



(12) 发明专利申请



(10) 申请公布号 CN 114641306 A

(43) 申请公布日 2022.06.17

(21) 申请号 202080072208.8

(22) 申请日 2020.10.17

(30) 优先权数据

62/916,854 2019.10.18 US

(85) PCT国际申请进入国家阶段日

2022.04.14

(86) PCT国际申请的申请数据

PCT/US2020/056197 2020.10.17

(87) PCT国际申请的公布数据

W02021/077051 EN 2021.04.22

(71) 申请人 免疫治疗有限公司

地址 美国马里兰州

(72) 发明人 特瑞·海兰

(74) 专利代理机构 中原信达知识产权代理有限
责任公司 11219

专利代理师 金海霞 刘慧

(51) Int.Cl.

A61K 39/00 (2006.01)

A61K 39/385 (2006.01)

A61P 35/00 (2006.01)

C07K 19/00 (2006.01)

C12N 15/62 (2006.01)

权利要求书2页 说明书54页
序列表215页 附图44页

(54) 发明名称

包含癌抗原的改良LAMP构建物

(57) 摘要

本发明提供了包含LAMP腔内结构域的特定片段的改良LAMP构建物,以将癌抗原递送到免疫细胞,用于增强加工。这些LAMP构建物可用于疾病、特别是过度增殖性障碍和/或癌症的治疗。所述改良LAMP构建物在施用于受试者时允许呈递正确配置的三维表位,用于产生免疫应答。所述改良LAMP构建物可以是多价分子,和/或可以被提供为含有两种或更多种LAMP构建物的多价疫苗的一部分。本文中所描述的改良LAMP构建物也可用于在施用于非人类脊椎动物时产生抗体。

1. 一种改良LAMP构建物,其包含:
 - a. LAMP蛋白的半胱氨酸保守片段;和
 - b. 至少一种癌抗原,其中所述癌抗原选自大T抗原、小T抗原、MAGE-A10、MAGE-A12、MAGE-A1、MAGE-A2、MAGE-A3、MAGE-A4、MAGE-A4、MAGE-A6、MAGE-A6、MAGE-A6、MAGE-A9、MAGE-B10、MAGE-B16、MAGE-B17、MAGE-B1、MAGE-B2、MAGE-B3、MAGE-B4、MAGE-B5、MAGE-B6、MAGE-C1、MAGE-C2、MAGE-C3、MAGE-D1、MAGE-D2、MAGE-D4、MAGE-E1、MAGE-E1_(MAGE1)、MAGE-E2、MAGE-F1、MAGE-H1或MAGEL2。
3. 根据权利要求1所述的改良LAMP构建物,其中:
 - a. 所述抗原被放置在所述半胱氨酸保守片段的N-端处;
 - b. 所述抗原被放置在单个半胱氨酸保守片段的C-端处;或
 - c. 所述抗原被放置在两个半胱氨酸保守片段之间。
3. 根据权利要求1或权利要求2所述的改良LAMP构建物,其中所述改良LAMP构建物包含表1的第1列或第4列中描述的至少一个片段/表位,并且优选地如ILC-1、ILC-2、ILC-3、ILC-4、ILC-5或ILC-6中所述来构建。
4. 根据权利要求3所述的改良LAMP构建物,其中每个抗原被连接物隔开,优选地其中所述连接物是氨基酸序列GPGPG (SEQ ID NO:152) 或PMGLP (SEQ ID NO:153)。
5. 根据前述权利要求中的任一项所述的改良LAMP构建物,其中所述改良LAMP构建物包含超过一个半胱氨酸保守片段。
6. 根据前述权利要求中的任一项所述的改良LAMP构建物,其中所述半胱氨酸保守片段包含LAMP蛋白的同源结构域。
7. 根据前述权利要求中的任一项所述的改良LAMP构建物,其中所述改良LAMP构建物还包含LAMP蛋白的跨膜结构域。
8. 根据前述权利要求中的任一项所述的改良LAMP构建物,其中所述改良LAMP构建物还包含信号序列,优选地其中所述信号序列源自于LAMP蛋白。
9. 根据前述权利要求中的任一项所述的改良LAMP构建物,其中所述LAMP蛋白选自LAMP-1、LAMP2、LAMP-3、LIMP 2、Macrosailin、Endolyn、LAMP5或LIMBIC。
10. 根据前述权利要求中的任一项所述的改良LAMP构建物,其中所述改良LAMP构建物包含:
 - A) 选自SEQ ID NO:1-113中的任一者的LAMP蛋白和选自SEQ ID NO:114-116中的任一者的癌抗原;
 - B) LT^{S220A}-LAMP的氨基酸序列 (SEQ ID NO:151);或
 - C) 与SEQ ID NO:117-150中的任一者组合的(A)或(B)。
11. 根据权利要求12所述的改良LAMP构建物,其中所述LAMP蛋白与SEQ ID NO:1-113具有至少约70%、至少约75%、至少约80%、至少约85%、至少约90%、至少约95%、96%、97%、98%或99%同一性,和/或所述癌抗原与SEQ ID NO:114-151具有至少约70%、至少约75%、至少约80%、至少约85%、至少约90%、至少约95%、96%、97%、98%或99%同一性。
12. 根据前述权利要求中的任一项所述的改良LAMP构建物,其中所述改良LAMP构建物包含SEQ ID NO:116的氨基酸序列,并且优选地其中所述LAMP蛋白是人类LAMP1,并且优选地其中所述LAMP构建物是ILC-4。

13. 一种多核苷酸,其编码根据权利要求1-12中的任一项所述的改良LAMP构建物。
14. 根据权利要求13所述的多核苷酸,其中所述多核苷酸是DNA疫苗。
15. 根据权利要求14所述的多核苷酸,其中所述多核苷酸是自我复制RNA疫苗。
16. 一种宿主细胞,其包含根据权利要求13-15中的任一项所述的多核苷酸。
17. 一种组合物,其包含根据权利要求1-12中的任一项所述的改良LAMP构建物、根据权利要求13-15中的任一项所述的多核苷酸或根据权利要求16所述的宿主细胞。
18. 一种治疗患有疾病或障碍的受试者的方法,其中所述方法包括以足以减轻或治疗所述疾病或障碍的量向需要的受试者施用根据权利要求1-12中的任一项所述的改良LAMP构建物、根据权利要求13-15中的任一项所述的多核苷酸、根据权利要求16所述的宿主细胞或根据权利要求17所述的组合物。
19. 根据权利要求18所述的方法,其中所述方法包括初免步骤和至少一个加强步骤。
20. 根据权利要求19所述的方法,其中将根据权利要求1-12中的任一项所述的改良LAMP构建物、根据权利要求13-15中的任一项所述的多核苷酸、根据权利要求16所述的宿主细胞或根据权利要求17所述的组合物用于所述初免步骤中。
21. 根据权利要求19或20所述的方法,其中所述加强步骤包括施用抗原、改良LAMP构建物、由改良LAMP构建物编码的多肽或包含所述改良LAMP构建物的细胞。
22. 根据权利要求18-21中的任一项所述的方法,其中:
 - a) 用于初免的抗原与用于加强的抗原相同;
 - b) 用于初免的抗原与用于加强的第二抗原源自于同一蛋白;
 - c) 将超过一种抗原用于初免和/或加强。
23. 根据权利要求18-22中的任一项所述的方法,其中所述受试者患有过度增殖性障碍。
24. 根据权利要求23所述的方法,其中所述过度增殖性障碍选自腺癌、肉瘤、皮肤癌(例如梅克尔细胞癌)、黑素瘤、膀胱癌、脑癌(包括多形性成胶质细胞瘤)、乳腺癌、子宫癌、卵巢癌、前列腺癌、肺癌(包括但不限于NSCLC、SCLC、鳞状细胞癌)、结肠直肠癌、肛门癌、直肠癌、宫颈癌、肝癌、头颈癌、口腔癌、唾液腺癌、食管癌、胰腺癌、胰腺导管腺癌(PDA)、肾细胞癌、胃癌、肾癌、多发性骨髓瘤或脑癌。
25. 根据权利要求23或24所述的方法,其中所述过度增殖性障碍由巨细胞病毒(CMV)引起。
26. 根据权利要求18-25中的任一项所述的方法,其中所述受试者还被施用检查点抑制剂,优选地其中所述检查点抑制剂是PD-1/PD-L1抑制剂或CTLA抑制剂。
27. 根据权利要求26所述的方法,其中所述检查点抑制剂选自派姆单抗(KeytrudaTM)、纳武单抗(OpdivoTM)、西米普利单抗(LibtayoTM)、阿特珠单抗(TecentriqTM)、阿维鲁单抗(BavencioTM)、德瓦鲁单抗(ImfinziTM)或伊匹单抗(YervoyTM)。

包含癌抗原的改良LAMP构建物

技术领域

[0001] 本发明涉及包含癌抗原的改良LAMP构建物以及它们在治疗患有过度增殖性障碍和/或癌症的受试者中的用途。还描述了利用本文描述的改良LAMP构建物的初免-加强方案。

背景技术

[0002] 在下面的讨论中,出于背景和介绍的目的将描述某些文章和方法。本文包含的任何内容都不应被解释为对现有技术的“承认”。申请人明确保留在适当情况下证明本文参考的文章和方法在适用的法律规定下不构成现有技术的权力。

[0003] DNA疫苗是用于开发预防性和治疗性疫苗两者的新的且有希望的候选物。它们被证明是安全的,并且如果需要重复的疫苗接种循环以获得临床益处,则缺少对载体骨架的免疫应答可能是明确的优势。然而,常规DNA疫苗的一种察觉到的缺点是它们在人类中的低免疫原性。基于表位的DNA疫苗的免疫原性中的关键限制步骤可能是表位进入II类主要组织相容性(MHC)呈递途径到达T细胞,这在不使用靶向技术的疫苗的情况下可能是随机的过程。

[0004] 美国专利号5,633,234描述了包含修饰的流感血凝素(HA)的抗原性结构域和胞质胞内体/溶酶体靶向信号的嵌合蛋白,所述靶向信号有效地将抗原靶向该区室。所述抗原性结构域被加工,并且来自于它的肽与II类MHC分子联合呈递在细胞表面上。LAMP-1的胞质尾区被用于形成所述嵌合蛋白的胞内体/溶酶体靶向结构域。

[0005] 美国专利号8,318,173扩展了这些初始的观察,描述了包含插入在LAMP-1的完整腔内结构域与跨膜结构域之间的HIV-1 Gag蛋白的嵌合蛋白(以及编码这些蛋白的相应DNA)。将这种构建物引入到树突状细胞中,所述细胞随后被报道为靶向MHC II途径。

[0006] 这种方法已被证明可用于提高针对几种病毒抗原的细胞和体液应答,所述病毒抗原是人类乳头瘤病毒E7、登革病毒膜蛋白、HIV-1gp160膜蛋白、HIV-1 p55 Gag、西尼罗病毒膜蛋白、丙型肝炎病毒NS3蛋白和巨细胞病毒pp65(参见例如Bonini等,J.Immunol.166:5250-5257,2001)。所述增强的免疫应答可以归因于LAMP与MHC II的共定位以及抗原性肽的更高效的加工和递送。此外,LAMP靶向据报道引起数目增加的免疫原性表位的呈递,因此与非靶向抗原相比诱导在定性水平上拓宽的免疫应答。例如,Fernandes等,2000,Eur.J.Immunol.30(8):2333-43证实了在痘苗病毒载体中编码的LAMP转运的OVA抗原的被呈递的肽的数目增加。在从外源供应的OVA产生的12种肽中,9种被OVA/LAMP嵌合体呈递,相比较而言只有2种被不含LAMP的构建物呈递。

[0007] 尽管已确定LAMP的胞质结构域是必需的(与信号序列和跨膜结构域相结合),但它对所有抗原的胞内体/溶酶体转运来说不总是足够的。相反,已显示LAMP的完整腔内结构域对于蛋白质向溶酶体囊泡途径的转运来说也是需要的。

[0008] 然而,即使存在LAMP的完整腔内结构域和完整跨膜/胞质尾区(“完全LAMP构建物”),但仍越来越多地发现,特定抗原引起免疫应答的效能高度依赖于在这些构建物中使

用的具体序列。事实上已发现,当被插入到完全LAMP构建物中时,同一蛋白的不同抗原性片段不引发相同的免疫应答。所述抗原片段有时产生免疫应答,其他时候则不产生。这些观察使得在使用完全LAMP构建物时,事先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。

[0009] 此外,在产生完全LAMP构建物中,已反复地观察到为了正确地表达和加工抗原,需要完整腔内结构域。例如,在Godinho等,PLoS ONE 9(6):e99887.doi:10.1371/journal.pone.0099887中,作者报道了所述完全和完整的腔内结构域是将抗原靶向溶酶体所需的最小必需区域,并且所述腔内结构域的片段不起作用。参见同上,第6页。

[0010] 具体来说,作者Godinho显示,通过完全去除第一腔内结构域和一部分第二腔内结构域(即T1-Lum/gag构建物),蛋白质表达和抗体应答两者降低。同样地,去除25%的第一腔内结构域单具有完整的第二腔内结构域(即T2-lum/gag),蛋白质表达和抗体应答两者相对提高,但仍低于使用完全LAMP构建物获得的结果。

[0011] 此外,所述作者承认引起免疫应答的能力取决于具体抗原和在这些完全LAMP构建物中使用的表位。例如,在第9页第2栏中,作者陈述道“因此,以前的研究证实,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,其也不同于由胞质Gag诱导的应答”。然而,正如文献中已经描述的抗原性序列在LAMP的完整腔内结构域与LAMP的完整跨膜/胞质结构域之间的插入产生如此大的多核苷酸序列,使得在商业化水平上生产变得过于昂贵或者从科学观点来看不现实。

[0012] 此前,本发明人发现,尽管在文献中已广泛报道了比LAMP-1的完整腔内结构域更小的片段不能有效地产生强大的免疫应答(参见例如Godinho等),但以某些方式排布的特定片段确实有效地将抗原呈递到免疫系统,产生强大的免疫应答,包括产生不同的抗体谱。例如,本发明人已鉴定到,有效产生强大免疫应答的最小LAMP腔内结构域片段不是完整腔内结构域(正如在文献中广泛报道的),而是LAMP蛋白的腔内结构域的单个同源结构域。因此,构建物可以不包含完整腔内结构域,而是包含LAMP蛋白的腔内结构域的单个同源结构域。然而,本发明人发现,在审的专利申请16/607,082中描述的名为ILC-4的优选构建物(描绘在本文的图1中)包含融合在LAMP蛋白的第一同源结构域与LAMP蛋白的第二同源结构域之间(或至少在两个半胱氨酸保守片段之间)的至少一个感兴趣的抗原,例如,所述至少一个感兴趣的抗原可以被放置在LAMP铰链区中。在优选实施方式中,该构建物还包含LAMP蛋白的跨膜结构域和/或LAMP蛋白的胞质尾区。所述两个同源结构域可以源自于例如LAMP-1、LAMP-2、LAMP-3或Endolyn蛋白。本发明人出人意料地发现,改良LAMP构建物例如ILC-4可以例如引发针对所述感兴趣的抗原的强烈T-细胞和抗体应答,使它们成为用作DNA疫苗的可行候选物。

[0013] 尽管如上所述,但对设计可用作疫苗以有效治疗例如过度增殖性障碍和/或癌症的新的改良LAMP构建物,仍存在着进一步需求。此外,在改良后,这些新的LAMP构建物可用于产生抗体。

发明内容

[0014] 提供本发明内容是为了以简化形式介绍所选的概念,所述概念在下文的详细描述中被进一步描述。本发明内容不打算鉴定要求保护的主体内容的关键或基本特征,也不打

算用于限制所述要求保护的主体内容的范围。根据下面书写的详细描述(包括在附图中图示和在随附的权利要求书中定义的那些方面),所述要求保护的主体内容的其他特征、细节、用途和优点将显而易见。

[0015] 本发明的一个目的是提供包含LAMP结构域的特定片段和/或变体的新的构建物(“改良LAMP构建物”),其将本文中指定的癌抗原有效地呈递到免疫系统,以产生增强的免疫应答。这些改良LAMP构建物有效地将所述抗原导向溶酶体/胞内体区室,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细胞被优先刺激和/或产生抗体。

[0016] 本文描述的改良LAMP构建物和方法可以在受试者中引发免疫应答。所述免疫应答可以是针对所述改良LAMP构建物(例如疫苗)中的抗原的表位的免疫应答。疫苗武装所述受试者的免疫系统,使得所述免疫系统可以检测并破坏所述受试者中含有所述疫苗的抗原的物质。本文描述的改良LAMP构建物和方法可以在所述受试者中引发Th1免疫应答。Th1免疫应答可以包括免疫细胞的亚类(例如抗原特异性T-细胞)分泌炎性细胞因子(例如IFN γ 、TNF α)。在某些情况下,所述炎性细胞因子活化另一种亚型的免疫细胞(例如细胞毒性T-细胞),其可以破坏所述受试者中含有所述抗原的物质。

[0017] 在某些情况下,在本文中描述的改良LAMP构建物和方法中使用的表位和/或抗原可以被受试者的免疫系统识别,以引发Th1免疫应答并释放I型细胞因子。所述Th1应答可能是由所述表位与所述T-细胞、更具体来说所述T-细胞表达的主要组织相容性复合物(MHC)之间的相互作用启动的。例如,表位与MHC受体的高亲和性结合可以刺激Th1应答。MHC受体可以是多种类型的MHC受体中的至少一种。接合在T-细胞上的MHC受体在群体中的个体之间可以不同。

[0018] 在某些情况下,所述免疫应答是I型免疫应答。在某些情况下,所述免疫应答的特征在于I型细胞因子生产与II型细胞因子生产之比大于1。在某些情况下,所述免疫应答的特征在于I型细胞因子生产与II型细胞因子生产之比小于1。在某些情况下,所述免疫应答的特征在于IFN γ 生产与IL-10生产之比大于1。在某些情况下,所述免疫应答的特征在于IFN γ 生产与IL-10生产之比小于1。

[0019] 还设想了初免-加强方案。例如,本发明还提供了一种在受试者中产生针对癌抗原的免疫应答的方法,所述方法包括用包含本文所描述的癌抗原的改良LAMP构建物对所述受试者进行初免,然后用所述抗原或相关抗原(例如源自于相同或高度相似的蛋白质序列的第二抗原)对所述受试者进行至少一次加强。在所述初免和加强步骤中的任一者或两者中,可以使用抗原的混合物。已显示,将改良LAMP构建物用于初免步骤然后进行抗原加强步骤明显产生更高的滴度,表明了LAMP在增强抗体应答方面的能力。

[0020] 在其他优选实施方式中,编码本文描述的改良LAMP构建物的核酸分子可以以提供初免-加强的方式使用,以在受试者中引发针对癌抗原的增强的免疫应答(例如包括显著更高的抗体滴度的免疫应答)。例如,可以使用包含本文描述的表位和/或癌抗原的改良LAMP构建物来引发免疫应答(即其中所述表位和/或抗原被加工并呈递到II类MHC分子,以便偏好性地刺激辅助性T细胞、启动记忆细胞和/或产生抗体),并且提供另一种癌表位和/或抗原的表达,用于例如通过扩大记忆应答来加强所述免疫应答,其中所述加强表位和/或抗原被分泌到所述受试者的循环中。所述用于引发免疫应答的癌表位和/或抗原与所述用于加

强免疫应答的表位和/或抗原可以相同或不同。

[0021] 本发明的另一个目的是提供治疗癌症和/或过度增殖性障碍的改进的方法(例如通过经辅助性T细胞的刺激引发抗肿瘤免疫应答)。

[0022] 本发明还提供了一种核酸分子,其编码包含本文描述的癌抗原、具体来说表1中列出的癌抗原的任何改良LAMP构建物,所述癌抗原包括下述癌抗原中的任一者:大T抗原,小T抗原,MAGE-A10,MAGE-A12,MAGE-A1,MAGE-A2,MAGE-A3,MAGE-A4,MAGE-A4,MAGE-A4,MAGE-A6,MAGE-A6,MAGE-A6,MAGE-A9,MAGE-B10,MAGE-B16,MAGE-B17,MAGE-B1,MAGE-B2,MAGE-B3,MAGE-B4,MAGE-B5,MAGE-B6,MAGE-C1,MAGE-C2,MAGE-C3,MAGE-D1,MAGE-D2,MAGE-D4,MAGE-E1,MAGE-E1_(MAGE1),MAGE-E2,MAGE-F1,MAGE-H1或MAGEL2。本发明还提供了本文描述的改良LAMP构建物,其中所述核酸分子可以例如包含编码至少一个用于初免的抗原的改良LAMP构建物的核酸序列,以及编码至少一个用于加强的抗原的核酸序列,其中所述核酸序列中的任一者或两者被可操作地连接到表达控制序列。在一种优选情况下,所述编码改良LAMP构建物的核酸分子是适合于对受试者进行疫苗接种的疫苗载体。另一方面,本发明提供了递送媒介,以便于将所述改良LAMP构建物、表位和/或抗原引入到细胞中。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。

[0023] 在优选实施方式中,本发明提供了一种可注射组合物,其包含含有感兴趣的癌抗原的改良LAMP构建物,用于在哺乳动物中引发针对所述癌抗原的免疫应答(例如抗体的产生)。在优选实施方式中,相对于Th2应答,这种疫苗优先产生Th1应答。所述改良LAMP构建物包含本文所描述的癌抗原的至少一个表位。

[0024] 本发明还提供了包含本文中描述的可用于产生免疫应答的任何改良LAMP构建物的细胞。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)或工程化改造的抗原呈递细胞(例如被工程化改造成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细胞,或者它们本身可以被工程化改造(例如突变或修饰以表现出所需性质,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,和/或所述任选的初免和加强抗原是自身抗原。

[0025] 本发明还提供了一种试剂盒,其包含含有本文中描述的任何改良LAMP构建物的多种细胞。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LAMP构建物。在一种情况下,提供了一种试剂盒,其包含改良LAMP构建物和用于接受所述载体的细胞。

[0026] 本发明还提供了一种转基因动物,其包含本文所描述的至少一种细胞和/或至少一种改良LAMP构建物。本发明还提供了一种转基因动物,其包含至少一种本文所描述的细胞。

[0027] 本发明还提供了一种在受试者(例如人类或非人类脊椎动物)中产生针对抗原的增强的免疫应答的方法,所述方法包括:向所述受试者施用如上所述的细胞,其中所述细胞在所述受试者中表达或可以被诱导表达所述改良LAMP构建物。在一种情况下,所述细胞包含与所述受试者的MHC蛋白相容的II类MHC分子,使得所述受试者不产生针对所述II类MHC

分子的免疫应答。在一种优选情况下,所述受试者是人类。

[0028] 另一方面,本发明提供了一种引发针对癌抗原的增强的免疫应答的方法,所述方法包括向受试者例如人类或非人类脊椎动物施用本文所描述的任何改良LAMP构建物。优选地,所述改良LAMP构建物对于所述受试者的细胞来说是感染性的。例如,所述改良LAMP构建物可以是病毒载体,例如痘苗病毒载体。

[0029] 例如,本发明还提供了一种在动物中产生针对癌抗原的免疫应答的方法,所述方法包括用包含本文所描述的癌抗原的改良LAMP构建物对所述动物进行初免,然后对所述动物进行至少一次加强。已显示,将改良LAMP构建物用于初免步骤然后进行抗原加强步骤明显产生更高的滴度,表明了LAMP在增强抗体应答方面的能力。

[0030] 在另一种情况下,从受试者获得细胞,将本文中描述的改良LAMP构建物(并任选地与加强表位和/或抗原一起)引入到所述细胞中,并将所述细胞或所述细胞的后代重新引入到所述受试者中。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。具体来说设想了人类患者的治疗以及兽医应用。

[0031] 本发明还包括在非人类脊椎动物中产生抗体的方法,其中将所述非人类脊椎动物用本文所描述的包含感兴趣的抗原的改良LAMP构建物注射。然后,在所述非人类脊椎动物中,将所述感兴趣的癌抗原在LAMP的帮助下高效呈递到免疫系统,以启动记忆细胞并产生针对所述抗原的抗体。

[0032] 具体来说,通过所述感兴趣的抗原与LAMP的组合呈递,所述抗原随后被有效地运输到胞质胞内体/溶酶体区室,在那里所述抗原可以被加工,并且来自于所述抗原的肽与II类主要组织相容性(MHC)分子相结合被呈递在细胞表面上。

[0033] 这些产生的抗体可以从所述脊椎动物的血液分离(作为多克隆),然后使用标准技术进一步分离以产生单克隆抗体。

[0034] 在优选实施方式中,所述非人类脊椎动物的基因组包含引入的部分人类免疫球蛋白区,所述引入的区域包含人类免疫球蛋白可变区基因座的编码序列和基于所述非人类脊椎动物的内源性免疫球蛋白可变区基因座的非编码序列。优选地,所述非人类脊椎动物的基因组被移除了至少一部分或所有的内源性免疫球蛋白区。

[0035] 在其他优选实施方式中,在非人类脊椎动物中生产人类单克隆抗体,要求所述宿主具有至少一个表达人类重链免疫球蛋白的基因座和至少一个表达人类轻链免疫球蛋白的基因座。

[0036] 在某些情况下,所述部分人类免疫球蛋白可变区基因座包含人类V_H编码序列和基于所述非人类脊椎动物的内源性V_H区的非编码V_H序列。在这些情况下,所述部分人类免疫球蛋白可变区基因座还包含人类D和J基因编码序列和基于所述非人类脊椎动物宿主的内源性基因组的非编码D和J基因序列。

[0037] 在其他情况下,所述免疫球蛋白区包含引入的区域,所述引入的区域含有人类V_L编码序列和基于所述非人类脊椎动物的内源性V_L区的非编码V_L序列。更优选地,所引入的包含人类V_L编码序列的部分人类免疫球蛋白区还包含人类J基因编码序列和基于所述非人类脊椎动物宿主的内源性基因组的非编码J基因序列。

[0038] 在某些情况下,所述脊椎动物是哺乳动物,并且优选地所述哺乳动物是啮齿动物例如小鼠或大鼠。在其他情况下,所述脊椎动物是禽类,例如鸡。其他非人类脊椎动物包括

兔、美洲驼、骆驼、奶牛、豚鼠、仓鼠、狗、猫、马、非人类灵长动物、猿猴(例如猴或猿)、猴(例如狨猴、狒狒、恒河猴)或猿(例如大猩猩、黑猩猩、猩猩、长臂猿)。

[0039] 在其他实施方式中,所述部分人类免疫球蛋白区包含人类 V_H 基因编码区,并且还包含i) 人类D和J基因编码序列,和ii) 基于所述非人类脊椎动物宿主的内源性基因组的非编码D和J基因和pre-DJ序列。在其他情况下,所述 V_H 基因编码区源自于(至少部分源自于)其他来源,例如它们可以是合理设计或以其他方式设计的序列,作为人类序列和其他设计序列的組合的序列,或来自于其他物种例如非人类灵长动物的序列。

[0040] 在另一种特定情况下,所述部分人类免疫球蛋白区包含人类 V_L 基因编码区,并且还包含i) 人类J基因编码序列,和ii) 基于所述非人类脊椎动物宿主的内源性基因组的非编码J基因序列。在特定情况下,所述部分人类免疫球蛋白区包含人类 V_H 编码区、人类D和J基因编码序列以及基于所述非人类脊椎动物宿主的内源性基因组的非编码D和J基因和pre-DJ序列。

[0041] 本文中描述的方法可用于诊断和治疗用途的抗体(包括完全人类抗体、人源化抗体、嵌合抗体)的生产和/或优化。生产这些抗体的杂交瘤也是本发明的另一个目的。

[0042] 下文中更详细地描述了这些以及其他的方面、目的和特征。

附图说明

[0043] 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征。

[0044] 图1示出了可以如本文中所述使用的不同类型的改良LAMP构建物(被鉴定为ILC-1、ILC-2、ILC-3、ILC-4、ILC-5和ILC-6)的总体方案。

[0045] 图2B示出了本文中定义的LAMP蛋白的结构域,而图2A定义了这些结构域的具体氨基酸边界,所述LAMP蛋白是人类LAMP-1 (SEQ ID NO:1)、人类LAMP-2 (SEQ ID NO:2)、人类LAMP-3 (SEQ ID NO:3)、人类LAMP-4 (SEQ ID NO:4)、人类Endolyn (SEQ ID NO:5)、人类Macrosailin (SEQ ID NO:80)、人类LAMP-5 (SEQ ID NO:93) 和人类LIMBIC (SEQ ID NO:67)。正如本文中描述的,所述LAMP腔内结构域、同源结构域、跨膜结构域、胞质尾区和所述信号序列可用于产生本文中所描述的改良LAMP构建物ILC-1、ILC-2、ILC-3、ILC-4、ILC-5和ILC-6。

[0046] 图3提供了在其他物种中发现的LAMP-1蛋白与人类LAMP-1 (SEQ ID NO:1) 相比的比对。这些其他物种的对等结构域可用于产生本文中描述的改良LAMP构建物,并且通过将图2和图3中为人类LAMP-1鉴定的结构域与图3中示出的比对进行比较可以容易地鉴定。

[0047] 图4提供了在其他物种中发现的LAMP-2蛋白与人类LAMP-2 (SEQ ID NO:2) 相比的比对。这些其他物种的对等结构域可用于产生本文中描述的改良LAMP构建物,并且通过将图2和图4中为人类LAMP-2鉴定的结构域与图4中示出的比对进行比较可以容易地鉴定。

[0048] 图5提供了在其他物种中发现的LAMP-3蛋白与人类LAMP-3 (SEQ ID NO:3) 相比的比对。这些其他物种的对等结构域可用于产生本文中描述的改良LAMP构建物,并且通过将图2和图5中为人类LAMP-3鉴定的结构域与图5中示出的比对进行比较可以容易地鉴定。

[0049] 图6提供了在其他物种中发现的LAMP-4蛋白与人类LAMP-4 (SEQ ID NO:4) 相比的比对。这些其他物种的对等结构域可用于产生本文中描述的改良LAMP构建物,并且通过将图2和图6中为人类LAMP-4鉴定的结构域与图6中示出的比对进行比较可以容易地鉴定。

[0050] 图7提供了在其他物种中发现的LIMBIC蛋白与人类LIMBIC (SEQ ID NO:67) 相比的比对。这些其他物种的对等结构域可用于产生本文中描述的改良LAMP构建物,并且通过将图2和图7中为人类LIMBIC鉴定的结构域与图7中示出的比对进行比较可以容易地鉴定。

[0051] 图8提供了在其他物种中发现的Endolyn蛋白与人类Endolyn (SEQ ID NO:5) 相比的比对。这些其他物种的对等结构域可用于产生本文中描述的改良LAMP构建物,并且通过将图2和图8中为人类Endolyn鉴定的结构域与图8中示出的比对进行比较可以容易地鉴定。

[0052] 图9提供了在其他物种中发现的Macrosailin蛋白与人类Macrosailin (SEQ ID NO:80) 相比的比对。这些其他物种的对等结构域可用于产生本文中描述的改良LAMP构建物,并且通过将图2和图9中为人类Macrosailin鉴定的结构域与图9中示出的比对进行比较可以容易地鉴定。

[0053] 图10提供了在其他物种中发现的LAMP-5蛋白与人类LAMP-5 (SEQ ID NO:93) 相比的比对。这些其他物种的对等结构域可用于产生本文中描述的改良LAMP构建物,并且通过将图2和图10中为人类LAMP-5鉴定的结构域与图10中示出的比对进行比较可以容易地鉴定。

[0054] 图11A提供了克隆在本文描述的改良LAMP构建物中的LT^{S220A}的氨基酸序列。优选地,使用ILC-4作为实例。图11B说明了研究设计。图11C示出了ILC-4中的LT^{S220A}在完整脾细胞中诱导IFN γ 肽回忆应答的结果。图11D示出了ILC-4中的LT^{S220A}在脾CD4⁺ T细胞但在脾CD8⁺ T细胞中在肽回忆应答中诱导IFN γ 和TNF α 产生。图11E示出了肽合并物2 (SEQ ID NO:114的aa141-160)、肽13 (SEQ ID NO:114的aa145-157) 以及在较小程度上肽6 (SEQ ID NO:114的aa117-129)、12 (SEQ ID NO:114的aa141-153) 和17 (SEQ ID NO:114的aa161-173) 在完整脾细胞中诱导观察到的IFN γ 肽回忆应答。

[0055] 图12A示出了在被提供有B16-LTS220A肿瘤的疫苗接种的小鼠中LT^{S220A}-LAMP延迟肿瘤发作。图12B报告了在用LT^{S220A}-LAMP疫苗接种的小鼠中,血液ELISPOT反应可能预测最终的肿瘤负荷。

[0056] 图13A示出了在B16-LTS220A模型中LT^{S220A}-LAMP显著延长生存期。图13B示出了LT^{S220A}-LAMP诱导包括CD4和CD8⁺ T细胞在内的CD45⁺免疫细胞的肿瘤浸润。图13C证实了LT^{S220A}-LAMP诱导NK和NKT细胞两者的肿瘤浸润。图13D示出了LT^{S220A}-LAMP改变肿瘤内的髓系细胞。图13E示出了LT^{S220A}-LAMP提高TME内调节性T细胞的数量,但Treg数量的增加与肿瘤负荷无关。图13F表明与LT^{S220A}-LAMP的组合疗法的价值。

具体实施方式

[0057] 本发明提供了可用于产生疫苗和/或用于产生抗体的改良LAMP构建物。所述改良LAMP构建物可用于调节或增强免疫应答。在一种优选情况下,本发明提供了一种通过提供包含一种或多种本文所描述的癌抗原的改良LAMP构建物来治疗患有癌症或过度增殖性障碍的患者的方法。所述改良LAMP构建物也可用于在非人类脊椎动物中、优选为非人类哺乳动物中产生抗体。

[0058] 定义

[0059] 为下面书面描述中使用的特定术语,提供了下述定义。

[0060] 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。

[0061] 当在本文中使用时，术语“包含”旨在意味着所述改良LAMP构建物和方法包括所叙述的要素，但不排除其他要素。当用于定义改良LAMP构建物和方法时，“基本上由……构成”意味着排除对所述组合具有任何其他意义的其他要素。因此，基本上由本文中所定义的要素构成的改良LAMP构建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施用本发明的改良LAMP构建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。

[0062] 术语“约”或“大约”对于特定值来说意味着在由本领域普通技术人员所确定的可接受的范围之内，所述范围部分依赖于测量或确定所述值的方法，例如测量系统的限制。例如，“约”可以意味着给定值的最高20%、优选地最高10%、更优选地最高5%、更优选地最高1%的范围。可选地，特别是对于生物系统或方法来说，所述术语可以意味着在值的一定数量级之内，优选地5倍之内，更优选地2倍之内。除非另有陈述，否则术语“约”对特定值来说意味着在可接受的误差范围例如 $\pm 1-20\%$ 、优选地 $\pm 1-10\%$ 、更优选地 $\pm 1-5\%$ 之内。

[0063] 在提供值的范围的情况下，应该理解在该范围的上限与下限之间的每个居间值和在该陈述的范围中的任何其他陈述的或居间值，被涵盖在本发明之内。这些较小范围的上限和下限可以被独立地包括在所述较小范围中，并且也被涵盖在本发明之内，除了在所述陈述的范围中任何具体排除的限值之外。在所述陈述的范围包括所述限值中的一者或两者的情况下，排除了那些被包括的限值中的任一者或两者的范围，也被包括在本发明中。

[0064] 当在本文中使用时，“溶酶体/胞内体区室”是指膜结合的酸性液泡，其含有在膜中的LAMP分子、在抗原加工中发挥作用的水解酶和用于抗原识别和呈递的II类MHC分子。该区室充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)。当在本文中使用时，术语“胞内体”涵盖溶酶体。

[0065] 当在本文中使用时，“溶酶体相关细胞器”是指包含溶菌酶的任何细胞器，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。

[0066] 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)。

[0067] 当在本文中使用时，术语“肽”是指两个或更多个亚单位氨基酸、氨基酸类似物或

肽模拟物的化合物。所述亚单位可以通过肽键或通过其他键(例如酯、醚等)连接。

[0068] 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。如果肽链短,三个或更多个氨基酸的肽通常被称为寡肽。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。

[0069] 当在本文中使用时,“LAMP蛋白”或“LAMP多肽”是指本文中所描述的哺乳动物溶酶体相关膜蛋白人类LAMP-1、人类LAMP-2、人类LAMP-3、人类LIMP-2、人类Endo1yn、人类LIMBIC、人类LAMP-5或人类Macrosailin,以及直系同源物(例如在图3-10中示出的LAMP蛋白)和等位基因变体中的任一者。

[0070] 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的剪接。

[0071] 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核酸序列的转录时,该核酸序列“可操作地连接”到所述表达控制序列。在另一种情形中,术语“可操作地连接”是指肽、多肽或蛋白质例如表位或抗原与信号序列例如分泌信号序列的连接,以引起所述肽、多肽或蛋白质从宿主细胞的分泌。

[0072] 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)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。该信号序列有时在多肽的成熟中被细胞切掉。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。

[0073] 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被转录并翻译成肽、多肽或蛋白质的序列。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′。

[0074] 当在本文中使用时,如果两个编码序列或它们的互补序列编码相同的氨基酸序列,则所述两个编码序列彼此“对应”。

[0075] 当在本文中使用时,“转运”是指改良LAMP构建物所编码的多肽的移动或进展,其通过从粗面内质网到发生抗原加工和与MHC II结合的胞内体/溶酶体区室或相关细胞器的途径中的细胞器或区室来进行。

[0076] 当在本文中使用时,“改良LAMP构建物”和“包含抗原的改良LAMP构建物”和“包含感兴趣的抗原的改良LAMP构建物”可互换使用。所述改良LAMP构建物的不同排列在图1中作为ILC1-ILC6示出。此外,“改良LAMP构建物”的使用涵盖了所述改良LAMP构建物的多核苷酸序列以及由所述改良LAMP构建物的多核苷酸序列编码的蛋白质两者。在优选实施方式中,所述改良LAMP构建物包含SEQ ID NO:151的氨基酸序列。

[0077] 当在本文中使用时,“癌抗原”或“抗原”被定义为表1中列出的癌抗原之一,并且具体来说是至少一种大T抗原、小T抗原、MAGE-A10、MAGE-A12、MAGE-A1、MAGE-A2、MAGE-A3、MAGE-A4、MAGE-A4、MAGE-A4、MAGE-A6、MAGE-A6、MAGE-A6、MAGE-A9、MAGE-B10、MAGE-B16、

MAGE-B17、MAGE-B1、MAGE-B2、MAGE-B3、MAGE-B4、MAGE-B5、MAGE-B6、MAGE-C1、MAGE-C2、MAGE-C3、MAGE-D1、MAGE-D2、MAGE-D4、MAGE-E1、MAGE-E1_(MAGE1)、MAGE-E2、MAGE-F1、MAGE-H1或MAGEL2。在优选实施方式中,所述抗原包含SEQ ID NO:115或SEQ ID NO:116。

[0078] 当在本文中使用,“改良LAMP构建物递送媒介”被定义为可以将改良LAMP构建物携带到宿主细胞中并且与本文中所描述的改良LAMP构建物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)。

[0079] 当在本文中使用,“改良LAMP构建物递送”或“改良LAMP构建物转移”是指将所述改良LAMP构建物引入到宿主细胞中,不论用于引入的方法如何。引入的改良LAMP构建物可以稳定地或暂时地维持在所述宿主细胞中。稳定维持通常要求引入的改良LAMP构建物含有与所述宿主细胞相容的复制起点,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。

[0080] 当在本文中使用,“改进的LAMP病毒构建物”是指包含待体内、离体或体外递送到宿主细胞中的所述改良LAMP构建物的病毒或病毒粒子。改进的LAMP病毒构建物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,改良LAMP构建物包括腺病毒基因组或其一部分,以及所选择的与腺病毒衣壳蛋白相结合的非腺病毒基因。

[0081] 当在本文中使用,“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改良LAMP构建物转移到宿主细胞中的过程。优选地,所述改良LAMP构建物能够在所述细胞内复制和/或整合并被转录。

[0082] 当在本文中使用,“腺病毒粒子”是指包含外部衣壳和改良LAMP构建物的单个腺病毒毒粒,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。

[0083] 当在本文中使用,术语“施用”或“免疫接种”或“注射”改良LAMP构建物是指用所述改良LAMP构建物转导、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),将改良LAMP构建物引入到所述靶细胞中。

[0084] 当在本文中使用,短语“初免-加强”描述了使用本文中描述的改良LAMP构建物来引发T-细胞应答,随后使用第二种包含抗原的改良LAMP构建物、包含抗原或重组抗原的DNA疫苗来加强所述应答(反之亦然)。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。使用包含抗原的改良LAMP构建物的初免启动了记忆细胞;所述加强步骤扩大了所述记忆应答。优选地,使用不引起针对彼此的应答的两种不同药剂,因此它们不干扰彼此的活性。在初免和/或加强步骤中特别考虑到了抗原的混合物。加强可以进行一次或多次。

[0085] 在其他实施方式中,可以使用编码改良LAMP构建物的核酸分子来提供初免-加强,以在受试者中引发增强的免疫应答(例如包含显著更高的抗体滴度的免疫应答)。例如,所述核酸分子(例如质粒或载体)可能提供:包含癌表位和/或抗原的改良LAMP构建物的表达,以引发免疫应答(在本文中被称作“初免表位”或“初免抗原”),其中所述初免表位和/或抗原被加工并呈递到II类MHC分子,以便偏好性地刺激辅助性T细胞,启动记忆细胞和/或产生

抗体;和通过扩大记忆应答来增强所述免疫应答的表位和/或抗原(在本文中被称为“加强表位”或“加强抗原”)的表达,其中所述加强表位和/或抗原被分泌到所述受试者的循环中。所述用于引发免疫应答的初免表位和/或抗原与所述用于加强免疫应答的加强表位和/或抗原可以相同或不同,然而,也具体设想了表位和抗原的混合物。

[0086] 当在本文中使用时,术语“分泌”是指细胞内的过程和途径,其导致肽、多肽或蛋白质被运输穿过细胞壁,使得所述肽、多肽或蛋白质被释放到细胞外环境中,并且可以例如进入受试者的循环。被运往细胞外环境(即待分泌)的肽、多肽或蛋白质通常被提供有分泌信号序列,通常位于N-端处,其指导核糖体将所述肽、多肽或蛋白质翻译到粗面内质网(粗面ER),从那里可以将新制造的肽、多肽或蛋白质并入到小的运输或分泌囊泡中,所述囊泡将所述肽、多肽或蛋白质转运到细胞表面进行释放。

[0087] 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反应的引发或核酶对多核苷酸的酶切割中的步骤。

[0088] 当在本文中使用时,与另一个序列具有一定百分比(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)的百分比。

[0089] 当在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,两个序列是“基本上同源的”或“基本上相似的”。同样地,当在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66%、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,两个多肽序列是“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℃下洗涤。严紧杂交条件的其他实例包括:约25℃至约37℃的温育温度;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的洗涤溶液。温和杂交条件的实例包括:约40℃至约50℃的温育温度;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的洗涤溶液。高严紧条件的实例包括:约55℃至约68℃的温育温度;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或去离子水的洗涤溶液。一般来说,杂交温育时间为5分钟至24小时,使用1、2或更多个洗涤步骤,并且洗涤温育时间为约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体系的SSC的等效物。相似性可以通过测序来验证,但优选地,也或可选地使用适合于所考虑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。

[0090] 术语“百分比(%)序列相似性”、“百分比(%)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。

[0091] 为了确定两个氨基酸序列或两个核酸分子之间的百分比同一性,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比同一性是所述序列共有的一致位置的数目的函数(即百分比同一性=一致位置的数目/位置(例如交叠的位置)的总数 $\times$ 100)。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比同一性可以使用与下面描述的相似的技术,在允许或不允许存在间隙的情况下来确定。在计算百分比序列同一性中,通常对完全匹配进行计数。

[0092] 两个序列之间的百分比同一性的确定,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中改良的。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/。

[0093] 用于序列比較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。

[0094] 在优选实施方式中,两个氨基酸序列之间的百分比同一性使用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比同一性使用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。

[0095] 可以确定百分比同一性的另一个非限制性实例是通过使用软件程序,例如在《现代分子生物学方法》(Current Protocols In Molecular Biology)(F.M.Ausubel等主编,1987)附录30,第7.7.18节,表7.7.1中描述的软件程序。优选地,将缺省参数用于比对。优选

的比对程序是使用缺省参数的BLAST。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>。

[0096] 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,统计学显著性被计算到 $p=0.05$ (5%)、更优选地 $p=0.01$ 、 $p=0.001$ 、 $p=0.0001$ 、 $p=0.000001$ 的水平。

[0097] 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所选择的(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)。

[0098] 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野生型蛋白的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)所述活性的生物活性。

[0099] 当在本文中使用时,“体内”核酸递送、核酸转移、核酸疗法等,是指将本文所描述的改良LAMP构建物(任选地与加强癌表位和/或抗原一起)直接引入到受试者例如人类或非人类哺乳动物的身体中,由此将所述改良LAMP构建物引入到这种生物体体内的细胞中。

[0100] 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,其中将所述改良LAMP构建物带到靶细胞附近(例如所述核酸不被全身性施用)。例如,原位递送方法包括但不限于将改良LAMP构建物直接注射在位点处(例如到组织例如肿瘤或心肌中),通过开放手术部位将所述改良LAMP构建物与细胞或组织接触,或使用医疗接入装置例如导管将所述改良LAMP构建物递送到位点。

[0101] 当在本文中使用时,术语“分离的”或“纯化的”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(或基本上不含所述组分)。例如,对于本文所描述的改良LAMP构建物来说,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。基本上不含或基本上纯化的,意味着至少50%、优选地至少70%、更优选地至少80%、甚至更优选地至少90%的所述群体不含在自然界中与它们缔合的组分。

