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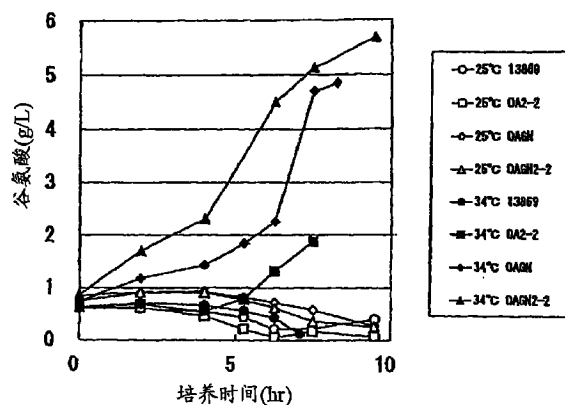
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(54) 发明名称

生产 L-谷氨酸的微生物和生产 L-谷氨酸的方法

(57) 摘要

本发明涉及具有 L-谷氨酸生产能力的棒状杆菌型细菌,其至少以与非突变菌株或野生型菌株相同的生长速率生长,而且其具有的胞内 α -酮戊二酸脱氢酶活性小于非突变或野生型菌株的一半,并通过将突变引入到染色体 *odhA* 基因的编码区或表达控制区而获得,所述染色体 *odhA* 基因编码 α -酮戊二酸脱氢酶复合物的 E1 α 亚基。



1. 生产 L- 谷氨酸的棒状杆菌型细菌,其包含
 - a) 胞内 α - 酮戊二酸脱氢酶活性,所述活性小于非突变或野生型菌株的一半,和
 - b) 在染色体 *odhA* 基因的编码区中的突变,所述染色体 *odhA* 基因编码 α - 酮戊二酸脱氢酶复合物的 E1 α 亚基,其中所述细菌几乎以与非突变或野生型菌株相同的生长速率生长,而且其中所述染色体 *odhA* 基因编码选自下组的蛋白质:
 - (A) 由 SEQ ID NO :10 的氨基酸序列组成的蛋白质,和
 - (B) 由 SEQ ID NO :10 的氨基酸 37 至 1257 组成的蛋白质,且其中将所述突变引入到由 SEQ ID NO :9 的核苷酸 2534 至 2548 组成的区域或由 SEQ ID NO :9 的核苷酸 1094 至 1114 组成的区域。
2. 根据权利要求 1 的棒状杆菌型细菌,其中所述 *odhA* 基因选自下组:
 - (a) 由 SEQ ID NO :9 的核苷酸 443 至 4213 组成的基因,和
 - (b) 由 SEQ ID NO :9 的核苷酸 551 至 4213 组成的基因。
3. 根据权利要求 1 的棒状杆菌型细菌,其中所述突变为在由 SEQ ID NO :10 的氨基酸 698 至 702 组成的区域中缺失一个或多个氨基酸。
4. 根据权利要求 1 的棒状杆菌型细菌,其中所述突变为氨基酸的替换,所述氨基酸从下组选择:SEQ ID NO :10 所示氨基酸序列中 698 位的 Lys、699 位的 Leu、700 位的 Arg、702 位的 Tyr、及其组合。
5. 根据权利要求 1 的棒状杆菌型细菌,其中所述突变为在由 SEQ ID NO :10 的氨基酸 218 至 224 组成的区域中缺失一个或多个氨基酸。
6. 根据权利要求 1 所述的棒状杆菌型细菌,其中所述细菌包含选自下组的编码突变的 α - 酮戊二酸脱氢酶的基因:
 - (a) 由从 SEQ ID NO :11、13 和 15 组成的组中选择的多核苷酸的核苷酸 443 至 4213 组成的基因,或者由从 SEQ ID NO :44、46 和 48 组成的组中选择的多核苷酸的核苷酸 443 至 4210 组成的基因,
 - (b) 由从 SEQ ID NO :11、13 和 15 组成的组中选择的多核苷酸的核苷酸 551 至 4213 组成的基因,或者由从 SEQ ID NO :44、46 和 48 组成的组中选择的多核苷酸的核苷酸 551 至 4210 组成的基因。
7. 根据权利要求 1 所述的棒状杆菌型细菌,其中所述细菌包含编码突变的 α - 酮戊二酸脱氢酶的基因:其中所述突变的 α - 酮戊二酸脱氢酶选自下组:
 - (a) 由从 SEQ ID NO :12、14、16、45、47 和 49 组成的组中选择的氨基酸序列组成的蛋白质,和
 - (b) 由从 SEQ ID NO :12、45、47 和 49 组成的组中选择的氨基酸序列的氨基酸 37 至 1256 组成的蛋白质,由氨基酸序列 SEQ ID NO :14 的氨基酸 37 至 1255 组成的蛋白质,或者由氨基酸序列 SEQ ID NO :16 的氨基酸 37 至 1254 组成的蛋白质。
8. 根据权利要求 1 所述的棒状杆菌型细菌,其中所述细菌是导入突变的 α - 酮戊二酸脱氢酶的基因的突变 ATCC13869 菌株。
9. 根据权利要求 1 所述的棒状杆菌型细菌,其中所述细菌是能表达突变的 α - 酮戊二酸脱氢酶的突变 ATCC13869 菌株。

10. 根据权利要求 1 所述的棒状杆菌型细菌,其包括属于棒杆菌属、短杆菌属的细菌。

11. 产生 L- 谷氨酸的方法,包括:

- a) 在培养基中培养根据权利要求 1 至 10 中任一项的棒状杆菌型细菌,和
- b) 从培养基和 / 或所述细菌收集 L- 谷氨酸。

12. 编码突变 α - 酮戊二酸脱氢酶的基因,选自下组:

(a) 由从 SEQ ID NO:11、13 和 15 组成的组中选择的多核苷酸的核苷酸 443 至 4213 组成的基因,或者由从 SEQ ID NO:44、46 和 48 组成的组中选择的多核苷酸的核苷酸 443 至 4210 组成的基因,和

(b) 由从 SEQ ID NO:11、13 和 15 组成的组中选择的多核苷酸的核苷酸 551 至 4213 组成的基因,或者由从 SEQ ID NO:44、46 和 48 组成的组中选择的多核苷酸的核苷酸 551 至 4210 组成的基因。

13. 突变 α - 酮戊二酸脱氢酶,选自下组:

(a) 由从 SEQ ID NO:12、14、16、45、47 和 49 组成的组中选择的氨基酸序列组成的蛋白质,和

(b) 由从 SEQ ID NO:12、45、47 和 49 组成的组中选择的氨基酸序列的氨基酸 37 至 1256 组成的蛋白质,由氨基酸序列 SEQ ID NO:14 的氨基酸 37 至 1255 组成的蛋白质,或者由氨基酸序列 SEQ ID NO:16 的氨基酸 37 至 1254 组成的蛋白质。

生产 L- 谷氨酸的微生物和生产 L- 谷氨酸的方法

技术领域

[0001] 本发明涉及生产 L- 谷氨酸的微生物和利用所述微生物生产 L- 谷氨酸的方法。L- 谷氨酸广泛用于食品工业,例如,作为生产调味品的原料。

[0002] 相关技术简述

[0003] 已通过发酵方法利用生产 L- 谷氨酸的棒状杆菌型细菌如属于短杆菌属 (*Brevibacterium*) 和棒杆菌属 (*Corynebacterium*) 的细菌以工业规模常规生产 L- 谷氨酸。为了提高棒状杆菌型细菌的 L- 谷氨酸生产能力,将从自然界分离的菌株或这些菌株的人工突变体用作生产 L- 谷氨酸的棒状杆菌型细菌。

[0004] 已经报导了许多使用重组 DNA 技术,通过增强 L- 谷氨酸生物合成酶活性而提高 L- 谷氨酸生产能力的技术。例如,已报导了具有扩增的柠檬酸合酶基因的棒状杆菌型细菌 (JP07-121228B),和具有扩增的谷氨酸脱氢酶基因的棒状杆菌型细菌 (EP 955368)。

[0005] 在物质的发酵生产中,维持细菌细胞的充分生长以充分生产目标物质是有必要的。相应地,培育目标物质的生物合成增强的菌株而不引起细菌生长下降是有必要的。在 L- 谷氨酸的生产中,已报导降低 α - 酮戊二酸脱氢酶活性是有利的 (JP06-237779A 和 W095/34672)。然而,还没有降低 α - 酮戊二酸脱氢酶活性同时维持足够的 L- 谷氨酸生产水平的报导。

发明内容

[0006] 本发明的目的是提供提高棒状杆菌型细菌的 L- 谷氨酸生产能力的技术,所述棒状杆菌型细菌用于 L- 谷氨酸的发酵生产。当 α - 酮戊二酸脱氢酶基因被破坏时,通过 TCA 循环产生的能量减少,导致细菌生长的阻滞。结果,可能无法获得足够的 L- 谷氨酸产率。

[0007] 因此,降解 L- 谷氨酸的能力降低同时维持正常的生长速率的突变菌株可用于有效地生产 L- 谷氨酸。通过将突变引入到编码棒状杆菌型细菌 α - 酮戊二酸脱氢酶复合物的 E1 α 亚基的染色体 *odhA* 基因而获得了突变菌株,所述突变菌株具有降低的 α - 酮戊二酸脱氢酶活性,并且保持了几乎与野生型菌株相同的生长速率。发现利用这样的突变菌株有效地生产 L- 谷氨酸。

[0008] 本发明的目的是提供生产 L- 谷氨酸的棒状杆菌型细菌,其包含

[0009] a) 胞内 α - 酮戊二酸脱氢酶活性,该活性小于非突变或野生型菌株的一半,和

[0010] b) 在染色体 *odhA* 基因的编码区或表达控制区中的突变,所述染色体 *odhA* 基因编码 α - 酮戊二酸脱氢酶复合物的 E1 α 亚基,

[0011] 其中所述细菌几乎以与非突变或野生型菌株相同的生长速率生长。

[0012] 本发明的又一目的是提供如上所述的棒状杆菌型细菌,其中所述 *odhA* 基因编码选自下组的蛋白质:

[0013] (A) 包含 SEQ ID NO:10 的氨基酸序列的蛋白质,

[0014] (B) 包含 SEQ ID NO:10 的氨基酸序列的蛋白质,其中在所述蛋白质中取代、缺失、插入、或添加了一个或几个氨基酸,并且其中所述蛋白质具有 α - 酮戊二酸脱氢酶复合物

的 E1o 亚基的活性,

[0015] (C) 包含 SEQ ID NO:10 的氨基酸 37 至 1257 的蛋白质,和

[0016] (D) 包含 SEQ ID NO:10 的氨基酸 37 至 1257 的蛋白质,其中在所述蛋白质中取代、缺失、插入、或添加了一个或几个氨基酸,并且其中所述蛋白质具有 α -酮戊二酸脱氢酶复合物的 E1o 亚基的活性。

[0017] 本发明的又一目的是提供如上所述的棒状杆菌型细菌,其中所述几个氨基酸是 2 至 20 个氨基酸。

[0018] 本发明的又一目的是提供如上所述的棒状杆菌型细菌,其中所述 *odhA* 基因选自下组:

[0019] (a) 包含 SEQ ID NO:9 的核苷酸 443 至 4213 的基因,

[0020] (b) 能够在严紧条件下与以下物质杂交的基因:包含 SEQ ID NO:9 的核苷酸 443 至 4213 的多核苷酸或由包含 SEQ ID NO:9 的核苷酸 443 至 4213 的多核苷酸制备的探针,并且其中所述基因编码蛋白质,该蛋白质具有 α -酮戊二酸脱氢酶复合物的 E1o 亚基的活性,

[0021] (c) 包含 SEQ ID NO:9 的核苷酸 551 至 4213 的基因,和

[0022] (d) 能够在严紧条件下与以下物质杂交的基因:包含 SEQ ID NO:9 的核苷酸 551 至 4213 的多核苷酸或由包含 SEQ ID NO:9 的核苷酸 551 至 4213 的多核苷酸制备的探针,并且其中所述基因编码蛋白质,该蛋白质具有 α -酮戊二酸脱氢酶复合物的 E1o 亚基的活性。

[0023] 本发明的又一目的是提供如上所述的棒状杆菌型细菌,其中所述突变被引入到编码焦磷酸硫胺素结合区的区域。

[0024] 本发明的又一目的是提供如上所述的棒状杆菌型细菌,其中所述突变包括氨基酸的缺失,所述氨基酸从下组选择:SEQ ID NO:10 所示氨基酸序列中 686 位的 Gly、687 位的 Leu、688 位的 Gly、713 位的 Asn、714 位的 Asn 及其组合。

[0025] 本发明的又一目的是提供如上所述的棒状杆菌型细菌,其中所述突变被引入到包含 SEQ ID NO:9 的核苷酸 2534 至 2548 的区域。

[0026] 本发明的又一目的是提供如上所述的棒状杆菌型细菌,其中所述突变包括在包含 SEQ ID NO:10 的氨基酸 698 至 702 的区域中缺失一个或多个氨基酸。

[0027] 本发明的又一目的是提供如上所述的棒状杆菌型细菌,其中所述突变包括氨基酸的替换,所述氨基酸从下组选择:SEQ ID NO:10 所示氨基酸序列中 698 位的 Lys、699 位的 Leu、700 位的 Arg、702 位的 Tyr、及其组合。

[0028] 本发明的又一目的是提供如上所述的棒状杆菌型细菌,其中所述突变被引入到包含 SEQ ID NO:9 的核苷酸 1094 至 1114 的区域。

[0029] 本发明的又一目的是提供如上所述的棒状杆菌型细菌,其中所述突变包括在包含 SEQ ID NO:10 的氨基酸 218 至 224 的区域中缺失一个或多个氨基酸。

[0030] 本发明的又一目的是提供生产 L-谷氨酸的方法,包括:

[0031] a) 在培养基中培养根据权利要求 1 的棒状杆菌型细菌和

[0032] b) 从培养基和/或所述细菌收集 L-谷氨酸。

[0033] 本发明的又一目的是提供编码突变的 α -酮戊二酸脱氢酶的基因,所述基因选自

下组：

[0034] (a) 包含从 SEQ ID NO :11、13 和 15 组成的组中选择的多核苷酸的核苷酸 443 至 4213 的基因,或者包含从 SEQ ID NO :44、46 和 48 组成的组中选择的多核苷酸的核苷酸 443 至 4210 的基因,

[0035] (b) 能够在严紧条件下与以下物质杂交的基因:包含从 SEQ ID NO :11、13 和 15 组成的组中选择的多核苷酸的核苷酸 443 至 4213 的多核苷酸、包含从 SEQ ID NO :44、46 和 48 组成的组中选择的多核苷酸的核苷酸 443 至 4210 的多核苷酸、由从 SEQ ID NO :11、13 和 15 组成的组中选择的多核苷酸的核苷酸 443 至 4213 制备的探针、或由从 SEQ ID NO :44、46 和 48 组成的组中选择的多核苷酸的核苷酸 443 至 4210 制备的探针,并且其中所述基因编码具有 α -酮戊二酸脱氢酶活性的蛋白质,通过与 E2o 和 E3 亚基形成复合物,该蛋白质的 α -酮戊二酸脱氢酶活性小于野生型或非突变菌株的 α -酮戊二酸脱氢酶活性的一半,

[0036] (c) 包含从 SEQ ID NO :11、13 和 15 组成的组中选择的多核苷酸的核苷酸 551 至 4213 的基因,或者包含从 SEQ ID NO :44、46 和 48 组成的组中选择的多核苷酸的核苷酸 551 至 4210 的基因,和

[0037] (d) 能够在严紧条件下与以下物质杂交的基因:包含从 SEQ ID NO :11、13 和 15 组成的组中选择的多核苷酸的核苷酸 551 至 4213 的多核苷酸、包含从 SEQ ID NO :44、46 和 48 组成的组中选择的多核苷酸的核苷酸 551 至 4210 的多核苷酸、由从 SEQ ID NO :11、13 和 15 组成的组中选择的多核苷酸的核苷酸 551 至 4213 制备的探针、或由从 SEQ ID NO :44、46 和 48 组成的组中选择的多核苷酸的核苷酸 551 至 4210 制备的探针,并且其中所述基因编码具有 α -酮戊二酸脱氢酶活性的蛋白质,通过与 E2o 和 E3 亚基形成复合物,该蛋白质的 α -酮戊二酸脱氢酶活性小于野生型或非突变菌株的 α -酮戊二酸脱氢酶活性的一半。

[0038] 本发明的又一目的是提供突变的 α -酮戊二酸脱氢酶,其选自下组：

[0039] (a) 从 SEQ ID NO :12、14、16、45、47 和 49 组成的组中选择的蛋白质,

[0040] (b) 从 SEQ ID NO :12、14、16、45、47 和 49 组成的组中选择的蛋白质,其中在所述蛋白质中取代、缺失或添加了一个或几个氨基酸,并且其中通过与 E2o 和 E3 亚基形成复合物,所述蛋白质显示的 α -酮戊二酸脱氢酶活性小于野生型或非突变菌株的 α -酮戊二酸脱氢酶活性的一半,

[0041] (c) 包含从 SEQ ID NO :12、45、47 和 49 组成的组中选择的氨基酸序列的氨基酸 37 至 1256 的蛋白质,包含氨基酸序列 SEQ ID NO :14 的氨基酸 37 至 1255 的蛋白质,或者包含氨基酸序列 SEQ ID NO :16 的氨基酸 37 至 1254 的蛋白质,和

[0042] (d) 包含从 SEQ ID NO :12、45、47 和 49 组成的组中选择的氨基酸序列的氨基酸 37 至 1256 的蛋白质,包含氨基酸序列 SEQ ID NO :14 的氨基酸 37 至 1255 的蛋白质,或者包含氨基酸序列 SEQ ID NO :16 的氨基酸 37 至 1254 的蛋白质,其中在所述蛋白质中取代、缺失、或添加了一个或几个氨基酸,并且其中通过与 E2o 和 E3 亚基形成复合物,所述蛋白质显示的 α -酮戊二酸脱氢酶活性小于野生型或非突变菌株的 α -酮戊二酸脱氢酶活性的一半。

附图说明

[0043] 图 1 显示质粒 pBS3 的构建。

[0044] 图 2 显示质粒 pBS4S 的构建。

- [0045] 图 3 显示质粒 pBSOAGN 的构建。
- [0046] 图 4 显示质粒 pBSOA2-2 的构建。
- [0047] 图 5 显示培养各菌株时 L- 谷氨酸浓度的变化。
- [0048] 图 6 显示各菌株的生长速率。
- [0049] 图 7 显示培养各菌株时残糖 (residual sugar) 量的变化。
- [0050] 优选实施方案的说明
- [0051] 以下将详细描述本发明。
- [0052] <1> 本发明的棒状杆菌型细菌
- [0053] 本发明的棒状杆菌型细菌具有生产 L- 谷氨酸的能力, 并且几乎以与非突变菌株或野生型菌株相同的生长速率生长。通过将突变引入到 *odhA* 基因的编码区或表达控制区, 本发明的棒状杆菌型细菌所具有的胞内 α - 酮戊二酸脱氢酶 (以下也称为 " α -KGDH") 活性小于非突变菌株或野生型菌株的活性的一半, 所述 *odhA* 基因编码 α -KGDH 复合物的 E1 α 亚基。
- [0054] α -KGDH 也称为酮戊二酸脱氢酶或 2- 酮戊二酸脱氢酶。
- [0055] 在本发明中, 棒状杆菌型细菌的例子包括常规的棒状杆菌型细菌, 也包括曾经分类为短杆菌属但目前分类为棒杆菌属的细菌 (Int. J. Syst. Bacteriol., 41, 255 (1991)), 以及非常接近棒杆菌属细菌的短杆菌属细菌。这样的棒状杆菌型细菌的例子包括下述的细菌。
- [0056] 嗜乙酰乙酸棒杆菌 (*Corynebacterium acetoacidophilum*)
- [0057] 醋谷棒杆菌 (*Corynebacterium acetoglutamicum*)
- [0058] 烷醇棒杆菌 (*Corynebacterium alkanolyticum*)
- [0059] 美棒杆菌 (*Corynebacterium callunae*)
- [0060] 谷氨酸棒杆菌 (*Corynebacterium glutamicum*)
- [0061] 百合花棒杆菌 (*Corynebacterium lilium*)
- [0062] 栖糖蜜棒杆菌 (*Corynebacterium melassecola*)
- [0063] 嗜热产氨棒杆菌 (*Corynebacterium thermoaminogenes*) (*Corynebacterium efficiens*)
- [0064] 力士棒杆菌 (*Corynebacterium herculis*)
- [0065] 二歧短杆菌 (*Brevibacterium divaricatum*)
- [0066] 黄色短杆菌 (*Brevibacterium flavum*)
- [0067] *Brevibacterium immariophilum*
- [0068] 乳发酵短杆菌 (*Brevibacterium lactofermentum*) (谷氨酸棒杆菌)
- [0069] 玫瑰色短杆菌 (*Brevibacterium roseum*)
- [0070] 解糖短杆菌 (*Brevibacterium saccharolyticum*)
- [0071] 生硫短杆菌 (*Brevibacterium thiogenitalis*)
- [0072] 产氨棒杆菌 (*Corynebacterium ammoniagenes*)
- [0073] 白色短杆菌 (*Brevibacterium album*)
- [0074] 蜡状短杆菌 (*Brevibacterium cerinum*)
- [0075] 嗜氨微杆菌 (*Microbacterium ammoniophilum*)

[0076] 棒状杆菌型细菌的具体实例如下：

[0077] 嗜乙酰乙酸棒杆菌 ATCC13870

[0078] 醋谷棒杆菌 ATCC15806

[0079] 烷醇棒杆菌 ATCC21511

[0080] 美棒杆菌 ATCC15991

[0081] 谷氨酸棒杆菌 ATCC13020, ATCC13032, ATCC13060, ATCC13869

[0082] 百合花棒杆菌 ATCC 15990

[0083] 栖糖蜜棒杆菌 ATCC 17965

[0084] *Corynebacterium efficiens* AJ12340 (FERM BP-1539)

[0085] 力士棒状杆菌 ATCC13868

[0086] 二歧短杆菌 ATCC14020

[0087] 黄色短杆菌 ATCC13826, ATCC14067, AJ12418 (FERM BP-2205)

[0088] *Brevibacterium immariophilum* ATCC 14068

[0089] 乳发酵短杆菌 (谷氨酸棒杆菌) ATCC13869

[0090] 玫瑰色短杆菌 ATCC13825

[0091] 解糖短杆菌 ATCC 14066

[0092] 生硫短杆菌 ATCC 19240

[0093] 产氨棒杆菌 ATCC6871, ATCC 6872

[0094] 白色短杆菌 ATCC15111

[0095] 蜡状短杆菌 ATCC15112

[0096] 嗜氨微杆菌 ATCC15354。

[0097] 这些菌株可从美国典型培养物保藏中心 (ATCC, 地址 :P. O. Box 1549, Manassas, VA 20108, United States of America) 获得。即, 给予每个菌株唯一的登记号, 该登记号列于 ATCC 的目录中。可以使用此登记号来定购菌株。根据布达佩斯条约的规定, 将 AJ12340 菌株于 1989 年 10 月 27 日保藏在通商产业省工业技术院生命工学工业技术研究所 (the National Institute of Bioscience and Human-Technology, Agency of Industrial Science and Technology, Ministry of International Trade and Industry) (目前为, 独立行政法人产业技术综合研究所特许微生物保藏中心 (International Patent Organism Depositary, National Institute of Advanced Industrial Science and Technology), 地址为 Tsukuba Central 6, 1-1, Higashi 1-chome, Tsukuba-shi, Ibaraki-ken, 305-5466, 日本), 并给予登记号 FERM BP-1539。根据布达佩斯条约的规定, 于 1989 年 1 月 5 日将 AJ12418 菌株保藏在通商产业省工业技术院生命工学工业技术研究所, 并给予登记号 FERM BP-2205。

[0098] 在本发明中, "L-谷氨酸生产能力" 指当在培养基中培养本发明的棒状杆菌型细菌时, 导致在培养基中累积足够量的 L-谷氨酸的能力。L-谷氨酸生产能力可以是培育本发明的棒状杆菌型细菌的亲本株的特性, 或者是通过突变、基因重组等等所赋予或增强的特性。另外, 可以通过向编码 α -酮戊二酸脱氢酶复合物的 E1 α 亚基的 *odhA* 基因中引入突变而赋予 L-谷氨酸生产能力。

[0099] 赋予 L-谷氨酸生产能力的方法的例子包括增强编码 L-谷氨酸生物合成酶的基因

的表达。涉及 L- 谷氨酸生物合成的酶的例子包括谷氨酸脱氢酶、谷氨酰胺合成酶、谷氨酸合成酶、异柠檬酸脱氢酶、乌头酸水合酶、柠檬酸合酶、磷酸烯醇丙酮酸羧化酶、丙酮酸羧化酶、丙酮酸脱氢酶、丙酮酸激酶、磷酸烯醇丙酮酸合酶、烯醇化酶、磷酸甘油酸变位酶、磷酸甘油酸激酶、甘油醛 -3- 磷酸脱氢酶、磷酸丙糖异构酶、果糖二磷酸醛缩酶、磷酸果糖激酶、和磷酸葡萄糖异构酶。

[0100] 这些基因表达的增强可以通过将包含这种基因的 DNA 片段整合到能够在棒状杆菌型细菌中自主复制的适当质粒中,并用所得质粒转化细菌细胞;通过同源重组、接合(conjugation)、移位(transposition)等等将这种基因整合到染色体中;或者将突变引入这种基因的启动子区来实现(WO/0018935)。

[0101] 当上述基因通过质粒引入或者被整合在染色体上时,用于所述基因表达的启动子可以是任何启动子,只要它能够在棒状杆菌型细菌中起作用。这种启动子的例子包括 lac 启动子、trp 启动子、trc 启动子、PS2 启动子、和 pL 启动子。也可以使用所述基因的天然启动子。

[0102] 经修饰而使柠檬酸合成酶基因、磷酸烯醇丙酮酸羧化酶基因、和 / 或谷氨酸脱氢酶基因表达增强的微生物的例子包括 JP2001-333769A(EP1078989A)、JP2000-106869A(EP955368A)、JP2000-189169A(EP952221A)、和 JP2001-333769A(EP1078989A) 中公开的那些微生物。

[0103] 赋予 L- 谷氨酸生产能力的修饰包括减小或消除酶的活性,所述酶催化合成除 L- 谷氨酸之外的化合物并由 L- 谷氨酸生物合成途径分支的反应。这些酶的例子包括异柠檬酸裂解酶、乙酰磷酸转移酶、乙酸激酶、乙酰羟酸合酶、乙酰乳酸合酶、乙酰甲酸转移酶、乳酸脱氢酶、谷氨酸脱羧酶、和 1- 焦磷酸脱氢酶。

[0104] 为了减小或消除上述酶的活性,可以将导致酶活性减小或丧失的突变或缺失引入到染色体上酶的基因中。这可以通过例如破坏染色体上编码酶的基因,或者通过修饰基因的表达控制序列如启动子和 / 或 Shine Dargarno(SD) 序列来实现。此外,可以通过引入导致氨基酸取代的错义突变、产生终止密码子的无义突变、或者在编码区中添加或缺失一个或两个核苷酸的移码突变、或者通过缺失基因的一部分来减小或消除这些酶的活性(Journal of biological Chemistry 272 :8611-8617(1997))。另外,可以通过构建其编码区被缺失的编码突变酶的基因,并通过同源重组用所得基因替换染色体基因来减小或消除这些酶的活性。

[0105] 也可以通过筛选对有机酸类似物或呼吸作用抑制剂有抗性的菌株,或者通过筛选对细胞壁合成抑制剂敏感的菌株来赋予 L- 谷氨酸生产能力。这些方法的例子包括赋予对于苯并吡喃酮(benzopirone)或萘醌(Naphtoquinone)的抗性(JP56-1889A)、赋予对于 HQNO 的抗性(JP56-140895A)、赋予对于 α -酮丙二酸的抗性(JP57-2689A)、赋予对于胍的抗性(JP56-35981A)、和赋予对于青霉素的敏感性(JP04-88994A)。

[0106] 这些细菌的具体例子包括下述菌株。

[0107] 黄色短杆菌 AJ11355(FERM P-5007 ;JP56-1889A)

[0108] 谷氨酸棒杆菌 AJ11355(FERM P-5020 ;JP56-1889A)

[0109] 黄色短杆菌 AJ11217(FERM P-4318 ;JP57-2689A)

[0110] 谷氨酸棒杆菌 AJ11218(FERM P-4319 ;JP57-2689A)

[0111] 黄色短杆菌 AJ11564 (FERM P-5472 ;JP56-140895A)

[0112] 黄色短杆菌 AJ11439 (FERM P-5136 ;JP56-35981A)

[0113] 谷氨酸棒杆菌 H7684 (FERM BP-3004 ;JP04-88994A)

[0114] 本发明的棒状杆菌型细菌可以通过向编码 α -KGDH 复合物 E1o 亚基的染色体 *odhA* 基因引入突变,并挑选几乎以与非突变菌株或野生型菌株相同的生长速率生长,其显示的 α -KGDH 活性小于非突变菌株或野生型菌株的活性的一半的那些菌株,从如前所述具有 L-谷氨酸生产能力的棒状杆菌型细菌获得。或者,可以首先将这种突变引入到 *odhA* 基因,之后赋予 L-氨基酸生产能力。

[0115] 本发明中, α -KGDH 活性指催化 α -酮戊二酸(2-酮戊二酸)的氧化脱羧反应,产生丁二酰-CoA 的活性。上述反应由 α -KGDH 复合物催化,所述 α -KGDH 复合物包括三种亚基,即 α -酮戊二酸脱氢酶(E1o, EC1.2.4.2)、二氢硫辛酰胺-S-琥珀酰转移酶(E2o, EC:2.3.1.61)、和二氢硫辛酰胺脱氢酶(E3, EC:1.8.1.4)。也就是说,这三种亚基催化下述各个反应:

[0116] E1o 亚基:

[0117] $2\text{-酮戊二酸} + [\text{二氢硫辛酰赖氨酸-残基琥珀酰转移酶}] \text{硫辛酰赖氨酸} = [\text{二氢硫辛酰赖氨酸-残基琥珀酰转移酶}] \text{S-琥珀酰二氢硫辛酰赖氨酸} + \text{CO}_2$

[0118] E2o 亚基:

[0119] $\text{CoA} + \text{酶 N6-(S-琥珀酰二氢硫辛酰)赖氨酸} = \text{丁二酰-CoA} + \text{酶 N6-(二氢硫辛酰)赖氨酸}$

[0120] E3 亚基:

[0121] $\text{蛋白质 N6-(二氢硫辛酰)赖氨酸} + \text{NAD}^+ = \text{蛋白质 N6-(硫辛酰)赖氨酸} + \text{NADH} + \text{H}^+$

[0122] " α -KGDH 复合物" 的活性指催化以上三种反应的总反应的活性。

[0123] 在大肠杆菌 (*Escherichia coli*) 中,这三种亚基形成复合物。

[0124] 在棒状杆菌型细菌的情况中,E1o 亚基由 *odhA* 基因编码,E3 亚基由 *lpd* 基因编码 (GenBank 登录号 Y16642 ;SEQ ID NO:17)。E2o 亚基是作为双功能蛋白与 E1o 亚基一起由 *odhA* 基因编码 (Usuda et al., Microbiology 1996 142,3347-3354),还是由 GenBank 数据库中登记为登录号 NC_003450 的 NCg12126 (SEQ ID NO:27) 的单独基因所编码存在争议。因此,除了 E1o 亚基之外,*odhA* 基因可编码 E2o 亚基。

[0125] 本发明的棒状杆菌型细菌在染色体 *odhA* 基因中具有突变。*odhA* 基因包括,例如,具有编码 SEQ ID NO:10 所示氨基酸序列的核苷酸序列的基因。*odhA* 基因还包括例如具有编码 SEQ ID NO:51 所示氨基酸序列的核苷酸序列的基因。此外,尽管 SEQ ID NO:9 的核苷酸序列中 551 至 553 位的 "gtg" 是 Val 的密码子,但有可能翻译为 Met,并可在该密码子启动翻译。因此,*odhA* 基因还包括具有编码 SEQ ID NO:10 的氨基酸 37 至 1257 的氨基酸序列的核苷酸序列的基因。另外,*odhA* 基因还可以是编码具有 SEQ ID NO:10 或 51 所示氨基酸序列,或 SEQ ID NO:10 的氨基酸 37 至 1257 的氨基酸序列的蛋白质的基因,其包括一个或几个氨基酸的取代、缺失、插入或添加,只要其显示 α -KGDH 复合物 E1o 亚基的活性。E1o 亚基本身的活性可以用 Massey et al. (Biochim. Biophys. Acta 38,447-460) 的方法测定。此处所用 "几个" 优选为 2 至 20 个,更优选 2 至 10 个,特别优选 2 至 5 个。

[0126] 更具体地,*odhA* 基因优选具有 SEQ ID NO:9 的核苷酸 443 至 4213 的核苷酸序列,

或 SEQ ID NO :9 的核苷酸 551 至 4213 的核苷酸序列。odhA 基因可以具有 SEQ ID NO :50 所示的核苷酸序列。另外,由于 odhA 基因的核苷酸序列在棒状杆菌型细菌的菌种或菌株之间可以有所不同,因而 odhA 基因可以为在严紧条件下与具有 SEQ ID NO :9 核苷酸 443 至 4213 的核苷酸序列的多核苷酸、具有 SEQ ID NO :50 所示核苷酸序列、或 SEQ ID NO :9 的核苷酸 551 至 4213 的核苷酸序列的多核苷酸、或者由所述核苷酸序列制备的探针杂交的基因,只要所述基因编码的蛋白质显示 α -KGDH 复合物 E1 α 亚基的活性。如此处所用的“严紧条件”为在此条件下形成所谓的特异性杂合体且不形成非特异性杂合体的条件。难以用任何的数值清楚地表示此条件。然而,严紧条件的例子包括在其条件下,DNA 于 Southern 杂交通常洗涤的盐浓度下互相杂交的条件,即在 1x SSC、0.1% SDS 在 60℃,优选 0.1x SSC、0.1% SDS 在 60℃,更优选 0.1x SSC、0.1% SDS 在 68℃洗涤一次或优选 2-3 次。

[0127] 本发明中,“突变被引入到染色体 odhA 基因中”包括其中染色体上的 odhA 基因被突变的 odhA 基因替换而产生基本相同的条件的情况,在该条件中突变被直接引入到染色体 odhA 基因中。

[0128] 上述突变不仅可以在编码区引入,还可以在 odhA 基因的表达控制区引入。表达控制区包括,例如启动子、SD 序列、和操纵子。odhA 基因的表达控制区包括 SEQ ID NO :9 的核苷酸 1 至 442 的核苷酸序列。odhA 基因的表达控制序列也可以通过基因分析软件如 GENETYX 或者通过 Goldstein et al. (Prokaryotic promoters in biotechnology. Biotechnol. Annu. Rev., 1995, 1, 105-128) 中公开的方法鉴定。

[0129] “ α -KGDH 活性小于非突变或野生型菌株的 α -KGDH 活性的一半”优选指培养 4 小时的本发明棒状杆菌型细菌的每单位细胞(每单位蛋白质重量)的 α -KGDH 活性小于在相同条件下培养的棒状杆菌型细菌的非突变菌株或野生型菌株活性的一半。这种 α -KGDH 活性减小的棒状杆菌型细菌的例子包括其中每个细胞的 α -KGDH 分子数目减少的细菌,和其中每个 α -KGDH 分子的活性减小的细菌。用作对照的野生型棒状杆菌型细菌的例子包括乳发酵短杆菌 ATCC 13869 菌株。本发明的棒状杆菌型细菌的胞内 α -KGDH 活性优选小于非突变或野生型菌株所述活性的 40%,更优选小于其 30%。虽然 α -KGDH 活性可以降低到不可检测的水平,但优选没有完全消除该活性。可以用 Shiio et al. 的方法(Isamu Shiio and Kyoko Ujigawa-Takeda, Agric. Biol. Chem., 44(8), 1897-1904, 1980) 测定 α -KGDH 活性(α -KGDH 复合物的活性)。

[0130] 作为胞内 α -KGDH 活性减小的结果,棒状杆菌型细菌的 L-谷氨酸生产能力提高。本发明中,“提高 L-谷氨酸生产能力”优选指当在培养基中培养已在 odhA 基因中引入突变的棒状杆菌型细菌菌株时,由突变的棒状杆菌型细菌累积在培养基中的 L-谷氨酸量大于由野生型或非突变菌株累积的量,或者突变的棒状杆菌型细菌生产 L-谷氨酸的速率高于野生型或非突变菌株的生产速率。

[0131] 短语“与野生型菌株或非突变菌株相比,细菌几乎以相同的生长速率生长”优选指本发明的细菌几乎以与野生型菌株如乳发酵短杆菌 ATCC13869 相同的生长速率生长。此处,“几乎以相同的生长速率”指野生型或非突变菌株生长速率的 80%或更高,更优选 90%、或更优选 95%或更高。本发明的棒状杆菌型细菌在任何培养温度下都几乎以与野生型或非突变菌株相同的生长速率生长不是必需的。也就是说,在低温下显示足够的生长速率但在高温下显示降低的生长速率的棒状杆菌型细菌,如实施例所示的 GN-2-2 菌株也

包括于本发明的棒状杆菌型细菌中。

[0132] 例如,可以通过在培养基中接种相同数目的各菌株的细胞,并在预定时间后比较活细胞数来比较本发明的菌株和野生型或非突变菌株的生长速率。当使用液体培养基时,可以根据例如预定时间后 600nm 波长的光密度 (OD) 或细菌细胞的重量计算活细胞数目。当使用固体培养基如平板培养基时,可以根据预定时间后出现的菌落数计算活细胞数目。

[0133] 向染色体上的 *odhA* 基因引入突变的方法的例子包括用 X- 射线或紫外线照射棒状杆菌型细菌,以及用诱变剂如 N- 甲基 -N' - 硝基 -N- 亚硝基胍处理棒状杆菌型细菌。也可以通过制备突变的 *odhA* 基因,并通过同源重组技术用此突变的 *odhA* 基因替换染色体 *odhA* 基因将突变引入到染色体上的 *odhA* 基因中。这种突变的 *odhA* 基因可以通过易错 PCR、DNA 改组、或 StEP-PCR(Firth AE, Patrick WM; Bioinformatics. 2005 Jun 2; Statistics of protein library construction.), 或重叠 - 延伸 PCR (overlap-extension PCR) (Urban, A., Neukirchen, S. and Jaeger, K. E., A rapid and efficient method for site-directed mutagenesis using one-step overlap extension PCR. Nucleic Acids Res, 25, 2227-8. (1997)) 制备。

[0134] 同源重组可以通过使用线性 DNA 的称为 " Red- 驱动的整合 (Red-driven integration) " 的方法 (Datsenko, K. A., PNAS, 97 (12), 6640-6645, 2000), 或者通过使用具有温度敏感性复制起点的质粒的方法 (USP6303383, 和 JP05-007491A) 来进行。向染色体 *odhA* 基因引入突变也可以通过使用不能在棒状杆菌型细菌细胞中复制的质粒或能够通过接合转移到棒状杆菌型细菌的质粒来进行。

[0135] 用于棒状杆菌型细菌的这种温度敏感性质粒的例子包括 p48K 和 pSFKT2 (JP2000-262288A)、pHSC4 (法 国 专 利 Laid-open 公 布 号 2667875, 1992 和 JP5-7491A)、pBS5T 等等。这些质粒在棒状杆菌型细菌中可以在至少 25°C 的温度自主复制,但不能在 37°C 的温度自主复制。含有 pHSC4 的 AJ12571 菌株依据布达佩斯条约的规定于 1991 年 8 月 26 日保藏在通商产业省工业技术院生命工学工业技术研究所 (National Institute of Bioscience and Human Technology, Agency of Industrial Science and Technology, Ministry of International Trade and Industry) (目前为产业技术综合研究所特许微生物保藏 中心 International Patent Organism Depository, National Institute of Advanced Industrial Science and Technology, 其地址为 Tsukuba Central 6, 1-1, Higashi-1-chome, Tsukuba-shi, Ibaraki-ken 305-5466, Japan), 给予保藏号 FERMBP-3524。

[0136] 不能在棒状杆菌型细菌细胞中复制的质粒优选为可在埃希氏菌属的细菌细胞中复制的质粒,其例子包括 pHSG299 (Takara Bio) 和 pHSG399 (Takara Bio)。能够通过接合转移到棒状杆菌型细菌的质粒的例子包括 pK19mobsacB (J. Bacteriology 174 : 5462-65 (1992))。

[0137] 将突变的 *odhA* 基因插入到温度敏感性质粒或者不能在棒状杆菌型细菌中复制的质粒中,所获得的重组质粒用于转化棒状杆菌型细菌。转化可以通过常规方法进行。例如,可以使用氯化钙处理感受态细胞以增加 DNA 通透性的方法,其已报导用于大肠杆菌 (Mandel, M. and Higa, A., J. Mol. Biol., 53, 159 (1970)), 和使用从生长细胞制备的感受态细胞以引入 DNA 的方法,其已报导用于枯草芽孢杆菌 (*Bacillus subtilis*) (Duncan, C. H.,

Wilson, G. A. and Young, R. E., *Gene*, 1, 153 (1977))。除了这些方法外,还可以使用将重组 DNA 引入到原生质体-样或原生质球-样 (protoplast-or spheroplast-like) 受体细胞中的方法,其已报导可用于枯草芽孢杆菌、放线菌类 (actinomycetes) 和酵母 (Chang, S. and Choen, S. N., *Molec. Gen. Genet.*, 168, 111 (1979); Bibb, M. J., Ward, J. M. and Hopwood, O. A., *Nature*, 274, 398 (1978); Hinnen, A. Hicks, J. B. and Fink, G. R., *Proc. Natl. Sci. USA*, 75, 1929 (1978))。此外,棒状杆菌型细菌的转化还可以通过电脉冲法进行 (Sugimoto et al., JP2-207791A)。

[0138] 在使用在棒状杆菌型细菌的细胞中无能的质粒的情况下,染色体上的野生型 *odhA* 基因由质粒上的突变 *odhA* 基因所替换。

[0139] 在使用温度敏感性质粒的情况下,在热敏感性复制起点不起作用的温度 (例如 25°C) 培养转化的菌株,以获得引入了所述质粒的菌株。然后,在高温下培养转化体以除去温度敏感性质粒,并涂布在含抗生素药物如卡那霉素的平板培养基上。虽然去除了所述质粒的菌株不能在含这种抗生素药物的平板上生长,但其中染色体 *odhA* 基因被突变的 *odhA* 基因替换的少数菌株能够生长并出现菌落。

[0140] 在这种如上所述将含突变 *odhA* 基因的重组 DNA 整合到染色体 DNA 中的菌株中,重组 DNA 导致与原来存在于染色体上的 *odhA* 基因重组,并将染色体 *odhA* 基因与突变 *odhA* 基因的融合基因插入到染色体,以使重组 DNA 的其它部分 (载体区段、温度敏感性复制起点和药物抗性标记) 存在于融合基因之间。然后,为了在染色体 DNA 上只留下突变的 *odhA* 基因,将一个拷贝的 *odhA* 基因连同载体区段 (包括温度敏感性复制起点和药物抗性标记) 从染色体 DNA 去除。在这种情况下,将正常 *odhA* 基因留在染色体 DNA 上,并将突变的 *odhA* 基因从染色体 DNA 切除,或者相反,将突变的 *odhA* 基因留在染色体 DNA 上,将正常 *odhA* 基因从染色体 DNA 切除。然后,可以使用 PCR、Southern 杂交等选择在染色体上只留下突变 *odhA* 基因的菌株。

[0141] 可以使用编码果聚糖蔗糖酶的 *sacB* 基因作为重组标志物来进行同源重组。编码果聚糖蔗糖酶的 *sacB* 基因用于有效选择菌株,在所述菌株中,染色体 *odhA* 基因被突变的 *odhA* 基因所替换,并从染色体消除 (cure) 载体部分 (Schafer, A. et al., *Gene* 145 (1994) 69-73)。也就是说,在棒状杆菌型细菌的情况中,当果聚糖蔗糖酶表达时,通过蔗糖同化产生的果聚糖对细菌来说变得致命,并由此细菌不能生长。因此,通过在含蔗糖平板上培养,可以选择其中在载体中的突变 *odhA* 基因和染色体 *odhA* 基因之间发生取代,并从中消除了载体的其它部分的菌株。

[0142] *sacB* 基因的例子包括下述基因。

[0143] 枯草芽孢杆菌 (*Bacillus subtilis*): *sacB* GenBank 登录号 X02730 (SEQ IDNO: 19)

[0144] 解淀粉芽孢杆菌 (*Bacillus amyloliquefaciens*): *sacB* GenBank 登录号 X52988
运动发酵单胞菌 (*Zymomonas mobilis*): *sacB* GenBank 登录号 L33402 嗜热脂肪芽孢杆菌 (*Bacillus stearothermophilus*): *surB* GenBank 登录号 U34874

[0145] *Lactobacillus sanfranciscensis*: *frfA* GenBank 登录号 AJ508391

[0146] *Acetobacter xylinus*: *lsxA* GenBank 登录号 AB034152

[0147] *Gluconacetobacter diazotrophicus*: *lsdA* GenBank 登录号 L41732

[0148] <2> 本发明的突变的 *odhA* 基因

[0149] 将要引入到染色体 *odhA* 基因中的突变没有具体限制,只要其为将 α -KGDH 活性降至低于非突变菌株或野生型菌株 α -KGDH 活性的一半,但不引起细菌生长延缓的突变。所述突变的具体例子包括下述突变。

[0150] (1) 焦磷酸硫胺素结合区中的突变

[0151] 该突变被引入到辅酶焦磷酸硫胺素的结合区。焦磷酸硫胺素结合区指相应于由 *odhA* 基因 (SEQ ID NO:9) 的核苷酸 2498 至 2584 编码区的区域。该区域的氨基酸序列如 SEQ ID NO:10 中氨基酸 686 至 714 所示。该区域中突变的例子包括导致一个或多个氨基酸残基缺失的突变,所述氨基酸残基选自下组:686 位的 Gly、687 位的 Leu、688 位的 Gly、713 位的 Asn、和 714 位的 Asn。

[0152] 也可以在 *odhA* 基因 (SEQ ID NO:9) 的核苷酸 2534 至 2548 的区域引入焦磷酸硫胺素结合区中的突变。该突变命名为 GN 型突变。GN 型突变优选为导致一个或多个氨基酸残基缺失和/或取代的突变,所述氨基酸残基选自下组:SEQ ID NO:10 中 698 位的 Lys、699 位的 Leu、700 位的 Arg、701 位的 Gly、和 702 位的 Tyr。这种突变的例子为缺失 SEQ ID NO:10 中 701 位的 Gly 的突变。具有该突变的突变 *odhA* 基因的例子包括具有 SEQ ID NO:13 的核苷酸 443 至 4213 的核苷酸序列的基因,和具有 SEQ ID NOS:44、46 或 48 的核苷酸 443 至 4210 的核苷酸序列的基因,和由这些基因编码的突变 α -KGDH 蛋白如 SEQ ID NOS:14、45、47、和 49 所示。具有该突变的突变 *odhA* 基因的例子还包括具有 SEQ ID NO:13 的核苷酸 551 至 4213 的核苷酸序列的基因和具有 SEQ ID NOS:44、46 或 48 的核苷酸 551 至 4210 的核苷酸序列的基因,由这些基因编码的突变 α -KGDH 蛋白如 SEQ ID NOS:14 的氨基酸 37 至 1255、和 SEQ ID NOS:45、47、和 49 的氨基酸 37 至 1256 所示。在 SEQ ID NO:13 的核苷酸序列中引入在 SEQ ID NO:9 的 2538 位缺失 "t" 和在 SEQ ID NO:9 的 2543 至 2547 位缺失 "ggcta" 的突变。

[0153] 另外,具有突变的突变 *odhA* 基因也是优选的,所述突变导致从 SEQ IDNO:10 中 698 位的 Lys、699 位的 Leu、700 位的 Arg、和 702 位的 Tyr 组成的组中选择一个或多个氨基酸残基被另一种氨基酸所替换。所述 "另一种氨基酸" 没有具体限制,只要其不同于原来的氨基酸,并选自天然氨基酸如 Lys、Glu、Thr、Val、Leu、Ile、Ser、Asp、Asn、Gln、Arg、Cys、Met、Phe、Trp、Tyr、Gly、Ala、Pro、和 His。然而,优选 698 位的 Lys 被除碱性氨基酸如 Arg 和 His 之外的氨基酸所替换,699 位的 Leu 被除疏水性脂肪族氨基酸如 Ile 和 Val 之外的氨基酸所替换,700 位的 Arg 被除碱性氨基酸如 Lys 和 His 之外的氨基酸所替换,702 位的 Tyr 被除羟基氨基酸如 Ser 和 Thr 之外的氨基酸所替换。特别优选 698 位的 Lys 被疏水性脂肪族氨基酸如 Ile、Leu、或 Val 所替换,699 位的 Leu 被羟基氨基酸如 Ser、Thr 或 Tyr 所替换,700 位的 Arg 被含硫氨基酸如 Cys 或 Met 所替换,702 位的 tyr 被疏水性脂肪族氨基酸如 Ile、Leu、或 Val 所替换。

