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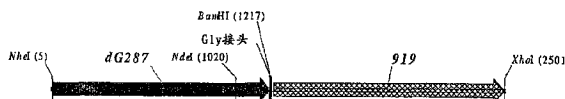
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(54) 发明名称

奈瑟球菌蛋白质的杂交表达

(57) 摘要

以单个杂交蛋白形式表达两种或多种奈瑟球菌的蛋白质 (如 A 和 B), 其可以式  $\text{NH}_2\text{-A-B-COOH}$  简单地表示。



1. 式  $\text{NH}_2\text{-A-B-COOH}$  的杂交蛋白,其特征在于,所述的 A 含  $\Delta\text{G287}$ , B 含 953,所述杂交蛋白的氨基酸序列如 SEQ ID NO :6 所示。
2. 如权利要求 1 所述的蛋白质,其特征在于,所述的  $\Delta\text{G287}$  来自脑膜炎奈瑟氏球菌菌株 2996 或 394/98。
3. 如权利要求 1 所述的蛋白质,其特征在于,所述 953 来自脑膜炎奈瑟氏球菌菌株 2996 或 394/98。
4. 如权利要求 1 所述的蛋白质,其特征在于,所述的 A 和 B 来自相同的菌株。
5. 如权利要求 1 所述的蛋白质,其特征在于,所述杂交蛋白的氨基酸序列如 SEQ ID NO :6 所示。

## 奈瑟球菌蛋白质的杂交表达

[0001] 本案是 2001.02.28 提交的申请号为 01808738.8, 名为奈瑟球菌蛋白质的杂交表达的分案申请。本文将所引用的全部文献都纳入作为参考。

### 技术领域

[0002] 本发明涉及蛋白质表达的领域。具体说, 本发明涉及奈瑟球菌 (如淋病奈瑟球菌或较佳地为脑膜炎奈瑟球菌) 的蛋白质的异源表达。

### 背景技术

[0003] 国际专利申请 W099/24578、W099/36544、W099/57280 和 W000/22430 公开了脑膜炎奈瑟球菌 (*Neisseria meningitidis*) 和淋病奈瑟球菌 (*Neisseria gonorrhoeae*) 的蛋白质。这些蛋白质一般是以 N-末端 GST- 融合体或 C-末端 His- 标记融合体在大肠杆菌中表达的 (即异源表达), 虽然也公开了其它表达系统 (包括在天然的奈瑟球菌中的表达)。

[0004] 本发明的目的是提供这些蛋白质的异源表达的其它或改进方法。这些方法通常影响表达的水平、纯化的简易程度、表达的细胞内定位和 / 或表达的蛋白质的免疫学特性。

[0005] 发明的公开

[0006] 在本发明中, 以单杂交蛋白表达本发明的两种或多种 (如 3、4、5、6 或更多) 蛋白质。较佳地, 不使用非奈瑟球菌的融合配体 (如 GST 或聚-His)。

[0007] 这有两个优点。其一, 可能不稳定或本身表达很差的蛋白质可以通过加入合适的克服该问题的杂交配体予以帮助。其二, 简化工业生产, 即制备两种分别有用的蛋白质只需要一次表达和纯化。

[0008] 因此, 本发明提供了同时异源表达本发明的两种或多种蛋白质的方法, 其中所述的本发明的两种或多种蛋白质是融合的 (即, 它们是作为单多肽链翻译的)。

[0009] 该方法通常包括如下步骤: 获得编码本发明第一种蛋白质的第一核酸; 获得编码本发明第二种蛋白质的第二核酸; 连接第一和第二核酸。将得到的核酸插入表达载体中, 或已作为表达载体的一部分。

[0010] 当仅连接两种蛋白质时, 可以式  $\text{NH}_2\text{-A-B-COOH}$  简单地表示杂交蛋白。A 和 B 各选自任何奈瑟球菌蛋白质, 尤其是那些以 SEQ#1-4326 表示的。该方法非常适合表达蛋白质 orf1、orf4、orf25、orf40、Orf46/46.1、orf83、233、287、292L、564、687、741、907、919、953、961 和 983。

[0011] 由式  $\text{NH}_2\text{-A-B-COOH}$  在下表中以 'X' 表示的 42 个杂交体是优选的:

[0012]

↓ AB →	ORF46.1	287	741	919	953	961	983
ORF46.1		×	×	×	×	×	×
287	×		×	×	×	×	×
741	×	×		×	×	×	×
919	×	×	×		×	×	×
953	×	×	×	×		×	×

961	×	×	×	×	×		×
983	×	×	×	×	×	×	

[0013] 因此,优选的以杂交体表达的蛋白质是 ORF46.1, 287, 741, 919, 953, 961 和 983。它们可以全长形式或多-甘氨酸缺失 ( $\Delta G$ ) 形式使用 (如  $\Delta G-287$ 、 $\Delta GTbp2$ 、 $\Delta G741$ 、 $\Delta G983$  等)、或以截短形式使用 (如  $\Delta 1-287$ 、 $\Delta 2-287$  等), 或以结构域缺失的形式使用 (如 287B、287C、287BC、ORF46<sub>1-433</sub>、ORF46<sub>433-608</sub>、ORF46、961c 等) 等。

[0014] 特别优选的是:(a) 含 919 和 287 的杂交蛋白;(b) 含 953 和 287 的杂交蛋白;(c) 含 287 和 ORF46.1 的杂交蛋白;(d) 含 ORF1 和 ORF46.1 的杂交蛋白;(e) 含 919 和 ORF46.1 的杂交蛋白;(f) 含 ORF46.1 和 919 的杂交蛋白;(g) 含 ORF46.1、287 和 919 的杂交蛋白;(h) 含 919 和 519 的杂交蛋白;和 (i) 含 ORF97 和 225 的杂交蛋白。

[0015] 附图中显示了其它优选例,它们包括  $\Delta G287-919$ 、 $\Delta G287-953$ 、 $\Delta G287-961$ 、 $\Delta G983-ORF46.1$ 、 $\Delta G983-741$ 、 $\Delta G983-961$ 、 $\Delta G983-961C$ 、 $\Delta G741-961$ 、 $\Delta G741-961C$ 、 $\Delta G741-983$ 、 $\Delta G741-ORF46.1$ 、ORF46.1-741、ORF46.1-961、ORF46.1-961C、961-ORF46.1、961-741、961-983、961C-ORF46.1、961C-741、961C-983、961CL-ORF46.1、961CL-741 和 961CL-983。

[0016] 当使用 287 时,其优先位于杂交体的 C- 末端;如果在 N- 末端使用它,则优先使用 287 的  $\Delta G$  形式 (如与 ORF46.1、919、953 或 961 杂交的杂交体的 N- 末端)。

[0017] 当使用 287 时,其优先为菌株 2996 或菌株 394/98 的。

[0018] 当使用 961 时,其优先在 N- 末端。可使用 961 的结构域形式。

[0019] W099/66741 公开了 ORF46、287、919 和 953 的多态形式的排序。本发明可以使用这些多态形式中的任一形式。

[0020] 较佳地,本发明杂交蛋白中的组成蛋白质 (A 和 B) 来源于是同一菌株。

[0021] 杂交体中的融合蛋白可以是直接相连的,或者是通过接头肽相连的,如通过聚-甘氨酸接头 (即, Gn, 其中 n = 3、4、5、6、7、8、9、10 或更多) 或通过协助克隆的短肽序列相连。显然不宜将  $\Delta G$  蛋白质连接于聚-甘氨酸接头的 C- 末端。

[0022] 融合蛋白可以缺失天然前导肽或可以包含 N- 末端融合配体的前导肽序列。

[0023] 宿主

[0024] 较佳地,利用异源宿主。异源宿主可以是原核的或真核的。优先为大肠杆菌,但其它合适的宿主包括枯草芽孢杆菌 (*Bacillus subtilis*)、霍乱弧菌 (*Vibrio cholerae*)、伤寒沙门氏菌 (*Salmonella typhi*)、鼠伤寒沙门氏菌 (*Salmonella typhimurium*)、脑膜炎奈瑟球菌、淋病奈瑟球菌、乳糖奈瑟球菌 (*Neisseria lactamica*)、灰色奈瑟球菌 (*Neisseria cinerea*)、分枝杆菌 (如结核分枝杆菌 (*M. tuberculosis*))、酵母等。

[0025] 载体、宿主等

[0026] 如上所述的方法,本发明提供了 (a) 用于这些方法的核酸和载体;(b) 含所述载体的宿主细胞;(c) 可用这些方法表达的或可表达的蛋白质;(d) 包含这些蛋白质的组合物,其可能适合作为疫苗、或例如诊断剂或免疫原性的组合物;(e) 用作药物 (如疫苗) 或诊断剂的组合物;(f) 这些组合物在制备以下物质中的用途 (1) 用于治疗或预防奈瑟球菌引起的感染的药物 (2) 检测奈瑟球菌或由奈瑟球菌引起的抗体存在与否的诊断剂,和 / 或 (3) 能产生抗奈瑟球菌抗体的药物;和 (g) 治疗患者的方法,其包括对该患者施用治疗有效量

的这些组合物。

[0027] 序列

[0028] 本发明还提供了具有以下实施例中所列出的任何的蛋白质或核酸。本发明还提供了具有与这些序列是序列相同性的蛋白质和核酸。如上所述，“序列相同性”的程度最好大于 50%（如 60%、70%、80%、90%、95%、99%或更大）。

[0029] 本文的命名

[0030] 本文参考在 W099/24578、W099/36544 和 W099/57280 中公开的 2166 个蛋白质序列，并将它们编号为如下的 SEQ#：

[0031]

申请	蛋白质序列	本文的 SEQ#
W099/24578	偶 SEQ ID2-892	SEQ#1-446
W099/36544	偶 SEQ ID2-90	SEQ#447-491
W099/57280	偶 SEQ ID2-3020	SEQ#492-2001
	偶 SEQ ID3040-3114	SEQ#2002-2039
	SEQ ID3115-3241	SEQ#2040-2166

[0032] 除了这种 SEQ# 编号外，本文还使用了 W099/24578、W099/36544 和 W099/27280 中的命名约定（如 W099/24578 和 W099/36544 中用的‘ORF4’、‘ORF40’、‘OFR40-1’等；W099/57280 中用的‘m919’、‘g919’和‘a919’等）。

[0033] 在本文中，将 Tettelin 等 [Science(2000)287:1809-1815] 中的从 NMB0001 到 NMB2160 的 2160 个蛋白质称为 SEQ#2167-4326 [参见 W000/66791]。

[0034] 本文采用的术语“本发明的蛋白质”指包含以下的蛋白质：

[0035] (a) SEQ#1-4326 中的一个序列；或

[0036] (b) 与 SEQ#1-4326 中的一个序列相同的序列；或

[0037] (c) SEQ#1-4326 中的一个序列的片段。

[0038] (b) 中的“序列相同性”的程度最好大于 50%（如 60%、70%、80%、90%、95%、99%或更大）。其包括突变体和等位基因变体 [如，参见 W000/66741]。相同性最好用 Smith-Waterman 同源性搜寻算法确定，如在 MPSRCH 程序 (OxfordMolecular) 中执行的，采用参数“缺口罚分 (gap open penalty)”为 12，“缺口延伸罚分 (gap extension penalty)”为 1 进行缺口仿射搜索。通常，将两种蛋白质之间 50%或更高的相同性视为功能等效的指示。

[0039] (c) 中的“片段”应包含 SEQ#1-4326 中一个序列的至少 n 个连续的氨基酸，且根据具体的序列 n 为 7 或更高（如 8、10、12、14、16、18、20、25、30、35、40、50、60、70、80、90、100 或更高）。较佳地，片段包含 SEQ#1-4326 中一个序列的表位。优选的片段是在 W000/71574 和 W001/04316 中公开的那些。

[0040] 本发明优选的蛋白质是在脑膜炎奈瑟球菌血清群 B 中发现的。

[0041] 根据本发明使用的优选蛋白质是血清群 B 脑膜炎奈瑟球菌菌株 2996 或菌株 394/98 (新西兰菌株)。除非特别指出，本文所述的蛋白质是脑膜炎奈瑟球菌菌株 2996 的蛋白质。但是，应该理解通常本发明并不受菌株的限制。参考具体的蛋白质（如‘287’、‘919’等）可以包括任何菌株的该蛋白质。

[0042] 应该理解术语“核酸”包括 DNA 和 RNA，以及它们的类似物，如含有修饰骨架的那些

类似物,还包括肽核酸(PNA)等。

[0043] 附图简述

[0044] 图 1-26 显示本发明的杂交蛋白。

[0045] 本发明的进行模式

[0046] 实施例 1-ORF46 的杂交体

[0047] 脑膜炎奈瑟球菌(血清群 B, 菌株 2996) 的完整 ORF46 蛋白质具有如下序列:

[0048] 1 LGISRKISLI LSILAVCLPM HAHASDLAND SFIRQVLDLDRQ HFEPDGKYHL

[0049] 51 FGSRGELAER SGHIGLGKIQ SHQLGNLMIQ QAAIKGNIGY IVRFSHDHGHE

[0050] 101 VHSPFDNHAS HSDSDEAGSP VDGFSLYRIH WDGYEHPAD GYDGPQGGGY

[0051] 151 PAPKGARDIY SYDIKVAQN IRLNLTDATRS TGQRLADRFH NAGSMLTQGV

[0052] 201 GDGFKRATRY SPELDRSGNA AEAFTGTADI VKNIIGAAGE IVGAGDAVQG

[0053] 251 ISEGSNIAVM HGLGLLSTEN KMARINDLAD MAQLKDYAAA AIRDWAVQNP

[0054] 301 NAAQGIEAVS NIFMAAIPK GICAVRGKYG LGGITAHPK RSQMGAIALP

[0055] 351 KGKSAVSDNF ADAAYAKYPS PYHSRNIRSN LEQRYGKNI TSSTVPPSNG

[0056] 401 KNVKLADQRH PKTGVPFDGK GFPNFEKHVK YDTKLDIQEL SGGGIPKAKP

[0057] 451 VSDAKPRWEV DRKLNKLTR EQVEKNVQET RNGNKNSNFS QHAQLEREIN

[0058] 501 KLKSADEINF ADGMGKFTDS MNDKAFSRLV KSVKENGFTN PVVEYVEING

[0059] 551 KAYIVRGNNR VFAAEYLGRI HELKFKKVDF PVPNTSWKNP TDVLNESGNV

[0060] 601 KRPRYRSK \*

[0061] 在前导肽下加下划线。

[0062] 可以在 W000/66741 中发现其它菌株的 ORF46 的序列。

[0063] ORF46 在其 C- 末端和 N- 末端与 287、919 和 ORF1 融合。该杂交蛋白通常是不溶解的,但产生一些良好的 ELISA 和杀菌结果(针对同源 2996 菌株):

[0064]

蛋白质	ELISA	杀菌 Ab
Orf1-Orf46. 1-His	850	256
919-Orf46. 1-His	12900	512
919-287-Orf46-His	n. d.	n. d.
Orf46. 1-287His	150	8192
Orf46. 1-919His	2800	2048
Orf46. 1-287-919His	3200	16384

[0065] 为了比较,构建了 ORF46. 1、287(以 GST 融合体或 $\Delta$  G287 的形式)和 919 的“三”杂交体,并针对各种菌株(包括同源 2996 菌株)将其与三种抗原的简单混合物相比。FCA 用作佐剂:

[0066]

	2996	BZ232	MC58	NGH38	F6124	BZ133
混合物	8192	256	512	1024	>2048	>2048
ORF46. 1-287-919his	16384	256	4096	8192	8192	8192
AG287-919-ORF46. 1his	8192	64	4096	8192	8192	16384
AG287-ORF46. 1-919his	4096	128	256	8192	512	1024

[0067] 同样,这些杂交体显示相当等的或更佳的免疫活性。

[0068] 针对各种异源菌株,将两种蛋白质(菌株 2996)的杂交体与单种蛋白质相比:

[0069]

	1000	MC58	F6124 (MenA)
ORF46.1-His	<4	4096	<4
ORF1-His	8	256	128
ORF1—ORF46.1-His	1024	512	1024

[0070] 再次,这些杂交体显示相等的或更佳的免疫活性。

[0071] 实施例 2-  $\Delta$  G287 的杂交体

[0072] 发现 287 中 (Gly)<sub>6</sub> 序列的缺失对蛋白质的表达有显著影响。将缺失 N- 末端氨基酸多达 GGGGGG 的蛋白质称为 ' $\Delta$  G287'。在菌株 MC58 中,它的基本序列(前导肽有下划线)为:

[0073] SPDVKS ADTL SKPAAP VVSEKETEAK EDAPQAGSQ QGAPSAQGSQ DMAAVSEENT

[0074] GNGGAVTADN PKNEDEVAQN DMPQNAAGTD SSTPNHTPDP NMLAGNMENQ ATDAGESSQP

[0075] ANQPDMANAA DGMQGDPSA GGQNAGNTAA QGANQAGNNQ AAGSSDPIPA SNPAPANGGS

[0076] NFRGVDLANG VLIDGPSQNI TLTHCKGDSC SGNNFLDEEV QLKSEFEKLS DADKISNYKK

[0077] DGKNDK FVGL VADSVQMKGI NQYIIFYKPK PTSFARFRRS ARSRRSLPAE MPLIPVNQAD

[0078] TLIVDGEAVS LTGHSGNIFA PEGNYRYLTY GAEKLPGGSY ALRVQGEPAK GEMLAGAAVY

[0079] NGEVLHFHTE NGRPYPTRGR FAAKVDFGSK SVDGIIDSGD DLHMG TQKFK AAIDGNGFKG

[0080] TWTENSGDV SGKFYGPAGE EVAGKYSYRP TDAEKGGFGV FAGKEQD \*

[0081] 与 ' $\Delta$  287-His' 或 ' $\Delta$  287<sup>未标记的</sup>' 相比,有或无 His- 标记的  $\Delta$  G287(分别为 ' $\Delta$  G287-His' 和 ' $\Delta$  G287K') 以很好的水平表达。

[0082] 在基因变异性数据的基础上,从许多 MenB 菌株(尤其是从菌株 2996、MC58、100 和 BZ232)的大肠杆菌中表达  $\Delta$  G287-His 的变体。结果也好 - 它们都具有很高的 ELISA 滴定度,且血清杀菌滴定度 >8192。由 pET-24b 表达的  $\Delta$  G287K 在 ELISA 和血清杀菌实验中有极佳滴定度。

[0083] 还将聚 -Gly 序列的缺失应用于 Tbp2(NMB0460)、741(NMB1870) 和 983(NMB1969)。在不编码其前导肽的序列且没有聚 -Gly(即,以 " $\Delta$  G 形式"),在 pET 载体中克隆并在大肠杆菌中表达时,观察到相同的作用 - 在携带聚 - 甘氨酸段缺失的克隆中表达很好,若在表达的蛋白中存在甘氨酸时则表达差或不表达。

[0084] 将  $\Delta$  G287 直接融合于 919、953、961(如下所示的序列)和 ORF46.1 的符合读框的上游:

[0085]  $\Delta$  G287-919

[0086] ATGGCTAGCCCGATGTTAAATCGGCCGACACGCTGTCAAACCGGCCGCTCCTGTTGTGTGCTGAAAAAGACAGAG

[0087] GTAAAAGAAGATCCGCCACAGGCAGGTTCTCAAGGACAGCCGCGCCATCCACACAAGGCAGCCAAGATATGCCGGCA

[0088] GTTTCGGCAGAAAATACACGCAATGGCGGTGCGGCAACAACCGAACAACCCAAAAATGAAGACGAGGGACCGAAAAAT

[0089] GATATGCCGCAAAAATCCGCCAATCCGCAAAATCAAACAGGGAACAACCAACCCGCCATTCTTCAGATTCCGCCCCC

[0090] GCGTCAAACCCGACCTGCGAATGGCGGTAGCAATTTTGAAGGGTTGATTTGGCTAATGGCGTTTTGATTGATGGG

[0091] CCGTCGCAAAAATATAACGTTGACCCACTGTAAAACGGGATTCTTGTAATGGTGATAATTTATTTGATGAAGAAGCACCG

[0092] TCAAAATCAGAAATTTGAAAAATTTAAATGAGTCTGAACGAATTGAGAAATATAAGAAAGATGGGAAAAGCGATAAAATTT

[0093] ACTAATTTGGTTGCGACAGCAGTTCAAGCTAATGGAACATAACAAATATGTCATCATTTATAAAGACAAGTCCGCTTCA

[0094] TCTTCATCTGCGGATTCAGGCGTTCTGCACGGTCGAGGAGTCGCTTCCTGCCGAGATGCCGCTAATCCCGTCAAT

[0095] CAGGCGGATACGCTGATTGTTCGATGGGGAAGCGGTCAGCCTGACGGGGCATTCGGCAATATCTTCGCGCCGAAGGG  
[0096] AATTACCGGTATCTGACTTACGGGGCGGAAAAATGCCCCGGCGGATCGTATGCCCTCCGTGTGCAAGGCGAAACCCGCA  
[0097] AAAGGCGAAATGCTTGTCTGGCACGGCCGTGTACAACGGCGAAGTGTGCATTTTCATACGGAAAAACGGCCGTCCGTAC  
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[0099] TTGCATATGGGTACGCAAAAAATCAAAGCCGCCATCGATGGAACGGCTTTAAGGGGACTTGGACGGAATAATGGCGGC  
[0100] GGGGATGTTTCCGGAAGGTTTTACGGCCCCGGCCGGAGGAAGTCGGCGGAAAAATACAGCTATCGCCCCGACAGATGCG  
[0101] GAAAAGGGCGGATTCCGGCGTGTTCGGCGCAAAAAAGAGCAGGATGGATCCGGAGGAGGAGGATGCCAAAGCAAGAGC  
[0102] ATCCAAACCTTTCGGCAACCCGACACATCCGTTCATCAACGGCCCCGACCGGCCGGTCCGCATCCCCGACCCCCCGCGA  
[0103] ACGACGGTCGGCGGGCGGGGGCCGTCTATACCGTTGTACCGCACCTGTCCCTGCCCCACTGGGCGGCGCAGGATTTTC  
[0104] GCCAAAAGCCTGCAATCCCTCCGCCTCGGCTGCGCCAATTTGAAAAACCGCAAGGCTGGCAGGATGTGTGCGCCCAA  
[0105] GCCTTTCAAACCCCCGTCCATTCCTTTTCAGGCAAAACAGTTTTTTTGAACGCTATTTTCAACCGCGTGGCAGGTTGCAGGC  
[0106] AACGGAAGCCTTTCGGGTACGGTTACCGGCTATTACGAGCCGGTGTGAAGGGCGACGACAGGCGGACGGCACAAGCC  
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[0108] GTCCGCATCAGGCAGACGGGAAAAAACAGCGGCACAATCGACAATACCGGCGGCACACATACCGCCGACCTCTCCCGA  
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[0113] GCCTATATGCGGCAAAATCCGCAACGCCTCGCGAAGTTTTGGGTCAAACCCAGCTATATCTTTTTCCGCGAGCTT  
[0114] GCCGGAAGCAGCAATGACGGTCCCGTCCGGCACTGGGCACGCCGTTGATGGGGGAATATGCCGGCGCAGTCGACCCG  
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[0116] ATGGCGCAGGATACCGGCAGCGGATTAAGGGCGCGGTGCGCGTGGATTATTTTTGGGGATACGGCGACGAAGCCGGC  
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[0119] 1 MASPDVKSAD TLSKPAAPVV AEKETE VKED APQAGSQGQG APSTQGSQDM  
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[0121] 101 DSAPASNPAP ANGGSNFGRV DLANGVLIDG PSQNILTHC KGDSNGDNL  
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[0123] 201 IYKDKSASSS SARFRRSARS RRSPLAEMPL IPVNQADTLI VDGEAVSLTG  
[0124] 251 HSGNIFAPEG NYRYLTYGAE KLPGGSYALR VQGEPKAGEM LAGTAVYNGE  
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[0126] 351 DGNGFKGTWT ENGGGDVSGR FYGPACEEVA GKYSYRPTDA EKGFGVFAG  
[0127] 401 KKEQDGS GGG GCQSKSIQTF P QPDTSVING PDRPVGIPDP AGTTVGGGGA  
[0128] 451 VYTVVPHLSL PHWAAQDFAK SLQSFRLGCA NLKNRQGWQD VCAQAFQTPV  
[0129] 501 HSFQAKQFFE RYFTPWQVAG NGSLAGTVTG YYEPVLKGDD RRTAQARFPI  
[0130] 551 YGIPDDFISV PLPAGLRSGK ALVRIRQTGK NSGTIDNTGG THTADLSRFP  
[0131] 601 ITARTTAIKG RFEGSRFLPY HTRNQINGGA LDGKAPILGY AEDPVELFFM  
[0132] 651 HIQSGRLKT PSGKYIRIGY ADKNEHPYVS IGRYMADKGY LKLGQTSMQG  
[0133] 701 IKAYMRQNPQ RLAEVLGQNP SYIFFRELAG SSNDGPV GAL GTPLMGEYAG



- [0134] 751 AVDRHYITLG APLFVATAHP VTRKALNRLI MAQDTGSAIK GAVRVDYFWG
- [0135] 801 YGDEAGELAG KQKTTGYVWQ LLPNGMKPEY RP \*
- [0136] Δ G287-953
- [0137] ATGGCTAGCCCCGATGTTAAATCGGCGGACACGCTGTCAAAACCGCCGCTCCTGTGTGTTGCTGAAAAAGAGACAGAG
- [0138] GTAAAAAGAAGATGCGCCACAGGCAGGTTCTCAAGGACAGGGCGCCATCCACACAAGGCAGCCAAGATATGGCGGCA
- [0139] GTTTCGGCAGAAAAATACAGGCAATGGCGGTGCGGCAACAACGGACAAACCCAAAAATGAAGACGAGGGACCGCAAAAT
- [0140] GATATGCCGCAAAATTCGCGCAATCCGCAATCAAACAGGGAACAACCAACCCGCGGATTTCTTCAGATTCGCCCCC
- [0141] GCGTCAAACCCCTGCACCTGCGAATGGCGGTAGCAATTTTGAAGGGTTGATTTGGCTAATGGCGTTTTGATTGATGGG
- [0142] CCGTCGCAAAATATAACGTTGACCCACTGTAAAGGCGATTCTTGTAAATGGTGATAATTTATTGGATGAAGAAGCACCG
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- [0144] ACTAATTTGGTTGCGACAGCAGTTCAAGCTAATGGAACTAACAAATATGTTCATCATTTATAAAGACAAGTCCGCTTCA
- [0145] TCTTCATCTGCGGATTCAGGCGTTCTGCACGGTCGAGGAGGTGCGTTCCCTGCCGAGATGCCGCTAATCCCCGTCAAT
- [0146] CAGGCGGATACGCTGATTTGTCGATGGGGAAGCGGTACGCTGACGGGGCATTCGGCAATATCTTCGCGCCCGAAGGG
- [0147] AATTACCGGTATCTGACTTACGGGGCGGAAAAATTTGGCCCGCGGATCGTATGCCCTCCGTGTGCAAGGCGAACCGGCA
- [0148] AAAGGCGAAATGCTTGTGTCGACGGCCGTGTACAACGGCGAAGTGTGCAATTTTCATACGGAAAAACGGCCGTCCGTAC
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- [0150] TTGCATATGGGTACGCAAAATTCAAAGCCGCCATCGATGGAACCGGCTTTAAGGGGACTTGGACGAAAAATGGCGGC
- [0151] GGGGATGTTTCCGGAAGGTTTTACGGCCCGCGCGGAGGAAGTGGCGGAAAAATACAGCTATCGCCCGACAGATGCG
- [0152] GAAAAGGGCGGATTCGGCGTGTTTGCCGGGCAAAAAAGAGCAGGATGGATCCGGAGGAGGAGCCACCTACAAAGTG
- [0153] GACGAATATCAGCCAACGCCCCGTTTCGCCATCGACCATTTCAACACCAGCACCAACGTCGGCGGTTTTTACGGTCTG
- [0154] ACCGGTTCCGTCGAGTTCGACCAAGCAAAACGCGACGGTAAAAATCGACATCAACCATCCCCGTTGCCAACCTGCAAAAGC
- [0155] GGTTCGCAACACTTTACCGACCCTGAAATCAGCCGACATCTTCGATGCCGCCAATATCCGGACATCCGCTTTGTT
- [0156] TCCACCAAATTCAACTTCAACGGCAAAAAACTGGTTTTCCGTTGACGGCAACCTGACCATGCACGGCAAAACCGCCCCC
- [0157] GTCAAACCTCAAAGCCGAAAAATTCAACTGCTACCAAAGCCCGATGGCGAAAAACCGAAGTTTGGCGCGCGGACTTCAGC
- [0158] ACCACCATCGACCGCACCAAAATGGGGCGTGGACTACCTCGTTAACGTTGGTATGACCAAAAGCGTCCGCATCGACATC
- [0159] CAAATCGAGGCAGCCAAACAAATAACTCGAG
- [0160] 1 MASPDVKSAD TLSKPAAPVV AEKETEVEKED APQAGSQGQG APSTQGSQDM
- [0161] 51 AAVSAENTGN GGAATTDKPK NEDEGPQNDM PQNSAESANQ TGNNQPADSS
- [0162] 101 DSAPASNPAP ANGGSNFGRV DLANGVLIDG PSQNITLTHC KGDSNGDNL
- [0163] 151 LDEEAPSKSE FENL NESERI EKYKKDGKSD KFTNLVATAV QANGTNKYVI
- [0164] 201 IYKDKSASSS SARFRRSARS RRSPLAEMPL IPVNQADTLI VDGEAVSLTG
- [0165] 251 HSGNIFAPEG NYRYLTYGAE KLPGGSYALR VQGEPKAGEM LAGTAVYNGE
- [0166] 301 VLHFHTENGR PYPTRGRFAA KVDFGSKSVD GIIDSGDDLH MGTQKFKAAI
- [0167] 351 DGNGFKGTWT ENGGGDVSGR FYGPAGEEVA GKYSYRPTDA EKGFGVFAG
- [0168] 401 KKEQDGS GGG GATYKVD EYH ANARFAIDHF NTSTNVGGFY GLTGSVEFDQ
- [0169] 451 AKRDGKIDIT IPVANLQSGS QHFTDHLKSA DIFDAAQYPD IRFVSTKFNF
- [0170] 501 NGKKLVSDG NLTMHGKTAP VKLKA EKTNC YQSPMAKTEV CGGDFSTTID
- [0171] 551 RTKWGVDYLV NVGMTKSVRI DIQIEAAKQ \*
- [0172] Δ G287-961

[0173] ATGGCTAGCCCGATGTTAAATCGGCGGACACGCTGTCAAAACCGGCCGCTCCTGTGTTGCTGAAAAAGAGACAGAG  
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[0175] GTTTCGGCAGAAAATACAGGCAATGGCGGTGCGGCAACAACGGACAAAACCCAAAAATGAAGACGAGGGACCGCAAAAT  
[0176] GATATGCCGCAAAATTCGCGCAATCCGCAATCAAACAGGGAACAACCAACCCGCGGATTTCTCAGATTCGCCCCC  
[0177] GCGTCAAACCCCTGCACCTGCGAATGGCGGTAGCAATTTTGAAGGGTTGATTTGGCTAATGGCGTTTTGATTGATGGG  
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[0187] GGGGATGTTTCCGGAAGGTTTTACGGCCCCGCGCGGAGGAAGTGGCGGAAAAATACAGCTATCGCCCGACAGATGCG  
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[0189] GATGTTAAAAAAGCTGCCACTGTGGCCATTGCTGCTGCCTACAACAATGGCCAAGAAATCAACGGTTTTCAAAGCTGGA  
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[0194] ACAAATATCGTAAAAATTTGATGAAAAATTTAGAAGCCGTGGCTGATACCGTCGACAAGCATGCCGAAGCATTCAACGAT  
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[0203] TCTTCCGCGACCTACCATGTGCGGCTCAATTACGAGTGGTAACTCGAG  
[0204] 1 MASPDVKSAD TLSKPAAPVV AEKETEVEKED APQAGSQGQG APSTQGSQDM  
[0205] 51 AAVSAENTGN GGAATTDKPK NEDEGPQNDM PQNSAESANQ TGNNQPADSS  
[0206] 101 DSAPASNPAP ANGGSNFGRV DLANGVLIDG PSQNILTLTHC KGDSNCNDNL  
[0207] 151 LDEEAPSKSE FENL NESERI EKYKKDGKSD KFTNLVATAV QANGTNKYVI  
[0208] 201 IYKDKSASSS SARFRRSARS RRSPLAEMPL IPVNQADTLI VDGGEAVSLTG  
[0209] 251 HSGNIFAPEG NYRYLTYGAE KLPGGSYALR VQGEPKAGEM LAGTAVYNGE  
[0210] 301 VLHFHTENGR PYPTRGRFAA KVDFGSKSVD GIIDSGDDLH MGTQKFKAAI  
[0211] 351 DGNFGKGTWT ENGGGDVSGR FYGPAGEEVA GKYSYRPTDA EKGFGVVFAG

[0212] 401 KKEQDGS GGG GATNDDVKK AATVAIAAAY NNGQEINGFK AGETIYDIDE  
 [0213] 451 DGTITKKDAT AADVEADDFK GLGLKKVVTN LTKTVNENKQ NVDKVKAAE  
 [0214] 501 SEIEKLTTKL ADTDAALADT DAALDATTNA LNKLGENTTT FAEETKTIV  
 [0215] 551 KIDEKLEAVA DTVDKHAEAF NDIADSLDET NTKADEAVKT ANEAKQTAEE  
 [0216] 601 TKQNVDAKVK AAETAAGKAE AAAGTANTAA DKAEAVAAKV TDIKADIATN  
 [0217] 651 KDNIAKKANS ADVYTREESD SKFVRIDGLN ATTEKLDTRL ASAEXSIADH  
 [0218] 701 DTRLNGLDKT VSDLRKETRQ GLAEQAALSG LFQPYNVGRF NVTAAVGGYKC  
 [0219] 751 SESAVAIGTG FRFTENFAAK AGVAVGTSSG SSAAYHVGVN YEW \*  
 [0220]

	ELISA	杀菌
△ G287-953-His	3834	65536
△ G287-961-His	108627	65536

[0221] 对 919 和 ORF46.1 而言,将针对杂交蛋白产生的抗体的杀菌效力(同源菌株)与针对组分抗原(用 287-GST)的简单混合物产生的抗体相比:

[0222]

	与 287 的混合物	与 △ G287 的杂交体
919	32000	128000
ORF46.1	128	16000

[0223] 还获得了针对异源 MenB 菌株和针对血清型 A 和 C 的杀菌活性的数据:

[0224]

菌株	919		ORF46.1	
	混合物	杂交体	混合物	杂交体
<b>NGH38</b>	<b>1024</b>	<b>32000</b>	-	<b>16384</b>
<b>MC58</b>	<b>512</b>	<b>8192</b>	-	<b>512</b>
<b>BZ232</b>	<b>512</b>	<b>512</b>	-	-
<b>MenA (F6124)</b>	<b>512</b>	<b>32000</b>	-	<b>8192</b>
<b>MenC (C11)</b>	<b>&gt;2048</b>	<b>&gt;2048</b>	-	-
<b>MenC (BZ133)</b>	<b>&gt;4096</b>	<b>64000</b>	-	<b>8192</b>

[0225] 因此,在 N-末端与 △ G287 的杂交蛋白在免疫学上优于与 △ G287-ORF46.1 的简单混合物,即使针对异源菌株也特别有效。可以在 pET-24b 中表达 △ G287-ORF46.1。

[0226] 用新西兰菌株 394/98,而非 2996,制备相同的杂交蛋白:

[0227] △ G287Nz-919

[0228] ATGGCTAGCCCGATGTCAAGTCGGCGGACACGCTGTCAAACCTGCCGCCCTGTTGTTCTGAAAAAGAGACAGAG

[0229] GCAAAGGAAGATGCGCCACAGGCAGGTTCTCAAGGACAGGGCGGCCATCCGCACAAGGGGTCAAGATATGGCGGGC

[0230] GTTTCGGAAGAAAATACAGGCAATGGCGGTGCGGCAGCAACGGACAAACCCAAAAATGAAGACGAGGGGGCGCAAAAT

[0231] GATATGCCGAAAATGCCCGGATACAGATAGTTTGACACCGAATCACACCCCGGCTTCGAATATGCCGGCCGAAAT

[0232] ATGGAACCAAGCACCGGATGCCGGGAATCGGAGCAGCGGCAAACCAACCGGATATGGCAAATACGGCGGACGGA

[0233] ATGCAGGGTGACGATCCGTCGGCAGGGGGAAAATGCCGGCAATACGGCTGCCAAGGTACAAATCAAGCCGAAAAC

[0234] AATCAAACCGCCGTTCTCAAAATCCTGCCTCTTCAACCAATCCTAGCGCCAGGAATAGCGGTGGTGATTTTGAAGG

[0235] ACGAACGTGGGCAATTCTGTGTGATTGACGGGCCGTCGAAAAATAACGTTGACCCACTGTAAAGCGGATTCTTGT  
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 [0245] GAAGTGGCGGGAAAAATACAGCTATCGCCCAACAGATGCGGAAAAAGGGCGGATTCCGGCGTGTTTGCGCGAAAAAACAG  
 [0246] CAGGATGGATCCGGAGGAGGAGGATGCCAAAGCAAGAGCATCCAAAACCTTTCCGCAACCCGACACATCCGTCATCAAC  
 [0247] GGCCCGACCGGGCCGTCGGCATCCCGACCCCGCCGGAACGACGGTCGGCGGGCGGGGGCCGTCATATACCGTTGTA  
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 [0263] 1 MASPDVKSAD TLSKPAAPVV SEKETEAKED APQAGSQGQG APSAQGGQDM  
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 [0265] 101 PAGNMENQAP DAGESEQPAN QPDMANTADG MQGDDPSAGG ENAGNTAAQG  
 [0266] 151 TNQAENNQTA GSQNPASSTN PSATNSGGDF GRTNVGNSVV IDGPSQNITL  
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 [0270] 351 SKGEMLAGTA VYNGEVLHFH TENGRPSPSR GRFAAKVDFG SKSVDGIIDS  
 [0271] 401 GDGLHMGTK FKA AIDGNGF KGTWTENGG DVSGKFGYGA GEEVAGKCYST  
 [0272] 451 RPTDAEKGGF GVFAKGKEQD GSGGGGQSK SIQTFPQPD SVINGPDRPV  
 [0273] 501 GIPDPAGTTV GGGGAVYTVV PHLSLPHWAA QDFAKSLQSF RLGCANLKNR

[0274] 551 QGWQDVCAQA FQTPVHSFQA KQFFERYFTP WQVAGNGSLA GTVTGYEYEPV  
 [0275] 601 LKGDDRRTAQ ARFPIYIGIPD DFISVPLPAG LRS GKALVRI RQTGKNSGTI  
 [0276] 651 DNTGGTHTAD LSRFPITART TAIKGRFEGS RFLPYHTRNQ INGGALDGA  
 [0277] 701 PILGYAEDPV ELFFMHIQGS GRLKTPSGKY IRIGYADKNE HPYVSIGRYM  
 [0278] 751 ADKGYLKLQ TSMQGIKAYM RQNPQRLAEV LGQNPYSYIFF RELAGSSNDG  
 [0279] 801 PVGALGTPLM GEYAGAVDRH YITLGAPLFV ATAHPVTRKA LNRLIMAQDT  
 [0280] 851 GSAIKGAVRV DYFWGYGDEA GELAGKQKTT GYVWQLLPNG MKPEYRP \*  
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 [0283] GCAAAGGAAGATGCGCCACAGGCAGGTTCTCAAGGACAGGGCGCCATCCGCACAAGCGGTCAAGATATGGCGGCG  
 [0284] GTTTCGGAAGAAAAATACAGGCAATGGCGGTGCGGCAGCAACGGACAAACCCAAAAATGAAGACGAGGGGGCGCAAAAT  
 [0285] GATATGCCGCAAAATGCCGCCGATACAGATAGTTTGACACCGAATCACACCCCGGCTTCGAATATGCCGGCCGAAAT  
 [0286] ATGGAACCAAGCACCGGATGCCGGGAATCGGAGCAGCCGCAACCAACCGGATATGGCAAAATACGGCGGACCGA  
 [0287] ATGCAGGTGACGATCCGTCGGCAGGCGGGAAAAATGCCGCAATACGGCTGCCCAAGGTACAAATCAAGCCGAAAAAC  
 [0288] AATCAAACCGCGGTTCTCAAAATCCTGCCTCTTCAACCAATCCTAGCGCCACGAATAGCGGTGGTGATTTTGGAAGG  
 [0289] ACGAACGTGGCAATTTCTGTGTGATTGACGGCCGTCGCAAAATATAACGTTGACCCACTGTAAAGGCGATTCTTGT  
 [0290] AGTGGCAATAATTTCTTGGATGAAGAAGTACAGCTAAAAATCAGAATTTGAAAAATTAAGTGATGCAGACAAAATAAGT  
 [0291] AATTACAAGAAAGATGGGAAGAATGACGGGAAGAATGATAAAATTTTGTGGTTTGGTTGCCGATAGTGTGCAGATGAAG  
 [0292] GGAATCAATCAATATATTATCTTTTATAAACCTAAACCCACTTCATTTGCGGATTTAGCGGTTCTGCACGGTCGAGG  
 [0293] CGGTGCTTCCGCGCGAGATGCCGCTGATTCOCGTCAATCAGGCGGATACGCTGATTGTGATGGGAAGCGGTCAGC  
 [0294] CTGACGGGGCATTCGGCAATATCTTCCGCGCCGAAGGGAATTAACGGTATCTGACTTACGGGGCGAAAAATTTGCC  
 [0295] GCGGATCGTATGCCCTCCGTGTTCAGGGCAACCTTCAAAAGGCGAAATGCTCGCGGCACGGCAGTGTACAACGGC  
 [0296] GAAGTGCTGCATTTTCATACGGAAAAACGGCGTCCGTCOCCTCCAGAGGCAGGTTTGGCCGAAAAAGTCGATTTCCGC  
 [0297] AGCAATCTGTGCACGGCATTATCGACAGCGCGATGGTTTGCATATGGGTACGCAAAATTCAAAGCCGCCATCGAT  
 [0298] GGAAACGGCTTTAAGGGGACTTGGACGAAAAATGGCGCGGGGATGTTTCCGAAAGTTTTACGGCCCGCGGGCGAG  
 [0299] GAAGTGGCGGAAAAATACAGCTATCGCCCAACAGATGCGGAAAAGGGCGGATTCGGCGTGTTTGCCGCAAAAAAGAG  
 [0300] CAGGATGGATCCGGAGGAGGAGGCCACTACAAAGTGGACGAATATCAGCCAAACGCCCCGTTTCGCCATCGACCAT  
 [0301] TTCAACACCAGCACCAACGTCGGCGGTTTTTACGGTCTGACCGGTTCCGTCGAGTTCCGACCAAGCAAAACGGACCGT  
 [0302] AAAATCGACATCAACATCCCCGTTGCCAACCTGCAAAGCGGTTCCGCAACACTTTACCGACCACTGAAATCGACCGGAC  
 [0303] ATCTTCGATGCCGCCAATATCCGGACATCCGTTTTGTTCACCAAAATTCAACTTCAACGGCAAAAACTGGTTTTCC  
 [0304] GTTGACGGCAACCTGACCATGCACGGCAAAACGCCCCCGTCAAACCTCAAAGCCGAAAAATTCAACTGCTACCAAAGC  
 [0305] CCGATGGCGAAAAACGAAGTTTGGCGGGCGACTTCAGCACCAACCATCGACCGCAACCAATGGGGCGTGGACTACCTC  
 [0306] GTTAACGTTGGTATGACCAAAAGCGTCCGCATCGACATCCAAATCGAGGCAGCCAAACAATAAAAAGCTT  
 [0307] 1 MASPDVKSAD TLSKPAAPVV SEKETEAKED APQAGSQGQG APSAQGGQDM  
 [0308] 51 AAVSEENTGN GGAAATDKPK NEDEGAQNDM PQNAADTDSL TPNHTPASNM  
 [0309] 101 PAGNMENQAP DAGESEQPAN QPDMANTADG MQGDDPSAGG ENAGNTAAQG  
 [0310] 151 TNQAENNQTA GSQNPASSTN PSATNSGGDF GRTNVGNSVV IDGPSQNITL  
 [0311] 201 THCKGDSCSG NNFLDEEVQL KSEFEKLSDA DKISNYKKDG KNDGKNDKFV  
 [0312] 251 GLVADSVQMK GINQYIIFYK PKPTS FARFR RSARSRRSLP AEMPLIPVQ