[0102] 当在本文中使用时,“靶细胞”或“受体细胞”是指期望成为或已经成为本文中描述的改良LAMP构建物的受体的个体细胞或细胞。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(在形态上或在基因组或总DNA互补上)。靶细胞可以与其他细胞相接触(例如在组织中),或者可能被发现生物体的身体内循环。

[0103] 当在本文中使用时,“受试者”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“受试者”是啮齿动物(例如大鼠、小鼠或兔)、美洲驼、骆驼、奶牛、豚鼠、仓鼠、狗、猫、马、非人类灵长动物、猿猴(例如猴或猿)、猴(例如狨猴、狒狒、恒河猴)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)。

[0104] 术语“癌症”、“赘生物”和“肿瘤”可以互换并以单数或复数形式使用,是指已经历恶性转化,使得它们对于宿主生物体来说成为病理性的细胞。原代癌细胞(即从恶性转化的位点附近获得的细胞)可以通过已确立的技术、特别是组织学检查,与非癌性细胞容易地区分开。当在本文中使用时,癌细胞的定义不仅包括原代癌细胞,还包括源自于癌细胞祖先的任何细胞。这包括转移的癌细胞和源自于癌细胞的体外培养物和细胞系。当指称通常表现为实体肿瘤的癌症类型时,“临床可检测的”肿瘤是在肿瘤块的基础上可以例如通过诸如CAT扫描、MR成像、X-射线、超声或触诊的程序检测,和/或由于在可以从患者获得的样品中一种或多种癌症特异性抗原的表达而可以检测的肿瘤。

[0105] 在优选实施方式中,所述癌症(包括所有发展阶段,包括增生)是腺癌、肉瘤、皮肤癌(例如梅克尔细胞癌)、黑素瘤、膀胱癌、脑癌(包括多形性成胶质细胞瘤)、乳腺癌、子宫癌、卵巢癌、前列腺癌、肺癌(包括但不限于NSCLC、SCLC、鳞状细胞癌)、结肠直肠癌、肛门癌、直肠癌、宫颈癌、肝癌、头颈癌、口腔癌、唾液腺癌、食管癌、胰腺癌、胰腺导管腺癌(PDA)、肾细胞癌(renal cancer)、胃癌、肾癌(kidney cancer)、多发性骨髓瘤或脑癌。此外,待使用本文描述的LAMP构建物进行治疗的优选疾病包括由巨细胞病毒(CMV)引起的过度增殖性障碍或癌症。

[0106] 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。包含所述改良LAMP构建物的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《马丁雷明顿药物科学》(Martin Remington's Pharm.Sci.)第15版(Mack Publ.Co., Easton(1975))。

[0107] 当改良LAMP构建物的核酸分子已被引入到细胞内部时,所述细胞已被这些核酸分子“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,改良LAMP构建物的核酸分子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改良LAMP构建物的核酸分子已整合在染色体中,使得它通过染色体复制被子细胞继承的细胞。这种稳定性由所述真核细胞建立包含有所述核酸分子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先产生的细胞群体。“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。

[0108] 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,例如所述改良LAMP构建物转化和/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施用、应用或给药中施用。在一种情况下,改良LAMP构建物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。

[0109] 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”是足以将疾病的临床显著特征例如肿瘤块尺寸、抗体产生、细胞因子产生、发热或白细胞计数等降低至少约30%、更优选地至少50%、最优选地至少90%的量。

[0110] “抗体”是结合特定抗原的任何免疫球蛋白,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区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。因此,术语抗体不仅涵盖了全抗体分子,而且涵盖了抗体片段以及抗体和抗体片段的变体(包括衍生物例如融合蛋白)。在本申请中用术语“抗体”描述的分子的实例包括但不限于:单链Fv(scFv), Fab片段, Fab'片段, F(ab')₂, 二硫键连接的Fv(sdFv), Fv, 以及包含VL或VH任一结构域或由其构成的片段。当在本文中使用时,术语“单链Fv”或“scFv”是指包含与抗体的VH结构域相连的抗体的VL结构域的多肽。参见Carter(2006) *Nature Rev. Immunol.* 6:243。

[0111] 此外,可以使用本文描述的改良LAMP构建物产生的抗体包括但不限于单克隆、多特异性、双特异性、人类、人源化、小鼠或嵌合抗体,单链抗体,骆驼抗体,Fab片段,F(ab')片段,抗独特型(抗Id)抗体(包括例如针对本发明的抗体的抗Id抗体),结构域抗体和任何上述抗体的表位结合片段。所述免疫球蛋白分子可以是任何类型(例如IgG、IgE、IgM、IgD、IgA和IgY)、类(例如IgG1、IgG2、IgG3、IgG4、IgA1和IgA2)或亚类的免疫球蛋白分子。

[0112] 最优选地,所述抗体是人类抗体。当在本文中使用时,“人类”抗体包括具有人类免疫球蛋白的氨基酸序列的抗体,并包括从人类免疫球蛋白文库和已被遗传工程改造成生产人类抗体的异种移植小鼠或其他生物体分离的抗体。本文中描述的改良LAMP构建物可以与在示例性流程中所描述的用于产生人类抗体和人类单克隆抗体的已知技术相组合使用,参见例如PCT公布WO 98/24893、WO 92/01047、WO 96/34096、WO 96/33735、欧洲专利号0 598 877、美国专利号5,413,923、5,625,126、5,633,425、5,569,825、5,661,016、5,545,806、5,814,318、5,885,793、5,916,771和5,939,598,以及Lonberg和Huszar, *Int. Rev. Immunol.* 13:65-93(1995)。

[0113] 人类抗体或“人源化”嵌合单克隆抗体可以使用所述改良LAMP构建物与本文中描述的或本领域中另外已知的技术相组合来生产。例如,用于生产嵌合抗体的标准方法在本领域中是已知的。对于综述,参见下述参考文献:Morrison, *Science* 229:1202(1985); Oi等, *BioTechniques* 4:214(1986); Cabilly等,美国专利号4,816,567; Taniguchi等, EP 171496; Morrison等, EP 173494; Neuberger等, WO 8601533; Robinson等, WO 8702671; Boulianne等, *Nature* 312:643(1984); Neuberger等, *Nature* 314:268(1985)。

[0114] 可以使用本文描述的改良LAMP构建物产生的抗体可以是单价、二价、三价或多价的。例如,单价scFv可以通过化学方法或通过另一种蛋白质或物质缔合被多聚体化。融合到六聚组氨酸标签或Flag标签的scFv可以使用Ni-NTA琼脂糖(Qiagen)或使用抗Flag抗体(Stratagene, Inc.)被多聚体化。此外,所述改良LAMP构建物可用于产生针对所述改良LAMP构建物中含有的编码的抗原的单特异性、双特异性、三特异性或更高的多特异性。参见例如PCT公布WO 93/17715、WO 92/08802、WO 91/00360、WO 92/05793; Tutt等, *J. Immunol.* 147: 60-69(1991); 美国专利号4,474,893、4,714,681、4,925,648、5,573,920、5,601,819;

Kostelny等, J. Immunol. 148:1547-1553 (1992)。

[0115] “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。如果两个表位可以被同一抗体特异性结合,则它们彼此对应。如果两个表位都能结合到相同的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。应该理解,多个表位可以组成抗原。

[0116] 当在本文中使用时,术语“抗原”或“感兴趣的抗原”覆盖了由克隆到所述改良LAMP构建物中的多核苷酸序列编码的任何多肽序列,其被用于引发先天性或适应性免疫应答,如表1和/或图11A中所述。“抗原”涵盖了克隆在所述改良LAMP构建物中的单个抗原以及多个抗原性序列(源自于相同或不同蛋白)两者。

[0117] 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。

[0118] 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从所述改良LAMP构建物表达的抗原。

[0119] 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。

[0120] 当在本文中使用时,“部分人类”是指具有来自于人类和非人类脊椎动物两者的序列的核酸。在部分人类序列的情形中,所述部分人类核酸具有人类免疫球蛋白编码区的序列和基于所述非人类脊椎动物的内源性免疫球蛋白区的非编码序列的序列。当指称来自于非人类脊椎动物的内源性非编码序列时,术语“基于”是指对应于所述非编码序列,并与所述宿主脊椎动物例如所述ES细胞所源自的非人类脊椎动物的内源性基因座的非编码序列具有相对高的同源性程度的序列。优选地,所述非编码序列与包含所述非编码序列的部分人类分子已被引入到其中的非人类脊椎动物宿主细胞的内源性基因座中存在的相应非编码序列具有至少80%、更优选地90%的同源性。

[0121] 当在本文中使用时,术语“免疫球蛋白可变区”是指编码抗体分子的全部或一部分可变区的核苷酸序列或控制抗体分子的表达的全部或一部分调控核苷酸序列。用于重链的免疫球蛋白区可以包括但不限于V、D、J和转换区的全部或一部分,包括内含子。用于轻链的免疫球蛋白区可以包括但不限于与轻链恒定区基因相关或相邻的V和J区、它们的上游侧翼序列、内含子。

[0122] “转基因动物”意味着具有作为染色体外元件存在于其部分细胞中或稳定整合在其种系DNA中(即在其大多数或所有细胞的基因组序列中)的外源核酸序列的非人类动物,通常为哺乳动物。在产生包含人类序列的转基因动物中,按照本领域中公知的方法,通过例

如所述宿主动物的胚胎或胚胎干细胞的遗传操作,将部分人类核酸引入到这些转基因动物的种系中。

[0123] “载体”包括不论是否自我复制,可用于转化或转染细胞的质粒和病毒和任何DNA或RNA分子。

[0124] “分离”或“纯化”的细胞群体基本上不含在自然界中与其相伴的细胞和材料。基本上游离或基本上纯化的APC意味着所述群体的至少50%是APC,优选地至少70%、更优选地至少80%、甚至更优选地至少90%不含在自然界中与其相伴的非APC细胞。

[0125] 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均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改良LAMP构建物以及基于反转录病毒的载体。

[0126] 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.Glover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)。

[0127] 除非另有定义,否则本文中使用的所有技术和科学术语具有与本发明所属领域的普通技术人员所通常理解的相同的意义。出于描述和公开可以与目前描述的发明相结合使用的装置、制剂和方法的目的,本文中提到的所有出版物通过引用并入本文。

[0128] 示例性实施方式

[0129] 下面是示例性的优选实施方式:

[0130] 1.一种改良LAMP构建物,其包含:

[0131] a.LAMP蛋白的半胱氨酸保守片段;和

[0132] b.至少一种癌抗原,其中所述癌抗原选自大T抗原、小T抗原、MAGE-A10、MAGE-A12、MAGE-A1、MAGE-A2、MAGE-A3、MAGE-A4、MAGE-A4、MAGE-A4、MAGE-A6、MAGE-A6、MAGE-A6、MAGE-A9、MAGE-B10、MAGE-B16、MAGE-B17、MAGE-B1、MAGE-B2、MAGE-B3、MAGE-B4、MAGE-B5、MAGE-B6、MAGE-C1、MAGE-C2、MAGE-C3、MAGE-D1、MAGE-D2、MAGE-D4、MAGE-E1、MAGE-E1_(MAGE1)、MAGE-E2、MAGE-F1、MAGE-H1或MAGEL2。

[0133] 2.根据权利要求1所述的改良LAMP构建物,其中:

[0134] a.所述抗原被放置在所述半胱氨酸保守片段的N-端处;

[0135] b.所述抗原被放置在单个半胱氨酸保守片段的C-端处;或

[0136] c.所述抗原被放置在两个半胱氨酸保守片段之间。

[0137] 3.根据权利要求1或权利要求2所述的改良LAMP构建物,其中所述改良LAMP构建物

包含表1的第1列或第4列中描述的至少一个片段/表位,并且优选地如ILC-1、ILC-2、ILC-3、ILC-4、ILC-5或ILC-6中所述来构建。

[0138] 4. 根据权利要求3所述的改良LAMP构建物,其中每个抗原被连接物隔开,优选地其中所述连接物是氨基酸序列GPGPG (SEQ ID NO:152) 或PMGLP (SEQ ID NO:153)。

[0139] 5. 根据前述权利要求中的任一项所述的改良LAMP构建物,其中所述改良LAMP构建物包含超过一个半胱氨酸保守片段。

[0140] 6. 根据前述权利要求中的任一项所述的改良LAMP构建物,其中所述半胱氨酸保守片段包含LAMP蛋白的同源结构域。

[0141] 7. 根据前述权利要求中的任一项所述的改良LAMP构建物,其中所述改良LAMP构建物还包含LAMP蛋白的跨膜结构域。

[0142] 8. 根据前述权利要求中的任一项所述的改良LAMP构建物,其中所述改良LAMP构建物还包含信号序列,优选地其中所述信号序列源自于LAMP蛋白。

[0143] 9. 根据前述权利要求中的任一项所述的改良LAMP构建物,其中所述LAMP蛋白选自LAMP-1、LAMP2、LAMP-3、LIMP 2、Macrosailin、Endolyn、LAMP5或LIMBIC。

[0144] 10. 根据前述权利要求中的任一项所述的改良LAMP构建物,其中所述改良LAMP构建物包含:

[0145] A) 选自SEQ ID NO:1-113中的任一者的LAMP蛋白和选自SEQ ID NO:114-116中的任一者的癌抗原;

[0146] B) LT^{S220A}-LAMP的氨基酸序列 (SEQ ID NO:151); 或

[0147] C) 与SEQ ID NO:117-150中的任一者组合的(A) 或(B)。

[0148] 11. 根据权利要求12所述的改良LAMP构建物,其中所述LAMP蛋白与SEQ ID NO:1-113具有至少约70%、至少约75%、至少约80%、至少约85%、至少约90%、至少约95%、96%、97%、98%或99%同一性,和/或所述癌抗原与SEQ ID NO:114-151具有至少约70%、至少约75%、至少约80%、至少约85%、至少约90%、至少约95%、96%、97%、98%或99%同一性。

[0149] 12. 根据前述权利要求中的任一项所述的改良LAMP构建物,其中所述改良LAMP构建物包含SEQ ID NO:116的氨基酸序列,并且优选地其中所述LAMP蛋白是人类LAMP1,并且优选地其中所述LAMP构建物是ILC-4。

[0150] 13. 一种多核苷酸,其编码根据权利要求1-12中的任一项所述的改良LAMP构建物。

[0151] 14. 根据权利要求13所述的多核苷酸,其中所述多核苷酸是DNA疫苗。

[0152] 15. 根据权利要求14所述的多核苷酸,其中所述多核苷酸是自我复制RNA疫苗。

[0153] 16. 一种宿主细胞,其包含根据权利要求13-15中的任一项所述的多核苷酸。

[0154] 17. 一种组合物,其包含根据权利要求1-12中的任一项所述的改良LAMP构建物、根据权利要求13-15中的任一项所述的多核苷酸或根据权利要求16所述的宿主细胞。

[0155] 18. 一种治疗患有疾病或障碍的受试者的方法,其中所述方法包括以足以减轻或治疗所述疾病或障碍的量向需要的受试者施用根据权利要求1-12中的任一项所述的改良LAMP构建物、根据权利要求13-15中的任一项所述的多核苷酸、根据权利要求16所述的宿主细胞或根据权利要求17所述的组合物。

[0156] 19. 根据权利要求18所述的方法,其中所述方法包括初免步骤和至少一个加强步

骤。

[0157] 20. 根据权利要求19所述的方法, 其中将根据权利要求1-12中的任一项所述的改良LAMP构建物、根据权利要求13-15中的任一项所述的多核苷酸、根据权利要求16所述的宿主细胞或根据权利要求17所述的组合物用于所述初免步骤中。

[0158] 21. 根据权利要求19或20所述的方法, 其中所述加强步骤包括施用抗原、改良LAMP构建物、由改良LAMP构建物编码的多肽或包含所述改良LAMP构建物的细胞。

[0159] 22. 根据权利要求18-21中的任一项所述的方法, 其中:

[0160] a) 用于初免的抗原与用于加强的抗原相同;

[0161] b) 用于初免的抗原与用于加强的第二抗原源自于同一蛋白;

[0162] c) 将超过一种抗原用于初免和/或加强。

[0163] 23. 根据权利要求18-22中的任一项所述的方法, 其中所述受试者患有过度增殖性障碍。

[0164] 24. 根据权利要求23所述的方法, 其中所述过度增殖性障碍选自腺癌、肉瘤、皮肤癌(例如梅克尔细胞癌)、黑素瘤、膀胱癌、脑癌(包括多形性成胶质细胞瘤)、乳腺癌、子宫癌、卵巢癌、前列腺癌、肺癌(包括但不限于NSCLC、SCLC、鳞状细胞癌)、结肠直肠癌、肛门癌、直肠癌、宫颈癌、肝癌、头颈癌、口腔癌、唾液腺癌、食管癌、胰腺癌、胰腺导管腺癌(PDA)、肾细胞癌、胃癌、肾癌、多发性骨髓瘤或脑癌。

[0165] 25. 根据权利要求23或24所述的方法, 其中所述过度增殖性障碍由巨细胞病毒(CMV)引起。

[0166] 26. 根据权利要求18-25中的任一项所述的方法, 其中所述受试者还被施用检查点抑制剂, 优选地其中所述检查点抑制剂是PD-1/PD-L1抑制剂或CTLA抑制剂。

[0167] 27. 根据权利要求26所述的方法, 其中所述检查点抑制剂选自派姆单抗(KeytrudaTM)、纳武单抗(OpdivoTM)、西米普利单抗(LibtayoTM)、阿特珠单抗(TecentriqTM)、阿维鲁单抗(BavencioTM)、德瓦鲁单抗(ImfinziTM)、伊匹单抗(YervoyTM)。

[0168] LAMP构建物

[0169] 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2A和2B。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22个残基的“铰链”区分隔开的两个大约160个残基的“同源结构域”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)。图2A示意性示出了LAMP-1、LAMP-2、LAMP-3、Endolyn、LIMBIC、LAMP5或Macrosailin之间的保守结构域。

[0170] 以前报道的LAMP构建物包含采取下面这种特定排列方式的下述元件:

[0171] (a) LAMP-1蛋白的完整腔内结构域, 所述抗原, 然后是LAMP-1蛋白的完整跨膜/胞质尾区; 或

[0172] (b) 所述抗原和LAMP-1蛋白的完整跨膜/胞质尾区。

[0173] 在实例(a)中, 所述抗原性序列被插入到LAMP-1蛋白的完整腔内结构域与LAMP-1

的完整跨膜结构域/胞质尾区之间。已显示两种构建物成功地将抗原性序列靶向到溶酶体/胞内体,如图1中所示将被称为“完全LAMP构建物”,相比于本文中描述的改良LAMP构建物 ILC1-ILC6。本文中描述的改良LAMP构建物不包括所述在现有技术中描述的完全LAMP构建物。

[0174] 此外,本文描述的改良LAMP构建物可以包含至少一个初免表位和/或感兴趣的抗原,其被融合到LAMP蛋白的腔内结构域的N-端、LAMP蛋白的至少一个同源结构域的N-或C-端、或LAMP蛋白的至少一个半胱氨酸保守片段的N-或C-端(参见例如图1的 ILC-1-ILC-6)。然而,一些优选的改良LAMP构建物包含至少一个初免表位和/或感兴趣的抗原,其被融合在LAMP蛋白的第一同源结构域与LAMP蛋白的第二同源结构域之间(或至少在两个半胱氨酸保守片段之间)(参见例如图1的 ILC-4)。例如,至少一个感兴趣的抗原可以被放置在LAMP铰链区中或者可以代替所述LAMP铰链区。在某些优选实施方式中,该构建物还包含LAMP蛋白的跨膜结构域和/或LAMP蛋白的胞质尾区。

[0175] 尽管在文献中已广泛报道了比LAMP-1的完整腔内结构域更小的片段在产生稳健的免疫应答中不是有效的(参见例如Godinho等),但相反,本发明人出人意料地发现,采取某些排列方式的特定片段事实上有效地将抗原呈递到免疫系统,在许多情况下产生更加稳健的免疫应答,包括产生不同的抗体谱。例如,本发明人已鉴定到,对产生稳健的免疫应答有效的最小LAMP腔内结构域片段不是所述完整腔内结构域(正如在文献中广泛报道的),而是LAMP蛋白的腔内结构域的单个同源结构域。

[0176] 例如,构建物可以不包含所述完整腔内结构域,而是代之以包含LAMP蛋白的腔内结构域的单个同源结构域。当在本文中使用时,所述“同源结构域”如图3-10中所示包含至少4个均匀间隔的半胱氨酸残基。如图3-10中所示,在每个同源结构域中这些半胱氨酸残基被标注为1、2、3和4(并且在LIMP-2和Macrosailin中鉴定到5个半胱氨酸,在LIMBIC中鉴定到6个半胱氨酸,在Endolyn中鉴定到8个半胱氨酸),并在本文中被定义为“半胱氨酸保守片段”。另外的氨基酸可以被包括到所述半胱氨酸保守片段的N-末端和/或C-末端,以产生多达并包括LAMP蛋白的完整同源结构域。这些另外添加的氨基酸可以源自于所述半胱氨酸保守片段所源自的同源结构域或其他LAMP蛋白同源结构域。因此,当在本文中使用时,LAMP同源结构域包含一个半胱氨酸保守片段和/或由一个半胱氨酸保守片段构成。至少两个LAMP同源结构域组成了LAMP-1、LAMP-2、LAMP-3或Endolyn的腔内结构域。

[0177] 具体来说,在一个优选实施方式中,所述改良LAMP构建物包含表1中描述的至少一个癌抗原(优选为表1的第4列中描述的序列/片段/表位)和/或段落[134]中描述的组合,其被融合到LAMP蛋白的腔内结构域、LAMP蛋白的至少一个同源结构域或LAMP蛋白的至少一个半胱氨酸保守片段的N-端。参见例如图1的 ILC-2和 ILC-6。在优选实施方式中,这些构建物还包含LAMP蛋白的跨膜结构域和/或LAMP蛋白的胞质尾区。在其他优选实施方式中,当抗原含有跨膜结构域时,所述LAMP蛋白的跨膜结构域和/或LAMP蛋白的胞质尾区是非必需的。在优选实施方式中,在所述改良LAMP构建物中包括两个同源结构域(例如图1的 ILC-1)。在其他优选实施方式中,所述两个同源结构域源自于LAMP-1、LAMP-2、LAMP-3或Endolyn蛋白。或者,所述两个同源结构域源自于不同的LAMP蛋白。在这些包含两个同源结构域的构建物中,也可以包括LAMP铰链结构域。本段中描述的改良LAMP构建物相对于现有技术来说是出人意料的,因为所述抗原总是被放置在所述完整腔内LAMP-1结构域与完整LAMP-1跨膜/胞质尾

区之间,因为尚未报道所述腔内结构域的片段在产生稳健的免疫应答中有效。

[0178] 在另一个优选实施方式中,所述改良LAMP构建物包含表1中描述的至少一个癌抗原(优选为表1的第4列中描述的序列/片段/表位)和/或段落[134]中描述的组,其被融合到LAMP蛋白的单个同源结构域或LAMP蛋白的单个半胱氨酸保守片段的C-端(例如图1的ILC-5)。在优选实施方式中,这些构建物还包含LAMP蛋白的跨膜结构域和/或LAMP蛋白的胞质尾区(例如图1的ILC-3)。在其他优选实施方式中,当抗原含有跨膜结构域时,所述LAMP蛋白的跨膜结构域和/或LAMP蛋白的胞质尾区是非必需的。表1中描述的癌抗原也可以插入到如图1中所描绘的完全LAMP构建物中。或者,可以使用来自于两种不同LAMP蛋白的两个同源结构域。本段中描述的改良LAMP构建物相对于现有技术来说是出人意料的,因为抗原总是被放置在完整的腔内LAMP-1结构域与完整的LAMP-1跨膜/胞质尾区之间,因为尚未报道过腔内结构域的片段能有效地产生稳健的免疫应答。

[0179] 因此,所述改良LAMP构建物包含表1中描述的至少一个癌抗原(优选为表1的第4列中描述的序列/片段/表位),其被融合到LAMP蛋白的单个同源结构域或LAMP蛋白的单个半胱氨酸保守片段的C-端。参见例如图1的ILC-3和ILC-5。在优选实施方式中,这些构建物还包含LAMP蛋白的跨膜结构域和/或LAMP蛋白的胞质尾区。在其他优选实施方式中,当抗原含有跨膜结构域时,LAMP蛋白的跨膜结构域和/或LAMP蛋白的胞质尾区是非必需的。如上所述,本段中描述的改良LAMP构建物相对于现有技术来说是出人意料的。

[0180] 在另一个优选实施方式中,所述改良LAMP构建物包含融合在LAMP蛋白的第一同源结构域与LAMP蛋白的第二同源结构域之间(或至少在两个半胱氨酸保守片段之间)的至少一个感兴趣的抗原。参见例如图1的ILC-4。在优选实施方式中,所述两个同源结构域源自于LAMP-1、LAMP-2、LAMP-3或Endolyn蛋白。在这些构建物中,所述抗原可以被放置在LAMP铰链区中。或者,可以使用来自于两种不同LAMP蛋白的两个同源结构域。表1中描述的至少一个癌抗原(优选为表1的第4列中描述的序列/片段/表位)融合在两个LAMP同源结构域(包括半胱氨酸保守片段)之间的这种排列方式相对于现有技术来说是出人意料的。

[0181] 上文描述的改良LAMP构建物可以使用图中定义的结构域来产生。例如,具体设想例如包括在图1中示出的改良LAMP构建物中的结构域可以起源于从直系同源序列衍生的序列。参见例如图3-10。明确设想对于直系同源系列来说,在图2A和2B中定义的对等结构域可用于产生图1中示出的改良LAMP构建物。此外,图3-10中示出的直系同源序列是可用于产生所述结构域的序列的代表。鉴定其他直系同源序列和/或同种型并将它们与图3-10中示出的比对进行比较,完全在本领域的技术范围之内。因此,通过使用图3-10中示出的比对为人类LAMP蛋白鉴定图2A和2B中定义的对等边界,人们可以产生图1中示出的改良LAMP构建物。

[0182] 正如专业技术人员充分理解的,每个结构域的边界是近似值,并且在克隆考虑和限制性酶放置的基础上可以调整至少1、2、3、4、5、6、7、8、9或10个氨基酸。因此,当特定结构域(例如LAMP同源结构域)被包括在所述改良LAMP构建物中时,所述结构域的起点和终点可以参照图2A中定义的边界调整至少1、2、3、4、5、6、7、8、9或10个氨基酸。

[0183] 本文描述的每个所述改良LAMP构建物可以另外包含信号序列和/或出于克隆目的在每个结构域之间包含另外的氨基酸,正如本领域中公知的。此外,所述LAMP同源结构域、LAMP腔内结构域、LAMP跨膜结构域和/或LAMP胞质尾区结构域可以起源于相同的LAMP蛋白

(例如人类LAMP-1)或不同的LAMP蛋白(例如腔内结构域来自于人类LAMP-1并且跨膜结构域来自于人类LAMP-2,和/或同一基因家族(例如LAMP-1)或不同基因家族(LAMP-1和LAMP-2)中的直系同源结构域的混合)。

[0184] 设想了所描述的LAMP构建物的多肽变体。例如,与本文中描述的任何改良LAMP构建物具有至少约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,以及编码这些变体的多核苷酸。所述改良LAMP构建物的变体保留了通过将所述抗原性序列靶向溶酶体而起作用的能力。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,即使包含所述嵌合序列的细胞产生足够的抗原呈递以使其增强免疫应答的效能,将膜和非膜抗原性材料两者转运到胞内体区室的能力。在一种情况下,通过构建含有卵清蛋白的良好表征的抗原性结构域、含有推测的溶酶体/胞内体靶向信号的蛋白的跨膜结构域和胞质结构域的改良LAMP构建物,可以鉴定含有适合的转运信号的序列。靶向的效率可以通过确定表达所述改良LAMP构建物的抗原呈递细胞刺激HA表位特异性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)。

[0185] 编码任何所描述的改良LAMP构建物的多核苷酸,以及与本文中描述的任何改良LAMP构建物的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,是本发明的优选实施方式。所述改良LAMP构建物的变体保留了通过将所述抗原性序列靶向到溶酶体而起作用的能力。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,即使包含所述嵌合序列的细胞产生足够的抗原呈递以使其增强免疫应答的效能,将膜和非膜抗原性材料两者转运到胞内体区室的能力。在一种情况下,通过构建含有卵清蛋白的良好表征的抗原性结构域、含有推测的溶酶体/胞内体靶向信号的蛋白的跨膜结构域和胞质结构域的改良LAMP构建物,可以鉴定含有适合的转运信号的序列。靶向的效率可以通过确定表达所述改良LAMP构建物的抗原呈递细胞刺激HA表位特异性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)。

[0186] 癌抗原

[0187] 下面表1中示出的抗原可以使用专业技术人员公知的技术克隆到本文描述的每个LAMP构建物中。第4列中描述的序列/片段/表位也可以克隆到本文所描述的改良LAMP构建物中。此外,具体设想了可以将表1中列出的任一癌抗原与表1中列出的任何其他抗原(包括在第4列中描述的序列/片段/表位)组合,并插入到本文所描述的改良LAMP构建物中。

[0188]

SEQ ID NO:	抗原的蛋白质名称	登记号/源自于	可以克隆到本文描述的 LAMP 构建物中的优选表位/片段, 至少包含
114	大 T 抗原	YP_009111421	SEQ ID NO: 114 的第 1-327 位氨基酸, 在第 220 位氨基酸处具有或没有突变, 其中野生型丝氨酸优选地被丙氨酸 (或其他失活性氨基酸) 代替 (例如 SEQ ID NO: 115-116), 使得 Rb 结合基序的磷酸化被抑制, 如 Sharma 等, 38, 1153-1162 (JC 2016) 中所述。也设想了 SEQ ID NO: 114 的第 1-327 位氨基酸的片段, 例如被示例为 SEQ ID NO: 115-116 的片段, 只要这些片段保留产生针对梅克尔细胞多瘤病毒 (MCPyV) 的抗体应答的能力即可。优选实施方式的一个实例包含 SEQ ID NO: 51 的氨基酸序列。
117	小 T 抗原	YP_009111422	MCPyVgp4 小 T 抗原, 全长和片段。
118	MAGE-A10	UniProtKB: A0A024RC14	SEQ ID NO: 118
119	MAGE-A12	UniProtKB: P43365	SEQ ID NO: 119
120	MAGE-A1	UniProtKB: P43355	SEQ ID NO: 120
121	MAGE-A2	UniProtKB: P43356	SEQ ID NO: 121
122	MAGE-A3	UniProtKB: P43357	SEQ ID NO: 122
123	MAGE-A4	UniProtKB: A0A024RC12	SEQ ID NO: 123
124	MAGE-A4	UniProtKB: P43358	SEQ ID NO: 124
125	MAGE-A4	UniProtKB: Q1RN33	SEQ ID NO: 125
126	MAGE-A6	UniProtKB: A8K072	SEQ ID NO: 126
127	MAGE-A6	UniProtKB: P43360	SEQ ID NO: 127
128	MAGE-A6	UniProtKB: Q6FHI5	SEQ ID NO: 128
129	MAGE-A9	UniProtKB: P43362	SEQ ID NO: 129
130	MAGE-B10	UniProtKB: Q96LZ2	SEQ ID NO: 130
131	MAGE-B16	UniProtKB: A2A368	SEQ ID NO: 131
132	MAGE-B17	UniProtKB: A8MXT2	SEQ ID NO: 132

[0189]

133	MAGE-B1	UniProtKB: Q96TG1	SEQ ID NO: 133
134	MAGE-B2	UniProtKB: O15479	SEQ ID NO: 134
135	MAGE-B3	UniProtKB: O15480	SEQ ID NO: 135
136	MAGE-B4	UniProtKB: O15481	SEQ ID NO: 136
137	MAGE-B5	UniProtKB: Q9BZ81	SEQ ID NO: 137
138	MAGE-B6	UniProtKB: Q8N7X4	SEQ ID NO: 138
139	MAGE-C1	UniProtKB: O60732	SEQ ID NO: 139
140	MAGE-C2	UniProtKB: Q9UBF1	SEQ ID NO: 140
141	MAGE-C3	UniProtKB: Q8TD91	SEQ ID NO: 141
142	MAGE-D1	UniProtKB: Q9Y5V3	SEQ ID NO: 142
143	MAGE-D2	UniProtKB: Q9UNF1	SEQ ID NO: 143
144	MAGE-D4	UniProtKB: Q96JG8	SEQ ID NO: 144
145	MAGE-E1	UniProtKB: Q6IAI7	SEQ ID NO: 145
146	MAGE-E1 (MAGE1)	UniProtKB: Q9HCL5	SEQ ID NO: 146
147	MAGE-E2	UniProtKB: Q8TD90	SEQ ID NO: 147
148	MAGE-F1	UniProtKB: Q9HAY2	SEQ ID NO: 148
149	MAGE-H1	UniProtKB: Q9H213	SEQ ID NO: 149
150	MAGE-L2	UniProtKB: Q9UJ55	SEQ ID NO: 150

[0190] 此外,可以将表1中描述的抗原(包括在第4列中示出的序列/片段/表位)单独地或彼此组合地克隆到本文描述的LAMP构建物中。因此,表1的第1列中示出的每一个序列、包括

表1的第4列中描述的表位/片段,可用于与也选自表1的第1列或第4列的另一个序列相组合来产生LAMP构建物。为了说明不同的可能组合但决不是限制本公开,可以将抗原(包括表1的第1列中示出的序列和/或表1的第4列中描述的序列/片段/表位)的组合克隆到本文所描述的LAMP构建物中。在特定LAMP构建物中抗原的组合次序可以变化。此外,具体设想了这些抗原可以合并单个LAMP构建物中,或者可以在包含多个LAMP构建物的组合物中递送。

[0191] 编码改良LAMP构建物的序列的组装

[0192] 用于构建包含所述感兴趣的抗原的改良LAMP构建物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。

[0193] 例如,使用重组DNA方法的常规程序,可以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中所描述的。

[0194] 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。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。

[0195] 在一种情况下,使用聚合酶链反应单个地分离编码所述改良LAMP构建物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核酸酶位点,其允许构建编码所述癌抗原序列的改良LAMP构建物。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。

[0196] 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。

[0197] 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)。

[0198] 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起点。

[0199] 核酸递送媒介

[0200] 在一种情况下,将包含改良LAMP构建物的疫苗组合物引入到细胞中。所述细胞可以是用于复制所述核酸或用于表达所述改良LAMP构建物的宿主细胞。优选地,用于表达所述改良LAMP构建物的宿主细胞是抗原呈递细胞(在下文进一步描述)。

[0201] 在优选实施方式中,所述改良LAMP构建物还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)中复制或被复制和/或将所述编码改良LAMP构建物的序列传送到靶细胞内的所需位置的其他序列。

[0202] 另一方面,本发明提供了一种核酸分子(例如质粒或载体),其包含:(i)第一多核苷酸序列,其编码本文所描述的改良LAMP构建物(例如在某些优选实施方式中,一种改良LAMP构建物,其中所述构建物包含融合在LAMP蛋白的第一同源结构域与LAMP蛋白的第二同源结构域之间(或至少在两个半胱氨酸保守片段之间)的至少一个初免表位和/或感兴趣的抗原,例如至少一个表位和/或感兴趣的抗原可以被放置在LAMP铰链区中,或者可以代替所述LAMP铰链区);和(ii)第二多核苷酸序列,其编码可操作地连接到分泌信号序列的至少一个加强表位和/或抗原,其中所述加强表位和/或抗原被分泌到受试者的循环中。所述用于引发免疫应答的表位和/或抗原与所述用于加强免疫应答的表位和/或抗原可以相同或不同,并且优选地选自表1。

[0203] 所述核酸分子可以作为疫苗组合物提供并引入到细胞中。所述细胞可以是用于复制所述核酸分子或用于表达所述改良LAMP构建物(提供初免表位和/或抗原)和所述可操作地连接到分泌信号序列的加强表位和/或抗原(使得所述加强表位和/或抗原从所述细胞分泌)的宿主细胞。优选地,所述宿主细胞是抗原呈递细胞(在下文中进一步描述)。

[0204] 在优选实施方式中,所述编码改良LAMP构建物的第一多核苷酸序列还包含用于插入到靶细胞中的多核苷酸序列和与其可操作连接以控制所述第一多核苷酸序列在所述细胞中的表达(例如转录和/或翻译)的表达控制序列。同样地,在优选实施方式中,所述编码加强表位和/或抗原的第二多核苷酸序列还包含用于插入到靶细胞中的多核苷酸序列和与其可操作地连接以控制所述第二多核苷酸序列在所述细胞中的表达(例如转录和/或翻译)的表达控制序列。所述包含第一和第二多核苷酸序列的核酸分子可以被提供为例如质粒、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)中复制或被复制和/或将所述编码改良LAMP构建物和/或加强表位和/或抗原的序列传送到靶细胞内的所需位置的其他序列。

[0205] 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,例如痘苗。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、以及痘苗和其他痘病毒,正如在例如Flexner, Adv. Pharmacol. 21:51, 1990中教导的。

[0206] 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。

[0207] 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者合成或克隆的共有序列。含有启动子和多核苷酸被可操作地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。

[0208] 为了优化表达和/或转录,可能必需去除、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——控制可操作地连接到它的多核苷酸序列的表达的序列——可用于这些载体中,以表达本发明的多核苷酸序列。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。

[0209] 所述第一和第二多核苷酸序列(编码所述改良LAMP构建物和加强表位和/或抗原)可以从相同或不同的表达控制序列表达。例如,单个启动子可用于编码所述改良LAMP构建物和加强表位和/或抗原两者的双顺反子mRNA分子的转录。本领域技术人员将会充分认识到,所述“第二”编码蛋白的翻译可以通过包含翻译增强元件例如内部核糖体进入位点(IRES) (Plank等, Wiley Interdiscip. Rev. RNA 3:195-212, 2012) 或非结构化连接序列以实现终止后的翻译重新起始 (Onishi等, G3 (Bethesda) 6 (12):4115-4125, 2016) 来实现。然而,在某些优选实施方式中,所述编码改良LAMP构建物和加强表位和/或抗原的多核苷酸序列从不同的表达控制序列(例如不同启动子)表达。

[0210] 为了实现至少一个加强表位和/或抗原的分泌,所述第二多核苷酸序列可以包括编码长度通常为16-30个氨基酸的分泌信号序列(也被称为前导序列)的多核苷酸序列,使得所述第二多核苷酸序列的表达产生可操作连接到所述分泌信号序列的加强表位和/或抗原。本领域技术人员熟知适合的分泌信号序列,它们包括例如白介素-2、CD5、免疫球蛋白κ轻链(在后文中被称为Igκ前导序列)、胰蛋白酶原、血清白蛋白和催乳素的信号序列 (Stern等, Trends Cell Mol. Biol. 2:1-17, 2007; Kober等, Biotechnol. Bioengin. 110:1164-1173, 2013)。在某些情况下,所述分泌信号序列可以是所述加强抗原本源的分泌信号序列。

[0211] 在一种情况下,所述核酸分子包含用于复制的复制原点。优选地,所述起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,适合的起点包括但不限于在细菌细胞(例如埃希氏杆菌 (*Escherichia* sp.)、沙门氏菌 (*Salmonella* sp.)、变形杆菌 (*Proteus* sp.)、梭菌 (*Clostridium* sp.)、克雷伯氏菌 (*Klebsiella* sp.)、芽孢杆菌 (*Bacillus* sp.)、链霉菌 (*Streptomyces* sp.) 和假单胞菌 (*Pseudomonas* sp.))、酵母(例如酿酒酵母 (*Saccharomyces* sp.) 或毕赤酵母 (*Pichia* sp.))、昆虫细胞和哺乳动物细胞中起作用的起点。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)中起作用的复制起点。在

另一种情况下,提供了至少两个复制起点,一个在宿主细胞中起作用,一个在靶细胞中起作用。

[0212] 所述核酸分子可以可替代地或附加性地包含促进所述核酸分子(例如递送载体)的至少一部分整合到靶细胞染色体中的多核苷酸序列。例如,所述核酸分子可以包含与靶细胞的染色体DNA同源的区域。在一种情况下,所述核酸分子被提供成递送载体,其包含与编码所述改良LAMP构建物和加强表位和/或抗原的核酸序列侧接的两个或更多个重组位点。

[0213] 所述载体可以另外包含可检测和/或可选择的标记物,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。这些标记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。

[0214] 可检测/可选择标记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的DNA区段(例如tRNA基因、营养缺陷标记物);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(例如表型标记物例如 β -半乳糖苷酶、荧光蛋白(GFP、CFP、YFP、BFP、RFP、EGFP、EYFP、EBFP、dsRed、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(例如限制性内切核酸酶)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。

[0215] 所述标记物基因可作为标记物,用于证实成功的基因转移和/或用于分离表达被转移的基因的细胞和/或从细胞回收被转移的基因。例如,在一种情况下,所述标记物基因被用于分离和纯化表达本文描述的改良LAMP构建物的抗原呈递细胞。

[0216] 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70%、高于80%、高于约90%并且优选地高于约95%的同一性的基因。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。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。

[0217] 所述编码任选地带有加强表位的改良LAMP构建物的核酸分子可以被提供为裸露核酸分子,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。

[0218] 基于脂质的制剂

[0219] 被设计用于促进改良LAMP构建物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改良LAMP构建物易位到细胞内的易位序列。

[0220] 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。

[0221] 本文描述的改良LAMP构建物可以任选地与加强抗原一起提供在包含脂质单层或双层的制剂中,以促进所述载体进行跨细胞膜转移。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施用,包括静脉内或口服施用。

[0222] 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:核酸分子(编码改良LAMP构建物以及任选的加强表位和/或抗原)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)。

[0223] 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。

[0224] 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,从而使尺寸较小的脂质体聚集体形成的风险最小化。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)。

[0225] 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ferrioxanine是优选的。

[0226] 本发明的改良LAMP构建物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。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,可以使得到的多层囊泡的尺寸分布向较小的尺寸转变。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。

[0227] 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)。

[0228] 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Transfectain™ (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)、DOTAP™ (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)。

[0229] 适合于与所述改良LAMP构建物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)。

[0230] 基于病毒的基因递送媒介

[0231] 在一种情况下,所述改良LAMP构建物和/或加强表位和/或抗原被提供为包含病毒或病毒粒子的递送媒介。在这种情况下,优选地,所述改良LAMP构建物包含病毒载体。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。

[0232] 优选地,包含本文中描述的改良LAMP构建物的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。

[0233] 优选的病毒载体可以源自于选自疱疹病毒、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。这些病毒载体在本领域中是公知的。

[0234] 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、晚期基因表达和剪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

起点,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。

[0235] 腺病毒载体可以被工程化改造成条件复制型 (CRAd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,保留编码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)的全部或一部分E3序列,可以是有利的。

[0236] 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,以便提高所表达的基因在被转导细胞中的长期表达(参见例如WO 94/28152;Lusky等,1998,J.Virol 72:2022-2032)。

[0237] 被引入到细胞中的所述改良LAMP构建物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。

[0238] 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)、禽类(Genbank参考号AAVEDSDNA)、牛类(例如BAV3;Reddy等,1998,J.Virol.72:13941402)、鼠类(Genbank参考号ADRMUSMAVI)、绵羊、猫科动物、猪或猿猴来源,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。

[0239] 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改良LAMP构建物,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。

[0240] 腺病毒粒子可以按照本领域中任何常规的技术(例如WO 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成补足缺陷的载体(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WO 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(例如层析、超离心,如在WO 96/27677、WO 98/00524、WO 98/26048和WO 00/50573中所描述)进一步纯化。

[0241] 细胞类型特异性靶向可以使用通过修饰病毒表面蛋白从具有广宿主范围的腺病毒衍生的载体来实现。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;WO 93/09221和WO 95/28494中。

[0242] 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的系统的几个特征表明它是用于递送的裸露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,主要的吸引人的特征在于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,形成对比的是裸露DNA的剂量为50ug或约 10^{15} 个拷贝。

[0243] 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DNase抗性粒子。

[0244] 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进行复制,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株系(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,所述改良LAMP构建物被插入到所述衣壳化序列下游,优选地以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。

[0245] 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对于所述反转录病毒载体来说有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基因的产物负责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293E16(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。

[0246] 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,Viol.179:247-266;Johnson等,1993,Viol.196:381-401)、Wyeth株系和修饰的Ankara(MVA)株系(Antoine等,1998,Viol.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 206 920;Mayr等,1975,Infection 3:6-14;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,例如非编码基因间区或其失活或缺失不显著损害病毒生长和复制的任何基因。

[0247] 痘病毒粒子如本领域中所所述来制备(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,通过在大肠埃希氏杆菌(*E.coli*)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,以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、冷冻/融化、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去除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。

[0248] 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个碱基对的外来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,痘病毒专门在感染的细胞的细胞质内复制,降低了重组病毒DNA与宿主染色体进行遗传交换的可能性。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。

[0249] 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.Natl'l.Acad.Sci,USA,79:4927,1982;Mackett等,Proc.Natl'l.Acad.Sci.USA,79:7415,1982)。

[0250] 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,可能通过所述改良LAMP构建物和任选的加强表位和/或抗原一起发生癌抗原的表达。已构建了极大地促进了外来基因的插入和表达的质粒载体(Mackett等,J.Viol,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核酸酶位点构成。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。

[0251] 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而使所述TK基因失

活。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。

[0252] 含有大肠埃希氏杆菌 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。

[0253] 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)。

[0254] 病毒的衣壳分子可以包括靶向组成部分以促进靶向和/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记物、组织特异性标记物、细胞受体、病毒抗原、抗原性表位或肿瘤相关标记物。

[0255] 基于病毒粒子的包含改良LAMP构建物以及任选的加强表位和/或抗原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。LAMP构建物的剂量优选地在 0.01 至 10 mg/kg之间,更特别地在 0.1 至 2 mg/kg之间。

[0256] 自我复制RNA

[0257] 自我复制RNA病毒载体也可使用本文中所描述的改良LAMP构建物来构建。例如,甲病毒、黄病毒、麻疹病毒和弹状病毒可用于产生自我复制RNA病毒疫苗。自我复制RNA病毒的优选株系包括但不限于狂犬病病毒(RABV)、水泡性口炎病毒(VSV)、西尼罗病毒、昆津病毒、塞姆利基森林病毒(SFV)、辛德毕斯病毒(SIN)和/或委内瑞拉马脑炎病毒(VEE)。