[0154] GN 型突变可以同时导致 701 位的 Gly 的缺失和从 SEQ ID NO:10 中 698 位的 Lys、699 位的 Leu、700 位的 Arg、和 702 位的 Tyr 组成的组中选择一个或多个氨基酸残基的替换。这种突变 *odhA* 基因的例子包括具有 SEQ IDNOS:44、46、和 48 的核苷酸 443 至 4210 的核苷酸序列的基因。由这些突变 *odhA* 基因编码的突变 α -KGDH 蛋白的氨基酸序列如 SEQ ID NOS:45、47、和 49 所示。这种突变 *odhA* 基因的例子还包括具有 SEQ ID NOS:44、46、和

48 的核苷酸 551 至 4210 的核苷酸序列的基因。由这些突变 *odhA* 基因编码的突变 α -KGDH 蛋白的氨基酸序列如 SEQ ID NOS:45、47、和 49 的氨基酸 37 至 1256 所示。然而,在焦磷酸硫胺素结合区具有突变的突变 *odhA* 基因不限于这些例子。

[0155] (2) 2-2 型突变

[0156] 这种类型的突变优选为引入到 *odhA* 基因 (SEQ ID NO:9) 的核苷酸 1094 至 1114 区域中的突变,其导致选自 SEQ ID NO:10 中选自 218 位的 Asp、219 位的 Val、220 位的 Ile、221 位的 Asp、222 位的 Gly、223 位的 Lys、和 224 位的 Pro 的一个或多个氨基酸残基的缺失和 / 或取代。2-2 型突变优选为在 SEQ ID NO:10 中 218 位缺失 Asp 的突变。具有此突变的 *odhA* 基因的例子包括具有 SEQ ID NO:11 的核苷酸 443 至 4213 的核苷酸序列的 *odhA* 基因,或者具有 SEQ ID NO:11 的核苷酸 551 至 4213 的核苷酸序列的 *odhA* 基因。由这些基因编码的突变 α -KGDH 的氨基酸序列分别如 SEQ ID NO:12 或 SEQ ID NO:12 的 37 至 1256 位氨基酸所示。SEQ ID NO:11 的核苷酸序列具有在 SEQ ID NO:9 所示核苷酸序列中缺失 1094 至 1098 的 "gacgt" 并用 "ggcc" 替换 1110 至 1111 的 "ag" 的突变。

[0157] 2-2 型突变还优选为替换选自 219 位的 Val、220 位的 Ile、221 位的 Asp、222 位的 Gly、和 223 位的 Lys 的一个或多个氨基酸的突变。虽然替换这些氨基酸的氨基酸没有具体限制,但优选除脂肪族疏水性氨基酸如 Ile 和 Leu 之外的氨基酸替换 219 位的 Val,用除脂肪族疏水性氨基酸如 Leu 之外的氨基酸替换 220 位的 Ile,用除酸性氨基酸如 Glu 之外的氨基酸替换 221 位的 Asp,以及用除简单氨基酸如 Ala 之外的氨基酸替换 222 位的 Gly。更优选用碱性氨基酸如 His、Arg 和 Lys 替换 219 位的 Val、220 位的 Ile、和 221 位的 Asp,用氨基酸如 Asp 和 Gln 替换 222 位的 Gly,以及用氨基酸如 Gly 和 Ala 替换 223 位的 Lys。

[0158] 然而,具有 2-2 型突变的突变 *odhA* 基因不限于这些例子。

[0159] (3) GN2-2 型突变

[0160] 该突变同时包括 GN 型突变和 2-2 型突变。具有此突变的 *odhA* 基因的例子包括具有 SEQ ID NO:15 的核苷酸 443 至 4213 的核苷酸序列的 *odhA* 基因,或者具有 SEQ ID NO:15 的核苷酸 551 至 4213 的核苷酸序列的 *odhA* 基因。由这些基因编码的突变 α -KGDH 的氨基酸序列分别如 SEQ ID NO:16 或 SEQ ID NO:16 的氨基酸 37 至 1254 所示。然而,具有 GN2-2 型突变的突变 *odhA* 基因不限于这些例子。

[0161] 用于本发明的其他类型的突变 *odhA* 基因可以利用 *ygg* 突变株,如以下实施例 5 中所述的 ATCC13869-L 来筛选。也就是说,将随机突变引入到 *odhA* 基因中,并用于转化 *ygg* 突变菌株。从转化体选择几乎与野生型菌株或非突变菌株相同的生长速率生长,并显示小于野生型菌株或非突变菌株的一半 α -KGDH 活性的菌株,之后测序。由此可以获得突变的 *odhA* 基因。

[0162] 由上述突变 *odhA* 基因编码的 α -KGDH 复合物的突变 E1o 亚基是蛋白质,其通过与 α -KGDH 复合物的 E2o 和 E3 亚基形成复合物,具有小于野生型或非突变菌株 α -KGDH 活性一半的 α -KGDH 活性,并且在棒状杆菌型细菌中表达时不引起棒状杆菌型细菌严重的生长延缓。

[0163] 认为即便是一个或几个氨基酸被其它氨基酸所替换,突变 E1o 亚基的这些特性也将保持,所述一个或几个氨基酸是除上述 GN 型或 2-2 型突变体中被替换的特定氨基酸之外的氨基酸,例如不影响酶活性的氨基酸。因此,在以上提到的突变 E1o 亚基蛋白的氨基酸序

列(例如,SEQ ID NOS:12、14、16、45、47 和 49,SEQ ID NOS:12、45、47 和 49 的氨基酸 37 至 1256,SEQ ID

[0164] NO:14 的氨基酸 37 至 1255,或者 SEQ ID NO:16 的氨基酸 37 至 1254) 中,可以替换除 GN 型或 2-2 型突变体中被取代的特定氨基酸之外的其它一个或几个氨基酸,只要所编码的蛋白质通过与 α -KGDH E2o 亚基和 E3 亚基蛋白一起形成复合物,显示小于野生型 α -KGDH 复合物一半的 α -KGDH 活性。此处“几个”优选指 2 至 20 个,更优选 2 至 10 个,并特别优选 2 至 5 个。这种氨基酸取代可以通过源于细菌个体差异和菌种差异的天然存在的突变所引起的取代,其中 *odhA* 基因由所述细菌衍生。例如,具有编码氨基酸序列 SEQ ID NO:51 的核苷酸序列的突变 *odhA* 基因也可用于本发明,其中对应于上述 GN- 型突变或 2-2 型突变的氨基酸被缺失和/或取代。氨基酸序列 SEQ ID NO:51 中对应于 GN- 型突变或 2-2 型突变的这些氨基酸可以很容易地通过比对 SEQ ID NOS:10 和 51 的氨基酸序列来鉴定。上述取代优选为保守性取代。在芳香族氨基酸的情况中,保守性取代指 phe、trp、和 tyr 之间的相互取代。在疏水性氨基酸的情况中,保守性取代指 leu、ile、和 val 之间的相互取代。在极性氨基酸的情况中,保守性取代指 gln 和 asn 之间的相互取代。在碱性氨基酸的情况中,保守性取代指 arg、lys、和 his 之间的相互取代。在酸性氨基酸的情况中,保守性取代为 asp 和 glu 之间的相互取代。在含羟基氨基酸的情况中,保守性取代指 ser 和 thr 之间的取代。保守性取代还包括:ser 或 thr 取代 ala, gln、his 或 lys 取代 arg; glu、gln、lys、his 或 asp 取代 asn; asn、glu 或 gln 取代 asp; ser 或 ala 取代 cys; asn、glu、lys、his、asp 或 arg 取代 gln; asn、gln、lys 或 asp 取代 glu; val 取代 gly; asn、lys、gln、arg 或 tyr 取代 his; leu、met、val 或 phe 取代 ile; ile、met、val 或 phe 取代 leu; asn、glu、gln、his 或 arg 取代 lys; ile、leu、val 或 phe 取代 met; trp、tyr、met、ile 或 leu 取代 phe; thr 或 ala 取代 ser; ser 或 ala 取代 thr; phe 或 tyr 取代 trp; his、phe、或 trp 取代 tyr; 以及 met、ile、或 leu 取代 val。

[0165] 当 E1o 亚基和 E2o 亚基由单个 *odhA* 基因编码时, α -KGDH 复合物可以包括 SEQ ID NO:10(或 SEQ ID NO:10 的氨基酸 37 至 1257) 的蛋白质和 SEQ ID NO:18 的蛋白质。当 E1o 亚基由 *odhA* 基因编码且 E2o 亚基由 SEQ ID NO:27 的基因编码时, α -KGDH 复合物可以包括 SEQ ID NO:10 的蛋白质、SEQ ID NO:18 的蛋白质、和 SEQ ID NO:28 的蛋白质。

[0166] 本发明的突变 *odhA* 基因是编码上述突变 α -KGDH E1o 亚基的基因。本发明的突变 *odhA* 基因可以是在严紧条件下,与各自具有 SEQ ID NO:11、13、或 15 的核苷酸 443 至 4213 的核苷酸序列的多核苷酸,与各自具有 SEQ ID NO:44、46 或 48 的核苷酸 443 至 4210 的核苷酸序列的多核苷酸,与 SEQ ID NO:11、13、或 15 的核苷酸 551 至 4213 的核苷酸序列,或与 SEQ ID NO:44、46、或 48 的核苷酸 443 至 4210 的核苷酸序列,或与从所述序列制备的探针杂交的基因,只要该基因编码通过与 E2o 亚基和 E3 亚基蛋白形成复合物,显示小于野生型 α -KGDH 复合物一半的 α -KGDH 活性的蛋白质。严紧条件的例子包括在其条件下,DNAs 于 Southern 杂交通常洗涤的盐浓度下互相杂交的条件,即在 1x SSC、0.1% SDS 在 60°C,优选 0.1x SSC、0.1% SDS 在 60°C,更优选 0.1x SSC、0.1% SDS 在 68°C 的条件下洗涤一次或优选 2-3 次。

[0167] <3> 生产 L-谷氨酸的方法

[0168] 可以通过在培养基中培养本发明的棒状杆菌型细菌,导致 L-谷氨酸在培养基中

和 / 或在细菌细胞中累积, 并从培养基和 / 或细菌细胞收集 L- 谷氨酸来生产 L- 谷氨酸。在本发明的生产方法中, 优选通过例如在 25 至 40℃ 培养本发明的棒状杆菌型细菌 8 至 120 小时来生产 L- 谷氨酸。如果在低温下显示足够的生长速率但在高温下显示减小的生长速率的菌株, 如实施例所示的 GN-2-2 菌株用于 L- 谷氨酸生产, 则优选在低温下如 25 至 30℃ 培养这种菌株 8 至 30 小时, 以使所述菌株能够生长; 然后在高温下如 34 至 40℃ 将所得细菌细胞保温 16 至 48 小时, 使所述菌株能够生产 L- 谷氨酸。

[0169] 所述培养基可以是包含碳源、氮源、无机盐、和任选有机微量营养物如氨基酸和维生素的常规培养基。合成培养基或天然培养基均可使用。可以使用任何种类的碳源和氮源, 只要它们能够被要培养的菌株所利用。

[0170] 糖类如葡萄糖、丙三醇、果糖、蔗糖、麦芽糖、甘露糖、半乳糖、淀粉水解物、和糖蜜可以用作碳源。此外, 有机酸如醋酸和柠檬酸、以及醇如乙醇也可以单独或组合作为碳源使用。氨、铵盐如硫酸铵、碳酸铵、氯化铵、磷酸铵、和乙酸铵、硝酸盐等可以用作氮源。氨基酸、维生素、脂肪酸、核酸、包含蛋白胨的物质、酪蛋白氨基酸、酵母提取物、和大豆蛋白分解产物可以以少量使用作为有机营养物。当使用其生长需要氨基酸等的营养缺陷型突变株时, 优选添加这种所需的营养物。磷酸盐、镁盐、钙盐、铁盐、锰盐等可以作为无机盐使用。

[0171] 优选通过控制发酵温度并将培养基的 pH 调节至 3 到 9 来进行需氧培养。培养期间 pH 降低时, 通过添加碱如碳酸钙或氨气来中和培养基。培养约 10 至约 120 小时使培养基中累积大量的 L- 谷氨酸。

[0172] 此外, 可以使用液体培养基进行培养, 所述液体培养基被调节至生产的 L- 谷氨酸结晶并析出的条件。L- 谷氨酸结晶的条件包括 pH 5.0 至 4.0, 优选 pH 4.5 至 4.0, 更优选 pH 4.3 至 4.0, 特别优选 pH 4.0 (EP1233069、EP1233070)。

[0173] 培养完成后, 可以通过常规方法从培养基收集 L- 谷氨酸。例如可以通过从培养基去除细菌细胞并浓缩 L- 谷氨酸或者通过使用离子交换层析来收集 L- 谷氨酸。当在 L- 谷氨酸结晶并析出的条件下进行培养时, 可以例如通过离心或过滤来收集结晶的 L- 谷氨酸。在这种情况下, 也可以在溶解的 L- 谷氨酸结晶后收集溶解在培养基中的 L- 谷氨酸。

[0174] 实施例

[0175] 以下本发明将通过参考以下非限制性实施例更具体地解释本发明。

[0176] 实施例 1

[0177] <1> 携带 sacB 基因的载体的构建

[0178] (A) pBS3 的构建

[0179] 使用枯草芽孢杆菌的染色体 DNA 作为模板, SEQ ID NOS :21 和 22 的寡核苷酸作为引物通过 PCR, 获得了 sacB 基因 (SEQ ID NO :19)。按照以下程序用 LA Taq (可由 TaKaRa 获得) 进行 PCR :94℃ 预变性 5 分钟的一个循环 ;94℃ 变性 30 秒、49℃ 退火 30 秒、72℃ 延伸 2 分钟的 25 个循环。用常规方法纯化所得 PCR 产物, 然后用 BglIII 和 BamHI 消化并平端化。将所述片段插入到已用 AvaII 消化且平端化的 pHS3299 中。所得 DNA 用于转化大肠杆菌 JM109 (可由 Takara Bio 获得) 的感受态细胞。然后, 将转化的细菌细胞涂布到含 25 μg/ml 卡那霉素 (以下缩写为 "Km") 的 LB 琼脂平板上, 保温一夜。此后, 选择出现的菌落作为转化体。从所得转化体分离质粒, 并将具有目的 PCR 产物插入物的质粒命名为 pBS3。图 1 显示构建 pBS3 的方法。

[0180] (B)pBS4S 的构建

[0181] 使用不引起氨基酸取代的交换 (cross-over)PCR 来破坏 pBS3 上卡那霉素抗性基因中的 SmaI 识别位点。首先使用 pBS3 作为模板, SEQ ID NOS :23 和 24 的合成 DNAs 作为引物进行 PCR,以获得卡那霉素抗性基因的 N 末端片段。另一方面,为了获得卡那霉素抗性基因的 C 末端片段,使用 pBS3 作为模板, SEQ ID NOS :25 和 26 的合成 DNAs 作为引物进行 PCR。按照以下程序用 Pyrobest DNA 聚合酶(可由 TaKaRa Bio 获得)进行 PCR :98℃ 预变性 5 分钟 ;及 98℃ 变性 10 秒、57℃ 退火 30 秒、72℃ 延伸 1 分钟的 25 个循环。SEQ ID NOS :24 和 25 相互之间部分互补,而且不包含 SmaI 识别位点。然后,为了获得不含 SmaI 识别位点的突变卡那霉素抗性基因的全长片段,将上述 N 末端和 C 末端基因产物以基本上等摩尔的量互相混合。使用所述基因产物作为模板, SEQ ID NOS :23 和 26 的合成 DNAs 作为引物进行 PCR,以获得引入了突变的 Km 抗性基因。按照以下程序用 Pyrobest DNA 聚合酶(可由 TaKaRaBio 获得)进行 PCR :98℃ 预变性 5 分钟 ;及 98℃ 变性 10 秒、57℃ 退火 30 秒、72℃ 延伸 1.5 分钟的 25 个循环。

[0182] 用常规方法纯化 PCR 产物,接下来用 BanII 消化,然后插入到 pBS3 的上述 BanII 识别位点中。所得质粒用于转化大肠杆菌 JM109(可由 Takara Bio 获得)的感受态细胞。即将转化的细菌细胞涂布到包含 25 μ g/ml 卡那霉素的 LB 琼脂培养基上,并保温一夜。此后,选择出现的菌落作为转化体。从所得转化体分离质粒,并将具有目的 PCR 产物插入物的质粒命名为 pBS4S。图 2 显示构建 pBS4S 的方法。

[0183] <2> 将 odhA 突变 (GN- 型) 引入到谷氨酸棒杆菌 ATCC13869 菌株中

[0184] 编码棒状杆菌型细菌 α - 酮戊二酸脱氢酶的 odhA 的序列已有报导 (Microbiology 142, 3347-3354 (1996), GenBank 登录号 D84102)。

[0185] 本发明的发明人成功培育的生产 L- 谷氨酸的细菌菌株 GN 的核苷酸序列分析显示,该菌株在 odhA 基因 (SEQ ID NO :9) 的核苷酸序列中具有核苷酸 2538 和核苷酸 2543 至 2547 的缺失,如表 1 所示。表 1 还显示了由突变 odhA 基因编码的突变 Elo 亚基的氨基酸序列。

[0186] 表 1

[0187]

菌株	odhA 基因的核苷酸序列
ATCC13869	GCT AAG CTG CGT GGC TAC GAC GTC GGA GGC ACC ATC
OAGN	GCT AAG C-G CGT-----C GAC GTC GGA GGC ACC ATC
菌株	Elo 亚基的氨基酸序列
ATCC13869	Ala Lys Leu Arg Gly Tyr Asp Val Gly Gly Thr Ile
OAGN	Ala Lys Arg Val-----Asp Val Gly Gly Thr Ile

[0188] 然后,将该突变 odhA 基因引入到谷氨酸棒杆菌 2256 菌株 (ATCC13869) 中并评估。首先制备用于将这些突变引入到谷氨酸棒杆菌 2256 菌株 (ATCC13869) 中的质粒。使用 Bacterial Genomic DNA Purif. 试剂盒(由 MStechsystems Co.,Ltd. 生产)从上述 GN 菌株提取染色体 DNA,使用所获得的染色体 DNA 作为模板, SEQ ID NOS :1 和 2 的寡核苷酸作为引物进行 PCR。按照以下程序使用 Pyrobest 聚合酶(可由 TaKaRa Bio 获得)进行 PCR 以扩增约 2.75kb 的片段 :98℃ 变性 10 秒、50℃ 退火 30 秒、72℃ 延伸 3 分钟的 30 个 循环。所述引物在 5' 端包含 BamHI 识别序列,并设计用于扩增 GenBank 登录号 D84102 序列的核苷酸 1521 至 4270 的区域。扩增的片段用 BamHI 消化,并连接到用 BarnHI 消化的 pBS4S 载

体 (Ligation kit Ver. 2, 使用可从 Takara Bio 获得的产品), 由此获得质粒 pBSOAGN (图 3 显示构建方法)。

[0189] 通过电脉冲法 (JP02-207791A) 将 pBSOAGN 导入到谷氨酸棒杆菌 ATCC13869 菌株中, 将所获得的细菌细胞涂布到含 25 μ g/ml 卡那霉素的 CM-Dex 琼脂培养基 (5g/l 葡萄糖、10g/l 多蛋白胨、10g/l 酵母提取物、1g/l KH_2PO_4 、0.4g/l $\text{MgSO}_4 \cdot 7\text{H}_2\text{O}$ 、0.01g/l $\text{FeSO}_4 \cdot 7\text{H}_2\text{O}$ 、0.01g/l $\text{MnSO}_4 \cdot 4\text{H}_2\text{O}$ 、3g/l 尿素、1.2g/l 大豆蛋白水解物、和 20g/l 琼脂, pH 调节到 7.5)。25°C 培养后, 通过使用 PCR 确认出现的菌落为一次重组菌株 (once recombinant strain), 在此菌株中, pBSOAGN 通过同源重组整合在染色体上。使用候选菌株的染色体 DNA 作为模板, 具有特异于 pBS4S 的序列 (SEQ ID NO:3) 的核苷酸序列的寡核苷酸和具有特异于染色体上的序列 (SEQ ID NO:4) 的核苷酸序列的寡核苷酸作为引物进行 PCR。也就是说, 由于 pBS4S 的序列在非重组菌株的染色体上不存在, 因而如果所述候选菌株不是重组菌株, 则没有片段通过 PCR 被扩增。将所获得的一次重组菌株在 25°C 在含 25 μ g/ml 卡那霉素的 CM-Dex 液体培养基中培养一天, 适当稀释所得培养物并涂布到 S10 平板上, 所述 S10 平板具有上述 CM-Dex 培养基的组成, 其中只是用 10g/l 的蔗糖替换 5g/l 的葡萄糖。选择了几个生长在 S10 平板上并显示卡那霉素敏感性的菌株, 然后通过 Sanger 的方法 (J. Mol. Biol., 143, 161 (1980)) 确认 *odhA* 序列的核苷酸序列。使用 BigDye 终止物测序试剂盒 (由 Applied Biosystems 生产) 通过遗传 Analyzer ABI310 (由 Applied Biosystems 生产) 分析核苷酸序列。将如此获得的携带 GN- 型突变 *odhA* 基因的菌株命名为 ATCC13869OAGN。

[0190] <3> 将 2-2 型突变 *odhA* 基因导入谷氨酸棒杆菌 ATCC13869 菌株中

[0191] 本发明的发明人成功培育的生产 L- 谷氨酸的 "2-2" 菌株的核苷酸序列分析显示, 该菌株在 *odhA* 基因 (SEQ ID NO:9) 中包含核苷酸 1094 至 1098 的缺失和以 "ggcc" 替换处于 1110 至 1111 的 "ag", 如表 2 所示。表 2 还显示了由突变 *odhA* 基因编码的突变 E1o 亚基的氨基酸序列。

[0192] 表 2

[0193]

菌株	<i>odhA</i> 基因的核苷酸序列
ATCC13869	AAC TCC TAC GAC GTC ATC GAC GGC AAG CCA ACC CTG
OA2-2	AAC TCC TAC—CAT CGA CGG CAG GCC CCA ACC CTG
菌株	E1o 亚基的氨基酸序列
ATCC13869	Asn Ser Tyr Asp Val Ile Asp Gly Lys Pro Thr Leu
OA2-2	Asn Ser Tyr—His Arg Arg Gln Ala Pro Thr Leu

[0194] 然后, 将该突变的 *odhA* 基因导入到谷氨酸棒杆菌 2256 菌株 (ATCC13869) 中并评估。首先制备用于将这些突变引入到谷氨酸棒杆菌 2256 中的质粒。用 Bacterial Genomic DNA Purif. 试剂盒 (由 MS Technosystems Co., Ltd. 生产) 从 2-2 菌株分离染色体 DNA, 使用此染色体 DNA 作为模板, SEQ ID NOS:5 和 6 的寡核苷酸作为引物进行 PCR。按照以下程序使用 TaKaRa Ex Taq (可由 TaKaRa Bio 获得) 进行 PCR 以扩增约 2.0kb 的片段: 94°C 变性 30 秒、55°C 退火 10 秒、72°C 延伸 2 分钟的 25 个循环。所述引物在 5' 端包含 BamHI 识别序列, 该引物设计用于扩增 GenBank 登录号 D84102 核苷酸序列的核苷酸 51 至 2150 区域。扩增的片段用 BamHI 消化, 并使用 Takara Bio 的 Ligation kit Ver. 2 连接到经 BamHI 消化的 pBS4S 载体, 由此获得质粒 pBSOA2-2 (图 4 显示构建图)。实施与实施例 1<2> 中所述相同的步骤以获得携带 2-2 型突变 *odhA* 基因的菌株 (ATCC13869OA2-2 菌株)。

[0195] <4> 将 2-2 型突变引入到 ATCC13869OAGN 菌株的 GN 型 *odhA* 基因中

[0196] 按照与实施例 1<2> 中所述相同的方法,将实施例 1<3> 中构建的质粒 pBSOA2-2 导入实施例 1<2> 中制备的 ATCC13869OAGN 菌株中,以获得 *odhA* 基因中同时携带 GN 型和 2-2 型突变的 ATCC13869 菌株。以下由 2-2 型突变和 GN 型突变组成的双突变也称为 GN2-2 突变。

[0197] 虽然在实施例 1<2> 至 <4> 中,所述突变株使用通过 PCR 扩增的突变 *odhA* 基因制备,所述 PCR 利用来自 GN 菌株或 2-2 菌株的染色体 DNA 作为模板,但它们也可以通过使用突变的 *odhA* 基因制备,所述突变的 *odhA* 基因通过定点诱变技术如使用 Mutan-Super Express Km 试剂盒 (Takara Bio) 的技术获得。例如,可以如以下所述获得具有类似于实施例 1<2> 中制备的 pBSOAGN 的结构 of 的质粒。即,使用 SEQ ID NOS :2 和 5 的合成 DNAs 作为引物,野生型 *odhA* 基因的染色体 DNA 作为模板,通过 PCR 制备 *odhA* 基因片段,并将所得 PCR 片段克隆到 Mutan-Super Express Km 试剂盒附带的质粒 pKF 19k 的 BamHI 识别位点。接下来,使用所得质粒模板和具有磷酸化的 5' - 末端的 SEQ ID NO :7 的合成 DNA 引物和 Mutan-Super Express Km 试剂盒附带的选择引物进行另一 PCR。用所得 PCR 产物转化 sup^0 大肠杆菌,例如 MV 1184 菌株 (可由 Takara Bio 获得),结果构建了包含突变 *odhA* 基因片段的质粒。最后,用 BamHI 消化所述片段并插入到 pBS4S 载体中,由此可以构建与 pBSOAGN 类似的质粒。

[0198] 类似地,为了获得包含 2-2 型突变的 *odhA* 基因,可以用具有磷酸化的 5' - 末端的 SEQ ID NO :8 的合成 DNA 代替上述方法中具有磷酸化的 5' - 末端的 SEQ ID NO :7 的合成 DNA 来构建类似于 pBSOA2-2 的质粒。

[0199] 此外,为了获得包含 GN2-2 双突变的 *odhA* 基因,从上述类似于 pBSOAGN 的质粒切除或 PCR 扩增包含 GN- 型突变的片段,并用于替换上述类似于 pBSOA2-2 的质粒上的相应片段。

[0200] 实施例 2

[0201] 菌株 ATCC13869OAGN、OA2-2、和 OAGN2-2 降解谷氨酸的能力的对比

[0202] 虽然携带野生型 *odhA* 基因的菌株能够同化培养基中的 L- 谷氨酸,但推测由于 *odhA* 突变而削弱或消除了 α -KGDH 活性的菌株也具有减小的降解谷氨酸的能力。然后,使用实施例 1<2> 至 <4> 中制备的各 *odhA* 突变株 ATCC13869OAGN、OA2-2、和 OAGN2-2 测定降解谷氨酸的能力。各菌株均在 CM-Dex 平板上在 25°C 培养一天,然后接种到液体培养基中,所述液体培养基由 20g/l 谷氨酸钠、2.64g/l $(\text{NH}_4)_2\text{SO}_4$ 、0.5g/l KH_2PO_4 、0.5g/l K_2HPO_4 、0.25g/l $\text{MgSO}_4 \cdot 7\text{H}_2\text{O}$ 、0.01g/l $\text{FeSO}_4 \cdot 7\text{H}_2\text{O}$ 、0.01g/l $\text{MnSO}_4 \cdot 4-5\text{H}_2\text{O}$ 、0.01g/l CaCl_2 、0.02mg/l CuSO_4 、40g/l MOPS、0.03g/l 原儿茶酸 (protocatechic acid)、200 $\mu\text{g/l}$ 维生素 B1、和 300 $\mu\text{g/l}$ 生物素 (用 NaOH 调节至 pH 6.7) 组成,之后在 25°C 和 34°C 培养 50 小时。分别测定起点、和培养 25 小时和 50 小时后谷氨酸的量,并比较 25°C 和 34°C 培养的菌株之间降解的 (degraded) 谷氨酸的量。表 3 显示结果。特别地,GN2-2 突变株显示降解的谷氨酸的量明显减小,尤其是当培养温度为 34°C 时。这些结果表明引入 GN2-2 突变能够有效地减小 α -KGDH 活性,具有此突变的菌株优选用于 L- 谷氨酸生产。

[0203] 表 3 :降解的谷氨酸的量

[0204]

菌株	25 小时		50 小时	
	25°C	34°C	25°C	34°C
ATCC13869	15	15	15.4	15.4
OAGN	3.8	5.8	9.4	10.0
OA2-2	11.7	15.1	15.4	15.4
OAGN2-2	0.7	0.5	4.9	1.0

[0205] (单位 :g/l)

[0206] 实施例 3

[0207] ATCC13869OAGN、OA2-2、和 OAGN2-2 菌株 α -KGDH 活性的对比

[0208] 菌株 ATCC13869OAGN、OA2-2、和 OAGN2-2 的 α -KGDH 活性如下所述使用实施例 4 中自培养起始 4 小时后收集的培养液测定。所述活性按照 Agric. Biol. Chem., 44(8), p1897(1980) 中所述方法测定。具体地,在用 0.2%氯化钠洗涤细菌细胞后,将其悬浮在含 30%甘油的 100mM TES-NaOH(pH 7.5) 缓冲溶液中。用 Bioruptor(Olympus) 超声处理细菌细胞,然后离心以去除未破裂的细菌细胞,之后使用 Sephadex-G25(Amersham Pharmacia) 用相同缓冲液凝胶过滤。将如此获得的制备物用作粗酶溶液。将所述粗制酶溶液添加到含 100mM TES-NaOH(pH 7.7)、5mM MgCl₂、0.2mM CoA、0.3mM 辅羧酶(cocarcboxylase)、1mM α -酮戊二酸、3mM L-半胱氨酸、和 1mM 乙酰吡啶-腺嘌呤-二核苷酸的反应体系,用 Hitachi 分光光度计 U-2001 在 31.5°C 在 365nm 测定吸收。在粗制酶溶液中蛋白浓度的测量中,使用蛋白质测试(Bio-Rad)。牛血清白蛋白用作标准蛋白质。

[0209] 表 4 显示测定 α -KGDH 活性的结果。与 ATCC13869 相比,引入 GN 型突变、2-2 型突变、和 GN2-2 型突变导致 α -KGDH 活性减小。特别地,在引入 GN2-2 型突变的菌株的情况中,观测到相当大的活性减小。这表明 GN 型突变、2-2 型突变、和 GN2-2 型突变是减小 α -KGDH 活性的突变。

[0210] 表 4 : α -KGDH 活性

[0211]

菌株	培养温度 25°C	培养温度 34°C
ATCC13869	0.036	0.021
OAGN	0.001	0.002
OA2-2	0.007	0.009
OAGN2-2	0.001>	0.001>

[0212] (单位 : Δ Abs/min/mg 蛋白质)

[0213] 实施例 4

[0214] 菌株 ATCC13869OAGN、OA2-2、和 OAGN2-2 的 L-谷氨酸生产能力的对比

[0215] 在发酵釜培养中检验菌株 ATCC13869OAGN、OA2-2、和 OAGN2-2 的 L-谷氨酸生产能力。首先,将上述四种菌株在 25°C 在 CM-Dex 琼脂培养基上培养一天,并将所得的细菌细胞接种在 300ml 灭菌的种子培养基(seed medium)中,所述种子培养基含 60g/l 葡萄糖、1.54g/l H₃PO₄、1.45g/l KOH、0.9g/l MgSO₄·7H₂O、0.01g/l FeSO₄·7H₂O、670 μ g/l 维生

素 B 1、3, 200 μ g/l 生物素、0.28g/l DL-Met、1.54g/l 大豆蛋白水解物、和 0.1ml/l 消泡剂 AZ-20R, 一直培养到糖被完全耗尽。在培养期间, 以 1/1 VVM 通气来搅拌培养基, 以使溶解氧的浓度保持在不小于 5%。用氨气将培养期间的 pH 控制到 pH 7.2。然后, 将 30ml 所得种子培养物接种到 270ml 含 80g/l 葡萄糖、3.46g/l KH_2PO_4 、1.0g/l $\text{MgSO}_4 \cdot 7\text{H}_2\text{O}$ 、0.01g/l $\text{FeSO}_4 \cdot 7\text{H}_2\text{O}$ 、0.01g/l $\text{MnSO}_4 \cdot 4\text{H}_2\text{O}$ 、230 μ g/l 维生素 B 1、525 μ g/l 生物素、0.35g/l 大豆蛋白水解物、和 0.2ml/l 消泡剂 AZ-20R 的主培养基中, 在 25°C 或 34°C 培养。培养期间如上所述进行通气。用氨气将培养期间的 pH 控制在 pH 7.3。

[0216] 表 5 显示自培养起始约 7.5 小时后累积的 L- 谷氨酸的量。图 5、6 和 7 分别显示 L- 谷氨酸累积、细菌细胞量、和残余糖分的时间进程。ATCC13869 菌株不累积 L- 谷氨酸, 而 OAGN 和 OAGN2-2 突变菌株累积 L- 谷氨酸。特别地, 当这些菌株在 34°C 培养时, 所累积的 L- 谷氨酸的量显著增加。每种引入突变的菌株都显示几乎与野生型菌株相同的生长速率。

[0217] 由这些结果证实 GN 型突变、2-2 型突变、和 GN2-2 型突变对增加 L- 谷氨酸生产是有效的。发现在这些突变当中, GN2-2 型突变对 L- 谷氨酸生产有最显著的影响。

[0218] 表 5 : 引入 *odhA* 突变的菌株所生产的 L- 谷氨酸 (Glu) 的量

[0219]

菌株	25°C	34°C
	Glu(g/L)	Glu(g/L)
ATCC13869	0.24	0.13
OAGN	0.18	1.88
OA2-2	0.59	4.70
OAGN2-2	0.38	5.13

[0220] 实施例 5

[0221] 用 *yggB* 突变菌株筛选 *odhA* 突变菌株

[0222] <L30 型 *yggB* 突变菌株的构建>

[0223] 首先, 由 ATCC13869 菌株构建在 *yggB* 基因中具有突变的突变菌株。L30 型突变为在 *yggB* 基因 (SEQ ID NO :29) 中用 " T " 替换 1768 位的 " C " 的突变。具有 L30 型突变的突变 *yggB* 基因如 SEQ ID NO :31 所示, 由该基因编码的氨基酸序列如 SEQ ID NO :32 所示。所述突变 *yggB* 基因以与实施例 1 中相同的方法构建。即, 使用 SEQ ID NOS :33 和 34 的引物和 ATCC13869 菌株的染色体 DNA 模板通过 PCR 制备编码 *ygg* 基因 N- 末端部分的片段。以类似的方式使用 SEQ ID NOS :35 和 36 的引物和 ATCC13869 菌株的染色体 DNA 模板通过 PCR 制备编码 *ygg* 基因 C- 末端部分的片段。随后, 利用 SEQ ID NOS :37 和 35 的引物以及等量的 N- 末端片段和 C- 末端片段的混合物模板通过 PCR 获得包含 L30 型突变的 *yggB* 基因片段。用 *SacI* 消化所得 PCR 产物并连接到 *SacI* 消化的 pBS4S, 由此获得用于引入所述突变的质粒 (pBS4 *yggB*-L)。将所得 pBS4*yggB*-L 整合到 ATCC13869 菌株的染色体中, 然后按照与实施例 1 中类似的方法将其从所述菌株消除。测定所得卡那霉素抗性菌株 *yggB* 基因的核苷酸序列, 并选择其中 *yggB* 基因被 L30 型替换的菌株。将具有 SEQ ID NO :31 的 *yggB* 基因的菌株命名为 ATCC 13869-L 菌株。该菌株可用于 *odhA* 突变基因的筛选。

[0224] <*ygg*、*odhA* 双突变菌株的构建>

[0225] 然后,将表 6 所示的各种突变引入到 ATCC13869-L 菌株的染色体 *odhA* 基因中。表 6 中显示了各菌株相应于 SEQ ID NO:9 的核苷酸 2528 至 2562 区域的核苷酸序列。表 7 中显示了各菌株相应于 SEQ ID NO:10 的氨基酸 696 至 707 区域的氨基酸序列。

[0226] 引入具有核苷酸序列 SEQ ID NO:42 的 *odhA* 基因的 L30sucA8 菌株可以如下获得。使用 SEQ ID NOS:2 和 5 的引物通过 PCR 制备突变的 *odhA* 基因片段。所得片段用 BamHI 消化并连接到 Mutan-Super Express Km(Takara Bio) 附带的质粒 pKF19m 的 BamHI 位点。然后,使用具有磷酸化的 5'-末端的引物 SEQ ID NO:38 和 Mutan-Super Express Km 的选择引物进行 PCR,所得 PCR 产物用于转化 *sup0-* 大肠杆菌菌株如 MV1184 菌株,以得到包含突变 *odhA* 片段的质粒。将该片段插入到 pBS4S 质粒中,按照与实施例 1 中类似的方法用所得质粒转化 ATCC13869-L 菌株,由此获得所述质粒整合到其染色体中的菌株。然后,从这些菌株中选择对蔗糖有抗性且对卡那霉素敏感的菌株。测定所选择菌株的 *odhA* 基因的核苷酸序列,并选择其中由于 *odhA* 基因中的移码突变而使 α -KGDH 功能缺陷的菌株作为 ATCC13869-L30sucA8(*odhA8*) 菌株。其它的 *odhA* 突变菌株可以使用 *yggB* 突变菌株通过类似的方法获得。

[0227] 引入了具有核苷酸序列 SEQ ID NO:44 的突变 *odhA* 基因的 *sucA801* 菌株可以通过与上述类似的方法获得,所述方法中,用具有磷酸化的 5'-末端的引物 SEQ ID NO:39 代替引物 SEQ ID NO:38。

[0228] 引入了具有核苷酸序列 SEQ ID NO:46 的突变 *odhA* 基因的 *sucA805* 菌株可以通过与上述类似的方法获得,所述方法中,用具有磷酸化的 5'-末端的引物 SEQ ID NO:40 代替引物 SEQ ID NO:38。

[0229] 引入了具有核苷酸序列 SEQ ID NO:48 的突变 *odhA* 基因的 *sucA77* 菌株可以通过与上述类似的方法获得,所述方法中,用具有磷酸化的 5'-末端的引物 SEQ ID NO:41 代替引物 SEQ ID NO:38。

[0230] L30sucA8 菌株没有胞内 α -KGDH,因为 *sucA8* 突变是引起 α -KGDH 蛋白不成熟截断的移码突变。另一方面,*sucA801* 菌株、*sucA805* 菌株和 *sucA77* 菌株具有减小的但有一些 α -KGDH 活性,因为这些突变不是移码突变,而且不引起 α -KGDH 蛋白的不成熟截断。

[0231] 表 6:*odhA* 突变基因的部分核苷酸序列

[0232]

菌株	<i>odhA</i> 基因的核苷酸序列
ATCC13869-L	CTG GCT AAG CTG CGT GGC TAC GAC GTCGGA GGC ACC
L30sucA8	CTG GCT AAG CTG CGT C GAC GTC GGAGGC ACC
L30sucA801	CTG GCT AAG CTG CGT CTC GAC GTC GGA GGC ACC
L30sucA805	CTG GCT AAA AGC TGC GTC GAC GTC GGA GGC ACC
L30sucA77	CTG GCT ATA AGC TGC GTC GAC GTC GGA GGC ACC

[0233] 表 7:*odhA* 突变体的氨基酸序列

[0234]

菌株	E1 α 亚基的氨基酸序列
野生的	Leu Ala Lys Leu Arg Gly Tyr Asp Val Gly Gly Thr
L30sucA8(Δ <i>sucA</i>)	Leu Ala Lys Leu Arg Arg Arg Arg Arg His

[0235]

L30sucA801	Leu Ala Lys Leu Arg---Leu Asp Val Gly Gly Thr
L30sucA805	Leu Ala Lys Ser Cys---Val Asp Val Gly Gly Thr
L30sucA77	Leu Ala Ile Ser Cys---Val Asp Val Gly Gly Thr

[0236] < 使用携带各种突变 odhA 基因的菌株生产 L- 谷氨酸 >

[0237] 通过在坂口 (Sakaguchi) 烧瓶中培养所得 odhA 突变菌株来评估这些菌株的 L- 谷氨酸生产力。将表 6 列出的各种菌株在 CM-Dex 琼脂培养基上在 31.5°C 培养过夜, 然后将 1/6 的培养物转移到 20ml 含 60g/l 葡萄糖、22.5g/l (NH₄)₂SO₄、1g/l KH₂PO₄、0.4g/l MgSO₄ · 7H₂O、0.01g/l FeSO₄ · 7H₂O、0.01g/l MnSO₄ · 4-5H₂O、200 μ g/l 维生素 B1、0.48g/l 大豆蛋白水解物、和 300 μ g/l 生物素 (用 KOH 调节至 pH 8.0) 的培养基中, 添加 CaCO₃ 并在 31.5°C、115rpm 搅动培养。培养 19 小时后累积的 L- 谷氨酸的量如表 8 所示。sucA801、sucA805、和 sucA77 菌株显示高于 ATCC13869-L 菌株和 sucA8 菌株的 L- 谷氨酸生产力, 其中 ATCC13869-L 菌株携带野生型 odhA 基因, 而 sucA8 菌株携带含有移码突变的 odhA 基因。这些结果显示, 通过将突变引入到 odhA 基因的焦磷酸硫胺素结合区附近区域中以调节 α -KGDH 活性, 从而有效地生产了 L- 谷氨酸。

[0238] 表 8 : odhA 突变菌株的 L- 谷氨酸生产

[0239]

菌株	L- 谷氨酸 (g/L)
ATCC13869-L	4.9
L30sucA8	19.8
L30sucA801	22.1
L30sucA805	23.8
L30sucA77	21.6

[0001]

序列表

<110> 味之素株式会社(Ajinomoto Co., Inc.)

