,X263F,X265F,X267N,X267V,X267M,X269I,X269R,X270C,X271F,X271V,X271I,X271P,X271H,X271M,X271T,X271L,X271A,X272F,X272R,X272F,X273I,X273F,和X274G,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0225] 本发明还提供包含芽孢杆菌属枯草杆菌蛋白酶的枯草杆菌蛋白酶变体的多肽,其中该枯草杆菌蛋白酶变体是具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:X16S,X18R,X20R,X22A,X24R,X43R/D,X45T,X76D,X101A,X103G,X104L,X111V,X128N,X148I,X230E,X242R,和X249R,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0226] 本发明还提供包含芽孢杆菌属枯草杆菌蛋白酶的枯草杆菌蛋白酶变体的多肽,其中该枯草杆菌蛋白酶变体是具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:X1R,X230E,X271L,X115R,X20R,X249R,X235F,X27V/F/L,X75E,X82R,X18R,X269R,X43D,X43R,X76D,X45T,X212F,X242R,X24R,X78R,X9A,X22R,X121E,X244R,X28E,X30E,X4R,和X241R,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0227] 本发明还提供包含芽孢杆菌属枯草杆菌蛋白酶的枯草杆菌蛋白酶变体的多肽,其中该枯草杆菌蛋白酶变体是具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:X062E-X158E,X103G-X158E,X128N-X158E,X016S-X158E,X104L-X158E,X089P-X158E,X111V-X158E,X022A-X158E,X101A-X158E,X148I-X158E,X129E-X158E,X022A-X089P,X016S-X089P,X062E-X089P,X062E-X271F,X158E-X271F,X186H-X271F,X129E-X271F,X111V-X271F,X209E-X271F,X016S-X271F,X188D-X271F,X022A-X271F,X159E-X271F,X104L-X271F,X101A-X271F,X089P-X271F,X128N-X271F,X103G-

X271F,X148I-X271F,X249R-X271F,X062E-X159E,X016S-X159E,X128N-X159E,X148I-X159E,X111V-X159E,X089P-X159E,X022A-X159E,X129E-X159E,X103G-X159E,X104L-X159E,X158E-X159E,X101A-X159E,X158E-X249R,X111V-X249R,X129E-X249R,X062E-X249R,X016S-X249R,X186H-X249R,X148I-X249R,X159E-X249R,X101A-X249R,X188D-X249R,X104L-X249R,X209E-X249R,X022A-X249R,X128N-X249R,X103G-X249R,X089P-X249R,X022A-X111V,X101A-X111V,X016S-X111V,X104L-X111V,X062E-X111V,X103G-X111V,X089P-X111V,X016S-X148I,X062E-X148I,X022A-X148I,X129E-X148I,X104L-X148I,X103G-X148I,X128N-X148I,X101A-X148I,X089P-X148I,X111V-X148I,X016S-X062E,X022A-X062E,X062E-X129E,X022A-X129E,X128N-X129E,X016S-X129E,X101A-X129E,X104L-X129E,X089P-X129E,X103G-X129E,X111V-X129E,X062E-X186H,X128N-X186H,X101A-X186H,X022A-X186H,X016S-X186H,X158E-X186H,X089P-X186H,X129E-X186H,X159E-X186H,X103G-X186H,X104L-X186H,X111V-X186H,X148I-X186H,X062E-X101A,X022A-X101A,X016S-X101A,X089P-X101A,X062E-X103G,X022A-X103G,X016S-X103G,X101A-X103G,X089P-X103G,X062E-X128N,X016S-X128N,X022A-X128N,X101A-X128N,X104L-X128N,X089P-X128N,X103G-X128N,X111V-X128N,X111V-X188D,X062E-X188D,X016S-X188D,X148I-X188D,X022A-X188D,X128N-X188D,X101A-X188D,X104L-X188D,X089P-X188D,X129E-X188D,X159E-X188D,X186H-X188D,X103G-X188D,X158E-X188D,X016S-X022A,X016S-X104L,X022A-X104L,X101A-X104L,X062E-X104L,X103G-X104L,X089P-X104L,X159E-X209E,X111V-X209E,X101A-X209E,X016S-X209E,X128N-X209E,X148I-X209E,X129E-X209E,X062E-X209E,X022A-X209E,X103G-X209E,X158E-X209E,X188D-X209E,X104L-X209E,X089P-X209E,和X186H-X209E,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0228] 本发明还提供包含芽孢杆菌属枯草杆菌蛋白酶的枯草杆菌蛋白酶变体的多肽,其中该枯草杆菌蛋白酶变体是具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:X018R-X241R,X020R-X241R,X024R-X241R,X009A-X241R,X020R-X241R,X004R-X241R,X043R-X241R,X078R-X241R,X022R-X241R,X115R-X241R,X001R-X241R,X212F-X241R,X082R-X241R,X018R-X244R,X024R-X244R,X078R-X244R,X020R-X244R,X212F-X244R,X009A-X244R,X082R-X244R,X001R-X244R,X043R-X244R,X022R-X244R,X004R-X244R,X115R-X244R,X241R-X244R,X242R-X244R,X001R-X004R,X009A-X022R,X018R-X022R,X020R-X022R,X004R-X022R,X001R-X022R,X024R-X242R,X018R-X242R,X004R-X242R,X020R-X242R,X212F-X242R,X082R-X242R,X078R-X242R,X001R-X242R,X009A-X242R,X022R-X242R,X115R-X242R,X043R-X242R,X241R-X242R,X018R-X212F,X022R-X212F,X004R-X212F,X024R-X212F,X001R-X212F,X115R-X212F,X020R-X212F,X009A-X212F,X043R-X212F,X078R-X212F,X082R-X212F,X009A-X078R,X020R-X078R,X024R-X078R,X022R-X078R,X018R-X078R,X004R-X078R,X001R-X078R,X043R-X078R,X022R-X024R,X020R-X024R,X018R-X024R,X001R-X024R,X004R-X024R,X009A-X024R,X004R-X009A,X001R-X009A,X242R-X269R,X024R-X269R,X020R-X269R,X022R-X269R,X249R-X269R,X212F-X269R,X043R-X269R,X244R-X269R,X001R-X269R,X018R-

X269R,X078R-X269R,X009A-X269R,X115R-X269R,X241R-X269R,X004R-X269R,X082R-X269R,X018R-X043R,X020R-X043R,X004R-X043R,X022R-X043R,X009A-X043R,X001R-X043R,X024R-X043R,X009A-X018R,X004R-X018R,X001R-X018R,X024R-X082R,X009A-X082R,X018R-X082R,X001R-X082R,X078R-X082R,X020R-X082R,X022R-X082R,X004R-X082R,X043R-X082R,X043R-X249R,X020R-X249R,X004R-X249R,X018R-X249R,X009A-X249R,X212F-X249R,X022R-X249R,X024R-X249R,X115R-X249R,X001R-X249R,X082R-X249R,X242R-X249R,X241R-X249R,X244R-X249R,X078R-X249R,X018R-X115R,X020R-X115R,X022R-X115R,X078R-X115R,X009A-X115R,X004R-X115R,X001R-X115R,X082R-X115R,X043R-X115R,X024R-X115R,X009A-X020R,X018R-X020R,X004R-X020R,X001R-X020R,X009A-X271L,X020R-X271L,X024R-X271L,X244R-X271L,X241R-X271L,X043R-X271L,X022R-X271L,X249R-X271L,X212F-X271L,X115R-X271L,X242R-X271L,X078R-X271L,X004R-X271L,X269R-X271L,X001R-X271L,X018R-X271L,和X082R-X271L,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0229] 本发明还提供分离的枯草杆菌蛋白酶变体,其中该枯草杆菌蛋白酶变体是具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:X020R-X043R,X020K-X062E,X024F-X116L,X020K-X024F,X024R-X174T,X024R-X118R,X024R-X235F,X024R-X086R,X024R-X086W,X078R-X118R,X033S-X118R,X033S-X235F,X209A-X241R,X020R-X076D,X018R-X245R,X024R-X045T,X232V-X245R,X118R-X172V,X118R-X194T,X008T-X024R,X235F-X243F,X018R-X103A,X018R-X104I,X086W-X118R,X086W-X243F,X086W-X209A,X024C-X033S,X024R-X232V,X024R-X243F,X024R-X239Q,X024R-X101G,X024R-X141G,X024R-X033S,X024R-X274I,X024R-X209A,X078R-X086W,X101G-X232V,X033S-X148F,X033S-X086W,X033S-X201S,X033S-X078R,X033S-X241R,X033S-X209A,X230E-X249R,X232V-X249R,X118R-X235F,X076D-X245R,X086W-X235F,X024R-X247H,X024R-X104A,X078R-X235F,X101G-X249R,X103A-X232V,X033S-X048T,X033S-X239T,X033S-X253A,X143A-X209A,X209A-X235F,X018R-X045T,X209A-X243F,X024R-X272P,X024R-X269C,X101G-X104I,X104I-X232V,X076D-X249R,和X024R-X076D,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0230] 本发明还提供分离的枯草杆菌蛋白酶变体,其中该枯草杆菌蛋白酶变体是具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:X020R-X076D,X024R-X045T,X230E-X249R,X018R-X045T,X018R-X245R,X101G-X232V,X024R-X232V,X232V-X245R,X024R-X101G,X018R-X104I,X018R-X103A,X101G-X249R,X232V-X249R,X103A-X232V,X076D-X245R,X101G-X104I,X104I-X232V,X076D-X249R,X024R-X076D,X024F-X116L,X020K-X024F,X020K-X062E,X033S-X118R,X024R-X086W,X024R-X118R,X024R-X086R,X209A-X241R,X024R-X241R,X024R-X235F,X118R-X209A,X078R-X118R,X033S-X235F,X024R-X174T,X086W-X209A,X008T-X024R,X086W-X118R,X033S-X241R,X024R-X243F,X024R-X209A,X033S-X086W,X024R-X033S,X086W-X243F,X033S-X201S,X024R-X239Q,X078R-X086W,X235F-X243F,X118R-X172V,X033S-X148F,X033S-

X078R,X033S-X243F,X024C-X033S,X118R-X194T,X033S-X209A,X024R-X141G,X024R-X274I,X086W-X235F,X015T-X033S,X209A-X235F,X024R-X247H,X078R-X235F,X024R-X104A,X033S-X048T,X118R-X235F,X033S-X253A,X143A-X209A,X033S-X239T,X209A-X243F,X024R-X272P,和X024R-X269C,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0231] 本发明还提供分离的枯草杆菌蛋白酶变体,其中该枯草杆菌蛋白酶变体是具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:X004R-X009A-X020R-X242R,X020R-X043R-X241R,X020R-X242R-X269R,X004R-X009A-X020R-X043R,X004R-X020R-X249R,X018R-X024R-X244R,X009A-X022R-X212F-X241R,X020R-X043R-X269R,X018R-X024R-X242R,X004R-X009A-X043R-X241R,X020R-X043R-X244R,X020R-X022R-X242R,X004R-X020R-X043R,X004R-X009A-X020R-X043R-X242R,X020R-X043R-X242R,X020R-X043R-X242R-X249R,X020R-X212F-X249R,X004R-X009A-X241R,X001R-X009A-X043R,X020R-X043R-X249R,X009A-X020R-X043R-X241R,X020R-X022R-X043R,X020R-X249R-X269R,X020R-X022R-X241R,X004R-X009A-X024R-X043R-X241R,X009A-X043R-X078R,X004R-X020R-X024R-X244R,X020R-X022R-X078R-X242R,X020R-X024R-X242R-X249R,X004R-X009A-X078R-X241R,X009A-X043R-X078R-X242R,X004R-X020R-X024R,X009A-X043R-X212F,X020R-X043R-X212F,X024R-X078R-X212F,X009A-X020R-X024R-X043R,X009A-X022R-X043R-X078R,X020R-X022R-X212F-X241R,X020R-X043R-X212F-X241R,X009A-X043R-X241R,X020R-X043R-X271L,X020R-X022R-X078R-X241R,X020R-X024R-X043R-X242R,X020R-X022R-X043R-X241R,X009A-X020R-X043R-X212F,X004R-X009A-X020R-X024R-X242R,X020R-X043R-X249R-X271L,X020R-X022R-X024R-X242R,X009A-X022R-X078R-X212F,X020R-X043R-X242R-X271L,X009A-X022R-X078R-X212F-X241R,X004R-X020R-X024R-X249R,X020R-X022R-X271L,X020R-X022R-X043R-X212F,X004R-X020R-X024R-X043R-X242R,X004R-X020R-X024R-X043R,X004R-X009A-X022R-X078R-X212F,X020R-X022R-X078R-X212F-X241R,和X020R-X022R-X269R,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0232] 本发明还提供分离的枯草杆菌蛋白酶变体,其中该枯草杆菌蛋白酶变体是具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:X018R-X020R-X043D-X045T-X230E,X018R-X043R-X045T-X242R-X249R,X024R-X043D-X249R,X018R-X020R-X045T,X020R-X024R-X076D-X249R,X024R-X043R-X230E-X242R,X018R-X024R-X043D-X230E,X020R-X076D,X018R-X024R-X043D-X076D-X249R,X024R-X043R-X076D-X249R,X018R-X024R-X045T-X242R,X020R-X043D-X076D-X230E-X249R,X020R-X043R-X045T-X242R,X018R-X024R-X076D-X249R,X018R-X020R-X024R-X043D-X045T-X233I-X242R,X024R-X043R-X230E,X018R-X020R-X043D,X043R-X242R-X249R,X020R-X043R-X045T-X230E,X043R-X076D-X242R-X249R,X020R-X024R-X045T-X230E-X242R,X024R-X045T-X076D-X230E-X242R-X249R,X024R-X045T,X024R-X043R-X045T-X076D-X230E-X249R,X018R-X024R-X043D-X045T-X249R,X018R-X043R-X045T-X249R,X024R-X043R-X242R,X018R-X020R-X043R-X076D-X249R,X020R-X024R-X043D-X249R,X020R-

X043R-X230E-X242R,X020R-X043R-X242R,X018R-X043R-X076D-X230E,X020R-X024R-X043D-X242R,X020R-X043R-X230E,X018R-X020R-X043R-X076D-X242R-X249R,X043D-X045T-X076D-X249R,X018R-X043R-X242R-X249R,X018R-X020R-X043R-X045T-X242R,X018R-X020R-X043D-X230E-X242R,X020R-X024R-X043R-X045T-X249R,X024R-X043R-X249R,X020R-X024R-X27E-X043R-X076D-X230E,X024R-X043R-X045T-X242R,X018R-X020R-X024R-X043R-X045T-X076D-X230E,X020R-X043R-X076D-X230E-X249R,X018R-X043R-X045T-X242R,X020R-X242R-X249R,X018R-X043R-X076D-X230E-X242R-X249R,X018R-X024R-X076D,X020R-X024R-X27R-X043D-X242R-X249R,X018R-X020R-X024R-X043D-X076D-X242R,X018R-X043R-X076D-X242R-X249R,X018R-X024R-X043D-X230E-X249R,X018R-X020R-X043D-X249R,X018R-X020R-X043D-X045T-X076D-X242R,X024R-X043R-X076D-X230E-X242R,X020R-X024R-X38I-X043R-X045T-X076D-X242R-X249R,X018R-X020R-X043R,X018R-X024R-X045T-X230E-X242R,X018R-X020R-X249R,X024R-X043R-X076D,X018R-X020R-X024R-X043R-X045T-X076D-X249R,X018R-X043D-X045T-X076D-X242R-X249R,X024R-X043D-X242R-X249R,X018R-X020R-X024R-X043D-X045T-X242R,X020R-X024R-X043R-X076D,X018R-X020R-X043D-X045T-X230E-X242R,X020R-X024R-X043R-X045T-X076D-X242R-X249R,X018R-X043R-X045T-X076D-X242R,X018R-X020R-X043R-X076D-X230E-X242R,X018R-X024R-X043D-X249R,X018R-X024R-X043R-X045T-X230E-X249R,X018R-X020R-X043R-X045T-X076D-X249R,X018R-X024R-X242R,X018R-X043R-X045T-X076D-X230E-X242R,X045T-X242R-X249R,X018R-X024R-X043D-X242R,X018R-X020R-X043D-X045T-X240P,X024R-X043R-X045T-X242R-X249R,X018R-X024R-X30S-X31S-X32I-X33Q-X34V-X35F,X018R-X020R-X043R-X076D,X020R-X043D-X045T-X076D-X242R-X249R,X018R-X024R-X043D-X230E-X242R,X018R-X024R-X043D-X242R-X249R,X024R-X043D-X045T-X242R-X249R,X043R-X230E-X249R,X024R-X043R-X076D-X230E-X249R,X020R-X024R-X043D-X076D-X249R,X024R-X045T-X242R-X273V,X020R-X024R-X045T-X076D-X242R-X249R,X018R-X024R-X043D-X076D-X242R,X018R-X043R-X076D-X230E-X249R,X018R-X020R-X043R-X045T-X249R,X018R-X043R-X045T-X230E-X242R,X020R-X024R-X043D-X045T-X230E-X242R,X018R-X043D-X230E-X249R,X018R-X043R-X076D-X242R,X018R-X020R-X076D,X018R-X020R-X043D-X076D-X242R-X249R,X020R-X024R-X043D-X076D-X242R-X249R,X043D-X242R-X249R,X018R-X020R-X024R-X043R-X076D,X018R-X020R-X043D-X045T-X076D-X249R,X018R-X020R-X043R-X045T-X076D-X230E-X249R,X018R-X076D-X242R,X020R-X043R-X249R,X018R-X076D-X242R-X249R,X018R-X024R-X045T-X230E-X249R,X230E-X249R,X018R-X045T-X249R,X020R-X043R-X076D,X043R-X045T-X249R,X018R-X043D-X076D-X242R-X249R,X043R-X076D-X249R,X018R-X045T,X020R-X076D-X230E-X242R,X020R-X024R-X043D-X045T,X024R-X043D-X076D-X242R-X249R,X020R-X045T-X249R,X043R-X076D-X153A-X249R,X043R-X076D-X230E-X249R,X018R-X043D-X076D-X249R,和X020R-X043R-X076D-X227I,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0233] 本发明还提供分离的枯草杆菌蛋白酶变体,其中该枯草杆菌蛋白酶变体是具有蛋

白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:X101G-X103A-X104I-X232V-X236H-X245R-X252K,X101G-X103A-X104I-X232V-X245R-X248R,X101G-X103A-X104I-X159R-X232V-X245R-X248D,X101G-X103A-X104I-X159D-X232V-X245R-X248R,X101G-X103A-X104I-X232V-X245R,X101G-X103A-X104I-X159D-X232V-X245R和X101G-X103A-X104I-X232V-X245R-X248D,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与如SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0234] 本发明还提供分离的枯草杆菌蛋白酶变体,其中该枯草杆菌蛋白酶变体是具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:X101G-X103A-X104I-X129E-X188D-X232V-X238R-X245R-X248D,X024R-X101G-X103A-X104I-X129E-X158E-X188D-X232V-X245R-X248D-X249R,X022A-X101G-X103A-X104I-X129E-X158E-X188D-X232V-X245R-X248D-X249R,X022A-X024R-X101G-X103A-X104I-X129E-X158E-X188D-X232V-X245R-X248D-X249R,X024R-X101G-X103A-X104I-X129E-X188D-X232V-X245R-X248D-X249R,X024R-X101G-X103A-X104I-X129E-X159E-X188D-X232V-X245R-X248D-X249R,X024R-X101G-X103A-X104I-X128N-X129E-X158E-X232V-X245R-X248D-X249R,X024R-X101G-X103A-X104I-X148I-X158E-X188D-X232V-X245R-X248D,X022A-X024R-X101G-X103A-X104I-X129E-X159E-X188D-X232V-X245R-X248D-X249R,X024R-X101G-X103A-X104I-X128N-X129E-X232V-X245R-X248D,X101G-X103A-X104I-X129E-X188D-X232V-X245R-X248D-X249R,X024R-X101G-X103A-X104I-X129E-X158E-X232V-X245R-X248D-X249R,X022A-X024R-X101G-X103A-X104I-X158E-X159E-X188D-X232V-X245R-X248D-X249R,X022A-X024R-X101G-X103A-X104I-X129E-X158E-X159E-X188D-X232V-X238R-X245R-X248D,X024R-X101G-X103A-X104I-X129E-X148I-X158E-X232V-X245R-X248D,X016S-X024R-X101G-X103A-X104I-X158E-X188D-X232V-X245R-X248D-X249R,X101G-X103A-X104I-X158E-X159E-X232V-X245R-X248D-X249R,X022A-X101G-X103A-X104I-X129E-X158E-X159E-X232V-X238R-X245R-X248D,X022A-X024R-X101G-X103A-X104I-X129E-X158E-X159E-X232V-X245R-X248D-X249R,X022A-X024R-X101G-X103A-X104I-X128N-X158E-X188D-X232V-X245R-X248D,X024R-X101G-X103A-X104I-X129E-X188D-X232V-X245R-X248D,X022A-X024R-X101G-X103A-X104I-X129E-X158E-X232V-X245R-X248D,X022A-X024R-X101G-X103A-X104I-X129E-X232V-X245R-X248D,X022A-X024R-X101G-X103A-X104I-X129E-X188D-X232V-X245R-X248D,X024R-X101G-X103A-X104I-X158E-X188D-X232V-X238R-X245R-X248D,X022A-X101G-X103A-X104I-X128N-X129E-X188D-X232V-X238R-X245R-X248D,X024R-X101G-X103A-X104I-X129E-X188D-X232V-X238R-X245R-X248D,X024R-X101G-X103A-X104I-X158E-X159E-X188D-X232V-X245R-X248D,X022A-X024R-X101G-X103A-X104I-X128N-X188D-X232V-X245R-X248D,X024R-X101G-X103A-X104I-X129E-X158E-X188D-X232V-X245R-X248D,X022A-X024R-X101G-X103A-X104I-X128N-X129E-X158E-X232V-X245R-X248D,X024R-X101G-X103A-X104I-X159E-X188D-X232V-X245R-X248D,X022A-X101G-X103A-X104I-X128N-X129E-X232V-X238R-X245R-X248D,X024R-X101G-X103A-X104I-X129E-X159E-X232V-X245R-X248D,X022A-X024R-X101G-X103A-X104I-X129E-X158E-X188D-X232V-

X238R-X245R-X248D,XO22A-XO24R-X101G-X103A-X104I-X158E-X159E-X188D-X232V-X245R-X248D,XO24R-X101G-X103A-X104I-X159E-X188D-X232V-X245R-X248D-X249R,XO22A-X101G-X103A-X104I-X129E-X158E-X232V-X238R-X245R-X248D,XO22A-XO24R-X101G-X103A-X104I-X129E-X158E-X232V-X245R-X248D-X249R,XO24R-X101G-X103A-X104I-X148I-X158E-X232V-X245R-X248D,XO22A-X101G-X103A-X104I-X158E-X159E-X188D-X232V-X245R-X248D-X249R,XO22A-X101G-X103A-X104I-X158E-X188D-X232V-X245R-X248D,XO22A-X101G-X103A-X104I-X129E-X188D-X232V-X238R-X245R-X248D,XO24R-X101G-X103A-X104I-X129E-X158E-X159E-X188D-X232V-X245R-X248D-X249R,XO22A-XO24R-X101G-X103A-X104I-X158E-X159E-X188D-X232V-X238R-X245R-X248D,X101G-X103A-X104I-X129E-X158E-X188D-X232V-X245R-X248D-X249R,XO24R-X101G-X103A-X104I-X128N-X158E-X232V-X245R-X248D,XO22A-XO24R-X101G-X103A-X104I-X128N-X129E-X188D-X232V-X245R-X248D,XO22A-X101G-X103A-X104I-X129E-X159E-X232V-X238R-X245R-X248D,X101G-X103A-X104I-X129E-X159E-X232V-X245R-X248D-X249R,XO22A-X101G-X103A-X104I-X129E-X158E-X232V-X245R-X248D-X249R,XO24R-X101G-X103A-X104I-X129E-X148I-X158E-X188D-X232V-X245R-X248D,XO22A-X101G-X103A-X104I-X129E-X159E-X232V-X245R-X248D-X249R,XO24R-X101G-X103A-X104I-X159E-X188D-X232V-X238R-X245R-X248D,XO24R-X101G-X103A-X104I-X129E-X158E-X159E-X232V-X245R-X248D-X249R,XO24R-X101G-X103A-X104I-X129E-X158E-X159E-X232V-X238R-X245R-X248D,XO24R-X101G-X103A-X104I-X128N-X159E-X188D-X232V-X245R-X248D,XO22A-X101G-X103A-X104I-X159E-X188D-X232V-X245R-X248D-X249R,XO24R-X101G-X103A-X104I-X129E-X159E-X188D-X232V-X238R-X245R-X248D,X101G-X103A-X104I-X158E-X232V-X238R-X245R-X248D,XO22A-X101G-X103A-X104I-X129E-X159E-X188D-X232V-X245R-X248D-X249R,XO24R-X101G-X103A-X104I-X129E-X148I-X188D-X232V-X245R-X248D,XO24R-X101G-X103A-X104I-X158E-X232V-X245R-X248D-X249R,XO22A-X101G-X103A-X104I-X158E-X159E-X232V-X238R-X245R-X248D,XO24R-X101G-X103A-X104I-X158E-X159E-X232V-X238R-X245R-X248D,XO22A-X101G-X103A-X104I-X129E-X158E-X159E-X232V-X245R-X248D-X249R,X101G-X103A-X104I-X129E-X158E-X188D-X232V-X238R-X245R-X248D,XO22A-XO24R-X101G-X103A-X104I-X129E-X158E-X159E-X232V-X245R-X248D,X101G-X103A-X104I-X188D-X232V-X238R-X245R-X248D,XO22A-XO24R-X101G-X103A-X104I-X158E-X232V-X245R-X248D-X249R,XO22A-XO24R-X101G-X103A-X104I-X148I-X158E-X232V-X245R-X248D,X101G-X103A-X104I-X129E-X158E-X159E-X232V-X238R-X245R-X248D,XO22A-X101G-X103A-X104I-X159E-X188D-X232V-X238R-X245R-X248D,XO22A-XO24R-X101G-X103A-X104I-X129E-X158E-X159E-X188D-X232V-X245R-X248D-X249R,XO22A-X101G-X103A-X104I-X129E-X232V-X238R-X245R-X248D,XO22A-XO24R-X101G-X103A-X104I-X188D-X232V-X245R-X248D-X249R,X101G-X103A-X104I-X129E-X158E-X159E-X232V-X245R-X248D-X249R,XO22A-X101G-X103A-X104I-X158E-X159E-X232V-X245R-X248D-X249R,X101G-X103A-X104I-X129E-X188D-X232V-X245R-X248D,XO24R-X101G-X103A-X104I-X129E-X159E-X232V-X238R-X245R-X248D,X101G-X103A-X104I-X128N-X129E-X232V-X245R-X248D,X101G-

X103A-X104I-X158E-X188D-X232V-X245R-X248D,X022A-X024R-X101G-X103A-X104I-X129E-X232V-X245R-X248D-X249R,X101G-X103A-X104I-X129E-X159E-X232V-X238R-X245R-X248D,X101G-X103A-X104I-X158E-X159E-X188D-X232V-X238R-X245R-X248D,X024R-X101G-X103A-X104I-X232V-X245R-X248D-X249R,X022A-X024R-X101G-X103A-X104I-X129E-X148I-X232V-X245R-X248D,X022A-X024R-X101G-X103A-X104I-X158E-X232V-X238R-X245R-X248D,X101G-X103A-X104I-X128N-X129E-X232V-X238R-X245R-X248D,X022A-X101G-X103A-X104I-X128N-X159E-X232V-X245R-X248D,X022A-X101G-X103A-X104I-X128N-X129E-X158E-X232V-X238R-X245R-X248D,X101G-X103A-X104I-X128N-X129E-X188D-X232V-X245R-X248D-X249R,X022A-X024R-X101G-X103A-X104I-X128N-X129E-X158E-X188D-X232V-X245R-X248D-X249R,X024R-X101G-X103A-X104I-X128N-X158E-X159E-X188D-X232V-X245R-X248D,X022A-X024K-X101G-X103A-X104I-X128N-X158E-X159E-X232V-X245R-X248D,X101G-X103A-X104I-X129E-X148I-X188D-X232V-X245R-X248D,X024R-X101G-X103A-X104I-X148I-X232V-X245R-X248D,X022A-X101G-X103A-X104I-X148I-X188D-X232V-X245R-X248D,X024R-X101G-X103A-X104I-X128N-X129E-X188D-X232V-X245R-X248D,X101G-X103A-X104I-X128N-X129E-X158E-X232V-X238R-X245R-X248D,X022A-X024R-X101G-X103A-X104I-X129E-X148I-X158E-X188D-X232V-X245R-X248D,X022A-X024R-X101G-X103A-X104I-X148I-X158E-X188D-X232V-X245R-X248D,X101G-X103A-X104I-X148I-X159E-X232V-X245R-X248D,X022A-X024R-X101G-X103A-X104I-X158E-X188D-X232V-X245R-X248D,和X101G-X103A-X104I-X128N-X129E-X158E-X232V-X245R-X248D-X249R,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0235] 本发明还提供分离的枯草杆菌蛋白酶变体,其中该枯草杆菌蛋白酶变体是具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:X022A-X024R-X101G-X103A-X104I-X158E-X232V-X245R-X248D-X249R,X022A-X024R-X101G-X103A-X104I-X129E-X232V-X245R-X248D-X249R,X024R-X101G-X103A-X104I-X158E-X159E-X232V-X238R-X245R-X248D,X024R-X101G-X103A-X104I-X232V-X245R-X248D-X249R,X101G-X103A-X104I-X158E-X232V-X245R-X248D-X249R,X101G-X103A-X104I-X188D-X232V-X245R-X248D-X249R,X024R-X101G-X103A-X104I-X159E-X188D-X232V-X245R-X248D-X249R,X022A-X024R-X101G-X103A-X104I-X158E-X232V-X238R-X245R-X248D,X024R-X101G-X103A-X104I-X159E-X188D-X232V-X238R-X245R-X248D,X022A-X024R-X101G-X103A-X104I-X129E-X232V-X245R-X248D,X024R-X101G-X103A-X104I-X148I-X232V-X245R-X248D,X024R-X101G-X103A-X104I-X129E-X158E-X232V-X245R-X248D-X249R,X024R-X101G-X103A-X104I-X148I-X158E-X232V-X245R-X248D,X022A-X024R-X101G-X103A-X104I-X129E-X158E-X232V-X245R-X248D-X249R,X016S-X024R-X101G-X103A-X104I-X158E-X188D-X232V-X245R-X248D-X249R,X024R-X101G-X103A-X104I-X129E-X159E-X232V-X238R-X245R-X248D,X024R-X101G-X103A-X104I-X129E-X188D-X232V-X245R-X248D-X249R,X022A-X101G-X103A-X104I-X129E-X232V-X238R-X245R-X248D,X022A-X024R-X101G-X103A-X104I-X148I-X158E-X232V-X245R-X248D,

X024R-X101G-X103A-X104I-X129E-X188D-X232V-X238R-X245R-X248D,X022A-X024R-X101G-X103A-X104I-X158E-X159E-X188D-X232V-X238R-X245R-X248D,X022A-X101G-X103A-X104I-X158E-X159E-X232V-X238R-X245R-X248D,X022A-X024R-X101G-X103A-X104I-X129E-X158E-X232V-X245R-X248D,X101G-X103A-X104I-X158E-X188D-X232V-X245R-X248D-X249R,X022A-X101G-X103A-X104I-X158E-X159E-X232V-X245R-X248D-X249R,和X024R-X101G-X103A-X104I-X158E-X159E-X232V-X245R-X248D,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0236] 本发明还提供分离的枯草杆菌蛋白酶变体,其中该枯草杆菌蛋白酶变体是具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:X104L-X128N-X158E-X186H-X249R,X128N-X158E-X188D-X249R,X062E-X128N-X158E-X159E-X271F,X062E-X158E-X188D-X249R-X271F,X062E-X158E-X186H-X249R-X271F,X128N-X158E-X188D-X209E-X271F,X062E-X159E-X188D-X249R,X016S-X062E-X158E-X186H-X249R,X062E-X158E-X159E-X249R,X101A-X128N-X158E-X209E-X249R,X128N-X158E-X186H-X271F,X062E-X158E-X188D-X249R,X062E-X158E-X186H-X271F,X062E-X158E-X186H-X249R,X062E-X101A-X186H-X249R,X062E-X101A-X158E-X186H-X271F,X062E-X104L-X158E-X188D-X249R-X271F,X062E-X159E-X186H-X249R,X062E-X159E-X249R,X128N-X158E-X186H-X249R,X128N-X158E-X188D-X271F,X062E-X158E-X249R,X062E-X186H-X188D-X249R-X271F,X128N-X158E-X209E-,X062E-X101A-X158E-X249R,X104L-X128N-X158E-X186H-X271F,X062E-X101A-X158E-X186H-X249R-X271F,X016S-X062E-X158E-X249R,X062E-X101A-X159E-X249R,X128N-X158E-X186H-X188D-X271F,X101A-X128N-X158E-X186H-X271F,X062E-X101A-X188D-X249R,X101A-X104L-X158E-X186H-X188D-X249R,X062E-X159E-X249R-X271F,X128N-X158E-X159E-X271F,X016S-X062E-X104L-X158E-X186H-X271F,X022A-X128N-X158E-X249R,X128N-X158E-X249R,X062E-X101A-X104L-X158E-X186H-X271F,X016S-X062E-X158E-X186H-X271F,X104L-X128N-X158E-X249R,X104L-X128N-X158E-X188D-X249R,X022A-X062E-X158E,X062E-X101A-X188D-X249R-X271F,X062E-X158E-X249R-X271F,X104L-X128N-X158E-X186H-X188D-X271F,X062E-X101A-X186H-X271F,X062E-X104L-X159E-X249R,X062E-X186H-X249R,X062E-X101A-X186H-X249R-X271F,X101A-X158E-X186H-X188D-X249R,X062E-X101A-X186H,X101A-X128N-X129E-X186H-X249R,X101A-X103G-X158E-X186H-X249R,X016S-X062E-X104L-X186H-X188D-X271F,X104L-X158E-X186H-X249R,X101A-X128N-X158E-X188D-X209E-X271F,X062E-X101A-X186H-X188D-X271F,X016S-X062E-X158E-X249R-X271F,X062E-X128N-X158E,X062E-X128N-X159E-X249R,X062E-X101A-X158E-X188D-X249R,X101A-X128N-X158E-X249R,X062E-X158E-X186H-X188D-X249R,X016S-X104L-X158E-X186H-X271F,X062E-X148I-X159E,X062E-X101A-X158E-X186H-X249R,X062E-X101A-X186H-X188D-X249R,X104L-X158E-X186H-X188D-X249R,X062E-X101A-X104L-X186H-X188D-X271F,X022A-X101A-X158E-X186H-X249R,X101A-X128N-X158E-X209E,X158E-X186H-X188D-X249R-X271F,X104L-X158E-X186H-X188D-X249R-X271F,X101A-X104L-X158E-X186H-X249R,X104L-X158E-X249R,X101A-X104L-X128N-X158E-X186H-

X271F,X016S-X104L-X188D-X249R,X101A-X104L-X158E-X186H-X188D-X271F,X104L-X128N-X159E-X271F,X104L-X158E-X186H-X249R-X271F,X158E-X186H-X249R,X101A-X158E-X186H-X249R,X104L-X158E-X188D-X249R-X271F,X016S-X128N-X158E-X186H,X104L-X128N-X186H-X188D-X249R,X016S-X101A-X128N-X186H,X016S-X062E-X128N-X186H-X271F,X016S-X128N-X186H-X271F,X128N-X129E-X186H,X158E-X186H-X249R-X271F,X016S-X158E-X249R,X016S-X158E-X186H-X249R,X016S-X022A-X158E-X186H-X271F,X089P-X101A-X129E-X186H,X022A-X128N-X158E-X186H,X101A-X104L-X128N-X158E-X186H,X022A-X128N-X186H-X188D-,X062E-X104L-X158E-X186H-X188D-X249R,X022A-X158E-X186H-X249R-X271F,X022A-X104L-X158E-X249R,X101A-X111V-X129E,X016S-X158E-X249R-X271F,X016S-X111V-X188D-,X022A-X104L-X186H-X188D-X249R,和X104L-X148I-X188D-X249R,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0237] 本发明还提供分离的枯草杆菌蛋白酶变体,其中该枯草杆菌蛋白酶变体是具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:X001R-X101G-X103A-X104I-X232V-X245R,X004R-X101G-X103A-X104I-X232V-X245R,X043R-X101G-X103A-X104I-X232V-X245R-X271L,X078R-X101G-X103A-X104I-X232V-X245R,X004R-X043R-X101G-X103A-X104I-X232V-X245R,X018R-X043R-X101G-X103A-X104I-X232V-X245R,X020R-X101G-X103A-X104I-X232V-X245R,X101G-X103A-X104I-X232V-X245R-X271L,X020R-X043R-X101G-X103A-X104I-X232V-X245R,X024R-X043R-X101G-X103A-X104I-X232V-X245R,X020R-X025R-X116A-X167W,X018R-X101G-X103A-X104I-X232V-X245R,X022R-X101G-X103A-X104I-X232V-X245R,X078R-X103N-X106G-X167W-X236N,X018R-X043D-X101G-X103A-X104I-X232V-X245R-X269R,X043R-X101G-X103A-X104I-X232V-X245R-X269R,X024R-X101A-X120F-X194F-X249R,X020R-X043D-X101G-X103A-X104I-X232V-X245R-X269R,X101G-X103A-X104I-X212F-X232V-X245R,X020R-X144R-X185I-X233C-X236N,X023A-X078R-X216F-X236N-X249R,X101G-X103A-X104I-X232V-X245R-X269R,X101G-X103A-X104I-X115R-X232V-X245R,X052N-X078R-X103N-X148I-X213A,X018R-X043D-X101G-X103A-X104I-X232V-X245R-X249R,X024R-X043D-X101G-X103A-X104I-X232V-X245R-X249R,X024R-X043D-X101G-X103A-X104I-X232V-X245R-X269R,X025R-X089I-X116A-X239S-X270C,X024R-X101G-X103A-X104I-X232V-X245R,X148I-X213A-X252R,X024R-X025R-X183D-X192W-X239S,X046R-X194F-X212M,X104L-X217E-X224A-X249R-X252R,X023A-X091F-X121F-X192W-X236N,X101G-X103A-X104I-X232V-X244R-X245R,X099F-X144R-X167W-X252R,X101G-X103A-X104I-X232V-X245R-X249R,X043R-X101G-X103A-X104I-X232V-X245R,X022W-X078R-X167W-X212M-X270C,X121F-X252R-X270C,X020R-X103N-X216F-X236N-X252R,X043R-X101G-X103A-X104I-X232V-X245R-X249R,X023A-X052N-X192W-X198L-X252R,X025R-X046R-X121F,X024R-X078R-X104L-X116A-X183D,X046R-X059A-X103N-X211Q-X212M,X020R-X052N-X062Q-X091F-X192W,X023A-X052N-X144R-X192W-X216F,X101G-X103A-X104I-X232V-X242R-X245R,X052N-X103N-X116A-X148I-X192W,X089I-X116A-X117F-X224A-X249R,X144R-X211Q-X238L-X239S-X249R,X043A-X062Q-X194F-X211Q,X020R-X024R-X052N-

X059A-X216F,X024R-X167W-X224A-X249R,X057R-X167W-X249R,X025R-X103N-X186K-X194F-X224A,X105T-X128N-X144R-X148I-X212M,X020R-X059A-X144R-X192W-X224A,X024R-X043A-X117F-X194F-X211Q,X117F-X194F-X213A-X270C,X078R-X091F-X121F-X233C-X252R,X057R-X099F-X105T-X198L-X213A,X023A-X091F-X101A-X198L-X252R,X062Q-X103N-X121F-X144R-X249R,X043R-X101G-X103A-X104I-X232V-X242R-X245R,X023A-X024R-X117F-X212M-X216F,X104L-X213A-X216F,X194F-X211Q-X236N,X062Q-X103N-X117F-X194F,X024R-X062Q-X104L-X106G-X249R,X057R-X089I-X198L,X046R-X059A-X106G-X217E-X249R,X117F-X213A-X215F,X101A-X120F-X192W-X215F-X224A,X043A-X057R-X117F-X144R-X183D,X046R-X183D-X238L,X025R-X043A-X089I-X117F,X078R-X104L-X213A-X215F-X224A,X091F-X099F-X101A-X105T-X167W,X106G-X117F-X238L,X046R-X089I-X091F-X101A-X116A,X020R-X062Q-X089I-X186K-X212M,X057R-X099F-X121F-X185I-X192W,X046R-X089I-X192W-X233C-X270C,X089I-X117F-X185I-X215F-X233C,X052N-X104L-X183D-X216F-X249R,X078R-X099F-X116A-X186K-X224A,X025R-X105T-X128N-X144R-X270C,X105T-X211Q-X216F,X024R-X046R-X091F-X121F,X106G-X185I-X216F-X236N,X062Q-X101A-X236N-X252R-X270C,X025R-X043A-X091F-X198L-X270C,X020R-X023A-X104L-X192W-X233C,X024R-X043A-X105T-X106G-X198L,X020R-X089I-X217E,X024R-X091F-X198L-X215F-X239S,X046R-X089I-X099F-X186K-X212M,X104L-X120F-X186K-X216F-X252R,X022W-X194F-X213A-X233C-X238L,X099F-X105T-X106G-X194F-X212M,X089I-X105T-X116A-X215F-X216F,X025R-X116A-X120F-X224A-X270C,X043A-X059A-X101A-X216F-X224A,X057R-X183D-X236N,X025R-X062Q-X128N-X144R-X185I,X103N-X120F-X167W-X198L-X233C,X022W-X089I-X216F,X024R-X106G-X116A-X212M-X224A,X020R-X052N-X101A-X198L-X233C,X089I-X091F-X185I-X211Q-X270C,X111I-X215F-X239S,X024R-X116A-X186K-X233C-X236N，和X023A-X103N-X106G-X212M-X215F，其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0238] 本发明还提供分离的枯草杆菌蛋白酶变体，其中该枯草杆菌蛋白酶变体是具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:X020R-X022W-X078R-X101A-X103A-X104I-X116S-X213A-X215F-X232V-X245R,X018R-X078R-X101G-X103A-X104I-X232V-X245R,X024R-X045T-X101G-X103A-X104I-X232V-X245R-X269R,X020R-X022W-X078R-X101G-X103A-X104I-X116A-X232V-X245R,X020R-X22W-X101G-X103A-X104I-X232V-X245R,X018R-X043R-X101G-X103A-X104I-X232V-X245R,X018R-X022W-X024R-X076D-X101A-X116A-X232V-X245R,X018R-X104I-X232V-X249R,X018R-X024R-X076D-X101A-X116A-X211Q-X249R,X018R-X043D-X078R-X101G-X103A-X104I-X217E-X232V-X245R,X018R-X043R-X101G-X103A-X104I-X232V-X245R-X269R,X018R-X045T-X076D-X101G-X103A-X104I-X232V-X245R-X269R,X076D-X078R-X101G-X103A-X104I-X232V-X245R-X269R,X020R-X043D-X078R-X101G-X103A-X104I-X232V-X245R,X018R-X043D-X076D-X101G-X103A-X104I-X232V-X245R-X269R,X024R-X045T-X076D-X078R-X101G-X103A-X104I-X232V-X245R-X269R,X018R-X103A-X232V-X249R,X018R-X101G-X104I-X232V-X245R,X020R-X024R-X101G-X103A-X104I-X217E-X232V-X245R-

X249R,X018R-X22K-X043D-X101G-X103A-X104I-X232V-X245R,X043R-X045T-X101G-X103A-X104I-X232V-X245R-X269R,X020R-X22W-X101G-X103A-X104I-X211Q-X232V-X245R,X024R-X076D-X078R-X101G-X103A-X104I-X232V-X245R-X269R,X020R-X22W-X078R-X101A-X103A-X104I-X116A-X183D-X232V,X018R-X024R-X076D-X116A-X215F-X249R,X018R-X043R-X045T-X101G-X103A-X104I-X232V-X245R,X024R-X043R-X076D-X101G-X103A-X104I-X232V-X245R,X020R-X022W-X101G-X103A-X104I-X232V-X245R,X020R-X022W-X101G-X103A-X104I-X211Q-X232V-X245R,X020R-X022W-X078R-X101G-X103A-X104I-X116A-X213A-X215F-X232V-X245R,X043D-X076D-X078R-X101G-X103A-X104I-X232V-X245R-X269R,X018R-X024R-X076D-X101A-X116A-X213A-X249R,X018R-X024R-X076D-X116A-X211Q-X249R,X043R-X045T-X076D-X078R-X101G-X103A-X104I-X232V-X245R,X018R-X101G-X245R,X020R-X22W-X101A-X103A-X104I-X211Q-X213A-X232V-X245R,X020R-X024R-X043D-X076D-X078R-X101G-X103A-X104I-X232V-X245R,X018R-X045T-X076D-X078R-X101G-X103A-X104I-X232V-X245R,X020R-X078R-X101G-X103A-X104I-X211Q-X213A-X215F-X232V-X245R,X045T-X078R-X101G-X103A-X104I-X232V-X245R-X269R,X024R-X043D-X101G-X103A-X104I-X232V-X245R-X269R,X018R-X101G-X103A-X249R,X018R-X22W-X024R-X076D-X101A-X116A-X232V-X245R,X018R-X101G-X104I-X232V-X249R,X020R-X22W-X101A-X103A-X104I-X215F-X232V-X245R,X018R-X024R-X076D-X211Q-X213A-X249R,X018R-X022W-X024R-X076D-X101A-X198L-X249R,X024R-X101G-X103A-X104I-X232V-X245R,X020R-X076D-X101G-X103A-X104I-X232V-X245R-X269R,X020R-X101G-X103A-X104I-X232V-X245R-X269R,X043D-X078R-X101G-X103A-X104I-X232V-X245R,X020R-X101G-X104I-X213A-X215F-X232V-X245R,X020R-X101G-X103A-X104I-X116A-X215F-X232V-X245R,X024R-X103A-X104I-X249R,X018R-X076D-X078R-X101G-X103A-X104I-X232V-X245R,X045T-X076D-X078R-X101G-X103A-X104I-X232V-X245R-X269R,X024R-X101G-X104I-X245R,X020R-X101G-X103A-X104I-X211Q-X213A-X215F-X232V-X245R,X024R-X103A-X104I-X232V-X249R,X018R-X024R-X076D-X116A-X211Q-X215F-X249R,X018R-X245R,X024R-X103A-X245R,X024R-X103A-X104I-X245R,X020R-X078R-X101G-X232V-X245R,X018R-X024R-X076D-X104I-X249R,X018R-X024R-X104I-X249R,X024R-X101G-X103A-X104I-X232V-X245R,X018R-X024R-X076D-X211Q-X215F-X249R,X019H-X020R-X022W-X078R-X101G-X103A-X104I-X211Q-X232V-X245R,X018R-X024R-X076D-X101A-X198L-X211Q-X213A-X249R,X018R-X024R-X043D-X101G-X103A-X104I-X232V-X245R,X020R-X22W-X103A-X104I-X232V-X245R,X018R-X103A-X104I-X249R,X018R-X022W-X024R-X076D-X101A-X198L-X215F-X249R,X018R-X024R-X101G-X104I-X232V,X078R-X101G-X103A-X104I-X232V-X245R-X269R,X024R-X043R-X076D-X078R-X101G-X103A-X104I-X232V-X245R,X018R-X020R-X043D-X076D-X101G-X103A-X104I-X232V-X245R,X018R-X22W-X024R-X076D-X116A-X213A-X249R,X018R-X024R-X101G-X104I,X020R-X101A-X103A-X104I-X215F-X232V-X245R,X018R-X045T-X078R-X101G-X103A-X104I-X232V-X245R,X018R-X101G-X103A-X245R,X043R-X076D-X078R-X101G-X103A-X104I-X232V-X245R,X020R-X022W-X101A-X103A-X104I-X211Q-X215F-X232V-X245R,X020R-X22W-X078R-X101G-X103A-X104I-X116A-X213A-X215F-X232V-X245R,X020R-X078R-X101G-X103A-

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X022W-X024R-X076D-X183D-X198L-X211Q-X215F-X249R,X018R-X022W-X024R-X076D-X183D-X249R,X018R-X022W-X024R-X076D-X101A-X183D-X198L-X215F-X249R,X018R-X020R-X043D-X045T-X076D-X101G-X103A-X104I-X232V-X245R,X020R-X022W-X101A-X103A-X104I-X183D-X198L-X215F-X232V-X245R,X076D-X101G-X103A-X104I-X249R,X018R-X020R-X024R-X076D-X183D-X198L-X215F-X249R,X018R-X020R-X022W-X024R-X076D-X101A-X183D-X215F-X249R,X018R-X020R-X024R-X076D-X211Q-X213A-X249R,X018R-X024R-X076D-X116A-X183D-X211Q-X213A-X249R,X018R-X024R-X076D-X116A-X183D-X198L-X249R,X018R-X020R-X024R-X076D-X211Q-X243D-X249R,X018R-X020R-X045T-X076D-X101G-X103A-X104I-X232V-X245R-X249R,X018R-X022W-X024R-X076D-X183D-X198L-X211Q-X213A-X249R,X018R-X024R-X076D-X101A-X116A-X183D-X198L-X211Q-X213A-X249R,X018R-X022W-X024R-X076D-X116A-X198L-X211Q-X213A-X215F-X249R,X024R-X076D-X101G,X018R-X020R-X024R-X076D-X101A-X198L-X213A-X215F-X249R,X018R-X022W-X024R-X076D-X116A-X183D-X211Q-X213A-X249R,X018R-X020R-X024R-X076D-X183D-X215F-X249R,X018R-X043D-X076D-X078R-X101G-X103A-X104I-X232V-X245R-X249R,X018R-X022W-X024R-X076D-X116A-X183D-X211Q-X213A-X245R,X020R-X024R-X076D-X078R-X101G-X103A-X104I-X232V-X245R-X249R,X018R-X020R-X045T-X101G-X103A-X104I-X232V-X245R-X249R,X018R-X024R-X076D-X101A-X183D-X198L-X211Q-X249R,X018R-X022W-X024R-X076D-X183D-X211Q-X213A-X249R,X018R-X020R-X024R-X076D-X116A-X198L-X211Q-X215F-X249R-X269S,X018R-X020R-X022W-X024R-X076D-X101A-X116A-X183D-X198L-X211Q-X215F-X249R,X020R-X022W-X101A-X103A-X104I-X183D-X213A-X215F-X232V-X245R,X018R-X024R-X076D-X086V-X101A-X183D-X198L-X211Q-X249R,X018R-X076D-X101G-X198T-X232V,X018R-X020R-X024R-X076D-X101A-X116A-X183D-X198L-X211Q-X215F-X249R,X018R-X022W-X024R-X076D-X101A-X116A-X183D-X213A-X215F-X249R,X018R-X022W-X024R-X076D-X101A-X183D-X211Q-X213A-X215F-X249R,X018R-X024R-X076D-X183D-X249R-X248T,X018R-X076D-X104I-X245R-X249R,X018R-X022W-X024R-X076D-X101A-X116A-X183D-X198L-X215F-X249R,X018R-X022W-X024R-X076D-X116A-X183D-X213A-X215F-X249R,X018R-X020R-X022W-X024R-X076D-X116A-X183D-X211Q-X213A-X215F-X249R,X018R-X020R-X024R-X076D-X101A-X249R,X018R-X020R-X024R-X076D-X101A-X116A-X213A-X215F-X249R,X018R-X022W-X024R-X076D-X116A-X183D-X211Q-X215F-X249R,X018R-X022W-X024R-X076D-X116A-X183D-X198L-X211Q-X213A-X249R,X043R-X045T-X078R-X101G-X103A-X104I-X217E-X232V-X245R,X043R-X045T-X101G-X103A-X104I-X232V-X245R-X249R,X018R-X076D-X101G-X104I,X020R-X045T-X076D-X078R-X101G-X103A-X104I-X232V-X245R-X249R,X043D-X076D-X101G-X103A-X104I-X232V-X245R,X018R-X020R-X022W-X024R-X076D-X101A-X116A-X183D-X198L-X249R,X018R-X076D-X104I,X018R-X020R-X043D-X101G-X103A-X104I-X232V-X245R-X249R,X018R-X020R-X022W-X024R-X076D-X183D-X211Q-X249R,X018R-X024R-X076D-X101A-X183D-X198L-X211Q-X215F-X249R,X101G-X104I,X018R-X022W-X024R-X076D-X116A-X183D-X198L-X211Q-X213A-X215F-X249R,X018R-X020R-X024R-X076D-X101A-X183D-X211Q-X213A-X215F-X249R,X018R-

X020R-X024R-X076D-X116A-X183D-X215F-X249R-X263D,X018R-X022W-X024R-X076D-X101A-X183D-X249R,X018R-X024R-X076D-X101A-X116A-X183D-X198L-X215F-X249R,X018R-X022W-X024R-X076D-X116A-X198L-X215F-X249R-X269H,X018R-X043D-X045T-X076D-X078R-X101G-X103A-X104I-X232V-X245R,X018R-X024R-X045T-X076D-X078R-X101G-X103A-X104I-X232V-X245R-X269R,X078R-X101G-X103A-X104I-X217E-X232V-X245R,X018R-X020R-X022W-X024R-X076D-X101A-X183D-X198L-X213A-X215F-X249R,X018R-X020R-X024R-X076D-X183D-X198L-X213A-X249R,X018R-X020R-X022W-X024R-X076D-X116A-X198L-X211Q-X215F-X249R,X018R-X020R-X022W-X024R-X076D-X116A-X183D-X211Q-X249R,X018R-X020R-X022W-X024R-X076D-X101A-X198L-X211Q-X213A-X249R,X018R-X020R-X022W-X024R-X076D-X249R,X020R-X022W-X101G-X103A-X104I-X116A-X183D-X198L-X211Q-X213A-X215F-X232V-X245R,X104I-X232V,X018R-X020R-X022W-X024R-X076D-X101A-X116A-X183D-X211Q-X215F-X249R,X018R-X020R-X022W-X024R-X076D-X101A-X116A-X183D-X198L-X211Q-X213A-X215F-X249R,X018R-X020R-X022W-X024R-X076D-X101A-X183D-X213A-X215F-X249R,X018R-X022W-X024R-X076D-X101A-X183D-X198L-X211Q-X213A-X249R,X018R-X022W-X024R-X076D-X101A-X183D-X198L-X249R,X043D-X045T-X101G-X103A-X104I-X232V-X245R-X269R,X018R-X020R-X024R-X076D-X101A-X183D-X198L-X211Q-X249R,X018R-X020R-X043R-X101G-X103A-X104I-X217E-X232V-X245R,X024R-X043R-X076D-X078R-X101G-X103A-X104I-X232V-X245R-X269R,X043R-X045T-X076D-X078R-X101G-X103A-X104I-X166F-X176P-X179V-X184T-X187P-X194P,X018R-X022W-X024R-X041E-X076D-X101A-X160T-X183D-X211Q-X213A-X249R,X018R-X020R-X022W-X024R-X076D-X116A-X183D-X198L-X211Q-X215F-X249R,X018R-X020R-X022W-X024R-X076D-X101A-X116A-X198L-X213A-X249R,X018R-X022W-X024R-X076D-X101A-X116A-X183D-X198L-X211Q-X213A-X249R,X018R-X020R-X024R-X076D-X198L-X213A-X249R,X018R-X020R-X022W-X024R-X076D-X116A-X183D-X198L-X211Q-X249R,X018R-X020R-X024R-X076D-X183D-X211Q-X215F-X249R,X024R-X076D-X104I,X018R-X076D-X101G-X232V,X018R-X024R-X076D-X101A-X116A-X183D-X198L-X211Q-X213A-X215F-X249R,X018R-X020R-X022W-X024R-X076D-X116A-X183D-X215F-X249R,X018R-X024R-X031F-X076D-X116A-X183D-X211Q-X213A-X215F-X249R,X018R-X024R-X076D-X101A-X116A-X183D-X198L-X213A-X249R-X269S,X018R-X020R-X024R-X076D-X101A-X116A-X198L-X215F-X249R,X018R-X043R-X076D-X078R-X101G-X103A-X104I-X232V-X245R-X269R,X018R-X020R-X024R-X076D-X101A-X114T-X198L-X211Q-X215F-X249R,X024R-X043R-X078R-X101G-X103A-X104I-X217E-X232V-X245R,X024R-X076D-X103A-X104I-X232V,X018R-X020R-X022W-X024R-X076D-X101A-X198L-X211Q-X215F-X249R,X101G-X104I-X232V,X018R-X022W-X024R-X076D-X183D-X198L-X213A-X215F-X249R,X018R-X022W-X024R-X076D-X183D-X198L-X211Q-X249R,X018R-X020R-X024R-X076D-X183D-X213A-X249R,X018R-X024R-X076D-X101A-X183D-X211Q-X215F-X249R,X018R-X020R-X022W-X024R-X076D-X116A-X211Q-X213A-X249R,X018R-X078R-X101G-X103A-X104I-X232V-X245R-X269R,X018R-X022W-X024R-X076D-X101A-X116A-X183D-X211Q-X215F-X249R-X260A,X076D-X249R,X018R-X022W-X024R-X076D-

X183D-X211Q-X215F-X249R,X018R-X020R-X024R-X076D-X116A-X211Q-X215F-X249R,X018R-X020R-X024R-X076D-X213A-X249R,X018R-X020R-X022W-X024R-X076D-X116A-X183D-X198L-X249R,X018R-X020R-X022W-X024R-X076D-X101A-X183D-X249R,X076D-X104I-X249R,X020R-X022W-X101A-X103A-X104I-X116A-X183D-X211Q-X213A-X215F-X232V-X245R,X024R-X043R-X045T-X078R-X101G-X103A-X104I-X217E-X232V-X245R,X018R-X020R-X022W-X024R-X076D-X183D-X198L-X215F-X249R,X018R-X076D-X101G-X103A,X020R-X024R-X101G-X103A-X104I-X232V-X245R-X269R,X018R-X020R-X024R-X076D-X101A-X116A-X183D-X211Q-X249R,X101G-X103A-X232V,X024R-X076D-X101G-X232V,X018R-X022W-X024R-X076D-X101A-X183D-X198L-X211Q-X249R,X018R-X020R-X024R-X076D-X101A-X183D-X198L-X211Q-X215F-X249R,X018R-X020R-X024R-X076D-X183D-X198L-X249R,X018R-X022W-X024R-X076D-X101A-X116A-X183D-X198L-X211Q-X249R,X018R-X020R-X024R-X076D-X116A-X156V-X183D-X211Q-X215F-X249R-X269S,X045T-X076D-X101G-X103A-X104I-X232V-X245R-X249R,X018R-X020R-X024R-X076D-X101A-X183D-X198L-X249R,X018R-X020R-X022W-X024R-X076D-X198L-X211Q-X215F-X249R,X018R-X020R-X022W-X024R-X076D-X101A-X116A-X198L-X211Q-X215F-X249R,X018R-X020R-X022W-X024R-X076D-X116A-X249R,X018R-X076D-X101G,X018R-X024R-X076D-X116A-X183D-X198L-X213A-X215F-X249R,X018R-X020R-X022W-X024R-X076D-X101A-X116A-X198L-X213A-X215F-X249R,X018R-X024R-X076D-X101A-X116A-X183D-X198L-X211Q-X249R,X018R-X076D-X232V,X018R-X020R-X024R-X076D-X101A-X232V-X245R,X018R-X043D-X045T-X076D-X101G-X103A-X104I-X232V-X245R,X018R-X022W-X024R-X076D-X183D-X213A-X215F-X249R,X018R-X024R-X076D-X101A-X116A-X211Q-X213A-X237D-X249R,X018R-X020R-X024R-X076D-X101A-X116A-X183D-X211Q-X249R-X275S,X018R-X022W-X024R-X076D-X101A-X116A-X183D-X198L-X211Q-X213A-X215F-X249R,X024R-X076D,X018R-X024R-X076D-X183D-X211Q-X215F-X249R,X018R-X022W-X024R-X076D-X116A-X183D-X198L-X213A-X215F-X249R,X076D-X104I-X232V-X249R,X018R-X076D-X103A-X232V,X018R-X020R-X024R-X076D-X101A-X116A-X183D-X198L-X211Q-X213A-X249R,X018R-X020R-X024R-X076D-X101A-X183D-X213A-X249R,X018R-X020R-X024R-X076D-X101A-X175E-X183D-X211Q-X215F-X249R,X018R-X020R-X043D-X078R-X101G-X103A-X104I-X217E-X232V-X245R-X273E,X020R-X024R-X043D-X045T-X076D-X101G-X103A-X104I-X232V-X245R,X005S-X101G-X103A-X104I-X232V-X245R-X249R,X103A-X104I-X232V,X018R-X020R-X024R-X068A-X076D-X101A-X116A-X213A-X215F-X249R,X018R-X022W-X024R-X076D-X101A-X198L-X215F-X249R-X275S,X018R-X024R-X076D-X183D-X198L-X211Q-X213A-X249R,和X043D-X045T-X101G-X103A-X104I-X232V-X245R,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0239] 本发明还提供分离的枯草杆菌蛋白酶变体,其中该枯草杆菌蛋白酶变体是具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:X018R-X024R-X043R-X076D-X249R-X269R,X018R-X022R-X024R-X043R-X076D-X249R,X018R-X043D-X101G-X103A-X104I-X232V-X245R,X020R-X043D-X101G-X103A-X104I-X232V-

X245R,X043D-X101G-X103A-X104I-X232V-X245R-X269R,X043D-X078R-X101G-X103A-X104I-X232V-X245R,X043R-X076D-X101G-X103A-X104I-X232V-X245R,X022R-X043R-X101G-X103A-X104I-X232V-X245R,X043R-X078R-X101G-X103A-X104I-X232V-X245R,X020R-X076D-X101G-X103A-X104I-X232V-X245R,X043R-X076D-X101G-X103A-X104I-X232V-X245R,X022R-X076D-X101G-X103A-X104I-X232V-X245R,X076D-X078R-X101G-X103A-X104I-X232V-X245R,X018R-X024R-X043R-X076D-X249R,X018R-X024R-X076D-X242R-X249R,X018R-X024R-X076D-X249R-X269R,X018R-X022R-X024R-X076D-X249R,X018R-X024R-X076D-X078R-X249R,X018R-X024R-X043D-X076D-X249R-X269R,X018R-X022R-X024R-X043D-X076D-X249R,X018R-X024R-X043D-X076D-X078R-X249R,X020R-X101G-X103G-X104I-X232V-X245R,X020R-X101G-X103A-X104L-X232V-X245R,X020R-X101G-X103A-X104V-X232V-X245R,X020R-X101G-X103S-X104I-X232V-X245R,X020R-X101G-X103S-X104L-X232V-X245R,X020R-X101S-X103S-X104I-X232V-X245R,X020R-X101S-X103S-X104L-X232V-X245R,X020R-X101A-X103A-X104L-X232V-X245R,X020R-X101S-X103S-X104V-X232V-X245R,X020R-X101S-X103A-X104I-X232V-X245R,X020R-X101S-X103A-X104V-X232V-X245R,X020R-X101S-X103G-X104I-X232V-X245R,X020R-X101S-X103G-X104V-X232V-X245R,X020R-X101A-X103A-X104V-X232V-X245R,X020R-X101A-X103S-X104I-X232V-X245R,X020R-X101A-X103S-X104V-X232V-X245R,X018R-X024R-X043R-X076D-X078R-X249R,X024R-X043D-X101G-X103A-X104I-X232V-X245R,X043D-X101G-X103A-X104I-X232V-X245R-X249R,X024R-X076D-X101G-X103A-X104I-X232V-X245R,X076D-X101G-X103A-X104I-X232V-X242R-X245R,X018R-X020R-X024R-X076D-X217E-X249R,X018R-X024R-X043R-X076D-X217E-X249R,X018R-X024R-X043D-X076D-X242R-X249R,X018R-X020R-X024R-X043R-X076D-X249R,X020R-X101A-X103G-X104V-X232V-X245R,X043D-X101G-X103A-X104I-X232V-X245R,X018R-X024R-X076D-X217E-X249R-X269R,和X018R-X024R-X076D-X217E-X242R-X249R,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0240] 本发明还提供分离的枯草杆菌蛋白酶变体,其中该枯草杆菌蛋白酶变体是具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:X020R-X101A-X103A-X104I-X118R-X232V-X245R,X020R-X024R-X116A-X213A,X043R-X101A-X116A-X215F-X269R,X024R-X043R-X101A-X116A,X024R-X043R-X101A-X116A-X215F-X269R,X020R-X101G-X103A-X104I-X215F-X232V-X245R,X043R-X101A-X269R,X024R-X043R-X116A-X213A-X269R,X020R-X024R-X043R-X045T-X101A-X213A,X024R-X043R-X116A-X215F-X269R,X020R-X024R-X213A-X215F,X020R-X116A-X269R,X024R-X116A-X213A-X269R,X043R-X101A-X116A-X269R,X101G-X103A-X104I-X116A-X213A-X232V-X245R-X269R,X024R-X043R-X045T-X101A-X116A-X215F-X269R,X020R-X043R-X101A-X269R,X101A-X103A-X104I-X213A-X232V-X245R-X269R,X024R-X215F-X269R,X043R-X101A-X116A-X213A-X215F-X269R,X043R-X101A-X213A-X269R,X020R-X024R-X043R-X045T-X116A-X213A,X101G-X103A-X104I-X232V-X245R-X269R,X024R-X043R-X045T-X101A-X116A-X213A-X269R,X024R-X043R-X045T-X269R,X020R-X043R-X045T-X101A-

X269R,X024R-X043R-X116A-X269R,X020R-X024R-X043R-X045T,X043R-X116A-X269R,X024R-X043R-X101A-X215F-X269R,X024R-X043R-X045T-X213A-X215F-X269R,X020R-X024R-X045T-X269R,X020R-X043R-X101A-X116A-X213A-X215F,X020R-X101G-X103A-X104I-X213A-X215F-X232V-X245R,X020R-X024R-X045T-X116A-X269R,X020R-X101A-X116A-X269R,X024R-X043R-X215F,X020R-X024R-X213A,X024R-X043R-X101A-X215F,X020R-X024R-X043R-X045T-X116A,X020R-X024R-X043R-X045T-X101A-X269R,X020R-X024R-X101A-X215F,X020R-X024R-X116A-X213A-X215F,X020R-X024R-X116A,X020R-X024R-X101A-X116A,X043R-X213A-X215F-X269R,X024R-X101A-X269R,X024R-X043R-X116A-X215F,X020R-X038A-X043R-X101A,X020R-X024R-X116A-X215F,X024R-X043R-X101A-X213A,X014L-X020R-X024R-X043R-X045T-X101A-X215F,X020R-X024R-X215F,X020R-X116A-X215F-X269R,X020R-X045T-X116A-X269R,X020R-X024R-X043R-X045T-X215F,和X020R-X024R-X043R-X045T-X116A-X213A-X215F,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0241] 本发明还提供分离的枯草杆菌蛋白酶变体,其中该枯草杆菌蛋白酶变体是具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:X043R-X076D-X101A-X103A-X104I-X158E-X188D-X232V-X245R-X248D-X249R-X271F,X024R-X043R-X076D-X101A-X103A-X104I-X158E-X188D-X217E-X232V-X245R-X248D-X249R,X101A-X103A-X104I-X158E-X188D-X232V-X245R-X248D-X249R-X271F-X271F,X101A-X103A-X104I-X158E-X188D-X217E-X232V-X245R-X248D-X249R-X271F,X076D-X101G-X103A-X104I-X114V-X158E-X188D-X232V-X245R-X248D-X249R-X271F,X024R-X076D-X101G-X103A-X104I-X158E-X188D-X232V-X245R-X248D-X249R-X271F,X024R-X043R-X101A-X103A-X104I-X158E-X188D-X217E-X232V-X245R-X248D-X249R,X024R-X043R-X101A-X103A-X104I-X158E-X188D-X232V-X245R-X248D-X249R,X024R-X101A-X103A-X104I-X158E-X166D-X188D-X217E-X232V-X245R-X248D-X249R,X076D-X101G-X103A-X104I-X128L-X158E-X188D-X232V-X245R-X248D-X249R-X271F,和X043R-X076D-X101G-X103A-X104I-X158E-X166D-X188D-X232V-X245R-X248D-X249R-X271F,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0242] 本发明还提供分离的枯草杆菌蛋白酶变体,其中该枯草杆菌蛋白酶变体是具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:X022A-X101G-X103A-X104I-X159D-X217E-X232V-X245R-X248D-X271F,X022A-X043R-X101G-X103A-X104I-X159D-X188D-X217E-X232V-X245R-X248D-X271F,X022A-X101G-X103A-X104I-X159D-X188D-X232V-X245R-X248D-X271F,X043R-X101A-X103A-X104I-X158E-X188D-X217E-X232V-X245R-X248D-X249R,X043R-X076D-X101A-X103A-X104I-X158E-X188D-X217E-X232V-X245R-X248D-X249R-X271F,X024R-X101G-X103A-X104I-X158E-X188D-X217E-X232V-X245R-X248D-X249R,X024R-X101G-X103A-X104I-X158E-X188D-X232V-X245R-X248D-X249R,X101G-X103A-X104I-X158E-X188D-X232V-X245R-X248D-X249R,X024R-X101G-X103A-X104I-X158E-X183D-X188D-X232V-X245R-X248D-X249R,

X022A-X076D-X101G-X103A-X104I-X159D-X188D-X232V-X245R-X248D-X271F,X022A-X043R-X076D-X101G-X103A-X104I-X159D-X188D-X232V-X245R-X248D-X271F,X022A-X076D-X101G-X103A-X104I-X159D-X232V-X245R-X248D-X271F,X022A-X101G-X103A-X104I-X159D-X232V-X245R-X248D-X271F,X076D-X101A-X103A-X104I-X158E-X188D-X232V-X245R-X248D-X249R-X271F,X043R-X101A-X103A-X104I-X158E-X166D-X188D-X232V-X245R-X248D-X249R,X024R-X076D-X101A-X103A-X104I-X158E-X166D-X188D-X232V-X245R-X248D-X249R-X271F,X076D-X101A-X103A-X104I-X158E-X188D-X232V-X245R-X248D-X249R,X101A-X103A-X104I-X158E-X166D-X188D-X232V-X245R-X248D-X249R-X271F,X043R-X076D-X101A-X103A-X104I-X158E-X166D-X188D-X232V-X245R-X248D-X249R-X271F,X101G-X103A-X104I-X158E-X166D-X188D-X232V-X245R-X248D-X249R-X271F,X101A-X103A-X104I-X158E-X188D-X232V-X245R-X248D-X249R-X271F,X101A-X103A-X104I-X158E-X188D-X217E-X232V-X245R-X248D-X249R,X076D-X101A-X103A-X104I-X158E-X166D-X188D-X232V-X245R-X248D-X249R-X271F,X101G-X103A-X104I-X158E-X183D-X188D-X232V-X245R-X248D-X249R,X024R-X101G-X103A-X104I-X128L-X158E-X188D-X232V-X245R-X248D-X249R,X076D-X101G-X103A-X104I-X158E-X166D-X188D-X232V-X245R-X248D-X249R-X271F,X043R-X076D-X101A-X103A-X104I-X158E-X166D-X188D-X232V-X245R-X248D-X249R,和X076D-X101A-X103A-X104I-X158E-X188D-X217E-X232V-X245R-X248D-X249R-X271F,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0243] 本发明还提供分离的枯草杆菌蛋白酶变体,其中该枯草杆菌蛋白酶变体是具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:X017R-X022A-X076D-X101G-X103A-X104I-X159D-X188D-X232V-X245R-X248D-X271F,X022A-X043R-X101G-X103A-X104I-X159D-X232V-X245R-X248D-X271F,X022A-X101G-X103A-X104I-X159D-X188D-X232V-X245R-X248D-X249R-X271F,X017R-X022A-X076D-X101G-X103A-X104I-X159D-X232V-X245R-X248D-X271F,X022A-X076D-X101G-X103A-X104I-X159D-X232V-X245R-X248D-X249R-X271F,X022A-X101G-X102A-X103A-X104I-X159D-X188D-X232V-X245R-X248D-X271F,和X022A-X043R-X076D-X101G-X103A-X104I-X159D-X232V-X245R-X248D-X249R-X271F,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0244] 本发明还提供分离的枯草杆菌蛋白酶变体,其中该枯草杆菌蛋白酶变体是具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:X101S-X103A-X104I-X158E-X188D-X232V-X245R-X248D-X249R,X101S-X103G-X104V-X158E-X188D-X232V-X245R-X248D-X249R,X101G-X103S-X104I-X158E-X188D-X232V-X245R-X248D-X249R,X101A-X103A-X104I-X158E-X188D-X232V-X245R-X248D-X249R,X101A-X103A-X104L-X158E-X188D-X232V-X245R-X248D-X249R,X101G-X103G-X104I-X158E-X188D-X232V-X245R-X248D-X249R,X101S-X103G-X104I-X158E-X188D-X232V-X245R-X248D-X249R,X101S-X103S-X104I-X158E-X188D-X232V-X245R-X248D-X249R,X101S-X103S-X104V-X158E-X188D-X232V-X245R-X248D-X249R,X101A-X103S-X104I-X158E-

X188D-X232V-X245R-X248D-X249R,X101A-X103S-X104I-X159E-X232V-X245R-X248D-X249R,X101S-X103A-X104I-X159E-X232V-X245R-X248D-X249R,X101G-X103A-X104L-X158E-X188D-X232V-X245R-X248D-X249R,X101A-X103A-X104L-X159E-X232V-X245R-X248D-X249R,X101A-X103S-X104L-X159E-X232V-X245R-X248D-X249R,X101G-X103S-X104L-X159E-X232V-X245R-X248D-X249R,X101S-X103A-X104L-X159E-X232V-X245R-X248D-X249R,X101A-X103G-X104V-X159E-X232V-X245R-X248D-X249R,和X101S-X103A-X104V-X159E-X232V-X245R-X248D-X249R,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0245] 本发明还提供分离的枯草杆菌蛋白酶变体,其中该枯草杆菌蛋白酶变体是具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:X026F-X051W-X104L-X106E,X026F-X031F-X078N-X102A-X160D,X020K-X100S-X116L-X158E-X166D-X243F,X033S-X043W-X218D-X239G-X243F,X022L-X038F-X048R-X062E-X100S-X186K,X101D-X103N-X116L-X144R-X215D,X104L-X105T-X213A-X217E-X256N,X043W-X101D-X212M-X243F,X026F-X048R-X105T-X213A-X218D-X224A,X024F-X101D-X118R-X215D-X250I-X272F,X121F-X185E-X224A-X239G,X022L-X031F-X102A-X128D-X224A-X243F,X062E-X078N-X102A-X116L-X144R-X250I,X022L-X038F-X121F-X160D-X272F,X026F-X078N-X159C-X186K-X243F,X024F-X048R-X118R-X166D-X217E,X023A-X038F-X078N-X100S-X212M-X215D,X100S-X116L-X158E-X213A,X078N-X104L-X118R-X128D,X102A-X103N-X105T-X194E,X022L-X078N-X128D-X213A,X027R-X100S-X118R-X160D-X188D-X243F,X024F-X102A-X186K-X213A-X217E-X243F,X033S-X105T-X188D-X216F,X023A-X100S-X194E-X212M,X048R-X128D-X185E-X239G,X020K-X024F-X033S-X129E-X194E,X020K-X027R-X129E-X166D-X239G,X022L-X023A-X027R-X101D-X104L-X216F,X033S-X118R-X129E-X194E-X239G,X022L-X078N-X116L-X129E-X256N,X027R-X101D-X103N-X105T-X272F,X048R-X078N-X116L-X185E-X217E-X239G,X023A-X024F-X027R-X062E,X024F-X103N-X104L-X118R-X188D,X026F-X104L-X256N-X272F,X024F-X043W-X104L-X121F-X129E,X062E-X078N-X116L-X224A,X023A-X024F-X051W-X158E,X027R-X038F-X102A-X116L,X062E-X078N-X144R-X212M,X031F-X116L-X256N-X272F,X022L-X033S-X104L-X116L-X160D-X186K,X024F-X118R-X129E-X186K-X213A,X043W-X105T-X213A-X215D-X216F,X031F-X105T-X186K-X188D,X026F-X194E-X213A-X256N,和X103N-X160D-X250I-X256N,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0246] 本发明还提供分离的枯草杆菌蛋白酶变体,其中该枯草杆菌蛋白酶变体是具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:X022A-X024R-X101D-X103A-X104I-X118R-X159D-X188D-X232V-X248D-X271F,X022A-X024R-X103A-X104I-X129E-X159D-X188D-X232V-X248D-X271F,X022A-X024R-X103A-X104I-X118R-X159D-X188D-X217D-X232V-X248D,X022A-X024R-X101D-X103A-X104I-X118R-X129E-X159D-X188D-X232V-X245R-X248D,X022A-X024R-X101D-X103A-X104I-X159D-X188D-X232V-X245R-X248D,X022A-X043R-X103A-X104I-X118R-X129E-X159D-X188D-

X232V-X245R-X248D,X022A-X043R-X103A-X104I-X118R-X128I-X129E-X159D-X188D-X232V-X248D,X022A-X043R-X101D-X103A-X104I-X118R-X129E-X159D-X188D-X232V-X248D-X271F,X022A-X024R-X043R-X101D-X103A-X104I-X159D-X188D-X232V-X245R-X248D,X022A-X103A-X104I-X159D-X188D-X232V-X248D,X022A-X024R-X103A-X104I-X118R-X129E-X159D-X188D-X232V-X248D-X271F,X022A-X024R-X103A-X104I-X159D-X188D-X217D-X232V-X245R-X248D-X271F,X022A-X043R-X062E-X103A-X104I-X159D-X188D-X232V-X245R-X248D-X271F,X022A-X043R-X103A-X104I-X129E-X159D-X188D-X232V-X245R-X248D,X022A-X024R-X103A-X104I-X159D-X188D-X217D-X232V-X248D-X271F,X022A-X103A-X104I-X118R-X159D-X188D-X217D-X232V-X245R-X248D,X022A-X024R-X101D-X103A-X104I-X118R-X128I-X159D-X188D-X232V-X245R-X248D,X022A-X024R-X043R-X103A-X104I-X159D-X188D-X217D-X232V-X248D-X271F,X022A-X043R-X103A-X104I-X118R-X159D-X188D-X217D-X232V-X248D-X271F,X022A-X043R-X103A-X104I-X118R-X159D-X188D-X232V-X248D-X271F,X022A-X103A-X104I-X128I-X129E-X159D-X188D-X232V-X248D-X271F,X022A-X103A-X104I-X159D-X188D-X217D-X232V-X245R-X248D-X271F,X022A-X043R-X103A-X104I-X128I-X159D-X188D-X232V-X245R-X248D,X022A-X101D-X103A-X104I-X118R-X159D-X188D-X217D-X232V-X245R-X248D-X271F,X022A-X103A-X104I-X118R-X129E-X159D-X188D-X232V-X245R-X248D-X271F,X022A-X024R-X043R-X103A-X104I-X118R-X159D-X188D-X217D-X232V-X248D,X022A-X062E-X103A-X104I-X118R-X159D-X188D-X232V-X245R-X248D,X022A-X043R-X101D-X103A-X104I-X118R-X129E-X159D-X188D-X217D-X232V,X022A-X024R-X103A-X104I-X159D-X188D-X217D-X232V-X248D,X022A-X024R-X043R-X103A-X104I-X118R-X128I-X129E-X159D-X188D-X217D-X232V-X248D-X271F,和X022A-X103A-X104I-X118R-X159D-X188D-X217D-X232V-X245R-X248D-X271F,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0247] 本发明还提供分离的枯草杆菌蛋白酶变体,其中该枯草杆菌蛋白酶变体是具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:X020K-X024F-X062E-X188D-X239G,X024F-X062E-X116L-X239G,X020K-X023A-X062E-X188D,X020K-X023A-X024F-X062E-X118R-X188D-X213A,X020K-X043W-X062E-X116L-X188D-X213A-X239G,X023A-X062E-X116L-X118R,X023A-X024F-X062E-X116L-X118R,X024F-X116L,X024F-X062E-X188D-X213A,X023A-X062E-X116L-X118R-X188D-X239G,X020K-X024F-X062E,X020K-X043W-X062E-X116L-X239G,X024F-X062E-X116L-X213A-X239G,X020K-X024F-X043W-X062E-X116L-X213A,X020K-X023A-X024F-X062E-X116L-X188D-X213A,X024F-X062E-X188D-X239G,X023A-X043W-X062E-X116L-X118R-X213A,X062E-X188D-X239G,X020K-X024F-X062E-X239G,X024F-X116L-X118R-X188D-X239G,X020K-X023A-X062E-X116L-X118R-X213A,X020K-X023A-X024F-X062E-X188D-X213A-X239G,X024F-X043W-X118R-X188D,X023A-X024F-X116L-X118R-X188D-X213A,X020K-X023A-X043W-X116L-X188D-X213A-X239G,X023A-X024F-X116L-X188D-X239G,X023A-X043W-X116L-X118R-X188D,X023A-X024F-X118R-X188D-X239G,X023A-X024F-X043W-X062E-

X116L-X118R,X020K-X043W-X188D-X213A,X024F-X062E-X118R-X239G,X023A-X043W-X188D-X213A,X020K-X024F-X043W-X062E-X116L-X118R-X188D-X239G,X020K-X116L-X188D-X239G,X020K-X043W-X062E-X118R,X020K-X043W-X116L-X188D-X213A,X020K-X024F,X023A-X043W-X116L-X239G,X023A-X024F-X043W-X116L-X118R-X188D-X239G,X020K-X023A-X043W-X213A,和X023A-X024F-X062E-X118R-X213A-X239G,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0248] 本发明还提供分离的枯草杆菌蛋白酶变体,其中该枯草杆菌蛋白酶变体是具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:X020K-X023A-X043W-X118R-X128I-X129E-X159D-X188D,X024F-X118R-X128I-X129E-X159D,X020K-X024F-X062E-X116L-X118R-X188D,X020K-X062E-X116L-X188D,X062E-X116L-X118R-X213A,X020K-X023A-X062E-X116L-X188D,X062E-X116L-X118R-X188D,X020K-X062E-X116L-X213A,X020K-X023A-X062E-X116L,X020K-X062E-X188D-X213A,X020K-X062E,X020K-X024F-X062E-X116L-X188D,X020K-X043W-X062E-X116L-X188D,X020K-X024F-X062E-X188D-X213A,X062E-X116L-X188D-X213A,X020K-X062E-X116L,X020K-X023A-X062E-X116L-X188D-X213A,X023A-X024F-X062E-X116L-X213A,X022A-X043R-X103A-X104I-X128I-X129E-X159D-X188D-X232V-X245R-X248D,X022A-X043R-X103A-X104I-X118R-X128I-X129E-X159D-X188D-X232V-X248D-X271F,X024F-X062E-X116L-X188D,X022A-X024R-X103A-X104I-X118R-X128I-X129E-X159D-X188D-X232V-X248D,X023A-X062E-X116L-X188D,X043W-X062E-X116L,X020K-X023A-X116L-X188D,X043W-X062E-X116L-X188D,X024F-X062E-X116L,X062E-X116L-X188D,和X022A-X024R-X103A-X104I-X128I-X159D-X188D-X232V-X248D,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0249] 本发明还提供分离的枯草杆菌蛋白酶变体,其中该枯草杆菌蛋白酶变体是具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:X087R-X101G-X103A-X104I-X109R-X212P-X232V-X245R-X271V,X101G-X103A-X104I-X109R-X232V-X245R,X101G-X103A-X104I-X109R-X212P-X232V-X245R-X271V,X101G-X103A-X104I-X109R-X212P-X232V-X245R,X076D-S87R-X103A-X104I-X212P-X271V,X076D-X103A-X104I-X109R,X076D-X103A-X104I-X212P-X271V,X076D-X103A-X104I-X109R-X245R,和X076D-X103A-X104I-X212P-X245L-X271V,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0250] 本发明还提供分离的枯草杆菌蛋白酶变体,其中该枯草杆菌蛋白酶变体是具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:X024R-X086W-X118R,X024R-X078R-X086W-X243F,X024R-X033S-X086S-X087N-X209A,X033S-X118R,X024R-X078R-X086W-X118R-X270T,X024R-X033S-X086W-X118R,X078R-X086W-X243F,X033S-X078R-X086W-X118R-X209A,X033S-X078R-X209A,X086W-X118R-X243F,X024R-X086W,X078R-X086W-X235F,X024R-X118R,X024R-X086R,X101G-X103A-X104I-

X232V,X024R-X033S-X078R-X086W-X118R,X024R-X118R-X209A,X209A-X241R,X033S-X086W-X243F,X033S-X172V-X209A,X118R-X209A-X243F,X024R-X086S-X141G,X024R-X118R-X209A-X243F,X024R-X033S-X086S-X085N-X235F,X024R-X033S-X133V,X024R-X033S-X078R-X086W,X024R-X086W-X209A,X024R-X241R,X033S-X118R-X243F,X024R-X235F,X024R-X078R-X086W,X024R-X118R-X209A-X235F,X024R-X209A-X241R,X033S-X118R-X241R,X086W-X118R-X209A,X033S-X118R-X159D-X209A,X033S-X078R-X086W,X024R-X086W-X243F,X118R-X209A,X024R-X086W-X118R-X203I,X078R-X209A-X235F,X024R-X033S-X241R,X078R-X118R,X033S-X118R-X209A-X243F,X021M-X024R-X033S,X024R-X033S-X086W,X033S-X235F,X078R-X086W-X209A,X024R-X033S-X209A-X235F,X033S-X086W-X118R,X024R-X033S-X078R-X209A,X033S-X086W-X118R-X209A-X243F,X086W-X209A-X243F,X005S-X078R-X118R-X241R,X024R-X174T,X033S-X209A-X243F,X086W-X118R-X133V,X024R-X033S-X118R,X024R-X086W-X209A-X235F,X086W-X209A,X008T-X024R,X086W-X118R,X033S-X241R,X005S-X024R-X033S-X243F,X024R-X209A-X242P,X024R-X033S-X078R-X118R,X024R-X033S-X194T,X024R-X243F,X024R-X209A,X024R-X033S-X118R-X209A,X033S-X086W,X024R-X033S,X024R-X033S-X078R-X243F,X086W-X243F,X033S-X118D-X138V-X209A,X033S-X209A-X235F,X024R-X086R-X118R,X033S-X201S,X024R-X239Q,X033S-X118R-X209A-,X078R-X086W,X235F-X243F,X024R-X209A-X235F,X118R-X172V,X017Y-X024R-X033S-X086W,X033S-X148F,X024R-X118R-X235F,X033S-X078R,X033S-X243F,X024C-X033S,X118R-X194T,X033S-X209A,X118R-X209A-X235F,X024R-X033S-X209A-X243F,X024R-X033S-X235F,X024R-X033S-X118R-X235F,X024R-X141G,X024R-X274I,X024R-X033S-X209A,X086W-X235F,X024R-X209A-X243F,X004E-X033S-X078R,X086W-X209A-X235F,X015T-X033S,X033S-X086W-X156L-X209A,X024R-X118R-X243F-X269H,X209A-X235F,X024R-X247H,X024R-X033S-X228T,X078R-X235F,X024R-X033S-X174V-X235F,X024R-X235F-X243F,X024R-X033S-X235F-X241R,X024R-X033S-X151V,X024R-X104A,X033S-X048T,X012H-X104A-X118R,X118R-X235F,X033S-X253A,X143A-X209A,X024R-X033S-X243F,X033S-X239T,X209A-X243F,X024R-X033S-X129H-X184D-X253M,X024R-X085V-X086W-X118R-X235F,X024R-X272P,和X024R-X269C,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0251] 本发明还提供分离的枯草杆菌蛋白酶变体,其中该枯草杆菌蛋白酶变体是具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:X020R-X087D-X101G-X103A-X104I-X232V-X245R,X020R-X101G-X103A-X104I-X150L-X232V-X245R,X018R-X020R-X024R-X076D-X087D-X249R,X018R-X020R-X024R-X076D-X150L-X249R,X018R-X024R-X043R-X076D-X087D-X249R,X018R-X024R-X043R-X076D-X150L-X249R,X018R-X024R-X076D-X078R-X087D-X249R,X018R-X024R-X076D-X078R-X150L-X249R,X018R-X024R-X076D-X087D-X249R-X269R,X018R-X024R-X076D-X087D-X242R-X249R,X018R-X024R-X076D-X087D-X150L-X249R,X018R-X024R-X076D-X150L-X249R,X018R-X087D-X101G-X103A-X104I-X232V-X245R,X018R-X101G-X103A-X104I-X150L-X232V-X245R,X018R-X022R-X024R-X076D-X087D-X249R,X018R-X022R-X024R-X076D-

X150L-X249R,X043R-X087D-X101G-X103A-X104I-X232V-X245R-X269R,X043R-X101G-X103A-X104I-X150L-X232V-X245R,X024R-X087D-X101G-X103A-X104I-X232V-X245R,X024R-X101G-X103A-X104I-X150L-X232V-X245R,X078R-X087D-X101G-X103A-X104I-X232V-X245R,X078R-X101G-X103A-X104I-X150L-X232V-X245R,X087D-X101G-X103A-X104I-X232V-X245R-X269R,X101G-X103A-X104I-X150L-X232V-X245R-X249R,X101G-X103A-X104I-X150L-X232V-X245R-X269R,X022R-X087D-X101G-X103A-X104I-X232V-X245R,X018R-X024R-X043D-X076D-X150L-X249R,X043R-X087D-X101G-X103A-X104I-X232V-X245R,X022R-X101G-X103A-X104I-X150L-X232V-X245R,X018R-X024R-X043D-X076D-X087D-X249R,X018R-X024R-X076D-X087D-X249R,X018R-X024R-X076D-X150L-X242R-X249R,X043R-X101G-X103A-X104I-X150L-X232V-X245R-X269R,X076D-X101G-X103A-X104I-X150L-X232V-X245R,X087D-X101G-X103A-X104I-X232V-X242R-X245R,X101G-X103A-X104I-X150L-X232V-X245R,X076D-X087D-X101G-X103A-X104I-X232V-X245R,X087D-X101G-X103A-X104I-X232V-X245R,和X101G-X103A-X104I-X150L-X232V-X242R-X245R,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0252] 本发明还提供分离的枯草杆菌蛋白酶变体,其中该枯草杆菌蛋白酶变体是具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:X024R-X101G-X103A-X104I-X129Q-X158E-X188D-X217E-X232V-X245R-X248D-X249R,X024R-X101G-X103A-X104I-X130A-X158E-X183D-X188D-X232V-X245R-X248D-X249R,X024R-X101G-X103A-X104I-X129Q-X158E-X183D-X188D-X232V-X245R-X248D-X249R,X101G-X103A-X104I-X130A-X158E-X188D-X232V-X245R-X248D-X249R,X024R-X101G-X103A-X104I-X129Q-X158E-X188D-X232V-X245R-X248D-X249R,X024R-X101G-X103A-X104I-X130A-X158E-X188D-X232V-X245R-X248D-X249R,X024R-X101G-X103A-X104I-X129Q-X130A-X158E-X183D-X188D-X232V-X245R-X248D-X249R,X024R-X101G-X103A-X104I-X128L-X129Q-X158E-X188D-X232V-X245R-X248D-X249R,X024R-X101G-X103A-X104I-X129Q-X130A-X158E-X188D-X232V-X245R-X248D-X249R,X101G-X103A-X104I-X129Q-X158E-X188D-X232V-X245R-X248D-X249R,X101G-X103A-X104I-X129Q-X130A-X158E-X188D-X232V-X245R-X248D-X249R,X024R-X101G-X103A-X104I-X128L-X129Q-X130A-X158E-X188D-X232V-X245R-X248D-X249R,X101G-X103A-X104I-X128L-X129Q-X158E-X188D-X232V-X245R-X248D-X249R,和X024R-X027R-X101G-X103A-X104I-X128L-X129Q-X130A-X158E-X188D-X232V-X245R-X248D-X249R,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0253] 本发明还提供分离的枯草杆菌蛋白酶变体,其中该枯草杆菌蛋白酶变体是具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:X101G-X103A-X104I-X232V-X222Q-X245R,X101G-X103A-X104I-X158E-X188D-X222S-X232V-X245R-X248D-X249R,X101G-X103A-X104I-X158E-X188D-X222Q-X232V-X245R-X248D-X249R,X076D-X101G-X103A-X104I-X232V-X222Q-X245R,X101G-X103A-X104I-X232V-X222S-X245R,X076D-X101G-X103A-X104I-X232V-X222S-X245R,和X076D-X101G-X103A-

X104I-X158E-X188D-X222S-X232V-X245R-X248D-X249R,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0254] 本发明还提供分离的枯草杆菌蛋白酶变体,其中该枯草杆菌蛋白酶变体是具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:X024R-X101G-X103A-X104I-X128L-X129Q-X158E-X188D-X232V-X245R-X248D-X249R,X101G-X103A-X104I-X130A-X158E-X188D-X232V-X245R-X248D-X249R,X024R-X101G-X103A-X104I-X158E-X188D-X232V-X245R-X248D-X249R,X101G-X103A-X104I-X128L-X129Q-X158E-X188D-X232V-X245R-X248D-X249R,X101G-X103A-X104I-X129Q-X130A-X158E-X188D-X232V-X245R-X248D-X249R,X101G-X103A-X104I-X130A-X158E-X183D-X188D-X217E-X232V-X245R-X248D-X249R,X024R-X101G-X103A-X104I-X128L-X129Q-X130A-X158E-X188D-X232V-X245R-X248D-X249R,X024R-X101G-X103A-X104I-X129Q-X158E-X188D-X217E-X232V-X245R-X248D-X249R,X101G-X103A-X104I-X128L-X130A-X158E-X188D-X217E-X232V-X245R-X248D-X249R,X024R-X101G-X103A-X104I-X128L-X129Q-X158E-X183D-X188D-X232V-X245R-X248D-X249R,X024R-X101G-X103A-X104I-X128L-X129Q-X130A-X158E-X183D-X188D-X232V-X245R-X248D-X249R,X024R-X101G-X103A-X104I-X128L-X129Q-X158E-X188D-X232V-X245R-X248D-X249R-X271G,X101G-X103A-X104I-X129Q-X158E-X183D-X188D-X232V-X245R-X248D-X249R,X024R-X101G-X103A-X104I-X130A-X158E-X188D-X217E-X232V-X245R-X248D-X249R,X024R-X101G-X103A-X104I-X128L-X158E-X183D-X188D-X232V-X245R-X248D-X249R,X101G-X103A-X104I-X129Q-X158E-X188D-X217E-X232V-X245R-X248D-X249R,和X024R-X101G-X103A-X104I-X128L-X130A-X158E-X188D-X232V-X245R-X248D-X249R,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0255] 本发明还提供包含芽孢杆菌属枯草杆菌蛋白酶的枯草杆菌蛋白酶变体的多肽,其中该枯草杆菌蛋白酶变体是具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:X101G-X103A-X104I,X22A-X101A-X209E,S103G-L111V-G159E,X22A-X103G-X159E,X22A-X111V-X159E,X22A-X128N-X271F-X209E,X22A-X103G-X111V,X62E-X111V-X128N,X22A-X111V-X128N,X22A-X62E-X111V,X101A-X103G-X104L-X188D,X101G-X103A-X104I-X159D,X101A-X103G-X104L-X128N,X22A-X101A-X159E,X101A-X103G-X104L,X101A-X103G-X104L-X159E,X22A-X101A-X103G-X104L,X101A-X103G-X104L-X209E,X22A-X209E-X271F,X22A-X101A-X271F,和X101A-X209E-X271F,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0256] 本发明还提供包含芽孢杆菌属枯草杆菌蛋白酶的枯草杆菌蛋白酶变体的多肽,其中该枯草杆菌蛋白酶变体是具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:X103A-X104I-X159D-X232V-X236H-X245R-X248D-X252K,X101G-X104I-X159D-X232V-X236H-X245R-X248D-X252K,X101G-X103A-X159D-X232V-X236H-X245R-X248D-X252K,X101G-X103A-X104L-X232V-X236H-X245R-X248D-X252K,X101G-

X103A-X104L-X159D-X236H-X245R-X248D-X252K,X101G-X103A-X104L-X159D-X232V-X245R-X248D-X252K,X101G-X103A-X104L-X159D-X232V-X236H-X248D-X252K,X101G-X103A-X104L-X159D-X232V-X236H-X245R-X252K,和X101G-X103A-X104L-X159D-X232V-X236H-X245R-X248D,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0257] 本发明还提供包含芽孢杆菌属枯草杆菌蛋白酶的枯草杆菌蛋白酶变体的多肽,其中该枯草杆菌蛋白酶变体是具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:X101G-X103A-X104I-X159D-X232V-X245R-X248D,X101G-X103A-X104I-X159D-X232V-X245R-X248D-X271F,X101G-X103A-X104I-X159D-X232V-X245R-X248D-X238R,X101G-X103A-X104I-X159D-X232V-X245R-X248D-X248R,X101G-X103A-X104I-X159D-X232V-X245R-X248D-X253R,X101G-X103A-X104I-X159D-X232V-X245R-X248D-X24R,X101G-X103A-X104I-X159D-X232V-X245R-X248D-X76D,X101G-X103A-X104I-X159E-X232V-X245R-X248D-X249R,X101G-X103A-X104I-X159E-X232V-X245R-X248D-X271F,X101G-X103A-X104I-X158E-X232V-X245R-X248D-X249R,X101G-X103A-X104I-X158E-X232V-X245R-X248D-X271F,X22A-X101G-X103A-X104I-X159D-X232V-X245R-X248D-X249R,X22A-X101G-X103A-X104I-X159D-X232V-X245R-X248D-X271F,X62E-X101G-X103A-X104I-X159D-X232V-X245R-X248D-X249R,和X62E-X101G-X103A-X104I-X159D-X232V-X245R-X248D-X271F,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0258] 本发明还提供包含芽孢杆菌属枯草杆菌蛋白酶的枯草杆菌蛋白酶变体的多肽,其中该枯草杆菌蛋白酶变体是具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:X20R-X43R-X249R,X20R-X22R-X43R,X20R-X43R-X242R,X20R-X43R-X271L,X20R-X43R-X244R,X20R-X24R-X43R-X242R,X9A-X22R-X78R-X212F-X241R,X9A-X20R-X43R-X212F,X9A-X43R-X212F,X20R-X43R-X212F,X20R-X22R-X43R-X212F,X24R-X78R-X212F,X9A-X43R-X78R,X9A-X43R-X78R-X242R,X9A-X20R-X43R-X78R,X20R-X24R-X43R-X78R-X242R,X22R-X24R-X78R-X212F,X9A-X20R-X43R-X78R-X242R,X20R-X43R-X78R-X249R,X20R-X43R-X78R,X9A-X78R-X212F,X9A-X22R-X43R-X78R,X9A-X20R-X24R-X43R,X9A-X22R-X78R-X212F,X4R-X9A-X22R-X78R-X212F,X20R-X24R-X43R,X1R-X9A-X43R,X20R-X24R-X43R-X115R,X9A-X24R-X43R,X20R-X22R-X24R-X43R,X1R-X24R-X43R,X9A-X20R-X24R-X43R-X242R,X9A-X20R-X22R-X78R-X212F,X9A-X24R-X43R-X244R,X9A-X24R-X43R-X242R,X4R-X9A-X22R-X24R-X212F,和X22R-X24R-X43R,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0259] 本发明还提供包含芽孢杆菌属枯草杆菌蛋白酶的枯草杆菌蛋白酶变体的多肽,其中该枯草杆菌蛋白酶变体是具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:X101G-X103A-X104I-X232V-X245R-X248D,X101G-X103A-X104I-X159D-X232V-X245R,X101G-X103A-X104I-X159R-X232V-X245R-X248D,X101G-X103A-X104I-X159D-X232V-X245R-X248R,X101G-X103A-X104I-X232V-X245R,X101G-X103A-X104I-X232V-X245R-X248R,X101G-X103A-X104I-X159R-X232V-X245R-X248R,以及X101G,

X103A,X104I,X232V,X236H,X245R,和X252K,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0260] 本发明还提供包含芽孢杆菌属枯草杆菌蛋白酶的枯草杆菌蛋白酶变体的多肽,其中该枯草杆菌蛋白酶变体是具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:X16S,X22A,X24R,X62E,X76D,X89P,X101A/G,X103G/A,X104L/I,X111V,X128N,X129E,X232V,X148I,X158E,X159D/E,X166D,X186H,X188D,X209E,X236H,X238R,X245R,X248D/R,X249R,X252K/R,X253R,和X271F,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0261] 本发明还提供包含芽孢杆菌属枯草杆菌蛋白酶的枯草杆菌蛋白酶变体的多肽,其中该枯草杆菌蛋白酶变体是具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:N062E-A158E,S103G-A158E,S128N-A158E,A016S-A158E,V104L-A158E,E089P-A158E,L111V-A158E,T022A-A158E,S101A-A158E,L148I-A158E,P129E-A158E,T022A-E089P,A016S-E089P,N062E-E089P,N062E-E271F,A158E-E271F,R186H-E271F,P129E-E271F,L111V-E271F,Y209E-E271F,A016S-E271F,S188D-E271F,T022A-E271F,G159E-E271F,V104L-E271F,S101A-E271F,E089P-E271F,S128N-E271F,S103G-E271F,L148I-E271F,H249R-E271F,N062E-G159E,A016S-G159E,S128N-G159E,L148I-G159E,L111V-G159E,E089P-G159E,T022A-G159E,P129E-G159E,S103G-G159E,V104L-G159E,A158E-G159E,S101A-G159E,A158E-H249R,L111V-H249R,P129E-H249R,N062E-H249R,A016S-H249R,R186H-H249R,L148I-H249R,G159E-H249R,S101A-H249R,S188D-H249R,V104L-H249R,Y209E-H249R,T022A-H249R,S128N-H249R,S103G-H249R,E089P-H249R,T022A-L111V,S101A-L111V,A016S-L111V,V104L-L111V,N062E-L111V,S103G-L111V,E089P-L111V,A016S-L148I,N062E-L148I,T022A-L148I,P129E-L148I,V104L-L148I,S103G-L148I,S128N-L148I,S101A-L148I,E089P-L148I,L111V-L148I,A016S-N062E,T022A-N062E,N062E-P129E,T022A-P129E,S128N-P129E,A016S-P129E,S101A-P129E,V104L-P129E,E089P-P129E,S103G-P129E,L111V-P129E,N062E-R186H,S128N-R186H,S101A-R186H,T022A-R186H,A016S-R186H,A158E-R186H,E089P-R186H,P129E-R186H,G159E-R186H,S103G-R186H,V104L-R186H,L111V-R186H,L148I-R186H,N062E-S101A,T022A-S101A,A016S-S101A,E089P-S101A,N062E-S103G,T022A-S103G,A016S-S103G,S101A-S103G,E089P-S103G,N062E-S128N,A016S-S128N,T022A-S128N,S101A-S128N,V104L-S128N,E089P-S128N,S103G-S128N,L111V-S128N,L111V-S188D,N062E-S188D,A016S-S188D,L148I-S188D,T022A-S188D,S128N-S188D,S101A-S188D,V104L-S188D,E089P-S188D,P129E-S188D,G159E-S188D,R186H-S188D,S103G-S188D,A158E-S188D,A016S-T022A,A016S-V104L,T022A-V104L,S101A-V104L,N062E-V104L,S103G-V104L,E089P-V104L,G159E-Y209E,L111V-Y209E,S101A-Y209E,A016S-Y209E,S128N-Y209E,L148I-Y209E,P129E-Y209E,N062E-Y209E,T022A-Y209E,S103G-Y209E,A158E-Y209E,S188D-Y209E,V104L-Y209E,E089P-Y209E,和R186H-Y209E,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸

序列的对应关系进行编号。

[0262] 本发明还提供包含具有蛋白水解活性的枯草杆菌蛋白酶变体的多肽，该枯草杆菌蛋白酶变体包含具有选自以下的氨基酸置换的组合的氨基酸序列：N018R-W241R,G020R-W241R,S024R-W241R,S009A-W241R,G020R-W241R,V004R-W241R,N043R-W241R,S078R-W241R,T022R-W241R,G115R-W241R,A001R-W241R,S212F-W241R,L082R-W241R,N018R-V244R,S024R-V244R,S078R-V244R,G020R-V244R,S212F-V244R,S009A-V244R,L082R-V244R,A001R-V244R,N043R-V244R,T022R-V244R,V004R-V244R,G115R-V244R,W241R-V244R,S242R-V244R,A001R-V004R,S009A-T022R,N018R-T022R,G020R-T022R,V004R-T022R,A001R-T022R,S024R-S242R,N018R-S242R,V004R-S242R,G020R-S242R,S212F-S242R,L082R-S242R,S078R-S242R,A001R-S242R,S009A-S242R,T022R-S242R,G115R-S242R,N043R-S242R,W241R-S242R,N018R-S212F,T022R-S212F,V004R-S212F,S024R-S212F,A001R-S212F,G115R-S212F,G020R-S212F,S009A-S212F,N043R-S212F,S078R-S212F,L082R-S212F,S009A-S078R,G020R-S078R,S024R-S078R,T022R-S078R,N018R-S078R,V004R-S078R,A001R-S078R,N043R-S078R,T022R-S024R,G020R-S024R,N018R-S024R,A001R-S024R,V004R-S024R,S009A-S024R,V004R-S009A,A001R-S009A,S242R-N269R,S024R-N269R,G020R-N269R,T022R-N269R,H249R-N269R,S212F-N269R,N043R-N269R,V244R-N269R,A001R-N269R,N018R-N269R,S078R-N269R,S009A-N269R,G115R-N269R,W241R-N269R,V004R-N269R,L082R-N269R,N018R-N043R,G020R-N043R,V004R-N043R,T022R-N043R,S009A-N043R,A001R-N043R,S024R-N043R,S009A-N018R,V004R-N018R,A001R-N018R,S024R-L082R,S009A-L082R,N018R-L082R,A001R-L082R,S078R-L082R,G020R-L082R,T022R-L082R,V004R-L082R,N043R-L082R,N043R-H249R,G020R-H249R,V004R-H249R,N018R-H249R,S009A-H249R,S212F-H249R,T022R-H249R,S024R-H249R,G115R-H249R,A001R-H249R,L082R-H249R,S242R-H249R,W241R-H249R,V244R-H249R,S078R-H249R,N018R-G115R,G020R-G115R,T022R-G115R,S078R-G115R,S009A-G115R,V004R-G115R,A001R-G115R,L082R-G115R,N043R-G115R,S024R-G115R,S009A-G020R,N018R-G020R,V004R-G020R,A001R-G020R,S009A-E271L,G020R-E271L,S024R-E271L,V244R-E271L,W241R-E271L,N043R-E271L,T022R-E271L,H249R-E271L,S212F-E271L,G115R-E271L,S242R-E271L,S078R-E271L,V004R-E271L,N269R-E271L,A001R-E271L,N018R-E271L，和L082R-E271L，其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0263] 本发明还提供分离的枯草杆菌蛋白酶变体，其中所述枯草杆菌蛋白酶变体是具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列：G020R-N043R,N062E-A158E,S103G-A158E,S128N-A158E,A016S-A158E,V104L-A158E,E089P-A158E,L111V-A158E,T022A-A158E,S101A-A158E,L148I-A158E,P129E-A158E,T022A-E089P,A016S-E089P,N062E-E089P,N062E-E271F,A158E-E271F,R186H-E271F,P129E-E271F,L111V-E271F,Y209E-E271F,A016S-E271F,S188D-E271F,T022A-E271F,G159E-E271F,V104L-E271F,S101A-E271F,E089P-E271F,S128N-E271F,S103G-E271F,L148I-E271F,H249R-E271F,N062E-G159E,A016S-G159E,S128N-G159E,L148I-G159E,L111V-G159E,E089P-G159E,T022A-G159E,P129E-G159E,S103G-G159E,V104L-G159E,A158E-

G159E,S101A-G159E,A158E-H249R,L111V-H249R,P129E-H249R,N062E-H249R,A016S-H249R,R186H-H249R,L148I-H249R,G159E-H249R,S101A-H249R,S188D-H249R,V104L-H249R,Y209E-H249R,T022A-H249R,S128N-H249R,S103G-H249R,E089P-H249R,T022A-L111V,S101A-L111V,A016S-L111V,V104L-L111V,N062E-L111V,S103G-L111V,E089P-L111V,A016S-L148I,N062E-L148I,T022A-L148I,P129E-L148I,V104L-L148I,S103G-L148I,S128N-L148I,S101A-L148I,E089P-L148I,L111V-L148I,A016S-N062E,T022A-N062E,N062E-P129E,T022A-P129E,S128N-P129E,A016S-P129E,S101A-P129E,V104L-P129E,E089P-P129E,S103G-P129E,L111V-P129E,N062E-R186H,S128N-R186H,S101A-R186H,T022A-R186H,A016S-R186H,A158E-R186H,E089P-R186H,P129E-R186H,G159E-R186H,S103G-R186H,V104L-R186H,L111V-R186H,L148I-R186H,N062E-S101A,T022A-S101A,A016S-S101A,E089P-S101A,N062E-S103G,T022A-S103G,A016S-S103G,S101A-S103G,E089P-S103G,N062E-S128N,A016S-S128N,T022A-S128N,S101A-S128N,V104L-S128N,E089P-S128N,S103G-S128N,L111V-S128N,L111V-S188D,N062E-S188D,A016S-S188D,L148I-S188D,T022A-S188D,S128N-S188D,S101A-S188D,V104L-S188D,E089P-S188D,P129E-S188D,G159E-S188D,R186H-S188D,S103G-S188D,A158E-S188D,A016S-T022A,A016S-V104L,T022A-V104L,S101A-V104L,N062E-V104L,S103G-V104L,E089P-V104L,G159E-Y209E,L111V-Y209E,S101A-Y209E,A016S-Y209E,S128N-Y209E,L148I-Y209E,P129E-Y209E,N062E-Y209E,T022A-Y209E,S103G-Y209E,A158E-Y209E,S188D-Y209E,V104L-Y209E,E089P-Y209E,R186H-Y209E,N018R-W241R,G020R-W241R,S024R-W241R,S009A-W241R,G020R-W241R,V004R-W241R,N043R-W241R,S078R-W241R,T022R-W241R,G115R-W241R,A001R-W241R,S212F-W241R,L082R-W241R,N018R-V244R,S024R-V244R,S078R-V244R,G020R-V244R,S212F-V244R,S009A-V244R,L082R-V244R,A001R-V244R,N043R-V244R,T022R-V244R,V004R-V244R,G115R-V244R,W241R-V244R,S242R-V244R,A001R-V004R,S009A-T022R,N018R-T022R,G020R-T022R,V004R-T022R,A001R-T022R,S024R-S242R,N018R-S242R,V004R-S242R,G020R-S242R,S212F-S242R,L082R-S242R,S078R-S242R,A001R-S242R,S009A-S242R,T022R-S242R,G115R-S242R,N043R-S242R,W241R-S242R,N018R-S212F,T022R-S212F,V004R-S212F,S024R-S212F,A001R-S212F,G115R-S212F,G020R-S212F,S009A-S212F,N043R-S212F,S078R-S212F,L082R-S212F,S009A-S078R,G020R-S078R,S024R-S078R,T022R-S078R,N018R-S078R,V004R-S078R,A001R-S078R,N043R-S078R,T022R-S024R,G020R-S024R,N018R-S024R,A001R-S024R,V004R-S024R,S009A-S024R,V004R-S009A,A001R-S009A,S242R-N269R,S024R-N269R,G020R-N269R,T022R-N269R,H249R-N269R,S212F-N269R,N043R-N269R,V244R-N269R,A001R-N269R,N018R-N269R,S078R-N269R,S009A-N269R,G115R-N269R,W241R-N269R,V004R-N269R,L082R-N269R,N018R-N043R,G020R-N043R,V004R-N043R,T022R-N043R,S009A-N043R,A001R-N043R,S024R-N043R,S009A-N018R,V004R-N018R,A001R-N018R,S024R-L082R,S009A-L082R,N018R-L082R,A001R-L082R,S078R-L082R,G020R-L082R,T022R-L082R,V004R-L082R,N043R-L082R,N043R-H249R,G020R-H249R,V004R-H249R,N018R-H249R,S009A-H249R,S212F-H249R,T022R-H249R,S024R-H249R,G115R-H249R,A001R-H249R,L082R-H249R,S242R-H249R,W241R-H249R,V244R-H249R,S078R-

H249R,N018R-G115R,G020R-G115R,T022R-G115R,S078R-G115R,S009A-G115R,V004R-G115R,A001R-G115R,L082R-G115R,N043R-G115R,S024R-G115R,S009A-G020R,N018R-G020R,V004R-G020R,A001R-G020R,S009A-E271L,G020R-E271L,S024R-E271L,V244R-E271L,W241R-E271L,N043R-E271L,T022R-E271L,H249R-E271L,S212F-E271L,G115R-E271L,S242R-E271L,S078R-E271L,V004R-E271L,N269R-E271L,A001R-E271L,N018R-E271L,和L082R-E271L,并且其中该变体的总净电荷相对于迟缓芽孢杆菌枯草杆菌蛋白酶GG36蛋白酶的总净电荷为0、+1、+2、+3、+4、+5、-1、-2、-3、-4或-5,并且其中总净电荷是通过一个或多个选自以下的置换获得:N43D,R45T,N62E,N76D,S101D,P129E,A158E,G159D,G159E,S166D,S188D,A230E,N18R,G20K,G20R,T22R,S24R,N43R,G118R,Q245R,H249R,N269R,E271F,和E271L,并且其中该蛋白酶变体的氨基酸位置根据SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列中对应的氨基酸位置的编号方式来进行编号。

[0264] 本发明还提供分离的枯草杆菌蛋白酶变体,其中该枯草杆菌蛋白酶变体是具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:G020R-N043R,G020K-N062E,S024F-N116L,G020K-S024F,S024R-A174T,S024R-G118R,S024R-K235F,S024R-P086R,S024R-P086W,S078R-G118R,T033S-G118R,T033S-K235F,Y209A-W241R,G020R-N076D,N018R-Q245R,S024R-R045T,A232V-Q245R,G118R-A172V,G118R-A194T,I008T-S024R,K235F-N243F,N018R-S103A,N018R-V104I,P086W-G118R,P086W-N243F,P086W-Y209A,S024C-T033S,S024R-A232V,S024R-N243F,S024R-P239Q,S024R-S101G,S024R-S141G,S024R-T033S,S024R-T274I,S024R-Y209A,S078R-P086W,S101G-A232V,T033S-L148F,T033S-P086W,T033S-P201S,T033S-S078R,T033S-W241R,T033S-Y209A,A230E-H249R,A232V-H249R,G118R-K235F,N076D-Q245R,P086W-K235F,S024R-R247H,S024R-V104A,S078R-K235F,S101G-H249R,S103A-A232V,T033S-A048T,T033S-P239T,T033S-T253A,T143A-Y209A,Y209A-K235F,N018R-R045T,Y209A-N243F,S024R-A272P,S024R-R269C,S101G-V104I,V104I-A232V,N076D-H249R,和S024R-N076D,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0265] 本发明还提供分离的枯草杆菌蛋白酶变体,其中该枯草杆菌蛋白酶变体是具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:G020R-N076D,S024R-R045T,A230E-H249R,N018R-R045T,N018R-Q245R,S101G-A232V,S024R-A232V,A232V-Q245R,S024R-S101G,N018R-V104I,N018R-S103A,S101G-H249R,A232V-H249R,S103A-A232V,N076D-Q245R,S101G-V104I,V104I-A232V,N076D-H249R,S024R-N076D,S024F-N116L,G020K-S024F,G020K-N062E,T033S-G118R,S024R-P086W,S024R-G118R,S024R-P086R,Y209A-W241R,S024R-W241R,S024R-K235F,G118R-Y209A,S078R-G118R,T033S-K235F,S024R-A174T,P086W-Y209A,I008T-S024R,P086W-G118R,T033S-W241R,S024R-N243F,S024R-Y209A,T033S-P086W,S024R-T033S,P086W-N243F,T033S-P201S,S024R-P239Q,S078R-P086W,K235F-N243F,G118R-A172V,T033S-L148F,T033S-S078R,T033S-N243F,S024C-T033S,G118R-A194T,T033S-Y209A,S024R-S141G,S024R-T274I,P086W-K235F,A015T-T033S,Y209A-K235F,S024R-R247H,S078R-K235F,S024R-V104A,T033S-A048T,G118R-K235F,T033S-T253A,T143A-Y209A,T033S-P239T,Y209A-

N243F,S024R-A272P,和S024R-R269C,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0266] 本发明还提供分离的枯草杆菌蛋白酶变体,其中该枯草杆菌蛋白酶变体是具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:V004R-S009A-G020R-S242R,G020R-N043R-W241R,G020R-S242R-N269R,V004R-S009A-G020R-N043R,V004R-G020R-H249R,N018R-S024R-V244R,S009A-T022R-S212F-W241R,G020R-N043R-N269R,N018R-S024R-S242R,V004R-S009A-N043R-W241R,G020R-N043R-V244R,G020R-T022R-S242R,V004R-G020R-N043R,V004R-S009A-G020R-N043R-S242R,G020R-N043R-S242R,G020R-N043R-S242R-H249R,G020R-S212F-H249R,V004R-S009A-W241R,A001R-S009A-N043R,G020R-N043R-H249R,S009A-G020R-N043R-W241R,G020R-T022R-N043R,G020R-H249R-N269R,G020R-T022R-W241R,V004R-S009A-S024R-N043R-W241R,S009A-N043R-S078R,V004R-G020R-S024R-V244R,G020R-T022R-S078R-S242R,G020R-S024R-S242R-H249R,V004R-S009A-S078R-W241R,S009A-N043R-S078R-S242R,V004R-G020R-S024R,S009A-N043R-S212F,G020R-N043R-S212F,S024R-S078R-S212F,S009A-G020R-S024R-N043R,S009A-T022R-N043R-S078R,G020R-T022R-S212F-W241R,G020R-N043R-S212F-W241R,S009A-N043R-W241R,G020R-N043R-E271L,G020R-T022R-S078R-W241R,G020R-S024R-N043R-S242R,G020R-T022R-N043R-W241R,S009A-G020R-N043R-S212F,V004R-S009A-G020R-S024R-S242R,G020R-N043R-H249R-E271L,G020R-T022R-S024R-S242R,S009A-T022R-S078R-S212F,G020R-N043R-S242R-E271L,S009A-T022R-S078R-S212F-W241R,V004R-G020R-S024R-H249R,G020R-T022R-E271L,G020R-T022R-N043R-S212F,V004R-G020R-S024R-N043R-S242R,V004R-G020R-S024R-N043R,V004R-S009A-T022R-S078R-S212F,G020R-T022R-S078R-S212F-W241R,和G020R-T022R-N269R,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0267] 本发明还提供分离的枯草杆菌蛋白酶变体,其中该枯草杆菌蛋白酶变体是具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:N018R-G020R-N043D-R045T-A230E,N018R-N043R-R045T-S242R-H249R,S024R-N043D-H249R,N018R-G020R-R045T,G020R-S024R-N076D-H249R,S024R-N043R-A230E-S242R,N018R-S024R-N043D-A230E,G020R-N076D,N018R-S024R-N043D-N076D-H249R,S024R-N043R-N076D-H249R,N018R-S024R-R045T-S242R,G020R-N043D-N076D-A230E-H249R,G020R-N043R-R045T-S242R,N018R-S024R-N076D-H249R,N018R-G020R-S024R-N043D-R045T-L233I-S242R,S024R-N043R-A230E,N018R-G020R-N043D,N043R-S242R-H249R,G020R-N043R-R045T-A230E,N043R-N076D-S242R-H249R,G020R-S024R-R045T-A230E-S242R,S024R-R045T-N076D-A230E-S242R-H249R,S024R-R045T,S024R-N043R-R045T-N076D-A230E-H249R,N018R-S024R-N043D-R045T-H249R,N018R-N043R-R045T-H249R,S024R-N043R-S242R,N018R-G020R-N043R-N076D-H249R,G020R-S024R-N043D-H249R,G020R-N043R-A230E-S242R,G020R-N043R-S242R,N018R-N043R-N076D-A230E,G020R-S024R-N043D-S242R,G020R-N043R-A230E,N018R-G020R-N043R-N076D-S242R-H249R,N043D-R045T-N076D-H249R,N018R-N043R-S242R-H249R,N018R-G020R-N043R-R045T-S242R,

N018R-G020R-N043D-A230E-S242R,G020R-S024R-N043R-R045T-H249R,S024R-N043R-H249R,G020R-S024R-K27E-N043R-N076D-A230E,S024R-N043R-R045T-S242R,N018R-G020R-S024R-N043R-R045T-N076D-A230E,G020R-N043R-N076D-A230E-H249R,N018R-N043R-R045T-S242R,G020R-S242R-H249R,N018R-N043R-N076D-A230E-S242R-H249R,N018R-S024R-N076D,G020R-S024R-K27R-N043D-S242R-H249R,N018R-G020R-S024R-N043D-N076D-S242R,N018R-N043R-N076D-S242R-H249R,N018R-S024R-N043D-A230E-H249R,N018R-G020R-N043D-H249R,N018R-G020R-N043D-R045T-N076D-S242R,S024R-N043R-N076D-A230E-S242R,G020R-S024R-T38I-N043R-R045T-N076D-S242R-H249R,N018R-G020R-N043R,N018R-S024R-R045T-A230E-S242R,N018R-G020R-H249R,S024R-N043R-N076D,N018R-G020R-S024R-N043R-R045T-N076D-H249R,N018R-N043D-R045T-N076D-S242R-H249R,S024R-N043D-S242R-H249R,N018R-G020R-S024R-N043D-R045T-S242R,G020R-S024R-N043R-N076D,N018R-G020R-N043D-R045T-A230E-S242R,G020R-S024R-N043R-R045T-N076D-S242R-H249R,N018R-N043R-R045T-N076D-S242R,N018R-G020R-N043R-N076D-A230E-S242R,N018R-S024R-N043D-H249R,N018R-S024R-N043R-R045T-A230E-H249R,N018R-G020R-N043R-R045T-N076D-H249R,N018R-S024R-S242R,N018R-N043R-R045T-N076D-A230E-S242R,R045T-S242R-H249R,N018R-S024R-N043D-S242R,N018R-G020R-N043D-R045T-S240P,S024R-N043R-R045T-S242R-H249R,N018R-S024R-V30S-L31S-D32I-T33Q-G34V-I35F,N018R-G020R-N043R-N076D,G020R-N043D-R045T-N076D-S242R-H249R,N018R-S024R-N043D-A230E-S242R,N018R-S024R-N043D-S242R-H249R,S024R-N043D-R045T-S242R-H249R,N043R-A230E-H249R,S024R-N043R-N076D-A230E-H249R,G020R-S024R-N043D-N076D-H249R,S024R-R045T-S242R-A273V,G020R-S024R-R045T-N076D-S242R-H249R,N018R-S024R-N043D-N076D-S242R,N018R-N043R-N076D-A230E-H249R,N018R-G020R-N043R-R045T-H249R,N018R-N043R-R045T-A230E-S242R,G020R-S024R-N043D-R045T-A230E-S242R,N018R-N043D-A230E-H249R,N018R-N043R-N076D-S242R,N018R-G020R-N076D,N018R-G020R-N043D-N076D-S242R-H249R,G020R-S024R-N043D-N076D-S242R-H249R,N043D-S242R-H249R,N018R-G020R-S024R-N043R-N076D,N018R-G020R-N043D-R045T-N076D-H249R,N018R-G020R-N043R-R045T-N076D-A230E-H249R,N018R-N076D-S242R,G020R-N043R-H249R,N018R-N076D-S242R-H249R,N018R-S024R-R045T-A230E-H249R,A230E-H249R,N018R-R045T-H249R,G020R-N043R-N076D,N043R-R045T-H249R,N018R-N043D-N076D-S242R-H249R,N043R-N076D-H249R,N018R-R045T,G020R-N076D-A230E-S242R,G020R-S024R-N043D-R045T,S024R-N043D-N076D-S242R-H249R,G020R-R045T-H249R,N043R-N076D-S153A-H249R,N043R-N076D-A230E-H249R,N018R-N043D-N076D-H249R,和G020R-N043R-N076D-V227I,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0268] 本发明还提供分离的枯草杆菌蛋白酶变体,其中该枯草杆菌蛋白酶变体是具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:S101G-S103A-V104I-A232V-Q236H-Q245R-N252K,S101G-S103A-V104I-A232V-Q245R-N248R,S101G-S103A-V104I-G159R-A232V-Q245R-N248D,S101G-S103A-V104I-G159D-A232V-

Q245R-N248R,S101G-S103A-V104I-A232V-Q245R,S101G-S103A-V104I-G159D-A232V-Q245R和S101G-S103A-V104I-A232V-Q245R-N248D,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0269] 本发明还提供分离的枯草杆菌蛋白酶变体,其中该枯草杆菌蛋白酶变体是具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:S101G-S103A-V104I-P129E-S188D-A232V-N238R-Q245R-N248D,S024R-S101G-S103A-V104I-P129E-A158E-S188D-A232V-Q245R-N248D-H249R,T022A-S101G-S103A-V104I-P129E-A158E-S188D-A232V-Q245R-N248D-H249R,T022A-S024R-S101G-S103A-V104I-P129E-A158E-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-P129E-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-P129E-G159E-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-S128N-P129E-A158E-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-L148I-A158E-S188D-A232V-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-P129E-G159E-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-S128N-P129E-A232V-Q245R-N248D,S101G-S103A-V104I-P129E-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-P129E-A158E-A232V-Q245R-N248D-H249R,T022A-S024R-S101G-S103A-V104I-A158E-G159E-S188D-A232V-Q245R-N248D-H249R,T022A-S024R-S101G-S103A-V104I-P129E-A158E-G159E-S188D-A232V-N238R-Q245R-N248D,S024R-S101G-S103A-V104I-P129E-L148I-A158E-A232V-Q245R-N248D,A016S-S024R-S101G-S103A-V104I-A158E-S188D-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-A158E-G159E-A232V-Q245R-N248D-H249R,T022A-S101G-S103A-V104I-P129E-A158E-G159E-A232V-N238R-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-P129E-A158E-G159E-A232V-Q245R-N248D-H249R,T022A-S024R-S101G-S103A-V104I-S128N-A158E-S188D-A232V-Q245R-N248D,S024R-S101G-S103A-V104I-P129E-S188D-A232V-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-P129E-A158E-A232V-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-P129E-A232V-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-P129E-S188D-A232V-Q245R-N248D,S024R-S101G-S103A-V104I-A158E-S188D-A232V-N238R-Q245R-N248D,T022A-S101G-S103A-V104I-S128N-P129E-S188D-A232V-N238R-Q245R-N248D,S024R-S101G-S103A-V104I-P129E-S188D-A232V-N238R-Q245R-N248D,S024R-S101G-S103A-V104I-A158E-G159E-S188D-A232V-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-S128N-S188D-A232V-Q245R-N248D,S024R-S101G-S103A-V104I-P129E-A158E-S188D-A232V-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-S128N-P129E-A158E-A232V-Q245R-N248D,S024R-S101G-S103A-V104I-G159E-S188D-A232V-Q245R-N248D,T022A-S101G-S103A-V104I-S128N-P129E-A232V-N238R-Q245R-N248D,S024R-S101G-S103A-V104I-P129E-G159E-A232V-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-P129E-A158E-S188D-A232V-N238R-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-A158E-G159E-S188D-A232V-Q245R-N248D,S024R-S101G-S103A-V104I-G159E-S188D-A232V-Q245R-N248D-H249R,T022A-S101G-S103A-V104I-P129E-A158E-A232V-N238R-Q245R-N248D,T022A-S024R-

S101G-S103A-V104I-P129E-A158E-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-L148I-A158E-A232V-Q245R-N248D,T022A-S101G-S103A-V104I-A158E-G159E-S188D-A232V-Q245R-N248D-H249R,T022A-S101G-S103A-V104I-A158E-S188D-A232V-Q245R-N248D,T022A-S101G-S103A-V104I-P129E-S188D-A232V-N238R-Q245R-N248D,S024R-S101G-S103A-V104I-P129E-A158E-G159E-S188D-A232V-Q245R-N248D-H249R,T022A-S024R-S101G-S103A-V104I-A158E-G159E-S188D-A232V-N238R-Q245R-N248D,S101G-S103A-V104I-P129E-A158E-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-S128N-A158E-A232V-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-S128N-P129E-S188D-A232V-Q245R-N248D,T022A-S101G-S103A-V104I-P129E-G159E-A232V-N238R-Q245R-N248D,S101G-S103A-V104I-P129E-G159E-A232V-Q245R-N248D-H249R,T022A-S101G-S103A-V104I-P129E-A158E-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-P129E-L148I-A158E-S188D-A232V-Q245R-N248D,T022A-S101G-S103A-V104I-P129E-G159E-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-G159E-S188D-A232V-N238R-Q245R-N248D,S024R-S101G-S103A-V104I-P129E-A158E-G159E-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-P129E-A158E-G159E-A232V-N238R-Q245R-N248D,S024R-S101G-S103A-V104I-S128N-G159E-S188D-A232V-Q245R-N248D,T022A-S101G-S103A-V104I-G159E-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-P129E-G159E-S188D-A232V-N238R-Q245R-N248D,S101G-S103A-V104I-A158E-A232V-N238R-Q245R-N248D,T022A-S101G-S103A-V104I-P129E-G159E-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-P129E-L148I-S188D-A232V-Q245R-N248D,S024R-S101G-S103A-V104I-A158E-A232V-Q245R-N248D-H249R,T022A-S101G-S103A-V104I-A158E-G159E-A232V-N238R-Q245R-N248D,S024R-S101G-S103A-V104I-A158E-G159E-A232V-N238R-Q245R-N248D,T022A-S101G-S103A-V104I-P129E-A158E-G159E-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-P129E-A158E-S188D-A232V-N238R-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-P129E-A158E-G159E-A232V-Q245R-N248D,S101G-S103A-V104I-S188D-A232V-N238R-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-A158E-A232V-Q245R-N248D-H249R,T022A-S024R-S101G-S103A-V104I-L148I-A158E-A232V-Q245R-N248D,S101G-S103A-V104I-P129E-A158E-G159E-A232V-N238R-Q245R-N248D,T022A-S101G-S103A-V104I-G159E-S188D-A232V-N238R-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-P129E-A158E-G159E-S188D-A232V-Q245R-N248D-H249R,T022A-S101G-S103A-V104I-P129E-A232V-N238R-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-S188D-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-P129E-A158E-G159E-A232V-Q245R-N248D-H249R,T022A-S101G-S103A-V104I-A158E-G159E-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-P129E-S188D-A232V-Q245R-N248D,S024R-S101G-S103A-V104I-P129E-G159E-A232V-N238R-Q245R-N248D,S101G-S103A-V104I-S128N-P129E-A232V-Q245R-N248D,S101G-S103A-V104I-A158E-S188D-A232V-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-P129E-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-P129E-G159E-A232V-N238R-Q245R-N248D,S101G-S103A-V104I-A158E-G159E-S188D-A232V-N238R-Q245R-N248D,

S024R-S101G-S103A-V104I-A232V-Q245R-N248D-H249R,T022A-S024R-S101G-S103A-V104I-P129E-L148I-A232V-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-A158E-A232V-N238R-Q245R-N248D,S101G-S103A-V104I-S128N-P129E-A232V-N238R-Q245R-N248D,T022A-S101G-S103A-V104I-S128N-G159E-A232V-Q245R-N248D,T022A-S101G-S103A-V104I-S128N-P129E-A158E-A232V-N238R-Q245R-N248D,S101G-S103A-V104I-S128N-P129E-S188D-A232V-Q245R-N248D-H249R,T022A-S024R-S101G-S103A-V104I-S128N-P129E-A158E-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-S128N-A158E-G159E-S188D-A232V-Q245R-N248D,T022A-S024K-S101G-S103A-V104I-S128N-A158E-G159E-A232V-Q245R-N248D,S101G-S103A-V104I-P129E-L148I-S188D-A232V-Q245R-N248D,S024R-S101G-S103A-V104I-L148I-A232V-Q245R-N248D,T022A-S101G-S103A-V104I-L148I-S188D-A232V-Q245R-N248D,S024R-S101G-S103A-V104I-S128N-P129E-S188D-A232V-Q245R-N248D,S101G-S103A-V104I-S128N-P129E-A158E-A232V-N238R-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-P129E-L148I-A158E-S188D-A232V-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-L148I-A158E-S188D-A232V-Q245R-N248D,S101G-S103A-V104I-L148I-G159E-A232V-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-A158E-S188D-A232V-Q245R-N248D,和S101G-S103A-V104I-S128N-P129E-A158E-A232V-Q245R-N248D-H249R,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0270] 本发明还提供分离的枯草杆菌蛋白酶变体,其中该枯草杆菌蛋白酶变体是具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:T022A-S024R-S101G-S103A-V104I-A158E-A232V-Q245R-N248D-H249R,T022A-S024R-S101G-S103A-V104I-P129E-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-A158E-G159E-A232V-N238R-Q245R-N248D,S024R-S101G-S103A-V104I-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-A158E-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-G159E-S188D-A232V-Q245R-N248D-H249R,T022A-S024R-S101G-S103A-V104I-A158E-A232V-N238R-Q245R-N248D,S024R-S101G-S103A-V104I-G159E-S188D-A232V-N238R-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-P129E-A232V-Q245R-N248D,S024R-S101G-S103A-V104I-L148I-A232V-Q245R-N248D,S024R-S101G-S103A-V104I-P129E-A158E-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-L148I-A158E-A232V-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-P129E-A158E-A232V-Q245R-N248D-H249R,A016S-S024R-S101G-S103A-V104I-A158E-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-P129E-G159E-A232V-N238R-Q245R-N248D,S024R-S101G-S103A-V104I-P129E-S188D-A232V-Q245R-N248D-H249R,T022A-S101G-S103A-V104I-P129E-A232V-N238R-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-L148I-A158E-A232V-Q245R-N248D,S024R-S101G-S103A-V104I-P129E-S188D-A232V-N238R-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-A158E-G159E-S188D-A232V-N238R-Q245R-N248D,T022A-S101G-S103A-V104I-A158E-G159E-A232V-N238R-Q245R-N248D,T022A-S024R-S101G-S103A-

V104I-P129E-A158E-A232V-Q245R-N248D,S101G-S103A-V104I-A158E-S188D-A232V-Q245R-N248D-H249R,T022A-S101G-S103A-V104I-A158E-G159E-A232V-Q245R-N248D-H249R,和S024R-S101G-S103A-V104I-A158E-G159E-A232V-Q245R-N248D,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0271] 本发明还提供分离的枯草杆菌蛋白酶变体,其中该枯草杆菌蛋白酶变体是具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:V104L-S128N-A158E-R186H-H249R,S128N-A158E-S188D-H249R,N062E-S128N-A158E-G159E-E271F,N062E-A158E-S188D-H249R-E271F,N062E-A158E-R186H-H249R-E271F,S128N-A158E-S188D-Y209E-E271F,N062E-G159E-S188D-H249R,A016S-N062E-A158E-R186H-H249R,N062E-A158E-G159E-H249R,S101A-S128N-A158E-Y209E-H249R,S128N-A158E-R186H-E271F,N062E-A158E-S188D-H249R,N062E-A158E-R186H-E271F,N062E-A158E-R186H-H249R,N062E-S101A-R186H-H249R,N062E-S101A-A158E-R186H-E271F,N062E-V104L-A158E-S188D-H249R-E271F,N062E-G159E-R186H-H249R,N062E-G159E-H249R,S128N-A158E-R186H-H249R,S128N-A158E-S188D-E271F,N062E-A158E-H249R,N062E-R186H-S188D-H249R-E271F,S128N-A158E-Y209E-,N062E-S101A-A158E-H249R,V104L-S128N-A158E-R186H-E271F,N062E-S101A-A158E-R186H-H249R-E271F,A016S-N062E-A158E-H249R,N062E-S101A-G159E-H249R,S128N-A158E-R186H-S188D-E271F,S101A-S128N-A158E-R186H-E271F,N062E-S101A-S188D-H249R,S101A-V104L-A158E-R186H-S188D-H249R,N062E-G159E-H249R-E271F,S128N-A158E-G159E-E271F,A016S-N062E-V104L-A158E-R186H-E271F,T022A-S128N-A158E-H249R,S128N-A158E-H249R,N062E-S101A-V104L-A158E-R186H-E271F,A016S-N062E-A158E-R186H-E271F,V104L-S128N-A158E-H249R,V104L-S128N-A158E-S188D-H249R,T022A-N062E-A158E,N062E-S101A-S188D-H249R-E271F,N062E-A158E-H249R-E271F,V104L-S128N-A158E-R186H-S188D-E271F,N062E-S101A-R186H-E271F,N062E-V104L-G159E-H249R,N062E-R186H-H249R,N062E-S101A-R186H-H249R-E271F,S101A-A158E-R186H-S188D-H249R,N062E-S101A-R186H,S101A-S128N-P129E-R186H-H249R,S101A-S103G-A158E-R186H-H249R,A016S-N062E-V104L-R186H-S188D-E271F,V104L-A158E-R186H-H249R,S101A-S128N-A158E-S188D-Y209E-E271F,N062E-S101A-R186H-S188D-E271F,A016S-N062E-A158E-H249R-E271F,N062E-S128N-A158E,N062E-S128N-G159E-H249R,N062E-S101A-A158E-S188D-H249R,S101A-S128N-A158E-H249R,N062E-A158E-R186H-S188D-H249R,A016S-V104L-A158E-R186H-E271F,N062E-L148I-G159E,N062E-S101A-A158E-R186H-H249R,N062E-S101A-R186H-S188D-H249R,V104L-A158E-R186H-S188D-H249R,N062E-S101A-V104L-R186H-S188D-E271F,T022A-S101A-A158E-R186H-H249R,S101A-S128N-A158E-Y209E,A158E-R186H-S188D-H249R-E271F,V104L-A158E-R186H-S188D-H249R-E271F,S101A-V104L-A158E-R186H-H249R,V104L-A158E-H249R,S101A-V104L-S128N-A158E-R186H-E271F,A016S-V104L-S188D-H249R,S101A-V104L-A158E-R186H-S188D-E271F,V104L-S128N-G159E-E271F,V104L-A158E-R186H-H249R-E271F,A158E-R186H-H249R,S101A-A158E-R186H-H249R,V104L-A158E-S188D-H249R-E271F,A016S-S128N-A158E-R186H,

V104L-S128N-R186H-S188D-H249R,A016S-S101A-S128N-R186H,A016S-N062E-S128N-R186H-E271F,A016S-S128N-R186H-E271F,S128N-P129E-R186H,A158E-R186H-H249R-E271F,A016S-A158E-H249R,A016S-A158E-R186H-H249R,A016S-T022A-A158E-R186H-E271F,E089P-S101A-P129E-R186H,T022A-S128N-A158E-R186H,S101A-V104L-S128N-A158E-R186H,T022A-S128N-R186H-S188D-,N062E-V104L-A158E-R186H-S188D-H249R,T022A-A158E-R186H-H249R-E271F,T022A-V104L-A158E-H249R,S101A-L111V-P129E,A016S-A158E-H249R-E271F,A016S-L111V-S188D-,T022A-V104L-R186H-S188D-H249R,和V104L-L148I-S188D-H249R,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0272] 本发明还提供分离的枯草杆菌蛋白酶变体,其中该枯草杆菌蛋白酶变体是具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:A001R-S101G-S103A-V104I-A232V-Q245R,V004R-S101G-S103A-V104I-A232V-Q245R,N043R-S101G-S103A-V104I-A232V-Q245R-E271L,S078R-S101G-S103A-V104I-A232V-Q245R,V004R-N043R-S101G-S103A-V104I-A232V-Q245R,N018R-N043R-S101G-S103A-V104I-A232V-Q245R,G020R-S101G-S103A-V104I-A232V-Q245R,S101G-S103A-V104I-A232V-Q245R-E271L,G020R-N043R-S101G-S103A-V104I-A232V-Q245R,S024R-N043R-S101G-S103A-V104I-A232V-Q245R,G020R-G025R-N116A-Y167W,N018R-S101G-S103A-V104I-A232V-Q245R,T022R-S101G-S103A-V104I-A232V-Q245R,S078R-S103N-S106G-Y167W-Q236N,N018R-N043D-S101G-S103A-V104I-A232V-Q245R-N269R,N043R-S101G-S103A-V104I-A232V-Q245R-N269R,S024R-S101A-H120F-A194F-H249R,G020R-N043D-S101G-S103A-V104I-A232V-Q245R-N269R,S101G-S103A-V104I-S212F-A232V-Q245R,G020R-S144R-N185I-L233C-Q236N,G023A-S078R-S216F-Q236N-H249R,S101G-S103A-V104I-A232V-Q245R-N269R,S101G-S103A-V104I-G115R-A232V-Q245R,P052N-S078R-S103N-L148I-T213A,N018R-N043D-S101G-S103A-V104I-A232V-Q245R-H249R,S024R-N043D-S101G-S103A-V104I-A232V-Q245R-H249R,S024R-N043D-S101G-S103A-V104I-A232V-Q245R-N269R,G025R-E089I-N116A-P239S-A270C,S024R-S101G-S103A-V104I-A232V-Q245R,L148I-T213A-N252R,S024R-G025R-N183D-Y192W-P239S,G046R-A194F-S212M,V104L-L217E-T224A-H249R-N252R,G023A-Y091F-V121F-Y192W-Q236N,S101G-S103A-V104I-A232V-V244R-Q245R,S099F-S144R-Y167W-N252R,S101G-S103A-V104I-A232V-Q245R-H249R,N043R-S101G-S103A-V104I-A232V-Q245R,T022W-S078R-Y167W-S212M-A270C,V121F-N252R-A270C,G020R-S103N-S216F-Q236N-N252R,N043R-S101G-S103A-V104I-A232V-Q245R-H249R,G023A-P052N-Y192W-I198L-N252R,G025R-G046R-V121F,S024R-S078R-V104L-N116A-N183D,G046R-Q059A-S103N-G211Q-S212M,G020R-P052N-N062Q-Y091F-Y192W,G023A-P052N-S144R-Y192W-S216F,S101G-S103A-V104I-A232V-S242R-Q245R,P052N-S103N-N116A-L148I-Y192W,E089I-N116A-N117F-T224A-H249R,S144R-G211Q-N238L-P239S-H249R,N043A-N062Q-A194F-G211Q,G020R-S024R-P052N-Q059A-S216F,S024R-Y167W-T224A-H249R,T057R-Y167W-H249R,G025R-S103N-R186K-A194F-T224A,S105T-S128N-S144R-L148I-S212M,G020R-Q059A-S144R-Y192W-T224A,S024R-N043A-N117F-A194F-G211Q,N117F-A194F-T213A-A270C,S078R-Y091F-V121F-

L233C-N252R,T057R-S099F-S105T-I198L-T213A,G023A-Y091F-S101A-I198L-N252R,N062Q-S103N-V121F-S144R-H249R,N043R-S101G-S103A-V104I-A232V-S242R-Q245R,G023A-S024R-N117F-S212M-S216F,V104L-T213A-S216F,A194F-G211Q-Q236N,N062Q-S103N-N117F-A194F,S024R-N062Q-V104L-S106G-H249R,T057R-E089I-I198L,G046R-Q059A-S106G-L217E-H249R,N117F-T213A-A215F,S101A-H120F-Y192W-A215F-T224A,N043A-T057R-N117F-S144R-N183D,G046R-N183D-N238L,G025R-N043A-E089I-N117F,S078R-V104L-T213A-A215F-T224A,Y091F-S099F-S101A-S105T-Y167W,S106G-N117F-N238L,G046R-E089I-Y091F-S101A-N116A,G020R-N062Q-E089I-R186K-S212M,T057R-S099F-V121F-N185I-Y192W,G046R-E089I-Y192W-L233C-A270C,E089I-N117F-N185I-A215F-L233C,P052N-V104L-N183D-S216F-H249R,S078R-S099F-N116A-R186K-T224A,G025R-S105T-S128N-S144R-A270C,S105T-G211Q-S216F,S024R-G046R-Y091F-V121F,S106G-N185I-S216F-Q236N,N062Q-S101A-Q236N-N252R-A270C,G025R-N043A-Y091F-I198L-A270C,G020R-G023A-V104L-Y192W-L233C,S024R-N043A-S105T-S106G-I198L,G020R-E089I-L217E,S024R-Y091F-I198L-A215F-P239S,G046R-E089I-S099F-R186K-S212M,V104L-H120F-R186K-S216F-N252R,T022W-A194F-T213A-L233C-N238L,S099F-S105T-S106G-A194F-S212M,E089I-S105T-N116A-A215F-S216F,G025R-N116A-H120F-T224A-A270C,N043A-Q059A-S101A-S216F-T224A,T057R-N183D-Q236N,G025R-N062Q-S128N-S144R-N185I,S103N-H120F-Y167W-I198L-L233C,T022W-E089I-S216F,S024R-S106G-N116A-S212M-T224A,G020R-P052N-S101A-I198L-L233C,E089I-Y091F-N185I-G211Q-A270C,L111I-A215F-P239S,S024R-N116A-R186K-L233C-Q236N,和G023A-S103N-S106G-S212M-A215F,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0273] 本发明还提供分离的枯草杆菌蛋白酶变体,其中该枯草杆菌蛋白酶变体是具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:G020R-T022W-S078R-S101A-S103A-V104I-N116S-T213A-A215F-A232V-Q245R,N018R-S078R-S101G-S103A-V104I-A232V-Q245R,S024R-R045T-S101G-S103A-V104I-A232V-Q245R-N269R,G020R-T022W-S078R-S101G-S103A-V104I-N116A-A232V-Q245R,G020R-T22W-S101G-S103A-V104I-A232V-Q245R,N018R-N043R-S101G-S103A-V104I-A232V-Q245R,N018R-T022W-S024R-N076D-S101A-N116A-A232V-Q245R,N018R-V104I-A232V-H249R,N018R-S024R-N076D-S101A-N116A-G211Q-H249R,N018R-N043D-S078R-S101G-S103A-V104I-L217E-A232V-Q245R,N018R-N043R-S101G-S103A-V104I-A232V-Q245R-N269R,N018R-R045T-N076D-S101G-S103A-V104I-A232V-Q245R-N269R,N076D-S078R-S101G-S103A-V104I-A232V-Q245R-N269R,G020R-N043D-S078R-S101G-S103A-V104I-A232V-Q245R,N018R-N043D-N076D-S101G-S103A-V104I-A232V-Q245R-N269R,S024R-R045T-N076D-S078R-S101G-S103A-V104I-A232V-Q245R-N269R,N018R-S103A-A232V-H249R,N018R-S101G-V104I-A232V-Q245R,G020R-S024R-S101G-S103A-V104I-L217E-A232V-Q245R-H249R,N018R-T22K-N043D-S101G-S103A-V104I-A232V-Q245R,N043R-R045T-S101G-S103A-V104I-A232V-Q245R-N269R,G020R-T22W-S101G-S103A-V104I-G211Q-A232V-Q245R,S024R-N076D-S078R-S101G-S103A-V104I-A232V-Q245R-N269R,G020R-T22W-S078R-S101A-S103A-

V104I-N116A-N183D-A232V,N018R-S024R-N076D-N116A-A215F-H249R,N018R-N043R-R045T-S101G-S103A-V104I-A232V-Q245R,S024R-N043R-N076D-S101G-S103A-V104I-A232V-Q245R,G020R-T022W-S101G-S103A-V104I-A232V-Q245R,G020R-T022W-S101G-S103A-V104I-G211Q-A232V-Q245R,G020R-T022W-S078R-S101G-S103A-V104I-N116A-T213A-A215F-A232V-Q245R,N043D-N076D-S078R-S101G-S103A-V104I-A232V-Q245R-N269R,N018R-S024R-N076D-S101A-N116A-T213A-H249R,N018R-S024R-N076D-N116A-G211Q-H249R,N043R-R045T-N076D-S078R-S101G-S103A-V104I-A232V-Q245R,N018R-S101G-Q245R,G020R-T22W-S101A-S103A-V104I-G211Q-T213A-A232V-Q245R,G020R-S024R-N043D-N076D-S078R-S101G-S103A-V104I-A232V-Q245R,N018R-R045T-N076D-S078R-S101G-S103A-V104I-A232V-Q245R,G020R-S078R-S101G-S103A-V104I-G211Q-T213A-A215F-A232V-Q245R,R045T-S078R-S101G-S103A-V104I-A232V-Q245R-N269R,S024R-N043D-S101G-S103A-V104I-A232V-Q245R-N269R,N018R-S101G-S103A-H249R,N018R-T22W-S024R-N076D-S101A-N116A-A232V-Q245R,N018R-S101G-V104I-A232V-H249R,G020R-T22W-S101A-S103A-V104I-A215F-A232V-Q245R,N018R-S024R-N076D-G211Q-T213A-H249R,N018R-T022W-S024R-N076D-S101A-I198L-H249R,S024R-S101G-S103A-V104I-A232V-Q245R,G020R-N076D-S101G-S103A-V104I-A232V-Q245R-N269R,G020R-S101G-S103A-V104I-A232V-Q245R-N269R,N043D-S078R-S101G-S103A-V104I-A232V-Q245R,G020R-S101G-V104I-T213A-A215F-A232V-Q245R,G020R-S101G-S103A-V104I-N116A-A215F-A232V-Q245R,S024R-S103A-V104I-H249R,N018R-N076D-S078R-S101G-S103A-V104I-A232V-Q245R,R045T-N076D-S078R-S101G-S103A-V104I-A232V-Q245R-N269R,S024R-S101G-V104I-Q245R,G020R-S101G-S103A-V104I-G211Q-T213A-A215F-A232V-Q245R,S024R-S103A-V104I-A232V-H249R,N018R-S024R-N076D-N116A-G211Q-A215F-H249R,N018R-Q245R,S024R-S103A-Q245R,S024R-S103A-V104I-Q245R,G020R-S078R-S101G-A232V-Q245R,N018R-S024R-N076D-V104I-H249R,N018R-S024R-V104I-H249R,S024R-S101G-S103A-V104I-A232V-Q245R,N018R-S024R-N076D-G211Q-A215F-H249R,R019H-G020R-T022W-S078R-S101G-S103A-V104I-G211Q-A232V-Q245R,N018R-S024R-N076D-S101A-I198L-G211Q-T213A-H249R,N018R-S024R-N043D-S101G-S103A-V104I-A232V-Q245R,G020R-T22W-S103A-V104I-A232V-Q245R,N018R-S103A-V104I-H249R,N018R-T022W-S024R-N076D-S101A-I198L-A215F-H249R,N018R-S024R-S101G-V104I-A232V,S078R-S101G-S103A-V104I-A232V-Q245R-N269R,S024R-N043R-N076D-S078R-S101G-S103A-V104I-A232V-Q245R,N018R-G020R-N043D-N076D-S101G-S103A-V104I-A232V-Q245R,N018R-T22W-S024R-N076D-N116A-T213A-H249R,N018R-S024R-S101G-V104I,G020R-S101A-S103A-V104I-A215F-A232V-Q245R,N018R-R045T-S078R-S101G-S103A-V104I-A232V-Q245R,N018R-S101G-S103A-Q245R,N043R-N076D-S078R-S101G-S103A-V104I-A232V-Q245R,G020R-T022W-S101A-S103A-V104I-G211Q-A215F-A232V-Q245R,G020R-T22W-S078R-S101G-S103A-V104I-N116A-T213A-A215F-A232V-Q245R,G020R-S078R-S101G-S103A-V104I-A215F-A232V-Q245R,G020R-T022W-S078R-S101G-S103A-V104I-N116A-N183D-A232V-Q245R,N076D-S101G-S103A-V104I-A232V-Q245R,N076D-S101G-S103A-V104I-A232V-Q245R-N269R,G020R-T22W-S101A-S103A-V104I-A232V-Q245R,G020R-S101G-S103A-

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S103A-V104I-N183D-I198L-A215F-A232V-Q245R,N076D-S101G-S103A-V104I-H249R,N018R-G020R-S024R-N076D-N183D-I198L-A215F-H249R,N018R-G020R-T022W-S024R-N076D-S101A-N183D-A215F-H249R,N018R-G020R-S024R-N076D-G211Q-T213A-H249R,N018R-S024R-N076D-N116A-N183D-G211Q-T213A-H249R,N018R-S024R-N076D-N116A-N183D-I198L-H249R,N018R-G020R-S024R-N076D-G211Q-N243D-H249R,N018R-G020R-R045T-N076D-S101G-S103A-V104I-A232V-Q245R-H249R,N018R-T022W-S024R-N076D-N183D-I198L-G211Q-T213A-H249R,N018R-S024R-N076D-S101A-N116A-N183D-I198L-G211Q-T213A-H249R,N018R-T022W-S024R-N076D-N116A-I198L-G211Q-T213A-A215F-H249R,S024R-N076D-S101G,N018R-G020R-S024R-N076D-S101A-I198L-T213A-A215F-H249R,N018R-T022W-S024R-N076D-N116A-N183D-G211Q-T213A-H249R,N018R-G020R-S024R-N076D-N183D-A215F-H249R,N018R-N043D-N076D-S078R-S101G-S103A-V104I-A232V-Q245R-H249R,N018R-T022W-S024R-N076D-N116A-N183D-G211Q-T213A-Q245R,G020R-S024R-N076D-S078R-S101G-S103A-V104I-A232V-Q245R-H249R,N018R-G020R-R045T-S101G-S103A-V104I-A232V-Q245R-H249R,N018R-S024R-N076D-S101A-N183D-I198L-G211Q-H249R,N018R-T022W-S024R-N076D-N183D-G211Q-T213A-H249R,N018R-G020R-S024R-N076D-N116A-I198L-G211Q-A215F-H249R-N269S,N018R-G020R-T022W-S024R-N076D-S101A-N116A-N183D-I198L-G211Q-A215F-H249R,G020R-T022W-S101A-S103A-V104I-N183D-T213A-A215F-A232V-Q245R,N018R-S024R-N076D-A086V-S101A-N183D-I198L-G211Q-H249R,N018R-N076D-S101G-I198T-A232V,N018R-G020R-S024R-N076D-S101A-N116A-N183D-I198L-G211Q-A215F-H249R,N018R-T022W-S024R-N076D-S101A-N116A-N183D-T213A-A215F-H249R,N018R-T022W-S024R-N076D-S101A-N183D-G211Q-T213A-A215F-H249R,N018R-S024R-N076D-N183D-H249R-A248T,N018R-N076D-V104I-Q245R-H249R,N018R-T022W-S024R-N076D-S101A-N116A-N183D-I198L-A215F-H249R,N018R-T022W-S024R-N076D-N116A-N183D-T213A-A215F-H249R,N018R-G020R-T022W-S024R-N076D-N116A-N183D-G211Q-T213A-A215F-H249R,N018R-G020R-S024R-N076D-S101A-H249R,N018R-G020R-S024R-N076D-S101A-N116A-T213A-A215F-H249R,N018R-T022W-S024R-N076D-N116A-N183D-G211Q-A215F-H249R,N018R-T022W-S024R-N076D-N116A-N183D-I198L-G211Q-T213A-H249R,N043R-R045T-S078R-S101G-S103A-V104I-L217E-A232V-Q245R,N043R-R045T-S101G-S103A-V104I-A232V-Q245R-H249R,N018R-N076D-S101G-V104I,G020R-R045T-N076D-S078R-S101G-S103A-V104I-A232V-Q245R-H249R,N043D-N076D-S101G-S103A-V104I-A232V-Q245R,N018R-G020R-T022W-S024R-N076D-S101A-N116A-N183D-I198L-H249R,N018R-N076D-V104I,N018R-G020R-N043D-S101G-S103A-V104I-A232V-Q245R-H249R,N018R-G020R-T022W-S024R-N076D-N183D-G211Q-H249R,N018R-S024R-N076D-S101A-N183D-I198L-G211Q-A215F-H249R,S101G-V104I,N018R-T022W-S024R-N076D-N116A-N183D-I198L-G211Q-T213A-A215F-H249R,N018R-G020R-S024R-N076D-S101A-N183D-G211Q-T213A-A215F-H249R,N018R-G020R-S024R-N076D-N116A-N183D-A215F-H249R-N263D,N018R-T022W-S024R-N076D-S101A-N183D-H249R,N018R-S024R-N076D-S101A-N116A-N183D-I198L-A215F-H249R,N018R-T022W-S024R-N076D-N116A-I198L-A215F-H249R-R269H,N018R-N043D-R045T-

N076D-S078R-S101G-S103A-V104I-A232V-Q245R,N018R-S024R-R045T-N076D-S078R-S101G-S103A-V104I-A232V-Q245R-N269R,S078R-S101G-S103A-V104I-L217E-A232V-Q245R,N018R-G020R-T022W-S024R-N076D-S101A-N183D-I198L-T213A-A215F-H249R,N018R-G020R-S024R-N076D-N183D-I198L-T213A-H249R,N018R-G020R-T022W-S024R-N076D-N116A-I198L-G211Q-A215F-H249R,N018R-G020R-T022W-S024R-N076D-N116A-N183D-G211Q-H249R,N018R-G020R-T022W-S024R-N076D-S101A-I198L-G211Q-T213A-H249R,N018R-G020R-T022W-S024R-N076D-H249R,G020R-T022W-S101G-S103A-V104I-N116A-N183D-I198L-G211Q-T213A-A215F-A232V-Q245R,V104I-A232V,N018R-G020R-T022W-S024R-N076D-S101A-N116A-N183D-G211Q-A215F-H249R,N018R-G020R-T022W-S024R-N076D-S101A-N116A-N183D-I198L-G211Q-T213A-A215F-H249R,N018R-G020R-T022W-S024R-N076D-S101A-N183D-T213A-A215F-H249R,N018R-T022W-S024R-N076D-S101A-N183D-I198L-G211Q-T213A-H249R,N018R-T022W-S024R-N076D-S101A-N183D-I198L-H249R,N043D-R045T-S101G-S103A-V104I-A232V-Q245R-N269R,N018R-G020R-S024R-N076D-S101A-N183D-I198L-G211Q-H249R,N018R-G020R-N043R-S101G-S103A-V104I-L217E-A232V-Q245R,S024R-N043R-N076D-S078R-S101G-S103A-V104I-A232V-Q245R-N269R,N043R-R045T-N076D-S078R-S101G-S103A-V104I-Y166F-A176P-A179V-N184T-A187P-A194P,N018R-T022W-S024R-D041E-N076D-S101A-S160T-N183D-G211Q-T213A-H249R,N018R-G020R-T022W-S024R-N076D-N116A-N183D-I198L-G211Q-A215F-H249R,N018R-G020R-T022W-S024R-N076D-S101A-N116A-I198L-T213A-H249R,N018R-T022W-S024R-N076D-S101A-N116A-N183D-I198L-G211Q-T213A-H249R,N018R-G020R-S024R-N076D-I198L-T213A-H249R,N018R-G020R-T022W-S024R-N076D-N116A-N183D-I198L-G211Q-H249R,N018R-G020R-S024R-N076D-N183D-G211Q-A215F-H249R,S024R-N076D-V104I,N018R-N076D-S101G-A232V,N018R-S024R-N076D-S101A-N116A-N183D-I198L-G211Q-T213A-A215F-H249R,N018R-G020R-T022W-S024R-N076D-N116A-N183D-A215F-H249R,N018R-S024R-L031F-N076D-N116A-N183D-G211Q-T213A-A215F-H249R,N018R-S024R-N076D-S101A-N116A-N183D-I198L-T213A-H249R-N269S,N018R-G020R-S024R-N076D-S101A-N116A-I198L-A215F-H249R,N018R-N043R-N076D-S078R-S101G-S103A-V104I-A232V-Q245R-N269R,N018R-G020R-S024R-N076D-S101A-N114T-I198L-G211Q-A215F-H249R,S024R-N043R-S078R-S101G-S103A-V104I-L217E-A232V-Q245R,S024R-N076D-S103A-V104I-A232V,N018R-G020R-T022W-S024R-N076D-S101A-I198L-G211Q-A215F-H249R,S101G-V104I-A232V,N018R-T022W-S024R-N076D-N183D-I198L-T213A-A215F-H249R,N018R-T022W-S024R-N076D-N183D-I198L-G211Q-H249R,N018R-G020R-S024R-N076D-N183D-T213A-H249R,N018R-S024R-N076D-S101A-N183D-G211Q-A215F-H249R,N018R-G020R-T022W-S024R-N076D-N116A-G211Q-T213A-H249R,N018R-S078R-S101G-S103A-V104I-A232V-Q245R-N269R,N018R-T022W-S024R-N076D-S101A-N116A-N183D-G211Q-A215F-H249R-T260A,N076D-H249R,N018R-T022W-S024R-N076D-N183D-G211Q-A215F-H249R,N018R-G020R-S024R-N076D-N116A-G211Q-A215F-H249R,N018R-G020R-S024R-N076D-T213A-H249R,N018R-G020R-T022W-S024R-N076D-N116A-N183D-I198L-H249R,N018R-G020R-T022W-S024R-N076D-S101A-N183D-H249R,N076D-

V104I-H249R,G020R-T022W-S101A-S103A-V104I-N116A-N183D-G211Q-T213A-A215F-A232V-Q245R,S024R-N043R-R045T-S078R-S101G-S103A-V104I-L217E-A232V-Q245R,N018R-G020R-T022W-S024R-N076D-N183D-I198L-A215F-H249R,N018R-N076D-S101G-S103A,G020R-S024R-S101G-S103A-V104I-A232V-Q245R-N269R,N018R-G020R-S024R-N076D-S101A-N116A-N183D-G211Q-H249R,S101G-S103A-A232V,S024R-N076D-S101G-A232V,N018R-T022W-S024R-N076D-S101A-N183D-I198L-G211Q-H249R,N018R-G020R-S024R-N076D-S101A-N183D-I198L-G211Q-A215F-H249R,N018R-G020R-S024R-N076D-N183D-I198L-H249R,N018R-T022W-S024R-N076D-S101A-N116A-N183D-I198L-G211Q-H249R,N018R-G020R-S024R-N076D-N116A-A156V-N183D-G211Q-A215F-H249R-N269S,R045T-N076D-S101G-S103A-V104I-A232V-Q245R-H249R,N018R-G020R-S024R-N076D-S101A-N183D-I198L-H249R,N018R-G020R-T022W-S024R-N076D-I198L-G211Q-A215F-H249R,N018R-G020R-T022W-S024R-N076D-S101A-N116A-I198L-G211Q-A215F-H249R,N018R-G020R-T022W-S024R-N076D-N116A-H249R,N018R-N076D-S101G,N018R-S024R-N076D-N116A-N183D-I198L-T213A-A215F-H249R,N018R-G020R-T022W-S024R-N076D-S101A-N116A-I198L-T213A-A215F-H249R,N018R-S024R-N076D-S101A-N116A-N183D-I198L-G211Q-H249R,N018R-N076D-A232V,N018R-G020R-S024R-N076D-S101A-A232V-Q245R,N018R-N043D-R045T-N076D-S101G-S103A-V104I-A232V-Q245R,N018R-T022W-S024R-N076D-N183D-T213A-A215F-H249R,N018R-S024R-N076D-S101A-N116A-G211Q-T213A-N237D-H249R,N018R-G020R-S024R-N076D-S101A-N116A-N183D-G211Q-H249R-R275S,N018R-T022W-S024R-N076D-S101A-N116A-N183D-I198L-G211Q-T213A-A215F-H249R,S024R-N076D,N018R-S024R-N076D-N183D-G211Q-A215F-H249R,N018R-T022W-S024R-N076D-N116A-N183D-I198L-T213A-A215F-H249R,N076D-V104I-A232V-H249R,N018R-N076D-S103A-A232V,N018R-G020R-S024R-N076D-S101A-N116A-N183D-I198L-G211Q-T213A-H249R,N018R-G020R-S024R-N076D-S101A-N183D-T213A-H249R,N018R-G020R-S024R-N076D-S101A-D175E-N183D-G211Q-A215F-H249R,N018R-G020R-N043D-S078R-S101G-S103A-V104I-L217E-A232V-Q245R-A273E,G020R-S024R-N043D-R045T-N076D-S101G-S103A-V104I-A232V-Q245R,P005S-S101G-S103A-V104I-A232V-Q245R-H249R,S103A-V104I-A232V,N018R-G020R-S024R-V068A-N076D-S101A-N116A-T213A-A215F-H249R,N018R-T022W-S024R-N076D-S101A-I198L-A215F-H249R-R275S,N018R-S024R-N076D-N183D-I198L-G211Q-T213A-H249R,和N043D-R045T-S101G-S103A-V104I-A232V-Q245R,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0274] 本发明还提供分离的枯草杆菌蛋白酶变体,其中该枯草杆菌蛋白酶变体是具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:N018R-S024R-N043R-N076D-H249R-N269R,N018R-T022R-S024R-N043R-N076D-H249R,N018R-N043D-S101G-S103A-V104I-A232V-Q245R,G020R-N043D-S101G-S103A-V104I-A232V-Q245R,N043D-S101G-S103A-V104I-A232V-Q245R-N269R,N043D-S078R-S101G-S103A-V104I-A232V-Q245R,N043R-N076D-S101G-S103A-V104I-A232V-Q245R,T022R-N043R-S101G-S103A-V104I-A232V-Q245R,N043R-S078R-S101G-S103A-V104I-A232V-Q245R,

G020R-N076D-S101G-S103A-V104I-A232V-Q245R,N043R-N076D-S101G-S103A-V104I-A232V-Q245R,T022R-N076D-S101G-S103A-V104I-A232V-Q245R,N076D-S078R-S101G-S103A-V104I-A232V-Q245R,N018R-S024R-N043R-N076D-H249R,N018R-S024R-N076D-S242R-H249R,N018R-S024R-N076D-H249R-N269R,N018R-T022R-S024R-N076D-H249R,N018R-S024R-N076D-S078R-H249R,N018R-S024R-N043D-N076D-H249R-N269R,N018R-T022R-S024R-N043D-N076D-H249R,N018R-S024R-N043D-N076D-S078R-H249R,G020R-S101G-S103G-V104I-A232V-Q245R,G020R-S101G-S103A-V104L-A232V-Q245R,G020R-S101G-S103A-V104V-A232V-Q245R,G020R-S101G-S103S-V104I-A232V-Q245R,G020R-S101G-S103S-V104L-A232V-Q245R,G020R-S101S-S103S-V104I-A232V-Q245R,G020R-S101S-S103S-V104L-A232V-Q245R,G020R-S101A-S103A-V104L-A232V-Q245R,G020R-S101S-S103S-V104V-A232V-Q245R,G020R-S101S-S103A-V104I-A232V-Q245R,G020R-S101S-S103A-V104V-A232V-Q245R,G020R-S101S-S103G-V104I-A232V-Q245R,G020R-S101S-S103G-V104V-A232V-Q245R,G020R-S101A-S103A-V104V-A232V-Q245R,G020R-S101A-S103S-V104I-A232V-Q245R,G020R-S101A-S103S-V104V-A232V-Q245R,N018R-S024R-N043R-N076D-S078R-H249R,S024R-N043D-S101G-S103A-V104I-A232V-Q245R,N043D-S101G-S103A-V104I-A232V-Q245R-H249R,S024R-N076D-S101G-S103A-V104I-A232V-Q245R,N076D-S101G-S103A-V104I-A232V-S242R-Q245R,N018R-G020R-S024R-N076D-L217E-H249R,N018R-S024R-N043R-N076D-L217E-H249R,N018R-S024R-N043D-N076D-S242R-H249R,N018R-G020R-S024R-N043R-N076D-H249R,G020R-S101A-S103G-V104V-A232V-Q245R,N043D-S101G-S103A-V104I-A232V-Q245R,N018R-S024R-N076D-L217E-H249R-N269R,和N018R-S024R-N076D-L217E-S242R-H249R,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0275] 本发明还提供分离的枯草杆菌蛋白酶变体,其中该枯草杆菌蛋白酶变体是具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:G020R-S101A-S103A-V104I-G118R-A232V-Q245R,G020R-S024R-N116A-T213A,N043R-S101A-N116A-A215F-N269R,S024R-N043R-S101A-N116A,S024R-N043R-S101A-N116A-A215F-N269R,G020R-S101G-S103A-V104I-A215F-A232V-Q245R,N043R-S101A-N269R,S024R-N043R-N116A-T213A-N269R,G020R-S024R-N043R-R045T-S101A-T213A,S024R-N043R-N116A-A215F-N269R,G020R-S024R-T213A-A215F,G020R-N116A-N269R,S024R-N116A-T213A-N269R,N043R-S101A-N116A-N269R,S101G-S103A-V104I-N116A-T213A-A232V-Q245R-N269R,S024R-N043R-R045T-S101A-N116A-A215F-N269R,G020R-N043R-S101A-N269R,S101A-S103A-V104I-T213A-A232V-Q245R-N269R,S024R-A215F-N269R,N043R-S101A-N116A-T213A-A215F-N269R,N043R-S101A-T213A-N269R,G020R-S024R-N043R-R045T-N116A-T213A,S101G-S103A-V104I-A232V-Q245R-N269R,S024R-N043R-R045T-S101A-N116A-T213A-N269R,S024R-N043R-R045T-N269R,G020R-N043R-R045T-S101A-N269R,S024R-N043R-N116A-N269R,G020R-S024R-N043R-R045T,N043R-N116A-N269R,S024R-N043R-S101A-A215F-N269R,S024R-N043R-R045T-T213A-A215F-N269R,G020R-S024R-R045T-N269R,G020R-N043R-S101A-N116A-T213A-A215F,G020R-S101G-S103A-

V104I-T213A-A215F-A232V-Q245R,G020R-S024R-R045T-N116A-N269R,G020R-S101A-N116A-N269R,S024R-N043R-A215F,G020R-S024R-T213A,S024R-N043R-S101A-A215F,G020R-S024R-N043R-R045T-N116A,G020R-S024R-N043R-R045T-S101A-N269R,G020R-S024R-S101A-A215F,G020R-S024R-N116A-T213A-A215F,G020R-S024R-N116A,G020R-S024R-S101A-N116A,N043R-T213A-A215F-N269R,S024R-S101A-N269R,S024R-N043R-N116A-A215F,G020R-T038A-N043R-S101A,G020R-S024R-N116A-A215F,S024R-N043R-S101A-T213A,P014L-G020R-S024R-N043R-R045T-S101A-A215F,G020R-S024R-A215F,G020R-N116A-A215F-N269R,G020R-R045T-N116A-N269R,G020R-S024R-N043R-R045T-A215F,和G020R-S024R-N043R-R045T-N116A-T213A-A215F,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0276] 本发明还提供分离的枯草杆菌蛋白酶变体,其中该枯草杆菌蛋白酶变体是具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:N043R-N076D-S101A-S103A-V104I-A158E-S188D-A232V-Q245R-N248D-H249R-E271F,S024R-N043R-N076D-S101A-S103A-V104I-A158E-S188D-L217E-A232V-Q245R-N248D-H249R,S101A-S103A-V104I-A158E-S188D-A232V-Q245R-N248D-H249R-E271F-E271F,S101A-S103A-V104I-A158E-S188D-L217E-A232V-Q245R-N248D-H249R-E271F,N076D-S101G-S103A-V104I-A114V-A158E-S188D-A232V-Q245R-N248D-H249R-E271F,S024R-N076D-S101G-S103A-V104I-A158E-S188D-A232V-Q245R-N248D-H249R-E271F,S024R-N043R-S101A-S103A-V104I-A158E-S188D-L217E-A232V-Q245R-N248D-H249R,S024R-N043R-S101A-S103A-V104I-A158E-S188D-A232V-Q245R-N248D-H249R,S024R-S101A-S103A-V104I-A158E-S166D-S188D-L217E-A232V-Q245R-N248D-H249R,N076D-S101G-S103A-V104I-S128L-A158E-S188D-A232V-Q245R-N248D-H249R-E271F,和N043R-N076D-S101G-S103A-V104I-A158E-S166D-S188D-A232V-Q245R-N248D-H249R-E271F,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0277] 本发明还提供分离的枯草杆菌蛋白酶变体,其中该枯草杆菌蛋白酶变体是具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:T022A-S101G-S103A-V104I-G159D-L217E-A232V-Q245R-N248D-E271F,T022A-N043R-S101G-S103A-V104I-G159D-S188D-L217E-A232V-Q245R-N248D-E271F,T022A-S101G-S103A-V104I-G159D-S188D-A232V-Q245R-N248D-E271F,N043R-S101A-S103A-V104I-A158E-S188D-L217E-A232V-Q245R-N248D-H249R,N043R-N076D-S101A-S103A-V104I-A158E-S188D-L217E-A232V-Q245R-N248D-H249R-E271F,S024R-S101G-S103A-V104I-A158E-S188D-L217E-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-A158E-S188D-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-A158E-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-A158E-N183D-S188D-A232V-Q245R-N248D-H249R,T022A-N076D-S101G-S103A-V104I-G159D-S188D-A232V-Q245R-N248D-E271F,T022A-N043R-N076D-S101G-S103A-V104I-G159D-S188D-A232V-Q245R-N248D-E271F,T022A-N076D-S101G-S103A-V104I-G159D-A232V-Q245R-N248D-E271F,T022A-S101G-S103A-

V104I-G159D-A232V-Q245R-N248D-E271F,N076D-S101A-S103A-V104I-A158E-S188D-A232V-Q245R-N248D-H249R-E271F,N043R-S101A-S103A-V104I-A158E-S166D-S188D-A232V-Q245R-N248D-H249R,S024R-N076D-S101A-S103A-V104I-A158E-S166D-S188D-A232V-Q245R-N248D-H249R-E271F,N076D-S101A-S103A-V104I-A158E-S188D-A232V-Q245R-N248D-H249R,S101A-S103A-V104I-A158E-S166D-S188D-A232V-Q245R-N248D-H249R-E271F,N043R-N076D-S101A-S103A-V104I-A158E-S166D-S188D-A232V-Q245R-N248D-H249R-E271F,S101G-S103A-V104I-A158E-S166D-S188D-A232V-Q245R-N248D-H249R-E271F,S101A-S103A-V104I-A158E-S188D-A232V-Q245R-N248D-H249R-E271F,S101A-S103A-V104I-A158E-S188D-L217E-A232V-Q245R-N248D-H249R,N076D-S101A-S103A-V104I-A158E-S166D-S188D-A232V-Q245R-N248D-H249R-E271F,S101G-S103A-V104I-A158E-N183D-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-S128L-A158E-S188D-A232V-Q245R-N248D-H249R,N076D-S101G-S103A-V104I-A158E-S166D-S188D-A232V-Q245R-N248D-H249R-E271F,N043R-N076D-S101A-S103A-V104I-A158E-S166D-S188D-A232V-Q245R-N248D-H249R,和N076D-S101A-S103A-V104I-A158E-S188D-L217E-A232V-Q245R-N248D-H249R-E271F,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0278] 本发明还提供分离的枯草杆菌蛋白酶变体,其中该枯草杆菌蛋白酶变体是具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:H017R-T022A-N076D-S101G-S103A-V104I-G159D-S188D-A232V-Q245R-N248D-E271F,T022A-N043R-S101G-S103A-V104I-G159D-A232V-Q245R-N248D-E271F,T022A-S101G-S103A-V104I-G159D-S188D-A232V-Q245R-N248D-H249R-E271F,H017R-T022A-N076D-S101G-S103A-V104I-G159D-A232V-Q245R-N248D-E271F,T022A-N076D-S101G-S103A-V104I-G159D-A232V-Q245R-N248D-H249R-E271F,T022A-S101G-G102A-S103A-V104I-G159D-S188D-A232V-Q245R-N248D-E271F,和T022A-N043R-N076D-S101G-S103A-V104I-G159D-A232V-Q245R-N248D-H249R-E271F,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0279] 本发明还提供分离的枯草杆菌蛋白酶变体,其中该枯草杆菌蛋白酶变体是具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:S101S-S103A-V104I-A158E-S188D-A232V-Q245R-N248D-H249R,S101S-S103G-V104V-A158E-S188D-A232V-Q245R-N248D-H249R,S101G-S103S-V104I-A158E-S188D-A232V-Q245R-N248D-H249R,S101A-S103A-V104I-A158E-S188D-A232V-Q245R-N248D-H249R,S101A-S103A-V104L-A158E-S188D-A232V-Q245R-N248D-H249R,S101G-S103G-V104I-A158E-S188D-A232V-Q245R-N248D-H249R,S101S-S103G-V104I-A158E-S188D-A232V-Q245R-N248D-H249R,S101S-S103S-V104I-A158E-S188D-A232V-Q245R-N248D-H249R,S101S-S103S-V104V-A158E-S188D-A232V-Q245R-N248D-H249R,S101A-S103S-V104I-A158E-S188D-A232V-Q245R-N248D-H249R,S101A-S103S-V104I-G159E-A232V-Q245R-N248D-H249R,S101S-S103A-V104I-G159E-A232V-Q245R-N248D-H249R,S101G-S103A-V104L-A158E-S188D-A232V-Q245R-N248D-H249R,S101A-S103A-V104L-G159E-A232V-Q245R-

N248D-H249R,S101A-S103S-V104L-G159E-A232V-Q245R-N248D-H249R,S101G-S103S-V104L-G159E-A232V-Q245R-N248D-H249R,S101S-S103A-V104L-G159E-A232V-Q245R-N248D-H249R,S101A-S103G-V104V-G159E-A232V-Q245R-N248D-H249R,和S101S-S103A-V104V-G159E-A232V-Q245R-N248D-H249R,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0280] 本发明还提供分离的枯草杆菌蛋白酶变体,其中该枯草杆菌蛋白酶变体是具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:V026F-V051W-V104L-S106E,V026F-L031F-S078N-G102A-S160D,G020K-G100S-N116L-A158E-S166D-N243F,T033S-N043W-N218D-P239G-N243F,T022L-T038F-A048R-N062E-G100S-R186K,S101D-S103N-N116L-S144R-A215D,V104L-S105T-T213A-L217E-S256N,N043W-S101D-S212M-N243F,V026F-A048R-S105T-T213A-N218D-T224A,S024F-S101D-G118R-A215D-L250I-A272F,V121F-N185E-T224A-P239G,T022L-L031F-G102A-S128D-T224A-N243F,N062E-S078N-G102A-N116L-S144R-L250I,T022L-T038F-V121F-S160D-A272F,V026F-S078N-G159C-R186K-N243F,S024F-A048R-G118R-S166D-L217E,G023A-T038F-S078N-G100S-S212M-A215D,G100S-N116L-A158E-T213A,S078N-V104L-G118R-S128D,G102A-S103N-S105T-A194E,T022L-S078N-S128D-T213A,K027R-G100S-G118R-S160D-S188D-N243F,S024F-G102A-R186K-T213A-L217E-N243F,T033S-S105T-S188D-S216F,G023A-G100S-A194E-S212M,A048R-S128D-N185E-P239G,G020K-S024F-T033S-P129E-A194E,G020K-K027R-P129E-S166D-P239G,T022L-G023A-K027R-S101D-V104L-S216F,T033S-G118R-P129E-A194E-P239G,T022L-S078N-N116L-P129E-S256N,K027R-S101D-S103N-S105T-A272F,A048R-S078N-N116L-N185E-L217E-P239G,G023A-S024F-K027R-N062E,S024F-S103N-V104L-G118R-S188D,V026F-V104L-S256N-A272F,S024F-N043W-V104L-V121F-P129E,N062E-S078N-N116L-T224A,G023A-S024F-V051W-A158E,K027R-T038F-G102A-N116L,N062E-S078N-S144R-S212M,L031F-N116L-S256N-A272F,T022L-T033S-V104L-N116L-S160D-R186K,S024F-G118R-P129E-R186K-T213A,N043W-S105T-T213A-A215D-S216F,L031F-S105T-R186K-S188D,V026F-A194E-T213A-S256N,和S103N-S160D-L250I-S256N,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0281] 本发明还提供分离的枯草杆菌蛋白酶变体,其中该枯草杆菌蛋白酶变体是具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:T022A-S024R-S101D-S103A-V104I-G118R-G159D-S188D-A232V-N248D-E271F,T022A-S024R-S103A-V104I-P129E-G159D-S188D-A232V-N248D-E271F,T022A-S024R-S103A-V104I-G118R-G159D-S188D-L217D-A232V-N248D,T022A-S024R-S101D-S103A-V104I-G118R-P129E-G159D-S188D-A232V-Q245R-N248D,T022A-S024R-S101D-S103A-V104I-G159D-S188D-A232V-Q245R-N248D,T022A-N043R-S103A-V104I-G118R-P129E-G159D-S188D-A232V-Q245R-N248D,T022A-N043R-S103A-V104I-G118R-S128I-P129E-G159D-S188D-A232V-N248D,T022A-N043R-S101D-S103A-V104I-G118R-P129E-G159D-S188D-A232V-N248D-E271F,T022A-S024R-N043R-S101D-S103A-V104I-G159D-S188D-A232V-Q245R-

N248D,T022A-S103A-V104I-G159D-S188D-A232V-N248D,T022A-S024R-S103A-V104I-G118R-P129E-G159D-S188D-A232V-N248D-E271F,T022A-S024R-S103A-V104I-G159D-S188D-L217D-A232V-Q245R-N248D-E271F,T022A-N043R-N062E-S103A-V104I-G159D-S188D-A232V-Q245R-N248D-E271F,T022A-N043R-S103A-V104I-P129E-G159D-S188D-A232V-Q245R-N248D,T022A-S024R-S103A-V104I-G159D-S188D-L217D-A232V-N248D-E271F,T022A-S103A-V104I-G118R-G159D-S188D-L217D-A232V-Q245R-N248D,T022A-S024R-S101D-S103A-V104I-G118R-S128I-G159D-S188D-A232V-Q245R-N248D,T022A-S024R-N043R-S103A-V104I-G159D-S188D-L217D-A232V-N248D-E271F,T022A-N043R-S103A-V104I-G118R-G159D-S188D-L217D-A232V-N248D-E271F,T022A-N043R-S103A-V104I-G118R-G159D-S188D-A232V-N248D-E271F,T022A-S103A-V104I-S128I-P129E-G159D-S188D-A232V-N248D-E271F,T022A-S103A-V104I-G159D-S188D-L217D-A232V-Q245R-N248D-E271F,T022A-N043R-S103A-V104I-S128I-G159D-S188D-A232V-Q245R-N248D,T022A-S101D-S103A-V104I-G118R-G159D-S188D-L217D-A232V-Q245R-N248D-E271F,T022A-S103A-V104I-G118R-P129E-G159D-S188D-A232V-Q245R-N248D-E271F,T022A-S024R-N043R-S103A-V104I-G118R-G159D-S188D-L217D-A232V-N248D,T022A-N062E-S103A-V104I-G118R-G159D-S188D-A232V-Q245R-N248D,T022A-N043R-S101D-S103A-V104I-G118R-P129E-G159D-S188D-L217D-A232V,T022A-S024R-S103A-V104I-G159D-S188D-L217D-A232V-N248D,T022A-S024R-N043R-S103A-V104I-G118R-S128I-P129E-G159D-S188D-L217D-A232V-N248D-E271F,和T022A-S103A-V104I-G118R-G159D-S188D-L217D-A232V-Q245R-N248D-E271F,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0282] 本发明还提供分离的枯草杆菌蛋白酶变体,其中该枯草杆菌蛋白酶变体是具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:G020K-S024F-N062E-S188D-P239G,S024F-N062E-N116L-P239G,G020K-G023A-N062E-S188D,G020K-G023A-S024F-N062E-G118R-S188D-T213A,G020K-N043W-N062E-N116L-S188D-T213A-P239G,G023A-N062E-N116L-G118R,G023A-S024F-N062E-N116L-G118R,S024F-N116L,S024F-N062E-S188D-T213A,G023A-N062E-N116L-G118R-S188D-P239G,G020K-S024F-N062E,G020K-N043W-N062E-N116L-P239G,S024F-N062E-N116L-T213A-P239G,G020K-S024F-N043W-N062E-N116L-T213A,G020K-G023A-S024F-N062E-N116L-S188D-T213A,S024F-N062E-S188D-P239G,G023A-N043W-N062E-N116L-G118R-T213A,N062E-S188D-P239G,G020K-S024F-N062E-P239G,S024F-N116L-G118R-S188D-P239G,G020K-G023A-N062E-N116L-G118R-T213A,G020K-G023A-S024F-N062E-S188D-T213A-P239G,S024F-N043W-G118R-S188D,G023A-S024F-N116L-G118R-S188D-T213A,G020K-G023A-N043W-N116L-S188D-T213A-P239G,G023A-S024F-N116L-S188D-P239G,G023A-N043W-N116L-G118R-S188D,G023A-S024F-G118R-S188D-P239G,G023A-S024F-N043W-N062E-N116L-G118R,G020K-N043W-S188D-T213A,S024F-N062E-G118R-P239G,G023A-N043W-S188D-T213A,G020K-S024F-N043W-N062E-N116L-G118R-S188D-P239G,G020K-N116L-S188D-P239G,G020K-N043W-N062E-G118R,G020K-N043W-N116L-S188D-T213A,G020K-

S024F,G023A-N043W-N116L-P239G,G023A-S024F-N043W-N116L-G118R-S188D-P239G,G020K-G023A-N043W-T213A,和G023A-S024F-N062E-G118R-T213A-P239G,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0283] 本发明还提供分离的枯草杆菌蛋白酶变体,其中该枯草杆菌蛋白酶变体是具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:G020K-G023A-N043W-G118R-S128I-P129E-G159D-S188D,S024F-G118R-S128I-P129E-G159D,G020K-S024F-N062E-N116L-G118R-S188D,G020K-N062E-N116L-S188D,N062E-N116L-G118R-T213A,G020K-G023A-N062E-N116L-S188D,N062E-N116L-G118R-S188D,G020K-N062E-N116L-T213A,G020K-G023A-N062E-N116L,G020K-N062E-S188D-T213A,G020K-N062E,G020K-S024F-N062E-N116L-S188D,G020K-N043W-N062E-N116L-S188D,G020K-S024F-N062E-S188D-T213A,N062E-N116L-S188D-T213A,G020K-N062E-N116L,G020K-G023A-N062E-N116L-S188D-T213A,G023A-S024F-N062E-N116L-T213A,T022A-N043R-S103A-V104I-S128I-P129E-G159D-S188D-A232V-Q245R-N248D,T022A-N043R-S103A-V104I-G118R-S128I-P129E-G159D-S188D-A232V-N248D-E271F,S024F-N062E-N116L-S188D,T022A-S024R-S103A-V104I-G118R-S128I-P129E-G159D-S188D-A232V-N248D,G023A-N062E-N116L-S188D,N043W-N062E-N116L,G020K-G023A-N116L-S188D,N043W-N062E-N116L-S188D,S024F-N062E-N116L,N062E-N116L-S188D,和T022A-S024R-S103A-V104I-S128I-G159D-S188D-A232V-N248D,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0284] 本发明还提供分离的枯草杆菌蛋白酶变体,其中该枯草杆菌蛋白酶变体是具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:S087R-S101G-S103A-V104I-Q109R-S212P-A232V-Q245R-E271V,S101G-S103A-V104I-Q109R-A232V-Q245R,S101G-S103A-V104I-Q109R-S212P-A232V-Q245R-E271V,S101G-S103A-V104I-Q109R-S212P-A232V-Q245R,N076D-S87R-S103A-V104I-S212P-E271V,N076D-S103A-V104I-Q109R,N076D-S103A-V104I-S212P-E271V,N076D-S103A-V104I-Q109R-Q245R,和N076D-S103A-V104I-S212P-Q245L-E271V,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0285] 本发明还提供分离的枯草杆菌蛋白酶变体,其中该枯草杆菌蛋白酶变体是具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:S024R-P086W-G118R,S024R-S078R-P086W-N243F,S024R-T033S-P086S-S087N-Y209A,T033S-G118R,S024R-S078R-P086W-G118R-A270T,S024R-T033S-P086W-G118R,S078R-P086W-N243F,T033S-S078R-P086W-G118R-Y209A,T033S-S078R-Y209A,P086W-G118R-N243F,S024R-P086W,S078R-P086W-K235F,S024R-G118R,S024R-P086R,S101G-S103A-V104I-A232V,S024R-T033S-S078R-P086W-G118R,S024R-G118R-Y209A,Y209A-W241R,T033S-P086W-N243F,T033S-A172V-Y209A,G118R-Y209A-N243F,S024R-P086S-S141G,S024R-G118R-Y209A-N243F,S024R-T033S-P086S-S085N-K235F,S024R-T033S-A133V,S024R-

T033S-S078R-P086W,S024R-P086W-Y209A,S024R-W241R,T033S-G118R-N243F,S024R-K235F,S024R-S078R-P086W,S024R-G118R-Y209A-K235F,S024R-Y209A-W241R,T033S-G118R-W241R,P086W-G118R-Y209A,T033S-G118R-G159D-Y209A,T033S-S078R-P086W,S024R-P086W-N243F,G118R-Y209A,S024R-P086W-G118R-V203I,S078R-Y209A-K235F,S024R-T033S-W241R,S078R-G118R,T033S-G118R-Y209A-N243F,L021M-S024R-T033S,S024R-T033S-P086W,T033S-K235F,S078R-P086W-Y209A,S024R-T033S-Y209A-K235F,T033S-P086W-G118R,S024R-T033S-S078R-Y209A,T033S-P086W-G118R-Y209A-N243F,P086W-Y209A-N243F,P005S-S078R-G118R-W241R,S024R-A174T,T033S-Y209A-N243F,P086W-G118R-A133V,S024R-T033S-G118R,S024R-P086W-Y209A-K235F,P086W-Y209A,I008T-S024R,P086W-G118R,T033S-W241R,P005S-S024R-T033S-N243F,S024R-Y209A-S242P,S024R-T033S-S078R-G118R,S024R-T033S-A194T,S024R-N243F,S024R-Y209A,S024R-T033S-G118R-Y209A,T033S-P086W,S024R-T033S,S024R-T033S-S078R-N243F,P086W-N243F,T033S-G118D-A138V-Y209A,T033S-Y209A-K235F,S024R-P086R-G118R,T033S-P201S,S024R-P239Q,T033S-G118R-Y209A-,S078R-P086W,K235F-N243F,S024R-Y209A-K235F,G118R-A172V,H017Y-S024R-T033S-P086W,T033S-L148F,S024R-G118R-K235F,T033S-S078R,T033S-N243F,S024C-T033S,G118R-A194T,T033S-Y209A,G118R-Y209A-K235F,S024R-T033S-Y209A-N243F,S024R-T033S-K235F,S024R-T033S-G118R-K235F,S024R-S141G,S024R-T274I,S024R-T033S-Y209A,P086W-K235F,S024R-Y209A-N243F,V004E-T033S-S078R,P086W-Y209A-K235F,A015T-T033S,T033S-P086W-S156L-Y209A,S024R-G118R-N243F-R269H,Y209A-K235F,S024R-R247H,S024R-T033S-A228T,S078R-K235F,S024R-T033S-A174V-K235F,S024R-K235F-N243F,S024R-T033S-K235F-W241R,S024R-T033S-A151V,S024R-V104A,T033S-A048T,Q012H-V104A-G118R,G118R-K235F,T033S-T253A,T143A-Y209A,S024R-T033S-N243F,T033S-P239T,Y209A-N243F,S024R-T033S-P129H-N184D-T253M,S024R-A085V-P086W-G118R-K235F,S024R-A272P,和S024R-R269C,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0286] 本发明还提供分离的蛋白酶变体,其中所述蛋白酶变体包含一个或多个,优选地两个或多个,或优选地三个或多个以下的突变:X1R,X2S,X4R,X4S,X9A,X10S,X14K,X16S,X17R,X18R,X20R,X22A,X22R,X24R,X24W,X25R,X25V,X26F,X42I,X43R,X43A,X46R,X52F,X52E,X52N,X57R,X59A,X62E,X62Q,X68A,X68C,X71G,X72C,X74C.X75A,X75F,X75R,X76D,X78R,X82R,X86W,X89P,X89T,X89G,X89H,X89I,X89V,X89W,X91N,X94N,X100S,X101A,X101N,X101G,X101D,X103G,X103N,X104L,X104I,X106V,X106G,X108I,X111V,X112V,X115K,X115R,X117F,X118I,X121F,X128D,X128F,X128L,X128N,X129E,X144R,X148I,X158E,X159E,X160D,X166D,X185E,X185I,X186H,X188E,X188D,X197F,X203E,X209S,X209N,X209F,X209T,X209E,X209H,X209G,X210R,X212I,X212F,X214F,X215N,X215D,X215E,X217E,X217N,X224A,X230E,X231I,X236F,X238R,X238K,X239K,X239G,X239R,X239S,X241R,X242R,X242L,X243R,X244R,X248I,X248V,X249R,X250I,X252R,X253R,X262D,X263F,X265F,X267V,X267N,X269I,X269R,X271F,X271I,X271H,X271P,X271T,X271V,X271L和X272F,以及任选地包含一个或多个以下的突变:X103A,X159D,X236H,

