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(54)发明名称

用于治疗过敏的核酸

(57)摘要

本发明提供了用于过敏反应的治疗或预防的DNA疫苗。所述疫苗包含与溶酶体相关膜蛋白(LAMP)的腔内结构域和LAMP的靶向序列框内融合的过敏原X或其片段的编码序列。所述疫苗在给药至对象时允许呈递正确配置的三维表位,用于产生免疫应答。所述疫苗可以是多价分子,和/或可以被提供为含有两种或更多种DNA构建物的多价疫苗的一部分。

1. 一种分离的编码多肽的核酸,所述多肽包含:
 - a. 溶酶体相关膜蛋白 (LAMP) 腔内结构域;
 - b. 如表1中所描述的至少一种过敏原X;和
 - c. LAMP跨膜结构域/胞质尾区。
2. 权利要求1的核酸,其中LAMP选自LAMP多肽 (LAMP-1)、DC-LAMP、LAMP-2、LAMP-3、LIMP II或ENDOLYN。
3. 权利要求2的核酸,其中所述LAMP腔内结构域源自于LAMP-1。
4. 权利要求3的核酸,其中所述LAMP腔内结构域包含如以下序列所示的氨基酸序列:
 - (a) SEQ ID NO:2;
 - (b) SEQ ID NO:3;
 - (c) SEQ ID NO:4的第29-381位氨基酸或SEQ ID NO:5的第25-370位氨基酸;或
 - (d) (a) - (c) 的变体,其中所述变体与 (a) - (c) 具有至少约60%、至少约70%、至少约75%、至少约80%、至少约85%、至少约90%、至少约95%、96%、97%、98%或99%同一性。
5. 权利要求1-4任一项的核酸,其中所述LAMP跨膜结构域/胞质尾区包含:
 - (a) SEQ ID NO:1;
 - (b) SEQ ID NO:4的第382-417位氨基酸或SEQ ID NO:5的第371-406位氨基酸;或
 - (c) (a) - (b) 的变体,其中所述变体与 (a) - (b) 具有至少约60%、至少约70%、至少约75%、至少约80%、至少约85%、至少约90%、至少约95%、96%、97%、98%或99%同一性。
6. 权利要求1-5任一项的核酸,其中过敏原X包含:
 - (a) SEQ ID NO:Y或SEQ ID NO:V中至少一者的氨基酸序列;或
 - (b) (a) 的变体,其中所述变体与 (a) 具有至少约60%、至少约70%、至少约75%、至少约80%、至少约85%、至少约90%、至少约95%、96%、97%、98%或99%同一性;并且其中所述变体保留 (a) 产生与它所源自的过敏原X发生交叉反应的抗体的能力,和/或 (b) 过敏原X的生物活性。
7. 权利要求1-6任一项的核酸,其中所述核酸包含:
 - (a) 表1中所示的SEQ ID NO:Z或SEQ ID NO:W的多核苷酸中的任一者;
 - (b) 编码多肽的多核苷酸,所述多肽由表1中所示的SEQ ID NO:Z或SEQ ID NO:W的多核苷酸中的任一者编码;
 - (c) 编码多肽的多核苷酸,所述多肽包含表1中所示的SEQ ID NO:Y或SEQ ID NO:V的氨基酸序列;
 - (d) 编码腔内结构域 (例如SEQ ID NO:2或3或者如SEQ ID NO:4或5中所示)、表1中所示的SEQ ID NO:Y中的一者或多者和转运结构域 (例如SEQ ID NO:1或者如SEQ ID NO:4或5中所示) 的多核苷酸;
 - (e) 编码腔内结构域 (例如SEQ ID NO:2或3或者如SEQ ID NO:4或5中所示) 和表1中所示的SEQ ID NO:Y中的一者或多者的多核苷酸;
 - (f) 编码表1中所示的SEQ ID NO:Y中的一者或多者和转运结构域 (例如SEQ ID NO:1或者如SEQ ID NO:4或5中所示) 的多核苷酸;或
 - (g) 与 (a) - (f) 的任一多核苷酸具有至少约60%、至少约70%、至少约75%、至少约80%、至少约85%、至少约90%、至少约95%、96%、97%、98%或99%同一性的多核苷酸。

8. 一种载体,其包含权利要求1-7任一项的核酸。
9. 一种宿主细胞,其包含权利要求1-7任一项的核酸或权利要求8的载体。
10. 一种多肽,其由权利要求1-7任一项的核酸、权利要求8的载体或权利要求9的宿主细胞编码。
11. 一种疫苗,其包含权利要求1-7任一项的核酸、权利要求8的载体、权利要求9的宿主细胞或权利要求10的多肽。
12. 一种治疗或预防过敏反应的方法,其中所述方法包括以足以减轻、抑制或阻止过敏反应的有效量向对象给药权利要求11的疫苗。
13. 权利要求12的方法,其中所述疫苗被治疗性给药。
14. 权利要求12的方法,其中所述疫苗被预防性给药。
15. 权利要求12-14任一项的方法,其中所述方法包括初免步骤和至少一个加强步骤。
16. 权利要求15的方法,其中:
 - (a) 使用所述LAMP构建物来初免所述对象;和/或
 - (b) 所述加强步骤包括给药过敏原、所述LAMP构建物、由所述LAMP构建物编码的多肽或包含所述LAMP构建物的细胞。
17. 权利要求15或16的方法,其中用于初免的过敏原与用于加强的过敏原相同。
18. 权利要求15-17任一项的方法,其中用于初免的过敏原与用于加强的过敏原源自于同一蛋白。
19. 权利要求15-18任一项的方法,其中超过一种过敏原被用于初免和/或加强。

用于治疗过敏的核酸

技术领域

[0001] 本发明涉及分子生物学和医学领域。更具体来说,本发明涉及用作DNA疫苗的核酸和使用它们来治疗遭受过敏反应或对过敏反应易感的对象的方法。还描述了利用本文描述的LAMP构建物的初免-加强(prime boost)方案。

背景技术

[0002] 当免疫系统对被成为过敏原的无害外来物质产生反应时,发生过敏反应。例如,由于过敏性休克(anaphylaxis)这种潜在致死的系统性休克的高风险,食物过敏是重要的公共健康问题(Sampson等,(1992) N.Engl. J. Med. 327:380-384;Bock等,(2001) J. Allergy Clin. Immunol. 107:191-193)。幼儿与普通公众相比具有发生食物过敏的更高风险(Lack等,(2003) N.Engl. J. Med. 348:977-985;Zimmerman等,(1989) J. Allergy Clin. Immunol. 83:764-770;Green等,(2007) Pediatrics 120:1304-1310)。在生命的前三年中,6-8%的儿童经历由食物引起的过敏反应(Bock (1987) Allergy 45:587-596;Burks和Sampson,(1993) Curr. Prob. Pediatr. 23:230-252;Jansen等,(1994) J. Allergy Clin. Immunol. 93:2:446-456;Sampson (1999) J. Allergy Clin. Immunol. 103:5:717-728)。坚果过敏例如花生和坚果过敏影响高达1-2%的人群,并且这种食物过敏的发生率据认为在总人群中正在增加,不成比例地影响亚洲族裔。

[0003] 由暴露于过敏原例如树坚果或花生导致的过敏性休克,引起以组胺的过量生产为特征的严重免疫反应,并且每年造成一半的美国过敏性休克急诊室就诊。例如,在美国,对坚果的极端反应每年引起超过30,000例过敏性休克和100-200例之间的死亡。痕量的坚果通常存在于数以千计的各种品牌但未标注的包装食品中。超过一百五十万美国人经历来自于坚果过敏的症状,并且症状通常持续终生。许多人在痕量暴露后经历危险的反应。

[0004] 对缓解坚果过敏症状不存在治疗方法。在最近十年中,坚果过敏的普及率已经加倍,影响2%的成年美国人(Sampson (1999) J. Allergy Clin. Immunol. 103:5:717-728;Sicherer等,(2003) J. Allergy Clin. Immunol. 112:1203-1207)。尽管许多其他过敏如枯草热和矮豚草花粉的症状不危及生命,但对于坚果过敏个体来说,摄入少至1/1000的坚果就可引起过敏性休克和死亡(Taylor等,(2002) J. Allergy Clin. Immunol. 109 (1):24-30;Wensing等,(2002) J. Allergy Clin. Immunol. 110 (6):915-920)。在偶然的摄入触发过敏性休克的情况下,使用肾上腺素注射剂打开气道通道(Stark和Sullivan,(1986) J. Allergy Clin. Immunol. 78:76-83;Sampson (2003) Pediatrics 111 (6):1601-1608)。

[0005] 当个体未能发展出口服耐受并且反而变得对后续过敏原暴露敏化时,发生食物过敏(Till等,(2004) J. Allergy Clin. Immunol. 113 (6):1025-1034)。在过敏患者中,过敏原偏好性地激活2型辅助性CD4+T淋巴细胞(Th2),其产生促过敏细胞因子白介素IL-4、IL-5和IL-13,它们帮助统筹安排作为大多数过敏症状的基础的炎症(Woodfolk (2007) J. Allergy Clin. Immunol. 118 (2):260-294)。IL-4指示产生抗体的B细胞分泌过敏原特异性免疫球蛋白(Ig) E (DeI Prete等,(1988) J. Immunol. 140:4193-4198;Swain等,(1990)

J.Immunol.145:3796-3806)。不同于中和性IgG,IgE结合到它的由肥大细胞和嗜曙红细胞表达的高亲和性受体Fc-εR1 (Blank等,(1989) Nature337:187-190;Benhamou等,(1990) J.Immunol.144:3071-3077),由此使这些细胞敏化。在后续暴露后,IgE结合攻击性过敏原,交联,并转导指示肥大细胞脱粒并释放出引发过敏反应的挥发性化学物质的信号。

[0006] 除了食物过敏之外,其他环境因子也可以在个体中产生如上所述的过敏反应。这些环境因子的实例包括但不限于花粉、狗皮屑、猫唾液或尘螨。

[0007] 给药剂量逐渐增加的过敏原以引起耐受的免疫疗法,是用于过敏性疾病的标准治疗,但由于频繁的过敏性休克反应而尚未被批准用于治疗坚果过敏 (Nelson等,(1997) J.Allergy Clin.Immunol99:6:744-751;Oppenheimer等,(1992) J.Allergy Clin.Immunol 90:256-262)。此外,免疫疗法的效用受到治疗长度限制,其需要长达36个月的每周或每两周一次的注射,并且导致不同程度的成功和依从性 (Bousquet等,(1998) J.Allergy Clin.Immunol 102:558-562;Rank和Li,(2007) Mayo Clin.Proc.82 (9):1119-1123; Ciprandi等,(2007) Allergy Asthma Proc.28:40-43)。

[0008] 已提出将DNA疫苗作为过敏性疾病的治疗 (Raz等,1996;Hartl等,2004;Hsu等,1996;Cramer 2007;Weiss等,2006)。潜在的基本原理是由DNA疫苗编码的过敏原蛋白将偏好性地激活过敏原特异性Th1细胞应答并通过APC、自然杀伤(NK)和T细胞产生干扰素,而不是特征性的Th2型应答,例如IL-4、IL-5和IL-13的分泌和通过B淋巴细胞形成IgE以及在后期反应中嗜曙红细胞的成熟和召集。然而,Th1和Th2 T-细胞表型的差异诱导背后的机制似乎涉及大量因素,例如疫苗制剂的细菌DNA的独特性质如未甲基化的和CpG DNA残基、由先天性免疫力引发的细胞因子环境和过敏原的细胞转运性质 (Chen等,2001;Kaeck等,2002)。

[0009] 一般来说,DNA疫苗是包括编码一个或多个表位的序列的工程化改造的核酸。将所述核酸递送到细胞、通常为抗原呈递细胞(APC),所述核酸被表达,并且存在于所表达的蛋白质上的表位在胞内体/溶酶体区室中被加工,并最终呈递在细胞表面上。例如,August等人的美国专利号5,633,234公开并表征了溶酶体相关膜蛋白(LAMP)的胞内体/溶酶体靶向序列,鉴定了所述蛋白的C-端区域中将所述蛋白靶向胞内体/溶酶体区室所必需的关键残基。此外,Harris等人的美国专利申请公布号2004/0157307公开了使用LAMP腔内结构域作为“转运结构域(trafficking domain)”来指导从DNA疫苗表达的嵌合蛋白通过一个或多个细胞区室/细胞器,例如通过溶酶体囊泡途径。所述嵌合蛋白包括LAMP多肽的腔内结构域、包含以前鉴定的并选自抗原蛋白的肽表位序列的抗原性结构域、跨膜结构域和胞内体/溶酶体靶向序列。

[0010] 尽管已提出大量LAMP嵌合疫苗,但在体内测试后它们发挥有效疫苗作用的能力是不一致的。例如,在Godinho等,PLoS ONE 9(6):e99887.doi:10.1371/journal.pone.0099887中,作者报告了完整的腔内结构域对于将抗原靶向溶酶体和外泌体分泌途径而言是必需的,并且所述腔内结构域的片段不总是有效。参见同上,第6页。此外,作者承认引起免疫应答的能力依赖于所使用的具体抗原和表位。例如,在第9页第二栏,作者陈述了“因此,前面的研究证实,产生作为VLP分泌或采取可溶形式的Gag的DNA疫苗诱导不同水平的T和B细胞活化,其也不同于由细胞质Gag诱导的应答”。

[0011] 因此,即使在两种LAMP结构域都存在的情况下,也已越来越多地发现特定抗原引起免疫应答的效能高度依赖于所使用的具体序列。事实上已发现,同一蛋白的不同抗原性

片段当插入到一致的LAMP疫苗载体中时,不引发相同的免疫应答。抗原片段有时产生免疫应答,其他时候则不产生。这些观察使得提前预测来自于感兴趣的蛋白质的哪个特定抗原性序列将引起免疫应答的能力变得困难。相反,在LAMP疫苗的情况下,免疫应答活性需要通过体内测试来确定。

[0012] 因此,对鉴定可用于有效治疗对过敏反应的易感性的新的和改进的LAMP嵌合疫苗,存在着需求。

发明内容

[0013] 本发明的一个目的是提供包含具有高免疫原性的特异性抗原的疫苗,特别是基因疫苗例如DNA或RNA疫苗。

[0014] 本发明的另一个目的是通过使用本公开的抗原提供更有效的疫苗接种方法,所述抗原被导向溶酶体/胞内体区室和相关的细胞器(例如MIIC、CIIV、黑素小体、分泌颗粒、Birbeck颗粒等),在那里它们被加工并呈递到II类主要组织相容性复合物(MHC)分子,使得辅助性T细胞被偏好性地刺激。

[0015] 本发明的核酸以及因此所编码的蛋白质、多肽和肽可用于治疗对象的方法中,所述对象特别是患有或可能发生过敏症的对象。一般来说,符合本发明的治疗方法包括将本发明的核酸以足以将所述核酸递送到一个或多个免疫细胞、优选为免疫系统的一个或多个抗原呈递细胞(APC)的量给药到对象。在递送后,所述核酸被表达,所编码的蛋白质在所述细胞内被加工,并且表位展示在所述细胞表面上。所述治疗方法可以被当作使用所述核酸和蛋白质以在患有或可能发生过敏症的对象中提供治疗性或预防性免疫应答的方法。

[0016] 一方面,本发明提供了一种嵌合蛋白,其包含:包含至少一个过敏原X的N-端结构域;和转运结构域;其中所述转运结构域在细胞中将过敏原X导向胞内体区室(例如溶酶体)。优选地,所述转运结构域包含LAMP多肽例如LAMP-1或LAMP-2多肽的腔内结构域。

[0017] 在另一种情况下,所述嵌合蛋白包含将至少一个过敏原X导向胞内体/溶酶体区室或相关细胞器以用于蛋白质加工和将肽表位结合到MHC II的靶向序列,例如四肽序列Tyr-Xaa-Xaa-Xbb,其中Xaa是任何氨基酸并且Xbb是疏水性氨基酸。在另一种情况下,所述靶向序列包含二亮氨酸序列。在另一种情况下,所述靶向序列包含来自于吞饮受体的胞质蛋白靶向结构域。适合的结构域包括但不限于C-型凝集素受体、DEC-205多肽、gp200-MR6蛋白或其同源物、直系同源物、变体或修饰形式的靶向结构域。

[0018] 在一种特别优选的情况下,所述蛋白质包含LAMP多的腔内结构域和包含四肽序列Tyr-Xaa-Xaa-Xbb的胞质结构域,其中Xaa是任何氨基酸并且Xbb是疏水性氨基酸。所述嵌合蛋白优选地还包含跨膜蛋白。更优选地,所述嵌合蛋白还包含信号传导结构域。

[0019] 过敏原X可用于产生嵌合蛋白。在一种情况下,优选的过敏原包含表1中所示的SEQ ID NO:Y中的任一者的过敏原X的氨基酸序列。可以编码过敏原X(SEQ ID NO:Y)的多核苷酸的代表性实例在表1中显示为SEQ ID NO:Z。这些多核苷酸被插入在转运结构域与靶向结构域之间。利用与SEQ ID NO:Y的氨基酸序列侧接的克隆序列,例如编码“Leu-Glu”和“Glu-Phe”的多核苷酸(例如“CTCGAG”和“GAATTC”),可以便于插入。

[0020] 本发明还提供了编码表1的任一过敏原X的核酸分子。本发明还提供了包含编码过敏原X的核酸例如SEQ ID NO:Z和SEQ ID NO:W的载体,其中所述核酸分子被可操作地连接

到表达控制序列。在一种优选情况下,所述载体是适合于针对过敏原X接种患者的疫苗载体。在另一种情况下,本发明提供了包含所述核酸分子的递送媒介,以便于将所述核酸分子引入到细胞中。所述递送媒介可以是基于脂质的(例如脂质体制剂)、基于病毒的(例如包含包封所述核酸分子的病毒蛋白)或基于细胞的。在一种优选情况下,所述载体是疫苗载体。

[0021] 本发明还提供了包含任何上述载体的细胞。在一种情况下,所述细胞是抗原呈递细胞。所述抗原呈递细胞可以是专业抗原呈递细胞(例如树突状细胞、巨噬细胞、B细胞等)或工程化的抗原呈递细胞(例如被工程化改造以表达抗原呈递所需的分子例如II类MHC分子的非专业抗原呈递细胞)。所述抗原呈递所需的分子可以源自于其他细胞,例如天然存在的,或者它们本身可以被工程化改造(例如被突变或修饰以表现所需性质,例如对抗原性表位更高或更低的亲和性)。在一种情况下,所述抗原呈递细胞不表达任何辅助刺激信号,并且所述抗原是自身抗原。

[0022] 此外,本发明提供了一种试剂盒,其包含含有任何上述载体的多种细胞。至少两种所述细胞表达不同的II类MHC分子,并且每种细胞包含相同的载体。在一种情况下,提供了一种试剂盒,其包含载体和用于接受所述载体的细胞。

[0023] 本发明还提供了一种转基因动物,其包含至少一种上述细胞。

[0024] 本发明还提供了一种在动物中产生针对过敏原X的免疫应答的方法,所述方法包括:向所述动物给药如上所述包含编码过敏原X的核酸序列(例如SEQ ID NO:Z或SEQ ID NO:W)的细胞或多核苷酸,其中所述细胞在所述动物中表达或可以被诱导以表达所述嵌合蛋白。在一种情况下,所述细胞包含与所述动物的MHC蛋白相容的II类MHC分子,使得所述动物不产生针对所述II类MHC分子的免疫应答。在一种优选情况下,所述动物是人类。

[0025] 一方面,本发明提供了一种治疗患有或可能发生对过敏原X的过敏症的患者的方法,所述方法包括向动物给药上述载体、宿主细胞、多核苷酸或多肽中的任一者。在一个实施方式中,所述载体对所述动物的细胞具有感染性。例如,所述载体可以是病毒载体例如牛痘载体。向所述动物给药的优选嵌合疫苗包括编码表1中所示的SEQ ID NO:Y的任一氨基酸序列的多核苷酸。

[0026] 还设想了初免-加强方案。例如,本发明还提供了一种用于在对象中产生针对过敏原X的免疫应答的方法,所述方法包括用本文中描述的LAMP构建物初免所述对象,然后使用过敏原X或相关抗原(例如源自于相同或高度相似的蛋白质序列的第二种过敏原)对所述对象进行至少一次加强。在初免和加强步骤任一者或两者中,可以使用过敏原的混合物。已显示,将LAMP构建物用于初免步骤并随后进行加强步骤明显产生更高的滴度,指示了LAMP在增强抗体应答中的效力。

[0027] 在另一种情况下,从患者获得细胞,将所述载体引入到所述细胞中,并将所述细胞或细胞的后代重新引入到所述患者中。在一种情况下,所述细胞是能够分化成抗原呈递细胞的干细胞。

附图说明

[0028] 参考下面的详细描述和附图,可以更好地理解本发明的目的和特点。

[0029] 图1提供了用于产生本文中描述的构建物的人类LAMP-1序列的不同部分。

[0030] 图2提供了人类Lamp-1蛋白(SEQ ID NO:4)的已知结构域和氨基酸序列。

[0031] 图3提供了小鼠Lamp-1蛋白 (SEQ ID NO:5) 的已知结构域和氨基酸序列。

[0032] 图4是作为表1提供的本文中描述的不同构建物的示意图。

[0033] 详细描述

[0034] 本发明提供了可用于产生针对过敏原X的疫苗的嵌合蛋白和编码这些蛋白的核酸。在一种情况下,嵌合蛋白包含过敏原X和用于将所述蛋白转运到胞内体/溶酶体区室或相关细胞器的结构域。在一种优选情况下,所述转运结构域包含LAMP多肽的腔内结构域。可替代地或附加性地,所述嵌合蛋白包含吞饮受体(例如C-型凝集素、DEC-205或gp200-MR6)的转运结构域。所述疫苗可用于调节免疫应答。在一种优选情况下,本发明提供了一种通过向患者提供包含过敏原X的嵌合蛋白或编码过敏原X的核酸,在所述患者中治疗或预防过敏反应的方法。

[0035] 定义

[0036] 为下面书面描述中使用的特定术语,提供了下述定义。

[0037] 当在本说明书和权利要求书中使用时,没有具体数目的指称包括复数指称物,除非上下文明确指示不是如此。例如,术语“细胞”包括多个细胞,包括其混合物。术语“核酸分子”包括多个核酸分子。

[0038] 当在本文中使用时,术语“包含”旨在意味着所述组合物和方法包括所叙述的要素,但不排除其他要素。“基本上由……构成”当用于定义组合物和方法时,意味着排除对所述组合具有任何重要意义的其他要素。因此,基本上由本文中所定义的要素构成的组合物将不排除来自于分离和纯化方法的痕量污染物和可药用载体,例如磷酸盐缓冲盐水、防腐剂等。“由……构成”意味着排除超过痕量的其他成分要素和用于给药本发明的组合物的实质性方法步骤。由每个这些过渡性术语定义的实施方式都在本发明的范围之内。

[0039] 当在本文中使用时,“溶酶体/胞内体区室”是指膜约束的酸性液泡,其含有在膜中的LAMP分子、在抗原加工中发挥作用的水解酶类和用于抗原识别和呈递的II类MHC分子。该区室允当通过各种不同机制包括胞吞、吞噬和胞饮中的任一者从细胞表面内化的外来物质和通过特化的自溶现象递送到该区室的细胞内物质的降解位点(de Duve, Eur.J.Biochem.137:391,1983)。当在本文和权利要求书中使用时,术语“胞内体”涵盖溶酶体。

[0040] 当在本文中使用时,“溶酶体相关细胞器”是指包含溶酶体的任何细胞器,并且包括但不限于MIIC、CIIV、黑素小体、分泌颗粒、裂解性颗粒、血小板致密颗粒、嗜碱粒、Birbeck颗粒、吞噬溶酶体、分泌溶酶体等。优选地,这种细胞器缺少甘露糖6-磷酸受体并包含LAMP,但可以包含或不包含II类MHC分子。对于综述,参见例如Blott和Griffiths, Nature Reviews, Molecular Cell Biology, 2002; Dell'Angelica等, The FASEB Journal 14:1265-1278, 2000。

[0041] 当在本文中使用时,术语“多核苷酸”和“核酸分子”可互换地用于指称任何长度的核苷酸的聚合形式。多核苷酸可以含有脱氧核糖核苷酸、核糖核苷酸和/或它们的类似物。核苷酸可以具有任何三维结构,并且可以执行任何已知或未知的功能。术语“多核苷酸”包括例如单链、双链和三螺旋分子、基因或基因片段、外显子、内含子、mRNA、tRNA、rRNA、核酶、反义分子、cDNA、重组多核苷酸、支链多核苷酸、适体、质粒、载体、分离的任何序列的DNA、分离的任何序列的RNA、核酸探针和引物。核酸分子也可以包含修饰的核酸分子(例如包含修

饰的碱基、糖和/或核苷酸间连接物)。

[0042] 当在本文中使用时,术语“肽”是指两个或更多个子单元氨基酸、氨基酸类似物或肽模拟物的化合物。所述子单元可以通过肽键或通过其他键(例如酯、醚等)连接。

[0043] 当在本文中使用时,术语“氨基酸”是指天然和/或非天然的或合成的氨基酸,包括甘氨酸和D或L光学异构体两者以及氨基酸类似物和肽模拟物。三个或更多个氨基酸的肽,如果肽链短,通常被称为寡肽。如果肽链长(例如大于约10个氨基酸),所述肽通常被称为多肽或蛋白质。尽管术语“蛋白质”涵盖术语“多肽”,但“多肽”可以小于全长蛋白质。

[0044] 当在本文中使用时,术语“过敏原X”是指在下表1中列出的特定基因/蛋白质、其片段或列出的蛋白质的混合物,其已知在重复地暴露于个体后引起过敏症、即IgE介导的反应。通常,过敏原是能够引起过敏反应的任何化合物、物质或材料。过敏原通常被理解为抗原的亚类,它们是能够唤起免疫应答的化合物、物质或材料。为了执行本发明,过敏原X尤其可以选自天然或本源过敏原、修饰的天然过敏原、合成过敏原、重组过敏原、类过敏原及其混合物或组合。特别感兴趣的是能够引起IgE介导的速发型超敏反应的过敏原X。

[0045]

表 1

过敏原 X	过敏原 X 的氨基酸 序列 (SEQ ID NO: Y)	编码 SEQ ID NO: Y 的 代表性多核苷酸序列 (SEQ ID NO: Z)	全长构建物的氨基 酸序列 (SEQ ID NO: V)	编码 SEQ ID NO: V 的 代表性多核苷酸序列 (SEQ ID NO: W)
Cor a 1	SEQ ID NO: 7	SEQ ID NO: 6		
Cor a 9	SEQ ID NO: 9	SEQ ID NO: 8		
Cor a 1 – Gly4 – Cor a 9	SEQ ID NO: 11	SEQ ID NO: 10		
Pru du 6	SEQ ID NO: 13	SEQ ID NO: 12		
Ana o 1	SEQ ID NO: 15	SEQ ID NO: 14		
Ana o 2	SEQ ID NO: 17	SEQ ID NO: 16		
Ana o 3	SEQ ID NO: 19	SEQ ID NO: 18		
Ana 0 2 – Gly4- Ana 0 1 – Gly4- Ana 0 3	SEQ ID NO: 21	SEQ ID NO: 20		
Jug n 1	SEQ ID NO: 23	SEQ ID NO: 22		
Jug r 2	SEQ ID NO: 25	SEQ ID NO: 24		
Jug n 1 – Gly4 – Jug r 2	SEQ ID NO: 27	SEQ ID NO: 26		
Amb a 1	SEQ ID NO: 29	SEQ ID NO: 28	SEQ ID NO: 31	SEQ ID NO: 30
Bet v 1-A	SEQ ID NO: 33	SEQ ID NO: 32	SEQ ID NO: 35	SEQ ID NO: 34
Can f 1	SEQ ID NO: 37	SEQ ID NO: 36	SEQ ID NO: 39	SEQ ID NO: 38
Cyn d 1	SEQ ID NO: 41	SEQ ID NO: 40	SEQ ID NO: 43	SEQ ID NO: 42
Der F 1 (19-321)	SEQ ID NO: 45	SEQ ID NO: 44	SEQ ID NO: 47	SEQ ID NO: 46
Der F 1 (99-321)	SEQ ID NO: 49	SEQ ID NO: 48	SEQ ID NO: 51	SEQ ID NO: 50

[0046]

Der P2	SEQ ID NO: 53	SEQ ID NO: 52	SEQ ID NO: 55	SEQ ID NO: 54
DerF2	SEQ ID NO: 57	SEQ ID NO: 56	SEQ ID NO: 59	SEQ ID NO: 58
DerP1 (del)	SEQ ID NO: 61	SEQ ID NO: 60	SEQ ID NO: 63	SEQ ID NO: 62
Fel D 1	SEQ ID NO: 65 SEQ ID NO: 66	SEQ ID NO: 64	SEQ ID NO: 68	SEQ ID NO: 67
Fel d 2	SEQ ID NO: 70	SEQ ID NO: 69	SEQ ID NO: 72	SEQ ID NO: 71
Fel d 4	SEQ ID NO: 74	SEQ ID NO: 73	SEQ ID NO: 76	SEQ ID NO: 75
Lit v 1	SEQ ID NO: 78	SEQ ID NO: 77	SEQ ID NO: 80	SEQ ID NO: 79
Lol p 5a	SEQ ID NO: 82	SEQ ID NO: 81	SEQ ID NO: 84	SEQ ID NO: 83
Phl p 1	SEQ ID NO: 86	SEQ ID NO: 85	SEQ ID NO: 88	SEQ ID NO: 87
Phl p 5	SEQ ID NO: 90	SEQ ID NO: 89	SEQ ID NO: 92	SEQ ID NO: 91
Der f 15	SEQ ID NO: 93			
Der f 18	SEQ ID NO: 94			
Zen-1	SEQ ID NO: 95			
Cte f 1	SEQ ID NO: 96			
Der F15-Der F18	SEQ ID NO: 109			
Der F1-Der F2	SEQ ID NO: 110			

[0047] 当在本文中使用时,过敏原X的氨基酸序列包含SEQ ID NO:Y中的任一者。可以编码过敏原X的多核苷酸的优选的代表性实例在表1中被显示为SEQ ID NO:Z。特别考虑到了

编码过敏原X多肽的多核苷酸。

[0048] 当在本文中使用时,“过敏原X”还涵盖过敏原X的变体。例如,优选实施方式包括与 SEQ ID NO:Y 具有至少约60%、至少约70%、至少约75%、至少约80%、至少约85%、至少约90%、至少约95%、96%、97%、98%或99%同一性的过敏原X多肽变体。这些变体保留了(a)产生与它所源自的过敏原X发生交叉反应的抗体的能力,和/或(b)过敏原X的生物活性。特别考虑到了编码这些变体过敏原X多肽的多核苷酸。

[0049] 此外,超过一种过敏原X可以被组合并作为本文中描述的疫苗给药。在被克隆时,构建物内过敏原X的组合的顺序可以变化。此外,具体设想了所述过敏原X的组合可以被克隆在单一疫苗构建物内,或者可以在包含多种疫苗构建物或过敏原X的组合物中递送。具体来说,如表1中所描述的过敏原X可以被单个地或彼此组合地克隆到本文描述的LAMP构建物中。当在本文这一段落中使用时,名称Cora1、Cora9、Prudu6、Anao1、Anao2、Anao3、Jugn1、Jugr2、Amba1、Betv1-A、Canf1、Cynd1、DerF1 (19-321)、DerF1 (99-321)、DerP2、DerF2、DerP1 (del)、FelD1、FelD2、FelD4、Litv1、Lolp5a、Phlp1、Phlp5、DerF15、DerF18、Zen-1和Ctef1是指表1中描述的过敏原X。具体来说,可以如下所述将过敏原X的组合克隆到本文描述的LAMP构建物中:(a) Cora1和下述至少一者:Cora9,Prudu6,Anao1,Anao2,Anao3,Jugn1,Jugr2,Amba1,Betv1-A,Canf1,Cynd1,DerF1 (19-321),DerF1 (99-321),DerP2,DerF2,DerP1 (del),FelD1,FelD2,FelD4,Litv1,Lolp5a,Phlp1,Phlp5,DerF15,DerF18,Zen-1和/或Ctef1;(b) Cora9和下述至少一者:Cora1,Prudu6,Anao1,Anao2,Anao3,Jugn1,Jugr2,Amba1,Betv1-A,Canf1,Cynd1,DerF1 (19-321),DerF1 (99-321),DerP2,DerF2,DerP1 (del),FelD1,FelD2,FelD4,Litv1,Lolp5a,Phlp1,Phlp5,DerF15,DerF18,Zen-1和/或Ctef1;(c) Prudu6和下述至少一者:Cora1,Cora9,Anao1,Anao2,Anao3,Jugn1,Jugr2,Amba1,Betv1-A,Canf1,Cynd1,DerF1 (19-321),DerF1 (99-321),DerP2,DerF2,DerP1 (del),FelD1,FelD2,FelD4,Litv1,Lolp5a,Phlp1,Phlp5,DerF15,DerF18,Zen-1和/或Ctef1;(d) Anao1和下述至少一者:Cora1,Cora9,Prudu6,Anao2,Anao3,Jugn1,Jugr2,Amba1,Betv1-A,Canf1,Cynd1,DerF1 (19-321),DerF1 (99-321),DerP2,DerF2,DerP1 (del),FelD1,FelD2,FelD4,Litv1,Lolp5a,Phlp1,Phlp5,DerF15,DerF18,Zen-1和/或Ctef1;(e) Anao2和下述至少一者:Cora1,Cora9,Prudu6,Anao1,Anao3,Jugn1,Jugr2,Amba1,Betv1-A,Canf1,Cynd1,DerF1 (19-321),DerF1 (99-321),DerP2,DerF2,DerP1 (del),FelD1,FelD2,FelD4,Litv1,Lolp5a,Phlp1,Phlp5,DerF15,DerF18,Zen-1和/或Ctef1;(f) Anao3和下述至少一者:Cora1,Cora9,Prudu6,Anao1,Anao2,Jugn1,Jugr2,Amba1,Betv1-A,Canf1,Cynd1,DerF1 (19-321),DerF1 (99-321),DerP2,DerF2,DerP1 (del),FelD1,FelD2,FelD4,Litv1,Lolp5a,Phlp1,Phlp5,DerF15,DerF18,Zen-1和/或Ctef1;(g) Jugn1和下述至少一者:Cora1,Cora9,Prudu6,Anao1,Anao2,Anao3,Jugn1,Jugr2,Amba1,Betv1-A,Canf1,Cynd1,DerF1 (19-321),DerF1 (99-321),DerP2,DerF2,DerP1 (del),FelD1,FelD2,FelD4,Litv1,Lolp5a,Phlp1,Phlp5,DerF15,DerF18,Zen-1和/或Ctef1;(h) Jugr2和下述至少一者:Cora1,Cora9,Prudu6,Anao1,Anao2,Anao3,Jugn1,Amba1,Betv1-A,Canf1,Cynd1,DerF1 (19-321),DerF1 (99-321),DerP2,DerF2,DerP1 (del),FelD1,FelD2,FelD4,Litv1,Lolp5a,Phlp1,Phlp5,DerF15,DerF18,Zen-1和/或Ctef1;(i) Betv1-A和下述至少一者:Cora1,Cora9,Prudu6,Anao1,Anao2,Anao3,Jugn1,Jugr2,Amba1,Canf1,Cynd1,DerF1 (19-321),DerF1 (99-321),

DerP2, DerF2, DerP1 (del), FelD1, FelD2, FelD4, Litv1, Lolp5a, Phlp1, Phlp5, DerF15, DerF18, Zen-1和/或Ctef1; (j) Canf1和下述至少一者: Cora9, Prudu6, Anao1, Anao2, Anao3, Jugn1, Jugr2, Amba1, Betv1-A, Cynd1, DerF1 (19-321), DerF1 (99-321), DerP2, DerF2, DerP1 (del), FelD1, FelD2, FelD4, Litv1, Lolp5a, Phlp1, Phlp5, DerF15, DerF18, Zen-1和/或Ctef1; (k) Cynd1和下述至少一者: Cora9, Prudu6, Anao1, Anao2, Anao3, Jugn1, Jugr2, Amba1, Betv1-A, Canf1, DerF1 (19-321), DerF1 (99-321), DerP2, DerF2, DerP1 (del), FelD1, FelD2, FelD4, Litv1, Lolp5a, Phlp1, Phlp5, DerF15, DerF18, Zen-1和/或Ctef1; (l) DerF1 (19-321)和下述至少一者: Cora9, Prudu6, Anao1, Anao2, Anao3, Jugn1, Jugr2, Amba1, Betv1-A, Canf1, Cynd1, DerF1 (99-321), DerP2, DerF2, DerP1 (del), FelD1, FelD2, FelD4, Litv1, Lolp5a, Phlp1, Phlp5, DerF15, DerF18, Zen-1和/或Ctef1; (m) DerF1 (99-321)和下述至少一者: Cora1, Cora9, Prudu6, Anao1, Anao2, Anao3, Jugn1, Jugr2, Amba1, Betv1-A, Canf1, Cynd1, DerF1 (19-321), DerP2, DerF2, DerP1 (del), FelD1, FelD2, FelD4, Litv1, Lolp5a, Phlp1, Phlp5, DerF15, DerF18, Zen-1和/或Ctef1; (n) DerP2和下述至少一者: Cora1, Cora9, Prudu6, Anao1, Anao2, Anao3, Jugn1, Jugr2, Amba1, Betv1-A, Canf1, Cynd1, DerF1 (19-321), DerF1 (99-321), DerF2, DerP1 (del), FelD1, FelD2, FelD4, Litv1, Lolp5a, Phlp1, Phlp5, DerF15, DerF18, Zen-1和/或Ctef1; (o) DerF2和下述至少一者: Cora1, Cora9, Prudu6, Anao1, Anao2, Anao3, Jugn1, Jugr2, Amba1, Betv1-A, Canf1, Cynd1, DerF1 (19-321), DerF1 (99-321), DerP2, DerP1 (del), FelD1, FelD2, FelD4, Litv1, Lolp5a, Phlp1, Phlp5, DerF15, DerF18, Zen-1和/或Ctef1; (p) DerP1 (del)和下述至少一者: Cora1, Cora9, Prudu6, Anao1, Anao2, Anao3, Jugn1, Jugr2, Amba1, Betv1-A, Canf1, Cynd1, DerF1 (19-321), DerF1 (99-321), DerP2, DerF2, FelD1, FelD2, FelD4, Litv1, Lolp5a, Phlp1, Phlp5, DerF15, DerF18, Zen-1和/或Ctef1; (q) FelD1和下述至少一者: Cora1, Cora9, Prudu6, Anao1, Anao2, Anao3, Jugn1, Jugr2, Amba1, Betv1-A, Canf1, Cynd1, DerF1 (19-321), DerF1 (99-321), DerP2, DerF2, DerP1 (del), FelD2, FelD4, Litv1, Lolp5a, Phlp1, Phlp5, DerF15, DerF18, Zen-1和/或Ctef1; (r) FelD2和下述至少一者: Cora1, Cora9, Prudu6, Anao1, Anao2, Anao3, Jugn1, Jugr2, Amba1, Betv1-A, Canf1, Cynd1, DerF1 (19-321), DerF1 (99-321), DerP2, DerF2, DerP1 (del), FelD1, FelD4, Litv1, Lolp5a, Phlp1, Phlp5, DerF15, DerF18, Zen-1和/或Ctef1; (s) FelD4和下述至少一者: Cora1, Cora9, Prudu6, Anao1, Anao2, Anao3, Jugn1, Jugr2, Amba1, Betv1-A, Canf1, Cynd1, DerF1 (19-321), DerF1 (99-321), DerP2, DerF2, DerP1 (del), FelD1, FelD2, Litv1, Lolp5a, Phlp1, Phlp5, DerF15, DerF18, Zen-1和/或Ctef1; (t) Litv1和下述至少一者: Cora1, Cora9, Prudu6, Anao1, Anao2, Anao3, Jugn1, Jugr2, Amba1, Betv1-A, Canf1, Cynd1, DerF1 (19-321), DerF1 (99-321), DerP2, DerF2, DerP1 (del), FelD1, FelD2, FelD4, Lolp5a, Phlp1, Phlp5, DerF15, DerF18, Zen-1和/或Ctef1; (u) Lolp5a和下述至少一者: Cora1, Cora9, Prudu6, Anao1, Anao2, Anao3, Jugn1, Jugr2, Amba1, Betv1-A, Canf1, Cynd1, DerF1 (19-321), DerF1 (99-321), DerP2, DerF2, DerP1 (del), FelD1, FelD2, FelD4, Litv1, Phlp1, Phlp5, DerF15, DerF18, Zen-1和/或Ctef1; (v) Phlp1和下述至少一者: Cora1, Cora9, Prudu6, Anao1, Anao2, Anao3, Jugn1, Jugr2, Amba1, Betv1-A, Canf1, Cynd1, DerF1 (19-321), DerF1 (99-321), DerP2, DerF2, DerP1 (del), FelD1, FelD2, FelD4, Litv1, Lolp5a, Phlp5, DerF15, DerF18, Zen-1和/或Ctef1; (w) Amba1和下述至少一者: Cora1,

Cora9, Prudu6, Anao1, Anao2, Anao3, Jugn1, Jugr2, Betv1-A, Canf1, Cynd1, DerF1 (19-321), DerF1 (99-321), DerP2, DerF2, DerP1 (del), FelD1, FelD2, FelD4, Litv1, Lolp5a, Phlp1, Phlp5, DerF15, DerF18, Zen-1 和/或 Ctef1; (x) Phlp5 和下述至少一者: Cora1, Cora9, Prudu6, Anao1, Anao2, Anao3, Jugn1, Jugr2, Amba1, Betv1-A, Canf1, Cynd1, DerF1 (19-321), DerF1 (99-321), DerP2, DerF2, DerP1 (del), FelD1, FelD2, FelD4, Litv1, Lolp5a, Phlp1, DerF15, DerF18, Zen-1 和/或 Ctef1; (y) DerF15 和下述至少一者: Cora1, Cora9, Prudu6, Anao1, Anao2, Anao3, Jugn1, Jugr2, Amba1, Betv1-A, Canf1, Cynd1, DerF1 (19-321), DerF1 (99-321), DerP2, DerF2, DerP1 (del), FelD1, FelD2, FelD4, Litv1, Lolp5a, Phlp1, Phlp5, DerF18, Zen-1 和/或 Ctef1; (z) DerF18 和下述至少一者: Cora1, Cora9, Prudu6, Anao1, Anao2, Anao3, Jugn1, Jugr2, Amba1, Betv1-A, Canf1, Cynd1, DerF1 (19-321), DerF1 (99-321), DerP2, DerF2, DerP1 (del), FelD1, FelD2, FelD4, Litv1, Lolp5a, Phlp1, Phlp5, DerF15, Zen-1 和/或 Ctef1; (aa) Zen-1 和下述至少一者: Cora1, Cora9, Prudu6, Anao1, Anao2, Anao3, Jugn1, Jugr2, Amba1, Betv1-A, Canf1, Cynd1, DerF1 (19-321), DerF1 (99-321), DerP2, DerF2, DerP1 (del), FelD1, FelD2, FelD4, Litv1, Lolp5a, Phlp1, Phlp5, DerF15, DerF18 和/或 Ctef1; 和/或 (bb) Ctef1 和下述至少一者: Cora1, Cora9, Prudu6, Anao1, Anao2, Anao3, Jugn1, Jugr2, Amba1, Betv1-A, Canf1, Cynd1, DerF1 (19-321), DerF1 (99-321), DerP2, DerF2, DerP1 (del), FelD1, FelD2, FelD4, Litv1, Lolp5a, Phlp1, Phlp5, DerF15, DerF18 和/或 Zen-1。

[0050] 在特定LAMP构建物中如上所述的抗原的组合顺序可以变化,因为这个列表描述了LAMP构建物包含的抗原并且不必定描述所述抗原在特定构建物内的排列。此外,特别设想了这些抗原可以合并并在单一LAMP构建物内,或者可以在包含多个LAMP构建物的组合物中递送。

[0051] 当在本文中使用时,“LAMP多肽”是指LAMP-1、LAMP-2、CD63/LAMP-3、DC-LAMP或任何溶酶体相关膜蛋白或同源物、直系同源物、变体(例如等位基因变体)和修饰形式(例如包含一个或多个天然存在的或工程化改造的突变)。在一种情况下,LAMP多肽是哺乳动物溶酶体相关膜蛋白,例如人类或小鼠溶酶体相关膜蛋白。更通常地,“溶酶体相关膜蛋白”是指包含存在于胞内体/溶酶体区室或溶酶体相关细胞器的膜中的结构域,并且还包含腔内结构域的任何蛋白质。LAMP-1多肽的代表性实例包括SEQ ID NO:4(人类LAMP-1)、SEQ ID NO:5(小鼠LAMP-1)或犬LAMP(XP_534193),并且任何这些序列可用于产生本文中所描述的DNA疫苗。

[0052] 当在本文中使用时,“吞饮受体”是指其C-端或N-末端朝向细胞质的跨膜蛋白,并且其包含用于将偶联到它(例如通过化学键)的多肽或肽运输到II类MHC分子或运输到细胞内区室以便随后与II类MHC分子结合的转运结构域(例如腔内结构域)。吞饮受体的实例包括但不限于Fc-受体、补体受体、清除剂受体、整合蛋白、凝集素(例如C-型凝集素)、DEC-205多肽、gp200-MR6多肽、Toll样受体、热休克蛋白受体(例如CD 91)凋亡小体或坏死小体受体(例如CD 14)或其同源物、直系同源物、变体(例如等位基因变体)和修饰形式(例如包含一个或多个天然存在的或工程化改造的突变)。

[0053] 当在本文中使用时,“表达”是指多核苷酸被转录成mRNA和/或翻译成肽、多肽或蛋白质的过程。如果所述多核苷酸源自于基因组DNA,表达可以包括从基因组DNA转录的mRNA

的拼接。

[0054] 当在本文中使用时,“在转录控制下”或“可操作地连接”是指由表达控制元件和编码序列的适合的并置所控制的多核苷酸序列的表达(例如转录或翻译)。在一种情况下,当表达控制序列控制并调节DNA序列的转录时,该DNA序列“可操作地连接”到所述表达控制序列。

[0055] 当在本文中使用时,“编码序列”是当置于适合的表达控制序列的控制之下时转录并翻译成多肽的序列。编码序列的边界由5′(氨基)端的起始密码子和3′(羧基)端的翻译终止密码子确定。编码序列可以包括但不限于原核序列、来自于真核mRNA的cDNA、来自于真核(例如哺乳动物)DNA的基因组DNA序列和甚至合成的DNA序列。多腺苷化信号和转录终止序列通常位于所述编码序列的3′。

[0056] 当在本文中使用时,两个编码序列,如果所述序列或它们的互补序列编码相同的氨基酸序列,则它们彼此“对应”。

[0057] 当在本文中使用时,“信号序列”是指内质网易位序列。该序列编码与细胞通讯的信号肽,以将它连接(例如通过化学键)到的多肽导向内质网囊泡区室,进入胞吐/胞吞细胞器,递送到细胞囊泡区室、细胞表面,或分泌所述多肽。该信号序列有时在蛋白质成熟中被细胞切掉。可以发现与原核生物和真核生物本源的各种不同蛋白质缔合的信号序列。

[0058] 当在本文中使用时,“转运”是指过敏原X多肽通过从粗面内质网到发生抗原加工和与MHC II的结合的胞内体/溶酶体区室或相关细胞器的途径中的所有细胞器或区室的移动或进展。“运输”是指将嵌合蛋白递送到一种特定类型的细胞区室。

[0059] 当在本文中使用时,与另一个转运序列基本上同源的“转运序列”,是与所述另一个转运序列享有显著同源性的转运序列;然而,用于显著同源性的最终测试是功能测定,其中包含与转运序列基本上同源的序列的多肽能够与所述转运序列共定位到同一胞内体区室。

[0060] 当在本文中使用时,“转运结构域”是指蛋白质中的一系列连续或不连续的氨基酸,其为所述蛋白质通过一个或多个细胞区室/细胞器的囊泡流动所需。转运结构域优选地包含适合的蛋白质折叠所必需的序列,以介导这种流动。在一种情况下,转运结构域包含腔内序列;优选地,这种序列包含用于与细胞折叠蛋白例如伴侣蛋白相互作用的一个或多个结合位点。

[0061] 当在本文中使用时,“靶向”是指多肽序列指导过敏原X向发生抗原加工和与MHC II的结合的优选位点或细胞器或区室的转运。

[0062] 相反,当在本文中使用时,“靶向结构域”是指向细胞区室/细胞器的递送所需的一系列氨基酸。优选地,靶向结构域是结合到接合体或AP蛋白(例如AP1、AP2或AP3蛋白)的序列。示例性的靶向结构域序列描述在De11’Angelica,2000,同上中。

[0063] “嵌合DNA”是较大的DNA分子内可识别的DNA区段,其在自然界中未发现与所述较大分子缔合。因此,当所述嵌合DNA编码蛋白质区段时,所述编码序列区段将侧接有在任何天然存在的基因组中不侧接所述编码序列的DNA。等位基因变异或天然存在的突变事件不产生本文中所定义的嵌合DNA。

[0064] 编码氨基酸的多核苷酸的短区段可以被包括在编码过敏原X的多核苷酸的末端处,以便于克隆到本文描述的任何载体中。例如,侧接于SEQ ID NO:Y的氨基酸序列的克隆

序列例如编码“Leu-Glu”和“Glu-Phe”的多核苷酸(例如“CTCGAG”和“GAATTC”)的使用,可以被包括在构建物设计中。

[0065] 当在本文中使用时,“核酸递送载体”是可以将感兴趣的多核苷酸运输到细胞中的核酸分子。优选地,这种载体包含可操作地连接到表达控制序列的编码序列。然而,感兴趣的多核苷酸序列可能不必定包含编码序列。例如,在一种情况下,感兴趣的多核苷酸序列是结合到靶分子的适体。在另一种情况下,感兴趣的序列是调控序列的互补序列,其结合到调控序列以抑制所述调控序列的调控。在另一种情况下,感兴趣的序列本身是调控序列(例如用于滴定出细胞中的调控因子)。

[0066] 当在本文中使用时,“核酸递送媒介”被定义为可以将多核苷酸携带到宿主细胞中并且与如上所述的核酸载体缔合出现的任何分子或成组分子或大分子(例如基因或基因片段、反义分子、核酶、适体等)。

[0067] 当在本文中使用时,“核酸递送”或“核酸转移”是指将外源多核苷酸(例如“转入基因”)引入到宿主细胞中,不论用于引入的方法如何。被引入的多核苷酸可以稳定地或暂时地维持在所述宿主细胞中。稳定维持通常要求被引入的多核苷酸含有与所述宿主细胞相容的复制原点,或整合到宿主细胞的复制子例如染色体外复制子(例如质粒)或核或线粒体染色体中。

[0068] 当在本文中使用时,“病毒载体”是指包含待体内、离体或体外递送到宿主细胞中的多核苷酸的病毒或病毒粒子。病毒载体的实例包括但不限于腺病毒载体、腺相关病毒载体、反转录病毒载体等。在基因转移由腺病毒载体介导的情况下,载体构建物是指与腺病毒衣壳蛋白相结合的包含腺病毒基因组或其一部分和选定的非腺病毒基因的多核苷酸。

[0069] 当在本文中使用时,“腺病毒介导的基因转移”或“腺病毒转导”是指利用进入细胞的腺病毒将基因或核酸序列转移到宿主细胞中的过程。优选地,所述病毒能够在所述细胞内复制和/或整合并被转录。

[0070] 当在本文中使用时,“腺病毒粒子”是指包含外部衣壳和内部核酸材料的单个腺病毒毒粒,其中所述衣壳进一步包含腺病毒包膜蛋白。所述腺病毒包膜蛋白可以被修饰以包含融合多肽,所述融合多肽含有共价附连到所述病毒蛋白质的多肽配体,例如用于将所述腺病毒粒子靶向到特定细胞和/或组织类型。

[0071] 当在本文中使用时,术语“向细胞给药分子”(例如表达载体、核酸、辅助因子、递送媒介、药剂等)是指用所述分子转导、转染、微注射、电穿孔或射击所述细胞。在某些情况下,通过将靶细胞与递送细胞相接触(例如通过细胞融合或通过所述递送细胞邻近所述靶细胞时将递送细胞裂解),将分子引入到所述靶细胞中。

[0072] 当在本文中使用时,短语“初免-加强”描述了本文中描述的LAMP构建物的用途,其用于引发T-细胞应答,随后使用包含过敏原的第二种LAMP构建物、包含过敏原或重组过敏原的DNA疫苗来加强所述应答。这些异源初免-加强免疫接种引发与通过用相同载体初免和加强所能实现的相比高度和广度更大的免疫应答。所述初免使用包含过敏原X记忆细胞的LAMP构建物;所述加强步骤扩大了所述记忆应答。优选地,所述两种药剂的使用不引起针对彼此的应答,因此不干扰彼此的活性。在初免和/或加强步骤中特别考虑到了过敏原的混合物。加强可以进行一次或多次。

[0073] 当在本文中使用时,“杂交”是指其中一个或多个多核苷酸进行反应,以形成通过

核苷酸残基的碱基之间的氢键键合稳定化的复合体的反应。所述氢键键合可以通过Watson-Crick碱基配对、Hoogsteen结合或以任何其他序列特异性方式进行。所述复合体可以包含形成双链体结构的两条链、形成多链复合体的三条或更多条链、自我杂交的单链或它们的任何组合。杂交反应可以构成更加广泛的过程例如PCR反应的引发或多核苷酸被核酶的酶切割中的步骤。

[0074] 当在本文中使用时,与另一个序列具有一定百分率(例如至少约50%、至少约60%、至少约70%、至少约80%、至少约85%、至少约90%、至少约95%、至少约99%)的“序列同一性”的多核苷酸或多核苷酸区域(或多肽或多肽区域),意味着在比较所述两个序列时,在使用本领域中常用的软件程序最大对齐时,相同的碱基(或氨基酸)的百分率。

[0075] 两个序列,当在所述DNA序列的确定长度内至少约50%、至少约60%、至少约70%、至少约75%、优选地至少约80%、且最优选地至少约90或95%的核苷酸匹配时,是“基本上同源的”或“基本上相似的”。同样地,两个多肽序列,当在所述多肽序列的确定长度内所述多肽的至少约50%、至少约60%、至少约65%、至少约70%、至少约75%、优选地至少约80%、且最优选地至少约90或95%的氨基酸残基匹配时,是“基本上同源的”或“基本上相似的”。基本上同源的序列可以通过使用序列数据库中可用的标准软件比较所述序列来鉴定。基本上同源的核酸序列也可以在Southern杂交实验中,在例如为该特定系统定义的严紧条件下鉴定。确定适合的杂交条件在本领域的技术范围之内。例如,严紧条件可以是:在5xSSC和50%甲酰胺和42℃下杂交,并在0.1xSSC和0.1%十二烷基硫酸钠和60℃下清洗。

[0076] 术语“百分(%)序列相似性”、“百分(%)序列同一性”等,通常是指可以具有或不具有共同进化起源的核酸分子的不同核苷酸序列或多肽的氨基酸序列之间的同一性或对应性程度(参见Reeck等,同上)。序列同一性可以使用大量可公开获得的序列比较算法例如BLAST、FASTA、DNA Strider、GCG (Genetics Computer Group,《GCG软件包程序手册》(Program Manual for the GCG Package),第7版,Madison,Wisconsin)等中的任一者来确定。

[0077] 为了确定两个氨基酸序列或两个核酸分子之间的百分同一性,出于最佳比较的目的将所述序列对齐。所述两个序列之间的百分同一性是所述序列共有的一致位置的数目的函数(即百分同一性=一致位置的数目/位置(例如交叠的位置)的总数x100)。在一个实施方式中,所述两个序列是相同长度或近似相同长度的。两个序列之间的百分同一性可以使用与下面描述的相似的技术,允许或不允许存在间隙来确定。在计算百分序列同一性中,通常对完全匹配进行计数。

[0078] 两个序列之间的百分同一性的确定,可以使用数学算法来实现。用于两个序列的比較的数学算法的非限制性实例是Karlin和Altschul,Proc.Natl.Acad.Sci.USA 1990,87:2264的算法,如在Karlin和Altschul,Proc.Natl.Acad.Sci.USA 1993,90:5873-5877中那样修改。这种算法被并入到Altschul等,J.Mol.Biol.1990;215:403的NBLAST和XBLAST程序中。BLAST核苷酸搜索可以使用NBLAST程序,计分=100,字长=12来进行,以获得与本发明的序列同源的核苷酸序列。BLAST蛋白质搜索可以使用XBLAST程序,计分=50,字长=3来进行,以获得与本发明的蛋白质序列同源的氨基酸序列。为了获得用于比较目的的带间隙的比对,可以利用如Altschul等,Nucleic Acids Res.1997,25:3389中所描述的Gapped BLAST。或者,可以使用PSI-Blast来进行检测分子之间的远缘关系的迭代搜索。参见

Altschul等,(1997),同上。当利用BLAST、Gapped BLAST和PSI-Blast程序时,可以使用相应程序(例如XBLAST和NBLAST)的缺省参数。参见万维网上的ncbi.nlm.nih.gov/BLAST/。

[0079] 用于序列比较的数学算法的另一个非限制性实例是Myers和Miller,CABIOS 1988;4:11-17的算法。这种算法被并入到ALIGN程序(2.0版)中,所述程序是GCG序列比对软件包的一部分。当利用ALIGN程序来比较氨基酸序列时,可以使用PAM120权重残基表、12的间隙长度罚分和4的间隙罚分。

[0080] 在优选实施方式中,两个氨基酸序列之间的百分同一性使用Needleman和Wunsch的算法(J.Mol.Biol.1970,48:444-453)来确定,所述算法已被并入到GCG软件包中的GAP程序内(Accelrys,Burlington,MA;可以在万维网上的accelrys.com处获得),使用Blossum62矩阵或PAM250矩阵,16、14、12、10、8、6或4的间隙权重和1、2、3、4、5或6的长度权重。在另一个优选实施方式中,两个核苷酸序列之间的百分同一性使用GCG软件包中的GAP程序来确定,使用NWSgapdna.CMP矩阵,40、50、60、70或80的间隙权重和1、2、3、4、5或6的长度权重。特别优选的一套参数(并且如果从业人员不确定应该使用什么参数来确定分子是否在本发明的序列同一性或同源性限度内的话,可以使用的一套参数)是使用Blossum 62计分矩阵,并且间隙开放罚分为12,间隙扩展罚分为4,移码间隙罚分为5。

[0081] 本文中描述的性质的统计分析可以通过标准检验例如t-检验、ANOVA或卡方检验来进行。通常,统计显著性被计算到 $p=0.05$ (5%)、更优选地 $p=0.01$ 、 $p=0.001$ 、 $p=0.0001$ 、 $p=0.000001$ 的水平。

[0082] 也可以提供结构域序列的“保守修饰的变体”。对于特定核酸序列来说,保守修饰的变体是指编码一致或基本上一致的氨基酸序列的核酸,或者在所述核酸不编码氨基酸序列的情况下,是指基本上一致的序列。具体来说,简并密码子替换可以通过产生其中一个或多个选定(或所有)密码子的第三个位置被混合碱基和/或脱氧肌苷残基替换的序列来实现(Batzer等,1991,Nucleic Acids Res.19:5081;Ohtsuka等,1985,J.Biol.Chem.260:2605-2608;Rossolini等,1994,Mol.Cell.Probes 8:91-98)。

[0083] 术语野生型蛋白的“生物活性片段”、“生物活性形式”、“生物活性等同物”和“功能性衍生物”,具有当使用适合于检测下述生物活性的测定法测量时至少基本上等于(例如不显著不同于)所述野生型蛋白的生物活性的生物活性。例如,包含转运结构域的生物活性片段是可以与包含所述转运结构域的全长多肽共定位到相同区室的片段。

[0084] 当在本文中使用时,“体内”核酸递送、核酸转移、核酸疗法等,是指将包含外源多核苷酸的载体直接引入到生物体例如人类或非人类哺乳动物的身体中,由此将所述外源多核苷酸引入到这种生物体体内的细胞中。

[0085] 当在本文中使用时,术语“原位”是指一种类型的体内核酸递送,其中将所述核酸带到靶细胞附近(例如所述核酸不被系统性给药)。例如,原位递送方法包括但不限于将核酸直接注射在位点处(例如到组织例如肿瘤或心肌中),通过开放手术部位将所述核酸与细胞或组织接触,或使用医疗接入装置例如导管将所述核酸递送到位点。

[0086] 当在本文中使用时,术语“分离的”意味着与所述多核苷酸、肽、多肽、蛋白质、抗体或其片段在自然界中通常缔合的细胞组分或其他组分分开。例如,对于多核苷酸来说,分离的多核苷酸是与通常在染色体中与其缔合的5'和3'序列分开的多核苷酸。正如对本领域技术人员来说显而易见的,非天然存在的多核苷酸、肽、多肽、蛋白质、抗体或其片段不需要

“分离”以将它与它的天然存在的对应物区分开。

[0087] 当在本文中使用时,“靶细胞”或“受体细胞”是指个体细胞或期望成为或已经成为外源核酸分子、多核苷酸和/或蛋白质的受体的细胞。该术语旨在也包括单个细胞的后代,并且所述后代由于天然、偶然或故意的突变,可以不必定与原始亲代细胞完全一致(在形态或基因组或整套DNA上)。靶细胞可以与其他细胞相接触(例如在组织中),或者可能被发现在生物体的身体内循环。

[0088] 当在本文中使用时,“对象”是脊椎动物,优选为哺乳动物,更优选为人类。哺乳动物包括但不限于鼠类、猿猴类、人类、家畜、运动动物(sport animal)和宠物。在其他优选实施方式中,所述“对象”是啮齿动物(例如豚鼠、仓鼠、大鼠、小鼠)、鼠科动物(例如小鼠)、犬科动物(例如狗)、猫科动物(例如猫)、马科动物(例如马)、灵长动物、猿猴(例如猴或猿)、猴(例如狨猴、狒狒)或猿(例如大猩猩、黑猩猩、猩猩、长臂猿)。在其他实施方式中,可以使用非人类哺乳动物,特别是常规作为模型用于证实在人类中的治疗效能的哺乳动物(例如鼠科动物、灵长动物、猪科动物、犬科动物或兔类动物)。

[0089] 当在本文中使用时,术语“可药用载体”涵盖了任何标准制药载体,例如磷酸盐缓冲盐水溶液、水和乳液例如油/水或水/油乳液,和各种不同类型的润湿剂。所述组合物还可以包括稳定剂和防腐剂。对于载体、稳定剂和佐剂的实例,参见Martin Remington's Pharm.Sci.第15版(Mack Publ.Co.,Easton(1975))。).

[0090] 当外源或异源核酸已被引入到细胞内部时,所述细胞已被这些核酸“转化”、“转导”或“转染”。转化DNA可以与或不与构成细胞基因组的染色体DNA整合(共价连接)。例如,在原核生物、酵母和哺乳动物细胞中,所述转化DNA可以维持在游离体元件例如质粒上。在真核细胞中,稳定转化的细胞是其中所述转化DNA已整合在染色体中的细胞,使得它通过染色体复制被子细胞继承。这种稳定性由所述真核细胞建立包含含有所述转化DNA的子细胞群体的细胞系或克隆的能力所证实。“克隆”是通过有丝分裂从单一细胞或共同祖产生的细胞群体。“细胞系”是能够在体外稳定生长许多代(例如至少约10代)的原代细胞的克隆。

[0091] 当在本文中使用时,“有效量”是足以实现有益或所需结果的量,例如核酸转化和/或表达和/或达到所需治疗终点的有效量。有效量可以在一次或多次给药、施用或剂量中给药。在一种情况下,核酸递送载体的有效量是足以在包含至少两个细胞的细胞群体中转化/转导/转染至少一个细胞的量。

[0092] 当在本文中使用时,“治疗有效量”在本文中用于表示足以防止、校正异常的生理响应和/或使异常的生理响应正常化的量。在一种情况下,“治疗有效量”是足以将例如疾病的临床显著特征例如抗体产生、细胞因子产生、发热或白细胞计数或组胺水平降低至少约30%、更优选地至少50%、最优选地至少90%的最。

[0093] 当在本文中使用时,在过敏症免疫疗法、过敏症治疗的背景中的术语“预防”或描述被设计用于过敏症患者的干预的其他术语,意味着在至少20%的所有患者中预防IgE应答。术语“预防”不意味着在所有患者中完全阻止IgE介导的疾病的发生,并且这种定义在用于通过减轻过敏症状的机制治疗过敏症的本发明的范围之外,并且与所述术语在本领域中的使用不一致。过敏症免疫疗法领域的技术人员公知,过敏症治疗不是在100%的患者中100%有效的,因此在本发明的情形中“预防”的绝对定义并不适用。本发明考虑本领域中公认的预防的概念。

[0094] 术语“口腔粘膜”给药是指将剂型置于舌下或口腔中任何其他地方以允许活性成分与患者的口腔或咽部的粘膜发生接触,以便获得所述活性成分的局部或系统性效应的给药途径。口腔粘膜给药途径的实例是舌下给药。术语“舌下给药”是指将剂型置于舌下以便获得活性成分的局部或系统性效应的给药途径。当在本文中使用时,术语“真皮内递送”意味着将疫苗递送到皮肤中的真皮。然而,所述疫苗不必定仅仅位于真皮中。在人类皮肤中,真皮是皮肤中位于距表面约1.0至约2.0mm之间的层,但在个体之间和身体的不同部分中存在一定量的变差。通常,通过进入皮肤表面之下1.5mm,可以预期到达真皮。真皮位于表面处的角质层和表皮与下方的皮下组织层之间。取决于给药方式,疫苗最终可以仅仅或主要位于真皮内,或者它最终可以分布在表皮和真皮内。

[0095] “抗体”是结合特定表位的任何免疫球蛋白,包括抗体及其片段。所述术语涵盖了多克隆、单克隆和嵌合抗体(例如双特异性抗体)。“抗体结合部位”是抗体分子的包含特异性结合抗原的重链和轻链可变和高变区的结构部分。示例性的抗体分子是完整免疫球蛋白分子、基本上完整的免疫球蛋白分子和免疫球蛋白分子的含有补位的那些部分,包括Fab、Fab'、F(ab')₂和F(v)部分,所述部分优选用于本文描述的治疗方法中。

[0096] “表位”是通常由短的肽序列或寡糖构成,被免疫系统的组分特异性识别或特异性结合的结构。通常已显示T-细胞表位是直链寡肽。两个表位,如果它们可以被同一抗体特异性结合,则彼此对应。两个表位,如果两者都能结合到相同的B细胞受体或相同的T细胞受体,并且一个抗体与其表位的结合基本上阻止了被另一个表位结合(例如低于约30%、优选地低于约20%、更优选地低于约10%、5%、1%或约0.1%的另一个表位结合),则两个表位彼此对应。在本发明中,可以将多种过敏原X组合以构成过敏原X抗原(参见例如SEQ ID NO: 11、21、27、109和110)。

[0097] 当在本文中使用时,术语“抗原性材料”覆盖了引发先天性或适应性免疫应答的任何物质。

[0098] 当在本文中使用时,术语“抗原呈递细胞”包括在表面上呈递与主要组织相容性复合物分子或其部分或一种或多种非经典MHC分子或其部分相结合的抗原的任何细胞。适合的APC的实例在下文中详细讨论,并且包括但不限于完整细胞例如巨噬细胞、树突状细胞、B细胞、杂交APC和培养的抗原呈递细胞。

[0099] 当在本文中使用时,“工程化改造的抗原呈递细胞”是指在其表面上具有非天然分子组成部分的抗原呈递细胞。例如,这种细胞可以在其表面上不天然具有辅助刺激分子,或者在其表面上除了天然辅助刺激分子之外可以还具有另外的人工辅助刺激分子,或者可能在其表面上表达非天然的II类分子。在优选实施方式中,所述工程化改造的抗原呈递细胞在其表面上具有一个或多个过敏原X。

[0100] 当在本文中使用时,“免疫效应细胞”是指能够结合抗原并介导免疫应答的细胞。这些细胞包括但不限于T细胞、B细胞、单核细胞、巨噬细胞、NK细胞和细胞毒性T淋巴细胞(CTL),例如CTL细胞系、CTL克隆和来自于肿瘤、炎性或其他浸润物的CTL。

[0101] 细胞的“分离”或“纯化”的群体是基本上不含天然与其相伴的细胞和材料的细胞群体。基本上游离或基本上纯化的APC,意味着至少50%的所述群体是APC,优选地至少70%、更优选地至少80%、甚至更优选地至少90%不含天然与它们相伴的非APC细胞。

[0102] 当在本文中使用时,“遗传修饰”是指对细胞的正常核苷酸的任何添加、缺失或破

坏。可以实现APC的遗传修饰的任何方法都在本发明的精神和范围之内。本领域公认的方法包括病毒介导的基因转移、脂质体介导的转移、转化、转染和转导,例如病毒介导的基因转移如使用基于DNA病毒例如腺病毒、腺相关病毒和疱疹病毒的载体以及基于反转录病毒的载体。

[0103] 除非另有指明,否则本发明的实践利用在本领域技术范围内的常规分子生物学、微生物学和重组DNA技术。这些技术在文献中充分解释。参见例如Maniatis,Fritsch& Sambrook,《分子克隆实验指南》(Molecular Cloning:A Laboratory Manual) (1982);《DNA克隆实用方法》(DNA Cloning:A Practical Approach),第I和II卷(D.N.Clover主编,1985);《寡核苷酸合成》(Oligonucleotide Synthesis) (M.J.Gait主编,1984);《核酸杂交》(Nucleic Acid Hybridization) (B.D.Hames&S.J.Higgins主编,1985);《转录和翻译》(Transcription and Translation) (B.D.Hames&S.I.Higgins主编,1984);《动物细胞培养》(Animal Cell Culture) (R.I.Freshney主编,1986);《固定化细胞和酶》(Immobilized Cells and Enzymes) (IRL Press,1986);B.Perbal,《分子克隆实用指南》(A Practical Guide to Molecular Cloning) (1984)。

[0104] 过敏原X的抗原序列

[0105] 本发明提供了针对过敏原X的聚核酸、聚氨基酸、宿主细胞、载体,和治疗需要这些聚核酸、聚氨基酸、宿主细胞或载体的对象的方法。广义来说,所述聚核酸可以被认为是用于过敏原性序列(聚氨基酸)的细胞内产生的核酸(例如DNA、RNA)疫苗,其在所述聚核酸给药至的对象体内引发保护性免疫应答。所述聚核酸在给药时,偏好性地通过MHC-II途径唤起细胞介导的免疫应答,并通过由APC、NK细胞和T细胞产生的干扰素激活过敏原特异性T辅助性细胞1型(Th1)细胞应答而不是涉及IgE抗体、粒细胞(例如嗜曙红细胞)和其他物质的产生的Th2型应答,来生产IgG抗体。在某种程度上,可以产生MHC-II和MHC-I应答两者;然而,本发明提供了主要或基本上是MHC-II应答的应答。优选地,所述核酸不编码抗生素抗性基因。

[0106] 本发明至少部分基于下述认识,即某些结构性以及因此功能性元件的组合为核酸疫苗和被编码的过敏原提供了有利性质,并允许满足本领域中未满足需求的过敏症治疗方法。在旨在被理解为单独作为独立实施方式和作为合并了所述独立实施方式的两种或更多种特征的实施方式的本发明的各种不同实施方式中,所述组合包括使用溶酶体转运结构域将过敏原X导向具有MHC II蛋白的溶酶体。这样做允许针对过敏原X的主要是IgG应答而不是IgE应答。此外,独立实施方式或实施方式的组合提供了含有足够长度的核酸序列(例如全长核酸序列或其片段、全长核酸序列的变体或其片段等)的构建物,以编码提供表位的天然存在的三维结构的氨基酸序列。在优选实施方式中,所述核酸序列编码过敏原X (SEQ ID NO:Y)。在其他实施方式中,所述核酸序列编码至少一种过敏原X。尽管在本领域中公认免疫应答可以针对表位的主要序列产生,但本发明认识到用于产生针对所编码表位的MHC-II免疫应答的核酸疫苗优选地使用编码足够序列数据的核酸构建物,以至少在过敏原X被递送到溶酶体进行加工时在包含过敏原X的区域中产生正确的三维肽结构。尽管不受任何特定分子理论限制,但据信三维折叠正确的蛋白质、多肽或肽向胞内体的递送改善了用于免疫应答的过敏原性表位的加工和呈递。

[0107] 因此,本发明提供了包含过敏原X和多肽的腔内序列的嵌合体,所述腔内序列引起

所述嵌合体转运到胞内体/溶酶体区室,用于抗原加工和抗原表位与MHC II的结合。在一种情况下,所述嵌合蛋白另外包含将所述嵌合体导向胞内体/溶酶体区室的胞质靶向序列。另外,所述嵌合蛋白也可以包含信号序列和/或跨膜序列。适合的转运结构域由LAMP-1、LAMP-2、DC-LAMP、Trp-1、DEC-205、gp200-MR6和如下文所讨论的其他多肽提供。所述信号序列和跨膜序列可以但不是必须来自于这些多肽。然而,在一种情况下,抗原/LAMP嵌合体包含全长LAMP多肽。

[0108] 过敏原X可用于产生嵌合蛋白。在一种情况下,优选的组合物包含如表1中所示的SEQ ID NO:Y中任一者的过敏原X的氨基酸序列,或编码SEQ ID NO:Y中的任一者的多核苷酸。可以编码过敏原X的多核苷酸的优选的代表性实例在表1中被显示为SEQ ID NO:Z。其他优选的代表性实施方式是包含过敏原X以及人类、鼠类或犬类LAMP序列的构建物(参见例如SEQ ID NO:W和SEQ ID NO:V)。如实施例中的表3中所述,令人吃惊地发现包含对应于SEQ ID NO:Y的特定过敏原X氨基酸序列的嵌合LAMP疫苗与试验的其他构建物相比产生出人意料地强健的免疫应答。

[0109] 过敏原X也可以包括过敏原X变体。例如,优选实施方式包括与SEQ ID NO:Y具有至少约60%、至少约70%、至少约75%、至少约80%、至少约85%、至少约90%、至少约95%、96%、97%、98%或99%同一性的过敏原X多肽变体。这些变体保留了(a)产生与它所源自的过敏原X发生交叉反应的抗体的能力,和/或(b)过敏原X生物活性。特别考虑了编码这些多肽的多核苷酸。

[0110] 合成的过敏原X抗原和改变的过敏原X抗原也可用于本文中描述的方法。合成的抗原性过敏原X肽表位相对于天然过敏原X序列具有修饰的氨基酸序列。术语“合成的过敏原X抗原性肽”还涵盖合成的抗原性过敏原X肽的多聚体(串联体),任选地包括居间的氨基酸序列。例如,本发明的合成的过敏原X抗原性肽表位可以在抗原性过敏原X肽表位的已知氨基酸序列的基础上设计。

[0111] 在本发明的范围内还包括在翻译期间或之后被不同修饰的抗原性过敏原X肽,例如通过磷酸化、糖基化、交联、酰化、蛋白水解切割、连接到抗体分子、膜分子或其他配体(Ferguson等,Ann.Rev.Biochem.57:285-320,1998)。

[0112] 分离的过敏原X肽可以使用适合的固相合成程序来合成(Steward和Young,《固相肽合成》(Solid Phase Peptide Synthesis),Freemantle,San Francisco,Calif.1968)。优选的方法是Merrifield方法(Merrifield,Recent Progress in Hormone Res.23:451,1967)。这些肽的过敏原X抗原性活性可以方便地使用例如本文中描述的测定法来测试。

[0113] 在获得分离的过敏原X肽后,它可以通过标准方法包括层析(例如离子交换、亲和和尺寸排阻柱层析)、离心、差异溶解度或通过用于蛋白质纯化的任何其他标准技术来纯化。对于免疫亲和层析来说,过敏原X表位可以通过将它结合到包含抗体的亲和柱来分离,所述抗体针对该肽或相关肽产生并被缀合到固定支持物。或者,可以将亲和标签例如六His(Invitrogen)、麦芽糖结合结构域(New England Biolabs)、流感病毒外壳蛋白序列(Kolodziej等,Methods Enzymol.194:508-509,1991)和谷胱甘肽-S-转移酶附连到所述肽,以允许经由在适合的亲和柱上通过而容易地纯化。分离的过敏原X肽也可以使用诸如蛋白水解、核磁共振和x-射线晶体学的技术进行物理表征。

[0114] 已经分离并鉴定所需表位的过敏原X肽序列后,包含编码这些表位的序列的核酸

可以被容易地测序。

[0115] 胞内体转运序列

[0116] 可以获得的数据表明在II类MHC分子的细胞内运输中的下述一系列事件:具有恒定链的II类MHC分子在内质网中被组装并与其他膜蛋白包括I类MHC一起被运输通过高尔基体。所述分子然后通过未知机制靶向到特定胞内体/溶酶体细胞器,与遵循组成性途径到达细胞表面的I类MHC分子分离开。在所述胞内体/溶酶体途径中,所述恒定链被在酸性环境中起作用的蛋白酶从II类MHC移除。同时,蛋白质的已经进入胞内体/溶酶体途径的抗原性片段被这些蛋白酶产生,得到的肽结合到所述II类分子并被携带到细胞表面。

[0117] 存在于溶酶体/胞内体区室中的水解酶类的生物合成和囊泡靶向机制已被广泛研究(Kornfeld和Mellman,Ann.Rev.Cell Biol.5:483,1989)。高尔基体中新合成的水解酶获得甘露糖6-磷酸基团,其充当特异性识别标志物用于将这些酶结合到甘露糖6-磷酸受体,其然后以某种未知方式靶向到前溶酶体囊泡。在那里所述受体-酶复合物被低pH解离,所述受体再循环到高尔基体,而含有酶的囊泡成熟成溶酶体。

[0118] 溶酶体膜糖蛋白的定位受到独立于明确确定的用于水解性溶酶体酶的甘露糖6-磷酸受体(MPR)途径的靶向机制控制(Kornfeld和Mellman,1989,同上)。最近的研究描述了一种独特的囊泡区室,其具有溶酶体性质,并以高浓度的溶酶体相关膜蛋白(LAMP-1)和II类MHC分子为特征(Peters等,EMBO J.9:3497,1990)。新合成的LAMP-1和其他类似蛋白的分子内运输和靶向的溶酶体/胞内体区室动力学分析表明,所述分子在内质网中合成,在高尔基体潴泡中加工,并在其生物合成的1小时内运输到溶酶体,在质膜中没有可检测的积累(Barriocanal等,J Biol.Chem.15:261(35):16755-63,1986;D'Sousa等,Arch.Biochem.Biophys.249:522,1986;Green等,J.Cell Biol.,105:1227,1987)。

[0119] 溶酶体膜的结构和功能的研究始于1981年August及其同事发现了由于主要位于溶酶体膜中而在随后被称为溶酶体相关膜蛋白1和2(LAMP-1和LAMP-2)的重要细胞糖蛋白(Hughes等,J.Biol.Chem.256:664,1981;Chen等,J.Cell Biol.101:85,1985)。随后在大鼠、鸡和人类细胞中鉴定到类似的蛋白质(Barriocanal等,1986,同上;Lewis等,J.Cell Biol.100:1839,1985;Fambourgh等,J.Cell Biol.106:61,1988;Mane等,Arch.Biochem.Biophys.268:360,1989)。