[0313] 301 ADTLIVDGEA VSLTGHSNI FAPEGNYRYL TYGAEKLP GG SYALRVQGEP  
[0314] 351 SKGEMLAGTA VYNGEVLHFH TENGRPSPSR GRFAAKVDFG SKSVDGITDS  
[0315] 401 GDGLHMG TQK FKA AIDGNGF KGTWTENGGG DVSGKFY GPA GEEVAGKYSY  
[0316] 451 RPTDAEKGGF GVFAGKKEQD GSGGGGATYK VDEYHANARF AIDHFNTSTN  
[0317] 501 VGGFYGLTGS VEFDAQKRDG KIDITIPVAN LQSGSQHF TD HLKSADIFDA  
[0318] 551 AQYPD I RFVS TKFNFNKKL VSVDGNLTMH GKTAPVKLKA EKFN CYQSPM  
[0319] 601 AKTEVCGGDF STTIDR TKWG VDYL VNVGMT KSVRIDIQIE AAKQ \*  
[0320] Δ G287Nz-961  
[0321] ATGGCTAGCCCGATGTCAAGTCGGCGGACACGCTGTCAAAACCTGCCGCCCTGTGTCTGAAAAAGAGACAGAG  
[0322] GCAAAGGAAGATGCGCCACAGGCAGGTTCTCAAGGACAGGCGGCCATCCGCACAAGGCGGTCAAGATATGGCGGGC  
[0323] GTTTCGGAAGAAAATACAGGCAATGGCGGTGCGGCAGCAACGGACAAACCCAAAAATGAAGACGAGGGGGCGCAAAAT  
[0324] GATATGCCGCAAAATGCCGCCGATACAGATAGTTTGACACCGAATCACACCCCGGCTTCGAATATGCCGGCCGAAAT  
[0325] ATGGAAAACCAAGCACCGGATGCCGGGAATCGGAGCAGCCGCAAAACCAACCGGATATGGCAAAATACGGCGGACGGA  
[0326] ATGCAGGTGACGATCCGTCGGCAGGCGGGAAAATGCCGGCAATACGGCTGCCAAGGTACAAAATCAAGCCGAAAAAC  
[0327] AATCAAACCGCGGTTCTCAAAATCCTGCCCTTCAACCAATCCTAGCGCCACGAATAGCGGTGGTGATTTTGGAAGG  
[0328] ACGAACGTGGGCAATTTCTGTGTGATTGACGGCCGTCGCAAAATATAACGTTGACCCACTGTAAAGGCGATTCTTGT  
[0329] AGTGGCAATAATTTCTTGGATGAAGAAGTACAGCTAAAATCAGAATTTGAAAAATTAAGTGATGCAGACAAAATAAGT  
[0330] AATTACAAGAAAGATGGGAAGAATCACGGGAAGAATGATAAATTTGTCGGTTTGGTTGCCGATAGTGTGCAGATGAAG  
[0331] GGAATCAATCAATATATTATCTTTTATAAACCTAAACCCACTTCATTTGCGGATTTAGGCGTTCTGCACGGTCGAGG  
[0332] CGGTGCTTCCGCGCGAGATGCCGCTGATTCCCGTCAATCAGGCGGATACGCTGATTGTGATGGGAAGCGGTCAGC  
[0333] CTGACGGGGCATTTCCGGCAATATCTTCCGCGCCGAAGGGAATTAACCGGATCTGACTTACGGGGCGAAAAATTTGCC  
[0334] GCGGATCGTATGCCCTCCGTGTTC AAGCGAACCTTCAAAAGGCGAAATGCTCGCGGCACGGCAGTGTACAACGGC  
[0335] GAAGTGCTGCATTTTCATACGGA AAAACGGCGTCCGTC CCGGTCAGAGGCAGGTTTGGCCGAAAAAGTCGATTTCCGC  
[0336] AGCAAACTGTGGACGGCATTATCGACAGCGCGATGGTTTG CATATGGGTACGCAAAAATTC AAAGCCGCCATCGAT  
[0337] GGAAACGGCTTTAAGGGGACTTGGACGGA AAAATGGCGCGGGGATGTTTCCGGAAGTTTACGGCCCGCGGGCGAG  
[0338] GAAGTGGCGGAAAAATACAGCTATCGCCCAACAGATGCGGAAAAGGGCGGATTCGGCGTGTTTGCCGCAAAAAGAG  
[0339] CAGGATGGATCCGGAGGAGGAGGCCAAAAACGACGAGATGTTAAAAAGCTGCCACTGTGGCCATTTGCTGCTGCC  
[0340] TACAACAATGGCCAAGAAATCAACGGTTTCAAAGCTGGAGAGACCATCTACGACATTGATGAAGACGGCACAATTAAC  
[0341] AAAAAAGACGCAACTGCAGCCGATGTTGAAGCGACGACTTTAAAGGCTTGGGCTGAAAAAAGTCGTGACTAACCTG  
[0342] ACCAAAAACCGTCAATGAAAACAAACAAAACGTCGATGCCAAAGTAAAAGCTGCAGAACTGAAAATAGAAAAGTTAACA  
[0343] ACCAAGTTAGCAGACTGATGCCGCTTTAGCAGATACTGATGCCGCTCTGGATGCAACCACCAACGCCCTTGAATAAA  
[0344] TTGGGAGAAAAATATAACGACATTTGCTGAAGAGACTAAGACAAATATCGTAAAAATTTGATGAAAAATTAGAAGCCGTG  
[0345] GCTGATACCGTCGACAAGCATGCCGAAGCATTC AAGGATATCGCGGATTCATTTGGATGAAACCAACACTAAGGCAGAC  
[0346] GAAGCGTCAAAAACCGCAATGAAGCCAAACAGACGGCCG AAGAAACCAACAAAACGTCGATGCCAAAGTAAAAGCT  
[0347] GCAGAACTGCAGCAGGCAAAGCCGAAAGCTGCCGCTGGCACAGCTAATACTGCAGCCGACAAGGCCGAAAGCTGTGCT  
[0348] GCAAAAGTTACCGACATCAAAGCTGATATCGCTACGAACAAAGATAATATTTGCTAAAAAAGCAAAACAGTCCGACGCTG  
[0349] TACACCAGAGAAGAGTCTGACAGCAAAATTTGTGAGAAATTTGATGGTCTGAAACGCTACTACCGAAAAATTTGGACACACGC  
[0350] TTGGCTTCTGCTGAAAAATCCATTTGCCGATCAGATACTCGCCTGAACGGTTTGGATAAAAACAGTGTGACACCTGGCG  
[0351] AAAGAAAACCGCAAGGCTTGCAGAACAAAGCGCGCTCTCCGCTCTGTTCCAACCTTACAACGTTGGGTCGGTTCAAT

- [0352] GTAACGGCTGCAGTCGGCGGCTACAAATCCGAATCGGCAGTCGCCATCGGTACCGGCTTCCGCTTTACCGAAAACITTT
- [0353] GCCGCCAAAGCAGCGGTGGCAGTCGGCACTTCGTCCGGTTCTTCCGCAGCCTACCATGTCCGGCTCAATTACGAGTGG
- [0354] TAAAAGCTT
- [0355] 1 MASPDVKSAD TLSKPAAPVV SEKETEAKED APQAGSQGQG APSAQGGQDM
- [0356] 51 AAVSEENTGN GGAAATDKPK NEDEGAQNDM PQNAADTDSL TPNHTPASNM
- [0357] 101 PAGNMENQAP DAGESEQPAN QPDMANTADG MQGDDPSAGG ENAGNTAAQG
- [0358] 151 TNQAENNQTA GSQNPASSTN PSATNSGGDF GRTNVGNVSVV IDGPSQNITL
- [0359] 201 THCKGDSCSG NNFLDEEVQL KSEFEKLSDA DKISNYKKDG KNDGKNDKTV
- [0360] 251 GLVADSVQMK GINQYIIFYK PKPTS FARFR RSARSRRSLP AEMPLIPVNQ
- [0361] 301 ADTLIVDGEA VSLTGHSCNI FAPEGNYRYL TYGAEKLP GG SYALRVQGEP
- [0362] 351 SKGEMLAGTA VYNGEVLHFH TENGRPSPSR GRFAAKVDFG SKSVDGIIDS
- [0363] 401 GDGLHMGTK FKAADGNGF KGTWTENGG DVSGKTYGPA GEEVAGKYSY
- [0364] 451 RPTDAEKGGF GVFAKGKEQD GSGGGGATND DDVKKAAATVA IAAAYNNGQE
- [0365] 501 INGFKAGETI YDIDEDGTIT KKDATAADVE ADDFKGLGLK KVVTNLT KTV
- [0366] 551 NENKQNVDAK VKAAESEIEK LTTKLADTDA ALADTDAALD ATTMALNKL G
- [0367] 601 ENITTFAEET KTNIVKIDEK IEAVADTVDK HAEAFNDIAD SLDETNTKAD
- [0368] 651 EAVKTANEAK QTAETKQNV DAKVKAAETA AGKAEAAAAGT ANTAADKAEA
- [0369] 701 VAAKVTDIKA DIATNKDNIA KKANSADVYT REESDSKFVR IDGLNATTEK
- [0370] 751 LDTRLASA EK SIADHDTRLN GLDKTVSDLR KETRQGLAEQ AALSGLFQPY
- [0371] 801 NVGRFNVTAA VGGYKSESAV AIGTGFRFTE NFAAKAGVAV GTSSGSSAAY
- [0372] 851 HVG VNYEW \*
- [0373] 实施例 3-  $\Delta$  G983 的杂交体
- [0374] 蛋白质 983 具有如下序列：
- [0375] 983 →  $\Delta$  G983
- [0376] 1 MRTTPTFPTK TFKPTAMALA VATTLSACLG GGGGGTSAPD FNAGGTGIGS
- [0377] 51 NSRATTAKSA AVSYAGIKNE MCKDRSMLCA GRDDVAVTDR DAKINAPPPN
- [0378] 101 LHTGDFPNPN DAYKNLNLK PAIEAGYTGR GVEVGIVDTG ESVGSISFPE
- [0379] 151 LYGRKEHGYN ENYKNYTAYM RKEAPEDGGG KDIEASFDD E AVIETEAKPT
- [0380] 201 DIRHVKEIGH IDLVSHIIGG RSV DGRPAGG IAPDATLHIM NTNDETKNEM
- [0381] 251 MVAAIRNAWV KLG ERGVRIV NNSFGTTSRA GTADLFQIAN SEEQYRQALL
- [0382] 301 DYSGGDKTDE GIRLMQSDY GNLSYHIRNK NMLFIFSTGN DAQAQPNTYA
- [0383] 351 LLPFYEKDAQ KGIITVAGVD RSGEKFKREM YGEPGTEPLE YGSNHCGITA
- [0384] 401 MWCLSAPYEA SVRFTRTNPI QIAGTSFSAP IVTGTAALLL QKYPWMSNDN
- [0385] 451 LRTLLTTAQ DIGAVGVDSK FGWGLLDAGK AMNGPASFPF GDFTADTKGT
- [0386] 501 SDIAYSFRND ISGTGGLIKK GGSQQLQHGN NTYTGKTIE GGSLVLYGNN
- [0387] 551 KSDMRVETKG ALIYNGAASG GSLNSDGI VY LADTDQSGAN ETVHIKGS LQ
- [0388] 601 LDGKGTLYTR LGKLLKVDGT AII GGKLYMS ARGKGAGYLN STGRRVPF LS
- [0389] 651 AAKIGQDYSF FTNIETD GGL LASLDSVEKT AGSEGDTLSY YVRRGNAART
- [0390] 701 ASAAAHSAPA GLKHAVEQGG SNLENLMVEL DASESSATPE TVE TAAADRT

[0391] 751 DMPGIRPYGA TFRAAAQVQH ANAADGVRIF NSLAATVYAD STAAHADMQG  
 [0392] 801 RRLKAVSDGL DHNGTGLRVI AQTQQDGGTW EQGGVEGKMR GSTQTVGIAA  
 [0393] 851 KTGENTTAAA TLGMGRSTWS ENSANAKTDS ISLFAGIRHD AGDIGYLKGL  
 [0394] 901 FSYGRYKNSI SRSTGADEHA EGSVNGTLMQ LGALGGVNPV FAATGDLTVE  
 [0395] 9. 51 GGLRYDLLKQ DAFAEKGSAL GWSGNSLTEG TLVGLAGLKL SQPLSDKAVL  
 [0396] 1001 FATAGVERDL NGRDYTVTGG FTGATAATGK TGARNMPHTR LVAGL GADVE  
 [0397] 1051 FGNGWNLAR YSYAGSKQYG NHSGRVGVGY RF\*

[0398] 因此△ G983 具有如下基本序列：

[0399] TSAPD FNAGGTGIGS  
 [0400] NSRATTAKSA AVSYAGIKNE MCKDRSMLCA GRDDVAVTDR DAKINAPPPN  
 [0401] LHTGDFPNPN DAYKNLNLK PAIEAGYTGR GVEVGIVDTG ESVGSISFPE  
 [0402] LYGRKEHGYN ENYKNYTAYM RKEAPEDGGG KDIEASFDDE AVIETEAKPT  
 [0403] DIRHVKEIGH IDLVSHIIGG RSVDRPAGG IAPDATLHTM NTNDETKNEM  
 [0404] MVAAIRNAWV KLGERGVRIV NNSFGTTSRA GTADLFQIAN SEEQYRQALL  
 [0405] DYSGGDKTDE GIRLMQQSDY GNLSYHIRNK NMLFIFSTGN DAQAQPNTYA  
 [0406] LLPFYEKDAQ KGIITVAGVD RSGEKFKREM YGEPGTEPLE YGSNHCGITA  
 [0407] MWCLSAPYEA SVRFTRTNPI QIAGTSFSAP IVTGTAALLL QKYPWMSNDN  
 [0408] LRTTLLTTAQ DIGAVGVDSK FGWGLLDAGK AMNGPASFPF GDFADTKGT  
 [0409] SDIAYSFRND ISGTGGLIKK GGSQQLHGN NTYTGKTIIE GGSLVLYGN  
 [0410] KSDMRVETKG ALTYNGAASG GSLNSDGIYV LADTDQSGAN ETVHIKGSLLQ  
 [0411] LDGKGTLYTR LGKLLKVDGT AIIGGKLYMS ARGKGAGYLN STGRRVPFLS  
 [0412] AAKIGQDYSF FTNIETDGG LSLDSVEKT AGSEGDLSY YVRRGNAART  
 [0413] ASAAAHSAPA GLKHAVEQGG SNLENLMVEL DASESSATPE TVETAAADR  
 [0414] DMPGIRPYGA TFRAAAQVQH ANAADGVRIF NSLAATVYAD STAAHADMQG  
 [0415] RRLKAVSDGL DHNGTGLRVI AQTQQDGGTW EQGGVEGKMRGSTQTVGIAA  
 [0416] KTGENTTAAA TLGMGRSTWS ENSANAKTDS ISLFAGIRHD AGDIGYLKGL  
 [0417] FSYGRYKNSI SRSTGADEHA EGSVNGTLMQ LGALGGVNPV FAATGDLTVE  
 [0418] GGLRYDLLKQ DAFAEKGSAL GWSGNSLTEG TLVGLAGLKL SQPLSDKAVL  
 [0419] FATAGVERDL NGRDYTVTGG FTGATAATGK TGARNMPHTR LVAGLGADVE  
 [0420] FGNGWNLAR YSYAGSKQYG NHSGRVGVGY RF\*

[0421] 将△ G983 作为在其 C- 末端与 ORF46. 1、741、961 或 961C 的杂交体表达：

[0422] △ G983-ORF46. 1

[0423] ATGACTTCTGCGCCGACTTCAATGCAGGCGGTACCGGTATCGGCAGCAACAGCAGACAAACACGCGAAATCAGCA  
 [0424] GCAGTATCTTACGCCGGTATCAAGAACGAAATGTGCAAAGACAGAAGCATGCTCTGTGCGCGGTCCGGATGACGTTGCC  
 [0425] GTTACAGACAGGGATGCCAAAATCAATGCCCCCCCCCGAATCTGCATACCGGAGACTTTCCAAAACCCAAATGACGCA  
 [0426] TACAAGAATTTGATCAACCTCAAACCTGCAATTGAAGCAGGCTATACAGGACGCGGGGTAGAGGTAGGTATCGTCGAC  
 [0427] ACAGGCGAATCCGTCGGCAGCATATCCTTTCCCGAACTGTATGGCAGAAAAGAACACCGCTATAACGAAAATTACAAA  
 [0428] AACTATACGGGTATATGCGGAAGGAAGCGCCTGAAGACGGAGCGGTAAAGACATTGAAGCTTCTTTCCGACGATGAG  
 [0429] GCCGTTATAGAGACTGAAGCAAAGCCGACGATATCCGCCACGTAAAAGAAAATCGGACACATCGATTTGGTCTCCCAT



[0430] ATTTATTGGCGGGCGTTCCGTGGACGGCAGACCTGCAGGCGGTATTGCGCCCGATGCGACGCTACACATAATGAATACG  
[0431] AATGATGAAACCAAGAAACGAAATGATGGTTGCAGCCATCCGCAATGCATGGGTCAAGCTGGGCGAAACGTGGCGTGGCG  
[0432] ATCGTCAATAACAGTTTTTGGAAACAACATCGAGGGCAGGCACCTGCCACCTTTTCCAAATAGCCAAATTCGGAGGAGCAG  
[0433] TACCGCCAAGCGTTGCTCGACTATTCCGGCGGTGATAAAAACAGACGAGGGTATCCGCCTGATGCAACAGAGCGATTAC  
[0434] GGCAACCTGTCTTACCACATCCGTAATAAAAAACATGCTTTTTCATCTTTTTCGACAGGCAATGACGCACAAGCTCAGCCC  
[0435] AACACATATGCCCTATTGCCATTTTATGAAAAAGACGCTCAAAAAGGCATTATCACAGTCGCAGGCGTAGACCCGAGT  
[0436] GGAGAAAAGTTCAAACGGGAAAATGTATGGAGAACCGGGTACAGAACCGCTTGAGTATGGCTCCAACCATTCGCGAATT  
[0437] ACTGCCATGTGGTGCCTGTGCGCACCCCTATGAAGCAAGCGTCCGTTTACCCGTACAAAACCCGATTCAAATTCGCCGA  
[0438] ACATCCTTTTCCGCACCCATCGTAACCGGCACGGCGGCTCTGCTGCTGCAGAAAATACCCGTGGATGAGCAACGACAAC  
[0439] CTGGGTACCACGTTGCTGACGACGGCTCAGGACATCGGTGCAGTCGGCGTGGACAGCAAGTTCCGGCTGGGACTGCTG  
[0440] GATGCGGGTAAGGCCATGAACGGACCCGCTCCTTTCCGTTTCGGCGACTTTACCGCCGATACGAAAGGTACATCCGAT  
[0441] ATTGCCCTACTCCTTCCGTAACGACATTTTCAGGCACGGGCGGCTGATCAAAAAAGGCGGCAGCCAACTGCAACTGCAC  
[0442] GGCAACAACACCTATAACGGGCAAAACCATTTATCGAAGGCGGTTTCGCTGGTGTGTGTACGGCAACAACAAATCGGATATG  
[0443] CGCGTCGAAACCAAAGGTGCGCTGATTTATAACGGGCGGCATCCGGCGGCAGCCTGAACAGCGACGGCATTTGTCTAT  
[0444] CTGGCAGATACCGACCAATCCGGCGCAAAACGAAACCGTACACATCAAAGGCAGTCTGCAGCTGGACGGCAAAGGTACG  
[0445] CTGTACACACGTTTGGGCAAACTGCTGAAAGTGGACGGTACGGCGATTATCGGGCGCAAGCTGTACATGTCGGCACGC  
[0446] GGCAAGGGGGCAGGCTATCTCAACAGTACCGACGACGTGTTCCCTTCCGAGTGCAGCCAAAATCGGGCAGGATTAT  
[0447] TCTTTCTTCAAAAACATCGAAAACCGACGGCGGCTGCTGGCTTCCCTCGACAGCGTCGAAAAACAGCGGGCAGTGAA  
[0448] GCGGACACGCTGTCTATTTATGTCGGTCGCGCAATGCGGCACGGACTGCTTCGGCAGCGGCACATTCGCGCCCGCC  
[0449] GGTCTGAAACACGCGCTAGAACAGGGCGGCAGCAATCTGGAAAACCTGATGGTTCGAACTGGATGCCTCCGAATCATCC  
[0450] GCAACACCCGAGACGGTTGAAAACGCGGCAGCCGACCGACAGATATGCCGGCATCCGCCCTACGGCGCAACTTTC  
[0451] CGCGCAGCGGCAGCCGTACAGCATGCGAATGCCCGGACGGTGTACGCATCTTCAACAGTCTCGCCGCTACCGTCTAT  
[0452] GCCGACAGTACCGCCGCCATGCCGATATGCAGGGACGCCGCTGAAAGCCGTATCGGACGGGTTGGACCACAACGGC  
[0453] ACGGTTCTGCGGTCATCGCGCAAACCCAAACAGGACGGTGGAACTGGGAAACAGGGCGGTGTTGAAGGCAAAATGCGC  
[0454] GGCAGTACCCAAACCGTCGGCATTTGCCGCAAAACCGGCGAAAATACGACAGCAGCCGCCACACTGGGCATGGGACGC  
[0455] AGCAGATGGAGCGAAAACAGTGCAAAATGCAAAAACCGACAGCATTAGTCTGTTTGCAGGCATACGGCACGATGCGGGC  
[0456] GATATCGGCTATCTCAAAGGCTGTTCTCCTACGGACGCTACAAAAACAGCATCAGCCGAGCACCGGTGCGGACGAA  
[0457] CATGCGGAAGGCAGCGTCAAACGGCACGCTGATGCAGCTGGGCGCACTGGGCGGTGTCAACTTCGTTTGGCCAAACG  
[0458] GGAGATTTGACGGTTCGAAGGCGGTCTGCGCTACGACCTGCTCAAACAGGATGCATTCGCGGAAAAAGGCAGTGCTTTG  
[0459] GGCTGGAGCGGCAACAGCCTCACTGAAGGCACGCTGGTTCGACTCGCGGTTCTGAAGCTGTGCAACCCCTTGAGCGAT  
[0460] AAAGCCGTCTGTTTGCACGGCGGGCGTGAACCGGACCTGAAACGGACGCGACTACAGGTAACGGGCGGCTTTACC  
[0461] GCGCGACTGCAGCAACCGCAAGACGGGGCACGCAATATGCCGCACCCGCTCTGGTTGCCGGCTGGGCGCGGAT  
[0462] GTCGAATTCGGCAACGGCTGGAACGGCTTGGCACGTTACAGCTACCGCGTTCCAAACAGTACGGCAACCACAGCGGA  
[0463] CGAGTCGGCTAGGCTACCGTTCCCTCGACGGTGGCGGAGGCACTGGATCCTCAGATTTGGCAAACGATTCTTTTATC  
[0464] CGGCAGGTTCTCGACGTCAGCATTTTCGAAACCGACGGGAAATACCCTATTTCGGCAGCAGGGGGAACTTCGCCAG  
[0465] CGCAGCGGCCATATCGGATTGGGAAAAATACAAAGCCATCAGTTGGGCAACCTGATGATTCAACAGGCGGCCATTA  
[0466] GGAAATATCGGCTACATTTGTCGGCTTTTCCGATCACGGCACGAAAGTCCATTCOCCCTTCGACAACCATGCCTCACAT  
[0467] TCCGATTTCTGATGAAGCCGTTAGTCCCGTTGACGGATTTAGCCTTTACCGCATCCATTTGGGACGGATACGAACCCAT  
[0468] CCCGCCGACGGCTATGACGGGCCACAGGGCGGCGCTATCCCGCTCCCAAAGGCGGAGGGATATATACAGCTACGAC

[0469] ATAAAAGGCGTTGCCAAAATATCCGCCTCAACCTGACCGACAACCGCAGCACCGGACAACGGCTTGCCGACCGTTTC  
 [0470] CACAATGCCGGTAGTATGCTGACGCAAGGAGTAGGCGACGGATTCAAACGCGCCACCCGATACAGCCCGAGCTGGAC  
 [0471] AGATCGGGCAATGCCGCCGAAGCCTTCAACGGCACTGCAGATATCGTTAAAAACATCATCGGCGCGCAGGAGAAATT  
 [0472] GTCGCGCAGGCGATGCCGTGCAGGGCATAAGCGAAGGCTCAAACATTGCTGTATGCACGGCTTGGGTCTGCTTTCC  
 [0473] ACCGAAAACAAGATGGCGCGCATCAACGATTTGGCAGATATGGCGCAACTCAAAGACTATGCCGCAGCAGCCATCCGC  
 [0474] GATTGGGCAGTCCAAAACCCCAATGCCGCACAAGGCATAGAAGCCGTCAGCAATATCTTTATGGCAGCCATCCCCATC  
 [0475] AAAGGGATTGGAGCTGTTCCGGGAAAATACGGCTTGGGCGGCATCACGGCACATCCTATCAAGCGGTGCGAGATGGGC  
 [0476] GCGATCGCATTGCCGAAAGGGAAAATCCGCGTCAGCGACAATTTTGGCGATGCGGCATACGCCAAATACCCGTCCCCT  
 [0477] TACCATTCCCAGAAATATCCGTTCAAACCTTGGAGCAGCGTTACGGCAAAGAAAACATCACCTCCTCAACCGTGCCGCCG  
 [0478] TCAAACGGCAAAAATGTCAAACCTGGCAGACCAACGCCACCCGAAGACAGGCGTACCGTTTGACGGTAAAGGGTTTCCG  
 [0479] AATTTTGAGAAGCACGTGAAATATGATACGCTCGAGCACCACCACCACCACCTGA  
 [0480] 1 MTSAPDFNAG GTGIGSNSRA TTAKSAAVSY AGIKNEMCKD RSMLCAGRDD  
 [0481] 51 VAVTDRDAKI NAPPPNLHTG DFPNPNDAYK NLINLKPAIE AGYTGRGVEV  
 [0482] 101 GIVDTGESVG SISFPELYGR KEHGYNENYK NYTAYMRKEA PEDGGGKDIE  
 [0483] 151 ASFDDEAVIE TEAKPTDIRH VKEIGHIDLK SHIIGGRSVD GRPAGGIAPD  
 [0484] 201 ATLHIMNTND ETKNEMVAA IRNAWVKLGE RGVRIVNNSF GTTSRAGTAD  
 [0485] 251 LFQIANSEEQ YRQALLDYSY GDKTDEGIRL MQQSDYGNLS YHIRNKNMLF  
 [0486] 301 IFSTGNDAQA QPNTYALLPF YEKDAQKGI TVAGVDRSGE KFKREMYGEP  
 [0487] 351 GTEPLEYGSN HCGITAMWCL SAPYEASVRF TRTNPIQIAG TSFSAPIVTG  
 [0488] 401 TAALLLQKYP WMSNDNLRTT LLTTAQDIGA VGVDSKFGWG LLDAGKAMNG  
 [0489] 451 PASFPFGDFT ADTKGTS DIA YSFRNDISGT GGLIKKGGSQ LQLHGNNTYT  
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 [0694] GCGGACACGCTGTCTATTTATGTCCGTCCGGCAATGCGGCACGGACTGCTTCGGCAGCGGCACATTCGGCGCCCGCC  
 [0695] GGTCTGAAACACGCGTAGAACAGGGCGGACGCAATCTGGAACCTGATGGTCCAACTGGATGCCTCCGAATCATCC  
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 [0697] CGCGCAGCGGCAGCCGTACAGCATGCGAATGCCCGGACGGTGTACGCATCTTCAACAGTCTCCCGCTACCGTCTAT  
 [0698] GCCGACAGTACCGCCGCCATGCCGATATGCAGGACGCGGCTGAAAGCGGTATCGGACGGGTTGGACCACAACGGC  
 [0699] ACCGGTCTGCGGTCATCCGCAAACCCAAACAGGACGGTGGAACTGGGAAACAGGGCGGTGTTGAAGGCAAAAATGCGC  
 [0700] GGCAGTACCCAAACCGTCCGCATTTGCCGGAACCGGGCGAAAATACGACAGCAGCCGCCACACTGGGCATGGGAACG  
 [0701] AGCACATGGAGCGAAAACAGTGCAAAATGCAAAAACCGACAGCATTAGTCTGTTTGCAGGCATACGGCACGATGCGGGC  
 [0702] GATATCGGCTATCTCAAAGGCTGTTCTCCTACGGACGCTACAAAAACAGCATCAGCCGACGACCCGGTGGGACGAA

[0703] CATGCGGAAGGCAGCGTCAACGGCACGCTGATGCAGCTGGGCGCACTGGGCGGTGTCAAAGTTCGGTTTGCCGCAACG  
[0704] GGAGARTTGACGGTTCGAAGGCGGTCTGCGCTACGACCTGCTCAAACAGGATGCATTCGCCGAAAAAGGCAGTGCTTTG  
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[0706] AAAGCCGTCCTGTTTGAACGGCGGGCGTGAACGCGACCTGAACGGACGCGACTACACGGTAACGGGCGGCTTTACC  
[0707] GGCGCGACTGCAGCAACCGGCAAGACGGGGCACGCAATATGCCGCACACCCGCTCTGGTTGCCGGCCTGGGCGCGGAT  
[0708] GTCGAATTCGGCAACGGCTGGAACGGCTTGGCACGTTAGAGCTACGCCGGTTCCAAACAGTACGGCAACCACAGCGGA  
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[0710] GCTGCCACTGTGGCCATTGCTGCTGCCTACAACAATGGCCAAGAAATCAACGGTTTCAAAGCTGGAGAGACCATCTAC  
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[0712] GGTCTGAAAAAGTCGTGACTAACCTGACCAAAACCGTCAATGAAAAACAAAACGTCGATGCCAAAAGTAAAAGCT  
[0713] GCAGAACTTGAAATAGAAAAAGTTAACAACCAAGTTAGCAGACACTGATGCCGCTTTAGCAGATACTGATGCCGCTCTG  
[0714] GATGCAACCACCAACGCCCTTGAATAAATTTGGGAGAAAATATAACGACATTTGCTGAAGAGACTAAGACAAATATCGTA  
[0715] AAAATTGATGAAAAATTAGAAGCCGTGGCTGATACCGTCGACAAGCATGCCGAAGCATTCAACGATATCGCCGATTCA  
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[0720] GCTACTACGAAAAAATGGACACACGCTTGGCTTCTGCTGAAAAATCCATTGCCGATCACGATACTCGCCTGAACGGT  
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[0722] CAACCTTACAACGTGGGTCTCGAGCACCACCACCACCACCCTGA  
[0723] 1 MTSAPDFNAG GTGIGSNSRA TTAKSAAVSY AGIKNEMCKD RSMCAGRDD  
[0724] 51 VAVTDRDAKI NAPPPNLHTG DFPNPNDAYK NLINLKPAIE AGYTGRGVEV  
[0725] 101 GIVDTGESVG SISFPELYGR KEHGYNENYK NYTAYMRKEA PEDGGGKDIE  
[0726] 151 ASFDDEAVIE TEAKPTDIRH VKEIGHIDL V SHIIGGRSVD GRPAGGIAPD  
[0727] 201 ATLHIMNTND ETKNEMVAA IRNAWVKLGE RGVRIVNSF GTTSRAGTAD  
[0728] 251 LFQIANSEEQ YRQALLDYSG GDKTDEGIRL MQQSDYGNLS YHIRNKNMLF  
[0729] 301 IFSTGNDAQA QPNTYALLPF YEKDAQKGI TVAGVDRSGE KFKREMYGEP  
[0730] 351 GTEPLEYGSN HCGITAMWCL SAPYEASVRF TRTNPIQIAG TSFSAPIVTG  
[0731] 401 TAALLLQKYP WMSNDNLRTT LLTTAQDIGA VGVDSKTGWG LLDAGKAMNG  
[0732] 451 PASFPFGDFT ADTKGTS DIA YSFRNDISGT GGLIKKGGSQ LQLHGNNTYT  
[0733] 501 GKTIIEGGSL VLYGNKSDM RVETKGALIY NGAASGGSLNSDGIVYLADT  
[0734] 551 DQSGANETVH IKGSLQLDGK GTLYTRLGKL LKVDGTATIG GKLYMSARGK  
[0735] 601 GAGYLNSTGR RVPFLSAAKI GQDYSFFTNI ETDGGLLASL DSVEKTAGSE  
[0736] 651 GD TLSYVRR GNAARTASAA AHSAPAGLKH AVEQGGSNLE NLMVELDASE  
[0737] 701 SSATPETVET AAADRTDMPG IRPYGATFRA AAAVQHANA DGVRIFNLSA  
[0738] 751 ATVYADSTAA HADMQRRLK AVSDGLDHNG TGLRVIAQTQ QDGGTWEQGG  
[0739] 801 VEGKMRGSTQ TVGIAAKTGE NTTAAATLGM GRSTWSENSA NAKTDSISLF  
[0740] 851 AGIRHDAGDI GTLKGLFSYG RYKNSISRST GADEHAEGSV NGTLMQLGAL  
[0741] 901 GGVNVPFAAT GDLTVEGGLR YDLLKQDAFA KKGSA LGWSG NSLTTEGTLVG



[0742] 951 LAGLKLSQPL SDKAVLFATA GVERDLNGRD YTVTGGFTGA TAATGKTGAR  
 [0743] 1001 NMPHTRLVAG LGADVEFGNG WNLARYSYA GSKQYGNHSG RVGVGYRFLE  
 [0744] 1051 GGGGTGSATN DDDVKKAATV AIAAAYNNGQ EINGFKAGET IYDIDEDGTI  
 [0745] 1101 TKKDATAADV EADDFKGLGL KKVVTNLTKT VVENKQNVDA KVKAASEIE  
 [0746] 1151 KLTTKLADTD AALADTDAAL DATTNALNKL GENITTFAE TKTNIIVKIDE  
 [0747] 1201 KLEAVADTVD KHAEAFNDIA DSLDETNTKA DEAVKTANEA KQTAEETKQN  
 [0748] 1251 VDAKVKAAET AAGKAEAAAAG TANTAADKAE AVAAKVTDIK ADIATNKDNI  
 [0749] 1301 AKKANSADV TREESDSKFV RIDGLNATTE KLDTRLASAE KSIADHDTRL  
 [0750] 1351 NGLDKTVSDL RKETRQGLAE QAALSGLFQP YNVGLEHHHH HH \*

[0751] 实施例 4-  $\Delta$  G741 的杂交体

[0752] 蛋白质 741 具有如下序列：

[0753] 1 VNRTAFCCLS LTTALILTAC SSGGGGVAAD IGAGLADALT APLDCHKDKGL  
 [0754] 51 QSLTLDQSVR KNEKLKLAQ GAEKTYGNGD SLNTGKLNK KVSRLFDFIRQ  
 [0755] 101 IEVDGQLITL ESGEFQVYKQ SHSALTAFQT EQIQDSEHSG KMAKRQFRI  
 [0756] 151 GDIAGEHTSF DKLPEGGRAT YRGTAFGSDD AGGKLYTID FAAKQNGKI  
 [0757] 201 EHLKSPENLV DLAAADIKPD GKRHAVISGS VLYNQAEKGS YSLGIFGGKA  
 [0758] 251 QEVAGSAEVK TVNGIRHIGL AAKQ \*

[0759] 因此， $\Delta$  G741 具有如下基本序列：

[0760] VAAD IGAGLADALT APLDCHKDKGL  
 [0761] QSLTLDQSVR KNEKLKLAQ GAEKTYGNGD SLNTGKLNK KVSRLFDFIRQ  
 [0762] IEVDGQLITL ESGEFQVYKQ SHSALTAFQT EQIQDSEHSG KMAKRQFRI  
 [0763] GDIAGEHTSF DKLPEGGRAT YRGTAFGSDD AGGKLYTID FAAKQNGKI  
 [0764] EHLKSPENLV DLAAADIKPD GKRHAVISGS VLYNQAEKGS YSLGIFGGKA  
 [0765] QEVAGSAEVK TVNGIRHIGL AAKQ \*

[0766] 将  $\Delta$  G741 直接融合于蛋白质 961、961C、983 和 ORF46.1 的符合读框的上游：

[0767]  $\Delta$  G741-961

[0768] ATGGTCGCCGCCGACATCGGTGCGGGCTTGGCGATGCACTAACCGCACCGCTCGACCATAAAGACAAAGGTTTGCAG  
 [0769] TCTTTGACGCTGGATCAGTCCGTCAGGAAAAACGAGAACTGAAGCTGGCGGCACAAGGTGCGGAAAAACTTATGGA  
 [0770] AACGGTGACAGCCTCAATACGGCAAATGAAGAACGACAAGGTCAGCCGTTTTCGACTTTATCCGCCAAATCGAAGTG  
 [0771] GACGGGCAGCTCATTTACCTTGGAGAGTGGAGAGTTCCAAGTATACAAACAAAGCCATTCGCCCTTAAACCGCTTTTCAG  
 [0772] ACCGAGCAAATACAAGATTCGGAGCATTCGGGAAGATGGTTGCGAAAACGCCAGTTTCAGAATCGGCGACATGGCGGGC  
 [0773] GAACATACATCTTTTGACAAGCTTCCCGAAGGCGGCAGGGCGACATATCGCGGGACGGCGTTCCGTTTCAGACGATGCC  
 [0774] GGCGAAAACTGACCTACACCATAGATTTCCGCCCAAGCAGGAAAACGGCAAAATCGAACATTTGAAATCGCCAGAA  
 [0775] CTCAATGTGACCTGGCCGCCGCCGATATCAAGCCGCATGGAAAAACCCATGCCGTCATCAGCGGTTCCGTTCTTTAC  
 [0776] AACCAAGCCGAGAAAGGCAGTTACTCCCTCGGTATCTTTGGCGAAAAGCCAGGAAGTTGCCGCGAGCGCGGAAGTG  
 [0777] AAAACCGTAAACCGCATAACCCATATCGCCCTTGGCGCAAGCAACTCGAGGGTGGCGGAGGCACTGGATCCGCCACA  
 [0778] AACGACGACGATGTTAAAAAGCTGCCACTGTGGCCATTGCTGCTGCCTACAACAATGGCCAAGAAATCAACGGTTTC  
 [0779] AAAGCTGGAGAGACCATCTACGACATTTGATGAAGACGGCACAATACCAAAAAAGACGCAACTGCAGCCGATGTTGAA  
 [0780] GCCGACGACTTTAAAGGTCTGGGTCTGAAAAAGTGTGACTAACCTGACCAAAACCGTCAATGAAAAACAAACAAAAC

[0781] GTCGATGCCAAAGTAAAAGCTGCAGAATCTGAAATAGAAAAGTTAACAACCAAGTTAGCAGACACTGATGCCGCTTTA  
 [0782] GCAGATACTGATGCCGCTCTGGATGCAACCACCAACGCCTTGAATAAATTTGGGAGAAAAATAACGACATTTGCTGAA  
 [0783] GAGACTAAGACAAATATCGTAAAAATTTGATGAAAAATTAGAAGCCGTGGCTGATACCGTCGACAAGCATGCCGAAGCA  
 [0784] TTCAACGATATCGCCGATTCATTTGGATGAAACCAACACTAAGGCAGACGAAAGCCGTCAAAAACCGCCAATGAAGCCAAA  
 [0785] CAGACGGCCGAAGAAACCAACAAAACGTCGATGCCAAAGTAAAAGCTGCAGAACTGCAGCAGGCAAAGCCGAAGCT  
 [0786] GCCGCTGGCACAGCTAATACTGCAGCCGACAAGGCCAAGCTGTCGCTGCAAAAAGTTACCGACATCAAAGCTGATATC  
 [0787] GCTACGAACAAAGATAATATTGCTAAAAAAGCAAACAGTGCAGCAGCTGTACACCAGAGAAGAGTCTGACAGCAAATTT  
 [0788] GTCAGAATTGATGGTCTGAACGCTACTACCGAAAAATTTGGACACACGCTTTGGCTTCTGCTGAAAAATCCATTGCCGAT  
 [0789] CACGATACTCGCCTGAACGGTTTGGATAAAACAGTGTTCAGACCTGCGCAAAGAAACCCGCCAAGGCCTTGCAGAAACAA  
 [0790] GCCGCGCTCTCCGGTCTGTTCACACCTTACAACGTTGGGTTCGCTTCAATGTAACGGCTGCAGTCCGCGGCTACAAAATCC  
 [0791] GAATCGGCAGTCCCATCGGTACCGGCTTCCGCTTTACCGAAAACTTTGCCGCCAAAGCAGGCGTGGCAGTCCGCACT  
 [0792] TCGTCCGGTCTTCCGCGAGCCTACCATGTCCGGCTCAATTACGAGTGGCTCGAGCACCACCACCACCACCCTGA  
 [0793] 1 MVAADIGAGL ADALTAPLDH KDKGLQSLTL DQSVRKNEKL KLAAQGA EKT  
 [0794] 51 YGNGLSLNTG KLKNDKVSFR DFIRQIEVDG QLITLES GEF QVYKQSHSAL  
 [0795] 101 TAFQTEQIQD SEHSGKMOVAK RQFRIGDIAG EHTSFDKLPE GGRATYRGT A  
 [0796] 151 FGSDDAGGKL TYTIDFAAKQ GNGKIEHLKS PELNVDLAAA DIKCPDGKRHA  
 [0797] 201 VISGSVLYNQ AEKGSYSLGI FGGKAQEVAG SAEVKT VNGI RHIGLAAKQL  
 [0798] 251 EGGGGTGSAT NDDDVKKAAT VAIAAAYNNG QEINGFKAGE TIYDIDEDGT  
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 [0800] 351 EKLTTKLADT DAALADTDAA LDATTNALNK LGEKNTTFAE ETKTNIVKID  
 [0801] 401 EKLEAVADTV DKHAEAFNDI ADSLDETNTK ADEAVKTANE AKQTAEETKQ  
 [0802] 451 NVDKVKAAE TAAGKAEAAA GTANTAADKA EAVA AKVTDI KADIATNKDN  
 [0803] 501 IAKKANSADV YTREESDSKF VRIDGLNATT EKLDTRLASA EKSIADHDTR  
 [0804] 551 LNGLDKTVSD LRKETRQGLA EQAALSGLFQ PYNVGRFNVT AAVGGYKSES  
 [0805] 601 AVAIGTGFRF TENFAAKAGV AVGTSSGSSA AYHVG VNYEW LEHHHHHHH \*  
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[0895] 51 YGNGDSLNTG KLKNDKVSFR DFIRQIEVDG QLITLESGEF QVYKQSHSAL  
[0896] 101 TAFQTEQIQD SEHSGKMVAK RQFRIGDIAG EHTSFDKLPE GGRATYRGTA  
[0897] 151 FGSDDAGGKL TYTIDFAAKQ GNGKIEHLKS PELNVDLAAA DIKPDGKRHA

[0898] 201 VISGSVLYNQ AKKGSYSLGI FGGKAQEVAG SAEVKTVNGI RHIGLAAKQL  
 [0899] 251 EGSGGGGTSA PDFNAGGTGI GSNSRATTAK SAAVSYAGIK NEMCKDRSML  
 [0900] 301 CAGRDDVAVT DRDAKINAPP PNLHTGDFPN PNDAYKNLIN LKPA 工 EAGYT  
 [0901] 351 GRGVEVGIVD TGESVGSISF PELYGRKEHG YNENYKNYTA YMRKEAPEDG  
 [0902] 401 GGDIEASFD DEAVIETEAK PTDIRHVKEI GHIDLVSHII GGRSVDGRPA  
 [0903] 451 GGIAPDATLH IMNTNDETKN EMMVAAIRNA WVKLGERGVR IVNNSFGTTS  
 [0904] 501 RAGTADLFQI ANSEEQYRQA LLDYSGGDKT DEGIRLMQQS DYGNLSYHIR  
 [0905] 551 NKNMLFIFST GNDAQAQPNT YALLPFYEKD AQKGIITVAG VDRSGEKFKR  
 [0906] 601 EMYGEPGTEP LEYGSNHCGI TAMWCLSAPY EASVRFTRTN PIQIAGTSFS  
 [0907] 651 APIVTGTAAL LLQKYPWMSN DNLRTLLTT AQDIGAVGVD SKFGWGLDA  
 [0908] 701 GKAMNGPASF PFGDFTADTK GTSDIAYSFR NDISGTGGLI KKGGSQQLLAH  
 [0909] 751 GNNTYTGKTI IEGGSLVLYG NNKSDMRVET KGALIYNGAA SGGSLNSDGI  
 [0910] 801 VYLADTDQSG ANETVHIKGS LQLDGKGTLY TRLGKLLKVD GTAIIGGKLY  
 [0911] 851 MSARGKGAGY LNSTGRRVPF LSAAKIGQDY SFFTNIETDG GLLASLDSVE  
 [0912] 901 KTAGSEGDTL SYVVRRGNAA RTASAAHSA PAGLKHAVEQ GGSNLENLMV  
 [0913] 951 ELDASESSAT PETVETAAAD RTDMPGIRPY GATFRAAAAV QHANAADGVR  
 [0914] 1001 IFNSLAATVY ADSTAAHADM QGRRRLKAVSD GLDHNGTGLR VIAQTQQDGG  
 [0915] 1051 TWEQGGVEGK MRGSTQTVGI AAKTGENTTA AATLGMGRST WSENSANAKT  
 [0916] 1101 DSISLFAGIR HDAGDIGYK GLFSYGRYKN SISRSTGADE HAEGSVNGTL  
 [0917] 1151 MQLGALGGVN VPFAATGDLT VEGGLRYDLL KQDAFAEKGS ALGWSGNSLT  
 [0918] 1201 EGTLVGLAGL KLSQPLSDKA VLFATAGVER DLNGRDYTVT GGFTGATAAT  
 [0919] 1251 GKTGARNMPH TRLVAGLGAD VEFNGWNGL ARYSYAGSKQ YGNHSGRVGV  
 [0920] 1301 GYRFLEHHHH HH \*  
 [0921] Δ G741-ORF46. 1  
 [0922] ATGGTCCCGCCGACATCCGGTCCGGGGCTTGCCGATGCACTAACCGCACCGCTCCACCATAAAGACAAAGGTTTGCAG  
 [0923] TCTTTGACGCTGGATCAGTCCGTCAGGAAAAACGAGAACTGAAGCTGGCGGCACAAGGTGCGGAAAAAATTATGGA  
 [0924] AACGGTGACAGCCTCAATACGGGCAAATGAAGAACGACAAGGTCAGCCGTTTCCGACTTTATCCGCCAAATCGAAGTG  
 [0925] GACGGGCAGCTCATTACCTTGGAGAGTGGAGAGTTCCAAGTATACAAACAAAGCCATTCGCCCTTAAACCGCTTTTCAG  
 [0926] ACCGAGCAAATACAAGATTCGGAGCATTCGGGAAGATGGTTGCGAAAACGCCAGTTTCAGAATCCGGCAGATAGCGGGC  
 [0927] GAACATACATCTTTTGACAAGCTTCCCGAAGGCGGCAGGGCGACATATCGCGGGACGGCGTTCCGGTTTCAGACGATGCC  
 [0928] GCGGAAAACTGACTACACCATAGATTTCCGCCCAAGCAGGGAAAACGGAAATCGAACATTTCCGAAATCGCCAGAA  
 [0929] CTCAATGTCCGCTGGCCGCCGCCGATATCAAGCCGGATGGAAAAACCCATGCCGTCATCAGCGGTTCCGTCCTTTAC  
 [0930] AACCAAGCCGAGAAAGGCAGTTACTCCCTCGGTATCTTTGGCGGAAAAGCCAGGAAGTTGCCGCCAGCGCGGAAGTG  
 [0931] AAAACCGTAAACGGCATAAGCCATATCGGCCTTGCCGCCAAGCAACTCGACGGTGGCGGAGGCACTGGATCCTCAGAT  
 [0932] TTGGCAAACGATCTTTTTATCCGGCAGGTTCTCGACCGTCAGCATTTTGAACCCGACGGGAAATACCACCTATTCGGC  
 [0933] AGCAGGGGGAACTTGCCGAGCGCAGCGCCATATCGGATTTGGGAAAAATACAAAGCCATCAGTTGGGCAACCTGATG  
 [0934] ATTCAACAGGCGGCCATTAAGGAAATATCGGCTACATTGTCCGCTTTTCCGATCACGGGCACGAAGTCCATTCCCC  
 [0935] TTCGACAACCATGCCTCACATTCGGATTTCTGATGAAGCCGGTAGTCCCGTTGACGGATTTAGCCTTTACCGCATCCAT  
 [0936] TGGGACGGATACGAACACCATCCCCCGACGGCTATGACGGGCCACAGGGCGGGCTATCCCGCTCCCAAAGGCGCG