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<130> 生产 L-谷氨酸的微生物和生产 L-谷氨酸的方法

<150> JP2004-264458

<151> 2004-09-10

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[0003]

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Pro Thr Thr Asn Val Thr Val Asp Lys Ile Lys Leu Asn Lys Pro Ser	
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Arg Ser Lys Glu Lys Arg Arg Val Pro Ala Val Ser Ser Ala Ser Thr	
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Phe Gly Gln Asn Ala Trp Leu Val Asp Glu Met Phe Gln Gln Phe Gln	
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Lys Asp Pro Lys Ser Val Asp Lys Glu Trp Arg Glu Leu Phe Glu Ala	
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Lys Ala Ala Pro Arg Val Glu Thr Lys Pro Ala Ala Lys Thr Ala Pro	
110 115 120	
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Lys Ala Lys Glu Ser Ser Val Pro Gln Gln Pro Lys Leu Pro Glu Pro	
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Gly Gln Thr Pro Ile Arg Gly Ile Phe Lys Ser Ile Ala Lys Asn Met	
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Asp Ile Ser Leu Glu Ile Pro Thr Ala Thr Ser Val Arg Asp Met Pro	
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Ala Arg Leu Met Phe Glu Asn Arg Ala Met Val Asn Asp Gln Leu Lys	
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Arg Thr Arg Gly Gly Lys Ile Ser Phe Thr His Ile Ile Gly Tyr Ala	
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Met Val Lys Ala Val Met Ala His Pro Asp Met Asn Asn Ser Tyr Asp	
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Val Ile Asp Gly Lys Pro Thr Leu Ile Val Pro Glu His Ile Asn Leu	
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Met Asp Asp Tyr Gln Gly Val Thr Val Ser Leu Thr Asn Pro Gly Gly	
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Ile Gly Thr Arg His Ser Val Pro Arg Leu Thr Lys Gly Gln Gly Thr	
300 305 310	

[0004]

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acc tcc acc tac gat cac cgc gtg atc cag ggt gct gtg tcc ggt gaa Thr Ser Thr Tyr Asp His Arg Val Ile Gln Gly Ala Val Ser Gly Glu 350 355 360	1528
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[0005]

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Gly Val Asp Gly Lys Thr Val Val Pro Leu Leu Leu His Gly Asp Ala	
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Leu Arg Gly Tyr Asp Val Gly Gly Thr Ile His Ile Val Val Asn Asn	
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Gln Ile Gly Phe Thr Thr Thr Pro Asp Ser Ser Arg Ser Met His Tyr	
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gca acc gac tac gcc aag gca ttc ggc tgc cca gtc ttc cac gtc aat	2680
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Tyr Arg Arg Arg Phe Gly Lys Asp Val Phe Ile Asp Leu Val Cys Tyr	
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Arg Leu Arg Gly His Asn Glu Ala Asp Asp Pro Ser Met Thr Gln Pro	
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Lys Met Tyr Glu Leu Ile Thr Gly Arg Glu Thr Val Arg Ala Gln Tyr	
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Gly Ser Leu Ala Asn Ser Gly Arg Leu Val Arg Leu Ala Gly Glu Asp	
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Ser Arg Arg Gly Thr Phe Thr Gln Arg His Ala Val Ala Ile Asp Pro	
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[0006]

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Gln Thr Ile Ile Asp Glu Tyr Val Ser Ser Gly Glu Ala Lys Trp	
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Gly Gln Gly Pro Asp His Ser Ser Ala Arg Ile Glu Arg Phe Leu	
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Pro Ala Asn His Phe His Leu Leu Arg Arg His Ala Leu Ser Asp	
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Lys Phe Gln Ser Val Ile Asp Asp Pro Asn Val Ala Asp Ala Ala	
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Lys Val Lys Lys Val Met Leu Val Ser Gly Lys Leu Tyr Tyr Glu	
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1155 1160 1165	
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Val Arg Ile Glu Met Leu His Pro Ile Pro Phe Asn Arg Ile Ser	
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Gln Asp Glu Pro Ala Asn Gln Gly Pro Trp Pro Phe Tyr Gln Glu	
1200 1205 1210	
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His Leu Pro Glu Leu Ile Pro Asn Met Pro Lys Met Arg Arg Val	
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[0007]

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Arg Val Pro Ala Val Ser Ser Ala Ser Thr Phe Gly Gln Asn Ala Trp
35      40      45
Leu Val Asp Glu Met Phe Gln Gln Phe Gln Lys Asp Pro Lys Ser Val
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Asp Lys Glu Trp Arg Glu Leu Phe Glu Ala Gln Gly Gly Pro Asn Ala
65      70      75      80
Thr Pro Ala Thr Thr Glu Ala Gln Pro Ser Ala Pro Lys Glu Ser Ala
85      90      95
Lys Pro Ala Pro Lys Ala Ala Pro Ala Ala Lys Ala Ala Pro Arg Val
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Glu Thr Lys Pro Ala Ala Lys Thr Ala Pro Lys Ala Lys Glu Ser Ser
115     120     125
Val Pro Gln Gln Pro Lys Leu Pro Glu Pro Gly Gln Thr Pro Ile Arg
130     135     140
Gly Ile Phe Lys Ser Ile Ala Lys Asn Met Asp Ile Ser Leu Glu Ile
145     150     155     160
Pro Thr Ala Thr Ser Val Arg Asp Met Pro Ala Arg Leu Met Phe Glu
165     170     175
Asn Arg Ala Met Val Asn Asp Gln Leu Lys Arg Thr Arg Gly Gly Lys
180     185     190
Ile Ser Phe Thr His Ile Ile Gly Tyr Ala Met Val Lys Ala Val Met
195     200     205
Ala His Pro Asp Met Asn Asn Ser Tyr Asp Val Ile Asp Gly Lys Pro
210     215     220
Thr Leu Ile Val Pro Glu His Ile Asn Leu Gly Leu Ala Ile Asp Leu
225     230     235     240
Pro Gln Lys Asp Gly Ser Arg Ala Leu Val Val Ala Ala Ile Lys Glu
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Thr Glu Lys Met Asn Phe Ser Glu Phe Leu Ala Ala Tyr Glu Asp Ile
260     265     270
Val Thr Arg Ser Arg Lys Gly Lys Leu Thr Met Asp Asp Tyr Gln Gly
275     280     285
Val Thr Val Ser Leu Thr Asn Pro Gly Gly Ile Gly Thr Arg His Ser
290     295     300
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305     310     315     320
Met Asp Tyr Pro Ala Glu Phe Gln Gly Ala Ser Glu Asp Arg Leu Ala
325     330     335
Glu Leu Gly Val Gly Lys Leu Val Thr Ile Thr Ser Thr Tyr Asp His
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Arg Leu Leu Thr Asp Asp Ser Phe Trp Asp Glu Ile Phe Asp Ala Met
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Asn Val Pro Tyr Thr Pro Met Arg Trp Ala Gln Asp Val Pro Asn Thr
385     390     395     400
Gly Val Asp Lys Asn Thr Arg Val Met Gln Leu Ile Glu Ala Tyr Arg
405     410     415
Ser Arg Gly His Leu Ile Ala Asp Thr Asn Pro Leu Ser Trp Val Gln
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435     440     445
Ser Leu Thr Ile Trp Asp Leu Asp Arg Thr Phe Ser Val Gly Gly Phe
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[0008]

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Arg Phe Ser Leu Glu Gly Ala Glu Ala Leu Ile Pro Leu Met Asp Ser					
545		550		555	
Ala Ile Asp Thr Ala Ala Gly Gln Gly Leu Asp Glu Val Val Ile Gly					
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Met Pro His Arg Gly Arg Leu Asn Val Leu Phe Asn Ile Val Gly Lys					
580		585		590	
Pro Leu Ala Ser Ile Phe Asn Glu Phe Glu Gly Gln Met Glu Gln Gly					
595		600		605	
Gln Ile Gly Gly Ser Gly Asp Val Lys Tyr His Leu Gly Ser Glu Gly					
610		615		620	
Gln His Leu Gln Met Phe Gly Asp Gly Glu Ile Lys Val Ser Leu Thr					
625		630		635	
Ala Asn Pro Ser His Leu Glu Ala Val Asn Pro Val Met Glu Gly Ile					
645		650		655	
Val Arg Ala Lys Gln Asp Tyr Leu Asp Lys Gly Val Asp Gly Lys Thr					
660		665		670	
Val Val Pro Leu Leu Leu His Gly Asp Ala Ala Phe Ala Gly Leu Gly					
675		680		685	
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690		695		700	
Gly Gly Thr Ile His Ile Val Val Asn Asn Gln Ile Gly Phe Thr Thr					
705		710		715	
Thr Pro Asp Ser Ser Arg Ser Met His Tyr Ala Thr Asp Tyr Ala Lys					
725		730		735	
Ala Phe Gly Cys Pro Val Phe His Val Asn Gly Asp Asp Pro Glu Ala					
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Val Val Trp Val Gly Gln Leu Ala Thr Glu Tyr Arg Arg Arg Phe Gly					
755		760		765	
Lys Asp Val Phe Ile Asp Leu Val Cys Tyr Arg Leu Arg Gly His Asn					
770		775		780	
Glu Ala Asp Asp Pro Ser Met Thr Gln Pro Lys Met Tyr Glu Leu Ile					
785		790		795	
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805		810		815	
Arg Gly Asp Leu Ser Asn Glu Asp Ala Glu Ala Val Val Arg Asp Phe					
820		825		830	
His Asp Gln Met Glu Ser Val Phe Asn Glu Val Lys Glu Gly Gly Lys					
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Lys Gln Ala Glu Ala Gln Thr Gly Ile Thr Gly Ser Gln Lys Leu Pro					
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His Gly Leu Glu Thr Asn Ile Ser Arg Glu Glu Leu Leu Glu Leu Gly					
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Gln Ala Phe Ala Asn Thr Pro Glu Gly Phe Asn Tyr His Pro Arg Val					
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Ala Pro Val Ala Lys Lys Arg Val Ser Ser Val Thr Glu Gly Gly Ile					
900		905		910	
Asp Trp Ala Trp Gly Glu Leu Leu Ala Phe Gly Ser Leu Ala Asn Ser					
915		920		925	
Gly Arg Leu Val Arg Leu Ala Gly Glu Asp Ser Arg Arg Gly Thr Phe					
930		935		940	
Thr Gln Arg His Ala Val Ala Ile Asp Pro Ala Thr Ala Glu Glu Phe					
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Asn Pro Leu His Glu Leu Ala Gln Ser Lys Gly Asn Asn Gly Lys Phe					
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Leu Val Tyr Asn Ser Ala Leu Thr Glu Tyr Ala Gly Met Gly Phe Glu					
980		985		990	

[0009]

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 His Pro Ile Pro Phe Asn Arg Ile Ser Glu Ala Leu Ala Gly Tyr
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 cgaagccacc tccaccctcg acccgcgcac cgaagccgtt atcctcaacg cctccgatcg 240
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 gttgtctgct aacggcacct acgccgcgat gtggcattta atggcctgac acgttatatt 420
 taggagaact gtcaacaaat ta atg cta caa ctg ggg ctt agg cat aat cag 472
 Met Leu Gln Leu Gly Leu Arg His Asn Gln
 1 5 10
 cca acg acc aac gtt aca gtg gat aaa ata aag ctc aat aaa ccc tca 520
 Pro Thr Thr Asn Val Thr Val Asp Lys Ile Lys Leu Asn Lys Pro Ser
 15 20 25
 aga agc aag gaa aag agg cga gta cct gcc gtg agc agc gct agt act 568
 Arg Ser Lys Glu Lys Arg Arg Val Pro Ala Val Ser Ser Ala Ser Thr
 30 35 40

[0010]

ttc ggc cag aat gcg tgg ctg gta gac gag atg ttc cag cag ttc cag Phe Gly Gln Asn Ala Trp Leu Val Asp Glu Met Phe Gln Gln Phe Gln 45 50 55	616
aag gac ccc aag tcc gtg gac aag gaa tgg aga gaa ctc ttt gag gcg Lys Asp Pro Lys Ser Val Asp Lys Glu Trp Arg Glu Leu Phe Glu Ala 60 65 70	664
cag ggg gga cca aat gct acc ccc gct aca aca gaa gca cag cct tca Gln Gly Gly Pro Asn Ala Thr Pro Ala Thr Thr Glu Ala Gln Pro Ser 75 80 85 90	712
gcg ccc aag gag tct gcg aaa cca gca cca aag gct gcc cct gca gcc Ala Pro Lys Glu Ser Ala Lys Pro Ala Pro Lys Ala Ala Pro Ala Ala 95 100 105	760
aag gca gca ccg cgc gta gaa acc aag ccg gcc gcc aag acc gcc cct Lys Ala Ala Pro Arg Val Glu Thr Lys Pro Ala Ala Lys Thr Ala Pro 110 115 120	808
aag gcc aag gag tcc tca gtg cca cag caa cct aag ctt ccg gag cca Lys Ala Lys Glu Ser Ser Val Pro Gln Gln Pro Lys Leu Pro Glu Pro 125 130 135	856
gga caa acc cca atc agg ggt att ttc aag tcc atc gcg aag aac atg Gly Gln Thr Pro Ile Arg Gly Ile Phe Lys Ser Ile Ala Lys Asn Met 140 145 150	904
gat atc tcc ctg gaa atc cca acc gca acc tcg gtt cgc gat atg cca Asp Ile Ser Leu Glu Ile Pro Thr Ala Thr Ser Val Arg Asp Met Pro 155 160 165 170	952
gct cgc ctc atg ttc gaa aac cgc gcg atg gtc aac gat cag ctc aag Ala Arg Leu Met Phe Glu Asn Arg Ala Met Val Asn Asp Gln Leu Lys 175 180 185	1000
cgc acc cgc ggt ggc aag atc tcc ttc acc cac atc att gcc tac gcc Arg Thr Arg Gly Lys Ile Ser Phe Thr His Ile Ile Gly Tyr Ala 190 195 200	1048
atg gtg aag gca gtc atg gct cac ccg gac atg aac aac tcc tac cat Met Val Lys Ala Val Met Ala His Pro Asp Met Asn Asn Ser Tyr His 205 210 215	1096
cga cgg cag gcc cca acc ctg atc gtg cct gag cac atc aac ctg ggc Arg Arg Gln Ala Pro Thr Leu Ile Val Pro Glu His Ile Asn Leu Gly 220 225 230	1144
ctt gcc atc gac ctt cct cag aag gac ggc tcc cgc gca ctt gtc gta Leu Ala Ile Asp Leu Pro Gln Lys Asp Gly Ser Arg Ala Leu Val Val 235 240 245 250	1192
gca gcc atc aag gaa acc gag aag atg aac ttc tcc gag ttc ctc gca Ala Ala Ile Lys Glu Thr Glu Lys Met Asn Phe Ser Glu Phe Leu Ala 255 260 265	1240
gca tac gaa gac atc gtg aca cgc tcc cgc aag ggc aag ctc acc atg Ala Tyr Glu Asp Ile Val Thr Arg Ser Arg Lys Gly Lys Leu Thr Met 270 275 280	1288
gat gac tac cag ggc gtt acc gtt tcc ttg acc aac cca ggt ggc atc Asp Asp Tyr Gln Gly Val Thr Val Ser Leu Thr Asn Pro Gly Gly Ile 285 290 295	1336
ggt acc cgc cac tct gtc cca cgt ctg acc aag ggc cag ggc acc atc Gly Thr Arg His Ser Val Pro Arg Leu Thr Lys Gly Gln Gly Thr Ile 300 305 310	1384
atc ggt gtc ggt tcc atg gat tac cca gca gag ttc cag ggc gct tcc Ile Gly Val Gly Ser Met Asp Tyr Pro Ala Glu Phe Gln Gly Ala Ser 315 320 325 330	1432
gaa gac cgc ctt gca gag ctc ggc gtt gga aag ctt gtc acc atc acc Glu Asp Arg Leu Ala Glu Leu Gly Val Gly Lys Leu Val Thr Ile Thr 335 340 345	1480
tcc acc tac gat cac cgc gtg atc cag ggt gct gtg tcc ggt gaa ttc Ser Thr Tyr Asp His Arg Val Ile Gln Gly Ala Val Ser Gly Glu Phe 350 355 360	1528
ctg cgt acc atg tct cgc ctg ctc acc gat gat tcc ttc tgg gat gag Leu Arg Thr Met Ser Arg Leu Leu Thr Asp Asp Ser Phe Trp Asp Glu 365 370 375	1576

[0011]

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gac gtt cca aac acc ggt gtt gat aag aac acc cgc gtc atg cag ctc Asp Val Pro Asn Thr Gly Val Asp Lys Asn Thr Arg Val Met Gln Leu 395 400 405 410	1672
att gag gca tac cgc tcc cgt gga cac ctc atc gct gac acc aac cca Ile Glu Ala Tyr Arg Ser Arg Gly His Leu Ile Ala Asp Thr Asn Pro 415 420 425	1720
ctt tca tgg gtt cag cct ggc atg cca gtt cca gac cac cgc gac ctc Leu Ser Trp Val Gln Pro Gly Met Pro Val Pro Asp His Arg Asp Leu 430 435 440	1768
gac atc gag acc cac agc ctg acc atc tgg gat ctg gac cgt acc ttc Asp Ile Glu Thr His Ser Leu Thr Ile Trp Asp Leu Asp Arg Thr Phe 445 450 455	1816
agc gtc ggt ggc ttc ggc ggc aag gag acc atg acc ctg cgc gag gta Ser Val Gly Gly Phe Gly Lys Glu Thr Met Thr Leu Arg Glu Val 460 465 470	1864
ctg tcc cgc ctg cgc gct gcc tac acc ttg aag gtc ggc tcc gaa tac Leu Ser Arg Leu Arg Ala Ala Tyr Thr Leu Lys Val Gly Ser Glu Tyr 475 480 485 490	1912
acc cac atc ctg gac cgc gac gag cgc acc tgg ctg cag gac cgc ctc Thr His Ile Leu Asp Arg Asp Glu Arg Thr Trp Leu Gln Asp Arg Leu 495 500 505	1960
gaa gcc gga atg cca aag cca acc cag gca gag cag aag tac atc ctg Glu Ala Gly Met Pro Lys Pro Thr Gln Ala Glu Gln Lys Tyr Ile Leu 510 515 520	2008
cag aag ctg aac gcc gca gag gct ttc gag aac ttc ctg cag acc aag Gln Lys Leu Asn Ala Ala Glu Ala Phe Glu Asn Phe Leu Gln Thr Lys 525 530 535	2056
tac gtc ggc cag aag cgc ttc tcc ctc gaa ggt gca gaa gct ctc atc Tyr Val Gly Gln Lys Arg Phe Ser Leu Glu Gly Ala Glu Ala Leu Ile 540 545 550	2104
cca ctg atg gac tcc gcc atc gac acc gcc gca ggc cag ggc ctc gac Pro Leu Met Asp Ser Ala Ile Asp Thr Ala Ala Gly Gln Gly Leu Asp 555 560 565 570	2152
gaa gtt gtc atc ggt atg cca cac cgt ggt cgc ctc aac gtg ctg ttc Glu Val Val Ile Gly Met Pro His Arg Gly Arg Leu Asn Val Leu Phe 575 580 585	2200
aac atc gtg ggc aag cca ctg gca tcc atc ttc aac gag ttt gaa ggc Asn Ile Val Gly Lys Pro Leu Ala Ser Ile Phe Asn Glu Phe Glu Gly 590 595 600	2248
caa atg gag cag ggc cag atc ggt ggc tcc ggt gac gtg aag tac cac Gln Met Glu Gln Gly Gln Ile Gly Gly Ser Gly Asp Val Lys Tyr His 605 610 615	2296
ctc ggt tcc gaa ggc cag cac ctg cag atg ttc ggc gac ggc gag atc Leu Gly Ser Glu Gly Gln His Leu Gln Met Phe Gly Asp Gly Glu Ile 620 625 630	2344
aag gtc tcc ctg act gct aac ccg tcc cac ctg gaa gct gtt aac cca Lys Val Ser Leu Thr Ala Asn Pro Ser His Leu Glu Ala Val Asn Pro 635 640 645 650	2392
gtg atg gaa ggt atc gtc cgc gca aag cag gac tac ctg gac aag ggc Val Met Glu Gly Ile Val Arg Ala Lys Gln Asp Tyr Leu Asp Lys Gly 655 660 665	2440
gta gac ggc aag act gtt gtg cca ctg ctg ctc cac ggt gac gct gca Val Asp Gly Lys Thr Val Val Pro Leu Leu Leu His Gly Asp Ala Ala 670 675 680	2488
ttc gca ggc ctg ggc atc gtg cca gaa acc atc aac ctg gct aag ctg Phe Ala Gly Leu Gly Ile Val Pro Glu Thr Ile Asn Leu Ala Lys Leu 685 690 695	2536
cgt ggc tac gac gtc gga ggc acc atc cac atc gtg gtg aac aac cag Arg Gly Tyr Asp Val Gly Gly Thr Ile His Ile Val Val Asn Asn Gln 700 705 710	2584

[0012]

atc ggc ttc acc acc acc cca gac tcc agc cgc tcc atg cac tac gca Ile Gly Phe Thr Thr Thr Pro Asp Ser Ser Arg Ser Met His Tyr Ala 715 720 725 730	2632
acc gac tac gcc aag gca ttc ggc tgc cca gtc ttc cac gtc aat ggt Thr Asp Tyr Ala Lys Ala Phe Gly Cys Pro Val Phe His Val Asn Gly 735 740 745	2680
gat gac cca gag gca gtt gtc tgg gtt ggc cag ctg gca acc gag tac Asp Asp Pro Glu Ala Val Val Trp Val Gly Gln Leu Ala Thr Glu Tyr 750 755 760	2728
cgt cgt cgc ttc ggc aag gac gtc ttc atc gac ctc gtt tgc tac cgc Arg Arg Arg Phe Gly Lys Asp Val Phe Ile Asp Leu Val Cys Tyr Arg 765 770 775	2776
ctc cgc ggc cac aac gaa gct gat gat cct tcc atg acc cag cca aag Leu Arg Gly His Asn Glu Ala Asp Asp Pro Ser Met Thr Gln Pro Lys 780 785 790	2824
atg tat gag ctc atc acc ggc cgc gag acc gtt cgt gct cag tac acc Met Tyr Glu Leu Ile Thr Gly Arg Glu Thr Val Arg Ala Gln Tyr Thr 795 800 805 810	2872
gaa gac ctg ctc gga cgt gga gac ctc tcc aac gaa gat gca gaa gca Glu Asp Leu Leu Gly Arg Gly Asp Leu Ser Asn Glu Asp Ala Glu Ala 815 820 825	2920
gtc gtc cgc gac ttc cac gac cag atg gaa tct gtg ttc aac gaa gtc Val Val Arg Asp Phe His Asp Gln Met Glu Ser Val Phe Asn Glu Val 830 835 840	2968
aag gaa ggc ggc aag aag cag gct gag gca cag acc ggc atc acc ggc Lys Glu Gly Gly Lys Lys Gln Ala Glu Ala Gln Thr Gly Ile Thr Gly 845 850 855	3016
tcc cag aag ctt cca cac ggc ctt gag acc aac atc tcc cgt gaa gag Ser Gln Lys Leu Pro His Gly Leu Glu Thr Asn Ile Ser Arg Glu Glu 860 865 870	3064
ctc ctg gaa ctg gga cag gct ttc gcc aac acc cca gaa ggc ttc aac Leu Leu Glu Leu Gly Gln Ala Phe Ala Asn Thr Pro Glu Gly Phe Asn 875 880 885 890	3112
tac cac cca cgt gtg gct cca gtt gct aag aag cgc gtc tcc tct gtc Tyr His Pro Arg Val Ala Pro Val Ala Lys Lys Arg Val Ser Ser Val 895 900 905	3160
acc gaa ggt ggc atc gac tgg gca tgg ggc gag ctc ctc gcc ttc ggt Thr Glu Gly Gly Ile Asp Trp Ala Trp Gly Glu Leu Leu Ala Phe Gly 910 915 920	3208
tcc ctg gct aac tcc ggc cgc ttg gtt cgc ctt gca ggt gaa gat tcc Ser Leu Ala Asn Ser Gly Arg Leu Val Arg Leu Ala Gly Glu Asp Ser 925 930 935	3256
cgc cgc ggt acc ttc acc cag cgc cac gca gtt gcc atc gac cca cgc Arg Arg Gly Thr Phe Thr Arg His Ala Val Ala Ile Asp Pro Ala 940 945 950	3304
acc gct gaa gag ttc aac cca ctc cac gag ctt gca cag tcc aag ggc Thr Ala Glu Glu Phe Asn Pro Leu His Glu Leu Ala Gln Ser Lys Gly 955 960 965 970	3352
aac aac ggt aag ttc ctg gtc tac aac tcc gca ctg acc gag tac gca Asn Asn Gly Lys Phe Leu Val Tyr Asn Ser Ala Leu Thr Glu Tyr Ala 975 980 985	3400
ggc atg ggc ttc gag tac ggc tac tcc gta gga aac gaa gac tcc gtc Gly Met Gly Phe Glu Tyr Gly Tyr Ser Val Gly Asn Glu Asp Ser Val 990 995 1000	3448
gtt gca tgg gaa gca cag ttc ggc gac ttc gcc aac ggc gct cag Val Ala Trp Glu Ala Gln Phe Gly Asp Phe Ala Asn Gly Ala Gln 1005 1010 1015	3493
acc atc atc gat gag tac gtc tcc tca ggc gaa gct aag tgg ggc Thr Ile Ile Asp Glu Tyr Val Ser Ser Gly Glu Ala Lys Trp Gly 1020 1025 1030	3538
cag acc tcc aag ctg atc ctt ctg ctg cct cac ggc tac gaa ggc Gln Thr Ser Lys Leu Ile Leu Leu Leu Pro His Gly Tyr Glu Gly 1035 1040 1045	3583

[0013]

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Gln Gly Pro Asp His Ser Ser Ala Arg Ile Glu Arg Phe Leu Gln
1050 1055 1060
ctg tgc gct gag ggt tcc atg act gtt gct cag cca tcc acc cca 3673
Leu Cys Ala Glu Gly Ser Met Thr Val Ala Gln Pro Ser Thr Pro
1065 1070 1075
gca aac cac ttc cac ctg ctg cgt cgt cac gct ctg tcc gac ctg 3718
Ala Asn His Phe His Leu Leu Arg Arg His Ala Leu Ser Asp Leu
1080 1085 1090
aag cgt cca ctg gtt atc ttc acc ccg aag tcc atg ctg cgt aac 3763
Lys Arg Pro Leu Val Ile Phe Thr Pro Lys Ser Met Leu Arg Asn
1095 1100 1105
aag gct gct gcc tcc gca cca gaa gac ttc act gag gtc acc aag 3808
Lys Ala Ala Ala Ser Ala Pro Glu Asp Phe Thr Glu Val Thr Lys
1110 1115 1120
ttc caa tcc gtg atc gac gat cca aac gtt gca gat gca gcc aag 3853
Phe Gln Ser Val Ile Asp Asp Pro Asn Val Ala Asp Ala Ala Lys
1125 1130 1135
gtg aag aag gtc atg ctg gtc tcc gcc aag ctg tac tac gaa ttg 3898
Val Lys Lys Val Met Leu Val Ser Gly Lys Leu Tyr Tyr Glu Leu
1140 1145 1150
gca aag cgc aag gag aag gac gga cgc gac gac atc cgc atc gtt 3943
Ala Lys Arg Lys Glu Lys Asp Gly Arg Asp Asp Ile Ala Ile Val
1155 1160 1165
cgt atc gaa atg ctc cac cca att ccg ttc aac cgc atc tcc gag 3988
Arg Ile Glu Met Leu His Pro Ile Pro Phe Asn Arg Ile Ser Glu
1170 1175 1180
gct ctt gcc gcc tac cct aac gct gag gaa gtc ctc ttc gtt cag 4033
Ala Leu Ala Gly Tyr Pro Asn Ala Glu Glu Val Leu Phe Val Gln
1185 1190 1195
gat gag cca gca aac cag gcc cca tgg ccg ttc tac cag gag cac 4078
Asp Glu Pro Ala Asn Gln Gly Pro Trp Pro Phe Tyr Gln Glu His
1200 1205 1210
ctc cca gag ctg atc ccg aac atg cca aag atg cgc cgc gtt tcc 4123
Leu Pro Glu Leu Ile Pro Asn Met Pro Lys Met Arg Arg Val Ser
1215 1220 1225
cgc cgc gct cag tcc tcc acc gca act ggt gtt gct aag gtg cac 4168
Arg Arg Ala Gln Ser Ser Thr Ala Thr Gly Val Ala Lys Val His
1230 1235 1240
cag ctg gag gag aag cag ctt atc gac gag gct ttc gag gct taa 4213
Gln Leu Glu Glu Lys Gln Leu Ile Asp Glu Ala Phe Glu Ala
1245 1250 1255
gtctttatag tctgcacta gcctagagg ccttatgcag tgtgaatcac acagcataag 4273
gccctttttg ctgccgtggt tgcctaaggt ggaaggcatg aaacgaatct gtgcggtcac 4333
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Arg Val Pro Ala Val Ser Ser Ala Ser Thr Phe Gly Gln Asn Ala Trp
35 40 45
Leu Val Asp Glu Met Phe Gln Gln Phe Gln Lys Asp Pro Lys Ser Val
50 55 60
Asp Lys Glu Trp Arg Glu Leu Phe Glu Ala Gln Gly Gly Pro Asn Ala
65 70 75 80

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[0014]

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Thr Pro Ala Thr Thr Glu Ala Gln Pro Ser Ala Pro Lys Glu Ser Ala
      85                      90                      95
Lys Pro Ala Pro Lys Ala Ala Pro Ala Ala Lys Ala Ala Pro Arg Val
      100                    105                    110
Glu Thr Lys Pro Ala Ala Lys Thr Ala Pro Lys Ala Lys Glu Ser Ser
      115                    120                    125
Val Pro Gln Gln Pro Lys Leu Pro Glu Pro Gly Gln Thr Pro Ile Arg
      130                    135                    140
Gly Ile Phe Lys Ser Ile Ala Lys Asn Met Asp Ile Ser Leu Glu Ile
      145                    150                    155                    160
Pro Thr Ala Thr Ser Val Arg Asp Met Pro Ala Arg Leu Met Phe Glu
      165                    170                    175
Asn Arg Ala Met Val Asn Asp Gln Leu Lys Arg Thr Arg Gly Gly Lys
      180                    185                    190
Ile Ser Phe Thr His Ile Ile Gly Tyr Ala Met Val Lys Ala Val Met
      195                    200                    205
Ala His Pro Asp Met Asn Asn Ser Tyr His Arg Arg Gln Ala Pro Thr
      210                    215                    220
Leu Ile Val Pro Glu His Ile Asn Leu Gly Leu Ala Ile Asp Leu Pro
      225                    230                    235                    240
Gln Lys Asp Gly Ser Arg Ala Leu Val Val Ala Ala Ile Lys Glu Thr
      245                    250                    255
Glu Lys Met Asn Phe Ser Glu Phe Leu Ala Ala Tyr Glu Asp Ile Val
      260                    265                    270
Thr Arg Ser Arg Lys Gly Lys Leu Thr Met Asp Asp Tyr Gln Gly Val
      275                    280                    285
Thr Val Ser Leu Thr Asn Pro Gly Gly Ile Gly Thr Arg His Ser Val
      290                    295                    300
Pro Arg Leu Thr Lys Gly Gln Gly Thr Ile Ile Gly Val Gly Ser Met
      305                    310                    315                    320
Asp Tyr Pro Ala Glu Phe Gln Gly Ala Ser Glu Asp Arg Leu Ala Glu
      325                    330                    335
Leu Gly Val Gly Lys Leu Val Thr Ile Thr Ser Thr Tyr Asp His Arg
      340                    345                    350
Val Ile Gln Gly Ala Val Ser Gly Glu Phe Leu Arg Thr Met Ser Arg
      355                    360                    365
Leu Leu Thr Asp Asp Ser Phe Trp Asp Glu Ile Phe Asp Ala Met Asn
      370                    375                    380
Val Pro Tyr Thr Pro Met Arg Trp Ala Gln Asp Val Pro Asn Thr Gly
      385                    390                    395                    400
Val Asp Lys Asn Thr Arg Val Met Gln Leu Ile Glu Ala Tyr Arg Ser
      405                    410                    415
Arg Gly His Leu Ile Ala Asp Thr Asn Pro Leu Ser Trp Val Gln Pro
      420                    425                    430
Gly Met Pro Val Pro Asp His Arg Asp Leu Asp Ile Glu Thr His Ser
      435                    440                    445
Leu Thr Ile Trp Asp Leu Asp Arg Thr Phe Ser Val Gly Gly Phe Gly
      450                    455                    460
Gly Lys Glu Thr Met Thr Leu Arg Glu Val Leu Ser Arg Leu Arg Ala
      465                    470                    475                    480
Ala Tyr Thr Leu Lys Val Gly Ser Glu Tyr Thr His Ile Leu Asp Arg
      485                    490                    495
Asp Glu Arg Thr Trp Leu Gln Asp Arg Leu Glu Ala Gly Met Pro Lys
      500                    505                    510
Pro Thr Gln Ala Glu Gln Lys Tyr Ile Leu Gln Lys Leu Asn Ala Ala
      515                    520                    525
Glu Ala Phe Glu Asn Phe Leu Gln Thr Lys Tyr Val Gly Gln Lys Arg
      530                    535                    540
Phe Ser Leu Glu Gly Ala Glu Ala Leu Ile Pro Leu Met Asp Ser Ala
      545                    550                    555                    560
Ile Asp Thr Ala Ala Gly Gln Gly Leu Asp Glu Val Val Ile Gly Met
      565                    570                    575
Pro His Arg Gly Arg Leu Asn Val Leu Phe Asn Ile Val Gly Lys Pro

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[0015]

580	585	590
Leu Ala Ser Ile Phe Asn Glu Phe Glu Gly Gln Met Glu Gln Gly Gln		
595	600	605
Ile Gly Gly Ser Gly Asp Val Lys Tyr His Leu Gly Ser Glu Gly Gln		
610	615	620
His Leu Gln Met Phe Gly Asp Gly Glu Ile Lys Val Ser Leu Thr Ala		
625	630	635
Asn Pro Ser His Leu Glu Ala Val Asn Pro Val Met Glu Gly Ile Val		
645	650	655
Arg Ala Lys Gln Asp Tyr Leu Asp Lys Gly Val Asp Gly Lys Thr Val		
660	665	670
Val Pro Leu Leu Leu His Gly Asp Ala Ala Phe Ala Gly Leu Gly Ile		
675	680	685
Val Pro Glu Thr Ile Asn Leu Ala Lys Leu Arg Gly Tyr Asp Val Gly		
690	695	700
Gly Thr Ile His Ile Val Val Asn Asn Gln Ile Gly Phe Thr Thr Thr		
705	710	715
Pro Asp Ser Ser Arg Ser Met His Tyr Ala Thr Asp Tyr Ala Lys Ala		
725	730	735
Phe Gly Cys Pro Val Phe His Val Asn Gly Asp Asp Pro Glu Ala Val		
740	745	750
Val Trp Val Gly Gln Leu Ala Thr Glu Tyr Arg Arg Arg Phe Gly Lys		
755	760	765
Asp Val Phe Ile Asp Leu Val Cys Tyr Arg Leu Arg Gly His Asn Glu		
770	775	780
Ala Asp Asp Pro Ser Met Thr Gln Pro Lys Met Tyr Glu Leu Ile Thr		
785	790	795
Gly Arg Glu Thr Val Arg Ala Gln Tyr Thr Glu Asp Leu Leu Gly Arg		
805	810	815
Gly Asp Leu Ser Asn Glu Asp Ala Glu Ala Val Val Arg Asp Phe His		
820	825	830
Asp Gln Met Glu Ser Val Phe Asn Glu Val Lys Glu Gly Gly Lys Lys		
835	840	845
Gln Ala Glu Ala Gln Thr Gly Ile Thr Gly Ser Gln Lys Leu Pro His		
850	855	860
Gly Leu Glu Thr Asn Ile Ser Arg Glu Glu Leu Leu Glu Leu Gly Gln		
865	870	875
Ala Phe Ala Asn Thr Pro Glu Gly Phe Asn Tyr His Pro Arg Val Ala		
885	890	895
Pro Val Ala Lys Lys Arg Val Ser Ser Val Thr Glu Gly Gly Ile Asp		
900	905	910
Trp Ala Trp Gly Glu Leu Leu Ala Phe Gly Ser Leu Ala Asn Ser Gly		
915	920	925
Arg Leu Val Arg Leu Ala Gly Glu Asp Ser Arg Arg Gly Thr Phe Thr		
930	935	940
Gln Arg His Ala Val Ala Ile Asp Pro Ala Thr Ala Glu Glu Phe Asn		
945	950	955
Pro Leu His Glu Leu Ala Gln Ser Lys Gly Asn Asn Gly Lys Phe Leu		
965	970	975
Val Tyr Asn Ser Ala Leu Thr Glu Tyr Ala Gly Met Gly Phe Glu Tyr		
980	985	990
Gly Tyr Ser Val Gly Asn Glu Asp Ser Val Val Ala Trp Glu Ala Gln		
995	1000	1005
Phe Gly Asp Phe Ala Asn Gly Ala Gln Thr Ile Ile Asp Glu Tyr		
1010	1015	1020
Val Ser Ser Gly Glu Ala Lys Trp Gly Gln Thr Ser Lys Leu Ile		
1025	1030	1035
Leu Leu Leu Pro His Gly Tyr Glu Gly Gln Gly Pro Asp His Ser		
1040	1045	1050
Ser Ala Arg Ile Glu Arg Phe Leu Gln Leu Cys Ala Glu Gly Ser		
1055	1060	1065
Met Thr Val Ala Gln Pro Ser Thr Pro Ala Asn His Phe His Leu		
1070	1075	1080

[0016]

Leu Arg Arg His Ala Leu Ser Asp Leu Lys Arg Pro Leu Val Ile
 1085 1090 1095
 Phe Thr Pro Lys Ser Met Leu Arg Asn Lys Ala Ala Ala Ser Ala
 1100 1105 1110
 Pro Glu Asp Phe Thr Glu Val Thr Lys Phe Gln Ser Val Ile Asp
 1115 1120 1125
 Asp Pro Asn Val Ala Asp Ala Ala Lys Val Lys Lys Val Met Leu
 1130 1135 1140
 Val Ser Gly Lys Leu Tyr Tyr Glu Leu Ala Lys Arg Lys Glu Lys
 1145 1150 1155
 Asp Gly Arg Asp Asp Ile Ala Ile Val Arg Ile Glu Met Leu His
 1160 1165 1170
 Pro Ile Pro Phe Asn Arg Ile Ser Glu Ala Leu Ala Gly Tyr Pro
 1175 1180 1185
 Asn Ala Glu Glu Val Leu Phe Val Gln Asp Glu Pro Ala Asn Gln
 1190 1195 1200
 Gly Pro Trp Pro Phe Tyr Gln Glu His Leu Pro Glu Leu Ile Pro
 1205 1210 1215
 Asn Met Pro Lys Met Arg Arg Val Ser Arg Arg Ala Gln Ser Ser
 1220 1225 1230
 Thr Ala Thr Gly Val Ala Lys Val His Gln Leu Glu Glu Lys Gln
 1235 1240 1245
 Leu Ile Asp Glu Ala Phe Glu Ala
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 gcgcgaactg atcgcgctgg cgcgcgccga actcatcgag ccttccatca tgcttctcga 180
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 cgaccgtatt cttgtttgtg aacaaggacg tatcattgag gacggatctc acgacgcgtt 360
 gtgtctctgt aacggcacct acgcccgcat gtggcattta atggcctgac acgttatatt 420
 taggagaact gtcaacaat ta atg cta caa ctg ggg ctt agg cat aat cag 472
 Met Leu Gln Leu Gly Leu Arg His Asn Gln
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 cca acg acc aac gtt aca gtg gat aaa ata aag ctc aat aaa ccc tca 520
 Pro Thr Thr Asn Val Thr Val Asp Lys Ile Lys Leu Asn Lys Pro Ser
 15 20 25
 aga agc aag gaa aag agg cga gta cct gcc gtg agc agc gct agt act 568
 Arg Ser Lys Glu Lys Arg Arg Val Pro Ala Val Ser Ser Ala Ser Thr
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 Phe Gly Gln Asn Ala Trp Leu Val Asp Glu Met Phe Gln Gln Phe Gln
 45 50 55
 aag gac ccc aag tcc gtg gac aag gaa tgg aga gaa ctc ttt gag gcg 664
 Lys Asp Pro Lys Ser Val Asp Lys Glu Trp Arg Glu Leu Phe Glu Ala
 60 65 70
 cag ggg gga cca aat gct acc ccc gct aca aca gaa gca cag cct tca 712
 Gln Gly Gly Pro Asn Ala Thr Pro Ala Thr Thr Glu Ala Gln Pro Ser
 75 80 85 90
 gcg ccc aag gag tct gcg aaa cca gca cca aag gct gcc cct gca gcc 760

[0017]

Ala Pro Lys Glu Ser Ala Lys Pro Ala Pro Lys Ala Ala Pro Ala Ala	
95 100 105	
aag gca gca ccg cgc gta gaa acc aag ccg gcc gcc aag acc gcc cct	808
Lys Ala Ala Pro Arg Val Glu Thr Lys Pro Ala Ala Lys Thr Ala Pro	
110 115 120	
aag gcc aag gag tcc tca gtg cca cag caa cct aag ctt ccg gag cca	856
Lys Ala Lys Glu Ser Ser Val Pro Gln Gln Pro Lys Leu Pro Glu Pro	
125 130 135	
gga caa acc cca atc agg ggt att ttc aag tcc atc gcg aag aac atg	904
Gly Gln Thr Pro Ile Arg Gly Ile Phe Lys Ser Ile Ala Lys Asn Met	
140 145 150	
gat atc tcc ctg gaa atc cca acc gca acc tcg gtt cgc gat atg cca	952
Asp Ile Ser Leu Glu Ile Pro Thr Ala Thr Ser Val Arg Asp Met Pro	
155 160 165 170	
gct cgc ctc atg ttc gaa aac cgc gcg atg gtc aac gat cag ctc aag	1000
Ala Arg Leu Met Phe Glu Asn Arg Ala Met Val Asn Asp Gln Leu Lys	
175 180 185	
cgc acc cgc ggt ggc aag atc tcc ttc acc cac atc att ggc tac gcc	1048
Arg Thr Arg Gly Lys Ile Ser Phe Thr His Ile Ile Gly Tyr Ala	
190 195 200	
atg gtg aag gca gtc atg gct cac ccg gac atg aac aac tcc tac gac	1096
Met Val Lys Ala Val Met Ala His Pro Asp Met Asn Asn Ser Tyr Asp	
205 210 215	
gtc atc gac ggc aag cca acc ctg atc gtg cct gag cac atc aac ctg	1144
Val Ile Asp Gly Lys Pro Thr Leu Ile Val Pro Glu His Ile Asn Leu	
220 225 230	
ggc ctt gcc atc gac ctt cct cag aag gac ggc tcc cgc gca ctt gtc	1192
Gly Leu Ala Ile Asp Leu Pro Gln Lys Asp Gly Ser Arg Ala Leu Val	
235 240 245 250	
gta gca gcc atc aag gaa acc gag aag atg aac ttc tcc gag ttc ctc	1240
Val Ala Ala Ile Lys Glu Thr Glu Lys Met Asn Phe Ser Glu Phe Leu	
255 260 265	
gca gca tac gaa gac atc gtg aca cgc tcc cgc aag ggc aag ctc acc	1288
Ala Ala Tyr Glu Asp Ile Val Thr Arg Ser Arg Lys Gly Lys Leu Thr	
270 275 280	
atg gat gac tac cag ggc gtt acc gtt tcc ttg acc aac cca ggt ggc	1336
Met Asp Asp Tyr Gln Gly Val Thr Val Ser Leu Thr Asn Pro Gly Gly	
285 290 295	
atc ggt acc cgc cac tct gtc cca cgt ctg acc aag ggc cag ggc acc	1384
Ile Gly Thr Arg His Ser Val Pro Arg Leu Thr Lys Gly Gln Gly Thr	
300 305 310	
atc atc ggt gtc ggt tcc atg gat tac cca gca gag ttc cag ggc gct	1432
Ile Ile Gly Val Gly Ser Met Asp Tyr Pro Ala Glu Phe Gln Gly Ala	
315 320 325 330	
tcc gaa gac cgc ctt gca gag ctc ggc gtt gga aag ctt gtc acc atc	1480
Ser Glu Asp Arg Leu Ala Glu Leu Gly Val Gly Lys Leu Val Thr Ile	
335 340 345	
acc tcc acc tac gat cac cgc gtg atc cag ggt gct gtg tcc ggt gaa	1528
Thr Ser Thr Tyr Asp His Arg Val Ile Gln Gly Ala Val Ser Gly Glu	
350 355 360	
ttc ctg cgt acc atg tct cgc ctg ctc acc gat gat tcc ttc tgg gat	1576
Phe Leu Arg Thr Met Ser Arg Leu Leu Thr Asp Asp Ser Phe Trp Asp	
365 370 375	
gag atc ttc gac gca atg aac gtt cct tac acc cca atg cgt tgg gca	1624
Glu Ile Phe Asp Ala Met Asn Val Pro Tyr Thr Pro Met Arg Trp Ala	
380 385 390	
cag gac gtt cca aac acc ggt gtt gat aag aac acc cgc gtc atg cag	1672
Gln Asp Val Pro Asn Thr Gly Val Asp Lys Asn Thr Arg Val Met Gln	
395 400 405 410	
ctc att gag gca tac cgc tcc cgt gga cac ctc atc gct gac acc aac	1720
Leu Ile Glu Ala Tyr Arg Ser Arg Gly His Leu Ile Ala Asp Thr Asn	
415 420 425	
cca ctt tca tgg gtt cag cct ggc atg cca gtt cca gac cac cgc gac	1768

[0018]

Pro	Leu	Ser	Trp	Val	Gln	Pro	Gly	Met	Pro	Val	Pro	Asp	His	Arg	Asp	
			430					435					440			
ctc	gac	atc	gag	acc	cac	agc	ctg	acc	atc	tgg	gat	ctg	gac	cgt	acc	1816
Leu	Asp	Ile	Glu	Thr	His	Ser	Leu	Thr	Ile	Trp	Asp	Leu	Asp	Arg	Thr	
		445						450					455			
ttc	agc	gtc	ggc	ggc	ttc	ggc	ggc	aag	gag	acc	atg	acc	ctg	cgc	gag	1864
Phe	Ser	Val	Gly	Gly	Phe	Gly	Gly	Lys	Glu	Thr	Met	Thr	Leu	Arg	Glu	
		460						465					470			
gta	ctg	tcc	cgc	ctg	cgc	gct	gcc	tac	acc	tgg	aag	gtc	ggc	tcc	gaa	1912
Val	Leu	Ser	Arg	Leu	Arg	Ala	Ala	Tyr	Thr	Leu	Lys	Val	Gly	Ser	Glu	
		475						480					485		490	
tac	acc	cac	atc	ctg	gac	cgc	gac	gag	cgc	acc	tgg	ctg	cag	gac	cgc	1960
Tyr	Thr	His	Ile	Leu	Asp	Arg	Asp	Glu	Arg	Thr	Trp	Leu	Gln	Asp	Arg	
			495						500					505		
ctc	gaa	gcc	gga	atg	cca	aag	cca	acc	cag	gca	gag	cag	aag	tac	atc	2008
Leu	Glu	Ala	Gly	Met	Pro	Lys	Pro	Thr	Gln	Ala	Glu	Gln	Lys	Tyr	Ile	
		510							515					520		
ctg	cag	aag	ctg	aac	gcc	gca	gag	gct	ttc	gag	aac	ttc	ctg	cag	acc	2056
Leu	Gln	Lys	Leu	Asn	Ala	Ala	Glu	Ala	Phe	Glu	Asn	Phe	Leu	Gln	Thr	
		525							530					535		
aag	tac	gtc	ggc	cag	aag	cgc	ttc	tcc	ctc	gaa	ggc	gca	gaa	gct	ctc	2104
Lys	Tyr	Val	Gly	Gln	Lys	Arg	Phe	Ser	Leu	Glu	Gly	Ala	Glu	Ala	Leu	
		540							545					550		
atc	cca	ctg	atg	gac	tcc	gcc	atc	gac	acc	gcc	gca	ggc	cag	ggc	ctc	2152
Ile	Pro	Leu	Met	Asp	Ser	Ala	Ile	Asp	Thr	Ala	Ala	Gly	Gln	Gly	Leu	
		555												560		
gac	gaa	gtt	gtc	atc	ggc	atg	cca	cac	cgt	ggc	cgc	ctc	aac	gtg	ctg	2200
Asp	Glu	Val	Val	Ile	Gly	Met	Pro	His	Arg	Gly	Arg	Leu	Asn	Val	Leu	
			575						580					585		
ttc	aac	atc	gtg	ggc	aag	cca	ctg	gca	tcc	atc	ttc	aac	gag	ttt	gaa	2248
Phe	Asn	Ile	Val	Gly	Lys	Pro	Leu	Ala	Ser	Ile	Phe	Asn	Glu	Phe	Glu	
			590						595					600		
ggc	caa	atg	gag	cag	ggc	cag	atc	ggc	ggc	tcc	ggc	gac	gtg	aag	tac	2296
Gly	Gln	Met	Glu	Gln	Gly	Gln	Ile	Gly	Gly	Ser	Gly	Asp	Val	Lys	Tyr	
		605							610					615		
cac	ctc	ggc	tcc	gaa	ggc	cag	cac	ctg	cag	atg	ttc	ggc	gac	ggc	gag	2344
His	Leu	Gly	Ser	Glu	Gly	Gln	His	Leu	Gln	Met	Phe	Gly	Asp	Gly	Glu	
		620							625					630		
atc	aag	gtc	tcc	ctg	act	gct	aac	cgc	tcc	cac	ctg	gaa	gct	gtt	aac	2392
Ile	Lys	Val	Ser	Leu	Thr	Ala	Asn	Pro	Ser	His	Leu	Glu	Ala	Val	Asn	
		635												640		
cca	gtg	atg	gaa	ggc	atc	gtc	cgc	gca	aag	cag	gac	tac	ctg	gac	aag	2440
Pro	Val	Met	Glu	Gly	Ile	Val	Arg	Ala	Lys	Gln	Asp	Tyr	Leu	Asp	Lys	
			655						660					665		
ggc	gta	gac	ggc	aag	act	gtt	gtg	cca	ctg	ctg	ctc	cac	ggc	gac	gct	2488
Gly	Val	Asp	Gly	Lys	Thr	Val	Val	Pro	Leu	Leu	Leu	His	Gly	Asp	Ala	
		670							675					680		
gca	ttc	gca	ggc	ctg	ggc	atc	gtg	cca	gaa	acc	atc	aac	ctg	gct	aag	2536
Ala	Phe	Ala	Gly	Leu	Gly	Ile	Val	Pro	Glu	Thr	Ile	Asn	Leu	Ala	Lys	
		685							690					695		
cgc	gtc	gac	gtc	gga	ggc	acc	atc	cac	atc	gtg	gtg	aac	aac	cag	atc	2584
Arg	Val	Asp	Val	Gly	Gly	Thr	Ile	His	Ile	Val	Val	Asn	Asn	Gln	Ile	
		700							705					710		
ggc	ttc	acc	acc	acc	cca	gac	tcc	agc	cgc	tcc	atg	cac	tac	gca	acc	2632
Gly	Phe	Thr	Thr	Thr	Pro	Asp	Ser	Ser	Arg	Ser	Met	His	Tyr	Ala	Thr	
		715							720					725		
gac	tac	gcc	aag	gca	ttc	ggc	tgc	cca	gtc	ttc	cac	gtc	aac	ggt	gat	2680
Asp	Tyr	Ala	Lys	Ala	Phe	Gly	Cys	Pro	Val	Phe	His	Val	Asn	Gly	Asp	
		735							740					745		
gac	cca	gag	gca	gtt	gtc	tgg	gtt	ggc	cag	ctg	gca	acc	gag	tac	cgt	2728
Asp	Pro	Glu	Ala	Val	Val	Trp	Val	Gly	Gln	Leu	Ala	Thr	Glu	Tyr	Arg	
		750							755					760		
cgt	cgc	ttc	ggc	aag	gac	gtc	ttc	atc	gac	ctc	gtt	tgc	tac	cgc	ctc	2776

[0019]

Arg Arg Phe Gly Lys Asp Val Phe Ile Asp Leu Val Cys Tyr Arg Leu	
765 770 775	
cgc ggc cac aac gaa gct gat gat cct tcc atg acc cag cca aag atg	2824
Arg Gly His Asn Glu Ala Asp Asp Pro Ser Met Thr Gln Pro Lys Met	
780 785 790	
tat gag ctc atc acc ggc cgc gag acc gtt cgt gct cag tac acc gaa	2872
Tyr Glu Leu Ile Thr Gly Arg Glu Thr Val Arg Ala Gln Tyr Thr Glu	
795 800 805 810	
gac ctg ctc gga cgt gga gac ctc tcc aac gaa gat gca gaa gca gtc	2920
Asp Leu Leu Gly Arg Gly Asp Leu Ser Asn Glu Asp Ala Glu Ala Val	
815 820 825	
gtc cgc gac ttc cac gac cag atg gaa tct gtg ttc aac gaa gtc aag	2968
Val Arg Asp Phe His Asp Gln Met Glu Ser Val Phe Asn Glu Val Lys	
830 835 840	
gaa ggc ggc aag aag cag gct gag gca cag acc ggc atc acc ggc tcc	3016
Glu Gly Gly Lys Lys Gln Ala Glu Ala Gln Thr Gly Ile Thr Gly Ser	
845 850 855	
cag aag ctt cca cac ggc ctt gag acc aac atc tcc cgt gaa gag ctc	3064
Gln Lys Leu Pro His Gly Leu Glu Thr Asn Ile Ser Arg Glu Glu Leu	
860 865 870	
ctg gaa ctg gga cag gct ttc gcc aac acc cca gaa ggc ttc aac tac	3112
Leu Glu Leu Gly Gln Ala Phe Ala Asn Thr Pro Glu Gly Phe Asn Tyr	
875 880 885 890	
cac cca cgt gtg gct cca gtt gct aag aag cgc gtc tcc tct gtc acc	3160
His Pro Arg Val Ala Pro Val Ala Lys Lys Arg Val Ser Ser Val Thr	
895 900 905	
gaa ggt ggc atc gac tgg gca tgg ggc gag ctc ctc gcc ttc ggt tcc	3208
Glu Gly Gly Ile Asp Trp Ala Trp Gly Glu Leu Leu Ala Phe Gly Ser	
910 915 920	
ctg gct aac tcc ggc cgc ttg gtt cgc ctt gca ggt gaa gat tcc cgc	3256
Leu Ala Asn Ser Gly Arg Leu Val Arg Leu Ala Gly Glu Asp Ser Arg	
925 930 935	
cgc ggt acc ttc acc cag cgc cac gca gtt gcc atc gac cca gcg acc	3304
Arg Gly Thr Phe Thr Gln Arg His Ala Val Ala Ile Asp Pro Ala Thr	
940 945 950	
gct gaa gag ttc aac cca ctc cac gag ctt gca cag tcc aag ggc aac	3352
Ala Glu Glu Phe Asn Pro Leu His Glu Leu Ala Gln Ser Lys Gly Asn	
955 960 965 970	
aac ggt aag ttc ctg gtc tac aac tcc gca ctg acc gag tac gca ggc	3400
Asn Gly Lys Phe Leu Val Tyr Asn Ser Ala Leu Thr Glu Tyr Ala Gly	
975 980 985	
atg ggc ttc gag tac ggc tac tcc gta gga aac gaa gac tcc gtc gtt	3448
Met Gly Phe Glu Tyr Gly Tyr Ser Val Gly Asn Glu Asp Ser Val Val	
990 995 1000	
gca tgg gaa gca cag ttc ggc gac ttc gcc aac ggc gct cag acc	3493
Ala Trp Glu Ala Gln Phe Gly Asp Phe Ala Asn Gly Ala Gln Thr	
1005 1010 1015	
atc atc gat gag tac gtc tcc tca ggc gaa gct aag tgg ggc cag	3538
Ile Ile Asp Glu Tyr Val Ser Ser Gly Glu Ala Lys Trp Gly Gln	
1020 1025 1030	
acc tcc aag ctg atc ctt ctg ctg cct cac ggc tac gaa ggc cag	3583
Thr Ser Lys Leu Ile Leu Leu Leu Pro His Gly Tyr Glu Gly Gln	
1035 1040 1045	
ggc cca gac cac tct tcc gca cgt atc gag cgc ttc ctg cag ctg	3628
Gly Pro Asp His Ser Ser Ala Arg Ile Glu Arg Phe Leu Gln Leu	
1050 1055 1060	
tgc gct gag ggt tcc atg act gtt gct cag cca tcc acc cca gca	3673
Cys Ala Glu Gly Ser Met Thr Val Ala Gln Pro Ser Thr Pro Ala	
1065 1070 1075	
aac cac ttc cac ctg ctg cgt cgt cac gct ctg tcc gac ctg aag	3718
Asn His Phe His Leu Leu Arg Arg His Ala Leu Ser Asp Leu Lys	
1080 1085 1090	
cgt cca ctg gtt atc ttc acc ccg aag tcc atg ctg cgt aac aag	3763