X245R,X248D和X252K。

[0287] 本发明还提供分离的蛋白酶变体,其中所述蛋白酶变体包含一个或多个以下的突变组:

[0288] a)G020K-G023A-N043W-G118R-S128I-P129E-G159D-S188D,G020K-G023A-N062E-N116L,G020K-G023A-N062E-N116L-S188D,G020K-G023A-N062E-N116L-S188D-T213A,G020K-G100S-N116L-A158E-S166D-N243F,G020K-N043W-N062E-N116L-S188D,G020K-N062E,G020K-N062E-N116L,G020K-N062E-N116L-S188D,G020K-N062E-N116L-T213A,G020K-N062E-S188D-T213A,G020K-S024F-N062E-N116L-G118R-S188D,G020K-S024F-N062E-N116L-S188D,G020K-S024F-N062E-S188D-T213A,G023A-N062E-N116L-S188D,G023A-S024F-N062E-N116L-T213A,N043R-N076D-S101A-S103A-V104I-A158E-S188D-L217E-A232V-Q245R-N248D-H249R-E271F,N043R-S101A-S103A-V104I-A158E-S188D-L217E-A232V-Q245R-N248D-H249R,N043W-N062E-N116L,N043W-S101D-S212M-N243F,N062E-N116L-G118R-S188D,N062E-N116L-G118R-T213A,N062E-N116L-S188D-T213A,S024F-G118R-S128I-P129E-G159D,S024F-N062E-N116L-S188D,S024R-S101G-S103A-V104I-A158E-N183D-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-A158E-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-A158E-S188D-L217E-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-P129Q-A158E-N183D-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-P129Q-A158E-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-P129Q-A158E-S188D-L217E-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-P129Q-S130A-A158E-N183D-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-S128L-P129Q-A158E-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-S130A-A158E-N183D-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-S130A-A158E-S188D-A232V-Q245R-N248D-H249R,S101D-S103N-N116L-S144R-A215D,S101G-S103A-V104I-A158E-S188D-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-S130A-A158E-S188D-A232V-Q245R-N248D-H249R,T022A-N043R-S101G-S103A-V104I-G159D-S188D-L217E-A232V-Q245R-N248D-E271F,T022A-N043R-S103A-V104I-G118R-S128I-P129E-G159D-S188D-A232V-N248D-E271F,T022A-N043R-S103A-V104I-S128I-P129E-G159D-S188D-A232V-Q245R-N248D,T022A-S024R-S103A-V104I-G118R-S128I-P129E-G159D-S188D-A232V-N248D,T022A-S101G-S103A-V104I-G159D-L217E-A232V-Q245R-N248D-E271F,T022A-S101G-S103A-V104I-G159D-S188D-A232V-Q245R-N248D-E271F,T022L-T038F-A048R-N062E-G100S-R186K,T033S-N043W-N218D-P239G-N243F,V026F-A048R-S105T-T213A-N218D-T224A,V026F-L031F-S078N-G102A-S160D,V026F-V051W-V104L-S106E,V104L-S105T-T213A-L217E-S256N,A016S-N062E-A158E-H249R,A016S-N062E-A158E-R186H-E271F,A016S-N062E-A158E-R186H-H249R,A016S-N062E-V104L-A158E-R186H-E271F,A016S-S024R-S101G-S103A-V104I-A158E-S188D-A232V-Q245R-N248D-H249R,G020K-G023A-N062E-S188D,G020K-G023A-S024F-N062E-G118R-S188D-T213A,G020K-N043W-N062E-N116L-S188D-T213A-P239G,G020K-S024F-N062E-S188D-P239G,G023A-N062E-N116L-G118R,G023A-N062E-N116L-G118R-S188D-P239G,G023A-S024F-N062E-

N116L-G118R,H017R-T022A-N076D-S101G-S103A-V104I-G159D-S188D-A232V-Q245R-N248D-E271F,N043R-N076D-S101A-S103A-V104I-A158E-S188D-A232V-Q245R-N248D-H249R-E271F,N062E-A158E-G159E-H249R,N062E-A158E-H249R,N062E-A158E-R186H-E271F,N062E-A158E-R186H-H249R,N062E-A158E-R186H-H249R-E271F,N062E-A158E-S188D-H249R,N062E-A158E-S188D-H249R-E271F,N062E-G159E-H249R,N062E-G159E-H249R-E271F,N062E-G159E-R186H-H249R,N062E-G159E-S188D-H249R,N062E-R186H-S188D-H249R-E271F,N062E-S101A-A158E-H249R,N062E-S101A-A158E-R186H-E271F,N062E-S101A-A158E-R186H-H249R-E271F,N062E-S101A-G159E-H249R,N062E-S101A-R186H-H249R,N062E-S101A-S188D-H249R,N062E-S101A-S188D-H249R-E271F,N062E-S101A-V104L-A158E-R186H-E271F,N062E-S128N-A158E-G159E-E271F,N062E-V104L-A158E-S188D-H249R-E271F,N076D-S101G-S103A-V104I-A232V-M222Q-Q245R,S024F-N062E-N116L-P239G,S024F-N062E-S188D-T213A,S024F-N116L,S024R-N043R-N076D-S101A-S103A-V104I-A158E-S188D-L217E-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-A158E-G159E-A232V-N238R-Q245R-N248D,S024R-S101G-S103A-V104I-A158E-G159E-S188D-A232V-Q245R-N248D,S024R-S101G-S103A-V104I-A158E-S188D-A232V-N238R-Q245R-N248D,S024R-S101G-S103A-V104I-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-G159E-S188D-A232V-N238R-Q245R-N248D,S024R-S101G-S103A-V104I-G159E-S188D-A232V-Q245R-N248D,S024R-S101G-S103A-V104I-G159E-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-L148I-A158E-A232V-Q245R-N248D,S024R-S101G-S103A-V104I-L148I-A158E-S188D-A232V-Q245R-N248D,S024R-S101G-S103A-V104I-L148I-A232V-Q245R-N248D,S024R-S101G-S103A-V104I-P129E-A158E-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-P129E-A158E-G159E-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-P129E-A158E-S188D-A232V-Q245R-N248D,S024R-S101G-S103A-V104I-P129E-A158E-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-P129E-G159E-A232V-Q245R-N248D,S024R-S101G-S103A-V104I-P129E-G159E-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-P129E-L148I-A158E-A232V-Q245R-N248D,S024R-S101G-S103A-V104I-P129E-S188D-A232V-N238R-Q245R-N248D,S024R-S101G-S103A-V104I-P129E-S188D-A232V-Q245R-N248D,S024R-S101G-S103A-V104I-P129E-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-S128N-A158E-A232V-Q245R-N248D,S024R-S101G-S103A-V104I-S128N-P129E-A158E-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-S128N-P129E-A232V-Q245R-N248D,S101A-S103A-V104I-A158E-S188D-A232V-Q245R-N248D-H249R,S101A-S103A-V104I-A158E-S188D-A232V-Q245R-N248D-H249R-E271F-E271F,S101A-S103A-V104L-A158E-S188D-A232V-Q245R-N248D-H249R,S101A-S128N-A158E-R186H-E271F,S101A-S128N-A158E-Y209E-H249R,S101A-V104L-A158E-R186H-S188D-H249R,S101G-S103A-V104I-A158E-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-A158E-G159E-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-A158E-S188D-M222Q-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-A158E-S188D-M222S-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-A232V-M222Q-Q245R,S101G-

S103A-V104I-P129E-A158E-S188D-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-P129E-G159E-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-P129E-S188D-A232V-N238R-Q245R-N248D,S101G-S103A-V104I-P129E-S188D-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-S188D-A232V-Q245R-N248D-H249R,S101G-S103G-V104I-A158E-S188D-A232V-Q245R-N248D-H249R,S101G-S103S-V104I-A158E-S188D-A232V-Q245R-N248D-H249R,S101S-S103A-V104I-A158E-S188D-A232V-Q245R-N248D-H249R,S101S-S103G-V104I-A158E-S188D-A232V-Q245R-N248D-H249R,S101S-S103G-V104V-A158E-S188D-A232V-Q245R-N248D-H249R,S128N-A158E-G159E-E271F,S128N-A158E-H249R,S128N-A158E-R186H-E271F,S128N-A158E-R186H-H249R,S128N-A158E-R186H-S188D-E271F,S128N-A158E-S188D-E271F,S128N-A158E-S188D-H249R,S128N-A158E-S188D-Y209E-E271F,S128N-A158E-Y209E-,T022A-N043R-S103A-V104I-G118R-P129E-G159D-S188D-A232V-Q245R-N248D,T022A-N062E-A158E,T022A-S024R-S101D-S103A-V104I-G118R-G159D-S188D-A232V-N248D-E271F,T022A-S024R-S101D-S103A-V104I-G118R-P129E-G159D-S188D-A232V-Q245R-N248D,T022A-S024R-S101D-S103A-V104I-G159D-S188D-A232V-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-A158E-A232V-N238R-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-A158E-A232V-Q245R-N248D-H249R,T022A-S024R-S101G-S103A-V104I-A158E-G159E-S188D-A232V-N238R-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-A158E-G159E-S188D-A232V-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-A158E-G159E-S188D-A232V-Q245R-N248D-H249R,T022A-S024R-S101G-S103A-V104I-P129E-A158E-A232V-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-P129E-A158E-A232V-Q245R-N248D-H249R,T022A-S024R-S101G-S103A-V104I-P129E-A158E-G159E-A232V-Q245R-N248D-H249R,T022A-S024R-S101G-S103A-V104I-P129E-A158E-G159E-S188D-A232V-N238R-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-P129E-A158E-S188D-A232V-N238R-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-P129E-A158E-S188D-A232V-Q245R-N248D-H249R,T022A-S024R-S101G-S103A-V104I-P129E-A232V-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-P129E-A232V-Q245R-N248D-H249R,T022A-S024R-S101G-S103A-V104I-P129E-G159E-S188D-A232V-Q245R-N248D-H249R,T022A-S024R-S101G-S103A-V104I-P129E-S188D-A232V-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-S128N-A158E-S188D-A232V-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-S128N-P129E-A158E-A232V-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-S128N-P129E-S188D-A232V-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-S128N-S188D-A232V-Q245R-N248D,T022A-S024R-S103A-V104I-G118R-G159D-S188D-L217D-A232V-N248D,T022A-S024R-S103A-V104I-P129E-G159D-S188D-A232V-N248D-E271F,T022A-S101G-S103A-V104I-A158E-G159E-S188D-A232V-Q245R-N248D-H249R,T022A-S101G-S103A-V104I-A158E-S188D-A232V-Q245R-N248D,T022A-S101G-S103A-V104I-P129E-A158E-A232V-N238R-Q245R-N248D,T022A-S101G-S103A-V104I-P129E-A158E-G159E-A232V-N238R-Q245R-N248D,T022A-S101G-S103A-V104I-P129E-A158E-S188D-A232V-Q245R-N248D-H249R,T022A-S101G-S103A-V104I-P129E-G159E-A232V-N238R-Q245R-N248D,T022A-S101G-S103A-V104I-P129E-

S188D-A232V-N238R-Q245R-N248D,T022A-S101G-S103A-V104I-S128N-P129E-A232V-N238R-Q245R-N248D,T022A-S101G-S103A-V104I-S128N-P129E-S188D-A232V-N238R-Q245R-N248D,T022A-S128N-A158E-H249R,V104L-S128N-A158E-H249R,V104L-S128N-A158E-R186H-E271F,V104L-S128N-A158E-R186H-H249R,和/或V104L-S128N-A158E-S188D-H249R;

[0289] b)A016S-N062E-A158E-H249R-E271F,A016S-N062E-S128N-R186H-E271F,A016S-N062E-V104L-R186H-S188D-E271F,A016S-S101A-S128N-R186H,A016S-S128N-A158E-R186H,A016S-V104L-A158E-R186H-E271F,A016S-V104L-S188D-H249R,A158E-R186H-H249R,A158E-R186H-S188D-H249R-E271F,G020K-G023A-N116L-S188D,G020K-G023A-S024F-N062E-N116L-S188D-T213A,G020K-N043W-N062E-N116L-P239G,G020K-S024F-N043W-N062E-N116L-T213A,G020K-S024F-N062E,G023A-N043W-N062E-N116L-G118R-T213A,G023A-T038F-S078N-G100S-S212M-A215D,G100S-N116L-A158E-T213A,G102A-S103N-S105T-A194E,H017R-T022A-N076D-S101G-S103A-V104I-G159D-A232V-Q245R-N248D-E271F,N043R-N076D-S101A-S103A-V104I-A158E-S166D-S188D-A232V-Q245R-N248D-H249R-E271F,N043R-S101A-S103A-V104I-A158E-S166D-S188D-A232V-Q245R-N248D-H249R,N043W-N062E-N116L-S188D,N062E-A158E-H249R-E271F,N062E-A158E-R186H-S188D-H249R,N062E-L148I-G159E,N062E-N116L-S188D,N062E-R186H-H249R,N062E-S078N-G102A-N116L-S144R-L250I,N062E-S101A-A158E-R186H-H249R,N062E-S101A-A158E-S188D-H249R,N062E-S101A-R186H,N062E-S101A-R186H-E271F,N062E-S101A-R186H-H249R-E271F,N062E-S101A-R186H-S188D-E271F,N062E-S101A-R186H-S188D-H249R,N062E-S101A-V104L-R186H-S188D-E271F,N062E-S128N-A158E,N062E-S128N-G159E-H249R,N062E-S188D-P239G,N062E-V104L-G159E-H249R,N076D-S101A-S103A-V104I-A158E-S166D-S188D-A232V-Q245R-N248D-H249R-E271F,N076D-S101A-S103A-V104I-A158E-S188D-A232V-Q245R-N248D-H249R,N076D-S101A-S103A-V104I-A158E-S188D-A232V-Q245R-N248D-H249R-E271F,N076D-S101G-S103A-V104I-A114V-A158E-S188D-A232V-Q245R-N248D-H249R-E271F,N076D-S101G-S103A-V104I-A232V-M222S-Q245R,S024F-A048R-G118R-S166D-L217E,S024F-N062E-N116L,S024F-N062E-N116L-T213A-P239G,S024F-N062E-S188D-P239G,S024F-S101D-G118R-A215D-L250I-A272F,S024R-K027R-S101G-S103A-V104I-S128L-P129Q-S130A-A158E-S188D-A232V-Q245R-N248D-H249R,S024R-N076D-S101A-S103A-V104I-A158E-S166D-S188D-A232V-Q245R-N248D-H249R-E271F,S024R-S101G-S103A-V104I-A158E-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-P129E-A158E-G159E-A232V-N238R-Q245R-N248D,S024R-S101G-S103A-V104I-P129E-A158E-G159E-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-P129E-G159E-A232V-N238R-Q245R-N248D,S024R-S101G-S103A-V104I-P129E-G159E-S188D-A232V-N238R-Q245R-N248D,S024R-S101G-S103A-V104I-P129E-L148I-A158E-S188D-A232V-Q245R-N248D,S024R-S101G-S103A-V104I-P129E-L148I-S188D-A232V-Q245R-N248D,S024R-S101G-S103A-V104I-P129Q-S130A-A158E-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-S128L-A158E-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-S128L-P129Q-S130A-A158E-

S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-S128N-G159E-S188D-A232V-Q245R-N248D,S078N-V104L-G118R-S128D,S101A-A158E-R186H-H249R,S101A-A158E-R186H-S188D-H249R,S101A-S103A-V104I-A158E-S166D-S188D-A232V-Q245R-N248D-H249R-E271F,S101A-S103A-V104I-A158E-S188D-A232V-Q245R-N248D-H249R-E271F,S101A-S103A-V104I-A158E-S188D-L217E-A232V-Q245R-N248D-H249R,S101A-S103A-V104I-A158E-S188D-L217E-A232V-Q245R-N248D-H249R-E271F,S101A-S103G-A158E-R186H-H249R,S101A-S103S-V104I-A158E-S188D-A232V-Q245R-N248D-H249R,S101A-S103S-V104I-G159E-A232V-Q245R-N248D-H249R,S101A-S128N-A158E-H249R,S101A-S128N-A158E-S188D-Y209E-E271F,S101A-S128N-A158E-Y209E,S101A-S128N-P129E-R186H-H249R,S101A-V104L-A158E-R186H-H249R,S101A-V104L-A158E-R186H-S188D-E271F,S101A-V104L-S128N-A158E-R186H-E271F,S101G-S103A-V104I-A158E-A232V-N238R-Q245R-N248D,S101G-S103A-V104I-A158E-G159E-S188D-A232V-N238R-Q245R-N248D,S101G-S103A-V104I-A158E-N183D-S188D-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-A158E-S166D-S188D-A232V-Q245R-N248D-H249R-E271F,S101G-S103A-V104I-A158E-S188D-A232V-Q245R-N248D,S101G-S103A-V104I-A232V-M222S-Q245R,S101G-S103A-V104I-P129E-A158E-G159E-A232V-N238R-Q245R-N248D,S101G-S103A-V104I-P129E-A158E-G159E-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-P129E-A158E-S188D-A232V-N238R-Q245R-N248D,S101G-S103A-V104I-P129E-G159E-A232V-N238R-Q245R-N248D,S101G-S103A-V104I-P129E-S188D-A232V-Q245R-N248D,S101G-S103A-V104I-P129Q-A158E-S188D-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-P129Q-S130A-A158E-S188D-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-S128L-P129Q-A158E-S188D-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-S128L-S130A-A158E-S188D-L217E-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-S128N-P129E-A232V-N238R-Q245R-N248D,S101G-S103A-V104I-S128N-P129E-A232V-Q245R-N248D,S101G-S103A-V104I-S130A-A158E-N183D-S188D-L217E-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-S188D-A232V-N238R-Q245R-N248D,S101G-S103A-V104L-A158E-S188D-A232V-Q245R-N248D-H249R,S101S-S103A-V104I-G159E-A232V-Q245R-N248D-H249R,S101S-S103S-V104I-A158E-S188D-A232V-Q245R-N248D-H249R,S101S-S103S-V104V-A158E-S188D-A232V-Q245R-N248D-H249R,T022A-N043R-N062E-S103A-V104I-G159D-S188D-A232V-Q245R-N248D-E271F,T022A-N043R-N076D-S101G-S103A-V104I-G159D-S188D-A232V-Q245R-N248D-E271F,T022A-N043R-S101D-S103A-V104I-G118R-P129E-G159D-S188D-A232V-N248D-E271F,T022A-N043R-S101G-S103A-V104I-G159D-A232V-Q245R-N248D-E271F,T022A-N043R-S103A-V104I-G118R-G159D-S188D-A232V-N248D-E271F,T022A-N043R-S103A-V104I-G118R-G159D-S188D-L217D-A232V-N248D-E271F,T022A-N043R-S103A-V104I-G118R-S128I-P129E-G159D-S188D-A232V-N248D,T022A-N043R-S103A-V104I-P129E-G159D-S188D-A232V-Q245R-N248D,T022A-N076D-S101G-S103A-V104I-G159D-A232V-Q245R-N248D-E271F,T022A-N076D-S101G-S103A-V104I-G159D-S188D-A232V-Q245R-N248D-E271F,T022A-S024R-N043R-S101D-S103A-V104I-G159D-S188D-A232V-Q245R-N248D,T022A-S024R-N043R-S103A-V104I-

G159D-S188D-L217D-A232V-N248D-E271F,T022A-S024R-S101D-S103A-V104I-G118R-S128I-G159D-S188D-A232V-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-L148I-A158E-A232V-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-P129E-A158E-G159E-A232V-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-P129E-A158E-G159E-S188D-A232V-Q245R-N248D-H249R,T022A-S024R-S101G-S103A-V104I-P129E-L148I-A232V-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-S188D-A232V-Q245R-N248D-H249R,T022A-S024R-S103A-V104I-G118R-P129E-G159D-S188D-A232V-N248D-E271F,T022A-S024R-S103A-V104I-G159D-S188D-L217D-A232V-N248D-E271F,T022A-S024R-S103A-V104I-G159D-S188D-L217D-A232V-Q245R-N248D-E271F,T022A-S101A-A158E-R186H-H249R,T022A-S101G-S103A-V104I-A158E-G159E-A232V-N238R-Q245R-N248D,T022A-S101G-S103A-V104I-A158E-G159E-A232V-Q245R-N248D-H249R,T022A-S101G-S103A-V104I-G159D-A232V-Q245R-N248D-E271F,T022A-S101G-S103A-V104I-G159D-S188D-A232V-Q245R-N248D-H249R-E271F,T022A-S101G-S103A-V104I-G159E-S188D-A232V-N238R-Q245R-N248D,T022A-S101G-S103A-V104I-G159E-S188D-A232V-Q245R-N248D-H249R,T022A-S101G-S103A-V104I-P129E-A158E-A232V-Q245R-N248D-H249R,T022A-S101G-S103A-V104I-P129E-A158E-G159E-A232V-Q245R-N248D-H249R,T022A-S101G-S103A-V104I-P129E-A232V-N238R-Q245R-N248D,T022A-S101G-S103A-V104I-P129E-G159E-A232V-Q245R-N248D-H249R,T022A-S101G-S103A-V104I-P129E-G159E-S188D-A232V-Q245R-N248D-H249R,T022A-S103A-V104I-G118R-G159D-S188D-L217D-A232V-Q245R-N248D,T022A-S103A-V104I-G159D-S188D-A232V-N248D,T022L-L031F-G102A-S128D-T224A-N243F,T022L-T038F-V121F-S160D-A272F,V026F-S078N-G159C-R186K-N243F,V104L-A158E-H249R,V104L-A158E-R186H-H249R,V104L-A158E-R186H-H249R-E271F,V104L-A158E-R186H-S188D-H249R,V104L-A158E-R186H-S188D-H249R-E271F,V104L-A158E-S188D-H249R-E271F,V104L-S128N-A158E-R186H-S188D-E271F,V104L-S128N-G159E-E271F,V104L-S128N-R186H-S188D-H249R,和/或V121F-N185E-T224A-P239G;

[0290] c)A016S-S128N-R186H-E271F,N076D-S101G-S103A-V104I-A158E-S188D-M222S-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-S128L-P129Q-A158E-N183D-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-S128L-P129Q-A158E-S188D-A232V-Q245R-N248D-H249R-E271G,S024R-S101G-S103A-V104I-S128L-P129Q-S130A-A158E-N183D-S188D-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-P129Q-A158E-N183D-S188D-A232V-Q245R-N248D-H249R,T022A-N076D-S101G-S103A-V104I-G159D-A232V-Q245R-N248D-H249R-E271F,T022A-S101G-G102A-S103A-V104I-G159D-S188D-A232V-Q245R-N248D-E271F,A016S-A158E-H249R,A016S-A158E-H249R-E271F,A016S-A158E-R186H-H249R,A016S-L111V-S188D-,A016S-T022A-A158E-R186H-E271F,A048R-S078N-N116L-N185E-L217E-P239G,A048R-S128D-N185E-P239G,A158E-R186H-H249R-E271F,E089P-S101A-P129E-R186H,G020K-G023A-N043W-N116L-S188D-T213A-P239G,G020K-G023A-N062E-N116L-G118R-T213A,G020K-G023A-S024F-N062E-S188D-T213A-P239G,G020K-K027R-P129E-S166D-P239G,G020K-S024F-N062E-P239G,G020K-S024F-T033S-P129E-A194E,G023A-G100S-A194E-S212M,G023A-N043W-N116L-G118R-

S188D,G023A-S024F-G118R-S188D-P239G,G023A-S024F-K027R-N062E,G023A-S024F-N043W-N062E-N116L-G118R,G023A-S024F-N116L-G118R-S188D-T213A,G023A-S024F-N116L-S188D-P239G,K027R-G100S-G118R-S160D-S188D-N243F,K027R-S101D-S103N-S105T-A272F,N043R-N076D-S101A-S103A-V104I-A158E-S166D-S188D-A232V-Q245R-N248D-H249R,N062E-S078N-N116L-T224A,N062E-V104L-A158E-R186H-S188D-H249R,N076D-S101A-S103A-V104I-A158E-S188D-L217E-A232V-Q245R-N248D-H249R-E271F,N076D-S101G-S103A-V104I-A158E-S166D-S188D-A232V-Q245R-N248D-H249R-E271F,S024F-G102A-R186K-T213A-L217E-N243F,S024F-N043W-G118R-S188D,S024F-N043W-V104L-V121F-P129E,S024F-N116L-G118R-S188D-P239G,S024F-S103N-V104L-G118R-S188D,S024R-N043R-S101A-S103A-V104I-A158E-S188D-A232V-Q245R-N248D-H249R,S024R-N043R-S101A-S103A-V104I-A158E-S188D-L217E-A232V-Q245R-N248D-H249R,S024R-N076D-S101G-S103A-V104I-A158E-S188D-A232V-Q245R-N248D-H249R-E271F,S024R-S101G-S103A-V104I-A158E-G159E-A232V-Q245R-N248D,S024R-S101G-S103A-V104I-S128N-A158E-G159E-S188D-A232V-Q245R-N248D,S024R-S101G-S103A-V104I-S128N-P129E-S188D-A232V-Q245R-N248D,S101A-L111V-P129E,S101A-S103A-V104L-G159E-A232V-Q245R-N248D-H249R,S101A-S103S-V104L-G159E-A232V-Q245R-N248D-H249R,S101A-V104L-S128N-A158E-R186H,S101G-S103A-V104I-P129E-L148I-S188D-A232V-Q245R-N248D,S101G-S103A-V104I-S128N-P129E-A158E-A232V-N238R-Q245R-N248D,S101G-S103A-V104I-S128N-P129E-S188D-A232V-Q245R-N248D-H249R,S101G-S103S-V104L-G159E-A232V-Q245R-N248D-H249R,S101S-S103A-V104L-G159E-A232V-Q245R-N248D-H249R,S128N-P129E-R186H,T022A-A158E-R186H-H249R-E271F,T022A-S024K-S101G-S103A-V104I-S128N-A158E-G159E-A232V-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-S128N-P129E-A158E-S188D-A232V-Q245R-N248D-H249R,T022A-S024R-S103A-V104I-S128I-G159D-S188D-A232V-N248D,T022A-S101G-S103A-V104I-L148I-S188D-A232V-Q245R-N248D,T022A-S101G-S103A-V104I-S128N-G159E-A232V-Q245R-N248D,T022A-S101G-S103A-V104I-S128N-P129E-A158E-A232V-N238R-Q245R-N248D,T022A-S128N-A158E-R186H,T022A-S128N-R186H-S188D-,T022A-V104L-A158E-H249R,T022A-V104L-R186H-S188D-H249R,T022L-G023A-K027R-S101D-V104L-S216F,T022L-S078N-N116L-P129E-S256N,T022L-S078N-S128D-T213A,T033S-G118R-P129E-A194E-P239G,T033S-S105T-S188D-S216F,V026F-V104L-S256N-A272F,T022A-N043R-S103A-V104I-S128I-G159D-S188D-A232V-Q245R-N248D,T022A-S024R-N043R-S103A-V104I-G118R-G159D-S188D-L217D-A232V-N248D,T022A-S101D-S103A-V104I-G118R-G159D-S188D-L217D-A232V-Q245R-N248D-E271F,T022A-S103A-V104I-G118R-P129E-G159D-S188D-A232V-Q245R-N248D-E271F,T022A-S103A-V104I-G159D-S188D-L217D-A232V-Q245R-N248D-E271F,和/或T022A-S103A-V104I-S128I-P129E-G159D-S188D-A232V-N248D-E271F;

[0291] d)G118R-Y209A,G118R-Y209A-N243F,L021M-S024R-T033S,P005S-S078R-G118R-W241R,P086W-G118R-A133V,P086W-G118R-N243F,P086W-G118R-Y209A,P086W-Y209A-N243F,S024R-A174T,S024R-G118R,S024R-G118R-Y209A,S024R-G118R-Y209A-K235F,

S024R-G118R-Y209A-N243F,S024R-K235F,S024R-P086R,S024R-P086S-S141G,S024R-P086W,S024R-P086W-G118R,S024R-P086W-G118R-V203I,S024R-P086W-N243F,S024R-P086W-Y209A,S024R-S078R-P086W,S024R-S078R-P086W-G118R-A270T,S024R-S078R-P086W-N243F,S024R-T033S-A133V,S024R-T033S-G118R,S024R-T033S-P086S-S085N-K235F,S024R-T033S-P086S-S087N-Y209A,S024R-T033S-P086W,S024R-T033S-P086W-G118R,S024R-T033S-S078R-P086W,S024R-T033S-S078R-P086W-G118R,S024R-T033S-S078R-Y209A,S024R-T033S-W241R,S024R-T033S-Y209A-K235F,S024R-Y209A-W241R,S078R-G118R,S078R-P086W-K235F,S078R-P086W-N243F,S078R-P086W-Y209A,S078R-Y209A-K235F,T033S-A172V-Y209A,T033S-G118R,T033S-G118R-G159D-Y209A,T033S-G118R-N243F,T033S-G118R-W241R,T033S-G118R-Y209A-N243F,T033S-K235F,T033S-P086W-G118R,T033S-P086W-G118R-Y209A-N243F,T033S-P086W-N243F,T033S-S078R-P086W,T033S-S078R-P086W-G118R-Y209A,T033S-S078R-Y209A,T033S-Y209A-N243F,Y209A-W241R,A001R-S009A-N043R,A001R-S101G-S103A-V104I-A232V-Q245R,A001T-N018R-S024R-N076D-N116A-T213A-H249R,A194F-G211Q-Q236N,E089I-N116A-N117F-T224A-H249R,G020R-G025R-N116A-Y167W,G020R-H249R-N269R,G020R-N043D-N076D-A230E-H249R,G020R-N043D-S078R-S101G-S103A-V104I-A232V-Q245R,G020R-N043D-S101G-S103A-V104I-A232V-Q245R,G020R-N043D-S101G-S103A-V104I-A232V-Q245R-N269R,G020R-N043R-A230E,G020R-N043R-A230E-S242R,G020R-N043R-E271L,G020R-N043R-H249R,G020R-N043R-H249R-E271L,G020R-N043R-N269R,G020R-N043R-R045T-A230E,G020R-N043R-R045T-S101A-N269R,G020R-N043R-R045T-S242R,G020R-N043R-S101A-N116A-T213A-A215F,G020R-N043R-S101A-N269R,G020R-N043R-S101G-S103A-V104I-A232V-Q245R,G020R-N043R-S212F,G020R-N043R-S212F-W241R,G020R-N043R-S242R,G020R-N043R-S242R-E271L,G020R-N043R-S242R-H249R,G020R-N043R-V244R,G020R-N043R-W241R,G020R-N062Q-E089I-R186K-S212M,G020R-N076D,G020R-N076D-S101G-S103A-V104I-A232V-Q245R,G020R-N076D-S101G-S103A-V104I-A232V-Q245R-N269R,G020R-N116A-N269R,G020R-P052N-N062Q-Y091F-Y192W,G020R-Q059A-S144R-Y192W-T224A,G020R-S024R-K27E-N043R-N076D-A230E,G020R-S024R-N043D-H249R,G020R-S024R-N043D-N076D-S078R-S101G-S103A-V104I-A232V-Q245R,G020R-S024R-N043D-S242R,G020R-S024R-N043R-R045T,G020R-S024R-N043R-R045T-H249R,G020R-S024R-N043R-R045T-N116A,G020R-S024R-N043R-R045T-N116A-T213A,G020R-S024R-N043R-R045T-S101A-N269R,G020R-S024R-N043R-R045T-S101A-T213A,G020R-S024R-N043R-S242R,G020R-S024R-N076D-H249R,G020R-S024R-N116A,G020R-S024R-N116A-A215F,G020R-S024R-N116A-T213A,G020R-S024R-N116A-T213A-A215F,G020R-S024R-P052N-Q059A-S216F,G020R-S024R-R045T-A230E-S242R,G020R-S024R-R045T-N116A-N269R,G020R-S024R-R045T-N269R,G020R-S024R-S101A-A215F,G020R-S024R-S101A-N116A,G020R-S024R-S101G-S103A-V104I-L217E-A232V-Q245R-H249R,G020R-S024R-S242R-H249R,G020R-S024R-T213A,G020R-S024R-T213A-A215F,G020R-S078R-S101A-S103A-V104I-N116A-N183D-T213A-A232V-Q245R,G020R-S078R-S101G-A232V-Q245R,G020R-S078R-S101G-S103A-V104I-A215F-A232V-Q245R,G020R-S078R-S101G-S103A-V104I-

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[0293] f)A015T-T033S,A016T-N043R-R045T-N076D-S101G-S103A-V104I-A232V-Q245R-N269R,A230E-H249R,A232V-H249R,E089I-S105T-N116A-A215F-S216F,E089I-Y091F-N185I-G211Q-A270C,G020R-A090S-S101G-S103A-V104I-N116A-N183D-T213A-A215F-A232V-Q245R,G020R-N043D-S078R-S101G-S103A-V104I-A232V-Q245R-H249R,G020R-N043R-N076D,G020R-N043R-R045T-S078R-S101G-S103A-V104I-A232V-Q245R,G020R-P052N-S101A-I198L-L233C,G020R-R045T-N076D-S078R-S101G-S103A-V104I-A232V-Q245R-N269R,G020R-S024R-N043D-N076D-H249R,G020R-S024R-N043D-N076D-S242R-H249R,G020R-S024R-N043D-R045T-A230E-S242R,G020R-S024R-N043D-S078R-S101G-S103A-V104I-A232V-Q245R,G020R-S024R-N043D-S078R-S101G-S103A-V104I-A232V-Q245R-H249R,G020R-S024R-N043R-S101G-S103A-V104I-A232V-Q245R,G020R-S024R-N076D-S078R-S101G-S103A-V104I-A232V-Q245R-H249R,G020R-S024R-R045T-N076D-S101G-S103A-V104I-A232V-Q245R,G020R-S024R-R045T-N076D-S242R-H249R,G020R-

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N076D-S103A-H249R,N018R-S024R-N076D-S103A-V104I-L135I-A232V,N018R-S024R-N076D-T213A-A215F-H249R-T260K,N018R-S024R-N076D-V150L-S242R-H249R,N018R-S024R-R045T-A230E-H249R,N018R-S101G-S103A-V104I-A232V-Q245R-H249R,N018R-T022R-S024R-N076D-S101A-N116A-N183D-G211Q-H249R,N018R-T022W-S024R-N076D-G211Q-A215F-H249R,N018R-T022W-S024R-N076D-I198L-G211Q-A215F-H249R,N018R-T022W-S024R-N076D-I198L-G211Q-T213A-H249R,N018R-T022W-S024R-N076D-I198L-H249R,N018R-T022W-S024R-N076D-I198L-T213A-H249R,N018R-T022W-S024R-N076D-N116A-A215F-H249R,N018R-T022W-S024R-N076D-N116A-G211Q-T213A-A215F-H249R,N018R-T022W-S024R-N076D-N116A-H249R,N018R-T022W-S024R-N076D-N116A-I198L-A215F-H249R,N018R-T022W-S024R-N076D-N116A-I198L-G211Q-A215F-H249R,N018R-T022W-S024R-N076D-N116A-I198L-G211Q-T213A-A215F-H249R,N018R-T022W-S024R-N076D-N116A-I198L-H249R,N018R-T022W-S024R-N076D-N116A-I198L-T213A-A215F-H249R,N018R-T022W-S024R-N076D-N116A-N183D-A215F-H249R,N018R-T022W-S024R-N076D-N116A-N183D-G211Q-A215F-H249R,N018R-T022W-S024R-N076D-N116A-N183D-G211Q-H249R,N018R-T022W-S024R-N076D-N116A-N183D-G211Q-T213A-H249R,N018R-T022W-S024R-N076D-N116A-N183D-G211Q-T213A-Q245R,N018R-T022W-S024R-N076D-N116A-N183D-I198L-A215F-H249R,N018R-T022W-S024R-N076D-N116A-N183D-I198L-G211Q-A215F-H249R,N018R-T022W-S024R-N076D-N116A-N183D-I198L-G211Q-H249R,N018R-T022W-S024R-N076D-N116A-N183D-I198L-G211Q-T213A-A209V-H249R,N018R-T022W-S024R-N076D-N116A-N183D-I198L-G211Q-T213A-H249R,N018R-T022W-S024R-N076D-N116A-N183D-I198L-H249R,N018R-T022W-S024R-N076D-N116A-N183D-I198L-Y209H-G211Q-H249R,N018R-T022W-S024R-N076D-N116A-N183D-T213A-A215F-H249R,N018R-T022W-S024R-N076D-N116A-N183D-T213A-H249R,N018R-T022W-S024R-N076D-N183D-G211Q-H249R,N018R-T022W-S024R-N076D-N183D-G211Q-T213A-A215F-H249R,N018R-T022W-S024R-N076D-N183D-G211Q-T213A-H249R,N018R-T022W-S024R-N076D-N183D-H249R,N018R-T022W-S024R-N076D-N183D-I198L-A215F-H249R,N018R-T022W-S024R-N076D-N183D-I198L-G211Q-A215F-H249R,N018R-T022W-S024R-N076D-N183D-I198L-G211Q-T213A-H249R,N018R-T022W-S024R-N076D-N183D-I198L-H249R,N018R-T022W-S024R-N076D-N183D-T213A-H249R,N018R-T022W-S024R-N076D-S101A-G211Q-A215F-H249R,N018R-T022W-S024R-N076D-S101A-I198L-G211Q-A215F-H249R,N018R-T022W-S024R-N076D-S101A-I198L-G211Q-H249R,N018R-T022W-S024R-N076D-S101A-I198L-G211Q-T213A-H249R,N018R-T022W-S024R-N076D-S101A-N116A-G211Q-T213A-A215F-H249R,N018R-T022W-S024R-N076D-S101A-N116A-H249R,N018R-T022W-S024R-N076D-S101A-N116A-N183D-A215F-H249R,N018R-T022W-S024R-N076D-S101A-N116A-N183D-G211Q-A215F-H249R,N018R-T022W-S024R-N076D-S101A-N116A-N183D-G211Q-H249R,N018R-T022W-S024R-N076D-S101A-N116A-N183D-G211Q-T213A-A215F-H249R,N018R-T022W-S024R-N076D-S101A-N116A-N183D-G211Q-T213A-H249R,N018R-T022W-S024R-N076D-S101A-N116A-N183D-H249R,N018R-T022W-S024R-N076D-S101A-N116A-N183D-I198L-A215F-H249R,N018R-T022W-S024R-N076D-S101A-N116A-N183D-I198L-

H249R,N018R-T022W-S024R-N076D-S101A-N116A-N183D-I198L-T213A-H249R,N018R-T022W-S024R-N076D-S101A-N116A-N183D-T213A-A215F-H249R,N018R-T022W-S024R-N076D-S101A-N116A-N183D-T213A-H249R,N018R-T022W-S024R-N076D-S101A-N116A-T213A-A215F-H249R,N018R-T022W-S024R-N076D-S101A-N116A-T213A-A215F-H249R-L267I,N018R-T022W-S024R-N076D-S101A-N116T-I198L-A215F-H249R,N018R-T022W-S024R-N076D-S101A-N183D-G211Q-A215F-H249R,N018R-T022W-S024R-N076D-S101A-N183D-G211Q-H249R,N018R-T022W-S024R-N076D-S101A-N183D-G211Q-T213A-A215F-H249R,N018R-T022W-S024R-N076D-S101A-N183D-G211Q-T213A-H249R,N018R-T022W-S024R-N076D-S101A-N183D-I198L-A215F-H249R,N018R-T022W-S024R-N076D-S101A-N183D-I198L-T213A-H249R,N018R-T022W-S024R-N076D-S101A-N183D-I198L-Y209H-H249R,N018R-T022W-S024R-N076D-S101A-N183D-T213A-A215F-H249R,N018R-T22W-S024R-N076D-G211Q-T213A-H249R,N018R-T22W-S024R-N076D-N116A-I198L-T213A-H249R,N018R-T22W-S024R-N076D-S101A-I198L-H249R,N018R-V104I-A232V,N043A-Q059A-S101A-S216F-T224A,N043D-N076D-S101G-S103A-V104I-A232V-Q245R-H249R,N043D-R045T-N076D-S078R-S101G-S103A-V104I-A232V-Q245R,N043D-R045T-S078R-S101G-S103A-V104I-A232V-Q245R,N043D-R045T-S078R-S101G-S103A-V104I-A232V-Q245R-N269R,N043D-S242R-H249R,N043R-A230E-H249R,N043R-N076D-S078R-S101G-S103A-V104I-A232V-Q245R-H249R,N043R-N076D-S078R-S101G-S103A-V104I-L217E-A232V-Q245R,N043R-N076D-S101G-S103T-V104I-A232V-Q245R-H249R-N269R,N043R-R045T-H249R,N043R-R045T-N076D-S101G-S103A-V104I-A232V-Q245R,N043R-R045T-S078R-S101G-S103A-V104I-A232V-Q245R-N269R,N043R-R045T-S078R-S101G-S103A-V104I-L217E-A232V-Q245R,N043R-R045T-S101G-S103A-V104I-A232V-Q245R-H249R,N043R-S078R-S101G-S103A-V104I-L217E-A232V-Q245R,N043R-S101G-S103A-V104I-Q245R-H249R,N043R-S101G-S103A-V104I-V150L-A232V-Q245R-N269R,N076D-A232V-Q245R,N076D-Q245R,N076D-S101G-A232V-Q245R,N076D-S101G-S103A-Q245R,N076D-S101G-S103A-V104I-A232V-H249R,N076D-S101G-S103A-V104I-H249R,N076D-S101G-S103A-V104I-V150L-A232V-Q245R,N076D-S101G-V104I-H249R,N076D-S101G-V104I-Q245R,N076D-S103A-V104I-A232V-Q245R,N076D-S103A-V104I-Q245R,N076D-V104I-A232V-Q245R,N076D-V104I-Q245R,P005S-N018R-T022W-S024R-N076D-S101A-T213A-A215F-H249R,P086W-K235F,P086W-Y209A-K235F,Q012H-V104A-G118R,R045T-N076D-S078R-S101G-S103A-V104I-A232V-Q245R-H249R,R045T-S101G-S103A-V104I-A232V-Q245R,S024R-G118R-N243F-R269H,S024R-K235F-N243F,S024R-N043D-N076D-S101G-S103A-V104I-A232V-Q245R-N269R,S024R-N043R-N076D-A230E-H249R,S024R-N076D-A232V-H249R,S024R-N076D-S078R-S101G-S103A-V104I-A232V-Q245R-H249R,S024R-N076D-S101G,S024R-N076D-S101G-A232V-H249R,S024R-N076D-S101G-S103A-A232V,S024R-N076D-S101G-S103A-V104I-M175L-H249R,S024R-N076D-S101G-S103A-V104I-Q245R,S024R-N076D-S101G-V104I-A232V-H249R,S024R-N076D-S103A-H249R,S024R-N076D-S103A-Q245R,S024R-N076D-S103A-V104I-H249R,S024R-R045T-N076D-S101G-S103A-V104I-A232V-Q245R-H249R,S024R-R045T-S242R-A273V,S024R-R247H,S024R-S101G-S103A,S024R-

S101G-S103A-A232V,S024R-S101G-S103A-V104I,S024R-S103A-Q245R-H249R,S024R-S103A-V104I,S024R-S106G-N116A-S212M-T224A,S024R-T033S-A151V,S024R-T033S-A174V-K235F,S024R-T033S-A228T,S024R-T033S-K235F-W241R,S024R-T033S-N243F,S024R-V104A,S024R-V104I-A232V,S024R-Y209A-N243F,S078R-K235F,S087D-S101G-S103A-V104I-A232V-S242R-Q245R,S099F-S105T-S106G-A194F-S212M,S101G-H249R,S101G-S103A-V104I,S101G-S103A-V104I-A232V-Q245R-N248D,S101G-S103A-V104I-G159D-A232V-Q245R,S101G-S103A-V104I-G159D-A232V-Q245R-N248R,S101G-S103A-V104I-V150L-A232V-Q245R,S103A-A232V,S103A-A232V-H249R,S103A-A232V-Q245R,S103A-V104I-Q245R,S103N-H120F-Y167W-I198L-L233C,T022W-A194F-T213A-L233C-N238L,T022W-E089I-S216F,T033S-A048T,T033S-P086W-S156L-Y209A,T033S-P239T,T033S-T253A,T057R-N183D-Q236N,T143A-Y209A,V004E-T033S-S078R,V004R-S009A-T022R-S078R-S212F,和/或Y209A-K235F;以及任选地包含一个或多个以下的突变:S103A,G159D,Q236H,Q245R,N248D和N252K。

[0294] 本发明还提供分离的蛋白酶变体,其中所述蛋白酶变体具有至少一个,或甚至两个或多个选自以下的带电突变:N062E,S101D,P129E,A158E,G159D/E,S166D,和/或S188D,该蛋白酶变体相对于SEQ ID NO:1的酶优选地具有0、-1、-2、-3、-4或-5的电荷,优选地0、-1、-2或-3,最优选地-1或-2。所述蛋白酶变体也可包括本申请中列出的任何变体。

[0295] 本发明还提供分离的蛋白酶变体,其中所述蛋白酶变体具有一个或两个或多个选自以下的带电突变:N018R,G020K/R,T022R,S024R,N043R,Q245R,H249R和/或N269R,该蛋白酶变体相对于SEQ ID NO:1的酶优选地具有0、+1、+2、+3、+4或+5的电荷,优选地+1、+2或+3,最优选地+2。所述蛋白酶变体也可包括本申请中列出的任何变体。

[0296] 本发明还提供分离的枯草杆菌蛋白酶变体,其中该枯草杆菌蛋白酶变体是具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:G020R-S087D-S101G-S103A-V104I-A232V-Q245R,G020R-S101G-S103A-V104I-V150L-A232V-Q245R,N018R-G020R-S024R-N076D-S087D-H249R,N018R-G020R-S024R-N076D-V150L-H249R,N018R-S024R-N043R-N076D-S087D-H249R,N018R-S024R-N043R-N076D-V150L-H249R,N018R-S024R-N076D-S078R-S087D-H249R,N018R-S024R-N076D-S078R-V150L-H249R,N018R-S024R-N076D-S087D-H249R-N269R,N018R-S024R-N076D-S087D-S242R-H249R,N018R-S024R-N076D-S087D-V150L-H249R,N018R-S024R-N076D-V150L-H249R,N018R-S087D-S101G-S103A-V104I-A232V-Q245R,N018R-S101G-S103A-V104I-V150L-A232V-Q245R,N018R-T022R-S024R-N076D-S087D-H249R,N018R-T022R-S024R-N076D-V150L-H249R,N043R-S087D-S101G-S103A-V104I-A232V-Q245R-N269R,N043R-S101G-S103A-V104I-V150L-A232V-Q245R,S024R-S087D-S101G-S103A-V104I-A232V-Q245R,S024R-S101G-S103A-V104I-V150L-A232V-Q245R,S078R-S087D-S101G-S103A-V104I-A232V-Q245R,S078R-S101G-S103A-V104I-V150L-A232V-Q245R,S087D-S101G-S103A-V104I-A232V-Q245R-N269R,S101G-S103A-V104I-V150L-A232V-Q245R-H249R,S101G-S103A-V104I-V150L-A232V-Q245R-N269R,T022R-S087D-S101G-S103A-V104I-A232V-Q245R,N018R-S024R-N043D-N076D-V150L-H249R,N043R-S087D-S101G-S103A-V104I-A232V-Q245R,T022R-S101G-S103A-V104I-V150L-A232V-Q245R,N018R-S024R-N043D-

N076D-S087D-H249R,N018R-S024R-N076D-S087D-H249R,N018R-S024R-N076D-V150L-S242R-H249R,N043R-S101G-S103A-V104I-V150L-A232V-Q245R-N269R,N076D-S101G-S103A-V104I-V150L-A232V-Q245R,S087D-S101G-S103A-V104I-A232V-S242R-Q245R,S101G-S103A-V104I-V150L-A232V-Q245R,N076D-S087D-S101G-S103A-V104I-A232V-Q245R,S087D-S101G-S103A-V104I-A232V-Q245R,和S101G-S103A-V104I-V150L-A232V-S242R-Q245R,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0297] 本发明还提供分离的枯草杆菌蛋白酶变体,其中该枯草杆菌蛋白酶变体是具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:S024R-S101G-S103A-V104I-P129Q-A158E-S188D-L217E-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-S130A-A158E-N183D-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-P129Q-A158E-N183D-S188D-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-S130A-A158E-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-P129Q-A158E-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-S130A-A158E-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-P129Q-S130A-A158E-N183D-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-S128L-P129Q-A158E-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-P129Q-S130A-A158E-S188D-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-P129Q-A158E-S188D-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-P129Q-S130A-A158E-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-S128L-P129Q-S130A-A158E-S188D-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-S128L-P129Q-A158E-S188D-A232V-Q245R-N248D-H249R,和S024R-K027R-S101G-S103A-V104I-S128L-P129Q-S130A-A158E-S188D-A232V-Q245R-N248D-H249R,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0298] 本发明还提供分离的枯草杆菌蛋白酶变体,其中该枯草杆菌蛋白酶变体是具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:S101G-S103A-V104I-A232V-M222Q-Q245R,S101G-S103A-V104I-A158E-S188D-M222S-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-A158E-S188D-M222Q-A232V-Q245R-N248D-H249R,N076D-S101G-S103A-V104I-A232V-M222Q-Q245R,S101G-S103A-V104I-A232V-M222S-Q245R,N076D-S101G-S103A-V104I-A232V-M222S-Q245R,和N076D-S101G-S103A-V104I-A158E-S188D-M222S-A232V-Q245R-N248D-H249R,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0299] 本发明还提供分离的枯草杆菌蛋白酶变体,其中该枯草杆菌蛋白酶变体是具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:S024R-S101G-S103A-V104I-S128L-P129Q-A158E-S188D-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-S130A-A158E-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-A158E-S188D-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-S128L-P129Q-

A158E-S188D-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-P129Q-S130A-A158E-S188D-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-S130A-A158E-N183D-S188D-L217E-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-S128L-P129Q-S130A-A158E-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-P129Q-A158E-S188D-L217E-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-S128L-S130A-A158E-S188D-L217E-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-S128L-P129Q-A158E-N183D-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-S128L-P129Q-S130A-A158E-N183D-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-S128L-P129Q-A158E-S188D-A232V-Q245R-N248D-H249R-E271G,S101G-S103A-V104I-P129Q-A158E-N183D-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-S130A-A158E-S188D-L217E-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-S128L-A158E-N183D-S188D-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-P129Q-A158E-S188D-L217E-A232V-Q245R-N248D-H249R,和S024R-S101G-S103A-V104I-S128L-S130A-A158E-S188D-A232V-Q245R-N248D-H249R,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0300] 本发明还提供包含具有蛋白水解活性的枯草杆菌蛋白酶变体的多肽,该枯草杆菌蛋白酶变体包含具有选自以下的氨基酸置换的组合的氨基酸序列:S101G-S103A-V104I,T22A-S101A-Y209E,S103G-L111V-G159E,T22A-S103G-G159E,T22A-L111V-G159E,T22A-S128N-E271F-Y209E,T22A-S103G-L111V,N62E-L111V-S128N,T22A-L111V-S128N,T22A-N62E-L111V,S101A-S103G-V104L-S188D,S101G-S103A-V104I-G159D,S101A-S103G-V104L-S128N,T22A-S101A-G159E,S101A-S103G-V104L,S101A-S103G-V104L-G159E,T22A-S101A-S103G-V104L,S101A-S103G-V104L-Y209E,T22A-Y209E-E271F,T22A-S101A-E271F,和S101A-Y209E-E271F,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0301] 本发明还提供包含具有蛋白水解活性的枯草杆菌蛋白酶变体的多肽,该枯草杆菌蛋白酶变体包含具有选自以下的氨基酸置换的组合的氨基酸序列:S103A-V104I-G159D-A232V-Q236H-Q245R-N248D-N252K,S101G-V104I-G159D-A232V-Q236H-Q245R-N248D-N252K,S101G-S103A-G159D-A232V-Q236H-Q245R-N248D-N252K,S101G-S103A-V104L-A232V-Q236H-Q245R-N248D-N252K,S101G-S103A-V104L-G159D-Q236H-Q245R-N248D-N252K,S101G-S103A-V104L-G159D-A232V-Q245R-N248D-N252K,S101G-S103A-V104L-G159D-A232V-Q236H-N248D-N252K,S101G-S103A-V104L-G159D-A232V-Q236H-Q245R-N252K,和S101G-S103A-V104L-G159D-A232V-Q236H-Q245R-N248D,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0302] 本发明还提供包含具有蛋白水解活性的枯草杆菌蛋白酶变体的多肽,该枯草杆菌蛋白酶变体包含具有选自以下的氨基酸置换的组合的氨基酸序列:S101G-S103A-V104I-G159D-A232V-Q245R-N248D,S101G-S103A-V104I-G159D-A232V-Q245R-N248D-E271F,S101G-S103A-V104I-G159D-A232V-Q245R-N248D-N238R,S101G-S103A-V104I-G159D-

A232V-Q245R-N248D-N248R,S101G-S103A-V104I-G159D-A232V-Q245R-N248D-T253R,S101G-S103A-V104I-G159D-A232V-Q245R-N248D-S24R,S101G-S103A-V104I-G159D-A232V-Q245R-N248D-N76D,S101G-S103A-V104I-G159E-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-G159E-A232V-Q245R-N248D-E271F,S101G-S103A-V104I-A158E-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-A158E-A232V-Q245R-N248D-E271F,T22A-S101G-S103A-V104I-G159D-A232V-Q245R-N248D-H249R,T22A-S101G-S103A-V104I-G159D-A232V-Q245R-N248D-E271F,N62E-S101G-S103A-V104I-G159D-A232V-Q245R-N248D-H249R,和N62E-S101G-S103A-V104I-G159D-A232V-Q245R-N248D-E271F,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0303] 本发明还提供包含具有蛋白水解活性的枯草杆菌蛋白酶变体的多肽,该枯草杆菌蛋白酶变体包含具有选自以下的氨基酸置换的组合的氨基酸序列:A1R,A230E,E271L,G115R,G20R,H249R,K235F,K27V/F/L,L75E,L82R,N18R,N269R,N43D,N43R,N76D,R45T,S212F,S242R,S24R,S78R,S9A,T22R,V121E,V244R,V28E,V30E,V4R,W241R,G20R-N43R-H249R,G20R-T22R-N43R,G20R-N43R-S242R,G20R-N43R-E271L,G20R-N43R-V244R,G20R-S24R-N43R-S242R,S9A-T22R-S78R-S212F-W241R,S9A-G20R-N43R-S212F,S9A-N43R-S212F,G20R-N43R-S212F,G20R-T22R-N43R-S212F,S24R-S78R-S212F,S9A-N43R-S78R,S9A-N43R-S78R-S242R,S9A-G20R-N43R-S78R,G20R-S24R-N43R-S78R-S242R,T22R-S24R-S78R-S212F,S9A-G20R-N43R-S78R-S242R,G20R-N43R-S78R-H249R,G20R-N43R-S78R,S9A-S78R-S212F,S9A-T22R-N43R-S78R,S9A-G20R-S24R-N43R,S9A-T22R-S78R-S212F,V4R-S9A-T22R-S78R-S212F,G20R-S24R-N43R,A1R-S9A-N43R,G20R-S24R-N43R-G115R,S9A-S24R-N43R,G20R-T22R-S24R-N43R,A1R-S24R-N43R,S9A-G20R-S24R-N43R-S242R,S9A-G20R-T22R-S78R-S212F,S9A-S24R-N43R-V244R,S9A-S24R-N43R-S242R,V4R-S9A-T22R-S24R-S212F,和T22R-S24R-N43R,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0304] 本发明还提供包含具有蛋白水解活性的枯草杆菌蛋白酶变体的多肽,并且该枯草杆菌蛋白酶变体包含具有选自以下的氨基酸置换的组合的氨基酸序列:S101G-S103A-V104I-A232V-Q245R-N248D,S101G-S103A-V104I-G159D-A232V-Q245R,S101G-S103A-V104I-G159R-A232V-Q245R-N248D,S101G-S103A-V104I-G159D-A232V-Q245R-N248R,S101G-S103A-V104I-A232V-Q245R,S101G-S103A-V104I-A232V-Q245R-N248R,S101G-S103A-V104I-G159R-A232V-Q245R-N248R,S101G,S103A,V104I,A232V,Q236H,和Q245R,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0305] 本发明还提供包含具有蛋白水解活性的枯草杆菌蛋白酶变体的多肽,并且该枯草杆菌蛋白酶变体包含具有选自以下的氨基酸置换的组合的氨基酸序列:A16S,T22A,S24R,N62E,N76D,E89P,S101A/G,S103G/A,V104L/I,L111V,S128N,P129E,A232V,L148I,A158E,G159D/E,R186H,S188D,Y209E,Q236H,Q245R,N248D/R,H249R,N252K/R,T253R,和E271F,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0306] 本发明还提供迟缓芽孢杆菌枯草杆菌蛋白酶GG36蛋白酶的蛋白酶变体，其中该迟缓芽孢杆菌枯草杆菌蛋白酶GG36蛋白酶包含SEQ ID NO:2所示氨基酸序列，其中该蛋白酶变体包含与SEQ ID NO:2的氨基酸序列相差不超过2、3、4、5、6、7、8、9、10、11、12、13、14、15、16、17、18、19、20、21、22、23、24或25个突变的氨基酸序列，所述突变选自:G20K,G20R,G23A,S24F,S24R,N43R,N43W,R45T,N62E,N76D,S101A,N116A,N116L,G118R,S128I,P129E,S188D,T213A,A215F,L217E,P239G，和N269R，其中该蛋白酶变体的氨基酸位置根据SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列中对应的氨基酸位置的编号方式来进行编号，这是通过该蛋白酶变体氨基酸序列与解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'氨基酸序列的比对来确定的。

[0307] 本发明还提供包含具有蛋白水解活性的枯草杆菌蛋白酶变体的多肽，并且该枯草杆菌蛋白酶变体包含具有选自以下的氨基酸置换的组合的氨基酸序列:A1R,Q2S,Q2M,Q2A,Q2R,Q2W,S3R,V4R,V4S,V4C,I8A,S9A,S9F,S9W,R10S,R10A,R10H,R10M,Q12F,Q12R,P14K,P14F,P14Q,A15R,A15F,A16S,H17R,H17M,H17F,N18R,N18K,G20F,G20K,G20R,T22A,T22R,T22Y,T22V,T22Q,T22L,T22W,G23A,G23S,G23F,S24R,S24F,S24W,S24Q,S24H,S24L,G25V,G25F,G25R,V26F,K27L,K27F,K27R,K27V,V28A,V28N,V28E,A29T,V30E,L31F,T33S,T33G,T33D,G34P,I35M,S36T,S36F,S36R,T38L,T38F,T38R,P40N,P40L,P40T,P40W,P40H,P40R,L42I,N43A,N43F,N43I,N43S,N43R,N43M,N43W,N43D,R45T,G46R,A48R,F50C,V51W,V51F,V51H,P52F,P52E,P52N,P55Y,T57R,Q59A,Q59F,Q59R,D60P,D60Q,D60A,N62E,N62Q,G63V,G63M,G63T,G63I,G63A,G63S,G63H,G63Q,G63D,G63E,G63P,H64F,H64T,V68A,V68C,A69N,A69T,A69P,A69W,T71G,T71G,I72C,A74C,L75A,L75F,L75E,L75R,N76D,S78R,S78N,S78I,S78R,I79W,I79Q,V81R,L82F,L82T,L82V,L82R,L82M,A85M,P86W,P86L,P86I,E89P,E89T,E89G,E89H,E89W,E89L,E89V,E89W,E89F,E89I,Y91N,Y91F,A92F,K94N,S99F,S99T,S99P,S99G,S99M,G100S,G100N,G100Q,G100I,S101A,S101N,S101G,S101D,S101T,S101D,S101E,S101P,S101F,G102A,G102T,G102N,G102H,G102E,S103G,S103N,S103D,S103A,V104L,V104I,V104E,V104D,S105T,S105E,S105Q,S106G,S106T,S106E,S106D,S106A,S106V,S106F,I107M,I107F,A108I,A108G,Q109M,L111V,L111I,E112V,E112L,E112Q,A114G,G115K,G115R,N116K,N116A,N116L,N117F,G118R,G118I,M119C,H120A,H120F,H120R,V121F,V121F,V121E,N123G,N123E,L124S,S128D,S128F,S128L,S128N,S128H,S128M,S128I,S128Q,P129E,S132A,S132E,A138G,S144R,V147L,L148I,A158E,G159D,G159E,G159C,S160D,S166D,S166E,Y167W,M175V,V177C,D181A,Q182R,N183I,N183D,N183M,N183R,N183F,N183R,N185E,N185V,N185I,R186H,R186K,S188E,S188D,S188R,Y192H,Y192W,A194E,A194V,A194F,D197F,D197F,I198L,I198F,V203E,V203C,T208S,Y209S,Y209N,Y209F,Y209T,Y209E,Y209H,Y209G,Y209L,P210R,P210V,P210L,G211Q,G211R,S212I,S212M,S212F,T213A,Y214F,A215N,A215D,A215E,A215H,A215F,S216F,S216A,L217E,L217N,L217D,N218D,N218P,N218E,T224A,T224G,V227I,A230E,A231I,A231C,A232V,L233C,V234F,K235F,Q236F,Q236N,Q236H,N238R,N238K,N238L,P239K,P239G,P239R,P239R,P239H,P239T,P239N,P239S,P239F,S240R,W241R,S242L,S242R,N243F,N243R,V244R,Q245R,I246S,N248D,N248V,N248I,N248R,H249R,H249T,L250I,K251R,K251S,N252I,N252F,N252R,N252K,N252H,T253I,T253R,T253F,A254C,S256N,G258R,

T260V,T260I,L262D,L262H,Y263F,S265F,L267V,L267N,L267M,N269I,N269R,A270C,E271I,E271H,E271V,E271H,E271M,E271L,E271P,E271A,E271F,E271T,A272F,A272F,A272R,A273F,A273I,和T274G,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0308] 本发明还提供包含迟缓芽孢杆菌枯草杆菌蛋白酶GG36蛋白酶的蛋白酶变体的多肽,其中该迟缓芽孢杆菌枯草杆菌蛋白酶GG36蛋白酶包含SEQ ID NO:2所示氨基酸序列,并且其中该蛋白酶变体包含与SEQ ID NO:2的氨基酸序列相差不超过2、3、4、5、6、7、8、9、10、11、12、13、14、15、16、17、18、19、20、21、22、23、24、25、30、35、40、45或50个突变的氨基酸序列,所述突变处于选自氨基酸1、2、3、4、8、9、10、12、14、15、16、17、18、20、22、23、24、25、26、27、28、29、30、31、33、34、35、36、38、40、42、43、45、46、48、50、51、52、55、57、59、60、62、63、64、68、69、71、72、74、75、76、78、79、81、82、85、86、89、91、92、94、99、100、101、102、103、104、105、106、107、108、109、111、112、114、115、116、117、118、119、120、121、123、124、128、129、132、138、44、147、148、158、159、160、166、167、175、177、181、182、183、185、186、188、192、194、197、198、203、208、209、210、211、212、213、214、215、216、217、218、224、227、230、231、233、234、235、236、236、238、238、239、240、241、242、243、244、246、248、249、250、251、252、253、254、256、258、260、262、263、265、267、269、270、271、272、273和274的氨基酸位置,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0309] 本发明还提供包含迟缓芽孢杆菌枯草杆菌蛋白酶GG36蛋白酶的蛋白酶变体的多肽,其中该迟缓芽孢杆菌枯草杆菌蛋白酶GG36蛋白酶包含SEQ ID NO:2所示氨基酸序列,并且其中该蛋白酶变体包含与SEQ ID NO:2的氨基酸序列相差不超过2、3、4、5、6、7、8、9、10、11、12、13、14、15、16、17、18、19、20、21、22、23、24、25、30、35、40、45或50个突变的氨基酸序列,所述突变选自:A1R,Q2S,Q2M,Q2A,Q2R,Q2W,S3R,V4R,V4S,V4C,I8A,S9A,S9F,S9W,R10S,R10A,R10H,R10M,Q12F,Q12R,P14K,P14F,P14Q,A15R,A15F,A16S,H17R,H17M,H17F,N18R,N18K,G20F,G20K,G20R,T22A,T22R,T22Y,T22V,T22Q,T22L,T22W,G23A,G23S,G23F,S24R,S24F,S24W,S24Q,S24H,S24L,G25V,G25F,G25R,V26F,K27L,K27F,K27R,K27V,V28A,V28N,V28E,A29T,V30E,L31F,T33S,T33G,T33D,G34P,I35M,S36T,S36F,S36R,T38L,T38F,T38R,P40N,P40L,P40T,P40W,P40H,P40R,L42I,N43A,N43F,N43I,N43S,N43R,N43M,N43W,N43D,R45T,G46R,A48R,F50C,V51W,V51F,V51H,P52F,P52E,P52N,P55Y,T57R,Q59A,Q59F,Q59R,D60P,D60Q,D60A,N62E,N62Q,G63V,G63M,G63T,G63I,G63A,G63S,G63H,G63Q,G63D,G63E,G63P,H64F,H64T,V68A,V68C,A69N,A69T,A69P,A69W,T71G,T71G,I72C,A74C,L75A,L75F,L75E,L75R,N76D,S78R,S78N,S78I,S78R,I79W,I79Q,V81R,L82F,L82T,L82V,L82R,L82M,A85M,P86W,P86L,P86I,E89P,E89T,E89G,E89H,E89W,E89L,E89V,E89W,E89F,E89I,Y91N,Y91F,A92F,K94N,S99F,S99T,S99P,S99G,S99M,G100S,G100N,G100Q,G100I,S101A,S101N,S101G,S101D,S101T,S101D,S101E,S101P,S101F,G102A,G102T,G102N,G102H,G102E,S103G,S103N,S103D,S103A,V104L,V104I,V104E,V104D,S105T,S105E,S105Q,S106G,S106T,S106E,S106D,S106A,S106V,S106F,I107M,I107F,A108I,A108G,Q109M,L111V,L111I,E112V,E112L,E112Q,A114G,G115K,G115R,N116K,N116A,N116L,N117F,G118R,G118I,M119C,H120A,H120F,H120R,V121F,V121F,V121E,N123G,N123E,L124S,S128D,

S128F,S128L,S128N,S128H,S128M,S128I,S128Q,P129E,S132A,S132E,A138G,S144R,V147L,L148I,A158E,G159D,G159E,G159C,S160D,S166D,S166E,Y167W,M175V,V177C,D181A,Q182R,N183I,N183D,N183M,N183R,N183F,N183R,N185E,N185V,N185I,R186H,R186K,S188E,S188D,S188R,Y192H,Y192W,A194E,A194V,A194F,D197F,D197F,I198L,I198F,V203E,V203C,T208S,Y209S,Y209N,Y209F,Y209T,Y209E,Y209H,Y209G,Y209L,P210R,P210V,P210L,G211Q,G211R,S212I,S212M,S212F,T213A,Y214F,A215N,A215D,A215E,A215H,A215F,S216F,S216A,L217E,L217N,L217D,N218D,N218P,N218E,T224A,T224G,V227I,A230E,A231I,A231C,A232V,L233C,V234F,K235F,Q236F,Q236N,Q236H,N238R,N238K,N238L,P239K,P239G,P239R,P239R,P239H,P239T,P239N,P239S,P239F,S240R,W241R,S242L,S242R,N243F,N243R,V244R,Q245R,I246S,N248D,N248V,N248I,N248R,H249R,H249T,L250I,K251R,K251S,N252I,N252F,N252R,N252K,N252H,T253I,T253R,T253F,A254C,S256N,G258R,T260V,T260I,L262D,L262H,Y263F,S265F,L267V,L267N,L267M,N269I,N269R,A270C,E271I,E271H,E271V,E271H,E271M,E271L,E271P,E271A,E271F,E271T,A272F,A272F,A272R,A273F,A273I,和T274G,其中该蛋白酶变体的氨基酸位置根据SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列中对应的氨基酸位置的编号方式来进行编号,这是通过该蛋白酶变体氨基酸序列与解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'氨基酸序列的比对来确定的。

[0310] 本发明还提供包含迟缓芽孢杆菌枯草杆菌蛋白酶GG36蛋白酶的蛋白酶变体的多肽,其中该迟缓芽孢杆菌枯草杆菌蛋白酶GG36蛋白酶包含SEQ ID NO:2所示氨基酸序列,并且其中该蛋白酶变体包含与SEQ ID NO:2的氨基酸序列相差不超过2、3、4、5、6、7、8、9、10、11、12、13、14、15、16、17、18、19、20、21、22、23、24、25、30、35、40、45或50个突变的氨基酸序列,所述突变选自:A1R,Q2S,V4R,V4S,S9A,R10S,P14K,A16S,H17R,N18R,G20R,T22A,T22R,S24R,S24W,G25R,G25V,V26F,L42I,N43R,N43A,G46R,P52F,P52E,P52N,T57R,Q59A,N62E,N62Q,V68A,V68C,T71G,I72C,A74C.L75A,L75F,L75R,N76D,S78R,L82R,P86W,E89P,E89T,E89G,E89H,E89I,E89V,E89W,Y91N,K94N,G100S,S101A,S101N,S101G,S101D,S103G,S103N,V104L,V104I,S106V,S106G,A108I,L111V,E112V,G115K,G115R,N117F,G118I,V121F,S128D,S128F,S128L,S128N,P129E,S144R,L148I,A158E,G159E,S160D,S166D,N185E,N185I,R186H,S188E,S188D,D197F,V203E,Y209S,Y209N,Y209F,Y209T,Y209E,Y209H,Y209G,P210R,S212I,S212F,Y214F,A215N,A215D,A215E,L217E,L217N,T224A,A230E,A231I,Q236F,N238R,N238K,P239K,P239G,P239R,P239S,W241R,S242R,S242L,N243R,V244R,N248I,N248V,H249R,L250I,N252R,T253R,L262D,Y263F,S265F,L267V,L267N.N269I,N269R,E271F,E271I,E271H,E271P,E271T,E271V,E271L和A272F,并且该蛋白酶变体任选地包含至少一个选自S103A,G159D,Q236H,Q245R,N248D和N252K,的突变,其中该蛋白酶变体的氨基酸位置根据SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列中对应的氨基酸位置的编号方式来进行编号,这是通过该蛋白酶变体氨基酸序列与解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'氨基酸序列的比对来确定的。

[0311] 本发明还提供包含迟缓芽孢杆菌枯草杆菌蛋白酶GG36蛋白酶的蛋白酶变体的多肽,其中该迟缓芽孢杆菌枯草杆菌蛋白酶GG36蛋白酶包含SEQ ID NO:2所示氨基酸序列,并且其中该蛋白酶变体包含与SEQ ID NO:2的氨基酸序列相差不超过2、3、4、5、6、7、8、9、10、

11、12、13、14、15、16、17、18、19、20、21、22、23、24、25、30、35、40、45或50个突变的氨基酸序列，所述突变选自：A1R,Q2S,V4R,V4S,S9A,R10S,P14K,A16S,H17R,N18R,G20R,T22A,T22R,S24R,S24W,G25R,G25V,V26F,L42I,N43R,N43A,G46R,P52F,P52E,P52N,T57R,Q59A,N62E,N62Q,V68A,V68C,T71G,I72C,A74C.L75A,L75F,L75R,N76D,S78R,L82R,P86W,E89P,E89T,E89G,E89H,E89I,E89V,E89W,Y91N,K94N,G100S,S101A,S101N,S101G,S101D,S103G,S103N,V104L,V104I,S106V,S106G,A108I,L111V,E112V,G115K,G115R,N117F,G118I,V121F,S128D,S128F,S128L,S128N,P129E,S144R,L148I,A158E.G159E,S160D,S166D,N185E,N185I,R186H,S188E,S188D,D197F,V203E,Y209S,Y209N,Y209F,Y209T,Y209E,Y209H,Y209G,P210R,S212I,S212F,Y214F,A215N,A215D,A215E,L217E,L217N,T224A,A230E,A231I,Q236F,N238R,N238K,P239K,P239G,P239R,P239S,W241R,S242R,S242L,N243R,V244R,N248I,N248V,H249R,L250I,N252R,T253R,L262D,Y263F,S265F,L267V,L267N.N269I,N269R,E271F,E271I,E271H,E271P,E271T,E271V,E271L和A272F，并且该蛋白酶变体任选地包含至少一个选自S103A,G159D,Q236H,Q245R,N248D和N252K,的突变，其中该蛋白酶变体的氨基酸位置根据SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列中对应的氨基酸位置的编号方式来进行编号，这是通过该蛋白酶变体氨基酸序列与解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'氨基酸序列的比对来确定的。

[0312] 本发明还提供包含迟缓芽孢杆菌枯草杆菌蛋白酶GG36蛋白酶的蛋白酶变体的多肽，其中该迟缓芽孢杆菌枯草杆菌蛋白酶GG36蛋白酶包含SEQ ID NO:2所示氨基酸序列，其中该蛋白酶变体包含与SEQ ID NO:2的氨基酸序列相差不超过2、3、4、5、6、7、8、9、10、11、12、13、14、15、16、17、18、19、20、21、22、23、24、25、30、35、40、45或50个突变的氨基酸序列，所述突变选自：A16S,T22A,S24R,N62E,N76D,E89P,S101A/G,S103G/A,V104L/I,L111V,S128N,P129E,A232V,L148I,A158E,G159D/E,R186H,S188D,Y209E,Q236H,Q245R,N248D/R,H249R,N252K/R,T253R,E271F,A1R,A230E,E271L,G115R,G20R,H249R,K235F,K27V/F/L,L75E,L82R,N18R,N269R,N43D,N43R,N76D,R45T,S212F,S242R,S24R,S78R,S9A,T22R,V121E,V244R,V28E,V30E,V4R，和W241R，并且其中该蛋白酶变体的氨基酸位置根据SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列中对应的氨基酸位置的编号方式来进行编号，这是通过该蛋白酶变体氨基酸序列与解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'氨基酸序列的比对来确定的。

[0313] 本发明还提供迟缓芽孢杆菌枯草杆菌蛋白酶GG36蛋白酶的蛋白酶变体，其中该迟缓芽孢杆菌枯草杆菌蛋白酶GG36蛋白酶包含SEQ ID NO:2所示氨基酸序列，其中该蛋白酶变体包含与SEQ ID NO:2的氨基酸序列相差不超过2、3、4、5、6、7、8、9、10、11、12、13、14、15、16、17、18、19、20、21、22、23、24或25个突变的氨基酸序列，所述突变选自：G20K,G20R,G23A,S24F,S24R,N43R,N43W,R45T,N62E,N76D,S101A,N116A,N116L,G118R,S128I,P129E,S188D,T213A,A215F,L217E,P239G，和N269R，其中该蛋白酶变体的氨基酸位置根据SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列中对应的氨基酸位置的编号方式来进行编号，这是通过该蛋白酶变体氨基酸序列与解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'氨基酸序列的比对来确定的。

[0314] 本发明还提供包含迟缓芽孢杆菌枯草杆菌蛋白酶GG36蛋白酶的蛋白酶变体的多肽，其中该迟缓芽孢杆菌枯草杆菌蛋白酶GG36蛋白酶包含SEQ ID NO:2所示氨基酸序列，并

且其中该蛋白酶变体包含与SEQ ID NO:2的氨基酸序列相差不超过2、3、4、5、6、7、8、9、10、11、12、13、14、15、16、17、18、19、20、21、22、23、24、25、30、35、40、45或50个突变的氨基酸序列，所述突变选自：A16S,T22A,S24R,N62E,N76D,E89P,S101A/G,S103G/A,V104L/I,L111V,S128N,P129E,A232V,L148I,A158E,G159D/E,R186H,S188D,Y209E,Q236H,Q245R,N248D/R,H249R,N252K/R,T253R,E271F,A1R,A230E,E271L,G115R,G20R,H249R,K235F,K27V/F/L,L75E,L82R,N18R,N269R,N43D,N43R,N76D,R45T,S212F,S242R,S24R,S78R,S9A,T22R,V121E,V244R,V28E,V30E,V4R，和W241R，其中该蛋白酶变体的氨基酸位置根据SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列中对应的氨基酸位置的编号方式来进行编号，这是通过该蛋白酶变体氨基酸序列与解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'氨基酸序列的比对来确定的。

[0315] 本发明还提供多肽，其包含具有与SEQ ID NO:2的氨基酸序列不同的氨基酸序列的蛋白酶变体，并且其中该蛋白酶变体的总净电荷相对于迟缓芽孢杆菌枯草杆菌蛋白酶GG36蛋白酶的总净电荷为0、+1、+2、+3、+4、+5、-1、-2、-3、-4或-5，并且其中该蛋白酶变体的氨基酸位置根据SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列中对应的氨基酸位置的编号方式来进行编号，这是通过该蛋白酶变体氨基酸序列与解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'氨基酸序列的比对来确定的。

[0316] 本发明还提供包含与SEQ ID NO:2的氨基酸序列不同的氨基酸序列的蛋白酶变体，并且其中该蛋白酶变体的总净电荷相对于迟缓芽孢杆菌枯草杆菌蛋白酶GG36蛋白酶的总净电荷为0，并且其中该蛋白酶变体的氨基酸位置根据SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列中对应的氨基酸位置的编号方式来进行编号，这是通过该蛋白酶变体氨基酸序列与解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'氨基酸序列的比对来确定的。

[0317] 本发明还提供包含与SEQ ID NO:2的氨基酸序列不同的氨基酸序列的蛋白酶变体，其中该蛋白酶变体是具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列：G020R-N043R,G020K-N062E,S024F-N116L,G020K-S024F,S024R-A174T,S024R-G118R,S024R-K235F,S024R-P086R,S024R-P086W,S078R-G118R,T033S-G118R,T033S-K235F,Y209A-W241R,G020R-N076D,N018R-Q245R,S024R-R045T,A232V-Q245R,G118R-A172V,G118R-A194T,I008T-S024R,K235F-N243F,N018R-S103A,N018R-V104I,P086W-G118R,P086W-N243F,P086W-Y209A,S024C-T033S,S024R-A232V,S024R-N243F,S024R-P239Q,S024R-S101G,S024R-S141G,S024R-T033S,S024R-T274I,S024R-Y209A,S078R-P086W,S101G-A232V,T033S-L148F,T033S-P086W,T033S-P201S,T033S-S078R,T033S-W241R,T033S-Y209A,A230E-H249R,A232V-H249R,G118R-K235F,N076D-Q245R,P086W-K235F,S024R-R247H,S024R-V104A,S078R-K235F,S101G-H249R,S103A-A232V,T033S-A048T,T033S-P239T,T033S-T253A,T143A-Y209A,Y209A-K235F,N018R-R045T,Y209A-N243F,S024R-A272P,S024R-R269C,S101G-V104I,V104I-A232V,N076D-H249R，和S024R-N076D，并且其中该蛋白酶变体的总净电荷相对于迟缓芽孢杆菌枯草杆菌蛋白酶GG36蛋白酶的总净电荷为0、+1、+2、+3、+4、+5、-1、-2、-3、-4或-5，并且其中总净电荷是通过一个或多个选自以下的置换获得：N43D,R45T,N62E,N76D,S101D,P129E,A158E,G159D,G159E,S166D,S188D,A230E,N18R,G20K,G20R,T22R,S24R,N43R,G118R,Q245R,

H249R,N269R,E271F,和E271L,并且其中该蛋白酶变体的氨基酸位置根据SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列中对应的氨基酸位置的编号方式来进行编号,这是通过该蛋白酶变体氨基酸序列与解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'氨基酸序列的比对来确定的。

[0318] 本发明还提供包含与SEQ ID NO:2的氨基酸序列不同的氨基酸序列的蛋白酶变体,其中该蛋白酶变体是具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:G020R-N076D,S024R-R045T,A230E-H249R,N018R-R045T,N018R-Q245R,S101G-A232V,S024R-A232V,A232V-Q245R,S024R-S101G,N018R-V104I,N018R-S103A,S101G-H249R,A232V-H249R,S103A-A232V,N076D-Q245R,S101G-V104I,V104I-A232V,N076D-H249R,S024R-N076D,S024F-N116L,G020K-S024F,G020K-N062E,T033S-G118R,S024R-P086W,S024R-G118R,S024R-P086R,Y209A-W241R,S024R-W241R,S024R-K235F,G118R-Y209A,S078R-G118R,T033S-K235F,S024R-A174T,P086W-Y209A,I008T-S024R,P086W-G118R,T033S-W241R,S024R-N243F,S024R-Y209A,T033S-P086W,S024R-T033S,P086W-N243F,T033S-P201S,S024R-P239Q,S078R-P086W,K235F-N243F,G118R-A172V,T033S-L148F,T033S-S078R,T033S-N243F,S024C-T033S,G118R-A194T,T033S-Y209A,S024R-S141G,S024R-T274I,P086W-K235F,A015T-T033S,Y209A-K235F,S024R-R247H,S078R-K235F,S024R-V104A,T033S-A048T,G118R-K235F,T033S-T253A,T143A-Y209A,T033S-P239T,Y209A-N243F,S024R-A272P,和S024R-R269C,并且其中该蛋白酶变体的总净电荷相对于迟缓芽孢杆菌枯草杆菌蛋白酶GG36蛋白酶的总净电荷为0、+1、+2、+3、+4、+5、-1、-2、-3、-4或-5,并且其中总净电荷是通过一个或多个选自以下的置换获得:N43D,R45T,N62E,N76D,S101D,P129E,A158E,G159D,G159E,S166D,S188D,A230E,N18R,G20K,G20R,T22R,S24R,N43R,G118R,Q245R,H249R,N269R,E271F,和E271L,并且其中该蛋白酶变体的氨基酸位置根据SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列中对应的氨基酸位置的编号方式来进行编号,这是通过该蛋白酶变体氨基酸序列与解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'氨基酸序列的比对来确定的。

[0319] 本发明还提供包含与SEQ ID NO:2的氨基酸序列不同的氨基酸序列的蛋白酶变体,其中该蛋白酶变体是具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:G020K-G023A-N043W-G118R-S128I-P129E-G159D-S188D,G020K-G023A-N062E-N116L,G020K-G023A-N062E-N116L-S188D,G020K-G023A-N062E-N116L-S188D-T213A,G020K-G100S-N116L-A158E-S166D-N243F,G020K-N043W-N062E-N116L-S188D,G020K-N062E,G020K-N062E-N116L,G020K-N062E-N116L-S188D,G020K-N062E-N116L-T213A,G020K-N062E-S188D-T213A,G020K-S024F-N062E-N116L-G118R-S188D,G020K-S024F-N062E-N116L-S188D,G020K-S024F-N062E-S188D-T213A,G023A-N062E-N116L-S188D,G023A-S024F-N062E-N116L-T213A,N043R-N076D-S101A-S103A-V104I-A158E-S188D-L217E-A232V-Q245R-N248D-H249R-E271F,N043R-S101A-S103A-V104I-A158E-S188D-L217E-A232V-Q245R-N248D-H249R,N043W-N062E-N116L,N043W-S101D-S212M-N243F,N062E-N116L-G118R-S188D,N062E-N116L-G118R-T213A,N062E-N116L-S188D-T213A,S024F-G118R-S128I-P129E-G159D,S024F-N062E-N116L-S188D,S024R-S101G-S103A-V104I-A158E-N183D-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-

S103A-V104I-A158E-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-A158E-S188D-L217E-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-P129Q-A158E-N183D-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-P129Q-A158E-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-P129Q-A158E-S188D-L217E-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-P129Q-S130A-A158E-N183D-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-S128L-P129Q-A158E-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-S130A-A158E-N183D-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-S130A-A158E-S188D-A232V-Q245R-N248D-H249R,S101D-S103N-N116L-S144R-A215D,S101G-S103A-V104I-A158E-S188D-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-S130A-A158E-S188D-A232V-Q245R-N248D-H249R,T022A-N043R-S101G-S103A-V104I-G159D-S188D-L217E-A232V-Q245R-N248D-E271F,T022A-N043R-S103A-V104I-G118R-S128I-P129E-G159D-S188D-A232V-N248D-E271F,T022A-N043R-S103A-V104I-S128I-P129E-G159D-S188D-A232V-Q245R-N248D,T022A-S024R-S103A-V104I-G118R-S128I-P129E-G159D-S188D-A232V-N248D,T022A-S101G-S103A-V104I-G159D-L217E-A232V-Q245R-N248D-E271F,T022A-S101G-S103A-V104I-G159D-S188D-A232V-Q245R-N248D-E271F,T022L-T038F-A048R-N062E-G100S-R186K,T033S-N043W-N218D-P239G-N243F,V026F-A048R-S105T-T213A-N218D-T224A,V026F-L031F-S078N-G102A-S160D,V026F-V051W-V104L-S106E,V104L-S105T-T213A-L217E-S256N,A016S-N062E-A158E-H249R,A016S-N062E-A158E-R186H-E271F,A016S-N062E-A158E-R186H-H249R,A016S-N062E-V104L-A158E-R186H-E271F,A016S-S024R-S101G-S103A-V104I-A158E-S188D-A232V-Q245R-N248D-H249R,G020K-G023A-N062E-S188D,G020K-G023A-S024F-N062E-G118R-S188D-T213A,G020K-N043W-N062E-N116L-S188D-T213A-P239G,G020K-S024F-N062E-S188D-P239G,G023A-N062E-N116L-G118R,G023A-N062E-N116L-G118R-S188D-P239G,G023A-S024F-N062E-N116L-G118R,H017R-T022A-N076D-S101G-S103A-V104I-G159D-S188D-A232V-Q245R-N248D-E271F,N043R-N076D-S101A-S103A-V104I-A158E-S188D-A232V-Q245R-N248D-H249R-E271F,N062E-A158E-G159E-H249R,N062E-A158E-H249R,N062E-A158E-R186H-E271F,N062E-A158E-R186H-H249R,N062E-A158E-R186H-H249R-E271F,N062E-A158E-S188D-H249R,N062E-A158E-S188D-H249R-E271F,N062E-G159E-H249R,N062E-G159E-H249R-E271F,N062E-G159E-R186H-H249R,N062E-G159E-S188D-H249R,N062E-R186H-S188D-H249R-E271F,N062E-S101A-A158E-H249R,N062E-S101A-A158E-R186H-E271F,N062E-S101A-A158E-R186H-H249R-E271F,N062E-S101A-G159E-H249R,N062E-S101A-R186H-H249R,N062E-S101A-S188D-H249R,N062E-S101A-S188D-H249R-E271F,N062E-S101A-V104L-A158E-R186H-E271F,N062E-S128N-A158E-G159E-E271F,N062E-V104L-A158E-S188D-H249R-E271F,N076D-S101G-S103A-V104I-A232V-M222Q-Q245R,S024F-N062E-N116L-P239G,S024F-N062E-S188D-T213A,S024F-N116L,S024R-N043R-N076D-S101A-S103A-V104I-A158E-S188D-L217E-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-A158E-G159E-A232V-N238R-Q245R-N248D,S024R-S101G-S103A-V104I-A158E-G159E-S188D-A232V-Q245R-N248D,S024R-S101G-S103A-V104I-

A158E-S188D-A232V-N238R-Q245R-N248D,S024R-S101G-S103A-V104I-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-G159E-S188D-A232V-N238R-Q245R-N248D,S024R-S101G-S103A-V104I-G159E-S188D-A232V-Q245R-N248D,S024R-S101G-S103A-V104I-G159E-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-L148I-A158E-A232V-Q245R-N248D,S024R-S101G-S103A-V104I-L148I-A158E-S188D-A232V-Q245R-N248D,S024R-S101G-S103A-V104I-L148I-A232V-Q245R-N248D,S024R-S101G-S103A-V104I-P129E-A158E-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-P129E-A158E-G159E-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-P129E-A158E-S188D-A232V-Q245R-N248D,S024R-S101G-S103A-V104I-P129E-A158E-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-P129E-G159E-A232V-Q245R-N248D,S024R-S101G-S103A-V104I-P129E-G159E-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-P129E-L148I-A158E-A232V-Q245R-N248D,S024R-S101G-S103A-V104I-P129E-S188D-A232V-N238R-Q245R-N248D,S024R-S101G-S103A-V104I-P129E-S188D-A232V-Q245R-N248D,S024R-S101G-S103A-V104I-P129E-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-S128N-A158E-A232V-Q245R-N248D,S024R-S101G-S103A-V104I-S128N-P129E-A158E-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-S128N-P129E-A232V-Q245R-N248D,S101A-S103A-V104I-A158E-S188D-A232V-Q245R-N248D-H249R,S101A-S103A-V104I-A158E-S188D-A232V-Q245R-N248D-H249R-E271F-E271F,S101A-S103A-V104L-A158E-S188D-A232V-Q245R-N248D-H249R,S101A-S128N-A158E-R186H-E271F,S101A-S128N-A158E-Y209E-H249R,S101A-V104L-A158E-R186H-S188D-H249R,S101G-S103A-V104I-A158E-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-A158E-G159E-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-A158E-S188D-M222Q-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-A158E-S188D-M222S-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-A232V-M222Q-Q245R,S101G-S103A-V104I-P129E-A158E-S188D-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-P129E-G159E-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-P129E-S188D-A232V-N238R-Q245R-N248D,S101G-S103A-V104I-P129E-S188D-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-S188D-A232V-Q245R-N248D-H249R,S101G-S103G-V104I-A158E-S188D-A232V-Q245R-N248D-H249R,S101G-S103S-V104I-A158E-S188D-A232V-Q245R-N248D-H249R,S101S-S103A-V104I-A158E-S188D-A232V-Q245R-N248D-H249R,S101S-S103G-V104I-A158E-S188D-A232V-Q245R-N248D-H249R,S101S-S103G-V104V-A158E-S188D-A232V-Q245R-N248D-H249R,S128N-A158E-G159E-E271F,S128N-A158E-H249R,S128N-A158E-R186H-E271F,S128N-A158E-R186H-H249R,S128N-A158E-R186H-S188D-E271F,S128N-A158E-S188D-E271F,S128N-A158E-S188D-H249R,S128N-A158E-S188D-Y209E-E271F,S128N-A158E-Y209E-,T022A-N043R-S103A-V104I-G118R-P129E-G159D-S188D-A232V-Q245R-N248D,T022A-N062E-A158E,T022A-S024R-S101D-S103A-V104I-G118R-G159D-S188D-A232V-N248D-E271F,T022A-S024R-S101D-S103A-V104I-G118R-P129E-G159D-S188D-A232V-Q245R-N248D,T022A-S024R-S101D-S103A-V104I-G159D-S188D-A232V-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-A158E-

A232V-N238R-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-A158E-A232V-Q245R-N248D-H249R,T022A-S024R-S101G-S103A-V104I-A158E-G159E-S188D-A232V-N238R-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-A158E-G159E-S188D-A232V-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-A158E-G159E-S188D-A232V-Q245R-N248D-H249R,T022A-S024R-S101G-S103A-V104I-P129E-A158E-A232V-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-P129E-A158E-A232V-Q245R-N248D-H249R,T022A-S024R-S101G-S103A-V104I-P129E-A158E-G159E-A232V-Q245R-N248D-H249R,T022A-S024R-S101G-S103A-V104I-P129E-A158E-G159E-S188D-A232V-N238R-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-P129E-A158E-S188D-A232V-N238R-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-P129E-A158E-S188D-A232V-Q245R-N248D-H249R,T022A-S024R-S101G-S103A-V104I-P129E-A232V-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-P129E-A232V-Q245R-N248D-H249R,T022A-S024R-S101G-S103A-V104I-P129E-G159E-S188D-A232V-Q245R-N248D-H249R,T022A-S024R-S101G-S103A-V104I-P129E-S188D-A232V-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-S128N-A158E-S188D-A232V-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-S128N-P129E-A158E-A232V-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-S128N-P129E-S188D-A232V-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-S128N-S188D-A232V-Q245R-N248D,T022A-S024R-S103A-V104I-G118R-G159D-S188D-L217D-A232V-N248D,T022A-S024R-S103A-V104I-P129E-G159D-S188D-A232V-N248D-E271F,T022A-S101G-S103A-V104I-A158E-G159E-S188D-A232V-Q245R-N248D-H249R,T022A-S101G-S103A-V104I-A158E-S188D-A232V-Q245R-N248D,T022A-S101G-S103A-V104I-P129E-A158E-A232V-N238R-Q245R-N248D,T022A-S101G-S103A-V104I-P129E-A158E-G159E-A232V-N238R-Q245R-N248D,T022A-S101G-S103A-V104I-P129E-A158E-S188D-A232V-Q245R-N248D-H249R,T022A-S101G-S103A-V104I-P129E-G159E-A232V-N238R-Q245R-N248D,T022A-S101G-S103A-V104I-P129E-S188D-A232V-N238R-Q245R-N248D,T022A-S101G-S103A-V104I-S128N-P129E-A232V-N238R-Q245R-N248D,T022A-S101G-S103A-V104I-S128N-P129E-S188D-A232V-N238R-Q245R-N248D,T022A-S128N-A158E-H249R,V104L-S128N-A158E-H249R,V104L-S128N-A158E-R186H-E271F,V104L-S128N-A158E-R186H-H249R,和V104L-S128N-A158E-S188D-H249R,并且其中该蛋白酶变体的总净电荷相对于迟缓芽孢杆菌枯草杆菌蛋白酶GG36蛋白酶的总净电荷为0、+1、+2、+3、+4、+5、-1、-2、-3、-4或-5,并且其中总净电荷是通过一个或多个选自以下的置换获得:N43D,R45T,N62E,N76D,S101D,P129E,A158E,G159D,G159E,S166D,S188D,A230E,N18R,G20K,G20R,T22R,S24R,N43R,G118R,Q245R,H249R,N269R,E271F,和E271L,并且其中该蛋白酶变体的氨基酸位置根据SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列中对应的氨基酸位置的编号方式来进行编号,这是通过该蛋白酶变体氨基酸序列与解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'氨基酸序列的比对来确定的。

[0320] 本发明还提供包含与SEQ ID NO:2的氨基酸序列不同的氨基酸序列的蛋白酶变体,其中该蛋白酶变体是具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:A016S-N062E-A158E-H249R-E271F,A016S-N062E-S128N-R186H-

E271F,A016S-N062E-V104L-R186H-S188D-E271F,A016S-S101A-S128N-R186H,A016S-S128N-A158E-R186H,A016S-V104L-A158E-R186H-E271F,A016S-V104L-S188D-H249R,A158E-R186H-H249R,A158E-R186H-S188D-H249R-E271F,G020K-G023A-N116L-S188D,G020K-G023A-S024F-N062E-N116L-S188D-T213A,G020K-N043W-N062E-N116L-P239G,G020K-S024F-N043W-N062E-N116L-T213A,G020K-S024F-N062E,G023A-N043W-N062E-N116L-G118R-T213A,G023A-T038F-S078N-G100S-S212M-A215D,G100S-N116L-A158E-T213A,G102A-S103N-S105T-A194E,H017R-T022A-N076D-S101G-S103A-V104I-G159D-A232V-Q245R-N248D-E271F,N043R-N076D-S101A-S103A-V104I-A158E-S166D-S188D-A232V-Q245R-N248D-H249R-E271F,N043R-S101A-S103A-V104I-A158E-S166D-S188D-A232V-Q245R-N248D-H249R,N043W-N062E-N116L-S188D,N062E-A158E-H249R-E271F,N062E-A158E-R186H-S188D-H249R,N062E-L148I-G159E,N062E-N116L-S188D,N062E-R186H-H249R,N062E-S078N-G102A-N116L-S144R-L250I,N062E-S101A-A158E-R186H-H249R,N062E-S101A-A158E-S188D-H249R,N062E-S101A-R186H,N062E-S101A-R186H-E271F,N062E-S101A-R186H-H249R-E271F,N062E-S101A-R186H-S188D-E271F,N062E-S101A-R186H-S188D-H249R,N062E-S101A-V104L-R186H-S188D-E271F,N062E-S128N-A158E,N062E-S128N-G159E-H249R,N062E-S188D-P239G,N062E-V104L-G159E-H249R,N076D-S101A-S103A-V104I-A158E-S166D-S188D-A232V-Q245R-N248D-H249R-E271F,N076D-S101A-S103A-V104I-A158E-S188D-A232V-Q245R-N248D-H249R,N076D-S101A-S103A-V104I-A158E-S188D-A232V-Q245R-N248D-H249R-E271F,N076D-S101G-S103A-V104I-A114V-A158E-S188D-A232V-Q245R-N248D-H249R-E271F,N076D-S101G-S103A-V104I-A232V-M222S-Q245R,S024F-A048R-G118R-S166D-L217E,S024F-N062E-N116L,S024F-N062E-N116L-T213A-P239G,S024F-N062E-S188D-P239G,S024F-S101D-G118R-A215D-L250I-A272F,S024R-K027R-S101G-S103A-V104I-S128L-P129Q-S130A-A158E-S188D-A232V-Q245R-N248D-H249R,S024R-N076D-S101A-S103A-V104I-A158E-S166D-S188D-A232V-Q245R-N248D-H249R-E271F,S024R-S101G-S103A-V104I-A158E-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-P129E-A158E-G159E-A232V-N238R-Q245R-N248D,S024R-S101G-S103A-V104I-P129E-A158E-G159E-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-P129E-G159E-A232V-N238R-Q245R-N248D,S024R-S101G-S103A-V104I-P129E-G159E-S188D-A232V-N238R-Q245R-N248D,S024R-S101G-S103A-V104I-P129E-L148I-A158E-S188D-A232V-Q245R-N248D,S024R-S101G-S103A-V104I-P129E-L148I-S188D-A232V-Q245R-N248D,S024R-S101G-S103A-V104I-P129Q-S130A-A158E-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-S128L-A158E-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-S128L-P129Q-S130A-A158E-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-S128N-G159E-S188D-A232V-Q245R-N248D,S078N-V104L-G118R-S128D,S101A-A158E-R186H-H249R,S101A-A158E-R186H-S188D-H249R,S101A-S103A-V104I-A158E-S166D-S188D-A232V-Q245R-N248D-H249R-E271F,S101A-S103A-V104I-A158E-S188D-A232V-Q245R-N248D-H249R-E271F,S101A-S103A-V104I-A158E-S188D-L217E-A232V-Q245R-N248D-H249R,S101A-S103A-V104I-A158E-S188D-L217E-A232V-Q245R-N248D-H249R-E271F,

S101A-S103G-A158E-R186H-H249R,S101A-S103S-V104I-A158E-S188D-A232V-Q245R-N248D-H249R,S101A-S103S-V104I-G159E-A232V-Q245R-N248D-H249R,S101A-S128N-A158E-H249R,S101A-S128N-A158E-S188D-Y209E-E271F,S101A-S128N-A158E-Y209E,S101A-S128N-P129E-R186H-H249R,S101A-V104L-A158E-R186H-H249R,S101A-V104L-A158E-R186H-S188D-E271F,S101A-V104L-S128N-A158E-R186H-E271F,S101G-S103A-V104I-A158E-A232V-N238R-Q245R-N248D,S101G-S103A-V104I-A158E-G159E-S188D-A232V-N238R-Q245R-N248D,S101G-S103A-V104I-A158E-N183D-S188D-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-A158E-S166D-S188D-A232V-Q245R-N248D-H249R-E271F,S101G-S103A-V104I-A158E-S188D-A232V-Q245R-N248D,S101G-S103A-V104I-A232V-M222S-Q245R,S101G-S103A-V104I-P129E-A158E-G159E-A232V-N238R-Q245R-N248D,S101G-S103A-V104I-P129E-A158E-G159E-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-P129E-A158E-S188D-A232V-N238R-Q245R-N248D,S101G-S103A-V104I-P129E-G159E-A232V-N238R-Q245R-N248D,S101G-S103A-V104I-P129E-S188D-A232V-Q245R-N248D,S101G-S103A-V104I-P129Q-A158E-S188D-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-P129Q-S130A-A158E-S188D-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-S128L-P129Q-A158E-S188D-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-S128L-S130A-A158E-S188D-L217E-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-S128N-P129E-A232V-N238R-Q245R-N248D,S101G-S103A-V104I-S128N-P129E-A232V-Q245R-N248D,S101G-S103A-V104I-S130A-A158E-N183D-S188D-L217E-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-S188D-A232V-N238R-Q245R-N248D,S101G-S103A-V104L-A158E-S188D-A232V-Q245R-N248D-H249R,S101S-S103A-V104I-G159E-A232V-Q245R-N248D-H249R,S101S-S103S-V104I-A158E-S188D-A232V-Q245R-N248D-H249R,S101S-S103S-V104V-A158E-S188D-A232V-Q245R-N248D-H249R,T022A-N043R-N062E-S103A-V104I-G159D-S188D-A232V-Q245R-N248D-E271F,T022A-N043R-N076D-S101G-S103A-V104I-G159D-S188D-A232V-Q245R-N248D-E271F,T022A-N043R-S101D-S103A-V104I-G118R-P129E-G159D-S188D-A232V-N248D-E271F,T022A-N043R-S101G-S103A-V104I-G159D-A232V-Q245R-N248D-E271F,T022A-N043R-S103A-V104I-G118R-G159D-S188D-A232V-N248D-E271F,T022A-N043R-S103A-V104I-G118R-G159D-S188D-L217D-A232V-N248D-E271F,T022A-N043R-S103A-V104I-G118R-S128I-P129E-G159D-S188D-A232V-N248D,T022A-N043R-S103A-V104I-P129E-G159D-S188D-A232V-Q245R-N248D,T022A-N076D-S101G-S103A-V104I-G159D-A232V-Q245R-N248D-E271F,T022A-N076D-S101G-S103A-V104I-G159D-S188D-A232V-Q245R-N248D-E271F,T022A-S024R-N043R-S101D-S103A-V104I-G159D-S188D-A232V-Q245R-N248D,T022A-S024R-N043R-S103A-V104I-G159D-S188D-L217D-A232V-N248D-E271F,T022A-S024R-S101D-S103A-V104I-G118R-S128I-G159D-S188D-A232V-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-L148I-A158E-A232V-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-P129E-A158E-G159E-A232V-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-P129E-A158E-G159E-S188D-A232V-Q245R-N248D-H249R,T022A-S024R-S101G-S103A-V104I-P129E-L148I-A232V-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-S188D-A232V-Q245R-

N248D-H249R,T022A-S024R-S103A-V104I-G118R-P129E-G159D-S188D-A232V-N248D-E271F,T022A-S024R-S103A-V104I-G159D-S188D-L217D-A232V-N248D-E271F,T022A-S024R-S103A-V104I-G159D-S188D-L217D-A232V-Q245R-N248D-E271F,T022A-S101A-A158E-R186H-H249R,T022A-S101G-S103A-V104I-A158E-G159E-A232V-N238R-Q245R-N248D,T022A-S101G-S103A-V104I-A158E-G159E-A232V-Q245R-N248D-H249R,T022A-S101G-S103A-V104I-G159D-A232V-Q245R-N248D-E271F,T022A-S101G-S103A-V104I-G159D-S188D-A232V-Q245R-N248D-H249R-E271F,T022A-S101G-S103A-V104I-G159E-S188D-A232V-N238R-Q245R-N248D,T022A-S101G-S103A-V104I-G159E-S188D-A232V-Q245R-N248D-H249R,T022A-S101G-S103A-V104I-P129E-A158E-A232V-Q245R-N248D-H249R,T022A-S101G-S103A-V104I-P129E-A158E-G159E-A232V-Q245R-N248D-H249R,T022A-S101G-S103A-V104I-P129E-A232V-N238R-Q245R-N248D,T022A-S101G-S103A-V104I-P129E-G159E-A232V-Q245R-N248D-H249R,T022A-S101G-S103A-V104I-P129E-G159E-S188D-A232V-Q245R-N248D-H249R,T022A-S103A-V104I-G118R-G159D-S188D-L217D-A232V-Q245R-N248D,T022A-S103A-V104I-G159D-S188D-A232V-N248D,T022L-L031F-G102A-S128D-T224A-N243F,T022L-T038F-V121F-S160D-A272F,V026F-S078N-G159C-R186K-N243F,V104L-A158E-H249R,V104L-A158E-R186H-H249R,V104L-A158E-R186H-H249R-E271F,V104L-A158E-R186H-S188D-H249R,V104L-A158E-R186H-S188D-H249R-E271F,V104L-A158E-S188D-H249R-E271F,V104L-S128N-A158E-R186H-S188D-E271F,V104L-S128N-G159E-E271F,V104L-S128N-R186H-S188D-H249R,和V121F-N185E-T224A-P239G,并且其中该蛋白酶变体的总净电荷相对于迟缓芽孢杆菌枯草杆菌蛋白酶GG36蛋白酶的总净电荷为0、+1、+2、+3、+4、+5、-1、-2、-3、-4或-5,并且其中总净电荷是通过一个或多个选自以下的置换获得:N43D,R45T,N62E,N76D,S101D,P129E,A158E,G159D,G159E,S166D,S188D,A230E,N18R,G20K,G20R,T22R,S24R,N43R,G118R,Q245R,H249R,N269R,E271F,和E271L,并且其中该蛋白酶变体的氨基酸位置根据SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列中对应的氨基酸位置的编号方式来进行编号,这是通过该蛋白酶变体氨基酸序列与解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'氨基酸序列的比对来确定的。

[0321] 本发明还提供包含与SEQ ID NO:2的氨基酸序列不同的氨基酸序列的蛋白酶变体,其中该蛋白酶变体是具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:A016S-S128N-R186H-E271F,N076D-S101G-S103A-V104I-A158E-S188D-M222S-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-S128L-P129Q-A158E-N183D-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-S128L-P129Q-A158E-S188D-A232V-Q245R-N248D-H249R-E271G,S024R-S101G-S103A-V104I-S128L-P129Q-S130A-A158E-N183D-S188D-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-P129Q-A158E-N183D-S188D-A232V-Q245R-N248D-H249R,T022A-N076D-S101G-S103A-V104I-G159D-A232V-Q245R-N248D-H249R-E271F,T022A-S101G-G102A-S103A-V104I-G159D-S188D-A232V-Q245R-N248D-E271F,A016S-A158E-H249R,A016S-A158E-H249R-E271F,A016S-A158E-R186H-H249R,A016S-L111V-S188D-,A016S-T022A-A158E-R186H-E271F,A048R-S078N-N116L-N185E-L217E-P239G,A048R-S128D-N185E-P239G,

A158E-R186H-H249R-E271F,E089P-S101A-P129E-R186H,G020K-G023A-N043W-N116L-S188D-T213A-P239G,G020K-G023A-N062E-N116L-G118R-T213A,G020K-G023A-S024F-N062E-S188D-T213A-P239G,G020K-K027R-P129E-S166D-P239G,G020K-S024F-N062E-P239G,G020K-S024F-T033S-P129E-A194E,G023A-G100S-A194E-S212M,G023A-N043W-N116L-G118R-S188D,G023A-S024F-G118R-S188D-P239G,G023A-S024F-K027R-N062E,G023A-S024F-N043W-N062E-N116L-G118R,G023A-S024F-N116L-G118R-S188D-T213A,G023A-S024F-N116L-S188D-P239G,K027R-G100S-G118R-S160D-S188D-N243F,K027R-S101D-S103N-S105T-A272F,N043R-N076D-S101A-S103A-V104I-A158E-S166D-S188D-A232V-Q245R-N248D-H249R,N062E-S078N-N116L-T224A,N062E-V104L-A158E-R186H-S188D-H249R,N076D-S101A-S103A-V104I-A158E-S188D-L217E-A232V-Q245R-N248D-H249R-E271F,N076D-S101G-S103A-V104I-A158E-S166D-S188D-A232V-Q245R-N248D-H249R-E271F,S024F-G102A-R186K-T213A-L217E-N243F,S024F-N043W-G118R-S188D,S024F-N043W-V104L-V121F-P129E,S024F-N116L-G118R-S188D-P239G,S024F-S103N-V104L-G118R-S188D,S024R-N043R-S101A-S103A-V104I-A158E-S188D-A232V-Q245R-N248D-H249R,S024R-N043R-S101A-S103A-V104I-A158E-S188D-L217E-A232V-Q245R-N248D-H249R,S024R-N076D-S101G-S103A-V104I-A158E-S188D-A232V-Q245R-N248D-H249R-E271F,S024R-S101G-S103A-V104I-A158E-G159E-A232V-Q245R-N248D,S024R-S101G-S103A-V104I-S128N-A158E-G159E-S188D-A232V-Q245R-N248D,S024R-S101G-S103A-V104I-S128N-P129E-S188D-A232V-Q245R-N248D,S101A-L111V-P129E,S101A-S103A-V104L-G159E-A232V-Q245R-N248D-H249R,S101A-S103S-V104L-G159E-A232V-Q245R-N248D-H249R,S101A-V104L-S128N-A158E-R186H,S101G-S103A-V104I-P129E-L148I-S188D-A232V-Q245R-N248D,S101G-S103A-V104I-S128N-P129E-A158E-A232V-N238R-Q245R-N248D,S101G-S103A-V104I-S128N-P129E-S188D-A232V-Q245R-N248D-H249R,S101G-S103S-V104L-G159E-A232V-Q245R-N248D-H249R,S101S-S103A-V104L-G159E-A232V-Q245R-N248D-H249R,S128N-P129E-R186H,T022A-A158E-R186H-H249R-E271F,T022A-S024K-S101G-S103A-V104I-S128N-A158E-G159E-A232V-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-S128N-P129E-A158E-S188D-A232V-Q245R-N248D-H249R,T022A-S024R-S103A-V104I-S128I-G159D-S188D-A232V-N248D,T022A-S101G-S103A-V104I-L148I-S188D-A232V-Q245R-N248D,T022A-S101G-S103A-V104I-S128N-G159E-A232V-Q245R-N248D,T022A-S101G-S103A-V104I-S128N-P129E-A158E-A232V-N238R-Q245R-N248D,T022A-S128N-A158E-R186H,T022A-S128N-R186H-S188D-,T022A-V104L-A158E-H249R,T022A-V104L-R186H-S188D-H249R,T022L-G023A-K027R-S101D-V104L-S216F,T022L-S078N-N116L-P129E-S256N,T022L-S078N-S128D-T213A,T033S-G118R-P129E-A194E-P239G,T033S-S105T-S188D-S216F,V026F-V104L-S256N-A272F,T022A-N043R-S103A-V104I-S128I-G159D-S188D-A232V-Q245R-N248D,T022A-S024R-N043R-S103A-V104I-G118R-G159D-S188D-L217D-A232V-N248D,T022A-S101D-S103A-V104I-G118R-G159D-S188D-L217D-A232V-Q245R-N248D-E271F,T022A-S103A-V104I-G118R-P129E-G159D-S188D-A232V-Q245R-N248D-E271F,T022A-S103A-V104I-G159D-S188D-L217D-A232V-Q245R-N248D-E271F,T022A-S103A-V104I-S128I-P129E-G159D-

S188D-A232V-N248D-E271F,T022A-S024R-S101G-S103A-V104I-P129E-L148I-A158E-S188D-A232V-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-L148I-A158E-S188D-A232V-Q245R-N248D,S101G-S103A-V104I-L148I-G159E-A232V-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-A158E-S188D-A232V-Q245R-N248D,S101G-S103A-V104I-S128N-P129E-A158E-A232V-Q245R-N248D-H249R,V104L-L148I-S188D-H249R,S024R-S101A-S103A-V104I-A158E-S166D-S188D-L217E-A232V-Q245R-N248D-H249R,N076D-S101G-S103A-V104I-S128L-A158E-S188D-A232V-Q245R-N248D-H249R-E271F,N043R-N076D-S101G-S103A-V104I-A158E-S166D-S188D-A232V-Q245R-N248D-H249R-E271F,T022A-N043R-N076D-S101G-S103A-V104I-G159D-A232V-Q245R-N248D-H249R-E271F,S101A-S103G-V104V-G159E-A232V-Q245R-N248D-H249R,S101S-S103A-V104V-G159E-A232V-Q245R-N248D-H249R,G023A-S024F-V051W-A158E,K027R-T038F-G102A-N116L,N062E-S078N-S144R-S212M,L031F-N116L-S256N-A272F,T022L-T033S-V104L-N116L-S160D-R186K,S024F-G118R-P129E-R186K-T213A,N043W-S105T-T213A-A215D-S216F,L031F-S105T-R186K-S188D,V026F-A194E-T213A-S256N,S103N-S160D-L250I-S256N,S024R-S101G-S103A-V104I-S130A-A158E-S188D-L217E-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-S128L-A158E-N183D-S188D-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-P129Q-A158E-S188D-L217E-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-S128L-S130A-A158E-S188D-A232V-Q245R-N248D-H249R,T022A-N062E-S103A-V104I-G118R-G159D-S188D-A232V-Q245R-N248D,T022A-N043R-S101D-S103A-V104I-G118R-P129E-G159D-S188D-L217D-A232V,T022A-S024R-S103A-V104I-G159D-S188D-L217D-A232V-N248D,T022A-S024R-N043R-S103A-V104I-G118R-S128I-P129E-G159D-S188D-L217D-A232V-N248D-E271F,T022A-S103A-V104I-G118R-G159D-S188D-L217D-A232V-Q245R-N248D-E271F,G020K-N043W-S188D-T213A,S024F-N062E-G118R-P239G,G023A-N043W-S188D-T213A,G020K-S024F-N043W-N062E-N116L-G118R-S188D-P239G,G020K-N116L-S188D-P239G,G020K-N043W-N062E-G118R,G020K-N043W-N116L-S188D-T213A,G020K-S024F,G023A-N043W-N116L-P239G,G023A-S024F-N043W-N116L-G118R-S188D-P239G,G020K-G023A-N043W-T213A,和G023A-S024F-N062E-G118R-T213A-P239G,并且其中该蛋白酶变体的总净电荷相对于迟缓芽孢杆菌枯草杆菌蛋白酶GG36蛋白酶的总净电荷为0、+1、+2、+3、+4、+5、-1、-2、-3、-4或-5,并且其中总净电荷是通过一个或多个选自以下的置换获得:N43D,R45T,N62E,N76D,S101D,P129E,A158E,G159D,G159E,S166D,S188D,A230E,N18R,G20K,G20R,T22R,S24R,N43R,G118R,Q245R,H249R,N269R,E271F,和E271L,并且其中该蛋白酶变体的氨基酸位置根据SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列中对应的氨基酸位置的编号方式来进行编号,这是通过该蛋白酶变体氨基酸序列与解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'氨基酸序列的比对来确定的。

[0322] 本发明还提供包含与SEQ ID NO:2的氨基酸序列不同的氨基酸序列的蛋白酶变体,其中该蛋白酶变体是具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:G118R-Y209A,G118R-Y209A-N243F,L021M-S024R-T033S,P005S-S078R-G118R-W241R,P086W-G118R-A133V,P086W-G118R-N243F,P086W-G118R-Y209A,

P086W-Y209A-N243F,S024R-A174T,S024R-G118R,S024R-G118R-Y209A,S024R-G118R-Y209A-K235F,S024R-G118R-Y209A-N243F,S024R-K235F,S024R-P086R,S024R-P086S-S141G,S024R-P086W,S024R-P086W-G118R,S024R-P086W-G118R-V203I,S024R-P086W-N243F,S024R-P086W-Y209A,S024R-S078R-P086W,S024R-S078R-P086W-G118R-A270T,S024R-S078R-P086W-N243F,S024R-T033S-A133V,S024R-T033S-G118R,S024R-T033S-P086S-S085N-K235F,S024R-T033S-P086S-S087N-Y209A,S024R-T033S-P086W,S024R-T033S-P086W-G118R,S024R-T033S-S078R-P086W,S024R-T033S-S078R-P086W-G118R,S024R-T033S-S078R-Y209A,S024R-T033S-W241R,S024R-T033S-Y209A-K235F,S024R-Y209A-W241R,S078R-G118R,S078R-P086W-K235F,S078R-P086W-N243F,S078R-P086W-Y209A,S078R-Y209A-K235F,T033S-A172V-Y209A,T033S-G118R,T033S-G118R-G159D-Y209A,T033S-G118R-N243F,T033S-G118R-W241R,T033S-G118R-Y209A-N243F,T033S-K235F,T033S-P086W-G118R,T033S-P086W-G118R-Y209A-N243F,T033S-P086W-N243F,T033S-S078R-P086W,T033S-S078R-P086W-G118R-Y209A,T033S-S078R-Y209A,T033S-Y209A-N243F,Y209A-W241R,A001R-S009A-N043R,A001R-S101G-S103A-V104I-A232V-Q245R,A001T-N018R-S024R-N076D-N116A-T213A-H249R,A194F-G211Q-Q236N,E089I-N116A-N117F-T224A-H249R,G020R-G025R-N116A-Y167W,G020R-H249R-N269R,G020R-N043D-N076D-A230E-H249R,G020R-N043D-S078R-S101G-S103A-V104I-A232V-Q245R,G020R-N043D-S101G-S103A-V104I-A232V-Q245R,G020R-N043D-S101G-S103A-V104I-A232V-Q245R-N269R,G020R-N043R-A230E,G020R-N043R-A230E-S242R,G020R-N043R-E271L,G020R-N043R-H249R,G020R-N043R-H249R-E271L,G020R-N043R-N269R,G020R-N043R-R045T-A230E,G020R-N043R-R045T-S101A-N269R,G020R-N043R-R045T-S242R,G020R-N043R-S101A-N116A-T213A-A215F,G020R-N043R-S101A-N269R,G020R-N043R-S101G-S103A-V104I-A232V-Q245R,G020R-N043R-S212F,G020R-N043R-S212F-W241R,G020R-N043R-S242R,G020R-N043R-S242R-E271L,G020R-N043R-S242R-H249R,G020R-N043R-V244R,G020R-N043R-W241R,G020R-N062Q-E089I-R186K-S212M,G020R-N076D,G020R-N076D-S101G-S103A-V104I-A232V-Q245R,G020R-N076D-S101G-S103A-V104I-A232V-Q245R-N269R,G020R-N116A-N269R,G020R-P052N-N062Q-Y091F-Y192W,G020R-Q059A-S144R-Y192W-T224A,G020R-S024R-K27E-N043R-N076D-A230E,G020R-S024R-N043D-H249R,G020R-S024R-N043D-N076D-S078R-S101G-S103A-V104I-A232V-Q245R,G020R-S024R-N043D-S242R,G020R-S024R-N043R-R045T,G020R-S024R-N043R-R045T-H249R,G020R-S024R-N043R-R045T-N116A,G020R-S024R-N043R-R045T-N116A-T213A,G020R-S024R-N043R-R045T-S101A-N269R,G020R-S024R-N043R-R045T-S101A-T213A,G020R-S024R-N043R-S242R,G020R-S024R-N076D-H249R,G020R-S024R-N116A,G020R-S024R-N116A-A215F,G020R-S024R-N116A-T213A,G020R-S024R-N116A-T213A-A215F,G020R-S024R-P052N-Q059A-S216F,G020R-S024R-R045T-A230E-S242R,G020R-S024R-R045T-N116A-N269R,G020R-S024R-R045T-N269R,G020R-S024R-S101A-A215F,G020R-S024R-S101A-N116A,G020R-S024R-S101G-S103A-V104I-L217E-A232V-Q245R-H249R,G020R-S024R-S242R-H249R,G020R-S024R-T213A,G020R-S024R-T213A-A215F,G020R-S078R-S101A-S103A-V104I-N116A-N183D-T213A-A232V-Q245R,G020R-S078R-S101G-A232V-

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[0323] 本发明还提供包含与SEQ ID NO:2的氨基酸序列不同的氨基酸序列的蛋白酶变体,其中该蛋白酶变体是具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:S101G-S103A-V104I-A232V-Q236H-Q245R-N252K,S101G-S103A-V104I-A232V-Q245R-N248R,S101G-S103A-V104I-G159R-A232V-Q245R-N248D,A232V-Q245R,E089I-N117F-N185I-A215F-L233C,G020R-E089I-L217E,G020R-G023A-V104L-Y192W-L233C,G020R-N043D-R045T-N076D-S242R-H249R,G020R-N043D-R045T-S078R-S101G-S103A-V104I-A232V-Q245R,G020R-N043D-S101G-S103A-V104I-A232V-Q245R-H249R,G020R-N043R-N076D-A230E-H249R,G020R-N043R-N076D-S101G-S103A-V104I-A232V-Q245R-N269R,G020R-N116A-A215F-N269R,G020R-R045T-N076D-S101G-S103A-V104I-A232V-Q245R,G020R-R045T-N076D-S101G-S103A-V104I-A232V-Q245R-H249R,G020R-R045T-N116A-N269R,G020R-R045T-S101G-S103A-V104I-A232V-Q245R,G020R-

S024R-A215F,G020R-S024R-K27R-N043D-S242R-H249R,G020R-S024R-N043D-N076D-S078R-S101G-S103A-V104I-A232V-Q245R-N269R,G020R-S024R-N043R-N076D,G020R-S024R-N043R-R045T-A215F,G020R-S024R-N043R-R045T-N076D-S242R-H249R,G020R-S024R-N043R-R045T-N116A-T213A-A215F,G020R-S024R-N076D-S101G-S103A-V104I-A232V-Q245R,G020R-S024R-T38I-N043R-R045T-N076D-S242R-H249R,G020R-S078R-S101A-S103A-V104I-A232V-Q245R,G020R-S078R-S101A-S103A-V104I-G211Q-T213A-A232V-Q245R,G020R-S078R-S101A-S103A-V104I-N116A-N183D-A232V-Q245R,G020R-S078R-S101A-S103A-V104I-N116A-N183D-G211Q-A232V-Q245R,G020R-S078R-S101A-S103A-V104I-N116A-N183D-G211Q-T213A-A215F-A232V-Q245R,G020R-S078R-S101A-S103A-V104I-N116A-N183D-G211Q-T213A-A232V-Q245R,G020R-S078R-S101A-S103A-V104I-N116A-N183D-I198L-A215F-A232V-Q245R,G020R-S078R-S101A-S103A-V104I-N183D-A215F-A232V-Q245R,G020R-S078R-S101G-S103A-V104I-N116A-A131V-N183D-T213A-A232V-Q245R,G020R-S078R-S101G-S103A-V104I-N116A-N183D-G211Q-T213A-A215F-A232V,G020R-S078R-S101G-S103A-V104I-N116A-N183D-G211Q-T213A-A215F-A232V-Q245R,G020R-S078R-S101G-S103A-V104I-N116A-N183D-T213A-A232V-Q245R,G020R-S078R-S101G-S103A-V104I-N183D-G211Q-T213A-A232V-Q245R-E271G,G020R-S078R-S101G-S103A-V104I-T180A-A232V-Q245R,G020R-S101A-S103A-V104I-N116A-N183D-G211Q-T213A-A215F-A232V-Q245R,G020R-S101A-S103A-V104I-N116A-N183D-T213A-A232V-Q245R,G020R-S101A-S103A-V104I-T213A-A215F-A232V-Q245R,G020R-S101A-S103G-V104V-A232V-Q245R,G020R-S101G-S103A-V104I-N116A-A232V-Q245R,G020R-S101G-S103A-V104I-N116A-G211Q-A232V-Q245R,G020R-S101G-S103A-V104I-N183D-G211Q-A232V-Q245R-,G020R-S103A-V104I-A232V-Q245R,G020R-S242R-H249R,G020R-T022W-S078R-S101A-S103A-V104I-A232V-Q245R,G020R-T022W-S078R-S101A-S103A-V104I-I198L-A232V-Q245R,G020R-T022W-S078R-S101A-S103A-V104I-N116A-N183D-G211Q-T213A-A215F-A232V-Q245R,G020R-T022W-S078R-S101A-S103A-V104I-N116A-N183D-T213A-A215F-A232V-Q245R,G020R-T022W-S078R-S101A-S103A-V104I-N183D-I198L-T213A-A215F-A232V-Q245R,G020R-T022W-S078R-S101G-S103A-V104I-G211Q-T213A-A232V-Q245R,G020R-T022W-S078R-S101G-S103A-V104I-N116A-N183D-A215F-A232V-Q245R,G020R-T022W-S101A-N116A-I198L-G211Q-T213A-A215F-H249R,G020R-T022W-S101A-S103A-V104I-A215F-A232V-Q245R,G020R-T022W-S101A-S103A-V104I-A232V-Q245R,G020R-T022W-S101A-S103A-V104I-G211Q-A232V-Q245R,G020R-T022W-S101A-S103A-V104I-G211Q-T213A-A232V-Q245R,G020R-T022W-S101A-S103A-V104I-I198L-G211Q-A215F-A232V-Q245R,G020R-T022W-S101A-S103A-V104I-N116A-G211Q-A215F-A232V-Q245R,G020R-T022W-S101A-S103A-V104I-N116A-G211Q-A232V-Q245R,G020R-T022W-S101A-S103A-V104I-N116A-G211Q-T213A-A215F-A232V-Q245R,G020R-T022W-S101A-S103A-V104I-N116A-N183D-A232V-Q245R,G020R-T022W-S101A-S103A-V104I-N116A-N183D-G211Q-A232V-Q245R,G020R-T022W-S101A-S103A-V104I-N116A-N183D-G211Q-T213A-A232V-Q245R,G020R-T022W-S101G-S103A-V104I-A114T-T213A-A215F-A232V-Q245R,G020R-T022W-S101G-S103A-V104I-G211Q-T213A-A215F-A232V-Q245R,

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通过一个或多个选自以下的置换获得:N43D,R45T,N62E,N76D,S101D,P129E,A158E,G159D,G159E,S166D,S188D,A230E,N18R,G20K,G20R,T22R,S24R,N43R,G118R,Q245R,H249R,N269R,E271F,和E271L,并且其中该蛋白酶变体的氨基酸位置根据SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列中对应的氨基酸位置的编号方式来进行编号,这是通过该蛋白酶变体氨基酸序列与解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'氨基酸序列的比对来确定的。

[0324] 本发明还提供包含与SEQ ID NO:2的氨基酸序列不同的氨基酸序列的蛋白酶变体,其中该蛋白酶变体是具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:A015T-T033S,A016T-N043R-R045T-N076D-S101G-S103A-V104I-A232V-Q245R-N269R,A230E-H249R,A232V-H249R,E089I-S105T-N116A-A215F-S216F,E089I-Y091F-N185I-G211Q-A270C,G020R-A090S-S101G-S103A-V104I-N116A-N183D-T213A-A215F-A232V-Q245R,G020R-N043D-S078R-S101G-S103A-V104I-A232V-Q245R-H249R,G020R-N043R-N076D,G020R-N043R-R045T-S078R-S101G-S103A-V104I-A232V-Q245R,G020R-P052N-S101A-I198L-L233C,G020R-R045T-N076D-S078R-S101G-S103A-V104I-A232V-Q245R-N269R,G020R-S024R-N043D-N076D-H249R,G020R-S024R-N043D-N076D-S242R-H249R,G020R-S024R-N043D-R045T-A230E-S242R,G020R-S024R-N043D-S078R-S101G-S103A-V104I-A232V-Q245R,G020R-S024R-N043D-S078R-S101G-S103A-V104I-A232V-Q245R-H249R,G020R-S024R-N043R-S101G-S103A-V104I-A232V-Q245R,G020R-S024R-N076D-S078R-S101G-S103A-V104I-A232V-Q245R-H249R,G020R-S024R-R045T-N076D-S101G-S103A-V104I-A232V-Q245R,G020R-S024R-R045T-N076D-S242R-H249R,G020R-S024R-R045T-S101G-S103A-V104I-A232V-Q245R,G020R-S078R-S101A-S103A-V104I-G115E-N116A-N183D-G211Q-T213A-A232V-Q245R,G020R-S101A-S103A-V104I-N116A-N183D-A215F-A232V-Q245R,G020R-S101A-S103A-V104I-N116A-N183D-A232V-Q245R,G020R-S101A-S103A-V104I-N116A-N183D-G211Q-A232V-Q245R,G020R-S101A-S103A-V104I-N116A-N183D-G211Q-A232V-Q245R-T274I,G020R-S101A-S103A-V104I-N116A-N183D-I198L-G211Q-T213A-A215F-A232V-Q245R,G020R-S101A-S103A-V104I-N116A-N183D-T213A-A215F-A232V-Q245R,G020R-S101A-S103A-V104I-T213A-A232V-Q245R,G020R-S101G-S103A-V104I-N116A-N183D-A232V-Q245R,G020R-S101G-S103A-V104I-N116A-N183D-G211Q-A215F-A232V-Q245R,G020R-S101G-S103A-V104I-N116A-N183D-G211Q-A232V-Q245R,G020R-S101G-S103A-V104I-N116A-N183D-G211Q-T213A-A215F-A232V-Q245R,G020R-S101G-S103A-V104I-N116A-N183D-G211Q-T213A-A232V-Q245R,G020R-S101G-S103A-V104I-N116A-N183D-T213A-A232V-Q245R,G020R-T022R-N269R,G020R-T022R-S078R-S212F-W241R,G020R-T022W-S101A-S103A-V104I-N116A-N183D-A215F-A232V-Q245R,G020R-T022W-S101A-S103A-V104I-N116A-N183D-A232V-Q245R-N269S,G020R-T022W-S101A-S103A-V104I-N116A-N183D-A232V-Q245R-T274I,G020R-T022W-S101A-S103A-V104I-N116A-N183D-G211Q-A215F-A232V-Q245R,G020R-T022W-S101A-S103A-V104I-N116A-N183D-I198L-G211Q-T213A-A215F-A232V-Q245R,G020R-T022W-S101A-S103A-V104I-N116A-N183D-T213A-A232V-Q245R,G020R-T022W-S101A-S103A-V104I-N183D-G211Q-T213A-A215F-A232V-Q245R,G020R-T022W-

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H249R,N018R-T022W-S024R-N076D-N183D-I198L-G211Q-H249R,N018R-G020R-S024R-N076D-N183D-T213A-H249R,N018R-S024R-N076D-S101A-N183D-G211Q-A215F-H249R,N018R-G020R-T022W-S024R-N076D-N116A-G211Q-T213A-H249R,N018R-S078R-S101G-S103A-V104I-A232V-Q245R-N269R,N018R-T022W-S024R-N076D-S101A-N116A-N183D-G211Q-A215F-H249R-T260A,N076D-H249R,N018R-T022W-S024R-N076D-N183D-G211Q-A215F-H249R,N018R-G020R-S024R-N076D-N116A-G211Q-A215F-H249R,N018R-G020R-S024R-N076D-T213A-H249R,N018R-G020R-T022W-S024R-N076D-N116A-N183D-I198L-H249R,N018R-G020R-T022W-S024R-N076D-S101A-N183D-H249R,N076D-V104I-H249R,G020R-T022W-S101A-S103A-V104I-N116A-N183D-G211Q-T213A-A215F-A232V-Q245R,S024R-N043R-R045T-S078R-S101G-S103A-V104I-L217E-A232V-Q245R,N018R-G020R-T022W-S024R-N076D-N183D-I198L-A215F-H249R,N018R-N076D-S101G-S103A,G020R-S024R-S101G-S103A-V104I-A232V-Q245R-N269R,N018R-G020R-S024R-N076D-S101A-N116A-N183D-G211Q-H249R,S101G-S103A-A232V,S024R-N076D-S101G-A232V,N018R-T022W-S024R-N076D-S101A-N183D-I198L-G211Q-H249R,N018R-G020R-S024R-N076D-S101A-N183D-I198L-G211Q-A215F-H249R,N018R-G020R-S024R-N076D-N183D-I198L-H249R,N018R-T022W-S024R-N076D-S101A-N116A-N183D-I198L-G211Q-H249R,N018R-G020R-S024R-N076D-N116A-A156V-N183D-G211Q-A215F-H249R-N269S,R045T-N076D-S101G-S103A-V104I-A232V-Q245R-H249R,N018R-G020R-S024R-N076D-S101A-N183D-I198L-H249R,N018R-G020R-T022W-S024R-N076D-I198L-G211Q-A215F-H249R,N018R-G020R-T022W-S024R-N076D-S101A-N116A-I198L-G211Q-A215F-H249R,N018R-G020R-T022W-S024R-N076D-N116A-H249R,N018R-N076D-S101G,N018R-S024R-N076D-N116A-N183D-I198L-T213A-A215F-H249R,N018R-G020R-T022W-S024R-N076D-S101A-N116A-I198L-T213A-A215F-H249R,N018R-S024R-N076D-S101A-N116A-N183D-I198L-G211Q-H249R,N018R-N076D-A232V,N018R-G020R-S024R-N076D-S101A-A232V-Q245R,N018R-N043D-R045T-N076D-S101G-S103A-V104I-A232V-Q245R,N018R-T022W-S024R-N076D-N183D-T213A-A215F-H249R,N018R-S024R-N076D-S101A-N116A-G211Q-T213A-N237D-H249R,N018R-G020R-S024R-N076D-S101A-N116A-N183D-G211Q-H249R-R275S,N018R-T022W-S024R-N076D-S101A-N116A-N183D-I198L-G211Q-T213A-A215F-H249R,S024R-N076D,N018R-S024R-N076D-N183D-G211Q-A215F-H249R,N018R-T022W-S024R-N076D-N116A-N183D-I198L-T213A-A215F-H249R,N076D-V104I-A232V-H249R,N018R-N076D-S103A-A232V,N018R-G020R-S024R-N076D-S101A-N116A-N183D-I198L-G211Q-T213A-H249R,N018R-G020R-S024R-N076D-S101A-N183D-T213A-H249R,N018R-G020R-S024R-N076D-S101A-D175E-N183D-G211Q-A215F-H249R,N018R-G020R-N043D-S078R-S101G-S103A-V104I-L217E-A232V-Q245R-A273E,G020R-S024R-N043D-R045T-N076D-S101G-S103A-V104I-A232V-Q245R,P005S-S101G-S103A-V104I-A232V-Q245R-H249R,S103A-V104I-A232V,N018R-G020R-S024R-V068A-N076D-S101A-N116A-T213A-A215F-H249R,N018R-T022W-S024R-N076D-S101A-I198L-A215F-H249R-R275S,N018R-S024R-N076D-N183D-I198L-G211Q-T213A-H249R,N043D-R045T-S101G-S103A-V104I-A232V-Q245R,N018R-S024R-N076D-L217E-S242R-H249R,N076D-S087D-S101G-S103A-V104I-A232V-

Q245R,S087D-S101G-S103A-V104I-A232V-Q245R,和S101G-S103A-V104I-V150L-A232V-S242R-Q245R,并且其中该蛋白酶变体的总净电荷相对于迟缓芽孢杆菌枯草杆菌蛋白酶GG36蛋白酶的总净电荷为0、+1、+2、+3、+4、+5、-1、-2、-3、-4或-5,并且其中总净电荷是通过一个或多个选自以下的置换获得:N43D,R45T,N62E,N76D,S101D,P129E,A158E,G159D,G159E,S166D,S188D,A230E,N18R,G20K,G20R,T22R,S24R,N43R,G118R,Q245R,H249R,N269R,E271F,和E271L,并且其中该蛋白酶变体的氨基酸位置根据SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列中对应的氨基酸位置的编号方式来进行编号,这是通过该蛋白酶变体氨基酸序列与解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'氨基酸序列的比对来确定的。

[0325] 在另一个方面,发明人发现优选的蛋白酶包含至少一个、或甚至两个或多个选自以下的带电突变:N062E,S101D,P129E,A158E,G159D/E,S166D,和/或S188D。此类蛋白酶对于掺入到这样的洗涤剂组合物中是尤其优选的,该洗涤剂组合物适用于加入水中来制成优选地具有低离子强度或低洗涤剂浓度的洗涤液体。因此,在本发明的一个优选方面,这些蛋白酶将构成洗涤剂组合物的一部分,该洗涤剂组合物为了手动洗涤或机器洗涤过程而加入水中(通常是洗衣机内的水中),以形成洗涤液体,其电导率为约0.1mS/cm至约3mS/cm,约0.3mS/cm至约2.5mS/cm,或甚至约0.5mS/cm至约2mS/cm。

[0326] 在另一个方面,此类蛋白酶包含至少一个,或甚至两个或多个选自以下的带电突变:N062E,S101D,P129E,A158E,G159D/E,S166D,和/或S188D,所述蛋白酶相对于SEQ ID NO:1的酶具有0、-1、-2、-3、-4或-5的电荷,优选地0、-1、-2或-3,最优选地-1或-2。

[0327] 根据本发明,用于本发明的尤其优选的蛋白酶:

[0328] (a)包含一个或多个选自以下的带电突变:N062E,S101D,P129E,A158E,G159D/E,S166D,和/或S188D;

[0329] (b)相对于SEQ ID NO:1的酶具有0、-1、-2、-3、-4或-5的电荷,优选地0、-1、-2或-3,最优选地-1或-2;以及

[0330] (c)包含一个、两个、三个或多个旨在达到所需的净电荷的突变,所述突变选自G20K,S024R,G118R,Q245R,H249R和/或E271F/L。

[0331] 所谓"旨在达到所需的净电荷的突变"旨在表示当该酶变体与迟缓芽孢杆菌枯草杆菌蛋白酶GG36蛋白酶比较时,可通过选择一个或多个另外的突变,优选地选自指定的突变,例如上述(c)中所列出的突变,来将该变体相对于迟缓芽孢杆菌枯草杆菌蛋白酶GG36的总净电荷调整至优选的范围内。

[0332] 优选地,这些优选的蛋白酶构成洗涤剂组合物的一部分,该洗涤剂组合物在手动或机器洗涤过程加入水中(通常是洗衣机内的水中),以形成洗涤液体,其电导率为约0.1mS/cm至约3mS/cm,约0.3mS/cm至约2.5mS/cm,或甚至约0.5mS/cm至约2mS/cm。

[0333] 不希望受理论的束缚,但认为这些旨在达到所需的净电荷的突变通过确保该分子对于低离子强度条件或具有低洗涤剂浓度的洗涤液体的最佳电荷来提供增强的总体蛋白酶性能—仅通过某些突变(其中这些突变是优选的)的仔细组合即可获得此类优选的蛋白酶。

[0334] 在另一个方面,发明人发现优选的蛋白酶包含至少一个或两个或多个选自以下的带电突变:N018R,G020K/R,T022R,S024R,N043R,Q245R,H249R和/或N269R。此类蛋白酶对于

掺入到这样的洗涤剂组合物中是尤其优选的，该洗涤剂组合物将被加入水中来制成优选地具有高离子强度或高洗涤剂浓度的洗涤液体。例如这些优选的蛋白酶可以构成洗涤剂组合物的一部分，该洗涤剂组合物为了手动洗涤或机器洗涤而加入水中(通常是洗衣机内的水中)，以形成洗涤液体，其电导率为大于约3mS/cm至约30mS/cm，约3.5mS/cm至约20mS/cm，或甚至约4mS/cm至约10mS/cm。

[0335] 在另一个方面，此类蛋白酶包含至少一个，或两个或甚至更多个选自以下的带电突变:N018R,G020K/R,T022R,S024R,N043R,Q245R,H249R和/或N269R，所述蛋白酶相对于SEQ ID NO:1的酶具有0、+1、+2、+3、+4或+5的电荷，优选地+1、+2或+3，最优选地+2。

[0336] 尤其优选的蛋白酶：

[0337] (a)包含一个或两个或多个选自以下的带电突变:N018R,G020K/R,T022R,S024R,N043R,Q245R,H249R和/或N269R；

[0338] (b)相对于SEQ ID NO:1的酶具有0、+1、+2、+3、+4或+5的电荷，优选地+1、+2或+3，最优选地+2；以及

[0339] (c)包含旨在达到所需的净电荷的突变，所述突变选自:N043D,R045T,N076D和/或A230E。

[0340] 优选地，这些蛋白酶构成这样的洗涤剂组合物的一部分，该洗涤剂组合物在手动或机器洗涤过程加入水中(通常是洗衣机内的水中)，以形成洗涤液体，其电导率为大于约3mS/cm至约30mS/cm，约3.5mS/cm至约20mS/cm，或甚至约4mS/cm至约10mS/cm。

[0341] 不希望受理论的束缚，但认为这些旨在达到所需的净电荷的突变在高离子强度或高洗涤剂浓度条件下提供增强的总体蛋白酶性能—仅通过某些突变(其中这些突变是优选的)的仔细组合即可获得此类优选的蛋白酶。

[0342] 本发明还提供包含具有以下特性中的一者或多者的蛋白酶变体的多肽:a)测试方法2性能指数为至少1.1、至少1.2、至少1.3、至少1.4、至少1.5、至少1.6、至少1.7、至少1.8、至少1.9、至少2、1.1至约10、1.1至约8或甚至1.1至约5；b)测试方法3性能指数为至少1.1、至少1.2、至少1.3、至少1.4、至少1.5、至少1.6、至少1.7、至少1.8、至少1.9、至少2、1.1至约10、1.1至约8或甚至1.1至约5；c)测试方法4性能指数为至少1.0、至少1.1、至少1.2、至少1.3、至少1.4、至少1.5、至少1.6、至少1.7、至少1.8、至少1.9、至少2、1.0至约10、1.0至约8或甚至1.0至约5；和/或d)测试方法6性能指数为至少1.0、至少1.1、至少1.2、至少1.3、至少1.4、至少1.5、至少1.6、至少1.7、至少1.8、至少1.9、至少2、1.0至约10、1.0至约8或甚至1.0至约5。测试方法2、测试方法3、测试方法4和测试方法6在下文的实例1题为“测试方法”的章节中明确地进行了描述。

[0343] 本发明的核酸

[0344] 本发明提供分离的、非天然存在的或重组的核酸(在本文中也称为“多核苷酸”)，其可统称为“本发明的核酸”或“本发明的多核苷酸”，其编码本发明的多肽。本发明的核酸(包括下文描述的全部核酸在内)可用于本发明多肽的重组生产(如表达)，通常是通过表达包含编码目的多肽或其片段的序列的质粒表达载体来进行。如上面所论述，多肽包括变体蛋白酶多肽，包括具有酶活性(如蛋白水解活性)的变体枯草杆菌蛋白酶多肽在内，其可用于清洁应用和清洁组合物，以供清洁需要进行清洁的物品或表面(如物品的表面)。

[0345] 在一些实施例中，本发明提供分离的、重组的、基本上纯的或非天然存在的核酸，

该核酸包含编码在以上题为“本发明的多肽”的章节中以及本文其他地方描述的任何本发明多肽(包括任何融合蛋白等)的核苷酸序列。本发明还提供分离的、重组的、基本上纯的或非天然存在的核酸,该核酸包含编码以上和本文其他地方描述的任何本发明多肽中的两种或更多种的组合的核苷酸序列。

[0346] 还提供分离的、重组的、基本上纯的或非天然存在的核酸,其包含编码具有蛋白水解活性的变体蛋白酶的多核苷酸序列,所述变体蛋白酶(如变体枯草杆菌蛋白酶)包含与SEQ ID NO:2的氨基酸序列相差不超过50、不超过40、不超过30、不超过35、不超过25、不超过20、不超过19、不超过18、不超过17、不超过16、不超过15、不超过14、不超过13、不超过12、不超过11、不超过10、不超过9、不超过8、不超过7、不超过6、不超过5、不超过4、不超过3、不超过2或不超过1个氨基酸残基的氨基酸序列,其中该变体枯草杆菌蛋白酶的氨基酸位置根据SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列中对应的氨基酸位置的编号方式来进行编号,这是通过该变体蛋白酶氨基酸序列与解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'氨基酸序列的比对来确定的。

[0347] 本发明提供编码芽孢杆菌属枯草杆菌蛋白酶的枯草杆菌蛋白酶变体的核酸,其中该枯草杆菌蛋白酶变体是具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:X1R,X2W,X2M,X2R,X2A,X2S,X3R,X4R,X4C,X4S,X8A,X9F,X9W,X9A,X10S,X10M,X10H,X10A,X12R,X12F,X14K,X14F,X14Q,X15R,X15F,X16S,X17R,X17M,X17F,X18R,X18K,X20F,X20R,X20K,X22Y,X22A,X22R,X22V,X22Q,X22W,X22L,X23F,X23S,X23A,X24W,X24R,X24H,X24F,X24Q,X24L,X25V,X25F,X25R,X26F,X27V,X27F,X27L,X27R,X28N,X28E,X28A,X29T,X30E,X31F,X33D,X33G,X33S,X34P,X35M,X36F,X36R,X36T,X38L,X38F,X38R,X40L,X40W,X40N,X40R,X40T,X40H,X42I,X43D,X43I,X43R,X43M,X43F,X43W,X43S,X43A,X45T,X46R,X48R,X50C,X51H,X51W,X51F,X52F,X52E,X52N,X55Y,X57R,X59R,X59A,X59F,X60A,X60Q,X60P,X62E,X62Q,X63I,X63V,X63T,X63P,X63D,X63M,X63H,X63Q,X63E,X63A,X63S,X64F,X64T,X68C,X68A,X69N,X69P,X69W,X69T,X71G,X72C,X74C,X75F,X75A,X75R,X75E,X76D,X78I,X78R,X78N,X79W,X79Q,X81R,X82V,X82T,X82F,X82M,X82R,X85M,X86L,X86I,X86W,X89P,X89T,X89V,X89G,X89W,X89H,X89F,X89L,X89I,X91N,X91F,X92F,X94N,X99G,X99F,X99M,X99T,X99P,X100I,X100S,X100N,X100Q,X101N,X101A,X101G,X101P,X101F,X101E,X101T,X101D,X102H,X102N,X102E,X102T,X102A,X103G,X103D,X103N,X104D,X104E,X104I,X104L,X105Q,X105E,X105T,X106F,X106V,X106G,X106E,X106T,X106D,X106A,X107F,X107M,X108G,X108I,X109M,X111V,X111I,X112V,X112L,X112Q,X114G,X115K,X115R,X116A,X116K,X116L,X117F,X118I,X118R,X119C,X120F,X120A,X120R,X121E,X121F,X123G,X123E,X124S,X128F,X128H,X128I,X128L,X128Q,X128N,X128M,X128D,X129E,X132E,X132A,X138G,X144R,X147L,X148I,X158E,X158E,X159E,X159C,X160D,X166D,X166E,X167W,X175V,X177C,X181A,X182R,X183F,X183I,X183D,X183R,X183M,X185E,X185I,X185V,X186H,X186K,X188R,X188E,X188D,X192H,X192W,X194V,X194F,X194E,X197F,X198L,X198F,X203E,X203C,X208S,X209N,X209F,X209E,X209S,X209H,X209G,X209T,X209L,X210R,X210V,X210L,X211R,X211Q,X212I,X212M,X212F,X213A,X214F,X215F,X215N,X215D,X215H,X215E,X216F,X216A,X217N,X217E,X217D,X218P,X218D,X218E,X224A,X224G,X227I,X230E,X231I,X231C,X233C,

X234F,X235F,X236F,X236N,X238L,X238K,X238R,X239K,X239S,X239T,X239G,X239H,X239R,X239N,X239F,X240R,X241R,X242L,X242R,X243R,X243F,X244R,X246S,X248I,X248V,X248R,X249R,X249T,X250I,X251S,X251R,X252I,X252F,X252H,X252R,X253F,X253I,X253R,X254C,X256N,X258R,X260V,X260I,X262H,X262D,X263F,X265F,X267N,X267V,X267M,X269I,X269R,X270C,X271F,X271V,X271I,X271P,X271H,X271M,X271T,X271L,X271A,X272F,X272R,X272F,X273I,X273F,和X274G,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0348] 本发明提供编码芽孢杆菌属枯草杆菌蛋白酶的核酸,其中该枯草杆菌蛋白酶变体是具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:X16S,X18R,X20R,X22A,X24R,X43R/D,X45T,X76D,X101A,X103G,X104L,X111V,X128N,X148I,X230E,X242R,和X249R,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0349] 本发明提供编码芽孢杆菌属枯草杆菌蛋白酶的核酸,其中该枯草杆菌蛋白酶变体是具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:X1R,X230E,X271L,X115R,X20R,X249R,X235F,X27V/F/L,X75E,X82R,X18R,X269R,X43D,X43R,X76D,X45T,X212F,X242R,X24R,X78R,X9A,X22R,X121E,X244R,X28E,X30E,X4R,和X241R,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ IDNO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0350] 本发明提供编码芽孢杆菌属枯草杆菌蛋白酶的核酸,其中该枯草杆菌蛋白酶变体是具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:X062E-X158E,X103G-X158E,X128N-X158E,X016S-X158E,X104L-X158E,X089P-X158E,X111V-X158E,X022A-X158E,X101A-X158E,X148I-X158E,X129E-X158E,X022A-X089P,X016S-X089P,X062E-X089P,X062E-X271F,X158E-X271F,X186H-X271F,X129E-X271F,X111V-X271F,X209E-X271F,X016S-X271F,X188D-X271F,X022A-X271F,X159E-X271F,X104L-X271F,X101A-X271F,X089P-X271F,X128N-X271F,X103G-X271F,X148I-X271F,X249R-X271F,X062E-X159E,X016S-X159E,X128N-X159E,X148I-X159E,X111V-X159E,X089P-X159E,X022A-X159E,X129E-X159E,X103G-X159E,X104L-X159E,X158E-X159E,X101A-X159E,X158E-X249R,X111V-X249R,X129E-X249R,X062E-X249R,X016S-X249R,X186H-X249R,X148I-X249R,X159E-X249R,X101A-X249R,X188D-X249R,X104L-X249R,X209E-X249R,X022A-X249R,X128N-X249R,X103G-X249R,X089P-X249R,X022A-X111V,X101A-X111V,X016S-X111V,X104L-X111V,X062E-X111V,X103G-X111V,X089P-X111V,X016S-X148I,X062E-X148I,X022A-X148I,X129E-X148I,X104L-X148I,X103G-X148I,X128N-X148I,X101A-X148I,X089P-X148I,X111V-X148I,X016S-X062E,X022A-X062E,X062E-X129E,X022A-X129E,X128N-X129E,X016S-X129E,X101A-X129E,X104L-X129E,X089P-X129E,X103G-X129E,X111V-X129E,X062E-X186H,X128N-X186H,X101A-X186H,X022A-X186H,X016S-X186H,X158E-X186H,X089P-X186H,X129E-X186H,X159E-X186H,X103G-X186H,X104L-X186H,X111V-X186H,X148I-X186H,X062E-X101A,X022A-X101A,X016S-X101A,X089P-X101A,X062E-X103G,X022A-X103G,X016S-X103G,X101A-X103G,

X089P-X103G,X062E-X128N,X016S-X128N,X022A-X128N,X101A-X128N,X104L-X128N,X089P-X128N,X103G-X128N,X111V-X128N,X111V-X188D,X062E-X188D,X016S-X188D,X148I-X188D,X022A-X188D,X128N-X188D,X101A-X188D,X104L-X188D,X089P-X188D,X129E-X188D,X159E-X188D,X186H-X188D,X103G-X188D,X158E-X188D,X016S-X022A,X016S-X104L,X022A-X104L,X101A-X104L,X062E-X104L,X103G-X104L,X089P-X104L,X159E-X209E,X111V-X209E,X101A-X209E,X016S-X209E,X128N-X209E,X148I-X209E,X129E-X209E,X062E-X209E,X022A-X209E,X103G-X209E,X158E-X209E,X188D-X209E,X104L-X209E,X089P-X209E,和X186H-X209E,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0351] 本发明提供编码芽孢杆菌属枯草杆菌蛋白酶变体的核酸,其中该枯草杆菌蛋白酶变体是具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:X018R-X241R,X020R-X241R,X024R-X241R,X009A-X241R,X020R-X241R,X004R-X241R,X043R-X241R,X078R-X241R,X022R-X241R,X115R-X241R,X001R-X241R,X212F-X241R,X082R-X241R,X018R-X244R,X024R-X244R,X078R-X244R,X020R-X244R,X212F-X244R,X009A-X244R,X082R-X244R,X001R-X244R,X043R-X244R,X022R-X244R,X004R-X244R,X115R-X244R,X241R-X244R,X242R-X244R,X001R-X004R,X009A-X022R,X018R-X022R,X020R-X022R,X004R-X022R,X001R-X022R,X024R-X242R,X018R-X242R,X004R-X242R,X020R-X242R,X212F-X242R,X082R-X242R,X078R-X242R,X001R-X242R,X009A-X242R,X022R-X242R,X115R-X242R,X043R-X242R,X241R-X242R,X018R-X212F,X022R-X212F,X004R-X212F,X024R-X212F,X001R-X212F,X115R-X212F,X020R-X212F,X009A-X212F,X043R-X212F,X078R-X212F,X082R-X212F,X009A-X078R,X020R-X078R,X024R-X078R,X022R-X078R,X018R-X078R,X004R-X078R,X001R-X078R,X043R-X078R,X022R-X024R,X020R-X024R,X018R-X024R,X001R-X024R,X004R-X024R,X009A-X024R,X004R-X009A,X001R-X009A,X242R-X269R,X024R-X269R,X020R-X269R,X022R-X269R,X249R-X269R,X212F-X269R,X043R-X269R,X244R-X269R,X001R-X269R,X018R-X269R,X078R-X269R,X009A-X269R,X115R-X269R,X241R-X269R,X004R-X269R,X082R-X269R,X018R-X043R,X020R-X043R,X004R-X043R,X022R-X043R,X009A-X043R,X001R-X043R,X024R-X043R,X009A-X018R,X004R-X018R,X001R-X018R,X024R-X082R,X009A-X082R,X018R-X082R,X001R-X082R,X078R-X082R,X020R-X082R,X022R-X082R,X004R-X082R,X043R-X082R,X043R-X249R,X020R-X249R,X004R-X249R,X018R-X249R,X009A-X249R,X212F-X249R,X022R-X249R,X024R-X249R,X115R-X249R,X001R-X249R,X082R-X249R,X242R-X249R,X241R-X249R,X244R-X249R,X078R-X249R,X018R-X115R,X020R-X115R,X022R-X115R,X078R-X115R,X009A-X115R,X004R-X115R,X001R-X115R,X082R-X115R,X043R-X115R,X024R-X115R,X009A-X020R,X018R-X020R,X004R-X020R,X001R-X020R,X009A-X271L,X020R-X271L,X024R-X271L,X244R-X271L,X241R-X271L,X043R-X271L,X022R-X271L,X249R-X271L,X212F-X271L,X115R-X271L,X242R-X271L,X078R-X271L,X004R-X271L,X269R-X271L,X001R-X271L,X018R-X271L,和X082R-X271L,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的

对应关系进行编号。

[0352] 本发明提供编码芽孢杆菌属枯草杆菌蛋白酶变体的核酸，其中该枯草杆菌蛋白酶变体是具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列：X020R-X-43R,X020K-X062E,X024F-X116L,X020K-X024F,X024R-X174T,X024R-X118R,X024R-X235F,X024R-X086R,X024R-X086W,X078R-X118R,X033S-X118R,X033S-X235F,X209A-X241R,X020R-X076D,X018R-X245R,X024R-X045T,X232V-X245R,X118R-X172V,X118R-X194T,X008T-X024R,X235F-X243F,X018R-X103A,X018R-X104I,X086W-X118R,X086W-X243F,X086W-X209A,X024C-X033S,X024R-X232V,X024R-X243F,X024R-X239Q,X024R-X101G,X024R-X141G,X024R-X033S,X024R-X274I,X024R-X209A,X078R-X086W,X101G-X232V,X033S-X148F,X033S-X086W,X033S-X201S,X033S-X078R,X033S-X241R,X033S-X209A,X230E-X249R,X232V-X249R,X118R-X235F,X076D-X245R,X086W-X235F,X024R-X247H,X024R-X104A,X078R-X235F,X101G-X249R,X103A-X232V,X033S-X048T,X033S-X239T,X033S-X253A,X143A-X209A,X209A-X235F,X018R-X045T,X209A-X243F,X024R-X272P,X024R-X269C,X101G-X104I,X104I-X232V,X076D-X249R，和X024R-X076D，其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0353] 本发明提供编码芽孢杆菌属枯草杆菌蛋白酶变体的核酸，其中该枯草杆菌蛋白酶变体是具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列：X020R-X076D,X024R-X045T,X230E-X249R,X018R-X045T,X018R-X245R,X101G-X232V,X024R-X232V,X232V-X245R,X024R-X101G,X018R-X104I,X018R-X103A,X101G-X249R,X232V-X249R,X103A-X232V,X076D-X245R,X101G-X104I,X104I-X232V,X076D-X249R,X024R-X076D,X024F-X116L,X020K-X024F,X020K-X062E,X033S-X118R,X024R-X086W,X024R-X118R,X024R-X086R,X209A-X241R,X024R-X241R,X024R-X235F,X118R-X209A,X078R-X118R,X033S-X235F,X024R-X174T,X086W-X209A,X008T-X024R,X086W-X118R,X033S-X241R,X024R-X243F,X024R-X209A,X033S-X086W,X024R-X033S,X086W-X243F,X033S-X201S,X024R-X239Q,X078R-X086W,X235F-X243F,X118R-X172V,X033S-X148F,X033S-X078R,X033S-X243F,X024C-X033S,X118R-X194T,X033S-X209A,X024R-X141G,X024R-X274I,X086W-X235F,X015T-X033S,X209A-X235F,X024R-X247H,X078R-X235F,X024R-X104A,X033S-X048T,X118R-X235F,X033S-X253A,X143A-X209A,X033S-X239T,X209A-X243F,X024R-X272P，和X024R-X269C，其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0354] 本发明提供编码芽孢杆菌属枯草杆菌蛋白酶变体的核酸，其中该枯草杆菌蛋白酶变体是具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列：X004R-X009A-X020R-X242R,X020R-X043R-X241R,X020R-X242R-X269R,X004R-X009A-X020R-X043R,X004R-X020R-X249R,X018R-X024R-X244R,X009A-X022R-X212F-X241R,X020R-X043R-X269R,X018R-X024R-X242R,X004R-X009A-X043R-X241R,X020R-X043R-X244R,X020R-X022R-X242R,X004R-X020R-X043R,X004R-X009A-X020R-X043R-X242R,X020R-X043R-X242R,X020R-X043R-X242R-X249R,X020R-X212F-X249R,X004R-X009A-

X241R,X001R-X009A-X043R,X020R-X043R-X249R,X009A-X020R-X043R-X241R,X020R-X022R-X043R,X020R-X249R-X269R,X020R-X022R-X241R,X004R-X009A-X024R-X043R-X241R,X009A-X043R-X078R,X004R-X020R-X024R-X244R,X020R-X022R-X078R-X242R,X020R-X024R-X242R-X249R,X004R-X009A-X078R-X241R,X009A-X043R-X078R-X242R,X004R-X020R-X024R,X009A-X043R-X212F,X020R-X043R-X212F,X024R-X078R-X212F,X009A-X020R-X024R-X043R,X009A-X022R-X043R-X078R,X020R-X022R-X212F-X241R,X020R-X043R-X212F-X241R,X009A-X043R-X241R,X020R-X043R-X271L,X020R-X022R-X078R-X241R,X020R-X024R-X043R-X242R,X020R-X022R-X043R-X241R,X009A-X020R-X043R-X212F,X004R-X009A-X020R-X024R-X242R,X020R-X043R-X249R-X271L,X020R-X022R-X024R-X242R,X009A-X022R-X078R-X212F,X020R-X043R-X242R-X271L,X009A-X022R-X078R-X212F-X241R,X004R-X020R-X024R-X249R,X020R-X022R-X271L,X020R-X022R-X043R-X212F,X004R-X020R-X024R-X043R-X242R,X004R-X020R-X024R-X043R,X004R-X009A-X022R-X078R-X212F,X020R-X022R-X078R-X212F-X241R,和X020R-X022R-X269R,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0355] 本发明提供编码芽孢杆菌属枯草杆菌蛋白酶变体的核酸,其中该枯草杆菌蛋白酶变体是具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:X018R-X020R-X043D-X045T-X230E,X018R-X043R-X045T-X242R-X249R,X024R-X043D-X249R,X018R-X020R-X045T,X020R-X024R-X076D-X249R,X024R-X043R-X230E-X242R,X018R-X024R-X043D-X230E,X020R-X076D,X018R-X024R-X043D-X076D-X249R,X024R-X043R-X076D-X249R,X018R-X024R-X045T-X242R,X020R-X043D-X076D-X230E-X249R,X020R-X043R-X045T-X242R,X018R-X024R-X076D-X249R,X018R-X020R-X024R-X043D-X045T-X233I-X242R,X024R-X043R-X230E,X018R-X020R-X043D,X043R-X242R-X249R,X020R-X043R-X045T-X230E,X043R-X076D-X242R-X249R,X020R-X024R-X045T-X230E-X242R,X024R-X045T-X076D-X230E-X242R-X249R,X024R-X045T,X024R-X043R-X045T-X076D-X230E-X249R,X018R-X024R-X043D-X045T-X249R,X018R-X043R-X045T-X249R,X024R-X043R-X242R,X018R-X020R-X043R-X076D-X249R,X020R-X024R-X043D-X249R,X020R-X043R-X230E-X242R,X020R-X043R-X242R,X018R-X043R-X076D-X230E,X020R-X024R-X043D-X242R,X020R-X043R-X230E,X018R-X020R-X043R-X076D-X242R-X249R,X043D-X045T-X076D-X249R,X018R-X043R-X242R-X249R,X018R-X020R-X043R-X045T-X242R,X018R-X020R-X043D-X230E-X242R,X020R-X024R-X043R-X045T-X249R,X024R-X043R-X249R,X020R-X024R-X27E-X043R-X076D-X230E,X024R-X043R-X045T-X242R,X018R-X020R-X024R-X043R-X045T-X076D-X230E,X020R-X043R-X076D-X230E-X249R,X018R-X043R-X045T-X242R,X020R-X242R-X249R,X018R-X043R-X076D-X230E-X242R-X249R,X018R-X024R-X076D,X020R-X024R-X27R-X043D-X242R-X249R,X018R-X020R-X024R-X043D-X076D-X242R,X018R-X043R-X076D-X242R-X249R,X018R-X024R-X043D-X230E-X249R,X018R-X020R-X043D-X249R,X018R-X020R-X043D-X045T-X076D-X242R,X024R-X043R-X076D-X230E-X242R,X020R-X024R-X38I-X043R-X045T-X076D-X242R-X249R,X018R-X020R-X043R,X018R-X024R-X045T-X230E-X242R,X018R-X020R-X249R,X024R-X043R-X076D,

X018R-X020R-X024R-X043R-X045T-X076D-X249R,X018R-X043D-X045T-X076D-X242R-X249R,X024R-X043D-X242R-X249R,X018R-X020R-X024R-X043D-X045T-X242R,X020R-X024R-X043R-X076D,X018R-X020R-X043D-X045T-X230E-X242R,X020R-X024R-X043R-X045T-X076D-X242R-X249R,X018R-X043R-X045T-X076D-X242R,X018R-X020R-X043R-X076D-X230E-X242R,X018R-X024R-X043D-X249R,X018R-X024R-X043R-X045T-X230E-X249R,X018R-X020R-X043R-X045T-X076D-X249R,X018R-X024R-X242R,X018R-X043R-X045T-X076D-X230E-X242R,X045T-X242R-X249R,X018R-X024R-X043D-X242R,X018R-X020R-X043D-X045T-X240P,X024R-X043R-X045T-X242R-X249R,X018R-X024R-X30S-X31S-X32I-X33Q-X34V-X35F,X018R-X020R-X043R-X076D,X020R-X043D-X045T-X076D-X242R-X249R,X018R-X024R-X043D-X230E-X242R,X018R-X024R-X043D-X242R-X249R,X024R-X043D-X045T-X242R-X249R,X043R-X230E-X249R,X024R-X043R-X076D-X230E-X249R,X020R-X024R-X043D-X076D-X249R,X024R-X045T-X242R-X273V,X020R-X024R-X045T-X076D-X242R-X249R,X018R-X024R-X043D-X076D-X242R,X018R-X043R-X076D-X230E-X249R,X018R-X020R-X043R-X045T-X249R,X018R-X043R-X045T-X230E-X242R,X020R-X024R-X043D-X045T-X230E-X242R,X018R-X043D-X230E-X249R,X018R-X043R-X076D-X242R,X018R-X020R-X076D,X018R-X020R-X043D-X076D-X242R-X249R,X020R-X024R-X043D-X076D-X242R-X249R,X043D-X242R-X249R,X018R-X020R-X024R-X043R-X076D,X018R-X020R-X043D-X045T-X076D-X249R,X018R-X020R-X043R-X045T-X076D-X230E-X249R,X018R-X076D-X242R,X020R-X043R-X249R,X018R-X076D-X242R-X249R,X018R-X024R-X045T-X230E-X249R,X230E-X249R,X018R-X045T-X249R,X020R-X043R-X076D,X043R-X045T-X249R,X018R-X043D-X076D-X242R-X249R,X043R-X076D-X249R,X018R-X045T,X020R-X076D-X230E-X242R,X020R-X024R-X043D-X045T,X024R-X043D-X076D-X242R-X249R,X020R-X045T-X249R,X043R-X076D-X153A-X249R,X043R-X076D-X230E-X249R,X018R-X043D-X076D-X249R,和X020R-X043R-X076D-X227I,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0356] 本发明提供编码芽孢杆菌属枯草杆菌蛋白酶变体的核酸,其中该枯草杆菌蛋白酶变体是具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:X101G-X103A-X104I-X232V-X236H-X245R-X252K,X101G-X103A-X104I-X232V-X245R-X248R,X101G-X103A-X104I-X159R-X232V-X245R-X248D,X101G-X103A-X104I-X159D-X232V-X245R-X248R,X101G-X103A-X104I-X232V-X245R,X101G-X103A-X104I-X159D-X232V-X245R和X101G-X103A-X104I-X232V-X245R-X248D,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0357] 本发明提供编码芽孢杆菌属枯草杆菌蛋白酶变体的核酸,其中该枯草杆菌蛋白酶变体是具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:X101G-X103A-X104I-X129E-X188D-X232V-X238R-X245R-X248D,X024R-X101G-X103A-X104I-X129E-X158E-X188D-X232V-X245R-X248D-X249R,X022A-X101G-X103A-X104I-X129E-X158E-X188D-X232V-X245R-X248D-X249R,X022A-X024R-X101G-X103A-X104I-

X129E-X158E-X188D-X232V-X245R-X248D-X249R,XO24R-X101G-X103A-X104I-X129E-X188D-X232V-X245R-X248D-X249R,XO24R-X101G-X103A-X104I-X129E-X159E-X188D-X232V-X245R-X248D-X249R,XO24R-X101G-X103A-X104I-X128N-X129E-X158E-X232V-X245R-X248D-X249R,XO24R-X101G-X103A-X104I-X148I-X158E-X188D-X232V-X245R-X248D,XO22A-XO24R-X101G-X103A-X104I-X129E-X159E-X188D-X232V-X245R-X248D-X249R,XO24R-X101G-X103A-X104I-X128N-X129E-X232V-X245R-X248D,X101G-X103A-X104I-X129E-X188D-X232V-X245R-X248D-X249R,XO24R-X101G-X103A-X104I-X129E-X158E-X232V-X245R-X248D-X249R,XO22A-XO24R-X101G-X103A-X104I-X158E-X159E-X188D-X232V-X245R-X248D-X249R,XO22A-XO24R-X101G-X103A-X104I-X129E-X158E-X159E-X188D-X232V-X238R-X245R-X248D,XO24R-X101G-X103A-X104I-X129E-X148I-X158E-X232V-X245R-X248D,XO16S-XO24R-X101G-X103A-X104I-X158E-X188D-X232V-X245R-X248D-X249R,X101G-X103A-X104I-X158E-X159E-X232V-X245R-X248D-X249R,XO22A-X101G-X103A-X104I-X129E-X158E-X159E-X232V-X238R-X245R-X248D,XO22A-XO24R-X101G-X103A-X104I-X129E-X158E-X159E-X232V-X245R-X248D-X249R,XO22A-XO24R-X101G-X103A-X104I-X128N-X158E-X188D-X232V-X245R-X248D,XO24R-X101G-X103A-X104I-X129E-X188D-X232V-X245R-X248D,XO22A-XO24R-X101G-X103A-X104I-X129E-X158E-X232V-X245R-X248D,XO22A-XO24R-X101G-X103A-X104I-X129E-X232V-X245R-X248D,XO22A-XO24R-X101G-X103A-X104I-X129E-X188D-X232V-X245R-X248D,XO24R-X101G-X103A-X104I-X158E-X188D-X232V-X238R-X245R-X248D,XO22A-X101G-X103A-X104I-X128N-X129E-X188D-X232V-X238R-X245R-X248D,XO24R-X101G-X103A-X104I-X129E-X188D-X232V-X238R-X245R-X248D,XO24R-X101G-X103A-X104I-X158E-X159E-X188D-X232V-X245R-X248D,XO22A-XO24R-X101G-X103A-X104I-X128N-X188D-X232V-X245R-X248D,XO24R-X101G-X103A-X104I-X129E-X158E-X188D-X232V-X245R-X248D,XO22A-XO24R-X101G-X103A-X104I-X128N-X129E-X158E-X232V-X245R-X248D,XO24R-X101G-X103A-X104I-X159E-X188D-X232V-X245R-X248D,XO22A-X101G-X103A-X104I-X128N-X129E-X232V-X238R-X245R-X248D,XO24R-X101G-X103A-X104I-X129E-X159E-X232V-X245R-X248D,XO22A-XO24R-X101G-X103A-X104I-X129E-X158E-X188D-X232V-X238R-X245R-X248D,XO22A-XO24R-X101G-X103A-X104I-X158E-X159E-X188D-X232V-X245R-X248D,XO24R-X101G-X103A-X104I-X159E-X188D-X232V-X245R-X248D-X249R,XO22A-X101G-X103A-X104I-X129E-X158E-X232V-X238R-X245R-X248D,XO22A-XO24R-X101G-X103A-X104I-X129E-X158E-X232V-X245R-X248D-X249R,XO24R-X101G-X103A-X104I-X148I-X158E-X232V-X245R-X248D,XO22A-X101G-X103A-X104I-X158E-X159E-X188D-X232V-X245R-X248D-X249R,XO22A-X101G-X103A-X104I-X158E-X188D-X232V-X245R-X248D,XO22A-X101G-X103A-X104I-X129E-X188D-X232V-X238R-X245R-X248D,XO24R-X101G-X103A-X104I-X129E-X158E-X159E-X188D-X232V-X245R-X248D-X249R,XO22A-XO24R-X101G-X103A-X104I-X158E-X159E-X188D-X232V-X238R-X245R-X248D,X101G-X103A-X104I-X129E-X158E-X188D-X232V-X245R-X248D-X249R,XO24R-X101G-X103A-X104I-X128N-X158E-X232V-X245R-X248D,XO22A-XO24R-X101G-X103A-X104I-X128N-X129E-X188D-X232V-X245R-X248D,XO22A-X101G-X103A-X104I-X129E-

X159E-X232V-X238R-X245R-X248D,X101G-X103A-X104I-X129E-X159E-X232V-X245R-X248D-X249R,X022A-X101G-X103A-X104I-X129E-X158E-X232V-X245R-X248D-X249R,X024R-X101G-X103A-X104I-X129E-X148I-X158E-X188D-X232V-X245R-X248D,X022A-X101G-X103A-X104I-X129E-X159E-X232V-X245R-X248D-X249R,X024R-X101G-X103A-X104I-X159E-X188D-X232V-X238R-X245R-X248D,X024R-X101G-X103A-X104I-X129E-X158E-X159E-X232V-X245R-X248D-X249R,X024R-X101G-X103A-X104I-X129E-X158E-X159E-X232V-X238R-X245R-X248D,X024R-X101G-X103A-X104I-X128N-X159E-X188D-X232V-X245R-X248D,X022A-X101G-X103A-X104I-X159E-X188D-X232V-X245R-X248D-X249R,X024R-X101G-X103A-X104I-X129E-X159E-X188D-X232V-X238R-X245R-X248D,X101G-X103A-X104I-X158E-X232V-X238R-X245R-X248D,X022A-X101G-X103A-X104I-X129E-X159E-X188D-X232V-X245R-X248D-X249R,X024R-X101G-X103A-X104I-X129E-X148I-X188D-X232V-X245R-X248D,X024R-X101G-X103A-X104I-X158E-X232V-X245R-X248D-X249R,X022A-X101G-X103A-X104I-X158E-X159E-X232V-X238R-X245R-X248D,X024R-X101G-X103A-X104I-X158E-X159E-X232V-X238R-X245R-X248D,X022A-X101G-X103A-X104I-X129E-X158E-X159E-X232V-X245R-X248D-X249R,X101G-X103A-X104I-X129E-X158E-X188D-X232V-X238R-X245R-X248D,X022A-X024R-X101G-X103A-X104I-X129E-X158E-X159E-X232V-X245R-X248D,X101G-X103A-X104I-X188D-X232V-X238R-X245R-X248D,X022A-X024R-X101G-X103A-X104I-X158E-X232V-X245R-X248D-X249R,X022A-X024R-X101G-X103A-X104I-X148I-X158E-X232V-X245R-X248D,X101G-X103A-X104I-X129E-X158E-X159E-X232V-X238R-X245R-X248D,X022A-X101G-X103A-X104I-X159E-X188D-X232V-X238R-X245R-X248D,X022A-X024R-X101G-X103A-X104I-X129E-X158E-X159E-X188D-X232V-X245R-X248D-X249R,X022A-X101G-X103A-X104I-X129E-X232V-X238R-X245R-X248D,X022A-X024R-X101G-X103A-X104I-X188D-X232V-X245R-X248D-X249R,X101G-X103A-X104I-X129E-X158E-X159E-X232V-X245R-X248D-X249R,X022A-X101G-X103A-X104I-X158E-X159E-X232V-X245R-X248D-X249R,X101G-X103A-X104I-X129E-X188D-X232V-X245R-X248D,X024R-X101G-X103A-X104I-X129E-X159E-X232V-X238R-X245R-X248D,X101G-X103A-X104I-X128N-X129E-X232V-X245R-X248D,X101G-X103A-X104I-X158E-X188D-X232V-X245R-X248D,X022A-X024R-X101G-X103A-X104I-X129E-X232V-X245R-X248D-X249R,X101G-X103A-X104I-X129E-X159E-X232V-X238R-X245R-X248D,X101G-X103A-X104I-X158E-X159E-X188D-X232V-X238R-X245R-X248D,X024R-X101G-X103A-X104I-X232V-X245R-X248D-X249R,X022A-X024R-X101G-X103A-X104I-X129E-X148I-X232V-X245R-X248D,X022A-X024R-X101G-X103A-X104I-X158E-X232V-X238R-X245R-X248D,X101G-X103A-X104I-X128N-X129E-X232V-X238R-X245R-X248D,X022A-X101G-X103A-X104I-X128N-X159E-X232V-X245R-X248D,X022A-X101G-X103A-X104I-X128N-X129E-X158E-X232V-X238R-X245R-X248D,X101G-X103A-X104I-X128N-X129E-X188D-X232V-X245R-X248D-X249R,X022A-X024R-X101G-X103A-X104I-X128N-X129E-X158E-X188D-X232V-X245R-X248D-X249R,X024R-X101G-X103A-X104I-X128N-X158E-X159E-X188D-X232V-X245R-X248D,X022A-X024K-X101G-X103A-X104I-X128N-X158E-X159E-X232V-X245R-X248D,X101G-X103A-X104I-X129E-X148I-

X188D-X232V-X245R-X248D,X024R-X101G-X103A-X104I-X148I-X232V-X245R-X248D,X022A-X101G-X103A-X104I-X148I-X188D-X232V-X245R-X248D,X024R-X101G-X103A-X104I-X128N-X129E-X188D-X232V-X245R-X248D,X101G-X103A-X104I-X128N-X129E-X158E-X232V-X238R-X245R-X248D,X022A-X024R-X101G-X103A-X104I-X129E-X148I-X158E-X188D-X232V-X245R-X248D,X022A-X024R-X101G-X103A-X104I-X148I-X158E-X188D-X232V-X245R-X248D,X101G-X103A-X104I-X148I-X159E-X232V-X245R-X248D,X022A-X024R-X101G-X103A-X104I-X158E-X188D-X232V-X245R-X248D,和X101G-X103A-X104I-X128N-X129E-X158E-X232V-X245R-X248D-X249R,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0358] 本发明提供编码芽孢杆菌属枯草杆菌蛋白酶变体的核酸,其中该枯草杆菌蛋白酶变体是具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:X022A-X024R-X101G-X103A-X104I-X158E-X232V-X245R-X248D-X249R,X022A-X024R-X101G-X103A-X104I-X129E-X232V-X245R-X248D-X249R,X024R-X101G-X103A-X104I-X158E-X159E-X232V-X238R-X245R-X248D,X024R-X101G-X103A-X104I-X232V-X245R-X248D-X249R,X101G-X103A-X104I-X158E-X232V-X245R-X248D-X249R,X101G-X103A-X104I-X188D-X232V-X245R-X248D-X249R,X024R-X101G-X103A-X104I-X159E-X188D-X232V-X245R-X248D-X249R,X022A-X024R-X101G-X103A-X104I-X158E-X232V-X238R-X245R-X248D,X024R-X101G-X103A-X104I-X159E-X188D-X232V-X238R-X245R-X248D,X022A-X024R-X101G-X103A-X104I-X129E-X232V-X245R-X248D,X024R-X101G-X103A-X104I-X148I-X232V-X245R-X248D,X024R-X101G-X103A-X104I-X129E-X158E-X232V-X245R-X248D-X249R,X024R-X101G-X103A-X104I-X148I-X158E-X232V-X245R-X248D,X022A-X024R-X101G-X103A-X104I-X129E-X158E-X232V-X245R-X248D-X249R,X016S-X024R-X101G-X103A-X104I-X158E-X188D-X232V-X245R-X248D-X249R,X024R-X101G-X103A-X104I-X129E-X159E-X232V-X238R-X245R-X248D,X024R-X101G-X103A-X104I-X129E-X188D-X232V-X245R-X248D-X249R,X022A-X101G-X103A-X104I-X129E-X232V-X238R-X245R-X248D,X022A-X024R-X101G-X103A-X104I-X148I-X158E-X232V-X245R-X248D,X024R-X101G-X103A-X104I-X129E-X188D-X232V-X238R-X245R-X248D,X022A-X024R-X101G-X103A-X104I-X158E-X159E-X188D-X232V-X238R-X245R-X248D,X022A-X101G-X103A-X104I-X158E-X159E-X232V-X238R-X245R-X248D,X022A-X024R-X101G-X103A-X104I-X129E-X158E-X232V-X245R-X248D,X101G-X103A-X104I-X158E-X188D-X232V-X245R-X248D-X249R,X022A-X101G-X103A-X104I-X158E-X159E-X232V-X245R-X248D-X249R,和X024R-X101G-X103A-X104I-X158E-X159E-X232V-X245R-X248D,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0359] 本发明提供编码芽孢杆菌属枯草杆菌蛋白酶变体的核酸,其中该枯草杆菌蛋白酶变体是具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:X104L-X128N-X158E-X186H-X249R,X128N-X158E-X188D-X249R,X062E-X128N-X158E-X159E-X271F,X062E-X158E-X188D-X249R-X271F,X062E-X158E-X186H-X249R-X271F,

X128N-X158E-X188D-X209E-X271F,X062E-X159E-X188D-X249R,X016S-X062E-X158E-X186H-X249R,X062E-X158E-X159E-X249R,X101A-X128N-X158E-X209E-X249R,X128N-X158E-X186H-X271F,X062E-X158E-X188D-X249R,X062E-X158E-X186H-X271F,X062E-X158E-X186H-X249R,X062E-X101A-X186H-X249R,X062E-X101A-X158E-X186H-X271F,X062E-X104L-X158E-X188D-X249R-X271F,X062E-X159E-X186H-X249R,X062E-X159E-X249R,X128N-X158E-X186H-X249R,X128N-X158E-X188D-X271F,X062E-X158E-X249R,X062E-X186H-X188D-X249R-X271F,X128N-X158E-X209E-,X062E-X101A-X158E-X249R,X104L-X128N-X158E-X186H-X271F,X062E-X101A-X158E-X186H-X249R-X271F,X016S-X062E-X158E-X249R,X062E-X101A-X159E-X249R,X128N-X158E-X186H-X188D-X271F,X101A-X128N-X158E-X186H-X271F,X062E-X101A-X188D-X249R,X101A-X104L-X158E-X186H-X188D-X249R,X062E-X159E-X249R-X271F,X128N-X158E-X159E-X271F,X016S-X062E-X104L-X158E-X186H-X271F,X022A-X128N-X158E-X249R,X128N-X158E-X249R,X062E-X101A-X104L-X158E-X186H-X271F,X016S-X062E-X158E-X186H-X271F,X104L-X128N-X158E-X249R,X104L-X128N-X158E-X188D-X249R,X022A-X062E-X158E,X062E-X101A-X188D-X249R-X271F,X062E-X158E-X249R-X271F,X104L-X128N-X158E-X186H-X188D-X271F,X062E-X101A-X186H-X271F,X062E-X104L-X159E-X249R,X062E-X186H-X249R,X062E-X101A-X186H-X249R-X271F,X101A-X158E-X186H-X188D-X249R,X062E-X101A-X186H,X101A-X128N-X129E-X186H-X249R,X101A-X103G-X158E-X186H-X249R,X016S-X062E-X104L-X186H-X188D-X271F,X104L-X158E-X186H-X249R,X101A-X128N-X158E-X188D-X209E-X271F,X062E-X101A-X186H-X188D-X271F,X016S-X062E-X158E-X249R-X271F,X062E-X128N-X158E,X062E-X128N-X159E-X249R,X062E-X101A-X158E-X188D-X249R,X101A-X128N-X158E-X249R,X062E-X158E-X186H-X188D-X249R,X016S-X104L-X158E-X186H-X271F,X062E-X148I-X159E,X062E-X101A-X158E-X186H-X249R,X062E-X101A-X186H-X188D-X249R,X104L-X158E-X186H-X188D-X249R,X062E-X101A-X104L-X186H-X188D-X271F,X022A-X101A-X158E-X186H-X249R,X101A-X128N-X158E-X209E,X158E-X186H-X188D-X249R-X271F,X104L-X158E-X186H-X188D-X249R-X271F,X101A-X104L-X158E-X186H-X249R,X104L-X158E-X249R,X101A-X104L-X128N-X158E-X186H-X271F,X016S-X104L-X188D-X249R,X101A-X104L-X158E-X186H-X188D-X271F,X104L-X128N-X159E-X271F,X104L-X158E-X186H-X249R-X271F,X158E-X186H-X249R,X101A-X158E-X186H-X249R,X104L-X158E-X188D-X249R-X271F,X016S-X128N-X158E-X186H,X104L-X128N-X186H-X188D-X249R,X016S-X101A-X128N-X186H,X016S-X062E-X128N-X186H-X271F,X016S-X128N-X186H-X271F,X128N-X129E-X186H,X158E-X186H-X249R-X271F,X016S-X158E-X249R,X016S-X158E-X186H-X249R,X016S-X022A-X158E-X186H-X271F,X089P-X101A-X129E-X186H,X022A-X128N-X158E-X186H,X101A-X104L-X128N-X158E-X186H,X022A-X128N-X186H-X188D-,X062E-X104L-X158E-X186H-X188D-X249R,X022A-X158E-X186H-X249R-X271F,X022A-X104L-X158E-X249R,X101A-X111V-X129E,X016S-X158E-X249R-X271F,X016S-X111V-X188D-,X022A-X104L-X186H-X188D-X249R,和X104L-X148I-X188D-X249R,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0360] 本发明提供编码芽孢杆菌属枯草杆菌蛋白酶变体的核酸，其中该枯草杆菌蛋白酶变体是具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列：X001R-X101G-X103A-X104I-X232V-X245R,X004R-X101G-X103A-X104I-X232V-X245R,X043R-X101G-X103A-X104I-X232V-X245R-X271L,X078R-X101G-X103A-X104I-X232V-X245R,X004R-X043R-X101G-X103A-X104I-X232V-X245R,X018R-X043R-X101G-X103A-X104I-X232V-X245R,X020R-X101G-X103A-X104I-X232V-X245R,X101G-X103A-X104I-X232V-X245R-X271L,X020R-X043R-X101G-X103A-X104I-X232V-X245R,X024R-X043R-X101G-X103A-X104I-X232V-X245R,X020R-X025R-X116A-X167W,X018R-X101G-X103A-X104I-X232V-X245R,X022R-X101G-X103A-X104I-X232V-X245R,X078R-X103N-X106G-X167W-X236N,X018R-X043D-X101G-X103A-X104I-X232V-X245R-X269R,X043R-X101G-X103A-X104I-X232V-X245R-X269R,X024R-X101A-X120F-X194F-X249R,X020R-X043D-X101G-X103A-X104I-X232V-X245R-X269R,X101G-X103A-X104I-X212F-X232V-X245R,X020R-X144R-X185I-X233C-X236N,X023A-X078R-X216F-X236N-X249R,X101G-X103A-X104I-X232V-X245R-X269R,X101G-X103A-X104I-X115R-X232V-X245R,X052N-X078R-X103N-X148I-X213A,X018R-X043D-X101G-X103A-X104I-X232V-X245R-X249R,X024R-X043D-X101G-X103A-X104I-X232V-X245R-X249R,X024R-X043D-X101G-X103A-X104I-X232V-X245R-X269R,X025R-X089I-X116A-X239S-X270C,X024R-X101G-X103A-X104I-X232V-X245R,X148I-X213A-X252R,X024R-X025R-X183D-X192W-X239S,X046R-X194F-X212M,X104L-X217E-X224A-X249R-X252R,X023A-X091F-X121F-X192W-X236N,X101G-X103A-X104I-X232V-X244R-X245R,X099F-X144R-X167W-X252R,X101G-X103A-X104I-X232V-X245R-X249R,X043R-X101G-X103A-X104I-X232V-X245R,X022W-X078R-X167W-X212M-X270C,X121F-X252R-X270C,X020R-X103N-X216F-X236N-X252R,X043R-X101G-X103A-X104I-X232V-X245R-X249R,X023A-X052N-X192W-X198L-X252R,X025R-X046R-X121F,X024R-X078R-X104L-X116A-X183D,X046R-X059A-X103N-X211Q-X212M,X020R-X052N-X062Q-X091F-X192W,X023A-X052N-X144R-X192W-X216F,X101G-X103A-X104I-X232V-X242R-X245R,X052N-X103N-X116A-X148I-X192W,X089I-X116A-X117F-X224A-X249R,X144R-X211Q-X238L-X239S-X249R,X043A-X062Q-X194F-X211Q,X020R-X024R-X052N-X059A-X216F,X024R-X167W-X224A-X249R,X057R-X167W-X249R,X025R-X103N-X186K-X194F-X224A,X105T-X128N-X144R-X148I-X212M,X020R-X059A-X144R-X192W-X224A,X024R-X043A-X117F-X194F-X211Q,X117F-X194F-X213A-X270C,X078R-X091F-X121F-X233C-X252R,X057R-X099F-X105T-X198L-X213A,X023A-X091F-X101A-X198L-X252R,X062Q-X103N-X121F-X144R-X249R,X043R-X101G-X103A-X104I-X232V-X242R-X245R,X023A-X024R-X117F-X212M-X216F,X104L-X213A-X216F,X194F-X211Q-X236N,X062Q-X103N-X117F-X194F,X024R-X062Q-X104L-X106G-X249R,X057R-X089I-X198L,X046R-X059A-X106G-X217E-X249R,X117F-X213A-X215F,X101A-X120F-X192W-X215F-X224A,X043A-X057R-X117F-X144R-X183D,X046R-X183D-X238L,X025R-X043A-X089I-X117F,X078R-X104L-X213A-X215F-X224A,X091F-X099F-X101A-X105T-X167W,X106G-X117F-X238L,X046R-X089I-X091F-X101A-X116A,X020R-X062Q-X089I-X186K-X212M,X057R-X099F-X121F-X185I-X192W,X046R-X089I-X192W-X233C-X270C,X089I-X117F-