[0120] 通常,正如从cDNA克隆所推演的(Chen等,J.Biol.Chem.263:8754,1988),LAMP-1由约382个氨基酸的多肽核心构成,具有大的(346个残基)腔内氨基端结构域,然后是24个残基的疏水性跨膜区和短的(12个残基)羧基端胞质尾区。参见图2和3。所述腔内结构域被高度糖基化,被约20个天冬酰胺连接的复合体类型的寡糖取代,并由被富含脯氨酸/丝氨酸的区域分隔开的2至约160个残基的同源性单元构成。每个这些同源结构域含有4个均匀间隔的半胱氨酸残基,二硫键合形成4个36-38个残基的环,其对称地位于腔内结构域的两半之内(Arterburn等,J.Biol.Chem.265:7419,1990;也参见Chen等,J.Biol.Chem.25:263(18):8754-8,1988)。LAMP-2分子在总体氨基酸序列上与LAMP-1高度相似(Cha等,J.Biol.Chem.265:5008,1990)。

[0121] LAMP-1和LAMP-2不特异性存在于抗原呈递细胞(树突状细胞)中。它们的准确功能是未知的,但推测它们以某种方式参与溶酶体功能。它们与MHC II在APC的多层MIIC囊泡区室中的共定位没有已知的与抗原加工或呈递的功能关联;然而,如上所讨论的包含LAMP胞

质结构域的嵌合抗原显示出增强的免疫原性(参见美国专利号5,633,234)。

[0122] 本发明提供了包含溶酶体相关膜蛋白的腔内结构域例如LAMP多肽或其生物活性片段或修饰形式(合称为“LAMP-腔内结构域”)的嵌合过敏原X蛋白。在一种情况下,所述LAMP腔内结构域包含至少两个同源性单元。优选地,每个同源性单元被富含脯氨酸/丝氨酸的区域分隔开。更优选地,每个同源结构域包含4个半胱氨酸残基,其在二硫键键合在一起时能够形成对称位于所述腔内结构域的两半之内的四个36-38个残基的环。最优选地,所述腔内结构域包含将它所连接(例如通过化学键)的多肽靶向并运输到胞内体/溶酶体区室或溶酶体相关细胞器所必需的序列,用于将所述多肽结合到II类MHC分子或递送到另一个区室/细胞器,在那里它结合到II类MHC分子。

[0123] 在优选实施方式中,可以在本发明中使用的LAMP-1的腔内结构域部分包括但不限于SEQ ID NO:2或3或SEQ ID NO:4的第29-381位氨基酸(或SEQ ID NO:5的相应序列)。在更优选实施方式中,LAMP-1的跨膜结构域/胞质尾区可用于本发明。例如,SEQ ID NO:1或SEQ ID NO:4的第382-417位氨基酸(或SEQ ID NO:5的相应序列)可用于本文中描述的嵌合疫苗中。此外,可以使用腔内结构域片段与跨膜结构域/胞质尾区片段的任何组合。

[0124] 在另一种情况下,所述嵌合蛋白附加性地或可替代地包含基于二亮氨酸的信号,所述信号包含至少一个亮氨酸-亮氨酸对或至少一个亮氨酸/异亮氨酸对。优选地,所述蛋白质在所述对的上游4-5个残基处包含酸性残基。更优选地,该信号结构域结合到AP复合多肽(参见例如Bonafacino和Dell'Angelica, J. Cell Biol. 145:923-926, 1999)。适合的基于二亮氨酸的结构域可以在例如酪氨酸酶(TM-X₁₀-EKQPLL-X₅-YHSL-X_S)(SEQ ID NO:97)、TRP-2(TM-X₇-EANQPLL-X₁₂)(SEQ ID NO:98)和Pme17(TM-X₃₄-ENSPLL-X₅)(SEQ ID NO:99)和P蛋白(参见例如Dell'Angelica, 2000, 同上)中找到。

[0125] 在优选情况下,所述嵌合蛋白还包含用于将嵌合过敏原X蛋白靶向和/或转运到胞内体/溶酶体区室或溶酶体相关细胞器的胞质结构域。在一种情况下,所述胞质结构域包含LAMP多肽的尾区。LAMP-1和其他相似的溶酶体膜糖蛋白的胞质尾区的11个氨基酸的序列具有下述序列:Arg-Lys-Arg-Ser-His-Ala-Gly-Tyr-Gln-Thr-Ile-COOH(Chen等, 1988, 同上)(SEQ ID NO:1的第25-35位残基)。在LAMP-1中,这些序列来自于全长多肽的第372-382位氨基酸。

[0126] 在表2中,已将溶酶体膜蛋白LAMP-1(Chen等, 1988, 同上)、LAMP-2(Cha等, 1990, 同上)和CD63(Hotta等, Cancer Res. 48:2955, 1988)的已知的胞质尾区序列与LAP的胞质尾区中含有Tyr的内化信号(Pohlman等, EMBO J. 7:2343, 1988)比对。已知所述Tyr残基为胞内体/溶酶体靶向所需,并且在美国专利号5,633,234中证实了将其他分子靶向溶酶体所需的完整序列需要Tyr-X-X-hyd序列(即“Tyr”基序),Tyr后面跟有两个氨基酸,随后是疏水性残基。

表2	
主要溶酶体膜蛋白的胞质尾区序列*	
[0127] LAMP-1	RKRSHA <u>GYQTI</u> (SEQ ID NO: 1的第25-35位残基)
LAMP-2	KHHHA <u>GYEQF</u> (SEQ ID NO: 100)
CD63	KSIRS <u>GVEVM</u> (SEQ ID NO: 101)
LAP	RMEAPP <u>GYRHVADGEDHA</u> (SEQ ID NO: 102)

[0128] *所描述的溶酶体膜蛋白的胞质结构域中保守的Gly-Tyr-X-X-疏水性残基基序被加上下划线,其中X是任何氨基酸。所述列出的蛋白质的完整的胞质尾区序列显示为从跨膜区到羧基端。

[0129] 从LAMP-1的Tyr-Gln-Thr-Ile序列(SEQ ID NO:1的第32-35位残基)的修饰获得的结果,显示了在羧基端位置处或附近的疏水性残基的重要性。在突变的cDNA分子中Ile被两个其他疏水性残基Leu或Phe和极性残基Thr替换。替换的Leu(Tyr-Gln-Thr-Leu)(SEQ ID NO:103)和Phe(Tyr-Gln-Thr-Phe)(SEQ ID NO:104)不影响溶酶体靶向,而含有Thr的突变蛋白(Tyr-Gln-Thr-Thr)(SEQ ID NO:105)在细胞表面处积累。含有Ala替换Gln(Tyr-Ala-Thr-Ile)(SEQ ID NO:106)、Thr(Tyr-Gln-Ala-Ile)(SEQ ID NO:107)和这两个残基(Tyr-Ala-Ala-Ile)(SEQ ID NO:108)的突变体对靶向到溶酶体膜没有影响,表明这些位置可以被带电荷、极性或非极性残基占据。

[0130] 因此,向溶酶体/胞内体区室的优选的靶向信号包括位于胞质结构域中靠近跨膜结构域并且也靠近C-端的四肽序列。胞质结构域优选为末端为游离羧基的短氨基酸序列(少于70个氨基酸,优选地少于30个氨基酸,最优选地少于20个氨基酸)。在更优选实施方式中,所述四肽在含有靶向信号的短胞质尾区的C-末端处,或处于与LAMP-1类似的背景中。

[0131] 适合于所述四肽的四氨基酸序列可以通过氨基酸替换来获得,只要所述基序由Tyr-X-X-Hyd(其中X可以是任何氨基酸并且Hyd表示疏水性氨基酸)构成,并且提供溶酶体/胞内体靶向的能力得以保留即可。特别优选的四肽具有序列Tyr-Gln-Thr-Ile(SEQ ID NO:1的第32-35位残基)。在所述最优选实施方式中,整个LAMP胞质尾区与其跨膜结构域结合,以及最优选地其腔内结构域,被偶联到抗原性结构域的一级序列,用于高效II类MHC加工和呈递。然而,所述胞质结构域不必促进转运,只要提供LAMP多肽的腔内结构域即可。

[0132] 在另一种情况下,所述胞内体靶向结构域包含跨膜序列。充当用于特定免疫刺激性构建物的抗原性结构域的来源的许多蛋白质是在其一级序列中包括跨膜结构域的表面抗原。这种跨膜结构域可以被保留,并且将胞质结构域用本文中所教导的溶酶体/胞内体靶向结构域(例如包含LAMP腔内结构域的结构域)代替。

[0133] 在一种优选情况下,将LAMP的跨膜结构域(参见Chen等,J.Biol.Chem.263:8754,1988)偶联到所述过敏原X来源的多肽的一级序列和所述腔内结构域的序列。多肽中跨膜结构域的结构在本领域中是已知的(参见例如Bangham,Anal.Biochem.174:142,1988;Klein等,Biochem.Biophys.Acta 815:468,1985;Kyle&Doolittle,J.Mol.Biol.157:105,1982)。

通常,所述跨膜区在一级序列中作为侧接有亲水性区域的20-25个疏水性氨基酸残基的序列出现。这些序列可以例如在Genbank列出的大多数细胞表面抗原序列以及许多其他膜蛋白中发现。具体的跨膜序列并不关键,只要它起到将抗原性结构域连接到腔内结构域和胞质尾区的作用并将所述构建物锚定在膜区室中即可。

[0134] 附加性的或可替选的分拣基序可以包括但不限于下述一者或多者:靶向结构域,如上所述的酪氨酸基序结构域;基于二亮氨酸和酪氨酸的结构域;富含脯氨酸的结构域;和S-V-V结构域(参见例如Blott和Griffitts, *Nature* 3:122-131, 2002)。

[0135] 吞饮受体序列

[0136] 抗原进入到抗原呈递细胞例如树突状细胞的MHC II囊泡区室,通常通过外来抗原的胞吞来进行。吞饮受体的转运结构域可用于产生嵌合多肽,以将过敏原X携带到胞内体/溶酶体区室或溶酶体相关细胞器,用于与II类MHC分子结合并进一步加工。

[0137] 因此,在一种情况下,本发明提供了至少一种连接到吞饮受体的转运结构域的过敏原X(例如通过编码转运结构域和抗原的核酸序列的框内融合)。所述转运结构域将过敏原X定位到胞内体/溶酶体区室或溶酶体相关细胞器,用于与所述区室/细胞器中的或过敏原X被递送到的后续区室中的II类MHC分子结合。

[0138] 符合本发明的吞饮受体包括但不限于用于微生物的受体, Fc受体(例如CD64、CD32、CD16、CD23和CD89), 补体受体(例如CR1或CD35、CR3、CR4), 清除剂受体或结合到乙酰化或修饰的脂蛋白、多核糖核苷酸、脂多糖和二氧化硅粒子的受体(例如SRA、MARCO), 整合蛋白(CD49e/CD29、CD49d/CD29、CD51/CD61), 凝集素类(例如dectin-1、C-型凝集素等), 和Toll样受体(例如TLR)。对于这些受体的综述, 参见例如Underhill和Ozinsky, *Annu. Rev. Immunol.* 20:825-52, 2002。

[0139] 在一种情况下,所述吞饮受体从专业的抗原呈递细胞例如树突状细胞获得。已经鉴定到大量树突状细胞的吞饮受体,包括巨噬细胞甘露糖受体(MMR)、磷脂酶A₂受体、Endo180和DEC-205及其人类同源物、gp200-MR6(McKay等, 1998)。DEC-205据报道不同于MMR,至少在于它将抗原性材料靶向胞内体/溶酶体区室,与LAMP和MHC II共定位,而MMR存在于缺少LAMP和MHC II的外周胞内体中(Mahnke等, *J. Cell Biol.* 151(3):673-684, 2000)。

[0140] 与MMR相比,DEC-205也表现出被胞吞抗原向CD4⁺T细胞的呈递的极大加强。所述两种分子之间的这种向MHC II的转运和抗原递送的差异,据报道是由于在DEC-205的胞质尾区中除了被膜小窝摄入序列之外还存在EDE三联体,而在MMR中缺少所述EDE三联体。据显示,所述胞质尾区的含有EDE序列的远端部分对于靶向含有LAMP和MHC II的较深胞内体/溶酶体区室而言是必需的,并且EDE不被AAA序列代替。Mahnke等, 2000, 同上, 也显示,这些胞质尾区转运信号足以将CD16嵌合体转运并再循环到MHC II/LAMP位点,并介导抗原呈递的100倍增加。

[0141] DEC-205与gp200-MR6之间的序列相似性,特别是在胞质结构域中,使得该序列也是适合的转运序列。此外,已显示gp200-MR6具有IL-4调控的其他重要性质。McKay等, *Eur J Immunol.* 28(12):4071-83, 1998显示, gp200-MR6的连接可以模拟IL-4并在免疫系统内具有抗增殖、促成熟的影响,引起B淋巴细胞上辅助刺激分子的上调。

[0142] 然而,DEC-205与LAMP的融合体不转移到胞内体区室而是定位到细胞表面。然而,合并了LAMP结构域和至少一个过敏原X和吞饮受体结构域例如DEC-205结构域的嵌合蛋白,

能够转运到胞内体区室,与内源LAMP共定位。

[0143] 因此,在优选情况下,本发明的嵌合过敏原X蛋白包含溶酶体膜多肽的腔内结构域(例如LAMP腔内结构域)和吞饮受体的靶向结构域(例如DEC-205或gp 200-MR6多肽)。这些构建物可以不仅显示出正确的靶向,而且显示出提高的抗原性。另一方面,吞饮受体的靶向和转运结构域两者与至少一种过敏原X一起提供。嵌合过敏原X蛋白可以附加性地或可替代地包含吞饮受体的腔内结构域。在另一种情况下,嵌合蛋白可以包含全长吞饮受体多肽以及至少一种过敏原X。

[0144] 在一种情况下,所述吞饮受体的靶向结构域包含DEC多肽的31个氨基酸的胞质结构域(参见例如Manhke等,2000,同上)。在另一种情况下,所述靶向结构域包含DEC-205胞质尾区的第7-9位残基。优选地,所述结构域包含Tyr基序。更优选地,所述靶向结构域还包含DEC-205胞质尾区的第18-27位残基。另一方面,所述靶向结构域包含EDE结构域。DEC-205的序列提供在Kato等,Immunogenetics 47 (6):442-50,1998中,而gp200-MR6的序列提供在例如McKay等,1998,同上中。

[0145] 所述嵌合过敏原X蛋白可以另外包含用于将至少一种过敏原X靶向胞内体/溶酶体区室或溶酶体相关细胞器的胞质靶向结构域(例如胞质LAMP结构域),以及一种或多种上文描述的其他结构域(例如信号序列、跨膜序列等)。如上所述,附加性的或可替代的分拣基序可以包括但不限于下述一者或多者:M6P结构域,酪氨酸基序结构域,基于二亮氨酸和酪氨酸的结构域,富含脯氨酸的结构域;和S-V-V结构域(参见例如Blott和Griffiths,Nature 3:122-131,2002)。

[0146] 疫苗组合物

[0147] 尽管已假设大量抗原能够与LAMP组合以产生新的嵌合疫苗,但在实际中在试验时,这些疫苗不总是起作用。

[0148] 因此,本发明提供了一种用于在哺乳动物中引发针对过敏原X的免疫应答的疫苗组合物。所述组合物包含疫苗载体,其包括含有编码至少一种过敏原X(SEQ ID NO:Y)的序列的嵌合DNA区段。优选地,所述DNA区段还包括编码溶酶体结合性膜多肽的腔内结构域(例如LAMP多肽(例如SEQ ID NO:2、3、4或5)、其同源物、直系同源物、变体或修饰形式)或吞饮受体的转运结构域的序列。优选地,所述腔内结构域或转运结构域将所述抗原转运到细胞的胞内体/溶酶体区室或溶酶体相关细胞器,在那里它结合到II类MHC分子或被加工以递送到另一个区室/细胞器,它随后在那里结合到II类MHC分子。更优选地,过敏原X在所述区室/细胞器(或它被递送到的后续区室)中被加工,以产生在细胞表面上呈递并被结合到II类MHC分子的过敏原X表位。

[0149] 所述载体也可以编码下述一者或多者:跨膜结构域,含有将蛋白质导向胞内体/溶酶体区室或溶酶体相关细胞器的胞内体/溶酶体靶向信号的胞质结构域,二亮氨酸结构域,Tyr基序,富含脯氨酸的结构域和/或S-V-V结构域。

[0150] 所述结构域可以被顺序提供或被编码连接物多肽或编码具有所需功能的其他氨基酸序列(例如蛋白质稳定化序列等)的核酸分隔开。通常,在包含连接物序列的情况下,它们编码范围为约1至约50个氨基酸的连接物多肽。所述载体的最低要求是它编码具有所需转运性质的嵌合过敏原X蛋白。这些性质可以使用本领域中常规的测定法容易地检验。

[0151] 例如,可以使用免疫荧光显微术来确认过敏原X嵌合蛋白向适合的区室/细胞器的

转运。35S甲硫氨酸脉冲追踪标记分析可用于监测过敏原X嵌合蛋白的合成和降解,以证实过敏原X嵌合蛋白的合成速率相比于内源过敏原X蛋白是基本上相等的,和/或所述过敏原X嵌合蛋白的加工正确地发生。

[0152] 在特定实施方式中,由所述嵌合DNA区段编码的蛋白质含有包含作为与II类主要组织相容性复合物(MHC)分子复合的肽的至少一个过敏原X表位的腔内结构域,如上所述的胞内体/溶酶体转运序列和含有胞内体/溶酶体靶向序列的胞质结构域。优选地,所述靶向序列包含四肽序列Tyr-Xaa-Xaa-Xbb,其中Xbb是疏水性氨基酸。

[0153] 在另一种情况下,由所述嵌合DNA区段编码的蛋白包含全长溶酶体膜结合性多肽例如LAMP多肽、其同源物、直系同源物、变体或修饰形式,其包含用于将膜结合和非膜结合的抗原性材料两者靶向和转运到胞内体/溶酶体区室的序列。

[0154] 在优选实施方式中,所述嵌合疫苗包含(a)如表1中所示的SEQ ID NO:Z或SEQ ID NO:W的任一多核苷酸;(b)编码被鉴定为如表1中所示的SEQ ID NO:Z或SEQ ID NO:W的任一多核苷酸所编码的多肽的多核苷酸;(c)编码包含如表1中所示的SEQ ID NO:Y或SEQ ID NO:V的氨基酸序列的多肽的多核苷酸;(d)编码腔内结构域(例如SEQ ID NO:2或3或如SEQ ID NO:4或5中所示)、如表1中所示的一个或多个SEQ ID NO:Y和转运结构域(例如SEQ ID NO:1或如SEQ ID NO:4或5中所示)的多核苷酸;(e)编码腔内结构域(例如SEQ ID NO:2或3或如SEQ ID NO:4或5中所示)和如表1中所示的一个或多个SEQ ID NO:Y的多核苷酸;(f)编码如表1中所示的一个或多个SEQ ID NO:Y和转运结构域(例如SEQ ID NO:1或如SEQ ID NO:4或5中所示)的多核苷酸;或(g)与(a)-(f)的任一多核苷酸具有至少约60%、至少约70%、至少约75%、至少约80%、至少约85%、至少约90%、至少约95%、96%、97%、98%或99%同一性的多核苷酸。

[0155] 编码过敏原X嵌合蛋白的序列的组装

[0156] 用于嵌合蛋白的构建的程序在本领域中是公知的(参见例如Williams等,J.Cell Biol.111:955,1990)。编码所需区段的DNA序列可以从容易获得的重组DNA材料例如可以从美国典型培养物保藏中心(American Type Culture Collection,12301 Parklawn Drive, Rockville,Md.20852,U.S.A.)或从含有所需DNA的DNA文库获得的重组DNA材料来获得。

[0157] 这些DNA区段至少包括:编码来自于所述过敏原X蛋白的抗原性结构域和用于将连接到腔内结构域的多肽转运到胞内体/溶酶体区室或溶酶体相关细胞器的溶酶体膜结合多肽的腔内结构域和/或用于转运到胞内体/溶酶体区室和/或溶酶体相关细胞器的吞饮受体的转运结构域的序列。其他的DNA区段可以包括但不限于编码下述序列的序列:用于将嵌合蛋白靶向到胞内体/溶酶体区室或溶酶体相关细胞器的胞质靶向序列,跨膜序列,信号序列,二亮氨酸序列,Tyr基序,富含脯氨酸的结构域,M6P序列,Ser-Val-Val序列以及克隆序列等。

[0158] 然后使用重组DNA方法的常规程序,将对应于所需结构域序列的DNA区段与适合的控制和信号序列组装。参见例如在美国专利号4,593,002和Langford等,Molec.Cell.Biol.6:3191,1986中所述。

[0159] 编码蛋白质或多肽的DNA序列可以被化学合成或通过几种方法之一被分离。所述待合成的DNA序列可以被设计成具有对所需氨基酸序列适合的密码子。通常,人们将选择对在其中表达所述序列的目标宿主来说优选的密码子。完整序列可以从通过标准方法制备并

组装成完整编码序列的交叠的寡核苷酸组装。参见例如Edge, Nature 292:756, 1981; Nambair等, Science 223:1299, 1984; Jay等, J. Biol. Chem. 259:6311, 1984。

[0160] 在一种情况下, 使用聚合酶链反应单个地分离编码所述嵌合蛋白的结构域序列的一种或多种核酸(M.A. Innis等, 《PCR方案: 方法和应用指南》(PCR Protocols: A Guide to Methods and Applications), Academic Press, 1990)。所述结构域优选地从已知含有它们的可公开获得的克隆分离, 但是它们也可以从基因组DNA或cDNA文库分离。优选地, 分离的片段在边缘具有相容的限制性内切酶位点, 其允许构建编码免疫原性蛋白质序列的嵌合DNA。这种技术对于本领域技术人员来说是公知的。结构域序列可以彼此直接融合(例如没有居间序列)或插入到彼此之中(例如其中结构域序列是不连续的), 或者可以被居间序列(例如连接物序列)分隔开。

[0161] 用于制备寡核苷酸引物、探针和DNA文库以及通过核酸杂交对它们进行筛选的基本策略, 对于本领域技术人员来说是公知的。参见例如Sambrook等, 1989, 同上; Perbal, 1984, 同上。适合的基因组DNA或cDNA文库的构建在本领域的技术范围之内。参见例如Perbal, 1984, 同上。或者, 适合的DNA文库或可公开获得的克隆可以从生物研究材料的供应商例如Clontech和Stratagene获得, 以及从公共保藏处例如美国典型培养物保藏中心(American Type Culture Collection)获得。

[0162] 选择可以通过从DNA的表达文库表达序列并通过免疫学方法检测表达的肽来实现。选择表达结合到MHC II分子并结合到所需抗体/T细胞受体的肽的克隆。这些选择程序对于本领域普通技术人员来说是公知的(参见例如Sambrook等, 1989, 同上)。

[0163] 在含有所需多肽序列的编码序列的克隆被制备或分离后, 可以将所述序列克隆到任何适合的载体中, 所述载体优选地包含用于在宿主细胞中维持所述序列的复制原点。

[0164] 在优选实施方式中, 所述嵌合蛋白由下述多核苷酸编码: (a) 如表1中所示的SEQ ID NO: Z或SEQ ID NO: W的任一多核苷酸; (b) 编码由表1中所示的SEQ ID NO: Z或SEQ ID NO: W的任一多核苷酸所编码的多肽的多核苷酸; (c) 编码包含如表1中所示的SEQ ID NO: Y或SEQ ID NO: V的氨基酸序列的多肽的多核苷酸; (d) 编码腔内结构域(例如SEQ ID NO: 2或3或如SEQ ID NO: 4或5中所示)、如表1中所示的一个或多个SEQ ID NO: Y和转运结构域(例如SEQ ID NO: 1或如SEQ ID NO: 4或5中所示)的多核苷酸; (e) 编码腔内结构域(例如SEQ ID NO: 2或3或如SEQ ID NO: 4或5中所示)和如表1中所示的一个或多个SEQ ID NO: Y的多核苷酸; (f) 编码如表1中所示的一个或多个SEQ ID NO: Y和转运结构域(例如SEQ ID NO: 1或如SEQ ID NO: 4或5中所示)的多核苷酸; 或(g) 与(a) - (f)的任一多核苷酸具有至少约60%、至少约70%、至少约75%、至少约80%、至少约85%、至少约90%、至少约95%、96%、97%、98%或99%同一性的多核苷酸。由这些多核苷酸编码的多肽是另外的优选实施方式。

[0165] 核酸递送媒介

[0166] 在一种情况下, 将编码嵌合疫苗的核酸载体引入到细胞中。所述细胞可以是用于复制所述核酸或用于表达所述嵌合疫苗的宿主细胞。优选地, 所述用于表达嵌合疫苗的宿主细胞是抗原呈递细胞(在下文进一步描述)。

[0167] 所述核酸载体至少包含用于插入到靶细胞中的多核苷酸序列和可操作地连接到所述多核苷酸序列以控制它在所述细胞中的表达(例如转录和/或翻译)的表达控制序列。实例包括质粒、噬菌体、自主复制序列(ARS)、着丝粒和能够在体外或在宿主细胞(例如细

菌、酵母或昆虫细胞)和/或靶细胞(例如哺乳动物细胞、优选为抗原呈递细胞)中复制或复制和/或将所述编码嵌合疫苗的序列传送到靶细胞内的所需位置的其他序列。

[0168] 在优选实施方式中,本文中描述的载体/媒介包含(a)如表1中所示的SEQ ID NO:Z或SEQ ID NO:W的任一多核苷酸;(b)编码由表1中所示的SEQ ID NO:Z或SEQ ID NO:W的任一多核苷酸所编码的多肽的多核苷酸;(c)编码包含如表1中所示的SEQ ID NO:Y或SEQ ID NO:V的氨基酸序列的多肽的多核苷酸;(d)编码腔内结构域(例如SEQ ID NO:2或3或如SEQ ID NO:4或5中所示)、如表1中所示的一个或多个SEQ ID NO:Y和转运结构域(例如SEQ ID NO:1或如SEQ ID NO:4或5中所示)的多核苷酸;(e)编码腔内结构域(例如SEQ ID NO:2或3或如SEQ ID NO:4或5中所示)和如表1中所示的一个或多个SEQ ID NO:Y的多核苷酸;(f)编码如表1中所示的一个或多个SEQ ID NO:Y和转运结构域(例如SEQ ID NO:1或如SEQ ID NO:4或5中所示)的多核苷酸;或(g)与(a)-(f)的任一多核苷酸具有至少约60%、至少约70%、至少约75%、至少约80%、至少约85%、至少约90%、至少约95%、96%、97%、98%或99%同一性的多核苷酸。

[0169] 重组表达载体可以源自于容易感染动物包括人、马、奶牛、猪、美洲驼、长颈鹿、狗、猫或鸡的微生物。优选的载体包括已被用作活疫苗的载体,例如牛痘。这些重组体可以被直接接种到宿主中,不仅提供针对所述微生物载体的免疫力,而且表达外来抗原。本文中设想作为活重组疫苗的优选载体包括RNA病毒、腺病毒、疱疹病毒、脊髓灰质炎病毒和痘苗和其他痘病毒,正如在例如Flexner, Adv. Pharmacol. 21:51, 1990中教导的。

[0170] 表达控制序列包括但不限于结合RNA聚合酶的启动子序列、分别结合到转录激活子和阻遏物的增强子序列或负调控元件和/或用于核糖体结合的翻译起始序列。例如,细菌表达载体可以包括启动子例如lac启动子和用于转录起始的序列、Shine-Dalgarno序列和起始密码子AUG (Sambrook等, 1989, 同上)。同样地,真核表达载体优选地包括用于RNA聚合酶II的异源、同源或嵌合启动子、下游多腺苷化信号、起始密码子AUG和用于核糖体脱离的终止密码子。

[0171] 表达控制序列可以从天然存在的基因获得,或者可以被设计。设计的表达控制序列包括但不限于突变的和/或嵌合的表达控制序列或合成或克隆的共有序列。含有启动子和多核苷酸可以被操作性连接到其中的克隆位点的载体,在本领域中是公知的。这些载体能够在体外或体内转录RNA,并且可以从诸如Stratagene (La Jolla, Calif.) 和Promega Biotech (Madison, Wis.) 的来源商购。

[0172] 为了优化表达和/或转录,可能必需除去、添加或改变所述载体的5'和/或3'非翻译部分,以消除额外的或可替选的翻译起始密码子或可能在转录或翻译水平上干扰或降低表达的其他序列。或者,可以将共有核糖体结合位点插入到紧邻起始密码子的5'以增强表达。广范围的各种不同表达控制序列——控制操作性连接到它的DNA序列的表达的序列——可用于这些载体中,以表达本发明的DNA序列。这些有用的表达控制序列包括例如SV40、CMV、痘苗病毒、多瘤病毒、腺病毒、疱疹病毒的早期或晚期启动子和已知控制哺乳动物细胞的基因表达的其他序列,及其各种不同组合。

[0173] 在一种情况下,所述核酸递送载体包含用于复制所述载体的复制原点。优选地,所述原点在至少一种类型的宿主细胞中起作用,所述宿主细胞可用于产生足够拷贝数的序列用于递送到靶细胞。因此,适合的原点包括但不限于在细菌细胞(例如埃希氏杆菌、沙门氏

菌、变形杆菌、梭菌、克雷伯氏菌、芽孢杆菌、链霉菌和假单胞菌)、酵母(例如酿酒酵母或毕赤酵母)、昆虫细胞和哺乳动物细胞中起作用的原点。在一种优选情况下,提供了在所述核酸递送媒介被引入到其中的靶细胞(例如哺乳动物细胞如人类细胞)中起作用的复制原点。在另一种情况下,提供了至少两个复制原点,一个在宿主细胞中起作用,一个在靶细胞中起作用。

[0174] 所述核酸递送载体可以可替代地或附加性地包含促进所述核酸递送载体的至少一部分整合到靶细胞染色体中的序列。例如,所述核酸递送载体可以包含与靶细胞的染色体DNA同源的区域。在一种情况下,所述递送载体包含与编码嵌合疫苗的核酸序列侧接的两个或更多个重组位点。

[0175] 所述载体可以另外包含可检测和/或可选择的标志物,以确认所述载体已被成功地引入到靶细胞中和/或可以被所述靶细胞表达。这些标志物可以编码活性例如但不限于RNA、肽或蛋白质的产生,或者可以提供用于RNA、肽、蛋白质、无机和有机化合物或组合物等的结合位点。

[0176] 可检测/可选择标志物基因的实例包括但不限于:编码提供针对原本有毒的化合物(例如抗生素)的抗性的产物的DNA区段;编码在受体细胞中原本缺少的产物(例如tRNA基因、营养缺陷标志物)的DNA区段;编码抑制基因产物的活性的产物的DNA区段;编码可以被容易地鉴定的产物(例如表型标志物例如 β -半乳糖苷酶、荧光蛋白(GFP、CFP、YFP、BFP、RFP、EGFP、EYFP、EBFP、dsRed及其突变、修饰或增强的形式等)和细胞表面蛋白)的DNA区段;结合原本对细胞存活和/或功能有害的产物的DNA区段;原本抑制其他核酸区段的活性的DNA区段(例如反义寡核苷酸);结合修饰底物的产物(例如限制性内切酶)的DNA区段;可用于分离或鉴定所需分子的DNA区段(例如编码特异性蛋白结合位点的区段);引物序列;在不存在时直接或间接提供对特定化合物的抗性或敏感性的DNA区段;和/或编码在受体细胞中有毒的产物的DNA区段。

[0177] 所述标志物基因可作为标志物,用于证实成功的基因转移和/或用于分离表达转入基因的细胞和/或从细胞回收被转移的基因。例如,在一种情况下,所述标志物基因被用于分离和纯化表达所述嵌合疫苗的抗原呈递细胞。

[0178] 正如上文时论的,可以使用任何结构域序列的同源物、变体和修饰形式,只要它们保留了使用它们相应的结构域功能起作用的能力即可。例如,修饰的腔内序列必须保留以与原始的结构域序列相比至少约50%、至少约60%、至少70%、至少约80%、至少约90%或至少约100%的效能将膜和非膜抗原性材料两者转运到胞内体区室的能力,所述效能即由包含所述嵌合序列的细胞产生足够的抗原呈递以使它产生免疫应答的效能。在一种情况下,含有适合的转运信号的序列可以通过构建嵌合DNA来鉴定,所述嵌合DNA含有充分表征的卵清蛋白的抗原性结构域、跨膜结构域和含有假定的溶酶体/胞内体靶向序列的蛋白质的胞质结构域。靶向的效率可以通过确定表达所述嵌合蛋白的抗原呈递细胞刺激HA表位特异性的II类MHC限制性T-细胞的能力来测量(参见例如美国专利号5,633,234的实施例5)。

[0179] 可以提供基本上相似的基因,例如与已知基因具有高于约50%、高于约60%、高于约70%、高于80%、高于约90%并且优选地高于约95%的同一性的基因。百分同一性可以使用本领域中已知的软件程序来确定,例如在《分子生物学现代方法》(Current Protocols In Molecular Biology)(F.M.Ausubel等主编,1987) Supplement 30, section 7.7.18,

Table 7.7.1中所描述的。优选地,将缺省参数用于比对。优选的比对程序是BLAST,使用缺省参数。具体来说,优选的程序是BLASTN和BLASTP,使用下述缺省参数:Genetic code=standard;filter=none;strand=both;cutoff=60;expect=10;Matrix=BLOSUM62;Descriptions=50sequences;sort by=HIGH SCORE;Databases=non-redundant;GenBank+EMBL+DDBJ+PDB+GenBank CDS translations+SwissProtein+SPupdate+PIR。这些程序的详情可以在下述英特网网址处找到:<http://www.ncbi.nlm.nih.gov/cgi-bin/BLAST>。

[0180] 也可以提供基因的“保守修饰的变体”。对于特定核酸序列来说,保守修饰的变体是指编码一致或基本上一致的氨基酸序列的核酸,或者在所述核酸不编码氨基酸序列的情况下,是指基本上一致的序列。具体来说,简并密码子替换可以通过产生其中一个或多个选定(或所有)密码子的第三个位置被混合碱基和/或脱氧肌苷残基替换的序列来实现(Batzer等,1991,Nucleic Acids Res.19:5081;Ohtsuka等,1985,J.Biol.Chem.260:2605-2608;Rossolini等,1994,Mol.Cell.Probes 8:91-98)。

[0181] 基本上相似的结构域序列可以首先通过选择在严紧杂交条件下特异性杂交到感兴趣的结构域序列的序列来鉴定。严紧杂交条件的实例包括:约25℃至约37℃的温浴温度;约6xSSC至约10xSSC的杂交缓冲液浓度;约0%至约25%的甲酰胺浓度;和约6xSSC的清洗溶液。中等杂交条件的实例包括:约40℃至约50℃的温浴温度;约9xSSC至约2xSSC的缓冲液浓度;约30%至约50%的甲酰胺浓度;和约5xSSC至约2xSSC的清洗溶液。高严紧性条件的实例包括:约55℃至约68℃的温浴温度;约1xSSC至约0.1xSSC的缓冲液浓度;约55%至约75%的甲酰胺浓度;和约1xSSC、0.1xSSC的清洗溶液或去离子水。通常,杂交温浴时间为5分钟至24小时,使用1、2或更多个清洗步骤,并且清洗温浴时间为约1、2或15分钟。SSC是0.15M NaCl和15mM柠檬酸盐缓冲液。应该理解,可以利用使用其他缓冲系统的SSC的等效物。相似性可以通过测序确认,但优选地也或可替代地使用适合于所讨论的特定结构域的测定法,通过功能(例如转运到胞内体区室的能力等)来验证。

[0182] 执行测定法以确定同源、变体或修饰的结构域序列的适合性仅仅是对表达适合活性的序列进行筛选的问题。这些筛选在本领域中是常规的。

[0183] 所述核酸递送载体可以被提供为裸露核酸,或与用于促进核酸进入到细胞中的一种或多种分子相结合提供在递送媒介中。适合的递送媒介包括但不限于:脂质体制剂,多肽,多糖,脂多糖,病毒制剂(例如包括病毒、病毒粒子、人工病毒包膜等),细胞递送媒介等。

[0184] 基于脂质的制剂

[0185] 被设计用于促进生物活性分子的细胞内递送的递送媒介,必须与非极性和极性环境两者相互作用(在例如质膜、组织液、细胞内的区室等中或其上)。因此,优选地,递送媒介被设计成含有极性和非极性结构域两者或用于将核酸易位到细胞内的易位序列。

[0186] 具有极性和非极性结构域的化合物被称为两亲物。阳离子型两亲物具有能够在生理pH下或附近带正电荷的极性基团,用于与带负电荷的多核苷酸例如DNA相互作用。

[0187] 上面描述的核酸载体可以提供在包含脂质单层或双层的制剂中,以便于所述载体跨过细胞膜的转移。可以使用脂质体或任何形式的脂质膜例如平面脂质膜或完整细胞例如红细胞的细胞膜。脂质体制剂可以通过任何手段来给药,包括静脉内或口服给药。

[0188] 脂质体和脂质体制剂可以按照标准方法来制备,并且在本领域中是公知的,参见

例如Remington's;Akimaru,1995,Cytokines Mol.Ther.1:197-210;Alving,1995,Immunol.Rev.145:5-31;Szoka,1980,Ann.Rev.Biophys.Bioeng.9:467;美国专利号4,235,871;美国专利号4,501,728;和美国专利号4,837,028。在一种情况下,所述脂质体包含靶向分子,用于将脂质体:核酸载体复合物靶向到特定细胞类型。在特别优选的情况下,靶向分子包含用于靶组织中存在的血管或细胞表面上的生物分子(例如受体或配体)的结合配偶体(例如配体或受体)。

[0189] 脂质体电荷是脂质体从血液清除的重要决定因素,其中带负电荷的脂质体被网状内皮系统更快地摄取(Juliano,1975,Biochem.Biophys.Res.Comm.63:651)并因此在血流中具有更短的半衰期。并入磷脂酰乙醇胺衍生物通过阻止脂质体聚集增加了循环时间。例如,将N-(ω -羧基)酰胺基磷脂酰乙醇胺并入到L- α -二硬脂酰基磷脂酰胆碱的大的单层囊泡,急剧提高了体内脂质体循环寿命(参见例如Ahl,1997,Biochim.Biophys.Acta 1329:370-382)。具有延长的循环半衰期的脂质体对于治疗和诊断用途来说通常是合乎需要的。关于药代动力学的一般性讨论,参见例如Remington's,第37-39章, Lee等,在《药代动力学分析实用方法》(Pharmacokinetic Analysis:A Practical Approach)(Technomic Publishing AG,Basel,Switzerland 1996)中。

[0190] 通常,使用约5至15摩尔%的带负电荷的磷脂例如磷脂酰甘油、磷脂酰丝氨酸或磷脂酰肌醇来制备脂质体。添加的带负电荷的磷脂例如磷脂酰甘油也起到阻止脂质体的自发聚集的作用,从而最小化尺寸较小的脂质体聚集体形成的风险。浓度为至少约50摩尔%的膜硬化剂例如神经鞘磷脂或饱和的中性磷脂和5至15摩尔%的单唾液酸化神经节苷脂,也可以合乎需要地提供脂质体性质例如刚性(参见例如美国专利号4,837,028)。

[0191] 此外,脂质体悬液可以包括脂质保护剂,其在储存时保护脂质以防自由基和脂质过氧化损伤。亲脂性自由基淬灭剂例如 α -生育酚和水溶性铁特异性螯合剂例如ferrioxianine,是优选的。

[0192] 本发明的核酸递送媒介可以包括尺寸不均一的多层囊泡。例如,可以将形成囊泡的脂质溶解在适合的有机溶剂或溶剂系统中,并在真空或惰性气体下干燥,以形成脂质薄膜。如果需要,可以将所述薄膜重新溶解在适合的溶剂例如叔丁醇中,然后冷冻干燥以形成采取更容易水合的粉末状形式的更均匀的脂质混合物。将这种薄膜用肽或多肽复合物的水溶液覆盖,并允许在搅拌下通常在15至60分钟的时间段内水合。得到的多层囊泡的尺寸分布,可以通过在更剧烈的搅拌条件下水合所述脂质或通过添加增溶性去污剂例如脱氧胆酸盐,向较小的尺寸转变。水合介质优选地包含浓度为最终脂质体悬液中脂质体的内部体积中所需的浓度的核酸。

[0193] 在脂质体制备后,可以将所述脂质体按尺寸筛分,以获得所需的尺寸范围和相对窄的脂质体尺寸分布。一个优选的尺寸范围是约0.2至0.4微米,其允许所述脂质体悬液通过常规滤器、通常为0.22微米滤器过滤来除菌。如果所述脂质体已按尺寸筛分到约0.2至0.4微米,则过滤除菌可以在高通量的基础上进行。几种技术可用于将脂质体按尺寸筛分到所需尺寸(参见例如美国专利号4,737,323)。

[0194] 适合的脂质包括但不限于DOTMA(Felgner等,1987,Proc.Natl.Acad.Sci.USA 84:7413-7417)、DOGS或TransfectainTM(Behr等,1989,Proc.Natl.Acad.Sci.USA 86:6982-6986)、DNERIE或DORIE(Felgner等,Methods 5:67-75)、DC-CHOL(Gao和Huang,1991,BBRC

179:280-285)、DOTAPTM (McLachlan等,1995, Gene Therapy 2:674-622)、Lipofectamine^{RTM}和甘油脂质化合物(参见例如EP901463和W098/37916)。

[0195] 适合于与核酸递送载体复合的其他分子包括阳离子型分子例如聚酰胺-胺(Haensler和Szoka,1993, Bioconjugate Chem. 4:372-379)、树枝状聚赖氨酸(WO 95/24221)、聚乙烯亚胺(polyethylene irinine)或聚丙烯亚胺(polypropylene h-nine)(WO 96/02655)、聚赖氨酸(美国专利号5,595,897;FR 2 719 316)、壳聚糖(美国专利号5,744,166)、DNA-明胶团聚体(参见例如美国专利号6,207,195;美国专利号6,025,337;美国专利号5,972,707)或DEAE葡聚糖(Lopata等,1984, Nucleic Acid Res. 12:5707-5717)。

[0196] 基于病毒的基因递送媒介

[0197] 在一种情况下,所述核酸递送媒介包含病毒或病毒粒子。在这种情况下,优选地,所述核酸载体包含病毒载体。病毒载体例如反转录病毒、腺病毒、腺相关病毒和疱疹病毒,通常由两种组分构成,修饰的病毒基因组和包围它的外壳结构(参见例如Smith等,1995, Ann. Rev. Microbiol. 49:807-838),尽管有时病毒载体以裸露形式引入或用病毒蛋白之外的蛋白包被。大多数当前的载体具有与野生型病毒相似的外壳结构。这种结构包装并保护病毒核酸,并提供结合和进入靶细胞的手段。

[0198] 优选地,病毒载体与野生型病毒基因组相比被修饰,以失去所述病毒在靶细胞中生长的能力,同时使所述病毒能够在用于制备感染性粒子的宿主细胞(例如包装或辅助细胞)中生长。载体核酸通常必需包含用于在辅助细胞系中复制和包装的顺式作用的病毒序列和用于调控被递送到靶细胞的多核苷酸的表达的表达控制序列。其他病毒功能在特定包装或辅助细胞系中反式表达,正如在本领域中已知的。

[0199] 优选的载体是从选自疱疹病毒、巨细胞病毒、泡沫病毒、慢病毒、Semliki森林病毒、AAV(腺相关病毒)、痘病毒、腺病毒和反转录病毒的病毒衍生的病毒载体。这些病毒载体在本领域中是公知的。

[0200] 在一种优选情况下,使用的病毒载体是腺病毒载体。腺病毒基因组由约36kb的线性双链DNA分子构成,带有超过约30个完成病毒复制周期所必需的基因。早期基因分为4个区(E1至E4),它们对于病毒复制来说是必需的,除了据信调节抗病毒宿主免疫应答的E3区之外。E1区(E1A和E1B)编码负责病毒基因组的转录调控的蛋白质。E2区基因(E2A和E2B)的表达导致病毒复制所需的多肽的合成。由E3区编码的蛋白质阻止由细胞毒性T细胞和肿瘤坏死因子造成的细胞溶解(Wold和Gooding,1991, Virology 184:1-8)。由E4区编码的蛋白质参与DNA复制、晚期基因表达和拼接以及宿主细胞关闭(Halbert等,1985, J. Virol. 56:250-257)。晚期基因通常编码对病毒衣壳有贡献的结构蛋白。此外,腺病毒基因组带有顺式作用的5'和3' ITR(末端反向重复序列)和DNA复制所必需的包装序列。所述ITR带有DNA复制原点,而衣壳化区对于腺病毒DNA包装到感染性粒子中而言是必需的。

[0201] 腺病毒载体可以被工程化改造成条件复制型(CRA载体),以便在特定细胞(例如增殖性细胞)中选择性复制,正如在Heise和Kim(2000, J. Clin. Invest. 105:847-851)中所描述的。在另一种情况下,腺病毒载体对于E1功能来说是复制缺陷的(例如通过E1的完全或部分缺失或突变)。所述载体的腺病毒骨架可以包含其他修饰(一个或多个病毒基因中的缺失、插入或突变)。E2修饰的一个实例通过位于DBP(DNA结合蛋白)编码基因上的热敏突变来说明(Ensinger等,1972, J. Virol. 10:328-339)。所述腺病毒序列也可以缺失全部或一部分

E4区(参见例如EP 974 668;Christ等,2000,Human Gene Ther.11:415-427;Lusky等,1999,J.Virol.73:8308-8319)。非必需的E3区内的其他缺失可以允许被递送的多核苷酸的尺寸增加(Yeh等,1997,FASEB Journal 11:615-623)。然而,保留为允许病毒避开免疫系统(Gooding等,1990,Critical Review of Immunology 10:53-71)或炎症反应(EP 00440267.3)的多肽(例如gp19k)编码的全部或一部分E3序列,可以是有利的。

[0202] 也可使用保留ITR和包装序列并包含实质性遗传修饰以废除病毒抗原的残留合成的第二代载体,以便提高待表达基因在被转导细胞中的长期表达(参见例如W0 94/28152;Lusky等,1998,J.Virol 72:2022-2032)。

[0203] 被引入到细胞中的多核苷酸可以插入到病毒基因组的除了顺式作用序列之外的任何位置中。优选地,它被插入以代替缺失区(E1、E3和/或E4),优选地在缺失的E1区内。

[0204] 腺病毒可以源自于任何人类或动物来源,特别是犬类(例如CAV-1或CAV-2,Genbank参考号分别为CAVIGENOM和CAV77082)、鸟类(Genbank参考号AAVEDSDNA)、牛类(例如BAV3;Reddy等,1998,J.Virol.72:13941402)、鼠类(Genbank参考号ADMUSMAVI)、绵羊、猫科动物、猪类或猿猴来源,或者可以是杂交病毒。可以使用任何血清型。然而,C亚类的人类腺病毒是优选的,特别是腺病毒2(Ad2)和5(Ad5)。这些病毒可以例如从ATCC获得。

[0205] 腺病毒粒子或空的腺病毒衣壳也可用于通过病毒介导的辅助内化过程来转移核酸递送载体,如在美国专利号5,928,944中所述。这一过程可以在阳离子试剂例如聚碳烯或包含一个或多个脂质层的脂质囊泡存在下实现。

[0206] 腺病毒粒子可以按照本领域中任何常规的技术(例如W0 96/17070),使用互补细胞系或辅助病毒来制备和繁殖,所述互补细胞系或辅助病毒反式供应丢失的对于病毒复制而言必需的病毒基因。细胞系293(Graham等,1977,J.Gen.Virol.36:59-72)和PERC6(Fallaux等,1998,Human Gene Therapy 9:1909-1917)常用于补足E1缺失。其他细胞系已被工程化改造,以补足缺陷的载体(Yeh等,1996,J.Virol.70:559-565;Kroughak和Graham,1995,Human Gene Ther.6:1575-1586;Wang等,1995,Gene Ther.2:775-783;Lusky等,1998,J.Virol.72:2022-203;EP 919627和W0 97/04119)。腺病毒粒子可以从培养上清液回收,但是也可以在裂解后从细胞回收,并任选地按照标准技术进一步纯化(例如层析、超离心,如在W0 96/27677、W0 98/00524、W0 98/26048和W0 00/50573中所描述)。

[0207] 细胞类型特异性靶向可以使用从具有广宿主范围的腺病毒通过修饰病毒表面蛋白而衍生的载体来实现。例如,腺病毒感染的特异性由与允许细胞的表面处存在的细胞受体的附连来决定。就此而言,在腺病毒衣壳表面处存在的纤维和五邻体,在细胞附连中发挥关键作用(Defer等,1990,J.Virol.64:3661-3673)。因此,腺病毒的细胞靶向可以通过编码纤维和/或五邻体的病毒基因的遗传修饰,以产生能够与独特的细胞表面受体特异性相互作用的修饰的纤维和/或五邻体,来进行。这些修饰的实例描述在Wickarn等,1997,J.Virol.71:8221-8229;Arriberg等,1997,Virol.Chem 268:6866-6869;Roux等,1989,Proc.Natl.Acad.Sci.USA 86:9079-9083;Miller和Vile,1995,FASEB J.9:190-199;W0 93/09221和W0 95/28494中。

[0208] 在特别优选的情况下,使用腺相关病毒序列作为载体。源自于人类细小病毒AAV-2(腺相关病毒2型)的载体是目前正在开发的最有前景的基因递送媒介之一。这种用于包装单链DNA的系统的几个特点表明它是用于递送基因疫苗的裸露DNA的可能的替代物。与其他

病毒载体例如痘苗或腺病毒形成对比,主要的吸引人的特点在于AAV载体不表达任何病毒基因。疫苗构建物中包括的唯一病毒DNA序列是145bp的末端反向重复序列(ITR)。因此,与在使用裸露DNA的免疫接种中相同,表达的唯一基因是抗原或抗原嵌合体的基因。此外,已知AAV载体转导分裂和非分裂细胞两者,例如人类外周血单核细胞衍生的树突状细胞,具有持久的转入基因表达,并具有口服和鼻内递送以产生粘膜免疫的可能性。此外,所需的DNA的量似乎大大减少几个数量级,最大应答在 10^{10} 至 10^{11} 个粒子或DNA拷贝的剂量下,形成对比的裸露DNA的剂量为50ug或约 10^{15} 个拷贝。

[0209] 在一种情况下,通过用编码AAV ITR嵌合蛋白的构建物中包含的DNA和含有AAV编码区(AAV rep和cap基因)而没有ITR的AAV辅助质粒ACG2共转染适合的细胞系(例如人类293细胞)来包装AAV载体。随后将所述细胞用腺病毒Ad5感染。载体可以使用本领域中已知的方法(例如氯化铯密度梯度超离心)从细胞裂解物纯化,并验证以确保它们不含可检测的能够复制的AAV或腺病毒(例如通过细胞病变效应生物测定法)。可以使用在用蛋白酶K消化后制备的病毒DNA样品,通过定量PCR来确定AAV滴度。优选地,通过这种方法产生的载体滴度为每ml约 5×10^{12} 至 1×10^{13} 个DNA酶抗性粒子。

[0210] 在其他情况下,使用反转录病毒载体。反转录病毒是一类整合型病毒,其使用病毒编码的反转录酶复制,以将病毒的RNA基因组复制成双链DNA,所述双链DNA被整合到被感染细胞(例如靶细胞)的染色体DNA中。这些载体包括源自于鼠白血病病毒、特别是Moloney (Gilboa等,1988,Adv.Exp.Med.Biol.241:29)或Friend's FB29毒株(WO 95/01447)的载体。通常,反转录病毒载体缺失病毒基因gag、pol和env的全部或一部分,并保留5'和3'LTR和衣壳化序列。这些元件可以被修饰以提高反转录病毒载体的表达水平或稳定性。这些修饰包括用反转录转座子之一例如VL30替换反转录病毒的衣壳化序列(参见例如美国专利号5,747,323)。优选地,感兴趣的多核苷酸被插入到所述衣壳化序列下游,优选地采取相对于反转录病毒基因组相反的方向。细胞特异性靶向可以通过抗体或抗体片段与反转录病毒的包膜蛋白的偶联来实现,正如本领域中已知的。

[0211] 反转录病毒粒子在辅助病毒存在下或在适合的互补(包装)细胞系中制备,所述细胞系含有整合在其基因组中的所述反转录病毒载体缺陷的反转录病毒基因(例如gag/pol和env)。这些细胞系描述在现有技术中(Miller和Rosman,1989,BioTechniques 7:980; Danos和Mulligan,1988,Proc.Natl.Acad.Sci.USA 85:6460;Markowitz等,1988,Virol.167:400)。所述env基因的产物造成病毒粒子与靶细胞表面上存在的病毒受体的结合,并因此决定所述反转录病毒粒子的宿主范围。在本发明的情形中,使用含有兼嗜性包膜蛋白的包装细胞系例如PA317细胞(ATCC CRL 9078)或293EI6(WO97/35996),以允许感染人类和其他物种的靶细胞,是有利的。所述反转录病毒粒子优选地从培养上清液回收,并且可以任选地按照标准技术(例如层析、超离心)进一步纯化。

[0212] 其他适合的病毒包括痘病毒。痘病毒科的几个成员的基因组已被作图并测序。痘病毒载体可以从痘病毒科的任何成员特别是金丝雀痘、鸡痘和痘苗病毒获得。适合的痘苗病毒包括但不限于Copenhagen株系(Goebel等,1990,Virol.179:247-266;Johnson等,1993,Virol.196:381-401)、Wyeth株和修饰的Ankara(MVA)株(Antoine等,1998,Virol.244:365-396)。用于构建痘苗病毒载体的一般性条件在本领域中是已知的(参见例如EP 83 286和EP 206920;Mayr等,1975,Infection3:6-14;Sutter和Moss,1992,

Proc.Natl.Acad.Sci.USA 89:10847-10851)。优选地,将感兴趣的多核苷酸插入到非必需基因座中,例如编码基因间区的n0D7或其失活或缺失不显著损害病毒生长和复制的任何基因。

[0213] 痘病毒粒子如本领域中所述来制备 (Piccini等,1987,Methods of Enzymology 153:545-563;美国专利号4,769,330;美国专利号4,772,848;美国专利号4,603,112;美国专利号5,100,587和美国专利号5,179,993)。通常,构建供体质粒,通过在大肠杆菌中生长进行扩增,并通过常规程序进行分离。然后,将它与痘病毒基因组一起引入到适合的细胞培养物(例如鸡胚成纤维细胞)中,通过同源重组产生痘病毒粒子。它们可以从培养上清液或在裂解步骤(例如化学裂解、冻/融、渗透压冲击、超声处理等)后从培养的细胞回收。可以使用连续的多轮噬斑纯化来除去污染性的野生型病毒。然后可以使用本领域中已知的技术(例如层析方法或在氯化铯或蔗糖梯度上超离心)来纯化病毒粒子。

[0214] 在全球根除天花的战役中痘苗作为活病毒疫苗的使用,使得痘苗成为开发作为活重组疫苗载体的明显选择。已经报道了表达接近100种不同外来蛋白质的活重组痘苗病毒,它们中的许多是有效的实验性疫苗(由Moss和Flexner,1987综述)。由于它的基因组尺寸大,能够接受至少25,000碱基对的外来DNA,以及它感染大多数真核细胞类型包括昆虫细胞的能力(出处同上),痘苗作为表达载体是特别通用的。不同于其他DNA病毒,痘病毒专门在被感染细胞的细胞质内复制,降低了重组病毒DNA与宿主染色体的遗传交换的可能性。已显示重组痘苗载体正确加工和表达来自于各种不同来源包括人、其他哺乳动物、寄生虫、RNA和DNA病毒、细菌和噬菌体的蛋白质。

[0215] 所述病毒能够感染大多数哺乳动物,使得它成为用于研究广范围的人类和动物疾病的有用载体。编码外来蛋白质的DNA的表达受到宿主病毒调控元件包括上游启动子序列和必要时RNA加工信号的控制。已通过同源重组进行了外来DNA在痘苗病毒基因组的非必需区中的插入 (Panicali等,Proc.Nat'l.Acad.Sci,USA,79:4927,1982;Mackett等,Proc.Nat'l.Acad.Sci.USA,79:7415,1982)。

[0216] 由于在插入位点处或其附近的转录调控元件,或通过更精确的遗传工程,外来基因通过DNA的表达可以发生。已构建了极大便于外来基因的插入和表达的质粒载体 (Mackett等,J.Virol,49:857,1982)。这些载体含有表达位点,其由痘苗转录启动子和用于插入侧接有来自于痘苗基因组的非必需区的DNA的外来编码序列的一个或多个独特的限制性内切酶位点构成。启动子的选择决定了表达的时间(例如早期或晚期)和水平,而侧接的DNA序列决定了同源重组的位点。

[0217] 通过这种程序产生的病毒粒子仅仅约千分之一是重组的。尽管重组病毒噬斑可以通过DNA杂交来鉴定,但已开发了高效的选择程序。通过使用非必需的痘苗病毒胸苷激酶(TK)基因的区段作为侧接序列,外来基因重组到TK基因座中并通过插入失活所述TK基因。TK病毒的选择通过在5-溴脱氧尿苷存在下在TK细胞中进行病毒噬斑测定法来实现。所述核苷类似物的磷酸化和随后致死性掺入到病毒DNA中,只发生在被TK+亲代病毒感染的细胞中。取决于转染和重组的效率,高达80%的噬斑是所需重组体,其余的是自发TK突变体。

[0218] 含有大肠杆菌 β -半乳糖苷酶基因以及用于第二个基因的表达位点的质粒载体,允许将重组体与亲代病毒区分开的可替代方法 (Chakrabarti等,Mol.Cell.Biol.,5:3403,1985)。由这些重组体形成的噬斑可以通过在添加适合的指示剂后形成的蓝色来正向鉴定。

通过将TK选择和 β -半乳糖苷酶表达两者组合,重组病毒被容易且快速地分离。然后通过适合的细胞系中繁殖来扩增所述重组体,并通过适合的酶学、免疫学或物理程序检查插入基因的表达。

[0219] 可以添加到痘苗病毒基因组的遗传信息的量的上限尚不知道。然而,接近25,000个碱基对的外来DNA的添加对病毒产量没有明显的有害效应(Smith等, Gene, 25:21, 1983)。在必要时,可以缺失痘苗病毒基因组的大的区段以提供额外的容量(Moss等, J.Virol. 40: 387, 1981)。

[0220] 病毒的衣壳分子可以包括靶向组成部分以便于靶向和/或进入到细胞中。适合的靶向分子包括但不限于:化学缀合物,脂质,糖脂,激素,糖,聚合物(例如PEG、聚赖氨酸、PEI等),肽,多肽(参见例如WO 94/40958),维生素,抗原,凝集素,抗体及其片段。优选地,这些靶向分子识别并结合到细胞特异性标志物、组织特异性标志物、细胞受体、病毒抗原、抗原性表位或肿瘤相关标志物。

[0221] 基于病毒粒子的组合物可以配制成 10 至 10^{14} i.u. (感染单位)之间、优选地 10 至 10^{11} i.u.之间的药剂的形式。所述滴度可以通过常规技术确定。核酸递送载体的剂量优选地在 0.01 至 10mg/kg 之间,更特别地在 0.1 至 2mg/kg 之间。

[0222] 基于细胞的递送媒介

[0223] 符合本发明的核酸载体可以利用包含所述载体的其它细胞(“递送细胞”)递送到靶细胞。将载体引入到细胞中的方法在本领域中是已知的,并包括将DNA微注射到细胞的核中(Capechi等, 1980, Cell 22:479-488),用 CaPO_4 转染(Chen和Okayama, 1987, Mol. Cell Biol. 7:2745-2752),电穿孔(Chu等, 1987, Nucleic Acid Res. 15:1311-1326),脂转染/脂质体融合(Feigner等, 1987, Proc. Natl. Acad. Sci. USA 84:7413-7417)和粒子轰击(Yang等, 1990, Proc. Natl. Acad. Sci. USA 87:9568-9572)。适合的细胞包括自体和非自体细胞,并且可以包括异种细胞。递送细胞可以被诱导通过诱导它们的死亡(例如通过向这些细胞提供可诱导的自杀基因),以将它们的内含物递送到靶细胞。

[0224] 辅助分子

[0225] 符合本发明的组合物可以包含用于促进将核酸递送载体引入到细胞中和/或用于增强特定治疗效果的一种或多种辅助分子。

[0226] 此外,符合本发明的组合物可以包括一种或多种稳定化物质例如脂质、核酸酶抑制剂、水凝胶、透明质酸酶(WO 98/53853)、胶原酶、聚合物、螯合剂(EP 890362),以便抑制在动物/人体内的降解和/或改善所述载体在靶细胞中的转染/感染。这些物质可以单独或组合(例如阳离子型和中性脂质)使用。

[0227] 也已显示,腺病毒蛋白能够使胞内体失稳并增强DNA被摄入到细胞内。腺病毒与含有脂质复合的DNA载体的溶液的混合物或将DNA结合到使用蛋白质交联剂共价附连到腺病毒的聚赖氨酸,可以显著提高核酸递送载体的摄入和表达(参见例如Curiel等, 1992, Am. J. Respir. Cell. Mol. Biol. 6:247-252)。

[0228] 宿主细胞

[0229] 符合本发明的核酸载体可以在各种不同的宿主细胞中表达,包括但不限于:原核细胞(例如大肠杆菌、葡萄球菌、芽孢杆菌),酵母细胞(例如酿酒酵母),昆虫细胞,线虫细胞,植物细胞,两栖类细胞(例如爪蟾),鸟类细胞,和哺乳动物细胞(例如人类细胞、小鼠细

胞、哺乳动物细胞系、原代培养的哺乳动物细胞例如来自于解剖组织的)。

[0230] 所述分子可以在从生物体分离的宿主细胞、作为生物体的一部分的宿主细胞或被引入到生物体中的宿主细胞中表达。在一种情况下,融合分子在体外例如在培养物中在宿主细胞中表达。在另一种情况下,融合分子在转基因生物体(例如转基因小鼠、大鼠、兔、猪、灵长动物等)中表达,所述生物体包括含有编码所述融合分子的核酸的体细胞和/或生殖系细胞。用于构建转基因动物的方法在本领域中是已知的并且是常规的。

[0231] 核酸载体也可以在体外被引入到细胞中,并且可以将所述细胞(例如干细胞、造血细胞、淋巴细胞等)引入到宿主生物体中。所述细胞对于宿主生物体来说可以是异源或自体的。例如,可以从所述宿主生物体获得细胞,将核酸载体在体外引入到所述细胞中,然后将所述细胞重新引入到宿主生物体中。

[0232] 抗原呈递细胞

[0233] 在本发明的优选情况下,将如上所述的核酸递送媒介引入到天然或工程化的抗原呈递细胞中。

[0234] 当在本文中使用时,术语“抗原呈递细胞”(APC)包括在其表面上呈递与主要组织相容性复合物分子、优选为II类分子或其部分结合的抗原的任何细胞。适合的APC的实例在下文中详细讨论,并且包括但不限于完整细胞例如巨噬细胞、树突状细胞、B细胞、杂交APC和培养的抗原呈递细胞。制造杂交APC的方法在本领域中已被描述并且已知。

[0235] 树突状细胞(DC)是强效抗原呈递细胞。已显示DC提供T细胞活化和增殖所需的所有信号。这些信号可以被分为两种类型。为免疫应答提供特异性的第一种类型通过T-细胞受体/CD3(“TCR/CD3”)复合物与APC表面上由I或II类主要组织相容性复合物(上文定义的“MHC”)蛋白呈递的抗原性肽之间的相互作用介导。这种相互作用对于发生T细胞活化来说是必要的但不是充分的。事实上,在没有第二种类型的信号时,所述第一种类型的信号可以导致T细胞无反应性。被称为辅助刺激信号的第二种类型的信号既不是抗原特异性的也不是MHC限制的,并且在第一种类型的信号存在下可以引起T细胞的完全增殖应答和T细胞效应功能的诱导。

[0236] 几种分子已显示出增强辅助刺激活性。它们包括但小限于热稳定抗原(HSA)、硫酸软骨素修饰的MHC恒定链(Ii-CS)、细胞内粘附分子I(ICAM-1)和APC表面上的B7辅助刺激分子及其在T细胞上的对应受体CD 28或CTLA-4。

[0237] 其他重要的辅助刺激分子是CD40、CD54、CD80、CD86。当在本文中使用时,术语“辅助刺激分子”涵盖了当与T细胞表面上的TCR所结合的肽/MHC复合物一起作用时,提供了实现结合所述肽的T细胞的活化的辅助刺激效果的任何单一分子或分子的组合。因此,所述术语涵盖了APC上的B7或其他辅助刺激分子及其片段(单独地,与另外的分子复合地或作为融合蛋白的一部分),它们与肽/MHC复合物一起结合到同族配体,并在T细胞表面上的TCR特异性结合所述肽时引起所述T细胞的活化。辅助刺激分子可以从各种不同的来源包括例如 Beckman Coulter 商购。

[0238] 在本发明的一种情况下,使用在Romani等,J.Immunol.Methods196:135-151,1996和Bender等,J.Imrnunol.Methods 196:121-135,1996中描述的方法,从哺乳动物例如鼠、猿猴或人类的外周血单核细胞(PBMC)产生不成熟和成熟的树突状细胞两者。简单来说,利用免疫磁性技术将分离的PBMC预处理以清除T-和B-细胞。然后将清除淋巴细胞的PBMC在增

补有人类血浆(优选为自体血浆)和GM-CSF/IL-4的RPMI培养基9中培养例如约7天,以产生树突状细胞。与它们的单核细胞祖先相比,树突状细胞是非贴壁的。因此,在大约第7天,将非贴壁细胞收获以进一步处理。

[0239] 在GM-CSF和IL-4存在下从PBMC衍生的所述树突状细胞是不成熟的,因为如果从培养物中除去细胞因子刺激物,它们可以失去它们的非贴壁性质并逆转回到巨噬细胞的细胞命运。所述处于不成熟状态下的树突状细胞,在加工本源蛋白质抗原用于II类MHC限制的途径中非常有效(Romani等,J.Exp.Med.169:1169,1989)。培养的树突状细胞的进一步成熟通过在含有必需的成熟因子的巨噬细胞调制的培养基(CM)中培养3天来完成。成熟的树突状细胞不太能够捕获新的蛋白质用于呈递,但是在刺激静息T细胞(CD4和CD8两者)以生长和分化方面好得多。

[0240] 成熟的树突状细胞可以通过它们的形态变化来鉴定,例如通过更加能动的细胞质过程的形成,通过它们的非贴壁性,通过存在下述标志物中的至少一者:CD83,CD68,HLA-DR或CD86,或通过Fc受体例如CD115的丧失(综述在Steinman,Annu.Rev.Immunol.9:271,1991中)。成熟的树突状细胞可以被收集,并使用典型的细胞荧光显影术和细胞分选技术和装置例如FACScan和FACStar来分析。用于流式细胞术的第一抗体是特异性针对成熟树突状细胞的细胞表面抗原的第一抗体,并且是可商购的。第二抗体可以是生物素化的Ig,随后是FITC-或PE-偶联的链亲合素。

[0241] 可替代地,其他人报道了用于上调(活化)树突状细胞和将单核细胞转化成活化的树突状细胞表型的方法。这种方法包括向培养基添加钙离子载体,以将单核细胞转变成活化的树突状细胞。例如在24-48小时的培养周期的开始时添加钙离子载体A23187,引起合并的“单核细胞加上DC”级分的均匀的活化和树突状细胞表型转化:特征性地,所述活化的群体均匀地变成CD 14 (Leu M3) 阴性,并且上调HLA-DR、HLA-DQ、ICAM-1,137.1和137.2。此外,这种活化的大量群体在最少的基础上也与进一步纯化时同样好地发挥作用。已将特定的细胞因子组合成功地用于扩增(或部分取代)使用钙离子载体实现的活化/转化:这些细胞因子包括但不限于G-CSF、GM-CSF、IL-2和IL-4。每种细胞因子在单独提供时不足以用于最佳的上调。

[0242] 用于分离APC的第二种方法是收集相对大量的已经在血液中循环的前定向APC。以前用于从人类外周血分离定向APC的技术包括物理程序的组合,例如甲泛葡胺梯度和粘附/非粘附步骤(Freudenthal等,PNAS 87:7698-7702,1990),Percoll梯度分离(Mehta-Damani等,J.Immunol.153:996-1003,1994),和荧光活化细胞分选技术(Thomas等,J.Immunol.151:6840-52,1993)。

[0243] 对于本领域技术人员来说,显然存在许多在本领域中常规用于分离专业抗原呈递细胞(或它们的前体)的方法,并且这些方法和可能开发的其他方法是非限制性的,并涵盖在本发明的范围之内。

[0244] 在一个实施方式中,所述APC和因此呈递一种或多种抗原的细胞是自体的。在另一个实施方式中,所述呈递抗原的APC是同种异体的,即源自于不同对象。

[0245] 正如上文讨论的,可以使用上述方法或本领域中已知的其他方法将编码嵌合分子的核酸引入到APC中,所述方法包括但不限于转染、电穿孔、融合、微注射、基于病毒的递送或基于细胞的递送.Arthur等,Cancer Gene Therapy 4(1):17-25,1997报道了在人类树突

状细胞中基因转移方法的比较。

[0246] 已知的、部分的和推测的人类白细胞抗原 (HLA)、人类MHC的基因指定、氨基酸和核苷酸序列包括共有序列,已被发表(参见例如Zemmour和Parham, *Immunogenetics* 33:310-320, 1991), 并且表达HLA变体的细胞系是已知的并且通常也可以获得,许多来自于美国典型培养物保藏中心(American Type Culture Collection) (“ATCC”)。因此,使用PCR,可以容易地将编码II类MHC的核苷酸序列操作性连接到本发明的表达载体,然后将其用于转化适合的细胞,以在其中表达。

[0247] 可以使用专业APC,例如巨噬细胞、B细胞、单核细胞、树突状细胞和朗格汉斯细胞。使用标准程序从下述供体的血液或组织收集这些细胞:1) 自体供体;2) 具有与待治疗的宿主不同的HLA特异性的异源供体;或3) 不同物种的异种供体(Coligan等,《免疫学现代方法》(*Current Protocols in Immunology*),第3和14节,1994)。所述细胞可以从正常宿主或具有传染病、癌症、自体免疫疾病或过敏症的患者分离。

[0248] 可以使用白细胞去除术和“FICOLL/HYPAQUE”密度梯度离心(通过Ficoll和不连续Percoll密度梯度逐步离心),从外周血获得专业APC。使用的程序避免了将所述APC暴露于可以被所述APC内化的抗原,引起不特异性针对目标抗原的T细胞的活化。

[0249] 不天然呈递抗原的细胞可以通过引入编码适合分子的序列,被工程化改造成抗原呈递细胞。例如,编码II类MHC分子、辅助分子、辅助刺激分子和抗原加工辅助分子的核酸序列,可以在直接合成、克隆、从含有这些基因的细胞纯化DNA等之后被引入。获得在本文描述的组合物和方法中使用的分子的编码基因的一种方便的手段,是使用选定的寡核苷酸引物对,在选定的核酸模板上进行聚合酶链反应(PCR)扩增。例如,可以使用上皮细胞、内皮细胞、肿瘤细胞、成纤维细胞、活化的T细胞、嗜曙红细胞、角化细胞、星形细胞、小胶质细胞、胸腺皮质上皮细胞、施旺细胞、视网膜色素上皮细胞、成肌细胞、血管平滑肌细胞、软骨细胞、肠上皮细胞、甲状腺细胞和肾小管细胞。它们可以是最近从宿主外植并且没有专门在细胞培养物中传代以形成确立细胞系的原代细胞,或者相对均质并且能够增殖许多代或无限增殖的确立细胞系。

[0250] 不是专业APC的细胞从它们所位于的自体供体、异源供体或异种供体的任何组织,使用各种不同的已知分离方法来分离(Darling,《动物细胞:培养和培养基》(*Animal Cells: Culture and Media*), J.Wiley, New York, 1994; Freshney,《动物细胞的培养》(*Culture of Animal Cells*), Alan R. Liss, Inc., New York, 1987)。非自体细胞例如异源或异种细胞,可以被离体工程化改造以表达匹配已知人类HLA特异性的I类和II类HLA分子。然后将这些细胞引入到匹配所述工程化细胞的HLA特异性的人类对象中。将所述细胞进一步离体工程化改造以表达符合本发明的一种或多种嵌合疫苗。

[0251] 将所述工程化改造的细胞通过标准的细胞培养方法维持在细胞培养物中(Darling,《动物细胞:培养和培养基》(*Animal Cells: Culture and Media*), J.Wiley, New York, 1994; Freshney,《动物细胞的培养》(*Culture of Animal Cells*), Alan R. Liss, Inc., New York, 1987)。在本发明中使用的细胞系从各种不同的来源获得(例如《ATCC细胞系和杂交瘤目录》(*ATCC Catalogue of Cell Lines & Hybridomas*), American Type Culture Collection, 第8版, 1995), 或者使用标准方法生产(Freshney,《永生化细胞的培养》(*Culture of Immortalized Cells*), Wiley-Liss, New York, 1996)。对于在人类对象中使

用来说,非转化的细胞系是优选的。

[0252] 在一种情况下,在GM-CSF的影响下分化成树突状细胞的CD34+前体从对象的身体获得,并将编码符合本发明的嵌合疫苗的核酸引入到所述细胞中,然后将其重新注射到所述对象中。利用含有连接到胞内体/溶酶体靶向信号的抗原性序列(并任选地包含LAMP样腔内多肽)的构建物,将增强源自于特定抗原的肽与转导的抗原呈递细胞上的II类MHC分子的结合,产生明显更加强力的系统性T细胞依赖性免疫应答。尽管在这种策略中转染的抗原呈递细胞优选为自体细胞,但如上所述,可以使用在所述宿主中有效呈递抗原的任何II类MHC细胞。

[0253] 肽疫苗

[0254] 在本发明的范围之内还包括含有无细胞肽免疫原的疫苗,其中所述免疫原含有至少一种过敏原X,其被融合到溶酶体膜多肽(例如LAMP多肽或其同源物、直系同源物、变体或修饰的版本)的序列或用于将过敏原X靶向并转运到胞内体/溶酶体区室或溶酶体相关细胞器以结合到II类MHC分子或用于递送到另一个区室/细胞器以结合到II类MHC分子的吞饮受体的序列。优选地,过敏原X在所述区室/细胞器(或它被递送到的后续区室/细胞器)内被加工,以产生能够调节免疫应答的结合到II类MHC分子的过敏原X表位。

[0255] 所述嵌合疫苗也可以包含跨膜区和/或胞质尾区和溶酶体靶向区(优选地来自于LAMP多肽)和/或二亮氨酸结构域、Tyr基序、MR6结构域、富含脯氨酸的结构域和/或Ser-Val-Val结构域。所述嵌合疫苗也可以被结合在膜结构中,以便于将它给药至生物体的身体。例如,所述嵌合疫苗可以被并入到脂质体中,如美国专利号4,448,765中所述。

[0256] 在优选实施方式中,本发明的肽疫苗包含:(a)由表1中所示的SEQ ID NO:Z或SEQ ID NO:W中的任一多核苷酸编码的多肽;(b)包含表1中所示的SEQ ID NO:Y或SEQ ID NO:V的氨基酸序列的多肽;(c)包含腔内结构域(例如SEQ ID NO:2或3或如SEQ ID NO:4或5中所示)、表1中所示的SEQ ID NO:Y中的一者或多者和转运结构域(例如SEQ ID NO:1或如SEQ ID NO:4或5中所示)的多肽;(d)包含腔内结构域(例如SEQ ID NO:2或3或如SEQ ID NO:4或5中所示)、表1中所示的SEQ ID NO:Y中的一者或多者的多肽;(e)包含表1中所示的SEQ ID NO:Y中的一者或多者和转运结构域(例如SEQ ID NO:1或如SEQ ID NO:4或5中所示)的多肽;或(f)与(a)-(e)的任一多肽具有至少约60%、至少约70%、至少约75%、至少约80%、至少约85%、至少约90%、至少约95%、96%、97%、98%或99%同一性的多肽。

[0257] 当蛋白质或多肽要被用作免疫原时,它可以通过在重组细胞中表达上述任一个或多个DNA构建物来生产,或者它可以通过化学合成来制备。例如,可以使用Merrifield技术(Journal of American Chemical Society,vol.85,pp.2149-2154,1968)。

[0258] 用作为多核苷酸的LAMP构建物、所述LAMP构建物的编码蛋白质和/或细胞(例如表达本文中描述的LAMP构建物的抗原呈递细胞)初免,然后用过敏原X加强,是本发明的优选实施方式。在其他优选实施方式中,具体设想了使用本文中描述的LAMP构建物初免,然后用过敏原、优选为源自于过敏原X所源自的蛋白质的过敏原加强,并且其可用于产生甚至更加稳健的免疫应答,特别是从抗体库的多样性和滴度的观点来看。

[0259] 给药

[0260] 符合本发明的疫苗材料可以含有上文描述的免疫刺激性构建物,或者可以是表达所述免疫刺激性构建物的重组微生物或抗原呈递细胞。含有符合本发明的疫苗材料的组合

物的制备和这些组合物用于个体免疫接种的给药,按照本领域技术人员公知的免疫接种原则来完成。

[0261] 大量的这些材料可以通过培养含有表达本文中描述的嵌合过敏原X蛋白的复制子的重组或转化的细胞来获得。培养方法对于本领域技术人员来说是公知的,并且在上文引用的一个或多个文献中教导。所述疫苗材料通常通过重组或转化的细胞的培养来生产,并配制在通常是生理相容的水性溶液的可药用溶液或悬液中,或配制在包衣片剂、片剂、胶囊、栓剂或一次性针剂中,如本领域中所述,例如通过参考并入本文的美国专利号4,446,128。给药可以是任何适合的途径,包括口、直肠、鼻内或通过注射给药,其中注射可以是例如透皮、皮下、肌肉内或静脉内注射。

[0262] 所述疫苗组合物以足以在哺乳动物中诱导免疫应答的量给药到所述哺乳动物。给药的最低优选量是引发抗体形成到至少4倍于给药前存在的浓度所需的量。典型的初始给药剂量,在静脉内、肌肉内或皮下给药时为10-5000微克或者 10^5 至 10^{11} 噬斑形成单位的重组载体,尽管这个量可以由进行给药的临床医生调整,正如在疫苗或诱导免疫应答的其他药剂的给药中通常发生的。单次给药通常可以足以诱导免疫,但可以进行多次给药以确保或加强所述应答(例如使用重组生产的源自于过敏原X所源自的同一蛋白的疫苗)。

[0263] 疫苗一开始可以在非人类哺乳动物(例如小鼠或灵长动物)中试验。例如可以使用接种小鼠的免疫应答的测定来证实与野生型抗原相比更多的抗体、T细胞增殖和对靶向溶酶体的嵌合蛋白的细胞毒性T细胞应答。可以在恒河猴中评估嵌合蛋白,以确定在小鼠中高度有效的DNA疫苗制剂是否也引发适合的猴免疫应答。在一种情况下,每只猴每次免疫接种接受总共5mg DNA,IM递送并分为2个位点,其中免疫接种在第0天和第4、8和20周进行,任选额外的药剂。可以测量抗体应答、ADCC、CD4+和CD8+T-细胞的细胞因子产生、CD4+和CD 8+T-细胞的抗原特异性细胞因子染色,以监测对所述疫苗的免疫应答。

[0264] 符合本发明的制剂和给药的适合方法的进一步描述,可以在美国专利号4,454,116(构建物)、美国专利号4,681,762(重组细菌)以及美国专利号4,592,002和4,920,209(重组病毒)中找到。