[0020]

Arg Pro Leu Val Ile Phe Thr Pro Lys Ser Met Leu Arg Asn Lys	
1095 1100 1105	
gct gct gcc tcc gca cca gaa gac ttc act gag gtc acc aag ttc	3808
Ala Ala Ala Ser Ala Pro Glu Asp Phe Thr Glu Val Thr Lys Phe	
1110 1115 1120	
caa tcc gtg atc gac gat cca aac gtt gca gat gca gcc aag gtg	3853
Gln Ser Val Ile Asp Asp Pro Asn Val Ala Asp Ala Ala Lys Val	
1125 1130 1135	
aag aag gtc atg ctg gtc tcc ggc aag ctg tac tac gaa ttg gca	3898
Lys Lys Val Met Leu Val Ser Gly Lys Leu Tyr Tyr Glu Leu Ala	
1140 1145 1150	
aag cgc aag gag aag gac gga cgc gac gac atc gcg atc gtt cgt	3943
Lys Arg Lys Glu Lys Asp Gly Arg Asp Asp Ile Ala Ile Val Arg	
1155 1160 1165	
atc gaa atg ctc cac cca att ccg ttc aac cgc atc tcc gag gct	3988
Ile Glu Met Leu His Pro Ile Pro Phe Asn Arg Ile Ser Glu Ala	
1170 1175 1180	
ctt gcc ggc tac cct aac gct gag gaa gtc ctc ttc gtt cag gat	4033
Leu Ala Gly Tyr Pro Asn Ala Glu Glu Val Leu Phe Val Gln Asp	
1185 1190 1195	
gag cca gca aac cag ggc cca tgg ccg ttc tac cag gag cac ctc	4078
Glu Pro Ala Asn Gln Gly Pro Trp Pro Phe Tyr Gln Glu His Leu	
1200 1205 1210	
cca gag ctg atc ccg aac atg cca aag atg cgc cgc gtt tcc cgc	4123
Pro Glu Leu Ile Pro Asn Met Pro Lys Met Arg Arg Val Ser Arg	
1215 1220 1225	
cgc gct cag tcc tcc acc gca act ggt gtt gct aag gtg cac cag	4168
Arg Ala Gln Ser Ser Thr Ala Thr Gly Val Ala Lys Val His Gln	
1230 1235 1240	
ctg gag gag aag cag ctt atc gac gag gct ttc gag gct taa gtc	4213
Leu Glu Glu Lys Gln Leu Ile Asp Glu Ala Phe Glu Ala Val	
1245 1250 1255	
tttatagtc tgcactagcc tagagggcct tatgcagtgt gaatacacaca gcataaggcc	4273
ctttttgctg ccgtggttgc ctaaggtgga aggcatagaaa cgaatctgtg cggtcacgat	4333
ctcttcagta cttttgctaa gtggctgctc ctccacttcc accacgcagc tcgag	4388

<210> 14
 <211> 1255
 <212> PRT
 <213> 谷氨酸棒杆菌

<400> 14
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 1 5 10 15
 Val Asp Lys Ile Lys Leu Asn Lys Pro Ser Arg Ser Lys Glu Lys Arg
 20 25 30
 Arg Val Pro Ala Val Ser Ser Ala Ser Thr Phe Gly Gln Asn Ala Trp
 35 40 45
 Leu Val Asp Glu Met Phe Gln Gln Phe Gln Lys Asp Pro Lys Ser Val
 50 55 60
 Asp Lys Glu Trp Arg Glu Leu Phe Glu Ala Gln Gly Gly Pro Asn Ala
 65 70 75 80
 Thr Pro Ala Thr Thr Glu Ala Gln Pro Ser Ala Pro Lys Glu Ser Ala
 85 90 95
 Lys Pro Ala Pro Lys Ala Ala Pro Ala Ala Lys Ala Ala Pro Arg Val
 100 105 110
 Glu Thr Lys Pro Ala Ala Lys Thr Ala Pro Lys Ala Lys Glu Ser Ser
 115 120 125
 Val Pro Gln Gln Pro Lys Leu Pro Glu Pro Gly Gln Thr Pro Ile Arg
 130 135 140
 Gly Ile Phe Lys Ser Ile Ala Lys Asn Met Asp Ile Ser Leu Glu Ile
 145 150 155 160

[0021]

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Pro Thr Ala Thr Ser Val Arg Asp Met Pro Ala Arg Leu Met Phe Glu
      165      170      175
Asn Arg Ala Met Val Asn Asp Gln Leu Lys Arg Thr Arg Gly Gly Lys
      180      185      190
Ile Ser Phe Thr His Ile Ile Gly Tyr Ala Met Val Lys Ala Val Met
      195      200      205
Ala His Pro Asp Met Asn Asn Ser Tyr Asp Val Ile Asp Gly Lys Pro
      210      215      220
Thr Leu Ile Val Pro Glu His Ile Asn Leu Gly Leu Ala Ile Asp Leu
      225      230      235      240
Pro Gln Lys Asp Gly Ser Arg Ala Leu Val Val Ala Ala Ile Lys Glu
      245      250      255
Thr Glu Lys Met Asn Phe Ser Glu Phe Leu Ala Ala Tyr Glu Asp Ile
      260      265      270
Val Thr Arg Ser Arg Lys Gly Lys Leu Thr Met Asp Asp Tyr Gln Gly
      275      280      285
Val Thr Val Ser Leu Thr Asn Pro Gly Gly Ile Gly Thr Arg His Ser
      290      295      300
Val Pro Arg Leu Thr Lys Gly Gln Gly Thr Ile Ile Gly Val Gly Ser
      305      310      315      320
Met Asp Tyr Pro Ala Glu Phe Gln Gly Ala Ser Glu Asp Arg Leu Ala
      325      330      335
Glu Leu Gly Val Gly Lys Leu Val Thr Ile Thr Ser Thr Tyr Asp His
      340      345      350
Arg Val Ile Gln Gly Ala Val Ser Gly Glu Phe Leu Arg Thr Met Ser
      355      360      365
Arg Leu Leu Thr Asp Asp Ser Phe Trp Asp Glu Ile Phe Asp Ala Met
      370      375      380
Asn Val Pro Tyr Thr Pro Met Arg Trp Ala Gln Asp Val Pro Asn Thr
      385      390      395      400
Gly Val Asp Lys Asn Thr Arg Val Met Gln Leu Ile Glu Ala Tyr Arg
      405      410      415
Ser Arg Gly His Leu Ile Ala Asp Thr Asn Pro Leu Ser Trp Val Gln
      420      425      430
Pro Gly Met Pro Val Pro Asp His Arg Asp Leu Asp Ile Glu Thr His
      435      440      445
Ser Leu Thr Ile Trp Asp Leu Asp Arg Thr Phe Ser Val Gly Gly Phe
      450      455      460
Gly Gly Lys Glu Thr Met Thr Leu Arg Glu Val Leu Ser Arg Leu Arg
      465      470      475      480
Ala Ala Tyr Thr Leu Lys Val Gly Ser Glu Tyr Thr His Ile Leu Asp
      485      490      495
Arg Asp Glu Arg Thr Trp Leu Gln Asp Arg Leu Glu Ala Gly Met Pro
      500      505      510
Lys Pro Thr Gln Ala Glu Gln Lys Tyr Ile Leu Gln Lys Leu Asn Ala
      515      520      525
Ala Glu Ala Phe Glu Asn Phe Leu Gln Thr Lys Tyr Val Gly Gln Lys
      530      535      540
Arg Phe Ser Leu Glu Gly Ala Glu Ala Leu Ile Pro Leu Met Asp Ser
      545      550      555      560
Ala Ile Asp Thr Ala Ala Gly Gln Gly Leu Asp Glu Val Val Ile Gly
      565      570      575
Met Pro His Arg Gly Arg Leu Asn Val Leu Phe Asn Ile Val Gly Lys
      580      585      590
Pro Leu Ala Ser Ile Phe Asn Glu Phe Glu Gly Gln Met Glu Gln Gly
      595      600      605
Gln Ile Gly Gly Ser Gly Asp Val Lys Tyr His Leu Gly Ser Glu Gly
      610      615      620
Gln His Leu Gln Met Phe Gly Asp Gly Glu Ile Lys Val Ser Leu Thr
      625      630      635      640
Ala Asn Pro Ser His Leu Glu Ala Val Asn Pro Val Met Glu Gly Ile
      645      650      655
Val Arg Ala Lys Gln Asp Tyr Leu Asp Lys Gly Val Asp Gly Lys Thr

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[0022]

660	665	670
Val Val Pro Leu Leu Leu His Gly Asp Ala Ala Phe Ala Gly Leu Gly		
675	680	685
Ile Val Pro Glu Thr Ile Asn Leu Ala Lys Arg Val Asp Val Gly Gly		
690	695	700
Thr Ile His Ile Val Val Asn Asn Gln Ile Gly Phe Thr Thr Thr Pro		
705	710	715
Asp Ser Ser Arg Ser Met His Tyr Ala Thr Asp Tyr Ala Lys Ala Phe		
725	730	735
Gly Cys Pro Val Phe His Val Asn Gly Asp Asp Pro Glu Ala Val Val		
740	745	750
Trp Val Gly Gln Leu Ala Thr Glu Tyr Arg Arg Arg Phe Gly Lys Asp		
755	760	765
Val Phe Ile Asp Leu Val Cys Tyr Arg Leu Arg Gly His Asn Glu Ala		
770	775	780
Asp Asp Pro Ser Met Thr Gln Pro Lys Met Tyr Glu Leu Ile Thr Gly		
785	790	795
Arg Glu Thr Val Arg Ala Gln Tyr Thr Glu Asp Leu Leu Gly Arg Gly		
805	810	815
Asp Leu Ser Asn Glu Asp Ala Glu Ala Val Val Arg Asp Phe His Asp		
820	825	830
Gln Met Glu Ser Val Phe Asn Glu Val Lys Glu Gly Gly Lys Lys Gln		
835	840	845
Ala Glu Ala Gln Thr Gly Ile Thr Gly Ser Gln Lys Leu Pro His Gly		
850	855	860
Leu Glu Thr Asn Ile Ser Arg Glu Glu Leu Leu Glu Leu Gly Gln Ala		
865	870	875
Phe Ala Asn Thr Pro Glu Gly Phe Asn Tyr His Pro Arg Val Ala Pro		
885	890	895
Val Ala Lys Lys Arg Val Ser Ser Val Thr Glu Gly Gly Ile Asp Trp		
900	905	910
Ala Trp Gly Glu Leu Leu Ala Phe Gly Ser Leu Ala Asn Ser Gly Arg		
915	920	925
Leu Val Arg Leu Ala Gly Glu Asp Ser Arg Arg Gly Thr Phe Thr Gln		
930	935	940
Arg His Ala Val Ala Ile Asp Pro Ala Thr Ala Glu Glu Phe Asn Pro		
945	950	955
Leu His Glu Leu Ala Gln Ser Lys Gly Asn Asn Gly Lys Phe Leu Val		
965	970	975
Tyr Asn Ser Ala Leu Thr Glu Tyr Ala Gly Met Gly Phe Glu Tyr Gly		
980	985	990
Tyr Ser Val Gly Asn Glu Asp Ser Val Val Ala Trp Glu Ala Gln Phe		
995	1000	1005
Gly Asp Phe Ala Asn Gly Ala Gln Thr Ile Ile Asp Glu Tyr Val		
1010	1015	1020
Ser Ser Gly Glu Ala Lys Trp Gly Gln Thr Ser Lys Leu Ile Leu		
1025	1030	1035
Leu Leu Pro His Gly Tyr Glu Gly Gln Gly Pro Asp His Ser Ser		
1040	1045	1050
Ala Arg Ile Glu Arg Phe Leu Gln Leu Cys Ala Glu Gly Ser Met		
1055	1060	1065
Thr Val Ala Gln Pro Ser Thr Pro Ala Asn His Phe His Leu Leu		
1070	1075	1080
Arg Arg His Ala Leu Ser Asp Leu Lys Arg Pro Leu Val Ile Phe		
1085	1090	1095
Thr Pro Lys Ser Met Leu Arg Asn Lys Ala Ala Ala Ser Ala Pro		
1100	1105	1110
Glu Asp Phe Thr Glu Val Thr Lys Phe Gln Ser Val Ile Asp Asp		
1115	1120	1125
Pro Asn Val Ala Asp Ala Ala Lys Val Lys Lys Val Met Leu Val		
1130	1135	1140
Ser Gly Lys Leu Tyr Tyr Glu Leu Ala Lys Arg Lys Glu Lys Asp		
1145	1150	1155

[0023]

Gly Arg Asp Asp Ile Ala Ile Val Arg Ile Glu Met Leu His Pro
 1160 1165 1170
 Ile Pro Phe Asn Arg Ile Ser Glu Ala Leu Ala Gly Tyr Pro Asn
 1175 1180 1185
 Ala Glu Glu Val Leu Phe Val Gln Asp Glu Pro Ala Asn Gln Gly
 1190 1195 1200
 Pro Trp Pro Phe Tyr Gln Glu His Leu Pro Glu Leu Ile Pro Asn
 1205 1210 1215
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 ggcgcaactg atcgcgctgg cgcgcgcgga actcatcgag ccttccatca tgcttctcga 180
 cgaagccacc tccaccctcg accccgccac cgaagccgtt atcctcaacg cctccgatcg 240
 agtcactaag ggacgcacca gcatcatcgt cgcgcaccgc ttggcaaccg ctaaaagggc 300
 cgaccgtatt ctgtgtgttg aacaaggacg tatcattgag gacggatctc acgacgcgtt 360
 gttgtctgct aacggcacct acgcccgcat gtggcattta atggcctgac acgttatatt 420
 taggagaact gtcaacaaat ta atg cta caa ctg ggg ctt agg cat aat cag 472
 Met Leu Gln Leu Gly Leu Arg His Asn Gln
 1 5 10
 cca acg acc aac gtt aca gtg gat aaa ata aag ctc aat aaa ccc tca 520
 Pro Thr Thr Asn Val Thr Val Asp Lys Ile Lys Leu Asn Lys Pro Ser
 15 20 25
 aga agc aag gaa aag agg cga gta cct gcc gtg agc agc gct agt act 568
 Arg Ser Lys Glu Lys Arg Arg Val Pro Ala Val Ser Ser Ala Ser Thr
 30 35 40
 ttc ggc cag aat gcg tgg ctg gta gac gag atg ttc cag cag ttc cag 616
 Phe Gly Gln Asn Ala Trp Leu Val Asp Glu Met Phe Gln Gln Phe Gln
 45 50 55
 aag gac ccc aag tcc gtg gac aag gaa tgg aga gaa ctc ttt gag gcg 664
 Lys Asp Pro Lys Ser Val Asp Lys Glu Trp Arg Glu Leu Phe Glu Ala
 60 65 70
 cag ggg gga cca aat gct acc ccc gct aca aca gaa gca cag cct tca 712
 Gln Gly Gly Pro Asn Ala Thr Pro Ala Thr Thr Glu Ala Gln Pro Ser
 75 80 85 90
 gcg ccc aag gag tct gcg aaa cca gca cca aag gct gcc cct gca gcc 760
 Ala Pro Lys Glu Ser Ala Lys Pro Ala Pro Lys Ala Ala Pro Ala Ala
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 aag gca gca ccg cgc gta gaa acc aag ccg gcc gcc aag acc gcc cct 808
 Lys Ala Ala Pro Arg Val Glu Thr Lys Pro Ala Ala Lys Thr Ala Pro
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 aag gcc aag gag tcc tca gtg cca cag caa cct aag ctt ccg gag cca 856
 Lys Ala Lys Glu Ser Ser Val Pro Gln Gln Pro Lys Leu Pro Glu Pro
 125 130 135
 gga caa acc cca atc agg ggt att ttc aag tcc atc gcg aag aac atg 904
 Gly Gln Thr Pro Ile Arg Gly Ile Phe Lys Ser Ile Ala Lys Asn Met
 140 145 150

[0024]

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Asp Ile Ser Leu Glu Ile Pro Thr Ala Thr Ser Val Arg Asp Met Pro	
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Ala Arg Leu Met Phe Glu Asn Arg Ala Met Val Asn Asp Gln Leu Lys	
175 180 185	
cgc acc cgc ggt ggc aag atc tcc ttc acc cac atc att ggc tac gcc	1048
Arg Thr Arg Gly Lys Ile Ser Phe Thr His Ile Ile Gly Tyr Ala	
190 195 200	
atg gtg aag gca gtc atg gct cac ccg gac atg aac aac tcc tac cat	1096
Met Val Lys Ala Val Met Ala His Pro Asp Met Asn Asn Ser Tyr His	
205 210 215	
cga cgg cag gcc cca acc ctg atc gtg cct gag cac atc aac ctg ggc	1144
Arg Arg Gln Ala Pro Thr Leu Ile Val Pro Glu His Ile Asn Leu Gly	
220 225 230	
ctt gcc atc gac ctt cct cag aag gac ggc tcc cgc gca ctt gtc gta	1192
Leu Ala Ile Asp Leu Pro Gln Lys Asp Gly Ser Arg Ala Leu Val Val	
235 240 245 250	
gca gcc atc aag gaa acc gag aag atg aac ttc tcc gag ttc ctc gca	1240
Ala Ala Ile Lys Glu Thr Glu Lys Met Asn Phe Ser Glu Phe Leu Ala	
255 260 265	
gca tac gaa gac atc gtg aca cgc tcc cgc aag ggc aag ctc acc atg	1288
Ala Tyr Glu Asp Ile Val Thr Arg Ser Arg Lys Gly Lys Leu Thr Met	
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gat gac tac cag ggc gtt acc gtt tcc ttg acc aac cca ggt ggc atc	1336
Asp Asp Tyr Gln Gly Val Thr Val Ser Leu Thr Asn Pro Gly Gly Ile	
285 290 295	
ggt acc cgc cac tct gtc cca cgt ctg acc aag ggc cag ggc acc atc	1384
Gly Thr Arg His Ser Val Pro Arg Leu Thr Lys Gly Gln Gly Thr Ile	
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atc ggt gtc ggt tcc atg gat tac cca gca gag ttc cag ggc gct tcc	1432
Ile Gly Val Gly Ser Met Asp Tyr Pro Ala Glu Phe Gln Gly Ala Ser	
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gaa gac cgc ctt gca gag ctc ggc gtt gga aag ctt gtc acc atc acc	1480
Glu Asp Arg Leu Ala Glu Leu Gly Val Gly Lys Leu Val Thr Ile Thr	
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tcc acc tac gat cac cgc gtg atc cag ggt gct gtg tcc ggt gaa ttc	1528
Ser Thr Tyr Asp His Arg Val Ile Gln Gly Ala Val Ser Gly Glu Phe	
350 355 360	
ctg cgt acc atg tct cgc ctg ctc acc gat gat tcc ttc tgg gat gag	1576
Leu Arg Thr Met Ser Arg Leu Leu Thr Asp Asp Ser Phe Trp Asp Glu	
365 370 375	
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Ile Phe Asp Ala Met Asn Val Pro Tyr Thr Pro Met Arg Trp Ala Gln	
380 385 390	
gac gtt cca aac acc ggt gtt gat aag aac acc cgc gtc atg cag ctc	1672
Asp Val Pro Asn Thr Gly Val Asp Lys Asn Thr Arg Val Met Gln Leu	
395 400 405 410	
att gag gca tac cgc tcc cgt gga cac ctc atc gct gac acc aac cca	1720
Ile Glu Ala Tyr Arg Ser Arg Gly His Leu Ile Ala Asp Thr Asn Pro	
415 420 425	
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Leu Ser Trp Val Gln Pro Gly Met Pro Val Pro Asp His Arg Asp Leu	
430 435 440	
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Asp Ile Glu Thr His Ser Leu Thr Ile Trp Asp Leu Asp Arg Thr Phe	
445 450 455	
agc gtc ggt ggc ttc ggc ggc aag gag acc atg acc ctg cgc gag gta	1864
Ser Val Gly Gly Phe Gly Gly Lys Glu Thr Met Thr Leu Arg Glu Val	
460 465 470	
ctg tcc cgc ctg cgc gct gcc tac acc ttg aag gtc ggc tcc gaa tac	1912
Leu Ser Arg Leu Arg Ala Ala Tyr Thr Leu Lys Val Gly Ser Glu Tyr	
475 480 485 490	

[0025]

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Thr His Ile Leu Asp Arg Asp Glu Arg Thr Trp Leu Gln Asp Arg Leu	
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gaa gcc gga atg cca aag cca acc cag gca gag cag aag tac atc ctg	2008
Glu Ala Gly Met Pro Lys Pro Thr Gln Ala Glu Gln Lys Tyr Ile Leu	
510 515 520	
cag aag ctg aac gcc gca gag gct ttc gag aac ttc ctg cag acc aag	2056
Gln Lys Leu Asn Ala Ala Glu Ala Phe Glu Asn Phe Leu Gln Thr Lys	
525 530 535	
tac gtc ggc cag aag cgc ttc tcc ctc gaa ggt gca gaa gct ctc atc	2104
Tyr Val Gly Gln Lys Arg Phe Ser Leu Glu Gly Ala Glu Ala Leu Ile	
540 545 550	
cca ctg atg gac tcc gcc atc gac acc gcc gca ggc cag ggc ctc gac	2152
Pro Leu Met Asp Ser Ala Ile Asp Thr Ala Ala Gly Gln Gly Leu Asp	
555 560 565 570	
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Glu Val Val Ile Gly Met Pro His Arg Gly Arg Leu Asn Val Leu Phe	
575 580 585	
aac atc gtg ggc aag cca ctg gca tcc atc ttc aac gag ttt gaa ggc	2248
Asn Ile Val Gly Lys Pro Leu Ala Ser Ile Phe Asn Glu Phe Glu Gly	
590 595 600	
caa atg gag cag ggc cag atc ggt ggc tcc ggt gac gtg aag tac cac	2296
Gln Met Glu Gln Gly Gln Ile Gly Gly Ser Gly Asp Val Lys Tyr His	
605 610 615	
ctc ggt tcc gaa ggc cag cac ctg cag atg ttc ggc gac ggc gag atc	2344
Leu Gly Ser Glu Gly Gln His Leu Gln Met Phe Gly Asp Gly Glu Ile	
620 625 630	
aag gtc tcc ctg act gct aac ccg tcc cac ctg gaa gct gtt aac cca	2392
Lys Val Ser Leu Thr Ala Asn Pro Ser His Leu Glu Ala Val Asn Pro	
635 640 645 650	
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Val Met Glu Gly Ile Val Arg Ala Lys Gln Asp Tyr Leu Asp Lys Gly	
655 660 665	
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Val Asp Gly Lys Thr Val Val Pro Leu Leu Leu His Gly Asp Ala Ala	
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Phe Ala Gly Leu Gly Ile Val Pro Glu Thr Ile Asn Leu Ala Lys Arg	
685 690 695	
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Val Asp Val Gly Gly Thr Ile His Ile Val Val Asn Asn Gln Ile Gly	
700 705 710	
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Phe Thr Thr Thr Pro Asp Ser Ser Arg Ser Met His Tyr Ala Thr Asp	
715 720 725 730	
tac gcc aag gca ttc ggc tgc cca gtc ttc cac gtc aat ggt gat gac	2680
Tyr Ala Lys Ala Phe Gly Cys Pro Val Phe His Val Asn Gly Asp Asp	
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Pro Glu Ala Val Val Trp Val Gly Gln Leu Ala Thr Glu Tyr Arg Arg	
750 755 760	
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Arg Phe Gly Lys Asp Val Phe Ile Asp Leu Val Cys Tyr Arg Leu Arg	
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Gly His Asn Glu Ala Asp Asp Pro Ser Met Thr Gln Pro Lys Met Tyr	
780 785 790	
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Glu Leu Ile Thr Gly Arg Glu Thr Val Arg Ala Gln Tyr Thr Glu Asp	
795 800 805 810	
ctg ctc gga cgt gga gac ctc tcc aac gaa gat gca gaa gca gtc gtc	2920
Leu Leu Gly Arg Gly Asp Leu Ser Asn Glu Asp Ala Glu Ala Val Val	
815 820 825	

[0026]

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ggc ggc aag aag cag gct gag gca cag acc ggc atc acc ggc tcc cag Gly Gly Lys Lys Gln Ala Glu Ala Gln Thr Gly Ile Thr Gly Ser Gln 845 850 855	3016
aag ctt cca cac ggc ctt gag acc aac atc tcc cgt gaa gag ctc ctg Lys Leu Pro His Gly Leu Glu Thr Asn Ile Ser Arg Glu Glu Leu Leu 860 865 870	3064
gaa ctg gga cag gct ttc gcc aac acc cca gaa ggc ttc aac tac cac Glu Leu Gly Gln Ala Phe Ala Asn Thr Pro Glu Gly Phe Asn Tyr His 875 880 885 890	3112
cca cgt gtg gct cca gtt gct aag aag cgc gtc tcc tct gtc acc gaa Pro Arg Val Ala Pro Val Ala Lys Lys Arg Val Ser Ser Val Thr Glu 895 900 905	3160
ggc ggc atc gac tgg gca tgg ggc gag ctc ctc gcc ttc ggt tcc ctg Gly Gly Ile Asp Trp Ala Trp Gly Glu Leu Leu Ala Phe Gly Ser Leu 910 915 920	3208
gct aac tcc ggc cgc ttg gtt cgc ctt gca ggt gaa gat tcc cgc cgc Ala Asn Ser Gly Arg Leu Val Arg Leu Ala Gly Glu Asp Ser Arg Arg 925 930 935	3256
ggt acc ttc acc cag cgc cac gca gtt gcc atc gac cca gcg acc gct Gly Thr Phe Thr Gln Arg His Ala Val Ala Ile Asp Pro Ala Thr Ala 940 945 950	3304
gaa gag ttc aac cca ctc cac gag ctt gca cag tcc aag ggc aac aac Glu Glu Phe Asn Pro Leu His Glu Leu Ala Gln Ser Lys Gly Asn Asn 955 960 965 970	3352
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cca gac cac tct tcc gca cgt atc gag cgc ttc ctg cag ctg tgc Pro Asp His Ser Ser Ala Arg Ile Glu Arg Phe Leu Gln Leu Cys 1050 1055 1060	3628
gct gag ggt tcc atg act gtt gct cag cca tcc acc cca gca aac Ala Glu Gly Ser Met Thr Val Ala Gln Pro Ser Thr Pro Ala Asn 1065 1070 1075	3673
cac ttc cac ctg ctg cgt cgt cac gct ctg tcc gac ctg aag cgt His Phe His Leu Leu Arg Arg His Ala Leu Ser Asp Leu Lys Arg 1080 1085 1090	3718
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gct gcc tcc gca cca gaa gac ttc act gag gtc acc aag ttc caa Ala Ala Ser Ala Pro Glu Asp Phe Thr Glu Val Thr Lys Phe Gln 1110 1115 1120	3808
tcc gtg atc gac gat cca aac gtt gca gat gca gcc aag gtg aag Ser Val Ile Asp Asp Pro Asn Val Ala Asp Ala Ala Lys Val Lys 1125 1130 1135	3853
aag gtc atg ctg gtc tcc ggc aag ctg tac tac gaa ttg gca aag Lys Val Met Leu Val Ser Gly Lys Leu Tyr Tyr Glu Leu Ala Lys 1140 1145 1150	3898

[0027]

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gaa atg ctc cac cca att ccg ttc aac cgc atc tcc gag gct ctt 3988
Glu Met Leu His Pro Ile Pro Phe Asn Arg Ile Ser Glu Ala Leu
1170 1175 1180
gcc gcc tac cct aac gct gag gaa gtc ctc ttc gtt cag gat gag 4033
Ala Gly Tyr Pro Asn Ala Glu Glu Val Leu Phe Val Gln Asp Glu
1185 1190 1195
cca gca aac cag gcc cca tgg ccg ttc tac cag gag cac ctc cca 4078
Pro Ala Asn Gln Gly Pro Trp Pro Phe Tyr Gln Glu His Leu Pro
1200 1205 1210
gag ctg atc ccg aac atg cca aag atg cgc cgc gtt tcc cgc cgc 4123
Glu Leu Ile Pro Asn Met Pro Lys Met Arg Arg Val Ser Arg Arg
1215 1220 1225
gct cag tcc tcc acc gca act ggt gtt gct aag gtg cac cag ctg 4168
Ala Gln Ser Ser Thr Ala Thr Gly Val Ala Lys Val His Gln Leu
1230 1235 1240
gag gag aag cag ctt atc gac gag gct ttc gag gct taa gtc ttt 4213
Glu Glu Lys Gln Leu Ile Asp Glu Ala Phe Glu Ala Val Phe
1245 1250 1255
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tttgctgccg tggttgccta aggtggaagg catgaaacga atctgtgcgg tcacgatctc 4333
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35 40 45
Leu Val Asp Glu Met Phe Gln Gln Phe Gln Lys Asp Pro Lys Ser Val
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Asp Lys Glu Trp Arg Glu Leu Phe Glu Ala Gln Gly Gly Pro Asn Ala
65 70 75 80
Thr Pro Ala Thr Thr Glu Ala Gln Pro Ser Ala Pro Lys Glu Ser Ala
85 90 95
Lys Pro Ala Pro Lys Ala Ala Pro Ala Ala Lys Ala Ala Pro Arg Val
100 105 110
Glu Thr Lys Pro Ala Ala Lys Thr Ala Pro Lys Ala Lys Glu Ser Ser
115 120 125
Val Pro Gln Gln Pro Lys Leu Pro Glu Pro Gly Gln Thr Pro Ile Arg
130 135 140
Gly Ile Phe Lys Ser Ile Ala Lys Asn Met Asp Ile Ser Leu Glu Ile
145 150 155 160
Pro Thr Ala Thr Ser Val Arg Asp Met Pro Ala Arg Leu Met Phe Glu
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Asn Arg Ala Met Val Asn Asp Gln Leu Lys Arg Thr Arg Gly Gly Lys
180 185 190
Ile Ser Phe Thr His Ile Ile Gly Tyr Ala Met Val Lys Ala Val Met
195 200 205
Ala His Pro Asp Met Asn Asn Ser Tyr His Arg Arg Gln Ala Pro Thr
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Leu Ile Val Pro Glu His Ile Asn Leu Gly Leu Ala Ile Asp Leu Pro
225 230 235 240
Gln Lys Asp Gly Ser Arg Ala Leu Val Val Ala Ala Ile Lys Glu Thr
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[0028]

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Thr Val Ser Leu Thr Asn Pro Gly Gly Ile Gly Thr Arg His Ser Val	
290	295 300
Pro Arg Leu Thr Lys Gly Gln Gly Thr Ile Ile Gly Val Gly Ser Met	
305	310 315 320
Asp Tyr Pro Ala Glu Phe Gln Gly Ala Ser Glu Asp Arg Leu Ala Glu	
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Leu Gly Val Gly Lys Leu Val Thr Ile Thr Ser Thr Tyr Asp His Arg	
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Val Ile Gln Gly Ala Val Ser Gly Glu Phe Leu Arg Thr Met Ser Arg	
	355 360 365
Leu Leu Thr Asp Asp Ser Phe Trp Asp Glu Ile Phe Asp Ala Met Asn	
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Val Pro Tyr Thr Pro Met Arg Trp Ala Gln Asp Val Pro Asn Thr Gly	
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Val Asp Lys Asn Thr Arg Val Met Gln Leu Ile Glu Ala Tyr Arg Ser	
	405 410 415
Arg Gly His Leu Ile Ala Asp Thr Asn Pro Leu Ser Trp Val Gln Pro	
	420 425 430
Gly Met Pro Val Pro Asp His Arg Asp Leu Asp Ile Glu Thr His Ser	
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Leu Thr Ile Trp Asp Leu Asp Arg Thr Phe Ser Val Gly Gly Phe Gly	
	450 455 460
Gly Lys Glu Thr Met Thr Leu Arg Glu Val Leu Ser Arg Leu Arg Ala	
465	470 475 480
Ala Tyr Thr Leu Lys Val Gly Ser Glu Tyr Thr His Ile Leu Asp Arg	
	485 490 495
Asp Glu Arg Thr Trp Leu Gln Asp Arg Leu Glu Ala Gly Met Pro Lys	
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Pro Thr Gln Ala Glu Gln Lys Tyr Ile Leu Gln Lys Leu Asn Ala Ala	
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Glu Ala Phe Glu Asn Phe Leu Gln Thr Lys Tyr Val Gly Gln Lys Arg	
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Ile Asp Thr Ala Ala Gly Gln Gly Leu Asp Glu Val Val Ile Gly Met	
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Pro His Arg Gly Arg Leu Asn Val Leu Phe Asn Ile Val Gly Lys Pro	
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Leu Ala Ser Ile Phe Asn Glu Phe Glu Gly Gln Met Glu Gln Gly Gln	
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His Leu Gln Met Phe Gly Asp Gly Glu Ile Lys Val Ser Leu Thr Ala	
625	630 635 640
Asn Pro Ser His Leu Glu Ala Val Asn Pro Val Met Glu Gly Ile Val	
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Arg Ala Lys Gln Asp Tyr Leu Asp Lys Gly Val Asp Gly Lys Thr Val	
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Val Pro Leu Leu Leu His Gly Asp Ala Ala Phe Ala Gly Leu Gly Ile	
	675 680 685
Val Pro Glu Thr Ile Asn Leu Ala Lys Arg Val Asp Val Gly Gly Thr	
	690 695 700
Ile His Ile Val Val Asn Asn Gln Ile Gly Phe Thr Thr Thr Pro Asp	
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Ser Ser Arg Ser Met His Tyr Ala Thr Asp Tyr Ala Lys Ala Phe Gly	
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Cys Pro Val Phe His Val Asn Gly Asp Asp Pro Glu Ala Val Val Trp	
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Val Gly Gln Leu Ala Thr Glu Tyr Arg Arg Arg Phe Gly Lys Asp Val	

[0029]

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770	775	780
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785	790	795
Glu Thr Val Arg Ala Gln Tyr Thr Glu Asp Leu Leu Gly Arg Gly Asp		
805	810	815
Leu Ser Asn Glu Asp Ala Glu Ala Val Val Arg Asp Phe His Asp Gln		
820	825	830
Met Glu Ser Val Phe Asn Glu Val Lys Glu Gly Gly Lys Lys Gln Ala		
835	840	845
Glu Ala Gln Thr Gly Ile Thr Gly Ser Gln Lys Leu Pro His Gly Leu		
850	855	860
Glu Thr Asn Ile Ser Arg Glu Glu Leu Leu Glu Leu Gly Gln Ala Phe		
865	870	875
Ala Asn Thr Pro Glu Gly Phe Asn Tyr His Pro Arg Val Ala Pro Val		
885	890	895
Ala Lys Lys Arg Val Ser Ser Val Thr Glu Gly Gly Ile Asp Trp Ala		
900	905	910
Trp Gly Glu Leu Leu Ala Phe Gly Ser Leu Ala Asn Ser Gly Arg Leu		
915	920	925
Val Arg Leu Ala Gly Glu Asp Ser Arg Arg Gly Thr Phe Thr Gln Arg		
930	935	940
His Ala Val Ala Ile Asp Pro Ala Thr Ala Glu Glu Phe Asn Pro Leu		
945	950	955
His Glu Leu Ala Gln Ser Lys Gly Asn Asn Gly Lys Phe Leu Val Tyr		
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980	985	990
Ser Val Gly Asn Glu Asp Ser Val Val Ala Trp Glu Ala Gln Phe Gly		
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Asp Phe Ala Asn Gly Ala Gln Thr Ile Ile Asp Glu Tyr Val Ser		
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Ser Gly Glu Ala Lys Trp Gly Gln Thr Ser Lys Leu Ile Leu Leu		
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Leu Pro His Gly Tyr Glu Gly Gln Gly Pro Asp His Ser Ser Ala		
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Arg Ile Glu Arg Phe Leu Gln Leu Cys Ala Glu Gly Ser Met Thr		
1055	1060	1065
Val Ala Gln Pro Ser Thr Pro Ala Asn His Phe His Leu Leu Arg		
1070	1075	1080
Arg His Ala Leu Ser Asp Leu Lys Arg Pro Leu Val Ile Phe Thr		
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Pro Lys Ser Met Leu Arg Asn Lys Ala Ala Ala Ser Ala Pro Glu		
1100	1105	1110
Asp Phe Thr Glu Val Thr Lys Phe Gln Ser Val Ile Asp Asp Pro		
1115	1120	1125
Asn Val Ala Asp Ala Ala Lys Val Lys Lys Val Met Leu Val Ser		
1130	1135	1140
Gly Lys Leu Tyr Tyr Glu Leu Ala Lys Arg Lys Glu Lys Asp Gly		
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Arg Asp Asp Ile Ala Ile Val Arg Ile Glu Met Leu His Pro Ile		
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Pro Phe Asn Arg Ile Ser Glu Ala Leu Ala Gly Tyr Pro Asn Ala		
1175	1180	1185
Glu Glu Val Leu Phe Val Gln Asp Glu Pro Ala Asn Gln Gly Pro		
1190	1195	1200
Trp Pro Phe Tyr Gln Glu His Leu Pro Glu Leu Ile Pro Asn Met		
1205	1210	1215
Pro Lys Met Arg Arg Val Ser Arg Arg Ala Gln Ser Ser Thr Ala		
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1235	1240	1245

[0030]

Asp Glu Ala Phe Glu Ala
1250

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<213> 谷氨酸棒杆菌

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ttcattttct tccactctaa aattaagtat ggaaaaccaa ccgcacccgg atgcacgaca 180
atgacccact aaacacgtat ccttgaatgc gtg act gaa cat tat gac gta gta 234
Met Thr Glu His Tyr Asp Val Val
1 5
gta ctc gga gcc ggc ccc ggt ggc tat gtc tcc gcc atc cgt gca gcg 282
Val Leu Gly Ala Gly Pro Gly Gly Tyr Val Ser Ala Ile Arg Ala Ala
10 15 20
cag ctt ggc aag aag gtt gct gta att gag aag cag tac tgg ggt ggt 330
Gln Leu Gly Lys Lys Val Ala Val Ile Glu Lys Gln Tyr Trp Gly Gly
25 30 35 40
gtt tgc cta aac gtg ggc tgc att cct tcc aag tct ctg atc aaa aac 378
Val Cys Leu Asn Val Gly Cys Ile Pro Ser Lys Ser Leu Ile Lys Asn
45 50 55
gct gaa gtt gcc cat acc ttt acc cat gag aag aag acc ttc ggc atc 426
Ala Glu Val Ala His Thr Phe Thr His Glu Lys Lys Thr Phe Gly Ile
60 65 70
aat ggc gaa gtg acc ttc aac tat gag gat gct cac aag cgt tcc cgt 474
Asn Gly Glu Val Thr Phe Asn Tyr Glu Asp Ala His Lys Arg Ser Arg
75 80 85
ggc gtt tcc gac aag atc gtt gga ggc gtt cat tac ttg atg aag aag 522
Gly Val Ser Asp Lys Ile Val Gly Gly Val His Tyr Leu Met Lys Lys
90 95 100
aac aag atc atc gaa att cat ggt ctt gga aac ttc aag gat gct aag 570
Asn Lys Ile Ile Glu Ile His Gly Leu Gly Asn Phe Lys Asp Ala Lys
105 110 115 120
act ctt gag gtc acc gac ggt aag gat gct ggc aag acc atc acc ttt 618
Thr Leu Glu Val Thr Asp Gly Lys Asp Ala Gly Lys Thr Ile Thr Phe
125 130 135
gat gac tgc atc atc gca acc ggt tgc gta gtc aac acc ctc cgt ggc 666
Asp Asp Cys Ile Ile Ala Thr Gly Ser Val Val Asn Thr Leu Arg Gly
140 145 150
gtt gac ttc tca gag aac gtt gtg tct ttt gaa gag cag att ctt aac 714
Val Asp Phe Ser Glu Asn Val Val Ser Phe Glu Glu Gln Ile Leu Asn
155 160 165
cct gtt gcg cca aag aag atg gtc att gtt ggt gca ggc gca att gga 762
Pro Val Ala Pro Lys Lys Met Val Ile Val Gly Ala Gly Ala Ile Gly
170 175 180
atg gaa ttc gcc tac gtt ctt ggt aac tac ggt gta gat gta acc gtc 810
Met Glu Phe Ala Tyr Val Leu Gly Asn Tyr Gly Val Asp Val Thr Val
185 190 195 200
atc gag ttc atg gat cgt gtg ctt cca aat gaa gat gct gaa gtc tcc 858
Ile Glu Phe Met Asp Arg Val Leu Pro Asn Glu Asp Ala Glu Val Ser
205 210 215
aag gtt att gca aag gcc tac aag aag atg ggc gtt aag ctt ctt cct 906
Lys Val Ile Ala Lys Ala Tyr Lys Lys Met Gly Val Lys Leu Leu Pro
220 225 230
ggc cat gca acc act gct gtt cgg gac aac ggt gac ttt gtc gag gtt 954

[0031]

Gly His Ala Thr Thr Ala Val Arg Asp Asn Gly Asp Phe Val Glu Val	
235 240 245	
gat tac cag aag aag ggc tct gac aag aca gag act ctt act gtt gat	1002
Asp Tyr Gln Lys Lys Gly Ser Asp Lys Thr Glu Thr Leu Thr Val Asp	
250 255 260	
cga gtc atg gtt tcc gtt ggt ttc cgt cca cgc gtt gag gga ttt ggt	1050
Arg Val Met Val Ser Val Gly Phe Arg Pro Arg Val Glu Gly Phe Gly	
265 270 275 280	
ctt gaa aac act ggc gtt aag ctc acc gag cgt ggc gca atc gag atc	1098
Leu Glu Asn Thr Gly Val Lys Leu Thr Glu Arg Gly Ala Ile Glu Ile	
285 290 295	
gat gat tac atg cgt acc aac gtc gat ggc att tac gcc atc ggt gac	1146
Asp Asp Tyr Met Arg Thr Asn Val Asp Gly Ile Tyr Ala Ile Gly Asp	
300 305 310	
gtg acc gcc aag ctt cag ctt gct cac gtc gca gaa gca cag ggc att	1194
Val Thr Ala Lys Leu Gln Leu Ala His Val Ala Glu Ala Gln Gly Ile	
315 320 325	
gtt gcc gca gag act att gct ggt gca gaa act cag act ctt ggt gat	1242
Val Ala Ala Glu Thr Ile Ala Gly Ala Glu Thr Gln Thr Leu Gly Asp	
330 335 340	
tac atg atg atg cca cgt gca acc ttc tgc aac cca cag gtt tct tcc	1290
Tyr Met Met Met Pro Arg Ala Thr Phe Cys Asn Pro Gln Val Ser Ser	
345 350 355 360	
ttt ggt tac acc gaa gag cag gcc aag gag aag tgg cca gat cgt gag	1338
Phe Gly Tyr Thr Glu Glu Gln Ala Lys Glu Lys Trp Pro Asp Arg Glu	
365 370 375	
atc aag gtt gct tcc ctc cca ttc tct gca aac ggt aaa gca gtt ggc	1386
Ile Lys Val Ala Ser Leu Pro Phe Ser Ala Asn Gly Lys Ala Val Gly	
380 385 390	
ctg gca gaa act gat ggt ttc gca aag atc gtt gct gat gca gaa ttc	1434
Leu Ala Glu Thr Asp Gly Phe Ala Lys Ile Val Ala Asp Ala Glu Phe	
395 400 405	
ggg gag ctg ctc ggt gca cac ctg gtt gga gca aat gca tca gag ctc	1482
Gly Glu Leu Leu Gly Ala His Leu Val Gly Ala Asn Ala Ser Glu Leu	
410 415 420	
atc aat gaa ttg gtg ctt gct cag aac tgg gat ctc acc act gaa gag	1530
Ile Asn Glu Leu Val Leu Ala Gln Asn Trp Asp Leu Thr Thr Glu Glu	
425 430 435 440	
atc tct cgt agc gtc cat att cac cca acg cta tct gag gca gtt aag	1578
Ile Ser Arg Ser Val His Ile His Pro Thr Leu Ser Glu Ala Val Lys	
445 450 455	
gaa gct gca cac ggt atc tct gga cac atg atc aac ttc tag	1620
Glu Ala Ala His Gly Ile Ser Gly His Met Ile Asn Phe	
460 465	
aatccacctc gttagccctg ttctgtatg gaaacagggc caaaaccgat ttccaatcca	1680
aaccgagtgct tggttagtgc tcatactcac aaaaactttt cgattatcaa agagaattat	1740
ttctaaaaatt cggatctgct taagaaatga gtttgccaat agctcagcat caaaatgctg	1800
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Tyr Val Ser Ala Ile Arg Ala Ala Gln Leu Gly Lys Lys Val Ala Val	
20 25 30	
Ile Glu Lys Gln Tyr Trp Gly Gly Val Cys Leu Asn Val Gly Cys Ile	
35 40 45	
Pro Ser Lys Ser Leu Ile Lys Asn Ala Glu Val Ala His Thr Phe Thr	
50 55 60	
His Glu Lys Lys Thr Phe Gly Ile Asn Gly Glu Val Thr Phe Asn Tyr	

[0032]

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65          70          75          80
Glu Asp Ala His Lys Arg Ser Arg Gly Val Ser Asp Lys Ile Val Gly
      85          90          95
Gly Val His Tyr Leu Met Lys Lys Asn Lys Ile Ile Glu Ile His Gly
      100         105         110
Leu Gly Asn Phe Lys Asp Ala Lys Thr Leu Glu Val Thr Asp Gly Lys
      115         120         125
Asp Ala Gly Lys Thr Ile Thr Phe Asp Asp Cys Ile Ile Ala Thr Gly
      130         135         140
Ser Val Val Asn Thr Leu Arg Gly Val Asp Phe Ser Glu Asn Val Val
      145         150         155         160
Ser Phe Glu Glu Gln Ile Leu Asn Pro Val Ala Pro Lys Lys Met Val
      165         170         175
Ile Val Gly Ala Gly Ala Ile Gly Met Glu Phe Ala Tyr Val Leu Gly
      180         185         190
Asn Tyr Gly Val Asp Val Thr Val Ile Glu Phe Met Asp Arg Val Leu
      195         200         205
Pro Asn Glu Asp Ala Glu Val Ser Lys Val Ile Ala Lys Ala Tyr Lys
      210         215         220
Lys Met Gly Val Lys Leu Leu Pro Gly His Ala Thr Thr Ala Val Arg
      225         230         235         240
Asp Asn Gly Asp Phe Val Glu Val Asp Tyr Gln Lys Lys Gly Ser Asp
      245         250         255
Lys Thr Glu Thr Leu Thr Val Asp Arg Val Met Val Ser Val Gly Phe
      260         265         270
Arg Pro Arg Val Glu Gly Phe Gly Leu Glu Asn Thr Gly Val Lys Leu
      275         280         285
Thr Glu Arg Gly Ala Ile Glu Ile Asp Asp Tyr Met Arg Thr Asn Val
      290         295         300
Asp Gly Ile Tyr Ala Ile Gly Asp Val Thr Ala Lys Leu Gln Leu Ala
      305         310         315         320
His Val Ala Glu Ala Gln Gly Ile Val Ala Ala Glu Thr Ile Ala Gly
      325         330         335
Ala Glu Thr Gln Thr Leu Gly Asp Tyr Met Met Met Pro Arg Ala Thr
      340         345         350
Phe Cys Asn Pro Gln Val Ser Ser Phe Gly Tyr Thr Glu Glu Gln Ala
      355         360         365
Lys Glu Lys Trp Pro Asp Arg Glu Ile Lys Val Ala Ser Leu Pro Phe
      370         375         380
Ser Ala Asn Gly Lys Ala Val Gly Leu Ala Glu Thr Asp Gly Phe Ala
      385         390         395         400
Lys Ile Val Ala Asp Ala Glu Phe Gly Glu Leu Leu Gly Ala His Leu
      405         410         415
Val Gly Ala Asn Ala Ser Glu Leu Ile Asn Glu Leu Val Leu Ala Gln
      420         425         430
Asn Trp Asp Leu Thr Thr Glu Glu Ile Ser Arg Ser Val His Ile His
      435         440         445
Pro Thr Leu Ser Glu Ala Val Lys Glu Ala Ala His Gly Ile Ser Gly
      450         455         460
His Met Ile Asn Phe
465