X185I-X215F-X233C,X052N-X104L-X183D-X216F-X249R,X078R-X099F-X116A-X186K-X224A,X025R-X105T-X128N-X144R-X270C,X105T-X211Q-X216F,X024R-X046R-X091F-X121F,X106G-X185I-X216F-X236N,X062Q-X101A-X236N-X252R-X270C,X025R-X043A-X091F-X198L-X270C,X020R-X023A-X104L-X192W-X233C,X024R-X043A-X105T-X106G-X198L,X020R-X089I-X217E,X024R-X091F-X198L-X215F-X239S,X046R-X089I-X099F-X186K-X212M,X104L-X120F-X186K-X216F-X252R,X022W-X194F-X213A-X233C-X238L,X099F-X105T-X106G-X194F-X212M,X089I-X105T-X116A-X215F-X216F,X025R-X116A-X120F-X224A-X270C,X043A-X059A-X101A-X216F-X224A,X057R-X183D-X236N,X025R-X062Q-X128N-X144R-X185I,X103N-X120F-X167W-X198L-X233C,X022W-X089I-X216F,X024R-X106G-X116A-X212M-X224A,X020R-X052N-X101A-X198L-X233C,X089I-X091F-X185I-X211Q-X270C,X111I-X215F-X239S,X024R-X116A-X186K-X233C-X236N,和X023A-X103N-X106G-X212M-X215F,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0361] 本发明提供编码芽孢杆菌属枯草杆菌蛋白酶变体的核酸,其中该枯草杆菌蛋白酶变体是具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:X020R-X022W-X078R-X101A-X103A-X104I-X116S-X213A-X215F-X232V-X245R,X018R-X078R-X101G-X103A-X104I-X232V-X245R,X024R-X045T-X101G-X103A-X104I-X232V-X245R-X269R,X020R-X022W-X078R-X101G-X103A-X104I-X116A-X232V-X245R,X020R-X22W-X101G-X103A-X104I-X232V-X245R,X018R-X043R-X101G-X103A-X104I-X232V-X245R,X018R-X022W-X024R-X076D-X101A-X116A-X232V-X245R,X018R-X104I-X232V-X249R,X018R-X024R-X076D-X101A-X116A-X211Q-X249R,X018R-X043D-X078R-X101G-X103A-X104I-X217E-X232V-X245R,X018R-X043R-X101G-X103A-X104I-X232V-X245R-X269R,X018R-X045T-X076D-X101G-X103A-X104I-X232V-X245R-X269R,X076D-X078R-X101G-X103A-X104I-X232V-X245R-X269R,X020R-X043D-X078R-X101G-X103A-X104I-X232V-X245R,X018R-X043D-X076D-X101G-X103A-X104I-X232V-X245R-X269R,X024R-X045T-X076D-X078R-X101G-X103A-X104I-X232V-X245R-X269R,X018R-X103A-X232V-X249R,X018R-X101G-X104I-X232V-X245R,X020R-X024R-X101G-X103A-X104I-X217E-X232V-X245R-X249R,X018R-X22K-X043D-X101G-X103A-X104I-X232V-X245R,X043R-X045T-X101G-X103A-X104I-X232V-X245R-X269R,X020R-X22W-X101G-X103A-X104I-X211Q-X232V-X245R,X024R-X076D-X078R-X101G-X103A-X104I-X232V-X245R-X269R,X020R-X22W-X078R-X101A-X103A-X104I-X116A-X183D-X232V,X018R-X024R-X076D-X116A-X215F-X249R,X018R-X043R-X045T-X101G-X103A-X104I-X232V-X245R,X024R-X043R-X076D-X101G-X103A-X104I-X232V-X245R,X020R-X022W-X101G-X103A-X104I-X232V-X245R,X020R-X022W-X101G-X103A-X104I-X211Q-X232V-X245R,X020R-X022W-X078R-X101G-X103A-X104I-X116A-X213A-X215F-X232V-X245R,X043D-X076D-X078R-X101G-X103A-X104I-X232V-X245R-X269R,X018R-X024R-X076D-X101A-X116A-X213A-X249R,X018R-X024R-X076D-X116A-X211Q-X249R,X043R-X045T-X076D-X078R-X101G-X103A-X104I-X232V-X245R,X018R-X101G-X245R,X020R-X22W-X101A-X103A-X104I-X211Q-X213A-X232V-X245R,X020R-X024R-X043D-X076D-X078R-X101G-X103A-X104I-X232V-X245R,X018R-X045T-X076D-

X078R-X101G-X103A-X104I-X232V-X245R,X020R-X078R-X101G-X103A-X104I-X211Q-X213A-X215F-X232V-X245R,X045T-X078R-X101G-X103A-X104I-X232V-X245R-X269R,X024R-X043D-X101G-X103A-X104I-X232V-X245R-X269R,X018R-X101G-X103A-X249R,X018R-X22W-X024R-X076D-X101A-X116A-X232V-X245R,X018R-X101G-X104I-X232V-X249R,X020R-X22W-X101A-X103A-X104I-X215F-X232V-X245R,X018R-X024R-X076D-X211Q-X213A-X249R,X018R-X022W-X024R-X076D-X101A-X198L-X249R,X024R-X101G-X103A-X104I-X232V-X245R,X020R-X076D-X101G-X103A-X104I-X232V-X245R-X269R,X020R-X101G-X103A-X104I-X232V-X245R-X269R,X043D-X078R-X101G-X103A-X104I-X232V-X245R,X020R-X101G-X104I-X213A-X215F-X232V-X245R,X020R-X101G-X103A-X104I-X116A-X215F-X232V-X245R,X024R-X103A-X104I-X249R,X018R-X076D-X078R-X101G-X103A-X104I-X232V-X245R,X045T-X076D-X078R-X101G-X103A-X104I-X232V-X245R-X269R,X024R-X101G-X104I-X245R,X020R-X101G-X103A-X104I-X211Q-X213A-X215F-X232V-X245R,X024R-X103A-X104I-X232V-X249R,X018R-X024R-X076D-X116A-X211Q-X215F-X249R,X018R-X245R,X024R-X103A-X245R,X024R-X103A-X104I-X245R,X020R-X078R-X101G-X232V-X245R,X018R-X024R-X076D-X104I-X249R,X018R-X024R-X104I-X249R,X024R-X101G-X103A-X104I-X232V-X245R,X018R-X024R-X076D-X211Q-X215F-X249R,X019H-X020R-X022W-X078R-X101G-X103A-X104I-X211Q-X232V-X245R,X018R-X024R-X076D-X101A-X198L-X211Q-X213A-X249R,X018R-X024R-X043D-X101G-X103A-X104I-X232V-X245R,X020R-X22W-X103A-X104I-X232V-X245R,X018R-X103A-X104I-X249R,X018R-X022W-X024R-X076D-X101A-X198L-X215F-X249R,X018R-X024R-X101G-X104I-X232V,X078R-X101G-X103A-X104I-X232V-X245R-X269R,X024R-X043R-X076D-X078R-X101G-X103A-X104I-X232V-X245R,X018R-X020R-X043D-X076D-X101G-X103A-X104I-X232V-X245R,X018R-X22W-X024R-X076D-X116A-X213A-X249R,X018R-X024R-X101G-X104I,X020R-X101A-X103A-X104I-X215F-X232V-X245R,X018R-X045T-X078R-X101G-X103A-X104I-X232V-X245R,X018R-X101G-X103A-X245R,X043R-X076D-X078R-X101G-X103A-X104I-X232V-X245R,X020R-X022W-X101A-X103A-X104I-X211Q-X215F-X232V-X245R,X020R-X22W-X078R-X101G-X103A-X104I-X116A-X213A-X215F-X232V-X245R,X020R-X078R-X101G-X103A-X104I-X215F-X232V-X245R,X020R-X022W-X078R-X101G-X103A-X104I-X116A-X183D-X232V-X245R,X076D-X101G-X103A-X104I-X232V-X245R,X076D-X101G-X103A-X104I-X232V-X245R-X269R,X020R-X22W-X101A-X103A-X104I-X232V-X245R,X020R-X101G-X103A-X232V-X245R,X020R-X022W-X078R-X101A-X103A-X104I-X116A-X183D-X232V-X245R,X018R-X020R-X024R-X045T-X076D-X101G-X103A-X104I-X232V-X245R-X269R,X043R-X045T-X078R-X101G-X103A-X104I-X232V-X245R,X018R-X101G-X104I-X249R,X020R-X22W-X078R-X101G-X103A-X104I-X116A-X183D-X232V-X245R,X020R-X022W-X101G-X103A-X104I-X198L-X211Q-X213A-X232V-X245R,X020R-X078R-X101A-X103A-X104I-X116A-X183D-X213A-X232V-X245R,X024R-X076D-X104I-X232V-X245R,X018R-X020R-X076D-X101G-X103A-X104I-X232V-X245R,X018R-X024R-X076D-X101G-X104I-X232V-X249R,X018R-X043D-X078R-X101G-X103A-X104I-X232V-X245R,X001T-X018R-X024R-X076D-X116A-X213A-X249R,X076D-X078R-X101G-X103A-X104I-X232V-X245R,X020R-

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X215F-X249R,X018R-X022W-X024R-X076D-X116A-X183D-X211Q-X213A-X249R,X018R-X020R-X024R-X076D-X183D-X215F-X249R,X018R-X043D-X076D-X078R-X101G-X103A-X104I-X232V-X245R-X249R,X018R-X022W-X024R-X076D-X116A-X183D-X211Q-X213A-X245R,X020R-X024R-X076D-X078R-X101G-X103A-X104I-X232V-X245R-X249R,X018R-X020R-X045T-X101G-X103A-X104I-X232V-X245R-X249R,X018R-X024R-X076D-X101A-X183D-X198L-X211Q-X249R,X018R-X022W-X024R-X076D-X183D-X211Q-X213A-X249R,X018R-X020R-X024R-X076D-X116A-X198L-X211Q-X215F-X249R-X269S,X018R-X020R-X022W-X024R-X076D-X101A-X116A-X183D-X198L-X211Q-X215F-X249R,X020R-X022W-X101A-X103A-X104I-X183D-X213A-X215F-X232V-X245R,X018R-X024R-X076D-X086V-X101A-X183D-X198L-X211Q-X249R,X018R-X076D-X101G-X198T-X232V,X018R-X020R-X024R-X076D-X101A-X116A-X183D-X198L-X211Q-X215F-X249R,X018R-X022W-X024R-X076D-X101A-X116A-X183D-X213A-X215F-X249R,X018R-X022W-X024R-X076D-X101A-X183D-X211Q-X213A-X215F-X249R,X018R-X024R-X076D-X183D-X249R-X248T,X018R-X076D-X104I-X245R-X249R,X018R-X022W-X024R-X076D-X101A-X116A-X183D-X198L-X215F-X249R,X018R-X022W-X024R-X076D-X116A-X183D-X213A-X215F-X249R,X018R-X020R-X022W-X024R-X076D-X116A-X183D-X211Q-X213A-X215F-X249R,X018R-X020R-X024R-X076D-X101A-X249R,X018R-X020R-X024R-X076D-X101A-X116A-X213A-X215F-X249R,X018R-X022W-X024R-X076D-X116A-X183D-X211Q-X215F-X249R,X018R-X022W-X024R-X076D-X116A-X183D-X198L-X211Q-X213A-X249R,X043R-X045T-X078R-X101G-X103A-X104I-X217E-X232V-X245R,X043R-X045T-X101G-X103A-X104I-X232V-X245R-X249R,X018R-X076D-X101G-X104I,X020R-X045T-X076D-X078R-X101G-X103A-X104I-X232V-X245R-X249R,X043D-X076D-X101G-X103A-X104I-X232V-X245R,X018R-X020R-X022W-X024R-X076D-X101A-X116A-X183D-X198L-X249R,X018R-X076D-X104I,X018R-X020R-X043D-X101G-X103A-X104I-X232V-X245R-X249R,X018R-X020R-X022W-X024R-X076D-X183D-X211Q-X249R,X018R-X024R-X076D-X101A-X183D-X198L-X211Q-X215F-X249R,X101G-X104I,X018R-X022W-X024R-X076D-X116A-X183D-X198L-X211Q-X213A-X215F-X249R,X018R-X020R-X024R-X076D-X101A-X183D-X211Q-X213A-X215F-X249R,X018R-X020R-X024R-X076D-X116A-X183D-X215F-X249R-X263D,X018R-X022W-X024R-X076D-X101A-X183D-X249R,X018R-X024R-X076D-X101A-X116A-X183D-X198L-X215F-X249R,X018R-X022W-X024R-X076D-X116A-X198L-X215F-X249R-X269H,X018R-X043D-X045T-X076D-X078R-X101G-X103A-X104I-X232V-X245R,X018R-X024R-X045T-X076D-X078R-X101G-X103A-X104I-X232V-X245R-X269R,X078R-X101G-X103A-X104I-X217E-X232V-X245R,X018R-X020R-X022W-X024R-X076D-X101A-X183D-X198L-X213A-X215F-X249R,X018R-X020R-X024R-X076D-X183D-X198L-X213A-X249R,X018R-X020R-X022W-X024R-X076D-X116A-X198L-X211Q-X215F-X249R,X018R-X020R-X022W-X024R-X076D-X116A-X183D-X211Q-X249R,X018R-X020R-X022W-X024R-X076D-X101A-X198L-X211Q-X213A-X249R,X018R-X020R-X022W-X024R-X076D-X249R,X020R-X022W-X101G-X103A-X104I-X116A-X183D-X198L-X211Q-X213A-X215F-X232V-X245R,X104I-X232V,X018R-X020R-X022W-X024R-X076D-X101A-X116A-X183D-X211Q-X215F-X249R,X018R-X020R-

X022W-X024R-X076D-X101A-X116A-X183D-X198L-X211Q-X213A-X215F-X249R,X018R-X020R-X022W-X024R-X076D-X101A-X183D-X213A-X215F-X249R,X018R-X022W-X024R-X076D-X101A-X183D-X198L-X211Q-X213A-X249R,X018R-X022W-X024R-X076D-X101A-X183D-X198L-X249R,X043D-X045T-X101G-X103A-X104I-X232V-X245R-X269R,X018R-X020R-X024R-X076D-X101A-X183D-X198L-X211Q-X249R,X018R-X020R-X043R-X101G-X103A-X104I-X217E-X232V-X245R,X024R-X043R-X076D-X078R-X101G-X103A-X104I-X232V-X245R-X269R,X043R-X045T-X076D-X078R-X101G-X103A-X104I-X166F-X176P-X179V-X184T-X187P-X194P,X018R-X022W-X024R-X041E-X076D-X101A-X160T-X183D-X211Q-X213A-X249R,X018R-X020R-X022W-X024R-X076D-X116A-X183D-X198L-X211Q-X215F-X249R,X018R-X020R-X022W-X024R-X076D-X101A-X116A-X198L-X213A-X249R,X018R-X022W-X024R-X076D-X101A-X116A-X183D-X198L-X211Q-X213A-X249R,X018R-X020R-X024R-X076D-X198L-X213A-X249R,X018R-X020R-X022W-X024R-X076D-X116A-X183D-X198L-X211Q-X249R,X018R-X020R-X024R-X076D-X183D-X211Q-X215F-X249R,X024R-X076D-X104I,X018R-X076D-X101G-X232V,X018R-X024R-X076D-X101A-X116A-X183D-X198L-X211Q-X213A-X215F-X249R,X018R-X020R-X022W-X024R-X076D-X116A-X183D-X215F-X249R,X018R-X024R-X031F-X076D-X116A-X183D-X211Q-X213A-X215F-X249R,X018R-X024R-X076D-X101A-X116A-X183D-X198L-X213A-X249R-X269S,X018R-X020R-X024R-X076D-X101A-X116A-X198L-X215F-X249R,X018R-X043R-X076D-X078R-X101G-X103A-X104I-X232V-X245R-X269R,X018R-X020R-X024R-X076D-X101A-X114T-X198L-X211Q-X215F-X249R,X024R-X043R-X078R-X101G-X103A-X104I-X217E-X232V-X245R,X024R-X076D-X103A-X104I-X232V,X018R-X020R-X022W-X024R-X076D-X101A-X198L-X211Q-X215F-X249R,X101G-X104I-X232V,X018R-X022W-X024R-X076D-X183D-X198L-X213A-X215F-X249R,X018R-X022W-X024R-X076D-X183D-X198L-X211Q-X249R,X018R-X020R-X024R-X076D-X183D-X213A-X249R,X018R-X024R-X076D-X101A-X183D-X211Q-X215F-X249R,X018R-X020R-X022W-X024R-X076D-X116A-X211Q-X213A-X249R,X018R-X078R-X101G-X103A-X104I-X232V-X245R-X269R,X018R-X022W-X024R-X076D-X101A-X116A-X183D-X211Q-X215F-X249R-X260A,X076D-X249R,X018R-X022W-X024R-X076D-X183D-X211Q-X215F-X249R,X018R-X020R-X024R-X076D-X116A-X211Q-X215F-X249R,X018R-X020R-X024R-X076D-X213A-X249R,X018R-X020R-X022W-X024R-X076D-X116A-X183D-X198L-X249R,X018R-X020R-X022W-X024R-X076D-X101A-X183D-X249R,X076D-X104I-X249R,X020R-X022W-X101A-X103A-X104I-X116A-X183D-X211Q-X213A-X215F-X232V-X245R,X024R-X043R-X045T-X078R-X101G-X103A-X104I-X217E-X232V-X245R,X018R-X020R-X022W-X024R-X076D-X183D-X198L-X215F-X249R,X018R-X076D-X101G-X103A,X020R-X024R-X101G-X103A-X104I-X232V-X245R-X269R,X018R-X020R-X024R-X076D-X101A-X116A-X183D-X211Q-X249R,X101G-X103A-X232V,X024R-X076D-X101G-X232V,X018R-X022W-X024R-X076D-X101A-X183D-X198L-X211Q-X249R,X018R-X020R-X024R-X076D-X101A-X183D-X198L-X211Q-X215F-X249R,X018R-X020R-X024R-X076D-X183D-X198L-X249R,X018R-X022W-X024R-X076D-X101A-X116A-X183D-X198L-X211Q-X249R,X018R-X020R-X024R-X076D-X116A-X156V-X183D-X211Q-X215F-X249R-

X269S,X045T-X076D-X101G-X103A-X104I-X232V-X245R-X249R,X018R-X020R-X024R-X076D-X101A-X183D-X198L-X249R,X018R-X020R-X022W-X024R-X076D-X198L-X211Q-X215F-X249R,X018R-X020R-X022W-X024R-X076D-X101A-X116A-X198L-X211Q-X215F-X249R,X018R-X020R-X022W-X024R-X076D-X116A-X249R,X018R-X076D-X101G,X018R-X024R-X076D-X116A-X183D-X198L-X213A-X215F-X249R,X018R-X020R-X022W-X024R-X076D-X101A-X116A-X198L-X213A-X215F-X249R,X018R-X024R-X076D-X101A-X116A-X183D-X198L-X211Q-X249R,X018R-X076D-X232V,X018R-X020R-X024R-X076D-X101A-X232V-X245R,X018R-X043D-X045T-X076D-X101G-X103A-X104I-X232V-X245R,X018R-X022W-X024R-X076D-X183D-X213A-X215F-X249R,X018R-X024R-X076D-X101A-X116A-X211Q-X213A-X237D-X249R,X018R-X020R-X024R-X076D-X101A-X116A-X183D-X211Q-X249R-X275S,X018R-X022W-X024R-X076D-X101A-X116A-X183D-X198L-X211Q-X213A-X215F-X249R,X024R-X076D,X018R-X024R-X076D-X183D-X211Q-X215F-X249R,X018R-X022W-X024R-X076D-X116A-X183D-X198L-X213A-X215F-X249R,X076D-X104I-X232V-X249R,X018R-X076D-X103A-X232V,X018R-X020R-X024R-X076D-X101A-X116A-X183D-X198L-X211Q-X213A-X249R,X018R-X020R-X024R-X076D-X101A-X183D-X213A-X249R,X018R-X020R-X024R-X076D-X101A-X175E-X183D-X211Q-X215F-X249R,X018R-X020R-X043D-X078R-X101G-X103A-X104I-X217E-X232V-X245R-X273E,X020R-X024R-X043D-X045T-X076D-X101G-X103A-X104I-X232V-X245R,X005S-X101G-X103A-X104I-X232V-X245R-X249R,X103A-X104I-X232V,X018R-X020R-X024R-X068A-X076D-X101A-X116A-X213A-X215F-X249R,X018R-X022W-X024R-X076D-X101A-X198L-X215F-X249R-X275S,X018R-X024R-X076D-X183D-X198L-X211Q-X213A-X249R,和X043D-X045T-X101G-X103A-X104I-X232V-X245R,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0362] 本发明提供编码芽孢杆菌属枯草杆菌蛋白酶变体的核酸,其中该枯草杆菌蛋白酶变体是具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:X018R-X024R-X043R-X076D-X249R-X269R,X018R-X022R-X024R-X043R-X076D-X249R,X018R-X043D-X101G-X103A-X104I-X232V-X245R,X020R-X043D-X101G-X103A-X104I-X232V-X245R,X043D-X101G-X103A-X104I-X232V-X245R-X269R,X043D-X078R-X101G-X103A-X104I-X232V-X245R,X043R-X076D-X101G-X103A-X104I-X232V-X245R,X022R-X043R-X101G-X103A-X104I-X232V-X245R,X043R-X078R-X101G-X103A-X104I-X232V-X245R,X020R-X076D-X101G-X103A-X104I-X232V-X245R,X043R-X076D-X101G-X103A-X104I-X232V-X245R,X022R-X076D-X101G-X103A-X104I-X232V-X245R,X076D-X078R-X101G-X103A-X104I-X232V-X245R,X018R-X024R-X043R-X076D-X249R,X018R-X024R-X076D-X242R-X249R,X018R-X024R-X076D-X249R-X269R,X018R-X022R-X024R-X076D-X249R,X018R-X024R-X076D-X078R-X249R,X018R-X024R-X043D-X076D-X249R-X269R,X018R-X022R-X024R-X043D-X076D-X249R,X018R-X024R-X043D-X076D-X078R-X249R,X020R-X101G-X103G-X104I-X232V-X245R,X020R-X101G-X103A-X104L-X232V-X245R,X020R-X101G-X103A-X104V-X232V-X245R,X020R-X101G-X103S-X104I-X232V-X245R,X020R-X101G-X103S-X104L-X232V-X245R,X020R-X101S-X103S-X104I-X232V-X245R,

X020R-X101S-X103S-X104L-X232V-X245R,X020R-X101A-X103A-X104L-X232V-X245R,X020R-X101S-X103S-X104V-X232V-X245R,X020R-X101S-X103A-X104I-X232V-X245R,X020R-X101S-X103A-X104V-X232V-X245R,X020R-X101S-X103G-X104I-X232V-X245R,X020R-X101S-X103G-X104V-X232V-X245R,X020R-X101A-X103A-X104V-X232V-X245R,X020R-X101A-X103S-X104I-X232V-X245R,X020R-X101A-X103S-X104V-X232V-X245R,X018R-X024R-X043R-X076D-X078R-X249R,X024R-X043D-X101G-X103A-X104I-X232V-X245R,X043D-X101G-X103A-X104I-X232V-X245R-X249R,X024R-X076D-X101G-X103A-X104I-X232V-X245R,X076D-X101G-X103A-X104I-X232V-X242R-X245R,X018R-X020R-X024R-X076D-X217E-X249R,X018R-X024R-X043R-X076D-X217E-X249R,X018R-X024R-X043D-X076D-X242R-X249R,X018R-X020R-X024R-X043R-X076D-X249R,X020R-X101A-X103G-X104V-X232V-X245R,X043D-X101G-X103A-X104I-X232V-X245R,X018R-X024R-X076D-X217E-X249R-X269R,和X018R-X024R-X076D-X217E-X242R-X249R,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0363] 本发明提供编码芽孢杆菌属枯草杆菌蛋白酶变体的核酸,其中该枯草杆菌蛋白酶变体是具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:X020R-X101A-X103A-X104I-X118R-X232V-X245R,X020R-X024R-X116A-X213A,X043R-X101A-X116A-X215F-X269R,X024R-X043R-X101A-X116A,X024R-X043R-X101A-X116A-X215F-X269R,X020R-X101G-X103A-X104I-X215F-X232V-X245R,X043R-X101A-X269R,X024R-X043R-X116A-X213A-X269R,X020R-X024R-X043R-X045T-X101A-X213A,X024R-X043R-X116A-X215F-X269R,X020R-X024R-X213A-X215F,X020R-X116A-X269R,X024R-X116A-X213A-X269R,X043R-X101A-X116A-X269R,X101G-X103A-X104I-X116A-X213A-X232V-X245R-X269R,X024R-X043R-X045T-X101A-X116A-X215F-X269R,X020R-X043R-X101A-X269R,X101A-X103A-X104I-X213A-X232V-X245R-X269R,X024R-X215F-X269R,X043R-X101A-X116A-X213A-X215F-X269R,X043R-X101A-X213A-X269R,X020R-X024R-X043R-X045T-X116A-X213A,X101G-X103A-X104I-X232V-X245R-X269R,X024R-X043R-X045T-X101A-X116A-X213A-X269R,X024R-X043R-X045T-X269R,X020R-X043R-X045T-X101A-X269R,X024R-X043R-X116A-X269R,X020R-X024R-X043R-X045T,X043R-X116A-X269R,X024R-X043R-X101A-X215F-X269R,X024R-X043R-X045T-X213A-X215F-X269R,X020R-X024R-X045T-X269R,X020R-X043R-X101A-X116A-X213A-X215F,X020R-X101G-X103A-X104I-X213A-X215F-X232V-X245R,X020R-X024R-X045T-X116A-X269R,X020R-X101A-X116A-X269R,X024R-X043R-X215F,X020R-X024R-X213A,X024R-X043R-X101A-X215F,X020R-X024R-X043R-X045T-X116A,X020R-X024R-X043R-X045T-X101A-X269R,X020R-X024R-X101A-X215F,X020R-X024R-X116A-X213A-X215F,X020R-X024R-X116A,X020R-X024R-X101A-X116A,X043R-X213A-X215F-X269R,X024R-X101A-X269R,X024R-X043R-X116A-X215F,X020R-X038A-X043R-X101A,X020R-X024R-X116A-X215F,X024R-X043R-X101A-X213A,X014L-X020R-X024R-X043R-X045T-X101A-X215F,X020R-X024R-X215F,X020R-X116A-X215F-X269R,X020R-X045T-X116A-X269R,X020R-X024R-X043R-X045T-X215F,和X020R-X024R-X043R-X045T-X116A-X213A-X215F,其中该枯草杆菌蛋白酶

变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0364] 本发明提供编码芽孢杆菌属枯草杆菌蛋白酶变体的核酸,其中该枯草杆菌蛋白酶变体是具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:X043R-X076D-X101A-X103A-X104I-X158E-X188D-X232V-X245R-X248D-X249R-X271F,X024R-X043R-X076D-X101A-X103A-X104I-X158E-X188D-X217E-X232V-X245R-X248D-X249R,X101A-X103A-X104I-X158E-X188D-X232V-X245R-X248D-X249R-X271F-X271F,X101A-X103A-X104I-X158E-X188D-X217E-X232V-X245R-X248D-X249R-X271F,X076D-X101G-X103A-X104I-X114V-X158E-X188D-X232V-X245R-X248D-X249R-X271F,X024R-X076D-X101G-X103A-X104I-X158E-X188D-X232V-X245R-X248D-X249R-X271F,X024R-X043R-X101A-X103A-X104I-X158E-X188D-X217E-X232V-X245R-X248D-X249R,X024R-X043R-X101A-X103A-X104I-X158E-X188D-X232V-X245R-X248D-X249R,X024R-X101A-X103A-X104I-X158E-X166D-X188D-X217E-X232V-X245R-X248D-X249R,X076D-X101G-X103A-X104I-X128L-X158E-X188D-X232V-X245R-X248D-X249R-X271F,和X043R-X076D-X101G-X103A-X104I-X158E-X166D-X188D-X232V-X245R-X248D-X249R-X271F,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0365] 本发明提供编码芽孢杆菌属枯草杆菌蛋白酶变体的核酸,其中该枯草杆菌蛋白酶变体是具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:X022A-X101G-X103A-X104I-X159D-X217E-X232V-X245R-X248D-X271F,X022A-X043R-X101G-X103A-X104I-X159D-X188D-X217E-X232V-X245R-X248D-X271F,X022A-X101G-X103A-X104I-X159D-X188D-X232V-X245R-X248D-X271F,X043R-X101A-X103A-X104I-X158E-X188D-X217E-X232V-X245R-X248D-X249R,X043R-X076D-X101A-X103A-X104I-X158E-X188D-X217E-X232V-X245R-X248D-X249R-X271F,X024R-X101G-X103A-X104I-X158E-X188D-X217E-X232V-X245R-X248D-X249R,X024R-X101G-X103A-X104I-X158E-X188D-X232V-X245R-X248D-X249R,X101G-X103A-X104I-X158E-X188D-X232V-X245R-X248D-X249R,X024R-X101G-X103A-X104I-X158E-X183D-X188D-X232V-X245R-X248D-X249R,X022A-X076D-X101G-X103A-X104I-X159D-X188D-X232V-X245R-X248D-X271F,X022A-X043R-X076D-X101G-X103A-X104I-X159D-X188D-X232V-X245R-X248D-X271F,X022A-X076D-X101G-X103A-X104I-X159D-X232V-X245R-X248D-X271F,X022A-X101G-X103A-X104I-X159D-X232V-X245R-X248D-X271F,X076D-X101A-X103A-X104I-X158E-X188D-X232V-X245R-X248D-X249R-X271F,X043R-X101A-X103A-X104I-X158E-X166D-X188D-X232V-X245R-X248D-X249R,X024R-X076D-X101A-X103A-X104I-X158E-X166D-X188D-X232V-X245R-X248D-X249R-X271F,X076D-X101A-X103A-X104I-X158E-X188D-X232V-X245R-X248D-X249R,X101A-X103A-X104I-X158E-X166D-X188D-X232V-X245R-X248D-X249R-X271F,X043R-X076D-X101A-X103A-X104I-X158E-X166D-X188D-X232V-X245R-X248D-X249R-X271F,X101G-X103A-X104I-X158E-X166D-X188D-X232V-X245R-X248D-X249R-X271F,X101A-X103A-X104I-X158E-X188D-X232V-X245R-X248D-X249R-X271F,X101A-X103A-X104I-X158E-X188D-X217E-X232V-X245R-X248D-X249R,X076D-

X101A-X103A-X104I-X158E-X166D-X188D-X232V-X245R-X248D-X249R-X271F,X101G-X103A-X104I-X158E-X183D-X188D-X232V-X245R-X248D-X249R,X024R-X101G-X103A-X104I-X128L-X158E-X188D-X232V-X245R-X248D-X249R,X076D-X101G-X103A-X104I-X158E-X166D-X188D-X232V-X245R-X248D-X249R-X271F,X043R-X076D-X101A-X103A-X104I-X158E-X166D-X188D-X232V-X245R-X248D-X249R,和X076D-X101A-X103A-X104I-X158E-X188D-X217E-X232V-X245R-X248D-X249R-X271F,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0366] 本发明提供编码芽孢杆菌属枯草杆菌蛋白酶变体的核酸,其中该枯草杆菌蛋白酶变体是具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:X017R-X022A-X076D-X101G-X103A-X104I-X159D-X188D-X232V-X245R-X248D-X271F,X022A-X043R-X101G-X103A-X104I-X159D-X232V-X245R-X248D-X271F,X022A-X101G-X103A-X104I-X159D-X188D-X232V-X245R-X248D-X249R-X271F,X017R-X022A-X076D-X101G-X103A-X104I-X159D-X232V-X245R-X248D-X271F,X022A-X076D-X101G-X103A-X104I-X159D-X232V-X245R-X248D-X249R-X271F,X022A-X101G-X102A-X103A-X104I-X159D-X188D-X232V-X245R-X248D-X271F,和X022A-X043R-X076D-X101G-X103A-X104I-X159D-X232V-X245R-X248D-X249R-X271F,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0367] 本发明提供编码芽孢杆菌属枯草杆菌蛋白酶变体的核酸,其中该枯草杆菌蛋白酶变体是具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:X101S-X103A-X104I-X158E-X188D-X232V-X245R-X248D-X249R,X101S-X103G-X104V-X158E-X188D-X232V-X245R-X248D-X249R,X101G-X103S-X104I-X158E-X188D-X232V-X245R-X248D-X249R,X101A-X103A-X104I-X158E-X188D-X232V-X245R-X248D-X249R,X101A-X103A-X104L-X158E-X188D-X232V-X245R-X248D-X249R,X101G-X103G-X104I-X158E-X188D-X232V-X245R-X248D-X249R,X101S-X103G-X104I-X158E-X188D-X232V-X245R-X248D-X249R,X101S-X103S-X104I-X158E-X188D-X232V-X245R-X248D-X249R,X101S-X103S-X104V-X158E-X188D-X232V-X245R-X248D-X249R,X101A-X103S-X104I-X158E-X188D-X232V-X245R-X248D-X249R,X101A-X103S-X104I-X159E-X232V-X245R-X248D-X249R,X101S-X103A-X104I-X159E-X232V-X245R-X248D-X249R,X101G-X103A-X104L-X158E-X188D-X232V-X245R-X248D-X249R,X101A-X103A-X104L-X159E-X232V-X245R-X248D-X249R,X101A-X103S-X104L-X159E-X232V-X245R-X248D-X249R,X101G-X103S-X104L-X159E-X232V-X245R-X248D-X249R,X101S-X103A-X104L-X159E-X232V-X245R-X248D-X249R,X101A-X103G-X104V-X159E-X232V-X245R-X248D-X249R,和X101S-X103A-X104V-X159E-X232V-X245R-X248D-X249R,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0368] 本发明提供编码芽孢杆菌属枯草杆菌蛋白酶变体的核酸,其中该枯草杆菌蛋白酶变体是具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸

序列:X026F-X051W-X104L-X106E,X026F-X031F-X078N-X102A-X160D,X020K-X100S-X116L-X158E-X166D-X243F,X033S-X043W-X218D-X239G-X243F,X022L-X038F-X048R-X062E-X100S-X186K,X101D-X103N-X116L-X144R-X215D,X104L-X105T-X213A-X217E-X256N,X043W-X101D-X212M-X243F,X026F-X048R-X105T-X213A-X218D-X224A,X024F-X101D-X118R-X215D-X250I-X272F,X121F-X185E-X224A-X239G,X022L-X031F-X102A-X128D-X224A-X243F,X062E-X078N-X102A-X116L-X144R-X250I,X022L-X038F-X121F-X160D-X272F,X026F-X078N-X159C-X186K-X243F,X024F-X048R-X118R-X166D-X217E,X023A-X038F-X078N-X100S-X212M-X215D,X100S-X116L-X158E-X213A,X078N-X104L-X118R-X128D,X102A-X103N-X105T-X194E,X022L-X078N-X128D-X213A,X027R-X100S-X118R-X160D-X188D-X243F,X024F-X102A-X186K-X213A-X217E-X243F,X033S-X105T-X188D-X216F,X023A-X100S-X194E-X212M,X048R-X128D-X185E-X239G,X020K-X024F-X033S-X129E-X194E,X020K-X027R-X129E-X166D-X239G,X022L-X023A-X027R-X101D-X104L-X216F,X033S-X118R-X129E-X194E-X239G,X022L-X078N-X116L-X129E-X256N,X027R-X101D-X103N-X105T-X272F,X048R-X078N-X116L-X185E-X217E-X239G,X023A-X024F-X027R-X062E,X024F-X103N-X104L-X118R-X188D,X026F-X104L-X256N-X272F,X024F-X043W-X104L-X121F-X129E,X062E-X078N-X116L-X224A,X023A-X024F-X051W-X158E,X027R-X038F-X102A-X116L,X062E-X078N-X144R-X212M,X031F-X116L-X256N-X272F,X022L-X033S-X104L-X116L-X160D-X186K,X024F-X118R-X129E-X186K-X213A,X043W-X105T-X213A-X215D-X216F,X031F-X105T-X186K-X188D,X026F-X194E-X213A-X256N,和X103N-X160D-X250I-X256N,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0369] 本发明提供编码芽孢杆菌属枯草杆菌蛋白酶变体的核酸,其中该枯草杆菌蛋白酶变体是具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:X022A-X024R-X101D-X103A-X104I-X118R-X159D-X188D-X232V-X248D-X271F,X022A-X024R-X103A-X104I-X129E-X159D-X188D-X232V-X248D-X271F,X022A-X024R-X103A-X104I-X118R-X159D-X188D-X217D-X232V-X248D,X022A-X024R-X101D-X103A-X104I-X118R-X129E-X159D-X188D-X232V-X245R-X248D,X022A-X024R-X101D-X103A-X104I-X159D-X188D-X232V-X245R-X248D,X022A-X043R-X103A-X104I-X118R-X129E-X159D-X188D-X232V-X245R-X248D,X022A-X043R-X103A-X104I-X118R-X128I-X129E-X159D-X188D-X232V-X248D,X022A-X043R-X101D-X103A-X104I-X118R-X129E-X159D-X188D-X232V-X248D-X271F,X022A-X024R-X043R-X101D-X103A-X104I-X159D-X188D-X232V-X245R-X248D,X022A-X103A-X104I-X159D-X188D-X232V-X248D,X022A-X024R-X103A-X104I-X118R-X129E-X159D-X188D-X232V-X248D-X271F,X022A-X024R-X103A-X104I-X159D-X188D-X217D-X232V-X245R-X248D-X271F,X022A-X043R-X062E-X103A-X104I-X159D-X188D-X232V-X245R-X248D-X271F,X022A-X043R-X103A-X104I-X129E-X159D-X188D-X232V-X245R-X248D,X022A-X024R-X103A-X104I-X159D-X188D-X217D-X232V-X248D-X271F,X022A-X103A-X104I-X118R-X159D-X188D-X217D-X232V-X245R-X248D,X022A-X024R-X101D-X103A-X104I-X118R-X128I-X159D-X188D-X232V-X245R-X248D,X022A-X024R-X043R-X103A-X104I-X159D-X188D-X217D-X232V-X248D-X271F,X022A-

X043R-X103A-X104I-X118R-X159D-X188D-X217D-X232V-X248D-X271F,X022A-X043R-X103A-X104I-X118R-X159D-X188D-X232V-X248D-X271F,X022A-X103A-X104I-X128I-X129E-X159D-X188D-X232V-X248D-X271F,X022A-X103A-X104I-X159D-X188D-X217D-X232V-X245R-X248D-X271F,X022A-X043R-X103A-X104I-X128I-X159D-X188D-X232V-X245R-X248D,X022A-X101D-X103A-X104I-X118R-X159D-X188D-X217D-X232V-X245R-X248D-X271F,X022A-X103A-X104I-X118R-X129E-X159D-X188D-X232V-X245R-X248D-X271F,X022A-X024R-X043R-X103A-X104I-X118R-X159D-X188D-X217D-X232V-X248D,X022A-X062E-X103A-X104I-X118R-X159D-X188D-X232V-X245R-X248D,X022A-X043R-X101D-X103A-X104I-X118R-X129E-X159D-X188D-X217D-X232V,X022A-X024R-X103A-X104I-X159D-X188D-X217D-X232V-X248D,X022A-X024R-X043R-X103A-X104I-X118R-X128I-X129E-X159D-X188D-X217D-X232V-X248D-X271F,和X022A-X103A-X104I-X118R-X159D-X188D-X217D-X232V-X245R-X248D-X271F,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0370] 本发明提供编码芽孢杆菌属枯草杆菌蛋白酶变体的核酸,其中该枯草杆菌蛋白酶变体是具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:X020K-X024F-X062E-X188D-X239G,X024F-X062E-X116L-X239G,X020K-X023A-X062E-X188D,X020K-X023A-X024F-X062E-X118R-X188D-X213A,X020K-X043W-X062E-X116L-X188D-X213A-X239G,X023A-X062E-X116L-X118R,X023A-X024F-X062E-X116L-X118R,X024F-X116L,X024F-X062E-X188D-X213A,X023A-X062E-X116L-X118R-X188D-X239G,X020K-X024F-X062E,X020K-X043W-X062E-X116L-X239G,X024F-X062E-X116L-X213A-X239G,X020K-X024F-X043W-X062E-X116L-X213A,X020K-X023A-X024F-X062E-X116L-X188D-X213A,X024F-X062E-X188D-X239G,X023A-X043W-X062E-X116L-X118R-X213A,X062E-X188D-X239G,X020K-X024F-X062E-X239G,X024F-X116L-X118R-X188D-X239G,X020K-X023A-X062E-X116L-X118R-X213A,X020K-X023A-X024F-X062E-X188D-X213A-X239G,X024F-X043W-X118R-X188D,X023A-X024F-X116L-X118R-X188D-X213A,X020K-X023A-X043W-X116L-X188D-X213A-X239G,X023A-X024F-X116L-X188D-X239G,X023A-X043W-X116L-X118R-X188D,X023A-X024F-X118R-X188D-X239G,X023A-X024F-X043W-X062E-X116L-X118R,X020K-X043W-X188D-X213A,X024F-X062E-X118R-X239G,X023A-X043W-X188D-X213A,X020K-X024F-X043W-X062E-X116L-X118R-X188D-X239G,X020K-X116L-X188D-X239G,X020K-X043W-X062E-X118R,X020K-X043W-X116L-X188D-X213A,X020K-X024F,X023A-X043W-X116L-X239G,X023A-X024F-X043W-X116L-X118R-X188D-X239G,X020K-X023A-X043W-X213A,和X023A-X024F-X062E-X118R-X213A-X239G,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0371] 本发明提供编码芽孢杆菌属枯草杆菌蛋白酶变体的核酸,其中该枯草杆菌蛋白酶变体是具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:X020K-X023A-X043W-X118R-X128I-X129E-X159D-X188D,X024F-X118R-X128I-X129E-X159D,X020K-X024F-X062E-X116L-X118R-X188D,X020K-X062E-X116L-X188D,X062E-

X116L-X118R-X213A,X020K-X023A-X062E-X116L-X188D,X062E-X116L-X118R-X188D,X020K-X062E-X116L-X213A,X020K-X023A-X062E-X116L,X020K-X062E-X188D-X213A,X020K-X062E,X020K-X024F-X062E-X116L-X188D,X020K-X043W-X062E-X116L-X188D,X020K-X024F-X062E-X188D-X213A,X062E-X116L-X188D-X213A,X020K-X062E-X116L,X020K-X023A-X062E-X116L-X188D-X213A,X023A-X024F-X062E-X116L-X213A,X022A-X043R-X103A-X104I-X128I-X129E-X159D-X188D-X232V-X245R-X248D,X022A-X043R-X103A-X104I-X118R-X128I-X129E-X159D-X188D-X232V-X248D-X271F,X024F-X062E-X116L-X188D,X022A-X024R-X103A-X104I-X118R-X128I-X129E-X159D-X188D-X232V-X248D,X023A-X062E-X116L-X188D,X043W-X062E-X116L,X020K-X023A-X116L-X188D,X043W-X062E-X116L-X188D,X024F-X062E-X116L,X062E-X116L-X188D,和X022A-X024R-X103A-X104I-X128I-X159D-X188D-X232V-X248D,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0372] 本发明提供编码芽孢杆菌属枯草杆菌蛋白酶变体的核酸,其中该枯草杆菌蛋白酶变体是具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:X087R-X101G-X103A-X104I-X109R-X212P-X232V-X245R-X271V,X101G-X103A-X104I-X109R-X232V-X245R,X101G-X103A-X104I-X109R-X212P-X232V-X245R-X271V,X101G-X103A-X104I-X109R-X212P-X232V-X245R,X076D-S87R-X103A-X104I-X212P-X271V,X076D-X103A-X104I-X109R,X076D-X103A-X104I-X212P-X271V,X076D-X103A-X104I-X109R-X245R,和X076D-X103A-X104I-X212P-X245L-X271V,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ IDNO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0373] 本发明提供编码芽孢杆菌属枯草杆菌蛋白酶变体的核酸,其中该枯草杆菌蛋白酶变体是具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:X024R-X086W-X118R,X024R-X078R-X086W-X243F,X024R-X033S-X086S-X087N-X209A,X033S-X118R,X024R-X078R-X086W-X118R-X270T,X024R-X033S-X086W-X118R,X078R-X086W-X243F,X033S-X078R-X086W-X118R-X209A,X033S-X078R-X209A,X086W-X118R-X243F,X024R-X086W,X078R-X086W-X235F,X024R-X118R,X024R-X086R,X101G-X103A-X104I-X232V,X024R-X033S-X078R-X086W-X118R,X024R-X118R-X209A,X209A-X241R,X033S-X086W-X243F,X033S-X172V-X209A,X118R-X209A-X243F,X024R-X086S-X141G,X024R-X118R-X209A-X243F,X024R-X033S-X086S-X085N-X235F,X024R-X033S-X133V,X024R-X033S-X078R-X086W,X024R-X086W-X209A,X024R-X241R,X033S-X118R-X243F,X024R-X235F,X024R-X078R-X086W,X024R-X118R-X209A-X235F,X024R-X209A-X241R,X033S-X118R-X241R,X086W-X118R-X209A,X033S-X118R-X159D-X209A,X033S-X078R-X086W,X024R-X086W-X243F,X118R-X209A,X024R-X086W-X118R-X203I,X078R-X209A-X235F,X024R-X033S-X241R,X078R-X118R,X033S-X118R-X209A-X243F,X021M-X024R-X033S,X024R-X033S-X086W,X033S-X235F,X078R-X086W-X209A,X024R-X033S-X209A-X235F,X033S-X086W-X118R,X024R-X033S-X078R-X209A,X033S-X086W-X118R-X209A-X243F,X086W-X209A-X243F,X005S-X078R-X118R-X241R,X024R-X174T,X033S-X209A-

X243F,X086W-X118R-X133V,X024R-X033S-X118R,X024R-X086W-X209A-X235F,X086W-X209A,X008T-X024R,X086W-X118R,X033S-X241R,X005S-X024R-X033S-X243F,X024R-X209A-X242P,X024R-X033S-X078R-X118R,X024R-X033S-X194T,X024R-X243F,X024R-X209A,X024R-X033S-X118R-X209A,X033S-X086W,X024R-X033S,X024R-X033S-X078R-X243F,X086W-X243F,X033S-X118D-X138V-X209A,X033S-X209A-X235F,X024R-X086R-X118R,X033S-X201S,X024R-X239Q,X033S-X118R-X209A-,X078R-X086W,X235F-X243F,X024R-X209A-X235F,X118R-X172V,X017Y-X024R-X033S-X086W,X033S-X148F,X024R-X118R-X235F,X033S-X078R,X033S-X243F,X024C-X033S,X118R-X194T,X033S-X209A,X118R-X209A-X235F,X024R-X033S-X209A-X243F,X024R-X033S-X235F,X024R-X033S-X118R-X235F,X024R-X141G,X024R-X274I,X024R-X033S-X209A,X086W-X235F,X024R-X209A-X243F,X004E-X033S-X078R,X086W-X209A-X235F,X015T-X033S,X033S-X086W-X156L-X209A,X024R-X118R-X243F-X269H,X209A-X235F,X024R-X247H,X024R-X033S-X228T,X078R-X235F,X024R-X033S-X174V-X235F,X024R-X235F-X243F,X024R-X033S-X235F-X241R,X024R-X033S-X151V,X024R-X104A,X033S-X048T,X012H-X104A-X118R,X118R-X235F,X033S-X253A,X143A-X209A,X024R-X033S-X243F,X033S-X239T,X209A-X243F,X024R-X033S-X129H-X184D-X253M,X024R-X085V-X086W-X118R-X235F,X024R-X272P,和X024R-X269C,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0374] 本发明提供编码芽孢杆菌属枯草杆菌蛋白酶变体的核酸,其中该枯草杆菌蛋白酶变体是具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:X020R-X087D-X101G-X103A-X104I-X232V-X245R,X020R-X101G-X103A-X104I-X150L-X232V-X245R,X018R-X020R-X024R-X076D-X087D-X249R,X018R-X020R-X024R-X076D-X150L-X249R,X018R-X024R-X043R-X076D-X087D-X249R,X018R-X024R-X043R-X076D-X150L-X249R,X018R-X024R-X076D-X078R-X087D-X249R,X018R-X024R-X076D-X078R-X150L-X249R,X018R-X024R-X076D-X087D-X249R-X269R,X018R-X024R-X076D-X087D-X242R-X249R,X018R-X024R-X076D-X087D-X150L-X249R,X018R-X024R-X076D-X150L-X249R,X018R-X087D-X101G-X103A-X104I-X232V-X245R,X018R-X101G-X103A-X104I-X150L-X232V-X245R,X018R-X022R-X024R-X076D-X087D-X249R,X018R-X022R-X024R-X076D-X150L-X249R,X043R-X087D-X101G-X103A-X104I-X232V-X245R-X269R,X043R-X101G-X103A-X104I-X150L-X232V-X245R,X024R-X087D-X101G-X103A-X104I-X232V-X245R,X024R-X101G-X103A-X104I-X150L-X232V-X245R,X078R-X087D-X101G-X103A-X104I-X232V-X245R,X078R-X101G-X103A-X104I-X150L-X232V-X245R,X087D-X101G-X103A-X104I-X232V-X245R-X269R,X101G-X103A-X104I-X150L-X232V-X245R-X249R,X101G-X103A-X104I-X150L-X232V-X245R-X269R,X022R-X087D-X101G-X103A-X104I-X232V-X245R,X018R-X024R-X043D-X076D-X150L-X249R,X043R-X087D-X101G-X103A-X104I-X232V-X245R,X022R-X101G-X103A-X104I-X150L-X232V-X245R,X018R-X024R-X043D-X076D-X087D-X249R,X018R-X024R-X076D-X087D-X249R,X018R-X024R-X076D-X150L-X242R-X249R,X043R-X101G-X103A-X104I-X150L-X232V-X245R-X269R,X076D-X101G-X103A-X104I-X150L-X232V-X245R,X087D-X101G-X103A-X104I-X232V-X242R-

X245R,X101G-X103A-X104I-X150L-X232V-X245R,X076D-X087D-X101G-X103A-X104I-X232V-X245R,X087D-X101G-X103A-X104I-X232V-X245R,和X101G-X103A-X104I-X150L-X232V-X242R-X245R,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0375] 本发明提供编码芽孢杆菌属枯草杆菌蛋白酶变体的核酸,其中该枯草杆菌蛋白酶变体是具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:X024R-X101G-X103A-X104I-X129Q-X158E-X188D-X217E-X232V-X245R-X248D-X249R,X024R-X101G-X103A-X104I-X130A-X158E-X183D-X188D-X232V-X245R-X248D-X249R,X024R-X101G-X103A-X104I-X129Q-X158E-X183D-X188D-X232V-X245R-X248D-X249R,X101G-X103A-X104I-X130A-X158E-X188D-X232V-X245R-X248D-X249R,X024R-X101G-X103A-X104I-X129Q-X158E-X188D-X232V-X245R-X248D-X249R,X024R-X101G-X103A-X104I-X130A-X158E-X188D-X232V-X245R-X248D-X249R,X024R-X101G-X103A-X104I-X129Q-X130A-X158E-X183D-X188D-X232V-X245R-X248D-X249R,X024R-X101G-X103A-X104I-X128L-X129Q-X158E-X188D-X232V-X245R-X248D-X249R,X024R-X101G-X103A-X104I-X129Q-X130A-X158E-X188D-X232V-X245R-X248D-X249R,X101G-X103A-X104I-X129Q-X158E-X188D-X232V-X245R-X248D-X249R,X101G-X103A-X104I-X129Q-X130A-X158E-X188D-X232V-X245R-X248D-X249R,X024R-X101G-X103A-X104I-X128L-X129Q-X130A-X158E-X188D-X232V-X245R-X248D-X249R,X101G-X103A-X104I-X128L-X129Q-X158E-X188D-X232V-X245R-X248D-X249R,和X024R-X027R-X101G-X103A-X104I-X128L-X129Q-X130A-X158E-X188D-X232V-X245R-X248D-X249R,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0376] 本发明提供编码芽孢杆菌属枯草杆菌蛋白酶变体的核酸,其中该枯草杆菌蛋白酶变体是具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:X101G-X103A-X104I-X232V-X222Q-X245R,X101G-X103A-X104I-X158E-X188D-X222S-X232V-X245R-X248D-X249R,X101G-X103A-X104I-X158E-X188D-X222Q-X232V-X245R-X248D-X249R,X076D-X101G-X103A-X104I-X232V-X222Q-X245R,X101G-X103A-X104I-X232V-X222S-X245R,X076D-X101G-X103A-X104I-X232V-X222S-X245R,和X076D-X101G-X103A-X104I-X158E-X188D-X222S-X232V-X245R-X248D-X249R,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0377] 本发明提供编码芽孢杆菌属枯草杆菌蛋白酶变体的核酸,其中该枯草杆菌蛋白酶变体是具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:X024R-X101G-X103A-X104I-X128L-X129Q-X158E-X188D-X232V-X245R-X248D-X249R,X101G-X103A-X104I-X130A-X158E-X188D-X232V-X245R-X248D-X249R,X024R-X101G-X103A-X104I-X158E-X188D-X232V-X245R-X248D-X249R,X101G-X103A-X104I-X128L-X129Q-X158E-X188D-X232V-X245R-X248D-X249R,X101G-X103A-X104I-X129Q-X130A-X158E-X188D-X232V-X245R-X248D-X249R,X101G-X103A-X104I-X130A-X158E-X183D-X188D-X217E-X232V-X245R-X248D-X249R,X024R-X101G-X103A-X104I-X128L-X129Q-

X130A-X158E-X188D-X232V-X245R-X248D-X249R,X024R-X101G-X103A-X104I-X129Q-X158E-X188D-X217E-X232V-X245R-X248D-X249R,X101G-X103A-X104I-X128L-X130A-X158E-X188D-X217E-X232V-X245R-X248D-X249R,X024R-X101G-X103A-X104I-X128L-X129Q-X158E-X183D-X188D-X232V-X245R-X248D-X249R,X024R-X101G-X103A-X104I-X128L-X129Q-X130A-X158E-X183D-X188D-X232V-X245R-X248D-X249R,X024R-X101G-X103A-X104I-X128L-X129Q-X158E-X188D-X232V-X245R-X248D-X249R-X271G,X101G-X103A-X104I-X129Q-X158E-X183D-X188D-X232V-X245R-X248D-X249R,X024R-X101G-X103A-X104I-X130A-X158E-X188D-X217E-X232V-X245R-X248D-X249R,X024R-X101G-X103A-X104I-X128L-X158E-X183D-X188D-X232V-X245R-X248D-X249R,X101G-X103A-X104I-X129Q-X158E-X188D-X217E-X232V-X245R-X248D-X249R,和X024R-X101G-X103A-X104I-X128L-X130A-X158E-X188D-X232V-X245R-X248D-X249R,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0378] 本发明提供编码芽孢杆菌属枯草杆菌蛋白酶变体的核酸,其中该枯草杆菌蛋白酶变体是具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:X101G-X103A-X104I,X22A-X101A-X209E,S103G-L111V-G159E,X22A-X103G-X159E,X22A-X111V-X159E,X22A-X128N-X271F-X209E,X22A-X103G-X111V,X62E-X111V-X128N,X22A-X111V-X128N,X22A-X62E-X111V,X101A-X103G-X104L-X188D,X101G-X103A-X104I-X159D,X101A-X103G-X104L-X128N,X22A-X101A-X159E,X101A-X103G-X104L,X101A-X103G-X104L-X159E,X22A-X101A-X103G-X104L,X101A-X103G-X104L-X209E,X22A-X209E-X271F,X22A-X101A-X271F,和X101A-X209E-X271F,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0379] 本发明提供编码芽孢杆菌属枯草杆菌蛋白酶的芽孢杆菌属枯草杆菌蛋白酶变体的核酸,其中该枯草杆菌蛋白酶变体是具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:X103A-X104I-X159D-X232V-X236H-X245R-X248D-X252K,X101G-X104I-X159D-X232V-X236H-X245R-X248D-X252K,X101G-X103A-X159D-X232V-X236H-X245R-X248D-X252K,X101G-X103A-X104L-X232V-X236H-X245R-X248D-X252K,X101G-X103A-X104L-X159D-X236H-X245R-X248D-X252K,X101G-X103A-X104L-X159D-X232V-X245R-X248D-X252K,X101G-X103A-X104L-X159D-X232V-X236H-X248D-X252K,X101G-X103A-X104L-X159D-X232V-X236H-X245R-X252K,和X101G-X103A-X104L-X159D-X232V-X236H-X245R-X248D,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0380] 本发明提供编码芽孢杆菌属枯草杆菌蛋白酶变体的核酸,其中该枯草杆菌蛋白酶变体是具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:X101G-X103A-X104I-X159D-X232V-X245R-X248D,X101G-X103A-X104I-X159D-X232V-X245R-X248D-X271F,X101G-X103A-X104I-X159D-X232V-X245R-X248D-X238R,X101G-X103A-X104I-X159D-X232V-X245R-X248D-X248R,X101G-X103A-X104I-X159D-X232V-X245R-X248D-X253R,X101G-X103A-X104I-X159D-X232V-X245R-X248D-X24R,X101G-X103A-

X104I-X159D-X232V-X245R-X248D-X76D,X101G-X103A-X104I-X159E-X232V-X245R-X248D-X249R,X101G-X103A-X104I-X159E-X232V-X245R-X248D-X271F,X101G-X103A-X104I-X158E-X232V-X245R-X248D-X249R,X101G-X103A-X104I-X158E-X232V-X245R-X248D-X271F,X22A-X101G-X103A-X104I-X159D-X232V-X245R-X248D-X249R,X22A-X101G-X103A-X104I-X159D-X232V-X245R-X248D-X271F,X62E-X101G-X103A-X104I-X159D-X232V-X245R-X248D-X249R,和X62E-X101G-X103A-X104I-X159D-X232V-X245R-X248D-X271F,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0381] 本发明提供编码芽孢杆菌属枯草杆菌蛋白酶的核酸,其中该枯草杆菌蛋白酶变体是具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:X20R-X43R-X249R,X20R-X22R-X43R,X20R-X43R-X242R,X20R-X43R-X271L,X20R-X43R-X244R,X20R-X24R-X43R-X242R,X9A-X22R-X78R-X212F-X241R,X9A-X20R-X43R-X212F,X9A-X43R-X212F,X20R-X43R-X212F,X20R-X22R-X43R-X212F,X24R-X78R-X212F,X9A-X43R-X78R,X9A-X43R-X78R-X242R,X9A-X20R-X43R-X78R,X20R-X24R-X43R-X78R-X242R,X22R-X24R-X78R-X212F,X9A-X20R-X43R-X78R-X242R,X20R-X43R-X78R-X249R,X20R-X43R-X78R,X9A-X78R-X212F,X9A-X22R-X43R-X78R,X9A-X20R-X24R-X43R,X9A-X22R-X78R-X212F,X4R-X9A-X22R-X78R-X212F,X20R-X24R-X43R,X1R-X9A-X43R,X20R-X24R-X43R-X115R,X9A-X24R-X43R,X20R-X22R-X24R-X43R,X1R-X24R-X43R,X9A-X20R-X24R-X43R-X242R,X9A-X20R-X22R-X78R-X212F,X9A-X24R-X43R-X244R,X9A-X24R-X43R-X242R,X4R-X9A-X22R-X24R-X212F,和X22R-X24R-X43R,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0382] 本发明提供编码芽孢杆菌属枯草杆菌蛋白酶的芽孢杆菌属枯草杆菌蛋白酶变体的核酸,其中该枯草杆菌蛋白酶变体是具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:X101G-X103A-X104I-X232V-X245R-X248D,X101G-X103A-X104I-X159D-X232V-X245R,X101G-X103A-X104I-X159R-X232V-X245R-X248D,X101G-X103A-X104I-X159D-X232V-X245R-X248R,X101G-X103A-X104I-X232V-X245R,X101G-X103A-X104I-X232V-X245R-X248R,X101G-X103A-X104I-X159R-X232V-X245R-X248R,以及X101G,X103A,X104I,X232V,X236H,X245R,和X252K,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0383] 本发明提供编码芽孢杆菌属枯草杆菌蛋白酶的核酸,其中该枯草杆菌蛋白酶变体是具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:X16S,X22A,X24R,X62E,X76D,X89P,X101A/G,X103G/A,X104L/I,X111V,X128N,X129E,X232V,X148I,X158E,X159D/E,X166D,X186H,X188D,X209E,X236H,X238R,X245R,X248D/R,X249R,X252K/R,X253R,和X271F,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0384] 本发明提供编码芽孢杆菌属枯草杆菌蛋白酶的核酸,其中该枯草杆菌蛋白酶变体是具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:N062E-A158E,S103G-A158E,S128N-A158E,A016S-A158E,V104L-A158E,E089P-A158E,

L111V-A158E,T022A-A158E,S101A-A158E,L148I-A158E,P129E-A158E,T022A-E089P,A016S-E089P,N062E-E089P,N062E-E271F,A158E-E271F,R186H-E271F,P129E-E271F,L111V-E271F,Y209E-E271F,A016S-E271F,S188D-E271F,T022A-E271F,G159E-E271F,V104L-E271F,S101A-E271F,E089P-E271F,S128N-E271F,S103G-E271F,L148I-E271F,H249R-E271F,N062E-G159E,A016S-G159E,S128N-G159E,L148I-G159E,L111V-G159E,E089P-G159E,T022A-G159E,P129E-G159E,S103G-G159E,V104L-G159E,A158E-G159E,S101A-G159E,A158E-H249R,L111V-H249R,P129E-H249R,N062E-H249R,A016S-H249R,R186H-H249R,L148I-H249R,G159E-H249R,S101A-H249R,S188D-H249R,V104L-H249R,Y209E-H249R,T022A-H249R,S128N-H249R,S103G-H249R,E089P-H249R,T022A-L111V,S101A-L111V,A016S-L111V,V104L-L111V,N062E-L111V,S103G-L111V,E089P-L111V,A016S-L148I,N062E-L148I,T022A-L148I,P129E-L148I,V104L-L148I,S103G-L148I,S128N-L148I,S101A-L148I,E089P-L148I,L111V-L148I,A016S-N062E,T022A-N062E,N062E-P129E,T022A-P129E,S128N-P129E,A016S-P129E,S101A-P129E,V104L-P129E,E089P-P129E,S103G-P129E,L111V-P129E,N062E-R186H,S128N-R186H,S101A-R186H,T022A-R186H,A016S-R186H,A158E-R186H,E089P-R186H,P129E-R186H,G159E-R186H,S103G-R186H,V104L-R186H,L111V-R186H,L148I-R186H,N062E-S101A,T022A-S101A,A016S-S101A,E089P-S101A,N062E-S103G,T022A-S103G,A016S-S103G,S101A-S103G,E089P-S103G,N062E-S128N,A016S-S128N,T022A-S128N,S101A-S128N,V104L-S128N,E089P-S128N,S103G-S128N,L111V-S128N,L111V-S188D,N062E-S188D,A016S-S188D,L148I-S188D,T022A-S188D,S128N-S188D,S101A-S188D,V104L-S188D,E089P-S188D,P129E-S188D,G159E-S188D,R186H-S188D,S103G-S188D,A158E-S188D,A016S-T022A,A016S-V104L,T022A-V104L,S101A-V104L,N062E-V104L,S103G-V104L,E089P-V104L,G159E-Y209E,L111V-Y209E,S101A-Y209E,A016S-Y209E,S128N-Y209E,L148I-Y209E,P129E-Y209E,N062E-Y209E,T022A-Y209E,S103G-Y209E,A158E-Y209E,S188D-Y209E,V104L-Y209E,E089P-Y209E,和R186H-Y209E,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0385] 本发明提供编码芽孢杆菌属枯草杆菌蛋白酶变体的核酸,该变体具有蛋白水解活性并包含具有选自以下的氨基酸置换的组合的氨基酸序列:N018R-W241R,G020R-W241R,S024R-W241R,S009A-W241R,G020R-W241R,V004R-W241R,N043R-W241R,S078R-W241R,T022R-W241R,G115R-W241R,A001R-W241R,S212F-W241R,L082R-W241R,N018R-V244R,S024R-V244R,S078R-V244R,G020R-V244R,S212F-V244R,S009A-V244R,L082R-V244R,A001R-V244R,N043R-V244R,T022R-V244R,V004R-V244R,G115R-V244R,W241R-V244R,S242R-V244R,A001R-V004R,S009A-T022R,N018R-T022R,G020R-T022R,V004R-T022R,A001R-T022R,S024R-S242R,N018R-S242R,V004R-S242R,G020R-S242R,S212F-S242R,L082R-S242R,S078R-S242R,A001R-S242R,S009A-S242R,T022R-S242R,G115R-S242R,N043R-S242R,W241R-S242R,N018R-S212F,T022R-S212F,V004R-S212F,S024R-S212F,A001R-S212F,G115R-S212F,G020R-S212F,S009A-S212F,N043R-S212F,S078R-S212F,L082R-S212F,S009A-S078R,G020R-S078R,S024R-S078R,T022R-S078R,N018R-S078R,

V004R-S078R,A001R-S078R,N043R-S078R,T022R-S024R,G020R-S024R,N018R-S024R,A001R-S024R,V004R-S024R,S009A-S024R,V004R-S009A,A001R-S009A,S242R-N269R,S024R-N269R,G020R-N269R,T022R-N269R,H249R-N269R,S212F-N269R,N043R-N269R,V244R-N269R,A001R-N269R,N018R-N269R,S078R-N269R,S009A-N269R,G115R-N269R,W241R-N269R,V004R-N269R,L082R-N269R,N018R-N043R,G020R-N043R,V004R-N043R,T022R-N043R,S009A-N043R,A001R-N043R,S024R-N043R,S009A-N018R,V004R-N018R,A001R-N018R,S024R-L082R,S009A-L082R,N018R-L082R,A001R-L082R,S078R-L082R,G020R-L082R,T022R-L082R,V004R-L082R,N043R-L082R,N043R-H249R,G020R-H249R,V004R-H249R,N018R-H249R,S009A-H249R,S212F-H249R,T022R-H249R,S024R-H249R,G115R-H249R,A001R-H249R,L082R-H249R,S242R-H249R,W241R-H249R,V244R-H249R,S078R-H249R,N018R-G115R,G020R-G115R,T022R-G115R,S078R-G115R,S009A-G115R,V004R-G115R,A001R-G115R,L082R-G115R,N043R-G115R,S024R-G115R,S009A-G020R,N018R-G020R,V004R-G020R,A001R-G020R,S009A-E271L,G020R-E271L,S024R-E271L,V244R-E271L,W241R-E271L,N043R-E271L,T022R-E271L,H249R-E271L,S212F-E271L,G115R-E271L,S242R-E271L,S078R-E271L,V004R-E271L,N269R-E271L,A001R-E271L,N018R-E271L,和L082R-E271L,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0386] 本发明提供编码芽孢杆菌属枯草杆菌蛋白酶变体的核酸,该变体具有蛋白水解活性并包含具有选自以下的氨基酸置换的组合的氨基酸序列:G020R-N043R,G020K-N062E,S024F-N116L,G020K-S024F,S024R-A174T,S024R-G118R,S024R-K235F,S024R-P086R,S024R-P086W,S078R-G118R,T033S-G118R,T033S-K235F,Y209A-W241R,G020R-N076D,N018R-Q245R,S024R-R045T,A232V-Q245R,G118R-A172V,G118R-A194T,I008T-S024R,K235F-N243F,N018R-S103A,N018R-V104I,P086W-G118R,P086W-N243F,P086W-Y209A,S024C-T033S,S024R-A232V,S024R-N243F,S024R-P239Q,S024R-S101G,S024R-S141G,S024R-T033S,S024R-T274I,S024R-Y209A,S078R-P086W,S101G-A232V,T033S-L148F,T033S-P086W,T033S-P201S,T033S-S078R,T033S-W241R,T033S-Y209A,A230E-H249R,A232V-H249R,G118R-K235F,N076D-Q245R,P086W-K235F,S024R-R247H,S024R-V104A,S078R-K235F,S101G-H249R,S103A-A232V,T033S-A048T,T033S-P239T,T033S-T253A,T143A-Y209A,Y209A-K235F,N018R-R045T,Y209A-N243F,S024R-A272P,S024R-R269C,S101G-V104I,V104I-A232V,N076D-H249R,和S024R-N076D,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0387] 本发明提供编码芽孢杆菌属枯草杆菌蛋白酶变体的核酸,该变体具有蛋白水解活性并包含具有选自以下的氨基酸置换的组合的氨基酸序列:G020R-N076D,S024R-R045T,A230E-H249R,N018R-R045T,N018R-Q245R,S101G-A232V,S024R-A232V,A232V-Q245R,S024R-S101G,N018R-V104I,N018R-S103A,S101G-H249R,A232V-H249R,S103A-A232V,N076D-Q245R,S101G-V104I,V104I-A232V,N076D-H249R,S024R-N076D,S024F-N116L,G020K-S024F,G020K-N062E,T033S-G118R,S024R-P086W,S024R-G118R,S024R-P086R,Y209A-W241R,S024R-W241R,S024R-K235F,G118R-Y209A,S078R-G118R,T033S-K235F,

S024R-A174T,P086W-Y209A,I008T-S024R,P086W-G118R,T033S-W241R,S024R-N243F,S024R-Y209A,T033S-P086W,S024R-T033S,P086W-N243F,T033S-P201S,S024R-P239Q,S078R-P086W,K235F-N243F,G118R-A172V,T033S-L148F,T033S-S078R,T033S-N243F,S024C-T033S,G118R-A194T,T033S-Y209A,S024R-S141G,S024R-T274I,P086W-K235F,A015T-T033S,Y209A-K235F,S024R-R247H,S078R-K235F,S024R-V104A,T033S-A048T,G118R-K235F,T033S-T253A,T143A-Y209A,T033S-P239T,Y209A-N243F,S024R-A272P,和S024R-R269C,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0388] 本发明提供编码芽孢杆菌属枯草杆菌蛋白酶变体的核酸,该变体具有蛋白水解活性并包含具有选自以下的氨基酸置换的组合的氨基酸序列:V004R-S009A-G020R-S242R,G020R-N043R-W241R,G020R-S242R-N269R,V004R-S009A-G020R-N043R,V004R-G020R-H249R,N018R-S024R-V244R,S009A-T022R-S212F-W241R,G020R-N043R-N269R,N018R-S024R-S242R,V004R-S009A-N043R-W241R,G020R-N043R-V244R,G020R-T022R-S242R,V004R-G020R-N043R,V004R-S009A-G020R-N043R-S242R,G020R-N043R-S242R,G020R-N043R-S242R-H249R,G020R-S212F-H249R,V004R-S009A-W241R,A001R-S009A-N043R,G020R-N043R-H249R,S009A-G020R-N043R-W241R,G020R-T022R-N043R,G020R-H249R-N269R,G020R-T022R-W241R,V004R-S009A-S024R-N043R-W241R,S009A-N043R-S078R,V004R-G020R-S024R-V244R,G020R-T022R-S078R-S242R,G020R-S024R-S242R-H249R,V004R-S009A-S078R-W241R,S009A-N043R-S078R-S242R,V004R-G020R-S024R,S009A-N043R-S212F,G020R-N043R-S212F,S024R-S078R-S212F,S009A-G020R-S024R-N043R,S009A-T022R-N043R-S078R,G020R-T022R-S212F-W241R,G020R-N043R-S212F-W241R,S009A-N043R-W241R,G020R-N043R-E271L,G020R-T022R-S078R-W241R,G020R-S024R-N043R-S242R,G020R-T022R-N043R-W241R,S009A-G020R-N043R-S212F,V004R-S009A-G020R-S024R-S242R,G020R-N043R-H249R-E271L,G020R-T022R-S024R-S242R,S009A-T022R-S078R-S212F,G020R-N043R-S242R-E271L,S009A-T022R-S078R-S212F-W241R,V004R-G020R-S024R-H249R,G020R-T022R-E271L,G020R-T022R-N043R-S212F,V004R-G020R-S024R-N043R-S242R,V004R-G020R-S024R-N043R,V004R-S009A-T022R-S078R-S212F,G020R-T022R-S078R-S212F-W241R,和G020R-T022R-N269R,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0389] 本发明提供编码芽孢杆菌属枯草杆菌蛋白酶变体的核酸,该变体具有蛋白水解活性并包含具有选自以下的氨基酸置换的组合的氨基酸序列:N018R-G020R-N043D-R045T-A230E,N018R-N043R-R045T-S242R-H249R,S024R-N043D-H249R,N018R-G020R-R045T,G020R-S024R-N076D-H249R,S024R-N043R-A230E-S242R,N018R-S024R-N043D-A230E,G020R-N076D,N018R-S024R-N043D-N076D-H249R,S024R-N043R-N076D-H249R,N018R-S024R-R045T-S242R,G020R-N043D-N076D-A230E-H249R,G020R-N043R-R045T-S242R,N018R-S024R-N076D-H249R,N018R-G020R-S024R-N043D-R045T-L233I-S242R,S024R-N043R-A230E,N018R-G020R-N043D,N043R-S242R-H249R,G020R-N043R-R045T-A230E,N043R-N076D-S242R-H249R,G020R-S024R-R045T-A230E-S242R,S024R-R045T-N076D-

A230E-S242R-H249R,S024R-R045T,S024R-N043R-R045T-N076D-A230E-H249R,N018R-S024R-N043D-R045T-H249R,N018R-N043R-R045T-H249R,S024R-N043R-S242R,N018R-G020R-N043R-N076D-H249R,G020R-S024R-N043D-H249R,G020R-N043R-A230E-S242R,G020R-N043R-S242R,N018R-N043R-N076D-A230E,G020R-S024R-N043D-S242R,G020R-N043R-A230E,N018R-G020R-N043R-N076D-S242R-H249R,N043D-R045T-N076D-H249R,N018R-N043R-S242R-H249R,N018R-G020R-N043R-R045T-S242R,N018R-G020R-N043D-A230E-S242R,G020R-S024R-N043R-R045T-H249R,S024R-N043R-H249R,G020R-S024R-K27E-N043R-N076D-A230E,S024R-N043R-R045T-S242R,N018R-G020R-S024R-N043R-R045T-N076D-A230E,G020R-N043R-N076D-A230E-H249R,N018R-N043R-R045T-S242R,G020R-S242R-H249R,N018R-N043R-N076D-A230E-S242R-H249R,N018R-S024R-N076D,G020R-S024R-K27R-N043D-S242R-H249R,N018R-G020R-S024R-N043D-N076D-S242R,N018R-N043R-N076D-S242R-H249R,N018R-S024R-N043D-A230E-H249R,N018R-G020R-N043D-H249R,N018R-G020R-N043D-R045T-N076D-S242R,S024R-N043R-N076D-A230E-S242R,G020R-S024R-T38I-N043R-R045T-N076D-S242R-H249R,N018R-G020R-N043R,N018R-S024R-R045T-A230E-S242R,N018R-G020R-H249R,S024R-N043R-N076D,N018R-G020R-S024R-N043R-R045T-N076D-H249R,N018R-N043D-R045T-N076D-S242R-H249R,S024R-N043D-S242R-H249R,N018R-G020R-S024R-N043D-R045T-S242R,G020R-S024R-N043R-N076D,N018R-G020R-N043D-R045T-A230E-S242R,G020R-S024R-N043R-R045T-N076D-S242R-H249R,N018R-N043R-R045T-N076D-S242R,N018R-G020R-N043R-N076D-A230E-S242R,N018R-S024R-N043D-H249R,N018R-S024R-N043R-R045T-A230E-H249R,N018R-G020R-N043R-R045T-N076D-H249R,N018R-S024R-S242R,N018R-N043R-R045T-N076D-A230E-S242R,R045T-S242R-H249R,N018R-S024R-N043D-S242R,N018R-G020R-N043D-R045T-S240P,S024R-N043R-R045T-S242R-H249R,N018R-S024R-V30S-L31S-D32I-T33Q-G34V-I35F,N018R-G020R-N043R-N076D,G020R-N043D-R045T-N076D-S242R-H249R,N018R-S024R-N043D-A230E-S242R,N018R-S024R-N043D-S242R-H249R,S024R-N043D-R045T-S242R-H249R,N043R-A230E-H249R,S024R-N043R-N076D-A230E-H249R,G020R-S024R-N043D-N076D-H249R,S024R-R045T-S242R-A273V,G020R-S024R-R045T-N076D-S242R-H249R,N018R-S024R-N043D-N076D-S242R,N018R-N043R-N076D-A230E-H249R,N018R-G020R-N043R-R045T-H249R,N018R-N043R-R045T-A230E-S242R,G020R-S024R-N043D-R045T-A230E-S242R,N018R-N043D-A230E-H249R,N018R-N043R-N076D-S242R,N018R-G020R-N076D,N018R-G020R-N043D-N076D-S242R-H249R,G020R-S024R-N043D-N076D-S242R-H249R,N043D-S242R-H249R,N018R-G020R-S024R-N043R-N076D,N018R-G020R-N043D-R045T-N076D-H249R,N018R-G020R-N043R-R045T-N076D-A230E-H249R,N018R-N076D-S242R,G020R-N043R-H249R,N018R-N076D-S242R-H249R,N018R-S024R-R045T-A230E-H249R,A230E-H249R,N018R-R045T-H249R,G020R-N043R-N076D,N043R-R045T-H249R,N018R-N043D-N076D-S242R-H249R,N043R-N076D-H249R,N018R-R045T,G020R-N076D-A230E-S242R,G020R-S024R-N043D-R045T,S024R-N043D-N076D-S242R-H249R,G020R-R045T-H249R,N043R-N076D-S153A-H249R,N043R-N076D-A230E-H249R,N018R-N043D-N076D-H249R,和G020R-N043R-N076D-V227I,其中该枯草杆菌蛋白酶变体的氨基酸位置通

过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0390] 本发明提供编码芽孢杆菌属枯草杆菌蛋白酶变体的核酸，该变体具有蛋白水解活性并包含具有选自以下的氨基酸置换的组合的氨基酸序列：S101G-S103A-V104I-A232V-Q236H-Q245R-N252K,S101G-S103A-V104I-A232V-Q245R-N248R,S101G-S103A-V104I-G159R-A232V-Q245R-N248D,S101G-S103A-V104I-G159D-A232V-Q245R-N248R,S101G-S103A-V104I-A232V-Q245R,S101G-S103A-V104I-G159D-A232V-Q245R和S101G-S103A-V104I-A232V-Q245R-N248D，其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0391] 本发明提供编码芽孢杆菌属枯草杆菌蛋白酶变体的核酸，该变体具有蛋白水解活性并包含具有选自以下的氨基酸置换的组合的氨基酸序列：S101G-S103A-V104I-P129E-S188D-A232V-N238R-Q245R-N248D,S024R-S101G-S103A-V104I-P129E-A158E-S188D-A232V-Q245R-N248D-H249R,T022A-S101G-S103A-V104I-P129E-A158E-S188D-A232V-Q245R-N248D-H249R,T022A-S024R-S101G-S103A-V104I-P129E-A158E-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-P129E-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-P129E-G159E-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-S128N-P129E-A158E-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-L148I-A158E-S188D-A232V-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-P129E-G159E-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-S128N-P129E-A232V-Q245R-N248D,S101G-S103A-V104I-P129E-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-P129E-A158E-A232V-Q245R-N248D-H249R,T022A-S024R-S101G-S103A-V104I-A158E-G159E-S188D-A232V-Q245R-N248D-H249R,T022A-S024R-S101G-S103A-V104I-P129E-A158E-G159E-S188D-A232V-N238R-Q245R-N248D,S024R-S101G-S103A-V104I-P129E-L148I-A158E-A232V-Q245R-N248D,A016S-S024R-S101G-S103A-V104I-A158E-S188D-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-A158E-G159E-A232V-Q245R-N248D-H249R,T022A-S101G-S103A-V104I-P129E-A158E-G159E-A232V-N238R-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-P129E-A158E-G159E-A232V-Q245R-N248D-H249R,T022A-S024R-S101G-S103A-V104I-S128N-A158E-S188D-A232V-Q245R-N248D,S024R-S101G-S103A-V104I-P129E-S188D-A232V-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-P129E-A158E-A232V-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-P129E-A232V-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-P129E-S188D-A232V-Q245R-N248D,S024R-S101G-S103A-V104I-A158E-S188D-A232V-N238R-Q245R-N248D,T022A-S101G-S103A-V104I-S128N-P129E-S188D-A232V-N238R-Q245R-N248D,S024R-S101G-S103A-V104I-P129E-S188D-A232V-N238R-Q245R-N248D,S024R-S101G-S103A-V104I-A158E-G159E-S188D-A232V-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-S128N-S188D-A232V-Q245R-N248D,S024R-S101G-S103A-V104I-P129E-A158E-S188D-A232V-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-S128N-P129E-A158E-A232V-Q245R-N248D,S024R-S101G-S103A-V104I-G159E-S188D-A232V-Q245R-N248D,T022A-S101G-S103A-V104I-S128N-P129E-A232V-

N238R-Q245R-N248D,S024R-S101G-S103A-V104I-P129E-G159E-A232V-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-P129E-A158E-S188D-A232V-N238R-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-A158E-G159E-S188D-A232V-Q245R-N248D,S024R-S101G-S103A-V104I-G159E-S188D-A232V-Q245R-N248D-H249R,T022A-S101G-S103A-V104I-P129E-A158E-A232V-N238R-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-P129E-A158E-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-L148I-A158E-A232V-Q245R-N248D,T022A-S101G-S103A-V104I-A158E-G159E-S188D-A232V-Q245R-N248D-H249R,T022A-S101G-S103A-V104I-A158E-S188D-A232V-Q245R-N248D,T022A-S101G-S103A-V104I-P129E-S188D-A232V-N238R-Q245R-N248D,S024R-S101G-S103A-V104I-P129E-A158E-G159E-S188D-A232V-Q245R-N248D-H249R,T022A-S024R-S101G-S103A-V104I-A158E-G159E-S188D-A232V-N238R-Q245R-N248D,S101G-S103A-V104I-P129E-A158E-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-S128N-A158E-A232V-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-S128N-P129E-S188D-A232V-Q245R-N248D,T022A-S101G-S103A-V104I-P129E-G159E-A232V-N238R-Q245R-N248D,S101G-S103A-V104I-P129E-G159E-A232V-Q245R-N248D-H249R,T022A-S101G-S103A-V104I-P129E-A158E-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-P129E-L148I-A158E-S188D-A232V-Q245R-N248D,T022A-S101G-S103A-V104I-P129E-G159E-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-G159E-S188D-A232V-N238R-Q245R-N248D,S024R-S101G-S103A-V104I-P129E-A158E-G159E-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-P129E-A158E-G159E-A232V-N238R-Q245R-N248D,S024R-S101G-S103A-V104I-S128N-G159E-S188D-A232V-Q245R-N248D,T022A-S101G-S103A-V104I-G159E-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-P129E-G159E-S188D-A232V-N238R-Q245R-N248D,S101G-S103A-V104I-A158E-A232V-N238R-Q245R-N248D,T022A-S101G-S103A-V104I-P129E-G159E-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-P129E-L148I-S188D-A232V-Q245R-N248D,S024R-S101G-S103A-V104I-A158E-A232V-Q245R-N248D-H249R,T022A-S101G-S103A-V104I-A158E-G159E-A232V-N238R-Q245R-N248D,S024R-S101G-S103A-V104I-A158E-G159E-A232V-N238R-Q245R-N248D,T022A-S101G-S103A-V104I-P129E-A158E-G159E-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-P129E-A158E-S188D-A232V-N238R-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-P129E-A158E-G159E-A232V-Q245R-N248D,S101G-S103A-V104I-S188D-A232V-N238R-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-A158E-A232V-Q245R-N248D-H249R,T022A-S024R-S101G-S103A-V104I-L148I-A158E-A232V-Q245R-N248D,S101G-S103A-V104I-P129E-A158E-G159E-A232V-N238R-Q245R-N248D,T022A-S101G-S103A-V104I-G159E-S188D-A232V-N238R-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-P129E-A158E-G159E-S188D-A232V-Q245R-N248D-H249R,T022A-S101G-S103A-V104I-P129E-A232V-N238R-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-S188D-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-P129E-A158E-G159E-A232V-Q245R-N248D-H249R,T022A-S101G-S103A-V104I-A158E-G159E-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-P129E-S188D-A232V-

Q245R-N248D,S024R-S101G-S103A-V104I-P129E-G159E-A232V-N238R-Q245R-N248D,S101G-S103A-V104I-S128N-P129E-A232V-Q245R-N248D,S101G-S103A-V104I-A158E-S188D-A232V-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-P129E-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-P129E-G159E-A232V-N238R-Q245R-N248D,S101G-S103A-V104I-A158E-G159E-S188D-A232V-N238R-Q245R-N248D,S024R-S101G-S103A-V104I-A232V-Q245R-N248D-H249R,T022A-S024R-S101G-S103A-V104I-P129E-L148I-A232V-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-A158E-A232V-N238R-Q245R-N248D,S101G-S103A-V104I-S128N-P129E-A232V-N238R-Q245R-N248D,T022A-S101G-S103A-V104I-S128N-G159E-A232V-Q245R-N248D,T022A-S101G-S103A-V104I-S128N-P129E-A158E-A232V-N238R-Q245R-N248D,S101G-S103A-V104I-S128N-P129E-S188D-A232V-Q245R-N248D-H249R,T022A-S024R-S101G-S103A-V104I-S128N-P129E-A158E-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-S128N-A158E-G159E-S188D-A232V-Q245R-N248D,T022A-S024K-S101G-S103A-V104I-S128N-A158E-G159E-A232V-Q245R-N248D,S101G-S103A-V104I-P129E-L148I-S188D-A232V-Q245R-N248D,S024R-S101G-S103A-V104I-L148I-A232V-Q245R-N248D,T022A-S101G-S103A-V104I-L148I-S188D-A232V-Q245R-N248D,S024R-S101G-S103A-V104I-S128N-P129E-S188D-A232V-Q245R-N248D,S101G-S103A-V104I-S128N-P129E-A158E-A232V-N238R-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-P129E-L148I-A158E-S188D-A232V-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-L148I-A158E-S188D-A232V-Q245R-N248D,S101G-S103A-V104I-L148I-G159E-A232V-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-A158E-S188D-A232V-Q245R-N248D,和S101G-S103A-V104I-S128N-P129E-A158E-A232V-Q245R-N248D-H249R,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0392] 本发明提供编码芽孢杆菌属枯草杆菌蛋白酶变体的核酸,该变体具有蛋白水解活性并包含具有选自以下的氨基酸置换的组合的氨基酸序列:T022A-S024R-S101G-S103A-V104I-A158E-A232V-Q245R-N248D-H249R,T022A-S024R-S101G-S103A-V104I-P129E-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-A158E-G159E-A232V-N238R-Q245R-N248D,S024R-S101G-S103A-V104I-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-A158E-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-G159E-S188D-A232V-Q245R-N248D-H249R,T022A-S024R-S101G-S103A-V104I-A158E-A232V-N238R-Q245R-N248D,S024R-S101G-S103A-V104I-G159E-S188D-A232V-N238R-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-P129E-A232V-Q245R-N248D,S024R-S101G-S103A-V104I-L148I-A232V-Q245R-N248D,S024R-S101G-S103A-V104I-P129E-A158E-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-L148I-A158E-A232V-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-P129E-A158E-A232V-Q245R-N248D-H249R,A016S-S024R-S101G-S103A-V104I-A158E-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-P129E-G159E-A232V-N238R-Q245R-N248D,S024R-S101G-S103A-V104I-P129E-S188D-A232V-Q245R-N248D-H249R,T022A-S101G-S103A-V104I-P129E-A232V-N238R-Q245R-N248D,T022A-

S024R-S101G-S103A-V104I-L148I-A158E-A232V-Q245R-N248D,S024R-S101G-S103A-V104I-P129E-S188D-A232V-N238R-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-A158E-G159E-S188D-A232V-N238R-Q245R-N248D,T022A-S101G-S103A-V104I-A158E-G159E-A232V-N238R-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-P129E-A158E-A232V-Q245R-N248D,S101G-S103A-V104I-A158E-S188D-A232V-Q245R-N248D-H249R,T022A-S101G-S103A-V104I-A158E-G159E-A232V-Q245R-N248D-H249R,和S024R-S101G-S103A-V104I-A158E-G159E-A232V-Q245R-N248D,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0393] 本发明提供编码芽孢杆菌属枯草杆菌蛋白酶变体的核酸,该变体具有蛋白水解活性并包含具有选自以下的氨基酸置换的组合的氨基酸序列:V104L-S128N-A158E-R186H-H249R,S128N-A158E-S188D-H249R,N062E-S128N-A158E-G159E-E271F,N062E-A158E-S188D-H249R-E271F,N062E-A158E-R186H-H249R-E271F,S128N-A158E-S188D-Y209E-E271F,N062E-G159E-S188D-H249R,A016S-N062E-A158E-R186H-H249R,N062E-A158E-G159E-H249R,S101A-S128N-A158E-Y209E-H249R,S128N-A158E-R186H-E271F,N062E-A158E-S188D-H249R,N062E-A158E-R186H-E271F,N062E-A158E-R186H-H249R,N062E-S101A-R186H-H249R,N062E-S101A-A158E-R186H-E271F,N062E-V104L-A158E-S188D-H249R-E271F,N062E-G159E-R186H-H249R,N062E-G159E-H249R,S128N-A158E-R186H-H249R,S128N-A158E-S188D-E271F,N062E-A158E-H249R,N062E-R186H-S188D-H249R-E271F,S128N-A158E-Y209E-,N062E-S101A-A158E-H249R,V104L-S128N-A158E-R186H-E271F,N062E-S101A-A158E-R186H-H249R-E271F,A016S-N062E-A158E-H249R,N062E-S101A-G159E-H249R,S128N-A158E-R186H-S188D-E271F,S101A-S128N-A158E-R186H-E271F,N062E-S101A-S188D-H249R,S101A-V104L-A158E-R186H-S188D-H249R,N062E-G159E-H249R-E271F,S128N-A158E-G159E-E271F,A016S-N062E-V104L-A158E-R186H-E271F,T022A-S128N-A158E-H249R,S128N-A158E-H249R,N062E-S101A-V104L-A158E-R186H-E271F,A016S-N062E-A158E-R186H-E271F,V104L-S128N-A158E-H249R,V104L-S128N-A158E-S188D-H249R,T022A-N062E-A158E,N062E-S101A-S188D-H249R-E271F,N062E-A158E-H249R-E271F,V104L-S128N-A158E-R186H-S188D-E271F,N062E-S101A-R186H-E271F,N062E-V104L-G159E-H249R,N062E-R186H-H249R,N062E-S101A-R186H-H249R-E271F,S101A-A158E-R186H-S188D-H249R,N062E-S101A-R186H,S101A-S128N-P129E-R186H-H249R,S101A-S103G-A158E-R186H-H249R,A016S-N062E-V104L-R186H-S188D-E271F,V104L-A158E-R186H-H249R,S101A-S128N-A158E-S188D-Y209E-E271F,N062E-S101A-R186H-S188D-E271F,A016S-N062E-A158E-H249R-E271F,N062E-S128N-A158E,N062E-S128N-G159E-H249R,N062E-S101A-A158E-S188D-H249R,S101A-S128N-A158E-H249R,N062E-A158E-R186H-S188D-H249R,A016S-V104L-A158E-R186H-E271F,N062E-L148I-G159E,N062E-S101A-A158E-R186H-H249R,N062E-S101A-R186H-S188D-H249R,V104L-A158E-R186H-S188D-H249R,N062E-S101A-V104L-R186H-S188D-E271F,T022A-S101A-A158E-R186H-H249R,S101A-S128N-A158E-Y209E,A158E-R186H-S188D-H249R-E271F,V104L-A158E-R186H-S188D-H249R-E271F,S101A-V104L-A158E-R186H-

H249R,V104L-A158E-H249R,S101A-V104L-S128N-A158E-R186H-E271F,A016S-V104L-S188D-H249R,S101A-V104L-A158E-R186H-S188D-E271F,V104L-S128N-G159E-E271F,V104L-A158E-R186H-H249R-E271F,A158E-R186H-H249R,S101A-A158E-R186H-H249R,V104L-A158E-S188D-H249R-E271F,A016S-S128N-A158E-R186H,V104L-S128N-R186H-S188D-H249R,A016S-S101A-S128N-R186H,A016S-N062E-S128N-R186H-E271F,A016S-S128N-R186H-E271F,S128N-P129E-R186H,A158E-R186H-H249R-E271F,A016S-A158E-H249R,A016S-A158E-R186H-H249R,A016S-T022A-A158E-R186H-E271F,E089P-S101A-P129E-R186H,T022A-S128N-A158E-R186H,S101A-V104L-S128N-A158E-R186H,T022A-S128N-R186H-S188D-,N062E-V104L-A158E-R186H-S188D-H249R,T022A-A158E-R186H-H249R-E271F,T022A-V104L-A158E-H249R,S101A-L111V-P129E,A016S-A158E-H249R-E271F,A016S-L111V-S188D-,T022A-V104L-R186H-S188D-H249R,和V104L-L148I-S188D-H249R,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0394] 本发明提供编码芽孢杆菌属枯草杆菌蛋白酶变体的核酸,该变体具有蛋白水解活性并包含具有选自以下的氨基酸置换的组合的氨基酸序列:A001R-S101G-S103A-V104I-A232V-Q245R,V004R-S101G-S103A-V104I-A232V-Q245R,N043R-S101G-S103A-V104I-A232V-Q245R-E271L,S078R-S101G-S103A-V104I-A232V-Q245R,V004R-N043R-S101G-S103A-V104I-A232V-Q245R,N018R-N043R-S101G-S103A-V104I-A232V-Q245R,G020R-S101G-S103A-V104I-A232V-Q245R,S101G-S103A-V104I-A232V-Q245R-E271L,G020R-N043R-S101G-S103A-V104I-A232V-Q245R,S024R-N043R-S101G-S103A-V104I-A232V-Q245R,G020R-G025R-N116A-Y167W,N018R-S101G-S103A-V104I-A232V-Q245R,T022R-S101G-S103A-V104I-A232V-Q245R,S078R-S103N-S106G-Y167W-Q236N,N018R-N043D-S101G-S103A-V104I-A232V-Q245R-N269R,N043R-S101G-S103A-V104I-A232V-Q245R-N269R,S024R-S101A-H120F-A194F-H249R,G020R-N043D-S101G-S103A-V104I-A232V-Q245R-N269R,S101G-S103A-V104I-S212F-A232V-Q245R,G020R-S144R-N185I-L233C-Q236N,G023A-S078R-S216F-Q236N-H249R,S101G-S103A-V104I-A232V-Q245R-N269R,S101G-S103A-V104I-G115R-A232V-Q245R,P052N-S078R-S103N-L148I-T213A,N018R-N043D-S101G-S103A-V104I-A232V-Q245R-H249R,S024R-N043D-S101G-S103A-V104I-A232V-Q245R-H249R,S024R-N043D-S101G-S103A-V104I-A232V-Q245R-N269R,G025R-E089I-N116A-P239S-A270C,S024R-S101G-S103A-V104I-A232V-Q245R,L148I-T213A-N252R,S024R-G025R-N183D-Y192W-P239S,G046R-A194F-S212M,V104L-L217E-T224A-H249R-N252R,G023A-Y091F-V121F-Y192W-Q236N,S101G-S103A-V104I-A232V-V244R-Q245R,S099F-S144R-Y167W-N252R,S101G-S103A-V104I-A232V-Q245R-H249R,N043R-S101G-S103A-V104I-A232V-Q245R,T022W-S078R-Y167W-S212M-A270C,V121F-N252R-A270C,G020R-S103N-S216F-Q236N-N252R,N043R-S101G-S103A-V104I-A232V-Q245R-H249R,G023A-P052N-Y192W-I198L-N252R,G025R-G046R-V121F,S024R-S078R-V104L-N116A-N183D,G046R-Q059A-S103N-G211Q-S212M,G020R-P052N-N062Q-Y091F-Y192W,G023A-P052N-S144R-Y192W-S216F,S101G-S103A-V104I-A232V-S242R-Q245R,P052N-S103N-N116A-L148I-Y192W,E089I-N116A-N117F-T224A-H249R,S144R-G211Q-N238L-

P239S-H249R,N043A-N062Q-A194F-G211Q,G020R-S024R-P052N-Q059A-S216F,S024R-Y167W-T224A-H249R,T057R-Y167W-H249R,G025R-S103N-R186K-A194F-T224A,S105T-S128N-S144R-L148I-S212M,G020R-Q059A-S144R-Y192W-T224A,S024R-N043A-N117F-A194F-G211Q,N117F-A194F-T213A-A270C,S078R-Y091F-V121F-L233C-N252R,T057R-S099F-S105T-I198L-T213A,G023A-Y091F-S101A-I198L-N252R,N062Q-S103N-V121F-S144R-H249R,N043R-S101G-S103A-V104I-A232V-S242R-Q245R,G023A-S024R-N117F-S212M-S216F,V104L-T213A-S216F,A194F-G211Q-Q236N,N062Q-S103N-N117F-A194F,S024R-N062Q-V104L-S106G-H249R,T057R-E089I-I198L,G046R-Q059A-S106G-L217E-H249R,N117F-T213A-A215F,S101A-H120F-Y192W-A215F-T224A,N043A-T057R-N117F-S144R-N183D,G046R-N183D-N238L,G025R-N043A-E089I-N117F,S078R-V104L-T213A-A215F-T224A,Y091F-S099F-S101A-S105T-Y167W,S106G-N117F-N238L,G046R-E089I-Y091F-S101A-N116A,G020R-N062Q-E089I-R186K-S212M,T057R-S099F-V121F-N185I-Y192W,G046R-E089I-Y192W-L233C-A270C,E089I-N117F-N185I-A215F-L233C,P052N-V104L-N183D-S216F-H249R,S078R-S099F-N116A-R186K-T224A,G025R-S105T-S128N-S144R-A270C,S105T-G211Q-S216F,S024R-G046R-Y091F-V121F,S106G-N185I-S216F-Q236N,N062Q-S101A-Q236N-N252R-A270C,G025R-N043A-Y091F-I198L-A270C,G020R-G023A-V104L-Y192W-L233C,S024R-N043A-S105T-S106G-I198L,G020R-E089I-L217E,S024R-Y091F-I198L-A215F-P239S,G046R-E089I-S099F-R186K-S212M,V104L-H120F-R186K-S216F-N252R,T022W-A194F-T213A-L233C-N238L,S099F-S105T-S106G-A194F-S212M,E089I-S105T-N116A-A215F-S216F,G025R-N116A-H120F-T224A-A270C,N043A-Q059A-S101A-S216F-T224A,T057R-N183D-Q236N,G025R-N062Q-S128N-S144R-N185I,S103N-H120F-Y167W-I198L-L233C,T022W-E089I-S216F,S024R-S106G-N116A-S212M-T224A,G020R-P052N-S101A-I198L-L233C,E089I-Y091F-N185I-G211Q-A270C,L111I-A215F-P239S,S024R-N116A-R186K-L233C-Q236N,和G023A-S103N-S106G-S212M-A215F,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0395] 本发明提供编码芽孢杆菌属枯草杆菌蛋白酶变体的核酸,该变体具有蛋白水解活性并包含具有选自以下的氨基酸置换的组合的氨基酸序列:G020R-T022W-S078R-S101A-S103A-V104I-N116S-T213A-A215F-A232V-Q245R,N018R-S078R-S101G-S103A-V104I-A232V-Q245R,S024R-R045T-S101G-S103A-V104I-A232V-Q245R-N269R,G020R-T022W-S078R-S101G-S103A-V104I-N116A-A232V-Q245R,G020R-T22W-S101G-S103A-V104I-A232V-Q245R,N018R-N043R-S101G-S103A-V104I-A232V-Q245R,N018R-T022W-S024R-N076D-S101A-N116A-A232V-Q245R,N018R-V104I-A232V-H249R,N018R-S024R-N076D-S101A-N116A-G211Q-H249R,N018R-N043D-S078R-S101G-S103A-V104I-L217E-A232V-Q245R,N018R-N043R-S101G-S103A-V104I-A232V-Q245R-N269R,N018R-R045T-N076D-S101G-S103A-V104I-A232V-Q245R-N269R,N076D-S078R-S101G-S103A-V104I-A232V-Q245R-N269R,G020R-N043D-S078R-S101G-S103A-V104I-A232V-Q245R,N018R-N043D-N076D-S101G-S103A-V104I-A232V-Q245R-N269R,S024R-R045T-N076D-S078R-S101G-S103A-V104I-A232V-Q245R-N269R,N018R-S103A-A232V-H249R,N018R-S101G-V104I-A232V-

Q245R,G020R-S024R-S101G-S103A-V104I-L217E-A232V-Q245R-H249R,N018R-T22K-N043D-S101G-S103A-V104I-A232V-Q245R,N043R-R045T-S101G-S103A-V104I-A232V-Q245R-N269R,G020R-T22W-S101G-S103A-V104I-G211Q-A232V-Q245R,S024R-N076D-S078R-S101G-S103A-V104I-A232V-Q245R-N269R,G020R-T22W-S078R-S101A-S103A-V104I-N116A-N183D-A232V,N018R-S024R-N076D-N116A-A215F-H249R,N018R-N043R-R045T-S101G-S103A-V104I-A232V-Q245R,S024R-N043R-N076D-S101G-S103A-V104I-A232V-Q245R,G020R-T022W-S101G-S103A-V104I-A232V-Q245R,G020R-T022W-S101G-S103A-V104I-G211Q-A232V-Q245R,G020R-T022W-S078R-S101G-S103A-V104I-N116A-T213A-A215F-A232V-Q245R,N043D-N076D-S078R-S101G-S103A-V104I-A232V-Q245R-N269R,N018R-S024R-N076D-S101A-N116A-T213A-H249R,N018R-S024R-N076D-N116A-G211Q-H249R,N043R-R045T-N076D-S078R-S101G-S103A-V104I-A232V-Q245R,N018R-S101G-Q245R,G020R-T22W-S101A-S103A-V104I-G211Q-T213A-A232V-Q245R,G020R-S024R-N043D-N076D-S078R-S101G-S103A-V104I-A232V-Q245R,N018R-R045T-N076D-S078R-S101G-S103A-V104I-A232V-Q245R,G020R-S078R-S101G-S103A-V104I-G211Q-T213A-A215F-A232V-Q245R,R045T-S078R-S101G-S103A-V104I-A232V-Q245R-N269R,S024R-N043D-S101G-S103A-V104I-A232V-Q245R-N269R,N018R-S101G-S103A-H249R,N018R-T22W-S024R-N076D-S101A-N116A-A232V-Q245R,N018R-S101G-V104I-A232V-H249R,G020R-T22W-S101A-S103A-V104I-A215F-A232V-Q245R,N018R-S024R-N076D-G211Q-T213A-H249R,N018R-T022W-S024R-N076D-S101A-I198L-H249R,S024R-S101G-S103A-V104I-A232V-Q245R,G020R-N076D-S101G-S103A-V104I-A232V-Q245R-N269R,G020R-S101G-S103A-V104I-A232V-Q245R-N269R,N043D-S078R-S101G-S103A-V104I-A232V-Q245R,G020R-S101G-V104I-T213A-A215F-A232V-Q245R,G020R-S101G-S103A-V104I-N116A-A215F-A232V-Q245R,S024R-S103A-V104I-H249R,N018R-N076D-S078R-S101G-S103A-V104I-A232V-Q245R,R045T-N076D-S078R-S101G-S103A-V104I-A232V-Q245R-N269R,S024R-S101G-V104I-Q245R,G020R-S101G-S103A-V104I-G211Q-T213A-A215F-A232V-Q245R,S024R-S103A-V104I-A232V-H249R,N018R-S024R-N076D-N116A-G211Q-A215F-H249R,N018R-Q245R,S024R-S103A-Q245R,S024R-S103A-V104I-Q245R,G020R-S078R-S101G-A232V-Q245R,N018R-S024R-N076D-V104I-H249R,N018R-S024R-V104I-H249R,S024R-S101G-S103A-V104I-A232V-Q245R,N018R-S024R-N076D-G211Q-A215F-H249R,R019H-G020R-T022W-S078R-S101G-S103A-V104I-G211Q-A232V-Q245R,N018R-S024R-N076D-S101A-I198L-G211Q-T213A-H249R,N018R-S024R-N043D-S101G-S103A-V104I-A232V-Q245R,G020R-T22W-S103A-V104I-A232V-Q245R,N018R-S103A-V104I-H249R,N018R-T022W-S024R-N076D-S101A-I198L-A215F-H249R,N018R-S024R-S101G-V104I-A232V,S078R-S101G-S103A-V104I-A232V-Q245R-N269R,S024R-N043R-N076D-S078R-S101G-S103A-V104I-A232V-Q245R,N018R-G020R-N043D-N076D-S101G-S103A-V104I-A232V-Q245R,N018R-T22W-S024R-N076D-N116A-T213A-H249R,N018R-S024R-S101G-V104I,G020R-S101A-S103A-V104I-A215F-A232V-Q245R,N018R-R045T-S078R-S101G-S103A-V104I-A232V-Q245R,N018R-S101G-S103A-Q245R,N043R-N076D-S078R-S101G-S103A-V104I-A232V-Q245R,G020R-T022W-S101A-S103A-V104I-G211Q-A215F-A232V-Q245R,G020R-T22W-S078R-S101G-S103A-V104I-

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A215F-H249R-T260A,N076D-H249R,N018R-T022W-S024R-N076D-N183D-G211Q-A215F-H249R,N018R-G020R-S024R-N076D-N116A-G211Q-A215F-H249R,N018R-G020R-S024R-N076D-T213A-H249R,N018R-G020R-T022W-S024R-N076D-N116A-N183D-I198L-H249R,N018R-G020R-T022W-S024R-N076D-S101A-N183D-H249R,N076D-V104I-H249R,G020R-T022W-S101A-S103A-V104I-N116A-N183D-G211Q-T213A-A215F-A232V-Q245R,S024R-N043R-R045T-S078R-S101G-S103A-V104I-L217E-A232V-Q245R,N018R-G020R-T022W-S024R-N076D-N183D-I198L-A215F-H249R,N018R-N076D-S101G-S103A,G020R-S024R-S101G-S103A-V104I-A232V-Q245R-N269R,N018R-G020R-S024R-N076D-S101A-N116A-N183D-G211Q-H249R,S101G-S103A-A232V,S024R-N076D-S101G-A232V,N018R-T022W-S024R-N076D-S101A-N183D-I198L-G211Q-H249R,N018R-G020R-S024R-N076D-S101A-N183D-I198L-G211Q-A215F-H249R,N018R-G020R-S024R-N076D-N183D-I198L-H249R,N018R-T022W-S024R-N076D-S101A-N116A-N183D-I198L-G211Q-H249R,N018R-G020R-S024R-N076D-N116A-A156V-N183D-G211Q-A215F-H249R-N269S,R045T-N076D-S101G-S103A-V104I-A232V-Q245R-H249R,N018R-G020R-S024R-N076D-S101A-N183D-I198L-H249R,N018R-G020R-T022W-S024R-N076D-I198L-G211Q-A215F-H249R,N018R-G020R-T022W-S024R-N076D-S101A-N116A-I198L-G211Q-A215F-H249R,N018R-G020R-T022W-S024R-N076D-N116A-H249R,N018R-N076D-S101G,N018R-S024R-N076D-N116A-N183D-I198L-T213A-A215F-H249R,N018R-G020R-T022W-S024R-N076D-S101A-N116A-I198L-T213A-A215F-H249R,N018R-S024R-N076D-S101A-N116A-N183D-I198L-G211Q-H249R,N018R-N076D-A232V,N018R-G020R-S024R-N076D-S101A-A232V-Q245R,N018R-N043D-R045T-N076D-S101G-S103A-V104I-A232V-Q245R,N018R-T022W-S024R-N076D-N183D-T213A-A215F-H249R,N018R-S024R-N076D-S101A-N116A-G211Q-T213A-N237D-H249R,N018R-G020R-S024R-N076D-S101A-N116A-N183D-G211Q-H249R-R275S,N018R-T022W-S024R-N076D-S101A-N116A-N183D-I198L-G211Q-T213A-A215F-H249R,S024R-N076D,N018R-S024R-N076D-N183D-G211Q-A215F-H249R,N018R-T022W-S024R-N076D-N116A-N183D-I198L-T213A-A215F-H249R,N076D-V104I-A232V-H249R,N018R-N076D-S103A-A232V,N018R-G020R-S024R-N076D-S101A-N116A-N183D-I198L-G211Q-T213A-H249R,N018R-G020R-S024R-N076D-S101A-N183D-T213A-H249R,N018R-G020R-S024R-N076D-S101A-D175E-N183D-G211Q-A215F-H249R,N018R-G020R-N043D-S078R-S101G-S103A-V104I-L217E-A232V-Q245R-A273E,G020R-S024R-N043D-R045T-N076D-S101G-S103A-V104I-A232V-Q245R,P005S-S101G-S103A-V104I-A232V-Q245R-H249R,S103A-V104I-A232V,N018R-G020R-S024R-V068A-N076D-S101A-N116A-T213A-A215F-H249R,N018R-T022W-S024R-N076D-S101A-I198L-A215F-H249R-R275S,N018R-S024R-N076D-N183D-I198L-G211Q-T213A-H249R,和N043D-R045T-S101G-S103A-V104I-A232V-Q245R,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0396] 本发明提供编码芽孢杆菌属枯草杆菌蛋白酶变体的核酸,该变体具有蛋白水解活性并包含具有选自以下的氨基酸置换的组合的氨基酸序列:N018R-S024R-N043R-N076D-H249R-N269R,N018R-T022R-S024R-N043R-N076D-H249R,N018R-N043D-S101G-S103A-

V104I-A232V-Q245R,G02OR-N043D-S101G-S103A-V104I-A232V-Q245R,N043D-S101G-S103A-V104I-A232V-Q245R-N269R,N043D-S078R-S101G-S103A-V104I-A232V-Q245R,N043R-N076D-S101G-S103A-V104I-A232V-Q245R,T022R-N043R-S101G-S103A-V104I-A232V-Q245R,N043R-S078R-S101G-S103A-V104I-A232V-Q245R,G02OR-N076D-S101G-S103A-V104I-A232V-Q245R,N043R-N076D-S101G-S103A-V104I-A232V-Q245R,T022R-N076D-S101G-S103A-V104I-A232V-Q245R,N076D-S078R-S101G-S103A-V104I-A232V-Q245R,N018R-S024R-N043R-N076D-H249R,N018R-S024R-N076D-S242R-H249R,N018R-S024R-N076D-H249R-N269R,N018R-T022R-S024R-N076D-H249R,N018R-S024R-N076D-S078R-H249R,N018R-S024R-N043D-N076D-H249R-N269R,N018R-T022R-S024R-N043D-N076D-H249R,N018R-S024R-N043D-N076D-S078R-H249R,G02OR-S101G-S103G-V104I-A232V-Q245R,G02OR-S101G-S103A-V104L-A232V-Q245R,G02OR-S101G-S103A-V104V-A232V-Q245R,G02OR-S101G-S103S-V104I-A232V-Q245R,G02OR-S101G-S103S-V104L-A232V-Q245R,G02OR-S101S-S103S-V104I-A232V-Q245R,G02OR-S101S-S103S-V104L-A232V-Q245R,G02OR-S101A-S103A-V104L-A232V-Q245R,G02OR-S101S-S103S-V104V-A232V-Q245R,G02OR-S101S-S103A-V104I-A232V-Q245R,G02OR-S101S-S103A-V104V-A232V-Q245R,G02OR-S101S-S103G-V104I-A232V-Q245R,G02OR-S101S-S103G-V104V-A232V-Q245R,G02OR-S101A-S103A-V104V-A232V-Q245R,G02OR-S101A-S103S-V104I-A232V-Q245R,G02OR-S101A-S103S-V104V-A232V-Q245R,N018R-S024R-N043R-N076D-S078R-H249R,S024R-N043D-S101G-S103A-V104I-A232V-Q245R,N043D-S101G-S103A-V104I-A232V-Q245R-H249R,S024R-N076D-S101G-S103A-V104I-A232V-Q245R,N076D-S101G-S103A-V104I-A232V-S242R-Q245R,N018R-G02OR-S024R-N076D-L217E-H249R,N018R-S024R-N043R-N076D-L217E-H249R,N018R-S024R-N043D-N076D-S242R-H249R,N018R-G02OR-S024R-N043R-N076D-H249R,G02OR-S101A-S103G-V104V-A232V-Q245R,N043D-S101G-S103A-V104I-A232V-Q245R,N018R-S024R-N076D-L217E-H249R-N269R,和N018R-S024R-N076D-L217E-S242R-H249R,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0397] 本发明提供编码芽孢杆菌属枯草杆菌蛋白酶变体的核酸,该变体具有蛋白水解活性并包含具有选自以下的氨基酸置换的组合的氨基酸序列:G02OR-S101A-S103A-V104I-G118R-A232V-Q245R,G02OR-S024R-N116A-T213A,N043R-S101A-N116A-A215F-N269R,S024R-N043R-S101A-N116A,S024R-N043R-S101A-N116A-A215F-N269R,G02OR-S101G-S103A-V104I-A215F-A232V-Q245R,N043R-S101A-N269R,S024R-N043R-N116A-T213A-N269R,G02OR-S024R-N043R-R045T-S101A-T213A,S024R-N043R-N116A-A215F-N269R,G02OR-S024R-T213A-A215F,G02OR-N116A-N269R,S024R-N116A-T213A-N269R,N043R-S101A-N116A-N269R,S101G-S103A-V104I-N116A-T213A-A232V-Q245R-N269R,S024R-N043R-R045T-S101A-N116A-A215F-N269R,G02OR-N043R-S101A-N269R,S101A-S103A-V104I-T213A-A232V-Q245R-N269R,S024R-A215F-N269R,N043R-S101A-N116A-T213A-A215F-N269R,N043R-S101A-T213A-N269R,G02OR-S024R-N043R-R045T-N116A-T213A,S101G-S103A-V104I-A232V-Q245R-N269R,S024R-N043R-R045T-S101A-N116A-T213A-

N269R,S024R-N043R-R045T-N269R,G020R-N043R-R045T-S101A-N269R,S024R-N043R-N116A-N269R,G020R-S024R-N043R-R045T,N043R-N116A-N269R,S024R-N043R-S101A-A215F-N269R,S024R-N043R-R045T-T213A-A215F-N269R,G020R-S024R-R045T-N269R,G020R-N043R-S101A-N116A-T213A-A215F,G020R-S101G-S103A-V104I-T213A-A215F-A232V-Q245R,G020R-S024R-R045T-N116A-N269R,G020R-S101A-N116A-N269R,S024R-N043R-A215F,G020R-S024R-T213A,S024R-N043R-S101A-A215F,G020R-S024R-N043R-R045T-N116A,G020R-S024R-N043R-R045T-S101A-N269R,G020R-S024R-S101A-A215F,G020R-S024R-N116A-T213A-A215F,G020R-S024R-N116A,G020R-S024R-S101A-N116A,N043R-T213A-A215F-N269R,S024R-S101A-N269R,S024R-N043R-N116A-A215F,G020R-T038A-N043R-S101A,G020R-S024R-N116A-A215F,S024R-N043R-S101A-T213A,P014L-G020R-S024R-N043R-R045T-S101A-A215F,G020R-S024R-A215F,G020R-N116A-A215F-N269R,G020R-R045T-N116A-N269R,G020R-S024R-N043R-R045T-A215F,和G020R-S024R-N043R-R045T-N116A-T213A-A215F,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0398] 本发明提供编码芽孢杆菌属枯草杆菌蛋白酶变体的核酸,该变体具有蛋白水解活性并包含具有选自以下的氨基酸置换的组合的氨基酸序列:N043R-N076D-S101A-S103A-V104I-A158E-S188D-A232V-Q245R-N248D-H249R-E271F,S024R-N043R-N076D-S101A-S103A-V104I-A158E-S188D-L217E-A232V-Q245R-N248D-H249R,S101A-S103A-V104I-A158E-S188D-A232V-Q245R-N248D-H249R-E271F-E271F,S101A-S103A-V104I-A158E-S188D-L217E-A232V-Q245R-N248D-H249R-E271F,N076D-S101G-S103A-V104I-A114V-A158E-S188D-A232V-Q245R-N248D-H249R-E271F,S024R-N076D-S101G-S103A-V104I-A158E-S188D-A232V-Q245R-N248D-H249R-E271F,S024R-N043R-S101A-S103A-V104I-A158E-S188D-L217E-A232V-Q245R-N248D-H249R,S024R-N043R-S101A-S103A-V104I-A158E-S188D-A232V-Q245R-N248D-H249R,S024R-S101A-S103A-V104I-A158E-S166D-S188D-L217E-A232V-Q245R-N248D-H249R,N076D-S101G-S103A-V104I-S128L-A158E-S188D-A232V-Q245R-N248D-H249R-E271F,和N043R-N076D-S101G-S103A-V104I-A158E-S166D-S188D-A232V-Q245R-N248D-H249R-E271F,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0399] 本发明提供编码芽孢杆菌属枯草杆菌蛋白酶变体的核酸,该变体具有蛋白水解活性并包含具有选自以下的氨基酸置换的组合的氨基酸序列:T022A-S101G-S103A-V104I-G159D-L217E-A232V-Q245R-N248D-E271F,T022A-N043R-S101G-S103A-V104I-G159D-S188D-L217E-A232V-Q245R-N248D-E271F,T022A-S101G-S103A-V104I-G159D-S188D-A232V-Q245R-N248D-E271F,N043R-S101A-S103A-V104I-A158E-S188D-L217E-A232V-Q245R-N248D-H249R,N043R-N076D-S101A-S103A-V104I-A158E-S188D-L217E-A232V-Q245R-N248D-H249R-E271F,S024R-S101G-S103A-V104I-A158E-S188D-L217E-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-A158E-S188D-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-A158E-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-A158E-N183D-S188D-A232V-Q245R-N248D-H249R,T022A-N076D-S101G-

S103A-V104I-G159D-S188D-A232V-Q245R-N248D-E271F,T022A-N043R-N076D-S101G-S103A-V104I-G159D-S188D-A232V-Q245R-N248D-E271F,T022A-N076D-S101G-S103A-V104I-G159D-A232V-Q245R-N248D-E271F,T022A-S101G-S103A-V104I-G159D-A232V-Q245R-N248D-E271F,N076D-S101A-S103A-V104I-A158E-S188D-A232V-Q245R-N248D-H249R-E271F,N043R-S101A-S103A-V104I-A158E-S166D-S188D-A232V-Q245R-N248D-H249R,S024R-N076D-S101A-S103A-V104I-A158E-S166D-S188D-A232V-Q245R-N248D-H249R-E271F,N076D-S101A-S103A-V104I-A158E-S188D-A232V-Q245R-N248D-H249R,S101A-S103A-V104I-A158E-S166D-S188D-A232V-Q245R-N248D-H249R-E271F,N043R-N076D-S101A-S103A-V104I-A158E-S166D-S188D-A232V-Q245R-N248D-H249R-E271F,S101G-S103A-V104I-A158E-S166D-S188D-A232V-Q245R-N248D-H249R-E271F,S101A-S103A-V104I-A158E-S188D-A232V-Q245R-N248D-H249R-E271F,S101A-S103A-V104I-A158E-S188D-L217E-A232V-Q245R-N248D-H249R,N076D-S101A-S103A-V104I-A158E-S166D-S188D-A232V-Q245R-N248D-H249R-E271F,S101G-S103A-V104I-A158E-N183D-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-S128L-A158E-S188D-A232V-Q245R-N248D-H249R,N076D-S101G-S103A-V104I-A158E-S166D-S188D-A232V-Q245R-N248D-H249R-E271F,N043R-N076D-S101A-S103A-V104I-A158E-S166D-S188D-A232V-Q245R-N248D-H249R,和N076D-S101A-S103A-V104I-A158E-S188D-L217E-A232V-Q245R-N248D-H249R-E271F,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0400] 本发明提供编码芽孢杆菌属枯草杆菌蛋白酶变体的核酸,该变体具有蛋白水解活性并包含具有选自以下的氨基酸置换的组合的氨基酸序列:H017R-T022A-N076D-S101G-S103A-V104I-G159D-S188D-A232V-Q245R-N248D-E271F,T022A-N043R-S101G-S103A-V104I-G159D-A232V-Q245R-N248D-E271F,T022A-S101G-S103A-V104I-G159D-S188D-A232V-Q245R-N248D-H249R-E271F,H017R-T022A-N076D-S101G-S103A-V104I-G159D-A232V-Q245R-N248D-E271F,T022A-N076D-S101G-S103A-V104I-G159D-A232V-Q245R-N248D-H249R-E271F,T022A-S101G-G102A-S103A-V104I-G159D-S188D-A232V-Q245R-N248D-E271F,和T022A-N043R-N076D-S101G-S103A-V104I-G159D-A232V-Q245R-N248D-H249R-E271F,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0401] 本发明提供编码芽孢杆菌属枯草杆菌蛋白酶变体的核酸,该变体具有蛋白水解活性并包含具有选自以下的氨基酸置换的组合的氨基酸序列:S101S-S103A-V104I-A158E-S188D-A232V-Q245R-N248D-H249R,S101S-S103G-V104V-A158E-S188D-A232V-Q245R-N248D-H249R,S101G-S103S-V104I-A158E-S188D-A232V-Q245R-N248D-H249R,S101A-S103A-V104I-A158E-S188D-A232V-Q245R-N248D-H249R,S101A-S103A-V104L-A158E-S188D-A232V-Q245R-N248D-H249R,S101G-S103G-V104I-A158E-S188D-A232V-Q245R-N248D-H249R,S101S-S103G-V104I-A158E-S188D-A232V-Q245R-N248D-H249R,S101S-S103S-V104I-A158E-S188D-A232V-Q245R-N248D-H249R,S101S-S103S-V104V-A158E-S188D-A232V-Q245R-N248D-H249R,S101A-S103S-V104I-A158E-S188D-A232V-Q245R-N248D-H249R,S101A-S103S-V104I-G159E-A232V-Q245R-N248D-H249R,S101S-S103A-

V104I-G159E-A232V-Q245R-N248D-H249R,S101G-S103A-V104L-A158E-S188D-A232V-Q245R-N248D-H249R,S101A-S103A-V104L-G159E-A232V-Q245R-N248D-H249R,S101A-S103S-V104L-G159E-A232V-Q245R-N248D-H249R,S101G-S103S-V104L-G159E-A232V-Q245R-N248D-H249R,S101S-S103A-V104L-G159E-A232V-Q245R-N248D-H249R,S101A-S103G-V104V-G159E-A232V-Q245R-N248D-H249R,和S101S-S103A-V104V-G159E-A232V-Q245R-N248D-H249R,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0402] 本发明提供编码芽孢杆菌属枯草杆菌蛋白酶变体的核酸,该变体具有蛋白水解活性并包含具有选自以下的氨基酸置换的组合的氨基酸序列:V026F-V051W-V104L-S106E,V026F-L031F-S078N-G102A-S160D,G020K-G100S-N116L-A158E-S166D-N243F,T033S-N043W-N218D-P239G-N243F,T022L-T038F-A048R-N062E-G100S-R186K,S101D-S103N-N116L-S144R-A215D,V104L-S105T-T213A-L217E-S256N,N043W-S101D-S212M-N243F,V026F-A048R-S105T-T213A-N218D-T224A,S024F-S101D-G118R-A215D-L250I-A272F,V121F-N185E-T224A-P239G,T022L-L031F-G102A-S128D-T224A-N243F,N062E-S078N-G102A-N116L-S144R-L250I,T022L-T038F-V121F-S160D-A272F,V026F-S078N-G159C-R186K-N243F,S024F-A048R-G118R-S166D-L217E,G023A-T038F-S078N-G100S-S212M-A215D,G100S-N116L-A158E-T213A,S078N-V104L-G118R-S128D,G102A-S103N-S105T-A194E,T022L-S078N-S128D-T213A,K027R-G100S-G118R-S160D-S188D-N243F,S024F-G102A-R186K-T213A-L217E-N243F,T033S-S105T-S188D-S216F,G023A-G100S-A194E-S212M,A048R-S128D-N185E-P239G,G020K-S024F-T033S-P129E-A194E,G020K-K027R-P129E-S166D-P239G,T022L-G023A-K027R-S101D-V104L-S216F,T033S-G118R-P129E-A194E-P239G,T022L-S078N-N116L-P129E-S256N,K027R-S101D-S103N-S105T-A272F,A048R-S078N-N116L-N185E-L217E-P239G,G023A-S024F-K027R-N062E,S024F-S103N-V104L-G118R-S188D,V026F-V104L-S256N-A272F,S024F-N043W-V104L-V121F-P129E,N062E-S078N-N116L-T224A,G023A-S024F-V051W-A158E,K027R-T038F-G102A-N116L,N062E-S078N-S144R-S212M,L031F-N116L-S256N-A272F,T022L-T033S-V104L-N116L-S160D-R186K,S024F-G118R-P129E-R186K-T213A,N043W-S105T-T213A-A215D-S216F,L031F-S105T-R186K-S188D,V026F-A194E-T213A-S256N,和S103N-S160D-L250I-S256N,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0403] 本发明提供编码芽孢杆菌属枯草杆菌蛋白酶变体的核酸,该变体具有蛋白水解活性并包含具有选自以下的氨基酸置换的组合的氨基酸序列:T022A-S024R-S101D-S103A-V104I-G118R-G159D-S188D-A232V-N248D-E271F,T022A-S024R-S103A-V104I-P129E-G159D-S188D-A232V-N248D-E271F,T022A-S024R-S103A-V104I-G118R-G159D-S188D-L217D-A232V-N248D,T022A-S024R-S101D-S103A-V104I-G118R-P129E-G159D-S188D-A232V-Q245R-N248D,T022A-S024R-S101D-S103A-V104I-G159D-S188D-A232V-Q245R-N248D,T022A-N043R-S103A-V104I-G118R-P129E-G159D-S188D-A232V-Q245R-N248D,T022A-N043R-S103A-V104I-G118R-S128I-P129E-G159D-S188D-A232V-N248D,T022A-N043R-S101D-S103A-V104I-G118R-P129E-G159D-S188D-A232V-N248D-E271F,T022A-

S024R-N043R-S101D-S103A-V104I-G159D-S188D-A232V-Q245R-N248D,T022A-S103A-V104I-G159D-S188D-A232V-N248D,T022A-S024R-S103A-V104I-G118R-P129E-G159D-S188D-A232V-N248D-E271F,T022A-S024R-S103A-V104I-G159D-S188D-L217D-A232V-Q245R-N248D-E271F,T022A-N043R-N062E-S103A-V104I-G159D-S188D-A232V-Q245R-N248D-E271F,T022A-N043R-S103A-V104I-P129E-G159D-S188D-A232V-Q245R-N248D,T022A-S024R-S103A-V104I-G159D-S188D-L217D-A232V-N248D-E271F,T022A-S103A-V104I-G118R-G159D-S188D-L217D-A232V-Q245R-N248D,T022A-S024R-S101D-S103A-V104I-G118R-S128I-G159D-S188D-A232V-Q245R-N248D,T022A-S024R-N043R-S103A-V104I-G159D-S188D-L217D-A232V-N248D-E271F,T022A-N043R-S103A-V104I-G118R-G159D-S188D-L217D-A232V-N248D-E271F,T022A-N043R-S103A-V104I-G118R-G159D-S188D-A232V-N248D-E271F,T022A-S103A-V104I-S128I-P129E-G159D-S188D-A232V-N248D-E271F,T022A-S103A-V104I-G159D-S188D-L217D-A232V-Q245R-N248D-E271F,T022A-N043R-S103A-V104I-S128I-G159D-S188D-A232V-Q245R-N248D,T022A-S101D-S103A-V104I-G118R-G159D-S188D-L217D-A232V-Q245R-N248D-E271F,T022A-S103A-V104I-G118R-P129E-G159D-S188D-A232V-Q245R-N248D-E271F,T022A-S024R-N043R-S103A-V104I-G118R-G159D-S188D-L217D-A232V-N248D,T022A-N062E-S103A-V104I-G118R-G159D-S188D-A232V-Q245R-N248D,T022A-N043R-S101D-S103A-V104I-G118R-P129E-G159D-S188D-L217D-A232V,T022A-S024R-S103A-V104I-G159D-S188D-L217D-A232V-N248D,T022A-S024R-N043R-S103A-V104I-G118R-S128I-P129E-G159D-S188D-L217D-A232V-N248D-E271F,和T022A-S103A-V104I-G118R-G159D-S188D-L217D-A232V-Q245R-N248D-E271F,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0404] 本发明提供编码芽孢杆菌属枯草杆菌蛋白酶变体的核酸,该变体具有蛋白水解活性并包含具有选自以下的氨基酸置换的组合的氨基酸序列:G020K-S024F-N062E-S188D-P239G,S024F-N062E-N116L-P239G,G020K-G023A-N062E-S188D,G020K-G023A-S024F-N062E-G118R-S188D-T213A,G020K-N043W-N062E-N116L-S188D-T213A-P239G,G023A-N062E-N116L-G118R,G023A-S024F-N062E-N116L-G118R,S024F-N116L,S024F-N062E-S188D-T213A,G023A-N062E-N116L-G118R-S188D-P239G,G020K-S024F-N062E,G020K-N043W-N062E-N116L-P239G,S024F-N062E-N116L-T213A-P239G,G020K-S024F-N043W-N062E-N116L-T213A,G020K-G023A-S024F-N062E-N116L-S188D-T213A,S024F-N062E-S188D-P239G,G023A-N043W-N062E-N116L-G118R-T213A,N062E-S188D-P239G,G020K-S024F-N062E-P239G,S024F-N116L-G118R-S188D-P239G,G020K-G023A-N062E-N116L-G118R-T213A,G020K-G023A-S024F-N062E-S188D-T213A-P239G,S024F-N043W-G118R-S188D,G023A-S024F-N116L-G118R-S188D-T213A,G020K-G023A-N043W-N116L-S188D-T213A-P239G,G023A-S024F-N116L-S188D-P239G,G023A-N043W-N116L-G118R-S188D,G023A-S024F-G118R-S188D-P239G,G023A-S024F-N043W-N062E-N116L-G118R,G020K-N043W-S188D-T213A,S024F-N062E-G118R-P239G,G023A-N043W-S188D-T213A,G020K-S024F-N043W-N062E-N116L-G118R-S188D-P239G,G020K-N116L-S188D-P239G,G020K-N043W-N062E-G118R,G020K-N043W-N116L-S188D-T213A,G020K-S024F,G023A-N043W-

N116L-P239G,G023A-S024F-N043W-N116L-G118R-S188D-P239G,G020K-G023A-N043W-T213A,和G023A-S024F-N062E-G118R-T213A-P239G,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0405] 本发明提供编码芽孢杆菌属枯草杆菌蛋白酶变体的核酸,该变体具有蛋白水解活性并包含具有选自以下的氨基酸置换的组合的氨基酸序列:G020K-G023A-N043W-G118R-S128I-P129E-G159D-S188D,S024F-G118R-S128I-P129E-G159D,G020K-S024F-N062E-N116L-G118R-S188D,G020K-N062E-N116L-S188D,N062E-N116L-G118R-T213A,G020K-G023A-N062E-N116L-S188D,N062E-N116L-G118R-S188D,G020K-N062E-N116L-T213A,G020K-G023A-N062E-N116L,G020K-N062E-S188D-T213A,G020K-N062E,G020K-S024F-N062E-N116L-S188D,G020K-N043W-N062E-N116L-S188D,G020K-S024F-N062E-S188D-T213A,N062E-N116L-S188D-T213A,G020K-N062E-N116L,G020K-G023A-N062E-N116L-S188D-T213A,G023A-S024F-N062E-N116L-T213A,T022A-N043R-S103A-V104I-S128I-P129E-G159D-S188D-A232V-Q245R-N248D,T022A-N043R-S103A-V104I-G118R-S128I-P129E-G159D-S188D-A232V-N248D-E271F,S024F-N062E-N116L-S188D,T022A-S024R-S103A-V104I-G118R-S128I-P129E-G159D-S188D-A232V-N248D,G023A-N062E-N116L-S188D,N043W-N062E-N116L,G020K-G023A-N116L-S188D,N043W-N062E-N116L-S188D,S024F-N062E-N116L,N062E-N116L-S188D,和T022A-S024R-S103A-V104I-S128I-G159D-S188D-A232V-N248D,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0406] 本发明提供编码芽孢杆菌属枯草杆菌蛋白酶变体的核酸,该变体具有蛋白水解活性并包含具有选自以下的氨基酸置换的组合的氨基酸序列:S087R-S101G-S103A-V104I-Q109R-S212P-A232V-Q245R-E271V,S101G-S103A-V104I-Q109R-A232V-Q245R,S101G-S103A-V104I-Q109R-S212P-A232V-Q245R-E271V,S101G-S103A-V104I-Q109R-S212P-A232V-Q245R,N076D-S87R-S103A-V104I-S212P-E271V,N076D-S103A-V104I-Q109R,N076D-S103A-V104I-S212P-E271V,N076D-S103A-V104I-Q109R-Q245R,和N076D-S103A-V104I-S212P-Q245L-E271V,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0407] 本发明提供编码芽孢杆菌属枯草杆菌蛋白酶变体的核酸,该变体具有蛋白水解活性并包含具有选自以下的氨基酸置换的组合的氨基酸序列:S024R-P086W-G118R,S024R-S078R-P086W-N243F,S024R-T033S-P086S-S087N-Y209A,T033S-G118R,S024R-S078R-P086W-G118R-A270T,S024R-T033S-P086W-G118R,S078R-P086W-N243F,T033S-S078R-P086W-G118R-Y209A,T033S-S078R-Y209A,P086W-G118R-N243F,S024R-P086W,S078R-P086W-K235F,S024R-G118R,S024R-P086R,S101G-S103A-V104I-A232V,S024R-T033S-S078R-P086W-G118R,S024R-G118R-Y209A,Y209A-W241R,T033S-P086W-N243F,T033S-A172V-Y209A,G118R-Y209A-N243F,S024R-P086S-S141G,S024R-G118R-Y209A-N243F,S024R-T033S-P086S-S085N-K235F,S024R-T033S-A133V,S024R-T033S-S078R-P086W,S024R-P086W-Y209A,S024R-W241R,T033S-G118R-N243F,S024R-K235F,S024R-S078R-P086W,S024R-G118R-Y209A-K235F,S024R-Y209A-W241R,T033S-G118R-W241R,P086W-

G118R-Y209A,T033S-G118R-G159D-Y209A,T033S-S078R-P086W,S024R-P086W-N243F,G118R-Y209A,S024R-P086W-G118R-V203I,S078R-Y209A-K235F,S024R-T033S-W241R,S078R-G118R,T033S-G118R-Y209A-N243F,L021M-S024R-T033S,S024R-T033S-P086W,T033S-K235F,S078R-P086W-Y209A,S024R-T033S-Y209A-K235F,T033S-P086W-G118R,S024R-T033S-S078R-Y209A,T033S-P086W-G118R-Y209A-N243F,P086W-Y209A-N243F,P005S-S078R-G118R-W241R,S024R-A174T,T033S-Y209A-N243F,P086W-G118R-A133V,S024R-T033S-G118R,S024R-P086W-Y209A-K235F,P086W-Y209A,I008T-S024R,P086W-G118R,T033S-W241R,P005S-S024R-T033S-N243F,S024R-Y209A-S242P,S024R-T033S-S078R-G118R,S024R-T033S-A194T,S024R-N243F,S024R-Y209A,S024R-T033S-G118R-Y209A,T033S-P086W,S024R-T033S,S024R-T033S-S078R-N243F,P086W-N243F,T033S-G118D-A138V-Y209A,T033S-Y209A-K235F,S024R-P086R-G118R,T033S-P201S,S024R-P239Q,T033S-G118R-Y209A-,S078R-P086W,K235F-N243F,S024R-Y209A-K235F,G118R-A172V,H017Y-S024R-T033S-P086W,T033S-L148F,S024R-G118R-K235F,T033S-S078R,T033S-N243F,S024C-T033S,G118R-A194T,T033S-Y209A,G118R-Y209A-K235F,S024R-T033S-Y209A-N243F,S024R-T033S-K235F,S024R-T033S-G118R-K235F,S024R-S141G,S024R-T274I,S024R-T033S-Y209A,P086W-K235F,S024R-Y209A-N243F,V004E-T033S-S078R,P086W-Y209A-K235F,A015T-T033S,T033S-P086W-S156L-Y209A,S024R-G118R-N243F-R269H,Y209A-K235F,S024R-R247H,S024R-T033S-A228T,S078R-K235F,S024R-T033S-A174V-K235F,S024R-K235F-N243F,S024R-T033S-K235F-W241R,S024R-T033S-A151V,S024R-V104A,T033S-A048T,Q012H-V104A-G118R,G118R-K235F,T033S-T253A,T143A-Y209A,S024R-T033S-N243F,T033S-P239T,Y209A-N243F,S024R-T033S-P129H-N184D-T253M,S024R-A085V-P086W-G118R-K235F,S024R-A272P,和S024R-R269C,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0408] 本发明提供编码芽孢杆菌属枯草杆菌蛋白酶变体的核酸,该变体具有蛋白水解活性并包含具有选自以下的氨基酸置换的组合的氨基酸序列:G020R-S087D-S101G-S103A-V104I-A232V-Q245R,G020R-S101G-S103A-V104I-V150L-A232V-Q245R,N018R-G020R-S024R-N076D-S087D-H249R,N018R-G020R-S024R-N076D-V150L-H249R,N018R-S024R-N043R-N076D-S087D-H249R,N018R-S024R-N043R-N076D-V150L-H249R,N018R-S024R-N076D-S078R-S087D-H249R,N018R-S024R-N076D-S078R-V150L-H249R,N018R-S024R-N076D-S087D-H249R-N269R,N018R-S024R-N076D-S087D-S242R-H249R,N018R-S024R-N076D-S087D-V150L-H249R,N018R-S024R-N076D-V150L-H249R,N018R-S087D-S101G-S103A-V104I-A232V-Q245R,N018R-S101G-S103A-V104I-V150L-A232V-Q245R,N018R-T022R-S024R-N076D-S087D-H249R,N018R-T022R-S024R-N076D-V150L-H249R,N043R-S087D-S101G-S103A-V104I-A232V-Q245R-N269R,N043R-S101G-S103A-V104I-V150L-A232V-Q245R,S024R-S087D-S101G-S103A-V104I-A232V-Q245R,S024R-S101G-S103A-V104I-V150L-A232V-Q245R,S078R-S087D-S101G-S103A-V104I-A232V-Q245R,S078R-S101G-S103A-V104I-V150L-A232V-Q245R,S087D-S101G-S103A-V104I-A232V-Q245R-N269R,S101G-S103A-V104I-V150L-A232V-Q245R-H249R,S101G-S103A-V104I-V150L-

A232V-Q245R-N269R,T022R-S087D-S101G-S103A-V104I-A232V-Q245R,N018R-S024R-N043D-N076D-V150L-H249R,N043R-S087D-S101G-S103A-V104I-A232V-Q245R,T022R-S101G-S103A-V104I-V150L-A232V-Q245R,N018R-S024R-N043D-N076D-S087D-H249R,N018R-S024R-N076D-S087D-H249R,N018R-S024R-N076D-V150L-S242R-H249R,N043R-S101G-S103A-V104I-V150L-A232V-Q245R-N269R,N076D-S101G-S103A-V104I-V150L-A232V-Q245R,S087D-S101G-S103A-V104I-A232V-S242R-Q245R,S101G-S103A-V104I-V150L-A232V-Q245R,N076D-S087D-S101G-S103A-V104I-A232V-Q245R,S087D-S101G-S103A-V104I-A232V-Q245R,和S101G-S103A-V104I-V150L-A232V-S242R-Q245R,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0409] 本发明提供编码芽孢杆菌属枯草杆菌蛋白酶变体的核酸,该变体具有蛋白水解活性并包含具有选自以下的氨基酸置换的组合的氨基酸序列:S024R-S101G-S103A-V104I-P129Q-A158E-S188D-L217E-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-S130A-A158E-N183D-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-P129Q-A158E-N183D-S188D-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-S130A-A158E-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-P129Q-A158E-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-S130A-A158E-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-P129Q-S130A-A158E-N183D-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-S128L-P129Q-A158E-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-P129Q-S130A-A158E-S188D-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-P129Q-A158E-S188D-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-P129Q-S130A-A158E-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-S128L-P129Q-S130A-A158E-S188D-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-S128L-P129Q-A158E-S188D-A232V-Q245R-N248D-H249R,和S024R-K027R-S101G-S103A-V104I-S128L-P129Q-S130A-A158E-S188D-A232V-Q245R-N248D-H249R,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0410] 本发明提供编码芽孢杆菌属枯草杆菌蛋白酶变体的核酸,该变体具有蛋白水解活性并包含具有选自以下的氨基酸置换的组合的氨基酸序列:S101G-S103A-V104I-A232V-M222Q-Q245R,S101G-S103A-V104I-A158E-S188D-M222S-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-A158E-S188D-M222Q-A232V-Q245R-N248D-H249R,N076D-S101G-S103A-V104I-A232V-M222Q-Q245R,S101G-S103A-V104I-A232V-M222S-Q245R,N076D-S101G-S103A-V104I-A232V-M222S-Q245R,和N076D-S101G-S103A-V104I-A158E-S188D-M222S-A232V-Q245R-N248D-H249R,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0411] 本发明提供编码芽孢杆菌属枯草杆菌蛋白酶变体的核酸,该变体具有蛋白水解活性并包含具有选自以下的氨基酸置换的组合的氨基酸序列:S024R-S101G-S103A-V104I-S128L-P129Q-A158E-S188D-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-S130A-A158E-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-A158E-S188D-

A232V-Q245R-N248D-H249R,S101G-S103A-V104I-S128L-P129Q-A158E-S188D-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-P129Q-S130A-A158E-S188D-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-S130A-A158E-N183D-S188D-L217E-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-S128L-P129Q-S130A-A158E-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-P129Q-A158E-S188D-L217E-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-S128L-S130A-A158E-S188D-L217E-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-S128L-P129Q-A158E-N183D-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-S128L-P129Q-S130A-A158E-N183D-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-S128L-P129Q-A158E-S188D-A232V-Q245R-N248D-H249R-E271G,S101G-S103A-V104I-P129Q-A158E-N183D-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-S130A-A158E-S188D-L217E-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-S128L-A158E-N183D-S188D-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-P129Q-A158E-S188D-L217E-A232V-Q245R-N248D-H249R,和S024R-S101G-S103A-V104I-S128L-S130A-A158E-S188D-A232V-Q245R-N248D-H249R,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0412] 本发明提供编码芽孢杆菌属枯草杆菌蛋白酶变体的核酸,该变体具有蛋白水解活性并包含具有选自以下的氨基酸置换的组合的氨基酸序列:S101G-S103A-V104I,T22A-S101A-Y209E,S103G-L111V-G159E,T22A-S103G-G159E,T22A-L111V-G159E,T22A-S128N-E271F-Y209E,T22A-S103G-L111V,N62E-L111V-S128N,T22A-L111V-S128N,T22A-N62E-L111V,S101A-S103G-V104L-S188D,S101G-S103A-V104I-G159D,S101A-S103G-V104L-S128N,T22A-S101A-G159E,S101A-S103G-V104L,S101A-S103G-V104L-G159E,T22A-S101A-S103G-V104L,S101A-S103G-V104L-Y209E,T22A-Y209E-E271F,T22A-S101A-E271F,和S101A-Y209E-E271F,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0413] 本发明提供编码芽孢杆菌属枯草杆菌蛋白酶变体的核酸,该变体具有蛋白水解活性并包含具有选自以下的氨基酸置换的组合的氨基酸序列:S103A-V104I-G159D-A232V-Q236H-Q245R-N248D-N252K,S101G-V104I-G159D-A232V-Q236H-Q245R-N248D-N252K,S101G-S103A-G159D-A232V-Q236H-Q245R-N248D-N252K,S101G-S103A-V104L-A232V-Q236H-Q245R-N248D-N252K,S101G-S103A-V104L-G159D-Q236H-Q245R-N248D-N252K,S101G-S103A-V104L-G159D-A232V-Q245R-N248D-N252K,S101G-S103A-V104L-G159D-A232V-Q236H-N248D-N252K,S101G-S103A-V104L-G159D-A232V-Q236H-Q245R-N252K,和S101G-S103A-V104L-G159D-A232V-Q236H-Q245R-N248D,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0414] 本发明提供编码芽孢杆菌属枯草杆菌蛋白酶变体的核酸,该变体具有蛋白水解活性并包含具有选自以下的氨基酸置换的组合的氨基酸序列:S101G-S103A-V104I-G159D-A232V-Q245R-N248D,S101G-S103A-V104I-G159D-A232V-Q245R-N248D-E271F,S101G-S103A-V104I-G159D-A232V-Q245R-N248D-N238R,S101G-S103A-V104I-G159D-A232V-

Q245R-N248D-N248R,S101G-S103A-V104I-G159D-A232V-Q245R-N248D-T253R,S101G-S103A-V104I-G159D-A232V-Q245R-N248D-S24R,S101G-S103A-V104I-G159D-A232V-Q245R-N248D-N76D,S101G-S103A-V104I-G159E-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-G159E-A232V-Q245R-N248D-E271F,S101G-S103A-V104I-A158E-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-A158E-A232V-Q245R-N248D-E271F,T22A-S101G-S103A-V104I-G159D-A232V-Q245R-N248D-H249R,T22A-S101G-S103A-V104I-G159D-A232V-Q245R-N248D-E271F,N62E-S101G-S103A-V104I-G159D-A232V-Q245R-N248D-H249R,和N62E-S101G-S103A-V104I-G159D-A232V-Q245R-N248D-E271F,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0415] 本发明提供编码芽孢杆菌属枯草杆菌蛋白酶变体的核酸,该变体具有蛋白水解活性并包含具有选自以下的氨基酸置换的组合的氨基酸序列:A1R,A230E,E271L,G115R,G20R,H249R,K235F,K27V/F/L,L75E,L82R,N18R,N269R,N43D,N43R,N76D,R45T,S212F,S242R,S24R,S78R,S9A,T22R,V121E,V244R,V28E,V30E,V4R,W241R,G20R-N43R-H249R,G20R-T22R-N43R,G20R-N43R-S242R,G20R-N43R-E271L,G20R-N43R-V244R,G20R-S24R-N43R-S242R,S9A-T22R-S78R-S212F-W241R,S9A-G20R-N43R-S212F,S9A-N43R-S212F,G20R-N43R-S212F,G20R-T22R-N43R-S212F,S24R-S78R-S212F,S9A-N43R-S78R,S9A-N43R-S78R-S242R,S9A-G20R-N43R-S78R,G20R-S24R-N43R-S78R-S242R,T22R-S24R-S78R-S212F,S9A-G20R-N43R-S78R-S242R,G20R-N43R-S78R-H249R,G20R-N43R-S78R,S9A-S78R-S212F,S9A-T22R-N43R-S78R,S9A-G20R-S24R-N43R,S9A-T22R-S78R-S212F,V4R-S9A-T22R-S78R-S212F,G20R-S24R-N43R,A1R-S9A-N43R,G20R-S24R-N43R-G115R,S9A-S24R-N43R,G20R-T22R-S24R-N43R,A1R-S24R-N43R,S9A-G20R-S24R-N43R-S242R,S9A-G20R-T22R-S78R-S212F,S9A-S24R-N43R-V244R,S9A-S24R-N43R-S242R,V4R-S9A-T22R-S24R-S212F,和T22R-S24R-N43R,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0416] 本发明提供编码芽孢杆菌属枯草杆菌蛋白酶变体的核酸,该变体具有蛋白水解活性并包含具有选自以下的氨基酸置换的组合的氨基酸序列:S101G-S103A-V104I-A232V-Q245R-N248D,S101G-S103A-V104I-G159D-A232V-Q245R,S101G-S103A-V104I-G159R-A232V-Q245R-N248D,S101G-S103A-V104I-G159D-A232V-Q245R-N248R,S101G-S103A-V104I-A232V-Q245R,S101G-S103A-V104I-A232V-Q245R-N248R,S101G-S103A-V104I-G159R-A232V-Q245R-N248R,S101G,S103A,V104I,A232V,Q236H,和Q245R,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0417] 本发明提供编码芽孢杆菌属枯草杆菌蛋白酶变体的核酸,该变体具有蛋白水解活性并包含具有选自以下的氨基酸置换的组合的氨基酸序列:A16S,T22A,S24R,N62E,N76D,E89P,S101A/G,S103G/A,V104L/I,L111V,S128N,P129E,A232V,L148I,A158E,G159D/E,R186H,S188D,Y209E,Q236H,Q245R,N248D/R,H249R,N252K/R,T253R,和E271F,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0418] 本发明还提供迟缓芽孢杆菌枯草杆菌蛋白酶GG36蛋白酶的蛋白酶变体，其中该迟缓芽孢杆菌枯草杆菌蛋白酶GG36蛋白酶包含SEQ ID NO:2所示氨基酸序列，其中该蛋白酶变体包含与SEQ ID NO:2的氨基酸序列相差不超过2、3、4、5、6、7、8、9、10、11、12、13、14、15、16、17、18、19、20、21、22、23、24或25个突变的氨基酸序列，所述突变选自:G20K,G20R,G23A,S24F,S24R,N43R,N43W,R45T,N62E,N76D,S101A,N116A,N116L,G118R,S128I,P129E,S188D,T213A,A215F,L217E,P239G，和N269R，其中该蛋白酶变体的氨基酸位置根据SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列中对应的氨基酸位置的编号方式来进行编号，这是通过该蛋白酶变体氨基酸序列与解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'氨基酸序列的比对来确定的。

[0419] 本发明提供编码芽孢杆菌属枯草杆菌蛋白酶变体的核酸，该变体具有蛋白水解活性并包含具有选自以下的氨基酸置换的组合的氨基酸序列:A1R,Q2S,Q2M,Q2A,Q2R,Q2W,S3R,V4R,V4S,V4C,I8A,S9A,S9F,S9W,R10S,R10A,R10H,R10M,Q12F,Q12R,P14K,P14F,P14Q,A15R,A15F,A16S,H17R,H17M,H17F,N18R,N18K,G20F,G20K,G20R,T22A,T22R,T22Y,T22V,T22Q,T22L,T22W,G23A,G23S,G23F,S24R,S24F,S24W,S24Q,S24H,S24L,G25V,G25F,G25R,V26F,K27L,K27F,K27R,K27V,V28A,V28N,V28E,A29T,V30E,L31F,T33S,T33G,T33D,G34P,I35M,S36T,S36F,S36R,T38L,T38F,T38R,P40N,P40L,P40T,P40W,P40H,P40R,L42I,N43A,N43F,N43I,N43S,N43R,N43M,N43W,N43D,R45T,G46R,A48R,F50C,V51W,V51F,V51H,P52F,P52E,P52N,P55Y,T57R,Q59A,Q59F,Q59R,D60P,D60Q,D60A,N62E,N62Q,G63V,G63M,G63T,G63I,G63A,G63S,G63H,G63Q,G63D,G63E,G63P,H64F,H64T,V68A,V68C,A69N,A69T,A69P,A69W,T71G,T71G,I72C,A74C,L75A,L75F,L75E,L75R,N76D,S78R,S78N,S78I,S78R,I79W,I79Q,V81R,L82F,L82T,L82V,L82R,L82M,A85M,P86W,P86L,P86I,E89P,E89T,E89G,E89H,E89W,E89L,E89V,E89W,E89F,E89I,Y91N,Y91F,A92F,K94N,S99F,S99T,S99P,S99G,S99M,G100S,G100N,G100Q,G100I,S101A,S101N,S101G,S101D,S101T,S101D,S101E,S101P,S101F,G102A,G102T,G102N,G102H,G102E,S103G,S103N,S103D,S103A,V104L,V104I,V104E,V104D,S105T,S105E,S105Q,S106G,S106T,S106E,S106D,S106A,S106V,S106F,I107M,I107F,A108I,A108G,Q109M,L111V,L111I,E112V,E112L,E112Q,A114G,G115K,G115R,N116K,N116A,N116L,N117F,G118R,G118I,M119C,H120A,H120F,H120R,V121F,V121F,V121E,N123G,N123E,L124S,S128D,S128F,S128L,S128N,S128H,S128M,S128I,S128Q,P129E,S132A,S132E,A138G,S144R,V147L,L148I,A158E,G159D,G159E,G159C,S160D,S166D,S166E,Y167W,M175V,V177C,D181A,Q182R,N183I,N183D,N183M,N183R,N183F,N183R,N185E,N185V,N185I,R186H,R186K,S188E,S188D,S188R,Y192H,Y192W,A194E,A194V,A194F,D197F,D197F,I198L,I198F,V203E,V203C,T208S,Y209S,Y209N,Y209F,Y209T,Y209E,Y209H,Y209G,Y209L,P210R,P210V,P210L,G211Q,G211R,S212I,S212M,S212F,T213A,Y214F,A215N,A215D,A215E,A215H,A215F,S216F,S216A,L217E,L217N,L217D,N218D,N218P,N218E,T224A,T224G,V227I,A230E,A231I,A231C,A232V,L233C,V234F,K235F,Q236F,Q236N,Q236H,N238R,N238K,N238L,P239K,P239G,P239R,P239R,P239H,P239T,P239N,P239S,P239F,S240R,W241R,S242L,S242R,N243F,N243R,V244R,Q245R,I246S,N248D,N248V,N248I,N248R,H249R,H249T,L250I,K251R,K251S,N252I,N252F,N252R,N252K,N252H,T253I,T253R,T253F,A254C,S256N,G258R,T260V,

T260I,L262D,L262H,Y263F,S265F,L267V,L267N,L267M,N269I,N269R,A270C,E271I,E271H,E271V,E271H,E271M,E271L,E271P,E271A,E271F,E271T,A272F,A272F,A272R,A273F,A273I,和T274G,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0420] 本发明提供编码迟缓芽孢杆菌枯草杆菌蛋白酶GG36蛋白酶的芽孢杆菌属枯草杆菌蛋白酶变体的核酸,其中该迟缓芽孢杆菌枯草杆菌蛋白酶GG36蛋白酶包含SEQ ID NO:2所示氨基酸序列,并且其中该蛋白酶变体包含与SEQ ID NO:2的氨基酸序列相差不超过2、3、4、5、6、7、8、9、10、11、12、13、14、15、16、17、18、19、20、21、22、23、24或25个突变的氨基酸序列,所述突变处于选自氨基酸1、2、3、4、8、9、10、12、14、15、16、17、18、20、22、23、24、25、26、27、28、29、30、31、33、34、35、36、38、40、42、43、45、46、48、50、51、52、55、57、59、60、62、63、64、68、69、71、72、74、75、76、78、79、81、82、85、86、89、91、92、94、99、100、101、102、103、104、105、106、107、108、109、111、112、114、115、116、117、118、119、120、121、123、124、128、129、132、138、44、147、148、158、159、160、166、167、175、177、181、182、183、185、186、188、192、194、197、198、203、208、209、210、211、212、213、214、215、216、217、218、224、227、230、231、233、234、235、236、236、238、238、239、240、241、242、243、244、246、248、249、250、251、252、253、254、256、258、260、262、263、265、267、269、270、271、272、273和274的氨基酸位置,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号,其中该蛋白酶变体的氨基酸位置根据SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列中对应的氨基酸位置的编号方式来进行编号,这是通过该变体蛋白酶氨基酸序列与解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'氨基酸序列的比对来确定的。

[0421] 本发明提供编码迟缓芽孢杆菌枯草杆菌蛋白酶GG36蛋白酶的芽孢杆菌属枯草杆菌蛋白酶变体的核酸,其中该迟缓芽孢杆菌枯草杆菌蛋白酶GG36蛋白酶包含SEQ ID NO:2所示氨基酸序列,并且其中该蛋白酶变体包含与SEQ ID NO:2的氨基酸序列相差不超过2、3、4、5、6、7、8、9、10、11、12、13、14、15、16、17、18、19、20、21、22、23、24、25、30、35、40、45或50个突变的氨基酸序列,所述突变选自:A1R,Q2S,Q2M,Q2A,Q2R,Q2W,S3R,V4R,V4S,V4C,I8A,S9A,S9F,S9W,R10S,R10A,R10H,R10M,Q12F,Q12R,P14K,P14F,P14Q,A15R,A15F,A16S,H17R,H17M,H17F,N18R,N18K,G20F,G20K,G20R,T22A,T22R,T22Y,T22V,T22Q,T22L,T22W,G23A,G23S,G23F,S24R,S24F,S24W,S24Q,S24H,S24L,G25V,G25F,G25R,V26F,K27L,K27F,K27R,K27V,V28A,V28N,V28E,A29T,V30E,L31F,T33S,T33G,T33D,G34P,I35M,S36T,S36F,S36R,T38L,T38F,T38R,P40N,P40L,P40T,P40W,P40H,P40R,L42I,N43A,N43F,N43I,N43S,N43R,N43M,N43W,N43D,R45T,G46R,A48R,F50C,V51W,V51F,V51H,P52F,P52E,P52N,P55Y,T57R,Q59A,Q59F,Q59R,D60P,D60Q,D60A,N62E,N62Q,G63V,G63M,G63T,G63I,G63A,G63S,G63H,G63Q,G63D,G63E,G63P,H64F,H64T,V68A,V68C,A69N,A69T,A69P,A69W,T71G,T71G,I72C,A74C,L75A,L75F,L75E,L75R,N76D,S78R,S78N,S78I,S78R,I79W,I79Q,V81R,L82F,L82T,L82V,L82R,L82M,A85M,P86W,P86L,P86I,E89P,E89T,E89G,E89H,E89W,E89L,E89V,E89W,E89F,E89I,Y91N,Y91F,A92F,K94N,S99F,S99T,S99P,S99G,S99M,G100S,G100N,G100Q,G100I,S101A,S101N,S101G,S101D,S101T,S101D,S101E,S101P,S101F,G102A,G102T,G102N,G102H,G102E,S103G,S103N,S103D,S103A,V104L,V104I,V104E,V104D,S105T,

S105E,S105Q,S106G,S106T,S106E,S106D,S106A,S106V,S106F,I107M,I107F,A108I,A108G,Q109M,L111V,L111I,E112V,E112L,E112Q,A114G,G115K,G115R,N116K,N116A,N116L,N117F,G118R,G118I,M119C,H120A,H120F,H120R,V121F,V121F,V121E,N123G,N123E,L124S,S128D,S128F,S128L,S128N,S128H,S128M,S128I,S128Q,P129E,S132A,S132E,A138G,S144R,V147L,L148I,A158E,G159D,G159E,G159C,S160D,S166D,S166E,Y167W,M175V,V177C,D181A,Q182R,N183I,N183D,N183M,N183R,N183F,N183R,N185E,N185V,N185I,R186H,R186K,S188E,S188D,S188R,Y192H,Y192W,A194E,A194V,A194F,D197F,D197F,I198L,I198F,V203E,V203C,T208S,Y209S,Y209N,Y209F,Y209T,Y209E,Y209H,Y209G,Y209L,P210R,P210V,P210L,G211Q,G211R,S212I,S212M,S212F,T213A,Y214F,A215N,A215D,A215E,A215H,A215F,S216F,S216A,L217E,L217N,L217D,N218D,N218P,N218E,T224A,T224G,V227I,A230E,A231I,A231C,A232V,L233C,V234F,K235F,Q236F,Q236N,Q236H,N238R,N238K,N238L,P239K,P239G,P239R,P239R,P239H,P239T,P239N,P239S,P239F,S240R,W241R,S242L,S242R,N243F,N243R,V244R,Q245R,I246S,N248D,N248V,N248I,N248R,H249R,H249T,L250I,K251R,K251S,N252I,N252F,N252R,N252K,N252H,T253I,T253R,T253F,A254C,S256N,G258R,T260V,T260I,L262D,L262H,Y263F,S265F,L267V,L267N,L267M,N269I,N269R,A270C,E271I,E271H,E271V,E271H,E271M,E271L,E271P,E271A,E271F,E271T,A272F,A272F,A272R,A273F,A273I,和T274G,其中该蛋白酶变体的氨基酸位置根据SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列中对应的氨基酸位置的编号方式来进行编号,这是通过该蛋白酶变体氨基酸序列与解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'氨基酸序列的比对来确定的。

[0422] 本发明提供编码迟缓芽孢杆菌枯草杆菌蛋白酶GG36蛋白酶的芽孢杆菌属枯草杆菌蛋白酶变体的核酸,其中该迟缓芽孢杆菌枯草杆菌蛋白酶GG36蛋白酶包含SEQ ID NO:2所示氨基酸序列,并且其中该蛋白酶变体包含与SEQ ID NO:2的氨基酸序列相差不超过2、3、4、5、6、7、8、9、10、11、12、13、14、15、16、17、18、19、20、21、22、23、24、25、30、35、40、45或50个突变的氨基酸序列,所述突变选自:A1R,Q2S,V4R,V4S,S9A,R10S,P14K,A16S,H17R,N18R,G20R,T22A,T22R,S24R,S24W,G25R,G25V,V26F,L42I,N43R,N43A,G46R,P52F,P52E,P52N,T57R,Q59A,N62E,N62Q,V68A,V68C,T71G,I72C,A74C.L75A,L75F,L75R,N76D,S78R,L82R,P86W,E89P,E89T,E89G,E89H,E89I,E89V,E89W,Y91N,K94N,G100S,S101A,S101N,S101G,S101D,S103G,S103N,V104L,V104I,S106V,S106G,A108I,L111V,E112V,G115K,G115R,N117F,G118I,V121F,S128D,S128F,S128L,S128N,P129E,S144R,L148I,A158E,G159E,S160D,S166D,N185E,N185I,R186H,S188E,S188D,D197F,V203E,Y209S,Y209N,Y209F,Y209T,Y209E,Y209H,Y209G,P210R,S212I,S212F,Y214F,A215N,A215D,A215E,L217E,L217N,T224A,A230E,A231I,Q236F,N238R,N238K,P239K,P239G,P239R,P239S,W241R,S242R,S242L,N243R,V244R,N248I,N248V,H249R,L250I,N252R,T253R,L262D,Y263F,S265F,L267V,L267N.N269I,N269R,E271F,E271I,E271H,E271P,E271T,E271V,E271L和A272F,并且该蛋白酶变体任选地包含至少一个选自S103A,G159D,Q236H,Q245R,N248D和N252K,的突变,其中该蛋白酶变体的氨基酸位置根据SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列中对应的氨基酸位置的编号方式来进行编号,这是通过该蛋白酶变体氨基酸序列与解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'氨基酸序列的比对来确定

的。

[0423] 本发明提供编码迟缓芽孢杆菌枯草杆菌蛋白酶GG36蛋白酶的芽孢杆菌属枯草杆菌蛋白酶变体的核酸，其中该迟缓芽孢杆菌枯草杆菌蛋白酶GG36蛋白酶包含SEQ ID NO:2所示氨基酸序列，并且其中该蛋白酶变体包含与SEQ ID NO:2的氨基酸序列相差不超过2、3、4、5、6、7、8、9、10、11、12、13、14、15、16、17、18、19、20、21、22、23、24、25、30、35、40、45或50个突变的氨基酸序列，所述突变选自:A1R,Q2S,V4R,V4S,S9A,R10S,P14K,A16S,H17R,N18R,G20R,T22A,T22R,S24R,S24W,G25R,G25V,V26F,L42I,N43R,N43A,G46R,P52F,P52E,P52N,T57R,Q59A,N62E,N62Q,V68A,V68C,T71G,I72C,A74C.L75A,L75F,L75R,N76D,S78R,L82R,P86W,E89P,E89T,E89G,E89H,E89I,E89V,E89W,Y91N,K94N,G100S,S101A,S101N,S101G,S101D,S103G,S103N,V104L,V104I,S106V,S106G,A108I,L111V,E112V,G115K,G115R,N117F,G118I,V121F,S128D,S128F,S128L,S128N,P129E,S144R,L148I,A158E.G159E,S160D,S166D,N185E,N185I,R186H,S188E,S188D,D197F,V203E,Y209S,Y209N,Y209F,Y209T,Y209E,Y209H,Y209G,P210R,S212I,S212F,Y214F,A215N,A215D,A215E,L217E,L217N,T224A,A230E,A231I,Q236F,N238R,N238K,P239K,P239G,P239R,P239S,W241R,S242R,S242L,N243R,V244R,N248I,N248V,H249R,L250I,N252R,T253R,L262D,Y263F,S265F,L267V,L267N.N269I,N269R,E271F,E271I,E271H,E271P,E271T,E271V,E271L和A272F，并且该蛋白酶变体任选地包含至少一个选自以下的突变:S103A,G159D,Q236H,Q245R,N248D和N252K，

[0424] 本发明提供编码迟缓芽孢杆菌枯草杆菌蛋白酶GG36蛋白酶的芽孢杆菌属枯草杆菌蛋白酶变体的核酸，其中该迟缓芽孢杆菌枯草杆菌蛋白酶GG36蛋白酶包含SEQ ID NO:2所示氨基酸序列，并且其中该蛋白酶变体包含与SEQ ID NO:2的氨基酸序列相差不超过2、3、4、5、6、7、8、9、10、11、12、13、14、15、16、17、18、19、20、21、22、23、24、25、30、35、40、45或50个突变的氨基酸序列，所述突变选自:A16S,T22A,S24R,N62E,N76D,E89P,S101A/G,S103G/A,V104L/I,L111V,S128N,P129E,A232V,L148I,A158E,G159D/E,R186H,S188D,Y209E,Q236H,Q245R,N248D/R,H249R,N252K/R,T253R,E271F,A1R,A230E,E271L,G115R,G20R,H249R,K235F,K27V/F/L,L75E,L82R,N18R,N269R,N43D,N43R,N76D,R45T,S212F,S242R,S24R,S78R,S9A,T22R,V121E,V244R,V28E,V30E,V4R，和W241R，并且其中该蛋白酶变体的氨基酸位置根据SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列中对应的氨基酸位置的编号方式来进行编号，这是通过该蛋白酶变体氨基酸序列与解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'氨基酸序列的比对来确定的。

[0425] 本发明还提供迟缓芽孢杆菌枯草杆菌蛋白酶GG36蛋白酶的蛋白酶变体，其中该迟缓芽孢杆菌枯草杆菌蛋白酶GG36蛋白酶包含SEQ ID NO:2所示氨基酸序列，其中该蛋白酶变体包含与SEQ ID NO:2的氨基酸序列相差不超过2、3、4、5、6、7、8、9、10、11、12、13、14、15、16、17、18、19、20、21、22、23、24或25个突变的氨基酸序列，所述突变选自:A16S,T22A,S24R,N62E,N76D,E89P,S101A/G,S103G/A,V104L/I,L111V,S128N,P129E,A232V,L148I,A158E,G159D/E,R186H,S188D,Y209E,Q236H,Q245R,N248D/R,H249R,N252K/R,T253R，和E271F，其中该蛋白酶变体的氨基酸位置根据SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列中对应的氨基酸位置的编号方式来进行编号，这是通过该蛋白酶变体氨基酸序列与解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'氨基酸序列的比对来确定的。

[0426] 本发明提供编码迟缓芽孢杆菌枯草杆菌蛋白酶GG36蛋白酶的芽孢杆菌属枯草杆菌蛋白酶变体的核酸，其中该迟缓芽孢杆菌枯草杆菌蛋白酶GG36蛋白酶包含SEQ ID NO:2所示氨基酸序列，并且其中该蛋白酶变体包含与SEQ ID NO:2的氨基酸序列相差不超过2、3、4、5、6、7、8、9、10、11、12、13、14、15、16、17、18、19、20、21、22、23、24、25、30、35、40、45或50个突变的氨基酸序列，所述突变选自:A16S,T22A,S24R,N62E,N76D,E89P,S101A/G,S103G/A,V104L/I,L111V,S128N,P129E,A232V,L148I,A158E,G159D/E,R186H,S188D,Y209E,Q236H,Q245R,N248D/R,H249R,N252K/R,T253R,E271F,A1R,A230E,E271L,G115R,G20R,H249R,K235F,K27V/F/L,L75E,L82R,N18R,N269R,N43D,N43R,N76D,R45T,S212F,S242R,S24R,S78R,S9A,T22R,V121E,V244R,V28E,V30E,V4R，和W241R，其中该蛋白酶变体的氨基酸位置根据SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列中对应的氨基酸位置的编号方式来进行编号，这是通过该蛋白酶变体氨基酸序列与解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'氨基酸序列的比对来确定的。

[0427] 本发明还提供迟缓芽孢杆菌枯草杆菌蛋白酶GG36蛋白酶的蛋白酶变体，其中该迟缓芽孢杆菌枯草杆菌蛋白酶GG36蛋白酶包含SEQ ID NO:2所示氨基酸序列，其中该蛋白酶变体包含与SEQ ID NO:2的氨基酸序列相差不超过2、3、4、5、6、7、8、9、10、11、12、13、14、15、16、17、18、19、20、21、22、23、24或25个突变的氨基酸序列，所述突变选自:G20K,G20R,G23A,S24F,S24R,N43R,N43W,R45T,N62E,N76D,S101A,N116A,N116L,G118R,S128I,P129E,S188D,T213A,A215F,L217E,P239G，和N269R，其中该蛋白酶变体的氨基酸位置根据SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列中对应的氨基酸位置的编号方式来进行编号，这是通过该蛋白酶变体氨基酸序列与解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'氨基酸序列的比对来确定的。

[0428] 本发明提供编码芽孢杆菌属枯草杆菌蛋白酶变体的核酸，该枯草杆菌蛋白酶变体包含与SEQ ID NO:2的氨基酸序列不同的氨基酸序列，并且其中该蛋白酶变体的总净电荷相对于迟缓芽孢杆菌枯草杆菌蛋白酶GG36蛋白酶的总净电荷为+1、+2、+3、+4、+5、0、-1、-2、-3、-4或-5，并且其中该蛋白酶变体的氨基酸位置根据SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列中对应的氨基酸位置的编号方式来进行编号，这是通过该蛋白酶变体氨基酸序列与解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'氨基酸序列的比对来确定的。

[0429] 本发明还提供包含与SEQ ID NO:2的氨基酸序列不同的氨基酸序列的蛋白酶变体，并且其中该蛋白酶变体的总净电荷相对于迟缓芽孢杆菌枯草杆菌蛋白酶GG36蛋白酶的总净电荷为0，并且其中该蛋白酶变体的氨基酸位置根据SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列中对应的氨基酸位置的编号方式来进行编号，这是通过该蛋白酶变体氨基酸序列与解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'氨基酸序列的比对来确定的。

[0430] 本发明提供编码具有以下特性中的一者或多者的芽孢杆菌属枯草杆菌蛋白酶变体的核酸:a)测试方法2性能指数为至少1.1、至少1.2、至少1.3、至少1.4、至少1.5、至少1.6、至少1.7、至少1.8、至少1.9、至少2、1.1至约10、1.1至约8或甚至1.1至约5;b)测试方法3性能指数为至少1.1、至少1.2、至少1.3、至少1.4、至少1.5、至少1.6、至少1.7、至少1.8、至少1.9、至少2、1.1至约10、1.1至约8或甚至1.1至约5;c)测试方法4性能指数为至少1.0、至

少1.1、至少1.2、至少1.3、至少1.4、至少1.5、至少1.6、至少1.7、至少1.8、至少1.9、至少2、1.0至约10、1.0至约8或甚至1.0至约5;和/或d)测试方法6性能指数为至少1.0、至少1.1、至少1.2、至少1.3、至少1.4、至少1.5、至少1.6、至少1.7、至少1.8、至少1.9、至少2、1.0至约10、1.0至约8或甚至1.0至约5。测试方法2、测试方法3、测试方法4和测试方法6在下文的实例1题为“测试方法”的章节中明确地进行了描述。

[0431] 如本文所指出,合适的冷水蛋白酶变体是亲本蛋白酶的变体,所述亲本蛋白酶的序列与SEQ ID NO:1的氨基酸序列具有至少97%、至少99%或100%同一性,所述蛋白酶变体具有以下特性中的一者或多者:

[0432] a)测试方法2性能指数为至少1.1、至少1.2、至少1.3、至少1.4、至少1.5、至少1.6、至少1.7、至少1.8、至少1.9、至少2、1.1至约10、1.1至约8或甚至1.1至约5;b)测试方法3性能指数为至少1.1、至少1.2、至少1.3、至少1.4、至少1.5、至少1.6、至少1.7、至少1.8、至少1.9、至少2、1.1至约10、1.1至约8或甚至1.1至约5;c)测试方法4性能指数为至少1.0、至少1.1、至少1.2、至少1.3、至少1.4、至少1.5、至少1.6、至少1.7、至少1.8、至少1.9、至少2、1.0至约10、1.0至约8或甚至1.0至约5;和/或d)测试方法6性能指数为至少1.0、至少1.1、至少1.2、至少1.3、至少1.4、至少1.5、至少1.6、至少1.7、至少1.8、至少1.9、至少2、1.0至约10、1.0至约8或甚至1.0至约5。测试方法2、测试方法3、测试方法4和测试方法6在下文的实例1题为“测试方法”的章节中明确地进行了描述。本文提及的所有突变均利用如图1所示的BPN’编号方案。在一些实施例中,本文提及的变体是指具有利用BPN’编号方案与SEQ ID NO:2的氨基酸序列相比较的氨基酸序列的变体。

[0433] 在一些实施例中,本文提供的变体是指亲本蛋白酶的变体,其中亲本蛋白酶的序列与SEQ ID NO:1的氨基酸序列具有至少97%、至少99%或100%同一性。

[0434] 合适的冷水蛋白酶可以衍生自枯草杆菌蛋白酶,尤其是衍生自SEQ ID NO:2的迟缓芽孢杆菌枯草杆菌蛋白酶GG36的那些蛋白酶,并且在一些实施例中,包含一个或多个以下的突变:A1R,Q2S,V4R,V4S,S9A,R10S,P14K,A16S,H17R,N18R,G20R,T22A,T22R,S24R,S24W,G25R,G25V,V26F,L42I,N43R,N43A,G46R,P52F,P52E,P52N,T57R,Q59A,N62E,N62Q,V68A,V68C,T71G,I72C,A74C.L75A,L75F,L75R,N76D,S78R,L82R,P86W,E89P,E89T,E89G,E89H,E89I,E89V,E89W,Y91N,K94N,G100S,S101A,S101N,S101G,S101D,S103G,S103N,V104L,V104I,S106V,S106G,A108I,L111V,E112V,G115K,G115R,N117F,G118I,V121F,S128D,S128F,S128L,S128N,P129E,S144R,L148I,A158E.G159E,S160D,S166D,N185E,N185I,R186H,S188E,S188D,D197F,V203E,Y209S,Y209N,Y209F,Y209T,Y209E,Y209H,Y209G,P210R,S212I,S212F,Y214F,A215N,A215D,A215E,L217E,L217N,T224A,A230E,A231I,Q236F,N238R,N238K,P239K,P239G,P239R,P239S,W241R,S242R,S242L,N243R,V244R,N248I,N248V,H249R,L250I,N252R,T253R,L262D,Y263F,S265F,L267V,L267N.N269I,N269R,E271F,E271I,E271H,E271P,E271T,E271V,E271L和/或A272F。

[0435] 在一些实施例中,合适的冷水蛋白酶变体包括枯草杆菌蛋白酶,尤其是衍生自SEQ ID NO:2的迟缓芽孢杆菌GG36的那些蛋白酶,其包含一个或多个以下的突变组:T022R-S024R,S009A-E271L,N018R-W241R,N018R-G115R,N043R-H249R,G020R-H249R,V004R-H249R,G020R-S024R,N018R-H249R,S009A-G020R,G020R-W241R,S009A-S078R,G020R-G115R,N018R-S024R,S024R-S242R,T022R-G115R,N018R-N043R,G020R-N043R,N018R-

S242R,S242R-N269R,N018R-V244R,S024R-N269R,G020R-E271L,S024R-E271L,V004R-S009A,G020R-N269R,A001R-S024R,V244R-E271L,S009A-N018R,W241R-E271L,V004R-S024R,S009A-H249R,S009A-T022R,N062E-P129E,N062E-G159E,A016S-L148I,A158E-H249R,A016S-N062E,L111V-S188D,T022A-N062E,N062E-L148I,T022A-P129E,N062E-E271F,N062E-A158E,A016S-G159E,N062E-R186H,S128N-G159E,N062E-S188D,N062E-S128N,L148I-G159E,S103G-A158E,L111V-G159E,A158E-E271F,A016S-S188D,T022A-L111V,S128N-A158E,A016S-A158E,V104L-A158E,S128N-R186H,G159E-Y209E,N062E-S101A,L111V-Y209E,L148I-S188D,S101A-Y209E,T022A-S188D,A016S-T022A,S128N-P129E,A016S-Y209E,A016S-S128N,T022A-E089P,S128N-Y209E,E089P-A158E,N062E-S103G,R186H-E271F,A016S-P129E,E089P-G159E,L111V-H249R,S101A-P129E,L148I-Y209E,T022A-G159E,P129E-H249R,P129E-Y209E,V104L-P129E,S128N-S188D,L111V-A158E,T022A-A158E,N062E-Y209E,N062E-H249R,S101A-R186H,E089P-P129E,P129E-E271,T22A-L111V-G159E,S101A-S103G-V104L-Y209E,S101A-S103G-V104L-G159E,S101A-S103G-V104L-S188D,S101G-S103A-V104I-G159D,T22A-S103G-G159E,T22A-S128N-E271F-Y209E,T22A-Y209E-E271F,T22A-S101A-Y209E,S101A-Y209E-E271F,T22A-L111V-S128N,T22A-S101A-G159E,S101A-S103G-V104L,T22A-S101A-S103G-V104L,S101A-S103G-V104L,S101G-S103A-V104I,S101A-S103G-V104L-S128N,S103A-V104I-G159D-A232V-Q236H-Q245R-N248D-N252K,S101G-V104I-G159D-A232V-Q236H-Q245R-N248D-N252K,S101G-S103A-G159D-A232V-Q236H-Q245R-N248D-N252K,S101G-S103A-V104L-A232V-Q236H-Q245R-N248D-N252K,S101G-S103A-V104L-G159D-Q236H-Q245R-N248D-N252K,S101G-S103A-V104L-G159D-A232V-Q245R-N248D-N252K,S101G-S103A-V104L-G159D-A232V-Q236H-N248D-N252K,S101G-S103A-V104L-G159D-A232V-Q236H-Q245R-N252K,S101G-S103A-V104L-G159D-A232V-Q236H-Q245R-N248D,N62E-S101G-S103A-V104I-G159D-A232V-Q245R-N248D-E271F,N62E-S101G-S103A-V104I-G159D-A232V-Q245R-N248D-H249R,T22A-S101G-S103A-V104I-G159D-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-G159D-A232V-Q245R-N248D-S24R,S101G-S103A-V104I-G159D-A232V-Q245R-N248D-T253R,S101G-S103A-V104I-A158E-A232V-Q245R-N248D-H249R,T22A-S101G-S103A-V104I-G159D-A232V-Q245R-N248D-E271F,S101G-S103A-V104I-G159E-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-G159D-A232V-Q245R-N248D-N238R,S101G-S103A-V104I-A158E-A232V-Q245R-N248D-E271F,S101G-S103A-V104I-G159D-A232V-Q245R-N248D,S101G-S103A-V104I-G159D-A232V-Q245R-N248D-E271F,S101G-S103A-V104I-G159D-A232V-Q245R-N248D-N76D,和/或S101G-S103A-V104I-G159E-A232V-Q245R-N248D-E271F。

[0436] 本发明还提供分离的枯草杆菌蛋白酶变体,其中该枯草杆菌蛋白酶变体是具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:G020R-N043R,G020K-N062E,S024F-N116L,G020K-S024F,S024R-A174T,S024R-G118R,S024R-K235F,S024R-P086R,S024R-P086W,S078R-G118R,T033S-G118R,T033S-K235F,Y209A-W241R,G020R-N076D,N018R-Q245R,S024R-R045T,A232V-Q245R,G118R-A172V,G118R-A194T,I008T-S024R,K235F-N243F,N018R-S103A,N018R-V104I,P086W-G118R,P086W-N243F,P086W-Y209A,S024C-T033S,S024R-A232V,S024R-N243F,S024R-P239Q,S024R-

S101G,S024R-S141G,S024R-T033S,S024R-T274I,S024R-Y209A,S078R-P086W,S101G-A232V,T033S-L148F,T033S-P086W,T033S-P201S,T033S-S078R,T033S-W241R,T033S-Y209A,A230E-H249R,A232V-H249R,G118R-K235F,N076D-Q245R,P086W-K235F,S024R-R247H,S024R-V104A,S078R-K235F,S101G-H249R,S103A-A232V,T033S-A048T,T033S-P239T,T033S-T253A,T143A-Y209A,Y209A-K235F,N018R-R045T,Y209A-N243F,S024R-A272P,S024R-R269C,S101G-V104I,V104I-A232V,N076D-H249R,和S024R-N076D,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0437] 本发明还提供分离的枯草杆菌蛋白酶变体,其中该枯草杆菌蛋白酶变体是具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:G020R-N076D,S024R-R045T,A230E-H249R,N018R-R045T,N018R-Q245R,S101G-A232V,S024R-A232V,A232V-Q245R,S024R-S101G,N018R-V104I,N018R-S103A,S101G-H249R,A232V-H249R,S103A-A232V,N076D-Q245R,S101G-V104I,V104I-A232V,N076D-H249R,S024R-N076D,S024F-N116L,G020K-S024F,G020K-N062E,T033S-G118R,S024R-P086W,S024R-G118R,S024R-P086R,Y209A-W241R,S024R-W241R,S024R-K235F,G118R-Y209A,S078R-G118R,T033S-K235F,S024R-A174T,P086W-Y209A,I008T-S024R,P086W-G118R,T033S-W241R,S024R-N243F,S024R-Y209A,T033S-P086W,S024R-T033S,P086W-N243F,T033S-P201S,S024R-P239Q,S078R-P086W,K235F-N243F,G118R-A172V,T033S-L148F,T033S-S078R,T033S-N243F,S024C-T033S,G118R-A194T,T033S-Y209A,S024R-S141G,S024R-T274I,P086W-K235F,A015T-T033S,Y209A-K235F,S024R-R247H,S078R-K235F,S024R-V104A,T033S-A048T,G118R-K235F,T033S-T253A,T143A-Y209A,T033S-P239T,Y209A-N243F,S024R-A272P,和S024R-R269C,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0438] 本发明还提供分离的枯草杆菌蛋白酶变体,其中该枯草杆菌蛋白酶变体是具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:V004R-S009A-G020R-S242R,G020R-N043R-W241R,G020R-S242R-N269R,V004R-S009A-G020R-N043R,V004R-G020R-H249R,N018R-S024R-V244R,S009A-T022R-S212F-W241R,G020R-N043R-N269R,N018R-S024R-S242R,V004R-S009A-N043R-W241R,G020R-N043R-V244R,G020R-T022R-S242R,V004R-G020R-N043R,V004R-S009A-G020R-N043R-S242R,G020R-N043R-S242R,G020R-N043R-S242R-H249R,G020R-S212F-H249R,V004R-S009A-W241R,A001R-S009A-N043R,G020R-N043R-H249R,S009A-G020R-N043R-W241R,G020R-T022R-N043R,G020R-H249R-N269R,G020R-T022R-W241R,V004R-S009A-S024R-N043R-W241R,S009A-N043R-S078R,V004R-G020R-S024R-V244R,G020R-T022R-S078R-S242R,G020R-S024R-S242R-H249R,V004R-S009A-S078R-W241R,S009A-N043R-S078R-S242R,V004R-G020R-S024R,S009A-N043R-S212F,G020R-N043R-S212F,S024R-S078R-S212F,S009A-G020R-S024R-N043R,S009A-T022R-N043R-S078R,G020R-T022R-S212F-W241R,G020R-N043R-S212F-W241R,S009A-N043R-W241R,G020R-N043R-E271L,G020R-T022R-S078R-W241R,G020R-S024R-N043R-S242R,G020R-T022R-N043R-W241R,S009A-G020R-N043R-S212F,V004R-S009A-G020R-S024R-S242R,G020R-N043R-H249R-E271L,G020R-T022R-

S024R-S242R,S009A-T022R-S078R-S212F,G020R-N043R-S242R-E271L,S009A-T022R-S078R-S212F-W241R,V004R-G020R-S024R-H249R,G020R-T022R-E271L,G020R-T022R-N043R-S212F,V004R-G020R-S024R-N043R-S242R,V004R-G020R-S024R-N043R,V004R-S009A-T022R-S078R-S212F,G020R-T022R-S078R-S212F-W241R,和G020R-T022R-N269R,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0439] 本发明还提供分离的枯草杆菌蛋白酶变体,其中该枯草杆菌蛋白酶变体是具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:N018R-G020R-N043D-R045T-A230E,N018R-N043R-R045T-S242R-H249R,S024R-N043D-H249R,N018R-G020R-R045T,G020R-S024R-N076D-H249R,S024R-N043R-A230E-S242R,N018R-S024R-N043D-A230E,G020R-N076D,N018R-S024R-N043D-N076D-H249R,S024R-N043R-N076D-H249R,N018R-S024R-R045T-S242R,G020R-N043D-N076D-A230E-H249R,G020R-N043R-R045T-S242R,N018R-S024R-N076D-H249R,N018R-G020R-S024R-N043D-R045T-L233I-S242R,S024R-N043R-A230E,N018R-G020R-N043D,N043R-S242R-H249R,G020R-N043R-R045T-A230E,N043R-N076D-S242R-H249R,G020R-S024R-R045T-A230E-S242R,S024R-R045T-N076D-A230E-S242R-H249R,S024R-R045T,S024R-N043R-R045T-N076D-A230E-H249R,N018R-S024R-N043D-R045T-H249R,N018R-N043R-R045T-H249R,S024R-N043R-S242R,N018R-G020R-N043R-N076D-H249R,G020R-S024R-N043D-H249R,G020R-N043R-A230E-S242R,G020R-N043R-S242R,N018R-N043R-N076D-A230E,G020R-S024R-N043D-S242R,G020R-N043R-A230E,N018R-G020R-N043R-N076D-S242R-H249R,N043D-R045T-N076D-H249R,N018R-N043R-S242R-H249R,N018R-G020R-N043R-R045T-S242R,N018R-G020R-N043D-A230E-S242R,G020R-S024R-N043R-R045T-H249R,S024R-N043R-H249R,G020R-S024R-K27E-N043R-N076D-A230E,S024R-N043R-R045T-S242R,N018R-G020R-S024R-N043R-R045T-N076D-A230E,G020R-N043R-N076D-A230E-H249R,N018R-N043R-R045T-S242R,G020R-S242R-H249R,N018R-N043R-N076D-A230E-S242R-H249R,N018R-S024R-N076D,G020R-S024R-K27R-N043D-S242R-H249R,N018R-G020R-S024R-N043D-N076D-S242R,N018R-N043R-N076D-S242R-H249R,N018R-S024R-N043D-A230E-H249R,N018R-G020R-N043D-H249R,N018R-G020R-N043D-R045T-N076D-S242R,S024R-N043R-N076D-A230E-S242R,G020R-S024R-T38I-N043R-R045T-N076D-S242R-H249R,N018R-G020R-N043R,N018R-S024R-R045T-A230E-S242R,N018R-G020R-H249R,S024R-N043R-N076D,N018R-G020R-S024R-N043R-R045T-N076D-H249R,N018R-N043D-R045T-N076D-S242R-H249R,S024R-N043D-S242R-H249R,N018R-G020R-S024R-N043D-R045T-S242R,G020R-S024R-N043R-N076D,N018R-G020R-N043D-R045T-A230E-S242R,G020R-S024R-N043R-R045T-N076D-S242R-H249R,N018R-N043R-R045T-N076D-S242R,N018R-G020R-N043R-N076D-A230E-S242R,N018R-S024R-N043D-H249R,N018R-S024R-N043R-R045T-A230E-H249R,N018R-G020R-N043R-R045T-N076D-H249R,N018R-S024R-S242R,N018R-N043R-R045T-N076D-A230E-S242R,R045T-S242R-H249R,N018R-S024R-N043D-S242R,N018R-G020R-N043D-R045T-S240P,S024R-N043R-R045T-S242R-H249R,N018R-S024R-V30S-L31S-D32I-T33Q-G34V-I35F,N018R-G020R-N043R-N076D,G020R-N043D-R045T-N076D-S242R-H249R,

N018R-S024R-N043D-A230E-S242R,N018R-S024R-N043D-S242R-H249R,S024R-N043D-R045T-S242R-H249R,N043R-A230E-H249R,S024R-N043R-N076D-A230E-H249R,G020R-S024R-N043D-N076D-H249R,S024R-R045T-S242R-A273V,G020R-S024R-R045T-N076D-S242R-H249R,N018R-S024R-N043D-N076D-S242R,N018R-N043R-N076D-A230E-H249R,N018R-G020R-N043R-R045T-H249R,N018R-N043R-R045T-A230E-S242R,G020R-S024R-N043D-R045T-A230E-S242R,N018R-N043D-A230E-H249R,N018R-N043R-N076D-S242R,N018R-G020R-N076D,N018R-G020R-N043D-N076D-S242R-H249R,G020R-S024R-N043D-N076D-S242R-H249R,N043D-S242R-H249R,N018R-G020R-S024R-N043R-N076D,N018R-G020R-N043D-R045T-N076D-H249R,N018R-G020R-N043R-R045T-N076D-A230E-H249R,N018R-N076D-S242R,G020R-N043R-H249R,N018R-N076D-S242R-H249R,N018R-S024R-R045T-A230E-H249R,A230E-H249R,N018R-R045T-H249R,G020R-N043R-N076D,N043R-R045T-H249R,N018R-N043D-N076D-S242R-H249R,N043R-N076D-H249R,N018R-R045T,G020R-N076D-A230E-S242R,G020R-S024R-N043D-R045T,S024R-N043D-N076D-S242R-H249R,G020R-R045T-H249R,N043R-N076D-S153A-H249R,N043R-N076D-A230E-H249R,N018R-N043D-N076D-H249R,和G020R-N043R-N076D-V227I,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0440] 本发明还提供分离的枯草杆菌蛋白酶变体,其中该枯草杆菌蛋白酶变体是具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:S101G-S103A-V104I-A232V-Q236H-Q245R-N252K,S101G-S103A-V104I-A232V-Q245R-N248R,S101G-S103A-V104I-G159R-A232V-Q245R-N248D,S101G-S103A-V104I-G159D-A232V-Q245R-N248R,S101G-S103A-V104I-A232V-Q245R,S101G-S103A-V104I-G159D-A232V-Q245R和S101G-S103A-V104I-A232V-Q245R-N248D,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0441] 本发明还提供分离的枯草杆菌蛋白酶变体,其中该枯草杆菌蛋白酶变体是具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:S101G-S103A-V104I-P129E-S188D-A232V-N238R-Q245R-N248D,S024R-S101G-S103A-V104I-P129E-A158E-S188D-A232V-Q245R-N248D-H249R,T022A-S101G-S103A-V104I-P129E-A158E-S188D-A232V-Q245R-N248D-H249R,T022A-S024R-S101G-S103A-V104I-P129E-A158E-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-P129E-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-P129E-G159E-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-S128N-P129E-A158E-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-L148I-A158E-S188D-A232V-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-P129E-G159E-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-S128N-P129E-A232V-Q245R-N248D,S101G-S103A-V104I-P129E-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-P129E-A158E-A232V-Q245R-N248D-H249R,T022A-S024R-S101G-S103A-V104I-A158E-G159E-S188D-A232V-Q245R-N248D-H249R,T022A-S024R-S101G-S103A-V104I-P129E-A158E-G159E-