[0265] 过敏症的治疗

[0266] 本发明提供了可用于治疗与过敏原X相关的花粉症的制剂。以前已确定,将编码过敏原的蛋白质编码序列的DNA质粒递送到动物,可以提高IFN- γ 产生并降低IL-4产生,这在治疗对所述特定过敏原过敏的动物中 useful。本发明提供了一种改进的疫苗组合物,用于治疗具有与过敏原X相关的过敏症的患者。本发明的融合蛋白具有与II类MHC囊泡交织的特定细胞内转运模式,并引起过敏原X向免疫系统的呈递提高,特别引起抗体应答增强。本发明提供的核酸和组合物对执行过敏症免疫疗法有用。

[0267] 本发明提供了一种当给药到细胞时引起特异性抗体应答提高的制剂。对过敏原X的抗体应答的提高,对治疗IgE介导的过敏疾病有用。IgE具有与其细胞限制和结合同族过敏原后导致的细胞内信号传导相关的某些性质。当B细胞接收到由Th2细胞分泌的IL-4时,产生针对过敏原的IgE。这帮助指导B细胞产生IgE类别的抗体。在被B细胞分泌后,IgE结合到它的由肥大细胞和嗜嗜红细胞表达的高亲和性受体Fc- ϵ RI,导致这些细胞和所述动物变得对将来的过敏原暴露敏化。结果,可以在摄入、吸入过敏原或与过敏原粘膜接触后引发过敏症的症状。由于抗体的结合性质,已提出减轻过敏症症状的一种方式是通过用其他抗体

类别竞争来整合可用于被IgE结合的游离过敏原。具体来说,已提出增加IgG的过敏症制剂是减轻过敏疾病的途径。本文描述的发明诱导IgG产生的增强,从而以临床上显著的方式引起IgE与IgG的比率的降低。

[0268] 在特别优选的实施方式中,本发明提供了一种治疗或预防针对过敏原X的过敏症的方法。在一种优选方法中,多核苷酸编码本文中描述的过敏原X和溶酶体相关膜多肽(例如LAMP多肽、其同源物、直系同源物、变体或修饰形式)的腔内转运结构域或吞饮受体的腔内转运结构域以及LAMP多肽、其同源物、直系同源物、变体或修饰形式或吞饮受体的胞质靶向结构域,所述靶向结构域用于将所述过敏原X抗原靶向到胞内体/溶酶体区室或溶酶体相关细胞器并用于与所述区室/细胞器内或所述抗原被递送到的其他区室/细胞器内的II类MHC分子结合。这些嵌合DNA分子可以编码如上所述的其他结构域序列(例如编码跨膜结构域、信号序列、用于靶向到胞内体/溶酶体区室或溶酶体相关细胞器的胞质结构域、二亮氨酸结构域、Tyr基序结构域、富含脯氨酸的结构域、Ser-Val-Val结构域等的序列)。

[0269] 更通常地,在一个实施方式中,本发明提供了一种用于在哺乳动物中调节针对过敏原X的免疫应答(即刺激、增强或减弱这种应答)的疫苗组合物。优选地,所述组合物包含疫苗载体,其中所述载体含有编码蛋白质的嵌合DNA区段,所述蛋白质含有过敏原X和溶酶体相关膜多肽(例如LAMP多肽、其同源物、直系同源物、变体或修饰形式)的腔内转运结构域或吞饮受体的腔内转运结构域以及靶向结构域、例如LAMP多肽、其同源物、直系同源物、变体或修饰形式或吞饮受体的胞质靶向结构域,所述靶向结构域用于将所述抗原靶向到胞内体/溶酶体区室或溶酶体相关细胞器并用于与所述区室/细胞器内或所述抗原被递送到的其他区室/细胞器内的II类MHC分子结合。这些嵌合DNA分子可以编码如上所述的其他结构域序列(例如编码跨膜结构域、信号序列、用于靶向到胞内体/溶酶体区室或溶酶体相关细胞器的胞质结构域、二亮氨酸结构域、Tyr基序结构域、富含脯氨酸的结构域、Ser-Val-Val结构域等的序列)。

[0270] 试剂盒

[0271] 本发明还包括便于执行本文中描述的方法的试剂盒。在一种情况下,试剂盒包含如上所述的核酸载体和用于接受所述载体的细胞。所述试剂盒可以另外包含用于将所述细胞工程化改造成专业APC的一种或多种核酸。然而,在一种情况下,所述细胞是专业APC。所述细胞可以表达或不表达辅助刺激分子。在优选情况下,当所述细胞不表达辅助刺激分子时,由所述载体编码的抗原是自体抗原。在另一种情况下,提供了表达不同MHC分子(例如已知在人类中表达的MHC分子)的一组细胞。在另一种情况下,所述试剂盒包含促进所述载体进入到细胞中的试剂(例如基于脂质的制剂、病毒包装材料、细胞等)。在另一种情况下,提供了对所述载体所编码的抗原特异的一种或多种T细胞系,以验证所述载体引发、调节或增强免疫应答的能力。

实施例

[0272] 现在将参考下面的实施例进一步说明本发明。应该认识到,下述内容仅仅是示例性的,并且可以对细节作出修改并仍落于本发明的范围之内。

[0273] 实施例1-过敏原X构建物的构建

[0274] 构建了编码如表1中所述的嵌合过敏原X疫苗的大量不同核酸构建物。包含SEQ ID

NO:Z的多核苷酸的质粒使用本领域中公知的技术来设计。具体来说,将包含编码基因融合物的多核苷酸的质粒插入到NTC 8382载体中,所述基因融合物包含一部分LAMP-1腔内结构域(SEQ ID NO:2)融合到过敏原X(SEQ ID NO:Y),然后融合到一部分LAMP-1跨膜/胞质尾区(SEQ ID NO:1)。这些构建的多核苷酸的代表性实例被提供为SEQ ID NO:W。将得到的构建物进行序列确认并确认蛋白质表达。

[0275] 实施例2-小鼠对编码过敏原X的质粒的免疫应答的评估

[0276] 使用在Su,Yan,Michael Connolly,Anthony Marketon和Teri Heiland,“用于日本红雪松过敏症的CryJ-LAMP DNA疫苗在鼠类模型中诱导稳健的Th1型免疫应答”(CryJ-LAMP DNA Vaccines for Japanese Red Cedar Allergy Induce Robust Th1-Type Immune Responses in Murine Model),Journal of Immunology Research 2016(2016): 1-15中描述的测定法,试验了如实施例1中所述的过敏原X抗原构建物调节免疫应答的能力。

[0277] 每种构建物的结果报告在表3中。除非另有指明,否则“对照”构建物是缺少过敏原序列的载体骨架。

[0278]

表3	
有活性	微弱/无活性
Cor a 1 (SEQ ID NO: 7) IgG1: 疫苗接种组: 4x10 ⁵ 终点滴度 IgG2a: 疫苗接种组: 3.5x10 ⁶ 终点滴度	IgG1: 对照组: 2.1x10 ⁴ 终点滴度 IgG2a: 对照组: 未检出
在移除全长Cor a 9的319-480aa氨基酸以产生SEQ ID NO: 9后: IgG1 疫苗接种组: 5.7x10 ⁵ 终点滴度 对照组: 未检出 IgG2a 疫苗接种组: 6.2x10 ⁵ 终点滴度 对照组: 未检出 移除特异性提高IgG2a:IgG1比率	除去之前 (包括319-480aa氨基酸的全长 Cor a 9序列) IgG1 疫苗接种组: 1.2x10 ⁶ 终点滴度 对照组: 2.7x10 ⁴ 终点滴度 IgG2a 疫苗接种组: 7.5x10 ⁵ 终点滴度 对照组: 未检出

[0279]

Cor a 1 – Gly4 – Cor a 9 (SEQ ID NO: 11) IgG1: 疫苗接种组: 1x10 ⁵ 终点滴度 IgG2a: 疫苗接种组: 3.3x10 ⁵ 终点滴度	IgG1: 对照组: 2.2x10 ³ 终点滴度 IgG2a: 对照组: 2.7x10 ³ 终点滴度
移除Pru du 6序列的aa 368-551以产生SEQ ID NO: 13: 移除后: IgG1 疫苗接种组: 1.6x10 ⁵ 终点滴度 对照组: 1.3x10 ⁴ 终点滴度 IgG2a 疫苗接种组: 5.5x10 ⁵ 终点滴度 对照组: 未检出 碱性链(368-551 aa)的移除改进了抗体应答并特异性提高IgG2a:IgG1的比率	带有aa 368-551的全长Pru du 6序列。 移除前: IgG1 疫苗接种组: 9.9x10 ⁵ 终点滴度 对照组: 1.3x10 ⁴ 终点滴度 IgG2a 疫苗接种组: 2.8x10 ⁵ 终点滴度 对照组: 未检出
Ana o 1 (SEQ ID NO: 15) IgG1: 疫苗接种组: 1.2x10 ⁶ 终点滴度	IgG1: 对照组: 4.9x10 ⁴ 终点滴度 IgG2a: 对照组: 未检出

[0280]

IgG2a: 疫苗接种组: 6×10^6 终点滴度	
Ana o 2 (SEQ ID NO: 17) IgG1: 疫苗接种组: 8.1×10^5 终点滴度 IgG2a: 疫苗接种组: 4×10^6 终点滴度	IgG1: 对照组: 1.6×10^4 终点滴度 IgG2a: 对照组: 未检出
Ana o 3 (SEQ ID NO: 19) IgG1: 疫苗接种组: 2×10^5 终点滴度 IgG2a: 疫苗接种组: 1.4×10^6 终点滴度	IgG1: 对照组: 5.4×10^3 终点滴度 IgG2a: 对照组: 未检出
Ana 0 2 -Gly4- Ana 0 1 - Gly4- Ana 0 3 (SEQ ID NO: 21) IgG1: 疫苗接种组: 5.5×10^5 终点滴度 IgG2a: 疫苗接种组: 3.4×10^6 终点滴度	IgG1: 对照组: 3.7×10^4 终点滴度 IgG2a: 对照组: 未检出
Jug n1 (SEQ ID NO: 23) IgG1: 疫苗接种组: 6×10^5 终点滴度 IgG2a: 疫苗接种组: 1.7×10^6 终点滴度	IgG1: 对照组: 7×10^4 终点滴度 IgG2a: 对照组: 1×10^3 终点滴度
Jug r 2 (SEQ ID NO: 25) IgG1: 疫苗接种组: 9.9×10^5 终点滴度 IgG2a: 疫苗接种组: 4.2×10^6 终点滴度	IgG1: 对照组: 7×10^4 终点滴度 IgG2a: 对照组: 2×10^3 终点滴度
Jug n1 - Gly4 - Jug r 2 (SEQ ID NO: 27) IgG1: 疫苗接种组: 2×10^5 终点滴度	IgG1: 对照组: 1×10^4 终点滴度 IgG2a: 对照组: 未检出

[0281]

IgG2a: 疫苗接种组: 1.7×10^5 终点滴度	
Amb a 1 (SEQ ID NO: 29) IgG1: 疫苗接种组: 4×10^5 终点滴度 IgG2a: 疫苗接种组: 3.5×10^6 终点滴度	IgG1: 对照组: 2.1×10^4 终点滴度 IgG2a: 对照组: 未检出
Bet v 1-A (SEQ ID NO: 33) IgG1: 疫苗接种组: 4×10^5 终点滴度 IgG2a: 疫苗接种组: 2×10^6 终点滴度	IgG1: 对照组: 5×10^3 终点滴度 IgG2a: 对照组: 5×10^3 终点滴度
Can f 1 (SEQ ID NO: 37) IgG1: 疫苗接种组: 4×10^5 终点滴度 IgG2a: 疫苗接种组: 2×10^6 终点滴度	IgG1: 对照组: 1.8×10^4 终点滴度 IgG2a: 对照组: 5×10^3 终点滴度
Cyn d 1 (SEQ ID NO: 41) IgG1: 疫苗接种组: 5×10^5 终点滴度 IgG2a: 疫苗接种组: 6×10^6 终点滴度	IgG1: 对照组: 4×10^4 终点滴度 IgG2a: 对照组: 5×10^3 终点滴度
Der F 1 (19-321) (SEQ ID NO: 45) IgG1: 疫苗接种组: 1.5×10^5 终点滴度 IgG2a: 疫苗接种组: 2×10^6 终点滴度	IgG1: 使用Der F 1 (99-321) (SEQ ID NO: 49) 的疫苗接种组: 5×10^4 终点滴度 对照组: 未检出

[0282]

	IgG2a 使用Der F 1 (99-321) (SEQ ID NO: 49) 的疫苗接种组: 1x10⁶终点滴度 对照组: 未检出
Der P2 (SEQ ID NO: 53) IgG1: 疫苗接种组: 1x10⁵终点滴度 IgG2a: 疫苗接种组: 1x10⁶终点滴度	IgG1: 对照组: 8x10³终点滴度 IgG2a: 对照组: 未检出
DerF2 (SEQ ID NO: 57) IgG1: 疫苗接种组: 6x10⁵终点滴度 IgG2a: 疫苗接种组: 1.2x10⁶终点滴度	IgG1: 对照组: 未检出 IgG2a: 对照组: 未检出
在缺失DerP1序列的第27-50位氨基酸 (SEQ ID NO: 61) 之后: IgG1 疫苗接种组: 3.5x10³终点滴度 对照组: 未检出 IgG2a 疫苗接种组: 4x10⁵终点滴度	在缺失DerP1序列的第27-50位氨基酸之前: IgG1 疫苗接种组: 2.3x10⁵终点滴度 对照组: 1.1x10⁴ IgG2a 疫苗接种组: 9.3x10⁴终点滴度 对照组: 未检出

[0283]

对照组：未检出	
移除序列改进了抗体应答并特异性提高IgG2a:IgG1的比率	
Fel D 1 (SEQ ID NO: 66) IgG1: 疫苗接种组: 4×10^5 终点滴度 IgG2a: 疫苗接种组: 2×10^6 终点滴度	IgG1: 对照组: 1.4×10^3 终点滴度 IgG2a: 对照组: 未检出
Fel d 4 (SEQ ID NO: 74) IgG1: 疫苗接种组: 2.5×10^4 终点滴度 IgG2a: 疫苗接种组: 7×10^4 终点滴度	IgG1: 对照组: 未检出 IgG2a: 对照组: 未检出
Lit v 1 (SEQ ID NO: 78) IgG1: 疫苗接种组: 6×10^5 终点滴度 IgG2a: 疫苗接种组: 1.1×10^6 终点滴度	IgG1: 对照组: 4.2×10^4 终点滴度 IgG2a: 对照组: 1.9×10^4 终点滴度
Lol p 5a (SEQ ID NO: 82) IgG1: 疫苗接种组: 1×10^6 终点滴度 IgG2a: 疫苗接种组: 1.5×10^6 终点滴度	IgG1: 对照组: 1.8×10^5 终点滴度 IgG2a: 对照组: 未检出
Phl p 1 (SEQ ID NO: 86) IgG1: 疫苗接种组: 5×10^5 终点滴度 IgG2a: 疫苗接种组: 1.5×10^6 终点滴度	IgG1: 对照组: 未检出 IgG2a: 对照组: 未检出

[0284]

Phl p 5 (SEQ ID NO: 90) IgG1: 疫苗接种组: 1×10^6 终点滴度 IgG2a: 疫苗接种组: 3×10^6 终点滴度	IgG1: 对照组: 5×10^4 终点滴度 IgG2a: 对照组: 未检出
Der f 15 (SEQ ID NO: 93) IgG1: 疫苗接种组: 1.2×10^6 终点滴度 IgG2a: 疫苗接种组: 4.4×10^6 终点滴度	IgG1: 对照组: 1×10^5 终点滴度 IgG2a: 对照组: 2.7×10^3 终点滴度
Der f 18 (SEQ ID NO: 94) IgG1: 疫苗接种组: 1.2×10^6 终点滴度 IgG2a: 疫苗接种组: 4.4×10^6 终点滴度	IgG1: 对照组: 1×10^5 终点滴度 IgG2a: 对照组: 2.7×10^3 终点滴度
Cte f 1 (SEQ ID NO: 96) IgG1: 疫苗接种组: 1.3×10^6 终点滴度 IgG2a: 疫苗接种组: 2.9×10^6 终点滴度	IgG1: 对照组: 1×10^6 终点滴度 IgG2a: 对照组: 2.3×10^5 终点滴度
Der F1-Der F2 (SEQ ID NO: 110) <u>F1</u> IgG1: 疫苗接种组: 1.8×10^5 终点滴度 IgG2: 疫苗接种组: 1.0×10^6 终点滴度 <u>F2</u> IgG1: 疫苗接种组: 9.4×10^3 终点滴度 IgG2: 疫苗接种组: 6.0×10^5 终点滴度	

[0285]

	Der F15 – Der F18 (SEQ ID NO: 109) F15 IgG1: 疫苗接种组: 3.8x10⁴终点滴度 IgG2: 疫苗接种组: 4.0x10⁵终点滴度 F18 IgG1: 疫苗接种组: 1.2x10⁵终点滴度 IgG2: 疫苗接种组: 1.1x10⁶终点滴度

[0286] 将6至8周龄雌性Ba1b/c小鼠用对照载体或疫苗治疗,并在第0、7和14天通过Bioject真皮内递送进行免疫接种。小鼠在第42天在铝佐剂存在下用重组过敏原(5μg/小

鼠)加强,并在第21、35和56天取血。

[0287] 将血清样品在含有1%BSA的PBS中稀释1:100(第21天)、1:2000(第35天)或1:5000(第56天)倍。将第56天的样品用7个点的1:3连续稀释进一步稀释,以测量终点抗体滴度。为了检测IgE,将血清用琼脂糖-蛋白G(Thermo Fisher Scientific,Rockford,IL)处理50分钟,然后将1:20稀释的样品装载到ELISA板。样品用山羊抗小鼠IgG1-HRP、山羊抗小鼠IgG2a-HRP(Southern Biotech,Birmingham,Al)或大鼠抗小鼠IgE-生物素(R35-118,BD Pharmingen,San Jose,CA),然后用Pierce链亲和素-HRP(Thermo Fisher Scientific,Rockford,IL)检测。反应用SureBlue TMB底物显色并用TMB终止溶液终止。使用Epoch ELISA读板器(BioTek,Winooski,VT)读板(OD450)。终点滴度通过减去背景平均(PBS)读数两次来确定。每个组的终点滴度或OD450值的平均值和标准误差使用Excel统计函数来分析。IgE数据使用Student T检验来分析。检验是双尾的,并且p值 ≤ 0.05 被认为是显著的。

[0288] 对于本领域普通技术人员来说,可以对本文中描述的内容进行改变、修改和其他操作,而不背离本发明和权利要求书的精神和范围。指明的所有专利、专利申请、国际申请和参考文献明确地以其整体通过引用并入本文。

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      Ile Asn Val Gly Leu Arg Arg Gln Gln Gln Arg Tyr Phe Gly
          1             5             10
gag tgc aat ctg gac cgg ctg aac gct ctg gaa ccc acc aac aga atc 96
Glu Cys Asn Leu Asp Arg Leu Asn Ala Leu Glu Pro Thr Asn Arg Ile
15             20             25             30
gag gcc gag gct tgc cag atc gag agc tgg gac cac aac gac cag cag 144
Glu Ala Glu Ala Cys Gln Ile Glu Ser Trp Asp His Asn Asp Gln Gln
          35             40             45
ttc cag tgt gct ggc gtg gcc gtg atc aga cgg acc atc gag ccc aac 192
Phe Gln Cys Ala Gly Val Ala Val Ile Arg Arg Thr Ile Glu Pro Asn
          50             55             60
gga ctg ctg ctg ccc cag tac agc aat gcc ccc gag ctg atc tac atc 240
Gly Leu Leu Leu Pro Gln Tyr Ser Asn Ala Pro Glu Leu Ile Tyr Ile
          65             70             75
gag cgg ggc aga gga atc acc ggc gtg ctg ttt ccc ggc tgc ccc gag 288
Glu Arg Gly Arg Gly Ile Thr Gly Val Leu Phe Pro Gly Cys Pro Glu
          80             85             90
aca ttc gag gac cct cag cag cag agc cag caa ggc cag aga caa ggc 336
Thr Phe Glu Asp Pro Gln Gln Gln Ser Gln Gln Gly Gln Arg Gln Gly
95             100             105             110
caa ggc cag tcc cag aga agc gag caa gac cgg cac cag aag atc cgg 384
Gln Gly Gln Ser Gln Arg Ser Glu Gln Asp Arg His Gln Lys Ile Arg
          115             120             125
cac ttc aga gag ggc gac atc att gct ctg cca gcc ggc gtg gcc cac 432
His Phe Arg Glu Gly Asp Ile Ile Ala Leu Pro Ala Gly Val Ala His
          130             135             140
tgg tgc tac aat gat ggc gat agc ccc gtc gtg acc gtg tct ctg ctg 480
Trp Cys Tyr Asn Asp Gly Asp Ser Pro Val Val Thr Val Ser Leu Leu
          145             150             155
cac acc aac aac tac gcc aac cag ctg gac gag aac ccc aga cac ttc 528
His Thr Asn Asn Tyr Ala Asn Gln Leu Asp Glu Asn Pro Arg His Phe
          160             165             170
tat ctg gcc ggc aac ccc gac gac gag cac cag agg caa ggg cag cag 576
Tyr Leu Ala Gly Asn Pro Asp Asp Glu His Gln Arg Gln Gly Gln Gln
175             180             185             190

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cag ttc ggc cag aga aga agg cag cag cag cac agc cat ggc gag caa 624
 Gln Phe Gly Gln Arg Arg Arg Gln Gln Gln His Ser His Gly Glu Gln
 195 200 205
 ggc gag caa gag cag caa ggc gag ggc aac aac gtg ttc agc ggc ttc 672
 Gly Glu Gln Glu Gln Gln Gly Glu Gly Asn Asn Val Phe Ser Gly Phe
 210 215 220
 gac gcc gag ttt ctg gcc gac gcc ttc aac gtg gac gtg gac aca gcc 720
 Asp Ala Glu Phe Leu Ala Asp Ala Phe Asn Val Asp Val Asp Thr Ala
 225 230 235
 aga cgg ctg cag tcc aac caa gac aag cgg cgg aac atc gtg aaa gtg 768
 Arg Arg Leu Gln Ser Asn Gln Asp Lys Arg Arg Asn Ile Val Lys Val
 240 245 250
 gaa ggc cgg ctc caa gtc gtg cgg ccc gag aga tct aga caa gag tgg 816
 Glu Gly Arg Leu Gln Val Val Arg Pro Glu Arg Ser Arg Gln Glu Trp
 255 260 265 270
 gag cgg caa gag cgg caa gaa cgc gag agc gag caa gag aga gag cgg 864
 Glu Arg Gln Glu Arg Gln Glu Arg Glu Ser Glu Gln Glu Arg Glu Arg
 275 280 285
 cag aga agg caa ggc ggc aga ggc aga gat gtg aac gaatt 905
 Gln Arg Arg Gln Gly Gly Arg Gly Arg Asp Val Asn
 290 295

<210> 9

<211> 298

<212> PRT

<213> 欧榛(*Corylus avellana*)

<400> 9

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

100	105	110
Gln Ser Gln Arg Ser Glu Gln Asp Arg His Gln Lys Ile Arg His Phe		
115	120	125
Arg Glu Gly Asp Ile Ile Ala Leu Pro Ala Gly Val Ala His Trp Cys		
130	135	140
Tyr Asn Asp Gly Asp Ser Pro Val Val Thr Val Ser Leu Leu His Thr		
145	150	155
Asn Asn Tyr Ala Asn Gln Leu Asp Glu Asn Pro Arg His Phe Tyr Leu		
165	170	175
Ala Gly Asn Pro Asp Asp Glu His Gln Arg Gln Gly Gln Gln Gln Phe		
180	185	190
Gly Gln Arg Arg Arg Gln Gln Gln His Ser His Gly Glu Gln Gly Glu		
195	200	205
Gln Glu Gln Gln Gly Glu Gly Asn Asn Val Phe Ser Gly Phe Asp Ala		
210	215	220
Glu Phe Leu Ala Asp Ala Phe Asn Val Asp Val Asp Thr Ala Arg Arg		
225	230	235
Leu Gln Ser Asn Gln Asp Lys Arg Arg Asn Ile Val Lys Val Glu Gly		
245	250	255
Arg Leu Gln Val Val Arg Pro Glu Arg Ser Arg Gln Glu Trp Glu Arg		
260	265	270
Gln Glu Arg Gln Glu Arg Glu Ser Glu Gln Glu Arg Glu Arg Gln Arg		
275	280	285
Arg Gln Gly Gly Arg Gly Arg Asp Val Asn		
290	295	

<210> 10

<211> 1410

<212> DNA

<213> 人工序列

<220>

<223> 合成构建物

<220>

<221> CDS

<222> (13) .. (1398)

<400> 10

catatgctcg ag atg ggc gtg ttc tgc tac gag gac gag gcc aca agc gtg 51

Met Gly Val Phe Cys Tyr Glu Asp Glu Ala Thr Ser Val

1

5

10

atc cct ccc gcc aga ctg ttc aag agc ttc gtg ctg gac gcc gac aat 99

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Ile Pro Pro Ala Arg Leu Phe Lys Ser Phe Val Leu Asp Ala Asp Asn
  15                      20                      25
ctg atc ccc aaa gtg gcc ccc cag cac ttc acc agc gcc gag aat ctg 147
Leu Ile Pro Lys Val Ala Pro Gln His Phe Thr Ser Ala Glu Asn Leu
  30                      35                      40                      45
gaa ggc aat ggc gga ccc ggc acc atc aag aag atc aca ttc gcc gag 195
Glu Gly Asn Gly Gly Pro Gly Thr Ile Lys Lys Ile Thr Phe Ala Glu
                      50                      55                      60
ggc aac gag ttc aag tac atg aag cac aaa gtg gaa gag atc gac cac 243
Gly Asn Glu Phe Lys Tyr Met Lys His Lys Val Glu Glu Ile Asp His
                      65                      70                      75
gcc aac ttc aag tac tgc tac agc atc atc gaa ggc ggc cct ctg ggc 291
Ala Asn Phe Lys Tyr Cys Tyr Ser Ile Ile Glu Gly Gly Pro Leu Gly
                      80                      85                      90
cac aca ctg gaa aag atc agc tac gag atc aag atg gcc gct gcc cct 339
His Thr Leu Glu Lys Ile Ser Tyr Glu Ile Lys Met Ala Ala Ala Pro
                      95                      100                      105
cac ggc gga ggc agc att ctg aag atc acc agc aag tac cac acc aag 387
His Gly Gly Gly Ser Ile Leu Lys Ile Thr Ser Lys Tyr His Thr Lys
110                      115                      120                      125
ggc aac gcc agc atc aac gag gaa gaa atc aag gcc ggc aaa gag aaa 435
Gly Asn Ala Ser Ile Asn Glu Glu Glu Ile Lys Ala Gly Lys Glu Lys
                      130                      135                      140
gcc gcc gga ctg ttt aag gcc gtg gaa gcc tat ctg ctg gcc cac ccc 483
Ala Ala Gly Leu Phe Lys Ala Val Glu Ala Tyr Leu Leu Ala His Pro
                      145                      150                      155
gat gcc tac ggc gga ggg ggc atc aac gtg gga ctg cgg aga cag cag 531
Asp Ala Tyr Gly Gly Gly Gly Ile Asn Val Gly Leu Arg Arg Gln Gln
                      160                      165                      170
cag cgg tac ttc ggc gag tgc aat ctg gac cgg ctg aac gct ctg gaa 579
Gln Arg Tyr Phe Gly Glu Cys Asn Leu Asp Arg Leu Asn Ala Leu Glu
                      175                      180                      185
ccc acc aac aga atc gag gcc gag gct tgc cag atc gag agc tgg gac 627
Pro Thr Asn Arg Ile Glu Ala Glu Ala Cys Gln Ile Glu Ser Trp Asp
190                      195                      200                      205
cac aac gac cag cag ttc cag tgt gct ggc gtg gcc gtg atc aga cgg 675
His Asn Asp Gln Gln Phe Gln Cys Ala Gly Val Ala Val Ile Arg Arg
                      210                      215                      220
acc atc gag ccc aac gga ctg ctg ctg ccc cag tac agc aat gcc ccc 723

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Thr Ile Glu Pro Asn Gly Leu Leu Leu Pro Gln Tyr Ser Asn Ala Pro			
225	230	235	
gag ctg atc tac atc gag cgg ggc aga gga atc acc ggc gtg ctg ttt	771		
Glu Leu Ile Tyr Ile Glu Arg Gly Arg Gly Ile Thr Gly Val Leu Phe			
240	245	250	
ccc ggc tgc ccc gag aca ttc gag gac cct cag cag cag agc cag caa	819		
Pro Gly Cys Pro Glu Thr Phe Glu Asp Pro Gln Gln Gln Ser Gln Gln			
255	260	265	
ggc cag aga caa ggc caa ggc cag tcc cag aga agc gag caa gac cgg	867		
Gly Gln Arg Gln Gly Gln Gly Gln Ser Gln Arg Ser Glu Gln Asp Arg			
270	275	280	285
cac cag aag atc cgg cac ttc aga gag ggc gac atc att gct ctg cca	915		
His Gln Lys Ile Arg His Phe Arg Glu Gly Asp Ile Ile Ala Leu Pro			
290	295	300	
gcc ggc gtg gcc cac tgg tgc tac aat gat ggc gat agc ccc gtc gtg	963		
Ala Gly Val Ala His Trp Cys Tyr Asn Asp Gly Asp Ser Pro Val Val			
305	310	315	
acc gtg tct ctg ctg cac acc aac aac tac gcc aac cag ctg gac gag	1011		
Thr Val Ser Leu Leu His Thr Asn Asn Tyr Ala Asn Gln Leu Asp Glu			
320	325	330	
aac ccc aga cac ttc tat ctg gcc ggc aac ccc gac gac gag cac cag	1059		
Asn Pro Arg His Phe Tyr Leu Ala Gly Asn Pro Asp Asp Glu His Gln			
335	340	345	
agg caa ggg cag cag cag ttc ggc cag aga aga agg cag cag cag cac	1107		
Arg Gln Gly Gln Gln Gln Phe Gly Gln Arg Arg Arg Gln Gln Gln His			
350	355	360	365
agc cat ggc gag caa ggc gag caa gag cag caa ggc gag ggc aac aac	1155		
Ser His Gly Glu Gln Gly Glu Gln Glu Gln Gln Gly Glu Gly Asn Asn			
370	375	380	
gtg ttc agc ggc ttc gac gcc gag ttt ctg gcc gac gcc ttc aac gtg	1203		
Val Phe Ser Gly Phe Asp Ala Glu Phe Leu Ala Asp Ala Phe Asn Val			
385	390	395	
gac gtg gac aca gcc aga cgg ctg cag tcc aac caa gac aag cgg cgg	1251		
Asp Val Asp Thr Ala Arg Arg Leu Gln Ser Asn Gln Asp Lys Arg Arg			
400	405	410	
aac atc gtg aaa gtg gaa ggc cgg ctc caa gtc gtg cgg ccc gag aga	1299		
Asn Ile Val Lys Val Glu Gly Arg Leu Gln Val Val Arg Pro Glu Arg			
415	420	425	
tct aga caa gag tgg gag cgg caa gag cgg caa gaa cgc gag agc gag	1347		

Ser Arg Gln Glu Trp Glu Arg Gln Glu Arg Gln Glu Arg Glu Ser Glu
 430 435 440 445
 caa gag aga gag cgg cag aga agg caa ggc ggc aga ggc aga gat gtg 1395
 Gln Glu Arg Glu Arg Gln Arg Arg Gln Gly Gly Arg Gly Arg Asp Val
 450 455 460
 aac gaattcgtcg ac 1410
 Asn
 <210> 11
 <211> 462
 <212> PRT
 <213> 人工序列
 <220>
 <223> 合成构建物
 <400> 11
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 1 5 10 15
 Ala Arg Leu Phe Lys Ser Phe Val Leu Asp Ala Asp Asn Leu Ile Pro
 20 25 30
 Lys Val Ala Pro Gln His Phe Thr Ser Ala Glu Asn Leu Glu Gly Asn
 35 40 45
 Gly Gly Pro Gly Thr Ile Lys Lys Ile Thr Phe Ala Glu Gly Asn Glu
 50 55 60
 Phe Lys Tyr Met Lys His Lys Val Glu Glu Ile Asp His Ala Asn Phe
 65 70 75 80
 Lys Tyr Cys Tyr Ser Ile Ile Glu Gly Gly Pro Leu Gly His Thr Leu
 85 90 95
 Glu Lys Ile Ser Tyr Glu Ile Lys Met Ala Ala Ala Pro His Gly Gly
 100 105 110
 Gly Ser Ile Leu Lys Ile Thr Ser Lys Tyr His Thr Lys Gly Asn Ala
 115 120 125
 Ser Ile Asn Glu Glu Glu Ile Lys Ala Gly Lys Glu Lys Ala Ala Gly
 130 135 140
 Leu Phe Lys Ala Val Glu Ala Tyr Leu Leu Ala His Pro Asp Ala Tyr
 145 150 155 160
 Gly Gly Gly Gly Ile Asn Val Gly Leu Arg Arg Gln Gln Gln Arg Tyr
 165 170 175
 Phe Gly Glu Cys Asn Leu Asp Arg Leu Asn Ala Leu Glu Pro Thr Asn
 180 185 190
 Arg Ile Glu Ala Glu Ala Cys Gln Ile Glu Ser Trp Asp His Asn Asp

195	200	205
Gln Gln Phe Gln Cys Ala Gly Val Ala Val Ile Arg Arg Thr Ile Glu		
210	215	220
Pro Asn Gly Leu Leu Leu Pro Gln Tyr Ser Asn Ala Pro Glu Leu Ile		
225	230	235
Tyr Ile Glu Arg Gly Arg Gly Ile Thr Gly Val Leu Phe Pro Gly Cys		
245	250	255
Pro Glu Thr Phe Glu Asp Pro Gln Gln Gln Ser Gln Gln Gly Gln Arg		
260	265	270
Gln Gly Gln Gly Gln Ser Gln Arg Ser Glu Gln Asp Arg His Gln Lys		
275	280	285
Ile Arg His Phe Arg Glu Gly Asp Ile Ile Ala Leu Pro Ala Gly Val		
290	295	300
Ala His Trp Cys Tyr Asn Asp Gly Asp Ser Pro Val Val Thr Val Ser		
305	310	315
Leu Leu His Thr Asn Asn Tyr Ala Asn Gln Leu Asp Glu Asn Pro Arg		
325	330	335
His Phe Tyr Leu Ala Gly Asn Pro Asp Asp Glu His Gln Arg Gln Gly		
340	345	350
Gln Gln Gln Phe Gly Gln Arg Arg Arg Gln Gln Gln His Ser His Gly		
355	360	365
Glu Gln Gly Glu Gln Glu Gln Gln Gly Glu Gly Asn Asn Val Phe Ser		
370	375	380
Gly Phe Asp Ala Glu Phe Leu Ala Asp Ala Phe Asn Val Asp Val Asp		
385	390	395
Thr Ala Arg Arg Leu Gln Ser Asn Gln Asp Lys Arg Arg Asn Ile Val		
405	410	415
Lys Val Glu Gly Arg Leu Gln Val Val Arg Pro Glu Arg Ser Arg Gln		
420	425	430
Glu Trp Glu Arg Gln Glu Arg Gln Glu Arg Glu Ser Glu Gln Glu Arg		
435	440	445
Glu Arg Gln Arg Arg Gln Gly Gly Arg Gly Arg Asp Val Asn		
450	455	460

<210> 12

<211> 1053

<212> DNA

<213> 扁桃(Prunus dulcis)

<220>

<221> CDS

<222> (7) .. (1047)

<400> 12

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      1              5              10
aac cag ctg caa gcc aga gag ccc gac aac cgg att caa gcc gag gcc 96
      Asn Gln Leu Gln Ala Arg Glu Pro Asp Asn Arg Ile Gln Ala Glu Ala
      15              20              25              30
ggc cag atc gag aca tgg aac ttc aac caa gag gac ttc cag tgt gcc 144
      Gly Gln Ile Glu Thr Trp Asn Phe Asn Gln Glu Asp Phe Gln Cys Ala
      35              40              45
ggc gtg gcc gcc agc aga atc acc atc cag cgg aac gga ctg cat ctg 192
      Gly Val Ala Ala Ser Arg Ile Thr Ile Gln Arg Asn Gly Leu His Leu
      50              55              60
ccc agc tac agc aac gcc ccc cag ctg atc tac atc gtg caa gcc aga 240
      Pro Ser Tyr Ser Asn Ala Pro Gln Leu Ile Tyr Ile Val Gln Gly Arg
      65              70              75
ggc gtg ctg ggc gcc gtg ttt agc gga tgc ccc gag aca ttc gag gaa 288
      Gly Val Leu Gly Ala Val Phe Ser Gly Cys Pro Glu Thr Phe Glu Glu
      80              85              90
agc cag cag agc agc cag caa ggc cgg cag caa gag caa gaa caa gag 336
      Ser Gln Gln Ser Ser Gln Gln Gly Arg Gln Gln Glu Gln Glu Gln Glu
      95              100             105             110
aga caa cag cag cag caa ggg gag caa ggc aga cag caa gga cag caa 384
      Arg Gln Gln Gln Gln Gln Gly Glu Gln Gly Arg Gln Gln Gly Gln Gln
      115             120             125
gag cag cag caa gag cgc caa gga cgg cag caa ggg cgc cag cag caa 432
      Glu Gln Gln Gln Glu Arg Gln Gly Arg Gln Gln Gly Arg Gln Gln Gln
      130             135             140
gaa gag ggc aga cag caa gaa cag cag caa ggc cag caa ggg cgg cct 480
      Glu Glu Gly Arg Gln Gln Glu Gln Gln Gln Gly Gln Gln Gly Arg Pro
      145             150             155
cag cag cag cag cag ttc cgg cag ttc gac cgg cac cag aaa acc cgg 528
      Gln Gln Gln Gln Gln Phe Arg Gln Phe Asp Arg His Gln Lys Thr Arg
      160             165             170
cgg atc aga gaa ggc gac gtg gtg gct att cca gcc ggg gtg gcc tac 576
      Arg Ile Arg Glu Gly Asp Val Val Ala Ile Pro Ala Gly Val Ala Tyr
      175             180             185             190
tgg tcc tac aac gac ggc gac caa gaa ctg gtg gcc gtg aat ctg ttc 624

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Trp Ser Tyr Asn Asp Gly Asp Gln Glu Leu Val Ala Val Asn Leu Phe
 195 200 205
 cac gtg tcc agc gac cac aac cag ctg gac cag aac ccc cgg aag ttc 672
 His Val Ser Ser Asp His Asn Gln Leu Asp Gln Asn Pro Arg Lys Phe
 210 215 220
 tat ctg gct ggc aac ccc gag aac gag ttc aac cag caa ggg cag agc 720
 Tyr Leu Ala Gly Asn Pro Glu Asn Glu Phe Asn Gln Gln Gly Gln Ser
 225 230 235
 cag ccc aga cag caa ggc gaa caa gga cgg ccc gga cag cac cag cag 768
 Gln Pro Arg Gln Gln Gly Glu Gln Gly Arg Pro Gly Gln His Gln Gln
 240 245 250
 cct ttc ggc aga cca cgg cag caa gag cag caa ggc agc ggc aac aac 816
 Pro Phe Gly Arg Pro Arg Gln Gln Glu Gln Gln Gly Ser Gly Asn Asn
 255 260 265 270
 gtg ttc agc ggc ttc aac acc cag ctg ctg gcc caa gct ctg aac gtg 864
 Val Phe Ser Gly Phe Asn Thr Gln Leu Leu Ala Gln Ala Leu Asn Val
 275 280 285
 aac gag gaa acc gcc cgg aat ctg caa ggc cag aac gac aac aga aac 912
 Asn Glu Glu Thr Ala Arg Asn Leu Gln Gly Gln Asn Asp Asn Arg Asn
 290 295 300
 cag atc atc aga gtg cgg ggc aat ctg gac ttc gtg cag ccc cct aga 960
 Gln Ile Ile Arg Val Arg Gly Asn Leu Asp Phe Val Gln Pro Pro Arg
 305 310 315
 ggg cgg caa gag aga gag cac gaa gag agg cag caa gaa cag ctg cag 1008
 Gly Arg Gln Glu Arg Glu His Glu Glu Arg Gln Gln Glu Gln Leu Gln
 320 325 330
 caa gag cgg cag cag caa ggc gga cag ctg atg gcc aac gaattc 1053
 Gln Glu Arg Gln Gln Gln Gly Gly Gln Leu Met Ala Asn
 335 340 345
 <210> 13
 <211> 347
 <212> PRT
 <213> 扁桃(Prunus dulcis)
 <400> 13
 Ala Arg Gln Ser Gln Leu Ser Pro Gln Asn Gln Cys Gln Leu Asn Gln
 1 5 10 15
 Leu Gln Ala Arg Glu Pro Asp Asn Arg Ile Gln Ala Glu Ala Gly Gln
 20 25 30
 Ile Glu Thr Trp Asn Phe Asn Gln Glu Asp Phe Gln Cys Ala Gly Val

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

<210> 14
<211> 1548
<212> DNA
<213> 腰果 (Anacardium occidentale)
<220>
<221> CDS
<222> (7) .. (1542)
<400> 14
ctcgag aag atc gac ccc gag ctg aag cag tgc aag cac cag tgc aaa 48
Lys Ile Asp Pro Glu Leu Lys Gln Cys Lys His Gln Cys Lys
1 5 10
gtg cag cgg cag tac gac gag cag cag aaa gaa cag tgc gtg aaa gag 96
Val Gln Arg Gln Tyr Asp Glu Gln Gln Lys Glu Gln Cys Val Lys Glu
15 20 25 30
tgc gag aag tac tac aaa gag aag aag ggc cgc gag cgc gag cac gaa 144
Cys Glu Lys Tyr Tyr Lys Glu Lys Lys Gly Arg Glu Arg Glu His Glu
35 40 45
gag gaa gag gaa gaa tgg ggc acc ggc gga gtg gac gag cct tct aca 192
Glu Glu Glu Glu Glu Trp Gly Thr Gly Gly Val Asp Glu Pro Ser Thr
50 55 60
cac gag ccc gcc gag aaa cat ctg agc cag tgc atg aga cag tgc gaa 240
His Glu Pro Ala Glu Lys His Leu Ser Gln Cys Met Arg Gln Cys Glu
65 70 75
cgg caa gag ggc ggc cag cag aaa cag ctg tgc cgg ttc cgg tgc caa 288
Arg Gln Glu Gly Gly Gln Gln Lys Gln Leu Cys Arg Phe Arg Cys Gln
80 85 90
gag cgg tac aag aaa gag cgg ggc cag cac aac tac aag aga gag gac 336
Glu Arg Tyr Lys Lys Glu Arg Gly Gln His Asn Tyr Lys Arg Glu Asp
95 100 105 110
gac gag gac gaa gat gag gac gag gct gag gaa gag gac gag aac ccc 384
Asp Glu Asp Glu Asp Glu Asp Glu Ala Glu Glu Glu Asp Glu Asn Pro
115 120 125
tac gtg ttc gag gat gag gac ttc acc acc aaa gtg aaa acc gag caa 432
Tyr Val Phe Glu Asp Glu Asp Phe Thr Thr Lys Val Lys Thr Glu Gln
130 135 140
ggc aaa gtg gtg ctg ctg ccc aag ttc acc cag aag tcc aag ctg ctg 480
Gly Lys Val Val Leu Leu Pro Lys Phe Thr Gln Lys Ser Lys Leu Leu
145 150 155
cac gct ctg gaa aag tac cgg ctg gcc gtt ctg gtg gcc aac cct caa 528

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His Ala Leu Glu Lys Tyr Arg Leu Ala Val Leu Val Ala Asn Pro Gln
160                               165                               170
gcc ttc gtg gtg ccc agc cac atg gac gcc gac agc atc ttc ttc gtg 576
Ala Phe Val Val Pro Ser His Met Asp Ala Asp Ser Ile Phe Phe Val
175                               180                               185                               190
tct tgg ggc aga ggc acc atc acc aag att ctg gaa aac aag cgc gag 624
Ser Trp Gly Arg Gly Thr Ile Thr Lys Ile Leu Glu Asn Lys Arg Glu
                               195                               200                               205
agc atc aac gtg cgg caa ggc gac atc gtg tcc atc agc agc ggc acc 672
Ser Ile Asn Val Arg Gln Gly Asp Ile Val Ser Ile Ser Ser Gly Thr
                               210                               215                               220
ccc ttc tac att gcc aac aac gac gag aac gag aag ctg tat ctg gtg 720
Pro Phe Tyr Ile Ala Asn Asn Asp Glu Asn Glu Lys Leu Tyr Leu Val
                               225                               230                               235
cag ttt ctg cgg ccc gtg aat ctg ccc ggc cac ttt gaa gtg ttc cac 768
Gln Phe Leu Arg Pro Val Asn Leu Pro Gly His Phe Glu Val Phe His
                               240                               245                               250
gga ccc ggc gga gag aac ccc gag agc ttc tac aga gcc ttc agc tgg 816
Gly Pro Gly Gly Glu Asn Pro Glu Ser Phe Tyr Arg Ala Phe Ser Trp
255                               260                               265                               270
gaa att ctg gaa gcc gct ctg aaa aca tcc aag gac aca ctg gaa aag 864
Glu Ile Leu Glu Ala Ala Leu Lys Thr Ser Lys Asp Thr Leu Glu Lys
                               275                               280                               285
ctg ttc gag aag caa gac caa ggg acc atc atg aag gcc agc aaa gaa 912
Leu Phe Glu Lys Gln Asp Gln Gly Thr Ile Met Lys Ala Ser Lys Glu
                               290                               295                               300
cag atc cgg gcc atg agc aga aga ggc gag ggc ccc aag atc tgg ccc 960
Gln Ile Arg Ala Met Ser Arg Arg Gly Glu Gly Pro Lys Ile Trp Pro
                               305                               310                               315
ttc acc gag gaa agc acc ggc agc ttc aag ctg ttt aag aag gac ccc 1008
Phe Thr Glu Glu Ser Thr Gly Ser Phe Lys Leu Phe Lys Lys Asp Pro
                               320                               325                               330
agc cag agc aac aaa tac ggg cag ctg ttt gag gcc gag cgg atc gac 1056
Ser Gln Ser Asn Lys Tyr Gly Gln Leu Phe Glu Ala Glu Arg Ile Asp
335                               340                               345                               350
tac ccc cca ctg gaa aag ctg gac atg gtg gtg tcc tac gcc aat atc 1104
Tyr Pro Pro Leu Glu Lys Leu Asp Met Val Val Ser Tyr Ala Asn Ile
                               355                               360                               365
acc aag ggc ggc atg agc gtg ccc ttt tac aac agc aga gcc acc aag 1152

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Thr Lys Gly Gly Met Ser Val Pro Phe Tyr Asn Ser Arg Ala Thr Lys
 370 375 380
 atc gcc atc gtg gtg tcc ggc gag ggc tgc gtg gaa atc gct tgc cct 1200
 Ile Ala Ile Val Val Ser Gly Glu Gly Cys Val Glu Ile Ala Cys Pro
 385 390 395
 cat ctg agc agc agc aag tcc agc cac ccc agc tac aag aag ctg cgg 1248
 His Leu Ser Ser Ser Lys Ser Ser His Pro Ser Tyr Lys Lys Leu Arg
 400 405 410
 gcc aga atc cgg aag gac acc gtg ttc atc gtg cca gcc ggc cac cct 1296
 Ala Arg Ile Arg Lys Asp Thr Val Phe Ile Val Pro Ala Gly His Pro
 415 420 425 430
 ttt gcc aca gtg gcc agc ggc aac gag aat ctg gaa atc gtg tgc ttc 1344
 Phe Ala Thr Val Ala Ser Gly Asn Glu Asn Leu Glu Ile Val Cys Phe
 435 440 445
 gaa gtg aac gcc gag ggc aac atc cgg tac aca ctg gcc ggc aag aag 1392
 Glu Val Asn Ala Glu Gly Asn Ile Arg Tyr Thr Leu Ala Gly Lys Lys
 450 455 460
 aac atc atc aaa gtg atg gaa aag gaa gcc aaa gaa ctg gcc ttt aag 1440
 Asn Ile Ile Lys Val Met Glu Lys Glu Ala Lys Glu Leu Ala Phe Lys
 465 470 475
 atg gaa ggc gag gaa gtg gac aaa gtg ttc ggc aag caa gat gaa gag 1488
 Met Glu Gly Glu Glu Val Asp Lys Val Phe Gly Lys Gln Asp Glu Glu
 480 485 490
 ttc ttc ttt caa ggc ccc gag tgg cgc aaa gag aaa gag ggc aga gcc 1536
 Phe Phe Phe Gln Gly Pro Glu Trp Arg Lys Glu Lys Glu Gly Arg Ala
 495 500 505 510
 gac gag gaattc 1548
 Asp Glu
 <210> 15
 <211> 512
 <212> PRT
 <213> 腰果 (Anacardium occidentale)
 <400> 15
 Lys Ile Asp Pro Glu Leu Lys Gln Cys Lys His Gln Cys Lys Val Gln
 1 5 10 15
 Arg Gln Tyr Asp Glu Gln Gln Lys Glu Gln Cys Val Lys Glu Cys Glu
 20 25 30
 Lys Tyr Tyr Lys Glu Lys Lys Gly Arg Glu Arg Glu His Glu Glu Glu
 35 40 45

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

355	360	365
Gly Gly Met Ser Val Pro Phe Tyr Asn Ser Arg Ala Thr Lys Ile Ala		
370	375	380
Ile Val Val Ser Gly Glu Gly Cys Val Glu Ile Ala Cys Pro His Leu		
385	390	395
Ser Ser Ser Lys Ser Ser His Pro Ser Tyr Lys Lys Leu Arg Ala Arg		
405	410	415
Ile Arg Lys Asp Thr Val Phe Ile Val Pro Ala Gly His Pro Phe Ala		
420	425	430
Thr Val Ala Ser Gly Asn Glu Asn Leu Glu Ile Val Cys Phe Glu Val		
435	440	445
Asn Ala Glu Gly Asn Ile Arg Tyr Thr Leu Ala Gly Lys Lys Asn Ile		
450	455	460
Ile Lys Val Met Glu Lys Glu Ala Lys Glu Leu Ala Phe Lys Met Glu		
465	470	475
Gly Glu Glu Val Asp Lys Val Phe Gly Lys Gln Asp Glu Glu Phe Phe		
485	490	495
Phe Gln Gly Pro Glu Trp Arg Lys Glu Lys Glu Gly Arg Ala Asp Glu		
500	505	510

<210> 16

<211> 1383

<212> DNA

<213> 腰果 (Anacardium occidentale)

<220>

<221> CDS

<222> (7) .. (1377)

<400> 16

ctcgag ctg agc gtg tgc ttt ctg att ctg ttc cac ggc tgt ctg gcc 48

Leu Ser Val Cys Phe Leu Ile Leu Phe His Gly Cys Leu Ala

1

5

10

agc cgg caa gaa tgg cag cag caa gac gag tgc cag atc gac cgg ctg 96

Ser Arg Gln Glu Trp Gln Gln Gln Asp Glu Cys Gln Ile Asp Arg Leu

15

20

25

30

gac gct ctg gaa ccc gac aac cgg gtg gaa tac gag gcc ggc aca gtg 144

Asp Ala Leu Glu Pro Asp Asn Arg Val Glu Tyr Glu Ala Gly Thr Val

35

40

45

gaa gct tgg gac ccc aac cac gag cag ttc aga tgt gcc ggc gtg gca 192

Glu Ala Trp Asp Pro Asn His Glu Gln Phe Arg Cys Ala Gly Val Ala

50

55

60

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ctc gtg cgg cac acc atc cag cca aac gga ctg ctg ctg ccc cag tac 240
Leu Val Arg His Thr Ile Gln Pro Asn Gly Leu Leu Leu Pro Gln Tyr
      65                      70                      75
agc aac gcc ccc cag ctg atc tat gtg gtg caa ggc gag ggc atg acc 288
Ser Asn Ala Pro Gln Leu Ile Tyr Val Val Gln Gly Glu Gly Met Thr
      80                      85                      90
ggc atc agc tat ccc ggc tgc ccc gag aca tat caa gcc cct cag caa 336
Gly Ile Ser Tyr Pro Gly Cys Pro Glu Thr Tyr Gln Ala Pro Gln Gln
      95                      100                     105                     110
ggc aga cag caa ggc cag agc ggc cgg ttc caa gac cgg cac cag aag 384
Gly Arg Gln Gln Gly Gln Ser Gly Arg Phe Gln Asp Arg His Gln Lys
      115                     120                     125
atc cgg cgg ttc aga cgg ggc gac atc att gcc att cca gcc ggg gtg 432
Ile Arg Arg Phe Arg Arg Gly Asp Ile Ile Ala Ile Pro Ala Gly Val
      130                     135                     140
gcc cac tgg tgc tac aac gag ggc aat agc ccc gtc gtg acc gtg aca 480
Ala His Trp Cys Tyr Asn Glu Gly Asn Ser Pro Val Val Thr Val Thr
      145                     150                     155
ctg ctg gac gtg tcc aac agc cag aac cag ctg gac cgg acc ccc cgg 528
Leu Leu Asp Val Ser Asn Ser Gln Asn Gln Leu Asp Arg Thr Pro Arg
      160                     165                     170
aag ttt cat ctg gcc ggc aac ccc aag gac gtg ttc cag caa cag cag 576
Lys Phe His Leu Ala Gly Asn Pro Lys Asp Val Phe Gln Gln Gln Gln
      175                     180                     185                     190
cag cac cag agc cgg ggc aga aat ctg ttc agc ggc ttc gac acc gag 624
Gln His Gln Ser Arg Gly Arg Asn Leu Phe Ser Gly Phe Asp Thr Glu
      195                     200                     205
ctg ctg gcc gag gct ttt caa gtg gac gag cgg ctg atc aag cag ctg 672
Leu Leu Ala Glu Ala Phe Gln Val Asp Glu Arg Leu Ile Lys Gln Leu
      210                     215                     220
aag tcc gag gac aac aga ggc ggc atc gtg aaa gtg aag gac gac gag 720
Lys Ser Glu Asp Asn Arg Gly Gly Ile Val Lys Val Lys Asp Asp Glu
      225                     230                     235
ctg aga gtg atc cgg ccc agc aga agc cag agc gag aga ggc agc gag 768
Leu Arg Val Ile Arg Pro Ser Arg Ser Gln Ser Glu Arg Gly Ser Glu
      240                     245                     250
agc gag gaa gag tct gag gac gag aag cgg aga tgg ggc cag cgg gac 816
Ser Glu Glu Glu Ser Glu Asp Glu Lys Arg Arg Trp Gly Gln Arg Asp
      255                     260                     265                     270

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aac ggc atc gaa gag aca atc tgc acc atg cgg ctg aaa gag aac atc 864
Asn Gly Ile Glu Glu Thr Ile Cys Thr Met Arg Leu Lys Glu Asn Ile
                275                280                285

aac gac ccc gcc aga gcc gac atc tac acc ccc gaa gtg ggc cgg ctg 912
Asn Asp Pro Ala Arg Ala Asp Ile Tyr Thr Pro Glu Val Gly Arg Leu
                290                295                300

aca act ctg aac tct ctg aat ctg ccc att ctg aag tgg ctg cag ctg 960
Thr Thr Leu Asn Ser Leu Asn Leu Pro Ile Leu Lys Trp Leu Gln Leu
                305                310                315

tcc gtg gaa aag ggg gtg ctg tac aag aac gct ctg gtg ctg cct cac 1008
Ser Val Glu Lys Gly Val Leu Tyr Lys Asn Ala Leu Val Leu Pro His
                320                325                330

tgg aat ctg aac agc cac agc atc atc tac ggc tgc aag ggc aag ggc 1056
Trp Asn Leu Asn Ser His Ser Ile Ile Tyr Gly Cys Lys Gly Lys Gly
335                340                345                350

caa gtc caa gtg gtg gac aac ttc ggc aac aga gtg ttc gac ggc gaa 1104
Gln Val Gln Val Val Asp Asn Phe Gly Asn Arg Val Phe Asp Gly Glu
                355                360                365

gtg cgc gag ggc cag atg ctc gtg gtg ccc cag aat ttc gcc gtc gtg 1152
Val Arg Glu Gly Gln Met Leu Val Val Pro Gln Asn Phe Ala Val Val
                370                375                380

aag cgg gcc aga gaa gaa aga ttc gag tgg atc agc ttc aag acc aac 1200
Lys Arg Ala Arg Glu Glu Arg Phe Glu Trp Ile Ser Phe Lys Thr Asn
                385                390                395

gac cgg gcc atg acc agc cct ctg gcc gga aga aca tct gtg ctg ggc 1248
Asp Arg Ala Met Thr Ser Pro Leu Ala Gly Arg Thr Ser Val Leu Gly
                400                405                410

ggc atg ccc gag gaa gtg ctg gct aac gcc ttc cag atc agc aga gag 1296
Gly Met Pro Glu Glu Val Leu Ala Asn Ala Phe Gln Ile Ser Arg Glu
415                420                425                430

gac gcc cgg aag atc aag ttc aac aac cag cag acc aca ctg acc agc 1344
Asp Ala Arg Lys Ile Lys Phe Asn Asn Gln Gln Thr Thr Leu Thr Ser
                435                440                445

ggc gag agc agc cac cac atg aga gat gac gcc gaattc 1383
Gly Glu Ser Ser His His Met Arg Asp Asp Ala
                450                455

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<210> 17

<211> 457

<212> PRT

<213> 腰果 (Anacardium occidentale)

<400> 17

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

290	295	300
Leu Asn Ser Leu Asn Leu Pro Ile Leu Lys Trp Leu Gln Leu Ser Val		
305	310	315
Glu Lys Gly Val Leu Tyr Lys Asn Ala Leu Val Leu Pro His Trp Asn		
	325	330
Leu Asn Ser His Ser Ile Ile Tyr Gly Cys Lys Gly Lys Gly Gln Val		
	340	345
Gln Val Val Asp Asn Phe Gly Asn Arg Val Phe Asp Gly Glu Val Arg		
	355	360
Glu Gly Gln Met Leu Val Val Pro Gln Asn Phe Ala Val Val Lys Arg		
370	375	380
Ala Arg Glu Glu Arg Phe Glu Trp Ile Ser Phe Lys Thr Asn Asp Arg		
385	390	395
Ala Met Thr Ser Pro Leu Ala Gly Arg Thr Ser Val Leu Gly Gly Met		
	405	410
Pro Glu Glu Val Leu Ala Asn Ala Phe Gln Ile Ser Arg Glu Asp Ala		
	420	425
Arg Lys Ile Lys Phe Asn Asn Gln Gln Thr Thr Leu Thr Ser Gly Glu		
435	440	445
Ser Ser His His Met Arg Asp Asp Ala		
450	455	

<210> 18

<211> 366

<212> DNA

<213> 腰果 (Anacardium occidentale)

<220>

<221> CDS

<222> (7) .. (360)

<400> 18

ctcgag agc atc tac cgg gcc atc gtg gaa gtg gaa gag gac agc ggc 48

Ser Ile Tyr Arg Ala Ile Val Glu Val Glu Glu Asp Ser Gly

1

5

10

aga gag cag agc tgc cag cgg cag ttc gag gaa cag cag cgg ttc aga 96

Arg Glu Gln Ser Cys Gln Arg Gln Phe Glu Glu Gln Gln Arg Phe Arg

15

20

25

30

aac tgc cag aga tac gtg aag caa gaa gtg cag aga ggc ggc aga tac 144

Asn Cys Gln Arg Tyr Val Lys Gln Glu Val Gln Arg Gly Gly Arg Tyr

35

40

45

aac cag aga caa gag tct ctg aga gag tgc tgc caa gag ctg caa gaa 192

Asn Gln Arg Gln Glu Ser Leu Arg Glu Cys Cys Gln Glu Leu Gln Glu
 50 55 60
 gtg gac cgg cgc tgc cgg tgc cag aat ctg gaa cag atg gtg cgc cag 240
 Val Asp Arg Arg Cys Arg Cys Gln Asn Leu Glu Gln Met Val Arg Gln
 65 70 75
 ctg cag cag caa gag cag atc aag ggc gag gaa gtg cgc gag ctg tac 288
 Leu Gln Gln Gln Glu Gln Ile Lys Gly Glu Glu Val Arg Glu Leu Tyr
 80 85 90
 gag aca gcc agc gag ctg cct cgg atc tgc agc atc agc cca agc caa 336
 Glu Thr Ala Ser Glu Leu Pro Arg Ile Cys Ser Ile Ser Pro Ser Gln
 95 100 105 110
 ggc tgc cag ttc cag agc agc tac gaattc 366
 Gly Cys Gln Phe Gln Ser Ser Tyr
 115

<210> 19

<211> 118

<212> PRT

<213> 腰果(Anacardium occidentale)

<400> 19

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

<210> 20

<211> 3297

<212> DNA

<213> 人工序列

<220>

<223> 合成构建物

<220>

<221> CDS

<222> (7) .. (3291)

<400> 20

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ctcgag ctg agc gtg tgc ttt ctg att ctg ttc cac ggc tgt ctg gcc 48
      Leu Ser Val Cys Phe Leu Ile Leu Phe His Gly Cys Leu Ala
          1              5                  10
agc cgg caa gaa tgg cag cag caa gac gag tgc cag atc gac cgg ctg 96
Ser Arg Gln Glu Trp Gln Gln Gln Asp Glu Cys Gln Ile Asp Arg Leu
15              20              25              30
gac gct ctg gaa ccc gac aac cgg gtg gaa tac gag gcc ggc aca gtg 144
Asp Ala Leu Glu Pro Asp Asn Arg Val Glu Tyr Glu Ala Gly Thr Val
          35              40              45
gaa gct tgg gac ccc aac cac gag cag ttc aga tgt gcc ggc gtg gca 192
Glu Ala Trp Asp Pro Asn His Glu Gln Phe Arg Cys Ala Gly Val Ala
          50              55              60
ctc gtg cgg cac acc atc cag cca aac gga ctg ctg ctg ccc cag tac 240
Leu Val Arg His Thr Ile Gln Pro Asn Gly Leu Leu Leu Pro Gln Tyr
          65              70              75
agc aac gcc ccc cag ctg atc tat gtg gtg caa ggc gag ggc atg acc 288
Ser Asn Ala Pro Gln Leu Ile Tyr Val Val Gln Gly Glu Gly Met Thr
          80              85              90
ggc atc agc tat ccc ggc tgc ccc gag aca tat caa gcc cct cag caa 336
Gly Ile Ser Tyr Pro Gly Cys Pro Glu Thr Tyr Gln Ala Pro Gln Gln
95              100              105              110
ggc aga cag caa ggc cag agc ggc cgg ttc caa gac cgg cac cag aag 384
Gly Arg Gln Gln Gly Gln Ser Gly Arg Phe Gln Asp Arg His Gln Lys
          115              120              125
atc cgg cgg ttc aga cgg ggc gac atc att gcc att cca gcc ggg gtg 432
Ile Arg Arg Phe Arg Arg Gly Asp Ile Ile Ala Ile Pro Ala Gly Val
          130              135              140
gcc cac tgg tgc tac aac gag ggc aat agc ccc gtc gtg acc gtg aca 480
Ala His Trp Cys Tyr Asn Glu Gly Asn Ser Pro Val Val Thr Val Thr
          145              150              155
ctg ctg gac gtg tcc aac agc cag aac cag ctg gac cgg acc ccc cgg 528
Leu Leu Asp Val Ser Asn Ser Gln Asn Gln Leu Asp Arg Thr Pro Arg
          160              165              170

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aag ttt cat ctg gcc ggc aac ccc aag gac gtg ttc cag caa cag cag 576
Lys Phe His Leu Ala Gly Asn Pro Lys Asp Val Phe Gln Gln Gln Gln
175                      180                      185                      190
cag cac cag agc cgg ggc aga aat ctg ttc agc ggc ttc gac acc gag 624
Gln His Gln Ser Arg Gly Arg Asn Leu Phe Ser Gly Phe Asp Thr Glu
                      195                      200                      205
ctg ctg gcc gag gct ttt caa gtg gac gag cgg ctg atc aag cag ctg 672
Leu Leu Ala Glu Ala Phe Gln Val Asp Glu Arg Leu Ile Lys Gln Leu
                      210                      215                      220
aag tcc gag gac aac aga ggc ggc atc gtg aaa gtg aag gac gac gag 720
Lys Ser Glu Asp Asn Arg Gly Gly Ile Val Lys Val Lys Asp Asp Glu
                      225                      230                      235
ctg aga gtg atc cgg ccc agc aga agc cag agc gag aga ggc agc gag 768
Leu Arg Val Ile Arg Pro Ser Arg Ser Gln Ser Glu Arg Gly Ser Glu
                      240                      245                      250
agc gag gaa gag tct gag gac gag aag cgg aga tgg ggc cag cgg gac 816
Ser Glu Glu Glu Ser Glu Asp Glu Lys Arg Arg Trp Gly Gln Arg Asp
255                      260                      265                      270
aac ggc atc gaa gag aca atc tgc acc atg cgg ctg aaa gag aac atc 864
Asn Gly Ile Glu Glu Thr Ile Cys Thr Met Arg Leu Lys Glu Asn Ile
                      275                      280                      285
aac gac ccc gcc aga gcc gac atc tac acc ccc gaa gtg ggc cgg ctg 912
Asn Asp Pro Ala Arg Ala Asp Ile Tyr Thr Pro Glu Val Gly Arg Leu
                      290                      295                      300
aca act ctg aac tct ctg aat ctg ccc att ctg aag tgg ctg cag ctg 960
Thr Thr Leu Asn Ser Leu Asn Leu Pro Ile Leu Lys Trp Leu Gln Leu
                      305                      310                      315
tcc gtg gaa aag ggg gtg ctg tac aag aac gct ctg gtg ctg cct cac 1008
Ser Val Glu Lys Gly Val Leu Tyr Lys Asn Ala Leu Val Leu Pro His
                      320                      325                      330
tgg aat ctg aac agc cac agc atc atc tac ggc tgc aag ggc aag ggc 1056
Trp Asn Leu Asn Ser His Ser Ile Ile Tyr Gly Cys Lys Gly Lys Gly
335                      340                      345                      350
caa gtc caa gtg gtg gac aac ttc ggc aac aga gtg ttc gac ggc gaa 1104
Gln Val Gln Val Val Asp Asn Phe Gly Asn Arg Val Phe Asp Gly Glu
                      355                      360                      365
gtg cgc gag ggc cag atg ctc gtg gtg ccc cag aat ttc gcc gtc gtg 1152
Val Arg Glu Gly Gln Met Leu Val Val Pro Gln Asn Phe Ala Val Val
                      370                      375                      380

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aag cgg gcc aga gaa gaa aga ttc gag tgg atc agc ttc aag acc aac 1200
Lys Arg Ala Arg Glu Glu Arg Phe Glu Trp Ile Ser Phe Lys Thr Asn
      385              390              395

gac cgg gcc atg acc agc cct ctg gcc gga aga aca tct gtg ctg ggc 1248
Asp Arg Ala Met Thr Ser Pro Leu Ala Gly Arg Thr Ser Val Leu Gly
      400              405              410

ggc atg ccc gag gaa gtg ctg gct aac gcc ttc cag atc agc aga gag 1296
Gly Met Pro Glu Glu Val Leu Ala Asn Ala Phe Gln Ile Ser Arg Glu
      415              420              425              430

gac gcc cgg aag atc aag ttc aac aac cag cag acc aca ctg acc agc 1344
Asp Ala Arg Lys Ile Lys Phe Asn Asn Gln Gln Thr Thr Leu Thr Ser
      435              440              445

ggc gag agc agc cac cac atg aga gat gac gcc ggc gga ggg ggc aag 1392
Gly Glu Ser Ser His His Met Arg Asp Asp Ala Gly Gly Gly Gly Lys
      450              455              460

atc gac ccc gag ctg aag cag tgc aag cac cag tgc aaa gtg cag cgg 1440
Ile Asp Pro Glu Leu Lys Gln Cys Lys His Gln Cys Lys Val Gln Arg
      465              470              475

cag tac gac gag cag cag aaa gaa cag tgc gtg aaa gag tgc gag aag 1488
Gln Tyr Asp Glu Gln Gln Lys Glu Gln Cys Val Lys Glu Cys Glu Lys
      480              485              490

tac tac aaa gag aag aag ggc cgc gag cgc gag cac gaa gag gaa gag 1536
Tyr Tyr Lys Glu Lys Lys Gly Arg Glu Arg Glu His Glu Glu Glu Glu
      495              500              505              510

gaa gaa tgg ggc acc ggc gga gtg gac gag cct tct aca cac gag ccc 1584
Glu Glu Trp Gly Thr Gly Gly Val Asp Glu Pro Ser Thr His Glu Pro
      515              520              525

gcc gag aaa cat ctg agc cag tgc atg aga cag tgc gaa cgg caa gag 1632
Ala Glu Lys His Leu Ser Gln Cys Met Arg Gln Cys Glu Arg Gln Glu
      530              535              540

ggc ggc cag cag aaa cag ctg tgc cgg ttc cgg tgc caa gag cgg tac 1680
Gly Gly Gln Gln Lys Gln Leu Cys Arg Phe Arg Cys Gln Glu Arg Tyr
      545              550              555

aag aaa gag cgg ggc cag cac aac tac aag aga gag gac gac gag gac 1728
Lys Lys Glu Arg Gly Gln His Asn Tyr Lys Arg Glu Asp Asp Glu Asp
      560              565              570

gaa gat gag gac gag gct gag gaa gag gac gag aac ccc tac gtg ttc 1776
Glu Asp Glu Asp Glu Ala Glu Glu Glu Asp Glu Asn Pro Tyr Val Phe
      575              580              585              590

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gag gat gag gac ttc acc acc aaa gtg aaa acc gag caa ggc aaa gtg 1824
Glu Asp Glu Asp Phe Thr Thr Lys Val Lys Thr Glu Gln Gly Lys Val
                    595                    600                    605

gtg ctg ctg ccc aag ttc acc cag aag tcc aag ctg ctg cac gct ctg 1872
Val Leu Leu Pro Lys Phe Thr Gln Lys Ser Lys Leu Leu His Ala Leu
                    610                    615                    620

gaa aag tac cgg ctg gcc gtt ctg gtg gcc aac cct caa gcc ttc gtg 1920
Glu Lys Tyr Arg Leu Ala Val Leu Val Ala Asn Pro Gln Ala Phe Val
                    625                    630                    635

gtg ccc agc cac atg gac gcc gac agc atc ttc ttc gtg tct tgg ggc 1968
Val Pro Ser His Met Asp Ala Asp Ser Ile Phe Phe Val Ser Trp Gly
                    640                    645                    650

aga ggc acc atc acc aag att ctg gaa aac aag cgc gag agc atc aac 2016
Arg Gly Thr Ile Thr Lys Ile Leu Glu Asn Lys Arg Glu Ser Ile Asn
655                    660                    665                    670

gtg cgg caa ggc gac atc gtg tcc atc agc agc ggc acc ccc ttc tac 2064
Val Arg Gln Gly Asp Ile Val Ser Ile Ser Ser Gly Thr Pro Phe Tyr
                    675                    680                    685

att gcc aac aac gac gag aac gag aag ctg tat ctg gtg cag ttt ctg 2112
Ile Ala Asn Asn Asp Glu Asn Glu Lys Leu Tyr Leu Val Gln Phe Leu
                    690                    695                    700

cgg ccc gtg aat ctg ccc ggc cac ttt gaa gtg ttc cac gga ccc ggc 2160
Arg Pro Val Asn Leu Pro Gly His Phe Glu Val Phe His Gly Pro Gly
                    705                    710                    715

gga gag aac ccc gag agc ttc tac aga gcc ttc agc tgg gaa att ctg 2208
Gly Glu Asn Pro Glu Ser Phe Tyr Arg Ala Phe Ser Trp Glu Ile Leu
                    720                    725                    730

gaa gcc gct ctg aaa aca tcc aag gac aca ctg gaa aag ctg ttc gag 2256
Glu Ala Ala Leu Lys Thr Ser Lys Asp Thr Leu Glu Lys Leu Phe Glu
735                    740                    745                    750

aag caa gac caa ggg acc atc atg aag gcc agc aaa gaa cag atc cgg 2304
Lys Gln Asp Gln Gly Thr Ile Met Lys Ala Ser Lys Glu Gln Ile Arg
                    755                    760                    765

gcc atg agc aga aga ggc gag ggc ccc aag atc tgg ccc ttc acc gag 2352
Ala Met Ser Arg Arg Gly Glu Gly Pro Lys Ile Trp Pro Phe Thr Glu
                    770                    775                    780

gaa agc acc ggc agc ttc aag ctg ttt aag aag gac ccc agc cag agc 2400
Glu Ser Thr Gly Ser Phe Lys Leu Phe Lys Lys Asp Pro Ser Gln Ser
                    785                    790                    795

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aac aaa tac ggg cag ctg ttt gag gcc gag cgg atc gac tac ccc cca 2448
Asn Lys Tyr Gly Gln Leu Phe Glu Ala Glu Arg Ile Asp Tyr Pro Pro
      800                      805                      810
ctg gaa aag ctg gac atg gtg gtg tcc tac gcc aat atc acc aag ggc 2496
Leu Glu Lys Leu Asp Met Val Val Ser Tyr Ala Asn Ile Thr Lys Gly
      815                      820                      825                      830
ggc atg agc gtg ccc ttt tac aac agc aga gcc acc aag atc gcc atc 2544
Gly Met Ser Val Pro Phe Tyr Asn Ser Arg Ala Thr Lys Ile Ala Ile
                      835                      840                      845
gtg gtg tcc ggc gag ggc tgc gtg gaa atc gct tgc cct cat ctg agc 2592
Val Val Ser Gly Glu Gly Cys Val Glu Ile Ala Cys Pro His Leu Ser
                      850                      855                      860
agc agc aag tcc agc cac ccc agc tac aag aag ctg cgg gcc aga atc 2640
Ser Ser Lys Ser Ser His Pro Ser Tyr Lys Lys Leu Arg Ala Arg Ile
                      865                      870                      875
cgg aag gac acc gtg ttc atc gtg cca gcc ggc cac cct ttt gcc aca 2688
Arg Lys Asp Thr Val Phe Ile Val Pro Ala Gly His Pro Phe Ala Thr
                      880                      885                      890
gtg gcc agc ggc aac gag aat ctg gaa atc gtg tgc ttc gaa gtg aac 2736
Val Ala Ser Gly Asn Glu Asn Leu Glu Ile Val Cys Phe Glu Val Asn
      895                      900                      905                      910
gcc gag ggc aac atc cgg tac aca ctg gcc ggc aag aag aac atc atc 2784
Ala Glu Gly Asn Ile Arg Tyr Thr Leu Ala Gly Lys Lys Asn Ile Ile
                      915                      920                      925
aaa gtg atg gaa aag gaa gcc aaa gaa ctg gcc ttt aag atg gaa ggc 2832
Lys Val Met Glu Lys Glu Ala Lys Glu Leu Ala Phe Lys Met Glu Gly
                      930                      935                      940
gag gaa gtg gac aaa gtg ttc ggc aag caa gat gaa gag ttc ttc ttt 2880
Glu Glu Val Asp Lys Val Phe Gly Lys Gln Asp Glu Glu Phe Phe Phe
                      945                      950                      955
caa ggc ccc gag tgg cgc aaa gag aaa gag ggc aga gcc gac gag ggc 2928
Gln Gly Pro Glu Trp Arg Lys Glu Lys Glu Gly Arg Ala Asp Glu Gly
      960                      965                      970
gga ggg ggc agc atc tac cgg gcc atc gtg gaa gtg gaa gag gac agc 2976
Gly Gly Gly Ser Ile Tyr Arg Ala Ile Val Glu Val Glu Glu Asp Ser
      975                      980                      985                      990
ggc aga gag cag agc tgc cag cgg cag ttc gag gaa cag cag cgg ttc 3024
Gly Arg Glu Gln Ser Cys Gln Arg Gln Phe Glu Glu Gln Gln Arg Phe
                      995                      1000                      1005

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aga aac tgc cag aga tac gtg aag caa gaa gtg cag aga ggc ggc 3069
Arg Asn Cys Gln Arg Tyr Val Lys Gln Glu Val Gln Arg Gly Gly
      1010      1015      1020
aga tac aac cag aga caa gag tct ctg aga gag tgc tgc caa gag 3114
Arg Tyr Asn Gln Arg Gln Glu Ser Leu Arg Glu Cys Cys Gln Glu
      1025      1030      1035
ctg caa gaa gtg gac cgg cgc tgc cgg tgc cag aat ctg gaa cag 3159
Leu Gln Glu Val Asp Arg Arg Cys Arg Cys Gln Asn Leu Glu Gln
      1040      1045      1050
atg gtg cgc cag ctg cag cag caa gag cag atc aag ggc gag gaa 3204
Met Val Arg Gln Leu Gln Gln Gln Glu Gln Ile Lys Gly Glu Glu
      1055      1060      1065
gtg cgc gag ctg tac gag aca gcc agc gag ctg cct cgg atc tgc 3249
Val Arg Glu Leu Tyr Glu Thr Ala Ser Glu Leu Pro Arg Ile Cys
      1070      1075      1080
agc atc agc cca agc caa ggc tgc cag ttc cag agc agc tac gaa ttc 3297
Ser Ile Ser Pro Ser Gln Gly Cys Gln Phe Gln Ser Ser Tyr
      1085      1090      1095
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<212> PRT
<213> 人工序列
<220>
<223> 合成构建物
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      20      25      30
Leu Glu Pro Asp Asn Arg Val Glu Tyr Glu Ala Gly Thr Val Glu Ala
      35      40      45
Trp Asp Pro Asn His Glu Gln Phe Arg Cys Ala Gly Val Ala Leu Val
      50      55      60
Arg His Thr Ile Gln Pro Asn Gly Leu Leu Leu Pro Gln Tyr Ser Asn
65           70           75           80
Ala Pro Gln Leu Ile Tyr Val Val Gln Gly Glu Gly Met Thr Gly Ile
      85      90      95
Ser Tyr Pro Gly Cys Pro Glu Thr Tyr Gln Ala Pro Gln Gln Gly Arg
      100      105      110