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<210> 19
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<212> DNA
<213> 枯草芽孢杆菌

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<222> (464)..(1885)
<223>

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[0033]

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aaaaataca gagaatgaaa agaacagat agatttttta gttctttagg cccgtagtct	180
gcaaatcctt ttatgatttt ctatcaaaca aaagaggaaa atagaccagt tgcaatccaa	240
acgagagtct aatagaatga ggtcgaaaag taaatcgcg gggtttgta ctgataaagc	300
aggcaagacc taaaatgtgt aaagggcaaa gtgtatactt tggcgtcacc ccttacatat	360
tttaggtctt tttttattgt gcgtaactaa cttgccatct tcaaacagga gggctggaag	420
aagcagaccg ctaacacagt acataaaaaa ggagacatga acg atg aac atc aaa	475
Met Asn Ile Lys	
1	
aag ttt gca aaa caa gca aca gta tta acc ttt act acc gca ctg ctg	523
Lys Phe Ala Lys Gln Ala Thr Val Leu Thr Phe Thr Thr Ala Leu Leu	
5 10 15 20	
gca gga ggc gca act caa gcg ttt gcg aaa gaa acg aac caa aag cca	571
Ala Gly Gly Ala Thr Gln Ala Phe Ala Lys Glu Thr Asn Gln Lys Pro	
25 30 35	
tat aag gaa aca tac ggc att tcc cat att aca cgc cat gat atg ctg	619
Tyr Lys Glu Thr Tyr Gly Ile Ser His Ile Thr Arg His Asp Met Leu	
40 45 50	
caa atc cct gaa cag caa aaa aat gaa aaa tat caa gtt cct gaa ttc	667
Gln Ile Pro Glu Gln Gln Lys Asn Glu Lys Tyr Gln Val Pro Glu Phe	
55 60 65	
gat tcg tcc aca att aaa aat atc tct tct gca aaa ggc ctg gac gtt	715
Asp Ser Ser Thr Ile Lys Asn Ile Ser Ser Ala Lys Gly Leu Asp Val	
70 75 80	
tgg gac agc tgg cca tta caa aac gct gac ggc act gtc gca aac tat	763
Trp Asp Ser Trp Pro Leu Gln Asn Ala Asp Gly Thr Val Ala Asn Tyr	
85 90 95 100	
cac ggc tac cac atc gtc ttt gca tta gcc gga gat cct aaa aat gcg	811
His Gly Tyr His Ile Val Phe Ala Leu Ala Gly Asp Pro Lys Asn Ala	
105 110 115	
gat gac aca tcg att tac atg ttc tat caa aaa gtc ggc gaa act tct	859
Asp Asp Thr Ser Ile Tyr Met Phe Tyr Gln Lys Val Gly Glu Thr Ser	
120 125 130	
att gac agc tgg aaa aac gct ggc cgc gtc ttt aaa gac agc gac aaa	907
Ile Asp Ser Trp Lys Asn Ala Gly Arg Val Phe Lys Asp Ser Asp Lys	
135 140 145	
ttc gat gca aat gat tct atc cta aaa gac caa aca caa gaa tgg tca	955
Phe Asp Ala Asn Asp Ser Ile Leu Lys Asp Gln Thr Gln Glu Trp Ser	
150 155 160	
ggt tca gcc aca ttt aca tct gac gga aaa atc cgt tta ttc tac act	1003
Gly Ser Ala Thr Phe Thr Ser Asp Gly Lys Ile Arg Leu Phe Tyr Thr	
165 170 175 180	
gat ttc tcc ggt aaa cat tac ggc aaa caa aca ctg aca act gca caa	1051
Asp Phe Ser Gly Lys His Tyr Gly Lys Gln Thr Leu Thr Thr Ala Gln	
185 190 195	
gtt aac gta tca gca tca gac agc tct ttg aac atc aac ggt gta gag	1099
Val Asn Val Ser Ala Ser Asp Ser Ser Leu Asn Ile Asn Gly Val Glu	
200 205 210	
gat tat aaa tca atc ttt gac ggt gac gga aaa acg tat caa aat gta	1147
Asp Tyr Lys Ser Ile Phe Asp Gly Asp Gly Lys Thr Tyr Gln Asn Val	
215 220 225	
cag cag ttc atc gat gaa ggc aac tac agc tca ggc gac aac cat acg	1195
Gln Gln Phe Ile Asp Glu Gly Asn Tyr Ser Ser Gly Asp Asn His Thr	
230 235 240	
ctg aga gat cct cac tac gta gaa gat aaa ggc cac aaa tac tta gta	1243
Leu Arg Asp Pro His Tyr Val Glu Asp Lys Gly His Lys Tyr Leu Val	
245 250 255 260	
ttt gaa gca aac act gga act gaa gat ggc tac caa ggc gaa gaa tct	1291
Phe Glu Ala Asn Thr Gly Thr Glu Asp Gly Tyr Gln Gly Glu Glu Ser	
265 270 275	
tta ttt aac aaa gca tac tat ggc aaa agc aca tca ttc ttc cgt caa	1339
Leu Phe Asn Lys Ala Tyr Tyr Gly Lys Ser Thr Ser Phe Phe Arg Gln	

[0034]

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      280      285      290
gaa agt caa aaa ctt ctg caa agc gat aaa aaa cgc acg gct gag tta 1387
Glu Ser Gln Lys Leu Leu Gln Ser Asp Lys Lys Arg Thr Ala Glu Leu
      295      300      305
gca aac ggc gct ctc ggt atg att gag cta aac gat gat tac aca ctg 1435
Ala Asn Gly Ala Leu Gly Met Ile Glu Leu Asn Asp Asp Tyr Thr Leu
      310      315      320
aaa aaa gtg atg aaa ccg ctg att gca tct aac aca gta aca gat gaa 1483
Lys Lys Val Met Lys Pro Leu Ile Ala Ser Asn Thr Val Thr Asp Glu
      325      330      335      340
att gaa cgc gcg aac gtc ttt aaa atg aac ggc aaa tgg tac ctg ttc 1531
Ile Glu Arg Ala Asn Val Phe Lys Met Asn Gly Lys Trp Tyr Leu Phe
      345      350      355
act gac tcc cgc gga tca aaa atg acg att gac ggc att acg tct aac 1579
Thr Asp Ser Arg Gly Ser Lys Met Thr Ile Asp Gly Ile Thr Ser Asn
      360      365      370
gat att tac atg ctt ggt tat gtt tct aat tct tta act ggc cca tac 1627
Asp Ile Tyr Met Leu Gly Tyr Val Ser Asn Ser Leu Thr Gly Pro Tyr
      375      380      385
aag ccg ctg aac aaa act ggc ctt gtg tta aaa atg gat ctt gat cct 1675
Lys Pro Leu Asn Lys Thr Gly Leu Val Leu Lys Met Asp Leu Asp Pro
      390      395      400
aac gat gta acc ttt act tac tca cac ttc gct gta cct caa gcg aaa 1723
Asn Asp Val Thr Phe Thr Tyr Ser His Phe Ala Val Pro Gln Ala Lys
      405      410      415      420
gga aac aat gtc gtg att aca agc tat atg aca aac aga gga ttc tac 1771
Gly Asn Asn Val Val Ile Thr Ser Tyr Met Thr Asn Arg Gly Phe Tyr
      425      430      435
gca gac aaa caa tca acg ttt gcg cca agc ttc ctg ctg aac atc aaa 1819
Ala Asp Lys Gln Ser Thr Phe Ala Pro Ser Phe Leu Leu Asn Ile Lys
      440      445      450
ggc aag aaa aca tct gtt gtc aaa gac agc atc ctt gaa caa gga caa 1867
Gly Lys Lys Thr Ser Val Val Lys Asp Ser Ile Leu Glu Gln Gly Gln
      455      460      465
tta aca gtt aac aaa taa aaacgcaaaa gaaaatgccg atatcctatt 1915
Leu Thr Val Asn Lys
      470
ggcattttct tttatttctt atcaacataa aggtgaatcc catatgaact atataaaagc 1975
aggcaaatgg ctaaccgtat tccaaacctt ttgaagatc 2014

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<210> 20
 <211> 473
 <212> PRT
 <213> 枯草芽孢杆菌

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

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[0035]

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

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<220>
 <223> 引物

<400> 21
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24

<210> 22
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 <212> DNA
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<220>
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[0036]

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<210> 24 <211> 44 <212> DNA <213> 人工的	
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<400> 25 cctgggaaaa cagcattcca ggtattag	28
<210> 26 <211> 23 <212> DNA <213> 人工的	
<220> <223> 引物	
<400> 26 tgcaggtcga ctctagagga tcc	23
<210> 27 <211> 2028 <212> DNA <213> 谷氨酸棒杆菌	
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[0037]

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ggc acg atc acc cag tgg ttg aag tct gtt ggt gac act gtt gag gta	96
Gly Thr Ile Thr Gln Trp Leu Lys Ser Val Gly Asp Thr Val Glu Val	
20 25 30	
gat gag ccg ttg ctc gag gtc tca act gac aag gtc gac acc gag att	144
Asp Glu Pro Leu Leu Glu Val Ser Thr Asp Lys Val Asp Thr Glu Ile	
35 40 45	
ccc tct cct gtc gcc ggt gtc atc cta gag att aag gct gaa gag gat	192
Pro Ser Pro Val Ala Gly Val Ile Leu Glu Ile Lys Ala Glu Glu Asp	
50 55 60	
gac acc gtc gac gtc ggc ggt gtc att gca ata atc ggc gat gct gat	240
Asp Thr Val Asp Val Gly Gly Val Ile Ala Ile Ile Gly Asp Ala Asp	
65 70 75 80	
gag act cct gcc aac gaa gct cct gcc gac gag gca cca gct cct gcc	288
Glu Thr Pro Ala Asn Glu Ala Pro Ala Asp Glu Ala Pro Ala Pro Ala	
85 90 95	
gaa gag gaa gaa cca gtt aag gaa gag cca aag aag gag gca gct cct	336
Glu Glu Glu Glu Pro Val Lys Glu Glu Pro Lys Lys Glu Ala Ala Pro	
100 105 110	
gaa gct cca gca gca act ggc gcc gca acc gat gtg gaa atg cca gaa	384
Glu Ala Pro Ala Ala Thr Gly Ala Ala Thr Asp Val Glu Met Pro Glu	
115 120 125	
ctc ggc gaa tcc gtc acc gaa ggc acc att acc cag tgg ctc aag gct	432
Leu Gly Glu Ser Val Thr Glu Gly Thr Ile Thr Gln Trp Leu Lys Ala	
130 135 140	
gtc ggc gac acc gtc gaa gta gac gaa cca ctt ctt gag gtc tcc acc	480
Val Gly Asp Thr Val Glu Val Asp Glu Pro Leu Leu Glu Val Ser Thr	
145 150 155 160	
gac aag gtc gac acc gaa atc cca tcc cca gta gca ggc acc atc gtg	528
Asp Lys Val Asp Thr Glu Ile Pro Ser Pro Val Ala Gly Thr Ile Val	
165 170 175	
gag atc ctt gca gag gaa gac gac acc gtc gac gtc ggc gca gtc atc	576
Glu Ile Leu Ala Asp Glu Asp Asp Thr Val Asp Val Gly Ala Val Ile	
180 185 190	
gcc cgc atc ggt gac gca aac gca gct gca gca cct gcc gaa gag gaa	624
Ala Arg Ile Gly Asp Ala Asn Ala Ala Ala Pro Ala Glu Glu Glu	
195 200 205	
gca gct cct gcc gaa gag gaa gaa cca gtt aag gaa gag cca aag aag	672
Ala Ala Pro Ala Glu Glu Glu Glu Pro Val Lys Glu Glu Pro Lys Lys	
210 215 220	
gag gca gct cct gaa gct cca gca gca act ggc gcc gca acc gat gtg	720
Glu Ala Ala Pro Glu Ala Pro Ala Ala Thr Gly Ala Ala Thr Asp Val	
225 230 235 240	
gaa atg cca gaa ctc ggc gaa tcc gtc acc gaa ggc acc att acc cag	768
Glu Met Pro Glu Leu Gly Glu Ser Val Thr Glu Gly Thr Ile Thr Gln	
245 250 255	
tgg ctc aag gct gtc ggc gac acc gtc gaa gta gac gaa cca ctt ctt	816
Trp Leu Lys Ala Val Gly Asp Thr Val Glu Val Asp Glu Pro Leu Leu	
260 265 270	
gag gtc tcc acc gac aag gtc gac acc gaa atc cca tcc cca gta gca	864
Glu Val Ser Thr Asp Lys Val Asp Thr Glu Ile Pro Ser Pro Val Ala	
275 280 285	
ggc acc atc gtg gag atc ctt gca gac gaa gac gac acc gtc gac gtc	912
Gly Thr Ile Val Glu Ile Leu Ala Asp Glu Asp Asp Thr Val Asp Val	
290 295 300	
ggc gca gtc atc gcc cgc atc ggt gac gca aac gca gct gca gca cct	960
Gly Ala Val Ile Ala Arg Ile Gly Asp Ala Asn Ala Ala Ala Pro	
305 310 315 320	
gcc gaa gag gaa gca gct cct gcc gaa gag gag gaa cca gtt aag gaa	1008
Ala Glu Glu Glu Ala Ala Pro Ala Glu Glu Glu Glu Pro Val Lys Glu	

[0038]

325	330	335	
gag cca aag aag gaa gag ccc aag aag gaa gag ccc aag aag gaa gca			1056
Glu Pro Lys Lys Glu Glu Pro Lys Lys Glu Glu Pro Lys Lys Glu Ala			
340	345	350	
gct act aca cct gct gcg gca tcc gca act gtg tcc gct tct ggc gac			1104
Ala Thr Thr Pro Ala Ala Ala Ser Ala Thr Val Ser Ala Ser Gly Asp			
355	360	365	
aac gtt cca tac gtc acc cca ctg gtg cgc aag ctt gct gaa aag cac			1152
Asn Val Pro Tyr Val Thr Pro Leu Val Arg Lys Leu Ala Glu Lys His			
370	375	380	
ggc gtt gac ttg aac acc gtg acc ggt acc ggt atc ggt ggc cgt atc			1200
Gly Val Asp Leu Asn Thr Val Thr Gly Thr Gly Ile Gly Gly Arg Ile			
385	390	395	400
cgc aag cag gat gtt ttg gct gct gcg aac ggc gag gct gca cct gct			1248
Arg Lys Gln Asp Val Leu Ala Ala Ala Asn Gly Glu Ala Ala Pro Ala			
405	410	415	
gag gct gct gct cct gtt tcc gct tgg tcc act aag tct gtt gac cct			1296
Glu Ala Ala Ala Pro Val Ser Ala Trp Ser Thr Lys Ser Val Asp Pro			
420	425	430	
gag aag gct aag ctc cgt ggt acc act cag aag gtc aac cgc atc cgt			1344
Glu Lys Ala Lys Leu Arg Gly Thr Thr Gln Lys Val Asn Arg Ile Arg			
435	440	445	
gag atc acc gcg atg aag acc gtc gag gct ctg cag att tct gct cag			1392
Glu Ile Thr Ala Met Lys Thr Val Glu Ala Leu Gln Ile Ser Ala Gln			
450	455	460	
ctc acc cag ctg cac gag gtc gat atg act cgc gtt gct gag ctg cgt			1440
Leu Thr Gln Leu His Glu Val Asp Met Thr Arg Val Ala Glu Leu Arg			
465	470	475	480
aag aag aac aag ccc gcg ttc atc gag aag cac ggt gtg aac ctc act			1488
Lys Lys Asn Lys Pro Ala Phe Ile Glu Lys His Gly Val Asn Leu Thr			
485	490	495	
tac ctg cca ttc ttc gtg aag gca gtt gtc gag gct ttg gtt tcc cat			1536
Tyr Leu Pro Phe Phe Val Lys Ala Val Val Glu Ala Leu Val Ser His			
500	505	510	
cca aac gtc aac gcg tct ttc aac gcg aag acc aag gag atg acc tac			1584
Pro Asn Val Asn Ala Ser Phe Asn Ala Lys Thr Lys Glu Met Thr Tyr			
515	520	525	
cac tcc tcc gtt aac ctc tcc atc gct gtt gat acc cca gct ggt ctg			1632
His Ser Ser Val Asn Leu Ser Ile Ala Val Asp Thr Pro Ala Gly Leu			
530	535	540	
ttg acc cca gtc att cac gat gct cag gat ctc tcc atc cca gag atc			1680
Leu Thr Pro Val Ile His Asp Ala Gln Asp Leu Ser Ile Pro Glu Ile			
545	550	555	560
gca aag gca att gtt gac ctg gct gat cgt tca cgc aac aac aag ctg			1728
Ala Lys Ala Ile Val Asp Leu Ala Asp Arg Ser Arg Asn Asn Lys Leu			
565	570	575	
aag cca aac gat ctg tcc ggt ggc acc ttc acc atc acc aac att ggt			1776
Lys Pro Asn Asp Leu Ser Gly Gly Thr Phe Thr Ile Thr Asn Ile Gly			
580	585	590	
tct gaa ggc gca ctg tct gat acc cca atc ctg gtt cca cca cag gct			1824
Ser Glu Gly Ala Leu Ser Asp Thr Pro Ile Leu Val Pro Pro Gln Ala			
595	600	605	
ggc atc ttg ggc acc ggc gcg atc gtg aag cgt cca gtt gtc atc acc			1872
Gly Ile Leu Gly Thr Gly Ala Ile Val Lys Arg Pro Val Val Ile Thr			
610	615	620	
gag gat gga att gat tcc atc gcg atc cgt cag atg gtc ttc cta cca			1920
Glu Asp Gly Ile Asp Ser Ile Ala Ile Arg Gln Met Val Phe Leu Pro			
625	630	635	640
ctg acc tac gac cac cag gtt gta gat ggc gca gat gct ggt cgc ttc			1968
Leu Thr Tyr Asp His Gln Val Val Asp Gly Ala Asp Ala Gly Arg Phe			
645	650	655	
ctg acc acc atc aag gac cgc ctt gag acc gct aac ttc gaa ggc gat			2016
Leu Thr Thr Ile Lys Asp Arg Leu Glu Thr Ala Asn Phe Glu Gly Asp			

[0039]

660
 ctg cag ctc taa
 Leu Gln Leu
 675

2028

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 <212> PRT
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 20 25 30
 Asp Glu Pro Leu Leu Glu Val Ser Thr Asp Lys Val Asp Thr Glu Ile
 35 40 45
 Pro Ser Pro Val Ala Gly Val Ile Leu Glu Ile Lys Ala Glu Glu Asp
 50 55 60
 Asp Thr Val Asp Val Gly Glu Val Ile Ala Ile Gly Asp Ala Asp
 65 70 75 80
 Glu Thr Pro Ala Asn Glu Ala Pro Ala Asp Glu Ala Pro Ala Pro Ala
 85 90 95
 Glu Glu Glu Glu Pro Val Lys Glu Glu Pro Lys Lys Glu Ala Ala Pro
 100 105 110
 Glu Ala Pro Ala Ala Thr Gly Ala Ala Thr Asp Val Glu Met Pro Glu
 115 120 125
 Leu Gly Glu Ser Val Thr Glu Gly Thr Ile Thr Gln Trp Leu Lys Ala
 130 135 140
 Val Gly Asp Thr Val Glu Val Asp Glu Pro Leu Leu Glu Val Ser Thr
 145 150 155 160
 Asp Lys Val Asp Thr Glu Ile Pro Ser Pro Val Ala Gly Thr Ile Val
 165 170 175
 Glu Ile Leu Ala Asp Glu Asp Asp Thr Val Asp Val Gly Ala Val Ile
 180 185 190
 Ala Arg Ile Gly Asp Ala Asn Ala Ala Ala Pro Ala Glu Glu Glu
 195 200 205
 Ala Ala Pro Ala Glu Glu Glu Glu Pro Val Lys Glu Glu Pro Lys Lys
 210 215 220
 Glu Ala Ala Pro Glu Ala Pro Ala Ala Thr Gly Ala Ala Thr Asp Val
 225 230 235 240
 Glu Met Pro Glu Leu Gly Glu Ser Val Thr Glu Gly Thr Ile Thr Gln
 245 250 255
 Trp Leu Lys Ala Val Gly Asp Thr Val Glu Val Asp Glu Pro Leu Leu
 260 265 270
 Glu Val Ser Thr Asp Lys Val Asp Thr Glu Ile Pro Ser Pro Val Ala
 275 280 285
 Gly Thr Ile Val Glu Ile Leu Ala Asp Glu Asp Asp Thr Val Asp Val
 290 295 300
 Gly Ala Val Ile Ala Arg Ile Gly Asp Ala Asn Ala Ala Ala Pro
 305 310 315 320
 Ala Glu Glu Glu Ala Ala Pro Ala Glu Glu Glu Glu Pro Val Lys Glu
 325 330 335
 Glu Pro Lys Lys Glu Glu Pro Lys Lys Glu Glu Pro Lys Lys Glu Ala
 340 345 350
 Ala Thr Thr Pro Ala Ala Ala Ser Ala Thr Val Ser Ala Ser Gly Asp
 355 360 365
 Asn Val Pro Tyr Val Thr Pro Leu Val Arg Lys Leu Ala Glu Lys His
 370 375 380
 Gly Val Asp Leu Asn Thr Val Thr Gly Thr Gly Ile Gly Gly Arg Ile
 385 390 395 400
 Arg Lys Gln Asp Val Leu Ala Ala Ala Asn Gly Glu Ala Ala Pro Ala

[0040]

405	410	415
Glu Ala Ala Ala Pro Val Ser Ala Trp Ser Thr Lys Ser Val Asp Pro		
420	425	430
Glu Lys Ala Lys Leu Arg Gly Thr Thr Gln Lys Val Asn Arg Ile Arg		
435	440	445
Glu Ile Thr Ala Met Lys Thr Val Glu Ala Leu Gln Ile Ser Ala Gln		
450	455	460
Leu Thr Gln Leu His Glu Val Asp Met Thr Arg Val Ala Glu Leu Arg		
465	470	475
Lys Lys Asn Lys Pro Ala Phe Ile Glu Lys His Gly Val Asn Leu Thr		
485	490	495
Tyr Leu Pro Phe Phe Val Lys Ala Val Val Glu Ala Leu Val Ser His		
500	505	510
Pro Asn Val Asn Ala Ser Phe Asn Ala Lys Thr Lys Glu Met Thr Tyr		
515	520	525
His Ser Ser Val Asn Leu Ser Ile Ala Val Asp Thr Pro Ala Gly Leu		
530	535	540
Leu Thr Pro Val Ile His Asp Ala Gln Asp Leu Ser Ile Pro Glu Ile		
545	550	555
Ala Lys Ala Ile Val Asp Leu Ala Asp Arg Ser Arg Asn Asn Lys Leu		
565	570	575
Lys Pro Asn Asp Leu Ser Gly Gly Thr Phe Thr Ile Thr Asn Ile Gly		
580	585	590
Ser Glu Gly Ala Leu Ser Asp Thr Pro Ile Leu Val Pro Pro Gln Ala		
595	600	605
Gly Ile Leu Gly Thr Gly Ala Ile Val Lys Arg Pro Val Val Ile Thr		
610	615	620
Glu Asp Gly Ile Asp Ser Ile Ala Ile Arg Gln Met Val Phe Leu Pro		
625	630	635
Leu Thr Tyr Asp His Gln Val Val Asp Gly Ala Asp Ala Gly Arg Phe		
645	650	655
Leu Thr Thr Ile Lys Asp Arg Leu Glu Thr Ala Asn Phe Glu Gly Asp		
660	665	670
Leu Gln Leu		
675		

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<211> 3481

<212> DNA

<213> 谷氨酸棒杆菌

<220>

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<222> (1437)..(3035)

<223> yggB

<400> 29

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gctgcgctgc agtgaccac cagcggacac agtgccatgc atgcctggca taccatgtg	180
cagctcgtgg gactctggga aggttcccag cgccatcaat gtggtgacaa ctggaatgcc	240
ggtgtgctca gcgaacgcac gaagctcttc gtgggcatca gccttgataa cgcgcgcc	300
aacgtaaaagg acaggcttct tagactcacc gatcagtttg acagcctgct caatctgtcg	360
agcatgcggt gttgaaactg ggcggtagcc tggcaggtcg atclttgggtg gccagacgaa	420
atccaattca gcgttctgaa catccttggg gatataccact agaacaggac cagggcgacc	480
agtaatcgcg aggtggaatg cctcagccaa tgcctgtgga atgtcgttgg ggttggtgac	540
catgaagtgt tgccttggtc ctggcatggt gatgccgcgg atatcggtt cctggaaagc	600
atcggtaacc agcaggctac ttccgacctg gccggtgatg gcaaccatgg gaacggagtc	660
caagtgtgca tcacgcgattg gggtaaccaa gttggttgcg cctgggccag aggttgcaat	720
gcagacgcca acgcgtccag taacctgcgc gtagccggtt gctgcgtggc ctgcgccctg	780
ctcgtggcgc actaggacgt ggcgcacctt tgtggaggaa tagagcgggt calacaccgg	840
tagcaccgca ccaccaggaa taccgaacac gatgtcggcg ttaagctcct cgagcgatcg	900
aacaattgcc tglgcacctg tcatccgctc agggcgggcg gatcgaccac ggcttgcaac	960

[0041]

cgtagcgagg	gtgggctgtt	gagaagctgc	cacattcacg	actttctggc	tcctttacta	1020
aataaggatt	ttcacaggac	ccgtccaagc	caagccgatt	tcaactcagc	ctaaagacaa	1080
agccctcatt	taaaattgtt	ccgacgcgga	tgcgtgtgca	cgcagtgcga	cagatgtctg	1140
ttgcaaagtt	ggctacttgg	gtcataacca	acaagaaagc	cctcgttcca	acactgtggt	1200
gagtgttgtc	gagggcgctt	gacgagacga	cttggaaggc	cgttacggca	ggcgccgcgc	1260
ggttactact	acaagtcgaa	taatggatcat	ggtgtgtcat	gtacacacac	tcgagtttcc	1320
aattccacaa	cgcacgaaaa	ttcccacccc	caaaactccc	ccacttcggt	taaggaaalca	1380
ggattctcac	aaagttcagg	caggctcccc	ctacttttca	gcgctaactct	tggtctc atg	1439
					Met	
					1	
att tta ggc gta ccc att caa tat ttg ctc tat tca ttg tgg aat tgg						1487
Ile Leu Gly Val Pro Ile Gln Tyr Leu Leu Tyr Ser Leu Trp Asn Trp						
	5		10		15	
att gtc gat acc ggt ttt gat gta gca att atc ctg gtc ttg gcg ttt						1535
Ile Val Asp Thr Gly Phe Asp Val Ala Ile Ile Leu Val Leu Ala Phe						
	20		25		30	
ttg att cca cgt atc ggc cga ctg gcc atg cgt att atc aag cag cga						1583
Leu Ile Pro Arg Ile Gly Arg Leu Ala Met Arg Ile Ile Lys Gln Arg						
	35		40		45	
gtg gag tct gca gcc gat gcg gac acc act aag aac cag ctc gcg ttc						1631
Val Glu Ser Ala Ala Asp Ala Asp Thr Thr Lys Asn Gln Leu Ala Phe						
	50		55		60	65
gct ggc gtt ggc gtt tat atc gcg caa att gtg gcg ttt ttc atg ctt						1679
Ala Gly Val Gly Val Tyr Ile Ala Gln Ile Val Ala Phe Phe Met Leu						
	70		75		80	
gcc gtc tcc gcg atg cag gct ttt ggt ttc tct ctc gcg ggc gct gcg						1727
Ala Val Ser Ala Met Gln Ala Phe Gly Phe Ser Leu Ala Gly Ala Ala						
	85		90		95	
att ccg gca acc att gcg tca gct gcc att ggt ctt ggt gcg cag tcg						1775
Ile Pro Ala Thr Ile Ala Ser Ala Ala Ile Gly Leu Gly Ala Gln Ser						
	100		105		110	
att gtt gcg gac ttc ttg gcc gga ttt ttc atc ctg acg gaa aag caa						1823
Ile Val Ala Asp Phe Leu Ala Gly Phe Phe Ile Leu Thr Glu Lys Gln						
	115		120		125	
ttc ggc gtg ggt gac tgg gtg cgc ttt gag ggc aac ggc atc gtt gtt						1871
Phe Gly Val Gly Asp Trp Val Arg Phe Glu Gly Asn Gly Ile Val Val						
	130		135		140	145
gaa ggc acc gtc att gag atc acc atg cgc gcg acc aaa att cgc acg						1919
Glu Gly Thr Val Ile Glu Ile Thr Met Arg Ala Thr Lys Ile Arg Thr						
	150		155		160	
att gca caa gag acc gtg atc atc ccg aac tcc acg gcg aaa gtg tgc						1967
Ile Ala Gln Glu Thr Val Ile Ile Pro Asn Ser Thr Ala Lys Val Cys						
	165		170		175	
atc aac aat tct aat aac tgg tcg cgt gcg gtt gtc gtt att ccg atc						2015
Ile Asn Asn Ser Asn Asn Trp Ser Arg Ala Val Val Val Ile Pro Ile						
	180		185		190	
ccc atg ttg ggt tct gaa aac atc aca gat gtc atc gcg cgc tct gaa						2063
Pro Met Leu Gly Ser Glu Asn Ile Thr Asp Val Ile Ala Arg Ser Glu						
	195		200		205	
gct gcg act cgt cgc gca ctt ggc cag gag aaa atc gca ccg gaa atc						2111
Ala Ala Thr Arg Arg Ala Leu Gly Gln Glu Lys Ile Ala Pro Glu Ile						
	210		215		220	225
ctc ggt gaa ctc gat gtg cac cca gcc acg gaa gtc aca ccg cca acg						2159
Leu Gly Glu Leu Asp Val His Pro Ala Thr Glu Val Thr Pro Pro Thr						
	230		235		240	
gtg gtc ggc atg ccg tgg atg gtc acc atg cgt ttc ctc gtg caa gtc						2207
Val Val Gly Met Pro Trp Met Val Thr Met Arg Phe Leu Val Gln Val						
	245		250		255	
acc gcc ggc aat caa tgg ctg gtc gaa cgc gcc atc cgc aca gaa atc						2255
Thr Ala Gly Asn Gln Trp Leu Val Glu Arg Ala Ile Arg Thr Glu Ile						
	260		265		270	
atc aac gaa ttc tgg gaa gaa tac ggc agc gca acc act aca tcg gga						2303
Ile Asn Glu Phe Trp Glu Glu Tyr Gly Ser Ala Thr Thr Thr Ser Gly						

[0042]

275	280	285	
acc ctc att gat tcc tta cac gtt gag cat gaa gag cca aag acc tcg			2351
Thr Leu Ile Asp Ser Leu His Val Glu His Glu Glu Pro Lys Thr Ser			
290	295	300	305
ctt atc gac gcc tcc ccc cag gct ctt aag gaa ccg aag ccg gag gct			2399
Leu Ile Asp Ala Ser Pro Gln Ala Leu Lys Glu Pro Lys Pro Glu Ala			
310	315	320	
gcg gcg acg gtt gca tcg cta gct gca tcg tct aac gac gat gca gac			2447
Ala Ala Thr Val Ala Ser Leu Ala Ala Ser Ser Asn Asp Asp Ala Asp			
325	330	335	
aat gca gac gcc tcg gcg atc aat gca ggc aat cca gag aag gaa ctt			2495
Asn Ala Asp Ala Ser Ala Ile Asn Ala Gly Asn Pro Glu Lys Glu Leu			
340	345	350	
gat tcc gat gtg ctg gaa caa gaa ctc tcc agc gaa gaa ccg gaa gaa			2543
Asp Ser Asp Val Leu Glu Gln Glu Leu Ser Ser Glu Glu Pro Glu Glu			
355	360	365	
aca gca aaa cca gat cac tct ctc cga ggc ttc ttc cgc act gat tac			2591
Thr Ala Lys Pro Asp His Ser Leu Arg Gly Phe Phe Arg Thr Asp Tyr			
370	375	380	385
tac cca aat cgg tgg cag aag atc ctg tcg ttt ggc gga cgt gtc cgc			2639
Tyr Pro Asn Arg Trp Gln Lys Ile Leu Ser Phe Gly Gly Arg Val Arg			
390	395	400	
atg agc act tcc ctg ttg ttg ggt gcg ctg ctc ttg ctg tca cta ttt			2687
Met Ser Thr Ser Leu Leu Leu Gly Ala Leu Leu Leu Leu Ser Leu Phe			
405	410	415	
aag gtc atg act gtg gaa cca agt gag aat tgg caa aac tcc agt gga			2735
Lys Val Met Thr Val Glu Pro Ser Glu Asn Trp Gln Asn Ser Ser Gly			
420	425	430	
tgg ctg tca cca agc act gcc acc tca act gcg gtg acc acc tcc gaa			2783
Trp Leu Ser Pro Ser Thr Ala Thr Ser Thr Ala Val Thr Thr Ser Glu			
435	440	445	
act tcc gcg cca gca agc acg cct tcg atg aca gtg ccc act acg gtg			2831
Thr Ser Ala Pro Ala Ser Thr Pro Ser Met Thr Val Pro Thr Thr Val			
450	455	460	465
gag gag acc cca acg atg gaa tct agc gtc gaa acg cag cag gaa acc			2879
Glu Glu Thr Pro Thr Met Glu Ser Ser Val Glu Thr Gln Gln Glu Thr			
470	475	480	
tca acc cct gca acc gca acg ccc cag cga gcc gac acc atc gaa ccg			2927
Ser Thr Pro Ala Thr Ala Thr Pro Gln Arg Ala Asp Thr Ile Glu Pro			
485	490	495	
acc gag gaa gcc acg tcg cag gag gaa acg act gca tcg cag acg cag			2975
Thr Glu Glu Ala Thr Ser Gln Glu Glu Thr Thr Ala Ser Gln Thr Gln			
500	505	510	
tct cca gca gtg gaa gca cca acc gcg gtc caa gaa aca gtt gcg ccg			3023
Ser Pro Ala Val Glu Ala Pro Thr Ala Val Gln Glu Thr Val Ala Pro			
515	520	525	
acg tcc acc cct taggacgtg attacagacg tgteccattt ctttactact			3075
Thr Ser Thr Pro			
530			
attggaatt atgagttcag acgcagaaaa ggcataccgtg gagctttccg aaaaatttca			3135
cccagaacgc acccatattt tgggcgcgct tgtttttggc ctgatctcat tattagtcac			3195
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<211>	533		
<212>	PRT		
<213>	谷氨酸棒杆菌		
<400>	30		

[0043]

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Trp Ile Val Asp Thr Gly Phe Asp Val Ala Ile Ile Leu Val Leu Ala
20           25           30
Phe Leu Ile Pro Arg Ile Gly Arg Leu Ala Met Arg Ile Ile Lys Gln
35           40           45
Arg Val Glu Ser Ala Ala Asp Ala Asp Thr Thr Lys Asn Gln Leu Ala
50           55           60
Phe Ala Gly Val Gly Val Tyr Ile Ala Gln Ile Val Ala Phe Phe Met
65           70           75           80
Leu Ala Val Ser Ala Met Gln Ala Phe Gly Phe Ser Leu Ala Gly Ala
85           90           95
Ala Ile Pro Ala Thr Ile Ala Ser Ala Ala Ile Gly Leu Gly Ala Gln
100          105          110
Ser Ile Val Ala Asp Phe Leu Ala Gly Phe Phe Ile Leu Thr Glu Lys
115          120          125
Gln Phe Gly Val Gly Asp Trp Val Arg Phe Glu Gly Asn Gly Ile Val
130          135          140
Val Glu Gly Thr Val Ile Glu Ile Thr Met Arg Ala Thr Lys Ile Arg
145          150          155          160
Thr Ile Ala Gln Glu Thr Val Ile Ile Pro Asn Ser Thr Ala Lys Val
165          170          175
Cys Ile Asn Asn Ser Asn Asn Trp Ser Arg Ala Val Val Val Ile Pro
180          185          190
Ile Pro Met Leu Gly Ser Glu Asn Ile Thr Asp Val Ile Ala Arg Ser
195          200          205
Glu Ala Ala Thr Arg Arg Ala Leu Gly Gln Glu Lys Ile Ala Pro Glu
210          215          220
Ile Leu Gly Glu Leu Asp Val His Pro Ala Thr Glu Val Thr Pro Pro
225          230          235          240
Thr Val Val Gly Met Pro Trp Met Val Thr Met Arg Phe Leu Val Gln
245          250          255
Val Thr Ala Gly Asn Gln Trp Leu Val Glu Arg Ala Ile Arg Thr Glu
260          265          270
Ile Ile Asn Glu Phe Trp Glu Glu Tyr Gly Ser Ala Thr Thr Thr Ser
275          280          285
Gly Thr Leu Ile Asp Ser Leu His Val Glu His Glu Glu Pro Lys Thr
290          295          300
Ser Leu Ile Asp Ala Ser Pro Gln Ala Leu Lys Glu Pro Lys Pro Glu
305          310          315          320
Ala Ala Ala Thr Val Ala Ser Leu Ala Ala Ser Ser Asn Asp Asp Ala
325          330          335
Asp Asn Ala Asp Ala Ser Ala Ile Asn Ala Gly Asn Pro Glu Lys Glu
340          345          350
Leu Asp Ser Asp Val Leu Glu Gln Glu Leu Ser Ser Glu Glu Pro Glu
355          360          365
Glu Thr Ala Lys Pro Asp His Ser Leu Arg Gly Phe Phe Arg Thr Asp
370          375          380
Tyr Tyr Pro Asn Arg Trp Gln Lys Ile Leu Ser Phe Gly Gly Arg Val
385          390          395          400
Arg Met Ser Thr Ser Leu Leu Leu Gly Ala Leu Leu Leu Ser Leu
405          410          415
Phe Lys Val Met Thr Val Glu Pro Ser Glu Asn Trp Gln Asn Ser Ser
420          425          430
Gly Trp Leu Ser Pro Ser Thr Ala Thr Ser Thr Ala Val Thr Thr Ser
435          440          445
Glu Thr Ser Ala Pro Ala Ser Thr Pro Ser Met Thr Val Pro Thr Thr
450          455          460
Val Glu Glu Thr Pro Thr Met Glu Ser Ser Val Glu Thr Gln Gln Glu
465          470          475          480
Thr Ser Thr Pro Ala Thr Ala Thr Pro Gln Arg Ala Asp Thr Ile Glu
485          490          495
Pro Thr Glu Glu Ala Thr Ser Gln Glu Glu Thr Thr Ala Ser Gln Thr

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[0044]

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 515 520 525
 Pro Thr Ser Thr Pro
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 <211> 3481
 <212> DNA
 <213> 谷氨酸棒杆菌

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 <222> (1437)..(3035)
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 cagctcgttg gactctggga aggttcccag cgcctatcaat gtggtgacaa ctggaatgcc 240
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 atcggtaccc agcagggtac ttccgacctg gccggtgatg gcaaccatgg gaacggagtc 660
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 att tta ggc gta ccc att caa tat ttg ctc tat tca ttg tgg aat tgg 1487
 Ile Leu Gly Val Pro Ile Gln Tyr Leu Leu Tyr Ser Leu Trp Asn Trp
 5 10 15
 att gtc gat acc ggt ttt gat gta gca att atc ctg gtc ttg gcg ttt 1535
 Ile Val Asp Thr Gly Phe Asp Val Ala Ile Ile Leu Val Leu Ala Phe
 20 25 30
 ttg att cca cgt atc ggc cga ctg gcc atg cgt att atc aag cag cga 1583
 Leu Ile Pro Arg Ile Gly Arg Leu Ala Met Arg Ile Ile Lys Gln Arg
 35 40 45
 gtg gag tct gca gcc gat gcg gac acc act aag aac cag ctc gcg ttc 1631
 Val Glu Ser Ala Ala Asp Thr Thr Lys Asn Gln Leu Ala Phe
 50 55 60 65
 gct ggc gtt ggc gtt tat atc gcg caa att gtg gcg ttt ttc atg ctt 1679
 Ala Gly Val Gly Val Tyr Ile Ala Gln Ile Val Ala Phe Phe Met Leu
 70 75 80
 gcc gtc tcc gcg atg cag gct ttt ggt ttc tct ctc gcg ggc gct gcg 1727
 Ala Val Ser Ala Met Gln Ala Phe Gly Phe Ser Leu Ala Gly Ala Ala
 85 90 95
 att ccg gca acc att gcg tca gct gcc att ggt ctt ggt gtg cag tcg 1775

[0045]

Ile Pro Ala Thr Ile Ala Ser Ala Ala Ile Gly Leu Gly Val Gln Ser	
100 105 110	
att gtt gcg gac ttc ttg gcc gga ttt ttc atc ctg acg gaa aag caa	1823
Ile Val Ala Asp Phe Leu Ala Gly Phe Phe Ile Leu Thr Glu Lys Gln	
115 120 125	
ttc ggc gtg ggt gac tgg gtg cgc ttt gag ggc aac ggc atc gtt gtt	1871
Phe Gly Val Gly Asp Trp Val Arg Phe Glu Gly Asn Gly Ile Val Val	
130 135 140 145	
gaa ggc acc gtc att gag atc acc atg cgc gcg acc aaa att cgc acg	1919
Glu Gly Thr Val Ile Glu Ile Thr Met Arg Ala Thr Lys Ile Arg Thr	
150 155 160	
att gca caa gag acc gtg atc atc ccg aac tcc acg gcg aaa gtg tgc	1967
Ile Ala Gln Glu Thr Val Ile Ile Pro Asn Ser Thr Ala Lys Val Cys	
165 170 175	
atc aac aat tct aat aac tgg tcg cgt gcg gtt gtc gtt att ccg atc	2015
Ile Asn Asn Ser Asn Asn Trp Ser Arg Ala Val Val Val Ile Pro Ile	
180 185 190	
ccc atg ttg ggt tct gaa aac atc aca gat gtc atc gcg cgc tct gaa	2063
Pro Met Leu Gly Ser Glu Asn Ile Thr Asp Val Ile Ala Arg Ser Glu	
195 200 205	
gct gcg act cgt cgc gca ctt ggc cag gag aaa atc gca ccg gaa atc	2111
Ala Ala Thr Arg Arg Ala Leu Gly Gln Glu Lys Ile Ala Pro Glu Ile	
210 215 220 225	
ctc ggt gaa ctc gat gtg cac cca gcc acg gaa gtc aca ccg cca acg	2159
Leu Gly Glu Leu Asp Val His Pro Ala Thr Glu Val Thr Pro Pro Thr	
230 235 240	
gtg gtc ggc atg ccg tgg atg gtc acc atg cgt ttc ctc gtg caa gtc	2207
Val Val Gly Met Pro Trp Met Val Thr Met Arg Phe Leu Val Gln Val	
245 250 255	
acc gcc ggc aat caa tgg ctg gtc gaa cgc gcc atc cgc aca gaa atc	2255
Thr Ala Gly Asn Gln Trp Leu Val Glu Arg Ala Ile Arg Thr Glu Ile	
260 265 270	
atc aac gaa ttc tgg gaa gaa tac ggc agc gca acc act aca tcg gga	2303
Ile Asn Glu Phe Trp Glu Glu Tyr Gly Ser Ala Thr Thr Thr Ser Gly	
275 280 285	
acc ctc att gat tcc tta cac gtt gag cat gaa gag cca aag acc tcg	2351
Thr Leu Ile Asp Ser Leu His Val Glu His Glu Glu Pro Lys Thr Ser	
290 295 300 305	
ctt atc gac gcc tcc ccc cag gct ctt aag gaa ccg aag ccg gag gct	2399
Leu Ile Asp Ala Ser Pro Gln Ala Leu Lys Glu Pro Lys Pro Glu Ala	
310 315 320	
gcg gcg acg gtt gca tcg cta gct gca tcg tct aac gac gat gca gac	2447
Ala Ala Thr Val Ala Ser Leu Ala Ala Ser Ser Asn Asp Asp Ala Asp	
325 330 335	
aat gca gac gcc tcg gcg atc aat gca ggc aat cca gag aag gaa ctt	2495
Asn Ala Asp Ala Ser Ala Ile Asn Ala Gly Asn Pro Glu Lys Glu Leu	
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gat tcc gat gtg ctg gaa caa gaa ctc tcc agc gaa gaa ccg gaa gaa	2543
Asp Ser Asp Val Leu Glu Gln Glu Leu Ser Ser Glu Glu Pro Glu Glu	
355 360 365	
aca gca aaa cca gat cac tct ctc cga ggc ttc ttc cgc act gat tac	2591
Thr Ala Lys Pro Asp His Ser Leu Arg Gly Phe Phe Arg Thr Asp Tyr	
370 375 380 385	
tac cca aat cgg tgg cag aag atc ctg tcg ttt ggc gga cgt gtc cgc	2639
Tyr Pro Asn Arg Trp Gln Lys Ile Leu Ser Phe Gly Gly Arg Val Arg	
390 395 400	
atg agc act tcc ctg ttg ttg ggt gcg ctg ctc ttg ctg tca cta ttt	2687
Met Ser Thr Ser Leu Leu Leu Gly Ala Leu Leu Leu Leu Ser Leu Phe	
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aag gtc atg act gtg gaa cca agt gag aat tgg caa aac tcc agt gga	2735
Lys Val Met Thr Val Glu Pro Ser Glu Asn Trp Gln Asn Ser Ser Gly	
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[0046]

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act tcc gcg cca gca agc acg cct tcg atg aca gtg ccc act acg gtg      2831
Thr Ser Ala Pro Ala Ser Thr Pro Ser Met Thr Val Pro Thr Thr Val
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gag gag acc cca acg atg gaa tct agc gtc gaa acg cag cag gaa acc      2879
Glu Glu Thr Pro Thr Met Glu Ser Ser Val Glu Thr Gln Gln Glu Thr
                               470                               475                               480
tca acc cct gca acc gca acg ccc cag cga gcc gac acc atc gaa ccg      2927
Ser Thr Pro Ala Thr Ala Thr Pro Gln Arg Ala Asp Thr Ile Glu Pro
                               485                               490                               495
acc gag gaa gcc acg tcg cag gag gaa acg act gca tcg cag acg cag      2975
Thr Glu Glu Ala Thr Ser Gln Glu Glu Thr Thr Ala Ser Gln Thr Gln
                               500                               505                               510
tct cca gca gtg gaa gca cca acc gcg gtc caa gaa aca gtt gcg ccg      3023
Ser Pro Ala Val Glu Ala Pro Thr Ala Val Gln Glu Thr Val Ala Pro
                               515                               520                               525
acg tcc acc cct taggacgtg attacagacg tgtcccatit ctttactact      3075
Thr Ser Thr Pro
530
attggaatt atgagttcag acgcagaaaa ggcacccgtg gagctttccg aaaaatttca      3135
cccagaacgc acccataatt tgggcgcctg tgtttttggc ctgatctcat tattagtcac      3195
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<213> 谷氨酸棒杆菌

<400> 32

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

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[0047]

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 260 265 270
 Ile Ile Asn Glu Phe Trp Glu Glu Tyr Gly Ser Ala Thr Thr Thr Ser
 275 280 285
 Gly Thr Leu Ile Asp Ser Leu His Val Glu His Glu Glu Pro Lys Thr
 290 295 300
 Ser Leu Ile Asp Ala Ser Pro Gln Ala Leu Lys Glu Pro Lys Pro Glu
 305 310 315 320
 Ala Ala Ala Thr Val Ala Ser Leu Ala Ala Ser Ser Asn Asp Asp Ala
 325 330 335
 Asp Asn Ala Asp Ala Ser Ala Ile Asn Ala Gly Asn Pro Glu Lys Glu
 340 345 350
 Leu Asp Ser Asp Val Leu Glu Gln Glu Leu Ser Ser Glu Glu Pro Glu
 355 360 365
 Glu Thr Ala Lys Pro Asp His Ser Leu Arg Gly Phe Phe Arg Thr Asp
 370 375 380
 Tyr Tyr Pro Asn Arg Trp Gln Lys Ile Leu Ser Phe Gly Gly Arg Val
 385 390 395 400
 Arg Met Ser Thr Ser Leu Leu Leu Gly Ala Leu Leu Leu Ser Leu
 405 410 415
 Phe Lys Val Met Thr Val Glu Pro Ser Glu Asn Trp Gln Asn Ser Ser
 420 425 430
 Gly Trp Leu Ser Pro Ser Thr Ala Thr Ser Thr Ala Val Thr Thr Ser
 435 440 445
 Glu Thr Ser Ala Pro Ala Ser Thr Pro Ser Met Thr Val Pro Thr Thr
 450 455 460
 Val Glu Glu Thr Pro Thr Met Glu Ser Ser Val Glu Thr Gln Gln Glu
 465 470 475 480
 Thr Ser Thr Pro Ala Thr Ala Thr Pro Gln Arg Ala Asp Thr Ile Glu
 485 490 495
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 500 505 510
 Gln Ser Pro Ala Val Glu Ala Pro Thr Ala Val Gln Glu Thr Val Ala
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 Pro Thr Ser Thr Pro
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29