S188D-A232V-N238R-Q245R-N248D,S024R-S101G-S103A-V104I-P129E-L148I-A158E-A232V-Q245R-N248D,A016S-S024R-S101G-S103A-V104I-A158E-S188D-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-A158E-G159E-A232V-Q245R-N248D-H249R,T022A-S101G-S103A-V104I-P129E-A158E-G159E-A232V-N238R-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-P129E-A158E-G159E-A232V-Q245R-N248D-H249R,T022A-S024R-S101G-S103A-V104I-S128N-A158E-S188D-A232V-Q245R-N248D,S024R-S101G-S103A-V104I-P129E-S188D-A232V-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-P129E-A158E-A232V-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-P129E-A232V-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-P129E-S188D-A232V-Q245R-N248D,S024R-S101G-S103A-V104I-A158E-S188D-A232V-N238R-Q245R-N248D,T022A-S101G-S103A-V104I-S128N-P129E-S188D-A232V-N238R-Q245R-N248D,S024R-S101G-S103A-V104I-P129E-S188D-A232V-N238R-Q245R-N248D,S024R-S101G-S103A-V104I-A158E-G159E-S188D-A232V-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-S128N-S188D-A232V-Q245R-N248D,S024R-S101G-S103A-V104I-P129E-A158E-S188D-A232V-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-S128N-P129E-A158E-A232V-Q245R-N248D,S024R-S101G-S103A-V104I-G159E-S188D-A232V-Q245R-N248D,T022A-S101G-S103A-V104I-S128N-P129E-A232V-N238R-Q245R-N248D,S024R-S101G-S103A-V104I-P129E-G159E-A232V-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-P129E-A158E-S188D-A232V-N238R-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-A158E-G159E-S188D-A232V-Q245R-N248D,S024R-S101G-S103A-V104I-G159E-S188D-A232V-Q245R-N248D-H249R,T022A-S101G-S103A-V104I-P129E-A158E-A232V-N238R-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-P129E-A158E-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-L148I-A158E-A232V-Q245R-N248D,T022A-S101G-S103A-V104I-A158E-G159E-S188D-A232V-Q245R-N248D-H249R,T022A-S101G-S103A-V104I-A158E-S188D-A232V-Q245R-N248D,T022A-S101G-S103A-V104I-P129E-S188D-A232V-N238R-Q245R-N248D,S024R-S101G-S103A-V104I-P129E-A158E-G159E-S188D-A232V-Q245R-N248D-H249R,T022A-S024R-S101G-S103A-V104I-A158E-G159E-S188D-A232V-N238R-Q245R-N248D,S101G-S103A-V104I-P129E-A158E-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-S128N-A158E-A232V-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-S128N-P129E-S188D-A232V-Q245R-N248D,T022A-S101G-S103A-V104I-P129E-G159E-A232V-N238R-Q245R-N248D,S101G-S103A-V104I-P129E-G159E-A232V-Q245R-N248D-H249R,T022A-S101G-S103A-V104I-P129E-A158E-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-P129E-L148I-A158E-S188D-A232V-Q245R-N248D,T022A-S101G-S103A-V104I-P129E-G159E-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-G159E-S188D-A232V-N238R-Q245R-N248D,S024R-S101G-S103A-V104I-P129E-A158E-G159E-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-P129E-A158E-G159E-A232V-N238R-Q245R-N248D,S024R-S101G-S103A-V104I-S128N-G159E-S188D-A232V-Q245R-N248D,T022A-S101G-S103A-V104I-G159E-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-P129E-G159E-S188D-A232V-N238R-Q245R-N248D,S101G-

S103A-V104I-A158E-A232V-N238R-Q245R-N248D,T022A-S101G-S103A-V104I-P129E-G159E-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-P129E-L148I-S188D-A232V-Q245R-N248D,S024R-S101G-S103A-V104I-A158E-A232V-Q245R-N248D-H249R,T022A-S101G-S103A-V104I-A158E-G159E-A232V-N238R-Q245R-N248D,S024R-S101G-S103A-V104I-A158E-G159E-A232V-N238R-Q245R-N248D,T022A-S101G-S103A-V104I-P129E-A158E-G159E-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-P129E-A158E-S188D-A232V-N238R-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-P129E-A158E-G159E-A232V-Q245R-N248D,S101G-S103A-V104I-S188D-A232V-N238R-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-A158E-A232V-Q245R-N248D-H249R,T022A-S024R-S101G-S103A-V104I-L148I-A158E-A232V-Q245R-N248D,S101G-S103A-V104I-P129E-A158E-G159E-A232V-N238R-Q245R-N248D,T022A-S101G-S103A-V104I-G159E-S188D-A232V-N238R-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-P129E-A158E-G159E-S188D-A232V-Q245R-N248D-H249R,T022A-S101G-S103A-V104I-P129E-A232V-N238R-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-S188D-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-P129E-A158E-G159E-A232V-Q245R-N248D-H249R,T022A-S101G-S103A-V104I-A158E-G159E-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-P129E-S188D-A232V-Q245R-N248D,S024R-S101G-S103A-V104I-P129E-G159E-A232V-N238R-Q245R-N248D,S101G-S103A-V104I-S128N-P129E-A232V-Q245R-N248D,S101G-S103A-V104I-A158E-S188D-A232V-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-P129E-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-P129E-G159E-A232V-N238R-Q245R-N248D,S101G-S103A-V104I-A158E-G159E-S188D-A232V-N238R-Q245R-N248D,S024R-S101G-S103A-V104I-A232V-Q245R-N248D-H249R,T022A-S024R-S101G-S103A-V104I-P129E-L148I-A232V-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-A158E-A232V-N238R-Q245R-N248D,S101G-S103A-V104I-S128N-P129E-A232V-N238R-Q245R-N248D,T022A-S101G-S103A-V104I-S128N-G159E-A232V-Q245R-N248D,T022A-S101G-S103A-V104I-S128N-P129E-A158E-A232V-N238R-Q245R-N248D,S101G-S103A-V104I-S128N-P129E-S188D-A232V-Q245R-N248D-H249R,T022A-S024R-S101G-S103A-V104I-S128N-P129E-A158E-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-S128N-A158E-G159E-S188D-A232V-Q245R-N248D,T022A-S024K-S101G-S103A-V104I-S128N-A158E-G159E-A232V-Q245R-N248D,S101G-S103A-V104I-P129E-L148I-S188D-A232V-Q245R-N248D,S024R-S101G-S103A-V104I-L148I-A232V-Q245R-N248D,T022A-S101G-S103A-V104I-L148I-S188D-A232V-Q245R-N248D,S024R-S101G-S103A-V104I-S128N-P129E-S188D-A232V-Q245R-N248D,S101G-S103A-V104I-S128N-P129E-A158E-A232V-N238R-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-P129E-L148I-A158E-S188D-A232V-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-L148I-A158E-S188D-A232V-Q245R-N248D,S101G-S103A-V104I-L148I-G159E-A232V-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-A158E-S188D-A232V-Q245R-N248D,和S101G-S103A-V104I-S128N-P129E-A158E-A232V-Q245R-N248D-H249R,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系

进行编号。

[0442] 本发明还提供分离的枯草杆菌蛋白酶变体，其中该枯草杆菌蛋白酶变体是具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列：T022A-S024R-S101G-S103A-V104I-A158E-A232V-Q245R-N248D-H249R，T022A-S024R-S101G-S103A-V104I-P129E-A232V-Q245R-N248D-H249R，S024R-S101G-S103A-V104I-A158E-G159E-A232V-N238R-Q245R-N248D，S024R-S101G-S103A-V104I-A232V-Q245R-N248D-H249R，S101G-S103A-V104I-A158E-A232V-Q245R-N248D-H249R，S101G-S103A-V104I-S188D-A232V-Q245R-N248D-H249R，S024R-S101G-S103A-V104I-G159E-S188D-A232V-Q245R-N248D-H249R，T022A-S024R-S101G-S103A-V104I-A158E-A232V-N238R-Q245R-N248D，S024R-S101G-S103A-V104I-G159E-S188D-A232V-N238R-Q245R-N248D，T022A-S024R-S101G-S103A-V104I-P129E-A232V-Q245R-N248D，S024R-S101G-S103A-V104I-L148I-A232V-Q245R-N248D，S024R-S101G-S103A-V104I-P129E-A158E-A232V-Q245R-N248D-H249R，S024R-S101G-S103A-V104I-L148I-A158E-A232V-Q245R-N248D，T022A-S024R-S101G-S103A-V104I-P129E-A158E-A232V-Q245R-N248D-H249R，A016S-S024R-S101G-S103A-V104I-A158E-S188D-A232V-Q245R-N248D-H249R，S024R-S101G-S103A-V104I-P129E-G159E-A232V-N238R-Q245R-N248D，S024R-S101G-S103A-V104I-P129E-S188D-A232V-Q245R-N248D-H249R，T022A-S101G-S103A-V104I-P129E-A232V-N238R-Q245R-N248D，T022A-S024R-S101G-S103A-V104I-L148I-A158E-A232V-Q245R-N248D，S024R-S101G-S103A-V104I-P129E-S188D-A232V-N238R-Q245R-N248D，T022A-S024R-S101G-S103A-V104I-A158E-G159E-S188D-A232V-N238R-Q245R-N248D，T022A-S101G-S103A-V104I-A158E-G159E-A232V-N238R-Q245R-N248D，T022A-S024R-S101G-S103A-V104I-P129E-A158E-A232V-Q245R-N248D，S101G-S103A-V104I-A158E-S188D-A232V-Q245R-N248D-H249R，T022A-S101G-S103A-V104I-A158E-G159E-A232V-Q245R-N248D-H249R，和S024R-S101G-S103A-V104I-A158E-G159E-A232V-Q245R-N248D，其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0443] 本发明还提供分离的枯草杆菌蛋白酶变体，其中该枯草杆菌蛋白酶变体是具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列：V104L-S128N-A158E-R186H-H249R，S128N-A158E-S188D-H249R，N062E-S128N-A158E-G159E-E271F，N062E-A158E-S188D-H249R-E271F，N062E-A158E-R186H-H249R-E271F，S128N-A158E-S188D-Y209E-E271F，N062E-G159E-S188D-H249R，A016S-N062E-A158E-R186H-H249R，N062E-A158E-G159E-H249R，S101A-S128N-A158E-Y209E-H249R，S128N-A158E-R186H-E271F，N062E-A158E-S188D-H249R，N062E-A158E-R186H-E271F，N062E-A158E-R186H-H249R，N062E-S101A-R186H-H249R，N062E-S101A-A158E-R186H-E271F，N062E-V104L-A158E-S188D-H249R-E271F，N062E-G159E-R186H-H249R，N062E-G159E-H249R，S128N-A158E-R186H-H249R，S128N-A158E-S188D-E271F，N062E-A158E-H249R，N062E-R186H-S188D-H249R-E271F，S128N-A158E-Y209E-，N062E-S101A-A158E-H249R，V104L-S128N-A158E-R186H-E271F，N062E-S101A-A158E-R186H-H249R-E271F，A016S-N062E-A158E-H249R，N062E-S101A-G159E-H249R，S128N-A158E-R186H-S188D-E271F，S101A-

S128N-A158E-R186H-E271F,N062E-S101A-S188D-H249R,S101A-V104L-A158E-R186H-S188D-H249R,N062E-G159E-H249R-E271F,S128N-A158E-G159E-E271F,A016S-N062E-V104L-A158E-R186H-E271F,T022A-S128N-A158E-H249R,S128N-A158E-H249R,N062E-S101A-V104L-A158E-R186H-E271F,A016S-N062E-A158E-R186H-E271F,V104L-S128N-A158E-H249R,V104L-S128N-A158E-S188D-H249R,T022A-N062E-A158E,N062E-S101A-S188D-H249R-E271F,N062E-A158E-H249R-E271F,V104L-S128N-A158E-R186H-S188D-E271F,N062E-S101A-R186H-E271F,N062E-V104L-G159E-H249R,N062E-R186H-H249R,N062E-S101A-R186H-H249R-E271F,S101A-A158E-R186H-S188D-H249R,N062E-S101A-R186H,S101A-S128N-P129E-R186H-H249R,S101A-S103G-A158E-R186H-H249R,A016S-N062E-V104L-R186H-S188D-E271F,V104L-A158E-R186H-H249R,S101A-S128N-A158E-S188D-Y209E-E271F,N062E-S101A-R186H-S188D-E271F,A016S-N062E-A158E-H249R-E271F,N062E-S128N-A158E,N062E-S128N-G159E-H249R,N062E-S101A-A158E-S188D-H249R,S101A-S128N-A158E-H249R,N062E-A158E-R186H-S188D-H249R,A016S-V104L-A158E-R186H-E271F,N062E-L148I-G159E,N062E-S101A-A158E-R186H-H249R,N062E-S101A-R186H-S188D-H249R,V104L-A158E-R186H-S188D-H249R,N062E-S101A-V104L-R186H-S188D-E271F,T022A-S101A-A158E-R186H-H249R,S101A-S128N-A158E-Y209E,A158E-R186H-S188D-H249R-E271F,V104L-A158E-R186H-S188D-H249R-E271F,S101A-V104L-A158E-R186H-H249R,V104L-A158E-H249R,S101A-V104L-S128N-A158E-R186H-E271F,A016S-V104L-S188D-H249R,S101A-V104L-A158E-R186H-S188D-E271F,V104L-S128N-G159E-E271F,V104L-A158E-R186H-H249R-E271F,A158E-R186H-H249R,S101A-A158E-R186H-H249R,V104L-A158E-S188D-H249R-E271F,A016S-S128N-A158E-R186H,V104L-S128N-R186H-S188D-H249R,A016S-S101A-S128N-R186H,A016S-N062E-S128N-R186H-E271F,A016S-S128N-R186H-E271F,S128N-P129E-R186H,A158E-R186H-H249R-E271F,A016S-A158E-H249R,A016S-A158E-R186H-H249R,A016S-T022A-A158E-R186H-E271F,E089P-S101A-P129E-R186H,T022A-S128N-A158E-R186H,S101A-V104L-S128N-A158E-R186H,T022A-S128N-R186H-S188D-,N062E-V104L-A158E-R186H-S188D-H249R,T022A-A158E-R186H-H249R-E271F,T022A-V104L-A158E-H249R,S101A-L111V-P129E,A016S-A158E-H249R-E271F,A016S-L111V-S188D-,T022A-V104L-R186H-S188D-H249R,和V104L-L148I-S188D-H249R,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0444] 本发明还提供分离的枯草杆菌蛋白酶变体,其中该枯草杆菌蛋白酶变体是具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:A001R-S101G-S103A-V104I-A232V-Q245R,V004R-S101G-S103A-V104I-A232V-Q245R,N043R-S101G-S103A-V104I-A232V-Q245R-E271L,S078R-S101G-S103A-V104I-A232V-Q245R,V004R-N043R-S101G-S103A-V104I-A232V-Q245R,N018R-N043R-S101G-S103A-V104I-A232V-Q245R,G020R-S101G-S103A-V104I-A232V-Q245R,S101G-S103A-V104I-A232V-Q245R-E271L,G020R-N043R-S101G-S103A-V104I-A232V-Q245R,S024R-N043R-S101G-S103A-V104I-A232V-Q245R,G020R-G025R-N116A-Y167W,N018R-S101G-S103A-V104I-A232V-Q245R,T022R-S101G-S103A-V104I-A232V-Q245R,S078R-S103N-S106G-Y167W-

Q236N,N018R-N043D-S101G-S103A-V104I-A232V-Q245R-N269R,N043R-S101G-S103A-V104I-A232V-Q245R-N269R,S024R-S101A-H120F-A194F-H249R,G020R-N043D-S101G-S103A-V104I-A232V-Q245R-N269R,S101G-S103A-V104I-S212F-A232V-Q245R,G020R-S144R-N185I-L233C-Q236N,G023A-S078R-S216F-Q236N-H249R,S101G-S103A-V104I-A232V-Q245R-N269R,S101G-S103A-V104I-G115R-A232V-Q245R,P052N-S078R-S103N-L148I-T213A,N018R-N043D-S101G-S103A-V104I-A232V-Q245R-H249R,S024R-N043D-S101G-S103A-V104I-A232V-Q245R-H249R,S024R-N043D-S101G-S103A-V104I-A232V-Q245R-N269R,G025R-E089I-N116A-P239S-A270C,S024R-S101G-S103A-V104I-A232V-Q245R,L148I-T213A-N252R,S024R-G025R-N183D-Y192W-P239S,G046R-A194F-S212M,V104L-L217E-T224A-H249R-N252R,G023A-Y091F-V121F-Y192W-Q236N,S101G-S103A-V104I-A232V-V244R-Q245R,S099F-S144R-Y167W-N252R,S101G-S103A-V104I-A232V-Q245R-H249R,N043R-S101G-S103A-V104I-A232V-Q245R,T022W-S078R-Y167W-S212M-A270C,V121F-N252R-A270C,G020R-S103N-S216F-Q236N-N252R,N043R-S101G-S103A-V104I-A232V-Q245R-H249R,G023A-P052N-Y192W-I198L-N252R,G025R-G046R-V121F,S024R-S078R-V104L-N116A-N183D,G046R-Q059A-S103N-G211Q-S212M,G020R-P052N-N062Q-Y091F-Y192W,G023A-P052N-S144R-Y192W-S216F,S101G-S103A-V104I-A232V-S242R-Q245R,P052N-S103N-N116A-L148I-Y192W,E089I-N116A-N117F-T224A-H249R,S144R-G211Q-N238L-P239S-H249R,N043A-N062Q-A194F-G211Q,G020R-S024R-P052N-Q059A-S216F,S024R-Y167W-T224A-H249R,T057R-Y167W-H249R,G025R-S103N-R186K-A194F-T224A,S105T-S128N-S144R-L148I-S212M,G020R-Q059A-S144R-Y192W-T224A,S024R-N043A-N117F-A194F-G211Q,N117F-A194F-T213A-A270C,S078R-Y091F-V121F-L233C-N252R,T057R-S099F-S105T-I198L-T213A,G023A-Y091F-S101A-I198L-N252R,N062Q-S103N-V121F-S144R-H249R,N043R-S101G-S103A-V104I-A232V-S242R-Q245R,G023A-S024R-N117F-S212M-S216F,V104L-T213A-S216F,A194F-G211Q-Q236N,N062Q-S103N-N117F-A194F,S024R-N062Q-V104L-S106G-H249R,T057R-E089I-I198L,G046R-Q059A-S106G-L217E-H249R,N117F-T213A-A215F,S101A-H120F-Y192W-A215F-T224A,N043A-T057R-N117F-S144R-N183D,G046R-N183D-N238L,G025R-N043A-E089I-N117F,S078R-V104L-T213A-A215F-T224A,Y091F-S099F-S101A-S105T-Y167W,S106G-N117F-N238L,G046R-E089I-Y091F-S101A-N116A,G020R-N062Q-E089I-R186K-S212M,T057R-S099F-V121F-N185I-Y192W,G046R-E089I-Y192W-L233C-A270C,E089I-N117F-N185I-A215F-L233C,P052N-V104L-N183D-S216F-H249R,S078R-S099F-N116A-R186K-T224A,G025R-S105T-S128N-S144R-A270C,S105T-G211Q-S216F,S024R-G046R-Y091F-V121F,S106G-N185I-S216F-Q236N,N062Q-S101A-Q236N-N252R-A270C,G025R-N043A-Y091F-I198L-A270C,G020R-G023A-V104L-Y192W-L233C,S024R-N043A-S105T-S106G-I198L,G020R-E089I-L217E,S024R-Y091F-I198L-A215F-P239S,G046R-E089I-S099F-R186K-S212M,V104L-H120F-R186K-S216F-N252R,T022W-A194F-T213A-L233C-N238L,S099F-S105T-S106G-A194F-S212M,E089I-S105T-N116A-A215F-S216F,G025R-N116A-H120F-T224A-A270C,N043A-Q059A-S101A-S216F-T224A,T057R-N183D-Q236N,G025R-N062Q-S128N-S144R-N185I,S103N-H120F-Y167W-I198L-L233C,T022W-E089I-S216F,S024R-

S106G-N116A-S212M-T224A,G020R-P052N-S101A-I198L-L233C,E089I-Y091F-N185I-G211Q-A270C,L111I-A215F-P239S,S024R-N116A-R186K-L233C-Q236N,和G023A-S103N-S106G-S212M-A215F,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0445] 本发明还提供分离的枯草杆菌蛋白酶变体,其中该枯草杆菌蛋白酶变体是具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:G020R-T022W-S078R-S101A-S103A-V104I-N116S-T213A-A215F-A232V-Q245R,N018R-S078R-S101G-S103A-V104I-A232V-Q245R,S024R-R045T-S101G-S103A-V104I-A232V-Q245R-N269R,G020R-T022W-S078R-S101G-S103A-V104I-N116A-A232V-Q245R,G020R-T22W-S101G-S103A-V104I-A232V-Q245R,N018R-N043R-S101G-S103A-V104I-A232V-Q245R,N018R-T022W-S024R-N076D-S101A-N116A-A232V-Q245R,N018R-V104I-A232V-H249R,N018R-S024R-N076D-S101A-N116A-G211Q-H249R,N018R-N043D-S078R-S101G-S103A-V104I-L217E-A232V-Q245R,N018R-N043R-S101G-S103A-V104I-A232V-Q245R-N269R,N018R-R045T-N076D-S101G-S103A-V104I-A232V-Q245R-N269R,N076D-S078R-S101G-S103A-V104I-A232V-Q245R-N269R,G020R-N043D-S078R-S101G-S103A-V104I-A232V-Q245R,N018R-N043D-N076D-S101G-S103A-V104I-A232V-Q245R-N269R,S024R-R045T-N076D-S078R-S101G-S103A-V104I-A232V-Q245R-N269R,N018R-S103A-A232V-H249R,N018R-S101G-V104I-A232V-Q245R,G020R-S024R-S101G-S103A-V104I-L217E-A232V-Q245R-H249R,N018R-T22K-N043D-S101G-S103A-V104I-A232V-Q245R,N043R-R045T-S101G-S103A-V104I-A232V-Q245R-N269R,G020R-T22W-S101G-S103A-V104I-G211Q-A232V-Q245R,S024R-N076D-S078R-S101G-S103A-V104I-A232V-Q245R-N269R,G020R-T22W-S078R-S101A-S103A-V104I-N116A-N183D-A232V,N018R-S024R-N076D-N116A-A215F-H249R,N018R-N043R-R045T-S101G-S103A-V104I-A232V-Q245R,S024R-N043R-N076D-S101G-S103A-V104I-A232V-Q245R,G020R-T022W-S101G-S103A-V104I-A232V-Q245R,G020R-T022W-S101G-S103A-V104I-G211Q-A232V-Q245R,G020R-T022W-S078R-S101G-S103A-V104I-N116A-T213A-A215F-A232V-Q245R,N043D-N076D-S078R-S101G-S103A-V104I-A232V-Q245R-N269R,N018R-S024R-N076D-S101A-N116A-T213A-H249R,N018R-S024R-N076D-N116A-G211Q-H249R,N043R-R045T-N076D-S078R-S101G-S103A-V104I-A232V-Q245R,N018R-S101G-Q245R,G020R-T22W-S101A-S103A-V104I-G211Q-T213A-A232V-Q245R,G020R-S024R-N043D-N076D-S078R-S101G-S103A-V104I-A232V-Q245R,N018R-R045T-N076D-S078R-S101G-S103A-V104I-A232V-Q245R,G020R-S078R-S101G-S103A-V104I-G211Q-T213A-A215F-A232V-Q245R,R045T-S078R-S101G-S103A-V104I-A232V-Q245R-N269R,S024R-N043D-S101G-S103A-V104I-A232V-Q245R-N269R,N018R-S101G-S103A-H249R,N018R-T22W-S024R-N076D-S101A-N116A-A232V-Q245R,N018R-S101G-V104I-A232V-H249R,G020R-T22W-S101A-S103A-V104I-A215F-A232V-Q245R,N018R-S024R-N076D-G211Q-T213A-H249R,N018R-T022W-S024R-N076D-S101A-I198L-H249R,S024R-S101G-S103A-V104I-A232V-Q245R,G020R-N076D-S101G-S103A-V104I-A232V-Q245R-N269R,G020R-S101G-S103A-V104I-A232V-Q245R-N269R,N043D-S078R-S101G-S103A-V104I-A232V-Q245R,G020R-S101G-V104I-T213A-A215F-A232V-Q245R,G020R-S101G-S103A-V104I-N116A-A215F-

A232V-Q245R,S024R-S103A-V104I-H249R,N018R-N076D-S078R-S101G-S103A-V104I-A232V-Q245R,R045T-N076D-S078R-S101G-S103A-V104I-A232V-Q245R-N269R,S024R-S101G-V104I-Q245R,G020R-S101G-S103A-V104I-G211Q-T213A-A215F-A232V-Q245R,S024R-S103A-V104I-A232V-H249R,N018R-S024R-N076D-N116A-G211Q-A215F-H249R,N018R-Q245R,S024R-S103A-Q245R,S024R-S103A-V104I-Q245R,G020R-S078R-S101G-A232V-Q245R,N018R-S024R-N076D-V104I-H249R,N018R-S024R-V104I-H249R,S024R-S101G-S103A-V104I-A232V-Q245R,N018R-S024R-N076D-G211Q-A215F-H249R,R019H-G020R-T022W-S078R-S101G-S103A-V104I-G211Q-A232V-Q245R,N018R-S024R-N076D-S101A-I198L-G211Q-T213A-H249R,N018R-S024R-N043D-S101G-S103A-V104I-A232V-Q245R,G020R-T22W-S103A-V104I-A232V-Q245R,N018R-S103A-V104I-H249R,N018R-T022W-S024R-N076D-S101A-I198L-A215F-H249R,N018R-S024R-S101G-V104I-A232V,S078R-S101G-S103A-V104I-A232V-Q245R-N269R,S024R-N043R-N076D-S078R-S101G-S103A-V104I-A232V-Q245R,N018R-G020R-N043D-N076D-S101G-S103A-V104I-A232V-Q245R,N018R-T22W-S024R-N076D-N116A-T213A-H249R,N018R-S024R-S101G-V104I,G020R-S101A-S103A-V104I-A215F-A232V-Q245R,N018R-R045T-S078R-S101G-S103A-V104I-A232V-Q245R,N018R-S101G-S103A-Q245R,N043R-N076D-S078R-S101G-S103A-V104I-A232V-Q245R,G020R-T022W-S101A-S103A-V104I-G211Q-A215F-A232V-Q245R,G020R-T22W-S078R-S101G-S103A-V104I-N116A-T213A-A215F-A232V-Q245R,G020R-S078R-S101G-S103A-V104I-A215F-A232V-Q245R,G020R-T022W-S078R-S101G-S103A-V104I-N116A-N183D-A232V-Q245R,N076D-S101G-S103A-V104I-A232V-Q245R,N076D-S101G-S103A-V104I-A232V-Q245R-N269R,G020R-T22W-S101A-S103A-V104I-A232V-Q245R,G020R-S101G-S103A-A232V-Q245R,G020R-T022W-S078R-S101A-S103A-V104I-N116A-N183D-A232V-Q245R,N018R-G020R-S024R-R045T-N076D-S101G-S103A-V104I-A232V-Q245R-N269R,N043R-R045T-S078R-S101G-S103A-V104I-A232V-Q245R,N018R-S101G-V104I-H249R,G020R-T22W-S078R-S101G-S103A-V104I-N116A-N183D-A232V-Q245R,G020R-T022W-S101G-S103A-V104I-I198L-G211Q-T213A-A232V-Q245R,G020R-S078R-S101A-S103A-V104I-N116A-N183D-T213A-A232V-Q245R,S024R-N076D-V104I-A232V-Q245R,N018R-G020R-N076D-S101G-S103A-V104I-A232V-Q245R,N018R-S024R-N076D-S101G-V104I-A232V-H249R,N018R-N043D-S078R-S101G-S103A-V104I-A232V-Q245R,A001T-N018R-S024R-N076D-N116A-T213A-H249R,N076D-S078R-S101G-S103A-V104I-A232V-Q245R,G020R-S078R-S101G-S103A-V104I-N116A-A232V-Q245R,N043R-N076D-S101G-S103A-V104I-A232V-Q245R,N018R-R045T-S101G-S103A-V104I-A232V-Q245R,N018R-N076D-S101G-V104I-A232V-Q245R,G020R-S078R-S101G-S103A-V104I-N116A-N183D-A232V-Q245R,N018R-S024R-N076D-S101A-G211Q-T213A-A215F-H249R,R045T-S078R-S101G-S103A-V104I-A232V-Q245R,N043R-N076D-S101G-S103A-V104I-A232V-Q245R-N269R,G020R-T022W-S078R-S101G-S103A-V104I-N116A-N183D-T213A-A232V-Q245R,G020R-T022W-S101G-S103A-V104I-N116A-N183D-T213A-A232V-Q245R,G020R-S101G-I198L-A215F-A232V-Q245R,N018R-S024R-N076D-T213A-A215F-H249R,G020R-S078R-S101G-S103A-V104I-N116A-G211Q-A232V-Q245R,G020R-T022W-S078R-S101A-S103A-V104I-N116A-N183D-

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H249R,N018R-G020R-T022W-S024R-N076D-S101A-N116A-I198L-T213A-H249R,N018R-T022W-S024R-N076D-S101A-N116A-N183D-I198L-G211Q-T213A-H249R,N018R-G020R-S024R-N076D-I198L-T213A-H249R,N018R-G020R-T022W-S024R-N076D-N116A-N183D-I198L-G211Q-H249R,N018R-G020R-S024R-N076D-N183D-G211Q-A215F-H249R,S024R-N076D-V104I,N018R-N076D-S101G-A232V,N018R-S024R-N076D-S101A-N116A-N183D-I198L-G211Q-T213A-A215F-H249R,N018R-G020R-T022W-S024R-N076D-N116A-N183D-A215F-H249R,N018R-S024R-L031F-N076D-N116A-N183D-G211Q-T213A-A215F-H249R,N018R-S024R-N076D-S101A-N116A-N183D-I198L-T213A-H249R-N269S,N018R-G020R-S024R-N076D-S101A-N116A-I198L-A215F-H249R,N018R-N043R-N076D-S078R-S101G-S103A-V104I-A232V-Q245R-N269R,N018R-G020R-S024R-N076D-S101A-N114T-I198L-G211Q-A215F-H249R,S024R-N043R-S078R-S101G-S103A-V104I-L217E-A232V-Q245R,S024R-N076D-S103A-V104I-A232V,N018R-G020R-T022W-S024R-N076D-S101A-I198L-G211Q-A215F-H249R,S101G-V104I-A232V,N018R-T022W-S024R-N076D-N183D-I198L-T213A-A215F-H249R,N018R-T022W-S024R-N076D-N183D-I198L-G211Q-H249R,N018R-G020R-S024R-N076D-N183D-T213A-H249R,N018R-S024R-N076D-S101A-N183D-G211Q-A215F-H249R,N018R-G020R-T022W-S024R-N076D-N116A-G211Q-T213A-H249R,N018R-S078R-S101G-S103A-V104I-A232V-Q245R-N269R,N018R-T022W-S024R-N076D-S101A-N116A-N183D-G211Q-A215F-H249R-T260A,N076D-H249R,N018R-T022W-S024R-N076D-N183D-G211Q-A215F-H249R,N018R-G020R-S024R-N076D-N116A-G211Q-A215F-H249R,N018R-G020R-S024R-N076D-T213A-H249R,N018R-G020R-T022W-S024R-N076D-N116A-N183D-I198L-H249R,N018R-G020R-T022W-S024R-N076D-S101A-N183D-H249R,N076D-V104I-H249R,G020R-T022W-S101A-S103A-V104I-N116A-N183D-G211Q-T213A-A215F-A232V-Q245R,S024R-N043R-R045T-S078R-S101G-S103A-V104I-L217E-A232V-Q245R,N018R-G020R-T022W-S024R-N076D-N183D-I198L-A215F-H249R,N018R-N076D-S101G-S103A,G020R-S024R-S101G-S103A-V104I-A232V-Q245R-N269R,N018R-G020R-S024R-N076D-S101A-N116A-N183D-G211Q-H249R,S101G-S103A-A232V,S024R-N076D-S101G-A232V,N018R-T022W-S024R-N076D-S101A-N183D-I198L-G211Q-H249R,N018R-G020R-S024R-N076D-S101A-N183D-I198L-G211Q-A215F-H249R,N018R-G020R-S024R-N076D-N183D-I198L-H249R,N018R-T022W-S024R-N076D-S101A-N116A-N183D-I198L-G211Q-H249R,N018R-G020R-S024R-N076D-N116A-A156V-N183D-G211Q-A215F-H249R-N269S,R045T-N076D-S101G-S103A-V104I-A232V-Q245R-H249R,N018R-G020R-S024R-N076D-S101A-N183D-I198L-H249R,N018R-G020R-T022W-S024R-N076D-I198L-G211Q-A215F-H249R,N018R-G020R-T022W-S024R-N076D-S101A-N116A-I198L-G211Q-A215F-H249R,N018R-G020R-T022W-S024R-N076D-N116A-H249R,N018R-N076D-S101G,N018R-S024R-N076D-N116A-N183D-I198L-T213A-A215F-H249R,N018R-G020R-T022W-S024R-N076D-S101A-N116A-I198L-T213A-A215F-H249R,N018R-S024R-N076D-S101A-N116A-N183D-I198L-G211Q-H249R,N018R-N076D-A232V,N018R-G020R-S024R-N076D-S101A-A232V-Q245R,N018R-N043D-R045T-N076D-S101G-S103A-V104I-A232V-Q245R,N018R-T022W-S024R-N076D-N183D-T213A-A215F-H249R,N018R-S024R-N076D-S101A-N116A-G211Q-

T213A-N237D-H249R,N018R-G020R-S024R-N076D-S101A-N116A-N183D-G211Q-H249R-R275S,N018R-T022W-S024R-N076D-S101A-N116A-N183D-I198L-G211Q-T213A-A215F-H249R,S024R-N076D,N018R-S024R-N076D-N183D-G211Q-A215F-H249R,N018R-T022W-S024R-N076D-N116A-N183D-I198L-T213A-A215F-H249R,N076D-V104I-A232V-H249R,N018R-N076D-S103A-A232V,N018R-G020R-S024R-N076D-S101A-N116A-N183D-I198L-G211Q-T213A-H249R,N018R-G020R-S024R-N076D-S101A-N183D-T213A-H249R,N018R-G020R-S024R-N076D-S101A-D175E-N183D-G211Q-A215F-H249R,N018R-G020R-N043D-S078R-S101G-S103A-V104I-L217E-A232V-Q245R-A273E,G020R-S024R-N043D-R045T-N076D-S101G-S103A-V104I-A232V-Q245R,P005S-S101G-S103A-V104I-A232V-Q245R-H249R,S103A-V104I-A232V,N018R-G020R-S024R-V068A-N076D-S101A-N116A-T213A-A215F-H249R,N018R-T022W-S024R-N076D-S101A-I198L-A215F-H249R-R275S,N018R-S024R-N076D-N183D-I198L-G211Q-T213A-H249R,和N043D-R045T-S101G-S103A-V104I-A232V-Q245R,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0446] 本发明还提供分离的枯草杆菌蛋白酶变体,其中该枯草杆菌蛋白酶变体是具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:N018R-S024R-N043R-N076D-H249R-N269R,N018R-T022R-S024R-N043R-N076D-H249R,N018R-N043D-S101G-S103A-V104I-A232V-Q245R,G020R-N043D-S101G-S103A-V104I-A232V-Q245R,N043D-S101G-S103A-V104I-A232V-Q245R-N269R,N043D-S078R-S101G-S103A-V104I-A232V-Q245R,N043R-N076D-S101G-S103A-V104I-A232V-Q245R,T022R-N043R-S101G-S103A-V104I-A232V-Q245R,N043R-S078R-S101G-S103A-V104I-A232V-Q245R,G020R-N076D-S101G-S103A-V104I-A232V-Q245R,N043R-N076D-S101G-S103A-V104I-A232V-Q245R,T022R-N076D-S101G-S103A-V104I-A232V-Q245R,N076D-S078R-S101G-S103A-V104I-A232V-Q245R,N018R-S024R-N043R-N076D-H249R,N018R-S024R-N076D-S242R-H249R,N018R-S024R-N076D-H249R-N269R,N018R-T022R-S024R-N076D-H249R,N018R-S024R-N076D-S078R-H249R,N018R-S024R-N043D-N076D-H249R-N269R,N018R-T022R-S024R-N043D-N076D-H249R,N018R-S024R-N043D-N076D-S078R-H249R,G020R-S101G-S103G-V104I-A232V-Q245R,G020R-S101G-S103A-V104L-A232V-Q245R,G020R-S101G-S103A-V104V-A232V-Q245R,G020R-S101G-S103S-V104I-A232V-Q245R,G020R-S101G-S103S-V104L-A232V-Q245R,G020R-S101S-S103S-V104I-A232V-Q245R,G020R-S101S-S103S-V104L-A232V-Q245R,G020R-S101A-S103A-V104L-A232V-Q245R,G020R-S101S-S103S-V104V-A232V-Q245R,G020R-S101S-S103A-V104I-A232V-Q245R,G020R-S101S-S103A-V104V-A232V-Q245R,G020R-S101S-S103G-V104I-A232V-Q245R,G020R-S101S-S103G-V104V-A232V-Q245R,G020R-S101A-S103A-V104V-A232V-Q245R,G020R-S101A-S103S-V104I-A232V-Q245R,G020R-S101A-S103S-V104V-A232V-Q245R,N018R-S024R-N043R-N076D-S078R-H249R,S024R-N043D-S101G-S103A-V104I-A232V-Q245R,N043D-S101G-S103A-V104I-A232V-Q245R-H249R,S024R-N076D-S101G-S103A-V104I-A232V-Q245R,N076D-S101G-S103A-V104I-A232V-S242R-Q245R,N018R-G020R-S024R-N076D-L217E-H249R,N018R-S024R-N043R-N076D-L217E-H249R,N018R-S024R-N043D-

N076D-S242R-H249R,N018R-G020R-S024R-N043R-N076D-H249R,G020R-S101A-S103G-V104V-A232V-Q245R,N043D-S101G-S103A-V104I-A232V-Q245R,N018R-S024R-N076D-L217E-H249R-N269R,和N018R-S024R-N076D-L217E-S242R-H249R,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0447] 本发明还提供分离的枯草杆菌蛋白酶变体,其中该枯草杆菌蛋白酶变体是具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:G020R-S101A-S103A-V104I-G118R-A232V-Q245R,G020R-S024R-N116A-T213A,N043R-S101A-N116A-A215F-N269R,S024R-N043R-S101A-N116A,S024R-N043R-S101A-N116A-A215F-N269R,G020R-S101G-S103A-V104I-A215F-A232V-Q245R,N043R-S101A-N269R,S024R-N043R-N116A-T213A-N269R,G020R-S024R-N043R-R045T-S101A-T213A,S024R-N043R-N116A-A215F-N269R,G020R-S024R-T213A-A215F,G020R-N116A-N269R,S024R-N116A-T213A-N269R,N043R-S101A-N116A-N269R,S101G-S103A-V104I-N116A-T213A-A232V-Q245R-N269R,S024R-N043R-R045T-S101A-N116A-A215F-N269R,G020R-N043R-S101A-N269R,S101A-S103A-V104I-T213A-A232V-Q245R-N269R,S024R-A215F-N269R,N043R-S101A-N116A-T213A-A215F-N269R,N043R-S101A-T213A-N269R,G020R-S024R-N043R-R045T-N116A-T213A,S101G-S103A-V104I-A232V-Q245R-N269R,S024R-N043R-R045T-S101A-N116A-T213A-N269R,S024R-N043R-R045T-N269R,G020R-N043R-R045T-S101A-N269R,S024R-N043R-N116A-N269R,G020R-S024R-N043R-R045T,N043R-N116A-N269R,S024R-N043R-S101A-A215F-N269R,S024R-N043R-R045T-T213A-A215F-N269R,G020R-S024R-R045T-N269R,G020R-N043R-S101A-N116A-T213A-A215F,G020R-S101G-S103A-V104I-T213A-A215F-A232V-Q245R,G020R-S024R-R045T-N116A-N269R,G020R-S101A-N116A-N269R,S024R-N043R-A215F,G020R-S024R-T213A,S024R-N043R-S101A-A215F,G020R-S024R-N043R-R045T-N116A,G020R-S024R-N043R-R045T-S101A-N269R,G020R-S024R-S101A-A215F,G020R-S024R-N116A-T213A-A215F,G020R-S024R-N116A,G020R-S024R-S101A-N116A,N043R-T213A-A215F-N269R,S024R-S101A-N269R,S024R-N043R-N116A-A215F,G020R-T038A-N043R-S101A,G020R-S024R-N116A-A215F,S024R-N043R-S101A-T213A,P014L-G020R-S024R-N043R-R045T-S101A-A215F,G020R-S024R-A215F,G020R-N116A-A215F-N269R,G020R-R045T-N116A-N269R,G020R-S024R-N043R-R045T-A215F,和G020R-S024R-N043R-R045T-N116A-T213A-A215F,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0448] 本发明还提供分离的枯草杆菌蛋白酶变体,其中该枯草杆菌蛋白酶变体是具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:N043R-N076D-S101A-S103A-V104I-A158E-S188D-A232V-Q245R-N248D-H249R-E271F,S024R-N043R-N076D-S101A-S103A-V104I-A158E-S188D-L217E-A232V-Q245R-N248D-H249R,S101A-S103A-V104I-A158E-S188D-A232V-Q245R-N248D-H249R-E271F-E271F,S101A-S103A-V104I-A158E-S188D-L217E-A232V-Q245R-N248D-H249R-E271F,N076D-S101G-S103A-V104I-A114V-A158E-S188D-A232V-Q245R-N248D-H249R-E271F,S024R-N076D-

S101G-S103A-V104I-A158E-S188D-A232V-Q245R-N248D-H249R-E271F,S024R-N043R-S101A-S103A-V104I-A158E-S188D-L217E-A232V-Q245R-N248D-H249R,S024R-N043R-S101A-S103A-V104I-A158E-S188D-A232V-Q245R-N248D-H249R,S024R-S101A-S103A-V104I-A158E-S166D-S188D-L217E-A232V-Q245R-N248D-H249R,N076D-S101G-S103A-V104I-S128L-A158E-S188D-A232V-Q245R-N248D-H249R-E271F,和N043R-N076D-S101G-S103A-V104I-A158E-S166D-S188D-A232V-Q245R-N248D-H249R-E271F,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0449] 本发明还提供分离的枯草杆菌蛋白酶变体,其中该枯草杆菌蛋白酶变体是具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:T022A-S101G-S103A-V104I-G159D-L217E-A232V-Q245R-N248D-E271F,T022A-N043R-S101G-S103A-V104I-G159D-S188D-L217E-A232V-Q245R-N248D-E271F,T022A-S101G-S103A-V104I-G159D-S188D-A232V-Q245R-N248D-E271F,N043R-S101A-S103A-V104I-A158E-S188D-L217E-A232V-Q245R-N248D-H249R,N043R-N076D-S101A-S103A-V104I-A158E-S188D-L217E-A232V-Q245R-N248D-H249R-E271F,S024R-S101G-S103A-V104I-A158E-S188D-L217E-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-A158E-S188D-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-A158E-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-A158E-N183D-S188D-A232V-Q245R-N248D-H249R,T022A-N076D-S101G-S103A-V104I-G159D-S188D-A232V-Q245R-N248D-E271F,T022A-N043R-N076D-S101G-S103A-V104I-G159D-S188D-A232V-Q245R-N248D-E271F,T022A-N076D-S101G-S103A-V104I-G159D-A232V-Q245R-N248D-E271F,T022A-S101G-S103A-V104I-G159D-A232V-Q245R-N248D-E271F,N076D-S101A-S103A-V104I-A158E-S188D-A232V-Q245R-N248D-H249R-E271F,N043R-S101A-S103A-V104I-A158E-S166D-S188D-A232V-Q245R-N248D-H249R,S024R-N076D-S101A-S103A-V104I-A158E-S166D-S188D-A232V-Q245R-N248D-H249R-E271F,N076D-S101A-S103A-V104I-A158E-S188D-A232V-Q245R-N248D-H249R,S101A-S103A-V104I-A158E-S166D-S188D-A232V-Q245R-N248D-H249R-E271F,N043R-N076D-S101A-S103A-V104I-A158E-S166D-S188D-A232V-Q245R-N248D-H249R-E271F,S101G-S103A-V104I-A158E-S166D-S188D-A232V-Q245R-N248D-H249R-E271F,S101A-S103A-V104I-A158E-S188D-A232V-Q245R-N248D-H249R-E271F,S101A-S103A-V104I-A158E-S188D-L217E-A232V-Q245R-N248D-H249R,N076D-S101A-S103A-V104I-A158E-S166D-S188D-A232V-Q245R-N248D-H249R-E271F,S101G-S103A-V104I-A158E-N183D-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-S128L-A158E-S188D-A232V-Q245R-N248D-H249R,N076D-S101G-S103A-V104I-A158E-S166D-S188D-A232V-Q245R-N248D-H249R-E271F,N043R-N076D-S101A-S103A-V104I-A158E-S166D-S188D-A232V-Q245R-N248D-H249R,和N076D-S101A-S103A-V104I-A158E-S188D-L217E-A232V-Q245R-N248D-H249R-E271F,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0450] 本发明还提供分离的枯草杆菌蛋白酶变体,其中该枯草杆菌蛋白酶变体是具有蛋

白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:H017R-T022A-N076D-S101G-S103A-V104I-G159D-S188D-A232V-Q245R-N248D-E271F,T022A-N043R-S101G-S103A-V104I-G159D-A232V-Q245R-N248D-E271F,T022A-S101G-S103A-V104I-G159D-S188D-A232V-Q245R-N248D-H249R-E271F,H017R-T022A-N076D-S101G-S103A-V104I-G159D-A232V-Q245R-N248D-E271F,T022A-N076D-S101G-S103A-V104I-G159D-A232V-Q245R-N248D-H249R-E271F,T022A-S101G-G102A-S103A-V104I-G159D-S188D-A232V-Q245R-N248D-E271F,和T022A-N043R-N076D-S101G-S103A-V104I-G159D-A232V-Q245R-N248D-H249R-E271F,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0451] 本发明还提供分离的枯草杆菌蛋白酶变体,其中该枯草杆菌蛋白酶变体是具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:S101S-S103A-V104I-A158E-S188D-A232V-Q245R-N248D-H249R,S101S-S103G-V104V-A158E-S188D-A232V-Q245R-N248D-H249R,S101G-S103S-V104I-A158E-S188D-A232V-Q245R-N248D-H249R,S101A-S103A-V104I-A158E-S188D-A232V-Q245R-N248D-H249R,S101A-S103A-V104L-A158E-S188D-A232V-Q245R-N248D-H249R,S101G-S103G-V104I-A158E-S188D-A232V-Q245R-N248D-H249R,S101S-S103G-V104I-A158E-S188D-A232V-Q245R-N248D-H249R,S101S-S103S-V104I-A158E-S188D-A232V-Q245R-N248D-H249R,S101S-S103S-V104V-A158E-S188D-A232V-Q245R-N248D-H249R,S101A-S103S-V104I-A158E-S188D-A232V-Q245R-N248D-H249R,S101A-S103S-V104I-G159E-A232V-Q245R-N248D-H249R,S101S-S103A-V104I-G159E-A232V-Q245R-N248D-H249R,S101G-S103A-V104L-A158E-S188D-A232V-Q245R-N248D-H249R,S101A-S103A-V104L-G159E-A232V-Q245R-N248D-H249R,S101A-S103S-V104L-G159E-A232V-Q245R-N248D-H249R,S101G-S103S-V104L-G159E-A232V-Q245R-N248D-H249R,S101S-S103A-V104L-G159E-A232V-Q245R-N248D-H249R,S101A-S103G-V104V-G159E-A232V-Q245R-N248D-H249R,和S101S-S103A-V104V-G159E-A232V-Q245R-N248D-H249R,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0452] 本发明还提供分离的枯草杆菌蛋白酶变体,其中该枯草杆菌蛋白酶变体是具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:V026F-V051W-V104L-S106E,V026F-L031F-S078N-G102A-S160D,G020K-G100S-N116L-A158E-S166D-N243F,T033S-N043W-N218D-P239G-N243F,T022L-T038F-A048R-N062E-G100S-R186K,S101D-S103N-N116L-S144R-A215D,V104L-S105T-T213A-L217E-S256N,N043W-S101D-S212M-N243F,V026F-A048R-S105T-T213A-N218D-T224A,S024F-S101D-G118R-A215D-L250I-A272F,V121F-N185E-T224A-P239G,T022L-L031F-G102A-S128D-T224A-N243F,N062E-S078N-G102A-N116L-S144R-L250I,T022L-T038F-V121F-S160D-A272F,V026F-S078N-G159C-R186K-N243F,S024F-A048R-G118R-S166D-L217E,G023A-T038F-S078N-G100S-S212M-A215D,G100S-N116L-A158E-T213A,S078N-V104L-G118R-S128D,G102A-S103N-S105T-A194E,T022L-S078N-S128D-T213A,K027R-G100S-G118R-S160D-S188D-N243F,S024F-G102A-R186K-T213A-L217E-N243F,T033S-S105T-S188D-S216F,

G023A-G100S-A194E-S212M,A048R-S128D-N185E-P239G,G020K-S024F-T033S-P129E-A194E,G020K-K027R-P129E-S166D-P239G,T022L-G023A-K027R-S101D-V104L-S216F,T033S-G118R-P129E-A194E-P239G,T022L-S078N-N116L-P129E-S256N,K027R-S101D-S103N-S105T-A272F,A048R-S078N-N116L-N185E-L217E-P239G,G023A-S024F-K027R-N062E,S024F-S103N-V104L-G118R-S188D,V026F-V104L-S256N-A272F,S024F-N043W-V104L-V121F-P129E,N062E-S078N-N116L-T224A,G023A-S024F-V051W-A158E,K027R-T038F-G102A-N116L,N062E-S078N-S144R-S212M,L031F-N116L-S256N-A272F,T022L-T033S-V104L-N116L-S160D-R186K,S024F-G118R-P129E-R186K-T213A,N043W-S105T-T213A-A215D-S216F,L031F-S105T-R186K-S188D,V026F-A194E-T213A-S256N,和S103N-S160D-L250I-S256N,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0453] 本发明还提供分离的枯草杆菌蛋白酶变体,其中该枯草杆菌蛋白酶变体是具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:T022A-S024R-S101D-S103A-V104I-G118R-G159D-S188D-A232V-N248D-E271F,T022A-S024R-S103A-V104I-P129E-G159D-S188D-A232V-N248D-E271F,T022A-S024R-S103A-V104I-G118R-G159D-S188D-L217D-A232V-N248D,T022A-S024R-S101D-S103A-V104I-G118R-P129E-G159D-S188D-A232V-Q245R-N248D,T022A-S024R-S101D-S103A-V104I-G159D-S188D-A232V-Q245R-N248D,T022A-N043R-S103A-V104I-G118R-P129E-G159D-S188D-A232V-Q245R-N248D,T022A-N043R-S103A-V104I-G118R-S128I-P129E-G159D-S188D-A232V-N248D,T022A-N043R-S101D-S103A-V104I-G118R-P129E-G159D-S188D-A232V-N248D-E271F,T022A-S024R-N043R-S101D-S103A-V104I-G159D-S188D-A232V-Q245R-N248D,T022A-S103A-V104I-G159D-S188D-A232V-N248D,T022A-S024R-S103A-V104I-G118R-P129E-G159D-S188D-A232V-N248D-E271F,T022A-S024R-S103A-V104I-G159D-S188D-L217D-A232V-Q245R-N248D-E271F,T022A-N043R-N062E-S103A-V104I-G159D-S188D-A232V-Q245R-N248D-E271F,T022A-N043R-S103A-V104I-P129E-G159D-S188D-A232V-Q245R-N248D,T022A-S024R-S103A-V104I-G159D-S188D-L217D-A232V-N248D-E271F,T022A-S103A-V104I-G118R-G159D-S188D-L217D-A232V-Q245R-N248D,T022A-S024R-S101D-S103A-V104I-G118R-S128I-G159D-S188D-A232V-Q245R-N248D,T022A-S024R-N043R-S103A-V104I-G159D-S188D-L217D-A232V-N248D-E271F,T022A-N043R-S103A-V104I-G118R-G159D-S188D-L217D-A232V-N248D-E271F,T022A-N043R-S103A-V104I-G118R-G159D-S188D-A232V-N248D-E271F,T022A-S103A-V104I-S128I-P129E-G159D-S188D-A232V-N248D-E271F,T022A-S103A-V104I-G159D-S188D-L217D-A232V-Q245R-N248D-E271F,T022A-N043R-S103A-V104I-S128I-G159D-S188D-A232V-Q245R-N248D,T022A-S101D-S103A-V104I-G118R-G159D-S188D-L217D-A232V-Q245R-N248D-E271F,T022A-S103A-V104I-G118R-P129E-G159D-S188D-A232V-Q245R-N248D-E271F,T022A-S024R-N043R-S103A-V104I-G118R-G159D-S188D-L217D-A232V-N248D,T022A-N062E-S103A-V104I-G118R-G159D-S188D-A232V-Q245R-N248D,T022A-N043R-S101D-S103A-V104I-G118R-P129E-G159D-S188D-L217D-A232V,T022A-S024R-S103A-V104I-G159D-S188D-L217D-A232V-N248D,T022A-S024R-N043R-S103A-V104I-G118R-S128I-

P129E-G159D-S188D-L217D-A232V-N248D-E271F，和T022A-S103A-V104I-G118R-G159D-S188D-L217D-A232V-Q245R-N248D-E271F，其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0454] 本发明还提供分离的枯草杆菌蛋白酶变体，其中该枯草杆菌蛋白酶变体是具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列：G020K-S024F-N062E-S188D-P239G，S024F-N062E-N116L-P239G，G020K-G023A-N062E-S188D，G020K-G023A-S024F-N062E-G118R-S188D-T213A，G020K-N043W-N062E-N116L-S188D-T213A-P239G，G023A-N062E-N116L-G118R，G023A-S024F-N062E-N116L-G118R，S024F-N116L，S024F-N062E-S188D-T213A，G023A-N062E-N116L-G118R-S188D-P239G，G020K-S024F-N062E，G020K-N043W-N062E-N116L-P239G，S024F-N062E-N116L-T213A-P239G，G020K-S024F-N043W-N062E-N116L-T213A，G020K-G023A-S024F-N062E-N116L-S188D-T213A，S024F-N062E-S188D-P239G，G023A-N043W-N062E-N116L-G118R-T213A，N062E-S188D-P239G，G020K-S024F-N062E-P239G，S024F-N116L-G118R-S188D-P239G，G020K-G023A-N062E-N116L-G118R-T213A，G020K-G023A-S024F-N062E-S188D-T213A-P239G，S024F-N043W-G118R-S188D，G023A-S024F-N116L-G118R-S188D-T213A，G020K-G023A-N043W-N116L-S188D-T213A-P239G，G023A-S024F-N116L-S188D-P239G，G023A-N043W-N116L-G118R-S188D，G023A-S024F-G118R-S188D-P239G，G023A-S024F-N043W-N062E-N116L-G118R，G020K-N043W-S188D-T213A，S024F-N062E-G118R-P239G，G023A-N043W-S188D-T213A，G020K-S024F-N043W-N062E-N116L-G118R-S188D-P239G，G020K-N116L-S188D-P239G，G020K-N043W-N062E-G118R，G020K-N043W-N116L-S188D-T213A，G020K-S024F，G023A-N043W-N116L-P239G，G023A-S024F-N043W-N116L-G118R-S188D-P239G，G020K-G023A-N043W-T213A，和G023A-S024F-N062E-G118R-T213A-P239G，其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0455] 本发明还提供分离的枯草杆菌蛋白酶变体，其中该枯草杆菌蛋白酶变体是具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列：G020K-G023A-N043W-G118R-S128I-P129E-G159D-S188D，S024F-G118R-S128I-P129E-G159D，G020K-S024F-N062E-N116L-G118R-S188D，G020K-N062E-N116L-S188D，N062E-N116L-G118R-T213A，G020K-G023A-N062E-N116L-S188D，N062E-N116L-G118R-S188D，G020K-N062E-N116L-T213A，G020K-G023A-N062E-N116L，G020K-N062E-S188D-T213A，G020K-N062E，G020K-S024F-N062E-N116L-S188D，G020K-N043W-N062E-N116L-S188D，G020K-S024F-N062E-S188D-T213A，N062E-N116L-S188D-T213A，G020K-N062E-N116L，G020K-G023A-N062E-N116L-S188D-T213A，G023A-S024F-N062E-N116L-T213A，T022A-N043R-S103A-V104I-S128I-P129E-G159D-S188D-A232V-Q245R-N248D，T022A-N043R-S103A-V104I-G118R-S128I-P129E-G159D-S188D-A232V-N248D-E271F，S024F-N062E-N116L-S188D，T022A-S024R-S103A-V104I-G118R-S128I-P129E-G159D-S188D-A232V-N248D，G023A-N062E-N116L-S188D，N043W-N062E-N116L，G020K-G023A-N116L-S188D，N043W-N062E-N116L-S188D，S024F-N062E-N116L，N062E-N116L-S188D，和T022A-S024R-S103A-

V104I-S128I-G159D-S188D-A232V-N248D，其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0456] 本发明还提供分离的枯草杆菌蛋白酶变体，其中该枯草杆菌蛋白酶变体是具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列：S087R-S101G-S103A-V104I-Q109R-S212P-A232V-Q245R-E271V，S101G-S103A-V104I-Q109R-A232V-Q245R，S101G-S103A-V104I-Q109R-S212P-A232V-Q245R-E271V，S101G-S103A-V104I-Q109R-S212P-A232V-Q245R，N076D-S87R-S103A-V104I-S212P-E271V，N076D-S103A-V104I-Q109R，N076D-S103A-V104I-S212P-E271V，N076D-S103A-V104I-Q109R-Q245R，和N076D-S103A-V104I-S212P-Q245L-E271V，其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0457] 本发明还提供分离的枯草杆菌蛋白酶变体，其中该枯草杆菌蛋白酶变体是具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列：S024R-P086W-G118R，S024R-S078R-P086W-N243F，S024R-T033S-P086S-S087N-Y209A，T033S-G118R，S024R-S078R-P086W-G118R-A270T，S024R-T033S-P086W-G118R，S078R-P086W-N243F，T033S-S078R-P086W-G118R-Y209A，T033S-S078R-Y209A，P086W-G118R-N243F，S024R-P086W，S078R-P086W-K235F，S024R-G118R，S024R-P086R，S101G-S103A-V104I-A232V，S024R-T033S-S078R-P086W-G118R，S024R-G118R-Y209A，Y209A-W241R，T033S-P086W-N243F，T033S-A172V-Y209A，G118R-Y209A-N243F，S024R-P086S-S141G，S024R-G118R-Y209A-N243F，S024R-T033S-P086S-S085N-K235F，S024R-T033S-A133V，S024R-T033S-S078R-P086W，S024R-P086W-Y209A，S024R-W241R，T033S-G118R-N243F，S024R-K235F，S024R-S078R-P086W，S024R-G118R-Y209A-K235F，S024R-Y209A-W241R，T033S-G118R-W241R，P086W-G118R-Y209A，T033S-G118R-G159D-Y209A，T033S-S078R-P086W，S024R-P086W-N243F，G118R-Y209A，S024R-P086W-G118R-V203I，S078R-Y209A-K235F，S024R-T033S-W241R，S078R-G118R，T033S-G118R-Y209A-N243F，L021M-S024R-T033S，S024R-T033S-P086W，T033S-K235F，S078R-P086W-Y209A，S024R-T033S-Y209A-K235F，T033S-P086W-G118R，S024R-T033S-S078R-Y209A，T033S-P086W-G118R-Y209A-N243F，P086W-Y209A-N243F，P005S-S078R-G118R-W241R，S024R-A174T，T033S-Y209A-N243F，P086W-G118R-A133V，S024R-T033S-G118R，S024R-P086W-Y209A-K235F，P086W-Y209A，I008T-S024R，P086W-G118R，T033S-W241R，P005S-S024R-T033S-N243F，S024R-Y209A-S242P，S024R-T033S-S078R-G118R，S024R-T033S-A194T，S024R-N243F，S024R-Y209A，S024R-T033S-G118R-Y209A，T033S-P086W，S024R-T033S，S024R-T033S-S078R-N243F，P086W-N243F，T033S-G118D-A138V-Y209A，T033S-Y209A-K235F，S024R-P086R-G118R，T033S-P201S，S024R-P239Q，T033S-G118R-Y209A-，S078R-P086W，K235F-N243F，S024R-Y209A-K235F，G118R-A172V，H017Y-S024R-T033S-P086W，T033S-L148F，S024R-G118R-K235F，T033S-S078R，T033S-N243F，S024C-T033S，G118R-A194T，T033S-Y209A，G118R-Y209A-K235F，S024R-T033S-Y209A-N243F，S024R-T033S-K235F，S024R-T033S-G118R-K235F，S024R-S141G，S024R-T274I，S024R-T033S-Y209A，P086W-K235F，S024R-Y209A-

N243F,V004E-T033S-S078R,P086W-Y209A-K235F,A015T-T033S,T033S-P086W-S156L-Y209A,S024R-G118R-N243F-R269H,Y209A-K235F,S024R-R247H,S024R-T033S-A228T,S078R-K235F,S024R-T033S-A174V-K235F,S024R-K235F-N243F,S024R-T033S-K235F-W241R,S024R-T033S-A151V,S024R-V104A,T033S-A048T,Q012H-V104A-G118R,G118R-K235F,T033S-T253A,T143A-Y209A,S024R-T033S-N243F,T033S-P239T,Y209A-N243F,S024R-T033S-P129H-N184D-T253M,S024R-A085V-P086W-G118R-K235F,S024R-A272P,和S024R-R269C,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0458] 本发明还提供分离的枯草杆菌蛋白酶变体,其中该枯草杆菌蛋白酶变体是具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:G020R-S087D-S101G-S103A-V104I-A232V-Q245R,G020R-S101G-S103A-V104I-V150L-A232V-Q245R,N018R-G020R-S024R-N076D-S087D-H249R,N018R-G020R-S024R-N076D-V150L-H249R,N018R-S024R-N043R-N076D-S087D-H249R,N018R-S024R-N043R-N076D-V150L-H249R,N018R-S024R-N076D-S078R-S087D-H249R,N018R-S024R-N076D-S078R-V150L-H249R,N018R-S024R-N076D-S087D-H249R-N269R,N018R-S024R-N076D-S087D-S242R-H249R,N018R-S024R-N076D-S087D-V150L-H249R,N018R-S024R-N076D-V150L-H249R,N018R-S087D-S101G-S103A-V104I-A232V-Q245R,N018R-S101G-S103A-V104I-V150L-A232V-Q245R,N018R-T022R-S024R-N076D-S087D-H249R,N018R-T022R-S024R-N076D-V150L-H249R,N043R-S087D-S101G-S103A-V104I-A232V-Q245R-N269R,N043R-S101G-S103A-V104I-V150L-A232V-Q245R,S024R-S087D-S101G-S103A-V104I-A232V-Q245R,S024R-S101G-S103A-V104I-V150L-A232V-Q245R,S078R-S087D-S101G-S103A-V104I-A232V-Q245R,S078R-S101G-S103A-V104I-V150L-A232V-Q245R,S087D-S101G-S103A-V104I-A232V-Q245R-N269R,S101G-S103A-V104I-V150L-A232V-Q245R-H249R,S101G-S103A-V104I-V150L-A232V-Q245R-N269R,T022R-S087D-S101G-S103A-V104I-A232V-Q245R,N018R-S024R-N043D-N076D-V150L-H249R,N043R-S087D-S101G-S103A-V104I-A232V-Q245R,T022R-S101G-S103A-V104I-V150L-A232V-Q245R,N018R-S024R-N043D-N076D-S087D-H249R,N018R-S024R-N076D-S087D-H249R,N018R-S024R-N076D-V150L-S242R-H249R,N043R-S101G-S103A-V104I-V150L-A232V-Q245R-N269R,N076D-S101G-S103A-V104I-V150L-A232V-Q245R,S087D-S101G-S103A-V104I-A232V-S242R-Q245R,S101G-S103A-V104I-V150L-A232V-Q245R,N076D-S087D-S101G-S103A-V104I-A232V-Q245R,S087D-S101G-S103A-V104I-A232V-Q245R,和S101G-S103A-V104I-V150L-A232V-S242R-Q245R,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0459] 本发明还提供分离的枯草杆菌蛋白酶变体,其中该枯草杆菌蛋白酶变体是具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:S024R-S101G-S103A-V104I-P129Q-A158E-S188D-L217E-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-S130A-A158E-N183D-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-P129Q-A158E-N183D-S188D-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-S130A-A158E-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-

V104I-P129Q-A158E-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-S130A-A158E-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-P129Q-S130A-A158E-N183D-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-S128L-P129Q-A158E-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-P129Q-S130A-A158E-S188D-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-P129Q-A158E-S188D-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-P129Q-S130A-A158E-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-S128L-P129Q-S130A-A158E-S188D-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-S128L-P129Q-A158E-S188D-A232V-Q245R-N248D-H249R,和S024R-K027R-S101G-S103A-V104I-S128L-P129Q-S130A-A158E-S188D-A232V-Q245R-N248D-H249R,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0460] 本发明还提供分离的枯草杆菌蛋白酶变体,其中该枯草杆菌蛋白酶变体是具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:S101G-S103A-V104I-A232V-M222Q-Q245R,S101G-S103A-V104I-A158E-S188D-M222S-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-A158E-S188D-M222Q-A232V-Q245R-N248D-H249R,N076D-S101G-S103A-V104I-A232V-M222Q-Q245R,S101G-S103A-V104I-A232V-M222S-Q245R,N076D-S101G-S103A-V104I-A232V-M222S-Q245R,和N076D-S101G-S103A-V104I-A158E-S188D-M222S-A232V-Q245R-N248D-H249R,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0461] 本发明还提供分离的枯草杆菌蛋白酶变体,其中该枯草杆菌蛋白酶变体是具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:S024R-S101G-S103A-V104I-S128L-P129Q-A158E-S188D-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-S130A-A158E-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-A158E-S188D-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-S128L-P129Q-A158E-S188D-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-P129Q-S130A-A158E-S188D-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-S130A-A158E-N183D-S188D-L217E-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-S128L-P129Q-S130A-A158E-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-P129Q-A158E-S188D-L217E-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-S128L-S130A-A158E-S188D-L217E-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-S128L-P129Q-A158E-N183D-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-S128L-P129Q-S130A-A158E-N183D-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-S128L-P129Q-A158E-S188D-A232V-Q245R-N248D-H249R-E271G,S101G-S103A-V104I-P129Q-A158E-N183D-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-S130A-A158E-S188D-L217E-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-S128L-A158E-N183D-S188D-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-P129Q-A158E-S188D-L217E-A232V-Q245R-N248D-H249R,和S024R-S101G-S103A-V104I-

S128L-S130A-A158E-S188D-A232V-Q245R-N248D-H249R,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0462] 在一些实施例中,合适的冷水蛋白酶变体包括枯草杆菌蛋白酶的变体,尤其是衍生自SEQ ID NO:2的迟缓芽孢杆菌GG36的那些变体,其中所述变体在包括位置1、2、4、9、10、14、16、17、18、20、22、24、25、26、42、43、46、52、57、59、62、68、71、72、74、75、76、78、82、86、89、91、94、100、101、103、104、106、108、111、112、115、117、118、121、128、129、144、148、158、159、160、166、185、186、188、197、203、209、210、212、214、215、217、224、230、231、236、238、239、241、242、243、244、248、249、250、252、253、262、263、265、267、269、271和272的一组位置内包含3、4、5、6、7、8、9、10、11、12、13、14 15、16、17、18、19、20、21、22、23、24或甚至25个突变。

[0463] 在一些实施例中,合适的冷水蛋白酶变体包括枯草杆菌蛋白酶的变体,尤其是衍生自SEQ ID NO:2的迟缓芽孢杆菌GG36的那些变体,其中所述变体包含总共3、4、5、6、7、8、9、10、11、12、13、14、15、16、17、18、19、20、21、22、23、24或甚至25个选自以下的突变:A1R,Q2S,V4R,V4S,S9A,R10S,P14K,A16S,H17R,N18R,G20R,T22A,T22R,S24R,S24W,G25R,G25V,V26F,L42I,N43R,N43A,G46R,P52F,P52E,P52N,T57R,Q59A,N62E,N62Q,V68A,V68C,T71G,I72C,A74C.L75A,L75F,L75R,N76D,S78R,L82R,P86W,E89P,E89T,E89G,E89H,E89I,E89V,E89W,Y91N,K94N,G100S,S101A,S101N,S101G,S101D,S103G,S103N,V104L,V104I,S106V,S106G,A108I,L111V,E112V,G115K,G115R,N117F,G118I,V121F,S128D,S128F,S128L,S128N,P129E,S144R,L148I,A158E.G159E,S160D,S166D,N185E,N185I,R186H,S188E,S188D,D197F,V203E,Y209S,Y209N,Y209F,Y209T,Y209E,Y209H,Y209G,P210R,S212I,S212F,Y214F,A215N,A215D,A215E,L217E,L217N,T224A,A230E,A231I,Q236F,N238R,N238K,P239K,P239G,P239R,P239S,W241R,S242R,S242L,N243R,V244R,N248I,N248V,H249R,L250I,N252R,T253R,L262D,Y263F,S265F,L267V,L267N,N269I,N269R,E271F,E271I,E271H,E271P,E271T,E271V,E271L和A272F;以及任选地包含一个或多个以下的突变:S103A,G159D,Q236H,Q245R,N248D和N252K。

[0464] 在一些实施例中,冷水蛋白酶变体包含一个或多个突变,并且相对于迟缓芽孢杆菌枯草杆菌蛋白酶GG36野生型(SEQ ID NO:2)具有-5、-4、-3、-2、-1或0的总净电荷

[0465] 在一些实施例中,冷水蛋白酶变体是低离子强度冷水蛋白酶变体。此类低离子强度冷水蛋白酶变体包含一个或多个突变,并且相对于迟缓芽孢杆菌枯草杆菌蛋白酶GG36蛋白酶野生型(SEQ ID NO:2)具有-5、-4、-3、-2、-1或0的总净电荷。在一些实施例中,这些突变选自两个或多个以下的突变:A1R,Q2S,V4R,V4S,S9A,R10S,P14K,A16S,T22A,T22R,S24R,G25V,V26F,L42I,P52F,P52E,P52N,N62E,N62Q,V68A,V68C,T71G,I72C,A74C.L75A,L75F,S78R,E89P,E89T,E89G,E89H,E89W,Y91N,K94N,G100S,S101A,S101N,S101G,S101D,S103G,S103N,V104L,V104I,A108I,L111V,E112V,G115K,N117F,V121F,S128D,S128F,S128L,S128N,P129E,L148I,A158E.G159E,S160D,S166D,N185E,R186H,S188E,S188D,V203E,Y209S,Y209N,Y209F,Y209T,Y209E,Y209H,Y209G,P210R,S212I,S212F,Y214F,A215N,A215D,A215E,L217E,L217N,T224A,A230E,A231I,Q236F,N238R,N238K,P239K,P239G,P239R,N248V,H249R,L250I,L262D,Y263F,S265F,L267V,L267N.N269I,N269R,E271F,

E271I,E271H和A272F;和/或一个或多个以下的突变组:N062E-P129E,N062E-G159E,A016S-L148I,A158E-H249R,A016S-N062E,L111V-S188D,T022A-N062E,N062E-L148I,T022A-P129E,N062E-E271F,N062E-A158E,A016S-G159E,N062E-R186H,S128N-G159E,N062E-S188D,N062E-S128N,L148I-G159E,S103G-A158E,L111V-G159E,A158E-E271F,A016S-S188D,T022A-L111V,S128N-A158E,A016S-A158E,V104L-A158E,S128N-R186H,G159E-Y209E,N062E-S101A,L111V-Y209E,L148I-S188D,S101A-Y209E,T022A-S188D,A016S-T022A,S128N-P129E,A016S-Y209E,A016S-S128N,T022A-E089P,S128N-Y209E,E089P-A158E,N062E-S103G,R186H-E271F,A016S-P129E,E089P-G159E,L111V-H249R,S101A-P129E,L148I-Y209E,T022A-G159E,P129E-H249R,P129E-Y209E,V104L-P129E,S128N-S188D,L111V-A158E,T022A-A158E,N062E-Y209E,N062E-H249R,S101A-R186H,E089P-P129E,P129E-E271F,T22A-L111V-G159E,S101A-S103G-V104L-Y209E,S101A-S103G-V104L-G159E,S101A-S103G-V104L-S188D,S101G-S103A-V104I-G159D,T22A-S103G-G159E,T22A-S128N-E271F-Y209E,T22A-Y209E-E271F,T22A-S101A-Y209E,S101A-Y209E-E271F,T22A-L111V-S128N,T22A-S101A-G159E,S101A-S103G-V104L,T22A-S101A-S103G-V104L,S101A-S103G-V104L,S101G-S103A-V104I,S101A-S103G-V104L-S128N,S103A-V104I-G159D-A232V-Q236H-Q245R-N248D-N252K,S101G-V104I-G159D-A232V-Q236H-Q245R-N248D-N252K,S101G-S103A-G159D-A232V-Q236H-Q245R-N248D-N252K,S101G-S103A-V104L-A232V-Q236H-Q245R-N248D-N252K,S101G-S103A-V104L-G159D-Q236H-Q245R-N248D-N252K,S101G-S103A-V104L-G159D-A232V-Q245R-N248D-N252K,S101G-S103A-V104L-G159D-A232V-Q236H-N248D-N252K,S101G-S103A-V104L-G159D-A232V-Q236H-Q245R-N252K,S101G-S103A-V104L-G159D-A232V-Q236H-Q245R-N248D,N62E-S101G-S103A-V104I-G159D-A232V-Q245R-N248D-E271F,N62E-S101G-S103A-V104I-G159D-A232V-Q245R-N248D-H249R,T22A-S101G-S103A-V104I-G159D-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-G159D-A232V-Q245R-N248D-S24R,S101G-S103A-V104I-G159D-A232V-Q245R-N248D-T253R,S101G-S103A-V104I-A158E-A232V-Q245R-N248D-H249R,T22A-S101G-S103A-V104I-G159D-A232V-Q245R-N248D-E271F,S101G-S103A-V104I-G159E-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-G159D-A232V-Q245R-N248D-N238R,S101G-S103A-V104I-A158E-A232V-Q245R-N248D-E271F,S101G-S103A-V104I-G159D-A232V-Q245R-N248D,S101G-S103A-V104I-G159D-A232V-Q245R-N248D-E271F,S101G-S103A-V104I-G159D-A232V-Q245R-N248D-N76D和S101G-S103A-V104I-G159E-A232V-Q245R-N248D-E271F。

[0466] 在一些实施例中,上述低离子强度冷水蛋白酶变体构成洗涤剂组合物的一部分,将该洗涤剂组合物稀释于水中,通常是洗衣机内的水中,以形成衣物洗涤剂洗涤液体,其电导率为约0.1mS/cm至约3mS/cm、约0.3mS/cm至约2.5mS/cm或甚至约0.5mS/cm至约2mS/cm

[0467] 在一些实施例中,冷水蛋白酶变体是高离子强度冷水蛋白酶变体。此类高离子强度冷水蛋白酶变体包含两个或多个突变,并且相对于迟缓芽孢杆菌枯草杆菌蛋白酶GG36蛋白酶野生型(SEQ ID NO:2)具有+5、+4、+3、+2、+1或0的总净电荷。在一些实施例中,这些突变选自两个或多个以下的突变:V4R,H17R,N18R,G20R,T22R,S24R,S24W,G25R,N43R,N43A,G46R,P52F,P52N,T57R,Q59A,N62Q,T71G,L75R,N76D,S78R,L82R,P86W,E89P,E89W,E89T,E89I,E89H,E89V,V104L,S106V,S106G,G115R,G118I,V121F,S144R,N185I,D197F,Y209N,

Y209S,L217E,A231I,P239R,P239S,W241R,S242R,S242L,N243R,V244R,N248I,H249R,N252R,T253R,E271T,E271V,E271L,E271H,E271F,E271P,A1R,S9A,S212F和N269R;和/或一个或多个以下的突变组:T022R-S024R,S009A-E271L,N018R-W241R,N018R-G115R,N043R-H249R,G020R-H249R,V004R-H249R,G020R-S024R,N018R-H249R,S009A-G020R,G020R-W241R,S009A-S078R,G020R-G115R,N018R-S024R,S024R-S242R,T022R-G115R,N018R-N043R,G020R-N043R,N018R-S242R,S242R-N269R,N018R-V244R,S024R-N269R,G020R-E271L,S024R-E271L,V004R-S009A,G020R-N269R,A001R-S024R,V244R-E271L,S009A-N018R,W241R-E271L,V004R-S024R,S009A-H249R,S009A-T022R,S101G-S103A-V104I-G159D-A232V-Q245R-N248D-E271F,S101G-S103A-V104I-A158E-A232V-Q245R-N248D-E271F,S101G-S103A-V104I-A158E-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-G159D-A232V-Q245R-N248D-S24R,S101G-S103A-V104L-G159D-A232V-Q236H-Q245R-N252K,S101G-S103A-V104L-A232V-Q236H-Q245R-N248D-N252K

[0468] 在一些实施例中,上述高离子强度冷水蛋白酶变体构成洗涤剂组合物的一部分,将该洗涤剂组合物稀释于水中,通常是洗衣机内的水中,以形成衣物洗涤剂洗涤液体,其电导率为约3mS/cm至约30mS/cm、约3.5mS/cm至约20mS/cm或甚至约4mS/cm至约10mS/cm。

[0469] 冷水蛋白酶变体的电荷是相对于具有SEQ ID NO:2的氨基酸序列的迟缓芽孢杆菌枯草杆菌蛋白酶GG36蛋白酶野生型来表示的。赋予单个负电荷的氨基酸为D和E,赋予单个正电荷的那些氨基酸为R、H和K。任何相对于SEQ ID NO:2可改变电荷的氨基酸变化均可用于计算冷水蛋白酶变体的电荷。例如,从野生型中性位置引入负电荷突变将给冷水蛋白酶变体添加净电荷-1,而从野生型正电荷氨基酸残基(R、H或K)引入负电荷突变(D或E)将添加净电荷-2。将冷水蛋白酶变体的相对于具有SEQ ID NO:2的氨基酸序列的迟缓芽孢杆菌枯草杆菌蛋白酶GG36蛋白酶野生型而言不同的所有氨基酸残基的电荷变化进行加和,可得到冷水蛋白酶变体的电荷变化。不希望受理论的束缚,但认为用于低电导率衣物洗涤剂溶液的冷水蛋白酶的优选电荷范围为-5、-4、-3、-2、-1、0,尤其是-2、-1;用于高电导率衣物洗涤剂溶液的冷水蛋白酶的优选电荷范围为+5、+4、+3、+2、+1、0,尤其是+2、+1。通过正确选择电荷,冷水清洁性能水平可得到出乎意料的改善。“低电导率衣物洗涤剂溶液”定义为具有约0.1mS/cm至约3mS/cm、约0.3mS/cm至约2.5mS/cm或甚至约0.5mS/cm至约2mS/cm的电导率。“高电导率衣物洗涤剂溶液”定义为具有约3mS/cm至约30mS/cm、约3.5mS/cm至约20mS/cm或甚至约4mS/cm至约10mS/cm的电导率。意图到,上述例子是非限制性的。一旦将各突变进行组合以优化冷水性能时,还可以通过在另外的位置的突变来平衡酶电荷。

[0470] 在一些实施例中,本发明提供分离的、重组的、基本上纯的或非天然存在的具有蛋白水解活性的变体蛋白酶(如变体枯草杆菌蛋白酶),所述变体蛋白酶包含与SEQ ID NO:2所示氨基酸序列相差不超过50、不超过45、不超过40、不超过35、不超过30、不超过25、不超过20、不超过19、不超过18、不超过17、不超过16、不超过15、不超过14、不超过13、不超过12、不超过11、不超过10、不超过9或不超过8个氨基酸残基的氨基酸序列,其中氨基酸位置根据SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列中对应的氨基酸位置的编号方式来进行编号,这是通过该变体蛋白酶氨基酸序列与解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'氨基酸序列的比对来确定的,其中该变体枯草杆菌蛋白酶包含置换101G/103A/104I/159D/232V/236H/245R/248D/252K。

[0471] 在一些实施例中，本发明提供分离的、重组的、基本上纯的或非天然存在的具有蛋白水解活性的变体蛋白酶(如变体枯草杆菌蛋白酶)，所述变体蛋白酶包含与SEQ ID NO:2所示氨基酸序列相差不超过50、不超过45、不超过40、不超过35、不超过30、不超过25、不超过20、不超过19、不超过18、不超过17、不超过16、不超过15、不超过14、不超过13、不超过12、不超过11、不超过10、不超过9、不超过6、不超过5、不超过4、不超过3、不超过2个氨基酸残基的氨基酸序列，其中氨基酸位置根据SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列中对应的氨基酸位置的编号方式来进行编号，这是通过该变体蛋白酶氨基酸序列与解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'氨基酸序列的比对来确定的，其中该变体枯草杆菌蛋白酶包含置换87N。

[0472] 本发明的核酸可通过使用任何合适的合成、操纵和/或分离技术或这些技术的组合来产生。例如，本发明的多核苷酸可用标准的核酸合成技术，如本领域技术人员所熟知的固相合成技术来制备。在这类技术中，通常合成多达50个或更多个核苷酸碱基的片段，然后连接(如通过酶连接方法或化学连接方法，或者聚合酶介导的重组方法连接)以形成基本上任何所需的连续核酸序列。还可通过本领域已知的任何合适的方法，包括但不限于使用经典的亚磷酰胺方法(参见例如Beaucage et al.Tetrahedron Letters 22:1859-69[1981](Beaucage等人，《四面体通讯》，第22卷，第1859-1869页，1981年))；或Matthes等人(参见Matthes et al.,EMBO J.3:801-805[1984](Matthes等人，《欧洲分子生物学组织杂志》，第3卷，第801-805页，1984年))描述的方法(其为自动合成方法中通常采用的)进行化学合成，来促进(或者完成)本发明核酸的合成。本发明的核酸也可以通过使用自动DNA合成仪来制备。定制的核酸可从多个商业来源订购(如Midland Certified Reagent Company、Great American Gene Company、Operon Technologies Inc.和DNA2.0)。其他合成核酸的技术和相关原理是本领域已知的(参见例如Itakura et al.,Ann.Rev.Biochem.53:323[1984](Itakura等人，《生物化学年评》，第53卷，第323页，1984年)和Itakura et al.,Science 198:1056[1984](Itakura等人，《科学》，第198卷，第1056页，1984年))。

[0473] 如上文所指出的，可用于修饰核酸的重组DNA技术是本领域所熟知的。例如，诸如限制性内切核酸酶消化、连接、逆转录和cDNA产生以及聚合酶链反应(如PCR)的技术是已知的并容易地由本领域技术人员采用。本发明的核苷酸还可以通过使用一种或多种可与编码本发明变体蛋白酶多肽的多核苷酸杂交或使之PCR扩增的寡核苷酸探针来筛选cDNA文库(如使用本领域通常使用的诱变技术(包括本文所述的那些)产生的cDNA文库)而获得。筛选和分离cDNA克隆的程序和PCR扩增程序是本领域技术人员所熟知的，并在本领域技术人员知道的标准参考文献中描述。本发明的一些核酸可通过利用例如已知的诱变程序(如定点诱变、点饱和诱变以及体外重组)改变天然存在的多核苷酸骨架(如编码酶或亲本蛋白酶的多核苷酸骨架)来获得。

[0474] 本发明的经修饰的变体蛋白酶的制备方法

[0475] 多种适用于产生编码本发明变体蛋白酶的本发明经修饰的多核苷酸的方法是本领域已知的，包括但不限于例如点饱和诱变、扫描诱变、插入诱变、缺失诱变、随机诱变、定点诱变和定向进化以及各种其他重组方法。制备经修饰的多核苷酸和蛋白质(如变体蛋白酶)的方法包括DNA改组方法，基于基因的非同源重组的方法，例如ITCHY(参见Ostermeier et al.,7:2139-44[1999](Ostermeier等人，《生物有机和药物化学》，第7卷，第2139-2144

页,1999年))、SCRACHY(参见Lutz et al.98:11248-53[2001](Lutz等人,《美国国家科学院院刊》,第98卷,第11248-11253页,2001年))、SHIPREC(参见Sieber et al.,19:456-60[2001](Sieber等人,《自然生物技术》,第19卷,第456-460页,2001年))和NRR(参见Bittker et al.,20:1024-9[2001](Bittker等人,《自然生物技术》,第20卷:第1024-1029页,2001年);Bittker et al.,101:7011-6[2004](Bittker等人,《美国国家科学院院刊》,第101卷,第7011-7016页,2004年)),以及依赖于使用寡核苷酸来插入随机和定向突变、缺失和/或插入的方法(参见Ness et al.,20:1251-5[2002](Ness等人,《自然生物技术》,第20卷,第1251-1255页,2002年);Coco et al.,20:1246-50[2002](Coco等人,《自然生物技术》,第20卷,第1246-1250页,2002年);Zha et al.,4:34-9[2003](Zha等人,《化学生物化学》,第4卷,第34-39页,2003年);Glaser et al.,149:3903-13[1992](Glaser等人,《免疫学杂志》,第149卷,第3903-3913页,1992年))。

[0476] 用于产生本发明的变体蛋白酶的载体、细胞和方法

[0477] 本发明提供分离的或重组的包含至少一种本文所述的本发明多核苷酸(如编码本文所述的本发明变体蛋白酶的多核苷酸)的载体;分离的或重组的包含至少一种本发明的核酸或多核苷酸的表达载体或表达盒;分离的、基本上纯的或重组的包含至少一种本发明的核酸或多核苷酸的DNA构建体;分离的或重组的包含至少一种本发明的多核苷酸的细胞;包含细胞的细胞培养物,该细胞包含至少一种本发明的多核苷酸;包含至少一种本发明的核酸或多核苷酸的细胞培养物;和包含一种或多种此类载体、核酸、表达载体、表达盒、DNA构建体、细胞、细胞培养物或它们的任何组合或混合物的组合物。

[0478] 在一些实施例中,本发明提供包含至少一种本发明的载体(如表达载体或DNA构建体)的重组细胞,所述载体包含至少一种本发明的核酸或多核苷酸。一些这类重组细胞转化有或转染有所述至少一种载体。这类细胞通常称为宿主细胞。一些此类细胞包括细菌细胞,包括但不限于芽孢杆菌细胞,例如枯草芽孢杆菌细胞。本发明还提供包含至少一种本发明的变体蛋白酶的重组细胞(如重组宿主细胞)。

[0479] 在一些实施例中,本发明提供包含本发明的核酸或多核苷酸的载体。在一些实施例中,载体是表达载体或表达盒,其中编码本发明变体蛋白酶的本发明多核苷酸序列有效连接至一个或多个为进行有效基因表达所需的核酸区段(例如与编码本发明变体蛋白酶的本发明多核苷酸有效连接的启动子)。载体可包含转录终止子和/或选择基因,如抗生素抗性基因,该抗性基因使得能通过在含有抗微生物剂的培养基中生长而对质粒感染的宿主细胞进行连续的培养维持。

[0480] 表达载体可衍生自质粒或病毒DNA,或在另选的实施例中,含有这二者的元件。示例性载体包括但不限于pXX、pC194、pJH101、pE194、pHP13(参见Harwood and Cutting[eds.],Chapter 3,Molecular Biological Methods for Bacillus,John Wiley&Sons[1990](Harwood和Cutting编辑,《芽孢杆菌的分子生物学方法》,第3章,约翰·威立父子出版公司,1990年);适于枯草芽孢杆菌的复制型质粒包括第92页列出的那些;还可参见Perego,Integrational Vectors for Genetic Manipulations in Bacillus subtilis,in Sonenshein et al.,[eds.]Bacillus subtilis and Other Gram-Positive Bacteria:Biochemistry,Physiology and Molecular Genetics,American Society for Microbiology,Washington,D.C.[1993],pp.615-624(Perego,“用于在枯草芽孢杆菌中进

行遗传操纵的整合载体”,载于Sonenshein等人编辑,《枯草芽孢杆菌和其他革兰氏阳性细菌:生物化学、生理学和分子遗传学》,美国微生物学学会,华盛顿哥伦比亚特区,1993年,第615-624页))。

[0481] 为了在细胞中表达和产生目的蛋白质(如变体蛋白酶),将至少一个包含至少一个拷贝(优选包含多个拷贝)的编码经修饰的蛋白酶的多核苷酸的表达载体在适于表达该蛋白酶的条件下转化进细胞中。在本发明的一些实施例中,将编码变体蛋白酶的多核苷酸序列(以及载体中包含的其他序列)整合进宿主细胞的基因组中,而在其他实施例中,将包含编码变体蛋白酶的多核苷酸序列的质粒载体在该细胞内保持为自主的染色体外元件。本发明提供染色体外核酸元件以及整合进宿主细胞基因组中的输入核苷酸序列二者。本文所述的载体可用于产生本发明的变体蛋白酶。在一些实施例中,编码变体蛋白酶的多核苷酸构建体存在于整合型载体上,该整合型载体使得编码变体蛋白酶的多核苷酸能整合以及任选扩增进细菌染色体中。整合位点的例子是本领域技术人员熟知的。在一些实施例中,编码本发明变体蛋白酶的多核苷酸的转录通过启动子来实现,该启动子对所选择的前体蛋白酶而言是野生型启动子。在一些其他实施例中,启动子对于前体蛋白酶而言是异源的,但在宿主细胞中有功能。具体而言,适用于细菌宿主细胞中的启动子的例子包括但不限于例如amyE、amyQ、amyL、pstS、sacB、pSPAC、pAprE、pVeg、pHpaII启动子、嗜热脂肪芽孢杆菌产麦芽糖淀粉酶基因的启动子、解淀粉芽孢杆菌(BAN)淀粉酶基因的启动子、枯草芽孢杆菌碱性蛋白酶基因的启动子、克劳氏芽孢杆菌碱性蛋白酶基因的启动子、短小芽孢杆菌(B.pumilis)木聚糖苷酶基因的启动子、苏云金芽孢杆菌cryIIIA启动子和地衣芽孢杆菌α-淀粉酶基因的启动子。另外的启动子包括但不限于A4启动子以及噬菌体λP_R或P_L启动子,和大肠杆菌(E.coli)lac、trp或tac启动子。

[0482] 本发明的变体蛋白酶可在任何合适的革兰氏阳性微生物(包括细菌和真菌)的宿主细胞中产生。例如,在一些实施例中,变体蛋白酶在真菌和/或细菌来源的宿主细胞中产生。在一些实施例中,宿主细胞是芽孢杆菌(Bacillus sp.)、链霉菌(Streptomyces sp.)、埃希杆菌(Escherichia sp.)或曲霉菌(Aspergillus sp.)。在一些实施例中,变体蛋白酶通过芽孢杆菌宿主细胞产生。可用于产生本发明变体蛋白酶的芽孢杆菌宿主细胞的例子包括但不限于地衣芽孢杆菌、迟缓芽孢杆菌、枯草芽孢杆菌、解淀粉芽孢杆菌、迟缓芽孢杆菌、短芽孢杆菌、嗜热脂肪芽孢杆菌、嗜碱芽孢杆菌、凝结芽孢杆菌、环状芽孢杆菌、短小芽孢杆菌、苏云金芽孢杆菌、克劳氏芽孢杆菌和巨大芽孢杆菌以及芽孢杆菌属内的其他生物体。在一些实施例中,枯草芽孢杆菌宿主细胞用于产生变体蛋白酶。美国专利5,264,366和4,760,025(RE 34,606)描述了各种可用于产生本发明变体蛋白酶的芽孢杆菌宿主菌株,但可以使用其他合适的菌株。

[0483] 几种可用于生产本发明变体蛋白酶的工业细菌菌株包括非重组(即野生型)的芽孢杆菌菌株,以及天然存在的菌株和/或重组菌株的变体。在一些实施例中,宿主菌株是重组菌株,其中编码目的多肽的多核苷酸已引入该宿主中。在一些实施例中,宿主菌株是枯草芽孢杆菌宿主菌株,尤其是重组枯草芽孢杆菌宿主菌株。许多枯草芽孢杆菌菌株是已知的,包括但不限于例如1A6(ATCC 39085)、168(1A01)、SB19、W23、Ts85、B637、PB1753至PB1758、PB3360、JH642、1A243(ATCC 39,087)、ATCC 21332、ATCC 6051、MI113、DE100(ATCC 39,094)、GX4931、PBT 110和PEP 211菌株(参见例如Hoch et al.,Genetics 73:215-228

[1973](Hoch等人,《遗传学》,第73卷,第215-228页,1973年);还可参见美国专利No.4,450,235和No.4,302,544以及EP 0134048,这些专利每一者全文以引用方式并入本文)。使用枯草芽孢杆菌作为表达宿主细胞是本领域熟知的(参见例如Palva et al.,Gene 19:81-87[1982](Palva等人,《基因》,第19卷,第81-87页,1982年);Fahnestock and Fischer,J.Bacteriol.,165:796-804[1986](Fahnestock和Fischer,《细菌学杂志》,第165卷,第796-804页,1986年)以及Wang et al.,Gene 69:39-47[1988](Wang等人,《基因》,第69卷,第39-47页,1988年))。

[0484] 在一些实施例中,芽孢杆菌宿主细胞是在以下基因中的至少一者中包括突变或缺失的芽孢杆菌:degU、degS、degR和degQ。优选地,突变在degU基因中,并且更优选地突变是degU(Hy)32(参见例如Msadek et al.,J.Bacteriol.172:824-834[1990](Msadek等人,《细菌学杂志》,第172卷,第824-834页,1990年)和Olmos et al.,Mol.Gen.Genet.253:562-567[1997](Olmos等人,《分子遗传学与普通遗传学》,第253卷,第562-567页,1997年))。一种合适的宿主菌株是携带degU32(Hy)突变的枯草芽孢杆菌。在一些实施例中,芽孢杆菌宿主包含在以下基因中的突变或缺失:scoC4(参见例如Caldwell et al.,J.Bacteriol.183:7329-7340[2001](Caldwell等人,《细菌学杂志》,第183卷,第7329-7340页,2001年))、spoIIE(参见例如Arigoni et al.,Mol.Microbiol.31:1407-1415[1999](Arigoni等人,《分子微生物学》,第31卷,第1407-1415页,1999年))和/或oppA或opp操纵子的其他基因(参见例如Perego et al.,Mol.Microbiol.5:173-185[1991](Perego等人,《分子微生物学》,第5卷,第173-185页,1991年))。实际上,设想到opp操纵子中的任何导致与oppA基因中的突变相同的表型的突变均将可用于本发明的改变的芽孢杆菌菌株的一些实施例。在一些实施例中,这些突变单独地出现,而在其他实施例中,存在突变的组合。在一些实施例中,可用于产生本发明的变体蛋白酶的改变的芽孢杆菌宿主细胞菌株是已在上述基因中的一者或多者中包含突变的芽孢杆菌宿主菌株。另外,可使用包含内源蛋白酶基因的突变和/或缺失的芽孢杆菌宿主细胞。在一些实施例中,芽孢杆菌宿主细胞包含aprE和nprE基因的缺失。在其他实施例中,芽孢杆菌宿主细胞包含5个蛋白酶基因的缺失,而在其他实施例中,芽孢杆菌宿主细胞包含9个蛋白酶基因的缺失(参见例如美国专利申请公开No.2005/0202535,该专利以引用方式并入本文)。

[0485] 使用任何合适的本领域已知的方法用至少一条编码至少一种本发明变体蛋白酶的核酸转化宿主细胞。无论是将核酸整合进载体中还是在不存在质粒DNA的情况下使用核酸,通常将其引入微生物中,在一些实施例中,优选引入大肠杆菌细胞或感受态芽孢杆菌细胞中。利用质粒DNA构建体或载体并将这类质粒DNA构建体或载体转化进芽孢杆菌细胞或大肠杆菌细胞中来将核酸(如DNA)引入这类细胞中的方法是众所周知的。在一些实施例中,随后从大肠杆菌细胞分离所述质粒并且转化进芽孢杆菌细胞中。然而,使用诸如大肠杆菌的中间微生物不是必需的,在一些实施例中,将DNA构建体或载体直接引入芽孢杆菌宿主中。

[0486] 本领域的技术人员十分了解适于将本发明的核酸或多核苷酸序列引入芽孢杆菌细胞中的方法(参见例如Ferrari et al.,"Genetics,"in Harwood et al.[eds.],Bacillus,Plenum Publishing Corp.[1989],pp.57-72(Ferrari等人,"遗传学",载于Harwood等人编辑,《芽孢杆菌》,普莱南出版公司,1989年,第57-72页);Saunders et al.,J.Bacteriol.157:718-726[1984](Saunders等人,《细菌学杂志》,第157卷,第718-726页,

1984年);Hoch et al.,J.Bacteriol.93:1925-1937[1967](Hoch等人,《细菌学杂志》,第93卷,第1925-1937页,1967年);Mann et al.,Current Microbiol.13:131-135[1986](Mann等人,《现代微生物学》,第13卷,第131-135页,1986年);Holubova,Folia Microbiol.30:97[1985](Holubova,Folia Microbiol.,第30卷,第97页,1985年);Chang et al.,Mol.Gen.Genet.168:11-115[1979](Chang等人,《分子遗传学和普通遗传学》,第168卷,第11-115页,1979年);Vorobjeva et al.,FEMS Microbiol.Lett.7:261-263[1980](Vorobjeva等人,《欧洲微生物学会联合会微生物学快报》,第7卷,第261-263页,1980年);Smith et al.,Appl.Env.Microbiol.51:634[1986](Smith等人,《应用和环境微生物学》,第51卷,第634页,1986年);Fisher et al.,Arch.Microbiol.139:213-217[1981](Fisher等人,《微生物学档案》,第139卷,第213-217页,1981年);以及McDonald,J.Gen.Microbiol.130:203[1984](McDonald,《普通微生物学杂志》,第130卷,第203页,1984年))。实际上,诸如转化(包括原生质体转化和中板集合(congression))、转导和原生质体融合之类的方法是众所周知的并且适用于本发明。使用转化方法将包含编码本发明变体蛋白酶的核酸的DNA构建体或载体引入宿主细胞中。本领域已知的转化芽孢杆菌细胞的方法包括诸如质粒标志补救转化的方法,质粒标志补救转化涉及携带部分同源的内生质粒的感受态细胞摄入供体质粒(参见Contente et al.,Plasmid 2:555-571[1979](Contente等人,《质粒》,第2卷,第555-571页,1979年);Haima et al.,Mol.Gen.Genet.223:185-191[1990](Haima等人,《分子遗传学和普通遗传学》,第223卷,第185-191页,1990年);Weinrauch et al.,J.Bacteriol.154:1077-1087[1983](Weinrauch等人,《细菌学杂志》,第154卷,第1077-1087页,1983年);以及Weinrauch et al.,J.Bacteriol.169:1205-1211[1987](Weinrauch等人,《细菌学杂志》,第169卷,第1205-1211页,1987年))。在这个方法中,输入的供体质粒与内生的“辅助”质粒的同源区在模拟染色体转化的过程中发生重组。

[0487] 除了通常使用的方法,在一些实施例中,将宿主细胞直接用包含编码本发明变体蛋白酶的核酸的DNA构建体或载体转化(即在引入到宿主细胞中之前,未使用中间细胞来扩增或以别的方式处理该DNA构建体或载体)。将本发明的DNA构建体或载体引入宿主细胞中包括本领域已知的那些在不插入质粒或载体的情况下将核酸序列(如DNA序列)引入宿主细胞中的物理和化学方法。这类方法包括但不限于氯化钙沉淀法、电穿孔法、裸DNA法、脂质体法等等。在另外的实施例中,将DNA构建体或载体与质粒共同转化,而不插入质粒中。在另一个实施例中,通过本领域已知的方法从已改变的芽孢杆菌菌株缺失掉选择标记(参见Stahl et al.,J.Bacteriol.158:411-418[1984](Stahl等人,《细菌学杂志》,第158卷,第411-418页,1984年);以及Palmeros et al.,Gene 247:255-264[2000](Palmeros等人,《基因》,第247卷,第255-264页,2000年))。

[0488] 在一些实施例中,将本发明的转化的细胞在常规营养培养基中培养。合适的具体培养条件,例如温度、pH等是本领域技术人员已知的,并且在科学文献中很好地进行了描述。在一些实施例中,本发明提供包含至少一种本发明的变体蛋白酶或至少一种本发明的核酸的培养物(如细胞培养物)。还提供的是包含至少一种本发明的核酸、载体或DNA构建体的组合物。

[0489] 在一些实施例中,将用至少一条编码至少一种本发明变体蛋白酶的多核苷酸序列转化的宿主细胞在允许本发明蛋白酶表达的条件下在合适的营养培养基中培养,此后从该

培养物回收所得的蛋白酶。用于培养细胞的培养基包含任何适于生长宿主细胞的常规培养基，如含有适当的补充成分的基本培养基和复合培养基。合适的培养基可从商业供应商获得或可根据公布的配方(参见，例如美国典型培养物保藏中心(American Type Culture Collection)的目录中公布的配方)制备。在一些实施例中，通过常规的程序从培养基回收由细胞产生的蛋白酶，包括但不限于例如，通过离心或过滤从培养基分离出宿主细胞，借助于盐(如硫酸铵)沉淀出上清液或滤液的蛋白质组分，进行色谱纯化(如离子交换色谱、凝胶过滤色谱、亲和色谱等)。任何适于回收或纯化变体蛋白酶的方法均可用于本发明。

[0490] 在一些实施例中，由重组宿主细胞产生的变体蛋白酶分泌进培养基中。编码利于纯化的结构域的核酸序列可用来利于可溶性蛋白质的纯化。包含编码变体蛋白酶的多核苷酸序列的载体或DNA构建体还可包含编码利于纯化的结构域的核酸序列，以利于纯化变体蛋白酶(参见例如Kroll et al.,DNA Cell Biol.12:441-53[1993](Kroll等人，《DNA细胞生物学》，第12卷，第441-453页，1993年))。此类利于纯化的结构域包括但不限于，例如金属螯合肽，如使得可以在固定化金属上进行纯化的组氨酸-色氨酸模块(参见Porath,Protein Expr.Purif.3:263-281[1992](Porath，《蛋白质表达和纯化》，第3卷，第263-281页，1992年))，使得可以在固定化免疫球蛋白上进行纯化的蛋白A结构域，以及用于FLAGS延伸/亲和纯化系统的结构域(如得自华盛顿州西雅图英姆纳克斯公司(Immunex Corp.,Seattle,WA)的蛋白A结构域)。在纯化结构域和异源蛋白质之间包括可切割的接头序列如XA因子或肠激酶(如得自加利福尼亚州圣地亚哥的英杰公司(Invitrogen,San Diego,CA)的序列)也可用于利于纯化。

[0491] 用于检测和测量酶(如本发明的变体蛋白酶)的酶活性的测定法是熟知的。各种用于检测和测量蛋白酶(例如本发明的变体蛋白酶)活性的测定法也是本领域一般技术人员已知的。具体地讲，可用于测量蛋白酶活性的测定法有基于酸可溶性肽从酪蛋白或血红蛋白的释放，以280nm处的吸光度进行测量或使用本领域的技术人员熟知的福林法进行比色测量。其他示例性的测定法涉及显色底物的增溶(参见例如Ward,“Proteinases,”in Fogarty(ed.).,Microbial Enzymes and Biotechnology,Applied Science,London,[1983],pp.251-317(Ward，“蛋白酶”，载于Fogarty编辑，《微生物酶和生物技术》，伦敦应用科学出版社，1983年，第251-317页))。其他示例性测定法包括但不限于琥珀酰-Ala-Ala-Pro-Phe-对硝基苯胺测定法(suc-AAPF-pNA)和2,4,6-三硝基苯磺酸钠盐测定法(TNBS测定法)。本领域人员知道的许多另外的参考文献提供了合适的方法(参见例如Wells et al.,Nucleic Acids Res.11:7911-7925[1983](Wells等人，《核酸研究》，第11卷，第7911-7925页，1983年)；Christianson et al.,Anal.Biochem.223:119-129[1994](Christianson等人，《分析生物化学》，第223卷，第119-129页，1994年)；以及Hsia et al.,Anal Biochem.242:221-227[1999](Hsia等人，《分析生物化学》，第242卷，第221-227页，1999年))。

[0492] 有多种方法可用于测定成熟蛋白酶(例如本发明的成熟变体蛋白酶)在宿主细胞中的产生水平。这类方法包括但不限于例如利用对该蛋白酶有特异性的多克隆或单克隆抗体的方法。示例性方法包括但不限于例如酶联免疫吸附测定法(ELISA)、放射免疫测定法(RIA)、荧光免疫测定法(FIA)和荧光激活细胞分选法(FACS)。这些和其他测定法是本领域所熟知的(参见例如Maddox et al.,J.Exp.Med.158:1211[1983](Maddox等人，《实验医学

杂志》,第158卷,第1211页,1983年))。

[0493] 在一些其他实施例中,本发明提供用于制备或产生本发明的成熟变体蛋白酶的方法。成熟变体蛋白酶不包含信号肽或前肽序列。一些方法包括在重组细菌宿主细胞,例如芽孢杆菌细胞(如枯草芽孢杆菌细胞)中制备或产生本发明的变体蛋白酶。在一些实施例中,本发明提供产生本发明的变体蛋白酶的方法,该方法包括在有利于产生该变体蛋白酶的条件下培养包含重组表达载体的重组宿主细胞,该重组表达载体包含编码本发明的变体蛋白酶的核酸。一些这类方法还包括从培养物回收变体蛋白酶。

[0494] 在一些实施例中,本发明提供产生本发明的变体蛋白酶的方法,该方法包括:(a)将包含编码本发明变体蛋白酶的核酸的重组表达载体引入细胞群(例如细菌细胞,如枯草芽孢杆菌细胞)中;以及(b)在有利于产生由该表达载体编码的变体蛋白酶的条件下在培养基中培养该细胞。一些此类方法还包括:(c)从细胞或培养基分离变体蛋白酶。

[0495] 织物和家庭护理产品

[0496] 在一些实施例中,本发明的蛋白酶变体可用于包含辅助材料和蛋白酶变体的组合物,其中该组合物为织物和家庭护理产品。

[0497] 在一些实施例中,织物和家庭护理产品组合物包含至少一种蛋白酶变体,该蛋白酶变体包含一个或多个,优选地两个或多个以下的突变:X1R,X2S,X4R,X4S,X9A,X10S,X14K,X16S,X17R,X18R,X20R,X22A,X22R,X24R,X24W,X25R,X25V,X26F,X42I,X43R,X43A,X46R,X52F,X52E,X52N,X57R,X59A,X62E,X62Q,X68A,X68C,X71G,X72C,X74C.X75A,X75F,X75R,X76D,X78R,X82R,X86W,X89P,X89T,X89G,X89H,X89I,X89V,X89W,X91N,X94N,X100S,X101A,X101N,X101G,X101D,X103G,X103N,X104L,X104I,X106V,X106G,X108I,X111V,X112V,X115K,X115R,X117F,X118I,X121F,X128D,X128F,X128L,X128N,X129E,X144R,X148I,X158E,X159E,X160D,X166D,X185E,X185I,X186H,X188E,X188D,X197F,X203E,X209S,X209N,X209F,X209T,X209E,X209H,X209G,X210R,X212I,X212F,X214F,X215N,X215D,X215E,X217E,X217N,X224A,X230E,X231I,X236F,X238R,X238K,X239K,X239G,X239R,X239S,X241R,X242R,X242L,X243R,X244R,X248I,X248V,X249R,X250I,X252R,X253R,X262D,X263F,X265F,X267V,X267N,X269I,X269R,X271F,X271I,X271H,X271P,X271T,X271V,X271L和X272F。

[0498] 在一些实施例中,织物和家庭护理产品组合物包含至少一种蛋白酶变体,该蛋白酶变体包含一个或多个以下的突变组:X022R-X024R,X009A-X271L,X018R-X241R,X018R-X115R,X043R-X249R,X020R-X249R,X004R-X249R,X020R-X024R,X018R-X249R,X009A-X020R,X020R-X241R,X009A-X078R,X020R-X115R,X018R-X024R,X024R-X242R,X022R-X115R,X018R-X043R,X020R-X043R,X018R-X242R,X242R-X269R,X018R-X244R,X024R-X269R,X020R-X271L,X024R-X271L,X004R-X009A,X020R-X269R,X001R-X024R,X244R-X271L,X009A-X018R,X241R-X271L,X004R-X024R,X009A-X249R,X009A-X022R,X062E-X129E,X062E-X159E,X016S-X148I,X158E-X249R,X016S-X062E,X111V-X188D,X022A-X062E,X062E-X148I,X022A-X129E,X062E-X271F,X062E-X158E,X016S-X159E,X062E-X186H,X128N-X159E,X062E-X188D,X062E-X128N,X148I-X159E,X103G-X158E,X111V-X159E,X158E-X271F,X016S-X188D,X022A-X111V,X128N-X158E,X016S-X158E,X104L-X158E,X128N-X186H,X159E-X209E,X062E-X101A,X111V-X209E,X148I-X188D,X101A-

X209E,X022A-X188D,X016S-X022A,X128N-X129E,X016S-X209E,X016S-X128N,X022A-X089P,X128N-X209E,X089P-X158E,X062E-X103G,X186H-X271F,X016S-X129E,X089P-X159E,X111V-X249R,X101A-X129E,X148I-X209E,X022A-X159E,X129E-X249R,X129E-X209E,X104L-X129E,X128N-X188D,X111V-X158E,X022A-X158E,X062E-X209E,X062E-X249R,X101A-X186H,X089P-X129E,X129E-X271,X22A-X111V-X159E,X101A-X103G-X104L-X209E,X101A-X103G-X104L-X159E,X101A-X103G-X104L-X188D,X101G-X103A-X104I-X159D,X22A-X103G-X159E,X22A-X128N-X271F-X209E,X22A-X209E-X271F,X22A-X101A-X209E,X101A-X209E-X271F,X22A-X111V-X128N,X22A-X101A-X159E,X101A-X103G-X104L,X22A-X101A-X103G-X104L,X101A-X103G-X104L,X101G-X103A-X104I,X101A-X103G-X104L-X128N,X103A-X104I-X159D-X232V-X236H-X245R-X248D-X252K,X101G-X104I-X159D-X232V-X236H-X245R-X248D-X252K,X101G-X103A-X159D-X232V-X236H-X245R-X248D-X252K,X101G-X103A-X104L-X232V-X236H-X245R-X248D-X252K,X101G-X103A-X104L-X159D-X236H-X245R-X248D-X252K,X101G-X103A-X104L-X159D-X232V-X245R-X248D-X252K,X101G-X103A-X104L-X159D-X232V-X236H-X248D-X252K,X101G-X103A-X104L-X159D-X232V-X236H-X245R-X252K,X101G-X103A-X104L-X159D-X232V-X236H-X245R-X248D,X62E-X101G-X103A-X104I-X159D-X232V-X245R-X248D-X271F,X62E-X101G-X103A-X104I-X159D-X232V-X245R-X248D-X249R,X22A-X101G-X103A-X104I-X159D-X232V-X245R-X248D-X249R,X101G-X103A-X104I-X159D-X232V-X245R-X248D-X24R,X101G-X103A-X104I-X159D-X232V-X245R-X248D-X253R,X101G-X103A-X104I-X158E-X232V-X245R-X248D-X249R,X22A-X101G-X103A-X104I-X159D-X232V-X245R-X248D-X271F,X101G-X103A-X104I-X159E-X232V-X245R-X248D-X249R,X101G-X103A-X104I-X159D-X232V-X245R-X248D-X238R,X101G-X103A-X104I-X158E-X232V-X245R-X248D-X271F,X101G-X103A-X104I-X159D-X232V-X245R-X248D,X101G-X103A-X104I-X159D-X232V-X245R-X248D-X271F,X101G-X103A-X104I-X159D-X232V-X245R-X248D-X76D和X101G-X103A-X104I-X159E-X232V-X245R-X248D-X271F。

[0499] 在一些实施例中,织物和家庭护理产品组合物包含至少一种蛋白酶变体,该蛋白酶变体包含一个或多个以下的突变组:X022R-X024R,X009A-X271L,X018R-X241R,X018R-X115R,X043R-X249R,X020R-X249R,X004R-X249R,X020R-X024R,X018R-X249R,X009A-X020R,X020R-X241R,X009A-X078R,X020R-X115R,X018R-X024R,X024R-X242R,X022R-X115R,X018R-X043R,X020R-X043R,X018R-X242R,X242R-X269R,X018R-X244R,X024R-X269R,X020R-X271L,X024R-X271L,X004R-X009A,X020R-X269R,X001R-X024R,X244R-X271L,X009A-X018R,X241R-X271L,X004R-X024R,X009A-X249R,X009A-X022R,X062E-X129E,X062E-X159E,X016S-X148I,X158E-X249R,X016S-X062E,X111V-X188D,X022A-X062E,X062E-X148I,X022A-X129E,X062E-X271F,X062E-X158E,X016S-X159E,X062E-X186H,X128N-X159E,X062E-X188D,X062E-X128N,X148I-X159E,X103G-X158E,X111V-X159E,X158E-X271F,X016S-X188D,X022A-X111V,X128N-X158E,X016S-X158E,X104L-X158E,X128N-X186H,X159E-X209E,X062E-X101A,X111V-X209E,X148I-X188D,X101A-X209E,X022A-X188D,X016S-X022A,X128N-X129E,X016S-X209E,X016S-X128N,X022A-X089P,X128N-X209E,X089P-X158E,X062E-X103G,X186H-X271F,X016S-X129E,X089P-

X159E,X111V-X249R,X101A-X129E,X148I-X209E,X022A-X159E,X129E-X249R,X129E-X209E,X104L-X129E,X128N-X188D,X111V-X158E,X022A-X158E,X062E-X209E,X062E-X249R,X101A-X186H,X089P-X129E,X129E-X271,X22A-X111V-X159E,X101A-X103G-X104L-X209E,X101A-X103G-X104L-X159E,X101A-X103G-X104L-X188D,X101G-X103A-X104I-X159D,X22A-X103G-X159E,X22A-X128N-X271F-X209E,X22A-X209E-X271F,X22A-X101A-X209E,X101A-X209E-X271F,X22A-X111V-X128N,X22A-X101A-X159E,X101A-X103G-X104L,X22A-X101A-X103G-X104L,X101A-X103G-X104L,X101G-X103A-X104I,X101A-X103G-X104L-X128N,X103A-X104I-X159D-X232V-X236H-X245R-X248D-X252K,X101G-X104I-X159D-X232V-X236H-X245R-X248D-X252K,X101G-X103A-X159D-X232V-X236H-X245R-X248D-X252K,X101G-X103A-X104L-X232V-X236H-X245R-X248D-X252K,X101G-X103A-X104L-X159D-X236H-X245R-X248D-X252K,X101G-X103A-X104L-X159D-X232V-X245R-X248D-X252K,X101G-X103A-X104L-X159D-X232V-X236H-X248D-X252K,X101G-X103A-X104L-X159D-X232V-X236H-X245R-X252K,X101G-X103A-X104L-X159D-X232V-X236H-X245R-X248D,X62E-X101G-X103A-X104I-X159D-X232V-X245R-X248D-X271F,X62E-X101G-X103A-X104I-X159D-X232V-X245R-X248D-X249R,X22A-X101G-X103A-X104I-X159D-X232V-X245R-X248D-X249R,X101G-X103A-X104I-X159D-X232V-X245R-X248D-X24R,X101G-X103A-X104I-X159D-X232V-X245R-X248D-X253R,X101G-X103A-X104I-X158E-X232V-X245R-X248D-X249R,X22A-X101G-X103A-X104I-X159D-X232V-X245R-X248D-X271F,X101G-X103A-X104I-X159E-X232V-X245R-X248D-X249R,X101G-X103A-X104I-X159D-X232V-X245R-X248D-X238R,X101G-X103A-X104I-X158E-X232V-X245R-X248D-X271F,X101G-X103A-X104I-X159D-X232V-X245R-X248D,X101G-X103A-X104I-X159D-X232V-X245R-X248D-X271F,X101G-X103A-X104I-X159D-X232V-X245R-X248D-X76D和X101G-X103A-X104I-X159E-X232V-X245R-X248D-X271F。

[0500] 在一些实施例中,织物和家庭护理产品组合物包含至少一种蛋白酶变体,该蛋白酶变体包含总共3、4、5、6、7、8、9、10、11、12、13、14、15、16、17、18、19、20、21、22、23、24或甚至25个选自以下的突变:X1R,X2S,V4R,V4S,X9A,X10S,X14K,X16S,H17R,X18R,X20R,X22A,X22R,X24R,X24W,X25R,X25V,X26F,X42I,X43R,X43A,G46R,X52F,X52E,X52N,T57R,Q59A,X62E,X62Q,X68A,X68C,X71G,X72C,X74C,X75A,X75F,X75R,X76D,X78R,L82R,P86W,X89P,X89T,X89G,X89H,X89I,X89V,X89W,X91N,X94N,X100S,X101A,X101N,X101G,X101D,X103G,X103N,X104L,X104I,X106V,X106G,X108I,X111V,X112V,X115K,X115R,X117F,X118I,X121F,X128D,X128F,X128L,X128N,X129E,X144R,X148I,X158E,X159E,X160D,X166D,X185E,X185I,X186H,X188E,X188D,D197F,X203E,X209S,X209N,X209F,X209T,X209E,X209H,X209G,X210R,X212I,X212F,X214F,X215N,X215D,X215E,X217E,X217N,X224A,X230E,X231I,X236F,X238R,X238K,X239K,X239G,X239R,X239S,X241R,X242R,X242L,X243R,X244R,X248I,X248V,X249R,X250I,X252R,X253R,X262D,X263F,X265F,X267V,X267N,X269I,X269R,X271F,X271I,X271H,X271P,X271T,X271V,X271L和X272F;以及任选地包含一个或多个以下的突变:X103A,X159D,X236H,X245R,X248D和X252K。

[0501] 在一些实施例中,织物和家庭护理产品组合物包含至少一种蛋白酶变体,该蛋白酶变体包含两个或多个以下的突变:X1R,X2S,V4R,V4S,X9A,X10S,X14K,X16S,X22A,X22R,

X24R,X25V,X26F,X42I,X52F,X52E,X52N,X62E,X62Q,X68A,X68C,X71G,X72C,X74C,X75A,X75F,X78R,X89P,X89T,X89G,X89H,X89W,X91N,X94N,X100S,X101A,X101N,X101G,X101D,X103G,X103N,X104L,X104I,X108I,X111V,X112V,X115K,X117F,X121F,X128D,X128F,X128L,X128N,X129E,X148I,X158E,X159E,X160D,X166D,X185E,X186H,X188E,X188D,X203E,X209S,X209N,X209F,X209T,X209E,X209H,X209G,X210R,X212I,X212F,X214F,X215N,X215D,X215E,X217E,X217N,X224A,X230E,X231I,X236F,X238R,X238K,X239K,X239G,X239R,X248V,X249R,X250I,X262D,X263F,X265F,X267V,X267N,X269I,X269R,X271F,X271I,X271H和X272F;和/或一个或多个以下的突变组:X062E-X129E,X062E-X159E,X016S-X148I,X158E-X249R,X016S-X062E,X111V-X188D,X022A-X062E,X062E-X148I,X022A-X129E,X062E-X271F,X062E-X158E,X016S-X159E,X062E-X186H,X128N-X159E,X062E-X188D,X062E-X128N,X148I-X159E,X103G-X158E,X111V-X159E,X158E-X271F,X016S-X188D,X022A-X111V,X128N-X158E,X016S-X158E,X104L-X158E,X128N-X186H,X159E-X209E,X062E-X101A,X111V-X209E,X148I-X188D,X101A-X209E,X022A-X188D,X016S-X022A,X128N-X129E,X016S-X209E,X016S-X128N,X022A-X089P,X128N-X209E,X089P-X158E,X062E-X103G,X186H-X271F,X016S-X129E,X089P-X159E,X111V-X249R,X101A-X129E,X148I-X209E,X022A-X159E,X129E-X249R,X129E-X209E,X104L-X129E,X128N-X188D,X111V-X158E,X022A-X158E,X062E-X209E,X062E-X249R,X101A-X186H,X089P-X129E,X129E-X271F,X22A-X111V-X159E,X101A-X103G-X104L-X209E,X101A-X103G-X104L-X159E,X101A-X103G-X104L-X188D,X101G-X103A-X104I-X159D,X22A-X103G-X159E,X22A-X128N-X271F-X209E,X22A-X209E-X271F,X22A-X101A-X209E,X101A-X209E-X271F,X22A-X111V-X128N,X22A-X101A-X159E,X101A-X103G-X104L,X22A-X101A-X103G-X104L,X101A-X103G-X104L,X101G-X103A-X104I,X101A-X103G-X104L-X128N,X103A-X104I-X159D-X232V-X236H-X245R-X248D-X252K,X101G-X104I-X159D-X232V-X236H-X245R-X248D-X252K,X101G-X103A-X159D-X232V-X236H-X245R-X248D-X252K,X101G-X103A-X104L-X232V-X236H-X245R-X248D-X252K,X101G-X103A-X104L-X159D-X236H-X245R-X248D-X252K,X101G-X103A-X104L-X159D-X232V-X245R-X248D-X252K,X101G-X103A-X104L-X159D-X232V-X236H-X248D-X252K,X101G-X103A-X104L-X159D-X232V-X236H-X245R-X252K,X101G-X103A-X104L-X159D-X232V-X236H-X245R-X248D,X62E-X101G-X103A-X104I-X159D-X232V-X245R-X248D-X271F,X62E-X101G-X103A-X104I-X159D-X232V-X245R-X248D-X249R,X22A-X101G-X103A-X104I-X159D-X232V-X245R-X248D-X249R,X101G-X103A-X104I-X159D-X232V-X245R-X248D-X24R,X101G-X103A-X104I-X159D-X232V-X245R-X248D-X253R,X101G-X103A-X104I-X158E-X232V-X245R-X248D-X249R,X22A-X101G-X103A-X104I-X159D-X232V-X245R-X248D-X271F,X101G-X103A-X104I-X159E-X232V-X245R-X248D-X249R,X101G-X103A-X104I-X159D-X232V-X245R-X248D-X238R,X101G-X103A-X104I-X158E-X232V-X245R-X248D-X271F,X101G-X103A-X104I-X159D-X232V-X245R-X248D,X101G-X103A-X104I-X159D-X232V-X245R-X248D-X271F,X101G-X103A-X104I-X159D-X232V-X245R-X248D-X76D和X101G-X103A-X104I-X159E-X232V-X245R-X248D-X271F;其中该至少一种蛋白酶变体相对于具有SEQ ID NO:2的氨基酸序列的迟缓芽孢杆菌枯草杆菌蛋白酶GG36蛋白酶具有0、-1、-2、-3、-4或-5的总净电荷。

[0502] 在一些实施例中，织物和家庭护理产品组合物包含至少一种蛋白酶变体，该蛋白酶变体包含两个或多个以下的突变：X4R,X17R,X18R,X20R,X22R,X24R,X24W,X25R,X43R,X43A,X46R,X52F,X52N,X57R,X59A,X62Q,X71G,X75R,X76D,X78R,X82R,X86W,X89P,X89W,X89T,X89I,X89H,X89V,X104L,X106V,X106G,X115R,X118I,X121F,X144R,X185I,X197F,X209N,X209S,X217E,X231I,X239R,X239S,X241R,X242R,X242L,X243R,X244R,X248I,X249R,X252R,X253R,X271T,X271V,X271L,X271H,X271F,X271P,X1R,X9A,X212F和X269R；和/或一个或多个以下的突变组：X022R-X024R,X009A-X271L,X018R-X241R,X018R-X115R,X043R-X249R,X020R-X249R,X004R-X249R,X020R-X024R,X018R-X249R,X009A-X020R,X020R-X241R,X009A-X078R,X020R-X115R,X018R-X024R,X024R-X242R,X022R-X115R,X018R-X043R,X020R-X043R,X018R-X242R,X242R-X269R,X018R-X244R,X024R-X269R,X020R-X271L,X024R-X271L,X004R-X009A,X020R-X269R,X001R-X024R,X244R-X271L,X009A-X018R,X241R-X271L,X004R-X024R,X009A-X249R,X009A-X022R,X101G-X103A-X104I-X159D-X232V-X245R-X248D-X271F,X101G-X103A-X104I-X158E-X232V-X245R-X248D-X271F,X101G-X103A-X104I-X158E-X232V-X245R-X248D-X249R,X101G-X103A-X104I-X159D-X232V-X245R-X248D-X24R,X101G-X103A-X104L-X159D-X232V-X236H-X245R-X252K,X101G-X103A-X104L-X232V-X236H-X245R-X248D-X252K；其中该至少一种蛋白酶变体相对于具有SEQ ID NO:2的氨基酸序列的迟缓芽孢杆菌枯草杆菌蛋白酶GG36蛋白酶具有0、+1、+2、+3、+4或+5的总净电荷。

[0503] 在一些实施例中，织物和家庭护理产品组合物的蛋白酶变体衍生自市售亲本蛋白酶(如诺维信公司(Novozymes A/S)生产的SAVINASE®、POLARZYME®、KANNASE®、LIQUINASE®、LIQUINASE ULTRA®、SAVINASE ULTRA®或OVOZYME®；杰能科国际(Genencor International)生产的MAXACAL®、PROPERASE®、PURAFECT®、FN3®、FN4®和PURAFECT OXP®、PURAFAST™、PURAFECT® PRIME或PURAMAX®)和得自汉高/凯米拉(Henkel/Kemira)的那些蛋白酶，即BLAP(US 5,352,604的图29中示出的序列，具有以下的突变：S99D+S101R+S103A+V104I+G159S，在下文中称为BLAP)和BLAP X(具有S3T+V4I+V205I的BLAP)。

[0504] 在一些实施例中，织物和家庭护理产品组合物包含至少一种蛋白酶变体，该蛋白酶变体的亲本具有蛋白水解活性，其中该变体蛋白酶包含与SEQ ID NO:2所示氨基酸序列相差不超过50、不超过40、不超过35、不超过30、不超过25、不超过20、不超过19、不超过18、不超过17、不超过16、不超过15、不超过14、不超过13、不超过12、不超过11、不超过10、不超过9或不超过8个氨基酸残基的氨基酸序列，其中氨基酸位置根据SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列中对应的氨基酸位置的编号方式来进行编号，这是通过该变体蛋白酶氨基酸序列与解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'氨基酸序列的比对来确定的，其中该变体枯草杆菌蛋白酶包含以下的置换组中的一者：X101G-X103A-X104I-X159D-X232V-X236H-X245R-X248D-X252K；或X87N；或X87N-S101G-V104N；或X76D,X103A-X104I；或Y167A-R170S-A194P；或X87N-G118V-X129Q-X130A

[0505] 在一些实施例中，织物和家庭护理产品组合物包含至少一种蛋白酶变体，该蛋白酶变体包含一个或多个，或甚至两个或多个以下的突变：A1R,Q2S,V4R,V4S,S9A,R10S,P14K,A16S,H17R,N18R,G20R,T22A,T22R,S24R,S24W,G25R,G25V,V26F,L42I,N43R,N43A,G46R,P52F,P52E,P52N,T57R,Q59A,N62E,N62Q,V68A,V68C,T71G,I72C,A74C.L75A,L75F,L75R,N76D,S78R,L82R,P86W,E89P,E89T,E89G,E89H,E89I,E89V,E89W,Y91N,K94N,G100S,S101A,S101N,S101G,S101D,S103G,S103N,V104L,V104I,S106V,S106G,A108I,L111V,E112V,G115K,G115R,N117F,G118I,V121F,S128D,S128F,S128L,S128N,P129E,S144R,L148I,A158E,G159E,S160D,S166D,N185E,N185I,R186H,S188E,S188D,D197F,V203E,Y209S,Y209N,Y209F,Y209T,Y209E,Y209H,Y209G,P210R,S212I,S212F,Y214F,A215N,A215D,A215E,L217E,L217N,T224A,A230E,A231I,Q236F,N238R,N238K,P239K,P239G,P239R,P239S,W241R,S242R,S242L,N243R,V244R,N248I,N248V,H249R,L250I,N252R,T253R,L262D,Y263F,S265F,L267V,L267N,N269I,N269R,E271F,E271I,E271H,E271P,E271T,E271V,E271L以及A272F

[0506] 在一些实施例中，织物和家庭护理产品组合物包含至少一种蛋白酶变体，该蛋白酶变体包含一个或多个以下的突变组：T022R-S024R,S009A-E271L,N018R-W241R,N018R-G115R,N043R-H249R,G020R-H249R,V004R-H249R,G020R-S024R,N018R-H249R,S009A-G020R,G020R-W241R,S009A-S078R,G020R-G115R,N018R-S024R,S024R-S242R,T022R-G115R,N018R-N043R,G020R-N043R,N018R-S242R,S242R-N269R,N018R-V244R,S024R-N269R,G020R-E271L,S024R-E271L,V004R-S009A,G020R-N269R,A001R-S024R,V244R-E271L,S009A-N018R,W241R-E271L,V004R-S024R,S009A-H249R,S009A-T022R,N062E-P129E,N062E-G159E,A016S-L148I,A158E-H249R,A016S-N062E,L111V-S188D,T022A-N062E,N062E-L148I,T022A-P129E,N062E-E271F,N062E-A158E,A016S-G159E,N062E-R186H,S128N-G159E,N062E-S188D,N062E-S128N,L148I-G159E,S103G-A158E,L111V-G159E,A158E-E271F,A016S-S188D,T022A-L111V,S128N-A158E,A016S-A158E,V104L-A158E,S128N-R186H,G159E-Y209E,N062E-S101A,L111V-Y209E,L148I-S188D,S101A-Y209E,T022A-S188D,A016S-T022A,S128N-P129E,A016S-Y209E,A016S-S128N,T022A-E089P,S128N-Y209E,E089P-A158E,N062E-S103G,R186H-E271F,A016S-P129E,E089P-G159E,L111V-H249R,S101A-P129E,L148I-Y209E,T022A-G159E,P129E-H249R,P129E-Y209E,V104L-P129E,S128N-S188D,L111V-A158E,T022A-A158E,N062E-Y209E,N062E-H249R,S101A-R186H,E089P-P129E,P129E-E271,T22A-L111V-G159E,S101A-S103G-V104L-Y209E,S101A-S103G-V104L-G159E,S101A-S103G-V104L-S188D,S101G-S103A-V104I-G159D,T22A-S103G-G159E,T22A-S128N-E271F-Y209E,T22A-Y209E-E271F,T22A-S101A-Y209E,S101A-Y209E-E271F,T22A-L111V-S128N,T22A-S101A-G159E,S101A-S103G-V104L,T22A-S101A-S103G-V104L,S101A-S103G-V104L,S101G-S103A-V104I,S101A-S103G-V104L-S128N,S103A-V104I-G159D-A232V-Q236H-Q245R-N248D-N252K,S101G-V104I-G159D-A232V-Q236H-Q245R-N248D-N252K,S101G-S103A-G159D-A232V-Q236H-Q245R-N248D-N252K,S101G-S103A-V104L-A232V-Q236H-Q245R-N248D-N252K,S101G-S103A-V104L-G159D-Q236H-Q245R-N248D-N252K,S101G-S103A-V104L-G159D-A232V-Q245R-N248D-N252K,S101G-S103A-V104L-G159D-A232V-Q236H-N248D-N252K,S101G-S103A-V104L-

G159D-A232V-Q236H-Q245R-N252K,S101G-S103A-V104L-G159D-A232V-Q236H-Q245R-N248D,N62E-S101G-S103A-V104I-G159D-A232V-Q245R-N248D-E271F,N62E-S101G-S103A-V104I-G159D-A232V-Q245R-N248D-H249R,T22A-S101G-S103A-V104I-G159D-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-G159D-A232V-Q245R-N248D-S24R,S101G-S103A-V104I-G159D-A232V-Q245R-N248D-T253R,S101G-S103A-V104I-A158E-A232V-Q245R-N248D-H249R,T22A-S101G-S103A-V104I-G159D-A232V-Q245R-N248D-E271F,S101G-S103A-V104I-G159E-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-G159D-A232V-Q245R-N248D-N238R,S101G-S103A-V104I-A158E-A232V-Q245R-N248D-E271F,S101G-S103A-V104I-G159D-A232V-Q245R-N248D,S101G-S103A-V104I-G159D-A232V-Q245R-N248D-E271F,S101G-S103A-V104I-G159D-A232V-Q245R-N248D-N76D和S101G-S103A-V104I-G159E-A232V-Q245R-N248D-E271F。

[0507] 在一些实施例中,织物和家庭护理产品组合物包含至少一种蛋白酶变体,该蛋白酶变体包含一个或多个以下的突变组:T022R-S024R,S009A-E271L,N018R-W241R,N018R-G115R,N043R-H249R,G020R-H249R,V004R-H249R,G020R-S024R,N018R-H249R,S009A-G020R,G020R-W241R,S009A-S078R,G020R-G115R,N018R-S024R,S024R-S242R,T022R-G115R,N018R-N043R,G020R-N043R,N018R-S242R,S242R-N269R,N018R-V244R,S024R-N269R,G020R-E271L,S024R-E271L,V004R-S009A,G020R-N269R,A001R-S024R,V244R-E271L,S009A-N018R,W241R-E271L,V004R-S024R,S009A-H249R,S009A-T022R,N062E-P129E,N062E-G159E,A016S-L148I,A158E-H249R,A016S-N062E,L111V-S188D,T022A-N062E,N062E-L148I,T022A-P129E,N062E-E271F,N062E-A158E,A016S-G159E,N062E-R186H,S128N-G159E,N062E-S188D,N062E-S128N,L148I-G159E,S103G-A158E,L111V-G159E,A158E-E271F,A016S-S188D,T022A-L111V,S128N-A158E,A016S-A158E,V104L-A158E,S128N-R186H,G159E-Y209E,N062E-S101A,L111V-Y209E,L148I-S188D,S101A-Y209E,T022A-S188D,A016S-T022A,S128N-P129E,A016S-Y209E,A016S-S128N,T022A-E089P,S128N-Y209E,E089P-A158E,N062E-S103G,R186H-E271F,A016S-P129E,E089P-G159E,L111V-H249R,S101A-P129E,L148I-Y209E,T022A-G159E,P129E-H249R,P129E-Y209E,V104L-P129E,S128N-S188D,L111V-A158E,T022A-A158E,N062E-Y209E,N062E-H249R,S101A-R186H,E089P-P129E,P129E-E271,T22A-L111V-G159E,S101A-S103G-V104L-Y209E,S101A-S103G-V104L-G159E,S101A-S103G-V104L-S188D,S101G-S103A-V104I-G159D,T22A-S103G-G159E,T22A-S128N-E271F-Y209E,T22A-Y209E-E271F,T22A-S101A-Y209E,S101A-Y209E-E271F,T22A-L111V-S128N,T22A-S101A-G159E,S101A-S103G-V104L,T22A-S101A-S103G-V104L,S101A-S103G-V104L,S101G-S103A-V104I,S101A-S103G-V104L-S128N,S103A-V104I-G159D-A232V-Q236H-Q245R-N248D-N252K,S101G-V104I-G159D-A232V-Q236H-Q245R-N248D-N252K,S101G-S103A-G159D-A232V-Q236H-Q245R-N248D-N252K,S101G-S103A-V104L-A232V-Q236H-Q245R-N248D-N252K,S101G-S103A-V104L-G159D-Q236H-Q245R-N248D-N252K,S101G-S103A-V104L-G159D-A232V-Q245R-N248D-N252K,S101G-S103A-V104L-G159D-A232V-Q236H-N248D-N252K,S101G-S103A-V104L-G159D-A232V-Q236H-Q245R-N252K,S101G-S103A-V104L-G159D-A232V-Q236H-Q245R-N248D,N62E-S101G-S103A-V104I-G159D-A232V-Q245R-N248D-E271F,N62E-S101G-S103A-

V104I-G159D-A232V-Q245R-N248D-H249R,T22A-S101G-S103A-V104I-G159D-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-G159D-A232V-Q245R-N248D-S24R,S101G-S103A-V104I-G159D-A232V-Q245R-N248D-T253R,S101G-S103A-V104I-A158E-A232V-Q245R-N248D-H249R,T22A-S101G-S103A-V104I-G159D-A232V-Q245R-N248D-E271F,S101G-S103A-V104I-G159E-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-G159D-A232V-Q245R-N248D-N238R,S101G-S103A-V104I-A158E-A232V-Q245R-N248D-E271F,S101G-S103A-V104I-G159D-A232V-Q245R-N248D,S101G-S103A-V104I-G159D-A232V-Q245R-N248D-E271F,S101G-S103A-V104I-G159D-A232V-Q245R-N248D-N76D和S101G-S103A-V104I-G159E-A232V-Q245R-N248D-E271F

[0508] 在一些实施例中,织物和家庭护理产品组合物包含至少一种蛋白酶变体,该蛋白酶变体在包括位置1、2、4、9、10、14、16、17、18、20、22、24、25、26、42、43、46、52、57、59、62、68、71、72、74、75、76、78、82、86、89、91、94、100、101、103、104、106、108、111、112、115、117、118、121、128、129、144、148、158、159、160、166、185、186、188、197、203、209、210、212、214、215、217、224、230、231、236、238、239、241、242、243、244、248、249、250、252、253、262、263、265、267、269、271和272的一组位置内包含3、4、5、6、7、8、9、10、11、12、13、14、15、16、17、18、19、20、21、22、23、24或甚至25个突变。

[0509] 在一些实施例中,织物和家庭护理产品组合物包含至少一种蛋白酶变体,该蛋白酶变体包含总共3、4、5、6、7、8、9、10、11、12、13、14、15、16、17、18、19、20、21、22、23、24或甚至25个选自以下的突变:A1R,Q2S,V4R,V4S,S9A,R10S,P14K,A16S,H17R,N18R,G20R,T22A,T22R,S24R,S24W,G25R,G25V,V26F,L42I,N43R,N43A,G46R,P52F,P52E,P52N,T57R,Q59A,N62E,N62Q,V68A,V68C,T71G,I72C,A74C,L75A,L75F,L75R,N76D,S78R,L82R,P86W,E89P,E89T,E89G,E89H,E89I,E89V,E89W,Y91N,K94N,G100S,S101A,S101N,S101G,S101D,S103G,S103N,V104L,V104I,S106V,S106G,A108I,L111V,E112V,G115K,G115R,N117F,G118I,V121F,S128D,S128F,S128L,S128N,P129E,S144R,L148I,A158E,G159E,S160D,S166D,N185E,N185I,R186H,S188E,S188D,D197F,V203E,Y209S,Y209N,Y209F,Y209T,Y209E,Y209H,Y209G,P210R,S212I,S212F,Y214F,A215N,A215D,A215E,L217E,L217N,T224A,A230E,A231I,Q236F,N238R,N238K,P239K,P239G,P239R,P239S,W241R,S242R,S242L,N243R,V244R,N248I,N248V,H249R,L250I,N252R,T253R,L262D,Y263F,S265F,L267V,L267N.N269I,N269R,E271F,E271I,E271H,E271P,E271T,E271V,E271L和A272F;以及任选地包含一个或多个以下的突变:S103A,G159D,Q236H,Q245R,N248D和N252K。

[0510] 在一些实施例中,织物和家庭护理产品组合物包含至少一种蛋白酶变体,该蛋白酶变体包含两个或多个以下的突变:A1R,Q2S,V4R,V4S,S9A,R10S,P14K,A16S,T22A,T22R,S24R,G25V,V26F,L42I,P52F,P52E,P52N,N62E,N62Q,V68A,V68C,T71G,I72C,A74C.L75A,L75F,S78R,E89P,E89T,E89G,E89H,E89W,Y91N,K94N,G100S,S101A,S101N,S101G,S101D,S103G,S103N,V104L,V104I,A108I,L111V,E112V,G115K,N117F,V121F,S128D,S128F,S128L,S128N,P129E,L148I,A158E,G159E,S160D,S166D,N185E,R186H,S188E,S188D,V203E,Y209S,Y209N,Y209F,Y209T,Y209E,Y209H,Y209G,P210R,S212I,S212F,Y214F,A215N,A215D,A215E,L217E,L217N,T224A,A230E,A231I,Q236F,N238R,N238K,P239K,P239G,P239R,N248V,H249R,L250I,L262D,Y263F,S265F,L267V,L267N,N269I,N269R,

E271F,E271I,E271H和A272F;和/或一个或多个以下的突变组:N062E-P129E,N062E-G159E,A016S-L148I,A158E-H249R,A016S-N062E,L111V-S188D,T022A-N062E,N062E-L148I,T022A-P129E,N062E-E271F,N062E-A158E,A016S-G159E,N062E-R186H,S128N-G159E,N062E-S188D,N062E-S128N,L148I-G159E,S103G-A158E,L111V-G159E,A158E-E271F,A016S-S188D,T022A-L111V,S128N-A158E,A016S-A158E,V104L-A158E,S128N-R186H,G159E-Y209E,N062E-S101A,L111V-Y209E,L148I-S188D,S101A-Y209E,T022A-S188D,A016S-T022A,S128N-P129E,A016S-Y209E,A016S-S128N,T022A-E089P,S128N-Y209E,E089P-A158E,N062E-S103G,R186H-E271F,A016S-P129E,E089P-G159E,L111V-H249R,S101A-P129E,L148I-Y209E,T022A-G159E,P129E-H249R,P129E-Y209E,V104L-P129E,S128N-S188D,L111V-A158E,T022A-A158E,N062E-Y209E,N062E-H249R,S101A-R186H,E089P-P129E,P129E-E271F,T22A-L111V-G159E,S101A-S103G-V104L-Y209E,S101A-S103G-V104L-G159E,S101A-S103G-V104L-S188D,S101G-S103A-V104I-G159D,T22A-S103G-G159E,T22A-S128N-E271F-Y209E,T22A-Y209E-E271F,T22A-S101A-Y209E,S101A-Y209E-E271F,T22A-L111V-S128N,T22A-S101A-G159E,S101A-S103G-V104L,T22A-S101A-S103G-V104L,S101A-S103G-V104L,S101G-S103A-V104I,S101A-S103G-V104L-S128N,S103A-V104I-G159D-A232V-Q236H-Q245R-N248D-N252K,S101G-V104I-G159D-A232V-Q236H-Q245R-N248D-N252K,S101G-S103A-G159D-A232V-Q236H-Q245R-N248D-N252K,S101G-S103A-V104L-A232V-Q236H-Q245R-N248D-N252K,S101G-S103A-V104L-G159D-Q236H-Q245R-N248D-N252K,S101G-S103A-V104L-G159D-A232V-Q245R-N248D-N252K,S101G-S103A-V104L-G159D-A232V-Q236H-N248D-N252K,S101G-S103A-V104L-G159D-A232V-Q236H-Q245R-N252K,S101G-S103A-V104L-G159D-A232V-Q236H-Q245R-N248D,N62E-S101G-S103A-V104I-G159D-A232V-Q245R-N248D-E271F,N62E-S101G-S103A-V104I-G159D-A232V-Q245R-N248D-H249R,T22A-S101G-S103A-V104I-G159D-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-G159D-A232V-Q245R-N248D-S24R,S101G-S103A-V104I-G159D-A232V-Q245R-N248D-T253R,S101G-S103A-V104I-A158E-A232V-Q245R-N248D-H249R,T22A-S101G-S103A-V104I-G159D-A232V-Q245R-N248D-E271F,S101G-S103A-V104I-G159E-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-G159D-A232V-Q245R-N248D-N238R,S101G-S103A-V104I-A158E-A232V-Q245R-N248D-E271F,S101G-S103A-V104I-G159D-A232V-Q245R-N248D,S101G-S103A-V104I-G159D-A232V-Q245R-N248D-E271F,S101G-S103A-V104I-G159D-A232V-Q245R-N248D-N76D和S101G-S103A-V104I-G159E-A232V-Q245R-N248D-E271F;其中该至少一种蛋白酶变体相对于具有SEQ ID NO:2的氨基酸序列的迟缓芽孢杆菌枯草杆菌蛋白酶GG36蛋白酶具有0、+1、+2、+3、+4或+5的总净电荷。

[0511] 在一些实施例中,织物和家庭护理产品组合物包含至少一种蛋白酶变体,其中至少一种蛋白酶变体是具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:X1R,X230E,X271L,X115R,X20R,X249R,X235F,X27V/F/L,X75E,X82R,X18R,X269R,X43D,X43R,X76D,X45T,X212F,X242R,X24R,X78R,X9A,X22R,X121E,X244R,X28E,X30E,X4R,和X241R,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0512] 在一些实施例中,织物和家庭护理产品组合物包含至少一种蛋白酶变体,其中至

少一种蛋白酶变体包含与SEQ ID NO:2的氨基酸序列相差不超过2、3、4、5、6、7、8、9、10、11、12、13、14、15、16、17、18、19、20、21、22、23、24或25个突变的氨基酸序列，所述突变选自：A1R,A230E,E271L,G115R,G20R,H249R,K235F,K27V/F/L,L75E,L82R,N18R,N269R,N43D,N43R,N76D,R45T,S212F,S242R,S24R,S78R,S9A,T22R,V121E,V244R,V28E,V30E,V4R，和W241R，其中该蛋白酶变体的氨基酸位置根据SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列中对应的氨基酸位置的编号方式来进行编号，这是通过该蛋白酶变体氨基酸序列与解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'氨基酸序列的比对来确定的。

[0513] 在一些实施例中，织物和家庭护理产品组合物包含至少一种蛋白酶变体，其中至少一种蛋白酶变体包含与SEQ ID NO:2的氨基酸序列相差不超过2、3、4、5、6、7、8、9、10、11、12、13、14、15、16、17、18、19、20、21、22、23、24或25个突变的氨基酸序列，所述突变选自：A1R,A230E,E271L,G115R,G20R,H249R,K235F,K27V/F/L,L75E,L82R,N18R,N269R,N43D,N43R,N76D,R45T,S212F,S242R,S24R,S78R,S9A,T22R,V121E,V244R,V28E,V30E,V4R，和W241R，并且该蛋白酶变体任选地包含至少一个选自以下的突变：S103A,G159D,Q236H,Q245R,N248D和N252K，其中该蛋白酶变体的氨基酸位置根据SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列中对应的氨基酸位置的编号方式来进行编号，这是通过该蛋白酶变体氨基酸序列与解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'氨基酸序列的比对来确定的。

[0514] 在一些实施例中，织物和家庭护理产品组合物包含至少一种蛋白酶变体，其中至少一种蛋白酶变体是具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列：X16S,X18R,X20R,X22A,X24R,X43R/D,X45T,X76D,X101A,X103G,X104L,X111V,X128N,X148I,X230E,X242R，和X249R，其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0515] 在一些实施例中，织物和家庭护理产品组合物包含至少一种蛋白酶变体，其中至少一种蛋白酶变体是具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列：A16S,N18R,G20R,T22A,S24R,N43R,N43D,R45T,N76D,S101A,S103G,V104L,L111V,S128N,L148I,A230E,S242R，和H249R，其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0516] 在一些实施例中，织物和家庭护理产品组合物包含至少一种蛋白酶变体，其中至少一种蛋白酶变体是具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列：X20R-X43R-X249R,X20R-X22R-X43R,X20R-X43R-X242R,X20R-X43R-X271L,X20R-X43R-X244R,X20R-X24R-X43R-X242R,X9A-X22R-X78R-X212F-X241R,X9A-X20R-X43R-X212F,X9A-X43R-X212F,X20R-X43R-X212F,X20R-X22R-X43R-X212F,X24R-X78R-X212F,X9A-X43R-X78R,X9A-X43R-X78R-X242R,X9A-X20R-X43R-X78R,X20R-X24R-X43R-X78R-X242R,X22R-X24R-X78R-X212F,X9A-X20R-X43R-X78R-X242R,X20R-X43R-X78R-X249R,X20R-X43R-X78R,X9A-X78R-X212F,X9A-X22R-X43R-X78R,X9A-X20R-X24R-X43R,X9A-X22R-X78R-X212F,X4R-X9A-X22R-X78R-X212F,X20R-X24R-X43R,X1R-X9A-X43R,X20R-X24R-X43R-X115R,X9A-X24R-X43R,X20R-X22R-X24R-X43R,X1R-X24R-X43R,X9A-X20R-

X24R-X43R-X242R,X9A-X20R-X22R-X78R-X212F,X9A-X24R-X43R-X244R,X9A-X24R-X43R-X242R,X4R-X9A-X22R-X24R-X212F,和X22R-X24R-X43R,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0517] 在一些实施例中,织物和家庭护理产品组合物包含至少一种蛋白酶变体,其中至少一种蛋白酶变体是具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:A1R,A230E,E271L,G115R,G20R,H249R,K235F,K27V/F/L,L75E,L82R,N18R,N269R,N43D,N43R,N76D,R45T,S212F,S242R,S24R,S78R,S9A,T22R,V121E,V244R,V28E,V30E,V4R,W241R,G20R-N43R-H249R,G20R-T22R-N43R,G20R-N43R-S242R,G20R-N43R-E271L,G20R-N43R-V244R,G20R-S24R-N43R-S242R,S9A-T22R-S78R-S212F-W241R,S9A-G20R-N43R-S212F,S9A-N43R-S212F,G20R-N43R-S212F,G20R-T22R-N43R-S212F,S24R-S78R-S212F,S9A-N43R-S78R,S9A-N43R-S78R-S242R,S9A-G20R-N43R-S78R,G20R-S24R-N43R-S78R-S242R,T22R-S24R-S78R-S212F,S9A-G20R-N43R-S78R-S242R,G20R-N43R-S78R-H249R,G20R-N43R-S78R,S9A-S78R-S212F,S9A-T22R-N43R-S78R,S9A-G20R-S24R-N43R,S9A-T22R-S78R-S212F,V4R-S9A-T22R-S78R-S212F,G20R-S24R-N43R,A1R-S9A-N43R,G20R-S24R-N43R-G115R,S9A-S24R-N43R,G20R-T22R-S24R-N43R,A1R-S24R-N43R,S9A-G20R-S24R-N43R-S242R,S9A-G20R-T22R-S78R-S212F,S9A-S24R-N43R-V244R,S9A-S24R-N43R-S242R,V4R-S9A-T22R-S24R-S212F,和T22R-S24R-N43R,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0518] 在一些实施例中,织物和家庭护理产品组合物包含至少一种蛋白酶变体,其中至少一种蛋白酶变体是具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:X101G-X103A-X104I-X232V-X245R-X248D,X101G-X103A-X104I-X159D-X232V-X245R,X101G-X103A-X104I-X159R-X232V-X245R-X248D,X101G-X103A-X104I-X159D-X232V-X245R-X248R,X101G-X103A-X104I-X232V-X245R,X101G-X103A-X104I-X232V-X245R-X248R,X101G-X103A-X104I-X159R-X232V-X245R-X248R,以及X101G,X103A,X104I,X232V,X236H,X245R,和X252K,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0519] 在一些实施例中,织物和家庭护理产品组合物包含至少一种蛋白酶变体,其中至少一种蛋白酶变体是具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:S101G-S103A-V104I-A232V-Q245R-N248D,S101G-S103A-V104I-G159D-A232V-Q245R,S101G-S103A-V104I-G159R-A232V-Q245R-N248D,S101G-S103A-V104I-G159D-A232V-Q245R-N248R,S101G-S103A-V104I-A232V-Q245R,S101G-S103A-V104I-A232V-Q245R-N248R,S101G-S103A-V104I-G159R-A232V-Q245R-N248R,S101G,S103A,V104I,A232V,Q236H,和Q245R,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0520] 在一个方面,所述组合物包含冷水蛋白酶变体,其中所述冷水蛋白酶变体是具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:X16S,X22A,X24R,X62E,X76D,X89P,X101A/G,X103G/A,X104L/I,X111V,X128N,X129E,X232V,

X148I,X158E,X159D/E,X166D,X186H,X188D,X209E,X236H,X238R,X245R,X248D/R,X249R,X252K/R,X253R,和X271F,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0521] 在一些实施例中,织物和家庭护理产品组合物包含至少一种蛋白酶变体,其中至少一种蛋白酶变体是具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:A16S,T22A,S24R,N62E,N76D,E89P,S101A/G,S103G/A,V104L/I,L111V,S128N,P129E,A232V,L148I,A158E,G159D/E,R186H,S188D,Y209E,Q236H,Q245R,N248D/R,H249R,N252K/R,T253R,和E271F,其中该枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[0522] 本发明还提供迟缓芽孢杆菌枯草杆菌蛋白酶GG36蛋白酶的蛋白酶变体,其中该迟缓芽孢杆菌枯草杆菌蛋白酶GG36蛋白酶包含SEQ ID NO:2所示氨基酸序列,其中该蛋白酶变体包含与SEQ ID NO:2的氨基酸序列相差不超过2、3、4、5、6、7、8、9、10、11、12、13、14、15、16、17、18、19、20、21、22、23、24或25个突变的氨基酸序列,所述突变选自A16S,T22A,S24R,N62E,N76D,E89P,S101A/G,S103G/A,V104L/I,L111V,S128N,P129E,A232V,L148I,A158E,G159D/E,R186H,S188D,Y209E,Q236H,Q245R,N248D/R,H249R,N252K/R,T253R,和E271F,其中该蛋白酶变体的氨基酸位置根据SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列中对应的氨基酸位置的编号方式来进行编号,这是通过该蛋白酶变体氨基酸序列与解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'氨基酸序列的比对来确定的。

[0523] 在一些实施例中,织物和家庭护理产品组合物包含至少一种蛋白酶变体,该蛋白酶变体包含与SEQ ID NO:2的氨基酸序列相差不超过2、3、4、5、6、7、8、9、10、11、12、13、14、15、16、17、18、19、20、21、22、23、24或25个突变的氨基酸序列,所述突变选自:A16S,T22A,S24R,N62E,N76D,E89P,S101A/G,S103G/A,V104L/I,L111V,S128N,P129E,A232V,L148I,A158E,G159D/E,R186H,S188D,Y209E,Q236H,Q245R,N248D/R,H249R,N252K/R,T253R,和E271F,其中该蛋白酶变体的氨基酸位置根据SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列中对应的氨基酸位置的编号方式来进行编号,这是通过该蛋白酶变体氨基酸序列与解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'氨基酸序列的比对来确定的。

[0524] 本发明还提供迟缓芽孢杆菌枯草杆菌蛋白酶GG36蛋白酶的蛋白酶变体,其中该迟缓芽孢杆菌枯草杆菌蛋白酶GG36蛋白酶包含SEQ ID NO:2所示氨基酸序列,其中该蛋白酶变体包含与SEQ ID NO:2的氨基酸序列相差不超过2、3、4、5、6、7、8、9、10、11、12、13、14、15、16、17、18、19、20、21、22、23、24或25个突变的氨基酸序列,所述突变选自A16S,T22A,S24R,N62E,N76D,E89P,S101A/G,S103G/A,V104L/I,L111V,S128N,P129E,A232V,L148I,A158E,G159D/E,R186H,S188D,Y209E,Q236H,Q245R,N248D/R,H249R,N252K/R,T253R,和E271F,其中该蛋白酶变体的氨基酸位置根据SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列中对应的氨基酸位置的编号方式来进行编号,这是通过该蛋白酶变体氨基酸序列与解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'氨基酸序列的比对来确定的。

[0525] 在一些实施例中,织物和家庭护理产品组合物包含至少一种蛋白酶变体,该蛋白酶变体包含与SEQ ID NO:2的氨基酸序列不同的氨基酸序列,并且其中该蛋白酶变体的总净电荷相对于迟缓芽孢杆菌枯草杆菌蛋白酶GG36蛋白酶的总净电荷为0、+1、+2、+3、+4、+5、-1、-2、-3、-4或-5,并且其中该蛋白酶变体的氨基酸位置根据SEQ ID NO:1所示解淀粉芽

孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列中对应的氨基酸位置的编号方式来进行编号，这是通过该蛋白酶变体氨基酸序列与解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'氨基酸序列的比对来确定的。

[0526] 在一些实施例中，织物和家庭护理产品组合物包含至少一种蛋白酶变体，该蛋白酶变体包含与SEQ ID NO:2的氨基酸序列相差不超过2、3、4、5、6、7、8、9、10、11、12、13、14、15、16、17、18、19、20、21、22、23、24或25个突变的氨基酸序列，所述突变选自：A1R,Q2S,V4R,V4S,S9A,R10S,P14K,A16S,H17R,N18R,G20R,T22A,T22R,S24R,S24W,G25R,G25V,V26F,L42I,N43R,N43A,G46R,P52F,P52E,P52N,T57R,Q59A,N62E,N62Q,V68A,V68C,T71G,I72C,A74C.L75A,L75F,L75R,N76D,S78R,L82R,P86W,E89P,E89T,E89G,E89H,E89I,E89V,E89W,Y91N,K94N,G100S,S101A,S101N,S101G,S101D,S103G,S103N,V104L,V104I,S106V,S106G,A108I,L111V,E112V,G115K,G115R,N117F,G118I,V121F,S128D,S128F,S128L,S128N,P129E,S144R,L148I,A158E,G159E,S160D,S166D,N185E,N185I,R186H,S188E,S188D,D197F,V203E,Y209S,Y209N,Y209F,Y209T,Y209E,Y209H,Y209G,P210R,S212I,S212F,Y214F,A215N,A215D,A215E,L217E,L217N,T224A,A230E,A231I,Q236F,N238R,N238K,P239K,P239G,P239R,P239S,W241R,S242R,S242L,N243R,V244R,N248I,N248V,H249R,L250I,N252R,T253R,L262D,Y263F,S265F,L267V,L267N.N269I,N269R,E271F,E271I,E271H,E271P,E271T,E271V,E271L和A272F，并且该蛋白酶变体任选地包含至少一个选自以下的突变：S103A,G159D,Q236H,Q245R,N248D和N252K，其中该蛋白酶变体的氨基酸位置根据SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列中对应的氨基酸位置的编号方式来进行编号，这是通过该蛋白酶变体氨基酸序列与解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'氨基酸序列的比对来确定的。

[0527] 在一些实施例中，织物和家庭护理产品组合物包含至少一种蛋白酶变体，该蛋白酶变体包含与SEQ ID NO:2的氨基酸序列相差不超过2、3、4、5、6、7、8、9、10、11、12、13、14、15、16、17、18、19、20、21、22、23、24或25个突变的氨基酸序列，所述突变选自：A16S,T22A,S24R,N62E,N76D,E89P,S101A/G,S103G/A,V104L/I,L111V,S128N,P129E,A232V,L148I,A158E,G159D/E,R186H,S188D,Y209E,Q236H,Q245R,N248D/R,H249R,N252K/R,T253R，和E271F，其中该蛋白酶变体的氨基酸位置根据SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列中对应的氨基酸位置的编号方式来进行编号，这是通过该蛋白酶变体氨基酸序列与解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'氨基酸序列的比对来确定的。

[0528] 在一些实施例中，织物和家庭护理产品组合物包含至少一种蛋白酶变体，该蛋白酶变体包含与SEQ ID NO:2的氨基酸序列相差不超过2、3、4、5、6、7、8、9、10、11、12、13、14、15、16、17、18、19、20、21、22、23、24或25个突变的氨基酸序列，所述突变选自：A1R,A230E,E271L,G115R,G20R,H249R,K235F,K27V/F/L,L75E,L82R,N18R,N269R,N43D,N43R,N76D,R45T,S212F,S242R,S24R,S78R,S9A,T22R,V121E,V244R,V28E,V30E,V4R，和W241R，其中该蛋白酶变体的氨基酸位置根据SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列中对应的氨基酸位置的编号方式来进行编号，这是通过该蛋白酶变体氨基酸序列与解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'氨基酸序列的比对来确定的。

[0529] 在一些实施例中，织物和家庭护理产品组合物包含至少一种蛋白酶变体，该蛋白酶变体包含与SEQ ID NO:2的氨基酸序列不同的氨基酸序列，其中所述蛋白酶变体包含与

SEQ ID NO:2的氨基酸序列相差不超过2、3、4、5、6、7、8、9、10、11、12、13、14、15、16、17、18、19、20、21、22、23、24或25个突变的氨基酸序列，所述突变选自：A1R,A230E,E271L,G115R,G20R,H249R,K235F,K27V/F/L,L75E,L82R,N18R,N269R,N43D,N43R,N76D,R45T,S212F,S242R,S24R,S78R,S9A,T22R,V121E,V244R,V28E,V30E,V4R，和W241R，并且该蛋白酶变体任选地包含至少一个选自以下的突变：S103A,G159D,Q236H,Q245R,N248D和N252K，其中该蛋白酶变体的氨基酸位置根据SEQ ID NO:1所示解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'的氨基酸序列中对应的氨基酸位置的编号方式来进行编号，这是通过该蛋白酶变体氨基酸序列与解淀粉芽孢杆菌枯草杆菌蛋白酶BPN'氨基酸序列的比对来确定的。

[0530] 在一些实施例中，织物和家庭护理产品组合物包含至少一种蛋白酶变体，该蛋白酶变体包含两个或多个以下的突变：V4R,H17R,N18R,G20R,T22R,S24R,S24W,G25R,N43R,N43A,G46R,P52F,P52N,T57R,Q59A,N62Q,T71G,L75R,N76D,S78R,L82R,P86W,E89P,E89W,E89T,E89I,E89H,E89V,V104L,S106V,S106G,G115R,G118I,V121F,S144R,N185I,D197F,Y209N,Y209S,L217E,A231I,P239R,P239S,W241R,S242R,S242L,N243R,V244R,N248I,H249R,N252R,T253R,E271T,E271V,E271L,E271H,E271F,E271P,A1R,S9A,S212F和N269R；和/或一个或多个以下的突变组：T022R-S024R,S009A-E271L,N018R-W241R,N018R-G115R,N043R-H249R,G020R-H249R,V004R-H249R,G020R-S024R,N018R-H249R,S009A-G020R,G020R-W241R,S009A-S078R,G020R-G115R,N018R-S024R,S024R-S242R,T022R-G115R,N018R-N043R,G020R-N043R,N018R-S242R,S242R-N269R,N018R-V244R,S024R-N269R,G020R-E271L,S024R-E271L,V004R-S009A,G020R-N269R,A001R-S024R,V244R-E271L,S009A-N018R,W241R-E271L,V004R-S024R,S009A-H249R,S009A-T022R,S101G-S103A-V104I-G159D-A232V-Q245R-N248D-E271F,S101G-S103A-V104I-A158E-A232V-Q245R-N248D-E271F,S101G-S103A-V104I-A158E-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-G159D-A232V-Q245R-N248D-S24R,S101G-S103A-V104L-G159D-A232V-Q236H-Q245R-N252K和S101G-S103A-V104L-A232V-Q236H-Q245R-N248D-N252K；其中该至少一种蛋白酶变体相对于具有SEQ ID NO:2的氨基酸序列的迟缓芽孢杆菌枯草杆菌蛋白酶GG36蛋白酶具有0、-1、-2、-3、-4或-5的总净电荷。

[0531] 在一些实施例中，织物和家庭护理产品组合物包含至少一种蛋白酶变体，该蛋白酶变体包含至少一种辅助材料，其选自包含香料的胶囊、调色剂、表面活性剂、助洗剂、螯合剂、染料转移抑制剂、分散剂、其他酶、酶稳定剂、催化材料、漂白活化剂、过氧化氢、过氧化氢源、预制过酸、聚合物分散剂、粘土去除/抗再沉淀剂、增白剂、抑泡剂、染料、香料、结构增塑剂、织物软化剂、载体、水溶助长剂、加工助剂、溶剂、颜料以及它们的混合物。

[0532] 在一些实施例中，织物和家庭护理产品组合物包含至少一种辅助材料，其选自香料胶囊；织物调色剂；冷水可溶性增白剂；漂白催化剂，漂白催化剂可包括选自以下的材料：亚铵阳离子、亚铵聚离子、亚铵两性离子、改性的胺、改性的氧化胺、N-磺酰基亚胺、N-膦酰基亚胺、N-酰基亚胺、噻二唑二氧化物、全氟亚胺、环状糖酮以及它们的混合物；第一洗涤脂肪酶first wash lipase)；细菌清洁纤维素酶；格尔贝特(Guerbet)非离子表面活性剂；以及它们的混合物。

[0533] 在一些实施例中，包含至少一种蛋白酶变体的织物和家庭护理产品组合物还包含至少一种另外的非免疫等同蛋白酶，其选自枯草杆菌蛋白酶(EC 3.4.21.62)、胰蛋白酶样

或胰凝乳蛋白酶样蛋白酶、金属蛋白酶以及它们的混合物。

[0534] 在一些实施例中，包含至少一种蛋白酶变体的织物和家庭护理产品组合物还包含至少一种另外的非免疫等同蛋白酶，其选自：衍生自枯草芽孢杆菌、解淀粉芽孢杆菌、短小芽孢杆菌(B.pumilus)和吉氏芽孢杆菌(B.gibsonii)的枯草杆菌蛋白酶(EC 3.4.21.62)；衍生自纤维单胞菌属(Cellulomonas)的胰蛋白酶和/或胰凝乳蛋白酶；衍生自解淀粉芽孢杆菌的金属蛋白酶；以及它们的混合物。

[0535] 在一些实施例中，包含至少一种蛋白酶变体的织物和家庭护理产品组合物还包含至少一种另外的酶，其选自半纤维素酶、过氧化物酶、蛋白酶、纤维素酶、纤维二糖脱氢酶、木葡聚糖酶、木聚糖酶、脂肪酶、磷脂酶、酯酶、角质酶、果胶酶、甘露聚糖酶、果胶酸裂解酶、角蛋白酶、还原酶、氧化酶、酚氧化酶、脂加氧酶、木质素酶、支链淀粉酶、鞣酸酶、戊聚糖酶、地衣聚糖酶、葡聚糖酶、阿拉伯糖苷酶、透明质酸酶、软骨素酶、漆酶、淀粉酶以及它们的混合物。

[0536] 在一些实施例中，包含至少一种蛋白酶变体的织物和家庭护理产品组合物还包含至少一种另外的酶，其选自第一洗涤脂肪酶、α-淀粉酶、细菌清洁纤维素酶以及它们的混合物。

[0537] 在一些实施例中，包含至少一种蛋白酶变体的织物和家庭护理产品组合物还包含以下组分中的至少一者：包含香料的胶囊，其包括香料微胶囊；调色剂，其包括选自以下的材料：碱性、酸性、疏水性、直接和聚合的染料，和峰值吸收波长为550nm至650nm的染料缀合物，以及它们的混合物；去污表面活性剂，其包括选自以下的材料：阴离子去污表面活性剂、非离子去污表面活性剂、阳离子去污表面活性剂、两性离子去污表面活性剂和两性去污表面活性剂以及它们的混合物；助洗剂，其包括选自以下的材料：沸石、磷酸盐以及它们的混合物；硅酸盐，其包括选自以下的材料：硅酸钠、硅酸钾以及它们的混合物；增白剂，其包括选自以下的材料：冷水可溶性增白剂以及它们的混合物；羧酸盐聚合物，其包括选自以下的材料：马来酸/丙烯酸随机共聚物或聚丙烯酸均聚物以及它们的混合物；去垢性聚合物，其包括选自以下的材料：对苯二甲酸共聚物以及它们的混合物；纤维素聚合物，其包括选自以下的材料：烷基纤维素、烷基烷氧基烷基纤维素、羧基烷基纤维素、烷基羧基烷基纤维素以及它们的混合物；漂白催化剂，其包括选自以下的材料：亚铵阳离子、亚铵聚离子、亚铵两性离子、改性的胺、改性的氧化胺、N-磺酰基亚胺、N-膦酰基亚胺、N-酰基亚胺、噻二唑二氧化物、全氟亚胺、环状糖酮以及它们的混合物；漂白活化剂，其包括选自以下的材料：十二烷酰氧基苯磺酸盐、癸酰氧基苯磺酸盐、癸酰氧基苯甲酸或它们的盐、3,5,5-三甲基己酰氧基苯磺酸盐、四乙酰基乙二胺(TAED)、壬酰氧基苯磺酸盐(NOBS)以及它们的混合物；过氧化氢源，其包括选自以下的材料：无机过氧化氢合物盐(包括碱金属盐例如过硼酸(通常为单水合物或四水合物)、过碳酸、过硫酸、过磷酸、过硅酸盐的钠盐)以及它们的混合物；螯合剂，其包括选自以下的材料：DTPA(二乙烯三胺五乙酸)、HEDP(羟基乙叉二膦酸)、DTPMP(二乙烯三胺五(甲叉膦酸))、乙二胺二琥珀酸(EDDS)、1,2-二羟基苯-3,5-二磺酸二钠盐水合物、所述螯合剂的衍生物以及它们的混合物。

[0538] 在一些实施例中，包含至少一种蛋白酶变体的织物和家庭护理产品组合物包含织物调色剂，该织物调色剂选自染料；包含至少一种阳离子-碱性染料和蒙脱石粘土的染料-粘土缀合物；以及它们的混合物。

[0539] 在一些实施例中，包含至少一种蛋白酶变体的织物和家庭护理产品组合物包含至少一种织物调色剂，该织物调色剂选自小分子染料、聚合物染料以及它们的混合物；包含至少一种阳离子-碱性染料和蒙脱石粘土的染料-粘土缀合物；以及它们的混合物。

[0540] 在一些实施例中，包含至少一种蛋白酶变体的织物和家庭护理产品组合物以单隔室或多隔室单位剂量提供。在一些实施例中，该组合物是多隔室单位剂量，其中该蛋白酶变体处于与任何过氧化氢源和/或螯合剂和/或另外的酶不同的隔室中。

[0541] 在一些实施例中，包含至少一种蛋白酶变体的织物和家庭护理产品组合物包含洗涤液体，其中至少一种蛋白酶变体包含两个或多个以下的突变：A1R,Q2S,V4R,V4S,S9A,R10S,P14K,A16S,T22A,T22R,S24R,G25V,V26F,L42I,P52F,P52E,P52N,N62E,N62Q,V68A,V68C,T71G,I72C,A74C.L75A,L75F,S78R,E89P,E89T,E89G,E89H,E89W,Y91N,K94N,G100S,S101A,S101N,S101G,S101D,S103G,S103N,V104L,V104I,A108I,L111V,E112V,G115K,N117F,V121F,S128D,S128F,S128L,S128N,P129E,L148I,A158E.G159E,S160D,S166D,N185E,R186H,S188E,S188D,V203E,Y209S,Y209N,Y209F,Y209T,Y209E,Y209H,Y209G,P210R,S212I,S212F,Y214F,A215N,A215D,A215E,L217E,L217N,T224A,A230E,A231I,Q236F,N238R,N238K,P239K,P239G,P239R,N248V,H249R,L250I,L262D,Y263F,S265F,L267V,L267N,N269I,N269R,E271F,E271I,E271H和A272F；和/或一个或多个以下的突变组：N062E-P129E,N062E-G159E,A016S-L148I,A158E-H249R,A016S-N062E,L111V-S188D,T022A-N062E,N062E-L148I,T022A-P129E,N062E-E271F,N062E-A158E,A016S-G159E,N062E-R186H,S128N-G159E,N062E-S188D,N062E-S128N,L148I-G159E,S103G-A158E,L111V-G159E,A158E-E271F,A016S-S188D,T022A-L111V,S128N-A158E,A016S-A158E,V104L-A158E,S128N-R186H,G159E-Y209E,N062E-S101A,L111V-Y209E,L148I-S188D,S101A-Y209E,T022A-S188D,A016S-T022A,S128N-P129E,A016S-Y209E,A016S-S128N,T022A-E089P,S128N-Y209E,E089P-A158E,N062E-S103G,R186H-E271F,A016S-P129E,E089P-G159E,L111V-H249R,S101A-P129E,L148I-Y209E,T022A-G159E,P129E-H249R,P129E-Y209E,V104L-P129E,S128N-S188D,L111V-A158E,T022A-A158E,N062E-Y209E,N062E-H249R,S101A-R186H,E089P-P129E,P129E-E271F,T22A-L111V-G159E,S101A-S103G-V104L-Y209E,S101A-S103G-V104L-G159E,S101A-S103G-V104L-S188D,S101G-S103A-V104I-G159D,T22A-S103G-G159E,T22A-S128N-E271F-Y209E,T22A-Y209E-E271F,T22A-S101A-Y209E,S101A-Y209E-E271F,T22A-L111V-S128N,T22A-S101A-G159E,S101A-S103G-V104L,T22A-S101A-S103G-V104L,S101A-S103G-V104L,S101G-S103A-V104I,S101A-S103G-V104L-S128N,S103A-V104I-G159D-A232V-Q236H-Q245R-N248D-N252K,S101G-V104I-G159D-A232V-Q236H-Q245R-N248D-N252K,S101G-S103A-G159D-A232V-Q236H-Q245R-N248D-N252K,S101G-S103A-V104L-A232V-Q236H-Q245R-N248D-N252K,S101G-S103A-V104L-G159D-Q236H-Q245R-N248D-N252K,S101G-S103A-V104L-G159D-A232V-Q245R-N248D-N252K,S101G-S103A-V104L-G159D-A232V-Q236H-N248D-N252K,S101G-S103A-V104L-G159D-A232V-Q236H-Q245R-N252K,S101G-S103A-V104L-G159D-A232V-Q236H-Q245R-N248D,N62E-S101G-S103A-V104I-G159D-A232V-Q245R-N248D-E271F,N62E-S101G-S103A-V104I-G159D-A232V-Q245R-N248D-H249R,T22A-S101G-S103A-V104I-G159D-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-G159D-A232V-Q245R-N248D-S24R,S101G-S103A-

V104I-G159D-A232V-Q245R-N248D-T253R,S101G-S103A-V104I-A158E-A232V-Q245R-N248D-H249R,T22A-S101G-S103A-V104I-G159D-A232V-Q245R-N248D-E271F,S101G-S103A-V104I-G159E-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-G159D-A232V-Q245R-N248D-N238R,S101G-S103A-V104I-A158E-A232V-Q245R-N248D-E271F,S101G-S103A-V104I-G159D-A232V-Q245R-N248D,S101G-S103A-V104I-G159D-A232V-Q245R-N248D-E271F,S101G-S103A-V104I-G159D-A232V-Q245R-N248D-N76D和S101G-S103A-V104I-G159E-A232V-Q245R-N248D-E271F;所述冷水蛋白酶变体相对于具有SEQ ID NO:1的氨基酸序列的迟缓芽孢杆菌枯草杆菌蛋白酶GG36蛋白酶具有+1、0、-1、-2、-3、-4或-5的总净电荷;并且其中洗涤液体具有约0.1mS/cm至约3mS/cm、约0.3mS/cm至约2.5mS/cm或甚至约0.5mS/cm至约2mS/cm的电导率。

[0542] 在一些实施例中,包含至少一种蛋白酶变体的织物和家庭护理产品组合物包含洗涤液体,该洗涤液体包含辅助材料,其中至少一种蛋白酶变体包含两个或多个以下的突变:V4R,H17R,N18R,G20R,T22R,S24R,S24W,G25R,N43R,N43A,G46R,P52F,P52N,T57R,Q59A,N62Q,T71G,L75R,N76D,S78R,L82R,P86W,E89P,E89W,E89T,E89I,E89H,E89V,V104L,S106V,S106G,G115R,G118I,V121F,S144R,N185I,D197F,Y209N,Y209S,L217E,A231I,P239R,P239S,W241R,S242R,S242L,N243R,V244R,N248I,H249R,N252R,T253R,E271T,E271V,E271L,E271H,E271F,E271P,A1R,S9A,S212F和N269R;和/或一个或多个以下的突变组:T022R-S024R,S009A-E271L,N018R-W241R,N018R-G115R,N043R-H249R,G020R-H249R,V004R-H249R,G020R-S024R,N018R-H249R,S009A-G020R,G020R-W241R,S009A-S078R,G020R-G115R,N018R-S024R,S024R-S242R,T022R-G115R,N018R-N043R,G020R-N043R,N018R-S242R,S242R-N269R,N018R-V244R,S024R-N269R,G020R-E271L,S024R-E271L,V004R-S009A,G020R-N269R,A001R-S024R,V244R-E271L,S009A-N018R,W241R-E271L,V004R-S024R,S009A-H249R,S009A-T022R,S101G-S103A-V104I-G159D-A232V-Q245R-N248D-E271F,S101G-S103A-V104I-A158E-A232V-Q245R-N248D-E271F,S101G-S103A-V104I-A158E-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-G159D-A232V-Q245R-N248D-S24R,S101G-S103A-V104L-G159D-A232V-Q236H-Q245R-N252K和S101G-S103A-V104L-A232V-Q236H-Q245R-N248D-N252K,所述冷水蛋白酶变体相对于具有SEQ ID NO:2的氨基酸序列的迟缓芽孢杆菌枯草杆菌蛋白酶GG36蛋白酶具有0、+1、+2、+3、+4或+5的总净电荷;并且所述衣物洗涤剂洗涤液体具有约3mS/cm至约30mS/cm、约3.5mS/cm至约20mS/cm或甚至约4mS/cm至约10mS/cm的电导率。

[0543] 在一些实施例中,包含至少一种蛋白酶变体的织物和家庭护理产品组合物包含一种或多种以下成分(基于总组合物重量计):约0.0005重量%至约0.1重量%、约0.001重量%至约0.05重量%或甚至约0.002重量%至约0.03重量%的所述冷水蛋白酶变体;以及一种或多种以下成分:约0.00003重量%至约0.1重量%的织物调色剂、约0.001重量%至约5重量%的香料胶囊、约0.001重量%至约1重量%的冷水可溶性增白剂、约0.00003重量%至约0.1重量%的漂白催化剂、约0.00003重量%至约0.1重量%的第一洗涤脂肪酶、约0.00003重量%至约0.1重量%的细菌清洁纤维素酶和/或约0.05重量%至约20重量%的格尔贝特非离子表面活性剂。

[0544] 在一些实施例中,织物和家庭护理产品组合物是不包含冷水蛋白酶的颗粒状或粉

末衣物洗涤剂。

[0545] 在一些实施例中，织物和家庭护理产品组合物是液体衣物洗涤剂、盘碟洗涤剂。

[0546] 意在使织物和家庭护理产品以任何合适的形式(包括流体或固体)提供。织物和家庭护理产品可以是单位剂量小袋的形式，尤其是液体的形式时，并且通常织物和家庭护理产品为至少部分地或甚至完全地被水溶性小袋封闭。此外，在包含至少一种蛋白酶变体的织物和家庭护理产品的一些实施例中，织物和家庭护理产品可以具有上面详述的参数和/或特性的任何组合。

[0547] 清洁组合物

[0548] 除非另作说明，否则本文提供的所有组分或组合物水平都是指所述组分或组合物的活性水平，而且市售来源中可能存在的杂质(例如残余溶剂或副产物)不包括在内。酶组分重量是以总活性蛋白质计。除非另作说明，否则所有百分比和比率都以重量计算。除非另作说明，否则所有百分比和比率都是以总组合物计算。在示例性的洗涤剂组合物中，酶水平是以纯酶占总组合物的重量比表示，并且除非另作规定，否则洗涤剂成分是以占总组合物的重量比表示。

[0549] 如本文所指出，在一些实施例中，本发明的清洁组合物还包含辅助材料，包括但不限于：表面活性剂、助洗剂、漂白剂、漂白活化剂、漂白催化剂、其他酶、酶稳定系统、螯合剂、荧光增白剂、去垢性聚合物、染料转移剂、分散剂、抑泡剂、染料、香料、着色剂、填料盐、水溶助长剂、光活化剂、荧光剂、织物调理剂、可水解表面活性剂、防腐剂、抗氧化剂、抗收缩剂、抗皱剂、杀菌剂、杀真菌剂、色粒、银护理剂、抗晦暗剂和/或抗腐蚀剂、碱度源、增溶剂、载体、加工助剂、颜料和pH控制剂(参见例如美国专利No.6,610,642、No.6,605,458、No.5,705,464、No.5,710,115、No.5,698,504、No.5,695,679、No.5,686,014和No.5,646,101，所有专利都以引用的方式并入本文)。特定清洁组合物材料的实施例在下文中举例说明。在清洁辅助材料与清洁组合物中的本发明变体蛋白酶不相容的实施例中，则使用合适的方法保持清洁辅助材料与蛋白酶分离(即，相互不接触)，直到两种组分适宜进行组合为止。这种分离方法包括本领域已知的任何合适方法(例如明胶胶囊法(gelcap)、包封法、片剂法、物理分离法等)。

[0550] 有利地，本发明的清洁组合物用于例如洗衣应用、硬质表面清洁、盘碟洗涤应用，以及美容应用，如假牙、牙齿、毛发和皮肤。此外，由于在较低温度溶液中效用提高的独特优势，本发明的酶理想地适合于衣物洗涤应用。此外，本发明的酶可用于颗粒状和液体组合物。

[0551] 本发明的变体蛋白酶还可用于清洁添加剂产品。在一些实施例中，可使用低温溶液清洁应用。在一些实施例中，本发明提供清洁添加剂产品，其包含至少一种本发明的酶，当需要额外漂白效用时，该清洁添加剂产品理想地适于包括在洗涤过程中。此类情形包括但不限于低温溶液清洁应用。在一些实施例中，添加剂产品为其最简单的形式，即一种或多种蛋白酶。在一些实施例中，添加剂被包装成用于添加到清洁过程中的剂型。在一些实施例中，添加剂被包装成用于添加到其中采用过氧源并需要增加的漂白效用的清洁过程中的剂型。任何合适的单一剂量单位形式都可用于本发明，包括但不限于：丸剂、片剂、明胶胶囊，或其他单一剂量单位例如预先计量的粉末或液体。在一些实施例中，包括填料或载体材料以增加所述组合物的体积。合适的填料或载体材料包括但不限于各种硫酸盐、碳酸盐和硅

酸盐，以及滑石、粘土等。适于液体组合物的填料或载体材料包括但不限于水或低分子量伯醇和仲醇，包括多元醇和二醇。这些醇的例子包括但不限于甲醇、乙醇、丙醇和异丙醇。在一些实施例中，组合物含有约5％至约90％的这类材料。酸性填料可用于降低pH。或者，在一些实施例中，清洁添加剂包含辅助成分，下文将予以更完整地描述。

[0552] 本发明清洁组合物和清洁添加剂需要有效量的本文所提供蛋白酶变体中的至少一种，其单独使用或与其他蛋白酶和/或另外的酶组合。所需的酶水平通过添加一种或多种本发明的蛋白酶变体来实现。通常，本发明清洁组合物包含至少约0.0001重量％、约0.0001至约10重量％、约0.001至约1重量％或甚至约0.01至约0.1重量％的至少一种本发明变体蛋白酶。

[0553] 通常将本文的清洁组合物配制成使得在水性清洁操作中使用期间，洗涤水的pH将为约5.0至约11.5或甚至约7.5至约10.5。液体产品制剂通常配制成净pH为约3.0至约9.0或甚至约3至约5。颗粒状洗衣用产品通常配制成pH为约9至约11。用于将pH控制在推荐的使用水平的技术包括使用缓冲液、碱、酸等，并且这些技术是本领域技术人员众所周知的。

[0554] 合适的“低pH清洁组合物”的净pH通常为约3至约5，并且通常不含在这种pH环境中水解的表面活性剂。这类表面活性剂包括包含至少一个环氧乙烷部分或甚至约1至约16摩尔的环氧乙烷的烷基硫酸钠表面活性剂。这类清洁组合物通常包含足量的pH调节剂，如氢氧化钠、单乙醇胺或盐酸，用以使此类清洁组合物的净pH为约3至约5。这些组合物通常包含至少一种酸稳定性酶。在一些实施例中，所述组合物为液体，而在其他实施例中，其为固体。这类液体组合物的pH通常是以净pH测量。这类固体组合物的pH是以所述组合物的10％固形物溶液测量，其中溶剂是蒸馏水。在这些实施例中，除非另作说明，否则所有pH测量值都是在20℃下取得。

[0555] 在一些实施例中，当颗粒组合物或液体中采用变体蛋白酶时，期望变体蛋白酶为封装颗粒的形式，以在存储过程中保护变体蛋白酶免受该颗粒组合物的其他组分的影响。此外，封装还是控制变体蛋白酶在清洁过程期间的利用度的方式。在一些实施例中，封装可增强变体蛋白酶和/或另外的酶的性能。就这一点而言，本发明的变体蛋白酶用本领域已知的任何合适的封装材料进行封装。在一些实施例中，封装材料通常包封本发明变体蛋白酶的催化剂的至少一部分。通常，封装材料是水溶性的和/或水分散性的。在一些实施例中，封装材料的玻璃化转变温度(Tg)为0℃或更高。玻璃化转变温度在WO 97/11151中进行了更详细的描述。封装材料通常选自以下：碳水化合物、天然的或合成的树胶、甲壳质、壳聚糖、纤维素和纤维素衍生物、硅酸盐、磷酸盐、硼酸盐、聚乙烯醇、聚乙二醇、石蜡以及它们的组合。当封装材料是碳水化合物时，其通常选自单糖、寡糖、多糖以及它们的组合。在一些典型的实施例中，封装材料是淀粉(例如参见EP 0 922 499;US 4,977,252;US 5,354,559;和US 5,935,826)。在一些实施例中，封装材料是由塑料例如热塑性塑料、丙烯腈、甲基丙烯腈、聚丙烯腈、聚甲基丙烯腈以及它们的混合物制成的微球体;适用的市售微球体包括但不限于以EXPANCEL®(瑞典斯Stockviksverke)和PM 6545、PM6550、PM 7220、PM 7228、EXTENDOSPHERES®、LUXSIL®、Q-CEL®和SPHERICEL®(宾夕法尼亚州福吉谷PQ公司(PQ Corp.,Valley Forge,PA))供应的那些微球体。

[0556] 如本文所述，本发明的变体蛋白酶尤其可用于清洁行业，包括但不限于衣物和盘

碟洗涤剂。这些应用使酶处于各种环境压力下。本发明的变体蛋白酶由于其在各种条件下的稳定性，提供了优于多种当前使用的酶的优点。

[0557] 实际上，洗涤中所涉及的蛋白酶会暴露于多种洗涤条件，包括不同的洗涤剂制剂、洗涤水体积、洗涤水温度和洗涤时间长度。此外，不同地理区域中使用的洗涤剂制剂在洗涤水中存在不同浓度的其相关组分。例如，欧洲的洗涤剂通常在洗涤水中具有约4500-5000ppm的洗涤剂组分，而日本的洗涤剂通常在洗涤水中具有大约667ppm的洗涤剂组分。在北美，尤其是在美国，洗涤剂通常在洗涤水中存在约975ppm的洗涤剂组分。

[0558] 低洗涤剂浓度系统包括在洗涤水中存在少于约800ppm的洗涤剂组分的洗涤剂。日本的洗涤剂通常被认为是低洗涤剂浓度系统，因为其在洗涤水中存在大约667ppm的洗涤剂组分。

[0559] 中等洗涤剂浓度包括在洗涤水中存在介于约800ppm至约2000ppm之间的洗涤剂组分的洗涤剂。北美的洗涤剂一般被认为是中等洗涤剂浓度系统，因为其在洗涤水中存在大约975ppm的洗涤剂组分。巴西通常在洗涤水中存在大约1500ppm的洗涤剂组分。

[0560] 高洗涤剂浓度系统包括在洗涤水中存在超过约2000ppm的洗涤剂组分的洗涤剂。欧洲的洗涤剂一般被认为是高洗涤剂浓度系统，因为其在洗涤水中具有大约4500-5000ppm的洗涤剂组分。

[0561] 拉丁美洲的洗涤剂一般是高泡磷酸盐助洗剂洗涤剂，而且拉丁美洲中使用的洗涤剂的范围可在中等洗涤剂浓度至高洗涤剂浓度之间，因为其在洗涤水中具有1500ppm至6000ppm的洗涤剂组分。如上所述，巴西通常在洗涤水中存在大约1500ppm的洗涤剂组分。然而，其他高泡磷酸盐助洗剂洗涤剂地理区域(不限于其他拉丁美洲国家)也可具有在洗涤水中存在最高达约6000ppm的洗涤剂组分的高洗涤剂浓度系统。

[0562] 按照前述内容，很明显在全世界范围内，典型洗涤溶液中洗涤剂组合物的浓度在低于约800ppm洗涤剂组合物(“低洗涤剂浓度地理区域”，例如在日本约667ppm)至介于约800ppm至约2000ppm之间(“中等洗涤剂浓度地理区域”，例如在美国约975ppm，在巴西约1500ppm)再到高于约2000ppm(“高洗涤剂浓度地理区域”，例如在欧洲约4500ppm至约5000ppm，以及在高泡磷酸盐助洗剂地理区域中约6000ppm)间变动。

[0563] 典型的洗涤溶液的浓度凭经验确定。例如，在美国，典型洗涤机器容纳约64.4L体积的洗涤溶液。因此，为了在洗涤溶液内获得约975ppm的洗涤剂浓度，须将约62.79g洗涤剂组合物添加至64.4L洗涤溶液中。这个量是由消费者使用随洗涤剂一起提供的量杯计量加到洗涤水中的典型量。

[0564] 再举个例子，不同地理区域使用不同的洗涤温度。日本的洗涤水温度通常低于欧洲所用的洗涤水温度。例如，北美和日本的洗涤水温度通常介于约10℃至约30℃之间(例如为约20℃)，而欧洲的洗涤水温度通常介于约30℃至约60℃之间(例如为约40℃)。然而，为了节省能源，许多消费者转向使用冷水洗涤。此外，在一些另外的区域中，通常将冷水用于洗衣以及餐具洗涤应用。在一些实施例中，本发明的“冷水洗涤”利用适用于在约10℃至约40℃，或约20℃至约30℃，或约15℃至约25℃，以及在约15℃至约35℃范围内的所有其他组合和在10℃至40℃内的所有范围的温度下进行洗涤的“冷水洗涤剂”。

[0565] 再举个例子，不同地理区域通常具有不同的水硬度。水硬度通常以每加仑混合的Ca^{2+}/Mg^{2+}的格令数来描述。硬度是水中钙(Ca^{2+})和镁(Mg^{2+})的量的量度。在美国，大多数水都

较硬，但硬度有波动。中等硬(60-120ppm)至硬(121-181ppm)水具有60至181ppm(ppm换算成每美制加仑格令数是ppm数除以17.1等于每加仑格令数)硬度的矿物质。

[0566]

水	每加仑格令数	份每一百万份
软	小于 1.0	小于 17
略硬	1.0 至 3.5	17 至 60
中等硬	3.5 至 7.0	60 至 120

[0567]

硬	7.0 至 10.5	120 至 180
极硬	大于 10.5	大于 180

[0568] 欧洲的水硬度通常是每加仑的混合的Ca^{2+}/Mg^{2+}高于约10.5(例如约10.5至约20.0)格令(例如每加仑的混合的Ca^{2+}/Mg^{2+}为约15格令)。北美的水硬度通常高于日本的水硬度，但小于欧洲的水硬度。例如，北美的水硬度可介于约3至约10格令、约3至约8格令之间或为约6格令。日本的水硬度通常小于北美的水硬度，通常小于约4，例如每加仑混合的Ca^{2+}/Mg^{2+}为约3格令。

[0569] 因此，在一些实施例中，本发明提供的变体蛋白酶在至少一组洗涤条件(如水温、水硬度和/或洗涤剂浓度)下显示出惊人的洗涤性能。在一些实施例中，本发明的变体蛋白酶与其他枯草杆菌蛋白酶的洗涤性能相当。在一些实施例中，与目前市售的枯草杆菌蛋白酶相比本发明的变体蛋白酶表现出增强的洗涤性能。因此，在本发明的一些实施例中，本文提供的变体蛋白酶表现出增强的氧化稳定性、增强的热稳定性、增强的在各种条件下的清洁能力和/或增强的螯合剂稳定性。此外，本发明的变体蛋白酶可用于不包含洗涤剂的清洁组合物，该变体蛋白酶同样是单独使用或与助洗剂和稳定剂组合。

[0570] 在本发明的一些实施例中，以组合物的重量计，清洁组合物包含水平为约0.00001％至约10％的至少一种本发明变体蛋白酶，以及以组合物的重量计，余量(例如约99.999％至约90.0％)包含清洁辅助材料。在本发明的一些其他实施例中，以组合物的重量计，本发明的清洁组合物包含水平为约0.0001％至约10％、约0.001％至约5％、约0.001％至约2％、或约0.005％至约0.5％的至少一种变体蛋白酶，清洁组合物的余量(如约99.9999重量％至约90.0重量％、约99.999重量％至约98重量％、约99.995重量％至约99.5重量％)包含清洁辅助材料。