[0258] 自我复制RNA病毒在递送到组织中之后表达本源抗原,因此模拟活的减毒疫苗而没有回归致病性的风险。它们也刺激先天性免疫系统,因此增强应答。参见例如Ljungberg, K.,“自我复制的甲病毒RNA疫苗”(Self-replicating alphavirus RNA vaccines),Expert Rev Vaccines (2):177-94 (2015);Lundstrom, K.,“癌症免疫疗法中的溶瘤甲病毒”(Oncolytic Alphaviruses in Cancer Immunotherapy),Vaccines 5:9 (2017);Lundstrom, K.,“作为疫苗的复制子RNA病毒载体”(Replicon RNA Viral Vectors as Vaccines),Vaccines 4:39 (2016) (整体通过引用并入本文)。包含本文中描述的改良LAMP构建物的自我复制疫苗的使用,也可用于初免-加强方案中。

[0259] 此外,自我复制RNA病毒也可以如本文中所述用脂质体包封,以改进递送和靶向。使用包含本文中描述的改良LAMP构建物的自我复制RNA病毒的免疫接种可以提供抗原的更高的瞬时表达水平,导致产生中和抗体应答和在安全条件下针对致命激惹的保护作用。

[0260] 基于细胞的递送媒介

[0261] 本发明的改良LAMP构建物可以利用包含所述构建物的其它细胞(“递送细胞”)递送到靶细胞。将改良LAMP构建物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CaPO₄转染(Chen和Okayama,1987,Mol.Cell Biol.7:27452752),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成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)来将它们的内含物递送到靶细胞。

[0262] 辅助分子

[0263] 本发明的包含改良LAMP构建物的组合物可以包含用于促进将改良LAMP构建物引入到细胞中和/或用于增强特定治疗效果和/或增加抗体生产的一种或多种辅助分子。

[0264] 此外,本发明的包含改良LAMP构建物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。

[0265] 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,可以显著提高改良LAMP构建物以及任选的加强表位和/或抗原的摄入和表达(参见例如Curiel等,1992,Am.I.Respir.Cell.Mol.Biol.6:247-252)。

[0266] 宿主细胞

[0267] 本发明的改良LAMP构建物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(例如大肠埃希氏杆菌、葡萄球菌(*Staphylococcus* sp.)、芽孢杆菌(*Bacillus* sp.)),酵母细胞(例如酿酒酵母(*Saccharomyces* sp.)),昆虫细胞,线虫细胞,植物细胞,两栖类细胞(例如爪蟾),禽类细胞,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)。

[0268] 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,改良LAMP构建物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,改良LAMP构建物在转基因生物体(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改良LAMP构建物以及加强表位和/或抗原的核酸的体细胞和/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。

[0269] 改良LAMP构建物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,可以将改良LAMP构建物(任选地与加强表位和/或抗原一起)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。

[0270] 抗原呈递细胞

[0271] 在本发明的优选情况下,将本文所述的改良LAMP构建物引入到天然或工程化的抗原呈递细胞中。

[0272] 当在本文中使用时,术语“抗原呈递细胞”(APC)意指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MHC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。

[0273] 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。

[0274] 几种分子已显示出增强辅助刺激活性。它们包括但不限于热稳定抗原(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。

[0275] 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。

[0276] 在本发明的一种情况下,使用在Romani等,J.Immunol.Methods 196:135-151,1996和Bender等,J.Immunol.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。

[0277] 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去除细胞因子刺激物,它们可以失去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。

[0278] 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,通过存在下述标记物中的至少一者:CD83,CD68,HLA-DR或CD86,或通过Fc受体例如CD 115的丧失来鉴定(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FACSscan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-偶联的链亲和素。

[0279] 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进一步纯化时在少量的基础上也发挥作用。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。

[0280] 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)。

[0281] 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)的其它方法,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。

[0282] 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,即源自于不同受试者。

[0283] 正如本文讨论的,可以使用上述方法或本领域中已知的其他方法将改良LAMP构建物引入到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。

[0284] 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。

[0285] 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感染性疾病、癌症、自体免疫疾病或过敏症的患者分离。

[0286] 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,引起不特异性针对感兴趣的抗原的T细胞的活化。

[0287] 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。获得在本文描述的改良LAMP构建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在细胞培养物中广泛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。

[0288] 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特异性的人类受试者中。将所述细胞进一步离体工程化改造以表达本发明的一种或多种LAMP构建物。

[0289] 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)。对于在人类受试者中使用来说,非转化的细胞系是优选的。

[0290] 在一种情况下,在GM-CSF的影响下分化成树突状细胞的CD34+前体从受试者的身体获得,并将编码改良LAMP构建物的核酸分子引入到所述细胞中,然后将所述细胞注射到所述受试者中。本文中所描述的改良LAMP构建物的使用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,产生显著更加强力的全身性T细胞依赖性免疫应答和/或抗体生产。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。

[0291] 肽疫苗

[0292] 在本发明的范围之内还包括由所述改良LAMP构建物编码的肽疫苗。优选地,所述抗原在所述区室/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分子的表位。

[0293] 由所述改良LAMP构建物编码的肽疫苗也可以被结合在膜结构中,以便于将它施用于生物体的身体。例如,由所述改良LAMP构建物编码的肽疫苗可以被并入到脂质体中,如美国专利号4,448,765中所述。

[0294] 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本文中描述的任一个或多个改良LAMP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)。

[0295] 使用LAMP构建物生产抗体的方法

[0296] 本文所描述的核酸分子和/或已引入所述核酸分子的细胞(例如表达本文中描述的改良LAMP构建物的抗原呈递细胞)可用于通过专业技术人员公知的方法例如本领域中描述的方法来产生抗体。参见例如Sutcliffe等,同上;Wilson等,同上;Chow等, Proc.Natl.Acad.Sci.USA 82:910-914 (1985);和Bittle等, J.Gen.Virol. 66:2347-2354 (1985)。如果使用体内免疫接种,则可以用由所述改良LAMP构建物编码的蛋白质和/或包含本文中所描述的含有抗原以及任选的加强表位和/或抗原的改良LAMP构建物的多核苷酸对动物进行免疫接种。使用作为多核苷酸的改良LAMP构建物、所述改良LAMP构建物的编码蛋白质和/或细胞(例如表达本文中描述的改良LAMP构建物的抗原呈递细胞)进行初免,然后用抗原进行加强,是本发明的优选实施方式。在其他优选实施方式中,具体设想了用本文中所描述的改良LAMP构建物进行初免,然后用抗原进行加强,并且这种方式可用于产生甚至更稳健的免疫应答,特别是从抗体谱多样性和滴度的观点来看。

[0297] 可以将包含所述抗原的改良LAMP构建物注射到所述非人类脊椎动物中以产生抗体。LAMP构建物的制备及其在非人类脊椎动物中的注射,可以按照本领域技术人员公知的动物免疫接种的原则来完成。

[0298] 使用改良LAMP构建物有效地呈递所述抗原,在一种情况下涉及所述抗原在胞吞后被抗原呈递细胞中的LAMP加工以及所述胞内体与溶酶体的融合。然后所述胞内体与来自于高尔基体的含有II类MHC分子的胞吐小泡融合,得到的肽结合到所述II类MHC分子。所述MHC-肽复合体然后转运到细胞质膜,在那里所述抗原可用于展示到CD4⁺T细胞。

[0299] 动物例如兔、大鼠、小鼠、美洲驼、骆驼和/或奶牛,可以用所述包含抗原的改良LAMP构建物和/或编码所述包含抗原的改良LAMP构建物的多核苷酸免疫接种。适合于免疫接种的其他动物包括非人类哺乳动物,例如啮齿动物(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、恒河猴)或猿(例如大猩猩、黑猩猩、猩猩、长臂猿)。

[0300] 例如,可以使用含有约100微克包含抗原或载体蛋白的改良LAMP构建物和弗氏佐剂或已知用于刺激免疫应答的任何其他佐剂的乳液的腹膜内和/或真皮内注射。可能需要例如以约2周的间隔进行几次加强注射(例如使用重组抗原蛋白),以提供可以例如使用直接或间接地(例如通过生物素化的AviTag)吸附到固相表面的游离抗原通过ELISA测定法检测的抗抗原抗体的有用滴度。来自于被免疫接种的动物的血清中抗抗原抗体的滴度可以通过抗抗体的选择来提高,例如按照本领域中公知的方法通过吸附到固相支持物上的抗原并洗脱所选择的抗体。

[0301] 此外,也可以将编码所述包含抗原(和任选的加强表位和/或抗原)的改良LAMP构建物的核酸分子直接引入到动物中。参见例如美国专利号5,676,954、6,875,748、5,661,133;Sahin等, Nat Rev Drug Discov, 2014 Oct;13(10):759-80;Kariko等, Mol Ther, 2008 Nov;16(11):1833-40;Kariko等, Nucleic Acid Res, 2011, Nov;39(21):e142;美国专利号

6,511,832。在一个实例中,将包含抗原的改良LAMP构建物直接注射到非人类脊椎动物中。在所述动物中的注射可以通过肌肉内、真皮内、鼻内、皮下、静脉内、气管内和鞘内递送来进行。使用重组抗原的后续加强,也可以被包括在所述抗体的产生中。

[0302] 此外,通过本公开的方法产生的抗体可以使用展示技术例如噬菌体展示、酵母展示或核糖体展示进行亲和力成熟。在一个实例中,筛选展示在噬菌体粒子表面上的单链抗体分子(“scFv”),以鉴定免疫特异性地结合到所述抗原和/或初始蛋白质的scFv。本发明涵盖了scFv及其被鉴定为免疫特异性地结合到所述抗原和/或初始蛋白质的部分两者。这些scFv可以通过将例如编码所述scFv的VH和/或VL结构域的核苷酸序列插入到含有恒定结构域序列的表达载体中,被常规地“转变”成免疫球蛋白分子,所述表达载体被工程化改造成指导所述免疫球蛋白分子的表达。

[0303] 使用本发明的包含抗原的改良LAMP构建物和编码所述包含抗原的改良LAMP构建物的多核苷酸产生的抗体(包括scFv、以及包含抗体片段或其变体或由抗体片段或其变体构成的其他分子(例如本发明的抗体的重链或轻链或其一部分或本发明的单链抗体))的重组表达,需要构建含有编码所述抗体或其片段或变体的多核苷酸的表达载体。一旦获得本发明的编码抗体分子(例如完全抗体、抗体的重链或轻链或其变体或一部分(优选但不必定含有所述重链或轻链可变结构域))的多核苷酸之后,用于生产所述抗体分子的载体可以使用本领域中公知的技术,通过重组DNA技术来生产。因此,在本文中描述了通过表达含有编码抗体的核苷酸序列的多核苷酸来制备抗体的方法。可以使用本领域技术人员公知的方法来构建含有抗体编码序列和适合的转录和翻译控制信号的表达载体。这些方法包括例如体外重组DNA技术、合成技术和体内遗传重组,并且在本文中描述。因此,本发明提供了可复制的载体,其包含可操作地连接到启动子的编码如本文中所述获得并分离的抗抗原抗体(例如完全抗体、抗体的重链或轻链、抗体的重链或轻链可变结构域或其一部分或重链或轻链CDR、单链Fv或其片段或变体)的核苷酸序列。这些载体可以包括编码抗体分子的恒定区的核苷酸序列(参见例如PCT公布W0 86/05807、PCT公布W0 89/01036和美国专利号5,122,464),并且可以将所述抗体的可变结构域克隆到这种载体中,用于表达完整重链、完整轻链或完整重链和轻链两者。

[0304] 可以通过常规技术将所述表达载体转移到宿主细胞,然后将所述转染的细胞通过常规技术进行培养,以生产任一种所述抗抗原抗体。因此,本发明包括宿主细胞,其含有可操作地连接到异源启动子的编码所述抗抗原抗体(例如完全抗体、其重链或轻链或其部分,或本发明的单链抗体或其片段或变体)的多核苷酸。在优选实施方式中,为了表达完整抗体分子,可以将编码重链和轻链两者的载体在所述宿主细胞中共表达,用于表达所述完整免疫球蛋白分子,正如下文详细描述。

[0305] 可以利用各种不同的宿主-表达载体系统来表达抗抗原抗体。这些宿主-表达系统代表了可以用于生产并随后纯化感兴趣的编码序列的媒介,但是也代表了当用适合的核苷酸编码序列转化或转染时可以表达所述抗抗原抗体的细胞。它们包括但不限于用含有序列的重组噬菌体DNA、质粒DNA或粘粒DNA表达载体转化的微生物例如细菌(例如大肠埃希氏杆菌、枯草芽孢杆菌(*B. subtilis*));用含有编码序列的重组酵母表达载体转化的酵母(例如酿酒酵母、毕赤酵母);用含有编码序列的重组病毒表达载体(例如杆状病毒)感染的昆虫细胞系统;用含有编码序列的重组病毒表达载体(例如花椰菜花叶病毒CaMV、烟草花叶病毒

TMV) 感染或用含有编码序列的重组质粒表达载体(例如Ti质粒)转化的植物细胞系统;或带有重组表达构建物的哺乳动物细胞系统(例如COS、CHO、BHK、293、3T3细胞),所述构建物含有源自于哺乳动物细胞的基因组的启动子(例如金属硫蛋白启动子)或源自于哺乳动物病毒的启动子(例如腺病毒晚期启动子、痘苗病毒7.5K启动子)。优选地,将细菌细胞例如大肠埃希氏杆菌、更优选地真核细胞用于所述抗抗原抗体的表达。例如,与载体例如来自于人类巨细胞病毒的主要立即早期基因启动子元件联合的哺乳动物细胞例如中华仓鼠卵巢细胞(CHO),是一种有效的表达系统(Foecking等, *Gene* 45:101 (1986);Cockett等, *Bio/Technology* 8:2 (1990))。

[0306] 在细菌系统中,大量表达载体可以有利地根据预定用途来选择。例如,当将要生产大量蛋白(用于抗体生产或所述改良LAMP构建物的编码多肽)时,指导容易纯化的融合蛋白产物的高水平表达的载体可能是合乎需要的。这样的载体包括但不限于大肠埃希氏杆菌表达载体pUR278(Ruther等, *EMBO J.* 1.2:1791 (1983)),其中所述编码序列可以被单个地连接到所述载体中,与lac Z编码区同框,以便产生融合蛋白;pIN载体(Inouye&Inouye, *Nucleic Acids Res.* 13:3101-3109 (1985);Van Heeke&Schuster, *J.Chem.* 24:5503-5509 (1989))等。pGEX载体也可用于将外来多肽表达为与谷胱甘肽S-转移酶(GST)的融合蛋白。通常,这些融合蛋白是可溶的,并且可以通过吸附并结合到基质谷胱甘肽琼脂糖珠,然后在游离谷胱甘肽存在下洗脱,从裂解的细胞容易地纯化。所述pGEX载体被设计成包括凝血酶或因因子Xa蛋白酶切割位点,以便可以将所述克隆的靶基因产物从GST组成部分释放。

[0307] 在昆虫系统中,可以使用苜蓿银纹夜蛾(*Autographa californica*)核多角体病毒(AcNPV)作为载体来表达抗抗原抗体或所述改良LAMP构建物的编码蛋白。所述病毒在草地贪夜蛾(*Spodoptera frugiperda*)细胞中生长。编码序列可以被单个地克隆在所述病毒的非必需区(例如多角体蛋白基因)中并置于AcNPV启动子(例如多角体蛋白启动子)的控制之下。

[0308] 在哺乳动物宿主细胞中,可以利用大量基于病毒的表达系统来表达抗抗原抗体或所述改良LAMP构建物的编码蛋白。在使用腺病毒作为表达载体的情况下,可以将感兴趣的编码序列连接到腺病毒转录/翻译控制复合物,例如晚期启动子和三联前导序列。然后将这个嵌合基因通过体外或体内重组插入到腺病毒基因组中。

[0309] 在病毒基因组的非必需区(例如E1或E3区)中的插入将产生在被感染的宿主中存活并且能够表达所述抗抗原抗体或所述改良LAMP构建物的编码多肽的重组病毒(例如参见Logan&Shenk, *Proc.Natl.Acad.Sci.USA* 81:355-359 (1984))。

[0310] 插入的编码序列的高效翻译也可能需要特定的起始信号。这些信号包括ATG起始密码子和相邻序列。此外,所述起始密码子必须与所需编码序列的阅读框同相,以确保整个插入序列的翻译。这些外源翻译控制信号和起始密码子可以是各种不同起源的,包括天然和合成的两者。表达的效率可以通过包含适合的转录增强子元件、转录终止子等来提高(参见例如Bittner等, *Methods in Enzymol.* 153:51-544 (1987))。

[0311] 此外,可以选择以所需的特定方式调节所述插入序列的表达或修饰和加工所述基因产物的宿主细胞株。蛋白质产物的这些修饰(例如糖基化)和加工(例如切割)对所述蛋白质的功能来说可能是重要的。不同宿主细胞具有特征性和特异性的机制用于蛋白质和基因产物的翻译后加工和修饰。可以选择适合的细胞系或宿主系统以确保表达的外来蛋白质的

正确修饰和加工,为此,可以使用具有用于原始转录本的正确加工、基因产物的糖基化和磷酸化的细胞机制的真核宿主细胞。这些哺乳动物宿主细胞包括但不限于CHO、VERY、BHK、Hela、COS、NSO、MDCK、293、3T3、W138,以及特别是乳腺癌细胞系例如BT483、Hs578T、HTB2、BT20和T47D和正常乳腺细胞系例如CRL7030和HsS78Bst。

[0312] 对于重组蛋白的长期、高得率生产来说,稳定的表达是优选的。例如,可以工程化改造稳定地表达抗抗原抗体或所述改良LAMP构建物的编码多肽的细胞系。代替使用含有病毒复制起点的表达载体,可以将宿主细胞用受到适合的表达控制元件(例如启动子、增强子、序列、转录终止子、多腺苷化位点等)控制的多核苷酸和选择标记物进行转化。在引入所述外来多核苷酸之后,可以允许工程化细胞在富集培养基中生长1-2天,然后切换到选择培养基。所述重组质粒中的选择标记物提供对所述选择的抗性,并允许细胞将所述质粒稳定地整合到它们的染色体中并生长以形成灶点,所述灶点进而可以被克隆并扩增成细胞系。这种方法可以被有利地用于工程化改造表达所述抗抗原抗体或所述改良LAMP构建物的编码多肽的细胞系。

[0313] 可以使用大量选择体系,包括但不限于可以分别用于tk⁻、hgprt⁻或aprt⁻细胞的单纯性疱疹病毒胸苷激酶(Wigler等,Cell 11:223(1977))、次黄嘌呤鸟嘌呤磷酸核糖基转移酶(Szybalska&Szybalski,Proc.Natl.Acad.Sci.USA 48:202(1992))和腺嘌呤磷酸核糖转移酶(Lowy等,Cell 22:817(1980))基因。此外,可以使用抗代谢物抗性作为下述基因的选择基础:dhfr,其提供对甲氨蝶呤的抗性(Wigler等,Natl.Acad.Sci.USA 77:357(1980); O'Hare等,Proc.Natl.Acad.Sci.USA 78:1527(1981));gpt,其提供对霉酚酸的抗性(Mulligan&Berg,Proc.Natl.Acad.Sci.USA 78:2072(1981));neo,其提供对氨基糖苷G-418的抗性(Goldspiel等,Clinical Pharmacy,12:488-505(1993);Wu和Wu,Biotherapy 3:87-95(1991);Tolstoshev,AnnPharmacol.Toxicol.32:573-596(1993);Mulligan,Science 260:926-932(1993);以及Morgan和Anderson,Ann.Rev.Biochem.62:191-217(1993);TIB TECH 11(5):155-215(May;1993));和hygro,其提供对潮霉素的抗性(Santerre等,Gene 30:147(1984))。重组DNA技术领域中公知的方法可以被常规应用于选择所需的重组克隆,并且这些方法被描述在例如Ausubel等(主编),《现代分子生物学方法》(Current Protocols in Molecular Biology),John Wiley&Sons,NY(1993);Kriegler,《基因转移和表达实验指南》(Gene Transfer and Expression,A Laboratory Manual),Stockton Press,NY(1990);以及Dracopoli等(主编),《人类遗传学现代方法》(Current Protocols in Human Genetics),John Wiley&Sons,NY(1994)的第12和13章;Colberre-Garapin等,J.Mol.Biol.150:1(1981)中。

[0314] 抗抗原抗体或所述改良LAMP构建物的编码多肽的表达水平可以通过载体扩增来提高(对于综述,参见Bebbington和Hentschel,在DNA克隆中基于基因扩增的载体用于在哺乳动物细胞中克隆基因的表达的用途(The Use Of Vectors Based On Gene Amplification For The Expression Of Cloned Genes In Mammalian Cells In DNA Cloning),Vol.3.(Academic Press,New York,1987))。当表达抗抗原抗体或所述改良LAMP构建物的编码多肽的载体系统中的标记物可扩增时,宿主细胞培养物中存在的抑制剂水平的提高将增加所述标记物的拷贝数。由于所述被扩增区与所述编码序列相连,因此所述抗抗原抗体或所述改良LAMP构建物的编码多肽的生产也提高(Crouse等,Mol.Cell.Biol.3:

257 (1983))。

[0315] 可以包括在载体序列中的其他元件包括异源信号肽(分泌信号)、膜锚定序列、内含子、可选剪接位点、翻译起始和终止信号、蛋白质内含子、生物素化位点和促进翻译后修饰的其他位点、纯化标签、编码与其他蛋白质或肽的融合蛋白的序列、被内部核糖体进入位点隔开的分隔编码区、编码例如提供可选择性(例如抗生素抗性)或可分拣性(例如荧光)的“标记物”蛋白的序列、修饰的核苷酸和其他已知的多核苷酸顺式作用零件,但不限于这些实例。

[0316] 所述宿主细胞可以用本发明的两种表达载体共转染,例如,编码重链来源的多肽的第一载体和编码轻链来源的多肽的第二载体。所述两个载体可能含有一致的选择标记物,能够使重链和轻链多肽相等地表达。或者,可以使用编码并且能够表达重链和轻链多肽两者的单一载体。在这种情况下,所述轻链优选被放置在重链之前,以避免有毒的游离重链的过量(Proudfoot, Nature 322:52 (1986); Kohler, Proc. Natl. Acad. Sci. USA 77:2 197 (1980))。所述重链和轻链的编码序列可以包含cDNA或基因组DNA或合成的DNA序列。

[0317] 一旦已通过重组表达生产了抗抗原抗体或所述改良LAMP构建物的编码多肽后,它可以通过本领域中已知的用于蛋白质纯化的任何方法进行纯化,例如通过层析(例如离子交换、亲和(特别是通过蛋白A亲和以及用于特定抗原的免疫亲和)和尺寸分离柱层析)、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。此外,可以将抗抗原抗体或所述改良LAMP构建物的编码多肽融合到本文中描述的或本领域中原本已知的异源多肽序列,以便于纯化。

[0318] 在一个实例中,所述抗抗原抗体或所述改良LAMP构建物的编码多肽可以与免疫球蛋白(IgA、IgE、IgG、IgM)的恒定结构域或其部分(CH1、CH2、CH3或其任何组合及其部分)或白蛋白(包括但不限于重组人类白蛋白或其片段或变体(参见例如1999年3月2日授权的美国专利号5,876,969、欧洲专利0 413 622和1998年6月16日授权的美国专利号5,766,883)融合,产生嵌合多肽。这些融合蛋白可以便于纯化,并且可以增加体内半衰期。这一点已被由人类CD4-多肽的前两个结构域和哺乳动物免疫球蛋白的重链或轻链的恒定区的各种不同结构域构成的嵌合蛋白显示。参见例如EP 394,827; Traunecker等, Nature, 331:84-86 (1988)。抗原跨过上皮屏障向免疫系统的递送的增加,已用偶联到FcRn结合配偶体例如IgG或Fe片段的抗原(例如胰岛素)得以证实(参见例如PCT公布WO 96/22024和WO 99/04813)。也已发现,由于IgG部分的二硫键而具有二硫键连接的二聚体结构的IgG融合蛋白,与单独的单体多肽或其片段相比在结合和中和其他分子中更加高效。参见例如Fountoulakis等, J. Biochem., 270:3958-3964 (1995)。编码本文中描述的抗抗原抗体或所述改良LAMP构建物的编码多肽的核酸也可以与作为表位标签(例如血凝素(“HA”)标签或flag标签)的感兴趣的基因重组,以帮助所表达的多肽的检测和纯化。例如,由Janknecht等人描述的系统允许容易地纯化在人类细胞系中表达的非变性融合蛋白(Janknecht等, 1991, Proc. Natl. Acad. Sci. USA 88:8972-897)。在这个系统中,将感兴趣的基因亚克隆在痘苗病毒重组质粒中,使得所述基因的开放阅读框在翻译上被融合到由6个组氨酸残基构成的氨基端标签。所述标签充当所述融合蛋白的基质结合结构域。将来自于用所述重组痘苗病毒感染的细胞的提取物装载到Ni²⁺次氨基乙酸-琼脂糖柱上,并且带有组氨酸标签的蛋白可以用含有咪唑的缓冲液选择性洗脱。

[0319] 施用

[0320] 本发明的疫苗材料可以含有编码本文中描述的免疫刺激性改良LAMP构建物(和所述加强表位和/或抗原)的核酸分子,或者可以是表达所述免疫刺激性改良LAMP构建物(和所述加强表位和/或抗原)的重组微生物或抗原呈递细胞。此类核酸分子的制备和用于个体免疫接种的施用按照本领域技术人员公知的免疫接种原则来完成。

[0321] 大量的这些材料可以通过培养含有所述核酸分子的重组体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。包含本文所描述的核酸分子的疫苗通常通过重组体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、栓剂或安瓿瓶中,如本领域所述,例如通过引用并入本文的美国专利号4,446,128中所述。施用可以是任何适合的途径,包括口服、直肠、鼻内或通过注射施用,其中注射可以是例如透皮、皮下、肌肉内或静脉内注射。

[0322] 本文所描述的核酸分子可以以足以在哺乳动物中诱导免疫应答的量施用于所述哺乳动物。施用的最低优选量是引发抗体形成到至少4倍于施用前存在的浓度所需的量。典型的初始施用剂量,在静脉内、肌肉内或皮下施用时为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所述施用的临床医生调整,正如在疫苗或诱导免疫应答的其他药剂的施用中通常发生的。单次施用通常可以足以诱导免疫,但可以进行多次施用以确保或加强所述应答。

[0323] 所述改良LAMP构建物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细胞增殖和对所述改良LAMP构建物的细胞毒性T细胞应答。可以在恒河猴中评估改良LAMP构建物,以确定在小鼠中高度有效的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核酸分子,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。

[0324] 本发明的制剂和施用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。

[0325] 癌症免疫疗法:预防和治疗的候选者

[0326] 本文描述的包含表1中描述的至少一种癌抗原的改良LAMP构建物可用于治疗患有癌症和/或过度增殖性障碍的患者。实例包括患有明确的Epstein-Barr病毒相关淋巴瘤的患者、患有HPV相关宫颈癌的患者、患有慢性HCV的患者或具有癌基因或肿瘤抑制基因的确定重排或突变的患者。其他优选实施方式包括患有由CMV感染引起的过度增殖性障碍、包括癌症的患者。

[0327] 在优选实施方式中,可以使用本文描述的改良LAMP构建物治疗的癌症包括但不限于下述癌症的所有发展阶段,包括增生:腺癌,肉瘤,皮肤癌(例如梅克尔细胞癌),黑素瘤,膀胱癌,脑癌(包括多形性成胶质细胞瘤),乳腺癌,子宫癌,卵巢癌,前列腺癌,肺癌(包括但不限于NSCLC、SCLC、鳞状细胞癌),结肠直肠癌,肛门癌,直肠癌,宫颈癌,肝癌,头颈癌,口腔

癌,唾液腺癌,食管癌,胰腺癌,胰腺导管腺癌(PDA),肾细胞癌,胃癌,肾癌,多发性骨髓瘤或脑癌。

[0328] 设想了一旦个体的癌症被鉴定后,使用改良LAMP构建物的疗法,例如在包含所述改良LAMP构建物的疫苗组合物的情况下,可以在所述个体的癌症进程期间的任何时期使用。在高风险患者中也可以进行疫苗接种,以便预防随后癌症的出现。还设想了基于蛋白质的LAMP构建物疫苗以及细胞疗法(例如包含LAMP构建物的树突状细胞疗法)和包含表1的癌抗原的自我复制构建物。

[0329] 用于疗法的程序

[0330] 在一个实施方式中,可以在患者恶性肿瘤的过程中的任何适合的时间点将所述改良LAMP构建物(任选地与加强表位和/或抗原一起)注入到所述患者中。例如,所述包含表1中描述的至少一种癌抗原的改良LAMP构建物可以在肿瘤负荷低的阶段时注射。在将所述改良LAMP构建物引入到个体的抗原呈递细胞(例如树突状细胞)中的可选实施方式中,从所述个体的骨髓或通过静脉穿刺从外周血抽取所述抗原呈递细胞的前体或成熟的抗原呈递细胞。将这些细胞建立培养物,然后用所述改良LAMP构建物转导。一旦转导发生后,将这些抗原呈递细胞注回所述患者中。

[0331] 在特别优选实施方式中,本发明提供了一种用于具有低肿瘤负荷的癌症患者的治疗方法,例如在疾病的早期、在赘生性肿瘤切除后或在以其他方式降低肿瘤细胞负荷时。在这种方法中,从所述患者获得含有能够分化成表达II类MHC分子的抗原呈递细胞的自体干细胞的细胞群体。将这些细胞培养并通过引入带有或不带有加强表位和/或抗原的改良LAMP构建物进行转化,以将所述待与II类MHC分子缔合的癌抗原递送到所述区室/细胞器内或所述抗原被递送到的另一个区室/细胞器内,并将所述加强抗原分泌到循环中。

[0332] 然后将所述转染的干细胞群体重新引入到所述患者中,在那里所述干细胞分化成抗原呈递细胞,其表达与来自于所述抗原的Th表位复合的II类MHC分子。通过增强所述辅助性T细胞群体的刺激,针对所述抗原的免疫应答将被增强。所述分泌的加强抗原通过例如扩大记忆应答来增强所述免疫应答。

[0333] 更通常地,在一个实施方式中,本发明提供了一种包含所述改良LAMP构建物(以及任选的加强表位和/或抗原)的疫苗组合物,用于在哺乳动物中调节针对抗原的免疫应答(即刺激、增强或降低这种应答)。

[0334] 试剂盒

[0335] 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,试剂盒包含本文中所述的改良LAMP构建物和任选的加强表位和/或抗原以及用于接受所述改良LAMP构建物的细胞。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。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,由所述改良LAMP构建物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改良LAMP构建物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,提供了对所述改良LAMP构建物所编码的抗原特异的一种或多种T细胞系,以验证所述改良LAMP构建物引发、调节或增强免疫应答的能力。

[0336] 实施例

[0337] 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。

[0338] 实施例1-LAMP构建物的构建

[0339] 图1中示出的改良LAMP构建物可以使用专业技术人员公知的标准分子生物学技术来构建。例如,可以设计包含所述多核苷酸的质粒,以产生图1中示出的不同结构ILC-1至ILC-6。图1中示出的LAMP结构域可以源自于图3-10中示出的氨基酸序列。优选地,所述LAMP结构域源自于图3-10中示出的人类LAMP蛋白。每个结构域的边界可以从图2A和图2B推演出来。设想了所述相应结构域也可以通过在与人类序列相比时鉴定对等的结构域,从直系同源序列克隆。如表1中所述,可以将所述癌抗原单个地或组合地克隆到所描述的LAMP构建物中。

[0340] 实施例2-小鼠对LAMP构建物的免疫应答的评估

[0341] 可以测试如实施例1中所描述的改良LAMP构建物调节免疫应答的能力。例如,雌性BALB/c小鼠可以在第0、14和28天,使用nanopass针头用100ul PBS中的50ug所述改良LAMP构建物和5ug GM-CSF进行i.d免疫接种。随后,实验将在最后一次给药后4周结束。

[0342] 用抗原性蛋白(10ug/ml)在T细胞培养基(含有10%热失活FBS、1%青霉素/链霉素和1X 2-ME的RPMI)中刺激脾细胞(3x10⁵/孔),72h后收集上清液。将上清液稀释(400ul上清液+200ul T细胞培养基),并通过ELISA评估细胞因子。IL-10或IL-4的生产可以通过ELISPOT测定法来测量。

[0343] 实施例3-使用LAMP构建物改进抗原呈递

[0344] 癌症是一组混杂的疾病,其中具有侵入其他身体部位的潜力的异常细胞生长控制着正常的内稳态,并且如果不及时且正确治疗,将变得致命。免疫疗法特异性靶向肿瘤细胞,从而避免了对非肿瘤细胞的附带损伤并诱导抗肿瘤应答。这种抗肿瘤应答也具有根除身体中远处的也许不可能通过手术切除的肿瘤的潜力。抗肿瘤免疫应答的诱导或增强在癌症中是艰巨的挑战,因为肿瘤细胞使用多种逃避策略并避免被免疫细胞检测或消除。

[0345] 本项目的目的是评估通过I.D.注射到BALB/c小鼠中的全新一代LAMP构建物的体内免疫应答。具体来说,通过真皮内注射将小鼠用50μg试验构建物进行免疫接种。未向这个试验添加佐剂。在一个月內,每组6只小鼠每7天用疫苗施用,总共三剂。在最后一次免疫接种后14天监测免疫应答。

[0346] 所述试验癌抗原LAMP构建物可以如本文中所述来产生,并且每个试验构建物的序列示出在图11中。用于IFN γ 的ELISPOT抗体对从Biolegend获得。荧光偶联的CD3、CD4、CD8、CD44、CD62L、IFN γ 、TNF α 、颗粒酶B、CD69单克隆抗体和Zombie aqua可固定存活率试剂盒购自BioLegend(San Diego,CA)。链亲和素-HRP购自Thermo Fisher(Waltham,MA)。SureBlue TMB微孔过氧化物酶底物和TMB终止溶液购自KPL(Gaithersburg,MD)。

[0347] 在优选实施方式中,对于Pharmajet来说,每只小鼠每剂使用100ul总体积中的50μg每种癌抗原LAMP构建物。在第0、7和14天,通过i.d.递送将小鼠用疫苗免疫接种。在第28天将小鼠取血,用于血清收集。收集血清并储存在-30℃。在第28天实验结束时收集脾脏并处理,用于ELISPOT和FACS,以评估T细胞应答。

[0348] 通过ELISA测量血浆抗原特异性总IgG。针对癌抗原的鼠类抗体应答可以通过间接

ELISA来评估。将ELISA板 (MaxiSorp) 用碳酸盐-碳酸氢盐缓冲液中的2 μ g/ml癌抗原包被过夜,然后用PBS中的2%BSA阻断。将血浆样品在阻断缓冲液中1:100稀释。用山羊抗小鼠IgG-HRP (Southern Biotech,Birmingham,AL) 检测样品。反应用SureBlue TMB底物进行显色并用来自于KPL (Gaithersburg,MD) 的TMB终止溶液终止。使用Epoch ELISA读板器 (BioTek, Winooski,VT) 读板 (OD450)。

[0349] 抗原特异性T细胞应答的评估。为了在用本文描述的癌抗原LAMP构建物疫苗接种过的小鼠中评估抗原特异性T细胞应答,通过酶联免疫斑点 (ELISPOT) 来评估来自于疫苗接种过的小鼠的脾细胞的抗原特异性IFN γ 生产。对于ELISPOT测定来说,将96孔硝酸纤维素板 (Millipore) 用100 μ l/孔的在PBS中的捕获单克隆抗体在4 $^{\circ}$ C包被过夜。将板用200 μ l/孔的PBS洗涤三次,并用200 μ l/孔的T细胞培养基在室温阻断至少2hr。将脾细胞以3 $\times 10^5$ 个细胞/孔铺板,并与2 μ g/ml癌抗原的合并肽 (表2) 或刀豆蛋白A (0.125 μ g/ml) 或单独的培养基,在总体积为200 μ l/孔的T细胞培养基 (含有L-谷氨酰胺和HEPES (ATCC)、1%青霉素、1%链霉素和5 $\times 10^{-5}$ M β -ME的RPMI-1640) 中,以3 $\times 10^5$ 个细胞/孔的密度在37 $^{\circ}$ C下和5%CO₂中共培养48h。将板用200 μ l/孔的PBS洗涤两次,并用200 μ l/孔的PBS-T (0.05%Tween/PBS) 洗涤两次。添加稀释的检测抗体 (50 μ l/孔,在PBS-T/0.5%BSA中),并将板在室温下振摇温育2hr。将板用PBS洗涤四次。添加在PBS中稀释的链亲和素-碱性磷酸酶 (50 μ l/孔) 并温育2h。将板用PBS洗涤四次,并用50 μ l/孔的3-氨基-9-乙基咔唑 (AEC,BD Bioscience) 底物显色10min。通过在流动自来水下洗涤来终止显色。在室温下在暗处干燥72h后,使用AID ELISPOT高分辨率读板器系统和AID ELISPOT软件3.5版 (Autoimmun Diagnostika GmbH) 对着色的斑点进行计数。

[0350] Western印迹。使用lipofectamine 2000试剂 (Invitrogen) 将293T细胞用所述试验构建物转染。将转染的细胞用PBS洗涤并悬浮在200 μ l含有停止蛋白酶抑制剂的RIPA裂解缓冲液 (Thermo Scientific,Waltham,MA) 中。将裂解物离心 (4 $^{\circ}$ C下700g 15分钟),然后使用Pierce BCA蛋白质测定试剂盒 (ThermoFisher Scientific,Waltham,MA) 测量澄清的上清液中的蛋白质浓度。将10 μ g蛋白质在预制 (4-20%) SDS-PAGE凝胶 (BioRad,Hercules,California) 中电泳,转移到硝酸纤维素膜 (BioRad) 上,并用针对hLAMP的mAb进行免疫印迹。将膜用DetectionTM阻断缓冲液 (KPL) 阻断,用兔抗人LAMP抗体 (Sino Biological Inc., Beijing,China) 或抗癌抗原抗体和山羊抗兔HRP抗体探测,然后用TMB (KPL) 显色。

[0351] 流式细胞术。将细胞首先用PBS中的Zombie aqua可固定存活性染料 (1:500稀释) 标记,然后用染色缓冲液 (含有4%FBS、2%兔血清、2%小鼠血清的PBS) 中的表面抗体 (1:100稀释) 标记。对于细胞内染色来说,将细胞用Zombie aqua染色,然后进行表面染色,用4%聚甲醛固定,并用通透化缓冲液 (含有1%FCS和0.1%皂苷的PBS) 中的细胞内抗体染色。样品可以在CytoFlex流式细胞仪 (Beckman Coulter) 上进行分析,并使用Kaluza软件 (Beckman Coulter) 进行分析。

[0352] 统计学。使用GraphPad Prism 6.0软件或R文件来进行双向ANOVA检验,以评估统计学显著性。从抗原活化的结果推导出每只小鼠的RPMI结果。

[0353] 疫苗和免疫接种。每只小鼠每剂使用25 μ l总体积中的对照、癌抗原+完全LAMP、癌抗原-ILC-1构建物、癌抗原-ILC-2、癌抗原-ILC-3和癌抗原-ILC-4构建物疫苗。在第0、7和14天将小鼠通过ID递送用所述疫苗免疫接种。在第-13和28天从小鼠取血,用于收集血清。

收集血清并储存在-30℃下。在第28天采集脾脏并加工,用于ELISPOT/ELISA测定。

[0354] 实施例4:LAMP构建物的治疗性治疗

[0355] 雌性BALB/c小鼠可以在第0天用7000个同基因4T1乳腺癌细胞s.c接种。在肿瘤可触知后,使用nanopass针头i.d给予100ul PBS中的50ug疫苗和5ug GM-CSF。使用卡尺测量原发肿瘤,并使用公式 $p/6 \times (长度 \times 宽度)^{3/2}$ 来计算肿瘤体积。可以测量平均肿瘤体积随肿瘤接种后的天数的变化。可以使用Kaplan-Meier图来显示结束点时的总存活率。

[0356] 实施例5-初免/加强方案

[0357] 编码本文描述的癌抗原构建物的DNA疫苗可用于治疗应用。在这种情况下,山羊抗小鼠IgG-HRP可以购自Southern Biotechnologies (Birmingham,AL)。SureBlue TMB微孔过氧化氢酶底物和TMB终止溶液可以购自KPL (Gaithersburg,MD)。ELISPOT板从EMD Millipore订购(Billerica,MA,目录号MAIPS4510)。在ELISPOT中使用的IFN- γ 抗体对购自BioLegend (San Diego,CA),并将克隆AN18和R46A2分别用于包被和检测。链亲和素-HRP和AEC底物购自BD Biosciences (San Jose,CA)。

[0358] 6至8周龄雌性Balb/c小鼠购自Harlan Laboratories (Frederick,MA),并且可以维持在Immunomic Therapeutics, Inc. (Rockville,MA)的动物房中。在第0、7和14天,通过电穿孔IM递送将小鼠(n=6)用10 μ g/剂的本文描述的癌抗原改良LAMP构建物(和适合的对照)进行治疗。在第35天,将小鼠用5 μ g癌抗原蛋白,在例如铝佐剂存在下通过i.p.注射进行加强。在第28和49天,将小鼠取血并分离血清,用于抗体检测。在第56天将小鼠处死,并通过ELISPOT测试脾细胞的IFN- γ 生产。

[0359] ELISA程序遵照Su等,J of Immunol Res; (10):1-15 (2016)。将板用5 μ g/ml癌抗原蛋白包被。数据使用Microsoft Excel和Prism 6软件进行分析。

[0360] 实施例6-在C57BL/6中验证LT^{S220A}

[0361] 梅克尔细胞癌(MCC)是一种罕见类型的皮肤癌,在美国每年影响约2500人。MCC表现为快速生长的肉色或蓝红色结节,通常位于面部、头部或颈部。MCC的发病率随着年龄的增长而增加,并与长期日晒和免疫抑制相关。MCC具有很强的侵袭性和高度转移性,治疗选择有限,表明需要针对这种疾病的新的靶向疗法。大约80%的MCC病例与梅克尔细胞多瘤病毒(MCP γ V)感染有关,所述病毒是一种环状双链DNA病毒,可克隆整合到皮肤内的梅克尔细胞中。MCP γ V感染被认为是常见的,并且所述病毒在人体皮肤微生物组中普遍表达。由于MCC非常罕见,因此疾病的发展显然是多因素的。

[0362] MCC细胞表达突变的病毒蛋白,其中主要是MCP γ V4的截短形式的大T(LT)抗原。来自于健康人和MCC患者两者的CD4⁺T细胞均识别LT,使其成为用于疫苗开发的有吸引力的潜在肿瘤相关抗原。LT作为一种癌蛋白,主要通过视网膜母细胞瘤蛋白(pRB)的N-端介导的隔离作用发挥作用。将第220位处的丝氨酸突变为丙氨酸消除了LT与pRB的结合,从而废除其促癌特性。Sharma等,38,1153-1162 (IJC 2016)。CD4⁺T细胞识别LTS220A和野生型LT两者,表明用LTS220A免疫接种可以诱导能够识别肿瘤中的内源性LT的免疫应答。

[0363] 除了本文所描述的溶酶体相关膜蛋白1(LAMP1)之外,我们还产生了编码LT^{S220A}(SEQ ID NO:151)的DNA疫苗。具体来说,构建了在第220位置处具有突变(丝氨酸被丙氨酸代替)的SEQ ID NO:116,并如ILC-4所述将其插入到LAMP的铰链区中。参见图11A和SEQ ID NO:151。

[0364] 我们报告了LT^{S220A}-LAMP诱导有效的全身性抗原特异性CD4 T细胞应答,正如通过IFN γ 和TNF α 两者的产生所度量的。本研究表明LT^{S220A}是有功能的,并且可以诱导针对LT-MCP γ V的全身性抗原特异性CD4 T细胞应答。

[0365] LT^{S220A}-LAMP由Nature Technology Corporation (Lincoln, NE) 制造。对照载体由ITI产生。跨越LT-MCP γ V的交叠肽文库由GenScript合成。将肽以50mg/ml重悬浮在DMSO中,产生5个各自含有25种肽的肽合并物,终浓度为2mg/ml。所有肽的工作浓度均为2ug/ml。伴刀豆球蛋白A (Sigma C5275) 以0.125ug/ml的浓度使用。使用的“培养基”是“T细胞培养基”(RPMI 1640, 10%FBS, 1%青霉素/链霉素, 0.1% β -巯基乙醇)。RBC裂解缓冲液购自Tonbo。将ELISPOT板 (Millipore MSIPS4510) 用纯化的抗小鼠IFN γ 抗体 (Biolegend 517902) 包被,并用生物素偶联的抗小鼠IFN γ 抗体 (Biolegend 505704)、链亲和素-HRP (BD 557630) 和AEC底物试剂盒 (BD 551015) 显色。对于细胞内流式细胞术来说,按照工作手册将细胞与布雷菲德菌素A (BD 555029)、莫能菌素 (BD 554724) 和/或细胞刺激混合物 (eBioscience 00-4970-03) 温育。将细胞用FACS缓冲液 (PBS, 2%FBS) 清洗,并用下述荧光染料偶联的针对表面靶的抗体染色:CD4 FITC (Biolegend 100406), CD8 PerCPCy5.5 (Biolegend 100734), CD44 PE-Cy7 (Biolegend 103030), CD3 A700 (Biolegend 100216), CD62L BV605 (Biolegend 104438)。然后将细胞固定 (BD 554714), 并通下述荧光染料偶联的针对细胞内靶的抗体染色:颗粒酶B PE (eBioscience 12-8898-82), TNF α APC (Biolegend 506308) 和IFN γ e450 (eBioscience 48-7311-82)。