[0937] AGGGATATATACAGCTACGACATAAAAAGGCGTTGCCAAAATATCCGCCTCAACCTGACCGACAACCGCAGCACCCGA  
 [0938] CAACGGCTTGCCGACCGTTTCCACAATGCCGGTAGTATGCTGACGCAAGGAGTAGGGCAGCGATTCAAACGCGCCACC  
 [0939] CGATACAGCCCCGAGCTGGACAGATCGGGCAATGCCGCCAAGCCTTCAACGGCACTGCAGATATCGTTAAAAACATC  
 [0940] ATCGGCGGGCAGGAGAAATTTGTCGGCGCAGGCGATGCCGTGCAGCGGCATAAGCGAAGGCTCAAACATTCCTGTTCATG  
 [0941] CACGGCTTGGGTCTGCTTCCACCGAAAACAAGATGGCGCGCATCAACGATTTGGCAGATATGGCGCAACTCAAAGAC  
 [0942] TATGCCGACAGCCATCCGCGATTGGGCAGTCCAAAACCCCAATGCCGCACAAGGCATAGAAGCCGTCAGCAATATC  
 [0943] TTTATGGCAGCCATCCCCATCAAAGGGATTTCGAGCTGTTCCGGGAAAATACGGCTTGGGCGGCATCACCGCACATCCT  
 [0944] ATCAACCGGTCGAGATGGGCGCGATCGCATTGCCGAAAAGGAAAATCCGCGTCAGCGACAATTTTGGCGATGCGGCA  
 [0945] TACGCCAAATACCCGTCCCTTACCATTCCCGAAAATATCCGTTCAAACCTTGGAGCAGCGTTACGGCAAAGAAAACATC  
 [0946] ACCTCCTCAACCGTCCCGCCGTCAAACGGCAAAAATGTCAAACCTGGCAGACCAACGCCACCCGAAGACAGGCGTACCG  
 [0947] TTTGACGGTAAAGGGTTTCCGAATTTTGAGAAGCACGTGAAATATGATACGCTCGAGCACCACCACCACCACCTCGA  
 [0948] 1 MVAADIGAGL ADALTAPLDH KDKGLQSLTL DQSVRKNEKL KLAAQGA EKT  
 [0949] 51 YGNGLSLNTG KLKNDKVSFR DFIRQIEVDG QLITLESGEF QVYKQSHSAL  
 [0950] 101 TAFQTEQIQD SEHSGKMOVAK RQFRIGDIAG EHTSFDKLPE GGRATYRGTA  
 [0951] 151 FGSDDAGGKL TYTIDFAAKQ GNGKIEHLKS PELNVDLAAA DIKPDGKRHA  
 [0952] 201 VISGSVLYNQ AEKGSYSLGI FGGKAQEVAG SAEVKTVNGI RHIGLAAKQL  
 [0953] 251 DGGGGTGSSD LANDSFIRQV LDRQHFEPDG KYHLFGSRGE LAERSGHIGL  
 [0954] 301 GKIQSHQLGN LMIQQA A IKG NIGYIVRFS D HGHEVHSPFD NHASHSDSDE  
 [0955] 351 AGSPVDGFSL YRIHWDGYEH HPADGYDGPQ GGGYPAPKGA RDIYSYDIKG  
 [0956] 401 VAQNIRLNLT DNRSTGQRLA DRFHNAGSML TQGVGDGFKRATRYSP ELDR  
 [0957] 451 SCNAAEAFNG TADIVKNIIG AAGEIVGAGD AVQGI SEGSN IAVMHGLG LL  
 [0958] 501 STENKMARIN DLADMAQLKD YAAAAIRDWA VQNPNA A QGI EAVSNIFMAA  
 [0959] 551 IPIKIGIAVR GKYGLGGITA HPIKRSQMG A IALPKGKSAV SDNFADAA YA  
 [0960] 601 KYPSPYHSRN IRSNLEQRYG KENITSSTVP PSNGKNV KLA DQRHPKTGVP  
 [0961] 651 FDGKGFPNFE KHVKYDTLEH HHHHH \*

[0962] 实施例 5-287 的杂交体

[0963] 以全长、具有 C-末端 His- 标记或无其前导肽但具有 C-末端 His- 标记的 287 的表达水平非常低。用 N-末端 GST- 融合实现了较好的表达。将 GST 用作 N-末端融合配体的替代方法，将 287 置于蛋白质 919 的 C-末端（‘919-287’）、蛋白质 953 的 C-端（‘953-287’）和蛋白质 ORF46.1 的 C-末端（‘ORF46.1-287’）。在这两种方法中，前导肽都是缺失的，且杂交体是直接的符合读框的融合。

[0964] 为了制备 953-287 杂交体，通过设计正向引物自各序列前导区的下游，除去两种蛋白质的前导肽；在 953 反向引物中除去终止密码子序列，但在 287 反向引物中包含终止密码子序列。对 953 基因而言，用于扩增的 5' 和 3' 引物分别包括 NdeI 和 BamHI 限制酶切位点，而对 287 基因的扩增而言，5' 和 3' 引物分别包括 BamHI 和 XhoI 限制酶切位点。用这种方法，用 NdeI-BamHI（克隆第一个基因）且随后用 BamHI-XhoI（克隆第二个基因），可以实现 pET21b+ 中两个基因的顺序定向克隆。

[0965] 通过将编码 287 的成熟部分的序列克隆入 pET21b+ 中的 919-His 克隆的 3' - 端的 XhoI 位点，可以得到 919-287 杂交体。设计用于扩增 287 基因的引物，从而在 PCR 片段

的 5' - 引入 SalI 限制酶切位点并在 3' - 引入 XhoI 位点。因为由 SalI 和 XhoI 限制酶产生的粘性末端是相容的,因此可以将由 SalI-XhoI 消化的 287PCR 产物插入到由 XhoI 切割的 pET21b-919 克隆中。

[0966] 类似地得到 ORF46.1-287 杂交体。

[0967] 将针对杂交蛋白产生的抗体的杀菌效力(同源菌株)与针对组分抗原的简单混合物产生的抗体相比:

[0968]

	与 287 的混合物	与 287 的杂交体
919	32000	16000
953	8192	8192
ORF46.1	128	8192

[0969] 对 919-287 和 953-287 而言,还获得了针对异源 MenB 菌株和针对血清型 A 和 C 的杀菌活性的数据:

[0970]

菌株	919		953		ORF46.1	
	混合物	杂交体	混合物	杂交体	混合物	杂交体
<b>MC58</b>	512	1024	512	1024	-	1024
<b>NGH38</b>	1024	2048	2048	4096	-	4096
<b>BZ232</b>	512	128	1024	16	-	-
<b>MenA (F6124)</b>	512	2048	2048	32	-	1024
<b>MenC (C11)</b>	>2048	n.d.	>2048	n.d.	-	n.d.
<b>MenC (BZ133)</b>	>4096	>8192	>4096	<16	-	2048

[0971] 还构建了 ORF46.1 和 919 的杂交体。在 N- 末端用 919 得到了最佳结果(高 4 倍的滴定度)。

[0972] 还测试了杂交体 919-519His、ORF97-225His 和 225-ORF97His。它们的 ELISA 滴定度和杀菌抗体应答结果中等。

[0973] 两种蛋白质 A 和 B 的杂交体可以是 NH<sub>2</sub>-A-B-COOH 或 NH<sub>2</sub>-B-A-COOH,用  $\Delta$  G287 还制得了在 N- 末端与 287 “反向”杂交的杂交体。使用一系列菌株,包括同源菌株 2996。FCA 用作佐剂:

[0974]

菌株	287 & 919		287 & 953		287 & ORF46.1	
	$\Delta$ G287-919	919-287	$\Delta$ G287-953	953-287	$\Delta$ G287-46.1	46.1-287
<b>2996</b>	128000	16000	65536	8192	16384	8192
<b>BZ232</b>	256	128	128	<4	<4	<4
<b>1000</b>	2048	<4	<4	<4	<4	<4
<b>MC58</b>	8192	1024	16384	1024	512	128
<b>NGH38</b>	32000	2048	>2048	4096	16384	4096
<b>394/98</b>	4096	32	256	128	128	16
<b>MenA (F6124)</b>	32000	2048	>2048	32	8192	1024
<b>MenC (BZ133)</b>	64000	>8192	>8192	<16	8192	2048

[0975] 通常在 N- 末端用 287 观察到较好的杀菌滴定度。

[0976] 当融合于蛋白质 961 [ 如上所示的 NH<sub>2</sub>- Δ G287-961-COOH- 序列 ] 时, 得到的蛋白质是不溶解的, 纯化必须将其变性和复性。在复性后, 发现约 50% 蛋白质仍不溶解。比较可溶和不溶蛋白质, 用可溶蛋白质得到更好的杀菌滴定度 (FCA 作为佐剂) :

[0977]

	2996	BZ232	MC58	NGH38	F6124	BZ133
可溶的	65536	128	4096	>2048	>2048	4096
不溶的	8192	<4	<4	16	n. d.	n. d.

[0978] 但用明矾佐剂替代, 可以改善不溶形式的蛋白质的滴定度 :

[0979]

不溶的	32768	128	4096	>2048	>2048	2048
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[0980] 还在杂交蛋白中使用 961C ( 见上 ) 。由于 961 及其结构域变体指导有效的表达, 它们非常适合作为杂交蛋白的 N- 末端部分。

[0981] 实施例 23- 其它杂交体

[0982] 附图中显示本发明的其它杂交蛋白, 它们具有如下所示的序列。当与单独蛋白质相比时, 这此杂交蛋白是有利的 :

[0983] ORF46. 1-741

[0984] ATGTCAGATTTGGCAAACGATTCTTTTATCCGGCAGGTTCTCGACCGTCAGCATTTCGAACCCGACGGGAAATACCAC

[0985] CTATTCGGCAGCAGGGGGAACTTGCCGAGCGCAGCGCCATATCGGATTGGGAAAAATACAAAGCCATCAGTTGGGC

[0986] AACCTGATGATTAACACAGGCGCCATTAAAGGAAATATCGGCTACATTGTCCGCTTTCCGATCACGGGCACGAAAGTC

[0987] CATTCCCCCTTCGACAACCATGCCTCACATTCCGATTCTGTATGAAGCCGGTAGTCCCGTTGACGCATTTAGCCTTTAC

[0988] CGCATCCATTGGGACGGATACGAACACCATCCCGCCGACGGCTATGACGGGCCACAGGGCGGGCTATCCCGCTCCC

[0989] AAAGGCGGAGGGATATATACAGCTACGACATAAAAGGCGTTGCCAAAAATATCCGCCTCAACCTGACCGACAACCGC

[0990] AGCACCGGACAACGGCTTGCCGACCGTTTCCACAATGCCGGTAGTATGCTGACGCAAGGAGTAGGCGACGGATTCAA

[0991] CGCGCCACCCGATACAGCCCCGAGCTGGACAGATCGGGCAATGCCCGGAAGCCTTCAAACGGCACTGCAGATATCGTT

[0992] AAAACATCATCGGCGGGCAGGAGAAATTTGCGGCGCAGGCGATGCCGTGACGGGCATTAAGCGAAGGCTCAAAACATT

[0993] GCTGTTCATGCACGGCTTGGGTCTGCTTTCCACCGAAAAACAAGATGGCGCGCATCAACGATTTGGCAGATATGGCGCAA

[0994] CTCAAAGACTATGCCGACGAGCCATCCGCGATTGGGCAGTCCAAAACCCCAATGCCGCACAAGGCATAGAAGCCGTC

[0995] AGCAATATCTTTATGGCAGCCATCCCCATCAAAGGATTTGGAGCTGTTCCGGGAAAAATACGGCTTGGGCGGCATCACG

[0996] GCACATCCTATCAAGCGGTGCGAGATGGGCGCGATCGCATTTGCCGAAAGGAAAAATCCCGCGTCAGCGACAATTTTGCC

[0997] GATGCGGCATACGCCAAATACCCGTCCCTTACCATTCCCGAAAATATCCGTTCAAACCTTGGAGCAGCGTTACGGCAA

[0998] GAAAACATCACCTCCTCAACCGTGCCGCGTCAAACGGCAAAAATGTCAAACCTGGCAGACCAACGCCACCCGAAGACA

[0999] GGCGTACCGTTTACGGTAAAGGGTTTCCGAATTTTGAGAAGCACGTGAAAATATGATACGGGATCCGGAGGGGGTGGT

[1000] GTCGCGCGACATCGGTGCGGGGCTTGCCGATGCACTAACCGCACCGCTCGACCATAAAGACAAAGGTTTGCAGTCT

[1001] TTGACGCTGGATCAGTCCGTCAGGAAAAACGAGAACTGAAGCTGGCGGCACAAGGTGCGGAAAAAATTTATGGAAAC

[1002] GGTGACAGCCTCAATACGGGCAAAATGAAGAACGACAAGGTCAGCCGTTTTCGACTTTATCCGCCAAATCGAAGTGGAC

[1003] GGGCAGCTCATTACCTTGGAGAGTGGAGAGTTCCAAGTATACAAAACAAAGCCATTCGCGCTTAAACCGCCTTTCAGACC

[1004] GAGCAAATACAAGATTCCGAGCATTCGGGAAGATGGTTGCGAAAACGCCAGTTTTCAGAAATCGGCGACATAGCGGGCGAA

[1005] CATACATCTTTTGACAAGCTTCCCGAAGGCGGCAGGGGACATATCGCGGACGGCGTTCCGTTTCAGACGATGCCGGC

[1006] GGAAAACCTGACCTACCCATAGATTTCCCGCCAAAGCAGGGAAAACGGCAAAAATCGAACATTTGAAATGCCAGAACTC



[1007] AATGTCGACCTGGCCGCCGCCGATATCAAGCCGGATGAAAAACGCCATGCCGTCATCAGCGGTTCCGTCCTTTACAAC  
 [1008] CAAGCCGAGAAAAGGCAGTTACTCCCTCGGTATCTTTGGCGGAAAAGCCCAGGAAGTTGCCGGCAGCGCGGAAGTGAAA  
 [1009] ACCGTAAACGGCATAAGCCATATCGGCCCTTGGCCCAAGCAACTCGAGCACCACCACCACCACCTGA  
 [1010] 1 MSDLANDSFI RQVLDRQHFE PDGKYHLFGS RGELAERSGH IGLGKIQSHQ  
 [1011] 51 LGNLMIQQA IKGNIGYIVR FSDHGHEVHS PFDNHASHSD SDEAGSPVDG  
 [1012] 101 FSLYRIHWDG YEHPADGYD GPQGGYPAP KGARDIYSYD IKGVAQNIRL  
 [1013] 151 NLTDNRSTGQ RLADRFHNAG SMLTQGVGDG FKRASTRYSPE LDRSGNAAEA  
 [1014] 201 FNGTADIVKN IIGAAGEIVG AGDAVQGI SE GSNIAMHGL GLLSTENKMA  
 [1015] 251 RINDLADMAQ LKDYAAAAIR DWAVQNPNA QGIEAVSNIF MAAIPIKIGI  
 [1016] 301 AVRGKYGLG ITHAPIKRSQ MGAIALPKGK SAVSDNFADA AYAKYPSPYH  
 [1017] 351 SRNIRSNELEQ RYKKNITSS TVPPSNGKNV KIADQRHPKT GVPFDGKGF  
 [1018] 401 NFEKHVKYDT GSGGGVVAAD IGAGLADALT APLDCHKDKGL QSLTLDQSVR  
 [1019] 451 KNEKLKLAQ GAKEYGNGD SLNTGKLNKND KVSRLFDFIRQ IEVDGQLITL  
 [1020] 501 ESGEFQVYKQ SHSALTAFT EQIQDSEHSG KMAKRQFRI GDIAGEHTSF  
 [1021] 551 DKLPEGGRAT YRGTAFGSD AGGKLYTID FAAKQNGKI EHLKSPELNV  
 [1022] 601 DLAAADLKP GKRHAVLSGS VLYNQAEGKS YSLGIFGGKA QEVAGSAEVK  
 [1023] 651 TVNGIRHIGL AAKQLEHHHH HH\*  
 [1024] ORF46. 1-961  
 [1025] ATGTCAGATTTGGCAAACGATTTCTTTTATCCGGCAGGTTCTCGACCGTCAGCATTTTCGAACCCGACGGGAAATACCAC  
 [1026] CTATTCGGCAGCAGGGGGAACTTGGCCGAGCGCAGCGCCATATCGGATTTGGGAAAAATACAAAGCCATCAGTTGGGC  
 [1027] AACCTGATGATTAACAGCGGCCATTAAGGAAATATCGGCTACATTTGTCGGCTTTTCCGATCACGGGCACGAAGTC  
 [1028] CATTCCTCCCTTCGACAACCATGCCTCACATTCGGATTTCTGATGAAGCCGGTAGTCCCGTTGACGGATTTAGCCTTTAC  
 [1029] CGCATCCATTTGGGACGGATACGAACACCATCCCGCCGACGGCTATGACGGGCCACAGGGCGGGCTATCCCGCTCCC  
 [1030] AAAGGCGGAGGGATATATACAGCTACGACATAAAAGGCGTTGCCAAAAATATCCGCTCAACCTGACCGACAACCGC  
 [1031] AGCACCGGACAACGGCTTGGCGACCGTTTCCACAATGCCGGTAGTATGCTGACGCAAGGAGTAGGCGACGGATTCAAA  
 [1032] CGCGCCACCGATACAGCCCGAGCTGGACAGATCGGGCAATGCCCGGAAGCCTTCAAACGGCACTGCAGATATCGTT  
 [1033] AAAACATCATCGGCGGGCAGGAGAAATTTGTCGGCGCAGGCGATGCCGTGACGGGCATAAGCGAAGGCTCAAACATT  
 [1034] GCTGTCATGCACGGCTTGGGTCTGCTTTCCACCGAAAAACAAGATGGCGCGCATCAACGATTTGGCAGATATGGCGCAA  
 [1035] CTCAAAGACTATGCCGAGCAGCCATCCGCGATTTGGGCAGTCCAAAACCCCAATGCCGCACAAGGCATAGAAGCGCTC  
 [1036] AGCAATATCTTTATGGCAGCCATCCCCATCAAAGGATTTGGAGCTGTTCCGGGAAAAATACGGCTTTGGGCGGCATCACG  
 [1037] GCACATCCTATCAAGCGGTCGAGATGGGCGGATCGCATTTGCCGAAAGGAAAAATCCGCGTCAGCGACAATTTGCC  
 [1038] GATGCGGCATACGCCAAATACCGTCCCCTTACCATTCCCAGAAATATCCGTTCAAACCTTGGAGCAGCGTTACGGCAA  
 [1039] GAAAACATCACCTCCTCAACCGTCCCGCGTCAAACGGCAAAAATGTCAAACCTGGCAGACCAACGCCACCCGAAGACA  
 [1040] GGCGTACCGTTTGGCGTAAAGGGTTTCCGAATTTTGAAGAAGCAGTGAATATGATACGGGATCCGGAGGAGGAGGA  
 [1041] GCCAAAAACGACGAGATGTTAAAAAGCTGCCACTGTGGCCATTTGCTGCTGCCTACAACAATGGCCAAGAAATCAAC  
 [1042] GGTTCAAAGCTGGAGAGACCATCTACGACATTTGATGAAGACGGCACAATTAACAAAAAGACGCAACTGCAGCCGAT  
 [1043] GTTGAAGCCGACGACTTTAAAGGTCTGGGTCTGAAAAAGTCTGACTAACCTGACCAAAAACCGTCAATGAAAAAAA  
 [1044] CAAAACGTCGATGCCAAAGTAAAAGCTGCAGAATCTGAAATAGAAAAGTTAAACAACCAAGTTAGCAGACACTGATGCC  
 [1045] GCTTTAGCAGATACTGATGCCGCTCTGGATGCAACCAACCGCTTGAATAAATTTGGGAGAAAAATATAACGACATTT

[1046] GCTGAAGAGACTAAGACAAATATCGTAAAAATTTGATGAAAAATTAGAAGCCGTGGCTGATACCGTCGACAAGCATGCC  
 [1047] GAAGCATTCAACGATATCGCCGATTTCATTGGATGAAACCAACACTAAGGCAGACGAAGCCGTCAAAACCGCCAATGAA  
 [1048] GCCAAACAGACGGCCGAAGAAAACAAACAAAACGTCGATGCCAAAGTAAAAGCTGCAGAAACTGCAGCAGGCAAAGCC  
 [1049] GAAGCTGCCGCTGGCACAGCTAATACTGCAGCCGACAAGGCCGAAGCTGTGCTGCAAAAAGTTACCGACATCAAAGCT  
 [1050] GATATCGCTACGAACAAAGATAATATTGCTAAAAAGCAAACAGTGGCCGACGTGTACACCAGAGAAGAGTCTGACAGC  
 [1051] AAATTTGTCAGAAATTGATGGTCTGAACGCTACTACCGAAAAATTTGGACACACGCTTGGCTTCTGCTGAAAAATCCATT  
 [1052] GCCGATCAGATACTCGCCTGAACGGTTTGGATAAAACAGTGTGACACCTGCGCAAAGAAAACCGCCAAGGCCCTTGCA  
 [1053] GAACAAGCCGCGCTCTCCGGTCTGTTCCAACCTTACAACGTTGGGTGGTTCAAATGTAACGGCTGCAGTCCGCGGCTAC  
 [1054] AAATCCGAATCGGCAGTCCGCATCCGTTACCGGCTTCCGCTTTACCGAAAACTTTGCCGCCAAAGCAGGCGTGGCAGTC  
 [1055] GGCATTTCGTCGGTCTTCCGCGACCTACCATGTGCGGCTCAATTACGAGTGGCTCGAGCACCACCACCACCACCAC  
 [1056] TGA  
 [1057] 1 MSDLANDSFI RQVLDRQHFE PDGKYHLFGS RGELAERSGH IGLGKIQSHQ  
 [1058] 51 LGNLMIQQA IKGNIGYIVR FSDHGHEVHS PFDNHASHSD SDEAGSPVDG  
 [1059] 101 FSLYRIHWDG YEHPADGYD GPQGGYPAP KGARDIYSYD IKGVAQNIRL  
 [1060] 151 NLTDNRSTGQ RLADRFHNAG SMLTQGVGDG FKRASTRYSPE LDRSGNAAEA  
 [1061] 201 FNGTADIVKN IIGAAGEIVG AGDAVQGI SE GSNIAMHGL GLLSTENKMA  
 [1062] 251 RINDLADMAQ LKDYAAAAIR DWAVQNPNA QGIEAVSNIF MAAPIKIGIG  
 [1063] 301 AVRGKYGLGG ITAHPIKRSQ MGAIALPKGK SAVSDNFADA AYAKYPSPYH  
 [1064] 351 SRNIRSLEQ RYKGENITSS TVPPSNGKNV KLADQRHPKT GVPFDGKGF  
 [1065] 401 NFEKHVKYDT GSGGGGATND DDVKAATVA IAAAYNNGQE INGFKAGETI  
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 [1624] 1151 WEQGGVEGKM RGSTQTVGIA AKTGENTTAA ATLGMRSTW SENSANAKTD  
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 [1628] 1351 KTGARNMPHT RLVAGLGADV EFGNGWNGLA RYSYAGSKQY GNHSGRNVG  
 [1629] 1401 YRF\*

[1630] 可以理解本发明仅以实施例的方式进行描述,在本发明的范围和精神内还可进行



改变。例如,设想可以使用其它菌株的蛋白质[如,参见 W000/66741, ORF4、ORF40、ORF46、225、235、287、519、726、919 和 953 的多态序列]。

[1631] 实验详述

[1632] 克隆策略和寡核苷酸设计

[1633] 用以脑膜炎奈瑟球菌 B MC58 的基因组序列为基础设计的寡核苷酸,通过 PCR 扩增编码感兴趣的抗原的基因。除非特别指出,通常将菌株 2996 的基因组 DNA 用作 PCR 反应的模板,将扩增的片段克隆入表达载体 pET21b+(Novagen),从而以 C-末端 His 标记的产物形式表达该蛋白,或将其克隆入 pET-24b+(Novagen) 以‘未标记的’形式(如 $\Delta$  G287K)表达该蛋白。

[1634] 不用融合配体和用其自身前导肽(如果存在时)表达蛋白质,进行开放读框(ATG 到终止密码子)的扩增。

[1635] 当蛋白质以‘未标记的’的形式表达时,通过从预定的前导序列设计 5'-端扩增引物下游除去前导肽。

[1636] 用于 PCR 的引物的解链温度取决于整个引物中杂交核苷酸的数量和类型,并用以下公式确定:

[1637]  $T_{m1} = 4(G+C) + 2(A+T)$  (除去尾部的)

[1638]  $T_{m2} = 64.9 + 0.41(\% GC) - 600/N$  (完整的引物)

[1639] 对整个低聚物而言,所选寡核苷酸的解链温度通常为 65-70°C,仅针对杂交区域,解链温度为 50-60°C。

[1640] 用 Perkin Elmer394DNA/RNA 合成仪合成寡核苷酸,将其从柱上洗脱到 2.0ml NH<sub>4</sub>OH 中,在 56°C 培育 5 小时以去保护。加入 0.3M 乙酸钠和 2 体积的乙醇沉淀寡聚物。将样品离心,将沉淀物重悬浮于水中。

[1641]

		序列	限制酶切位点
<b>fu (961)-</b>	Fwd	<b>CGCGGATCC</b> -GGAGGGGGTGGTGTCC	<b>BamHI</b>
<b>741(MC58)-His</b>	Rev	<b>CCCGCTCGAG</b> -TTGCTTGGCGGCAAGGC	<b>XhoI</b>
<b>fu (961)-983-His</b>	Fwd	<b>CGCGGATCC</b> - GCGGAGGCGGCACTT	<b>BamHI</b>
	Rev	<b>CCCGCTCGAG</b> -GAACCGGTAGCCTACG	<b>XhoI</b>

[1642]

fu (961)- Orf46.1- His	Fwd	CGCGGATCCGGTGGTGGTGGT-TCAGATTTGGCAAACGATTC	BamHI
	Rev	CCCGCTCGAG-CGTATCATATTTACGTGC	XhoI
fu (961 c-L)- 741(MC58)	Fwd	CGCGGATCC -GGAGGGGGTGGTGTCG	BamHI
	Rev	CCCGCTCGAG-TTATTGCTTGGCGCAAG	XhoI
fu (961c-L)-983	Fwd	CGCGGATCC - GGCGGAGGCGCACTT	BamHI
	Rev	CCCGCTCGAG-TCAGAACCGGTAGCCTAC	XhoI
fu (961c-L)- Orf46.1	Fwd	CGCGGATCCGGTGGTGGTGGT-TCAGATTTGGCAAACGATTC	BamHI
	Rev	CCCGCTCGAG-TTACGTATCATATTTACGTGC	XhoI
fu-(ΔG287)-919- His	Fwd	CGCGGATCCGGTGGTGGTGGT-CAAAGCAAGAGCATCCAAACC	BamHI
	Rev	CCCAAGCTT-TTCGGGCGGTATTTCGGGCTTC	HindIII
fu-(ΔG287)-953- His	Fwd	CGCGGATCCGGTGGTGGTGGT-GCCACCTACAAAGTGGAC	BamHI
	Rev	GCCCAAGCTT-TTGTTTGGCTGCCTCGAT	HindIII
fu-(ΔG287)-961- His	Fwd	CGCGGATCCGGTGGTGGTGGT-ACAAGCGACGACG	BamHI
	Rev	GCCCAAGCTT-CCACTCGTAATTGACGCC	HindIII
fu-(ΔG287)- Orf46.1-His	Fwd	CGCGGATCCGGTGGTGGTGGT-TCAGATTTGGCAAACGATTC	BamHI
	Rev	CCCAAGCTT-CGTATCATATTTACGTGC	HindIII
fu-(ΔG287-919)- Orf46.1-His	Fwd	CCCAAGCTTGGTGGTGGTGGTGGT-TCAGATTTGGCAAACGATTC	HindIII
	Rev	CCCGCTCGAG-CGTATCATATTTACGTGC	XhoI
fu-(ΔG287- Orf46.1)-919-His	Fwd	CCCAAGCTTGGTGGTGGTGGTGGT-CAAAGCAAGAGCATCCAAACC	HindIII
	Rev	CCCGCTCGAG-CGGGCGGTATTTCGGGCTT	XhoI
fu ΔG287(394.98)- ...	Fwd	CGCGGATCCGCTAGC-CCCGATGTTAAATCGGC	NheI
	Rev	CGGGGATCC-ATCCTGCTCTTTTTGCCGG	BamHI
fu Orf1-(Orf46.1)- His	Fwd	CGCGGATCCGCTAGC-GGACACACTTATTTTCGGCATC	NheI
	Rev	CGCGGATCC-CCAGCGGTAGCCTAATTTGAT	
fu (Orf1)-Orf46.1- His	Fwd	CGCGGATCCGGTGGTGGTGGT-TCAGATTTGGCAAACGATTC	BamHI
	Rev	CCCAAGCTT-CGTATCATATTTACGTGC	HindIII
fu (919)-Orf46.1- His	Fwd1	GCGGCGTTCGACGGTGGCGGAGGCACTGGATCCTCAG	SalI
	Fwd2	GGAGGCACTGGATCCTCAGATTTGGCAAACGATTC	
	Rev	CCCGCTCGAG-CGTATCATATTTACGTGC	XhoI
Fu (orf46)-287-His	Fwd	CGGGGATCCGGGGGCGGGCGGTGGCG	BamHI
	Rev	CCCAAGCTTATCCTGCTCTTTTTGCCGGC	HindIII
Fu (orf46)-919-His	Fwd	CGCGGATCCGGTGGTGGTGGTCAAAGCAAGAGCATCCA AACC	BamHI
	Rev	CCCAAGCTTTCGGGCGGTATTTCGGGCTTC	HindIII

[1643]

<b>Fu (orf46-919)-287-His</b>	Fwd	CCCCAAGCTTGGGGGCGGCGGTGGCG	HindIII
	Rev	CCCGCTCGAGATCCTGCTCTTTTTTGCCGGC	XhoI
<b>Fu (orf46-287)-919-His</b>	Fwd	CCCAAGCTTGGTGGTGGTGGTGGTCAAAGCAAGAGCAT CCAAACC	HindIII
	Rev	CCCGCTCGAGCGGGCGGTATTCGGGCTT	XhoI
<b>(ΔG741)-961c-His</b>	Fwd1	GGAGGCACTGGATCCGCAGCCACAAACGACGACGA	XhoI
	Fwd2	GCGGCCTCGAG-GGTGGCGGAGGCACTGGATCCGCAG	
	Rev	CCCGCTCGAG-ACCCAGCTTGTAAGGTTG	XhoI
<b>(ΔG741)-961-His</b>	Fwd1	GGAGGCACTGGATCCGCAGCCACAAACGACGACGA	XhoI
	Fwd2	GCGGCCTCGAG-GGTGGCGGAGGCACTGGATCCGCAG	
	Rev	CCCGCTCGAG-CCACTCGTAATTGACGCC	XhoI
<b>(ΔG741)-983-His</b>	Fwd	GCGGCCTCGAG- GGATCCGGCGGAGGCGGCACTTCTGCG	XhoI
	Rev	CCCGCTCGAG-GAACCGGTAGCCTACG	
<b>(ΔG741)-orf46.1-His</b>	Fwd1	GGAGGCACTGGATCCTCAGATTTGGCAAACGATTC	SalI
	Fwd2	GCGGCCTCGAGCGGTGGCGGAGGCACTGGATCCTCAGA	
	Rev	CCCGCTCGAG-CGTATCATATTTACGTGC	XhoI
<b>(ΔG983)-741(MC58)-His</b>	Fwd	GCGGCCTCGAG-GGATCCGGAGGGGGTGGTGTCCGCC	XhoI
	Rev	CCCGCTCGAG-TTGCTTGGCGGCAAG	
<b>(ΔG983)-961c-His</b>	Fwd1	GGAGGCACTGGATCCGCAGCCACAAACGACGACGA	XhoI
	Fwd2	GCGGCCTCGAG-GGTGGCGGAGGCACTGGATCCGCAG	
	Rev	CCCGCTCGAG-ACCCAGCTTGTAAGGTTG	XhoI
<b>(ΔG983)-961-His</b>	Fwd1	GGAGGCACTGGATCCGCAGCCACAAACGACGACGA	XhoI
	Fwd2	GCGGCCTCGAG-GGTGGCGGAGGCACTGGATCCGCAG	
	Rev	CCCGCTCGAG-CCACTCGTAATTGACGCC	XhoI
<b>(ΔG983)-Orf46.1-His</b>	Fwd1	GGAGGCACTGGATCCTCAGATTTGGCAAACGATTC	SalI
	Fwd2	GCGGCCTCGAGCGGTGGCGGAGGCACTGGATCCTCAGA	
	Rev	CCCGCTCGAG-CGTATCATATTTACGTGC	XhoI

[1644] \* 将该引物用作反向引物,将所有 287 的 C 末端融合于 His- 标记。

[1645] § 与 287-His 反向引物联用的正向引物。

[1646] NB- 所有 PCR 反应使用菌株 2996,除非特别指出(如菌株 MC58)。

[1647] 在所有以 ATG 起始不跟随唯一 NheI 位点的构建物中,ATG 密码子是用于克隆的 NdeI 位点的一部分。在 5' 端用 NheI 作为克隆位点制备的构建物(如所有那些在 N- 末端包含 287 的)另有两个融合于抗原的编码序列的密码子(GCTAGC)。

[1648] 染色体 DNA 模板的制备

[1649] 在 100ml GC 培养基中使脑膜炎奈瑟球菌前株 2996、MC58、394.98、1000 和 BZ232(及其它)生长至指数期,离心收获,并重悬浮于 5ml 缓冲液(20% w/v 蔗糖、50mM Tris-HCl、50mM EDTA、pH8)中。在冰上培育 10 分钟后,加入 10ml 裂解液(50mM NaCl、1% 十二烷基肌氨酸钠(Na-Sarkosyl)、50 μg/ml 蛋白酶 K)裂解细菌,悬浮液在 37°C 培育 2 小时。进行 2 次苯酚提取(平衡至 pH8)和一次 CHCl<sub>3</sub>/异戊醇(24:1)提取。加入 0.3M 乙酸钠和 2 体积乙醇沉降 DNA,并离心收集。用 70% (v/v) 乙醇洗涤沉淀物 1 次,并重溶解于 4.0ml TE 缓冲液(10mM Tris-HCl、1mM EDTA、pH8.0)。读取 OD<sub>260</sub> 测定 DNA 浓度。

[1650] PCR 扩增

[1651] 标准的 PCR 过程:进行如下在 40 μM 各寡核苷酸引物、400-800 μM dNTP 溶液、1x

PCR 缓冲液（包含 1.5mM MgCl<sub>2</sub>）、2.5 单位 TaqI DNA 聚合酶（用 Perkin-Elmer AmpliTaq, Boehringer Mannheim Expand™ 长模板）存在时,将 200ng2996、MC581000、或 BZ232 菌株的基因组 DNA 或 10ng 重组克隆的质粒 DNA 制备物用作模板。

[1652] 将整个混合物在 95℃ 初步培育 3 分钟后,每份样品进行 2- 步的扩增:用除去引物 (T<sub>m1</sub>) 的限制酶尾部的杂交温度进行前 5 轮。然后按全长低聚物 (T<sub>m2</sub>) 计算的杂交温度进行 30 轮。根据要扩增的 Orf 的长度,在 68℃ 或 72℃ 进行的延伸时间各不相同。对 Orf1 而言,自 3 分钟开始的延伸时间每轮递增 15 秒。以在 72℃ 10 分钟延伸步骤完成循环。

[1653] 将扩增的 DNA 直接加到 1% 琼脂糖凝胶上。按制造商的说明,用 Qiagen 凝胶提取试剂盒纯化相应于正确大小条带的 DNA 片段。

[1654] PCR 片段和克隆载体的消化

[1655] 用合适的限制酶消化相应于扩增片段的纯化 DNA,从而克隆入 pET-21b+、pET22b+、或 pET-24b+。用 QIAquick PCR 纯化试剂盒（按制造商的说明）纯化消化的片段,用 H<sub>2</sub>O 或 10mM Tris (pH8.5) 洗脱。用合适的限制酶消化质粒载体,加到 1.0% 琼脂糖凝胶上,用 Qiagen AIAquick 凝胶提取试剂盒纯化相应于消化的载体的条带。

[1656] 克隆

[1657] 将预先消化和纯化的、相应于各基因的片段连接到 pET21b+、pET22b+ 或 pET-24b+ 中。将在连接缓冲液（由制造商提供）中的 T4DNA 连接酶用于摩尔比为 3:1 的片段/载体。

[1658] 通过在冰上培育连接酶反应溶液和细菌 40 分钟,然后在 37℃ 培育 3 分钟,将重组质粒转化入感受态大肠杆菌 DH5 或 HB101 中。

[1659] 然后添加 800 μl LB 肉汤,并在 37℃ 培育 20 分钟。在 Eppendorf 微型离心机中以最高速度离心这些细胞,并重悬浮于约 200 μl 的上清液中,并涂布在 LB 氨苄青霉素 (100mg/ml) 琼脂上。

[1660] 在 4.0ml LB 肉汤 +100 μg/ml 氨苄青霉素中培育随机选择的集落过夜,进行重组集落的筛选。使细胞沉淀,并按制造商的说明用 Qiagen QIAprep SpinMiniprep 试剂盒提取质粒 DNA。用合适的限制酶消化约 1 μg 的各微型制备物,将消化物加到 1-1.5% 琼脂糖凝胶（取决于预计的插入大小）与分子量标记 (1kbDNA Ladder, GIBCO) 平行。根据插入的大小选择阳性克隆。

[1661] 表达

[1662] 各基因克隆入表达载体后,将重组质粒转化入适合表达重组蛋白的大肠杆菌菌株中。如上所述,用 1 μl 各构建物转化大肠杆菌 BL21-DE3。将单重组集落接种入 2ml LB+Amp (100 μg/ml) 中,在 37℃ 培育过夜,然后在 100ml 烧瓶中用 20ml LB+Amp (100 μg/ml) 以 1:30 稀释,使 OD<sub>600</sub> 在 0.1-0.2 之间。将烧瓶置于旋转式水浴摇床中于 30℃ 或 37℃ 培育,直到 OD<sub>600</sub> 显示适合诱导表达的指数生长期 (0.4-0.8OD)。加入 1.0mM IPTG 诱导蛋白质表达。在 30℃ 或 37℃ 培育 3 小时后,测定 OD<sub>600</sub> 并检测表达。用微型离心机离心 1.0ml 各样品,将沉淀物重悬浮于 PBS 中,用 SDS-PAGE 和考马斯蓝染色分析。

[1663] His- 标记的蛋白质的纯化

[1664] 从菌株 2996 和 MC58 中克隆了 287 的各种形式。用 C- 末端 His 标记的融合体进行构建,其包括成熟形式 (aa18-427)、含缺失 (Δ 1、Δ 2、Δ 3 和 Δ 4) 的构建物和由 B

或 C 结构域组成的克隆。对以 His- 融合体纯化的各克隆而言,划线接种单集落,并且在 37°C LB/Amp(100 μg/ml) 琼脂板上培育过夜。将从该平板上分离的集落接种到 20ml LB/Amp(100 μg/ml) 的液体培养基中,并在 37°C 振荡生长过夜。以 1:30 将过夜培养物稀释到 1.0L LB/Amp(100 μg/ml) 液体培养基中,让其在最佳温度(30 或 37°C)生长,直到 OD<sub>550</sub> 达到 0.6-0.8。添加 IPTG(终浓度为 1.0mM)诱导重组蛋白的表达,再培育培养物 3 小时。于 4°C,以 8000g 离心 15 分钟收获细菌。将细菌沉淀物重悬浮于 7.5ml (i) 冷缓冲液 A(300mM NaCl、50mM 磷酸盐缓冲液、10mM 咪唑、pH8.0),用于可溶性蛋白质;或 (ii) 缓冲液 B(10mM Tris-HCl、100mM 磷酸盐缓冲液,pH8.8 和任选地 8M 尿素),用于不溶性蛋白质。以可溶形式纯化的蛋白质包括 287-His、△ 1、△ 2、△ 3 和 △ 4287-His、△ 4287MC58-His、287c-His 和 287cMC58-His。蛋白质 287bMC58-His 是不溶的并相应地纯化。用 Branson Sonifier450,在冰上以 40W、30 秒超声处理破坏细胞 4 次,并于 4°C 以 13000xg 离心 30 分钟。对于不溶蛋白质,将沉淀物重悬浮于 2.0ml 缓冲液 C(6M 盐酸胍、100mM 磷酸盐缓冲液、10mM Tris-HCl、pH7.5),并用 Dounce 匀浆器处理 10 次。以 13000g 离心匀浆 30 分钟并保留上清液。将可溶的和不可溶制备物的上清液与 150 μl Ni<sup>2+</sup>- 树脂(预先用缓冲液 A 或缓冲液 B 平衡)混合,并在室温温和振荡培育 30 分钟。树脂是按制造商说明制备的 ChelatingSepharose Fast Flow(Pharmacia)。于 4°C,以 700g 离心分批制备物 5 分钟,弃去上清液。用 10ml 缓冲液 A 或 B 洗涤树脂 2 次(分批)10 分钟,重悬浮于 1.0ml 缓冲液 A 或 B 中,加到一次性柱上。用 (i) 缓冲液 A(4°C) 或 (ii) 缓冲液 B(室温)持续洗涤树脂,直到流出物的 OD<sub>280</sub> 达到 0.02-0.01。再用 (i) 冷缓冲液 C(300mM NaCl、50mM 磷酸盐缓冲液、20mM 咪唑、pH8.0) 或 (ii) 缓冲液 D(10mM Tris-HCl、100mM 磷酸盐缓冲液、pH6.3 和任选地 8M 尿素)进一步洗涤树脂,直到流出物的 OD<sub>280</sub> 达到 0.02-0.01。加入 700 μl (i) 冷洗脱缓冲液 A(300mM NaCl、50mM 磷酸盐缓冲液、250mM 咪唑、pH8.0) 或 (ii) 洗脱缓冲液 B(10mM Tris-HCl、100mM 磷酸盐缓冲液、pH4.5 和任选地 8M 尿素)洗脱 His- 融合蛋白,收集组分直到 OD<sub>280</sub> 显示获得了所有重组蛋白。用 SDS-PAGE 分析 20 μl 量的各洗脱组分。用 Bradford 试验法计算蛋白质浓度。