[0571] 在一些实施例中，本发明的清洁组合物包含一种或多种另外的洗涤酶，该酶可提供清洁性能和/或织物护理和/或盘碟洗涤益处。合适的酶的例子包括但不限于：半纤维素酶、纤维素酶、过氧化物酶、蛋白酶、木聚糖酶、脂肪酶、磷脂酶、酯酶、角质酶、果胶酶、果胶酸裂解酶、甘露聚糖酶、角蛋白酶、还原酶、氧化酶、酚氧化酶、脂加氧酶、木质素酶、支链淀粉酶、鞣酸酶、戊聚糖酶、malanase、β-葡聚糖酶、阿拉伯糖苷酶、透明质酸酶、软骨素酶、漆酶和淀粉酶或它们的任何组合或混合物。在一些实施例中，使用包含常规应用性酶的酶组合(即“混合物(cocktail)”)，如使用蛋白酶、脂肪酶、角质酶和/或纤维素酶联合淀粉酶。

[0572] 除本文提供的蛋白酶变体之外，任何其他合适的蛋白酶均可用于本发明的组合物。合适的蛋白酶包括动物、植物或微生物来源的酶。在一些实施例中，使用微生物蛋白酶。在一些实施例中，包括经化学或遗传修饰的突变体。在一些实施例中，蛋白酶是丝氨酸蛋白酶，优选碱性微生物蛋白酶或胰蛋白酶样蛋白酶。碱性蛋白酶的例子包括枯草杆菌蛋白酶，

尤其是衍生自芽孢杆菌属的那些(如枯草杆菌蛋白酶、迟缓芽孢杆菌、解淀粉芽孢杆菌、枯草杆菌蛋白酶Carlsberg、枯草杆菌蛋白酶309、枯草杆菌蛋白酶147和枯草杆菌蛋白酶168)。另外的例子包括美国专利No.RE34,606、No.5,955,340、No.5,700,676、No.6,312,936和No.6,482,628中描述的那些突变型蛋白酶,所有这些专利以引用方式并入本文。另外的蛋白酶的例子包括但不限于胰蛋白酶(如猪或牛来源的胰蛋白酶)和WO89/06270中描述的镰孢菌属(Fusarium)蛋白酶。在一些实施例中,可用于本发明的市售蛋白酶包括但不限于MAXATASE®、MAXACAL™、MAXAPEM™、OPTICLEAN®、OPTIMASE®、PROPERASE®、PURAFECT®、PURAFECT® OXP、PURAMAX™、EXCELLASE™和PURAFAST™(杰能科公司(Genencor));ALCALASE®、SAVINASE®、PRIMASE®、DURAZYM™、POLARZYME®、OVOZYME®、KANNASE®、LIQUANASE®、NEUTRASE®、RELASE®和ESPERASE®(诺维信公司(Novozymes));BLAP™和BLAP™变体(德国杜塞尔多夫汉高公司(Henkel Kommanditgesellschaft auf Aktien,Duesseldorf,Germany))和KAP(嗜碱芽孢杆菌枯草杆菌蛋白酶;日本东京花王公司(Kao Corp.,Tokyo,Japan))。各种蛋白酶在WO95/23221、WO92/21760、美国专利公开No.2008/0090747和美国专利No.5,801,039、No.5,340,735、No.5,500,364、No.5,855,625、US RE 34,606、No.5,955,340、No.5,700,676、No.6,312,936和No.6,482,628以及各种其他专利中有描述。在一些其他实施例中,金属蛋白酶可用于本发明,包括但不限于WO 07/044993中描述的中性金属蛋白酶。

[0573] 此外,任何合适的脂肪酶可用于本发明。合适的脂肪酶包括但不限于细菌或真菌来源的酶。本发明涵盖经过化学方式或遗传修饰的突变体。可用的脂肪酶的例子包括:绵毛状腐质菌(Humicola lanuginosa)脂肪酶(参见例如EP 258 068和EP 305 216);米黑根毛霉(Rhizomucor miehei)脂肪酶(参见例如EP 238 023);假丝酵母属(Candida)脂肪酶,例如南极假丝酵母(C.antarctica)脂肪酶(例如南极假丝酵母脂肪酶A或B;参见例如EP 214 761);假单胞菌属(Pseudomonas)脂肪酶,例如产碱假单胞菌(P.alcaligenes)脂肪酶和类产碱假单胞菌(P.pseudoalcaligenes)脂肪酶(参见例如EP 218 272)、洋葱假单胞菌(P.cepacia)脂肪酶(参见例如EP 331 376)、施氏假单胞菌(P.stutzeri)脂肪酶(参见例如GB 1,372,034)、荧光假单胞菌(P.fluorescens)脂肪酶;芽孢杆菌属脂肪酶(例如枯草芽孢杆菌脂肪酶[Dartois et al.,Biochem.Biophys.Acta 1131:253-260[1993](Dartois等人,《生物化学与生物物理学报》,第1131卷,第253-260页,1993年)];嗜热脂肪芽孢杆菌脂肪酶[参见例如JP 64/744992];和短小芽孢杆菌脂肪酶[参见例如WO 91/16422])。

[0574] 此外,多种克隆的脂肪酶可用于本发明一些实施例中,包括但不限于:卡门柏青霉(Penicillium camembertii)脂肪酶(参见Yamaguchi et al.,Gene 103:61-67[1991](Yamaguchi等人,《基因》,第103卷,第61-67页,1991年))、白地霉(Geotricum candidum)脂肪酶(参见Schimada et al.,J.Biochem.,106:383-388[1989](Schimada等人,《生物化学杂志》,第106卷,第383-388页,1989年))以及各种根霉属(Rhizopus)脂肪酶,例如德氏根霉(R.delemar)脂肪酶(参见Hass et al.,Gene 109:117-113[1991](Hass等人,《基因》,第109卷,第117-113页,1991年))、雪白根霉(R.niveus)脂肪酶(Kugimiya et al.,

Biosci.Biotech.Biochem.56:716-719[1992](Kugimiya等人,《生物科学、生物技术和生物化学》,第56卷,第716-719页,1992年))和米根霉(R.oryzae)脂肪酶。

[0575] 其他类型的脂肪分解酶(例如角质酶)也可用于本发明的一些实施例,包括但不限于衍生自门多萨假单胞菌(Pseudomonas mendocina)的角质酶(参见WO 88/09367)和衍生自豌豆根腐镰孢菌(Fusarium solani pisi)的角质酶(参见WO 90/09446)。

[0576] 另外合适的脂肪酶包括市售的脂肪酶,例如M1LIPASE™、LUMA FAST™和LIPOMAX™(杰能科公司(Genencor))、LIPEX®、LIPOLASE®和LIPOLASE® ULTRA(诺维信公司(Novozymes))和LIPASE P™"Amano"(日本天野制药株式会社(Amano Pharmaceutical Co.Ltd.,Japan))。

[0577] 在本发明一些实施例中,以本发明清洁组合物重量计,本发明清洁组合物还包含水平为约0.00001%至约10%的另外的脂肪酶,以组合物重量计余量为清洁辅助材料。在本发明的一些其他实施例中,以本发明清洁组合物重量计,本发明清洁组合物还包含水平为约0.0001%至约10%、约0.001%至约5%、约0.001%至约2%、约0.005%至约0.5%脂肪酶的脂肪酶。

[0578] 在本发明的一些实施例中,任何合适的淀粉酶都可用于本发明。在一些实施例中,也可使用任何适用于碱性溶液中的淀粉酶(例如α和/或β淀粉酶)。合适的淀粉酶包括但不限于细菌或真菌来源的酶。在一些实施例中包括经化学或遗传修饰的突变体。可用于本发明的淀粉酶包括但不限于从地衣芽孢杆菌获得的α-淀粉酶(参见例如GB 1,296,839)。可用于本发明的市售淀粉酶包括但不限于:DURAMYL®、TERMAMYL®、FUNGAMYL®、STAINZYME®、STAINZYME PLUS®、STAINZYME ULTRA®和BAN™(诺维信公司(Novozymes))以及POWERASE™、RAPIDASE®和MAXAMYL® P(杰能科公司(Genencor))。

[0579] 在本发明一些实施例中,以本发明清洁组合物重量计,本发明清洁组合物还包含水平为约0.00001%至约10%另外淀粉酶的淀粉酶,以组合物重量计余量为清洁辅助材料。在本发明的一些其他实施例中,以本发明清洁组合物重量计,本发明清洁组合物还包含水平为约0.0001%至约10%、约0.001%至约5%、约0.001%至约2%、约0.005%至约0.5%淀粉酶的淀粉酶。

[0580] 在一些其他实施例中,任何合适的纤维素酶都都可用于本发明的清洁组合物。合适的纤维素酶包括但不限于细菌或真菌来源的酶。在一些实施例中包括经化学或遗传修饰的突变体。合适的纤维素酶包括但不限于特异腐质霉(Humicola insolens)纤维素酶(参见例如美国专利No.4,435,307)。特别合适的纤维素酶是具有颜色护理有益效果的纤维素酶(参见例如EP 0 495 257)。可用于本发明中的市售纤维素酶包括但不限于:CELLUZYME®、CAREZYME®(诺维信公司)以及KAC-500(B)™(花王公司(Kao Corporation))。在一些实施例中,纤维素酶作为成熟野生型纤维素酶或变体纤维素酶的部分或片段掺入,其中N末端的一部分缺失(例如参见美国专利No.5,874,276)。在一些实施例中,以本发明清洁组合物重量计,本发明清洁组合物还包含水平为约0.00001%至约10%另外纤维素酶的纤维素酶,并且以组合物重量计,余量为清洁辅助材料。在本发明的一些其他

实施例中，以本发明清洁组合物重量计，本发明清洁组合物还包含水平为约0.0001％至约10％、约0.001％至约5％、约0.001％至约2％、约0.005％至约0.5％纤维素酶的纤维素酶。

[0581] 任何适用于洗涤剂组合物中的甘露聚糖酶也可用于本发明。合适的甘露聚糖酶包括但不限于细菌或真菌来源的酶。在一些实施例中包括经化学或遗传修饰的突变体。各种可用于本发明的甘露聚糖酶是已知的(参见例如美国专利No.6,566,114、美国专利No.6,602,842和美国专利No.6,440,991，所有这些专利均以引用方式并入本文)。在一些实施例中，以本发明清洁组合物重量计，本发明清洁组合物还包含水平为约0.00001％至约10％另外甘露聚糖酶的甘露聚糖酶，并且以组合物重量计，余量为清洁辅助材料。在本发明的一些其他实施例中，以本发明清洁组合物重量计，本发明清洁组合物还包含水平为约0.0001％至约10％、约0.001％至约5％、约0.001％至约2％、约0.005％至约0.5％甘露聚糖酶的甘露聚糖酶。

[0582] 在一些实施例中，过氧化物酶与过氧化氢或其来源(例如过碳酸盐、过硼酸盐或过硫酸盐)组合用于本发明组合物中。在一些另选的实施例中，氧化酶与氧联合使用。这两种类型的酶优选连同增强剂一起用于“溶液漂白”(即，当各种织物在洗涤液中一起洗涤时防止纺织品染料从染色的织物转移到另一织物)(参见例如WO 94/12621和WO 95/01426)。合适的过氧化物酶/氧化酶包括但不限于植物、细菌或真菌来源的酶。在一些实施例中包括经化学或遗传修饰的突变体。在一些实施例中，以本发明清洁组合物的重量计，本发明清洁组合物还包含水平为约0.00001％至约10％另外过氧化物酶和/或氧化酶的过氧化物酶和/或氧化酶，并且以组合物的重量计，余量为清洁辅助材料。在本发明的一些其他实施例中，以本发明清洁组合物的重量计，本发明清洁组合物还包含水平为约0.0001％至约10％、约0.001％至约5％、约0.001％至约2％、约0.005％至约0.5％过氧化物酶和/或氧化酶的过氧化物酶和/或氧化酶。

[0583] 在一些实施例中，可使用另外的酶，包括但不限于过水解酶(例如参见WO 05/056782)。此外，在一些实施例中，本文涵盖上述酶的混合物，尤其是一种或多种另外的蛋白酶、淀粉酶、脂肪酶、甘露聚糖酶和/或至少一种纤维素酶。实际上，设想到这些酶的各种混合物都可用于本发明。还设想到，变体蛋白酶与一种或多种另外的酶的不同水平都可独立地在最高达约10％的范围内，该清洁组合物的余量为清洁辅助材料。易于通过考虑待清洁的表面、物体、物品或织物以及对使用期间(例如通过使用洗涤剂)的清洁条件理想的组合物形式，来具体选择清洁辅助材料。

[0584] 合适的清洁辅助材料的例子包括但不限于表面活性剂、助洗剂、漂白剂、漂白活化剂、漂白催化剂、其他酶、酶稳定系统、螯合剂、荧光增白剂、去垢性聚合物、染料转移剂、染料转移抑制剂、催化材料、过氧化氢、过氧化氢源、预先形成的过酸、聚合物分散剂、粘土污垢去除剂、结构增弹性剂(elasticizing agent)、分散剂、抑泡剂、染料、香料、着色剂、填料盐、水溶助长剂、光活化剂、荧光剂、织物调理剂、织物软化剂、载体、水溶助长剂、加工助剂、溶剂、颜料、可水解表面活性剂、防腐剂、抗氧化剂、抗收缩剂、抗皱剂、杀菌剂、杀真菌剂、色粒、银护理剂、抗晦暗剂和/或抗腐蚀剂、碱度源、增溶剂、载体、加工助剂、颜料和pH控制剂(参见例如美国专利No.6,610,642、No.6,605,458、No.5,705,464、No.5,710,115、No.5,698,504、No.5,695,679、No.5,686,014和No.5,646,101，所有这些专利均以引用方式并入本文)。特定清洁组合物材料的实施例在下文中举例说明。在清洁辅助材料与清洁组合物中

的本发明变体蛋白酶不相容的实施例中，则使用合适的方法保持清洁辅助材料与蛋白酶分离(即，相互不接触)，直到两种组分适宜进行组合为止。这种分离方法包括本领域已知的任何合适方法(例如明胶胶囊法(gelcap)、包封法、片剂法、物理分离法等)。

[0585] 在一些实施例中，在可用于清洁多种需要去除蛋白质污渍的表面的组合物中包含有效量的一种或多种本文提供的变体蛋白酶。这些清洁组合物包括用于诸如清洁硬质表面、织物和餐具之类的应用的清洁组合物。实际上，在一些实施例中，本发明提供织物清洁组合物，而在其他实施例中，本发明提供非织物清洁组合物。值得注意的是，本发明还提供适于个人护理的清洁组合物，包括口腔护理(包括洁牙剂、牙膏、漱口水等，以及假牙清洁组合物)、皮肤和毛发清洁组合物。意在使本发明涵盖任何形式(即，液体、颗粒状、条状、半固体、凝胶、乳液、片剂、胶囊等)的洗涤剂组合物。

[0586] 举例来说，在下文更详细地描述了几种在其中可使用本发明变体蛋白酶的清洁组合物。在本发明的清洁组合物被配制成适合在洗衣机洗涤方法中使用的组合物的一些实施例中，本发明组合物优选地包含至少一种表面活性剂和至少一种助洗剂化合物，以及一种或多种清洁辅助材料，所述清洁辅助材料优选地选自有机聚合化合物、漂白剂、另外的酶、抑泡剂、分散剂、石灰皂分散剂、悬污剂和抗再沉积剂以及腐蚀抑制剂。在一些实施例中，洗衣组合物还含有软化剂(即作为额外的清洁辅助材料)。本发明组合物还可使用固体或液体形式的洗涤添加剂产品。所述添加剂产品旨在补充和/或提高常规洗涤剂组合物的性能，并且可在洗涤过程的任何阶段添加。在一些实施例中，在20℃下测量时，本文中衣物洗涤剂组合物的密度在约400至约1200g/L的范围内，而在其他实施例中，其在约500至约950g/L组合物的范围内。

[0587] 在配制为在人工盘碟洗涤方法中使用的组合物的实施例中，本发明组合物优选地包含至少一种表面活性剂，以及优选地至少一种另外的选自以下的清洁辅助材料：有机聚合化合物、泡沫增强剂、II族金属离子、溶剂、水溶助长剂和另外的酶。

[0588] 在一些实施例中，各种清洁组合物(例如美国专利No.6,605,458中提供的组合物)可与本发明的变体蛋白酶一起使用。因此，在一些实施例中，包含至少一种本发明的变体蛋白酶的组合物是致密的颗粒状织物清洁组合物，而在其他实施例中，所述组合物是可用于清洗有色织物的颗粒状织物清洁组合物，在另外的实施例中，所述组合物是提供通过洗涤软化的能力(softening through the wash capacit)的颗粒状织物清洁组合物，在其他实施例中，所述组合物是重垢液体织物清洁组合物。在一些实施例中，包含至少一种本发明变体蛋白酶的组合物是织物清洁组合物，例如美国专利No.6,610,642和No.6,376,450中所述的那些组合物。此外，本发明的变体蛋白酶可用于在欧洲或日本洗涤条件下特别具有实用性的颗粒状衣物洗涤组合物中(参见例如美国专利No.6,610,642)。

[0589] 在一些另选的实施例中，本发明提供包含至少一种本文提供的变体蛋白酶的硬质表面清洁组合物。因此，在一些实施例中，包含至少一种本发明变体蛋白酶的组合物是硬质表面清洁组合物，例如美国专利No.6,610,642、No.6,376,450和No.6,376,450中所述的组合物。

[0590] 在另外其他实施例中，本发明提供包含至少一种本文提供的变体蛋白酶的盘碟洗涤组合物。因此，在一些实施例中，包含至少一种本发明变体蛋白酶的组合物是硬质表面清洁组合物，例如美国专利No.6,610,642和No.6,376,450中所述的那些组合物。在一些其他

实施例中，本发明提供包含至少一种本文提供的变体蛋白酶的盘碟洗涤组合物。在一些其他实施例中，包含至少一种本发明变体蛋白酶的组合物包含口腔护理组合物，例如美国专利No.6,376,450和No.6,376,450中所述的那些组合物。上述美国专利No.6,376,450、No.6,605,458、No.6,605,458和No.6,610,642中所包含的化合物和清洁辅助材料的配制和描述可用于本文提供的变体蛋白酶。

[0591] 本发明清洁组合物被配制成任何合适的形式并且由配制者选择的任何方法制备，其非限制性例子描述于美国专利No.5,879,584、No.5,691,297、No.5,574,005、No.5,569,645、No.5,565,422、No.5,516,448、No.5,489,392和No.5,486,303中，所有这些专利均以引用方式并入本文。当需要低pH清洁组合物时，通过添加诸如单乙醇胺或酸性材料(如HCl)之类的材料来调整此类组合物的pH。

[0592] 尽管不是实现本发明目的所必需的，但下文示例的辅助材料的非限制性名单适用于本发明清洁组合物。在一些实施例中，掺入这些辅助材料，例如以帮助或增强清洁性能以便处理待清洁的基材，或改变清洁组合物的美观性，如芳香剂、着色剂、染料等情形就是如此。应当理解，这些助剂是本发明的变体蛋白酶的补充。这些另外的组分的精确性质以及其掺入的水平将取决于组合物的物理形式和打算使用组合物的清洁操作的性质。合适的辅助材料包括但不限于：表面活性剂、助洗剂、螯合剂、染料转移抑制剂、沉积助剂、分散剂、另外的酶和酶稳定剂、催化材料、漂白活化剂、漂白增强剂、过氧化氢、过氧化氢源、预先形成的过酸、聚合物分散剂、粘土污垢去除剂/抗再沉积剂、增亮剂、抑泡剂、染料、芳香剂、结构增弹剂、织物软化剂、载体、水溶助长剂、加工助剂和/或颜料。除下文的公开内容外，此类其他助剂及使用水平的适合例子见于美国专利No.5,576,282、No.6,306,812和No.6,326,348(以引用的方式并入本文)中。上述辅助成分可构成本发明清洁组合物的余量。

[0593] 在一些实施例中，根据本发明的清洁组合物包含至少一种表面活性剂和/或表面活性剂系统，其中表面活性剂选自非离子表面活性剂、阴离子表面活性剂、阳离子表面活性剂、两性表面活性剂、两性离子表面活性剂、半极性非离子表面活性剂以及它们的混合物。在一些低pH清洁组合物实施例(例如净pH为约3至约5的组合物)中，组合物通常不含烷基乙氧基化硫酸盐，因为据信此类表面活性剂可能会被所述组合物的酸性内含物水解。在一些实施例中，以清洁组合物的重量计，表面活性剂以约0.1％至约60％的水平存在，而在另选的实施例中，所述水平为约1％至约50％，而在其他实施例中，所述水平为约5％至约40％。

[0594] 在一些实施例中，本发明的清洁组合物包含一种或多种洗涤剂助剂或助洗剂体系。在一些掺入至少一种助洗剂的实施例中，以清洁组合物的重量计，清洁组合物包含至少约1％、约3％至约60％或甚至约5％至约40％的助洗剂。助洗剂包括但不限于：聚磷酸的碱金属盐、铵盐和链烷醇铵盐；碱金属硅酸盐；碱土金属和碱金属碳酸盐；铝硅酸盐；聚羧酸盐化合物；醚羟基聚羧酸盐；马来酸酐与乙烯或乙烯基甲基醚的共聚物；1,3,5-三羟基苯-2,4,6-三磺酸；和羧甲基氧基琥珀酸；聚乙酸(如乙二胺四乙酸和次氮基三乙酸)的各种碱金属盐、铵盐和取代的铵盐；以及聚羧酸盐，如苯六甲酸、琥珀酸、柠檬酸、氧基二琥珀酸、聚马来酸、苯1,3,5-三甲酸、羧甲基氧基琥珀酸以及它们的可溶性盐。实际上，设想到任何合适的助洗剂都将可用于本发明各个实施例中。

[0595] 在一些实施例中，助洗剂形成水溶性硬度离子络合物(例如螯合助洗剂)，如柠檬酸盐和聚磷酸盐(例如三聚磷酸钠和六水合三聚磷酸钠、三聚磷酸钾以及三聚磷酸钠与三

聚磷酸钾的混合物等)。设想到,任何合适的助洗剂都将可用于本发明,包括本领域已知的那些助洗剂在内(参见例如EP 2 100 949)。

[0596] 在一些实施例中,本发明的清洁组合物包含至少一种螯合剂。合适的螯合剂包括但不限于:铜、铁和/或锰螯合剂以及它们的混合物。在使用至少一种螯合剂的实施例中,以本发明主题清洁组合物的重量计,本发明清洁组合物包含约0.1%至约15%或甚至约3.0%至约10%的螯合剂。

[0597] 在一些其他实施例中,本文中提供的清洁组合物含有至少一种沉积助剂。合适的沉积助剂包括但不限于:聚乙二醇;聚丙二醇;聚羧酸盐;去垢性聚合物,如聚对苯二甲酸;粘土,如高岭土、蒙脱土、绿坡缕石(atapulgite)、伊利石、膨润土、多水高岭土以及它们的混合物。

[0598] 如本文所指出,在一些实施例中,抗再沉积剂可用于本发明的一些实施例。在一些实施例中,可使用非离子型表面活性剂。例如,在自动盘碟洗涤实施例中,非离子型表面活性剂可用于表面修饰目的,尤其用于薄板(sheeting),以避免成膜和起斑以及用于改善光泽度。这些非离子型表面活性剂也可用于防止污垢再沉积。在一些实施例中,抗再沉积剂是本领域已知的非离子表面活性剂(参见例如EP 2 100 949)。

[0599] 在一些实施例中,本发明清洁组合物包含一种或多种染料转移抑制剂。合适的聚合物染料转移抑制剂包括但不限于:聚乙烯吡咯烷酮聚合物、聚胺N-氧化物聚合物、N-乙烯吡咯烷酮与N-乙烯咪唑的共聚物、聚乙烯噁唑烷酮和聚乙烯咪唑或它们的混合物。在使用至少一种染料转移抑制剂的实施例中,以清洁组合物的重量计,本发明清洁组合物包含约0.0001%至约10%、约0.01%至约5%或甚至约0.1%至约3%。

[0600] 在一些实施例中,硅酸盐包含在本发明的组合物中。在一些此类实施例中,使用硅酸钠(例如二硅酸钠、偏硅酸钠和结晶页硅酸盐)。在一些实施例中,硅酸盐以约1%至约20%的水平存在。在一些实施例中,以组合物的重量计,硅酸盐以约5%至约15%的水平存在。

[0601] 在一些另外的实施例中,本发明清洁组合物还包含分散剂。合适的水溶性有机材料包括但不限于均聚酸或共聚酸或它们的盐,其中多聚羧酸包含至少两个彼此相隔不超过两个碳原子的羧基。

[0602] 在一些其他实施例中,通过任何合适的技术使清洁组合物中使用的酶稳定。在一些实施例中,本文所用的酶由成品组合物中存在的可给该酶提供钙和/或镁离子的水溶性钙和/或镁离子源来稳定。在一些实施例中,酶稳定剂包括寡糖、多糖和无机二价金属盐(包括碱土金属,如钙盐)。设想到,各种酶稳定化技术将可用于本发明。例如,在一些实施例中,本文所采用的酶由成品组合物中存在的可给该酶提供锌(II)、钙(II)和/或镁(II)离子的水溶性的这类离子源,以及其他金属离子(例如钡(II)、钪(II)、铁(II)、锰(II)、铝(III)、锡(II)、钴(II)、铜(II)、镍(II)和氧钒(IV))来稳定。氯化物和硫酸盐也可用于本发明的一些实施例中。合适的寡糖和多糖(例如糊精)的例子是本领域已知的(参见例如WO 07/145964)。在一些实施例中,也可使用可逆的蛋白酶抑制剂,如含硼化合物(例如硼酸盐、4-甲酰基苯基硼酸)和/或必要时,可使用三肽醛进一步改进稳定性。

[0603] 在一些实施例中,漂白剂、漂白活化剂和/或漂白催化剂存在于本发明的组合物中。在一些实施例中,本发明的清洁组合物包含无机和/或有机漂白化合物。无机漂白剂包

括但不限于过氧化氢合物盐(例如过硼酸盐、过碳酸盐、过磷酸盐、过硫酸盐和过硅酸盐)。在一些实施例中,无机过氧化氢合物盐是碱金属盐。在一些实施例中,所包括的无机过氧化氢合物盐为结晶固体形式,无额外保护,但在一些另外的实施例中,所述盐被包覆。本领域已知的任何适合的盐都可用于本发明(参见例如EP 2 100949)。

[0604] 在一些实施例中,将漂白活化剂用于本发明的组合物中。漂白活化剂通常为有机过酸前体,这些有机过酸前体在60℃和低于60℃温度下进行的清洁过程中会增强漂白作用。适用于本发明的漂白活化剂包括这样的化合物,其在过氧化氢解条件下产生优选具有约1至约10个碳原子、尤其约2至约4个碳原子的脂族过氧羧酸,和/或任选取代的过苯甲酸。另外的漂白活化剂是本领域已知的并且可用于本发明(参见例如EP 2 100 949)。

[0605] 此外,在一些实施例中以及如本文中进一步描述的,本发明的清洁组合物还包含至少一种漂白催化剂。在一些实施例中,可使用三氮杂环壬烷锰和相关络合物,以及钴、铜、锰和铁络合物。其他漂白催化剂可用于本发明中(参见例如US 4,246,612、5,227,084、4,810410、WO 99/06521和EP 2 100 949)。

[0606] 在一些实施例中,本发明的清洁组合物含有一种或多种催化性金属络合物。在一些实施例中,可使用含金属漂白催化剂。在一些实施例中,金属漂白催化剂包含催化剂系统,所述催化剂系统包含具有确定的漂白催化活性的过渡金属阳离子(例如铜、铁、钛、钌、钨、钼或锰阳离子)、具有极低漂白催化活性或无漂白催化活性的辅助性金属阳离子(例如锌或铝阳离子),和对催化性和辅助性金属阳离子具有确定的稳定性常数的螯合剂(sequestrate),尤其可使用乙二胺四乙酸、乙二胺四(亚甲基膦酸)以及它们的水溶性盐(参见例如美国专利No.4,430,243)。在一些实施例中,借助于锰化合物来催化本发明的清洁组合物。这些化合物及其使用水平是本领域众所周知的(参见例如美国专利No.5,576,282)。在另外的实施例中,钴漂白催化剂可用于本发明的清洁组合物中。各种钴漂白催化剂是本领域已知的(参见例如美国专利No.5,597,936和No.5,595,967)且易于用已知程序制备。

[0607] 在一些另外的实施例中,本发明的清洁组合物包括巨多环刚性配体(MRL)的过渡金属络合物。作为一种实践(但绝非限制),在一些实施例中,对本发明提供的组合物和清洁方法进行调整以在含水洗涤介质中提供约至少1ppm的活性MRL物质,而在一些实施例中在洗涤液中提供约0.005ppm至约25ppm、更优选约0.05ppm至约10ppm且最优选约0.1ppm至约5ppm的MRL。

[0608] 在一些实施例中,本发明过渡金属漂白催化剂中的过渡金属包括(但不限于)锰、铁和铬。MRL还包括(但不限于)交叉桥接的特殊超刚性配体(例如5,12-二乙基-1,5,8,12-四氮杂双环[6.6.2]十六烷)。合适的过渡金属MRL易于用已知程序制备(参见例如WO 2000/32601和美国专利No.6,225,464)。

[0609] 在一些实施例中,本发明的清洁组合物包含金属护理剂。金属护理剂可用于防止和/或减少包括铝、不锈钢和非铁金属(例如银和铜)在内的金属的锈污、腐蚀和/或氧化。合适的金属护理剂包括EP 2 100 949、WO 9426860和WO 94/26859中所述的那些金属护理剂。在一些实施例中,金属护理剂是锌盐。在一些其他实施例中,本发明清洁组合物包含约0.1重量%至约5重量%的一种或多种金属护理剂。

[0610] 如上文所指出的,本发明的清洁组合物配制成任何合适的形式并由配制者选择的

任何方法制备，其非限制性例子描述于美国专利No.5,879,584、No.5,691,297、No.5,574,005、No.5,569,645、No.5,516,448、No.5,489,392和No.5,486,303中，所有这些专利都以引用的方式并入本文中。在一些需要低pH清洁组合物的实施例中，通过添加诸如HCl的酸性材料来调整此类组合物的pH。

[0611] 本文所公开的清洁组合物可用于清洁位置(situs)(例如表面、物品、盘碟或织物)。通常，使所述位置的至少一部分与纯的形式或在洗涤液中稀释的本发明清洁组合物实施例接触，随后任选洗涤和/或漂洗所述位置。出于本发明的目的，“洗涤”包括(但不限于)擦洗和机械搅动。在一些实施例中，清洁组合物在溶液中通常以约500ppm至约15,000ppm的浓度使用。当洗涤溶剂是水时，水温通常在约5℃至约90℃的范围内，并且当所述位置包括织物时，水与织物的质量比通常为约1:1至约30:1。

[0612] 清洁组合物的制备和使用方法

[0613] 本发明的清洁组合物被配制成任何合适的形式并通过配制者所选择的任何合适方法制备(参见例如美国专利No.5,879,584、5,691,297、5,574,005、5,569,645、5,565,422、5,516,448、5,489,392、5,486,303、4,515,705、4,537,706、4,515,707、4,550,862、4,561,998、4,597,898、4,968,451、5,565,145、5,929,022、6,294,514和6,376,445)。

[0614] 在一些实施例中，本发明的清洁组合物以单位剂型提供，包括片剂、胶囊剂、扁囊剂、袋剂和多隔室袋剂。在一些实施例中，对单位剂量形式进行设计以提供多隔室小袋(或其他单位剂量形式)内的成分的控制释放。合适的单位剂量和控制释放形式是本领域已知的(参见例如EP 2 100 949、WO 02/102955、美国专利No.4,765,916和4,972,017，以及WO 04/111178关于适用于单位剂量和控制释放形式的材料)。在一些实施例中，单位剂型以包有水溶性膜或水溶性小袋的片剂提供。各种用于单位剂量的形式在EP 2 100 947中提供，并且是本领域已知的。

[0615] 使用方法

[0616] 在一些实施例中，本发明的清洁组合物可用于清洁表面(如盘碟)、衣物、硬质表面、隐形眼镜等。在一些实施例中，该表面的至少一部分与纯形式的或在洗涤液中稀释的本发明清洁组合物的至少一个实施例接触，随后任选地洗涤和/或漂洗所述表面。出于本发明的目的，“洗涤”包括(但不限于)擦洗和机械洗涤。在一些实施例中，本发明的清洁组合物在溶液中以约500ppm至约15,000ppm的浓度使用。在一些其中洗涤溶剂为水的实施例中，水温通常在约5℃至约90℃的范围内。

[0617] 本发明提供用于清洁或洗涤需要清洁的物品或表面(如硬质表面)的方法，包括(但不限于)清洁或洗涤盘碟物品、餐具物品、织物物品、衣物物品、个人护理物品等的方法，以及清洁或洗涤硬质或软质表面(如物品的硬质表面)的方法。

[0618] 在一些实施例中，本发明提供清洁需要清洁的物品、物体或表面的方法，该方法包括使物品或表面(或希望进行清洁的物品或表面的一部分)与至少一种本发明的变体枯草杆菌蛋白酶或本发明的组合物接触足以清洁所述物品、物体或表面至所需程度的时间，和/或在适于和/或有效清洁所述物品、物体或表面至所需程度的条件下进行接触。一些这类方法还包括用水漂洗物品、物体或表面。对于一些这类方法，清洁组合物是盘碟洗涤剂组合物，而待清洁的物品或物体是盘碟物品或餐具物品。如本文所用，“盘碟物品”是通常用于供给食物或食用食物的物品。盘碟物品可以是但不限于例如盘子、碟子、杯子、碗等等。如本文

所用，“餐具”是更广泛的术语，其包括(但不限于)例如器皿、刀具、餐刀、餐叉、匙、筷子、玻璃器具、罐壶、调味汁碟、饮用容器、盛菜物品等。预期“餐具物品”包括这些或相似的用于供应食物或食用食物的物品中的任何一种。对于一些这类方法，清洁组合物是自动盘碟洗涤剂组合物或手动盘碟洗涤剂组合物，而待清洁的物品或物体是盘碟或餐具物品。对于一些这类方法，清洁组合物是衣物洗涤剂组合物(例如粉末衣物洗涤剂组合物或液体衣物洗涤剂组合物)，而待清洁的物品是织物物品。在一些其他实施例中，清洁组合物是衣物预处理组合物。

[0619] 在一些实施例中，本发明提供用于清洁或洗涤任选需要分别清洁或洗涤的织物物品的方法。在一些实施例中，所述方法包括提供包含变体蛋白酶的组合物(包括但不限于织物或衣物清洁组合物)和需要清洁的织物物品或衣物物品，并使该织物物品或衣物物品(希望进行清洁的物品的一部分)与该组合物在足以或有效清洁或洗涤该织物或衣物物品至所需程度的条件下接触。

[0620] 在一些实施例中，本发明提供清洁或洗涤任选需要清洁的物品或表面(如硬质表面)的方法，该方法包括提供待清洁或洗涤的物品或表面，使该物品或表面(希望进行清洁或洗涤的物品或表面的一部分)与至少一种本发明的枯草杆菌蛋白酶变体或包含至少一种这类枯草杆菌蛋白酶变体的本发明组合物接触足以清洁或洗涤该物品或表面至所需程度的时间，和/或在足以或有效清洁或洗涤该物品或表面至所需程度的条件下接触。这类组合物包括但不限于例如本发明的清洁组合物或洗涤剂组合物(如手动盘碟洗涤剂组合物、手动盘碟洗涤清洁组合物、衣物洗涤剂组合物或织物洗涤剂组合物或者衣物或织物清洁组合物、液体衣物洗涤剂、液体衣物清洁组合物、粉末衣物洗涤剂组合物、粉末衣物清洁组合物、自动盘碟洗涤剂组合物、衣物助洗剂清洁组合物或洗涤剂组合物、衣物清洁添加剂和衣物预洗剂组合物等)。在一些实施例中，将该方法重复一次或多次，尤其是如果需要额外的清洁或洗涤的话。例如，在某些情况下，该方法任选还包括让物品或表面与至少一种变体蛋白酶或组合物保持接触足以或有效清洁或洗涤该物品或表面至所需程度的一段时间。在一些实施例中，这些方法还包括用水和/或另一种液体漂洗物品或表面。在一些实施例中，这些方法还包括再次用至少一种本发明的变体蛋白酶或本发明的组合物接触物品或表面，并且让该物品或表面与至少一种变体蛋白酶或组合物保持接触足以清洁或洗涤该物品或表面至所需程度的一段时间。在一些实施例中，清洁组合物是盘碟洗涤剂组合物，而待清洁的物品是盘碟或餐具物品。在本发明方法的一些实施例中，清洁组合物是自动盘碟洗涤剂组合物或手动盘碟洗涤剂组合物，而待清洁的物品是盘碟或餐具物品。在所述方法的一些实施例中，清洁组合物是衣物洗涤剂组合物，而待清洁的物品是织物物品。

[0621] 本发明还提供在自动洗碗机中清洁餐具或盘碟物品的方法，该方法包括提供自动洗碗机，在机器中放入足以清洁餐具或盘碟物品的一定量的包含至少一种本发明枯草杆菌蛋白酶变体或本发明组合物的自动盘碟洗涤组合物(例如，通过将该组合物置于机器中的合适的或提供的洗涤剂隔室或分配器中)，将盘碟或餐具物品放入该机器中，运行该机器以清洁该餐具或盘碟物品(例如按照生产商的说明书)。在一些实施例中，所述方法包括本文所述的任何自动盘碟洗涤组合物，其包含(但不限于)至少一种本文提供的枯草杆菌蛋白酶变体。待使用的自动盘碟洗涤组合物的量可根据生产商的说明书或建议容易地确定，并可采用任何形式的包含至少一种本发明变体蛋白酶的自动盘碟洗涤组合物(例如液体、粉末、

固体、凝胶、片剂等)，包括本文所述的任何组合物在内。

[0622] 本发明还提供清洁任选需要清洁的表面、物品或物体的方法，该方法包括使物品或表面(或希望进行清洁的物品或表面的一部分)与纯形式的或在洗涤液中稀释的至少一种本发明变体枯草杆菌蛋白酶或本发明清洁组合物接触足以清洁或洗涤该物品或表面至所需程度的时间和/或在足以或有效清洁或洗涤该物品或表面至所需程度的条件下进行接触。然后如果需要，可对表面、物品或物体(任选)进行洗涤和/或漂洗。出于本发明的目的，“洗涤”包括(但不限于)例如擦洗和机械搅动。在一些实施例中，清洁组合物在溶液(如水溶液)中以约500ppm至约15,000ppm的浓度使用。当洗涤溶剂是水时，水温通常在约5℃至约90℃的范围内，并且当表面、物品或物体包括织物时，水与织物的质量比通常为约1:1至约30:1。

[0623] 本发明还提供在洗涤机中清洁衣物或织物物品的方法，该方法包括提供洗涤机，将足以清洁衣物或织物物品的一定量的包含至少一种本发明变体枯草杆菌蛋白酶的衣物洗涤剂组合物置于该机器中(例如通过将该组合物置于机器中的合适的或提供的洗涤剂隔室中或分配器中)，将衣物或织物物品置于该机器中，运行该机器以清洁衣物或织物物品(例如，按照生产商的说明书)。本发明的方法包括本文所述的任何衣物洗涤剂组合物，其包含(但不限于)本文提供的任何变体枯草杆菌蛋白酶中的至少一种。要使用的衣物洗涤剂组合物的量可根据生产商的说明书或建议容易地确定，并可采用任何形式的包含至少一种本发明变体蛋白酶的衣物洗涤剂组合物(例如固体、粉末、液体、片剂、凝胶等)，包括本文所述的任何组合物在内。

[0624] 实验

[0625] 在以下实例中更详细地描述本发明，所述实例不是旨在以任何方式限制受权利要求书保护的本发明的范围。

[0626] 在接下来的实验公开中，适用以下缩写:PI(性能指数)、ppm(份每一百万份);M(摩尔/升);mM(毫摩尔/升);μM(微摩尔/升);nM(纳摩尔/升);mol(摩尔);mmol(毫摩尔);μmol(微摩尔);nmol(纳摩尔);gm(克);mg(毫克);μg(微克);pg(皮克);L(升);ml和mL(毫升);μl和μL(微升);cm(厘米);mm(毫米);μm(微米);nm(纳米);U(单位);V(伏);MW(分子量);sec(秒);min(分钟);h和hr(小时);℃(摄氏度);QS(足量);ND(未进行);rpm(每分钟转数);GH(德国硬度度数);H_2O(水);dH_2O(去离子水);HCl(盐酸);aa(氨基酸);bp(碱基对);kb(千碱基对);kD(千道尔顿);cDNA(拷贝DNA或互补DNA);DNA(脱氧核糖核酸);ssDNA(单链DNA);dsDNA(双链DNA);dNTP(脱氧核苷三磷酸);RNA(核糖核酸);$MgCl_2$(氯化镁);NaCl(氯化钠);w/v(重量/体积比);v/v(体积比);w/w(重量比);g(重力);OD(光密度);ppm(份每一百万份);达尔伯克氏磷酸盐缓冲溶液(DPBS);SOC(2％细菌培养用胰蛋白胨、0.5％细菌培养用酵母提取物、10mM NaCl、2.5mM KCl);极品肉汤(TB;12g/l细菌培养用胰蛋白胨、24g/l甘油、2.31g/l KH_2PO_4和12.54g/l K_2HPO_4);OD_{280}(280nm处的光密度);OD_{600}(600nm处的光密度);A_{405}(405nm处的吸光度);Vmax(酶催化反应的最大初速度);PAGE(聚丙烯酰胺凝胶电泳);PBS(磷酸盐缓冲盐水[150mM NaCl,10mM磷酸钠缓冲剂,pH7.2]);PBST(PBS+0.25％TWEEN®-20);PEG(聚乙二醇);PCR(聚合酶链反应);RT-PCR(反转录PCR);SDS(十二烷基硫酸钠);Tris(三(羟甲基)氨基甲烷);HEPES(N-[2-羟乙基]哌嗪-N-[2-乙磺酸]);HBS(HEPES缓冲盐水);Tris-HCl(三[羟甲基]氨基甲烷-盐酸盐);Tricine(N-[三-(羟甲基)-甲

基]-甘氨酸);CHES(2-(N-环己基氨基)乙烷磺酸);TAPS(3-{[三-(羟甲基)-甲基]-氨基}-丙磺酸);CAPS(3-(环己基氨基)-丙烷磺酸);DMSO(二甲基亚砜);DTT(1,4-二硫代-DL-苏糖醇);SA(芥子酸(s,5-二甲氧基-4-羟基肉桂酸);TCA(三氯乙酸);Glut和GSH(还原型谷胱甘肽);GSSG(氧化型谷胱甘肽);TCEP(三[2-羧乙基]膦);Ci(居里);mCi(毫居里);μCi(微居里);HPLC(高压液相色谱法);RP-HPLC(反相高压液相色谱法);TLC(薄层色谱法);MALDI-TOF(基质辅助激光解吸/电离-飞行时间质谱);Ts(甲苯磺酰基);Bn(苄基);Ph(苯基);Ms(甲磺酰基);Et(乙基);Me(甲基);Taq(水生栖热菌(Thermus aquaticus)DNA聚合酶);Klenow(DNA聚合酶I大(Klenow)片段);EGTA(乙二醇双(β-氨基乙基醚)N,N,N',N'-四乙酸);EDTA(乙二胺四乙酸);bla(β-内酰胺酶或氨苄青霉素抗性基因);HDL(高密度液体);HDD(重垢粉末洗涤剂);HSG(高泡沫颗粒状洗涤剂);CEE(中欧和东欧);WE(西欧);当用于指洗涤剂时,NA(北美);当用于指洗涤剂时,JPN(日本);MJ Research(MJ Research公司,内华达州里诺(Reno,NV));Baseclear(Baseclear BV有限公司,荷兰莱顿(Leiden,the Netherlands));PerSeptive(PerSeptive Biosystems公司,马萨诸塞州弗雷明汉(Framingham,MA));ThermoFinnigan(菲尼根质谱公司(ThermoFinnigan),加利福尼亚州圣何塞(San Jose,CA));Argo(Argo BioAnalytica公司,新泽西州莫里斯普莱恩斯(Morris Plains,NJ));Seitz EKS(SeitzSchenk Filtersystems股份有限公司,德国巴特克罗伊茨纳赫(Bad Kreuznach,Germany));Pall(颇尔公司(Pall Corp.),纽约州东希尔斯(East Hills,NY)和德国巴特克罗伊茨纳赫);Spectrum(频谱实验室公司(Spectrum Laboratories),加利福尼亚州多明格斯牧场(Dominguez Rancho,CA));Molecular Structure(分子结构公司(Molecular Structure Corp.),得克萨斯州伍德兰兹(Woodlands,TX));Accelrys(Accelrys有限公司(Accelrys,Inc.),加利福尼亚州圣地亚哥(San Diego,CA));Chemical Computing(化学计算公司(Chemical Computing Corp.),加拿大蒙特利尔(Montreal,Canada));New Brunswick(新布朗什维克科学公司(New Brunswick Scientific,Co.),新泽西州爱迪生(Edison,NJ));CFT(材料测试中心(Center for Test Materials),荷兰费拉尔丁恩(Vlaardingen,The Netherlands));P&G和Procter&Gamble(宝洁公司(Procter&Gamble,Inc.),俄亥俄州辛辛那提(Cincinnati,OH));GE Healthcare(通用电气医疗集团(GE Healthcare),英国查尔芬特-圣贾尔斯(Chalfont St.Giles,United Kingdom));DNA2.0(DNA2.0公司,加利福尼亚州门洛帕克(Menlo Park,CA));OXOID(Oxoid公司,英国汉普郡贝辛斯托克(Basingstoke,Hampshire,UK));Megazyme(美格兹密国际爱尔兰有限公司(Megazyme International Ireland Ltd.),爱尔兰威克洛郡博雷商业圈博雷公司(Bray Business Park,Bray,Co.,Wicklow,Ireland));Finnzymes(Finnzymes Oy公司,芬兰埃斯波(Espoo,Finland));Kelco(斯比凯可公司(CP Kelco),特拉华州威尔明顿(Wilmington,DE));Corning(康宁生命科学(Corning Life Sciences),纽约州科宁(Corning,NY)));NEN(NEN生命科学产品公司(NEN Life Science Products),马萨诸塞州波士顿(Boston,MA));Pharma AS(Pharma AS公司,挪威奥斯陆(Oslo,Norway));Dynal(Dynal公司,挪威奥斯陆);Bio-Synthesis(生物合成公司(Bio-Synthesis),得克萨斯州路易斯维尔(Lewisville,TX));ATCC(美国典型培养物保藏中心(American Type Culture Collection),马里兰州罗克维尔(Rockville,MD));Gibco/BRL(Gibco/BRL公司,纽约州格兰德岛(Grand Island,NY));Sigma(西格玛化工有限

公司(Sigma Chemical Co.),密苏里州圣路易斯(St.Louis,MO));Pharmacia(法玛西亚生物技术公司(Pharmacia Biotech),新泽西州皮斯卡特维(Piscataway,NJ));NCBI(美国国家生物技术信息中心);Applied Biosystems(应用生物系统公司(Applied Biosystems),加利福尼亚州福斯特市(Foster City,CA));BD Biosciences和/或Clontech(碧迪生物科学克隆技术实验室(BD Biosciences CLONTECH Laboratories),加利福尼亚州帕罗奥图(Palo Alto,CA));Operon Technologies(欧佩沦科技有限公司(Operon Technologies,Inc.),加利福尼亚州阿拉米达(Alameda,CA));MWG Biotech(MWG生物科技公司(MWG Biotech),北卡罗来纳州海波因特(High Point,NC));Oligos Etc(Oligos Etc.有限公司,俄勒冈州威尔逊维尔(Wilsonville,OR));Bachem(巴亨生物科学公司(Bachem Bioscience,Inc.),宾夕法尼亚州普鲁士王(King of Prussia,PA));Difco(东方科技公司(Difco Laboratories),密歇根州底特律(Detroit,MI));Mediatech(敏达科技公司(Mediatech),弗吉尼亚州赫恩登(Herndon,VA));Santa Cruz(圣克鲁斯生物技术有限公司(Santa Cruz Biotechnology,Inc.),加利福尼亚州圣克鲁斯(Santa Cruz,CA));Oxoid(Oxoid有限公司,纽约州奥格登斯堡(Ogdensburg,NY));Worthington(沃辛顿生化公司(Worthington Biochemical Corp.),新泽西州弗里霍尔德(Freehold,NJ));GIBCO BRL或Gibco BRL(生命科技有限公司(Life Technologies,Inc.),马里兰州盖瑟斯堡(Gaithersburg,MD));Millipore(密理博公司(Millipore),马萨诸塞州比尔里卡(Billerica,MA));Bio-Rad(伯乐公司(Bio-Rad),加利福尼亚州赫尔克里士(Hercules,CA));Invitrogen(英杰公司(Invitrogen Corp.),加利福尼亚州圣地亚哥(San Diego,CA));NEB(纽英伦生物技术公司(New England Biolabs),马萨诸塞州贝弗利(Beverly,MA));Sigma(西格玛化工有限公司(Sigma Chemical Co.),密苏里州圣路易斯(St.Louis,MO));Pierce(皮尔斯生物技术公司(Pierce Biotechnology),伊利诺伊州罗克福德(Rockford,IL));Takara(宝生物工程株式会社(Takara Bio Inc.),日本大津(Otsu,Japan));Roche(霍夫曼-罗氏公司(Hoffmann-La Roche),瑞士巴塞尔(Basel,Switzerland));EM Science(EM科学公司(EM Science),新泽西州吉布斯敦(Gibbstown,NJ));Qiagen(凯杰公司(Qiagen,Inc.),加利福尼亚州瓦伦西亚(Valencia,CA));Biodesign(生物设计国际公司(Biodesign Intl.),缅因州萨科(Saco,Maine));Aptagen(Aptagen有限公司,弗吉尼亚州赫恩登);Sorvall(科峻仪器公司索福分公司(Sorvall brand,from Kendro Laboratory Products),北卡罗来纳州阿什维尔(Asheville,NC));Molecular Devices(分子仪器公司(Molecular Devices Corp.),加利福尼亚州森尼韦尔(Sunnyvale,CA));R&D Systems(安迪生物科技公司(R&D Systems),明尼苏达州明尼阿波利斯(Minneapolis,MN));Siegfried Handel(齐格弗里德汉德尔AG公司,瑞士祖芬根(Zofingen,Switzerland));Stratagene(Stratagene Cloning Systems公司,加利福尼亚州拉荷雅(La Jolla,CA));Marsh(马氏生物科学公司(Marsh Biosciences),纽约州罗彻斯特(Rochester,NY));Geneart(Geneart股份有限公司(Geneart GmbH),德国雷根斯堡(Regensburg,Germany));Bio-Tek(生物技术仪器公司(Bio-Tek Instruments),佛蒙特州威努斯基(Winooski,VT));Biacore(Biacore有限公司,新泽西州皮斯卡特维(Piscataway,NJ));PeproTech(派普泰克公司(PeproTech),新泽西州罗基希尔(Rocky Hill,NJ));SynPep(SynPep公司,加利福尼亚州都柏林(Dublin,CA));New Objective(科学仪器服务有

限公司新目标分公司(New Objective brand;Scientific Instrument Services,Inc.),新泽西州灵戈斯(Ringoes,NJ));Waters(沃特世公司(Waters,Inc.),马萨诸塞州米尔福德(Milford,MA));Matrix Science(矩阵科技公司(Matrix Science),马萨诸塞州波士顿(Boston,MA));Dionex(戴安公司(Dionex,Corp.),加利福尼亚州森尼韦尔(Sunnyvale,CA));Monsanto(孟山都公司(Monsanto Co.),密苏里州圣路易斯(St.Louis,MO));Wintershall(温特斯霍尔公司(Wintershall AG),德国卡塞尔(Kassel,Germany));BASF(巴斯夫公司(BASF Co.),新泽西州弗洛勒姆帕克(Florham Park,NJ));Huntsman(亨斯迈石化公司(Huntsman Petrochemical Corp.),犹他州盐湖城(Salt Lake City,UT));Shell Chemicals(壳牌化学公司(Shell Chemicals,Inc.),英国伦敦(London,UK));Stepan(斯泰潘公司(Stepan),伊利诺伊州诺斯菲尔德(Northfield,IL));Clariant(科莱恩公司(Clariant),德国苏尔茨巴赫(Sulzbach,Germany));Industrial Zeolite(工业沸石有限责任公司(Industrial Zeolite Ltd.),英国埃塞克斯郡格雷斯(Grays,Essex,UK));Jungbunzlauer(君布莱尔公司(Jungbunzlauer),瑞士巴塞尔);Solvay(苏威公司(Solvay),比利时布鲁塞尔(Brussels,Belgium));3V Sigma(3V西格玛公司(3V Sigma),意大利贝加莫省(Bergamo,Italy));Innospec(因诺斯派克公司(Innospec),英国埃尔斯米尔港(Ellesmere Port,UK));Thermphos(天富公司(Thermphos),荷兰弗利辛恩(Vlissiggen-Ost,the Netherlands));Ciba Specialty(汽巴精化有限公司(Ciba Specialty Chemicals),瑞士巴塞尔);Dow Corning(道康宁公司(Dow Corning),英国巴里(Barry,UK));Enichem(Enichem Iberica公司,西班牙巴萨罗那(Barcelona,Spain));Fluka Chemie AG(Fluka Chemie AG公司,瑞士布克斯(Buchs,Switzerland));Gist-Brocades(吉斯特-布罗卡德斯公司(Gist-Brocades,NV),荷兰代夫特(Delft,The Netherlands));Dow Corning(道康宁公司(Dow Corning Corp.),密歇根州米德兰(Midland,MI));Mettler-Toledo(梅特勒-托利多有限公司(Mettler-Toledo Inc.),俄亥俄州哥伦布(Columbus,OH));RB(英国斯劳利洁时公司(Reckitt-Benckiser,Slough,UK));以及Microsoft(微软公司(Microsoft,Inc.),华盛顿州雷德蒙德(Redmond,WA))。

[0627] 如本文所用,在一些列表中,标出了前置的“0”,以提供每个位点的三位数名称(例如,“001”与“1”相同,因此“A001C”与“A1C”相同)。在一些列表中,未包括前面的“0”。此外,如本文所用,“X”是指任何氨基酸。

[0628] 在本文提供的示例性洗涤剂组合物中,酶水平是以总组合物重量计的纯酶表示,除非另外指明,否则洗涤剂成分是以总组合物的重量表示。其中的缩写的组分标识具有以下含义:

缩写		成分
LAS	:	直链 C_{11-13} 烷基苯磺酸钠。
NaC16-17HSAS	:	C_{16-17} 高可溶性烷基硫酸钠
TAS	:	牛油烷基硫酸钠。
CxyAS	:	C_{1x} - C_{1y} 烷基硫酸钠。
CxyEz	:	与平均 z 摩尔环氧乙烷缩合的 C_{1x} - C_{1y} 主要直链的伯醇。
CxyAEzS	:	与平均 z 摩尔环氧乙烷缩合的 C_{1x} - C_{1y} 烷基硫酸钠。在实例中增添分子名称。
非离子型	:	混合的乙氧基化/丙氧基化脂肪醇，如 Plurafac LF404 为平均乙氧基化度为 3.8 且平均丙氧基化度为 4.5 的醇。

[0629]

QAS	:	$R_2 = C_{12}$-C_{14} 的 $R_2.N+(CH_3)_2(C_2H_4OH)$。
硅酸盐	:	无定形硅酸钠（SiO_2:Na_2O 比率= 1.6-3.2:1）。
偏硅酸盐	:	偏硅酸钠（SiO_2:Na_2O 比率= 1.0）。
沸石 A	:	式 $Na_{12}(A1O_2SiO_2)_{12}. 27H_2O$ 的水合硅铝酸盐
SKS-6	:	式 δ-$Na_2Si_2O_5$ 的结晶层状硅酸盐。
硫酸盐	:	无水硫酸钠。
STPP	:	三聚磷酸钠。
MA/AA	:	4:1 丙烯酸系(acrylate)/马来酸系(maleate)的无规共聚物，平均分子量为约 70,000-80,000。
AA	:	平均分子量为 4,500 的聚丙烯酸钠聚合物。

缩写		成分
聚羧酸系	:	分子量范围为 2,000-80,000 之间的、包含羧化单体如丙烯酸系、马来酸系和甲基丙烯酸系的混合物的共聚物，例如可从 BASF 商购获得的 Sokolan，其为丙烯酸的共聚物，分子量为 4,500。
BB1	:	3-(3,4-二氢异喹啉)丙磺酸盐
BB2		1-(3,4-二氢异喹啉)-癸烷-2-硫酸盐
PB1	:	过硼酸钠一水合物。
PB4	:	标称化学式为 $NaBO_3 4H_2O$ 的过硼酸钠四水合物。
过碳酸盐	:	标称化学式为 $2Na_2CO_3.3H_2O_2$ 的过碳酸钠。
TAED	:	四乙酰基乙二胺。
NOBS	:	钠盐形式的壬酰氧基苯磺酸盐。
DTPA	:	二亚乙基三胺五乙酸。
HEDP	:	1,1-羟基乙烷二膦酸。
DETPMP	:	二乙基三胺五(亚甲基)膦酸，由 Monsanto 公司以商品名 Dequest 2060 销售。
EDDS	:	其钠盐形式的乙二胺-N,N'-二琥珀酸，(S,S)异构体
二胺	:	二甲基氨基丙胺；1,6-己二胺；1,3-丙二胺；2-甲基-1,5-戊二胺；1,3-戊二胺；1-甲基-二氨基丙烷。
[0630] DETBCHD		5, 12-二乙基-1,5,8,12-四氮杂双环[6,6,2]十六烷，二氯化物，Mn(II)盐
PAAC	:	五胺乙酸钴(III)盐。
石蜡	:	石蜡油，由 Wintershall 公司以商品名 Winog 70 销售。
石蜡烃磺酸盐	:	其中一些氢原子已被磺酸根基团取代的石蜡油或蜡。
醛糖氧化酶	:	氧化酶，由诺维信公司以商品名醛糖氧化酶(Aldose Oxidase)销售
半乳糖氧化酶	:	购自 Sigma 的半乳糖氧化酶
nprE	:	在枯草芽孢杆菌中表达的重组形式的中性金属蛋白酶（参见例如 WO 07/044993）
PMN	:	纯化的来自解淀粉芽孢杆菌的中性金属蛋白酶。
淀粉酶	:	合适的淀粉分解酶，例如由杰能科公司以商品名 PURAFECT® Ox（在 WO 94/18314、WO96/05295 中有描述）销售的那些；NATALASE®、TERMAMYL®、FUNGAMYl®以及 DURAMYL™，全部可得自诺维信公司。
脂肪酶	:	合适的脂肪分解酶，如由诺维信公司以商品名 LIPEX®、LIPOLASE®、LIPOLASE® Ultra 销售的以及由吉斯特-布罗卡德斯公司(Gist-Brocades)以 Lipomax™销售的那些。

[0631]

缩写		成分
纤维素酶	:	合适的纤维素分解酶，如由诺维信公司以商品名CAREZYME®、CELLUZYME®和/或 ENDOLASE®销售的那些。
果胶裂解酶	:	合适的果胶裂解酶，如可得自诺维信公司的以商品名PECTAWAY®和 PECTAWASH®销售的那些。
PVP	:	平均分子量为 60,000 的聚乙烯基吡咯烷酮
PVNO	:	聚乙烯基吡啶-N-氧化物，平均分子量为 50,000。
PVPVI	:	乙烯基咪唑和乙烯基吡咯烷酮的共聚物，平均分子量为 20,000。
增白剂 1	:	4,4'-双(2-磺基苯乙烯基)联苯二钠。
有机硅消泡剂	:	以硅氧烷-氧化烯共聚物作为分散剂的聚二甲基硅氧烷泡沫控制剂，所述泡沫控制剂与所述分散剂的比例为 10:1 至 100:1。
抑泡剂	:	12%有机硅/硅石，18%硬脂醇，70%颗粒形式的淀粉。
SRP 1	:	阴离子封端的聚酯。
PEG X	:	分子量为 x 的聚乙二醇。
PVP K60 ®	:	乙烯基吡咯烷酮均聚物（平均分子量为 160,000）
Jeffamine ® ED-2001	:	得自 Huntsman 的封端的聚乙二醇
Isachem ® AS	:	得自 Enichem 的支链醇烷基硫酸盐
MME PEG (2000)	:	得自 Fluka Chemie AG 公司的聚乙二醇单甲醚(MW 2000)。
DC3225C	:	有机硅抑泡剂，得自 Dow Corning 公司的硅油和硅石混合物。
TEPAE	:	四亚乙基五胺乙氧基化物。
BTA	:	苯并三唑。
甜菜碱	:	$(CH_3)_3N^+CH_2COO^-$
糖	:	工业级 D-葡萄糖或食品级糖
CFAA	:	C_{12}-C_{14}烷基 N-甲基葡糖酰胺
TPKFA	:	C_{12}-C_{14}拔顶全馏份脂肪酸(topped whole cut fatty)。
粘土	:	通式为 $Al_2O_3SiO_2 \cdot xH_2O$ 的水合硅酸铝。类型：高岭石、蒙脱石、凹凸棒石、伊利石、膨润土、多水高岭土。
pH	:	在 20℃下以 1%蒸馏水溶液测量。

[0632] 对于北美(NA)和西欧(WE)重垢液体衣物(HDL)洗涤剂，通过将预称重的液体洗涤剂(于玻璃瓶中)置于95℃水浴中2小时对市售洗涤剂中存在的酶进行热灭活。热灭活NA和WE自动餐具洗涤(ADW)洗涤剂的温育时间是8小时。未加热的和加热过的洗涤剂二者均在溶解该洗涤剂5分钟内测定，以便精确地测定灭活百分比。通过AAPF测定法测试酶活性。

[0633] 为了测试在热灭活洗涤剂中的酶活性，由热灭活的储备液制备洗涤剂的工作溶液。添加适当量的水硬度(例如6gpg或12gpg)和缓冲液至该洗涤剂溶液以匹配所需的条件。通过涡旋或倒转瓶子来混合溶液。下表提供了关于本文所用的一些市售洗涤剂和测试条件的信息。在一些实验中，另外的和/或其他的市售洗涤剂可用于以下实例。

[0634]

表 A: 衣物和盘碟洗涤条件

地区	形式	剂量	洗涤剂*	缓冲液	Gpg	pH	T（℃）
衣物（重垢液体和颗粒）							
NA	HDL	0.78g/l	P&G TIDE® 2X	5mM HEPES	6	8.0	20
WE	HDL	5.0g/L	Henkel PERSIL™	5mM HEPES	12	8.2	40
WE	HDG	8.0g/L	P&G ARIEL®	2mM Na_2CO_3	12	10.5	40
JPN	HDG	0.7g/L	P&G TIDE®	2mM Na_2CO_3	6	10.0	20
NA	HDG	1.0g/L	P&G TIDE®	2mM Na_2CO_3	6	10.0	20
自动餐具洗涤							
WE	ADW	3.0g/L	RB CALGONIT™	2mM Na_2CO_3	21	10.0	40
NA	ADW	3.0g/L	P&G CASCADE®	2mM Na_2CO_3	9	10.0	40

[0635] 在一些另外的实例中,可使用以下溶液：

[0636]

表 B: 工作洗涤剂溶液

洗涤剂	温度（℃）	洗涤剂 g/L	pH	缓冲液	Gpg
TIDE® 2X Cold	16	0.98	8	5mM HEPES	6
TIDE® 2X Cold	32	0.98	8	5mM HEPES	6
TIDE® 2X Cold	16	0.98	7	5mM MOPS	6

[0637] 表C提供了根据本发明制备的适于洗涤织物的颗粒状衣物洗涤剂组合物。

[0638]

表 C: 颗粒状衣物洗涤剂组合物及它们的组分

组分	洗涤剂组合物					
	1	2	3	4	5	6

[0639]

表 C: 颗粒状衣物洗涤剂组合物及它们的组分

组分	洗涤剂组合物					
	1	2	3	4	5	6
具有脂族碳链长 C_{11}-C_{12} 的直链烷基苯磺酸盐	15	12	20	10	12	13
其他表面活性剂	1.6	1.2	1.9	3.2	0.5	1.2
磷酸盐助洗剂	2	3	4			
沸石		1		1	4	1
硅酸盐	4	5	2	3	3	5
碳酸钠	2	5	5	4	0	3
聚丙烯酸酯(MW 4500)	1	0.6	1	1	1.5	1
羧甲基纤维素（来自 CPKelco 的 Finnfix BDA）	1	-	0.3	-	1.1	-
Celluclean® (15.6mg/g)	0.23	0.17	0.5	0.2	0.2	0.6
冷水蛋白酶*	0.23	0.17	0.05	0.2	0.03	0.1
Stainzyme Plus® (14mg/g)	0.23	0.17	0.5	0.2	0.2	0.6
Mannaway 4.0T (4mg/g)	0.1			0.1		0.1
Lipex 100T (18.6mg/g)	0.2		0.1		0.3	
荧光增白剂	0.16	0.06	0.16	0.18	0.16	0.16
二亚乙基三胺五乙酸或乙二胺四乙酸	0.6		0.6	0.25	0.6	0.6
$MgSO_4$	1	1	1	0.5	1	1
漂白剂和漂白活化剂	6.88		6.12	2.09	1.17	4.66
乙氧基化的噻吩调色染料[5]	0.002	0.001	0.003	0.003	-	-
直接紫 9 (Direct Violet 9)（来自 Ciba Specialty Chemicals）				0.0006	0.0004	0.0006
硫酸盐/柠檬酸/碳酸氢钠/水分/香料	补足至 100%					

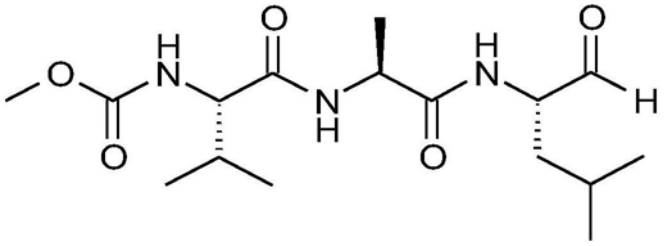
[0640] [1]无规接枝共聚物是聚乙酸乙烯酯接枝的聚环氧乙烷共聚物，其具有聚环氧乙烷主链和多条聚乙酸乙烯酯侧链。聚环氧乙烷主链的分子量为约6000，聚环氧乙烷与聚乙酸乙烯酯的重量比为约40至60，并且每50个环氧乙烷单元不超过1个接枝点。

[0641] [2]聚乙烯亚胺(MW＝600)，每个-NH具有20个乙氧基化基团。

[0642] [3]两亲性烷氧基化油脂清洁聚合物是聚乙烯亚胺(MW＝600)，每个-NH具有24个乙氧基化基团，每个-NH具有16个丙氧基化基团

[0643] [4]以下结构的可逆蛋白酶抑制剂：

[0644]



[0645] [5]乙氧基化的噻吩调色染料是如US 7,208,459 B2中描述的。

[0646] 在表C中，所有酶水平均以酶原料的百分比表示，(本发明的)冷水蛋白酶除外，其

以添加至产品的活性蛋白质的百分比表示。

[0647] 表D提供了适用于顶开式自动洗衣机的颗粒状衣物洗涤剂组合物(洗涤剂组合物7-9)和前开式洗衣机的颗粒状衣物洗涤剂组合物(洗涤剂组合物10-11)。将测试的GG36蛋白酶变体和/或本发明的冷水蛋白酶分别添加至这些制剂。

[0648]

表 D: 颗粒状衣物洗涤剂组合物及它们的组分

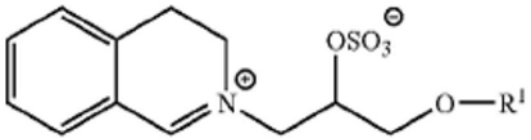
组分	洗涤剂组合物				
	7	8	9	10	11
表面活性剂					
C_{16-17} 支链烷基硫酸盐	3.55	15.8			
C_{12-14} 烷基硫酸盐			1.5		
具有脂族链长 C_{11}-C_{12} 的直链烷基苯磺酸钠	9.6		10.6	7.5	9
$C_{14/15}$ 醇乙氧基–3-硫酸钠	1.15			2.88	
$C_{14/15}$ 烷基硫酸钠	2.37				
具有平均 7 摩尔乙氧基化的 $C_{14/15}$ 醇乙氧基化物				1.17	1
单 C_{8-10} 烷基单羟乙基二甲基季铵氯化物					0.45
二甲基羟乙基月桂基氯化铵			0.18		
沸石 A	13.9	4.7	0.01	2.9	1.8
硅酸钠 1.6.比率	4	0.2		4	4
硅酸钠 2.35.比率			8		
柠檬酸				2.5	1.4
三聚磷酸钠			5		
碳酸钠	24.1	30	16.9	24.4	21

表 D：颗粒状衣物洗涤剂组合物及它们的组分

组分	洗涤剂组合物				
	7	8	9	10	11
壬酰氧基苯磺酸盐	5.78	2.81	0.96		
基于噁吖丙啶鎓(oxaziridinium)的漂白增强剂				0.03	0.017
S,S,-乙二胺二琥珀酸四钠				0.2	
二亚乙基三胺五(亚甲基膦酸)，七钠盐	0.61				0.33
羟基乙烷二亚甲基膦酸				0.29	0.45
乙二胺四乙酸盐			0.27		
硫酸镁			0.47	0.5994	0.782
过碳酸钠	7	4.4		15.9	19.1
四乙酰基乙二胺				3.3	4.6
过硼酸钠一水合物			1.2		
羧甲基纤维素（例如来自 CPKelco 的 Finnfix BDA）	0.1		0.17	1.69	0.23
丙烯酸/马来酸共聚物钠盐(70/30)	0.0236	3.8		2	2.5
聚丙烯酸钠(Sokalan PA30 CL)	4		0.84		
对苯二甲酸酯聚合物				0.23	
聚乙二醇/乙酸乙烯基酯无规接枝共聚物			0.89	0.89	0.91
光漂白剂-四磺酸基酞菁锌			0.005	0.001	0.002
C.I.荧光增白剂 260	0.11	0.15	0.04	0.23	0.15
C.I.荧光增白剂 351 (Tinopal® CBS)			0.1		
抑泡剂颗粒		0.25		0.07	0.04
疏水改性的羧甲基纤维素(Finnifix® SH-1)			0.019	0.028	
膨润土			8.35		
杂项（染料、香料、加工助剂、水分和硫酸钠）	余量	余量	余量	余量	余量

[0649]

[0650] 在表D中，表面活性剂成分可获自任何合适的供应商，包括但不限于BASF(例如LUTENSOL®)、Shell Chemicals、Stepan、Huntsman和Clariant(例如PRAEPAGEN®)。沸石可获自诸如Industrial Zeolite的来源。柠檬酸和柠檬酸钠可获自诸如Jungbunzlauer的来源。过碳酸钠、碳酸钠、碳酸氢钠和倍半碳酸钠可获自诸如Solvay的来源。丙烯酸系/马来酸系共聚物可获自诸如BASF的来源。羧甲基纤维素和疏水改性的羧甲基纤维素可获自诸如CPKelco的来源。C.I.荧光增白剂260可获自3V Sigma(例如OPTIBLANC®、OPTIBLANC® 2M/G、OPTIBLANC® 2MG/LT Extra或OPTIBLANC®Ecobright。S,S-乙二胺二琥珀酸四钠可获自诸如Innospec的来源。对苯二甲酸酯共聚物可获自Clariant(例如REPELOTEX SF 2)。另外，1-羟基乙烷-1,1-二膦酸可获自Thermphos。基于噁吖丙啶鎓的漂白增强剂具有以下结构，其中R1＝2-丁基辛基，并根据US 2006/0089284A1制备。

[0651] 

[0652] 酶NATALASE®、TERMAMYL®、STAINZYME PLUS®、CELLUCLEAN®和MANNAWAY®可从Novozymes获得。四磺酸基酞菁锌可从Ciba Specialty Chemicals获得(例如TINOLUX® BMC)。抑泡剂颗粒可从Dow Corning获得。在这些洗涤剂组合物中,无规接枝共聚物是聚乙酸乙烯酯接枝的聚环氧乙烷共聚物,其具有聚环氧乙烷主链和多条聚乙酸乙烯酯侧链。聚环氧乙烷主链的分子量为约6000,聚环氧乙烷与聚乙酸乙烯酯的重量比为约40至60,并且每50个环氧乙烷单元不超过1个接枝点。

[0653] 表E-G提供了适用于洗涤机的另外的颗粒状洗涤剂组合物(洗涤剂36a-n)。将测试的GG36蛋白酶变体或本发明的冷水蛋白酶分别添加至这些制剂。

[0654]

表 E: 另外的颗粒状衣物洗涤剂组合物及它们的组分

	洗涤剂组合物				
组分	36a	36b	36c	36d	36e
表面活性剂					
C_{10}非离子型				0.1843	
C_{16-17}支链烷基硫酸盐	3.53	3.53	3.53		
C_{12-14}烷基硫酸盐					
具有脂族链长C_{11}-C_{12}的直链烷基苯磺酸钠	8.98	8.98	8.98	13.58	14.75

[0655]

$C_{14/15}$醇乙氧基–3-硫酸钠	1.28	1.28	1.28		
$C_{14/15}$烷基硫酸钠	2.36	2.36	2.36		
具有平均 7 摩尔乙氧基化的 $C_{14/15}$醇乙氧基化物					
单 C_{8-10}烷基单羟乙基二甲基季铵氯化物					
二甲基羟乙基月桂基氯化铵				0.1803	
沸石 A	15.31	15.31	15.31		4.47
膨润土				8.35	
硅酸钠 1.6.比率					0.16
硅酸钠 2.0.比率	3.72	3.72	3.72	8.41	
硅酸钠 2.35.比率					
柠檬酸				0.0066	
三聚磷酸钠				5.06	
碳酸钠	26.1	26.18	26.1	15.9	29.0
壬酰氧基苯磺酸盐	5.78	5.78	5.78	1.17	1.86
基于噁吖丙啶鎓的漂白增强剂	0.037	0.037	0.037		
S,S,-乙二胺二琥珀酸四钠					
二亚乙基三胺五(亚甲基膦酸)，七钠盐	0.62	0.62	0.62		
羟基乙烷二亚甲基膦酸					
乙二胺四乙酸盐				0.2701	
硫酸镁	0.056	0.056	0.056	0.47	
过碳酸钠		7.06	7.06		3.64
四乙酰基乙二胺					
过硼酸钠一水合物				1.47	
羧甲基纤维素（例如来自 CPKelco 的 Finnfix BDA）	0.38	0.38	0.38	0.173	
丙烯酸/马来酸共聚物钠盐(70/30)	3.79	3.78	3.79		3.64
聚丙烯酸钠(Sokalan PA30 CL)	3.78	3.78	3.78	0.842	
对苯二甲酸酯聚合物					
聚乙二醇/乙酸乙烯基酯无规接枝共聚物				0.89	
光漂白剂-四磺酸基酞菁锌					
C.I.荧光增白剂 260	0.1125	0.1125	0.1125	0.043	0.15
C.I.荧光增白剂 351 (Tinopal® CBS)				0.0952	
抑泡剂颗粒	0.015	0.015	0.015		0.031
疏水改性的羧甲基纤维素(Finnifix® SH-1)					
膨润土					

[0656]

杂项（染料、香料、加工助剂、水分和硫酸钠）	余量	余量	余量	余量	余量

[0657]

表 F：另外的颗粒状衣物洗涤剂组合物及它们的组分					
	洗涤剂组合物				
组分	36f	36g	36h	36i	36j
表面活性剂					
C_{10} 非离子型	0.1142	0.2894	0.1885	0.1846	0.1885
C_{16-17} 支链烷基硫酸盐					
C_{12-14} 烷基硫酸盐					
具有脂族链长 C_{11}-C_{12} 的直链烷基苯磺酸钠	12.94	15.69	9.01	8.42	9.51
$C_{14/15}$ 醇乙氧基–3-硫酸钠					
$C_{14/15}$ 烷基硫酸钠					
具有平均 7 摩尔乙氧基化的 $C_{12/14}$ 醇乙氧基化物	2.9				
具有平均 3 摩尔乙氧基化的 $C_{12/14}$ 醇乙氧基化物				2.44	
具有平均 7 摩尔乙氧基化的 $C_{14/15}$ 醇乙氧基化物			0.97	1.17	0.97
单 C_{8-10} 烷基单羟乙基二甲基季铵氯化物			0.45		
二甲基羟乙基月桂基氯化铵		0.195			0.45
沸石 A	2.01	0.39	1.83	2.58	0.59
硅酸钠 1.6.比率			4.53	5.62	4.53
硅酸钠 2.0.比率		10.1			
硅酸钠 2.35.比率	7.05				
柠檬酸			1.4	1.84	1.0
三聚磷酸钠		5.73			
碳酸钠	12.65	15.93	21.0	27.31	20.2
壬酰氧基苯磺酸盐		1.73			
基于噁吖丙啶鎓的漂白增强剂			0.0168	0.0333	0.024
S,S,-乙二胺二琥珀酸四钠					
二亚乙基三胺五(亚甲基膦酸)，七钠盐			0.327		0.3272
羟基乙烷二亚甲基膦酸			0.45	0.2911	0.45
乙二胺四乙酸盐		0.28		0.1957	
硫酸镁		0.54	0.79	0.6494	0.793
过碳酸钠			19.1	15.85	22.5
四乙酰基乙二胺			4.554	3.71	5.24
过硼酸钠一水合物		5.55			

[0658]

羧甲基纤维素（例如来自 CPKelco 的 Finnfix BDA）	0.62	0.21	0.23	1.07	0.2622
丙烯酸/马来酸共聚物钠盐(70/30)	0.40	2.61	2.5	2.00	1.75
聚丙烯酸钠(Sokalan PA30 CL)			0.0055	0.011	0.008
对苯二甲酸酯聚合物				0.231	
聚乙二醇/乙酸乙烯基酯无规接枝共聚物	0.55	1.40	0.911	0.8924	0.911
光漂白剂-四磺酸基酞菁锌					
C.I.荧光增白剂 260	0.1174	0.048	0.1455	0.2252	0.1455
C.I.荧光增白剂 351 (Tinopal® CBS)		0.1049			
抑泡剂颗粒			0.04	0.0658	0.04
疏水改性的羧甲基纤维素(Finnifix® SH-1)					
膨润土					
杂项（染料、香料、加工助剂、水分和硫酸钠）	余量	余量	余量	余量	余量

[0659]

表 G: 另外的颗粒状衣物洗涤剂组合物及它们的组分

	洗涤剂组合物				
组分	36k	36l	36m	36n	
表面活性剂					
C_{10} 非离子型	0.1979	0.1979	0.1979	0.1979	
$C_{16\text{-}17}$ 支链烷基硫酸盐					
$C_{12\text{-}14}$ 烷基硫酸盐					
具有脂族链长 C_{11}-C_{12} 的直链烷基苯磺酸钠	8.92	8.92	11.5	11.5	
$C_{14/15}$ 醇乙氧基–3-硫酸钠	1.62	1.62	1.125	1.125	
$C_{14/15}$ 烷基硫酸钠					
具有平均 7 摩尔乙氧基化的 $C_{14/15}$ 醇乙氧基化物	1.0	1.0	1.5	1.5	
单 $C_{8\text{-}10}$ 烷基单羟乙基二甲基季铵氯化物					
二甲基羟乙基月桂基氯化铵					
沸石 A	1.63	1.63	2.0	2.0	
硅酸钠 1.6.比率	4.75	4.75	4.75	4.75	
硅酸钠 2.0.比率			0.06	0.06	
硅酸钠 2.35.比率					
柠檬酸	1.10	1.10	1.1	1.1	
三聚磷酸钠					
碳酸钠	23.3	23.3	23.3	23.3	

[0660]

壬酰氧基苯磺酸盐					
基于噁吖丙啶鎓的漂白增强剂	0.021	0.021	0.015	0.015	
S,S,-乙二胺二琥珀酸四钠	0.26	0.26	0.26	0.26	
二亚乙基三胺五(亚甲基膦酸)，七钠盐					
羟基乙烷二亚甲基膦酸	0.47	0.47	0.47	0.47	
乙二胺四乙酸盐					
硫酸镁	0.83	0.83	0.82	0.82	
过碳酸钠	19.35	19.35	19.35	19.35	
四乙酰基乙二胺	4.51	4.51	4.51	4.51	
过硼酸钠一水合物					
羧甲基纤维素（例如来自 CPKelco 的 Finnfix BDA）	1.01	1.01	1.01	1.01	
丙烯酸/马来酸共聚物钠盐(70/30)	1.84	1.84	1.84	1.84	
聚丙烯酸钠(Sokalan PA30 CL)	0.007	0.007	0.005	0.005	
对苯二甲酸酯聚合物	0.179	0.179	0.179	0.179	
聚乙二醇/乙酸乙烯基酯无规接枝共聚物	0.96	0.96	0.96	0.96	
光漂白剂-四磺酸基酞菁锌					
C.I.荧光增白剂 260	0.153	0.153	0.171	0.171	
C.I.荧光增白剂 351 (Tinopal® CBS)					
抑泡剂颗粒	0.042	0.042	0.042	0.042	
疏水改性的羧甲基纤维素(Finnifix® SH-1)					
膨润土					
杂项（染料、香料、加工助剂、水分和硫酸钠）	余量	余量	余量	余量	余量

[0661] 表E、F、G中的洗涤剂组合物36a-n的注释：

[0662] 表面活性剂成分可得自德国路德维希港巴斯夫公司(BASF,Ludwigshafen,Germany)(Lutensol®)；英国伦敦壳牌化学公司(Shell Chemicals,London,UK)；美国伊利诺伊州诺斯菲尔德斯泰潘公司(Stepan,Northfield,Illinois,USA)；美国犹他州盐湖城亨斯迈公司(Huntsman,Salt Lake City,Utah,USA)；德国苏尔茨巴赫科莱恩公司(Clariant,Sulzbach,Germany)(Praepagen®)。

[0663] 沸石可得自英国埃塞克斯郡格雷斯工业沸石有限责任公司(Industrial Zeolite(UK)Ltd,Grays,Essex,UK)。

[0664] 柠檬酸和柠檬酸钠可得自瑞士巴塞尔君布莱尔公司(Jungbunzlauer,Basel,Switzerland)。

[0665] 过碳酸钠、碳酸钠、碳酸氢钠和倍半碳酸钠可得自比利时布鲁塞尔市苏威公司(Solvay,Brussels,Belgium)。

[0666] 丙烯酸系/马来酸系共聚物可得自德国路德维希港巴斯夫公司(BASF,Ludwigshafen,Germany)。

[0667] 羧甲基纤维素和疏水改性的羧甲基纤维素可得自荷兰阿纳姆斯比凯可公司

(CPKelco,Arnhem,The Netherlands)。

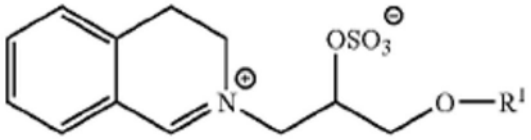
[0668] C.I.荧光增白剂260可以商品名Optiblanc®、 Optiblanc® 2M/G、Optiblanc® 2MG/LT Extra或Optiblanc® Ecobright得自意大利贝加莫省3V西格玛公司(3V Sigma,Bergamo,Italy)。

[0669] S,S-乙二胺二琥珀酸四钠可得自英国埃尔斯米尔港因诺斯派克公司(Innospec,Ellesmere Port,UK)。

[0670] 对苯二甲酸酯共聚物可以商品名Repelotex SF 2得自科莱恩公司(Clariant)。

[0671] 1-羟基乙烷-1,1-二膦酸可得自荷兰弗利辛恩天富公司(Thermphos,Vlissingen-Oost,The Netherlands)。

[0672] 基于噁吖丙啶鎓的漂白增强剂具有以下结构,其中R1＝2-丁基辛基,并根据US 2006/0089284A1制备。

[0673] 

[0674] 酶Natalase®、Termamyl®、Stainzyme Plus®、Celluclean®和Mannaway®可得自丹麦鲍斯韦诺维信公司(Novozymes,Bagsvaerd,Denmark)。

[0675] 四磺酸基酞菁锌可以商品名Tinolux® BMC得自瑞士巴塞尔汽巴精化有限公司(Ciba Specialty Chemicals,Basel,Switzerland)。

[0676] 抑泡剂颗粒可得自英国巴里道康宁公司(Dow Corning,Barry,UK)。

[0677] 无规接枝共聚物是聚乙酸乙烯酯接枝的聚环氧乙烷共聚物,其具有聚环氧乙烷主链和多条聚乙酸乙烯酯侧链。聚环氧乙烷主链的分子量为约6000,聚环氧乙烷与聚乙酸乙烯酯的重量比为约40至60,并且每50个环氧乙烷单元不超过1个接枝点。

[0678] 实例1

[0679] 测定法和测试方法

[0680] 本实例描述了用于开发本发明的多种测试方法和测定法。任何偏离于所提供的方案的地方均在相关的实例中指出。

[0681] 这些测定法用Biomek FX机械手(贝克曼库尔特公司(Beckman Coulter))或多通道移液器(例如Rainin PipetLite,梅特勒-托利多公司(Mettler-Toledo))和SpectraMAX MTP读板机(340型;美国分子仪器公司(Molecular Devices))进行。

[0682] A.测试方法

[0683] 测试方法1

[0684] 下面提供了用来确定染料或颜料材料是否是用于本发明目的的织物调色剂的方案:

[0685] 1)向两个tergotometer去污机罐中装入800ml英国泰恩河畔纽卡斯尔城市用水(Newcastle upon Tyne,UK,City Water)(约12格令/美加仑总硬度,由英国达勒姆郡Pity Me城诺森伯兰水务公司供应(Northumbrian Water,Pity Me,Durham,Co.Durham,UK))。

[0686] 2)将罐插入tergotometer去污机中,在实验期间水温控制在30℃并且搅拌设定在

40rpm。

[0687] 3)向每个罐添加4.8g的IEC-B洗涤剂(B型IEC 60456洗衣机参考基础洗涤剂(IEC 60456Washing Machine Reference Base Detergent Type B),由德国Brüggen-Bracht的wfk公司提供)。

[0688] 4)两分钟后,向第一个罐添加2.0mg活性着色剂。

[0689] 5)一分钟后,向每个罐添加切成5cm×5cm样本的50g扁平棉背心(由英国达勒姆郡康塞特(Consett,County Durham,UK)的Warwick Equest公司提供)。

[0690] 6)10分钟后,将罐中水排出并重新装上水硬度为14.4英式克拉克(Clark)度硬度的冷水(16℃),钙镁摩尔比为3:1。

[0691] 7)2分钟漂洗后,移出织物。

[0692] 8)使用相同的处理再重复步骤3-7三个循环。

[0693] 9)收集织物并在室内挂干12小时。

[0694] 10)用装配有D65光源和UVA减光滤光片的Hunter Miniscan光谱仪分析样本,以获得Hunter a(红绿轴)和Hunter b(黄蓝轴)值。

[0695] 11)将每组的织物的Hunter a值和Hunter b值取平均值。如果用评估的着色剂处理过的织物在a轴或b轴上显示出大于0.2个单位的平均色调差异,则其被认为是用于本发明目的的织物调色剂。

[0696] 测试方法2

[0697] 对于测试方法2,用颗粒状洗涤剂组合物10(参见上面的表D)进行下面提供的BMI微样本测定法。将衣物洗涤剂溶解于硬度为12gpg且调节至温度为16℃的水中,添加目的蛋白酶变体酶。然后按照所描述的BMI微样本测定法测定蛋白酶变体酶的性能。通过将蛋白酶变体酶的性能与具有SEQ ID NO:2的氨基酸序列的迟缓芽孢杆菌GG36枯草杆菌蛋白酶的性能相比较来确定性能指数,在所有情况中,酶剂量范围为0.1-5ppm。性能指数为1.1或更大的蛋白酶变体酶被视为是冷水蛋白酶。

[0698] 测试方法3

[0699] 对于测试方法3,用颗粒状衣物洗涤剂组合物7(参见上面的表D)进行下面提供的BMI微样本测定法。将衣物洗涤剂溶解于硬度为6gpg且调节至温度为16℃的水中,添加目的GG36蛋白酶变体酶。然后按照所描述的BMI微样本测定法测定GG36蛋白酶变体酶的性能。通过将GG36蛋白酶变体酶的性能与具有SEQ ID NO:2的氨基酸序列的迟缓芽孢杆菌GG36枯草杆菌蛋白酶的性能相比较来确定性能指数,在所有情况中,酶剂量范围为0.1-5ppm。性能指数为1.1或更大的GG36蛋白酶变体酶被视为是冷水蛋白酶。

[0700] 测试方法4

[0701] 对于测试方法4,用颗粒状衣物洗涤剂组合物7(参见上面的表D)进行BMI微样本测定法。将衣物洗涤剂溶解于硬度为6gpg且调节至温度为16℃的水中,添加目的GG36蛋白酶变体酶。然后按照所描述的BMI微样本测定法测定GG36蛋白酶变体酶的性能。通过将GG36蛋白酶变体酶的性能与参考酶GG36-A158E,的性能相比较来确定性能指数,所述GG36-A158E参考酶由在位置158处具有丙氨酸置换为谷氨酸的单一置换(即A158E突变)的SEQ ID NO:2的迟缓芽孢杆菌枯草杆菌蛋白酶GG36蛋白酶氨基酸序列组成,在所有情况中酶剂量范围为0.1-5ppm。性能指数为1.0或更大的GG36蛋白酶变体酶被视为是冷水蛋白酶。

[0702] 测试方法6

[0703] 对于测试方法6,使用表1-2中的洗涤剂36a-36n中的一种进行BMI微样本测定法。将洗涤剂溶解于具有如表1-2中指定的硬度且调节至温度为16℃的水中。然后按照所描述的BMI微样本测定法测定变体酶的性能。通过将变体的性能与具有SEQ ID NO:2的酶的性能相比较来确定性能指数,在所有情况下酶剂量范围为0.1-5ppm。性能指数为1.1或更大的酶被视为是冷水蛋白酶。

[0704] B.测定法

[0705] 96孔微量滴定板中测定蛋白质含量的TCA测定法

[0706] 在潮湿通风环境下,将枯草芽孢杆菌培养物在37℃下培养2-3天,同时以250-300rpm振摇。通过离心和/或过滤将细胞从包含酶的培养上清液中移除。使用TCA沉淀测定法测定蛋白酶/蛋白质/酶浓度。将培养上清液的等分试样(20-25ul)转移到包含100微升/孔0.25N HCl的96孔平底微量滴定板(MTP;Costar 9017中结合力透明聚苯乙烯板)。在混合5秒后,通过在405nm处的光散射/吸光度读数确定“基线”读数。将100微升/孔的30%(w/v)三氯乙酸(TCA)添加到含HCl的板中,并在室温下温育10分钟,以促进蛋白质沉淀。混合5秒后,测定该“测试”板在405nm处的光散射/吸光度。样品中浊度/光散射的增加与培养上清液中可沉淀蛋白质的总量相关。通过从“测试”读数(添加TCA后得到)减去“基线”读数(添加HCl后得到)进行计算,从而得到存在的总蛋白质的相对量度。如果需要,可通过用具有已知比活性的克隆的AAPF蛋白酶测定法(参见下文)校正TCA读数,来生成标准曲线。然而,TCA结果对于50至500份每一百万份(ppm)的蛋白质(其中1ppm对应于1mg/L)的蛋白质浓度而言是线性的,因而可相对于酶性能直接绘图以选择具有所需性能的变体。

[0707] 96孔微量滴定板中的AAPF蛋白酶测定法

[0708] 为了测定丝氨酸蛋白酶变体的蛋白酶活性,对N-琥珀酰-L-丙氨酰-L-丙氨酰-L-脯氨酰-L-苯基-对硝基苯胺(suc-AAPF-pNA)的水解进行了测量。所用试剂溶液为:100mM Tris/HCl,pH 8.6,包含0.005% TWEEN®-80(Tris稀释缓冲液);100mM Tris缓冲液,pH 8.6,包含1mM $CaCl_2$和0.005% TWEEN®-80(Tris/Ca缓冲液);以及160mM suc-AAPF-pNA的DMSO溶液(suc-AAPF-pNA储备溶液)(Sigma:S-7388)。为制备suc-AAPF-pNA工作溶液,将1ml suc-AAPF-pNA储备溶液添加至100ml Tris/Ca缓冲液并充分混合至少10秒。通过添加10μl的稀释蛋白酶溶液至96孔MTP的每个孔,随即添加190μL的1mg/ml suc-AAPF-pNA工作溶液来进行该测定法。将溶液混合5秒,25℃下在MTP读板机中在405nm处读取动力学模式的吸光度变化(5分钟内25个读数)。蛋白酶活性表示为AU(活性=$\Delta OD \cdot min^{-1}\ ml^{-1}$)。

[0709] 水蛭抑制剂C抑制测定法

[0710] 如本文所述,通过用称为水蛭抑制剂c的抑制剂进行滴定来测定丝氨酸蛋白酶浓度和比活性。来自水蛭欧洲医蛭(Hirudo medicinalis)的水蛭抑制剂c为枯草杆菌蛋白酶和天冬氨酸蛋白酶的紧密结合蛋白抑制剂(Heinz et al.,Biochemistry,31:8755-66[1992](Heinz等人,《生物化学》,第31卷:第8755-8766页,1992年)),并因此可用于测量蛋白酶的酶浓度,继而可计算比活性。通过标准方法合成了水蛭抑制剂c的基因并在大肠杆菌中进行了表达。其特性和抑制效力与购自Sigma的水蛭抑制剂c相同。

[0711] (i)水蛭抑制剂C储备溶液的浓度测定

[0712] 将已知比活性的迟缓芽孢杆菌枯草杆菌蛋白酶的样品稀释于含有1mM $CaCl_2$和0.005％ TWEEN®-80的100mM Tris缓冲液(pH 8.6)(Tris/Ca缓冲液)中，至适于上述AAPF蛋白酶测定法的浓度。也在该Tris/Ca缓冲液中制备了水蛭抑制剂c储备溶液的若干稀释液。将每种稀释的水蛭抑制剂c溶液的等分试样与等体积的稀释的迟缓芽孢杆菌枯草杆菌蛋白酶溶液混合。也将仅含Tris/Ca缓冲液而不含水蛭抑制剂c的等分试样与等体积的稀释的迟缓芽孢杆菌枯草杆菌蛋白酶溶液混合，以测量在不存在水蛭抑制剂c的情况下的未受抑制的枯草杆菌蛋白酶活性。将混合的溶液在室温下温育15-30分钟，然后通过上述AAPF测定法测量每份样品的蛋白酶活性。利用迟缓芽孢杆菌枯草杆菌蛋白酶的已知比活性，测定每份样品中活性蛋白酶的浓度。然后根据与仅与Tris/Ca缓冲液(无水蛭抑制剂c)混合的未受抑制的枯草杆菌蛋白酶样品相比较所观察到的蛋白酶活性的下降，计算每份样品中水蛭抑制剂c的浓度。因而，利用已知稀释度和体积的水蛭抑制剂c溶液，储备溶液中水蛭抑制剂c的浓度得以测定。

[0713] (ii)枯草杆菌蛋白酶变体的浓度和比活性测定

[0714] 将枯草杆菌蛋白酶变体的样品稀释于含有1mM $CaCl_2$和0.005％ TWEEN®-80的100mM Tris缓冲液(pH 8.6)(Tris/Ca缓冲液)中。还在该Tris/Ca缓冲液中制备已知浓度的水蛭抑制剂c储备溶液的若干稀释液。将每个稀释的水蛭抑制剂c溶液的等分试样与等体积的枯草杆菌蛋白酶变体溶液混合。将混合的溶液在室温下温育15-30分钟，然后通过AAPF测定法测量每份样品的蛋白酶活性。利用在添加每份水蛭抑制剂c样品时观察到的蛋白酶活性的降低和水蛭抑制剂c的已知浓度，完全抑制每种枯草杆菌蛋白酶变体所需的水蛭抑制剂C的浓度得以计算。这个浓度等同于样品中的酶浓度。也将仅Tris/Ca缓冲液(无水蛭抑制剂c)的等分试样与每份枯草杆菌蛋白酶变体样品混合，通过AAPF测定法测量在不存在水蛭抑制剂c的情况下的蛋白酶活性。然后利用如上面测定的酶浓度计算枯草杆菌蛋白酶变体的比活性。

[0715] BMI微样本测定法(BMI测定法)

[0716] 在96孔微量滴定板(MTP;Corning 3641)中的经预漂洗并裁成5.5毫米直径圆片的被血液、奶及油墨(BMI)染污的微样本(EMPA116)得自测试材料BV中心(Center for Testmaterials BV)(荷兰费拉尔丁恩(Vlaardingen,The Netherlands))。

[0717] 通过以下方式制备洗涤剂7-11和36a-n(表D-G)：在2mM碳酸钠中混合至少30分钟，如表1-1和表1-2中所述在Milli-Q水中以适当水平的水硬度(3:1Ca:Mg-$CaCl_2$:$MgCl_2 \cdot 6H_2O$)缓冲到pH 10.3。将洗涤剂等分到50ml圆锥管(Falcon)中，离心除去沉淀，并且在使用之前在冰上冷却30分钟。

[0718] 使酶浓度相对于纯化的GG36的标准品调整(equalize)至20-50ppm范围内的所需固定浓度。使用以AAPF作为底物的GG36的比活性将扣除基线的TCA值换算为酶浓度(ppm)。一旦测定了酶浓度(ppm)，使用以下简单的公式计算为添加到固定体积的缓冲液(300-600μL)以达到所需储备酶浓度而需要的每种变体的体积：

[0719] x＝(目标ppm)(v_b)/(y-目标ppm)

[0720] 其中x＝酶体积，y＝酶浓度，v_b＝缓冲液体积

[0721] 使用具有Versispan 8通道臂的珀金埃尔默(Perkin-Elmer)Janus机械手的导电

尖端，将可变体积的酶从源板(爱思进(Axygen)半深孔板，具有集中的收获的用于TCA酶浓度测定法的变体)分配到填充有缓冲液的目标板中。通过用移液管上下吹吸来将样品混合三次。通过测量经调整的板的AAPF活性来验证酶稀释液的精确度，并将其与源板的AAPF活性相比较，来证实是否已制得恰当的稀释液。

[0722] 调整后，将5-15μL酶溶液添加到填充有洗涤剂的BMI微样本板以达到约200μL的最终体积。在某些情况下，酶样品未经调整，相反全部从储备板同样地稀释以达到0.1-5ppm的工作范围。从剂量响应曲线确定每种测定法的最佳目标浓度，从而测量给定洗涤剂在该范围内的清洁活性。

[0723] 用箔(Bio-Rad)密封MTP，并且在设置为4℃的冷藏室中或在32℃下，在工作台上的预设为16℃的iEMS温育器/振荡器(Thermo/Labsystems)中以1400rpm温育30分钟。温育后，将120μL上清液转移到新的MTP(Corning 9017)中并使用SpectraMax读板机在600nm下读数。通过从每个值扣除空白对照(不含酶)而得到真实的吸光度读数。

[0724] 计算每种变体的性能指数(PI)。性能指数为在固定酶浓度下通过变体酶清洁制得的上清液的吸光度与通过GG36清洁制得的上清液的吸光度的比率。对于经调整的板而言，通过用变体吸光度除以给定板上对照物的吸光度计算PI值。对于非经调整的板而言，由对照物的活性和酶浓度生成标准曲线(例如朗缪尔(Langmuir)或四参数逻辑非线性回归模型拟合)。使用此标准曲线，可在任何酶浓度下直接将变体性能与对照物性能相比较。通过用变体吸光度除以在相同酶浓度下计算的对照物吸光度来确定PI。

[0725] 大于1的性能指数(PI)(PI>1)指示与标准品(例如GG36)相比优越的变体清洁能力，而等于1的PI(PI＝1)指示与标准品表现相同的变体，小于1的PI(PI<1)指示比标准品表现差的变体。

[0726]

表 1-1：用于 BMI 微样本测定法的最终洗涤剂、水硬度和缓冲液浓度

洗涤剂组合物	最终洗涤剂浓度(g/L)	最终水硬度*(gpg)	最终碳酸钠缓冲液浓度(mM)
7	0.808	6	2
8	1	3	2
9	2.3	12	2
10	5.9	12	2
11	8.3	12	2

[0727] *(3:1Ca:Mg)浓度如文中详述。

[0728]

表 1-2: 用于 BMI 微样本测定法的最终洗涤剂、水硬度和缓冲液浓度

洗涤剂组合物	最终洗涤剂浓度 (g/L)	最终水硬度* (gpg)	最终碳酸钠缓冲液浓度(mM)
36a	0.75	6	2
36b	0.808	6	2
36c	0.808	6	2
36d	2.25	12	2
36e	1	3	2
36f	1.2	12	2
36g	3.96	12	2
36h	7.69	20	2
36i	5	10	2
36j	7.69	20	2
36k	7.69	20	2
36l	6.15	10	2
36m	7.69	20	2
36n	6.15	20	2

[0729] *(3:1Ca:Mg)浓度如文中详述。

[0730] LAS/EDTA稳定性测定法

[0731] 在限定条件下温育后测量蛋白酶变体在存在代表性阴离子型表面活性剂(LAS＝直链烷基苯磺酸盐,十二烷基苯磺酸钠-DOBS)和乙二胺四乙酸二钠的情况下的稳定性,并使用如上所述的AAPF测定法测定残余的活性。所用试剂为十二烷基苯磺酸钠盐(DOBS;Sigma No.D-2525);TWEEN®-80(Sigma No.P-8074);乙二胺四乙酸二钠(Siegfried Handel No.164599-02);HEPES(Sigma No.H-7523);非应激缓冲液:50mM HEPES(11.9g/l)+0.005% TWEEN®-80,pH 8.0;应激缓冲液:50mM HEPES(11.9g/l)、0.1%(w/v)DOBS(1g/l)、10mM EDTA(3.36g/l),pH 8.0;包含200-400μg/ml蛋白质的参考蛋白酶和蛋白酶变体培养上清液。使用的设备是作为稀释板的V形或U形底MTP(分别是Greiner 651101和650161)、用于非应激板、LAS/EDTA缓冲液板以及用于suc-AAPF-pNA板的F形底MTP(Corning 9017)、Biomek FX(Beckman Coulter)、Spectramax Plus 384MTP读板机(Molecular Devices)和iEMS温育器/振荡器(Thermo/Labsystems)。

[0732] 将iEMS温育器/振荡器(Thermo/Labsystems)设定为29℃。将培养上清液稀释到装有非应激缓冲液的板中至约25ppm的浓度(母稀释板)。对于该测定法,将20μL来自母稀释板的样品添加至装有180μL非应激缓冲液的板以得到2.5ppm的最终温育浓度。将内容物混合并保持在室温下,对这个板进行AAPF测定法。另外,将20μl来自母稀释板的样品也添加至装有180μl应激缓冲液(50mM HEPES(11.9g/l)、0.1%(w/v)DOBS(1g/l)、10mM EDTA(3.36g/l),pH 8.0)的板。将溶液混合并立刻置于29℃iEMS震荡器中400rpm下30分钟。温育30分钟后,对该应激板进行AAPF测定法。通过如下计算残余和初始AAPF活性的比率来确定样品的稳定性:残余活性(%)＝[mOD.min-1应激]*100/[mOD.min-1非应激]。

[0733] 根据要使用的测定体系(例如北美、日本、西欧或中欧条件)确定最终的洗涤剂、水硬度和缓冲液浓度。在一些实施例中,在市售的洗涤剂中测定蛋白酶变体的去污性能。商业洗涤剂制剂的热灭活用于破坏任何蛋白质组分的酶活性而同时保留非酶组分的特性。因

而,这个方法适于制备用于测试本发明的酶变体的商购洗涤剂。

[0734] 烘蛋微量滴定测定法

[0735] 对于这个测定法,从鸡蛋黄制备96孔烘蛋黄基材板。将鸡蛋黄与蛋白分离,从囊膜释放出来,用Milli-Q水稀释成20%(体积/重量)。用磁力搅拌器将稀释的蛋黄在室温下搅拌15分钟。用8通道移液管小心吸移5μL到96孔V形底板(Costar#3894)的每个孔的中央。将板在90℃下烘焙1小时并在室温下冷却。将烘蛋黄基材板在室温下保存并在制备的一周内使用。如本文所述制备自动餐具洗涤剂并预加热至50℃。用8通道移液管将190μL的等分洗涤剂添加至96孔板的每孔。用96通道移液装置将10μL稀释的酶添加至每孔。将板小心地用胶粘箔密封器密封,在振荡下于50℃温育30分钟。将120μL反应混合物转移至新的96孔平底板,在405nm处测定吸光度/光散射。405nm处的吸光度/光散射与蛋黄移除量成比例。

[0736] 蛋黄微样本测定法("CS-38微样本测定法";或"EGG"或"餐具")

[0737] 如本文所述制备自动餐具洗涤剂。所使用的设备包括New Brunswick Innova 4230振荡器/温育器和SpectraMAX(340型)MTP读板机。MTP获自Costar(9017型)。带有颜料的老化蛋黄样本(CS-38)获自材料测试中心(Center for Test Materials,荷兰费拉尔丁恩)。在切制0.25英寸圆形微样本之前,用水洗涤织物。在96孔微量滴定板的每个孔中放置一个微样本。将测试洗涤剂在50℃下平衡。将190μl洗涤剂溶液添加至MTP的每个装有微样本的孔。向这个混合物添加10μL稀释的酶溶液。用胶粘箔密封MTP,置于温育器中30分钟,同时伴随振动。温育后,将100μL来自每个孔的溶液转移至新MTP中。用SpectraMax MTP读板机在405nm处对这个MTP进行读数。还包括了空白对照以及装有微样本和洗涤剂但无酶的对照。

[0738] 在一些实施例中,可使用预先洗涤过的微样本。将这个类型的微样本在环境温度下在去离子水中预先洗涤20分钟。在预洗涤步骤后,将样本置于纸巾上干燥。然后将风干的样本在冲出式压机上用-1/4"圆形冲模打孔。最后将两个微样本竖直放到96孔MTP的每个孔中以暴露整个表面积(即不平躺在孔的底部)。

[0739] 待测试的蛋白酶变体的样品获自在MTP板中生长的培养物的过滤过的培养液。所用的设备为Biomek FX机械手(Beckman Coulter)、SpectraMAX MTP读板机(型号340;Molecular Devices)、iEMS温育器/振荡器(Thermo/Labsystems)、平底MTP(Costar 9017型,用于在温育后对反应板进行读数),以及V形底MTP(Greiner 651101,用于上清液的预先稀释)。在这个测定法中,蛋白酶水解该基材并从该基材释放颜料和不溶性粒子。因而,浊度的速率是酶活性的量度。

[0740] 在MTP规模上在市售的洗涤剂(Calgonit 5in1)中测定参考丝氨酸蛋白酶及其变体对微样本的去污性能。将从费拉尔丁恩测试材料BV中心(CFT Vlaardingen)获得的CS-38微样本(带染料的蛋黄,通过加热老化)用作基材。每个孔使用两个样本。来自Calgonit 5in1的ADW片剂用于制备洗涤剂溶液。为了使所述片剂中存在的蛋白酶活性失活,将21g片剂溶解于在水浴中加热至60℃温度的Milli-Q水中。使溶液冷却至室温,将水的体积调节至700ml。用水进一步稀释该溶液以达到3g/l的最终浓度。通过添加1.46ml的Ca/Mg混合物(Ca/Mg混合物[(3:1),1.92M $CaCl_2$=282.3g/L $CaCl_2.2H_20$;0.64M $MgCl_2$=130.1g/L $MgCl_2.6H_2O$],15000gpg)将水硬度调节至21°GH。将酶样品在10mM NaCl、0.1mM $CaCl_2$、0.005% TWEEN®-80溶液中预先稀释,并在适当浓度下测试。

[0741] 将温育器设定在50℃的所需温度。将72μL的稀释缓冲液添加至空的V形底板(即“稀释板”),然后添加8μL上清液。将来自稀释板的9μL添加至装有在171μL洗涤剂溶液中温育过的微样本的板中。将来自稀释板的9μL添加至装有所述微样本的板以得到200X的上清液总稀释度。将该微样本板(具有洗涤剂和酶)用胶带覆盖并置于温育器/振荡器中1400rpm下30分钟。温育后,将75μL反应混合物转移至空的平底板,在用吹风机去泡后在MTP读板机中读取405nm处的吸光度。在该测试中还包括了空白对照(装有一个或两个微样本和洗涤剂但未添加含参考蛋白酶的样品)。

[0742] 然后针对空白值(无酶的基材)校正获得的吸光度值,从而提供水解活性的度量。对每个样品(变体)计算性能指数。该性能指数将相同蛋白质浓度下变体的性能(实际值)和标准酶的性能(理论值)相比较。另外,可用标准酶的朗缪尔方程的参数来计算理论值。

[0743] 不锈钢上的蛋黄污渍

[0744] 将这些实验中使用的不锈钢板(10×15cm;一侧擦刷过)在实验室用餐具洗涤机中用高碱度市售洗涤剂(例如ECOLAB®洗涤剂;Henkel)在95℃下彻底洗涤,以提供清洁且无油脂的钢片。在第一次使用这些钢片之前对它们清理毛刺。将钢片在热柜中80℃下干燥30分钟,然后用蛋黄染污。在进行染污之前不接触待擦刷的表面。另外,在表面上不允许有水渍或尘块。在染污之前对冷却的钢片进行称重。

[0745] 通过将大约10-11个蛋的蛋黄(200g蛋黄)与蛋白分离来制备蛋黄。将蛋黄用叉子在玻璃烧杯中搅拌以匀化蛋黄悬浮液。然后使蛋黄通过滤器(大约0.5mm网孔)以除去粗颗粒和任何蛋壳碎片。

[0746] 用平刷(2.5″)将1.0±0.1g蛋黄悬浮液尽可能均匀地施加在每个不锈钢板的擦刷过的侧面上的140cm^{2}面积上,留下大约1cm宽的未染污的边缘(如果需要的话,使用胶带)。将染污的钢板在室温下水平干燥(以防止在钢板的边缘形成小滴)4小时(最多24小时)。

[0747] 为进行变性,将钢片浸没在煮沸的软化水中30秒(如果需要的话,使用夹持装置)。然后,将钢片在80℃下再次干燥30分钟。干燥并冷却后,对钢片进行称重。称重后,使钢片静置至少24小时(20℃,40-60%相对湿度)后再让其接受洗涤测试。为了满足测试要求,仅将具有500±100mg/140cm^2(变性后的蛋黄)的钢片用于测试。在进行洗涤测试后,将钢片在热柜中80℃下干燥30分钟,冷却后再次称重。通过将(洗涤释放的蛋黄(mg)×100)除以(施加的变性蛋黄(mg))测定清洁性能百分数。

[0748] 瓷盘上的肉糜

[0749] 对于这些实验,使用符合EN 50242,form 1495,No.0219的直径19cm的甜点盘(Arzberg公司,白釉瓷器)。在除去可见的脂肪后,将总共225g猪瘦肉和牛肉(一样一半)切细并冷却。将混合物两次通过碎肉器。避免温度高于35℃。然后,将225g肉糜与75g蛋(蛋白和蛋黄混合在一起)混合。然后在使用前,将制备物-18℃下冷冻最多三个月。如果没有猪肉可用,则使用牛肉。

[0750] 使该肉糜和鸡蛋混合物(300g)升至室温并与80ml合成水混合。然后使用厨房手动混合器将该混合物匀化2分钟。然后,使用叉子将3g肉糜/蛋/水混合物铺展在每个白色瓷盘上,在边缘周围留下大约2cm宽的未染污的空白区。施加的量为11.8±0.5mg/cm^2。将瓷盘在120℃的预热热柜中干燥2小时。盘一冷却,它们即备好待用。将盘堆叠,每个盘之间放纸巾。

[0751] 洗涤后,将盘喷以茚三酮溶液(1%乙醇)以更好地鉴别肉糜残余物。为了促进该颜

色反应，将盘在热柜中80℃下加热10分钟。通过参照IKW图卡(photographic catalogue)(IKW)目测检查肉糜残余物的颜色反应来进行对洗涤性能的评价。

[0752] 不锈钢上的蛋/奶污渍

[0753] 将这些实验中使用的不锈钢板(10×15cm;一侧擦刷过)在实验室用餐具洗涤机中用高碱度市售洗涤剂在95℃下彻底洗涤，以移除油脂和清洁钢片。用纤维素布将钢片擦亮擦干。在进行染污之前不接触待擦刷的表面。另外，在表面上不允许有水渍或尘块。在进行染污之前，将钢片置于80℃的热柜中30分钟。在染污之前对冷却的钢片进行称重。

[0754] 将完整生鸡蛋(3-4个蛋;160g/蛋)的蛋黄和蛋白放置在碗中，用搅蛋器搅拌。然后，将50ml半脱脂UHT(1.5％脂肪，超高温，匀化的)奶添加至该混合物。在不产生泡沫的情况下将该奶和蛋混合。用平刷将1.0±0.1g蛋/奶混合物均匀分布在不锈钢板的经擦刷的一侧上，用天平检查分布。在钢片的短侧边周围留下大约1.0cm的空白区。将染污的钢板在室温下水平干燥(以防止在钢板的边缘形成小滴)4小时(最多24小时)。

[0755] 然后将钢片浸没在煮沸的软化水中30秒(如果需要的话，使用夹持装置)。然后，将钢片在80℃下再次干燥30分钟。干燥并冷却后，对钢片进行称重。称重后，使钢片静置至少24小时(20℃，40-60％相对湿度)后再让其接受洗涤测试。为了满足测试要求，仅使用具有190±10mg蛋黄的钢片。

[0756] 在进行洗涤测试后，将钢片在热柜中80℃下干燥30分钟，冷却后再次称重。通过将(洗涤释放的蛋/奶(mg)×100)除以(施加的蛋/奶(mg))测定清洁性能百分数。

[0757] 瓷盘上的意大利面条混合污渍的制备

[0758] 将意大利面酱(390g)与150g煮熟的意大利面、25g肉糜(改进的IKW组合物，为225克无脂肪肉糜和75克蛋黄的组合)和50g Grozette Formaggio奶酪混合。用勺子将3g的这个混合物铺展在每个白色陶瓷盘(Arzberg公司，19cm直径，白釉瓷器，符合EN 50242,form 1495,No.0219)上，在边缘周围留下大约2cm宽的未染污空白区。通过将盘在烘箱中120℃下烘焙2小时使盘干燥。盘一冷却，它们即备好待用。将盘堆叠，每个盘之间放纸巾，用于保存。洗涤后，将盘喷以碘溶液(0.05N)以更好地鉴别碳水化合物残余物。通过参照IKW图卡(IKW)目视检查碳水化合物残余物的颜色反应来进行对洗涤性能的评价，并按0-10的等级(10为清洁)评分。

[0759] 性能指数

[0760] 该性能指数将相同蛋白质浓度下变体的性能(测量值)与标准酶的性能(理论值)相比较。另外，可用标准蛋白酶的性能剂量响应曲线的参数计算理论值。

[0761] 实例2

[0762] 用位点评价文库(SEL)产生GG36单突变体

[0763] 本实例中描述的GG36SEL的构建由GENEART使用他们的用于基因优化、基因合成、文库产生和分析的专有方法和技术平台(WO 2004/059556A3、欧洲专利No.0 200 362和No.0 201 184;以及美国专利No.4,683,195、No.4,683,202和No.6,472,184)进行。使用pHPLT-GG36枯草芽孢杆菌表达质粒(参见图2)，在本发明人预先选择的位置处产生GG36SEL。这个枯草芽孢杆菌表达质粒含有下面示出的GG36表达盒、地衣芽孢杆菌LAT启动子(Plat)和来自pUB110(McKenzie et al.,Plasmid,15:93-103,1986(McKenzie等人，《质粒》，第15卷：第93-103页，1986年))的包括复制酶基因(reppUB)、新霉素/卡那霉素抗性基

因(neo)和博来霉素抗性标记(bleo)在内的额外元件(美国专利No.6,566,112中的图4)。pHPLT-GG36质粒图谱在图2提供。GG36表达盒序列在下文提供。

[0764] GG36的DNA序列(信号序列以小写字母示出,前肽以小写带下划线的文本示出,GG36成熟序列以大写字母示出)在下面提供:

[0765] GtgagaagcaaaaaattgtggatcgtcgcgtcgaccgcactactcatttctgttgctttcagttcatcgatcgcatcggctgctgaagaagcaaaagaaaaatatttaattggctttaatgagcaggaagctgtcagtgagtttgtagaacaagtagaggcaaatgacgaggtcgccattctctctgaggaagaggaagtcgaaattgaattgcttcatgaatttgaaacgattcctgttttatccgttgagttaagcccagaagatgtggacgcgcttgagctcgatccagcgatttcttatattgaagaggatgcagaagtaacgacaatgGCGCAATCAGTGCCATGGGGAATTAGCCGTGTGCAAGCCCCAGCTGCCCATAACCGTGGATTGACAGGTTCTGGTGTAAAAGTTGCTGTCCTCGATACAGGTATTTCCACTCATCCAGACTTAAATATTCGTGGTGGCGCTAGCTTTGTACCAGGGGAACCATCCACTCAAGATGGGAATGGGCATGGCACGCATGTGGCCGGGACGATTGCTGCTTTAAACAATTCGATTGGCGTTCTTGGCGTAGCGCCGAGCGCGGAACTATACGCTGTTAAAGTATTAGGGGCGAGCGGTTCAGGTTCGGTCAGCTCGATTGCCCAAGGATTGGAATGGGCAGGGAACAATGGCATGCACGTTGCTAATTTGAGTTTAGGAAGCCCTTCGCCAAGTGCCACACTTGAGCAAGCTGTTAATAGCGCGACTTCTAGAGGCGTTCTTGTTGTAGCGGCATCTGGAAATTCAGGTGCAGGCTCAATCAGCTATCCGGCCCGTTATGCGAACGCAATGGCAGTCGGAGCTACTGACCAAAACAACAACCGCGCCAGCTTTTCACAGTATGGCGCAGGGCTTGACATTGTCGCACCAGGTGTAAACGTGCAGAGCACATACCCAGGTTCAACGTATGCCAGCTTAAACGGTACATCGATGGCTACTCCTCATGTTGCAGGTGCAGCAGCCCTTGTTAAACAAAAGAACCCATCTTGGTCCAATGTACAAATCCGCAATCATCTAAAGAATACGGCAACGAGCTTAGGAAGCACGAACTTGTATGGAAGCGGACTTGTCAATGCAGAAGCTGCAACTCGTTAA(SEQ ID NO:3)

[0766] GG36的蛋白质序列(信号序列以小写字母示出,前肽以小写带下划线的文本示出,GG36成熟蛋白酶序列以大写字母示出)在下面提供:

[0767] vrskklwivastallisvafsssiasaaeeakekyligfneqeavsefveqveandevailseeeeveiellhefetipvlsvelspedvdaleldpaisyieedaevttmAQSVPWGISRVQAPAAHNRGLTGSGVKVAVLDTGISTHPDLNIRGGASFVPGEPSTQDGNGHGTHVAGTIAALNNSIGVLGVAPSAELYAVKVLGASGSGSVSSIAQGLEWAGNNGMHVANLSLGSPSPSATLEQAVNSATSRGVLVVAASGNSGAGSISYPARYANAMAVGATDQNNNRASFSQYGAGLDIVAPGVNVQSTYPGSTYASLNGTSMATPHVAGAAALVKQKNPSWSNVQIRNHLKNTATSLGSTNLYGSGLVNAEAATR(SEQ ID NO:4)。

[0768] 诱变的方法是基于密码子特异性突变方法,其中使用在目的位点含有简并密码子NNS((A、C、T或G)、(A、C、T或G)、(C或G))的正向和反向诱变引物在特定目的密码子处同时产生所有可能的氨基酸置换。为构建每个GG36SEL,进行了三个PCR反应:两个诱变反应(初次PCR1和PCR2),以利用NNS正向和反向诱变引物(长25-45个核苷酸)在成熟GG36DNA序列中引入目的突变密码子,和第三个反应,以将两个诱变PCR产物融合在一起来构建在成熟GG36序列中具有所需的突变密码子的pHPLT-GG36表达载体。

[0769] 这个实例中使用的引物序列在下面提供:

[0770]

表 2-1: 引物	
序列	引物名称
CGCGCTT**GAGCTC**GATCCAGCGATTTC (SEQ ID NO:9)	SacI-Fw
GTCTCC**AAGCTT**TAACGAGTTGCAG (SEQ ID NO:10)	HindIII-Rv
GCAATTC**AGATCT**TCCTTCAGGTTATGACC (SEQ ID NO:11)	pHPLT-BglII-Fw
GCATCGA**AGATCT**GATTGCTTAACTGCTTC (SEQ ID NO:12)	pHPLT-BglII-Rv

[0771] Phusion高保真DNA聚合酶(Finnzymes目录号F-530L)用于所有的PCR,反应根据随同该聚合酶提供的生产商的方案执行。具体来讲,对于初次PCR 1,使用1μL(10μM)的pHPLT-BglII-Fw引物和NNS反向诱变引物每一者,对于初次PCR 2,使用1μL(10μM)的pHPLT-BglII-Rv引物和NNS正向诱变引物。每种反应物还包括1μL的pHPLT-GG36质粒模板DNA(0.1-1ng/μL)。用MJ Research PTC-200Peltier热循环仪进行PCR。反应产生出在目的GG36密码子周围具有大约30个核苷酸重叠的大约2至3kb的两个片段。所获得的片段在类似于上述PCR的第三PCR中融合,该第三PCR使用1μL初次PCR 1反应混合物、1μL初次PCR 2反应混合物和1μL(10μM)的正向和反向SacI-Fw和HindIII-Rv引物的每一者。将扩增的编码GG36变体基因的859bp线性片段纯化(使用QIAGEN®Qiaquick PCR纯化试剂盒)并用SacI和HindIIII限制酶消化以在融合片段的两侧产生粘性末端。约50ng的质粒pHPLT-GG36也在用SacI和HindIIII消化后进行纯化,从而得到3.9kb载体骨架片段。按照生产商关于克隆粘性末端的方案,使用T4DNA连接酶(Invitrogen)将消化后的载体片段与50ng消化后的编码变体酶的859bp片段连接。随后,使用连接混合物转化如所述(WO2002/014490)的枯草芽孢杆菌细胞(ΔaprE,ΔnprE,oppA,ΔspoIIE,degUHy32,ΔamyE::[xylR,pxylA-comK])。

[0772] 为了表达变体蛋白用于进一步生化分析,将携带GG36变体质粒的枯草芽孢杆菌菌株接种到装有150μl补充有10μg/ml新霉素的Luria肉汤培养基的微量滴定板中。使用Enzyscreen微量滴定板盖(Enzyscreen),将板在37℃下以300rpm振荡和80%湿度进行培养。将来自过夜培养板的10微升用于接种装有190μl含10ug/ml新霉素的MBD培养基(基于MOPS的成分确定的培养基)的新微量滴定板。基本上如本领域所知(参见Neidhardt et al.,J.Bacteriol.,119:736-747[1974](Neidhardt等人,《细菌学杂志》,第119卷:第736-747页,1974年))来制备MBD培养基,不同的是在基础培养基中省掉NH_4Cl_2、$FeSO_4$和$CaCl_2$,使用3mM K_2HPO_4,并且基础培养基补充有60mM尿素和100ml由210g/l葡萄糖和350g/l麦芽糖糊精制成的溶液。补足微量营养素,营养素为100X储备溶液,其1升含有400mg $FeSO_4$ $7H_2O$、100mg $MnSO_4.H_2O$、100mg $ZnSO_4$ $7H_2O$、50mg $CuCl_2$ $2H_2O$、100mg $CoCl_2$ $6H_2O$、100mg $NaMoO_4$ $2H_2O$、100mg $Na_2B_4O_7$ $10H_2O$、10ml 1M $CaCl_2$和10ml 0.5M柠檬酸钠。使用Enzyscreen盖(Enzyscreen),将装有MBD培养基的微量滴定板在37℃、300rpm和80%湿度下培养68小时,以测定蛋白质表达。第二天,将培养物滤过微过滤器板(0.22μm;Millipore),将所得的滤液用于生化分析。如实例1中所述进行洗涤剂组合物7-11的TCA和BMI微样本测定法。也如实例1中关于BMI测定法的描述内容所述计算性能指数,并将性能指数相对于GG36示于表2-2中。在下面的各表中,洗涤剂组合物与上面的表D中所示的那些组合物相对应。另外,如所指出,氨基酸位置根据BPN'编号方式列出。

[0773]

表 2-2：在洗涤剂 7-11 中在 TCA 或 16℃下 BMI 微样本清洁中，相对于 GG36 而言性能指数为至少 0.2 的 GG36 单变体。		
GG36 氨基酸位置（BPN'的编号方式）	野生型残基	突变残基
1	A	R

表 2-2：在洗涤剂 7-11 中在 TCA 或 16℃下 BMI 微样本清洁中，相对于 GG36 而言性能指数为至少 0.2 的 GG36 单变体。		
2	Q	A
2	Q	R
2	Q	S
2	Q	M
2	Q	W

[0774]

表 2-2：在洗涤剂 7-11 中在 TCA 或 16℃下 BMI 微样本清洁中，相对于 GG36 而言性能指数为至少 0.2 的 GG36 单变体。		
3	S	R
4	V	R
4	V	S
4	V	C
8	I	A
9	S	W
9	S	F
9	S	A
10	R	A
10	R	M
10	R	S
10	R	H
12	Q	F
12	Q	R
14	P	F
14	P	K
14	P	Q
15	A	R
15	A	F
16	A	S
17	H	R
17	H	F
17	H	M
18	N	R
18	N	K
20	G	R
20	G	K
20	G	F
22	T	R
22	T	Q
22	T	L
22	T	V
22	T	W
22	T	Y
22	T	A
23	G	A
23	G	S
23	G	F
24	S	R
24	S	W
24	S	H

表 2-2：在洗涤剂 7-11 中在 TCA 或 16℃下 BMI 微样本清洁中，相对于 GG36 而言性能指数为至少 0.2 的 GG36 单变体。		
24	S	L
24	S	Q
24	S	F
25	G	R
25	G	F
25	G	V
26	V	F
27	K	R
27	K	L
27	K	V
27	K	F
28	V	A
28	V	E
28	V	N
29	A	T
30	V	E
31	L	F
33	T	S
33	T	G
33	T	D
34	G	P
35	I	M
36	S	T
36	S	F
36	S	R
38	T	R
38	T	F
38	T	L
40	P	H
40	P	W
40	P	R
40	P	N
40	P	T
40	P	L
42	L	I
43	N	R
43	N	A
43	N	S
43	N	W
43	N	F
43	N	I

[0775]

表 2-2：在洗涤剂 7-11 中在 TCA 或 16℃下 BMI 微样本清洁中，相对于 GG36 而言性能指数为至少 0.2 的 GG36 单变体。		
43	N	D
43	N	M
45	R	T
46	G	R
48	A	R
50	F	C
51	V	W
51	V	F
51	V	H
52	P	F
52	P	N
52	P	E
55	P	Y
57	T	R
59	Q	A
59	Q	F
59	Q	R
60	D	P
60	D	A
60	D	Q
62	N	Q
62	N	E
63	G	S
63	G	A
63	G	M
63	G	V
63	G	T
63	G	H
63	G	Q
63	G	I
63	G	D
63	G	E
63	G	P
64	H	F
64	H	T
68	V	A
68	V	C
69	A	N
69	A	T
69	A	W
69	A	P

表 2-2：在洗涤剂 7-11 中在 TCA 或 16℃下 BMI 微样本清洁中，相对于 GG36 而言性能指数为至少 0.2 的 GG36 单变体。		
71	T	G
72	I	C
74	A	C
75	L	R
75	L	A
75	L	E
75	L	F
78	S	R
78	S	I
78	S	N
79	I	Q
79	I	W
81	V	R
82	L	R
82	L	T
82	L	M
82	L	F
82	L	V
85	A	M
86	P	W
86	P	I
86	P	L
89	E	P
89	E	W
89	E	T
89	E	I
89	E	H
89	E	V
89	E	F
89	E	L
89	E	W
89	E	G
91	Y	F
91	Y	N
92	A	F
94	K	N
99	S	F
99	S	T
99	S	M
99	S	G
99	S	P

[0776]

表 2-2：在洗涤剂 7-11 中在 TCA 或 16℃下 BMI 微样本清洁中，相对于 GG36 而言性能指数为至少 0.2 的 GG36 单变体。		
100	G	I
100	G	S
100	G	N
100	G	Q
101	S	N
101	S	G
101	S	T
101	S	A
101	S	D
101	S	F
101	S	D
101	S	E
101	S	P
102	G	A
102	G	N
102	G	T
102	G	E
102	G	H
103	S	N
103	S	G
103	S	D
104	V	L
104	V	I
104	V	E
104	V	D
105	S	T
105	S	Q
105	S	E
106	S	V
106	S	G
106	S	T
106	S	A
106	S	E
106	S	D
106	S	F
107	I	F
107	I	M
108	A	I
108	A	G
109	Q	M
111	L	V

表 2-2：在洗涤剂 7-11 中在 TCA 或 16℃下 BMI 微样本清洁中，相对于 GG36 而言性能指数为至少 0.2 的 GG36 单变体。		
111	L	I
112	E	V
112	E	L
112	E	Q
114	A	G
115	G	R
115	G	K
116	N	L
116	N	A
116	N	K
117	N	F
118	G	I
118	G	R
119	M	C
120	H	A
120	H	F
120	H	R
121	V	E
121	V	F
123	N	G
123	N	E
124	L	S
128	S	N
128	S	M
128	S	H
128	S	Q
128	S	I
128	S	F
128	S	L
128	S	D
129	P	E
132	S	A
132	S	E
138	A	G
144	S	R
147	V	L
148	L	I
158	A	E
159	G	C
159	G	E
160	S	D

[0777]

表 2-2：在洗涤剂 7-11 中在 TCA 或 16℃下 BMI 微样本清洁中，相对于 GG36 而言性能指数为至少 0.2 的 GG36 单变体。		
166	S	E
166	S	D
167	Y	W
175	M	V
177	V	C
181	D	A
182	Q	R
183	N	D
183	N	R
183	N	I
183	N	F
183	N	M
185	N	I
185	N	E
185	N	V
186	R	H
186	R	K
188	S	R
188	S	E
188	S	D
192	Y	W
192	Y	H
194	A	V
194	A	F
194	A	E
197	D	F
198	I	L
198	I	F
203	V	E
203	V	C
208	T	S
209	Y	N
209	Y	S
209	Y	F
209	Y	T
209	Y	H
209	Y	L
209	Y	G
209	Y	E
210	P	V
210	P	R

表 2-2：在洗涤剂 7-11 中在 TCA 或 16℃下 BMI 微样本清洁中，相对于 GG36 而言性能指数为至少 0.2 的 GG36 单变体。		
210	P	L
211	G	R
211	G	Q
212	S	I
212	S	F
212	S	M
213	T	A
214	Y	F
215	A	F
215	A	N
215	A	H
215	A	E
215	A	D
216	S	F
216	S	A
217	L	E
217	L	N
217	L	D
218	N	P
218	N	E
218	N	D
224	T	A
224	T	G
227	V	I
230	A	E
231	A	I
231	A	C
233	L	C
234	V	F
235	K	F
236	Q	N
236	Q	F
238	N	R
238	N	K
238	N	L
239	P	R
239	P	S
239	P	R
239	P	H
239	P	N
239	P	K

[0778]

表 2-2：在洗涤剂 7-11 中在 TCA 或 16℃下 BMI 微样本清洁中，相对于 GG36 而言性能指数为至少 0.2 的 GG36 单变体。		
239	P	T
239	P	F
239	P	G
240	S	R
241	W	R
242	S	R
242	S	L
243	N	R
243	N	F
244	V	R
246	I	S
248	N	I
248	N	V
248	N	R
249	H	R
249	H	T
250	L	I
251	K	R
251	K	S
252	N	R
252	N	F
252	N	H
252	N	I
253	T	R
253	T	F
253	T	I
254	A	C
256	S	N

表 2-2：在洗涤剂 7-11 中在 TCA 或 16℃下 BMI 微样本清洁中，相对于 GG36 而言性能指数为至少 0.2 的 GG36 单变体。		
258	G	R
260	T	V
260	T	I
262	L	H
262	L	D
263	Y	F
265	S	F
267	L	N
267	L	M
267	L	V
269	N	R
269	N	I
270	A	C
271	E	T
271	E	V
271	E	L
271	E	H
271	E	F
271	E	P
271	E	A
271	E	M
271	E	I
272	A	F
272	A	R
273	A	I
273	A	F
274	T	G

[0779]

表 2-3：在洗涤剂 7 中在 32℃下 BMI 微样本清洁中，相对于 GG36 而言性能指数为至少 1.5 的 GG36 单变体。
GG36 变体
N62E
A158E
G159E

[0780]

表 2-4：在洗涤剂 10 中在 32℃下 BMI 微样本清洁中，相对于 GG36 而言性能指数为至少 1.2 的 GG36 单变体。
GG36 变体
A1R
S78R
V244R
N269R
E271L

[0781] 实例3

[0782] NHJ1组和WCE1组GG36变体的构建及清洁性能

[0783] 本文描述的NHJ1组和WCE1组GG36变体在DNA 2.0有限公司(DNA2.0,Inc.)利用上述pHPLT-GG36枯草芽孢杆菌表达质粒(图2)进行构建。如实例2中所述在枯草芽孢杆菌细胞(基因型：ΔaprE,ΔnprE,amyE::xylRPxylAcomK-phleo)中表达变体，并用实例1中所述的用于蛋白质含量测定的TCA测定法、LAS/EDTA稳定性测定法和BMI微样本清洁测定法进一步表征。这些结果在表3-1和3-2中示出。在下面的各表中，洗涤剂组合物与上面的表D中所示的那些组合物相对应。另外，如所指出，氨基酸位置根据BPN’编号方式列出。

[0784]

表 3-1：在洗涤剂 7、8 或 9 中在 TCA、LAS/EDTA 稳定性或 16℃下 BMI 微样本清洁任一者中，相对于 GG36 而言性能指数为至少 0.25 的 NHJ1 变体。
GG36 变体（BPN'编号方式）
N062E-A158E
S103G-A158E
S128N-A158E
A016S-A158E
V104L-A158E
E089P-A158E
L111V-A158E
T022A-A158E
S101A-A158E

表 3-1：在洗涤剂 7、8 或 9 中在 TCA、LAS/EDTA 稳定性或 16℃下 BMI 微样本清洁任一者中，相对于 GG36 而言性能指数为至少 0.25 的 NHJ1 变体。
GG36 变体（BPN'编号方式）
L148I-A158E
P129E-A158E
T022A-E089P
A016S-E089P
N062E-E089P
N062E-E271F
A158E-E271F
R186H-E271F
P129E-E271F

[0785]

表 3-1：在洗涤剂 7、8 或 9 中在 TCA、LAS/EDTA 稳定性或 16℃下 BMI 微样本清洁任一者中，相对于 GG36 而言性能指数为至少 0.25 的 NHJ1 变体。
GG36 变体（BPN'编号方式）
L111V-E271F
Y209E-E271F
A016S-E271F
S188D-E271F
T022A-E271F
G159E-E271F
V104L-E271F
S101A-E271F
E089P-E271F
S128N-E271F
S103G-E271F
L148I-E271F
H249R-E271F
N062E-G159E
A016S-G159E
S128N-G159E
L148I-G159E
L111V-G159E
E089P-G159E
T022A-G159E
P129E-G159E
S103G-G159E
V104L-G159E
A158E-G159E
S101A-G159E
A158E-H249R
L111V-H249R
P129E-H249R
N062E-H249R
A016S-H249R
R186H-H249R
L148I-H249R
G159E-H249R
S101A-H249R
S188D-H249R
V104L-H249R
Y209E-H249R
T022A-H249R

表 3-1：在洗涤剂 7、8 或 9 中在 TCA、LAS/EDTA 稳定性或 16℃下 BMI 微样本清洁任一者中，相对于 GG36 而言性能指数为至少 0.25 的 NHJ1 变体。
GG36 变体（BPN'编号方式）
S128N-H249R
S103G-H249R
E089P-H249R
T022A-L111V
S101A-L111V
A016S-L111V
V104L-L111V
N062E-L111V
S103G-L111V
E089P-L111V
A016S-L148I
N062E-L148I
T022A-L148I
P129E-L148I
V104L-L148I
S103G-L148I
S128N-L148I
S101A-L148I
E089P-L148I
L111V-L148I
A016S-N062E
T022A-N062E
N062E-P129E
T022A-P129E
S128N-P129E
A016S-P129E
S101A-P129E
V104L-P129E
E089P-P129E
S103G-P129E
L111V-P129E
N062E-R186H
S128N-R186H
S101A-R186H
T022A-R186H
A016S-R186H
A158E-R186H
E089P-R186H

[0786]

表 3-1：在洗涤剂 7、8 或 9 中在 TCA、LAS/EDTA 稳定性或 16℃下 BMI 微样本清洁任一者中，相对于 GG36 而言性能指数为至少 0.25 的 NHJ1 变体。
GG36 变体 （BPN'编号方式）
P129E-R186H
G159E-R186H
S103G-R186H
V104L-R186H
L111V-R186H
L148I-R186H
N062E-S101A
T022A-S101A
A016S-S101A
E089P-S101A
N062E-S103G
T022A-S103G
A016S-S103G
S101A-S103G
E089P-S103G
N062E-S128N
A016S-S128N
T022A-S128N
S101A-S128N
V104L-S128N
E089P-S128N
S103G-S128N
L111V-S128N
L111V-S188D
N062E-S188D
A016S-S188D
L148I-S188D
T022A-S188D
S128N-S188D
S101A-S188D
V104L-S188D
E089P-S188D
P129E-S188D
G159E-S188D
R186H-S188D
S103G-S188D
A158E-S188D

表 3-1：在洗涤剂 7、8 或 9 中在 TCA、LAS/EDTA 稳定性或 16℃下 BMI 微样本清洁任一者中，相对于 GG36 而言性能指数为至少 0.25 的 NHJ1 变体。
GG36 变体 （BPN'编号方式）
A016S-T022A
A016S-V104L
T022A-V104L
S101A-V104L
N062E-V104L
S103G-V104L
E089P-V104L
G159E-Y209E
L111V-Y209E
S101A-Y209E
A016S-Y209E
S128N-Y209E
L148I-Y209E
P129E-Y209E
N062E-Y209E
T022A-Y209E
S103G-Y209E
A158E-Y209E
S188D-Y209E
V104L-Y209E
E089P-Y209E
R186H-Y209E
GG36

[0787]

表 3-2：在洗涤剂 10 或 11 中在 TCA、LAS/EDTA 稳定性或 16℃下 BMI 微样本清洁任一者中，相对于 GG36 而言性能指数为至少 0.2 的 WCE1 变体。
GG36 变体（BPN'编号方式）
N018R-W241R
G020R-W241R
S024R-W241R
S009A-W241R
G020R-W241R
V004R-W241R
N043R-W241R
S078R-W241R
T022R-W241R
G115R-W241R
A001R-W241R
S212F-W241R
L082R-W241R
N018R-V244R
S024R-V244R
S078R-V244R
G020R-V244R
S212F-V244R
S009A-V244R
L082R-V244R
A001R-V244R
N043R-V244R
T022R-V244R
V004R-V244R
G115R-V244R
W241R-V244R
S242R-V244R
A001R-V004R
S009A-T022R
N018R-T022R
G020R-T022R
V004R-T022R
A001R-T022R
S024R-S242R
N018R-S242R
V004R-S242R
G020R-S242R

[0788]

表 3-2：在洗涤剂 10 或 11 中在 TCA、LAS/EDTA 稳定性或 16℃下 BMI 微样本清洁任一者中，相对于 GG36 而言性能指数为至少 0.2 的 WCE1 变体。
GG36 变体（BPN'编号方式）
S212F-S242R
L082R-S242R
S078R-S242R
A001R-S242R
S009A-S242R
T022R-S242R
G115R-S242R
N043R-S242R
W241R-S242R
N018R-S212F
T022R-S212F
V004R-S212F
S024R-S212F
A001R-S212F
G115R-S212F
G020R-S212F
S009A-S212F
N043R-S212F
S078R-S212F
L082R-S212F
S009A-S078R
G020R-S078R
S024R-S078R
T022R-S078R
N018R-S078R
V004R-S078R
A001R-S078R
N043R-S078R
T022R-S024R
G020R-S024R
N018R-S024R
A001R-S024R
V004R-S024R
S009A-S024R
V004R-S009A
A001R-S009A
S242R-N269R
S024R-N269R
G020R-N269R

[0789]

表 3-2：在洗涤剂 10 或 11 中在 TCA、LAS/EDTA 稳定性或 16℃下 BMI 微样本清洁任一者中，相对于 GG36 而言性能指数为至少 0.2 的 WCE1 变体。
GG36 变体（BPN'编号方式）
T022R-N269R
H249R-N269R
S212F-N269R
N043R-N269R
V244R-N269R
A001R-N269R
N018R-N269R
S078R-N269R
S009A-N269R
G115R-N269R
W241R-N269R
V004R-N269R
L082R-N269R
N018R-N043R
G020R-N043R
V004R-N043R
T022R-N043R
S009A-N043R
A001R-N043R
S024R-N043R
S009A-N018R
V004R-N018R
A001R-N018R
S024R-L082R
S009A-L082R
N018R-L082R
A001R-L082R
S078R-L082R
G020R-L082R
T022R-L082R
V004R-L082R
N043R-L082R
N043R-H249R
G020R-H249R
V004R-H249R
N018R-H249R
S009A-H249R
S212F-H249R
T022R-H249R

[0790]

表 3-2：在洗涤剂 10 或 11 中在 TCA、LAS/EDTA 稳定性或 16℃下 BMI 微样本清洁任一者中，相对于 GG36 而言性能指数为至少 0.2 的 WCE1 变体。
GG36 变体（BPN'编号方式）
S024R-H249R
G115R-H249R
A001R-H249R
L082R-H249R
S242R-H249R
W241R-H249R
V244R-H249R
S078R-H249R
N018R-G115R
G020R-G115R
T022R-G115R
S078R-G115R
S009A-G115R
V004R-G115R
A001R-G115R
L082R-G115R
N043R-G115R
S024R-G115R
S009A-G020R
N018R-G020R
V004R-G020R
A001R-G020R
S009A-E271L
G020R-E271L
S024R-E271L
V244R-E271L
W241R-E271L
N043R-E271L
T022R-E271L
H249R-E271L
S212F-E271L
G115R-E271L
S242R-E271L
S078R-E271L
V004R-E271L
N269R-E271L
A001R-E271L
N018R-E271L
L082R-E271L

[0791]

表 3-2：在洗涤剂 10 或 11 中在 TCA、LAS/EDTA 稳定性或 16℃下 BMI 微样本清洁任一者中，相对于 GG36 而言性能指数为至少 0.2 的 WCE1 变体。
GG36 变体（BPN'编号方式）
GG36

[0792] 实例4

[0793] NHJ4组GG36变体的构建及清洁性能

[0794] 如下所述使用PCR融合或QUIKCHANGE® 多定点诱变试剂盒(“QCMS试剂盒”;Stratagene),利用pHPLT-GG36枯草芽孢杆菌表达质粒(图2),构建下面表4-4中所述的NHJ4组GG36变体。

[0795] a)通过QUIKCHANGE® 多定点诱变构建NHJ4变体

[0796] 利用QUIKCHANGE® 多定点诱变产生的变体在表4-4中示出。根据生产商的说明书,使用2微克的DNA和Dam甲基化酶(NEB)对亲本质粒pHPLT-GG36(模板DNA)进行甲基化。按照生产商的方案,通过QuikChange® 多定点诱变试剂盒(“QCMS试剂盒”;Stratagene)制备定点突变体(参见表4-1的引物序列)。为了有效转化枯草芽孢杆菌,使用Illustra Templiphi试剂盒(GE Healthcare)通过滚环扩增(RCA)来扩增来自QCMS反应混合物的DNA,根据生产商的方案进行该反应。用1微升10倍稀释的经扩增的DNA转化50μl感受态枯草芽孢杆菌细胞(基因型:Δ aprE,Δ nprE,amyE::xylRPxylAcomK-phleo)。将该转化混合物在37℃下振荡1小时。将转化混合物的10微升等分试样接种于补充有10μg/ml新霉素(Teknova)的脱脂乳(1.6%)Luria琼脂板上。随后,将在脱脂乳板上形成透明区域(晕圈)的菌落接种在包含10μg/mL新霉素的120μl LB培养基中,用于质粒DNA提取(QIAprep Spin Miniprep试剂盒,Qiagen)。将提取的质粒进行测序以确认所需的突变的存在。

[0797]

表 4-1：用于构建 NHJ4 变体的引物序列

引入的突变（BPN'编号方式）	引物名称	引物序列（5'-磷酸化的）
S101A S103G V104L	P5939	AAAGTATTAGGGGCGAGCGGTGCAGGTGGACTTAGCTCG ATTGCCCAAGGATTG (SEQ ID NO:13)
G159E	P5940	CATCTGGAAATTCAGGTGCAGAATCAATCAGCTATCCGGC CCGTTA (SEQ ID NO:14)
T22A	P5941	CTGCCCATAACCGTGGATTGGCAGGTTCTGGTGTAAAAGT TGCTG (SEQ ID NO:15)
Y209E	P5942	AGGTGTAAACGTGCAGAGCACAGAACCAGGTTCAACGTA TGCCAG(SEQ ID NO:16)
E271F	P5943	GAAGCGGACTTGTCAATGCATTCGCTGCAACTCGTTAAAG CTTG (SEQ ID NO:17)
S101A	P5944	AAAGTATTAGGGGCGAGCGGTGCAGGTTCGGTCAGCTCG ATTGCCCAA (SEQ ID NO:18)
S103G	P5945	TATTAGGGGCGAGCGGTTCAGGTGGAGTCAGCTCGATTGC CCAAGGA (SEQ ID NO:19)
L111V	P5946	GTCAGCTCGATTGCCCAAGGAGTAGAATGGGCAGGGAAC AATGGCA (SEQ ID NO:20)
S128N	P5947	CGTTGCTAATTTGAGTTTAGGAAACCCTTCGCCAAGTGCC ACACTTGA (SEQ ID NO:21)
N62E	P5948	GAACCATCCACTCAAGATGGGGAAGGGCATGGCACGCAT GTG (SEQ ID NO:22)
S188D	P5949	ACCAAAACAACAACCGCGCCGACTTTTCACAGTATGGCGC AGGGCTT (SEQ ID NO:23)

[0798] b)通过延伸PCR构建NHJ4变体

[0799] 通过延伸PCR产生GG36的10个组合突变体。用于这个目的的pHPLT-GG36质粒和引物中引入的突变的列表示于表4-2中。为产生每个突变体，通过表4-2中所示引物扩增若干片段(表4-3)。每个PCR扩增反应物含有30皮摩尔的每种引物和100ng的DNA模板即pHPLT-GG36质粒。用Vent DNA聚合酶(NEB)进行扩增。一开始将该PCR反应物(20μL)在95℃下加热2.5分钟，然后30个循环的：94℃下变性15秒，55℃下退火15秒，72℃下延伸1分钟。扩增后，使用QIAGEN®凝胶带纯化试剂盒对每种变体的2至4个PCR片段(表4-3)进行凝胶纯化并混合(50ng的每种片段)。这些混合物用作DNA模板以供通过引物P5954和P5955进行延伸PCR以产生全长基因片段。PCR条件与上面描述的相同，例外的是延伸阶段，其在72℃下进行2分钟。将该全长DNA片段用QIAGEN®凝胶带纯化试剂盒进行凝胶纯化，用BamHI和HindIII限制酶消化并与用相同限制酶消化的pHPLT-GG36连接。通过Illustra Templiphi试剂盒根据生产商的说明书(GE Healthcare)利用滚环扩增对1微升的连接混合物进行扩增，以产生用于转化到枯草芽孢杆菌中的多聚体DNA。将该滚环扩增的产物稀释100倍并用于转化枯草芽孢杆菌细胞(基因型：ΔaprE,ΔnprE,amyE::xylRPxylAcomK-phleo)。将转化混合物的等分试样平板接种于包含1.6％脱脂乳和10μg/mL新霉素的LB板上，并在37℃下温育过夜。随后，将具有晕圈的菌落接种到包含10μg/mL新霉素的120μl Luria肉汤培养基中，用于质粒DNA提取(QIAprep Spin Miniprep试剂盒，Qiagen)。将提取的质粒进行测序以确认所需的突变

的存在。由延伸PCR产生的变体在表4-4中示出。

[0800]

表 4-2: 用于通过延伸 PCR 构建 NHJ4 变体的引物的列表

突变（BPN'编号方式）	引物名称	正向或反向	引物序列
	P5950 侧翼	正向	CATATGAGTTATGCAGTTTGTAG (SEQ ID NO:24)
	P5951 侧翼	反向	TGTTTTTCTTGGAATTGTGCTGT (SEQ ID NO:25)
	P5954 侧翼	正向	CAGTTTGTAGAATGCAAAAAGTG (SEQ ID NO:26)
	P5955 侧翼	反向	GACAAGGTAAAGGATAAAACAGC (SEQ ID NO:27)
T22A	P5956	正向	CATAACCGTGGATTGGCAGGTTCT GGTGTAAAAGTTGCTG (SEQ ID NO:28)
T22A	P5957	反向	ACTTTTACACCAGAACCTGCCAAT CCACGGTTATGGGCAG (SEQ ID NO:29)
N62E	P5958	正向	CACTCAAGATGGGGAAGGGCATG GCACGCATGTGG (SEQ ID NO:30)
N62E	P5959	反向	ATGCGTGCCATGCCCTTCCCCATC TTGAGTGGATGGTTC (SEQ ID NO:31)
S103G	P5960	正向	GCGAGCGGTTCAGGTGGAGTCAG CTCGATTGCCCAAGGA (SEQ ID NO:32)
S103G	P5961	反向	TGGGCAATCGAGCTGACTCCACCT GAACCGCTCGCCCCTA (SEQ ID NO:33)

[0801]

表 4-2：用于通过延伸 PCR 构建 NHJ4 变体的引物的列表

突变（BPN'编号方式）	引物名称	正向或反向	引物序列
S103G L111V	P5962	正向	GTGGAGTCAGCTCGATTGCCCAAG GAGTAGAATGGGCAGGGAACAATGGCAT (SEQ ID NO:34)
S103G L111V	P5963	反向	CATTCTACTCCTTGGGCAATCGAG CTGACTCCACCTGAACCGCTCGCCCCTA (SEQ ID NO:35)
S101G S103A V104I	P5964	正向	GCGAGCGGTGGAGGTGCGATCAGCTC GATTGCCCAAGGATTG (SEQ ID NO:36)
S101G S103A V104I	P5965	反向	CTTGGGCAATCGAGCTGATCGCACCT CCACCGCTCGCCCCTAATACTTTA (SEQ ID NO:37)
S101A S103G V104L	P5966	正向	GCGAGCGGTGCAGGTGGACTTAGCTC GATTGCCCAAGGATTG (SEQ ID NO:38)
S101A S103G V104L	P5967	反向	CTTGGGCAATCGAGCTAAGTCCACCT GCACCGCTCGCCCCTAATACTTTA (SEQ ID NO:39)
S101A	P5968	正向	TATTAGGGGCGAGCGGTGCAGGTTCGG TCAGCTCGATTGC (SEQ ID NO:40)
S101A	P5969	反向	ATCGAGCTGACCGAACCTGCACCGCTC GCCCCTAATACTTTA (SEQ ID NO:41)
S128N	P5970	正向	CTAATTTGAGTTTAGGAAACCCTTCGC CAAGTGCCACACTT (SEQ ID NO:42)
S128N	P5971	反向	GCACTTGGCGAAGGGTTTCCTAAACTC AAATTAGCAACGTG (SEQ ID NO:43)
G159D	P5972	正向	GAAATTCAGGTGCAGACTCAATCAGCT ATCCGGCCCGTT (SEQ ID NO:44)
G159D	P5973	反向	GGATAGCTGATTGAGTCTGCACCTGAA TTTCCAGATGC (SEQ ID NO:45)
G159E	P5974	正向	GAAATTCAGGTGCAGAATCAATCAGCT ATCCGGCCCGTT (SEQ ID NO:46)
G159E	P5975	反向	GGATAGCTGATTGATTCTGCACCTGAAT TTCCAGATGC (SEQ ID NO:47)
Y209E	P5976	正向	AACGTGCAGAGCACAGAACCAGGTTCA ACGTATGCCAGCTT (SEQ ID NO:48)
Y209E	P5977	反向	CATACGTTGAACCTGGTTCTGTGCTCTG CACGTTTACACC (SEQ ID NO:49)
L111V	P5978	正向	TCGATTGCCCAAGGAGTAGAATGGGCA GGGAACAATGGCAT (SEQ ID NO:50)
L111V	P5979	反向	CATTGTTCCCTGCCCATTCTACTCCTTGG GCAATCGAGCTGAC (SEQ ID NO:51)

表 4-3：通过延伸 PCR 产生的组合变体

变体编号	变体（BPN 编号方式）	片段	PCR 片段
NHJ4-1	S101G S103A V104I	1 2	P5950+P5965 P5964+P5951
NHJ4-2	S101G S103A V104I G159D	3 4 5	P5950+P5965 P5964+P5973 P5972+P5951
NHJ4-3	S101A S103G V104L	6 7	P5950+P5967 P5966+P5951
NHJ4-4	S101A S103G V104L G159E	8 9 10	P5950+P5967 P5966+P5975 P5974+P5951
NHJ4-5	S101A S103G V104L T22A	11 12 13	P5950+P5957 P5956+P5967 P5966+P5951
NHJ4-10	T22A S101A Y209E	14 15 16 17	P5950+P5957 P5956+P5969 P5968+P5977 P5976+P5951
NHJ4-11	S103G L111V G159E	18 19 20	P5950+P5963 P5962+P5975 P5974+P5951
NHJ4-12	T22A S103G G159E	21 22 23 24	P5950+P5957 P5956+P5961 P5960+P5975 P5974+P5951
NHJ4-18	T22A N62E L111V	25 26 27 28	P5950+P5957 P5956+P5959 P5958+P5979 P5978+P5951
NHJ4-20	S101A S103G V104L S128N	29 30 31	P5950+P5967 P5966+P5971 P5970+P5951

[0802]

[0803] 为表达NHJ4组的变体蛋白用于进一步生化分析，将携带变体质粒的枯草芽孢杆菌菌株接种到装有150μl补充有10μg/ml新霉素的Luria肉汤培养基的微量滴定板中。如实例2中所述使培养物生长以进行蛋白质表达，同样如实例2中所述将它们滤过微过滤器板(0.22μm;Millipore)。将所得的滤液用于生化分析。如实例1中所述进行用于蛋白质含量测定的水蛭抑制剂c抑制测定法和在各种洗涤剂中测试的BMI微样本测定法。还如实例1中关于BMI测定法描述内容所述计算性能指数。表4-4提供了关于这些多突变变体和它们所获得的结果的信息。PI值是相对于GG36而言的。在下面的各表中，洗涤剂组合物与上面的表D中所示的那些组合物相对应。另外，如所指出，氨基酸位置根据BPN’编号方式列出。

[0804]

表 4-4：在 16℃洗涤剂 7、8 或 9 中，相对于 GG36 而言 BMI 清洁性能指数为至少 0.2 的 NHJ4 多突变变体。

变体名称	产生方式	突变（BPN'编号方式）
		GG36
NHJ4-1	延伸 PCR	S101G S103A V104I
NHJ4-10	延伸 PCR	T22A S101A Y209E
NHJ4-11	延伸 PCR	S103G L111V G159E
NHJ4-12	延伸 PCR	T22A S103G G159E
NHJ4-13	QCMS	T22A L111V G159E
NHJ4-14	QCMS	T22A S128N E271F Y209E
NHJ4-15	QCMS	T22A S103G L111V
NHJ4-16	QCMS	N62E L111V S128N
NHJ4-17	QCMS	T22A L111V S128N
NHJ4-18	延伸 PCR	T22A N62E L111V
NHJ4-19	QCMS	S101A S103G V104L S188D
NHJ4-2	延伸 PCR	S101G S103A V104I G159D
NHJ4-20	延伸 PCR	S101A S103G V104L S128N
NHJ4-24	QCMS	T22A S101A G159E
NHJ4-3	延伸 PCR	S101A S103G V104L
NHJ4-4	延伸 PCR	S101A S103G V104L G159E
NHJ4-5	延伸 PCR	T22A S101A S103G V104L
NHJ4-6	QCMS	S101A S103G V104L Y209E
NHJ4-7	QCMS	T22A Y209E E271F
NHJ4-8	QCMS	T22A S101A E271F
NHJ4-9	QCMS	S101A Y209E E271F

[0805] 实例5

[0806] NHJ3组的GG36变体的构建及清洁性能

[0807] 本文所述NHJ3组的变体是基于含有以下突变的GG36的变体(称为GG36-9):S101G,S103A,V104I,G159D,A232V,Q236H,Q245R,N248D,和N252K(BPN'编号方式)。这些变体用QUIKCHANGE®Lightning定点诱变试剂盒(QCLDS试剂盒;Stratagene),以pRA68质粒(参见图3)作为DNA模板产生。质粒pRA68衍生自pBN3载体(参见Babéet al.,Biotech.Appl.Biochem.27:117-124[1998](Babé等人,《生物技术与应用生物化学》,第27卷,第117-124页,1998年))。

[0808] GG36-9变体的DNA序列(信号序列以小写字母示出,前肽以小写带下划线的文字示出,GG36-9成熟序列以大写字母示出)在下面提供:

[0809] GtgagaagcaaaaaattgtggatcgtcgcgtcgaccgcactactcatttctgttgcttttagttcatcgatcgcatcggctgctgaagaagcaaaagaaaaatatttaattggctttaatgagcaggaagctgtcagtgagtttgtagaacaagtagaggcaaatgacgaggtcgccattctctctgaggaagaggaagtcgaaattgaattgcttcatgaatttgaaacgattcctgttttatccgttgagttaagcccagaagatgtggacgcgcttgaactcgatccagcgatttcttatattgaagaggatgcagaagtaacgacaatgGCGCAATCAGTGCCATGGGGAATTAGCCGTGTGCAAGCC

CCGGCTGCCCATAACCGTGGATTGACAGGTTCTGGTGTAAAAGTTGCTGTCCTCGATACAGGTATTTCCACTCATC
CAGACTTAAATATTCGTGGTGGCGCTAGCTTTGTACCAGGGGAACCATCCACTCAAGATGGGAATGGGCATGGCAC
GCATGTGGCCGGGACGATTGCTGCTCTAAACAATTCGATTGGCGTACTTGGCGTAGCGCCGAGCGCGGAACTATAC
GCTGTTAAAGTATTAGGGGCGAGCGGTGGGGGCGCCATCAGCTCGATTGCCCAAGGATTGGAATGGGCAGGGAACA
ATGGCATGCACGTTGCTAATTTGAGTTTAGGAAGCCCTTCGCCAAGTGCCACACTTGAGCAAGCTGTTAATAGCGC
GACTTCTAGGGGCGTTCTTGTTGTAGCGGCATCTGGAAATTCGGGTGCAGACTCAATCAGCTATCCGGCCCGTTAT
GCGAACGCAATGGCAGTCGGAGCTACTGACCAAAACAACAACCGCGCCAGCTTTTCACAGTATGGCGCAGGGCTTG
ACATCGTCGCACCAGGTGTAAACGTGCAGAGCACATACCCAGGTTCAACGTATGCCAGCTTAAACGGTACATCGAT
GGCTACTCCTCATGTTGCAGGTGCAGCAGTCCTTGTTAAACATAAGAACCCATCTTGGTCCAATGTACGAATCCGC
GATCATCTAAAGAAAACGGCAACGAGCTTAGGAAGCACGAACTTGTATGGAAGCGGACTTGTCAATGCCGAAGCTG
CAACTCGTTAA(SEQ ID NO:5)

[0810] GG36-9变体的蛋白质序列(信号序列以小写字母示出,前肽以小写带下划线的文本示出,GG36-9成熟蛋白酶序列以大写字母示出)在下面提供:

[0811] vrskklwivastallisvafsssiasaaeeakekyligfneqeavsefveqveandevailseeeeveiellhefetipvlsvelspedvdaleldpaisyieedaevttmAQSVPWGISRVQAPAAHNRGLTGSGVKVAVLDTGISTHPDLNIRGGASFVPGEPSTQDGNGHGTHVAGTIAALNNSIGVLGVAPSAELYAVKVLGASGGGAISSIAQGLEWAGNNGMHVANLSLGSPSPSATLEQAVNSATSRGVLVVAASGNSGADSISYPARYANAMAVGATDQNNNRASFSQYGAGLDIVAPGVNVQSTYPGSTYASLNGTSMATPHVAGAAVLVKHKNPSWSNVRIRDHLKKTATSLGSTNLYGSGLVNAEAATR(SEQ ID NO:6)

[0812] 为了用QCLSD试剂盒产生NHJ3变体,针对每种变体设计了如表5-1中所示的诱变引物。按照生产商的说明书,每种变体的诱变反应物由以下组成:0.5μl 10X缓冲液、0.5μL pRA68质粒DNA(168ng/μL)、0.5μl正向“f”诱变引物(25μM)、0.5μl反向“r”诱变引物(25μM)、1μl dNTP(在QCLSD试剂盒中提供)、1.5μl Quik溶液(在QCLMS试剂盒中提供)、1μl酶混合物(在QCLSD试剂盒中提供)和补足至50μL反应体积的40μl蒸馏去离子水。循环程序为1个循环的95℃2分钟,18个循环的:95℃20秒,60℃10秒以及68℃3分钟22秒,以及最后一个循环的68℃5分钟。接着,用1μL的在该试剂盒中提供的DpnI限制酶消化该反应物中的质粒DNA,然后用2μL的反应物转化TOP 10大肠杆菌感受态细菌(Invitrogen)。37℃下培养过夜后,在含有50μg/mL(ppm)羧苄青霉素的Luria肉汤培养基板上选择大肠杆菌转化株。使用QIAprep spin miniprep试剂盒(Qiagen),从4-8个在含有50μg/mL(ppm)羧苄青霉素的LA培养基中培养的大肠杆菌菌落提取质粒DNA。将质粒进行测序以确认所需的突变的存在。然后如实例2中所述将变体质粒转化到枯草芽孢杆菌细胞中。如实例2中所述培养枯草芽孢杆菌变体菌株用于进一步生化分析,如使用水蛭抑制剂c抑制测定法进行的蛋白质含量测定(实例1)以及BMI微样本清洁测定法(实例1)。结果在下面的表5-2和5-3中给出。PI是相对于GG36而言的。在下面的各表中,洗涤剂组合物与上面的表D中所示的那些组合物相对应。另外,如所指出,氨基酸位置根据BPN’编号方式列出。

[0813]

表 5-1. 用于产生 NHJ3 组的变体的诱变引物的列表
（“f”是指正向引物，“r”是指反向引物）

变体	掺入的突变（BPN'编号方式）	诱变引物名称	诱变引物序列 5'至 3'
NHJ3-1	G101S	p158_G101S f	GTTAAAGTATTAGGGGCGAGCGGTAGCGGCGCCATCAGCTCGATTGCC (SEQ ID NO:53)
		p159_G101S r	GGCAATCGAGCTGATGGCGCCGCTACCGCTCGCCCCTAATACTTTAAC (SEQ ID NO:54)
NHJ3-2	A103S	p160_A1013 f	GTATTAGGGGCGAGCGGTGGGGGCAGCATCAGCTCGATTGCCCAAGGATTG (SEQ ID NO:55)
		p161_A1013 r	CAATCCTTGGGCAATCGAGCTGATGCTGCCCCCACCGCTCGCCCCTAATAC (SEQ ID NO:56)
NHJ3-3	I104V	p142_I104V f	GGGCGAGCGGTGGGGGCGCCGTTAGCTCGATTGC CCAAGGATTG (SEQ ID NO:57)
		p143_I104V r	CAATCCTTGGGCAATCGAGCTAACGGCGCCCCCA CCGCTCGCCC (SEQ ID NO:58)
NHJ3-4	D159G	p144_D159G f	GCATCTGGAAATTCGGGTGCAGGCTCAATCAGCT ATCCGGCCCGT (SEQ ID NO:59)
		p145_D159G r	ACGGGCCGGATAGCTGATTGAGCCTGCACCCGAA TTTCCAGATGC (SEQ ID NO:60)
NHJ3-5	V232A	p146_V232A f	CTCATGTTGCAGGTGCAGCAGCACTTGTTAAACAT AAGAACCC (SEQ ID NO:61)
		p147_V232A r	GGGTTCTTATGTTTAACAAGTGCTGCTGCACCTGC AACATGAG (SEQ ID NO:62)

[0814]

表 5-1. 用于产生 NHJ3 组的变体的诱变引物的列表
（“f”是指正向引物，“r”是指反向引物）

变体	掺入的突变（BPN'编号方式）	诱变引物名称	诱变引物序列 5'至 3'
NHJ3-6	H236Q	p148_H236Q f	GTGCAGCAGTCCTTGTTAAACAAAAGAACCCATC TTGGTCCAAT (SEQ ID NO:63)
		p149_H236Q r	ATTGGACCAAGATGGGTTCTTTTGTTTAACAAGG ACTGCTGCAC (SEQ ID NO:64)
NHJ3-7	R245Q	p150_R245Q f	CCATCTTGGTCCAATGTACAAATCCGCGATCATC TAAAGAAAAC (SEQ ID NO:65)
		p151_R245Q r	GTTTTCTTTAGATGATCGCGGATTTGTACATTGG ACCAAGATGG (SEQ ID NO:66)
NHJ3-8	D248N	P152_D248N f	GGTCCAATGTACGAATCCGCAATCATCTAAAGA AAACGGCAAC (SEQ ID NO:67)
		P153_D248N r	GTTGCCGTTTTCTTTAGATGATTGCGGATTCGTA CATTGGACC (SEQ ID NO:68)
NHJ3-9	K252N	P154_K252N f	GAATCCGCGATCATCTAAAGAATACGGCAACGA GCTTAGGAAG (SEQ ID NO:69)
		P155_K252N r	CTTCCTAAGCTCGTTGCCGTATTCTTTAGATGATC GCGGATTC (SEQ ID NO:70)

[0815]

表 5-2. 在 16℃洗涤剂 7、8 或 9 中，相对于 GG36 而言 BMI 清洁性能指数为至少 1.1 的 NHJ3 多突变变体。

变体	相对于 GG36 的变体序列（BPN'编号方式）
	GG36
NHJ3-1	S103A-V104I-G159D-A232V-Q236H-Q245R-N248D-N252K
NHJ3-2	S101G-V104I-G159D-A232V-Q236H-Q245R-N248D-N252K
NHJ3-3	S101G-S103A-G159D-A232V-Q236H-Q245R-N248D-N252K
NHJ3-4	S101G-S103A-V104L-A232V-Q236H-Q245R-N248D-N252K
NHJ3-5	S101G-S103A-V104L-G159D-Q236H-Q245R-N248D-N252K
NHJ3-6	S101G-S103A-V104L-G159D-A232V-Q245R-N248D-N252K
NHJ3-7	S101G-S103A-V104L-G159D-A232V-Q236H-N248D-N252K
NHJ3-8	S101G-S103A-V104L-G159D-A232V-Q236H-Q245R-N252K
NHJ3-9	S101G-S103A-V104L-G159D-A232V-Q236H-Q245R-N248D

[0816]

表 5-3：在 16℃洗涤剂 10 或 11 中，相对于 GG36 而言 BMI 清洁性能指数为至少 0.3 的 NHJ3 多突变变体。

变体	相对于 GG36 的变体序列（BPN'编号方式）
	GG36
NHJ3-1	S103A-V104I-G159D-A232V-Q236H-Q245R-N248D-N252K
NHJ3-2	S101G-V104I-G159D-A232V-Q236H-Q245R-N248D-N252K
NHJ3-3	S101G-S103A-G159D-A232V-Q236H-Q245R-N248D-N252K
NHJ3-4	S101G-S103A-V104L-A232V-Q236H-Q245R-N248D-N252K
NHJ3-5	S101G-S103A-V104L-G159D-Q236H-Q245R-N248D-N252K
NHJ3-6	S101G-S103A-V104L-G159D-A232V-Q245R-N248D-N252K
NHJ3-7	S101G-S103A-V104L-G159D-A232V-Q236H-N248D-N252K
NHJ3-8	S101G-S103A-V104L-G159D-A232V-Q236H-Q245R-N252K
NHJ3-9	S101G-S103A-V104L-G159D-A232V-Q236H-Q245R-N248D

[0817] 实例6

[0818] NHJ5组的GG36变体的构建及清洁性能

[0819] 本文所述的NHJ5组的变体是基于含有以下突变的GG36的变体(称为GG36-7)：S101G,S103A,V104I,G159D,A232V,Q245R,和N248D,(BPN'编号方式)。这些变体用QUIKCHANGE®Lightning多定点诱变试剂盒("QCLMS试剂盒")，以pRA96质粒作为DNA模板(参见图4)产生。掺入在GG36-7中的突变以及用于在GG36-7中引入突变的引物的序列示于表6-1中。使用实例4中所述方法产生变体。如实例2中所述培养枯草芽孢杆菌变体菌株用于进一步生化分析，如使用水蛭抑制剂c抑制测定法进行的蛋白质含量测定(实例1)以及BMI微样本清洁测定法(实例1)。结果在下面的表6-2中给出。PI值是相对于GG36而言的。在下面的各表中，洗涤剂组合物与上面的表D中所示的那些组合物相对应。另外，如所指出，氨基酸位置根据BPN'编号方式列出。

[0820] GG36-7变体的DNA序列(信号序列以小写字母示出，前肽以小写带下划线的文本示

出,GG36-7成熟蛋白酶序列以大写字母示出)在下面提供:

[0821] Gtgagaagcaaaaaattgtggatcgtcgcgtcgaccgcactactcatttctgttgcttttagttcatc gatcgcatcggctgctgaagaagcaaaagaaaaatatttaattggctttaatgagcaggaagctgtcagtgagttt gtagaacaagtagaggcaaatgacgaggtcgccattctctctgaggaagaggaagtcgaaattgaattgcttcatg aatttgaaacgattcctgttttatccgttgagttaagcccagaagatgtggacgcgcttgaactcgatccagcgat ttcttatattgaagaggatgcagaagtaacgacaatgGCGCAATCAGTGCCATGGGGAATTAGCCGTGTGCAAGCC CCGGCTGCCCATAACCGTGGATTGACAGGTTCTGGTGTAAAAGTTGCTGTCCTCGATACAGGTATTTCCACTCATC CAGACTTAAATATTCGTGGTGGCGCTAGCTTTGTACCAGGGGAACCATCCACTCAAGATGGGAATGGGCATGGCAC GCATGTGGCCGGGACGATTGCTGCTCTAAACAATTCGATTGGCGTACTTGGCGTAGCGCCGAGCGCGGAACTATAC GCTGTTAAAGTATTAGGGGCGAGCGGTGGGGGCGCCATCAGCTCGATTGCCCAAGGATTGGAATGGGCAGGGAACA ATGGCATGCACGTTGCTAATTTGAGTTTAGGAAGCCCTTCGCCAAGTGCCACACTTGAGCAAGCTGTTAATAGCGC GACTTCTAGGGGCGTTCTTGTTGTAGCGGCATCTGGAAATTCGGGTGCAGACTCAATCAGCTATCCGGCCCGTTAT GCGAACGCAATGGCAGTCGGAGCTACTGACCAAAACAACAACCGCGCCAGCTTTTCACAGTATGGCGCAGGGCTTG ACATCGTCGCACCAGGTGTAAACGTGCAGAGCACATACCCAGGTTCAACGTATGCCAGCTTAAACGGTACATCGAT GGCTACTCCTCATGTTGCAGGTGCAGCAGTCCTTGTTAAACAAAAGAACCCATCTTGGTCCAATGTACGAATCCGC GATCATCTAAAGAATACGGCAACGAGCTTAGGAAGCACGAACTTGTATGGAAGCGGACTTGTCAATGCCGAAGCTG CAACTCGT(SEQ ID NO:7)

[0822] GG36-7变体的蛋白质序列(信号序列以小写字母示出,前肽以小写带下划线的文本示出,GG36-7成熟蛋白酶序列以大写字母示出)在下面提供:

[0823] vrskklwivastallisvafsssiasaaeeakekyligfneqeavsefveqveandevailseeeeve iellhefetipvlsvelspedvdaleldpaisyieedaevttmAQSVPWGISRVQAPAAHNRGLTGSGVKVAVLDT GISTHPDLNIRGGASFVPGEPSTQDGNGHGTHVAGTIAALNNSIGVLGVAPSAELYAVKVLGASGGGAISSIAQGL EWAGNNGMHVANLSLGSPSPSATLEQAVNSATSRGVLVVAASGNSGADSISYPARYANAMAVGATDQNNNRASFSQ YGAGLDIVAPGVNVQSTYPGSTYASLNGTSMATPHVAGAAVLVKQKNPSWSNVRIRDHLKNTATSLGSTNLYGSGL VNAEAATR(SEQ ID NO:8)

[0824]

表 6-1：用于产生 NHJ5 组的变体的引物的列表

引物编号	所用突变 GG36 编号方式（BPN'编号方式在括号中示出）	引物序列
168	H243R (H249R)	GTACGAATCCGCGATAGACTAAAGAATACGGCAACGAG (SEQ ID NO:71)
170	E265F (E271F)	GCGGACTTGTCAATGCCTTTGCTGCAACTCGTTAAAGCTTACAT (SEQ ID NO:72)
172	D157E (D159E)	GGAAATTCGGGTGCAGAATCAATCAGCTATCCGGCCCGTTA (SEQ ID NO:73)
174	A156E (A158E)	CTGGAAATTCGGGTGAAGACTCAATCAGCTATCCGGCC (SEQ ID NO:74)
176	A156E-D157G (A158E- D159E)	CGGCATCTGGAAATTCGGGTGAAGGCTCAATCAGCTATCCGGCCCGTTATG (SEQ ID NO:75)
178	T22A	CATAACCGTGGATTGGCAGGTTCTGGTGTAAAAGTTGCTGTC (SEQ ID NO:76)
180	N60E (N62E)	TCCACTCAAGATGGGGGAAGGGCATGGCACGCATGTGGC (SEQ ID NO:77)
182	N232R (N238R)	CTTGTTAAACAAAAGAGACCATCTTGGTCCAATGTACGAATC (SEQ ID NO:78)
184	D242R (D248R)	AATGTACGAATCCGCAGACATCTAAAGAATACGGCAACGAGC (SEQ ID NO:79)
186	T247R (T253R)	CGATCATCTAAAGAATAGAGCAACGAGCTTAGGAAGCACGAAC (SEQ ID NO:80)
188	S24R	GTGGATTGACAGGTAGAGGTGTAAAAGTTGCTGTCCTCGATA (SEQ ID NO:81)
190	N74D (N76D)	ACGATTGCTGCTCTAGATAATTCGATTGGCGTACTTGGCGTAG (SEQ ID NO:82)

[0825]

表 6-2：在 16℃洗涤剂 7-11 中，相对于 GG36 而言 BMI 清洁性能指数为至少 0.6 的 NHJ5 多突变变体。

变体	相对于 GG36 的变体序列（BPN'编号方式）
	GG36
GG36-7	S101G-S103A-V104I-G159D-A232V-Q245R-N248D
NHJ5-1	S101G-S103A-V104I-G159D-A232V-Q245R-N248D-E271F
NHJ5-2	S101G-S103A-V104I-G159D-A232V-Q245R-N248D-N238R
NHJ5-3	S101G-S103A-V104I-G159D-A232V-Q245R-N248D-N248R
NHJ5-4	S101G-S103A-V104I-G159D-A232V-Q245R-N248D-T253R
NHJ5-5	S101G-S103A-V104I-G159D-A232V-Q245R-N248D-S24R
NHJ5-6	S101G-S103A-V104I-G159D-A232V-Q245R-N248D-N76D
NHJ5-7	S101G-S103A-V104I-G159E-A232V-Q245R-N248D-H249R
NHJ5-8	S101G-S103A-V104I-G159E-A232V-Q245R-N248D-E271F
NHJ5-9	S101G-S103A-V104I-A158E-A232V-Q245R-N248D-H249R
NHJ5-10	S101G-S103A-V104I-A158E-A232V-Q245R-N248D-E271F
NHJ5-11	T22A-S101G-S103A-V104I-G159D-A232V-Q245R-N248D-H249R
NHJ5-12	T22A-S101G-S103A-V104I-G159D-A232V-Q245R-N248D-E271F
NHJ5-13	N62E-S101G-S103A-V104I-G159D-A232V-Q245R-N248D-H249R
NHJ5-14	N62E-S101G-S103A-V104I-G159D-A232V-Q245R-N248D-E271F

[0826] 实例7

[0827] NHJ2组合文库的构建

[0828] 本实例描述了涉及一种或多种以下突变的GG36组合文库的构建：A16S,T22A,S101A,S103G,V104L,L111V,S128N,和L148I(BPN'编号方式)。将pHPLT-GG36枯草芽孢杆菌表达质粒提供给DNA 2.0Inc.公司用于产生NHJ2组合文库。构建的NHJ2文库的连接反应物由DNA 2.0Inc.公司提供，用于转化到枯草芽孢杆菌菌株(基因型：ΔaprE,ΔnprE,amyE::xylRPxylAcomK-phleo)中。可使用本文所述的方法和洗涤剂组合物对所产生的包含一个或若干个本文所述突变的变体进行冷水清洁应用测试。

[0829] 实例8

[0830] 另外的文库和GG36变体的构建

[0831] 使用以下组的突变构建另外的文库和变体：A1R,A230E,E271L,G115R G20R,H249R,K235F,K27V/F/L,L75E,L82R,N18R,N269R,N43D,N43R,N76D,R45T,S212F,S242R,S24R,S78R,S9A,T22R,V121E,V244R,V28E,V30E,V4R,W241R(BPN'编号方式)。在DNA 2.0Inc.公司使用pHPLT-GG36枯草芽孢杆菌表达质粒构建文库和变体。将所述文库或变体的连接反应物转化到枯草芽孢杆菌菌株(基因型：ΔaprE,ΔnprE,amyE::xylRPxylAcomK-phleo)中。在BMI微样本清洁测定法(实例1)中，使用本文所述的方法和洗涤剂组合物对所产生的包含一个或若干个这些突变的变体进行冷水清洁测试。结果在下面的表8-1中给出。在下面的各表中，洗涤剂组合物与上面的表1-2中所示的那些组合物相对应。另外，如所指出，氨基酸位置根据BPN'编号方式列出。

[0832] 构建了另外的GG36变体组并使用本文所述的方法和洗涤剂组合物测试了冷水清

洁应用，包括：G20R-N43R-H249R,G20R-T22R-N43R,G20R-N43R-S242R,G20R-N43R-E271L,G20R-N43R-V244R,G20R-S24R-N43R-S242R,S9A-T22R-S78R-S212F-W241R,S9A-G20R-N43R-S212F,S9A-N43R-S212F,G20R-N43R-S212F,G20R-T22R-N43R-S212F,S24R-S78R-S212F,S9A-N43R-S78R,S9A-N43R-S78R-S242R,S9A-G20R-N43R-S78R,G20R-S24R-N43R-S78R-S242R,T22R-S24R-S78R-S212F,S9A-G20R-N43R-S78R-S242R,G20R-N43R-S78R-H249R,G20R-N43R-S78R,S9A-S78R-S212F,S9A-T22R-N43R-S78R,S9A-G20R-S24R-N43R,S9A-T22R-S78R-S212F,V4R-S9A-T22R-S78R-S212F,G20R-S24R-N43R,A1R-S9A-N43R,G20R-S24R-N43R-G115R,S9A-S24R-N43R,G20R-T22R-S24R-N43R,A1R-S24R-N43R,S9A-G20R-S24R-N43R-S242R,S9A-G20R-T22R-S78R-S212F,S9A-S24R-N43R-V244R,S9A-S24R-N43R-S242R,V4R-S9A-T22R-S24R-S212F，和T22R-S24R-N43R(BPN’编号方式)。

[0833]

表 7-1: WCE4 变体的 BMI 清洁性能

PI=相对于 GG36 的性能指数

在洗涤剂 36k 或 36l 中，PI>或=1.5 为+++; PI 介于 1.49 和 1.3 之间=++; PI 介于 1.29 和 1.0 之间=+

[0834]

GG36 变体的序列（BPN'编号方式）	相对于 GG36 的 PI；洗涤剂 36k 或 36l，BMI 测定法，16℃
V004R-S009A-G020R-S242R	+++
G020R-N043R-W241R	+++
G020R-S242R-N269R	+++
V004R-S009A-G020R-N043R-	+++
V004R-G020R-H249R-	+++
N018R-S024R-V244R	+++
S009A-T022R-S212F-W241R	+++
G020R-N043R-N269R-	+++
N018R-S024R-S242R	+++
V004R-S009A-N043R-W241R-	+++
G020R-N043R-V244R-	+++
G020R-T022R-S242R-	+++
V004R-G020R-N043R-	+++
V004R-S009A-G020R-N043R-S242R-	+++
G020R-N043R-S242R-	+++
G020R-N043R-S242R-H249R-	+++
G020R-S212F-H249R-	+++
V004R-S009A-W241R-	+++
A001R-S009A-N043R-	+++
G020R-N043R-H249R-	+++
S009A-G020R-N043R-W241R	+++
G020R-T022R-N043R-	+++
G020R-H249R-N269R-	+++
G020R-T022R-W241R-	+++
V004R-S009A-S024R-N043R-W241R-	+++
S009A-N043R-S078R	+++
V004R-G020R-S024R-V244R-	+++
G020R-T022R-S078R-S242R-	+++
G020R-S024R-S242R-H249R-	+++
V004R-S009A-S078R-W241R-	+++
S009A-N043R-S078R-S242R	+++
V004R-G020R-S024R-	+++
S009A-N043R-S212F	+++
G020R-N043R-S212F-	+++
S024R-S078R-S212F-	+++
S009A-G020R-S024R-N043R	+++
S009A-T022R-N043R-S078R	+++
G020R-T022R-S212F-W241R-	+++
G020R-N043R-S212F-W241R-	+++
S009A-N043R-W241R	+++
G020R-N043R-E271L	+++
G020R-T022R-S078R-W241R-	+++

表 7-1：WCE4 变体的 BMI 清洁性能

PI=相对于 GG36 的性能指数

在洗涤剂 36k 或 36l 中，PI>或=1.5 为+++；PI 介于 1.49 和 1.3 之间=++；PI 介于 1.29 和 1.0 之间=+

[0835]

GG36 变体的序列（BPN'编号方式）	相对于 GG36 的 PI；洗涤剂 36k 或 36l，BMI 测定法，16℃
G020R-S024R-N043R-S242R-	+++
G020R-T022R-N043R-W241R-	+++
S009A-G020R-N043R-S212F	+++
V004R-S009A-G020R-S024R-S242R-	+++
G020R-N043R-H249R-E271L	+++
G020R-T022R-S024R-S242R-	+++
S009A-T022R-S078R-S212F	+++
G020R-N043R-S242R-E271L	+++
S009A-T022R-S078R-S212F-W241R	+++
V004R-G020R-S024R-H249R-	+++
G020R-T022R-E271L	+++
G020R-T022R-N043R-S212F-	+++
V004R-G020R-S024R-N043R-S242R-	+++
V004R-G020R-S024R-N043R-	+++
V004R-S009A-T022R-S078R-S212F-	+
G020R-T022R-S078R-S212F-W241R-	+
G020R-T022R-N269R-	+

[0836] 实例9

[0837] GG36文库WCE2的构建及清洁性能

[0838] WCE2组合文库由DNA 2.0,Inc.公司使用pHPLT-GG36枯草芽孢杆菌表达质粒产生。将构建的WCE2文库的连接反应物转化到枯草芽孢杆菌菌株(基因型：ΔaprE,ΔnprE,amyE::xylRPxylAcomK-phleo)中。用于产生WCE2文库的突变组为A230E,G20R,H249R,N18R,N43R/D,N76D,R45T,S242R,和S24R(BPN'编号方式)。在BMI微样本清洁测定法(实例1)中,使用本文所述的方法和洗涤剂组合物对所产生的包含一个或若干个这些突变的变体进行冷水清洁测试。结果在下面的表9-1中给出。在下面的各表中,洗涤剂组合物与上面的表1-2中所示的那些组合物相对应。另外,如所指出,氨基酸位置根据BPN'编号方式列出。

[0839]

表 8-1：GG36 的 WCE2 文库变体的 BMI 清洁性能。

PI=相对于 GG36 的性能指数

在洗涤剂 36h 或 36i 中，PI>或=1.5 为+++；PI 介于 1.49 和 1.3 之间=++；PI 介于 1.29 和 1.0 之间=+

GG36 变体的序列（BPN'编号方式）	相对于 GG36 的 PI；BMI 测定法，洗涤剂 36h 或 36i，16℃
N018R-G020R-N043D-R045T-A230E	+++
N018R-N043R-R045T-S242R-H249R	+++
S024R-N043D-H249R	+++
N018R-G020R-R045T	+++
G020R-S024R-N076D-H249R	+++
S024R-N043R-A230E-S242R	+++
N018R-S024R-N043D-A230E	++
G020R-N076D	++
N018R-S024R-N043D-N076D-H249R	++
S024R-N043R-N076D-H249R	+++
N018R-S024R-R045T-S242R	++
G020R-N043D-N076D-A230E-H249R	++
G020R-N043R-R045T-S242R	+++
N018R-S024R-N076D-H249R	++
N018R-G020R-S024R-N043D-R045T-L233I-S242R	+++
S024R-N043R-A230E	+++
N018R-G020R-N043D	+++
N043R-S242R-H249R	+++
G020R-N043R-R045T-A230E	+++
N043R-N076D-S242R-H249R	+++
G020R-S024R-R045T-A230E-S242R	+++
S024R-R045T-N076D-A230E-S242R-H249R	+++
S024R-R045T	+++
S024R-N043R-R045T-N076D-A230E-H249R	++
N018R-S024R-N043D-R045T-H249R	++
N018R-N043R-R045T-H249R	+++
S024R-N043R-S242R	+++
N018R-G020R-N043R-N076D-H249R	+++
G020R-S024R-N043D-H249R	+++
G020R-N043R-A230E-S242R	+++
G020R-N043R-S242R	+++
N018R-N043R-N076D-A230E	++
G020R-S024R-N043D-S242R	+++
G020R-N043R-A230E	+++

[0840]

表 8-1：GG36 的 WCE2 文库变体的 BMI 清洁性能。

PI=相对于 GG36 的性能指数

在洗涤剂 36h 或 36i 中，PI>或=1.5 为+++；PI 介于 1.49 和 1.3 之间=++；PI 介于 1.29 和 1.0 之间=+

GG36 变体的序列（BPN'编号方式）	相对于 GG36 的 PI；BMI 测定法，洗涤剂 36h 或 36i，16℃
N018R-G020R-N043R-N076D-S242R-H249R	+++
N043D-R045T-N076D-H249R	+
N018R-N043R-S242R-H249R	+++
N018R-G020R-N043R-R045T-S242R	+++
N018R-G020R-N043D-A230E-S242R	+++
G020R-S024R-N043R-R045T-H249R	+++
S024R-N043R-H249R	+++
G020R-S024R-K027E-N043R-N076D-A230E	+++
S024R-N043R-R045T-S242R	+++
N018R-G020R-S024R-N043R-R045T-N076D-A230E	+++
G020R-N043R-N076D-A230E-H249R	+++
N018R-N043R-R045T-S242R	+++
G020R-S242R-H249R	+++
N018R-N043R-N076D-A230E-S242R-H249R	++
N018R-S024R-N076D	++
G020R-S024R-K27R-N043D-S242R-H249R	+++
N018R-G020R-S024R-N043D-N076D-S242R	++
N018R-N043R-N076D-S242R-H249R	+++
N018R-S024R-N043D-A230E-H249R	+++
N018R-G020R-N043D-H249R	++
N018R-G020R-N043D-R045T-N076D-S242R	+++
S024R-N043R-N076D-A230E-S242R	+++
G020R-S024R-T38I-N043R-R045T-N076D-S242R-H249R	+++
N018R-G020R-N043R	+++
N018R-S024R-R045T-A230E-S242R	++
N018R-G020R-H249R	+++
S024R-N043R-N076D	+++
N018R-G020R-S024R-N043R-R045T-N076D-H249R	++
N018R-N043D-R045T-N076D-S242R-H249R	+++
S024R-N043D-S242R-H249R	+++
N018R-G020R-S024R-N043D-R045T-S242R	++
G020R-S024R-N043R-N076D	++
N018R-G020R-N043D-R045T-A230E-S242R	++

[0841]

表 8-1：GG36 的 WCE2 文库变体的 BMI 清洁性能。

PI=相对于 GG36 的性能指数

在洗涤剂 36h 或 36i 中，PI>或=1.5 为+++；PI 介于 1.49 和 1.3 之间=++；PI 介于 1.29 和 1.0 之间=+

GG36 变体的序列（BPN'编号方式）	相对于 GG36 的 PI；BMI 测定法，洗涤剂 36h 或 36i，16℃
G020R-S024R-N043R-R045T-N076D-S242R-H249R	++
N018R-N043R-R045T-N076D-S242R	++
N018R-G020R-N043R-N076D-A230E-S242R	++
N018R-S024R-N043D-H249R	++
N018R-S024R-N043R-R045T-A230E-H249R	++
N018R-G020R-N043R-R045T-N076D-H249R	+++
N018R-S024R-S242R	++
N018R-N043R-R045T-N076D-A230E-S242R	++
R045T-S242R-H249R	+++
N018R-S024R-N043D-S242R	+++
N018R-G020R-N043D-R045T-S240P	++
S024R-N043R-R045T-S242R-H249R	++
N018R-S024R-V30S-L31S-D32I-T33Q-G34V-I35F	++
N018R-G020R-N043R-N076D	+++
G020R-N043D-R045T-N076D-S242R-H249R	++
N018R-S024R-N043D-A230E-S242R	++
N018R-S024R-N043D-S242R-H249R	+++
S024R-N043D-R045T-S242R-H249R	++
N043R-A230E-H249R	+
N043R-A230E-H249R	+
G020R-S024R-N043D-N076D-H249R	++
S024R-R045T-S242R-A273V	+
G020R-S024R-R045T-N076D-S242R-H249R	+
N018R-S024R-N043D-N076D-S242R	+
N018R-N043R-N076D-A230E-H249R	+
N018R-G020R-N043R-R045T-H249R	+
N018R-N043R-R045T-A230E-S242R	+
G020R-S024R-N043D-R045T-A230E-S242R	+
N018R-N043D-A230E-H249R	+
N018R-N043R-N076D-S242R	+++
N018R-G020R-N076D	+
N018R-G020R-N043D-N076D-S242R-H249R	+
G020R-S024R-N043D-N076D-S242R-H249R	+++
N043D-S242R-H249R	+++

[0842]