[0366] 免疫接种和细胞因子测量。7-8周龄雌性C57BL/6小鼠购自Jackson Laboratories (Bar Harbor, MA) 并维持在ITI动物房 (Rockville, MD) 中。从第0天开始每周在耳部 (ID/EP) 给药每周剂量的疫苗共4剂。在最后的疫苗接种后两周将小鼠安乐死,收集血清和脾细胞,并将RBC裂解。脾细胞在分析之前在10%DMSO中冷冻。在融化后,将活的脾细胞用于通ELISPOT和细胞内细胞因子染色来测定细胞因子生产。数据使用CytoFLEX流式细胞仪 (Beckman Coulter)、AID读板器、FlowJo、Microsoft Excel和Prism 6软件进行分析。

[0367] 结果。如图11C中所示,LT^{S220A}-LAMP在完整脾细胞中诱导IFN γ 肽回忆应答。如图11B中所示将小鼠用LT^{S220A}-LAMP疫苗接种。在安乐死时,将脾细胞在10%DMSO中冷冻。在融化后,将每孔 3×10^5 个活的脾细胞在用纯化的抗小鼠IFN γ 抗体包被的ELISPOT板中铺板。添加适合的刺激物,包括5个含有横跨LT-MCP γ V的交叠肽文库的区段的独立的肽合并物 (2ug/ml) 和作为阳性对照的伴刀豆球蛋白A。在温育48小时后,将ELISPOT板清洗并用生物素偶联的抗小鼠IFN γ 抗体、链亲和素-HRP和AEC底物显色。将所述板干燥并用AID ELISPOT读板器成像。

[0368] 在来自于用LT^{S220A}-LAMP疫苗接种的小鼠的脾细胞中,肽合并物2和5产生最强的回忆应答。在确认实验中,在任何条件下在任何组中未能检测到IL-10产生 (数据未示出)。值得注意的是,肽合并物5含有额外的非交叠肽,包括以前被其他研究组鉴定为CD8和CD4 T细胞两者的免疫显性表位的肽。所述免疫显性CD8表位也存在于合并物1中,并且所述免疫显性CD4表位也存在于合并物2中。这些ELISPOT数据表明在这种模型中CD4 T细胞可能是IFN γ 的主要生产者,与以前的研究相一致。此外,由于与合并物5相比针对肽合并物2的回忆应答更强,因此合并物2可能含有在LT^{S220A}-LAMP的情形中用作免疫显性表位的额外的肽和/或进一步优化的肽。进一步的研究应该表征肽合并物2中诱导IFN γ 产生的特定肽。

[0369] 图11D:LT^{S220A}-LAMP在脾脏CD4 T细胞中但不在脾脏CD8 T细胞中在肽回忆应答中诱导IFN γ 和TNF α 产生。如图11B中所示将小鼠用LT^{S220A}-LAMP疫苗接种。在安乐死时,将脾细胞在10%DMSO中冷冻。在融化后,将每孔约2E6个脾细胞在布雷菲德菌素A、莫能菌素和5个含有横跨LT-MCP γ V的交叠肽文库的区段的独立的肽合并物(2ug/ml)存在下铺板。将两个孔与PMA/离子霉素温育,用作阳性和同型对照。也将每个脾细胞样品铺板,作为无肽对照。在温育5小时后,将细胞清洗,用荧光染料偶联的抗体染色,并在CytoFLEX流式细胞仪上分析。

[0370] 所述细胞内细胞因子染色数据与ELISPOT数据一致,其中肽合并物2和5在来自于用LT^{S220A}-LAMP疫苗接种的小鼠的脾细胞中产生最强的回忆应答。此外,正如预测,在这个模型中CD4 T细胞是IFN γ 和TNF α 两者的主要生产者,而对CD8 T细胞的影响可忽略不计。

[0371] 图11E示出了肽合并物2(SEQ ID NO:114的aa141-160)、肽13(SEQ ID NO:114的aa145-157)以及在较小程度上肽6(SEQ ID NO:114的aa117-129)、12(SEQ ID NO:114的aa141-153)和17(SEQ ID NO:114的aa161-173)在完整脾细胞中诱导所述观察到的IFN γ 肽回忆应答。如上所述在结束的当天将脾细胞冷冻,在15天后融化,并将各个小鼠合并成组。将每孔 3×10^5 个活的脾细胞在用纯化的抗小鼠IFN γ 抗体包被的ELISPOT板中铺板。将来自于肽合并物2的25种肽中的每一者以2ug/ml的终浓度进行测试。也测试了已知的CD4和CD8表位用于参比,并测试了单独的培养基和作为阳性对照的伴刀豆球蛋白A。在温育48小时后,将ELISPOT板清洗并用生物素偶联的抗小鼠IFN γ 抗体、链亲和素-HRP和AEC底物显色。将所述板干燥并用AID ELISPOT读板器成像。

[0372] 来自于合并物2的肽13诱导最强的IFN γ 肽回忆应答,甚至比使用已知的以前鉴定的CD4免疫显性表位观察到的应答更强。肽13显示出与两种已知表位的交叠,但是独一无二的。当在LAMP的情形中对抗原进行加工时,这种肽可能是最佳的。其他的肽也显示出IFN γ 肽回忆应答,包括不与所述已知表位交叠的肽6和17。

[0373] 实施例8:C57BL/6中的预防性B16-LT^{S220A}研究

[0374] 本研究测试了LT^{S220A}-LAMP在B16小鼠模型中阻止肿瘤生长的能力。将C57BL/6小鼠通过真皮内施用而不使用电穿孔每周疫苗接种共3次。在最后一次疫苗接种后一周,分析外周血的IFN γ 肽回忆应答,以评估对使用LT^{S220A}-LAMP的疫苗接种的免疫应答。在最后一次疫苗接种后两周,在右肋中向小鼠皮下给予2E5个B16-LT^{S220A}肿瘤细胞。随时间测量肿瘤生长和总生存期。出人意料的是,使用LT^{S220A}-LAMP3000的预防性疫苗接种将肿瘤生长的开始显著延迟了大约30天。在疫苗接种的小鼠中观察到肿瘤生长后,每周给予另外的LT^{S220A}-LAMP药剂共5剂。大约50%的疫苗接种的小鼠在肿瘤生长开始后显示出进一步延迟的肿瘤动力学。10只疫苗接种的小鼠中的1只(10%)在肿瘤细胞的初始注射后70天仍保持无肿瘤。本研究证实了LT^{S220A}-LAMP当在预防性情景中给药时能够显著延迟和/或阻止B16-LT^{S220A}肿瘤的生长。

[0375] 具体来说,图12A示出了在给予B16-LTS220A肿瘤的疫苗接种的小鼠中LT^{S220A}-LAMP延迟肿瘤发作。将小鼠用LT^{S220A}-LAMP疫苗接种。将2E5个B16-LTS220A肿瘤细胞皮下注射到右肋中,并随时间测量肿瘤生长和动力学。当肿瘤尺寸在任何方向上达到20mm或达到2000mm³时,或者当肿瘤具有超过2mm的溃疡时,或者当小鼠显示出腹膜肿瘤的窘境或迹象,表明肿瘤已生长通过腹膜壁时,将小鼠安乐死。

[0376] 正如预期,用对照载体疫苗接种的小鼠经历快速、不受控制的肿瘤生长,并且到肿瘤注射后20天为止,100%的动物被安乐死。100%的疫苗接种的小鼠显示出B16-LTS220A肿瘤生长的显著延迟,其中10%的动物在肿瘤注射后70天仍保持无肿瘤。在继续发展肿瘤的疫苗接种的小鼠中,50%表现出对重复的疫苗接种的部分响应,在大约三周的时间段中肿瘤生长减少。

[0377] 图12B报告了在血液ELISPOT反应可以预测用LT^{S220A}-LAMP疫苗接种的小鼠中的最终肿瘤负荷。如上所述的来自于血液ELISPOT的数据与图11A中所示的肿瘤动力学相关。将血液ELISPOT数据归一化到伴刀豆球蛋白A信号,并与肿瘤起始后的存活率进行比较。对使用LT^{S220A}-LAMP的进一步疫苗接种有响应的小鼠(图12A)被称为“响应者”。尽管这些数据在统计上不显著,但它们正趋向于显著($p=0.059$)。

[0378] 实施例9:在C57BL/6中LTS220A DNA疫苗对抗B16-LTS220A的治疗性研究

[0379] 本研究测试了LT^{S220A}-LAMP在上述B16-LTS220A小鼠模型中在预防或延迟肿瘤生长方面的治疗效能。从在右肋中皮下注射 5×10^4 个B16-LTS220A肿瘤细胞后三天开始,每周使用电穿孔通过真皮内施用对C57BL/6小鼠进行疫苗接种,共4次。随时间测量肿瘤生长和总生存期。在肿瘤起始后第17天,通过流式细胞术在8只疫苗接种和8只未疫苗接种的小鼠中检查肿瘤微环境(TME)的细胞组成。如图13中所示,使用LT^{S220A}-LAMP的疫苗接种在治疗情景中出人意料且显著地提高生存期($p=0.003$),生存期中位数比在未疫苗接种的小鼠中观察到的长7天(31天相比于24天)。与以前的研究一致,LT^{S220A}-LAMP在TME中诱导显著的细胞变化。LT^{S220A}-LAMP疫苗接种的小鼠显示出包括CD4和CD8 T细胞和NK细胞在内的免疫细胞大量流入肿瘤内。

[0380] 具体来说,图13A示出了在B16-LTS220A模型中LT^{S220A}-LAMP显著延长生存期。在疫苗接种的小鼠中总生存期显著增加,其中生存期中位数在LT^{S220A}-LAMP疫苗接种的小鼠中为31天,在对照疫苗接种的小鼠中为24天。50% (5/10) 的疫苗接种的动物显示出对所述疫苗的最强响应。

[0381] 图13B示出了LT^{S220A}-LAMP诱导包括CD4和CD8 T细胞在内的CD45+免疫细胞的肿瘤浸润。在肿瘤起始后第17天,将每个治疗组中的8只小鼠用布雷菲德菌素A腹膜内注射。在注射后4小时,将小鼠安乐死,收集脾脏和肿瘤,加工,并通过流式细胞术进行分析。使用LT^{S220A}-LAMP的治疗性疫苗接种引起TME中CD45+免疫细胞的显著增加,包括总T细胞数目的增加以及总CD45+细胞群体的T细胞频率的增加。在疫苗接种的小鼠中每克肿瘤的CD4和CD8 T细胞增加。在这些CD4 T细胞中,疫苗接种的小鼠中PD-1+细胞的频率更高。

[0382] 图13C证实了LT^{S220A}-LAMP诱导NK和NKT细胞两者的肿瘤浸润。使用LT^{S220A}-LAMP的治疗性疫苗接种引起TME中NK细胞的显著增加,每克肿瘤的总数和总CD45+CD3-细胞的频率两者均增加。来自于疫苗接种的小鼠的肿瘤中的NK细胞也显示出更高的CD11b表达,表明表型更加成熟。疫苗接种的小鼠在TME中还具有增加的总NKT细胞。

[0383] 图13D示出了LT^{S220A}-LAMP改变肿瘤内的髓系细胞。使用LT^{S220A}-LAMP的治疗性疫苗接种引起TME中主体CD11b+髓系细胞频率的降低。此外,疫苗接种的小鼠在肿瘤相关巨噬细胞中显示出朝向iNOS生产增强的趋势。

[0384] 图13E示出了LT^{S220A}-LAMP增加TME中调节性T细胞的数目,但Treg数目的增加与肿瘤负荷无关。使用LT^{S220A}-LAMP的治疗性疫苗接种引起疫苗接种的动物的TME中调节性T细胞

(Treg) 数目的增加。然而, Treg 的频率不变, 并且 Treg 的绝对数目和总 CD4⁺ T 细胞的 Treg 频率均与肿瘤负荷无关。

[0385] 图 13F 表明与 LT^{S220A}-LAMP 的组合疗法的潜在价值。正如上文证实的, 使用 LT^{S220A}-LAMP 的治疗性疫苗接种引起浸润 TME 的 T 细胞的相对频率提高, 同时浸润 TME 的髓系细胞的频率降低。无论疫苗接种状态如何, CD8⁺ T 细胞上增加的 PD-1 与肿瘤负荷提高相关, 表明将 LT^{S220A}-LAMP 与 PD-1 阻断相组合可能是一种有效的治疗策略。PD-1 阻断是一种用于梅克尔细胞癌的 FDA 批准的治疗方法。无论疫苗接种状态如何, TME 中髓系细胞的频率也与肿瘤负荷提高相关, 表明靶向 TME 中髓系细胞的召集和/或极化可能增强 LT^{S220A}-LAMP 的有效性。因此, 这些结果支持本文描述的改良 LAMP 构建物、优选为 LT^{S220A}-LAMP 与检查点抑制剂的组合疗法。检查点抑制剂的实例包括但不限于 PD-1/PD-L1 抑制剂或 CTLA 抑制剂, 例如派姆单抗 (KeytrudaTM)、纳武单抗 (OpdivoTM)、西米普利单抗 (LibtayoTM)、阿特珠单抗 (TecentriqTM)、阿维鲁单抗 (BavencioTM)、德瓦鲁单抗 (Imfinzi) 或伊匹单抗 (YervoyTM)。

[0386] 实施例 10: 从多肽生产抗体

[0387] 抗抗原抗体可以使用动物注射, 通过各种不同的产生抗体的标准方法来制备 (参见《现代方法》(Current Protocols), 第 2 章)。例如, 将表达本文中描述的包含癌抗原的改良 LAMP 构建物的细胞施用于非人类脊椎动物, 以诱导含有单克隆抗体的血清的生产。在优选方法中, 制备并纯化所述 LAMP/抗原蛋白的制备物, 以使它基本上不含天然污染物。然后将这种制备物引入到非人类脊椎动物中, 以产生具有更高特异性活性的多克隆抗血清。

[0388] 在最优选的方法中, 本发明的抗抗原抗体是单克隆抗体 (或其蛋白结合片段)。这种单克隆抗体可以使用杂交瘤技术来制备 (Kohler 等, Nature 256:495 (1975); ; Kohler 等, Eur. J. Immunol. 6:511 (1976); Kohler 等, Eur. J. Immunol. 6:292 (1976); Hammerling 等, 《单克隆抗体和 T-细胞杂交瘤》(Monoclonal Antibodies and T-Cell Hybridomas), Elsevier, N.Y., pp.563-681 (1981))。一般来说, 这些程序包括用包含抗原的改良 LAMP 构建物、包含抗原的改良 LAMP 构建物的编码蛋白或更优选地用表达改良 LAMP 构建物的细胞对非人类脊椎动物 (优选为兔、小鼠、奶牛、骆驼、美洲驼) 进行免疫接种。这些细胞可以在任何适合的组织培养基中培养; 然而, 优选地在增补有 10% 胎牛血清 (在约 56°C 下失活) 并增补有约 10g/l 的非必需氨基酸、约 1,000U/ml 的青霉素和约 100ug/ml 的链霉素的 Earle's 改良的 Eagle's 培养基中培养细胞。

[0389] 提取这些非人类脊椎动物宿主 (例如小鼠) 的脾细胞, 并将其与适合的骨髓瘤细胞系融合。根据本发明, 可以使用任何适合的骨髓瘤细胞系; 然而, 优选地使用可以从 ATCCTM 获得的亲本骨髓瘤细胞系 (SP20)。在融合后, 将得到的杂交瘤细胞选择性维持在 HAT 培养基中, 然后如 Wands 等人所述 (Gastroenterology 80:225-232 (1981)) 通过有限稀释法进行克隆。然后测定通过这种选择获得的杂交瘤细胞, 以鉴定分泌能够结合所述抗原的抗体的克隆。

[0390] 应该认识到, 根据本文公开的方法, 可以使用所述抗抗原抗体的 Fab 和 F(ab')₂ 以及其他片段。通常通过蛋白水解切割, 使用酶例如木瓜蛋白酶 (以产生 Fab 片段) 或胃蛋白酶 (以产生 F(ab')₂ 片段) 产生这些片段。或者, 可以通过使用重组 DNA 技术或通过合成化学来生产分泌的蛋白结合片段。

[0391] 对于抗体在人类中的体内使用来说, 使用“人源化”嵌合单克隆抗体可能是优选

的。这些抗体可以使用源自于上述产生所述单克隆抗体的杂交瘤细胞的遗传构建物来生产。用于生产嵌合抗体的方法在本领域中是已知的(对于综述,参见Morrison, Science 229:1202 (1985); Oi等, BioTechniques 4:214 (1986); Cabilly等, 美国专利号4,816,567; Taniguchi等, EP 171496; Morrison等, EP 173494; Neuberger等, WO 8601533; Robinson等, WO 8702671; Boulianne等, Nature 312:643 (1984); Neuberger等, Nature 314:268 (1985))。

[0392] 实施例11:使用多核苷酸产生多克隆和单克隆抗体

[0393] 将多核苷酸直接注射到动物中的方法在本领域中已充分描述。参见例如美国专利号5,676,954、6,875,748、5,661,133。例如,可以将编码包含抗原(以及任选的加强表位和/或抗原)的改良LAMP构建物的多核苷酸注射到受约束的清醒小鼠(雌性6-12周龄BALB/c或裸小鼠nu/nu,来自于Harlan Sprague Dawley, Indianapolis, Ind.)的四头肌中。在一个实施方式中,使用一次性无菌塑料胰岛素注射器和装配有从微量移液器头切下的塑料套环的28G1/2针头(Becton-Dickinson, Franklin Lakes, N.J., 目录号329430), 50 μ l溶液中的50 μ g多核苷酸可用于注射小鼠,如Hartikka, J.等, Hum. Gene Ther. 7:1205-1217 (1996)中所述。

[0394] 或者,在注射前24小时开始,可以向6周龄Sprague Dawley雌性小鼠(体重20-25克)在饮用水中提供5000ppm ZnSO₄。已显示该锌量能够激活金属硫蛋白启动子。然后使用25号针头通过微静脉穿刺,用30 μ l总体积中的与150 μ g脂质体(LipofectionTM)复合的30 μ g编码含有抗原(以及任选的加强表位和/或抗原)的改良LAMP构建物的多核苷酸静脉内注射每只小鼠。动物看护应该在整个研究期间维持,并且应该遵照“实验室动物使用和护理指南”(Guide for the Use and Care of Laboratory Animals, Institute of Laboratory Animal Resources, Commission on Life Sciences, National Research Council, National Academy Press)来进行。

[0395] 在所述注射的编码包含抗原的改良LAMP构建物的多核苷酸被递送到动物中的细胞内之后,所述抗原被递送到胞内体/溶酶体,加工并作为初免抗原呈递到免疫系统,而所述加强表位和/或抗原从细胞分泌。然后所述包含抗原的改良LAMP构建物可以刺激特异性针对所述抗原的抗体的产生,并且所述加强抗原可以增强这种特异性针对所述抗原的抗体的生产。这些抗体可以被分离并用作多克隆混合物,或者被进一步分离成单一物类或单克隆。免疫应答的过程和针对外来抗原的抗体的体内生产,在本领域中是公知的。

[0396] 在第三种动物模型中,将Balb/c 3T3 A31细胞通过电穿孔用编码包含抗原的改良LAMP构建物的多核苷酸转染。表达包含抗原的LAMP构建物的G418抗性克隆通过它们结合人类RBC的能力来鉴定。为了产生多克隆抗体,将Balb/c小鼠以14天的时间间隔,用10⁷个包含所述含有抗原的改良LAMP构建物的细胞进行两次腹膜内免疫接种。在最后一次加强后,收集免疫血清,将IgG通过蛋白G Sepharose纯化,并在通过将1.0mg纯化的抗原偶联到溴化氰活化的Sepharose CL-4B而制备的抗原柱上通过。结合的IgG可以用0.1M pH 2.5的甘氨酸缓冲液洗脱,并用0.1体积的pH 8.0的0.1M Tris中和。为了产生单克隆抗体(mAb),将Balb/c小鼠用包含抗原的LAMP构建物免疫接种,并按照标准方法(28)通过将免疫脾细胞与SP2骨髓瘤融合来产生杂交瘤。可以通过如本领域中所述的酶联免疫吸附测定法来鉴定特异性与抗原反应的阳性孔。将所述杂交瘤通过有限稀释法克隆三次,以产生抗体。

[0397] 实施例12:包含癌抗原的改良LAMP构建物的免疫接种

[0398] 在哺乳动物中产生抗体的方法在本领域中是公知的。在一个实例中,通过在两个月的时间段内用总共500 μ g包含抗原的改良LAMP构建物免疫接种无病原体的兔,产生针对包含抗原的LAMP构建物的多克隆抗血清。例如,可以将所述包含抗原的改良LAMP构建物溶解在PBS中,并用等体积的弗氏佐剂乳化。在最后一次加强后,可以分离所述兔的血清以确定多克隆抗血清的滴度。

[0399] 在另一个动物模型中,可以将5只小鼠(C57BL/6J; Jackson Labs)的组用在铝佐剂中乳化的5 μ g无内毒素的包含抗原的LAMP构建物皮下免疫接种。三周后,对小鼠取血,并且可以通过ELISA通过滴定所述血清来确定抗抗原特异性抗体的存在(血清中的抗体直接结合到直接或间接地(通过生物素化标签和链亲和素)包被在孔上的野生型BPTI或APP-KI)。

[0400] 为了获得单克隆抗体,可以将4-6周龄Ba1b/c小鼠用包含抗原的改良LAMP构建物免疫接种(例如以2周的时间间隔用10-100 μ g/注射来免疫接种四次,第一次注射时溶解在弗氏完全佐剂中,随后的免疫接种时溶解在弗氏不完全佐剂中)。分离脾细胞并与融合细胞系例如Sp2/0骨髓瘤细胞融合,然后进行有限稀释。生长的克隆使用例如酶联免疫吸附测定法(ELISA)来筛选。将96孔板用包含抗原的改良LAMP构建物或用对照蛋白包被。添加培养上清液,然后洗涤并添加用于检测的标记的抗小鼠抗体。在有限稀释后,获得产生所述抗抗原抗体的稳定杂交瘤的克隆。从每种细胞收集上清液,并且通过使用蛋白A琼脂糖柱的亲和层析,可以纯化单克隆抗体。

[0401] 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。

序列表

<110> 免疫治疗有限公司(Immunomic Therapeutics, Inc.)

<120> 改良LAMP构建物

<130> ITI-15-PCT

<150> US 62/916,854

<151> 2019-10-18

<160> 153

<170> PatentIn version 3.5

<210> 1

<211> 417

<212> PRT

<213> 智人(Homo sapiens)

<400> 1

```

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

```

195	200	205
Ser Pro Ser Pro Val Pro Lys	Ser Pro Ser Val Asp Lys Tyr Asn Val	
210	215	220
Ser Gly Thr Asn Gly Thr Cys Leu Leu Ala Ser Met Gly Leu Gln Leu		
225	230	235
240		
Asn Leu Thr Tyr Glu Arg Lys Asp Asn Thr Thr Val Thr Arg Leu Leu		
245	250	255
Asn Ile Asn Pro Asn Lys Thr Ser Ala Ser Gly Ser Cys Gly Ala His		
260	265	270
Leu Val Thr Leu Glu Leu His Ser Glu Gly Thr Thr Val Leu Leu Phe		
275	280	285
Gln Phe Gly Met Asn Ala Ser Ser Ser Arg Phe Phe Leu Gln Gly Ile		
290	295	300
Gln Leu Asn Thr Ile Leu Pro Asp Ala Arg Asp Pro Ala Phe Lys Ala		
305	310	315
320		
Ala Asn Gly Ser Leu Arg Ala Leu Gln Ala Thr Val Gly Asn Ser Tyr		
325	330	335
Lys Cys Asn Ala Glu Glu His Val Arg Val Thr Lys Ala Phe Ser Val		
340	345	350
Asn Ile Phe Lys Val Trp Val Gln Ala Phe Lys Val Glu Gly Gly Gln		
355	360	365
Phe Gly Ser Val Glu Glu Cys Leu Leu Asp Glu Asn Ser Met Leu Ile		
370	375	380
Pro Ile Ala Val Gly Gly Ala Leu Ala Gly Leu Val Leu Ile Val Leu		
385	390	395
400		
Ile Ala Tyr Leu Val Gly Arg Lys Arg Ser His Ala Gly Tyr Gln Thr		
405	410	415
Ile		
<210> 2		
<211> 410		
<212> PRT		
<213> 智人(Homo sapiens)		
<400> 2		
Met Val Cys Phe Arg Leu Phe Pro Val Pro Gly Ser Gly Leu Val Leu		
1	5	10
15		
Val Cys Leu Val Leu Gly Ala Val Arg Ser Tyr Ala Leu Glu Leu Asn		
20	25	30
Leu Thr Asp Ser Glu Asn Ala Thr Cys Leu Tyr Ala Lys Trp Gln Met		
35	40	45

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

355	360	365
Ser Ala Asp Asp Asp Asn Phe	Leu Val Pro Ile Ala Val Gly Ala Ala	
370	375	380
Leu Ala Gly Val Leu Ile Leu Val Leu Leu Ala Tyr Phe Ile Gly Leu		
385	390	395
Lys His His His Ala Gly Tyr Glu Gln Phe		400
	405	410
<210> 3		
<211> 416		
<212> PRT		
<213> 智人(Homo sapiens)		
<400> 3		
Met Pro Arg Gln Leu Ser Ala Ala Ala Ala Leu Phe Ala Ser Leu Ala		
1	5	10
Val Ile Leu His Asp Gly Ser Gln Met Arg Ala Lys Ala Phe Pro Glu		
	20	25
Thr Arg Asp Tyr Ser Gln Pro Thr Ala Ala Ala Thr Val Gln Asp Ile		
	35	40
Lys Lys Pro Val Gln Gln Pro Ala Lys Gln Ala Pro His Gln Thr Leu		
	50	55
Ala Ala Arg Phe Met Asp Gly His Ile Thr Phe Gln Thr Ala Ala Thr		
65	70	75
Val Lys Ile Pro Thr Thr Thr Pro Ala Thr Thr Lys Asn Thr Ala Thr		
	85	90
Thr Ser Pro Ile Thr Tyr Thr Leu Val Thr Thr Gln Ala Thr Pro Asn		
	100	105
Asn Ser His Thr Ala Pro Pro Val Thr Glu Val Thr Val Gly Pro Ser		
	115	120
Leu Ala Pro Tyr Ser Leu Pro Pro Thr Ile Thr Pro Pro Ala His Thr		
	130	135
Thr Gly Thr Ser Ser Ser Thr Val Ser His Thr Thr Gly Asn Thr Thr		
145	150	155
Gln Pro Ser Asn Gln Thr Thr Leu Pro Ala Thr Leu Ser Ile Ala Leu		
	165	170
His Lys Ser Thr Thr Gly Gln Lys Pro Val Gln Pro Thr His Ala Pro		
	180	185
Gly Thr Thr Ala Ala Ala His Asn Thr Thr Arg Thr Ala Ala Pro Ala		
	195	200
Ser Thr Val Pro Gly Pro Thr Leu Ala Pro Gln Pro Ser Ser Val Lys		205

210	215	220
Thr Gly Ile Tyr Gln Val Leu Asn Gly Ser Arg Leu Cys Ile Lys Ala		
225	230	235
Glu Met Gly Ile Gln Leu Ile Val Gln Asp Lys Glu Ser Val Phe Ser		240
245	250	255
Pro Arg Arg Tyr Phe Asn Ile Asp Pro Asn Ala Thr Gln Ala Ser Gly		
260	265	270
Asn Cys Gly Thr Arg Lys Ser Asn Leu Leu Leu Asn Phe Gln Gly Gly		
275	280	285
Phe Val Asn Leu Thr Phe Thr Lys Asp Glu Glu Ser Tyr Tyr Ile Ser		
290	295	300
Glu Val Gly Ala Tyr Leu Thr Val Ser Asp Pro Glu Thr Ile Tyr Gln		
305	310	315
Gly Ile Lys His Ala Val Val Met Phe Gln Thr Ala Val Gly His Ser		320
325	330	335
Phe Lys Cys Val Ser Glu Gln Ser Leu Gln Leu Ser Ala His Leu Gln		
340	345	350
Val Lys Thr Thr Asp Val Gln Leu Gln Ala Phe Asp Phe Glu Asp Asp		
355	360	365
His Phe Gly Asn Val Asp Glu Cys Ser Ser Asp Tyr Thr Ile Val Leu		
370	375	380
Pro Val Ile Gly Ala Ile Val Val Gly Leu Cys Leu Met Gly Met Gly		
385	390	395
Val Tyr Lys Ile Arg Leu Arg Cys Gln Ser Ser Gly Tyr Gln Arg Ile		400
405	410	415
<210> 4		
<211> 478		
<212> PRT		
<213> 智人(Homo sapiens)		
<400> 4		
Met Gly Arg Cys Cys Phe Tyr Thr Ala Gly Thr Leu Ser Leu Leu Leu		
1	5	10
Leu Val Thr Ser Val Thr Leu Leu Val Ala Arg Val Phe Gln Lys Ala		
20	25	30
Val Asp Gln Ser Ile Glu Lys Lys Ile Val Leu Arg Asn Gly Thr Glu		
35	40	45
Ala Phe Asp Ser Trp Glu Lys Pro Pro Leu Pro Val Tyr Thr Gln Phe		
50	55	60
Tyr Phe Phe Asn Val Thr Asn Pro Glu Glu Ile Leu Arg Gly Glu Thr		

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

Ile Asn Ile Tyr Val Lys Lys Leu Asp Asp Phe Val Glu Thr Gly Asp			
385	390	395	400
Ile Arg Thr Met Val Phe Pro Val Met Tyr Leu Asn Glu Ser Val His			
	405	410	415
Ile Asp Lys Glu Thr Ala Ser Arg Leu Lys Ser Met Ile Asn Thr Thr			
	420	425	430
Leu Ile Ile Thr Asn Ile Pro Tyr Ile Ile Met Ala Leu Gly Val Phe			
	435	440	445
Phe Gly Leu Val Phe Thr Trp Leu Ala Cys Lys Gly Gln Gly Ser Met			
	450	455	460
Asp Glu Gly Thr Ala Asp Glu Arg Ala Pro Leu Ile Arg Thr			
465	470	475	
<210> 5			
<211> 197			
<212> PRT			
<213> 智人(Homo sapiens)			
<400> 5			
Met Ser Arg Leu Ser Arg Ser Leu Leu Trp Ala Ala Thr Cys Leu Gly			
1	5	10	15
Val Leu Cys Val Leu Ser Ala Asp Lys Asn Thr Thr Gln His Pro Asn			
	20	25	30
Val Thr Thr Leu Ala Pro Ile Ser Asn Val Thr Ser Ala Pro Val Thr			
	35	40	45
Ser Leu Pro Leu Val Thr Thr Pro Ala Pro Glu Thr Cys Glu Gly Arg			
	50	55	60
Asn Ser Cys Val Ser Cys Phe Asn Val Ser Val Val Asn Thr Thr Cys			
65	70	75	80
Phe Trp Ile Glu Cys Lys Asp Glu Ser Tyr Cys Ser His Asn Ser Thr			
	85	90	95
Val Ser Asp Cys Gln Val Gly Asn Thr Thr Asp Phe Cys Ser Val Ser			
	100	105	110
Thr Ala Thr Pro Val Pro Thr Ala Asn Ser Thr Ala Lys Pro Thr Val			
	115	120	125
Gln Pro Ser Pro Ser Thr Thr Ser Lys Thr Val Thr Thr Ser Gly Thr			
	130	135	140
Thr Asn Asn Thr Val Thr Pro Thr Ser Gln Pro Val Arg Lys Ser Thr			
145	150	155	160
Phe Asp Ala Ala Ser Phe Ile Gly Gly Ile Val Leu Val Leu Gly Val			
	165	170	175

Gln Ala Val Ile Phe Phe Leu Tyr Lys Phe Cys Lys Ser Lys Glu Arg
 180 185 190
 Asn Tyr His Thr Leu
 195
 <210> 6
 <211> 406
 <212> PRT
 <213> 小鼠 (Mus musculus)
 <400> 6
 Met Ala Ala Pro Gly Ala Arg Arg Pro Leu Leu Leu Leu Leu Ala
 1 5 10 15
 Gly Leu Ala His Gly Ala Ser Ala Leu Phe Glu Val Lys Asn Asn Gly
 20 25 30
 Thr Thr Cys Ile Met Ala Ser Phe Ser Ala Ser Phe Leu Thr Thr Tyr
 35 40 45
 Glu Thr Ala Asn Gly Ser Gln Ile Val Asn Ile Ser Leu Pro Ala Ser
 50 55 60
 Ala Glu Val Leu Lys Asn Gly Ser Ser Cys Gly Lys Glu Asn Val Ser
 65 70 75 80
 Asp Pro Ser Leu Thr Ile Thr Phe Gly Arg Gly Tyr Leu Leu Thr Leu
 85 90 95
 Asn Phe Thr Lys Asn Thr Thr Arg Tyr Ser Val Gln His Met Tyr Phe
 100 105 110
 Thr Tyr Asn Leu Ser Asp Thr Glu His Phe Pro Asn Ala Ile Ser Lys
 115 120 125
 Glu Ile Tyr Thr Met Asp Ser Thr Thr Asp Ile Lys Ala Asp Ile Asn
 130 135 140
 Lys Ala Tyr Arg Cys Val Ser Asp Ile Arg Val Tyr Met Lys Asn Val
 145 150 155 160
 Thr Val Val Leu Arg Asp Ala Thr Ile Gln Ala Tyr Leu Ser Ser Gly
 165 170 175
 Asn Phe Ser Lys Glu Glu Thr His Cys Thr Gln Asp Gly Pro Ser Pro
 180 185 190
 Thr Thr Gly Pro Pro Ser Pro Ser Pro Pro Leu Val Pro Thr Asn Pro
 195 200 205
 Thr Val Ser Lys Tyr Asn Val Thr Gly Asn Asn Gly Thr Cys Leu Leu
 210 215 220
 Ala Ser Met Ala Leu Gln Leu Asn Ile Thr Tyr Leu Lys Lys Asp Asn
 225 230 235 240

Lys Thr Val Thr Arg Ala Phe Asn Ile Ser Pro Asn Asp Thr Ser Ser
 245 250 255
 Gly Ser Cys Gly Ile Asn Leu Val Thr Leu Lys Val Glu Asn Lys Asn
 260 265 270
 Arg Ala Leu Glu Leu Gln Phe Gly Met Asn Ala Ser Ser Ser Leu Phe
 275 280 285
 Phe Leu Gln Gly Val Arg Leu Asn Met Thr Leu Pro Asp Ala Leu Val
 290 295 300
 Pro Thr Phe Ser Ile Ser Asn His Ser Leu Lys Ala Leu Gln Ala Thr
 305 310 315 320
 Val Gly Asn Ser Tyr Lys Cys Asn Thr Glu Glu His Ile Phe Val Ser
 325 330 335
 Lys Met Leu Ser Leu Asn Val Phe Ser Val Gln Val Gln Ala Phe Lys
 340 345 350
 Val Asp Ser Asp Arg Phe Gly Ser Val Glu Glu Cys Val Gln Asp Gly
 355 360 365
 Asn Asn Met Leu Ile Pro Ile Ala Val Gly Gly Ala Leu Ala Gly Leu
 370 375 380
 Val Leu Ile Val Leu Ile Ala Tyr Leu Ile Gly Arg Lys Arg Ser His
 385 390 395 400
 Ala Gly Tyr Gln Thr Ile
 405

<210> 7

<211> 411

<212> PRT

<213> 斑马鱼 (Danio rerio)

<400> 7

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

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

405	410
<210> 8	
<211> 417	
<212> PRT	
<213> 非洲爪蟾(Xenopus laevis)	
<400> 8	
Met Ser Trp Arg Gln Val Lys Met Pro Val Tyr Trp Met Ala Val Met	
1 5 10 15	
Leu Leu Ile Gly Val Val Gln Val Ala Thr Ala Val Gln Phe Glu Val	
20 25 30	
Lys Asp Gly Lys Thr Asn Ile Thr Cys Ile Leu Ala Asp Leu Ser Ile	
35 40 45	
Asn Phe Ser Val Ser Tyr Asn Val Ser Ser Lys Met Glu Leu Ala Thr	
50 55 60	
Phe Val Leu Pro Ser Glu Ala Val Thr Asn Ile Asn Lys Ser Ser Cys	
65 70 75 80	
Gly Val Glu Asn Thr Thr Ala Pro Val Leu Ala Ile Gln Phe Gly Ser	
85 90 95	
Asn His Ser Leu Ser Ile His Phe Ala Arg Asn Asn Thr Arg Tyr Glu	
100 105 110	
Val Ala Glu Leu Val Met Ser Tyr Asn Leu Ser Asp Lys Ile Ile Phe	
115 120 125	
Pro Asn Ala Ser Glu Asn Gly Thr Lys Thr Val Ser Thr Asn Lys Thr	
130 135 140	
Ala Val Leu Ala Glu Asn Asp Thr Val Tyr Lys Cys Met Asn Pro His	
145 150 155 160	
Leu Ile Arg Met Asp Asn Ala Asn Ala Thr Phe His Asp Ile Arg Leu	
165 170 175	
Glu Ala Tyr Leu Lys Gln Ser Asn Phe Ser Gln Lys Val Ser Thr Cys	
180 185 190	
Ser Glu Asp Ile Thr Pro Thr Ser Ala Pro Ala Pro Val Thr Thr Thr	
195 200 205	
Ala Pro Val Pro Ala Pro Val Pro Asp Pro Pro Val Val Gln Tyr Ser	
210 215 220	
Val Asn Arg Ser Ser Glu Pro Cys Leu Leu Ala Lys Val Gly Leu Gln	
225 230 235 240	
Met Asn Ile Thr Tyr Thr Thr Lys Asp Gly Lys Asn Gly Ser Tyr Val	
245 250 255	
Phe Asn Ile Glu Ser Lys Gly Val Thr Val Asp Gly Asn Cys Thr Asn	

260	265	270
Thr Thr Ala Tyr Leu Ser Leu Ser Thr Gly Ser Ile Asp Leu Arg Phe		
275	280	285
Asn Phe Thr Leu Asn Ser Ser Leu Glu Val Phe Tyr Leu Asp Gly Val		
290	295	300
Ser Leu Ser Thr Gly Leu Pro Ala Asp Ala Asn Asp Thr His Phe Glu		
305	310	315
Ala Ala Asn Ser Ser Leu Asn Tyr Met Gln Thr Asn Val His Lys Ser		
325	330	335
Phe Lys Cys Asn Ser Lys Gln Thr Leu Gln Ile Thr Asp Pro Phe Thr		
340	345	350
Val Asn Thr Tyr His Leu Gln Val Gln Ala Phe Asn Ser Asp Asn Thr		
355	360	365
Phe Ala Ser Ala Val Glu Cys Ser Leu Asp Glu Asn Gly Met Leu Val		
370	375	380
Pro Ile Val Val Gly Ala Ala Leu Ala Gly Leu Val Leu Ile Val Leu		
385	390	395
Ile Ala Tyr Leu Ile Gly Arg Lys Arg Ser His Ala Gly Tyr Gln Thr		
405	410	415
Ile		
<210> 9		
<211> 417		
<212> PRT		
<213> 黑猩猩 (Pan troglodytes)		
<400> 9		
Met Ala Ala Pro Gly Ser Ala Arg Arg Pro Leu Leu Leu Leu Leu Leu		
1	5	10
Leu Leu Leu Leu Gly Leu Val His Cys Ala Ser Ala Ala Met Phe Met		
20	25	30
Val Lys Asn Gly Asn Gly Thr Ala Cys Ile Met Ala Asn Phe Ser Ala		
35	40	45
Ser Phe Ser Val Asn Tyr Asp Thr Lys Ser Gly Pro Lys Asn Met Thr		
50	55	60
Phe Asp Leu Pro Ser Asp Ala Thr Val Val Leu Asn Arg Ser Ser Cys		
65	70	75
Gly Lys Glu Asn Thr Ser Asp Pro Ser Leu Val Ile Ala Phe Gly Arg		
85	90	95
Gly His Thr Leu Thr Leu Asn Phe Thr Arg Asn Ala Thr Arg Tyr Ser		
100	105	110

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

<210> 10

<211> 415

<212> PRT

<213> 猕猴 (Macaca mulatta)

<400> 10

```

Met Ala Ala Pro Gly Ser Ala Arg Arg Ser Leu Leu Leu Leu Leu
1           5           10           15
Leu Leu Leu Gly Leu Thr His Cys Ala Ser Ala Ala Met Phe Ile 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 Phe
           50           55           60
Asp Leu Pro Ser Asp Ala Lys Val Val Leu Asn Ser 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
Gln 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 Glu 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 Glu 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 Leu Ala Ser Gly Ser Cys Gly Ala His Leu
           260          265          270

```

Val Thr Leu Glu Leu His Ser Glu Gly Ser 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 Thr Leu Pro Asp Ala Arg Asp Pro Ala Phe Lys Ala Ala		
305	310	315
Asn Ser 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 Asn Met Leu Ile Pro		
	370	375
Ile Ala Val Gly Gly Ala Leu Ala Gly Leu Val Leu Ile Val Leu Ile		
385	390	395
Ala Tyr Leu Val Gly Arg Lys Arg Ser His Ala Gly Tyr Gln Thr		
	405	410
<210> 11		415
<211> 413		
<212> PRT		
<213> 家犬(Canis lupus familiaris)		
<400> 11		
Met Ala Ala Phe Gly Gly Ala Arg Pro Arg Pro Leu Leu Leu Leu Leu		
1	5	10
Leu Ala Gly Leu Val His Gly Ala Ala Val Phe Val Val Lys Asp		
	20	25
Ala Asn Gly Thr Ala Cys Ile Met Ala Asn Phe Ser Ala Ala Phe Leu		
	35	40
Ala Ser Tyr Glu Thr Arg Ser Gly Pro Lys Asn Val Thr Phe Asp Leu		
	50	55
Pro Ser Asp Ala Val Val Leu Asn Ser Ser Ser Cys Gly Lys Glu Asn		
65	70	75
Thr Ser Asp Pro Ser Leu Met Ile Ala Phe Gly Lys Gly His Gly Leu		
	85	90
Thr Leu Asn Phe Thr Arg Asn Ala Thr Arg Tyr Ser Val Gln Leu Met		
	100	105
Ser Phe Ile Tyr Asn Leu Ser Asp Thr Gln Ile Phe Pro Asn Ala Ser		
	115	120
		125

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

<210> 12

<211> 417

<212> PRT

<213> 家兔 (*Oryctolagus cuniculus*)

<400> 12

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

290	295	300
Val Leu Leu Asn Thr Thr Leu Pro Asp Ala Arg Glu Pro Ala Phe Ser		
305	310	315
Ala Ser Asn Ser Ser Leu Arg Ala Leu Gln Ala Thr Leu Gly Asn Ser		320
	325	330
Tyr Lys Cys Asn Ser Glu Glu His Val Arg Val Thr Pro Ala Phe Ser		335
	340	345
Leu Ser Ile Phe Lys Val Trp Val Gln Ala Phe Gln Val Lys Gly Asp		350
	355	360
Lys Phe Gly Ser Val Glu Glu Cys Leu Leu Asp Gln Asp Ser Met Leu		365
	370	380
Ile Pro Ile Ala Val Gly Gly Ala Leu Ala Gly Leu Val Leu Val Val		
385	390	395
Leu Ile Ala Tyr Leu Ile Gly Arg Lys Arg Ser His Ala Gly Tyr Gln		400
	405	410
		415
Thr		
<210> 13		
<211> 409		
<212> PRT		
<213> 家牛 (Bos taurus)		
<400> 13		
Met Ala Ala Pro Gly Gly Ala Arg Arg Arg Pro Leu Leu Leu Leu Leu		
1	5	10
Phe Ala Gly Leu Val His Gly Ala Ser Ala Val Phe Val Val Lys Asn		
	20	25
		30
Gly Asn Gly Thr Ala Cys Ile Met Ala Asp Phe Ser Ala Thr Phe Leu		
	35	40
		45
Thr Ser Tyr Asp Thr Arg Ser Gly Pro Gln Asn Lys Ser Phe Glu Leu		
	50	55
		60
Pro Ala Gly Ala Glu Val Ser Asn Ser Ser Ser Cys Gly Lys Glu Asn		
65	70	75
		80
Ala Ser Asp Ser Ser Leu Val Ile Thr Phe Gly Arg Gly His Thr Leu		
	85	90
		95
Thr Leu Ile Phe Thr Arg Asn Ala Thr Arg Tyr Glu Val Gln Leu Met		
	100	105
		110
Arg Phe Ala Tyr Asn Leu Ser Asp Thr Asp Thr Phe Pro Asn Ser Ser		
	115	120
		125
Ser Thr Gly Val Lys Thr Val Glu Ser Ala Thr Asp Ile Lys Ala Asp		
	130	135
		140

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

<210> 14

<211> 407

<212> PRT

<213> 褐家鼠(Rattus norvegicus)