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Gln Gln Gly Gln Ser Gly Arg Phe Gln Asp Arg His Gln Lys Ile Arg		
115	120	125
Arg Phe Arg Arg Gly Asp Ile Ile Ala Ile Pro Ala Gly Val Ala His		
130	135	140
Trp Cys Tyr Asn Glu Gly Asn Ser Pro Val Val Thr Val Thr Leu Leu		
145	150	155
Asp Val Ser Asn Ser Gln Asn Gln Leu Asp Arg Thr Pro Arg Lys Phe		
165	170	175
His Leu Ala Gly Asn Pro Lys Asp Val Phe Gln Gln Gln Gln Gln His		
180	185	190
Gln Ser Arg Gly Arg Asn Leu Phe Ser Gly Phe Asp Thr Glu Leu Leu		
195	200	205
Ala Glu Ala Phe Gln Val Asp Glu Arg Leu Ile Lys Gln Leu Lys Ser		
210	215	220
Glu Asp Asn Arg Gly Gly Ile Val Lys Val Lys Asp Asp Glu Leu Arg		
225	230	235
Val Ile Arg Pro Ser Arg Ser Gln Ser Glu Arg Gly Ser Glu Ser Glu		
245	250	255
Glu Glu Ser Glu Asp Glu Lys Arg Arg Trp Gly Gln Arg Asp Asn Gly		
260	265	270
Ile Glu Glu Thr Ile Cys Thr Met Arg Leu Lys Glu Asn Ile Asn Asp		
275	280	285
Pro Ala Arg Ala Asp Ile Tyr Thr Pro Glu Val Gly Arg Leu Thr Thr		
290	295	300
Leu Asn Ser Leu Asn Leu Pro Ile Leu Lys Trp Leu Gln Leu Ser Val		
305	310	315
Glu Lys Gly Val Leu Tyr Lys Asn Ala Leu Val Leu Pro His Trp Asn		
325	330	335
Leu Asn Ser His Ser Ile Ile Tyr Gly Cys Lys Gly Lys Gly Gln Val		
340	345	350
Gln Val Val Asp Asn Phe Gly Asn Arg Val Phe Asp Gly Glu Val Arg		
355	360	365
Glu Gly Gln Met Leu Val Val Pro Gln Asn Phe Ala Val Val Lys Arg		
370	375	380
Ala Arg Glu Glu Arg Phe Glu Trp Ile Ser Phe Lys Thr Asn Asp Arg		
385	390	395
Ala Met Thr Ser Pro Leu Ala Gly Arg Thr Ser Val Leu Gly Gly Met		
405	410	415
Pro Glu Glu Val Leu Ala Asn Ala Phe Gln Ile Ser Arg Glu Asp Ala		

420	425	430
Arg Lys Ile Lys Phe Asn Asn Gln Gln Thr Thr Leu Thr Ser Gly Glu		
435	440	445
Ser Ser His His Met Arg Asp Asp Ala Gly Gly Gly Gly Lys Ile Asp		
450	455	460
Pro Glu Leu Lys Gln Cys Lys His Gln Cys Lys Val Gln Arg Gln Tyr		
465	470	475
Asp Glu Gln Gln Lys Glu Gln Cys Val Lys Glu Cys Glu Lys Tyr Tyr		
485	490	495
Lys Glu Lys Lys Gly Arg Glu Arg Glu His Glu Glu Glu Glu Glu Glu		
500	505	510
Trp Gly Thr Gly Gly Val Asp Glu Pro Ser Thr His Glu Pro Ala Glu		
515	520	525
Lys His Leu Ser Gln Cys Met Arg Gln Cys Glu Arg Gln Glu Gly Gly		
530	535	540
Gln Gln Lys Gln Leu Cys Arg Phe Arg Cys Gln Glu Arg Tyr Lys Lys		
545	550	555
Glu Arg Gly Gln His Asn Tyr Lys Arg Glu Asp Asp Glu Asp Glu Asp		
565	570	575
Glu Asp Glu Ala Glu Glu Glu Asp Glu Asn Pro Tyr Val Phe Glu Asp		
580	585	590
Glu Asp Phe Thr Thr Lys Val Lys Thr Glu Gln Gly Lys Val Val Leu		
595	600	605
Leu Pro Lys Phe Thr Gln Lys Ser Lys Leu Leu His Ala Leu Glu Lys		
610	615	620
Tyr Arg Leu Ala Val Leu Val Ala Asn Pro Gln Ala Phe Val Val Pro		
625	630	635
Ser His Met Asp Ala Asp Ser Ile Phe Phe Val Ser Trp Gly Arg Gly		
645	650	655
Thr Ile Thr Lys Ile Leu Glu Asn Lys Arg Glu Ser Ile Asn Val Arg		
660	665	670
Gln Gly Asp Ile Val Ser Ile Ser Ser Gly Thr Pro Phe Tyr Ile Ala		
675	680	685
Asn Asn Asp Glu Asn Glu Lys Leu Tyr Leu Val Gln Phe Leu Arg Pro		
690	695	700
Val Asn Leu Pro Gly His Phe Glu Val Phe His Gly Pro Gly Gly Glu		
705	710	715
Asn Pro Glu Ser Phe Tyr Arg Ala Phe Ser Trp Glu Ile Leu Glu Ala		
725	730	735

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

1040	1045	1050
Arg Gln Leu Gln Gln Gln Glu Gln Ile Lys Gly	Glu Glu Val Arg	
1055	1060	1065
Glu Leu Tyr Glu Thr Ala Ser Glu Leu Pro Arg	Ile Cys Ser Ile	
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1	5	10
aac ccc aga aga aga ggc gag ggc tgc caa gag cag atc cag cgg cag 96		
Asn Pro Arg Arg Arg Gly Glu Gly Cys Gln Glu Gln Ile Gln Arg Gln		
15	20	25
cag aat ctg aac cac tgc cag tac tat ctg agg cag cag agc aga agc 144		
Gln Asn Leu Asn His Cys Gln Tyr Tyr Leu Arg Gln Gln Ser Arg Ser		
35	40	45
ggc ggc tac gac gag gat aac cag aga cag cac ttc aga cag tgc tgc 192		
Gly Gly Tyr Asp Glu Asp Asn Gln Arg Gln His Phe Arg Gln Cys Cys		
50	55	60
cag cag ctg agc cag atc gag gaa cag tgc cag tgc gag gga ctg aga 240		
Gln Gln Leu Ser Gln Ile Glu Glu Gln Cys Gln Cys Glu Gly Leu Arg		
65	70	75
caa gcc gtg cgg aga caa cag cag cag caa gga ctg cgg ggc gaa gag 288		
Gln Ala Val Arg Arg Gln Gln Gln Gln Gln Gly Leu Arg Gly Glu Glu		
80	85	90
atg gaa gaa atg gtg cag agc gcc aga gat ctg ccc aaa gag tgc ggc 336		
Met Glu Glu Met Val Gln Ser Ala Arg Asp Leu Pro Lys Glu Cys Gly		
95	100	105
atc agc agc cag aga tgc gag atc cgg cgg agt tgg ttc gaattc 381		
Ile Ser Ser Gln Arg Cys Glu Ile Arg Arg Ser Trp Phe		
115	120	

<210> 23

<211> 123

<212> PRT

<213> 黑核桃(Juglans nigra)

<400> 23

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

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<211> 1791

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<220>

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<222> (7) .. (1785)

<400> 24

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cgc gag cag tac cgg cag tgc caa gag tac tgc aga agg caa ggc caa 96
Arg Glu Gln Tyr Arg Gln Cys Gln Glu Tyr Cys Arg Arg Gln Gly Gln
15           20           25           30
ggc cag aga cag cag cag cag tgc cag atc aga tgc gag gaa cgg ctg 144
Gly Gln Arg Gln Gln Gln Gln Cys Gln Ile Arg Cys Glu Glu Arg Leu
           35           40           45
gaa gag gac cag cgg agc caa gag gaa cgc gag cgg aga aga ggc aga 192

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Glu Glu Asp Gln Arg Ser Gln Glu Glu Arg Glu Arg Arg Arg Gly Arg	
50	55 60
gat gtg gac gac cag aac ccc cgg gac ccc gag cag aga tac gag cag	240
Asp Val Asp Asp Gln Asn Pro Arg Asp Pro Glu Gln Arg Tyr Glu Gln	
65	70 75
tgt cag cag cag tgt gaa cgg cag cgg aga ggc caa gag cag aca ctg	288
Cys Gln Gln Gln Cys Glu Arg Gln Arg Arg Gly Gln Glu Gln Thr Leu	
80	85 90
tgt cgg cgg aga tgc gag cag cgg cgg cag caa gag gaa aga gaa cgc	336
Cys Arg Arg Arg Cys Glu Gln Arg Arg Gln Gln Glu Glu Arg Glu Arg	
95	100 105 110
cag cgg ggc aga gac aga caa gac ccc cag cag cag tac cac cgg tgc	384
Gln Arg Gly Arg Asp Arg Gln Asp Pro Gln Gln Gln Tyr His Arg Cys	
115	120 125
cag aga aga tgc cag atc caa gaa cag agc ccc gag cgg cag cgc cag	432
Gln Arg Arg Cys Gln Ile Gln Glu Gln Ser Pro Glu Arg Gln Arg Gln	
130	135 140
tgc cag cag aga tgc gaa aga cag tac aaa gag cag caa ggc aga gag	480
Cys Gln Gln Arg Cys Glu Arg Gln Tyr Lys Glu Gln Gln Gly Arg Glu	
145	150 155
agg ggc cca gag gcc agc cct aga aga gag tcc aga gga cgg gaa gaa	528
Arg Gly Pro Glu Ala Ser Pro Arg Arg Glu Ser Arg Gly Arg Glu Glu	
160	165 170
gaa cag cag cgg cac aac ccc tac tac ttc cac agc cag agc atc aga	576
Glu Gln Gln Arg His Asn Pro Tyr Tyr Phe His Ser Gln Ser Ile Arg	
175	180 185 190
agc cgg cac gag agc gaa gag ggc gaa gtg aag tat ctg gaa cgg ttc	624
Ser Arg His Glu Ser Glu Glu Gly Glu Val Lys Tyr Leu Glu Arg Phe	
195	200 205
acc gag cgg acc gag ctg ctg aga ggc atc gag aac tac cgg gtc gtg	672
Thr Glu Arg Thr Glu Leu Leu Arg Gly Ile Glu Asn Tyr Arg Val Val	
210	215 220
att ctg gac gcc aac ccc aac aca tcc atg ctg ccc cac cac aag gac	720
Ile Leu Asp Ala Asn Pro Asn Thr Ser Met Leu Pro His His Lys Asp	
225	230 235
gcc gag tct gtg gcc gtc gtg aca agg ggc aga gcc aca ctg aca ctg	768
Ala Glu Ser Val Ala Val Val Thr Arg Gly Arg Ala Thr Leu Thr Leu	
240	245 250
gtg tcc caa gag act cgc gag agc ttc aat ctg gaa tgc ggc gac gtg	816

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Val Ser Gln Glu Thr Arg Glu Ser Phe Asn Leu Glu Cys Gly Asp Val
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atc cgg gtg cca gct ggg gct aca gtg tac gtg atc aac caa gac agc 864
Ile Arg Val Pro Ala Gly Ala Thr Val Tyr Val Ile Asn Gln Asp Ser
                275                280                285
aac gag cgg ctg gaa atg gtc aag ctg ctg cag ccc gtg aac aac ccc 912
Asn Glu Arg Leu Glu Met Val Lys Leu Leu Gln Pro Val Asn Asn Pro
                290                295                300
ggc cag ttc aga gag tac tac gcc gct ggc gcc aag tcc ccc gac cag 960
Gly Gln Phe Arg Glu Tyr Tyr Ala Ala Gly Ala Lys Ser Pro Asp Gln
                305                310                315
agc tat ctg cgg gtg ttc agc aac gac att ctg gtg gcc gct ctg aat 1008
Ser Tyr Leu Arg Val Phe Ser Asn Asp Ile Leu Val Ala Ala Leu Asn
                320                325                330
acc cct cgg gac aga ctg gaa aga ttc ttc gat cag caa gag cag cgc 1056
Thr Pro Arg Asp Arg Leu Glu Arg Phe Phe Asp Gln Gln Glu Gln Arg
335                340                345                350
gag ggc gtg atc atc aga gcc agc caa gag aag ctg cgg gct ctg agc 1104
Glu Gly Val Ile Ile Arg Ala Ser Gln Glu Lys Leu Arg Ala Leu Ser
                355                360                365
cag cac gcc atg tct gct gga cag agg cct tgg ggc aga aga agc tct 1152
Gln His Ala Met Ser Ala Gly Gln Arg Pro Trp Gly Arg Arg Ser Ser
                370                375                380
ggc ggc cct atc tct ctg aag tcc gag agc ccc tcc tac agc aac cag 1200
Gly Gly Pro Ile Ser Leu Lys Ser Glu Ser Pro Ser Tyr Ser Asn Gln
                385                390                395
ttt ggc cag ttc ttc gag gct tgc ccc gag gaa cac cgg cag ctg caa 1248
Phe Gly Gln Phe Phe Glu Ala Cys Pro Glu Glu His Arg Gln Leu Gln
                400                405                410
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Glu Met Asp Val Leu Val Asn Tyr Ala Glu Ile Lys Arg Gly Ala Met
415                420                425                430
atg gtg ccc cac tac aac agc aag gcc acc gtg gtg gtg tac gtg gtg 1344
Met Val Pro His Tyr Asn Ser Lys Ala Thr Val Val Val Tyr Val Val
                435                440                445
gaa ggc acc ggc aga tac gag atg gca tgc ccc cac gtg tcc agc cag 1392
Glu Gly Thr Gly Arg Tyr Glu Met Ala Cys Pro His Val Ser Ser Gln
                450                455                460
tct tac gag ggc caa gga cgc aga gag caa gaa gag gaa gag tcc acc 1440

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Ser Tyr Glu Gly Gln Gly Arg Arg Glu Gln Glu Glu Glu Ser Thr
 465 470 475
 gga cgg ttc cag aaa gtg acc gcc aga ctg gcc aga ggc gac atc ttc 1488
 Gly Arg Phe Gln Lys Val Thr Ala Arg Leu Ala Arg Gly Asp Ile Phe
 480 485 490
 gtg atc cca gcc gga cac cct atc gcc atc acc gcc agc cag aac gag 1536
 Val Ile Pro Ala Gly His Pro Ile Ala Ile Thr Ala Ser Gln Asn Glu
 495 500 505 510
 aat ctg cgg ctg ctg ggc ttc gac atc aac ggc gag aac aac cag cgg 1584
 Asn Leu Arg Leu Leu Gly Phe Asp Ile Asn Gly Glu Asn Asn Gln Arg
 515 520 525
 gac ttt ctg gcc gga cag aac aac atc atc aac cag ctg gaa cgg gaa 1632
 Asp Phe Leu Ala Gly Gln Asn Asn Ile Ile Asn Gln Leu Glu Arg Glu
 530 535 540
 gcc aaa gaa ctg agc ttc aac atg ccc cgc gag gaa atc gaa gag att 1680
 Ala Lys Glu Leu Ser Phe Asn Met Pro Arg Glu Glu Ile Glu Glu Ile
 545 550 555
 ttc gag agc cag atg gaa agc tac ttc gtg ccc acc gag cgc cag agc 1728
 Phe Glu Ser Gln Met Glu Ser Tyr Phe Val Pro Thr Glu Arg Gln Ser
 560 565 570
 aga agg ggc caa ggg cgg gat cac cca ctg gcc tct att ctg gat ttc 1776
 Arg Arg Gly Gln Gly Arg Asp His Pro Leu Ala Ser Ile Leu Asp Phe
 575 580 585 590
 gcc ttc ttc gaattc 1791
 Ala Phe Phe
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 Gln Tyr Arg Gln Cys Gln Glu Tyr Cys Arg Arg Gln Gly Gln Gly Gln
 20 25 30
 Arg Gln Gln Gln Gln Cys Gln Ile Arg Cys Glu Glu Arg Leu Glu Glu
 35 40 45
 Asp Gln Arg Ser Gln Glu Glu Arg Glu Arg Arg Gly Arg Asp Val
 50 55 60
 Asp Asp Gln Asn Pro Arg Asp Pro Glu Gln Arg Tyr Glu Gln Cys Gln

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

Pro	Ile	Ser	Leu	Lys	Ser	Glu	Ser	Pro	Ser	Tyr	Ser	Asn	Gln	Phe	Gly
385						390					395				400
Gln	Phe	Phe	Glu	Ala	Cys	Pro	Glu	Glu	His	Arg	Gln	Leu	Gln	Glu	Met
				405					410					415	
Asp	Val	Leu	Val	Asn	Tyr	Ala	Glu	Ile	Lys	Arg	Gly	Ala	Met	Met	Val
			420					425					430		
Pro	His	Tyr	Asn	Ser	Lys	Ala	Thr	Val	Val	Val	Tyr	Val	Val	Glu	Gly
		435					440					445			
Thr	Gly	Arg	Tyr	Glu	Met	Ala	Cys	Pro	His	Val	Ser	Ser	Gln	Ser	Tyr
	450					455					460				
Glu	Gly	Gln	Gly	Arg	Arg	Glu	Gln	Glu	Glu	Glu	Glu	Ser	Thr	Gly	Arg
465					470					475					480
Phe	Gln	Lys	Val	Thr	Ala	Arg	Leu	Ala	Arg	Gly	Asp	Ile	Phe	Val	Ile
				485					490					495	
Pro	Ala	Gly	His	Pro	Ile	Ala	Ile	Thr	Ala	Ser	Gln	Asn	Glu	Asn	Leu
		500						505					510		
Arg	Leu	Leu	Gly	Phe	Asp	Ile	Asn	Gly	Glu	Asn	Asn	Gln	Arg	Asp	Phe
		515					520					525			
Leu	Ala	Gly	Gln	Asn	Asn	Ile	Ile	Asn	Gln	Leu	Glu	Arg	Glu	Ala	Lys
	530					535					540				
Glu	Leu	Ser	Phe	Asn	Met	Pro	Arg	Glu	Glu	Ile	Glu	Glu	Ile	Phe	Glu
545					550					555					560
Ser	Gln	Met	Glu	Ser	Tyr	Phe	Val	Pro	Thr	Glu	Arg	Gln	Ser	Arg	Arg
				565					570				575		
Gly	Gln	Gly	Arg	Asp	His	Pro	Leu	Ala	Ser	Ile	Leu	Asp	Phe	Ala	Phe
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Phe

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<211> 2172

<212> DNA

<213> 人工序列

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<223> 合成构建物

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<222> (7) .. (2166)

<400> 26

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aac ccc aga aga aga ggc gag ggc tgc caa gag cag atc cag cgg cag			96
Asn Pro Arg Arg Arg Gly Glu Gly Cys Gln Glu Gln Ile Gln Arg Gln			
15	20	25	30
cag aat ctg aac cac tgc cag tac tat ctg agg cag cag agc aga agc			144
Gln Asn Leu Asn His Cys Gln Tyr Tyr Leu Arg Gln Gln Ser Arg Ser			
	35	40	45
ggc ggc tac gac gag gat aac cag aga cag cac ttc aga cag tgc tgc			192
Gly Gly Tyr Asp Glu Asp Asn Gln Arg Gln His Phe Arg Gln Cys Cys			
	50	55	60
cag cag ctg agc cag atc gag gaa cag tgc cag tgc gag gga ctg aga			240
Gln Gln Leu Ser Gln Ile Glu Glu Gln Cys Gln Cys Glu Gly Leu Arg			
	65	70	75
caa gcc gtg cgg aga caa cag cag cag caa gga ctg cgg ggc gaa gag			288
Gln Ala Val Arg Arg Gln Gln Gln Gln Gln Gly Leu Arg Gly Glu Glu			
	80	85	90
atg gaa gaa atg gtg cag agc gcc aga gat ctg ccc aaa gag tgc ggc			336
Met Glu Glu Met Val Gln Ser Ala Arg Asp Leu Pro Lys Glu Cys Gly			
95	100	105	110
atc agc agc cag aga tgc gag atc cgg cgg agt tgg ttc ggc gga ggg			384
Ile Ser Ser Gln Arg Cys Glu Ile Arg Arg Ser Trp Phe Gly Gly Gly			
	115	120	125
ggc aga ggc cgg gac gac gac gat gag gaa aac ccc aga gat ccc cgc			432
Gly Arg Gly Arg Asp Asp Asp Asp Glu Glu Asn Pro Arg Asp Pro Arg			
	130	135	140
gag cag tac cgg cag tgc caa gag tac tgc aga agg caa ggc caa ggc			480
Glu Gln Tyr Arg Gln Cys Gln Glu Tyr Cys Arg Arg Gln Gly Gln Gly			
	145	150	155
cag aga cag cag cag cag tgc cag atc aga tgc gag gaa cgg ctg gaa			528
Gln Arg Gln Gln Gln Gln Cys Gln Ile Arg Cys Glu Glu Arg Leu Glu			
	160	165	170
gag gac cag cgg agc caa gag gaa cgc gag cgg aga aga ggc aga gat			576
Glu Asp Gln Arg Ser Gln Glu Glu Arg Glu Arg Arg Arg Gly Arg Asp			
175	180	185	190
gtg gac gac cag aac ccc cgg gac ccc gag cag aga tac gag cag tgt			624
Val Asp Asp Gln Asn Pro Arg Asp Pro Glu Gln Arg Tyr Glu Gln Cys			
	195	200	205
cag cag cag tgt gaa cgg cag cgg aga ggc caa gag cag aca ctg tgt			672
Gln Gln Gln Cys Glu Arg Gln Arg Arg Gly Gln Glu Gln Thr Leu Cys			

210	215	220
cgg cgg aga tgc gag cag cgg cgg cag caa gag gaa aga gaa cgc cag 720		
Arg Arg Arg Cys Glu Gln Arg Arg Gln Gln Glu Glu Arg Glu Arg Gln		
225	230	235
cgg ggc aga gac aga caa gac ccc cag cag cag tac cac cgg tgc cag 768		
Arg Gly Arg Asp Arg Gln Asp Pro Gln Gln Gln Tyr His Arg Cys Gln		
240	245	250
aga aga tgc cag atc caa gaa cag agc ccc gag cgg cag cgc cag tgc 816		
Arg Arg Cys Gln Ile Gln Glu Gln Ser Pro Glu Arg Gln Arg Gln Cys		
255	260	265
cag cag aga tgc gaa aga cag tac aaa gag cag caa ggc aga gag agg 864		
Gln Gln Arg Cys Glu Arg Gln Tyr Lys Glu Gln Gln Gly Arg Glu Arg		
275	280	285
ggc cca gag gcc agc cct aga aga gag tcc aga gga cgg gaa gaa gaa 912		
Gly Pro Glu Ala Ser Pro Arg Arg Glu Ser Arg Gly Arg Glu Glu Glu		
290	295	300
cag cag cgg cac aac ccc tac tac ttc cac agc cag agc atc aga agc 960		
Gln Gln Arg His Asn Pro Tyr Tyr Phe His Ser Gln Ser Ile Arg Ser		
305	310	315
cgg cac gag agc gaa gag ggc gaa gtg aag tat ctg gaa cgg ttc acc 1008		
Arg His Glu Ser Glu Glu Gly Glu Val Lys Tyr Leu Glu Arg Phe Thr		
320	325	330
gag cgg acc gag ctg ctg aga ggc atc gag aac tac cgg gtc gtg att 1056		
Glu Arg Thr Glu Leu Leu Arg Gly Ile Glu Asn Tyr Arg Val Val Ile		
335	340	345
ctg gac gcc aac ccc aac aca tcc atg ctg ccc cac cac aag gac gcc 1104		
Leu Asp Ala Asn Pro Asn Thr Ser Met Leu Pro His His Lys Asp Ala		
355	360	365
gag tct gtg gcc gtc gtg aca agg ggc aga gcc aca ctg aca ctg gtg 1152		
Glu Ser Val Ala Val Val Thr Arg Gly Arg Ala Thr Leu Thr Leu Val		
370	375	380
tcc caa gag act cgc gag agc ttc aat ctg gaa tgc ggc gac gtg atc 1200		
Ser Gln Glu Thr Arg Glu Ser Phe Asn Leu Glu Cys Gly Asp Val Ile		
385	390	395
cgg gtg cca gct ggg gct aca gtg tac gtg atc aac caa gac agc aac 1248		
Arg Val Pro Ala Gly Ala Thr Val Tyr Val Ile Asn Gln Asp Ser Asn		
400	405	410
gag cgg ctg gaa atg gtc aag ctg ctg cag ccc gtg aac aac ccc ggc 1296		
Glu Arg Leu Glu Met Val Lys Leu Leu Gln Pro Val Asn Asn Pro Gly		

415	420	425	430
cag ttc aga gag tac tac gcc gct ggc gcc aag tcc ccc gac cag agc	1344		
Gln Phe Arg Glu Tyr Tyr Ala Ala Gly Ala Lys Ser Pro Asp Gln Ser			
435	440	445	
tat ctg cgg gtg ttc agc aac gac att ctg gtg gcc gct ctg aat acc	1392		
Tyr Leu Arg Val Phe Ser Asn Asp Ile Leu Val Ala Ala Leu Asn Thr			
450	455	460	
cct cgg gac aga ctg gaa aga ttc ttc gat cag caa gag cag cgc gag	1440		
Pro Arg Asp Arg Leu Glu Arg Phe Phe Asp Gln Gln Glu Gln Arg Glu			
465	470	475	
ggc gtg atc atc aga gcc agc caa gag aag ctg cgg gct ctg agc cag	1488		
Gly Val Ile Ile Arg Ala Ser Gln Glu Lys Leu Arg Ala Leu Ser Gln			
480	485	490	
cac gcc atg tct gct gga cag agg cct tgg ggc aga aga agc tct ggc	1536		
His Ala Met Ser Ala Gly Gln Arg Pro Trp Gly Arg Arg Ser Ser Gly			
495	500	505	510
ggc cct atc tct ctg aag tcc gag agc ccc tcc tac agc aac cag ttt	1584		
Gly Pro Ile Ser Leu Lys Ser Glu Ser Pro Ser Tyr Ser Asn Gln Phe			
515	520	525	
ggc cag ttc ttc gag gct tgc ccc gag gaa cac cgg cag ctg caa gaa	1632		
Gly Gln Phe Phe Glu Ala Cys Pro Glu Glu His Arg Gln Leu Gln Glu			
530	535	540	
atg gac gtg ctc gtg aac tac gcc gag atc aag agg ggc gcc atg atg	1680		
Met Asp Val Leu Val Asn Tyr Ala Glu Ile Lys Arg Gly Ala Met Met			
545	550	555	
gtg ccc cac tac aac agc aag gcc acc gtg gtg gtg tac gtg gtg gaa	1728		
Val Pro His Tyr Asn Ser Lys Ala Thr Val Val Val Tyr Val Val Glu			
560	565	570	
ggc acc ggc aga tac gag atg gca tgc ccc cac gtg tcc agc cag tct	1776		
Gly Thr Gly Arg Tyr Glu Met Ala Cys Pro His Val Ser Ser Gln Ser			
575	580	585	590
tac gag ggc caa gga cgc aga gag caa gaa gag gaa gag tcc acc gga	1824		
Tyr Glu Gly Gln Gly Arg Arg Glu Gln Glu Glu Glu Ser Thr Gly			
595	600	605	
cgg ttc cag aaa gtg acc gcc aga ctg gcc aga ggc gac atc ttc gtg	1872		
Arg Phe Gln Lys Val Thr Ala Arg Leu Ala Arg Gly Asp Ile Phe Val			
610	615	620	
atc cca gcc gga cac cct atc gcc atc acc gcc agc cag aac gag aat	1920		
Ile Pro Ala Gly His Pro Ile Ala Ile Thr Ala Ser Gln Asn Glu Asn			

625	630	635
ctg cgg ctg ctg ggc ttc gac atc aac ggc gag aac aac cag cgg gac	1968	
Leu Arg Leu Leu Gly Phe Asp Ile Asn Gly Glu Asn Asn Gln Arg Asp		
640	645	650
ttt ctg gcc gga cag aac aac atc atc aac cag ctg gaa cgg gaa gcc	2016	
Phe Leu Ala Gly Gln Asn Asn Ile Ile Asn Gln Leu Glu Arg Glu Ala		
655	660	665
aaa gaa ctg agc ttc aac atg ccc cgc gag gaa atc gaa gag att ttc	2064	
Lys Glu Leu Ser Phe Asn Met Pro Arg Glu Glu Ile Glu Glu Ile Phe		
675	680	685
gag agc cag atg gaa agc tac ttc gtg ccc acc gag cgc cag agc aga	2112	
Glu Ser Gln Met Glu Ser Tyr Phe Val Pro Thr Glu Arg Gln Ser Arg		
690	695	700
agg ggc caa ggg cgg gat cac cca ctg gcc tct att ctg gat ttc gcc	2160	
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ttc ttc gaattc	2172	
Phe Phe		
720		
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Leu Asn His Cys Gln Tyr Tyr Leu Arg Gln Gln Ser Arg Ser Gly Gly		
35 40 45		
Tyr Asp Glu Asp Asn Gln Arg Gln His Phe Arg Gln Cys Cys Gln Gln		
50 55 60		
Leu Ser Gln Ile Glu Glu Gln Cys Gln Cys Glu Gly Leu Arg Gln Ala		
65 70 75 80		
Val Arg Arg Gln Gln Gln Gln Gly Leu Arg Gly Glu Glu Met Glu		
85 90 95		
Glu Met Val Gln Ser Ala Arg Asp Leu Pro Lys Glu Cys Gly Ile Ser		

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

Leu	Glu	Met	Val	Lys	Leu	Leu	Gln	Pro	Val	Asn	Asn	Pro	Gly	Gln	Phe	
Arg	Glu	Tyr	Tyr	Ala	Ala	Gly	Ala	Lys	Ser	Pro	Asp	Gln	Ser	Tyr	Leu	
Arg	Val	Phe	Ser	Asn	Asp	Ile	Leu	Val	Ala	Ala	Leu	Asn	Thr	Pro	Arg	
Asp	Arg	Leu	Glu	Arg	Phe	Phe	Asp	Gln	Gln	Glu	Gln	Arg	Glu	Gly	Val	
Ile	Ile	Arg	Ala	Ser	Gln	Glu	Lys	Leu	Arg	Ala	Leu	Ser	Gln	His	Ala	
Met	Ser	Ala	Gly	Gln	Arg	Pro	Trp	Gly	Arg	Arg	Ser	Ser	Gly	Gly	Pro	
Ile	Ser	Leu	Lys	Ser	Glu	Ser	Pro	Ser	Tyr	Ser	Asn	Gln	Phe	Gly	Gln	
Phe	Phe	Glu	Ala	Cys	Pro	Glu	Glu	His	Arg	Gln	Leu	Gln	Glu	Met	Asp	
Val	Leu	Val	Asn	Tyr	Ala	Glu	Ile	Lys	Arg	Gly	Ala	Met	Met	Val	Pro	
His	Tyr	Asn	Ser	Lys	Ala	Thr	Val	Val	Val	Tyr	Val	Val	Glu	Gly	Thr	
Gly	Arg	Tyr	Glu	Met	Ala	Cys	Pro	His	Val	Ser	Ser	Gln	Ser	Tyr	Glu	
Gly	Gln	Gly	Arg	Arg	Glu	Gln	Glu	Glu	Glu	Glu	Ser	Thr	Gly	Arg	Phe	
Gln	Lys	Val	Thr	Ala	Arg	Leu	Ala	Arg	Gly	Asp	Ile	Phe	Val	Ile	Pro	
Ala	Gly	His	Pro	Ile	Ala	Ile	Thr	Ala	Ser	Gln	Asn	Glu	Asn	Leu	Arg	
Leu	Leu	Gly	Phe	Asp	Ile	Asn	Gly	Glu	Asn	Asn	Gln	Arg	Asp	Phe	Leu	
Ala	Gly	Gln	Asn	Asn	Ile	Ile	Asn	Gln	Leu	Glu	Arg	Glu	Ala	Lys	Glu	
Leu	Ser	Phe	Asn	Met	Pro	Arg	Glu	Glu	Ile	Glu	Glu	Ile	Phe	Glu	Ser	
Gln	Met	Glu	Ser	Tyr	Phe	Val	Pro	Thr	Glu	Arg	Gln	Ser	Arg	Arg	Gly	
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<210> 28

<211> 1125

<212> DNA

<213> 豚草(Ambrosia artemisiifolia)

<220>

<221> CDS

<222> (7) .. (1119)

<400> 28

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1

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Arg Leu Thr Thr Ser Gly Ala Tyr Asn Ile Ile Asp Gly Cys Trp Arg

15

20

25

30

ggc aag gcc gat tgg gcc gag aac aga aag gct ctg gcc gat tgc gcc 144

Gly Lys Ala Asp Trp Ala Glu Asn Arg Lys Ala Leu Ala Asp Cys Ala

35

40

45

caa ggc ttc ggc aag gga aca gtg ggc ggc aag gac ggc gac atc tac 192

Gln Gly Phe Gly Lys Gly Thr Val Gly Gly Lys Asp Gly Asp Ile Tyr

50

55

60

acc gtg acc agc gag ctg gac gac gac gtg gcc aat ccc aaa gag ggc 240

Thr Val Thr Ser Glu Leu Asp Asp Asp Val Ala Asn Pro Lys Glu Gly

65

70

75

aca ctg aga ttc gga gcc gcc cag aac cgg cct ctg tgg atc atc ttc 288

Thr Leu Arg Phe Gly Ala Ala Gln Asn Arg Pro Leu Trp Ile Ile Phe

80

85

90

gag cgg gac atg gtc atc cgg ctg gac aaa gaa atg gtc gtg aac agc 336

Glu Arg Asp Met Val Ile Arg Leu Asp Lys Glu Met Val Val Asn Ser

95

100

105

110

gac aag acc atc gac gga aga ggc gcc aaa gtg gaa atc atc aac gcc 384

Asp Lys Thr Ile Asp Gly Arg Gly Ala Lys Val Glu Ile Ile Asn Ala

115

120

125

ggc ttc aca ctg aac ggc gtg aag aac gtg atc atc cac aac atc aac 432

Gly Phe Thr Leu Asn Gly Val Lys Asn Val Ile Ile His Asn Ile Asn

130

135

140

atg cac gac gtg aaa gtg aat ccc ggc gga ctg atc aag agc aac gat 480

Met His Asp Val Lys Val Asn Pro Gly Gly Leu Ile Lys Ser Asn Asp

145

150

155

ggc cca gcc gcc cct aga gcc gga tct gat ggc gac gcc att tcc atc 528

Gly Pro Ala Ala Pro Arg Ala Gly Ser Asp Gly Asp Ala Ile Ser Ile

160	165	170	
agc ggc agc tct cag atc tgg atc gac cac tgc tct ctg agc aag agc	576		
Ser Gly Ser Ser Gln Ile Trp Ile Asp His Cys Ser Leu Ser Lys Ser			
175	180	185	190
gtg gac gga ctc gtg gac gcc aag ctg ggc acc aca aga ctg acc gtg	624		
Val Asp Gly Leu Val Asp Ala Lys Leu Gly Thr Thr Arg Leu Thr Val			
195	200	205	
tcc aac tct ctg ttc acc cag cac cag ttc gtg ctg ctg ttc ggc gct	672		
Ser Asn Ser Leu Phe Thr Gln His Gln Phe Val Leu Leu Phe Gly Ala			
210	215	220	
ggc gac gag aac atc gag gat agg ggc atg ctg gcc acc gtg gcc ttc	720		
Gly Asp Glu Asn Ile Glu Asp Arg Gly Met Leu Ala Thr Val Ala Phe			
225	230	235	
aac aca ttc acc gac aac gtg gac cag cgg atg ccc aga tgc cgg cac	768		
Asn Thr Phe Thr Asp Asn Val Asp Gln Arg Met Pro Arg Cys Arg His			
240	245	250	
ggc ttc ttc caa gtc gtg aac aac aac tac gat aag tgg ggc agc tac	816		
Gly Phe Phe Gln Val Val Asn Asn Asn Tyr Asp Lys Trp Gly Ser Tyr			
255	260	265	270
gcc atc ggc ggc tct gcc agc cct acc att ctg agc caa ggc aac cgg	864		
Ala Ile Gly Gly Ser Ala Ser Pro Thr Ile Leu Ser Gln Gly Asn Arg			
275	280	285	
ttc tgc gcc cca gac gag cgg agc aag aag aat gtg ctg gga cgg cac	912		
Phe Cys Ala Pro Asp Glu Arg Ser Lys Lys Asn Val Leu Gly Arg His			
290	295	300	
ggc gaa gcc gcc gct gaa tcc atg aag tgg aac tgg cgg acc aac aag	960		
Gly Glu Ala Ala Ala Glu Ser Met Lys Trp Asn Trp Arg Thr Asn Lys			
305	310	315	
gac gtg ctg gaa aac ggc gcc atc ttc gtg gcc tct ggc gtg gac cca	1008		
Asp Val Leu Glu Asn Gly Ala Ile Phe Val Ala Ser Gly Val Asp Pro			
320	325	330	
gtg ctg aca cca gaa cag agc gcc ggc atg att cca gcc gag ccc ggc	1056		
Val Leu Thr Pro Glu Gln Ser Ala Gly Met Ile Pro Ala Glu Pro Gly			
335	340	345	350
gaa tct gct ctg tct ctg aca agc tct gcc ggc gtg ctg agc tgt cag	1104		
Glu Ser Ala Leu Ser Leu Thr Ser Ser Ala Gly Val Leu Ser Cys Gln			
355	360	365	
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Pro Gly Ala Pro Cys			

370

<210> 29

<211> 371

<212> PRT

<213> 豚草(Ambrosia artemisiifolia)

<400> 29

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Thr	Thr	Ser	Gly	Ala	Tyr	Asn	Ile	Ile	Asp	Gly	Cys	Trp	Arg	Gly	Lys
			20					25					30		
Ala	Asp	Trp	Ala	Glu	Asn	Arg	Lys	Ala	Leu	Ala	Asp	Cys	Ala	Gln	Gly
		35					40					45			
Phe	Gly	Lys	Gly	Thr	Val	Gly	Gly	Lys	Asp	Gly	Asp	Ile	Tyr	Thr	Val
	50					55					60				
Thr	Ser	Glu	Leu	Asp	Asp	Asp	Val	Ala	Asn	Pro	Lys	Glu	Gly	Thr	Leu
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Arg	Phe	Gly	Ala	Ala	Gln	Asn	Arg	Pro	Leu	Trp	Ile	Ile	Phe	Glu	Arg
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Asp	Met	Val	Ile	Arg	Leu	Asp	Lys	Glu	Met	Val	Val	Asn	Ser	Asp	Lys
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Thr	Ile	Asp	Gly	Arg	Gly	Ala	Lys	Val	Glu	Ile	Ile	Asn	Ala	Gly	Phe
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Asp	Val	Lys	Val	Asn	Pro	Gly	Gly	Leu	Ile	Lys	Ser	Asn	Asp	Gly	Pro
145					150					155					160
Ala	Ala	Pro	Arg	Ala	Gly	Ser	Asp	Gly	Asp	Ala	Ile	Ser	Ile	Ser	Gly
				165					170					175	
Ser	Ser	Gln	Ile	Trp	Ile	Asp	His	Cys	Ser	Leu	Ser	Lys	Ser	Val	Asp
		180					185						190		
Gly	Leu	Val	Asp	Ala	Lys	Leu	Gly	Thr	Thr	Arg	Leu	Thr	Val	Ser	Asn
		195					200						205		
Ser	Leu	Phe	Thr	Gln	His	Gln	Phe	Val	Leu	Leu	Phe	Gly	Ala	Gly	Asp
	210					215					220				
Glu	Asn	Ile	Glu	Asp	Arg	Gly	Met	Leu	Ala	Thr	Val	Ala	Phe	Asn	Thr
225					230					235					240
Phe	Thr	Asp	Asn	Val	Asp	Gln	Arg	Met	Pro	Arg	Cys	Arg	His	Gly	Phe
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Ala Pro Asp Glu Arg Ser Lys Lys Asn Val Leu Gly Arg His Gly Glu		
290	295	300
Ala Ala Ala Glu Ser Met Lys Trp Asn Trp Arg Thr Asn Lys Asp Val		
305	310	315
Leu Glu Asn Gly Ala Ile Phe Val Ala Ser Gly Val Asp Pro Val Leu		
325	330	335
Thr Pro Glu Gln Ser Ala Gly Met Ile Pro Ala Glu Pro Gly Glu Ser		
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ctg ctg ctc ggc ctc atg cat tgt gcg tca gca gca atg ttt atg gtg 96		
Leu Leu Leu Gly Leu Met His Cys Ala Ser Ala Ala Met Phe Met Val		
20 25 30		
aaa aat ggc aac ggg acc gcg tgc ata atg gcc aac ttc tct gct gcc 144		
Lys Asn Gly Asn Gly Thr Ala Cys Ile Met Ala Asn Phe Ser Ala Ala		
35 40 45		
ttc tca gtg aac tac gac acc aag agt ggc cct aag aac atg acc ctt 192		
Phe Ser Val Asn Tyr Asp Thr Lys Ser Gly Pro Lys Asn Met Thr Leu		
50 55 60		
gac ctg cca tca gat gcc aca gtg gtg ctc aac cgc agc tcc tgt gga 240		
Asp Leu Pro Ser Asp Ala Thr Val Val Leu Asn Arg Ser Ser Cys Gly		

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aaa gag aac act tct gac ccc agt ctc gtg att gct ttt gga aga gga	288		
Lys Glu Asn Thr Ser Asp Pro Ser Leu Val Ile Ala Phe Gly Arg Gly			
85	90	95	
cat aca ctc act ctc aat ttc acg aga aat gca aca cgt tac agc gtc	336		
His Thr Leu Thr Leu Asn Phe Thr Arg Asn Ala Thr Arg Tyr Ser Val			
100	105	110	
cag ctc atg agt ttt gtt tat aac ttg tca gac aca cac ctt ttc ccc	384		
Gln Leu Met Ser Phe Val Tyr Asn Leu Ser Asp Thr His Leu Phe Pro			
115	120	125	
aat gcg agc tcc aaa gaa atc aag act gtg gaa tct ata act gac atc	432		
Asn Ala Ser Ser Lys Glu Ile Lys Thr Val Glu Ser Ile Thr Asp Ile			
130	135	140	
agg gca gat ata gat aaa aaa tac aga tgt gtt agt ggc acc cag gtc	480		
Arg Ala Asp Ile Asp Lys Lys Tyr Arg Cys Val Ser Gly Thr Gln Val			
145	150	155	160
cac atg aac aac gtg acc gta acg ctc cat gat gcc acc atc cag gcg	528		
His Met Asn Asn Val Thr Val Thr Leu His Asp Ala Thr Ile Gln Ala			
165	170	175	
tac ctt tcc aac agc agc ttc agc cgg gga gag aca cgc tgt gaa caa	576		
Tyr Leu Ser Asn Ser Ser Phe Ser Arg Gly Glu Thr Arg Cys Glu Gln			
180	185	190	
gac agg cct tcc cca acc aca gcg ccc cct gcg cca ccc agc ccc tcg	624		
Asp Arg Pro Ser Pro Thr Thr Ala Pro Pro Ala Pro Pro Ser Pro Ser			
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Pro Ser Pro Val Pro Lys Ser Pro Ser Val Asp Lys Tyr Asn Val Ser			
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Gly Thr Asn Gly Thr Cys Leu Leu Ala Ser Met Gly Leu Gln Leu Asn			
225	230	235	240
ctc acc tat gag agg aag gac aac acg acg gtg aca agg ctt ctc aac	768		
Leu Thr Tyr Glu Arg Lys Asp Asn Thr Thr Val Thr Arg Leu Leu Asn			
245	250	255	
atc aac ccc aac aag acc tcg gcc agc ggg agc tgc ggc gcc cac ctg	816		
Ile Asn Pro Asn Lys Thr Ser Ala Ser Gly Ser Cys Gly Ala His Leu			
260	265	270	
gtg act ctg gag ctg cac agc gag ggc acc acc gtc ctg ctc ttc cag	864		
Val Thr Leu Glu Leu His Ser Glu Gly Thr Thr Val Leu Leu Phe Gln			

275	280	285
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Phe Gly Met Asn Ala Ser Ser Ser Arg Phe Phe Leu Gln Gly Ile Gln		
290	295	300
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305	310	315
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325	330	335
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Cys Asn Ala Glu Glu His Val Arg Val Thr Lys Ala Phe Ser Val Asn		
340	345	350
ata ttc aaa gtg tgg gtc cag gct ttc aag gtg gaa ggt ggc cag ttt 1104		
Ile Phe Lys Val Trp Val Gln Ala Phe Lys Val Glu Gly Gly Gln Phe		
355	360	365
ggc tct gtg gag gag tgt ctg ctg gac gag aac agc ctc gag gcc gag 1152		
Gly Ser Val Glu Glu Cys Leu Leu Asp Glu Asn Ser Leu Glu Ala Glu		
370	375	380
gat ctg caa gag att ctg ccc gtg aac gag aca cgg cgg ctg aca aca 1200		
Asp Leu Gln Glu Ile Leu Pro Val Asn Glu Thr Arg Arg Leu Thr Thr		
385	390	395
agc ggc gcc tac aac atc atc gac ggc tgc tgg cgg ggc aag gcc gat 1248		
Ser Gly Ala Tyr Asn Ile Ile Asp Gly Cys Trp Arg Gly Lys Ala Asp		
405	410	415
tgg gcc gag aac aga aag gct ctg gcc gat tgc gcc caa ggc ttc ggc 1296		
Trp Ala Glu Asn Arg Lys Ala Leu Ala Asp Cys Ala Gln Gly Phe Gly		
420	425	430
aag gga aca gtg ggc ggc aag gac ggc gac atc tac acc gtg acc agc 1344		
Lys Gly Thr Val Gly Gly Lys Asp Gly Asp Ile Tyr Thr Val Thr Ser		
435	440	445
gag ctg gac gac gac gtg gcc aat ccc aaa gag ggc aca ctg aga ttc 1392		
Glu Leu Asp Asp Asp Val Ala Asn Pro Lys Glu Gly Thr Leu Arg Phe		
450	455	460
gga gcc gcc cag aac cgg cct ctg tgg atc atc ttc gag cgg gac atg 1440		
Gly Ala Ala Gln Asn Arg Pro Leu Trp Ile Ile Phe Glu Arg Asp Met		
465	470	475
gtc atc cgg ctg gac aaa gaa atg gtc gtg aac agc gac aag acc atc 1488		
Val Ile Arg Leu Asp Lys Glu Met Val Val Asn Ser Asp Lys Thr Ile		

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gac gga aga ggc gcc aaa gtg gaa atc atc aac gcc ggc ttc aca ctg 1536		
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aac ggc gtg aag aac gtg atc atc cac aac atc aac atg cac gac gtg 1584		
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Lys Val Asn Pro Gly Gly Leu Ile Lys Ser Asn Asp Gly Pro Ala Ala		
530	535	540
cct aga gcc gga tct gat ggc gac gcc att tcc atc agc ggc agc tct 1680		
Pro Arg Ala Gly Ser Asp Gly Asp Ala Ile Ser Ile Ser Gly Ser Ser		
545	550	555
cag atc tgg atc gac cac tgc tct ctg agc aag agc gtg gac gga ctc 1728		
Gln Ile Trp Ile Asp His Cys Ser Leu Ser Lys Ser Val Asp Gly Leu		
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atc gag gat agg ggc atg ctg gcc acc gtg gcc ttc aac aca ttc acc 1872		
Ile Glu Asp Arg Gly Met Leu Ala Thr Val Ala Phe Asn Thr Phe Thr		
610	615	620
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Asp Asn Val Asp Gln Arg Met Pro Arg Cys Arg His Gly Phe Phe Gln		
625	630	635
gtc gtg aac aac aac tac gat aag tgg ggc agc tac gcc atc ggc ggc 1968		
Val Val Asn Asn Asn Tyr Asp Lys Trp Gly Ser Tyr Ala Ile Gly Gly		
645	650	655
tct gcc agc cct acc att ctg agc caa ggc aac cgg ttc tgc gcc cca 2016		
Ser Ala Ser Pro Thr Ile Leu Ser Gln Gly Asn Arg Phe Cys Ala Pro		
660	665	670
gac gag cgg agc aag aag aat gtg ctg gga cgg cac ggc gaa gcc gcc 2064		
Asp Glu Arg Ser Lys Lys Asn Val Leu Gly Arg His Gly Glu Ala Ala		
675	680	685
gct gaa tcc atg aag tgg aac tgg cgg acc aac aag gac gtg ctg gaa 2112		
Ala Glu Ser Met Lys Trp Asn Trp Arg Thr Asn Lys Asp Val Leu Glu		

690	695	700
aac ggc gcc atc ttc gtg gcc tct ggc gtg gac cca gtg ctg aca cca	2160	
Asn Gly Ala Ile Phe Val Ala Ser Gly Val Asp Pro Val Leu Thr Pro		
705	710	715
720		
gaa cag agc gcc ggc atg att cca gcc gag ccc ggc gaa tct gct ctg	2208	
Glu Gln Ser Ala Gly Met Ile Pro Ala Glu Pro Gly Glu Ser Ala Leu		
725	730	735
tct ctg aca agc tct gcc ggc gtg ctg agc tgt cag ccc gga gca cca	2256	
Ser Leu Thr Ser Ser Ala Gly Val Leu Ser Cys Gln Pro Gly Ala Pro		
740	745	750
tgt gaa ttc acg ctg atc ccc atc gct gtg ggt ggt gcc ctg gcg ggg	2304	
Cys Glu Phe Thr Leu Ile Pro Ile Ala Val Gly Gly Ala Leu Ala Gly		
755	760	765
ctg gtc ctc atc gtc ctc atc gcc tac ctc gtc ggc agg aag agg agt	2352	
Leu Val Leu Ile Val Leu Ile Ala Tyr Leu Val Gly Arg Lys Arg Ser		
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Lys Asn Gly Asn Gly Thr Ala Cys Ile Met Ala Asn Phe Ser Ala Ala		
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Phe Ser Val Asn Tyr Asp Thr Lys Ser Gly Pro Lys Asn Met Thr Leu		
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Asp Leu Pro Ser Asp Ala Thr Val Val Leu Asn Arg Ser Ser Cys Gly		
65	70	75
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Lys Glu Asn Thr Ser Asp Pro Ser Leu Val Ile Ala Phe Gly Arg Gly		
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His Thr Leu Thr Leu Asn Phe Thr Arg Asn Ala Thr Arg Tyr Ser Val		

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Gln Leu Met Ser Phe Val Tyr Asn Leu Ser Asp Thr His Leu Phe Pro					
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Asn Ala Ser Ser Lys Glu Ile Lys Thr Val Glu Ser Ile Thr Asp Ile					
130		135		140	
Arg Ala Asp Ile Asp Lys Lys Tyr Arg Cys Val Ser Gly Thr Gln Val					
145		150		155	160
His Met Asn Asn Val Thr Val Thr Leu His Asp Ala Thr Ile Gln Ala					
165		170		175	
Tyr Leu Ser Asn Ser Ser Phe Ser Arg Gly Glu Thr Arg Cys Glu Gln					
180		185		190	
Asp Arg Pro Ser Pro Thr Thr Ala Pro Pro Ala Pro Pro Ser Pro Ser					
195		200		205	
Pro Ser Pro Val Pro Lys Ser Pro Ser Val Asp Lys Tyr Asn Val Ser					
210		215		220	
Gly Thr Asn Gly Thr Cys Leu Leu Ala Ser Met Gly Leu Gln Leu Asn					
225		230		235	240
Leu Thr Tyr Glu Arg Lys Asp Asn Thr Thr Val Thr Arg Leu Leu Asn					
245		250		255	
Ile Asn Pro Asn Lys Thr Ser Ala Ser Gly Ser Cys Gly Ala His Leu					
260		265		270	
Val Thr Leu Glu Leu His Ser Glu Gly Thr Thr Val Leu Leu Phe Gln					
275		280		285	
Phe Gly Met Asn Ala Ser Ser Ser Arg Phe Phe Leu Gln Gly Ile Gln					
290		295		300	
Leu Asn Thr Ile Leu Pro Asp Ala Arg Asp Pro Ala Phe Lys Ala Ala					
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Asn Gly Ser Leu Arg Ala Leu Gln Ala Thr Val Gly Asn Ser Tyr Lys					
325		330		335	
Cys Asn Ala Glu Glu His Val Arg Val Thr Lys Ala Phe Ser Val Asn					
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370		375		380	
Asp Leu Gln Glu Ile Leu Pro Val Asn Glu Thr Arg Arg Leu Thr Thr					
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Ser Gly Ala Tyr Asn Ile Ile Asp Gly Cys Trp Arg Gly Lys Ala Asp					
405		410		415	

Trp	Ala	Glu	Asn	Arg	Lys	Ala	Leu	Ala	Asp	Cys	Ala	Gln	Gly	Phe	Gly			
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Lys	Gly	Thr	Val	Gly	Gly	Lys	Asp	Gly	Asp	Ile	Tyr	Thr	Val	Thr	Ser			
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Glu	Leu	Asp	Asp	Asp	Val	Ala	Asn	Pro	Lys	Glu	Gly	Thr	Leu	Arg	Phe			
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Gly	Ala	Ala	Gln	Asn	Arg	Pro	Leu	Trp	Ile	Ile	Phe	Glu	Arg	Asp	Met			
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Val	Ile	Arg	Leu	Asp	Lys	Glu	Met	Val	Val	Asn	Ser	Asp	Lys	Thr	Ile			
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Asp	Gly	Arg	Gly	Ala	Lys	Val	Glu	Ile	Ile	Asn	Ala	Gly	Phe	Thr	Leu			
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Pro	Arg	Ala	Gly	Ser	Asp	Gly	Asp	Ala	Ile	Ser	Ile	Ser	Gly	Ser	Ser			
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Gln	Ile	Trp	Ile	Asp	His	Cys	Ser	Leu	Ser	Lys	Ser	Val	Asp	Gly	Leu			
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Val	Asp	Ala	Lys	Leu	Gly	Thr	Thr	Arg	Leu	Thr	Val	Ser	Asn	Ser	Leu			
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Phe	Thr	Gln	His	Gln	Phe	Val	Leu	Leu	Phe	Gly	Ala	Gly	Asp	Glu	Asn			
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Ile	Glu	Asp	Arg	Gly	Met	Leu	Ala	Thr	Val	Ala	Phe	Asn	Thr	Phe	Thr			
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Asp	Asn	Val	Asp	Gln	Arg	Met	Pro	Arg	Cys	Arg	His	Gly	Phe	Phe	Gln			
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Val	Val	Asn	Asn	Asn	Tyr	Asp	Lys	Trp	Gly	Ser	Tyr	Ala	Ile	Gly	Gly			
																645	650	655
Ser	Ala	Ser	Pro	Thr	Ile	Leu	Ser	Gln	Gly	Asn	Arg	Phe	Cys	Ala	Pro			
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Asp	Glu	Arg	Ser	Lys	Lys	Asn	Val	Leu	Gly	Arg	His	Gly	Glu	Ala	Ala			
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Ala	Glu	Ser	Met	Lys	Trp	Asn	Trp	Arg	Thr	Asn	Lys	Asp	Val	Leu	Glu			
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Asn	Gly	Ala	Ile	Phe	Val	Ala	Ser	Gly	Val	Asp	Pro	Val	Leu	Thr	Pro			
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Glu	Gln	Ser	Ala	Gly	Met	Ile	Pro	Ala	Glu	Pro	Gly	Glu	Ser	Ala	Leu			

	725		730		735										
Ser	Leu	Thr	Ser	Ser	Ala	Gly	Val	Leu	Ser	Cys	Gln	Pro	Gly	Ala	Pro
	740		745		750										
Cys	Glu	Phe	Thr	Leu	Ile	Pro	Ile	Ala	Val	Gly	Gly	Ala	Leu	Ala	Gly
	755		760		765										
Leu	Val	Leu	Ile	Val	Leu	Ile	Ala	Tyr	Leu	Val	Gly	Arg	Lys	Arg	Ser
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ccc aaa gtg gcc ccc caa gcc atc agc agc gtg gaa aac atc gag ggc 144
Pro Lys Val Ala Pro Gln Ala Ile Ser Ser Val Glu Asn Ile Glu Gly
          35              40              45

aat ggc gga ccc ggc acc atc aag aag atc agc ttc ccc gag ggc ttc 192
Asn Gly Gly Pro Gly Thr Ile Lys Lys Ile Ser Phe Pro Glu Gly Phe
          50              55              60

cca ttc aaa tac gtg aag gac cgg gtg gac gaa gtg gac cac acc aac 240
Pro Phe Lys Tyr Val Lys Asp Arg Val Asp Glu Val Asp His Thr Asn
          65              70              75

ttc aag tac aac tac tcc gtg atc gag ggc gga ccc atc ggc gac aca 288
Phe Lys Tyr Asn Tyr Ser Val Ile Glu Gly Gly Pro Ile Gly Asp Thr
          80              85              90

ctg gaa aag atc agc aac gag atc aag atc gtg gcc acc ccc gac ggc 336
Leu Glu Lys Ile Ser Asn Glu Ile Lys Ile Val Ala Thr Pro Asp Gly
95              100              105              110

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 Glu Val Lys Ala Glu Gln Val Lys Ala Ser Lys Glu Met Gly Glu Thr
 130 135 140
 ctg ctg cgg gcc gtg gaa agc tat ctg ctg gcc cac agc gac gcc tac 480
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<213> 垂枝桦(*Betula pendula*)

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 35 40 45
 Gly Pro Gly Thr Ile Lys Lys Ile Ser Phe Pro Glu Gly Phe Pro Phe
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 Lys Tyr Val Lys Asp Arg Val Asp Glu Val Asp His Thr Asn Phe Lys
 65 70 75 80
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 Lys Ile Ser Asn Glu Ile Lys Ile Val Ala Thr Pro Asp Gly Gly Ser
 100 105 110
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Leu Leu Leu Gly Leu Met His Cys Ala Ser Ala Ala Met Phe Met Val
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Lys Asn Gly Asn Gly Thr Ala Cys Ile Met Ala Asn Phe Ser Ala Ala
           35           40           45
ttc tca gtg aac tac gac acc aag agt ggc cct aag aac atg acc ctt 192
Phe Ser Val Asn Tyr Asp Thr Lys Ser Gly Pro Lys Asn Met Thr Leu
           50           55           60
gac ctg cca tca gat gcc aca gtg gtg ctc aac cgc agc tcc tgt gga 240
Asp Leu Pro Ser Asp Ala Thr Val Val Leu Asn Arg Ser Ser Cys Gly
65           70           75           80
aaa gag aac act tct gac ccc agt ctc gtg att gct ttt gga aga gga 288
Lys Glu Asn Thr Ser Asp Pro Ser Leu Val Ile Ala Phe Gly Arg Gly
           85           90           95
cat aca ctc act ctc aat ttc acg aga aat gca aca cgt tac agc gtc 336
His Thr Leu Thr Leu Asn Phe Thr Arg Asn Ala Thr Arg Tyr Ser Val
           100          105          110
cag ctc atg agt ttt gtt tat aac ttg tca gac aca cac ctt ttc ccc 384
Gln Leu Met Ser Phe Val Tyr Asn Leu Ser Asp Thr His Leu Phe Pro
           115          120          125
aat gcg agc tcc aaa gaa atc aag act gtg gaa tct ata act gac atc 432
Asn Ala Ser Ser Lys Glu Ile Lys Thr Val Glu Ser Ile Thr Asp Ile
           130          135          140
agg gca gat ata gat aaa aaa tac aga tgt gtt agt ggc acc cag gtc 480
Arg Ala Asp Ile Asp Lys Lys Tyr Arg Cys Val Ser Gly Thr Gln Val
145          150          155          160
cac atg aac aac gtg acc gta acg ctc cat gat gcc acc atc cag gcg 528
His Met Asn Asn Val Thr Val Thr Leu His Asp Ala Thr Ile Gln Ala
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tac ctt tcc aac agc agc ttc agc cgg gga gag aca cgc tgt gaa caa 576
Tyr Leu Ser Asn Ser Ser Phe Ser Arg Gly Glu Thr Arg Cys Glu Gln
      180              185              190
gac agg cct tcc cca acc aca gcg ccc cct gcg cca ccc agc ccc tcg 624
Asp Arg Pro Ser Pro Thr Thr Ala Pro Pro Ala Pro Pro Ser Pro Ser
      195              200              205
ccc tca ccc gtg ccc aag agc ccc tct gtg gac aag tac aac gtg agc 672
Pro Ser Pro Val Pro Lys Ser Pro Ser Val Asp Lys Tyr Asn Val Ser
      210              215              220
ggc acc aac ggg acc tgc ctg ctg gcc agc atg ggg ctg cag ctg aac 720
Gly Thr Asn Gly Thr Cys Leu Leu Ala Ser Met Gly Leu Gln Leu Asn
225              230              235              240
ctc acc tat gag agg aag gac aac acg acg gtg aca agg ctt ctc aac 768
Leu Thr Tyr Glu Arg Lys Asp Asn Thr Thr Val Thr Arg Leu Leu Asn
      245              250              255
atc aac ccc aac aag acc tcg gcc agc ggg agc tgc ggc gcc cac ctg 816
Ile Asn Pro Asn Lys Thr Ser Ala Ser Gly Ser Cys Gly Ala His Leu
      260              265              270
gtg act ctg gag ctg cac agc gag ggc acc acc gtc ctg ctc ttc cag 864
Val Thr Leu Glu Leu His Ser Glu Gly Thr Thr Val Leu Leu Phe Gln
      275              280              285
ttc ggg atg aat gca agt tct agc cgg ttt ttc cta caa gga atc cag 912
Phe Gly Met Asn Ala Ser Ser Ser Arg Phe Phe Leu Gln Gly Ile Gln
      290              295              300
ttg aat aca att ctt cct gac gcc aga gac cct gcc ttt aaa gct gcc 960
Leu Asn Thr Ile Leu Pro Asp Ala Arg Asp Pro Ala Phe Lys Ala Ala
305              310              315              320
aac ggc tcc ctg cga gcg ctg cag gcc aca gtc ggc aat tcc tac aag 1008
Asn Gly Ser Leu Arg Ala Leu Gln Ala Thr Val Gly Asn Ser Tyr Lys
      325              330              335
tgc aac gcg gag gag cac gtc cgt gtc acg aag gcg ttt tca gtc aat 1056
Cys Asn Ala Glu Glu His Val Arg Val Thr Lys Ala Phe Ser Val Asn
      340              345              350
ata ttc aaa gtg tgg gtc cag gct ttc aag gtg gaa ggt ggc cag ttt 1104
Ile Phe Lys Val Trp Val Gln Ala Phe Lys Val Glu Gly Gly Gln Phe
      355              360              365
ggc tct gtg gag gag tgt ctg ctg gac gag aac agc ctc gag ggc gtg 1152
Gly Ser Val Glu Glu Cys Leu Leu Asp Glu Asn Ser Leu Glu Gly Val
      370              375              380

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ttc aac tac gag aca gag aca acc agc gtg atc cca gcc gcc aga ctg 1200
Phe Asn Tyr Glu Thr Glu Thr Thr Ser Val Ile Pro Ala Ala Arg Leu
385                390                395                400
ttc aag gcc ttc att ctg gac ggc gac aat ctg ttc ccc aaa gtg gcc 1248
Phe Lys Ala Phe Ile Leu Asp Gly Asp Asn Leu Phe Pro Lys Val Ala
                405                410                415
ccc caa gcc atc agc agc gtg gaa aac atc gag ggc aat ggc gga ccc 1296
Pro Gln Ala Ile Ser Ser Val Glu Asn Ile Glu Gly Asn Gly Gly Pro
                420                425                430
ggc acc atc aag aag atc agc ttc ccc gag ggc ttc cca ttc aaa tac 1344
Gly Thr Ile Lys Lys Ile Ser Phe Pro Glu Gly Phe Pro Phe Lys Tyr
                435                440                445
gtg aag gac cgg gtg gac gaa gtg gac cac acc aac ttc aag tac aac 1392
Val Lys Asp Arg Val Asp Glu Val Asp His Thr Asn Phe Lys Tyr Asn
                450                455                460
tac tcc gtg atc gag ggc gga ccc atc ggc gac aca ctg gaa aag atc 1440
Tyr Ser Val Ile Glu Gly Gly Pro Ile Gly Asp Thr Leu Glu Lys Ile
465                470                475                480
agc aac gag atc aag atc gtg gcc acc ccc gac ggc ggc agc att ctg 1488
Ser Asn Glu Ile Lys Ile Val Ala Thr Pro Asp Gly Gly Ser Ile Leu
                485                490                495
aag atc tcc aac aag tac cac aca aag ggc gac cac gaa gtg aag gcc 1536
Lys Ile Ser Asn Lys Tyr His Thr Lys Gly Asp His Glu Val Lys Ala
                500                505                510
gaa caa gtg aaa gcc agc aaa gag atg ggc gag aca ctg ctg cgg gcc 1584
Glu Gln Val Lys Ala Ser Lys Glu Met Gly Glu Thr Leu Leu Arg Ala
                515                520                525
gtg gaa agc tat ctg ctg gcc cac agc gac gcc tac aac gaa ttc acg 1632
Val Glu Ser Tyr Leu Leu Ala His Ser Asp Ala Tyr Asn Glu Phe Thr
                530                535                540
ctg atc ccc atc gct gtg ggt ggt gcc ctg gcg ggg ctg gtc ctc atc 1680
Leu Ile Pro Ile Ala Val Gly Gly Ala Leu Ala Gly Leu Val Leu Ile
545                550                555                560
gtc ctc atc gcc tac ctc gtc ggc agg aag agg agt cac gca ggc tac 1728
Val Leu Ile Ala Tyr Leu Val Gly Arg Lys Arg Ser His Ala Gly Tyr
                565                570                575
cag act atc tag taa 1743
Gln Thr Ile
<210> 35

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<211> 579

<212> PRT

<213> 人工序列

<220>

<223> 合成构建物

<400> 35

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

```

260	265	270
Val Thr Leu Glu Leu His Ser Glu Gly Thr Thr Val Leu Leu Phe Gln		
275	280	285
Phe Gly Met Asn Ala Ser Ser Ser Arg Phe Phe Leu Gln Gly Ile Gln		
290	295	300
Leu Asn Thr Ile Leu Pro Asp Ala Arg Asp Pro Ala Phe Lys Ala Ala		
305	310	315
Asn Gly Ser Leu Arg Ala Leu Gln Ala Thr Val Gly Asn Ser Tyr Lys		
325	330	335
Cys Asn Ala Glu Glu His Val Arg Val Thr Lys Ala Phe Ser Val Asn		
340	345	350
Ile Phe Lys Val Trp Val Gln Ala Phe Lys Val Glu Gly Gly Gln Phe		
355	360	365
Gly Ser Val Glu Glu Cys Leu Leu Asp Glu Asn Ser Leu Glu Gly Val		
370	375	380
Phe Asn Tyr Glu Thr Glu Thr Thr Ser Val Ile Pro Ala Ala Arg Leu		
385	390	395
Phe Lys Ala Phe Ile Leu Asp Gly Asp Asn Leu Phe Pro Lys Val Ala		
405	410	415
Pro Gln Ala Ile Ser Ser Val Glu Asn Ile Glu Gly Asn Gly Gly Pro		
420	425	430
Gly Thr Ile Lys Lys Ile Ser Phe Pro Glu Gly Phe Pro Phe Lys Tyr		
435	440	445
Val Lys Asp Arg Val Asp Glu Val Asp His Thr Asn Phe Lys Tyr Asn		
450	455	460
Tyr Ser Val Ile Glu Gly Gly Pro Ile Gly Asp Thr Leu Glu Lys Ile		
465	470	475
Ser Asn Glu Ile Lys Ile Val Ala Thr Pro Asp Gly Gly Ser Ile Leu		
485	490	495
Lys Ile Ser Asn Lys Tyr His Thr Lys Gly Asp His Glu Val Lys Ala		
500	505	510
Glu Gln Val Lys Ala Ser Lys Glu Met Gly Glu Thr Leu Leu Arg Ala		
515	520	525
Val Glu Ser Tyr Leu Leu Ala His Ser Asp Ala Tyr Asn Glu Phe Thr		
530	535	540
Leu Ile Pro Ile Ala Val Gly Gly Ala Leu Ala Gly Leu Val Leu Ile		
545	550	555
Val Leu Ile Ala Tyr Leu Val Gly Arg Lys Arg Ser His Ala Gly Tyr		
565	570	575

Gln Thr Ile

<210> 36

<211> 480

<212> DNA

<213> 灰狼 (Canis lupus)

<220>

<221> CDS

<222> (7) .. (474)

<400> 36

ctcgag caa gac acc ccc gct ctg ggc aag gat acc gtg gcc gtg tcc 48

Gln Asp Thr Pro Ala Leu Gly Lys Asp Thr Val Ala Val Ser

1

5

10

ggc aag tgg tat ctg aag gcc atg acc gcc gac caa gaa gtg ccc gag 96

Gly Lys Trp Tyr Leu Lys Ala Met Thr Ala Asp Gln Glu Val Pro Glu

15

20

25

30

aag ccc gat agc gtg acc ccc atg att ctg aaa gcc cag aag ggc ggc 144

Lys Pro Asp Ser Val Thr Pro Met Ile Leu Lys Ala Gln Lys Gly Gly

35

40

45

aat ctg gaa gcc aag atc acc atg ctg acc aac ggc cag tgc cag aac 192

Asn Leu Glu Ala Lys Ile Thr Met Leu Thr Asn Gly Gln Cys Gln Asn

50

55

60

atc acc gtg gtg ctg cac aag acc agc gag ccc ggc aag tac aca gcc 240

Ile Thr Val Val Leu His Lys Thr Ser Glu Pro Gly Lys Tyr Thr Ala

65

70

75

tac gag ggc cag cgg gtg gtg ttc atc cag cct tct cca gtg cgg gat 288

Tyr Glu Gly Gln Arg Val Val Phe Ile Gln Pro Ser Pro Val Arg Asp

80

85

90

cac tac att ctg tac tgc gag ggc gag ctg cac ggc cgg cag atc aga 336

His Tyr Ile Leu Tyr Cys Glu Gly Glu Leu His Gly Arg Gln Ile Arg

95

100

105

110

atg gcc aag ctg ctg ggc aga gat ccc gag cag agc caa gag gct ctg 384

Met Ala Lys Leu Leu Gly Arg Asp Pro Glu Gln Ser Gln Glu Ala Leu

115

120

125

gaa gat ttc aga gag ttc agc cgg gcc aag gga ctg aac caa gag att 432

Glu Asp Phe Arg Glu Phe Ser Arg Ala Lys Gly Leu Asn Gln Glu Ile

130

135

140

ctg gaa ctg gct cag agc gag aca tgc tct ccc ggc gga caa gaattc 480

Leu Glu Leu Ala Gln Ser Glu Thr Cys Ser Pro Gly Gly Gln

145

150

155

<210> 37

<211> 156

<212> PRT

<213> 灰狼 (Canis lupus)

<400> 37

```

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

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<210> 38

<211> 1734

<212> DNA

<213> 人工序列

<220>

<223> 合成构建物

<220>

<221> CDS

<222> (1) .. (1734)

<400> 38

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atg gcg ccc cgc agc gcc cgg cga ccc ctg ctg ctg cta ctg ctg ttg 48
Met Ala Pro Arg Ser Ala Arg Arg Pro Leu Leu Leu Leu Leu Leu
1          5          10          15
ctg ctg ctc ggc ctc atg cat tgt gcg tca gca gca atg ttt atg gtg 96