表 8-1：GG36 的 WCE2 文库变体的 BMI 清洁性能。

PI=相对于 GG36 的性能指数

在洗涤剂 36h 或 36i 中，PI>或=1.5 为+++；PI 介于 1.49 和 1.3 之间=++；PI 介于 1.29 和 1.0 之间=+

GG36 变体的序列（BPN'编号方式）	相对于 GG36 的 PI；BMI 测定法，洗涤剂 36h 或 36i，16℃
N018R-G020R-S024R-N043R-N076D	+
N018R-G020R-N043D-R045T-N076D-H249R	+
N018R-G020R-N043R-R045T-N076D-A230E-H249R	+
N018R-N076D-S242R	+
G020R-N043R-H249R	+
N018R-N076D-S242R-H249R	+
N018R-S024R-R045T-A230E-H249R	+
A230E-H249R	+++
N018R-R045T-H249R	+
G020R-N043R-N076D	+++
N043R-R045T-H249R	+++
N018R-N043D-N076D-S242R-H249R	+
N043R-N076D-H249R	+++
N018R-R045T	+
G020R-N076D-A230E-S242R	+
G020R-S024R-N043D-R045T	+++
S024R-N043D-N076D-S242R-H249R	+++
G020R-R045T-H249R	+
N043R-N076D-S153A-H249R	+
N043R-N076D-A230E-H249R	+++
N018R-N043D-N076D-H249R	+
G020R-N043R-N076D-V227I	+

[0843] 实例10

[0844] WCE3组的GG36变体的构建及清洁性能

[0845] 本实例描述了基于GG36变体、GG36-7(实例5)和GG36-9(实例4)的WCE3组的突变体。这些变体是:S101G-S103A-V104I-A232V-Q245R-N248D,S101G-S103A-V104I-G159D-A232V-Q245R,S101G-S103A-V104I-G159R-A232V-Q245R-N248D,S101G-S103A-V104I-G159D-A232V-Q245R-N248R,S101G-S103A-V104I-A232V-Q245R,S101G-S103A-V104I-A232V-Q245R-N248R,S101G-S103A-V104I-G159R-A232V-Q245R-N248R,和S101G,S103A,V104I,A232V,Q236H,Q245R,以及N252K。它们用QuikChange® Lightning多定点诱变试剂盒(QCLMS试剂盒;Stratagene),如实例5中所述以pRA96质粒作为DNA模板产生。在BMI微样本测定法(实例1)中,使用表1-2中所述洗涤剂对产生的变体测试了冷水清洁。

[0846]

表 9-1：WCE3 变体的 BMI 清洁性能。

PI=相对于 GG36 的性能指数

在洗涤剂 36h 或 36i 中，PI>或=1.5 为+++；PI 介于 1.49 和 1.3 之间=++；PI 介于 1.29 和 1.0 之间=+

GG36 变体的序列（BPN'编号方式）	相对于 GG36 的 PI；BMI 测定法，洗涤剂 36h 或 36i，16℃
S101G-S103A-V104I-A232V-Q236H-Q245R-N252K	++
S101G-S103A-V104I-A232V-Q245R-N248R	++
S101G-S103A-V104I-G159R-A232V-Q245R-N248D	++
S101G-S103A-V104I-G159D-A232V-Q245R-N248R	+
S101G-S103A-V104I-A232V-Q245R	+
S101G-S103A-V104I-G159D-A232V-Q245R	+
S101G-S103A-V104I-A232V-Q245R-N248D	+

[0847] 实例11

[0848] 另外的GG36文库和变体的构建

[0849] 本实例描述了使用以下突变中的一者或多者由枯草芽孢杆菌表达质粒(例如pHPLT-GG36;图2)构建GG36变体和文库:A16S,T22A,S24R,N62E,N76D,E89P,S101A/G,S103G/A,V104L/I,L111V,S128N,P129E,A232V,L148I,A158E,G159D/E,S166D,R186H,S188D,Y209E,Q236H,N238R,Q245R,N248D/R,H249R,N252K/R,T253R,E271F(BPN'编号方式)。组合变体由DNA2.0,Inc.公司使用枯草芽孢杆菌表达质粒(例如pHPLT-GG36;图2)和枯草芽孢杆菌菌株(基因型:ΔaprE,ΔnprE,amyE::xylRPxylAcomK-phleo)构建。就DNA文库而言,将使用枯草芽孢杆菌表达质粒(例如pHPLT-GG36;图2)构建的每个文库的连接反应物转化到枯草芽孢杆菌菌株(基因型:ΔaprE,ΔnprE,amyE::xylRPxylAcomK-phleo)中。在BMI微样本测定法(实例1)中,使用表1-2中所述的洗涤剂组合物对产生的包含上文所列突变中的一者或多者的变体进行了冷水清洁测试。

[0850]

表 10-1：NHJ6 文库变体的 BMI 清洁性能。

PI=性能指数

在洗涤剂 36b、36d 或 36e 中，PI>或=1.5 为+++；PI 介于 1.49 和 1.3 之间=++；PI 介于 1.29 和 1.0 之间=+

GG36 变体的序列（BPN'编号方式）	相对于 GG36 的 PI; BMI 测定法；洗涤剂 36b、36d 或 36e，16℃
S101G-S103A-V104I-P129E-S188D-A232V-N238R-*Q245R-N248D*	+++
S024R-S101G-S103A-V104I-P129E-A158E-S188D-A232V-Q245R-N248D-H249R	+++
T022A-S101G-S103A-V104I-P129E-A158E-S188D-A232V-Q245R-N248D-H249R	+++
T022A-S024R-S101G-S103A-V104I-P129E-A158E-S188D-A232V-Q245R-N248D-H249R	+++
S024R-S101G-S103A-V104I-P129E-S188D-A232V-Q245R-N248D-H249R	+++
S024R-S101G-S103A-V104I-P129E-G159E-S188D-A232V-Q245R-N248D-H249R	+++
S024R-S101G-S103A-V104I-S128N-P129E-A158E-A232V-Q245R-N248D-H249R	+++
S024R-S101G-S103A-V104I-L148I-A158E-S188D-A232V-Q245R-N248D	+++
T022A-S024R-S101G-S103A-V104I-P129E-G159E-S188D-A232V-Q245R-N248D-H249R	+++
S024R-S101G-S103A-V104I-S128N-P129E-A232V-Q245R-N248D	+++
S101G-S103A-V104I-P129E-S188D-A232V-Q245R-N248D-H249R	+++
S024R-S101G-S103A-V104I-P129E-A158E-A232V-Q245R-N248D-H249R	+++
T022A-S024R-S101G-S103A-V104I-A158E-G159E-S188D-A232V-Q245R-N248D-H249R	+++

[0851]

表 10-1：NHJ6 文库变体的 BMI 清洁性能。 PI=性能指数 在洗涤剂 36b、36d 或 36e 中，PI>或=1.5 为+++；PI 介于 1.49 和 1.3 之间=++；PI 介于 1.29 和 1.0 之间=+	
GG36 变体的序列（BPN'编号方式）	相对于 GG36 的 PI；BMI 测定法；洗涤剂 36b、36d 或 36e，16℃
T022A-S024R-S101G-S103A-V104I-P129E-A158E-G159E-S188D-A232V-N238R-Q245R-N248D	+++
S024R-S101G-S103A-V104I-P129E-L148I-A158E-A232V-Q245R-N248D	+++
A016S-S024R-S101G-S103A-V104I-A158E-S188D-A232V-Q245R-N248D-H249R	+++
S101G-S103A-V104I-A158E-G159E-A232V-Q245R-N248D-H249R	+++
T022A-S101G-S103A-V104I-P129E-A158E-G159E-A232V-N238R-Q245R-N248D	+++
T022A-S024R-S101G-S103A-V104I-P129E-A158E-G159E-A232V-Q245R-N248D-H249R	+++
T022A-S024R-S101G-S103A-V104I-S128N-A158E-S188D-A232V-Q245R-N248D	+++
S024R-S101G-S103A-V104I-P129E-S188D-A232V-Q245R-N248D	+++
T022A-S024R-S101G-S103A-V104I-P129E-A158E-A232V-Q245R-N248D	+++
T022A-S024R-S101G-S103A-V104I-P129E-A232V-Q245R-N248D	+++
T022A-S024R-S101G-S103A-V104I-P129E-S188D-A232V-Q245R-N248D	+++
S024R-S101G-S103A-V104I-A158E-S188D-A232V-N238R-Q245R-N248D	+++
T022A-S101G-S103A-V104I-S128N-P129E-S188D-A232V-N238R-Q245R-N248D	+++
S024R-S101G-S103A-V104I-P129E-S188D-A232V-N238R-Q245R-N248D	+++
S024R-S101G-S103A-V104I-A158E-G159E-S188D-A232V-Q245R-N248D	+++
T022A-S024R-S101G-S103A-V104I-S128N-S188D-A232V-Q245R-N248D	+++
S024R-S101G-S103A-V104I-P129E-A158E-S188D-A232V-Q245R-N248D	+++
T022A-S024R-S101G-S103A-V104I-S128N-P129E-A158E-A232V-Q245R-N248D	+++

[0852]

表 10-1：NHJ6 文库变体的 BMI 清洁性能。

PI=性能指数

在洗涤剂 36b、36d 或 36e 中，PI>或=1.5 为+++；PI 介于 1.49 和 1.3 之间=++；PI 介于 1.29 和 1.0 之间=+

GG36 变体的序列（BPN'编号方式）	相对于 GG36 的 PI；BMI 测定法；洗涤剂 36b、36d 或 36e，16℃
S024R-S101G-S103A-V104I-G159E-S188D-A232V-Q245R-N248D	+++
T022A-S101G-S103A-V104I-S128N-P129E-A232V-N238R-Q245R-N248D	+++
S024R-S101G-S103A-V104I-P129E-G159E-A232V-Q245R-N248D	+++
T022A-S024R-S101G-S103A-V104I-P129E-A158E-S188D-A232V-N238R-Q245R-N248D	+++
T022A-S024R-S101G-S103A-V104I-A158E-G159E-S188D-A232V-Q245R-N248D	+++
S024R-S101G-S103A-V104I-G159E-S188D-A232V-Q245R-N248D-H249R	+++
T022A-S101G-S103A-V104I-P129E-A158E-A232V-N238R-Q245R-N248D	+++
T022A-S024R-S101G-S103A-V104I-P129E-A158E-A232V-Q245R-N248D-H249R	+++
S024R-S101G-S103A-V104I-L148I-A158E-A232V-Q245R-N248D	+++
T022A-S101G-S103A-V104I-A158E-G159E-S188D-A232V-Q245R-N248D-H249R	+++
T022A-S101G-S103A-V104I-A158E-S188D-A232V-Q245R-N248D	+++
T022A-S101G-S103A-V104I-P129E-S188D-A232V-N238R-Q245R-N248D	+++
S024R-S101G-S103A-V104I-P129E-A158E-G159E-S188D-A232V-Q245R-N248D-H249R	+++
T022A-S024R-S101G-S103A-V104I-A158E-G159E-S188D-A232V-N238R-Q245R-N248D	+++
S101G-S103A-V104I-P129E-A158E-S188D-A232V-Q245R-N248D-H249R	+++
S024R-S101G-S103A-V104I-S128N-A158E-A232V-Q245R-N248D	+++
T022A-S024R-S101G-S103A-V104I-S128N-P129E-S188D-A232V-Q245R-N248D	+++
T022A-S101G-S103A-V104I-P129E-G159E-A232V-N238R-Q245R-N248D	+++

[0853]

表 10-1：NHJ6 文库变体的 BMI 清洁性能。

PI=性能指数

在洗涤剂 36b、36d 或 36e 中，PI>或=1.5 为+++；PI 介于 1.49 和 1.3 之间=++；PI 介于 1.29 和 1.0 之间=+

GG36 变体的序列（BPN'编号方式）	相对于 GG36 的 PI; BMI 测定法；洗涤剂 36b、36d 或 36e，16℃
S101G-S103A-V104I-P129E-G159E-A232V-Q245R-N248D-H249R	+++
T022A-S101G-S103A-V104I-P129E-A158E-A232V-Q245R-N248D-H249R	++
S024R-S101G-S103A-V104I-P129E-L148I-A158E-S188D-A232V-Q245R-N248D	++
T022A-S101G-S103A-V104I-P129E-G159E-A232V-Q245R-N248D-H249R	++
S024R-S101G-S103A-V104I-G159E-S188D-A232V-N238R-Q245R-N248D	++
S024R-S101G-S103A-V104I-P129E-A158E-G159E-A232V-Q245R-N248D-H249R	++
S024R-S101G-S103A-V104I-P129E-A158E-G159E-A232V-N238R-Q245R-N248D	++
S024R-S101G-S103A-V104I-S128N-G159E-S188D-A232V-Q245R-N248D	++
T022A-S101G-S103A-V104I-G159E-S188D-A232V-Q245R-N248D-H249R	++
S024R-S101G-S103A-V104I-P129E-G159E-S188D-A232V-N238R-Q245R-N248D	++
S101G-S103A-V104I-A158E-A232V-N238R-Q245R-N248D	++
T022A-S101G-S103A-V104I-P129E-G159E-S188D-A232V-Q245R-N248D-H249R	++
S024R-S101G-S103A-V104I-P129E-L148I-S188D-A232V-Q245R-N248D	++
S024R-S101G-S103A-V104I-A158E-A232V-Q245R-N248D-H249R	++
T022A-S101G-S103A-V104I-A158E-G159E-A232V-N238R-Q245R-N248D	++
S024R-S101G-S103A-V104I-A158E-G159E-A232V-N238R-Q245R-N248D	++
T022A-S101G-S103A-V104I-P129E-A158E-G159E-A232V-Q245R-N248D-H249R	++
S101G-S103A-V104I-P129E-A158E-S188D-A232V-N238R-Q245R-N248D	++

[0854]

表 10-1：NHJ6 文库变体的 BMI 清洁性能。

PI=性能指数

在洗涤剂 36b、36d 或 36e 中，PI>或=1.5 为+++；PI 介于 1.49 和 1.3 之间=++；PI 介于 1.29 和 1.0 之间=+

GG36 变体的序列（BPN'编号方式）	相对于 GG36 的 PI；BMI 测定法；洗涤剂 36b、36d 或 36e，16℃
T022A-S024R-S101G-S103A-V104I-P129E-A158E-G159E-A232V-Q245R-N248D	++
S101G-S103A-V104I-S188D-A232V-N238R-Q245R-N248D	++
T022A-S024R-S101G-S103A-V104I-A158E-A232V-Q245R-N248D-H249R	++
T022A-S024R-S101G-S103A-V104I-L148I-A158E-A232V-Q245R-N248D	++
S101G-S103A-V104I-P129E-A158E-G159E-A232V-N238R-Q245R-N248D	++
T022A-S101G-S103A-V104I-G159E-S188D-A232V-N238R-Q245R-N248D	++
T022A-S024R-S101G-S103A-V104I-P129E-A158E-G159E-S188D-A232V-Q245R-N248D-H249R	++
T022A-S101G-S103A-V104I-P129E-A232V-N238R-Q245R-N248D	++
T022A-S024R-S101G-S103A-V104I-S188D-A232V-Q245R-N248D-H249R	++
S101G-S103A-V104I-P129E-A158E-G159E-A232V-Q245R-N248D-H249R	++
T022A-S101G-S103A-V104I-A158E-G159E-A232V-Q245R-N248D-H249R	++
S101G-S103A-V104I-P129E-S188D-A232V-Q245R-N248D	++
S024R-S101G-S103A-V104I-P129E-G159E-A232V-N238R-Q245R-N248D	++
S101G-S103A-V104I-S128N-P129E-A232V-Q245R-N248D	++
S101G-S103A-V104I-A158E-S188D-A232V-Q245R-N248D	++
T022A-S024R-S101G-S103A-V104I-P129E-A232V-Q245R-N248D-H249R	++
S101G-S103A-V104I-P129E-G159E-A232V-N238R-Q245R-N248D	++
S101G-S103A-V104I-A158E-G159E-S188D-A232V-N238R-Q245R-N248D	++
S024R-S101G-S103A-V104I-A232V-Q245R-N248D-H249R	++
T022A-S024R-S101G-S103A-V104I-P129E-L148I-A232V-Q245R-N248D	++

[0855]

表 10-1：NHJ6 文库变体的 BMI 清洁性能。

PI=性能指数

在洗涤剂 36b、36d 或 36e 中，PI>或=1.5 为+++；PI 介于 1.49 和 1.3 之间=++；PI 介于 1.29 和 1.0 之间=+

GG36 变体的序列（BPN'编号方式）	相对于 GG36 的 PI; BMI 测定法；洗涤剂 36b、36d 或 36e，16℃
T022A-S024R-S101G-S103A-V104I-A158E-A232V-N238R-Q245R-N248D	++
S101G-S103A-V104I-S128N-P129E-A232V-N238R-Q245R-N248D	++
T022A-S101G-S103A-V104I-S128N-G159E-A232V-Q245R-N248D	+
T022A-S101G-S103A-V104I-S128N-P129E-A158E-A232V-N238R-Q245R-N248D	+
S101G-S103A-V104I-S128N-P129E-S188D-A232V-Q245R-N248D-H249R	+
T022A-S024R-S101G-S103A-V104I-S128N-P129E-A158E-S188D-A232V-Q245R-N248D-H249R	+
S024R-S101G-S103A-V104I-S128N-A158E-G159E-S188D-A232V-Q245R-N248D	+
T022A-S024K-S101G-S103A-V104I-S128N-A158E-G159E-A232V-Q245R-N248D	+
S101G-S103A-V104I-P129E-L148I-S188D-A232V-Q245R-N248D	+
S024R-S101G-S103A-V104I-L148I-A232V-Q245R-N248D	+
T022A-S101G-S103A-V104I-L148I-S188D-A232V-Q245R-N248D	+
S024R-S101G-S103A-V104I-S128N-P129E-S188D-A232V-Q245R-N248D	+
S101G-S103A-V104I-S128N-P129E-A158E-A232V-N238R-Q245R-N248D	+
T022A-S024R-S101G-S103A-V104I-P129E-L148I-A158E-S188D-A232V-Q245R-N248D	+
T022A-S024R-S101G-S103A-V104I-L148I-A158E-S188D-A232V-Q245R-N248D	+
S101G-S103A-V104I-L148I-G159E-A232V-Q245R-N248D	+
T022A-S024R-S101G-S103A-V104I-A158E-S188D-A232V-Q245R-N248D	+
S101G-S103A-V104I-S128N-P129E-A158E-A232V-Q245R-N248D-H249R	+

[0856]

表 10-2：NHJ6 文库变体的 BMI 清洁性能。

PI=性能指数

PI>或=1.5 为+++；PI 介于 1.49 和 1.3 之间=++；PI 介于 1.29 和 1.0 之间=+

GG36 变体的序列（BPN'编号方式）	相对于 GG36 的 PI；BMI 测定法，洗涤剂 36g，16℃
T022A-S024R-S101G-S103A-V104I-A158E-A232V-Q245R-N248D-H249R	+++
T022A-S024R-S101G-S103A-V104I-P129E-A232V-Q245R-N248D-H249R	+++
S024R-S101G-S103A-V104I-A158E-G159E-A232V-N238R-Q245R-N248D	+++
S024R-S101G-S103A-V104I-A232V-Q245R-N248D-H249R	+++
S101G-S103A-V104I-A158E-A232V-Q245R-N248D-H249R	+++
S101G-S103A-V104I-S188D-A232V-Q245R-N248D-H249R	+++
S024R-S101G-S103A-V104I-G159E-S188D-A232V-Q245R-N248D-H249R	+++
T022A-S024R-S101G-S103A-V104I-A158E-A232V-N238R-Q245R-N248D	+++
S024R-S101G-S103A-V104I-G159E-S188D-A232V-N238R-Q245R-N248D	+++
T022A-S024R-S101G-S103A-V104I-P129E-A232V-Q245R-N248D	+++
S024R-S101G-S103A-V104I-L148I-A232V-Q245R-N248D	+++
S024R-S101G-S103A-V104I-P129E-A158E-A232V-Q245R-N248D-H249R	++
S024R-S101G-S103A-V104I-L148I-A158E-A232V-Q245R-N248D	++
T022A-S024R-S101G-S103A-V104I-P129E-A158E-A232V-Q245R-N248D-H249R	++
A016S-S024R-S101G-S103A-V104I-A158E-S188D-A232V-Q245R-N248D-H249R	++
S024R-S101G-S103A-V104I-P129E-G159E-A232V-N238R-Q245R-N248D	++
S024R-S101G-S103A-V104I-P129E-S188D-A232V-Q245R-N248D-H249R	++
T022A-S101G-S103A-V104I-P129E-A232V-N238R-Q245R-N248D	++
T022A-S024R-S101G-S103A-V104I-L148I-A158E-A232V-Q245R-N248D	+
S024R-S101G-S103A-V104I-P129E-S188D-A232V-N238R-Q245R-N248D	+
T022A-S024R-S101G-S103A-V104I-A158E-G159E-S188D-A232V-N238R-Q245R-N248D	+
T022A-S101G-S103A-V104I-A158E-G159E-A232V-N238R-Q245R-N248D	+

[0857]

表 10-2：NHJ6 文库变体的 BMI 清洁性能。

PI=性能指数

PI>或=1.5 为+++；PI 介于 1.49 和 1.3 之间=++；PI 介于 1.29 和 1.0 之间=+

GG36 变体的序列（BPN'编号方式）	相对于 GG36 的 PI；BMI 测定法，洗涤剂 36g，16℃
T022A-S024R-S101G-S103A-V104I-P129E-A158E-A232V-Q245R-N248D	+
S101G-S103A-V104I-A158E-S188D-A232V-Q245R-N248D-H249R	+
T022A-S101G-S103A-V104I-A158E-G159E-A232V-Q245R-N248D-H249R	+
S024R-S101G-S103A-V104I-A158E-G159E-A232V-Q245R-N248D	+

[0858]

表 10-3：NHJ7 组合变体的 BMI 清洁性能。

PI=性能指数

在洗涤剂 36b、36d 或 36e 中，PI>或=1.5 为+++；PI 介于 1.49 和 1.3 之间=++；PI 介于 1.29 和 1.0 之间=+

GG36 变体的序列（BPN'编号方式）	相对于 GG36 的 PI；BMI 测定法，洗涤剂 36b、36d 或 36e，16℃
V104L-S128N-A158E-R186H-H249R	+++
S128N-A158E-S188D-H249R	+++
N062E-S128N-A158E-G159E-E271F	+++
N062E-A158E-S188D-H249R-E271F	+++
N062E-A158E-R186H-H249R-E271F	+++
S128N-A158E-S188D-Y209E-E271F	+++
N062E-G159E-S188D-H249R	+++
A016S-N062E-A158E-R186H-H249R	+++
N062E-A158E-G159E-H249R	+++
S101A-S128N-A158E-Y209E-H249R	+++
S128N-A158E-R186H-E271F	+++
N062E-A158E-S188D-H249R	+++
N062E-A158E-R186H-E271F	+++
N062E-A158E-R186H-H249R	+++
N062E-S101A-R186H-H249R	+++
N062E-S101A-A158E-R186H-E271F	+++
N062E-V104L-A158E-S188D-H249R-E271F	+++
N062E-G159E-R186H-H249R	+++
N062E-G159E-H249R	+++

[0859]

表 10-3：NHJ7 组合变体的 BMI 清洁性能。

PI=性能指数

在洗涤剂 36b、36d 或 36e 中，PI>或=1.5 为+++；PI 介于 1.49 和 1.3 之间=++；PI 介于 1.29 和 1.0 之间=+

GG36 变体的序列（BPN'编号方式）	相对于 GG36 的 PI；BMI 测定法，洗涤剂 36b、36d 或 36e，16℃
S128N-A158E-R186H-H249R	+++
S128N-A158E-S188D-E271F	+++
N062E-A158E-H249R	+++
N062E-R186H-S188D-H249R-E271F	+++
S128N-A158E-Y209E-	+++
N062E-S101A-A158E-H249R	+++
V104L-S128N-A158E-R186H-E271F	+++
N062E-S101A-A158E-R186H-H249R-E271F	+++
A016S-N062E-A158E-H249R	+++
N062E-S101A-G159E-H249R	+++
S128N-A158E-R186H-S188D-E271F	+++
S101A-S128N-A158E-R186H-E271F	+++
N062E-S101A-S188D-H249R	+++
S101A-V104L-A158E-R186H-S188D-H249R	+++
N062E-G159E-H249R-E271F	+++
S128N-A158E-G159E-E271F	+++
A016S-N062E-V104L-A158E-R186H-E271F	+++
T022A-S128N-A158E-H249R	+++
S128N-A158E-H249R	+++
N062E-S101A-V104L-A158E-R186H-E271F	+++
A016S-N062E-A158E-R186H-E271F	+++
V104L-S128N-A158E-H249R	+++
V104L-S128N-A158E-S188D-H249R	+++
T022A-N062E-A158E	+++
N062E-S101A-S188D-H249R-E271F	+++
N062E-A158E-H249R-E271F	++
V104L-S128N-A158E-R186H-S188D-E271F	++
N062E-S101A-R186H-E271F	++
N062E-V104L-G159E-H249R	++
N062E-R186H-H249R	++
N062E-S101A-R186H-H249R-E271F	++
S101A-A158E-R186H-S188D-H249R	++
N062E-S101A-R186H	++
S101A-S128N-P129E-R186H-H249R	++
S101A-S103G-A158E-R186H-H249R	++
A016S-N062E-V104L-R186H-S188D-E271F	++

[0860]

表 10-3：NHJ7 组合变体的 BMI 清洁性能。

PI=性能指数

在洗涤剂 36b、36d 或 36e 中，PI>或=1.5 为+++；PI 介于 1.49 和 1.3 之间=++；PI 介于 1.29 和 1.0 之间=+

GG36 变体的序列（BPN'编号方式）	相对于 GG36 的 PI；BMI 测定法，洗涤剂 36b、36d 或 36e，16℃
V104L-A158E-R186H-H249R	++
S101A-S128N-A158E-S188D-Y209E-E271F	++
N062E-S101A-R186H-S188D-E271F	++
A016S-N062E-A158E-H249R-E271F	++
N062E-S128N-A158E	++
N062E-S128N-G159E-H249R	++
N062E-S101A-A158E-S188D-H249R	++
S101A-S128N-A158E-H249R	++
N062E-A158E-R186H-S188D-H249R	++
A016S-V104L-A158E-R186H-E271F	++
N062E-L148I-G159E	++
N062E-S101A-A158E-R186H-H249R	++
N062E-S101A-R186H-S188D-H249R	++
V104L-A158E-R186H-S188D-H249R	++
N062E-S101A-V104L-R186H-S188D-E271F	++
T022A-S101A-A158E-R186H-H249R	++
S101A-S128N-A158E-Y209E	++
A158E-R186H-S188D-H249R-E271F	++
V104L-A158E-R186H-S188D-H249R-E271F	++
S101A-V104L-A158E-R186H-H249R	++
V104L-A158E-H249R	++
S101A-V104L-S128N-A158E-R186H-E271F	++
A016S-V104L-S188D-H249R	++
S101A-V104L-A158E-R186H-S188D-E271F	++
V104L-S128N-G159E-E271F	++
V104L-A158E-R186H-H249R-E271F	++
A158E-R186H-H249R	++
S101A-A158E-R186H-H249R	++
V104L-A158E-S188D-H249R-E271F	++
A016S-S128N-A158E-R186H	++
V104L-S128N-R186H-S188D-H249R	++
A016S-S101A-S128N-R186H	++
A016S-N062E-S128N-R186H-E271F	++
A016S-S128N-R186H-E271F	+
S128N-P129E-R186H	+
A158E-R186H-H249R-E271F	+

[0861]

表 10-3：NHJ7 组合变体的 BMI 清洁性能。

PI=性能指数

在洗涤剂 36b、36d 或 36e 中，PI>或=1.5 为+++；PI 介于 1.49 和 1.3 之间=++；PI 介于 1.29 和 1.0 之间=+

GG36 变体的序列（BPN'编号方式）	相对于 GG36 的 PI；BMI 测定法，洗涤剂 36b、36d 或 36e，16℃
A016S-A158E-H249R	+
A016S-A158E-R186H-H249R	+
A016S-T022A-A158E-R186H-E271F	+
E089P-S101A-P129E-R186H	+
T022A-S128N-A158E-R186H	+
S101A-V104L-S128N-A158E-R186H	+
T022A-S128N-R186H-S188D-	+
N062E-V104L-A158E-R186H-S188D-H249R	+
T022A-A158E-R186H-H249R-E271F	+
T022A-V104L-A158E-H249R	+
S101A-L111V-P129E	+
A016S-A158E-H249R-E271F	+
A016S-L111V-S188D-	+
T022A-V104L-R186H-S188D-H249R	+
V104L-L148I-S188D-H249R	+

[0862] 实例12

[0863] 另外的GG36文库和变体的构建

[0864] 本实例描述了在枯草芽孢杆菌中使用以下突变中的一者或多者(BPN'编号方式)构建GG36变体和文库:A1R,Q2S,Q2M,Q2A,Q2R,Q2W,S3R,V4R,V4S,V4C,I8A,S9A,S9F,S9W,R10S,R10A,R10H,R10M,Q12F,Q12R,P14K,P14F,P14Q,A15R,A15F,A16S,H17R,H17M,H17F,N18R,N18K,G20F,G20K,G20R,T22A,T22R,T22Y,T22V,T22Q,T22L,T22W,G23A,G23S,G23F,S24R,S24F,S24W,S24Q,S24H,S24L,G25V,G25F,G25R,V26F,K27L,K27F,K27R,K27V,V28A,V28N,V28E,A29T,V30E,L31F,T33S,T33G,T33D,G34P,I35M,S36T,S36F,S36R,T38L,T38F,T38R,P40N,P40L,P40T,P40W,P40H,P40R,L42I,N43A,N43F,N43I,N43S,N43R,N43M,N43W,N43D,R45T,G46R,A48R,F50C,V51W,V51F,V51H,P52F,P52E,P52N,P55Y,T57R,Q59A,Q59F,Q59R,D60P,D60Q,D60A,N62E,N62Q,G63V,G63M,G63T,G63I,G63A,G63S,G63H,G63Q,G63D,G63E,G63P,H64F,H64T,V68A,V68C,A69N,A69T,A69P,A69W,T71G,I72C,A74C,L75A,L75F,L75E,L75R,N76D,S78R,S78N,S78I,I79W,I79Q,V81R,L82F,L82T,L82V,L82R,L82M,A85M,P86W,P86L,P86I,E89P,E89T,E89G,E89H,E89L,E89V,E89W,E89F,E89I,Y91N,Y91F,A92F,K94N,S99F,S99T,S99P,S99G,S99M,G100S,G100N,G100Q,G100I,S101A,S101N,S101G,S101T,S101D,S101E,S101P,S101F,G102A,G102T,G102N,G102H,G102E,S103G,S103N,S103D,S103A,V104L,V104I,V104E,V104D,S105T,S105E,S105Q,S106G,S106T,S106E,S106D,S106A,S106V,S106F,I107M,I107F,A108I,A108G,Q109M,L111V,L111I,E112V,E112L,E112Q,A114G,G115K,G115R,N116K,N116A,N116L,N117F,G118R,G118I,M119C,H120A,H120F,H120R,V121F,V121E,N123G,N123E,L124S,S128D,S128F,S128L,S128N,

S128H,S128M,S128I,S128Q,P129E,S132A,S132E,A138G,S144R,V147L,L148I,A158E,G159D,G159E,G159C,S160D,S166D,S166E,Y167W,M175V,V177C,D181A,Q182R,N183I,N183D,N183M,N183F,N183R,N185E,N185V,N185I,R186H,R186K,S188E,S188D,S188R,Y192H,Y192W,A194E,A194V,A194F,D197F,I198L,I198F,V203E,V203C,T208S,Y209S,Y209N,Y209F,Y209T,Y209E,Y209H,Y209G,Y209L,P210R,P210V,P210L,G211Q,G211R,S212I,S212M,S212F,T213A,Y214F,A215N,A215D,A215E,A215H,A215F,S216F,S216A,L217E,L217N,L217D,N218D,N218P,N218E,T224A,T224G,V227I,A230E,A231I,A231C,A232V,L233C,V234F,K235F,Q236F,Q236N,Q236H,N238R,N238K,N238L,P239K,P239G,P239R,P239H,P239T,P239N,P239S,P239F,S240R,W241R,S242L,S242R,N243F,N243R,V244R,Q245R,I246S,N248D,N248V,N248I,N248R,H249R,H249T,L250I,K251R,K251S,N252I,N252F,N252R,N252K,N252H,T253I,T253R,T253F,A254C,S256N,G258R,T260V,T260I,L262D,L262H,Y263F,S265F,L267V,L267N,L267M,N269I,N269R,A270C,E271I,E271V,E271H,E271M,E271L,E271P,E271A,E271F,E271T,A272F,A272F,A272R,A273F,A273I,和T274G。变体和文库由DNA2.0,Inc.公司如实例11中所述进行构建。在BMI微样本测定法(实例1)中,使用表1-2中所述的洗涤剂组合物对所产生的包含一个或若干个这些突变的变体进行冷水清洁测试。

[0865]

表 11-1：WCE6 和 WCE8 变体的 BMI 清洁性能。
PI=性能指数

在洗涤剂 36k 或 36l 中，PI>或=1.5 为+++；PI 介于 1.49 和 1.3 之间=++；PI 介于 1.29 和 1.0 之间=+

GG36 变体的序列（BPN'编号方式）	相对于 GG36 的 PI；BMI 测定法，洗涤剂 36k 或 36l，16℃
A001R-S101G-S103A-V104I-A232V-Q245R	+++
V004R-S101G-S103A-V104I-A232V-Q245R	+++
N043R-S101G-S103A-V104I-A232V-Q245R-E271L	+++
S078R-S101G-S103A-V104I-A232V-Q245R	+++
V004R-N043R-S101G-S103A-V104I-A232V-Q245R	+++
N018R-N043R-S101G-S103A-V104I-A232V-Q245R	+++
G020R-S101G-S103A-V104I-A232V-Q245R	+++
S101G-S103A-V104I-A232V-Q245R-E271L	+++
G020R-N043R-S101G-S103A-V104I-A232V-Q245R	+++
S024R-N043R-S101G-S103A-V104I-A232V-Q245R	+++
G020R-G025R-N116A-Y167W	+++
N018R-S101G-S103A-V104I-A232V-Q245R	+++
T022R-S101G-S103A-V104I-A232V-Q245R	+++
S078R-S103N-S106G-Y167W-Q236N	+++
N018R-N043D-S101G-S103A-V104I-A232V-Q245R-N269R	+++
N043R-S101G-S103A-V104I-A232V-Q245R-N269R	+++
S024R-S101A-H120F-A194F-H249R	+++
G020R-N043D-S101G-S103A-V104I-A232V-Q245R-N269R	+++
S101G-S103A-V104I-S212F-A232V-Q245R	+++
G020R-S144R-N185I-L233C-Q236N	+++
G023A-S078R-S216F-Q236N-H249R	+++
S101G-S103A-V104I-A232V-Q245R-N269R	+++
S101G-S103A-V104I-G115R-A232V-Q245R	+++
P052N-S078R-S103N-L148I-T213A	+++
N018R-N043D-S101G-S103A-V104I-A232V-Q245R-H249R	+++
S024R-N043D-S101G-S103A-V104I-A232V-Q245R-H249R	+++
S024R-N043D-S101G-S103A-V104I-A232V-Q245R-N269R	+++
G025R-E089I-N116A-P239S-A270C	+++
S024R-S101G-S103A-V104I-A232V-Q245R	+++

表 11-1：WCE6 和 WCE8 变体的 BMI 清洁性能。
PI=性能指数

在洗涤剂 36k 或 36l 中，PI>或=1.5 为+++；PI 介于 1.49 和 1.3 之间=++；PI 介于 1.29 和 1.0 之间=+

[0866]

GG36 变体的序列（BPN'编号方式）	相对于 GG36 的 PI；BMI 测定法，洗涤剂 36k 或 36l，16℃
L148I-T213A-N252R	+++
S024R-G025R-N183D-Y192W-P239S	+++
G046R-A194F-S212M	+++
V104L-L217E-T224A-H249R-N252R	+++
G023A-Y091F-V121F-Y192W-Q236N	+++
S101G-S103A-V104I-A232V-V244R-Q245R	+++
S099F-S144R-Y167W-N252R	+++
S101G-S103A-V104I-A232V-Q245R-H249R	+++
N043R-S101G-S103A-V104I-A232V-Q245R	+++
T022W-S078R-Y167W-S212M-A270C	+++
V121F-N252R-A270C	+++
G020R-S103N-S216F-Q236N-N252R	+++
N043R-S101G-S103A-V104I-A232V-Q245R-H249R	+++
G023A-P052N-Y192W-I198L-N252R	+++
G025R-G046R-V121F	+++
S024R-S078R-V104L-N116A-N183D	+++
G046R-Q059A-S103N-G211Q-S212M	+++
G020R-P052N-N062Q-Y091F-Y192W	+++
G023A-P052N-S144R-Y192W-S216F	+++
S101G-S103A-V104I-A232V-S242R-Q245R	+++
P052N-S103N-N116A-L148I-Y192W	+++
E089I-N116A-N117F-T224A-H249R	+++
S144R-G211Q-N238L-P239S-H249R	+++
N043A-N062Q-A194F-G211Q	+++
G020R-S024R-P052N-Q059A-S216F	+++
S024R-Y167W-T224A-H249R	+++
T057R-Y167W-H249R	+++
G025R-S103N-R186K-A194F-T224A	+++
S105T-S128N-S144R-L148I-S212M	+++
G020R-Q059A-S144R-Y192W-T224A	+++
S024R-N043A-N117F-A194F-G211Q	+++
N117F-A194F-T213A-A270C	+++
S078R-Y091F-V121F-L233C-N252R	+++
T057R-S099F-S105T-I198L-T213A	+++
G023A-Y091F-S101A-I198L-N252R	+++
N062Q-S103N-V121F-S144R-H249R	+++

[0867]

表 11-1：WCE6 和 WCE8 变体的 BMI 清洁性能。
PI=性能指数

在洗涤剂 36k 或 36l 中，PI>或=1.5 为+++；PI 介于 1.49 和 1.3 之间=++；PI 介于 1.29 和 1.0 之间=+

GG36 变体的序列（BPN'编号方式）	相对于 GG36 的 PI；BMI 测定法，洗涤剂 36k 或 36l，16℃
N043R-S101G-S103A-V104I-A232V-S242R-Q245R	+++
G023A-S024R-N117F-S212M-S216F	+++
V104L-T213A-S216F	+++
A194F-G211Q-Q236N	+++
N062Q-S103N-N117F-A194F	+++
S024R-N062Q-V104L-S106G-H249R	+++
T057R-E089I-I198L	+++
G046R-Q059A-S106G-L217E-H249R	+++
N117F-T213A-A215F	+++
S101A-H120F-Y192W-A215F-T224A	+++
N043A-T057R-N117F-S144R-N183D	+++
G046R-N183D-N238L	+++
G025R-N043A-E089I-N117F	+++
S078R-V104L-T213A-A215F-T224A	+++
Y091F-S099F-S101A-S105T-Y167W	+++
S106G-N117F-N238L	+++
G046R-E089I-Y091F-S101A-N116A	+++
G020R-N062Q-E089I-R186K-S212M	+++
T057R-S099F-V121F-N185I-Y192W	+++
G046R-E089I-Y192W-L233C-A270C	+++
E089I-N117F-N185I-A215F-L233C	++
P052N-V104L-N183D-S216F-H249R	++
S078R-S099F-N116A-R186K-T224A	++
G025R-S105T-S128N-S144R-A270C	++
S105T-G211Q-S216F	++
S024R-G046R-Y091F-V121F	++
S106G-N185I-S216F-Q236N	++
N062Q-S101A-Q236N-N252R-A270C	++
G025R-N043A-Y091F-I198L-A270C	++
G020R-G023A-V104L-Y192W-L233C	++
S024R-N043A-S105T-S106G-I198L	++
G020R-E089I-L217E	++
S024R-Y091F-I198L-A215F-P239S	++
G046R-E089I-S099F-R186K-S212M	++
V104L-H120F-R186K-S216F-N252R	++
T022W-A194F-T213A-L233C-N238L	+

表 11-1：WCE6 和 WCE8 变体的 BMI 清洁性能。
PI=性能指数

在洗涤剂 36k 或 36l 中，PI>或=1.5 为+++；PI 介于 1.49 和 1.3 之间=++；PI 介于 1.29 和 1.0 之间=+

[0868]

GG36 变体的序列（BPN'编号方式）	相对于 GG36 的 PI；BMI 测定法，洗涤剂 36k 或 36l，16℃
S099F-S105T-S106G-A194F-S212M	+
E089I-S105T-N116A-A215F-S216F	+
G025R-N116A-H120F-T224A-A270C	+
N043A-Q059A-S101A-S216F-T224A	+
T057R-N183D-Q236N	+
G025R-N062Q-S128N-S144R-N185I	+
S103N-H120F-Y167W-I198L-L233C	+
T022W-E089I-S216F	+
S024R-S106G-N116A-S212M-T224A	+
G020R-P052N-S101A-I198L-L233C	+
E089I-Y091F-N185I-G211Q-A270C	+
L111I-A215F-P239S	+
S024R-N116A-R186K-L233C-Q236N	+
G023A-S103N-S106G-S212M-A215F	+

表 11-2：WCE10 至 WCE14 文库变体的 BMI 清洁性能。
PI=性能指数
在洗涤剂 36k 或 36l 中，PI>或=1.5 为+++；PI 介于 1.49 和 1.3 之间=++；PI 介于 1.29 和 1.0 之间=+

[0869]

GG36 变体的序列（BPN'编号方式）	相对于 GG36 的 PI；BMI 测定法，洗涤剂 36k 或 36l，16℃
G020R-T022W-S078R-S101A-S103A-V104I-N116S-T213A-A215F-A232V-Q245R	+++
N018R-S078R-S101G-S103A-V104I-A232V-Q245R	+++
S024R-R045T-S101G-S103A-V104I-A232V-Q245R-N269R	+++
G020R-T022W-S078R-S101G-S103A-V104I-N116A-A232V-Q245R	+++
G020R-T22W-S101G-S103A-V104I-A232V-Q245R	+++
N018R-N043R-S101G-S103A-V104I-A232V-Q245R	+++
N018R-T022W-S024R-N076D-S101A-N116A-A232V-Q245R	+++
N018R-V104I-A232V-H249R	+++
N018R-S024R-N076D-S101A-N116A-G211Q-H249R	+++
N018R-N043D-S078R-S101G-S103A-V104I-L217E-A232V-Q245R	+++

[0870]

表 11-2：WCE10 至 WCE14 文库变体的 BMI 清洁性能。
PI=性能指数
在洗涤剂 36k 或 36l 中，PI>或=1.5 为+++；PI 介于 1.49 和 1.3 之间=++；PI 介于 1.29 和 1.0 之间=+

GG36 变体的序列（BPN'编号方式）	相对于 GG36 的 PI; BMI 测定法，洗涤剂 36k 或 36l，16℃
N018R-N043R-S101G-S103A-V104I-A232V-Q245R-N269R	+++
N018R-R045T-N076D-S101G-S103A-V104I-A232V-Q245R-N269R	+++
N076D-S078R-S101G-S103A-V104I-A232V-Q245R-N269R	+++
G020R-N043D-S078R-S101G-S103A-V104I-A232V-Q245R	+++
N018R-N043D-N076D-S101G-S103A-V104I-A232V-Q245R-N269R	+++
S024R-R045T-N076D-S078R-S101G-S103A-V104I-A232V-Q245R-N269R	+++
N018R-S103A-A232V-H249R	+++
N018R-S101G-V104I-A232V-Q245R	+++
G020R-S024R-S101G-S103A-V104I-L217E-A232V-Q245R-H249R	+++
N018R-T22K-N043D-S101G-S103A-V104I-A232V-Q245R	+++
N043R-R045T-S101G-S103A-V104I-A232V-Q245R-N269R	+++
G020R-T22W-S101G-S103A-V104I-G211Q-A232V-Q245R	+++
S024R-N076D-S078R-S101G-S103A-V104I-A232V-Q245R-N269R	+++
G020R-T22W-S078R-S101A-S103A-V104I-N116A-N183D-A232V	+++
N018R-S024R-N076D-N116A-A215F-H249R	+++
N018R-N043R-R045T-S101G-S103A-V104I-A232V-Q245R	+++
S024R-N043R-N076D-S101G-S103A-V104I-A232V-Q245R	+++
G020R-T022W-S101G-S103A-V104I-A232V-Q245R	+++
G020R-T022W-S101G-S103A-V104I-G211Q-A232V-Q245R	+++
G020R-T022W-S078R-S101G-S103A-V104I-N116A-T213A-A215F-A232V-Q245R	+++
N043D-N076D-S078R-S101G-S103A-V104I-A232V-Q245R-N269R	+++
N018R-S024R-N076D-S101A-N116A-T213A-H249R	+++
N018R-S024R-N076D-N116A-G211Q-H249R	+++
N043R-R045T-N076D-S078R-S101G-S103A-V104I-A232V-Q245R	+++
N018R-S101G-Q245R	+++
G020R-T22W-S101A-S103A-V104I-G211Q-T213A-A232V-Q245R	+++
G020R-S024R-N043D-N076D-S078R-S101G-S103A-V104I-A232V-Q245R	+++
N018R-R045T-N076D-S078R-S101G-S103A-V104I-A232V-Q245R	+++
G020R-S078R-S101G-S103A-V104I-G211Q-T213A-A215F-A232V-Q245R	+++
R045T-S078R-S101G-S103A-V104I-A232V-Q245R-N269R	+++
S024R-N043D-S101G-S103A-V104I-A232V-Q245R-N269R	+++

表 11-2：WCE10 至 WCE14 文库变体的 BMI 清洁性能。
PI=性能指数
在洗涤剂 36k 或 36l 中，PI>或=1.5 为+++；PI 介于 1.49 和 1.3 之间=++；PI 介于 1.29 和 1.0 之间=+

[0871]

GG36 变体的序列（BPN'编号方式）	相对于 GG36 的 PI；BMI 测定法，洗涤剂 36k 或 36l，16℃
N018R-S101G-S103A-H249R	+++
N018R-T22W-S024R-N076D-S101A-N116A-A232V-Q245R	+++
N018R-S101G-V104I-A232V-H249R	+++
G020R-T22W-S101A-S103A-V104I-A215F-A232V-Q245R	+++
N018R-S024R-N076D-G211Q-T213A-H249R	+++
N018R-T022W-S024R-N076D-S101A-I198L-H249R	+++
S024R-S101G-S103A-V104I-A232V-Q245R	+++
G020R-N076D-S101G-S103A-V104I-A232V-Q245R-N269R	+++
G020R-S101G-S103A-V104I-A232V-Q245R-N269R	+++
N043D-S078R-S101G-S103A-V104I-A232V-Q245R	+++
G020R-S101G-V104I-T213A-A215F-A232V-Q245R	+++
G020R-S101G-S103A-V104I-N116A-A215F-A232V-Q245R	+++
S024R-S103A-V104I-H249R	+++
N018R-N076D-S078R-S101G-S103A-V104I-A232V-Q245R	+++
R045T-N076D-S078R-S101G-S103A-V104I-A232V-Q245R-N269R	+++
S024R-S101G-V104I-Q245R	+++
G020R-S101G-S103A-V104I-G211Q-T213A-A215F-A232V-Q245R	+++
S024R-S103A-V104I-A232V-H249R	+++
N018R-S024R-N076D-N116A-G211Q-A215F-H249R	+++
N018R-Q245R	+++
S024R-S103A-Q245R	+++
S024R-S103A-V104I-Q245R	+++
G020R-S078R-S101G-A232V-Q245R	+++
N018R-S024R-N076D-V104I-H249R	+++
N018R-S024R-V104I-H249R	+++
S024R-S101G-S103A-V104I-A232V-Q245R	+++
N018R-S024R-N076D-G211Q-A215F-H249R	+++
R019H-G020R-T022W-S078R-S101G-S103A-V104I-G211Q-A232V-Q245R	+++
N018R-S024R-N076D-S101A-I198L-G211Q-T213A-H249R	+++
N018R-S024R-N043D-S101G-S103A-V104I-A232V-Q245R	+++
G020R-T22W-S103A-V104I-A232V-Q245R	+++
N018R-S103A-V104I-H249R	+++
N018R-T022W-S024R-N076D-S101A-I198L-A215F-H249R	+++
N018R-S024R-S101G-V104I-A232V	+++
S078R-S101G-S103A-V104I-A232V-Q245R-N269R	+++

[0872]

表 11-2：WCE10 至 WCE14 文库变体的 BMI 清洁性能。
PI=性能指数
在洗涤剂 36k 或 36l 中，PI>或=1.5 为+++；PI 介于 1.49 和 1.3 之间=++；PI 介于 1.29 和 1.0 之间=+

GG36 变体的序列（BPN'编号方式）	相对于 GG36 的 PI; BMI 测定法，洗涤剂 36k 或 36l，16℃
S024R-N043R-N076D-S078R-S101G-S103A-V104I-A232V-Q245R	+++
N018R-G020R-N043D-N076D-S101G-S103A-V104I-A232V-Q245R	+++
N018R-T22W-S024R-N076D-N116A-T213A-H249R	+++
N018R-S024R-S101G-V104I	+++
G020R-S101A-S103A-V104I-A215F-A232V-Q245R	+++
N018R-R045T-S078R-S101G-S103A-V104I-A232V-Q245R	+++
N018R-S101G-S103A-Q245R	+++
N043R-N076D-S078R-S101G-S103A-V104I-A232V-Q245R	+++
G020R-T022W-S101A-S103A-V104I-G211Q-A215F-A232V-Q245R	+++
G020R-T22W-S078R-S101G-S103A-V104I-N116A-T213A-A215F-A232V-Q245R	+++
G020R-S078R-S101G-S103A-V104I-A215F-A232V-Q245R	+++
G020R-T022W-S078R-S101G-S103A-V104I-N116A-N183D-A232V-Q245R	+++
N076D-S101G-S103A-V104I-A232V-Q245R	+++
N076D-S101G-S103A-V104I-A232V-Q245R-N269R	+++
G020R-T22W-S101A-S103A-V104I-A232V-Q245R	+++
G020R-S101G-S103A-A232V-Q245R	+++
G020R-T022W-S078R-S101A-S103A-V104I-N116A-N183D-A232V-Q245R	+++
N018R-G020R-S024R-R045T-N076D-S101G-S103A-V104I-A232V-Q245R-N269R	+++
N043R-R045T-S078R-S101G-S103A-V104I-A232V-Q245R	+++
N018R-S101G-V104I-H249R	+++
G020R-T22W-S078R-S101G-S103A-V104I-N116A-N183D-A232V-Q245R	+++
G020R-T022W-S101G-S103A-V104I-I198L-G211Q-T213A-A232V-Q245R	+++
G020R-S078R-S101A-S103A-V104I-N116A-N183D-T213A-A232V-Q245R	+++
S024R-N076D-V104I-A232V-Q245R	+++
N018R-G020R-N076D-S101G-S103A-V104I-A232V-Q245R	+++
N018R-S024R-N076D-S101G-V104I-A232V-H249R	+++
N018R-N043D-S078R-S101G-S103A-V104I-A232V-Q245R	+++
A001T-N018R-S024R-N076D-N116A-T213A-H249R	+++

[0873]

表 11-2：WCE10 至 WCE14 文库变体的 BMI 清洁性能。
PI=性能指数
在洗涤剂 36k 或 36l 中，PI>或=1.5 为+++；PI 介于 1.49 和 1.3 之间=++；PI 介于 1.29 和 1.0 之间=+

GG36 变体的序列（BPN'编号方式）	相对于 GG36 的 PI; BMI 测定法，洗涤剂 36k 或 36l，16℃
N076D-S078R-S101G-S103A-V104I-A232V-Q245R	+++
G020R-S078R-S101G-S103A-V104I-N116A-A232V-Q245R	+++
N043R-N076D-S101G-S103A-V104I-A232V-Q245R	+++
N018R-R045T-S101G-S103A-V104I-A232V-Q245R	+++
N018R-N076D-S101G-V104I-A232V-Q245R	+++
G020R-S078R-S101G-S103A-V104I-N116A-N183D-A232V-Q245R	+++
N018R-S024R-N076D-S101A-G211Q-T213A-A215F-H249R	+++
R045T-S078R-S101G-S103A-V104I-A232V-Q245R	+++
N043R-N076D-S101G-S103A-V104I-A232V-Q245R-N269R	+++
G020R-T022W-S078R-S101G-S103A-V104I-N116A-N183D-T213A-A232V-Q245R	+++
G020R-T022W-S101G-S103A-V104I-N116A-N183D-T213A-A232V-Q245R	+++
G020R-S101G-I198L-A215F-A232V-Q245R	+++
N018R-S024R-N076D-T213A-A215F-H249R	+++
G020R-S078R-S101G-S103A-V104I-N116A-G211Q-A232V-Q245R	+++
G020R-T022W-S078R-S101A-S103A-V104I-N116A-N183D-A215F-A232V-Q245R	+++
G020R-T022W-S078R-S101A-S103A-V104I-N116A-N183D-T213A-A232V-Q245R	+++
S024R-A232V-Q245R	+++
N018R-S024R-N043D-S101G-S103A-V104I-A232V-Q245R-N269R	+++
N018R-S024R-N076D-S101A-A215F-H249R	+++
N018R-T022W-S024R-N076D-N116A-T213A-H249R	+++
S101G-S103A-V104I-A232V-Q245R	+++
N018R-S024R-N076D-G211Q-T213A-A215F-H249R	+++
N018R-S024R-N076D-N116A-T213A-A215F-H249R	+++
N043D-N076D-S078R-S101G-S103A-V104I-A232V-Q245R-N269R	+++
N043D-S078R-S101G-S103A-V104I-A232V-Q245R-H249R	+++
G020R-T022W-S078R-S101G-S103A-V104I-N116A-N183D-G211Q-A232V-Q245R	+++
N018R-S024R-N076D-S101A-I198L-G211Q-A215V-H249R	+++
N018R-T022W-S024R-N076D-N116A-G211Q-H249R	+++
G020R-S103A-V104I-A232V-Q245R	++
G020R-T22W-S101A-S103A-V104I-G211Q-A215F-A232V-Q245R	++
S024R-N076D-S101G-S103A-V104I-A232V-Q245R	++

[0874]

表 11-2：WCE10 至 WCE14 文库变体的 BMI 清洁性能。
PI=性能指数
在洗涤剂 36k 或 36l 中，PI>或=1.5 为+++；PI 介于 1.49 和 1.3 之间=++；PI 介于 1.29 和 1.0 之间=+

GG36 变体的序列（BPN'编号方式）	相对于 GG36 的 PI; BMI 测定法，洗涤剂 36k 或 36l，16℃
G020R-S101G-S103A-V104I-N116A-A232V-Q245R	++
N018R-T22W-S024R-N076D-I198L-A215F-H249R	++
G020R-T022W-S103A-V104I-A232V-Q245R	++
G020R-T022W-S101A-S103A-V104I-G211Q-T213A-A232V-Q245R	++
G020R-T022W-S101G-S103A-V104I-G211Q-T213A-A215F-A232V-Q245R	++
N018R-N043R-R045T-N076D-S101G-S103A-V104I-A232V-Q245R	++
N018R-T022W-S024R-N076D-S101A-I198L-T213A-A215F-H249R	++
N018R-T22W-S024R-N076D-S101A-A215F-H249R	++
G020R-R045T-S101G-S103A-V104I-A232V-Q245R	++
G020R-S078R-S101G-S103A-V104I-T180A-A232V-Q245R	++
G020R-T022W-S078R-S101G-S103A-V104I-N116A-N183D-A215F-A232V-Q245R	++
N018R-S101G-S103A-V104I	++
G020R-T22W-S101A-S103A-V104I-N116A-G211Q-T213A-A215F-A232V-Q245R	++
N018R-S024R-N076D-S103A-A232V-Q245R	++
G020R-S078R-S101A-S103A-V104I-N116A-N183D-A232V-Q245R	++
N018R-S024R-N076D-G211Q-H249R	++
G020R-S101A-S103A-V104I-T213A-A215F-A232V-Q245R	++
N018R-G020R-N043D-S101G-S103A-V104I-A232V-Q245R	++
G020R-T022W-S101A-S103A-V104I-G211Q-A232V-Q245R	++
G020R-T022W-S101A-S103A-V104I-N116A-G211Q-A215F-A232V-Q245R	++
G020R-T022W-S101A-S103A-V104I-N116A-G211Q-A232V-Q245R	++
N018R-S024R-N076D-A232V-H249R	++
N018R-S024R-R045T-N076D-S101G-S103A-V104I-A232V-Q245R-N269R	++
N018R-N076D-Q245R	++
S024R-V104I-Q245R	++
S101G-A232V	++
G020R-T22W-S101A-S103A-V104I-N116A-G211Q-A215F-A232V-Q245R	++
N018R-G020R-T022W-S024R-N076D-N116A-N183D-I198L-T213A-H249R	++

[0875]

表 11-2：WCE10 至 WCE14 文库变体的 BMI 清洁性能。
PI=性能指数
在洗涤剂 36k 或 36l 中，PI>或=1.5 为+++；PI 介于 1.49 和 1.3 之间=++；PI 介于 1.29 和 1.0 之间=+

GG36 变体的序列（BPN'编号方式）	相对于 GG36 的 PI; BMI 测定法，洗涤剂 36k 或 36l，16℃
G020R-T022W-S078R-S101A-S103A-V104I-A232V-Q245R	++
G020R-T022W-S078R-S101A-S103A-V104I-I198L-A232V-Q245R	++
S024R-Q245R-H249R	++
G020R-S101G-S103A-V104I-N116A-G211Q-A232V-Q245R	++
N018R-T22W-S024R-N076D-N116A-G211Q-H249R	++
S024R-S101G-V104I-H249R	++
N018R-S024R-N076D-N116A-I198L-G211Q-T213A-A215F-H249R	++
N018R-S024R-V104I	++
G020R-T022W-S078R-S101A-S103A-V104I-N183D-I198L-T213A-A215F-A232V-Q245R	++
N018R-G020R-T22W-S024R-N076D-N116A-N183D-I198L-T213A-H249R	++
G020R-T022W-S101A-S103A-V104I-A232V-Q245R	++
Q012H-G020R-S078R-S101G-S103A-V104I-I198L-G211Q-T213A-A232V-Q245R	++
N018R-S024R-N076D-S101A-G211Q-A215F-H249R	++
N018R-S024R-N076D-T213A-H249R	++
S024R-V104I-H249R	++
N018R-T022W-S024R-N076D-G211Q-H249R	++
N018R-N076D-S103A-V104I-H249R	++
N043R-N076D-S101G-S103A-V104I-L217E-A232V-Q245R	++
G020R-S078R-S101G-S103A-V104I-N183D-G211Q-T213A-A232V-Q245R-E271G	++
N018R-T022W-S024R-N076D-S101A-N116A-I198L-A215F-H249R	++
N018R-S024R-N043D-N076D-S101G-S103A-V104I-A232V-Q245R	++
N018R-S024R-N076D-S101A-I198L-A215F-H249R	++
N018R-T022W-S024R-N076D-N116A-I198L-G211Q-T213A-H249R	++
N018R-S024R-N076D-S101A-N116A-T213A-A215F-H249R	++
G020R-N043D-R045T-S078R-S101G-S103A-V104I-A232V-Q245R	++
R045T-S078R-S101G-S103A-V104I-A232V-Q245R-H249R	++
N018R-T22W-S024R-N076D-S101A-N116A-A215F-H249R	++
N043D-S101G-S103A-V104I-A232V-Q245R-N269R	++
G020R-T022W-S078R-S101A-S103A-V104I-N116A-N183D-T213A-A215F-A232V-Q245R	++
N018R-S024R-N076D-N116A-G211Q-T213A-A215F-H249R	++

[0876]

表 11-2：WCE10 至 WCE14 文库变体的 BMI 清洁性能。
PI=性能指数
在洗涤剂 36k 或 36l 中，PI>或=1.5 为+++；PI 介于 1.49 和 1.3 之间=++；PI 介于 1.29 和 1.0 之间=+

GG36 变体的序列（BPN'编号方式）	相对于 GG36 的 PI; BMI 测定法，洗涤剂 36k 或 36l，16℃
S024R-S103A-M175L-A232V-H249R	++
N018R-S024R-N076D-N116A-T213A-H249R	++
G020R-R045T-N076D-S101G-S103A-V104I-A232V-Q245R	++
G020R-S078R-S101A-S103A-V104I-N116A-N183D-G211Q-T213A-A215F-A232V-Q245R	++
S024R-N043R-R045T-N076D-S078R-S101G-S103A-V104I-A232V-Q245R	++
N018R-S024R-N076D-S101A-N116A-I198L-T213A-A215F-H249R	++
N043R-R045T-S101G-S103A-V104I-A232V-Q245R	++
N018R-T022W-S024R-N076D-S101A-I198L-G211Q-Q245R	++
G020R-S024R-N043D-N076D-S078R-S101G-S103A-V104I-A232V-Q245R-N269R	++
S024R-A232V	++
G020R-S078R-S101A-S103A-V104I-N116A-N183D-G211Q-A232V-Q245R	++
S024R-N076D-S101G-A232V-Q245R	++
N018R-N076D-S101G-S103A-V104I-H249R	++
N018R-S024R-N076D-I198M-G211Q-T213A-A215F-H249R	++
N018R-T22W-S024R-N076D-S101A-I198L-A215F-H249R	++
N018R-N043R-N076D-S101G-S103A-V104I-A232V-Q245R-N269R	++
G020R-T022W-S103A-G211Q-T213A-A215F-A232V-Q245R	++
G020R-S078R-S101A-S103A-V104I-N116A-N183D-G211Q-T213A-A232V-Q245R	++
R045T-N076D-S101G-S103A-V104I-A232V-Q245R-N269R	++
N018R-T22W-S024R-N076D-S101A-G211Q-T213A-H249R	++
N018R-S024R-N076D-N116A-I198L-A215F-H249R-V268G	++
N018R-T022W-S024R-N076D-S101A-G211Q-H249R	++
N018R-T022W-S024R-N076D-S101A-N116A-I198L-G211Q-H249R	++
S101G-S103A-V104I-Q245R	++
N018R-N076D-S101G-A232V-Q245R	++
N018R-G020R-R045T-S101G-S103A-V104I-A232V-Q245R	++
N018R-T022W-S024R-N076D-S101A-N116A-I198L-H249R	++
N018R-T022W-S024R-N076D-N116A-I198L-T213A-H249R	++
S078R-S101G-S103A-V104I-A232V-Q245R-H249R	++
N018R-S078R-S101G-S103A-V104I-L217E-A232V-Q245R	++

[0877]

表 11-2：WCE10 至 WCE14 文库变体的 BMI 清洁性能。
PI=性能指数
在洗涤剂 36k 或 36l 中，PI>或=1.5 为+++；PI 介于 1.49 和 1.3 之间=++；PI 介于 1.29 和 1.0 之间=+

GG36 变体的序列（BPN'编号方式）	相对于 GG36 的 PI；BMI 测定法，洗涤剂 36k 或 36l，16℃
G020R-N043R-N076D-S101G-S103A-V104I-A232V-Q245R-N269R	++
N018R-N043D-N076D-S101G-S103A-V104I-A232V-Q245R-H249R	++
R045T-S101G-S103A-V104I-A232V-Q245R-N269R	++
S024R-S103A-A232V	++
N018R-S024R-N076D-S101A-G211Q-H249R	++
N043D-S101G-S103A-V104I-A232V-Q245R-H249R	++
N018R-N043R-R045T-N076D-S076T-S101G-S103A-V104I-A232V-Q245R-A273T	++
N018R-G020R-N043D-S078R-S101G-S103A-V104I-A232V-Q245R	++
G020R-S078R-S101A-S103A-V104I-N183D-A215F-A232V-Q245R	++
N018R-S024R-N076D-S101G-A232V	++
A232V-Q245R	++
N043R-R045T-N076D-S078R-S101G-S103A-V104I-A232V-V234I-Q245R	++
S024R-N076D-S103A-V104I-Q245R	++
G020R-S078R-S101A-S103A-V104I-G211Q-T213A-A232V-Q245R	++
N043D-S078R-S101G-S103A-V104I-A232V-Q245R-N269R-A272V	++
N018R-G020R-S024R-N076D-N116A-N183D-I198L-G211Q-H249R	++
N018R-S103A-V104I-A232V	++
G020R-T022W-S101G-S103A-V104I-N116A-N183D-T213A-A215F-A232V-Q245R	++
S024R-N043R-N076D-S101G-S103A-V104I-A232V-Q245R-N269R	++
N018R-T022W-S024R-N076D-T213A-A215F-H249R	++
N018R-S024R-N076D-S101A-N116A-I198L-G211Q-T213A-H249R	++
G020R-T22W-S078R-S101A-S103A-V104I-N116A-N183D-T213A-A232V-Q245R	++
G020R-T022W-S078R-S101G-S103A-V104I-G211Q-T213A-A232V-Q245R	++
G020R-T022W-S101A-S103A-V104I-A215F-A232V-Q245R	++
N018R-G020R-S024R-N076D-N116A-N183D-A215F-H249R	++
N018R-S024R-N076D-N116A-M117I-N183D-T213A-H249R	++
N018R-T022W-S024R-N076D-S101A-N116A-I198L-T213A-H249R	++
N018R-T22W-S024R-N076D-S101A-I198L-T213A-A215F-H249R	++
N018R-N043D-S078R-S101G-S103A-V104I-A232V-Q245R-H249R	++

[0878]

表 11-2：WCE10 至 WCE14 文库变体的 BMI 清洁性能。
PI=性能指数
在洗涤剂 36k 或 36l 中，PI>或=1.5 为+++；PI 介于 1.49 和 1.3 之间=++；PI 介于 1.29 和 1.0 之间=+

GG36 变体的序列（BPN'编号方式）	相对于 GG36 的 PI；BMI 测定法，洗涤剂 36k 或 36l，16℃
N018R-N076D-S101G-S103A-V104I-A232V-Q245R-H249R	++
G020R-T022W-S101G-S103A-V104I-N116A-N183D-I198L-A232V-Q245R	++
N018R-N043R-R045T-N076D-S101G-S103A-V104I-A232V-Q245R-N269R	++
N018R-S024R-N076D-N116A-I198L-Y209H-T213A-H249R	++
G020R-T022W-S101A-S103A-V104I-N116A-N183D-G211Q-T213A-A232V-Q245R	++
S024R-N076D-S101G-M175L-A232V-Q245R	++
N018R-N043D-R045T-S101G-S103A-V104I-A232V-Q245R	++
R045T-N076D-S078R-S101G-S103A-V104I-A232V-Q245R	++
G020R-S078R-S101A-S103A-V104I-N116A-N183D-I198L-A215F-A232V-Q245R	++
N043R-N076D-S101G-S103A-V104I-A232V-Q245R-H249R	++
N018R-S024R-N076D-I198L-T213A-A215F-H249R	++
N018R-T022W-S024R-N076D-I198L-A215F-H249R	++
N018R-T022W-S024R-N076D-N116A-T213A-A215F-H249R	++
N018R-T022W-S024R-N076D-S101A-N116A-I198L-T213A-A215F-H249R	++
N018R-T022W-S024R-N076D-N116A-G211Q-T213A-H249R	++
N018R-S024R-Q245R	++
N018R-T022W-S024R-N076D-S101A-N116A-A215F-H249R	++
S024R-N076D-V104I-Q245R	++
K027R-N043R-S101G-S103A-V104I-A232V-Q245R-N269R	++
N018R-S024R-N076D-N116A-I198L-G211Q-T213A-H249R	++
N018R-S024R-N076D-N116A-I198L-H249R	++
N018R-S024R-N076D-N183D-I198L-G211Q-T213A-A215F-H249R	++
G020R-T022W-S101A-S103A-V104I-N116A-G211Q-T213A-A215F-A232V-Q245R	++
N018R-N043D-R045T-S078R-S101G-S103A-V104I-A232V-Q245R	++
N043R-R045T-N076D-S078R-S101G-S103A-V104I-A232V-Q245R-N269R	++
N018R-T22W-S024R-N076D-N116A-T213A-A215F-H249R	++
N018R-T022W-S024R-N076D-N116A-G211Q-A215F-H249R	++
G020R-S078R-S101G-S103A-V104I-N116A-N183D-T213A-A232V-Q245R	++
N018R-N076D-S101G-S103A-V104I-A232V-Q245R	++

[0879]

表 11-2：WCE10 至 WCE14 文库变体的 BMI 清洁性能。
PI=性能指数
在洗涤剂 36k 或 36l 中，PI>或=1.5 为+++；PI 介于 1.49 和 1.3 之间=++；PI 介于 1.29 和 1.0 之间=+

GG36 变体的序列（BPN'编号方式）	相对于 GG36 的 PI; BMI 测定法，洗涤剂 36k 或 36l，16℃
N018R-S101G-V104I	++
G020R-S078R-S101G-S103A-V104I-N116A-N183D-G211Q-T213A-A215F-A232V-Q245R	++
G020R-S078R-S101A-S103A-V104I-A232V-Q245R	++
N018R-S024R-N076D-S101A-I198L-G211Q-H249R	++
N018R-S024R-N076D-I198L-G211Q-T213A-H249R	++
N018R-T022W-S024R-N076D-S101A-N116A-I198L-G211Q-T213A-H249R	++
N018R-N076D-H249R	++
N018R-G020R-S024R-N076D-S101A-N116A-N183D-I198L-H249R	++
N018R-S024R-N076D-S101A-N116A-G211Q-T213A-H249R	++
G020R-T022W-S078R-S101A-S103A-V104I-N116A-N183D-G211Q-T213A-A215F-A232V-Q245R	++
G020R-T022W-S101G-S103A-V104I-A114T-T213A-A215F-A232V-Q245R	++
N018R-T22W-S024R-N076D-N116A-G211Q-T213A-H249R	++
N018R-G020R-T022W-S024R-N076D-S101A-N116A-N183D-H249R	++
G020R-S101A-S103A-V104I-N116A-N183D-T213A-A232V-Q245R	++
N018R-T022W-S024R-N076D-S101A-G211Q-T213A-H249R	++
N018R-T022K-N043D-S101G-S103A-V104I-A232V-Q245R	++
N018R-S101G-S103A-V104I-A232V-Q245R-N269R	++
G020R-S078R-S101G-S103A-V104I-N116A-N183D-G211Q-T213A-A215F-A232V	++
N018R-S024R-N076D-N116A-H249R	++
G020R-S024R-N076D-S101G-S103A-V104I-A232V-Q245R	++
N043D-N076D-S101G-S103A-V104I-A232V-Q245R-N269R	++
N018R-S024R-N076D-S101A-N116A-I198L-G211Q-H249R	++
N018R-T022W-S024R-N076D-I198L-T213A-A215F-H249R	++
N018R-N043D-N076D-S078R-S101G-S103A-V104I-A232V-Q245R-N269R	++
G020R-T22W-S101G-S103A-V104I-N116A-N183D-T213A-A215F-A232V-Q245R	++
G020R-S101G-S103A-V104I-N183D-G211Q-A232V-Q245R-	++
N018R-S024R-N076D-S101A-I198L-T213A-H249R	++
N018R-S024R-N076D-S101A-I198L-H249R	++

[0880]

表 11-2：WCE10 至 WCE14 文库变体的 BMI 清洁性能。
PI=性能指数
在洗涤剂 36k 或 36l 中，PI>或=1.5 为+++；PI 介于 1.49 和 1.3 之间=++；PI 介于 1.29 和 1.0 之间=+

GG36 变体的序列（BPN'编号方式）	相对于 GG36 的 PI; BMI 测定法，洗涤剂 36k 或 36l，16℃
N018R-S024R-R045T-N076D-S101G-S103A-V104I-A232V-Q245R-H249R	++
N018R-S024R-N076D-S101A-N183D-T213A-H249R	++
N018R-N043D-N076D-S078R-S101G-S103A-V104I-A232V-Q245R	++
G020R-S078R-S101G-S103A-V104I-N116A-A131V-N183D-T213A-A232V-Q245R	++
N018R-R045T-N076D-S101G-S103A-V104I-A232V-Q245R	++
N018R-S024R-N076D-S101A-N183D-G211Q-H249R	++
N076D-S101G-S103A-V104I-A232V-Q245R-H249R	++
S024R-S101G-Q245R	++
S024R-N076D-S101G-Q245R	++
N076D-S078R-S101G-S103A-V104I-A232V-Q245R-H249R	++
N018R-G020R-S024R-N076D-S101A-N183D-G211Q-A215F-H249R	++
S024R-S101G	++
N018R-T22W-S024R-N076D-T213A-A215F-H249R	++
G020R-N043D-S101G-S103A-V104I-A232V-Q245R	++
G020R-T022W-S101G-S103A-V104I-N183D-I198L-T213A-A215F-A232V-Q245R	++
N018R-N043D-R045T-S101G-S103A-V104I-A232V-Q245R-N269R	++
N043D-N076D-S078R-S101G-S103A-V104I-A232V-Q245R	++
S024R-R045T-N076D-S101G-S103A-V104I-A232V-Q245R-N269R	++
G020R-T022W-S101A-S103A-V104I-I198L-G211Q-A215F-A232V-Q245R	++
G020R-T022W-S101G-S103A-V104I-N116A-N183D-A215F-A232V-Q245R	++
N018R-G020R-N076D-S101G-S103A-V104I-A232V-Q245R-H249R	++
N018R-T022W-S024R-N076D-S101A-A215F-H249R	++
N018R-V104I	++
N018R-S024R-N076D-N116A-I198L-A215F-H249R	++
N018R-S024R-N076D-L088I-S101A-N116A-I198L-G211Q-A215F-H249R	++
N018R-T022W-S024R-N076D-S101A-N116A-G211Q-T213A-H249R	++
N043R-R045T-N076D-S101G-S103A-V104I-A232V-Q245R-N269R	++
N018R-N076D-S101G-V104I-H249R	++

[0881]

表 11-2：WCE10 至 WCE14 文库变体的 BMI 清洁性能。
PI=性能指数
在洗涤剂 36k 或 36l 中，PI>或=1.5 为+++；PI 介于 1.49 和 1.3 之间=++；PI 介于 1.29 和 1.0 之间=+

GG36 变体的序列（BPN'编号方式）	相对于 GG36 的 PI；BMI 测定法，洗涤剂 36k 或 36l，16℃
N018R-T022W-S024R-N076D-S101A-T213A-A215F-H249R	++
N018R-T22W-S024R-N076D-S101A-N116A-I198L-A215F-H249R	++
N018R-G020R-S101G-S103A-V104I-A232V-Q245R-H249R	++
S101G-S103A-V104I-A232V-Q245R-H249R-N269R	++
S024R-N076D-Q245R	++
N018R-G020R-N043R-R045T-N076D-S101G-S103A-V104I-A232V-Q245R	++
N018R-G020R-S024R-N076D-A215F-H249R	++
N018R-S024R-N076D-S101A-N116A-N183D-I198L-T213A-H249R	++
N018R-G020R-S024R-N076D-G211Q-A215F-H249R	++
N043D-S101G-S103A-V104I-A232V-Q245R	++
G020R-T22W-S078R-S101A-S103A-V104I-N116A-N183D-A215F-A232V-Q245R	++
N018R-S024R-N076D-I198L-G211Q-A215F-H249R	++
N043R-N076D-S078R-S101G-S103A-V104I-A232V-Q245R-N269R	++
N043R-S078R-S101G-S103A-V104I-A232V-Q245R-N269R	++
G020R-N043D-S101G-S103A-V104I-A232V-Q245R-H249R	++
N018R-T022W-S024R-N076D-S101A-T213A-H249R	++
G020R-T022W-S101A-N116A-I198L-G211Q-T213A-A215F-H249R	++
N043R-R045T-S078R-S101G-S103A-V104I-N218S-A232V-Q245R	++
N018R-S103A	++
G020R-T22W-S101G-S103A-V104I-N116A-N183D-A215F-A232V-Q245R	++
N018R-S024R-N076D-S101A-H249R	++
N018R-T022W-S024R-N076D-G211Q-T213A-H249R	++
S024R-N043R-R045T-N076D-S101G-S103A-V104I-A232V-Q245R	++
G020R-T022W-S101A-S103A-V104I-N116A-N183D-A232V-Q245R	++
G020R-S101A-S103A-V104I-N116A-N183D-G211Q-T213A-A215F-A232V-Q245R	++
K027R-R045T-N076D-S078R-S101G-S103A-V104I-A232V-Q245R-N269R	++
G020R-R045T-N076D-S101G-S103A-V104I-A232V-Q245R-H249R	++
N018R-G020R-S024R-N076D-N116A-N183D-T213A-A215F-H249R	++
N018R-S024R-N076D-V104I	++

[0882]

表 11-2：WCE10 至 WCE14 文库变体的 BMI 清洁性能。
PI=性能指数
在洗涤剂 36k 或 36l 中，PI>或=1.5 为+++；PI 介于 1.49 和 1.3 之间=++；PI 介于 1.29 和 1.0 之间=+

GG36 变体的序列（BPN'编号方式）	相对于 GG36 的 PI; BMI 测定法，洗涤剂 36k 或 36l，16℃
S101G-S103A-V104I-A232V-H249R	++
N018R-S024R-N076D-N116A-N183D-G211Q-H249R	++
N018R-G020R-S024R-N076D-N116A-A215F-H249R	++
N018R-S024R-N076D-N183D-T213A-A215F-H249R	++
N018R-T022W-S024R-N076D-I198L-G211Q-H249R	++
N043D-S078R-S101G-S103A-V104I-A232V-Q245R-N269R-R275S	++
G020R-T022W-S101A-S103A-V104I-N116A-N183D-G211Q-A232V-Q245R	++
N018R-T022W-S024R-N076D-S101A-I198L-G211Q-T213A-A215F-H249R	++
N018R-T022W-S024R-N076D-S101A-N116A-I198L-G211Q-T213A-A215F-H249R	++
N018R-G020R-S024R-N076D-N183D-H249R	++
N018R-S024R-N076D-N116A-I198L-T213A-H249R	++
N018R-T022W-S024R-N076D-S101A-N116A-G211Q-H249R	++
V004M-N018R-S024R-N076D-N116A-I198L-G211Q-T213A-H249R	++
V104I-A232V-H249R	++
G020R-T022W-S101G-S103A-V104I-N116A-N183D-G211Q-A215F-A232V-Q245R	++
G020R-S101A-S103A-V104I-N116A-N183D-G211Q-A232V-Q245R-T274I	+
G020R-S101A-S103A-V104I-T213A-A232V-Q245R	+
G020R-S101G-S103A-V104I-N116A-N183D-G211Q-T213A-A232V-Q245R	+
G020R-S024R-N043D-S078R-S101G-S103A-V104I-A232V-Q245R	+
N018R-S024R-N076D-S103A-H249R	+
N018R-G020R-S024R-N076D-S101A-N116A-N183D-G211Q-A215F-H249R	+
N018R-G020R-S024R-N076D-N116A-N183D-I198L-H249R	+
N018R-T022W-S024R-N076D-N116A-I198L-A215F-H249R	+
N018R-S024R-N076D-S101A-G211Q-T213A-A215F-H249R-A270V	+
N018R-N043D-R045T-N076D-S078R-S101G-S103A-V104I-A232V-Q245R-N269R	+
G020R-T022W-S101G-S103A-V104I-N183D-A232V-Q245R	+

[0883]

表 11-2：WCE10 至 WCE14 文库变体的 BMI 清洁性能。
PI=性能指数
在洗涤剂 36k 或 36l 中，PI>或=1.5 为+++；PI 介于 1.49 和 1.3 之间=++；PI 介于 1.29 和 1.0 之间=+

GG36 变体的序列（BPN'编号方式）	相对于 GG36 的 PI; BMI 测定法，洗涤剂 36k 或 36l，16℃
N018R-G020R-T022W-S024R-N076D-S101A-N116A-T213A-H249R	+
N018R-T022W-S024R-N076D-I198L-G211Q-A215F-H249R	+
N018R-T022W-S024R-N076D-I198L-T213A-H249R	+
G020R-T022W-S101G-S103A-V104I-N116A-N183D-A232V-Q245R	+
N018R-T22W-S024R-N076D-N116A-I198L-T213A-H249R	+
N043R-R045T-S078R-S101G-S103A-V104I-A232V-Q245R-N269R	+
N018R-S024R-N076D-S101G-S103A-V104I-A232V	+
S101G-H249R	+
S024R-N076D-S101G-S103A-V104I-M175L-H249R	+
G020R-T022W-S101A-S103A-V104I-N116A-N183D-A232V-Q245R-N269S	+
N018R-S024R-N076D-S101A-N116A-I198L-H249R	+
N018R-T022W-S024R-N076D-N116A-H249R	+
N018R-G020R-S024R-N076D-S101A-N183D-I198L-A215F-H249R	+
N018R-S024R-N076D-T213A-A215F-H249R-T260K	+
N018R-S024R-N076D-N116A-G211Q-T213A-H249R	+
N018R-G020R-T022W-S024R-N076D-N116A-I198L-H249R	+
S024R-N076D-S101G-S103A-V104I-Q245R	+
S024R-N076D-S103A-H249R	+
N018R-S101G-S103A-V104I-A232V-Q245R-H249R	+
N018R-S024R-N076D-I198L-G211Q-H249R	+
N018R-T022W-S024R-N076D-S101A-I198L-G211Q-T213A-H249R	+
G020R-S024R-R045T-S101G-S103A-V104I-A232V-Q245R	+
N018R-G020R-S024R-N076D-N183D-G211Q-T213A-H249R	+
N018R-N043D-R045T-S078R-S101G-S103A-V104I-A232V-Q245R-A272D	+
N018R-S024R-N076D-N116A-I198L-T213A-A215F-H249R	+
N018R-T22W-S024R-N076D-S101A-I198L-H249R	+
N018R-T022W-S024R-N076D-N116A-I198L-H249R	+
S024R-N076D-S101G-S103A-A232V	+
S024R-S103A-V104I	+
N018R-S024R-N076D-S101A-N116A-N183D-G211Q-A215F-H249R	+
S024R-R045T-N076D-S101G-S103A-V104I-A232V-Q245R-H249R	+

[0884]

表 11-2：WCE10 至 WCE14 文库变体的 BMI 清洁性能。
PI=性能指数
在洗涤剂 36k 或 36l 中，PI>或=1.5 为+++；PI 介于 1.49 和 1.3 之间=++；PI 介于 1.29 和 1.0 之间=+

GG36 变体的序列（BPN'编号方式）	相对于 GG36 的 PI; BMI 测定法，洗涤剂 36k 或 36l，16℃
G020R-S101G-S103A-V104I-N116A-N183D-A232V-Q245R	+
S024R-N043D-N076D-S101G-S103A-V104I-A232V-Q245R-N269R	+
G020R-T022W-S101A-S103A-V104I-N183D-G211Q-T213A-A215F-A232V-Q245R	+
G020R-R045T-N076D-S078R-S101G-S103A-V104I-A232V-Q245R-N269R	+
N018R-S024R-N076D-S101A-N116A-I198L-G211Q-A215F-H249R	+
G020R-S101A-S103A-V104I-N116A-N183D-A215F-A232V-Q245R	+
N018R-N043R-S101G-S103A-V104I-A232V-Q245R-H249R	+
N018R-S024R-N076D-I198L-T213A-H249R	+
N018R-S024R-N076D-N116A-N183D-T213A-H249R	+
G020R-N043D-S101G-S103A-V104I-A232V-Q245R-N269R	+
S024R-N076D-S103A-Q245R	+
N018R-T022W-S024R-N076D-S101A-N116A-G211Q-T213A-A215F-H249R	+
S103A-V104I-Q245R	+
N018R-T022W-S024R-N076D-G211Q-A215F-H249R	+
N018R-T022W-S024R-N076D-N116A-N183D-I198L-H249R	+
N018R-T022W-S024R-N076D-I198L-G211Q-T213A-H249R	+
N018R-S024R-N076D-N116A-N183D-G211Q-T213A-A215F-H249R	+
N018R-G020R-N043D-R045T-N076D-S101G-S103A-V104I-A232V-Q245R-N269R	+
N018R-G020R-T022W-S024R-N076D-S101A-G211Q-T213A-A215F-H249R	+
A016T-N043R-R045T-N076D-S101G-S103A-V104I-A232V-Q245R-N269R	+
N018R-T022W-S024R-N076D-N116A-A215F-H249R	+
N043R-N076D-S101G-S103T-V104I-A232V-Q245R-H249R-N269R	+
G020R-S078R-S101A-S103A-V104I-G115E-N116A-N183D-G211Q-T213A-A232V-Q245R	+
N018R-S024R-N076D-I198L-H249R	+
N018R-S024R-N076D-S101A-N116A-N183D-H249R	+
G020R-S101G-S103A-V104I-N116A-N183D-G211Q-A232V-Q245R	+
N018R-S024R-N076D-S101G	+
N076D-S101G-A232V-Q245R	+

表 11-2：WCE10 至 WCE14 文库变体的 BMI 清洁性能。
PI=性能指数
在洗涤剂 36k 或 36l 中，PI>或=1.5 为+++；PI 介于 1.49 和 1.3 之间=++；PI 介于 1.29 和 1.0 之间=+

[0885]

GG36 变体的序列（BPN'编号方式）	相对于 GG36 的 PI；BMI 测定法，洗涤剂 36k 或 36l，16℃
N018R-N076D-S101G-S103A-V104I-Q245R	+
N018R-R045T-S101G-S103A-V104I-A232V-Q245R-H249R	+
N018R-S024R-N076D-A215F-H249R	+
N018R-V104I-A232V	+
N043D-R045T-N076D-S078R-S101G-S103A-V104I-A232V-Q245R	+
S024R-N076D-S101G-A232V-H249R	+
S103A-A232V-Q245R	+
G020R-S101G-S103A-V104I-N116A-N183D-G211Q-T213A-A215F-A232V-Q245R	+
N018R-G020R-S024R-N076D-N116A-N183D-I198L-G211Q-A215F-H249R	+
N018R-T022W-S024R-N076D-S101A-I198L-G211Q-A215F-H249R	+
S024R-N076D-S103A-V104I-H249R	+
S024R-S101G-S103A-V104I	+
G020R-S101G-S103A-V104I-N116A-N183D-G211Q-A215F-A232V-Q245R	+
N018R-T022W-S024R-N076D-S101A-N116A-N183D-A215F-H249R	+
G020R-T022W-S101G-S103A-V104I-N116A-N183D-G211Q-T213A-A215F-A232V-Q245R	+
G020R-S024R-R045T-N076D-S101G-S103A-V104I-A232V-Q245R	+
N018R-T022W-S024R-N076D-N116A-N183D-T213A-H249R	+
N018R-G020R-S024R-N076D-A131T-A215F-H249R	+
N018R-S024R-N076D-S101A-N116A-N183D-G211Q-T213A-A215F-H249R	+
N018R-S024R-N076D-S101A-N116A-G211Q-T213A-A215F-H249R	+
N018R-S024R-N076D-I198L-A215F-H249R	+
N018R-T022W-S024R-N076D-N183D-G211Q-H249R	+
N018R-T022W-S024R-N076D-S101A-N116A-T213A-A215F-H249R	+
N018R-G020R-S024R-R045T-N076D-S101G-S103A-V104I-A232V-Q245R	+
N043R-S101G-S103A-V104I-Q245R-H249R	+
N018R-N076D-A232V-H249R	+
N018K-N076D-S078R-S101G-S103A-V104I-L217E-A232V-Q245R-N269R	+

[0886]

表 11-2：WCE10 至 WCE14 文库变体的 BMI 清洁性能。
PI=性能指数
在洗涤剂 36k 或 36l 中，PI>或=1.5 为+++；PI 介于 1.49 和 1.3 之间=++；PI 介于 1.29 和 1.0 之间=+

GG36 变体的序列（BPN'编号方式）	相对于 GG36 的 PI；BMI 测定法，洗涤剂 36k 或 36l，16℃
N018R-G020R-S024R-N043D-N076D-S078R-S101G-S103A-V104I-A232V-Q245R	+
N018R-T022W-S024R-N076D-S101A-N116A-T213A-A215F-H249R-L267I	+
A232V-H249R	+
N018R-G020R-S024R-N076D-N116A-G211Q-T213A-A215F-H249R	+
N076D-V104I-Q245R	+
N018R-G020R-S024R-N076D-N183D-I198L-G211Q-A215F-H249R	+
N018R-S024R-N076D-S101A-G211Q-T213A-H249R	+
S024R-S101G-S103A-A232V	+
N018R-G020R-T022W-S024R-N076D-N116A-N183D-I198L-T213A-A215F-H249R	+
N018R-G020R-S024R-N076D-N116A-N183D-I198L-G211Q-T213A-H249R	+
N018R-G020R-T022W-S024R-N076D-S101A-A215F-H249R	+
G020R-T022W-S101A-S103A-V104I-N116A-N183D-G211Q-A215F-A232V-Q245R	+
N018R-S024R-N076D-N116A-I198L-G211Q-H249R	+
S103A-A232V-H249R	+
N018R-G020R-S024R-N076D-N116A-N183D-I198L-A215F-H249R	+
N018R-S024R-N076D-N116A-N183D-I198L-T213A-H249R	+
N018R-T022W-S024R-N076D-N183D-T213A-H249R	+
N018R-S024R-N076D-S101A-T213A-A215F-H249R	+
N018R-T022W-S024R-N076D-S101A-N116A-N183D-G211Q-H249R	+
N018R-R045T-S101G-S103A-V104I-A232V-Q245R-N269R	+
N018R-G020R-R045T-N076D-S078R-S101G-S103A-V104I-A232V-Q245R	+
N018R-T022W-S024R-N076D-N116A-I198L-T213A-A215F-H249R	+
G020R-T022W-S101G-S103A-V104I-N116A-N183D-G211Q-T213A-A232V-Q245R	+
N018R-G020R-S024R-N076D-I198L-H249R	+
N018R-G020R-T022W-S024R-N076D-S101A-N116A-G211Q-H249R	+
G020R-T022W-S101A-S103A-V104I-N116A-N183D-A232V-Q245R-T274I	+

[0887]

表 11-2：WCE10 至 WCE14 文库变体的 BMI 清洁性能。
PI=性能指数
在洗涤剂 36k 或 36l 中，PI>或=1.5 为+++；PI 介于 1.49 和 1.3 之间=++；PI 介于 1.29 和 1.0 之间=+

GG36 变体的序列（BPN'编号方式）	相对于 GG36 的 PI; BMI 测定法，洗涤剂 36k 或 36l，16℃
S024R-S103A-Q245R-H249R	+
N018R-T022W-S024R-N076D-S101A-N116A-N183D-I198L-H249R	+
N018R-S024R-N076D-S101A-I198L-G211Q-A215F-H249R	+
N018R-T022W-S024R-N076D-N116A-I198L-G211Q-A215F-H249R	+
N018R-G020R-T022W-S024R-N076D-N116A-N183D-T213A-H249R	+
N018R-N043D-R045T-N076D-S101G-S103A-V104I-A232V-Q245R-N269R	+
N018R-T022W-S024R-N076D-N116A-G211Q-T213A-A215F-H249R	+
N018R-S024R-N076D-S101A-N183D-I198L-T213A-H249R	+
N043D-N076D-S101G-S103A-V104I-A232V-Q245R-H249R	+
N018R-S024R-N076D-I198L-G211Q-T213A-A215F-H249R	+
N018R-G020R-S024R-N076D-N116A-N183D-T213A-H249R	+
S103A-A232V	+
N018R-T022W-S024R-N076D-N116A-N183D-A215F-H249R	+
N018R-S024R-N076D-S101A-N116A-H249R	+
N018R-N043R-S078R-S101G-S103A-V104I-A232V-Q245R	+
N018R-G020R-T022W-S024R-N076D-S101A-N183D-G211Q-A215F-H249R	+
N043R-N076D-S078R-S101G-S103A-V104I-A232V-Q245R-H249R	+
N018R-G020R-S024R-N076D-S101A-N116A-N183D-I198L-T213A-H249R	+
N018R-S024R-N076D-N183D-I198L-T213A-H249R	+
N018R-T022W-S024R-N076D-S101A-N183D-G211Q-H249R	+
N018R-G020R-S024R-N076D-I198L-T213A-A215F-H249R	+
N018R-G020R-T022W-S024R-N076D-N183D-G211Q-T213A-H249R	+
N018R-T022W-S024R-N076D-I198L-H249R	+
N018R-S024R-N076D-N183D-I198L-G211Q-H249R	+
G020R-T022W-S101A-S103A-V104I-N116A-N183D-T213A-A232V-Q245R	+
N018R-G020R-S024R-N076D-N116A-N183D-G211Q-T213A-H249R	+

[0888]

表 11-2：WCE10 至 WCE14 文库变体的 BMI 清洁性能。
PI=性能指数
在洗涤剂 36k 或 36l 中，PI>或=1.5 为+++；PI 介于 1.49 和 1.3 之间=++；PI 介于 1.29 和 1.0 之间=+

GG36 变体的序列（BPN'编号方式）	相对于 GG36 的 PI; BMI 测定法，洗涤剂 36k 或 36l，16℃
N018R-S024R-N076D-N116A-N183D-I198L-G211Q-T213A-A215F-H249R	+
G020R-T022W-S101A-S103A-V104I-N116A-N183D-A215F-A232V-Q245R	+
N018R-S024R-N076D-S101A-N183D-H249R	+
N018R-S024R-N076D-A232V	+
N018R-T022W-S024R-N076D-S101A-N116A-H249R	+
G020R-S101A-S103A-V104I-N116A-N183D-I198L-G211Q-T213A-A215F-A232V-Q245R	+
G020R-T022W-S101G-S103A-V104I-N116A-N183D-G211Q-A232V-Q245R-N263S	+
S024R-N076D-S101G-V104I-A232V-H249R	+
N043R-S078R-S101G-S103A-V104I-A232V-Q245R	+
S024R-N076D-S078R-S101G-S103A-V104I-A232V-Q245R-H249R	+
N018R-S024R-N076D-S101A-N183D-I198L-T213A-A215F-H249R	+
N018R-G020R-S024R-N076D-I198L-A215F-H249R	+
N018R-G020R-S024R-N076D-S101A-N116A-T213A-H249R	+
N018R-S024R-N076D-S101A-V197A-T213A-A215F-H249R	+
S024R-S101G-S103A	+
N018R-S024R-N076D-S101A-N116A-G211Q-A215F-H249R	+
N043R-N076D-S078R-S101G-S103A-V104I-L217E-A232V-Q245R	+
S024R-V104I-A232V	+
N018R-S024R-N076D-N183D-G211Q-H249R	+
G020R-N043R-R045T-S078R-S101G-S103A-V104I-A232V-Q245R	+
N018R-G020R-T022W-S024R-N076D-S101A-N116A-N183D-T213A-H249R	+
N018R-S024R-N076D-N116A-A150T-T213A-H249R	+
N018R-S024R-N076D-N183D-T213A-H249R	+
N018R-G020R-S024R-N076D-N116A-N183D-G211Q-A215F-H249R	+
N018R-G020R-S024R-N076D-G211Q-H249R	+
N018R-S024R-N076D-S101A-N116A-N183D-I198L-H249R	+
S024R-N076D-A232V-H249R	+
N018R-G020R-T022W-S024R-N076D-S101A-N116A-N183D-I198L-G211Q-T213A-H249R	+
N018R-T022W-S024R-N076D-S101A-N116T-I198L-A215F-H249R	+
N018R-S024R-N076D-N183D-I198L-G211Q-A215F-H249R	+

[0889]

表 11-2：WCE10 至 WCE14 文库变体的 BMI 清洁性能。
PI=性能指数
在洗涤剂 36k 或 36l 中，PI>或=1.5 为+++；PI 介于 1.49 和 1.3 之间=++；PI 介于 1.29 和 1.0 之间=+

GG36 变体的序列（BPN'编号方式）	相对于 GG36 的 PI; BMI 测定法，洗涤剂 36k 或 36l，16℃
N018R-T022R-S024R-N076D-S101A-N116A-N183D-G211Q-H249R	+
R045T-S101G-S103A-V104I-A232V-Q245R	+
N018R-G020R-S024R-N076D-S101A-N183D-G211Q-H249R	+
G020R-S101G-S103A-V104I-N116A-N183D-T213A-A232V-Q245R	+
N076D-S101G-S103A-Q245R	+
G020R-N043D-S078R-S101G-S103A-V104I-A232V-Q245R-H249R	+
N018R-S024R-N076D-N116A-N183D-H249R	+
N018R-S024R-N076D-S101A-N183D-G211Q-T213A-A215F-H249R	+
N018R-G020R-T022W-S024R-N076D-S101A-N116A-I198L-H249R	+
N018R-T22W-S024R-N076D-G211Q-T213A-H249R	+
N018R-G020R-S024R-N076D-N183D-G211Q-H249R	+
N018R-G020R-S024R-N076D-S101A-N116A-N183D-T213A-H249R	+
N043R-S078R-S101G-S103A-V104I-L217E-A232V-Q245R	+
N018R-T022W-S024R-N076D-S101A-A215F-H249R	+
N018R-G020R-S024R-N076D-S101A-N183D-I198L-G211Q-T213A-H249R	+
N076D-S101G-V104I-H249R	+
N018R-T022W-S024R-N076D-S101A-N116A-N183D-T213A-H249R	+
N018R-S024R-N076D-N183D-H249R	+
N018R-S024R-N076D-S101A-N183D-I198L-A215F-H249R	+
N018R-T022W-S024R-N076D-N183D-I198L-A215F-H249R	+
N018R-T022W-S024R-N076D-S101A-I198L-G211Q-H249R	+
G020R-S101A-S103A-V104I-N116A-N183D-A232V-Q245R	+
N018R-S024R-N076D-N116A-N183D-I198L-G211Q-H249R	+
N018R-G020R-S024R-S101G-S103A-V104I-A232V-Q245R	+
N018R-N076D-S078R-S101G-S103A-V104I-L217E-A232V-Q245R	+
G020R-S101A-S103A-V104I-N116A-N183D-G211Q-A232V-Q245R	+
N018R-T022W-S024R-N076D-S101A-N183D-I198L-Y209H-H249R	+
N018R-S024R-N076D-N183D-I198L-T213A-A215F-H249R	+

[0890]

表 11-2：WCE10 至 WCE14 文库变体的 BMI 清洁性能。
PI=性能指数
在洗涤剂 36k 或 36l 中，PI>或=1.5 为+++；PI 介于 1.49 和 1.3 之间=++；PI 介于 1.29 和 1.0 之间=+

GG36 变体的序列（BPN'编号方式）	相对于 GG36 的 PI；BMI 测定法，洗涤剂 36k 或 36l，16℃
N018R-S024R-N076D-S101A-N116A-N183D-G211Q-T213A-H249R	+
N018R-T022W-S024R-N076D-S101A-N116A-N183D-G211Q-T213A-H249R	+
N018R-S024R-N076D-N183D-I198L-H249R	+
N018R-S024R-N076D-N183D-A215F-H249R	+
N018R-G020R-S024R-N076D-G211Q-T213A-A215F-H249R	+
N076D-Q245R	+
N076D-S101G-V104I-Q245R	+
N018R-T022W-S024R-N076D-S101A-G211Q-A215F-H249R	+
N018R-T022W-S024R-N076D-S101A-N116A-N183D-G211Q-A215F-H249R	+
N018R-G020R-T022W-S024R-N076D-S101A-G211Q-T213A-H249R	+
G020R-S024R-N043R-S101G-S103A-V104I-A232V-Q245R	+
N018R-S024R-N076D-N116A-N183D-G211Q-A215F-H249R	+
G020R-S101A-S103A-V104I-N116A-N183D-T213A-A215F-A232V-Q245R	+
S101G-S103A-V104I	+
N018R-G020R-S024R-N076D-S101A-N116A-N183D-G211Q-T213A-H249R	+
N018R-G020R-S024R-N076D-N204D-T213A-H249R	+
N018R-T022W-S024R-N076D-N183D-I198L-H249R	+
N018R-S024R-N076D-S101A-N116A-N183D-A215F-H249R	+
N018R-T022W-S024R-N076D-N116A-N183D-I198L-G211Q-T213A-A209V-H249R	+
N018R-T022W-S024R-N076D-S101A-N116A-N183D-G211Q-T213A-A215F-H249R	+
N018R-S024R-N076D-S101A-N116A-I198L-T213A-H249R	+
N018R-G020R-S024R-N076D-S101A-N116A-G211Q-T213A-H249R	+
N018R-G020R-T022W-S024R-N076D-S101A-N116A-N183D-G211Q-T213A-A215F-H249R	+
N018R-S024R-N076D-S101A-N116A-N183D-T213A-A215F-H249R	+
N018R-S024R-N076D-S101A-N183D-I198L-G211Q-T213A-A215F-H249R	+

[0891]

表 11-2：WCE10 至 WCE14 文库变体的 BMI 清洁性能。
PI=性能指数
在洗涤剂 36k 或 36l 中，PI>或=1.5 为+++；PI 介于 1.49 和 1.3 之间=++；PI 介于 1.29 和 1.0 之间=+

GG36 变体的序列（BPN'编号方式）	相对于 GG36 的 PI; BMI 测定法，洗涤剂 36k 或 36l，16℃
N018R-S024R-N076D-S101A-N183D-I198L-G211Q-T213A-H249R	+
N018R-N043R-R045T-S078R-S101G-S103A-V104I-L217E-A232V-Q245R	+
N018R-S024R-N076D-N183D-G211Q-T213A-A215F-H249R	+
N018R-T022W-S024R-N076D-N116A-N183D-I198L-A215F-H249R	+
N018R-G020R-S024R-N076D-N116A-H249R	+
N018R-G020R-T022W-S024R-N076D-S101A-G211Q-A215F-H249R	+
N018R-G020R-S024R-N076D-N183D-G211Q-T213A-A215F-H249R	+
N018R-G020R-T022W-S024R-N076D-I198L-T213A-H249R	+
N018R-G020R-S024R-N076D-S101A-G211Q-A215F-H249R-N269D	+
N018R-G020R-N043D-S101G-S103A-V104I-A232V-Q245R-N269R	+
N018R-T022W-S024R-N076D-S101A-N183D-I198L-T213A-H249R	+
G020R-T022W-S101G-S103A-V104I-N183D-A215F-A232V-Q245R	+
N018R-T022W-S024R-N076D-N116A-N183D-I198L-Y209H-G211Q-H249R	+
N018R-G020R-T022W-S024R-N076D-S101A-N116A-N183D-G211Q-H249R	+
N076D-A232V-Q245R	+
N043D-R045T-S078R-S101G-S103A-V104I-A232V-Q245R	+
N018R-G020R-S024R-N076D-N116A-I198L-G211Q-A215F-Q245R	+
N018R-G020R-T022W-S024R-N076D-T213A-H249R	+
G020R-S024R-N043D-S078R-S101G-S103A-V104I-A232V-Q245R-H249R	+
N018R-G020R-T022W-S024R-N076D-S101A-I198L-A215F-H249R	+
G020R-A090S-S101G-S103A-V104I-N116A-N183D-T213A-A215F-A232V-Q245R	+
N018R-G020R-T022W-S024R-N076D-S101A-I198L-G211Q-T213A-A215F-H249R	+
N018R-G020R-S024R-N076D-S101A-N183D-T213A-A215F-H249R	+

[0892]

表 11-2：WCE10 至 WCE14 文库变体的 BMI 清洁性能。
PI=性能指数
在洗涤剂 36k 或 36l 中，PI>或=1.5 为+++；PI 介于 1.49 和 1.3 之间=++；PI 介于 1.29 和 1.0 之间=+

GG36 变体的序列（BPN'编号方式）	相对于 GG36 的 PI；BMI 测定法，洗涤剂 36k 或 36l，16℃
N018R-S024R-N076D-N116A-N183D-I198L-G211Q-T213A-H249R	+
N043D-R045T-S078R-S101G-S103A-V104I-A232V-Q245R-N269R	+
N018R-S024R-N076D-S101A-N183D-A215F-H249R	+
N018R-G020R-S024R-N076D-S101A-N183D-I198L-T213A-H249R	+
G020R-T022W-S101A-S103A-V104I-N116A-N183D-I198L-G211Q-T213A-A215F-A232V-Q245R	+
N018R-G020R-S024R-N043D-N076D-S101G-S103A-V104I-A232V-Q245R-N269R	+
N018R-S024R-N076D-S101A-N183D-T213A-A215F-H249R	+
N018R-G020R-T022W-S024R-N076D-S101A-N116A-I198L-G211Q-T213A-A215F-H249R	+
N018R-G020R-N043D-S101G-S103A-V104I-L217E-A232V-Q245R	+
N076D-S103A-V104I-A232V-Q245R	+
R045T-N076D-S078R-S101G-S103A-V104I-A232V-Q245R-H249R	+
N018R-T022W-S024R-N076D-S101A-N183D-G211Q-A215F-H249R	+
N018R-T022W-S024R-N076D-S101A-N116A-N183D-H249R	+
N018R-S024R-N076D-N116A-N183D-I198L-G211Q-A215F-H249R	+
N018R-G020R-N043D-N076D-S078R-S101G-S103A-V104I-L217E-A232V-Q245R	+
N076D-S103A-V104I-Q245R	+
N018R-G020R-S024R-N076D-S101A-N116A-G211Q-T213A-A215F-H249R	+
N018R-S024R-N076D-S101A-N183D-I198L-H249R	+
N018R-T022W-S024R-N076D-N116A-N183D-I198L-G211Q-A215F-H249R	+
N018R-S024R-N076D-N116A-N183D-T213A-A215F-H249R	+
N018R-T022W-S024R-N076D-N116A-N183D-I198L-G211Q-H249R	+
N018R-S024R-N076D-S101G-Q245R	+
N018R-S024R-N076D-S101A-N116A-N183D-I198L-T213A-A215F-H249R	+
N043R-R045T-N076D-S101G-S103A-V104I-A232V-Q245R	+
N018R-G020R-T022W-S024R-N076D-N116A-I198L-T213A-A215F-H249R	+
N076D-V104I-A232V-Q245R	+

[0893]

表 11-2：WCE10 至 WCE14 文库变体的 BMI 清洁性能。
PI=性能指数
在洗涤剂 36k 或 36l 中，PI>或=1.5 为+++；PI 介于 1.49 和 1.3 之间=++；PI 介于 1.29 和 1.0 之间=+

GG36 变体的序列（BPN'编号方式）	相对于 GG36 的 PI；BMI 测定法，洗涤剂 36k 或 36l，16℃
K027R-N043R-R045T-N076D-S101G-S103A-V104I-A232V-Q245R	+
N018R-T022W-S024R-N076D-S101A-N183D-T213A-A215F-H249R	+
N018R-S024R-N076D-S103A-V104I-L135I-A232V	+
N018R-G020R-T022W-S024R-N076D-N183D-I198L-G211Q-H249R	+
N018R-G020R-T022W-S024R-N076D-S101A-N116A-N183D-I198L-A215F-H249R	+
N018R-S024R-N076D-S101A-N116A-N183D-G211Q-H249R	+
N018R-T022W-S024R-N076D-N183D-G211Q-T213A-A215F-H249R	+
N076D-S101G-S103A-V104I-A232V-H249R	+
P005S-N018R-T022W-S024R-N076D-S101A-T213A-A215F-H249R	+
N018R-S024R-N076D-N116A-N183D-A215F-H249R	+
N018R-S024R-N076D-N183D-I198L-A215F-H249R	+
N018R-G020R-S024R-N076D-S101A-N116A-N183D-H249R	+
N018R-T022W-S024R-N076D-N116A-N183D-G211Q-H249R	+
N018R-G020R-T022W-S024R-N076D-S101A-N116A-H249R	+
N018R-T022W-S024R-N076D-S101A-N116A-N183D-I198L-T213A-H249R	+
N018R-T022W-S024R-N076D-S101A-N183D-G211Q-T213A-H249R	+
N018R-G020R-S024R-N076D-N116A-I198L-H249R	+
N018R-S024R-N076D-N183D-G211Q-T213A-H249R	+
N018R-S024R-N076D-S101A-N116A-N183D-T213A-H249R	+
N018R-S024R-N076D-N116A-N183D-I198L-A215F-H249R	+
N018R-T022W-S024R-N076D-N183D-I198L-G211Q-A215F-H249R	+
N018R-T022W-S024R-N076D-N183D-H249R	+
N018R-T022W-S024R-N076D-S101A-N183D-I198L-A215F-H249R	+
N018R-G020R-N043D-R045T-N076D-S101G-S103A-V104I-A232V-Q245R	+
G020R-T022W-S101A-S103A-V104I-N183D-I198L-A215F-A232V-Q245R	+
N076D-S101G-S103A-V104I-H249R	+
N018R-G020R-S024R-N076D-N183D-I198L-A215F-H249R	+

[0894]

表 11-2：WCE10 至 WCE14 文库变体的 BMI 清洁性能。
PI=性能指数
在洗涤剂 36k 或 36l 中，PI>或=1.5 为+++；PI 介于 1.49 和 1.3 之间=++；PI 介于 1.29 和 1.0 之间=+

GG36 变体的序列（BPN'编号方式）	相对于 GG36 的 PI; BMI 测定法，洗涤剂 36k 或 36l，16℃
N018R-G020R-T022W-S024R-N076D-S101A-N183D-A215F-H249R	+
N018R-G020R-S024R-N076D-G211Q-T213A-H249R	+
N018R-S024R-N076D-N116A-N183D-G211Q-T213A-H249R	+
N018R-S024R-N076D-N116A-N183D-I198L-H249R	+
N018R-G020R-S024R-N076D-G211Q-N243D-H249R	+
N018R-G020R-R045T-N076D-S101G-S103A-V104I-A232V-Q245R-H249R	+
N018R-T022W-S024R-N076D-N183D-I198L-G211Q-T213A-H249R	+
N018R-S024R-N076D-S101A-N116A-N183D-I198L-G211Q-T213A-H249R	+
N018R-T022W-S024R-N076D-N116A-I198L-G211Q-T213A-A215F-H249R	+
S024R-N076D-S101G	+
N018R-G020R-S024R-N076D-S101A-I198L-T213A-A215F-H249R	+
N018R-T022W-S024R-N076D-N116A-N183D-G211Q-T213A-H249R	+
N018R-G020R-S024R-N076D-N183D-A215F-H249R	+
N018R-N043D-N076D-S078R-S101G-S103A-V104I-A232V-Q245R-H249R	+
N018R-T022W-S024R-N076D-N116A-N183D-G211Q-T213A-Q245R	+
G020R-S024R-N076D-S078R-S101G-S103A-V104I-A232V-Q245R-H249R	+
N018R-G020R-R045T-S101G-S103A-V104I-A232V-Q245R-H249R	+
N018R-S024R-N076D-S101A-N183D-I198L-G211Q-H249R	+
N018R-T022W-S024R-N076D-N183D-G211Q-T213A-H249R	+
N018R-G020R-S024R-N076D-N116A-I198L-G211Q-A215F-H249R-N269S	+
N018R-G020R-T022W-S024R-N076D-S101A-N116A-N183D-I198L-G211Q-A215F-H249R	+
G020R-T022W-S101A-S103A-V104I-N183D-T213A-A215F-A232V-Q245R	+
N018R-S024R-N076D-A086V-S101A-N183D-I198L-G211Q-H249R	+
N018R-N076D-S101G-I198T-A232V	+

[0895]

表 11-2：WCE10 至 WCE14 文库变体的 BMI 清洁性能。
PI=性能指数
在洗涤剂 36k 或 36l 中，PI>或=1.5 为+++；PI 介于 1.49 和 1.3 之间=++；PI 介于 1.29 和 1.0 之间=+

GG36 变体的序列（BPN'编号方式）	相对于 GG36 的 PI; BMI 测定法，洗涤剂 36k 或 36l，16℃
N018R-G020R-S024R-N076D-S101A-N116A-N183D-I198L-G211Q-A215F-H249R	+
N018R-T022W-S024R-N076D-S101A-N116A-N183D-T213A-A215F-H249R	+
N018R-T022W-S024R-N076D-S101A-N183D-G211Q-T213A-A215F-H249R	+
N018R-S024R-N076D-N183D-H249R-A248T	+
N018R-N076D-V104I-Q245R-H249R	+
N018R-T022W-S024R-N076D-S101A-N116A-N183D-I198L-A215F-H249R	+
N018R-T022W-S024R-N076D-N116A-N183D-T213A-A215F-H249R	+
N018R-G020R-T022W-S024R-N076D-N116A-N183D-G211Q-T213A-A215F-H249R	+
N018R-G020R-S024R-N076D-S101A-H249R	+
N018R-G020R-S024R-N076D-S101A-N116A-T213A-A215F-H249R	+
N018R-T022W-S024R-N076D-N116A-N183D-G211Q-A215F-H249R	+
N018R-T022W-S024R-N076D-N116A-N183D-I198L-G211Q-T213A-H249R	+
N043R-R045T-S078R-S101G-S103A-V104I-L217E-A232V-Q245R	+
N043R-R045T-S101G-S103A-V104I-A232V-Q245R-H249R	+
N018R-N076D-S101G-V104I	+
G020R-R045T-N076D-S078R-S101G-S103A-V104I-A232V-Q245R-H249R	+
N043D-N076D-S101G-S103A-V104I-A232V-Q245R	+
N018R-G020R-T022W-S024R-N076D-S101A-N116A-N183D-I198L-H249R	+
N018R-N076D-V104I	+
N018R-G020R-N043D-S101G-S103A-V104I-A232V-Q245R-H249R	+
N018R-G020R-T022W-S024R-N076D-N183D-G211Q-H249R	+
N018R-S024R-N076D-S101A-N183D-I198L-G211Q-A215F-H249R	+
S101G-V104I	+
N018R-T022W-S024R-N076D-N116A-N183D-I198L-G211Q-T213A-A215F-H249R	+

[0896]

表 11-2：WCE10 至 WCE14 文库变体的 BMI 清洁性能。
PI=性能指数
在洗涤剂 36k 或 36l 中，PI>或=1.5 为+++；PI 介于 1.49 和 1.3 之间=++；PI 介于 1.29 和 1.0 之间=+

GG36 变体的序列（BPN'编号方式）	相对于 GG36 的 PI; BMI 测定法，洗涤剂 36k 或 36l，16℃
N018R-G020R-S024R-N076D-S101A-N183D-G211Q-T213A-A215F-H249R	+
N018R-G020R-S024R-N076D-N116A-N183D-A215F-H249R-N263D	+
N018R-T022W-S024R-N076D-S101A-N183D-H249R	+
N018R-S024R-N076D-S101A-N116A-N183D-I198L-A215F-H249R	+
N018R-T022W-S024R-N076D-N116A-I198L-A215F-H249R-R269H	+
N018R-N043D-R045T-N076D-S078R-S101G-S103A-V104I-A232V-Q245R	+
N018R-S024R-R045T-N076D-S078R-S101G-S103A-V104I-A232V-Q245R-N269R	+
S078R-S101G-S103A-V104I-L217E-A232V-Q245R	+
N018R-G020R-T022W-S024R-N076D-S101A-N183D-I198L-T213A-A215F-H249R	+
N018R-G020R-S024R-N076D-N183D-I198L-T213A-H249R	+
N018R-G020R-T022W-S024R-N076D-N116A-I198L-G211Q-A215F-H249R	+
N018R-G020R-T022W-S024R-N076D-N116A-N183D-G211Q-H249R	+
N018R-G020R-T022W-S024R-N076D-S101A-I198L-G211Q-T213A-H249R	+
N018R-G020R-T022W-S024R-N076D-H249R	+
G020R-T022W-S101G-S103A-V104I-N116A-N183D-I198L-G211Q-T213A-A215F-A232V-Q245R	+
V104I-A232V	+
N018R-G020R-T022W-S024R-N076D-S101A-N116A-N183D-G211Q-A215F-H249R	+
N018R-G020R-T022W-S024R-N076D-S101A-N116A-N183D-I198L-G211Q-T213A-A215F-H249R	+
N018R-G020R-T022W-S024R-N076D-S101A-N183D-T213A-A215F-H249R	+
N018R-T022W-S024R-N076D-S101A-N183D-I198L-G211Q-T213A-H249R	+
N018R-T022W-S024R-N076D-S101A-N183D-I198L-H249R	+
N043D-R045T-S101G-S103A-V104I-A232V-Q245R-N269R	+
N018R-G020R-S024R-N076D-S101A-N183D-I198L-G211Q-H249R	+

[0897]

表 11-2：WCE10 至 WCE14 文库变体的 BMI 清洁性能。
PI=性能指数
在洗涤剂 36k 或 36l 中，PI>或=1.5 为+++；PI 介于 1.49 和 1.3 之间=++；PI 介于 1.29 和 1.0 之间=+

GG36 变体的序列（BPN'编号方式）	相对于 GG36 的 PI; BMI 测定法，洗涤剂 36k 或 36l，16℃
N018R-G020R-N043R-S101G-S103A-V104I-L217E-A232V-Q245R	+
S024R-N043R-N076D-S078R-S101G-S103A-V104I-A232V-Q245R-N269R	+
N043R-R045T-N076D-S078R-S101G-S103A-V104I-Y166F-A176P-A179V-N184T-A187P-A194P	+
N018R-T022W-S024R-D041E-N076D-S101A-S160T-N183D-G211Q-T213A-H249R	+
N018R-G020R-T022W-S024R-N076D-N116A-N183D-I198L-G211Q-A215F-H249R	+
N018R-G020R-T022W-S024R-N076D-S101A-N116A-I198L-T213A-H249R	+
N018R-T022W-S024R-N076D-S101A-N116A-N183D-I198L-G211Q-T213A-H249R	+
N018R-G020R-S024R-N076D-I198L-T213A-H249R	+
N018R-G020R-T022W-S024R-N076D-N116A-N183D-I198L-G211Q-H249R	+
N018R-G020R-S024R-N076D-N183D-G211Q-A215F-H249R	+
S024R-N076D-V104I	+
N018R-N076D-S101G-A232V	+
N018R-S024R-N076D-S101A-N116A-N183D-I198L-G211Q-T213A-A215F-H249R	+
N018R-G020R-T022W-S024R-N076D-N116A-N183D-A215F-H249R	+
N018R-S024R-L031F-N076D-N116A-N183D-G211Q-T213A-A215F-H249R	+
N018R-S024R-N076D-S101A-N116A-N183D-I198L-T213A-H249R-N269S	+
N018R-G020R-S024R-N076D-S101A-N116A-I198L-A215F-H249R	+
N018R-N043R-N076D-S078R-S101G-S103A-V104I-A232V-Q245R-N269R	+
N018R-G020R-S024R-N076D-S101A-N114T-I198L-G211Q-A215F-H249R	+
S024R-N043R-S078R-S101G-S103A-V104I-L217E-A232V-Q245R	+
S024R-N076D-S103A-V104I-A232V	+
N018R-G020R-T022W-S024R-N076D-S101A-I198L-G211Q-A215F-H249R	+
S101G-V104I-A232V	+

[0898]

表 11-2：WCE10 至 WCE14 文库变体的 BMI 清洁性能。
PI=性能指数
在洗涤剂 36k 或 36l 中，PI>或=1.5 为+++；PI 介于 1.49 和 1.3 之间=++；PI 介于 1.29 和 1.0 之间=+

GG36 变体的序列（BPN'编号方式）	相对于 GG36 的 PI; BMI 测定法，洗涤剂 36k 或 36l，16℃
N018R-T022W-S024R-N076D-N183D-I198L-T213A-A215F-H249R	+
N018R-T022W-S024R-N076D-N183D-I198L-G211Q-H249R	+
N018R-G020R-S024R-N076D-N183D-T213A-H249R	+
N018R-S024R-N076D-S101A-N183D-G211Q-A215F-H249R	+
N018R-G020R-T022W-S024R-N076D-N116A-G211Q-T213A-H249R	+
N018R-S078R-S101G-S103A-V104I-A232V-Q245R-N269R	+
N018R-T022W-S024R-N076D-S101A-N116A-N183D-G211Q-A215F-H249R-T260A	+
N076D-H249R	+
N018R-T022W-S024R-N076D-N183D-G211Q-A215F-H249R	+
N018R-G020R-S024R-N076D-N116A-G211Q-A215F-H249R	+
N018R-G020R-S024R-N076D-T213A-H249R	+
N018R-G020R-T022W-S024R-N076D-N116A-N183D-I198L-H249R	+
N018R-G020R-T022W-S024R-N076D-S101A-N183D-H249R	+
N076D-V104I-H249R	+
G020R-T022W-S101A-S103A-V104I-N116A-N183D-G211Q-T213A-A215F-A232V-Q245R	+
S024R-N043R-R045T-S078R-S101G-S103A-V104I-L217E-A232V-Q245R	+
N018R-G020R-T022W-S024R-N076D-N183D-I198L-A215F-H249R	+
N018R-N076D-S101G-S103A	+
G020R-S024R-S101G-S103A-V104I-A232V-Q245R-N269R	+
N018R-G020R-S024R-N076D-S101A-N116A-N183D-G211Q-H249R	+
S101G-S103A-A232V	+
S024R-N076D-S101G-A232V	+
N018R-T022W-S024R-N076D-S101A-N183D-I198L-G211Q-H249R	+
N018R-G020R-S024R-N076D-S101A-N183D-I198L-G211Q-A215F-H249R	+
N018R-G020R-S024R-N076D-N183D-I198L-H249R	+
N018R-T022W-S024R-N076D-S101A-N116A-N183D-I198L-G211Q-H249R	+

[0899]

表 11-2：WCE10 至 WCE14 文库变体的 BMI 清洁性能。
PI=性能指数
在洗涤剂 36k 或 36l 中，PI>或=1.5 为+++；PI 介于 1.49 和 1.3 之间=++；PI 介于 1.29 和 1.0 之间=+

GG36 变体的序列（BPN'编号方式）	相对于 GG36 的 PI；BMI 测定法，洗涤剂 36k 或 36l，16℃
N018R-G020R-S024R-N076D-N116A-A156V-N183D-G211Q-A215F-H249R-N269S	+
R045T-N076D-S101G-S103A-V104I-A232V-Q245R-H249R	+
N018R-G020R-S024R-N076D-S101A-N183D-I198L-H249R	+
N018R-G020R-T022W-S024R-N076D-I198L-G211Q-A215F-H249R	+
N018R-G020R-T022W-S024R-N076D-S101A-N116A-I198L-G211Q-A215F-H249R	+
N018R-G020R-T022W-S024R-N076D-N116A-H249R	+
N018R-N076D-S101G	+
N018R-S024R-N076D-N116A-N183D-I198L-T213A-A215F-H249R	+
N018R-G020R-T022W-S024R-N076D-S101A-N116A-I198L-T213A-A215F-H249R	+
N018R-S024R-N076D-S101A-N116A-N183D-I198L-G211Q-H249R	+
N018R-N076D-A232V	+
N018R-G020R-S024R-N076D-S101A-A232V-Q245R	+
N018R-N043D-R045T-N076D-S101G-S103A-V104I-A232V-Q245R	+
N018R-T022W-S024R-N076D-N183D-T213A-A215F-H249R	+
N018R-S024R-N076D-S101A-N116A-G211Q-T213A-N237D-H249R	+
N018R-G020R-S024R-N076D-S101A-N116A-N183D-G211Q-H249R-R275S	+
N018R-T022W-S024R-N076D-S101A-N116A-N183D-I198L-G211Q-T213A-A215F-H249R	+
S024R-N076D	+
N018R-S024R-N076D-N183D-G211Q-A215F-H249R	+
N018R-T022W-S024R-N076D-N116A-N183D-I198L-T213A-A215F-H249R	+
N076D-V104I-A232V-H249R	+
N018R-N076D-S103A-A232V	+
N018R-G020R-S024R-N076D-S101A-N116A-N183D-I198L-G211Q-T213A-H249R	+
N018R-G020R-S024R-N076D-S101A-N183D-T213A-H249R	+
N018R-G020R-S024R-N076D-S101A-D175E-N183D-G211Q-A215F-H249R	+
N018R-G020R-N043D-S078R-S101G-S103A-V104I-L217E-A232V-Q245R-A273E	+

[0900]

表 11-2：WCE10 至 WCE14 文库变体的 BMI 清洁性能。
PI=性能指数
在洗涤剂 36k 或 36l 中，PI>或=1.5 为+++；PI 介于 1.49 和 1.3 之间=++；PI 介于 1.29 和 1.0 之间=+

GG36 变体的序列（BPN'编号方式）	相对于 GG36 的 PI；BMI 测定法，洗涤剂 36k 或 36l，16℃
G020R-S024R-N043D-R045T-N076D-S101G-S103A-V104I-A232V-Q245R	+
P005S-S101G-S103A-V104I-A232V-Q245R-H249R	+
S103A-V104I-A232V	+
N018R-G020R-S024R-V068A-N076D-S101A-N116A-T213A-A215F-H249R	+
N018R-T022W-S024R-N076D-S101A-I198L-A215F-H249R-R275S	+
N018R-S024R-N076D-N183D-I198L-G211Q-T213A-H249R	+
N043D-R045T-S101G-S103A-V104I-A232V-Q245R	+

[0901]

表 11-3：WCE15 和 WCE16 变体的 BMI 清洁性能。
PI=性能指数
在洗涤剂 36m 中，PI>或=1.5 为+++；PI 介于 1.49 和 1.3 之间=++；PI 介于 1.29 和 1.0 之间=+

GG36 变体的序列（BPN'编号方式）	相对于 GG36 的 PI；洗涤剂 36m，BMI，16℃
N018R-S024R-N043R-N076D-H249R-N269R	+++
N018R-T022R-S024R-N043R-N076D-H249R	+++
N018R-N043D-S101G-S103A-V104I-A232V-Q245R	+++
G020R-N043D-S101G-S103A-V104I-A232V-Q245R	+++
N043D-S101G-S103A-V104I-A232V-Q245R-N269R	+++
N043D-S078R-S101G-S103A-V104I-A232V-Q245R	+++
N043R-N076D-S101G-S103A-V104I-A232V-Q245R	+++
T022R-N043R-S101G-S103A-V104I-A232V-Q245R	+++
N043R-S078R-S101G-S103A-V104I-A232V-Q245R	+++
G020R-N076D-S101G-S103A-V104I-A232V-Q245R	+++
N043R-N076D-S101G-S103A-V104I-A232V-Q245R	+++
T022R-N076D-S101G-S103A-V104I-A232V-Q245R	+++
N076D-S078R-S101G-S103A-V104I-A232V-Q245R	+++
N018R-S024R-N043R-N076D-H249R	+++
N018R-S024R-N076D-S242R-H249R	+++
N018R-S024R-N076D-H249R-N269R	+++
N018R-T022R-S024R-N076D-H249R	+++
N018R-S024R-N076D-S078R-H249R	+++
N018R-S024R-N043D-N076D-H249R-N269R	+++

[0902]

表 11-3：WCE15 和 WCE16 变体的 BMI 清洁性能。
PI=性能指数
在洗涤剂 36m 中，PI>或=1.5 为+++；PI 介于 1.49 和 1.3 之间=++；PI 介于 1.29 和 1.0 之间=+

GG36 变体的序列（BPN'编号方式）	相对于 GG36 的 PI；洗涤剂 36m，BMI，16℃
N018R-T022R-S024R-N043D-N076D-H249R	+++
N018R-S024R-N043D-N076D-S078R-H249R	+++
G020R-S101G-S103G-V104I-A232V-Q245R	+++
G020R-S101G-S103A-V104L-A232V-Q245R	+++
G020R-S101G-S103A-V104V-A232V-Q245R	+++
G020R-S101G-S103S-V104I-A232V-Q245R	+++
G020R-S101G-S103S-V104L-A232V-Q245R	+++
G020R-S101S-S103S-V104I-A232V-Q245R	+++
G020R-S101S-S103S-V104L-A232V-Q245R	+++
G020R-S101A-S103A-V104L-A232V-Q245R	+++
G020R-S101S-S103S-V104V-A232V-Q245R	+++
G020R-S101S-S103A-V104I-A232V-Q245R	+++
G020R-S101S-S103A-V104V-A232V-Q245R	+++
G020R-S101S-S103G-V104I-A232V-Q245R	+++
G020R-S101S-S103G-V104V-A232V-Q245R	+++
G020R-S101A-S103A-V104V-A232V-Q245R	+++
G020R-S101A-S103S-V104I-A232V-Q245R	+++
G020R-S101A-S103S-V104V-A232V-Q245R	+++
N018R-S024R-N043R-N076D-S078R-H249R	++
S024R-N043D-S101G-S103A-V104I-A232V-Q245R	++
N043D-S101G-S103A-V104I-A232V-Q245R-H249R	++
S024R-N076D-S101G-S103A-V104I-A232V-Q245R	++
N076D-S101G-S103A-V104I-A232V-S242R-Q245R	++
N018R-G020R-S024R-N076D-L217E-H249R	++
N018R-S024R-N043R-N076D-L217E-H249R	++
N018R-S024R-N043D-N076D-S242R-H249R	++
N018R-G020R-S024R-N043R-N076D-H249R	++
G020R-S101A-S103G-V104V-A232V-Q245R	++
N043D-S101G-S103A-V104I-A232V-Q245R	+
N018R-S024R-N076D-L217E-H249R-N269R	+
N018R-S024R-N076D-L217E-S242R-H249R	+

[0903]

表 11-4：WCE20 和 WCE21 文库变体的 BMI 清洁性能。
PI=性能指数
在洗涤剂 36m 或 36n 中，PI>或=1.5 为+++；PI 介于 1.49 和 1.3 之间=++；PI 介于 1.29 和 1.0 之间=+

[0904]

GG36 变体的序列（BPN'编号方式）	相对于 GG36 的 PI；BMI 测定法，洗涤剂 36m 或 36n，16℃
G020R-S101A-S103A-V104I-G118R-A232V-Q245R	+++
G020R-S024R-N116A-T213A	+++
N043R-S101A-N116A-A215F-N269R	+++
S024R-N043R-S101A-N116A	+++
S024R-N043R-S101A-N116A-A215F-N269R	+++
G020R-S101G-S103A-V104I-A215F-A232V-Q245R	+++
N043R-S101A-N269R	+++
S024R-N043R-N116A-T213A-N269R	+++
G020R-S024R-N043R-R045T-S101A-T213A	+++
S024R-N043R-N116A-A215F-N269R	+++
G020R-S024R-T213A-A215F	+++
G020R-N116A-N269R	+++
S024R-N116A-T213A-N269R	+++
N043R-S101A-N116A-N269R	+++
S101G-S103A-V104I-N116A-T213A-A232V-Q245R-N269R	+++
S024R-N043R-R045T-S101A-N116A-A215F-N269R	+++
G020R-N043R-S101A-N269R	+++
S101A-S103A-V104I-T213A-A232V-Q245R-N269R	+++
S024R-A215F-N269R	+++
N043R-S101A-N116A-T213A-A215F-N269R	+++
N043R-S101A-T213A-N269R	+++
G020R-S024R-N043R-R045T-N116A-T213A	+++
S101G-S103A-V104I-A232V-Q245R-N269R	+++
S024R-N043R-R045T-S101A-N116A-T213A-N269R	+++
S024R-N043R-R045T-N269R	+++
G020R-N043R-R045T-S101A-N269R	+++
S024R-N043R-N116A-N269R	+++
G020R-S024R-N043R-R045T	+++
N043R-N116A-N269R	+++
S024R-N043R-S101A-A215F-N269R	+++
S024R-N043R-R045T-T213A-A215F-N269R	+++
G020R-S024R-R045T-N269R	+++
G020R-N043R-S101A-N116A-T213A-A215F	+++
G020R-S101G-S103A-V104I-T213A-A215F-A232V-Q245R	+++
G020R-S024R-R045T-N116A-N269R	+++
G020R-S101A-N116A-N269R	+++
S024R-N043R-A215F	+++
G020R-S024R-T213A	+++
S024R-N043R-S101A-A215F	+++
G020R-S024R-N043R-R045T-N116A	+++

[0905]

表 11-4：WCE20 和 WCE21 文库变体的 BMI 清洁性能。
PI=性能指数
在洗涤剂 36m 或 36n 中，PI>或=1.5 为+++；PI 介于 1.49 和 1.3 之间=++；PI 介于 1.29 和 1.0 之间=+

GG36 变体的序列（BPN'编号方式）	相对于 GG36 的 PI；BMI 测定法，洗涤剂 36m 或 36n，16℃
G020R-S024R-N043R-R045T-S101A-N269R	+++
G020R-S024R-S101A-A215F	+++
G020R-S024R-N116A-T213A-A215F	+++
G020R-S024R-N116A	+++
G020R-S024R-S101A-N116A	+++
N043R-T213A-A215F-N269R	+++
S024R-S101A-N269R	+++
S024R-N043R-N116A-A215F	+++
G020R-T038A-N043R-S101A	+++
G020R-S024R-N116A-A215F	+++
S024R-N043R-S101A-T213A	++
P014L-G020R-S024R-N043R-R045T-S101A-A215F	++
G020R-S024R-A215F	++
G020R-N116A-A215F-N269R	++
G020R-R045T-N116A-N269R	++
G020R-S024R-N043R-R045T-A215F	++
G020R-S024R-N043R-R045T-N116A-T213A-A215F	++

[0906]

表 11-5：NHJ8 文库变体的 BMI 清洁性能。
PI=性能指数
在洗涤剂 36f 中，PI>或=1.3 为+++；PI 介于 1.29 和 1.2 之间=++；PI 介于 1.19 和 1.0 之间=+

GG36 变体的序列（BPN'编号方式）	相对于 GG36 的 PI；BMI 测定法，洗涤剂 36f，16℃
N043R-N076D-S101A-S103A-V104I-A158E-S188D-A232V-Q245R-N248D-H249R-E271F	+++
S024R-N043R-N076D-S101A-S103A-V104I-A158E-S188D-L217E-A232V-Q245R-N248D-H249R	+++
S101A-S103A-V104I-A158E-S188D-A232V-Q245R-N248D-H249R-E271F-E271F	+++
S101A-S103A-V104I-A158E-S188D-L217E-A232V-Q245R-N248D-H249R-E271F	++
N076D-S101G-S103A-V104I-A114V-A158E-S188D-A232V-Q245R-N248D-H249R-E271F	++

[0907]

表 11-5：NHJ8 文库变体的 BMI 清洁性能。
PI=性能指数
在洗涤剂 36f 中，PI>或=1.3 为+++；PI 介于 1.29 和 1.2 之间=++；PI 介于 1.19 和 1.0 之间=+

GG36 变体的序列（BPN'编号方式）	相对于 GG36 的 PI；BMI 测定法，洗涤剂 36f，16℃
S024R-N076D-S101G-S103A-V104I-A158E-S188D-A232V-Q245R-N248D-H249R-E271F	+
S024R-N043R-S101A-S103A-V104I-A158E-S188D-L217E-A232V-Q245R-N248D-H249R	+
S024R-N043R-S101A-S103A-V104I-A158E-S188D-A232V-Q245R-N248D-H249R	+
S024R-S101A-S103A-V104I-A158E-S166D-S188D-L217E-A232V-Q245R-N248D-H249R	+
N076D-S101G-S103A-V104I-S128L-A158E-S188D-A232V-Q245R-N248D-H249R-E271F	+
N043R-N076D-S101G-S103A-V104I-A158E-S166D-S188D-A232V-Q245R-N248D-H249R-E271F	+

[0908]

表 11-6：NHJ8、NHJ9、NHJ14 文库变体的 BMI 清洁性能。
PI=性能指数
在洗涤剂 36c 中，PI>或=1.5 为+++；PI 介于 1.49 和 1.3 之间=++；PI 介于 1.29 和 1.0 之间=+

GG36 变体的序列（BPN'编号方式）	相对于 GG36 的 PI；BMI 测定法，洗涤剂 36c，16℃
T022A-S101G-S103A-V104I-G159D-L217E-A232V-Q245R-N248D-E271F	+++
T022A-N043R-S101G-S103A-V104I-G159D-S188D-L217E-A232V-Q245R-N248D-E271F	+++
T022A-S101G-S103A-V104I-G159D-S188D-A232V-Q245R-N248D-E271F	+++
N043R-S101A-S103A-V104I-A158E-S188D-L217E-A232V-Q245R-N248D-H249R	+++
N043R-N076D-S101A-S103A-V104I-A158E-S188D-L217E-A232V-Q245R-N248D-H249R-E271F	+++
S024R-S101G-S103A-V104I-A158E-S188D-L217E-A232V-Q245R-N248D-H249R	+++
S024R-S101G-S103A-V104I-A158E-S188D-A232V-Q245R-N248D-H249R	+++
S101G-S103A-V104I-A158E-S188D-A232V-Q245R-N248D-H249R	+++

[0909]

表 11-6: NHJ8、NHJ9、NHJ14 文库变体的 BMI 清洁性能。
PI=性能指数
在洗涤剂 36c 中，PI>或=1.5 为+++；PI 介于 1.49 和 1.3 之间=++；PI 介于 1.29 和 1.0 之间=+

GG36 变体的序列（BPN'编号方式）	相对于 GG36 的 PI；BMI 测定法，洗涤剂 36c，16℃
S024R-S101G-S103A-V104I-A158E-N183D-S188D-A232V-Q245R-N248D-H249R	+++
T022A-N076D-S101G-S103A-V104I-G159D-S188D-A232V-Q245R-N248D-E271F	++
T022A-N043R-N076D-S101G-S103A-V104I-G159D-S188D-A232V-Q245R-N248D-E271F	++
T022A-N076D-S101G-S103A-V104I-G159D-A232V-Q245R-N248D-E271F	++
T022A-S101G-S103A-V104I-G159D-A232V-Q245R-N248D-E271F	++
N076D-S101A-S103A-V104I-A158E-S188D-A232V-Q245R-N248D-H249R-E271F	++
N043R-S101A-S103A-V104I-A158E-S166D-S188D-A232V-Q245R-N248D-H249R	++
S024R-N076D-S101A-S103A-V104I-A158E-S166D-S188D-A232V-Q245R-N248D-H249R-E271F	++
N076D-S101A-S103A-V104I-A158E-S188D-A232V-Q245R-N248D-H249R	++
S101A-S103A-V104I-A158E-S166D-S188D-A232V-Q245R-N248D-H249R-E271F	++
N043R-N076D-S101A-S103A-V104I-A158E-S166D-S188D-A232V-Q245R-N248D-H249R-E271F	++
S101G-S103A-V104I-A158E-S166D-S188D-A232V-Q245R-N248D-H249R-E271F	++
S101A-S103A-V104I-A158E-S188D-A232V-Q245R-N248D-H249R-E271F	++
S101A-S103A-V104I-A158E-S188D-L217E-A232V-Q245R-N248D-H249R	++
N076D-S101A-S103A-V104I-A158E-S166D-S188D-A232V-Q245R-N248D-H249R-E271F	++
S101G-S103A-V104I-A158E-N183D-S188D-A232V-Q245R-N248D-H249R	++
S024R-S101G-S103A-V104I-S128L-A158E-S188D-A232V-Q245R-N248D-H249R	++
N076D-S101G-S103A-V104I-A158E-S166D-S188D-A232V-Q245R-N248D-H249R-E271F	+
N043R-N076D-S101A-S103A-V104I-A158E-S166D-S188D-A232V-Q245R-N248D-H249R	+

[0910]

表 11-6：NHJ8、NHJ9、NHJ14 文库变体的 BMI 清洁性能。
PI=性能指数
在洗涤剂 36c 中，PI>或=1.5 为+++；PI 介于 1.49 和 1.3 之间=++；PI 介于 1.29 和 1.0 之间=+

GG36 变体的序列（BPN'编号方式）	相对于 GG36 的 PI；BMI 测定法，洗涤剂 36c，16℃
N076D-S101A-S103A-V104I-A158E-S188D-L217E-A232V-Q245R-N248D-H249R-E271F	+

[0911]

表 11-7：NHJ9 文库变体的 BMI 清洁性能。
PI=性能指数
对于洗涤剂 36f，PI>或=1.3 为+++；PI 介于 1.29 和 1.2 之间=++；PI 介于 1.19 和 1.0 之间=+

GG36 变体的序列（BPN'编号方式）	相对于 GG36 的 PI；BMI 测定法；洗涤剂 36f，16℃
H017R-T022A-N076D-S101G-S103A-V104I-G159D-S188D-A232V-Q245R-N248D-E271F	+++
T022A-N043R-S101G-S103A-V104I-G159D-A232V-Q245R-N248D-E271F	++
T022A-S101G-S103A-V104I-G159D-S188D-A232V-Q245R-N248D-H249R-E271F	++
H017R-T022A-N076D-S101G-S103A-V104I-G159D-A232V-Q245R-N248D-E271F	++
T022A-N076D-S101G-S103A-V104I-G159D-A232V-Q245R-N248D-H249R-E271F	+
T022A-S101G-G102A-S103A-V104I-G159D-S188D-A232V-Q245R-N248D-E271F	+
T022A-N043R-N076D-S101G-S103A-V104I-G159D-A232V-Q245R-N248D-H249R-E271F	+

[0912]

表 11-8：NHJ11 变体的 BMI 清洁性能。
PI=性能指数
在洗涤剂 36a 或 36c 中，PI>或=1.5 为+++；PI 介于 1.49 和 1.3 之间=++；PI 介于 1.29 和 1.0 之间=+

GG36 变体的序列（BPN'编号方式）	相对于 GG36 的 PI；BMI 测定法，洗涤剂 36a 或 36c1，无漂白剂，16℃
S101S-S103A-V104I-A158E-S188D-A232V-Q245R-N248D-H249R	+++

[0913]

S101S-S103G-V104V-A158E-S188D-A232V-Q245R-N248D-H249R	+++
S101G-S103S-V104I-A158E-S188D-A232V-Q245R-N248D-H249R	+++
S101A-S103A-V104I-A158E-S188D-A232V-Q245R-N248D-H249R	+++
S101A-S103A-V104L-A158E-S188D-A232V-Q245R-N248D-H249R	+++
S101G-S103G-V104I-A158E-S188D-A232V-Q245R-N248D-H249R	+++
S101S-S103G-V104I-A158E-S188D-A232V-Q245R-N248D-H249R	+++
S101S-S103S-V104I-A158E-S188D-A232V-Q245R-N248D-H249R	++
S101S-S103S-V104V-A158E-S188D-A232V-Q245R-N248D-H249R	++
S101A-S103S-V104I-A158E-S188D-A232V-Q245R-N248D-H249R	++
S101A-S103S-V104I-G159E-A232V-Q245R-N248D-H249R	++
S101S-S103A-V104I-G159E-A232V-Q245R-N248D-H249R	++
S101G-S103A-V104L-A158E-S188D-A232V-Q245R-N248D-H249R	++
S101A-S103A-V104L-G159E-A232V-Q245R-N248D-H249R	+
S101A-S103S-V104L-G159E-A232V-Q245R-N248D-H249R	+
S101G-S103S-V104L-G159E-A232V-Q245R-N248D-H249R	+
S101S-S103A-V104L-G159E-A232V-Q245R-N248D-H249R	+
S101A-S103G-V104V-G159E-A232V-Q245R-N248D-H249R	+
S101S-S103A-V104V-G159E-A232V-Q245R-N248D-H249R	+

[0914]

表 11-9: NHJ12 变体的 BMI 清洁性能
PI=性能指数
在洗涤剂 36a 中，PI>或=1.3 为+++；PI 介于 1.29 和 1.2 之间=++；PI 介于 1.19 和 1.0 之间=+

GG36 变体的序列（BPN'编号方式）	相对于 GG36 的 PI; BMI 测定法，洗涤剂 36a，16℃
V026F-V051W-V104L-S106E	+++
V026F-L031F-S078N-G102A-S160D	+++
G020K-G100S-N116L-A158E-S166D-N243F	+++
T033S-N043W-N218D-P239G-N243F	+++
T022L-T038F-A048R-N062E-G100S-R186K	+++
S101D-S103N-N116L-S144R-A215D	+++
V104L-S105T-T213A-L217E-S256N	+++
N043W-S101D-S212M-N243F	+++
V026F-A048R-S105T-T213A-N218D-T224A	+++
S024F-S101D-G118R-A215D-L250I-A272F	++
V121F-N185E-T224A-P239G	++
T022L-L031F-G102A-S128D-T224A-N243F	++

[0915]

表 11-9：NHJ12 变体的 BMI 清洁性能
PI=性能指数
在洗涤剂 36a 中，PI>或=1.3 为+++；PI 介于 1.29 和 1.2 之间=++；PI 介于 1.19 和 1.0 之间=+

GG36 变体的序列（BPN'编号方式）	相对于 GG36 的 PI; BMI 测定法，洗涤剂 36a，16℃
N062E-S078N-G102A-N116L-S144R-L250I	++
T022L-T038F-V121F-S160D-A272F	++
V026F-S078N-G159C-R186K-N243F	++
S024F-A048R-G118R-S166D-L217E	++
G023A-T038F-S078N-G100S-S212M-A215D	++
G100S-N116L-A158E-T213A	++
S078N-V104L-G118R-S128D	++
G102A-S103N-S105T-A194E	++
T022L-S078N-S128D-T213A	+
K027R-G100S-G118R-S160D-S188D-N243F	+
S024F-G102A-R186K-T213A-L217E-N243F	+
T033S-S105T-S188D-S216F	+
G023A-G100S-A194E-S212M	+
A048R-S128D-N185E-P239G	+
G020K-S024F-T033S-P129E-A194E	+
G020K-K027R-P129E-S166D-P239G	+
T022L-G023A-K027R-S101D-V104L-S216F	+
T033S-G118R-P129E-A194E-P239G	+
T022L-S078N-N116L-P129E-S256N	+
K027R-S101D-S103N-S105T-A272F	+
A048R-S078N-N116L-N185E-L217E-P239G	+
G023A-S024F-K027R-N062E	+
S024F-S103N-V104L-G118R-S188D	+
V026F-V104L-S256N-A272F	+
S024F-N043W-V104L-V121F-P129E	+
N062E-S078N-N116L-T224A	+
G023A-S024F-V051W-A158E	+
K027R-T038F-G102A-N116L	+
N062E-S078N-S144R-S212M	+
L031F-N116L-S256N-A272F	+
T022L-T033S-V104L-N116L-S160D-R186K	+
S024F-G118R-P129E-R186K-T213A	+
N043W-S105T-T213A-A215D-S216F	+
L031F-S105T-R186K-S188D	+
V026F-A194E-T213A-S256N	+
S103N-S160D-L250I-S256N	+

[0916]

表 11-10：NHJ15 文库变体的 BMI 清洁性能。
PI=性能指数
在洗涤剂 36a 中，PI>或=1.3 为+++；PI 介于 1.29 和 1.2 之间=++；PI 介于 1.19 和 1.0 之间=+

GG36 变体的序列（BPN'编号方式）	相对于 GG36 的 PI；BMI 测定法，洗涤剂 36a，16℃
T022A-S024R-S101D-S103A-V104I-G118R-G159D-S188D-A232V-N248D-E271F	+++
T022A-S024R-S103A-V104I-P129E-G159D-S188D-A232V-N248D-E271F	+++
T022A-S024R-S103A-V104I-G118R-G159D-S188D-L217D-A232V-N248D	+++
T022A-S024R-S101D-S103A-V104I-G118R-P129E-G159D-S188D-A232V-Q245R-N248D	+++
T022A-S024R-S101D-S103A-V104I-G159D-S188D-A232V-Q245R-N248D	+++
T022A-N043R-S103A-V104I-G118R-P129E-G159D-S188D-A232V-Q245R-N248D	+++
T022A-N043R-S103A-V104I-G118R-S128I-P129E-G159D-S188D-A232V-N248D	++
T022A-N043R-S101D-S103A-V104I-G118R-P129E-G159D-S188D-A232V-N248D-E271F	++
T022A-S024R-N043R-S101D-S103A-V104I-G159D-S188D-A232V-Q245R-N248D	++
T022A-S103A-V104I-G159D-S188D-A232V-N248D	++
T022A-S024R-S103A-V104I-G118R-P129E-G159D-S188D-A232V-N248D-E271F	++
T022A-S024R-S103A-V104I-G159D-S188D-L217D-A232V-Q245R-N248D-E271F	++
T022A-N043R-N062E-S103A-V104I-G159D-S188D-A232V-Q245R-N248D-E271F	++
T022A-N043R-S103A-V104I-P129E-G159D-S188D-A232V-Q245R-N248D	++
T022A-S024R-S103A-V104I-G159D-S188D-L217D-A232V-N248D-E271F	++
T022A-S103A-V104I-G118R-G159D-S188D-L217D-A232V-Q245R-N248D	++
T022A-S024R-S101D-S103A-V104I-G118R-S128I-G159D-S188D-A232V-Q245R-N248D	++
T022A-S024R-N043R-S103A-V104I-G159D-S188D-L217D-A232V-N248D-E271F	++

[0917]

表 11-10：NHJ15 文库变体的 BMI 清洁性能。
PI=性能指数
在洗涤剂 36a 中，PI>或=1.3 为+++；PI 介于 1.29 和 1.2 之间=++；PI 介于 1.19 和 1.0 之间=+

GG36 变体的序列（BPN'编号方式）	相对于 GG36 的 PI；BMI 测定法，洗涤剂 36a，16℃
T022A-N043R-S103A-V104I-G118R-G159D-S188D-L217D-A232V-N248D-E271F	++
T022A-N043R-S103A-V104I-G118R-G159D-S188D-A232V-N248D-E271F	++
T022A-S103A-V104I-S128I-P129E-G159D-S188D-A232V-N248D-E271F	+
T022A-S103A-V104I-G159D-S188D-L217D-A232V-Q245R-N248D-E271F	+
T022A-N043R-S103A-V104I-S128I-G159D-S188D-A232V-Q245R-N248D	+
T022A-S101D-S103A-V104I-G118R-G159D-S188D-L217D-A232V-Q245R-N248D-E271F	+
T022A-S103A-V104I-G118R-P129E-G159D-S188D-A232V-Q245R-N248D-E271F	+
T022A-S024R-N043R-S103A-V104I-G118R-G159D-S188D-L217D-A232V-N248D	+
T022A-N062E-S103A-V104I-G118R-G159D-S188D-A232V-Q245R-N248D	+
T022A-N043R-S101D-S103A-V104I-G118R-P129E-G159D-S188D-L217D-A232V	+
T022A-S024R-S103A-V104I-G159D-S188D-L217D-A232V-N248D	+
T022A-S024R-N043R-S103A-V104I-G118R-S128I-P129E-G159D-S188D-L217D-A232V-N248D-E271F	+
T022A-S103A-V104I-G118R-G159D-S188D-L217D-A232V-Q245R-N248D-E271F	+

[0918]

表 11-11：NHJ16 文库变体的 BMI 清洁性能。
PI=性能指数
在洗涤剂 36a 中，PI>或=1.3 为+++；PI 介于 1.29 和 1.2 之间=++；PI 介于 1.19 和 1.0 之间=+

GG36 变体的序列（BPN'编号方式）	相对于 GG36 的 PI；洗涤剂 36a，16℃
G020K-S024F-N062E-S188D-P239G	+++
S024F-N062E-N116L-P239G	+++
G020K-G023A-N062E-S188D	+++

表 11-11：NHJ16 文库变体的 BMI 清洁性能。
PI=性能指数
在洗涤剂 36a 中，PI>或=1.3 为+++；PI 介于 1.29 和 1.2 之间=++；PI 介于 1.19 和 1.0 之间=+

[0919]

GG36 变体的序列（BPN'编号方式）	相对于 GG36 的 PI；洗涤剂 36a，16℃
G020K-G023A-S024F-N062E-G118R-S188D-T213A	+++
G020K-N043W-N062E-N116L-S188D-T213A-P239G	+++
G023A-N062E-N116L-G118R	+++
G023A-S024F-N062E-N116L-G118R	+++
S024F-N116L	+++
S024F-N062E-S188D-T213A	+++
G023A-N062E-N116L-G118R-S188D-P239G	+++
G020K-S024F-N062E	++
G020K-N043W-N062E-N116L-P239G	++
S024F-N062E-N116L-T213A-P239G	++
G020K-S024F-N043W-N062E-N116L-T213A	++
G020K-G023A-S024F-N062E-N116L-S188D-T213A	++
S024F-N062E-S188D-P239G	++
G023A-N043W-N062E-N116L-G118R-T213A	++
N062E-S188D-P239G	++
G020K-S024F-N062E-P239G	+
S024F-N116L-G118R-S188D-P239G	+
G020K-G023A-N062E-N116L-G118R-T213A	+
G020K-G023A-S024F-N062E-S188D-T213A-P239G	+
S024F-N043W-G118R-S188D	+
G023A-S024F-N116L-G118R-S188D-T213A	+
G020K-G023A-N043W-N116L-S188D-T213A-P239G	+
G023A-S024F-N116L-S188D-P239G	+
G023A-N043W-N116L-G118R-S188D	+
G023A-S024F-G118R-S188D-P239G	+
G023A-S024F-N043W-N062E-N116L-G118R	+
G020K-N043W-S188D-T213A	+
S024F-N062E-G118R-P239G	+
G023A-N043W-S188D-T213A	+
G020K-S024F-N043W-N062E-N116L-G118R-S188D-P239G	+
G020K-N116L-S188D-P239G	+
G020K-N043W-N062E-G118R	+
G020K-N043W-N116L-S188D-T213A	+
G020K-S024F	+
G023A-N043W-N116L-P239G	+
G023A-S024F-N043W-N116L-G118R-S188D-P239G	+

[0920]

表 11-11：NHJ16 文库变体的 BMI 清洁性能。
PI=性能指数
在洗涤剂 36a 中，PI>或=1.3 为+++；PI 介于 1.29 和 1.2 之间=++；PI 介于 1.19 和 1.0 之间=+

GG36 变体的序列（BPN'编号方式）	相对于 GG36 的 PI；洗涤剂 36a，16℃
G020K-G023A-N043W-T213A	+
G023A-S024F-N062E-G118R-T213A-P239G	+

[0921]

表 11-12：NHJ15 和 NHJ16 文库变体的 BMI 清洁性能。
PI=性能指数
在洗涤剂 36a、36d 或 36f 中，PI>或=1.3 为+++；PI 介于 1.29 和 1.2 之间=++；PI 介于 1.19 和 1.0 之间=+

GG36 变体的序列（BPN'编号方式）	相对于 GG36 的 PI；BMI 洗涤剂 36a、36d 或 36f；16℃
G020K-G023A-N043W-G118R-S128I-P129E-G159D-S188D	+++
S024F-G118R-S128I-P129E-G159D	+++
G020K-S024F-N062E-N116L-G118R-S188D	+++
G020K-N062E-N116L-S188D	+++
N062E-N116L-G118R-T213A	+++
G020K-G023A-N062E-N116L-S188D	+++
N062E-N116L-G118R-S188D	+++
G020K-N062E-N116L-T213A	+++
G020K-G023A-N062E-N116L	+++
G020K-N062E-S188D-T213A	+++
G020K-N062E	+++
G020K-S024F-N062E-N116L-S188D	+++
G020K-N043W-N062E-N116L-S188D	+++
G020K-S024F-N062E-S188D-T213A	+++
N062E-N116L-S188D-T213A	+++
G020K-N062E-N116L	+++
G020K-G023A-N062E-N116L-S188D-T213A	+++
G023A-S024F-N062E-N116L-T213A	+++
T022A-N043R-S103A-V104I-S128I-P129E-G159D-S188D-A232V-Q245R-N248D	+++
T022A-N043R-S103A-V104I-G118R-S128I-P129E-G159D-S188D-A232V-N248D-E271F	+++
S024F-N062E-N116L-S188D	+++
T022A-S024R-S103A-V104I-G118R-S128I-P129E-G159D-S188D-A232V-N248D	+++

[0922]

表 11-12: NHJ15 和 NHJ16 文库变体的 BMI 清洁性能。
PI=性能指数
在洗涤剂 36a、36d 或 36f 中，PI>或=1.3 为+++; PI 介于 1.29 和 1.2 之间=++; PI 介于 1.19 和 1.0 之间=+

GG36 变体的序列（BPN'编号方式）	相对于 GG36 的 PI; BMI 洗涤剂 36a、36d 或 36f; 16℃
G023A-N062E-N116L-S188D	+++
N043W-N062E-N116L	+++
G020K-G023A-N116L-S188D	++
N043W-N062E-N116L-S188D	++
S024F-N062E-N116L	++
N062E-N116L-S188D	++
T022A-S024R-S103A-V104I-S128I-G159D-S188D-A232V-N248D	+

[0923] 实例13

[0924] 另外的GG36文库和变体的构建

[0925] 本实例描述了在枯草芽孢杆菌中构建的另外的GG36变体和文库的冷水清洁，大部分DNA文库由DNA2.0,Inc.公司使用pHPLT-GG36枯草芽孢杆菌表达质粒合成。使用如实例4中所述的滚环扩增进行DNA扩增后，将构建的文库的连接反应物转化到枯草芽孢杆菌菌株(基因型：Δ aprE, Δ nprE,amyE::xylRPxylAcomK-phleo)中。通过延伸PCR或QuickChange诱变(参见实例4的方法说明)产生WCE9和NHJ10文库和变体。还使用pHPLT-GG36枯草芽孢杆菌表达质粒产生WCE9和NHJ10文库和变体。如实例1中所述在枯草芽孢杆菌细胞(基因型：Δ aprE, Δ nprE,amyE::xylRPxylAcomK-phleo)中表达变体，并用如实例1中所述的BMI微样本清洁测定法进一步表征。在下面的各表中，洗涤剂组合物与上面的表1-2中所示的那些组合物相对应。另外，如所指出，氨基酸位置根据BPN’编号方式列出。

[0926]

表 12-1: WCE5 变体的 BMI 清洁性能。
PI=性能指数

在洗涤剂 36k 或 36l 中，PI>或=1.5 为+++; PI 介于 1.49 和 1.3 之间=++; PI 介于 1.29 和 1.0 之间=+

[0927]

GG36 变体的序列（BPN'编号方式）	相对于 GG36 的 PI；BMI 测定法，洗涤剂 36k 或 36l，16℃
S087R-S101G-S103A-V104I-Q109R-S212P-A232V-Q245R-E271V	+++
S101G-S103A-V104I-Q109R-A232V-Q245R	+++
S101G-S103A-V104I-Q109R-S212P-A232V-Q245R-E271V	+++
S101G-S103A-V104I-Q109R-S212P-A232V-Q245R	+++
N076D-S87R-S103A-V104I-S212P-E271V	+++
N076D-S103A-V104I-Q109R	+++
N076D-S103A-V104I-S212P-E271V	+++
N076D-S103A-V104I-Q109R-Q245R	+++
N076D-S103A-V104I-S212P-Q245L-E271V	+++

[0928]

表 12-2：WCE9 变体的 BMI 清洁性能。
PI=性能指数
在洗涤剂 36j、36d 或 36e 中，PI>或=1.5 为+++；PI 介于 1.49 和 1.3 之间=++；PI 介于 1.29 和 1.0 之间=+

相对于 GG36 的序列（BPN'编号方式）	相对于 GG36 的 PI；BMI 测定法，洗涤剂 36j、36d 或 36e，16℃
S024R-P086W-G118R	+++
S024R-S078R-P086W-N243F	+++
S024R-T033S-P086S-S087N-Y209A	+++
T033S-G118R	+++
S024R-S078R-P086W-G118R-A270T	+++
S024R-T033S-P086W-G118R	+++
S078R-P086W-N243F	+++
T033S-S078R-P086W-G118R-Y209A	+++
T033S-S078R-Y209A	+++
P086W-G118R-N243F	+++
S024R-P086W	+++
S078R-P086W-K235F	+++
S024R-G118R	+++
S024R-P086R	+++
S101G-S103A-V104I-A232V	+++
S024R-T033S-S078R-P086W-G118R	+++
S024R-G118R-Y209A	+++
Y209A-W241R	+++
T033S-P086W-N243F	+++

表 12-2：WCE9 变体的 BMI 清洁性能。
PI=性能指数
在洗涤剂 36j、36d 或 36e 中，PI>或=1.5 为+++；PI 介于 1.49 和 1.3 之间=++；PI 介于 1.29 和 1.0 之间=+

[0929]

相对于 GG36 的序列（BPN'编号方式）	相对于 GG36 的 PI；BMI 测定法，洗涤剂 36j、36d 或 36e，16℃
T033S-A172V-Y209A	+++
G118R-Y209A-N243F	+++
S024R-P086S-S141G	+++
S024R-G118R-Y209A-N243F	+++
S024R-T033S-P086S-S085N-K235F	+++
S024R-T033S-A133V	+++
S024R-T033S-S078R-P086W	+++
S024R-P086W-Y209A	+++
S024R-W241R	+++
T033S-G118R-N243F	+++
S024R-K235F	+++
S024R-S078R-P086W	+++
S024R-G118R-Y209A-K235F	+++
S024R-Y209A-W241R	+++
T033S-G118R-W241R	+++
P086W-G118R-Y209A	+++
T033S-G118R-G159D-Y209A	+++
T033S-S078R-P086W	+++
S024R-P086W-N243F	+++
G118R-Y209A	+++
S024R-P086W-G118R-V203I	+++
S078R-Y209A-K235F	+++
S024R-T033S-W241R	+++
S078R-G118R	+++
T033S-G118R-Y209A-N243F	+++
L021M-S024R-T033S	+++
S024R-T033S-P086W	+++
T033S-K235F	+++
S078R-P086W-Y209A	+++
S024R-T033S-Y209A-K235F	+++
T033S-P086W-G118R	+++
S024R-T033S-S078R-Y209A	+++
T033S-P086W-G118R-Y209A-N243F	+++
P086W-Y209A-N243F	+++
P005S-S078R-G118R-W241R	+++

[0930]

表 12-2：WCE9 变体的 BMI 清洁性能。
PI=性能指数
在洗涤剂 36j、36d 或 36e 中，PI>或=1.5 为+++；PI 介于 1.49 和 1.3 之间=++；PI 介于 1.29 和 1.0 之间=+

相对于 GG36 的序列（BPN'编号方式）	相对于 GG36 的 PI；BMI 测定法，洗涤剂 36j、36d 或 36e，16℃
S024R-A174T	+++
T033S-Y209A-N243F	+++
P086W-G118R-A133V	+++
S024R-T033S-G118R	+++
S024R-P086W-Y209A-K235F	++
P086W-Y209A	++
I008T-S024R	++
P086W-G118R	++
T033S-W241R	++
P005S-S024R-T033S-N243F	++
S024R-Y209A-S242P	++
S024R-T033S-S078R-G118R	++
S024R-T033S-A194T	++
S024R-N243F	++
S024R-Y209A	++
S024R-T033S-G118R-Y209A	++
T033S-P086W	++
S024R-T033S	++
S024R-T033S-S078R-N243F	++
P086W-N243F	++
T033S-G118D-A138V-Y209A	++
T033S-Y209A-K235F	++
S024R-P086R-G118R	++
T033S-P201S	++
S024R-P239Q	++
T033S-G118R-Y209A-	++
S078R-P086W	++
K235F-N243F	++
S024R-Y209A-K235F	++
G118R-A172V	++
H017Y-S024R-T033S-P086W	++
T033S-L148F	++
S024R-G118R-K235F	++
T033S-S078R	++
T033S-N243F	++

表 12-2：WCE9 变体的 BMI 清洁性能。
PI=性能指数
在洗涤剂 36j、36d 或 36e 中，PI>或=1.5 为+++；PI 介于 1.49 和 1.3 之间=++；PI 介于 1.29 和 1.0 之间=+

[0931]

相对于 GG36 的序列（BPN'编号方式）	相对于 GG36 的 PI；BMI 测定法，洗涤剂 36j、36d 或 36e，16℃
S024C-T033S	++
G118R-A194T	++
T033S-Y209A	++
G118R-Y209A-K235F	++
S024R-T033S-Y209A-N243F	++
S024R-T033S-K235F	++
S024R-T033S-G118R-K235F	++
S024R-S141G	++
S024R-T274I	++
S024R-T033S-Y209A	++
P086W-K235F	+
S024R-Y209A-N243F	+
V004E-T033S-S078R	+
P086W-Y209A-K235F	+
A015T-T033S	+
T033S-P086W-S156L-Y209A	+
S024R-G118R-N243F-R269H	+
Y209A-K235F	+
S024R-R247H	+
S024R-T033S-A228T	+
S078R-K235F	+
S024R-T033S-A174V-K235F	+
S024R-K235F-N243F	+
S024R-T033S-K235F-W241R	+
S024R-T033S-A151V	+
S024R-V104A	+
T033S-A048T	+
Q012H-V104A-G118R	+
G118R-K235F	+
T033S-T253A	+
T143A-Y209A	+
S024R-T033S-N243F	+
T033S-P239T	+
Y209A-N243F	+
S024R-T033S-P129H-N184D-T253M	+

表 12-2：WCE9 变体的 BMI 清洁性能。
PI=性能指数
在洗涤剂 36j、36d 或 36e 中，PI>或=1.5 为+++；PI 介于 1.49 和 1.3 之间=++；PI 介于 1.29 和 1.0 之间=+

[0932]

相对于 GG36 的序列（BPN'编号方式）	相对于 GG36 的 PI；BMI 测定法，洗涤剂 36j、36d 或 36e，16℃
S024R-A085V-P086W-G118R-K235F	+
S024R-A272P	+
S024R-R269C	+

表 12-3：WCE15 变体的 BMI 清洁性能。
PI=性能指数
在洗涤剂 36m 中，PI>或=1.5 为+++；PI 介于 1.49 和 1.3 之间=++；PI 介于 1.29 和 1.0 之间=+

[0933]

GG36 变体的序列（BPN'编号方式）	相对于 GG36 的 PI；BMI 测定法，洗涤剂 36m，16℃
G020R-S087D-S101G-S103A-V104I-A232V-Q245R	+++
G020R-S101G-S103A-V104I-V150L-A232V-Q245R	+++
N018R-G020R-S024R-N076D-S087D-H249R	+++
N018R-G020R-S024R-N076D-V150L-H249R	+++
N018R-S024R-N043R-N076D-S087D-H249R	+++
N018R-S024R-N043R-N076D-V150L-H249R	+++
N018R-S024R-N076D-S078R-S087D-H249R	+++
N018R-S024R-N076D-S078R-V150L-H249R	+++
N018R-S024R-N076D-S087D-H249R-N269R	+++
N018R-S024R-N076D-S087D-S242R-H249R	+++
N018R-S024R-N076D-S087D-V150L-H249R	+++
N018R-S024R-N076D-V150L-H249R	+++
N018R-S087D-S101G-S103A-V104I-A232V-Q245R	+++
N018R-S101G-S103A-V104I-V150L-A232V-Q245R	+++
N018R-T022R-S024R-N076D-S087D-H249R	+++
N018R-T022R-S024R-N076D-V150L-H249R	+++
N043R-S087D-S101G-S103A-V104I-A232V-Q245R-N269R	+++
N043R-S101G-S103A-V104I-V150L-A232V-Q245R	+++
S024R-S087D-S101G-S103A-V104I-A232V-Q245R	+++
S024R-S101G-S103A-V104I-V150L-A232V-Q245R	+++
S078R-S087D-S101G-S103A-V104I-A232V-Q245R	+++
S078R-S101G-S103A-V104I-V150L-A232V-Q245R	+++
S087D-S101G-S103A-V104I-A232V-Q245R-N269R	+++
S101G-S103A-V104I-V150L-A232V-Q245R-H249R	+++

[0934]

表 12-3：WCE15 变体的 BMI 清洁性能。
PI=性能指数
在洗涤剂 36m 中，PI>或=1.5 为+++；PI 介于 1.49 和 1.3 之间=++；PI 介于 1.29 和 1.0 之间=+

GG36 变体的序列（BPN'编号方式）	相对于 GG36 的 PI；BMI 测定法，洗涤剂 36m，16℃
S101G-S103A-V104I-V150L-A232V-Q245R-N269R	+++
T022R-S087D-S101G-S103A-V104I-A232V-Q245R	+++
N018R-S024R-N043D-N076D-V150L-H249R	++
N043R-S087D-S101G-S103A-V104I-A232V-Q245R	++
T022R-S101G-S103A-V104I-V150L-A232V-Q245R	++
N018R-S024R-N043D-N076D-S087D-H249R	+
N018R-S024R-N076D-S087D-H249R	+
N018R-S024R-N076D-V150L-S242R-H249R	+
N043R-S101G-S103A-V104I-V150L-A232V-Q245R-N269R	+
N076D-S101G-S103A-V104I-V150L-A232V-Q245R	+
S087D-S101G-S103A-V104I-A232V-S242R-Q245R	+
S101G-S103A-V104I-V150L-A232V-Q245R	+
N076D-S087D-S101G-S103A-V104I-A232V-Q245R	+
S087D-S101G-S103A-V104I-A232V-Q245R	+
S101G-S103A-V104I-V150L-A232V-S242R-Q245R	+

[0935]

表 12-4：NHJ14 文库变体的 BMI 清洁性能。
PI=性能指数
在实例 36c 的洗涤剂中，PI>或=1.5 为+++；PI 介于 1.49 和 1.3 之间=++；PI 介于 1.29 和 1.0 之间=+

GG36 变体的序列（BPN'编号方式）	相对于 GG36 的 PI；BMI 测定法，洗涤剂 36c，16℃
S024R-S101G-S103A-V104I-P129Q-A158E-S188D-L217E-A232V-Q245R-N248D-H249R	+++
S024R-S101G-S103A-V104I-S130A-A158E-N183D-S188D-A232V-Q245R-N248D-H249R	+++
S024R-S101G-S103A-V104I-P129Q-A158E-N183D-S188D-A232V-Q245R-N248D-H249R	+++
S101G-S103A-V104I-S130A-A158E-S188D-A232V-Q245R-N248D-H249R	+++
S024R-S101G-S103A-V104I-P129Q-A158E-S188D-A232V-Q245R-N248D-H249R	+++
S024R-S101G-S103A-V104I-S130A-A158E-S188D-A232V-Q245R-N248D-H249R	+++
S024R-S101G-S103A-V104I-P129Q-S130A-A158E-N183D-S188D-A232V-Q245R-N248D-H249R	+++

[0936]

表 12-4：NHJ14 文库变体的 BMI 清洁性能。
PI=性能指数
在实例 36c 的洗涤剂中，PI>或=1.5 为+++；PI 介于 1.49 和 1.3 之间=++；PI 介于 1.29 和 1.0 之间=+

GG36 变体的序列（BPN'编号方式）	相对于 GG36 的 PI；BMI 测定法，洗涤剂 36c，16℃
S024R-S101G-S103A-V104I-S128L-P129Q-A158E-S188D-A232V-Q245R-N248D-H249R	+++
S024R-S101G-S103A-V104I-P129Q-S130A-A158E-S188D-A232V-Q245R-N248D-H249R	++
S101G-S103A-V104I-P129Q-A158E-S188D-A232V-Q245R-N248D-H249R	++
S101G-S103A-V104I-P129Q-S130A-A158E-S188D-A232V-Q245R-N248D-H249R	++
S024R-S101G-S103A-V104I-S128L-P129Q-S130A-A158E-S188D-A232V-Q245R-N248D-H249R	++
S101G-S103A-V104I-S128L-P129Q-A158E-S188D-A232V-Q245R-N248D-H249R	++
S024R-K027R-S101G-S103A-V104I-S128L-P129Q-S130A-A158E-S188D-A232V-Q245R-N248D-H249R	++

[0937]

表 12-5：NHJ10 变体的 BMI 清洁性能。
PI=性能指数
在洗涤剂 36a 中，PI>或=1.3 为+++；PI 介于 1.29 和 1.2 之间=++；PI 介于 1.19 和 1.0 之间=+

GG36 变体的序列（BPN'编号方式）	相对于 GG36 的 PI；BMI 测定法，洗涤剂 36a，16℃
S101G-S103A-V104I-A232V-M222Q-Q245R	+++
S101G-S103A-V104I-A158E-S188D-M222S-A232V-Q245R-N248D-H249R	+++
S101G-S103A-V104I-A158E-S188D-M222Q-A232V-Q245R-N248D-H249R	+++
N076D-S101G-S103A-V104I-A232V-M222Q-Q245R	+++
S101G-S103A-V104I-A232V-M222S-Q245R	++
N076D-S101G-S103A-V104I-A232V-M222S-Q245R	++
N076D-S101G-S103A-V104I-A158E-S188D-M222S-A232V-Q245R-N248D-H249R	+

[0938]

表 12-6：NHJ14 文库变体的 BMI 清洁性能。
PI=性能指数
在洗涤剂 36f 中，PI>或=1.3 为+++；PI 介于 1.29 和 1.2 之间=++；PI 介于 1.19 和 1.0 之间=+

GG36 变体的序列（BPN'编号方式）	相对于 GG36 的 PI；BMI 测定法，洗涤剂 36f，16℃
S024R-S101G-S103A-V104I-S128L-P129Q-A158E-S188D-A232V-Q245R-N248D-H249R	+++
S101G-S103A-V104I-S130A-A158E-S188D-A232V-Q245R-N248D-H249R	+++
S024R-S101G-S103A-V104I-A158E-S188D-A232V-Q245R-N248D-H249R	++
S101G-S103A-V104I-S128L-P129Q-A158E-S188D-A232V-Q245R-N248D-H249R	++
S101G-S103A-V104I-P129Q-S130A-A158E-S188D-A232V-Q245R-N248D-H249R	++
S101G-S103A-V104I-S130A-A158E-N183D-S188D-L217E-A232V-Q245R-N248D-H249R	++
S024R-S101G-S103A-V104I-S128L-P129Q-S130A-A158E-S188D-A232V-Q245R-N248D-H249R	++
S024R-S101G-S103A-V104I-P129Q-A158E-S188D-L217E-A232V-Q245R-N248D-H249R	++
S101G-S103A-V104I-S128L-S130A-A158E-S188D-L217E-A232V-Q245R-N248D-H249R	++
S024R-S101G-S103A-V104I-S128L-P129Q-A158E-N183D-S188D-A232V-Q245R-N248D-H249R	+
S024R-S101G-S103A-V104I-S128L-P129Q-S130A-A158E-N183D-S188D-A232V-Q245R-N248D-H249R	+
S024R-S101G-S103A-V104I-S128L-P129Q-A158E-S188D-A232V-Q245R-N248D-H249R-E271G	+
S101G-S103A-V104I-P129Q-A158E-N183D-S188D-A232V-Q245R-N248D-H249R	+
S024R-S101G-S103A-V104I-S130A-A158E-S188D-L217E-A232V-Q245R-N248D-H249R	+
S024R-S101G-S103A-V104I-S128L-A158E-N183D-S188D-A232V-Q245R-N248D-H249R	+
S101G-S103A-V104I-P129Q-A158E-S188D-L217E-A232V-Q245R-N248D-H249R	+
S024R-S101G-S103A-V104I-S128L-S130A-A158E-S188D-A232V-Q245R-N248D-H249R	+

[0939] 实例14

[0940] 颗粒状和/或片状洗衣组合物

[0941] 本实例提供了颗粒状和/或片状衣物洗涤剂的各种制剂。以下的本发明洗衣组合物在下面提供，该洗衣组合物可以是颗粒或片剂的形式。在这些制剂的每一者中，包含浓度为约0.0001至约10重量%的至少一种本文所提供的蛋白酶变体。在一些另选的实施例中，配制者可根据其需求决定使用其他浓度。

表 13-1：颗粒状和/或片状洗衣组合物

化合物	制剂				
	I	II	III	IV	V
基础产品					
C_{14}-C_{15}AS 或 TAS	8.0	5.0	3.0	3.0	3.0
LAS	8.0	-	8.0	-	7.0
C_{12}-$C_{15}AE_3S$	0.5	2.0	1.0	-	-
C_{12}-$C_{15}E_5$ 或 E_3	2.0	-	5.0	2.0	2.0
QAS	-	-	-	1.0	1.0
沸石 A	20.0	18.0	11.0	-	10.0
SKS-6（干加）	-	-	9.0	-	-
MA/AA	2.0	2.0	2.0	-	-
AA	-	-	-	-	4.0
二水合柠檬酸三钠	-	2.0	-	-	-
柠檬酸（无水）	2.0	-	1.5	2.0	-
DTPA	0.2	0.2	-	-	-
[0942] EDDS	-	-	0.5	0.1	-
HEDP	-	-	0.2	0.1	-
PB1	3.0	4.8	-	-	4.0
过碳酸盐	-	-	3.8	5.2	-
NOBS	1.9	-	-	-	-
NACA OBS	-	-	2.0	-	-
TAED	0.5	2.0	2.0	5.0	1.00
BB1	0.06	-	0.34	-	0.14
BB2	-	0.14	-	0.20	-
无水碳酸钠	15.0	18.0	-	15.0	15.0
硫酸盐	5.0	12.0	5.0	17.0	3.0
硅酸盐	-	1.0	-	-	8.0
nprE（任选）	0.03	-	0.1	0.06	-
PMN	-	0.05	-	-	0.1
蛋白酶 B（任选）	-	0.01	-	-	-
蛋白酶 C（任选）	-	-	-	0.01	-
脂肪酶	-	0.008	-	-	-
淀粉酶	0.001	-	-	-	0.001

表 13-1：颗粒状和/或片状洗衣组合物

化合物	制剂				
	I	II	III	IV	V
[0943] 纤维素酶	-	0.0014	-	-	-
果胶裂解酶	0.001	0.001	0.001	0.001	0.001
醛糖氧化酶	0.03	-	0.05	-	-
PAAC	-	0.01	-	-	0.05
余量为水分和/或微量物质*，补足至 100%					

[0944] *香料、染料、增白剂/SRP1/羧甲基纤维素钠/光漂白剂/$MgSO_4$/PVPVI/抑泡剂/高分子PEG/粘土。

[0945] 实例15

[0946] 片状洗涤剂组合物

[0947] 本实例提供各种片状洗涤剂制剂。通过用标准的12头旋转压片机以13KN/cm^2的压力压制颗粒状盘碟洗涤剂组合物，制备以下的本发明片状洗涤剂组合物。在这些制剂的每一者中，包含浓度为约0.0001至约10重量%的至少一种本文所提供的蛋白酶变体。在一些另选的实施例中，配制者可根据其需求决定使用其他浓度。

[0948]

表 14-1：片状洗涤剂组合物

化合物	制剂							
	I	II	III	IV	V	VI	VII	VIII
STPP	-	48.8	44.7	38.2	-	42.4	46.1	46.0
二水合柠檬酸三钠	20.0	-	-	-	35.9	-	-	-
碳酸钠	20.0	5.0	14.0	15.4	8.0	23.0	20.0	-
硅酸盐	15.0	14.8	15.0	12.6	23.4	2.9	4.3	4.2
脂肪酶	0.001	-	0.01	-	0.02	-	-	-
蛋白酶 B（任选）	0.01	-	-	-	-	-	-	-
蛋白酶 C（任选）	-	-	-	-	-	0.01	-	-
nprE（任选）	0.01	0.08	-	0.04	-	0.023	-	0.05
PMN	-	-	0.05	-	0.052	-	0.023	-
淀粉酶	0.012	0.012	0.012	-	0.015	-	0.017	0.002
果胶裂解酶	0.005	-	-	0.002	-	-	-	-
醛糖氧化酶	-	0.03	-	0.02	0.02	-	0.03	-
PB1	-	-	3.8	-	7.8	-	-	4.5
过碳酸盐	6.0	-	-	6.0	-	5.0	-	-

[0949]

表 14-1：片状洗涤剂组合物

化合物	制剂							
	I	II	III	IV	V	VI	VII	VIII
BB1	0.2	-	0.5	-	0.3	0.2	-	-
BB2	-	0.2	-	0.5	-	-	0.1	0.2
非离子型	1.5	2.0	2.0	2.2	1.0	4.2	4.0	6.5
PAAC	0.01	0.01	0.02	-	-	-	-	-
DETBCHD	-	-	-	0.02	0.02	-	-	-
TAED	-	-	-	-	-	2.1	-	1.6
HEDP	1.0	-	-	0.9	-	0.4	0.2	-
DETPMP	0.7	-	-	-	-	-	-	-
石蜡	0.4	0.5	0.5	0.5	-	-	0.5	-
BTA	0.2	0.3	0.3	0.3	0.3	0.3	0.3	-
聚羧酸系	4.0	-	-	-	4.9	0.6	0.8	-
PEG 400-30,000	-	-	-	-	-	2.0	-	2.0
甘油	-	-	-	-	-	0.4	-	0.5
香料	-	-	-	0.05	0.2	0.2	0.2	0.2
余量为水分和/或微量物质*，补足至 100%								

[0950] *增白剂/SRP1/羧甲基纤维素钠/光漂白剂/$MgSO_4$/PVPVI/抑泡剂/高分子PEG/粘土。

[0951] 实例15(I)至15(VII)的pH为约10至约11.5;15(VIII)的pH为8-10。实例15(I)至15(VIII)的片重为约20克至约30克。

[0952] 实例16

[0953] 液体衣物洗涤剂组合物

[0954] 在本实例中,提供液体衣物洗涤剂组合物的各种制剂。以下的本发明液体衣物洗涤剂组合物如下所示制备。在这些制剂的每一者中,包含浓度为约0.0001至约10重量%的至少一种本文所提供的蛋白酶变体。在一些另选的实施例中,配制者可根据其需求决定使用其他浓度。

[0955] 表 15-1: 液体衣物洗涤剂组合物

化合物	制剂				
	I	II	III	IV	V
LAS	24.0	32.0	6.0	3.0	6.0
NaC_{16}-C_{17} HSAS	-	-	-	5.0	-
C_{12}-C_{15} $AE_{1.8}S$	-	-	8.0	7.0	5.0
C_8-C_{10} 丙基二甲胺	2.0	2.0	2.0	2.0	1.0
C_{12}-C_{14} 烷基二甲基氧化胺	-	-	-	-	2.0

[0956]

表 15-1：液体衣物洗涤剂组合物

化合物	制剂				
	I	II	III	IV	V
C_{12}-C_{15} AS	-	-	17.0	-	8.0
CFAA	-	5.0	4.0	4.0	3.0
C_{12}-C_{14}脂肪醇乙氧基化物	12.0	6.0	1.0	1.0	1.0
C_{12}-C_{18}脂肪酸	3.0	-	4.0	2.0	3.0
柠檬酸（无水）	4.5	5.0	3.0	2.0	1.0
DETPMP	-	-	1.0	1.0	0.5
单乙醇胺	5.0	5.0	5.0	5.0	2.0
氢氧化钠	-	-	2.5	1.0	1.5
1N HCl 水溶液	#1	#1	-	-	-
丙二醇	12.7	14.5	13.1	10.	8.0
乙醇	1.8	2.4	4.7	5.4	1.0
DTPA	0.5	0.4	0.3	0.4	0.5
果胶裂解酶	-	-	-	0.005	-
淀粉酶	0.001	0.002	-	-	-
纤维素酶	-	-	0.0002	-	0.0001
脂肪酶	0.1	-	0.1	-	0.1
nprE（任选）	0.05	0.3	-	0.5	0.2
PMN	-	-	0.08	-	-
蛋白酶 A（任选）	-	-	-	-	0.1
醛糖氧化酶	-	-	0.3	-	0.003
ZnCl2	0.1	0.05	0.05	0.05	0.02
甲酸钙	0.05	0.07	0.05	0.06	0.07
DETBCHD	-	-	0.02	0.01	-
SRP1	0.5	0.5	-	0.3	0.3
硼酸	-	-	-	-	2.4
二甲苯磺酸钠	-	-	3.0	-	-
枯烯磺酸钠	-	-	-	0.3	0.5
DC 3225C	1.0	1.0	1.0	1.0	1.0
2-丁基-辛醇	0.03	0.04	0.04	0.03	0.03
增白剂 1	0.12	0.10	0.18	0.08	0.10
余量为香料/染料和/或水，补足到 100%					

[0957] #1：添加1N HCl水溶液以将制剂的净pH调到约3至约5的范围内。

[0958] 上面实例16(I)-(II)的pH为约5至约7，实例16(III)-(V)的pH为约7.5至约8.5。

表 15-2：液体衣物洗涤剂

化合物	制剂					
	I	II	III	IV	V	VI
LAS	11.5	11.5	9.0	-	4.0	-
C_{12}-$C_{15}AE_{2.85}S$	-	-	3.0	18.0	-	16.0
C_{14}-$C_{15}E_{2.5}S$	11.5	11.5	3.0	-	16.0	-
C_{12}-$C_{13}E_9$	-	-	3.0	2.0	2.0	1.0
C_{12}-$C_{13}E_7$	3.2	3.2	-	-	-	-
CFAA	-	-	-	5.0	-	3.0
TPKFA	2.0	2.0	-	2.0	0.5	2.0
柠檬酸（无水）	3.2	3.2	0.5	1.2	2.0	1.2
甲酸钙	0.1	0.1	0.06	0.1	-	-
甲酸钠	0.5	0.5	0.06	0.1	0.05	0.05
ZnCl2	0.1	0.05	0.06	0.03	0.05	0.05
枯烯磺酸钠	4.0	4.0	1.0	3.0	1.2	-
硼酸盐	0.6	0.6	1.5	-	-	-
氢氧化钠	6.0	6.0	2.0	3.5	4.0	3.0
乙醇	2.0	2.0	1.0	4.0	4.0	3.0
1,2 丙二醇	3.0	3.0	2.0	8.0	8.0	5.0
单乙醇胺	3.0	3.0	1.5	1.0	2.5	1.0
TEPAE	2.0	2.0	-	1.0	1.0	1.0
nprE（任选）	0.03	0.05	-	0.03	-	0.02
PMN	-	-	0.01	-	0.08	-
蛋白酶 A（任选）	-	-	0.01	-	-	-
脂肪酶	-	-	-	0.002	-	-
淀粉酶	-	-	-	-	0.002	-
纤维素酶	-	-	-	-	-	0.0001
果胶裂解酶	0.005	0.005	-		-	-
醛糖氧化酶	0.05	-	-	0.05	-	0.02
半乳糖氧化酶	-	0.04				
PAAC	0.03	0.03	0.02	-	-	-
DETBCHD	-	-	-	0.02	0.01	-
SRP 1	0.2	0.2	-	0.1	-	-
DTPA	-	-	-	0.3	-	-
PVNO	-	-	-	0.3	-	0.2
增白剂 1	0.2	0.2	0.07	0.1	-	-
有机硅消泡剂	0.04	0.04	0.02	0.1	0.1	0.1
余量为香料/染料和/或水，补足至 100%						

[0959]

[0960] 实例17

[0961] 手工盘碟液体洗涤剂组合物

[0962] 在本实例中，提供各种手工盘碟液体洗涤剂制剂。以下的本发明手工盘碟液体洗涤剂组合物在下面提供。在这些制剂的每一者中，包含浓度为约0.0001至约10重量％的至少一种本文所提供的蛋白酶变体。在一些另选的实施例中，配制者可根据其需求决定使用

其他浓度。

[0963]

表 16-1：手工盘碟液体洗涤剂组合物

化合物	制剂					
	I	II	III	IV	V	VI
C_{12}-$C_{15}AE_{1.8}S$	30.0	28.0	25.0	-	15.0	10.0
LAS	-	-	-	5.0	15.0	12.0
石蜡烃磺酸盐	-	-	-	20.0	-	-
C_{10}-C_{18}烷基二甲基氧化胺	5.0	3.0	7.0	-	-	-
甜菜碱	3.0	-	1.0	3.0	1.0	-
C_{12}多羟基脂肪酸酰胺	-	-	-	3.0	-	1.0
C_{14}多羟基脂肪酸酰胺	-	1.5	-	-	-	-
$C_{11}E_9$	2.0	-	4.0	-	-	20.0
DTPA	-	-	-	-	0.2	-
脱水柠檬酸三钠	0.25	-	-	0.7	-	-
二胺	1.0	5.0	7.0	1.0	5.0	7.0
$MgCl_2$	0.25	-	-	1.0	-	-
nprE（任选）	0.02	0.01	-	0.01	-	0.05
PMN	-	-	0.03	-	0.02	-
蛋白酶 A（任选）	-	0.01	-	-	-	-
淀粉酶	0.001	-	-	0.002	-	0.001
醛糖氧化酶	0.03	-	0.02	-	0.05	-
枯烯磺酸钠	-	-	-	2.0	1.5	3.0
PAAC	0.01	0.01	0.02	-	-	-
DETBCHD	-	-	-	0.01	0.02	0.01
余量为香料/染料和/或水，补足到 100%						

[0964] 实例17(I)-(VI)的pH为约8至约11。

[0965] 实例18

[0966] 液体自动盘碟洗涤剂组合物

[0967] 在本实例中，提供各种液体自动盘碟洗涤剂制剂。以下的本发明手工盘碟液体洗涤剂组合物在下面提供。在这些制剂的每一者中，包括浓度为约0.0001至约10重量%的至少一种本文所提供的蛋白酶变体。在一些另选的实施例中，配制者可根据其需求决定使用其他浓度。

表 17-1：液体自动盘碟洗涤剂组合物

化合物	制剂				
	I	II	III	IV	V
STPP	16	16	18	16	16
硫酸钾	-	10	8	-	10
1,2 丙二醇	6.0	0.5	2.0	6.0	0.5
硼酸	-	-	-	4.0	3.0
$CaCl_2$ 二水合物	0.04	0.04	0.04	0.04	0.04
非离子型	0.5	0.5	0.5	0.5	0.5
nprE（任选）	0.1	0.03	-	0.03	-
PMN	-	-	0.05	-	0.06
蛋白酶 B（任选）	-	-	-	0.01	-
淀粉酶	0.02	-	0.02	0.02	-
醛糖氧化酶	-	0.15	0.02	-	0.01
半乳糖氧化酶	-	-	0.01	-	0.01
PAAC	0.01	-	-	0.01	-
DETBCHD	-	0.01	-	-	0.01
余量为香料/染料和/或水，补足到 100%					

[0968]

[0969] 实例19

[0970] 高密度盘碟洗涤剂

[0971] 本实例提供高密度盘碟洗涤剂的各种制剂。以下的本发明紧凑型高密度盘碟洗涤剂在下文提供。这些制剂的每一者中，包含浓度为约0.0001至约10重量％的至少一种本文所提供的蛋白酶变体。在一些另选的实例中，配制者可根据其需求决定使用其他浓度。

表 18-1：高密度盘碟洗涤剂

化合物	制剂					
	I	II	III	IV	V	VI
STPP	-	45.0	45.0	-	-	40.0
二水合柠檬酸三钠	17.0	-	-	50.0	40.2	-
碳酸钠	17.5	14.0	20.0	-	8.0	33.6
碳酸氢盐	-	-	-	26.0	-	-
硅酸盐	15.0	15.0	8.0	-	25.0	3.6
偏硅酸盐	2.5	4.5	4.5	-	-	-
PB1	-	-	4.5	-	-	-
PB4	-	-	-	5.0	-	-

[0972]

[0973]