<400> 14

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

305	310	315	320
Ser Val Gly Asn Ser Tyr Lys Cys Asn Ser Glu Glu His Ile Phe Val			
	325	330	335
Ser Lys Ala Leu Ala Leu Asn Val Phe Ser Val Gln Val Gln Ala Phe			
	340	345	350
Arg Val Glu Ser Asp Arg Phe Gly Ser Val Glu Glu Cys Val Gln Asp			
	355	360	365
Gly Asn Asn Met Leu Ile Pro Ile Ala Val Gly Gly Ala Leu Ala Gly			
	370	375	380
Leu Val Leu Ile Val Leu Ile Ala Tyr Leu Ile Gly Arg Lys Arg Ser			
385	390	395	400
His Ala Gly Tyr Gln Thr Ile			
	405		
<210> 15			
<211> 414			
<212> PRT			
<213> 原鸡(Gallus gallus)			
<400> 15			
Met Gly Gly Ala Ala Arg Ala Val Leu Leu Gly Phe Leu Gln Ala Ser			
1	5	10	15
Ser Ser Phe Asp Val Arg Asp Ser Thr Gly Lys Val Cys Ile Ile Ala			
	20	25	30
Asn Leu Thr Val Ala Phe Ser Val Glu Tyr Lys Ser Ser Gly Gln Lys			
	35	40	45
Gln Phe Ala His Phe Phe Leu Pro Gln Asn Ala Thr Ser Gln Ser His			
	50	55	60
Ser Ser Cys Gly Glu Gly Asn Thr Ser His Pro Ile Leu Ala Leu Ser			
65	70	75	80
Phe Gly Ala Gly His Leu Ile Ser Leu Asn Phe Ser Lys Thr Leu Asp			
	85	90	95
Lys Tyr Gln Val Glu Glu Leu Thr Phe His Tyr Asn Leu Ser Asp Glu			
	100	105	110
Thr Leu Phe Pro Asn Ala Thr Glu Gly Lys Val Met Val Ala Thr Gln			
	115	120	125
Lys Ser Val Ile Gln Ala Arg Ile Gly Thr Glu Tyr Arg Cys Ile Asn			
	130	135	140
Ser Lys Tyr Val Arg Met Lys His Val Asn Ile Thr Phe Ser Asn Val			
145	150	155	160
Thr Leu Glu Ala Tyr Pro Thr Asn Asp Thr Phe Ser Ala Asn Lys Thr			

165																170				175					
Glu	Cys	Arg	Glu	Asp	Met	Val	Ser	Thr	Thr	Thr	Val	Ala	Pro	Thr	Thr										
180																185				190					
Pro	Lys	His	Ala	Thr	Ser	Gln	Val	Pro	Thr	Thr	Ser	Pro	Ala	Pro	Thr										
195																200				205					
Ala	Ala	Pro	Ser	Ser	Pro	Ala	Val	Gly	Lys	Tyr	Asn	Val	Thr	Gly	Ala										
210																215				220					
Asn	Gly	Thr	Cys	Val	Leu	Ala	Ser	Met	Gly	Leu	Gln	Leu	Asn	Ile	Thr										
225																230				235				240	
Tyr	Val	Lys	Lys	Asp	Glu	Lys	Met	Gly	Leu	Asp	Leu	Leu	Asn	Phe	Ile										
245																250				255					
Pro	His	Asn	Thr	Ser	Ala	Ser	Gly	Met	Cys	Glu	Ser	Thr	Ser	Ala	Phe										
260																265				270					
Leu	Asn	Leu	Ala	Phe	Glu	Lys	Thr	Lys	Ile	Thr	Phe	His	Phe	Val	Leu										
275																280				285					
Asn	Ala	Ser	Ser	Glu	Lys	Phe	Phe	Leu	Gln	Gly	Val	Asn	Val	Ser	Thr										
290																295				300					
Thr	Leu	Pro	Ser	Glu	Ala	Lys	Ala	Pro	Thr	Phe	Glu	Ala	Ser	Asn	Asp										
305																310				315				320	
Ser	Met	Ser	Glu	Ser	Arg	Ala	Thr	Val	Gly	Asn	Ser	Tyr	Lys	Cys	Ser										
325																330				335					
Ala	Glu	Glu	Asn	Phe	Gln	Val	Thr	Asp	Lys	Ala	Leu	Val	Asn	Val	Phe										
340																345				350					
Asn	Val	Gln	Val	Gln	Ala	Phe	Lys	Val	Asp	Gly	Asp	Lys	Phe	Gly	Ala										
355																360				365					
Met	Glu	Glu	Cys	Gln	Leu	Asp	Glu	Asn	Asn	Met	Leu	Ile	Pro	Ile	Ile										
370																375				380					
Val	Gly	Ala	Ala	Leu	Ala	Gly	Leu	Val	Leu	Ile	Val	Leu	Ile	Ala	Tyr										
385																390				395				400	
Leu	Ile	Gly	Arg	Lys	Arg	Ser	His	Ala	Gly	Tyr	Gln	Thr	Ile												
405																410									
<210> 16																									
<211> 413																									
<212> PRT																									
<213> 野猪 (Sus scrofa)																									
<400> 16																									
Met	Ala	Ala	Pro	Gly	Gly	Ala	Trp	Arg	Arg	Pro	Leu	Leu	Leu	Leu	Leu										
1	5															10				15					
Leu	Leu	Leu	Gly	Leu	Ala	Arg	Gly	Ala	Ser	Ala	Val	Phe	Val	Val	Ser										

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

Glu Gln Arg Leu Gln Val Thr Glu Ala Phe Ala Leu Asn Val Phe Gln
 340 345 350
 Val Arg Val Gln Ala Phe Arg Val Asp Gly Asp Lys Phe Gly Pro Ala
 355 360 365
 Glu Glu Cys Gln Leu Asp Glu Asn Ser Met Leu Ile Pro Ile Ala Val
 370 375 380
 Gly Gly Ala Leu Ala Gly Leu Val Leu Val Val Leu Met Ala Tyr Leu
 385 390 395 400
 Val Gly Arg Lys Arg Ser His Ala Gly Tyr Gln Thr Ile
 405 410

<210> 17

<211> 422

<212> PRT

<213> 短尾负鼠 (*Monodelphis domestica*)

<400> 17

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

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

<210> 18

<211> 415

<212> PRT

<213> 火鸡(Meleagris gallopavo)

<400> 18

Met Ala Arg Ala Leu Leu Ala Ala Val Leu Leu Gly Phe Leu Gln Ala
 1 5 10 15
 Ser Ser Ser Phe Asp Val Arg Asp Ser Thr Gly Lys Val Cys Ile Ile
 20 25 30

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

340	345	350
Phe Asn Val Gln Val Gln Ala Phe Lys Val Asp Gly Asp Lys Phe Gly		
355	360	365
Ala Val Glu Glu Cys Gln Leu Asp Glu Asn Asn Met Leu Ile Pro Ile		
370	375	380
Ile Val Gly Ala Ala Leu Ala Gly Leu Val Leu Ile Val Leu Ile Ala		
385	390	395
Tyr Leu Ile Gly Arg Lys Arg Ser His Ala Gly Tyr Gln Thr Ile		400
405	410	415
<210> 19		
<211> 415		
<212> PRT		
<213> 斑胸草雀(Taeniopygia guttata)		
<400> 19		
Met Ala Arg Gly Leu Leu Ala Ala Ala Leu Leu Gly Phe Leu Gln		
1	5	10
Ala Ser Ser Ser Phe Glu Val Lys Asp Ser Ser Gly Lys Val Cys Ile		
20	25	30
Leu Ala Asp Leu Thr Val Ala Phe Ser Val Glu Tyr Lys Thr Asn Val		
35	40	45
Gln Lys Glu Phe Val His Phe Phe Leu Pro Gln Asn Ala Ser Val Asp		
50	55	60
Ser Gln Ser Ser Cys Gly Lys Asp Asn Ala Ser His Pro Ile Leu Val		
65	70	75
Leu Asp Phe Gly Gly Gly His Ser Leu Ser Leu Asn Phe Ser Glu Ser		
85	90	95
Ala Asp Lys Tyr Gln Val Glu Glu Leu Val Phe His Tyr Asn Leu Ser		
100	105	110
Asp Ala Thr Leu Phe Pro Asn Ser Ser Thr Gly Gly Met Lys Thr Val		
115	120	125
Ser His Lys Ser Ile Ile Gln Ala His Met Gly Thr Gln Tyr Arg Cys		
130	135	140
Ile Asn Ser Lys His Ile Asn Met Lys Asn Val Asn Val Thr Phe Ser		
145	150	155
Asn Val Thr Leu Glu Ala Tyr Leu Thr Asn Gly Thr Leu Ser Val Asn		
165	170	175
Lys Thr Glu Cys Ala Glu Asp Arg Val Ser Thr Thr Thr Met Val Pro		
180	185	190
Thr Thr Pro Lys Gln Thr Thr Ser Gln Ser Pro Thr Thr Gly Pro Ala		

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

<210> 20

<211> 418

<212> PRT

<213> 变色蜥(*Anolis carolinensis*)

<400> 20

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

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

Lys Phe Gly Ala Val Glu Glu Cys Gln Leu Asp Glu Asn Asn Met Leu
 370 375 380
 Ile Pro Ile Ile Val Gly Ala Ala Leu Ala Gly Leu Val Leu Ile Val
 385 390 395 400
 Leu Ile Ala Tyr Leu Ile Gly Arg Lys Arg Ser His Ala Gly Tyr Gln
 405 410 415
 Thr Ile
 <210> 21
 <211> 418
 <212> PRT
 <213> 青鳉 (*Oryzias latipes*)
 <400> 21
 Met Lys Ser Phe Pro Ser Phe Val Ala Leu Phe Ile Val Cys Ser Ala
 1 5 10 15
 Val Leu Ala Asp Thr Gln Ala Val Val Thr Leu Glu Val Lys Glu Gly
 20 25 30
 Asn Ser Thr Cys Ile Lys Ala Glu Phe Ser Ala Val Phe Ser Ile Thr
 35 40 45
 Tyr Asn Thr Thr Asn Asp Thr Arg Thr Val Ser Val Phe Leu Pro Asn
 50 55 60
 Ser Thr Thr Val Asp Ser Ala Asn Ser Ser Cys Gly Ser Asn Gly Ser
 65 70 75 80
 Thr Pro Gly Leu Met Ala Lys Phe Gly Pro Gly His Tyr Phe Gly Met
 85 90 95
 Asn Phe Ser Thr Asn Gly Ser Leu Tyr Ser Val Asp Thr Leu Phe Leu
 100 105 110
 Arg Tyr Asn Leu Ser Asp Ala Ser Leu Phe Pro Glu Ala Asn Ser Ser
 115 120 125
 Gly Pro Val Asp Phe Glu Leu Ser Ala Ser Val Gly Ile Trp Ala Pro
 130 135 140
 Thr Asn Thr Thr Tyr Arg Cys Leu Ser Pro Thr Thr Ile Thr Ile Thr
 145 150 155 160
 Arg Pro Ser Val Thr Phe Ser Glu Met Lys Leu Glu Ala Tyr Met Pro
 165 170 175
 Gly Asn Asp Phe Ser Pro Ala Glu Arg Val Cys Ala Ala Asp Gln Thr
 180 185 190
 Thr Thr Gly Ala Pro Thr Thr Thr Thr Ser Ala Ala Thr Pro Thr Thr
 195 200 205
 Pro Ser Pro Thr Pro Ala Gly Thr Pro Glu Gln Gly Ser Tyr Ser Val

210	215	220
Lys Asn Ala Ser Gly Thr Val Cys Leu Met Ala Lys Met Gly Val Gln		
225	230	235
Leu Asn Val Ser Tyr Phe Ser Gln Ser Gln Asn Lys Thr Val Gln Glu		240
	245	250
Leu Leu Asn Leu Thr Pro Asn Leu Thr Ser Ser Ser Gly Leu Cys Gly		255
	260	265
Gly Thr Asn Ala Thr Leu Val Leu Ala Gln Glu Glu Thr Thr Val Leu		270
	275	280
Ser Phe Leu Phe Thr Val Asn Ser Thr Ser Asn Lys Tyr His Leu Ser		285
290	295	300
Gly Ile Thr Leu Gln Ala Asn Trp Thr Asp Met Met Ser Pro Phe Ser		
305	310	315
Ala Ser Asn Thr Ser Leu Asp Tyr Leu Arg Ser Ser Leu Gly His Ser		320
	325	330
Tyr Met Cys Asn Ala Glu Gln Thr Leu Phe Val Val Ser Thr Phe Ser		335
	340	345
Ile Asn Met Phe Glu Leu Gln Val Gln Pro Phe Gly Val Thr Ser Thr		350
	355	360
Gln Phe Ala Ser Ala Glu Val Cys Gln Ile Asp Gln Asp Gln Met Leu		365
	370	375
Ile Pro Ile Ile Val Gly Ala Ala Leu Ala Gly Leu Val Leu Ile Val		380
385	390	395
Leu Ile Ala Tyr Leu Ile Gly Arg Lys Arg Ser His Ala Gly Tyr Gln		400
	405	410
		415
Thr Ile		
<210> 22		
<211> 420		
<212> PRT		
<213> 红鳍东方鲀(Takifugu rubripes)		
<400> 22		
Met Lys Arg Ser His Ala Leu Val Val Leu Ile Ile Ala Trp Phe Ser		
1	5	10
Leu Ser Gly Cys Ile Gln Ala Val Ser Leu Glu Val Lys Glu Gly Asn		15
	20	25
Ser Thr Cys Ile Lys Ala Asn Leu Ser Ala Tyr Phe Ser Ile Thr Tyr		30
	35	40
Asn Thr Ser Ser Ser Thr Arg Thr Ala Gln Phe Ile Leu Pro Asp Ser		45
50	55	60

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

370	375	380
Met Leu Ile Pro Ile Ile Val Gly Ala Ser Leu Ala Gly Leu Val Leu		
385	390	395
Ile Val Leu Ile Ala Tyr Leu Ile Gly Arg Lys Lys Ser His Ala Gly		400
	405	410
		415
Tyr Gln Thr Ile		
420		
<210> 23		
<211> 419		
<212> PRT		
<213> 安大略鲑(Salmo salar)		
<400> 23		
Met Thr Arg Thr Cys Pro Phe Val Val Gly Ile Ala Cys Phe Ala Ile		
1	5	10
Leu Gly Cys Val Thr Val Val Gln Ser Gln Val Thr Leu Glu Val Thr		15
	20	25
		30
Glu Gly Asn Ser Thr Cys Ile Lys Ala Glu Leu Ser Ala Ser Phe Ser		
	35	40
		45
Ile Thr Tyr Asp Thr Ala Asn Gly Thr Arg Thr Val Met Val Pro Leu		
	50	55
		60
Pro Gly Ser Ala Val Val Gly Val Ala Ser Ser Cys Gly Gly Asp Gly		
65	70	75
		80
Arg Ser Pro Trp Leu Val Ala Leu Phe Gly Asp Gly His Ala Leu Gly		
	85	90
		95
Leu Gly Phe Ser Ser Asn Asp Ser Leu Tyr Ser Val Ala Lys Leu Thr		
	100	105
		110
Leu Gln Tyr Asn Leu Ser Asp Val Ser Asn Phe Pro Glu Ala Asn Ser		
	115	120
		125
Thr Asp Val Val Thr Val Glu Thr Thr Ser Val Gly Met Val Ala Arg		
	130	135
		140
Val Asn Thr Thr Tyr Arg Cys Ile Ser Ala Ser Pro Val Ile Val Gly		
145	150	155
		160
Gly Ala Thr Val Thr Phe Ser Asn Val Thr Met Glu Ala Phe Met Thr		
	165	170
		175
Gly Glu Asp Leu Ser Pro Asn Glu Ser Val Cys Thr Ala Asp Gln Ser		
	180	185
		190
Phe Thr Thr Ala Pro Pro Pro Pro Pro Ser Thr Thr Thr Ala Ala Pro		
	195	200
		205
Ala Pro Val Pro Thr Pro Pro Gly Thr Pro Ser Gln Gly Ser Tyr Ser		

210	215	220
Val Ser Asn Ser Asn Gly Thr Val Cys Leu Leu Ala Arg Met Ala Leu		
225	230	235
Gln Leu Asn Ile Ser His Phe Ser Ala Ser Gln Asn Lys Thr Ile Gln		240
	245	250
Glu Val Val Asn Leu Leu Pro Asn Gln Thr Thr Ser Ser Gly Ser Cys		255
	260	265
Asp Pro Thr Ser Ala Thr Leu Val Leu Thr Gln Ala Asn Ala Thr Asn		270
	275	280
Leu Ser Phe Leu Phe Thr Leu Asn Ser Thr Ser Asn Arg Tyr His Leu		285
	290	295
Thr Gly Leu Ser Val Val Ala Ala Trp Ser Asp Met Thr Ala Pro Phe		300
305	310	315
Asn Thr Ser Asn Ser Ser Leu Asp Tyr Gln Arg Gly Ser Leu Gly Arg		320
	325	330
Ser Tyr Met Cys Ile Ser Glu Gln Thr Leu Val Val Asp Gln Asn Phe		335
	340	345
Ser Leu Asn Thr Phe Gln Leu Gln Val Gln Pro Phe Gly Ile Thr Arg		350
	355	360
Gly Gln Phe Ala Gln Ala Glu Glu Cys Gln Leu Asp Gln Asp Asn Met		365
	370	375
Leu Ile Pro Ile Val Val Gly Ala Ala Leu Ala Gly Leu Val Leu Ile		380
385	390	395
Val Leu Ile Ala Tyr Leu Ile Gly Arg Lys Arg Ser His Ala Gly Tyr		400
	405	410
		415
Gln Thr Ile		
<210> 24		
<211> 247		
<212> PRT		
<213> 罗非鱼(Oreochromis niloticus)		
<400> 24		
Met Val Gln Ile Cys Arg Val Gln Ser Trp Phe Val Gly Val Thr Pro		
1	5	10
Leu Leu Ile Phe Ala Thr Val Leu His Gln Gly Phe Ala Thr Val Ala		15
	20	25
Pro Pro Thr Pro Ala Pro His Lys Glu Pro Gly Arg Pro Glu Arg Gly		30
	35	40
Tyr Tyr Asn Val Thr Asn His Asn Gly Thr Ile Cys Leu Met Ala Tyr		45
	50	55
		60

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

<210> 25

<211> 415

<212> PRT

<213> 小鼠 (Mus musculus)

<400> 25

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

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

385	390	395	400
Tyr Leu Ile Gly Arg Arg Lys Thr Tyr Ala Gly Tyr Gln Thr Leu			
	405	410	415
<210> 26			
<211> 415			
<212> PRT			
<213> 非洲爪蟾 (<i>Xenopus laevis</i>)			
<400> 26			
Met Gly Asp Thr Gly Ala Met Glu Arg Cys Ala Cys Pro Ala Ala Val			
1	5	10	15
Leu Leu Leu Ser Leu Val Leu Met Gly Ala Thr Ala Phe Glu Val Glu			
	20	25	30
Ile Lys Asp Asp Lys Asn Ala Thr Cys Ile Tyr Ala Lys Leu Ser Val			
	35	40	45
Asn Ile Thr Val Gln Tyr Glu Thr Asp Thr Ser Ser Ser Lys Asn Ile			
	50	55	60
Thr Phe Pro Val Pro Ser Asp Val Thr Thr Asn Gly Ser Ser Cys Gly			
65	70	75	80
Ser Asp Gly Lys Ala Pro Leu Leu Val Ile Asn Phe Gly Asn Ser Gln			
	85	90	95
Ser Trp Ser Leu Asn Phe Thr Arg Asn Asn Ser Thr Tyr Ser Gly Ser			
	100	105	110
Ala Leu Ile Phe Thr Tyr Asn Thr Asn Asp Thr Ile Leu Phe Pro Asp			
	115	120	125
Ala Leu Arg Lys Gly Leu Ile Ser Ser Thr Ala Met Phe Leu Gly Pro			
	130	135	140
Val Pro Leu Asn Ser Thr Tyr Lys Cys Ile Ser Arg Glu Val Val Val			
145	150	155	160
Ser Glu Asn Val Thr Gln Ile Ile Tyr Asp Val Lys Leu Glu Ala Phe			
	165	170	175
Met Ala Asn Gly Thr Leu Gly Lys Glu Ile Ile Cys Asp Ala Asp Lys			
	180	185	190
Pro Ser Pro Val Pro Ser Pro Thr Gln Pro Ser Thr Thr Ala Ser Thr			
	195	200	205
Ala Ile Pro Ala Pro Thr Ser Lys Pro Leu Asp Lys Pro Thr Met Gly			
	210	215	220
Asn Tyr Thr Val Ser Asp Ala Ser Gly Ile Cys Leu Leu Ala Ser Met			
225	230	235	240
Gly Leu Gln Ile Asn Thr Ser Leu Leu Ser Glu Gly Lys Asn Ile Trp			

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

100	105	110
Asn Thr Thr Asn Ser Thr Thr Glu Pro Pro Thr Thr Thr Gly His Asn		
115	120	125
Thr Thr Asn Ser Thr Thr Asp Ala Pro Thr Thr Thr His Thr Asn Ala		
130	135	140
Thr Val Ala Pro Thr Pro Pro Pro Thr Thr Pro Ser Val Pro Lys Pro		
145	150	155
Thr Val Gly Asn Tyr Ser Val Lys Thr Asp Asn Val Ser Asp Cys Leu		
165	170	175
Leu Ala Lys Met Gly Leu Gln Phe Ser Phe Lys Ile Ser Gly Asn Ala		
180	185	190
Ser Leu Gln Thr Val Asn Leu Asp Pro Asn Val Thr Lys Val Asn Gly		
195	200	205
Thr Cys Gly Ser Gly Gly Ser Asp Ser Ser Leu Phe Leu Thr Ser Lys		
210	215	220
Asp Ile Thr Val His Phe Val Phe Thr Asn Asp Ser Gln Lys Phe Arg		
225	230	235
Leu His Ala Leu Thr Leu Thr Val Asp Leu Gly Asn Gly Asn Ile Phe		
245	250	255
Asn Asp Ser Asn Thr Asn Leu Ser Leu Trp Glu Ala Ser Val Gly Ser		
260	265	270
Ser Tyr Met Cys Arg Lys Glu Gln Ser Tyr Asn Ile Ser Asp Lys Leu		
275	280	285
Thr Leu Asn Thr Phe Glu Leu Gln Val Gln Pro Phe Asp Val Lys Lys		
290	295	300
Asn Ser Phe Ser Thr Ala His Glu Cys Ser Leu Asp Asp Thr Ser Leu		
305	310	315
Leu Ile Pro Ile Ile Val Gly Ala Ala Leu Ala Gly Leu Ile Phe Ile		
325	330	335
Val Val Ile Ala Tyr Val Ile Gly Arg Arg Arg Thr Tyr Val Gly Tyr		
340	345	350
Gln Thr Leu		
355		
<210> 28		
<211> 411		
<212> PRT		
<213> 东非狒狒(Papio anubis)		
<400> 28		
Met Val Cys Phe Arg Leu Phe Pro Val Pro Gly Ser Gly Leu Val Leu		

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

Trp Asp Ala Pro Leu Gly Ser Ser Tyr Met Cys Asn Lys Glu Gln Thr
 325 330 335
 Val Ser Val Ser Gly Ala Phe Gln Ile Asn Thr Phe Asp Leu Arg Val
 340 345 350
 Gln Pro Phe Asn Val Thr Gln Gly Lys Tyr Ser Thr Ala Glu Glu Cys
 355 360 365
 Ser Ala Asp Ser Asp Leu Asn Phe Leu Ile Pro Val Ala Val Gly Val
 370 375 380
 Ala Leu Gly Phe Leu Ile Ile Val Val Phe Ile Ser Tyr Met Ile Gly
 385 390 395 400
 Arg Arg Lys Ser Arg Thr Gly Tyr Gln Ser Val
 405 410
 <210> 29
 <211> 410
 <212> PRT
 <213> 猕猴 (Macaca mulatta)
 <400> 29
 Met Val Cys Phe Arg Leu Phe Pro Val Pro Gly Ser Gly Leu Val Leu
 1 5 10 15
 Val Cys Leu Val Leu Gly Ala Val Gln Ser Tyr Ala Leu Glu Leu Asn
 20 25 30
 Leu Thr Asp Ser Gly Lys Ala Thr Cys Leu Tyr Ala Lys Trp Gln Met
 35 40 45
 Asn Phe Thr Val Arg Tyr Glu Thr Thr Asn Lys Thr Tyr Lys Thr Val
 50 55 60
 Thr Ile Ser Asp Arg Gly Thr Val Thr Tyr Asn Gly Ser Ile Cys Gly
 65 70 75 80
 Asp Asp Gln Asn Gly Pro Lys Ile Ala Val Gln Phe Gly Pro Gly Phe
 85 90 95
 Ser Trp Ile Ala Asn Phe Ser Lys Ala Ala Ser Thr Tyr Ser Ile Asp
 100 105 110
 Ser Ile Ser Phe Ser Tyr Asn Thr Gly Asp Asn Thr Thr Phe Pro Asp
 115 120 125
 Ala Glu Asp Lys Gly Ile Ile Thr Val Asp Glu Leu Leu Ala Ile Lys
 130 135 140
 Ile Pro Leu Asn Asp Leu Phe Arg Cys Asn Ser Leu Ser Thr Leu Glu
 145 150 155 160
 Lys Asn Asp Val Val Gln Asn Tyr Trp Asp Val Leu Val Gln Ala Phe
 165 170 175

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

<210> 30

<211> 364

<212> PRT

<213> 黑猩猩 (Pan troglodytes)

<220>

<221> SITE

<222> (200) .. (200)

<223> Xaa可以是任何天然存在的氨基酸

<400> 30

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

305	310	315	320
Cys Ser Ala Asp Ser Asp Leu Asn Phe Leu Ile Pro Val Ala Val Gly			
	325	330	335
Val Ala Leu Gly Phe Leu Ile Ile Val Val Phe Ile Ser Tyr Met Ile			
	340	345	350
Gly Arg Arg Lys Ser Arg Thr Gly Tyr Gln Ser Val			
	355	360	
<210> 31			
<211> 411			
<212> PRT			
<213> 家犬(Canis lupus familiaris)			
<400> 31			
Met Val Cys Phe Arg Leu Ser Pro Ala Pro Gly Ser Gly Leu Val Leu			
1	5	10	15
Leu Cys Leu Val Leu Gly Ala Val Ser Ser Tyr Ala Leu Glu Val Asn			
	20	25	30
Val Thr Asp Ser Glu Lys Ala Thr Cys Leu Tyr Ala Lys Trp Gln Met			
	35	40	45
Asn Phe Thr Ile Gln Tyr Asn Thr Thr Ser Lys Asn Phe Lys Thr Ala			
	50	55	60
Thr Ile Ser Asp Phe Ser Thr Ala Thr Tyr Asn Gly Ser Val Cys Gly			
65	70	75	80
Asn Asp Gln Asn Asn Pro Lys Ile Val Val Gln Phe Gly Ser Gly Phe			
	85	90	95
Ser Trp Ile Val Asn Phe Thr Lys Lys Glu Ser Ala Tyr Leu Ile Asp			
	100	105	110
Ser Ile Ser Phe Ser Tyr Asn Leu Ser Asp Asn Ala Thr Phe Pro Asp			
	115	120	125
Ala Lys Glu Lys Gly Ile Leu Thr Val His Asp Leu Val Gly Phe Arg			
	130	135	140
Ile Pro Leu Asn Asn Ile Phe Arg Cys Asn Ser Leu Ser Thr Leu Glu			
145	150	155	160
Lys Asn Gly Val Val Gln Tyr Tyr Trp Asp Val His Val Gln Ala Phe			
	165	170	175
Val Gln Asn Gly Thr Val Ser Thr Lys Glu Phe Leu Cys Glu Lys Asp			
	180	185	190
Lys Thr Ser Thr Thr Val Val Pro Thr Ile Ser Thr Thr Thr Pro Ser			
	195	200	205
Pro Thr Thr Thr Pro Thr Pro Lys Glu Lys Pro Glu Val Gly Ser Tyr			

210	215	220
Ser Val Asn Asn Ser Asn Gly Thr Cys Leu Leu Ala Thr Met Gly Leu		
225	230	235
Gln Leu Asn Ile Thr His Asn Lys Val Ala Ser Val Ile Asn Ile Asn		240
	245	250
Pro Asn Thr Thr Asp Phe Thr Gly Ser Cys Gln Pro Gln Thr Ala Leu		255
	260	265
Leu Arg Leu Asn Ser Ser Asn Ile Lys Tyr Leu Asp Phe Val Phe Ala		270
	275	280
Val Lys Asn Glu Asn Arg Phe Tyr Leu Lys Glu Val Asn Val Ser Met		285
290	295	300
Tyr Leu Val Asn Gly Ser Val Phe Ser Ile Ala Asn Asn Asn Leu Ser		
305	310	315
Tyr Trp Asp Ala Pro Leu Gly Ser Ser Tyr Met Cys Asn Lys Glu Gln		320
	325	330
Thr Val Ser Val Ser Gly Ala Phe Gln Ile Asn Thr Phe Asp Leu Arg		335
	340	345
Val Gln Pro Phe Asn Val Met Glu Gly Lys Tyr Ser Thr Ala Gln Glu		350
	355	360
Cys Ser Leu Asp Asp Asp Thr Ile Leu Ile Pro Ile Ile Val Gly Ala		365
370	375	380
Gly Leu Ser Gly Leu Ile Ile Val Ile Val Ile Ala Tyr Leu Ile Gly		
385	390	395
Arg Arg Lys Ser Tyr Ala Gly Tyr Gln Thr Leu		400
	405	410
<210> 32		
<211> 417		
<212> PRT		
<213> 家马(Equus caballus)		
<400> 32		
Met Val Cys Phe Arg Leu Ser Pro Val Pro Gly Ser Gly Leu Val Leu		
1	5	10
Leu Cys Leu Val Leu Gly Ala Val Ser Ser Tyr Ala Leu Glu Leu Asn		
	20	25
Leu Thr Asp Ser Glu Lys Ala Leu Cys Leu Tyr Ala Lys Trp Gln Met		30
	35	40
Asn Phe Thr Ile Pro Tyr Glu Thr Thr Ser Lys Ser Tyr Lys Thr Val		45
50	55	60
Thr Ile Ser Asn Phe Gly Thr Pro Thr Tyr Asn Gly Ser Ile Cys Gly		

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

Pro Ile Ala Val Gly Ala Ala Leu Ala Gly Val Leu Ile Leu Val Leu
 385 390 395 400
 Leu Ala Tyr Phe Ile Gly Leu Lys Arg His His Ala Gly Tyr Glu Gln
 405 410 415
 Phe
 <210> 33
 <211> 407
 <212> PRT
 <213> 家牛 (Bos taurus)
 <400> 33
 Met Val Cys Phe Arg Leu Ala Pro Val Pro Gly Ser Gly Phe Leu Leu
 1 5 10 15
 Leu Cys Leu Val Leu Gly Ala Val Ser Ser Tyr Ala Leu Glu Leu Asn
 20 25 30
 Leu Thr Asp Ser Ser Asn Ala Thr Cys Leu Tyr Ala Lys Trp Gln Met
 35 40 45
 Asn Phe Thr Ile Arg Tyr Glu Thr Thr Asp Lys His Asn Lys Thr Val
 50 55 60
 Pro Ile Ser Asp Leu Gly Ala Ala Thr Tyr Asn Gly Ser Phe Cys Gly
 65 70 75 80
 Asp Asp Gln Asn Gly Pro Lys Ile Ala Val Gln Phe Gly Ser Gly Phe
 85 90 95
 Ser Trp Ile Val Asn Phe Thr Lys Glu Ala Ala Ser Pro Ser Thr Tyr
 100 105 110
 Leu Val Asp Thr Ile Ser Phe Ser Tyr Asn Thr Asn Asp Asn Lys Thr
 115 120 125
 Phe Pro Asp Ala Lys Glu Lys Glu Val Phe Thr Val Asn Asn Arg Val
 130 135 140
 Ala Leu Lys Ile Pro Leu Asn Asp Ile Phe Arg Cys Asn Ser Leu Ser
 145 150 155 160
 Thr Leu Glu Asn Arg Asp Val Val Gln His Tyr Trp Asp Val His Val
 165 170 175
 Gln Ala Phe Val Gln Asn Gly Thr Val Ser Thr Thr Glu Phe Leu Cys
 180 185 190
 Asp Lys Asp Lys Thr Val Thr Thr Ala Val Pro Ile Val Pro Thr Thr
 195 200 205
 Leu Pro Ser Pro Thr Lys Pro Val Val Gly Ser Tyr Ser Val Val Asn
 210 215 220
 Ser Asn Gly Thr Cys Leu Leu Ala Thr Met Gly Leu Gln Leu Asn Ile

225	230	235	240
Thr His Asp Lys Val	Ala Ser Val Phe Asn Ile	Asn Pro Asn Thr Thr	
	245	250	255
Asn Ala Thr Gly Ser Cys Gln Pro Gln Thr	Ala Leu Leu Arg Leu Ser		
	260	265	270
Ser Ser Asn Ile Lys Tyr Leu Asp Phe Val Phe	Ala Val Lys Asn Glu		
	275	280	285
Asn Arg Phe Tyr Leu Lys Glu Val Asn Val Ser Met	Ile Leu Val Asn		
	290	295	300
Gly Ser Val Tyr Ser Ile Ser Asn Thr Asn Leu Ser Tyr Trp	Asp Ala		
305	310	315	320
Pro Leu Gly Ser Ser Tyr Met Cys Asn Lys Glu Gln Thr Val Ser Val			
	325	330	335
Ser Gly Ala Phe Gln Ile Asn Thr Phe Asp Leu Arg Val Gln Pro Phe			
	340	345	350
Ser Val Thr Glu Gly Lys Tyr Ser Thr Ala Gln Glu Cys Ser Leu Asp			
	355	360	365
Asp Asp Thr Ile Leu Ile Pro Ile Ile Val Gly Ala Gly Leu Ser Gly			
	370	375	380
Leu Ile Ile Val Ile Val Ile Ala Tyr Leu Ile Gly Arg Arg Lys Ser			
385	390	395	400
Tyr Ala Gly Tyr Gln Thr Leu			
	405		

<210> 34

<211> 411

<212> PRT

<213> 野猪(Sus scrofa)

<400> 34

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

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

Leu Lys Arg His His Ala Gly Tyr Glu Gln Phe
 405 410
 <210> 35
 <211> 408
 <212> PRT
 <213> 绵羊 (Ovis aries)
 <400> 35
 Met Val Cys Phe Arg Leu Ala Pro Val Pro Gly Cys Gly Phe Leu Leu
 1 5 10 15
 Phe Cys Leu Val Leu Gly Thr Val Ser Ser Tyr Ala Leu Glu Leu Asn
 20 25 30
 Leu Thr Asp Ser Ser Lys Ala Thr Cys Leu Tyr Ala Lys Trp Gln Met
 35 40 45
 Asn Phe Thr Ile Arg Tyr Glu Thr Thr Asp Lys His Asn Lys Thr Val
 50 55 60
 Thr Ile Ser Asp Phe Asp Ala Ala Ala Tyr Asn Gly Ser Val Cys Gly
 65 70 75 80
 Asp Asp Gln Asn Gly Pro Lys Ile Ala Val Gln Phe Gly Ser Gly Phe
 85 90 95
 Ser Trp Ile Val Asn Phe Thr Lys Glu Ala Ser Ser Thr Ser Thr Tyr
 100 105 110
 Leu Val Asp Ser Ile Ser Phe Ser Tyr Asn Thr Asn Asp Asn Ala Thr
 115 120 125
 Phe Pro Asp Ala Lys Glu Lys Gly Val Phe Thr Val Asn Asn Arg Val
 130 135 140
 Ala Leu Lys Ile Pro Leu Asn Asp Ile Phe Arg Cys Asn Ser Leu Ser
 145 150 155 160
 Thr Leu Glu Lys Ser Asp Val Val Gln His Tyr Trp Asp Val His Val
 165 170 175
 Gln Ala Phe Val Gln Asn Gly Thr Val Ser Thr Thr Glu Phe Leu Cys
 180 185 190
 Asp Lys Asp Lys Thr Val Thr Thr Ala Met Pro Ile Val Pro Thr Thr
 195 200 205
 Ala Pro Ser Pro Thr Lys Pro Val Val Gly Ser Tyr Ser Val Val Asn
 210 215 220
 Ser Asn Gly Thr Cys Leu Leu Ala Thr Met Gly Leu Gln Leu Asn Ile
 225 230 235 240
 Thr His Asp Lys Val Ala Ser Val Phe Asn Ile Asn Pro Asn Thr Thr
 245 250 255

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

<210> 36

<211> 411

<212> PRT

<213> 褐家鼠 (*Rattus norvegicus*)

<400> 36

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

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

<210> 37

<211> 570

<212> PRT

<213> 鸭嘴兽 (Ornithorhynchus anatinus)

<400> 37

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

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

<210> 38

<211> 425

<212> PRT

<213> 原鸡(Gallus gallus)

<400> 38

```

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

```


Thr	Leu	Ile	Asp	Phe	Thr	Phe	Ile	Val	Asn	Ala	Ser	Ala	Ser	Val	Gln
290									295			300			
Lys	Phe	Tyr	Leu	Arg	Glu	Val	Asn	Val	Thr	Leu	Leu	Asn	Tyr	Gln	Asn
305					310				315					320	
Gly	Ser	Val	Ile	Leu	Ser	Ala	Asp	Asn	Asn	Asn	Leu	Ser	Lys	Trp	Asp
			325					330						335	
Ala	Ser	Leu	Gly	Asn	Ser	Tyr	Met	Cys	Arg	Lys	Glu	Gln	Thr	Leu	Glu
			340					345						350	
Ile	Asn	Glu	Asn	Leu	Gln	Val	His	Thr	Phe	Asn	Leu	Trp	Val	Gln	Pro
		355					360					365			
Phe	Leu	Val	Lys	Glu	Asn	Lys	Phe	Ser	Ile	Ala	Glu	Glu	Cys	Phe	Ala
		370				375				380					
Asp	Ser	Asp	Leu	Asn	Phe	Leu	Ile	Pro	Val	Ala	Val	Gly	Met	Ala	Leu
385				390						395					400
Gly	Phe	Leu	Ile	Ile	Leu	Val	Phe	Ile	Ser	Tyr	Ile	Ile	Gly	Arg	Arg
			405					410						415	
Lys	Ser	Arg	Thr	Gly	Tyr	Gln	Ser	Val							
		420					425								

<210> 39

<211> 556

<212> PRT

<213> 斑胸草雀(Taeniopygia guttata)

<400> 39

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

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

435	440	445
Arg Leu Asn Gly Ser Val Ile Ser Ser Ala Asp Asn Ser Asn Leu Ser		
450	455	460
Lys Trp Asp Ala Phe Leu Gly Ser Ser Tyr Met Cys Arg Lys Glu Gln		
465	470	475
Thr Leu Gln Ile Asn Glu Asn Val Gln Val His Thr Phe Asn Leu Trp		
485	490	495
Ile Gln Pro Phe Leu Val Glu Ala Asn Lys Phe Ala Thr Ala Glu Glu		
500	505	510
Cys Ile Ala Asp Ser Asp Leu Asn Phe Leu Ile Pro Ile Ala Val Gly		
515	520	525
Val Ala Leu Gly Phe Leu Ile Ile Leu Val Phe Ile Ser Tyr Ile Ile		
530	535	540
Gly Arg Arg Lys Ser Arg Thr Gly Tyr Gln Ser Val		
545	550	555
<210> 40		
<211> 408		
<212> PRT		
<213> 热带爪蟾(Xenopus tropicalis)		
<400> 40		
Met Glu Arg Cys Ala Cys Pro Ala Ala Leu Leu Leu Leu Ser Leu Val		
1	5	10
Leu Met Gly Ala Met Ala Phe Asp Val Glu Ile Lys Asp Asp Lys Asn		
20	25	30
Ala Thr Cys Ile Tyr Ala Lys Leu Ser Val Asn Val Thr Val Gln Tyr		
35	40	45
Glu Thr Asn Thr Ser Ser Thr Lys Asn Val Thr Phe Ser Val Pro Ser		
50	55	60
Glu Val Thr Thr Asn Gly Ser Ser Cys Gly Ser Asn Gly Lys Ala Pro		
65	70	75
Ile Leu Val Ile Asn Phe Gly Asn Gly His Ser Trp Ser Leu Asn Phe		
85	90	95
Thr Arg Asn Asp Ser Met Tyr Ser Gly Gly Ala Leu Ile Phe Thr Tyr		
100	105	110
Asn Thr Asn Asp Ser Thr Leu Phe Pro Asp Ala Leu Lys Glu Gly Leu		
115	120	125
Ile Ser Ser Thr Ala Ala Phe Leu Gly Pro Ile Pro Leu Asn Ser Thr		
130	135	140
Tyr Lys Cys Ile Ser Ser Glu Val Val Val Ser Glu Asn Val Thr Gln		

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

<210> 41

<211> 404

<212> PRT

<213> 安大略鲑 (Salmo salar)

<400> 41

Met Phe Arg Cys Ala Phe Leu Ile Leu Phe Leu Ala Leu Gly Asn Glu

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

Ser Ser Tyr Met Cys Asn Lys Glu Gln Thr Leu Asn Val Thr Asp Thr
 325 330 335
 Leu Thr Leu Tyr Thr Phe Glu Leu Arg Val Gln Pro Phe Glu Val Asn
 340 345 350
 Lys Gly Glu Phe Ala Thr Ala His Glu Cys Ser Leu Asp Asp Thr Ser
 355 360 365
 Ile Leu Ile Pro Ile Ile Val Gly Ala Ala Leu Ala Gly Leu Ile Leu
 370 375 380
 Ile Val Val Ile Ala Tyr Val Ile Gly Arg Arg Lys Thr Tyr Val Gly
 385 390 395 400
 Tyr Gln Thr Leu
 <210> 42
 <211> 410
 <212> PRT
 <213> 罗非鱼 (*Oreochromis niloticus*)
 <400> 42
 Met Lys Val Ser His Ala Thr Ala Gly Leu Val Val Trp Phe Val Val
 1 5 10 15
 Leu Gly Cys Ile Asp Ala Val Thr Leu Glu Val Lys Glu Ser Asn Thr
 20 25 30
 Thr Cys Ile Lys Ala Asp Leu Ser Ala Ser Phe Ser Ile Ile Tyr Asn
 35 40 45
 Thr Thr His Ala Glu Arg Thr Val Gln Val Leu Leu Pro Asn Ser Thr
 50 55 60
 Thr Val Asp Thr Ala Asn Ser Thr Cys Gly Lys Asp Gly Ser Ser Pro
 65 70 75 80
 Arg Leu Val Ala Val Phe Gly Ser Gly Tyr Thr Leu Gly Leu Asn Phe
 85 90 95
 Ser Thr Asn Gly Thr Leu Tyr Gln Val Ser Ser Leu Thr Leu Gln Tyr
 100 105 110
 Asn Leu Ser Asp Thr Ser Val Phe Pro Asn Ala Thr Ile Ser Gly Val
 115 120 125
 Val Thr Leu Val Ser Ala Ser Val Gly Ile Glu Ala Asn Val Asn Thr
 130 135 140
 Thr Tyr Lys Cys Ala Ser Pro Thr Val Ile Asp Val Ala Thr Ala Lys
 145 150 155 160
 Val Asn Phe Thr Asp Met Arg Leu Glu Ala Tyr Met Pro Gly Asn Glu
 165 170 175
 Leu Ser Pro Asn Glu Thr Val Cys Phe Ala Asp Gln Thr Ser Thr Thr

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

<210> 43

<211> 249

<212> PRT

<213> 红鳍东方鲀(Takifugu rubripes)

<400> 43

Met Thr Gln Ile Gly Gly Val Gln Pro Val Phe Leu Ala Val Thr Val		
1	5	10
His Leu Ile Leu Ala Thr Val Leu His Gln Thr Phe Ala Thr Val Thr		
20	25	30
Pro Pro Val Thr Thr Ala Val Pro His Lys Glu Pro Gly Arg Pro Asp		

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

<210> 44

<211> 418

<212> PRT

<213> 黑猩猩 (Pan troglodytes)

<400> 44

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

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

Asp Asp His Phe Gly Asn Val Asp Glu Cys Ser Ser Asp Tyr Thr Ile
 370 375 380
 Val Leu Pro Val Ile Gly Ala Ile Val Val Gly Leu Cys Leu Met Gly
 385 390 395 400
 Met Gly Val Tyr Lys Ile Arg Leu Arg Cys Gln Ser Ser Gly Tyr Gln
 405 410 415
 Arg Ile
 <210> 45
 <211> 416
 <212> PRT
 <213> 东非狒狒(Papio anubis)
 <400> 45
 Met Pro Arg Gln Leu Ser Ala Ala Ala Val Leu Phe Ala Ser Leu Ala
 1 5 10 15
 Val Ile Leu His Asp Gly Ser Gln Met Arg Ala Lys Ala Phe Pro Lys
 20 25 30
 Thr Arg Asp Tyr Ser Gln Pro Thr Ala Ala Ala Thr Gly Gln Asp Ile
 35 40 45
 Ala Lys Pro Val Gln Gln Pro Ala Asn Gln Ala Pro His Gln Thr Leu
 50 55 60
 Ala Ala Arg Leu Met Asp Gly His Ile Thr Phe Gln Thr Ala Ala Thr
 65 70 75 80
 Ile Lys Thr Pro Thr Thr Thr Pro Val Thr Thr Lys Asn Thr Pro Thr
 85 90 95
 Thr Ser Pro Ile Ile Tyr Thr Leu Val Thr Thr Gln Ala Thr Ser Asn
 100 105 110
 Asn Ser His Thr Ala Pro Pro Leu Thr Lys Val Thr Val Gly Pro Ser
 115 120 125
 Leu Ala Pro Tyr Ser Leu Pro Pro Thr Ile Thr Pro Pro Ala His Thr
 130 135 140
 Thr Gly Thr Ser Ser Ser Thr Val Asn His Thr Thr Gly Asn Ala Thr
 145 150 155 160
 Gln Pro Ser Asn Gln Thr Thr Leu Pro Ala Thr Leu Ser Ile Ala Leu
 165 170 175
 His Lys Ser Thr Thr Gly Gln Lys Pro Val Gln Pro Thr His Ala Pro
 180 185 190
 Gly Thr Thr Ala Ala Ala His Asn Thr Thr Arg Thr Ala Ala Pro Ala
 195 200 205
 Ser Thr Val Pro Gly Ser Thr Leu Ala Pro Gln Pro Ser Ser Val Lys