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```

Leu Leu Leu Gly Leu Met His Cys Ala Ser Ala Ala Met Phe Met Val
      20                      25                      30
aaa aat ggc aac ggg acc gcg tgc ata atg gcc aac ttc tct gct gcc 144
Lys Asn Gly Asn Gly Thr Ala Cys Ile Met Ala Asn Phe Ser Ala Ala
      35                      40                      45
ttc tca gtg aac tac gac acc aag agt ggc cct aag aac atg acc ctt 192
Phe Ser Val Asn Tyr Asp Thr Lys Ser Gly Pro Lys Asn Met Thr Leu
      50                      55                      60
gac ctg cca tca gat gcc aca gtg gtg ctc aac cgc agc tcc tgt gga 240
Asp Leu Pro Ser Asp Ala Thr Val Val Leu Asn Arg Ser Ser Cys Gly
      65                      70                      75                      80
aaa gag aac act tct gac ccc agt ctc gtg att gct ttt gga aga gga 288
Lys Glu Asn Thr Ser Asp Pro Ser Leu Val Ile Ala Phe Gly Arg Gly
      85                      90                      95
cat aca ctc act ctc aat ttc acg aga aat gca aca cgt tac agc gtc 336
His Thr Leu Thr Leu Asn Phe Thr Arg Asn Ala Thr Arg Tyr Ser Val
      100                     105                     110
cag ctc atg agt ttt gtt tat aac ttg tca gac aca cac ctt ttc ccc 384
Gln Leu Met Ser Phe Val Tyr Asn Leu Ser Asp Thr His Leu Phe Pro
      115                     120                     125
aat gcg agc tcc aaa gaa atc aag act gtg gaa tct ata act gac atc 432
Asn Ala Ser Ser Lys Glu Ile Lys Thr Val Glu Ser Ile Thr Asp Ile
      130                     135                     140
agg gca gat ata gat aaa aaa tac aga tgt gtt agt ggc acc cag gtc 480
Arg Ala Asp Ile Asp Lys Lys Tyr Arg Cys Val Ser Gly Thr Gln Val
      145                     150                     155                     160
cac atg aac aac gtg acc gta acg ctc cat gat gcc acc atc cag gcg 528
His Met Asn Asn Val Thr Val Thr Leu His Asp Ala Thr Ile Gln Ala
      165                     170                     175
tac ctt tcc aac agc agc ttc agc cgg gga gag aca cgc tgt gaa caa 576
Tyr Leu Ser Asn Ser Ser Phe Ser Arg Gly Glu Thr Arg Cys Glu Gln
      180                     185                     190
gac agg cct tcc cca acc aca gcg ccc cct gcg cca ccc agc ccc tcg 624
Asp Arg Pro Ser Pro Thr Thr Ala Pro Pro Ala Pro Pro Ser Pro Ser
      195                     200                     205
ccc tca ccc gtg ccc aag agc ccc tct gtg gac aag tac aac gtg agc 672
Pro Ser Pro Val Pro Lys Ser Pro Ser Val Asp Lys Tyr Asn Val Ser
      210                     215                     220
ggc acc aac ggg acc tgc ctg ctg gcc agc atg ggg ctg cag ctg aac 720

```

Gly Thr Asn Gly Thr Cys Leu Leu Ala Ser Met Gly Leu Gln Leu Asn
 225 230 235 240
 ctc acc tat gag agg aag gac aac acg acg gtg aca agg ctt ctc aac 768
 Leu Thr Tyr Glu Arg Lys Asp Asn Thr Thr Val Thr Arg Leu Leu Asn
 245 250 255
 atc aac ccc aac aag acc tcg gcc agc ggg agc tgc ggc gcc cac ctg 816
 Ile Asn Pro Asn Lys Thr Ser Ala Ser Gly Ser Cys Gly Ala His Leu
 260 265 270
 gtg act ctg gag ctg cac agc gag ggc acc acc gtc ctg ctc ttc cag 864
 Val Thr Leu Glu Leu His Ser Glu Gly Thr Thr Val Leu Leu Phe Gln
 275 280 285
 ttc ggg atg aat gca agt tct agc cgg ttt ttc cta caa gga atc cag 912
 Phe Gly Met Asn Ala Ser Ser Ser Arg Phe Phe Leu Gln Gly Ile Gln
 290 295 300
 ttg aat aca att ctt cct gac gcc aga gac cct gcc ttt aaa gct gcc 960
 Leu Asn Thr Ile Leu Pro Asp Ala Arg Asp Pro Ala Phe Lys Ala Ala
 305 310 315 320
 aac ggc tcc ctg cga gcg ctg cag gcc aca gtc ggc aat tcc tac aag 1008
 Asn Gly Ser Leu Arg Ala Leu Gln Ala Thr Val Gly Asn Ser Tyr Lys
 325 330 335
 tgc aac gcg gag gag cac gtc cgt gtc acg aag gcg ttt tca gtc aat 1056
 Cys Asn Ala Glu Glu His Val Arg Val Thr Lys Ala Phe Ser Val Asn
 340 345 350
 ata ttc aaa gtg tgg gtc cag gct ttc aag gtg gaa ggt ggc cag ttt 1104
 Ile Phe Lys Val Trp Val Gln Ala Phe Lys Val Glu Gly Gly Gln Phe
 355 360 365
 ggc tct gtg gag gag tgt ctg ctg gac gag aac agc ctc gag caa gac 1152
 Gly Ser Val Glu Glu Cys Leu Leu Asp Glu Asn Ser Leu Glu Gln Asp
 370 375 380
 acc ccc gct ctg ggc aag gat acc gtg gcc gtg tcc ggc aag tgg tat 1200
 Thr Pro Ala Leu Gly Lys Asp Thr Val Ala Val Ser Gly Lys Trp Tyr
 385 390 395 400
 ctg aag gcc atg acc gcc gac caa gaa gtg ccc gag aag ccc gat agc 1248
 Leu Lys Ala Met Thr Ala Asp Gln Glu Val Pro Glu Lys Pro Asp Ser
 405 410 415
 gtg acc ccc atg att ctg aaa gcc cag aag ggc ggc aat ctg gaa gcc 1296
 Val Thr Pro Met Ile Leu Lys Ala Gln Lys Gly Gly Asn Leu Glu Ala
 420 425 430
 aag atc acc atg ctg acc aac ggc cag tgc cag aac atc acc gtg gtg 1344

Lys Ile Thr Met Leu Thr Asn Gly Gln Cys Gln Asn Ile Thr Val Val
 435 440 445
 ctg cac aag acc agc gag ccc ggc aag tac aca gcc tac gag ggc cag 1392
 Leu His Lys Thr Ser Glu Pro Gly Lys Tyr Thr Ala Tyr Glu Gly Gln
 450 455 460
 cgg gtg gtg ttc atc cag cct tct cca gtg cgg gat cac tac att ctg 1440
 Arg Val Val Phe Ile Gln Pro Ser Pro Val Arg Asp His Tyr Ile Leu
 465 470 475 480
 tac tgc gag ggc gag ctg cac ggc cgg cag atc aga atg gcc aag ctg 1488
 Tyr Cys Glu Gly Glu Leu His Gly Arg Gln Ile Arg Met Ala Lys Leu
 485 490 495
 ctg ggc aga gat ccc gag cag agc caa gag gct ctg gaa gat ttc aga 1536
 Leu Gly Arg Asp Pro Glu Gln Ser Gln Glu Ala Leu Glu Asp Phe Arg
 500 505 510
 gag ttc agc cgg gcc aag gga ctg aac caa gag att ctg gaa ctg gct 1584
 Glu Phe Ser Arg Ala Lys Gly Leu Asn Gln Glu Ile Leu Glu Leu Ala
 515 520 525
 cag agc gag aca tgc tct ccc ggc gga caa gaa ttc acg ctg atc ccc 1632
 Gln Ser Glu Thr Cys Ser Pro Gly Gly Gln Glu Phe Thr Leu Ile Pro
 530 535 540
 atc gct gtg ggt ggt gcc ctg gcg ggg ctg gtc ctc atc gtc ctc atc 1680
 Ile Ala Val Gly Gly Ala Leu Ala Gly Leu Val Leu Ile Val Leu Ile
 545 550 555 560
 gcc tac ctc gtc ggc agg aag agg agt cac gca ggc tac cag act atc 1728
 Ala Tyr Leu Val Gly Arg Lys Arg Ser His Ala Gly Tyr Gln Thr Ile
 565 570 575
 tag taa 1734
 <210> 39
 <211> 576
 <212> PRT
 <213> 人工序列
 <220>
 <223> 合成构建物
 <400> 39
 Met Ala Pro Arg Ser Ala Arg Arg Pro Leu Leu Leu Leu Leu Leu Leu
 1 5 10 15
 Leu Leu Leu Gly Leu Met His Cys Ala Ser Ala Ala Met Phe Met Val
 20 25 30
 Lys Asn Gly Asn Gly Thr Ala Cys Ile Met Ala Asn Phe Ser Ala Ala

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

Ile Phe Lys Val Trp Val Gln Ala Phe Lys Val Glu Gly Gly Gln Phe		
355	360	365
Gly Ser Val Glu Glu Cys Leu Leu Asp Glu Asn Ser Leu Glu Gln Asp		
370	375	380
Thr Pro Ala Leu Gly Lys Asp Thr Val Ala Val Ser Gly Lys Trp Tyr		
385	390	395
Leu Lys Ala Met Thr Ala Asp Gln Glu Val Pro Glu Lys Pro Asp Ser		
405	410	415
Val Thr Pro Met Ile Leu Lys Ala Gln Lys Gly Gly Asn Leu Glu Ala		
420	425	430
Lys Ile Thr Met Leu Thr Asn Gly Gln Cys Gln Asn Ile Thr Val Val		
435	440	445
Leu His Lys Thr Ser Glu Pro Gly Lys Tyr Thr Ala Tyr Glu Gly Gln		
450	455	460
Arg Val Val Phe Ile Gln Pro Ser Pro Val Arg Asp His Tyr Ile Leu		
465	470	475
Tyr Cys Glu Gly Glu Leu His Gly Arg Gln Ile Arg Met Ala Lys Leu		
485	490	495
Leu Gly Arg Asp Pro Glu Gln Ser Gln Glu Ala Leu Glu Asp Phe Arg		
500	505	510
Glu Phe Ser Arg Ala Lys Gly Leu Asn Gln Glu Ile Leu Glu Leu Ala		
515	520	525
Gln Ser Glu Thr Cys Ser Pro Gly Gly Gln Glu Phe Thr Leu Ile Pro		
530	535	540
Ile Ala Val Gly Gly Ala Leu Ala Gly Leu Val Leu Ile Val Leu Ile		
545	550	555
Ala Tyr Leu Val Gly Arg Lys Arg Ser His Ala Gly Tyr Gln Thr Ile		
565	570	575

<210> 40

<211> 750

<212> DNA

<213> 狗牙根 (Cynodon dactylon)

<220>

<221> CDS

<222> (7) .. (744)

<400> 40

ctcgag gcc atc ggc gat aag ccc gga ccc aac atc acc gcc aca tac 48

Ala Ile Gly Asp Lys Pro Gly Pro Asn Ile Thr Ala Thr Tyr

1

5

10

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ggc agc aag tgg ctg gaa gcc aga gcc aca ttc tac ggc tcc aac ccc 96
Gly Ser Lys Trp Leu Glu Ala Arg Ala Thr Phe Tyr Gly Ser Asn Pro
15                20                25                30
aga ggc gcc gct ccc gat gat cat ggc gga gct tgc ggc tac aag gac 144
Arg Gly Ala Ala Pro Asp Asp His Gly Gly Ala Cys Gly Tyr Lys Asp
35                40                45
gtg gac aag ccc ccc ttc gac ggc atg acc gct tgc ggc aac gag ccc 192
Val Asp Lys Pro Pro Phe Asp Gly Met Thr Ala Cys Gly Asn Glu Pro
50                55                60
atc ttc aag gac gga ctg ggc tgc cgg gct tgc tac gag atc aag tgc 240
Ile Phe Lys Asp Gly Leu Gly Cys Arg Ala Cys Tyr Glu Ile Lys Cys
65                70                75
aaa gaa ccc gtg gaa tgc agc ggc gag ccc gtg ctc gtg aag atc acc 288
Lys Glu Pro Val Glu Cys Ser Gly Glu Pro Val Leu Val Lys Ile Thr
80                85                90
gac aag aac tac gag cac att gcc gcc tac cac ttc gat ctg agc ggc 336
Asp Lys Asn Tyr Glu His Ile Ala Ala Tyr His Phe Asp Leu Ser Gly
95                100                105                110
aag gcc ttt ggc gcc atg gcc aag aag ggc caa gag gac aag ctg cgg 384
Lys Ala Phe Gly Ala Met Ala Lys Lys Gly Gln Glu Asp Lys Leu Arg
115                120                125
aag gcc ggc gaa ctg aca ctg cag ttt cgg aga gtg aag tgc aag tac 432
Lys Ala Gly Glu Leu Thr Leu Gln Phe Arg Arg Val Lys Cys Lys Tyr
130                135                140
ccc agc ggc acc aag atc aca ttc cac atc gag aag ggc agc aac gat 480
Pro Ser Gly Thr Lys Ile Thr Phe His Ile Glu Lys Gly Ser Asn Asp
145                150                155
cac tat ctg gct ctg ctc gtg aaa tac gcc gct ggc gac ggc aac atc 528
His Tyr Leu Ala Leu Leu Val Lys Tyr Ala Ala Gly Asp Gly Asn Ile
160                165                170
gtg gcc gtg gac atc aag ccc aga gac agc gac gag ttc atc ccc atg 576
Val Ala Val Asp Ile Lys Pro Arg Asp Ser Asp Glu Phe Ile Pro Met
175                180                185                190
aag tcc agc tgg ggc gcc atc tgg cgg atc gac cca aag aag cct ctg 624
Lys Ser Ser Trp Gly Ala Ile Trp Arg Ile Asp Pro Lys Lys Pro Leu
195                200                205
aag ggc ccc ttc tcc atc cgg ctg aca tct gag ggc gga gca cat ctg 672
Lys Gly Pro Phe Ser Ile Arg Leu Thr Ser Glu Gly Gly Ala His Leu
210                215                220

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gtg caa gac gac gtg atc ccc gcc aac tgg aag ccc gac acc gtg tac 720
Val Gln Asp Asp Val Ile Pro Ala Asn Trp Lys Pro Asp Thr Val Tyr
      225              230              235

acc agc aag ctg cag ttt ggc gcc gaattc 750
Thr Ser Lys Leu Gln Phe Gly Ala
      240              245

<210> 41
<211> 246
<212> PRT
<213> 狗牙根 (Cynodon dactylon)
<400> 41
Ala Ile Gly Asp Lys Pro Gly Pro Asn Ile Thr Ala Thr Tyr Gly Ser
1              5              10              15
Lys Trp Leu Glu Ala Arg Ala Thr Phe Tyr Gly Ser Asn Pro Arg Gly
      20              25              30
Ala Ala Pro Asp Asp His Gly Gly Ala Cys Gly Tyr Lys Asp Val Asp
      35              40              45
Lys Pro Pro Phe Asp Gly Met Thr Ala Cys Gly Asn Glu Pro Ile Phe
      50              55              60
Lys Asp Gly Leu Gly Cys Arg Ala Cys Tyr Glu Ile Lys Cys Lys Glu
65              70              75              80
Pro Val Glu Cys Ser Gly Glu Pro Val Leu Val Lys Ile Thr Asp Lys
      85              90              95
Asn Tyr Glu His Ile Ala Ala Tyr His Phe Asp Leu Ser Gly Lys Ala
      100             105             110
Phe Gly Ala Met Ala Lys Lys Gly Gln Glu Asp Lys Leu Arg Lys Ala
      115             120             125
Gly Glu Leu Thr Leu Gln Phe Arg Arg Val Lys Cys Lys Tyr Pro Ser
      130             135             140
Gly Thr Lys Ile Thr Phe His Ile Glu Lys Gly Ser Asn Asp His Tyr
145             150             155             160
Leu Ala Leu Leu Val Lys Tyr Ala Ala Gly Asp Gly Asn Ile Val Ala
      165             170             175
Val Asp Ile Lys Pro Arg Asp Ser Asp Glu Phe Ile Pro Met Lys Ser
      180             185             190
Ser Trp Gly Ala Ile Trp Arg Ile Asp Pro Lys Lys Pro Leu Lys Gly
      195             200             205
Pro Phe Ser Ile Arg Leu Thr Ser Glu Gly Gly Ala His Leu Val Gln
      210             215             220

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Asp Asp Val Ile Pro Ala Asn Trp Lys Pro Asp Thr Val Tyr Thr Ser
 225 230 235 240
 Lys Leu Gln Phe Gly Ala
 245
 <210> 42
 <211> 2004
 <212> DNA
 <213> 人工序列
 <220>
 <223> 合成构建物
 <220>
 <221> CDS
 <222> (1) .. (2004)
 <400> 42
 atg gcg ccc cgc agc gcc cgg cga ccc ctg ctg ctg cta ctg ctg ttg 48
 Met Ala Pro Arg Ser Ala Arg Arg Pro Leu Leu Leu Leu Leu Leu
 1 5 10 15
 ctg ctg ctc ggc ctc atg cat tgt gcg tca gca gca atg ttt atg gtg 96
 Leu Leu Leu Gly Leu Met His Cys Ala Ser Ala Ala Met Phe Met Val
 20 25 30
 aaa aat ggc aac ggg acc gcg tgc ata atg gcc aac ttc tct gct gcc 144
 Lys Asn Gly Asn Gly Thr Ala Cys Ile Met Ala Asn Phe Ser Ala Ala
 35 40 45
 ttc tca gtg aac tac gac acc aag agt ggc cct aag aac atg acc ctt 192
 Phe Ser Val Asn Tyr Asp Thr Lys Ser Gly Pro Lys Asn Met Thr Leu
 50 55 60
 gac ctg cca tca gat gcc aca gtg gtg ctc aac cgc agc tcc tgt gga 240
 Asp Leu Pro Ser Asp Ala Thr Val Val Leu Asn Arg Ser Ser Cys Gly
 65 70 75 80
 aaa gag aac act tct gac ccc agt ctc gtg att gct ttt gga aga gga 288
 Lys Glu Asn Thr Ser Asp Pro Ser Leu Val Ile Ala Phe Gly Arg Gly
 85 90 95
 cat aca ctc act ctc aat ttc acg aga aat gca aca cgt tac agc gtc 336
 His Thr Leu Thr Leu Asn Phe Thr Arg Asn Ala Thr Arg Tyr Ser Val
 100 105 110
 cag ctc atg agt ttt gtt tat aac ttg tca gac aca cac ctt ttc ccc 384
 Gln Leu Met Ser Phe Val Tyr Asn Leu Ser Asp Thr His Leu Phe Pro
 115 120 125
 aat gcg agc tcc aaa gaa atc aag act gtg gaa tct ata act gac atc 432

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Asn Ala Ser Ser Lys Glu Ile Lys Thr Val Glu Ser Ile Thr Asp Ile
 130                      135                      140
agg gca gat ata gat aaa aaa tac aga tgt gtt agt ggc acc cag gtc 480
Arg Ala Asp Ile Asp Lys Lys Tyr Arg Cys Val Ser Gly Thr Gln Val
145                      150                      155                      160
cac atg aac aac gtg acc gta acg ctc cat gat gcc acc atc cag gcg 528
His Met Asn Asn Val Thr Val Thr Leu His Asp Ala Thr Ile Gln Ala
                      165                      170                      175
tac ctt tcc aac agc agc ttc agc cgg gga gag aca cgc tgt gaa caa 576
Tyr Leu Ser Asn Ser Ser Phe Ser Arg Gly Glu Thr Arg Cys Glu Gln
                      180                      185                      190
gac agg cct tcc cca acc aca gcg ccc cct gcg cca ccc agc ccc tcg 624
Asp Arg Pro Ser Pro Thr Thr Ala Pro Pro Ala Pro Pro Ser Pro Ser
                      195                      200                      205
ccc tca ccc gtg ccc aag agc ccc tct gtg gac aag tac aac gtg agc 672
Pro Ser Pro Val Pro Lys Ser Pro Ser Val Asp Lys Tyr Asn Val Ser
                      210                      215                      220
ggc acc aac ggg acc tgc ctg ctg gcc agc atg ggg ctg cag ctg aac 720
Gly Thr Asn Gly Thr Cys Leu Leu Ala Ser Met Gly Leu Gln Leu Asn
225                      230                      235                      240
ctc acc tat gag agg aag gac aac acg acg gtg aca agg ctt ctc aac 768
Leu Thr Tyr Glu Arg Lys Asp Asn Thr Thr Val Thr Arg Leu Leu Asn
                      245                      250                      255
atc aac ccc aac aag acc tcg gcc agc ggg agc tgc ggc gcc cac ctg 816
Ile Asn Pro Asn Lys Thr Ser Ala Ser Gly Ser Cys Gly Ala His Leu
                      260                      265                      270
gtg act ctg gag ctg cac agc gag ggc acc acc gtc ctg ctc ttc cag 864
Val Thr Leu Glu Leu His Ser Glu Gly Thr Thr Val Leu Leu Phe Gln
                      275                      280                      285
ttc ggg atg aat gca agt tct agc cgg ttt ttc cta caa gga atc cag 912
Phe Gly Met Asn Ala Ser Ser Ser Arg Phe Phe Leu Gln Gly Ile Gln
                      290                      295                      300
ttg aat aca att ctt cct gac gcc aga gac cct gcc ttt aaa gct gcc 960
Leu Asn Thr Ile Leu Pro Asp Ala Arg Asp Pro Ala Phe Lys Ala Ala
305                      310                      315                      320
aac ggc tcc ctg cga gcg ctg cag gcc aca gtc ggc aat tcc tac aag 1008
Asn Gly Ser Leu Arg Ala Leu Gln Ala Thr Val Gly Asn Ser Tyr Lys
                      325                      330                      335
tgc aac gcg gag gag cac gtc cgt gtc acg aag gcg ttt tca gtc aat 1056

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Cys Asn Ala Glu Glu His Val Arg Val Thr Lys Ala Phe Ser Val Asn		
340	345	350
ata ttc aaa gtg tgg gtc cag gct ttc aag gtg gaa ggt ggc cag ttt	1104	
Ile Phe Lys Val Trp Val Gln Ala Phe Lys Val Glu Gly Gly Gln Phe		
355	360	365
ggc tct gtg gag gag tgt ctg ctg gac gag aac agc ctc gag gcc atc	1152	
Gly Ser Val Glu Glu Cys Leu Leu Asp Glu Asn Ser Leu Glu Ala Ile		
370	375	380
ggc gat aag ccc gga ccc aac atc acc gcc aca tac ggc agc aag tgg	1200	
Gly Asp Lys Pro Gly Pro Asn Ile Thr Ala Thr Tyr Gly Ser Lys Trp		
385	390	395
ctg gaa gcc aga gcc aca ttc tac ggc tcc aac ccc aga ggc gcc gct	1248	
Leu Glu Ala Arg Ala Thr Phe Tyr Gly Ser Asn Pro Arg Gly Ala Ala		
405	410	415
ccc gat gat cat ggc gga gct tgc ggc tac aag gac gtg gac aag ccc	1296	
Pro Asp Asp His Gly Gly Ala Cys Gly Tyr Lys Asp Val Asp Lys Pro		
420	425	430
ccc ttc gac ggc atg acc gct tgc ggc aac gag ccc atc ttc aag gac	1344	
Pro Phe Asp Gly Met Thr Ala Cys Gly Asn Glu Pro Ile Phe Lys Asp		
435	440	445
gga ctg ggc tgc cgg gct tgc tac gag atc aag tgc aaa gaa ccc gtg	1392	
Gly Leu Gly Cys Arg Ala Cys Tyr Glu Ile Lys Cys Lys Glu Pro Val		
450	455	460
gaa tgc agc ggc gag ccc gtg ctc gtg aag atc acc gac aag aac tac	1440	
Glu Cys Ser Gly Glu Pro Val Leu Val Lys Ile Thr Asp Lys Asn Tyr		
465	470	475
gag cac att gcc gcc tac cac ttc gat ctg agc ggc aag gcc ttt ggc	1488	
Glu His Ile Ala Ala Tyr His Phe Asp Leu Ser Gly Lys Ala Phe Gly		
485	490	495
gcc atg gcc aag aag ggc caa gag gac aag ctg cgg aag gcc ggc gaa	1536	
Ala Met Ala Lys Lys Gly Gln Glu Asp Lys Leu Arg Lys Ala Gly Glu		
500	505	510
ctg aca ctg cag ttt cgg aga gtg aag tgc aag tac ccc agc ggc acc	1584	
Leu Thr Leu Gln Phe Arg Arg Val Lys Cys Lys Tyr Pro Ser Gly Thr		
515	520	525
aag atc aca ttc cac atc gag aag ggc agc aac gat cac tat ctg gct	1632	
Lys Ile Thr Phe His Ile Glu Lys Gly Ser Asn Asp His Tyr Leu Ala		
530	535	540
ctg ctc gtg aaa tac gcc gct ggc gac ggc aac atc gtg gcc gtg gac	1680	

Leu Leu Val Lys Tyr Ala Ala Gly Asp Gly Asn Ile Val Ala Val Asp
 545 550 555 560
 atc aag ccc aga gac agc gac gag ttc atc ccc atg aag tcc agc tgg 1728
 Ile Lys Pro Arg Asp Ser Asp Glu Phe Ile Pro Met Lys Ser Ser Trp
 565 570 575
 ggc gcc atc tgg cgg atc gac cca aag aag cct ctg aag ggc ccc ttc 1776
 Gly Ala Ile Trp Arg Ile Asp Pro Lys Lys Pro Leu Lys Gly Pro Phe
 580 585 590
 tcc atc cgg ctg aca tct gag ggc gga gca cat ctg gtg caa gac gac 1824
 Ser Ile Arg Leu Thr Ser Glu Gly Gly Ala His Leu Val Gln Asp Asp
 595 600 605
 gtg atc ccc gcc aac tgg aag ccc gac acc gtg tac acc agc aag ctg 1872
 Val Ile Pro Ala Asn Trp Lys Pro Asp Thr Val Tyr Thr Ser Lys Leu
 610 615 620
 cag ttt ggc gcc gaa ttc acg ctg atc ccc atc gct gtg ggt ggt gcc 1920
 Gln Phe Gly Ala Glu Phe Thr Leu Ile Pro Ile Ala Val Gly Gly Ala
 625 630 635 640
 ctg gcg ggg ctg gtc ctc atc gtc ctc atc gcc tac ctc gtc ggc agg 1968
 Leu Ala Gly Leu Val Leu Ile Val Leu Ile Ala Tyr Leu Val Gly Arg
 645 650 655
 aag agg agt cac gca ggc tac cag act atc tag taa 2004
 Lys Arg Ser His Ala Gly Tyr Gln Thr Ile
 660 665

<210> 43

<211> 666

<212> PRT

<213> 人工序列

<220>

<223> 合成构建物

<400> 43

Met Ala Pro Arg Ser Ala Arg Arg Pro Leu Leu Leu Leu Leu Leu Leu
 1 5 10 15
 Leu Leu Leu Gly Leu Met His Cys Ala Ser Ala Ala Met Phe Met Val
 20 25 30
 Lys Asn Gly Asn Gly Thr Ala Cys Ile Met Ala Asn Phe Ser Ala Ala
 35 40 45
 Phe Ser Val Asn Tyr Asp Thr Lys Ser Gly Pro Lys Asn Met Thr Leu
 50 55 60
 Asp Leu Pro Ser Asp Ala Thr Val Val Leu Asn Arg Ser Ser Cys Gly

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

Gly Asp Lys Pro Gly Pro Asn Ile Thr Ala Thr Tyr Gly Ser Lys Trp			
385	390	395	400
Leu Glu Ala Arg Ala Thr Phe Tyr Gly Ser Asn Pro Arg Gly Ala Ala			
	405	410	415
Pro Asp Asp His Gly Gly Ala Cys Gly Tyr Lys Asp Val Asp Lys Pro			
	420	425	430
Pro Phe Asp Gly Met Thr Ala Cys Gly Asn Glu Pro Ile Phe Lys Asp			
	435	440	445
Gly Leu Gly Cys Arg Ala Cys Tyr Glu Ile Lys Cys Lys Glu Pro Val			
	450	455	460
Glu Cys Ser Gly Glu Pro Val Leu Val Lys Ile Thr Asp Lys Asn Tyr			
465	470	475	480
Glu His Ile Ala Ala Tyr His Phe Asp Leu Ser Gly Lys Ala Phe Gly			
	485	490	495
Ala Met Ala Lys Lys Gly Gln Glu Asp Lys Leu Arg Lys Ala Gly Glu			
	500	505	510
Leu Thr Leu Gln Phe Arg Arg Val Lys Cys Lys Tyr Pro Ser Gly Thr			
	515	520	525
Lys Ile Thr Phe His Ile Glu Lys Gly Ser Asn Asp His Tyr Leu Ala			
	530	535	540
Leu Leu Val Lys Tyr Ala Ala Gly Asp Gly Asn Ile Val Ala Val Asp			
545	550	555	560
Ile Lys Pro Arg Asp Ser Asp Glu Phe Ile Pro Met Lys Ser Ser Trp			
	565	570	575
Gly Ala Ile Trp Arg Ile Asp Pro Lys Lys Pro Leu Lys Gly Pro Phe			
	580	585	590
Ser Ile Arg Leu Thr Ser Glu Gly Gly Ala His Leu Val Gln Asp Asp			
	595	600	605
Val Ile Pro Ala Asn Trp Lys Pro Asp Thr Val Tyr Thr Ser Lys Leu			
	610	615	620
Gln Phe Gly Ala Glu Phe Thr Leu Ile Pro Ile Ala Val Gly Gly Ala			
625	630	635	640
Leu Ala Gly Leu Val Leu Ile Val Leu Ile Ala Tyr Leu Val Gly Arg			
	645	650	655
Lys Arg Ser His Ala Gly Tyr Gln Thr Ile			
	660	665	

<210> 44

<211> 921

<212> DNA

<213> 粉尘螨(Dermatophagoides farinae)

<220>

<221> CDS

<222> (7) .. (915)

<400> 44

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ctcgag agg ccc gcc agc atc aag aca ttc gaa gag ttc aag aag gcc 48
      Arg Pro Ala Ser Ile Lys Thr Phe Glu Glu Phe Lys Lys Ala
          1              5              10

ttt aac aag aac tac gcc acc gtg gaa gag gaa gaa gtg gcc cgg aag 96
Phe Asn Lys Asn Tyr Ala Thr Val Glu Glu Glu Glu Val Ala Arg Lys
15              20              25              30

aac ttt ctg gaa tct ctg aaa tac gtg gaa gcc aac aag ggc gcc atc 144
Asn Phe Leu Glu Ser Leu Lys Tyr Val Glu Ala Asn Lys Gly Ala Ile
          35              40              45

aac cat ctg agc gat ctg tct ctg gac gag ttt aag aac cgg tat ctg 192
Asn His Leu Ser Asp Leu Ser Leu Asp Glu Phe Lys Asn Arg Tyr Leu
          50              55              60

atg agc gcc gag gcc ttc gag cag ctg aaa acc cag ttc gat ctg aac 240
Met Ser Ala Glu Ala Phe Glu Gln Leu Lys Thr Gln Phe Asp Leu Asn
          65              70              75

gcc gaa acc agc gct tgc cgg atc aac agc gtg aac gtg ccc agc gag 288
Ala Glu Thr Ser Ala Cys Arg Ile Asn Ser Val Asn Val Pro Ser Glu
          80              85              90

ctg gat ctg aga tct ctg aga acc gtg acc ccc atc aga atg caa ggc 336
Leu Asp Leu Arg Ser Leu Arg Thr Val Thr Pro Ile Arg Met Gln Gly
95              100              105              110

ggc tgc ggc agc tgc tgg gcc ttt agc gga gtg gcc gcc aca gag tct 384
Gly Cys Gly Ser Cys Trp Ala Phe Ser Gly Val Ala Ala Thr Glu Ser
          115              120              125

gcc tat ctg gcc tac cgg aac aca tct ctg gat ctg tcc gag caa gaa 432
Ala Tyr Leu Ala Tyr Arg Asn Thr Ser Leu Asp Leu Ser Glu Gln Glu
          130              135              140

ctc gtg gac tgc gcc agc cag cac ggc tgt cac ggc gat aca atc ccc 480
Leu Val Asp Cys Ala Ser Gln His Gly Cys His Gly Asp Thr Ile Pro
          145              150              155

aga ggc atc gag tac atc cag cag aac ggc gtc gtg gaa gaa cgg tcc 528
Arg Gly Ile Glu Tyr Ile Gln Gln Asn Gly Val Val Glu Glu Arg Ser
          160              165              170

tac cct tac gtg gcc cgc gag cag aga tgc aga agg ccc aac tct cag 576

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Tyr Pro Tyr Val Ala Arg Glu Gln Arg Cys Arg Arg Pro Asn Ser Gln
 175 180 185 190
 cac tac ggc atc agc aac tac tgc cag atc tac ccc ccc gac gtg aag 624
 His Tyr Gly Ile Ser Asn Tyr Cys Gln Ile Tyr Pro Pro Asp Val Lys
 195 200 205
 cag atc aga gag gct ctg acc cag acc cac acc gcc att gcc gtg atc 672
 Gln Ile Arg Glu Ala Leu Thr Gln Thr His Thr Ala Ile Ala Val Ile
 210 215 220
 atc gga atc aag gat ctg cgg gcc ttc cag cac tat gac ggc cgg acc 720
 Ile Gly Ile Lys Asp Leu Arg Ala Phe Gln His Tyr Asp Gly Arg Thr
 225 230 235
 atc atc cag cac gac aac ggc tac cag ccc aac tac cac gcc gtg aac 768
 Ile Ile Gln His Asp Asn Gly Tyr Gln Pro Asn Tyr His Ala Val Asn
 240 245 250
 atc gtg ggc tac ggc agc aca caa ggc gac gac tac tgg atc gtg cgg 816
 Ile Val Gly Tyr Gly Ser Thr Gln Gly Asp Asp Tyr Trp Ile Val Arg
 255 260 265 270
 aac agc tgg gac acc aca tgg ggc gat agc ggc tac ggc tac ttc caa 864
 Asn Ser Trp Asp Thr Thr Trp Gly Asp Ser Gly Tyr Gly Tyr Phe Gln
 275 280 285
 gcc ggc aac aat ctg atg atg atc gag cag tac ccc tac gtc gtg atc 912
 Ala Gly Asn Asn Leu Met Met Ile Glu Gln Tyr Pro Tyr Val Val Ile
 290 295 300

atg gaattc 921

Met

<210> 45

<211> 303

<212> PRT

<213> 粉尘螨(Dermatophagoides farinae)

<400> 45

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

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

<210> 46

<211> 2175

<212> DNA

<213> 人工序列

<220>

<223> 合成构建物

<220>

<221> CDS

<222> (1) .. (2175)

<400> 46

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atg gcg ccc cgc agc gcc cgg cga ccc ctg ctg ctg cta ctg ctg ttg 48
Met Ala Pro Arg Ser Ala Arg Arg Pro Leu Leu Leu Leu Leu Leu
1           5           10           15
ctg ctg ctc ggc ctc atg cat tgt gcg tca gca gca atg ttt atg gtg 96
Leu Leu Leu Gly Leu Met His Cys Ala Ser Ala Ala Met Phe Met Val
20           25           30
aaa aat ggc aac ggg acc gcg tgc ata atg gcc aac ttc tct gct gcc 144
Lys Asn Gly Asn Gly Thr Ala Cys Ile Met Ala Asn Phe Ser Ala Ala
35           40           45
ttc tca gtg aac tac gac acc aag agt ggc cct aag aac atg acc ctt 192
Phe Ser Val Asn Tyr Asp Thr Lys Ser Gly Pro Lys Asn Met Thr Leu
50           55           60
gac ctg cca tca gat gcc aca gtg gtg ctc aac cgc agc tcc tgt gga 240
Asp Leu Pro Ser Asp Ala Thr Val Val Leu Asn Arg Ser Ser Cys Gly
65           70           75           80
aaa gag aac act tct gac ccc agt ctc gtg att gct ttt gga aga gga 288
Lys Glu Asn Thr Ser Asp Pro Ser Leu Val Ile Ala Phe Gly Arg Gly
85           90           95
cat aca ctc act ctc aat ttc acg aga aat gca aca cgt tac agc gtc 336
His Thr Leu Thr Leu Asn Phe Thr Arg Asn Ala Thr Arg Tyr Ser Val
100          105          110
cag ctc atg agt ttt gtt tat aac ttg tca gac aca cac ctt ttc ccc 384
Gln Leu Met Ser Phe Val Tyr Asn Leu Ser Asp Thr His Leu Phe Pro
115          120          125
aat gcg agc tcc aaa gaa atc aag act gtg gaa tct ata act gac atc 432
Asn Ala Ser Ser Lys Glu Ile Lys Thr Val Glu Ser Ile Thr Asp Ile
130          135          140
agg gca gat ata gat aaa aaa tac aga tgt gtt agt ggc acc cag gtc 480
Arg Ala Asp Ile Asp Lys Lys Tyr Arg Cys Val Ser Gly Thr Gln Val
145          150          155          160
cac atg aac aac gtg acc gta acg ctc cat gat gcc acc atc cag gcg 528
His Met Asn Asn Val Thr Val Thr Leu His Asp Ala Thr Ile Gln Ala
165          170          175
tac ctt tcc aac agc agc ttc agc cgg gga gag aca cgc tgt gaa caa 576
Tyr Leu Ser Asn Ser Ser Phe Ser Arg Gly Glu Thr Arg Cys Glu Gln
180          185          190
gac agg cct tcc cca acc aca gcg ccc cct gcg cca ccc agc ccc tcg 624
Asp Arg Pro Ser Pro Thr Thr Ala Pro Pro Ala Pro Pro Ser Pro Ser
195          200          205

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ccc tca ccc gtg ccc aag agc ccc tct gtg gac aag tac aac gtg agc 672
Pro Ser Pro Val Pro Lys Ser Pro Ser Val Asp Lys Tyr Asn Val Ser
      210                      215                      220

ggc acc aac ggg acc tgc ctg ctg gcc agc atg ggg ctg cag ctg aac 720
Gly Thr Asn Gly Thr Cys Leu Leu Ala Ser Met Gly Leu Gln Leu Asn
225                      230                      235                      240

ctc acc tat gag agg aag gac aac acg acg gtg aca agg ctt ctc aac 768
Leu Thr Tyr Glu Arg Lys Asp Asn Thr Thr Val Thr Arg Leu Leu Asn
      245                      250                      255

atc aac ccc aac aag acc tcg gcc agc ggg agc tgc ggc gcc cac ctg 816
Ile Asn Pro Asn Lys Thr Ser Ala Ser Gly Ser Cys Gly Ala His Leu
      260                      265                      270

gtg act ctg gag ctg cac agc gag ggc acc acc gtc ctg ctc ttc cag 864
Val Thr Leu Glu Leu His Ser Glu Gly Thr Thr Val Leu Leu Phe Gln
      275                      280                      285

ttc ggg atg aat gca agt tct agc cgg ttt ttc cta caa gga atc cag 912
Phe Gly Met Asn Ala Ser Ser Ser Arg Phe Phe Leu Gln Gly Ile Gln
      290                      295                      300

ttg aat aca att ctt cct gac gcc aga gac cct gcc ttt aaa gct gcc 960
Leu Asn Thr Ile Leu Pro Asp Ala Arg Asp Pro Ala Phe Lys Ala Ala
305                      310                      315                      320

aac ggc tcc ctg cga gcg ctg cag gcc aca gtc ggc aat tcc tac aag 1008
Asn Gly Ser Leu Arg Ala Leu Gln Ala Thr Val Gly Asn Ser Tyr Lys
      325                      330                      335

tgc aac gcg gag gag cac gtc cgt gtc acg aag gcg ttt tca gtc aat 1056
Cys Asn Ala Glu Glu His Val Arg Val Thr Lys Ala Phe Ser Val Asn
      340                      345                      350

ata ttc aaa gtg tgg gtc cag gct ttc aag gtg gaa ggt ggc cag ttt 1104
Ile Phe Lys Val Trp Val Gln Ala Phe Lys Val Glu Gly Gly Gln Phe
      355                      360                      365

ggc tct gtg gag gag tgt ctg ctg gac gag aac agc ctc gag agg ccc 1152
Gly Ser Val Glu Glu Cys Leu Leu Asp Glu Asn Ser Leu Glu Arg Pro
      370                      375                      380

gcc agc atc aag aca ttc gaa gag ttc aag aag gcc ttt aac aag aac 1200
Ala Ser Ile Lys Thr Phe Glu Glu Phe Lys Lys Ala Phe Asn Lys Asn
385                      390                      395                      400

tac gcc acc gtg gaa gag gaa gaa gtg gcc cgg aag aac ttt ctg gaa 1248
Tyr Ala Thr Val Glu Glu Glu Glu Val Ala Arg Lys Asn Phe Leu Glu
      405                      410                      415

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tct ctg aaa tac gtg gaa gcc aac aag ggc gcc atc aac cat ctg agc 1296
Ser Leu Lys Tyr Val Glu Ala Asn Lys Gly Ala Ile Asn His Leu Ser
      420                      425                      430

gat ctg tct ctg gac gag ttt aag aac cgg tat ctg atg agc gcc gag 1344
Asp Leu Ser Leu Asp Glu Phe Lys Asn Arg Tyr Leu Met Ser Ala Glu
      435                      440                      445

gcc ttc gag cag ctg aaa acc cag ttc gat ctg aac gcc gaa acc agc 1392
Ala Phe Glu Gln Leu Lys Thr Gln Phe Asp Leu Asn Ala Glu Thr Ser
      450                      455                      460

gct tgc cgg atc aac agc gtg aac gtg ccc agc gag ctg gat ctg aga 1440
Ala Cys Arg Ile Asn Ser Val Asn Val Pro Ser Glu Leu Asp Leu Arg
465                      470                      475                      480

tct ctg aga acc gtg acc ccc atc aga atg caa ggc ggc tgc ggc agc 1488
Ser Leu Arg Thr Val Thr Pro Ile Arg Met Gln Gly Gly Cys Gly Ser
      485                      490                      495

tgc tgg gcc ttt agc gga gtg gcc gcc aca gag tct gcc tat ctg gcc 1536
Cys Trp Ala Phe Ser Gly Val Ala Ala Thr Glu Ser Ala Tyr Leu Ala
      500                      505                      510

tac cgg aac aca tct ctg gat ctg tcc gag caa gaa ctc gtg gac tgc 1584
Tyr Arg Asn Thr Ser Leu Asp Leu Ser Glu Gln Glu Leu Val Asp Cys
      515                      520                      525

gcc agc cag cac ggc tgt cac ggc gat aca atc ccc aga ggc atc gag 1632
Ala Ser Gln His Gly Cys His Gly Asp Thr Ile Pro Arg Gly Ile Glu
      530                      535                      540

tac atc cag cag aac ggc gtc gtg gaa gaa cgg tcc tac cct tac gtg 1680
Tyr Ile Gln Gln Asn Gly Val Val Glu Glu Arg Ser Tyr Pro Tyr Val
545                      550                      555                      560

gcc cgc gag cag aga tgc aga agg ccc aac tct cag cac tac ggc atc 1728
Ala Arg Glu Gln Arg Cys Arg Arg Pro Asn Ser Gln His Tyr Gly Ile
      565                      570                      575

agc aac tac tgc cag atc tac ccc ccc gac gtg aag cag atc aga gag 1776
Ser Asn Tyr Cys Gln Ile Tyr Pro Pro Asp Val Lys Gln Ile Arg Glu
      580                      585                      590

gct ctg acc cag acc cac acc gcc att gcc gtg atc atc gga atc aag 1824
Ala Leu Thr Gln Thr His Thr Ala Ile Ala Val Ile Ile Gly Ile Lys
      595                      600                      605

gat ctg cgg gcc ttc cag cac tat gac ggc cgg acc atc atc cag cac 1872
Asp Leu Arg Ala Phe Gln His Tyr Asp Gly Arg Thr Ile Ile Gln His
      610                      615                      620

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gac aac ggc tac cag ccc aac tac cac gcc gtg aac atc gtg ggc tac 1920
 Asp Asn Gly Tyr Gln Pro Asn Tyr His Ala Val Asn Ile Val Gly Tyr
 625 630 635 640
 ggc agc aca caa ggc gac gac tac tgg atc gtg cgg aac agc tgg gac 1968
 Gly Ser Thr Gln Gly Asp Asp Tyr Trp Ile Val Arg Asn Ser Trp Asp
 645 650 655
 acc aca tgg ggc gat agc ggc tac ggc tac ttc caa gcc ggc aac aat 2016
 Thr Thr Trp Gly Asp Ser Gly Tyr Gly Tyr Phe Gln Ala Gly Asn Asn
 660 665 670
 ctg atg atg atc gag cag tac ccc tac gtc gtg atc atg gaa ttc acg 2064
 Leu Met Met Ile Glu Gln Tyr Pro Tyr Val Val Ile Met Glu Phe Thr
 675 680 685
 ctg atc ccc atc gct gtg ggt ggt gcc ctg gcg ggg ctg gtc ctc atc 2112
 Leu Ile Pro Ile Ala Val Gly Gly Ala Leu Ala Gly Leu Val Leu Ile
 690 695 700
 gtc ctc atc gcc tac ctc gtc ggc agg aag agg agt cac gca ggc tac 2160
 Val Leu Ile Ala Tyr Leu Val Gly Arg Lys Arg Ser His Ala Gly Tyr
 705 710 715 720
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 Gln Thr Ile
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 <400> 47
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 Leu Leu Leu Gly Leu Met His Cys Ala Ser Ala Ala Met Phe Met Val
 20 25 30
 Lys Asn Gly Asn Gly Thr Ala Cys Ile Met Ala Asn Phe Ser Ala Ala
 35 40 45
 Phe Ser Val Asn Tyr Asp Thr Lys Ser Gly Pro Lys Asn Met Thr Leu
 50 55 60
 Asp Leu Pro Ser Asp Ala Thr Val Val Leu Asn Arg Ser Ser Cys Gly
 65 70 75 80
 Lys Glu Asn Thr Ser Asp Pro Ser Leu Val Ile Ala Phe Gly Arg Gly
 85 90 95

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

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

Gln Thr Ile

<210> 48

<211> 681

<212> DNA

<213> 粉尘螨(Dermatophagoides farinae)

<220>

<221> CDS

<222> (7) .. (675)

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Thr Ser Ala Cys Arg Ile Asn Ser Val Asn Val Pro Ser Glu

1

5

10

ctg gat ctg aga tct ctg aga acc gtg acc ccc atc aga atg caa ggc 96

Leu Asp Leu Arg Ser Leu Arg Thr Val Thr Pro Ile Arg Met Gln Gly

15

20

25

30

ggc tgc ggc agc tgc tgg gcc ttt agc gga gtg gcc gcc aca gag tct 144

Gly Cys Gly Ser Cys Trp Ala Phe Ser Gly Val Ala Ala Thr Glu Ser

35

40

45

gcc tat ctg gcc tac cgg aac aca tct ctg gat ctg tcc gag caa gaa 192

Ala Tyr Leu Ala Tyr Arg Asn Thr Ser Leu Asp Leu Ser Glu Gln Glu

50

55

60

ctc gtg gac tgc gcc agc cag cac ggc tgt cac ggc gat aca atc ccc 240

Leu Val Asp Cys Ala Ser Gln His Gly Cys His Gly Asp Thr Ile Pro

65

70

75

aga ggc atc gag tac atc cag cag aac ggc gtc gtg gaa gaa cgg tcc 288

Arg Gly Ile Glu Tyr Ile Gln Gln Asn Gly Val Val Glu Glu Arg Ser

80

85

90

tac cct tac gtg gcc cgc gag cag aga tgc aga agg ccc aac tct cag 336

Tyr Pro Tyr Val Ala Arg Glu Gln Arg Cys Arg Arg Pro Asn Ser Gln

95

100

105

110

cac tac ggc atc agc aac tac tgc cag atc tac ccc ccc gac gtg aag 384

His Tyr Gly Ile Ser Asn Tyr Cys Gln Ile Tyr Pro Pro Asp Val Lys

115

120

125

cag atc aga gag gct ctg acc cag acc cac acc gcc att gcc gtg atc 432

Gln Ile Arg Glu Ala Leu Thr Gln Thr His Thr Ala Ile Ala Val Ile

130

135

140

atc gga atc aag gat ctg cgg gcc ttc cag cac tat gac ggc cgg acc 480

Ile Gly Ile Lys Asp Leu Arg Ala Phe Gln His Tyr Asp Gly Arg Thr

145

150

155

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atc atc cag cac gac aac ggc tac cag ccc aac tac cac gcc gtg aac 528
Ile Ile Gln His Asp Asn Gly Tyr Gln Pro Asn Tyr His Ala Val Asn
    160                      165                      170
atc gtg ggc tac ggc agc aca caa ggc gac gac tac tgg atc gtg cgg 576
Ile Val Gly Tyr Gly Ser Thr Gln Gly Asp Asp Tyr Trp Ile Val Arg
    175                      180                      185                      190
aac agc tgg gac acc aca tgg ggc gat agc ggc tac ggc tac ttc caa 624
Asn Ser Trp Asp Thr Thr Trp Gly Asp Ser Gly Tyr Gly Tyr Phe Gln
                      195                      200                      205
gcc ggc aac aat ctg atg atg atc gag cag tac ccc tac gtc gtg atc 672
Ala Gly Asn Asn Leu Met Met Ile Glu Gln Tyr Pro Tyr Val Val Ile
                      210                      215                      220
atg gaattc 681
Met
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          20          25          30
Gly Ser Cys Trp Ala Phe Ser Gly Val Ala Ala Thr Glu Ser Ala Tyr
          35          40          45
Leu Ala Tyr Arg Asn Thr Ser Leu Asp Leu Ser Glu Gln Glu Leu Val
          50          55          60
Asp Cys Ala Ser Gln His Gly Cys His Gly Asp Thr Ile Pro Arg Gly
65          70          75          80
Ile Glu Tyr Ile Gln Gln Asn Gly Val Val Glu Glu Arg Ser Tyr Pro
          85          90          95
Tyr Val Ala Arg Glu Gln Arg Cys Arg Arg Pro Asn Ser Gln His Tyr
          100         105         110
Gly Ile Ser Asn Tyr Cys Gln Ile Tyr Pro Pro Asp Val Lys Gln Ile
          115         120         125
Arg Glu Ala Leu Thr Gln Thr His Thr Ala Ile Ala Val Ile Ile Gly
          130         135         140
Ile Lys Asp Leu Arg Ala Phe Gln His Tyr Asp Gly Arg Thr Ile Ile
145         150         155         160

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Gln His Asp Asn Gly Tyr Gln Pro Asn Tyr His Ala Val Asn Ile Val
 165 170 175
 Gly Tyr Gly Ser Thr Gln Gly Asp Asp Tyr Trp Ile Val Arg Asn Ser
 180 185 190
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 Asn Asn Leu Met Met Ile Glu Gln Tyr Pro Tyr Val Val Ile Met
 210 215 220
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 ctg ctg ctc ggc ctc atg cat tgt gcg tca gca gca atg ttt atg gtg 96
 Leu Leu Leu Gly Leu Met His Cys Ala Ser Ala Ala Met Phe Met Val
 20 25 30
 aaa aat ggc aac ggg acc gcg tgc ata atg gcc aac ttc tct gct gcc 144
 Lys Asn Gly Asn Gly Thr Ala Cys Ile Met Ala Asn Phe Ser Ala Ala
 35 40 45
 ttc tca gtg aac tac gac acc aag agt ggc cct aag aac atg acc ctt 192
 Phe Ser Val Asn Tyr Asp Thr Lys Ser Gly Pro Lys Asn Met Thr Leu
 50 55 60
 gac ctg cca tca gat gcc aca gtg gtg ctc aac cgc agc tcc tgt gga 240
 Asp Leu Pro Ser Asp Ala Thr Val Val Leu Asn Arg Ser Ser Cys Gly
 65 70 75 80
 aaa gag aac act tct gac ccc agt ctc gtg att gct ttt gga aga gga 288
 Lys Glu Asn Thr Ser Asp Pro Ser Leu Val Ile Ala Phe Gly Arg Gly
 85 90 95
 cat aca ctc act ctc aat ttc acg aga aat gca aca cgt tac agc gtc 336
 His Thr Leu Thr Leu Asn Phe Thr Arg Asn Ala Thr Arg Tyr Ser Val
 100 105 110

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cag ctc atg agt ttt gtt tat aac ttg tca gac aca cac ctt ttc ccc 384
Gln Leu Met Ser Phe Val Tyr Asn Leu Ser Asp Thr His Leu Phe Pro
      115                      120                      125
aat gcg agc tcc aaa gaa atc aag act gtg gaa tct ata act gac atc 432
Asn Ala Ser Ser Lys Glu Ile Lys Thr Val Glu Ser Ile Thr Asp Ile
      130                      135                      140
agg gca gat ata gat aaa aaa tac aga tgt gtt agt ggc acc cag gtc 480
Arg Ala Asp Ile Asp Lys Lys Tyr Arg Cys Val Ser Gly Thr Gln Val
      145                      150                      155                      160
cac atg aac aac gtg acc gta acg ctc cat gat gcc acc atc cag gcg 528
His Met Asn Asn Val Thr Val Thr Leu His Asp Ala Thr Ile Gln Ala
      165                      170                      175
tac ctt tcc aac agc agc ttc agc cgg gga gag aca cgc tgt gaa caa 576
Tyr Leu Ser Asn Ser Ser Phe Ser Arg Gly Glu Thr Arg Cys Glu Gln
      180                      185                      190
gac agg cct tcc cca acc aca gcg ccc cct gcg cca ccc agc ccc tcg 624
Asp Arg Pro Ser Pro Thr Thr Ala Pro Pro Ala Pro Pro Ser Pro Ser
      195                      200                      205
ccc tca ccc gtg ccc aag agc ccc tct gtg gac aag tac aac gtg agc 672
Pro Ser Pro Val Pro Lys Ser Pro Ser Val Asp Lys Tyr Asn Val Ser
      210                      215                      220
ggc acc aac ggg acc tgc ctg ctg gcc agc atg ggg ctg cag ctg aac 720
Gly Thr Asn Gly Thr Cys Leu Leu Ala Ser Met Gly Leu Gln Leu Asn
      225                      230                      235                      240
ctc acc tat gag agg aag gac aac acg acg gtg aca agg ctt ctc aac 768
Leu Thr Tyr Glu Arg Lys Asp Asn Thr Thr Val Thr Arg Leu Leu Asn
      245                      250                      255
atc aac ccc aac aag acc tcg gcc agc ggg agc tgc ggc gcc cac ctg 816
Ile Asn Pro Asn Lys Thr Ser Ala Ser Gly Ser Cys Gly Ala His Leu
      260                      265                      270
gtg act ctg gag ctg cac agc gag ggc acc acc gtc ctg ctc ttc cag 864
Val Thr Leu Glu Leu His Ser Glu Gly Thr Thr Val Leu Leu Phe Gln
      275                      280                      285
ttc ggg atg aat gca agt tct agc cgg ttt ttc cta caa gga atc cag 912
Phe Gly Met Asn Ala Ser Ser Ser Arg Phe Phe Leu Gln Gly Ile Gln
      290                      295                      300
ttg aat aca att ctt cct gac gcc aga gac cct gcc ttt aaa gct gcc 960
Leu Asn Thr Ile Leu Pro Asp Ala Arg Asp Pro Ala Phe Lys Ala Ala
      305                      310                      315                      320

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aac ggc tcc ctg cga gcg ctg cag gcc aca gtc ggc aat tcc tac aag 1008
Asn Gly Ser Leu Arg Ala Leu Gln Ala Thr Val Gly Asn Ser Tyr Lys
          325                      330                      335

tgc aac gcg gag gag cac gtc cgt gtc acg aag gcg ttt tca gtc aat 1056
Cys Asn Ala Glu Glu His Val Arg Val Thr Lys Ala Phe Ser Val Asn
          340                      345                      350

ata ttc aaa gtg tgg gtc cag gct ttc aag gtg gaa ggt ggc cag ttt 1104
Ile Phe Lys Val Trp Val Gln Ala Phe Lys Val Glu Gly Gly Gln Phe
          355                      360                      365

ggc tct gtg gag gag tgt ctg ctg gac gag aac agc ctc gag acc agc 1152
Gly Ser Val Glu Glu Cys Leu Leu Asp Glu Asn Ser Leu Glu Thr Ser
          370                      375                      380

gct tgc cgg atc aac agc gtg aac gtg ccc agc gag ctg gat ctg aga 1200
Ala Cys Arg Ile Asn Ser Val Asn Val Pro Ser Glu Leu Asp Leu Arg
          385                      390                      395                      400

tct ctg aga acc gtg acc ccc atc aga atg caa ggc ggc tgc ggc agc 1248
Ser Leu Arg Thr Val Thr Pro Ile Arg Met Gln Gly Gly Cys Gly Ser
          405                      410                      415

tgc tgg gcc ttt agc gga gtg gcc gcc aca gag tct gcc tat ctg gcc 1296
Cys Trp Ala Phe Ser Gly Val Ala Ala Thr Glu Ser Ala Tyr Leu Ala
          420                      425                      430

tac cgg aac aca tct ctg gat ctg tcc gag caa gaa ctc gtg gac tgc 1344
Tyr Arg Asn Thr Ser Leu Asp Leu Ser Glu Gln Glu Leu Val Asp Cys
          435                      440                      445

gcc agc cag cac ggc tgt cac ggc gat aca atc ccc aga ggc atc gag 1392
Ala Ser Gln His Gly Cys His Gly Asp Thr Ile Pro Arg Gly Ile Glu
          450                      455                      460

tac atc cag cag aac ggc gtc gtg gaa gaa cgg tcc tac cct tac gtg 1440
Tyr Ile Gln Gln Asn Gly Val Val Glu Glu Arg Ser Tyr Pro Tyr Val
          465                      470                      475                      480

gcc cgc gag cag aga tgc aga agg ccc aac tct cag cac tac ggc atc 1488
Ala Arg Glu Gln Arg Cys Arg Arg Pro Asn Ser Gln His Tyr Gly Ile
          485                      490                      495

agc aac tac tgc cag atc tac ccc ccc gac gtg aag cag atc aga gag 1536
Ser Asn Tyr Cys Gln Ile Tyr Pro Pro Asp Val Lys Gln Ile Arg Glu
          500                      505                      510

gct ctg acc cag acc cac acc gcc att gcc gtg atc atc gga atc aag 1584
Ala Leu Thr Gln Thr His Thr Ala Ile Ala Val Ile Ile Gly Ile Lys
          515                      520                      525

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gat ctg cgg gcc ttc cag cac tat gac ggc cgg acc atc atc cag cac 1632
Asp Leu Arg Ala Phe Gln His Tyr Asp Gly Arg Thr Ile Ile Gln His
      530                      535                      540
gac aac ggc tac cag ccc aac tac cac gcc gtg aac atc gtg ggc tac 1680
Asp Asn Gly Tyr Gln Pro Asn Tyr His Ala Val Asn Ile Val Gly Tyr
      545                      550                      555                      560
ggc agc aca caa ggc gac gac tac tgg atc gtg cgg aac agc tgg gac 1728
Gly Ser Thr Gln Gly Asp Asp Tyr Trp Ile Val Arg Asn Ser Trp Asp
                      565                      570                      575
acc aca tgg ggc gat agc ggc tac ggc tac ttc caa gcc ggc aac aat 1776
Thr Thr Trp Gly Asp Ser Gly Tyr Gly Tyr Phe Gln Ala Gly Asn Asn
                      580                      585                      590
ctg atg atg atc gag cag tac ccc tac gtc gtg atc atg gaa ttc acg 1824
Leu Met Met Ile Glu Gln Tyr Pro Tyr Val Val Ile Met Glu Phe Thr
                      595                      600                      605
ctg atc ccc atc gct gtg ggt ggt gcc ctg gcg ggg ctg gtc ctc atc 1872
Leu Ile Pro Ile Ala Val Gly Gly Ala Leu Ala Gly Leu Val Leu Ile
      610                      615                      620
gtc ctc atc gcc tac ctc gtc ggc agg aag agg agt cac gca ggc tac 1920
Val Leu Ile Ala Tyr Leu Val Gly Arg Lys Arg Ser His Ala Gly Tyr
      625                      630                      635                      640
cag act atc tag taa 1935
Gln Thr Ile
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<400> 51
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1          5          10          15
Leu Leu Leu Gly Leu Met His Cys Ala Ser Ala Ala Met Phe Met Val
      20          25          30
Lys Asn Gly Asn Gly Thr Ala Cys Ile Met Ala Asn Phe Ser Ala Ala
      35          40          45
Phe Ser Val Asn Tyr Asp Thr Lys Ser Gly Pro Lys Asn Met Thr Leu
      50          55          60
Asp Leu Pro Ser Asp Ala Thr Val Val Leu Asn Arg Ser Ser Cys Gly

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

Ala Cys Arg Ile Asn Ser Val Asn Val Pro Ser Glu Leu Asp Leu Arg			
385	390	395	400
Ser Leu Arg Thr Val Thr Pro Ile Arg Met Gln Gly Gly Cys Gly Ser			
	405	410	415
Cys Trp Ala Phe Ser Gly Val Ala Ala Thr Glu Ser Ala Tyr Leu Ala			
	420	425	430
Tyr Arg Asn Thr Ser Leu Asp Leu Ser Glu Gln Glu Leu Val Asp Cys			
	435	440	445
Ala Ser Gln His Gly Cys His Gly Asp Thr Ile Pro Arg Gly Ile Glu			
	450	455	460
Tyr Ile Gln Gln Asn Gly Val Val Glu Glu Arg Ser Tyr Pro Tyr Val			
465	470	475	480
Ala Arg Glu Gln Arg Cys Arg Arg Pro Asn Ser Gln His Tyr Gly Ile			
	485	490	495
Ser Asn Tyr Cys Gln Ile Tyr Pro Pro Asp Val Lys Gln Ile Arg Glu			
	500	505	510
Ala Leu Thr Gln Thr His Thr Ala Ile Ala Val Ile Ile Gly Ile Lys			
	515	520	525
Asp Leu Arg Ala Phe Gln His Tyr Asp Gly Arg Thr Ile Ile Gln His			
	530	535	540
Asp Asn Gly Tyr Gln Pro Asn Tyr His Ala Val Asn Ile Val Gly Tyr			
545	550	555	560
Gly Ser Thr Gln Gly Asp Asp Tyr Trp Ile Val Arg Asn Ser Trp Asp			
	565	570	575
Thr Thr Trp Gly Asp Ser Gly Tyr Gly Tyr Phe Gln Ala Gly Asn Asn			
	580	585	590
Leu Met Met Ile Glu Gln Tyr Pro Tyr Val Val Ile Met Glu Phe Thr			
	595	600	605
Leu Ile Pro Ile Ala Val Gly Gly Ala Leu Ala Gly Leu Val Leu Ile			
	610	615	620
Val Leu Ile Ala Tyr Leu Val Gly Arg Lys Arg Ser His Ala Gly Tyr			
625	630	635	640
Gln Thr Ile			
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<221> CDS			

<222> (7) .. (393)

<400> 52

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Asp Gln Val Asp Val Lys Asp Cys Ala Asn His Glu Ile Lys

1

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aaa gtg ctg gtg ccc ggc tgc cac ggc agc gag cct tgt atc atc cac 96

Lys Val Leu Val Pro Gly Cys His Gly Ser Glu Pro Cys Ile Ile His

15

20

25

30

cgg ggc aag ccc ttt cag ctg gaa gcc gtg ttc gag gcc aac cag aac 144

Arg Gly Lys Pro Phe Gln Leu Glu Ala Val Phe Glu Ala Asn Gln Asn

35

40

45

acc aag acc gcc aag att gag atc aag gcc agc atc gac gga ctg gaa 192

Thr Lys Thr Ala Lys Ile Glu Ile Lys Ala Ser Ile Asp Gly Leu Glu

50

55

60

gtg gat gtg ccc ggc atc gac ccc aac gct tgt cac tac atg aag tgc 240

Val Asp Val Pro Gly Ile Asp Pro Asn Ala Cys His Tyr Met Lys Cys

65

70

75

cct ctc gtg aag ggc cag cag tac gac atc aag tac aca tgg aac gtg 288

Pro Leu Val Lys Gly Gln Gln Tyr Asp Ile Lys Tyr Thr Trp Asn Val

80

85

90

ccc aag atc gcc ccc aag agc gag aac gtc gtc gtg acc gtg aaa gtg 336

Pro Lys Ile Ala Pro Lys Ser Glu Asn Val Val Val Thr Val Lys Val

95

100

105

110

atg ggc gac gac ggc gtg ctg gct tgc gcc att gcc aca cac gcc aag 384

Met Gly Asp Asp Gly Val Leu Ala Cys Ala Ile Ala Thr His Ala Lys

115

120

125

atc cgg gac gaattc 399

Ile Arg Asp

<210> 53

<211> 129

<212> PRT

<213> 屋尘螨(Dermatophagoides pteronyssinus)

<400> 53

Asp Gln Val Asp Val Lys Asp Cys Ala Asn His Glu Ile Lys Lys Val

1

5

10

15

Leu Val Pro Gly Cys His Gly Ser Glu Pro Cys Ile Ile His Arg Gly

20

25

30

Lys Pro Phe Gln Leu Glu Ala Val Phe Glu Ala Asn Gln Asn Thr Lys

35

40

45

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Thr Ala Lys Ile Glu Ile Lys Ala Ser Ile Asp Gly Leu Glu Val Asp
  50                      55                      60
Val Pro Gly Ile Asp Pro Asn Ala Cys His Tyr Met Lys Cys Pro Leu
  65                      70                      75                      80
Val Lys Gly Gln Gln Tyr Asp Ile Lys Tyr Thr Trp Asn Val Pro Lys
                      85                      90                      95
Ile Ala Pro Lys Ser Glu Asn Val Val Val Thr Val Lys Val Met Gly
                      100                    105                    110
Asp Asp Gly Val Leu Ala Cys Ala Ile Ala Thr His Ala Lys Ile Arg
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Asp

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<211> 1653

<212> DNA

<213> 人工序列

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<223> 合成构建物

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<222> (1) .. (1653)

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Met Ala Pro Arg Ser Ala Arg Arg Pro Leu Leu Leu Leu Leu Leu
  1                      5                      10                      15
ctg ctg ctc ggc ctc atg cat tgt gcg tca gca gca atg ttt atg gtg 96
Leu Leu Leu Gly Leu Met His Cys Ala Ser Ala Ala Met Phe Met Val
                      20                      25                      30
aaa aat ggc aac ggg acc gcg tgc ata atg gcc aac ttc tct gct gcc 144
Lys Asn Gly Asn Gly Thr Ala Cys Ile Met Ala Asn Phe Ser Ala Ala
                      35                      40                      45
ttc tca gtg aac tac gac acc aag agt ggc cct aag aac atg acc ctt 192
Phe Ser Val Asn Tyr Asp Thr Lys Ser Gly Pro Lys Asn Met Thr Leu
                      50                      55                      60
gac ctg cca tca gat gcc aca gtg gtg ctc aac cgc agc tcc tgt gga 240
Asp Leu Pro Ser Asp Ala Thr Val Val Leu Asn Arg Ser Ser Cys Gly
  65                      70                      75                      80
aaa gag aac act tct gac ccc agt ctc gtg att gct ttt gga aga gga 288
Lys Glu Asn Thr Ser Asp Pro Ser Leu Val Ile Ala Phe Gly Arg Gly
                      85                      90                      95

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cat aca ctc act ctc aat ttc acg aga aat gca aca cgt tac agc gtc 336
His Thr Leu Thr Leu Asn Phe Thr Arg Asn Ala Thr Arg Tyr Ser Val
      100                      105                      110
cag ctc atg agt ttt gtt tat aac ttg tca gac aca cac ctt ttc ccc 384
Gln Leu Met Ser Phe Val Tyr Asn Leu Ser Asp Thr His Leu Phe Pro
      115                      120                      125
aat gcg agc tcc aaa gaa atc aag act gtg gaa tct ata act gac atc 432
Asn Ala Ser Ser Lys Glu Ile Lys Thr Val Glu Ser Ile Thr Asp Ile
      130                      135                      140
agg gca gat ata gat aaa aaa tac aga tgt gtt agt ggc acc cag gtc 480
Arg Ala Asp Ile Asp Lys Lys Tyr Arg Cys Val Ser Gly Thr Gln Val
145                      150                      155                      160
cac atg aac aac gtg acc gta acg ctc cat gat gcc acc atc cag gcg 528
His Met Asn Asn Val Thr Val Thr Leu His Asp Ala Thr Ile Gln Ala
      165                      170                      175
tac ctt tcc aac agc agc ttc agc cgg gga gag aca cgc tgt gaa caa 576
Tyr Leu Ser Asn Ser Ser Phe Ser Arg Gly Glu Thr Arg Cys Glu Gln
      180                      185                      190
gac agg cct tcc cca acc aca gcg ccc cct gcg cca ccc agc ccc tcg 624
Asp Arg Pro Ser Pro Thr Thr Ala Pro Pro Ala Pro Pro Ser Pro Ser
      195                      200                      205
ccc tca ccc gtg ccc aag agc ccc tct gtg gac aag tac aac gtg agc 672
Pro Ser Pro Val Pro Lys Ser Pro Ser Val Asp Lys Tyr Asn Val Ser
      210                      215                      220
ggc acc aac ggg acc tgc ctg ctg gcc agc atg ggg ctg cag ctg aac 720
Gly Thr Asn Gly Thr Cys Leu Leu Ala Ser Met Gly Leu Gln Leu Asn
225                      230                      235                      240
ctc acc tat gag agg aag gac aac acg acg gtg aca agg ctt ctc aac 768
Leu Thr Tyr Glu Arg Lys Asp Asn Thr Thr Val Thr Arg Leu Leu Asn
      245                      250                      255
atc aac ccc aac aag acc tcg gcc agc ggg agc tgc ggc gcc cac ctg 816
Ile Asn Pro Asn Lys Thr Ser Ala Ser Gly Ser Cys Gly Ala His Leu
      260                      265                      270
gtg act ctg gag ctg cac agc gag ggc acc acc gtc ctg ctc ttc cag 864
Val Thr Leu Glu Leu His Ser Glu Gly Thr Thr Val Leu Leu Phe Gln
      275                      280                      285
ttc ggg atg aat gca agt tct agc cgg ttt ttc cta caa gga atc cag 912
Phe Gly Met Asn Ala Ser Ser Ser Arg Phe Phe Leu Gln Gly Ile Gln
      290                      295                      300

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ttg aat aca att ctt cct gac gcc aga gac cct gcc ttt aaa gct gcc 960
Leu Asn Thr Ile Leu Pro Asp Ala Arg Asp Pro Ala Phe Lys Ala Ala
305                310                315                320
aac ggc tcc ctg cga gcg ctg cag gcc aca gtc ggc aat tcc tac aag 1008
Asn Gly Ser Leu Arg Ala Leu Gln Ala Thr Val Gly Asn Ser Tyr Lys
                325                330                335
tgc aac gcg gag gag cac gtc cgt gtc acg aag gcg ttt tca gtc aat 1056
Cys Asn Ala Glu Glu His Val Arg Val Thr Lys Ala Phe Ser Val Asn
                340                345                350
ata ttc aaa gtg tgg gtc cag gct ttc aag gtg gaa ggt ggc cag ttt 1104
Ile Phe Lys Val Trp Val Gln Ala Phe Lys Val Glu Gly Gly Gln Phe
                355                360                365
ggc tct gtg gag gag tgt ctg ctg gac gag aac agc ctc gag gac caa 1152
Gly Ser Val Glu Glu Cys Leu Leu Asp Glu Asn Ser Leu Glu Asp Gln
                370                375                380
gtg gac gtg aag gac tgc gcc aac cac gag atc aag aaa gtg ctg gtg 1200
Val Asp Val Lys Asp Cys Ala Asn His Glu Ile Lys Lys Val Leu Val
385                390                395                400
ccc ggc tgc cac ggc agc gag cct tgt atc atc cac cgg ggc aag ccc 1248
Pro Gly Cys His Gly Ser Glu Pro Cys Ile Ile His Arg Gly Lys Pro
                405                410                415
ttt cag ctg gaa gcc gtg ttc gag gcc aac cag aac acc aag acc gcc 1296
Phe Gln Leu Glu Ala Val Phe Glu Ala Asn Gln Asn Thr Lys Thr Ala
                420                425                430
aag att gag atc aag gcc agc atc gac gga ctg gaa gtg gat gtg ccc 1344
Lys Ile Glu Ile Lys Ala Ser Ile Asp Gly Leu Glu Val Asp Val Pro
                435                440                445
ggc atc gac ccc aac gct tgt cac tac atg aag tgc cct ctc gtg aag 1392
Gly Ile Asp Pro Asn Ala Cys His Tyr Met Lys Cys Pro Leu Val Lys
                450                455                460
ggc cag cag tac gac atc aag tac aca tgg aac gtg ccc aag atc gcc 1440
Gly Gln Gln Tyr Asp Ile Lys Tyr Thr Trp Asn Val Pro Lys Ile Ala
465                470                475                480
ccc aag agc gag aac gtc gtc gtg acc gtg aaa gtg atg ggc gac gac 1488
Pro Lys Ser Glu Asn Val Val Val Thr Val Lys Val Met Gly Asp Asp
                485                490                495
ggc gtg ctg gct tgc gcc att gcc aca cac gcc aag atc cgg gac gaa 1536
Gly Val Leu Ala Cys Ala Ile Ala Thr His Ala Lys Ile Arg Asp Glu
                500                505                510

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ttc acg ctg atc ccc atc gct gtg ggt ggt gcc ctg gcg ggg ctg gtc 1584
Phe Thr Leu Ile Pro Ile Ala Val Gly Gly Ala Leu Ala Gly Leu Val
515 520 525
ctc atc gtc ctc atc gcc tac ctc gtc ggc agg aag agg agt cac gca 1632
Leu Ile Val Leu Ile Ala Tyr Leu Val Gly Arg Lys Arg Ser His Ala
530 535 540
ggc tac cag act atc tag taa 1653
Gly Tyr Gln Thr Ile
545
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Leu Leu Leu Gly Leu Met His Cys Ala Ser Ala Ala Met Phe Met Val
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Lys Asn Gly Asn Gly Thr Ala Cys Ile Met Ala Asn Phe Ser Ala Ala
35 40 45
Phe Ser Val Asn Tyr Asp Thr Lys Ser Gly Pro Lys Asn Met Thr Leu
50 55 60
Asp Leu Pro Ser Asp Ala Thr Val Val Leu Asn Arg Ser Ser Cys Gly
65 70 75 80
Lys Glu Asn Thr Ser Asp Pro Ser Leu Val Ile Ala Phe Gly Arg Gly
85 90 95
His Thr Leu Thr Leu Asn Phe Thr Arg Asn Ala Thr Arg Tyr Ser Val
100 105 110
Gln Leu Met Ser Phe Val Tyr Asn Leu Ser Asp Thr His Leu Phe Pro
115 120 125
Asn Ala Ser Ser Lys Glu Ile Lys Thr Val Glu Ser Ile Thr Asp Ile
130 135 140
Arg Ala Asp Ile Asp Lys Lys Tyr Arg Cys Val Ser Gly Thr Gln Val
145 150 155 160
His Met Asn Asn Val Thr Val Thr Leu His Asp Ala Thr Ile Gln Ala
165 170 175
Tyr Leu Ser Asn Ser Ser Phe Ser Arg Gly Glu Thr Arg Cys Glu Gln

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

Gly Val Leu Ala Cys Ala Ile Ala Thr His Ala Lys Ile Arg Asp Glu
 500 505 510
 Phe Thr Leu Ile Pro Ile Ala Val Gly Gly Ala Leu Ala Gly Leu Val
 515 520 525
 Leu Ile Val Leu Ile Ala Tyr Leu Val Gly Arg Lys Arg Ser His Ala
 530 535 540
 Gly Tyr Gln Thr Ile
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 1 5 10
 aaa gtc atg gtg gac gga tgt cac ggg agc gac ccc tgt att atc cac 96
 Lys Val Met Val Asp Gly Cys His Gly Ser Asp Pro Cys Ile Ile His
 15 20 25 30
 cgg gga aag ccc ttc aca ctg gag gcc ctg ttt gat gct aac cag aat 144
 Arg Gly Lys Pro Phe Thr Leu Glu Ala Leu Phe Asp Ala Asn Gln Asn
 35 40 45
 acc aag aca gca aaa atc gag gtc aaa gcc agc ctg gac ggc ctg gaa 192
 Thr Lys Thr Ala Lys Ile Glu Val Lys Ala Ser Leu Asp Gly Leu Glu
 50 55 60
 atc gat gtg cca ggg att gac acc aac gct tgc cat ttc gtc aag tgt 240
 Ile Asp Val Pro Gly Ile Asp Thr Asn Ala Cys His Phe Val Lys Cys
 65 70 75
 ccc ctg gtg aaa ggc cag cag tac gac atc aag tat act tgg aac gtc 288
 Pro Leu Val Lys Gly Gln Gln Tyr Asp Ile Lys Tyr Thr Trp Asn Val
 80 85 90
 ccc aag att gcc cct aaa tcc gaa aat gtg gtc gtg acc gtg aaa ctg 336
 Pro Lys Ile Ala Pro Lys Ser Glu Asn Val Val Val Thr Val Lys Leu
 95 100 105 110
 att gga gac aac ggc gtc ctg gcc tgt gct atc gca act cac ggg aag 384
 Ile Gly Asp Asn Gly Val Leu Ala Cys Ala Ile Ala Thr His Gly Lys

	115	120	125
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Ile Arg Asp			
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Asp Gln Val	Asp Val Lys Asp Cys Ala Asn Asn Glu Ile Lys Lys Val		
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	20	25	30
Lys Pro Phe Thr Leu Glu Ala Leu Phe Asp Ala Asn Gln Asn Thr Lys			
	35	40	45
Thr Ala Lys Ile Glu Val Lys Ala Ser Leu Asp Gly Leu Glu Ile Asp			
	50	55	60
Val Pro Gly Ile Asp Thr Asn Ala Cys His Phe Val Lys Cys Pro Leu			
65	70	75	80
Val Lys Gly Gln Gln Tyr Asp Ile Lys Tyr Thr Trp Asn Val Pro Lys			
	85	90	95
Ile Ala Pro Lys Ser Glu Asn Val Val Val Thr Val Lys Leu Ile Gly			
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Asp Asn Gly Val Leu Ala Cys Ala Ile Ala Thr His Gly Lys Ile Arg			
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1	5	10	15
ctg ctg ctc ggc ctc atg cat tgt gcg tca gca gca atg ttt atg gtg 96			

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Leu Leu Leu Gly Leu Met His Cys Ala Ser Ala Ala Met Phe Met Val
      20                      25                      30
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Lys Asn Gly Asn Gly Thr Ala Cys Ile Met Ala Asn Phe Ser Ala Ala
      35                      40                      45
ttc tca gtg aac tac gac acc aag agt ggc cct aag aac atg acc ctt 192
Phe Ser Val Asn Tyr Asp Thr Lys Ser Gly Pro Lys Asn Met Thr Leu
      50                      55                      60
gac ctg cca tca gat gcc aca gtg gtg ctc aac cgc agc tcc tgt gga 240
Asp Leu Pro Ser Asp Ala Thr Val Val Leu Asn Arg Ser Ser Cys Gly
      65                      70                      75                      80
aaa gag aac act tct gac ccc agt ctc gtg att gct ttt gga aga gga 288
Lys Glu Asn Thr Ser Asp Pro Ser Leu Val Ile Ala Phe Gly Arg Gly
      85                      90                      95
cat aca ctc act ctc aat ttc acg aga aat gca aca cgt tac agc gtc 336
His Thr Leu Thr Leu Asn Phe Thr Arg Asn Ala Thr Arg Tyr Ser Val
      100                     105                     110
cag ctc atg agt ttt gtt tat aac ttg tca gac aca cac ctt ttc ccc 384
Gln Leu Met Ser Phe Val Tyr Asn Leu Ser Asp Thr His Leu Phe Pro
      115                     120                     125
aat gcg agc tcc aaa gaa atc aag act gtg gaa tct ata act gac atc 432
Asn Ala Ser Ser Lys Glu Ile Lys Thr Val Glu Ser Ile Thr Asp Ile
      130                     135                     140
agg gca gat ata gat aaa aaa tac aga tgt gtt agt ggc acc cag gtc 480
Arg Ala Asp Ile Asp Lys Lys Tyr Arg Cys Val Ser Gly Thr Gln Val
      145                     150                     155                     160
cac atg aac aac gtg acc gta acg ctc cat gat gcc acc atc cag gcg 528
His Met Asn Asn Val Thr Val Thr Leu His Asp Ala Thr Ile Gln Ala
      165                     170                     175
tac ctt tcc aac agc agc ttc agc cgg gga gag aca cgc tgt gaa caa 576
Tyr Leu Ser Asn Ser Ser Phe Ser Arg Gly Glu Thr Arg Cys Glu Gln
      180                     185                     190
gac agg cct tcc cca acc aca gcg ccc cct gcg cca ccc agc ccc tcg 624
Asp Arg Pro Ser Pro Thr Thr Ala Pro Pro Ala Pro Pro Ser Pro Ser
      195                     200                     205
ccc tca ccc gtg ccc aag agc ccc tct gtg gac aag tac aac gtg agc 672
Pro Ser Pro Val Pro Lys Ser Pro Ser Val Asp Lys Tyr Asn Val Ser
      210                     215                     220
ggc acc aac ggg acc tgc ctg ctg gcc agc atg ggg ctg cag ctg aac 720

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Gly Thr Asn Gly Thr Cys Leu Leu Ala Ser Met Gly Leu Gln Leu Asn
 225 230 235 240
 ctc acc tat gag agg aag gac aac acg acg gtg aca agg ctt ctc aac 768
 Leu Thr Tyr Glu Arg Lys Asp Asn Thr Thr Val Thr Arg Leu Leu Asn
 245 250 255
 atc aac ccc aac aag acc tcg gcc agc ggg agc tgc ggc gcc cac ctg 816
 Ile Asn Pro Asn Lys Thr Ser Ala Ser Gly Ser Cys Gly Ala His Leu
 260 265 270
 gtg act ctg gag ctg cac agc gag ggc acc acc gtc ctg ctc ttc cag 864
 Val Thr Leu Glu Leu His Ser Glu Gly Thr Thr Val Leu Leu Phe Gln
 275 280 285
 ttc ggg atg aat gca agt tct agc cgg ttt ttc cta caa gga atc cag 912
 Phe Gly Met Asn Ala Ser Ser Ser Arg Phe Phe Leu Gln Gly Ile Gln
 290 295 300
 ttg aat aca att ctt cct gac gcc aga gac cct gcc ttt aaa gct gcc 960
 Leu Asn Thr Ile Leu Pro Asp Ala Arg Asp Pro Ala Phe Lys Ala Ala
 305 310 315 320
 aac ggc tcc ctg cga gcg ctg cag gcc aca gtc ggc aat tcc tac aag 1008
 Asn Gly Ser Leu Arg Ala Leu Gln Ala Thr Val Gly Asn Ser Tyr Lys
 325 330 335
 tgc aac gcg gag gag cac gtc cgt gtc acg aag gcg ttt tca gtc aat 1056
 Cys Asn Ala Glu Glu His Val Arg Val Thr Lys Ala Phe Ser Val Asn
 340 345 350
 ata ttc aaa gtg tgg gtc cag gct ttc aag gtg gaa ggt ggc cag ttt 1104
 Ile Phe Lys Val Trp Val Gln Ala Phe Lys Val Glu Gly Gly Gln Phe
 355 360 365
 ggc tct gtg gag gag tgt ctg ctg gac gag aac agc ctc gag gat cag 1152
 Gly Ser Val Glu Glu Cys Leu Leu Asp Glu Asn Ser Leu Glu Asp Gln
 370 375 380
 gtg gat gtc aag gac tgt gct aac aac gaa atc aag aaa gtc atg gtg 1200
 Val Asp Val Lys Asp Cys Ala Asn Asn Glu Ile Lys Lys Val Met Val
 385 390 395 400
 gac gga tgt cac ggg agc gac ccc tgt att atc cac cgg gga aag ccc 1248
 Asp Gly Cys His Gly Ser Asp Pro Cys Ile Ile His Arg Gly Lys Pro
 405 410 415
 ttc aca ctg gag gcc ctg ttt gat gct aac cag aat acc aag aca gca 1296
 Phe Thr Leu Glu Ala Leu Phe Asp Ala Asn Gln Asn Thr Lys Thr Ala
 420 425 430
 aaa atc gag gtc aaa gcc agc ctg gac ggc ctg gaa atc gat gtg cca 1344

Lys Ile Glu Val Lys Ala Ser Leu Asp Gly Leu Glu Ile Asp Val Pro
 435 440 445
 ggg att gac acc aac gct tgc cat ttc gtc aag tgt ccc ctg gtg aaa 1392
 Gly Ile Asp Thr Asn Ala Cys His Phe Val Lys Cys Pro Leu Val Lys
 450 455 460
 ggc cag cag tac gac atc aag tat act tgg aac gtc ccc aag att gcc 1440
 Gly Gln Gln Tyr Asp Ile Lys Tyr Thr Trp Asn Val Pro Lys Ile Ala
 465 470 475 480
 cct aaa tcc gaa aat gtg gtc gtg acc gtg aaa ctg att gga gac aac 1488
 Pro Lys Ser Glu Asn Val Val Val Thr Val Lys Leu Ile Gly Asp Asn
 485 490 495
 ggc gtc ctg gcc tgt gct atc gca act cac ggg aag att aga gac gaa 1536
 Gly Val Leu Ala Cys Ala Ile Ala Thr His Gly Lys Ile Arg Asp Glu
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 Phe Thr Leu Ile Pro Ile Ala Val Gly Gly Ala Leu Ala Gly Leu Val
 515 520 525
 ctc atc gtc ctc atc gcc tac ctc gtc ggc agg aag agg agt cac gca 1632
 Leu Ile Val Leu Ile Ala Tyr Leu Val Gly Arg Lys Arg Ser His Ala
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 Gly Tyr Gln Thr Ile
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 Met Ala Pro Arg Ser Ala Arg Arg Pro Leu Leu Leu Leu Leu Leu Leu
 1 5 10 15
 Leu Leu Leu Gly Leu Met His Cys Ala Ser Ala Ala Met Phe Met Val
 20 25 30
 Lys Asn Gly Asn Gly Thr Ala Cys Ile Met Ala Asn Phe Ser Ala Ala
 35 40 45
 Phe Ser Val Asn Tyr Asp Thr Lys Ser Gly Pro Lys Asn Met Thr Leu
 50 55 60
 Asp Leu Pro Ser Asp Ala Thr Val Val Leu Asn Arg Ser Ser Cys Gly

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

Val Asp Val Lys Asp Cys Ala Asn Asn Glu Ile Lys Lys Val Met Val
 385 390 395 400
 Asp Gly Cys His Gly Ser Asp Pro Cys Ile Ile His Arg Gly Lys Pro
 405 410 415
 Phe Thr Leu Glu Ala Leu Phe Asp Ala Asn Gln Asn Thr Lys Thr Ala
 420 425 430
 Lys Ile Glu Val Lys Ala Ser Leu Asp Gly Leu Glu Ile Asp Val Pro
 435 440 445
 Gly Ile Asp Thr Asn Ala Cys His Phe Val Lys Cys Pro Leu Val Lys
 450 455 460
 Gly Gln Gln Tyr Asp Ile Lys Tyr Thr Trp Asn Val Pro Lys Ile Ala
 465 470 475 480
 Pro Lys Ser Glu Asn Val Val Val Thr Val Lys Leu Ile Gly Asp Asn
 485 490 495
 Gly Val Leu Ala Cys Ala Ile Ala Thr His Gly Lys Ile Arg Asp Glu
 500 505 510
 Phe Thr Leu Ile Pro Ile Ala Val Gly Gly Ala Leu Ala Gly Leu Val
 515 520 525
 Leu Ile Val Leu Ile Ala Tyr Leu Val Gly Arg Lys Arg Ser His Ala
 530 535 540
 Gly Tyr Gln Thr Ile

545

<210> 60

<211> 648

<212> DNA

<213> 屋尘螨(Dermatophagoides pteronyssinus)

<220>

<221> CDS

<222> (7) .. (642)

<400> 60

ctcgag acc aac gct tgc tct atc aac gga aac gcc ccc gcc gaa atc 48