[1665] 变性的 His- 融合蛋白的复性

[1666] 需要变性以稳定 287bMC8,因此在免疫接种前需进行复性步骤。将甘油加到上述得到的变性组分中,使终浓度为 10% v/v。用透析缓冲液 I(10% v/v 甘油,0.5M 精氨酸、50mM 磷酸盐缓冲液、5.0mM 还原的谷胱甘肽、0.5mM 氧化的谷胱甘肽、2.0M 尿素,pH8.8)将蛋白质稀释至 200 μg/ml,用相同的缓冲液在 4°C 透析 12-14 小时。于 4°C,用缓冲液 II(10% v/v 甘油,0.5M 精氨酸、50mM 磷酸盐缓冲液、5.0mM 还原的谷胱甘肽、0.5mM 氧化的谷胱甘肽、pH8.8)再进行透析 12-14 小时。用以下公式计算蛋白质的浓度:

$$[1667] \quad \text{蛋白质 (mg/ml)} = (1.55 \times \text{OD}_{280}) - (0.76 \times \text{OD}_{260})$$

[1668] 免疫接种

[1669] 在第 0、21 和 35 天,用抗原免疫接种 Balb/C 小鼠,在第 49 天分析血清。

[1670] 血清分析 -ELISA

[1671] 将不包囊的 MenB M7 和包囊的菌株置于巧克力琼脂板上,在 37°C、5% CO<sub>2</sub> 中培育过夜。用无菌 Dracon 刷从琼脂板上收集细菌菌落,并接种到含有 0.25% 葡萄糖的 Mueller-Hinton 肉汤(Difco)中。每 30 分钟监测一次细菌的生长,随后测定 OD<sub>620</sub>。让细菌

生长直到 OD 达到 0.4-0.5。将培养物以 4000rpm 离心 10 分钟。弃去上清液,用 PBS 洗涤细菌 2 次,重悬浮于含有 0.025% 甲醛的 PBS 中,并在 37°C 培育 1 小时,然后在 4°C 搅拌培育过夜。在 96 孔 Greiner 板的各孔中添加 100  $\mu$ l 细菌细胞,并在 4°C 培育过夜。然后用 PBT 洗涤缓冲液 (0.1% Tween-20 的 PBS 溶液) 冲洗这些孔 3 次。在各孔中加入 200  $\mu$ l 饱和和缓冲液 (2.7% 聚乙烯吡咯烷酮 10 的水溶液),将这些平板在 37°C 培育 2 小时。用 PBT 冲洗这些孔 3 次。在各孔中加入 200  $\mu$ l 稀释的血清 (稀释缓冲液:1% BSA、0.1% Tween-20、0.1% NaN<sub>3</sub> 的 PBS 溶液),将这些平板在 37°C 培育 2 小时。用 PBT 冲洗这些孔 3 次。在各孔中加入 100  $\mu$ l HRP- 缀合的兔抗 - 小鼠 (Dako) 血清 (用稀释缓冲液以 1:2000 稀释),将这些平板置于 37°C 培育 90 分钟。用 PBT 缓冲液洗涤这些孔 3 次。在各孔中加入 100  $\mu$ l HRP 的底物缓冲液 (25ml 柠檬酸缓冲液 pH5, 10mg 邻 - 苯二胺 (phenildiamine) 和 10  $\mu$ l H<sub>2</sub>O<sub>2</sub>),并将平板在室温中静置 20 分钟。在各孔中加入 100  $\mu$ l 12.5% H<sub>2</sub>SO<sub>4</sub>,随后测定 OD<sub>490</sub>。计算 ELISA 滴定度,即高于预先免疫血清稀释度的、OD<sub>490</sub> 值为 0.4 的血清稀释度。当 OD<sub>490</sub> 值为 0.4 的血清稀释度高于 1:400 时,将 ELISA 视为阳性。

#### [1672] 血清分析 - FACS 扫描细菌结合分析

[1673] 将不包囊的 MenB M7 菌株置于巧克力琼脂板上,在 37°C、5% CO<sub>2</sub> 中培育过夜。用无菌 Dracon 刷从琼脂板上收集菌落,并接种到 4 支装有 0.25% 葡萄糖的 8ml Mueller-Hinton 肉汤 (Difco) 试管中。每 30 分钟监测细菌的生长,然后测定 OD<sub>620</sub>。让细菌生长直到 OD 达到 0.35-0.5。将培养物以 4000rpm 离心 10 分钟。弃去上清液,用封阻缓冲液 (1% BSA 的 PBS 溶液,0.4% NaN<sub>3</sub>) 重悬浮沉淀物,并以 4000rpm 离心 5 分钟。将细胞重悬浮于封阻缓冲液,使 OD<sub>620</sub> 达到 0.05。在 96 孔 Costar 板的各孔中添加 100  $\mu$ l 细菌细胞。在各孔中加入 100  $\mu$ l 稀释的 (1:100、1:200、1:400) 血清 (以封阻缓冲液配制),并将这些平板在 4°C 培育 2 小时。以 4000rpm 离心细胞 5 分钟,吸出上清液,在各孔中加入 200  $\mu$ l/孔封阻缓冲液洗少涂细胞。在各孔中加入 100  $\mu$ l R-Phicoerytrin 缀合的 F(ab)<sub>2</sub> 山羊抗 - 小鼠 (以 1:100 稀释),将平板置于 4°C 培育 1 小时。以 4000rpm 离心 5 分钟以沉淀细胞,添加 200  $\mu$ l/孔封阻缓冲液洗涤细胞。吸出上清液,细胞重悬浮于 200  $\mu$ l/孔 PBS、0.25% 甲醛。将样品转移到 FACScan 管中并读数。FACScan (Laser Power15mW) 的条件设定为:FL2 开;FSC-H 阈值:92;FSC PMT 电压:E01;SSCPMT:474;Amp. Gains6.1;FL-2PMT:586;补偿值:0。

#### [1674] 血清分析 - 杀菌试验

[1675] 于 37°C,在 5% CO<sub>2</sub>、在巧克力琼脂板 (以冷冻原液起始) 上培育脑膜炎奈瑟球菌菌株 2996 过夜。收集菌落,并将其接种到 7ml 含有 0.25% 葡萄糖的 Mueller-Hinton 肉汤中,使 OD<sub>620</sub> 达到 0.05-0.08。在 37°C 振荡培育约 1.5 小时,直到 OD<sub>620</sub> 达到 0.23-0.24。用 50mM 磷酸盐缓冲液 (pH7.2,含 10mM MgCl<sub>2</sub>、10mM CaCl<sub>2</sub> 和 0.5% (w/v) BSA (分析缓冲液)) 以 10<sup>5</sup>CFU/ml 工作稀释度稀释细菌。最终反应混合物的总体积为 50  $\mu$ l,其中 25  $\mu$ l 连续 2 倍稀释的测试血清,12.5  $\mu$ l 工作稀释度的细菌,12.5  $\mu$ l 幼兔补体 (终浓度 25%)。

[1676] 对照包括:用补体血清培育的细菌、用细菌培育并在 56°C 加热 30 分钟补充灭活的免疫血清。在加入幼兔补体后,用斜置方法立即将 10  $\mu$ l 对照置于 Mueller-Hinton 琼脂板上 (0 时间)。37°C 旋转培育 96 孔板 1 小时。将每份样品的 7  $\mu$ l 涂布在 Mueller-Hinton 琼脂板上作为斑点,而用斜置方法将 10  $\mu$ l 对照涂布在 Mueller-Hinton 琼脂板上 (1 时间)。37°C 培育琼脂板 18 小时,计算相应于 0 时间和 1 时间的菌落数量。

[1677] 血清分析 -Western 印迹法

[1678] 将纯化的蛋白质 (500ng/泳道)、外膜小泡 (5 μg) 和 MenB 菌株 2996 衍生的全细胞提取物 (25 μg) 加到 12% SDS-聚丙烯酰胺凝胶上,并转移到硝基纤维素膜上。用转化缓冲液 (0.3% Tris 碱,1.14% 甘氨酸、20% (v/v) 甲醇) 在 4℃、150mA 进行转化 2 小时。于 4℃,在饱和缓冲液 (10% 脱脂乳、0.1% Triton X100 的 PBS 溶液) 中培育过夜使膜饱和。用冲洗缓冲液 (3% 脱脂乳、0.1% Triton X100 的 PBS 溶液) 冲洗膜 2 次,并在 37℃ 与用洗涤缓冲液以 1:200 稀释的小鼠血清一起培育 2 小时。冲洗膜 2 次,与 1:2000 稀释的辣根过氧化物酶标记的抗 - 小鼠 Ig 一起培育 90 分钟。用 0.1% Triton X100 的 PBS 溶液冲洗膜 2 次,用 Opti-4CN 底物试剂盒 (Bio-Rad) 显色。加入水终止反应。

[1679] 如下制备 OMV:于 37℃、5% CO<sub>2</sub>,在 5 个 GC 板上让脑膜炎奈瑟球菌 2996 生长过夜,用接种环收获,并重悬浮于 10ml20mM Tris-HCl pH7.5、2mM EDTA 中。在 56℃ 热灭活 45 分钟,在冰上超声处理破碎细胞 5 分钟 (50% 负载循环 (dutycycle)、50% 输出,Branson 超声仪 3mm 微型针头)。以 5000g 离心 10 分钟除去未被破坏的细胞,回收含有完整细胞包膜组分的上清液,于 4℃ 以 50000g 进一步离心过夜。将含有膜的沉淀物重悬浮于 2% 二烷基肌氨酸钠、20mM Tris-HClpH7.5、2mM EDTA 中,在室温培育 20 分钟以溶解内膜。以 10000g 离心上清液 10 分钟除去聚集体,以 50000g 进一步离心上清液 3 小时。用 PBS 冲洗含有外膜的沉淀物,并重悬浮于相同的缓冲液中。用 BSA 作为标准,由 D. C. Bio-Rad 蛋白分析 (改进的 Lowry 方法) 测定蛋白质的浓度。

[1680] 如下制备全细胞提取物:使脑膜炎奈瑟球菌在 GC 板上培育过夜,用接种环收获,并重悬浮于 1ml20mM Tris-HCl 中。在 56℃ 热灭活 30 分钟。

[1681] 序列表

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[1689] <160>121

[1690] <170>SeqWin99, version1.02

[1691] <210>1

[1692] <211>608

[1693] <212>PRT

[1694] <213> 脑膜炎奈瑟氏菌 (*Neisseria meningitidis*)

[1695] <400>1

[1696]





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 Ala Arg Ile Asn Asp Leu Ala Asp Met Ala Gln Leu Lys Asp Tyr Ala  
 275 280 285  
 Ala Ala Ala Ile Arg Asp Trp Ala Val Gln Asn Pro Asn Ala Ala Gln  
 290 295 300  
 Gly Ile Glu Ala Val Ser Asn Ile Phe Met Ala Ala Ile Pro Ile Lys  
 305 310 315 320  
 Gly Ile Gly Ala Val Arg Gly Lys Tyr Gly Leu Gly Gly Ile Thr Ala  
 325 330 335  
 His Pro Ile Lys Arg Ser Gln Met Gly Ala Ile Ala Leu Pro Lys Gly  
 340 345 350  
 Lys Ser Ala Val Ser Asp Asn Phe Ala Asp Ala Ala Tyr Ala Lys Tyr  
 355 360 365  
 Pro Ser Pro Tyr His Ser Arg Asn Ile Arg Ser Asn Leu Glu Gln Arg  
 370 375 380  
 Tyr Gly Lys Glu Asn Ile Thr Ser Ser Thr Val Pro Pro Ser Asn Gly  
 385 390 395 400  
 Lys Asn Val Lys Leu Ala Asp Gln Arg His Pro Lys Thr Gly Val Pro  
 405 410 415  
 Phe Asp Gly Lys Gly Phe Pro Asn Phe Glu Lys His Val Lys Tyr Asp  
 420 425 430  
 Thr Lys Leu Asp Ile Gln Glu Leu Ser Gly Gly Gly Ile Pro Lys Ala  
 435 440 445  
 Lys Pro Val Ser Asp Ala Lys Pro Arg Trp Glu Val Asp Arg Lys Leu  
 450 455 460  
 Asn Lys Leu Thr Thr Arg Glu Gln Val Glu Lys Asn Val Gln Glu Ile  
 465 470 475 480  
 Arg Asn Gly Asn Lys Asn Ser Asn Phe Ser Gln His Ala Gln Leu Glu  
 485 490 495  
 Arg Glu Ile Asn Lys Leu Lys Ser Ala Asp Glu Ile Asn Phe Ala Asp  
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 Gly Met Gly Lys Phe Thr Asp Ser Met Asn Asp Lys Ala Phe Ser Arg  
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 Leu Val Lys Ser Val Lys Glu Asn Gly Phe Thr Asn Pro Val Val Glu  
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 Tyr Val Glu Ile Asn Gly Lys Ala Tyr Ile Val Arg Gly Asn Asn Arg  
 545 550 555 560  
 Val Phe Ala Ala Glu Tyr Leu Gly Arg Ile His Glu Leu Lys Phe Lys  
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[1699] &lt;211&gt;464

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[1701] &lt;213&gt;人工序列

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[1703] <223> Δ G287

[1704] <400>2

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 35 40 45  
 Ala Ala Val Ser Glu Glu Asn Thr Gly Asn Gly Gly Ala Val Thr Ala  
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 Asp Asn Pro Lys Asn Glu Asp Glu Val Ala Gln Asn Asp Met Pro Gln  
 65 70 75 80  
 Asn Ala Ala Gly Thr Asp Ser Ser Thr Pro Asn His Thr Pro Asp Pro  
 85 90 95  
 Asn Met Leu Ala Gly Asn Met Glu Asn Gln Ala Thr Asp Ala Gly Glu  
 100 105 110  
 Ser Ser Gln Pro Ala Asn Gln Pro Asp Met Ala Asn Ala Ala Asp Gly  
 115 120 125  
 Met Gln Gly Asp Asp Pro Ser Ala Gly Gly Gln Asn Ala Gly Asn Thr  
 130 135 140  
 Ala Ala Gln Gly Ala Asn Gln Ala Gly Asn Asn Gln Ala Ala Gly Ser  
 145 150 155 160  
 Ser Asp Pro Ile Pro Ala Ser Asn Pro Ala Pro Ala Asn Gly Gly Ser  
 165 170 175  
 Asn Phe Gly Arg Val Asp Leu Ala Asn Gly Val Leu Ile Asp Gly Pro  
 180 185 190  
 Ser Gln Asn Ile Thr Leu Thr His Cys Lys Gly Asp Ser Cys Ser Gly  
 195 200 205  
 Asn Asn Phe Leu Asp Glu Glu Val Gln Leu Lys Ser Glu Phe Glu Lys  
 210 215 220  
 Leu Ser Asp Ala Asp Lys Ile Ser Asn Tyr Lys Lys Asp Gly Lys Asn  
 225 230 235 240  
 Asp Lys Phe Val Gly Leu Val Ala Asp Ser Val Gln Met Lys Gly Ile  
 245 250 255  
 Asn Gln Tyr Ile Ile Phe Tyr Lys Pro Lys Pro Thr Ser Phe Ala Arg  
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 Phe Arg Arg Ser Ala Arg Ser Arg Arg Ser Leu Pro Ala Glu Met Pro  
 275 280 285  
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 Val Ser Leu Thr Gly His Ser Gly Asn Ile Phe Ala Pro Glu Gly Asn  
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 Tyr Arg Tyr Leu Thr Tyr Gly Ala Glu Lys Leu Pro Gly Gly Ser Tyr  
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 Ala Leu Arg Val Gln Gly Glu Pro Ala Lys Gly Glu Met Leu Ala Gly  
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 Ala Ala Val Tyr Asn Gly Glu Val Leu His Phe His Thr Glu Asn Gly  
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 370 375 380

[1706]

Ser	Lys	Ser	Val	Asp	Gly	Ile	Ile	Asp	Ser	Gly	Asp	Asp	Leu	His	Met
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Gly	Thr	Gln	Lys	Phe	Lys	Ala	Ala	Ile	Asp	Gly	Asn	Gly	Phe	Lys	Gly
				405					410						415
Thr	Trp	Thr	Glu	Asn	Gly	Ser	Gly	Asp	Val	Ser	Gly	Lys	Phe	Tyr	Gly
			420					425						430	
Pro	Ala	Gly	Glu	Glu	Val	Ala	Gly	Lys	Tyr	Ser	Tyr	Arg	Pro	Thr	Asp
		435					440					445			
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- [1709] <212>DNA
- [1710] <213> 人工序列
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- [1712] <223> Δ G287-919
- [1713] <400>3
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gcgccatcca cacaaggcag ccaagatatg gcggcagttt cggcagaaaa tacaggcaat	180
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ccgcaaaatt ccgccgaatc cgcaaatcaa acagggaaaca accaaccgcg cgattcttca	300
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atttataaag acaagtcgc ttcattctca tctgcgcgat tcaggcgtt tgcacggctg	660
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[1723]

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           35           40           45
Asp Met Ala Ala Val Ser Ala Glu Asn Thr Gly Asn Gly Gly Ala Ala
           50           55           60
Thr Thr Asp Lys Pro Lys Asn Glu Asp Glu Gly Pro Gln Asn Asp Met
65           70           75           80
Pro Gln Asn Ser Ala Glu Ser Ala Asn Gln Thr Gly Asn Asn Gln Pro
           85           90           95
Ala Asp Ser Ser Asp Ser Ala Pro Ala Ser Asn Pro Ala Pro Ala Asn
           100          105          110
Gly Gly Ser Asn Phe Gly Arg Val Asp Leu Ala Asn Gly Val Leu Ile
           115          120          125
Asp Gly Pro Ser Gln Asn Ile Thr Leu Thr His Cys Lys Gly Asp Ser
           130          135          140
Cys Asn Gly Asp Asn Leu Leu Asp Glu Glu Ala Pro Ser Lys Ser Glu
145          150          155          160
Phe Glu Asn Leu Asn Glu Ser Glu Arg Ile Glu Lys Tyr Lys Lys Asp
           165          170          175
Gly Lys Ser Asp Lys Phe Thr Asn Leu Val Ala Thr Ala Val Gln Ala
           180          185          190
Asn Gly Thr Asn Lys Tyr Val Ile Ile Tyr Lys Asp Lys Ser Ala Ser
           195          200          205
Ser Ser Ser Ala Arg Phe Arg Arg Ser Ala Arg Ser Arg Arg Ser Leu
           210          215          220
Pro Ala Glu Met Pro Leu Ile Pro Val Asn Gln Ala Asp Thr Leu Ile
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Val Asp Gly Glu Ala Val Ser Leu Thr Gly His Ser Gly Asn Ile Phe
           245          250          255

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[1724]

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 His Thr Glu Asn Gly Arg Pro Tyr Pro Thr Arg Gly Arg Phe Ala Ala  
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 Lys Val Asp Phe Gly Ser Lys Ser Val Asp Gly Ile Ile Asp Ser Gly  
 325 330 335  
 Asp Asp Leu His Met Gly Thr Gln Lys Phe Lys Ala Ala Ile Asp Gly  
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 Asn Gly Phe Lys Gly Thr Trp Thr Glu Asn Gly Gly Gly Asp Val Ser  
 355 360 365  
 Gly Arg Phe Tyr Gly Pro Ala Gly Glu Glu Val Ala Gly Lys Tyr Ser  
 370 375 380  
 Tyr Arg Pro Thr Asp Ala Glu Lys Gly Gly Phe Gly Val Phe Ala Gly  
 385 390 395 400  
 Lys Lys Glu Gln Asp Gly Ser Gly Gly Gly Gly Cys Gln Ser Lys Ser  
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 Ile Gln Thr Phe Pro Gln Pro Asp Thr Ser Val Ile Asn Gly Pro Asp  
 420 425 430  
 Arg Pro Val Gly Ile Pro Asp Pro Ala Gly Thr Thr Val Gly Gly Gly  
 435 440 445  
 Gly Ala Val Tyr Thr Val Val Pro His Leu Ser Leu Pro His Trp Ala  
 450 455 460  
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 485 490 495  
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 500 505 510  
 Phe Thr Pro Trp Gln Val Ala Gly Asn Gly Ser Leu Ala Gly Thr Val  
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 Thr Gly Tyr Tyr Glu Pro Val Leu Lys Gly Asp Asp Arg Arg Thr Ala  
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 Gln Ala Arg Phe Pro Ile Tyr Gly Ile Pro Asp Asp Phe Ile Ser Val  
 545 550 555 560  
 Pro Leu Pro Ala Gly Leu Arg Ser Gly Lys Ala Leu Val Arg Ile Arg  
 565 570 575  
 Gln Thr Gly Lys Asn Ser Gly Thr Ile Asp Asn Thr Gly Gly Thr His  
 580 585 590  
 Thr Ala Asp Leu Ser Arg Phe Pro Ile Thr Ala Arg Thr Thr Ala Ile  
 595 600 605  
 Lys Gly Arg Phe Glu Gly Ser Arg Phe Leu Pro Tyr His Thr Arg Asn  
 610 615 620  
 Gln Ile Asn Gly Gly Ala Leu Asp Gly Lys Ala Pro Ile Leu Gly Tyr  
 625 630 635 640  
 Ala Glu Asp Pro Val Glu Leu Phe Phe Met His Ile Gln Gly Ser Gly  
 645 650 655  
 Arg Leu Lys Thr Pro Ser Gly Lys Tyr Ile Arg Ile Gly Tyr Ala Asp  
 660 665 670

[1725]

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 690 695 700  
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 705 710 715 720  
 Ser Tyr Ile Phe Phe Arg Glu Leu Ala Gly Ser Ser Asn Asp Gly Pro  
 725 730 735  
 Val Gly Ala Leu Gly Thr Pro Leu Met Gly Glu Tyr Ala Gly Ala Val  
 740 745 750  
 Asp Arg His Tyr Ile Thr Leu Gly Ala Pro Leu Phe Val Ala Thr Ala  
 755 760 765  
 His Pro Val Thr Arg Lys Ala Leu Asn Arg Leu Ile Met Ala Gln Asp  
 770 775 780  
 Thr Gly Ser Ala Ile Lys Gly Ala Val Arg Val Asp Tyr Phe Trp Gly  
 785 790 795 800  
 Tyr Gly Asp Glu Ala Gly Glu Leu Ala Gly Lys Gln Lys Thr Thr Gly  
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- [1728] <212>DNA
- [1729] <213>人工序列
- [1730] <220>
- [1731] <223>Δ G287-953
- [1732] <400>5
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gcccattcca cacaaggcag ccaagatatg gcggcagttt cggcagaaaa tacaggcaat 180
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[1734]

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[1736] &lt;211&gt;579

[1737] &lt;212&gt;PRT

[1738] &lt;213&gt; 人工序列

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[1740] &lt;223&gt; Δ G287-953

[1741] &lt;400&gt;6

[1742]

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 35 40 45  
 Asp Met Ala Ala Val Ser Ala Glu Asn Thr Gly Asn Gly Gly Ala Ala  
 50 55 60  
 Thr Thr Asp Lys Pro Lys Asn Glu Asp Glu Gly Pro Gln Asn Asp Met  
 65 70 75 80  
 Pro Gln Asn Ser Ala Glu Ser Ala Asn Gln Thr Gly Asn Asn Gln Pro  
 85 90 95  
 Ala Asp Ser Ser Asp Ser Ala Pro Ala Ser Asn Pro Ala Pro Ala Asn  
 100 105 110  
 Gly Gly Ser Asn Phe Gly Arg Val Asp Leu Ala Asn Gly Val Leu Ile  
 115 120 125  
 Asp Gly Pro Ser Gln Asn Ile Thr Leu Thr His Cys Lys Gly Asp Ser  
 130 135 140  
 Cys Asn Gly Asp Asn Leu Leu Asp Glu Glu Ala Pro Ser Lys Ser Glu  
 145 150 155 160  
 Phe Glu Asn Leu Asn Glu Ser Glu Arg Ile Glu Lys Tyr Lys Lys Asp  
 165 170 175  
 Gly Lys Ser Asp Lys Phe Thr Asn Leu Val Ala Thr Ala Val Gln Ala  
 180 185 190  
 Asn Gly Thr Asn Lys Tyr Val Ile Ile Tyr Lys Asp Lys Ser Ala Ser  
 195 200 205  
 Ser Ser Ser Ala Arg Phe Arg Arg Ser Ala Arg Ser Arg Arg Ser Leu  
 210 215 220  
 Pro Ala Glu Met Pro Leu Ile Pro Val Asn Gln Ala Asp Thr Leu Ile  
 225 230 235 240  
 Val Asp Gly Glu Ala Val Ser Leu Thr Gly His Ser Gly Asn Ile Phe  
 245 250 255  
 Ala Pro Glu Gly Asn Tyr Arg Tyr Leu Thr Tyr Gly Ala Glu Lys Leu

[1743]

	260		265		270
Pro Gly Gly Ser Tyr Ala Leu Arg Val Gln Gly Glu Pro Ala Lys Gly					
	275		280		285
Glu Met Leu Ala Gly Thr Ala Val Tyr Asn Gly Glu Val Leu His Phe					
	290		295		300
His Thr Glu Asn Gly Arg Pro Tyr Pro Thr Arg Gly Arg Phe Ala Ala					
305		310		315	320
Lys Val Asp Phe Gly Ser Lys Ser Val Asp Gly Ile Ile Asp Ser Gly					
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Asp Asp Leu His Met Gly Thr Gln Lys Phe Lys Ala Ala Ile Asp Gly					
	340		345		350
Asn Gly Phe Lys Gly Thr Trp Thr Glu Asn Gly Gly Gly Asp Val Ser					
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Gly Arg Phe Tyr Gly Pro Ala Gly Glu Glu Val Ala Gly Lys Tyr Ser					
	370		375		380
Tyr Arg Pro Thr Asp Ala Glu Lys Gly Gly Phe Gly Val Phe Ala Gly					
385		390		395	400
Lys Lys Glu Gln Asp Gly Ser Gly Gly Gly Gly Ala Thr Tyr Lys Val					
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Asp Glu Tyr His Ala Asn Ala Arg Phe Ala Ile Asp His Phe Asn Thr					
	420		425		430
Ser Thr Asn Val Gly Gly Phe Tyr Gly Leu Thr Gly Ser Val Glu Phe					
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Asp Gln Ala Lys Arg Asp Gly Lys Ile Asp Ile Thr Ile Pro Val Ala					
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Asn Leu Gln Ser Gly Ser Gln His Phe Thr Asp His Leu Lys Ser Ala					
465		470		475	480
Asp Ile Phe Asp Ala Ala Gln Tyr Pro Asp Ile Arg Phe Val Ser Thr					
	485		490		495
Lys Phe Asn Phe Asn Gly Lys Lys Leu Val Ser Val Asp Gly Asn Leu					
	500		505		510
Thr Met His Gly Lys Thr Ala Pro Val Lys Leu Lys Ala Glu Lys Phe					
	515		520		525
Asn Cys Tyr Gln Ser Pro Met Ala Lys Thr Glu Val Cys Gly Gly Asp					
	530		535		540
Phe Ser Thr Thr Ile Asp Arg Thr Lys Trp Gly Val Asp Tyr Leu Val					
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Asn Val Gly Met Thr Lys Ser Val Arg Ile Asp Ile Gln Ile Glu Ala					
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Ala Lys Gln

[1744] &lt;210&gt;7

[1745] &lt;211&gt;2388

[1746] &lt;212&gt;DNA

[1747] &lt;213&gt;人工序列

[1748] &lt;220&gt;

[1749] &lt;223&gt;ΔG287-961

[1750] &lt;400&gt;7

[1751]

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[1752]

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[1753] &lt;210&gt;8

[1754] &lt;211&gt;793

[1755] &lt;212&gt;PRT

[1756] &lt;213&gt; 人工序列

[1757] &lt;220&gt;

[1758] &lt;223&gt; Δ G287-961

[1759] &lt;400&gt;8

[1760]

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[1761]

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Thr	Thr	Asp	Lys	Pro	Lys	Asn	Glu	Asp	Glu	Gly	Pro	Gln	Asn	Asp	Met
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Cys	Asn	Gly	Asp	Asn	Leu	Leu	Asp	Glu	Glu	Ala	Pro	Ser	Lys	Ser	Glu
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Glu	Met	Leu	Ala	Gly	Thr	Ala	Val	Tyr	Asn	Gly	Glu	Val	Leu	His	Phe
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		340						345					350		
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Lys	Lys	Glu	Gln	Asp	Gly	Ser	Gly	Gly	Gly	Gly	Ala	Thr	Asn	Asp	Asp
			405							410				415	
Asp	Val	Lys	Lys	Ala	Ala	Thr	Val	Ala	Ile	Ala	Ala	Ala	Tyr	Asn	Asn
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[1762]



[1768] &lt;223&gt; Δ G287NZ-919

[1769] &lt;400&gt;9

[1770]

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[1771] &lt;210&gt;10

[1772] &lt;211&gt;897



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 35 40 45  
 Asp Met Ala Ala Val Ser Glu Glu Asn Thr Gly Asn Gly Gly Ala Ala  
 50 55 60  
 Ala Thr Asp Lys Pro Lys Asn Glu Asp Glu Gly Ala Gln Asn Asp Met  
 65 70 75 80  
 Pro Gln Asn Ala Ala Asp Thr Asp Ser Leu Thr Pro Asn His Thr Pro  
 85 90 95  
 Ala Ser Asn Met Pro Ala Gly Asn Met Glu Asn Gln Ala Pro Asp Ala  
 100 105 110  
 Gly Glu Ser Glu Gln Pro Ala Asn Gln Pro Asp Met Ala Asn Thr Ala  
 115 120 125  
 Asp Gly Met Gln Gly Asp Asp Pro Ser Ala Gly Gly Glu Asn Ala Gly  
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 Ser Gly Asn Asn Phe Leu Asp Glu Glu Val Gln Leu Lys Ser Glu Phe  
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 Glu Lys Leu Ser Asp Ala Asp Lys Ile Ser Asn Tyr Lys Lys Asp Gly  
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 Ile Val Asp Gly Glu Ala Val Ser Leu Thr Gly His Ser Gly Asn Ile  
 305 310 315 320  
 Phe Ala Pro Glu Gly Asn Tyr Arg Tyr Leu Thr Tyr Gly Ala Glu Lys  
 325 330 335  
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 Gly Glu Met Leu Ala Gly Thr Ala Val Tyr Asn Gly Glu Val Leu His  
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[1779]

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 595 600 605  
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 Val Pro Leu Pro Ala Gly Leu Arg Ser Gly Lys Ala Leu Val Arg Ile  
 625 630 635 640  
 Arg Gln Thr Gly Lys Asn Ser Gly Thr Ile Asp Asn Thr Gly Gly Thr  
 645 650 655  
 His Thr Ala Asp Leu Ser Arg Phe Pro Ile Thr Ala Arg Thr Thr Ala  
 660 665 670  
 Ile Lys Gly Arg Phe Glu Gly Ser Arg Phe Leu Pro Tyr His Thr Arg  
 675 680 685  
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 690 695 700  
 Tyr Ala Glu Asp Pro Val Glu Leu Phe Phe Met His Ile Gln Gly Ser  
 705 710 715 720  
 Gly Arg Leu Lys Thr Pro Ser Gly Lys Tyr Ile Arg Ile Gly Tyr Ala  
 725 730 735  
 Asp Lys Asn Glu His Pro Tyr Val Ser Ile Gly Arg Tyr Met Ala Asp  
 740 745 750  
 Lys Gly Tyr Leu Lys Leu Gly Gln Thr Ser Met Gln Gly Ile Lys Ala  
 755 760 765  
 Tyr Met Arg Gln Asn Pro Gln Arg Leu Ala Glu Val Leu Gly Gln Asn  
 770 775 780

[1780]

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 785 790 795 800  
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 Val Asp Arg His Tyr Ile Thr Leu Gly Ala Pro Leu Phe Val Ala Thr  
 820 825 830  
 Ala His Pro Val Thr Arg Lys Ala Leu Asn Arg Leu Ile Met Ala Gln  
 835 840 845  
 Asp Thr Gly Ser Ala Ile Lys Gly Ala Val Arg Val Asp Tyr Phe Trp  
 850 855 860  
 Gly Tyr Gly Asp Glu Ala Gly Glu Leu Ala Gly Lys Gln Lys Thr Thr  
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gcgaaaaccg aagtttgcg cggcgacttc agcaccacca tcgaccgcac caaatggggc 1860  
gtggactacc tcgttaacgt tggatgacc aaaagcgtcc gcatcgacat ccaaatcgag 1920  
gcagccaaac aataaaagct t 1941

[1790] &lt;210&gt;12

[1791] &lt;211&gt;644

[1792] &lt;212&gt;PRT

[1793] &lt;213&gt; 人工序列

[1794] &lt;220&gt;

[1795] &lt;223&gt; Δ G287NZ-953

[1796] &lt;400&gt;12

[1797]

Met Ala Ser Pro Asp Val Lys Ser Ala Asp Thr Leu Ser Lys Pro Ala  
 1                                   5                                   10                                   15  
 Ala Pro Val Val Ser Glu Lys Glu Thr Glu Ala Lys Glu Asp Ala Pro  
                                   20                                   25                                   30  
 Gln Ala Gly Ser Gln Gly Gln Gly Ala Pro Ser Ala Gln Gly Gly Gln  
                                   35                                   40                                   45  
 Asp Met Ala Ala Val Ser Glu Glu Asn Thr Gly Asn Gly Gly Ala Ala  
                                   50                                   55                                   60  
 Ala Thr Asp Lys Pro Lys Asn Glu Asp Glu Gly Ala Gln Asn Asp Met  
 65                                   70                                   75                                   80  
 Pro Gln Asn Ala Ala Asp Thr Asp Ser Leu Thr Pro Asn His Thr Pro  
                                   85                                   90                                   95  
 Ala Ser Asn Met Pro Ala Gly Asn Met Glu Asn Gln Ala Pro Asp Ala  
                                   100                                   105                                   110  
 Gly Glu Ser Glu Gln Pro Ala Asn Gln Pro Asp Met Ala Asn Thr Ala  
                                   115                                   120                                   125  
 Asp Gly Met Gln Gly Asp Asp Pro Ser Ala Gly Gly Glu Asn Ala Gly  
                                   130                                   135                                   140  
 Asn Thr Ala Ala Gln Gly Thr Asn Gln Ala Glu Asn Asn Gln Thr Ala  
 145                                   150                                   155                                   160  
 Gly Ser Gln Asn Pro Ala Ser Ser Thr Asn Pro Ser Ala Thr Asn Ser  
                                   165                                   170                                   175  
 Gly Gly Asp Phe Gly Arg Thr Asn Val Gly Asn Ser Val Val Ile Asp  
                                   180                                   185                                   190  
 Gly Pro Ser Gln Asn Ile Thr Leu Thr His Cys Lys Gly Asp Ser Cys  
                                   195                                   200                                   205  
 Ser Gly Asn Asn Phe Leu Asp Glu Glu Val Gln Leu Lys Ser Glu Phe  
                                   210                                   215                                   220  
 Glu Lys Leu Ser Asp Ala Asp Lys Ile Ser Asn Tyr Lys Lys Asp Gly  
 225                                   230                                   235                                   240  
 Lys Asn Asp Gly Lys Asn Asp Lys Phe Val Gly Leu Val Ala Asp Ser  
                                   245                                   250                                   255  
 Val Gln Met Lys Gly Ile Asn Gln Tyr Ile Ile Phe Tyr Lys Pro Lys  
                                   260                                   265                                   270  
 Pro Thr Ser Phe Ala Arg Phe Arg Arg Ser Ala Arg Ser Arg Arg Ser

[1798]

275	280	285
Leu Pro Ala Glu Met Pro Leu Ile Pro Val Asn Gln Ala Asp Thr Leu		
290	295	300
Ile Val Asp Gly Glu Ala Val Ser Leu Thr Gly His Ser Gly Asn Ile		
305	310	315
Phe Ala Pro Glu Gly Asn Tyr Arg Tyr Leu Thr Tyr Gly Ala Glu Lys		
	325	330
Leu Pro Gly Gly Ser Tyr Ala Leu Arg Val Gln Gly Glu Pro Ser Lys		
	340	345
Gly Glu Met Leu Ala Gly Thr Ala Val Tyr Asn Gly Glu Val Leu His		
	355	360
Phe His Thr Glu Asn Gly Arg Pro Ser Pro Ser Arg Gly Arg Phe Ala		
370	375	380
Ala Lys Val Asp Phe Gly Ser Lys Ser Val Asp Gly Ile Ile Asp Ser		
385	390	395
Gly Asp Gly Leu His Met Gly Thr Gln Lys Phe Lys Ala Ala Ile Asp		
	405	410
Gly Asn Gly Phe Lys Gly Thr Trp Thr Glu Asn Gly Gly Gly Asp Val		
	420	425
Ser Gly Lys Phe Tyr Gly Pro Ala Gly Glu Glu Val Ala Gly Lys Tyr		
	435	440
Ser Tyr Arg Pro Thr Asp Ala Glu Lys Gly Gly Phe Gly Val Phe Ala		
450	455	460
Gly Lys Lys Glu Gln Asp Gly Ser Gly Gly Gly Gly Ala Thr Tyr Lys		
465	470	475
Val Asp Glu Tyr His Ala Asn Ala Arg Phe Ala Ile Asp His Phe Asn		
	485	490
Thr Ser Thr Asn Val Gly Gly Phe Tyr Gly Leu Thr Gly Ser Val Glu		
	500	505
Phe Asp Gln Ala Lys Arg Asp Gly Lys Ile Asp Ile Thr Ile Pro Val		
	515	520
Ala Asn Leu Gln Ser Gly Ser Gln His Phe Thr Asp His Leu Lys Ser		
	530	535
Ala Asp Ile Phe Asp Ala Ala Gln Tyr Pro Asp Ile Arg Phe Val Ser		
545	550	555
Thr Lys Phe Asn Phe Asn Gly Lys Lys Leu Val Ser Val Asp Gly Asn		
	565	570
Leu Thr Met His Gly Lys Thr Ala Pro Val Lys Leu Lys Ala Glu Lys		
	580	585
Phe Asn Cys Tyr Gln Ser Pro Met Ala Lys Thr Glu Val Cys Gly Gly		
	595	600
Asp Phe Ser Thr Thr Ile Asp Arg Thr Lys Trp Gly Val Asp Tyr Leu		
610	615	620
Val Asn Val Gly Met Thr Lys Ser Val Arg Ile Asp Ile Gln Ile Glu		
625	630	635
Ala Ala Lys Gln		

[1799] &lt;210&gt;13

[1800] &lt;211&gt;2583

[1801] &lt;212&gt;DNA

[1802] &lt;213&gt;人工序列

[1803] &lt;220&gt;

[1804] &lt;223&gt; Δ G287NZ-961

[1805] &lt;400&gt;13

[1806]

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gcgccatccg cacaaggcgg tcaagatatg gcggcggttt cggaagaaaa tacaggcaat 180
ggcggtgccg cagcaacgga caaacccaaa aatgaagacg agggggcgca aatgatgatg 240
ccgcaaaatg ccgccgatac agatagtttg acaccgaatc acaccccggc ttcgaatatg 300
ccggccggaa atatggaaaa ccaagcaccg gatgccgggg aatcggagca gccggcaaac 360
caaccgata tggcaaatat ggcggacgga atgcagggtg acgatccgtc ggcaggcggg 420
gaaaatgccg gcaatacggc tgcccaaggt acaaatcaag ccgaaaacaa tcaaaccgcc 480
ggttctcaaa atcctgccte ttcaaccaat cctagcgcca cgaatagcgg tggatgattt 540
ggaaggacga acgtgggcaa ttctgttgtg attgacgggc cgtcgcaaaa tataacgttg 600
accactgta aaggcgattc ttgtagtggc aataatttct tggatgaaga agtacagcta 660
aaatcagaat ttgaaaaatt aagtgatgca gacaaaataa gtaattacaa gaaagatggg 720
aagaatgacg ggaagaatga taaatttgtc ggtttggttg ccgatagtg gcagatgaag 780
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cgttctgcac ggtcgaggcg gtcgcttccg gccgagatgc cgctgattcc cgtcaatcag 900
gcggatacgc tgattgtcga tggggaagcg gtcagcctga cggggcattc cggcaatatac 960
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gtgtacaacg gcgaagtgtc gcattttcat acggaacacg gccgtccgtc cccgtccaga 1140
ggcaggttg ccgcaaaagt cgatttcggc agcaaatctg tggacggcat tatcgacagc 1200
ggcgtatggt tgcatatggg tacgcaaaaa ttcaaagccg ccatcgatgg aaacggcttt 1260
aaggggactt ggacgaaaa tggcggcggg gatgtttccg gaaagtitta cggcccggcc 1320
ggcgaggaa tggcgggaaa atacagctat cgcccaacag atgcggaaaa gggcggattc 1380
ggcgtgttg ccgcaaaaa agagcaggat ggatccggag gaggaggagc cacaacgac 1440
gacgatgta aaaaagctgc cacigtggcc attgctgtct cctacaacaa tggccaagaa 1500
atcaacggt tcaaagctgg agagaccatc tacgacattg atgaagacgg cacaattacc 1560
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gctttagcag atactgatgc cgtcttgat gcaaccacca acgcctttaa taaattggga 1800
gaaaatataa cgacatttgc tgaagagact aagacaaata tcgtaaaaat tgatgaaaaa 1860
ttagaagccg tggctgatac cgtcgacaag catgccgaag cattcaacga tatcgccgat 1920
tcattggatg aaaccaacac taaggcagac gaagccgtca aaaccgcaa tgaagccaaa 1980
cagacggccg aagaaccaa acaaaacgtc gatgccaaag taaaagctgc agaaactgca 2040
gcaggcaaa cgaagctgc cgctggcaca gctaatactg cagccgacaa ggccgaagct 2100
gtcgtgcaa aagttaccga catcaaagct gatatcgta cgaacaaga taatattgct 2160
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aacgtgggtc ggttcaatgt aacggctgca gtcggcggct acaaatccga atcggcagtc 2460
gccatcggtc cggcttccg cttaccgaa aactttgccg ccaaagcagg cgtggcagtc 2520
ggcacttcgt ccggttcttc cgcagcctac catgtcggcg tcaattacga gtgtaaaaag 2580
ctt

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[1807] &lt;210&gt;14

[1808] &lt;211&gt;858



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- [1809] <212>PRT
  - [1810] <213> 人工序列
  - [1811] <220>
  - [1812] <223>  $\Delta$  G287NZ-961
  - [1813] <400>14
  - [1814]

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 Ala Pro Val Val Ser Glu Lys Glu Thr Glu Ala Lys Glu Asp Ala Pro  
 20 25 30  
 Gln Ala Gly Ser Gln Gly Gln Gly Ala Pro Ser Ala Gln Gly Gly Gln  
 35 40 45  
 Asp Met Ala Ala Val Ser Glu Glu Asn Thr Gly Asn Gly Gly Ala Ala  
 50 55 60  
 Ala Thr Asp Lys Pro Lys Asn Glu Asp Glu Gly Ala Gln Asn Asp Met  
 65 70 75 80  
 Pro Gln Asn Ala Ala Asp Thr Asp Ser Leu Thr Pro Asn His Thr Pro  
 85 90 95  
 Ala Ser Asn Met Pro Ala Gly Asn Met Glu Asn Gln Ala Pro Asp Ala  
 100 105 110  
 Gly Glu Ser Glu Gln Pro Ala Asn Gln Pro Asp Met Ala Asn Thr Ala  
 115 120 125  
 Asp Gly Met Gln Gly Asp Asp Pro Ser Ala Gly Gly Glu Asn Ala Gly  
 130 135 140  
 Asn Thr Ala Ala Gln Gly Thr Asn Gln Ala Glu Asn Asn Gln Thr Ala  
 145 150 155 160  
 Gly Ser Gln Asn Pro Ala Ser Ser Thr Asn Pro Ser Ala Thr Asn Ser  
 165 170 175  
 Gly Gly Asp Phe Gly Arg Thr Asn Val Gly Asn Ser Val Val Ile Asp  
 180 185 190  
 Gly Pro Ser Gln Asn Ile Thr Leu Thr His Cys Lys Gly Asp Ser Cys  
 195 200 205  
 Ser Gly Asn Asn Phe Leu Asp Glu Glu Val Gln Leu Lys Ser Glu Phe  
 210 215 220  
 Glu Lys Leu Ser Asp Ala Asp Lys Ile Ser Asn Tyr Lys Lys Asp Gly  
 225 230 235 240  
 Lys Asn Asp Gly Lys Asn Asp Lys Phe Val Gly Leu Val Ala Asp Ser  
 245 250 255  
 Val Gln Met Lys Gly Ile Asn Gln Tyr Ile Ile Phe Tyr Lys Pro Lys  
 260 265 270  
 Pro Thr Ser Phe Ala Arg Phe Arg Arg Ser Ala Arg Ser Arg Arg Ser  
 275 280 285  
 Leu Pro Ala Glu Met Pro Leu Ile Pro Val Asn Gln Ala Asp Thr Leu  
 290 295 300  
 Ile Val Asp Gly Glu Ala Val Ser Leu Thr Gly His Ser Gly Asn Ile  
 305 310 315 320  
 Phe Ala Pro Glu Gly Asn Tyr Arg Tyr Leu Thr Tyr Gly Ala Glu Lys  
 325 330 335  
 Leu Pro Gly Gly Ser Tyr Ala Leu Arg Val Gln Gly Glu Pro Ser Lys  
 340 345 350  
 Gly Glu Met Leu Ala Gly Thr Ala Val Tyr Asn Gly Glu Val Leu His

[1815]