表 18-1：高密度盘碟洗涤剂

化合物	制剂					
	I	II	III	IV	V	VI
过碳酸盐	-	-	-	-	-	4.8
BB1	-	0.1	0.1	-	0.5	-
BB2	0.2	0.05	-	0.1	-	0.6
非离子型	2.0	1.5	1.5	3.0	1.9	5.9
HEDP	1.0	-	-	-	-	-
DETPMP	0.6	-	-	-	-	-
PAAC	0.03	0.05	0.02	-	-	-
石蜡	0.5	0.4	0.4	0.6	-	-
nprE（任选）	0.072	0.053	-	0.026	-	0.01
PMN	-	-	0.053	-	0.059	-
蛋白酶 B（任选）	-	-	-	-	-	0.01
淀粉酶	0.012	-	0.012	-	0.021	0.006
脂肪酶	-	0.001	-	0.005	-	-
果胶裂解酶	0.001	0.001	0.001	-	-	-
醛糖氧化酶	0.05	0.05	0.03	0.01	0.02	0.01
BTA	0.3	0.2	0.2	0.3	0.3	0.3
聚羧酸系	6.0	-	-	-	4.0	0.9
香料	0.2	0.1	0.1	0.2	0.2	0.2
余量为水分和/或微量物质*，补足至 100%						

[0974] *增白剂/染料/SRP1/羧甲基纤维素钠/光漂白剂/$MgSO_4$/PVPVI/抑泡剂/高分子PEG/粘土。

[0975] 实例19(I)至(VI)的pH为约9.6至约11.3。

[0976] 实例20

[0977] 液体硬质表面清洁洗涤剂

[0978] 本实例提供液体硬质表面清洁洗涤剂的各种制剂。以下的本发明液体硬质表面清洁洗涤剂组合物在下文提供。在这些制剂的每一者中，包含浓度为约0.0001至约10重量%的至少一种本文所提供的蛋白酶变体。在一些另选的实施例中，配制者可根据其需求决定使用其他浓度。

[0979]

表 19-1：液体硬质表面清洁洗涤剂

化合物	制剂						
	I	II	III	IV	V	VI	VII
C_9-$C_{11}E_5$	2.4	1.9	2.5	2.5	2.5	2.4	2.5

[0980]

表 19-1：液体硬质表面清洁洗涤剂

化合物	制剂						
	I	II	III	IV	V	VI	VII
C_{12}-$C_{14}E_5$	3.6	2.9	2.5	2.5	2.5	3.6	2.5
C_7-C_9E_6	-	-	-	-	8.0	-	-
C_{12}-$C_{14}E_{21}$	1.0	0.8	4.0	2.0	2.0	1.0	2.0
LAS	-	-	-	0.8	0.8	-	0.8
枯烯磺酸钠	1.5	2.6	-	1.5	1.5	1.5	1.5
Isachem® AS	0.6	0.6	-	-	-	0.6	-
Na_2CO_3	0.6	0.13	0.6	0.1	0.2	0.6	0.2
二水合柠檬酸三钠	0.5	0.56	0.5	0.6	0.75	0.5	0.75
NaOH	0.3	0.33	0.3	0.3	0.5	0.3	0.5
脂肪酸	0.6	0.13	0.6	0.1	0.4	0.6	0.4
2-丁基辛醇	0.3	0.3	-	0.3	0.3	0.3	0.3
PEG DME-2000®	0.4	-	0.3	0.35	0.5	-	-
PVP	0.3	0.4	0.6	0.3	0.5	-	-
MME PEG (2000)®	-	-	-	-	-	0.5	0.5
Jeffamine® ED-2001	-	0.4	-	-	0.5	-	-
PAAC	-	-	-	0.03	0.03	0.03	-
DETBCHD	0.03	0.05	0.05	-	-	-	-
nprE（任选）	0.07	-	0.08	0.03	-	0.01	0.04
PMN	-	0.05	-	-	0.06	-	-
蛋白酶 B（任选）	-	-	-	-	-	0.01	-
淀粉酶	0.12	0.01	0.01	-	0.02	-	0.01
脂肪酶	-	0.001	-	0.005	-	0.005	-
果胶裂解酶	0.001	-	0.001	-	-	-	0.002
ZnCl2	0.02	0.01	0.03	0.05	0.1	0.05	0.02
甲酸钙	0.03	0.03	0.01	-	-	-	-
PB1	-	4.6	-	3.8	-	-	-
醛糖氧化酶	0.05	-	0.03	-	0.02	0.02	0.05
余量为香料/染料和/或水，补足到 100%							

[0981] 实例20(I)至(VII)的pH为约7.4至约9.5。

[0982] 实例21

[0983] 自动盘碟洗涤性能测试

[0984] 在本实例中，描述了用于使用一些市售的盘碟洗涤剂测定蛋白酶变体的洗涤性能的方法。这些蛋白酶变体中各种条件下测试。这些洗涤剂可从WFK商购获得并通过下文提供的名称来指代。下面提供了用于每种污渍类型(肉糜、蛋黄和含有奶的蛋黄)的方案。在可将各污垢类型施加至测试盘碟之前，必须对餐具进行彻底洗涤。这是特别必要的，因为某些持久污渍的残余物可能会仍存在于来自之前的测试的盘碟上。在新盘碟在测试中第一次使用前，也将其进行三次彻底洗涤。

[0985] 洗涤测试通常在自动盘碟洗涤机(例如Miele:G690SC)中进行，该盘碟洗涤剂装配有染污的盘碟和不锈钢板，如上所述。使用定量的洗涤剂，如下面结果表格中所指出的。在一些实验中，测试的温度为45℃、55℃和65℃。在一些实验中，水硬度为9°或21°GH(德国硬度)(374ppm Ca)。

[0986] 如上所指出，在洗涤后，利用0至10的照片等级量表对用肉糜或意大利面食/调味料/肉/奶酪染污的盘子进行视觉评估，其中“0”表示完全脏的盘子，“10”表示清洁的盘子。这些值与含酶洗涤剂的污渍或污垢移除(SR)能力相对应。

[0987] 将洗涤过的污染有蛋黄和/或蛋黄奶的不锈钢板通过重量测定法进行分析，以测定洗涤后残余污渍的量。

[0988] 下面提供了一些示例性的洗涤剂。

[0989]

表 20-1：无磷酸盐洗涤剂 IEC-60436 WFK B 型（pH=10.4，3g/l）	
组分	重量%
脱水柠檬酸钠	30.0
马来酸/丙烯酸共聚物钠盐（SOKALAN® CP5；BASF）	12.0
过硼酸钠一水合物	5.0
TAED	2.0
二硅酸钠：Protil A (Cognis)	25.0
直链脂肪醇乙氧基化物	2.0
无水碳酸钠	加至 100

[0990]

表 20-2：含磷酸盐洗涤剂：IEC-60436 WFK C 型（pH=10.5，3g/l）	
组分	重量%

[0991]

表 20-2：含磷酸盐洗涤剂：IEC-60436 WFK C 型（pH=10.5，3g/l）	
组分	重量%
三聚磷酸钠	23.0
脱水柠檬酸钠	22.3
马来酸/丙烯酸共聚物钠盐	4.0
过硼酸钠一水合物	6.0
TAED	2.0
二硅酸钠：Protil A (Cognis)	5.0
直链脂肪醇乙氧基化物	2.0
无水碳酸钠	加至 100

[0992] 本申请要求保护以下技术方案：

[0993] 1.一种分离的枯草杆菌蛋白酶变体,其中所述枯草杆菌蛋白酶变体为具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:G020R-N043R,N062E-A158E,S103G-A158E,S128N-A158E,A016S-A158E,V104L-A158E,E089P-A158E,L111V-A158E,T022A-A158E,S101A-A158E,L148I-A158E,P129E-A158E,T022A-E089P,A016S-E089P,N062E-E089P,N062E-E271F,A158E-E271F,R186H-E271F,P129E-E271F,L111V-E271F,Y209E-E271F,A016S-E271F,S188D-E271F,T022A-E271F,G159E-E271F,V104L-E271F,S101A-E271F,E089P-E271F,S128N-E271F,S103G-E271F,L148I-E271F,H249R-E271F,N062E-G159E,A016S-G159E,S128N-G159E,L148I-G159E,L111V-G159E,E089P-G159E,T022A-G159E,P129E-G159E,S103G-G159E,V104L-G159E,A158E-G159E,S101A-G159E,A158E-H249R,L111V-H249R,P129E-H249R,N062E-H249R,A016S-H249R,R186H-H249R,L148I-H249R,G159E-H249R,S101A-H249R,S188D-H249R,V104L-H249R,Y209E-H249R,T022A-H249R,S128N-H249R,S103G-H249R,E089P-H249R,T022A-L111V,S101A-L111V,A016S-L111V,V104L-L111V,N062E-L111V,S103G-L111V,E089P-L111V,A016S-L148I,N062E-L148I,T022A-L148I,P129E-L148I,V104L-L148I,S103G-L148I,S128N-L148I,S101A-L148I,E089P-L148I,L111V-L148I,A016S-N062E,T022A-N062E,N062E-P129E,T022A-P129E,S128N-P129E,A016S-P129E,S101A-P129E,V104L-P129E,E089P-P129E,S103G-P129E,L111V-P129E,N062E-R186H,S128N-R186H,S101A-R186H,T022A-R186H,A016S-R186H,A158E-R186H,E089P-R186H,P129E-R186H,G159E-R186H,S103G-R186H,V104L-R186H,L111V-R186H,L148I-R186H,N062E-S101A,T022A-S101A,A016S-S101A,E089P-S101A,N062E-S103G,T022A-S103G,A016S-S103G,S101A-S103G,E089P-S103G,N062E-S128N,A016S-S128N,T022A-S128N,S101A-S128N,V104L-S128N,E089P-S128N,S103G-S128N,L111V-S128N,L111V-S188D,N062E-S188D,A016S-S188D,L148I-S188D,T022A-S188D,S128N-S188D,S101A-S188D,V104L-S188D,E089P-S188D,P129E-S188D,G159E-S188D,R186H-S188D,S103G-S188D,A158E-S188D,A016S-T022A,A016S-V104L,T022A-V104L,S101A-V104L,N062E-V104L,S103G-V104L,E089P-V104L,G159E-Y209E,L111V-Y209E,S101A-Y209E,A016S-Y209E,S128N-Y209E,L148I-Y209E,P129E-Y209E,N062E-Y209E,T022A-Y209E,S103G-Y209E,A158E-Y209E,S188D-Y209E,V104L-Y209E,E089P-Y209E,R186H-Y209E,N018R-W241R,G020R-W241R,S024R-W241R,S009A-W241R,G020R-W241R,V004R-W241R,N043R-W241R,S078R-W241R,T022R-W241R,G115R-W241R,A001R-W241R,S212F-W241R,L082R-W241R,N018R-V244R,S024R-V244R,S078R-V244R,G020R-V244R,S212F-V244R,S009A-V244R,L082R-V244R,A001R-V244R,N043R-V244R,T022R-V244R,V004R-V244R,G115R-V244R,W241R-V244R,S242R-V244R,A001R-V004R,S009A-T022R,N018R-T022R,G020R-T022R,V004R-T022R,A001R-T022R,S024R-S242R,N018R-S242R,V004R-S242R,G020R-S242R,S212F-S242R,L082R-S242R,S078R-S242R,A001R-S242R,S009A-S242R,T022R-S242R,G115R-S242R,N043R-S242R,W241R-S242R,N018R-S212F,T022R-S212F,V004R-S212F,S024R-S212F,A001R-S212F,G115R-S212F,G020R-S212F,S009A-S212F,N043R-S212F,S078R-S212F,L082R-S212F,S009A-S078R,G020R-S078R,S024R-S078R,T022R-S078R,N018R-S078R,V004R-S078R,A001R-S078R,N043R-S078R,T022R-S024R,G020R-S024R,N018R-S024R,A001R-S024R,

V004R-S024R,S009A-S024R,V004R-S009A,A001R-S009A,S242R-N269R,S024R-N269R,G020R-N269R,T022R-N269R,H249R-N269R,S212F-N269R,N043R-N269R,V244R-N269R,A001R-N269R,N018R-N269R,S078R-N269R,S009A-N269R,G115R-N269R,W241R-N269R,V004R-N269R,L082R-N269R,N018R-N043R,G020R-N043R,V004R-N043R,T022R-N043R,S009A-N043R,A001R-N043R,S024R-N043R,S009A-N018R,V004R-N018R,A001R-N018R,S024R-L082R,S009A-L082R,N018R-L082R,A001R-L082R,S078R-L082R,G020R-L082R,T022R-L082R,V004R-L082R,N043R-L082R,N043R-H249R,G020R-H249R,V004R-H249R,N018R-H249R,S009A-H249R,S212F-H249R,T022R-H249R,S024R-H249R,G115R-H249R,A001R-H249R,L082R-H249R,S242R-H249R,W241R-H249R,V244R-H249R,S078R-H249R,N018R-G115R,G020R-G115R,T022R-G115R,S078R-G115R,S009A-G115R,V004R-G115R,A001R-G115R,L082R-G115R,N043R-G115R,S024R-G115R,S009A-G020R,N018R-G020R,V004R-G020R,A001R-G020R,S009A-E271L,G020R-E271L,S024R-E271L,V244R-E271L,W241R-E271L,N043R-E271L,T022R-E271L,H249R-E271L,S212F-E271L,G115R-E271L,S242R-E271L,S078R-E271L,V004R-E271L,N269R-E271L,A001R-E271L,N018R-E271L,和L082R-E271L,并且其中所述变体的总净电荷相对于迟缓芽孢杆菌(Bacillus lentus)枯草杆菌蛋白酶GG36蛋白酶的总净电荷为0、+1、+2、+3、+4、+5、-1、-2、-3、-4或-5,并且其中所述总净电荷是通过一种或多种选自以下的置换来获得的:N43D,R45T,N62E,N76D,S101D,P129E,A158E,G159D,G159E,S166D,S188D,A230E,N18R,G20K,G20R,T22R,S24R,N43R,G118R,Q245R,H249R,N269R,E271F,和E271L,并且其中所述蛋白酶变体的氨基酸位置根据SEQ ID NO:1所示解淀粉芽孢杆菌(Bacillus amyloliquefaciens)枯草杆菌蛋白酶BPN'的氨基酸序列中对应的氨基酸位置的编号方式来进行编号。

[0994] 2.一种分离的枯草杆菌蛋白酶变体,其中所述枯草杆菌蛋白酶变体为具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:G020R-N043R,G020K-N062E,S024F-N116L,G020K-S024F,S024R-A174T,S024R-G118R,S024R-K235F,S024R-P086R,S024R-P086W,S078R-G118R,T033S-G118R,T033S-K235F,Y209A-W241R,G020R-N076D,N018R-Q245R,S024R-R045T,A232V-Q245R,G118R-A172V,G118R-A194T,I008T-S024R,K235F-N243F,N018R-S103A,N018R-V104I,P086W-G118R,P086W-N243F,P086W-Y209A,S024C-T033S,S024R-A232V,S024R-N243F,S024R-P239Q,S024R-S101G,S024R-S141G,S024R-T033S,S024R-T274I,S024R-Y209A,S078R-P086W,S101G-A232V,T033S-L148F,T033S-P086W,T033S-P201S,T033S-S078R,T033S-W241R,T033S-Y209A,A230E-H249R,A232V-H249R,G118R-K235F,N076D-Q245R,P086W-K235F,S024R-R247H,S024R-V104A,S078R-K235F,S101G-H249R,S103A-A232V,T033S-A048T,T033S-P239T,T033S-T253A,T143A-Y209A,Y209A-K235F,N018R-R045T,Y209A-N243F,S024R-A272P,S024R-R269C,S101G-V104I,V104I-A232V,N076D-H249R,和S024R-N076D,并且其中所述变体的总净电荷相对于迟缓芽孢杆菌(Bacillus lentus)枯草杆菌蛋白酶GG36蛋白酶的总净电荷为0、+1、+2、+3、+4、+5、-1、-2、-3、-4或-5,并且其中所述总净电荷是通过一种或多种选自以下的置换来获得的:N43D,R45T,N62E,N76D,S101D,P129E,A158E,G159D,G159E,S166D,S188D,A230E,N18R,G20K,G20R,T22R,S24R,N43R,G118R,Q245R,H249R,N269R,E271F,和E271L,并且其中所述蛋白酶变体的氨基酸位置根据SEQ ID NO:1所示解淀粉芽孢杆菌

(Bacillus amyloliquefaciens)枯草杆菌蛋白酶BPN'的氨基酸序列中对应的氨基酸位置的编号方式来进行编号。

[0995] 3.一种分离的枯草杆菌蛋白酶变体,其中所述枯草杆菌蛋白酶变体为具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:G020R-N076D,S024R-R045T,A230E-H249R,N018R-R045T,N018R-Q245R,S101G-A232V,S024R-A232V,A232V-Q245R,S024R-S101G,N018R-V104I,N018R-S103A,S101G-H249R,A232V-H249R,S103A-A232V,N076D-Q245R,S101G-V104I,V104I-A232V,N076D-H249R,S024R-N076D,S024F-N116L,G020K-S024F,G020K-N062E,T033S-G118R,S024R-P086W,S024R-G118R,S024R-P086R,Y209A-W241R,S024R-W241R,S024R-K235F,G118R-Y209A,S078R-G118R,T033S-K235F,S024R-A174T,P086W-Y209A,I008T-S024R,P086W-G118R,T033S-W241R,S024R-N243F,S024R-Y209A,T033S-P086W,S024R-T033S,P086W-N243F,T033S-P201S,S024R-P239Q,S078R-P086W,K235F-N243F,G118R-A172V,T033S-L148F,T033S-S078R,T033S-N243F,S024C-T033S,G118R-A194T,T033S-Y209A,S024R-S141G,S024R-T274I,P086W-K235F,A015T-T033S,Y209A-K235F,S024R-R247H,S078R-K235F,S024R-V104A,T033S-A048T,G118R-K235F,T033S-T253A,T143A-Y209A,T033S-P239T,Y209A-N243F,S024R-A272P,和S024R-R269C,并且其中所述变体的总净电荷相对于迟缓芽孢杆菌(Bacillus lentus)枯草杆菌蛋白酶GG36蛋白酶的总净电荷为0、+1、+2、+3、+4、+5、-1、-2、-3、-4或-5,并且其中所述总净电荷是通过一种或多种选自以下的置换来获得的:N43D,R45T,N62E,N76D,S101D,P129E,A158E,G159D,G159E,S166D,S188D,A230E,N18R,G20K,G20R,T22R,S24R,N43R,G118R,Q245R,H249R,N269R,E271F,和E271L,并且其中所述蛋白酶变体的氨基酸位置根据SEQ ID NO:1所示解淀粉芽孢杆菌(Bacillus amyloliquefaciens)枯草杆菌蛋白酶BPN'的氨基酸序列中对应的氨基酸位置的编号方式来进行编号。

[0996] 4.一种分离的枯草杆菌蛋白酶变体,其中所述枯草杆菌蛋白酶变体为具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:G020K-G023A-N043W-G118R-S128I-P129E-G159D-S188D,G020K-G023A-N062E-N116L,G020K-G023A-N062E-N116L-S188D,G020K-G023A-N062E-N116L-S188D-T213A,G020K-G100S-N116L-A158E-S166D-N243F,G020K-N043W-N062E-N116L-S188D,G020K-N062E,G020K-N062E-N116L,G020K-N062E-N116L-S188D,G020K-N062E-N116L-T213A,G020K-N062E-S188D-T213A,G020K-S024F-N062E-N116L-G118R-S188D,G020K-S024F-N062E-N116L-S188D,G020K-S024F-N062E-S188D-T213A,G023A-N062E-N116L-S188D,G023A-S024F-N062E-N116L-T213A,N043R-N076D-S101A-S103A-V104I-A158E-S188D-L217E-A232V-Q245R-N248D-H249R-E271F,N043R-S101A-S103A-V104I-A158E-S188D-L217E-A232V-Q245R-N248D-H249R,N043W-N062E-N116L,N043W-S101D-S212M-N243F,N062E-N116L-G118R-S188D,N062E-N116L-G118R-T213A,N062E-N116L-S188D-T213A,S024F-G118R-S128I-P129E-G159D,S024F-N062E-N116L-S188D,S024R-S101G-S103A-V104I-A158E-N183D-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-A158E-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-A158E-S188D-L217E-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-P129Q-A158E-N183D-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-P129Q-A158E-S188D-A232V-Q245R-N248D-

H249R,S024R-S101G-S103A-V104I-P129Q-A158E-S188D-L217E-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-P129Q-S130A-A158E-N183D-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-S128L-P129Q-A158E-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-S130A-A158E-N183D-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-S130A-A158E-S188D-A232V-Q245R-N248D-H249R,S101D-S103N-N116L-S144R-A215D,S101G-S103A-V104I-A158E-S188D-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-S130A-A158E-S188D-A232V-Q245R-N248D-H249R,T022A-N043R-S101G-S103A-V104I-G159D-S188D-L217E-A232V-Q245R-N248D-E271F,T022A-N043R-S103A-V104I-G118R-S128I-P129E-G159D-S188D-A232V-N248D-E271F,T022A-N043R-S103A-V104I-S128I-P129E-G159D-S188D-A232V-Q245R-N248D,T022A-S024R-S103A-V104I-G118R-S128I-P129E-G159D-S188D-A232V-N248D,T022A-S101G-S103A-V104I-G159D-L217E-A232V-Q245R-N248D-E271F,T022A-S101G-S103A-V104I-G159D-S188D-A232V-Q245R-N248D-E271F,T022L-T038F-A048R-N062E-G100S-R186K,T033S-N043W-N218D-P239G-N243F,V026F-A048R-S105T-T213A-N218D-T224A,V026F-L031F-S078N-G102A-S160D,V026F-V051W-V104L-S106E,V104L-S105T-T213A-L217E-S256N,A016S-N062E-A158E-H249R,A016S-N062E-A158E-R186H-E271F,A016S-N062E-A158E-R186H-H249R,A016S-N062E-V104L-A158E-R186H-E271F,A016S-S024R-S101G-S103A-V104I-A158E-S188D-A232V-Q245R-N248D-H249R,G020K-G023A-N062E-S188D,G020K-G023A-S024F-N062E-G118R-S188D-T213A,G020K-N043W-N062E-N116L-S188D-T213A-P239G,G020K-S024F-N062E-S188D-P239G,G023A-N062E-N116L-G118R,G023A-N062E-N116L-G118R-S188D-P239G,G023A-S024F-N062E-N116L-G118R,H017R-T022A-N076D-S101G-S103A-V104I-G159D-S188D-A232V-Q245R-N248D-E271F,N043R-N076D-S101A-S103A-V104I-A158E-S188D-A232V-Q245R-N248D-H249R-E271F,N062E-A158E-G159E-H249R,N062E-A158E-H249R,N062E-A158E-R186H-E271F,N062E-A158E-R186H-H249R,N062E-A158E-R186H-H249R-E271F,N062E-A158E-S188D-H249R,N062E-A158E-S188D-H249R-E271F,N062E-G159E-H249R,N062E-G159E-H249R-E271F,N062E-G159E-R186H-H249R,N062E-G159E-S188D-H249R,N062E-R186H-S188D-H249R-E271F,N062E-S101A-A158E-H249R,N062E-S101A-A158E-R186H-E271F,N062E-S101A-A158E-R186H-H249R-E271F,N062E-S101A-G159E-H249R,N062E-S101A-R186H-H249R,N062E-S101A-S188D-H249R,N062E-S101A-S188D-H249R-E271F,N062E-S101A-V104L-A158E-R186H-E271F,N062E-S128N-A158E-G159E-E271F,N062E-V104L-A158E-S188D-H249R-E271F,N076D-S101G-S103A-V104I-A232V-M222Q-Q245R,S024F-N062E-N116L-P239G,S024F-N062E-S188D-T213A,S024F-N116L,S024R-N043R-N076D-S101A-S103A-V104I-A158E-S188D-L217E-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-A158E-G159E-A232V-N238R-Q245R-N248D,S024R-S101G-S103A-V104I-A158E-G159E-S188D-A232V-Q245R-N248D,S024R-S101G-S103A-V104I-A158E-S188D-A232V-N238R-Q245R-N248D,S024R-S101G-S103A-V104I-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-G159E-S188D-A232V-N238R-Q245R-N248D,S024R-S101G-S103A-V104I-G159E-S188D-A232V-Q245R-N248D,S024R-S101G-S103A-V104I-G159E-S188D-A232V-Q245R-

N248D-H249R,S024R-S101G-S103A-V104I-L148I-A158E-A232V-Q245R-N248D,S024R-S101G-S103A-V104I-L148I-A158E-S188D-A232V-Q245R-N248D,S024R-S101G-S103A-V104I-L148I-A232V-Q245R-N248D,S024R-S101G-S103A-V104I-P129E-A158E-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-P129E-A158E-G159E-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-P129E-A158E-S188D-A232V-Q245R-N248D,S024R-S101G-S103A-V104I-P129E-A158E-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-P129E-G159E-A232V-Q245R-N248D,S024R-S101G-S103A-V104I-P129E-G159E-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-P129E-L148I-A158E-A232V-Q245R-N248D,S024R-S101G-S103A-V104I-P129E-S188D-A232V-N238R-Q245R-N248D,S024R-S101G-S103A-V104I-P129E-S188D-A232V-Q245R-N248D,S024R-S101G-S103A-V104I-P129E-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-S128N-A158E-A232V-Q245R-N248D,S024R-S101G-S103A-V104I-S128N-P129E-A158E-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-S128N-P129E-A232V-Q245R-N248D,S101A-S103A-V104I-A158E-S188D-A232V-Q245R-N248D-H249R,S101A-S103A-V104I-A158E-S188D-A232V-Q245R-N248D-H249R-E271F-E271F,S101A-S103A-V104L-A158E-S188D-A232V-Q245R-N248D-H249R,S101A-S128N-A158E-R186H-E271F,S101A-S128N-A158E-Y209E-H249R,S101A-V104L-A158E-R186H-S188D-H249R,S101G-S103A-V104I-A158E-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-A158E-G159E-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-A158E-S188D-M222Q-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-A158E-S188D-M222S-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-A232V-M222Q-Q245R,S101G-S103A-V104I-P129E-A158E-S188D-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-P129E-G159E-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-P129E-S188D-A232V-N238R-Q245R-N248D,S101G-S103A-V104I-P129E-S188D-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-S188D-A232V-Q245R-N248D-H249R,S101G-S103G-V104I-A158E-S188D-A232V-Q245R-N248D-H249R,S101G-S103S-V104I-A158E-S188D-A232V-Q245R-N248D-H249R,S101S-S103A-V104I-A158E-S188D-A232V-Q245R-N248D-H249R,S101S-S103G-V104I-A158E-S188D-A232V-Q245R-N248D-H249R,S101S-S103G-V104V-A158E-S188D-A232V-Q245R-N248D-H249R,S128N-A158E-G159E-E271F,S128N-A158E-H249R,S128N-A158E-R186H-E271F,S128N-A158E-R186H-H249R,S128N-A158E-R186H-S188D-E271F,S128N-A158E-S188D-E271F,S128N-A158E-S188D-H249R,S128N-A158E-S188D-Y209E-E271F,S128N-A158E-Y209E-,T022A-N043R-S103A-V104I-G118R-P129E-G159D-S188D-A232V-Q245R-N248D,T022A-N062E-A158E,T022A-S024R-S101D-S103A-V104I-G118R-G159D-S188D-A232V-N248D-E271F,T022A-S024R-S101D-S103A-V104I-G118R-P129E-G159D-S188D-A232V-Q245R-N248D,T022A-S024R-S101D-S103A-V104I-G159D-S188D-A232V-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-A158E-A232V-N238R-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-A158E-A232V-Q245R-N248D-H249R,T022A-S024R-S101G-S103A-V104I-A158E-G159E-S188D-A232V-N238R-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-A158E-G159E-S188D-A232V-Q245R-N248D,T022A-S024R-S101G-S103A-

V104I-A158E-G159E-S188D-A232V-Q245R-N248D-H249R,T022A-S024R-S101G-S103A-V104I-P129E-A158E-A232V-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-P129E-A158E-A232V-Q245R-N248D-H249R,T022A-S024R-S101G-S103A-V104I-P129E-A158E-G159E-A232V-Q245R-N248D-H249R,T022A-S024R-S101G-S103A-V104I-P129E-A158E-G159E-S188D-A232V-N238R-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-P129E-A158E-S188D-A232V-N238R-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-P129E-A158E-S188D-A232V-Q245R-N248D-H249R,T022A-S024R-S101G-S103A-V104I-P129E-A232V-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-P129E-A232V-Q245R-N248D-H249R,T022A-S024R-S101G-S103A-V104I-P129E-G159E-S188D-A232V-Q245R-N248D-H249R,T022A-S024R-S101G-S103A-V104I-P129E-S188D-A232V-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-S128N-A158E-S188D-A232V-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-S128N-P129E-A158E-A232V-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-S128N-P129E-S188D-A232V-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-S128N-S188D-A232V-Q245R-N248D,T022A-S024R-S103A-V104I-G118R-G159D-S188D-L217D-A232V-N248D,T022A-S024R-S103A-V104I-P129E-G159D-S188D-A232V-N248D-E271F,T022A-S101G-S103A-V104I-A158E-G159E-S188D-A232V-Q245R-N248D-H249R,T022A-S101G-S103A-V104I-A158E-S188D-A232V-Q245R-N248D,T022A-S101G-S103A-V104I-P129E-A158E-A232V-N238R-Q245R-N248D,T022A-S101G-S103A-V104I-P129E-A158E-G159E-A232V-N238R-Q245R-N248D,T022A-S101G-S103A-V104I-P129E-A158E-S188D-A232V-Q245R-N248D-H249R,T022A-S101G-S103A-V104I-P129E-G159E-A232V-N238R-Q245R-N248D,T022A-S101G-S103A-V104I-P129E-S188D-A232V-N238R-Q245R-N248D,T022A-S101G-S103A-V104I-S128N-P129E-A232V-N238R-Q245R-N248D,T022A-S101G-S103A-V104I-S128N-P129E-S188D-A232V-N238R-Q245R-N248D,T022A-S128N-A158E-H249R,V104L-S128N-A158E-H249R,V104L-S128N-A158E-R186H-E271F,V104L-S128N-A158E-R186H-H249R,和V104L-S128N-A158E-S188D-H249R,并且其中所述变体的总净电荷相对于迟缓芽孢杆菌(Bacillus lentus)枯草杆菌蛋白酶GG36蛋白酶的总净电荷为0、+1、+2、+3、+4、+5、-1、-2、-3、-4或-5,并且其中所述总净电荷是通过一种或多种选自以下的置换来获得的:N43D,R45T,N62E,N76D,S101D,P129E,A158E,G159D,G159E,S166D,S188D,A230E,N18R,G20K,G20R,T22R,S24R,N43R,G118R,Q245R,H249R,N269R,E271F,和E271L,并且其中所述蛋白酶变体的氨基酸位置根据SEQ ID NO:1所示解淀粉芽孢杆菌(Bacillus amyloliquefaciens)枯草杆菌蛋白酶BPN'的氨基酸序列中对应的氨基酸位置的编号方式来进行编号。

[0997] 5.一种分离的枯草杆菌蛋白酶变体,其中所述枯草杆菌蛋白酶变体为具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:A016S-N062E-A158E-H249R-E271F,A016S-N062E-S128N-R186H-E271F,A016S-N062E-V104L-R186H-S188D-E271F,A016S-S101A-S128N-R186H,A016S-S128N-A158E-R186H,A016S-V104L-A158E-R186H-E271F,A016S-V104L-S188D-H249R,A158E-R186H-H249R,A158E-R186H-S188D-H249R-E271F,G020K-G023A-N116L-S188D,G020K-G023A-S024F-N062E-N116L-S188D-T213A,G020K-N043W-N062E-N116L-P239G,G020K-S024F-N043W-N062E-N116L-

T213A,G020K-S024F-N062E,G023A-N043W-N062E-N116L-G118R-T213A,G023A-T038F-S078N-G100S-S212M-A215D,G100S-N116L-A158E-T213A,G102A-S103N-S105T-A194E,H017R-T022A-N076D-S101G-S103A-V104I-G159D-A232V-Q245R-N248D-E271F,N043R-N076D-S101A-S103A-V104I-A158E-S166D-S188D-A232V-Q245R-N248D-H249R-E271F,N043R-S101A-S103A-V104I-A158E-S166D-S188D-A232V-Q245R-N248D-H249R,N043W-N062E-N116L-S188D,N062E-A158E-H249R-E271F,N062E-A158E-R186H-S188D-H249R,N062E-L148I-G159E,N062E-N116L-S188D,N062E-R186H-H249R,N062E-S078N-G102A-N116L-S144R-L250I,N062E-S101A-A158E-R186H-H249R,N062E-S101A-A158E-S188D-H249R,N062E-S101A-R186H,N062E-S101A-R186H-E271F,N062E-S101A-R186H-H249R-E271F,N062E-S101A-R186H-S188D-E271F,N062E-S101A-R186H-S188D-H249R,N062E-S101A-V104L-R186H-S188D-E271F,N062E-S128N-A158E,N062E-S128N-G159E-H249R,N062E-S188D-P239G,N062E-V104L-G159E-H249R,N076D-S101A-S103A-V104I-A158E-S166D-S188D-A232V-Q245R-N248D-H249R-E271F,N076D-S101A-S103A-V104I-A158E-S188D-A232V-Q245R-N248D-H249R,N076D-S101A-S103A-V104I-A158E-S188D-A232V-Q245R-N248D-H249R-E271F,N076D-S101G-S103A-V104I-A114V-A158E-S188D-A232V-Q245R-N248D-H249R-E271F,N076D-S101G-S103A-V104I-A232V-M222S-Q245R,S024F-A048R-G118R-S166D-L217E,S024F-N062E-N116L,S024F-N062E-N116L-T213A-P239G,S024F-N062E-S188D-P239G,S024F-S101D-G118R-A215D-L250I-A272F,S024R-K027R-S101G-S103A-V104I-S128L-P129Q-S130A-A158E-S188D-A232V-Q245R-N248D-H249R,S024R-N076D-S101A-S103A-V104I-A158E-S166D-S188D-A232V-Q245R-N248D-H249R-E271F,S024R-S101G-S103A-V104I-A158E-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-P129E-A158E-G159E-A232V-N238R-Q245R-N248D,S024R-S101G-S103A-V104I-P129E-A158E-G159E-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-P129E-G159E-A232V-N238R-Q245R-N248D,S024R-S101G-S103A-V104I-P129E-G159E-S188D-A232V-N238R-Q245R-N248D,S024R-S101G-S103A-V104I-P129E-L148I-A158E-S188D-A232V-Q245R-N248D,S024R-S101G-S103A-V104I-P129E-L148I-S188D-A232V-Q245R-N248D,S024R-S101G-S103A-V104I-P129Q-S130A-A158E-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-S128L-A158E-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-S128L-P129Q-S130A-A158E-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-S128N-G159E-S188D-A232V-Q245R-N248D,S078N-V104L-G118R-S128D,S101A-A158E-R186H-H249R,S101A-A158E-R186H-S188D-H249R,S101A-S103A-V104I-A158E-S166D-S188D-A232V-Q245R-N248D-H249R-E271F,S101A-S103A-V104I-A158E-S188D-A232V-Q245R-N248D-H249R-E271F,S101A-S103A-V104I-A158E-S188D-L217E-A232V-Q245R-N248D-H249R,S101A-S103A-V104I-A158E-S188D-L217E-A232V-Q245R-N248D-H249R-E271F,S101A-S103G-A158E-R186H-H249R,S101A-S103S-V104I-A158E-S188D-A232V-Q245R-N248D-H249R,S101A-S103S-V104I-G159E-A232V-Q245R-N248D-H249R,S101A-S128N-A158E-H249R,S101A-S128N-A158E-S188D-Y209E-E271F,S101A-S128N-A158E-Y209E,S101A-S128N-P129E-R186H-H249R,S101A-V104L-A158E-R186H-H249R,S101A-V104L-A158E-R186H-S188D-E271F,S101A-

V104L-S128N-A158E-R186H-E271F,S101G-S103A-V104I-A158E-A232V-N238R-Q245R-N248D,S101G-S103A-V104I-A158E-G159E-S188D-A232V-N238R-Q245R-N248D,S101G-S103A-V104I-A158E-N183D-S188D-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-A158E-S166D-S188D-A232V-Q245R-N248D-H249R-E271F,S101G-S103A-V104I-A158E-S188D-A232V-Q245R-N248D,S101G-S103A-V104I-A232V-M222S-Q245R,S101G-S103A-V104I-P129E-A158E-G159E-A232V-N238R-Q245R-N248D,S101G-S103A-V104I-P129E-A158E-G159E-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-P129E-A158E-S188D-A232V-N238R-Q245R-N248D,S101G-S103A-V104I-P129E-G159E-A232V-N238R-Q245R-N248D,S101G-S103A-V104I-P129E-S188D-A232V-Q245R-N248D,S101G-S103A-V104I-P129Q-A158E-S188D-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-P129Q-S130A-A158E-S188D-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-S128L-P129Q-A158E-S188D-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-S128L-S130A-A158E-S188D-L217E-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-S128N-P129E-A232V-N238R-Q245R-N248D,S101G-S103A-V104I-S128N-P129E-A232V-Q245R-N248D,S101G-S103A-V104I-S130A-A158E-N183D-S188D-L217E-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-S188D-A232V-N238R-Q245R-N248D,S101G-S103A-V104L-A158E-S188D-A232V-Q245R-N248D-H249R,S101S-S103A-V104I-G159E-A232V-Q245R-N248D-H249R,S101S-S103S-V104I-A158E-S188D-A232V-Q245R-N248D-H249R,S101S-S103S-V104V-A158E-S188D-A232V-Q245R-N248D-H249R,T022A-N043R-N062E-S103A-V104I-G159D-S188D-A232V-Q245R-N248D-E271F,T022A-N043R-N076D-S101G-S103A-V104I-G159D-S188D-A232V-Q245R-N248D-E271F,T022A-N043R-S101D-S103A-V104I-G118R-P129E-G159D-S188D-A232V-N248D-E271F,T022A-N043R-S101G-S103A-V104I-G159D-A232V-Q245R-N248D-E271F,T022A-N043R-S103A-V104I-G118R-G159D-S188D-A232V-N248D-E271F,T022A-N043R-S103A-V104I-G118R-G159D-S188D-L217D-A232V-N248D-E271F,T022A-N043R-S103A-V104I-G118R-S128I-P129E-G159D-S188D-A232V-N248D,T022A-N043R-S103A-V104I-P129E-G159D-S188D-A232V-Q245R-N248D,T022A-N076D-S101G-S103A-V104I-G159D-A232V-Q245R-N248D-E271F,T022A-N076D-S101G-S103A-V104I-G159D-S188D-A232V-Q245R-N248D-E271F,T022A-S024R-N043R-S101D-S103A-V104I-G159D-S188D-A232V-Q245R-N248D,T022A-S024R-N043R-S103A-V104I-G159D-S188D-L217D-A232V-N248D-E271F,T022A-S024R-S101D-S103A-V104I-G118R-S128I-G159D-S188D-A232V-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-L148I-A158E-A232V-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-P129E-A158E-G159E-A232V-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-P129E-A158E-G159E-S188D-A232V-Q245R-N248D-H249R,T022A-S024R-S101G-S103A-V104I-P129E-L148I-A232V-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-S188D-A232V-Q245R-N248D-H249R,T022A-S024R-S103A-V104I-G118R-P129E-G159D-S188D-A232V-N248D-E271F,T022A-S024R-S103A-V104I-G159D-S188D-L217D-A232V-N248D-E271F,T022A-S024R-S103A-V104I-G159D-S188D-L217D-A232V-Q245R-N248D-E271F,T022A-S101A-A158E-R186H-H249R,T022A-S101G-S103A-V104I-A158E-G159E-A232V-N238R-Q245R-N248D,T022A-S101G-S103A-V104I-

A158E-G159E-A232V-Q245R-N248D-H249R,T022A-S101G-S103A-V104I-G159D-A232V-Q245R-N248D-E271F,T022A-S101G-S103A-V104I-G159D-S188D-A232V-Q245R-N248D-H249R-E271F,T022A-S101G-S103A-V104I-G159E-S188D-A232V-N238R-Q245R-N248D,T022A-S101G-S103A-V104I-G159E-S188D-A232V-Q245R-N248D-H249R,T022A-S101G-S103A-V104I-P129E-A158E-A232V-Q245R-N248D-H249R,T022A-S101G-S103A-V104I-P129E-A158E-G159E-A232V-Q245R-N248D-H249R,T022A-S101G-S103A-V104I-P129E-A232V-N238R-Q245R-N248D,T022A-S101G-S103A-V104I-P129E-G159E-A232V-Q245R-N248D-H249R,T022A-S101G-S103A-V104I-P129E-G159E-S188D-A232V-Q245R-N248D-H249R,T022A-S103A-V104I-G118R-G159D-S188D-L217D-A232V-Q245R-N248D,T022A-S103A-V104I-G159D-S188D-A232V-N248D,T022L-L031F-G102A-S128D-T224A-N243F,T022L-T038F-V121F-S160D-A272F,V026F-S078N-G159C-R186K-N243F,V104L-A158E-H249R,V104L-A158E-R186H-H249R,V104L-A158E-R186H-H249R-E271F,V104L-A158E-R186H-S188D-H249R,V104L-A158E-R186H-S188D-H249R-E271F,V104L-A158E-S188D-H249R-E271F,V104L-S128N-A158E-R186H-S188D-E271F,V104L-S128N-G159E-E271F,V104L-S128N-R186H-S188D-H249R,和V121F-N185E-T224A-P239G,并且其中所述变体的总净电荷相对于迟缓芽孢杆菌(Bacillus lentus)枯草杆菌蛋白酶GG36蛋白酶的总净电荷为0、+1、+2、+3、+4、+5、-1、-2、-3、-4或-5,并且其中所述总净电荷是通过一种或多种选自以下的置换来获得的:N43D,R45T,N62E,N76D,S101D,P129E,A158E,G159D,G159E,S166D,S188D,A230E,N18R,G20K,G20R,T22R,S24R,N43R,G118R,Q245R,H249R,N269R,E271F,和E271L,并且其中所述蛋白酶变体的氨基酸位置根据SEQ ID NO:1所示解淀粉芽孢杆菌(Bacillus amyloliquefaciens)枯草杆菌蛋白酶BPN'的氨基酸序列中对应的氨基酸位置的编号方式来进行编号。

[0998] 6.一种分离的枯草杆菌蛋白酶变体,其中所述枯草杆菌蛋白酶变体为具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:G118R-Y209A,G118R-Y209A-N243F,L021M-S024R-T033S,P005S-S078R-G118R-W241R,P086W-G118R-A133V,P086W-G118R-N243F,P086W-G118R-Y209A,P086W-Y209A-N243F,S024R-A174T,S024R-G118R,S024R-G118R-Y209A,S024R-G118R-Y209A-K235F,S024R-G118R-Y209A-N243F,S024R-K235F,S024R-P086R,S024R-P086S-S141G,S024R-P086W,S024R-P086W-G118R,S024R-P086W-G118R-V203I,S024R-P086W-N243F,S024R-P086W-Y209A,S024R-S078R-P086W,S024R-S078R-P086W-G118R-A270T,S024R-S078R-P086W-N243F,S024R-T033S-A133V,S024R-T033S-G118R,S024R-T033S-P086S-S085N-K235F,S024R-T033S-P086S-S087N-Y209A,S024R-T033S-P086W,S024R-T033S-P086W-G118R,S024R-T033S-S078R-P086W,S024R-T033S-S078R-P086W-G118R,S024R-T033S-S078R-Y209A,S024R-T033S-W241R,S024R-T033S-Y209A-K235F,S024R-Y209A-W241R,S078R-G118R,S078R-P086W-K235F,S078R-P086W-N243F,S078R-P086W-Y209A,S078R-Y209A-K235F,T033S-A172V-Y209A,T033S-G118R,T033S-G118R-G159D-Y209A,T033S-G118R-N243F,T033S-G118R-W241R,T033S-G118R-Y209A-N243F,T033S-K235F,T033S-P086W-G118R,T033S-P086W-G118R-Y209A-N243F,T033S-P086W-N243F,T033S-S078R-P086W,T033S-S078R-P086W-G118R-Y209A,T033S-S078R-Y209A,T033S-Y209A-N243F,Y209A-W241R,A001R-

S009A-N043R,A001R-S101G-S103A-V104I-A232V-Q245R,A001T-N018R-S024R-N076D-N116A-T213A-H249R,A194F-G211Q-Q236N,E089I-N116A-N117F-T224A-H249R,G020R-G025R-N116A-Y167W,G020R-H249R-N269R,G020R-N043D-N076D-A230E-H249R,G020R-N043D-S078R-S101G-S103A-V104I-A232V-Q245R,G020R-N043D-S101G-S103A-V104I-A232V-Q245R,G020R-N043D-S101G-S103A-V104I-A232V-Q245R-N269R,G020R-N043R-A230E,G020R-N043R-A230E-S242R,G020R-N043R-E271L,G020R-N043R-H249R,G020R-N043R-H249R-E271L,G020R-N043R-N269R,G020R-N043R-R045T-A230E,G020R-N043R-R045T-S101A-N269R,G020R-N043R-R045T-S242R,G020R-N043R-S101A-N116A-T213A-A215F,G020R-N043R-S101A-N269R,G020R-N043R-S101G-S103A-V104I-A232V-Q245R,G020R-N043R-S212F,G020R-N043R-S212F-W241R,G020R-N043R-S242R,G020R-N043R-S242R-E271L,G020R-N043R-S242R-H249R,G020R-N043R-V244R,G020R-N043R-W241R,G020R-N062Q-E089I-R186K-S212M,G020R-N076D,G020R-N076D-S101G-S103A-V104I-A232V-Q245R,G020R-N076D-S101G-S103A-V104I-A232V-Q245R-N269R,G020R-N116A-N269R,G020R-P052N-N062Q-Y091F-Y192W,G020R-Q059A-S144R-Y192W-T224A,G020R-S024R-K27E-N043R-N076D-A230E,G020R-S024R-N043D-H249R,G020R-S024R-N043D-N076D-S078R-S101G-S103A-V104I-A232V-Q245R,G020R-S024R-N043D-S242R,G020R-S024R-N043R-R045T,G020R-S024R-N043R-R045T-H249R,G020R-S024R-N043R-R045T-N116A,G020R-S024R-N043R-R045T-N116A-T213A,G020R-S024R-N043R-R045T-S101A-N269R,G020R-S024R-N043R-R045T-S101A-T213A,G020R-S024R-N043R-S242R,G020R-S024R-N076D-H249R,G020R-S024R-N116A,G020R-S024R-N116A-A215F,G020R-S024R-N116A-T213A,G020R-S024R-N116A-T213A-A215F,G020R-S024R-P052N-Q059A-S216F,G020R-S024R-R045T-A230E-S242R,G020R-S024R-R045T-N116A-N269R,G020R-S024R-R045T-N269R,G020R-S024R-S101A-A215F,G020R-S024R-S101A-N116A,G020R-S024R-S101G-S103A-V104I-L217E-A232V-Q245R-H249R,G020R-S024R-S242R-H249R,G020R-S024R-T213A,G020R-S024R-T213A-A215F,G020R-S078R-S101A-S103A-V104I-N116A-N183D-T213A-A232V-Q245R,G020R-S078R-S101G-A232V-Q245R,G020R-S078R-S101G-S103A-V104I-A215F-A232V-Q245R,G020R-S078R-S101G-S103A-V104I-G211Q-T213A-A215F-A232V-Q245R,G020R-S078R-S101G-S103A-V104I-N116A-A232V-Q245R,G020R-S078R-S101G-S103A-V104I-N116A-G211Q-A232V-Q245R,G020R-S078R-S101G-S103A-V104I-N116A-N183D-A232V-Q245R,G020R-S087D-S101G-S103A-V104I-A232V-Q245R,G020R-S101A-N116A-N269R,G020R-S101A-S103A-V104I-A215F-A232V-Q245R,G020R-S101A-S103A-V104I-G118R-A232V-Q245R,G020R-S101A-S103A-V104L-A232V-Q245R,G020R-S101A-S103A-V104V-A232V-Q245R,G020R-S101A-S103S-V104I-A232V-Q245R,G020R-S101A-S103S-V104V-A232V-Q245R,G020R-S101G-I198L-A215F-A232V-Q245R,G020R-S101G-S103A-A232V-Q245R,G020R-S101G-S103A-V104I-A215F-A232V-Q245R,G020R-S101G-S103A-V104I-A232V-Q245R,G020R-S101G-S103A-V104I-A232V-Q245R-N269R,G020R-S101G-S103A-V104I-G211Q-T213A-A215F-A232V-Q245R,G020R-S101G-S103A-V104I-N116A-A215F-A232V-Q245R,G020R-S101G-S103A-V104I-T213A-A215F-A232V-Q245R,G020R-S101G-S103A-V104I-V150L-A232V-Q245R,G020R-S101G-S103A-V104L-

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V004R-G020R-N043R,V004R-G020R-S024R,V004R-G020R-S024R-H249R,V004R-G020R-S024R-N043R,V004R-G020R-S024R-N043R-S242R,V004R-G020R-S024R-V244R,V004R-N043R-S101G-S103A-V104I-A232V-Q245R,V004R-S009A-G020R-N043R,V004R-S009A-G020R-N043R-S242R,V004R-S009A-G020R-S024R-S242R,V004R-S009A-G020R-S242R,V004R-S009A-N043R-W241R,V004R-S009A-S024R-N043R-W241R,V004R-S009A-S078R-W241R,V004R-S009A-W241R,V004R-S101G-S103A-V104I-A232V-Q245R,V104L-L217E-T224A-H249R-N252R,V104L-T213A-S216F,V121F-N252R-A270C,Y091F-S099F-S101A-S105T-Y167W,N043R-N076D-A230E-H249R,S024R-N043D-N076D-S242R-H249R,G020R-S024R-N043D-R045T,N043R-N076D-H249R,N043R-R045T-H249R,G020R-N043R-N076D,A230E-H249R,N043D-S242R-H249R,G020R-S024R-N043D-N076D-S242R-H249R,S024R-N043D-S242R-H249R,N018R-N043D-R045T-N076D-S242R-H249R,S024R-N043R-N076D,N018R-G020R-H249R,N018R-G020R-N043R,G020R-S024R-T38I-N043R-R045T-N076D-S242R-H249R,S024R-N043R-N076D-A230E-S242R,N018R-G020R-N043D-R045T-N076D-S242R,N018R-S024R-N043D-A230E-H249R,N018R-N043R-N076D-S242R-H249R,G020R-S024R-K27R-N043D-S242R-H249R,G020R-S242R-H249R,N018R-N043R-R045T-S242R,G020R-N043R-N076D-A230E-H249R,N018R-N043R-N076D-S242R,N018R-G020R-N043R-N076D,N018R-S024R-N043D-S242R,R045T-S242R-H249R,N018R-G020R-N043R-R045T-N076D-H249R,并且其中所述变体的总净电荷相对于迟缓芽孢杆菌(Bacillus lentus)枯草杆菌蛋白酶GG36蛋白酶的总净电荷为0、+1、+2、+3、+4、+5、-1、-2、-3、-4或-5,并且其中所述总净电荷是通过一种或多种选自以下的置换来获得的:N43D,R45T,N62E,N76D,S101D,P129E,A158E,G159D,G159E,S166D,S188D,A230E,N18R,G20K,G20R,T22R,S24R,N43R,G118R,Q245R,H249R,N269R,E271F,和E271L,并且其中所述蛋白酶变体的氨基酸位置根据SEQ ID NO:1所示解淀粉芽孢杆菌(Bacillus amyloliquefaciens)枯草杆菌蛋白酶BPN'的氨基酸序列中对应的氨基酸位置的编号方式来进行编号。

[0999] 7.一种分离的枯草杆菌蛋白酶变体,其中所述枯草杆菌蛋白酶变体为具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:A016S-S128N-R186H-E271F,N076D-S101G-S103A-V104I-A158E-S188D-M222S-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-S128L-P129Q-A158E-N183D-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-S128L-P129Q-A158E-S188D-A232V-Q245R-N248D-H249R-E271G,S024R-S101G-S103A-V104I-S128L-P129Q-S130A-A158E-N183D-S188D-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-P129Q-A158E-N183D-S188D-A232V-Q245R-N248D-H249R,T022A-N076D-S101G-S103A-V104I-G159D-A232V-Q245R-N248D-H249R-E271F,T022A-S101G-G102A-S103A-V104I-G159D-S188D-A232V-Q245R-N248D-E271F,A016S-A158E-H249R,A016S-A158E-H249R-E271F,A016S-A158E-R186H-H249R,A016S-L111V-S188D-,A016S-T022A-A158E-R186H-E271F,A048R-S078N-N116L-N185E-L217E-P239G,A048R-S128D-N185E-P239G,A158E-R186H-H249R-E271F,E089P-S101A-P129E-R186H,G020K-G023A-N043W-N116L-S188D-T213A-P239G,G020K-G023A-N062E-N116L-G118R-T213A,G020K-G023A-S024F-N062E-S188D-T213A-P239G,G020K-K027R-P129E-S166D-P239G,G020K-S024F-N062E-P239G,G020K-S024F-T033S-P129E-

A194E,G023A-G100S-A194E-S212M,G023A-N043W-N116L-G118R-S188D,G023A-S024F-G118R-S188D-P239G,G023A-S024F-K027R-N062E,G023A-S024F-N043W-N062E-N116L-G118R,G023A-S024F-N116L-G118R-S188D-T213A,G023A-S024F-N116L-S188D-P239G,K027R-G100S-G118R-S160D-S188D-N243F,K027R-S101D-S103N-S105T-A272F,N043R-N076D-S101A-S103A-V104I-A158E-S166D-S188D-A232V-Q245R-N248D-H249R,N062E-S078N-N116L-T224A,N062E-V104L-A158E-R186H-S188D-H249R,N076D-S101A-S103A-V104I-A158E-S188D-L217E-A232V-Q245R-N248D-H249R-E271F,N076D-S101G-S103A-V104I-A158E-S166D-S188D-A232V-Q245R-N248D-H249R-E271F,S024F-G102A-R186K-T213A-L217E-N243F,S024F-N043W-G118R-S188D,S024F-N043W-V104L-V121F-P129E,S024F-N116L-G118R-S188D-P239G,S024F-S103N-V104L-G118R-S188D,S024R-N043R-S101A-S103A-V104I-A158E-S188D-A232V-Q245R-N248D-H249R,S024R-N043R-S101A-S103A-V104I-A158E-S188D-L217E-A232V-Q245R-N248D-H249R,S024R-N076D-S101G-S103A-V104I-A158E-S188D-A232V-Q245R-N248D-H249R-E271F,S024R-S101G-S103A-V104I-A158E-G159E-A232V-Q245R-N248D,S024R-S101G-S103A-V104I-S128N-A158E-G159E-S188D-A232V-Q245R-N248D,S024R-S101G-S103A-V104I-S128N-P129E-S188D-A232V-Q245R-N248D,S101A-L111V-P129E,S101A-S103A-V104L-G159E-A232V-Q245R-N248D-H249R,S101A-S103S-V104L-G159E-A232V-Q245R-N248D-H249R,S101A-V104L-S128N-A158E-R186H,S101G-S103A-V104I-P129E-L148I-S188D-A232V-Q245R-N248D,S101G-S103A-V104I-S128N-P129E-A158E-A232V-N238R-Q245R-N248D,S101G-S103A-V104I-S128N-P129E-S188D-A232V-Q245R-N248D-H249R,S101G-S103S-V104L-G159E-A232V-Q245R-N248D-H249R,S101S-S103A-V104L-G159E-A232V-Q245R-N248D-H249R,S128N-P129E-R186H,T022A-A158E-R186H-H249R-E271F,T022A-S024K-S101G-S103A-V104I-S128N-A158E-G159E-A232V-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-S128N-P129E-A158E-S188D-A232V-Q245R-N248D-H249R,T022A-S024R-S103A-V104I-S128I-G159D-S188D-A232V-N248D,T022A-S101G-S103A-V104I-L148I-S188D-A232V-Q245R-N248D,T022A-S101G-S103A-V104I-S128N-G159E-A232V-Q245R-N248D,T022A-S101G-S103A-V104I-S128N-P129E-A158E-A232V-N238R-Q245R-N248D,T022A-S128N-A158E-R186H,T022A-S128N-R186H-S188D-,T022A-V104L-A158E-H249R,T022A-V104L-R186H-S188D-H249R,T022L-G023A-K027R-S101D-V104L-S216F,T022L-S078N-N116L-P129E-S256N,T022L-S078N-S128D-T213A,T033S-G118R-P129E-A194E-P239G,T033S-S105T-S188D-S216F,V026F-V104L-S256N-A272F,T022A-N043R-S103A-V104I-S128I-G159D-S188D-A232V-Q245R-N248D,T022A-S024R-N043R-S103A-V104I-G118R-G159D-S188D-L217D-A232V-N248D,T022A-S101D-S103A-V104I-G118R-G159D-S188D-L217D-A232V-Q245R-N248D-E271F,T022A-S103A-V104I-G118R-P129E-G159D-S188D-A232V-Q245R-N248D-E271F,T022A-S103A-V104I-G159D-S188D-L217D-A232V-Q245R-N248D-E271F,T022A-S103A-V104I-S128I-P129E-G159D-S188D-A232V-N248D-E271F,T022A-S024R-S101G-S103A-V104I-P129E-L148I-A158E-S188D-A232V-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-L148I-A158E-S188D-A232V-Q245R-N248D,S101G-S103A-V104I-L148I-G159E-A232V-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-A158E-

S188D-A232V-Q245R-N248D,S101G-S103A-V104I-S128N-P129E-A158E-A232V-Q245R-N248D-H249R,V104L-L148I-S188D-H249R,S024R-S101A-S103A-V104I-A158E-S166D-S188D-L217E-A232V-Q245R-N248D-H249R,N076D-S101G-S103A-V104I-S128L-A158E-S188D-A232V-Q245R-N248D-H249R-E271F,N043R-N076D-S101G-S103A-V104I-A158E-S166D-S188D-A232V-Q245R-N248D-H249R-E271F,T022A-N043R-N076D-S101G-S103A-V104I-G159D-A232V-Q245R-N248D-H249R-E271F,S101A-S103G-V104V-G159E-A232V-Q245R-N248D-H249R,S101S-S103A-V104V-G159E-A232V-Q245R-N248D-H249R,G023A-S024F-V051W-A158E,K027R-T038F-G102A-N116L,N062E-S078N-S144R-S212M,L031F-N116L-S256N-A272F,T022L-T033S-V104L-N116L-S160D-R186K,S024F-G118R-P129E-R186K-T213A,N043W-S105T-T213A-A215D-S216F,L031F-S105T-R186K-S188D,V026F-A194E-T213A-S256N,S103N-S160D-L250I-S256N,S024R-S101G-S103A-V104I-S130A-A158E-S188D-L217E-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-S128L-A158E-N183D-S188D-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-P129Q-A158E-S188D-L217E-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-S128L-S130A-A158E-S188D-A232V-Q245R-N248D-H249R,T022A-N062E-S103A-V104I-G118R-G159D-S188D-A232V-Q245R-N248D,T022A-N043R-S101D-S103A-V104I-G118R-P129E-G159D-S188D-L217D-A232V,T022A-S024R-S103A-V104I-G159D-S188D-L217D-A232V-N248D,T022A-S024R-N043R-S103A-V104I-G118R-S128I-P129E-G159D-S188D-L217D-A232V-N248D-E271F,T022A-S103A-V104I-G118R-G159D-S188D-L217D-A232V-Q245R-N248D-E271F,G020K-N043W-S188D-T213A,S024F-N062E-G118R-P239G,G023A-N043W-S188D-T213A,G020K-S024F-N043W-N062E-N116L-G118R-S188D-P239G,G020K-N116L-S188D-P239G,G020K-N043W-N062E-G118R,G020K-N043W-N116L-S188D-T213A,G020K-S024F,G023A-N043W-N116L-P239G,G023A-S024F-N043W-N116L-G118R-S188D-P239G,G020K-G023A-N043W-T213A,和G023A-S024F-N062E-G118R-T213A-P239G,并且其中所述变体的总净电荷相对于迟缓芽孢杆菌(Bacillus lentus)枯草杆菌蛋白酶GG36蛋白酶的总净电荷为0、+1、+2、+3、+4、+5、-1、-2、-3、-4或-5,并且其中所述总净电荷是通过一种或多种选自以下的置换来获得的:N43D,R45T,N62E,N76D,S101D,P129E,A158E,G159D,G159E,S166D,S188D,A230E,N18R,G20K,G20R,T22R,S24R,N43R,G118R,Q245R,H249R,N269R,E271F,和E271L,并且其中所述蛋白酶变体的氨基酸位置根据SEQ ID NO:1所示解淀粉芽孢杆菌(Bacillus amyloliquefaciens)枯草杆菌蛋白酶BPN'的氨基酸序列中对应的氨基酸位置的编号方式来进行编号。

[1000] 8.一种分离的枯草杆菌蛋白酶变体,其中所述枯草杆菌蛋白酶变体为具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:S101G-S103A-V104I-A232V-Q236H-Q245R-N252K,S101G-S103A-V104I-A232V-Q245R-N248R,S101G-S103A-V104I-G159R-A232V-Q245R-N248D,A232V-Q245R,E089I-N117F-N185I-A215F-L233C,G020R-E089I-L217E,G020R-G023A-V104L-Y192W-L233C,G020R-N043D-R045T-N076D-S242R-H249R,G020R-N043D-R045T-S078R-S101G-S103A-V104I-A232V-Q245R,G020R-N043D-S101G-S103A-V104I-A232V-Q245R-H249R,G020R-N043R-N076D-A230E-H249R,G020R-N043R-N076D-S101G-S103A-V104I-A232V-Q245R-N269R,G020R-N116A-

A215F-N269R,G020R-R045T-N076D-S101G-S103A-V104I-A232V-Q245R,G020R-R045T-N076D-S101G-S103A-V104I-A232V-Q245R-H249R,G020R-R045T-N116A-N269R,G020R-R045T-S101G-S103A-V104I-A232V-Q245R,G020R-S024R-A215F,G020R-S024R-K27R-N043D-S242R-H249R,G020R-S024R-N043D-N076D-S078R-S101G-S103A-V104I-A232V-Q245R-N269R,G020R-S024R-N043R-N076D,G020R-S024R-N043R-R045T-A215F,G020R-S024R-N043R-R045T-N076D-S242R-H249R,G020R-S024R-N043R-R045T-N116A-T213A-A215F,G020R-S024R-N076D-S101G-S103A-V104I-A232V-Q245R,G020R-S024R-T38I-N043R-R045T-N076D-S242R-H249R,G020R-S078R-S101A-S103A-V104I-A232V-Q245R,G020R-S078R-S101A-S103A-V104I-G211Q-T213A-A232V-Q245R,G020R-S078R-S101A-S103A-V104I-N116A-N183D-A232V-Q245R,G020R-S078R-S101A-S103A-V104I-N116A-N183D-G211Q-A232V-Q245R,G020R-S078R-S101A-S103A-V104I-N116A-N183D-G211Q-T213A-A215F-A232V-Q245R,G020R-S078R-S101A-S103A-V104I-N116A-N183D-G211Q-T213A-A232V-Q245R,G020R-S078R-S101A-S103A-V104I-N116A-N183D-I198L-A215F-A232V-Q245R,G020R-S078R-S101A-S103A-V104I-N183D-A215F-A232V-Q245R,G020R-S078R-S101G-S103A-V104I-N116A-A131V-N183D-T213A-A232V-Q245R,G020R-S078R-S101G-S103A-V104I-N116A-N183D-G211Q-T213A-A215F-A232V,G020R-S078R-S101G-S103A-V104I-N116A-N183D-G211Q-T213A-A215F-A232V-Q245R,G020R-S078R-S101G-S103A-V104I-N116A-N183D-T213A-A232V-Q245R,G020R-S078R-S101G-S103A-V104I-N183D-G211Q-T213A-A232V-Q245R-E271G,G020R-S078R-S101G-S103A-V104I-T180A-A232V-Q245R,G020R-S101A-S103A-V104I-N116A-N183D-G211Q-T213A-A215F-A232V-Q245R,G020R-S101A-S103A-V104I-N116A-N183D-T213A-A232V-Q245R,G020R-S101A-S103A-V104I-T213A-A215F-A232V-Q245R,G020R-S101A-S103G-V104V-A232V-Q245R,G020R-S101G-S103A-V104I-N116A-A232V-Q245R,G020R-S101G-S103A-V104I-N116A-G211Q-A232V-Q245R,G020R-S101G-S103A-V104I-N183D-G211Q-A232V-Q245R-,G020R-S103A-V104I-A232V-Q245R,G020R-S242R-H249R,G020R-T022W-S078R-S101A-S103A-V104I-A232V-Q245R,G020R-T022W-S078R-S101A-S103A-V104I-I198L-A232V-Q245R,G020R-T022W-S078R-S101A-S103A-V104I-N116A-N183D-G211Q-T213A-A215F-A232V-Q245R,G020R-T022W-S078R-S101A-S103A-V104I-N116A-N183D-T213A-A215F-A232V-Q245R,G020R-T022W-S078R-S101A-S103A-V104I-N183D-I198L-T213A-A215F-A232V-Q245R,G020R-T022W-S078R-S101G-S103A-V104I-G211Q-T213A-A232V-Q245R,G020R-T022W-S078R-S101G-S103A-V104I-N116A-N183D-A215F-A232V-Q245R,G020R-T022W-S101A-N116A-I198L-G211Q-T213A-A215F-H249R,G020R-T022W-S101A-S103A-V104I-A215F-A232V-Q245R,G020R-T022W-S101A-S103A-V104I-A232V-Q245R,G020R-T022W-S101A-S103A-V104I-G211Q-A232V-Q245R,G020R-T022W-S101A-S103A-V104I-G211Q-T213A-A232V-Q245R,G020R-T022W-S101A-S103A-V104I-I198L-G211Q-A215F-A232V-Q245R,G020R-T022W-S101A-S103A-V104I-N116A-G211Q-A215F-A232V-Q245R,G020R-T022W-S101A-S103A-V104I-N116A-G211Q-A232V-Q245R,G020R-T022W-S101A-S103A-V104I-N116A-G211Q-T213A-A215F-A232V-Q245R,G020R-T022W-S101A-S103A-V104I-N116A-N183D-A232V-Q245R,G020R-T022W-S101A-S103A-V104I-N116A-N183D-G211Q-A232V-Q245R,

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N076D-S242R-H249R,N018R-N043D-R045T-S078R-S101G-S103A-V104I-A232V-Q245R,N018R-N043D-R045T-S101G-S103A-V104I-A232V-Q245R,N018R-N043D-R045T-S101G-S103A-V104I-A232V-Q245R-N269R,N018R-N043D-S078R-S101G-S103A-V104I-A232V-Q245R-H249R,N018R-N043R-N076D-A230E-S242R-H249R,N018R-N043R-N076D-S101G-S103A-V104I-A232V-Q245R-N269R,N018R-N043R-N076D-S242R-H249R,N018R-N043R-R045T-N076D-A230E-S242R,N018R-N043R-R045T-N076D-S076T-S101G-S103A-V104I-A232V-Q245R-A273T,N018R-N043R-R045T-N076D-S101G-S103A-V104I-A232V-Q245R,N018R-N043R-R045T-N076D-S101G-S103A-V104I-A232V-Q245R-N269R,N018R-N043R-R045T-N076D-S242R,N018R-N043R-R045T-S242R,N018R-N076D-H249R,N018R-N076D-Q245R,N018R-N076D-S101G-A232V-Q245R,N018R-N076D-S101G-S103A-V104I-A232V-Q245R,N018R-N076D-S101G-S103A-V104I-A232V-Q245R-H249R,N018R-N076D-S101G-S103A-V104I-H249R,N018R-N076D-S101G-V104I-H249R,N018R-N076D-S103A-V104I-H249R,N018R-R045T-N076D-S101G-S103A-V104I-A232V-Q245R,N018R-S024R-N043D-A230E-H249R,N018R-S024R-N043D-A230E-S242R,N018R-S024R-N043D-H249R,N018R-S024R-N043D-N076D-S101G-S103A-V104I-A232V-Q245R,N018R-S024R-N043D-N076D-S242R-H249R,N018R-S024R-N043D-N076D-V150L-H249R,N018R-S024R-N043D-S242R,N018R-S024R-N043D-S242R-H249R,N018R-S024R-N043R-N076D-L217E-H249R,N018R-S024R-N043R-N076D-S078R-H249R,N018R-S024R-N043R-R045T-A230E-H249R,N018R-S024R-N076D,N018R-S024R-N076D-A232V-H249R,N018R-S024R-N076D-G211Q-H249R,N018R-S024R-N076D-I198L-G211Q-A215F-H249R,N018R-S024R-N076D-I198L-G211Q-T213A-H249R,N018R-S024R-N076D-I198L-T213A-A215F-H249R,N018R-S024R-N076D-I198M-G211Q-T213A-A215F-H249R,N018R-S024R-N076D-L088I-S101A-N116A-I198L-G211Q-A215F-H249R,N018R-S024R-N076D-N116A-G211Q-T213A-A215F-H249R,N018R-S024R-N076D-N116A-H249R,N018R-S024R-N076D-N116A-I198L-A215F-H249R,N018R-S024R-N076D-N116A-I198L-A215F-H249R-V268G,N018R-S024R-N076D-N116A-I198L-G211Q-T213A-A215F-H249R,N018R-S024R-N076D-N116A-I198L-G211Q-T213A-H249R,N018R-S024R-N076D-N116A-I198L-H249R,N018R-S024R-N076D-N116A-I198L-T213A-H249R,N018R-S024R-N076D-N116A-I198L-Y209H-T213A-H249R,N018R-S024R-N076D-N116A-M117I-N183D-T213A-H249R,N018R-S024R-N076D-N116A-N183D-G211Q-H249R,N018R-S024R-N076D-N116A-T213A-H249R,N018R-S024R-N076D-N183D-I198L-G211Q-T213A-A215F-H249R,N018R-S024R-N076D-N183D-T213A-A215F-H249R,N018R-S024R-N076D-S101A-G211Q-A215F-H249R,N018R-S024R-N076D-S101A-G211Q-H249R,N018R-S024R-N076D-S101A-H249R,N018R-S024R-N076D-S101A-I198L-A215F-H249R,N018R-S024R-N076D-S101A-I198L-G211Q-H249R,N018R-S024R-N076D-S101A-I198L-H249R,N018R-S024R-N076D-S101A-I198L-T213A-H249R,N018R-S024R-N076D-S101A-N116A-G211Q-T213A-H249R,N018R-S024R-N076D-S101A-N116A-I198L-G211Q-H249R,N018R-S024R-N076D-S101A-N116A-I198L-G211Q-T213A-H249R,N018R-S024R-N076D-S101A-N116A-I198L-T213A-A215F-H249R,N018R-S024R-N076D-S101A-N116A-N183D-I198L-T213A-H249R,N018R-S024R-N076D-S101A-N116A-T213A-A215F-H249R,N018R-S024R-

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S101G-S103A-V104I-A232V-Q245R-H249R,N043R-N076D-S078R-S101G-S103A-V104I-A232V-Q245R-N269R,N043R-N076D-S101G-S103A-V104I-A232V-Q245R-H249R,N043R-N076D-S101G-S103A-V104I-L217E-A232V-Q245R,N043R-R045T-N076D-S078R-S101G-S103A-V104I-A232V-Q245R-N269R,N043R-R045T-N076D-S078R-S101G-S103A-V104I-A232V-V234I-Q245R,N043R-R045T-N076D-S101G-S103A-V104I-A232V-Q245R-N269R,N043R-R045T-S078R-S101G-S103A-V104I-N218S-A232V-Q245R,N043R-R045T-S101G-S103A-V104I-A232V-Q245R,N043R-S078R-S101G-S103A-V104I-A232V-Q245R-N269R,N043R-S087D-S101G-S103A-V104I-A232V-Q245R,N062Q-S101A-Q236N-N252R-A270C,N076D-S078R-S101G-S103A-V104I-A232V-Q245R-H249R,N076D-S101G-S103A-V104I-A232V-Q245R-H249R,N076D-S101G-S103A-V104I-A232V-S242R-Q245R,P005S-S024R-T033S-N243F,P014L-G020R-S024R-N043R-R045T-S101A-A215F,P052N-V104L-N183D-S216F-H249R,P086W-G118R,P086W-N243F,P086W-Y209A,Q012H-G020R-S078R-S101G-S103A-V104I-I198L-G211Q-T213A-A232V-Q245R,R045T-N076D-S078R-S101G-S103A-V104I-A232V-Q245R,R045T-N076D-S101G-S103A-V104I-A232V-Q245R-N269R,R045T-S078R-S101G-S103A-V104I-A232V-Q245R-H249R,R045T-S101G-S103A-V104I-A232V-Q245R-N269R,R045T-S242R-H249R,S024C-T033S,S024R-A232V,S024R-G046R-Y091F-V121F,S024R-G118R-K235F,S024R-N043A-S105T-S106G-I198L,S024R-N043D-R045T-S242R-H249R,S024R-N043D-S101G-S103A-V104I-A232V-Q245R,S024R-N043D-S242R-H249R,S024R-N043R-N076D,S024R-N043R-N076D-A230E-S242R,S024R-N043R-N076D-S101G-S103A-V104I-A232V-Q245R-N269R,S024R-N043R-R045T-N076D-S078R-S101G-S103A-V104I-A232V-Q245R,S024R-N043R-R045T-N076D-S101G-S103A-V104I-A232V-Q245R,S024R-N043R-R045T-S242R-H249R,S024R-N043R-S101A-T213A,S024R-N076D-Q245R,S024R-N076D-S101G-A232V-Q245R,S024R-N076D-S101G-M175L-A232V-Q245R,S024R-N076D-S101G-Q245R,S024R-N076D-S101G-S103A-V104I-A232V-Q245R,S024R-N076D-S103A-V104I-Q245R,S024R-N076D-V104I-Q245R,S024R-N243F,S024R-P086R-G118R,S024R-P086W-Y209A-K235F,S024R-P239Q,S024R-Q245R-H249R,S024R-R045T-N076D-S101G-S103A-V104I-A232V-Q245R-N269R,S024R-S101G,S024R-S101G-Q245R,S024R-S101G-V104I-H249R,S024R-S103A-A232V,S024R-S103A-M175L-A232V-H249R,S024R-S141G,S024R-T033S,S024R-T033S-A194T,S024R-T033S-G118R-K235F,S024R-T033S-G118R-Y209A,S024R-T033S-K235F,S024R-T033S-S078R-G118R,S024R-T033S-S078R-N243F,S024R-T033S-Y209A,S024R-T033S-Y209A-N243F,S024R-T274I,S024R-V104I-H249R,S024R-V104I-Q245R,S024R-Y091F-I198L-A215F-P239S,S024R-Y209A,S024R-Y209A-K235F,S024R-Y209A-S242P,S078R-P086W,S078R-S099F-N116A-R186K-T224A,S078R-S101G-S103A-V104I-A232V-Q245R-H249R,S101G-A232V,S101G-S103A-V104I-A232V-H249R,S101G-S103A-V104I-A232V-Q245R-H249R-N269R,S101G-S103A-V104I-Q245R,S105T-G211Q-S216F,S106G-N185I-S216F-Q236N,T022R-S101G-S103A-V104I-V150L-A232V-Q245R,T033S-G118D-A138V-Y209A,T033S-G118R-Y209A-,T033S-L148F,T033S-N243F,T033S-P086W,T033S-P201S,T033S-S078R,T033S-W241R,T033S-Y209A,T033S-Y209A-K235F,V004M-N018R-S024R-N076D-N116A-I198L-G211Q-T213A-

H249R,V104I-A232V-H249R,和V104L-H120F-R186K-S216F-N252R,并且其中所述蛋白酶变体的总净电荷相对于迟缓芽孢杆菌(Bacillus lentus)枯草杆菌蛋白酶GG36蛋白酶的总净电荷为0、+1、+2、+3、+4、+5、-1、-2、-3、-4或-5,并且其中所述总净电荷是通过一种或多种选自以下的置换来获得的:N43D,R45T,N62E,N76D,S101D,P129E,A158E,G159D,G159E,S166D,S188D,A230E,N18R,G20K,G20R,T22R,S24R,N43R,G118R,Q245R,H249R,N269R,E271F,和E271L,并且其中所述蛋白酶变体的氨基酸位置根据SEQ ID NO:1所示解淀粉芽孢杆菌(Bacillus amyloliquefaciens)枯草杆菌蛋白酶BPN'的氨基酸序列中对应的氨基酸位置的编号方式来进行编号。

[1001] 9.一种分离的枯草杆菌蛋白酶变体,其中所述枯草杆菌蛋白酶变体为具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:A015T-T033S,A016T-N043R-R045T-N076D-S101G-S103A-V104I-A232V-Q245R-N269R,A230E-H249R,A232V-H249R,E089I-S105T-N116A-A215F-S216F,E089I-Y091F-N185I-G211Q-A270C,G020R-A090S-S101G-S103A-V104I-N116A-N183D-T213A-A215F-A232V-Q245R,G020R-N043D-S078R-S101G-S103A-V104I-A232V-Q245R-H249R,G020R-N043R-N076D,G020R-N043R-R045T-S078R-S101G-S103A-V104I-A232V-Q245R,G020R-P052N-S101A-I198L-L233C,G020R-R045T-N076D-S078R-S101G-S103A-V104I-A232V-Q245R-N269R,G020R-S024R-N043D-N076D-H249R,G020R-S024R-N043D-N076D-S242R-H249R,G020R-S024R-N043D-R045T-A230E-S242R,G020R-S024R-N043D-S078R-S101G-S103A-V104I-A232V-Q245R,G020R-S024R-N043D-S078R-S101G-S103A-V104I-A232V-Q245R-H249R,G020R-S024R-N043R-S101G-S103A-V104I-A232V-Q245R,G020R-S024R-N076D-S078R-S101G-S103A-V104I-A232V-Q245R-H249R,G020R-S024R-R045T-N076D-S101G-S103A-V104I-A232V-Q245R,G020R-S024R-R045T-N076D-S242R-H249R,G020R-S024R-R045T-S101G-S103A-V104I-A232V-Q245R,G020R-S078R-S101A-S103A-V104I-G115E-N116A-N183D-G211Q-T213A-A232V-Q245R,G020R-S101A-S103A-V104I-N116A-N183D-A215F-A232V-Q245R,G020R-S101A-S103A-V104I-N116A-N183D-A232V-Q245R,G020R-S101A-S103A-V104I-N116A-N183D-G211Q-A232V-Q245R,G020R-S101A-S103A-V104I-N116A-N183D-G211Q-A232V-Q245R-T274I,G020R-S101A-S103A-V104I-N116A-N183D-I198L-G211Q-T213A-A215F-A232V-Q245R,G020R-S101A-S103A-V104I-N116A-N183D-T213A-A215F-A232V-Q245R,G020R-S101A-S103A-V104I-T213A-A232V-Q245R,G020R-S101G-S103A-V104I-N116A-N183D-A232V-Q245R,G020R-S101G-S103A-V104I-N116A-N183D-G211Q-A215F-A232V-Q245R,G020R-S101G-S103A-V104I-N116A-N183D-G211Q-A232V-Q245R,G020R-S101G-S103A-V104I-N116A-N183D-G211Q-T213A-A215F-A232V-Q245R,G020R-S101G-S103A-V104I-N116A-N183D-G211Q-T213A-A232V-Q245R,G020R-S101G-S103A-V104I-N116A-N183D-T213A-A232V-Q245R,G020R-T022R-N269R,G020R-T022R-S078R-S212F-W241R,G020R-T022W-S101A-S103A-V104I-N116A-N183D-A215F-A232V-Q245R,G020R-T022W-S101A-S103A-V104I-N116A-N183D-A232V-Q245R-N269S,G020R-T022W-S101A-S103A-V104I-N116A-N183D-A232V-Q245R-T274I,G020R-T022W-S101A-S103A-V104I-N116A-N183D-G211Q-A215F-A232V-Q245R,G020R-T022W-S101A-S103A-V104I-N116A-N183D-I198L-G211Q-T213A-A215F-A232V-Q245R,G020R-T022W-S101A-S103A-

V104I-N116A-N183D-T213A-A232V-Q245R,G02OR-TO22W-S101A-S103A-V104I-N183D-G211Q-T213A-A215F-A232V-Q245R,G02OR-TO22W-S101A-S103A-V104I-N183D-I198L-A215F-A232V-Q245R,G02OR-TO22W-S101A-S103A-V104I-N183D-T213A-A215F-A232V-Q245R,G02OR-TO22W-S101G-S103A-V104I-N116A-N183D-A232V-Q245R,G02OR-TO22W-S101G-S103A-V104I-N116A-N183D-G211Q-A232V-Q245R-N263S,G02OR-TO22W-S101G-S103A-V104I-N116A-N183D-G211Q-T213A-A215F-A232V-Q245R,G02OR-TO22W-S101G-S103A-V104I-N116A-N183D-G211Q-T213A-A232V-Q245R,G02OR-TO22W-S101G-S103A-V104I-N183D-A215F-A232V-Q245R,G02OR-TO22W-S101G-S103A-V104I-N183D-A232V-Q245R,G025R-NO62Q-S128N-S144R-N185I,G025R-N116A-H12OF-T224A-A27OC,G118R-K235F,K027R-NO43R-RO45T-NO76D-S101G-S103A-V104I-A232V-Q245R,NO18K-NO76D-SO78R-S101G-S103A-V104I-L217E-A232V-Q245R-N269R,NO18R-G02OR-NO43D-NO76D-SO78R-S101G-S103A-V104I-L217E-A232V-Q245R,NO18R-G02OR-NO43D-NO76D-S242R-H249R,NO18R-G02OR-NO43D-RO45T-NO76D-H249R,NO18R-G02OR-NO43D-RO45T-NO76D-S101G-S103A-V104I-A232V-Q245R,NO18R-G02OR-NO43D-RO45T-NO76D-S101G-S103A-V104I-A232V-Q245R-N269R,NO18R-G02OR-NO43D-S101G-S103A-V104I-A232V-Q245R-N269R,NO18R-G02OR-NO43D-S101G-S103A-V104I-L217E-A232V-Q245R,NO18R-G02OR-NO43R-RO45T-H249R,NO18R-G02OR-NO43R-RO45T-NO76D-A23OE-H249R,NO18R-G02OR-NO76D,NO18R-G02OR-RO45T-NO76D-SO78R-S101G-S103A-V104I-A232V-Q245R,NO18R-G02OR-RO45T-NO76D-S101G-S103A-V104I-A232V-Q245R-H249R,NO18R-G02OR-RO45T-S101G-S103A-V104I-A232V-Q245R-H249R,NO18R-G02OR-SO24R-NO43D-NO76D-SO78R-S101G-S103A-V104I-A232V-Q245R,NO18R-G02OR-SO24R-NO43D-NO76D-S101G-S103A-V104I-A232V-Q245R-N269R,NO18R-G02OR-SO24R-NO43R-NO76D,NO18R-G02OR-SO24R-NO76D-A131T-A215F-H249R,NO18R-G02OR-SO24R-NO76D-G211Q-H249R,NO18R-G02OR-SO24R-NO76D-G211Q-N243D-H249R,NO18R-G02OR-SO24R-NO76D-G211Q-T213A-A215F-H249R,NO18R-G02OR-SO24R-NO76D-G211Q-T213A-H249R,NO18R-G02OR-SO24R-NO76D-I198L-A215F-H249R,NO18R-G02OR-SO24R-NO76D-I198L-H249R,NO18R-G02OR-SO24R-NO76D-I198L-T213A-A215F-H249R,NO18R-G02OR-SO24R-NO76D-N116A-G211Q-T213A-A215F-H249R,NO18R-G02OR-SO24R-NO76D-N116A-H249R,NO18R-G02OR-SO24R-NO76D-N116A-I198L-G211Q-A215F-H249R-N269S,NO18R-G02OR-SO24R-NO76D-N116A-I198L-G211Q-A215F-Q245R,NO18R-G02OR-SO24R-NO76D-N116A-I198L-H249R,NO18R-G02OR-SO24R-NO76D-N116A-N183D-G211Q-A215F-H249R,NO18R-G02OR-SO24R-NO76D-N116A-N183D-G211Q-T213A-H249R,NO18R-G02OR-SO24R-NO76D-N116A-N183D-I198L-A215F-H249R,NO18R-G02OR-SO24R-NO76D-N116A-N183D-I198L-G211Q-A215F-H249R,NO18R-G02OR-SO24R-NO76D-N116A-N183D-I198L-G211Q-T213A-H249R,NO18R-G02OR-SO24R-NO76D-N116A-N183D-I198L-H249R,NO18R-G02OR-SO24R-NO76D-N116A-N183D-T213A-H249R,NO18R-G02OR-SO24R-NO76D-N183D-A215F-H249R,NO18R-G02OR-SO24R-NO76D-N183D-G211Q-H249R,NO18R-G02OR-SO24R-NO76D-N183D-G211Q-T213A-A215F-H249R,NO18R-G02OR-SO24R-NO76D-N183D-G211Q-T213A-H249R,NO18R-G02OR-SO24R-NO76D-N183D-I198L-A215F-H249R,NO18R-G02OR-SO24R-NO76D-N183D-I198L-G211Q-A215F-

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N043R-N076D-S078R-S101G-S103A-V104I-L217E-A232V-Q245R,N043R-N076D-S101G-S103T-V104I-A232V-Q245R-H249R-N269R,N043R-R045T-H249R,N043R-R045T-N076D-S101G-S103A-V104I-A232V-Q245R,N043R-R045T-S078R-S101G-S103A-V104I-A232V-Q245R-N269R,N043R-R045T-S078R-S101G-S103A-V104I-L217E-A232V-Q245R,N043R-R045T-S101G-S103A-V104I-A232V-Q245R-H249R,N043R-S078R-S101G-S103A-V104I-L217E-A232V-Q245R,N043R-S101G-S103A-V104I-Q245R-H249R,N043R-S101G-S103A-V104I-V150L-A232V-Q245R-N269R,N076D-A232V-Q245R,N076D-Q245R,N076D-S101G-A232V-Q245R,N076D-S101G-S103A-Q245R,N076D-S101G-S103A-V104I-A232V-H249R,N076D-S101G-S103A-V104I-H249R,N076D-S101G-S103A-V104I-V150L-A232V-Q245R,N076D-S101G-V104I-H249R,N076D-S101G-V104I-Q245R,N076D-S103A-V104I-A232V-Q245R,N076D-S103A-V104I-Q245R,N076D-V104I-A232V-Q245R,N076D-V104I-Q245R,P005S-N018R-T022W-S024R-N076D-S101A-T213A-A215F-H249R,P086W-K235F,P086W-Y209A-K235F,Q012H-V104A-G118R,R045T-N076D-S078R-S101G-S103A-V104I-A232V-Q245R-H249R,R045T-S101G-S103A-V104I-A232V-Q245R,S024R-G118R-N243F-R269H,S024R-K235F-N243F,S024R-N043D-N076D-S101G-S103A-V104I-A232V-Q245R-N269R,S024R-N043R-N076D-A230E-H249R,S024R-N076D-A232V-H249R,S024R-N076D-S078R-S101G-S103A-V104I-A232V-Q245R-H249R,S024R-N076D-S101G,S024R-N076D-S101G-A232V-H249R,S024R-N076D-S101G-S103A-A232V,S024R-N076D-S101G-S103A-V104I-M175L-H249R,S024R-N076D-S101G-S103A-V104I-Q245R,S024R-N076D-S101G-V104I-A232V-H249R,S024R-N076D-S103A-H249R,S024R-N076D-S103A-Q245R,S024R-N076D-S103A-V104I-H249R,S024R-R045T-N076D-S101G-S103A-V104I-A232V-Q245R-H249R,S024R-R045T-S242R-A273V,S024R-R247H,S024R-S101G-S103A,S024R-S101G-S103A-A232V,S024R-S101G-S103A-V104I,S024R-S103A-Q245R-H249R,S024R-S103A-V104I,S024R-S106G-N116A-S212M-T224A,S024R-T033S-A151V,S024R-T033S-A174V-K235F,S024R-T033S-A228T,S024R-T033S-K235F-W241R,S024R-T033S-N243F,S024R-V104A,S024R-V104I-A232V,S024R-Y209A-N243F,S078R-K235F,S087D-S101G-S103A-V104I-A232V-S242R-Q245R,S099F-S105T-S106G-A194F-S212M,S101G-H249R,S101G-S103A-V104I,S101G-S103A-V104I-A232V-Q245R-N248D,S101G-S103A-V104I-G159D-A232V-Q245R,S101G-S103A-V104I-G159D-A232V-Q245R-N248R,S101G-S103A-V104I-V150L-A232V-Q245R,S103A-A232V,S103A-A232V-H249R,S103A-A232V-Q245R,S103A-V104I-Q245R,S103N-H120F-Y167W-I198L-L233C,T022W-A194F-T213A-L233C-N238L,T022W-E089I-S216F,T033S-A048T,T033S-P086W-S156L-Y209A,T033S-P239T,T033S-T253A,T057R-N183D-Q236N,T143A-Y209A,V004E-T033S-S078R,V004R-S009A-T022R-S078R-S212F,Y209A-K235F,N043R-N076D-H249R,N018R-R045T,G020R-N076D-A230E-S242R,G020R-S024R-N043D-R045T,S024R-N043D-N076D-S242R-H249R,G020R-R045T-H249R,N043R-N076D-S153A-H249R,N043R-N076D-A230E-H249R,N018R-N043D-N076D-H249R,G020R-N043R-N076D-V227I,L111I-A215F-P239S,S024R-N116A-R186K-L233C-Q236N,G023A-S103N-S106G-S212M-A215F,Y209A-N243F,S024R-T033S-P129H-N184D-T253M,S024R-A085V-P086W-G118R-K235F,S024R-A272P,S024R-R269C,G020R-R045T-N076D-

S078R-S101G-S103A-V104I-A232V-Q245R-H249R,N043D-N076D-S101G-S103A-V104I-A232V-Q245R,N018R-G020R-T022W-S024R-N076D-S101A-N116A-N183D-I198L-H249R,N018R-N076D-V104I,N018R-G020R-N043D-S101G-S103A-V104I-A232V-Q245R-H249R,N018R-G020R-T022W-S024R-N076D-N183D-G211Q-H249R,N018R-S024R-N076D-S101A-N183D-I198L-G211Q-A215F-H249R,S101G-V104I,N018R-T022W-S024R-N076D-N116A-N183D-I198L-G211Q-T213A-A215F-H249R,N018R-G020R-S024R-N076D-S101A-N183D-G211Q-T213A-A215F-H249R,N018R-G020R-S024R-N076D-N116A-N183D-A215F-H249R-N263D,N018R-T022W-S024R-N076D-S101A-N183D-H249R,N018R-S024R-N076D-S101A-N116A-N183D-I198L-A215F-H249R,N018R-T022W-S024R-N076D-N116A-I198L-A215F-H249R-R269H,N018R-N043D-R045T-N076D-S078R-S101G-S103A-V104I-A232V-Q245R,N018R-S024R-R045T-N076D-S078R-S101G-S103A-V104I-A232V-Q245R-N269R,S078R-S101G-S103A-V104I-L217E-A232V-Q245R,N018R-G020R-T022W-S024R-N076D-S101A-N183D-I198L-T213A-A215F-H249R,N018R-G020R-S024R-N076D-N183D-I198L-T213A-H249R,N018R-G020R-T022W-S024R-N076D-N116A-I198L-G211Q-A215F-H249R,N018R-G020R-T022W-S024R-N076D-N116A-N183D-G211Q-H249R,N018R-G020R-T022W-S024R-N076D-S101A-I198L-G211Q-T213A-H249R,N018R-G020R-T022W-S024R-N076D-H249R,G020R-T022W-S101G-S103A-V104I-N116A-N183D-I198L-G211Q-T213A-A215F-A232V-Q245R,V104I-A232V,N018R-G020R-T022W-S024R-N076D-S101A-N116A-N183D-G211Q-A215F-H249R,N018R-G020R-T022W-S024R-N076D-S101A-N116A-N183D-I198L-G211Q-T213A-A215F-H249R,N018R-G020R-T022W-S024R-N076D-S101A-N183D-T213A-A215F-H249R,N018R-T022W-S024R-N076D-S101A-N183D-I198L-G211Q-T213A-H249R,N018R-T022W-S024R-N076D-S101A-N183D-I198L-H249R,N043D-R045T-S101G-S103A-V104I-A232V-Q245R-N269R,N018R-G020R-S024R-N076D-S101A-N183D-I198L-G211Q-H249R,N018R-G020R-N043R-S101G-S103A-V104I-L217E-A232V-Q245R,S024R-N043R-N076D-S078R-S101G-S103A-V104I-A232V-Q245R-N269R,N043R-R045T-N076D-S078R-S101G-S103A-V104I-Y166F-A176P-A179V-N184T-A187P-A194P,N018R-T022W-S024R-D041E-N076D-S101A-S160T-N183D-G211Q-T213A-H249R,N018R-G020R-T022W-S024R-N076D-N116A-N183D-I198L-G211Q-A215F-H249R,N018R-G020R-T022W-S024R-N076D-S101A-N116A-I198L-T213A-H249R,N018R-T022W-S024R-N076D-S101A-N116A-N183D-I198L-G211Q-T213A-H249R,N018R-G020R-S024R-N076D-I198L-T213A-H249R,N018R-G020R-T022W-S024R-N076D-N116A-N183D-I198L-G211Q-H249R,N018R-G020R-S024R-N076D-N183D-G211Q-A215F-H249R,S024R-N076D-V104I,N018R-N076D-S101G-A232V,N018R-S024R-N076D-S101A-N116A-N183D-I198L-G211Q-T213A-A215F-H249R,N018R-G020R-T022W-S024R-N076D-N116A-N183D-A215F-H249R,N018R-S024R-L031F-N076D-N116A-N183D-G211Q-T213A-A215F-H249R,N018R-S024R-N076D-S101A-N116A-N183D-I198L-T213A-H249R-N269S,N018R-G020R-S024R-N076D-S101A-N116A-I198L-A215F-H249R,N018R-N043R-N076D-S078R-S101G-S103A-V104I-A232V-Q245R-N269R,N018R-G020R-S024R-N076D-S101A-N114T-I198L-G211Q-A215F-H249R,S024R-N043R-S078R-S101G-S103A-V104I-L217E-A232V-Q245R,S024R-N076D-S103A-V104I-A232V,N018R-G020R-

T022W-S024R-N076D-S101A-I198L-G211Q-A215F-H249R,S101G-V104I-A232V,N018R-T022W-S024R-N076D-N183D-I198L-T213A-A215F-H249R,N018R-T022W-S024R-N076D-N183D-I198L-G211Q-H249R,N018R-G020R-S024R-N076D-N183D-T213A-H249R,N018R-S024R-N076D-S101A-N183D-G211Q-A215F-H249R,N018R-G020R-T022W-S024R-N076D-N116A-G211Q-T213A-H249R,N018R-S078R-S101G-S103A-V104I-A232V-Q245R-N269R,N018R-T022W-S024R-N076D-S101A-N116A-N183D-G211Q-A215F-H249R-T260A,N076D-H249R,N018R-T022W-S024R-N076D-N183D-G211Q-A215F-H249R,N018R-G020R-S024R-N076D-N116A-G211Q-A215F-H249R,N018R-G020R-S024R-N076D-T213A-H249R,N018R-G020R-T022W-S024R-N076D-N116A-N183D-I198L-H249R,N018R-G020R-T022W-S024R-N076D-S101A-N183D-H249R,N076D-V104I-H249R,G020R-T022W-S101A-S103A-V104I-N116A-N183D-G211Q-T213A-A215F-A232V-Q245R,S024R-N043R-R045T-S078R-S101G-S103A-V104I-L217E-A232V-Q245R,N018R-G020R-T022W-S024R-N076D-N183D-I198L-A215F-H249R,N018R-N076D-S101G-S103A,G020R-S024R-S101G-S103A-V104I-A232V-Q245R-N269R,N018R-G020R-S024R-N076D-S101A-N116A-N183D-G211Q-H249R,S101G-S103A-A232V,S024R-N076D-S101G-A232V,N018R-T022W-S024R-N076D-S101A-N183D-I198L-G211Q-H249R,N018R-G020R-S024R-N076D-S101A-N183D-I198L-G211Q-A215F-H249R,N018R-G020R-S024R-N076D-N183D-I198L-H249R,N018R-T022W-S024R-N076D-S101A-N116A-N183D-I198L-G211Q-H249R,N018R-G020R-S024R-N076D-N116A-A156V-N183D-G211Q-A215F-H249R-N269S,R045T-N076D-S101G-S103A-V104I-A232V-Q245R-H249R,N018R-G020R-S024R-N076D-S101A-N183D-I198L-H249R,N018R-G020R-T022W-S024R-N076D-I198L-G211Q-A215F-H249R,N018R-G020R-T022W-S024R-N076D-S101A-N116A-I198L-G211Q-A215F-H249R,N018R-G020R-T022W-S024R-N076D-N116A-H249R,N018R-N076D-S101G,N018R-S024R-N076D-N116A-N183D-I198L-T213A-A215F-H249R,N018R-G020R-T022W-S024R-N076D-S101A-N116A-I198L-T213A-A215F-H249R,N018R-S024R-N076D-S101A-N116A-N183D-I198L-G211Q-H249R,N018R-N076D-A232V,N018R-G020R-S024R-N076D-S101A-A232V-Q245R,N018R-N043D-R045T-N076D-S101G-S103A-V104I-A232V-Q245R,N018R-T022W-S024R-N076D-N183D-T213A-A215F-H249R,N018R-S024R-N076D-S101A-N116A-G211Q-T213A-N237D-H249R,N018R-G020R-S024R-N076D-S101A-N116A-N183D-G211Q-H249R-R275S,N018R-T022W-S024R-N076D-S101A-N116A-N183D-I198L-G211Q-T213A-A215F-H249R,S024R-N076D,N018R-S024R-N076D-N183D-G211Q-A215F-H249R,N018R-T022W-S024R-N076D-N116A-N183D-I198L-T213A-A215F-H249R,N076D-V104I-A232V-H249R,N018R-N076D-S103A-A232V,N018R-G020R-S024R-N076D-S101A-N116A-N183D-I198L-G211Q-T213A-H249R,N018R-G020R-S024R-N076D-S101A-N183D-T213A-H249R,N018R-G020R-S024R-N076D-S101A-D175E-N183D-G211Q-A215F-H249R,N018R-G020R-N043D-S078R-S101G-S103A-V104I-L217E-A232V-Q245R-A273E,G020R-S024R-N043D-R045T-N076D-S101G-S103A-V104I-A232V-Q245R,P005S-S101G-S103A-V104I-A232V-Q245R-H249R,S103A-V104I-A232V,N018R-G020R-S024R-V068A-N076D-S101A-N116A-T213A-A215F-H249R,N018R-T022W-S024R-N076D-S101A-I198L-A215F-H249R-R275S,N018R-S024R-N076D-N183D-I198L-G211Q-T213A-H249R,

N043D-R045T-S101G-S103A-V104I-A232V-Q245R,N018R-S024R-N076D-L217E-S242R-H249R,N076D-S087D-S101G-S103A-V104I-A232V-Q245R,S087D-S101G-S103A-V104I-A232V-Q245R,和S101G-S103A-V104I-V150L-A232V-S242R-Q245R,并且其中所述蛋白酶变体的总净电荷相对于迟缓芽孢杆菌(Bacillus lentus)枯草杆菌蛋白酶GG36蛋白酶的总净电荷为0、+1、+2、+3、+4、+5、-1、-2、-3、-4或-5,并且其中所述总净电荷是通过一种或多种选自以下的置换来获得的:N43D,R45T,N62E,N76D,S101D,P129E,A158E,G159D,G159E,S166D,S188D,A230E,N18R,G20K,G20R,T22R,S24R,N43R,G118R,Q245R,H249R,N269R,E271F,和E271L,并且其中所述蛋白酶变体的氨基酸位置根据SEQ ID NO:1所示解淀粉芽孢杆菌(Bacillus amyloliquefaciens)枯草杆菌蛋白酶BPN'的氨基酸序列中对应的氨基酸位置的编号方式来进行编号。

[1002] 10.一种分离的枯草杆菌蛋白酶变体,其中所述枯草杆菌蛋白酶变体为具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:X020R-X-43R,X020K-X062E,X024F-X116L,X020K-X024F,X024R-X174T,X024R-X118R,X024R-X235F,X024R-X086R,X024R-X086W,X078R-X118R,X033S-X118R,X033S-X235F,X209A-X241R,X020R-X076D,X018R-X245R,X024R-X045T,X232V-X245R,X118R-X172V,X118R-X194T,X008T-X024R,X235F-X243F,X018R-X103A,X018R-X104I,X086W-X118R,X086W-X243F,X086W-X209A,X024C-X033S,X024R-X232V,X024R-X243F,X024R-X239Q,X024R-X101G,X024R-X141G,X024R-X033S,X024R-X274I,X024R-X209A,X078R-X086W,X101G-X232V,X033S-X148F,X033S-X086W,X033S-X201S,X033S-X078R,X033S-X241R,X033S-X209A,X230E-X249R,X232V-X249R,X118R-X235F,X076D-X245R,X086W-X235F,X024R-X247H,X024R-X104A,X078R-X235F,X101G-X249R,X103A-X232V,X033S-X048T,X033S-X239T,X033S-X253A,X143A-X209A,X209A-X235F,X018R-X045T,X209A-X243F,X024R-X272P,X024R-X269C,X101G-X104I,X104I-X232V,X076D-X249R,和X024R-X076D,其中所述枯草杆菌蛋白酶变体的氨基酸位置通过与如SEQ ID NO:1所示解淀粉芽孢杆菌(B.amyloliquefaciens)枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[1003] 11.一种分离的枯草杆菌蛋白酶变体,其中所述枯草杆菌蛋白酶变体为具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:X020R-X076D,X024R-X045T,X230E-X249R,X018R-X045T,X018R-X245R,X101G-X232V,X024R-X232V,X232V-X245R,X024R-X101G,X018R-X104I,X018R-X103A,X101G-X249R,X232V-X249R,X103A-X232V,X076D-X245R,X101G-X104I,X104I-X232V,X076D-X249R,X024R-X076D,X024F-X116L,X020K-X024F,X020K-X062E,X033S-X118R,X024R-X086W,X024R-X118R,X024R-X086R,X209A-X241R,X024R-X241R,X024R-X235F,X118R-X209A,X078R-X118R,X033S-X235F,X024R-X174T,X086W-X209A,X008T-X024R,X086W-X118R,X033S-X241R,X024R-X243F,X024R-X209A,X033S-X086W,X024R-X033S,X086W-X243F,X033S-X201S,X024R-X239Q,X078R-X086W,X235F-X243F,X118R-X172V,X033S-X148F,X033S-X078R,X033S-X243F,X024C-X033S,X118R-X194T,X033S-X209A,X024R-X141G,X024R-X274I,X086W-X235F,X015T-X033S,X209A-X235F,X024R-X247H,X078R-X235F,X024R-X104A,X033S-X048T,X118R-X235F,X033S-X253A,X143A-X209A,X033S-X239T,X209A-X243F,X024R-X272P,和X024R-X269C,其中所述枯草杆菌蛋白酶变体的氨基酸位置通过与

如SEQ ID NO:1所示解淀粉芽孢杆菌(B.amyloliquefaciens)枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[1004] 12.一种分离的枯草杆菌蛋白酶变体,其中所述枯草杆菌蛋白酶变体为具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:X004R-X009A-X020R-X242R,X020R-X043R-X241R,X020R-X242R-X269R,X004R-X009A-X020R-X043R,X004R-X020R-X249R,X018R-X024R-X244R,X009A-X022R-X212F-X241R,X020R-X043R-X269R,X018R-X024R-X242R,X004R-X009A-X043R-X241R,X020R-X043R-X244R,X020R-X022R-X242R,X004R-X020R-X043R,X004R-X009A-X020R-X043R-X242R,X020R-X043R-X242R,X020R-X043R-X242R-X249R,X020R-X212F-X249R,X004R-X009A-X241R,X001R-X009A-X043R,X020R-X043R-X249R,X009A-X020R-X043R-X241R,X020R-X022R-X043R,X020R-X249R-X269R,X020R-X022R-X241R,X004R-X009A-X024R-X043R-X241R,X009A-X043R-X078R,X004R-X020R-X024R-X244R,X020R-X022R-X078R-X242R,X020R-X024R-X242R-X249R,X004R-X009A-X078R-X241R,X009A-X043R-X078R-X242R,X004R-X020R-X024R,X009A-X043R-X212F,X020R-X043R-X212F,X024R-X078R-X212F,X009A-X020R-X024R-X043R,X009A-X022R-X043R-X078R,X020R-X022R-X212F-X241R,X020R-X043R-X212F-X241R,X009A-X043R-X241R,X020R-X043R-X271L,X020R-X022R-X078R-X241R,X020R-X024R-X043R-X242R,X020R-X022R-X043R-X241R,X009A-X020R-X043R-X212F,X004R-X009A-X020R-X024R-X242R,X020R-X043R-X249R-X271L,X020R-X022R-X024R-X242R,X009A-X022R-X078R-X212F,X020R-X043R-X242R-X271L,X009A-X022R-X078R-X212F-X241R,X004R-X020R-X024R-X249R,X020R-X022R-X271L,X020R-X022R-X043R-X212F,X004R-X020R-X024R-X043R-X242R,X004R-X020R-X024R-X043R,X004R-X009A-X022R-X078R-X212F,X020R-X022R-X078R-X212F-X241R,和X020R-X022R-X269R,其中所述枯草杆菌蛋白酶变体的氨基酸位置通过与如SEQ ID NO:1所示解淀粉芽孢杆菌(B.amyloliquefaciens)枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[1005] 13.一种分离的枯草杆菌蛋白酶变体,其中所述枯草杆菌蛋白酶变体为具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:X018R-X020R-X043D-X045T-X230E,X018R-X043R-X045T-X242R-X249R,X024R-X043D-X249R,X018R-X020R-X045T,X020R-X024R-X076D-X249R,X024R-X043R-X230E-X242R,X018R-X024R-X043D-X230E,X020R-X076D,X018R-X024R-X043D-X076D-X249R,X024R-X043R-X076D-X249R,X018R-X024R-X045T-X242R,X020R-X043D-X076D-X230E-X249R,X020R-X043R-X045T-X242R,X018R-X024R-X076D-X249R,X018R-X020R-X024R-X043D-X045T-X233I-X242R,X024R-X043R-X230E,X018R-X020R-X043D,X043R-X242R-X249R,X020R-X043R-X045T-X230E,X043R-X076D-X242R-X249R,X020R-X024R-X045T-X230E-X242R,X024R-X045T-X076D-X230E-X242R-X249R,X024R-X045T,X024R-X043R-X045T-X076D-X230E-X249R,X018R-X024R-X043D-X045T-X249R,X018R-X043R-X045T-X249R,X024R-X043R-X242R,X018R-X020R-X043R-X076D-X249R,X020R-X024R-X043D-X249R,X020R-X043R-X230E-X242R,X020R-X043R-X242R,X018R-X043R-X076D-X230E,X020R-X024R-X043D-X242R,X020R-X043R-X230E,X018R-X020R-X043R-X076D-X242R-X249R,X043D-X045T-X076D-X249R,X018R-X043R-X242R-X249R,X018R-X020R-X043R-X045T-X242R,

X018R-X020R-X043D-X230E-X242R,X020R-X024R-X043R-X045T-X249R,X024R-X043R-X249R,X020R-X024R-X27E-X043R-X076D-X230E,X024R-X043R-X045T-X242R,X018R-X020R-X024R-X043R-X045T-X076D-X230E,X020R-X043R-X076D-X230E-X249R,X018R-X043R-X045T-X242R,X020R-X242R-X249R,X018R-X043R-X076D-X230E-X242R-X249R,X018R-X024R-X076D,X020R-X024R-X27R-X043D-X242R-X249R,X018R-X020R-X024R-X043D-X076D-X242R,X018R-X043R-X076D-X242R-X249R,X018R-X024R-X043D-X230E-X249R,X018R-X020R-X043D-X249R,X018R-X020R-X043D-X045T-X076D-X242R,X024R-X043R-X076D-X230E-X242R,X020R-X024R-X38I-X043R-X045T-X076D-X242R-X249R,X018R-X020R-X043R,X018R-X024R-X045T-X230E-X242R,X018R-X020R-X249R,X024R-X043R-X076D,X018R-X020R-X024R-X043R-X045T-X076D-X249R,X018R-X043D-X045T-X076D-X242R-X249R,X024R-X043D-X242R-X249R,X018R-X020R-X024R-X043D-X045T-X242R,X020R-X024R-X043R-X076D,X018R-X020R-X043D-X045T-X230E-X242R,X020R-X024R-X043R-X045T-X076D-X242R-X249R,X018R-X043R-X045T-X076D-X242R,X018R-X020R-X043R-X076D-X230E-X242R,X018R-X024R-X043D-X249R,X018R-X024R-X043R-X045T-X230E-X249R,X018R-X020R-X043R-X045T-X076D-X249R,X018R-X024R-X242R,X018R-X043R-X045T-X076D-X230E-X242R,X045T-X242R-X249R,X018R-X024R-X043D-X242R,X018R-X020R-X043D-X045T-X240P,X024R-X043R-X045T-X242R-X249R,X018R-X024R-X30S-X31S-X32I-X33Q-X34V-X35F,X018R-X020R-X043R-X076D,X020R-X043D-X045T-X076D-X242R-X249R,X018R-X024R-X043D-X230E-X242R,X018R-X024R-X043D-X242R-X249R,X024R-X043D-X045T-X242R-X249R,X043R-X230E-X249R,X024R-X043R-X076D-X230E-X249R,X020R-X024R-X043D-X076D-X249R,X024R-X045T-X242R-X273V,X020R-X024R-X045T-X076D-X242R-X249R,X018R-X024R-X043D-X076D-X242R,X018R-X043R-X076D-X230E-X249R,X018R-X020R-X043R-X045T-X249R,X018R-X043R-X045T-X230E-X242R,X020R-X024R-X043D-X045T-X230E-X242R,X018R-X043D-X230E-X249R,X018R-X043R-X076D-X242R,X018R-X020R-X076D,X018R-X020R-X043D-X076D-X242R-X249R,X020R-X024R-X043D-X076D-X242R-X249R,X043D-X242R-X249R,X018R-X020R-X024R-X043R-X076D,X018R-X020R-X043D-X045T-X076D-X249R,X018R-X020R-X043R-X045T-X076D-X230E-X249R,X018R-X076D-X242R,X020R-X043R-X249R,X018R-X076D-X242R-X249R,X018R-X024R-X045T-X230E-X249R,X230E-X249R,X018R-X045T-X249R,X020R-X043R-X076D,X043R-X045T-X249R,X018R-X043D-X076D-X242R-X249R,X043R-X076D-X249R,X018R-X045T,X020R-X076D-X230E-X242R,X020R-X024R-X043D-X045T,X024R-X043D-X076D-X242R-X249R,X020R-X045T-X249R,X043R-X076D-X153A-X249R,X043R-X076D-X230E-X249R,X018R-X043D-X076D-X249R,和X020R-X043R-X076D-X227I,其中所述枯草杆菌蛋白酶变体的氨基酸位置通过与如SEQ ID NO:1所示解淀粉芽孢杆菌(B.amyloliquefaciens)枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[1006] 14.一种分离的枯草杆菌蛋白酶变体,其中所述枯草杆菌蛋白酶变体为具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:X101G-X103A-X104I-X232V-X236H-X245R-X252K,X101G-X103A-X104I-X232V-X245R-X248R,X101G-X103A-X104I-X159R-X232V-X245R-X248D,X101G-X103A-X104I-X159D-X232V-

X245R-X248R,X101G-X103A-X104I-X232V-X245R,X101G-X103A-X104I-X159D-X232V-X245R和X101G-X103A-X104I-X232V-X245R-X248D,其中所述枯草杆菌蛋白酶变体的氨基酸位置通过与如SEQ ID NO:1所示解淀粉芽孢杆菌(B.amyloliquefaciens)枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[1007] 15.一种分离的枯草杆菌蛋白酶变体,其中所述枯草杆菌蛋白酶变体为具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:X101G-X103A-X104I-X129E-X188D-X232V-X238R-X245R-X248D,X024R-X101G-X103A-X104I-X129E-X158E-X188D-X232V-X245R-X248D-X249R,X022A-X101G-X103A-X104I-X129E-X158E-X188D-X232V-X245R-X248D-X249R,X022A-X024R-X101G-X103A-X104I-X129E-X158E-X188D-X232V-X245R-X248D-X249R,X024R-X101G-X103A-X104I-X129E-X188D-X232V-X245R-X248D-X249R,X024R-X101G-X103A-X104I-X129E-X159E-X188D-X232V-X245R-X248D-X249R,X024R-X101G-X103A-X104I-X128N-X129E-X158E-X232V-X245R-X248D-X249R,X024R-X101G-X103A-X104I-X148I-X158E-X188D-X232V-X245R-X248D,X022A-X024R-X101G-X103A-X104I-X129E-X159E-X188D-X232V-X245R-X248D-X249R,X024R-X101G-X103A-X104I-X128N-X129E-X232V-X245R-X248D,X101G-X103A-X104I-X129E-X188D-X232V-X245R-X248D-X249R,X024R-X101G-X103A-X104I-X129E-X158E-X232V-X245R-X248D-X249R,X022A-X024R-X101G-X103A-X104I-X158E-X159E-X188D-X232V-X245R-X248D-X249R,X022A-X024R-X101G-X103A-X104I-X129E-X158E-X159E-X188D-X232V-X238R-X245R-X248D,X024R-X101G-X103A-X104I-X129E-X148I-X158E-X232V-X245R-X248D,X016S-X024R-X101G-X103A-X104I-X158E-X188D-X232V-X245R-X248D-X249R,X101G-X103A-X104I-X158E-X159E-X232V-X245R-X248D-X249R,X022A-X101G-X103A-X104I-X129E-X158E-X159E-X232V-X238R-X245R-X248D,X022A-X024R-X101G-X103A-X104I-X129E-X158E-X159E-X232V-X245R-X248D-X249R,X022A-X024R-X101G-X103A-X104I-X128N-X158E-X188D-X232V-X245R-X248D,X024R-X101G-X103A-X104I-X129E-X188D-X232V-X245R-X248D,X022A-X024R-X101G-X103A-X104I-X129E-X158E-X232V-X245R-X248D,X022A-X024R-X101G-X103A-X104I-X129E-X232V-X245R-X248D,X022A-X024R-X101G-X103A-X104I-X129E-X188D-X232V-X245R-X248D,X024R-X101G-X103A-X104I-X158E-X188D-X232V-X238R-X245R-X248D,X022A-X101G-X103A-X104I-X128N-X129E-X188D-X232V-X238R-X245R-X248D,X024R-X101G-X103A-X104I-X129E-X188D-X232V-X238R-X245R-X248D,X024R-X101G-X103A-X104I-X158E-X159E-X188D-X232V-X245R-X248D,X022A-X024R-X101G-X103A-X104I-X128N-X188D-X232V-X245R-X248D,X024R-X101G-X103A-X104I-X129E-X158E-X188D-X232V-X245R-X248D,X022A-X024R-X101G-X103A-X104I-X128N-X129E-X158E-X232V-X245R-X248D,X024R-X101G-X103A-X104I-X159E-X188D-X232V-X245R-X248D,X022A-X101G-X103A-X104I-X128N-X129E-X232V-X238R-X245R-X248D,X024R-X101G-X103A-X104I-X129E-X159E-X232V-X245R-X248D,X022A-X024R-X101G-X103A-X104I-X129E-X158E-X188D-X232V-X238R-X245R-X248D,X022A-X024R-X101G-X103A-X104I-X158E-X159E-X188D-X232V-X245R-X248D,X024R-X101G-X103A-X104I-X159E-X188D-X232V-X245R-X248D-X249R,X022A-X101G-X103A-X104I-X129E-X158E-X232V-X238R-X245R-X248D,X022A-X024R-

X101G-X103A-X104I-X129E-X158E-X232V-X245R-X248D-X249R,XO24R-X101G-X103A-X104I-X148I-X158E-X232V-X245R-X248D,XO22A-X101G-X103A-X104I-X158E-X159E-X188D-X232V-X245R-X248D-X249R,XO22A-X101G-X103A-X104I-X158E-X188D-X232V-X245R-X248D,XO22A-X101G-X103A-X104I-X129E-X188D-X232V-X238R-X245R-X248D,XO24R-X101G-X103A-X104I-X129E-X158E-X159E-X188D-X232V-X245R-X248D-X249R,XO22A-XO24R-X101G-X103A-X104I-X158E-X159E-X188D-X232V-X238R-X245R-X248D,X101G-X103A-X104I-X129E-X158E-X188D-X232V-X245R-X248D-X249R,XO24R-X101G-X103A-X104I-X128N-X158E-X232V-X245R-X248D,XO22A-XO24R-X101G-X103A-X104I-X128N-X129E-X188D-X232V-X245R-X248D,XO22A-X101G-X103A-X104I-X129E-X159E-X232V-X238R-X245R-X248D,X101G-X103A-X104I-X129E-X159E-X232V-X245R-X248D-X249R,XO22A-X101G-X103A-X104I-X129E-X158E-X232V-X245R-X248D-X249R,XO24R-X101G-X103A-X104I-X129E-X148I-X158E-X188D-X232V-X245R-X248D,XO22A-X101G-X103A-X104I-X129E-X159E-X232V-X245R-X248D-X249R,XO24R-X101G-X103A-X104I-X159E-X188D-X232V-X238R-X245R-X248D,XO24R-X101G-X103A-X104I-X129E-X158E-X159E-X232V-X245R-X248D-X249R,XO24R-X101G-X103A-X104I-X129E-X158E-X159E-X232V-X238R-X245R-X248D,XO24R-X101G-X103A-X104I-X128N-X159E-X188D-X232V-X245R-X248D,XO22A-X101G-X103A-X104I-X159E-X188D-X232V-X238R-X245R-X248D-X249R,XO24R-X101G-X103A-X104I-X129E-X159E-X188D-X232V-X238R-X245R-X248D,X101G-X103A-X104I-X158E-X232V-X238R-X245R-X248D,XO22A-X101G-X103A-X104I-X129E-X159E-X188D-X232V-X245R-X248D-X249R,XO24R-X101G-X103A-X104I-X129E-X148I-X188D-X232V-X245R-X248D,XO24R-X101G-X103A-X104I-X158E-X232V-X245R-X248D-X249R,XO22A-X101G-X103A-X104I-X158E-X159E-X232V-X238R-X245R-X248D,XO24R-X101G-X103A-X104I-X158E-X159E-X232V-X238R-X245R-X248D,XO22A-X101G-X103A-X104I-X129E-X158E-X159E-X232V-X245R-X248D-X249R,X101G-X103A-X104I-X129E-X158E-X188D-X232V-X238R-X245R-X248D,XO22A-XO24R-X101G-X103A-X104I-X129E-X158E-X159E-X232V-X245R-X248D,X101G-X103A-X104I-X188D-X232V-X238R-X245R-X248D,XO22A-XO24R-X101G-X103A-X104I-X158E-X232V-X245R-X248D-X249R,XO22A-XO24R-X101G-X103A-X104I-X148I-X158E-X232V-X245R-X248D,X101G-X103A-X104I-X129E-X158E-X159E-X232V-X238R-X245R-X248D,XO22A-X101G-X103A-X104I-X159E-X188D-X232V-X238R-X245R-X248D,XO22A-XO24R-X101G-X103A-X104I-X129E-X158E-X159E-X188D-X232V-X245R-X248D-X249R,XO22A-X101G-X103A-X104I-X129E-X232V-X238R-X245R-X248D,XO22A-XO24R-X101G-X103A-X104I-X188D-X232V-X245R-X248D-X249R,X101G-X103A-X104I-X129E-X158E-X159E-X232V-X245R-X248D-X249R,XO22A-X101G-X103A-X104I-X158E-X159E-X232V-X245R-X248D-X249R,X101G-X103A-X104I-X129E-X188D-X232V-X245R-X248D,XO24R-X101G-X103A-X104I-X129E-X159E-X232V-X238R-X245R-X248D,X101G-X103A-X104I-X128N-X129E-X232V-X245R-X248D,X101G-X103A-X104I-X158E-X188D-X232V-X245R-X248D,XO22A-XO24R-X101G-X103A-X104I-X129E-X232V-X245R-X248D-X249R,X101G-X103A-X104I-X129E-X159E-X232V-X238R-X245R-X248D,X101G-X103A-X104I-X158E-X159E-X188D-X232V-X238R-X245R-X248D,

X024R-X101G-X103A-X104I-X232V-X245R-X248D-X249R,X022A-X024R-X101G-X103A-X104I-X129E-X148I-X232V-X245R-X248D,X022A-X024R-X101G-X103A-X104I-X158E-X232V-X238R-X245R-X248D,X101G-X103A-X104I-X128N-X129E-X232V-X238R-X245R-X248D,X022A-X101G-X103A-X104I-X128N-X159E-X232V-X245R-X248D,X022A-X101G-X103A-X104I-X128N-X129E-X158E-X232V-X238R-X245R-X248D,X101G-X103A-X104I-X128N-X129E-X188D-X232V-X245R-X248D-X249R,X022A-X024R-X101G-X103A-X104I-X128N-X129E-X158E-X188D-X232V-X245R-X248D-X249R,X024R-X101G-X103A-X104I-X128N-X158E-X159E-X188D-X232V-X245R-X248D,X022A-X024K-X101G-X103A-X104I-X128N-X158E-X159E-X232V-X245R-X248D,X101G-X103A-X104I-X129E-X148I-X188D-X232V-X245R-X248D,X024R-X101G-X103A-X104I-X148I-X232V-X245R-X248D,X022A-X101G-X103A-X104I-X148I-X188D-X232V-X245R-X248D,X024R-X101G-X103A-X104I-X128N-X129E-X188D-X232V-X245R-X248D,X101G-X103A-X104I-X128N-X129E-X158E-X232V-X238R-X245R-X248D,X022A-X024R-X101G-X103A-X104I-X129E-X148I-X158E-X188D-X232V-X245R-X248D,X022A-X024R-X101G-X103A-X104I-X148I-X158E-X188D-X232V-X245R-X248D,X101G-X103A-X104I-X148I-X159E-X232V-X245R-X248D,X022A-X024R-X101G-X103A-X104I-X158E-X188D-X232V-X245R-X248D,和X101G-X103A-X104I-X128N-X129E-X158E-X232V-X245R-X248D-X249R,其中所述枯草杆菌蛋白酶变体的氨基酸位置通过与如SEQ ID NO:1所示解淀粉芽孢杆菌(B.amyloliquefaciens)枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[1008] 16.一种分离的枯草杆菌蛋白酶变体,其中所述枯草杆菌蛋白酶变体为具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:X022A-X024R-X101G-X103A-X104I-X158E-X232V-X245R-X248D-X249R,X022A-X024R-X101G-X103A-X104I-X129E-X232V-X245R-X248D-X249R,X024R-X101G-X103A-X104I-X158E-X159E-X232V-X238R-X245R-X248D,X024R-X101G-X103A-X104I-X232V-X245R-X248D-X249R,X101G-X103A-X104I-X158E-X232V-X245R-X248D-X249R,X101G-X103A-X104I-X188D-X232V-X245R-X248D-X249R,X024R-X101G-X103A-X104I-X159E-X188D-X232V-X245R-X248D-X249R,X022A-X024R-X101G-X103A-X104I-X158E-X232V-X238R-X245R-X248D,X024R-X101G-X103A-X104I-X159E-X188D-X232V-X238R-X245R-X248D,X022A-X024R-X101G-X103A-X104I-X129E-X232V-X245R-X248D,X024R-X101G-X103A-X104I-X148I-X232V-X245R-X248D,X024R-X101G-X103A-X104I-X129E-X158E-X232V-X245R-X248D-X249R,X024R-X101G-X103A-X104I-X148I-X158E-X232V-X245R-X248D,X022A-X024R-X101G-X103A-X104I-X129E-X158E-X232V-X245R-X248D-X249R,X016S-X024R-X101G-X103A-X104I-X158E-X188D-X232V-X245R-X248D-X249R,X024R-X101G-X103A-X104I-X129E-X159E-X232V-X238R-X245R-X248D,X024R-X101G-X103A-X104I-X129E-X188D-X232V-X245R-X248D-X249R,X022A-X101G-X103A-X104I-X129E-X232V-X238R-X245R-X248D,X022A-X024R-X101G-X103A-X104I-X148I-X158E-X232V-X245R-X248D,X024R-X101G-X103A-X104I-X129E-X188D-X232V-X238R-X245R-X248D,X022A-X024R-X101G-X103A-X104I-X158E-X159E-X188D-X232V-X238R-X245R-X248D,X022A-X101G-X103A-X104I-X158E-X159E-X232V-X238R-X245R-X248D,X022A-X024R-X101G-X103A-

X104I-X129E-X158E-X232V-X245R-X248D,X101G-X103A-X104I-X158E-X188D-X232V-X245R-X248D-X249R,X022A-X101G-X103A-X104I-X158E-X159E-X232V-X245R-X248D-X249R,和X024R-X101G-X103A-X104I-X158E-X159E-X232V-X245R-X248D,其中所述枯草杆菌蛋白酶变体的氨基酸位置通过与如SEQ ID NO:1所示解淀粉芽孢杆菌(B.amyloliquefaciens)枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[1009] 17.一种分离的枯草杆菌蛋白酶变体,其中所述枯草杆菌蛋白酶变体为具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:X104L-X128N-X158E-X186H-X249R,X128N-X158E-X188D-X249R,X062E-X128N-X158E-X159E-X271F,X062E-X158E-X188D-X249R-X271F,X062E-X158E-X186H-X249R-X271F,X128N-X158E-X188D-X209E-X271F,X062E-X159E-X188D-X249R,X016S-X062E-X158E-X186H-X249R,X062E-X158E-X159E-X249R,X101A-X128N-X158E-X209E-X249R,X128N-X158E-X186H-X271F,X062E-X158E-X188D-X249R,X062E-X158E-X186H-X271F,X062E-X158E-X186H-X249R,X062E-X101A-X186H-X249R,X062E-X101A-X158E-X186H-X271F,X062E-X104L-X158E-X188D-X249R-X271F,X062E-X159E-X186H-X249R,X062E-X159E-X249R,X128N-X158E-X186H-X249R,X128N-X158E-X188D-X271F,X062E-X158E-X249R,X062E-X186H-X188D-X249R-X271F,X128N-X158E-X209E-,X062E-X101A-X158E-X249R,X104L-X128N-X158E-X186H-X271F,X062E-X101A-X158E-X186H-X249R-X271F,X016S-X062E-X158E-X249R,X062E-X101A-X159E-X249R,X128N-X158E-X186H-X188D-X271F,X101A-X128N-X158E-X186H-X271F,X062E-X101A-X188D-X249R,X101A-X104L-X158E-X186H-X188D-X249R,X062E-X159E-X249R-X271F,X128N-X158E-X159E-X271F,X016S-X062E-X104L-X158E-X186H-X271F,X022A-X128N-X158E-X249R,X128N-X158E-X249R,X062E-X101A-X104L-X158E-X186H-X271F,X016S-X062E-X158E-X186H-X271F,X104L-X128N-X158E-X249R,X104L-X128N-X158E-X188D-X249R,X022A-X062E-X158E,X062E-X101A-X188D-X249R-X271F,X062E-X158E-X249R-X271F,X104L-X128N-X158E-X186H-X188D-X271F,X062E-X101A-X186H-X271F,X062E-X104L-X159E-X249R,X062E-X186H-X249R,X062E-X101A-X186H-X249R-X271F,X101A-X158E-X186H-X188D-X249R,X062E-X101A-X186H,X101A-X128N-X129E-X186H-X249R,X101A-X103G-X158E-X186H-X249R,X016S-X062E-X104L-X186H-X188D-X271F,X104L-X158E-X186H-X249R,X101A-X128N-X158E-X188D-X209E-X271F,X062E-X101A-X186H-X188D-X271F,X016S-X062E-X158E-X249R-X271F,X062E-X128N-X158E,X062E-X128N-X159E-X249R,X062E-X101A-X158E-X188D-X249R,X101A-X128N-X158E-X249R,X062E-X158E-X186H-X188D-X249R,X016S-X104L-X158E-X186H-X271F,X062E-X148I-X159E,X062E-X101A-X158E-X186H-X249R,X062E-X101A-X186H-X188D-X249R,X104L-X158E-X186H-X188D-X249R,X062E-X101A-X104L-X186H-X188D-X271F,X022A-X101A-X158E-X186H-X249R,X101A-X128N-X158E-X209E,X158E-X186H-X188D-X249R-X271F,X104L-X158E-X186H-X188D-X249R-X271F,X101A-X104L-X158E-X186H-X249R,X104L-X158E-X249R,X101A-X104L-X128N-X158E-X186H-X271F,X016S-X104L-X188D-X249R,X101A-X104L-X158E-X186H-X188D-X271F,X104L-X128N-X159E-X271F,X104L-X158E-X186H-X249R-X271F,X158E-X186H-X249R,X101A-X158E-X186H-X249R,X104L-X158E-X188D-X249R-X271F,X016S-X128N-X158E-X186H,

X104L-X128N-X186H-X188D-X249R,X016S-X101A-X128N-X186H,X016S-X062E-X128N-X186H-X271F,X016S-X128N-X186H-X271F,X128N-X129E-X186H,X158E-X186H-X249R-X271F,X016S-X158E-X249R,X016S-X158E-X186H-X249R,X016S-X022A-X158E-X186H-X271F,X089P-X101A-X129E-X186H,X022A-X128N-X158E-X186H,X101A-X104L-X128N-X158E-X186H,X022A-X128N-X186H-X188D-,X062E-X104L-X158E-X186H-X188D-X249R,X022A-X158E-X186H-X249R-X271F,X022A-X104L-X158E-X249R,X101A-X111V-X129E,X016S-X158E-X249R-X271F,X016S-X111V-X188D-,X022A-X104L-X186H-X188D-X249R,和X104L-X148I-X188D-X249R,其中所述枯草杆菌蛋白酶变体的氨基酸位置通过与如SEQ ID NO:1所示解淀粉芽孢杆菌(B.amyloliquefaciens)枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[1010] 18.一种分离的枯草杆菌蛋白酶变体,其中所述枯草杆菌蛋白酶变体为具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:X001R-X101G-X103A-X104I-X232V-X245R,X004R-X101G-X103A-X104I-X232V-X245R,X043R-X101G-X103A-X104I-X232V-X245R-X271L,X078R-X101G-X103A-X104I-X232V-X245R,X004R-X043R-X101G-X103A-X104I-X232V-X245R,X018R-X043R-X101G-X103A-X104I-X232V-X245R,X020R-X101G-X103A-X104I-X232V-X245R,X101G-X103A-X104I-X232V-X245R-X271L,X020R-X043R-X101G-X103A-X104I-X232V-X245R,X024R-X043R-X101G-X103A-X104I-X232V-X245R,X020R-X025R-X116A-X167W,X018R-X101G-X103A-X104I-X232V-X245R,X022R-X101G-X103A-X104I-X232V-X245R,X078R-X103N-X106G-X167W-X236N,X018R-X043D-X101G-X103A-X104I-X232V-X245R-X269R,X043R-X101G-X103A-X104I-X232V-X245R-X269R,X024R-X101A-X120F-X194F-X249R,X020R-X043D-X101G-X103A-X104I-X232V-X245R-X269R,X101G-X103A-X104I-X212F-X232V-X245R,X020R-X144R-X185I-X233C-X236N,X023A-X078R-X216F-X236N-X249R,X101G-X103A-X104I-X232V-X245R-X269R,X101G-X103A-X104I-X115R-X232V-X245R,X052N-X078R-X103N-X148I-X213A,X018R-X043D-X101G-X103A-X104I-X232V-X245R-X249R,X024R-X043D-X101G-X103A-X104I-X232V-X245R-X249R,X024R-X043D-X101G-X103A-X104I-X232V-X245R-X269R,X025R-X089I-X116A-X239S-X270C,X024R-X101G-X103A-X104I-X232V-X245R,X148I-X213A-X252R,X024R-X025R-X183D-X192W-X239S,X046R-X194F-X212M,X104L-X217E-X224A-X249R-X252R,X023A-X091F-X121F-X192W-X236N,X101G-X103A-X104I-X232V-X244R-X245R,X099F-X144R-X167W-X252R,X101G-X103A-X104I-X232V-X245R-X249R,X043R-X101G-X103A-X104I-X232V-X245R,X022W-X078R-X167W-X212M-X270C,X121F-X252R-X270C,X020R-X103N-X216F-X236N-X252R,X043R-X101G-X103A-X104I-X232V-X245R-X249R,X023A-X052N-X192W-X198L-X252R,X025R-X046R-X121F,X024R-X078R-X104L-X116A-X183D,X046R-X059A-X103N-X211Q-X212M,X020R-X052N-X062Q-X091F-X192W,X023A-X052N-X144R-X192W-X216F,X101G-X103A-X104I-X232V-X242R-X245R,X052N-X103N-X116A-X148I-X192W,X089I-X116A-X117F-X224A-X249R,X144R-X211Q-X238L-X239S-X249R,X043A-X062Q-X194F-X211Q,X020R-X024R-X052N-X059A-X216F,X024R-X167W-X224A-X249R,X057R-X167W-X249R,X025R-X103N-X186K-X194F-X224A,X105T-X128N-X144R-X148I-X212M,X020R-X059A-X144R-X192W-X224A,

X024R-X043A-X117F-X194F-X211Q,X117F-X194F-X213A-X270C,X078R-X091F-X121F-X233C-X252R,X057R-X099F-X105T-X198L-X213A,X023A-X091F-X101A-X198L-X252R,X062Q-X103N-X121F-X144R-X249R,X043R-X101G-X103A-X104I-X232V-X242R-X245R,X023A-X024R-X117F-X212M-X216F,X104L-X213A-X216F,X194F-X211Q-X236N,X062Q-X103N-X117F-X194F,X024R-X062Q-X104L-X106G-X249R,X057R-X089I-X198L,X046R-X059A-X106G-X217E-X249R,X117F-X213A-X215F,X101A-X120F-X192W-X215F-X224A,X043A-X057R-X117F-X144R-X183D,X046R-X183D-X238L,X025R-X043A-X089I-X117F,X078R-X104L-X213A-X215F-X224A,X091F-X099F-X101A-X105T-X167W,X106G-X117F-X238L,X046R-X089I-X091F-X101A-X116A,X020R-X062Q-X089I-X186K-X212M,X057R-X099F-X121F-X185I-X192W,X046R-X089I-X192W-X233C-X270C,X089I-X117F-X185I-X215F-X233C,X052N-X104L-X183D-X216F-X249R,X078R-X099F-X116A-X186K-X224A,X025R-X105T-X128N-X144R-X270C,X105T-X211Q-X216F,X024R-X046R-X091F-X121F,X106G-X185I-X216F-X236N,X062Q-X101A-X236N-X252R-X270C,X025R-X043A-X091F-X198L-X270C,X020R-X023A-X104L-X192W-X233C,X024R-X043A-X105T-X106G-X198L,X020R-X089I-X217E,X024R-X091F-X198L-X215F-X239S,X046R-X089I-X099F-X186K-X212M,X104L-X120F-X186K-X216F-X252R,X022W-X194F-X213A-X233C-X238L,X099F-X105T-X106G-X194F-X212M,X089I-X105T-X116A-X215F-X216F,X025R-X116A-X120F-X224A-X270C,X043A-X059A-X101A-X216F-X224A,X057R-X183D-X236N,X025R-X062Q-X128N-X144R-X185I,X103N-X120F-X167W-X198L-X233C,X022W-X089I-X216F,X024R-X106G-X116A-X212M-X224A,X020R-X052N-X101A-X198L-X233C,X089I-X091F-X185I-X211Q-X270C,X111I-X215F-X239S,X024R-X116A-X186K-X233C-X236N,和X023A-X103N-X106G-X212M-X215F,其中所述枯草杆菌蛋白酶变体的氨基酸位置通过与如SEQ ID NO:1所示解淀粉芽孢杆菌(B.amyloliquefaciens)枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[1011] 19.一种分离的枯草杆菌蛋白酶变体,其中所述枯草杆菌蛋白酶变体为具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:X020R-X022W-X078R-X101A-X103A-X104I-X116S-X213A-X215F-X232V-X245R,X018R-X078R-X101G-X103A-X104I-X232V-X245R,X024R-X045T-X101G-X103A-X104I-X232V-X245R-X269R,X020R-X022W-X078R-X101G-X103A-X104I-X116A-X232V-X245R,X020R-X22W-X101G-X103A-X104I-X232V-X245R,X018R-X043R-X101G-X103A-X104I-X232V-X245R,X018R-X022W-X024R-X076D-X101A-X116A-X232V-X245R,X018R-X104I-X232V-X249R,X018R-X024R-X076D-X101A-X116A-X211Q-X249R,X018R-X043D-X078R-X101G-X103A-X104I-X217E-X232V-X245R,X018R-X043R-X101G-X103A-X104I-X232V-X245R-X269R,X018R-X045T-X076D-X101G-X103A-X104I-X232V-X245R-X269R,X076D-X078R-X101G-X103A-X104I-X232V-X245R-X269R,X020R-X043D-X078R-X101G-X103A-X104I-X232V-X245R,X018R-X043D-X076D-X101G-X103A-X104I-X232V-X245R-X269R,X024R-X045T-X076D-X078R-X101G-X103A-X104I-X232V-X245R-X269R,X018R-X103A-X232V-X249R,X018R-X101G-X104I-X232V-X245R,X020R-X024R-X101G-X103A-X104I-X217E-X232V-X245R-X249R,X018R-X22K-X043D-X101G-X103A-X104I-X232V-X245R,X043R-X045T-X101G-X103A-

X104I-X232V-X245R-X269R,X020R-X22W-X101G-X103A-X104I-X211Q-X232V-X245R,X024R-X076D-X078R-X101G-X103A-X104I-X232V-X245R-X269R,X020R-X22W-X078R-X101A-X103A-X104I-X116A-X183D-X232V,X018R-X024R-X076D-X116A-X215F-X249R,X018R-X043R-X045T-X101G-X103A-X104I-X232V-X245R,X024R-X043R-X076D-X101G-X103A-X104I-X232V-X245R,X020R-X022W-X101G-X103A-X104I-X232V-X245R,X020R-X022W-X101G-X103A-X104I-X211Q-X232V-X245R,X020R-X022W-X078R-X101G-X103A-X104I-X116A-X213A-X215F-X232V-X245R,X043D-X076D-X078R-X101G-X103A-X104I-X232V-X245R-X269R,X018R-X024R-X076D-X101A-X116A-X213A-X249R,X018R-X024R-X076D-X116A-X211Q-X249R,X043R-X045T-X076D-X078R-X101G-X103A-X104I-X232V-X245R,X018R-X101G-X245R,X020R-X22W-X101A-X103A-X104I-X211Q-X213A-X232V-X245R,X020R-X024R-X043D-X076D-X078R-X101G-X103A-X104I-X232V-X245R,X018R-X045T-X076D-X078R-X101G-X103A-X104I-X232V-X245R,X020R-X078R-X101G-X103A-X104I-X211Q-X213A-X215F-X232V-X245R,X045T-X078R-X101G-X103A-X104I-X232V-X245R-X269R,X024R-X043D-X101G-X103A-X104I-X232V-X245R-X269R,X018R-X101G-X103A-X249R,X018R-X22W-X024R-X076D-X101A-X116A-X232V-X245R,X018R-X101G-X104I-X232V-X249R,X020R-X22W-X101A-X103A-X104I-X215F-X232V-X245R,X018R-X024R-X076D-X211Q-X213A-X249R,X018R-X022W-X024R-X076D-X101A-X198L-X249R,X024R-X101G-X103A-X104I-X232V-X245R,X020R-X076D-X101G-X103A-X104I-X232V-X245R-X269R,X020R-X101G-X103A-X104I-X232V-X245R-X269R,X043D-X078R-X101G-X103A-X104I-X232V-X245R,X020R-X101G-X104I-X213A-X215F-X232V-X245R,X020R-X101G-X103A-X104I-X116A-X215F-X232V-X245R,X024R-X103A-X104I-X249R,X018R-X076D-X078R-X101G-X103A-X104I-X232V-X245R,X045T-X076D-X078R-X101G-X103A-X104I-X232V-X245R-X269R,X024R-X101G-X104I-X245R,X020R-X101G-X103A-X104I-X211Q-X213A-X215F-X232V-X245R,X024R-X103A-X104I-X232V-X249R,X018R-X024R-X076D-X116A-X211Q-X215F-X249R,X018R-X245R,X024R-X103A-X245R,X024R-X103A-X104I-X245R,X020R-X078R-X101G-X232V-X245R,X018R-X024R-X076D-X104I-X249R,X018R-X024R-X104I-X249R,X024R-X101G-X103A-X104I-X232V-X245R,X018R-X024R-X076D-X211Q-X215F-X249R,X019H-X020R-X022W-X078R-X101G-X103A-X104I-X211Q-X232V-X245R,X018R-X024R-X076D-X101A-X198L-X211Q-X213A-X249R,X018R-X024R-X043D-X101G-X103A-X104I-X232V-X245R,X020R-X22W-X103A-X104I-X232V-X245R,X018R-X103A-X104I-X249R,X018R-X022W-X024R-X076D-X101A-X198L-X215F-X249R,X018R-X024R-X101G-X104I-X232V,X078R-X101G-X103A-X104I-X232V-X245R-X269R,X024R-X043R-X076D-X078R-X101G-X103A-X104I-X232V-X245R,X018R-X020R-X043D-X076D-X101G-X103A-X104I-X232V-X245R,X018R-X22W-X024R-X076D-X116A-X213A-X249R,X018R-X024R-X101G-X104I,X020R-X101A-X103A-X104I-X215F-X232V-X245R,X018R-X045T-X078R-X101G-X103A-X104I-X232V-X245R,X018R-X101G-X103A-X245R,X043R-X076D-X078R-X101G-X103A-X104I-X232V-X245R,X020R-X022W-X101A-X103A-X104I-X211Q-X215F-X232V-X245R,X020R-X22W-X078R-X101G-X103A-X104I-X116A-X213A-X215F-X232V-X245R,X020R-X078R-X101G-X103A-X104I-X215F-X232V-X245R,X020R-X022W-X078R-X101G-X103A-X104I-X116A-X183D-

X232V-X245R,X076D-X101G-X103A-X104I-X232V-X245R,X076D-X101G-X103A-X104I-X232V-X245R-X269R,X020R-X22W-X101A-X103A-X104I-X232V-X245R,X020R-X101G-X103A-X232V-X245R,X020R-X022W-X078R-X101A-X103A-X104I-X116A-X183D-X232V-X245R,X018R-X020R-X024R-X045T-X076D-X101G-X103A-X104I-X232V-X245R-X269R,X043R-X045T-X078R-X101G-X103A-X104I-X232V-X245R,X018R-X101G-X104I-X249R,X020R-X22W-X078R-X101G-X103A-X104I-X116A-X183D-X232V-X245R,X020R-X022W-X101G-X103A-X104I-X198L-X211Q-X213A-X232V-X245R,X020R-X078R-X101A-X103A-X104I-X116A-X183D-X213A-X232V-X245R,X024R-X076D-X104I-X232V-X245R,X018R-X020R-X076D-X101G-X103A-X104I-X232V-X245R,X018R-X024R-X076D-X101G-X104I-X232V-X249R,X018R-X043D-X078R-X101G-X103A-X104I-X232V-X245R,X001T-X018R-X024R-X076D-X116A-X213A-X249R,X076D-X078R-X101G-X103A-X104I-X232V-X245R,X020R-X078R-X101G-X103A-X104I-X116A-X232V-X245R,X043R-X076D-X101G-X103A-X104I-X232V-X245R,X018R-X045T-X101G-X103A-X104I-X232V-X245R,X018R-X076D-X101G-X104I-X232V-X245R,X020R-X078R-X101G-X103A-X104I-X116A-X183D-X232V-X245R,X018R-X024R-X076D-X101A-X211Q-X213A-X215F-X249R,X045T-X078R-X101G-X103A-X104I-X232V-X245R,X043R-X076D-X101G-X103A-X104I-X232V-X245R-X269R,X020R-X022W-X078R-X101G-X103A-X104I-X116A-X183D-X213A-X232V-X245R,X020R-X022W-X101G-X103A-X104I-X116A-X183D-X213A-X232V-X245R,X020R-X101G-X198L-X215F-X232V-X245R,X018R-X024R-X076D-X213A-X215F-X249R,X020R-X078R-X101G-X103A-X104I-X116A-X211Q-X232V-X245R,X020R-X022W-X078R-X101A-X103A-X104I-X116A-X183D-X215F-X232V-X245R,X020R-X022W-X078R-X101A-X103A-X104I-X116A-X183D-X213A-X232V-X245R,X024R-X232V-X245R,X018R-X024R-X043D-X101G-X103A-X104I-X232V-X245R-X269R,X018R-X024R-X076D-X101A-X215F-X249R,X018R-X022W-X024R-X076D-X116A-X213A-X249R,X101G-X103A-X104I-X232V-X245R,X018R-X024R-X076D-X211Q-X213A-X215F-X249R,X018R-X024R-X076D-X116A-X213A-X215F-X249R,X043D-X076D-X078R-X101G-X103A-X104I-X232V-X245R-X269R,X043D-X078R-X101G-X103A-X104I-X232V-X245R-X249R,X020R-X022W-X078R-X101G-X103A-X104I-X116A-X183D-X211Q-X232V-X245R,X018R-X024R-X076D-X101A-X198L-X211Q-X215V-X249R,X018R-X022W-X024R-X076D-X116A-X211Q-X249R,X020R-X103A-X104I-X232V-X245R,X020R-X22W-X101A-X103A-X104I-X211Q-X215F-X232V-X245R,X024R-X076D-X101G-X103A-X104I-X232V-X245R,X020R-X101G-X103A-X104I-X116A-X232V-X245R,X018R-X22W-X024R-X076D-X198L-X215F-X249R,X020R-X022W-X103A-X104I-X232V-X245R,X020R-X022W-X101A-X103A-X104I-X211Q-X213A-X232V-X245R,X020R-X022W-X101G-X103A-X104I-X211Q-X213A-X215F-X232V-X245R,X018R-X043R-X045T-X076D-X101G-X103A-X104I-X232V-X245R,X018R-X022W-X024R-X076D-X101A-X198L-X213A-X215F-X249R,X018R-X22W-X024R-X076D-X101A-X215F-X249R,X020R-X045T-X101G-X103A-X104I-X232V-X245R,X020R-X078R-X101G-X103A-X104I-X180A-X232V-X245R,X020R-X022W-X078R-X101G-X103A-X104I-X116A-X183D-X215F-X232V-X245R,X018R-X101G-X103A-X104I,X020R-X22W-X101A-X103A-X104I-X116A-X211Q-X213A-X215F-X232V-X245R,X018R-X024R-X076D-X103A-X232V-

X245R,X020R-X078R-X101A-X103A-X104I-X116A-X183D-X232V-X245R,X018R-X024R-X076D-X211Q-X249R,X020R-X101A-X103A-X104I-X213A-X215F-X232V-X245R,X018R-X020R-X043D-X101G-X103A-X104I-X232V-X245R,X020R-X022W-X101A-X103A-X104I-X211Q-X232V-X245R,X020R-X022W-X101A-X103A-X104I-X116A-X211Q-X215F-X232V-X245R,X020R-X022W-X101A-X103A-X104I-X116A-X211Q-X232V-X245R,X018R-X024R-X076D-X232V-X249R,X018R-X024R-X045T-X076D-X101G-X103A-X104I-X232V-X245R-X269R,X018R-X076D-X245R,X024R-X104I-X245R,X101G-X232V,X020R-X22W-X101A-X103A-X104I-X116A-X211Q-X215F-X232V-X245R,X018R-X020R-X022W-X024R-X076D-X116A-X183D-X198L-X213A-X249R,X020R-X022W-X078R-X101A-X103A-X104I-X232V-X245R,X020R-X022W-X078R-X101A-X103A-X104I-X198L-X232V-X245R,X024R-X245R-X249R,X020R-X101G-X103A-X104I-X116A-X211Q-X232V-X245R,X018R-X22W-X024R-X076D-X116A-X211Q-X249R,X024R-X101G-X104I-X249R,X018R-X024R-X076D-X116A-X198L-X211Q-X213A-X215F-X249R,X018R-X024R-X104I,X020R-X022W-X078R-X101A-X103A-X104I-X183D-X198L-X213A-X215F-X232V-X245R,X018R-X020R-X22W-X024R-X076D-X116A-X183D-X198L-X213A-X249R,X020R-X022W-X101A-X103A-X104I-X232V-X245R,X012H-X020R-X078R-X101G-X103A-X104I-X198L-X211Q-X213A-X232V-X245R,X018R-X024R-X076D-X101A-X211Q-X215F-X249R,X018R-X024R-X076D-X213A-X249R,X024R-X104I-X249R,X018R-X022W-X024R-X076D-X211Q-X249R,X018R-X076D-X103A-X104I-X249R,X043R-X076D-X101G-X103A-X104I-X217E-X232V-X245R,X020R-X078R-X101G-X103A-X104I-X183D-X211Q-X213A-X232V-X245R-X271G,X018R-X022W-X024R-X076D-X101A-X116A-X198L-X215F-X249R,X018R-X024R-X043D-X076D-X101G-X103A-X104I-X232V-X245R,X018R-X024R-X076D-X101A-X198L-X215F-X249R,X018R-X022W-X024R-X076D-X116A-X198L-X211Q-X213A-X249R,X018R-X024R-X076D-X101A-X116A-X213A-X215F-X249R,X020R-X043D-X045T-X078R-X101G-X103A-X104I-X232V-X245R,X045T-X078R-X101G-X103A-X104I-X232V-X245R-X249R,X018R-X22W-X024R-X076D-X101A-X116A-X215F-X249R,X043D-X101G-X103A-X104I-X232V-X245R-X269R,X020R-X022W-X078R-X101A-X103A-X104I-X116A-X183D-X213A-X215F-X232V-X245R,X018R-X024R-X076D-X116A-X211Q-X213A-X215F-X249R,X024R-X103A-X175L-X232V-X249R,X018R-X024R-X076D-X116A-X213A-X249R,X020R-X045T-X076D-X101G-X103A-X104I-X232V-X245R,X020R-X078R-X101A-X103A-X104I-X116A-X183D-X211Q-X213A-X215F-X232V-X245R,X024R-X043R-X045T-X076D-X078R-X101G-X103A-X104I-X232V-X245R,X018R-X024R-X076D-X101A-X116A-X198L-X213A-X215F-X249R,X043R-X045T-X101G-X103A-X104I-X232V-X245R,X018R-X022W-X024R-X076D-X101A-X198L-X211Q-X245R,X020R-X024R-X043D-X076D-X078R-X101G-X103A-X104I-X232V-X245R-X269R,X024R-X232V,X020R-X078R-X101A-X103A-X104I-X116A-X183D-X211Q-X232V-X245R,X024R-X076D-X101G-X232V-X245R,X018R-X076D-X101G-X103A-X104I-X249R,X018R-X024R-X076D-X198M-X211Q-X213A-X215F-X249R,X018R-X22W-X024R-X076D-X101A-X198L-X215F-X249R,X018R-X043R-X076D-X101G-X103A-X104I-X232V-X245R-X269R,X020R-X022W-X103A-X211Q-X213A-X215F-X232V-X245R,X020R-X078R-X101A-X103A-X104I-X116A-X183D-X211Q-X213A-X232V-

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X183D-X249R,X018R-X022W-X024R-X076D-X101A-X183D-X198L-X215F-X249R,X018R-X020R-X043D-X045T-X076D-X101G-X103A-X104I-X232V-X245R,X020R-X022W-X101A-X103A-X104I-X183D-X198L-X215F-X232V-X245R,X076D-X101G-X103A-X104I-X249R,X018R-X020R-X024R-X076D-X183D-X198L-X215F-X249R,X018R-X020R-X022W-X024R-X076D-X101A-X183D-X215F-X249R,X018R-X020R-X024R-X076D-X211Q-X213A-X249R,X018R-X024R-X076D-X116A-X183D-X211Q-X213A-X249R,X018R-X024R-X076D-X116A-X183D-X198L-X249R,X018R-X020R-X024R-X076D-X211Q-X243D-X249R,X018R-X020R-X045T-X076D-X101G-X103A-X104I-X232V-X245R-X249R,X018R-X022W-X024R-X076D-X183D-X198L-X211Q-X213A-X249R,X018R-X024R-X076D-X101A-X116A-X183D-X198L-X211Q-X213A-X249R,X018R-X022W-X024R-X076D-X116A-X198L-X211Q-X213A-X215F-X249R,X024R-X076D-X101G,X018R-X020R-X024R-X076D-X101A-X198L-X213A-X215F-X249R,X018R-X022W-X024R-X076D-X116A-X183D-X211Q-X213A-X249R,X018R-X020R-X024R-X076D-X183D-X215F-X249R,X018R-X043D-X076D-X078R-X101G-X103A-X104I-X232V-X245R-X249R,X018R-X022W-X024R-X076D-X116A-X183D-X211Q-X213A-X245R,X020R-X024R-X076D-X078R-X101G-X103A-X104I-X232V-X245R-X249R,X018R-X020R-X045T-X101G-X103A-X104I-X232V-X245R-X249R,X018R-X024R-X076D-X101A-X183D-X198L-X211Q-X249R,X018R-X022W-X024R-X076D-X183D-X211Q-X213A-X249R,X018R-X020R-X024R-X076D-X116A-X198L-X211Q-X215F-X249R-X269S,X018R-X020R-X022W-X024R-X076D-X101A-X116A-X183D-X198L-X211Q-X215F-X249R,X020R-X022W-X101A-X103A-X104I-X183D-X213A-X215F-X232V-X245R,X018R-X024R-X076D-X086V-X101A-X183D-X198L-X211Q-X249R,X018R-X076D-X101G-X198T-X232V,X018R-X020R-X024R-X076D-X101A-X116A-X183D-X198L-X211Q-X215F-X249R,X018R-X022W-X024R-X076D-X101A-X116A-X183D-X213A-X215F-X249R,X018R-X022W-X024R-X076D-X101A-X183D-X211Q-X213A-X215F-X249R,X018R-X024R-X076D-X183D-X249R-X248T,X018R-X076D-X104I-X245R-X249R,X018R-X022W-X024R-X076D-X101A-X116A-X183D-X198L-X215F-X249R,X018R-X022W-X024R-X076D-X116A-X183D-X213A-X215F-X249R,X018R-X020R-X022W-X024R-X076D-X116A-X183D-X211Q-X213A-X215F-X249R,X018R-X020R-X024R-X076D-X101A-X249R,X018R-X020R-X024R-X076D-X101A-X116A-X213A-X215F-X249R,X018R-X022W-X024R-X076D-X116A-X183D-X211Q-X215F-X249R,X018R-X022W-X024R-X076D-X116A-X183D-X198L-X211Q-X213A-X249R,X043R-X045T-X078R-X101G-X103A-X104I-X217E-X232V-X245R,X043R-X045T-X101G-X103A-X104I-X232V-X245R-X249R,X018R-X076D-X101G-X104I,X020R-X045T-X076D-X078R-X101G-X103A-X104I-X232V-X245R-X249R,X043D-X076D-X101G-X103A-X104I-X232V-X245R,X018R-X020R-X022W-X024R-X076D-X101A-X116A-X183D-X198L-X249R,X018R-X076D-X104I,X018R-X020R-X043D-X101G-X103A-X104I-X232V-X245R-X249R,X018R-X020R-X022W-X024R-X076D-X183D-X211Q-X249R,X018R-X024R-X076D-X101A-X183D-X198L-X211Q-X215F-X249R,X101G-X104I,X018R-X022W-X024R-X076D-X116A-X183D-X198L-X211Q-X213A-X215F-X249R,X018R-X020R-X024R-X076D-X101A-X183D-X211Q-X213A-X215F-X249R,X018R-X020R-X024R-X076D-X116A-X183D-X215F-X249R-X263D,X018R-X022W-X024R-X076D-

X101A-X183D-X249R,X018R-X024R-X076D-X101A-X116A-X183D-X198L-X215F-X249R,X018R-X022W-X024R-X076D-X116A-X198L-X215F-X249R-X269H,X018R-X043D-X045T-X076D-X078R-X101G-X103A-X104I-X232V-X245R,X018R-X024R-X045T-X076D-X078R-X101G-X103A-X104I-X232V-X245R-X269R,X078R-X101G-X103A-X104I-X217E-X232V-X245R,X018R-X020R-X022W-X024R-X076D-X101A-X183D-X198L-X213A-X215F-X249R,X018R-X020R-X024R-X076D-X183D-X198L-X213A-X249R,X018R-X020R-X022W-X024R-X076D-X116A-X198L-X211Q-X215F-X249R,X018R-X020R-X022W-X024R-X076D-X116A-X183D-X211Q-X249R,X018R-X020R-X022W-X024R-X076D-X101A-X198L-X211Q-X213A-X249R,X018R-X020R-X022W-X024R-X076D-X249R,X020R-X022W-X101G-X103A-X104I-X116A-X183D-X198L-X211Q-X213A-X215F-X232V-X245R,X104I-X232V,X018R-X020R-X022W-X024R-X076D-X101A-X116A-X183D-X211Q-X215F-X249R,X018R-X020R-X022W-X024R-X076D-X101A-X116A-X183D-X198L-X211Q-X213A-X215F-X249R,X018R-X020R-X022W-X024R-X076D-X101A-X183D-X213A-X215F-X249R,X018R-X022W-X024R-X076D-X101A-X183D-X198L-X211Q-X213A-X249R,X018R-X022W-X024R-X076D-X101A-X183D-X198L-X249R,X043D-X045T-X101G-X103A-X104I-X232V-X245R-X269R,X018R-X020R-X024R-X076D-X101A-X183D-X198L-X211Q-X249R,X018R-X020R-X043R-X101G-X103A-X104I-X217E-X232V-X245R,X024R-X043R-X076D-X078R-X101G-X103A-X104I-X232V-X245R-X269R,X043R-X045T-X076D-X078R-X101G-X103A-X104I-X166F-X176P-X179V-X184T-X187P-X194P,X018R-X022W-X024R-X041E-X076D-X101A-X160T-X183D-X211Q-X213A-X249R,X018R-X020R-X022W-X024R-X076D-X116A-X183D-X198L-X211Q-X215F-X249R,X018R-X020R-X022W-X024R-X076D-X101A-X116A-X198L-X213A-X249R,X018R-X022W-X024R-X076D-X101A-X116A-X183D-X198L-X211Q-X213A-X249R,X018R-X020R-X024R-X076D-X198L-X213A-X249R,X018R-X020R-X022W-X024R-X076D-X116A-X183D-X198L-X211Q-X249R,X018R-X020R-X024R-X076D-X183D-X211Q-X215F-X249R,X024R-X076D-X104I,X018R-X076D-X101G-X232V,X018R-X024R-X076D-X101A-X116A-X183D-X198L-X211Q-X213A-X215F-X249R,X018R-X020R-X022W-X024R-X076D-X116A-X183D-X215F-X249R,X018R-X024R-X031F-X076D-X116A-X183D-X211Q-X213A-X215F-X249R,X018R-X024R-X076D-X101A-X116A-X183D-X198L-X213A-X249R-X269S,X018R-X020R-X024R-X076D-X101A-X116A-X198L-X215F-X249R,X018R-X043R-X076D-X078R-X101G-X103A-X104I-X232V-X245R-X269R,X018R-X020R-X024R-X076D-X101A-X114T-X198L-X211Q-X215F-X249R,X024R-X043R-X078R-X101G-X103A-X104I-X217E-X232V-X245R,X024R-X076D-X103A-X104I-X232V,X018R-X020R-X022W-X024R-X076D-X101A-X198L-X211Q-X215F-X249R,X101G-X104I-X232V,X018R-X022W-X024R-X076D-X183D-X198L-X213A-X215F-X249R,X018R-X022W-X024R-X076D-X183D-X198L-X211Q-X249R,X018R-X020R-X024R-X076D-X183D-X213A-X249R,X018R-X024R-X076D-X101A-X183D-X211Q-X215F-X249R,X018R-X020R-X022W-X024R-X076D-X116A-X211Q-X213A-X249R,X018R-X078R-X101G-X103A-X104I-X232V-X245R-X269R,X018R-X022W-X024R-X076D-X101A-X116A-X183D-X211Q-X215F-X249R-X260A,X076D-X249R,X018R-X022W-X024R-X076D-X183D-X211Q-X215F-X249R,X018R-X020R-X024R-X076D-X116A-X211Q-X215F-X249R,

X018R-X020R-X024R-X076D-X213A-X249R,X018R-X020R-X022W-X024R-X076D-X116A-X183D-X198L-X249R,X018R-X020R-X022W-X024R-X076D-X101A-X183D-X249R,X076D-X104I-X249R,X020R-X022W-X101A-X103A-X104I-X116A-X183D-X211Q-X213A-X215F-X232V-X245R,X024R-X043R-X045T-X078R-X101G-X103A-X104I-X217E-X232V-X245R,X018R-X020R-X022W-X024R-X076D-X183D-X198L-X215F-X249R,X018R-X076D-X101G-X103A,X020R-X024R-X101G-X103A-X104I-X232V-X245R-X269R,X018R-X020R-X024R-X076D-X101A-X116A-X183D-X211Q-X249R,X101G-X103A-X232V,X024R-X076D-X101G-X232V,X018R-X022W-X024R-X076D-X101A-X183D-X198L-X211Q-X249R,X018R-X020R-X024R-X076D-X101A-X183D-X198L-X211Q-X215F-X249R,X018R-X020R-X024R-X076D-X183D-X198L-X249R,X018R-X022W-X024R-X076D-X101A-X116A-X183D-X198L-X211Q-X249R,X018R-X020R-X024R-X076D-X116A-X156V-X183D-X211Q-X215F-X249R-X269S,X045T-X076D-X101G-X103A-X104I-X232V-X245R-X249R,X018R-X020R-X024R-X076D-X101A-X183D-X198L-X249R,X018R-X020R-X022W-X024R-X076D-X198L-X211Q-X215F-X249R,X018R-X020R-X022W-X024R-X076D-X101A-X116A-X198L-X211Q-X215F-X249R,X018R-X020R-X022W-X024R-X076D-X116A-X249R,X018R-X076D-X101G,X018R-X024R-X076D-X116A-X183D-X198L-X213A-X215F-X249R,X018R-X020R-X022W-X024R-X076D-X101A-X116A-X198L-X213A-X215F-X249R,X018R-X024R-X076D-X101A-X116A-X183D-X198L-X211Q-X249R,X018R-X076D-X232V,X018R-X020R-X024R-X076D-X101A-X232V-X245R,X018R-X043D-X045T-X076D-X101G-X103A-X104I-X232V-X245R,X018R-X022W-X024R-X076D-X183D-X213A-X215F-X249R,X018R-X024R-X076D-X101A-X116A-X211Q-X213A-X237D-X249R,X018R-X020R-X024R-X076D-X101A-X116A-X183D-X211Q-X249R-X275S,X018R-X022W-X024R-X076D-X101A-X116A-X183D-X198L-X211Q-X213A-X215F-X249R,X024R-X076D,X018R-X024R-X076D-X183D-X211Q-X215F-X249R,X018R-X022W-X024R-X076D-X116A-X183D-X198L-X213A-X215F-X249R,X076D-X104I-X232V-X249R,X018R-X076D-X103A-X232V,X018R-X020R-X024R-X076D-X101A-X116A-X183D-X198L-X211Q-X213A-X249R,X018R-X020R-X024R-X076D-X101A-X183D-X213A-X249R,X018R-X020R-X024R-X076D-X101A-X175E-X183D-X211Q-X215F-X249R,X018R-X020R-X043D-X078R-X101G-X103A-X104I-X217E-X232V-X245R-X273E,X020R-X024R-X043D-X045T-X076D-X101G-X103A-X104I-X232V-X245R,X005S-X101G-X103A-X104I-X232V-X245R-X249R,X103A-X104I-X232V,X018R-X020R-X024R-X068A-X076D-X101A-X116A-X213A-X215F-X249R,X018R-X022W-X024R-X076D-X101A-X198L-X215F-X249R-X275S,X018R-X024R-X076D-X183D-X198L-X211Q-X213A-X249R,和X043D-X045T-X101G-X103A-X104I-X232V-X245R,其中所述枯草杆菌蛋白酶变体的氨基酸位置通过与如SEQ ID NO:1所示解淀粉芽孢杆菌(B.amyloliquefaciens)枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[1012] 20.一种分离的枯草杆菌蛋白酶变体,其中所述枯草杆菌蛋白酶变体为具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:X018R-X024R-X043R-X076D-X249R-X269R,X018R-X022R-X024R-X043R-X076D-X249R,X018R-X043D-X101G-X103A-X104I-X232V-X245R,X020R-X043D-X101G-X103A-X104I-X232V-

X245R,X043D-X101G-X103A-X104I-X232V-X245R-X269R,X043D-X078R-X101G-X103A-X104I-X232V-X245R,X043R-X076D-X101G-X103A-X104I-X232V-X245R,X022R-X043R-X101G-X103A-X104I-X232V-X245R,X043R-X078R-X101G-X103A-X104I-X232V-X245R,X020R-X076D-X101G-X103A-X104I-X232V-X245R,X043R-X076D-X101G-X103A-X104I-X232V-X245R,X022R-X076D-X101G-X103A-X104I-X232V-X245R,X076D-X078R-X101G-X103A-X104I-X232V-X245R,X018R-X024R-X043R-X076D-X249R,X018R-X024R-X076D-X242R-X249R,X018R-X024R-X076D-X249R-X269R,X018R-X022R-X024R-X076D-X249R,X018R-X024R-X076D-X078R-X249R,X018R-X024R-X043D-X076D-X249R-X269R,X018R-X022R-X024R-X043D-X076D-X249R,X018R-X024R-X043D-X076D-X078R-X249R,X020R-X101G-X103G-X104I-X232V-X245R,X020R-X101G-X103A-X104L-X232V-X245R,X020R-X101G-X103A-X104V-X232V-X245R,X020R-X101G-X103S-X104I-X232V-X245R,X020R-X101G-X103S-X104L-X232V-X245R,X020R-X101S-X103S-X104I-X232V-X245R,X020R-X101S-X103S-X104L-X232V-X245R,X020R-X101A-X103A-X104L-X232V-X245R,X020R-X101S-X103S-X104V-X232V-X245R,X020R-X101S-X103A-X104I-X232V-X245R,X020R-X101S-X103A-X104V-X232V-X245R,X020R-X101S-X103G-X104I-X232V-X245R,X020R-X101S-X103G-X104V-X232V-X245R,X020R-X101A-X103A-X104V-X232V-X245R,X020R-X101A-X103S-X104I-X232V-X245R,X020R-X101A-X103S-X104V-X232V-X245R,X018R-X024R-X043R-X076D-X078R-X249R,X024R-X043D-X101G-X103A-X104I-X232V-X245R,X043D-X101G-X103A-X104I-X232V-X245R-X249R,X024R-X076D-X101G-X103A-X104I-X232V-X245R,X076D-X101G-X103A-X104I-X232V-X242R-X245R,X018R-X020R-X024R-X076D-X217E-X249R,X018R-X024R-X043R-X076D-X217E-X249R,X018R-X024R-X043D-X076D-X242R-X249R,X018R-X020R-X024R-X043R-X076D-X249R,X020R-X101A-X103G-X104V-X232V-X245R,X043D-X101G-X103A-X104I-X232V-X245R,X018R-X024R-X076D-X217E-X249R-X269R,和X018R-X024R-X076D-X217E-X242R-X249R,其中所述枯草杆菌蛋白酶变体的氨基酸位置通过与如SEQ ID NO:1所示解淀粉芽孢杆菌(B.amyloliquefaciens)枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[1013] 21.一种分离的枯草杆菌蛋白酶变体,其中所述枯草杆菌蛋白酶变体为具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:X020R-X101A-X103A-X104I-X118R-X232V-X245R,X020R-X024R-X116A-X213A,X043R-X101A-X116A-X215F-X269R,X024R-X043R-X101A-X116A,X024R-X043R-X101A-X116A-X215F-X269R,X020R-X101G-X103A-X104I-X215F-X232V-X245R,X043R-X101A-X269R,X024R-X043R-X116A-X213A-X269R,X020R-X024R-X043R-X045T-X101A-X213A,X024R-X043R-X116A-X215F-X269R,X020R-X024R-X213A-X215F,X020R-X116A-X269R,X024R-X116A-X213A-X269R,X043R-X101A-X116A-X269R,X101G-X103A-X104I-X116A-X213A-X232V-X245R-X269R,X024R-X043R-X045T-X101A-X116A-X215F-X269R,X020R-X043R-X101A-X269R,X101A-X103A-X104I-X213A-X232V-X245R-X269R,X024R-X215F-X269R,X043R-X101A-X116A-X213A-X215F-X269R,X043R-X101A-X213A-X269R,X020R-X024R-X043R-X045T-X116A-X213A,X101G-X103A-X104I-X232V-X245R-X269R,X024R-X043R-X045T-X101A-X116A-X213A-X269R,X024R-X043R-X045T-X269R,X020R-X043R-X045T-X101A-

X269R,X024R-X043R-X116A-X269R,X020R-X024R-X043R-X045T,X043R-X116A-X269R,X024R-X043R-X101A-X215F-X269R,X024R-X043R-X045T-X213A-X215F-X269R,X020R-X024R-X045T-X269R,X020R-X043R-X101A-X116A-X213A-X215F,X020R-X101G-X103A-X104I-X213A-X215F-X232V-X245R,X020R-X024R-X045T-X116A-X269R,X020R-X101A-X116A-X269R,X024R-X043R-X215F,X020R-X024R-X213A,X024R-X043R-X101A-X215F,X020R-X024R-X043R-X045T-X116A,X020R-X024R-X043R-X045T-X101A-X269R,X020R-X024R-X101A-X215F,X020R-X024R-X116A-X213A-X215F,X020R-X024R-X116A,X020R-X024R-X101A-X116A,X043R-X213A-X215F-X269R,X024R-X101A-X269R,X024R-X043R-X116A-X215F,X020R-X038A-X043R-X101A,X020R-X024R-X116A-X215F,X024R-X043R-X101A-X213A,X014L-X020R-X024R-X043R-X045T-X101A-X215F,X020R-X024R-X215F,X020R-X116A-X215F-X269R,X020R-X045T-X116A-X269R,X020R-X024R-X043R-X045T-X215F,和X020R-X024R-X043R-X045T-X116A-X213A-X215F,其中所述枯草杆菌蛋白酶变体的氨基酸位置通过与如SEQ ID NO:1所示解淀粉芽孢杆菌(B.amyloliquefaciens)枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[1014] 22.一种分离的枯草杆菌蛋白酶变体,其中所述枯草杆菌蛋白酶变体为具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:X043R-X076D-X101A-X103A-X104I-X158E-X188D-X232V-X245R-X248D-X249R-X271F,X024R-X043R-X076D-X101A-X103A-X104I-X158E-X188D-X217E-X232V-X245R-X248D-X249R,X101A-X103A-X104I-X158E-X188D-X232V-X245R-X248D-X249R-X271F-X271F,X101A-X103A-X104I-X158E-X188D-X217E-X232V-X245R-X248D-X249R-X271F,X076D-X101G-X103A-X104I-X114V-X158E-X188D-X232V-X245R-X248D-X249R-X271F,X024R-X076D-X101G-X103A-X104I-X158E-X188D-X232V-X245R-X248D-X249R-X271F,X024R-X043R-X101A-X103A-X104I-X158E-X188D-X217E-X232V-X245R-X248D-X249R,X024R-X043R-X101A-X103A-X104I-X158E-X188D-X232V-X245R-X248D-X249R,X024R-X101A-X103A-X104I-X158E-X166D-X188D-X217E-X232V-X245R-X248D-X249R,X076D-X101G-X103A-X104I-X128L-X158E-X188D-X232V-X245R-X248D-X249R-X271F,和X043R-X076D-X101G-X103A-X104I-X158E-X166D-X188D-X232V-X245R-X248D-X249R-X271F,其中所述枯草杆菌蛋白酶变体的氨基酸位置通过与如SEQ ID NO:1所示解淀粉芽孢杆菌(B.amyloliquefaciens)枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[1015] 23.一种分离的枯草杆菌蛋白酶变体,其中所述枯草杆菌蛋白酶变体为具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:X022A-X101G-X103A-X104I-X159D-X217E-X232V-X245R-X248D-X271F,X022A-X043R-X101G-X103A-X104I-X159D-X188D-X217E-X232V-X245R-X248D-X271F,X022A-X101G-X103A-X104I-X159D-X188D-X232V-X245R-X248D-X271F,X043R-X101A-X103A-X104I-X158E-X188D-X217E-X232V-X245R-X248D-X249R,X043R-X076D-X101A-X103A-X104I-X158E-X188D-X217E-X232V-X245R-X248D-X249R-X271F,X024R-X101G-X103A-X104I-X158E-X188D-X217E-X232V-X245R-X248D-X249R,X024R-X101G-X103A-X104I-X158E-X188D-X232V-X245R-X248D-X249R,X101G-X103A-X104I-X158E-X188D-X232V-X245R-X248D-X249R,X024R-X101G-X103A-X104I-X158E-X183D-X188D-X232V-X245R-X248D-X249R,

X022A-X076D-X101G-X103A-X104I-X159D-X188D-X232V-X245R-X248D-X271F,X022A-X043R-X076D-X101G-X103A-X104I-X159D-X188D-X232V-X245R-X248D-X271F,X022A-X076D-X101G-X103A-X104I-X159D-X232V-X245R-X248D-X271F,X022A-X101G-X103A-X104I-X159D-X232V-X245R-X248D-X271F,X076D-X101A-X103A-X104I-X158E-X188D-X232V-X245R-X248D-X249R-X271F,X043R-X101A-X103A-X104I-X158E-X166D-X188D-X232V-X245R-X248D-X249R,X024R-X076D-X101A-X103A-X104I-X158E-X166D-X188D-X232V-X245R-X248D-X249R-X271F,X076D-X101A-X103A-X104I-X158E-X188D-X232V-X245R-X248D-X249R,X101A-X103A-X104I-X158E-X166D-X188D-X232V-X245R-X248D-X249R-X271F,X043R-X076D-X101A-X103A-X104I-X158E-X166D-X188D-X232V-X245R-X248D-X249R-X271F,X101G-X103A-X104I-X158E-X166D-X188D-X232V-X245R-X248D-X249R-X271F,X101A-X103A-X104I-X158E-X188D-X232V-X245R-X248D-X249R-X271F,X101A-X103A-X104I-X158E-X188D-X217E-X232V-X245R-X248D-X249R,X076D-X101A-X103A-X104I-X158E-X166D-X188D-X232V-X245R-X248D-X249R-X271F,X101G-X103A-X104I-X158E-X183D-X188D-X232V-X245R-X248D-X249R,X024R-X101G-X103A-X104I-X128L-X158E-X188D-X232V-X245R-X248D-X249R,X076D-X101G-X103A-X104I-X158E-X166D-X188D-X232V-X245R-X248D-X249R-X271F,X043R-X076D-X101A-X103A-X104I-X158E-X166D-X188D-X232V-X245R-X248D-X249R,和X076D-X101A-X103A-X104I-X158E-X188D-X217E-X232V-X245R-X248D-X249R-X271F,其中所述枯草杆菌蛋白酶变体的氨基酸位置通过与如SEQ ID NO:1所示解淀粉芽孢杆菌(B.amyloliquefaciens)枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[1016] 24.一种分离的枯草杆菌蛋白酶变体,其中所述枯草杆菌蛋白酶变体为具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:X017R-X022A-X076D-X101G-X103A-X104I-X159D-X188D-X232V-X245R-X248D-X271F,X022A-X043R-X101G-X103A-X104I-X159D-X232V-X245R-X248D-X271F,X022A-X101G-X103A-X104I-X159D-X188D-X232V-X245R-X248D-X249R-X271F,X017R-X022A-X076D-X101G-X103A-X104I-X159D-X232V-X245R-X248D-X271F,X022A-X076D-X101G-X103A-X104I-X159D-X232V-X245R-X248D-X249R-X271F,X022A-X101G-X102A-X103A-X104I-X159D-X188D-X232V-X245R-X248D-X271F,和X022A-X043R-X076D-X101G-X103A-X104I-X159D-X232V-X245R-X248D-X249R-X271F,其中所述枯草杆菌蛋白酶变体的氨基酸位置通过与如SEQ ID NO:1所示解淀粉芽孢杆菌(B.amyloliquefaciens)枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[1017] 25.一种分离的枯草杆菌蛋白酶变体,其中所述枯草杆菌蛋白酶变体为具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:X101S-X103A-X104I-X158E-X188D-X232V-X245R-X248D-X249R,X101S-X103G-X104V-X158E-X188D-X232V-X245R-X248D-X249R,X101G-X103S-X104I-X158E-X188D-X232V-X245R-X248D-X249R,X101A-X103A-X104I-X158E-X188D-X232V-X245R-X248D-X249R,X101A-X103A-X104L-X158E-X188D-X232V-X245R-X248D-X249R,X101G-X103G-X104I-X158E-X188D-X232V-X245R-X248D-X249R,X101S-X103G-X104I-X158E-X188D-X232V-X245R-X248D-X249R,X101S-X103S-X104I-X158E-X188D-X232V-X245R-X248D-X249R,X101S-

X103S-X104V-X158E-X188D-X232V-X245R-X248D-X249R,X101A-X103S-X104I-X158E-X188D-X232V-X245R-X248D-X249R,X101A-X103S-X104I-X159E-X232V-X245R-X248D-X249R,X101S-X103A-X104I-X159E-X232V-X245R-X248D-X249R,X101G-X103A-X104L-X158E-X188D-X232V-X245R-X248D-X249R,X101A-X103A-X104L-X159E-X232V-X245R-X248D-X249R,X101A-X103S-X104L-X159E-X232V-X245R-X248D-X249R,X101G-X103S-X104L-X159E-X232V-X245R-X248D-X249R,X101S-X103A-X104L-X159E-X232V-X245R-X248D-X249R,X101A-X103G-X104V-X159E-X232V-X245R-X248D-X249R,和X101S-X103A-X104V-X159E-X232V-X245R-X248D-X249R,其中所述枯草杆菌蛋白酶变体的氨基酸位置通过与如SEQ ID NO:1所示解淀粉芽孢杆菌(B.amyloliquefaciens)枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[1018] 26.一种分离的枯草杆菌蛋白酶变体,其中所述枯草杆菌蛋白酶变体为具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:X026F-X051W-X104L-X106E,X026F-X031F-X078N-X102A-X160D,X020K-X100S-X116L-X158E-X166D-X243F,X033S-X043W-X218D-X239G-X243F,X022L-X038F-X048R-X062E-X100S-X186K,X101D-X103N-X116L-X144R-X215D,X104L-X105T-X213A-X217E-X256N,X043W-X101D-X212M-X243F,X026F-X048R-X105T-X213A-X218D-X224A,X024F-X101D-X118R-X215D-X250I-X272F,X121F-X185E-X224A-X239G,X022L-X031F-X102A-X128D-X224A-X243F,X062E-X078N-X102A-X116L-X144R-X250I,X022L-X038F-X121F-X160D-X272F,X026F-X078N-X159C-X186K-X243F,X024F-X048R-X118R-X166D-X217E,X023A-X038F-X078N-X100S-X212M-X215D,X100S-X116L-X158E-X213A,X078N-X104L-X118R-X128D,X102A-X103N-X105T-X194E,X022L-X078N-X128D-X213A,X027R-X100S-X118R-X160D-X188D-X243F,X024F-X102A-X186K-X213A-X217E-X243F,X033S-X105T-X188D-X216F,X023A-X100S-X194E-X212M,X048R-X128D-X185E-X239G,X020K-X024F-X033S-X129E-X194E,X020K-X027R-X129E-X166D-X239G,X022L-X023A-X027R-X101D-X104L-X216F,X033S-X118R-X129E-X194E-X239G,X022L-X078N-X116L-X129E-X256N,X027R-X101D-X103N-X105T-X272F,X048R-X078N-X116L-X185E-X217E-X239G,X023A-X024F-X027R-X062E,X024F-X103N-X104L-X118R-X188D,X026F-X104L-X256N-X272F,X024F-X043W-X104L-X121F-X129E,X062E-X078N-X116L-X224A,X023A-X024F-X051W-X158E,X027R-X038F-X102A-X116L,X062E-X078N-X144R-X212M,X031F-X116L-X256N-X272F,X022L-X033S-X104L-X116L-X160D-X186K,X024F-X118R-X129E-X186K-X213A,X043W-X105T-X213A-X215D-X216F,X031F-X105T-X186K-X188D,X026F-X194E-X213A-X256N,和X103N-X160D-X250I-X256N,其中所述枯草杆菌蛋白酶变体的氨基酸位置通过与如SEQ ID NO:1所示解淀粉芽孢杆菌(B.amyloliquefaciens)枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[1019] 27.一种分离的枯草杆菌蛋白酶变体,其中所述枯草杆菌蛋白酶变体为具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:X022A-X024R-X101D-X103A-X104I-X118R-X159D-X188D-X232V-X248D-X271F,X022A-X024R-X103A-X104I-X129E-X159D-X188D-X232V-X248D-X271F,X022A-X024R-X103A-X104I-X118R-X159D-X188D-X217D-X232V-X248D,X022A-X024R-X101D-X103A-X104I-X118R-

X129E-X159D-X188D-X232V-X245R-X248D,X022A-X024R-X101D-X103A-X104I-X159D-X188D-X232V-X245R-X248D,X022A-X043R-X103A-X104I-X118R-X129E-X159D-X188D-X232V-X245R-X248D,X022A-X043R-X103A-X104I-X118R-X128I-X129E-X159D-X188D-X232V-X248D,X022A-X043R-X101D-X103A-X104I-X118R-X129E-X159D-X188D-X232V-X248D-X271F,X022A-X024R-X043R-X101D-X103A-X104I-X159D-X188D-X232V-X245R-X248D,X022A-X103A-X104I-X159D-X188D-X232V-X248D,X022A-X024R-X103A-X104I-X118R-X129E-X159D-X188D-X232V-X248D-X271F,X022A-X024R-X103A-X104I-X159D-X188D-X217D-X232V-X245R-X248D-X271F,X022A-X043R-X062E-X103A-X104I-X159D-X188D-X232V-X245R-X248D-X271F,X022A-X043R-X103A-X104I-X129E-X159D-X188D-X232V-X245R-X248D,X022A-X024R-X103A-X104I-X159D-X188D-X217D-X232V-X248D-X271F,X022A-X103A-X104I-X118R-X159D-X188D-X217D-X232V-X245R-X248D,X022A-X024R-X101D-X103A-X104I-X118R-X128I-X159D-X188D-X232V-X245R-X248D,X022A-X024R-X043R-X103A-X104I-X159D-X188D-X217D-X232V-X248D-X271F,X022A-X043R-X103A-X104I-X118R-X159D-X188D-X217D-X232V-X248D-X271F,X022A-X043R-X103A-X104I-X118R-X159D-X188D-X232V-X248D-X271F,X022A-X103A-X104I-X128I-X129E-X159D-X188D-X232V-X248D-X271F,X022A-X103A-X104I-X159D-X188D-X217D-X232V-X245R-X248D-X271F,X022A-X043R-X103A-X104I-X128I-X159D-X188D-X232V-X245R-X248D,X022A-X101D-X103A-X104I-X118R-X159D-X188D-X217D-X232V-X245R-X248D-X271F,X022A-X103A-X104I-X118R-X129E-X159D-X188D-X232V-X245R-X248D-X271F,X022A-X024R-X043R-X103A-X104I-X118R-X159D-X188D-X217D-X232V-X248D,X022A-X062E-X103A-X104I-X118R-X159D-X188D-X232V-X245R-X248D,X022A-X043R-X101D-X103A-X104I-X118R-X129E-X159D-X188D-X217D-X232V,X022A-X024R-X103A-X104I-X159D-X188D-X217D-X232V-X248D,X022A-X024R-X043R-X103A-X104I-X118R-X128I-X129E-X159D-X188D-X217D-X232V-X248D-X271F,和X022A-X103A-X104I-X118R-X159D-X188D-X217D-X232V-X245R-X248D-X271F,其中所述枯草杆菌蛋白酶变体的氨基酸位置通过与如SEQ ID NO:1所示解淀粉芽孢杆菌(B.amyloliquefaciens)枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[1020] 28.一种分离的枯草杆菌蛋白酶变体,其中所述枯草杆菌蛋白酶变体为具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:X020K-X024F-X062E-X188D-X239G,X024F-X062E-X116L-X239G,X020K-X023A-X062E-X188D,X020K-X023A-X024F-X062E-X118R-X188D-X213A,X020K-X043W-X062E-X116L-X188D-X213A-X239G,X023A-X062E-X116L-X118R,X023A-X024F-X062E-X116L-X118R,X024F-X116L,X024F-X062E-X188D-X213A,X023A-X062E-X116L-X118R-X188D-X239G,X020K-X024F-X062E,X020K-X043W-X062E-X116L-X239G,X024F-X062E-X116L-X213A-X239G,X020K-X024F-X043W-X062E-X116L-X213A,X020K-X023A-X024F-X062E-X116L-X188D-X213A,X024F-X062E-X188D-X239G,X023A-X043W-X062E-X116L-X118R-X213A,X062E-X188D-X239G,X020K-X024F-X062E-X239G,X024F-X116L-X118R-X188D-X239G,X020K-X023A-X062E-X116L-X118R-X213A,X020K-X023A-X024F-X062E-X188D-X213A-X239G,X024F-X043W-X118R-X188D,X023A-X024F-X116L-X118R-X188D-X213A,X020K-X023A-

X043W-X116L-X188D-X213A-X239G,X023A-X024F-X116L-X188D-X239G,X023A-X043W-X116L-X118R-X188D,X023A-X024F-X118R-X188D-X239G,X023A-X024F-X043W-X062E-X116L-X118R,X020K-X043W-X188D-X213A,X024F-X062E-X118R-X239G,X023A-X043W-X188D-X213A,X020K-X024F-X043W-X062E-X116L-X118R-X188D-X239G,X020K-X116L-X188D-X239G,X020K-X043W-X062E-X118R,X020K-X043W-X116L-X188D-X213A,X020K-X024F,X023A-X043W-X116L-X239G,X023A-X024F-X043W-X116L-X118R-X188D-X239G,X020K-X023A-X043W-X213A,和X023A-X024F-X062E-X118R-X213A-X239G,其中所述枯草杆菌蛋白酶变体的氨基酸位置通过与如SEQ ID NO:1所示解淀粉芽孢杆菌(B.amyloliquefaciens)枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[1021] 29.一种分离的枯草杆菌蛋白酶变体,其中所述枯草杆菌蛋白酶变体为具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:X020K-X023A-X043W-X118R-X128I-X129E-X159D-X188D,X024F-X118R-X128I-X129E-X159D,X020K-X024F-X062E-X116L-X118R-X188D,X020K-X062E-X116L-X188D,X062E-X116L-X118R-X213A,X020K-X023A-X062E-X116L-X188D,X062E-X116L-X118R-X188D,X020K-X062E-X116L-X213A,X020K-X023A-X062E-X116L,X020K-X062E-X188D-X213A,X020K-X062E,X020K-X024F-X062E-X116L-X188D,X020K-X043W-X062E-X116L-X188D,X020K-X024F-X062E-X188D-X213A,X062E-X116L-X188D-X213A,X020K-X062E-X116L,X020K-X023A-X062E-X116L-X188D-X213A,X023A-X024F-X062E-X116L-X213A,X022A-X043R-X103A-X104I-X128I-X129E-X159D-X188D-X232V-X245R-X248D,X022A-X043R-X103A-X104I-X118R-X128I-X129E-X159D-X188D-X232V-X248D-X271F,X024F-X062E-X116L-X188D,X022A-X024R-X103A-X104I-X118R-X128I-X129E-X159D-X188D-X232V-X248D,X023A-X062E-X116L-X188D,X043W-X062E-X116L,X020K-X023A-X116L-X188D,X043W-X062E-X116L-X188D,X024F-X062E-X116L,X062E-X116L-X188D,和X022A-X024R-X103A-X104I-X128I-X159D-X188D-X232V-X248D,其中所述枯草杆菌蛋白酶变体的氨基酸位置通过与如SEQ ID NO:1所示解淀粉芽孢杆菌(B.amyloliquefaciens)枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[1022] 30.一种分离的枯草杆菌蛋白酶变体,其中所述枯草杆菌蛋白酶变体为具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:X020K-X023A-X043W-X118R-X128I-X129E-X159D-X188D,X024F-X118R-X128I-X129E-X159D,X020K-X024F-X062E-X116L-X118R-X188D,X020K-X062E-X116L-X188D,X062E-X116L-X118R-X213A,X020K-X023A-X062E-X116L-X188D,X062E-X116L-X118R-X188D,X020K-X062E-X116L-X213A,X020K-X023A-X062E-X116L,X020K-X062E-X188D-X213A,X020K-X062E,X020K-X024F-X062E-X116L-X188D,X020K-X043W-X062E-X116L-X188D,X020K-X024F-X062E-X188D-X213A,X062E-X116L-X188D-X213A,X020K-X062E-X116L,X020K-X023A-X062E-X116L-X188D-X213A,X023A-X024F-X062E-X116L-X213A,X022A-X043R-X103A-X104I-X128I-X129E-X159D-X188D-X232V-X245R-X248D,X022A-X043R-X103A-X104I-X118R-X128I-X129E-X159D-X188D-X232V-X248D-X271F,X024F-X062E-X116L-X188D,X022A-X024R-X103A-X104I-X118R-X128I-X129E-X159D-X188D-X232V-X248D,X023A-X062E-X116L-X188D,X043W-X062E-X116L,X020K-X023A-X116L-X188D,X043W-