Thr Asn Ala Cys Ser Ile Asn Gly Asn Ala Pro Ala Glu Ile

1

5

10

gac ctg agg cag atg agg act gtc aca ccc att agg tcc gga gtg gcc 96

Asp Leu Arg Gln Met Arg Thr Val Thr Pro Ile Arg Ser Gly Val Ala

15

20

25

30

gct act gag tct gcc tac ctg gct tat cga aat cag agt ctg gac ctg 144

Ala Thr Glu Ser Ala Tyr Leu Ala Tyr Arg Asn Gln Ser Leu Asp Leu

35

40

45

gca gag cag gaa ctg gtg gat tgc gcc agc cag cac aat ggg tgt cat 192
 Ala Glu Gln Glu Leu Val Asp Cys Ala Ser Gln His Asn Gly Cys His
 50 55 60
 gga gac acc atc cca agg gga atc gaa tac att cag cac aac ggc gtg 240
 Gly Asp Thr Ile Pro Arg Gly Ile Glu Tyr Ile Gln His Asn Gly Val
 65 70 75
 gtc cag gag tca tac tat aga tat gtg gcc cgc gaa cag agc tgc cga 288
 Val Gln Glu Ser Tyr Tyr Arg Tyr Val Ala Arg Glu Gln Ser Cys Arg
 80 85 90
 aga cca aat gct cag agg ttc ggc atc agt aac tac tgt cag att tat 336
 Arg Pro Asn Ala Gln Arg Phe Gly Ile Ser Asn Tyr Cys Gln Ile Tyr
 95 100 105 110
 cct cag aac gtg aat aag atc cga gag gca ctg gca cag acc cac tcc 384
 Pro Gln Asn Val Asn Lys Ile Arg Glu Ala Leu Ala Gln Thr His Ser
 115 120 125
 gct atc gca gtc atc att ggg att aaa gac ctg gat gcc ttt cga cat 432
 Ala Ile Ala Val Ile Ile Gly Ile Lys Asp Leu Asp Ala Phe Arg His
 130 135 140
 tac gac ggg cgg aca atc att cag aga gat aac gga tac cag ccc aat 480
 Tyr Asp Gly Arg Thr Ile Ile Gln Arg Asp Asn Gly Tyr Gln Pro Asn
 145 150 155
 tat cat gct gtg aac atc gtc ggc tac tcc aat gca cag ggg gtg gat 528
 Tyr His Ala Val Asn Ile Val Gly Tyr Ser Asn Ala Gln Gly Val Asp
 160 165 170
 tat tgg att gtc cgg aac tct tgg gac aca aac tgg ggc gat aat gga 576
 Tyr Trp Ile Val Arg Asn Ser Trp Asp Thr Asn Trp Gly Asp Asn Gly
 175 180 185 190
 tat ggc tat ttc gcc gcc aac att gac ctg atg atg att gaa gag tat 624
 Tyr Gly Tyr Phe Ala Ala Asn Ile Asp Leu Met Met Ile Glu Glu Tyr
 195 200 205
 cct tac gtg gtg atc ctg gaattc 648
 Pro Tyr Val Val Ile Leu
 210
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 <211> 212
 <212> PRT
 <213> 屋尘螨(Dermatophagoides pteronyssinus)
 <400> 61
 Thr Asn Ala Cys Ser Ile Asn Gly Asn Ala Pro Ala Glu Ile Asp Leu

1	5	10	15
Arg Gln Met Arg Thr Val Thr Pro Ile Arg Ser Gly Val Ala Ala Thr			
	20	25	30
Glu Ser Ala Tyr Leu Ala Tyr Arg Asn Gln Ser Leu Asp Leu Ala Glu			
	35	40	45
Gln Glu Leu Val Asp Cys Ala Ser Gln His Asn Gly Cys His Gly Asp			
	50	55	60
Thr Ile Pro Arg Gly Ile Glu Tyr Ile Gln His Asn Gly Val Val Gln			
65	70	75	80
Glu Ser Tyr Tyr Arg Tyr Val Ala Arg Glu Gln Ser Cys Arg Arg Pro			
	85	90	95
Asn Ala Gln Arg Phe Gly Ile Ser Asn Tyr Cys Gln Ile Tyr Pro Gln			
	100	105	110
Asn Val Asn Lys Ile Arg Glu Ala Leu Ala Gln Thr His Ser Ala Ile			
	115	120	125
Ala Val Ile Ile Gly Ile Lys Asp Leu Asp Ala Phe Arg His Tyr Asp			
	130	135	140
Gly Arg Thr Ile Ile Gln Arg Asp Asn Gly Tyr Gln Pro Asn Tyr His			
145	150	155	160
Ala Val Asn Ile Val Gly Tyr Ser Asn Ala Gln Gly Val Asp Tyr Trp			
	165	170	175
Ile Val Arg Asn Ser Trp Asp Thr Asn Trp Gly Asp Asn Gly Tyr Gly			
	180	185	190
Tyr Phe Ala Ala Asn Ile Asp Leu Met Met Ile Glu Glu Tyr Pro Tyr			
	195	200	205
Val Val Ile Leu			
210			
<210> 62			
<211> 1902			
<212> DNA			
<213> 人工序列			
<220>			
<223> 合成构建物			
<220>			
<221> CDS			
<222> (1) .. (1902)			
<400> 62			
atg gcg ccc cgc agc gcc cgg cga ccc ctg ctg ctg cta ctg ctg ttg 48			
Met Ala Pro Arg Ser Ala Arg Arg Pro Leu Leu Leu Leu Leu Leu Leu			

1	5	10	15
ctg ctg ctc ggc ctc atg cat tgt gcg tca gca gca atg ttt atg gtg	96		
Leu Leu Leu Gly Leu Met His Cys Ala Ser Ala Ala Met Phe Met Val			
20	25	30	
aaa aat ggc aac ggg acc gcg tgc ata atg gcc aac ttc tct gct gcc	144		
Lys Asn Gly Asn Gly Thr Ala Cys Ile Met Ala Asn Phe Ser Ala Ala			
35	40	45	
ttc tca gtg aac tac gac acc aag agt ggc cct aag aac atg acc ctt	192		
Phe Ser Val Asn Tyr Asp Thr Lys Ser Gly Pro Lys Asn Met Thr Leu			
50	55	60	
gac ctg cca tca gat gcc aca gtg gtg ctc aac cgc agc tcc tgt gga	240		
Asp Leu Pro Ser Asp Ala Thr Val Val Leu Asn Arg Ser Ser Cys Gly			
65	70	75	80
aaa gag aac act tct gac ccc agt ctc gtg att gct ttt gga aga gga	288		
Lys Glu Asn Thr Ser Asp Pro Ser Leu Val Ile Ala Phe Gly Arg Gly			
85	90	95	
cat aca ctc act ctc aat ttc acg aga aat gca aca cgt tac agc gtc	336		
His Thr Leu Thr Leu Asn Phe Thr Arg Asn Ala Thr Arg Tyr Ser Val			
100	105	110	
cag ctc atg agt ttt gtt tat aac ttg tca gac aca cac ctt ttc ccc	384		
Gln Leu Met Ser Phe Val Tyr Asn Leu Ser Asp Thr His Leu Phe Pro			
115	120	125	
aat gcg agc tcc aaa gaa atc aag act gtg gaa tct ata act gac atc	432		
Asn Ala Ser Ser Lys Glu Ile Lys Thr Val Glu Ser Ile Thr Asp Ile			
130	135	140	
agg gca gat ata gat aaa aaa tac aga tgt gtt agt ggc acc cag gtc	480		
Arg Ala Asp Ile Asp Lys Lys Tyr Arg Cys Val Ser Gly Thr Gln Val			
145	150	155	160
cac atg aac aac gtg acc gta acg ctc cat gat gcc acc atc cag gcg	528		
His Met Asn Asn Val Thr Val Thr Leu His Asp Ala Thr Ile Gln Ala			
165	170	175	
tac ctt tcc aac agc agc ttc agc cgg gga gag aca cgc tgt gaa caa	576		
Tyr Leu Ser Asn Ser Ser Phe Ser Arg Gly Glu Thr Arg Cys Glu Gln			
180	185	190	
gac agg cct tcc cca acc aca gcg ccc cct gcg cca ccc agc ccc tcg	624		
Asp Arg Pro Ser Pro Thr Thr Ala Pro Pro Ala Pro Pro Ser Pro Ser			
195	200	205	
ccc tca ccc gtg ccc aag agc ccc tct gtg gac aag tac aac gtg agc	672		
Pro Ser Pro Val Pro Lys Ser Pro Ser Val Asp Lys Tyr Asn Val Ser			

210	215	220	
ggc acc aac ggg acc tgc ctg ctg gcc agc atg ggg ctg cag ctg aac	720		
Gly Thr Asn Gly Thr Cys Leu Leu Ala Ser Met Gly Leu Gln Leu Asn			
225	230	235	240
ctc acc tat gag agg aag gac aac acg acg gtg aca agg ctt ctc aac	768		
Leu Thr Tyr Glu Arg Lys Asp Asn Thr Thr Val Thr Arg Leu Leu Asn			
245	250	255	
atc aac ccc aac aag acc tcg gcc agc ggg agc tgc ggc gcc cac ctg	816		
Ile Asn Pro Asn Lys Thr Ser Ala Ser Gly Ser Cys Gly Ala His Leu			
260	265	270	
gtg act ctg gag ctg cac agc gag ggc acc acc gtc ctg ctc ttc cag	864		
Val Thr Leu Glu Leu His Ser Glu Gly Thr Thr Val Leu Leu Phe Gln			
275	280	285	
ttc ggg atg aat gca agt tct agc cgg ttt ttc cta caa gga atc cag	912		
Phe Gly Met Asn Ala Ser Ser Ser Arg Phe Phe Leu Gln Gly Ile Gln			
290	295	300	
ttg aat aca att ctt cct gac gcc aga gac cct gcc ttt aaa gct gcc	960		
Leu Asn Thr Ile Leu Pro Asp Ala Arg Asp Pro Ala Phe Lys Ala Ala			
305	310	315	320
aac ggc tcc ctg cga gcg ctg cag gcc aca gtc ggc aat tcc tac aag	1008		
Asn Gly Ser Leu Arg Ala Leu Gln Ala Thr Val Gly Asn Ser Tyr Lys			
325	330	335	
tgc aac gcg gag gag cac gtc cgt gtc acg aag gcg ttt tca gtc aat	1056		
Cys Asn Ala Glu Glu His Val Arg Val Thr Lys Ala Phe Ser Val Asn			
340	345	350	
ata ttc aaa gtg tgg gtc cag gct ttc aag gtg gaa ggt ggc cag ttt	1104		
Ile Phe Lys Val Trp Val Gln Ala Phe Lys Val Glu Gly Gly Gln Phe			
355	360	365	
ggc tct gtg gag gag tgt ctg ctg gac gag aac agc ctc gag acc aac	1152		
Gly Ser Val Glu Glu Cys Leu Leu Asp Glu Asn Ser Leu Glu Thr Asn			
370	375	380	
gct tgc tct atc aac gga aac gcc ccc gcc gaa atc gac ctg agg cag	1200		
Ala Cys Ser Ile Asn Gly Asn Ala Pro Ala Glu Ile Asp Leu Arg Gln			
385	390	395	400
atg agg act gtc aca ccc att agg tcc gga gtg gcc gct act gag tct	1248		
Met Arg Thr Val Thr Pro Ile Arg Ser Gly Val Ala Ala Thr Glu Ser			
405	410	415	
gcc tac ctg gct tat cga aat cag agt ctg gac ctg gca gag cag gaa	1296		
Ala Tyr Leu Ala Tyr Arg Asn Gln Ser Leu Asp Leu Ala Glu Gln Glu			

420	425	430	
ctg gtg gat tgc gcc agc cag cac aat ggg tgt cat gga gac acc atc			1344
Leu Val Asp Cys Ala Ser Gln His Asn Gly Cys His Gly Asp Thr Ile			
435	440	445	
cca agg gga atc gaa tac att cag cac aac ggc gtg gtc cag gag tca			1392
Pro Arg Gly Ile Glu Tyr Ile Gln His Asn Gly Val Val Gln Glu Ser			
450	455	460	
tac tat aga tat gtg gcc cgc gaa cag agc tgc cga aga cca aat gct			1440
Tyr Tyr Arg Tyr Val Ala Arg Glu Gln Ser Cys Arg Arg Pro Asn Ala			
465	470	475	480
cag agg ttc ggc atc agt aac tac tgt cag att tat cct cag aac gtg			1488
Gln Arg Phe Gly Ile Ser Asn Tyr Cys Gln Ile Tyr Pro Gln Asn Val			
485	490	495	
aat aag atc cga gag gca ctg gca cag acc cac tcc gct atc gca gtc			1536
Asn Lys Ile Arg Glu Ala Leu Ala Gln Thr His Ser Ala Ile Ala Val			
500	505	510	
atc att ggg att aaa gac ctg gat gcc ttt cga cat tac gac ggg cgg			1584
Ile Ile Gly Ile Lys Asp Leu Asp Ala Phe Arg His Tyr Asp Gly Arg			
515	520	525	
aca atc att cag aga gat aac gga tac cag ccc aat tat cat gct gtg			1632
Thr Ile Ile Gln Arg Asp Asn Gly Tyr Gln Pro Asn Tyr His Ala Val			
530	535	540	
aac atc gtc ggc tac tcc aat gca cag ggg gtg gat tat tgg att gtc			1680
Asn Ile Val Gly Tyr Ser Asn Ala Gln Gly Val Asp Tyr Trp Ile Val			
545	550	555	560
cgg aac tct tgg gac aca aac tgg ggc gat aat gga tat ggc tat ttc			1728
Arg Asn Ser Trp Asp Thr Asn Trp Gly Asp Asn Gly Tyr Gly Tyr Phe			
565	570	575	
gcc gcc aac att gac ctg atg atg att gaa gag tat cct tac gtg gtg			1776
Ala Ala Asn Ile Asp Leu Met Met Ile Glu Glu Tyr Pro Tyr Val Val			
580	585	590	
atc ctg gaa ttc acg ctg atc ccc atc gct gtg ggt ggt gcc ctg gcg			1824
Ile Leu Glu Phe Thr Leu Ile Pro Ile Ala Val Gly Gly Ala Leu Ala			
595	600	605	
ggg ctg gtc ctc atc gtc ctc atc gcc tac ctc gtc ggc agg aag agg			1872
Gly Leu Val Leu Ile Val Leu Ile Ala Tyr Leu Val Gly Arg Lys Arg			
610	615	620	
agt cac gca ggc tac cag act atc tag taa			1902
Ser His Ala Gly Tyr Gln Thr Ile			

172

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

Arg Asn Ser Trp Asp Thr Asn Trp Gly Asp Asn Gly Tyr Gly Tyr Phe
 565 570 575
 Ala Ala Asn Ile Asp Leu Met Met Ile Glu Glu Tyr Pro Tyr Val Val
 580 585 590
 Ile Leu Glu Phe Thr Leu Ile Pro Ile Ala Val Gly Gly Ala Leu Ala
 595 600 605
 Gly Leu Val Leu Ile Val Leu Ile Ala Tyr Leu Val Gly Arg Lys Arg
 610 615 620
 Ser His Ala Gly Tyr Gln Thr Ile
 625 630
 <210> 64
 <211> 543
 <212> DNA
 <213> 家猫(Felis catus)
 <220>
 <221> CDS
 <222> (7) .. (537)
 <400> 64
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 Glu Ile Cys Pro Ala Val Lys Arg Asp Val Asp Leu Phe Leu
 1 5 10
 acc ggc acc ccc gac gag tac gtg gaa caa gtg gcc cag tac aag gct 96
 Thr Gly Thr Pro Asp Glu Tyr Val Glu Gln Val Ala Gln Tyr Lys Ala
 15 20 25 30
 ctg ccc gtg gtg ctg gaa aac gcc cgg att ctg aag aac tgc gtg gac 144
 Leu Pro Val Val Leu Glu Asn Ala Arg Ile Leu Lys Asn Cys Val Asp
 35 40 45
 gcc aag atg acc gaa gag gac aaa gag aac gct ctg tct ctg ctg gac 192
 Ala Lys Met Thr Glu Glu Asp Lys Glu Asn Ala Leu Ser Leu Leu Asp
 50 55 60
 aag atc tac acc agc cct ctg tgt ggc ggc gga gga tct ggc gga ggc 240
 Lys Ile Tyr Thr Ser Pro Leu Cys Gly Gly Gly Gly Ser Gly Gly Gly
 65 70 75
 gga agt ggc gga ggg ggc tct gtg aag atg gcc gag aca tgc ccc atc 288
 Gly Ser Gly Gly Gly Gly Ser Val Lys Met Ala Glu Thr Cys Pro Ile
 80 85 90
 ttc tac gac gtg ttc ttc gcc gtg gcc aac ggc aac gag ctg ctg ctg 336
 Phe Tyr Asp Val Phe Phe Ala Val Ala Asn Gly Asn Glu Leu Leu Leu
 95 100 105 110

gat ctg agt ctg acc aaa gtg aac gcc acc gag ccc gag cgg acc gcc 384
Asp Leu Ser Leu Thr Lys Val Asn Ala Thr Glu Pro Glu Arg Thr Ala
115 120 125
atg aag aag atc caa gac tgc tac gtg gaa aac gga ctg atc agc cgg 432
Met Lys Lys Ile Gln Asp Cys Tyr Val Glu Asn Gly Leu Ile Ser Arg
130 135 140
gtg ctg gac gga ctc gtg atg acc acc atc agc agc tcc aag gac tgc 480
Val Leu Asp Gly Leu Val Met Thr Thr Ile Ser Ser Ser Lys Asp Cys
145 150 155
atg ggc gag gcc gtg cag aac acc gtg gaa gat ctg aag ctg aac aca 528
Met Gly Glu Ala Val Gln Asn Thr Val Glu Asp Leu Lys Leu Asn Thr
160 165 170
ctg ggc cgg gaattc 543
Leu Gly Arg
175
<210> 65
<211> 177
<212> PRT
<213> 家猫(Felis catus)
<400> 65
Glu Ile Cys Pro Ala Val Lys Arg Asp Val Asp Leu Phe Leu Thr Gly
1 5 10 15
Thr Pro Asp Glu Tyr Val Glu Gln Val Ala Gln Tyr Lys Ala Leu Pro
20 25 30
Val Val Leu Glu Asn Ala Arg Ile Leu Lys Asn Cys Val Asp Ala Lys
35 40 45
Met Thr Glu Glu Asp Lys Glu Asn Ala Leu Ser Leu Leu Asp Lys Ile
50 55 60
Tyr Thr Ser Pro Leu Cys Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
65 70 75 80
Gly Gly Gly Gly Ser Val Lys Met Ala Glu Thr Cys Pro Ile Phe Tyr
85 90 95
Asp Val Phe Phe Ala Val Ala Asn Gly Asn Glu Leu Leu Leu Asp Leu
100 105 110
Ser Leu Thr Lys Val Asn Ala Thr Glu Pro Glu Arg Thr Ala Met Lys
115 120 125
Lys Ile Gln Asp Cys Tyr Val Glu Asn Gly Leu Ile Ser Arg Val Leu
130 135 140
Asp Gly Leu Val Met Thr Thr Ile Ser Ser Ser Lys Asp Cys Met Gly

145	150	155	160
Glu Ala Val Gln Asn Thr Val Glu Asp Leu Lys Leu Asn Thr Leu Gly			
	165	170	175

Arg

<210> 66

<211> 162

<212> PRT

<213> 家猫(Felis catus)

<400> 66

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

Gly Arg

<210> 67

<211> 1797

<212> DNA

<213> 人工序列

<220>

<223> 合成构建物

<220>

<221> CDS

<222> (1) .. (1797)

<400> 67

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atg gcg ccc cgc agc gcc cgg cga ccc ctg ctg ctg cta ctg ctg ttg 48
Met Ala Pro Arg Ser Ala Arg Arg Pro Leu Leu Leu Leu Leu Leu
1           5           10           15
ctg ctg ctc ggc ctc atg cat tgt gcg tca gca gca atg ttt atg gtg 96
Leu Leu Leu Gly Leu Met His Cys Ala Ser Ala Ala Met Phe Met Val
           20           25           30
aaa aat ggc aac ggg acc gcg tgc ata atg gcc aac ttc tct gct gcc 144
Lys Asn Gly Asn Gly Thr Ala Cys Ile Met Ala Asn Phe Ser Ala Ala
           35           40           45
ttc tca gtg aac tac gac acc aag agt ggc cct aag aac atg acc ctt 192
Phe Ser Val Asn Tyr Asp Thr Lys Ser Gly Pro Lys Asn Met Thr Leu
           50           55           60
gac ctg cca tca gat gcc aca gtg gtg ctc aac cgc agc tcc tgt gga 240
Asp Leu Pro Ser Asp Ala Thr Val Val Leu Asn Arg Ser Ser Cys Gly
65           70           75           80
aaa gag aac act tct gac ccc agt ctc gtg att gct ttt gga aga gga 288
Lys Glu Asn Thr Ser Asp Pro Ser Leu Val Ile Ala Phe Gly Arg Gly
           85           90           95
cat aca ctc act ctc aat ttc acg aga aat gca aca cgt tac agc gtc 336
His Thr Leu Thr Leu Asn Phe Thr Arg Asn Ala Thr Arg Tyr Ser Val
           100          105          110
cag ctc atg agt ttt gtt tat aac ttg tca gac aca cac ctt ttc ccc 384
Gln Leu Met Ser Phe Val Tyr Asn Leu Ser Asp Thr His Leu Phe Pro
           115          120          125
aat gcg agc tcc aaa gaa atc aag act gtg gaa tct ata act gac atc 432
Asn Ala Ser Ser Lys Glu Ile Lys Thr Val Glu Ser Ile Thr Asp Ile
           130          135          140
agg gca gat ata gat aaa aaa tac aga tgt gtt agt ggc acc cag gtc 480
Arg Ala Asp Ile Asp Lys Lys Tyr Arg Cys Val Ser Gly Thr Gln Val
145          150          155          160
cac atg aac aac gtg acc gta acg ctc cat gat gcc acc atc cag gcg 528
His Met Asn Asn Val Thr Val Thr Leu His Asp Ala Thr Ile Gln Ala
           165          170          175
tac ctt tcc aac agc agc ttc agc cgg gga gag aca cgc tgt gaa caa 576
Tyr Leu Ser Asn Ser Ser Phe Ser Arg Gly Glu Thr Arg Cys Glu Gln
           180          185          190
gac agg cct tcc cca acc aca gcg ccc cct gcg cca ccc agc ccc tcg 624
Asp Arg Pro Ser Pro Thr Thr Ala Pro Pro Ala Pro Pro Ser Pro Ser

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195	200	205
ccc tca ccc gtg ccc aag agc ccc tct gtg gac aag tac aac gtg agc 672		
Pro Ser Pro Val Pro Lys Ser Pro Ser Val Asp Lys Tyr Asn Val Ser		
210	215	220
ggc acc aac ggg acc tgc ctg ctg gcc agc atg ggg ctg cag ctg aac 720		
Gly Thr Asn Gly Thr Cys Leu Leu Ala Ser Met Gly Leu Gln Leu Asn		
225	230	235
ctc acc tat gag agg aag gac aac acg acg gtg aca agg ctt ctc aac 768		
Leu Thr Tyr Glu Arg Lys Asp Asn Thr Thr Val Thr Arg Leu Leu Asn		
245	250	255
atc aac ccc aac aag acc tcg gcc agc ggg agc tgc ggc gcc cac ctg 816		
Ile Asn Pro Asn Lys Thr Ser Ala Ser Gly Ser Cys Gly Ala His Leu		
260	265	270
gtg act ctg gag ctg cac agc gag ggc acc acc gtc ctg ctc ttc cag 864		
Val Thr Leu Glu Leu His Ser Glu Gly Thr Thr Val Leu Leu Phe Gln		
275	280	285
ttc ggg atg aat gca agt tct agc cgg ttt ttc cta caa gga atc cag 912		
Phe Gly Met Asn Ala Ser Ser Ser Arg Phe Phe Leu Gln Gly Ile Gln		
290	295	300
ttg aat aca att ctt cct gac gcc aga gac cct gcc ttt aaa gct gcc 960		
Leu Asn Thr Ile Leu Pro Asp Ala Arg Asp Pro Ala Phe Lys Ala Ala		
305	310	315
aac ggc tcc ctg cga gcg ctg cag gcc aca gtc ggc aat tcc tac aag 1008		
Asn Gly Ser Leu Arg Ala Leu Gln Ala Thr Val Gly Asn Ser Tyr Lys		
325	330	335
tgc aac gcg gag gag cac gtc cgt gtc acg aag gcg ttt tca gtc aat 1056		
Cys Asn Ala Glu Glu His Val Arg Val Thr Lys Ala Phe Ser Val Asn		
340	345	350
ata ttc aaa gtg tgg gtc cag gct ttc aag gtg gaa ggt ggc cag ttt 1104		
Ile Phe Lys Val Trp Val Gln Ala Phe Lys Val Glu Gly Gly Gln Phe		
355	360	365
ggc tct gtg gag gag tgt ctg ctg gac gag aac agc ctc gag gaa atc 1152		
Gly Ser Val Glu Glu Cys Leu Leu Asp Glu Asn Ser Leu Glu Glu Ile		
370	375	380
tgc cca gcc gtg aag cgg gat gtg gat ctg ttt ctg acc ggc acc ccc 1200		
Cys Pro Ala Val Lys Arg Asp Val Asp Leu Phe Leu Thr Gly Thr Pro		
385	390	395
gac gag tac gtg gaa caa gtg gcc cag tac aag gct ctg ccc gtg gtg 1248		
Asp Glu Tyr Val Glu Gln Val Ala Gln Tyr Lys Ala Leu Pro Val Val		

405	410	415
ctg gaa aac gcc cgg att ctg aag aac tgc gtg gac gcc aag atg acc 1296		
Leu Glu Asn Ala Arg Ile Leu Lys Asn Cys Val Asp Ala Lys Met Thr		
420	425	430
gaa gag gac aaa gag aac gct ctg tct ctg ctg gac aag atc tac acc 1344		
Glu Glu Asp Lys Glu Asn Ala Leu Ser Leu Leu Asp Lys Ile Tyr Thr		
435	440	445
agc cct ctg tgt ggc ggc gga gga tct ggc gga ggc gga agt ggc gga 1392		
Ser Pro Leu Cys Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly		
450	455	460
ggg ggc tct gtg aag atg gcc gag aca tgc ccc atc ttc tac gac gtg 1440		
Gly Gly Ser Val Lys Met Ala Glu Thr Cys Pro Ile Phe Tyr Asp Val		
465	470	475
ttc ttc gcc gtg gcc aac ggc aac gag ctg ctg ctg gat ctg agt ctg 1488		
Phe Phe Ala Val Ala Asn Gly Asn Glu Leu Leu Leu Asp Leu Ser Leu		
485	490	495
acc aaa gtg aac gcc acc gag ccc gag cgg acc gcc atg aag aag atc 1536		
Thr Lys Val Asn Ala Thr Glu Pro Glu Arg Thr Ala Met Lys Lys Ile		
500	505	510
caa gac tgc tac gtg gaa aac gga ctg atc agc cgg gtg ctg gac gga 1584		
Gln Asp Cys Tyr Val Glu Asn Gly Leu Ile Ser Arg Val Leu Asp Gly		
515	520	525
ctc gtg atg acc acc atc agc agc tcc aag gac tgc atg ggc gag gcc 1632		
Leu Val Met Thr Thr Ile Ser Ser Ser Lys Asp Cys Met Gly Glu Ala		
530	535	540
gtg cag aac acc gtg gaa gat ctg aag ctg aac aca ctg ggc cgg gaa 1680		
Val Gln Asn Thr Val Glu Asp Leu Lys Leu Asn Thr Leu Gly Arg Glu		
545	550	555
ttc acg ctg atc ccc atc gct gtg ggt ggt gcc ctg gcg ggg ctg gtc 1728		
Phe Thr Leu Ile Pro Ile Ala Val Gly Gly Ala Leu Ala Gly Leu Val		
565	570	575
ctc atc gtc ctc atc gcc tac ctc gtc ggc agg aag agg agt cac gca 1776		
Leu Ile Val Leu Ile Ala Tyr Leu Val Gly Arg Lys Arg Ser His Ala		
580	585	590
ggc tac cag act atc tag taa 1797		
Gly Tyr Gln Thr Ile		
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<223> 合成构建物

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

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

580	585	590
Gly Tyr Gln Thr Ile		
595		
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ggc gag gaa cac ttc cgg gga ctg gtt ctc gtg gcc ttc agc cag tat 96		
Gly Glu Glu His Phe Arg Gly Leu Val Leu Val Ala Phe Ser Gln Tyr		
15 20 25 30		
ctg cag cag tgc ccc ttc gag gac cac gtg aag ctc gtg aac gaa gtg 144		
Leu Gln Gln Cys Pro Phe Glu Asp His Val Lys Leu Val Asn Glu Val		
35 40 45		
acc gag ttc gcc aag ggc tgc gtg gcc gat cag tct gcc gcc aac tgc 192		
Thr Glu Phe Ala Lys Gly Cys Val Ala Asp Gln Ser Ala Ala Asn Cys		
50 55 60		
gag aag tct ctg cac gag ctg ctg ggc gac aag ctg tgt acc gtg gcc 240		
Glu Lys Ser Leu His Glu Leu Leu Gly Asp Lys Leu Cys Thr Val Ala		
65 70 75		
tct ctg cgg gat aag tac ggc gag atg gcc gac tgt tgc gag aag aaa 288		
Ser Leu Arg Asp Lys Tyr Gly Glu Met Ala Asp Cys Cys Glu Lys Lys		
80 85 90		
gag ccc gag cgg aac gag tgc ttt ctg cag cac aag gac gac aac ccc 336		
Glu Pro Glu Arg Asn Glu Cys Phe Leu Gln His Lys Asp Asp Asn Pro		
95 100 105 110		
ggc ttc ggc cag ctc gtg aca cca gag gcc gat gcc atg tgc acc gcc 384		
Gly Phe Gly Gln Leu Val Thr Pro Glu Ala Asp Ala Met Cys Thr Ala		
115 120 125		
ttc cac gag aat gag cag cgg ttt ctg ggc aag tat ctg tac gag att 432		
Phe His Glu Asn Glu Gln Arg Phe Leu Gly Lys Tyr Leu Tyr Glu Ile		
130 135 140		
gcc aga cgg cac ccc tac ttc tac gcc cca gag ctg ctg tac tac gcc 480		

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Ala Arg Arg His Pro Tyr Phe Tyr Ala Pro Glu Leu Leu Tyr Tyr Ala
      145                      150                      155
gaa gag tac aag ggc gtg ttc acc gag tgc tgc gag gcc gcc gat aag 528
Glu Glu Tyr Lys Gly Val Phe Thr Glu Cys Cys Glu Ala Ala Asp Lys
      160                      165                      170
gcc gct tgt ctg acc ccc aaa gtg gac gca ctg cgc gag aaa gtg ctg 576
Ala Ala Cys Leu Thr Pro Lys Val Asp Ala Leu Arg Glu Lys Val Leu
      175                      180                      185                      190
gcc tcc agc gcc aaa gaa cgg ctg aag tgc gct tct ctg cag aag ttc 624
Ala Ser Ser Ala Lys Glu Arg Leu Lys Cys Ala Ser Leu Gln Lys Phe
                      195                      200                      205
ggc gag cgg gcc ttc aag gct tgg agc gtg gca aga ctg agc cag aag 672
Gly Glu Arg Ala Phe Lys Ala Trp Ser Val Ala Arg Leu Ser Gln Lys
                      210                      215                      220
ttc ccc aag gcc gag ttt gcc gag atc agc aag ctc gtg acc gat ctg 720
Phe Pro Lys Ala Glu Phe Ala Glu Ile Ser Lys Leu Val Thr Asp Leu
                      225                      230                      235
gcc aag atc cac aaa gag tgc tgc cac ggc gat ctg ctg gaa tgc gcc 768
Ala Lys Ile His Lys Glu Cys Cys His Gly Asp Leu Leu Glu Cys Ala
                      240                      245                      250
gac gac aga gct gat ctg gct aag tac atc tgc gag aat caa gac agc 816
Asp Asp Arg Ala Asp Leu Ala Lys Tyr Ile Cys Glu Asn Gln Asp Ser
      255                      260                      265                      270
atc agc acc aag ctg aaa gag tgt tgc ggc aag ccc gtg ctg gaa aag 864
Ile Ser Thr Lys Leu Lys Glu Cys Cys Gly Lys Pro Val Leu Glu Lys
                      275                      280                      285
agc cac tgc atc agc gaa gtg gaa cgg gac gag ctg ccc gct gat ctg 912
Ser His Cys Ile Ser Glu Val Glu Arg Asp Glu Leu Pro Ala Asp Leu
                      290                      295                      300
cct cct ctg gcc gtg gac ttc gtg gag gac aaa gaa gtg tgc aag aac 960
Pro Pro Leu Ala Val Asp Phe Val Glu Asp Lys Glu Val Cys Lys Asn
                      305                      310                      315
tac caa gag gcc aag gat gtg ttt ctg ggg aca ttt ctg tat gag tac 1008
Tyr Gln Glu Ala Lys Asp Val Phe Leu Gly Thr Phe Leu Tyr Glu Tyr
                      320                      325                      330
tct cgg cgg cac ccc gag tac tcc gtg tct ctg ctg ctg cgg ctg gcc 1056
Ser Arg Arg His Pro Glu Tyr Ser Val Ser Leu Leu Leu Arg Leu Ala
      335                      340                      345                      350
aaa gag tac gag gcc aca ctg gaa aag tgc tgc gcc acc gac gat ccc 1104

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Lys Glu Tyr Glu Ala Thr Leu Glu Lys Cys Cys Ala Thr Asp Asp Pro
          355                      360                      365
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Pro Ala Cys Tyr Ala His Val Phe Asp Glu Phe Lys Pro Leu Val Glu
          370                      375                      380
gaa ccc cac aat ctc gtg aaa aca aac tgc gag ctg ttc gag aag ctg 1200
Glu Pro His Asn Leu Val Lys Thr Asn Cys Glu Leu Phe Glu Lys Leu
          385                      390                      395
ggc gag tac ggc ttc cag aac gca ctg ctc gtg cgg tac acc aag aaa 1248
Gly Glu Tyr Gly Phe Gln Asn Ala Leu Leu Val Arg Tyr Thr Lys Lys
          400                      405                      410
gtg ccc caa gtg tcc acc ccc aca ctc gtg gaa gtg tcc aga tct ctg 1296
Val Pro Gln Val Ser Thr Pro Thr Leu Val Glu Val Ser Arg Ser Leu
          415                      420                      425                      430
ggc aaa gtg ggc agc aag tgc tgc acc cac ccc gag gcc gag aga ctg 1344
Gly Lys Val Gly Ser Lys Cys Cys Thr His Pro Glu Ala Glu Arg Leu
          435                      440                      445
tct tgc gcc gag gac tat ctg agc gtg gtg ctg aac cgg ctg tgc gtg 1392
Ser Cys Ala Glu Asp Tyr Leu Ser Val Val Leu Asn Arg Leu Cys Val
          450                      455                      460
ctg cac gag aaa acc ccc gtg tcc gag cgc gtg acc aag tgc tgt acc 1440
Leu His Glu Lys Thr Pro Val Ser Glu Arg Val Thr Lys Cys Cys Thr
          465                      470                      475
gag tct ctc gtg aac aga cgg cct tgc ttc agc gct ctg caa gtg gac 1488
Glu Ser Leu Val Asn Arg Arg Pro Cys Phe Ser Ala Leu Gln Val Asp
          480                      485                      490
gag aca tac gtg ccc aaa gag ttc agc gcc gag aca ttc aca ttc cac 1536
Glu Thr Tyr Val Pro Lys Glu Phe Ser Ala Glu Thr Phe Thr Phe His
          495                      500                      505                      510
gcc gat ctg tgc aca ctg ccc gaa gcc gag aag cag atc aag aaa cag 1584
Ala Asp Leu Cys Thr Leu Pro Glu Ala Glu Lys Gln Ile Lys Lys Gln
          515                      520                      525
tcc gct ctc gtg gaa ctg ctg aag cac aag ccc aag gcc acc gag gaa 1632
Ser Ala Leu Val Glu Leu Leu Lys His Lys Pro Lys Ala Thr Glu Glu
          530                      535                      540
cag ctg aaa acc gtg atg ggc gac ttc ggc agc ttc gtg gat aag tgc 1680
Gln Leu Lys Thr Val Met Gly Asp Phe Gly Ser Phe Val Asp Lys Cys
          545                      550                      555
tgt gcc gct gag gac aaa gag gct tgc ttc gcc gaa gag ggc ccc aaa 1728

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Cys Ala Ala Glu Asp Lys Glu Ala Cys Phe Ala Glu Glu Gly Pro Lys
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 ctc gtg gct gct gct caa gct gct ctg gcc gaattc 1764
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 575 580
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 Gln Cys Pro Phe Glu Asp His Val Lys Leu Val Asn Glu Val Thr Glu
 35 40 45
 Phe Ala Lys Gly Cys Val Ala Asp Gln Ser Ala Ala Asn Cys Glu Lys
 50 55 60
 Ser Leu His Glu Leu Leu Gly Asp Lys Leu Cys Thr Val Ala Ser Leu
 65 70 75 80
 Arg Asp Lys Tyr Gly Glu Met Ala Asp Cys Cys Glu Lys Lys Glu Pro
 85 90 95
 Glu Arg Asn Glu Cys Phe Leu Gln His Lys Asp Asp Asn Pro Gly Phe
 100 105 110
 Gly Gln Leu Val Thr Pro Glu Ala Asp Ala Met Cys Thr Ala Phe His
 115 120 125
 Glu Asn Glu Gln Arg Phe Leu Gly Lys Tyr Leu Tyr Glu Ile Ala Arg
 130 135 140
 Arg His Pro Tyr Phe Tyr Ala Pro Glu Leu Leu Tyr Tyr Ala Glu Glu
 145 150 155 160
 Tyr Lys Gly Val Phe Thr Glu Cys Cys Glu Ala Ala Asp Lys Ala Ala
 165 170 175
 Cys Leu Thr Pro Lys Val Asp Ala Leu Arg Glu Lys Val Leu Ala Ser
 180 185 190
 Ser Ala Lys Glu Arg Leu Lys Cys Ala Ser Leu Gln Lys Phe Gly Glu
 195 200 205
 Arg Ala Phe Lys Ala Trp Ser Val Ala Arg Leu Ser Gln Lys Phe Pro
 210 215 220
 Lys Ala Glu Phe Ala Glu Ile Ser Lys Leu Val Thr Asp Leu Ala Lys

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

Lys Thr Val Met Gly Asp Phe Gly Ser Phe Val Asp Lys Cys Cys Ala
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 Leu Leu Leu Gly Leu Met His Cys Ala Ser Ala Ala Met Phe Met Val
 20 25 30
 aaa aat ggc aac ggg acc gcg tgc ata atg gcc aac ttc tct gct gcc 144
 Lys Asn Gly Asn Gly Thr Ala Cys Ile Met Ala Asn Phe Ser Ala Ala
 35 40 45
 ttc tca gtg aac tac gac acc aag agt ggc cct aag aac atg acc ctt 192
 Phe Ser Val Asn Tyr Asp Thr Lys Ser Gly Pro Lys Asn Met Thr Leu
 50 55 60
 gac ctg cca tca gat gcc aca gtg gtg ctc aac cgc agc tcc tgt gga 240
 Asp Leu Pro Ser Asp Ala Thr Val Val Leu Asn Arg Ser Ser Cys Gly
 65 70 75 80
 aaa gag aac act tct gac ccc agt ctc gtg att gct ttt gga aga gga 288
 Lys Glu Asn Thr Ser Asp Pro Ser Leu Val Ile Ala Phe Gly Arg Gly
 85 90 95
 cat aca ctc act ctc aat ttc acg aga aat gca aca cgt tac agc gtc 336
 His Thr Leu Thr Leu Asn Phe Thr Arg Asn Ala Thr Arg Tyr Ser Val
 100 105 110
 cag ctc atg agt ttt gtt tat aac ttg tca gac aca cac ctt ttc ccc 384
 Gln Leu Met Ser Phe Val Tyr Asn Leu Ser Asp Thr His Leu Phe Pro

115	120	125
aat gcg agc tcc aaa gaa atc aag act gtg gaa tct ata act gac atc 432		
Asn Ala Ser Ser Lys Glu Ile Lys Thr Val Glu Ser Ile Thr Asp Ile		
130	135	140
agg gca gat ata gat aaa aaa tac aga tgt gtt agt ggc acc cag gtc 480		
Arg Ala Asp Ile Asp Lys Lys Tyr Arg Cys Val Ser Gly Thr Gln Val		
145	150	155
cac atg aac aac gtg acc gta acg ctc cat gat gcc acc atc cag gcg 528		
His Met Asn Asn Val Thr Val Thr Leu His Asp Ala Thr Ile Gln Ala		
165	170	175
tac ctt tcc aac agc agc ttc agc cgg gga gag aca cgc tgt gaa caa 576		
Tyr Leu Ser Asn Ser Ser Phe Ser Arg Gly Glu Thr Arg Cys Glu Gln		
180	185	190
gac agg cct tcc cca acc aca gcg ccc cct gcg cca ccc agc ccc tcg 624		
Asp Arg Pro Ser Pro Thr Thr Ala Pro Pro Ala Pro Pro Ser Pro Ser		
195	200	205
ccc tca ccc gtg ccc aag agc ccc tct gtg gac aag tac aac gtg agc 672		
Pro Ser Pro Val Pro Lys Ser Pro Ser Val Asp Lys Tyr Asn Val Ser		
210	215	220
ggc acc aac ggg acc tgc ctg ctg gcc agc atg ggg ctg cag ctg aac 720		
Gly Thr Asn Gly Thr Cys Leu Leu Ala Ser Met Gly Leu Gln Leu Asn		
225	230	235
ctc acc tat gag agg aag gac aac acg acg gtg aca agg ctt ctc aac 768		
Leu Thr Tyr Glu Arg Lys Asp Asn Thr Thr Val Thr Arg Leu Leu Asn		
245	250	255
atc aac ccc aac aag acc tcg gcc agc ggg agc tgc ggc gcc cac ctg 816		
Ile Asn Pro Asn Lys Thr Ser Ala Ser Gly Ser Cys Gly Ala His Leu		
260	265	270
gtg act ctg gag ctg cac agc gag ggc acc acc gtc ctg ctc ttc cag 864		
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Phe Gly Met Asn Ala Ser Ser Ser Arg Phe Phe Leu Gln Gly Ile Gln		
290	295	300
ttg aat aca att ctt cct gac gcc aga gac cct gcc ttt aaa gct gcc 960		
Leu Asn Thr Ile Leu Pro Asp Ala Arg Asp Pro Ala Phe Lys Ala Ala		
305	310	315
aac ggc tcc ctg cga gcg ctg cag gcc aca gtc ggc aat tcc tac aag 1008		
Asn Gly Ser Leu Arg Ala Leu Gln Ala Thr Val Gly Asn Ser Tyr Lys		

325	330	335
tgc aac gcg gag gag cac gtc cgt gtc acg aag gcg ttt tca gtc aat 1056		
Cys Asn Ala Glu Glu His Val Arg Val Thr Lys Ala Phe Ser Val Asn		
340	345	350
ata ttc aaa gtg tgg gtc cag gct ttc aag gtg gaa ggt ggc cag ttt 1104		
Ile Phe Lys Val Trp Val Gln Ala Phe Lys Val Glu Gly Gly Gln Phe		
355	360	365
ggc tct gtg gag gag tgt ctg ctg gac gag aac agc ctc gag gaa gcc 1152		
Gly Ser Val Glu Glu Cys Leu Leu Asp Glu Asn Ser Leu Glu Glu Ala		
370	375	380
cat cag agc gag atc gcc cac cgg ttc aac gat ctg ggc gag gaa cac 1200		
His Gln Ser Glu Ile Ala His Arg Phe Asn Asp Leu Gly Glu Glu His		
385	390	395
ttc cgg gga ctg gtt ctc gtg gcc ttc agc cag tat ctg cag cag tgc 1248		
Phe Arg Gly Leu Val Leu Val Ala Phe Ser Gln Tyr Leu Gln Gln Cys		
405	410	415
ccc ttc gag gac cac gtg aag ctc gtg aac gaa gtg acc gag ttc gcc 1296		
Pro Phe Glu Asp His Val Lys Leu Val Asn Glu Val Thr Glu Phe Ala		
420	425	430
aag ggc tgc gtg gcc gat cag tct gcc gcc aac tgc gag aag tct ctg 1344		
Lys Gly Cys Val Ala Asp Gln Ser Ala Ala Asn Cys Glu Lys Ser Leu		
435	440	445
cac gag ctg ctg ggc gac aag ctg tgt acc gtg gcc tct ctg cgg gat 1392		
His Glu Leu Leu Gly Asp Lys Leu Cys Thr Val Ala Ser Leu Arg Asp		
450	455	460
aag tac ggc gag atg gcc gac tgt tgc gag aag aaa gag ccc gag cgg 1440		
Lys Tyr Gly Glu Met Ala Asp Cys Cys Glu Lys Lys Glu Pro Glu Arg		
465	470	475
aac gag tgc ttt ctg cag cac aag gac gac aac ccc ggc ttc ggc cag 1488		
Asn Glu Cys Phe Leu Gln His Lys Asp Asp Asn Pro Gly Phe Gly Gln		
485	490	495
ctc gtg aca cca gag gcc gat gcc atg tgc acc gcc ttc cac gag aat 1536		
Leu Val Thr Pro Glu Ala Asp Ala Met Cys Thr Ala Phe His Glu Asn		
500	505	510
gag cag cgg ttt ctg ggc aag tat ctg tac gag att gcc aga cgg cac 1584		
Glu Gln Arg Phe Leu Gly Lys Tyr Leu Tyr Glu Ile Ala Arg Arg His		
515	520	525
ccc tac ttc tac gcc cca gag ctg ctg tac tac gcc gaa gag tac aag 1632		
Pro Tyr Phe Tyr Ala Pro Glu Leu Leu Tyr Tyr Ala Glu Glu Tyr Lys		

530	535	540	
ggc gtg ttc acc gag tgc tgc gag gcc gcc gat aag gcc gct tgt ctg	1680		
Gly Val Phe Thr Glu Cys Cys Glu Ala Ala Asp Lys Ala Ala Cys Leu			
545	550	555	560
acc ccc aaa gtg gac gca ctg cgc gag aaa gtg ctg gcc tcc agc gcc	1728		
Thr Pro Lys Val Asp Ala Leu Arg Glu Lys Val Leu Ala Ser Ser Ala			
565	570	575	
aaa gaa cgg ctg aag tgc gct tct ctg cag aag ttc gcc gag cgg gcc	1776		
Lys Glu Arg Leu Lys Cys Ala Ser Leu Gln Lys Phe Gly Glu Arg Ala			
580	585	590	
ttc aag gct tgg agc gtg gca aga ctg agc cag aag ttc ccc aag gcc	1824		
Phe Lys Ala Trp Ser Val Ala Arg Leu Ser Gln Lys Phe Pro Lys Ala			
595	600	605	
gag ttt gcc gag atc agc aag ctc gtg acc gat ctg gcc aag atc cac	1872		
Glu Phe Ala Glu Ile Ser Lys Leu Val Thr Asp Leu Ala Lys Ile His			
610	615	620	
aaa gag tgc tgc cac gcc gat ctg ctg gaa tgc gcc gac gac aga gct	1920		
Lys Glu Cys Cys His Gly Asp Leu Leu Glu Cys Ala Asp Asp Arg Ala			
625	630	635	640
gat ctg gct aag tac atc tgc gag aat caa gac agc atc agc acc aag	1968		
Asp Leu Ala Lys Tyr Ile Cys Glu Asn Gln Asp Ser Ile Ser Thr Lys			
645	650	655	
ctg aaa gag tgt tgc gcc aag ccc gtg ctg gaa aag agc cac tgc atc	2016		
Leu Lys Glu Cys Cys Gly Lys Pro Val Leu Glu Lys Ser His Cys Ile			
660	665	670	
agc gaa gtg gaa cgg gac gag ctg ccc gct gat ctg cct cct ctg gcc	2064		
Ser Glu Val Glu Arg Asp Glu Leu Pro Ala Asp Leu Pro Pro Leu Ala			
675	680	685	
gtg gac ttc gtg gag gac aaa gaa gtg tgc aag aac tac caa gag gcc	2112		
Val Asp Phe Val Glu Asp Lys Glu Val Cys Lys Asn Tyr Gln Glu Ala			
690	695	700	
aag gat gtg ttt ctg ggg aca ttt ctg tat gag tac tct cgg cgg cac	2160		
Lys Asp Val Phe Leu Gly Thr Phe Leu Tyr Glu Tyr Ser Arg Arg His			
705	710	715	720
ccc gag tac tcc gtg tct ctg ctg ctg cgg ctg gcc aaa gag tac gag	2208		
Pro Glu Tyr Ser Val Ser Leu Leu Leu Arg Leu Ala Lys Glu Tyr Glu			
725	730	735	
gcc aca ctg gaa aag tgc tgc gcc acc gac gat ccc ccc gct tgt tat	2256		
Ala Thr Leu Glu Lys Cys Cys Ala Thr Asp Asp Pro Pro Ala Cys Tyr			

740	745	750
gcc cac gtg ttc gac gag ttc aag cca ctc gtg gaa gaa ccc cac aat 2304		
Ala His Val Phe Asp Glu Phe Lys Pro Leu Val Glu Glu Pro His Asn		
755	760	765
ctc gtg aaa aca aac tgc gag ctg ttc gag aag ctg ggc gag tac ggc 2352		
Leu Val Lys Thr Asn Cys Glu Leu Phe Glu Lys Leu Gly Glu Tyr Gly		
770	775	780
ttc cag aac gca ctg ctc gtg cgg tac acc aag aaa gtg ccc caa gtg 2400		
Phe Gln Asn Ala Leu Leu Val Arg Tyr Thr Lys Lys Val Pro Gln Val		
785	790	795
tcc acc ccc aca ctc gtg gaa gtg tcc aga tct ctg ggc aaa gtg ggc 2448		
Ser Thr Pro Thr Leu Val Glu Val Ser Arg Ser Leu Gly Lys Val Gly		
805	810	815
agc aag tgc tgc acc cac ccc gag gcc gag aga ctg tct tgc gcc gag 2496		
Ser Lys Cys Cys Thr His Pro Glu Ala Glu Arg Leu Ser Cys Ala Glu		
820	825	830
gac tat ctg agc gtg gtg ctg aac cgg ctg tgc gtg ctg cac gag aaa 2544		
Asp Tyr Leu Ser Val Val Leu Asn Arg Leu Cys Val Leu His Glu Lys		
835	840	845
acc ccc gtg tcc gag cgc gtg acc aag tgc tgt acc gag tct ctc gtg 2592		
Thr Pro Val Ser Glu Arg Val Thr Lys Cys Cys Thr Glu Ser Leu Val		
850	855	860
aac aga cgg cct tgc ttc agc gct ctg caa gtg gac gag aca tac gtg 2640		
Asn Arg Arg Pro Cys Phe Ser Ala Leu Gln Val Asp Glu Thr Tyr Val		
865	870	875
ccc aaa gag ttc agc gcc gag aca ttc aca ttc cac gcc gat ctg tgc 2688		
Pro Lys Glu Phe Ser Ala Glu Thr Phe Thr Phe His Ala Asp Leu Cys		
885	890	895
aca ctg ccc gaa gcc gag aag cag atc aag aaa cag tcc gct ctc gtg 2736		
Thr Leu Pro Glu Ala Glu Lys Gln Ile Lys Lys Gln Ser Ala Leu Val		
900	905	910
gaa ctg ctg aag cac aag ccc aag gcc acc gag gaa cag ctg aaa acc 2784		
Glu Leu Leu Lys His Lys Pro Lys Ala Thr Glu Glu Gln Leu Lys Thr		
915	920	925
gtg atg ggc gac ttc ggc agc ttc gtg gat aag tgc tgt gcc gct gag 2832		
Val Met Gly Asp Phe Gly Ser Phe Val Asp Lys Cys Cys Ala Ala Glu		
930	935	940
gac aaa gag gct tgc ttc gcc gaa gag ggc ccc aaa ctc gtg gct gct 2880		
Asp Lys Glu Ala Cys Phe Ala Glu Glu Gly Pro Lys Leu Val Ala Ala		

945	950	955	960
gct caa gct gct ctg gcc gaa ttc acg ctg atc ccc atc gct gtg ggt	2928		
Ala Gln Ala Ala Leu Ala Glu Phe Thr Leu Ile Pro Ile Ala Val Gly			
965	970	975	
ggt gcc ctg gcg ggg ctg gtc ctc atc gtc ctc atc gcc tac ctc gtc	2976		
Gly Ala Leu Ala Gly Leu Val Leu Ile Val Leu Ile Ala Tyr Leu Val			
980	985	990	
ggc agg aag agg agt cac gca ggc tac cag act atc tag taa	3018		
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995	1000		
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Lys Asn Gly Asn Gly Thr Ala Cys Ile Met Ala Asn Phe Ser Ala Ala			
35 40 45			
Phe Ser Val Asn Tyr Asp Thr Lys Ser Gly Pro Lys Asn Met Thr Leu			
50 55 60			
Asp Leu Pro Ser Asp Ala Thr Val Val Leu Asn Arg Ser Ser Cys Gly			
65 70 75 80			
Lys Glu Asn Thr Ser Asp Pro Ser Leu Val Ile Ala Phe Gly Arg Gly			
85 90 95			
His Thr Leu Thr Leu Asn Phe Thr Arg Asn Ala Thr Arg Tyr Ser Val			
100 105 110			
Gln Leu Met Ser Phe Val Tyr Asn Leu Ser Asp Thr His Leu Phe Pro			
115 120 125			
Asn Ala Ser Ser Lys Glu Ile Lys Thr Val Glu Ser Ile Thr Asp Ile			
130 135 140			
Arg Ala Asp Ile Asp Lys Lys Tyr Arg Cys Val Ser Gly Thr Gln Val			
145 150 155 160			
His Met Asn Asn Val Thr Val Thr Leu His Asp Ala Thr Ile Gln Ala			
165 170 175			

Tyr	Leu	Ser	Asn	Ser	Ser	Phe	Ser	Arg	Gly	Glu	Thr	Arg	Cys	Glu	Gln	
180						185				190						
Asp	Arg	Pro	Ser	Pro	Thr	Thr	Ala	Pro	Pro	Ala	Pro	Pro	Ser	Pro	Ser	
195						200				205						
Pro	Ser	Pro	Val	Pro	Lys	Ser	Pro	Ser	Val	Asp	Lys	Tyr	Asn	Val	Ser	
210						215				220						
Gly	Thr	Asn	Gly	Thr	Cys	Leu	Leu	Ala	Ser	Met	Gly	Leu	Gln	Leu	Asn	
225						230				235					240	
Leu	Thr	Tyr	Glu	Arg	Lys	Asp	Asn	Thr	Thr	Val	Thr	Arg	Leu	Leu	Asn	
245						250				255						
Ile	Asn	Pro	Asn	Lys	Thr	Ser	Ala	Ser	Gly	Ser	Cys	Gly	Ala	His	Leu	
260						265				270						
Val	Thr	Leu	Glu	Leu	His	Ser	Glu	Gly	Thr	Thr	Val	Leu	Leu	Phe	Gln	
275						280				285						
Phe	Gly	Met	Asn	Ala	Ser	Ser	Ser	Arg	Phe	Phe	Leu	Gln	Gly	Ile	Gln	
290						295				300						
Leu	Asn	Thr	Ile	Leu	Pro	Asp	Ala	Arg	Asp	Pro	Ala	Phe	Lys	Ala	Ala	
305						310				315					320	
Asn	Gly	Ser	Leu	Arg	Ala	Leu	Gln	Ala	Thr	Val	Gly	Asn	Ser	Tyr	Lys	
325						330				335						
Cys	Asn	Ala	Glu	Glu	His	Val	Arg	Val	Thr	Lys	Ala	Phe	Ser	Val	Asn	
340						345				350						
Ile	Phe	Lys	Val	Trp	Val	Gln	Ala	Phe	Lys	Val	Glu	Gly	Gly	Gln	Phe	
355						360				365						
Gly	Ser	Val	Glu	Glu	Cys	Leu	Leu	Asp	Glu	Asn	Ser	Leu	Glu	Glu	Ala	
370						375				380						
His	Gln	Ser	Glu	Ile	Ala	His	Arg	Phe	Asn	Asp	Leu	Gly	Glu	Glu	His	
385						390				395					400	
Phe	Arg	Gly	Leu	Val	Leu	Val	Ala	Phe	Ser	Gln	Tyr	Leu	Gln	Gln	Cys	
405						410				415						
Pro	Phe	Glu	Asp	His	Val	Lys	Leu	Val	Asn	Glu	Val	Thr	Glu	Phe	Ala	
420						425				430						
Lys	Gly	Cys	Val	Ala	Asp	Gln	Ser	Ala	Ala	Asn	Cys	Glu	Lys	Ser	Leu	
435						440				445						
His	Glu	Leu	Leu	Gly	Asp	Lys	Leu	Cys	Thr	Val	Ala	Ser	Leu	Arg	Asp	
450						455				460						
Lys	Tyr	Gly	Glu	Met	Ala	Asp	Cys	Cys	Glu	Lys	Lys	Glu	Pro	Glu	Arg	
465						470				475					480	
Asn	Glu	Cys	Phe	Leu	Gln	His	Lys	Asp	Asp	Asn	Pro	Gly	Phe	Gly	Gln	

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

Ser Thr Pro Thr Leu Val Glu Val Ser Arg Ser Leu Gly Lys Val Gly
 805 810 815
 Ser Lys Cys Cys Thr His Pro Glu Ala Glu Arg Leu Ser Cys Ala Glu
 820 825 830
 Asp Tyr Leu Ser Val Val Leu Asn Arg Leu Cys Val Leu His Glu Lys
 835 840 845
 Thr Pro Val Ser Glu Arg Val Thr Lys Cys Cys Thr Glu Ser Leu Val
 850 855 860
 Asn Arg Arg Pro Cys Phe Ser Ala Leu Gln Val Asp Glu Thr Tyr Val
 865 870 875 880
 Pro Lys Glu Phe Ser Ala Glu Thr Phe Thr Phe His Ala Asp Leu Cys
 885 890 895
 Thr Leu Pro Glu Ala Glu Lys Gln Ile Lys Lys Gln Ser Ala Leu Val
 900 905 910
 Glu Leu Leu Lys His Lys Pro Lys Ala Thr Glu Glu Gln Leu Lys Thr
 915 920 925
 Val Met Gly Asp Phe Gly Ser Phe Val Asp Lys Cys Cys Ala Ala Glu
 930 935 940
 Asp Lys Glu Ala Cys Phe Ala Glu Glu Gly Pro Lys Leu Val Ala Ala
 945 950 955 960
 Ala Gln Ala Ala Leu Ala Glu Phe Thr Leu Ile Pro Ile Ala Val Gly
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 Gly Ala Leu Ala Gly Leu Val Leu Ile Val Leu Ile Ala Tyr Leu Val
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<221> CDS

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aag atc agc ggc gag tgg tac agc att ctg ctg gcc tcc gac gtg aaa 96

Lys Ile Ser Gly Glu Trp Tyr Ser Ile Leu Leu Ala Ser Asp Val Lys

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gag aag atc gaa gaa aac ggc agc atg cgg gtg ttc gtg gaa cac atc	144		
Glu Lys Ile Glu Glu Asn Gly Ser Met Arg Val Phe Val Glu His Ile			
35	40	45	
aag gct ctg gac aac agc tct ctg agc ttc gtg ttc cac acc aaa gaa	192		
Lys Ala Leu Asp Asn Ser Ser Leu Ser Phe Val Phe His Thr Lys Glu			
50	55	60	
aat ggc aag tgc acc gag atc ttt ctc gtg gcc gac aag acc aag gac	240		
Asn Gly Lys Cys Thr Glu Ile Phe Leu Val Ala Asp Lys Thr Lys Asp			
65	70	75	
ggc gtg tac acc gtg gtg tac gac ggc tac aac gtg ttc agc atc gtg	288		
Gly Val Tyr Thr Val Val Tyr Asp Gly Tyr Asn Val Phe Ser Ile Val			
80	85	90	
gaa acc gtg tac gat gag tac att ctg ctg cat ctg ctg aac ttc gac	336		
Glu Thr Val Tyr Asp Glu Tyr Ile Leu Leu His Leu Leu Asn Phe Asp			
95	100	105	110
aag aca cgg ccc ttc caa ctc gtg gag ttc tac gcc aga gaa ccc gac	384		
Lys Thr Arg Pro Phe Gln Leu Val Glu Phe Tyr Ala Arg Glu Pro Asp			
115	120	125	
gtg tcc cag aag ctg aaa gaa aag ttc gtg aag tac tgc caa gag cac	432		
Val Ser Gln Lys Leu Lys Glu Lys Phe Val Lys Tyr Cys Gln Glu His			
130	135	140	
ggc atc gtg aac att ctg gat ctg acc gaa gtg gac cgg tgt ctg caa	480		
Gly Ile Val Asn Ile Leu Asp Leu Thr Glu Val Asp Arg Cys Leu Gln			
145	150	155	
gcc aga ggc agc gaa gtg gcc caa gac agc agc gtg gaa gaattc	525		
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160	165	170	
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<213> 家猫(Felis catus)			
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His Glu Glu Glu Asn Val Val Arg Ser Asn Ile Asp Ile Ser Lys Ile			
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Ser Gly Glu Trp Tyr Ser Ile Leu Leu Ala Ser Asp Val Lys Glu Lys			
20	25	30	
Ile Glu Glu Asn Gly Ser Met Arg Val Phe Val Glu His Ile Lys Ala			
35	40	45	

Leu Asp Asn Ser Ser Leu Ser Phe Val Phe His Thr Lys Glu Asn Gly
 50 55 60
 Lys Cys Thr Glu Ile Phe Leu Val Ala Asp Lys Thr Lys Asp Gly Val
 65 70 75 80
 Tyr Thr Val Val Tyr Asp Gly Tyr Asn Val Phe Ser Ile Val Glu Thr
 85 90 95
 Val Tyr Asp Glu Tyr Ile Leu Leu His Leu Leu Asn Phe Asp Lys Thr
 100 105 110
 Arg Pro Phe Gln Leu Val Glu Phe Tyr Ala Arg Glu Pro Asp Val Ser
 115 120 125
 Gln Lys Leu Lys Glu Lys Phe Val Lys Tyr Cys Gln Glu His Gly Ile
 130 135 140
 Val Asn Ile Leu Asp Leu Thr Glu Val Asp Arg Cys Leu Gln Ala Arg
 145 150 155 160
 Gly Ser Glu Val Ala Gln Asp Ser Ser Val Glu
 165 170

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<212> DNA

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 ctg ctg ctc ggc ctc atg cat tgt gcg tca gca gca atg ttt atg gtg 96
 Leu Leu Leu Gly Leu Met His Cys Ala Ser Ala Ala Met Phe Met Val
 20 25 30
 aaa aat ggc aac ggg acc gcg tgc ata atg gcc aac ttc tct gct gcc 144
 Lys Asn Gly Asn Gly Thr Ala Cys Ile Met Ala Asn Phe Ser Ala Ala
 35 40 45
 ttc tca gtg aac tac gac acc aag agt ggc cct aag aac atg acc ctt 192
 Phe Ser Val Asn Tyr Asp Thr Lys Ser Gly Pro Lys Asn Met Thr Leu
 50 55 60
 gac ctg cca tca gat gcc aca gtg gtg ctc aac cgc agc tcc tgt gga 240

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Asp Leu Pro Ser Asp Ala Thr Val Val Leu Asn Arg Ser Ser Cys Gly
65              70              75              80
aaa gag aac act tct gac ccc agt ctc gtg att gct ttt gga aga gga 288
Lys Glu Asn Thr Ser Asp Pro Ser Leu Val Ile Ala Phe Gly Arg Gly
              85              90              95
cat aca ctc act ctc aat ttc acg aga aat gca aca cgt tac agc gtc 336
His Thr Leu Thr Leu Asn Phe Thr Arg Asn Ala Thr Arg Tyr Ser Val
              100              105              110
cag ctc atg agt ttt gtt tat aac ttg tca gac aca cac ctt ttc ccc 384
Gln Leu Met Ser Phe Val Tyr Asn Leu Ser Asp Thr His Leu Phe Pro
              115              120              125
aat gcg agc tcc aaa gaa atc aag act gtg gaa tct ata act gac atc 432
Asn Ala Ser Ser Lys Glu Ile Lys Thr Val Glu Ser Ile Thr Asp Ile
              130              135              140
agg gca gat ata gat aaa aaa tac aga tgt gtt agt ggc acc cag gtc 480
Arg Ala Asp Ile Asp Lys Lys Tyr Arg Cys Val Ser Gly Thr Gln Val
145              150              155              160
cac atg aac aac gtg acc gta acg ctc cat gat gcc acc atc cag gcg 528
His Met Asn Asn Val Thr Val Thr Leu His Asp Ala Thr Ile Gln Ala
              165              170              175
tac ctt tcc aac agc agc ttc agc cgg gga gag aca cgc tgt gaa caa 576
Tyr Leu Ser Asn Ser Ser Phe Ser Arg Gly Glu Thr Arg Cys Glu Gln
              180              185              190
gac agg cct tcc cca acc aca gcg ccc cct gcg cca ccc agc ccc tcg 624
Asp Arg Pro Ser Pro Thr Thr Ala Pro Pro Ala Pro Pro Ser Pro Ser
              195              200              205
ccc tca ccc gtg ccc aag agc ccc tct gtg gac aag tac aac gtg agc 672
Pro Ser Pro Val Pro Lys Ser Pro Ser Val Asp Lys Tyr Asn Val Ser
              210              215              220
ggc acc aac ggg acc tgc ctg ctg gcc agc atg ggg ctg cag ctg aac 720
Gly Thr Asn Gly Thr Cys Leu Leu Ala Ser Met Gly Leu Gln Leu Asn
225              230              235              240
ctc acc tat gag agg aag gac aac acg acg gtg aca agg ctt ctc aac 768
Leu Thr Tyr Glu Arg Lys Asp Asn Thr Thr Val Thr Arg Leu Leu Asn
              245              250              255
atc aac ccc aac aag acc tcg gcc agc ggg agc tgc ggc gcc cac ctg 816
Ile Asn Pro Asn Lys Thr Ser Ala Ser Gly Ser Cys Gly Ala His Leu
              260              265              270
gtg act ctg gag ctg cac agc gag ggc acc acc gtc ctg ctc ttc cag 864

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Val Thr Leu Glu Leu His Ser Glu Gly Thr Thr Val Leu Leu Phe Gln		
275	280	285
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Phe Gly Met Asn Ala Ser Ser Ser Arg Phe Phe Leu Gln Gly Ile Gln		
290	295	300
ttg aat aca att ctt cct gac gcc aga gac cct gcc ttt aaa gct gcc	960	
Leu Asn Thr Ile Leu Pro Asp Ala Arg Asp Pro Ala Phe Lys Ala Ala		
305	310	315
aac ggc tcc ctg cga gcg ctg cag gcc aca gtc ggc aat tcc tac aag	1008	
Asn Gly Ser Leu Arg Ala Leu Gln Ala Thr Val Gly Asn Ser Tyr Lys		
325	330	335
tgc aac gcg gag gag cac gtc cgt gtc acg aag gcg ttt tca gtc aat	1056	
Cys Asn Ala Glu Glu His Val Arg Val Thr Lys Ala Phe Ser Val Asn		
340	345	350
ata ttc aaa gtg tgg gtc cag gct ttc aag gtg gaa ggt ggc cag ttt	1104	
Ile Phe Lys Val Trp Val Gln Ala Phe Lys Val Glu Gly Gly Gln Phe		
355	360	365
ggc tct gtg gag gag tgt ctg ctg gac gag aac agc ctc gag cac gag	1152	
Gly Ser Val Glu Glu Cys Leu Leu Asp Glu Asn Ser Leu Glu His Glu		
370	375	380
gaa gag aac gtc gtg cgg agc aac atc gac atc agc aag atc agc ggc	1200	
Glu Glu Asn Val Val Arg Ser Asn Ile Asp Ile Ser Lys Ile Ser Gly		
385	390	395
gag tgg tac agc att ctg ctg gcc tcc gac gtg aaa gag aag atc gaa	1248	
Glu Trp Tyr Ser Ile Leu Leu Ala Ser Asp Val Lys Glu Lys Ile Glu		
405	410	415
gaa aac ggc agc atg cgg gtg ttc gtg gaa cac atc aag gct ctg gac	1296	
Glu Asn Gly Ser Met Arg Val Phe Val Glu His Ile Lys Ala Leu Asp		
420	425	430
aac agc tct ctg agc ttc gtg ttc cac acc aaa gaa aat ggc aag tgc	1344	
Asn Ser Ser Leu Ser Phe Val Phe His Thr Lys Glu Asn Gly Lys Cys		
435	440	445
acc gag atc ttt ctc gtg gcc gac aag acc aag gac ggc gtg tac acc	1392	
Thr Glu Ile Phe Leu Val Ala Asp Lys Thr Lys Asp Gly Val Tyr Thr		
450	455	460
gtg gtg tac gac ggc tac aac gtg ttc agc atc gtg gaa acc gtg tac	1440	
Val Val Tyr Asp Gly Tyr Asn Val Phe Ser Ile Val Glu Thr Val Tyr		
465	470	475
gat gag tac att ctg ctg cat ctg ctg aac ttc gac aag aca cgg ccc	1488	

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Asp Glu Tyr Ile Leu Leu His Leu Leu Asn Phe Asp Lys Thr Arg Pro
      485                      490                      495
ttc caa ctc gtg gag ttc tac gcc aga gaa ccc gac gtg tcc cag aag 1536
Phe Gln Leu Val Glu Phe Tyr Ala Arg Glu Pro Asp Val Ser Gln Lys
      500                      505                      510
ctg aaa gaa aag ttc gtg aag tac tgc caa gag cac ggc atc gtg aac 1584
Leu Lys Glu Lys Phe Val Lys Tyr Cys Gln Glu His Gly Ile Val Asn
      515                      520                      525
att ctg gat ctg acc gaa gtg gac cgg tgt ctg caa gcc aga ggc agc 1632
Ile Leu Asp Leu Thr Glu Val Asp Arg Cys Leu Gln Ala Arg Gly Ser
      530                      535                      540
gaa gtg gcc caa gac agc agc gtg gaa gaa ttc acg ctg atc ccc atc 1680
Glu Val Ala Gln Asp Ser Ser Val Glu Glu Phe Thr Leu Ile Pro Ile
      545                      550                      555                      560
gct gtg ggt ggt gcc ctg gcg ggg ctg gtc ctc atc gtc ctc atc gcc 1728
Ala Val Gly Gly Ala Leu Ala Gly Leu Val Leu Ile Val Leu Ile Ala
      565                      570                      575
tac ctc gtc ggc agg aag agg agt cac gca ggc tac cag act atc tag 1776
Tyr Leu Val Gly Arg Lys Arg Ser His Ala Gly Tyr Gln Thr Ile
      580                      585                      590
taa 1779
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Leu Leu Leu Gly Leu Met His Cys Ala Ser Ala Ala Met Phe Met Val
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Lys Asn Gly Asn Gly Thr Ala Cys Ile Met Ala Asn Phe Ser Ala Ala
      35          40          45
Phe Ser Val Asn Tyr Asp Thr Lys Ser Gly Pro Lys Asn Met Thr Leu
      50          55          60
Asp Leu Pro Ser Asp Ala Thr Val Val Leu Asn Arg Ser Ser Cys Gly
65          70          75          80
Lys Glu Asn Thr Ser Asp Pro Ser Leu Val Ile Ala Phe Gly Arg Gly

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

Glu Trp Tyr Ser Ile Leu Leu Ala Ser Asp Val Lys Glu Lys Ile Glu
 405 410 415
 Glu Asn Gly Ser Met Arg Val Phe Val Glu His Ile Lys Ala Leu Asp
 420 425 430
 Asn Ser Ser Leu Ser Phe Val Phe His Thr Lys Glu Asn Gly Lys Cys
 435 440 445
 Thr Glu Ile Phe Leu Val Ala Asp Lys Thr Lys Asp Gly Val Tyr Thr
 450 455 460
 Val Val Tyr Asp Gly Tyr Asn Val Phe Ser Ile Val Glu Thr Val Tyr
 465 470 475 480
 Asp Glu Tyr Ile Leu Leu His Leu Leu Asn Phe Asp Lys Thr Arg Pro
 485 490 495
 Phe Gln Leu Val Glu Phe Tyr Ala Arg Glu Pro Asp Val Ser Gln Lys
 500 505 510
 Leu Lys Glu Lys Phe Val Lys Tyr Cys Gln Glu His Gly Ile Val Asn
 515 520 525
 Ile Leu Asp Leu Thr Glu Val Asp Arg Cys Leu Gln Ala Arg Gly Ser
 530 535 540
 Glu Val Ala Gln Asp Ser Ser Val Glu Glu Phe Thr Leu Ile Pro Ile
 545 550 555 560
 Ala Val Gly Gly Ala Leu Ala Gly Leu Val Leu Ile Val Leu Ile Ala
 565 570 575
 Tyr Leu Val Gly Arg Lys Arg Ser His Ala Gly Tyr Gln Thr Ile
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<211> 864

<212> DNA

<213> 凡纳滨对虾(Litopenaeus vannamei)

<220>

<221> CDS

<222> (7) .. (858)

<400> 77

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Met Asp Ala Ile Lys Lys Lys Met Gln Ala Met Lys Leu Glu

1

5

10

aag gac aac gcc atg gac cgg gcc gac aca ctg gaa cag cag aac aaa 96

Lys Asp Asn Ala Met Asp Arg Ala Asp Thr Leu Glu Gln Gln Asn Lys

15

20

25

30

gag gcc aac aat cgg gcc gag aag tcc gag gaa gaa gtg cac aat ctg 144

Glu Ala Asn Asn Arg Ala Glu Lys Ser Glu Glu Glu Val His Asn Leu
 35 40 45
 cag aaa cgg atg cag cag ctg gaa aac gat ctg gac caa gtg caa gag 192
 Gln Lys Arg Met Gln Gln Leu Glu Asn Asp Leu Asp Gln Val Gln Glu
 50 55 60
 tct ctg ctg aag gcc aac atc caa ctc gtg gaa aag gat aag gct ctg 240
 Ser Leu Leu Lys Ala Asn Ile Gln Leu Val Glu Lys Asp Lys Ala Leu
 65 70 75
 agc aac gcc gag ggc gaa gtg gcc gct ctg aac aga cgg att cag ctg 288
 Ser Asn Ala Glu Gly Glu Val Ala Ala Leu Asn Arg Arg Ile Gln Leu
 80 85 90
 ctg gaa gag gat ctg gaa aga agc gag gaa cgg ctg aac acc gcc aca 336
 Leu Glu Glu Asp Leu Glu Arg Ser Glu Glu Arg Leu Asn Thr Ala Thr
 95 100 105 110
 aca aag ctg gcc gaa gcc agc caa gcc gcc gac gag agc gag cgg atg 384
 Thr Lys Leu Ala Glu Ala Ser Gln Ala Ala Asp Glu Ser Glu Arg Met
 115 120 125
 cgg aaa gtg ctg gaa aac cgc tct ctg agc gac gag gaa aga atg gac 432
 Arg Lys Val Leu Glu Asn Arg Ser Leu Ser Asp Glu Glu Arg Met Asp
 130 135 140
 gct ctg gaa aat cag ctg aaa gag gcc cgg ttt ctg gcc gag gaa gcc 480
 Ala Leu Glu Asn Gln Leu Lys Glu Ala Arg Phe Leu Ala Glu Glu Ala
 145 150 155
 gac cgg aag tac gat gaa gtg gcc cgg aag ctg gcc atg gtc gag gct 528
 Asp Arg Lys Tyr Asp Glu Val Ala Arg Lys Leu Ala Met Val Glu Ala
 160 165 170
 gat ctg gaa cgg gcc gaa gag aga gcc gaa acc ggc gag agc aag atc 576
 Asp Leu Glu Arg Ala Glu Glu Arg Ala Glu Thr Gly Glu Ser Lys Ile
 175 180 185 190
 gtg gaa ctg gaa gag gaa ctg cgg gtc gtg ggc aac aat ctg aag tct 624
 Val Glu Leu Glu Glu Glu Leu Arg Val Val Gly Asn Asn Leu Lys Ser
 195 200 205
 ctg gaa gtg tcc gaa gag aag gcc aat cag aga gag gaa gcc tac aaa 672
 Leu Glu Val Ser Glu Glu Lys Ala Asn Gln Arg Glu Glu Ala Tyr Lys
 210 215 220
 gag cag atc aag aca ctg acc aac aag ctg aag gct gcc gag gcc aga 720
 Glu Gln Ile Lys Thr Leu Thr Asn Lys Leu Lys Ala Ala Glu Ala Arg
 225 230 235
 gcc gag ttc gcc gag aga agc gtg cag aaa ctg cag aaa gaa gtg gac 768

Ala Glu Phe Ala Glu Arg Ser Val Gln Lys Leu Gln Lys Glu Val Asp
 240 245 250
 cgg ctg gaa gat gag ctc gtg aac gag aaa gag aag tac aag agc atc 816
 Arg Leu Glu Asp Glu Leu Val Asn Glu Lys Glu Lys Tyr Lys Ser Ile
 255 260 265 270
 acc gac gag ctg gac cag aca ttc agc gag ctg agc ggc tac gaattc 864
 Thr Asp Glu Leu Asp Gln Thr Phe Ser Glu Leu Ser Gly Tyr
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 35 40 45
 Arg Met Gln Gln Leu Glu Asn Asp Leu Asp Gln Val Gln Glu Ser Leu
 50 55 60
 Leu Lys Ala Asn Ile Gln Leu Val Glu Lys Asp Lys Ala Leu Ser Asn
 65 70 75 80
 Ala Glu Gly Glu Val Ala Ala Leu Asn Arg Arg Ile Gln Leu Leu Glu
 85 90 95
 Glu Asp Leu Glu Arg Ser Glu Glu Arg Leu Asn Thr Ala Thr Thr Lys
 100 105 110
 Leu Ala Glu Ala Ser Gln Ala Ala Asp Glu Ser Glu Arg Met Arg Lys
 115 120 125
 Val Leu Glu Asn Arg Ser Leu Ser Asp Glu Glu Arg Met Asp Ala Leu
 130 135 140
 Glu Asn Gln Leu Lys Glu Ala Arg Phe Leu Ala Glu Glu Ala Asp Arg
 145 150 155 160
 Lys Tyr Asp Glu Val Ala Arg Lys Leu Ala Met Val Glu Ala Asp Leu
 165 170 175
 Glu Arg Ala Glu Glu Arg Ala Glu Thr Gly Glu Ser Lys Ile Val Glu
 180 185 190
 Leu Glu Glu Glu Leu Arg Val Val Gly Asn Asn Leu Lys Ser Leu Glu
 195 200 205

Val Ser Glu Glu Lys Ala Asn Gln Arg Glu Glu Ala Tyr Lys Glu Gln
210 215 220
Ile Lys Thr Leu Thr Asn Lys Leu Lys Ala Ala Glu Ala Arg Ala Glu
225 230 235 240
Phe Ala Glu Arg Ser Val Gln Lys Leu Gln Lys Glu Val Asp Arg Leu
245 250 255
Glu Asp Glu Leu Val Asn Glu Lys Glu Lys Tyr Lys Ser Ile Thr Asp
260 265 270
Glu Leu Asp Gln Thr Phe Ser Glu Leu Ser Gly Tyr
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<210> 79

<211> 2118

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<222> (1) .. (2118)

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ctg ctg ctc ggc ctc atg cat tgt gcg tca gca gca atg ttt atg gtg 96
Leu Leu Leu Gly Leu Met His Cys Ala Ser Ala Ala Met Phe Met Val
20 25 30
aaa aat ggc aac ggg acc gcg tgc ata atg gcc aac ttc tct gct gcc 144
Lys Asn Gly Asn Gly Thr Ala Cys Ile Met Ala Asn Phe Ser Ala Ala
35 40 45
ttc tca gtg aac tac gac acc aag agt ggc cct aag aac atg acc ctt 192
Phe Ser Val Asn Tyr Asp Thr Lys Ser Gly Pro Lys Asn Met Thr Leu
50 55 60
gac ctg cca tca gat gcc aca gtg gtg ctc aac cgc agc tcc tgt gga 240
Asp Leu Pro Ser Asp Ala Thr Val Val Leu Asn Arg Ser Ser Cys Gly
65 70 75 80
aaa gag aac act tct gac ccc agt ctc gtg att gct ttt gga aga gga 288
Lys Glu Asn Thr Ser Asp Pro Ser Leu Val Ile Ala Phe Gly Arg Gly
85 90 95
cat aca ctc act ctc aat ttc acg aga aat gca aca cgt tac agc gtc 336

His Thr Leu Thr Leu Asn Phe Thr Arg Asn Ala Thr Arg Tyr Ser Val		
100	105	110
cag ctc atg agt ttt gtt tat aac ttg tca gac aca cac ctt ttc ccc	384	
Gln Leu Met Ser Phe Val Tyr Asn Leu Ser Asp Thr His Leu Phe Pro		
115	120	125
aat gcg agc tcc aaa gaa atc aag act gtg gaa tct ata act gac atc	432	
Asn Ala Ser Ser Lys Glu Ile Lys Thr Val Glu Ser Ile Thr Asp Ile		
130	135	140
agg gca gat ata gat aaa aaa tac aga tgt gtt agt ggc acc cag gtc	480	
Arg Ala Asp Ile Asp Lys Lys Tyr Arg Cys Val Ser Gly Thr Gln Val		
145	150	155
cac atg aac aac gtg acc gta acg ctc cat gat gcc acc atc cag gcg	528	
His Met Asn Asn Val Thr Val Thr Leu His Asp Ala Thr Ile Gln Ala		
165	170	175
tac ctt tcc aac agc agc ttc agc cgg gga gag aca cgc tgt gaa caa	576	
Tyr Leu Ser Asn Ser Ser Phe Ser Arg Gly Glu Thr Arg Cys Glu Gln		
180	185	190
gac agg cct tcc cca acc aca gcg ccc cct gcg cca ccc agc ccc tcg	624	
Asp Arg Pro Ser Pro Thr Thr Ala Pro Pro Ala Pro Pro Ser Pro Ser		
195	200	205
ccc tca ccc gtg ccc aag agc ccc tct gtg gac aag tac aac gtg agc	672	
Pro Ser Pro Val Pro Lys Ser Pro Ser Val Asp Lys Tyr Asn Val Ser		
210	215	220
ggc acc aac ggg acc tgc ctg ctg gcc agc atg ggg ctg cag ctg aac	720	
Gly Thr Asn Gly Thr Cys Leu Leu Ala Ser Met Gly Leu Gln Leu Asn		
225	230	235
ctc acc tat gag agg aag gac aac acg acg gtg aca agg ctt ctc aac	768	
Leu Thr Tyr Glu Arg Lys Asp Asn Thr Thr Val Thr Arg Leu Leu Asn		
245	250	255
atc aac ccc aac aag acc tcg gcc agc ggg agc tgc ggc gcc cac ctg	816	
Ile Asn Pro Asn Lys Thr Ser Ala Ser Gly Ser Cys Gly Ala His Leu		
260	265	270
gtg act ctg gag ctg cac agc gag ggc acc acc gtc ctg ctc ttc cag	864	
Val Thr Leu Glu Leu His Ser Glu Gly Thr Thr Val Leu Leu Phe Gln		
275	280	285
ttc ggg atg aat gca agt tct agc cgg ttt ttc cta caa gga atc cag	912	
Phe Gly Met Asn Ala Ser Ser Ser Arg Phe Phe Leu Gln Gly Ile Gln		
290	295	300
ttg aat aca att ctt cct gac gcc aga gac cct gcc ttt aaa gct gcc	960	

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Leu Asn Thr Ile Leu Pro Asp Ala Arg Asp Pro Ala Phe Lys Ala Ala
305                310                315                320
aac ggc tcc ctg cga gcg ctg cag gcc aca gtc ggc aat tcc tac aag 1008
Asn Gly Ser Leu Arg Ala Leu Gln Ala Thr Val Gly Asn Ser Tyr Lys
                325                330                335
tgc aac gcg gag gag cac gtc cgt gtc acg aag gcg ttt tca gtc aat 1056
Cys Asn Ala Glu Glu His Val Arg Val Thr Lys Ala Phe Ser Val Asn
                340                345                350
ata ttc aaa gtg tgg gtc cag gct ttc aag gtg gaa ggt ggc cag ttt 1104
Ile Phe Lys Val Trp Val Gln Ala Phe Lys Val Glu Gly Gly Gln Phe
                355                360                365
ggc tct gtg gag gag tgt ctg ctg gac gag aac agc ctc gag atg gac 1152
Gly Ser Val Glu Glu Cys Leu Leu Asp Glu Asn Ser Leu Glu Met Asp
                370                375                380
gcc atc aag aag aaa atg caa gcc atg aag ctg gaa aag gac aac gcc 1200
Ala Ile Lys Lys Lys Met Gln Ala Met Lys Leu Glu Lys Asp Asn Ala
385                390                395                400
atg gac cgg gcc gac aca ctg gaa cag cag aac aaa gag gcc aac aat 1248
Met Asp Arg Ala Asp Thr Leu Glu Gln Gln Asn Lys Glu Ala Asn Asn
                405                410                415
cgg gcc gag aag tcc gag gaa gaa gtg cac aat ctg cag aaa cgg atg 1296
Arg Ala Glu Lys Ser Glu Glu Glu Val His Asn Leu Gln Lys Arg Met
                420                425                430
cag cag ctg gaa aac gat ctg gac caa gtg caa gag tct ctg ctg aag 1344
Gln Gln Leu Glu Asn Asp Leu Asp Gln Val Gln Glu Ser Leu Leu Lys
                435                440                445
gcc aac atc caa ctc gtg gaa aag gat aag gct ctg agc aac gcc gag 1392
Ala Asn Ile Gln Leu Val Glu Lys Asp Lys Ala Leu Ser Asn Ala Glu
                450                455                460
ggc gaa gtg gcc gct ctg aac aga cgg att cag ctg ctg gaa gag gat 1440
Gly Glu Val Ala Ala Leu Asn Arg Arg Ile Gln Leu Leu Glu Glu Asp
465                470                475                480
ctg gaa aga agc gag gaa cgg ctg aac acc gcc aca aca aag ctg gcc 1488
Leu Glu Arg Ser Glu Glu Arg Leu Asn Thr Ala Thr Thr Lys Leu Ala
                485                490                495
gaa gcc agc caa gcc gcc gac gag agc gag cgg atg cgg aaa gtg ctg 1536
Glu Ala Ser Gln Ala Ala Asp Glu Ser Glu Arg Met Arg Lys Val Leu
                500                505                510
gaa aac cgc tct ctg agc gac gag gaa aga atg gac gct ctg gaa aat 1584

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Glu Asn Arg Ser Leu Ser Asp Glu Glu Arg Met Asp Ala Leu Glu Asn
 515 520 525
 cag ctg aaa gag gcc cgg ttt ctg gcc gag gaa gcc gac cgg aag tac 1632
 Gln Leu Lys Glu Ala Arg Phe Leu Ala Glu Glu Ala Asp Arg Lys Tyr
 530 535 540
 gat gaa gtg gcc cgg aag ctg gcc atg gtc gag gct gat ctg gaa cgg 1680
 Asp Glu Val Ala Arg Lys Leu Ala Met Val Glu Ala Asp Leu Glu Arg
 545 550 555 560
 gcc gaa gag aga gcc gaa acc ggc gag agc aag atc gtg gaa ctg gaa 1728
 Ala Glu Glu Arg Ala Glu Thr Gly Glu Ser Lys Ile Val Glu Leu Glu
 565 570 575
 gag gaa ctg cgg gtc gtg ggc aac aat ctg aag tct ctg gaa gtg tcc 1776
 Glu Glu Leu Arg Val Val Gly Asn Asn Leu Lys Ser Leu Glu Val Ser
 580 585 590
 gaa gag aag gcc aat cag aga gag gaa gcc tac aaa gag cag atc aag 1824
 Glu Glu Lys Ala Asn Gln Arg Glu Glu Ala Tyr Lys Glu Gln Ile Lys
 595 600 605
 aca ctg acc aac aag ctg aag gct gcc gag gcc aga gcc gag ttc gcc 1872
 Thr Leu Thr Asn Lys Leu Lys Ala Ala Glu Ala Arg Ala Glu Phe Ala
 610 615 620
 gag aga agc gtg cag aaa ctg cag aaa gaa gtg gac cgg ctg gaa gat 1920
 Glu Arg Ser Val Gln Lys Leu Gln Lys Glu Val Asp Arg Leu Glu Asp
 625 630 635 640
 gag ctc gtg aac gag aaa gag aag tac aag agc atc acc gac gag ctg 1968
 Glu Leu Val Asn Glu Lys Glu Lys Tyr Lys Ser Ile Thr Asp Glu Leu
 645 650 655
 gac cag aca ttc agc gag ctg agc ggc tac gaa ttc acg ctg atc ccc 2016
 Asp Gln Thr Phe Ser Glu Leu Ser Gly Tyr Glu Phe Thr Leu Ile Pro
 660 665 670
 atc gct gtg ggt ggt gcc ctg gcg ggg ctg gtc ctc atc gtc ctc atc 2064
 Ile Ala Val Gly Gly Ala Leu Ala Gly Leu Val Leu Ile Val Leu Ile
 675 680 685
 gcc tac ctc gtc ggc agg aag agg agt cac gca ggc tac cag act atc 2112
 Ala Tyr Leu Val Gly Arg Lys Arg Ser His Ala Gly Tyr Gln Thr Ile
 690 695 700
 tag taa 2118
 <210> 80
 <211> 704
 <212> PRT

<213> 人工序列

<220>

<223> 合成构建物

<400> 80

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

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275	280	285
Phe Gly Met Asn Ala Ser Ser Ser Arg Phe Phe Leu Gln Gly Ile Gln		
290	295	300
Leu Asn Thr Ile Leu Pro Asp Ala Arg Asp Pro Ala Phe Lys Ala Ala		
305	310	315
Asn Gly Ser Leu Arg Ala Leu Gln Ala Thr Val Gly Asn Ser Tyr Lys		
325	330	335
Cys Asn Ala Glu Glu His Val Arg Val Thr Lys Ala Phe Ser Val Asn		
340	345	350
Ile Phe Lys Val Trp Val Gln Ala Phe Lys Val Glu Gly Gly Gln Phe		
355	360	365
Gly Ser Val Glu Glu Cys Leu Leu Asp Glu Asn Ser Leu Glu Met Asp		
370	375	380
Ala Ile Lys Lys Lys Met Gln Ala Met Lys Leu Glu Lys Asp Asn Ala		
385	390	395
Met Asp Arg Ala Asp Thr Leu Glu Gln Gln Asn Lys Glu Ala Asn Asn		
405	410	415
Arg Ala Glu Lys Ser Glu Glu Glu Val His Asn Leu Gln Lys Arg Met		
420	425	430
Gln Gln Leu Glu Asn Asp Leu Asp Gln Val Gln Glu Ser Leu Leu Lys		
435	440	445
Ala Asn Ile Gln Leu Val Glu Lys Asp Lys Ala Leu Ser Asn Ala Glu		
450	455	460
Gly Glu Val Ala Ala Leu Asn Arg Arg Ile Gln Leu Leu Glu Glu Asp		
465	470	475
Leu Glu Arg Ser Glu Glu Arg Leu Asn Thr Ala Thr Thr Lys Leu Ala		
485	490	495
Glu Ala Ser Gln Ala Ala Asp Glu Ser Glu Arg Met Arg Lys Val Leu		
500	505	510
Glu Asn Arg Ser Leu Ser Asp Glu Glu Arg Met Asp Ala Leu Glu Asn		
515	520	525
Gln Leu Lys Glu Ala Arg Phe Leu Ala Glu Glu Ala Asp Arg Lys Tyr		
530	535	540
Asp Glu Val Ala Arg Lys Leu Ala Met Val Glu Ala Asp Leu Glu Arg		
545	550	555
Ala Glu Glu Arg Ala Glu Thr Gly Glu Ser Lys Ile Val Glu Leu Glu		
565	570	575
Glu Glu Leu Arg Val Val Gly Asn Asn Leu Lys Ser Leu Glu Val Ser		
580	585	590

Glu Glu Lys Ala Asn Gln Arg Glu Glu Ala Tyr Lys Glu Gln Ile Lys
 595 600 605
 Thr Leu Thr Asn Lys Leu Lys Ala Ala Glu Ala Arg Ala Glu Phe Ala
 610 615 620
 Glu Arg Ser Val Gln Lys Leu Gln Lys Glu Val Asp Arg Leu Glu Asp
 625 630 635 640
 Glu Leu Val Asn Glu Lys Glu Lys Tyr Lys Ser Ile Thr Asp Glu Leu
 645 650 655
 Asp Gln Thr Phe Ser Glu Leu Ser Gly Tyr Glu Phe Thr Leu Ile Pro
 660 665 670
 Ile Ala Val Gly Gly Ala Leu Ala Gly Leu Val Leu Ile Val Leu Ile
 675 680 685
 Ala Tyr Leu Val Gly Arg Lys Arg Ser His Ala Gly Tyr Gln Thr Ile
 690 695 700

<210> 81

<211> 753

<212> DNA

<213> 黑麦草(Lolium perenne)

<220>

<221> CDS

<222> (7) .. (747)

<400> 81

ctcgag gcc gat gcc ggc tac aca cca gcc gct gct gct aca cca gcc 48
 Ala Asp Ala Gly Tyr Thr Pro Ala Ala Ala Ala Thr Pro Ala
 1 5 10
 act cca gca gca aca cca gca gcc gct ggc ggc aag gcc aca acc gat 96
 Thr Pro Ala Ala Thr Pro Ala Ala Ala Gly Gly Lys Ala Thr Thr Asp
 15 20 25 30
 gag cag aaa ctg ctg gaa gat gtg aac gcc ggc ttc aag gcc gcc gtg 144
 Glu Gln Lys Leu Leu Glu Asp Val Asn Ala Gly Phe Lys Ala Ala Val
 35 40 45
 gct gct gct gca aat gcc cct ccc gcc gac aag ttc aag atc ttc gag 192
 Ala Ala Ala Ala Asn Ala Pro Pro Ala Asp Lys Phe Lys Ile Phe Glu
 50 55 60
 gcc gcc ttc agc gag agc agc aag gga ctg ctg gcc aca tct gcc gcc 240
 Ala Ala Phe Ser Glu Ser Ser Lys Gly Leu Leu Ala Thr Ser Ala Ala
 65 70 75
 aaa gcc ccc gga ctg atc ccc aag ctg gac acc gcc tac gac gtg gcc 288
 Lys Ala Pro Gly Leu Ile Pro Lys Leu Asp Thr Ala Tyr Asp Val Ala

80	85	90	
tac aaa gcc gcc gag gcc acc cca gag gcc aaa tac gat gcc ttc gtg			336
Tyr Lys Ala Ala Glu Ala Thr Pro Glu Ala Lys Tyr Asp Ala Phe Val			
95	100	105	110
acc gct ctg acc gag gct ctg aga gtg att gcc ggc gct ctg gaa gtg			384
Thr Ala Leu Thr Glu Ala Leu Arg Val Ile Ala Gly Ala Leu Glu Val			
	115	120	125
cac gcc gtg aag cca gcc acc gaa gaa gtg ctg gcc gcc aag att cct			432
His Ala Val Lys Pro Ala Thr Glu Glu Val Leu Ala Ala Lys Ile Pro			
	130	135	140
acc ggc gag ctg cag atc gtg gac aag atc gac gcc gcc ttt aag atc			480
Thr Gly Glu Leu Gln Ile Val Asp Lys Ile Asp Ala Ala Phe Lys Ile			
	145	150	155
gcc gcc acc gcc gca aat gcc gcc cct acc aac gat aag ttc acc gtg			528
Ala Ala Thr Ala Ala Asn Ala Ala Pro Thr Asn Asp Lys Phe Thr Val			
	160	165	170
ttc gag agc gcc ttc aac aag gct ctg aac gag tgc acc ggc gga gcc			576
Phe Glu Ser Ala Phe Asn Lys Ala Leu Asn Glu Cys Thr Gly Gly Ala			
175	180	185	190
tac gag aca tac aag ttc atc cca tct ctg gaa gcc gct gtg aag caa			624
Tyr Glu Thr Tyr Lys Phe Ile Pro Ser Leu Glu Ala Ala Val Lys Gln			
	195	200	205
gcc tac gcc gcc aca gtg gcc gct gcc ccc gaa gtg aag tac gcc gtg			672
Ala Tyr Ala Ala Thr Val Ala Ala Ala Pro Glu Val Lys Tyr Ala Val			
	210	215	220
ttt gag gcc gca ctg acc aag gcc atc acc gcc atg aca caa gcc cag			720
Phe Glu Ala Ala Leu Thr Lys Ala Ile Thr Ala Met Thr Gln Ala Gln			
	225	230	235
aag gcc ggc aaa cca gct gct gca gct gaattc			753
Lys Ala Gly Lys Pro Ala Ala Ala Ala			
	240	245	
<210> 82			
<211> 247			
<212> PRT			
<213> 黑麦草(Lolium perenne)			
<400> 82			
Ala Asp Ala Gly Tyr Thr Pro Ala Ala Ala Ala Thr Pro Ala Thr Pro			
1	5	10	15
Ala Ala Thr Pro Ala Ala Ala Gly Gly Lys Ala Thr Thr Asp Glu Gln			

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

<210> 83

<211> 2007

<212> DNA

<213> 人工序列

<220>

<223> 合成构建物

<220>

<221> CDS

<222> (1) .. (2007)

<400> 83

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Met Ala Pro Arg Ser Ala Arg Arg Pro Leu Leu Leu Leu Leu Leu
1           5           10           15
ctg ctg ctc ggc ctc atg cat tgt gcg tca gca gca atg ttt atg gtg 96
Leu Leu Leu Gly Leu Met His Cys Ala Ser Ala Ala Met Phe Met Val
20           25           30