210	215	220
Thr Gly Ile Tyr Gln Val Leu Asn Gly Ser Arg Leu Cys Ile Lys Ala		
225	230	235
Glu Met Gly Ile Gln Leu Ile Val Gln Asp Lys Glu Ser Val Phe Ser		240
	245	250
Pro Arg Arg Tyr Phe Asn Leu Asp Pro Asn Ala Thr Gln Ala Ser Gly		255
	260	265
Asn Cys Gly Thr Arg Asn Ser Asn Leu Leu Leu Asn Phe Gln Gly Gly		270
	275	280
Phe Val Asn Leu Thr Phe Thr Lys Asp Glu Gly Ser Tyr Tyr Ile Ser		285
290	295	300
Glu Val Gly Ala Cys Leu Thr Val Ser Asp Pro Glu Thr Ile Tyr Gln		
305	310	315
Gly Met Lys His Ala Val Val Met Phe Gln Thr Ala Val Gly His Ser		320
	325	330
Phe Lys Cys Val Ser Glu Gln Ser Leu Gln Leu Ser Ala His Leu Gln		335
	340	345
Leu Lys Thr Thr Asn Val Gln Leu Gln Ala Phe Asp Phe Glu Asp Asp		350
355	360	365
His Phe Gly Asn Val Asp Glu Cys Ser Ser Asp Tyr Thr Ile Val Leu		
370	375	380
Pro Val Ile Gly Ala Ile Val Val Gly Leu Cys Leu Val Gly Ile Gly		
385	390	395
Val Tyr Lys Ile Arg Leu Arg Cys Gln Ser Ser Gly Tyr Gln Arg Ile		400
	405	410
		415

<210> 46

<211> 416

<212> PRT

<213> 猕猴 (Macaca mulatta)

<400> 46

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

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

Pro	Val	Ile	Gly	Ala	Ile	Val	Val	Gly	Leu	Cys	Leu	Val	Gly	Met	Gly
385										390					400
Val	Tyr	Lys	Ile	Arg	Leu	Arg	Cys	Gln	Ser	Ser	Gly	Tyr	Gln	Arg	Ile
					405				410						415
<210> 47															
<211> 428															
<212> PRT															
<213> 家犬(Canis lupus familiaris)															
<400> 47															
Met	Ser	Trp	Gln	Leu	Ser	Ala	Ala	Val	Ala	Leu	Phe	Val	Ser	Leu	Ala
1				5					10					15	
Leu	Ile	Leu	His	Tyr	Gly	Ser	Gln	Ile	Arg	Ala	Lys	Met	Phe	Pro	Glu
			20					25					30		
Thr	Val	Asp	Phe	Gln	Pro	Thr	Thr	Ala	Ala	Thr	Val	Arg	Ala	Thr	Ala
		35						40				45			
Lys	Pro	Phe	Leu	His	Leu	Thr	Asn	Gln	Val	Pro	Ser	Gln	Thr	Leu	Ala
	50					55					60				
Ala	Arg	Ser	Met	Asp	Gly	His	Ile	Ala	Ser	Gln	Arg	Ala	Ala	Thr	Thr
65					70					75					80
Ser	Ser	Ser	Glu	Pro	Pro	Thr	Thr	His	Thr	Thr	Val	Lys	Thr	Leu	Val
				85					90					95	
Thr	Thr	Ser	Leu	Val	Thr	Ala	Asn	Ser	Thr	Pro	Ser	Ser	Ser	Pro	Ile
			100						105					110	
Ile	Tyr	Thr	Leu	Val	Thr	Thr	Ile	Val	Thr	Pro	Asn	Asn	Ser	Asn	Thr
		115						120					125		
Ala	Ala	Pro	Val	Thr	Glu	Ala	Thr	Ile	Gly	Pro	Ser	Ala	Asp	Pro	Gly
		130					135					140			
Ser	Leu	Pro	Thr	Thr	Ser	Thr	Pro	Leu	Ala	His	Thr	Thr	Arg	Thr	Asn
145						150					155				160
Pro	Ser	Thr	Leu	Ser	His	Lys	Thr	Arg	Lys	Thr	Thr	His	Phe	Gly	Asn
					165					170				175	
Gln	Thr	Thr	Leu	Pro	Ala	Thr	Leu	Ser	Thr	Ser	Thr	His	Lys	Ser	Thr
			180						185				190		
Ser	Ser	His	Lys	Ser	Ala	Gln	Ser	Thr	His	Ala	Pro	Gly	Pro	Thr	Thr
		195						200					205		
Ala	Ala	His	Asn	Thr	Thr	Gln	Thr	Ala	Ser	Pro	Ala	Thr	Pro	Ala	Ser
		210					215					220			
Gly	Pro	Thr	Leu	Ala	Pro	Gln	Pro	Ser	Ser	Pro	Lys	Thr	Gly	Ile	Tyr
225						230					235				240

Gln Val Leu Asn Gly Ser Arg Leu Cys Ile Lys Ala Glu Met Gly Ile
 245 250 255
 Glu Leu Met Val Gln Asp Thr Lys Ser Val Phe Ser Pro Gln Arg Tyr
 260 265 270
 Phe Asn Ile Asp Pro Asn Ala Thr Gln Thr Ser Gly Asn Cys Gly Ser
 275 280 285
 Gln Lys Ser Asn Leu Leu Leu Asn Phe Gln Gly Gly Phe Val Asn Leu
 290 295 300
 Thr Phe Leu Lys Asp Glu Asn Ser Tyr Tyr Ile Asn Glu Val Gly Ala
 305 310 315 320
 Tyr Leu Ala Val Ser Asn Pro Glu Lys Ile Tyr Gln Gly Met Lys Ser
 325 330 335
 Ser Val Val Met Phe Glu Thr Gly Val Gly His Ser Phe Lys Cys Val
 340 345 350
 Ser Glu Gln Ser Ile Gln Leu Ser Thr His Leu Gln Leu Lys Thr Met
 355 360 365
 Asn Val Gln Phe Gln Ala Phe Asp Phe Glu Asp Asp His Phe Gly Asn
 370 375 380
 Val Asp Glu Cys Ser Ser Asp Tyr Thr Val Val Leu Pro Val Ile Gly
 385 390 395 400
 Ala Ile Val Leu Gly Leu Cys Ala Val Gly Leu Ile Val Tyr Gly Ile
 405 410 415
 His Leu Arg Arg Glu Ser Ser Gly Tyr Gln Arg Ile
 420 425

<210> 48

<211> 430

<212> PRT

<213> 野猪(Sus scrofa)

<400> 48

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

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

385	390	395	400
Ile Gly Ala Ile Val Leu Gly Leu Cys Ala Val Gly Leu Ile Val Tyr			
	405	410	415
Gly Ile Arg Leu Lys Arg Glu Ser Ser Glu Tyr Gln Arg Ile			
	420	425	430
<210> 49			
<211> 259			
<212> PRT			
<213> 斑马鱼 (Danio rerio)			
<400> 49			
Met Thr Gln Ser Ser Arg Ser Val Leu Leu Leu Met Leu Ser Ser Leu			
1	5	10	15
His Cys Leu Gly Ser Ser Leu Glu Ser Asn Pro Lys Asp Pro Ser Val			
	20	25	30
Leu Ala Glu Ala Pro Gly Gln Asn Lys Arg Asp Ser Asp Ile Ser Leu			
	35	40	45
Val Pro Gln Met Pro Val Leu Gln Pro Lys Glu Thr Ala Pro Pro Leu			
	50	55	60
Val Thr Tyr Thr Ile Arg Asn Pro Gln Gly Lys Val Cys Val Arg Ala			
65	70	75	80
Ser Phe Gly Val Glu Phe Val Val Arg Glu Asn Lys Lys Lys Tyr Tyr			
	85	90	95
Phe Asn Leu Thr Pro Asn Ser Ala Arg Ala Thr Gly Tyr Cys Ala Asn			
	100	105	110
Gln Lys Thr Val Leu Ser Leu Glu Phe Ser Gly Gly Asn Leu Glu Phe			
	115	120	125
Thr Phe Ile Lys Asp Gly Asp Gln Ser Tyr Val Lys Thr Val Lys Gly			
	130	135	140
Ser Leu Arg Ala Ala Pro Pro Cys Lys Asn Cys Pro Ser Lys Ile Tyr			
145	150	155	160
Val Gly Leu Val Asp Asn Glu Lys Leu Phe Lys Ala Lys Asn Gly Leu			
	165	170	175
Ser Phe Asn Cys Lys Ser Glu Thr Met Leu Ile Leu Ala Asp Tyr Phe			
	180	185	190
Arg Leu Lys Leu Val Pro Leu Gln Ile Gln Ala Phe Asp Leu Val Asn			
	195	200	205
Gly Ala Phe Gly Lys Glu Val Glu Cys Trp Ala Asp Tyr Asn Lys Arg			
	210	215	220
Met Ile Pro Ile Ile Leu Gly Ala Val Ala Ala Ala Ile Cys Leu Ile			

225	230	235	240
Ala Ile Leu Thr Tyr Val Leu Val Arg Glu His Arg Asn Gln Gly Tyr			
	245	250	255
Glu Gln Leu			
<210> 50			
<211> 432			
<212> PRT			
<213> 家马(Equus caballus)			
<400> 50			
Met Ala Trp Gln Leu Ser Ala Val Val Val Leu Phe Val Ser Leu Ala			
1	5	10	15
Val Ile Leu Tyr Tyr Gly Ser His Val Arg Ala Asn Val Phe Pro Glu			
	20	25	30
Ile Thr Asp Tyr Ser Gln Pro Thr Thr Ala Ala Thr Ile Gln Thr Arg			
	35	40	45
Ala Gln Pro Ser Leu Ser Gln Pro Thr Asn Gln Val Pro His Lys Thr			
	50	55	60
Leu Ala Thr Arg Ser Met Asp Gly Gln Val Thr Ser Gln Thr Ala Ala			
65	70	75	80
Thr Thr Val Asn Pro Glu Thr Pro Val Thr His Thr Thr Ile Lys Thr			
	85	90	95
Ala Ala Ala Thr Ser Leu Val Thr Thr Asn Ser Thr Leu Ser Thr Ser			
	100	105	110
Pro Ile Thr Asn Thr Leu Leu Thr Thr Leu Ala Thr Pro Asp Asn Thr			
	115	120	125
His Thr Thr Thr Pro Val Thr Glu Ala Thr Ile Gly Pro Ser Ala Gly			
	130	135	140
Pro Gly Ser Pro Pro Thr Thr Ile Thr Thr Thr Ser Ser Ala Tyr Thr			
145	150	155	160
Thr Gly Thr Arg Ser Ser Thr Val Ser His Thr Thr Gly Lys Thr Thr			
	165	170	175
Gln Leu Ser Asn Gln Thr Thr Leu Pro Ala Thr Leu Ser Thr Ser Pro			
	180	185	190
His Asn Ser Thr Thr Ser Gln Asn Pro Ala His Ser Thr His Thr Pro			
	195	200	205
Gly Pro Thr Thr Gly Thr Cys Asn Thr Thr Gln Thr Ala Ser Pro Thr			
	210	215	220
Thr Thr Ala Pro Gly Pro Thr Leu Ala Pro Gln Pro Ser Ser Ala Lys			
225	230	235	240

Thr Gly Met Tyr Gln Ile Leu Asn Gly Ser Lys Leu Cys Ile Lys Ala		
	245	250 255
Glu Met Gly Ile Gln Leu Thr Val Gln Asp Thr Lys Ser Ala Ser Pro		
	260	265 270
Pro Gln Gly Tyr Phe Asn Ile Asp Pro Asn Thr Thr Gln Val Ser Gly		
	275	280 285
Ile Cys Gly Ser Arg Lys Ser Asn Leu Leu Leu Asn Phe Trp Gly Gly		
	290	295 300
Phe Val Asn Leu Thr Phe Thr Lys Asp Glu Asn Ser Tyr Tyr Ile Ser		
305	310	315 320
Glu Val Gly Ala Tyr Leu Thr Val Ser Asn Pro Glu Lys Thr Tyr Gln		
	325	330 335
Gly Met Lys Ser Pro Val Val Met Phe Glu Thr Val Ile Gly His Ser		
	340	345 350
Phe Lys Cys Val Ser Glu Gln Ser Leu Glu Leu Ser Thr Gln Leu His		
	355	360 365
Leu Lys Thr Thr Asn Val Gln Leu Gln Ala Phe Asp Phe Glu Asp Asp		
	370	375 380
Asn Phe Gly Asn Val Asp Glu Cys Ser Ser Asp Tyr Thr Val Val Leu		
385	390	395 400
Pro Val Ile Gly Ala Ile Val Leu Gly Leu Phe Ala Val Gly Leu Ile		
	405	410 415
Val Tyr Gly Val Arg Val Arg Arg Glu Ala Ser Gly Tyr Gln Arg Ile		
	420	425 430

<210> 51

<211> 433

<212> PRT

<213> 家牛(Bos taurus)

<400> 51

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

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

385	390	395	400
Pro Val Ala Val Gly Leu Ser Ile Ala Val Leu Leu Ala Val Leu Leu			
	405	410	415
Thr Ala Cys Leu Val Thr Arg Lys Arg Pro Ser Arg Gly Tyr Glu Arg			
	420	425	430
Met			
<210> 52			
<211> 429			
<212> PRT			
<213> 绵羊 (Ovis aries)			
<400> 52			
Met Ser Trp Gln Ile Ser Ala Val Val Leu Phe Phe Val Ser Leu Ala			
1	5	10	15
Val Ile Trp Tyr Tyr Asp Ser His Met Lys Ala Asn Val Phe Pro Glu			
	20	25	30
Ile Thr Gly Tyr Ser Ser Pro Thr Thr Gly Gln Ala Thr Val Lys Pro			
	35	40	45
Ser Leu Leu Gln Pro Thr Asn His Val Pro Cys Asn Thr Ala Ala Ala			
	50	55	60
Lys Ser Thr Asp Gly His Val Thr Ser Gln Thr Val Ala Lys Thr Ser			
65	70	75	80
Ser Pro Glu Thr Leu Thr Thr Asn Thr Thr Ile Glu Val Leu Val Thr			
	85	90	95
Thr Ser Pro Val Thr Thr Gln Ser Thr Leu Pro Thr Thr Pro Thr Thr			
	100	105	110
His Thr Leu Val Thr Thr Leu Ala Thr Pro Ser Lys Ser His Val Thr			
	115	120	125
Phe Pro Val Thr Glu Ala Lys Ala Gly Leu Ser Ile Gly Pro Ser Ser			
	130	135	140
Pro Pro Val Thr Ile Asn Pro Ala Ala His Thr Thr Gly Asn Arg Pro			
145	150	155	160
Ser Thr Ala Ser His Thr Thr Gly Lys Thr Thr Gln Leu Ser Asn Gln			
	165	170	175
Thr Thr Leu Pro Ala Thr Leu Ser Thr Ser Pro His Asn Ile Thr Thr			
	180	185	190
Ser Gln Lys Pro Thr Gln Pro Thr His Thr Pro Gly Pro Thr Thr Ala			
	195	200	205
Ala Asn Asn Thr Thr His Thr Ala Ser Pro Ala Thr Ile Ala Pro Arg			
	210	215	220

Pro Thr Leu Ala Pro Gln Pro Leu Ser Pro Lys Thr Gly Leu Tyr Gln															
225						230					235				240
Val Leu Asn Gly Ser Lys Leu Cys Ile Lys Ala Glu Met Gly Ile Gln															
						245					250				255
Leu Thr Val Gln Asp Ser Val Ser Val Phe Ser Pro Gln Lys Tyr Phe															
						260					265				270
Asn Ile Asp Pro Asn Ala Thr Gln Ala Ser Gly Asn Cys Gly Ser Arg															
						275									285
Lys Ser Asn Leu Leu Leu Asn Phe Gln Gly Gly Phe Val Asn Leu Thr															
						290									300
Phe Ile Lys Asp Glu Asn Ser Tyr Tyr Ile Ser Glu Val Glu Ala Tyr															
305						310					315				320
Leu Thr Val Ser Asn Pro Ala Lys Val Tyr Gln Gly Met Lys Tyr Ala															
						325					330				335
Met Met Met Phe Glu Thr Val Val Gly His Ser Phe Lys Cys Val Ser															
						340					345				350
Glu Gln Ser Ile Gln Leu Ser Asn His Leu Gln Leu Lys Thr Val Asn															
						355									365
Val Gln Leu Gln Ala Phe Asp Phe Glu Asp Asp Arg Phe Gly Asn Ala															
						370									380
Asp Glu Cys Ile Ser Asp Arg Asn Arg Arg Glu Ile Pro Val Ala Val															
385						390					395				400
Gly Leu Ser Ile Ala Val Leu Leu Ala Val Leu Leu Thr Ala Cys Leu															
						405					410				415
Val Thr Arg Lys Arg Pro Ser Arg Gly Tyr Glu Arg Met															
						420									425
<210> 53															
<211> 408															
<212> PRT															
<213> 褐家鼠 (Rattus norvegicus)															
<400> 53															
Met Pro Gly Gln Thr Ser Ala Val Ala Val Leu Leu Cys Leu Ala Val															
1						5					10				15
Ile Leu His Gly Tyr Gln Ile Arg Glu Lys Glu Phe Pro Glu Ala Arg															
						20					25				30
Gly Tyr Leu Gln Tyr Thr Ala Thr Thr Thr Glu Gln Ile Thr Ala Lys															
						35					40				45
Pro Pro Leu Pro Leu Thr Asn Gln Thr Ser His Ala Thr Leu Ala Ser															
						50					55				60

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

370	375	380
Val Leu Cys Val Val Gly Leu Gly Ile Tyr Lys Ile Arg Gln Arg Arg		
385	390	395
Gln Ser Ser Ala Tyr Gln Arg Ile		400
	405	
<210> 54		
<211> 411		
<212> PRT		
<213> 小鼠 (Mus musculus)		
<400> 54		
Met Pro Gly Gln Ile Ser Ala Val Ala Val Leu Phe Leu Ser Leu Thr		
1	5	10
Val Ile Leu His Gly Tyr Gln Ile Arg Glu Lys Glu Phe Pro Lys Ala		
	20	25
Arg Gly Tyr Leu Gln Tyr Thr Ala Thr Ser Ala Glu Gln Ile Thr Thr		30
	35	40
Lys Pro Leu Leu Gln Leu Ile Asn Gln Arg Ser His Ile Thr Leu Ala		45
	50	55
Ser Arg Phe Lys Asp Asp Tyr Ile Gln Met Ala Ala Glu Thr Ser Ala		60
65	70	75
Ile Glu Asn Thr Ala His Ile Thr Met Lys Thr Val Thr Pro Val Thr		80
	85	90
Thr Lys Ser Leu Pro Pro Ile Ser Ser Ala Ser Tyr Thr Phe Val Arg		95
	100	105
Ser Asn Asn Ala His Met Thr Ala Ser Ser Thr Asp Asp Thr Ile Gly		110
	115	120
Ser Gly Ser Ile Ala His Leu Pro Val Pro Thr Thr Arg Ala Ser Leu		125
	130	135
Ala Ile Val Asn Tyr Ile Thr Gly Arg Ala Thr Gln Leu Gly Gly Gln		140
145	150	155
Thr Thr Leu Pro Lys Thr Phe Phe Thr Ala Ser His Lys Ser Thr Thr		160
	165	170
Asn Gln Arg Pro Thr Leu Ser Thr Asn Val Leu Gly Thr Ser Thr Pro		175
	180	185
Thr His Lys Asp Arg Ser Thr Thr Ser Pro Val Pro Leu Val Pro Arg		190
	195	200
Pro Thr Leu Val Thr Trp Ser Ser Pro Ala Lys Ile Gly Thr Tyr Glu		205
	210	215
Val Leu Asn Gly Ser Arg Leu Cys Ile Lys Ala Glu Met Gly Leu Ala		220

225	230	235	240
Leu Ile Val Gln Glu Lys Asp Leu Asp Ser Ala Thr Gln Arg Tyr Phe			
	245	250	255
Asn Ile Asp Pro Ser Leu Thr His Ala Ser Gly Lys Cys Asp Ser Gln			
	260	265	270
Lys Ser Asn Leu Phe Leu Asn Phe Gln Gly Gly Ser Val Asn Ile Thr			
	275	280	285
Phe Thr Lys Glu Glu Asn Leu Tyr Tyr Ile Ser Glu Val Gly Ala Tyr			
	290	295	300
Leu Thr Ile Ser Asn Thr Glu Lys Thr Tyr Gln Gly Lys Lys Asn Thr			
305	310	315	320
Leu Met Met Phe Glu Thr Val Val Gly His Ser Phe Lys Cys Val Ser			
	325	330	335
Glu Gln Ser Ile Gln Leu Ser Ala Gln Leu Gln Met Lys Thr Met Asn			
	340	345	350
Ile His Leu Gln Ala Phe Asp Phe Glu Gly Asp Ser Phe Gly Asn Val			
	355	360	365
Asn Glu Cys Leu Ser Asp Tyr Thr Val Val Leu Pro Met Val Ala Ile			
	370	375	380
Ile Val Val Val Ile Cys Val Val Gly Leu Ser Val Tyr Lys Ile Arg			
385	390	395	400
Gln Arg His Gln Ser Ser Ala Tyr Gln Arg Ile			
	405	410	

<210> 55

<211> 314

<212> PRT

<213> 热带爪蟾 (*Xenopus tropicalis*)

<400> 55

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

				85					90					95			
Thr	Thr	Thr	Thr	His	Ser	Val	Thr	Thr	Thr	Lys	Thr	Ala	Ser	Thr	Thr		
				100					105					110			
Thr	Pro	Thr	Pro	Thr	Leu	Glu	Pro	Lys	Pro	Ser	Pro	Pro	Glu	Thr	Gly		
				115					120					125			
Asn	Tyr	Thr	Val	Lys	Ile	Lys	Asn	Glu	Phe	Cys	Ile	Glu	Ala	Leu	Met		
				130					135					140			
Gly	Leu	Glu	Leu	Glu	Leu	Thr	Asn	Ser	Thr	Lys	Thr	Gln	Gln	Tyr	Phe		
				145					150					155			160
Asn	Ile	Val	Pro	Ser	Gln	Ile	Asn	Ser	Asn	Gly	Thr	Cys	Glu	Lys	Ser		
				165					170					175			
Lys	Ala	Asn	Leu	Asn	Leu	Thr	Phe	Ala	Asn	Ser	Tyr	Ile	Asn	Phe	Val		
				180					185					190			
Phe	Ala	Gln	Asp	Asp	Asn	Ser	Tyr	Tyr	Leu	Asp	Asn	Val	Thr	Val	Tyr		
				195					200					205			
Phe	Asn	Leu	Thr	Arg	Ser	Glu	Ser	Trp	Tyr	Gly	Asn	Ala	Thr	Asn	Gln		
				210					215					220			
Lys	Leu	Leu	Lys	Thr	Glu	Asn	Gly	Tyr	Ser	Val	Lys	Cys	Lys	Asn	Thr		
				225					230					235			240
Pro	Lys	Ile	Gln	Leu	Gly	Asp	Thr	Met	Asn	Leu	Val	Met	Thr	Asn	Val		
				245					250					255			
Lys	Leu	Gln	Val	Phe	Asn	Phe	Lys	Asp	Asn	Ser	Phe	Gly	Lys	Glu	Thr		
				260					265					270			
Thr	Cys	Lys	Tyr	Asp	His	Asn	Phe	Gly	Leu	Met	Ile	Ala	Gly	Ile	Val		
				275					280					285			
Ile	Val	Val	Ile	Val	Val	Leu	Gly	Val	Ile	Ile	Tyr	Phe	Ile	Trp	His		
				290					295					300			
Lys	Arg	Lys	Ser	Ser	Gly	Tyr	Gln	Arg	Ile								
				305					310								
<210> 56																	
<211> 478																	
<212> PRT																	
<213> 黑猩猩 (Pan troglodytes)																	
<400> 56																	
Met	Gly	Arg	Cys	Cys	Phe	Tyr	Thr	Ala	Gly	Thr	Leu	Ser	Leu	Leu	Leu		
				5					10					15			
Leu	Val	Thr	Ser	Val	Thr	Leu	Leu	Val	Ala	Arg	Val	Phe	Gln	Lys	Ala		
				20					25					30			
Val	Asp	Gln	Ser	Ile	Glu	Lys	Lys	Ile	Val	Leu	Arg	Asn	Gly	Thr	Glu		

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

Ile Glu Gly Met His Pro Asn Lys Glu Asp His Glu Thr Phe Val Asp		
355	360	365
Ile Asn Pro Leu Thr Gly Ile Ile Leu Lys Ala Ala Lys Arg Phe Gln		
370	375	380
Ile Asn Ile Tyr Val Lys Lys Leu Asp Asp Phe Val Glu Thr Gly Asp		
385	390	395
Ile Arg Thr Met Val Phe Pro Val Met Tyr Leu Asn Glu Ser Val His		
	405	410
Ile Asp Lys Glu Thr Ala Ser Arg Leu Lys Ser Met Ile Asn Thr Thr		
	420	425
Leu Ile Ile Thr Asn Ile Pro Tyr Ile Ile Met Ala Leu Gly Val Phe		
	435	440
Phe Gly Leu Val Phe Thr Trp Leu Ala Cys Lys Gly Gln Gly Ser Met		
	450	455
Asp Glu Gly Thr Ala Asp Glu Arg Ala Pro Leu Ile Arg Thr		
465	470	475
<210> 57		
<211> 478		
<212> PRT		
<213> 猕猴 (Macaca mulatta)		
<400> 57		
Met Gly Arg Cys Cys Phe Tyr Thr Ala Gly Thr Leu Ser Leu Leu Leu		
1	5	10
Leu Val Thr Ser Val Thr Leu Leu Val Ala Arg Val Phe Gln Lys Ala		
	20	25
Val Asp Gln Ser Ile Glu Lys Lys Ile Val Leu Arg Asn Gly Thr Glu		
	35	40
Ala Phe Asp Ser Trp Glu Lys Pro Pro Leu Pro Val Tyr Thr Gln Phe		
	50	55
Tyr Phe Phe Asn Val Thr Asn Pro Glu Glu Ile Leu Arg Gly Glu Thr		
65	70	75
Pro Arg Val Glu Glu Val Gly Pro Tyr Thr Tyr Arg Glu Leu Arg Asn		
	85	90
Lys Ala Asn Val Gln Phe Gly Asp Asn Gly Thr Thr Ile Ser Ala Val		
	100	105
Ser Asn Lys Ala Tyr Val Phe Glu Arg Asp Gln Ser Val Gly Asp Pro		
	115	120
Lys Ile Asp Leu Ile Arg Thr Leu Asn Ile Pro Val Leu Thr Val Ile		
130	135	140

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

450	455	460
Asp Glu Gly Thr Ala	Asp Glu Arg Ala Pro Leu	Ile Arg Thr
465	470	475
<210> 58		
<211> 478		
<212> PRT		
<213> 家犬(Canis lupus familiaris)		
<400> 58		
Met Gly Arg Cys Cys Phe Tyr Thr Val Gly Thr Leu Ser Leu Leu Leu		
1	5	10
Leu Val Thr Ser Ile Ala Leu Leu Val Ala Arg Val Phe Gln Lys Ala		15
	20	25
Val Asp Gln Thr Ile Glu Lys Asn Ile Val Leu Arg Asn Gly Ser Glu		30
	35	40
Thr Phe Asp Ser Trp Lys Lys Pro Pro Leu Pro Val Tyr Ala Gln Phe		45
	50	55
Tyr Phe Phe Asn Val Thr Asn Pro Glu Glu Ile Leu Arg Gly Glu Ile		60
65	70	75
Pro Arg Leu Glu Glu Val Gly Pro Tyr Thr Tyr Arg Glu Leu Arg Asp		80
	85	90
Lys Ala Asp Ile Gln Phe Gly Asp Asn Gly Thr Thr Ile Ser Ala Val		95
	100	105
Ser Asn Lys Ala Tyr Val Phe Glu Arg Asn Gln Ser Val Gly Asp Pro		110
	115	120
Lys Thr Asp Leu Ile Arg Thr Leu Asn Ile Pro Ala Val Thr Ala Met		125
	130	135
Glu Trp Ala His Leu His Phe Phe Arg Glu Leu Ile Glu Ala Leu Leu		140
145	150	155
Lys Ala Tyr Gln Gln Thr Leu Phe Val Thr His Thr Val Asp Glu Leu		160
	165	170
Leu Trp Gly Tyr Lys Asp Glu Ile Leu Ser Leu Ile Asn Val Phe Lys		175
	180	185
Pro Glu Ile Ser Pro Tyr Phe Gly Leu Tyr Tyr Gly Lys Asn Gly Thr		190
	195	200
Asn Asp Gly Asp Tyr Val Phe Leu Thr Gly Glu Asp Asn Tyr Leu Asn		205
	210	215
Phe Ser Lys Ile Val Glu Trp Asn Gly Lys Thr Ser Leu Asp Trp Trp		220
225	230	235
Thr Thr Asp Lys Cys Asn Met Ile Asn Gly Thr Asp Gly Asp Ser Phe		240

	245		250		255
His Pro Leu Ile Asp Lys Asp Glu Ile Leu Tyr Val Phe Pro Ser Glu					
	260		265		270
Phe Cys Arg Ser Val Tyr Ile Thr Phe Ser Asp Phe Lys Ser Val Gln					
	275		280		285
Gly Leu Pro Ala Phe Arg Tyr Lys Val Pro Gly Glu Val Leu Ala Asn					
	290		295		300
Thr Ser Asp Asn Ala Gly Phe Cys Val Pro Lys Gly Asn Cys Leu Gly					
305		310		315	320
Ser Gly Val Leu Asn Ile Ser Ile Cys Lys Asn Gly Ala Pro Ile Ile					
	325		330		335
Ile Ser Phe Pro His Phe Tyr Glu Ala Asp Lys Lys Phe Val Ser Ala					
	340		345		350
Ile Asp Gly Met Arg Pro Asn Lys Asp Tyr His Glu Thr Phe Val Asp					
	355		360		365
Ile Asn Pro Leu Thr Gly Ile Ile Leu Arg Ala Ala Lys Arg Phe Gln					
	370		375		380
Ile Asn Val Tyr Val Lys Lys Leu Asp Asp Phe Ile Glu Thr Gly Asn					
385		390		395	400
Ile Arg Thr Met Val Phe Pro Val Met Tyr Ile Asn Glu Ser Val Leu					
	405		410		415
Ile Asp Lys Asp Thr Ala Ser Arg Leu Lys Ser Val Ile Asn Thr Thr					
	420		425		430
Leu Ile Ile Thr Asn Ile Pro Tyr Ile Val Met Ala Leu Gly Val Phe					
	435		440		445
Phe Gly Leu Ile Phe Thr Trp Leu Ala Cys Arg Gly Gln Gly Ser Met					
	450		455		460
Asp Glu Gly Thr Pro Asp Glu Arg Ala Pro Leu Ile Arg Thr					
465		470		475	
<210> 59					
<211> 478					
<212> PRT					
<213> 家牛(Bos taurus)					
<400> 59					
Met Gly Arg Cys Cys Phe Tyr Ala Val Gly Thr Leu Ser Leu Leu Leu					
1		5		10	15
Leu Val Thr Ser Ile Thr Leu Leu Val Ala Arg Val Phe Gln Lys Ala					
	20		25		30
Val Asp Gln Thr Ile Glu Lys Asn Ile Val Leu Arg Asn Gly Ser Glu					

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

Ile Gly Gly Met His Pro Asn Lys Glu Tyr His Glu Thr Phe Val Asp		
355	360	365
Ile Asn Pro Leu Thr Gly Ile Ile Leu Arg Ala Ala Lys Arg Phe Gln		
370	375	380
Ile Asn Val Tyr Val Arg Lys Leu Asp Asp Phe Val Glu Thr Gly Asn		
385	390	395
Ile Gln Thr Leu Val Phe Pro Val Met Tyr Ile Asn Glu Ser Val Leu		
	405	410
		415
Ile Asp Lys Glu Thr Ala Ser Arg Leu Lys Ser Val Ile Asn Thr Thr		
	420	425
		430
Leu Ile Val Thr Asn Ile Pro Tyr Ile Ile Met Ala Leu Gly Val Phe		
	435	440
		445
Phe Gly Leu Ile Phe Thr Trp Leu Ala Cys Arg Gly Gln Gly Ser Thr		
	450	455
		460
Asp Glu Gly Thr Ala Asp Glu Arg Ala Pro Leu Ile Arg Thr		
465	470	475
<210> 60		
<211> 478		
<212> PRT		
<213> 小鼠 (Mus musculus)		
<400> 60		
Met Gly Arg Cys Cys Phe Tyr Thr Ala Gly Thr Leu Ser Leu Leu Leu		
1	5	10
		15
Leu Val Thr Ser Val Thr Leu Leu Val Ala Arg Val Phe Gln Lys Ala		
	20	25
		30
Val Asp Gln Thr Ile Glu Lys Asn Met Val Leu Gln Asn Gly Thr Lys		
	35	40
		45
Val Phe Asn Ser Trp Glu Lys Pro Pro Leu Pro Val Tyr Ile Gln Phe		
	50	55
		60
Tyr Phe Phe Asn Val Thr Asn Pro Glu Glu Ile Leu Gln Gly Glu Ile		
65	70	75
		80
Pro Leu Leu Glu Glu Val Gly Pro Tyr Thr Tyr Arg Glu Leu Arg Asn		
	85	90
		95
Lys Ala Asn Ile Gln Phe Gly Glu Asn Gly Thr Thr Ile Ser Ala Val		
	100	105
		110
Thr Asn Lys Ala Tyr Val Phe Glu Arg Asn Gln Ser Val Gly Asp Pro		
	115	120
		125
Asn Val Asp Leu Ile Arg Thr Ile Asn Ile Pro Leu Leu Thr Val Val		
	130	135
		140

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

450	455	460
Asp Glu Gly Thr Ala	Asp Glu Arg Ala Pro Leu	Ile Arg Thr
465	470	475
<210> 61		
<211> 531		
<212> PRT		
<213> 斑马鱼 (Danio rerio)		
<400> 61		
Met Thr Arg Arg Ser Cys Thr Ile Tyr Ala Thr Gly Ile Val Cys Ala		
1	5	10
His Leu Leu Ile Leu Gly Ile Ala Leu Leu Leu Ala Gln Val Phe Gln		
20	25	30
Thr Met Ile Gln Glu Arg Ile Lys Lys Glu Ile Thr Leu Ala Glu Asn		
35	40	45
Ser Arg Val Leu Asp Gly Trp Ile Asn Pro Pro Pro Pro Val Tyr Met		
50	55	60
Gln Tyr Phe Phe Phe Asn Val Thr Asn Pro Asp Glu Phe Leu Ala Gly		
65	70	75
Lys Glu Lys Ala Lys Val Thr Gln Met Gly Pro Tyr Thr Tyr Arg Glu		
85	90	95
Tyr Arg Pro Arg Glu Asn Val Thr Tyr Leu Glu Asn Gly Thr Lys Ile		
100	105	110
Phe Ala Thr Asn Pro Lys Ser Phe Val Phe Leu Arg Asn Met Ser Ala		
115	120	125
Gly Asp Pro Glu Val Asp Arg Val Thr Thr Val Asn Ile Pro Met Ile		
130	135	140
Ala Val Met Asn Glu Leu Asn Ser Tyr Ser Phe Phe Val Arg Thr Ala		
145	150	155
Val Ser Met Tyr Met Gly Ser Met Gly Met Gly Leu Phe Met Asn Arg		
165	170	175
Thr Val His Glu Ile Leu Trp Gly Phe Lys Asp Pro Leu Leu Thr Lys		
180	185	190
Leu His Ala Met Arg Pro Glu Val Asp Glu His Phe Gly Leu Met Tyr		
195	200	205
Asn Lys Asn Gly Thr His Glu Gly Glu Phe Val Phe His Thr Gly Glu		
210	215	220
Lys Asn Tyr Met Asn Tyr Gly Lys Ile Asp Thr Trp Asn Gly Ile Ser		
225	230	235
Gln Met Asn Trp Trp Ser Ser Asn Gln Ser Asn Met Ile Asn Gly Thr		

	245		250		255
Asp Gly Ser Val Phe His Thr Phe Leu Ser Arg Lys Glu Leu Leu Tyr					
	260		265		270
Ile Phe Ala Ala Asp Leu Cys Arg Ser Ile His Leu Gly Tyr Val Arg					
	275		280		285
Asp Met Glu Val Lys Gly Ile Pro Ala Phe Arg Phe Ala Pro Pro Ser					
	290		295		300
Asp Val Leu Ala Pro Pro Asp Glu Asn Pro Ala Asn Ala Gly Phe Cys					
305		310		315	320
Val Pro Ala Gly Asp Cys Leu Gly Lys Gly Val Leu Lys Val Ser Val					
	325		330		335
Cys Arg Gln Gly Ala Pro Ile Val Val Ser Phe Pro His Phe Tyr Gln					
	340		345		350
Ala Asp Glu Arg Tyr Ile Asn Ala Ile Glu Gly Met Asn Pro Asn Glu					
	355		360		365
Glu Glu His Glu Thr Tyr Leu Asp Ile Asn Pro Thr Thr Gly Val Pro					
	370		375		380
Ile Arg Ala Cys Lys Arg Ala Gln Leu Asn Ile Ile Leu Lys Arg Val					
385		390		395	400
Arg Gly Phe Pro Asn Thr Lys Phe Leu Asn Glu Thr Ile Phe Pro Ile					
	405		410		415
Met Tyr Val Asn Glu Thr Ala Thr Ile Asp Asp Glu Ser Ala Ala Gln					
	420		425		430
Met Arg Met Leu Leu Leu Ile Val Thr Val Val Ser Asn Phe Pro Val					
	435		440		445
Ile Ile Leu Ala Leu Gly Val Ile Leu Leu Val Val Leu Ile Phe Leu					
	450		455		460
Val Cys Arg Asn Arg Gln Arg Lys Asn Glu Val Lys Arg Ile Asp Phe					
465		470		475	480
Thr Glu Ala Phe His Ser Phe Ala Thr Thr Lys Asp Glu Thr Ala Tyr					
	485		490		495
Thr Gln Val Ser Asn Gln Ala Glu Asp Ser Pro Glu Asn Arg Asn Asn					
	500		505		510
Gln Pro Leu Arg Asn Gly Ser Tyr Ile Ala Met Ser Pro Val Glu Ala					
	515		520		525
Gln Lys Cys					
	530				
<210> 62					
<211> 478					

<212> PRT

<213> 褐家鼠 (*Rattus norvegicus*)

<400> 62

```

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

```

Gly	Leu	Pro	Ala	Phe	Arg	Tyr	Lys	Val	Pro	Ala	Glu	Ile	Leu	Ala	Asn
290						295					300				
Ser	Ser	Glu	Asn	Ala	Gly	Phe	Cys	Ile	Pro	Glu	Gly	Asn	Cys	Met	Asp
305					310					315				320	
Ala	Gly	Val	Leu	Asn	Val	Ser	Ile	Cys	Lys	Asn	Gly	Ala	Pro	Ile	Ile
				325					330					335	
Met	Ser	Phe	Pro	His	Phe	Tyr	Gln	Ala	Asp	Glu	Lys	Phe	Val	Ser	Ala
			340					345					350		
Ile	Lys	Gly	Met	Arg	Pro	Asn	Lys	Glu	Glu	His	Glu	Ser	Phe	Val	Asp
		355					360					365			
Ile	Asn	Pro	Leu	Thr	Gly	Ile	Ile	Leu	Arg	Gly	Ala	Lys	Arg	Phe	Gln
		370				375					380				
Ile	Asn	Thr	Tyr	Val	Lys	Lys	Leu	Asp	Asp	Phe	Val	Glu	Thr	Gly	Asn
385					390					395				400	
Ile	Arg	Thr	Met	Val	Phe	Pro	Val	Met	Tyr	Leu	Asn	Glu	Ser	Val	Leu
			405						410					415	
Ile	Asp	Lys	Glu	Thr	Ala	Ser	Gln	Leu	Lys	Ser	Val	Ile	Asn	Thr	Thr
			420					425					430		
Leu	Ile	Val	Thr	Asn	Ile	Pro	Tyr	Ile	Ile	Met	Ala	Leu	Gly	Val	Phe
		435						440				445			
Phe	Gly	Leu	Ile	Phe	Thr	Trp	Leu	Ala	Cys	Arg	Gly	Gln	Gly	Ser	Thr
		450					455				460				
Asp	Glu	Gly	Thr	Ala	Asp	Glu	Arg	Ala	Pro	Leu	Ile	Arg	Thr		
465					470					475					
<210> 63															
<211> 481															
<212> PRT															
<213> 原鸡(Gallus gallus)															
<400> 63															
Met	Arg	Ser	Leu	Cys	Leu	Val	Thr	Val	Gly	Val	Leu	Ala	Leu	Thr	Leu
1				5					10					15	
Leu	Ile	Ala	Ser	Ile	Ser	Leu	Leu	Val	Ala	His	Val	Phe	Gln	Thr	Val
			20					25					30		
Val	Asp	Leu	Gln	Val	Lys	Gln	Gly	Thr	Val	Leu	Lys	Asn	Gly	Thr	Glu
		35					40					45			
Thr	Phe	Glu	Ala	Trp	Glu	Asp	Pro	Pro	Pro	Pro	Val	Tyr	Met	Gln	Phe
		50				55					60				
Tyr	Phe	Phe	Asn	Val	Thr	Asn	Pro	Leu	Glu	Val	Leu	Gln	Gly	Ala	Thr
65					70					75				80	

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

385	390	395	400
Thr Gly Asn Ile Arg	Thr Leu Ile Phe	Pro Val Met Tyr	Ile Asn Glu
405	410	415	
Ser Val Leu Ile Asp	Glu Ala Ser Ala	Asn Lys Leu Lys	His Val Leu
420	425	430	
Leu Glu Ala Ser Val	Val Thr Gly Ile	Pro Phe Val Ile	Met Ala Ile
435	440	445	
Gly Ile Val Phe Gly	Ile Val Phe Ser	Val Leu Val Cys	Arg Ala Gln
450	455	460	
Gly Ala Arg Glu Glu	Ser Thr Glu Glu	Glu Arg Ser Pro	Leu Ile Arg
465	470	475	480
Thr			
<210> 64			
<211> 483			
<212> PRT			
<213> 热带爪蟾(Xenopus tropicalis)			
<400> 64			
Met Val Lys Trp Ala	Val Phe Gly Thr	Ala Ala Val Ser	Val Thr Leu
1	5	10	15
Leu Ile Val Ser Ile	Val Leu Leu Leu	Thr His Thr Phe	Met Asp Ile
20	25	30	
Val Glu Gly Gln Val	Lys Gln Ala Ile	Val Leu Lys Asn	Glu Ser Glu
35	40	45	
Val Phe Glu Asp Trp	Ala Asn Pro Pro	Pro Pro Val Tyr	Met Gln Phe
50	55	60	
Tyr Phe Phe Asn Val	Thr Asn Pro Leu	Glu Val Leu Ser	Gly Glu Lys
65	70	75	80
Pro Phe Val Asp Glu	Ile Gly Pro Tyr	Thr Tyr Arg Glu	Tyr Arg Pro
85	90	95	
Arg Glu Asn Ile Thr	Phe Ser Val Asn	Gly Thr Glu Val	Ser Ala Val
100	105	110	
Thr Pro Lys Thr Tyr	Val Phe Glu Pro	Glu Lys Ser Ile	Gly Asp Pro
115	120	125	
Lys Val Asp Leu Ile	Arg Thr Val Asn	Ile Pro Leu Val	Thr Ile Leu
130	135	140	
Glu Met Thr Lys Asp	Ser Ser Leu Leu	Arg Pro Phe Ile	Ile Ala Ala
145	150	155	160
Leu Lys Thr Tyr Lys	Glu Gly Met Phe	Val Thr Arg Thr	Val Asp Glu
165	170	175	

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

<210> 65

<211> 551

<212> PRT

<213> 黑腹果蝇 (*Drosophila melanogaster*)

<400> 65

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

Tyr Gly Ile Ile Asp Asn Phe Asn Gly Arg Thr His Leu Pro His Trp		
275	280	285
Thr Thr Asp Ala Cys Asn Thr Leu Ala Gly Thr Asp Gly Ser Ile Phe		
290	295	300
Pro Pro His Ile Asp His Asp Arg Ile Leu His Val Tyr Asp Lys Asp		
305	310	315
Leu Cys Arg Leu Leu Pro Leu Val Phe Glu Lys Glu Val Met Thr Ser		
	325	330
Asn Glu Val Pro Gly Tyr Arg Phe Thr Pro Pro Glu Trp Val Phe Ala		
	340	345
Asp Val Asp Ser His Pro Asp Asn Met Cys Phe Cys Pro Ala Gly Lys		
	355	360
Pro Ser Cys Ser Pro Asn Gly Leu Phe Asn Val Ser Leu Cys Gln Tyr		
	370	375
Asp Ser Pro Ile Met Leu Ser Phe Pro His Phe Tyr Leu Ala Asp Glu		
385	390	395
Ser Leu Arg Thr Gln Val Glu Gly Ile Ser Pro Pro Met Lys Glu Lys		
	405	410
His Gln Phe Phe Phe Asp Val Gln Pro Lys Met Gly Thr Thr Leu Arg		
	420	425
Val Arg Ala Arg Ile Gln Ile Asn Leu Ala Val Ser Gln Val Phe Asp		
	435	440
Ile Lys Gln Val Ala Asn Phe Pro Asp Ile Ile Phe Pro Ile Leu Trp		
	450	455
Phe Glu Glu Gly Ile Asp Asn Leu Pro Asp Glu Val Thr Asp Leu Met		
465	470	475
Arg Phe Ala Glu Gln Val Pro Pro Lys Ile Arg Val Ala Leu Ile Val		
	485	490
Gly Leu Cys Ala Leu Gly Val Ile Leu Leu Leu Leu Ser Thr Phe Cys		
	500	505
Leu Ile Arg Asn Ser His Arg Gln Ser Thr Leu His Leu Glu Gly Ser		
	515	520
Asn Tyr Leu Ala Thr Ala Gln Val Asp Met Asn Lys Lys Gln Asn Lys		
	530	535
Asp Asn Gln Pro Ala Arg Tyr		
545	550	
<210> 66		
<211> 522		
<212> PRT		