355 360 365  
 Phe His Thr Glu Asn Gly Arg Pro Ser Pro Ser Arg Gly Arg Phe Ala  
 370 375 380  
 Ala Lys Val Asp Phe Gly Ser Lys Ser Val Asp Gly Ile Ile Asp Ser  
 385 390 395 400  
 Gly Asp Gly Leu His Met Gly Thr Gln Lys Phe Lys Ala Ala Ile Asp  
 405 410 415  
 Gly Asn Gly Phe Lys Gly Thr Trp Thr Glu Asn Gly Gly Gly Asp Val  
 420 425 430  
 Ser Gly Lys Phe Tyr Gly Pro Ala Gly Glu Glu Val Ala Gly Lys Tyr  
 435 440 445  
 Ser Tyr Arg Pro Thr Asp Ala Glu Lys Gly Gly Phe Gly Val Phe Ala  
 450 455 460  
 Gly Lys Lys Glu Gln Asp Gly Ser Gly Gly Gly Gly Ala Thr Asn Asp  
 465 470 475 480  
 Asp Asp Val Lys Lys Ala Ala Thr Val Ala Ile Ala Ala Ala Tyr Asn  
 485 490 495  
 Asn Gly Gln Glu Ile Asn Gly Phe Lys Ala Gly Glu Thr Ile Tyr Asp  
 500 505 510  
 Ile Asp Glu Asp Gly Thr Ile Thr Lys Lys Asp Ala Thr Ala Ala Asp  
 515 520 525  
 Val Glu Ala Asp Asp Phe Lys Gly Leu Gly Leu Lys Lys Val Val Thr  
 530 535 540  
 Asn Leu Thr Lys Thr Val Asn Glu Asn Lys Gln Asn Val Asp Ala Lys  
 545 550 555 560  
 Val Lys Ala Ala Glu Ser Glu Ile Glu Lys Leu Thr Thr Lys Leu Ala  
 565 570 575  
 Asp Thr Asp Ala Ala Leu Ala Asp Thr Asp Ala Ala Leu Asp Ala Thr  
 580 585 590  
 Thr Asn Ala Leu Asn Lys Leu Gly Glu Asn Ile Thr Thr Phe Ala Glu  
 595 600 605  
 Glu Thr Lys Thr Asn Ile Val Lys Ile Asp Glu Lys Leu Glu Ala Val  
 610 615 620  
 Ala Asp Thr Val Asp Lys His Ala Glu Ala Phe Asn Asp Ile Ala Asp  
 625 630 635 640  
 Ser Leu Asp Glu Thr Asn Thr Lys Ala Asp Glu Ala Val Lys Thr Ala  
 645 650 655  
 Asn Glu Ala Lys Gln Thr Ala Glu Glu Thr Lys Gln Asn Val Asp Ala  
 660 665 670  
 Lys Val Lys Ala Ala Glu Thr Ala Ala Gly Lys Ala Glu Ala Ala Ala  
 675 680 685  
 Gly Thr Ala Asn Thr Ala Ala Asp Lys Ala Glu Ala Val Ala Ala Lys  
 690 695 700  
 Val Thr Asp Ile Lys Ala Asp Ile Ala Thr Asn Lys Asp Asn Ile Ala  
 705 710 715 720  
 Lys Lys Ala Asn Ser Ala Asp Val Tyr Thr Arg Glu Glu Ser Asp Ser  
 725 730 735  
 Lys Phe Val Arg Ile Asp Gly Leu Asn Ala Thr Thr Glu Lys Leu Asp  
 740 745 750  
 Thr Arg Leu Ala Ser Ala Glu Lys Ser Ile Ala Asp His Asp Thr Arg  
 755 760 765  
 Leu Asn Gly Leu Asp Lys Thr Val Ser Asp Leu Arg Lys Glu Thr Arg

[1816]

	770					775						780				
	Gln	Gly	Leu	Ala	Glu	Gln	Ala	Ala	Leu	Ser	Gly	Leu	Phe	Gln	Pro	Tyr
785						790					795					800
Asn	Val	Gly	Arg	Phe	Asn	Val	Thr	Ala	Ala	Val	Gly	Gly	Tyr	Lys	Ser	
				805						810						815
Glu	Ser	Ala	Val	Ala	Ile	Gly	Thr	Gly	Phe	Arg	Phe	Thr	Glu	Asn	Phe	
				820						825						830
Ala	Ala	Lys	Ala	Gly	Val	Ala	Val	Gly	Thr	Ser	Ser	Gly	Ser	Ser	Ala	
				835						840						845
Ala	Tyr	His	Val	Gly	Val	Asn	Tyr	Glu	Trp							
				850												
																855

- [1817] <210>15
- [1818] <211>1082
- [1819] <212>PRT
- [1820] <213>人工序列
- [1821] <220>
- [1822] <223>983
- [1823] <400>15
- [1824]

Met Arg Thr Thr Pro Thr Phe Pro Thr Lys Thr Phe Lys Pro Thr Ala  
 1 5 10 15  
 Met Ala Leu Ala Val Ala Thr Thr Leu Ser Ala Cys Leu Gly Gly Gly  
 20 25 30  
 Gly Gly Gly Thr Ser Ala Pro Asp Phe Asn Ala Gly Gly Thr Gly Ile  
 35 40 45  
 Gly Ser Asn Ser Arg Ala Thr Thr Ala Lys Ser Ala Ala Val Ser Tyr  
 50 55 60  
 Ala Gly Ile Lys Asn Glu Met Cys Lys Asp Arg Ser Met Leu Cys Ala  
 65 70 75 80  
 Gly Arg Asp Asp Val Ala Val Thr Asp Arg Asp Ala Lys Ile Asn Ala  
 85 90 95  
 Pro Pro Pro Asn Leu His Thr Gly Asp Phe Pro Asn Pro Asn Asp Ala  
 100 105 110  
 Tyr Lys Asn Leu Ile Asn Leu Lys Pro Ala Ile Glu Ala Gly Tyr Thr  
 115 120 125  
 Gly Arg Gly Val Glu Val Gly Ile Val Asp Thr Gly Glu Ser Val Gly  
 130 135 140  
 Ser Ile Ser Phe Pro Glu Leu Tyr Gly Arg Lys Glu His Gly Tyr Asn  
 145 150 155 160  
 Glu Asn Tyr Lys Asn Tyr Thr Ala Tyr Met Arg Lys Glu Ala Pro Glu  
 165 170 175  
 Asp Gly Gly Gly Lys Asp Ile Glu Ala Ser Phe Asp Asp Glu Ala Val  
 180 185 190  
 Ile Glu Thr Glu Ala Lys Pro Thr Asp Ile Arg His Val Lys Glu Ile  
 195 200 205  
 Gly His Ile Asp Leu Val Ser His Ile Ile Gly Gly Arg Ser Val Asp  
 210 215 220  
 Gly Arg Pro Ala Gly Gly Ile Ala Pro Asp Ala Thr Leu His Ile Met  
 225 230 235 240  
 Asn Thr Asn Asp Glu Thr Lys Asn Glu Met Met Val Ala Ala Ile Arg

[1825]

	245		250		255
Asn Ala Trp Val Lys Leu Gly Glu Arg Gly Val Arg Ile Val Asn Asn					
	260		265		270
Ser Phe Gly Thr Thr Ser Arg Ala Gly Thr Ala Asp Leu Phe Gln Ile					
	275		280		285
Ala Asn Ser Glu Glu Gln Tyr Arg Gln Ala Leu Leu Asp Tyr Ser Gly					
	290		295		300
Gly Asp Lys Thr Asp Glu Gly Ile Arg Leu Met Gln Gln Ser Asp Tyr					
305		310		315	320
Gly Asn Leu Ser Tyr His Ile Arg Asn Lys Asn Met Leu Phe Ile Phe					
	325		330		335
Ser Thr Gly Asn Asp Ala Gln Ala Gln Pro Asn Thr Tyr Ala Leu Leu					
	340		345		350
Pro Phe Tyr Glu Lys Asp Ala Gln Lys Gly Ile Ile Thr Val Ala Gly					
	355		360		365
Val Asp Arg Ser Gly Glu Lys Phe Lys Arg Glu Met Tyr Gly Glu Pro					
	370		375		380
Gly Thr Glu Pro Leu Glu Tyr Gly Ser Asn His Cys Gly Ile Thr Ala					
385		390		395	400
Met Trp Cys Leu Ser Ala Pro Tyr Glu Ala Ser Val Arg Phe Thr Arg					
	405		410		415
Thr Asn Pro Ile Gln Ile Ala Gly Thr Ser Phe Ser Ala Pro Ile Val					
	420		425		430
Thr Gly Thr Ala Ala Leu Leu Leu Gln Lys Tyr Pro Trp Met Ser Asn					
	435		440		445
Asp Asn Leu Arg Thr Thr Leu Leu Thr Thr Ala Gln Asp Ile Gly Ala					
	450		455		460
Val Gly Val Asp Ser Lys Phe Gly Trp Gly Leu Leu Asp Ala Gly Lys					
465		470		475	480
Ala Met Asn Gly Pro Ala Ser Phe Pro Phe Gly Asp Phe Thr Ala Asp					
	485		490		495
Thr Lys Gly Thr Ser Asp Ile Ala Tyr Ser Phe Arg Asn Asp Ile Ser					
	500		505		510
Gly Thr Gly Gly Leu Ile Lys Lys Gly Gly Ser Gln Leu Gln Leu His					
	515		520		525
Gly Asn Asn Thr Tyr Thr Gly Lys Thr Ile Ile Glu Gly Gly Ser Leu					
	530		535		540
Val Leu Tyr Gly Asn Asn Lys Ser Asp Met Arg Val Glu Thr Lys Gly					
545		550		555	560
Ala Leu Ile Tyr Asn Gly Ala Ala Ser Gly Gly Ser Leu Asn Ser Asp					
	565		570		575
Gly Ile Val Tyr Leu Ala Asp Thr Asp Gln Ser Gly Ala Asn Glu Thr					
	580		585		590
Val His Ile Lys Gly Ser Leu Gln Leu Asp Gly Lys Gly Thr Leu Tyr					
	595		600		605
Thr Arg Leu Gly Lys Leu Leu Lys Val Asp Gly Thr Ala Ile Ile Gly					
	610		615		620
Gly Lys Leu Tyr Met Ser Ala Arg Gly Lys Gly Ala Gly Tyr Leu Asn					
625		630		635	640
Ser Thr Gly Arg Arg Val Pro Phe Leu Ser Ala Ala Lys Ile Gly Gln					
	645		650		655
Asp Tyr Ser Phe Phe Thr Asn Ile Glu Thr Asp Gly Gly Leu Leu Ala					

[1826]

660 665 670  
 Ser Leu Asp Ser Val Glu Lys Thr Ala Gly Ser Glu Gly Asp Thr Leu  
 675 680 685  
 Ser Tyr Tyr Val Arg Arg Gly Asn Ala Ala Arg Thr Ala Ser Ala Ala  
 690 695 700  
 Ala His Ser Ala Pro Ala Gly Leu Lys His Ala Val Glu Gln Gly Gly  
 705 710 715 720  
 Ser Asn Leu Glu Asn Leu Met Val Glu Leu Asp Ala Ser Glu Ser Ser  
 725 730 735  
 Ala Thr Pro Glu Thr Val Glu Thr Ala Ala Ala Asp Arg Thr Asp Met  
 740 745 750  
 Pro Gly Ile Arg Pro Tyr Gly Ala Thr Phe Arg Ala Ala Ala Val  
 755 760 765  
 Gln His Ala Asn Ala Ala Asp Gly Val Arg Ile Phe Asn Ser Leu Ala  
 770 775 780  
 Ala Thr Val Tyr Ala Asp Ser Thr Ala Ala His Ala Asp Met Gln Gly  
 785 790 795 800  
 Arg Arg Leu Lys Ala Val Ser Asp Gly Leu Asp His Asn Gly Thr Gly  
 805 810 815  
 Leu Arg Val Ile Ala Gln Thr Gln Gln Asp Gly Gly Thr Trp Glu Gln  
 820 825 830  
 Gly Gly Val Glu Gly Lys Met Arg Gly Ser Thr Gln Thr Val Gly Ile  
 835 840 845  
 Ala Ala Lys Thr Gly Glu Asn Thr Thr Ala Ala Ala Thr Leu Gly Met  
 850 855 860  
 Gly Arg Ser Thr Trp Ser Glu Asn Ser Ala Asn Ala Lys Thr Asp Ser  
 865 870 875 880  
 Ile Ser Leu Phe Ala Gly Ile Arg His Asp Ala Gly Asp Ile Gly Tyr  
 885 890 895  
 Leu Lys Gly Leu Phe Ser Tyr Gly Arg Tyr Lys Asn Ser Ile Ser Arg  
 900 905 910  
 Ser Thr Gly Ala Asp Glu His Ala Glu Gly Ser Val Asn Gly Thr Leu  
 915 920 925  
 Met Gln Leu Gly Ala Leu Gly Gly Val Asn Val Pro Phe Ala Ala Thr  
 930 935 940  
 Gly Asp Leu Thr Val Glu Gly Gly Leu Arg Tyr Asp Leu Leu Lys Gln  
 945 950 955 960  
 Asp Ala Phe Ala Glu Lys Gly Ser Ala Leu Gly Trp Ser Gly Asn Ser  
 965 970 975  
 Leu Thr Glu Gly Thr Leu Val Gly Leu Ala Gly Leu Lys Leu Ser Gln  
 980 985 990  
 Pro Leu Ser Asp Lys Ala Val Leu Phe Ala Thr Ala Gly Val Glu Arg  
 995 1000 1005  
 Asp Leu Asn Gly Arg Asp Tyr Thr Val Thr Gly Gly Phe Thr Gly Ala  
 1010 1015 1020  
 Thr Ala Ala Thr Gly Lys Thr Gly Ala Arg Asn Met Pro His Thr Arg  
 1025 1030 1035 1040  
 Leu Val Ala Gly Leu Gly Ala Asp Val Glu Phe Gly Asn Gly Trp Asn  
 1045 1050 1055  
 Gly Leu Ala Arg Tyr Ser Tyr Ala Gly Ser Lys Gln Tyr Gly Asn His  
 1060 1065 1070  
 Ser Gly Arg Val Gly Val Gly Tyr Arg Phe  
 1075 1080

[1827]

- [1828] <210>16  
 [1829] <211>1047  
 [1830] <212>PRT  
 [1831] <213>人工序列  
 [1832] <220>  
 [1833] <223> $\Delta$ G983  
 [1834] <400>16  
 [1835]

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  Ser Arg Ala Thr Thr Ala Lys Ser Ala Ala Val Ser Tyr Ala Gly Ile
           20           25           30
  Lys Asn Glu Met Cys Lys Asp Arg Ser Met Leu Cys Ala Gly Arg Asp
           35           40           45
  Asp Val Ala Val Thr Asp Arg Asp Ala Lys Ile Asn Ala Pro Pro Pro
  50           55           60
  Asn Leu His Thr Gly Asp Phe Pro Asn Pro Asn Asp Ala Tyr Lys Asn
  65           70           75           80
  Leu Ile Asn Leu Lys Pro Ala Ile Glu Ala Gly Tyr Thr Gly Arg Gly
           85           90           95
  Val Glu Val Gly Ile Val Asp Thr Gly Glu Ser Val Gly Ser Ile Ser
           100          105          110
  Phe Pro Glu Leu Tyr Gly Arg Lys Glu His Gly Tyr Asn Glu Asn Tyr
           115          120          125
  Lys Asn Tyr Thr Ala Tyr Met Arg Lys Glu Ala Pro Glu Asp Gly Gly
           130          135          140
  Gly Lys Asp Ile Glu Ala Ser Phe Asp Asp Glu Ala Val Ile Glu Thr
  145          150          155          160
  Glu Ala Lys Pro Thr Asp Ile Arg His Val Lys Glu Ile Gly His Ile
           165          170          175
  Asp Leu Val Ser His Ile Ile Gly Gly Arg Ser Val Asp Gly Arg Pro
           180          185          190
  Ala Gly Gly Ile Ala Pro Asp Ala Thr Leu His Ile Met Asn Thr Asn
           195          200          205
  Asp Glu Thr Lys Asn Glu Met Met Val Ala Ala Ile Arg Asn Ala Trp
           210          215          220
  Val Lys Leu Gly Glu Arg Gly Val Arg Ile Val Asn Asn Ser Phe Gly
  225          230          235          240
  Thr Thr Ser Arg Ala Gly Thr Ala Asp Leu Phe Gln Ile Ala Asn Ser
           245          250          255
  Glu Glu Gln Tyr Arg Gln Ala Leu Leu Asp Tyr Ser Gly Gly Asp Lys
           260          265          270
  Thr Asp Glu Gly Ile Arg Leu Met Gln Gln Ser Asp Tyr Gly Asn Leu
           275          280          285
  Ser Tyr His Ile Arg Asn Lys Asn Met Leu Phe Ile Phe Ser Thr Gly
           290          295          300
  Asn Asp Ala Gln Ala Gln Pro Asn Thr Tyr Ala Leu Leu Pro Phe Tyr
  305          310          315          320
  Glu Lys Asp Ala Gln Lys Gly Ile Ile Thr Val Ala Gly Val Asp Arg

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[1836]

				325					330					335	
Ser	Gly	Glu	Lys	Phe	Lys	Arg	Glu	Met	Tyr	Gly	Glu	Pro	Gly	Thr	Glu
				340					345					350	
Pro	Leu	Glu	Tyr	Gly	Ser	Asn	His	Cys	Gly	Ile	Thr	Ala	Met	Trp	Cys
				355					360					365	
Leu	Ser	Ala	Pro	Tyr	Glu	Ala	Ser	Val	Arg	Phe	Thr	Arg	Thr	Asn	Pro
				370					375					380	
Ile	Gln	Ile	Ala	Gly	Thr	Ser	Phe	Ser	Ala	Pro	Ile	Val	Thr	Gly	Thr
				385					390					395	400
Ala	Ala	Leu	Leu	Leu	Gln	Lys	Tyr	Pro	Trp	Met	Ser	Asn	Asp	Asn	Leu
				405					410					415	
Arg	Thr	Thr	Leu	Leu	Thr	Thr	Ala	Gln	Asp	Ile	Gly	Ala	Val	Gly	Val
				420					425					430	
Asp	Ser	Lys	Phe	Gly	Trp	Gly	Leu	Leu	Asp	Ala	Gly	Lys	Ala	Met	Asn
				435					440					445	
Gly	Pro	Ala	Ser	Phe	Pro	Phe	Gly	Asp	Phe	Thr	Ala	Asp	Thr	Lys	Gly
				450					455					460	
Thr	Ser	Asp	Ile	Ala	Tyr	Ser	Phe	Arg	Asn	Asp	Ile	Ser	Gly	Thr	Gly
				465					470					475	480
Gly	Leu	Ile	Lys	Lys	Gly	Gly	Ser	Gln	Leu	Gln	Leu	His	Gly	Asn	Asn
				485					490					495	
Thr	Tyr	Thr	Gly	Lys	Thr	Ile	Ile	Glu	Gly	Gly	Ser	Leu	Val	Leu	Tyr
				500					505					510	
Gly	Asn	Asn	Lys	Ser	Asp	Met	Arg	Val	Glu	Thr	Lys	Gly	Ala	Leu	Ile
				515					520					525	
Tyr	Asn	Gly	Ala	Ala	Ser	Gly	Gly	Ser	Leu	Asn	Ser	Asp	Gly	Ile	Val
				530					535					540	
Tyr	Leu	Ala	Asp	Thr	Asp	Gln	Ser	Gly	Ala	Asn	Glu	Thr	Val	His	Ile
				545					550					555	560
Lys	Gly	Ser	Leu	Gln	Leu	Asp	Gly	Lys	Gly	Thr	Leu	Tyr	Thr	Arg	Leu
				565					570					575	
Gly	Lys	Leu	Leu	Lys	Val	Asp	Gly	Thr	Ala	Ile	Ile	Gly	Gly	Lys	Leu
				580					585					590	
Tyr	Met	Ser	Ala	Arg	Gly	Lys	Gly	Ala	Gly	Tyr	Leu	Asn	Ser	Thr	Gly
				595					600					605	
Arg	Arg	Val	Pro	Phe	Leu	Ser	Ala	Ala	Lys	Ile	Gly	Gln	Asp	Tyr	Ser
				610					615					620	
Phe	Phe	Thr	Asn	Ile	Glu	Thr	Asp	Gly	Gly	Leu	Leu	Ala	Ser	Leu	Asp
				625					630					635	640
Scr	Val	Glu	Lys	Thr	Ala	Gly	Ser	Glu	Gly	Asp	Thr	Leu	Ser	Tyr	Tyr
				645					650					655	
Val	Arg	Arg	Gly	Asn	Ala	Ala	Arg	Thr	Ala	Ser	Ala	Ala	Ala	His	Ser
				660					665					670	
Ala	Pro	Ala	Gly	Leu	Lys	His	Ala	Val	Glu	Gln	Gly	Gly	Ser	Asn	Leu
				675					680					685	
Glu	Asn	Leu	Met	Val	Glu	Leu	Asp	Ala	Ser	Glu	Ser	Ser	Ala	Thr	Pro
				690					695					700	
Glu	Thr	Val	Glu	Thr	Ala	Ala	Ala	Asp	Arg	Thr	Asp	Met	Pro	Gly	Ile
				705					710					715	720
Arg	Pro	Tyr	Gly	Ala	Thr	Phe	Arg	Ala	Ala	Ala	Ala	Val	Gln	His	Ala
				725					730					735	
Asn	Ala	Ala	Asp	Gly	Val	Arg	Ile	Phe	Asn	Ser	Leu	Ala	Ala	Thr	Val

[1837]

	740		745		750										
Tyr	Ala	Asp	Ser	Thr	Ala	Ala	His	Ala	Asp	Met	Gln	Gly	Arg	Arg	Leu
	755		760		765										
Lys	Ala	Val	Ser	Asp	Gly	Leu	Asp	His	Asn	Gly	Thr	Gly	Leu	Arg	Val
	770		775		780										
Ile	Ala	Gln	Thr	Gln	Gln	Asp	Gly	Gly	Thr	Trp	Glu	Gln	Gly	Gly	Val
	785		790		795										800
Glu	Gly	Lys	Met	Arg	Gly	Ser	Thr	Gln	Thr	Val	Gly	Ile	Ala	Ala	Lys
			805		810										815
Thr	Gly	Glu	Asn	Thr	Thr	Ala	Ala	Ala	Thr	Leu	Gly	Met	Gly	Arg	Ser
	820		825		830										
Thr	Trp	Ser	Glu	Asn	Ser	Ala	Asn	Ala	Lys	Thr	Asp	Ser	Ile	Ser	Leu
	835		840		845										
Phe	Ala	Gly	Ile	Arg	His	Asp	Ala	Gly	Asp	Ile	Gly	Tyr	Leu	Lys	Gly
	850		855		860										
Leu	Phe	Ser	Tyr	Gly	Arg	Tyr	Lys	Asn	Ser	Ile	Ser	Arg	Ser	Thr	Gly
	865		870		875										880
Ala	Asp	Glu	His	Ala	Glu	Gly	Ser	Val	Asn	Gly	Thr	Leu	Met	Gln	Leu
			885		890										895
Gly	Ala	Leu	Gly	Gly	Val	Asn	Val	Pro	Phe	Ala	Ala	Thr	Gly	Asp	Leu
	900		905		910										
Thr	Val	Glu	Gly	Gly	Leu	Arg	Tyr	Asp	Leu	Leu	Lys	Gln	Asp	Ala	Phe
	915		920		925										
Ala	Glu	Lys	Gly	Ser	Ala	Leu	Gly	Trp	Ser	Gly	Asn	Ser	Leu	Thr	Glu
	930		935		940										
Gly	Thr	Leu	Val	Gly	Leu	Ala	Gly	Leu	Lys	Leu	Ser	Gln	Pro	Leu	Ser
	945		950		955										960
Asp	Lys	Ala	Val	Leu	Phe	Ala	Thr	Ala	Gly	Val	Glu	Arg	Asp	Leu	Asn
			965		970										975
Gly	Arg	Asp	Tyr	Thr	Val	Thr	Gly	Gly	Phe	Thr	Gly	Ala	Thr	Ala	Ala
	980		985		990										
Thr	Gly	Lys	Thr	Gly	Ala	Arg	Asn	Met	Pro	His	Thr	Arg	Leu	Val	Ala
	995		1000		1005										
Gly	Leu	Gly	Ala	Asp	Val	Glu	Phe	Gly	Asn	Gly	Trp	Asn	Gly	Leu	Ala
	1010		1015		1020										
Arg	Tyr	Ser	Tyr	Ala	Gly	Ser	Lys	Gln	Tyr	Gly	Asn	His	Ser	Gly	Arg
	1025		1030		1035										1040
Val	Gly	Val	Gly	Tyr	Arg	Phe									
			1045												

[1838] &lt;210&gt;17

[1839] &lt;211&gt;4425

[1840] &lt;212&gt;DNA

[1841] &lt;213&gt; 人工序列

[1842] &lt;220&gt;

[1843] &lt;223&gt; Δ G983-ORF46. 1

[1844] &lt;400&gt;17

[1845]	atgacttctg	cgcccgactt	caatgcaggc	ggtaccggta	tcggcagcaa	cagcagagca	60
	acaacagcga	aatcagcagc	agtatcttac	gccggtatca	agaacgaaat	gtgcaaagac	120
	agaagcatgc	tctgtgccgg	tcgggatgac	gttgcgggta	cagacaggga	tgccaaaatc	180

aatgcccc	ccccgaatct	gcataccgga	gactttccaa	acccaaatga	cgcatacaag	240
aatttgatca	acctcaaacc	tgcaattgaa	gcaggctata	caggacgagg	ggtagaggta	300
ggtatcgctg	acacaggcga	atccgctggc	agcatacct	ttcccgaact	gtatggcaga	360
aaagaacacg	gctataacga	aaattacaaa	aactatacgg	cgtatatgcg	gaaggaagcg	420
cctgaagacg	gaggcggtaa	agacattgaa	gcttctttcg	acgatgaggc	cgttatagag	480
actgaagcaa	agccgacgga	tatccgccac	gtaaaagaaa	tcggacacal	cgatttggtc	540
tcccataatta	ttggcgggcg	ttccgtggac	ggcagacctg	caggcggat	tgcgccgat	600
gcgacgctac	acataatgaa	tacgaatgat	gaaaccaaga	acgaaatgat	ggttgacgcc	660
atccgcaatg	catgggtcaa	gctgggcgaa	cgtggcgtgc	gcacgtcaa	taacagttt	720
ggaacaacat	cgagggcagg	cactgccgac	cttttccaaa	tagccaattc	ggaggagcag	780
taccgccaag	cgttgctcga	ctattccggc	ggtgataaaa	cagacgaggg	tatccgctg	840
atgcaacaga	gcgattacgg	caacctgtcc	taccacatcc	gtaataaaaa	catgcttttc	900
atcttttcga	caggcaatga	cgcaacaaget	cagcccaaca	catatgccct	atlgccatit	960
tatgaaaaag	acgctcaaaa	aggcattatc	acagtcgcag	gcgtagaccg	cagtgagaaa	1020
aagttcaaac	gggaaatgta	tggagaaccg	ggtacagaac	cgcttgagta	tggctccaac	1080
cattgcggaa	ttactgccat	gtgggtcctg	tcggcacct	atgaagcaag	cgctccgttc	1140
accgglacaa	acccgattca	aattgccgga	acatcctttt	ccgcacccat	cgtaaccggc	1200
acggcggctc	tgctgctgca	gaaatacccg	tggatgagca	acgacaacct	gcgtaccacg	1260
ttgctgacga	cggtcagga	catcggtgca	gtcggcgtgg	acagcaagtt	cggttgggga	1320
ctgctggatg	gggtaaggc	catgaacgga	cccgcgtcct	ttccgttcgg	cgactttacc	1380
gcegatcga	aaggtacatc	cgatattgcc	tactccttcc	gtaacgacat	ttcaggcaccg	1440
ggcggcctga	tcaaaaaagg	cggcagccaa	ctgcaactgc	acggcaacaa	cacctatacg	1500
ggcaaaacca	ttatcgaagg	cggttcgtctg	gtgttgtagc	gcaacaacaa	atcgatgatg	1560
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gccgtagaac	agggcggcag	caatctggaa	aacctgatgg	tcgaaactgga	tgcttccgaa	2100
tcacgcgcaa	caccgagac	ggttgaaact	gcggcagccg	accgcacaga	tatgccgggc	2160
atccgccct	acggcgaac	tttccgcgca	gcggcagccg	lacagcatgc	gaatgccgcc	2220
gacggtgtac	gcacttcaa	cagtcctgcc	gctaccgtct	atgccgacag	taccgccgcc	2280
catgccgata	tgcagggacg	ccgctgaaa	gccgtatcgg	acgggttggg	ccacaacggc	2340
acgggtctgc	gcgtcatcgc	gcaaacccaa	caggacggtg	gaacgtggga	acagggcggt	2400
ggtgaaaggca	aaatgcggcg	cagtacccaa	accgtcggca	ttgccgcgaa	aaccggcgaa	2460
aatacgcagc	cagccgccac	actgggcatg	ggacgcagca	catggagcga	aaacagtgca	2520
aatgcaaaaa	ccgacagcat	tagtctgttt	cgaggcatac	ggcacgatgc	ggcgatatac	2580
ggctatctca	aaggcctgtt	ctcctacgga	cgctacaaaa	acagcatcag	ccgcagcacc	2640
ggtgcggacg	aacatgcgga	aggcagcgtc	aacggcacgc	tgatgcagct	ggcgccactg	2700
ggcgggtgca	acgttccggt	tgcgcgaacg	ggagatttga	cggtcgaagg	cggtctgcgc	2760
tacgacctgc	tcaaacagga	tgcattcgcc	gaaaaaggca	gtgctttggg	ctggagcggc	2820
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agcgataaag	ccgtctctgt	tgcaacggcg	ggcgtggaac	gcgacctgaa	cggacgcgac	2940
tacacggtaa	cgggcggtt	taccggcggc	actgcagcaa	ccggcaagac	gggggeacgc	3000
aatatgccgc	acaccctct	ggttgcggcg	ctgggcggcg	atgtcgaatt	cggcaacggc	3060
tggaaaggct	tggcacgtta	cagctacgcc	ggttccaaac	agtacggcaa	ccacagcgga	3120
cgagtcggcg	taggctaccg	gttccctgac	ggtggcggag	gcactggatc	ctcagatttg	3180
gcaaacgatt	cttttatccg	gcaggttctc	gaccgtcagc	atttcaacc	cgacgggaaa	3240
taccacctat	tcggcagcag	gggggaactt	gccgagcgcg	cgcccatat	cggattggga	3300

[1846]

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aaaatacaaaa gccatcagtt gggcaacctg atgattcaac aggcggccat taaaggaaat 3360
atcggctaca ttgtccgctt tccgatcac gggcacgaag tccattcccc ctgcacaac 3420
catgcctcac attccgattc tgatgaagcc ggtagtcccg ttgacggatt tagcctttac 3480
cgcacccatt gggacggata cgaacacccat cccgccgacg gctatgacgg gccacagggc 3540
ggcggctatc ccgctcccaa aggcgcgagg gatataata gctacgacat aaaaggcggt 3600
gccccaaaata tccgcctcaa cctgaccgac aaccgcagca ccggacaacg gcttgccgac 3660
cgtttccaca atgccggtag tatgctgac caaggagtag gcgacggatt caaacgcgcc 3720
accgataca gccccgagct ggacagatcg ggcaatgccg ccgaagcctt caacggcact 3780
gcagatatcg ttaaaaacat catcggcgcg gcaggagaaa ttgtcggcgc aggcgatgcc 3840
gtgcagggca taagcgaagg ctcaaacatt gctgtcatgc acggcttggg tctgctttcc 3900
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gccgcagcag ccattccgca ttgggcagtc caaaacccca atgccgcaca aggcatagaa 4020
gccgtcagca atatctttat ggcagccatc cccatcaaag ggattggagc tgttcgggga 4080
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gcattgccga aagggaate cgccgtcagc gacaattttg ccgatgcggc atacgcaaaa 4200
taccgctccc cttaccattc ccgaaatate cgttcaaact tggagcagcg ttacggcaaa 4260
gaaaacatca cctcctcaac cgtgccgccc tcaaacggca aaaatgtcaa actggcagac 4320
caacgccacc cgaagacagg cgtaccgttt gacggtaaag gtttccgaa ttttgagaag 4380
cacgtgaaat atgatacgtc cgagcaccac caccaccacc actga 4425

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[1847] &lt;210&gt;18

[1848] &lt;211&gt;1474

[1849] &lt;212&gt;PRT

[1850] &lt;213&gt;人工序列

[1851] &lt;220&gt;

[1852] &lt;223&gt;Δ G983-ORF46. 1

[1853] &lt;400&gt;18

[1854]

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Met Thr Ser Ala Pro Asp Phe Asn Ala Gly Gly Thr Gly Ile Gly Ser
1           5           10           15
Asn Ser Arg Ala Thr Thr Ala Lys Ser Ala Ala Val Ser Tyr Ala Gly
20           25           30
Ile Lys Asn Glu Met Cys Lys Asp Arg Ser Met Leu Cys Ala Gly Arg
35           40           45
Asp Asp Val Ala Val Thr Asp Arg Asp Ala Lys Ile Asn Ala Pro Pro
50           55           60
Pro Asn Leu His Thr Gly Asp Phe Pro Asn Pro Asn Asp Ala Tyr Lys
65           70           75           80
Asn Leu Ile Asn Leu Lys Pro Ala Ile Glu Ala Gly Tyr Thr Gly Arg
85           90           95
Gly Val Glu Val Gly Ile Val Asp Thr Gly Glu Ser Val Gly Ser Ile
100          105          110
Ser Phe Pro Glu Leu Tyr Gly Arg Lys Glu His Gly Tyr Asn Glu Asn
115          120          125
Tyr Lys Asn Tyr Thr Ala Tyr Met Arg Lys Glu Ala Pro Glu Asp Gly
130          135          140
Gly Gly Lys Asp Ile Glu Ala Ser Phe Asp Asp Glu Ala Val Ile Glu
145          150          155          160
Thr Glu Ala Lys Pro Thr Asp Ile Arg His Val Lys Glu Ile Gly His
165          170          175

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[1855]

Ile Asp Leu Val Ser His Ile Ile Gly Gly Arg Scr Val Asp Gly Arg  
 180 185 190  
 Pro Ala Gly Gly Ile Ala Pro Asp Ala Thr Leu His Ile Met Asn Thr  
 195 200 205  
 Asn Asp Glu Thr Lys Asn Glu Met Met Val Ala Ala Ile Arg Asn Ala  
 210 215 220  
 Trp Val Lys Leu Gly Glu Arg Gly Val Arg Ile Val Asn Asn Ser Phe  
 225 230 235 240  
 Gly Thr Thr Ser Arg Ala Gly Thr Ala Asp Leu Phe Gln Ile Ala Asn  
 245 250 255  
 Ser Glu Glu Gln Tyr Arg Gln Ala Leu Leu Asp Tyr Ser Gly Gly Asp  
 260 265 270  
 Lys Thr Asp Glu Gly Ile Arg Leu Met Gln Gln Ser Asp Tyr Gly Asn  
 275 280 285  
 Leu Ser Tyr His Ile Arg Asn Lys Asn Met Leu Phe Ile Phe Ser Thr  
 290 295 300  
 Gly Asn Asp Ala Gln Ala Gln Pro Asn Thr Tyr Ala Leu Leu Pro Phe  
 305 310 315 320  
 Tyr Glu Lys Asp Ala Gln Lys Gly Ile Ile Thr Val Ala Gly Val Asp  
 325 330 335  
 Arg Ser Gly Glu Lys Phe Lys Arg Glu Met Tyr Gly Glu Pro Gly Thr  
 340 345 350  
 Glu Pro Leu Glu Tyr Gly Ser Asn His Cys Gly Ile Thr Ala Met Trp  
 355 360 365  
 Cys Leu Ser Ala Pro Tyr Glu Ala Ser Val Arg Phe Thr Arg Thr Asn  
 370 375 380  
 Pro Ile Gln Ile Ala Gly Thr Ser Phe Ser Ala Pro Ile Val Thr Gly  
 385 390 395 400  
 Thr Ala Ala Leu Leu Leu Gln Lys Tyr Pro Trp Met Ser Asn Asp Asn  
 405 410 415  
 Leu Arg Thr Thr Leu Leu Thr Thr Ala Gln Asp Ile Gly Ala Val Gly  
 420 425 430  
 Val Asp Ser Lys Phe Gly Trp Gly Leu Leu Asp Ala Gly Lys Ala Met  
 435 440 445  
 Asn Gly Pro Ala Ser Phe Pro Phe Gly Asp Phe Thr Ala Asp Thr Lys  
 450 455 460  
 Gly Thr Ser Asp Ile Ala Tyr Ser Phe Arg Asn Asp Ile Ser Gly Thr  
 465 470 475 480  
 Gly Gly Leu Ile Lys Lys Gly Gly Ser Gln Leu Gln Leu His Gly Asn  
 485 490 495  
 Asn Thr Tyr Thr Gly Lys Thr Ile Ile Glu Gly Gly Ser Leu Val Leu  
 500 505 510  
 Tyr Gly Asn Asn Lys Ser Asp Met Arg Val Glu Thr Lys Gly Ala Leu  
 515 520 525  
 Ile Tyr Asn Gly Ala Ala Ser Gly Gly Scr Leu Asn Ser Asp Gly Ile  
 530 535 540  
 Val Tyr Leu Ala Asp Thr Asp Gln Ser Gly Ala Asn Glu Thr Val His  
 545 550 555 560  
 Ile Lys Gly Ser Leu Gln Leu Asp Gly Lys Gly Thr Leu Tyr Thr Arg  
 565 570 575  
 Leu Gly Lys Leu Leu Lys Val Asp Gly Thr Ala Ile Ile Gly Gly Lys  
 580 585 590

[1856]

Leu Tyr Met Ser Ala Arg Gly Lys Gly Ala Gly Tyr Leu Asn Ser Thr  
 595 600 605  
 Gly Arg Arg Val Pro Phe Leu Ser Ala Ala Lys Ile Gly Gln Asp Tyr  
 610 615 620  
 Ser Phe Phe Thr Asn Ile Glu Thr Asp Gly Gly Leu Leu Ala Ser Leu  
 625 630 635 640  
 Asp Ser Val Glu Lys Thr Ala Gly Ser Glu Gly Asp Thr Leu Ser Tyr  
 645 650 655  
 Tyr Val Arg Arg Gly Asn Ala Ala Arg Thr Ala Ser Ala Ala Ala His  
 660 665 670  
 Ser Ala Pro Ala Gly Leu Lys His Ala Val Glu Gln Gly Gly Ser Asn  
 675 680 685  
 Leu Glu Asn Leu Met Val Glu Leu Asp Ala Ser Glu Ser Ser Ala Thr  
 690 695 700  
 Pro Glu Thr Val Glu Thr Ala Ala Ala Asp Arg Thr Asp Met Pro Gly  
 705 710 715 720  
 Ile Arg Pro Tyr Gly Ala Thr Phe Arg Ala Ala Ala Ala Val Gln His  
 725 730 735  
 Ala Asn Ala Ala Asp Gly Val Arg Ile Phe Asn Ser Leu Ala Ala Thr  
 740 745 750  
 Val Tyr Ala Asp Ser Thr Ala Ala His Ala Asp Met Gln Gly Arg Arg  
 755 760 765  
 Leu Lys Ala Val Ser Asp Gly Leu Asp His Asn Gly Thr Gly Leu Arg  
 770 775 780  
 Val Ile Ala Gln Thr Gln Gln Asp Gly Gly Thr Trp Glu Gln Gly Gly  
 785 790 795 800  
 Val Glu Gly Lys Met Arg Gly Ser Thr Gln Thr Val Gly Ile Ala Ala  
 805 810 815  
 Lys Thr Gly Glu Asn Thr Thr Ala Ala Ala Thr Leu Gly Met Gly Arg  
 820 825 830  
 Ser Thr Trp Ser Glu Asn Ser Ala Asn Ala Lys Thr Asp Ser Ile Ser  
 835 840 845  
 Leu Phe Ala Gly Ile Arg His Asp Ala Gly Asp Ile Gly Tyr Leu Lys  
 850 855 860  
 Gly Leu Phe Ser Tyr Gly Arg Tyr Lys Asn Ser Ile Ser Arg Ser Thr  
 865 870 875 880  
 Gly Ala Asp Glu His Ala Glu Gly Ser Val Asn Gly Thr Leu Met Gln  
 885 890 895  
 Leu Gly Ala Leu Gly Gly Val Asn Val Pro Phe Ala Ala Thr Gly Asp  
 900 905 910  
 Leu Thr Val Glu Gly Gly Leu Arg Tyr Asp Leu Leu Lys Gln Asp Ala  
 915 920 925  
 Phe Ala Glu Lys Gly Ser Ala Leu Gly Trp Ser Gly Asn Ser Leu Thr  
 930 935 940  
 Glu Gly Thr Leu Val Gly Leu Ala Gly Leu Lys Leu Ser Gln Pro Leu  
 945 950 955 960  
 Ser Asp Lys Ala Val Leu Phe Ala Thr Ala Gly Val Glu Arg Asp Leu  
 965 970 975  
 Asn Gly Arg Asp Tyr Thr Val Thr Gly Gly Phe Thr Gly Ala Thr Ala  
 980 985 990  
 Ala Thr Gly Lys Thr Gly Ala Arg Asn Met Pro His Thr Arg Leu Val  
 995 1000 1005

[1857]

Ala Gly Leu Gly Ala Asp Val Glu Phe Gly Asn Gly Trp Asn Gly Leu  
 1010 1015 1020  
 Ala Arg Tyr Ser Tyr Ala Gly Ser Lys Gln Tyr Gly Asn His Ser Gly  
 1025 1030 1035 1040  
 Arg Val Gly Val Gly Tyr Arg Phe Leu Asp Gly Gly Gly Thr Gly  
 1045 1050 1055  
 Ser Ser Asp Leu Ala Asn Asp Ser Phe Ile Arg Gln Val Leu Asp Arg  
 1060 1065 1070  
 Gln His Phe Glu Pro Asp Gly Lys Tyr His Leu Phe Gly Ser Arg Gly  
 1075 1080 1085  
 Glu Leu Ala Glu Arg Ser Gly His Ile Gly Leu Gly Lys Ile Gln Ser  
 1090 1095 1100  
 His Gln Leu Gly Asn Leu Met Ile Gln Gln Ala Ala Ile Lys Gly Asn  
 1105 1110 1115 1120  
 Ile Gly Tyr Ile Val Arg Phe Ser Asp His Gly His Glu Val His Ser  
 1125 1130 1135  
 Pro Phe Asp Asn His Ala Ser His Ser Asp Ser Asp Glu Ala Gly Ser  
 1140 1145 1150  
 Pro Val Asp Gly Phe Ser Leu Tyr Arg Ile His Trp Asp Gly Tyr Glu  
 1155 1160 1165  
 His His Pro Ala Asp Gly Tyr Asp Gly Pro Gln Gly Gly Gly Tyr Pro  
 1170 1175 1180  
 Ala Pro Lys Gly Ala Arg Asp Ile Tyr Ser Tyr Asp Ile Lys Gly Val  
 1185 1190 1195 1200  
 Ala Gln Asn Ile Arg Leu Asn Leu Thr Asp Asn Arg Ser Thr Gly Gln  
 1205 1210 1215  
 Arg Leu Ala Asp Arg Phe His Asn Ala Gly Ser Met Leu Thr Gln Gly  
 1220 1225 1230  
 Val Gly Asp Gly Phe Lys Arg Ala Thr Arg Tyr Ser Pro Glu Leu Asp  
 1235 1240 1245  
 Arg Ser Gly Asn Ala Ala Glu Ala Phe Asn Gly Thr Ala Asp Ile Val  
 1250 1255 1260  
 Lys Asn Ile Ile Gly Ala Ala Gly Glu Ile Val Gly Ala Gly Asp Ala  
 1265 1270 1275 1280  
 Val Gln Gly Ile Ser Glu Gly Ser Asn Ile Ala Val Met His Gly Leu  
 1285 1290 1295  
 Gly Leu Leu Ser Thr Glu Asn Lys Met Ala Arg Ile Asn Asp Leu Ala  
 1300 1305 1310  
 Asp Met Ala Gln Leu Lys Asp Tyr Ala Ala Ala Ile Arg Asp Trp  
 1315 1320 1325  
 Ala Val Gln Asn Pro Asn Ala Ala Gln Gly Ile Glu Ala Val Ser Asn  
 1330 1335 1340  
 Ile Phe Met Ala Ala Ile Pro Ile Lys Gly Ile Gly Ala Val Arg Gly  
 1345 1350 1355 1360  
 Lys Tyr Gly Leu Gly Gly Ile Thr Ala His Pro Ile Lys Arg Ser Gln  
 1365 1370 1375  
 Met Gly Ala Ile Ala Leu Pro Lys Gly Lys Ser Ala Val Ser Asp Asn  
 1380 1385 1390  
 Phe Ala Asp Ala Ala Tyr Ala Lys Tyr Pro Ser Pro Tyr His Ser Arg  
 1395 1400 1405  
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 1410 1415 1420

[1858]

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 Gln Arg His Pro Lys Thr Gly Val Pro Phe Asp Gly Lys Gly Phe Pro  
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 His His

- [1859] <210>19
- [1860] <211>3939
- [1861] <212>DNA
- [1862] <213> 人工序列
- [1863] <220>
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- [1865] <400>19
- [1866]

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[1867]