aaa aat ggc aac ggg acc gcg tgc ata atg gcc aac ttc tct gct gcc 144
Lys Asn Gly Asn Gly Thr Ala Cys Ile Met Ala Asn Phe Ser Ala Ala
35           40           45
ttc tca gtg aac tac gac acc aag agt ggc cct aag aac atg acc ctt 192
Phe Ser Val Asn Tyr Asp Thr Lys Ser Gly Pro Lys Asn Met Thr Leu
50           55           60
gac ctg cca tca gat gcc aca gtg gtg ctc aac cgc agc tcc tgt gga 240
Asp Leu Pro Ser Asp Ala Thr Val Val Leu Asn Arg Ser Ser Cys Gly
65           70           75           80
aaa gag aac act tct gac ccc agt ctc gtg att gct ttt gga aga gga 288
Lys Glu Asn Thr Ser Asp Pro Ser Leu Val Ile Ala Phe Gly Arg Gly
85           90           95
cat aca ctc act ctc aat ttc acg aga aat gca aca cgt tac agc gtc 336
His Thr Leu Thr Leu Asn Phe Thr Arg Asn Ala Thr Arg Tyr Ser Val
100          105          110
cag ctc atg agt ttt gtt tat aac ttg tca gac aca cac ctt ttc ccc 384
Gln Leu Met Ser Phe Val Tyr Asn Leu Ser Asp Thr His Leu Phe Pro
115          120          125
aat gcg agc tcc aaa gaa atc aag act gtg gaa tct ata act gac atc 432
Asn Ala Ser Ser Lys Glu Ile Lys Thr Val Glu Ser Ile Thr Asp Ile
130          135          140
agg gca gat ata gat aaa aaa tac aga tgt gtt agt ggc acc cag gtc 480
Arg Ala Asp Ile Asp Lys Lys Tyr Arg Cys Val Ser Gly Thr Gln Val
145          150          155          160
cac atg aac aac gtg acc gta acg ctc cat gat gcc acc atc cag gcg 528
His Met Asn Asn Val Thr Val Thr Leu His Asp Ala Thr Ile Gln Ala
165          170          175
tac ctt tcc aac agc agc ttc agc cgg gga gag aca cgc tgt gaa caa 576
Tyr Leu Ser Asn Ser Ser Phe Ser Arg Gly Glu Thr Arg Cys Glu Gln
180          185          190
gac agg cct tcc cca acc aca gcg ccc cct gcg cca ccc agc ccc tcg 624
Asp Arg Pro Ser Pro Thr Thr Ala Pro Pro Ala Pro Pro Ser Pro Ser
195          200          205

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ccc tca ccc gtg ccc aag agc ccc tct gtg gac aag tac aac gtg agc 672
Pro Ser Pro Val Pro Lys Ser Pro Ser Val Asp Lys Tyr Asn Val Ser
      210                      215                      220
ggc acc aac ggg acc tgc ctg ctg gcc agc atg ggg ctg cag ctg aac 720
Gly Thr Asn Gly Thr Cys Leu Leu Ala Ser Met Gly Leu Gln Leu Asn
225                      230                      235                      240
ctc acc tat gag agg aag gac aac acg acg gtg aca agg ctt ctc aac 768
Leu Thr Tyr Glu Arg Lys Asp Asn Thr Thr Val Thr Arg Leu Leu Asn
      245                      250                      255
atc aac ccc aac aag acc tcg gcc agc ggg agc tgc ggc gcc cac ctg 816
Ile Asn Pro Asn Lys Thr Ser Ala Ser Gly Ser Cys Gly Ala His Leu
      260                      265                      270
gtg act ctg gag ctg cac agc gag ggc acc acc gtc ctg ctc ttc cag 864
Val Thr Leu Glu Leu His Ser Glu Gly Thr Thr Val Leu Leu Phe Gln
      275                      280                      285
ttc ggg atg aat gca agt tct agc cgg ttt ttc cta caa gga atc cag 912
Phe Gly Met Asn Ala Ser Ser Ser Arg Phe Phe Leu Gln Gly Ile Gln
      290                      295                      300
ttg aat aca att ctt cct gac gcc aga gac cct gcc ttt aaa gct gcc 960
Leu Asn Thr Ile Leu Pro Asp Ala Arg Asp Pro Ala Phe Lys Ala Ala
305                      310                      315                      320
aac ggc tcc ctg cga gcg ctg cag gcc aca gtc ggc aat tcc tac aag 1008
Asn Gly Ser Leu Arg Ala Leu Gln Ala Thr Val Gly Asn Ser Tyr Lys
      325                      330                      335
tgc aac gcg gag gag cac gtc cgt gtc acg aag gcg ttt tca gtc aat 1056
Cys Asn Ala Glu Glu His Val Arg Val Thr Lys Ala Phe Ser Val Asn
      340                      345                      350
ata ttc aaa gtg tgg gtc cag gct ttc aag gtg gaa ggt ggc cag ttt 1104
Ile Phe Lys Val Trp Val Gln Ala Phe Lys Val Glu Gly Gly Gln Phe
      355                      360                      365
ggc tct gtg gag gag tgt ctg ctg gac gag aac agc ctc gag gcc gat 1152
Gly Ser Val Glu Glu Cys Leu Leu Asp Glu Asn Ser Leu Glu Ala Asp
      370                      375                      380
gcc ggc tac aca cca gcc gct gct gct aca cca gcc act cca gca gca 1200
Ala Gly Tyr Thr Pro Ala Ala Ala Ala Thr Pro Ala Thr Pro Ala Ala
385                      390                      395                      400
aca cca gca gcc gct ggc ggc aag gcc aca acc gat gag cag aaa ctg 1248
Thr Pro Ala Ala Ala Gly Gly Lys Ala Thr Thr Asp Glu Gln Lys Leu
      405                      410                      415

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ctg gaa gat gtg aac gcc ggc ttc aag gcc gcc gtg gct gct gct gca 1296
Leu Glu Asp Val Asn Ala Gly Phe Lys Ala Ala Val Ala Ala Ala Ala
      420              425              430
aat gcc cct ccc gcc gac aag ttc aag atc ttc gag gcc gcc ttc agc 1344
Asn Ala Pro Pro Ala Asp Lys Phe Lys Ile Phe Glu Ala Ala Phe Ser
      435              440              445
gag agc agc aag gga ctg ctg gcc aca tct gcc gcc aaa gcc ccc gga 1392
Glu Ser Ser Lys Gly Leu Leu Ala Thr Ser Ala Ala Lys Ala Pro Gly
      450              455              460
ctg atc ccc aag ctg gac acc gcc tac gac gtg gcc tac aaa gcc gcc 1440
Leu Ile Pro Lys Leu Asp Thr Ala Tyr Asp Val Ala Tyr Lys Ala Ala
465              470              475              480
gag gcc acc cca gag gcc aaa tac gat gcc ttc gtg acc gct ctg acc 1488
Glu Ala Thr Pro Glu Ala Lys Tyr Asp Ala Phe Val Thr Ala Leu Thr
      485              490              495
gag gct ctg aga gtg att gcc ggc gct ctg gaa gtg cac gcc gtg aag 1536
Glu Ala Leu Arg Val Ile Ala Gly Ala Leu Glu Val His Ala Val Lys
      500              505              510
cca gcc acc gaa gaa gtg ctg gcc gcc aag att cct acc ggc gag ctg 1584
Pro Ala Thr Glu Glu Val Leu Ala Ala Lys Ile Pro Thr Gly Glu Leu
      515              520              525
cag atc gtg gac aag atc gac gcc gcc ttt aag atc gcc gcc acc gcc 1632
Gln Ile Val Asp Lys Ile Asp Ala Ala Phe Lys Ile Ala Ala Thr Ala
      530              535              540
gca aat gcc gcc cct acc aac gat aag ttc acc gtg ttc gag agc gcc 1680
Ala Asn Ala Ala Pro Thr Asn Asp Lys Phe Thr Val Phe Glu Ser Ala
545              550              555              560
ttc aac aag gct ctg aac gag tgc acc ggc gga gcc tac gag aca tac 1728
Phe Asn Lys Ala Leu Asn Glu Cys Thr Gly Gly Ala Tyr Glu Thr Tyr
      565              570              575
aag ttc atc cca tct ctg gaa gcc gct gtg aag caa gcc tac gcc gcc 1776
Lys Phe Ile Pro Ser Leu Glu Ala Ala Val Lys Gln Ala Tyr Ala Ala
      580              585              590
aca gtg gcc gct gcc ccc gaa gtg aag tac gcc gtg ttt gag gcc gca 1824
Thr Val Ala Ala Ala Pro Glu Val Lys Tyr Ala Val Phe Glu Ala Ala
      595              600              605
ctg acc aag gcc atc acc gcc atg aca caa gcc cag aag gcc ggc aaa 1872
Leu Thr Lys Ala Ile Thr Ala Met Thr Gln Ala Gln Lys Ala Gly Lys
      610              615              620

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cca gct gct gca gct gaa ttc acg ctg atc ccc atc gct gtg ggt ggt 1920
Pro Ala Ala Ala Ala Glu Phe Thr Leu Ile Pro Ile Ala Val Gly Gly
625          630          635          640
gcc ctg gcg ggg ctg gtc ctc atc gtc ctc atc gcc tac ctc gtc ggc 1968
Ala Leu Ala Gly Leu Val Leu Ile Val Leu Ile Ala Tyr Leu Val Gly
          645          650          655
agg aag agg agt cac gca ggc tac cag act atc tag taa 2007
Arg Lys Arg Ser His Ala Gly Tyr Gln Thr Ile
          660          665

<210> 84
<211> 667
<212> PRT
<213> 人工序列
<220>
<223> 合成构建物
<400> 84
Met Ala Pro Arg Ser Ala Arg Arg Pro Leu Leu Leu Leu Leu Leu Leu
1          5          10          15
Leu Leu Leu Gly Leu Met His Cys Ala Ser Ala Ala Met Phe Met Val
          20          25          30
Lys Asn Gly Asn Gly Thr Ala Cys Ile Met Ala Asn Phe Ser Ala Ala
          35          40          45
Phe Ser Val Asn Tyr Asp Thr Lys Ser Gly Pro Lys Asn Met Thr Leu
          50          55          60
Asp Leu Pro Ser Asp Ala Thr Val Val Leu Asn Arg Ser Ser Cys Gly
65          70          75          80
Lys Glu Asn Thr Ser Asp Pro Ser Leu Val Ile Ala Phe Gly Arg Gly
          85          90          95
His Thr Leu Thr Leu Asn Phe Thr Arg Asn Ala Thr Arg Tyr Ser Val
          100          105          110
Gln Leu Met Ser Phe Val Tyr Asn Leu Ser Asp Thr His Leu Phe Pro
          115          120          125
Asn Ala Ser Ser Lys Glu Ile Lys Thr Val Glu Ser Ile Thr Asp Ile
          130          135          140
Arg Ala Asp Ile Asp Lys Lys Tyr Arg Cys Val Ser Gly Thr Gln Val
145          150          155          160
His Met Asn Asn Val Thr Val Thr Leu His Asp Ala Thr Ile Gln Ala
          165          170          175
Tyr Leu Ser Asn Ser Ser Phe Ser Arg Gly Glu Thr Arg Cys Glu Gln

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

Glu Ala Leu Arg Val Ile Ala Gly Ala Leu Glu Val His Ala Val Lys
 500 505 510
 Pro Ala Thr Glu Glu Val Leu Ala Ala Lys Ile Pro Thr Gly Glu Leu
 515 520 525
 Gln Ile Val Asp Lys Ile Asp Ala Ala Phe Lys Ile Ala Ala Thr Ala
 530 535 540
 Ala Asn Ala Ala Pro Thr Asn Asp Lys Phe Thr Val Phe Glu Ser Ala
 545 550 555 560
 Phe Asn Lys Ala Leu Asn Glu Cys Thr Gly Gly Ala Tyr Glu Thr Tyr
 565 570 575
 Lys Phe Ile Pro Ser Leu Glu Ala Ala Val Lys Gln Ala Tyr Ala Ala
 580 585 590
 Thr Val Ala Ala Ala Pro Glu Val Lys Tyr Ala Val Phe Glu Ala Ala
 595 600 605
 Leu Thr Lys Ala Ile Thr Ala Met Thr Gln Ala Gln Lys Ala Gly Lys
 610 615 620
 Pro Ala Ala Ala Ala Glu Phe Thr Leu Ile Pro Ile Ala Val Gly Gly
 625 630 635 640
 Ala Leu Ala Gly Leu Val Leu Ile Val Leu Ile Ala Tyr Leu Val Gly
 645 650 655
 Arg Lys Arg Ser His Ala Gly Tyr Gln Thr Ile
 660 665

<210> 85

<211> 732

<212> DNA

<213> 梯牧草(Phleum pratense)

<220>

<221> CDS

<222> (7) .. (726)

<400> 85

ctcgag atc ccc aaa gtg cct ccc ggc cca aac atc acc gcc aca tac 48

Ile Pro Lys Val Pro Pro Gly Pro Asn Ile Thr Ala Thr Tyr

1

5

10

ggc gac aag tgg ctg gac gcc aag agc act tgg tac ggc aag cct act 96

Gly Asp Lys Trp Leu Asp Ala Lys Ser Thr Trp Tyr Gly Lys Pro Thr

15

20

25

30

ggc gcc gga ccc aag gac aat ggc ggc gct tgt ggc tac aag gac gtg 144

Gly Ala Gly Pro Lys Asp Asn Gly Gly Ala Cys Gly Tyr Lys Asp Val

35

40

45

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gac aag ccc ccc ttc tct ggc atg acc ggc tgc ggc aac acc ccc atc 192
Asp Lys Pro Pro Phe Ser Gly Met Thr Gly Cys Gly Asn Thr Pro Ile
          50                      55                      60

ttc aag agc ggc aga ggc tgt ggc agc tgc ttc gag atc aag tgc acc 240
Phe Lys Ser Gly Arg Gly Cys Gly Ser Cys Phe Glu Ile Lys Cys Thr
          65                      70                      75

aag ccc gag gct tgc agc ggc gaa cca gtc gtg gtg cac atc acc gac 288
Lys Pro Glu Ala Cys Ser Gly Glu Pro Val Val Val His Ile Thr Asp
          80                      85                      90

gac aac gag gaa ccc att gcc ccc tac cac ttc gat ctg agc ggc cac 336
Asp Asn Glu Glu Pro Ile Ala Pro Tyr His Phe Asp Leu Ser Gly His
          95                      100                      105                      110

gcc ttt ggc gcc atg gcc aag aaa ggc gac gag cag aag ctg aga tct 384
Ala Phe Gly Ala Met Ala Lys Lys Gly Asp Glu Gln Lys Leu Arg Ser
          115                      120                      125

gcc ggc gag ctg gaa ctg cag ttt cgg aga gtg aag tgc aag tac ccc 432
Ala Gly Glu Leu Glu Leu Gln Phe Arg Arg Val Lys Cys Lys Tyr Pro
          130                      135                      140

gag ggc acc aaa gtg aca ttt cac gtg gaa aag ggc agc aac ccc aac 480
Glu Gly Thr Lys Val Thr Phe His Val Glu Lys Gly Ser Asn Pro Asn
          145                      150                      155

tat ctg gct ctg ctc gtg aaa tac gtg aac ggc gac ggc gac gtc gtg 528
Tyr Leu Ala Leu Leu Val Lys Tyr Val Asn Gly Asp Gly Asp Val Val
          160                      165                      170

gcc gtg gac atc aaa gag aag ggc aag gac aag tgg atc gag ctg aaa 576
Ala Val Asp Ile Lys Glu Lys Gly Lys Asp Lys Trp Ile Glu Leu Lys
          175                      180                      185                      190

gag agc tgg ggc gcc atc tgg cgg atc gac acc cca gat aag ctg acc 624
Glu Ser Trp Gly Ala Ile Trp Arg Ile Asp Thr Pro Asp Lys Leu Thr
          195                      200                      205

ggc cct ttc acc gtg cgg tac aca aca gag ggc ggc acc aag aca gag 672
Gly Pro Phe Thr Val Arg Tyr Thr Thr Glu Gly Gly Thr Lys Thr Glu
          210                      215                      220

gcc gag gat gtg atc cca gag ggc tgg aag gcc gac acc agc tac gag 720
Ala Glu Asp Val Ile Pro Glu Gly Trp Lys Ala Asp Thr Ser Tyr Glu
          225                      230                      235

agc aaa gaattc 732
Ser Lys
          240

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<210> 86

<211> 240

<212> PRT

<213> 梯牧草(*Phleum pratense*)

<400> 86

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

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<210> 87

<211> 1986

<212> DNA

<213> 人工序列

<220>

<223> 合成构建物

<220>

<221> CDS

<222> (1) .. (1986)

<400> 87

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atg gcg ccc cgc agc gcc cgg cga ccc ctg ctg ctg cta ctg ctg ttg 48
Met Ala Pro Arg Ser Ala Arg Arg Pro Leu Leu Leu Leu Leu Leu Leu
1           5           10           15
ctg ctg ctc ggc ctc atg cat tgt gcg tca gca gca atg ttt atg gtg 96
Leu Leu Leu Gly Leu Met His Cys Ala Ser Ala Ala Met Phe Met Val
           20           25           30
aaa aat ggc aac ggg acc gcg tgc ata atg gcc aac ttc tct gct gcc 144
Lys Asn Gly Asn Gly Thr Ala Cys Ile Met Ala Asn Phe Ser Ala Ala
           35           40           45
ttc tca gtg aac tac gac acc aag agt ggc cct aag aac atg acc ctt 192
Phe Ser Val Asn Tyr Asp Thr Lys Ser Gly Pro Lys Asn Met Thr Leu
           50           55           60
gac ctg cca tca gat gcc aca gtg gtg ctc aac cgc agc tcc tgt gga 240
Asp Leu Pro Ser Asp Ala Thr Val Val Leu Asn Arg Ser Ser Cys Gly
           65           70           75           80
aaa gag aac act tct gac ccc agt ctc gtg att gct ttt gga aga gga 288
Lys Glu Asn Thr Ser Asp Pro Ser Leu Val Ile Ala Phe Gly Arg Gly
           85           90           95
cat aca ctc act ctc aat ttc acg aga aat gca aca cgt tac agc gtc 336
His Thr Leu Thr Leu Asn Phe Thr Arg Asn Ala Thr Arg Tyr Ser Val
           100          105          110
cag ctc atg agt ttt gtt tat aac ttg tca gac aca cac ctt ttc ccc 384
Gln Leu Met Ser Phe Val Tyr Asn Leu Ser Asp Thr His Leu Phe Pro
           115          120          125
aat gcg agc tcc aaa gaa atc aag act gtg gaa tct ata act gac atc 432
Asn Ala Ser Ser Lys Glu Ile Lys Thr Val Glu Ser Ile Thr Asp Ile
           130          135          140
agg gca gat ata gat aaa aaa tac aga tgt gtt agt ggc acc cag gtc 480
Arg Ala Asp Ile Asp Lys Lys Tyr Arg Cys Val Ser Gly Thr Gln Val
           145          150          155          160
cac atg aac aac gtg acc gta acg ctc cat gat gcc acc atc cag gcg 528
His Met Asn Asn Val Thr Val Thr Leu His Asp Ala Thr Ile Gln Ala
           165          170          175

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tac ctt tcc aac agc agc ttc agc cgg gga gag aca cgc tgt gaa caa 576
Tyr Leu Ser Asn Ser Ser Phe Ser Arg Gly Glu Thr Arg Cys Glu Gln
      180                      185                      190
gac agg cct tcc cca acc aca gcg ccc cct gcg cca ccc agc ccc tcg 624
Asp Arg Pro Ser Pro Thr Thr Ala Pro Pro Ala Pro Pro Ser Pro Ser
      195                      200                      205
ccc tca ccc gtg ccc aag agc ccc tct gtg gac aag tac aac gtg agc 672
Pro Ser Pro Val Pro Lys Ser Pro Ser Val Asp Lys Tyr Asn Val Ser
      210                      215                      220
ggc acc aac ggg acc tgc ctg ctg gcc agc atg ggg ctg cag ctg aac 720
Gly Thr Asn Gly Thr Cys Leu Leu Ala Ser Met Gly Leu Gln Leu Asn
      225                      230                      235                      240
ctc acc tat gag agg aag gac aac acg acg gtg aca agg ctt ctc aac 768
Leu Thr Tyr Glu Arg Lys Asp Asn Thr Thr Val Thr Arg Leu Leu Asn
      245                      250                      255
atc aac ccc aac aag acc tcg gcc agc ggg agc tgc ggc gcc cac ctg 816
Ile Asn Pro Asn Lys Thr Ser Ala Ser Gly Ser Cys Gly Ala His Leu
      260                      265                      270
gtg act ctg gag ctg cac agc gag ggc acc acc gtc ctg ctc ttc cag 864
Val Thr Leu Glu Leu His Ser Glu Gly Thr Thr Val Leu Leu Phe Gln
      275                      280                      285
ttc ggg atg aat gca agt tct agc cgg ttt ttc cta caa gga atc cag 912
Phe Gly Met Asn Ala Ser Ser Ser Arg Phe Phe Leu Gln Gly Ile Gln
      290                      295                      300
ttg aat aca att ctt cct gac gcc aga gac cct gcc ttt aaa gct gcc 960
Leu Asn Thr Ile Leu Pro Asp Ala Arg Asp Pro Ala Phe Lys Ala Ala
      305                      310                      315                      320
aac ggc tcc ctg cga gcg ctg cag gcc aca gtc ggc aat tcc tac aag 1008
Asn Gly Ser Leu Arg Ala Leu Gln Ala Thr Val Gly Asn Ser Tyr Lys
      325                      330                      335
tgc aac gcg gag gag cac gtc cgt gtc acg aag gcg ttt tca gtc aat 1056
Cys Asn Ala Glu Glu His Val Arg Val Thr Lys Ala Phe Ser Val Asn
      340                      345                      350
ata ttc aaa gtg tgg gtc cag gct ttc aag gtg gaa ggt ggc cag ttt 1104
Ile Phe Lys Val Trp Val Gln Ala Phe Lys Val Glu Gly Gly Gln Phe
      355                      360                      365
ggc tct gtg gag gag tgt ctg ctg gac gag aac agc ctc gag atc ccc 1152
Gly Ser Val Glu Glu Cys Leu Leu Asp Glu Asn Ser Leu Glu Ile Pro
      370                      375                      380

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aaa gtg cct ccc ggc cca aac atc acc gcc aca tac ggc gac aag tgg 1200
Lys Val Pro Pro Gly Pro Asn Ile Thr Ala Thr Tyr Gly Asp Lys Trp
385                390                395                400
ctg gac gcc aag agc act tgg tac ggc aag cct act ggc gcc gga ccc 1248
Leu Asp Ala Lys Ser Thr Trp Tyr Gly Lys Pro Thr Gly Ala Gly Pro
                405                410                415
aag gac aat ggc ggc gct tgt ggc tac aag gac gtg gac aag ccc ccc 1296
Lys Asp Asn Gly Gly Ala Cys Gly Tyr Lys Asp Val Asp Lys Pro Pro
                420                425                430
ttc tct ggc atg acc ggc tgc ggc aac acc ccc atc ttc aag agc ggc 1344
Phe Ser Gly Met Thr Gly Cys Gly Asn Thr Pro Ile Phe Lys Ser Gly
                435                440                445
aga ggc tgt ggc agc tgc ttc gag atc aag tgc acc aag ccc gag gct 1392
Arg Gly Cys Gly Ser Cys Phe Glu Ile Lys Cys Thr Lys Pro Glu Ala
                450                455                460
tgc agc ggc gaa cca gtc gtg gtg cac atc acc gac gac aac gag gaa 1440
Cys Ser Gly Glu Pro Val Val Val His Ile Thr Asp Asp Asn Glu Glu
465                470                475                480
ccc att gcc ccc tac cac ttc gat ctg agc ggc cac gcc ttt ggc gcc 1488
Pro Ile Ala Pro Tyr His Phe Asp Leu Ser Gly His Ala Phe Gly Ala
                485                490                495
atg gcc aag aaa ggc gac gag cag aag ctg aga tct gcc ggc gag ctg 1536
Met Ala Lys Lys Gly Asp Glu Gln Lys Leu Arg Ser Ala Gly Glu Leu
                500                505                510
gaa ctg cag ttt cgg aga gtg aag tgc aag tac ccc gag ggc acc aaa 1584
Glu Leu Gln Phe Arg Arg Val Lys Cys Lys Tyr Pro Glu Gly Thr Lys
                515                520                525
gtg aca ttt cac gtg gaa aag ggc agc aac ccc aac tat ctg gct ctg 1632
Val Thr Phe His Val Glu Lys Gly Ser Asn Pro Asn Tyr Leu Ala Leu
                530                535                540
ctc gtg aaa tac gtg aac ggc gac ggc gac gtc gtg gcc gtg gac atc 1680
Leu Val Lys Tyr Val Asn Gly Asp Gly Asp Val Val Ala Val Asp Ile
545                550                555                560
aaa gag aag ggc aag gac aag tgg atc gag ctg aaa gag agc tgg ggc 1728
Lys Glu Lys Gly Lys Asp Lys Trp Ile Glu Leu Lys Glu Ser Trp Gly
                565                570                575
gcc atc tgg cgg atc gac acc cca gat aag ctg acc ggc cct ttc acc 1776
Ala Ile Trp Arg Ile Asp Thr Pro Asp Lys Leu Thr Gly Pro Phe Thr
                580                585                590

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gtg cgg tac aca aca gag ggc ggc acc aag aca gag gcc gag gat gtg 1824
Val Arg Tyr Thr Thr Glu Gly Gly Thr Lys Thr Glu Ala Glu Asp Val
595 600 605
atc cca gag ggc tgg aag gcc gac acc agc tac gag agc aaa gaa ttc 1872
Ile Pro Glu Gly Trp Lys Ala Asp Thr Ser Tyr Glu Ser Lys Glu Phe
610 615 620
acg ctg atc ccc atc gct gtg ggt ggt gcc ctg gcg ggg ctg gtc ctc 1920
Thr Leu Ile Pro Ile Ala Val Gly Gly Ala Leu Ala Gly Leu Val Leu
625 630 635 640
atc gtc ctc atc gcc tac ctc gtc ggc agg aag agg agt cac gca ggc 1968
Ile Val Leu Ile Ala Tyr Leu Val Gly Arg Lys Arg Ser His Ala Gly
645 650 655
tac cag act atc tag taa 1986
Tyr Gln Thr Ile
660

<210> 88

<211> 660

<212> PRT

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<220>

<223> 合成构建物

<400> 88

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

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

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

<210> 89

<211> 804

<212> DNA

<213> 梯牧草 (Phleum pratense)

<220>

<221> CDS

<222> (7) .. (798)

<400> 89

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Ala Ala Asp Leu Gly Tyr Gly Pro Ala Thr Pro Ala Ala Pro

1

5

10

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Ala Ala Gly Tyr Thr Pro Ala Thr Pro Ala Ala Pro Ala Glu Ala Ala
15                20                25                30
cca gct gga aag gcc aca acc gag gaa cag aag ctg atc gag aag atc 144
Pro Ala Gly Lys Ala Thr Thr Glu Glu Gln Lys Leu Ile Glu Lys Ile
35                40                45
aac gcc ggc ttc aag gcc gct ctg gct gca gct gct ggg gtg cag cca 192
Asn Ala Gly Phe Lys Ala Ala Leu Ala Ala Ala Ala Gly Val Gln Pro
50                55                60
gcc gac aag tac aga aca ttc gtg gcc aca ttc gga gcc gcc agc aac 240
Ala Asp Lys Tyr Arg Thr Phe Val Ala Thr Phe Gly Ala Ala Ser Asn
65                70                75
aag gcc ttt gcc gag gga ctg agc ggc gag cct aaa ggc gcc gct gag 288
Lys Ala Phe Ala Glu Gly Leu Ser Gly Glu Pro Lys Gly Ala Ala Glu
80                85                90
tct agc agc aag gcc gca ctg acc agc aag ctg gac gcc gcc tac aag 336
Ser Ser Ser Lys Ala Ala Leu Thr Ser Lys Leu Asp Ala Ala Tyr Lys
95                100                105                110
ctg gcc tac aag aca gcc gaa ggc gcc acc ccc gag gcc aaa tac gat 384
Leu Ala Tyr Lys Thr Ala Glu Gly Ala Thr Pro Glu Ala Lys Tyr Asp
115                120                125
gcc tac gtg gcc act ctg agc gag gct ctg aga atc att gcc ggc aca 432
Ala Tyr Val Ala Thr Leu Ser Glu Ala Leu Arg Ile Ile Ala Gly Thr
130                135                140
ctg gaa gtg cac gcc gtg aag cca gcc gct gag gaa gtg aaa gtg atc 480
Leu Glu Val His Ala Val Lys Pro Ala Ala Glu Glu Val Lys Val Ile
145                150                155
cca gcc ggc gag ctc caa gtg att gag aaa gtg gat gcc gcc ttc aaa 528
Pro Ala Gly Glu Leu Gln Val Ile Glu Lys Val Asp Ala Ala Phe Lys
160                165                170
gtg gcc gcc acc gct gcc aat gcc gcc cca gcc aat gac aag ttc acc 576
Val Ala Ala Thr Ala Ala Asn Ala Ala Pro Ala Asn Asp Lys Phe Thr
175                180                185                190
gtg ttt gag gcc gcc ttt aac gac gcc atc aag gcc tct acc ggc gga 624
Val Phe Glu Ala Ala Phe Asn Asp Ala Ile Lys Ala Ser Thr Gly Gly
195                200                205
gcc tac gag agc tac aag ttc atc ccc gct ctg gaa gcc gcc gtg aaa 672
Ala Tyr Glu Ser Tyr Lys Phe Ile Pro Ala Leu Glu Ala Ala Val Lys
210                215                220

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caa gcc tat gcc gcc aca gtg gcc aca gcc ccc gaa gtg aag tac aca 720
Gln Ala Tyr Ala Ala Thr Val Ala Thr Ala Pro Glu Val Lys Tyr Thr
      225              230              235

gtg ttc gag aca gct ctg aag aaa gcc atc acc gcc atg tcc gag gcc 768
Val Phe Glu Thr Ala Leu Lys Lys Ala Ile Thr Ala Met Ser Glu Ala
      240              245              250

cag aag gcc gcc aaa cca gct gct gct gct gaattc 804
Gln Lys Ala Ala Lys Pro Ala Ala Ala Ala
255              260

<210> 90
<211> 264
<212> PRT
<213> 梯牧草(Phleum pratense)
<400> 90

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

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195	200	205
Glu Ser Tyr Lys Phe Ile Pro Ala Leu Glu Ala Ala Val Lys Gln Ala		
210	215	220
Tyr Ala Ala Thr Val Ala Thr Ala Pro Glu Val Lys Tyr Thr Val Phe		
225	230	235
Glu Thr Ala Leu Lys Lys Ala Ile Thr Ala Met Ser Glu Ala Gln Lys		
245	250	255
Ala Ala Lys Pro Ala Ala Ala Ala		
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1 5 10 15		
ctg ctg ctc ggc ctc atg cat tgt gcg tca gca gca atg ttt atg gtg 96		
Leu Leu Leu Gly Leu Met His Cys Ala Ser Ala Ala Met Phe Met Val		
20 25 30		
aaa aat ggc aac ggg acc gcg tgc ata atg gcc aac ttc tct gct gcc 144		
Lys Asn Gly Asn Gly Thr Ala Cys Ile Met Ala Asn Phe Ser Ala Ala		
35 40 45		
ttc tca gtg aac tac gac acc aag agt ggc cct aag aac atg acc ctt 192		
Phe Ser Val Asn Tyr Asp Thr Lys Ser Gly Pro Lys Asn Met Thr Leu		
50 55 60		
gac ctg cca tca gat gcc aca gtg gtg ctc aac cgc agc tcc tgt gga 240		
Asp Leu Pro Ser Asp Ala Thr Val Val Leu Asn Arg Ser Ser Cys Gly		
65 70 75 80		
aaa gag aac act tct gac ccc agt ctc gtg att gct ttt gga aga gga 288		
Lys Glu Asn Thr Ser Asp Pro Ser Leu Val Ile Ala Phe Gly Arg Gly		
85 90 95		
cat aca ctc act ctc aat ttc acg aga aat gca aca cgt tac agc gtc 336		
His Thr Leu Thr Leu Asn Phe Thr Arg Asn Ala Thr Arg Tyr Ser Val		

100	105	110
cag ctc atg agt ttt gtt tat aac ttg tca gac aca cac ctt ttc ccc 384		
Gln Leu Met Ser Phe Val Tyr Asn Leu Ser Asp Thr His Leu Phe Pro		
115	120	125
aat gcg agc tcc aaa gaa atc aag act gtg gaa tct ata act gac atc 432		
Asn Ala Ser Ser Lys Glu Ile Lys Thr Val Glu Ser Ile Thr Asp Ile		
130	135	140
agg gca gat ata gat aaa aaa tac aga tgt gtt agt ggc acc cag gtc 480		
Arg Ala Asp Ile Asp Lys Lys Tyr Arg Cys Val Ser Gly Thr Gln Val		
145	150	155
cac atg aac aac gtg acc gta acg ctc cat gat gcc acc atc cag gcg 528		
His Met Asn Asn Val Thr Val Thr Leu His Asp Ala Thr Ile Gln Ala		
165	170	175
tac ctt tcc aac agc agc ttc agc cgg gga gag aca cgc tgt gaa caa 576		
Tyr Leu Ser Asn Ser Ser Phe Ser Arg Gly Glu Thr Arg Cys Glu Gln		
180	185	190
gac agg cct tcc cca acc aca gcg ccc cct gcg cca ccc agc ccc tcg 624		
Asp Arg Pro Ser Pro Thr Thr Ala Pro Pro Ala Pro Pro Ser Pro Ser		
195	200	205
ccc tca ccc gtg ccc aag agc ccc tct gtg gac aag tac aac gtg agc 672		
Pro Ser Pro Val Pro Lys Ser Pro Ser Val Asp Lys Tyr Asn Val Ser		
210	215	220
ggc acc aac ggg acc tgc ctg ctg gcc agc atg ggg ctg cag ctg aac 720		
Gly Thr Asn Gly Thr Cys Leu Leu Ala Ser Met Gly Leu Gln Leu Asn		
225	230	235
ctc acc tat gag agg aag gac aac acg acg gtg aca agg ctt ctc aac 768		
Leu Thr Tyr Glu Arg Lys Asp Asn Thr Thr Val Thr Arg Leu Leu Asn		
245	250	255
atc aac ccc aac aag acc tcg gcc agc ggg agc tgc ggc gcc cac ctg 816		
Ile Asn Pro Asn Lys Thr Ser Ala Ser Gly Ser Cys Gly Ala His Leu		
260	265	270
gtg act ctg gag ctg cac agc gag ggc acc acc gtc ctg ctc ttc cag 864		
Val Thr Leu Glu Leu His Ser Glu Gly Thr Thr Val Leu Leu Phe Gln		
275	280	285
ttc ggg atg aat gca agt tct agc cgg ttt ttc cta caa gga atc cag 912		
Phe Gly Met Asn Ala Ser Ser Ser Arg Phe Phe Leu Gln Gly Ile Gln		
290	295	300
ttg aat aca att ctt cct gac gcc aga gac cct gcc ttt aaa gct gcc 960		
Leu Asn Thr Ile Leu Pro Asp Ala Arg Asp Pro Ala Phe Lys Ala Ala		

305	310	315	320
aac ggc tcc ctg cga gcg ctg cag gcc aca gtc ggc aat tcc tac aag	1008		
Asn Gly Ser Leu Arg Ala Leu Gln Ala Thr Val Gly Asn Ser Tyr Lys			
325	330	335	
tgc aac gcg gag gag cac gtc cgt gtc acg aag gcg ttt tca gtc aat	1056		
Cys Asn Ala Glu Glu His Val Arg Val Thr Lys Ala Phe Ser Val Asn			
340	345	350	
ata ttc aaa gtg tgg gtc cag gct ttc aag gtg gaa ggt ggc cag ttt	1104		
Ile Phe Lys Val Trp Val Gln Ala Phe Lys Val Glu Gly Gly Gln Phe			
355	360	365	
ggc tct gtg gag gag tgt ctg ctg gac gag aac agc ctc gag gcc gcc	1152		
Gly Ser Val Glu Glu Cys Leu Leu Asp Glu Asn Ser Leu Glu Ala Ala			
370	375	380	
gat ctg ggc tat ggc cca gct aca cca gct gcc cca gcc gcc gga tac	1200		
Asp Leu Gly Tyr Gly Pro Ala Thr Pro Ala Ala Pro Ala Ala Gly Tyr			
385	390	395	400
aca cca gca act cca gcc gct cca gct gaa gca gcc cca gct gga aag	1248		
Thr Pro Ala Thr Pro Ala Ala Pro Ala Glu Ala Ala Pro Ala Gly Lys			
405	410	415	
gcc aca acc gag gaa cag aag ctg atc gag aag atc aac gcc ggc ttc	1296		
Ala Thr Thr Glu Glu Gln Lys Leu Ile Glu Lys Ile Asn Ala Gly Phe			
420	425	430	
aag gcc gct ctg gct gca gct gct ggg gtg cag cca gcc gac aag tac	1344		
Lys Ala Ala Leu Ala Ala Ala Ala Gly Val Gln Pro Ala Asp Lys Tyr			
435	440	445	
aga aca ttc gtg gcc aca ttc gga gcc gcc agc aac aag gcc ttt gcc	1392		
Arg Thr Phe Val Ala Thr Phe Gly Ala Ala Ser Asn Lys Ala Phe Ala			
450	455	460	
gag gga ctg agc ggc gag cct aaa ggc gcc gct gag tct agc agc aag	1440		
Glu Gly Leu Ser Gly Glu Pro Lys Gly Ala Ala Glu Ser Ser Ser Lys			
465	470	475	480
gcc gca ctg acc agc aag ctg gac gcc gcc tac aag ctg gcc tac aag	1488		
Ala Ala Leu Thr Ser Lys Leu Asp Ala Ala Tyr Lys Leu Ala Tyr Lys			
485	490	495	
aca gcc gaa ggc gcc acc ccc gag gcc aaa tac gat gcc tac gtg gcc	1536		
Thr Ala Glu Gly Ala Thr Pro Glu Ala Lys Tyr Asp Ala Tyr Val Ala			
500	505	510	
act ctg agc gag gct ctg aga atc att gcc ggc aca ctg gaa gtg cac	1584		
Thr Leu Ser Glu Ala Leu Arg Ile Ile Ala Gly Thr Leu Glu Val His			

515	520	525	
gcc gtg aag cca gcc gct gag gaa gtg aaa gtg atc cca gcc ggc gag			1632
Ala Val Lys Pro Ala Ala Glu Glu Val Lys Val Ile Pro Ala Gly Glu			
530	535	540	
ctc caa gtg att gag aaa gtg gat gcc gcc ttc aaa gtg gcc gcc acc			1680
Leu Gln Val Ile Glu Lys Val Asp Ala Ala Phe Lys Val Ala Ala Thr			
545	550	555	560
gct gcc aat gcc gcc cca gcc aat gac aag ttc acc gtg ttt gag gcc			1728
Ala Ala Asn Ala Ala Pro Ala Asn Asp Lys Phe Thr Val Phe Glu Ala			
	565	570	575
gcc ttt aac gac gcc atc aag gcc tct acc ggc gga gcc tac gag agc			1776
Ala Phe Asn Asp Ala Ile Lys Ala Ser Thr Gly Gly Ala Tyr Glu Ser			
	580	585	590
tac aag ttc atc ccc gct ctg gaa gcc gcc gtg aaa caa gcc tat gcc			1824
Tyr Lys Phe Ile Pro Ala Leu Glu Ala Ala Val Lys Gln Ala Tyr Ala			
	595	600	605
gcc aca gtg gcc aca gcc ccc gaa gtg aag tac aca gtg ttc gag aca			1872
Ala Thr Val Ala Thr Ala Pro Glu Val Lys Tyr Thr Val Phe Glu Thr			
	610	615	620
gct ctg aag aaa gcc atc acc gcc atg tcc gag gcc cag aag gcc gcc			1920
Ala Leu Lys Lys Ala Ile Thr Ala Met Ser Glu Ala Gln Lys Ala Ala			
625	630	635	640
aaa cca gct gct gct gct gaa ttc acg ctg atc ccc atc gct gtg ggt			1968
Lys Pro Ala Ala Ala Ala Glu Phe Thr Leu Ile Pro Ile Ala Val Gly			
	645	650	655
ggt gcc ctg gcg ggg ctg gtc ctc atc gtc ctc atc gcc tac ctc gtc			2016
Gly Ala Leu Ala Gly Leu Val Leu Ile Val Leu Ile Ala Tyr Leu Val			
	660	665	670
ggc agg aag agg agt cac gca ggc tac cag act atc tag taa			2058
Gly Arg Lys Arg Ser His Ala Gly Tyr Gln Thr Ile			
675	680		
<210> 92			
<211> 684			
<212> PRT			
<213> 人工序列			
<220>			
<223> 合成构建物			
<400> 92			
Met Ala Pro Arg Ser Ala Arg Arg Pro Leu Leu Leu Leu Leu Leu			

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

Asn Gly Ser Leu Arg Ala Leu Gln Ala Thr Val Gly Asn Ser Tyr Lys		
325	330	335
Cys Asn Ala Glu Glu His Val Arg Val Thr Lys Ala Phe Ser Val Asn		
340	345	350
Ile Phe Lys Val Trp Val Gln Ala Phe Lys Val Glu Gly Gly Gln Phe		
355	360	365
Gly Ser Val Glu Glu Cys Leu Leu Asp Glu Asn Ser Leu Glu Ala Ala		
370	375	380
Asp Leu Gly Tyr Gly Pro Ala Thr Pro Ala Ala Pro Ala Ala Gly Tyr		
385	390	400
Thr Pro Ala Thr Pro Ala Ala Pro Ala Glu Ala Ala Pro Ala Gly Lys		
405	410	415
Ala Thr Thr Glu Glu Gln Lys Leu Ile Glu Lys Ile Asn Ala Gly Phe		
420	425	430
Lys Ala Ala Leu Ala Ala Ala Ala Gly Val Gln Pro Ala Asp Lys Tyr		
435	440	445
Arg Thr Phe Val Ala Thr Phe Gly Ala Ala Ser Asn Lys Ala Phe Ala		
450	455	460
Glu Gly Leu Ser Gly Glu Pro Lys Gly Ala Ala Glu Ser Ser Ser Lys		
465	470	480
Ala Ala Leu Thr Ser Lys Leu Asp Ala Ala Tyr Lys Leu Ala Tyr Lys		
485	490	495
Thr Ala Glu Gly Ala Thr Pro Glu Ala Lys Tyr Asp Ala Tyr Val Ala		
500	505	510
Thr Leu Ser Glu Ala Leu Arg Ile Ile Ala Gly Thr Leu Glu Val His		
515	520	525
Ala Val Lys Pro Ala Ala Glu Glu Val Lys Val Ile Pro Ala Gly Glu		
530	535	540
Leu Gln Val Ile Glu Lys Val Asp Ala Ala Phe Lys Val Ala Ala Thr		
545	550	560
Ala Ala Asn Ala Ala Pro Ala Asn Asp Lys Phe Thr Val Phe Glu Ala		
565	570	575
Ala Phe Asn Asp Ala Ile Lys Ala Ser Thr Gly Gly Ala Tyr Glu Ser		
580	585	590
Tyr Lys Phe Ile Pro Ala Leu Glu Ala Ala Val Lys Gln Ala Tyr Ala		
595	600	605
Ala Thr Val Ala Thr Ala Pro Glu Val Lys Tyr Thr Val Phe Glu Thr		
610	615	620
Ala Leu Lys Lys Ala Ile Thr Ala Met Ser Glu Ala Gln Lys Ala Ala		

625	630	635	640
Lys Pro Ala Ala Ala Ala Glu Phe Thr Leu Ile Pro Ile Ala Val Gly			
	645	650	655
Gly Ala Leu Ala Gly Leu Val Leu Ile Val Leu Ile Ala Tyr Leu Val			
660	665	670	
Gly Arg Lys Arg Ser His Ala Gly Tyr Gln Thr Ile			
675	680		
<210> 93			
<211> 536			
<212> PRT			
<213> 粉尘螨(Dermatophagoides farinae)			
<400> 93			
Ser Ile Lys Arg Asp His Asn Asp Tyr Ser Lys Asn Pro Met Arg Ile			
1	5	10	15
Val Cys Tyr Val Gly Thr Trp Ser Val Tyr His Lys Val Asp Pro Tyr			
20	25	30	
Thr Ile Glu Asp Ile Asp Pro Phe Lys Cys Thr His Leu Met Tyr Gly			
35	40	45	
Phe Ala Lys Ile Asp Glu Tyr Lys Tyr Thr Ile Gln Val Phe Asp Pro			
50	55	60	
Tyr Gln Asp Asp Asn His Asn Ser Trp Glu Lys Arg Gly Tyr Glu Arg			
65	70	75	80
Phe Asn Asn Leu Arg Leu Lys Asn Pro Glu Leu Thr Thr Met Ile Ser			
85	90	95	
Leu Gly Gly Trp Tyr Glu Gly Ser Glu Lys Tyr Ser Asp Met Ala Ala			
100	105	110	
Asn Pro Thr Tyr Arg Gln Gln Phe Ile Gln Ser Val Leu Asp Phe Leu			
115	120	125	
Gln Glu Tyr Lys Phe Asp Gly Leu Asp Leu Asp Trp Glu Tyr Pro Gly			
130	135	140	
Ser Arg Leu Gly Asn Pro Lys Ile Asp Lys Gln Asn Tyr Leu Ala Leu			
145	150	155	160
Val Arg Glu Leu Lys Asp Ala Phe Glu Pro His Gly Tyr Leu Leu Thr			
165	170	175	
Ala Ala Val Ser Pro Gly Lys Asp Lys Ile Asp Arg Ala Tyr Asp Ile			
180	185	190	
Lys Glu Leu Asn Lys Leu Phe Asp Trp Met Asn Val Met Thr Tyr Asp			
195	200	205	
Tyr His Gly Gly Trp Glu Asn Phe Tyr Gly His Asn Ala Pro Leu Tyr			

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

Glu Lys Leu Thr Cys Ile Gly Glu

530

535

<210> 94

<211> 424

<212> PRT

<213> 粉尘螨(Dermatophagoides farinae)

<400> 94

Ser Asn Ile Arg Pro Asn Val Ala Thr Leu Glu Pro Lys Thr Val Cys

1

5

10

15

Tyr Tyr Glu Ser Trp Val His Trp Arg Gln Gly Glu Gly Lys Met Asp

20

25

30

Pro Glu Asp Ile Asp Thr Ser Leu Cys Thr His Ile Val Tyr Ser Tyr

35

40

45

Phe Gly Ile Asp Ala Ala Thr His Glu Ile Lys Leu Leu Asp Glu Tyr

50

55

60

Leu Met Lys Asp Leu His Asp Met Glu His Phe Thr Gln His Lys Gly

65

70

75

80

Asn Ala Lys Ala Met Ile Ala Val Gly Gly Ser Thr Met Ser Asp Gln

85

90

95

Phe Ser Lys Thr Ala Ala Val Glu His Tyr Arg Glu Thr Phe Val Val

100

105

110

Ser Thr Val Asp Leu Met Thr Arg Tyr Gly Phe Asp Gly Val Met Ile

115

120

125

Asp Trp Ser Gly Met Gln Ala Lys Asp Ser Asp Asn Phe Ile Lys Leu

130

135

140

Leu Asp Lys Phe Asp Glu Asn Tyr Asn Ile Pro Ala Ile Ser Asn Tyr

145

150

155

160

Val Asp Phe Met Asn Val Leu Ser Leu Asp Tyr Thr Gly Ser Trp Ala

165

170

175

His Thr Val Gly His Ala Ser Pro Phe Pro Glu Gln Leu Lys Thr Leu

180

185

190

Glu Ala Tyr His Lys Arg Gly Ala Pro Arg His Lys Met Val Met Ala

195

200

205

Val Pro Phe Tyr Ala Arg Thr Trp Ile Leu Glu Lys Met Asn Lys Gln

210

215

220

Asp Ile Gly Asp Lys Ala Ser Gly Pro Gly Pro Arg Gly Gln Phe Thr

225

230

235

240

Gln Thr Asp Gly Phe Leu Ser Tyr Asn Glu Leu Cys Val Gln Ile Gln

245

250

255

Ala	Glu	Thr	Asn	Ala	Phe	Thr	Ile	Thr	Arg	Asp	His	Asp	Asn	Thr	Ala
260				265				270							
Ile	Tyr	Ala	Val	Tyr	Val	His	Ser	Asn	His	Ala	Glu	Trp	Ile	Ser	Phe
275				280				285							
Glu	Asp	Arg	His	Thr	Leu	Gly	Glu	Lys	Ala	Lys	Asn	Ile	Thr	Gln	Gln
290				295				300							
Gly	Tyr	Ala	Gly	Met	Ser	Val	Tyr	Thr	Leu	Ser	Asn	Glu	Asp	Val	His
305				310				315				320			
Gly	Val	Cys	Gly	Asp	Lys	Asn	Pro	Leu	Leu	His	Ala	Ile	Gln	Ser	Asn
325				330				335							
Tyr	Tyr	His	Gly	Val	Val	Thr	Glu	Pro	Thr	Val	Val	Thr	Leu	Pro	Pro
340				345				350							
Val	Thr	His	Thr	Thr	Glu	His	Val	Thr	Asp	Ile	Pro	Gly	Val	Phe	His
355				360				365							
Cys	His	Glu	Glu	Gly	Phe	Phe	Arg	Asp	Lys	Thr	Tyr	Cys	Ala	Thr	Tyr
370				375				380							
Tyr	Glu	Cys	Lys	Lys	Gly	Asp	Phe	Gly	Leu	Glu	Lys	Thr	Val	His	His
385				390				395				400			
Cys	Ala	Asn	His	Leu	Gln	Ala	Phe	Asp	Glu	Val	Ser	Arg	Thr	Cys	Ile
405				410				415							
Asp	His	Thr	Lys	Ile	Pro	Gly	Cys								
420															

<210> 95

<211> 478

<212> PRT

<213> 粉尘螨(Dermatophagoides farinae)

<400> 95

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

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

	405		410		415
Thr Pro Glu Pro Thr Thr Leu Asn Ser Thr Thr Pro Glu Pro Thr Thr					
	420		425		430
Leu Asn Ser Thr Thr Pro Glu Pro Thr Thr Ser Asn Ser Thr Thr Ser					
	435		440		445
Glu Pro Thr Asn Ser Ile Asn Arg Lys Thr Ser Glu Ile Ser Phe Leu					
	450		455		460
Ser Asp Trp Phe His Lys Ile Arg Thr Arg Phe Asn Ile Phe					
465		470		475	
<210> 96					
<211> 158					
<212> PRT					
<213> 猫蚤(Ctenocephalides felis)					
<400> 96					
Glu Asp Ile Trp Lys Val Asn Lys Lys Cys Thr Ser Gly Gly Lys Asn					
1	5		10		15
Gln Asp Arg Lys Leu Asp Gln Ile Ile Gln Lys Gly Gln Gln Val Lys					
	20		25		30
Ile Gln Asn Ile Cys Lys Leu Ile Arg Asp Lys Pro His Thr Asn Gln					
	35		40		45
Glu Lys Glu Lys Cys Met Lys Phe Cys Lys Lys Val Cys Lys Gly Tyr					
	50		55		60
Arg Gly Ala Cys Asp Gly Asn Ile Cys Tyr Cys Ser Arg Pro Ser Asn					
65		70		75	80
Leu Gly Pro Asp Trp Lys Val Ser Lys Glu Cys Lys Asp Pro Asn Asn					
	85		90		95
Lys Asp Ser Arg Pro Thr Glu Ile Val Pro Tyr Arg Gln Gln Leu Ala					
	100		105		110
Ile Pro Asn Ile Cys Lys Leu Lys Asn Ser Glu Thr Asn Glu Asp Ser					
	115		120		125
Lys Cys Lys Lys His Cys Lys Glu Lys Cys Arg Gly Gly Asn Asp Ala					
	130		135		140
Gly Cys Asp Gly Asn Phe Cys Tyr Cys Arg Pro Lys Asn Lys					
145		150		155	
<210> 97					
<211> 30					
<212> PRT					
<213> 未知					
<220>					

<223> 因为该物种可以是几种可能性之一,所以它是未知的。

<220>

<221> 不确定

<222> (1) .. (10)

<223> 每个Xaa可以是des-Xaa或任何天然存在的氨基酸

<220>

<221> 不确定

<222> (17) .. (21)

<223> 每个Xaa可以是des-Xaa或任何天然存在的氨基酸

<220>

<221> 不确定

<222> (26) .. (30)

<223> 每个Xaa可以是des-Xaa或任何天然存在的氨基酸

<400> 97

Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Glu	Lys	Gln	Pro	Leu	Leu
1				5					10					15	
Xaa	Xaa	Xaa	Xaa	Xaa	Tyr	His	Ser	Leu	Xaa	Xaa	Xaa	Xaa	Xaa		
				20				25					30		

<210> 98

<211> 26

<212> PRT

<213> 未知

<220>

<223> 因为该物种可以是几种可能性之一,所以它是未知的。

<220>

<221> 不确定

<222> (1) .. (7)

<223> 每个Xaa可以是des-Xaa或任何天然存在的氨基酸

<220>

<221> 不确定

<222> (15) .. (26)

<223> 每个Xaa可以是des-Xaa或任何天然存在的氨基酸

<400> 98

Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Glu	Ala	Asn	Gln	Pro	Leu	Leu	Xaa	Xaa
1				5					10					15	
Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa						
				20				25							

<210> 99

<211> 45

<212> PRT

<213> 未知

<220>

<223> 因为该物种可以是几种可能性之一,所以它是未知的。

<220>

<221> 不确定

<222> (1) .. (34)

<223> 每个Xaa可以是des-Xaa或任何天然存在的氨基酸

<220>

<221> 不确定

<222> (41) .. (45)

<223> 每个Xaa可以是des-Xaa或任何天然存在的氨基酸

<400> 99

Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa
1				5						10					15	
Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa
				20						25					30	
Xaa	Xaa	Glu	Asn	Ser	Pro	Leu	Leu	Xaa	Xaa	Xaa	Xaa	Xaa				
		35					40							45		

<210> 100

<211> 10

<212> PRT

<213> 智人(Homo sapiens)

<400> 100

Lys	His	His	His	Ala	Gly	Tyr	Glu	Gln	Phe
1				5					10

<210> 101

<211> 10

<212> PRT

<213> 智人(Homo sapiens)

<400> 101

Lys	Ser	Ile	Arg	Ser	Gly	Tyr	Glu	Val	Met
1				5					10

<210> 102

<211> 18

<212> PRT

<213> 未知

<220>

<223> 因为该物种可以是几种可能性之一,所以它是未知的。

<400> 102

Arg Met Glu Ala Pro Pro Gly Tyr Arg His Val Ala Asp Gly Gln Asp

1

5

10

15

His Ala

<210> 103

<211> 4

<212> PRT

<213> 人工序列

<220>

<223> 合成构建物

<400> 103

Tyr Gln Thr Leu

1

<210> 104

<211> 4

<212> PRT

<213> 人工序列

<220>

<223> 合成构建物

<400> 104

Tyr Gln Thr Phe

1

<210> 105

<211> 4

<212> PRT

<213> 人工序列

<220>

<223> 合成构建物

<400> 105

Tyr Gln Thr Thr

1

<210> 106

<211> 4

<212> PRT

<213> 人工序列

<220>

<223> 合成构建物

<400> 106

Tyr Ala Thr Ile

1

<210> 107

<211> 4

<212> PRT

<213> 人工序列

<220>

<223> 合成构建物

<400> 107

Tyr Gln Ala Ile

1

<210> 108

<211> 4

<212> PRT

<213> 人工序列

<220>

<223> 合成构建物

<400> 108

Tyr Ala Ala Ile

1

<210> 109

<211> 965

<212> PRT

<213> 人工序列

<220>

<223> 合成构建物

<400> 109

Ser Ile Lys Arg Asp His Asn Asp Tyr Ser Lys Asn Pro Met Arg Ile

1

5

10

15

Val Cys Tyr Val Gly Thr Trp Ser Val Tyr His Lys Val Asp Pro Tyr

20

25

30

Thr Ile Glu Asp Ile Asp Pro Phe Lys Cys Thr His Leu Met Tyr Gly

35

40

45

Phe Ala Lys Ile Asp Glu Tyr Lys Tyr Thr Ile Gln Val Phe Asp Pro

50

55

60

Tyr Gln Asp Asp Asn His Asn Ser Trp Glu Lys Arg Gly Tyr Glu Arg

65

70

75

80

Phe Asn Asn Leu Arg Leu Lys Asn Pro Glu Leu Thr Thr Met Ile Ser

85

90

95

Leu Gly Gly Trp Tyr Glu Gly Ser Glu Lys Tyr Ser Asp Met Ala Ala

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

Pro	Ser	Pro	Thr	Thr	Pro	Thr	Thr	Thr	Pro	Ser	Pro	Thr	Thr	Pro	Thr
420				425				430							
Thr	Thr	Pro	Ser	Pro	Thr	Thr	Pro	Thr	Thr	Thr	Pro	Ser	Pro	Thr	Thr
435				440				445							
Pro	Thr	Pro	Thr	Thr	Pro	Thr	Pro	Ala	Pro	Thr	Thr	Ser	Thr	Pro	Ser
450				455				460							
Pro	Thr	Thr	Thr	Glu	His	Thr	Ser	Glu	Thr	Pro	Lys	Tyr	Thr	Thr	Tyr
465				470				475				480			
Val	Asp	Gly	His	Leu	Ile	Lys	Cys	Tyr	Lys	Glu	Gly	Asp	Ile	Pro	His
485				490				495							
Pro	Thr	Asn	Ile	His	Lys	Tyr	Leu	Val	Cys	Glu	Phe	Val	Asn	Gly	Gly
500				505				510							
Trp	Trp	Val	His	Ile	Met	Pro	Cys	Pro	Pro	Gly	Thr	Ile	Trp	Cys	Gln
515				520				525							
Glu	Lys	Leu	Thr	Cys	Ile	Gly	Glu	Gly	Pro	Gly	Pro	Gly	Ser	Asn	Ile
530				535				540							
Arg	Pro	Asn	Val	Ala	Thr	Leu	Glu	Pro	Lys	Thr	Val	Cys	Tyr	Tyr	Glu
545				550				555				560			
Ser	Trp	Val	His	Trp	Arg	Gln	Gly	Glu	Gly	Lys	Met	Asp	Pro	Glu	Asp
565				570				575							
Ile	Asp	Thr	Ser	Leu	Cys	Thr	His	Ile	Val	Tyr	Ser	Tyr	Phe	Gly	Ile
580				585				590							
Asp	Ala	Ala	Thr	His	Glu	Ile	Lys	Leu	Leu	Asp	Glu	Tyr	Leu	Met	Lys
595				600				605							
Asp	Leu	His	Asp	Met	Glu	His	Phe	Thr	Gln	His	Lys	Gly	Asn	Ala	Lys
610				615				620							
Ala	Met	Ile	Ala	Val	Gly	Gly	Ser	Thr	Met	Ser	Asp	Gln	Phe	Ser	Lys
625				630				635				640			
Thr	Ala	Ala	Val	Glu	His	Tyr	Arg	Glu	Thr	Phe	Val	Val	Ser	Thr	Val
645				650				655							
Asp	Leu	Met	Thr	Arg	Tyr	Gly	Phe	Asp	Gly	Val	Met	Ile	Asp	Trp	Ser
660				665				670							
Gly	Met	Gln	Ala	Lys	Asp	Ser	Asp	Asn	Phe	Ile	Lys	Leu	Leu	Asp	Lys
675				680				685							
Phe	Asp	Glu	Asn	Tyr	Asn	Ile	Pro	Ala	Ile	Ser	Asn	Tyr	Val	Asp	Phe
690				695				700							
Met	Asn	Val	Leu	Ser	Leu	Asp	Tyr	Thr	Gly	Ser	Trp	Ala	His	Thr	Val
705				710				715				720			
Gly	His	Ala	Ser	Pro	Phe	Pro	Glu	Gln	Leu	Lys	Thr	Leu	Glu	Ala	Tyr

	725		730		735
His Lys Arg Gly Ala Pro Arg His Lys Met Val Met Ala Val Pro Phe					
	740		745		750
Tyr Ala Arg Thr Trp Ile Leu Glu Lys Met Asn Lys Gln Asp Ile Gly					
	755		760		765
Asp Lys Ala Ser Gly Pro Gly Pro Arg Gly Gln Phe Thr Gln Thr Asp					
	770		775		780
Gly Phe Leu Ser Tyr Asn Glu Leu Cys Val Gln Ile Gln Ala Glu Thr					
785		790		795	800
Asn Ala Phe Thr Ile Thr Arg Asp His Asp Asn Thr Ala Ile Tyr Ala					
	805		810		815
Val Tyr Val His Ser Asn His Ala Glu Trp Ile Ser Phe Glu Asp Arg					
	820		825		830
His Thr Leu Gly Glu Lys Ala Lys Asn Ile Thr Gln Gln Gly Tyr Ala					
	835		840		845
Gly Met Ser Val Tyr Thr Leu Ser Asn Glu Asp Val His Gly Val Cys					
	850		855		860
Gly Asp Lys Asn Pro Leu Leu His Ala Ile Gln Ser Asn Tyr Tyr His					
865		870		875	880
Gly Val Val Thr Glu Pro Thr Val Val Thr Leu Pro Pro Val Thr His					
	885		890		895
Thr Thr Glu His Val Thr Asp Ile Pro Gly Val Phe His Cys His Glu					
	900		905		910
Glu Gly Phe Phe Arg Asp Lys Thr Tyr Cys Ala Thr Tyr Tyr Glu Cys					
	915		920		925
Lys Lys Gly Asp Phe Gly Leu Glu Lys Thr Val His His Cys Ala Asn					
	930		935		940
His Leu Gln Ala Phe Asp Glu Val Ser Arg Thr Cys Ile Asp His Thr					
945		950		955	960
Lys Ile Pro Gly Cys					
	965				

<210> 110

<211> 965

<212> PRT

<213> 人工

<220>

<223> 合成构建物

<400> 110

Ser Ile Lys Arg Asp His Asn Asp Tyr Ser Lys Asn Pro Met Arg Ile

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

Ala Pro Tyr Gly Tyr Asn Asp Lys Ile Trp Val Gly Tyr Asp Asp Leu		
325	330	335
Ala Ser Ile Ser Cys Lys Leu Ala Phe Leu Lys Glu Leu Gly Val Ser		
340	345	350
Gly Val Met Val Trp Ser Leu Glu Asn Asp Asp Phe Lys Gly His Cys		
355	360	365
Gly Pro Lys Asn Pro Leu Leu Asn Lys Val His Asn Met Ile Asn Gly		
370	375	380
Asp Glu Lys Asn Ser Phe Glu Cys Ile Leu Gly Pro Ser Thr Thr Thr		
385	390	395
Pro Thr Pro Thr Thr Thr Pro Thr Thr Pro Thr Thr Thr Pro Thr Thr		
405	410	415
Pro Ser Pro Thr Thr Pro Thr Thr Thr Pro Ser Pro Thr Thr Pro Thr		
420	425	430
Thr Thr Pro Ser Pro Thr Thr Pro Thr Thr Thr Pro Ser Pro Thr Thr		
435	440	445
Pro Thr Pro Thr Thr Pro Thr Pro Ala Pro Thr Thr Ser Thr Pro Ser		
450	455	460
Pro Thr Thr Thr Glu His Thr Ser Glu Thr Pro Lys Tyr Thr Thr Tyr		
465	470	475
Val Asp Gly His Leu Ile Lys Cys Tyr Lys Glu Gly Asp Ile Pro His		
485	490	495
Pro Thr Asn Ile His Lys Tyr Leu Val Cys Glu Phe Val Asn Gly Gly		
500	505	510
Trp Trp Val His Ile Met Pro Cys Pro Pro Gly Thr Ile Trp Cys Gln		
515	520	525
Glu Lys Leu Thr Cys Ile Gly Glu Gly Pro Gly Pro Gly Ser Asn Ile		
530	535	540
Arg Pro Asn Val Ala Thr Leu Glu Pro Lys Thr Val Cys Tyr Tyr Glu		
545	550	555
Ser Trp Val His Trp Arg Gln Gly Glu Gly Lys Met Asp Pro Glu Asp		
565	570	575
Ile Asp Thr Ser Leu Cys Thr His Ile Val Tyr Ser Tyr Phe Gly Ile		
580	585	590
Asp Ala Ala Thr His Glu Ile Lys Leu Leu Asp Glu Tyr Leu Met Lys		
595	600	605
Asp Leu His Asp Met Glu His Phe Thr Gln His Lys Gly Asn Ala Lys		
610	615	620
Ala Met Ile Ala Val Gly Gly Ser Thr Met Ser Asp Gln Phe Ser Lys		

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

His	Leu	Gln	Ala	Phe	Asp	Glu	Val	Ser	Arg	Thr	Cys	Ile	Asp	His	Thr
945					950					955					960
Lys	Ile	Pro	Gly	Cys											
				965											

在构建物中使用的人类LAMP-1跨膜/胞质尾区的部分

(人类全长Lamp-1序列的第383-417位氨基酸) (SEQ ID NO: 1)

LIPIAVGGALAGLVLIIVLIAYLVGRKRSHAGYQTI

在构建物中使用的人类LAMP-1腔内结构域的部分 (全长Lamp-1序列的第3-381位氨基酸) (SEQ ID NO: 2)

APRSARRPLLLLLLLLLLLGLMHCAAMFMVKNNGTACIMANFSAAFVNNDTKSGPK
NMTLDLPSDATVVLNRSSCGKENTSDPSLVIAFGRGHTLTNLNFTRNATRYSVQLMSFVY
NLSDTLHLPNASSKEIKTVESITDIRADIDKKYRCVSGTQVHMNNVTVTLHDATIQAYL
SNSFSRGETRCEQDRPSPTTAPPAPPSPSPSPVVKSPSVDKYNVSGTNGTCLLASMGL
QLNLTYERKDNTTVTRLLNINPNKTSASGSCGAHLVTLELHSEGTTVLLFQFGMNASS
RFFLQGIQLNTILPDARDPAFKAANGSLRALQATVGNSYKCNAAEEHVRVTKAFSVNIFK
VWVQAFKVEGGQFGSVEECLLDENS

构建物中包含的5' 序列 (SEQ ID NO: 3)

MAPRSARRPLLLLLLLLLLLGLMHCAAMFMVKNNGTACIMANFSAAFVNNDTKSGP
KNMTLDLPSDATVVLNRSSCGKENTSDPSLVIAFGRGHTLTNLNFTRNATRYSVQLMSFV
YNLSDTLHLPNASSKEIKTVESITDIRADIDKKYRCVSGTQVHMNNVTVTLHDATIQAY
LSNSSFSRGETRCEQDRPSPTTAPPAPPSPSPSPVVKSPSVDKYNVSGTNGTCLLASM
LQLNLTYERKDNTTVTRLLNINPNKTSASGSCGAHLVTLELHSEGTTVLLFQFGMNASS
SRFFLQGIQLNTILPDARDPAFKAANGSLRALQATVGNSYKCNAAEEHVRVTKAFSVNIF
KVWVQAFKVEGGQFGSVEECLLDENSLE

图1

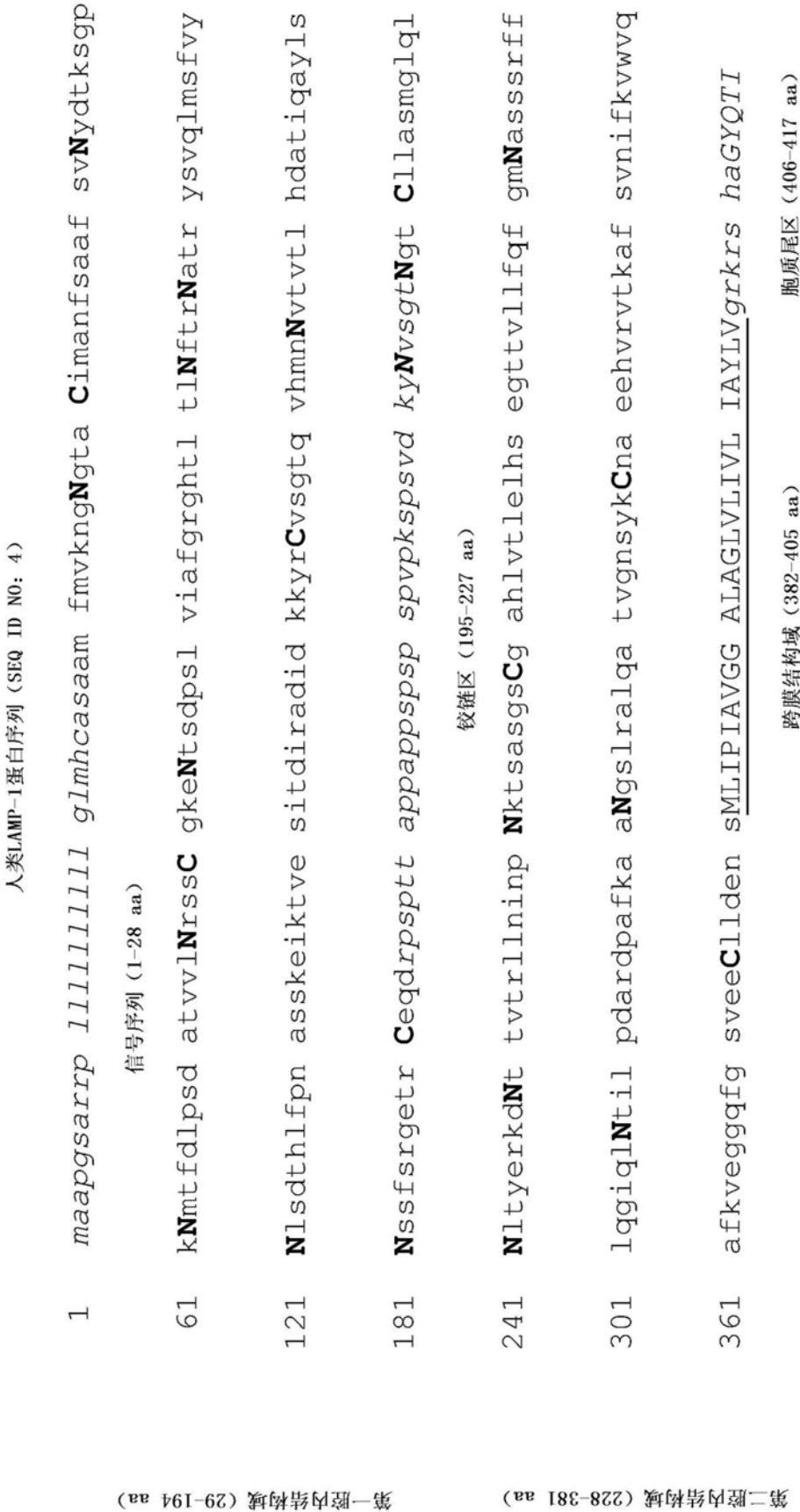


图2

254

对于构建物, 将序列高亮显示如下: **hLAMP 信号肽-hLAMP 腔内结构域-CTCGAG-抗原-GAATTC-hLAMP TM 和 Cyto 结构域**

SEQ ID NO:7 Cor a 1 氨基酸 (1-159)

MGVFCYEDEATSVIPPARLFKSFVLDADNLIPKVAPQHFTSAENLEGNGGPGTIKKITFAEGNEFKYMKH
KVVEIDHANFKYCYSIIIEGGPLGHTLEKISYEIKMAAAPHHGGGSILKITSKYHTKGNASINEEEIKAGKE
KAAGLFKAVEAYLLAHPDAY

编码Cor a 1的多核苷酸序列(侧接大写字母的XhoI-EcoRI)(SEQ ID NO:6)

CTCGAGatgggcggtgttctgctacgaggacgaggccacaagcgatccctcccgccagactgttcaaga
gcttcgtgctggacgcccgaacatctgatcccaaaagtggccccccagcacttcaccagcgccgagaatct
ggaaggcaatggcggacccggcaccatcaagaagatcacattcgccgagggcaacgagttcaagtacatg
aagcacaaagtggagagatcgaccacgccaacttcaagtactgctacagcatcatcgaaggcggccctc
tgggcccacacactggaaaagatcagctacgagatcaagatggccgctgcccctcacggcggagggcagcat
tctgaagatcaccagcaagtaccacaccaagggaacgcccagcatcaacgaggaagaaatcaaggccggc
aaagagaaagccgcccggactgtttaaggccgtggaagcctatctgctggcccaccccgatgcctacGAAT
TC

SEQ ID NO:9 Cor a 9 氨基酸 (24-320)

INVGLRRQQQRYFGECNLDRLNALEPTNRIEAEACQIESWDHNDQQFQCAGVAVIRRTIEPNGLLLPQYS
NAPELIYIERGRGITGVLFPGCPETFEDPQQQSQQGQROGQSQRSEQDRHQKIRHFREGDIIALPAGV
AHWCYNDGDSPPVTVSLHTNNYANQLDENPRHFYLAGNPDDHQRQGGQQFGQRRRQQQHSHEQGEQE
QQGEGNNVFSGFDAEFLADAFNVDVDTARRLQSNQDKRNRIVKVEGRLQVVRPERSRQEWERQERQERES
EQERERQRRQGGGRDGVN

编码Cor a 9的多核苷酸(改进的)(侧接大写字母的XhoI-EcoRI)(SEQ ID NO:8)

CTCGAGatcaacgtgggactgaggagacagcagcagcggtacttcggcgagtgcaatctggaccggctga
acgctctggaaccaccaaagagaatcgaggccgaggttgccagatcgagagctgggaccacaacgacca
gcagttccagtgtgctggcgtggcgtgatcagacggaccatcgagcccaacggactgctgctgccccag
tacagcaatgccccgagctgatctacatcgagcggggcagaggaatcaccggcgtgctgtttccgggt
gccccgagacattcgaggaccctcagcagcagagccagcaaggccagagacaaggccaaggccagtccca
gagaagcgagcaagaccggcaccagaagatccggcacttcagagagggcgacatcattgctctgccagcc
ggcgtggcccactggtgctacaatgatggcgatagcccgtcgtagccgtgtctctgctgcacaccaaca
actacgccaaccagctggacgagaaccccagacacttctatctggccggcaaccccagcagcagcagca
gaggcaaggggcagcagcagttcgccagagaagaaggcagcagcagcagccatggcgagcaaggcgag
caagagcagcaaggcgagggcaacaacgtgttcagcggcttcgacgccgagtttctggccgacgccttca
acgtggacgtggacacagccagacggctgcagtcacaacgaagacaagcggcggaacatcgtgaaagtgga
aggccggctccaagtcgtgcccggcagagatctagacaagagtgggagcggcaagagcggcaagaacgc
gagagcgagcaagagagagagcggcagagaaggcaaggcggcagagggcagagatgtgaacGAATTC

SEQ ID NO:11 Cor a 1-Gly 4-Cor a 9 氨基酸

MGVFCYEDEATSVIPPARLFKSFVLDADNLIPKVAPQHFTSAENLEGNGGPGTIKKITFAEGNEFKYMKH
KVVEIDHANFKYCYSIIIEGGPLGHTLEKISYEIKMAAAPHHGGGSILKITSKYHTKGNASINEEEIKAGKE

对于构建物，将序列高亮显示如下：**hLAMP 信号肽-hLAMP 腔内结构域-CTCGAG-抗原-GAATTC-hLAMP TM 和 Cyto 结构域**

KAAGLFKAVEAYLLAHPDAYGGGGINVGLRRQQRYFGEENLDRLNALEPTNRIEAEACQIESWDHNDQQ
FQCAGVAVIRRTIEPNGLLLPQYSNAPELIYIERGRGITGVLFPGCPETFEDPQQQSQQGQRQGGQSQR
SEQDRHQKIRHFREGDIIALPAGVAHWCYNDGSDPVVTVSLLHTNNYANQLDENPRHFYLAGNPDEHQR
QGQQQFGQRRRQQQHSHEGEQEQGEGNNVFSGFDAEFLADAFNVDVDTARRLQSNQDKRRNIVKVEG
RLQVVRPERSRQEWERQERERESEQERERQRRQGGGRDGVN

编码Cor a 1-GLY4-Cor a 9的多核苷酸 (SEQ ID NO:10) (大写字母的XhoI-EcoRI和Gly4连接物)

CATATGCTCGAGatgggctgttctgctacgaggacgaggccacaagcgtgatccctcccgcagactgt
tcaagagcttctgctggacgcccacaatctgatccccaaagtggccccccagcacttcaaccagcgccga
gaatctggaaggcaatggcggaccggcaccatcaagaagatcacattcgccgaggggcaacgagttcaag
tacatgaagcacaagtggaagagatcgaccagccaaacttcaagtactgctacagcatcatcgaaggcg
gcccctctggccacacactggaagagatcagctacgagatcaagatggccgctgcccctcacggcgagg
cagcattctgaagatcaccagcaagtaccacaccaaggggcaacgccagcatcaacgaggaagaaatcaag
gcccggcaagagaaagccgcccgaactgtttaaggccgtggaagcctatctgctggcccaccccgatgct
acGGCGGAGGGGGCcatcaacgtgggactgaggagacagcagcagcggacttctggcgagtgcaatctgga
ccggtgaacgctctggaaccaccaacagaatcgaggccgaggcttgccagatcgagagctgggaccac
aacgaccagcagttccagtgtgctggcgtggcgtgatcagacggaccatcgagcccaacggactgctgc
tgccccagtacagcaatgccccgagctgatctacatcgagcggggcagaggaatcacggcgctgctgtt
tccccgctgccccgagacattcgaggaccctcagcagcagagccagcaaggccagagacaaggccaaggc
cagtcaccagagaagcgagcaagaccggcaccagaagatccggcacttcagagagggcgacatcattgctc
tgccagccggcgtggccactggtgctacaatgatggcgatagccccgtcgtgaccgtgtctctgctgca
caccaacaactacgccaaccagctggacgagaaccccagacacttctatctggccggcaaccccagcagc
gagcaccagaggcaaggcgagcagcagcttcggccagagaagaaggcagcagcagcagcagccatggcgagc
aaggcgagcaagagcagcaaggcgagggaacaacgtgttcagcggcttcgacgccgagtttctggccga
cgcttcaacgtggacgtggacacagccagacggctgcagtccaaccaagacaagcgccggaacatcgtg
aaagtggaaggccggctccaagtcgtgcgcccgagagatctagacaagagtgaggagcggaagagcggc
aagaacgcgagagcgagcaagagagagagcggcagagaaggcaaggcgccagaggcagagatgtgaacGA
ATTCGTCGAC

SEQ ID NO:13 Pru du 6 氨基酸 (26-272)

ARQSQLSPQNQCQLNQLQAREPDNRIQAEAGQIETWNFNQEDFQCAGVAASRITIQRNLHLPSYSNAPQ
LIYIVQGRGVLGAVFSGCPETFEESSQSSQQGRQEQEQEQERQQQQQGEQGRQQQQEQEQQERQGRQQGRQ
QQEEGRQQEQQQGQQGRPQQQQQFRQFDRHQKTRRIREGDVVAIPAGVAYWSYNDGDQELVAVNLFHVSS
DHNQLDQNPVKFYLAGNPENEFNQGGQSQPRQQGEQGRPGQHQQPFGRPRQQEQQGSGNNVFSGFNTQLL
AQAQNVNEETARNLQGQNDNRNQIIRVRGNLDFVQPPRGRQEREHEERQQEQQLQEQERQQQGGQLMAN

编码Pru du 6的多核苷酸 (SEQ ID NO:12) (侧接大写字母的XhoI-EcoRI)

CTCGAGgccagacagagccagctgagccccagaatcagtgccagctgaaccagctgcaagccagagagc
ccgacaaccggattcaagccgaggccggccagatcgagacatggaacttcaaccaagaggacttccagtg
tgccggcgtggccgcccagcagaatcaccatccagcggaaacggactgcattgcccagctacagcaacgcc
ccccagctgatctacatcgtgcaaggcagaggcgtgctggcgccgtgtttagcggatgccccgagacat
tcgaggaaagccagcagagcagccagcaaggccggcagcaagagcaagaacaagagagacaacagcagca
gcaaggggagcaaggcagacagcaaggacagcaagagcagcagcaagagcgccaaggacggcagcaagg
cgccagcagcaagaagaggcgacagcaagaacagcagcaaggccagcaaggcgccctcagcagcagc

对于构建物，将序列高亮显示如下：**hLAMP 信号肽**-**hLAMP 腔内结构域**-**CTCGAG-抗原-GAATTC-hLAMP TM 和 Cyto 结构域**

agcagttccggcagttcgaccggcaccagaaaacccggcgatcagagaaggcgacgtggtggctattcc
agccgggggtggcctactggtcctacaacgacggcgaccaagaactggtggcgtgaatctgttccacgtg
tccagcgaccacaaccagctggaccagaacccccggaagttctatctggctggcaaccccgagaacgagt
tcaaccagcaagggcagagccagcccagacagcaaggcggaacaaggacggcccgacagcaccagcagcc
tttcggcagaccacggcagcaagagcagcaaggcagcggcaacaacgtgttcagcggcttcaacaccag
ctgctggcccaagctctgaacgtgaacgaggaacccggccgaatctgcaaggccagaacgacaacagaa
accagatcatcagagtgccggggcaatctggacttctgagccccctagagggcggaagagagagagca
cgaagagaggcagcaagaacagctgcagcaagagcggcagcagcaaggcgacagctgatggccaacGAA
TTC

SEQ ID NO:15 Ana o 1 氨基酸 (27-538)

KIDPELKQCKHQCKVQRQYDEQQKEQCVKECEKYKKEKGREREHEEEEEEWGTGGVDEPSTHEPAEKHL
SQCMRQCERQEGGQQQLCRFRCQERYKKERGQHNYKREDDDEDEDEAEEDENPYVFEDEDFTTKVKT
EQGKVLLPKFTQKSKLLHALEKYRLAVLVANPQAFVVP SHMDADSIFFVSWGRGTITKILENKRESINV
RQGDIVSISSTGPFYIANNDENEKLYLVQFLRPVNLPGHFVVFHGPGENPESFYRAFWEILEAALKTS
KDTLEKLFQKQDQGTIMKASKEQIRAMSRRGEGPKIWPFTTEESTGSFKLFKKDPSQSNKYQLFEAERID
YPPLEKLDVVSYANITKGGMSVFPFYNRSRATKIAIVVSGEGCVEIACPHLSSSKSSHPSYKKLRARIRKD
TVFIVPAGHPFATVASGNENLEIVCFEVNAEGNIRYTLAGKKNIIKVMEKEAKELEAFKMEGEEVDKVF GK
QDEEFFFGPEWRKEKEGRADE

编码Ana o 1的多核苷酸 (SEQ ID NO:14) (侧接大写字母的XhoI-EcoRI)

CTCGAGaagatcgaccccgagctgaagcagtgcaagcaccagtgcaaagtgcagcggcagtagcagcagc
agcagaaaagaacagtgctgaaagagtgcgagaaagtactacaaagagaagaagggccgcgagcgcgagca
cgaagaggaagaggaagaatggggcaccggcgagtgacgagccttctacacacgagcccgccgagaaa
catctgagccagtgcatgagacagtgcaaacggcaagagggcgccagcagaaaacagctgtgccggttcc
gggtgccaagagcgggtacaagaaagagcggggccagcacaaactacaagagagaggacgacgaggacgaaga
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aaaaccgagcaaggcaaaagtgggtgctgctgcccaggttcacccagaagtccaagctgctgcacgctctgg
aaaagtaccggctggcgttctgggtggccaaccctcaagccttcgtgggtgccagccaatggacgccga
cagcatcttctctgctgtcttggggcagaggcaccatcaccaagattctggaaaacaagcgcgagagcatc
aacgtgcggaaggcgacatcgtgtccatcagcagcggcaccoccttctacattgccaacaacgacgaga
acgagaagctgtatctgggtgcagtttctgcggcccgatgaatctgcccgccactttgaagtgttccacgg
accggcgagagagaaccccgagagcttctacagagccttcagctgggaaattctggaagccgctctgaaa
acatccaaggacacactggaaaagctgttcgagaagcaagaccaagggaaccatcatgaaggccagcaaa
aacagatccggggccatgagcagaagaggcgagggccccaagatctggcccttcaccgaggaaagcaccgg
cagcttcaagctgtttaagaaggaccccagccagagcaacaaatacgggcagctgtttgaggccgagcgg
atcgactacccccactggaaaagctggacatgggtggtgtcctacgccaatcaccaaggcgccgcatga
gcgtgcccttttacaacagcagagccaccaagatcgccatcgtggtgtccggcgagggtgcgtggaaat
cgcttgccctcatctgagcagcagcaagtcagccaccccagctacaagaagctgcggggccagaatccgg
aaggacaccgtgttcctgctgccagccggccacccttttgccacagtgccagcggcaacgagaatctgg
aaatcgtgtgcttcgaagtgaacgccgaggggaacatccggtacacactggccggcaagaagaacatcat
caaagtgatggaaaaggaagccaaagaactggcctttaagatggaaggcgagggaagtggacaaagtgttc
ggcaagcaagatgaagagttcttctttcaaggccccgagtggcgcaagagaaaagagggcgagccgacg
agGAATTC

SEQ ID NO:17 Ana o 2 氨基酸 (1-457)

对于构建物，将序列高亮显示如下：**hLAMP 信号肽**-hLAMP 腔内结构

域-CTCGAG-抗原-GAATTC-hLAMP TM 和 Cyto 结构域

LSVCFLLILFHGCLASRQEWQQQDECQIDRLDALEPDNRVEYEAGTVEAWDPNHEQFRCAGVALVRHTIQP
NGLLLPQYSNAPQLIYVVQEGMTGISYPGCPETYQAPQQGRQQGQSGRFQDRHQKIRRFRRGDIIAIPA
GVAHWCYNEGNSPVVTVTLDDVSNSQNQLDRTPRKFHLAAGNPKDVFQQQQHQSRGRNLFSGFDTELLAE
AFQVDERLIKQLKSEDNRRGIVKVKDDELVRIRPSRSQSERGSESEEESEDEKRRWGQRDNIEETICTM
RLKENINDPARADIYTPEVGRLTTLNSLNLPIILKWLQLSVEKGVLYKNALVLPWNLSHSIIYGCKGKG
QVQVVDNFGNRVFDGEVREGQMLVVPQNFVVKRAREERFEWISFKTNDRAMTSPLAGRTSVLGGMPPEEV
LANAFQISREDARKIKFNNQQTTLTSGESSHMRDDA

编码Ana o 2的多核苷酸 (SEQ ID NO:16) (侧接大写字母的XhoI-EcoRI)

CTCGAGctgagcgtgtgctttctgattctgttccacggctgtctggccagccgggaagaatggcagcagc
aagacgagtgccagatcgaccggctggacgctctggaacccgacaaccgggtggaatacgagggcggcac
agtggaagcttgggaccccaaccacgagcagttcagatgtgccggcgtggcactcgtgccgcacaccatc
cagccaaacggactgctgctgccccagtagcgaacgccccccagctgatctatgtggtgcaaggcgagg
gcatgaccggcatcagctatcccggtgccccgagacatatcaagcccctcagcaaggcagacagcaagg
ccagagcggcggttccaagaccggcaccagaagatccggcggttcagacggggcgacatcattgccatt
ccagccgggggtggcccactggtgctacaacgaggggcaatagccccgtcgtgaccgtgacactgctggacg
tgtccaacagccagaaccagctggaccggaccccccggaagtttcatctggccgggaaccccaaggacgt
gttccagcaacagcagcagcaccagagccggggcagaaatctgttcagcgggttcgacaccgagctgctg
gccgaggttttcaagtggacgagcggctgatcaagcagctgaagtcgaggacaacagaggcggcatcg
tgaaagtgaaggacgacgagctgagagtgatccggcccagcagaagccagagcgagagaggcagcgagag
cgaggaagagtctgaggacgagaagcggagatggggccagcgggacaacggcatcgaagagacaatctgc
accatgcggtgaaagagaacatcaacgacccccgacagagccgacatctacacccccgaagtgggcgggc
tgacaactctgaactctctgaatctgcccattctgaagtggctgcagctgtccgtggaaaaggggggtgct
gtacaagaacgctctggtgctgctcactggaatctgaacagccacagcatcatctacggctgcaagggc
aagggccaagtccaagtggaggacaacttcggcaacagagtggttcgacggcggaagtgcgcgagggccaga
tgctcgtggtgccccagaatttcgccgtcgtgaagcggggccagagaagaaagattcgagtggtatcagctt
caagaccaacgaccgggcatgaccagccctctggccggaagaacatctgtgctgggcggcatgcccgag
gaagtgtggttaacgccttcagatcagcagagaggacgcccgggaagatcaagttcaacaaccagcaga
ccactgaccagcggcgagagcagccaccacatgagagatgacgccGAATTC

SEQ ID NO:19 Ana o 3 氨基酸 (21-138)

SIYRAIVEVEEDSGREQSCQRQFEEQQRFRNCQRYVKQEVQRGGRYNQRQESLRECCQELQEVDRRCRCQ
NLEQMVRQLQQQEIKGEEVRELYETASELPRICSISPSQGCQFQSSY

编码Ana o 3的多核苷酸 (SEQ ID NO:18) (侧接大写字母的XhoI-EcoRI)

CTCGAGagcatctaccgggcatcgtggaagtggaagaggacagcggcagagagcagagctgccagcggc
agttcgaggaacagcagcgggttcagaaactgccagagatacgtgaagcaagaagtgcagagaggcggcag
atacaaccagagacaagagtctctgagagagtgctgccaagagctgcaagaagtggaccggcgctgccgg
tgccagaatctggaacagatggtgcgccagctgcagcagcaagagcagatcaagggcgaggaagtgcgcg
agctgtacgagacagccagcagctgcctcgatctgcagcatcagcccaagccaaggctgccagttcca
gacagctacGAATTC

SEQ ID NO:21 Ana o 2-Gly4-Ana o 1-Gly4-Ana o 3 氨基酸

LSVCFLLILFHGCLASRQEWQQQDECQIDRLDALEPDNRVEYEAGTVEAWDPNHEQFRCAGVALVRHTIQP
NGLLLPQYSNAPQLIYVVQEGMTGISYPGCPETYQAPQQGRQQGQSGRFQDRHQKIRRFRRGDIIAIPA

对于构建物，将序列高亮显示如下：**hLAMP 信号肽**-hLAMP 腔内结构

域-CTCGAG-抗原-GAATTC-hLAMP TM 和 Cyto 结构域

GVAHWCYNEGNSPVVTVTLLDVSNSQNLDRTPRKFLHAGNPKDVFQOQOQHOSRGRNLFSGFDTELLAE
AFQVDERLIKQLKSEDNRRGGIVKVKDELVRIPSRSSQSERGSESEEESEDEKRRWGORNDNGIETICTM
RLKENINDPARADIYTPEVGRLLTTLNSLNLPLILKWLQLSVEKGVLYKNALVLPWWNLNSHSIIYGCKGKG
QVQVVDNFGNRVFDGEVREGQMLVVPQNFVAVVKRAREERFEWISFKTNDRAMTSPLAGRTSVLGGMPPEEV
LANAFQISREDARKIKFNNQQTTLTSGESSHMRDDA**GGGG**KIDPELKQCKHQCKVQRQYDEQQKEQCV
KECEKYYKEKKGREREHEEEEEEWGTGGVDEPSTHEPAEKHLSQCMRQCERQEGGQKQLCRFRQCERYK
KERGQHNYKREDEDEDEDEAEEDENPYVFEDEDFTTKVKTEQGKVLLPKFTQKSKLLHALEKYRLAV
LVANPQAFVVP SHMDADSIFFVSWGRGTITKILENKRESINVRQGDIVSISGTFPIYIANNDENEKLYLV
QFLRPVNLPGHFVFGPGGENPESFYRAF SWEILEAALKTSKDTLEKLFKQDQGTIMKASKEQIRAMS
RRGEGPKIWPFTTEESTGSFKLFKKDPSQSNKYQLFEAERIDYPPLEKLDVVSYANITKGGMSVPPFYN
RATKIAIVVSGEGCVEIACPHLSSSKSSHP SYKKLRARIRKDTVFIVPAGHPFATVASGNENLEIVCFEV
NAEGNIRYTLAGKKNIIKVMEKEAKELAFKMEGEEVDKVF GKQDEEFFFGPEWRKEKEGRADE**GGGGS**
IYRAIVEVEEDSGREQSCQRQFEEQQRFRNCQRYVKQEVQRGGRYNQREQSLRECCQELQEVDRRCRCQN
LEQMVRQLQQQEIQIKGEEVRELYETASELPRICSISSPQGCQFQSSY

编码Ana 0 2-Gly4-Ana 0 1-Gly4-Ana 0 3的多核苷酸 (SEQ ID NO:20)

CTCGAGctgagcgtgtgctttctgattctgttccacggctgtctggccagccggcaagaatggcagcagc
aagacgagtgccagatcgaccggctggacgctctggaacccgacaaccgggtggaatcagagccgggcac
agtggagcttgggaccccaaccacgagcagttcagatgtgccggcgtggcactcgtgccgcacaccatc
cagccaaacggactgctgctgcccagtagcgaacgccccccagctgatctatgtggtgcaaggcgagg
gcatgaccggcatcagctatcccggtgccccgagacatataagccctcagcaaggcagacagcaagg
ccagagcggcggttccaagaccggcaccagaagatccggcggttcagacggggcgacatcattgccatt
ccagcgggggtggccactggtgctacaacgagggcaatagcccgctcgtgaccgtgacactgctggacg
tgtccaacagccagaaccagctggaccggaccccccggaagtttcatctggccggcaaccccaaggacgt
gttccagcaacagcagcagcaccagagccggggcgagaaatctgttcagcggttcgacaccgagctgctg
gccgaggttttcaagtggacgagcggctgatcaagcagctgaagtccgaggacaacagaggcgccatcg
tgaaagtgaaggacgagcagctgagagtgatccggcccagcagaagccagagcgagagagggcagcgagag
cgaggaagagctgaggagcagaagcggagatggggccagcgggacaacggcatcgaagagacaatctgc
accatcggtgctgaaagagaacatcaacgaccccgccagagccgacatctacaccccggaagtgggcggc
tgacaactctgaactctctgaatctgccattctgaagtggctgcagctgtccgtggaaaagggggtgct
gtacaagaacgctctggtgctgctcactggaatctgaacagccacagcatcatctacggctgcaagggc
aagggccaagtccaagtggtggacaacttcggcaacagagtggtcgacggcggaagtgcgcgagggccaga
tgctcgtggtgccccagaatttcgccgtcgtgaagcggggccagagaagaaagattcgagtgatcagctt
caagaccaacgacccgggcatgaccagccctctggccggaagaacatctgtgctgggcggcatgcccgag
gaagtgctggttaacgccttcagatcagcagagaggacgcccgggaagatcaagttcaacaaccagcaga
ccacactgaccagcggcgagagcagccaccacatgagagatgacgcc**GGCGGAGGGGGC**aagatcgacc
cgagctgaagcagtgcaagcaccagtgcaagtgtagcgggcagtagcagcagcagcagaagaacagtg
gtgaaagagtgcgagaagtagtactacaagagaagaagggccgagcgcgagcagcagaagaggaaggaag
aatggggcaccggcgagtgtagcagccttctacacacgagcccgccagaaacatctgagccagtgcat
gagacagtgcaacggcaagagggcgccagcagaacagctgtgccggttcgggtgccaagagcggtac
aagaaagagcggggccagcacaactacaagagagaggacgacgaggacgaagatgaggacgaggctgagg
aagaggacgagaacccctacgtgttcgaggatgaggacttcaccaccaaagtgaaaaccgagcaaggcaa
agtgggtgctgctgcccagttcaccacagaagccaagctgctgcacgctctggaaaagtaccggctggcc
gttctggtggccaacccctcaagccttcgtggtgcccagccacatggacgcccagacagcatcttctctggt
cttggggcagaggcaccatcaccaagattctggaaaacaagcgcgagagcatcaacgtgcggcaaggcga

对于构建物，将序列高亮显示如下：**hLAMP 信号肽**-hLAMP 腔内结构

域-CTCGAG-抗原-GAATTC-hLAMP TM 和 Cyto 结构域

catcgtgtccatcagcagcggcacccttctacattgccacaacgacgagaacgagaagctgtatctg
gtgcagtttctgcgcccgctgaatctgcccgccactttgaagtgttccacggaccggcgagagaacc
ccgagagcttctacagagccttcagctgggaattctggaagccgctctgaaaacatccaaggacacact
ggaaaagctgttcgagaagcaagaccaaggaccatcatgaaggccagcaaagaacagatccgggccatg
agcagaagaggcgaggggccccaagatctggcccttcaccgaggaaagcacccggcagcttcaagctgttta
agaaggaccccagccagagcaacaaatcgggcagctgtttgaggccgagcggatcgactacccccact
ggaaaagctggacatggtggtgtcctacgccaatatcaccaaggcgccatgagcgtgcccttttacaac
agcagagccaccaagatcgccatcgtggtgtcggcgagggtgctggtggaatcgcttgccctcatctga
gcagcagcaagtccagccaccccagctacaagaagctgcgggccagaatccggaaggacaccgtgttcac
cgtgccagccggccacccttttgccacagtggccagcggaacgagaatctggaaatcgtgtgcttcgaa
gtgaacgccgagggcaacatccggtacacactggccggcaagaagaacatcatcaaagtgatggaaaagg
aagccaaagaactggcctttaagatggaaggcgagggaagtggacaaagtgttcggcaagcaagatgaaga
gttcttctttcaaggccccgagtgccgcaagagaaagagggcgagagccgacgag**GGCGGAGGGGGC**agc
atctaccgggccatcgtggaagtggaagaggacagcggcgagagagcagagctgccagcggcagttcgagg
aacagcagcgggttcagaaactgccagagatcgtgaagcaagaagtgcagagaggcggcagatacaacca
gagacaagagtctctgagagagtgtgccaagagctgcaagaagtggaccggcgctgccggtgccagaat
ctggaacagatggtgcccagctgcagcagcaagagcagatcaaggcgagggaagtgcgcgagctgtacg
agacagccagcagctgcctcggatctgcagcatcagcccaagccaaggctgccagttccagagcagcta
cGAATTC

SEQ ID NO:23 Jug n 1 氨基酸 (39-161)

RTTITIMEIDEDIDNPRRRGEGCQEQIQRQQLNHCQYYLRQQSRSGGYDEDNQHQHFRQCCQQLSQIEE
QCQCEGLRQAVRRQQQQGLRGEEMEEMVQSARDLPKECGISSQRCEIRRSWF

编码Jug n 1的多核苷酸 (SEQ ID NO:22) (侧接大写字母的XhoI-EcoRI)

CTCGAGcggaccaccatcaccaccatggaaatcgacgaggacatcgacaaccccagaagaagaggcgagg
gctgccaagagcagatccagcggcagcagaatctgaaccactgccagtactatctgaggcagcagagcag
aagcggcggtctacgacgaggataaccagagacagcacttcagacagtgtgcccagcagctgagccagatc
gaggaacagtgccagtgcgagggactgagacaagccgtgcggagacaacagcagcagcaaggactgcggg
gcgaagagatggaagaaatggtgcagagcgccagagatctgcccgaagagtgcggcatcagcagccagag
atgcgagatccggcggagttggttcGAATTC

SEQ ID NO:25 Jug r 2 氨基酸 (1-593)

RGRDDDEENPRDPREYRQCQEYCRQGQGRQQQQCQIRCEERLEEDQRSQEERERRRGRDVEDDQNPR
DPEQRYEQCQQQCERQRRGQEQTLRRRCERRRQEEERERQRGRDRQDPQQYHRCQRCQIQEQSPERQ
RQCQQRCEQYKEQQGRERGPEASPRRESRGREEEQQRHNPYYFHSQSIRSRHESEEGEVKYLERTERT
ELLRGIENYRVVILDANPNTSMLPHHKDAESVAVVTRGRATLTLVSQETRESFNLECGDVIRVPAGATVY
VINQDSNERLEMVKLLQPVNNPGQFREYYAAGAKSPDQSYLRVFSNDILVAALNTPRDRLERFFDQQEQR
EGVIRASQEKLRALSQHAMSAGQRPWGRSSGGPISLKSESPSYSNQFGQFFEACPEEHRQLQEMDVLV
NYAEIKRGAMMVPYNSKATVVVYVVEGTGRYEMACPHVSSQSYEGQGRREQEEEEESTGRFQKVTLARLAR
GDIFVIPAGHPAITASQENENLRLGFDINGENNQRDFLAGQNNIINQLEREAKELSFNMPREEIEEIFE
SQMESYFVPTERQSRRGQGRDHPLASILDFAFF

编码Jug r 2的多核苷酸 (SEQ ID NO:24) (侧接大写字母的XhoI-EcoRI)

对于构建物，将序列高亮显示如下：**hLAMP 信号肽-hLAMP 腔内结构**

域-CTCGAG-抗原-GAATTC-hLAMP TM 和 Cyto 结构域

CTCGAGagaggccgggacgacgacgatgaggaaaacccagagatccccgcgagcagtagccggcagtgcc
aagagtactgcagaaggcaaggccaaggccagagacagcagcagcagtgccagatcagatgcgaggaacg
gctggaagaggaccagcggagccaagaggaacgcgagcgggagaagaggcagagatgtggacgaccagaac
ccccgggaccccgagcagagatacgagcagtggtcagcagcagtggtgaacggcagcggagaggccaagagc
agacactgtgtcggcggagatgcgagcagcggcggcagcaagaggaaagagaacgccagcggggcagaga
cagacaagacccccagcagcagtagccaccgggtgccagagaagatgccagatccaagaacagagccccgag
cggcagcggcagtgccagcagagatgcgaaagacagtagcaaaagagcagcaaggcagagagagggggccag
aggccagccctagaagagagtgccagaggacgggaagaagaacagcagcggcacaaccctactacttcca
cagccagagcatcagaagccggcagcagagcgaagagggcggaagtgaagtatctggaacgggttcaccgag
cggaccgagctgctgagaggcatcgagaactaccgggtcgtgattctggacgccaacccaacacatcca
tgctgccccaccacaaggacgcgcagtgctgtggcggcgtcgtgacaaggggcagagccacactgacactggt
gtcccaagagactcgcgagagcttcaatctggaatgcggcgacgtgatccgggtgccagctgggggtaca
gtgtacgtgatcaaccaagacagcaacgagcgggtggaatggtcaagctgctgcagcccgtagaacaacc
ccggccagttcagagagtagtacgcgcgtggcgccaagtccccgaccagagctatctgcgggtgttcag
caacgacattctggtggcgcgtctgaataccctcgggacagactggaagattcttcgatcagcaagag
cagcgcgagggcgctgatcatcagagccagccaagagaagctgcgggctctgagccagcagccatgtctg
ctggacagaggccttggggcagaagaagctctggcgccctatctctctgaagtccgagagccctccta
cagcaaccagtttggccagttcttcgaggcttgcgccgaggaacaccggcagctgcaagaaatggacgtg
ctcgtgaactacgcgcgagatcaagaggggcgcctatgatggtgccccactacaacagcaaggccaccgtgg
tgggtgtacgtggtggaaggcaccggcagatcagagatggcatgccccacgtgtccagccagctcttacga
gggccaaggacgcagagagcaagaagaggaagagtgccaccggacgggtccagaaagtgaccgccagactg
gccagaggcgacatcttcgtgatcccagccggacaccctatcgccatcaccgccagccagaacgagaatc
tgccgctgctgggcttcgacatcaacggcgagaacaaccagcgggactttctggccggacagaacaacat
catcaaccagctggaacgggaagccaagaactgagcttcaacatgccccgcgaggaaatcgaagagatt
ttcgagagccagatggaagctacttcgtgcccaccgagcgcgcagagcagaaggggccaaggcgggatc
accactggcctctattctggatttcgccttcttcGAATTC

SEQ ID NO:27 Jug n 1-Gly4-Jug r 2 氨基酸

RTTITIMEIDEDIDNPRRRGEGCQEIQRQQLNHCQYYLRQQSRSGGYDEDNQRQHFRQCCQQLSQIEE
QCQCEGLRQAVRRQQQQQLRGEEMEEMVQSARDLPKECGISSQRCEIRRSWFGGGGRGRDDDDDEENPRD
PREQYRQCQEYCRRRQGQQRQQQCQIRCEERLEEDQRSQEERERRRRGRDVEDDQNPDPPEQRYEQCQQQC
ERQRRGQEQTLCRRRCQEQRQQEERERQRGRDRQDPQQQYHRCQRRRCQIQEQSPERQRCQQRRCERQYKE
QQGRERGPEASPRRESRGREEEQQRHNPYYFHSQSIRSRHESEEVEVKYLERFTELLRGIENYRVVI
LDANPNTSMLPHHKDAESVAVVTRGRATLTLVSQETRESFNLECGDVIRVPAGATVYVINQDSNERLEMV
KLLQPVNPNPGQFREYYAAGAKSPDQSYLRVFSNDILVAALNTPRDLERFFDQEQREGVIIRASQEKLR
ALSQHAMSAGQRPWGRSSGGPISLKSESPSYSNQFGQFFEACPEEHRQLQEMDVLVNYAEIKRGAMVP
HYNKATVVVYVVEGTGRYEMACPHVSSQSYEGQGRREQEEEEESTGRFQKVITARLARGDIFVIPAGHP
IATASQENENLRLLGFDINGENNQRDFLAGQNNIINQLEREAKELSFNMPREEIEEIFESQMESYFVPTERQ
SRRGQGRDHPLASILDFAFF

编码Jug n 1-Gly4-Jug r 2的多核苷酸（侧接大写字母的XhoI-EcoRI）(SEQ ID NO:26)

CTCGAGcggaccaccatcaccaccatggaaatcgacgaggacatcgacaaccccagaagaagaggcgagg
gctgccaagagcagatccagcggcagcagaatctgaaccactgccagtagctatctgaggcagcagagcag
aagcggcggtctacgacgaggataaaccagagacagcacttcagacagtgctgccagcagctgagccagatc
gaggaacagtgccagtgcgagggactgagacaagccgtgcggagacaacagcagcagcaaggactgcggg
gcgaagagatggaagaaatggtgcagagcgcgcagagatctgcccgaagagtgccggcatcagcagccagag

对于构建物，将序列高亮显示如下：**hLAMP 信号肽**-hLAMP 腔内结构

域-CTCGAG-抗原-GAATTC-hLAMP TM 和 Cyto 结构域