<213> 冈比亚按蚊 (*Anopheles gambiae*)

<400> 66

```

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

```

290	295	300
Arg Gly Gly Val Lys Gly Tyr Arg Phe Thr Pro Ser Pro Asp Val Phe		
305	310	315
Ala Ser Val Asp Lys Asn Pro Asn Asn Met Cys Tyr Cys Pro Ala Gly		320
	325	330
Pro Pro Cys Ala Pro His Gly Leu Phe Asn Val Ser Leu Cys Gln Tyr		335
	340	345
Asp Ser Pro Ile Leu Leu Ser Phe Pro His Phe Tyr Met Ala Asp Gln		350
	355	360
Thr Leu Arg Thr Ala Val Glu Gly Ile Ser Pro Pro Glu Lys Asp Lys		365
	370	380
His Gln Leu Phe Ile Asp Val Gln Pro Asp Met Gly Thr Ala Leu Arg		
385	390	395
Ala Arg Ala Arg Ile Gln Ile Asn Leu Ala Val Ser Gln Val Val Asp		400
	405	410
Ile Lys Gln Val Ala Asn Phe Pro Asp Ile Val Phe Pro Ile Leu Trp		415
	420	425
Phe Glu Glu Gly Ile Asp Ser Leu Pro Asp Glu Ile Leu Asp Leu Met		430
	435	440
Lys Val Ala Thr Asn Ile Pro Pro Arg Ala Lys Phe Ile Leu Thr Ile		445
	450	455
Ala Leu Phe Gly Leu Gly Gly Phe Leu Phe Val Val Ala Val Ile Cys		460
465	470	475
Leu Val Arg Lys Ser His Arg Gln Ser Thr Leu His Leu Glu Gly Ser		480
	485	490
Asn Tyr Leu Ala Thr Ala Ser Val Asp Gln Ala Lys Lys Lys Ala Lys		495
	500	505
Met Asp Asn Gly Met Ser Ser Lys Ser Asn		510
	515	520
<210> 67		
<211> 338		
<212> PRT		
<213> 智人(Homo sapiens)		
<400> 67		
Met Val Arg Arg Val Gln Pro Asp Arg Lys Gln Leu Pro Leu Val Leu		
1	5	10
Leu Arg Leu Leu Cys Leu Leu Pro Thr Gly Leu Pro Val Arg Ser Val		
	20	25
Asp Phe Asn Arg Gly Thr Asp Asn Ile Thr Val Arg Gln Gly Asp Thr		30

35					40					45						
Ala	Ile	Leu	Arg	Cys	Val	Val	Glu	Asp	Lys	Asn	Ser	Lys	Val	Ala	Trp	
50					55					60						
Leu	Asn	Arg	Ser	Gly	Ile	Ile	Phe	Ala	Gly	His	Asp	Lys	Trp	Ser	Leu	
65					70					75					80	
Asp	Pro	Arg	Val	Glu	Leu	Glu	Lys	Arg	His	Ser	Leu	Glu	Tyr	Ser	Leu	
85					90					95						
Arg	Ile	Gln	Lys	Val	Asp	Val	Tyr	Asp	Glu	Gly	Ser	Tyr	Thr	Cys	Ser	
100					105					110						
Val	Gln	Thr	Gln	His	Glu	Pro	Lys	Thr	Ser	Gln	Val	Tyr	Leu	Ile	Val	
115					120					125						
Gln	Val	Pro	Pro	Lys	Ile	Ser	Asn	Ile	Ser	Ser	Asp	Val	Thr	Val	Asn	
130					135					140						
Glu	Gly	Ser	Asn	Val	Thr	Leu	Val	Cys	Met	Ala	Asn	Gly	Arg	Pro	Glu	
145					150					155					160	
Pro	Val	Ile	Thr	Trp	Arg	His	Leu	Thr	Pro	Thr	Gly	Arg	Glu	Phe	Glu	
165					170					175						
Gly	Glu	Glu	Glu	Tyr	Leu	Glu	Ile	Leu	Gly	Ile	Thr	Arg	Glu	Gln	Ser	
180					185					190						
Gly	Lys	Tyr	Glu	Cys	Lys	Ala	Ala	Asn	Glu	Val	Ser	Ser	Ala	Asp	Val	
195					200					205						
Lys	Gln	Val	Lys	Val	Thr	Val	Asn	Tyr	Pro	Pro	Thr	Ile	Thr	Glu	Ser	
210					215					220						
Lys	Ser	Asn	Glu	Ala	Thr	Thr	Gly	Arg	Gln	Ala	Ser	Leu	Lys	Cys	Glu	
225					230					235					240	
Ala	Ser	Ala	Val	Pro	Ala	Pro	Asp	Phe	Glu	Trp	Tyr	Arg	Asp	Asp	Thr	
245					250					255						
Arg	Ile	Asn	Ser	Ala	Asn	Gly	Leu	Glu	Ile	Lys	Ser	Thr	Glu	Gly	Gln	
260					265					270						
Ser	Ser	Leu	Thr	Val	Thr	Asn	Val	Thr	Glu	Glu	His	Tyr	Gly	Asn	Tyr	
275					280					285						
Thr	Cys	Val	Ala	Ala	Asn	Lys	Leu	Gly	Val	Thr	Asn	Ala	Ser	Leu	Val	
290					295					300						
Leu	Phe	Arg	Pro	Gly	Ser	Val	Arg	Gly	Ile	Asn	Gly	Ser	Ile	Ser	Leu	
305					310					315					320	
Ala	Val	Pro	Leu	Trp	Leu	Leu	Ala	Ala	Ser	Leu	Leu	Cys	Leu	Leu	Ser	
325					330					335						
Lys Cys																
<210> 68																

<211> 338

<212> PRT

<213> 黑猩猩(Pan troglodytes)

<400> 68

```

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

```

275	280	285
Thr Cys Val Ala Ala Asn Lys Leu Gly Val Thr Asn Ala Ser Leu Val		
290	295	300
Leu Phe Arg Pro Gly Ser Val Arg Gly Ile Asn Gly Ser Ile Ser Leu		
305	310	315
Ala Val Pro Leu Trp Leu Leu Ala Ala Ser Leu Leu Cys Leu Leu Ser		
325	330	335
Lys Cys		
<210> 69		
<211> 338		
<212> PRT		
<213> 家兔 (<i>Oryctolagus cuniculus</i>)		
<400> 69		
Met Gly Ala Arg Val Gln Pro Asp Arg Lys Gln Leu Pro Leu Val Leu		
1	5	10
Leu Arg Leu Leu Cys Leu Leu Pro Thr Gly Leu Pro Val Arg Ser Val		
20	25	30
Asp Phe Asn Arg Gly Thr Asp Asn Ile Thr Val Arg Gln Gly Asp Thr		
35	40	45
Ala Ile Leu Arg Cys Val Val Glu Asp Lys Asn Ser Lys Val Ala Trp		
50	55	60
Leu Asn Arg Ser Gly Ile Ile Phe Ala Gly His Asp Lys Trp Ser Leu		
65	70	75
Asp Pro Arg Val Glu Leu Glu Lys Arg His Ser Leu Glu Tyr Ser Leu		
85	90	95
Arg Ile Gln Lys Val Asp Val Tyr Asp Glu Gly Ser Tyr Thr Cys Ser		
100	105	110
Val Gln Thr Gln His Glu Pro Lys Thr Ser Gln Val Tyr Leu Ile Val		
115	120	125
Gln Val Pro Pro Lys Ile Ser Asn Ile Ser Ser Asp Val Thr Val Asn		
130	135	140
Glu Gly Ser Asn Val Thr Leu Val Cys Met Ala Asn Gly Arg Pro Glu		
145	150	155
Pro Val Ile Thr Trp Arg His Leu Thr Pro Thr Gly Arg Glu Phe Glu		
165	170	175
Gly Glu Glu Glu Tyr Leu Glu Ile Leu Gly Ile Thr Arg Glu Gln Ser		
180	185	190
Gly Lys Tyr Glu Cys Lys Ala Ala Asn Glu Val Ser Ser Ala Asp Val		
195	200	205

Lys Gln Val Lys Val Thr Val Asn Tyr Pro Pro Thr Ile Thr Glu Ser
 210 215 220
 Lys Ser Asn Glu Ala Thr Thr Gly Arg Gln Ala Ser Leu Lys Cys Glu
 225 230 235 240
 Ala Ser Ala Val Pro Ala Pro Asp Phe Glu Trp Tyr Arg Asp Asp Thr
 245 250 255
 Arg Ile Asn Ser Ala Asn Gly Leu Glu Ile Lys Ser Thr Glu Gly Gln
 260 265 270
 Ser Ser Leu Thr Val Thr Asn Val Thr Glu Glu His Tyr Gly Asn Tyr
 275 280 285
 Thr Cys Val Ala Ala Asn Lys Leu Gly Val Thr Asn Ala Ser Leu Val
 290 295 300
 Leu Phe Arg Pro Gly Ser Val Arg Gly Ile Asn Gly Ser Ile Ser Leu
 305 310 315 320
 Ala Val Pro Leu Trp Leu Leu Ala Ala Ser Leu Leu Cys Leu Leu Ser
 325 330 335
 Lys Cys
 <210> 70
 <211> 341
 <212> PRT
 <213> 小鼠 (Mus musculus)
 <400> 70
 Met Val Gly Arg Val Gln Pro Asp Arg Lys Gln Leu Pro Leu Val Leu
 1 5 10 15
 Leu Arg Leu Leu Cys Leu Leu Pro Thr Gly Leu Pro Val Arg Ser Val
 20 25 30
 Asp Phe Asn Arg Gly Thr Asp Asn Ile Thr Val Arg Gln Gly Asp Thr
 35 40 45
 Ala Ile Leu Arg Cys Val Val Glu Asp Lys Asn Ser Lys Val Ala Trp
 50 55 60
 Leu Asn Arg Ser Gly Ile Ile Phe Ala Gly His Asp Lys Trp Ser Leu
 65 70 75 80
 Asp Pro Arg Val Glu Leu Glu Lys Arg His Ala Leu Glu Tyr Ser Leu
 85 90 95
 Arg Ile Gln Lys Val Asp Val Tyr Asp Glu Gly Ser Tyr Thr Cys Ser
 100 105 110
 Val Gln Thr Gln His Glu Pro Lys Thr Ser Gln Val Tyr Leu Ile Val
 115 120 125
 Gln Val Pro Pro Lys Ile Ser Asn Ile Ser Ser Asp Val Thr Val Asn

130	135	140
Glu Gly Ser Asn Val Thr Leu Val Cys Met Ala Asn Gly Arg Pro Glu		
145	150	155
Pro Val Ile Thr Trp Arg His Leu Thr Pro Leu Gly Arg Glu Phe Glu		
	165	170
Gly Glu Glu Glu Tyr Leu Glu Ile Leu Gly Ile Thr Arg Glu Gln Ser		
	180	185
Gly Lys Tyr Glu Cys Lys Ala Ala Asn Glu Val Ser Ser Ala Asp Val		
	195	200
Lys Gln Val Lys Val Thr Val Asn Tyr Pro Pro Thr Ile Thr Glu Ser		
	210	220
Lys Ser Asn Glu Ala Thr Thr Gly Arg Gln Ala Ser Leu Lys Cys Glu		
225	230	235
Ala Ser Ala Val Pro Ala Pro Asp Phe Glu Trp Tyr Arg Asp Asp Thr		
	245	250
Arg Ile Asn Ser Ala Asn Gly Leu Glu Ile Lys Ser Thr Glu Gly Gln		
	260	265
Ser Ser Leu Thr Val Thr Asn Val Thr Glu Glu His Tyr Gly Asn Tyr		
	275	280
Thr Cys Val Ala Ala Asn Lys Leu Gly Val Thr Asn Ala Ser Leu Val		
	290	295
Leu Phe Ser Lys Tyr Ala Lys Thr Glu Pro Asp Ser Met Gln Val Ile		
305	310	315
Glu Phe Leu His Ile Asp Leu Lys Ser Ile Arg His Pro Leu Lys Val		
	325	330
Asn Pro Ile Gln Lys		335
	340	
<210> 71		
<211> 337		
<212> PRT		
<213> 非洲爪蟾 (Xenopus laevis)		
<400> 71		
Met Val Gly Arg Ser Gln Ser Asp Arg Asn Gln Leu Pro Leu Phe Leu		
1	5	10
Leu Arg Leu Leu Cys Leu Leu Pro Thr Gly Leu Pro Val Arg Ser Gly		
	20	25
Asp Phe Asn Arg Ser Thr Asp Asn Met Thr Val Arg Gln Gly Asp Thr		
	35	40
Ala Ile Leu Arg Cys Phe Val Glu Asp Lys Ser Ser Lys Val Ala Trp		

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

Cys

<210> 72

<211> 333

<212> PRT

<213> 斑马鱼 (Danio rerio)

<400> 72

```

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

```

290	295	300
Met Gly Arg Asp Ile Asn Ser Ala Gly Cys Ile Cys Gln Ser Leu Trp		
305	310	315
Leu Leu Leu Leu Cys Val Ser Ser Ala Leu Leu Gln Cys		320
	325	330
<210> 73		
<211> 197		
<212> PRT		
<213> 小鼠 (Mus musculus)		
<400> 73		
Met Ser Gly Ser Ser Arg Arg Leu Leu Trp Ala Ala Thr Cys Leu Ala		
1	5	10
Val Leu Cys Val Ser Ala Ala Gln Pro Asn Ile Thr Thr Leu Ala Pro		15
	20	25
Asn Val Thr Glu Val Pro Thr Thr Thr Thr Lys Val Val Pro Thr Thr		30
	35	40
Gln Met Pro Thr Val Leu Pro Glu Thr Cys Ala Ser Phe Asn Ser Cys		45
	50	55
Val Ser Cys Val Asn Ala Thr Phe Thr Asn Asn Ile Thr Cys Phe Trp		60
65	70	75
Leu His Cys Gln Glu Ala Asn Lys Thr Tyr Cys Ala Asn Glu Pro Leu		80
	85	90
Ser Asn Cys Ser Gln Val Asn Arg Thr Asp Leu Cys Ser Val Ile Pro		95
	100	105
Pro Thr Thr Pro Val Pro Thr Asn Ser Thr Ala Lys Pro Thr Thr Arg		110
	115	120
Pro Ser Ser Pro Thr Pro Thr Pro Ser Val Val Thr Ser Ala Gly Thr		125
	130	135
Thr Asn Thr Thr Leu Thr Pro Thr Ser Gln Pro Glu Arg Lys Ser Thr		140
145	150	155
Phe Asp Ala Ala Ser Phe Ile Gly Gly Ile Val Leu Val Leu Gly Val		160
	165	170
Gln Ala Val Ile Phe Phe Leu Tyr Lys Phe Cys Lys Ser Lys Glu Arg		175
	180	185
Asn Tyr His Thr Leu		190
	195	
<210> 74		
<211> 197		
<212> PRT		

<213> 猕猴 (*Macaca mulatta*)

<400> 74

```

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

```

<210> 75

<211> 194

<212> PRT

<213> 野猪 (*Sus scrofa*)

<400> 75

```

Met Leu Gly Leu Ser Arg Gln Leu Leu Trp Ala Val Gly Cys Leu Ala
1           5           10           15
Ala Leu Cys Val Leu Thr Ala Ala Lys Asn Ser Thr Ile Leu Pro Pro
          20           25           30
Ser Thr Thr Thr Pro Trp Leu Ser Pro Pro Thr Thr Gln Thr Thr Ser
          35           40           45

```

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

Thr Leu

<210> 76

<211> 198

<212> PRT

<213> 家牛(Bos taurus)

<400> 76

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

115	120	125
Thr Leu Pro Ser Thr Thr Thr Thr Ser Thr Thr Ala Thr Thr Ser Gly		
130	135	140
Thr Thr Asn Thr Thr Leu Ser Pro Thr Ile Gln Pro Thr Arg Lys Ser		
145	150	155
Thr Phe Asp Ala Ala Ser Phe Ile Gly Gly Ile Val Leu Val Leu Gly		
165	170	175
Val Gln Ala Val Ile Phe Phe Leu Tyr Lys Phe Cys Lys Ser Lys Glu		
180	185	190
Arg Asn Tyr His Thr Leu		
195		
<210> 77		
<211> 198		
<212> PRT		
<213> 绵羊 (Ovis aries)		
<400> 77		
Met Ser Gly Leu Ser Arg Pro Leu Leu Leu Ala Val Gly Tyr Leu Ala		
1	5	10
Ala Leu Cys Val Ile Thr Ala Ala Arg Asn Thr Thr Val Thr Pro Asn		
20	25	30
Val Thr Thr Pro Ser Ser Pro Pro Pro Thr Thr Ala Thr Val Pro Val		
35	40	45
Ser Pro Thr Thr Leu Thr Pro Pro Pro Val Thr Thr Pro Ala Pro Asp		
50	55	60
Ile Cys Gly Ser Arg Asn Ser Cys Ile Ser Cys Val Asp Gly Asn Ala		
65	70	75
Thr Cys Phe Trp Ile Glu Cys Lys Gly Lys Ser Tyr Cys Ser Asp Asn		
85	90	95
Ser Thr Val Ser Asp Cys Lys Val Val Asn Thr Thr Gly Phe Cys Ala		
100	105	110
Val Pro Thr Thr Thr Pro Thr Pro Thr Asn Ser Thr Ala Lys Thr Thr		
115	120	125
Thr Leu Pro Ser Thr Thr Thr Thr Ser Thr Thr Ala Thr Thr Ser Gly		
130	135	140
Thr Ala Asn Thr Thr Leu Thr Pro Thr Ile Gln Pro Met Arg Lys Ser		
145	150	155
Thr Phe Asp Ala Ala Ser Phe Ile Gly Gly Ile Val Leu Val Leu Gly		
165	170	175
Val Gln Ala Val Ile Phe Phe Leu Tyr Lys Phe Cys Lys Ser Lys Glu		

180	185	190
Arg Asn Tyr His Thr Leu		
195		
<210> 78		
<211> 198		
<212> PRT		
<213> 家犬(Canis lupus familiaris)		
<400> 78		
Met Ser Gly Leu Ser Arg Gln Leu Cys Trp Ala Ala Ala Cys Leu Ala		
1 5 10 15		
Ala Leu Cys Ala Leu Thr Ala Ala Gln Ser Phe Ser Ser Asp Pro Asn		
20 25 30		
Gly Thr Thr Thr Thr Thr Gln Ala Thr Thr Asp Ala Ala Thr Thr Arg		
35 40 45		
Val Thr Thr Ala Ala Pro Ala Thr Thr Pro Ala Pro Asp Pro Cys Asp		
50 55 60		
Asn Arg Asn Ser Cys Val Ser Cys Val Asn Thr Ser Val Asp Ala Thr		
65 70 75 80		
Ala Cys Ser Trp Ile Glu Cys Lys Glu Lys Ser Tyr Cys Ser His Asn		
85 90 95		
Thr Thr Val Ser Asp Cys Gln Val Val Asn Ser Thr Gln Leu Cys Ser		
100 105 110		
Ala Pro Glu Pro Thr Met Met Pro Thr Asn Ser Thr Ala Lys Thr Thr		
115 120 125		
Thr Gln Pro Ser Ser Ser Thr Ala Thr Thr Thr Ala Thr Thr Ser Gly		
130 135 140		
Thr Thr Asn Ile Thr Leu Ser Pro Thr Ser Gln Pro Gly Arg Lys Ser		
145 150 155 160		
Thr Phe Asp Ala Ala Ser Phe Ile Gly Gly Ile Val Leu Ile Leu Gly		
165 170 175		
Val Gln Ala Val Ile Phe Phe Leu Tyr Lys Phe Cys Lys Ser Lys Glu		
180 185 190		
Arg Asn Tyr His Thr Leu		
195		
<210> 79		
<211> 195		
<212> PRT		
<213> 褐家鼠(Rattus norvegicus)		
<400> 79		

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

His Thr Leu
195

<210> 80

<211> 354

<212> PRT

<213> 智人(Homo sapiens)

<400> 80

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

Thr Thr Thr Gly Thr Thr Ser His Gly Pro Thr Thr Ala Thr His Asn			
65	70	75	80
Pro Thr Thr Thr Ser His Gly Asn Val Thr Val His Pro Thr Ser Asn			
	85	90	95
Ser Thr Ala Thr Ser Gln Gly Pro Ser Thr Ala Thr His Ser Pro Ala			
	100	105	110
Thr Thr Ser His Gly Asn Ala Thr Val His Pro Thr Ser Asn Ser Thr			
	115	120	125
Ala Thr Ser Pro Gly Phe Thr Ser Ser Ala His Pro Glu Pro Pro Pro			
	130	135	140
Pro Ser Pro Ser Pro Ser Pro Thr Ser Lys Glu Thr Ile Gly Asp Tyr			
145	150	155	160
Thr Trp Thr Asn Gly Ser Gln Pro Cys Val His Leu Gln Ala Gln Ile			
	165	170	175
Gln Ile Arg Val Met Tyr Thr Thr Gln Gly Gly Gly Glu Ala Trp Gly			
	180	185	190
Ile Ser Val Leu Asn Pro Asn Lys Thr Lys Val Gln Gly Ser Cys Glu			
	195	200	205
Gly Ala His Pro His Leu Leu Leu Ser Phe Pro Tyr Gly His Leu Ser			
	210	215	220
Phe Gly Phe Met Gln Asp Leu Gln Gln Lys Val Val Tyr Leu Ser Tyr			
225	230	235	240
Met Ala Val Glu Tyr Asn Val Ser Phe Pro His Ala Ala Gln Trp Thr			
	245	250	255
Phe Ser Ala Gln Asn Ala Ser Leu Arg Asp Leu Gln Ala Pro Leu Gly			
	260	265	270
Gln Ser Phe Ser Cys Ser Asn Ser Ser Ile Ile Leu Ser Pro Ala Val			
	275	280	285
His Leu Asp Leu Leu Ser Leu Arg Leu Gln Ala Ala Gln Leu Pro His			
	290	295	300
Thr Gly Val Phe Gly Gln Ser Phe Ser Cys Pro Ser Asp Arg Ser Ile			
305	310	315	320
Leu Leu Pro Leu Ile Ile Gly Leu Ile Leu Leu Gly Leu Leu Ala Leu			
	325	330	335
Val Leu Ile Ala Phe Cys Ile Ile Arg Arg Arg Pro Ser Ala Tyr Gln			
	340	345	350
Ala Leu			
<210> 81			
<211> 354			

<212> PRT

<213> 黑猩猩(Pan troglodytes)

<400> 81

```

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

```

His Leu Asp Leu Leu Ser Leu Arg Leu Gln Ala Ala Gln Leu Pro His
 290 295 300
 Thr Gly Val Phe Gly Gln Ser Phe Ser Cys Pro Ser Asp Arg Ser Ile
 305 310 315 320
 Leu Leu Pro Leu Ile Ile Gly Leu Ile Leu Leu Gly Leu Leu Ala Leu
 325 330 335
 Val Leu Ile Ala Phe Cys Ile Ile Arg Arg Arg Pro Ser Ala Tyr Gln
 340 345 350
 Ala Leu
 <210> 82
 <211> 335
 <212> PRT
 <213> 家牛(Bos taurus)
 <400> 82
 Met Arg Leu Ala Val Phe Phe Ser Gly Ala Leu Leu Gly Leu Leu Ala
 1 5 10 15
 Ala Gln Gly Thr Gly Asn Asp Cys Pro His Lys Lys Ser Ala Thr Leu
 20 25 30
 Leu Pro Ser Phe Thr Val Thr Pro Thr Ala Thr Glu Ser Thr Pro Ser
 35 40 45
 Pro Gly Thr Thr Ser His Arg Thr Thr Lys Ser His Arg Thr Thr Thr
 50 55 60
 Trp Arg Ile Ser Thr Thr Thr His Thr Thr Asn Thr Thr Gly Thr Thr
 65 70 75 80
 Ser Ser Glu Ser Pro Thr Ala Thr His Ser Pro Ala Thr Thr Thr Ser
 85 90 95
 His Gln Asn Thr Thr Val His Pro Thr Ser Asn Ile Thr Ala Thr Ser
 100 105 110
 Pro Gly Pro Ser Thr Arg Ser Pro His Pro Glu Pro Pro Pro Ser Pro
 115 120 125
 Ser Pro Ser Pro Gly Ser Lys Glu Ala Ile Gly Asp Tyr Thr Trp Ser
 130 135 140
 Asn Gly Ser Gln Pro Cys Val Arg Leu Gln Ala Gln Ile Gln Ile Arg
 145 150 155 160
 Val Leu Tyr Pro Thr Gln Gly Gly Gly Glu Ala Trp Gly Ile Ser Val
 165 170 175
 Leu Asn Pro Asn Arg Thr Lys Ala Gln Gly Gly Cys Glu Gly Thr His
 180 185 190
 Ser His Leu Leu Leu Ser Phe Pro Ser Gly Gln Leu Ser Phe Gly Phe

195	200	205
Lys Gln Asp Pro Leu Gln Ser Ala Val Tyr Leu Asn Tyr Met Ala Val		
210	215	220
Glu Tyr Asn Val Ser Phe Pro Gln Ala Val Gln Trp Thr Phe Ser Val		
225	230	235
Gln Asn Ser Ser Leu Arg Asp Leu Gln Thr Pro Leu Gly His Ser Phe		
245	250	255
Ser Cys Arg Asn Ala Ser Ile Ile Val Ser Pro Ala Leu His Leu Asp		
260	265	270
Leu Leu Ser Leu Lys Leu Gln Ala Ala Gln Leu Ser Pro Ser Gly Ala		
275	280	285
Phe Gly Pro Ser Phe Ser Cys Pro Asn Asp Lys Ser Ile Leu Leu Pro		
290	295	300
Leu Ile Ile Gly Leu Ile Leu Leu Gly Leu Leu Thr Leu Val Leu Val		
305	310	315
Thr Phe Cys Ile Ile Arg Arg Arg Pro Pro Thr Tyr Gln Pro Leu		
325	330	335
<210> 83		
<211> 335		
<212> PRT		
<213> 小鼠 (Mus musculus)		
<400> 83		
Met Arg Leu Pro Val Cys Leu Ile Leu Leu Gly Pro Leu Ile Ala Gln		
1	5	10
Gly Thr Glu Glu Asp Cys Pro His Lys Lys Ala Val Thr Leu Leu Pro		
20	25	30
Ser Phe Thr Met Thr Pro Thr Ala Thr Glu Ser Thr Ala Ser Pro Thr		
35	40	45
Thr Ser His Arg Pro Thr Thr Thr Ser His Gly Asn Val Thr Val His		
50	55	60
Thr Ser Ser Gly Pro Thr Thr Val Thr His Asn Pro Ala Thr Thr Thr		
65	70	75
Ser His Gly Asn Ala Thr Ile Ser His Ala Thr Val Ser Pro Thr Thr		
85	90	95
Asn Gly Thr Ala Thr Ser Pro Arg Ser Ser Thr Val Gly Pro His Pro		
100	105	110
Gly Pro Pro Pro Pro Ser Pro Ser Pro Arg Ser Lys Gly Ala Leu Gly		
115	120	125
Asn Tyr Thr Trp Ala Asn Gly Ser Gln Pro Cys Val Gln Leu Gln Ala		

130	135	140
Gln Ile Gln Ile Arg Ile Leu Tyr Pro Ile Gln Gly Gly Arg Lys Val		
145	150	155
Lys Leu Lys Trp Gly Leu Lys Arg Ala Trp Gly Ile Ser Val Leu Asn		
165	170	175
Pro Asn Lys Thr Lys Val Gln Gly Gly Cys Asp Gly Thr His Pro His		
180	185	190
Leu Ser Leu Ser Phe Pro Tyr Gly Gln Leu Thr Phe Gly Phe Lys Gln		
195	200	205
Asp Leu His Gln Ser Pro Ser Thr Val Tyr Leu Asp Tyr Met Ala Val		
210	215	220
Glu Tyr Asn Val Ser Phe Pro Gln Ala Ala Gln Trp Thr Phe Met Ala		
225	230	235
Gln Asn Ser Ser Leu Arg Glu Leu Gln Ala Pro Leu Gly Gln Ser Phe		
245	250	255
Cys Cys Gly Asn Ala Ser Ile Val Leu Ser Pro Ala Val His Leu Asp		
260	265	270
Leu Leu Ser Leu Arg Leu Gln Ala Ala Gln Leu Pro Asp Lys Gly His		
275	280	285
Phe Gly Pro Cys Phe Ser Cys Asn Arg Asp Gln Ser Leu Leu Leu Pro		
290	295	300
Leu Ile Ile Gly Leu Val Leu Leu Gly Leu Leu Thr Leu Val Leu Ile		
305	310	315
Ala Phe Cys Ile Thr Arg Arg Arg Gln Ser Thr Tyr Gln Pro Leu		
325	330	335
<210> 84		
<211> 354		
<212> PRT		
<213> 猕猴 (Macaca mulatta)		
<400> 84		
Met Arg Leu Ala Val Leu Phe Leu Gly Ala Leu Leu Gly Leu Leu Ala		
1	5	10
Ala Gln Gly Thr Gly Asn Asp Cys Pro His Lys Lys Ser Ala Thr Leu		
20	25	30
Leu Pro Ser Phe Thr Val Thr Pro Thr Ala Thr Glu Ser Thr Gly Thr		
35	40	45
Thr Ser His Arg Thr Thr Lys Ser His Lys Thr Thr Thr His Arg Thr		
50	55	60
Thr Thr Thr Gly Thr Thr Ser His Arg Pro Thr Thr Ala Thr His Asn		

65	70	75	80
Pro Thr Thr Thr Ser His Arg Asn Ala Thr Val His Pro Thr Ser Asn			
	85	90	95
Ser Thr Ala Thr Ser Gln Gly Pro Ser Thr Ala Thr His Arg Pro Ala			
	100	105	110
Thr Thr Ser His Gly Asn Ala Thr Val His Pro Thr Ser Asn Ser Thr			
	115	120	125
Ala Thr Ser Pro Gly Leu Thr Ser Ser Ala His Pro Gly Pro Pro Pro			
	130	135	140
Pro Ser Pro Ser Pro Ser Pro Ala Ser Lys Glu Thr Ile Gly Asp Tyr			
145	150	155	160
Met Trp Thr Asn Gly Ser Gln Pro Cys Val His Leu Gln Ala Gln Ile			
	165	170	175
Gln Ile Arg Val Met Tyr Thr Thr Gln Gly Gly Gly Glu Ala Trp Gly			
	180	185	190
Ile Ser Val Leu Asn Pro Asn Lys Thr Lys Val Gln Gly Ser Cys Glu			
	195	200	205
Gly Ala His Pro His Leu Leu Leu Ser Phe Pro Tyr Gly His Leu Ser			
	210	215	220
Phe Gly Phe Met Gln Asp Leu Gln Gln Arg Val Val Tyr Leu Ser Tyr			
225	230	235	240
Met Ala Val Glu Tyr Asn Val Ser Phe Pro His Ala Ala Gln Trp Thr			
	245	250	255
Phe Ser Ala Gln Asn Ala Ser Leu Arg Asp Leu Gln Ala Pro Leu Gly			
	260	265	270
Gln Ser Phe Ser Cys Ser Asn Ser Ser Ile Ile Leu Ser Pro Ala Val			
	275	280	285
His Leu Asp Leu Leu Ser Leu Arg Leu Gln Ala Ala Gln Leu Pro His			
	290	295	300
Thr Gly Val Phe Gly Gln Ser Phe Ser Cys Pro Ser Asp Arg Ser Ile			
305	310	315	320
Leu Leu Pro Leu Ile Ile Gly Leu Val Leu Leu Gly Leu Leu Ala Leu			
	325	330	335
Val Leu Ile Ala Phe Cys Ile Val Arg Arg Arg Pro Ser Ala Tyr Gln			
	340	345	350
Ala Leu			
<210> 85			
<211> 330			
<212> PRT			

<213> 褐家鼠 (*Rattus norvegicus*)

<400> 85

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

290	295	300
Val Leu Leu Gly Leu Leu Thr Leu Val Leu Ile Ala Phe Cys Val Thr		
305	310	315
Arg Arg Arg Gln Ser Thr Tyr Gln Pro Leu		320
	325	330
<210> 86		
<211> 329		
<212> PRT		
<213> 家犬(Canis lupus familiaris)		
<400> 86		
Met Arg Pro Ala Val Phe Phe Leu Gly Ala Leu Val Gly Leu Leu Ala		
1	5	10
Ala Gln Gly Thr Arg Ser Asp Cys Pro His Lys Lys Ser Ala Thr Leu		15
	20	25
Leu Pro Ser Phe Thr Val Thr Pro Thr Ala Thr Glu Ser Thr Gly Ser		30
	35	40
Pro Gly Thr Thr Ser His Ser Thr Thr Thr Ala Glu Thr Thr Ser His		45
	50	55
Ala Pro Asn Thr Thr Thr His Gln Ala Pro Thr Thr Pro Gly His Arg		60
65	70	75
Asn Thr Thr Ile His Pro Thr Thr Ser Asn Ser Thr Ser Asn Thr Thr		80
	85	90
Gly Thr Thr Gly Thr Gly Lys Pro His Thr Ser Thr Ser Tyr Thr Gln		95
	100	105
Pro Gly Pro Gly Pro Arg Pro Pro Pro Pro Ser Pro Gly Pro Gly Pro		110
	115	120
Gln Asp Ala Ile Gly Asp Tyr Thr Trp Thr Thr Gly Ser Gln Pro Cys		125
	130	135
Ala Arg Leu Gln Ala Arg Ile Gln Ile Gly Val Val Tyr Pro Thr Gln		140
145	150	155
Ala Gly Gly Gln Ala Trp Gly Ile Ser Val Leu Asn Pro Asn Ser Thr		160
	165	170
Lys Pro Trp Gly Asp Cys Asp Gly Ala Arg Pro His Leu Leu Leu Ser		175
	180	185
Phe Pro Phe Gly Gln Leu Ser Phe Gly Phe Thr Gln Glu Pro Gln Gln		190
	195	200
Gly Ser Val Tyr Leu Asp Tyr Leu Ala Leu Gln Tyr Asn Val Ser Phe		205
	210	215
Pro Gln Ala Ala Gln Trp Thr Phe Ser Gly Gln Asn Ala Ser Leu Arg		220

225	230	235	240
Ala Leu Gln Ala Pro	Leu Gly Gln Ser Phe	Ser Cys Arg Asn Ala Ser	
	245	250	255
Ile Leu Leu Thr Pro	Ala Leu Arg Leu Asp	Leu Leu His Leu Lys Leu	
	260	265	270
Gln Ala Ala Gln Leu	Pro Pro Ser Gly Ala	Phe Gly Pro Ser Phe Ser	
	275	280	285
Cys Pro Ser Glu His	Phe Asn Leu Leu Pro	Leu Ile Val Gly Val Ile	
	290	295	300
Ser Leu Gly Leu Leu	Ala Leu Ala Leu Val	Thr Phe Cys Ile Ile Arg	
305	310	315	320
Arg Arg Pro Pro Thr	Tyr Gln Pro Leu		
	325		

<210> 87

<211> 322

<212> PRT

<213> 家马 (Equus caballus)

<400> 87

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

				165				170				175				
Cys	Ala	His	Pro	His	Leu	Leu	Leu	Ser	Phe	Pro	Tyr	Gly	Gln	Leu	Ser	
				180				185				190				
Phe	Gly	Phe	Lys	Gln	Glu	Pro	Leu	Gln	Ser	Thr	Val	Tyr	Leu	Asn	Tyr	
				195				200				205				
Ile	Ala	Val	Glu	Tyr	Asn	Val	Ser	Phe	Pro	Gln	Ala	Ala	Gln	Trp	Thr	
				210				215				220				
Phe	Leu	Val	Gln	Asn	Ser	Ser	Leu	Arg	Asp	Leu	Gln	Ala	Pro	Leu	Gly	
225					230				235				240			
Gln	Arg	Phe	Ser	Cys	Arg	Asn	Ala	Ser	Ile	Ala	Leu	Ser	Pro	Ala	Phe	
				245				250				255				
His	Leu	Asp	Leu	Leu	Ser	Leu	Lys	Leu	Gln	Ala	Ala	Gln	Leu	Thr	Pro	
				260				265				270				
Thr	Gly	Ala	Phe	Gly	Pro	Ser	Phe	Ser	Cys	Pro	Ser	Asp	Gln	Ser	Ile	
				275				280				285				
Leu	Leu	Pro	Leu	Ile	Ile	Gly	Leu	Ile	Leu	Leu	Gly	Leu	Phe	Ala	Leu	
				290				295				300				
Val	Leu	Ile	Thr	Phe	Cys	Val	Ile	Arg	Arg	Arg	Pro	Pro	Thr	Tyr	Gln	
305					310				315				320			
Ala Leu																
<210> 88																
<211> 305																
<212> PRT																
<213> 家兔(Oryctolagus cuniculus)																
<400> 88																
Met	Arg	Leu	Pro	Val	Leu	Phe	Leu	Ala	Leu	Leu	Gly	Leu	His	Ala	Ala	
1					5				10				15			
Ser	Ser	Gly	Thr	Thr	Ser	His	Arg	Thr	Thr	Lys	Asn	Pro	His	Thr	Thr	
				20				25				30				
Ser	His	Ser	Thr	Ala	Thr	Pro	Gly	Thr	Thr	Ser	His	Arg	Pro	Thr	Thr	
				35				40				45				
Ala	Thr	Pro	Thr	Thr	Gly	His	Gly	Asn	Val	Thr	Val	His	Pro	Thr	Thr	
				50				55				60				
Ser	Asn	Thr	Thr	Ser	Asn	Thr	Thr	Thr	Thr	Thr	Gly	Thr	Ser	Pro	Gly	
65					70				75				80			
Phe	Ser	Thr	Ser	Thr	Pro	His	Pro	Gly	Pro	Pro	Pro	Pro	Pro	Pro	Ser	
				85				90				95				
Pro	Ser	Pro	Gly	Ser	Arg	Glu	Ala	Val	Gly	Asn	Tyr	Thr	Trp	Thr	Asn	
				100				105				110				

Gly Ser Gln Pro Cys Val Gln Leu Gln Ala Gln Ile Gln Ile Arg Val															
115								120						125	
Leu Tyr Pro Thr Gln Gly Gly Gly Gln Ala Trp Gly Met Ser Val Leu															
130								135						140	
Asn Pro Asn Arg Thr Lys Ala Gln Gly Gly Cys Glu Gly Pro Arg Pro															
145								150						155	160
His Leu Leu Leu Ser Phe Pro Tyr Gly Gln Leu Ser Phe Gly Phe Lys															
														165	170
															175
Gln Asp Pro Gly Gln Gly Gln Ser Ala Val Tyr Leu Ser Tyr Leu Ala															
														180	185
															190
Val Glu Tyr Asn Val Ser Phe Pro Gln Ala Ala Arg Trp Thr Phe Ser															
														195	200
															205
Ala Gln Asn Ala Ser Leu Arg Asp Leu Gln Ala Pro Leu Gly Gln Ser															
														210	215
															220
Phe Ser Cys Arg Asn Ala Ser Ile Ala Val Ser Pro Ala Leu His Leu															
225														230	235
															240
Asp Leu Leu Ser Leu Arg Val Gln Ala Ala Gln Leu Pro Arg Thr Gly															
														245	250
															255
Ile Phe Gly Pro Ser Phe Ser Cys Pro Ala Asp His Pro Ser Ile Leu															
														260	265
															270
Val Pro Leu Ile Ile Gly Leu Ile Leu Val Gly Leu Leu Ala Leu Val															
														275	280
															285
Leu Val Ala Phe Cys Ile Ala Arg Arg Arg Pro Ser Ala Tyr Gln Ala															
														290	295
															300
Leu															
305															
<210> 89															
<211> 291															
<212> PRT															
<213> 野猪(Sus scrofa)															
<400> 89															
Met Thr Leu Ala Val Leu Phe Leu Gly Ala Leu Leu Gly Leu Leu Ala															
1														5	10
															15
Glu Ser Thr Thr Ser His Arg Thr Thr Thr Pro Arg Thr Thr Thr Thr															
														20	25
															30
Gly Thr Thr Ser His Gly Pro Thr Thr Val Thr His Asn Pro Ala Thr															
														35	40
															45
Thr Thr Ser His Gly Asn Ala Thr Val His Pro Thr Ser Ser Ser Thr															
														50	55
															60

Ala Thr Ser Pro Gly Ser Ser Thr Arg Pro Pro His Pro Gly Pro Pro			
65	70	75	80
Pro Pro Ser Pro Ser Pro Ser Pro Gly Ser Gln Glu Ala Ile Gly Asp			
	85	90	95
Tyr Thr Trp Thr Asn Gly Ser Gln Pro Cys Val Gln Leu Gln Ala Gln			
	100	105	110
Ile Gln Ile Arg Val Leu Tyr Pro Thr Gln Gly Gly Gly Glu Ala Trp			
	115	120	125
Gly Ile Ser Val Leu Asn Pro Asn Lys Thr Lys Ala Leu Gly Gly Cys			
	130	135	140
Glu Gly Ala His Pro His Val Arg Leu Ser Phe Pro Tyr Gly Gln Leu			
145	150	155	160
Thr Phe Gly Phe Lys Gln Gln Pro Gln Glu Ser Thr Val Tyr Leu Asn			
	165	170	175
Tyr Met Ala Val Glu Tyr Asn Val Ser Phe Pro Arg Ala Ala Gln Trp			
	180	185	190
Thr Phe Ser Val Gln Asn Ser Ser Leu Arg Asp Leu Gln Thr Pro Val			
	195	200	205
Gly Arg Ser Tyr Ser Cys Arg Asn Ala Ser Ile Ile Leu Ser Thr Ala			
	210	215	220
Phe His Leu Asp Leu Leu Ser Leu Lys Leu Gln Ala Ala Gln Leu Pro			
225	230	235	240
Pro Thr Gly Asn Phe Gly Pro Ser Phe Ser Cys Pro Ser Asp Gln Thr			
	245	250	255
Ile Leu Leu Pro Leu Ile Ile Gly Leu Ile Phe Leu Gly Leu Leu Ile			
	260	265	270
Leu Val Leu Val Thr Phe Cys Ile Ile Arg Arg Arg Pro Pro Ala Tyr			
	275	280	285
Gln Pro Leu			
290			
<210> 90			
<211> 354			
<212> PRT			
<213> 东非狒狒(Papio anubis)			
<400> 90			
Met Arg Leu Ala Val Leu Phe Ser Gly Ala Leu Leu Gly Leu Leu Ala			
1	5	10	15
Ala Gln Gly Thr Gly Asn Asp Cys Pro His Lys Lys Ser Ala Thr Leu			
	20	25	30

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

340	345	350
Ala Leu		
<210> 91		
<211> 323		
<212> PRT		
<213> 短尾负鼠 (Monodelphis domestica)		
<400> 91		
Met Arg Leu Ser Leu Leu Leu Ser Gly Ile Leu Leu Gly Leu Leu Ala		
1 5 10 15		
Glu Gln Gly Ala Gly Asp Lys Cys Pro Gln Glu Lys Ser Val Thr Leu		
20 25 30		
Val Pro Ser Phe Thr Val Thr Thr Ile Ala Thr Glu Arg Ser Thr Thr		
35 40 45		
Ser Pro Glu Thr Thr Thr Ser Ser Gly Ser Thr Ala Thr Thr Tyr Arg		
50 55 60		
Thr Ser Thr Ala Ala Thr Thr Pro His Ser Asn Ser Thr Ala Thr Ser		
65 70 75 80		
Tyr Ser Thr Thr Ser Glu Gly Thr Ala Val Thr His Gly Thr Thr Thr		
85 90 95		
Ser Pro Arg Asn Thr Ser Thr Thr Ser Thr Ser Gln Ser Val Pro Val		
100 105 110		
Pro Pro Ser Pro Gln Pro Thr Ser Ser Pro Ser Gly Ala Val Gly Asp		
115 120 125		
Tyr Ile Gly Ala Asn Gly Ser Gln Leu Cys Val His Leu Arg Ala Gln		
130 135 140		
Ile Gln Met Arg Val Leu Tyr Gln Ala Ser Gly Gly Gly Lys Leu Trp		
145 150 155 160		
Gly Ile Phe Val Leu Asn Pro Asn Arg Thr Met Ala Gln Gly Asn Cys		
165 170 175		
Glu Ala Asn His Ser Ser Leu Ile Leu Ser Phe Pro Asn Gly Lys Leu		
180 185 190		
Ile Phe Gly Phe Lys Gln Asp Ser Ile Lys Lys Ile Val Tyr Leu Ser		
195 200 205		
His Leu Ala Thr Glu Phe Asn Val Ser Phe Pro Ser Ala Thr Arg Trp		
210 215 220		
Ile Phe Ser Val Glu Asn Ser Ser Leu Gln Asp Leu Gln Thr Pro Leu		
225 230 235 240		
Gly His Ser Phe Ser Cys Arg Asn Arg Ser Ile Ala Leu Ser Pro Asp		
245 250 255		