X062E-X116L-X188D,X024F-X062E-X116L,X062E-X116L-X188D,和X022A-X024R-X103A-X104I-X128I-X159D-X188D-X232V-X248D,其中所述枯草杆菌蛋白酶变体的氨基酸位置通过与如SEQ ID NO:1所示解淀粉芽孢杆菌(B.amyloliquefaciens)枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[1023] 31.一种分离的枯草杆菌蛋白酶变体,其中所述枯草杆菌蛋白酶变体为具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:X024R-X086W-X118R,X024R-X078R-X086W-X243F,X024R-X033S-X086S-X087N-X209A,X033S-X118R,X024R-X078R-X086W-X118R-X270T,X024R-X033S-X086W-X118R,X078R-X086W-X243F,X033S-X078R-X086W-X118R-X209A,X033S-X078R-X209A,X086W-X118R-X243F,X024R-X086W,X078R-X086W-X235F,X024R-X118R,X024R-X086R,X101G-X103A-X104I-X232V,X024R-X033S-X078R-X086W-X118R,X024R-X118R-X209A,X209A-X241R,X033S-X086W-X243F,X033S-X172V-X209A,X118R-X209A-X243F,X024R-X086S-X141G,X024R-X118R-X209A-X243F,X024R-X033S-X086S-X085N-X235F,X024R-X033S-X133V,X024R-X033S-X078R-X086W,X024R-X086W-X209A,X024R-X241R,X033S-X118R-X243F,X024R-X235F,X024R-X078R-X086W,X024R-X118R-X209A-X235F,X024R-X209A-X241R,X033S-X118R-X241R,X086W-X118R-X209A,X033S-X118R-X159D-X209A,X033S-X078R-X086W,X024R-X086W-X243F,X118R-X209A,X024R-X086W-X118R-X203I,X078R-X209A-X235F,X024R-X033S-X241R,X078R-X118R,X033S-X118R-X209A-X243F,X021M-X024R-X033S,X024R-X033S-X086W,X033S-X235F,X078R-X086W-X209A,X024R-X033S-X209A-X235F,X033S-X086W-X118R,X024R-X033S-X078R-X209A,X033S-X086W-X118R-X209A-X243F,X086W-X209A-X243F,X005S-X078R-X118R-X241R,X024R-X174T,X033S-X209A-X243F,X086W-X118R-X133V,X024R-X033S-X118R,X024R-X086W-X209A-X235F,X086W-X209A,X008T-X024R,X086W-X118R,X033S-X241R,X005S-X024R-X033S-X243F,X024R-X209A-X242P,X024R-X033S-X078R-X118R,X024R-X033S-X194T,X024R-X243F,X024R-X209A,X024R-X033S-X118R-X209A,X033S-X086W,X024R-X033S,X024R-X033S-X078R-X243F,X086W-X243F,X033S-X118D-X138V-X209A,X033S-X209A-X235F,X024R-X086R-X118R,X033S-X201S,X024R-X239Q,X033S-X118R-X209A-,X078R-X086W,X235F-X243F,X024R-X209A-X235F,X118R-X172V,X017Y-X024R-X033S-X086W,X033S-X148F,X024R-X118R-X235F,X033S-X078R,X033S-X243F,X024C-X033S,X118R-X194T,X033S-X209A,X118R-X209A-X235F,X024R-X033S-X209A-X243F,X024R-X033S-X235F,X024R-X033S-X118R-X235F,X024R-X141G,X024R-X274I,X024R-X033S-X209A,X086W-X235F,X024R-X209A-X243F,X004E-X033S-X078R,X086W-X209A-X235F,X015T-X033S,X033S-X086W-X156L-X209A,X024R-X118R-X243F-X269H,X209A-X235F,X024R-X247H,X024R-X033S-X228T,X078R-X235F,X024R-X033S-X174V-X235F,X024R-X235F-X243F,X024R-X033S-X235F-X241R,X024R-X033S-X151V,X024R-X104A,X033S-X048T,X012H-X104A-X118R,X118R-X235F,X033S-X253A,X143A-X209A,X024R-X033S-X243F,X033S-X239T,X209A-X243F,X024R-X033S-X129H-X184D-X253M,X024R-X085V-X086W-X118R-X235F,X024R-X272P,和X024R-X269C,其中所述枯草杆菌蛋白酶变体的氨基酸位置通过与如SEQ ID NO:1所示解淀粉芽孢杆菌(B.amyloliquefaciens)枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编

号。

[1024] 32.一种分离的枯草杆菌蛋白酶变体,其中所述枯草杆菌蛋白酶变体为具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:X020R-X087D-X101G-X103A-X104I-X232V-X245R,X020R-X101G-X103A-X104I-X150L-X232V-X245R,X018R-X020R-X024R-X076D-X087D-X249R,X018R-X020R-X024R-X076D-X150L-X249R,X018R-X024R-X043R-X076D-X087D-X249R,X018R-X024R-X043R-X076D-X150L-X249R,X018R-X024R-X076D-X078R-X087D-X249R,X018R-X024R-X076D-X078R-X150L-X249R,X018R-X024R-X076D-X087D-X249R-X269R,X018R-X024R-X076D-X087D-X242R-X249R,X018R-X024R-X076D-X087D-X150L-X249R,X018R-X024R-X076D-X150L-X249R,X018R-X087D-X101G-X103A-X104I-X232V-X245R,X018R-X101G-X103A-X104I-X150L-X232V-X245R,X018R-X022R-X024R-X076D-X087D-X249R,X018R-X022R-X024R-X076D-X150L-X249R,X043R-X087D-X101G-X103A-X104I-X232V-X245R-X269R,X043R-X101G-X103A-X104I-X150L-X232V-X245R,X024R-X087D-X101G-X103A-X104I-X232V-X245R,X024R-X101G-X103A-X104I-X150L-X232V-X245R,X078R-X087D-X101G-X103A-X104I-X232V-X245R,X078R-X101G-X103A-X104I-X150L-X232V-X245R,X087D-X101G-X103A-X104I-X232V-X245R-X269R,X101G-X103A-X104I-X150L-X232V-X245R-X249R,X101G-X103A-X104I-X150L-X232V-X245R-X269R,X022R-X087D-X101G-X103A-X104I-X232V-X245R,X018R-X024R-X043D-X076D-X150L-X249R,X043R-X087D-X101G-X103A-X104I-X232V-X245R,X022R-X101G-X103A-X104I-X150L-X232V-X245R,X018R-X024R-X043D-X076D-X087D-X249R,X018R-X024R-X076D-X087D-X249R,X018R-X024R-X076D-X150L-X242R-X249R,X043R-X101G-X103A-X104I-X150L-X232V-X245R-X269R,X076D-X101G-X103A-X104I-X150L-X232V-X245R,X087D-X101G-X103A-X104I-X232V-X242R-X245R,X101G-X103A-X104I-X150L-X232V-X245R,X076D-X087D-X101G-X103A-X104I-X232V-X245R,X087D-X101G-X103A-X104I-X232V-X245R,和X101G-X103A-X104I-X150L-X232V-X242R-X245R,其中所述枯草杆菌蛋白酶变体的氨基酸位置通过与如SEQ ID NO:1所示解淀粉芽孢杆菌(B.amyloliquefaciens)枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[1025] 33.一种分离的枯草杆菌蛋白酶变体,其中所述枯草杆菌蛋白酶变体为具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:X024R-X101G-X103A-X104I-X129Q-X158E-X188D-X217E-X232V-X245R-X248D-X249R,X024R-X101G-X103A-X104I-X130A-X158E-X183D-X188D-X232V-X245R-X248D-X249R,X024R-X101G-X103A-X104I-X129Q-X158E-X183D-X188D-X232V-X245R-X248D-X249R,X101G-X103A-X104I-X130A-X158E-X188D-X232V-X245R-X248D-X249R,X024R-X101G-X103A-X104I-X129Q-X158E-X188D-X232V-X245R-X248D-X249R,X024R-X101G-X103A-X104I-X130A-X158E-X188D-X232V-X245R-X248D-X249R,X024R-X101G-X103A-X104I-X129Q-X130A-X158E-X183D-X188D-X232V-X245R-X248D-X249R,X024R-X101G-X103A-X104I-X128L-X129Q-X158E-X188D-X232V-X245R-X248D-X249R,X024R-X101G-X103A-X104I-X129Q-X130A-X158E-X188D-X232V-X245R-X248D-X249R,X101G-X103A-X104I-X129Q-X158E-X188D-X232V-X245R-X248D-X249R,X101G-X103A-X104I-X129Q-X130A-X158E-

X188D-X232V-X245R-X248D-X249R,X024R-X101G-X103A-X104I-X128L-X129Q-X130A-X158E-X188D-X232V-X245R-X248D-X249R,X101G-X103A-X104I-X128L-X129Q-X158E-X188D-X232V-X245R-X248D-X249R,和X024R-X027R-X101G-X103A-X104I-X128L-X129Q-X130A-X158E-X188D-X232V-X245R-X248D-X249R,其中所述枯草杆菌蛋白酶变体的氨基酸位置通过与如SEQ ID NO:1所示解淀粉芽孢杆菌(B.amyloliquefaciens)枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[1026] 34.一种分离的枯草杆菌蛋白酶变体,其中所述枯草杆菌蛋白酶变体为具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:X101G-X103A-X104I-X232V-X222Q-X245R,X101G-X103A-X104I-X158E-X188D-X222S-X232V-X245R-X248D-X249R,X101G-X103A-X104I-X158E-X188D-X222Q-X232V-X245R-X248D-X249R,X076D-X101G-X103A-X104I-X232V-X222Q-X245R,X101G-X103A-X104I-X232V-X222S-X245R,X076D-X101G-X103A-X104I-X232V-X222S-X245R,和X076D-X101G-X103A-X104I-X158E-X188D-X222S-X232V-X245R-X248D-X249R,其中所述枯草杆菌蛋白酶变体的氨基酸位置通过与如SEQ ID NO:1所示解淀粉芽孢杆菌(B.amyloliquefaciens)枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[1027] 35.一种分离的枯草杆菌蛋白酶变体,其中所述枯草杆菌蛋白酶变体为具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:X024R-X101G-X103A-X104I-X128L-X129Q-X158E-X188D-X232V-X245R-X248D-X249R,X101G-X103A-X104I-X130A-X158E-X188D-X232V-X245R-X248D-X249R,X024R-X101G-X103A-X104I-X158E-X188D-X232V-X245R-X248D-X249R,X101G-X103A-X104I-X128L-X129Q-X158E-X188D-X232V-X245R-X248D-X249R,X101G-X103A-X104I-X129Q-X130A-X158E-X188D-X232V-X245R-X248D-X249R,X101G-X103A-X104I-X130A-X158E-X183D-X188D-X217E-X232V-X245R-X248D-X249R,X024R-X101G-X103A-X104I-X128L-X129Q-X130A-X158E-X188D-X232V-X245R-X248D-X249R,X024R-X101G-X103A-X104I-X129Q-X158E-X188D-X217E-X232V-X245R-X248D-X249R,X101G-X103A-X104I-X128L-X130A-X158E-X188D-X217E-X232V-X245R-X248D-X249R,X024R-X101G-X103A-X104I-X128L-X129Q-X158E-X183D-X188D-X232V-X245R-X248D-X249R,X024R-X101G-X103A-X104I-X128L-X129Q-X130A-X158E-X183D-X188D-X232V-X245R-X248D-X249R,X024R-X101G-X103A-X104I-X128L-X129Q-X158E-X188D-X232V-X245R-X248D-X249R-X271G,X101G-X103A-X104I-X129Q-X158E-X183D-X188D-X232V-X245R-X248D-X249R,X024R-X101G-X103A-X104I-X130A-X158E-X188D-X217E-X232V-X245R-X248D-X249R,X024R-X101G-X103A-X104I-X128L-X158E-X183D-X188D-X232V-X245R-X248D-X249R,X101G-X103A-X104I-X129Q-X158E-X188D-X217E-X232V-X245R-X248D-X249R,和X024R-X101G-X103A-X104I-X128L-X130A-X158E-X188D-X232V-X245R-X248D-X249R,其中所述枯草杆菌蛋白酶变体的氨基酸位置通过与如SEQ ID NO:1所示解淀粉芽孢杆菌(B.amyloliquefaciens)枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[1028] 36.一种分离的枯草杆菌蛋白酶变体,其中所述枯草杆菌蛋白酶变体为具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:X1R,X2W,X2M,X2R,X2A,X2S,X3R,X4R,X4C,X4S,X8A,X9F,X9W,X9A,X10S,X10M,X10H,X10A,X12R,

X12F,X14K,X14F,X14Q,X15R,X15F,X16S,X17R,X17M,X17F,X18R,X18K,X20F,X20R,X20K,X22Y,X22A,X22R,X22V,X22Q,X22W,X22L,X23F,X23S,X23A,X24W,X24R,X24H,X24F,X24Q,X24L,X25V,X25F,X25R,X26F,X27V,X27F,X27L,X27R,X28N,X28E,X28A,X29T,X30E,X31F,X33D,X33G,X33S,X34P,X35M,X36F,X36R,X36T,X38L,X38F,X38R,X40L,X40W,X40N,X40R,X40T,X40H,X42I,X43D,X43I,X43R,X43M,X43F,X43W,X43S,X43A,X45T,X46R,X48R,X50C,X51H,X51W,X51F,X52F,X52E,X52N,X55Y,X57R,X59R,X59A,X59F,X60A,X60Q,X60P,X62E,X62Q,X63I,X63V,X63T,X63P,X63D,X63M,X63H,X63Q,X63E,X63A,X63S,X64F,X64T,X68C,X68A,X69N,X69P,X69W,X69T,X71G,X72C,X74C,X75F,X75A,X75R,X75E,X76D,X78I,X78R,X78N,X79W,X79Q,X81R,X82V,X82T,X82F,X82M,X82R,X85M,X86L,X86I,X86W,X89P,X89T,X89V,X89G,X89W,X89H,X89F,X89L,X89I,X91N,X91F,X92F,X94N,X99G,X99F,X99M,X99T,X99P,X100I,X100S,X100N,X100Q,X101N,X101A,X101G,X101P,X101F,X101E,X101T,X101D,X102H,X102N,X102E,X102T,X102A,X103G,X103D,X103N,X104D,X104E,X104I,X104L,X105Q,X105E,X105T,X106F,X106V,X106G,X106E,X106T,X106D,X106A,X107F,X107M,X108G,X108I,X109M,X111V,X111I,X112V,X112L,X112Q,X114G,X115K,X115R,X116A,X116K,X116L,X117F,X118I,X118R,X119C,X120F,X120A,X120R,X121E,X121F,X123G,X123E,X124S,X128F,X128H,X128I,X128L,X128Q,X128N,X128M,X128D,X129E,X132E,X132A,X138G,X144R,X147L,X148I,X158E,X158E,X159E,X159C,X160D,X166D,X166E,X167W,X175V,X177C,X181A,X182R,X183F,X183I,X183D,X183R,X183M,X185E,X185I,X185V,X186H,X186K,X188R,X188E,X188D,X192H,X192W,X194V,X194F,X194E,X197F,X198L,X198F,X203E,X203C,X208S,X209N,X209F,X209E,X209S,X209H,X209G,X209T,X209L,X210R,X210V,X210L,X211R,X211Q,X212I,X212M,X212F,X213A,X214F,X215F,X215N,X215D,X215H,X215E,X216F,X216A,X217N,X217E,X217D,X218P,X218D,X218E,X224A,X224G,X227I,X230E,X231I,X231C,X233C,X234F,X235F,X236F,X236N,X238L,X238K,X238R,X239K,X239S,X239T,X239G,X239H,X239R,X239N,X239F,X240R,X241R,X242L,X242R,X243R,X243F,X244R,X246S,X248I,X248V,X248R,X249R,X249T,X250I,X251S,X251R,X252I,X252F,X252H,X252R,X253F,X253I,X253R,X254C,X256N,X258R,X260V,X260I,X262H,X262D,X263F,X265F,X267N,X267V,X267M,X269I,X269R,X270C,X271F,X271V,X271I,X271P,X271H,X271M,X271T,X271L,X271A,X272F,X272R,X272F,X273I,X273F,和X274G,其中所述枯草杆菌蛋白酶变体的氨基酸位置通过与如SEQ ID NO:1所示解淀粉芽孢杆菌(B.amyloliquefaciens)枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[1029] 37.根据实施方式35所述的分离的枯草杆菌蛋白酶变体,其中所述枯草杆菌蛋白酶变体为具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:X16S,X18R,X20R,X22A,X24R,X43R/D,X45T,X76D,X101A,X103G,X104L,X111V,X128N,X148I,X230E,X242R,和X249R,其中所述枯草杆菌蛋白酶变体的氨基酸位置通过与如SEQ ID NO:1所示解淀粉芽孢杆菌(B.amyloliquefaciens)枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[1030] 38.一种分离的枯草杆菌蛋白酶变体,其中所述枯草杆菌蛋白酶变体为具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:X1R,X230E,

X271L,X115R,X20R,X249R,X235F,X27V/F/L,X75E,X82R,X18R,X269R,X43D,X43R,X76D,X45T,X212F,X242R,X24R,X78R,X9A,X22R,X121E,X244R,X28E,X30E,X4R,和X241R,其中所述枯草杆菌蛋白酶变体的氨基酸位置通过与如SEQ ID NO:1所示解淀粉芽孢杆菌(B.amyloliquefaciens)枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[1031] 39.一种分离的枯草杆菌蛋白酶变体,其中所述枯草杆菌蛋白酶变体为具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:X062E-X158E,X103G-X158E,X128N-X158E,X016S-X158E,X104L-X158E,X089P-X158E,X111V-X158E,X022A-X158E,X101A-X158E,X148I-X158E,X129E-X158E,X022A-X089P,X016S-X089P,X062E-X089P,X062E-X271F,X158E-X271F,X186H-X271F,X129E-X271F,X111V-X271F,X209E-X271F,X016S-X271F,X188D-X271F,X022A-X271F,X159E-X271F,X104L-X271F,X101A-X271F,X089P-X271F,X128N-X271F,X103G-X271F,X148I-X271F,X249R-X271F,X062E-X159E,X016S-X159E,X128N-X159E,X148I-X159E,X111V-X159E,X089P-X159E,X022A-X159E,X129E-X159E,X103G-X159E,X104L-X159E,X158E-X159E,X101A-X159E,X158E-X249R,X111V-X249R,X129E-X249R,X062E-X249R,X016S-X249R,X186H-X249R,X148I-X249R,X159E-X249R,X101A-X249R,X188D-X249R,X104L-X249R,X209E-X249R,X022A-X249R,X128N-X249R,X103G-X249R,X089P-X249R,X022A-X111V,X101A-X111V,X016S-X111V,X104L-X111V,X062E-X111V,X103G-X111V,X089P-X111V,X016S-X148I,X062E-X148I,X022A-X148I,X129E-X148I,X104L-X148I,X103G-X148I,X128N-X148I,X101A-X148I,X089P-X148I,X111V-X148I,X016S-X062E,X022A-X062E,X062E-X129E,X022A-X129E,X128N-X129E,X016S-X129E,X101A-X129E,X104L-X129E,X089P-X129E,X103G-X129E,X111V-X129E,X062E-X186H,X128N-X186H,X101A-X186H,X022A-X186H,X016S-X186H,X158E-X186H,X089P-X186H,X129E-X186H,X159E-X186H,X103G-X186H,X104L-X186H,X111V-X186H,X148I-X186H,X062E-X101A,X022A-X101A,X016S-X101A,X089P-X101A,X062E-X103G,X022A-X103G,X016S-X103G,X101A-X103G,X089P-X103G,X062E-X128N,X016S-X128N,X022A-X128N,X101A-X128N,X104L-X128N,X089P-X128N,X103G-X128N,X111V-X128N,X111V-X188D,X062E-X188D,X016S-X188D,X148I-X188D,X022A-X188D,X128N-X188D,X101A-X188D,X104L-X188D,X089P-X188D,X129E-X188D,X159E-X188D,X186H-X188D,X103G-X188D,X158E-X188D,X016S-X022A,X016S-X104L,X022A-X104L,X101A-X104L,X062E-X104L,X103G-X104L,X089P-X104L,X159E-X209E,X111V-X209E,X101A-X209E,X016S-X209E,X128N-X209E,X148I-X209E,X129E-X209E,X062E-X209E,X022A-X209E,X103G-X209E,X158E-X209E,X188D-X209E,X104L-X209E,X089P-X209E,和X186H-X209E,其中所述枯草杆菌蛋白酶变体的氨基酸位置通过与如SEQ ID NO:1所示解淀粉芽孢杆菌(B.amyloliquefaciens)枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[1032] 40.一种分离的枯草杆菌蛋白酶变体,其中所述枯草杆菌蛋白酶变体为具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:X018R-X241R,X020R-X241R,X024R-X241R,X009A-X241R,X020R-X241R,X004R-X241R,X043R-X241R,X078R-X241R,X022R-X241R,X115R-X241R,X001R-X241R,X212F-X241R,X082R-X241R,X018R-X244R,X024R-X244R,X078R-X244R,X020R-X244R,X212F-X244R,X009A-

X244R,X082R-X244R,X001R-X244R,X043R-X244R,X022R-X244R,X004R-X244R,X115R-X244R,X241R-X244R,X242R-X244R,X001R-X004R,X009A-X022R,X018R-X022R,X020R-X022R,X004R-X022R,X001R-X022R,X024R-X242R,X018R-X242R,X004R-X242R,X020R-X242R,X212F-X242R,X082R-X242R,X078R-X242R,X001R-X242R,X009A-X242R,X022R-X242R,X115R-X242R,X043R-X242R,X241R-X242R,X018R-X212F,X022R-X212F,X004R-X212F,X024R-X212F,X001R-X212F,X115R-X212F,X020R-X212F,X009A-X212F,X043R-X212F,X078R-X212F,X082R-X212F,X009A-X078R,X020R-X078R,X024R-X078R,X022R-X078R,X018R-X078R,X004R-X078R,X001R-X078R,X043R-X078R,X022R-X024R,X020R-X024R,X018R-X024R,X001R-X024R,X004R-X024R,X009A-X024R,X004R-X009A,X001R-X009A,X242R-X269R,X024R-X269R,X020R-X269R,X022R-X269R,X249R-X269R,X212F-X269R,X043R-X269R,X244R-X269R,X001R-X269R,X018R-X269R,X078R-X269R,X009A-X269R,X115R-X269R,X241R-X269R,X004R-X269R,X082R-X269R,X018R-X043R,X020R-X043R,X004R-X043R,X022R-X043R,X009A-X043R,X001R-X043R,X024R-X043R,X009A-X018R,X004R-X018R,X001R-X018R,X024R-X082R,X009A-X082R,X018R-X082R,X001R-X082R,X078R-X082R,X020R-X082R,X022R-X082R,X004R-X082R,X043R-X082R,X043R-X249R,X020R-X249R,X004R-X249R,X018R-X249R,X009A-X249R,X212F-X249R,X022R-X249R,X024R-X249R,X115R-X249R,X001R-X249R,X082R-X249R,X242R-X249R,X241R-X249R,X244R-X249R,X078R-X249R,X018R-X115R,X020R-X115R,X022R-X115R,X078R-X115R,X009A-X115R,X004R-X115R,X001R-X115R,X082R-X115R,X043R-X115R,X024R-X115R,X009A-X020R,X018R-X020R,X004R-X020R,X001R-X020R,X009A-X271L,X020R-X271L,X024R-X271L,X244R-X271L,X241R-X271L,X043R-X271L,X022R-X271L,X249R-X271L,X212F-X271L,X115R-X271L,X242R-X271L,X078R-X271L,X004R-X271L,X269R-X271L,X001R-X271L,X018R-X271L,和X082R-X271L,其中所述枯草杆菌蛋白酶变体的氨基酸位置通过与如SEQ ID NO:1所示解淀粉芽孢杆菌(B.amyloliquefaciens)枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[1033] 41.一种分离的枯草杆菌蛋白酶变体,其中所述枯草杆菌蛋白酶变体为具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:X101G-X103A-X104I,X22A-X101A-X209E,S103G-L111V-G159E,X22A-X103G-X159E,X22A-X111V-X159E,X22A-X128N-X271F-X209E,X22A-X103G-X111V,X62E-X111V-X128N,X22A-X111V-X128N,X22A-X62E-X111V,X101A-X103G-X104L-X188D,X101G-X103A-X104I-X159D,X101A-X103G-X104L-X128N,X22A-X101A-X159E,X101A-X103G-X104L,X101A-X103G-X104L-X159E,X22A-X101A-X103G-X104L,X101A-X103G-X104L-X209E,X22A-X209E-X271F,X22A-X101A-X271F,和X101A-X209E-X271F,其中所述枯草杆菌蛋白酶变体的氨基酸位置通过与如SEQ ID NO:1所示解淀粉芽孢杆菌(B.amyloliquefaciens)枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[1034] 42.一种分离的枯草杆菌蛋白酶变体,其中所述枯草杆菌蛋白酶变体为具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:X103A-X104I-X159D-X232V-X236H-X245R-X248D-X252K,X101G-X104I-X159D-X232V-X236H-X245R-X248D-X252K,X101G-X103A-X159D-X232V-X236H-X245R-X248D-X252K,X101G-

X103A-X104L-X232V-X236H-X245R-X248D-X252K,X101G-X103A-X104L-X159D-X236H-X245R-X248D-X252K,X101G-X103A-X104L-X159D-X232V-X245R-X248D-X252K,X101G-X103A-X104L-X159D-X232V-X236H-X248D-X252K,X101G-X103A-X104L-X159D-X232V-X236H-X245R-X252K,和X101G-X103A-X104L-X159D-X232V-X236H-X245R-X248D,其中所述枯草杆菌蛋白酶变体的氨基酸位置通过与如SEQ ID NO:1所示解淀粉芽孢杆菌(B.amyloliquefaciens)枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[1035] 43.一种分离的枯草杆菌蛋白酶变体,其中所述枯草杆菌蛋白酶变体为具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:X101G-X103A-X104I-X159D-X232V-X245R-X248D,X101G-X103A-X104I-X159D-X232V-X245R-X248D-X271F,X101G-X103A-X104I-X159D-X232V-X245R-X248D-X238R,X101G-X103A-X104I-X159D-X232V-X245R-X248D-X248R,X101G-X103A-X104I-X159D-X232V-X245R-X248D-X253R,X101G-X103A-X104I-X159D-X232V-X245R-X248D-X24R,X101G-X103A-X104I-X159D-X232V-X245R-X248D-X76D,X101G-X103A-X104I-X159E-X232V-X245R-X248D-X249R,X101G-X103A-X104I-X159E-X232V-X245R-X248D-X271F,X101G-X103A-X104I-X158E-X232V-X245R-X248D-X249R,X101G-X103A-X104I-X158E-X232V-X245R-X248D-X271F,X22A-X101G-X103A-X104I-X159D-X232V-X245R-X248D-X249R,X22A-X101G-X103A-X104I-X159D-X232V-X245R-X248D-X271F,X62E-X101G-X103A-X104I-X159D-X232V-X245R-X248D-X249R,和X62E-X101G-X103A-X104I-X159D-X232V-X245R-X248D-X271F,其中所述枯草杆菌蛋白酶变体的氨基酸位置通过与如SEQ ID NO:1所示解淀粉芽孢杆菌(B.amyloliquefaciens)枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[1036] 44.一种分离的枯草杆菌蛋白酶变体,其中所述枯草杆菌蛋白酶变体为具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:X20R-X43R-X249R,X20R-X22R-X43R,X20R-X43R-X242R,X20R-X43R-X271L,X20R-X43R-X244R,X20R-X24R-X43R-X242R,X9A-X22R-X78R-X212F-X241R,X9A-X20R-X43R-X212F,X9A-X43R-X212F,X20R-X43R-X212F,X20R-X22R-X43R-X212F,X24R-X78R-X212F,X9A-X43R-X78R,X9A-X43R-X78R-X242R,X9A-X20R-X43R-X78R,X20R-X24R-X43R-X78R-X242R,X22R-X24R-X78R-X212F,X9A-X20R-X43R-X78R-X242R,X20R-X43R-X78R-X249R,X20R-X43R-X78R,X9A-X78R-X212F,X9A-X22R-X43R-X78R,X9A-X20R-X24R-X43R,X9A-X22R-X78R-X212F,X4R-X9A-X22R-X78R-X212F,X20R-X24R-X43R,X1R-X9A-X43R,X20R-X24R-X43R-X115R,X9A-X24R-X43R,X20R-X22R-X24R-X43R,X1R-X24R-X43R,X9A-X20R-X24R-X43R-X242R,X9A-X20R-X22R-X78R-X212F,X9A-X24R-X43R-X244R,X9A-X24R-X43R-X242R,X4R-X9A-X22R-X24R-X212F,以及X22R-X24R-X43R,其中所述枯草杆菌蛋白酶变体的氨基酸位置通过与如SEQ ID NO:1所示解淀粉芽孢杆菌(B.amyloliquefaciens)枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[1037] 45.一种分离的枯草杆菌蛋白酶变体,其中所述枯草杆菌蛋白酶变体为具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:X101G-X103A-X104I-X232V-X245R-X248D,X101G-X103A-X104I-X159D-X232V-X245R,X101G-X103A-X104I-X159R-X232V-X245R-X248D,X101G-X103A-X104I-X159D-X232V-X245R-X248R,X101G-X103A-X104I-X232V-X245R,X101G-X103A-X104I-X232V-X245R-X248R,

X101G-X103A-X104I-X159R-X232V-X245R-X248R,以及X101G,X103A,X104I,X232V,X236H,X245R,和X252K,其中所述枯草杆菌蛋白酶变体的氨基酸位置通过与如SEQ ID NO:1所示解淀粉芽孢杆菌(B.amyloliquefaciens)枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[1038] 46.一种分离的枯草杆菌蛋白酶变体,其中所述枯草杆菌蛋白酶变体为具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:X16S,X22A,X24R,X62E,X76D,X89P,X101A/G,X103G/A,X104L/I,X111V,X128N,X129E,X232V,X148I,X158E,X159D/E,X166D,X186H,X188D,X209E,X236H,X238R,X245R,X248D/R,X249R,X252K/R,X253R,和X271F,其中所述枯草杆菌蛋白酶变体的氨基酸位置通过与如SEQ ID NO:1所示解淀粉芽孢杆菌(B.amyloliquefaciens)枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[1039] 47.一种分离的枯草杆菌蛋白酶变体,其中所述枯草杆菌蛋白酶变体为具有蛋白水解活性的成熟形式并包含具有选自以下的氨基酸置换的组合的氨基酸序列:N062E-A158E,S103G-A158E,S128N-A158E,A016S-A158E,V104L-A158E,E089P-A158E,L111V-A158E,T022A-A158E,S101A-A158E,L148I-A158E,P129E-A158E,T022A-E089P,A016S-E089P,N062E-E089P,N062E-E271F,A158E-E271F,R186H-E271F,P129E-E271F,L111V-E271F,Y209E-E271F,A016S-E271F,S188D-E271F,T022A-E271F,G159E-E271F,V104L-E271F,S101A-E271F,E089P-E271F,S128N-E271F,S103G-E271F,L148I-E271F,H249R-E271F,N062E-G159E,A016S-G159E,S128N-G159E,L148I-G159E,L111V-G159E,E089P-G159E,T022A-G159E,P129E-G159E,S103G-G159E,V104L-G159E,A158E-G159E,S101A-G159E,A158E-H249R,L111V-H249R,P129E-H249R,N062E-H249R,A016S-H249R,R186H-H249R,L148I-H249R,G159E-H249R,S101A-H249R,S188D-H249R,V104L-H249R,Y209E-H249R,T022A-H249R,S128N-H249R,S103G-H249R,E089P-H249R,T022A-L111V,S101A-L111V,A016S-L111V,V104L-L111V,N062E-L111V,S103G-L111V,E089P-L111V,A016S-L148I,N062E-L148I,T022A-L148I,P129E-L148I,V104L-L148I,S103G-L148I,S128N-L148I,S101A-L148I,E089P-L148I,L111V-L148I,A016S-N062E,T022A-N062E,N062E-P129E,T022A-P129E,S128N-P129E,A016S-P129E,S101A-P129E,V104L-P129E,E089P-P129E,S103G-P129E,L111V-P129E,N062E-R186H,S128N-R186H,S101A-R186H,T022A-R186H,A016S-R186H,A158E-R186H,E089P-R186H,P129E-R186H,G159E-R186H,S103G-R186H,V104L-R186H,L111V-R186H,L148I-R186H,N062E-S101A,T022A-S101A,A016S-S101A,E089P-S101A,N062E-S103G,T022A-S103G,A016S-S103G,S101A-S103G,E089P-S103G,N062E-S128N,A016S-S128N,T022A-S128N,S101A-S128N,V104L-S128N,E089P-S128N,S103G-S128N,L111V-S128N,L111V-S188D,N062E-S188D,A016S-S188D,L148I-S188D,T022A-S188D,S128N-S188D,S101A-S188D,V104L-S188D,E089P-S188D,P129E-S188D,G159E-S188D,R186H-S188D,S103G-S188D,A158E-S188D,A016S-T022A,A016S-V104L,T022A-V104L,S101A-V104L,N062E-V104L,S103G-V104L,E089P-V104L,G159E-Y209E,L111V-Y209E,S101A-Y209E,A016S-Y209E,S128N-Y209E,L148I-Y209E,P129E-Y209E,N062E-Y209E,T022A-Y209E,S103G-Y209E,A158E-Y209E,S188D-Y209E,V104L-Y209E,E089P-Y209E,和R186H-Y209E,其中所述枯草杆菌蛋白酶变体的氨基酸位置通过与

如SEQ ID NO:1所示解淀粉芽孢杆菌(B.amyloliquefaciens)枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[1040] 48.一种分离的枯草杆菌蛋白酶变体,所述枯草杆菌蛋白酶变体具有蛋白水解活性并包含具有选自以下的氨基酸置换的组合的氨基酸序列:N018R-W241R,G020R-W241R,S024R-W241R,S009A-W241R,G020R-W241R,V004R-W241R,N043R-W241R,S078R-W241R,T022R-W241R,G115R-W241R,A001R-W241R,S212F-W241R,L082R-W241R,N018R-V244R,S024R-V244R,S078R-V244R,G020R-V244R,S212F-V244R,S009A-V244R,L082R-V244R,A001R-V244R,N043R-V244R,T022R-V244R,V004R-V244R,G115R-V244R,W241R-V244R,S242R-V244R,A001R-V004R,S009A-T022R,N018R-T022R,G020R-T022R,V004R-T022R,A001R-T022R,S024R-S242R,N018R-S242R,V004R-S242R,G020R-S242R,S212F-S242R,L082R-S242R,S078R-S242R,A001R-S242R,S009A-S242R,T022R-S242R,G115R-S242R,N043R-S242R,W241R-S242R,N018R-S212F,T022R-S212F,V004R-S212F,S024R-S212F,A001R-S212F,G115R-S212F,G020R-S212F,S009A-S212F,N043R-S212F,S078R-S212F,L082R-S212F,S009A-S078R,G020R-S078R,S024R-S078R,T022R-S078R,N018R-S078R,V004R-S078R,A001R-S078R,N043R-S078R,T022R-S024R,G020R-S024R,N018R-S024R,A001R-S024R,V004R-S024R,S009A-S024R,V004R-S009A,A001R-S009A,S242R-N269R,S024R-N269R,G020R-N269R,T022R-N269R,H249R-N269R,S212F-N269R,N043R-N269R,V244R-N269R,A001R-N269R,N018R-N269R,S078R-N269R,S009A-N269R,G115R-N269R,W241R-N269R,V004R-N269R,L082R-N269R,N018R-N043R,G020R-N043R,V004R-N043R,T022R-N043R,S009A-N043R,A001R-N043R,S024R-N043R,S009A-N018R,V004R-N018R,A001R-N018R,S024R-L082R,S009A-L082R,N018R-L082R,A001R-L082R,S078R-L082R,G020R-L082R,T022R-L082R,V004R-L082R,N043R-L082R,N043R-H249R,G020R-H249R,V004R-H249R,N018R-H249R,S009A-H249R,S212F-H249R,T022R-H249R,S024R-H249R,G115R-H249R,A001R-H249R,L082R-H249R,S242R-H249R,W241R-H249R,V244R-H249R,S078R-H249R,N018R-G115R,G020R-G115R,T022R-G115R,S078R-G115R,S009A-G115R,V004R-G115R,A001R-G115R,L082R-G115R,N043R-G115R,S024R-G115R,S009A-G020R,N018R-G020R,V004R-G020R,A001R-G020R,S009A-E271L,G020R-E271L,S024R-E271L,V244R-E271L,W241R-E271L,N043R-E271L,T022R-E271L,H249R-E271L,S212F-E271L,G115R-E271L,S242R-E271L,S078R-E271L,V004R-E271L,N269R-E271L,A001R-E271L,N018R-E271L,和L082R-E271L,其中所述枯草杆菌蛋白酶变体的氨基酸位置通过与如SEQ ID NO:1所示解淀粉芽孢杆菌(B.amyloliquefaciens)枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[1041] 49.一种分离的枯草杆菌蛋白酶变体,所述枯草杆菌蛋白酶变体具有蛋白水解活性并包含具有选自以下的氨基酸置换的组合的氨基酸序列:G020R-N043R,G020K-N062E,S024F-N116L,G020K-S024F,S024R-A174T,S024R-G118R,S024R-K235F,S024R-P086R,S024R-P086W,S078R-G118R,T033S-G118R,T033S-K235F,Y209A-W241R,G020R-N076D,N018R-Q245R,S024R-R045T,A232V-Q245R,G118R-A172V,G118R-A194T,I008T-S024R,K235F-N243F,N018R-S103A,N018R-V104I,P086W-G118R,P086W-N243F,P086W-Y209A,S024C-T033S,S024R-A232V,S024R-N243F,S024R-P239Q,S024R-S101G,S024R-S141G,

S024R-T033S,S024R-T274I,S024R-Y209A,S078R-P086W,S101G-A232V,T033S-L148F,T033S-P086W,T033S-P201S,T033S-S078R,T033S-W241R,T033S-Y209A,A230E-H249R,A232V-H249R,G118R-K235F,N076D-Q245R,P086W-K235F,S024R-R247H,S024R-V104A,S078R-K235F,S101G-H249R,S103A-A232V,T033S-A048T,T033S-P239T,T033S-T253A,T143A-Y209A,Y209A-K235F,N018R-R045T,Y209A-N243F,S024R-A272P,S024R-R269C,S101G-V104I,V104I-A232V,N076D-H249R,和S024R-N076D,其中所述枯草杆菌蛋白酶变体的氨基酸位置通过与如SEQ ID NO:1所示解淀粉芽孢杆菌(B.amyloliquefaciens)枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[1042] 50.一种分离的枯草杆菌蛋白酶变体,所述枯草杆菌蛋白酶变体具有蛋白水解活性并包含具有选自以下的氨基酸置换的组合的氨基酸序列:G020R-N076D,S024R-R045T,A230E-H249R,N018R-R045T,N018R-Q245R,S101G-A232V,S024R-A232V,A232V-Q245R,S024R-S101G,N018R-V104I,N018R-S103A,S101G-H249R,A232V-H249R,S103A-A232V,N076D-Q245R,S101G-V104I,V104I-A232V,N076D-H249R,S024R-N076D,S024F-N116L,G020K-S024F,G020K-N062E,T033S-G118R,S024R-P086W,S024R-G118R,S024R-P086R,Y209A-W241R,S024R-W241R,S024R-K235F,G118R-Y209A,S078R-G118R,T033S-K235F,S024R-A174T,P086W-Y209A,I008T-S024R,P086W-G118R,T033S-W241R,S024R-N243F,S024R-Y209A,T033S-P086W,S024R-T033S,P086W-N243F,T033S-P201S,S024R-P239Q,S078R-P086W,K235F-N243F,G118R-A172V,T033S-L148F,T033S-S078R,T033S-N243F,S024C-T033S,G118R-A194T,T033S-Y209A,S024R-S141G,S024R-T274I,P086W-K235F,A015T-T033S,Y209A-K235F,S024R-R247H,S078R-K235F,S024R-V104A,T033S-A048T,G118R-K235F,T033S-T253A,T143A-Y209A,T033S-P239T,Y209A-N243F,S024R-A272P,和S024R-R269C,其中所述枯草杆菌蛋白酶变体的氨基酸位置通过与如SEQ ID NO:1所示解淀粉芽孢杆菌(B.amyloliquefaciens)枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[1043] 51.一种分离的枯草杆菌蛋白酶变体,所述枯草杆菌蛋白酶变体具有蛋白水解活性并包含具有选自以下的氨基酸置换的组合的氨基酸序列:V004R-S009A-G020R-S242R,G020R-N043R-W241R,G020R-S242R-N269R,V004R-S009A-G020R-N043R,V004R-G020R-H249R,N018R-S024R-V244R,S009A-T022R-S212F-W241R,G020R-N043R-N269R,N018R-S024R-S242R,V004R-S009A-N043R-W241R,G020R-N043R-V244R,G020R-T022R-S242R,V004R-G020R-N043R,V004R-S009A-G020R-N043R-S242R,G020R-N043R-S242R,G020R-N043R-S242R-H249R,G020R-S212F-H249R,V004R-S009A-W241R,A001R-S009A-N043R,G020R-N043R-H249R,S009A-G020R-N043R-W241R,G020R-T022R-N043R,G020R-H249R-N269R,G020R-T022R-W241R,V004R-S009A-S024R-N043R-W241R,S009A-N043R-S078R,V004R-G020R-S024R-V244R,G020R-T022R-S078R-S242R,G020R-S024R-S242R-H249R,V004R-S009A-S078R-W241R,S009A-N043R-S078R-S242R,V004R-G020R-S024R,S009A-N043R-S212F,G020R-N043R-S212F,S024R-S078R-S212F,S009A-G020R-S024R-N043R,S009A-T022R-N043R-S078R,G020R-T022R-S212F-W241R,G020R-N043R-S212F-W241R,S009A-N043R-W241R,G020R-N043R-E271L,G020R-T022R-S078R-W241R,G020R-S024R-N043R-S242R,G020R-T022R-N043R-W241R,S009A-G020R-N043R-S212F,V004R-S009A-

G020R-S024R-S242R,G020R-N043R-H249R-E271L,G020R-T022R-S024R-S242R,S009A-T022R-S078R-S212F,G020R-N043R-S242R-E271L,S009A-T022R-S078R-S212F-W241R,V004R-G020R-S024R-H249R,G020R-T022R-E271L,G020R-T022R-N043R-S212F,V004R-G020R-S024R-N043R-S242R,V004R-G020R-S024R-N043R,V004R-S009A-T022R-S078R-S212F,G020R-T022R-S078R-S212F-W241R,和G020R-T022R-N269R,其中所述枯草杆菌蛋白酶变体的氨基酸位置通过与如SEQ ID NO:1所示解淀粉芽孢杆菌(B.amyloliquefaciens)枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[1044] 52.一种分离的枯草杆菌蛋白酶变体,所述枯草杆菌蛋白酶变体具有蛋白水解活性并包含具有选自以下的氨基酸置换的组合的氨基酸序列:N018R-G020R-N043D-R045T-A230E,N018R-N043R-R045T-S242R-H249R,S024R-N043D-H249R,N018R-G020R-R045T,G020R-S024R-N076D-H249R,S024R-N043R-A230E-S242R,N018R-S024R-N043D-A230E,G020R-N076D,N018R-S024R-N043D-N076D-H249R,S024R-N043R-N076D-H249R,N018R-S024R-R045T-S242R,G020R-N043D-N076D-A230E-H249R,G020R-N043R-R045T-S242R,N018R-S024R-N076D-H249R,N018R-G020R-S024R-N043D-R045T-L233I-S242R,S024R-N043R-A230E,N018R-G020R-N043D,N043R-S242R-H249R,G020R-N043R-R045T-A230E,N043R-N076D-S242R-H249R,G020R-S024R-R045T-A230E-S242R,S024R-R045T-N076D-A230E-S242R-H249R,S024R-R045T,S024R-N043R-R045T-N076D-A230E-H249R,N018R-S024R-N043D-R045T-H249R,N018R-N043R-R045T-H249R,S024R-N043R-S242R,N018R-G020R-N043R-N076D-H249R,G020R-S024R-N043D-H249R,G020R-N043R-A230E-S242R,G020R-N043R-S242R,N018R-N043R-N076D-A230E,G020R-S024R-N043D-S242R,G020R-N043R-A230E,N018R-G020R-N043R-N076D-S242R-H249R,N043D-R045T-N076D-H249R,N018R-N043R-S242R-H249R,N018R-G020R-N043R-R045T-S242R,N018R-G020R-N043D-A230E-S242R,G020R-S024R-N043R-R045T-H249R,S024R-N043R-H249R,G020R-S024R-K27E-N043R-N076D-A230E,S024R-N043R-R045T-S242R,N018R-G020R-S024R-N043R-R045T-N076D-A230E,G020R-N043R-N076D-A230E-H249R,N018R-N043R-R045T-S242R,G020R-S242R-H249R,N018R-N043R-N076D-A230E-S242R-H249R,N018R-S024R-N076D,G020R-S024R-K27R-N043D-S242R-H249R,N018R-G020R-S024R-N043D-N076D-S242R,N018R-N043R-N076D-S242R-H249R,N018R-S024R-N043D-A230E-H249R,N018R-G020R-N043D-H249R,N018R-G020R-N043D-R045T-N076D-S242R,S024R-N043R-N076D-A230E-S242R,G020R-S024R-T38I-N043R-R045T-N076D-S242R-H249R,N018R-G020R-N043R,N018R-S024R-R045T-A230E-S242R,N018R-G020R-H249R,S024R-N043R-N076D,N018R-G020R-S024R-N043R-R045T-N076D-H249R,N018R-N043D-R045T-N076D-S242R-H249R,S024R-N043D-S242R-H249R,N018R-G020R-S024R-N043D-R045T-S242R,G020R-S024R-N043R-N076D,N018R-G020R-N043D-R045T-A230E-S242R,G020R-S024R-N043R-R045T-N076D-S242R-H249R,N018R-N043R-R045T-N076D-S242R,N018R-G020R-N043R-N076D-A230E-S242R,N018R-S024R-N043D-H249R,N018R-S024R-N043R-R045T-A230E-H249R,N018R-G020R-N043R-R045T-N076D-H249R,N018R-S024R-S242R,N018R-N043R-R045T-N076D-A230E-S242R,R045T-S242R-H249R,N018R-S024R-N043D-S242R,N018R-G020R-N043D-R045T-S240P,S024R-N043R-R045T-S242R-H249R,N018R-S024R-V30S-L31S-D32I-T33Q-G34V-I35F,

N018R-G020R-N043R-N076D,G020R-N043D-R045T-N076D-S242R-H249R,N018R-S024R-N043D-A230E-S242R,N018R-S024R-N043D-S242R-H249R,S024R-N043D-R045T-S242R-H249R,N043R-A230E-H249R,S024R-N043R-N076D-A230E-H249R,G020R-S024R-N043D-N076D-H249R,S024R-R045T-S242R-A273V,G020R-S024R-R045T-N076D-S242R-H249R,N018R-S024R-N043D-N076D-S242R,N018R-N043R-N076D-A230E-H249R,N018R-G020R-N043R-R045T-H249R,N018R-N043R-R045T-A230E-S242R,G020R-S024R-N043D-R045T-A230E-S242R,N018R-N043D-A230E-H249R,N018R-N043R-N076D-S242R,N018R-G020R-N076D,N018R-G020R-N043D-N076D-S242R-H249R,G020R-S024R-N043D-N076D-S242R-H249R,N043D-S242R-H249R,N018R-G020R-S024R-N043R-N076D,N018R-G020R-N043D-R045T-N076D-H249R,N018R-G020R-N043R-R045T-N076D-A230E-H249R,N018R-N076D-S242R,G020R-N043R-H249R,N018R-N076D-S242R-H249R,N018R-S024R-R045T-A230E-H249R,A230E-H249R,N018R-R045T-H249R,G020R-N043R-N076D,N043R-R045T-H249R,N018R-N043D-N076D-S242R-H249R,N043R-N076D-H249R,N018R-R045T,G020R-N076D-A230E-S242R,G020R-S024R-N043D-R045T,S024R-N043D-N076D-S242R-H249R,G020R-R045T-H249R,N043R-N076D-S153A-H249R,N043R-N076D-A230E-H249R,N018R-N043D-N076D-H249R,和G020R-N043R-N076D-V227I,其中所述枯草杆菌蛋白酶变体的氨基酸位置通过与如SEQ ID NO:1所示解淀粉芽孢杆菌(B.amyloliquefaciens)枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[1045] 53.一种分离的枯草杆菌蛋白酶变体,所述枯草杆菌蛋白酶变体具有蛋白水解活性并包含具有选自以下的氨基酸置换的组合的氨基酸序列:S101G-S103A-V104I-A232V-Q236H-Q245R-N252K,S101G-S103A-V104I-A232V-Q245R-N248R,S101G-S103A-V104I-G159R-A232V-Q245R-N248D,S101G-S103A-V104I-G159D-A232V-Q245R-N248R,S101G-S103A-V104I-A232V-Q245R,S101G-S103A-V104I-G159D-A232V-Q245R和S101G-S103A-V104I-A232V-Q245R-N248D,其中所述枯草杆菌蛋白酶变体的氨基酸位置通过与如SEQ ID NO:1所示解淀粉芽孢杆菌(B.amyloliquefaciens)枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[1046] 54.一种分离的枯草杆菌蛋白酶变体,所述枯草杆菌蛋白酶变体具有蛋白水解活性并包含具有选自以下的氨基酸置换的组合的氨基酸序列:S101G-S103A-V104I-P129E-S188D-A232V-N238R-Q245R-N248D,S024R-S101G-S103A-V104I-P129E-A158E-S188D-A232V-Q245R-N248D-H249R,T022A-S101G-S103A-V104I-P129E-A158E-S188D-A232V-Q245R-N248D-H249R,T022A-S024R-S101G-S103A-V104I-P129E-A158E-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-P129E-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-P129E-G159E-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-S128N-P129E-A158E-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-L148I-A158E-S188D-A232V-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-P129E-G159E-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-S128N-P129E-A232V-Q245R-N248D,S101G-S103A-V104I-P129E-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-P129E-A158E-A232V-Q245R-N248D-H249R,T022A-S024R-S101G-S103A-V104I-A158E-G159E-S188D-A232V-Q245R-N248D-

H249R,T022A-S024R-S101G-S103A-V104I-P129E-A158E-G159E-S188D-A232V-N238R-Q245R-N248D,S024R-S101G-S103A-V104I-P129E-L148I-A158E-A232V-Q245R-N248D,A016S-S024R-S101G-S103A-V104I-A158E-S188D-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-A158E-G159E-A232V-Q245R-N248D-H249R,T022A-S101G-S103A-V104I-P129E-A158E-G159E-A232V-N238R-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-P129E-A158E-G159E-A232V-Q245R-N248D-H249R,T022A-S024R-S101G-S103A-V104I-S128N-A158E-S188D-A232V-Q245R-N248D,S024R-S101G-S103A-V104I-P129E-S188D-A232V-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-P129E-A158E-A232V-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-P129E-A232V-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-P129E-S188D-A232V-Q245R-N248D,S024R-S101G-S103A-V104I-A158E-S188D-A232V-N238R-Q245R-N248D,T022A-S101G-S103A-V104I-S128N-P129E-S188D-A232V-N238R-Q245R-N248D,S024R-S101G-S103A-V104I-P129E-S188D-A232V-N238R-Q245R-N248D,S024R-S101G-S103A-V104I-A158E-G159E-S188D-A232V-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-S128N-S188D-A232V-Q245R-N248D,S024R-S101G-S103A-V104I-P129E-A158E-S188D-A232V-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-S128N-P129E-A158E-A232V-Q245R-N248D,S024R-S101G-S103A-V104I-G159E-S188D-A232V-Q245R-N248D,T022A-S101G-S103A-V104I-S128N-P129E-A232V-N238R-Q245R-N248D,S024R-S101G-S103A-V104I-P129E-G159E-A232V-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-P129E-A158E-S188D-A232V-N238R-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-A158E-G159E-S188D-A232V-Q245R-N248D,S024R-S101G-S103A-V104I-G159E-S188D-A232V-Q245R-N248D-H249R,T022A-S101G-S103A-V104I-P129E-A158E-A232V-N238R-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-P129E-A158E-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-L148I-A158E-A232V-Q245R-N248D,T022A-S101G-S103A-V104I-A158E-G159E-S188D-A232V-Q245R-N248D-H249R,T022A-S101G-S103A-V104I-A158E-S188D-A232V-Q245R-N248D,T022A-S101G-S103A-V104I-P129E-S188D-A232V-N238R-Q245R-N248D,S024R-S101G-S103A-V104I-P129E-A158E-G159E-S188D-A232V-Q245R-N248D-H249R,T022A-S024R-S101G-S103A-V104I-A158E-G159E-S188D-A232V-N238R-Q245R-N248D,S101G-S103A-V104I-P129E-A158E-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-S128N-A158E-A232V-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-S128N-P129E-S188D-A232V-Q245R-N248D,T022A-S101G-S103A-V104I-P129E-G159E-A232V-N238R-Q245R-N248D,S101G-S103A-V104I-P129E-G159E-A232V-Q245R-N248D-H249R,T022A-S101G-S103A-V104I-P129E-A158E-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-P129E-L148I-A158E-S188D-A232V-Q245R-N248D,T022A-S101G-S103A-V104I-P129E-G159E-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-G159E-S188D-A232V-N238R-Q245R-N248D,S024R-S101G-S103A-V104I-P129E-A158E-G159E-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-P129E-A158E-G159E-A232V-N238R-Q245R-N248D,S024R-S101G-S103A-V104I-S128N-G159E-S188D-A232V-Q245R-N248D,T022A-S101G-S103A-V104I-G159E-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-

V104I-P129E-G159E-S188D-A232V-N238R-Q245R-N248D,S101G-S103A-V104I-A158E-A232V-N238R-Q245R-N248D,T022A-S101G-S103A-V104I-P129E-G159E-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-P129E-L148I-S188D-A232V-Q245R-N248D,S024R-S101G-S103A-V104I-A158E-A232V-Q245R-N248D-H249R,T022A-S101G-S103A-V104I-A158E-G159E-A232V-N238R-Q245R-N248D,S024R-S101G-S103A-V104I-A158E-G159E-A232V-N238R-Q245R-N248D,T022A-S101G-S103A-V104I-P129E-A158E-G159E-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-P129E-A158E-S188D-A232V-N238R-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-P129E-A158E-G159E-A232V-Q245R-N248D,S101G-S103A-V104I-S188D-A232V-N238R-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-A158E-A232V-Q245R-N248D-H249R,T022A-S024R-S101G-S103A-V104I-L148I-A158E-A232V-Q245R-N248D,S101G-S103A-V104I-P129E-A158E-G159E-A232V-N238R-Q245R-N248D,T022A-S101G-S103A-V104I-G159E-S188D-A232V-N238R-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-P129E-A158E-G159E-S188D-A232V-Q245R-N248D-H249R,T022A-S101G-S103A-V104I-P129E-A232V-N238R-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-S188D-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-P129E-A158E-G159E-A232V-Q245R-N248D-H249R,T022A-S101G-S103A-V104I-A158E-G159E-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-P129E-S188D-A232V-Q245R-N248D,S024R-S101G-S103A-V104I-P129E-G159E-A232V-N238R-Q245R-N248D,S101G-S103A-V104I-S128N-P129E-A232V-Q245R-N248D,S101G-S103A-V104I-A158E-S188D-A232V-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-P129E-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-P129E-G159E-A232V-N238R-Q245R-N248D,S101G-S103A-V104I-A158E-G159E-S188D-A232V-N238R-Q245R-N248D,S024R-S101G-S103A-V104I-A232V-Q245R-N248D-H249R,T022A-S024R-S101G-S103A-V104I-P129E-L148I-A232V-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-A158E-A232V-N238R-Q245R-N248D,S101G-S103A-V104I-S128N-P129E-A232V-N238R-Q245R-N248D,T022A-S101G-S103A-V104I-S128N-G159E-A232V-Q245R-N248D,T022A-S101G-S103A-V104I-S128N-P129E-A158E-A232V-N238R-Q245R-N248D,S101G-S103A-V104I-S128N-P129E-S188D-A232V-Q245R-N248D-H249R,T022A-S024R-S101G-S103A-V104I-S128N-P129E-A158E-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-S128N-A158E-G159E-S188D-A232V-Q245R-N248D,T022A-S024K-S101G-S103A-V104I-S128N-A158E-G159E-A232V-Q245R-N248D,S101G-S103A-V104I-P129E-L148I-S188D-A232V-Q245R-N248D,S024R-S101G-S103A-V104I-L148I-A232V-Q245R-N248D,T022A-S101G-S103A-V104I-L148I-S188D-A232V-Q245R-N248D,S024R-S101G-S103A-V104I-S128N-P129E-S188D-A232V-Q245R-N248D,S101G-S103A-V104I-S128N-P129E-A158E-A232V-N238R-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-P129E-L148I-A158E-S188D-A232V-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-L148I-A158E-S188D-A232V-Q245R-N248D,S101G-S103A-V104I-L148I-G159E-A232V-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-A158E-S188D-A232V-Q245R-N248D,和S101G-S103A-V104I-S128N-P129E-A158E-A232V-Q245R-N248D-H249R,其中所述枯草杆菌蛋白酶变体的氨基酸位置通过与如SEQ ID

NO:1所示解淀粉芽孢杆菌(B.amyloliquefaciens)枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[1047] 55.一种分离的枯草杆菌蛋白酶变体,所述枯草杆菌蛋白酶变体具有蛋白水解活性并包含具有选自以下的氨基酸置换的组合的氨基酸序列:T022A-S024R-S101G-S103A-V104I-A158E-A232V-Q245R-N248D-H249R,T022A-S024R-S101G-S103A-V104I-P129E-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-A158E-G159E-A232V-N238R-Q245R-N248D,S024R-S101G-S103A-V104I-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-A158E-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-G159E-S188D-A232V-Q245R-N248D-H249R,T022A-S024R-S101G-S103A-V104I-A158E-A232V-N238R-Q245R-N248D,S024R-S101G-S103A-V104I-G159E-S188D-A232V-N238R-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-P129E-A232V-Q245R-N248D,S024R-S101G-S103A-V104I-L148I-A232V-Q245R-N248D,S024R-S101G-S103A-V104I-P129E-A158E-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-L148I-A158E-A232V-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-P129E-A158E-A232V-Q245R-N248D-H249R,A016S-S024R-S101G-S103A-V104I-A158E-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-P129E-G159E-A232V-N238R-Q245R-N248D,S024R-S101G-S103A-V104I-P129E-S188D-A232V-Q245R-N248D-H249R,T022A-S101G-S103A-V104I-P129E-A232V-N238R-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-L148I-A158E-A232V-Q245R-N248D,S024R-S101G-S103A-V104I-P129E-S188D-A232V-N238R-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-A158E-G159E-S188D-A232V-N238R-Q245R-N248D,T022A-S101G-S103A-V104I-A158E-G159E-A232V-N238R-Q245R-N248D,T022A-S024R-S101G-S103A-V104I-P129E-A158E-A232V-Q245R-N248D,S101G-S103A-V104I-A158E-S188D-A232V-Q245R-N248D-H249R,T022A-S101G-S103A-V104I-A158E-G159E-A232V-Q245R-N248D-H249R,和S024R-S101G-S103A-V104I-A158E-G159E-A232V-Q245R-N248D,其中所述枯草杆菌蛋白酶变体的氨基酸位置通过与如SEQ ID NO:1所示解淀粉芽孢杆菌(B.amyloliquefaciens)枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[1048] 56.一种分离的枯草杆菌蛋白酶变体,所述枯草杆菌蛋白酶变体具有蛋白水解活性并包含具有选自以下的氨基酸置换的组合的氨基酸序列:V104L-S128N-A158E-R186H-H249R,S128N-A158E-S188D-H249R,N062E-S128N-A158E-G159E-E271F,N062E-A158E-S188D-H249R-E271F,N062E-A158E-R186H-H249R-E271F,S128N-A158E-S188D-Y209E-E271F,N062E-G159E-S188D-H249R,A016S-N062E-A158E-R186H-H249R,N062E-A158E-G159E-H249R,S101A-S128N-A158E-Y209E-H249R,S128N-A158E-R186H-E271F,N062E-A158E-S188D-H249R,N062E-A158E-R186H-E271F,N062E-A158E-R186H-H249R,N062E-S101A-R186H-H249R,N062E-S101A-A158E-R186H-E271F,N062E-V104L-A158E-S188D-H249R-E271F,N062E-G159E-R186H-H249R,N062E-G159E-H249R,S128N-A158E-R186H-H249R,S128N-A158E-S188D-E271F,N062E-A158E-H249R,N062E-R186H-S188D-H249R-E271F,S128N-A158E-Y209E-,N062E-S101A-A158E-H249R,V104L-S128N-A158E-R186H-E271F,N062E-S101A-A158E-R186H-H249R-E271F,A016S-N062E-A158E-H249R,N062E-

S101A-G159E-H249R,S128N-A158E-R186H-S188D-E271F,S101A-S128N-A158E-R186H-E271F,N062E-S101A-S188D-H249R,S101A-V104L-A158E-R186H-S188D-H249R,N062E-G159E-H249R-E271F,S128N-A158E-G159E-E271F,A016S-N062E-V104L-A158E-R186H-E271F,T022A-S128N-A158E-H249R,S128N-A158E-H249R,N062E-S101A-V104L-A158E-R186H-E271F,A016S-N062E-A158E-R186H-E271F,V104L-S128N-A158E-H249R,V104L-S128N-A158E-S188D-H249R,T022A-N062E-A158E,N062E-S101A-S188D-H249R-E271F,N062E-A158E-H249R-E271F,V104L-S128N-A158E-R186H-S188D-E271F,N062E-S101A-R186H-E271F,N062E-V104L-G159E-H249R,N062E-R186H-H249R,N062E-S101A-R186H-H249R-E271F,S101A-A158E-R186H-S188D-H249R,N062E-S101A-R186H,S101A-S128N-P129E-R186H-H249R,S101A-S103G-A158E-R186H-H249R,A016S-N062E-V104L-R186H-S188D-E271F,V104L-A158E-R186H-H249R,S101A-S128N-A158E-S188D-Y209E-E271F,N062E-S101A-R186H-S188D-E271F,A016S-N062E-A158E-H249R-E271F,N062E-S128N-A158E,N062E-S128N-G159E-H249R,N062E-S101A-A158E-S188D-H249R,S101A-S128N-A158E-H249R,N062E-A158E-R186H-S188D-H249R,A016S-V104L-A158E-R186H-E271F,N062E-L148I-G159E,N062E-S101A-A158E-R186H-H249R,N062E-S101A-R186H-S188D-H249R,V104L-A158E-R186H-S188D-H249R,N062E-S101A-V104L-R186H-S188D-E271F,T022A-S101A-A158E-R186H-H249R,S101A-S128N-A158E-Y209E,A158E-R186H-S188D-H249R-E271F,V104L-A158E-R186H-S188D-H249R-E271F,S101A-V104L-A158E-R186H-H249R,V104L-A158E-H249R,S101A-V104L-S128N-A158E-R186H-E271F,A016S-V104L-S188D-H249R,S101A-V104L-A158E-R186H-S188D-E271F,V104L-S128N-G159E-E271F,V104L-A158E-R186H-H249R-E271F,A158E-R186H-H249R,S101A-A158E-R186H-H249R,V104L-A158E-S188D-H249R-E271F,A016S-S128N-A158E-R186H,V104L-S128N-R186H-S188D-H249R,A016S-S101A-S128N-R186H,A016S-N062E-S128N-R186H-E271F,A016S-S128N-R186H-E271F,S128N-P129E-R186H,A158E-R186H-H249R-E271F,A016S-A158E-H249R,A016S-A158E-R186H-H249R,A016S-T022A-A158E-R186H-E271F,E089P-S101A-P129E-R186H,T022A-S128N-A158E-R186H,S101A-V104L-S128N-A158E-R186H,T022A-S128N-R186H-S188D-,N062E-V104L-A158E-R186H-S188D-H249R,T022A-A158E-R186H-H249R-E271F,T022A-V104L-A158E-H249R,S101A-L111V-P129E,A016S-A158E-H249R-E271F,A016S-L111V-S188D-,T022A-V104L-R186H-S188D-H249R,和V104L-L148I-S188D-H249R,其中所述枯草杆菌蛋白酶变体的氨基酸位置通过与如SEQ ID NO:1所示解淀粉芽孢杆菌(B.amyloliquefaciens)枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[1049] 57.一种分离的枯草杆菌蛋白酶变体,所述枯草杆菌蛋白酶变体具有蛋白水解活性并包含具有选自以下的氨基酸置换的组合的氨基酸序列:A001R-S101G-S103A-V104I-A232V-Q245R,V004R-S101G-S103A-V104I-A232V-Q245R,N043R-S101G-S103A-V104I-A232V-Q245R-E271L,S078R-S101G-S103A-V104I-A232V-Q245R,V004R-N043R-S101G-S103A-V104I-A232V-Q245R,N018R-N043R-S101G-S103A-V104I-A232V-Q245R,G020R-S101G-S103A-V104I-A232V-Q245R,S101G-S103A-V104I-A232V-Q245R-E271L,G020R-N043R-S101G-S103A-V104I-A232V-Q245R,S024R-N043R-S101G-S103A-V104I-A232V-Q245R,G020R-G025R-N116A-Y167W,N018R-S101G-S103A-V104I-A232V-Q245R,T022R-

S101G-S103A-V104I-A232V-Q245R,S078R-S103N-S106G-Y167W-Q236N,N018R-N043D-S101G-S103A-V104I-A232V-Q245R-N269R,N043R-S101G-S103A-V104I-A232V-Q245R-N269R,S024R-S101A-H120F-A194F-H249R,G020R-N043D-S101G-S103A-V104I-A232V-Q245R-N269R,S101G-S103A-V104I-S212F-A232V-Q245R,G020R-S144R-N185I-L233C-Q236N,G023A-S078R-S216F-Q236N-H249R,S101G-S103A-V104I-A232V-Q245R-N269R,S101G-S103A-V104I-G115R-A232V-Q245R,P052N-S078R-S103N-L148I-T213A,N018R-N043D-S101G-S103A-V104I-A232V-Q245R-H249R,S024R-N043D-S101G-S103A-V104I-A232V-Q245R-H249R,S024R-N043D-S101G-S103A-V104I-A232V-Q245R-N269R,G025R-E089I-N116A-P239S-A270C,S024R-S101G-S103A-V104I-A232V-Q245R,L148I-T213A-N252R,S024R-G025R-N183D-Y192W-P239S,G046R-A194F-S212M,V104L-L217E-T224A-H249R-N252R,G023A-Y091F-V121F-Y192W-Q236N,S101G-S103A-V104I-A232V-V244R-Q245R,S099F-S144R-Y167W-N252R,S101G-S103A-V104I-A232V-Q245R-H249R,N043R-S101G-S103A-V104I-A232V-Q245R,T022W-S078R-Y167W-S212M-A270C,V121F-N252R-A270C,G020R-S103N-S216F-Q236N-N252R,N043R-S101G-S103A-V104I-A232V-Q245R-H249R,G023A-P052N-Y192W-I198L-N252R,G025R-G046R-V121F,S024R-S078R-V104L-N116A-N183D,G046R-Q059A-S103N-G211Q-S212M,G020R-P052N-N062Q-Y091F-Y192W,G023A-P052N-S144R-Y192W-S216F,S101G-S103A-V104I-A232V-S242R-Q245R,P052N-S103N-N116A-L148I-Y192W,E089I-N116A-N117F-T224A-H249R,S144R-G211Q-N238L-P239S-H249R,N043A-N062Q-A194F-G211Q,G020R-S024R-P052N-Q059A-S216F,S024R-Y167W-T224A-H249R,T057R-Y167W-H249R,G025R-S103N-R186K-A194F-T224A,S105T-S128N-S144R-L148I-S212M,G020R-Q059A-S144R-Y192W-T224A,S024R-N043A-N117F-A194F-G211Q,N117F-A194F-T213A-A270C,S078R-Y091F-V121F-L233C-N252R,T057R-S099F-S105T-I198L-T213A,G023A-Y091F-S101A-I198L-N252R,N062Q-S103N-V121F-S144R-H249R,N043R-S101G-S103A-V104I-A232V-S242R-Q245R,G023A-S024R-N117F-S212M-S216F,V104L-T213A-S216F,A194F-G211Q-Q236N,N062Q-S103N-N117F-A194F,S024R-N062Q-V104L-S106G-H249R,T057R-E089I-I198L,G046R-Q059A-S106G-L217E-H249R,N117F-T213A-A215F,S101A-H120F-Y192W-A215F-T224A,N043A-T057R-N117F-S144R-N183D,G046R-N183D-N238L,G025R-N043A-E089I-N117F,S078R-V104L-T213A-A215F-T224A,Y091F-S099F-S101A-S105T-Y167W,S106G-N117F-N238L,G046R-E089I-Y091F-S101A-N116A,G020R-N062Q-E089I-R186K-S212M,T057R-S099F-V121F-N185I-Y192W,G046R-E089I-Y192W-L233C-A270C,E089I-N117F-N185I-A215F-L233C,P052N-V104L-N183D-S216F-H249R,S078R-S099F-N116A-R186K-T224A,G025R-S105T-S128N-S144R-A270C,S105T-G211Q-S216F,S024R-G046R-Y091F-V121F,S106G-N185I-S216F-Q236N,N062Q-S101A-Q236N-N252R-A270C,G025R-N043A-Y091F-I198L-A270C,G020R-G023A-V104L-Y192W-L233C,S024R-N043A-S105T-S106G-I198L,G020R-E089I-L217E,S024R-Y091F-I198L-A215F-P239S,G046R-E089I-S099F-R186K-S212M,V104L-H120F-R186K-S216F-N252R,T022W-A194F-T213A-L233C-N238L,S099F-S105T-S106G-A194F-S212M,E089I-S105T-N116A-A215F-S216F,G025R-N116A-H120F-T224A-A270C,N043A-Q059A-S101A-S216F-T224A,T057R-N183D-Q236N,G025R-N062Q-S128N-S144R-N185I,

S103N-H120F-Y167W-I198L-L233C,T022W-E089I-S216F,S024R-S106G-N116A-S212M-T224A,G020R-P052N-S101A-I198L-L233C,E089I-Y091F-N185I-G211Q-A270C,L111I-A215F-P239S,S024R-N116A-R186K-L233C-Q236N,和G023A-S103N-S106G-S212M-A215F,其中所述枯草杆菌蛋白酶变体的氨基酸位置通过与如SEQ ID NO:1所示解淀粉芽孢杆菌(B.amyloliquefaciens)枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[1050] 58.一种分离的枯草杆菌蛋白酶变体,所述枯草杆菌蛋白酶变体具有蛋白水解活性并包含具有选自以下的氨基酸置换的组合的氨基酸序列:G020R-T022W-S078R-S101A-S103A-V104I-N116S-T213A-A215F-A232V-Q245R,N018R-S078R-S101G-S103A-V104I-A232V-Q245R,S024R-R045T-S101G-S103A-V104I-A232V-Q245R-N269R,G020R-T022W-S078R-S101G-S103A-V104I-N116A-A232V-Q245R,G020R-T22W-S101G-S103A-V104I-A232V-Q245R,N018R-N043R-S101G-S103A-V104I-A232V-Q245R,N018R-T022W-S024R-N076D-S101A-N116A-A232V-Q245R,N018R-V104I-A232V-H249R,N018R-S024R-N076D-S101A-N116A-G211Q-H249R,N018R-N043D-S078R-S101G-S103A-V104I-L217E-A232V-Q245R,N018R-N043R-S101G-S103A-V104I-A232V-Q245R-N269R,N018R-R045T-N076D-S101G-S103A-V104I-A232V-Q245R-N269R,N076D-S078R-S101G-S103A-V104I-A232V-Q245R-N269R,G020R-N043D-S078R-S101G-S103A-V104I-A232V-Q245R,N018R-N043D-N076D-S101G-S103A-V104I-A232V-Q245R-N269R,S024R-R045T-N076D-S078R-S101G-S103A-V104I-A232V-Q245R-N269R,N018R-S103A-A232V-H249R,N018R-S101G-V104I-A232V-Q245R,G020R-S024R-S101G-S103A-V104I-L217E-A232V-Q245R-H249R,N018R-T22K-N043D-S101G-S103A-V104I-A232V-Q245R,N043R-R045T-S101G-S103A-V104I-A232V-Q245R-N269R,G020R-T22W-S101G-S103A-V104I-G211Q-A232V-Q245R,S024R-N076D-S078R-S101G-S103A-V104I-A232V-Q245R-N269R,G020R-T22W-S078R-S101A-S103A-V104I-N116A-N183D-A232V,N018R-S024R-N076D-N116A-A215F-H249R,N018R-N043R-R045T-S101G-S103A-V104I-A232V-Q245R,S024R-N043R-N076D-S101G-S103A-V104I-A232V-Q245R,G020R-T022W-S101G-S103A-V104I-A232V-Q245R,G020R-T022W-S101G-S103A-V104I-G211Q-A232V-Q245R,G020R-T022W-S078R-S101G-S103A-V104I-N116A-T213A-A215F-A232V-Q245R,N043D-N076D-S078R-S101G-S103A-V104I-A232V-Q245R-N269R,N018R-S024R-N076D-S101A-N116A-T213A-H249R,N018R-S024R-N076D-N116A-G211Q-H249R,N043R-R045T-N076D-S078R-S101G-S103A-V104I-A232V-Q245R,N018R-S101G-Q245R,G020R-T22W-S101A-S103A-V104I-G211Q-T213A-A232V-Q245R,G020R-S024R-N043D-N076D-S078R-S101G-S103A-V104I-A232V-Q245R,N018R-R045T-N076D-S078R-S101G-S103A-V104I-A232V-Q245R,G020R-S078R-S101G-S103A-V104I-G211Q-T213A-A215F-A232V-Q245R,R045T-S078R-S101G-S103A-V104I-A232V-Q245R-N269R,S024R-N043D-S101G-S103A-V104I-A232V-Q245R-N269R,N018R-S101G-S103A-H249R,N018R-T22W-S024R-N076D-S101A-N116A-A232V-Q245R,N018R-S101G-V104I-A232V-H249R,G020R-T22W-S101A-S103A-V104I-A215F-A232V-Q245R,N018R-S024R-N076D-G211Q-T213A-H249R,N018R-T022W-S024R-N076D-S101A-I198L-H249R,S024R-S101G-S103A-V104I-A232V-Q245R,G020R-N076D-S101G-S103A-V104I-A232V-Q245R-N269R,G020R-S101G-S103A-V104I-A232V-Q245R-N269R,N043D-S078R-S101G-S103A-V104I-A232V-Q245R,G020R-S101G-V104I-T213A-

A215F-A232V-Q245R,G02OR-S101G-S103A-V104I-N116A-A215F-A232V-Q245R,S024R-S103A-V104I-H249R,N018R-N076D-S078R-S101G-S103A-V104I-A232V-Q245R,R045T-N076D-S078R-S101G-S103A-V104I-A232V-Q245R-N269R,S024R-S101G-V104I-Q245R,G02OR-S101G-S103A-V104I-G211Q-T213A-A215F-A232V-Q245R,S024R-S103A-V104I-A232V-H249R,N018R-S024R-N076D-N116A-G211Q-A215F-H249R,N018R-Q245R,S024R-S103A-Q245R,S024R-S103A-V104I-Q245R,G02OR-S078R-S101G-A232V-Q245R,N018R-S024R-N076D-V104I-H249R,N018R-S024R-V104I-H249R,S024R-S101G-S103A-V104I-A232V-Q245R,N018R-S024R-N076D-G211Q-A215F-H249R,R019H-G02OR-T022W-S078R-S101G-S103A-V104I-G211Q-A232V-Q245R,N018R-S024R-N076D-S101A-I198L-G211Q-T213A-H249R,N018R-S024R-N043D-S101G-S103A-V104I-A232V-Q245R,G02OR-T22W-S103A-V104I-A232V-Q245R,N018R-S103A-V104I-H249R,N018R-T022W-S024R-N076D-S101A-I198L-A215F-H249R,N018R-S024R-S101G-V104I-A232V,S078R-S101G-S103A-V104I-A232V-Q245R-N269R,S024R-N043R-N076D-S078R-S101G-S103A-V104I-A232V-Q245R,N018R-G02OR-N043D-N076D-S101G-S103A-V104I-A232V-Q245R,N018R-T22W-S024R-N076D-N116A-T213A-H249R,N018R-S024R-S101G-V104I,G02OR-S101A-S103A-V104I-A215F-A232V-Q245R,N018R-R045T-S078R-S101G-S103A-V104I-A232V-Q245R,N018R-S101G-S103A-Q245R,N043R-N076D-S078R-S101G-S103A-V104I-A232V-Q245R,G02OR-T022W-S101A-S103A-V104I-G211Q-A215F-A232V-Q245R,G02OR-T22W-S078R-S101G-S103A-V104I-N116A-T213A-A215F-A232V-Q245R,G02OR-S078R-S101G-S103A-V104I-A215F-A232V-Q245R,G02OR-T022W-S078R-S101G-S103A-V104I-N116A-N183D-A232V-Q245R,N076D-S101G-S103A-V104I-A232V-Q245R,N076D-S101G-S103A-V104I-A232V-Q245R-N269R,G02OR-T22W-S101A-S103A-V104I-A232V-Q245R,G02OR-S101G-S103A-A232V-Q245R,G02OR-T022W-S078R-S101A-S103A-V104I-N116A-N183D-A232V-Q245R,N018R-G02OR-S024R-R045T-N076D-S101G-S103A-V104I-A232V-Q245R-N269R,N043R-R045T-S078R-S101G-S103A-V104I-A232V-Q245R,N018R-S101G-V104I-H249R,G02OR-T22W-S078R-S101G-S103A-V104I-N116A-N183D-A232V-Q245R,G02OR-T022W-S101G-S103A-V104I-I198L-G211Q-T213A-A232V-Q245R,G02OR-S078R-S101A-S103A-V104I-N116A-N183D-T213A-A232V-Q245R,S024R-N076D-V104I-A232V-Q245R,N018R-G02OR-N076D-S101G-S103A-V104I-A232V-Q245R,N018R-S024R-N076D-S101G-V104I-A232V-H249R,N018R-N043D-S078R-S101G-S103A-V104I-A232V-Q245R,A001T-N018R-S024R-N076D-N116A-T213A-H249R,N076D-S078R-S101G-S103A-V104I-A232V-Q245R,G02OR-S078R-S101G-S103A-V104I-N116A-A232V-Q245R,N043R-N076D-S101G-S103A-V104I-A232V-Q245R,N018R-R045T-S101G-S103A-V104I-A232V-Q245R,N018R-N076D-S101G-V104I-A232V-Q245R,G02OR-S078R-S101G-S103A-V104I-N116A-N183D-A232V-Q245R,N018R-S024R-N076D-S101A-G211Q-T213A-A215F-H249R,R045T-S078R-S101G-S103A-V104I-A232V-Q245R,N043R-N076D-S101G-S103A-V104I-A232V-Q245R-N269R,G02OR-T022W-S078R-S101G-S103A-V104I-N116A-N183D-T213A-A232V-Q245R,G02OR-T022W-S101G-S103A-V104I-N116A-N183D-T213A-A232V-Q245R,G02OR-S101G-I198L-A215F-A232V-Q245R,N018R-S024R-N076D-T213A-A215F-H249R,G02OR-S078R-S101G-S103A-V104I-N116A-G211Q-A232V-

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T213A-A215F-A232V-Q245R,N018R-S024R-N076D-A086V-S101A-N183D-I198L-G211Q-H249R,N018R-N076D-S101G-I198T-A232V,N018R-G020R-S024R-N076D-S101A-N116A-N183D-I198L-G211Q-A215F-H249R,N018R-T022W-S024R-N076D-S101A-N116A-N183D-T213A-A215F-H249R,N018R-T022W-S024R-N076D-S101A-N183D-G211Q-T213A-A215F-H249R,N018R-S024R-N076D-N183D-H249R-A248T,N018R-N076D-V104I-Q245R-H249R,N018R-T022W-S024R-N076D-S101A-N116A-N183D-I198L-A215F-H249R,N018R-T022W-S024R-N076D-N116A-N183D-T213A-A215F-H249R,N018R-G020R-T022W-S024R-N076D-N116A-N183D-G211Q-T213A-A215F-H249R,N018R-G020R-S024R-N076D-S101A-H249R,N018R-G020R-S024R-N076D-S101A-N116A-T213A-A215F-H249R,N018R-T022W-S024R-N076D-N116A-N183D-G211Q-A215F-H249R,N018R-T022W-S024R-N076D-N116A-N183D-I198L-G211Q-T213A-H249R,N043R-R045T-S078R-S101G-S103A-V104I-L217E-A232V-Q245R,N043R-R045T-S101G-S103A-V104I-A232V-Q245R-H249R,N018R-N076D-S101G-V104I,G020R-R045T-N076D-S078R-S101G-S103A-V104I-A232V-Q245R-H249R,N043D-N076D-S101G-S103A-V104I-A232V-Q245R,N018R-G020R-T022W-S024R-N076D-S101A-N116A-N183D-I198L-H249R,N018R-N076D-V104I,N018R-G020R-N043D-S101G-S103A-V104I-A232V-Q245R-H249R,N018R-G020R-T022W-S024R-N076D-N183D-G211Q-H249R,N018R-S024R-N076D-S101A-N183D-I198L-G211Q-A215F-H249R,S101G-V104I,N018R-T022W-S024R-N076D-N116A-N183D-I198L-G211Q-T213A-A215F-H249R,N018R-G020R-S024R-N076D-S101A-N183D-G211Q-T213A-A215F-H249R,N018R-G020R-S024R-N076D-N116A-N183D-A215F-H249R-N263D,N018R-T022W-S024R-N076D-S101A-N183D-H249R,N018R-S024R-N076D-S101A-N116A-N183D-I198L-A215F-H249R,N018R-T022W-S024R-N076D-N116A-I198L-A215F-H249R-R269H,N018R-N043D-R045T-N076D-S078R-S101G-S103A-V104I-A232V-Q245R,N018R-S024R-R045T-N076D-S078R-S101G-S103A-V104I-A232V-Q245R-N269R,S078R-S101G-S103A-V104I-L217E-A232V-Q245R,N018R-G020R-T022W-S024R-N076D-S101A-N183D-I198L-T213A-A215F-H249R,N018R-G020R-S024R-N076D-N183D-I198L-T213A-H249R,N018R-G020R-T022W-S024R-N076D-N116A-I198L-G211Q-A215F-H249R,N018R-G020R-T022W-S024R-N076D-N116A-N183D-G211Q-H249R,N018R-G020R-T022W-S024R-N076D-S101A-I198L-G211Q-T213A-H249R,N018R-G020R-T022W-S024R-N076D-H249R,G020R-T022W-S101G-S103A-V104I-N116A-N183D-I198L-G211Q-T213A-A215F-A232V-Q245R,V104I-A232V,N018R-G020R-T022W-S024R-N076D-S101A-N116A-N183D-G211Q-A215F-H249R,N018R-G020R-T022W-S024R-N076D-S101A-N116A-N183D-I198L-G211Q-T213A-A215F-H249R,N018R-G020R-T022W-S024R-N076D-S101A-N183D-T213A-A215F-H249R,N018R-T022W-S024R-N076D-S101A-N183D-I198L-G211Q-T213A-H249R,N018R-T022W-S024R-N076D-S101A-N183D-I198L-H249R,N043D-R045T-S101G-S103A-V104I-A232V-Q245R-N269R,N018R-G020R-S024R-N076D-S101A-N183D-I198L-G211Q-H249R,N018R-G020R-N043R-S101G-S103A-V104I-L217E-A232V-Q245R,S024R-N043R-N076D-S078R-S101G-S103A-V104I-A232V-Q245R-N269R,N043R-R045T-N076D-S078R-S101G-S103A-V104I-Y166F-A176P-A179V-N184T-A187P-A194P,N018R-T022W-S024R-D041E-N076D-S101A-S160T-N183D-G211Q-T213A-H249R,N018R-

G020R-T022W-S024R-N076D-N116A-N183D-I198L-G211Q-A215F-H249R,N018R-G020R-T022W-S024R-N076D-S101A-N116A-I198L-T213A-H249R,N018R-T022W-S024R-N076D-S101A-N116A-N183D-I198L-G211Q-T213A-H249R,N018R-G020R-S024R-N076D-I198L-T213A-H249R,N018R-G020R-T022W-S024R-N076D-N116A-N183D-I198L-G211Q-H249R,N018R-G020R-S024R-N076D-N183D-G211Q-A215F-H249R,S024R-N076D-V104I,N018R-N076D-S101G-A232V,N018R-S024R-N076D-S101A-N116A-N183D-I198L-G211Q-T213A-A215F-H249R,N018R-G020R-T022W-S024R-N076D-N116A-N183D-A215F-H249R,N018R-S024R-L031F-N076D-N116A-N183D-G211Q-T213A-A215F-H249R,N018R-S024R-N076D-S101A-N116A-N183D-I198L-T213A-H249R-N269S,N018R-G020R-S024R-N076D-S101A-N116A-I198L-A215F-H249R,N018R-N043R-N076D-S078R-S101G-S103A-V104I-A232V-Q245R-N269R,N018R-G020R-S024R-N076D-S101A-N114T-I198L-G211Q-A215F-H249R,S024R-N043R-S078R-S101G-S103A-V104I-L217E-A232V-Q245R,S024R-N076D-S103A-V104I-A232V,N018R-G020R-T022W-S024R-N076D-S101A-I198L-G211Q-A215F-H249R,S101G-V104I-A232V,N018R-T022W-S024R-N076D-N183D-I198L-T213A-A215F-H249R,N018R-T022W-S024R-N076D-N183D-I198L-G211Q-H249R,N018R-G020R-S024R-N076D-N183D-T213A-H249R,N018R-S024R-N076D-S101A-N183D-G211Q-A215F-H249R,N018R-G020R-T022W-S024R-N076D-N116A-G211Q-T213A-H249R,N018R-S078R-S101G-S103A-V104I-A232V-Q245R-N269R,N018R-T022W-S024R-N076D-S101A-N116A-N183D-G211Q-A215F-H249R-T260A,N076D-H249R,N018R-T022W-S024R-N076D-N183D-G211Q-A215F-H249R,N018R-G020R-S024R-N076D-N116A-G211Q-A215F-H249R,N018R-G020R-S024R-N076D-T213A-H249R,N018R-G020R-T022W-S024R-N076D-N116A-N183D-I198L-H249R,N018R-G020R-T022W-S024R-N076D-S101A-N183D-H249R,N076D-V104I-H249R,G020R-T022W-S101A-S103A-V104I-N116A-N183D-G211Q-T213A-A215F-A232V-Q245R,S024R-N043R-R045T-S078R-S101G-S103A-V104I-L217E-A232V-Q245R,N018R-G020R-T022W-S024R-N076D-N183D-I198L-A215F-H249R,N018R-N076D-S101G-S103A,G020R-S024R-S101G-S103A-V104I-A232V-Q245R-N269R,N018R-G020R-S024R-N076D-S101A-N116A-N183D-G211Q-H249R,S101G-S103A-A232V,S024R-N076D-S101G-A232V,N018R-T022W-S024R-N076D-S101A-N183D-I198L-G211Q-H249R,N018R-G020R-S024R-N076D-S101A-N183D-I198L-G211Q-A215F-H249R,N018R-G020R-S024R-N076D-N183D-I198L-H249R,N018R-T022W-S024R-N076D-S101A-N116A-N183D-I198L-G211Q-H249R,N018R-G020R-S024R-N076D-N116A-A156V-N183D-G211Q-A215F-H249R-N269S,R045T-N076D-S101G-S103A-V104I-A232V-Q245R-H249R,N018R-G020R-S024R-N076D-S101A-N183D-I198L-H249R,N018R-G020R-T022W-S024R-N076D-I198L-G211Q-A215F-H249R,N018R-G020R-T022W-S024R-N076D-S101A-N116A-I198L-G211Q-A215F-H249R,N018R-G020R-T022W-S024R-N076D-N116A-H249R,N018R-N076D-S101G,N018R-S024R-N076D-N116A-N183D-I198L-T213A-A215F-H249R,N018R-G020R-T022W-S024R-N076D-S101A-N116A-I198L-T213A-A215F-H249R,N018R-S024R-N076D-S101A-N116A-N183D-I198L-G211Q-H249R,N018R-N076D-A232V,N018R-G020R-S024R-N076D-S101A-A232V-Q245R,N018R-N043D-R045T-N076D-S101G-S103A-V104I-A232V-Q245R,N018R-T022W-S024R-N076D-N183D-

T213A-A215F-H249R,N018R-S024R-N076D-S101A-N116A-G211Q-T213A-N237D-H249R,N018R-G020R-S024R-N076D-S101A-N116A-N183D-G211Q-H249R-R275S,N018R-T022W-S024R-N076D-S101A-N116A-N183D-I198L-G211Q-T213A-A215F-H249R,S024R-N076D,N018R-S024R-N076D-N183D-G211Q-A215F-H249R,N018R-T022W-S024R-N076D-N116A-N183D-I198L-T213A-A215F-H249R,N076D-V104I-A232V-H249R,N018R-N076D-S103A-A232V,N018R-G020R-S024R-N076D-S101A-N116A-N183D-I198L-G211Q-T213A-H249R,N018R-G020R-S024R-N076D-S101A-N183D-T213A-H249R,N018R-G020R-S024R-N076D-S101A-D175E-N183D-G211Q-A215F-H249R,N018R-G020R-N043D-S078R-S101G-S103A-V104I-L217E-A232V-Q245R-A273E,G020R-S024R-N043D-R045T-N076D-S101G-S103A-V104I-A232V-Q245R,P005S-S101G-S103A-V104I-A232V-Q245R-H249R,S103A-V104I-A232V,N018R-G020R-S024R-V068A-N076D-S101A-N116A-T213A-A215F-H249R,N018R-T022W-S024R-N076D-S101A-I198L-A215F-H249R-R275S,N018R-S024R-N076D-N183D-I198L-G211Q-T213A-H249R,和N043D-R045T-S101G-S103A-V104I-A232V-Q245R,其中所述枯草杆菌蛋白酶变体的氨基酸位置通过与如SEQ ID NO:1所示解淀粉芽孢杆菌(B.amyloliquefaciens)枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[1051] 59.一种分离的枯草杆菌蛋白酶变体,所述枯草杆菌蛋白酶变体具有蛋白水解活性并包含具有选自以下的氨基酸置换的组合的氨基酸序列:N018R-S024R-N043R-N076D-H249R-N269R,N018R-T022R-S024R-N043R-N076D-H249R,N018R-N043D-S101G-S103A-V104I-A232V-Q245R,G020R-N043D-S101G-S103A-V104I-A232V-Q245R,N043D-S101G-S103A-V104I-A232V-Q245R-N269R,N043D-S078R-S101G-S103A-V104I-A232V-Q245R,N043R-N076D-S101G-S103A-V104I-A232V-Q245R,T022R-N043R-S101G-S103A-V104I-A232V-Q245R,N043R-S078R-S101G-S103A-V104I-A232V-Q245R,G020R-N076D-S101G-S103A-V104I-A232V-Q245R,N043R-N076D-S101G-S103A-V104I-A232V-Q245R,T022R-N076D-S101G-S103A-V104I-A232V-Q245R,N076D-S078R-S101G-S103A-V104I-A232V-Q245R,N018R-S024R-N043R-N076D-H249R,N018R-S024R-N076D-S242R-H249R,N018R-S024R-N076D-H249R-N269R,N018R-T022R-S024R-N076D-H249R,N018R-S024R-N076D-S078R-H249R,N018R-S024R-N043D-N076D-H249R-N269R,N018R-T022R-S024R-N043D-N076D-H249R,N018R-S024R-N043D-N076D-S078R-H249R,G020R-S101G-S103G-V104I-A232V-Q245R,G020R-S101G-S103A-V104L-A232V-Q245R,G020R-S101G-S103A-V104V-A232V-Q245R,G020R-S101G-S103S-V104I-A232V-Q245R,G020R-S101G-S103S-V104L-A232V-Q245R,G020R-S101S-S103S-V104I-A232V-Q245R,G020R-S101S-S103S-V104L-A232V-Q245R,G020R-S101A-S103A-V104L-A232V-Q245R,G020R-S101S-S103S-V104V-A232V-Q245R,G020R-S101S-S103A-V104I-A232V-Q245R,G020R-S101S-S103A-V104V-A232V-Q245R,G020R-S101S-S103G-V104I-A232V-Q245R,G020R-S101S-S103G-V104V-A232V-Q245R,G020R-S101A-S103A-V104V-A232V-Q245R,G020R-S101A-S103S-V104I-A232V-Q245R,G020R-S101A-S103S-V104V-A232V-Q245R,N018R-S024R-N043R-N076D-S078R-H249R,S024R-N043D-S101G-S103A-V104I-A232V-Q245R,N043D-S101G-S103A-V104I-A232V-Q245R-H249R,S024R-N076D-S101G-S103A-V104I-A232V-Q245R,N076D-S101G-S103A-V104I-A232V-S242R-Q245R,N018R-G020R-S024R-N076D-L217E-H249R,

N018R-S024R-N043R-N076D-L217E-H249R,N018R-S024R-N043D-N076D-S242R-H249R,N018R-G020R-S024R-N043R-N076D-H249R,G020R-S101A-S103G-V104V-A232V-Q245R,N043D-S101G-S103A-V104I-A232V-Q245R,N018R-S024R-N076D-L217E-H249R-N269R,和N018R-S024R-N076D-L217E-S242R-H249R,其中所述枯草杆菌蛋白酶变体的氨基酸位置通过与如SEQ ID NO:1所示解淀粉芽孢杆菌(B.amyloliquefaciens)枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[1052] 60.一种分离的枯草杆菌蛋白酶变体,所述枯草杆菌蛋白酶变体具有蛋白水解活性并包含具有选自以下的氨基酸置换的组合的氨基酸序列:G020R-S101A-S103A-V104I-G118R-A232V-Q245R,G020R-S024R-N116A-T213A,N043R-S101A-N116A-A215F-N269R,S024R-N043R-S101A-N116A,S024R-N043R-S101A-N116A-A215F-N269R,G020R-S101G-S103A-V104I-A215F-A232V-Q245R,N043R-S101A-N269R,S024R-N043R-N116A-T213A-N269R,G020R-S024R-N043R-R045T-S101A-T213A,S024R-N043R-N116A-A215F-N269R,G020R-S024R-T213A-A215F,G020R-N116A-N269R,S024R-N116A-T213A-N269R,N043R-S101A-N116A-N269R,S101G-S103A-V104I-N116A-T213A-A232V-Q245R-N269R,S024R-N043R-R045T-S101A-N116A-A215F-N269R,G020R-N043R-S101A-N269R,S101A-S103A-V104I-T213A-A232V-Q245R-N269R,S024R-A215F-N269R,N043R-S101A-N116A-T213A-A215F-N269R,N043R-S101A-T213A-N269R,G020R-S024R-N043R-R045T-N116A-T213A,S101G-S103A-V104I-A232V-Q245R-N269R,S024R-N043R-R045T-S101A-N116A-T213A-N269R,S024R-N043R-R045T-N269R,G020R-N043R-R045T-S101A-N269R,S024R-N043R-N116A-N269R,G020R-S024R-N043R-R045T,N043R-N116A-N269R,S024R-N043R-S101A-A215F-N269R,S024R-N043R-R045T-T213A-A215F-N269R,G020R-S024R-R045T-N269R,G020R-N043R-S101A-N116A-T213A-A215F,G020R-S101G-S103A-V104I-T213A-A215F-A232V-Q245R,G020R-S024R-R045T-N116A-N269R,G020R-S101A-N116A-N269R,S024R-N043R-A215F,G020R-S024R-T213A,S024R-N043R-S101A-A215F,G020R-S024R-N043R-R045T-N116A,G020R-S024R-N043R-R045T-S101A-N269R,G020R-S024R-S101A-A215F,G020R-S024R-N116A-T213A-A215F,G020R-S024R-N116A,G020R-S024R-S101A-N116A,N043R-T213A-A215F-N269R,S024R-S101A-N269R,S024R-N043R-N116A-A215F,G020R-T038A-N043R-S101A,G020R-S024R-N116A-A215F,S024R-N043R-S101A-T213A,P014L-G020R-S024R-N043R-R045T-S101A-A215F,G020R-S024R-A215F,G020R-N116A-A215F-N269R,G020R-R045T-N116A-N269R,G020R-S024R-N043R-R045T-A215F,和G020R-S024R-N043R-R045T-N116A-T213A-A215F,其中所述枯草杆菌蛋白酶变体的氨基酸位置通过与如SEQ ID NO:1所示解淀粉芽孢杆菌(B.amyloliquefaciens)枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[1053] 61.一种分离的枯草杆菌蛋白酶变体,所述枯草杆菌蛋白酶变体具有蛋白水解活性并包含具有选自以下的氨基酸置换的组合的氨基酸序列:N043R-N076D-S101A-S103A-V104I-A158E-S188D-A232V-Q245R-N248D-H249R-E271F,S024R-N043R-N076D-S101A-S103A-V104I-A158E-S188D-L217E-A232V-Q245R-N248D-H249R,S101A-S103A-V104I-A158E-S188D-A232V-Q245R-N248D-H249R-E271F-E271F,S101A-S103A-V104I-A158E-S188D-L217E-A232V-Q245R-N248D-H249R-E271F,N076D-S101G-S103A-V104I-A114V-

A158E-S188D-A232V-Q245R-N248D-H249R-E271F,S024R-N076D-S101G-S103A-V104I-A158E-S188D-A232V-Q245R-N248D-H249R-E271F,S024R-N043R-S101A-S103A-V104I-A158E-S188D-L217E-A232V-Q245R-N248D-H249R,S024R-N043R-S101A-S103A-V104I-A158E-S188D-A232V-Q245R-N248D-H249R,S024R-S101A-S103A-V104I-A158E-S166D-S188D-L217E-A232V-Q245R-N248D-H249R,N076D-S101G-S103A-V104I-S128L-A158E-S188D-A232V-Q245R-N248D-H249R-E271F,和N043R-N076D-S101G-S103A-V104I-A158E-S166D-S188D-A232V-Q245R-N248D-H249R-E271F,其中所述枯草杆菌蛋白酶变体的氨基酸位置通过与如SEQ ID NO:1所示解淀粉芽孢杆菌(B.amyloliquefaciens)枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[1054] 62.一种分离的枯草杆菌蛋白酶变体,所述枯草杆菌蛋白酶变体具有蛋白水解活性并包含具有选自以下的氨基酸置换的组合的氨基酸序列:T022A-S101G-S103A-V104I-G159D-L217E-A232V-Q245R-N248D-E271F,T022A-N043R-S101G-S103A-V104I-G159D-S188D-L217E-A232V-Q245R-N248D-E271F,T022A-S101G-S103A-V104I-G159D-S188D-A232V-Q245R-N248D-E271F,N043R-S101A-S103A-V104I-A158E-S188D-L217E-A232V-Q245R-N248D-H249R,N043R-N076D-S101A-S103A-V104I-A158E-S188D-L217E-A232V-Q245R-N248D-H249R-E271F,S024R-S101G-S103A-V104I-A158E-S188D-L217E-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-A158E-S188D-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-A158E-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-A158E-N183D-S188D-A232V-Q245R-N248D-H249R,T022A-N076D-S101G-S103A-V104I-G159D-S188D-A232V-Q245R-N248D-E271F,T022A-N043R-N076D-S101G-S103A-V104I-G159D-S188D-A232V-Q245R-N248D-E271F,T022A-N076D-S101G-S103A-V104I-G159D-A232V-Q245R-N248D-E271F,T022A-S101G-S103A-V104I-G159D-A232V-Q245R-N248D-E271F,N076D-S101A-S103A-V104I-A158E-S188D-A232V-Q245R-N248D-H249R-E271F,N043R-S101A-S103A-V104I-A158E-S166D-S188D-A232V-Q245R-N248D-H249R,S024R-N076D-S101A-S103A-V104I-A158E-S166D-S188D-A232V-Q245R-N248D-H249R-E271F,N076D-S101A-S103A-V104I-A158E-S188D-A232V-Q245R-N248D-H249R,S101A-S103A-V104I-A158E-S166D-S188D-A232V-Q245R-N248D-H249R-E271F,N043R-N076D-S101A-S103A-V104I-A158E-S166D-S188D-A232V-Q245R-N248D-H249R-E271F,S101G-S103A-V104I-A158E-S166D-S188D-A232V-Q245R-N248D-H249R-E271F,S101A-S103A-V104I-A158E-S188D-A232V-Q245R-N248D-H249R-E271F,S101A-S103A-V104I-A158E-S188D-L217E-A232V-Q245R-N248D-H249R,N076D-S101A-S103A-V104I-A158E-S166D-S188D-A232V-Q245R-N248D-H249R-E271F,S101G-S103A-V104I-A158E-N183D-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-S128L-A158E-S188D-A232V-Q245R-N248D-H249R,N076D-S101G-S103A-V104I-A158E-S166D-S188D-A232V-Q245R-N248D-H249R-E271F,N043R-N076D-S101A-S103A-V104I-A158E-S166D-S188D-A232V-Q245R-N248D-H249R,和N076D-S101A-S103A-V104I-A158E-S188D-L217E-A232V-Q245R-N248D-H249R-E271F,其中所述枯草杆菌蛋白酶变体的氨基酸位置通过与如SEQ ID NO:1所示解淀粉芽孢杆菌(B.amyloliquefaciens)枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[1055] 63.一种分离的枯草杆菌蛋白酶变体,所述枯草杆菌蛋白酶变体具有蛋白水解活性并包含具有选自以下的氨基酸置换的组合的氨基酸序列:H017R-T022A-N076D-S101G-S103A-V104I-G159D-S188D-A232V-Q245R-N248D-E271F,T022A-N043R-S101G-S103A-V104I-G159D-A232V-Q245R-N248D-E271F,T022A-S101G-S103A-V104I-G159D-S188D-A232V-Q245R-N248D-H249R-E271F,H017R-T022A-N076D-S101G-S103A-V104I-G159D-A232V-Q245R-N248D-E271F,T022A-N076D-S101G-S103A-V104I-G159D-A232V-Q245R-N248D-H249R-E271F,T022A-S101G-G102A-S103A-V104I-G159D-S188D-A232V-Q245R-N248D-E271F,和T022A-N043R-N076D-S101G-S103A-V104I-G159D-A232V-Q245R-N248D-H249R-E271F,其中所述枯草杆菌蛋白酶变体的氨基酸位置通过与如SEQ ID NO:1所示解淀粉芽孢杆菌(B.amyloliquefaciens)枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[1056] 64.一种分离的枯草杆菌蛋白酶变体,所述枯草杆菌蛋白酶变体具有蛋白水解活性并包含具有选自以下的氨基酸置换的组合的氨基酸序列:S101S-S103A-V104I-A158E-S188D-A232V-Q245R-N248D-H249R,S101S-S103G-V104V-A158E-S188D-A232V-Q245R-N248D-H249R,S101G-S103S-V104I-A158E-S188D-A232V-Q245R-N248D-H249R,S101A-S103A-V104I-A158E-S188D-A232V-Q245R-N248D-H249R,S101A-S103A-V104L-A158E-S188D-A232V-Q245R-N248D-H249R,S101G-S103G-V104I-A158E-S188D-A232V-Q245R-N248D-H249R,S101S-S103G-V104I-A158E-S188D-A232V-Q245R-N248D-H249R,S101S-S103S-V104I-A158E-S188D-A232V-Q245R-N248D-H249R,S101S-S103S-V104V-A158E-S188D-A232V-Q245R-N248D-H249R,S101A-S103S-V104I-A158E-S188D-A232V-Q245R-N248D-H249R,S101A-S103S-V104I-G159E-A232V-Q245R-N248D-H249R,S101S-S103A-V104I-G159E-A232V-Q245R-N248D-H249R,S101G-S103A-V104L-A158E-S188D-A232V-Q245R-N248D-H249R,S101A-S103A-V104L-G159E-A232V-Q245R-N248D-H249R,S101A-S103S-V104L-G159E-A232V-Q245R-N248D-H249R,S101G-S103S-V104L-G159E-A232V-Q245R-N248D-H249R,S101S-S103A-V104L-G159E-A232V-Q245R-N248D-H249R,S101A-S103G-V104V-G159E-A232V-Q245R-N248D-H249R,和S101S-S103A-V104V-G159E-A232V-Q245R-N248D-H249R,其中所述枯草杆菌蛋白酶变体的氨基酸位置通过与如SEQ ID NO:1所示解淀粉芽孢杆菌(B.amyloliquefaciens)枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[1057] 65.一种分离的枯草杆菌蛋白酶变体,所述枯草杆菌蛋白酶变体具有蛋白水解活性并包含具有选自以下的氨基酸置换的组合的氨基酸序列:V026F-V051W-V104L-S106E,V026F-L031F-S078N-G102A-S160D,G020K-G100S-N116L-A158E-S166D-N243F,T033S-N043W-N218D-P239G-N243F,T022L-T038F-A048R-N062E-G100S-R186K,S101D-S103N-N116L-S144R-A215D,V104L-S105T-T213A-L217E-S256N,N043W-S101D-S212M-N243F,V026F-A048R-S105T-T213A-N218D-T224A,S024F-S101D-G118R-A215D-L250I-A272F,V121F-N185E-T224A-P239G,T022L-L031F-G102A-S128D-T224A-N243F,N062E-S078N-G102A-N116L-S144R-L250I,T022L-T038F-V121F-S160D-A272F,V026F-S078N-G159C-R186K-N243F,S024F-A048R-G118R-S166D-L217E,G023A-T038F-S078N-G100S-S212M-A215D,G100S-N116L-A158E-T213A,S078N-V104L-G118R-S128D,G102A-S103N-S105T-

A194E,T022L-S078N-S128D-T213A,K027R-G100S-G118R-S160D-S188D-N243F,S024F-G102A-R186K-T213A-L217E-N243F,T033S-S105T-S188D-S216F,G023A-G100S-A194E-S212M,A048R-S128D-N185E-P239G,G020K-S024F-T033S-P129E-A194E,G020K-K027R-P129E-S166D-P239G,T022L-G023A-K027R-S101D-V104L-S216F,T033S-G118R-P129E-A194E-P239G,T022L-S078N-N116L-P129E-S256N,K027R-S101D-S103N-S105T-A272F,A048R-S078N-N116L-N185E-L217E-P239G,G023A-S024F-K027R-N062E,S024F-S103N-V104L-G118R-S188D,V026F-V104L-S256N-A272F,S024F-N043W-V104L-V121F-P129E,N062E-S078N-N116L-T224A,G023A-S024F-V051W-A158E,K027R-T038F-G102A-N116L,N062E-S078N-S144R-S212M,L031F-N116L-S256N-A272F,T022L-T033S-V104L-N116L-S160D-R186K,S024F-G118R-P129E-R186K-T213A,N043W-S105T-T213A-A215D-S216F,L031F-S105T-R186K-S188D,V026F-A194E-T213A-S256N,和S103N-S160D-L250I-S256N,其中所述枯草杆菌蛋白酶变体的氨基酸位置通过与如SEQ ID NO:1所示解淀粉芽孢杆菌(B.amyloliquefaciens)枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[1058] 66.一种分离的枯草杆菌蛋白酶变体,所述枯草杆菌蛋白酶变体具有蛋白水解活性并包含具有选自以下的氨基酸置换的组合的氨基酸序列:T022A-S024R-S101D-S103A-V104I-G118R-G159D-S188D-A232V-N248D-E271F,T022A-S024R-S103A-V104I-P129E-G159D-S188D-A232V-N248D-E271F,T022A-S024R-S103A-V104I-G118R-G159D-S188D-L217D-A232V-N248D,T022A-S024R-S101D-S103A-V104I-G118R-P129E-G159D-S188D-A232V-Q245R-N248D,T022A-S024R-S101D-S103A-V104I-G159D-S188D-A232V-Q245R-N248D,T022A-N043R-S103A-V104I-G118R-P129E-G159D-S188D-A232V-Q245R-N248D,T022A-N043R-S103A-V104I-G118R-S128I-P129E-G159D-S188D-A232V-N248D,T022A-N043R-S101D-S103A-V104I-G118R-P129E-G159D-S188D-A232V-N248D-E271F,T022A-S024R-N043R-S101D-S103A-V104I-G159D-S188D-A232V-Q245R-N248D,T022A-S103A-V104I-G159D-S188D-A232V-N248D,T022A-S024R-S103A-V104I-G118R-P129E-G159D-S188D-A232V-N248D-E271F,T022A-S024R-S103A-V104I-G159D-S188D-L217D-A232V-Q245R-N248D-E271F,T022A-N043R-N062E-S103A-V104I-G159D-S188D-A232V-Q245R-N248D-E271F,T022A-N043R-S103A-V104I-P129E-G159D-S188D-A232V-Q245R-N248D,T022A-S024R-S103A-V104I-G159D-S188D-L217D-A232V-N248D-E271F,T022A-S103A-V104I-G118R-G159D-S188D-L217D-A232V-Q245R-N248D,T022A-S024R-S101D-S103A-V104I-G118R-S128I-G159D-S188D-A232V-Q245R-N248D,T022A-S024R-N043R-S103A-V104I-G159D-S188D-L217D-A232V-N248D-E271F,T022A-N043R-S103A-V104I-G118R-G159D-S188D-L217D-A232V-N248D-E271F,T022A-N043R-S103A-V104I-G118R-G159D-S188D-A232V-N248D-E271F,T022A-S103A-V104I-S128I-P129E-G159D-S188D-A232V-N248D-E271F,T022A-S103A-V104I-G159D-S188D-L217D-A232V-Q245R-N248D-E271F,T022A-N043R-S103A-V104I-S128I-G159D-S188D-A232V-Q245R-N248D,T022A-S101D-S103A-V104I-G118R-G159D-S188D-L217D-A232V-Q245R-N248D-E271F,T022A-S103A-V104I-G118R-P129E-G159D-S188D-A232V-Q245R-N248D-E271F,T022A-S024R-N043R-S103A-V104I-G118R-G159D-S188D-L217D-A232V-N248D,T022A-N062E-S103A-V104I-G118R-G159D-S188D-A232V-Q245R-N248D,T022A-N043R-S101D-S103A-V104I-G118R-

P129E-G159D-S188D-L217D-A232V,T022A-S024R-S103A-V104I-G159D-S188D-L217D-A232V-N248D,T022A-S024R-N043R-S103A-V104I-G118R-S128I-P129E-G159D-S188D-L217D-A232V-N248D-E271F,和T022A-S103A-V104I-G118R-G159D-S188D-L217D-A232V-Q245R-N248D-E271F,其中所述枯草杆菌蛋白酶变体的氨基酸位置通过与如SEQ ID NO:1所示解淀粉芽孢杆菌(B.amyloliquefaciens)枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[1059] 67.一种分离的枯草杆菌蛋白酶变体,所述枯草杆菌蛋白酶变体具有蛋白水解活性并包含具有选自以下的氨基酸置换的组合的氨基酸序列:G020K-S024F-N062E-S188D-P239G,S024F-N062E-N116L-P239G,G020K-G023A-N062E-S188D,G020K-G023A-S024F-N062E-G118R-S188D-T213A,G020K-N043W-N062E-N116L-S188D-T213A-P239G,G023A-N062E-N116L-G118R,G023A-S024F-N062E-N116L-G118R,S024F-N116L,S024F-N062E-S188D-T213A,G023A-N062E-N116L-G118R-S188D-P239G,G020K-S024F-N062E,G020K-N043W-N062E-N116L-P239G,S024F-N062E-N116L-T213A-P239G,G020K-S024F-N043W-N062E-N116L-T213A,G020K-G023A-S024F-N062E-N116L-S188D-T213A,S024F-N062E-S188D-P239G,G023A-N043W-N062E-N116L-G118R-T213A,N062E-S188D-P239G,G020K-S024F-N062E-P239G,S024F-N116L-G118R-S188D-P239G,G020K-G023A-N062E-N116L-G118R-T213A,G020K-G023A-S024F-N062E-S188D-T213A-P239G,S024F-N043W-G118R-S188D,G023A-S024F-N116L-G118R-S188D-T213A,G020K-G023A-N043W-N116L-S188D-T213A-P239G,G023A-S024F-N116L-S188D-P239G,G023A-N043W-N116L-G118R-S188D,G023A-S024F-G118R-S188D-P239G,G023A-S024F-N043W-N062E-N116L-G118R,G020K-N043W-S188D-T213A,S024F-N062E-G118R-P239G,G023A-N043W-S188D-T213A,G020K-S024F-N043W-N062E-N116L-G118R-S188D-P239G,G020K-N116L-S188D-P239G,G020K-N043W-N062E-G118R,G020K-N043W-N116L-S188D-T213A,G020K-S024F,G023A-N043W-N116L-P239G,G023A-S024F-N043W-N116L-G118R-S188D-P239G,G020K-G023A-N043W-T213A,和G023A-S024F-N062E-G118R-T213A-P239G,其中所述枯草杆菌蛋白酶变体的氨基酸位置通过与如SEQ ID NO:1所示解淀粉芽孢杆菌(B.amyloliquefaciens)枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[1060] 68.一种分离的枯草杆菌蛋白酶变体,所述枯草杆菌蛋白酶变体具有蛋白水解活性并包含具有选自以下的氨基酸置换的组合的氨基酸序列:G020K-G023A-N043W-G118R-S128I-P129E-G159D-S188D,S024F-G118R-S128I-P129E-G159D,G020K-S024F-N062E-N116L-G118R-S188D,G020K-N062E-N116L-S188D,N062E-N116L-G118R-T213A,G020K-G023A-N062E-N116L-S188D,N062E-N116L-G118R-S188D,G020K-N062E-N116L-T213A,G020K-G023A-N062E-N116L,G020K-N062E-S188D-T213A,G020K-N062E,G020K-S024F-N062E-N116L-S188D,G020K-N043W-N062E-N116L-S188D,G020K-S024F-N062E-S188D-T213A,N062E-N116L-S188D-T213A,G020K-N062E-N116L,G020K-G023A-N062E-N116L-S188D-T213A,G023A-S024F-N062E-N116L-T213A,T022A-N043R-S103A-V104I-S128I-P129E-G159D-S188D-A232V-Q245R-N248D,T022A-N043R-S103A-V104I-G118R-S128I-P129E-G159D-S188D-A232V-N248D-E271F,S024F-N062E-N116L-S188D,T022A-S024R-S103A-V104I-G118R-S128I-P129E-G159D-S188D-A232V-N248D,G023A-N062E-N116L-

S188D,N043W-N062E-N116L,G020K-G023A-N116L-S188D,N043W-N062E-N116L-S188D,S024F-N062E-N116L,N062E-N116L-S188D,和T022A-S024R-S103A-V104I-S128I-G159D-S188D-A232V-N248D,其中所述枯草杆菌蛋白酶变体的氨基酸位置通过与如SEQ ID NO:1所示解淀粉芽孢杆菌(B.amyloliquefaciens)枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[1061] 69.一种分离的枯草杆菌蛋白酶变体,所述枯草杆菌蛋白酶变体具有蛋白水解活性并包含具有选自以下的氨基酸置换的组合的氨基酸序列:S087R-S101G-S103A-V104I-Q109R-S212P-A232V-Q245R-E271V,S101G-S103A-V104I-Q109R-A232V-Q245R,S101G-S103A-V104I-Q109R-S212P-A232V-Q245R-E271V,S101G-S103A-V104I-Q109R-S212P-A232V-Q245R,N076D-S87R-S103A-V104I-S212P-E271V,N076D-S103A-V104I-Q109R,N076D-S103A-V104I-S212P-E271V,N076D-S103A-V104I-Q109R-Q245R,和N076D-S103A-V104I-S212P-Q245L-E271V,其中所述枯草杆菌蛋白酶变体的氨基酸位置通过与如SEQ ID NO:1所示解淀粉芽孢杆菌(B.amyloliquefaciens)枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[1062] 70.一种分离的枯草杆菌蛋白酶变体,所述枯草杆菌蛋白酶变体具有蛋白水解活性并包含具有选自以下的氨基酸置换的组合的氨基酸序列:S024R-P086W-G118R,S024R-S078R-P086W-N243F,S024R-T033S-P086S-S087N-Y209A,T033S-G118R,S024R-S078R-P086W-G118R-A270T,S024R-T033S-P086W-G118R,S078R-P086W-N243F,T033S-S078R-P086W-G118R-Y209A,T033S-S078R-Y209A,P086W-G118R-N243F,S024R-P086W,S078R-P086W-K235F,S024R-G118R,S024R-P086R,S101G-S103A-V104I-A232V,S024R-T033S-S078R-P086W-G118R,S024R-G118R-Y209A,Y209A-W241R,T033S-P086W-N243F,T033S-A172V-Y209A,G118R-Y209A-N243F,S024R-P086S-S141G,S024R-G118R-Y209A-N243F,S024R-T033S-P086S-S085N-K235F,S024R-T033S-A133V,S024R-T033S-S078R-P086W,S024R-P086W-Y209A,S024R-W241R,T033S-G118R-N243F,S024R-K235F,S024R-S078R-P086W,S024R-G118R-Y209A-K235F,S024R-Y209A-W241R,T033S-G118R-W241R,P086W-G118R-Y209A,T033S-G118R-G159D-Y209A,T033S-S078R-P086W,S024R-P086W-N243F,G118R-Y209A,S024R-P086W-G118R-V203I,S078R-Y209A-K235F,S024R-T033S-W241R,S078R-G118R,T033S-G118R-Y209A-N243F,L021M-S024R-T033S,S024R-T033S-P086W,T033S-K235F,S078R-P086W-Y209A,S024R-T033S-Y209A-K235F,T033S-P086W-G118R,S024R-T033S-S078R-Y209A,T033S-P086W-G118R-Y209A-N243F,P086W-Y209A-N243F,P005S-S078R-G118R-W241R,S024R-A174T,T033S-Y209A-N243F,P086W-G118R-A133V,S024R-T033S-G118R,S024R-P086W-Y209A-K235F,P086W-Y209A,I008T-S024R,P086W-G118R,T033S-W241R,P005S-S024R-T033S-N243F,S024R-Y209A-S242P,S024R-T033S-S078R-G118R,S024R-T033S-A194T,S024R-N243F,S024R-Y209A,S024R-T033S-G118R-Y209A,T033S-P086W,S024R-T033S,S024R-T033S-S078R-N243F,P086W-N243F,T033S-G118D-A138V-Y209A,T033S-Y209A-K235F,S024R-P086R-G118R,T033S-P201S,S024R-P239Q,T033S-G118R-Y209A-,S078R-P086W,K235F-N243F,S024R-Y209A-K235F,G118R-A172V,H017Y-S024R-T033S-P086W,T033S-L148F,S024R-G118R-K235F,T033S-S078R,T033S-N243F,S024C-T033S,G118R-A194T,T033S-Y209A,G118R-Y209A-K235F,S024R-

T033S-Y209A-N243F,S024R-T033S-K235F,S024R-T033S-G118R-K235F,S024R-S141G,S024R-T274I,S024R-T033S-Y209A,P086W-K235F,S024R-Y209A-N243F,V004E-T033S-S078R,P086W-Y209A-K235F,A015T-T033S,T033S-P086W-S156L-Y209A,S024R-G118R-N243F-R269H,Y209A-K235F,S024R-R247H,S024R-T033S-A228T,S078R-K235F,S024R-T033S-A174V-K235F,S024R-K235F-N243F,S024R-T033S-K235F-W241R,S024R-T033S-A151V,S024R-V104A,T033S-A048T,Q012H-V104A-G118R,G118R-K235F,T033S-T253A,T143A-Y209A,S024R-T033S-N243F,T033S-P239T,Y209A-N243F,S024R-T033S-P129H-N184D-T253M,S024R-A085V-P086W-G118R-K235F,S024R-A272P,和S024R-R269C,其中所述枯草杆菌蛋白酶变体的氨基酸位置通过与如SEQ ID NO:1所示解淀粉芽孢杆菌(B.amyloliquefaciens)枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[1063] 71.一种分离的枯草杆菌蛋白酶变体,所述枯草杆菌蛋白酶变体具有蛋白水解活性并包含具有选自以下的氨基酸置换的组合的氨基酸序列:G020R-S087D-S101G-S103A-V104I-A232V-Q245R,G020R-S101G-S103A-V104I-V150L-A232V-Q245R,N018R-G020R-S024R-N076D-S087D-H249R,N018R-G020R-S024R-N076D-V150L-H249R,N018R-S024R-N043R-N076D-S087D-H249R,N018R-S024R-N043R-N076D-V150L-H249R,N018R-S024R-N076D-S078R-S087D-H249R,N018R-S024R-N076D-S078R-V150L-H249R,N018R-S024R-N076D-S087D-H249R-N269R,N018R-S024R-N076D-S087D-S242R-H249R,N018R-S024R-N076D-S087D-V150L-H249R,N018R-S024R-N076D-V150L-H249R,N018R-S087D-S101G-S103A-V104I-A232V-Q245R,N018R-S101G-S103A-V104I-V150L-A232V-Q245R,N018R-T022R-S024R-N076D-S087D-H249R,N018R-T022R-S024R-N076D-V150L-H249R,N043R-S087D-S101G-S103A-V104I-A232V-Q245R-N269R,N043R-S101G-S103A-V104I-V150L-A232V-Q245R,S024R-S087D-S101G-S103A-V104I-A232V-Q245R,S024R-S101G-S103A-V104I-V150L-A232V-Q245R,S078R-S087D-S101G-S103A-V104I-A232V-Q245R,S078R-S101G-S103A-V104I-V150L-A232V-Q245R,S087D-S101G-S103A-V104I-A232V-Q245R-N269R,S101G-S103A-V104I-V150L-A232V-Q245R-H249R,S101G-S103A-V104I-V150L-A232V-Q245R-N269R,T022R-S087D-S101G-S103A-V104I-A232V-Q245R,N018R-S024R-N043D-N076D-V150L-H249R,N043R-S087D-S101G-S103A-V104I-A232V-Q245R,T022R-S101G-S103A-V104I-V150L-A232V-Q245R,N018R-S024R-N043D-N076D-S087D-H249R,N018R-S024R-N076D-S087D-H249R,N018R-S024R-N076D-V150L-S242R-H249R,N043R-S101G-S103A-V104I-V150L-A232V-Q245R-N269R,N076D-S101G-S103A-V104I-V150L-A232V-Q245R,S087D-S101G-S103A-V104I-A232V-S242R-Q245R,S101G-S103A-V104I-V150L-A232V-Q245R,N076D-S087D-S101G-S103A-V104I-A232V-Q245R,S087D-S101G-S103A-V104I-A232V-Q245R,和S101G-S103A-V104I-V150L-A232V-S242R-Q245R,其中所述枯草杆菌蛋白酶变体的氨基酸位置通过与如SEQ ID NO:1所示解淀粉芽孢杆菌(B.amyloliquefaciens)枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[1064] 72.一种分离的枯草杆菌蛋白酶变体,所述枯草杆菌蛋白酶变体具有蛋白水解活性并包含具有选自以下的氨基酸置换的组合的氨基酸序列:S024R-S101G-S103A-V104I-P129Q-A158E-S188D-L217E-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-S130A-A158E-N183D-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-

P129Q-A158E-N183D-S188D-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-S130A-A158E-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-P129Q-A158E-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-S130A-A158E-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-P129Q-S130A-A158E-N183D-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-S128L-P129Q-A158E-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-P129Q-S130A-A158E-S188D-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-P129Q-A158E-S188D-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-P129Q-S130A-A158E-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-S128L-P129Q-S130A-A158E-S188D-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-S128L-P129Q-A158E-S188D-A232V-Q245R-N248D-H249R,和S024R-K027R-S101G-S103A-V104I-S128L-P129Q-S130A-A158E-S188D-A232V-Q245R-N248D-H249R,其中所述枯草杆菌蛋白酶变体的氨基酸位置通过与如SEQ ID NO:1所示解淀粉芽孢杆菌(B.amyloliquefaciens)枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[1065] 73.一种分离的枯草杆菌蛋白酶变体,所述枯草杆菌蛋白酶变体具有蛋白水解活性并包含具有选自以下的氨基酸置换的组合的氨基酸序列:S101G-S103A-V104I-A232V-M222Q-Q245R,S101G-S103A-V104I-A158E-S188D-M222S-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-A158E-S188D-M222Q-A232V-Q245R-N248D-H249R,N076D-S101G-S103A-V104I-A232V-M222Q-Q245R,S101G-S103A-V104I-A232V-M222S-Q245R,N076D-S101G-S103A-V104I-A232V-M222S-Q245R,和N076D-S101G-S103A-V104I-A158E-S188D-M222S-A232V-Q245R-N248D-H249R,其中所述枯草杆菌蛋白酶变体的氨基酸位置通过与如SEQ ID NO:1所示解淀粉芽孢杆菌(B.amyloliquefaciens)枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[1066] 74.一种分离的枯草杆菌蛋白酶变体,所述枯草杆菌蛋白酶变体具有蛋白水解活性并包含具有选自以下的氨基酸置换的组合的氨基酸序列:S024R-S101G-S103A-V104I-S128L-P129Q-A158E-S188D-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-S130A-A158E-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-A158E-S188D-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-S128L-P129Q-A158E-S188D-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-P129Q-S130A-A158E-S188D-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-S130A-A158E-N183D-S188D-L217E-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-S128L-P129Q-S130A-A158E-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-P129Q-A158E-S188D-L217E-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-S128L-S130A-A158E-S188D-L217E-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-S128L-P129Q-A158E-N183D-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-S128L-P129Q-S130A-A158E-N183D-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-S128L-P129Q-A158E-S188D-A232V-Q245R-N248D-H249R-E271G,S101G-S103A-V104I-P129Q-A158E-N183D-S188D-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-S130A-A158E-S188D-L217E-A232V-Q245R-N248D-H249R,S024R-S101G-S103A-V104I-S128L-A158E-

N183D-S188D-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-P129Q-A158E-S188D-L217E-A232V-Q245R-N248D-H249R,和S024R-S101G-S103A-V104I-S128L-S130A-A158E-S188D-A232V-Q245R-N248D-H249R,其中所述枯草杆菌蛋白酶变体的氨基酸位置通过与如SEQ ID NO:1所示解淀粉芽孢杆菌(B.amyloliquefaciens)枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[1067] 75.一种分离的枯草杆菌蛋白酶变体,所述枯草杆菌蛋白酶变体具有蛋白水解活性并包含具有选自以下的氨基酸置换的组合的氨基酸序列:S101G-S103A-V104I,T22A-S101A-Y209E,S103G-L111V-G159E,T22A-S103G-G159E,T22A-L111V-G159E,T22A-S128N-E271F-Y209E,T22A-S103G-L111V,N62E-L111V-S128N,T22A-L111V-S128N,T22A-N62E-L111V,S101A-S103G-V104L-S188D,S101G-S103A-V104I-G159D,S101A-S103G-V104L-S128N,T22A-S101A-G159E,S101A-S103G-V104L,S101A-S103G-V104L-G159E,T22A-S101A-S103G-V104L,S101A-S103G-V104L-Y209E,T22A-Y209E-E271F,T22A-S101A-E271F,和S101A-Y209E-E271F,其中所述枯草杆菌蛋白酶变体的氨基酸位置通过与如SEQ ID NO:1所示解淀粉芽孢杆菌(B.amyloliquefaciens)枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[1068] 76.一种分离的枯草杆菌蛋白酶变体,所述枯草杆菌蛋白酶变体具有蛋白水解活性并包含具有选自以下的氨基酸置换的组合的氨基酸序列:S103A-V104I-G159D-A232V-Q236H-Q245R-N248D-N252K,S101G-V104I-G159D-A232V-Q236H-Q245R-N248D-N252K,S101G-S103A-G159D-A232V-Q236H-Q245R-N248D-N252K,S101G-S103A-V104L-A232V-Q236H-Q245R-N248D-N252K,S101G-S103A-V104L-G159D-Q236H-Q245R-N248D-N252K,S101G-S103A-V104L-G159D-A232V-Q245R-N248D-N252K,S101G-S103A-V104L-G159D-A232V-Q236H-N248D-N252K,S101G-S103A-V104L-G159D-A232V-Q236H-Q245R-N252K,和S101G-S103A-V104L-G159D-A232V-Q236H-Q245R-N248D,其中所述枯草杆菌蛋白酶变体的氨基酸位置通过与如SEQ ID NO:1所示解淀粉芽孢杆菌(B.amyloliquefaciens)枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[1069] 77.一种分离的枯草杆菌蛋白酶变体,所述枯草杆菌蛋白酶变体具有蛋白水解活性并包含具有选自以下的氨基酸置换的组合的氨基酸序列:S101G-S103A-V104I-G159D-A232V-Q245R-N248D,S101G-S103A-V104I-G159D-A232V-Q245R-N248D-E271F,S101G-S103A-V104I-G159D-A232V-Q245R-N248D-N238R,S101G-S103A-V104I-G159D-A232V-Q245R-N248D-N248R,S101G-S103A-V104I-G159D-A232V-Q245R-N248D-T253R,S101G-S103A-V104I-G159D-A232V-Q245R-N248D-S24R,S101G-S103A-V104I-G159D-A232V-Q245R-N248D-N76D,S101G-S103A-V104I-G159E-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-G159E-A232V-Q245R-N248D-E271F,S101G-S103A-V104I-A158E-A232V-Q245R-N248D-H249R,S101G-S103A-V104I-A158E-A232V-Q245R-N248D-E271F,T22A-S101G-S103A-V104I-G159D-A232V-Q245R-N248D-H249R,T22A-S101G-S103A-V104I-G159D-A232V-Q245R-N248D-E271F,N62E-S101G-S103A-V104I-G159D-A232V-Q245R-N248D-H249R,和N62E-S101G-S103A-V104I-G159D-A232V-Q245R-N248D-E271F,其中所述枯草杆菌蛋白酶变体的氨基酸位置通过与如SEQ ID NO:1所示解淀粉芽孢杆菌(B.amyloliquefaciens)枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[1070] 78.一种分离的枯草杆菌蛋白酶变体,所述枯草杆菌蛋白酶变体具有蛋白水解活性并包含具有选自以下的氨基酸置换的组合的氨基酸序列:A1R,A230E,E271L,G115R,G20R,H249R,K235F,K27V/F/L,L75E,L82R,N18R,N269R,N43D,N43R,N76D,R45T,S212F,S242R,S24R,S78R,S9A,T22R,V121E,V244R,V28E,V30E,V4R,W241R,G20R-N43R-H249R,G20R-T22R-N43R,G20R-N43R-S242R,G20R-N43R-E271L,G20R-N43R-V244R,G20R-S24R-N43R-S242R,S9A-T22R-S78R-S212F-W241R,S9A-G20R-N43R-S212F,S9A-N43R-S212F,G20R-N43R-S212F,G20R-T22R-N43R-S212F,S24R-S78R-S212F,S9A-N43R-S78R,S9A-N43R-S78R-S242R,S9A-G20R-N43R-S78R,G20R-S24R-N43R-S78R-S242R,T22R-S24R-S78R-S212F,S9A-G20R-N43R-S78R-S242R,G20R-N43R-S78R-H249R,G20R-N43R-S78R,S9A-S78R-S212F,S9A-T22R-N43R-S78R,S9A-G20R-S24R-N43R,S9A-T22R-S78R-S212F,V4R-S9A-T22R-S78R-S212F,G20R-S24R-N43R,A1R-S9A-N43R,G20R-S24R-N43R-G115R,S9A-S24R-N43R,G20R-T22R-S24R-N43R,A1R-S24R-N43R,S9A-G20R-S24R-N43R-S242R,S9A-G20R-T22R-S78R-S212F,S9A-S24R-N43R-V244R,S9A-S24R-N43R-S242R,V4R-S9A-T22R-S24R-S212F,和T22R-S24R-N43R,其中所述枯草杆菌蛋白酶变体的氨基酸位置通过与如SEQ ID NO:1所示解淀粉芽孢杆菌(B.amyloliquefaciens)枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[1071] 79.一种分离的枯草杆菌蛋白酶变体,所述枯草杆菌蛋白酶变体具有蛋白水解活性并包含具有选自以下的氨基酸置换的组合的氨基酸序列:S101G-S103A-V104I-A232V-Q245R-N248D,S101G-S103A-V104I-G159D-A232V-Q245R,S101G-S103A-V104I-G159R-A232V-Q245R-N248D,S101G-S103A-V104I-G159D-A232V-Q245R-N248R,S101G-S103A-V104I-A232V-Q245R,S101G-S103A-V104I-A232V-Q245R-N248R,S101G-S103A-V104I-G159R-A232V-Q245R-N248R,S101G,S103A,V104I,A232V,Q236H,和Q245R,其中所述枯草杆菌蛋白酶变体的氨基酸位置通过与如SEQ ID NO:1所示解淀粉芽孢杆菌(B.amyloliquefaciens)枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[1072] 80.一种分离的枯草杆菌蛋白酶变体,所述枯草杆菌蛋白酶变体具有蛋白水解活性并包含具有选自以下的氨基酸置换的组合的氨基酸序列:A16S,T22A,S24R,N62E,N76D,E89P,S101A/G,S103G/A,V104L/I,L111V,S128N,P129E,A232V,L148I,A158E,G159D/E,R186H,S188D,Y209E,Q236H,Q245R,N248D/R,H249R,N252K/R,T253R,和E271F,其中所述枯草杆菌蛋白酶变体的氨基酸位置通过与如SEQ ID NO:1所示解淀粉芽孢杆菌(B.amyloliquefaciens)枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[1073] 81.一种分离的枯草杆菌蛋白酶变体,所述枯草杆菌蛋白酶变体具有蛋白水解活性并包含具有选自以下的氨基酸置换的组合的氨基酸序列:A1R,Q2S,Q2M,Q2A,Q2R,Q2W,S3R,V4R,V4S,V4C,I8A,S9A,S9F,S9W,R10S,R10A,R10H,R10M,Q12F,Q12R,P14K,P14F,P14Q,A15R,A15F,A16S,H17R,H17M,H17F,N18R,N18K,G20F,G20K,G20R,T22A,T22R,T22Y,T22V,T22Q,T22L,T22W,G23A,G23S,G23F,S24R,S24F,S24W,S24Q,S24H,S24L,G25V,G25F,G25R,V26F,K27L,K27F,K27R,K27V,V28A,V28N,V28E,A29T,V30E,L31F,T33S,T33G,T33D,G34P,I35M,S36T,S36F,S36R,T38L,T38F,T38R,P40N,P40L,P40T,P40W,P40H,P40R,L42I,N43A,N43F,N43I,N43S,N43R,N43M,N43W,N43D,R45T,G46R,A48R,F50C,V51W,V51F,V51H,P52F,P52E,P52N,P55Y,T57R,Q59A,Q59F,Q59R,D60P,D60Q,D60A,N62E,N62Q,G63V,G63M,G63T,

G63I,G63A,G63S,G63H,G63Q,G63D,G63E,G63P,H64F,H64T,V68A,V68C,A69N,A69T,A69P,A69W,T71G,T71G,I72C,A74C,L75A,L75F,L75E,L75R,N76D,S78R,S78N,S78I,S78R,I79W,I79Q,V81R,L82F,L82T,L82V,L82R,L82M,A85M,P86W,P86L,P86I,E89P,E89T,E89G,E89H,E89W,E89L,E89V,E89W,E89F,E89I,Y91N,Y91F,A92F,K94N,S99F,S99T,S99P,S99G,S99M,G100S,G100N,G100Q,G100I,S101A,S101N,S101G,S101D,S101T,S101D,S101E,S101P,S101F,G102A,G102T,G102N,G102H,G102E,S103G,S103N,S103D,S103A,V104L,V104I,V104E,V104D,S105T,S105E,S105Q,S106G,S106T,S106E,S106D,S106A,S106V,S106F,I107M,I107F,A108I,A108G,Q109M,L111V,L111I,E112V,E112L,E112Q,A114G,G115K,G115R,N116K,N116A,N116L,N117F,G118R,G118I,M119C,H120A,H120F,H120R,V121F,V121F,V121E,N123G,N123E,L124S,S128D,S128F,S128L,S128N,S128H,S128M,S128I,S128Q,P129E,S132A,S132E,A138G,S144R,V147L,L148I,A158E,G159D,G159E,G159C,S160D,S166D,S166E,Y167W,M175V,V177C,D181A,Q182R,N183I,N183D,N183M,N183R,N183F,N183R,N185E,N185V,N185I,R186H,R186K,S188E,S188D,S188R,Y192H,Y192W,A194E,A194V,A194F,D197F,D197F,I198L,I198F,V203E,V203C,T208S,Y209S,Y209N,Y209F,Y209T,Y209E,Y209H,Y209G,Y209L,P210R,P210V,P210L,G211Q,G211R,S212I,S212M,S212F,T213A,Y214F,A215N,A215D,A215E,A215H,A215F,S216F,S216A,L217E,L217N,L217D,N218D,N218P,N218E,T224A,T224G,V227I,A230E,A231I,A231C,A232V,L233C,V234F,K235F,Q236F,Q236N,Q236H,N238R,N238K,N238L,P239K,P239G,P239R,P239R,P239H,P239T,P239N,P239S,P239F,S240R,W241R,S242L,S242R,N243F,N243R,V244R,Q245R,I246S,N248D,N248V,N248I,N248R,H249R,H249T,L250I,K251R,K251S,N252I,N252F,N252R,N252K,N252H,T253I,T253R,T253F,A254C,S256N,G258R,T260V,T260I,L262D,L262H,Y263F,S265F,L267V,L267N,L267M,N269I,N269R,A270C,E271I,E271H,E271V,E271H,E271M,E271L,E271P,E271A,E271F,E271T,A272F,A272F,A272R,A273F,A273I,和T274G,其中所述枯草杆菌蛋白酶变体的氨基酸位置通过与如SEQ ID NO:1所示解淀粉芽孢杆菌(B.amyloliquefaciens)枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号。

[1074] 82.一种迟缓芽孢杆菌(Bacillus lentus)枯草杆菌蛋白酶GG36蛋白酶的蛋白酶变体,其中所述迟缓芽孢杆菌(Bacillus lentus)枯草杆菌蛋白酶GG36蛋白酶包含SEQ ID NO:2所示氨基酸序列,并且其中所述蛋白酶变体包含与SEQ ID NO:2的氨基酸序列相差不超过2、3、4、5、6、7、8、9、10、11、12、13、14、15、16、17、18、19、20、21、22、23、24或25个突变的氨基酸序列,所述突变处于选自氨基酸1、2、3、4、8、9、10、12、14、15、16、17、18、20、22、23、24、25、26、27、28、29、30、31、33、34、35、36、38、40、42、43、45、46、48、50、51、52、55、57、59、60、62、63、64、68、69、71、72、74、75、76、78、79、81、82、85、86、89、91、92、94、99、100、101、102、103、104、105、106、107、108、109、111、112、114、115、116、117、118、119、120、121、123、124、128、129、132、138、44、147、148、158、159、160、166、167、175、177、181、182、183、185、186、188、192、194、197、198、203、208、209、210、211、212、213、214、215、216、217、218、224、227、230、231、233、234、235、236、236、238、238、239、240、241、242、243、244、246、248、249、250、251、252、253、254、256、258、260、262、263、265、267、269、270、271、272、273和274的氨基酸位置,其中所述枯草杆菌蛋白酶变体的氨基酸位置通过与SEQ ID NO:1所示解淀粉芽

孢杆菌(B.amyloliquefaciens)枯草杆菌蛋白酶BPN'的氨基酸序列的对应关系进行编号，其中所述蛋白酶变体的氨基酸位置根据SEQ ID NO:1所示解淀粉芽孢杆菌(Bacillus amyloliquefaciens)枯草杆菌蛋白酶BPN'的氨基酸序列中对应的氨基酸位置的编号方式来进行编号，这是通过所述变体蛋白酶氨基酸序列与所述解淀粉芽孢杆菌(Bacillus amyloliquefaciens)枯草杆菌蛋白酶BPN'氨基酸序列的比对来确定的。

[1075] 83.一种迟缓芽孢杆菌(Bacillus lentus)枯草杆菌蛋白酶GG36蛋白酶的蛋白酶变体，其中所述迟缓芽孢杆菌(Bacillus lentus)枯草杆菌蛋白酶GG36蛋白酶包含SEQ ID NO:2所示氨基酸序列，并且其中所述蛋白酶变体包含与SEQ ID NO:2的氨基酸序列相差不超过2、3、4、5、6、7、8、9、10、11、12、13、14、15、16、17、18、19、20、21、22、23、24或25个突变的氨基酸序列，所述突变选自A1R,Q2S,Q2M,Q2A,Q2R,Q2W,S3R,V4R,V4S,V4C,I8A,S9A,S9F,S9W,R10S,R10A,R10H,R10M,Q12F,Q12R,P14K,P14F,P14Q,A15R,A15F,A16S,H17R,H17M,H17F,N18R,N18K,G20F,G20K,G20R,T22A,T22R,T22Y,T22V,T22Q,T22L,T22W,G23A,G23S,G23F,S24R,S24F,S24W,S24Q,S24H,S24L,G25V,G25F,G25R,V26F,K27L,K27F,K27R,K27V,V28A,V28N,V28E,A29T,V30E,L31F,T33S,T33G,T33D,G34P,I35M,S36T,S36F,S36R,T38L,T38F,T38R,P40N,P40L,P40T,P40W,P40H,P40R,L42I,N43A,N43F,N43I,N43S,N43R,N43M,N43W,N43D,R45T,G46R,A48R,F50C,V51W,V51F,V51H,P52F,P52E,P52N,P55Y,T57R,Q59A,Q59F,Q59R,D60P,D60Q,D60A,N62E,N62Q,G63V,G63M,G63T,G63I,G63A,G63S,G63H,G63Q,G63D,G63E,G63P,H64F,H64T,V68A,V68C,A69N,A69T,A69P,A69W,T71G,T71G,I72C,A74C,L75A,L75F,L75E,L75R,N76D,S78R,S78N,S78I,S78R,I79W,I79Q,V81R,L82F,L82T,L82V,L82R,L82M,A85M,P86W,P86L,P86I,E89P,E89T,E89G,E89H,E89W,E89L,E89V,E89W,E89F,E89I,Y91N,Y91F,A92F,K94N,S99F,S99T,S99P,S99G,S99M,G100S,G100N,G100Q,G100I,S101A,S101N,S101G,S101D,S101T,S101D,S101E,S101P,S101F,G102A,G102T,G102N,G102H,G102E,S103G,S103N,S103D,S103A,V104L,V104I,V104E,V104D,S105T,S105E,S105Q,S106G,S106T,S106E,S106D,S106A,S106V,S106F,I107M,I107F,A108I,A108G,Q109M,L111V,L111I,E112V,E112L,E112Q,A114G,G115K,G115R,N116K,N116A,N116L,N117F,G118R,G118I,M119C,H120A,H120F,H120R,V121F,V121F,V121E,N123G,N123E,L124S,S128D,S128F,S128L,S128N,S128H,S128M,S128I,S128Q,P129E,S132A,S132E,A138G,S144R,V147L,L148I,A158E,G159D,G159E,G159C,S160D,S166D,S166E,Y167W,M175V,V177C,D181A,Q182R,N183I,N183D,N183M,N183R,N183F,N183R,N185E,N185V,N185I,R186H,R186K,S188E,S188D,S188R,Y192H,Y192W,A194E,A194V,A194F,D197F,D197F,I198L,I198F,V203E,V203C,T208S,Y209S,Y209N,Y209F,Y209T,Y209E,Y209H,Y209G,Y209L,P210R,P210V,P210L,G211Q,G211R,S212I,S212M,S212F,T213A,Y214F,A215N,A215D,A215E,A215H,A215F,S216F,S216A,L217E,L217N,L217D,N218D,N218P,N218E,T224A,T224G,V227I,A230E,A231I,A231C,A232V,L233C,V234F,K235F,Q236F,Q236N,Q236H,N238R,N238K,N238L,P239K,P239G,P239R,P239R,P239H,P239T,P239N,P239S,P239F,S240R,W241R,S242L,S242R,N243F,N243R,V244R,Q245R,I246S,N248D,N248V,N248I,N248R,H249R,H249T,L250I,K251R,K251S,N252I,N252F,N252R,N252K,N252H,T253I,T253R,T253F,A254C,S256N,G258R,T260V,T260I,L262D,L262H,Y263F,S265F,L267V,L267N,L267M,N269I,N269R,A270C,E271I,E271H,E271V,E271H,E271M,

E271L,E271P,E271A,E271F,E271T,A272F,A272F,A272R,A273F,A273I,和T274G,其中所述蛋白酶变体的氨基酸位置根据SEQ ID NO:1所示解淀粉芽孢杆菌(Bacillus amyloliquefaciens)枯草杆菌蛋白酶BPN'的氨基酸序列中对应的氨基酸位置的编号方式来进行编号,这是通过所述蛋白酶变体氨基酸序列与所述解淀粉芽孢杆菌(Bacillusamyloliquefaciens)枯草杆菌蛋白酶BPN'氨基酸序列的比对来确定的。

[1076] 84.一种迟缓芽孢杆菌(Bacillus lentus)枯草杆菌蛋白酶GG36蛋白酶的蛋白酶变体,其中所述迟缓芽孢杆菌(Bacillus lentus)枯草杆菌蛋白酶GG36蛋白酶包含SEQ ID NO:2所示氨基酸序列,其中所述蛋白酶变体包含与SEQ ID NO:2的氨基酸序列相差不超过2、3、4、5、6、7、8、9、10、11、12、13、14、15、16、17、18、19、20、21、22、23、24或25个突变的氨基酸序列,所述突变选自A1R,Q2S,V4R,V4S,S9A,R10S,P14K,A16S,H17R,N18R,G20R,T22A,T22R,S24R,S24W,G25R,G25V,V26F,L42I,N43R,N43A,G46R,P52F,P52E,P52N,T57R,Q59A,N62E,N62Q,V68A,V68C,T71G,I72C,A74C.L75A,L75F,L75R,N76D,S78R,L82R,P86W,E89P,E89T,E89G,E89H,E89I,E89V,E89W,Y91N,K94N,G100S,S101A,S101N,S101G,S101D,S103G,S103N,V104L,V104I,S106V,S106G,A108I,L111V,E112V,G115K,G115R,N117F,G118I,V121F,S128D,S128F,S128L,S128N,P129E,S144R,L148I,A158E,G159E,S160D,S166D,N185E,N185I,R186H,S188E,S188D,D197F,V203E,Y209S,Y209N,Y209F,Y209T,Y209E,Y209H,Y209G,P210R,S212I,S212F,Y214F,A215N,A215D,A215E,L217E,L217N,T224A,A230E,A231I,Q236F,N238R,N238K,P239K,P239G,P239R,P239S,W241R,S242R,S242L,N243R,V244R,N248I,N248V,H249R,L250I,N252R,T253R,L262D,Y263F,S265F,L267V,L267N、N269I,N269R,E271F,E271I,E271H,E271P,E271T,E271V,E271L和A272F,并且所述蛋白酶变体任选地包含至少一个选自S103A,G159D,Q236H,Q245R,N248D和N252K的突变,其中所述蛋白酶变体的氨基酸位置根据SEQ ID NO:1所示解淀粉芽孢杆菌(Bacillus amyloliquefaciens)枯草杆菌蛋白酶BPN'的氨基酸序列中对应的氨基酸位置的编号方式来进行编号,这是通过所述蛋白酶变体氨基酸序列与所述解淀粉芽孢杆菌(Bacillus amyloliquefaciens)枯草杆菌蛋白酶BPN'氨基酸序列的比对来确定的。

[1077] 85.一种迟缓芽孢杆菌(Bacillus lentus)枯草杆菌蛋白酶GG36蛋白酶的蛋白酶变体,其中所述迟缓芽孢杆菌(Bacillus lentus)枯草杆菌蛋白酶GG36蛋白酶包含SEQ ID NO:2所示氨基酸序列,其中所述蛋白酶变体包含与SEQ ID NO:2的氨基酸序列相差不超过2、3、4、5、6、7、8、9、10、11、12、13、14、15、16、17、18、19、20、21、22、23、24或25个突变的氨基酸序列,所述突变选自G20K,G20R,G23A,S24F,S24R,N43R,N43W,R45T,N62E,N76D,S101A,N116A,N116L,G118R,S128I,P129E,S188D,T213A,A215F,L217E,P239G,和N269R,其中所述蛋白酶变体的氨基酸位置根据SEQ ID NO:1所示解淀粉芽孢杆菌(Bacillus amyloliquefaciens)枯草杆菌蛋白酶BPN'的氨基酸序列中对应的氨基酸位置的编号方式来进行编号,这是通过所述蛋白酶变体氨基酸序列与所述解淀粉芽孢杆菌(Bacillus amyloliquefaciens)枯草杆菌蛋白酶BPN'氨基酸序列的比对来确定的。

[1078] 86.一种迟缓芽孢杆菌(Bacillus lentus)枯草杆菌蛋白酶GG36蛋白酶的蛋白酶变体,其中所述迟缓芽孢杆菌(Bacillus lentus)枯草杆菌蛋白酶GG36蛋白酶包含SEQ ID NO:2所示氨基酸序列,并且其中所述蛋白酶变体包含与SEQ ID NO:2的氨基酸序列相差不超过2、3、4、5、6、7、8、9、10、11、12、13、14、15、16、17、18、19、20、21、22、23、24或25个突变的

氨基酸序列,所述突变选自A16S,T22A,S24R,N62E,N76D,E89P,S101A/G,S103G/A,V104L/I,L111V,S128N,P129E,A232V,L148I,A158E,G159D/E,R186H,S188D,Y209E,Q236H,Q245R,N248D/R,H249R,N252K/R,T253R,和E271F,其中所述蛋白酶变体的氨基酸位置根据SEQ ID NO:1所示解淀粉芽孢杆菌(Bacillus amyloliquefaciens)枯草杆菌蛋白酶BPN'的氨基酸序列中对应的氨基酸位置的编号方式来进行编号,这是通过所述蛋白酶变体氨基酸序列与所述解淀粉芽孢杆菌(Bacillus amyloliquefaciens)枯草杆菌蛋白酶BPN'氨基酸序列的比对来确定的。

[1079] 87.一种迟缓芽孢杆菌(Bacillus lentus)枯草杆菌蛋白酶GG36蛋白酶的蛋白酶变体,其中所述迟缓芽孢杆菌(Bacillus lentus)枯草杆菌蛋白酶GG36蛋白酶包含SEQ ID NO:2所示氨基酸序列,并且其中所述蛋白酶变体包含与SEQ ID NO:2的氨基酸序列相差不超过2、3、4、5、6、7、8、9、10、11、12、13、14、15、16、17、18、19、20、21、22、23、24或25个突变的氨基酸序列,所述突变选自A1R,A230E,E271L,G115R,G20R,H249R,K235F,K27V/F/L,L75E,L82R,N18R,N269R,N43D,N43R,N76D,R45T,S212F,S242R,S24R,S78R,S9A,T22R,V121E,V244R,V28E,V30E,V4R,和W241R,其中所述蛋白酶变体的氨基酸位置根据SEQ ID NO:1所示解淀粉芽孢杆菌(Bacillus amyloliquefaciens)枯草杆菌蛋白酶BPN'的氨基酸序列中对应的氨基酸位置的编号方式来进行编号,这是通过所述蛋白酶变体氨基酸序列与所述解淀粉芽孢杆菌(Bacillus amyloliquefaciens)枯草杆菌蛋白酶BPN'氨基酸序列的比对来确定的。

[1080] 88.一种迟缓芽孢杆菌(Bacillus lentus)枯草杆菌蛋白酶GG36蛋白酶的蛋白酶变体,其中所述迟缓芽孢杆菌(Bacillus lentus)枯草杆菌蛋白酶GG36蛋白酶包含SEQ ID NO:2所示氨基酸序列,并且其中所述蛋白酶变体包含与SEQ ID NO:2的氨基酸序列相差不超过2、3、4、5、6、7、8、9、10、11、12、13、14、15、16、17、18、19、20、21、22、23、24或25个突变的氨基酸序列,所述突变选自A1R,A230E,E271L,G115R,G20R,H249R,K235F,K27V/F/L,L75E,L82R,N18R,N269R,N43D,N43R,N76D,R45T,S212F,S242R,S24R,S78R,S9A,T22R,V121E,V244R,V28E,V30E,V4R,和W241R,并且所述蛋白酶变体任选地包含至少一个选自S103A,G159D,Q236H,Q245R,N248D和N252K的突变,其中所述蛋白酶变体的氨基酸位置根据SEQ ID NO:1所示解淀粉芽孢杆菌(Bacillus amyloliquefaciens)枯草杆菌蛋白酶BPN'的氨基酸序列中对应的氨基酸位置的编号方式来进行编号,这是通过所述蛋白酶变体氨基酸序列与所述解淀粉芽孢杆菌(Bacillus amyloliquefaciens)枯草杆菌蛋白酶BPN'氨基酸序列的比对来确定的。

[1081] 89.根据实施方式1-26中任一项所述的蛋白酶变体,其中所述蛋白酶变体包含不同于SEQ ID NO:2的氨基酸序列的氨基酸序列,并且其中所述蛋白酶变体的总净电荷相对于迟缓芽孢杆菌(Bacillus lentus)枯草杆菌蛋白酶GG36蛋白酶的总净电荷为0、+1、+2、+3、+4、5、-1、-2、-3、-4或-5,其中亲本蛋白酶为GG36,并且其中所述蛋白酶变体的氨基酸位置根据SEQ ID NO:1所示解淀粉芽孢杆菌(Bacillus amyloliquefaciens)枯草杆菌蛋白酶BPN'的氨基酸序列中的对应氨基酸位置的编号方式来进行编号,这是通过所述蛋白酶变体氨基酸序列与所述解淀粉芽孢杆菌(Bacillus amyloliquefaciens)枯草杆菌蛋白酶BPN'氨基酸序列的比对来确定的。

[1082] 90.根据实施方式1-89中任一项所述的蛋白酶变体,其中所述蛋白酶变体具有以

下特性中的一者或多者:a)测试方法2性能指数为至少1.1、至少1.2、至少1.3、至少1.4、至少1.5、至少1.6、至少1.7、至少1.8、至少1.9、至少2、1.1至约10、1.1至约8、或甚至1.1至约5;b)测试方法3性能指数为至少1.1、至少1.2、至少1.3、至少1.4、至少1.5、至少1.6、至少1.7、至少1.8、至少1.9、至少2、1.1至约10、1.1至约8、或甚至1.1至约5;c)测试方法4性能指数为至少1.0、至少1.1、至少1.2、至少1.3、至少1.4、至少1.5、至少1.6、至少1.7、至少1.8、至少1.9、至少2、1.0至约10、1.0至约8、或甚至1.0至约5;和/或d)测试方法6性能指数为至少1.0、至少1.1、至少1.2、至少1.3、至少1.4、至少1.5、至少1.6、至少1.7、至少1.8、至少1.9、至少2、1.0至约10、1.0至约8、或甚至1.0至约5。

[1083] 91.一种分离的核酸,其包含编码实施方式1-90中任一项提供的枯草杆菌蛋白酶变体的多核苷酸序列。

[1084] 92.一种表达载体,其包含根据实施方式91所述的核酸。

[1085] 93.一种宿主细胞,其包含根据实施方式92所述的表达载体。

[1086] 94.一种用于产生芽孢杆菌属(Bacillus)枯草杆菌蛋白酶的至少一种枯草杆菌蛋白酶变体的方法,所述方法包括:

[1087] a)用包含至少一种编码至少一种根据实施方式1-90中任一项所述的枯草杆菌蛋白酶变体的核酸的表达载体来转化宿主细胞,以产生转化的宿主细胞;并且

[1088] b)在适于产生至少一种枯草杆菌蛋白酶变体的条件下培养所述转化的宿主细胞,以产生至少一种枯草杆菌蛋白酶变体。

[1089] 95.根据实施方式94所述的方法,还包括收获所产生的枯草杆菌蛋白酶变体。

[1090] 96.根据实施方式92所述的表达载体,其中所述至少一种核酸与启动子有效连接。

[1091] 97.根据实施方式94-95中任一项所述的方法,其中所述宿主细胞为芽孢杆菌属(Bacillus)的种。

[1092] 98.根据实施方式97所述的方法,其中所述芽孢杆菌属(Bacillus)的种为枯草芽孢杆菌(B.subtilis)。

[1093] 99.一种包含至少一种根据实施方式1-90中任一项所述的枯草杆菌蛋白酶变体的组合物,其中所述组合物不是织物和家庭护理产品。

[1094] 100.根据实施方式99所述的组合物,其中所述组合物为清洁组合物。

[1095] 101.根据实施方式99-100中任一项所述的组合物,其中所述清洁组合物为颗粒、粉末、固体、条棒、液体、片剂、凝胶或糊剂组合物。

[1096] 102.根据实施方式99-101中任一项所述的组合物,还包含至少一种漂白剂。

[1097] 103.根据实施方式99-102中任一项所述的组合物,其中所述清洁组合物不含磷酸盐。

[1098] 104.根据实施方式99-103中任一项所述的组合物,其中所述清洁组合物含有磷酸盐。

[1099] 105.根据实施方式99-104中任一项所述的组合物,还包含至少一种另外的酶。

[1100] 106.根据实施方式105所述的组合物,其中所述至少一种另外的酶选自半纤维素酶、纤维素酶、过氧化物酶、蛋白酶、金属蛋白酶、木聚糖酶、脂肪酶、磷脂酶、酯酶、过水解酶、角质酶、果胶酶、果胶酸裂解酶、甘露聚糖酶、角蛋白酶、还原酶、氧化酶、酚氧化酶、脂加氧酶、木质素酶、支链淀粉酶、鞣酸酶、戊聚糖酶、malanase、β-葡聚糖酶、阿拉伯糖苷酶、透

明质酸酶、软骨素酶、漆酶和淀粉酶或它们的任何组合。

[1101] 107.根据实施方式99-106中任一项所述的组合物，其中所述枯草杆菌蛋白酶变体不是冷水蛋白酶变体。

[1102] 108.一种清洁方法，包括用包含至少一种根据实施方式1-90中任一项所述的枯草杆菌蛋白酶变体的清洁组合物来接触表面或物品。

[1103] 109.一种清洁方法，包括用实施方式100-107中任一项示出的清洁组合物来接触表面或物品。

[1104] 110.根据实施方式108-109中任一项所述的方法，还包括在用所述清洁组合物分别接触所述表面或物品之后漂洗所述表面或物品。

[1105] 111.根据实施方式108-110中任一项所述的方法，还包括在用所述清洁组合物接触所述表面或物品之后漂洗所述表面或物品的步骤。

[1106] 112.根据实施方式111所述的方法，还包括在所述表面或物品的所述漂洗之后干燥所述表面或物品的步骤。

[1107] 113.一种清洁表面或物品的方法，包括：提供实施方式100-107中任一项示出的清洁组合物和需要清洁的表面或物品；以及在适于清洁所述表面或物品的所述表面的条件下使所述清洁组合物接触所述需要清洁的表面或物品，以得到洁净的表面或物品。

[1108] 114.根据实施方式113所述的方法，还包括漂洗所述洁净的表面或物品以得到漂洗过的表面或物品的步骤。

[1109] 115.根据实施方式113-114中任一项所述的方法，还包括干燥所述漂洗过的表面或物品的步骤。

[1110] 116.根据实施方式108-115中的任一项所述的方法，其中所述枯草杆菌蛋白酶变体不是冷水蛋白酶变体。

序列表

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<120> 包含枯草杆菌蛋白酶变体的组合物和方法

<130> 31528WO-2

<140> PCT/US2011/035389
<141> 2011-05-05

<150> US 61/332,151
<151> 2010-05-06

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<151> 2010-10-12

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<151> 2010-10-12

<160> 82

[0001] <170> PatentIn version 3.5

<210> 1
<211> 275
<212> PRT
<213> 解淀粉芽孢杆菌

<400> 1

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Ala Gln Ser Val Pro Tyr Gly Val Ser Gln Ile Lys Ala Pro Ala Leu
1               5                  10                  15
His Ser Gln Gly Tyr Thr Gly Ser Asn Val Lys Val Ala Val Ile Asp
            20                  25                  30
Ser Gly Ile Asp Ser Ser His Pro Asp Leu Lys Val Ala Gly Gly Ala
        35                  40                  45
Ser Met Val Pro Ser Glu Thr Asn Pro Phe Gln Asp Asn Asn Ser His
    50                  55                  60
Gly Thr His Val Ala Gly Thr Val Ala Ala Leu Asn Asn Ser Ile Gly
65                  70                  75                  80
Val Leu Gly Val Ala Pro Ser Ala Ser Leu Tyr Ala Val Lys Val Leu
                85                  90                  95
Gly Ala Asp Gly Ser Gly Gln Tyr Ser Trp Ile Ile Asn Gly Ile Glu
            100                 105                 110
Trp Ala Ile Ala Asn Asn Met Asp Val Ile Asn Met Ser Leu Gly Gly
        115                 120                 125
Pro Ser Gly Ser Ala Ala Leu Lys Ala Ala Val Asp Lys Ala Val Ala
    130                 135                 140
Ser Gly Val Val Val Val Ala Ala Ala Gly Asn Glu Gly Thr Ser Gly
145                 150                 155                 160
Ser Ser Ser Thr Val Gly Tyr Pro Gly Lys Tyr Pro Ser Val Ile Ala
                165                 170                 175
Val Gly Ala Val Asp Ser Ser Asn Gln Arg Ala Ser Phe Ser Ser Val
            180                 185                 190
Gly Pro Glu Leu Asp Val Met Ala Pro Gly Val Ser Ile Gln Ser Thr
        195                 200                 205
Leu Pro Gly Asn Lys Tyr Gly Ala Tyr Asn Gly Thr Ser Met Ala Ser
    210                 215                 220
Pro His Val Ala Gly Ala Ala Ala Leu Ile Leu Ser Lys His Pro Asn
225                 230                 235                 240
Trp Thr Asn Thr Gln Val Arg Ser Ser Leu Glu Asn Thr Thr Thr Lys
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245 250 255
Leu Gly Asp Ser Phe Tyr Tyr Gly Lys Gly Leu Ile Asn Val Gln Ala
260 265 270
Ala Ala Gln
275

<210> 2
<211> 269
<212> PRT
<213> 迟缓芽孢杆菌

<400> 2
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20 25 30
Thr Gly Ile Ser Thr His Pro Asp Leu Asn Ile Arg Gly Gly Ala Ser
35 40 45
Phe Val Pro Gly Glu Pro Ser Thr Gln Asp Gly Asn Gly His Gly Thr
50 55 60
His Val Ala Gly Thr Ile Ala Ala Leu Asn Asn Ser Ile Gly Val Leu
65 70 75 80
Gly Val Ala Pro Ser Ala Glu Leu Tyr Ala Val Lys Val Leu Gly Ala
85 90 95
Ser Gly Ser Gly Ser Val Ser Ser Ile Ala Gln Gly Leu Glu Trp Ala
100 105 110
Gly Asn Asn Gly Met His Val Ala Asn Leu Ser Leu Gly Ser Pro Ser
115 120 125
Pro Ser Ala Thr Leu Glu Gln Ala Val Asn Ser Ala Thr Ser Arg Gly
130 135 140
Val Leu Val Val Ala Ala Ser Gly Asn Ser Gly Ala Gly Ser Ile Ser
145 150 155 160
Tyr Pro Ala Arg Tyr Ala Asn Ala Met Ala Val Gly Ala Thr Asp Gln
165 170 175
Asn Asn Asn Arg Ala Ser Phe Ser Gln Tyr Gly Ala Gly Leu Asp Ile
180 185 190
Val Ala Pro Gly Val Asn Val Gln Ser Thr Tyr Pro Gly Ser Thr Tyr
195 200 205
[0002] Ala Ser Leu Asn Gly Thr Ser Met Ala Thr Pro His Val Ala Gly Ala
210 215 220
Ala Ala Leu Val Lys Gln Lys Asn Pro Ser Trp Ser Asn Val Gln Ile
225 230 235 240
Arg Asn His Leu Lys Asn Thr Ala Thr Ser Leu Gly Ser Thr Asn Leu
245 250 255
Tyr Gly Ser Gly Leu Val Asn Ala Glu Ala Ala Thr Arg
260 265

<210> 3
<211> 1143
<212> DNA
<213> 迟缓芽孢杆菌

<400> 3
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agttcatcga tcgcatcggc tgctgaagaa gcaaaagaaa aatatttaat tggctttaat 120
gagcaggaag ctgtcagtga gtttgtagaa caagtagagg caaatgacga ggtcgccatt 180
ctctctgagg aagaggaagt cgaaattgaa ttgcttcatg aatttgaaac gattcctgtt 240
ttatccgttg agttaagccc agaagatgtg gacgcgcttg agctcgatcc agcgatttct 300
tatattgaag aggatgcaga agtaacgaca atggcgcaat cagtgccatg gggaattagc 360
cgtgtgcaag ccccagctgc ccataaccgt ggattgacag gttctggtgt aaaagttgct 420
gtcctcgata caggtatttc cactcatcca gacttaaata ttcgtggtgg cgctagcttt 480
gtaccagggg aaccatccac tcaagatggg aatgggcatg gcacgcatgt ggccgggacg 540
attgctgctt taaacaattc gattggcgtt cttggcgtag cgccgagcgc ggaactatac 600
gctgttaaag tattaggggc gagcggttca ggttcggtca gctcgattgc ccaaggattg 660
gaatgggcag ggaacaatgg catgcacgtt gctaatttga gtttaggaag cccttcgcca 720
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gcatctggaa attcaggtgc aggctcaatc agctatccgg cccgttatgc gaacgcaatg 840
gcagtcggag ctactgacca aaacaacaac cgcgccagct tttcacagta tggcgcaggg 900
cttgacattg tcgcaccagg tgtaaacgtg cagagcacat acccaggttc aacgtatgcc 960
agcttaaacg gtacatcgat ggctactcct catgttgcag gtgcagcagc ccttgttaaa 1020
caaaagaacc catcttggtc caatgtacaa atccgcaatc atctaaagaa tacggcaacg 1080
agcttaggaa gcacgaactt gtatggaagc ggacttgtca atgcagaagc tgcaactcgt 1140
taa 1143

<210> 4
<211> 380

<212> PRT
<213> 迟缓芽孢杆菌

<400> 4

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1               5                  10                  15
Ser Val Ala Phe Ser Ser Ser Ile Ala Ser Ala Ala Glu Glu Ala Lys
            20                  25                  30
Glu Lys Tyr Leu Ile Gly Phe Asn Glu Gln Glu Ala Val Ser Glu Phe
        35                  40                  45
Val Glu Gln Val Glu Ala Asn Asp Glu Val Ala Ile Leu Ser Glu Glu
    50                  55                  60
Glu Glu Val Glu Ile Glu Leu Leu His Glu Phe Glu Thr Ile Pro Val
65                  70                  75                  80
Leu Ser Val Glu Leu Ser Pro Glu Asp Val Asp Ala Leu Glu Leu Asp
                85                  90                  95
Pro Ala Ile Ser Tyr Ile Glu Glu Asp Ala Glu Val Thr Thr Met Ala
            100                 105                 110
Gln Ser Val Pro Trp Gly Ile Ser Arg Val Gln Ala Pro Ala Ala His
        115                 120                 125
Asn Arg Gly Leu Thr Gly Ser Gly Val Lys Val Ala Val Leu Asp Thr
    130                 135                 140
Gly Ile Ser Thr His Pro Asp Leu Asn Ile Arg Gly Gly Ala Ser Phe
145                 150                 155                 160
Val Pro Gly Glu Pro Ser Thr Gln Asp Gly Asn Gly His Gly Thr His
                165                 170                 175
Val Ala Gly Thr Ile Ala Ala Leu Asn Asn Ser Ile Gly Val Leu Gly
            180                 185                 190
Val Ala Pro Ser Ala Glu Leu Tyr Ala Val Lys Val Leu Gly Ala Ser
        195                 200                 205
Gly Ser Gly Ser Val Ser Ser Ile Ala Gln Gly Leu Glu Trp Ala Gly
    210                 215                 220
Asn Asn Gly Met His Val Ala Asn Leu Ser Leu Gly Ser Pro Ser Pro
225                 230                 235                 240
Ser Ala Thr Leu Glu Gln Ala Val Asn Ser Ala Thr Ser Arg Gly Val
                245                 250                 255
Leu Val Val Ala Ala Ser Gly Asn Ser Gly Ala Gly Ser Ile Ser Tyr
            260                 265                 270
Pro Ala Arg Tyr Ala Asn Ala Met Ala Val Gly Ala Thr Asp Gln Asn
        275                 280                 285
Asn Asn Arg Ala Ser Phe Ser Gln Tyr Gly Ala Gly Leu Asp Ile Val
    290                 295                 300
Ala Pro Gly Val Asn Val Gln Ser Thr Tyr Pro Gly Ser Thr Tyr Ala
305                 310                 315                 320
Ser Leu Asn Gly Thr Ser Met Ala Thr Pro His Val Ala Gly Ala Ala
                325                 330                 335
Ala Leu Val Lys Gln Lys Asn Pro Ser Trp Ser Asn Val Gln Ile Arg
            340                 345                 350
Asn His Leu Lys Asn Thr Ala Thr Ser Leu Gly Ser Thr Asn Leu Tyr
        355                 360                 365
Gly Ser Gly Leu Val Asn Ala Glu Ala Ala Thr Arg
    370                 375                 380
```

[0003]

<210> 5
<211> 1143
<212> DNA
<213> 人工序列

<220>
<223> 合成的GG36-9变体

<400> 5

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gtgagaagca aaaaattgtg gatcgtcgcg tcgaccgcac tactcatttc tgttgctttt      60
agttcatcga tcgcatcggc tgctgaagaa gcaaaagaaa aatatttaat tggctttaat     120
gagcaggaag ctgtcagtga gtttgtagaa caagtagagg caaatgacga ggtcgccatt     180
ctctctgagg aagaggaagt cgaaattgaa ttgcttcatg aatttgaaac gattcctgtt     240
ttatccgttg agttaagccc agaagatgtg gacgcgcttg aactcgatcc agcgatttct     300
tatattgaag aggatgcaga agtaacgaca atggcgcaat cagtgccatg gggaattagc     360
cgtgtgcaag ccccggctgc ccataaccgt ggattgacag gttctggtgt aaaagttgct     420
gtcctcgata caggtatttc cactcatcca gacttaaata ttcgtggtgg cgctagcttt     480
gtaccagggg aaccatccac tcaagatggg aatgggcatg gcacgcatgt ggccgggacg     540
attgctgctc taaacaattc gattggcgta cttggcgtag cgccgagcgc ggaactatac     600
gctgttaaag tattaggggc gagcggtggg ggcgccatca gctcgattgc ccaaggattg     660
gaatgggcag ggaacaatgg catgcacgtt gctaatttga gtttaggaag cccttcgcca     720
agtgccacac ttgagcaagc tgttaatagc gcgacttcta ggggcgttct tgttgtagcg     780
gcatctggaa attcgggtgc agactcaatc agctatccgg cccgttatgc gaacgcaatg     840
```

```
gcagtcggag ctactgacca aaacaacaac cgcgccagct tttcacagta tggcgcaggg      900
cttgacatcg tcgcaccagg tgtaaacgtg cagagcacat acccaggttc aacgtatgcc      960
agcttaaacg gtacatcgat ggctactcct catgttgcag gtgcagcagt ccttgttaaa     1020
cataagaacc catcttggtc caatgtacga atccgcgatc atctaaagaa aacggcaacg     1080
agcttaggaa gcacgaactt gtatggaagc ggacttgtca atgccgaagc tgcaactcgt     1140
taa                                                                  1143
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<210> 6
<211> 380
<212> PRT
<213> 人工序列

<220>
<223> 合成的GG36-9变体

<400> 6

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Val Arg Ser Lys Lys Leu Trp Ile Val Ala Ser Thr Ala Leu Leu Ile
1               5                  10                  15
Ser Val Ala Phe Ser Ser Ser Ile Ala Ser Ala Ala Glu Glu Ala Lys
            20                  25                  30
Glu Lys Tyr Leu Ile Gly Phe Asn Glu Gln Glu Ala Val Ser Glu Phe
        35                  40                  45
Val Glu Gln Val Glu Ala Asn Asp Glu Val Ala Ile Leu Ser Glu Glu
    50                  55                  60
Glu Glu Val Glu Ile Glu Leu Leu His Glu Phe Glu Thr Ile Pro Val
65                  70                  75                  80
Leu Ser Val Glu Leu Ser Pro Glu Asp Val Asp Ala Leu Glu Leu Asp
                85                  90                  95
Pro Ala Ile Ser Tyr Ile Glu Glu Asp Ala Glu Val Thr Thr Met Ala
            100                 105                 110
Gln Ser Val Pro Trp Gly Ile Ser Arg Val Gln Ala Pro Ala Ala His
        115                 120                 125
Asn Arg Gly Leu Thr Gly Ser Gly Val Lys Val Ala Val Leu Asp Thr
    130                 135                 140
Gly Ile Ser Thr His Pro Asp Leu Asn Ile Arg Gly Gly Ala Ser Phe
145                 150                 155                 160
Val Pro Gly Glu Pro Ser Thr Gln Asp Gly Asn Gly His Gly Thr His
                165                 170                 175
Val Ala Gly Thr Ile Ala Ala Leu Asn Asn Ser Ile Gly Val Leu Gly
            180                 185                 190
Val Ala Pro Ser Ala Glu Leu Tyr Ala Val Lys Val Leu Gly Ala Ser
        195                 200                 205
Gly Gly Gly Ala Ile Ser Ser Ile Ala Gln Gly Leu Glu Trp Ala Gly
    210                 215                 220
Asn Asn Gly Met His Val Ala Asn Leu Ser Leu Gly Ser Pro Ser Pro
225                 230                 235                 240
Ser Ala Thr Leu Glu Gln Ala Val Asn Ser Ala Thr Ser Arg Gly Val
                245                 250                 255
Leu Val Val Ala Ala Ser Gly Asn Ser Gly Ala Asp Ser Ile Ser Tyr
            260                 265                 270
Pro Ala Arg Tyr Ala Asn Ala Met Ala Val Gly Ala Thr Asp Gln Asn
        275                 280                 285
Asn Asn Arg Ala Ser Phe Ser Gln Tyr Gly Ala Gly Leu Asp Ile Val
    290                 295                 300
Ala Pro Gly Val Asn Val Gln Ser Thr Tyr Pro Gly Ser Thr Tyr Ala
305                 310                 315                 320
Ser Leu Asn Gly Thr Ser Met Ala Thr Pro His Val Ala Gly Ala Ala
                325                 330                 335
Val Leu Val Lys His Lys Asn Pro Ser Trp Ser Asn Val Arg Ile Arg
            340                 345                 350
Asp His Leu Lys Lys Thr Ala Thr Ser Leu Gly Ser Thr Asn Leu Tyr
        355                 360                 365
Gly Ser Gly Leu Val Asn Ala Glu Ala Ala Thr Arg
    370                 375                 380
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<210> 7
<211> 1140
<212> DNA
<213> 人工序列

<220>
<223> 合成的GG36-7变体

<400> 7

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gtgagaagca aaaaattgtg gatcgtcgcg tcgaccgcac tactcatttc tgttgctttt       60
agttcatcga tcgcatcggc tgctgaagaa gcaaaagaaa aatatttaat tggctttaat      120
```

[0004]

```
gagcaggaag ctgtcagtga gtttgtagaa caagtagagg caaatgacga ggtcgccatt      180
ctctctgagg aagaggaagt cgaaattgaa ttgcttcatg aatttgaaac gattcctgtt      240
ttatccgttg agttaagccc agaagatgtg gacgcgcttg aactcgatcc agcgatttct      300
tatattgaag aggatgcaga agtaacgaca atggcgcaat cagtgccatg gggaattagc      360
cgtgtgcaag ccccggctgc ccataaccgt ggattgacag gttctggtgt aaaagttgct      420
gtcctcgata caggtatttc cactcatcca gacttaaata ttcgtggtgg cgctagcttt      480
gtaccagggg aaccatccac tcaagatggg aatgggcatg gcacgcatgt ggccgggacg      540
attgctgctc taaacaattc gattggcgta cttggcgtag cgccgagcgc ggaactatac      600
gctgttaaag tattaggggc gagcggtggg ggcgccatca gctcgattgc ccaaggattg      660
gaatgggcag ggaacaatgg catgcacgtt gctaatttga gtttaggaag cccttcgcca      720
agtgccacac ttgagcaagc tgttaatagc gcgacttcta ggggcgttct tgttgtagcg      780
gcatctggaa attcgggtgc agactcaatc agctatccgg cccgttatgc gaacgcaatg      840
gcagtcggag ctactgacca aaacaacaac cgcgccagct tttcacagta tggcgcaggg      900
cttgacatcg tcgcaccagg tgtaaacgtg cagagcacat acccaggttc aacgtatgcc      960
agcttaaacg gtacatcgat ggctactcct catgttgcag gtgcagcagt ccttgttaaa     1020
caaaagaacc catcttggtc caatgtacga atccgcgatc atctaaagaa tacggcaacg     1080
agcttaggaa gcacgaactt gtatggaagc ggacttgtca atgccgaagc tgcaactcgt     1140
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<210> 8
<211> 380
<212> PRT
<213> 人工序列

<220>
<223> 合成的GG36-7变体

<400> 8

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Val Arg Ser Lys Lys Leu Trp Ile Val Ala Ser Thr Ala Leu Leu Ile
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            20                  25                  30
Glu Lys Tyr Leu Ile Gly Phe Asn Glu Gln Glu Ala Val Ser Glu Phe
        35                  40                  45
Val Glu Gln Val Glu Ala Asn Asp Glu Val Ala Ile Leu Ser Glu Glu
    50                  55                  60
Glu Glu Val Glu Ile Glu Leu Leu His Glu Phe Glu Thr Ile Pro Val
65                  70                  75                  80
Leu Ser Val Glu Leu Ser Pro Glu Asp Val Asp Ala Leu Glu Leu Asp
                85                  90                  95
Pro Ala Ile Ser Tyr Ile Glu Glu Asp Ala Glu Val Thr Thr Met Ala
            100                 105                 110
Gln Ser Val Pro Trp Gly Ile Ser Arg Val Gln Ala Pro Ala Ala His
        115                 120                 125
Asn Arg Gly Leu Thr Gly Ser Gly Val Lys Val Ala Val Leu Asp Thr
    130                 135                 140
Gly Ile Ser Thr His Pro Asp Leu Asn Ile Arg Gly Gly Ala Ser Phe
145                 150                 155                 160
Val Pro Gly Glu Pro Ser Thr Gln Asp Gly Asn Gly His Gly Thr His
                165                 170                 175
Val Ala Gly Thr Ile Ala Ala Leu Asn Asn Ser Ile Gly Val Leu Gly
            180                 185                 190
Val Ala Pro Ser Ala Glu Leu Tyr Ala Val Lys Val Leu Gly Ala Ser
        195                 200                 205
Gly Gly Gly Ala Ile Ser Ser Ile Ala Gln Gly Leu Glu Trp Ala Gly
    210                 215                 220
Asn Asn Gly Met His Val Ala Asn Leu Ser Leu Gly Ser Pro Ser Pro
225                 230                 235                 240
Ser Ala Thr Leu Glu Gln Ala Val Asn Ser Ala Thr Ser Arg Gly Val
                245                 250                 255
Leu Val Val Ala Ala Ser Gly Asn Ser Gly Ala Asp Ser Ile Ser Tyr
            260                 265                 270
Pro Ala Arg Tyr Ala Asn Ala Met Ala Val Gly Ala Thr Asp Gln Asn
        275                 280                 285
Asn Asn Arg Ala Ser Phe Ser Gln Tyr Gly Ala Gly Leu Asp Ile Val
    290                 295                 300
Ala Pro Gly Val Asn Val Gln Ser Thr Tyr Pro Gly Ser Thr Tyr Ala
305                 310                 315                 320
Ser Leu Asn Gly Thr Ser Met Ala Thr Pro His Val Ala Gly Ala Ala
                325                 330                 335
Val Leu Val Lys Gln Lys Asn Pro Ser Trp Ser Asn Val Arg Ile Arg
            340                 345                 350
Asp His Leu Lys Asn Thr Ala Thr Ser Leu Gly Ser Thr Asn Leu Tyr
        355                 360                 365
Gly Ser Gly Leu Val Asn Ala Glu Ala Ala Thr Arg
    370                 375                 380
```

[0005]

<210> 9
<211> 27
<212> DNA
<213> 人工序列

<220>
<223> 合成的引物

<400> 9
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<210> 10
<211> 25
<212> DNA
<213> 人工序列

<220>
<223> 合成的引物

<400> 10
gtctccaagc tttaacgagt tgcag 25

<210> 11
<211> 30
<212> DNA
<213> 人工序列

<220>
<223> 合成的引物

<400> 11
gcaattcaga tcttccttca ggttatgacc 30

<210> 12
<211> 30
<212> DNA
<213> 人工序列

[0006]

<220>
<223> 合成的引物

<400> 12
gcatcgaaga tctgattgct taactgcttc 30

<210> 13
<211> 54
<212> DNA
<213> 人工序列

<220>
<223> 合成的引物

<400> 13
aaagtattag gggcgagcgg tgcaggtgga cttagctcga ttgcccaagg attg 54

<210> 14
<211> 46
<212> DNA
<213> 人工序列

<220>
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<400> 14
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<210> 15
<211> 45
<212> DNA
<213> 人工序列

<220>
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<400> 15
ctgcccataa ccgtggattg gcaggttctg gtgtaaaagt tgctg 45

<210> 16
<211> 45
<212> DNA
<213> 人工序列

<220>
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<400> 16
aggtgtaaac gtgcagagca cagaaccagg ttcaacgtat gccag 45

<210> 17
<211> 44
<212> DNA
<213> 人工序列

<220>
<223> 合成的引物

<400> 17
gaagcggact tgtcaatgca ttcgctgcaa ctcgttaaag cttg 44

<210> 18
<211> 48
<212> DNA
<213> 人工序列

<220>
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<400> 18
aaagtattag gggcgagcgg tgcaggttcg gtcagctcga ttgcccaa 48

<210> 19
<211> 47
<212> DNA
<213> 人工序列

[0007]

<220>
<223> 合成的引物

<400> 19
tattaggggc gagcggttca ggtggagtca gctcgattgc ccaagga 47

<210> 20
<211> 46
<212> DNA
<213> 人工序列

<220>
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<400> 20
gtcagctcga ttgcccaagg agtagaatgg gcagggaaca atggca 46

<210> 21
<211> 48
<212> DNA
<213> 人工序列

<220>
<223> 合成的引物

<400> 21
cgttgctaat ttgagtttag gaaacccttc gccaagtgcc acacttga 48

<210> 22
<211> 42
<212> DNA
<213> 人工序列

<220>
<223> 合成的引物

<400> 22

gaaccatcca ctcaagatgg ggaagggcat ggcacgcatg tg 42

<210> 23
<211> 47
<212> DNA
<213> 人工序列

<220>
<223> 合成的引物

<400> 23
accaaaacaa caaccgcgcc gacttttcac agtatggcgc agggctt 47

<210> 24
<211> 23
<212> DNA
<213> 人工序列

<220>
<223> 合成的引物

<400> 24
catatgagtt atgcagtttg tag 23

<210> 25
<211> 23
<212> DNA
<213> 人工序列

<220>
<223> 合成的引物

<400> 25
tgtttttctt ggaattgtgc tgt 23

[0008]

<210> 26
<211> 23
<212> DNA
<213> 人工序列

<220>
<223> 合成的引物

<400> 26
cagtttgtag aatgcaaaaa gtg 23

<210> 27
<211> 23
<212> DNA
<213> 人工序列

<220>
<223> 合成的引物

<400> 27
gacaaggtaa aggataaaac agc 23

<210> 28
<211> 40
<212> DNA
<213> 人工序列

<220>
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<400> 28
cataaccgtg gattggcagg ttctggtgta aaagttgctg 40

<210> 29
<211> 40
<212> DNA
<213> 人工序列

<220>
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<400> 29
actttacac cagaacctgc caatccacgg ttatgggcag 40

<210> 30
<211> 35
<212> DNA
<213> 人工序列

<220>
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<400> 30
cactcaagat ggggaagggc atggcacgca tgtgg 35

<210> 31
<211> 39
<212> DNA
<213> 人工序列

<220>
<223> 合成的引物

<400> 31
atgcgtgcca tgcccttccc catcttgagt ggatggttc 39

<210> 32
<211> 39
<212> DNA
<213> 人工序列

<220>
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<210> 33
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<400> 33
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<210> 34
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<212> DNA
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<210> 35
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<400> 35
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<210> 36
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<400> 36
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<400> 37
cttgggcaat cgagctgatc gcacctccac cgctcgcccc taatacttta 50

<210> 38
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<400> 38
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<210> 40
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<400> 41
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<210> 42
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<400> 42
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<400> 43
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<210> 44
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<400> 44
gaaattcagg tgcagactca atcagctatc cggcccgtt 39

<210> 45
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<400> 45
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<210> 46
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<400> 46
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<210> 47
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<400> 47
ggatagctga ttgattctgc acctgaattt ccagatgc 38

<210> 48
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<400> 48
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<210> 49
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<212> DNA
<213> 人工序列

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<400> 49
catacgttga acctggttct gtgctctgca cgtttacacc 40

<210> 50
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<400> 50
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<210> 51
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<400> 51
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<210> 52
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<223> 合成的底物

<400> 52
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<210> 53
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<400> 54
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<400> 56
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<400> 57
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<400> 59
gcatctggaa attcgggtgc aggctcaatc agctatccgg cccgt 45

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<400> 63
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<400> 65
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<400> 66
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<210> 67
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<400> 67
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<210> 69
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<400> 69
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<400> 70
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<211> 38
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<223> 合成的引物

<400> 73
ggaaattcgg gtgcagaatc aatcagctat ccggcccgtt a 41

<210> 74
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<213> 人工序列

[0015] <220>
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<400> 75
cggcatctgg aaattcgggt gaaggctcaa tcagctatcc ggcccgttat g 51

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<400> 76
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<400> 77
tccactcaag atggggaagg gcatggcacg catgtggc 38

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<400> 78
cttgttaaac aaaagagacc atcttggtcc aatgtacgaa tc 42

<210> 79
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<400> 79
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[0016]

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<400> 80
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<210> 81
<211> 42
<212> DNA
<213> 人工序列

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<400> 81
gtggattgac aggtagaggt gtaaaagttg ctgtcctcga ta 42

<210> 82
<211> 43
<212> DNA
<213> 人工序列

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<400> 82
acgattgctg ctctagataa ttcgattggc gtacttggcg tag 43

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GG36    1     AQSVPWGISR VQAPAAHNRG LTGSGVKVAV LDTGIS-THP DLNIRGGASF VPGEPST-QD

BPN'   61 NNSHGTHVAG TVAALNNSIG VLGVAPSASL YAVKVLGADG SGQYSWIING IEWAIANNMD
GG36   59 GNGHGTHVAG TIAALNNSIG VLGVAPSAEL YAVKVLGASG SGSVSSIAQG LEWAGNNGMH

BPN'  121 VINMSLGGPS GSAALKAAVD KAVASGVVVV AAAGNEGTSG SSSTVGYPGK YPSVIAVGAV
GG36  119 VANLSLGSPS PSATLEQAVN SATSRGVLVV AASGNSGAGS ----ISYPAR YANAMAVGAT

BPN'  181 DSSNQRASFS SVGPELDVMA PGVSIQSTLP GNKYGAYNGT SMASPHVAGA AALILSKHPN
GG36  175 DQNNNRASFS QYGAGLDIVA PGVNVQSTYP GSTYASLNGT SMATPHVAGA AALVKQKNPS

BPN'  241 WTNTQVRSSL ENTTTKLGDS FYYGKGLINV QAAAQ
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图1

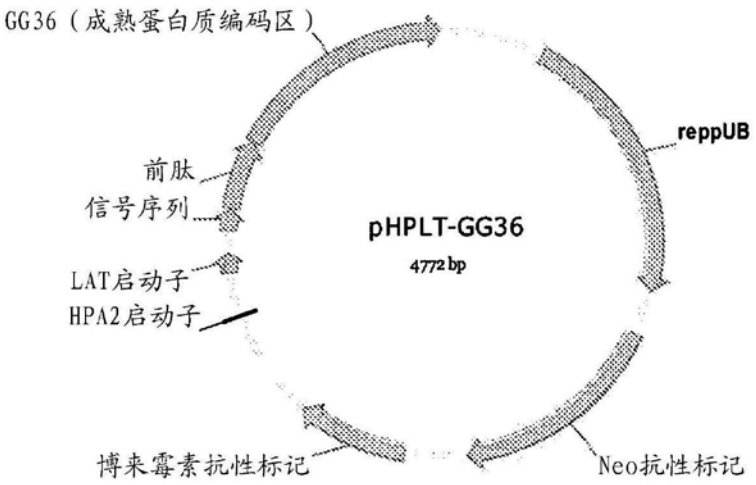

图2

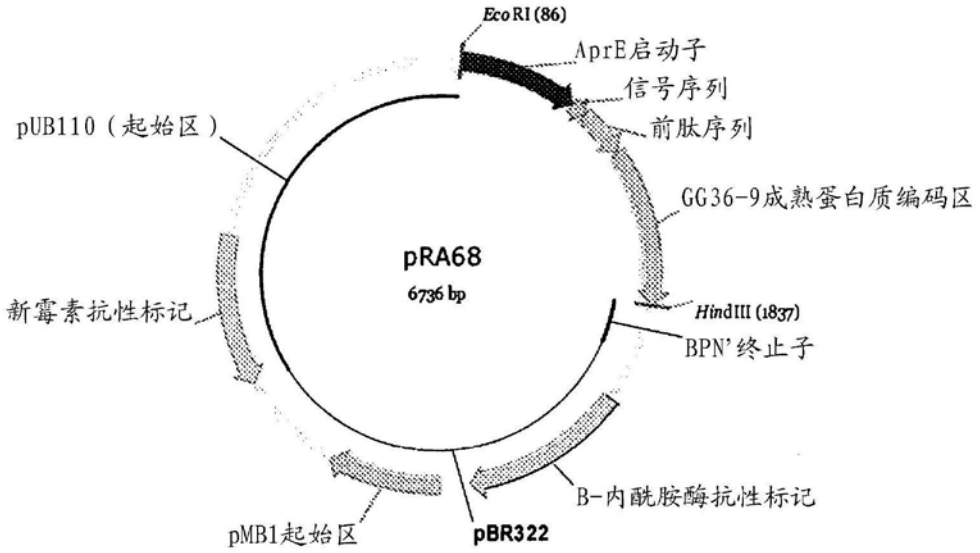
EcoRI (86)
AprE启动子
信号序列
前肽序列
GG36-9成熟蛋白质编码区
HindIII (1837)
BPN'终止子
B-内酰胺酶抗性标记
pBR322
pMB1起始区
新霉素抗性标记
pUB110（起始区）
pRA68
6736 bp

图3

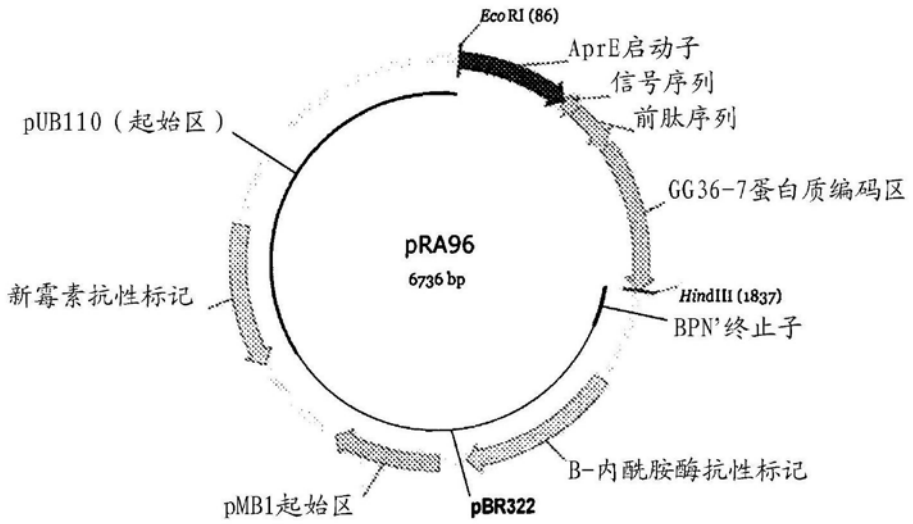
EcoRI (86)
AprE启动子
信号序列
前肽序列
GG36-7蛋白质编码区
HindIII (1837)
BPN'终止子
B-内酰胺酶抗性标记
pBR322
pMB1起始区
新霉素抗性标记
pUB110（起始区）
pRA96
6736 bp

图4