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[1871] &lt;213&gt;人工序列

[1872] &lt;220&gt;

[1873] &lt;223&gt;Δ G983-741

[1874] &lt;400&gt;20

[1875]

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		35					40					45			
Asp	Asp	Val	Ala	Val	Thr	Asp	Arg	Asp	Ala	Lys	Ile	Asn	Ala	Pro	Pro
	50					55					60				
Pro	Asn	Leu	His	Thr	Gly	Asp	Phe	Pro	Asn	Pro	Asn	Asp	Ala	Tyr	Lys
65					70					75					80

[1876]

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 115 120 125  
 Tyr Lys Asn Tyr Thr Ala Tyr Met Arg Lys Glu Ala Pro Glu Asp Gly  
 130 135 140  
 Gly Gly Lys Asp Ile Glu Ala Ser Phe Asp Asp Glu Ala Val Ile Glu  
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 Thr Glu Ala Lys Pro Thr Asp Ile Arg His Val Lys Glu Ile Gly His  
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 Ser Glu Glu Gln Tyr Arg Gln Ala Leu Leu Asp Tyr Ser Gly Gly Asp  
 260 265 270  
 Lys Thr Asp Glu Gly Ile Arg Leu Met Gln Gln Ser Asp Tyr Gly Asn  
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 325 330 335  
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 Val Asp Ser Lys Phe Gly Trp Gly Leu Leu Asp Ala Gly Lys Ala Met  
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 Asn Gly Pro Ala Ser Phe Pro Phe Gly Asp Phe Thr Ala Asp Thr Lys  
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 Gly Thr Ser Asp Ile Ala Tyr Ser Phe Arg Asn Asp Ile Ser Gly Thr  
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 Gly Gly Leu Ile Lys Lys Gly Gly Ser Gln Leu Gln Leu His Gly Asn  
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[1877]

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 Asp Ser Val Glu Lys Thr Ala Gly Ser Glu Gly Asp Thr Leu Ser Tyr  
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 Gly Leu Phe Ser Tyr Gly Arg Tyr Lys Asn Ser Ile Ser Arg Ser Thr  
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[1878]

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 Ser Asp Lys Ala Val Leu Phe Ala Thr Ala Gly Val Glu Arg Asp Leu  
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 Asn Gly Arg Asp Tyr Thr Val Thr Gly Gly Phe Thr Gly Ala Thr Ala  
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 Thr Tyr Gly Asn Gly Asp Ser Leu Asn Thr Gly Lys Leu Lys Asn Asp  
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[1887]

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aatccattg ccgatcacga tactcgctg aacggttgg ataaaacagt gtcagacctg	4080
cgcaaagaaa cccgccaagg ccttgcagaa caagccgcgc tctccggtct gtccaacct	4140
tacaacgtgg gtcggttcaa tgtaacggct gcagtcggcg gctacaaatc cgaatcggca	4200
gtcgccatcg gtaccggctt ccgctttacc gaaaactttg ccgccaaaagc aggcgtggca	4260
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[1894] <400>22	
[1895]	

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1				5					10					15	
Asn	Ser	Arg	Ala	Thr	Thr	Ala	Lys	Ser	Ala	Ala	Val	Ser	Tyr	Ala	Gly
			20					25					30		
Ile	Lys	Asn	Glu	Met	Cys	Lys	Asp	Arg	Ser	Met	Leu	Cys	Ala	Gly	Arg
		35					40					45			
Asp	Asp	Val	Ala	Val	Thr	Asp	Arg	Asp	Ala	Lys	Ile	Asn	Ala	Pro	Pro
	50					55					60				
Pro	Asn	Leu	His	Thr	Gly	Asp	Phe	Pro	Asn	Pro	Asn	Asp	Ala	Tyr	Lys
65					70					75				80	
Asn	Leu	Ile	Asn	Leu	Lys	Pro	Ala	Ile	Glu	Ala	Gly	Tyr	Thr	Gly	Arg
				85					90					95	

[1896]



Gly Val Glu Val Gly Ile Val Asp Thr Gly Glu Ser Val Gly Ser Ile  
 100 105 110  
 Ser Phe Pro Glu Leu Tyr Gly Arg Lys Glu His Gly Tyr Asn Glu Asn  
 115 120 125  
 Tyr Lys Asn Tyr Thr Ala Tyr Met Arg Lys Glu Ala Pro Glu Asp Gly  
 130 135 140  
 Gly Gly Lys Asp Ile Glu Ala Ser Phe Asp Asp Glu Ala Val Ile Glu  
 145 150 155 160  
 Thr Glu Ala Lys Pro Thr Asp Ile Arg His Val Lys Glu Ile Gly His  
 165 170 175  
 Ile Asp Leu Val Scr His Ile Ile Gly Gly Arg Ser Val Asp Gly Arg  
 180 185 190  
 Pro Ala Gly Gly Ile Ala Pro Asp Ala Thr Leu His Ile Met Asn Thr  
 195 200 205  
 Asn Asp Glu Thr Lys Asn Glu Met Met Val Ala Ala Ile Arg Asn Ala  
 210 215 220  
 Trp Val Lys Leu Gly Glu Arg Gly Val Arg Ile Val Asn Asn Ser Phe  
 225 230 235 240  
 Gly Thr Thr Ser Arg Ala Gly Thr Ala Asp Leu Phe Gln Ile Ala Asn  
 245 250 255  
 Ser Glu Glu Gln Tyr Arg Gln Ala Leu Leu Asp Tyr Ser Gly Gly Asp  
 260 265 270  
 Lys Thr Asp Glu Gly Ile Arg Leu Met Gln Gln Ser Asp Tyr Gly Asn  
 275 280 285  
 Leu Ser Tyr His Ile Arg Asn Lys Asn Met Leu Phe Ile Phe Ser Thr  
 290 295 300  
 Gly Asn Asp Ala Gln Ala Gln Pro Asn Thr Tyr Ala Leu Leu Pro Phe  
 305 310 315 320  
 Tyr Glu Lys Asp Ala Gln Lys Gly Ile Ile Thr Val Ala Gly Val Asp  
 325 330 335  
 Arg Ser Gly Glu Lys Phe Lys Arg Glu Met Tyr Gly Glu Pro Gly Thr  
 340 345 350  
 Glu Pro Leu Glu Tyr Gly Ser Asn His Cys Gly Ile Thr Ala Met Trp  
 355 360 365  
 Cys Leu Ser Ala Pro Tyr Glu Ala Ser Val Arg Phe Thr Arg Thr Asn  
 370 375 380  
 Pro Ile Gln Ile Ala Gly Thr Ser Phe Ser Ala Pro Ile Val Thr Gly  
 385 390 395 400  
 Thr Ala Ala Leu Leu Leu Gln Lys Tyr Pro Trp Met Ser Asn Asp Asn  
 405 410 415  
 Leu Arg Thr Thr Leu Leu Thr Thr Ala Gln Asp Ile Gly Ala Val Gly  
 420 425 430  
 Val Asp Ser Lys Phe Gly Trp Gly Leu Leu Asp Ala Gly Lys Ala Met  
 435 440 445  
 Asn Gly Pro Ala Ser Phe Pro Phe Gly Asp Phe Thr Ala Asp Thr Lys  
 450 455 460  
 Gly Thr Ser Asp Ile Ala Tyr Ser Phe Arg Asn Asp Ile Ser Gly Thr  
 465 470 475 480  
 Gly Gly Leu Ile Lys Lys Gly Gly Ser Gln Leu Gln Leu His Gly Asn  
 485 490 495  
 Asn Thr Tyr Thr Gly Lys Thr Ile Ile Glu Gly Gly Ser Leu Val Leu  
 500 505 510

[1897]

Tyr Gly Asn Asn Lys Ser Asp Met Arg Val Glu Thr Lys Gly Ala Leu  
 515 520 525  
 Ile Tyr Asn Gly Ala Ala Ser Gly Gly Ser Leu Asn Ser Asp Gly Ile  
 530 535 540  
 Val Tyr Leu Ala Asp Thr Asp Gln Ser Gly Ala Asn Glu Thr Val His  
 545 550 555 560  
 Ile Lys Gly Ser Leu Gln Leu Asp Gly Lys Gly Thr Leu Tyr Thr Arg  
 565 570 575  
 Leu Gly Lys Leu Leu Lys Val Asp Gly Thr Ala Ile Ile Gly Gly Lys  
 580 585 590  
 Leu Tyr Met Ser Ala Arg Gly Lys Gly Ala Gly Tyr Leu Asn Ser Thr  
 595 600 605  
 Gly Arg Arg Val Pro Phe Leu Ser Ala Ala Lys Ile Gly Gln Asp Tyr  
 610 615 620  
 Ser Phe Phe Thr Asn Ile Glu Thr Asp Gly Gly Leu Leu Ala Ser Leu  
 625 630 635 640  
  
 Asp Ser Val Glu Lys Thr Ala Gly Ser Glu Gly Asp Thr Leu Ser Tyr  
 645 650 655  
 Tyr Val Arg Arg Gly Asn Ala Ala Arg Thr Ala Ser Ala Ala Ala His  
 660 665 670  
 Ser Ala Pro Ala Gly Leu Lys His Ala Val Glu Gln Gly Gly Ser Asn  
 675 680 685  
 Leu Glu Asn Leu Met Val Glu Leu Asp Ala Ser Glu Ser Ser Ala Thr  
 690 695 700  
 Pro Glu Thr Val Glu Thr Ala Ala Ala Asp Arg Thr Asp Met Pro Gly  
 705 710 715 720  
 Ile Arg Pro Tyr Gly Ala Thr Phe Arg Ala Ala Ala Val Gln His  
 725 730 735  
 Ala Asn Ala Ala Asp Gly Val Arg Ile Phe Asn Ser Leu Ala Ala Thr  
 740 745 750  
 Val Tyr Ala Asp Ser Thr Ala Ala His Ala Asp Met Gln Gly Arg Arg  
 755 760 765  
 Leu Lys Ala Val Ser Asp Gly Leu Asp His Asn Gly Thr Gly Leu Arg  
 770 775 780  
 Val Ile Ala Gln Thr Gln Gln Asp Gly Gly Thr Trp Glu Gln Gly Gly  
 785 790 795 800  
 Val Glu Gly Lys Met Arg Gly Ser Thr Gln Thr Val Gly Ile Ala Ala  
 805 810 815  
 Lys Thr Gly Glu Asn Thr Thr Ala Ala Ala Thr Leu Gly Met Gly Arg  
 820 825 830  
 Ser Thr Trp Ser Glu Asn Ser Ala Asn Ala Lys Thr Asp Ser Ile Ser  
 835 840 845  
 Leu Phe Ala Gly Ile Arg His Asp Ala Gly Asp Ile Gly Tyr Leu Lys  
 850 855 860  
 Gly Leu Phe Ser Tyr Gly Arg Tyr Lys Asn Ser Ile Ser Arg Ser Thr  
 865 870 875 880  
 Gly Ala Asp Glu His Ala Glu Gly Ser Val Asn Gly Thr Leu Met Gln  
 885 890 895  
 Leu Gly Ala Leu Gly Gly Val Asn Val Pro Phe Ala Ala Thr Gly Asp  
 900 905 910  
 Leu Thr Val Glu Gly Gly Leu Arg Tyr Asp Leu Leu Lys Gln Asp Ala

[1898]



1330	1335	1340
Asp His Asp Thr Arg Leu Asn Gly Leu Asp Lys Thr Val Ser Asp Leu		
1345	1350	1355
Arg Lys Glu Thr Arg Gln Gly Leu Ala Glu Gln Ala Ala Leu Ser Gly		1360
	1365	1370
Leu Phe Gln Pro Tyr Asn Val Gly Arg Phe Asn Val Thr Ala Ala Val		1375
	1380	1385
Gly Gly Tyr Lys Ser Glu Ser Ala Val Ala Ile Gly Thr Gly Phe Arg		1390
	1395	1400
Phe Thr Glu Asn Phe Ala Ala Lys Ala Gly Val Ala Val Gly Thr Ser		1405
	1410	1415
Ser Gly Ser Ser Ala Ala Tyr His Val Gly Val Asn Tyr Glu Trp Leu		1420
1425	1430	1435
Glu His His His His His His		1440
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- [1903] <213> 人工序列
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[1908]

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[1914] <223>Δ G983-961c

[1915] &lt;400&gt;24

[1916]

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 Ile Lys Asn Glu Met Cys Lys Asp Arg Ser Met Leu Cys Ala Gly Arg  
 35 40 45  
 Asp Asp Val Ala Val Thr Asp Arg Asp Ala Lys Ile Asn Ala Pro Pro  
 50 55 60  
 Pro Asn Leu His Thr Gly Asp Phe Pro Asn Pro Asn Asp Ala Tyr Lys  
 65 70 75 80  
 Asn Leu Ile Asn Leu Lys Pro Ala Ile Glu Ala Gly Tyr Thr Gly Arg  
 85 90 95  
 Gly Val Glu Val Gly Ile Val Asp Thr Gly Glu Ser Val Gly Ser Ile  
 100 105 110  
 Ser Phe Pro Glu Leu Tyr Gly Arg Lys Glu His Gly Tyr Asn Glu Asn  
 115 120 125  
 Tyr Lys Asn Tyr Thr Ala Tyr Met Arg Lys Glu Ala Pro Glu Asp Gly  
 130 135 140  
 Gly Gly Lys Asp Ile Glu Ala Ser Phe Asp Asp Glu Ala Val Ile Glu  
 145 150 155 160  
 Thr Glu Ala Lys Pro Thr Asp Ile Arg His Val Lys Glu Ile Gly His  
 165 170 175  
 Ile Asp Leu Val Ser His Ile Ile Gly Gly Arg Ser Val Asp Gly Arg  
 180 185 190  
 Pro Ala Gly Gly Ile Ala Pro Asp Ala Thr Leu His Ile Met Asn Thr  
 195 200 205  
 Asn Asp Glu Thr Lys Asn Glu Met Met Val Ala Ala Ile Arg Asn Ala  
 210 215 220  
 Trp Val Lys Leu Gly Glu Arg Gly Val Arg Ile Val Asn Asn Ser Phe  
 225 230 235 240  
 Gly Thr Thr Ser Arg Ala Gly Thr Ala Asp Leu Phe Gln Ile Ala Asn  
 245 250 255  
 Ser Glu Glu Gln Tyr Arg Gln Ala Leu Leu Asp Tyr Ser Gly Gly Asp  
 260 265 270  
 Lys Thr Asp Glu Gly Ile Arg Leu Met Gln Gln Ser Asp Tyr Gly Asn  
 275 280 285  
 Leu Ser Tyr His Ile Arg Asn Lys Asn Met Leu Phe Ile Phe Ser Thr  
 290 295 300  
 Gly Asn Asp Ala Gln Ala Gln Pro Asn Thr Tyr Ala Leu Leu Pro Phe  
 305 310 315 320  
 Tyr Glu Lys Asp Ala Gln Lys Gly Ile Ile Thr Val Ala Gly Val Asp  
 325 330 335  
 Arg Ser Gly Glu Lys Phe Lys Arg Glu Met Tyr Gly Glu Pro Gly Thr  
 340 345 350  
 Glu Pro Leu Glu Tyr Gly Ser Asn His Cys Gly Ile Thr Ala Met Trp  
 355 360 365  
 Cys Leu Ser Ala Pro Tyr Glu Ala Ser Val Arg Phe Thr Arg Thr Asn  
 370 375 380  
 Pro Ile Gln Ile Ala Gly Thr Ser Phe Ser Ala Pro Ile Val Thr Gly  
 385 390 395 400  
 Thr Ala Ala Leu Leu Leu Gln Lys Tyr Pro Trp Met Ser Asn Asp Asn

[1917]

				405					410					415	
Leu	Arg	Thr	Thr	Leu	Leu	Thr	Thr	Ala	Gln	Asp	Ile	Gly	Ala	Val	Gly
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Val	Asp	Ser	Lys	Phe	Gly	Trp	Gly	Leu	Leu	Asp	Ala	Gly	Lys	Ala	Met
			435				440					445			
Asn	Gly	Pro	Ala	Ser	Phe	Pro	Phe	Gly	Asp	Phe	Thr	Ala	Asp	Thr	Lys
			450			455					460				
Gly	Thr	Ser	Asp	Ile	Ala	Tyr	Ser	Phe	Arg	Asn	Asp	Ile	Ser	Gly	Thr
			465			470					475			480	
Gly	Gly	Leu	Ile	Lys	Lys	Gly	Gly	Ser	Gln	Leu	Gln	Leu	His	Gly	Asn
				485					490					495	
Asn	Thr	Tyr	Thr	Gly	Lys	Thr	Ile	Ile	Glu	Gly	Gly	Ser	Leu	Val	Leu
			500					505					510		
Tyr	Gly	Asn	Asn	Lys	Ser	Asp	Met	Arg	Val	Glu	Thr	Lys	Gly	Ala	Leu
			515				520					525			
Ile	Tyr	Asn	Gly	Ala	Ala	Ser	Gly	Gly	Ser	Leu	Asn	Ser	Asp	Gly	Ile
			530			535						540			
Val	Tyr	Leu	Ala	Asp	Thr	Asp	Gln	Ser	Gly	Ala	Asn	Glu	Thr	Val	His
			545			550					555				560
Ile	Lys	Gly	Ser	Leu	Gln	Leu	Asp	Gly	Lys	Gly	Thr	Leu	Tyr	Thr	Arg
				565					570					575	
Leu	Gly	Lys	Leu	Leu	Lys	Val	Asp	Gly	Thr	Ala	Ile	Ile	Gly	Gly	Lys
			580					585					590		
Leu	Tyr	Met	Ser	Ala	Arg	Gly	Lys	Gly	Ala	Gly	Tyr	Leu	Asn	Ser	Thr
			595				600					605			
Gly	Arg	Arg	Val	Pro	Phe	Leu	Ser	Ala	Ala	Lys	Ile	Gly	Gln	Asp	Tyr
			610			615						620			
Ser	Phe	Phe	Thr	Asn	Ile	Glu	Thr	Asp	Gly	Gly	Leu	Leu	Ala	Ser	Leu
			625			630					635				640
Asp	Ser	Val	Glu	Lys	Thr	Ala	Gly	Ser	Glu	Gly	Asp	Thr	Leu	Ser	Tyr
				645					650					655	
Tyr	Val	Arg	Arg	Gly	Asn	Ala	Ala	Arg	Thr	Ala	Ser	Ala	Ala	Ala	His
				660				665						670	
Ser	Ala	Pro	Ala	Gly	Leu	Lys	His	Ala	Val	Glu	Gln	Gly	Gly	Ser	Asn
			675				680					685			
Leu	Glu	Asn	Leu	Met	Val	Glu	Leu	Asp	Ala	Ser	Glu	Ser	Ser	Ala	Thr
			690			695						700			
Pro	Glu	Thr	Val	Glu	Thr	Ala	Ala	Ala	Asp	Arg	Thr	Asp	Met	Pro	Gly
			705			710					715				720
Ile	Arg	Pro	Tyr	Gly	Ala	Thr	Phe	Arg	Ala	Ala	Ala	Ala	Val	Gln	His
				725					730					735	
Ala	Asn	Ala	Ala	Asp	Gly	Val	Arg	Ile	Phe	Asn	Ser	Leu	Ala	Ala	Thr
				740				745						750	
Val	Tyr	Ala	Asp	Ser	Thr	Ala	Ala	His	Ala	Asp	Met	Gln	Gly	Arg	Arg
			755				760					765			
Leu	Lys	Ala	Val	Ser	Asp	Gly	Leu	Asp	His	Asn	Gly	Thr	Gly	Leu	Arg
			770				775					780			
Val	Ile	Ala	Gln	Thr	Gln	Gln	Asp	Gly	Gly	Thr	Trp	Glu	Gln	Gly	Gly
			785			790					795				800
Val	Glu	Gly	Lys	Met	Arg	Gly	Ser	Thr	Gln	Thr	Val	Gly	Ile	Ala	Ala
				805					810					815	
Lys	Thr	Gly	Glu	Asn	Thr	Thr	Ala	Ala	Ala	Thr	Leu	Gly	Met	Gly	Arg

[1918]



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Leu Phe Ala Gly Ile Arg His Asp Ala Gly Asp Ile Gly Tyr Leu Lys					
	850		855		860
Gly Leu Phe Ser Tyr Gly Arg Tyr Lys Asn Ser Ile Ser Arg Ser Thr					
865		870		875	880
Gly Ala Asp Glu His Ala Glu Gly Ser Val Asn Gly Thr Leu Met Gln					
	885		890		895
Leu Gly Ala Leu Gly Gly Val Asn Val Pro Phe Ala Ala Thr Gly Asp					
	900		905		910
Leu Thr Val Glu Gly Gly Leu Arg Tyr Asp Leu Leu Lys Gln Asp Ala					
	915		920		925
Phe Ala Glu Lys Gly Ser Ala Leu Gly Trp Ser Gly Asn Ser Leu Thr					
	930		935		940
Glu Gly Thr Leu Val Gly Leu Ala Gly Leu Lys Leu Ser Gln Pro Leu					
945		950		955	960
Scr Asp Lys Ala Val Leu Phe Ala Thr Ala Gly Val Glu Arg Asp Leu					
	965		970		975
Asn Gly Arg Asp Tyr Thr Val Thr Gly Gly Phe Thr Gly Ala Thr Ala					
	980		985		990
Ala Thr Gly Lys Thr Gly Ala Arg Asn Met Pro His Thr Arg Leu Val					
	995		1000		1005
Ala Gly Leu Gly Ala Asp Val Glu Phe Gly Asn Gly Trp Asn Gly Leu					
	1010		1015		1020
Ala Arg Tyr Ser Tyr Ala Gly Ser Lys Gln Tyr Gly Asn His Ser Gly					
1025		1030		1035	1040
Arg Val Gly Val Gly Tyr Arg Phe Leu Glu Gly Gly Gly Thr Gly					
	1045		1050		1055
Ser Ala Thr Asn Asp Asp Asp Val Lys Lys Ala Ala Thr Val Ala Ile					
	1060		1065		1070
Ala Ala Ala Tyr Asn Asn Gly Gln Glu Ile Asn Gly Phe Lys Ala Gly					
	1075		1080		1085
Glu Thr Ile Tyr Asp Ile Asp Glu Asp Gly Thr Ile Thr Lys Lys Asp					
	1090		1095		1100
Ala Thr Ala Ala Asp Val Glu Ala Asp Asp Phe Lys Gly Leu Gly Leu					
1105		1110		1115	1120
Lys Lys Val Val Thr Asn Leu Thr Lys Thr Val Asn Glu Asn Lys Gln					
	1125		1130		1135
Asn Val Asp Ala Lys Val Lys Ala Ala Glu Ser Glu Ile Glu Lys Leu					
	1140		1145		1150
Thr Thr Lys Leu Ala Asp Thr Asp Ala Ala Leu Ala Asp Thr Asp Ala					
	1155		1160		1165
Ala Leu Asp Ala Thr Thr Asn Ala Leu Asn Lys Leu Gly Glu Asn Ile					
	1170		1175		1180
Thr Thr Phe Ala Glu Glu Thr Lys Thr Asn Ile Val Lys Ile Asp Glu					
1185		1190		1195	1200
Lys Leu Glu Ala Val Ala Asp Thr Val Asp Lys His Ala Glu Ala Phe					
	1205		1210		1215
Asn Asp Ile Ala Asp Ser Leu Asp Glu Thr Asn Thr Lys Ala Asp Glu					
	1220		1225		1230
Ala Val Lys Thr Ala Asn Glu Ala Lys Gln Thr Ala Glu Glu Thr Lys					

[1919]

	1235	1240	1245
Gln Asn Val Asp Ala Lys Val Lys Ala Ala Glu Thr Ala Ala Gly Lys			
1250	1255	1260	
Ala Glu Ala Ala Ala Gly Thr Ala Asn Thr Ala Ala Asp Lys Ala Glu			
1265	1270	1275	1280
Ala Val Ala Ala Lys Val Thr Asp Ile Lys Ala Asp Ile Ala Thr Asn			
	1285	1290	1295
Lys Asp Asn Ile Ala Lys Lys Ala Asn Ser Ala Asp Val Tyr Thr Arg			
	1300	1305	1310
Glu Glu Ser Asp Ser Lys Phe Val Arg Ile Asp Gly Leu Asn Ala Thr			
	1315	1320	1325
Thr Glu Lys Leu Asp Thr Arg Leu Ala Ser Ala Glu Lys Ser Ile Ala			
	1330	1335	1340
Asp His Asp Thr Arg Leu Asn Gly Leu Asp Lys Thr Val Ser Asp Leu			
1345	1350	1355	1360
Arg Lys Glu Thr Arg Gln Gly Leu Ala Glu Gln Ala Ala Leu Ser Gly			
	1365	1370	1375
Leu Phe Gln Pro Tyr Asn Val Gly Leu Glu His His His His His His			
	1380	1385	1390

[1920] &lt;210&gt;25

[1921] &lt;211&gt;274

[1922] &lt;212&gt;PRT

[1923] &lt;213&gt;人工序列

[1924] &lt;220&gt;

[1925] &lt;223&gt;741

[1926] &lt;400&gt;25

[1927]

Val Asn Arg Thr Ala Phe Cys Cys Leu Ser Leu Thr Thr Ala Leu Ile			
1	5	10	15
Leu Thr Ala Cys Ser Ser Gly Gly Gly Gly Val Ala Ala Asp Ile Gly			
	20	25	30
Ala Gly Leu Ala Asp Ala Leu Thr Ala Pro Leu Asp His Lys Asp Lys			
	35	40	45
Gly Leu Gln Ser Leu Thr Leu Asp Gln Ser Val Arg Lys Asn Glu Lys			
	50	55	60
Leu Lys Leu Ala Ala Gln Gly Ala Glu Lys Thr Tyr Gly Asn Gly Asp			
65	70	75	80
Ser Leu Asn Thr Gly Lys Leu Lys Asn Asp Lys Val Ser Arg Phe Asp			
	85	90	95
Phe Ile Arg Gln Ile Glu Val Asp Gly Gln Leu Ile Thr Leu Glu Ser			
	100	105	110
Gly Glu Phe Gln Val Tyr Lys Gln Ser His Ser Ala Leu Thr Ala Phe			
	115	120	125
Gln Thr Glu Gln Ile Gln Asp Ser Glu His Ser Gly Lys Met Val Ala			
	130	135	140
Lys Arg Gln Phe Arg Ile Gly Asp Ile Ala Gly Glu His Thr Ser Phe			
145	150	155	160
Asp Lys Leu Pro Glu Gly Gly Arg Ala Thr Tyr Arg Gly Thr Ala Phe			
	165	170	175

[1928]

Gly Ser Asp Asp Ala Gly Gly Lys Leu Thr Tyr Thr Ile Asp Phe Ala  
                   180                  185                  190  
 Ala Lys Gln Gly Asn Gly Lys Ile Glu His Leu Lys Ser Pro Glu Leu  
                   195                  200                  205  
 Asn Val Asp Leu Ala Ala Ala Asp Ile Lys Pro Asp Gly Lys Arg His  
                   210                  215                  220  
 Ala Val Ile Ser Gly Ser Val Leu Tyr Asn Gln Ala Glu Lys Gly Ser  
 225                  230                  235                  240  
 Tyr Ser Leu Gly Ile Phe Gly Gly Lys Ala Gln Glu Val Ala Gly Ser  
                   245                  250                  255  
 Ala Glu Val Lys Thr Val Asn Gly Ile Arg His Ile Gly Leu Ala Ala  
                   260                  265                  270  
 Lys Gln

[1929] &lt;210&gt;26

[1930] &lt;211&gt;248

[1931] &lt;212&gt;PRT

[1932] &lt;213&gt; 人工序列

[1933] &lt;220&gt;

[1934] &lt;223&gt; Δ G741

[1935] &lt;400&gt;26

[1936]

Val	Ala	Ala	Asp	Ile	Gly	Ala	Gly	Leu	Ala	Asp	Ala	Leu	Thr	Ala	Pro
1				5					10					15	
Leu	Asp	His	Lys	Asp	Lys	Gly	Leu	Gln	Ser	Leu	Thr	Leu	Asp	Gln	Ser
			20					25					30		
Val	Arg	Lys	Asn	Glu	Lys	Leu	Lys	Leu	Ala	Ala	Gln	Gly	Ala	Glu	Lys
			35					40					45		
Thr	Tyr	Gly	Asn	Gly	Asp	Ser	Leu	Asn	Thr	Gly	Lys	Leu	Lys	Asn	Asp
			50				55					60			
Lys	Val	Ser	Arg	Phe	Asp	Phe	Ile	Arg	Gln	Ile	Glu	Val	Asp	Gly	Gln
65					70					75					80
Leu	Ile	Thr	Leu	Glu	Ser	Gly	Glu	Phe	Gln	Val	Tyr	Lys	Gln	Ser	His
				85					90					95	
Ser	Ala	Leu	Thr	Ala	Phe	Gln	Thr	Glu	Gln	Ile	Gln	Asp	Ser	Glu	His
			100					105						110	
Ser	Gly	Lys	Met	Val	Ala	Lys	Arg	Gln	Phe	Arg	Ile	Gly	Asp	Ile	Ala
			115				120						125		
Gly	Glu	His	Thr	Ser	Phe	Asp	Lys	Leu	Pro	Glu	Gly	Gly	Arg	Ala	Thr
			130				135					140			
Tyr	Arg	Gly	Thr	Ala	Phe	Gly	Ser	Asp	Asp	Ala	Gly	Gly	Lys	Leu	Thr
145					150					155					160
Tyr	Thr	Ile	Asp	Phe	Ala	Ala	Lys	Gln	Gly	Asn	Gly	Lys	Ile	Glu	His
				165					170					175	
Leu	Lys	Ser	Pro	Glu	Leu	Asn	Val	Asp	Leu	Ala	Ala	Ala	Asp	Ile	Lys
			180					185						190	
Pro	Asp	Gly	Lys	Arg	His	Ala	Val	Ile	Ser	Gly	Ser	Val	Leu	Tyr	Asn
			195				200						205		
Gln	Ala	Glu	Lys	Gly	Ser	Tyr	Ser	Leu	Gly	Ile	Phe	Gly	Gly	Lys	Ala
			210				215					220			
[1937]															
Gln	Glu	Val	Ala	Gly	Ser	Ala	Glu	Val	Lys	Thr	Val	Asn	Gly	Ile	Arg
225						230				235					240
His	Ile	Gly	Leu	Ala	Ala	Lys	Gln								
						245									

[1938] &lt;210&gt;27

[1939] &lt;211&gt;1947

[1940] &lt;212&gt;DNA

[1941] &lt;213&gt; 人工序列

[1942] &lt;220&gt;

[1943] &lt;223&gt; Δ G741-961

[1944] &lt;400&gt;27

[1945]

atggtcgccg cggacatcgg tgcggggcct gccgatgcac taaccgcacc gctcgacat	60
aaagacaaaag gtttcgagtc tttagcgtg gatcagtcg tcaggaaaaa cgagaaactg	120
aagctggcgg cacaaggtgc ggaaaaaact tatggaaacg gtgacagcct caatacgggc	180
aaattgaaga acgacaaggt cagccgtttc gactttatcc gccaaatcga agtggacggg	240
cagctcatta ccttgagag tggagagttc caagtataca acaaaagcca ttccgcctta	300
accgcctttc agaccgagca aatacaagat tccggagcatt ccgggaagat gtttgcgaaa	360
cgccagtta gaatcggcga catagcgggc gaacatacat cttttgacaa gcttcccgaa	420
ggcggcaggc cgacatatcg cgggacggcg ttccggttcag acgatgccgg cggaaaactg	480
acctacacca tagatttcgc gcccaagcag ggaaacggca aaatcgaaca tttgaaatcg	540
ccagaactca atgtcgacct ggccgcccgc gatatcaagc cggatggaaa acgcatgcc	600
gtcatcagcg gttccgtcct ttacaaccaa gccgagaaag gcagtactc cctcggatc	660
tttggcggaa aagcccagga agttgccggc agcgcgggaag tgaaaaccgt aaacggcata	720
cgccatatcg gccttgccgc caagcaactc gagggtggcg gaggcactgg atccgccaca	780
aacgacgacg atgttaaaaa agctgccact gtggccattg ctgtgccta caacaatggc	840
caagaaatca acggtttcaa agctggagag accatctacg acattgatga agacggcaca	900
attacaaaaa aagacgcaac tgcagccgat gttgaagccg acgactttaa aggtctgggt	960
ctgaaaaaag tctgactaa cctgaccaa accgtcaatg aaaacaaca aaacgtcgat	1020
gccaaagtaa aagctgcaga atctgaaata gaaaagttaa caaccaagtt agcagacact	1080
gatgccgctt tagcagatac tgatgccgct ctggatgcaa ccaccaacgc ctgaaataa	1140
ttgggagaaa atataacgac atttgctgaa gagactaaga caaatatcgt aaaaattgat	1200
gaaaaattag aagccgtggc tgataccgct gacaagcatg ccgaagcatt caacgatatc	1260
gccgattcat tggatgaaac caacactaag gcagacgaag ccgtcaaac cgccaatgaa	1320
gccaaacaga cggccgaaga aaccaacaa aacgtcgatg ccaaagtaa agctgcagaa	1380
actgcagcag gcaaaagcca agctgccgct ggcacagcta atactgcagc cgacaaggcc	1440
gaagctgtcg ctgcaaaagt taccgacatc aaagctgata tcgctacgaa caaagataat	1500
attgctaaaa aagcaaacag tgccgacgtg tacaccagag aagagtctga cagcaaattt	1560
gtcagaattg atggtctgaa cgctactacc gaaaaattgg acacacgctt ggcttctgct	1620
gaaaaatcca ttgccgatca cgatactgc ctgaacggtt tggataaaac agtgtcagac	1680
ctgcgcaaag aaaccgcca aggcccttga gaacaagccg cgctctccgg tctgttccaa	1740
ccttacaacg tgggtcgggt caatgtaacg gctgcagtcg gcggctacaa atccgaatcg	1800
gcagtcgcca tcggtaccgg ctccgccttt accgaaaact ttgccgcaa agcaggcgtg	1860
gcagtcggca cttcgtccgg ttcttcgcga gcctaccatg tcggcgtcaa ttacgagttg	1920
ctcgagcacc accaccacca ccactga	1947

[1946] &lt;210&gt;28

[1947] &lt;211&gt;648

[1948] &lt;212&gt;PRT

[1949] &lt;213&gt;人工序列

[1950] &lt;220&gt;

[1951] &lt;223&gt; Δ G741-961

[1952] &lt;400&gt;28

[1953]

Met Val Ala Ala Asp Ile Gly Ala Gly Leu Ala Asp Ala Leu Thr Ala  
 1 5 10 15  
 Pro Leu Asp His Lys Asp Lys Gly Leu Gln Ser Leu Thr Leu Asp Gln  
 20 25 30  
 Ser Val Arg Lys Asn Glu Lys Leu Lys Leu Ala Ala Gln Gly Ala Glu  
 35 40 45  
 Lys Thr Tyr Gly Asn Gly Asp Ser Leu Asn Thr Gly Lys Leu Lys Asn  
 50 55 60  
 Asp Lys Val Ser Arg Phe Asp Phe Ile Arg Gln Ile Glu Val Asp Gly  
 65 70 75 80  
 Gln Leu Ile Thr Leu Glu Ser Gly Glu Phe Gln Val Tyr Lys Gln Ser  
 85 90 95  
 His Ser Ala Leu Thr Ala Phe Gln Thr Glu Gln Ile Gln Asp Ser Glu  
 100 105 110  
 His Ser Gly Lys Met Val Ala Lys Arg Gln Phe Arg Ile Gly Asp Ile  
 115 120 125  
 Ala Gly Glu His Thr Ser Phe Asp Lys Leu Pro Glu Gly Gly Arg Ala  
 130 135 140  
 Thr Tyr Arg Gly Thr Ala Phe Gly Ser Asp Asp Ala Gly Gly Lys Leu  
 145 150 155 160  
 Thr Tyr Thr Ile Asp Phe Ala Ala Lys Gln Gly Asn Gly Lys Ile Glu  
 165 170 175  
 His Leu Lys Ser Pro Glu Leu Asn Val Asp Leu Ala Ala Ala Asp Ile  
 180 185 190  
 Lys Pro Asp Gly Lys Arg His Ala Val Ile Ser Gly Ser Val Leu Tyr  
 195 200 205  
 Asn Gln Ala Glu Lys Gly Ser Tyr Ser Leu Gly Ile Phe Gly Gly Lys  
 210 215 220  
 Ala Gln Glu Val Ala Gly Ser Ala Glu Val Lys Thr Val Asn Gly Ile  
 225 230 235 240  
 Arg His Ile Gly Leu Ala Ala Lys Gln Leu Glu Gly Gly Gly Thr  
 245 250 255  
 Gly Ser Ala Thr Asn Asp Asp Asp Val Lys Lys Ala Ala Thr Val Ala  
 260 265 270  
 Ile Ala Ala Ala Tyr Asn Asn Gly Gln Glu Ile Asn Gly Phe Lys Ala  
 275 280 285  
 Gly Glu Thr Ile Tyr Asp Ile Asp Glu Asp Gly Thr Ile Thr Lys Lys  
 290 295 300  
 Asp Ala Thr Ala Ala Asp Val Glu Ala Asp Asp Phe Lys Gly Leu Gly  
 305 310 315 320  
 Leu Lys Lys Val Val Thr Asn Leu Thr Lys Thr Val Asn Glu Asn Lys  
 325 330 335  
 Gln Asn Val Asp Ala Lys Val Lys Ala Ala Glu Ser Glu Ile Glu Lys  
 340 345 350  
 Leu Thr Thr Lys Leu Ala Asp Thr Asp Ala Ala Leu Ala Asp Thr Asp  
 355 360 365  
 Ala Ala Leu Asp Ala Thr Thr Asn Ala Leu Asn Lys Leu Gly Glu Asn

[1954]

370	375	380
Ile Thr Thr Phe Ala Glu Glu Thr Lys Thr Asn Ile Val Lys Ile Asp		
385	390	395
Glu Lys Leu Glu Ala Val Ala Asp Thr Val Asp Lys His Ala Glu Ala		400
	405	410
Phe Asn Asp Ile Ala Asp Ser Leu Asp Glu Thr Asn Thr Lys Ala Asp		415
	420	425
Glu Ala Val Lys Thr Ala Asn Glu Ala Lys Gln Thr Ala Glu Glu Thr		430
	435	440
Lys Gln Asn Val Asp Ala Lys Val Lys Ala Ala Glu Thr Ala Ala Gly		445
	450	455
Lys Ala Glu Ala Ala Ala Gly Thr Ala Asn Thr Ala Ala Asp Lys Ala		460
465	470	475
Glu Ala Val Ala Ala Lys Val Thr Asp Ile Lys Ala Asp Ile Ala Thr		480
	485	490
Asn Lys Asp Asn Ile Ala Lys Lys Ala Asn Ser Ala Asp Val Tyr Thr		495
	500	505
Arg Glu Glu Ser Asp Ser Lys Phe Val Arg Ile Asp Gly Leu Asn Ala		510
	515	520
Thr Thr Glu Lys Leu Asp Thr Arg Leu Ala Ser Ala Glu Lys Ser Ile		525
	530	535
Ala Asp His Asp Thr Arg Leu Asn Gly Leu Asp Lys Thr Val Ser Asp		540
545	550	555
Leu Arg Lys Glu Thr Arg Gln Gly Leu Ala Glu Gln Ala Ala Leu Ser		560
	565	570
Gly Leu Phe Gln Pro Tyr Asn Val Gly Arg Phe Asn Val Thr Ala Ala		575
	580	585
Val Gly Gly Tyr Lys Ser Glu Ser Ala Val Ala Ile Gly Thr Gly Phe		590
	595	600
Arg Phe Thr Glu Asn Phe Ala Ala Lys Ala Gly Val Ala Val Gly Thr		605
	610	615
Ser Ser Gly Ser Ser Ala Ala Tyr His Val Gly Val Asn Tyr Glu Trp		620
625	630	635
Leu Glu His His His His His His		640
	645	

[1955] &lt;210&gt;29

[1956] &lt;211&gt;1782

[1957] &lt;212&gt;DNA

[1958] &lt;213&gt;人工序列

[1959] &lt;220&gt;

[1960] <223> $\Delta$ G741-961c

[1961] &lt;400&gt;29

[1962]

	atggtcgccg cgcacatcgg tgcggggcct gccgatgcac taaccgcacc gctcgacat	60
	aaagacaaag gtttgagtc tttgacgctg gatcagtcgc tcaggaaaa cgagaaactg	120
	aagctggcgg cacaaggtgc gaaaaaact tatggaaacg gtgacagcct caatacgggc	180
	aaattgaaga acgacaaggt cagccgtttc gactttatcc gccaaatcga agtggacggg	240
	cagctcatta ccttggagag tggagagttc caagtataca aacaaagcca ttccgcctta	300
	accgcctttc agaccgagca aatacaagat tcggagcatt ccgggaagat ggttgcgaaa	360
[1963]	cgccagtcca gaatcggcga catagcgggc gaacatacat cttttgacaa gcttcccga	420
	ggcggcaggg cgacatatcg cgggacggcg ttcggttcag acgatgccgg cggaaaactg	480
	acctacacca tagatttcgc cgccaagcag ggaaacggca aaatcgaaca ttgaaatcg	540
	ccagaactca atgtcgacct ggccgcccgc gatatcaagc cggatggaaa acgcatgcc	600
	gtcatcagcg gttccgtect ttacaaccaa gccgagaaag gcagttactc ctcggtatc	660
	tttggcggaa aagcccagga agttgccggc agcgcggaag tgaaccctg aaacggcata	720
	cgccatatcg gccttgccgc caagcaactc gagggcggcg gaggcactgg atccgccaca	780
	aacgacgacg atgttaaaaa agctgccact gtggccattg ctgctgccta caacaatggc	840
	caagaaatca acggtttcaa agctggagag accatctacg acattgatga agacggcaca	900
	attacaaaa aagacgcaac tgcagccgat gttgaagccg acgactttaa aggtctgggt	960
	ctgaaaaaag tcgtgactaa cctgaccaa accgtcaatg aaaacaaaca aaacgtcgat	1020
	gccaaagtaa aagctgcaga atctgaaata gaaaagttaa caaccaagtt agcagacact	1080
	gatgccgctt tagcagatac tgatgccgct ctggatgcaa ccaccaacgc ctgtaataaa	1140
	ttgggagaaa atataacgac atttgctgaa gagactaaga caaatatcgt aaaaattgat	1200
	gaaaaattag aagccgtggc tgataccgtc gacaagcatg ccgaagcatt caacgatatc	1260
	gccgattcat tggatgaaac caacactaag gcagacgaag ccgtcaaac cgccaatgaa	1320
	gccaaacaga cggccgaaga aaccaaaca aacgtcgatg ccaaagtaa agctgcagaa	1380
	actgcagcag gcaaagccga agctgccgct ggacacagcta atactgcagc cgacaagcc	1440
	gaagctgtcg ctgcaaaagt taccgacatc aaagctgata tcgctacgaa caagataat	1500
	attgctaaaa aagcaaacag tgccgacgtg tacaccagag aagagtctga cagcaattt	1560
	gtcagaattg atggtctgaa cgctactacc gaaaaattgg acacacgctt ggcttctgct	1620
	gaaaaatcca ttgccgatca cgatactcgc ctgaacggtt tggataaac agtgtcagac	1680
	ctgcgcaaag aaaccgcca aggccttgca gaacaagccg cgctctccgg tctgttccaa	1740
	cettacaacg tgggtctcga gcaccaccac caccaccact ga	1782
[1964]	<210>30	
[1965]	<211>593	
[1966]	<212>PRT	
[1967]	<213> 人工序列	
[1968]	<220>	
[1969]	<223> Δ G741-961c	
[1970]	<400>30	
[1971]		



Met Val Ala Ala Asp Ile Gly Ala Gly Leu Ala Asp Ala Leu Thr Ala  
 1                                   5                                   10                                   15  
 Pro Leu Asp His Lys Asp Lys Gly Leu Gln Ser Leu Thr Leu Asp Gln  
                                   20                                   25                                   30  
 Ser Val Arg Lys Asn Glu Lys Leu Lys Leu Ala Ala Gln Gly Ala Glu  
                                   35                                   40                                   45  
 Lys Thr Tyr Gly Asn Gly Asp Ser Leu Asn Thr Gly Lys Leu Lys Asn  
                                   50                                   55                                   60  
 Asp Lys Val Ser Arg Phe Asp Phe Ile Arg Gln Ile Glu Val Asp Gly  
 65                                   70                                   75                                   80  
 Gln Leu Ile Thr Leu Glu Ser Gly Glu Phe Gln Val Tyr Lys Gln Ser  
                                   85                                   90                                   95  
 His Ser Ala Leu Thr Ala Phe Gln Thr Glu Gln Ile Gln Asp Ser Glu  
                                   100                                   105                                   110  
 His Ser Gly Lys Met Val Ala Lys Arg Gln Phe Arg Ile Gly Asp Ile  
                                   115                                   120                                   125  
 Ala Gly Glu His Thr Ser Phe Asp Lys Leu Pro Glu Gly Gly Arg Ala  
                                   130                                   135                                   140  
 Thr Tyr Arg Gly Thr Ala Phe Gly Ser Asp Asp Ala Gly Gly Lys Leu

[1972]