[0048]

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[0049]

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gcgccaactg atcgcgctgg cgcgcgccga actcatcgag ccttccatca tgcttctcga		180
cgaagccacc tccaccctcg accccgccac cgaagccggt atcctcaacg cctccgatcg		240
agtcactaag ggacgcacca gcatcatcgt cgcgcaccgc ttggcaaccg ctaaaagggc		300
cgaccgtatt cttgttgttg aacaaggacg tatcattgag gacggatctc acgacgcgtt		360
gttgctctgct aacggcaccct acgcccgcgt gtggcattta atggcctgac acgttatatt		420
taggagaact gtcaacaaat ta atg cta caa ctg ggg ctt agg cat aat cag		472
Met Leu Gln Leu Gly Leu Arg His Asn Gln		
1 5 10		
cca acg acc aac gtt aca gtg gat aaa ata aag ctc aat aaa ccc tca		520
Pro Thr Thr Asn Val Thr Val Asp Lys Ile Lys Leu Asn Lys Pro Ser		
15 20 25		
aga agc aag gaa aag agg cga gta cct gcc gtg agc agc gct agt act		568
Arg Ser Lys Lys Glu Lys Arg Arg Val Pro Ala Val Ser Ser Ala Ser Thr		
30 35 40		
ttc ggc cag aat gcg tgg ctg gta gac gag atg ttc cag cag ttc cag		616
Phe Gly Gln Asn Ala Trp Leu Val Asp Glu Met Phe Gln Gln Phe Gln		
45 50 55		
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Lys Asp Pro Lys Ser Val Asp Lys Glu Trp Arg Glu Leu Phe Glu Ala		
60 65 70		
cag ggg gga cca aat gct acc ccc gct aca aca gaa gca cag cct tca		712
Gln Gly Gly Pro Asn Ala Thr Pro Ala Thr Thr Glu Ala Gln Pro Ser		
75 80 85 90		
gcg ccc aag gag tct gcg aaa cca gca cca aag gct gcc cct gca gcc		760
Ala Pro Lys Glu Ser Ala Lys Pro Ala Pro Lys Ala Ala Pro Ala Ala		
95 100 105		
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[0050]

Lys Ala Ala Pro Arg Val Glu Thr Lys Pro Ala Ala Lys Thr Ala Pro	
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aag gcc aag gag tcc tca gtg cca cag caa cct aag ctt ccg gag cca	856
Lys Ala Lys Glu Ser Ser Val Pro Gln Gln Pro Lys Leu Pro Glu Pro	
125 130 135	
gga caa acc cca atc agg ggt att ttc aag tcc atc gcg aag aac atg	904
Gly Gln Thr Pro Ile Arg Gly Ile Phe Lys Ser Ile Ala Lys Asn Met	
140 145 150	
gat atc tcc ctg gaa atc cca acc gca acc tcg gtt cgc gat atg cca	952
Asp Ile Ser Leu Glu Ile Pro Thr Ala Thr Ser Val Arg Asp Met Pro	
155 160 165 170	
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Ala Arg Leu Met Phe Glu Asn Arg Ala Met Val Asn Asp Gln Leu Lys	
175 180 185	
cgc acc cgc ggt ggc aag atc tcc ttc acc cac atc att ggc tac gcc	1048
Arg Thr Arg Gly Lys Ile Ser Phe Thr His Ile Ile Gly Tyr Ala	
190 195 200	
atg gtg aag gca gtc atg gct cac ccg gac atg aac aac tcc tac gac	1096
Met Val Lys Ala Val Met Ala His Pro Asp Met Asn Asn Ser Tyr Asp	
205 210 215	
gtc atc gac ggc aag cca acc ctg atc gtg cct gag cac atc aac ctg	1144
Val Ile Asp Gly Lys Pro Thr Leu Ile Val Pro Glu His Ile Asn Leu	
220 225 230	
ggc ctt gcc atc gac ctt cct cag aag gac ggc tcc cgc gca ctt gtc	1192
Gly Leu Ala Ile Asp Leu Pro Gln Lys Asp Gly Ser Arg Ala Leu Val	
235 240 245 250	
gta gca gcc atc aag gaa acc gag aag atg aac ttc tcc gag ttc ctc	1240
Val Ala Ala Ile Lys Glu Thr Glu Lys Met Asn Phe Ser Glu Phe Leu	
255 260 265	
gca gca tac gaa gac atc gtg aca cgc tcc cgc aag ggc aag ctc acc	1288
Ala Ala Tyr Glu Asp Ile Val Thr Arg Ser Arg Lys Gly Lys Leu Thr	
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Met Asp Asp Tyr Gln Gly Val Thr Val Ser Leu Thr Asn Pro Gly Gly	
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Ile Gly Thr Arg His Ser Val Pro Arg Leu Thr Lys Gly Gln Gly Thr	
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Ile Ile Gly Val Gly Ser Met Asp Tyr Pro Ala Glu Phe Gln Gly Ala	
315 320 325 330	
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Ser Glu Asp Arg Leu Ala Glu Leu Gly Val Gly Lys Leu Val Thr Ile	
335 340 345	
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Thr Ser Thr Tyr Asp His Arg Val Ile Gln Gly Ala Val Ser Gly Glu	
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Phe Leu Arg Thr Met Ser Arg Leu Leu Thr Asp Asp Ser Phe Trp Asp	
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Glu Ile Phe Asp Ala Met Asn Val Pro Tyr Thr Pro Met Arg Trp Ala	
380 385 390	
cag gac gtt cca aac acc ggt gtt gat aag aac acc cgc gtc atg cag	1672
Gln Asp Val Pro Asn Thr Gly Val Asp Lys Asn Thr Arg Val Met Gln	
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Leu Ile Glu Ala Tyr Arg Ser Arg Gly His Leu Ile Ala Asp Thr Asn	
415 420 425	
cca ctt tca tgg gtt cag cct ggc atg cca gtt cca gac cac cgc gac	1768
Pro Leu Ser Trp Val Gln Pro Gly Met Pro Val Pro Asp His Arg Asp	
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[0051]

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Phe Ser Val Gly Gly Phe Gly Gly Lys Glu Thr Met Thr Leu Arg Glu	
460 465 470	
gta ctg tcc cgc ctg cgc gct gcc tac acc ttg aag gtc ggc tcc gaa	1912
Val Leu Ser Arg Leu Arg Ala Ala Tyr Thr Leu Lys Val Gly Ser Glu	
475 480 485 490	
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Tyr Thr His Ile Leu Asp Arg Asp Glu Arg Thr Trp Leu Gln Asp Arg	
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Leu Glu Ala Gly Met Pro Lys Pro Thr Gln Ala Glu Gln Lys Tyr Ile	
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Leu Gln Lys Leu Asn Ala Ala Glu Ala Phe Glu Asn Phe Leu Gln Thr	
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Lys Tyr Val Gly Gln Lys Arg Phe Ser Leu Glu Gly Ala Glu Ala Leu	
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Phe Asn Ile Val Gly Lys Pro Leu Ala Ser Ile Phe Asn Glu Phe Glu	
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Gly Gln Met Glu Gln Gly Gln Ile Gly Gly Ser Gly Asp Val Lys Tyr	
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Ile Lys Val Ser Leu Thr Ala Asn Pro Ser His Leu Glu Ala Val Asn	
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Gly Val Asp Gly Lys Thr Val Val Pro Leu Leu Leu His Gly Asp Ala	
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Leu Arg	
700	
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[0052]

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aggacggcag cgacgacatc gcgatcgttc gtatcgaaat gctccacca attccgttca 3972
accgcatctc cgaggctctt gccggctacc ctaacgctga ggaagtcctc ttcgttcagg 4032
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cgaacatgcc aaagatgcgc cgcgtttccc gccgcgtcga gtcctccacc gcaactggtg 4152
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tctttatagt cctgcactag cctagagggc cttatgcagt gtgaatcaca cagcataagg 4272
ccctttttgc tgcctgtgtt gcctaagggt gaaggcatga aacgaatctg tgcggtcacg 4332
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<210> 43

<211> 700

<212> PRT

<213> 谷氨酸棒杆菌

<400> 43

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

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[0053]

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305          310          315          320
Met Asp Tyr Pro Ala Glu Phe Gln Gly Ala Ser Glu Asp Arg Leu Ala
          325          330          335
Glu Leu Gly Val Gly Lys Leu Val Thr Ile Thr Ser Thr Tyr Asp His
          340          345          350
Arg Val Ile Gln Gly Ala Val Ser Gly Glu Phe Leu Arg Thr Met Ser
          355          360          365
Arg Leu Leu Thr Asp Asp Ser Phe Trp Asp Glu Ile Phe Asp Ala Met
          370          375          380
Asn Val Pro Tyr Thr Pro Met Arg Trp Ala Gln Asp Val Pro Asn Thr
          385          390          395          400
Gly Val Asp Lys Asn Thr Arg Val Met Gln Leu Ile Glu Ala Tyr Arg
          405          410          415
Ser Arg Gly His Leu Ile Ala Asp Thr Asn Pro Leu Ser Trp Val Gln
          420          425          430
Pro Gly Met Pro Val Pro Asp His Arg Asp Leu Asp Ile Glu Thr His
          435          440          445
Ser Leu Thr Ile Trp Asp Leu Asp Arg Thr Phe Ser Val Gly Gly Phe
          450          455          460
Gly Gly Lys Glu Thr Met Thr Leu Arg Glu Val Leu Ser Arg Leu Arg
          465          470          475          480
Ala Ala Tyr Thr Leu Lys Val Gly Ser Glu Tyr Thr His Ile Leu Asp
          485          490          495
Arg Asp Glu Arg Thr Trp Leu Gln Asp Arg Leu Glu Ala Gly Met Pro
          500          505          510
Lys Pro Thr Gln Ala Glu Gln Lys Tyr Ile Leu Gln Lys Leu Asn Ala
          515          520          525
Ala Glu Ala Phe Glu Asn Phe Leu Gln Thr Lys Tyr Val Gly Gln Lys
          530          535          540
Arg Phe Ser Leu Glu Gly Ala Glu Ala Leu Ile Pro Leu Met Asp Ser
          545          550          555          560
Ala Ile Asp Thr Ala Ala Gly Gln Gly Leu Asp Glu Val Val Ile Gly
          565          570          575
Met Pro His Arg Gly Arg Leu Asn Val Leu Phe Asn Ile Val Gly Lys
          580          585          590
Pro Leu Ala Ser Ile Phe Asn Glu Phe Glu Gly Gln Met Glu Gln Gly
          595          600          605
Gln Ile Gly Gly Ser Gly Asp Val Lys Tyr His Leu Gly Ser Glu Gly
          610          615          620
Gln His Leu Gln Met Phe Gly Asp Gly Glu Ile Lys Val Ser Leu Thr
          625          630          635          640
Ala Asn Pro Ser His Leu Glu Ala Val Asn Pro Val Met Glu Gly Ile
          645          650          655
Val Arg Ala Lys Gln Asp Tyr Leu Asp Lys Gly Val Asp Gly Lys Thr
          660          665          670
Val Val Pro Leu Leu Leu His Gly Asp Ala Ala Phe Ala Gly Leu Gly
          675          680          685
Ile Val Pro Glu Thr Ile Asn Leu Ala Lys Leu Arg
          690          695          700

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<210> 44
 <211> 4391
 <212> DNA
 <213> 谷氨酸棒杆菌

<220>
 <221> CDS
 <222> (443)..(4210)
 <223> sucA801

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gcgccaactg atcgcgctgg cgcgcgcga actcatcgag ccttccatca tgcttctcga	180
cgaagccacc tccaccctcg accccgcac cgaagccgtt atctcaacg cctccgatcg	240
agtcactaag ggaagcacca gcatcatcgt cgcgcaccgc ttggcaaccg ctaaaagggc	300
cgaccgtatt cttgttgttg aacaaggacg tatcattgag gacggatctc acgacgcgtt	360
gttgtctgct aacggcacct acgcccgcgt gtggcattta atggcctgac acgttatatt	420
taggagaact gtcaacaaat ta atg cta caa ctg ggg ctt agg cat aat cag	472
Met Leu Gln Leu Gly Leu Arg His Asn Gln	
1 5 10	
cca acg acc aac gtt aca gtg gat aaa ata aag ctc aat aaa ccc tca	520
Pro Thr Thr Asn Val Thr Val Asp Lys Ile Lys Leu Asn Lys Pro Ser	
15 20 25	
aga agc aag gaa aag agg cga gta cct gcc gtg agc agc gct agt act	568
Arg Ser Lys Glu Lys Arg Arg Val Pro Ala Val Ser Ser Ala Ser Thr	
30 35 40	
ttc ggc cag aat gcg tgg ctg gta gac gag atg ttc cag cag ttc cag	616
Phe Gly Gln Asn Ala Trp Leu Val Asp Glu Met Phe Gln Gln Phe Gln	
45 50 55	
aag gac ccc aag tcc gtg gac aag gaa tgg aga gaa ctc ttt gag gcg	664
Lys Asp Pro Lys Ser Val Asp Lys Glu Trp Arg Glu Leu Phe Glu Ala	
60 65 70	
cag ggg gga cca aat gct acc ccc gct aca aca gaa gca cag cct tca	712
Gln Gly Gly Pro Asn Ala Thr Pro Ala Thr Thr Glu Ala Gln Pro Ser	
75 80 85 90	
gcg ccc aag gag tct gcg aaa cca gca cca aag gct gcc cct gca gcc	760
Ala Pro Lys Glu Ser Ala Lys Pro Ala Pro Lys Ala Ala Pro Ala Ala	
95 100 105	
aag gca gca ccg cgc gta gaa acc aag ccg gcc gcc aag acc gcc cct	808
Lys Ala Ala Pro Arg Val Glu Thr Lys Pro Ala Ala Lys Thr Ala Pro	
110 115 120	
aag gcc aag gag tcc tca gtg cca cag caa cct aag ctt ccg gag cca	856
Lys Ala Lys Glu Ser Ser Val Pro Gln Gln Pro Lys Leu Pro Glu Pro	
125 130 135	
gga caa acc cca atc agg ggt att ttc aag tcc atc gcg aag aac atg	904
Gly Gln Thr Pro Ile Arg Gly Ile Phe Lys Ser Ile Ala Lys Asn Met	
140 145 150	
gat atc tcc ctg gaa atc cca acc gca acc tcg gtt cgc gat atg cca	952
Asp Ile Ser Leu Glu Ile Pro Thr Ala Thr Ser Val Arg Asp Met Pro	
155 160 165 170	
gct cgc ctc atg ttc gaa aac cgc gcg atg gtc aac gat cag ctc aag	1000
Ala Arg Leu Met Phe Glu Asn Arg Ala Met Val Asn Asp Gln Leu Lys	
175 180 185	
cgc acc cgc ggt ggc aag atc tcc ttc acc cac atc att gcc tac gcc	1048
Arg Thr Arg Gly Gly Lys Ile Ser Phe Thr His Ile Ile Gly Tyr Ala	
190 195 200	
atg gtg aag gca gtc atg gct cac ccg gac atg aac aac tcc tac gac	1096
Met Val Lys Ala Val Met Ala His Pro Asp Met Asn Asn Ser Tyr Asp	
205 210 215	
gtc atc gac ggc aag cca acc ctg atc gtg cct gag cac atc aac ctg	1144
Val Ile Asp Gly Lys Pro Thr Leu Ile Val Pro Glu His Ile Asn Leu	
220 225 230	
ggc ctt gcc atc gac ctt cct cag aag gac ggc tcc cgc gca ctt gtc	1192
Gly Leu Ala Ile Asp Leu Pro Gln Lys Asp Gly Ser Arg Ala Leu Val	
235 240 245 250	
gta gca gcc atc aag gaa acc gag aag atg aac ttc tcc gag ttc ctc	1240
Val Ala Ala Ile Lys Glu Thr Glu Lys Met Asn Phe Ser Glu Phe Leu	
255 260 265	
gca gca tac gaa gac atc gtg aca cgc tcc cgc aag ggc aag ctc acc	1288
Ala Ala Tyr Glu Asp Ile Val Thr Arg Ser Arg Lys Gly Lys Leu Thr	
270 275 280	
atg gat gac tac cag ggc gtt acc gtt tcc ttg acc aac cca ggt ggc	1336
Met Asp Asp Tyr Gln Gly Val Thr Val Ser Leu Thr Asn Pro Gly Gly	
285 290 295	
atc ggt acc cgc cac tct gtc cca cgt ctg acc aag ggc cag ggc acc	1384

[0055]

Ile Gly Thr Arg His Ser Val Pro Arg Leu Thr Lys Gly Gln Gly Thr	
300 305 310	
atc atc ggt gtc ggt tcc atg gat tac cca gca gag ttc cag ggc gct	1432
Ile Ile Gly Val Gly Ser Met Asp Tyr Pro Ala Glu Phe Gln Gly Ala	
315 320 325 330	
tcc gaa gac cgc ctt gca gag ctc ggc gtt gga aag ctt gtc acc atc	1480
Ser Glu Asp Arg Leu Ala Glu Leu Gly Val Gly Lys Leu Val Thr Ile	
335 340 345	
acc tcc acc tac gat cac cgc gtg atc cag ggt gct gtg tcc ggt gaa	1528
Thr Ser Thr Tyr Asp His Arg Val Ile Gln Gly Ala Val Ser Gly Glu	
350 355 360	
ttc ctg cgt acc atg tct cgc ctg ctc acc gat gat tcc ttc tgg gat	1576
Phe Leu Arg Thr Met Ser Arg Leu Leu Thr Asp Asp Ser Phe Trp Asp	
365 370 375	
gag atc ttc gac gca atg aac gtt cct tac acc cca atg cgt tgg gca	1624
Glu Ile Phe Asp Ala Met Asn Val Pro Tyr Thr Pro Met Arg Trp Ala	
380 385 390	
cag gac gtt cca aac acc ggt gtt gat aag aac acc cgc gtc atg cag	1672
Gln Asp Val Pro Asn Thr Gly Val Asp Lys Asn Thr Arg Val Met Gln	
395 400 405 410	
ctc att gag gca tac cgc tcc cgt gga cac ctc atc gct gac acc aac	1720
Leu Ile Glu Ala Tyr Arg Ser Arg Gly His Leu Ile Ala Asp Thr Asn	
415 420 425	
cca ctt tca tgg gtt cag cct ggc atg cca gtt cca gac cac cgc gac	1768
Pro Leu Ser Trp Val Gln Pro Gly Met Pro Val Pro Asp His Arg Asp	
430 435 440	
ctc gac atc gag acc cac agc ctg acc atc tgg gat ctg gac cgt acc	1816
Leu Asp Ile Glu Thr His Ser Leu Thr Ile Trp Asp Leu Asp Arg Thr	
445 450 455	
ttc agc gtc ggt ggc ttc ggc ggc aag gag acc atg acc ctg cgc gag	1864
Phe Ser Val Gly Gly Phe Gly Gly Lys Glu Thr Met Thr Leu Arg Glu	
460 465 470	
gta ctg tcc cgc ctg cgc gct gcc tac acc ttg aag gtc ggc tcc gaa	1912
Val Leu Ser Arg Leu Arg Ala Ala Tyr Thr Leu Lys Val Gly Ser Glu	
475 480 485 490	
tac acc cac atc ctg gac cgc gac gag cgc acc tgg ctg cag gac cgc	1960
Tyr Thr His Ile Leu Asp Arg Asp Glu Arg Thr Trp Leu Gln Asp Arg	
495 500 505	
ctc gaa gcc gga atg cca aag cca acc cag gca gag cag aag tac atc	2008
Leu Glu Ala Gly Met Pro Lys Pro Thr Gln Ala Glu Gln Lys Tyr Ile	
510 515 520	
ctg cag aag ctg aac gcc gca gag gct ttc gag aac ttc ctg cag acc	2056
Leu Gln Lys Leu Asn Ala Ala Glu Ala Phe Glu Asn Phe Leu Gln Thr	
525 530 535	
aag tac gtc ggc cag aag cgc ttc tcc ctc gaa ggt gca gaa gct ctc	2104
Lys Tyr Val Gly Gln Lys Arg Phe Ser Leu Glu Gly Ala Glu Ala Leu	
540 545 550	
atc cca ctg atg gac tcc gcc atc gac acc gcc gca ggc cag ggc ctc	2152
Ile Pro Leu Met Asp Ser Ala Ile Asp Thr Ala Ala Gly Gln Gly Leu	
555 560 565 570	
gac gaa gtt gtc atc ggt atg cca cac cgt ggt cgc ctc aac gtg ctg	2200
Asp Glu Val Val Ile Gly Met Pro His Arg Gly Arg Leu Asn Val Leu	
575 580 585	
ttc aac atc gtg ggc aag cca ctg gca tcc atc ttc aac gag ttt gaa	2248
Phe Asn Ile Val Gly Lys Pro Leu Ala Ser Ile Phe Asn Glu Phe Glu	
590 595 600	
ggc caa atg gag cag ggc cag atc ggt ggc tcc ggt gac gtg aag tac	2296
Gly Gln Met Glu Gln Gly Gln Ile Gly Gly Ser Gly Asp Val Lys Tyr	
605 610 615	
cac ctc ggt tcc gaa ggc cag cac ctg cag atg ttc ggc gac ggc gag	2344
His Leu Gly Ser Glu Gly Gln His Leu Gln Met Phe Gly Asp Gly Glu	
620 625 630	
atc aag gtc tcc ctg act gct aac ccg tcc cac ctg gaa gct gtt aac	2392

[0056]

Ile Lys Val Ser Leu Thr Ala Asn Pro Ser His Leu Glu Ala Val Asn	
635 640 645 650	
cca gtg atg gaa ggt atc gtc cgc gca aag cag gac tac ctg gac aag	2440
Pro Val Met Glu Gly Ile Val Arg Ala Lys Gln Asp Tyr Leu Asp Lys	
655 660 665	
ggc gta gac ggc aag act gtt gtg cca ctg ctg ctc cac ggt gac gct	2488
Gly Val Asp Gly Lys Thr Val Val Pro Leu Leu Leu His Gly Asp Ala	
670 675 680	
gca ttc gca ggc ctg ggc atc gtg cca gaa acc atc aac ctg gct aag	2536
Ala Phe Ala Gly Leu Gly Ile Val Pro Glu Thr Ile Asn Leu Ala Lys	
685 690 695	
ctg cgt ctc gac gtc gga ggc acc atc cac atc gtg gtg aac aac cag	2584
Leu Arg Leu Asp Val Gly Gly Thr Ile His Ile Val Val Asn Asn Gln	
700 705 710	
atc ggc ttc acc acc acc cca gac tcc agc cgc tcc atg cac tac gca	2632
Ile Gly Phe Thr Thr Thr Pro Asp Ser Ser Arg Ser Met His Tyr Ala	
715 720 725 730	
acc gac tac gcc aag gca ttc ggc tgc cca gtc ttc cac gtc aat ggt	2680
Thr Asp Tyr Ala Lys Ala Phe Gly Cys Pro Val Phe His Val Asn Gly	
735 740 745	
gat gac cca gag gca gtt gtc tgg gtt ggc cag ctg gca acc gag tac	2728
Asp Asp Pro Glu Ala Val Val Trp Val Gly Gln Leu Ala Thr Glu Tyr	
750 755 760	
cgt cgt cgc ttc ggc aag gac gtc ttc atc gac ctc gtt tgc tac cgc	2776
Arg Arg Arg Phe Gly Lys Asp Val Phe Ile Asp Leu Val Cys Tyr Arg	
765 770 775	
ctc cgc ggc cac aac gaa gct gat gat cct tcc atg acc cag cca aag	2824
Leu Arg Gly His Asn Glu Ala Asp Asp Pro Ser Met Thr Gln Pro Lys	
780 785 790	
atg tat gag ctc atc acc ggc cgc gag acc gtt cgt gct cag tac acc	2872
Met Tyr Glu Leu Ile Thr Gly Arg Glu Thr Val Arg Ala Gln Tyr Thr	
795 800 805 810	
gaa gac ctg ctc gga cgt gga gac ctc tcc aac gaa gat gca gaa gca	2920
Glu Asp Leu Leu Gly Arg Gly Asp Leu Ser Asn Glu Asp Ala Glu Ala	
815 820 825	
gtc gtc cgc gac ttc cac gac cag atg gaa tct gtg ttc aac gaa gtc	2968
Val Val Arg Asp Phe His Asp Gln Met Glu Ser Val Phe Asn Glu Val	
830 835 840	
aag gaa ggc ggc aag aag cag gct gag gca cag acc ggc atc acc ggc	3016
Lys Glu Gly Gly Lys Lys Gln Ala Glu Ala Gln Thr Gly Ile Thr Gly	
845 850 855	
tcc cag aag ctt cca cac ggc ctt gag acc aac atc tcc cgt gaa gag	3064
Ser Gln Lys Leu Pro His Gly Leu Glu Thr Asn Ile Ser Arg Glu Glu	
860 865 870	
ctc ctg gaa ctg gga cag gct ttc gcc aac acc cca gaa ggc ttc aac	3112
Leu Leu Glu Leu Gly Gln Ala Phe Ala Asn Thr Pro Glu Gly Phe Asn	
875 880 885 890	
tac cac cca cgt gtg gct cca gtt gct aag aag cgc gtc tcc tct gtc	3160
Tyr His Pro Arg Val Ala Pro Val Ala Lys Lys Arg Val Ser Ser Val	
895 900 905	
acc gaa ggt ggc atc gac tgg gca tgg ggc gag ctc ctc gcc ttc ggt	3208
Thr Glu Gly Gly Ile Asp Trp Ala Trp Gly Glu Leu Leu Ala Phe Gly	
910 915 920	
tcc ctg gct aac tcc ggc cgc ttg gtt cgc ctt gca ggt gaa gat tcc	3256
Ser Leu Ala Asn Ser Gly Arg Leu Val Arg Leu Ala Gly Glu Asp Ser	
925 930 935	
cgc cgc ggt acc ttc acc cag cgc cac gca gtt gcc atc gac cca gcg	3304
Arg Arg Gly Thr Phe Thr Gln Arg His Ala Val Ala Ile Asp Pro Ala	
940 945 950	
acc gct gaa gag ttc aac cca ctc cac gag ctt gca cag tcc aag ggc	3352
Thr Ala Glu Glu Phe Asn Pro Leu His Glu Leu Ala Gln Ser Lys Gly	
955 960 965 970	
aac aac ggt aag ttc ctg gtc tac aac tcc gca ctg acc gag tac gca	3400

[0057]

Asn Asn Gly Lys Phe Leu Val Tyr Asn Ser Ala Leu Thr Glu Tyr Ala	
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ggc atg ggc ttc gag tac ggc tac tcc gta gga aac gaa gac tcc gtc	3448
Gly Met Gly Phe Glu Tyr Gly Tyr Ser Val Gly Asn Glu Asp Ser Val	
990 995 1000	
ggt gca tgg gaa gca cag ttc ggc gac ttc gcc aac ggc gct cag	3493
Val Ala Trp Glu Ala Gln Phe Gly Asp Phe Ala Asn Gly Ala Gln	
1005 1010 1015	
acc atc atc gat gag tac gtc tcc tca ggc gaa gct aag tgg ggc	3538
Thr Ile Ile Asp Glu Tyr Val Ser Ser Gly Glu Ala Lys Trp Gly	
1020 1025 1030	
cag acc tcc aag ctg atc ctt ctg ctg cct cac ggc tac gaa ggc	3583
Gln Thr Ser Lys Leu Ile Leu Leu Leu Pro His Gly Tyr Glu Gly	
1035 1040 1045	
cag ggc cca gac cac tct tcc gca cgt atc gag cgc ttc ctg cag	3628
Gln Gly Pro Asp His Ser Ser Ala Arg Ile Glu Arg Phe Leu Gln	
1050 1055 1060	
ctg tgc gct gag ggt tcc atg act gtt gct cag cca tcc acc cca	3673
Leu Cys Ala Glu Gly Ser Met Thr Val Ala Gln Pro Ser Thr Pro	
1065 1070 1075	
gca aac cac ttc cac ctg ctg cgt cgt cac gct ctg tcc gac ctg	3718
Ala Asn His Phe His Leu Leu Arg Arg His Ala Leu Ser Asp Leu	
1080 1085 1090	
aag cgt cca ctg gtt atc ttc acc ccg aag tcc atg ctg cgt aac	3763
Lys Arg Pro Leu Val Ile Phe Thr Pro Lys Ser Met Leu Arg Asn	
1095 1100 1105	
aag gct gct gcc tcc gca cca gaa gac ttc act gag gtc acc aag	3808
Lys Ala Ala Ala Ser Ala Pro Glu Asp Phe Thr Glu Val Thr Lys	
1110 1115 1120	
ttc caa tcc gtg atc gac gat cca aac gtt gca gat gca gcc aag	3853
Phe Gln Ser Val Ile Asp Asp Pro Asn Val Ala Asp Ala Ala Lys	
1125 1130 1135	
gtg aag aag gtc atg ctg gtc tcc ggc aag ctg tac tac gaa ttg	3898
Val Lys Lys Val Met Leu Val Ser Gly Lys Leu Tyr Tyr Glu Leu	
1140 1145 1150	
gca aag cgc aag gag aag gac gga cgc gac gac atc gcg atc gtt	3943
Ala Lys Arg Lys Glu Lys Asp Gly Arg Asp Asp Ile Ala Ile Val	
1155 1160 1165	
cgt atc gaa atg ctc cac cca att ccg ttc aac cgc atc tcc gag	3988
Arg Ile Glu Met Leu His Pro Ile Pro Phe Asn Arg Ile Ser Glu	
1170 1175 1180	
gct ctt gcc ggc tac cct aac gct gag gaa gtc ctc ttc gtt cag	4033
Ala Leu Ala Gly Tyr Pro Asn Ala Glu Glu Val Leu Phe Val Gln	
1185 1190 1195	
gat gag cca gca aac cag ggc cca tgg ccg ttc tac cag gag cac	4078
Asp Glu Pro Ala Asn Gln Gly Pro Trp Pro Phe Tyr Gln Glu His	
1200 1205 1210	
ctc cca gag ctg atc ccg aac atg cca aag atg cgc cgc gtt tcc	4123
Leu Pro Glu Leu Ile Pro Asn Met Pro Lys Met Arg Arg Val Ser	
1215 1220 1225	
cgc cgc gct cag tcc tcc acc gca act ggt gtt gct aag gtg cac	4168
Arg Arg Ala Gln Ser Ser Thr Ala Thr Gly Val Ala Lys Val His	
1230 1235 1240	
cag ctg gag gag aag cag ctt atc gac gag gct ttc gag gct	4210
Gln Leu Glu Glu Lys Gln Leu Ile Asp Glu Ala Phe Glu Ala	
1245 1250 1255	
taagtcttta tagtcctgca ctagecctaga gggccttatg cagtgtgaat cacacagcat	4270
aaggcccttt ttgctgccgt ggttgccctaa ggtggaaggc atgaaacgaa tctgtgcggt	4330
cacgatctct tcagtacttt tgctaagtgg ctgctectcc acttccacca cgcagctcga	4390
g	4391

<210> 45

<211> 1256

[0058]

<212> PRT

<213> 谷氨酸棒杆菌

<400> 45

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20      25      30
Arg Val Pro Ala Val Ser Ser Ala Ser Thr Phe Gly Gln Asn Ala Trp
35      40      45
Leu Val Asp Glu Met Phe Gln Gln Phe Gln Lys Asp Pro Lys Ser Val
50      55      60
Asp Lys Glu Trp Arg Glu Leu Phe Glu Ala Gln Gly Gly Pro Asn Ala
65      70      75      80
Thr Pro Ala Thr Thr Glu Ala Gln Pro Ser Ala Pro Lys Glu Ser Ala
85      90      95
Lys Pro Ala Pro Lys Ala Ala Pro Ala Ala Lys Ala Ala Pro Arg Val
100     105     110
Glu Thr Lys Pro Ala Ala Lys Thr Ala Pro Lys Ala Lys Glu Ser Ser
115     120     125
Val Pro Gln Gln Pro Lys Leu Pro Glu Pro Gly Gln Thr Pro Ile Arg
130     135     140
Gly Ile Phe Lys Ser Ile Ala Lys Asn Met Asp Ile Ser Leu Glu Ile
145     150     155     160
Pro Thr Ala Thr Ser Val Arg Asp Met Pro Ala Arg Leu Met Phe Glu
165     170     175
Asn Arg Ala Met Val Asn Asp Gln Leu Lys Arg Thr Arg Gly Gly Lys
180     185     190
Ile Ser Phe Thr His Ile Ile Gly Tyr Ala Met Val Lys Ala Val Met
195     200     205
Ala His Pro Asp Met Asn Asn Ser Tyr Asp Val Ile Asp Gly Lys Pro
210     215     220
Thr Leu Ile Val Pro Glu His Ile Asn Leu Gly Leu Ala Ile Asp Leu
225     230     235     240
Pro Gln Lys Asp Gly Ser Arg Ala Leu Val Val Ala Ala Ile Lys Glu
245     250     255
Thr Glu Lys Met Asn Phe Ser Glu Phe Leu Ala Ala Tyr Glu Asp Ile
260     265     270
Val Thr Arg Ser Arg Lys Gly Lys Leu Thr Met Asp Asp Tyr Gln Gly
275     280     285
Val Thr Val Ser Leu Thr Asn Pro Gly Gly Ile Gly Thr Arg His Ser
290     295     300
Val Pro Arg Leu Thr Lys Gly Gln Gly Thr Ile Ile Gly Val Gly Ser
305     310     315     320
Met Asp Tyr Pro Ala Glu Phe Gln Gly Ala Ser Glu Asp Arg Leu Ala
325     330     335
Glu Leu Gly Val Gly Lys Leu Val Thr Ile Thr Ser Thr Tyr Asp His
340     345     350
Arg Val Ile Gln Gly Ala Val Ser Gly Glu Phe Leu Arg Thr Met Ser
355     360     365
Arg Leu Leu Thr Asp Asp Ser Phe Trp Asp Glu Ile Phe Asp Ala Met
370     375     380
Asn Val Pro Tyr Thr Pro Met Arg Trp Ala Gln Asp Val Pro Asn Thr
385     390     395     400
Gly Val Asp Lys Asn Thr Arg Val Met Gln Leu Ile Glu Ala Tyr Arg
405     410     415
Ser Arg Gly His Leu Ile Ala Asp Thr Asn Pro Leu Ser Trp Val Gln
420     425     430
Pro Gly Met Pro Val Pro Asp His Arg Asp Leu Asp Ile Glu Thr His
435     440     445
Ser Leu Thr Ile Trp Asp Leu Asp Arg Thr Phe Ser Val Gly Gly Phe
450     455     460
Gly Gly Lys Glu Thr Met Thr Leu Arg Glu Val Leu Ser Arg Leu Arg

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[0059]

465	470	475	480
Ala Ala Tyr Thr Leu Lys Val Gly Ser Glu Tyr Thr His Ile Leu Asp			
	485	490	495
Arg Asp Glu Arg Thr Trp Leu Gln Asp Arg Leu Glu Ala Gly Met Pro			
	500	505	510
Lys Pro Thr Gln Ala Glu Gln Lys Tyr Ile Leu Gln Lys Leu Asn Ala			
	515	520	525
Ala Glu Ala Phe Glu Asn Phe Leu Gln Thr Lys Tyr Val Gly Gln Lys			
	530	535	540
Arg Phe Ser Leu Glu Gly Ala Glu Ala Leu Ile Pro Leu Met Asp Ser			
	545	550	555
Ala Ile Asp Thr Ala Ala Gly Gln Gly Leu Asp Glu Val Val Ile Gly			
	565	570	575
Met Pro His Arg Gly Arg Leu Asn Val Leu Phe Asn Ile Val Gly Lys			
	580	585	590
Pro Leu Ala Ser Ile Phe Asn Glu Phe Glu Gly Gln Met Glu Gln Gly			
	595	600	605
Gln Ile Gly Gly Ser Gly Asp Val Lys Tyr His Leu Gly Ser Glu Gly			
	610	615	620
Gln His Leu Gln Met Phe Gly Asp Gly Glu Ile Lys Val Ser Leu Thr			
	625	630	635
Ala Asn Pro Ser His Leu Glu Ala Val Asn Pro Val Met Glu Gly Ile			
	645	650	655
Val Arg Ala Lys Gln Asp Tyr Leu Asp Lys Gly Val Asp Gly Lys Thr			
	660	665	670
Val Val Pro Leu Leu Leu His Gly Asp Ala Ala Phe Ala Gly Leu Gly			
	675	680	685
Ile Val Pro Glu Thr Ile Asn Leu Ala Lys Leu Arg Leu Asp Val Gly			
	690	695	700
Gly Thr Ile His Ile Val Val Asn Asn Gln Ile Gly Phe Thr Thr Thr			
	705	710	715
Pro Asp Ser Ser Arg Ser Met His Tyr Ala Thr Asp Tyr Ala Lys Ala			
	725	730	735
Phe Gly Cys Pro Val Phe His Val Asn Gly Asp Asp Pro Glu Ala Val			
	740	745	750
Val Trp Val Gly Gln Leu Ala Thr Glu Tyr Arg Arg Arg Phe Gly Lys			
	755	760	765
Asp Val Phe Ile Asp Leu Val Cys Tyr Arg Leu Arg Gly His Asn Glu			
	770	775	780
Ala Asp Asp Pro Ser Met Thr Gln Pro Lys Met Tyr Glu Leu Ile Thr			
	785	790	795
Gly Arg Glu Thr Val Arg Ala Gln Tyr Thr Glu Asp Leu Leu Gly Arg			
	805	810	815
Gly Asp Leu Ser Asn Glu Asp Ala Glu Ala Val Val Arg Asp Phe His			
	820	825	830
Asp Gln Met Glu Ser Val Phe Asn Glu Val Lys Glu Gly Gly Lys Lys			
	835	840	845
Gln Ala Glu Ala Gln Thr Gly Ile Thr Gly Ser Gln Lys Leu Pro His			
	850	855	860
Gly Leu Glu Thr Asn Ile Ser Arg Glu Glu Leu Leu Glu Leu Gly Gln			
	865	870	875
Ala Phe Ala Asn Thr Pro Glu Gly Phe Asn Tyr His Pro Arg Val Ala			
	885	890	895
Pro Val Ala Lys Lys Arg Val Ser Ser Val Thr Glu Gly Gly Ile Asp			
	900	905	910
Trp Ala Trp Gly Glu Leu Leu Ala Phe Gly Ser Leu Ala Asn Ser Gly			
	915	920	925
Arg Leu Val Arg Leu Ala Gly Glu Asp Ser Arg Arg Gly Thr Phe Thr			
	930	935	940
Gln Arg His Ala Val Ala Ile Asp Pro Ala Thr Ala Glu Glu Phe Asn			
	945	950	955
Pro Leu His Glu Leu Ala Gln Ser Lys Gly Asn Asn Gly Lys Phe Leu			
	965	970	975

[0060]

Val Tyr Asn Ser Ala Leu Thr Glu Tyr Ala Gly Met Gly Phe Glu Tyr
 980 985 990
 Gly Tyr Ser Val Gly Asn Glu Asp Ser Val Val Ala Trp Glu Ala Gln
 995 1000 1005
 Phe Gly Asp Phe Ala Asn Gly Ala Gln Thr Ile Ile Asp Glu Tyr
 1010 1015 1020
 Val Ser Ser Gly Glu Ala Lys Trp Gly Gln Thr Ser Lys Leu Ile
 1025 1030 1035
 Leu Leu Leu Pro His Gly Tyr Glu Gly Gln Gly Pro Asp His Ser
 1040 1045 1050
 Ser Ala Arg Ile Glu Arg Phe Leu Gln Leu Cys Ala Glu Gly Ser
 1055 1060 1065
 Met Thr Val Ala Gln Pro Ser Thr Pro Ala Asn His Phe His Leu
 1070 1075 1080
 Leu Arg Arg His Ala Leu Ser Asp Leu Lys Arg Pro Leu Val Ile
 1085 1090 1095
 Phe Thr Pro Lys Ser Met Leu Arg Asn Lys Ala Ala Ala Ser Ala
 1100 1105 1110
 Pro Glu Asp Phe Thr Glu Val Thr Lys Phe Gln Ser Val Ile Asp
 1115 1120 1125
 Asp Pro Asn Val Ala Asp Ala Ala Lys Val Lys Lys Val Met Leu
 1130 1135 1140
 Val Ser Gly Lys Leu Tyr Tyr Glu Leu Ala Lys Arg Lys Glu Lys
 1145 1150 1155
 Asp Gly Arg Asp Asp Ile Ala Ile Val Arg Ile Glu Met Leu His
 1160 1165 1170
 Pro Ile Pro Phe Asn Arg Ile Ser Glu Ala Leu Ala Gly Tyr Pro
 1175 1180 1185
 Asn Ala Glu Glu Val Leu Phe Val Gln Asp Glu Pro Ala Asn Gln
 1190 1195 1200
 Gly Pro Trp Pro Phe Tyr Gln Glu His Leu Pro Glu Leu Ile Pro
 1205 1210 1215
 Asn Met Pro Lys Met Arg Arg Val Ser Arg Arg Ala Gln Ser Ser
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 Thr Ala Thr Gly Val Ala Lys Val His Gln Leu Glu Glu Lys Gln
 1235 1240 1245
 Leu Ile Asp Glu Ala Phe Glu Ala
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 gcgccaactg atcgcgctgg cgcgcgccga actcatcgag ccttccatca tgcttctcga 180
 cgaagccacc tcacacctcg accccgccac cgaagccggt atcctcaacg cctccgatcg 240
 agtcactaag ggacgcacca gcatcatcgt cgcgcaccgc ttggcaaccg ctaaaagggc 300
 cgaccgtatt cttgtgttg aacaaggacg tatcattgag gacggatctc acgacgcgtt 360
 gttgtctgct aacggcacct acgccgcgcat gtggcattta atggcctgac acgttatatt 420
 taggagaact gtcaacaaat ta atg cta caa ctg ggg ctt agg cat aat cag 472
 Met Leu Gln Leu Gly Leu Arg His Asn Gln
 1 5 10
 cca acg acc aac gtt aca gtg gat aaa ata aag ctc aat aaa ccc tca 520
 Pro Thr Thr Asn Val Thr Val Asp Lys Ile Lys Leu Asn Lys Pro Ser
 15 20 25

[0061]

aga agc aag gaa aag agg cga gta cct gcc gtg agc agc gct agt act	568
Arg Ser Lys Glu Lys Arg Arg Val Pro Ala Val Ser Ser Ala Ser Thr	
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ttc ggc cag aat gcg tgg ctg gta gac gag atg ttc cag cag ttc cag	616
Phe Gly Gln Asn Ala Trp Leu Val Asp Glu Met Phe Gln Gln Phe Gln	
45 50 55	
aag gac ccc aag tcc gtg gac aag gaa tgg aga gaa ctc ttt gag gcg	664
Lys Asp Pro Lys Ser Val Asp Lys Glu Trp Arg Glu Leu Phe Glu Ala	
60 65 70	
cag ggg gga cca aat gct acc ccc gct aca aca gaa gca cag cct tca	712
Gln Gly Gly Pro Asn Ala Thr Pro Ala Thr Thr Glu Ala Gln Pro Ser	
75 80 85 90	
gcg ccc aag gag tct gcg aaa cca gca cca aag gct gcc cct gca gcc	760
Ala Pro Lys Glu Ser Ala Lys Pro Ala Pro Lys Ala Ala Pro Ala Ala	
95 100 105	
aag gca gca cgc gcg gta gaa acc aag ccg gcc gcc aag acc gcc cct	808
Lys Ala Ala Pro Arg Val Glu Thr Lys Pro Ala Ala Lys Thr Ala Pro	
110 115 120	
aag gcc aag gag tcc tca gtg cca cag caa cct aag ctt ccg gag cca	856
Lys Ala Lys Glu Ser Ser Val Pro Gln Gln Pro Lys Leu Pro Glu Pro	
125 130 135	
gga caa acc cca atc agg ggt att ttc aag tcc atc gcg aag aac atg	904
Gly Gln Thr Pro Ile Arg Gly Ile Phe Lys Ser Ile Ala Lys Asn Met	
140 145 150	
gat atc tcc ctg gaa atc cca acc gca acc tcg gtt cgc gat atg cca	952
Asp Ile Ser Leu Glu Ile Pro Thr Ala Thr Ser Val Arg Asp Met Pro	
155 160 165 170	
gct cgc ctc atg ttc gaa aac cgc gcg atg gtc aac gat cag ctc aag	1000
Ala Arg Leu Met Phe Glu Asn Arg Ala Met Val Asn Asp Gln Leu Lys	
175 180 185	
cgc acc cgc ggt ggc aag atc tcc ttc acc cac atc att ggc tac gcc	1048
Arg Thr Arg Gly Gly Lys Ile Ser Phe Thr His Ile Ile Gly Tyr Ala	
190 195 200	
atg gtg aag gca gtc atg gct cac ccg gac atg aac aac tcc tac gac	1096
Met Val Lys Ala Val Met Ala His Pro Asp Met Asn Asn Ser Tyr Asp	
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gtc atc gac ggc aag cca acc ctg atc gtg cct gag cac atc aac ctg	1144
Val Ile Asp Gly Lys Pro Thr Leu Ile Val Pro Glu His Ile Asn Leu	
220 225 230	
ggc ctt gcc atc gac ctt cct cag aag gac ggc tcc cgc gca ctt gtc	1192
Gly Leu Ala Ile Asp Leu Pro Gln Lys Asp Gly Ser Arg Ala Leu Val	
235 240 245 250	
gta gca gcc atc aag gaa acc gag aag atg aac ttc tcc gag ttc ctc	1240
Val Ala Ala Ile Lys Glu Thr Glu Lys Met Asn Phe Ser Glu Phe Leu	
255 260 265	
gca gca tac gaa gac atc gtg aca cgc tcc cgc aag ggc aag ctc acc	1288
Ala Ala Tyr Glu Asp Ile Val Thr Arg Ser Arg Lys Gly Lys Leu Thr	
270 275 280	
atg gat gac tac cag ggc gtt acc gtt tcc ttg acc aac cca ggt ggc	1336
Met Asp Asp Tyr Gln Gly Val Thr Val Ser Leu Thr Asn Pro Gly Gly	
285 290 295	
atc ggt acc cgc cac tct gtc cca cgt ctg acc aag ggc cag ggc acc	1384
Ile Gly Thr Arg His Ser Val Pro Arg Leu Thr Lys Gly Gln Gly Thr	
300 305 310	
atc atc ggt gtc ggt tcc atg gat tac cca gca gag ttc cag ggc gct	1432
Ile Ile Gly Val Gly Ser Met Asp Tyr Pro Ala Glu Phe Gln Gly Ala	
315 320 325 330	
tcc gaa gac cgc ctt gca gag ctc ggc gtt gga aag ctt gtc acc atc	1480
Ser Glu Asp Arg Leu Ala Glu Leu Gly Val Gly Lys Leu Val Thr Ile	
335 340 345	
acc tcc acc tac gat cac cgc gtg atc cag ggt gct gtg tcc ggt gaa	1528
Thr Ser Thr Tyr Asp His Arg Val Ile Gln Gly Ala Val Ser Gly Glu	
350 355 360	

[0062]