```
atgcgagatccggcgaggttggttcGGCGGAGGGGGCagaggccgggacgacacgatgaggaacccccc  
agagatccccgcgagcagtagccggcagtgccaagagtactgcagaaggcaaggccaaggccagagacagc  
agcagcagtgccagatcagatgcgaggaacggctggaagaggaccagcggagccaagaggaacgcgagcg  
gagaagaggcagagatgtggacgaccagaacccccgggacccccgagcagagatacagcagtggtcagcag  
cagtggtgaacggcagcggagaggccaagagcagacactgtgtcggcggagatgagcagcagcggcgccagc  
aagaggaaagagaacgccagcggggcagagacagacaagacccccagcagcagtagccaccgggtgccagag  
aagatgccagatccaagaacagagccccgagcggcagcggcagtgccagcagagatgcaaaagacagtagc  
aaagagcagcaaggcagagagagggggcccagaggccagccctagaagagagtgccagaggacgggaagaag  
aacagcagcggcacaacccccactacttccacagccagagcagtagcagaagccggcagcagagcgaagagg  
cgaagtgaagtatctggaacgggtcaccgagcggacccagagtgctgagaggcatcgagaactaccgggtc  
gtgattctggacgccaaacccccacacatccatgtgtccccaccacaaggacgccgagtgctgtggcgtcg  
tgacaaggggcagagccacactgacactgggtgtcccaagagactcgcgagagcttcaatctggaatggg  
cgacgtgatccgggtgccagtggtggtacagtgtagtgatcaaccaagacagcaacgagcgggtggaa  
atggtcaagctgctgcagcccgtagaacaacccccggccagtgccagagtagtagcccgctggcgccaagt  
ccccgaccagagctatctgcggtgttcagcaacgacattctggtggccgctctgaataccctcgggg  
cagactggaaagattcttcgatcagcaagagcagcgcgagggcgtagcatcagagccagccaagagaag  
ctgcgggtctgagccagcagccatgtgtgtggacagaggccttggggcagaagaagctctggcgggc  
ctatctctctgaagtccgagagccccctctacagcaaccagtggtggccagtgcttcgagggcttgccccga  
ggaacaccggcagctgcaagaaatggacgtgctcgtgaactacgccgagatcaagaggggagccatgatg  
gtgccccactacaacagcaaggccaccgtggtggtgtacgtggtggaaggcaccggcagatacagatgg  
catgccccacgtgtccagccagtgcttacgaggggccaaggacgcagagagcaagaagaggaagagtagc  
cggacggttccagaaagtgaccgcccagactggccagaggcgacatcttcgtgatccagccggacaccct  
atcgccatcaccgcccagccagaacgagaatctgcggctgctgggcttcgacatcaacggcgagaacaacc  
agcgggactttctggcggacagaacaacatcatcaaccagctggaacgggaagccaagaactgagctt  
caacatgccccgcgaggaatcgaagagattttcgagagccagatggaaagctacttcgtgcccaccgag  
cgccagagcagaagggggccaagggcgggatcacccactggcctctattctggatttcgccttcttcGAAT  
TC
```

SEQ ID NO:29 Amb a 1 氨基酸 (26-296)

AEDLQEILPVNETRRLTTSAYNIIDGCRWKADWAENRKALADCAQGFKGKTVGGKDGDIYTVTSELDD
DVANPKEGTLLRFAGAAQNRPLWIIIFERDMVIRLDKEMVNSDKTIDGRGAKVEIINAGFTLNGVKNV
IHNINMHDVKVNPGLIKSNDGPAAPRAGSDGDAISISGSSQIWDHCSLSKSVLDGLVDKLGTT
RLTVSNSLFTQHQFVLLFGAGDENIEDRGMLATVAFNTFTDNDQRMPCRHRGFFQVNNNYDKWGS
YAIGGSASPTILSQGNRFCAPDERSKKNVLGRHGEAAAESMKWNWRTNKDVLENGAI FVASGVDP
VLTPEQSAGMIPAEPEGESALSLTSSAGVLSCQPGAPC

SEQ ID NO:33 Bet v 1-A 氨基酸 (2-160)

GVFNYETETTSVIPAAARLFKAFILDGDNLFKVPAPQAISSVENIEGNGGPGTIKKISFPEGFP
FKYVKDRVDEV DHTNFKYNSVIEGGPIGDTLEKISNEIKIVATPDGGSILKISNKYHTKGD
HEVKAEQVKASKEMGETLLRAVESYLLAHSDAYN

SEQ ID NO:37 Can f 1 氨基酸 (19-174)

QDTPALGKDTVAVSGKWYLKAMTADQEVPEKPDSTVPMILKAQKGGNLEAKITMLTNGQCQNIT
VVLHKTSEPGKYTAYEGQRVFIQPSVRDHYILYCEGELHGRQIRMAKLLGRDPEQSQEAL
EDFREFSRAKGLNQEILELAQSETCSPGGQ

SEQ ID NO:41 Cyn d 1 氨基酸 (1-246)

对于构建物，将序列高亮显示如下：**hLAMP 信号肽**-hLAMP 腔内结构

域-CTCGAG-抗原-GAATTC-hLAMP TM 和 Cyto 结构域

AIGDKPGPNITATYGSKWLEARATFYGSNPRGAAPDDHGGACGYKDVKPPFDGMTACGNEPIFKDGLGC
RACYEIKCKEPVECSGEPVLVKITDKNYEHIAAYHFDLSGKAFGAMAKKGQEDKLKAGELTLQFRRVKC
KYPSTGKITFHIKGSNDHYLALLVKYAAGDGNIVAVDIKPRDSDEFIPMKSSWGAIWRIIDPKPLKGP
SIRLTSEGAHLVQDDVIPANWKPDVTYTSKLQFGA

SEQ ID NO:45 Der f 1 氨基酸 (19-321)

RPASIKTFEEFKAFNKNYATVEEEVARKNFLES�KYVEANKGAINHLSLDEFKNRYLMSAEAFEQ
LKTQFDLNAETSACRINSVNVPSSELDLRLSLRTVTPIRMQGGCGSCWAFSGVAATESAYLAYRNTSLDLSE
QELVDCASQHGCHGDTIPRGIEYIQQNGVVEERSYPYVAREQRCRRPNSQHYGISNYCQIYPPDVVKQIRE
ALTQHTAIAVIGIKDLRAFQHYDGRITIIQHDNGYQPNYHAVNIVGYGSTQGDDYWIVRNSWDTTWGDS
GYGYFQAGNNLMMIEQYPYVIM

SEQ ID NO:49 Der f 1 氨基酸 (99-321)

TSACRINSVNVPSSELDLRLSLRTVTPIRMQGGCGSCWAFSGVAATESAYLAYRNTSLDLSEQELVDCASQ
HGCHGDTIPRGIEYIQQNGVVEERSYPYVAREQRCRRPNSQHYGISNYCQIYPPDVVKQIREALTQHTAIA
VIGIKDLRAFQHYDGRITIIQHDNGYQPNYHAVNIVGYGSTQGDDYWIVRNSWDTTWGDSGYGYFQAGNN
LMMIEQYPYVIM

SEQ ID NO:53 Der p 2 氨基酸 (18-146)

DQVDVKDCANHEIKKVLVPGCHGSEPCIIHRGKPFQLEAVFEANQNTKTAKIEIKASIDGLEVDVPGIDP
NACHYMKCPLVKGQYDIKYTWNVPKIAPKSENVVTVKVMGDDGVLACAIATHAKIRD

SEQ ID NO:57 Der f 2 氨基酸 (18-146)

DQVDVKDCANNEIKKVMVDGCHGSDPCIIHRGKPFLEALFDANQNTKTAKIEVKASLDGLEIDVPGIDT
NACHFVKCPLVKGQYDIKYTWNVPKIAPKSENVVTVKLIGDNGVLACAIATHGKIRD

SEQ ID NO:61 Der p 1 (DEL) 氨基酸 (1-26:38-223)

TNACSINGNAPAEIDLRQMRTVTPIRSGVAATESAYLAYRNQSLDLAEQELVDCASQHNGCHGDTIPRGI
EYIQHNGVVQESYRYVAREQSCRPNQRFGISNYCQIYPQNVNKIREALQTHSAIAVIGIKDLDAF
RHYDGRITIIQRDNGYQPNYHAVNIVGYSNAQGVYWIVRNSWDTNWGDNGYGYFAANIDLMMIEEYPYV
IL

SEQ ID NO:66 Fel d 1 链1-链2氨基酸 (23-92/18-109)

EICPAVKRDVDLFLTGTDPDEYVEQVAQYKALPVVLENARILKNCVDAKMTEEDKENALSLLDKIYTSPLC
VKMAETCPIFYDVFFAVANGNELLLDLSTKVNATEPERTAMKKIQDCYVENGLISRVLGGLVMTTISS
KDCMGEAVQNTVEDLKLNTLGR

SEQ ID NO:65 Fel d 1 链1-链2氨基酸 (23-92/18-109)

EICPAVKRDVDLFLTGTDPDEYVEQVAQYKALPVVLENARILKNCVDAKMTEEDKENALSLLDKIYTSPLC
GGGSGGGSGGGSGGKMAETCPIFYDVFFAVANGNELLLDLSTKVNATEPERTAMKKIQDCYVENGLI
SRVLGGLVMTTISSKDCMGEAVQNTVEDLKLNTLGR

SEQ ID NO:70 Fel d 2 氨基酸 (25-608)

EAHQSEIAHRFNDLGEHFRGLVLVAFSQYLQCCPFEDHVKLVNEVTEFAKGCVADQSAANCEKSLHELL
GDKLCTVASLRDKYEMADCEKKEPERNECFQHKDDNPGFGQLVTPEADAMCTAFHENEQRFLGKYLY
EIARRHPYFYAPELLYAAEYKGVFTECCEAADKAACLTpkVDALREKVLASSAKERLKCASLQKFGERA

对于构建物，将序列高亮显示如下：**hLAMP 信号肽-hLAMP 腔内结构**

域-CTCGAG-抗原-GAATTC-hLAMP TM 和 Cyto 结构域

FKAWSVARLSQKFPKAEFAEISKLVTDLAKIHKECCHGDLLECADDRADLAKYICENQDSISTKLKECCG
KPVLEKSHCISEVERDELPADLPPLAVDFVEDKEVCNKYQEAQDVFLGTFLYEYSRRHPEYSVSLLLRLA
KEYEATLEKCCATDDPPACYAHVFDEFKPLVEEPHNLVKTNCELFEKLGEYGFQNALLVRYTKKVPQVST
PTLVEVSRSLGKVGSKCCTHPEAERLSAEDYLSVVLNRLCVLHEKTPVSEVTKCCTESLVNRRPCFSA
LQVDETYVPKEFSAETFTFHADLCTLPEAEKQIKKQSALVELLKHKPKATEEQKKTVMGDFGSGFVDKCCA
AEDKEACFAEEGPKLVAAAQAALA

SEQ ID NO:74 Fel d 4 氨基酸 (16-186)

HEEENVVRNIDISKISGEWYSILLASDVKEKIEENGSMRVFVEHIKALDNSSLSFVFHTKENGKCTEIF
LVADKTKDGVYTVVYDGYNVFSIVETVYDEYILLHLLNFDKTRPFQLVEFYAREPDVSQKLKEKFVKYCQ
EHGIVNILDLETVDRCLQARGSEVAQDSSVE

SEQ ID NO:78 Lit v 1 氨基酸 (1-284)

MDAIIKKMQAMKLEKDNAMDRADTLEQQNKEANNRAEKSEEEVHNLQKRMQQLENDLDQVQESLLKANIQ
LVEKDKALSNAEGEVAALNRRIQLLEEDLERSEERLNTATTKLAEASQAADSESRMRKVLNRSLSDEER
MDALENQLKEARFLAEEADRKYDEVARKLAMVEADLERAEERAETGESKIVELEELRVVGNLKSLEVS
EEKANQREEAYKEQIKTLTNKLKAAEARAEFAERSVQKLQKEVDRLEDELVNEKEKYKSITDELDQTFSE
LSGY

SEQ ID NO:82 Lol p 5a 氨基酸 (26-272)

ADAGYTPAAAATPATPAATPAAAGGKATTDEQKILLEDVNAGFKA AVAAAANAPPADKFKIFEAAFSESSK
GLLATSAKAPGLIPKLDAYDVAYKAAEATPEAKYDAFVTALTEALRVIAGALEVHAVKPATEEVLAAK
IPTGELQIVDKIDAAFKIAATAANAAPTNDKFTVFESAFNKALNECTGGAYETYKFIPSLEAAVKQAYAA
TVAAAPEVKYAVFEAALTKAITAMTQAQKAGKAPAAA

SEQ ID NO:86 Phl p 1 氨基酸 (24-263)

IPKVPPGPNITATYGDKWLDKSTWYGKPTGAGPKDNGGACGYKDVDKPPFSGMTGCGNTPIFKSGRGCG
SCFEIKCTKPEACSGEPVVVHITDDNEEPIAPYHFDLSGHAFGAMAKKGDEQKLSAGELELQFRRVKCK
YPEGTVTFHVEKGSNPNYLALLVKYVNGDGDVVAVDIKEKGDKWIELKESWGAIWRIDTPDKLTGPFT
VRYTTEGGTKTEAEDVIPEGWKADTSYESK

SEQ ID NO:90 Phl p 5 氨基酸 (25-288)

AADLGYPATPAAPAAGYTPATPAAPAEAAPAGKATTEEQKLIKINAGFKAALAAAAGVQPADKYRTFV
ATFGAASNKAFAEGLSGEPKGAAESSKAALTSKLDAAAYKLAYKTAEGATPEAKYDAYVATLSEALRIIA
GTLEVHAVKPAAEEVKVIPAGELQVIEKVDAAFKVAATAANAAPANDKFTVFEEAFNDAIKASTGGAYES
YKFIPALEAAVKQAYAATVATAPEVKYTVFETALKKAITAMSEAQAAPAAA

SEQ ID NO:93 Der f 15 氨基酸 (20-555)

SIKRDHNDYSKNPMRIVCYVGTWSVYHKVDPYTIEDIDPFKCTHLMYGFAKIDEYKYTIQVFDPYQDDNH
NSWEKRGYERFNNLRLKNPELTMTISLGGWYEGSEKYSDMAANPTYRQQFIQSVLDFLQYKFDGLDLWD
EYPGSRGLGNPKIDKQNYLALVRELKDAFEPHGYLLTAAVSPGDKIDRAYDIKELNKLFDWMNVMTYDYH
GGWENFYGHNAPLYKRPDETDELHTYFNVNYTMHYLLNNGATRDKLVMGVPFYGRAWSIEDRSKLLGDP
AKGMSPPGFISGEEGVLSYIELCQLFQKEEWHIQYDEYYNAPYGYNDKIWVGYYDDLASISCKLAFLELG
VSGVMVWSLENDDFKGHCGPKNPLLNKVHNMINGDEKNSFECILGPSTTTPTTTPTTTPTTTPTTPTTPT
TPTTTPTTPTTTPTTPTTPTTPTTPTTPTTPTTPTTPTTPTTPTTPTTPTTPTTPTTPTTPTTPTTPTTPT
EGDIPHTNIHKYLVCEFVNGGWVHIMCPPGTIWCQEKLTICGE

域-CTCGAG-抗原-GAATTC-hLAMPTM和Cyto结构域

SIKRHDNDYSKNPMRIVCYVGTWSVYHKVDPTYTIEDIDPFKCTHLMYGFKAIDYEKYTIQVDPYQDDNHNNSWEKRGV
ERFNNLR LKNPELTTMISLGGWYEGSEKYSDMAANPTYRQQFIQSVLDFLQEQKFDGLDLDEWYEPGSR LGNPKIDKQN
YLALVRELKDAFEPHGYLLTAAVSPGKDKIDRAYDIKELNKLFDWMNVMTYDYHGGWENFYGHNAPLYKRPDETDEL
HTYFNVNVTMHYYLNNGATRDKLVMGVPFYGRAWSIEDRSK LKLGDPAKGMSPPGFISGEEGVLSYIELQLFQKEEW

对于构建物，将序列高亮显示如下：**hLAMP 信号肽**-hLAMP 腔内结构

域-CTCGAG-抗原-GAATTC-hLAMP TM 和 Cyto 结构域

ctgtcagcccgagcaccatgtGAATTCacgtgatcccatcgctgtgggtggcgccctggcggggctggtcctcatcgctcctcatcgctacctcgt
cggcaggaagaggagtcacgcaggctaccagactatctagtaa (SEQ ID NO:30)

过敏原X是Bet v 1-A

atggcgccccgagcgcggcgacccctgctgctgctactgctgttgcctgctgctcggcctcatgcattgtgcgtcagcagcaatgtttatggtg
aaaaatggcaacgggaccgctgcataatggccaacttctctgctgccttctcagtgaaactacgacaccaagagtgccctaagaacatgaccttga
cctgccatcagatgccacagtggtgctcaaccgcagctcctgtggaaaagagaacacttctgacccagtcctgtattgctttggaaggagacatac
actcactctcaatttcagagaaatgcaacacgttacagcgtccagctcatgagtttgtttataacttgcagacacacacctttcccaatgcgagct
ccaaagaaatcaagactgtggaatctataactgacatcaggcgagatagataaaaaatacagatgtttagtgaccagggtccacatgaaca
acgtgaccgtaacgctccatgatgccaccatccaggcgctacctttcaacagcagcttcagccgggagagacacgctgtgaacaagacaggccttc
cccaaccacagcgcggcctgcgcccagccctcgccctcaccgctgccaagagccctctgtggacaagtacaacgtgagcggcaccaacggg
acctgcctgctggcagcatgggctgcagctgaacctcacctatgagaggaaggacaacacgaggtgacaaggcttcaacatcaacccaaca
agacctcggcagcgggagctgcggcgccacctggtgactctggagctgcacagcgagggcaccaccgtcctgcttccagttcgggtagaatga
agttctagccggttttctacaaggaaatccagttgaatacaattctctgacgcagagaccctgcctttaagctgccaacggctccctgcgagcgc
tgaggccacagtcggcaattctacaagtgaacgcggaggagcacgtccgtgtcacgaaggcgttttcagtaatatattcaagtggtggctcag
gctttcaagtggaagggtggcagtttggctgtgaggagtgctgctggacgagaacagcCTCGAGggcgtgttcaactacgagacagagaca
accagcgtgatccagccgacagactgttaaggccttcattctggacggcgacaatctgttcccaagtggtgcccccaagccatcagcagcgtgga
aaacatcgagggcaatggcggacccggcaccatcaagaagatcagcttccccgagggttccattcaaatacgtgaaggaccgggtggacgaagt
ggaccacaccaactcaagtacaactactcgtgatcgaggcgacccatcgcgacacactggaaaagatcagcaacgagatcaagatcgtggc
caccgccagcggcgagcattctgaagatctcaacaagtaccacacaaaaggcgaccacgaagtgaaggccgaacaagtgaagccagcaaag
agatggcgagacactgctcgggcccgtgaaaagctatctgctgcccacagcagcctacaacGAATTCacgtgatcccatcgctgtgggtg
gtgcccggcgggctggtcctcatcgctcctcatcgctacctcgtcggcaggaagaggagtcacgcaggctaccagactatctagtaa (SEQ ID
NO:34)

atggcgccccgagcgcggcgacccctgctgctgctactgctgttgcctgctgctcggcctcatgcattgtgcgtcagcagcaatgtttatggtg
aaaaatggcaacgggaccgctgcataatggccaacttctctgctgccttctcagtgaaactacgacaccaagagtgccctaagaacatgaccttga
cctgccatcagatgccacagtggtgctcaaccgcagctcctgtggaaaagagaacacttctgacccagtcctgtattgctttggaaggagacatac
actcactctcaatttcagagaaatgcaacacgttacagcgtccagctcatgagtttgtttataacttgcagacacacacctttcccaatgcgagct
ccaaagaaatcaagactgtggaatctataactgacatcaggcgagatagataaaaaatacagatgtttagtgaccagggtccacatgaaca
acgtgaccgtaacgctccatgatgccaccatccaggcgctacctttcaacagcagcttcagccgggagagacacgctgtgaacaagacaggccttc

对于构建物，将序列高亮显示如下：**hLAMP 信号肽**-hLAMP 腔内结构域-CTCGAG-抗原-GAATTC-hLAMP TM 和 Cyto 结构域

cccaaccacagcgcgccacccagccctcgccctcaccgtgcccaagagccctctgtggacaagtacaacgtgagcggcaccacacggg
acctgcctgctggccagcatggggctgagctgaacctcacctatgagaggaaggacaacacgacggtgacaaggcttctcaacatcaacccaaca
agacctcggccagcgggagctgcccacccctggtgactctggagctgcacagcaggggaccaccgtcctgctctccagttcgggatgaatgca
agttctagccggttttctacaaggaatccagttgaatacaattcttctgacgccagagaccctgcctttaaagctgccaacggctcctgcgagcgc
tgcaggccacagtcggcaattcctacaagtgaacgcggaggagcacgtccgtgtcacgaaggcgtttcagtaatatattcaaagtgtgggtccag
gctttcaagggtggaaggtggccagtttggtctgtggaggagtgtctgctggacgagaacagcCTCGAGcaagacacccccgctctgggcaaggat
accgtggcctgtccgcaagtgtatctgaaggccatgaccgccgaccaagaagtgcggagaagcccgatagcgtgacccccatgattctgaaag
cccagaaggcgccgaatctggaagccaagatcacctgctgaccaacggccagtgcagaacatcacctgggtctgcacaagaccagcgagcccg
gcaagtacacagcctacgaggccagcgggtggttcatccagccttctccagtgcgggatcactacattctgtactgcgagggcgagctgcacggc
cggcagatcagaatggccaagctgctgggcagagatcccagcagagccaagaggctctggaagatttcagagagttcagccgggccaagggactg
aaccaagagattctggaactggctcagagcgagacatgctctccggcgggacaaGAATTCacgctgatcccatcgctgtgggtggtccctggcg
gggctggtcctcatgctcctcatgcctacctcgtcggcaggaagaggagtcacgcaggctaccagactatctagtaa (SEQ ID NO:38)

过敏原X是Cyn d 1

atggcgccccgcagcgcggcgaccctgctgctgactgctgttggctgctgctggcctcatgcattgtgctgagcgaacatgttatgggtg
aaaaatggcaacgggaccgctgcataatggccaacttctgctgctccttctcagtgaaactacgacaccaagagtgccctaagaacatgaccttga
cctgccatcagatgccacagtggtgctcaaccgcagctcctgtggaaaagagaacacttctgacccagctcgtgattgcttttggagaggacatac
actcactctcaatttcacgagaatgcaacacgttacagcgtccagctcatgattttgtttataacttgcagacacacacctttcccaatgcgagct
ccaaagaaatcaagactgtggaatctataactgacatcagggcagatatagataaaaaatacagatgtgttagtgccaccaggtccacatgaaca
acgtgaccgtaacgctcatgatgccaccatccaggcgtacctttcaacagcagcttcagccgggagagacacgctgtgaacaagacaggccttc
cccaaccacagcgcgccacccagccctcgccctcaccgtgcccaagagccctctgtggacaagtacaacgtgagcggcaccacacggg
acctgcctgctggccagcatggggctgagctgaacctcacctatgagaggaaggacaacacgacggtgacaaggcttctcaacatcaacccaaca
agacctcggccagcgggagctgcccacccctggtgactctggagctgcacagcaggggaccaccgtcctgctctccagttcgggatgaatgca
agttctagccggttttctacaaggaatccagttgaatacaattcttctgacgccagagaccctgcctttaaagctgccaacggctcctgcgagcgc
tgcaggccacagtcggcaattcctacaagtgaacgcggaggagcacgtccgtgtcacgaaggcgtttcagtaatatattcaaagtgtgggtccag
gctttcaagggtggaaggtggccagtttggtctgtggaggagtgtctgctggacgagaacagcCTCGAGgccatcggcgataagcccgacccaa
catcaccgccacatagcgcagcaagtggctggaagccagagccacattctacggctccaacccagaggcgccgctcccgatgatgacggagct
tgcggctacaaggacgtggacaagcccccttcgacggcatgaccgcttgcggcaacgagcccatcttcaaggacggactgggctgccgggcttgct
acgagatcaagtgcagaagaacccgtggaatgcagcggcgagccgctgctgtgaagatcaccgacaagaactacgagcacattgccgctaccat
tcgatctgagcggcaaggcctttggcgccatggccaagaaggccaagaggacaagctgcggaaggccggcgaactgacactgcagtttcggagag
tgaagtgaagtacccagcggcaccgaagatcacattccacatcgagaagggcagcaacgatcactatctggctctgctgtgaaatagccgctgg

对于构建物，将序列高亮显示如下：**hLAMP 信号肽**-hLAMP 腔内结构域-CTCGAG-抗原-GAATTC-hLAMP TM 和 Cyto 结构域

cgacggcaacatcgtggccgtggacatcaagcccagagacagcgacgagttcatccccatgaagtcagctggggcgccatctggcggatcgaccc
aaagaagcctctgaagggcccttctccatccggctgacatctgaggcgaggacacatctggtgcaagacgacgtgatccccgccaactggaagccc
gacaccgtgtacaccagcaagctgcagtttggcgccGAATTCacgctgatccccatcgctgtgggtggcgccctggcggggctggtcctcatcgctct
catcgctacctcgctcggcaggaagaggagtcacgcaggctaccagactatctagtaa (SEQ ID NO:42)

过敏原X是 Der F 1 (19-321)

atggcgccccgacgcgccccggcgaccctgctgctgactgctgttggctgctgctcgccctcatgcattgtgctcagcagcaatgtttatggtg
aaaaatggcaacgggaccgctgcataatggccaacttctctgctgcttctcagtgaaactacgacaccaagagtgccctaagaacatgacccttga
cctgccatcagatgccacagtggtgctcaaccgcagctcctgtgaaaagagaacacttctgacccagtcctgtgattgcttttgaagaggacatac
actcactctcaatttcacgagaaatgcaacacgttacagcgtccagctcatgagttttgtttataactgtcagacacacaccttttccccaatgcgagct
ccaaagaaatcaagactgtggaatctataactgacatcagggcagatatagataaaaaatacagatgtgttagtgacccaggtccacatgaaca
acgtgaccgtaacgctccatgatgccaccatccaggcgtacctttccaacagcagcttcagccgggagagacacgctgtgaacaagacaggccttc
cccaaccacagcgccccctgcccacccagccccctgcacctcaccgtgcccagagccccctctgtggacaagtacaacgtgagcggcaccacagg
acctgcctgctggccagcatggggctgcagctgaacctcacctatgagaggaaggacaacacgaggtgacaaggcttctcaacatcaacccaaca
agacctcggccagcgaggctgcggcgccacctggtgactctggagctgcacagcgagggcaccacgctcctgctctccagttcgggatgaatgca
agttctagccggttttctacaaggaatccagttgaatacaatttctctgacgcagagaccctgcctttaaagctgccaacggctccctgcgagcgc
tgcaggccacagtcggcaattctacaagtgaacgcggaggagcagctcgtgtcacgaaggcggttttcagtcataatattcaaatgtgggtccag
gctttcaaggtggaaggtggccagtttgctctgtggaggagtgctgctggacgagaacagcCTCGAGaggccccgacgcatcaagacattcgaa
gagttcaagaaggcctttaacaagaactacgccacgtggaagaggaagaagtggcccggaagaactttctggaatctctgaaatacgtggaagcc
aacaaggcgccatcaacatctgagcgtctgtctctggacgagtttaagaaccggtatctgatgagcgccgaggccttcgagcagctgaaaaccc
agttcgatctgaacgccgaaaccagcgttgccggatcaacagcgtgaacgtgccagcgagctggatctgagatctctgagaaccgtgacccccatc
agaatgcaaggcggctgcggcagctgctggccttttagcggagtggccgccacagagctgcctatctggcctaccggaacacatctctggatctgc
cgagcaagaactcgtggactgcgccagccagcacggctgtcacggcgatacaatccccagaggcatcgagtacatccagcagaacggcgtcgtgga
agaacggctctacccttacgtggccccgagcagagatgcagaaggcccaactctcagcactacggcatcagcaactactgccagatctaccccccc
gacgtgaagcagatcagagaggctctgacccagacccacaccgccattgccgtgatcatcggaatcaaggatctcgggccttcagcactatgacg
gccggaccatcatccagcacgacaacggctaccagcccaactaccacgccgtgaacatcgtgggctacggcagcacacaaggcgacgactactgga
tcgtgcggaacagctgggacaccacatggggcgatagcggctacggctacttccaagccggcaacaatctgatgatgagcagtagccctacgt
cgtgatcatgGAATTCacgctgatccccatcgctgtgggtggcgccctggcggggctggtcctcatcgctcctcatcgctacctcgtcggcaggaaga
ggagtcacgcaggctaccagactatctagtaa (SEQ ID NO:46)

对于构建物，将序列高亮显示如下：**hLAMP 信号肽**-hLAMP 腔内结构

域-CTCGAG-抗原-GAATTC-hLAMP TM 和 Cyto 结构域

过敏原X是 **Der F 1 (99-321)**

atggcgccccgagcgccccgagccccctgctgctactgctgttctgctgctcggcctcatgcattgtgctcagcagcaatgtttatggtg
aaaaatggcaacgggacgcgtgcataatggccaacttctctgctgccttctcagtgaactacgacaccaagagtggccctaagaacatgaccttga
cctgccatcagatgccacagtggtgctcaaccgcagctcctgtggaagagaacacttctgacccagctcctgtgattgcttttgaagaggacatac
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ccaaagaaatcaagactgtggaatctataactgacatcagggcagatatagataaaaaatacagatgtgttagtggcaccaggtccacatgaaca
acgtgaccgtaacgctccatgatgccaccatccaggcgtacctttccaacagcagcttcagccggggagagacacgctgtgaacaagacaggccttc
cccaaccacagcgccccctgcgccaccagccccctgcctcaccctgccccagagccccctctgtggaagtagacaacgtgagcggcaccaacggg
acctgctgctggccagcatggggctgcagctgaacctcacctatgagaggaaggacaacacgacggtgacaaggcttctcaacatcaacccaaca
agacctcgccagcgggagctgcggcgccacctggtgactctggagctgcacagcagggcaccacgctcctgctcttcagttcgggatgaatgca
agttctagccggttttctacaaggaatccagttgaatacaattcttctgacgacagacacctgcctttaagctccaacggctccctgcgagcgc
tgaggccacagtcggcaattctacaagtgaacgcggaggagcacgtccgtgtcacgaaggcgttttcagtaatatattcaagtggtgggtccag
gctttcaaggtggaaggtagccagtttggtctgtggaggagtgtctgctggacgagaacagcCTCGAGaccagcgcttgcgggatcaacacgctg
aacgtgccagcagcgtggtatctgagatctctgagaacctgacccccatcagaatgaaggcggctgcggcagctgctggccttttagcggagtg
ccgccacagagctgcctatctggcctaccggaacacatctctggatctgtccgagcaagaactcgtggactgcgccagccagcacggctgtcacggc
gataaatccccagaggcatcagatcatccagcagaacggcgtcgtggaagaacggtcctaccctacgtggcccgagcagagatgcagaagg
cccaactctcagcactacggcatcagcaactactgcagatctaccccccgacgtgaagcagatcagagaggctctgaccagacccacaccgcca
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ggcgtgaacatcgtgggtacggcagcacacaaggcgacgactactggatcgtgcggaacagctgggacaccacatggggcatagcggctacggc
tactccaagccggcaacaatctgatgatgatcagcagtagccctacgtcgtgatcatgGAATTCacgctgatccccatcgtgtgggtggtgcct
ggcggggctggtcctcatcgtcctcatcgcctacctcgtcggcaggaaggaggtcacgcaggctaccagactatctagtaa (SEQ ID NO:50)

过敏原X是 **Der P2**

atggcgccccgagcgccccgagccccctgctgctactgctgttctgctgctcggcctcatgcattgtgctcagcagcaatgtttatggtg
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(SEQ ID NO:54)

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 ID NO:8)

对于构建物，将序列高亮显示如下：**hLAMP 信号肽**-**hLAMP 腔内结构域**-**CTCGAG-抗原-GAATTC**-**hLAMP TM** 和 **Cyto 结构域**

过敏原X是 **DerP1 (del)**

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对于构建物，将序列高亮显示如下：**hLAMP 信号肽**-hLAMP 腔内结构

域-CTCGAG-抗原-GAATTC-hLAMP TM 和 Cyto 结构域

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对于构建物，将序列高亮显示如下：**hLAMP 信号肽**-hLAMP 腔内结构

域-CTCGAG-抗原-GAATTC-hLAMP TM 和 Cyto 结构域

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ID NO:79)

过敏原X是 Lol p 5a

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对于构建物，将序列高亮显示如下：**hLAMP 信号肽-hLAMP 腔内结构域-CTCGAG-抗原-GAATTC-hLAMP TM 和 Cyto 结构域**

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aagcccagaaggccggcaaaccagctgtctgagctGAATTCacgctgatccccatcgctgtgggtggtgcctggcgggctggtcctcatcgctct
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过敏原X是 **Phl p 1**

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对于构建物，将序列高亮显示如下：**hLAMP 信号肽**-hLAMP 腔内结构域-CTCGAG-**抗原**-GAATTC-**hLAMP TM** 和 **Cyto 结构域**

过敏原X是 **Phl p 5**

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图4