	565	570	575	
	Gly Leu Phe Gln Pro Tyr Asn Val Gly Leu Glu His His His His His			
	580	585	590	
	His			
[1974]	<210>31			
[1975]	<211>3939			
[1976]	<212>DNA			
[1977]	<213>人工序列			
[1978]	<220>			
[1979]	<223>Δ G741-983			
[1980]	<400>31			
[1981]				
	atggtcgccg cgcacatcgg tgcggggcct gccgatgcac taaccgcacc gctcgacct			60
	aaagacaaaag gtttcagctc tttagacgtg gatcagtcgc tcaggaaaaa cgagaaactg			120
	aagctggcgg cacaaggtgc gaaaaaaact tatggaaacg gtgacagcct caatacgggc			180
	aaattgaaga acgacaaggt cagccgtttc gactttatcc gccaaatcga agtggacggg			240
	cagctcatta ccttggagag tggagagtcc caagtataca aacaaagcca ttccgcctta			300
	accgcctttc agaccgagca aatacaagat tcggagcatt ccgggaagat ggttgcgaaa			360
	cgccagtcca gaatcggcga catagcgggc gaacatacat cttttgacaa gcttcccga			420
	ggcggcaggc cgacatatcg cgggacggcg ttcggttcag acgatgccgg cggaaaactg			480
	acctacacca tagatttcgc cgccaagcag ggaaacggca aaatcgaaca ttgaaatcg			540
	ccagaactca atgtcgacct ggccgcccgc gatatcaagc cggatggaaa acgcatgcc			600
	gtcatcagcg gttcgcctct ttacaaccaa gccgagaaag gcagttactc cctcggatc			660
	tttggcggaa aagcccagga agttgccggc agcgcggaag tgaaaaccgt aaacggcata			720
	cgccatatcg gccttgcgc caagcaactc gagggatccg ggggaggcgg cacttctgcg			780
	cccgacttca atgcaggcgg taccggatc gccagcaaca gcagagcaac aacagcgaaa			840
	tcagcagcag tatcttacgc cggatatcaag aacgaaatgt gcaaagacag aagcatgctc			900
	tgtgccggtc gggatgacgt tgcggttaca gacagggatg ccaaaatcaa tgccccccc			960
	ccgaatctgc ataccggaga ctttccaaac ccaaatgacg catacaagaa ttgatcaac			1020
	ctcaaactg caattgaagc aggctataca ggacgcgggg tagaggtagg tctcgtcgac			1080
	acaggcgaat ccgtcggcag catatccttt cccgaactgt atggcagaaa agaacacggc			1140
	tataacgaaa attacaaaa ctatacggcg tatatgcgga aggaagcgc tgaagacgga			1200
	ggcggtaaag acattgaagc ttctttcgac gatgaggccg ttatagagac tgaagcaaag			1260
	ccgacggata tccgccacgt aaaagaaatc ggacacatcg atttggtctc ccatattatt			1320
	ggcggggcgtt ccgtggacgg cagacctgca ggcggtatg cgcccgatgc gacgctacac			1380
	ataatgaata cgaatgatga aaccaagaac gaaatgatgg ttgcagccat ccgcaatgca			1440
	tgggtcaagc tgggcgaacg tggcgtgcgc atcgtcaata acagttttgg aacaacatcg			1500
	agggcaggca ctgccacct tttccaaata gccaatcggc aggagcagta ccgccaagcg			1560
	ttgctcgact attccggcgg tgataaaaca gacgagggta tccgcctgat gcaacagagc			1620
	gattacggca acctgtccta ccacatccgt aataaaaaaca tgcttttcat cttttcgaca			1680
	ggcaatgacg cacaagctca gcccaacaca tatgcctat tgccatttta tgaaaaagac			1740
	gctcaaaaag gcattatcac agtcgcaggc gtagaccgca gtggagaaaa gttcaaacgg			1800
	gaaatgtatg gagaaccggg tacagaaccg cttgagtatg gctccaacca ttgcggaatt			1860
	actgccatgt ggtgcctgtc ggcaccctat gaagcaagcg tccgtttcac ccgtacaaac			1920
	ccgattcaaa ttgccggaac atccttttcc gcaccatcg taaccggcac ggcggctctg			1980
	ctgctgcaga aatacccggt gatgagcaac gacaacctgc gtaccacgtt gctgacgacg			2040
	gctcaggaca tcggtgcagt cggcgtggac agcaagttcg gctggggact gctggatgcg			2100
	ggtaaggcca tgaacggacc cgcgtccttt ccgttcggcg actttaccgc cgatacga			2160
	ggtacatccg atattgccta ctcttccgt aacgacattt caggcacggg cggcctgatc			2220

[1982]

aaaaaaggcg	gcagccaact	gcaactgcac	ggcaacaaca	cctatacggg	caaaaccatt	2280
atcgaaggcg	gttcgctggt	gttgtacggc	aacaacaaat	cggatatgcg	cgtcgaaacc	2340
aaaggtcgc	tgatttataa	cggggcggca	tccggcggca	gcctgaacag	cgacggcatt	2400
gtctatctgg	cagataccga	ccaatccggc	gcaaacgaaa	ccgtacacat	caaaggcagt	2460
ctgcagctgg	acggcaaagg	tacgctgtac	acacgtttgg	gcaaactgct	gaaagtggac	2520
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gccgccacac	tgggcatggg	acgcagcaca	tggagcga	acagtgcaa	tgcaaaaacc	3300
gacagcat	gtctgtttgc	aggcatacgg	cacgatgcgg	gcgatatcgg	ctatctcaa	3360
ggcctgttct	cctacggacg	ctacaaaaac	agcatcagcc	gcagcaccgg	tgccggacgaa	3420
catgcggaag	gcagcgtcaa	cggcacgctg	atgcagctgg	gcgcaactggg	cggtgtcaac	3480
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gtcctgtttg	caacggcggg	cgltggaacgc	gacctgaacg	gacgcgacta	cacggtaacg	3720
ggcggettta	ccggcgcgac	tcagcaacc	ggcaagacgg	gggcacgcaa	tatgccgcac	3780
accgtcttgg	ttgccggcct	ggcgcgggat	gtcgaattcg	gcaacggctg	gaacggcttg	3840
gcaggttaca	gctacgccgg	ttccaacag	tacggcaacc	acagcggacg	agtcggcgta	3900
ggctaccggt	tcctcgagca	ccaccaccac	caccactga			3939

[1983] &lt;210&gt;32

[1984] &lt;211&gt;1312

[1985] &lt;212&gt;PRT

[1986] &lt;213&gt; 人工序列

[1987] &lt;220&gt;

[1988] &lt;223&gt; Δ G741-983

[1989] &lt;400&gt;32

[1990]

Met Val Ala Ala Asp Ile Gly Ala Gly Leu Ala Asp Ala Leu Thr Ala  
 1                                   5                                   10                                   15  
 Pro Leu Asp His Lys Asp Lys Gly Leu Gln Ser Leu Thr Leu Asp Gln  
                                   20                                   25                                   30  
 Ser Val Arg Lys Asn Glu Lys Leu Lys Leu Ala Ala Gln Gly Ala Glu  
                                   35                                   40                                   45  
 Lys Thr Tyr Gly Asn Gly Asp Ser Leu Asn Thr Gly Lys Leu Lys Asn  
                                   50                                   55                                   60  
 Asp Lys Val Ser Arg Phe Asp Phe Ile Arg Gln Ile Glu Val Asp Gly  
 65                                   70                                   75                                   80  
 Gln Leu Ile Thr Leu Glu Ser Gly Glu Phe Gln Val Tyr Lys Gln Ser  
                                   85                                   90                                   95  
 His Ser Ala Leu Thr Ala Phe Gln Thr Glu Gln Ile Gln Asp Ser Glu

[1991]

	100		105		110
His Ser Gly Lys Met Val Ala Lys Arg Gln Phe Arg Ile Gly Asp Ile					
	115		120		125
Ala Gly Glu His Thr Ser Phe Asp Lys Leu Pro Glu Gly Gly Arg Ala					
	130		135		140
Thr Tyr Arg Gly Thr Ala Phe Gly Ser Asp Asp Ala Gly Gly Lys Leu					
	145		150		155
Thr Tyr Thr Ile Asp Phe Ala Ala Lys Gln Gly Asn Gly Lys Ile Glu					
	165		170		175
His Leu Lys Ser Pro Glu Leu Asn Val Asp Leu Ala Ala Ala Asp Ile					
	180		185		190
Lys Pro Asp Gly Lys Arg His Ala Val Ile Ser Gly Ser Val Leu Tyr					
	195		200		205
Asn Gln Ala Glu Lys Gly Ser Tyr Ser Leu Gly Ile Phe Gly Gly Lys					
	210		215		220
Ala Gln Glu Val Ala Gly Ser Ala Glu Val Lys Thr Val Asn Gly Ile					
	225		230		235
Arg His Ile Gly Leu Ala Ala Lys Gln Leu Glu Gly Ser Gly Gly Gly					
	245		250		255
Gly Thr Ser Ala Pro Asp Phe Asn Ala Gly Gly Thr Gly Ile Gly Ser					
	260		265		270
Asn Ser Arg Ala Thr Thr Ala Lys Ser Ala Ala Val Ser Tyr Ala Gly					
	275		280		285
Ile Lys Asn Glu Met Cys Lys Asp Arg Ser Met Leu Cys Ala Gly Arg					
	290		295		300
Asp Asp Val Ala Val Thr Asp Arg Asp Ala Lys Ile Asn Ala Pro Pro					
	305		310		315
Pro Asn Leu His Thr Gly Asp Phe Pro Asn Pro Asn Asp Ala Tyr Lys					
	325		330		335
Asn Leu Ile Asn Leu Lys Pro Ala Ile Glu Ala Gly Tyr Thr Gly Arg					
	340		345		350
Gly Val Glu Val Gly Ile Val Asp Thr Gly Glu Ser Val Gly Ser Ile					
	355		360		365
Ser Phe Pro Glu Leu Tyr Gly Arg Lys Glu His Gly Tyr Asn Glu Asn					
	370		375		380
Tyr Lys Asn Tyr Thr Ala Tyr Met Arg Lys Glu Ala Pro Glu Asp Gly					
	385		390		395
Gly Gly Lys Asp Ile Glu Ala Ser Phe Asp Asp Glu Ala Val Ile Glu					
	405		410		415
Thr Glu Ala Lys Pro Thr Asp Ile Arg His Val Lys Glu Ile Gly His					
	420		425		430
Ile Asp Leu Val Ser His Ile Ile Gly Gly Arg Ser Val Asp Gly Arg					
	435		440		445
Pro Ala Gly Gly Ile Ala Pro Asp Ala Thr Leu His Ile Met Asn Thr					
	450		455		460
Asn Asp Glu Thr Lys Asn Glu Met Met Val Ala Ala Ile Arg Asn Ala					
	465		470		475
Trp Val Lys Leu Gly Glu Arg Gly Val Arg Ile Val Asn Asn Ser Phe					
	485		490		495
Gly Thr Thr Ser Arg Ala Gly Thr Ala Asp Leu Phe Gln Ile Ala Asn					
	500		505		510
Ser Glu Glu Gln Tyr Arg Gln Ala Leu Leu Asp Tyr Ser Gly Gly Asp					

[1992]

515	520	525
Lys Thr Asp Glu Gly Ile Arg Leu Met Gln Gln Ser Asp Tyr Gly Asn		
530	535	540
Leu Ser Tyr His Ile Arg Asn Lys Asn Met Leu Phe Ile Phe Ser Thr		
545	550	555
Gly Asn Asp Ala Gln Ala Gln Pro Asn Thr Tyr Ala Leu Leu Pro Phe		
565	570	575
Tyr Glu Lys Asp Ala Gln Lys Gly Ile Thr Val Ala Gly Val Asp		
580	585	590
Arg Ser Gly Glu Lys Phe Lys Arg Glu Met Tyr Gly Glu Pro Gly Thr		
595	600	605
Glu Pro Leu Glu Tyr Gly Ser Asn His Cys Gly Ile Thr Ala Met Trp		
610	615	620
Cys Leu Ser Ala Pro Tyr Glu Ala Ser Val Arg Phe Thr Arg Thr Asn		
625	630	635
Pro Ile Gln Ile Ala Gly Thr Ser Phe Ser Ala Pro Ile Val Thr Gly		
645	650	655
Thr Ala Ala Leu Leu Leu Gln Lys Tyr Pro Trp Met Ser Asn Asp Asn		
660	665	670
Leu Arg Thr Thr Leu Leu Thr Thr Ala Gln Asp Ile Gly Ala Val Gly		
675	680	685
Val Asp Ser Lys Phe Gly Trp Gly Leu Leu Asp Ala Gly Lys Ala Met		
690	695	700
Asn Gly Pro Ala Ser Phe Pro Phe Gly Asp Phe Thr Ala Asp Thr Lys		
705	710	715
Gly Thr Ser Asp Ile Ala Tyr Ser Phe Arg Asn Asp Ile Ser Gly Thr		
725	730	735
Gly Gly Leu Ile Lys Lys Gly Gly Ser Gln Leu Gln Leu His Gly Asn		
740	745	750
Asn Thr Tyr Thr Gly Lys Thr Ile Ile Glu Gly Gly Ser Leu Val Leu		
755	760	765
Tyr Gly Asn Asn Lys Ser Asp Met Arg Val Glu Thr Lys Gly Ala Leu		
770	775	780
Ile Tyr Asn Gly Ala Ala Ser Gly Gly Ser Leu Asn Ser Asp Gly Ile		
785	790	795
Val Tyr Leu Ala Asp Thr Asp Gln Ser Gly Ala Asn Glu Thr Val His		
805	810	815
Ile Lys Gly Ser Leu Gln Leu Asp Gly Lys Gly Thr Leu Tyr Thr Arg		
820	825	830
Leu Gly Lys Leu Leu Lys Val Asp Gly Thr Ala Ile Ile Gly Gly Lys		
835	840	845
Leu Tyr Met Ser Ala Arg Gly Lys Gly Ala Gly Tyr Leu Asn Ser Thr		
850	855	860
Gly Arg Arg Val Pro Phe Leu Ser Ala Ala Lys Ile Gly Gln Asp Tyr		
865	870	875
Ser Phe Phe Thr Asn Ile Glu Thr Asp Gly Gly Leu Leu Ala Ser Leu		
885	890	895
Asp Ser Val Glu Lys Thr Ala Gly Ser Glu Gly Asp Thr Leu Ser Tyr		
900	905	910
Tyr Val Arg Arg Gly Asn Ala Ala Arg Thr Ala Ser Ala Ala Ala His		
915	920	925
Scr Ala Pro Ala Gly Leu Lys His Ala Val Glu Gln Gly Gly Ser Asn		

[1993]

930	935	940
Leu Glu Asn Leu Met Val Glu Leu Asp Ala Ser Glu Ser Ser Ala Thr		
945	950	955
Pro Glu Thr Val Glu Thr Ala Ala Ala Asp Arg Thr Asp Met Pro Gly		
	965	970
Ile Arg Pro Tyr Gly Ala Thr Phe Arg Ala Ala Ala Ala Val Gln His		
	980	985
Ala Asn Ala Ala Asp Gly Val Arg Ile Phe Asn Ser Leu Ala Ala Thr		
	995	1000
Val Tyr Ala Asp Ser Thr Ala Ala His Ala Asp Met Gln Gly Arg Arg		
	1010	1015
Leu Lys Ala Val Ser Asp Gly Leu Asp His Asn Gly Thr Gly Leu Arg		
1025	1030	1035
Val Ile Ala Gln Thr Gln Gln Asp Gly Gly Thr Trp Glu Gln Gly Gly		
	1045	1050
Val Glu Gly Lys Met Arg Gly Ser Thr Gln Thr Val Gly Ile Ala Ala		
	1060	1065
Lys Thr Gly Glu Asn Thr Thr Ala Ala Ala Thr Leu Gly Met Gly Arg		
	1075	1080
Ser Thr Trp Ser Glu Asn Ser Ala Asn Ala Lys Thr Asp Ser Ile Ser		
	1090	1095
Leu Phe Ala Gly Ile Arg His Asp Ala Gly Asp Ile Gly Tyr Leu Lys		
1105	1110	1115
Gly Leu Phe Ser Tyr Gly Arg Tyr Lys Asn Ser Ile Ser Arg Ser Thr		
	1125	1130
Gly Ala Asp Glu His Ala Glu Gly Ser Val Asn Gly Thr Leu Met Gln		
	1140	1145
Leu Gly Ala Leu Gly Gly Val Asn Val Pro Phe Ala Ala Thr Gly Asp		
	1155	1160
Leu Thr Val Glu Gly Gly Leu Arg Tyr Asp Leu Leu Lys Gln Asp Ala		
	1170	1175
Phe Ala Glu Lys Gly Ser Ala Leu Gly Trp Ser Gly Asn Ser Leu Thr		
1185	1190	1195
Glu Gly Thr Leu Val Gly Leu Ala Gly Leu Lys Leu Ser Gln Pro Leu		
	1205	1210
Ser Asp Lys Ala Val Leu Phe Ala Thr Ala Gly Val Glu Arg Asp Leu		
	1220	1225
Asn Gly Arg Asp Tyr Thr Val Thr Gly Gly Phe Thr Gly Ala Thr Ala		
	1235	1240
Ala Thr Gly Lys Thr Gly Ala Arg Asn Met Pro His Thr Arg Leu Val		
	1250	1255
Ala Gly Leu Gly Ala Asp Val Glu Phe Gly Asn Gly Trp Asn Gly Leu		
1265	1270	1275
Ala Arg Tyr Ser Tyr Ala Gly Ser Lys Gln Tyr Gly Asn His Ser Gly		
	1285	1290
Arg Val Gly Val Gly Tyr Arg Phe Leu Glu His His His His His His		
	1300	1305
		1310

[1994] &lt;210&gt;33

[1995] &lt;211&gt;2028

[1996] &lt;212&gt;DNA



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	aaagacaaag gtttgcagtc tttgacgctg gatcagtccg tcaggaaaaa cgagaaactg	120
	aagctggcgg cacaaggtgc ggaaaaaact tatggaaacg gtgacagcct caatacgggc	180
	aaattgaaga acgacaaggt cagccgtttc gactttatcc gccaaatcga agtggacggg	240
	cagctcatta ccttggagag tggagagttc caagtataca acaaaagcca ttccgcctta	300
	accgcctttc agaccgagca aatacaagat tcggagcatt ccgggaagat ggttgcgaaa	360
	cgccagtcca gaatcggcga catagcgggc gaacatacat cttttgacaa gcttcccga	420
	ggcggcaggg cgacatatcg cgggacggcg ttcggttcag acgatgccgg cggaaaactg	480
	acctacacca tagatttcgc cgccaagcag ggaaacggca aaatcgaaca tttgaaatcg	540
	ccagaactca atgtcgacct ggccgcccgc gatatcaagc cggatggaaa acgcatgcc	600
	gtcatcagcg gttccgtcct ttacaaccaa gccgagaaag gcagttactc cctcggtatc	660
	tttggcggaa aagcccagga agttgccggc agcgcggaag tgaaaaccgt aaacggcata	720
	cgccatatcg gcttggcgc caagcaactc gacggtggcg gaggeactgg atcctcagat	780
	ttggcaaacg attcttttat ccggcaggtt ctcgaccgtc agcatttcga acccgacggg	840
	aaataccacc tattcggcag caggggggaa cttgccgagc gcagcggcca tatecgattg	900
	ggaaaaatac aaagccatca gttgggcaac ctgatgattc aacaggcggc cattaagga	960
	aatatcggct acattgtccg cttttccgat cacgggcacg aagtccattc ccccttcgac	1020
	aacctgcct cacattccga ttctgatgaa gccggtagtc ccggtgacgg atttagcctt	1080
	taccgatcc attgggacgg atacgaacac catcccgcg acggctatga cgggccacag	1140
	ggcggcggt atcccgtcc caaaggcgc agggatatac acagctacga cataaaaggc	1200
	gttgccc aaa ataccgct caacctgacc gacaaccgca gcaccggaca acggcttgc	1260
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	gccaccgat acagccccga gctggacaga tcgggcaatg ccgccgaagc cttaacggc	1380
	actgcagata tcgttaaaaa catcatcggc gcggcaggag aaattgtcgg cgcaggcgt	1440
	gccgtgcagg gcataagcga aggcctcaaac attgctgtca tgcacggctt gggctctgctt	1500
	tccaccgaaa acaagatggc gcgcatcaac gatttggcag atatggcgca actcaaagac	1560
	tatgccgag cagccatccg cgattgggca gtccaaaacc ccaatgccgc acaaggcata	1620
	gaagccgtca gcaatatctt tatggcagcc atccccatca aagggttgg agctgttcgg	1680
	ggaaaatac gcttggcgg catcacggca catcctatca agcggtcgca gatgggcgcg	1740
	atcgcatgc cgaagggaa atccgcccgc agcgacaatt ttgccgatgc ggcatagcc	1800
	aaataccgt ccccttacca ttcccgaat atccgttcaa acttggagca gcgttacggc	1860
	aaagaaaaca tcacctcctc aaccgtgcc cgctcaaacg gcaaaaatgt caaactggca	1920
	gaccaacgcc acccgaagac aggcgtaccg tttgacggta aagggtttcc gaattttgag	1980
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[2008]	<400>34	
[2009]		

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1                                    5                                    10                                    15  
Pro Leu Asp His Lys Asp Lys Gly Leu Gln Ser Leu Thr Leu Asp Gln

[2010]

20 25 30  
 Ser Val Arg Lys Asn Glu Lys Leu Lys Leu Ala Ala Gln Gly Ala Glu  
 35 40 45  
 Lys Thr Tyr Gly Asn Gly Asp Ser Leu Asn Thr Gly Lys Leu Lys Asn  
 50 55 60  
 Asp Lys Val Ser Arg Phe Asp Phe Ile Arg Gln Ile Glu Val Asp Gly  
 65 70 75 80  
 Gln Leu Ile Thr Leu Glu Ser Gly Glu Phe Gln Val Tyr Lys Gln Ser  
 85 90 95  
 His Ser Ala Leu Thr Ala Phe Gln Thr Glu Gln Ile Gln Asp Ser Glu  
 100 105 110  
 His Ser Gly Lys Met Val Ala Lys Arg Gln Phe Arg Ile Gly Asp Ile  
 115 120 125  
 Ala Gly Glu His Thr Ser Phe Asp Lys Leu Pro Glu Gly Gly Arg Ala  
 130 135 140  
 Thr Tyr Arg Gly Thr Ala Phe Gly Ser Asp Asp Ala Gly Gly Lys Leu  
 145 150 155 160  
 Thr Tyr Thr Ile Asp Phe Ala Ala Lys Gln Gly Asn Gly Lys Ile Glu  
 165 170 175  
 His Leu Lys Ser Pro Glu Leu Asn Val Asp Leu Ala Ala Ala Asp Ile  
 180 185 190  
 Lys Pro Asp Gly Lys Arg His Ala Val Ile Ser Gly Ser Val Leu Tyr  
 195 200 205  
 Asn Gln Ala Glu Lys Gly Ser Tyr Ser Leu Gly Ile Phe Gly Gly Lys  
 210 215 220  
 Ala Gln Glu Val Ala Gly Ser Ala Glu Val Lys Thr Val Asn Gly Ile  
 225 230 235 240  
 Arg His Ile Gly Leu Ala Ala Lys Gln Leu Asp Gly Gly Gly Gly Thr  
 245 250 255  
 Gly Ser Ser Asp Leu Ala Asn Asp Ser Phe Ile Arg Gln Val Leu Asp  
 260 265 270  
 Arg Gln His Phe Glu Pro Asp Gly Lys Tyr His Leu Phe Gly Ser Arg  
 275 280 285  
 Gly Glu Leu Ala Glu Arg Ser Gly His Ile Gly Leu Gly Lys Ile Gln  
 290 295 300  
 Ser His Gln Leu Gly Asn Leu Met Ile Gln Gln Ala Ala Ile Lys Gly  
 305 310 315 320  
 Asn Ile Gly Tyr Ile Val Arg Phe Ser Asp His Gly His Glu Val His  
 325 330 335  
 Ser Pro Phe Asp Asn His Ala Ser His Ser Asp Ser Asp Glu Ala Gly  
 340 345 350  
 Ser Pro Val Asp Gly Phe Ser Leu Tyr Arg Ile His Trp Asp Gly Tyr  
 355 360 365  
 Glu His His Pro Ala Asp Gly Tyr Asp Gly Pro Gln Gly Gly Gly Tyr  
 370 375 380  
 Pro Ala Pro Lys Gly Ala Arg Asp Ile Tyr Ser Tyr Asp Ile Lys Gly  
 385 390 395 400  
 Val Ala Gln Asn Ile Arg Leu Asn Leu Thr Asp Asn Arg Ser Thr Gly  
 405 410 415  
 Gln Arg Leu Ala Asp Arg Phe His Asn Ala Gly Ser Met Leu Thr Gln  
 420 425 430  
 Gly Val Gly Asp Gly Phe Lys Arg Ala Thr Arg Tyr Ser Pro Glu Leu

[2011]

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          435                440                445
Asp Arg Ser Gly Asn Ala Ala Glu Ala Phe Asn Gly Thr Ala Asp Ile
  450                455                460
Val Lys Asn Ile Ile Gly Ala Ala Gly Glu Ile Val Gly Ala Gly Asp
  465                470                475                480
Ala Val Gln Gly Ile Ser Glu Gly Ser Asn Ile Ala Val Met His Gly
          485                490                495
Leu Gly Leu Leu Ser Thr Glu Asn Lys Met Ala Arg Ile Asn Asp Leu
          500                505                510
Ala Asp Met Ala Gln Leu Lys Asp Tyr Ala Ala Ala Ala Ile Arg Asp
          515                520                525
Trp Ala Val Gln Asn Pro Asn Ala Ala Gln Gly Ile Glu Ala Val Ser
          530                535                540
Asn Ile Phe Met Ala Ala Ile Pro Ile Lys Gly Ile Gly Ala Val Arg
          545                550                555                560
Gly Lys Tyr Gly Leu Gly Gly Ile Thr Ala His Pro Ile Lys Arg Ser
          565                570                575
Gln Met Gly Ala Ile Ala Leu Pro Lys Gly Lys Ser Ala Val Ser Asp
          580                585                590
Asn Phe Ala Asp Ala Ala Tyr Ala Lys Tyr Pro Ser Pro Tyr His Ser
          595                600                605
Arg Asn Ile Arg Ser Asn Leu Glu Gln Arg Tyr Gly Lys Glu Asn Ile
          610                615                620
Thr Ser Ser Thr Val Pro Pro Ser Asn Gly Lys Asn Val Lys Leu Ala
          625                630                635                640
Asp Gln Arg His Pro Lys Thr Gly Val Pro Phe Asp Gly Lys Gly Phe
          645                650                655
Pro Asn Phe Glu Lys His Val Lys Tyr Asp Thr Leu Glu His His His
          660                665                670
His His His
          675

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[2012] &lt;210&gt;35

[2013] &lt;211&gt;2019

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[2015] &lt;213&gt; 人工序列

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	attaaaggaa atatcggtta cattgtccgc ttttccgatac acgggcacga agtccattcc	240
	cccttcgaca accatgcctc acattccgat tctgatgaag ccggtagtcc cgttgacgga	300
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	gggccacagg gggcggtta tcccgtccc aaaggcgcga gggatatata cagctacgac	420
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	ctcaaagact atgccgcagc agccatccgc gattgggcag tccaaaacc caatgccga	840
	caaggcatag aagccgtcag caatatcttt atggcagcca tccccatcaa agggattgga	900
	gctgttcggg gaaaatacgg cttgggcggc atcacggcac atcctatcaa gcggtcgcag	960
	atgggcgcga tcgattgcc gaaagggaaa tccgccgtca gcgacaattt tgccgatgcg	1020
	gcatacgcca aatacccgtc cccttaccat tcccgaata tccgttcaa cttggagcag	1080
	cgttacggca aagaaaacat cacctcctca accgtgccgc cgtcaaacgg caaaaatgtc	1140
	aaactggcag accaacgcca ccgaagaca ggcgtaccgt ttgacggtaa agggtttccg	1200
	aattttgaga agcacgtgaa atatgatac ggatccggag ggggtggtgt gcgcccgac	1260
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          20                   25                   30  
Glu Leu Ala Glu Arg Ser Gly His Ile Gly Leu Gly Lys Ile Gln Ser  
          35                   40                   45  
His Gln Leu Gly Asn Leu Met Ile Gln Gln Ala Ala Ile Lys Gly Asn  
          50                   55                   60  
Ile Gly Tyr Ile Val Arg Phe Ser Asp His Gly His Glu Val His Ser  
65                   70                   75                   80  
Pro Phe Asp Asn His Ala Ser His Ser Asp Ser Asp Glu Ala Gly Ser  
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Pro Val Asp Gly Phe Ser Leu Tyr Arg Ile His Trp Asp Gly Tyr Glu  
          100                   105                   110  
His His Pro Ala Asp Gly Tyr Asp Gly Pro Gln Gly Gly Gly Tyr Pro  
          115                   120                   125  
Ala Pro Lys Gly Ala Arg Asp Ile Tyr Ser Tyr Asp Ile Lys Gly Val  
          130                   135                   140  
Ala Gln Asn Ile Arg Leu Asn Leu Thr Asp Asn Arg Ser Thr Gly Gln

[2029]

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Arg Leu Ala Asp Arg Phe His Asn Ala Gly Ser Met Leu Thr Gln Gly						
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Val Gly Asp Gly Phe Lys Arg Ala Thr Arg Tyr Ser Pro Glu Leu Asp						
	180		185			190
Arg Ser Gly Asn Ala Ala Glu Ala Phe Asn Gly Thr Ala Asp Ile Val						
	195		200			205
Lys Asn Ile Ile Gly Ala Ala Gly Glu Ile Val Gly Ala Gly Asp Ala						
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Val Gln Gly Ile Ser Glu Gly Ser Asn Ile Ala Val Met His Gly Leu						
225		230		235		240
Gly Leu Leu Ser Thr Glu Asn Lys Met Ala Arg Ile Asn Asp Leu Ala						
	245			250		255
Asp Met Ala Gln Leu Lys Asp Tyr Ala Ala Ala Ala Ile Arg Asp Trp						
	260			265		270
Ala Val Gln Asn Pro Asn Ala Ala Gln Gly Ile Glu Ala Val Ser Asn						
	275		280			285
Ile Phe Met Ala Ala Ile Pro Ile Lys Gly Ile Gly Ala Val Arg Gly						
	290		295			300
Lys Tyr Gly Leu Gly Gly Ile Thr Ala His Pro Ile Lys Arg Ser Gln						
305		310		315		320
Met Gly Ala Ile Ala Leu Pro Lys Gly Lys Ser Ala Val Ser Asp Asn						
	325			330		335
Phe Ala Asp Ala Ala Tyr Ala Lys Tyr Pro Ser Pro Tyr His Ser Arg						
	340			345		350
Asn Ile Arg Ser Asn Leu Glu Gln Arg Tyr Gly Lys Glu Asn Ile Thr						
	355		360			365
Ser Ser Thr Val Pro Pro Ser Asn Gly Lys Asn Val Lys Leu Ala Asp						
	370		375			380
Gln Arg His Pro Lys Thr Gly Val Pro Phe Asp Gly Lys Gly Phe Pro						
385		390		395		400
Asn Phe Glu Lys His Val Lys Tyr Asp Thr Gly Ser Gly Gly Gly Gly						
	405			410		415
Val Ala Ala Asp Ile Gly Ala Gly Leu Ala Asp Ala Leu Thr Ala Pro						
	420			425		430
Leu Asp His Lys Asp Lys Gly Leu Gln Ser Leu Thr Leu Asp Gln Ser						
	435		440			445
Val Arg Lys Asn Glu Lys Leu Lys Leu Ala Ala Gln Gly Ala Glu Lys						
	450		455			460
Thr Tyr Gly Asn Gly Asp Ser Leu Asn Thr Gly Lys Leu Lys Asn Asp						
465		470		475		480
Lys Val Ser Arg Phe Asp Phe Ile Arg Gln Ile Glu Val Asp Gly Gln						
	485			490		495
Leu Ile Thr Leu Glu Ser Gly Glu Phe Gln Val Tyr Lys Gln Ser His						
	500			505		510
Ser Ala Leu Thr Ala Phe Gln Thr Glu Gln Ile Gln Asp Ser Glu His						
	515			520		525
Ser Gly Lys Met Val Ala Lys Arg Gln Phe Arg Ile Gly Asp Ile Ala						
	530			535		540
Gly Glu His Thr Ser Phe Asp Lys Leu Pro Glu Gly Gly Arg Ala Thr						
545		550		555		560
Tyr Arg Gly Thr Ala Phe Gly Ser Asp Asp Ala Gly Gly Lys Leu Thr						

[2030]

				565					570					575	
Tyr	Thr	Ile	Asp	Phe	Ala	Ala	Lys	Gln	Gly	Asn	Gly	Lys	Ile	Glu	His
				580					585					590	
Leu	Lys	Ser	Pro	Glu	Leu	Asn	Val	Asp	Leu	Ala	Ala	Ala	Asp	Ile	Lys
				595				600						605	
Pro	Asp	Gly	Lys	Arg	His	Ala	Val	Ile	Ser	Gly	Ser	Val	Leu	Tyr	Asn
				610				615						620	
Gln	Ala	Glu	Lys	Gly	Ser	Tyr	Ser	Leu	Gly	Ile	Phe	Gly	Gly	Lys	Ala
				625				630				635			640
Gln	Glu	Val	Ala	Gly	Ser	Ala	Glu	Val	Lys	Thr	Val	Asn	Gly	Ile	Arg
				645					650						655
His	Ile	Gly	Leu	Ala	Ala	Lys	Gln	Leu	Glu	His	His	His	His	His	His
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	cagacggccg	aagaaacca	acaaaacgtc	gatgccaaag	taaaagctgc	agaaactgca	1860
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           20                   25                   30  
 Glu Leu Ala Glu Arg Ser Gly His Ile Gly Leu Gly Lys Ile Gln Ser  
           35                   40                   45  
 His Gln Leu Gly Asn Leu Met Ile Gln Gln Ala Ala Ile Lys Gly Asn  
           50                   55                   60  
 Ile Gly Tyr Ile Val Arg Phe Ser Asp His Gly His Glu Val His Ser  
 65                   70                   75                   80  
 Pro Phe Asp Asn His Ala Ser His Ser Asp Ser Asp Glu Ala Gly Ser  
           85                   90                   95  
 Pro Val Asp Gly Phe Ser Leu Tyr Arg Ile His Trp Asp Gly Tyr Glu  
           100                   105                   110  
 His His Pro Ala Asp Gly Tyr Asp Gly Pro Gln Gly Gly Gly Tyr Pro  
           115                   120                   125  
 Ala Pro Lys Gly Ala Arg Asp Ile Tyr Ser Tyr Asp Ile Lys Gly Val  
           130                   135                   140  
 Ala Gln Asn Ile Arg Leu Asn Leu Thr Asp Asn Arg Ser Thr Gly Gln  
 145                   150                   155                   160  
 Arg Leu Ala Asp Arg Phe His Asn Ala Gly Ser Met Leu Thr Gln Gly  
           165                   170                   175  
 Val Gly Asp Gly Phe Lys Arg Ala Thr Arg Tyr Ser Pro Glu Leu Asp  
           180                   185                   190  
 Arg Ser Gly Asn Ala Ala Glu Ala Phe Asn Gly Thr Ala Asp Ile Val  
           195                   200                   205  
 Lys Asn Ile Ile Gly Ala Ala Gly Glu Ile Val Gly Ala Gly Asp Ala  
           210                   215                   220  
 Val Gln Gly Ile Ser Glu Gly Ser Asn Ile Ala Val Met His Gly Leu  
 225                   230                   235                   240

[2048]

Gly Leu Leu Ser Thr Glu Asn Lys Met Ala Arg Ile Asn Asp Leu Ala  
 245 250 255  
 Asp Met Ala Gln Leu Lys Asp Tyr Ala Ala Ala Ala Ile Arg Asp Trp  
 260 265 270  
 Ala Val Gln Asn Pro Asn Ala Ala Gln Gly Ile Glu Ala Val Ser Asn  
 275 280 285  
 Ile Phe Met Ala Ala Ile Pro Ile Lys Gly Ile Gly Ala Val Arg Gly  
 290 295 300  
 Lys Tyr Gly Leu Gly Gly Ile Thr Ala His Pro Ile Lys Arg Ser Gln  
 305 310 315 320  
 Met Gly Ala Ile Ala Leu Pro Lys Gly Lys Ser Ala Val Ser Asp Asn  
 325 330 335  
 Phe Ala Asp Ala Ala Tyr Ala Lys Tyr Pro Ser Pro Tyr His Ser Arg  
 340 345 350  
 Asn Ile Arg Ser Asn Leu Glu Gln Arg Tyr Gly Lys Glu Asn Ile Thr  
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 Ser Ser Thr Val Pro Pro Ser Asn Gly Lys Asn Val Lys Leu Ala Asp  
 370 375 380  
 Gln Arg His Pro Lys Thr Gly Val Pro Phe Asp Gly Lys Gly Phe Pro  
 385 390 395 400  
 Asn Phe Glu Lys His Val Lys Tyr Asp Thr Gly Ser Gly Gly Gly Gly  
 405 410 415  
 Ala Thr Asn Asp Asp Asp Val Lys Lys Ala Ala Thr Val Ala Ile Ala  
 420 425 430  
 Ala Ala Tyr Asn Asn Gly Gln Glu Ile Asn Gly Phe Lys Ala Gly Glu  
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 Thr Ile Tyr Asp Ile Asp Glu Asp Gly Thr Ile Thr Lys Lys Asp Ala  
 450 455 460  
 Thr Ala Ala Asp Val Glu Ala Asp Asp Phe Lys Gly Leu Gly Leu Lys  
 465 470 475 480  
 Lys Val Val Thr Asn Leu Thr Lys Thr Val Asn Glu Asn Lys Gln Asn  
 485 490 495  
 Val Asp Ala Lys Val Lys Ala Ala Glu Ser Glu Ile Glu Lys Leu Thr  
 500 505 510  
 Thr Lys Leu Ala Asp Thr Asp Ala Ala Leu Ala Asp Thr Asp Ala Ala  
 515 520 525  
 Leu Asp Ala Thr Thr Asn Ala Leu Asn Lys Leu Gly Glu Asn Ile Thr  
 530 535 540  
 Thr Phe Ala Glu Glu Thr Lys Thr Asn Ile Val Lys Ile Asp Glu Lys  
 545 550 555 560  
 Leu Glu Ala Val Ala Asp Thr Val Asp Lys His Ala Glu Ala Phe Asn  
 565 570 575  
 Asp Ile Ala Asp Ser Leu Asp Glu Thr Asn Thr Lys Ala Asp Glu Ala  
 580 585 590  
 Val Lys Thr Ala Asn Glu Ala Lys Gln Thr Ala Glu Glu Thr Lys Gln  
 595 600 605  
 Asn Val Asp Ala Lys Val Lys Ala Ala Glu Thr Ala Ala Gly Lys Ala  
 610 615 620  
 Glu Ala Ala Ala Gly Thr Ala Asn Thr Ala Ala Asp Lys Ala Glu Ala  
 625 630 635 640  
 Val Ala Ala Lys Val Thr Asp Ile Lys Ala Asp Ile Ala Thr Asn Lys  
 645 650 655

[2049]

Asp Asn Ile Ala Lys Lys Ala Asn Ser Ala Asp Val Tyr Thr Arg Glu  
 660 665 670  
 Glu Ser Asp Ser Lys Phe Val Arg Ile Asp Gly Leu Asn Ala Thr Thr  
 675 680 685  
 Glu Lys Leu Asp Thr Arg Leu Ala Ser Ala Glu Lys Ser Ile Ala Asp  
 690 695 700  
 His Asp Thr Arg Leu Asn Gly Leu Asp Lys Thr Val Ser Asp Leu Arg  
 705 710 715 720  
 Lys Glu Thr Arg Gln Gly Leu Ala Glu Gln Ala Ala Leu Ser Gly Leu  
 725 730 735  
 Phe Gln Pro Tyr Asn Val Gly Arg Phe Asn Val Thr Ala Ala Val Gly  
 740 745 750  
 Gly Tyr Lys Ser Glu Ser Ala Val Ala Ile Gly Thr Gly Phe Arg Phe  
 755 760 765  
 Thr Glu Asn Phe Ala Ala Lys Ala Gly Val Ala Val Gly Thr Ser Ser  
 770 775 780  
 Gly Ser Ser Ala Ala Tyr His Val Gly Val Asn Tyr Glu Trp Leu Glu  
 785 790 795 800  
 His His His His His His  
 805

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Glu	Leu	Ala	Glu	Arg	Ser	Gly	His	Ile	Gly	Leu	Gly	Lys	Ile	Gln	Ser
		35				40						45			
His	Gln	Leu	Gly	Asn	Leu	Met	Ile	Gln	Gln	Ala	Ala	Ile	Lys	Gly	Asn
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Ile	Gly	Tyr	Ile	Val	Arg	Phe	Ser	Asp	His	Gly	His	Glu	Val	His	Ser
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Pro	Phe	Asp	Asn	His	Ala	Ser	His	Ser	Asp	Ser	Asp	Glu	Ala	Gly	Ser
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Pro	Val	Asp	Gly	Phe	Ser	Leu	Tyr	Arg	Ile	His	Trp	Asp	Gly	Tyr	Glu
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Ala	Pro	Lys	Gly	Ala	Arg	Asp	Ile	Tyr	Ser	Tyr	Asp	Ile	Lys	Gly	Val
		130				135					140				
Ala	Gln	Asn	Ile	Arg	Leu	Asn	Leu	Thr	Asp	Asn	Arg	Ser	Thr	Gly	Gln
145					150					155					160
Arg	Leu	Ala	Asp	Arg	Phe	His	Asn	Ala	Gly	Ser	Met	Leu	Thr	Gln	Gly
				165					170					175	
Val	Gly	Asp	Gly	Phe	Lys	Arg	Ala	Thr	Arg	Tyr	Ser	Pro	Glu	Leu	Asp
			180					185					190		
Arg	Ser	Gly	Asn	Ala	Ala	Glu	Ala	Phe	Asn	Gly	Thr	Ala	Asp	Ile	Val
			195				200						205		

[2067]

Lys Asn Ile Ile Gly Ala Ala Gly Glu Ile Val Gly Ala Gly Asp Ala  
 210 215 220  
 Val Gln Gly Ile Ser Glu Gly Ser Asn Ile Ala Val Met His Gly Leu  
 225 230 235 240  
 Gly Leu Leu Ser Thr Glu Asn Lys Met Ala Arg Ile Asn Asp Leu Ala  
 245 250 255  
 Asp Met Ala Gln Leu Lys Asp Tyr Ala Ala Ala Ile Arg Asp Trp  
 260 265 270  
 Ala Val Gln Asn Pro Asn Ala Ala Gln Gly Ile Glu Ala Val Ser Asn  
 275 280 285  
 Ile Phe Met Ala Ala Ile Pro Ile Lys Gly Ile Gly Ala Val Arg Gly  
 290 295 300  
 Lys Tyr Gly Leu Gly Gly Ile Thr Ala His Pro Ile Lys Arg Ser Gln  
 305 310 315 320  
 Met Gly Ala Ile Ala Leu Pro Lys Gly Lys Ser Ala Val Ser Asp Asn  
 325 330 335  
 Phe Ala Asp Ala Ala Tyr Ala Lys Tyr Pro Ser Pro Tyr His Ser Arg  
 340 345 350  
 Asn Ile Arg Ser Asn Leu Glu Gln Arg Tyr Gly Lys Glu Asn Ile Thr  
 355 360 365  
 Ser Ser Thr Val Pro Pro Ser Asn Gly Lys Asn Val Lys Leu Ala Asp  
 370 375 380  
 Gln Arg His Pro Lys Thr Gly Val Pro Phe Asp Gly Lys Gly Phe Pro  
 385 390 395 400  
 Asn Phe Glu Lys His Val Lys Tyr Asp Thr Gly Ser Gly Gly Gly  
 405 410 415  
 Ala Thr Asn Asp Asp Asp Val Lys Lys Ala Ala Thr Val Ala Ile Ala  
 420 425 430  
 Ala Ala Tyr Asn Asn Gly Gln Glu Ile Asn Gly Phe Lys Ala Gly Glu  
 435 440 445  
 Thr Ile Tyr Asp Ile Asp Glu Asp Gly Thr Ile Thr Lys Lys Asp Ala  
 450 455 460  
 Thr Ala Ala Asp Val Glu Ala Asp Asp Phe Lys Gly Leu Gly Leu Lys  
 465 470 475 480  
 Lys Val Val Thr Asn Leu Thr Lys Thr Val Asn Glu Asn Lys Gln Asn  
 485 490 495  
 Val Asp Ala Lys Val Lys Ala Ala Glu Ser Glu Ile Glu Lys Leu Thr  
 500 505 510  
 Thr Lys Leu Ala Asp Thr Asp Ala Ala Leu Ala Asp Thr Asp Ala Ala  
 515 520 525  
 Leu Asp Ala Thr Thr Asn Ala Leu Asn Lys Leu Gly Glu Asn Ile Thr  
 530 535 540  
 Thr Phe Ala Glu Glu Thr Lys Thr Asn Ile Val Lys Ile Asp Glu Lys  
 545 550 555 560  
 Leu Glu Ala Val Ala Asp Thr Val Asp Lys His Ala Glu Ala Phe Asn  
 565 570 575  
 Asp Ile Ala Asp Ser Leu Asp Glu Thr Asn Thr Lys Ala Asp Glu Ala  
 580 585 590  
 Val Lys Thr Ala Asn Glu Ala Lys Gln Thr Ala Glu Glu Thr Lys Gln  
 595 600 605  
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[2068]