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Phe Leu Arg Thr Met Ser Arg Leu Leu Thr Asp Asp Ser Phe Trp Asp	
365 370 375	
gag atc ttc gac gca atg aac gtt cct tac acc cca atg cgt tgg gca	1624
Glu Ile Phe Asp Ala Met Asn Val Pro Tyr Thr Pro Met Arg Trp Ala	
380 385 390	
cag gac gtt cca aac acc ggt gtt gat aag aac acc cgc gtc atg cag	1672
Gln Asp Val Pro Asn Thr Gly Val Asp Lys Asn Thr Arg Val Met Gln	
395 400 405 410	
ctc att gag gca tac cgc tcc cgt gga cac ctc atc gct gac acc aac	1720
Leu Ile Glu Ala Tyr Arg Ser Arg Gly His Leu Ile Ala Asp Thr Asn	
415 420 425	
cca ctt tca tgg gtt cag cct ggc atg cca gtt cca gac cac cgc gac	1768
Pro Leu Ser Trp Val Gln Pro Gly Met Pro Val Pro Asp His Arg Asp	
430 435 440	
ctc gac atc gag acc cac agc ctg acc atc tgg gat ctg gac cgt acc	1816
Leu Asp Ile Glu Thr His Ser Leu Thr Ile Trp Asp Leu Asp Arg Thr	
445 450 455	
ttc agc gtc ggt ggc ttc ggc ggc aag gag acc atg acc ctg cgc gag	1864
Phe Ser Val Gly Gly Phe Gly Gly Lys Glu Thr Met Thr Leu Arg Glu	
460 465 470	
gta ctg tcc cgc ctg cgc gct gcc tac acc ttg aag gtc ggc tcc gaa	1912
Val Leu Ser Arg Leu Arg Ala Ala Tyr Thr Leu Lys Val Gly Ser Glu	
475 480 485 490	
tac acc cac atc ctg gac cgc gac gag cgc acc tgg ctg cag gac cgc	1960
Tyr Thr His Ile Leu Asp Arg Asp Glu Arg Thr Trp Leu Gln Asp Arg	
495 500 505	
ctc gaa gcc gga atg cca aag cca acc cag gca gag cag aag tac atc	2008
Leu Glu Ala Gly Met Pro Lys Pro Thr Gln Ala Glu Gln Lys Tyr Ile	
510 515 520	
ctg cag aag ctg aac gcc gca gag gct ttc gag aac ttc ctg cag acc	2056
Leu Gln Lys Leu Asn Ala Ala Glu Ala Phe Glu Asn Phe Leu Gln Thr	
525 530 535	
aag tac gtc ggc cag aag cgc ttc tcc ctc gaa ggt gca gaa gct ctc	2104
Lys Tyr Val Gly Gln Lys Arg Phe Ser Leu Glu Gly Ala Glu Ala Leu	
540 545 550	
atc cca ctg atg gac tcc gcc atc gac acc gcc gca ggc cag ggc ctc	2152
Ile Pro Leu Met Asp Ser Ala Ile Asp Thr Ala Ala Gly Gln Gly Leu	
555 560 565 570	
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Asp Glu Val Val Ile Gly Met Pro His Arg Gly Arg Leu Asn Val Leu	
575 580 585	
ttc aac atc gtg ggc aag cca ctg gca tcc atc ttc aac gag ttt gaa	2248
Phe Asn Ile Val Gly Lys Pro Leu Ala Ser Ile Phe Asn Glu Phe Glu	
590 595 600	
ggc caa atg gag cag ggc cag atc ggt ggc tcc ggt gac gtg aag tac	2296
Gly Gln Met Glu Gln Gly Gln Ile Gly Gly Ser Gly Asp Val Lys Tyr	
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His Leu Gly Ser Glu Gly Gln His Leu Gln Met Phe Gly Asp Gly Glu	
620 625 630	
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Ile Lys Val Ser Leu Thr Ala Asn Pro Ser His Leu Glu Ala Val Asn	
635 640 645 650	
cca gtg atg gaa ggt atc gtc cgc gca aag cag gac tac ctg gac aag	2440
Pro Val Met Glu Gly Ile Val Arg Ala Lys Gln Asp Tyr Leu Asp Lys	
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ggc gta gac ggc aag act gtt gtg cca ctg ctg ctc cac ggt gac gct	2488
Gly Val Asp Gly Lys Thr Val Val Pro Leu Leu Leu His Gly Asp Ala	
670 675 680	
gca ttc gca ggc ctg ggc atc gtg cca gaa acc atc aac ctg gct aaa	2536
Ala Phe Ala Gly Leu Gly Ile Val Pro Glu Thr Ile Asn Leu Ala Lys	
685 690 695	

[0063]

agc tgc gtc gac gtc gga ggc acc atc cac atc gtg gtg aac aac cag Ser Cys Val Asp Val Gly Gly Thr Ile His Ile Val Val Asn Asn Gln 700 705 710	2584
atc ggc ttc acc acc acc cca gac tcc agc cgc tcc atg cac tac gca Ile Gly Phe Thr Thr Thr Pro Asp Ser Ser Arg Ser Met His Tyr Ala 715 720 725 730	2632
acc gac tac gcc aag gca ttc ggc tgc cca gtc ttc cac gtc aat ggt Thr Asp Tyr Ala Lys Ala Phe Gly Cys Pro Val Phe His Val Asn Gly 735 740 745	2680
gat gac cca gag gca gtt gtc tgg gtt ggc cag ctg gca acc gag tac Asp Asp Pro Glu Ala Val Val Trp Val Gly Gln Leu Ala Thr Glu Tyr 750 755 760	2728
cgt cgt cgc ttc ggc aag gac gtc ttc atc gac ctc gtt tgc tac cgc Arg Arg Arg Phe Gly Lys Asp Val Phe Ile Asp Leu Val Cys Tyr Arg 765 770 775	2776
ctc cgc ggc cac aac gaa gct gat gat cct tcc atg acc cag cca aag Leu Arg Gly His Asn Glu Ala Asp Asp Pro Ser Met Thr Gln Pro Lys 780 785 790	2824
atg tat gag ctc atc acc ggc cgc gag acc gtt cgt gct cag tac acc Met Tyr Glu Leu Ile Thr Gly Arg Glu Thr Val Arg Ala Gln Tyr Thr 795 800 805 810	2872
gaa gac ctg ctc gga cgt gga gac ctc tcc aac gaa gat gca gaa gca Glu Asp Leu Leu Gly Arg Gly Asp Leu Ser Asn Glu Asp Ala Glu Ala 815 820 825	2920
gtc gtc cgc gac ttc cac gac cag atg gaa tct gtg ttc aac gaa gtc Val Val Arg Asp Phe His Asp Gln Met Glu Ser Val Phe Asn Glu Val 830 835 840	2968
aag gaa ggc ggc aag aag cag gct gag gca cag acc ggc atc acc ggc Lys Glu Gly Gly Lys Lys Gln Ala Glu Ala Gln Thr Gly Ile Thr Gly 845 850 855	3016
tcc cag aag ctt cca cac ggc ctt gag acc aac atc tcc cgt gaa gag Ser Gln Lys Leu Pro His Gly Leu Glu Thr Asn Ile Ser Arg Glu Glu 860 865 870	3064
ctc ctg gaa ctg gga cag gct ttc gcc aac acc cca gaa ggc ttc aac Leu Leu Glu Leu Gly Gln Ala Phe Ala Asn Thr Pro Glu Gly Phe Asn 875 880 885 890	3112
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acc gaa ggt ggc atc gac tgg gca tgg ggc gag ctc ctc gcc ttc ggt Thr Glu Gly Gly Ile Asp Trp Ala Trp Gly Glu Leu Leu Ala Phe Gly 910 915 920	3208
tcc ctg gct aac tcc ggc cgc ttg gtt cgc ctt gca ggt gaa gat tcc Ser Leu Ala Asn Ser Gly Arg Leu Val Arg Leu Ala Gly Glu Asp Ser 925 930 935	3256
cgc cgc ggt acc ttc acc cag cgc cac gca gtt gcc atc gac cca gcg Arg Arg Gly Thr Phe Thr Gln Arg His Ala Val Ala Ile Asp Pro Ala 940 945 950	3304
acc gct gaa gag ttc aac cca ctc cac gag ctt gca cag tcc aag ggc Thr Ala Glu Glu Phe Asn Pro Leu His Glu Leu Ala Gln Ser Lys Gly 955 960 965 970	3352
aac aac ggt aag ttc ctg gtc tac aac tcc gca ctg acc gag tac gca Asn Asn Gly Lys Phe Leu Val Tyr Asn Ser Ala Leu Thr Glu Tyr Ala 975 980 985	3400
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gtt gca tgg gaa gca cag ttc ggc gac ttc gcc aac ggc gct cag Val Ala Trp Glu Ala Gln Phe Gly Asp Phe Ala Asn Gly Ala Gln 1005 1010 1015	3493
acc atc atc gat gag tac gtc tcc tca ggc gaa gct aag tgg ggc Thr Ile Ile Asp Glu Tyr Val Ser Ser Gly Glu Ala Lys Trp Gly 1020 1025 1030	3538

[0064]

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cag acc tcc aag ctg atc ctt ctg ctg cct cac ggc tac gaa ggc 3583
Gln Thr Ser Lys Leu Ile Leu Leu Leu Pro His Gly Tyr Glu Gly
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Gln Gly Pro Asp His Ser Ser Ala Arg Ile Glu Arg Phe Leu Gln
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ctg tgc gct gag ggt tcc atg act gtt gct cag cca tcc acc cca 3673
Leu Cys Ala Glu Gly Ser Met Thr Val Ala Gln Pro Ser Thr Pro
1065 1070 1075
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Ala Asn His Phe His Leu Leu Arg Arg His Ala Leu Ser Asp Leu
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aag cgt cca ctg gtt atc ttc acc ccg aag tcc atg ctg cgt aac 3763
Lys Arg Pro Leu Val Ile Phe Thr Pro Lys Ser Met Leu Arg Asn
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Lys Ala Ala Ala Ser Ala Pro Glu Asp Phe Thr Glu Val Thr Lys
1110 1115 1120
ttc caa tcc gtg atc gac gat cca aac gtt gca gat gca gcc aag 3853
Phe Gln Ser Val Ile Asp Asp Pro Asn Val Ala Asp Ala Ala Lys
1125 1130 1135
gtg aag aag gtc atg ctg gtc tcc ggc aag ctg tac tac gaa ttg 3898
Val Lys Lys Val Met Leu Val Ser Gly Lys Leu Tyr Tyr Glu Leu
1140 1145 1150
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Ala Lys Arg Lys Glu Lys Asp Gly Arg Asp Asp Ile Ala Ile Val
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Arg Ile Glu Met Leu His Pro Ile Pro Phe Asn Arg Ile Ser Glu
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gct ctt gcc ggc tac cct aac gct gag gaa gtc ctc ttc gtt cag 4033
Ala Leu Ala Gly Tyr Pro Asn Ala Glu Glu Val Leu Phe Val Gln
1185 1190 1195
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Asp Glu Pro Ala Asn Gln Gly Pro Trp Pro Phe Tyr Gln Glu His
1200 1205 1210
ctc cca gag ctg atc ccg aac atg cca aag atg cgc cgc gtt tcc 4123
Leu Pro Glu Leu Ile Pro Asn Met Pro Lys Met Arg Arg Val Ser
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Arg Arg Ala Gln Ser Ser Thr Ala Thr Gly Val Ala Lys Val His
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Gln Leu Glu Glu Lys Gln Leu Ile Asp Glu Ala Phe Glu Ala
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aaggcccttt ttgctgccgt ggttgccctaa ggtggaaggc atgaaacgaa tctgtgcggt 4330
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 35 40 45
 Leu Val Asp Glu Met Phe Gln Gln Phe Gln Lys Asp Pro Lys Ser Val

[0065]

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65	70	75
Thr Pro Ala Thr Thr Glu Ala Gln Pro Ser Ala Pro Lys Glu Ser Ala		
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Lys Pro Ala Pro Lys Ala Ala Pro Ala Ala Lys Ala Ala Pro Arg Val		
	100	105
Glu Thr Lys Pro Ala Ala Lys Thr Ala Pro Lys Ala Lys Glu Ser Ser		
	115	120
Val Pro Gln Gln Pro Lys Leu Pro Glu Pro Gly Gln Thr Pro Ile Arg		
	130	135
Gly Ile Phe Lys Ser Ile Ala Lys Asn Met Asp Ile Ser Leu Glu Ile		
	145	150
Pro Thr Ala Thr Ser Val Arg Asp Met Pro Ala Arg Leu Met Phe Glu		
	165	170
Asn Arg Ala Met Val Asn Asp Gln Leu Lys Arg Thr Arg Gly Gly Lys		
	180	185
Ile Ser Phe Thr His Ile Ile Gly Tyr Ala Met Val Lys Ala Val Met		
	195	200
Ala His Pro Asp Met Asn Asn Ser Tyr Asp Val Ile Asp Gly Lys Pro		
	210	215
Thr Leu Ile Val Pro Glu His Ile Asn Leu Gly Leu Ala Ile Asp Leu		
	225	230
Pro Gln Lys Asp Gly Ser Arg Ala Leu Val Val Ala Ala Ile Lys Glu		
	245	250
Thr Glu Lys Met Asn Phe Ser Glu Phe Leu Ala Ala Tyr Glu Asp Ile		
	260	265
Val Thr Arg Ser Arg Lys Gly Lys Leu Thr Met Asp Asp Tyr Gln Gly		
	275	280
Val Thr Val Ser Leu Thr Asn Pro Gly Gly Ile Gly Thr Arg His Ser		
	290	295
Val Pro Arg Leu Thr Lys Gly Gln Gly Thr Ile Ile Gly Val Gly Ser		
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Met Asp Tyr Pro Ala Glu Phe Gln Gly Ala Ser Glu Asp Arg Leu Ala		
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Glu Leu Gly Val Gly Lys Leu Val Thr Ile Thr Ser Thr Tyr Asp His		
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Arg Val Ile Gln Gly Ala Val Ser Gly Glu Phe Leu Arg Thr Met Ser		
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Arg Leu Leu Thr Asp Asp Ser Phe Trp Asp Glu Ile Phe Asp Ala Met		
	370	375
Asn Val Pro Tyr Thr Pro Met Arg Trp Ala Gln Asp Val Pro Asn Thr		
	385	390
Gly Val Asp Lys Asn Thr Arg Val Met Gln Leu Ile Glu Ala Tyr Arg		
	405	410
Ser Arg Gly His Leu Ile Ala Asp Thr Asn Pro Leu Ser Trp Val Gln		
	420	425
Pro Gly Met Pro Val Pro Asp His Arg Asp Leu Asp Ile Glu Thr His		
	435	440
Ser Leu Thr Ile Trp Asp Leu Asp Arg Thr Phe Ser Val Gly Gly Phe		
	450	455
Gly Gly Lys Glu Thr Met Thr Leu Arg Glu Val Leu Ser Arg Leu Arg		
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	485	490
Arg Asp Glu Arg Thr Trp Leu Gln Asp Arg Leu Glu Ala Gly Met Pro		
	500	505
Lys Pro Thr Gln Ala Glu Gln Lys Tyr Ile Leu Gln Lys Leu Asn Ala		
	515	520
Ala Glu Ala Phe Glu Asn Phe Leu Gln Thr Lys Tyr Val Gly Gln Lys		
	530	535
Arg Phe Ser Leu Glu Gly Ala Glu Ala Leu Ile Pro Leu Met Asp Ser		
	545	550
		555
		560

[0066]

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Ala Ile Asp Thr Ala Ala Gly Gln Gly Leu Asp Glu Val Val Ile Gly
      565                      570                      575
Met Pro His Arg Gly Arg Leu Asn Val Leu Phe Asn Ile Val Gly Lys
      580                      585                      590
Pro Leu Ala Ser Ile Phe Asn Glu Phe Glu Gly Gln Met Glu Gln Gly
      595                      600                      605
Gln Ile Gly Gly Ser Gly Asp Val Lys Tyr His Leu Gly Ser Glu Gly
      610                      615                      620
Gln His Leu Gln Met Phe Gly Asp Gly Glu Ile Lys Val Ser Leu Thr
      625                      630                      635                      640
Ala Asn Pro Ser His Leu Glu Ala Val Asn Pro Val Met Glu Gly Ile
      645                      650                      655
Val Arg Ala Lys Gln Asp Tyr Leu Asp Lys Gly Val Asp Gly Lys Thr
      660                      665                      670
Val Val Pro Leu Leu Leu His Gly Asp Ala Ala Phe Ala Gly Leu Gly
      675                      680                      685
Ile Val Pro Glu Thr Ile Asn Leu Ala Lys Ser Cys Val Asp Val Gly
      690                      695                      700
Gly Thr Ile His Ile Val Val Asn Asn Gln Ile Gly Phe Thr Thr Thr
      705                      710                      715                      720
Pro Asp Ser Ser Arg Ser Met His Tyr Ala Thr Asp Tyr Ala Lys Ala
      725                      730                      735
Phe Gly Cys Pro Val Phe His Val Asn Gly Asp Asp Pro Glu Ala Val
      740                      745                      750
Val Trp Val Gly Gln Leu Ala Thr Glu Tyr Arg Arg Arg Phe Gly Lys
      755                      760                      765
Asp Val Phe Ile Asp Leu Val Cys Tyr Arg Leu Arg Gly His Asn Glu
      770                      775                      780
Ala Asp Asp Pro Ser Met Thr Gln Pro Lys Met Tyr Glu Leu Ile Thr
      785                      790                      795                      800
Gly Arg Glu Thr Val Arg Ala Gln Tyr Thr Glu Asp Leu Leu Gly Arg
      805                      810                      815
Gly Asp Leu Ser Asn Glu Asp Ala Glu Ala Val Val Arg Asp Phe His
      820                      825                      830
Asp Gln Met Glu Ser Val Phe Asn Glu Val Lys Glu Gly Gly Lys Lys
      835                      840                      845
Gln Ala Glu Ala Gln Thr Gly Ile Thr Gly Ser Gln Lys Leu Pro His
      850                      855                      860
Gly Leu Glu Thr Asn Ile Ser Arg Glu Glu Leu Leu Glu Leu Gly Gln
      865                      870                      875                      880
Ala Phe Ala Asn Thr Pro Glu Gly Phe Asn Tyr His Pro Arg Val Ala
      885                      890                      895
Pro Val Ala Lys Lys Arg Val Ser Ser Val Thr Glu Gly Gly Ile Asp
      900                      905                      910
Trp Ala Trp Gly Glu Leu Leu Ala Phe Gly Ser Leu Ala Asn Ser Gly
      915                      920                      925
Arg Leu Val Arg Leu Ala Gly Glu Asp Ser Arg Arg Gly Thr Phe Thr
      930                      935                      940
Gln Arg His Ala Val Ala Ile Asp Pro Ala Thr Ala Glu Glu Phe Asn
      945                      950                      955                      960
Pro Leu His Glu Leu Ala Gln Ser Lys Gly Asn Asn Gly Lys Phe Leu
      965                      970                      975
Val Tyr Asn Ser Ala Leu Thr Glu Tyr Ala Gly Met Gly Phe Glu Tyr
      980                      985                      990
Gly Tyr Ser Val Gly Asn Glu Asp Ser Val Val Ala Trp Glu Ala Gln
      995                      1000                      1005
Phe Gly Asp Phe Ala Asn Gly Ala Gln Thr Ile Ile Asp Glu Tyr
      1010                      1015                      1020
Val Ser Ser Gly Glu Ala Lys Trp Gly Gln Thr Ser Lys Leu Ile
      1025                      1030                      1035
Leu Leu Leu Pro His Gly Tyr Glu Gly Gln Gly Pro Asp His Ser
      1040                      1045                      1050
Ser Ala Arg Ile Glu Arg Phe Leu Gln Leu Cys Ala Glu Gly Ser

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[0067]

1055	1060	1065
Met Thr Val Ala Gln Pro Ser	Thr Pro Ala Asn His	Phe His Leu
1070	1075	1080
Leu Arg Arg His Ala Leu Ser	Asp Leu Lys Arg Pro	Leu Val Ile
1085	1090	1095
Phe Thr Pro Lys Ser Met	Leu Arg Asn Lys Ala Ala	Ala Ser Ala
1100	1105	1110
Pro Glu Asp Phe Thr Glu Val	Thr Lys Phe Gln Ser	Val Ile Asp
1115	1120	1125
Asp Pro Asn Val Ala Asp	Ala Ala Lys Val Lys Lys	Val Met Leu
1130	1135	1140
Val Ser Gly Lys Leu Tyr Tyr	Glu Leu Ala Lys Arg	Lys Glu Lys
1145	1150	1155
Asp Gly Arg Asp Asp Ile	Ala Ile Val Arg Ile Glu	Met Leu His
1160	1165	1170
Pro Ile Pro Phe Asn Arg	Ile Ser Glu Ala Leu Ala	Gly Tyr Pro
1175	1180	1185
Asn Ala Glu Glu Val Leu Phe	Val Gln Asp Glu Pro	Ala Asn Gln
1190	1195	1200
Gly Pro Trp Pro Phe Tyr Gln	Glu His Leu Pro Glu	Leu Ile Pro
1205	1210	1215
Asn Met Pro Lys Met Arg Arg	Val Ser Arg Arg Ala	Gln Ser Ser
1220	1225	1230
Thr Ala Thr Gly Val Ala Lys	Val His Gln Leu Glu	Glu Lys Gln
1235	1240	1245
Leu Ile Asp Glu Ala Phe	Glu Ala	
1250	1255	

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 catccctgat ggtttcaatc atcaagtcgg tgaacgcggg cgcaacctgt catccggaca 120
 gcgccaactg atcgcgctgg cgcgcgcgga actcatcgag ccttccatca tgcttctcga 180
 cgaagccacc tccaccctcg accccgcac cgaagccgtt atcctcaacg cctccgatcg 240
 agtcactaag ggacgcacca gcatcatcgt cgcgcaccgc ttggcaaccg ctaaaagggc 300
 cgaccgtatt ctgtgtgtg aacaaggacg tatcattgag gacggatctc acgacgcgtt 360
 gttgtctgct aacggcacct acgcccgcgt gtggcattta atggcctgac acgttatatt 420
 taggagaact gtcaacaaat ta atg cta caa ctg ggg ctt agg cat aat cag 472
 Met Leu Gln Leu Gly Leu Arg His Asn Gln
 1 5 10
 cca acg acc aac gtt aca gtg gat aaa ata aag ctc aat aaa ccc tca 520
 Pro Thr Thr Asn Val Thr Val Asp Lys Ile Lys Leu Asn Lys Pro Ser
 15 20 25
 aga agc aag gaa aag agg cga gta cct gcc gtg agc agc gct agt act 568
 Arg Ser Lys Glu Lys Arg Arg Val Pro Ala Val Ser Ser Ala Ser Thr
 30 35 40
 ttc ggc cag aat gcg tgg ctg gta gac gag atg ttc cag cag ttc cag 616
 Phe Gly Gln Asn Ala Trp Leu Val Asp Glu Met Phe Gln Gln Phe Gln
 45 50 55
 aag gac ccc aag tcc gtg gac aag gaa tgg aga gaa ctc ttt gag gcg 664
 Lys Asp Pro Lys Ser Val Asp Lys Glu Trp Arg Glu Leu Phe Glu Ala
 60 65 70
 cag ggg gga cca aat gct acc ccc gct aca aca gaa gca cag cct tca 712
 Gln Gly Gly Pro Asn Ala Thr Pro Ala Thr Thr Glu Ala Gln Pro Ser

[0068]

75	80	85	90	
gcg ccc aag gag tct gcg aaa cca gca cca aag gct gcc cct gca gcc				760
Ala Pro Lys Glu Ser Ala Lys Pro Ala Pro Lys Ala Ala Pro Ala Ala				
95	100	105		
aag gca gca ccg cgc gta gaa acc aag ccg gcc gcc aag acc gcc cct				808
Lys Ala Ala Pro Arg Val Glu Thr Lys Pro Ala Ala Lys Thr Ala Pro				
110	115	120		
aag gcc aag gag tcc tca gtg cca cag caa cct aag ctt ccg gag cca				856
Lys Ala Lys Glu Ser Ser Val Pro Gln Gln Pro Lys Leu Pro Glu Pro				
125	130	135		
gga caa acc cca atc agg ggt att ttc aag tcc atc gcg aag aac atg				904
Gly Gln Thr Pro Ile Arg Gly Ile Phe Lys Ser Ile Ala Lys Asn Met				
140	145	150		
gat atc tcc ctg gaa atc cca acc gca acc tcg gtt cgc gat atg cca				952
Asp Ile Ser Leu Glu Ile Pro Thr Ala Thr Ser Val Arg Asp Met Pro				
155	160	165	170	
gct cgc ctc atg ttc gaa aac cgc gcg atg gtc aac gat cag ctc aag				1000
Ala Arg Leu Met Phe Glu Asn Arg Ala Met Val Asn Asp Gln Leu Lys				
175	180	185		
cgc acc cgc ggt ggc aag atc tcc ttc acc cac atc att ggc tac gcc				1048
Arg Thr Arg Gly Gly Lys Ile Ser Phe Thr His Ile Ile Gly Tyr Ala				
190	195	200		
atg gtg aag gca gtc atg gct cac ccg gac atg aac aac tcc tac gac				1096
Met Val Lys Ala Val Met Ala His Pro Asp Met Asn Asn Ser Tyr Asp				
205	210	215		
gtc atc gac ggc aag cca acc ctg atc gtg cct gag cac atc aac ctg				1144
Val Ile Asp Gly Lys Pro Thr Leu Ile Val Pro Glu His Ile Asn Leu				
220	225	230		
ggc ctt gcc atc gac ctt cct cag aag gac ggc tcc cgc gca ctt gtc				1192
Gly Leu Ala Ile Asp Leu Pro Gln Lys Asp Gly Ser Arg Ala Leu Val				
235	240	245	250	
gta gca gcc atc aag gaa acc gag aag atg aac ttc tcc gag ttc ctc				1240
Val Ala Ala Ile Lys Glu Thr Glu Lys Met Asn Phe Ser Glu Phe Leu				
255	260	265		
gca gca tac gaa gac atc gtg aca cgc tcc cgc aag ggc aag ctc acc				1288
Ala Ala Tyr Glu Asp Ile Val Thr Arg Ser Arg Lys Gly Lys Leu Thr				
270	275	280		
atg gat gac tac cag ggc gtt acc gtt tcc ttg acc aac cca ggt ggc				1336
Met Asp Asp Tyr Gln Gly Val Thr Val Ser Leu Thr Asn Pro Gly Gly				
285	290	295		
atc ggt acc cgc cac tct gtc cca cgt ctg acc aag ggc cag ggc acc				1384
Ile Gly Thr Arg His Ser Val Pro Arg Leu Thr Lys Gly Gln Gly Thr				
300	305	310		
atc atc ggt gtc ggt tcc atg gat tac cca gca gag ttc cag ggc gct				1432
Ile Ile Gly Val Gly Ser Met Asp Tyr Pro Ala Glu Phe Gln Gly Ala				
315	320	325	330	
tcc gaa gac cgc ctt gca gag ctc ggc gtt gga aag ctt gtc acc atc				1480
Ser Glu Asp Arg Leu Ala Glu Leu Gly Val Gly Lys Leu Val Thr Ile				
335	340	345		
acc tcc acc tac gat cac cgc gtg atc cag ggt gct gtg tcc ggt gaa				1528
Thr Ser Thr Tyr Asp His Arg Val Ile Gln Gly Ala Val Ser Gly Glu				
350	355	360		
ttc ctg cgt acc atg tct cgc ctg ctc acc gat gat tcc ttc tgg gat				1576
Phe Leu Arg Thr Met Ser Arg Leu Leu Thr Asp Asp Ser Phe Trp Asp				
365	370	375		
gag atc ttc gac gca atg aac gtt cct tac acc cca atg cgt tgg gca				1624
Glu Ile Phe Asp Ala Met Asn Val Pro Tyr Thr Pro Met Arg Trp Ala				
380	385	390		
cag gac gtt cca aac acc ggt gtt gat aag aac acc cgc gtc atg cag				1672
Gln Asp Val Pro Asn Thr Gly Val Asp Lys Asn Thr Arg Val Met Gln				
395	400	405	410	
ctc att gag gca tac cgc tcc cgt gga cac ctc atc gct gac acc aac				1720
Leu Ile Glu Ala Tyr Arg Ser Arg Gly His Leu Ile Ala Asp Thr Asn				

[0069]

cca ctt tca tgg gtt cag cct ggc atg cca gtt cca gac cac cgc gac	415	420	425	1768
Pro Leu Ser Trp Val Gln Pro Gly Met Pro Val Pro Asp His Arg Asp				
ctc gac atc gag acc cac agc ctg acc atc tgg gat ctg gac cgt acc	430	435	440	1816
Leu Asp Ile Glu Thr His Ser Leu Thr Ile Trp Asp Leu Asp Arg Thr				
ttc agc gtc ggt ggc ttc ggc ggc aag gag acc atg acc ctg cgc gag	445	450	455	1864
Phe Ser Val Gly Gly Phe Gly Gly Lys Glu Thr Met Thr Leu Arg Glu				
gta ctg tcc cgc ctg cgc gct gcc tac acc ttg aag gtc ggc tcc gaa	460	465	470	1912
Val Leu Ser Arg Leu Arg Ala Ala Tyr Thr Leu Lys Val Gly Ser Glu				
tac acc cac atc ctg gac cgc gag cgc acc tgg ctg cag gac cgc	475	480	485	1960
Tyr Thr His Ile Leu Asp Arg Asp Glu Arg Thr Trp Leu Gln Asp Arg				
ctc gaa gcc gga atg cca aag cca acc cag gca gag cag aag tac atc	495	500	505	2008
Leu Glu Ala Gly Met Pro Lys Pro Thr Gln Ala Glu Gln Lys Tyr Ile				
ctg cag aag ctg aac gcc gca gag gct ttc gag aac ttc ctg cag acc	510	515	520	2056
Leu Gln Lys Leu Asn Ala Ala Glu Ala Phe Glu Asn Phe Leu Gln Thr				
aag tac gtc ggc cag aag cgc ttc tcc ctc gaa ggt gca gaa gct ctc	525	530	535	2104
Lys Tyr Val Gly Gln Lys Arg Phe Ser Leu Glu Gly Ala Glu Ala Leu				
atc cca ctg atg gac tcc gcc atc gac acc gcc gca ggc cag ggc ctc	540	545	550	2152
Ile Pro Leu Met Asp Ser Ala Ile Asp Thr Ala Ala Gly Gln Gly Leu				
gac gaa gtt gtc atc ggt atg cca cac cgt ggt cgc ctc aac gtg ctg	555	560	565	2200
Asp Glu Val Val Ile Gly Met Pro His Arg Gly Arg Leu Asn Val Leu				
ttc aac atc gtg ggc aag cca ctg gca tcc atc ttc aac gag ttt gaa	575	580	585	2248
Phe Asn Ile Val Gly Lys Pro Leu Ala Ser Ile Phe Asn Glu Phe Glu				
ggc caa atg gag cag ggc cag atc ggt ggc tcc ggt gac gtg aag tac	590	595	600	2296
Gly Gln Met Glu Gln Gly Gln Ile Gly Gly Ser Gly Asp Val Lys Tyr				
cac ctc ggt tcc gaa ggc cag cac ctg cag atg ttc ggc gac ggc gag	605	610	615	2344
His Leu Gly Ser Glu Gly Gln His Leu Gln Met Phe Gly Asp Gly Glu				
atc aag gtc tcc ctg act gct aac ccg tcc cac ctg gaa gct gtt aac	620	625	630	2392
Ile Lys Val Ser Leu Thr Ala Asn Pro Ser His Leu Glu Ala Val Asn				
cca gtg atg gaa ggt atc gtc cgc gca aag cag gac tac ctg gac aag	635	640	645	2440
Pro Val Met Glu Gly Ile Val Arg Ala Lys Gln Asp Tyr Leu Asp Lys				
ggc gta gac ggc aag act gtt gtg cca ctg ctg ctc cac ggt gac gct	655	660	665	2488
Gly Val Asp Gly Lys Thr Val Val Pro Leu Leu Leu His Gly Asp Ala				
gca ttc gca ggc ctg ggc atc gtg cca gaa acc atc aac ctg gct ata	670	675	680	2536
Ala Phe Ala Gly Leu Gly Ile Val Pro Glu Thr Ile Asn Leu Ala Ile				
agc tgc gtc gac gtc gga ggc acc atc cac atc gtg gtg aac aac cag	685	690	695	2584
Ser Cys Val Asp Val Gly Gly Thr Ile His Ile Val Val Asn Asn Gln				
atc ggc ttc acc acc acc cca gac tcc agc cgc tcc atg cac tac gca	700	705	710	2632
Ile Gly Phe Thr Thr Thr Pro Asp Ser Ser Arg Ser Met His Tyr Ala				
acc gac tac gcc aag gca ttc ggc tgc cca gtc ttc cac gtc aat ggt	715	720	725	2680
Thr Asp Tyr Ala Lys Ala Phe Gly Cys Pro Val Phe His Val Asn Gly				
gat gac cca gag gca gtt gtc tgg gtt ggc cag ctg gca acc gag tac	735	740	745	2728
Asp Asp Pro Glu Ala Val Val Trp Val Gly Gln Leu Ala Thr Glu Tyr				

[0070]

750	755	760	
cg t cg t cg c ttc ggc aag gac gtc ttc atc gac ctc gtt tgc tac cgc			2776
Arg Arg Arg Phe Gly Lys Asp Val Phe Ile Asp Leu Val Cys Tyr Arg			
765	770	775	
ctc cgc ggc cac aac gaa gct gat gat cct tcc atg acc cag cca aag			2824
Leu Arg Gly His Asn Glu Ala Asp Asp Pro Ser Met Thr Gln Pro Lys			
780	785	790	
atg tat gag ctc atc acc ggc cgc gag acc gtt cgt gct cag tac acc			2872
Met Tyr Glu Leu Ile Thr Gly Arg Glu Thr Val Arg Ala Gln Tyr Thr			
795	800	805	810
gaa gac ctg ctc gga cgt gga gac ctc tcc aac gaa gat gca gaa gca			2920
Glu Asp Leu Leu Gly Arg Gly Asp Leu Ser Asn Glu Asp Ala Glu Ala			
815	820	825	
gtc gtc cgc gac ttc cac gac cag atg gaa tct gtg ttc aac gaa gtc			2968
Val Val Arg Asp Phe His Asp Gln Met Glu Ser Val Phe Asn Glu Val			
830	835	840	
aag gaa ggc ggc aag aag cag gct gag gca cag acc ggc atc acc ggc			3016
Lys Glu Gly Gly Lys Lys Gln Ala Glu Ala Gln Thr Gly Ile Thr Gly			
845	850	855	
tcc cag aag ctt cca cac ggc ctt gag acc aac atc tcc cgt gaa gag			3064
Ser Gln Lys Leu Pro His Gly Leu Glu Thr Asn Ile Ser Arg Glu Glu			
860	865	870	
ctc ctg gaa ctg gga cag gct ttc gcc aac acc cca gaa ggc ttc aac			3112
Leu Leu Glu Leu Gly Gln Ala Phe Ala Asn Thr Pro Glu Gly Phe Asn			
875	880	885	890
tac cac cca cgt gtg gct cca gtt gct aag aag cgc gtc tcc tct gtc			3160
Tyr His Pro Arg Val Ala Pro Val Ala Lys Lys Arg Val Ser Ser Val			
895	900	905	
acc gaa ggt ggc atc gac tgg gca tgg ggc gag ctc ctc gcc ttc ggt			3208
Thr Glu Gly Gly Ile Asp Trp Ala Trp Gly Glu Leu Leu Ala Phe Gly			
910	915	920	
tcc ctg gct aac tcc ggc cgc ttg gtt cgc ctt gca ggt gaa gat tcc			3256
Ser Leu Ala Asn Ser Gly Arg Leu Val Arg Leu Ala Gly Glu Asp Ser			
925	930	935	
cgc cgc ggt acc ttc acc cag cgc cac gca gtt gcc atc gac cca gcg			3304
Arg Arg Gly Thr Phe Thr Gln Arg His Ala Val Ala Ile Asp Pro Ala			
940	945	950	
acc gct gaa gag ttc aac cca ctc cac gag ctt gca cag tcc aag ggc			3352
Thr Ala Glu Glu Phe Asn Pro Leu His Glu Leu Ala Gln Ser Lys Gly			
955	960	965	970
aac aac ggt aag ttc ctg gtc tac aac tcc gca ctg acc gag tac gca			3400
Asn Asn Gly Lys Phe Leu Val Tyr Asn Ser Ala Leu Thr Glu Tyr Ala			
975	980	985	
ggc atg ggc ttc gag tac ggc tac tcc gta gga aac gaa gac tcc gtc			3448
Gly Met Gly Phe Glu Tyr Gly Tyr Ser Val Gly Asn Glu Asp Ser Val			
990	995	1000	
gtt gca tgg gaa gca cag ttc ggc gac ttc gcc aac ggc gct cag			3493
Val Ala Trp Glu Ala Gln Phe Gly Asp Phe Ala Asn Gly Ala Gln			
1005	1010	1015	
acc atc atc gat gag tac gtc tcc tca ggc gaa gct aag tgg ggc			3538
Thr Ile Ile Asp Glu Tyr Val Ser Ser Gly Glu Ala Lys Trp Gly			
1020	1025	1030	
cag acc tcc aag ctg atc ctt ctg ctg cct cac ggc tac gaa ggc			3583
Gln Thr Ser Lys Leu Ile Leu Leu Leu Pro His Gly Tyr Glu Gly			
1035	1040	1045	
cag ggc cca gac cac tet tcc gca cgt atc gag cgc ttc ctg cag			3628
Gln Gly Pro Asp His Ser Ser Ala Arg Ile Glu Arg Phe Leu Gln			
1050	1055	1060	
ctg tgc gct gag ggt tcc atg act gtt gct cag cca tcc acc cca			3673
Leu Cys Ala Glu Gly Ser Met Thr Val Ala Gln Pro Ser Thr Pro			
1065	1070	1075	
gca aac cac ttc cac ctg ctg cgt cgt cac gct ctg tcc gac ctg			3718
Ala Asn His Phe His Leu Leu Arg Arg His Ala Leu Ser Asp Leu			

[0071]

1080	1085	1090	
aag cgt cca ctg gtt atc ttc acc ccg aag tcc atg ctg cgt aac			3763
Lys Arg Pro Leu Val Ile Phe Thr Pro Lys Ser Met Leu Arg Asn			
1095	1100	1105	
aag gct gct gcc tcc gca cca gaa gac ttc act gag gtc acc aag			3808
Lys Ala Ala Ala Ser Ala Pro Glu Asp Phe Thr Glu Val Thr Lys			
1110	1115	1120	
ttc caa tcc gtg atc gac gat cca aac gtt gca gat gca gcc aag			3853
Phe Gln Ser Val Ile Asp Asp Pro Asn Val Ala Asp Ala Ala Lys			
1125	1130	1135	
gtg aag aag gtc atg ctg gtc tcc ggc aag ctg tac tac gaa ttg			3898
Val Lys Lys Val Met Leu Val Ser Gly Lys Leu Tyr Tyr Glu Leu			
1140	1145	1150	
gca aag cgc aag gag aag gac gga cgc gac gac atc cgc atc gtt			3943
Ala Lys Arg Lys Glu Lys Asp Gly Arg Asp Asp Ile Ala Ile Val			
1155	1160	1165	
cgt atc gaa atg ctc cac cca att ccg ttc aac cgc atc tcc gag			3988
Arg Ile Glu Met Leu His Pro Ile Pro Phe Asn Arg Ile Ser Glu			
1170	1175	1180	
gct ctt gcc ggc tac cct aac gct gag gaa gtc ctc ttc gtt cag			4033
Ala Leu Ala Gly Tyr Pro Asn Ala Glu Glu Val Leu Phe Val Gln			
1185	1190	1195	
gat gag cca gca aac cag ggc cca tgg ccg ttc tac cag gag cac			4078
Asp Glu Pro Ala Asn Gln Gly Pro Trp Pro Phe Tyr Gln Glu His			
1200	1205	1210	
ctc cca gag ctg atc ccg aac atg cca aag atg cgc cgc gtt tcc			4123
Leu Pro Glu Leu Ile Pro Asn Met Pro Lys Met Arg Arg Val Ser			
1215	1220	1225	
cgc cgc gct cag tcc tcc acc gca act ggt gtt gct aag gtg cac			4168
Arg Arg Ala Gln Ser Ser Thr Ala Thr Gly Val Ala Lys Val His			
1230	1235	1240	
cag ctg gag gag aag cag ctt atc gac gag gct ttc gag gct			4210
Gln Leu Glu Glu Lys Gln Leu Ile Asp Glu Ala Phe Glu Ala			
1245	1250	1255	
taagtccttta tagtcctgca ctacgctaga gggccttatg cagtgtgaat cacacagcat			4270
aaggcccttt ttgctgccgt gggtgcctaa ggtggaaggc atgaaacgaa tctgtcgggt			4330
cacgatctct tcagtacttt tgetaagtgg ctgctcctcc acttcacca cgcagctcga			4390
g			4391

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

[0072]

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Gly Ile Phe Lys Ser Ile Ala Lys Asn Met Asp Ile Ser Leu Glu Ile
145                150                155                160
Pro Thr Ala Thr Ser Val Arg Asp Met Pro Ala Arg Leu Met Phe Glu
                165                170                175
Asn Arg Ala Met Val Asn Asp Gln Leu Lys Arg Thr Arg Gly Gly Lys
                180                185                190
Ile Ser Phe Thr His Ile Ile Gly Tyr Ala Met Val Lys Ala Val Met
                195                200                205
Ala His Pro Asp Met Asn Asn Ser Tyr Asp Val Ile Asp Gly Lys Pro
                210                215                220
Thr Leu Ile Val Pro Glu His Ile Asn Leu Gly Leu Ala Ile Asp Leu
225                230                235                240
Pro Gln Lys Asp Gly Ser Arg Ala Leu Val Val Ala Ala Ile Lys Glu
                245                250                255
Thr Glu Lys Met Asn Phe Ser Glu Phe Leu Ala Ala Tyr Glu Asp Ile
                260                265                270
Val Thr Arg Ser Arg Lys Gly Lys Leu Thr Met Asp Asp Tyr Gln Gly
                275                280                285
Val Thr Val Ser Leu Thr Asn Pro Gly Gly Ile Gly Thr Arg His Ser
                290                295                300
Val Pro Arg Leu Thr Lys Gly Gln Gly Thr Ile Ile Gly Val Gly Ser
305                310                315                320
Met Asp Tyr Pro Ala Glu Phe Gln Gly Ala Ser Glu Asp Arg Leu Ala
                325                330                335
Glu Leu Gly Val Gly Lys Leu Val Thr Ile Thr Ser Thr Tyr Asp His
                340                345                350
Arg Val Ile Gln Gly Ala Val Ser Gly Glu Phe Leu Arg Thr Met Ser
                355                360                365
Arg Leu Leu Thr Asp Asp Ser Phe Trp Asp Glu Ile Phe Asp Ala Met
                370                375                380
Asn Val Pro Tyr Thr Pro Met Arg Trp Ala Gln Asp Val Pro Asn Thr
385                390                395                400
Gly Val Asp Lys Asn Thr Arg Val Met Gln Leu Ile Glu Ala Tyr Arg
                405                410                415
Ser Arg Gly His Leu Ile Ala Asp Thr Asn Pro Leu Ser Trp Val Gln
                420                425                430
Pro Gly Met Pro Val Pro Asp His Arg Asp Leu Asp Ile Glu Thr His
                435                440                445
Ser Leu Thr Ile Trp Asp Leu Asp Arg Thr Phe Ser Val Gly Gly Phe
                450                455                460
Gly Gly Lys Glu Thr Met Thr Leu Arg Glu Val Leu Ser Arg Leu Arg
465                470                475                480
Ala Ala Tyr Thr Leu Lys Val Gly Ser Glu Tyr Thr His Ile Leu Asp
                485                490                495
Arg Asp Glu Arg Thr Trp Leu Gln Asp Arg Leu Glu Ala Gly Met Pro
                500                505                510
Lys Pro Thr Gln Ala Glu Gln Lys Tyr Ile Leu Gln Lys Leu Asn Ala
                515                520                525
Ala Glu Ala Phe Glu Asn Phe Leu Gln Thr Lys Tyr Val Gly Gln Lys
                530                535                540
Arg Phe Ser Leu Glu Gly Ala Glu Ala Leu Ile Pro Leu Met Asp Ser
545                550                555                560
Ala Ile Asp Thr Ala Ala Gly Gln Gly Leu Asp Glu Val Val Ile Gly
                565                570                575
Met Pro His Arg Gly Arg Leu Asn Val Leu Phe Asn Ile Val Gly Lys
                580                585                590
Pro Leu Ala Ser Ile Phe Asn Glu Phe Glu Gly Gln Met Glu Gln Gly
                595                600                605
Gln Ile Gly Gly Ser Gly Asp Val Lys Tyr His Leu Gly Ser Glu Gly
                610                615                620
Gln His Leu Gln Met Phe Gly Asp Gly Glu Ile Lys Val Ser Leu Thr
625                630                635                640
Ala Asn Pro Ser His Leu Glu Ala Val Asn Pro Val Met Glu Gly Ile

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[0073]

Val	Arg	Ala	Lys	Gln	Asp	Tyr	Leu	Asp	Lys	Gly	Val	Asp	Gly	Lys	Thr
645			650			655									
660			665			670									
Val	Val	Pro	Leu	Leu	Leu	His	Gly	Asp	Ala	Ala	Phe	Ala	Gly	Leu	Gly
675			680			685									
Ile	Val	Pro	Glu	Thr	Ile	Asn	Leu	Ala	Ile	Ser	Cys	Val	Asp	Val	Gly
690			695			700									
Gly	Thr	Ile	His	Ile	Val	Val	Asn	Asn	Gln	Ile	Gly	Phe	Thr	Thr	Thr
705			710			715			720						
Pro	Asp	Ser	Ser	Arg	Ser	Met	His	Tyr	Ala	Thr	Asp	Tyr	Ala	Lys	Ala
725			730			735									
Phe	Gly	Cys	Pro	Val	Phe	His	Val	Asn	Gly	Asp	Asp	Pro	Glu	Ala	Val
740			745			750									
Val	Trp	Val	Gly	Gln	Leu	Ala	Thr	Glu	Tyr	Arg	Arg	Arg	Phe	Gly	Lys
755			760			765									
Asp	Val	Phe	Ile	Asp	Leu	Val	Cys	Tyr	Arg	Leu	Arg	Gly	His	Asn	Glu
770			775			780									
Ala	Asp	Asp	Pro	Ser	Met	Thr	Gln	Pro	Lys	Met	Tyr	Glu	Leu	Ile	Thr
785			790			795			800						
Gly	Arg	Glu	Thr	Val	Arg	Ala	Gln	Tyr	Thr	Glu	Asp	Leu	Leu	Gly	Arg
805			810			815									
Gly	Asp	Leu	Ser	Asn	Glu	Asp	Ala	Glu	Ala	Val	Val	Arg	Asp	Phe	His
820			825			830									
Asp	Gln	Met	Glu	Ser	Val	Phe	Asn	Glu	Val	Lys	Glu	Gly	Gly	Lys	Lys
835			840			845									
Gln	Ala	Glu	Ala	Gln	Thr	Gly	Ile	Thr	Gly	Ser	Gln	Lys	Leu	Pro	His
850			855			860									
Gly	Leu	Glu	Thr	Asn	Ile	Ser	Arg	Glu	Glu	Leu	Glu	Leu	Gly	Gln	
865			870			875			880						
Ala	Phe	Ala	Asn	Thr	Pro	Glu	Gly	Phe	Asn	Tyr	His	Pro	Arg	Val	Ala
885			890			895									
Pro	Val	Ala	Lys	Lys	Arg	Val	Ser	Ser	Val	Thr	Glu	Gly	Gly	Ile	Asp
900			905			910									
Trp	Ala	Trp	Gly	Glu	Leu	Leu	Ala	Phe	Gly	Ser	Leu	Ala	Asn	Ser	Gly
915			920			925									
Arg	Leu	Val	Arg	Leu	Ala	Gly	Glu	Asp	Ser	Arg	Arg	Gly	Thr	Phe	Thr
930			935			940									
Gln	Arg	His	Ala	Val	Ala	Ile	Asp	Pro	Ala	Thr	Ala	Glu	Glu	Phe	Asn
945			950			955			960						
Pro	Leu	His	Glu	Leu	Ala	Gln	Ser	Lys	Gly	Asn	Asn	Gly	Lys	Phe	Leu
965			970			975									
Val	Tyr	Asn	Ser	Ala	Leu	Thr	Glu	Tyr	Ala	Gly	Met	Gly	Phe	Glu	Tyr
980			985			990									
Gly	Tyr	Ser	Val	Gly	Asn	Glu	Asp	Ser	Val	Val	Ala	Trp	Glu	Ala	Gln
995			1000			1005									
Phe	Gly	Asp	Phe	Ala	Asn	Gly	Ala	Gln	Thr	Ile	Ile	Asp	Glu	Tyr	
1010			1015			1020									
Val	Ser	Ser	Gly	Glu	Ala	Lys	Trp	Gly	Gln	Thr	Ser	Lys	Leu	Ile	
1025			1030			1035									
Leu	Leu	Leu	Pro	His	Gly	Tyr	Glu	Gly	Gln	Gly	Pro	Asp	His	Ser	
1040			1045			1050									
Ser	Ala	Arg	Ile	Glu	Arg	Phe	Leu	Gln	Leu	Cys	Ala	Glu	Gly	Ser	
1055			1060			1065									
Met	Thr	Val	Ala	Gln	Pro	Ser	Thr	Pro	Ala	Asn	His	Phe	His	Leu	
1070			1075			1080									
Leu	Arg	Arg	His	Ala	Leu	Ser	Asp	Leu	Lys	Arg	Pro	Leu	Val	Ile	
1085			1090			1095									
Phe	Thr	Pro	Lys	Ser	Met	Leu	Arg	Asn	Lys	Ala	Ala	Ala	Ser	Ala	
1100			1105			1110									
Pro	Glu	Asp	Phe	Thr	Glu	Val	Thr	Lys	Phe	Gln	Ser	Val	Ile	Asp	
1115			1120			1125									
Asp	Pro	Asn	Val	Ala	Asp	Ala	Ala	Lys	Val	Lys	Lys	Val	Met	Leu	
1130			1135			1140									