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660 665 670  
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[2086]

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Thr Glu Lys Leu Asp Thr Arg Leu Ala Ser Ala Glu Lys Ser Ile Ala		270
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Asp His Asp Thr Arg Leu Asn Gly Leu Asp Lys Thr Val Ser Asp Leu		285
290	295	300
Arg Lys Glu Thr Arg Gln Gly Leu Ala Glu Gln Ala Ala Leu Ser Gly		
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Leu Phe Gln Pro Tyr Asn Val Gly Arg Phe Asn Val Thr Ala Ala Val		
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Gly Gly Tyr Lys Ser Glu Ser Ala Val Ala Ile Gly Thr Gly Phe Arg		335
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Phe Thr Glu Asn Phe Ala Ala Lys Ala Gly Val Ala Val Gly Thr Ser		350
	355	360
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Ser Gly Gly Gly Gly Ser Asp Leu Ala Asn Asp Ser Phe Ile Arg Gln		
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Val Leu Asp Arg Gln His Phe Glu Pro Asp Gly Lys Tyr His Leu Phe		
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Gly Ser Arg Gly Glu Leu Ala Glu Arg Ser Gly His Ile Gly Leu Gly		415
	420	425
Lys Ile Gln Ser His Gln Leu Gly Asn Leu Met Ile Gln Gln Ala Ala		430
435	440	445
Ile Lys Gly Asn Ile Gly Tyr Ile Val Arg Phe Ser Asp His Gly His		
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Glu Val His Ser Pro Phe Asp Asn His Ala Ser His Ser Asp Ser Asp		
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Glu Ala Gly Ser Pro Val Asp Gly Phe Ser Leu Tyr Arg Ile His Trp		
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Ile Lys Gly Val Ala Gln Asn Ile Arg Leu Asn Leu Thr Asp Asn Arg		
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Leu Thr Gln Gly Val Gly Asp Gly Phe Lys Arg Ala Thr Arg Tyr Ser		560
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Pro Glu Leu Asp Arg Ser Gly Asn Ala Ala Glu Ala Phe Asn Gly Thr		575
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Ala Gly Asp Ala Val Gln Gly Ile Ser Glu Gly Ser Asn Ile Ala Val		
610	615	620
Met His Gly Leu Gly Leu Leu Ser Thr Glu Asn Lys Met Ala Arg Ile		

[2087]

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Ile Arg Asp Trp Ala Val Gln Asn Pro Asn Ala Ala Gln Gly Ile Glu						
		660		665		670
Ala Val Ser Asn Ile Phe Met Ala Ala Ile Pro Ile Lys Gly Ile Gly						
		675		680		685
Ala Val Arg Gly Lys Tyr Gly Leu Gly Gly Ile Thr Ala His Pro Ile						
		690		695		700
Lys Arg Ser Gln Met Gly Ala Ile Ala Leu Pro Lys Gly Lys Ser Ala						
		705		710		715
Val Ser Asp Asn Phe Ala Asp Ala Ala Tyr Ala Lys Tyr Pro Ser Pro						
		725		730		735
Tyr His Ser Arg Asn Ile Arg Ser Asn Leu Glu Gln Arg Tyr Gly Lys						
		740		745		750
Glu Asn Ile Thr Ser Ser Thr Val Pro Pro Ser Asn Gly Lys Asn Val						
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Lys Leu Ala Asp Gln Arg His Pro Lys Thr Gly Val Pro Phe Asp Gly						
		770		775		780
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 210 215 220

[2105]

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 260 265 270  
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[2115]



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caccaccacc actga 4335

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- [2116] <210>46
- [2117] <211>1444
- [2118] <212>PRT
- [2119] <213> 人工序列
- [2120] <220>
- [2121] <223>961-983
- [2122] <400>46
- [2123]

Met Ala Thr Asn Asp Asp Asp Val Lys Lys Ala Ala Thr Val Ala Ile  
1                                   5                                   10                                   15  
Ala Ala Ala Tyr Asn Asn Gly Gln Glu Ile Asn Gly Phe Lys Ala Gly  
                                  20                                   25                                   30  
Glu Thr Ile Tyr Asp Ile Asp Glu Asp Gly Thr Ile Thr Lys Lys Asp  
                                  35                                   40                                   45  
Ala Thr Ala Ala Asp Val Glu Ala Asp Asp Phe Lys Gly Leu Gly Leu  
                                  50                                   55                                   60  
Lys Lys Val Val Thr Asn Leu Thr Lys Thr Val Asn Glu Asn Lys Gln

[2124]

65		70		75		80
Asn Val Asp Ala Lys	Val Lys Ala Ala	Glu Ser Glu Ile	Glu Lys Leu			
	85		90		95	
Thr Thr Lys Leu Ala	Asp Thr Asp Ala	Ala Leu Ala Asp	Thr Asp Ala			
	100		105		110	
Ala Leu Asp Ala Thr	Thr Asn Ala Leu	Asn Lys Leu Gly	Glu Asn Ile			
	115		120		125	
Thr Thr Phe Ala Glu	Glu Thr Lys Thr	Asn Ile Val Lys	Ile Asp Glu			
	130		135		140	
Lys Leu Glu Ala Val	Ala Asp Thr Val	Asp Lys His Ala	Glu Ala Phe			
	145		150		155	
Asn Asp Ile Ala Asp	Ser Leu Asp Glu	Thr Asn Thr Lys	Ala Asp Glu			
	165		170		175	
Ala Val Lys Thr Ala	Asn Glu Ala Lys	Gln Thr Ala Glu	Glu Thr Lys			
	180		185		190	
Gln Asn Val Asp Ala	Lys Val Lys Ala	Ala Glu Thr Ala	Ala Gly Lys			
	195		200		205	
Ala Glu Ala Ala Ala	Gly Thr Ala Asn	Thr Ala Ala Asp	Lys Ala Glu			
	210		215		220	
Ala Val Ala Ala Lys	Val Thr Asp Ile	Lys Ala Asp Ile	Ala Thr Asn			
	225		230		235	
Lys Asp Asn Ile Ala	Lys Lys Ala Asn	Ser Ala Asp Val	Tyr Thr Arg			
	245		250		255	
Glu Glu Ser Asp Ser	Lys Phe Val Arg	Ile Asp Gly Leu	Asn Ala Thr			
	260		265		270	
Thr Glu Lys Leu Asp	Thr Arg Leu Ala	Ser Ala Glu Lys	Ser Ile Ala			
	275		280		285	
Asp His Asp Thr Arg	Leu Asn Gly Leu	Asp Lys Thr Val	Ser Asp Leu			
	290		295		300	
Arg Lys Glu Thr Arg	Gln Gly Leu Ala	Glu Gln Ala Ala	Leu Ser Gly			
	305		310		315	
Leu Phe Gln Pro Tyr	Asn Val Gly Arg	Phe Asn Val Thr	Ala Ala Val			
	325		330		335	
Gly Gly Tyr Lys Ser	Glu Ser Ala Val	Ala Ile Gly Thr	Gly Phe Arg			
	340		345		350	
Phe Thr Glu Asn Phe	Ala Ala Lys Ala	Gly Val Ala Val	Gly Thr Ser			
	355		360		365	
Ser Gly Ser Ser Ala	Ala Tyr His Val	Gly Val Asn Tyr	Glu Trp Gly			
	370		375		380	
Ser Gly Gly Gly Gly	Thr Ser Ala Pro	Asp Phe Asn Ala	Gly Gly Thr			
	385		390		395	
Gly Ile Gly Ser Asn	Ser Arg Ala Thr	Thr Ala Lys Ser	Ala Ala Val			
	405		410		415	
Ser Tyr Ala Gly Ile	Lys Asn Glu Met	Cys Lys Asp Arg	Ser Met Leu			
	420		425		430	
Cys Ala Gly Arg Asp	Asp Val Ala Val	Thr Asp Arg Asp	Ala Lys Ile			
	435		440		445	
Asn Ala Pro Pro Pro	Asn Leu His Thr	Gly Asp Phe Pro	Asn Pro Asn			
	450		455		460	
Asp Ala Tyr Lys Asn	Leu Ile Asn Leu	Lys Pro Ala Ile	Glu Ala Gly			
	465		470		475	
Tyr Thr Gly Arg Gly	Val Glu Val Gly	Ile Val Asp Thr	Gly Glu Ser			

[2125]

				485					490					495	
Val	Gly	Ser	Ile	Ser	Phe	Pro	Glu	Leu	Tyr	Gly	Arg	Lys	Glu	His	Gly
				500					505					510	
Tyr	Asn	Glu	Asn	Tyr	Lys	Asn	Tyr	Thr	Ala	Tyr	Met	Arg	Lys	Glu	Ala
				515				520						525	
Pro	Glu	Asp	Gly	Gly	Gly	Lys	Asp	Ile	Glu	Ala	Ser	Phe	Asp	Asp	Glu
				530				535						540	
Ala	Val	Ile	Glu	Thr	Glu	Ala	Lys	Pro	Thr	Asp	Ile	Arg	His	Val	Lys
				545				550				555			560
Glu	Ile	Gly	His	Ile	Asp	Leu	Val	Ser	His	Ile	Ile	Gly	Gly	Arg	Ser
				565					570						575
Val	Asp	Gly	Arg	Pro	Ala	Gly	Gly	Ile	Ala	Pro	Asp	Ala	Thr	Leu	His
				580					585						590
Ile	Met	Asn	Thr	Asn	Asp	Glu	Thr	Lys	Asn	Glu	Met	Met	Val	Ala	Ala
				595				600							605
Ile	Arg	Asn	Ala	Trp	Val	Lys	Leu	Gly	Glu	Arg	Gly	Val	Arg	Ile	Val
				610				615							620
Asn	Asn	Ser	Phe	Gly	Thr	Thr	Ser	Arg	Ala	Gly	Thr	Ala	Asp	Leu	Phe
				625					630						635
Gln	Ile	Ala	Asn	Ser	Glu	Glu	Gln	Tyr	Arg	Gln	Ala	Leu	Leu	Asp	Tyr
				645											650
Ser	Gly	Gly	Asp	Lys	Thr	Asp	Glu	Gly	Ile	Arg	Leu	Met	Gln	Gln	Ser
				660					665						670
Asp	Tyr	Gly	Asn	Leu	Ser	Tyr	His	Ile	Arg	Asn	Lys	Asn	Met	Leu	Phe
				675				680							685
Ile	Phe	Ser	Thr	Gly	Asn	Asp	Ala	Gln	Ala	Gln	Pro	Asn	Thr	Tyr	Ala
				690				695							700
Leu	Leu	Pro	Phe	Tyr	Glu	Lys	Asp	Ala	Gln	Lys	Gly	Ile	Ile	Thr	Val
				705											710
Ala	Gly	Val	Asp	Arg	Ser	Gly	Glu	Lys	Phe	Lys	Arg	Glu	Met	Tyr	Gly
				715											720
Glu	Pro	Gly	Thr	Glu	Pro	Leu	Glu	Tyr	Gly	Ser	Asn	His	Cys	Gly	Ile
				725											730
Thr	Ala	Met	Trp	Cys	Leu	Ser	Ala	Pro	Tyr	Glu	Ala	Ser	Val	Arg	Phe
				735											740
Thr	Arg	Thr	Asn	Pro	Ile	Gln	Ile	Ala	Gly	Thr	Ser	Phe	Ser	Ala	Pro
				745											750
Ile	Val	Thr	Gly	Thr	Ala	Ala	Leu	Leu	Leu	Gln	Lys	Tyr	Pro	Trp	Met
				755											760
Ser	Asn	Asp	Asn	Leu	Arg	Thr	Thr	Leu	Leu	Thr	Thr	Ala	Gln	Asp	Ile
				765											770
Gly	Ala	Val	Gly	Val	Asp	Ser	Lys	Phe	Gly	Trp	Gly	Leu	Leu	Asp	Ala
				775											780
Gly	Lys	Ala	Met	Asn	Gly	Pro	Ala	Ser	Phe	Pro	Phe	Gly	Asp	Phe	Thr
				785											790
Ala	Asp	Thr	Lys	Gly	Thr	Ser	Asp	Ile	Ala	Tyr	Ser	Phe	Arg	Asn	Asp
				795											800
Ile	Ser	Gly	Thr	Gly	Gly	Leu	Ile	Lys	Lys	Gly	Gly	Ser	Gln	Leu	Gln
				805											810
Leu	His	Gly	Asn	Asn	Thr	Tyr	Thr	Gly	Lys	Thr	Ile	Ile	Glu	Gly	Gly
				815											820
Ser	Leu	Val	Leu	Tyr	Gly	Asn	Asn	Lys	Ser	Asp	Met	Arg	Val	Glu	Thr
				825											830
				835											840
				845											850
				855											860
				865											870
				875											880
				885											890
				895											900

[2126]

	900		905		910
Lys Gly Ala Leu Ile Tyr Asn Gly Ala Ala Ser Gly Gly Ser Leu Asn					
	915		920		925
Ser Asp Gly Ile Val Tyr Leu Ala Asp Thr Asp Gln Ser Gly Ala Asn					
	930		935		940
Glu Thr Val His Ile Lys Gly Ser Leu Gln Leu Asp Gly Lys Gly Thr					
945		950		955	960
Leu Tyr Thr Arg Leu Gly Lys Leu Leu Lys Val Asp Gly Thr Ala Ile					
	965		970		975
Ile Gly Gly Lys Leu Tyr Met Ser Ala Arg Gly Lys Gly Ala Gly Tyr					
	980		985		990
Leu Asn Ser Thr Gly Arg Arg Val Pro Phe Leu Ser Ala Ala Lys Ile					
	995		1000		1005
Gly Gln Asp Tyr Ser Phe Phe Thr Asn Ile Glu Thr Asp Gly Gly Leu					
	1010		1015		1020
Leu Ala Ser Leu Asp Ser Val Glu Lys Thr Ala Gly Ser Glu Gly Asp					
1025		1030		1035	1040
Thr Leu Ser Tyr Tyr Val Arg Arg Gly Asn Ala Ala Arg Thr Ala Ser					
	1045		1050		1055
Ala Ala Ala His Ser Ala Pro Ala Gly Leu Lys His Ala Val Glu Gln					
	1060		1065		1070
Gly Gly Ser Asn Leu Glu Asn Leu Met Val Glu Leu Asp Ala Ser Glu					
	1075		1080		1085
Ser Ser Ala Thr Pro Glu Thr Val Glu Thr Ala Ala Ala Asp Arg Thr					
	1090		1095		1100
Asp Met Pro Gly Ile Arg Pro Tyr Gly Ala Thr Phe Arg Ala Ala Ala					
1105		1110		1115	1120
Ala Val Gln His Ala Asn Ala Ala Asp Gly Val Arg Ile Phe Asn Ser					
	1125		1130		1135
Leu Ala Ala Thr Val Tyr Ala Asp Ser Thr Ala Ala His Ala Asp Met					
	1140		1145		1150
Gln Gly Arg Arg Leu Lys Ala Val Ser Asp Gly Leu Asp His Asn Gly					
	1155		1160		1165
Thr Gly Leu Arg Val Ile Ala Gln Thr Gln Gln Asp Gly Gly Thr Trp					
	1170		1175		1180
Glu Gln Gly Gly Val Glu Gly Lys Met Arg Gly Ser Thr Gln Thr Val					
1185		1190		1195	1200
Gly Ile Ala Ala Lys Thr Gly Glu Asn Thr Thr Ala Ala Ala Thr Leu					
	1205		1210		1215
Gly Met Gly Arg Ser Thr Trp Ser Glu Asn Ser Ala Asn Ala Lys Thr					
	1220		1225		1230
Asp Ser Ile Ser Leu Phe Ala Gly Ile Arg His Asp Ala Gly Asp Ile					
	1235		1240		1245
Gly Tyr Leu Lys Gly Leu Phe Ser Tyr Gly Arg Tyr Lys Asn Ser Ile					
	1250		1255		1260
Ser Arg Ser Thr Gly Ala Asp Glu His Ala Glu Gly Ser Val Asn Gly					
1265		1270		1275	1280
Thr Leu Met Gln Leu Gly Ala Leu Gly Gly Val Asn Val Pro Phe Ala					
	1285		1290		1295
Ala Thr Gly Asp Leu Thr Val Glu Gly Gly Leu Arg Tyr Asp Leu Leu					
	1300		1305		1310
Lys Gln Asp Ala Phe Ala Glu Lys Gly Ser Ala Leu Gly Trp Ser Gly					

[2127]

1315	1320	1325	
Asn Ser Leu Thr Glu Gly Thr Leu Val Gly Leu Ala Gly Leu Lys Leu			
1330	1335	1340	
Ser Gln Pro Leu Ser Asp Lys Ala Val Leu Phe Ala Thr Ala Gly Val			
1345	1350	1355	1360
Glu Arg Asp Leu Asn Gly Arg Asp Tyr Thr Val Thr Gly Gly Phe Thr			
1365	1370	1375	
Gly Ala Thr Ala Ala Thr Gly Lys Thr Gly Ala Arg Asn Met Pro His			
1380	1385	1390	
Thr Arg Leu Val Ala Gly Leu Gly Ala Asp Val Glu Phe Gly Asn Gly			
1395	1400	1405	
Trp Asn Gly Leu Ala Arg Tyr Ser Tyr Ala Gly Ser Lys Gln Tyr Gly			
1410	1415	1420	
Asn His Ser Gly Arg Val Gly Val Gly Tyr Arg Phe Leu Glu His His			
1425	1430	1435	1440
His His His His			

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- [2129] <211>2256
- [2130] <212>DNA
- [2131] <213> 人工序列
- [2132] <220>
- [2133] <223>961c-ORF46. 1
- [2134] <400>47
- [2135]

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ggtctgggtc tgaaaaaagt cgtgactaac ctgacaaaaa ccgtcaatga aaacaaacia 240
aacgtcgatg ccaaagtaaa agctgcagaa tctgaaatag aaaagttaac aaccaagtta 300
gcagacactg atgccgcttt agcagatact gatgccgctc tggatgcaac caccaacgcc 360
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[2136]

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acctcctcaa ccgtgccgcc gtcaaacggc aaaaatgtca aactggcaga ccaacgccac 2160
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[2137] &lt;210&gt;48

[2138] &lt;211&gt;751

[2139] &lt;212&gt;PRT

[2140] &lt;213&gt; 人工序列

[2141] &lt;220&gt;

[2142] &lt;223&gt;961c-ORF46.1

[2143] &lt;400&gt;48

[2144]

Met Ala Thr Asn Asp Asp Asp Val Lys Lys Ala Ala Thr Val Ala Ile  
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 Ala Ala Ala Tyr Asn Asn Gly Gln Glu Ile Asn Gly Phe Lys Ala Gly  
                                   20                                    25                                    30  
 Glu Thr Ile Tyr Asp Ile Asp Glu Asp Gly Thr Ile Thr Lys Lys Asp  
                                   35                                    40                                    45  
 Ala Thr Ala Ala Asp Val Glu Ala Asp Asp Phe Lys Gly Leu Gly Leu  
                                   50                                    55                                    60  
 Lys Lys Val Val Thr Asn Leu Thr Lys Thr Val Asn Glu Asn Lys Gln  
 65                                    70                                    75                                    80  
 Asn Val Asp Ala Lys Val Lys Ala Ala Glu Ser Glu Ile Glu Lys Leu  
                                   85                                    90                                    95  
 Thr Thr Lys Leu Ala Asp Thr Asp Ala Ala Leu Ala Asp Thr Asp Ala  
                                   100                                    105                                    110  
 Ala Leu Asp Ala Thr Thr Asn Ala Leu Asn Lys Leu Gly Glu Asn Ile  
                                   115                                    120                                    125  
 Thr Thr Phe Ala Glu Glu Thr Lys Thr Asn Ile Val Lys Ile Asp Glu  
                                   130                                    135                                    140  
 Lys Leu Glu Ala Val Ala Asp Thr Val Asp Lys His Ala Glu Ala Phe  
 145                                    150                                    155                                    160  
 Asn Asp Ile Ala Asp Ser Leu Asp Glu Thr Asn Thr Lys Ala Asp Glu  
                                   165                                    170                                    175  
 Ala Val Lys Thr Ala Asn Glu Ala Lys Gln Thr Ala Glu Glu Thr Lys  
                                   180                                    185                                    190  
 Gln Asn Val Asp Ala Lys Val Lys Ala Ala Glu Thr Ala Ala Gly Lys  
                                   195                                    200                                    205  
 Ala Glu Ala Ala Ala Gly Thr Ala Asn Thr Ala Ala Asp Lys Ala Glu  
                                   210                                    215                                    220  
 Ala Val Ala Ala Lys Val Thr Asp Ile Lys Ala Asp Ile Ala Thr Asn

[2145]



225 230 235 240  
Lys Asp Asn Ile Ala Lys Lys Ala Asn Ser Ala Asp Val Tyr Thr Arg  
245 250 255  
Glu Glu Ser Asp Ser Lys Phe Val Arg Ile Asp Gly Leu Asn Ala Thr  
260 265 270  
Thr Glu Lys Leu Asp Thr Arg Leu Ala Ser Ala Glu Lys Ser Ile Ala  
275 280 285  
Asp His Asp Thr Arg Leu Asn Gly Leu Asp Lys Thr Val Ser Asp Leu  
290 295 300  
Arg Lys Glu Thr Arg Gln Gly Leu Ala Glu Gln Ala Ala Leu Ser Gly  
305 310 315 320  
Leu Phe Gln Pro Tyr Asn Val Gly Gly Ser Gly Gly Gly Ser Asp  
325 330 335  
Leu Ala Asn Asp Ser Phe Ile Arg Gln Val Leu Asp Arg Gln His Phe  
340 345 350  
Glu Pro Asp Gly Lys Tyr His Leu Phe Gly Ser Arg Gly Glu Leu Ala  
355 360 365  
Glu Arg Ser Gly His Ile Gly Leu Gly Lys Ile Gln Ser His Gln Leu  
370 375 380  
Gly Asn Leu Met Ile Gln Gln Ala Ala Ile Lys Gly Asn Ile Gly Tyr  
385 390 395 400  
Ile Val Arg Phe Ser Asp His Gly His Glu Val His Ser Pro Phe Asp  
405 410 415  
Asn His Ala Ser His Ser Asp Ser Asp Glu Ala Gly Ser Pro Val Asp  
420 425 430  
Gly Phe Ser Leu Tyr Arg Ile His Trp Asp Gly Tyr Glu His His Pro  
435 440 445  
Ala Asp Gly Tyr Asp Gly Pro Gln Gly Gly Tyr Pro Ala Pro Lys  
450 455 460  
Gly Ala Arg Asp Ile Tyr Ser Tyr Asp Ile Lys Gly Val Ala Gln Asn  
465 470 475 480  
Ile Arg Leu Asn Leu Thr Asp Asn Arg Ser Thr Gly Gln Arg Leu Ala  
485 490 495  
Asp Arg Phe His Asn Ala Gly Ser Met Leu Thr Gln Gly Val Gly Asp  
500 505 510  
Gly Phe Lys Arg Ala Thr Arg Tyr Ser Pro Glu Leu Asp Arg Ser Gly  
515 520 525  
Asn Ala Ala Glu Ala Phe Asn Gly Thr Ala Asp Ile Val Lys Asn Ile  
530 535 540  
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545 550 555 560  
Ile Ser Glu Gly Ser Asn Ile Ala Val Met His Gly Leu Gly Leu Leu  
565 570 575  
Ser Thr Glu Asn Lys Met Ala Arg Ile Asn Asp Leu Ala Asp Met Ala  
580 585 590  
Gln Leu Lys Asp Tyr Ala Ala Ala Ala Ile Arg Asp Trp Ala Val Gln  
595 600 605  
Asn Pro Asn Ala Ala Gln Gly Ile Glu Ala Val Ser Asn Ile Phe Met  
610 615 620  
Ala Ala Ile Pro Ile Lys Gly Ile Gly Ala Val Arg Gly Lys Tyr Gly  
625 630 635 640  
Leu Gly Gly Ile Thr Ala His Pro Ile Lys Arg Ser Gln Met Gly Ala

[2146]

				645					650					655	
Ile	Ala	Leu	Pro	Lys	Gly	Lys	Ser	Ala	Val	Ser	Asp	Asn	Phe	Ala	Asp
				660					665					670	
Ala	Ala	Tyr	Ala	Lys	Tyr	Pro	Ser	Pro	Tyr	His	Ser	Arg	Asn	Ile	Arg
		675						680						685	
Ser	Asn	Leu	Glu	Gln	Arg	Tyr	Gly	Lys	Glu	Asn	Ile	Thr	Ser	Ser	Thr
		690						695						700	
Val	Pro	Pro	Ser	Asn	Gly	Lys	Asn	Val	Lys	Leu	Ala	Asp	Gln	Arg	His
		705				710						715			720
Pro	Lys	Thr	Gly	Val	Pro	Phe	Asp	Gly	Lys	Gly	Phe	Pro	Asn	Phe	Glu
				725								730			735
Lys	His	Val	Lys	Tyr	Asp	Thr	Leu	Glu	His	His	His	His	His	His	His
				740					745						750

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	gacggcacia ttaccaaaaa agacgcaact gcagccgatg ttgaagccga cgactttaa	180
	ggtctgggtc tgaaaaaagt cgtgactaac ctgacaaaaa ccgtcaatga aaacaaacia	240
	aacgtcgatg ccaaagtaaa agctgcagaa tctgaaatag aaaagttaac aaccaagtta	300
	gcagacactg atgccgcttt agcagatact gatgccgctc tggatgcaac caccaacgcc	360
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 Gln Asn Val Asp Ala Lys Val Lys Ala Ala Glu Thr Ala Ala Gly Lys  
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 225 230 235 240  
 Lys Asp Asn Ile Ala Lys Lys Ala Asn Ser Ala Asp Val Tyr Thr Arg  
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Lys Asn Glu Lys Leu Lys Leu Ala Ala Gln Gly Ala Glu Lys Thr Tyr					
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Gly Asn Gly Asp Ser Leu Asn Thr Gly Lys Leu Lys Asn Asp Lys Val					
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Ser Arg Phe Asp Phe Ile Arg Gln Ile Glu Val Asp Gly Gln Leu Ile					
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Thr Leu Glu Ser Gly Glu Phe Gln Val Tyr Lys Gln Ser His Ser Ala					
	420		425		430
Leu Thr Ala Phe Gln Thr Glu Gln Ile Gln Asp Ser Glu His Ser Gly					
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Ser Pro Glu Leu Asn Val Asp Leu Ala Ala Ala Asp Ile Lys Pro Asp					
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Gly Lys Arg His Ala Val Ile Ser Gly Ser Val Leu Tyr Asn Gln Ala					
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Glu Lys Gly Ser Tyr Ser Leu Gly Ile Phe Gly Gly Lys Ala Gln Glu					
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 Asn Val Asp Ala Lys Val Lys Ala Ala Glu Ser Glu Ile Glu Lys Leu  
 85 90 95  
 Thr Thr Lys Leu Ala Asp Thr Asp Ala Ala Leu Ala Asp Thr Asp Ala  
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 Ala Leu Asp Ala Thr Thr Asn Ala Leu Asn Lys Leu Gly Glu Asn Ile  
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 Lys Leu Glu Ala Val Ala Asp Thr Val Asp Lys His Ala Glu Ala Phe  
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[2183]



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 785 790 795 800  
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 Gly Ala Ala Ser Gly Gly Ser Leu Asn Ser Asp Gly Ile Val Tyr Leu  
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 885 890 895  
 Scr Leu Gln Leu Asp Gly Lys Gly Thr Leu Tyr Thr Arg Leu Gly Lys  
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 Val Pro Phe Leu Ser Ala Ala Lys Ile Gly Gln Asp Tyr Scr Phe Phe  
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 Arg Gly Asn Ala Ala Arg Thr Ala Ser Ala Ala Ala His Ser Ala Pro  
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 Ser Glu Asn Ser Ala Asn Ala Lys Thr Asp Ser Ile Ser Leu Phe Ala  
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 Gly Ile Arg His Asp Ala Gly Asp Ile Gly Tyr Leu Lys Gly Leu Phe  
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Ala Ala Thr Val Ala Ile Ala Ala Ala Tyr Asn Asn Gly Gln Glu Ile  
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Asn Gly Phe Lys Ala Gly Glu Thr Ile Tyr Asp Ile Asp Glu Asp Gly

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Lys Gly Val Ala	Gln Asn Ile Arg Leu Asn Leu Thr Asp Asn Arg Ser					
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Thr Gly Gln Arg	Leu Ala Asp Arg Phe His Asn Ala Gly Ser Met Leu					
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Thr Gln Gly Val	Gly Asp Gly Phe Lys Arg Ala Thr Arg Tyr Ser Pro					
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Glu Leu Asp Arg	Ser Gly Asn Ala Ala Glu Ala Phe Asn Gly Thr Ala					
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Asp Ile Val Lys	Asn Ile Ile Gly Ala Ala Gly Glu Ile Val Gly Ala					
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Gly Asp Ala Val	Gln Gly Ile Ser Glu Gly Ser Asn Ile Ala Val Met					
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His Gly Leu Gly	Leu Leu Ser Thr Glu Asn Lys Met Ala Arg Ile Asn					
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Asp Leu Ala Asp	Met Ala Gln Leu Lys Asp Tyr Ala Ala Ala Ala Ile					
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Arg Asp Trp Ala	Val Gln Asn Pro Asn Ala Ala Gln Gly Ile Glu Ala					
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Val Ser Asn Ile	Phe Met Ala Ala Ile Pro Ile Lys Gly Ile Gly Ala					
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Val Arg Gly Lys	Tyr Gly Leu Gly Gly Ile Thr Ala His Pro Ile Lys					
		660		665		670
Arg Ser Gln Met	Gly Ala Ile Ala Leu Pro Lys Gly Lys Ser Ala Val					
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Ser Asp Asn Phe	Ala Asp Ala Ala Tyr Ala Lys Tyr Pro Ser Pro Tyr					
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His Ser Arg Asn	Ile Arg Ser Asn Leu Glu Gln Arg Tyr Gly Lys Glu					
		705		710		715
Asn Ile Thr Ser	Ser Thr Val Pro Pro Ser Asn Gly Lys Asn Val Lys					
		725		730		735
Leu Ala Asp Gln	Arg His Pro Lys Thr Gly Val Pro Phe Asp Gly Lys					
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Gly Phe Pro Asn	Phe Glu Lys His Val Lys Tyr Asp Thr					
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Phe	Lys	Gly	Leu	Gly	Leu	Lys	Lys	Val	Val	Thr	Asn	Leu	Thr	Lys	Thr
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Val	Asn	Glu	Asn	Lys	Gln	Asn	Val	Asp	Ala	Lys	Val	Lys	Ala	Ala	Glu
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 165 170 175  
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 Asn Thr Lys Ala Asp Glu Ala Val Lys Thr Ala Asn Glu Ala Lys Gln  
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 355 360 365  
 Leu Thr Ala Pro Leu Asp His Lys Asp Lys Gly Leu Gln Ser Leu Thr  
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 385 390 395 400  
 Gly Ala Glu Lys Thr Tyr Gly Asn Gly Asp Ser Leu Asn Thr Gly Lys  
 405 410 415  
 Leu Lys Asn Asp Lys Val Ser Arg Phe Asp Phe Ile Arg Gln Ile Glu  
 420 425 430  
 Val Asp Gly Gln Leu Ile Thr Leu Glu Ser Gly Glu Phe Gln Val Tyr  
 435 440 445  
 Lys Gln Ser His Ser Ala Leu Thr Ala Phe Gln Thr Glu Gln Ile Gln  
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 Asp Ser Glu His Ser Gly Lys Met Val Ala Lys Arg Gln Phe Arg Ile  
 465 470 475 480  
 Gly Asp Ile Ala Gly Glu His Thr Ser Phe Asp Lys Leu Pro Glu Gly  
 485 490 495  
 Gly Arg Ala Thr Tyr Arg Gly Thr Ala Phe Gly Ser Asp Asp Ala Gly  
 500 505 510  
 Gly Lys Leu Thr Tyr Thr Ile Asp Phe Ala Ala Lys Gln Gly Asn Gly  
 515 520 525  
 Lys Ile Glu His Leu Lys Ser Pro Glu Leu Asn Val Asp Leu Ala Ala  
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[2223]



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[2241]







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	885	890
Asp Gly Ile Val Tyr	Leu Ala Asp Thr Asp Gln Ser Gly Ala Asn Glu	
	900	905
Thr Val His Ile Lys	Gly Ser Leu Gln Leu Asp Gly Lys Gly Thr Leu	
	915	920
Tyr Thr Arg Leu Gly	Lys Leu Leu Lys Val Asp Gly Thr Ala Ile Ile	
	930	935
Gly Gly Lys Leu Tyr	Met Ser Ala Arg Gly Lys Gly Ala Gly Tyr Leu	
	945	950
Asn Ser Thr Gly Arg	Arg Val Pro Phe Leu Ser Ala Ala Lys Ile Gly	
	965	970
Gln Asp Tyr Ser Phe	Phe Thr Asn Ile Glu Thr Asp Gly Gly Leu Leu	
	980	985
Ala Ser Leu Asp Ser	Val Glu Lys Thr Ala Gly Ser Glu Gly Asp Thr	
	995	1000
Leu Ser Tyr Tyr Val	Arg Arg Gly Asn Ala Ala Arg Thr Ala Ser Ala	
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Ala Ala His Ser Ala	Pro Ala Gly Leu Lys His Ala Val Glu Gln Gly	
	1025	1030
Gly Ser Asn Leu Glu	Asn Leu Met Val Glu Leu Asp Ala Ser Glu Ser	
	1045	1050
Ser Ala Thr Pro Glu	Thr Val Glu Thr Ala Ala Ala Asp Arg Thr Asp	
	1060	1065
Met Pro Gly Ile Arg	Pro Tyr Gly Ala Thr Phe Arg Ala Ala Ala Ala	
	1075	1080
Val Gln His Ala Asn	Ala Ala Asp Gly Val Arg Ile Phe Asn Ser Leu	
	1090	1095
Ala Ala Thr Val Tyr	Ala Asp Ser Thr Ala Ala His Ala Asp Met Gln	
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Gly Arg Arg Leu Lys	Ala Val Ser Asp Gly Leu Asp His Asn Gly Thr	
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Gly Leu Arg Val Ile	Ala Gln Thr Gln Gln Asp Gly Gly Thr Trp Glu	
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Gln Gly Gly Val Glu	Gly Lys Met Arg Gly Ser Thr Gln Thr Val Gly	
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Ile Ala Ala Lys Thr	Gly Glu Asn Thr Thr Ala Ala Ala Thr Leu Gly	
	1170	1175
Met Gly Arg Ser Thr	Trp Ser Glu Asn Ser Ala Asn Ala Lys Thr Asp	
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Ser Ile Ser Leu Phe	Ala Gly Ile Arg His Asp Ala Gly Asp Ile Gly	
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Arg Ser Thr Gly Ala	Asp Glu His Ala Glu Gly Ser Val Asn Gly Thr	
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Leu Met Gln Leu Gly	Ala Leu Gly Gly Val Asn Val Pro Phe Ala Ala	
	1250	1255
Thr Gly Asp Leu Thr	Val Glu Gly Gly Leu Arg Tyr Asp Leu Leu Lys	

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	1285	1290	1295
Ser Leu Thr Glu Gly Thr Leu Val Gly	Leu Ala Gly Leu Lys Leu Ser		
	1300	1305	1310
Gln Pro Leu Ser Asp Lys Ala Val Leu Phe	Ala Thr Ala Gly Val Glu		
	1315	1320	1325
Arg Asp Leu Asn Gly Arg Asp Tyr Thr	Val Thr Gly Gly Phe Thr Gly		
	1330	1335	1340
Ala Thr Ala Ala Thr Gly Lys Thr Gly	Ala Arg Asn Met Pro His Thr		
	1345	1350	1355
Arg Leu Val Ala Gly Leu Gly Ala Asp	Val Glu Phe Gly Asn Gly Trp		
	1365	1370	1375
Asn Gly Leu Ala Arg Tyr Ser Tyr Ala	Gly Ser Lys Gln Tyr Gly Asn		
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His Ser Gly Arg Val Gly Val Gly Tyr	Arg Phe		
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图 1 —  $\Delta G287-919$

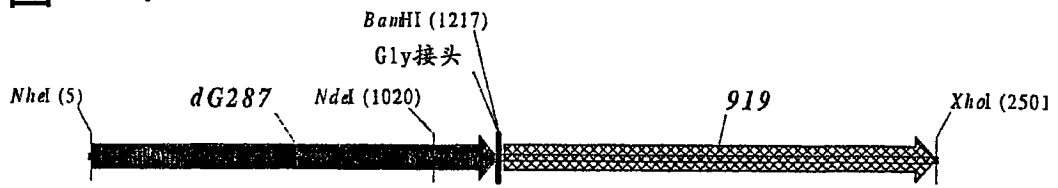


图 2 —  $\Delta G287-953$

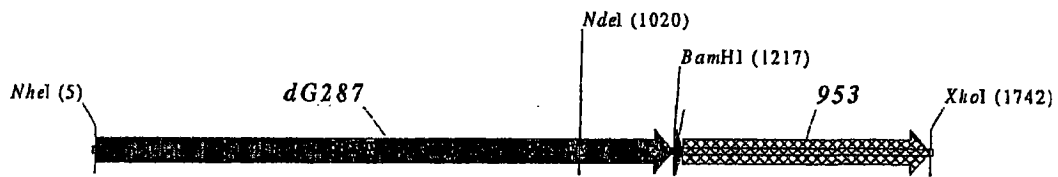


图 3 —  $\Delta G287-961$

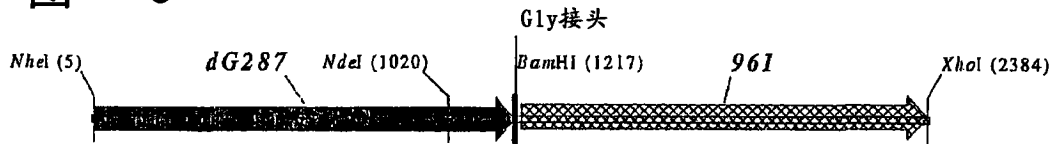


图 4 —  $\Delta G287NZ-919$



图 5 — ΔG287NZ—953



图 6 — ΔG287NZ—961

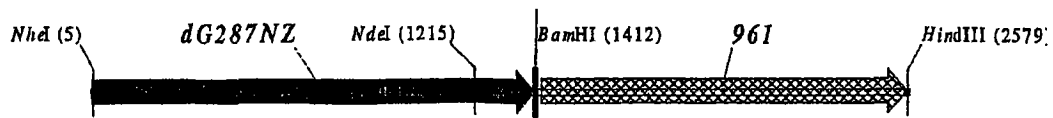


图 7 — ΔG983-ORF46.1



图 8 — ΔG983-741



图 9 —  $\Delta G983-961$



图 10 —  $\Delta G983-961c$



图 11 —  $\Delta G741-961$

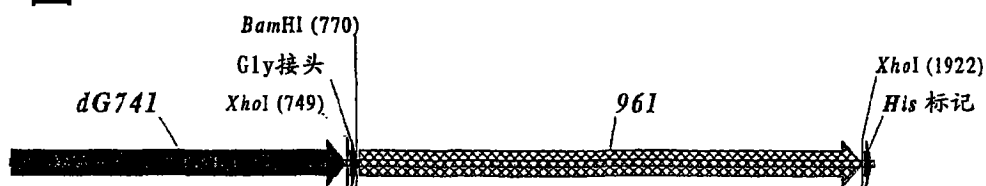


图 12 —  $\Delta G741-961c$



图 13 —  $\Delta G741-983$

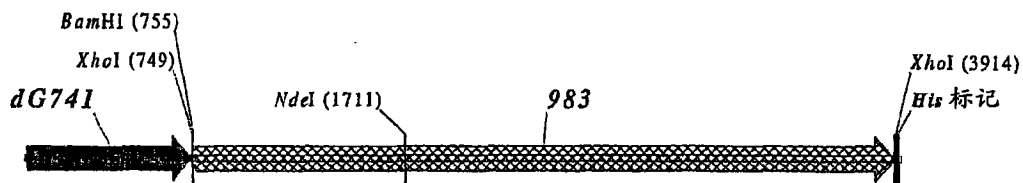


图 14 —  $\Delta G741-ORF46.1$

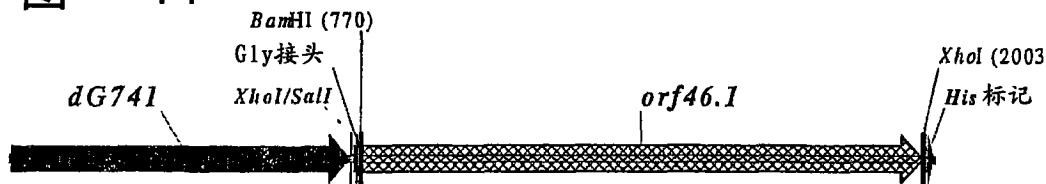


图 15 — *ORF46.1-741*

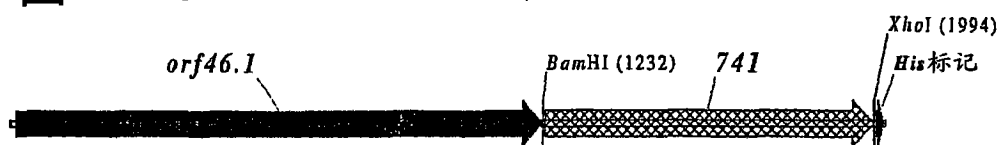


图 16 — *ORF46.1-961*



图 17 — *ORF46.1-961c*



图 18 — 961-ORF46.1



图 19 — 961-741

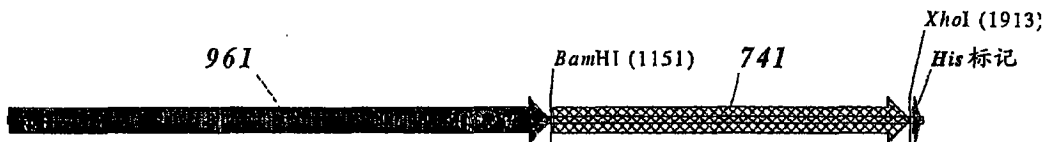


图 20 — 961-983

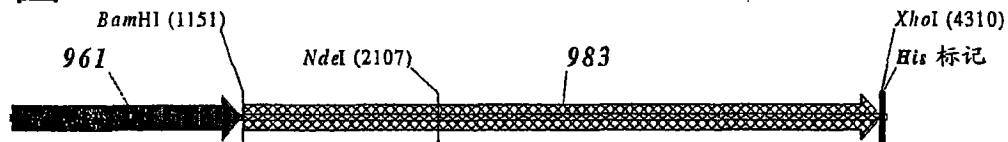


图 21 — 961c-ORF46.1



图 22 — 961c-741

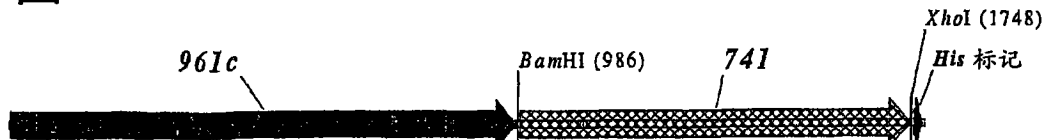


图 23 — 961c-983

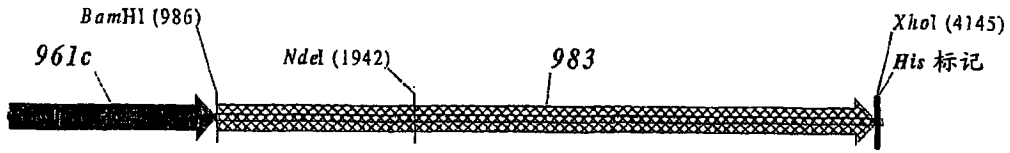


图 24 — 961cL-ORF46.1

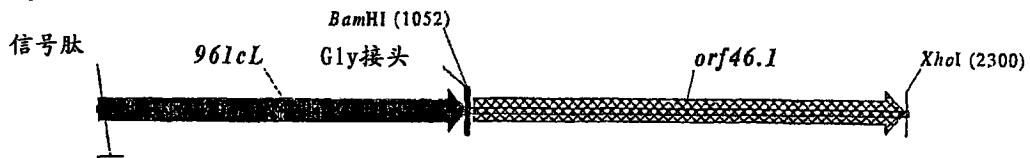


图 25 — 961cL-741

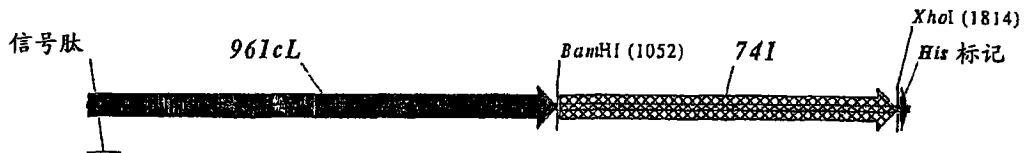


图 26 — 961cL-983