[0074]

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Val Ser Gly Lys Leu Tyr Tyr Glu Leu Ala Lys Arg Lys Glu Lys
1145 1150 1155
Asp Gly Arg Asp Asp Ile Ala Ile Val Arg Ile Glu Met Leu His
1160 1165 1170
Pro Ile Pro Phe Asn Arg Ile Ser Glu Ala Leu Ala Gly Tyr Pro
1175 1180 1185
Asn Ala Glu Glu Val Leu Phe Val Gln Asp Glu Pro Ala Asn Gln
1190 1195 1200
Gly Pro Trp Pro Phe Tyr Gln Glu His Leu Pro Glu Leu Ile Pro
1205 1210 1215
Asn Met Pro Lys Met Arg Arg Val Ser Arg Arg Ala Gln Ser Ser
1220 1225 1230
Thr Ala Thr Gly Val Ala Lys Val His Gln Leu Glu Glu Lys Gln
1235 1240 1245
Leu Ile Asp Glu Ala Phe Glu Ala
1250 1255

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Met Leu Gln Leu Gly Leu Arg His Asn Gln Pro Thr Thr Asn Val Thr
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gtg gat aaa aca aag ctc aat aaa ccc tca aga agc aag gaa aag agg 96
Val Asp Lys Thr Lys Leu Asn Lys Pro Ser Arg Ser Lys Glu Lys Arg
20 25 30
cga gta cct gcc gtg agc agc gct agt act ttc ggc cag aat gcg tgg 144
Arg Val Pro Ala Val Ser Ser Ala Ser Thr Phe Gly Gln Asn Ala Trp
35 40 45
ctg gta gac gag atg ttc cag cag ttc cag aag gac ccc aag tcc gtg 192
Leu Val Asp Glu Met Phe Gln Gln Phe Gln Lys Asp Pro Lys Ser Val
50 55 60
gac aag gaa tgg aga gaa ctc ttt gag gcg cag ggg gga cca aat act 240
Asp Lys Glu Trp Arg Glu Leu Phe Glu Ala Gln Gly Gly Pro Asn Thr
65 70 75 80
acc ccc gct aca aca gaa gca cag cct tca gcg ccc aag gag tct gcg 288
Thr Pro Ala Thr Thr Glu Ala Gln Pro Ser Ala Pro Lys Glu Ser Ala
85 90 95
aaa cca gca cca aag gct gcc cct gca gcc aag gca gca ccg cgc gta 336
Lys Pro Ala Pro Lys Ala Ala Pro Ala Ala Lys Ala Ala Pro Arg Val
100 105 110
gaa acc aag ccg gcc gac aag acc gcc cct aag gcc aag gag tcc tca 384
Glu Thr Lys Pro Ala Asp Lys Thr Ala Pro Lys Ala Lys Glu Ser Ser
115 120 125
gtg cca cag caa cct aag ctt ccg gag cca gga caa acc cca atc agg 432
Val Pro Gln Gln Pro Lys Leu Pro Glu Pro Gly Gln Thr Pro Ile Arg
130 135 140
ggg att ttc aag tcc atc gcg aag aac atg gat atc tcc ctg gaa atc 480
Gly Ile Phe Lys Ser Ile Ala Lys Asn Met Asp Ile Ser Leu Glu Ile
145 150 155 160
cca acc gca acc tcg gtt cgc gat atg cca gct cgc etc atg ttc gaa 528
Pro Thr Ala Thr Ser Val Arg Asp Met Pro Ala Arg Leu Met Phe Glu
165 170 175
aac cgc gcg atg gtc aac gat cag etc aag cgc acc cgc ggt ggc aag 576
Asn Arg Ala Met Val Asn Asp Gln Leu Lys Arg Thr Arg Gly Gly Lys

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[0075]

180	185	190	
atc tcc ttc acc cac atc att ggc tac gcc atg gtg aag gca gtc atg			624
Ile Ser Phe Thr His Ile Ile Gly Tyr Ala Met Val Lys Ala Val Met			
195	200	205	
gct cac ccg gac atg aac aac tcc tac gac gtc atc gac ggc aag cca			672
Ala His Pro Asp Met Asn Asn Ser Tyr Asp Val Ile Asp Gly Lys Pro			
210	215	220	
acc ctg atc gtg cct gag cac atc aac ctg ggc ctt gct atc gac ctt			720
Thr Leu Ile Val Pro Glu His Ile Asn Leu Gly Leu Ala Ile Asp Leu			
225	230	235	240
cct cag aag gac ggc tcc cgc gca ctt gtc gta gca gcc atc aag gaa			768
Pro Gln Lys Asp Gly Ser Arg Ala Leu Val Val Ala Ala Ile Lys Glu			
245	250	255	
acc gag aag atg aac ttc tcc gag ttc ctc gca gcc tac gaa gac atc			816
Thr Glu Lys Met Asn Phe Ser Glu Phe Leu Ala Ala Tyr Glu Asp Ile			
260	265	270	
gtg gca cgc tcc cgc aag ggc aag ctc acc atg gat gac tac cag ggc			864
Val Ala Arg Ser Arg Lys Gly Lys Leu Thr Met Asp Asp Tyr Gln Gly			
275	280	285	
gtt acc gtt tcc ttg acc aac cca ggt ggc atc ggt acc cgc cac tct			912
Val Thr Val Ser Leu Thr Asn Pro Gly Gly Ile Gly Thr Arg His Ser			
290	295	300	
gtt cca cgt cta acc aag ggc cag ggc acc atc atc ggt gtc ggt tcc			960
Val Pro Arg Leu Thr Lys Gly Gln Gly Thr Ile Ile Gly Val Gly Ser			
305	310	315	320
atg gat tac cca gca gag ttc cag ggc gct tca gaa gac cgc ctt gca			1008
Met Asp Tyr Pro Ala Glu Phe Gln Gly Ala Ser Glu Asp Arg Leu Ala			
325	330	335	
gag ctc ggc gtt ggc aaa ctt gtc acc atc acc tcc acc tac gat cac			1056
Glu Leu Gly Val Gly Lys Leu Val Thr Ile Thr Ser Thr Tyr Asp His			
340	345	350	
cgc gtg atc cag ggt gct gtg tcc ggt gaa ttc ctg cgc acc atg tct			1104
Arg Val Ile Gln Gly Ala Val Ser Gly Glu Phe Leu Arg Thr Met Ser			
355	360	365	
cgc ctg ctc acc gat gat tcc ttc tgg gat gag atc ttc gac gca atg			1152
Arg Leu Leu Thr Asp Asp Ser Phe Trp Asp Glu Ile Phe Asp Ala Met			
370	375	380	
aac gtt cct tac acc cca atg cgt tgg gca cag gac gtt cca aac acc			1200
Asn Val Pro Tyr Thr Pro Met Arg Trp Ala Gln Asp Val Pro Asn Thr			
385	390	395	400
ggt gtt gat aag aac acc cgc gtc atg cag ctc att gag gca tac cgc			1248
Gly Val Asp Lys Asn Thr Arg Val Met Gln Leu Ile Glu Ala Tyr Arg			
405	410	415	
tcc cgt gga cac ctc atc gct gac acc aac cca ctt tca tgg gtt cag			1296
Ser Arg Gly His Leu Ile Ala Asp Thr Asn Pro Leu Ser Trp Val Gln			
420	425	430	
cct ggc atg cca gtt cca gac cac cgc gac ctc gac atc gag acc cac			1344
Pro Gly Met Pro Val Pro Asp His Arg Asp Leu Asp Ile Glu Thr His			
435	440	445	
aac ctg acc atc tgg gat ctg gac cgt acc ttc aac gtc ggt ggc ttc			1392
Asn Leu Thr Ile Trp Asp Leu Asp Arg Thr Phe Asn Val Gly Gly Phe			
450	455	460	
ggc ggc aag gag acc atg acc ctg cgc gag gta ctg tcc cgc ctc cgc			1440
Gly Gly Lys Glu Thr Met Thr Leu Arg Glu Val Leu Ser Arg Leu Arg			
465	470	475	480
gct cgc tac acc ctc aag gtc ggc tcc gaa tac acc cac atc ctg gac			1488
Ala Ala Tyr Thr Leu Lys Val Gly Ser Glu Tyr Thr His Ile Leu Asp			
485	490	495	
cgc gac gag cgc acc tgg ctg cag gac cgc ctc gag gcc gga atg cca			1536
Arg Asp Glu Arg Thr Trp Leu Gln Asp Arg Leu Glu Ala Gly Met Pro			
500	505	510	
aag cca acc cag gca gag cag aag tac atc ctg cag aag ctg aac gcc			1584
Lys Pro Thr Gln Ala Glu Gln Lys Tyr Ile Leu Gln Lys Leu Asn Ala			

[0076]

515	520	525	1632
gcg gag gct ttc gag aac ttc	ctg cag acc aag tac gtc ggc cag aag		
Ala Glu Ala Phe Glu Asn Phe	Leu Gln Thr Lys Tyr Val Gly Gln Lys		
530	535	540	
cgc ttc tcc ctc gaa ggt gca	gaa gca ctt atc cca ctg atg gac tcc		1680
Arg Phe Ser Leu Glu Gly Ala	Glu Ala Leu Ile Pro Leu Met Asp Ser		
545	550	555	560
gcc atc gac acc gcc gca ggc	caa ggc ctc gac gaa gtt gtc atc ggt		1728
Ala Ile Asp Thr Ala Ala Gly	Gln Gly Leu Asp Glu Val Val Ile Gly		
565	570	575	
atg cca cac cgt ggt cgc ctc	aac gtg ctg ttc aac atc gtg ggc aag		1776
Met Pro His Arg Gly Arg Leu	Asn Val Leu Phe Asn Ile Val Gly Lys		
580	585	590	
cca ctg gca tcc atc ttc aac	gag ttt gaa ggc caa atg gag cag ggc		1824
Pro Leu Ala Ser Ile Phe Asn	Glu Phe Glu Gly Gln Met Glu Gln Gly		
595	600	605	
cag atc ggt ggc tcc ggt gac	gtg aag tac cac ctc ggt tcc gaa ggc		1872
Gln Ile Gly Gly Ser Gly Asp	Val Lys Tyr His Leu Gly Ser Glu Gly		
610	615	620	
cag cac ctg cag atg ttc ggc	gac ggc gag atc aag gtc tcc ctg act		1920
Gln His Leu Gln Met Phe Gly	Asp Gly Glu Ile Lys Val Ser Leu Thr		
625	630	635	640
gct aac ccg tcc cac ctg gaa	gct gtt aac cca gtg atg gaa ggt atc		1968
Ala Asn Pro Ser His Leu Glu	Ala Val Asn Pro Val Met Glu Gly Ile		
645	650	655	
gtc cgc gca aag cag gac tac	ctg gac aag ggc gta gac ggc aag act		2016
Val Arg Ala Lys Gln Asp Tyr	Leu Asp Lys Gly Val Asp Gly Lys Thr		
660	665	670	
gtt gtg cca ctg ctg ctc cac	ggt gac gct gca ttc gca ggc ctg ggc		2064
Val Val Pro Leu Leu Leu His	Gly Asp Ala Ala Phe Ala Gly Leu Gly		
675	680	685	
atc gtg cca gaa acc atc aac	ctg gct aag ctg cgt ggc tac gac gtc		2112
Ile Val Pro Glu Thr Ile Asn	Leu Ala Lys Leu Arg Gly Tyr Asp Val		
690	695	700	
ggc ggc acc atc cac atc gtg	gtg aac aac cag atc ggc ttc acc acc		2160
Gly Gly Thr Ile His Ile Val	Val Val Asn Asn Gln Ile Gly Phe Thr Thr		
705	710	715	720
acc cca gac tcc agc cgc tcc	atg cac tac gca acc gac tac gcc aag		2208
Thr Pro Asp Ser Ser Arg Ser	Met His Tyr Ala Thr Asp Tyr Ala Lys		
725	730	735	
gca ttc ggc tgc cca gtc ttc	cac gtc aac ggc gac gac cca gag gca		2256
Ala Phe Gly Cys Pro Val Phe	His Val Asn Gly Asp Asp Pro Glu Ala		
740	745	750	
gtt gtc tgg gtt ggc cag ctg	gcc acc gag tac cgt cgt cgc ttc ggc		2304
Val Val Trp Val Gly Gln Leu	Ala Thr Glu Tyr Arg Arg Arg Phe Gly		
755	760	765	
aag gac gtc ttc atc gac ctc	gtc tgc tac cgc ctc cgc ggc cac aac		2352
Lys Asp Val Phe Ile Asp Leu	Val Cys Tyr Arg Leu Arg Gly His Asn		
770	775	780	
gaa gct gat gat cct tcc atg	acc cag cca aag atg tat gag ctc atc		2400
Glu Ala Asp Asp Pro Ser Met	Thr Gln Pro Lys Met Tyr Glu Leu Ile		
785	790	795	800
acc ggc cgc gag acc gtt cgt	gct cag tac acc gaa gac ctg ctc gga		2448
Thr Gly Arg Glu Thr Val Arg	Ala Gln Tyr Thr Glu Asp Leu Leu Gly		
805	810	815	
cgt gga gac ctc tcc aac gaa	gat gca gaa gca gtc gtc cgc gac ttc		2496
Arg Gly Asp Leu Ser Asn Glu	Asp Ala Glu Ala Val Val Arg Asp Phe		
820	825	830	
cac gac cag atg gaa tct gtg	ttc aac gaa gtc aag gaa ggc ggc aag		2544
His Asp Gln Met Glu Ser Val	Phe Asn Glu Val Lys Glu Gly Gly Lys		
835	840	845	
aag cag gct gag gca cag acc	ggc atc acc ggc tcc cag aag ctt cca		2592
Lys Gln Ala Glu Ala Gln Thr	Gly Ile Thr Gly Ser Gln Lys Leu Pro		

[0077]

850	855	860	
cac ggc ctt gag acc aac atc tcc cgt gaa gag ctc ctg gaa ctg gga			2640
His Gly Leu Glu Thr Asn Ile Ser Arg Glu Glu Leu Leu Glu Leu Gly			
865	870	875	880
cag gct ttc gcc aac acc cca gaa ggc ttc aac tac cac cca cgt gtg			2688
Gln Ala Phe Ala Asn Thr Pro Glu Gly Phe Asn Tyr His Pro Arg Val			
885	890	895	
gct ccc gtt gct aag aag cgc gtc tcc tct gtc acc gaa ggt ggc atc			2736
Ala Pro Val Ala Lys Lys Arg Val Ser Ser Val Thr Glu Gly Gly Ile			
900	905	910	
gac tgg gca tgg ggc gag ctc ctc gcc ttc ggt tcc ctg gct aac tcc			2784
Asp Trp Ala Trp Gly Glu Leu Leu Ala Phe Gly Ser Leu Ala Asn Ser			
915	920	925	
ggc cgc ttg gtt cgc ctt gca ggt gaa gat tcc cgc cgc ggt acc ttc			2832
Gly Arg Leu Val Arg Leu Ala Gly Glu Asp Ser Arg Arg Gly Thr Phe			
930	935	940	
acc cag cgc cac gca gtt gcc atc gac cca gcg acc gct gaa gag ttc			2880
Thr Gln Arg His Ala Val Ala Ile Asp Pro Ala Thr Ala Glu Glu Phe			
945	950	955	960
aac cca ctc cac gag ctt gca cag tcc aag ggc aac aac ggt aag ttc			2928
Asn Pro Leu His Glu Leu Ala Gln Ser Lys Gly Asn Asn Gly Lys Phe			
965	970	975	
ctg gtc tac aac tcc gca ctg acc gag tac gca ggc atg ggc ttc gag			2976
Leu Val Tyr Asn Ser Ala Leu Thr Glu Tyr Ala Gly Met Gly Phe Glu			
980	985	990	
tac ggc tac tcc gta gga aac gaa gac tcc atc gtt gca tgg gaa gca			3024
Tyr Gly Tyr Ser Val Gly Asn Glu Asp Ser Ile Val Ala Trp Glu Ala			
995	1000	1005	
cag ttc ggc gac ttc gcc aac ggc gct cag acc atc atc gat gag			3069
Gln Phe Gly Asp Phe Ala Asn Gly Ala Gln Thr Ile Ile Asp Glu			
1010	1015	1020	
tac gtc tcc tca ggc gaa gct aag tgg ggc cag acc tcc aag ctg			3114
Tyr Val Ser Ser Gly Glu Ala Lys Trp Gly Gln Thr Ser Lys Leu			
1025	1030	1035	
atc ctt ctg ctg cct cac ggc tac gaa ggc cag ggc cca gac cac			3159
Ile Leu Leu Leu Pro His Gly Tyr Glu Gly Gln Gly Pro Asp His			
1040	1045	1050	
tct tcc gca cgt atc gag cgc ttc ctg cag ctg tgc gct gag ggt			3204
Ser Ser Ala Arg Ile Glu Arg Phe Leu Gln Leu Cys Ala Glu Gly			
1055	1060	1065	
tcc atg act gtt gct cag cca tcc acc cca gca aac cac ttc cac			3249
Ser Met Thr Val Ala Gln Pro Ser Thr Pro Ala Asn His Phe His			
1070	1075	1080	
cta ctg cgt cgt cac gct ctg tcc gac ctg aag cgt cca ctg gtt			3294
Leu Leu Arg Arg His Ala Leu Ser Asp Leu Lys Arg Pro Leu Val			
1085	1090	1095	
atc ttc acc ccg aag tcc atg ctg cgt aac aag gct gct gcc tcc			3339
Ile Phe Thr Pro Lys Ser Met Leu Arg Asn Lys Ala Ala Ala Ser			
1100	1105	1110	
gca cca gaa gac ttc act gag gtc acc aag ttc cag tcc gtg atc			3384
Ala Pro Glu Asp Phe Thr Glu Val Thr Lys Phe Gln Ser Val Ile			
1115	1120	1125	
aac gat cca aac gtt gca gat gca gcc aag gtg aag aag gtc atg			3429
Asn Asp Pro Asn Val Ala Asp Ala Ala Lys Val Lys Lys Val Met			
1130	1135	1140	
ctg gtc tcc ggc aag ctg tac tac gaa ttg gca aag cgc aag gag			3474
Leu Val Ser Gly Lys Leu Tyr Tyr Glu Leu Ala Lys Arg Lys Glu			
1145	1150	1155	
aag gac gga cgc gac gac atc gcg atc gtt cgt atc gaa atg ctc			3519
Lys Asp Gly Arg Asp Asp Ile Ala Ile Val Arg Ile Glu Met Leu			
1160	1165	1170	
cac cca att ccg ttc aac cgc atc tcc gag gct ctt gcc ggc tac			3564
His Pro Ile Pro Phe Asn Arg Ile Ser Glu Ala Leu Ala Gly Tyr			

[0078]

1175	1180	1185	
cct aac gct gag gaa gtc ctc	ttc gtt cag gat gag	cca gca aac	3609
Pro Asn Ala Glu Glu Val Leu	Phe Val Gln Asp Glu	Pro Ala Asn	
1190	1195	1200	
cag ggc cca tgg ccg ttc tac	cag gag cac ctc cca	gag ctg atc	3654
Gln Gly Pro Trp Pro Phe Tyr	Gln Glu His Leu Pro	Glu Leu Ile	
1205	1210	1215	
ccg aac atg cca aag atg cgc	cgc gtt tcc cgc cgc	gct cag tcc	3699
Pro Asn Met Pro Lys Met Arg	Arg Val Ser Arg Arg	Ala Gln Ser	
1220	1225	1230	
tcc acc gca act ggt gtt gcc	aag gtg cac cag ctg	gag gag aag	3744
Ser Thr Ala Thr Gly Val Ala	Lys Val His Gln Leu	Glu Glu Lys	
1235	1240	1245	
cag ctt atc gac gag gct ttc	gag gct taa		3774
Gln Leu Ile Asp Glu Ala Phe	Glu Ala		
1250	1255		

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 <212> PRT
 <213> 谷氨酸棒杆菌

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

[0079]

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305          310          315          320
Met Asp Tyr Pro Ala Glu Phe Gln Gly Ala Ser Glu Asp Arg Leu Ala
          325          330          335
Glu Leu Gly Val Gly Lys Leu Val Thr Ile Thr Ser Thr Tyr Asp His
          340          345          350
Arg Val Ile Gln Gly Ala Val Ser Gly Glu Phe Leu Arg Thr Met Ser
          355          360          365
Arg Leu Leu Thr Asp Asp Ser Phe Trp Asp Glu Ile Phe Asp Ala Met
          370          375          380
Asn Val Pro Tyr Thr Pro Met Arg Trp Ala Gln Asp Val Pro Asn Thr
385          390          395          400
Gly Val Asp Lys Asn Thr Arg Val Met Gln Leu Ile Glu Ala Tyr Arg
          405          410          415
Ser Arg Gly His Leu Ile Ala Asp Thr Asn Pro Leu Ser Trp Val Gln
          420          425          430
Pro Gly Met Pro Val Pro Asp His Arg Asp Leu Asp Ile Glu Thr His
          435          440          445
Asn Leu Thr Ile Trp Asp Leu Asp Arg Thr Phe Asn Val Gly Gly Phe
450          455          460
Gly Gly Lys Glu Thr Met Thr Leu Arg Glu Val Leu Ser Arg Leu Arg
465          470          475          480
Ala Ala Tyr Thr Leu Lys Val Gly Ser Glu Tyr Thr His Ile Leu Asp
          485          490          495
Arg Asp Glu Arg Thr Trp Leu Gln Asp Arg Leu Glu Ala Gly Met Pro
          500          505          510
Lys Pro Thr Gln Ala Glu Gln Lys Tyr Ile Leu Gln Lys Leu Asn Ala
          515          520          525
Ala Glu Ala Phe Glu Asn Phe Leu Gln Thr Lys Tyr Val Gly Gln Lys
          530          535          540
Arg Phe Ser Leu Glu Gly Ala Glu Ala Leu Ile Pro Leu Met Asp Ser
545          550          555          560
Ala Ile Asp Thr Ala Ala Gly Gln Gly Leu Asp Glu Val Val Ile Gly
          565          570          575
Met Pro His Arg Gly Arg Leu Asn Val Leu Phe Asn Ile Val Gly Lys
          580          585          590
Pro Leu Ala Ser Ile Phe Asn Glu Phe Glu Gly Gln Met Glu Gln Gly
          595          600          605
Gln Ile Gly Gly Ser Gly Asp Val Lys Tyr His Leu Gly Ser Glu Gly
          610          615          620
Gln His Leu Gln Met Phe Gly Asp Gly Glu Ile Lys Val Ser Leu Thr
625          630          635          640
Ala Asn Pro Ser His Leu Glu Ala Val Asn Pro Val Met Glu Gly Ile
          645          650          655
Val Arg Ala Lys Gln Asp Tyr Leu Asp Lys Gly Val Asp Gly Lys Thr
          660          665          670
Val Val Pro Leu Leu Leu His Gly Asp Ala Ala Phe Ala Gly Leu Gly
          675          680          685
Ile Val Pro Glu Thr Ile Asn Leu Ala Lys Leu Arg Gly Tyr Asp Val
          690          695          700
Gly Gly Thr Ile His Ile Val Val Asn Asn Gln Ile Gly Phe Thr Thr
705          710          715          720
Thr Pro Asp Ser Ser Arg Ser Met His Tyr Ala Thr Asp Tyr Ala Lys
          725          730          735
Ala Phe Gly Cys Pro Val Phe His Val Asn Gly Asp Asp Pro Glu Ala
          740          745          750
Val Val Trp Val Gly Gln Leu Ala Thr Glu Tyr Arg Arg Arg Phe Gly
          755          760          765
Lys Asp Val Phe Ile Asp Leu Val Cys Tyr Arg Leu Arg Gly His Asn
          770          775          780
Glu Ala Asp Asp Pro Ser Met Thr Gln Pro Lys Met Tyr Glu Leu Ile
785          790          795          800
Thr Gly Arg Glu Thr Val Arg Ala Gln Tyr Thr Glu Asp Leu Leu Gly
          805          810          815

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[0080]

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Arg Gly Asp Leu Ser Asn Glu Asp Ala Glu Ala Val Val Arg Asp Phe
      820              825              830
His Asp Gln Met Glu Ser Val Phe Asn Glu Val Lys Glu Gly Gly Lys
      835              840              845
Lys Gln Ala Glu Ala Gln Thr Gly Ile Thr Gly Ser Gln Lys Leu Pro
      850              855              860
His Gly Leu Glu Thr Asn Ile Ser Arg Glu Glu Leu Leu Glu Leu Gly
      865              870              875              880
Gln Ala Phe Ala Asn Thr Pro Glu Gly Phe Asn Tyr His Pro Arg Val
      885              890              895
Ala Pro Val Ala Lys Lys Arg Val Ser Ser Val Thr Glu Gly Gly Ile
      900              905              910
Asp Trp Ala Trp Gly Glu Leu Leu Ala Phe Gly Ser Leu Ala Asn Ser
      915              920              925
Gly Arg Leu Val Arg Leu Ala Gly Glu Asp Ser Arg Arg Gly Thr Phe
      930              935              940
Thr Gln Arg His Ala Val Ala Ile Asp Pro Ala Thr Ala Glu Glu Phe
      945              950              955              960
Asn Pro Leu His Glu Leu Ala Gln Ser Lys Gly Asn Asn Gly Lys Phe
      965              970              975
Leu Val Tyr Asn Ser Ala Leu Thr Glu Tyr Ala Gly Met Gly Phe Glu
      980              985              990
Tyr Gly Tyr Ser Val Gly Asn Glu Asp Ser Ile Val Ala Trp Glu Ala
      995              1000              1005
Gln Phe Gly Asp Phe Ala Asn Gly Ala Gln Thr Ile Ile Asp Glu
      1010              1015              1020
Tyr Val Ser Ser Gly Glu Ala Lys Trp Gly Gln Thr Ser Lys Leu
      1025              1030              1035
Ile Leu Leu Leu Pro His Gly Tyr Glu Gly Gln Gly Pro Asp His
      1040              1045              1050
Ser Ser Ala Arg Ile Glu Arg Phe Leu Gln Leu Cys Ala Glu Gly
      1055              1060              1065
Ser Met Thr Val Ala Gln Pro Ser Thr Pro Ala Asn His Phe His
      1070              1075              1080
Leu Leu Arg Arg His Ala Leu Ser Asp Leu Lys Arg Pro Leu Val
      1085              1090              1095
Ile Phe Thr Pro Lys Ser Met Leu Arg Asn Lys Ala Ala Ala Ser
      1100              1105              1110
Ala Pro Glu Asp Phe Thr Glu Val Thr Lys Phe Gln Ser Val Ile
      1115              1120              1125
Asn Asp Pro Asn Val Ala Asp Ala Ala Lys Val Lys Lys Val Met
      1130              1135              1140
Leu Val Ser Gly Lys Leu Tyr Tyr Glu Leu Ala Lys Arg Lys Glu
      1145              1150              1155
Lys Asp Gly Arg Asp Asp Ile Ala Ile Val Arg Ile Glu Met Leu
      1160              1165              1170
His Pro Ile Pro Phe Asn Arg Ile Ser Glu Ala Leu Ala Gly Tyr
      1175              1180              1185
Pro Asn Ala Glu Glu Val Leu Phe Val Gln Asp Glu Pro Ala Asn
      1190              1195              1200
Gln Gly Pro Trp Pro Phe Tyr Gln Glu His Leu Pro Glu Leu Ile
      1205              1210              1215
Pro Asn Met Pro Lys Met Arg Arg Val Ser Arg Arg Ala Gln Ser
      1220              1225              1230
Ser Thr Ala Thr Gly Val Ala Lys Val His Gln Leu Glu Glu Lys
      1235              1240              1245
Gln Leu Ile Asp Glu Ala Phe Glu Ala
      1250              1255

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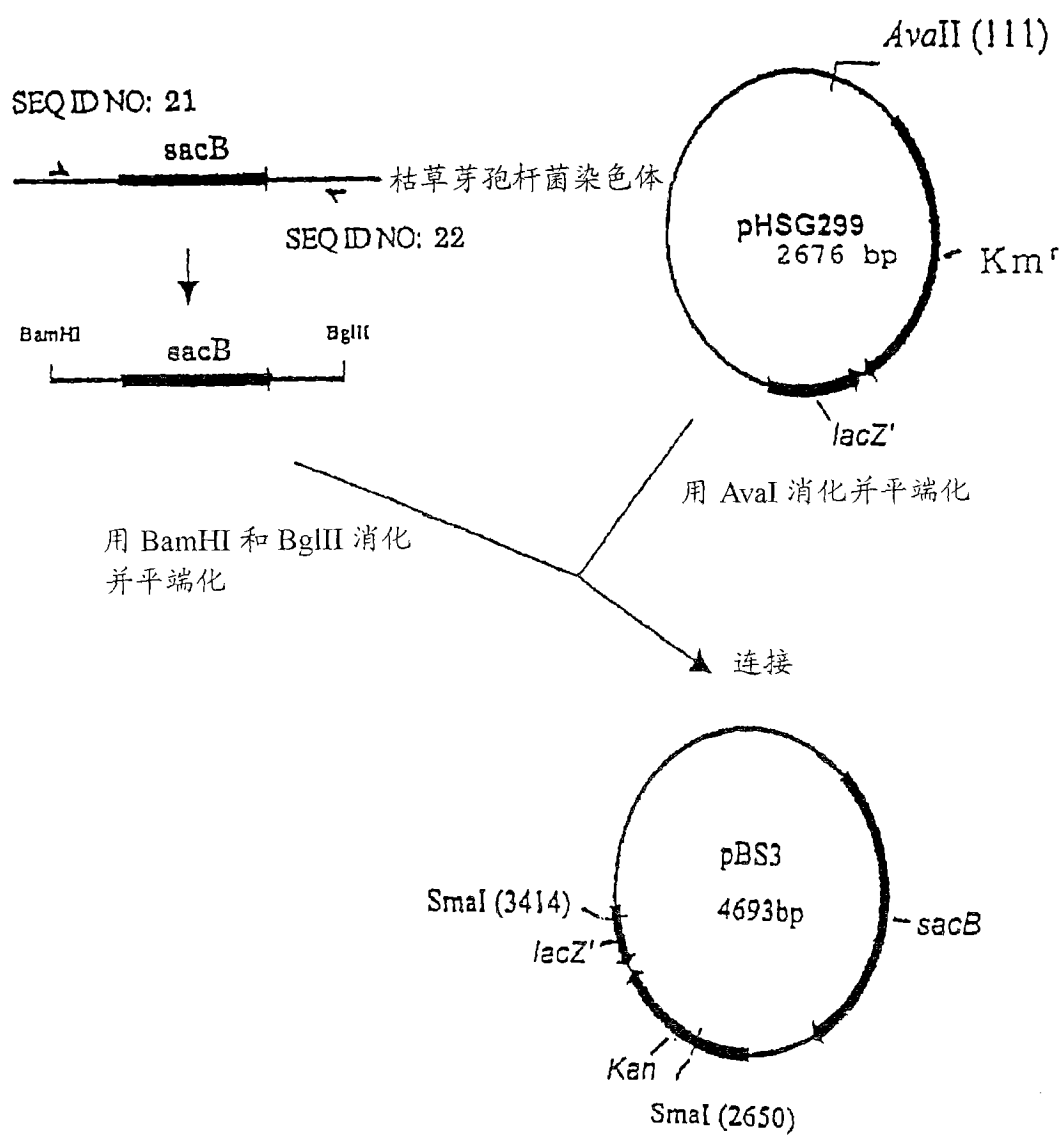


图 1

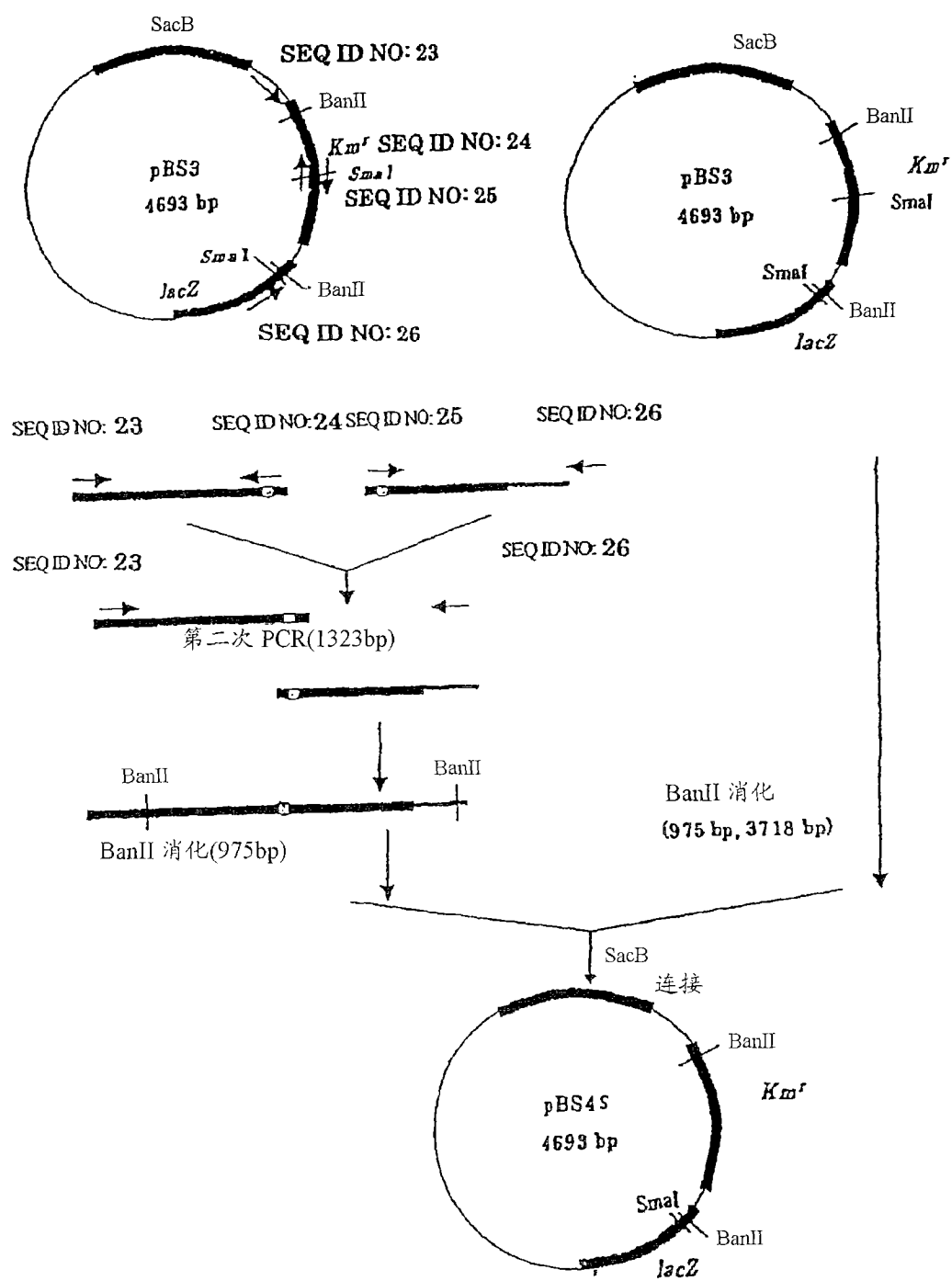


图 2

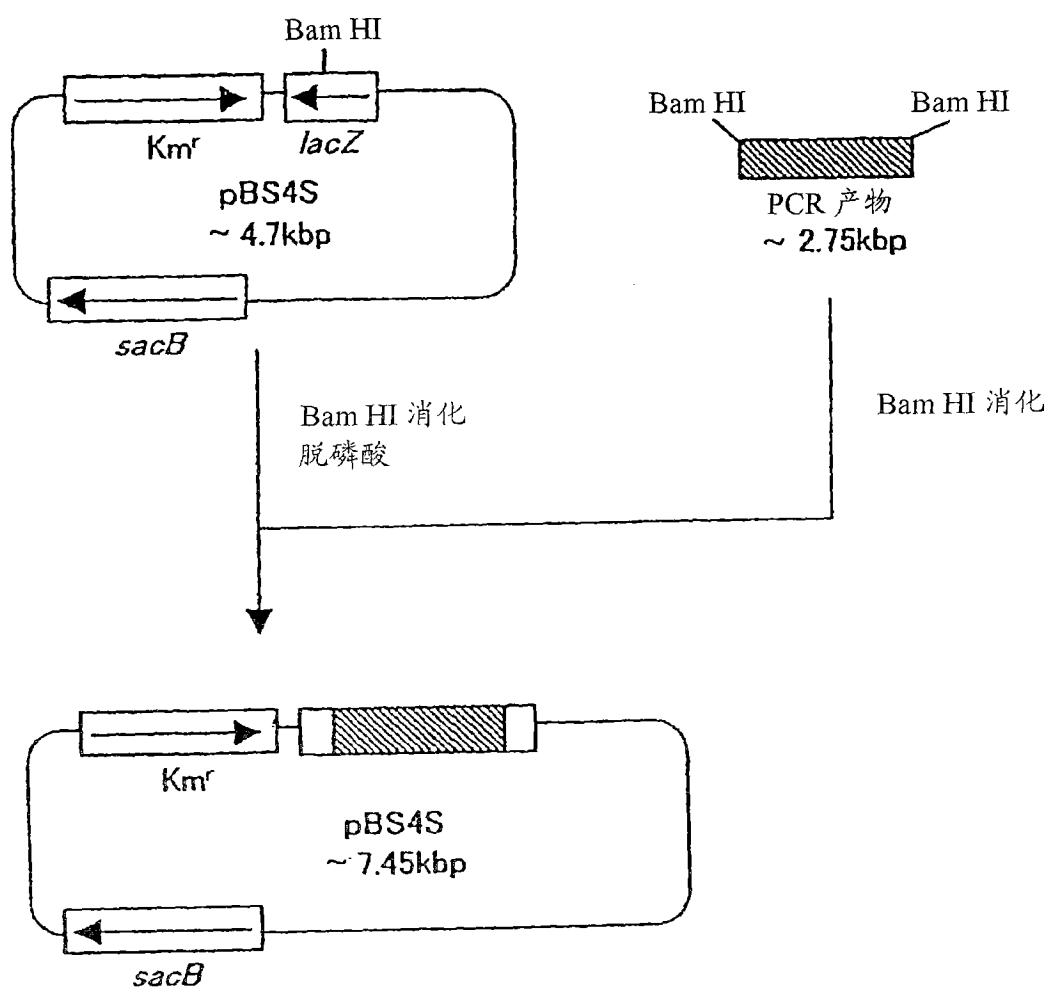


图 3

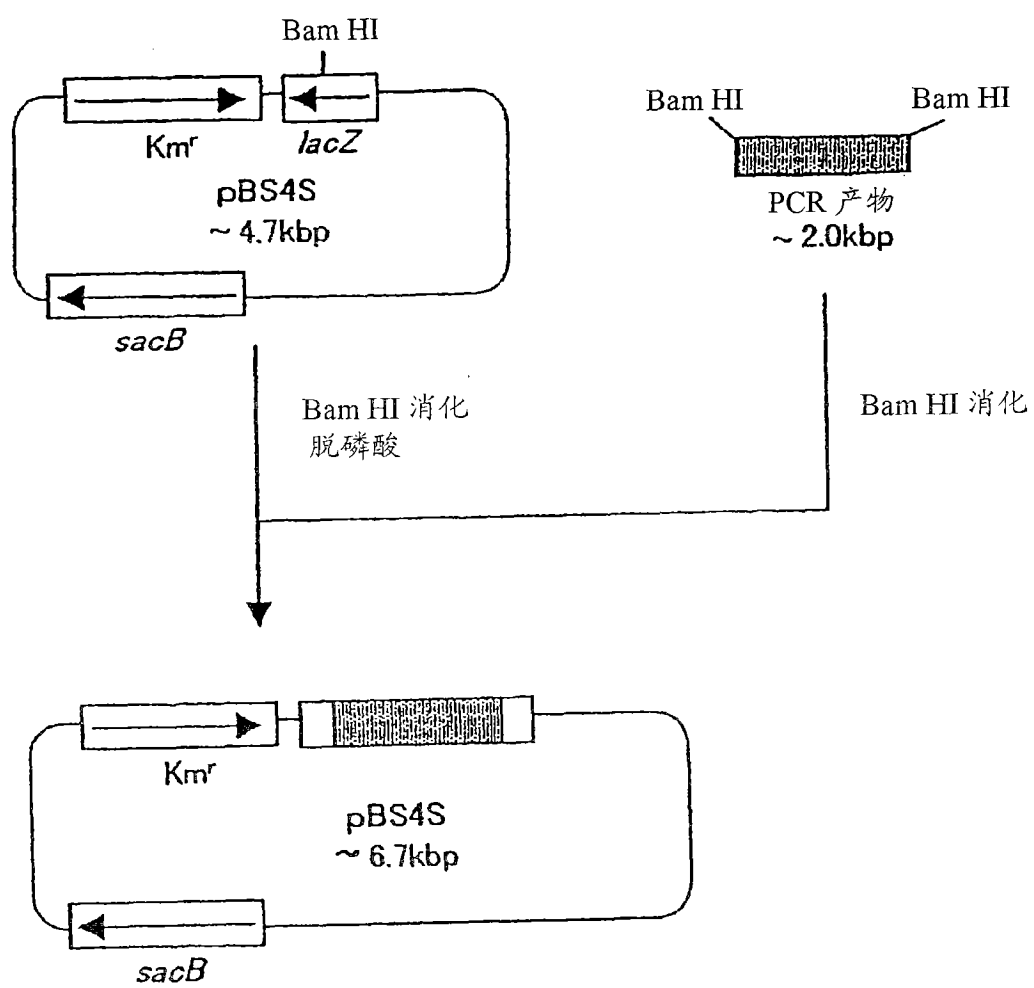


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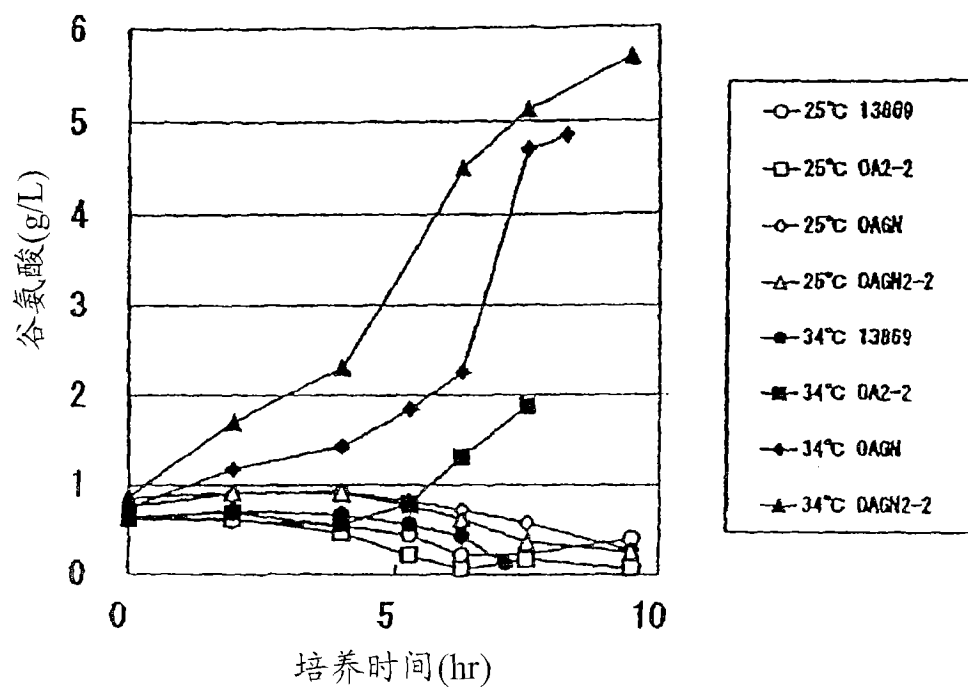


图 5

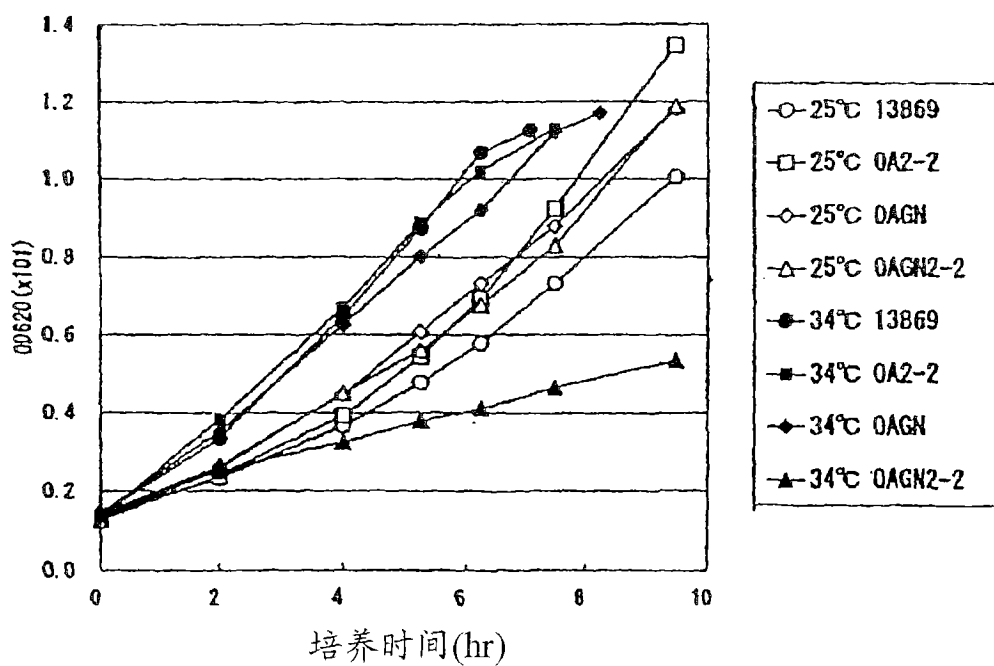


图 6

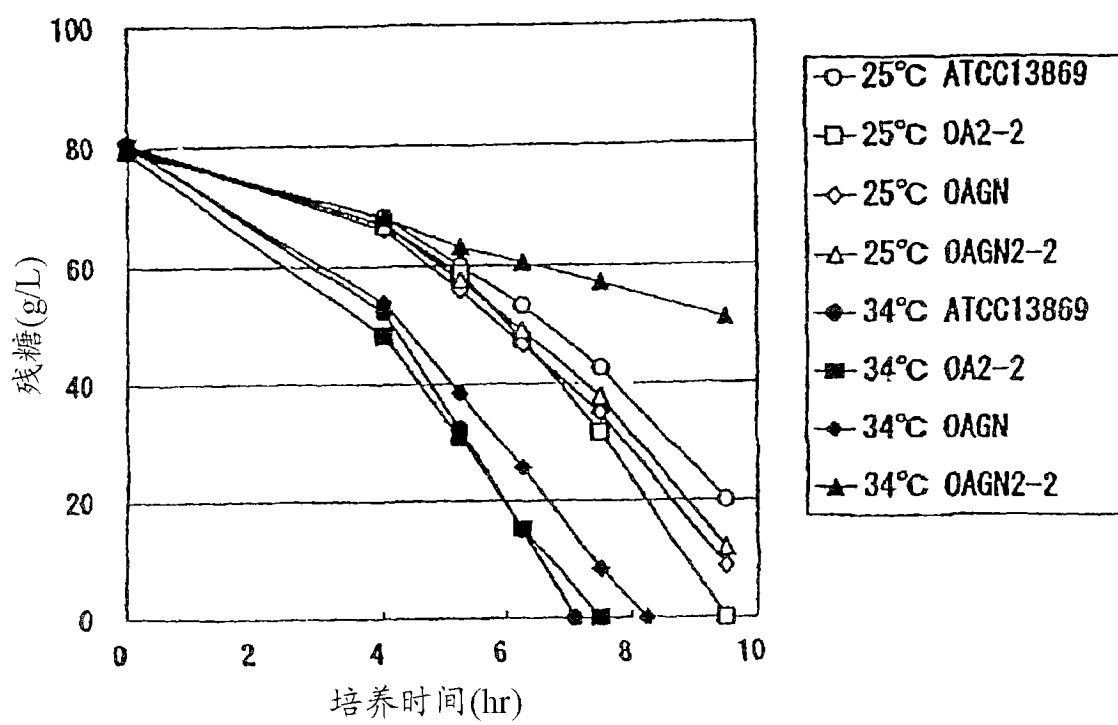


图 7