Ile His Leu Asp Leu Leu Ser Leu Gln Leu Gln Ala Ala Gln Leu Ser
 260 265 270
 Ser Ser Gly Ala Phe Gly Ala Ala Phe Ser Cys Ser Ala Asp Leu Asn
 275 280 285
 Ile Leu Val Pro Leu Val Val Gly Leu Val Leu Leu Thr Leu Leu Ile
 290 295 300
 Leu Val Leu Ser Ala Phe Cys Ile Ser Arg Arg Arg Pro Pro Ala Tyr
 305 310 315 320
 Gln Pro Leu
 <210> 92
 <211> 263
 <212> PRT
 <213> 鸭嘴兽 (Ornithorhynchus anatinus)
 <400> 92
 Met Gly Leu Thr Leu Pro Leu Pro Ala Gln Gly Ser Gln Cys Arg Ala
 1 5 10 15
 Asn Cys Pro His Lys Lys Ser Ala Thr Leu Val Pro Ser Phe Thr Val
 20 25 30
 Thr Pro Thr Ala Thr Ser Gly Pro Thr Thr Thr Ala His Gln Thr Thr
 35 40 45
 Thr Asp His Gly Thr Thr Thr Ser His Glu Thr Thr Thr Ser Gln Gly
 50 55 60
 Thr Ser Thr His Gly Thr Ser Thr Pro His Thr Thr Thr Thr Gly His
 65 70 75 80
 Gly Thr Thr Thr Gly His Gln Asn Thr Ser His Ser Thr Thr Thr Ser
 85 90 95
 His Gly Thr Ser Thr Pro His Lys Thr Thr Thr Arg His Pro Thr Thr
 100 105 110
 Ser His Gly Thr Thr Thr Ser His Gly Thr Ser Thr Gly His Trp Thr
 115 120 125
 Ala Arg Pro Thr Ile Arg Pro Gly Pro Pro Pro Pro Pro Pro Ser Pro
 130 135 140
 Gly Lys Ala Val Gly Asn Tyr Thr Val Phe Asn Gly Ser Gln Pro Cys
 145 150 155 160
 Leu Arg Leu Arg Ala Glu Ile Arg Leu Trp Val Leu Tyr Gln Ala Gln
 165 170 175
 Glu Glu Gly Glu Ala Pro Pro Val Ser Gly Ala Ala Ser Phe Pro Pro
 180 185 190
 Pro Arg Pro Arg Pro Val Ala Gly Glu Gly Asp Gly Glu Arg Ser Arg

195	200	205
Val Thr Pro Val Ala Ser Ala Met Thr Val Glu Gly Gly Ser Arg Ala		
210	215	220
Gly Phe Ala Met Leu Gly Ala Glu Val Arg Ser Arg Ala Pro Ser Leu		
225	230	235
Gly Arg Ala Gly Lys Thr Arg Leu Arg Ile His Gln Pro Val Val Val		
245	250	255
Leu Gln His Thr Tyr Tyr Val		
260		
<210> 93		
<211> 280		
<212> PRT		
<213> 智人(Homo sapiens)		
<400> 93		
Met Asp Leu Gln Gly Arg Gly Val Pro Ser Ile Asp Arg Leu Arg Val		
1	5	10
Leu Leu Met Leu Phe His Thr Met Ala Gln Ile Met Ala Glu Gln Glu		
20	25	30
Val Glu Asn Leu Ser Gly Leu Ser Thr Asn Pro Glu Lys Asp Ile Phe		
35	40	45
Val Val Arg Glu Asn Gly Thr Thr Cys Leu Met Ala Glu Phe Ala Ala		
50	55	60
Lys Phe Ile Val Pro Tyr Asp Val Trp Ala Ser Asn Tyr Val Asp Leu		
65	70	75
Ile Thr Glu Gln Ala Asp Ile Ala Leu Thr Arg Gly Ala Glu Val Lys		
85	90	95
Gly Arg Cys Gly His Ser Gln Ser Glu Leu Gln Val Phe Trp Val Asp		
100	105	110
Arg Ala Tyr Ala Leu Lys Met Leu Phe Val Lys Glu Ser His Asn Met		
115	120	125
Ser Lys Gly Pro Glu Ala Thr Trp Arg Leu Ser Lys Val Gln Phe Val		
130	135	140
Tyr Asp Ser Ser Glu Lys Thr His Phe Lys Asp Ala Val Ser Ala Gly		
145	150	155
Lys His Thr Ala Asn Ser His His Leu Ser Ala Leu Val Thr Pro Ala		
165	170	175
Gly Lys Ser Tyr Glu Cys Gln Ala Gln Gln Thr Ile Ser Leu Ala Ser		
180	185	190
Ser Asp Pro Gln Lys Thr Val Thr Met Ile Leu Ser Ala Val His Ile		

195	200	205
Gln Pro Phe Asp Ile Ile Ser Asp Phe Val Phe Ser Glu Glu His Lys		
210	215	220
Cys Pro Val Asp Glu Arg Glu Gln Leu Glu Glu Thr Leu Pro Leu Ile		
225	230	235
Leu Gly Leu Ile Leu Gly Leu Val Ile Met Val Thr Leu Ala Ile Tyr		
245	250	255
His Val His His Lys Met Thr Ala Asn Gln Val Gln Ile Pro Arg Asp		
260	265	270
Arg Ser Gln Tyr Lys His Met Gly		
275	280	
<210> 94		
<211> 280		
<212> PRT		
<213> 黑猩猩 (Pan troglodytes)		
<400> 94		
Met Asp Leu Arg Gly Arg Ala Val Pro Ser Ile Asp Arg Leu Arg Val		
1	5	10
Leu Leu Met Leu Phe His Thr Met Ala Gln Ile Met Ala Glu Gln Glu		
20	25	30
Val Glu Asn Leu Ser Gly Leu Ser Thr Asn Pro Glu Lys Asp Ile Phe		
35	40	45
Val Val Arg Glu Asn Gly Thr Thr Cys Leu Met Ala Glu Phe Ala Ala		
50	55	60
Lys Phe Ile Val Pro Tyr Asp Val Trp Ala Ser Asn Tyr Val Asp Leu		
65	70	75
Ile Thr Glu Gln Ala Asp Ile Ala Leu Thr Arg Gly Ala Glu Val Lys		
85	90	95
Gly Arg Cys Gly His Ser Glu Ser Glu Leu Gln Val Phe Trp Val Asp		
100	105	110
Arg Ala Tyr Ala Leu Lys Met Leu Phe Val Lys Glu Ser His Asn Met		
115	120	125
Ser Lys Gly Pro Glu Ala Thr Trp Arg Leu Ser Lys Val Gln Phe Val		
130	135	140
Tyr Asp Ser Ser Glu Lys Thr His Phe Lys Asp Ala Val Ser Ala Gly		
145	150	155
Lys His Thr Ala Asn Ser His His Leu Ser Ala Leu Val Thr Pro Ala		
165	170	175
Gly Lys Ser Tyr Glu Cys Gln Ala Gln Gln Thr Ile Ser Leu Ala Ser		

180	185	190
Ser Asp Leu Gln Lys Thr Val Thr Met Ile Leu Ser Ala Val His Ile		
195	200	205
Gln Pro Phe Asp Ile Ile Ser Asp Phe Val Phe Ser Glu Glu His Lys		
210	215	220
Cys Pro Val Asp Glu Arg Glu Gln Leu Glu Glu Thr Leu Pro Leu Ile		
225	230	235
240		
Leu Gly Leu Ile Leu Gly Leu Val Ile Met Val Thr Leu Ala Ile Tyr		
245	250	255
His Val His His Lys Met Thr Ala Asn Gln Val Gln Ile Pro Arg Asp		
260	265	270
Arg Ser Gln Tyr Lys His Met Gly		
275	280	
<210> 95		
<211> 280		
<212> PRT		
<213> 猕猴 (Macaca mulatta)		
<400> 95		
Met Asp Leu Gln Gly Arg Ala Val Pro Ser Val Asp Arg Leu Arg Val		
1	5	10
15		
Leu Leu Met Leu Phe His Thr Met Ala Gln Ile Met Ala Glu Gln Glu		
20	25	30
35		
Val Glu Asn Leu Ser Gly Leu Ser Thr Asn Pro Glu Lys Asp Ile Phe		
40	45	
50		
Val Val Arg Glu Asn Gly Thr Thr Cys Leu Met Ala Glu Phe Ala Ala		
55	60	
65		
Lys Phe Ile Val Pro Tyr Asp Val Trp Ala Ser Asn Tyr Val Asp Leu		
70	75	80
85		
Ile Thr Glu Gln Ala Asp Ile Ala Leu Thr Arg Gly Ala Glu Val Lys		
90	95	
100		
Gly Arg Cys Gly His Ser Glu Ser Glu Leu Gln Val Phe Trp Val Asp		
105	110	
115		
Arg Ala Tyr Ala Leu Lys Met Leu Phe Val Lys Glu Ser His Asn Thr		
120	125	
130		
Ser Lys Gly Pro Glu Ala Thr Trp Arg Leu Ser Lys Val Gln Phe Val		
135	140	
145		
Tyr Asp Ser Ser Glu Lys Thr His Phe Lys Asp Ala Val Ser Ala Gly		
150	155	160
165		
Lys His Thr Ala Asn Ser His His Leu Ser Ala Leu Val Thr Pro Ala		

				165					170					175			
Gly	Lys	Ser	Tyr	Glu	Cys	Gln	Ala	Gln	Gln	Thr	Ile	Ser	Leu	Ala	Ser		
				180					185					190			
Ser	Asp	Pro	Gln	Lys	Met	Val	Thr	Met	Ile	Leu	Ser	Ala	Val	His	Ile		
				195					200					205			
Gln	Pro	Phe	Asp	Ile	Ile	Ser	Asp	Phe	Val	Phe	Ser	Glu	Glu	His	Lys		
				210					215					220			
Cys	Pro	Val	Asp	Glu	Arg	Glu	Gln	Leu	Glu	Glu	Thr	Leu	Pro	Leu	Ile		
225																	
Leu	Gly	Leu	Ile	Leu	Gly	Leu	Val	Ile	Val	Val	Thr	Leu	Thr	Ile	Tyr		
				245													
His	Val	His	His	Lys	Met	Thr	Ala	Asn	Gln	Val	Gln	Ile	Pro	Arg	Asp		
				260													
Arg	Ser	Gln	Tyr	Lys	His	Met	Gly										
				275													
<210>	96																
<211>	280																
<212>	PRT																
<213>	家犬 (Canis lupus familiaris)																
<400>	96																
Met	Asp	Leu	Arg	Gly	Arg	Ala	Phe	Pro	Ser	Val	Tyr	Arg	Leu	Arg	Val		
1				5					10					15			
Leu	Leu	Met	Leu	Phe	Tyr	Thr	Met	Ala	Arg	Ile	Thr	Ala	Glu	Gln	Glu		
				20					25					30			
Val	Glu	Asn	Leu	Ser	Gly	Leu	Ser	Thr	Asn	Pro	Glu	Lys	Asp	Ile	Phe		
				35					40					45			
Val	Val	Arg	Glu	Asn	Gly	Thr	Thr	Cys	Leu	Met	Ala	Glu	Phe	Ala	Ala		
				50					55					60			
Lys	Phe	Ile	Val	Pro	Tyr	Asp	Val	Trp	Ala	Ser	Asn	Tyr	Val	Asp	Leu		
65									70					75			
Ile	Thr	Glu	Gln	Ala	Asp	Ile	Ser	Leu	Thr	Arg	Gly	Ala	Glu	Val	Lys		
				85										90			
Gly	His	Cys	Gly	His	Asn	Glu	Ser	Glu	Leu	Gln	Val	Phe	Trp	Val	Asp		
				100													
Arg	Ala	Tyr	Ala	Leu	Lys	Met	Leu	Phe	Val	Lys	Glu	Ser	Arg	Asn	Ala		
				115													
Ser	Lys	Gly	Pro	Glu	Ala	Thr	Trp	Arg	Leu	Ser	Lys	Val	Gln	Phe	Val		
				130													
Tyr	Asp	Ser	Ser	Glu	Lys	Thr	His	Phe	Lys	Asp	Ala	Val	Ser	Ala	Gly		

145	150	155	160
Lys His Thr Ala Asn Ser His Arg Leu Ser Ala Leu Val Thr Pro Ala			
	165	170	175
Gly Lys Ser Tyr Glu Cys Gln Ala Gln Gln Ser Ile Ser Leu Ala Ser			
	180	185	190
Ser Asp Pro Gln Lys Thr Val Thr Met Ile Leu Ser Ala Val His Ile			
	195	200	205
Gln Pro Phe Asp Ile Ile Ser Asp Phe Val Phe Ser Glu Glu His Lys			
	210	215	220
Cys Pro Val Asp Glu Arg Glu Gln Leu Glu Glu Thr Leu Pro Leu Ile			
225	230	235	240
Leu Gly Leu Ile Leu Gly Leu Val Ile Val Val Thr Leu Ala Ile Tyr			
	245	250	255
His Ile His His Lys Met Thr Ala Asn Gln Val Gln Ile Pro Arg Asp			
	260	265	270
Arg Ser Gln Tyr Lys His Met Gly			
	275	280	
<210> 97			
<211> 280			
<212> PRT			
<213> 家牛(Bos taurus)			
<400> 97			
Met Asp Leu Arg Arg Arg Ala Leu Leu Gly Val Asp Gly Leu Arg Val			
1	5	10	15
Leu Leu Met Leu Phe His Thr Val Thr Arg Ile Met Ala Glu Gln Glu			
	20	25	30
Val Glu Asn Leu Ser Gly Leu Ser Thr Asn Pro Glu Lys Asp Ile Phe			
	35	40	45
Val Val Arg Glu Asn Gly Thr Thr Cys Leu Met Ala Glu Phe Ala Ala			
	50	55	60
Lys Phe Ile Val Pro Tyr Asp Val Trp Ala Ser Asn Tyr Val Asp Leu			
65	70	75	80
Ile Thr Glu Gln Ala Asp Ile Ser Leu Thr Arg Gly Ala Glu Val Lys			
	85	90	95
Gly His Cys Gly His Asp Glu Ser Glu Leu Gln Val Phe Trp Val Asp			
	100	105	110
Arg Ala Tyr Ala Leu Lys Met Leu Phe Leu Lys Glu Ser His Asn Thr			
	115	120	125
Pro Lys Gly Pro Glu Ala Thr Trp Lys Leu Ser Lys Val Gln Phe Val			

130	135	140
Tyr Asp Ser Ser Glu Lys Thr His Phe Lys Asp Ala Val Ser Ala Gly		
145	150	155
Lys His Thr Ala Asn Ser His His Leu Ser Ala Leu Val Thr Pro Ala		
165	170	175
Gly Lys Ser Tyr Glu Cys Gln Ala Gln Gln Thr Ile Ser Leu Ala Ser		
180	185	190
Ser Asp Pro Gln Lys Thr Val Thr Met Ile Leu Ser Ala Val His Ile		
195	200	205
Gln Pro Phe Asp Ile Ile Ser Asp Phe Val Phe Ser Glu Glu His Lys		
210	215	220
Cys Pro Val Asp Glu Arg Glu Gln Leu Glu Glu Thr Leu Pro Leu Ile		
225	230	235
Leu Gly Leu Ile Leu Gly Leu Val Ile Val Val Thr Leu Val Ile Tyr		
245	250	255
His Ile His His Lys Met Thr Ala Asn Gln Val Gln Ile Pro Arg Asp		
260	265	270
Arg Ser Gln Tyr Lys His Met Gly		
275	280	
<210> 98		
<211> 280		
<212> PRT		
<213> 小鼠 (Mus musculus)		
<400> 98		
Met Asp Leu Arg Val Arg Thr Leu Leu Gly Gly Asp Arg Leu Arg Ile		
1	5	10
Leu Leu Met Phe Phe His Val Met Val Gln Thr Val Ala Glu Gln Glu		
20	25	30
Val Glu Asn Leu Ser Gly Leu Ser Thr Asn Pro Glu Lys Asp Ile Phe		
35	40	45
Val Val Arg Glu Asn Gly Thr Thr Cys Leu Met Ala Glu Phe Ala Ala		
50	55	60
Lys Phe Ile Val Pro Tyr Asp Val Trp Ala Ser Asn Tyr Val Asp Leu		
65	70	75
Ile Thr Glu Gln Ala Glu Ile Ser Leu Thr Arg Gly Ala Glu Val Lys		
85	90	95
Gly His Cys Gly His Asn Glu Ser Glu Leu Glu Val Phe Trp Val Asp		
100	105	110
His Ala Tyr Thr Leu Arg Met Leu Phe Val Lys Glu Ser His Asn Thr		

115	120	125
Ser Lys Gly Pro Glu Ala Thr Trp Asn Leu Asn Lys Val His Phe Val		
130	135	140
Tyr Asp Ser Ser Glu Lys Thr His Phe Lys Ala Pro Val Lys Val Asn		
145	150	155
Lys Tyr Ile Ala Ser Ser His His Leu Ser Ala Leu Val Thr Pro Ala		
165	170	175
Gly Met Ser Tyr Glu Cys Gln Ala Gln Gln Thr Ile Ser Leu Ala Ser		
180	185	190
Ser Asp Pro Gln Lys Thr Val Thr Met Ile Leu Ser Ala Val His Ile		
195	200	205
Gln Pro Phe Asp Ile Ile Ser Asp Phe Val Phe Ser Glu Glu His Lys		
210	215	220
Cys Pro Val Asp Glu Gln Glu Gln Leu Glu Glu Thr Leu Pro Leu Ile		
225	230	235
Leu Gly Leu Ile Leu Gly Leu Val Ile Val Ile Thr Leu Val Ile Tyr		
245	250	255
His Ile His His Lys Met Thr Ala Asn Gln Val Gln Ile Pro Arg Asp		
260	265	270
Arg Ser Gln Tyr Lys His Met Gly		
275	280	
<210> 99		
<211> 280		
<212> PRT		
<213> 褐家鼠 (Rattus norvegicus)		
<400> 99		
Met Asp Leu Arg Gly Arg Ala Leu Leu Gly Gly Asp Arg Leu Arg Ile		
1	5	10
Leu Leu Met Phe Phe His Ala Met Ala Gln Thr Val Ala Glu Gln Glu		
20	25	30
Val Glu Asn Leu Ser Gly Leu Ser Thr Asn Pro Glu Lys Asp Ile Phe		
35	40	45
Val Val Arg Glu Asn Gly Thr Thr Cys Leu Met Ala Glu Phe Ala Ala		
50	55	60
Lys Phe Ile Val Pro Tyr Asp Val Trp Ala Ser Asn Tyr Val Asp Leu		
65	70	75
Ile Thr Glu Gln Ala Glu Ile Ser Leu Thr Arg Gly Ala Glu Val Lys		
85	90	95
Gly Arg Cys Gly His Asn Glu Ser Glu Leu Gln Val Phe Trp Val Asp		

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

<210> 100

<211> 299

<212> PRT

<213> 原鸡(Gallus gallus)

<400> 100

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

	85		90		95
Glu Leu Glu Ile Ser Trp Leu Glu Arg Ala Tyr Thr Leu Lys Leu Phe					
	100		105		110
Phe Leu Lys Val Arg Gly Cys Pro Arg Arg Leu Gly Arg Gly Arg Cys					
	115		120		125
Ala Ala Ala Leu Arg Gly Pro Asp Gln Pro Cys Pro Pro Gln Glu Gly					
	130		135		140
His Asn Thr Ser Arg Gly Pro Glu Ala Phe Trp Arg Leu Ser Arg Ile					
145		150		155	160
Gln Phe Ser Tyr Asp Thr Ser Glu Arg Thr Tyr Phe Lys Asp Ala Val					
	165		170		175
Ser Pro Gly Lys His Thr Ala Ser Ser His Arg Leu Ser Ala Leu Val					
	180		185		190
Thr Pro Ala Gly Lys Ser Tyr Glu Cys Gln Ala Gln Gln Thr Ile Ser					
	195		200		205
Leu Ile Ser Ser Asp His Gln Lys Ser Val Gln Leu Leu Leu Ser Glu					
	210		215		220
Val Arg Ile Gln Pro Phe Asp Ile Thr Ala Asp Phe Val Phe Ser Glu					
225		230		235	240
Glu His Lys Cys Pro Val Asp Gln Arg Glu Gln Leu Glu Glu Thr Leu					
	245		250		255
Pro Leu Ile Leu Gly Leu Ile Leu Gly Leu Val Ile Val Ile Thr Leu					
	260		265		270
Cys Val Tyr His Ile His His Lys Leu Thr Ala Asn Gln Val Gln Ile					
	275		280		285
Pro Arg Asp Arg Ser Gln Tyr Lys His Met Gly					
	290		295		
<210> 101					
<211> 276					
<212> PRT					
<213> 热带爪蟾 (<i>Xenopus tropicalis</i>)					
<400> 101					
Met Asp Tyr Arg Ala Cys Thr Ser Ala Leu Arg Met Pro Val Leu Leu					
1	5		10		15
Leu Leu Leu Cys Thr Phe Ser Cys Asn Leu Ala Glu Gln Glu Val Glu					
	20		25		30
Asn Leu Ser Gly Leu Ser Ser Asn Pro Asp Lys Asn Ile Phe Ala Ile					
	35		40		45
Arg Glu Asn Gly Thr Thr Cys Leu Met Ala Glu Phe Ser Ala Arg Ile					

50	55	60
Leu Val Pro Tyr Glu	Val Pro Ser Ser Asn Glu	Val Asp Trp Asp Leu
65	70	75
Glu Glu Ala Ser Ile	Gln Leu Pro Arg Asp Thr	Glu Ile Arg Gly Lys
85	90	95
Cys Trp Asn Asn Glu	Ser Glu Leu His Leu	Ser Trp Leu Asp Lys Ala
100	105	110
Tyr Thr Leu Lys Leu	Phe Phe Ser Lys Glu Gly	Gln Asp Ala Ser Lys
115	120	125
Ser Arg Ser Trp Lys	Met Ser Lys Ile Gln Phe	Leu Tyr Asp Pro Ser
130	135	140
Glu His Thr Ile Phe	Lys Ser Gly Ala Arg Pro	Gly Arg His Thr Ala
145	150	155
Asn Ser His His Leu	Ser Leu Met Val Thr Pro	Ala Gly Met Ser Tyr
165	170	175
Glu Cys Glu Ala Thr	Gln Arg Ile Ser Leu Thr	Ser Thr Asp His Gln
180	185	190
Lys Ile Val Val Leu	Tyr Leu Ser Glu Val His	Leu Gln Pro Phe Asp
195	200	205
Ile Lys Ser Asp Phe	Val Tyr Ser Glu Glu Tyr	Lys Cys Pro Thr Asp
210	215	220
Gln Arg Lys Gln Leu	Glu Glu Thr Leu Pro Leu	Ile Leu Gly Leu Thr
225	230	235
Leu Gly Val Ala Ile	Leu Ile Ile Val Ala Val	Tyr His Ile His His
245	250	255
Lys Met Thr Ala Asn	Gln Val Gln Ile Pro Arg	Asp Arg Ser Leu Tyr
260	265	270
Lys His Met Gly		
275		
<210> 102		
<211> 338		
<212> PRT		
<213> 褐家鼠 (Rattus norvegicus)		
<400> 102		
Met Val Gly Arg Val	Gln Pro Asp Arg Lys	Gln Leu Pro Leu Val Leu
1	5	10
Leu Arg Leu Leu Cys	Leu Leu Pro Thr Gly	Leu Pro Val Arg Ser Val
20	25	30
Asp Phe Asn Arg Gly	Thr Asp Asn Ile Thr	Val Arg Gln Gly Asp Thr

35					40					45						
Ala	Ile	Leu	Arg	Cys	Val	Val	Glu	Asp	Lys	Asn	Ser	Lys	Val	Ala	Trp	
50					55					60						
Leu	Asn	Arg	Ser	Gly	Ile	Ile	Phe	Ala	Gly	His	Asp	Lys	Trp	Ser	Leu	
65					70					75					80	
Asp	Pro	Arg	Val	Glu	Leu	Glu	Lys	Arg	His	Ala	Leu	Glu	Tyr	Ser	Leu	
85					90					95						
Arg	Ile	Gln	Lys	Val	Asp	Val	Tyr	Asp	Glu	Gly	Ser	Tyr	Thr	Cys	Ser	
100					105					110						
Val	Gln	Thr	Gln	His	Glu	Pro	Lys	Thr	Ser	Gln	Val	Tyr	Leu	Ile	Val	
115					120					125						
Gln	Val	Pro	Pro	Lys	Ile	Ser	Asn	Ile	Ser	Ser	Asp	Val	Thr	Val	Asn	
130					135					140						
Glu	Gly	Ser	Asn	Val	Thr	Leu	Val	Cys	Met	Ala	Asn	Gly	Arg	Pro	Glu	
145					150					155					160	
Pro	Val	Ile	Thr	Trp	Arg	His	Leu	Thr	Pro	Leu	Gly	Arg	Glu	Phe	Glu	
165					170					175						
Gly	Glu	Glu	Glu	Tyr	Leu	Glu	Ile	Leu	Gly	Ile	Thr	Arg	Glu	Gln	Ser	
180					185					190						
Gly	Lys	Tyr	Glu	Cys	Lys	Ala	Ala	Asn	Glu	Val	Ser	Ser	Ala	Asp	Val	
195					200					205						
Lys	Gln	Val	Lys	Val	Thr	Val	Asn	Tyr	Pro	Pro	Thr	Ile	Thr	Glu	Ser	
210					215					220						
Lys	Ser	Asn	Glu	Ala	Thr	Thr	Gly	Arg	Gln	Ala	Ser	Leu	Lys	Cys	Glu	
225					230					235					240	
Ala	Ser	Ala	Val	Pro	Ala	Pro	Asp	Phe	Glu	Trp	Tyr	Arg	Asp	Asp	Thr	
245					250					255						
Arg	Ile	Asn	Ser	Ala	Asn	Gly	Leu	Glu	Ile	Lys	Ser	Thr	Glu	Gly	Gln	
260					265					270						
Ser	Ser	Leu	Thr	Val	Thr	Asn	Val	Thr	Glu	Glu	His	Tyr	Gly	Asn	Tyr	
275					280					285						
Thr	Cys	Val	Ala	Ala	Asn	Lys	Leu	Gly	Val	Thr	Asn	Ala	Ser	Leu	Val	
290					295					300						
Leu	Phe	Arg	Pro	Gly	Ser	Val	Arg	Gly	Ile	Asn	Gly	Ser	Ile	Ser	Leu	
305					310					315					320	
Ala	Val	Pro	Leu	Trp	Leu	Leu	Ala	Ala	Ser	Leu	Phe	Cys	Leu	Leu	Ser	
325					330					335						
Lys Cys																
<210> 103																

<211> 338

<212> PRT

<213> 家马(Equus caballus)

<400> 103

```

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

```

275	280	285
Thr Cys Val Ala Ala Asn Asn Leu Gly Val Thr Asn Ala Ser Leu Val		
290	295	300
Leu Phe Arg Pro Gly Ser Val Arg Gly Ile Asn Gly Ser Ile Ser Leu		
305	310	315
Ala Val Pro Leu Trp Leu Leu Ala Ala Ser Leu Leu Cys Leu Leu Ser		
325	330	335
Lys Cys		
<210> 104		
<211> 338		
<212> PRT		
<213> 野猪 (Sus scrofa)		
<400> 104		
Met Val Ala Arg Val Gln Pro Asp Arg Lys Gln Leu Pro Leu Val Leu		
1	5	10
Leu Arg Leu Leu Cys Leu Leu Pro Thr Gly Leu Pro Val Arg Ser Val		
20	25	30
Asp Phe Asn Arg Gly Thr Asp Asn Ile Thr Val Arg Gln Gly Asp Thr		
35	40	45
Ala Ile Leu Arg Cys Val Val Glu Asp Lys Asn Ser Lys Val Ala Trp		
50	55	60
Leu Asn Arg Ser Gly Ile Ile Phe Ala Gly His Asp Lys Trp Ser Leu		
65	70	75
Asp Pro Arg Val Glu Leu Glu Lys Arg His Ser Leu Glu Tyr Ser Leu		
85	90	95
Arg Ile Gln Lys Val Asp Val Tyr Asp Glu Gly Ser Tyr Thr Cys Ser		
100	105	110
Val Gln Thr Gln His Glu Pro Lys Thr Ser Gln Val Tyr Leu Ile Val		
115	120	125
Gln Val Pro Pro Lys Ile Ser Asn Ile Ser Ser Asp Val Thr Val Asn		
130	135	140
Glu Gly Ser Asn Val Thr Leu Val Cys Met Ala Asn Gly Arg Pro Glu		
145	150	155
Pro Val Ile Thr Trp Arg His Leu Thr Pro Thr Gly Arg Glu Leu Glu		
165	170	175
Gly Glu Glu Glu Tyr Leu Glu Ile Leu Gly Ile Thr Arg Glu Gln Ser		
180	185	190
Gly Lys Tyr Glu Cys Lys Ala Ala Asn Glu Val Ser Ser Ala Asp Val		
195	200	205

Lys Gln Val Lys Val Thr Val Asn Tyr Pro Pro Thr Ile Thr Glu Ser
 210 215 220
 Lys Ser Asn Glu Ala Thr Thr Gly Arg Lys Ala Ser Leu Lys Cys Glu
 225 230 235 240
 Ala Ser Ala Val Pro Ala Pro Asp Phe Glu Trp Tyr Arg Asp Asp Thr
 245 250 255
 Arg Ile Asn Ser Ala Asn Gly Leu Glu Ile Lys Ser Thr Glu Gly Gln
 260 265 270
 Ser Ser Leu Thr Val Thr Asn Val Thr Glu Glu His Tyr Gly Asn Tyr
 275 280 285
 Thr Cys Val Ala Ala Asn Asn Leu Gly Val Thr Asn Ala Ser Leu Val
 290 295 300
 Leu Phe Arg Pro Gly Ser Val Arg Gly Ile Asn Gly Ser Ile Ser Leu
 305 310 315 320
 Ala Val Pro Leu Trp Leu Leu Ala Ala Ser Leu Leu Cys Leu Leu Ser
 325 330 335
 Lys Cys
 <210> 105
 <211> 338
 <212> PRT
 <213> 家牛(Bos taurus)
 <400> 105
 Met Val Ala Arg Val Gln Pro Asp Arg Lys Gln Leu Pro Leu Val Leu
 1 5 10 15
 Leu Arg Leu Leu Cys Leu Leu Pro Thr Gly Leu Pro Val Arg Ser Val
 20 25 30
 Asp Phe Asn Arg Gly Thr Asp Asn Ile Thr Val Arg Gln Gly Asp Thr
 35 40 45
 Ala Ile Leu Arg Cys Val Val Glu Asp Lys Asn Ser Lys Val Ala Trp
 50 55 60
 Leu Asn Arg Ser Gly Ile Ile Phe Ala Gly His Asp Lys Trp Ser Leu
 65 70 75 80
 Asp Pro Arg Val Glu Leu Glu Lys Arg His Ser Leu Glu Tyr Ser Leu
 85 90 95
 Arg Ile Gln Lys Val Asp Val Tyr Asp Glu Gly Ser Tyr Thr Cys Ser
 100 105 110
 Val Gln Thr Gln His Glu Pro Lys Thr Ser Gln Val Tyr Leu Ile Val
 115 120 125
 Gln Val Pro Pro Lys Ile Ser Asn Ile Ser Ser Asp Val Thr Val Asn

130	135	140
Glu Gly Ser Asn Val Thr Leu Val Cys Met Ala Asn Gly Arg Pro Glu		
145	150	155
Pro Val Ile Thr Trp Arg His Leu Thr Pro Thr Gly Arg Glu Phe Glu		
	165	170
Gly Glu Glu Glu Tyr Leu Glu Ile Leu Gly Ile Thr Arg Glu Gln Ser		
	180	185
Gly Lys Tyr Glu Cys Lys Ala Ala Asn Glu Val Ser Ser Ala Asp Val		
	195	200
Lys Gln Val Lys Val Thr Val Asn Tyr Pro Pro Thr Ile Thr Glu Ser		
	210	220
Lys Ser Asn Glu Ala Thr Thr Gly Arg Lys Ala Ser Leu Lys Cys Glu		
225	230	235
Ala Ser Ala Val Pro Ala Pro Asp Phe Glu Trp Tyr Arg Asp Asp Thr		
	245	250
Arg Ile Asn Ser Ala Asn Gly Leu Glu Ile Lys Ser Thr Glu Gly Gln		
	260	265
Ser Ser Leu Thr Val Thr Asn Val Thr Glu Glu His Tyr Gly Asn Tyr		
	275	280
Thr Cys Val Ala Ala Asn Asn Leu Gly Met Thr Asn Ala Ser Leu Val		
	290	295
Leu Phe Arg Pro Gly Ser Val Arg Gly Ile Asn Gly Ser Ile Ser Leu		
305	310	315
Ala Val Pro Leu Trp Leu Leu Ala Ala Ser Leu Leu Cys Leu Leu Ser		
	325	330
		335
Lys Cys		
<210> 106		
<211> 417		
<212> PRT		
<213> 冈比亚按蚊(<i>Anopheles gambiae</i>)		
<400> 106		
Met Ser Phe Ala Gly Glu Ala Ala Ser Gln Ile Leu Asn Lys Ala Glu		
1	5	10
Pro Leu Phe Ile Ser Arg Ser Glu Ala Phe Lys Phe Ala Val Gly Asp		
	20	25
Thr Ile Thr Leu Pro Cys Glu Val Ala Ser Pro Gly Thr Tyr Val Leu		
	35	40
Ala Trp Lys Arg Gly Ile Ala Ile Leu Thr Ala Gly Ser Val Lys Val		
50	55	60

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

370	375	380
Ser Arg Asn Arg Tyr Gly Trp Ser Asp Phe Ser Glu Ser Phe Leu Phe		
385	390	395
Thr Thr Ser Asn Thr Gly Lys Trp Met Gly Gln Cys Cys Thr Asn Pro		400
	405	410
		415
Gly		
<210> 107		
<211> 334		
<212> PRT		
<213> 热带爪蟾 (<i>Xenopus tropicalis</i>)		
<400> 107		
Met Arg Pro Cys Leu Leu His Ser Ile Trp Met Leu Gly Phe Val Leu		
1	5	10
Cys Leu Leu Ser Leu Gln Gly Leu Pro Val Arg Ser Gly Asp Phe Asn		
	20	25
		30
Arg Ser Thr Asp Asn Ile Thr Val Arg Gln Gly Asp Thr Ala Ile Leu		
	35	40
		45
Arg Cys Phe Val Glu Asp Arg Ser Ser Arg Val Ala Trp Leu Asn Arg		
	50	55
		60
Ser Gly Ile Ile Phe Ala Gly Asp Asp Lys Trp Ser Leu Asp Pro Arg		
65	70	75
		80
Val Glu Leu Glu Lys Arg Ser Leu Leu Glu Tyr Ser Leu Arg Ile Gln		
	85	90
		95
Lys Val Asp Val Ser Asp Glu Gly Pro Tyr Thr Cys Ser Val Gln Thr		
	100	105
		110
Lys Gln His Thr Lys Thr Thr Gln Val Tyr Leu Ile Val Gln Val Pro		
	115	120
		125
Pro Lys Ile Ser Asn Ile Ser Ala Asp Ile Thr Val Asn Glu Gly Ser		
	130	135
		140
Asn Val Thr Leu Met Cys Ile Ala Tyr Gly Arg Pro Glu Pro Met Ile		
145	150	155
		160
Thr Trp Arg His Leu Thr Pro Thr Ala Arg Asp Phe Glu Gly Glu Glu		
	165	170
		175
Glu Phe Leu Glu Ile Gln Gly Ile Thr Arg Glu Gln Ser Gly Arg Tyr		
	180	185
		190
Glu Cys Lys Ala Ala Asn Glu Val Ala Ser Ala Asp Val Lys Gln Val		
	195	200
		205
Arg Val Thr Val Asn Tyr Pro Pro Ile Ile Thr Glu Ser Lys Ser Asn		
210	215	220

Glu Ala Thr Thr Gly Lys Gln Ala Ile Leu Arg Cys Glu Ala Ser Ala
 225 230 235 240
 Val Pro Ala Pro Asp Phe Glu Trp Tyr Lys Asp Asp Thr Arg Ile Asn
 245 250 255
 Ser Ala Gln Gly Leu Glu Ile Arg Asn Thr Gly Ser Arg Ser Val Leu
 260 265 270
 Met Val Ala Asn Val Thr Glu Glu His Tyr Gly Asn Tyr Thr Cys Val
 275 280 285
 Ala Ala Asn Lys Leu Gly Ile Thr Asn Thr Ser Leu Tyr Leu Tyr Ile
 290 295 300
 Gly Pro Gly Thr Pro Ile Asp Ser Ala Thr Ser Leu Ala Ala Ser Leu
 305 310 315 320
 Trp Leu Met Ala Asn Leu Leu Phe Cys Leu Phe Cys Thr Cys
 325 330

<210> 108

<211> 338

<212> PRT

<213> 家犬(Canis lupus familiaris)

<400> 108

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

Pro	Val	Ile	Thr	Trp	Arg	His	Leu	Thr	Pro	Thr	Gly	Arg	Glu	Phe	Glu			
																165	170	175
Gly	Glu	Glu	Glu	Tyr	Leu	Glu	Ile	Leu	Gly	Ile	Thr	Arg	Glu	Gln	Ser			
																180	185	190
Gly	Lys	Tyr	Glu	Cys	Lys	Ala	Ala	Asn	Glu	Val	Ser	Ser	Ala	Asp	Val			
																195	200	205
Arg	Gln	Val	Lys	Val	Thr	Val	Asn	Tyr	Pro	Pro	Thr	Ile	Thr	Glu	Ser			
																210	215	220
Lys	Ser	Asn	Glu	Ala	Thr	Thr	Gly	Arg	Lys	Ala	Ser	Leu	Lys	Cys	Glu			
																225	230	235
Ala	Ser	Ala	Val	Pro	Ala	Pro	Asp	Phe	Glu	Trp	Tyr	Arg	Asp	Asp	Thr			
																245	250	255
Arg	Ile	Asn	Ser	Ala	Asn	Gly	Leu	Glu	Ile	Lys	Ser	Thr	Glu	Gly	Gln			
																260	265	270
Ser	Ser	Leu	Thr	Val	Thr	Asn	Val	Thr	Glu	Glu	His	Tyr	Gly	Asn	Tyr			
																275	280	285
Thr	Cys	Val	Ala	Ala	Asn	Asn	Leu	Gly	Val	Thr	Asn	Ala	Ser	Leu	Val			
																290	295	300
Leu	Phe	Arg	Pro	Gly	Ser	Val	Arg	Gly	Ile	Asn	Gly	Ser	Ile	Ser	Leu			
																305	310	315
Ala	Val	Pro	Leu	Trp	Leu	Leu	Ala	Ala	Ser	Leu	Leu	Cys	Leu	Leu	Ser			
																325	330	335

Lys Cys

<210> 109

<211> 338

<212> PRT

<213> 短尾负鼠 (Monodelphis domestica)

<400> 109

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

	85		90		95
Arg Ile Gln Lys Val Asp Val Tyr Asp Glu Gly Ser Tyr Thr Cys Ser					
100		105		110	
Val Gln Thr Gln His Gln Pro Lys Thr Ser Gln Val Tyr Leu Ile Val					
115		120		125	
Gln Val Pro Pro Lys Ile Ser Asn Ile Ser Ser Asp Val Thr Val Asn					
130		135		140	
Glu Gly Ser Asn Val Thr Leu Val Cys Met Ala Asn Gly Arg Pro Glu					
145		150		155	
Pro Val Ile Thr Trp Arg His Leu Thr Pro Thr Gly Arg Glu Phe Glu					
165		170		175	
Gly Glu Glu Glu Tyr Leu Glu Ile Leu Gly Ile Thr Arg Glu Gln Ser					
180		185		190	
Gly Lys Tyr Glu Cys Lys Ala Ala Asn Glu Val Ser Ser Ala Asp Val					
195		200		205	
Lys Gln Val Lys Val Thr Val Asn Tyr Pro Pro Thr Ile Thr Glu Ser					
210		215		220	
Lys Ser Asn Glu Ala Thr Thr Gly Arg Gln Ala Ser Leu Lys Cys Glu					
225		230		235	
Ala Ser Ala Val Pro Ala Pro Asp Phe Glu Trp Tyr Arg Asp Asp Thr					
245		250		255	
Arg Ile Asn Ser Ala Asn Gly Leu Glu Ile Lys Ser Ile Glu Gly Gln					
260		265		270	
Ser Leu Leu Met Val Thr Asn Val Thr Glu Glu His Tyr Gly Asn Tyr					
275		280		285	
Thr Cys Val Ala Ala Asn Lys Leu Gly Val Thr Asn Ala Ser Leu Ile					
290		295		300	
Leu Phe Arg Pro Gly Ser Val Arg Gly Ile Asn Gly Ser Ile Ser Leu					
305		310		315	
Ala Val Pro Leu Trp Leu Leu Ala Ala Ser Leu Phe Cys Leu Leu Ser					
325		330		335	
Lys Cys					
<210> 110					
<211> 338					
<212> PRT					
<213> 原鸡(Gallus gallus)					
<400> 110					
Met Val Ala Arg Ala Gln Pro Asp Arg Lys Gln Leu Pro Leu Val Leu					
1	5	10		15	

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

	325	330	335
Lys Cys			
<210> 111			
<211> 335			
<212> PRT			
<213> 斑胸草雀(Taeniopygia guttata)			
<400> 111			
Met Arg Thr Tyr Trp Leu His Ser Ile Trp Val Leu Gly Phe Phe Leu			
1 5 10 15			
Ser Leu Phe Ser Leu Gln Gly Leu Pro Val Arg Ser Val Asp Phe Thr			
20 25 30			
Arg Gly Thr Asp Asn Ile Thr Val Arg Gln Gly Asp Thr Ala Ile Leu			
35 40 45			
Arg Cys Tyr Val Glu Asp Arg Ser Ser Lys Val Ala Trp Leu Asn Arg			
50 55 60			
Ser Gly Ile Ile Phe Ala Gly Glu Asp Lys Trp Ser Leu Asp Pro Arg			
65 70 75 80			
Val Glu Leu Glu Lys Arg Asn Pro Leu Glu Tyr Ser Leu Arg Ile Gln			
85 90 95			
Lys Val Asp Val Tyr Asp Glu Gly Ser Tyr Thr Cys Ser Val Gln Thr			
100 105 110			
Gln His His Pro Lys Thr Ser Gln Val Tyr Leu Ile Val Gln Val Pro			
115 120 125			
Pro Lys Ile Ser Asn Ile Ser Ser Asp Ile Thr Val Asn Glu Gly Ser			
130 135 140			
Asn Val Thr Leu Val Cys Met Ala Asn Gly Arg Pro Glu Pro Val Ile			
145 150 155 160			
Thr Trp Arg His Leu Thr Pro Thr Gly Lys Glu Phe Glu Gly Glu Glu			
165 170 175			
Glu Tyr Leu Glu Ile Leu Gly Ile Thr Arg Glu Gln Ser Gly Lys Tyr			
180 185 190			
Glu Cys Lys Ala Ala Asn Glu Val Ala Ser Ala Asp Val Lys Gln Val			
195 200 205			
Arg Val Thr Val Asn Tyr Pro Pro Thr Ile Thr Glu Ser Lys Ser Asn			
210 215 220			
Glu Ala Ala Thr Gly Arg Gln Ala Leu Leu Arg Cys Glu Ala Ser Ala			
225 230 235 240			
Val Pro Thr Pro Asp Phe Glu Trp Tyr Arg Asp Asp Thr Arg Ile Asn			
245 250 255			

Ser	Ala	Asn	Gly	Leu	Glu	Ile	Lys	Ser	Thr	Gly	Ser	Gln	Ser	Leu	Leu
				260				265					270		
Met	Val	Ala	Asn	Val	Thr	Glu	Glu	His	Tyr	Gly	Asn	Tyr	Thr	Cys	Val
				275				280					285		
Ala	Ala	Asn	Lys	Leu	Gly	Val	Thr	Asn	Ala	Ser	Leu	Tyr	Leu	Tyr	Arg
				290				295					300		
Pro	Gly	Thr	Gly	Arg	Val	Asp	Asn	Gly	Ser	Met	Ser	Leu	Ala	Val	Pro
305					310					315					320
Leu	Trp	Leu	Leu	Ala	Ala	Ser	Leu	Leu	Cys	Leu	Leu	Ser	Lys	Cys	
				325					330					335	
<210> 112															
<211> 334															
<212> PRT															
<213> 热带爪蟾(Xenopus tropicalis)															
<400> 112															
Met	Arg	Pro	Cys	Leu	Leu	His	Ser	Ile	Trp	Met	Leu	Gly	Phe	Val	Leu
1				5					10					15	
Cys	Leu	Leu	Ser	Leu	Gln	Gly	Leu	Pro	Val	Arg	Ser	Gly	Asp	Phe	Asn
				20				25						30	
Arg	Ser	Thr	Asp	Asn	Ile	Thr	Val	Arg	Gln	Gly	Asp	Thr	Ala	Ile	Leu
				35				40						45	
Arg	Cys	Phe	Val	Glu	Asp	Arg	Ser	Ser	Arg	Val	Ala	Trp	Leu	Asn	Arg
				50				55						60	
Ser	Gly	Ile	Ile	Phe	Ala	Gly	Asp	Asp	Lys	Trp	Ser	Leu	Asp	Pro	Arg
65					70					75					80
Val	Glu	Leu	Glu	Lys	Arg	Ser	Leu	Leu	Glu	Tyr	Ser	Leu	Arg	Ile	Gln
				85					90					95	
Lys	Val	Asp	Val	Ser	Asp	Glu	Gly	Pro	Tyr	Thr	Cys	Ser	Val	Gln	Thr
				100				105						110	
Lys	Gln	His	Thr	Lys	Thr	Thr	Gln	Val	Tyr	Leu	Ile	Val	Gln	Val	Pro
				115				120						125	
Pro	Lys	Ile	Ser	Asn	Ile	Ser	Ala	Asp	Ile	Thr	Val	Asn	Glu	Gly	Ser
				130				135						140	
Asn	Val	Thr	Leu	Met	Cys	Ile	Ala	Tyr	Gly	Arg	Pro	Glu	Pro	Met	Ile
145					150					155					160
Thr	Trp	Arg	His	Leu	Thr	Pro	Thr	Ala	Arg	Asp	Phe	Glu	Gly	Glu	Glu
				165					170					175	
Glu	Phe	Leu	Glu	Ile	Gln	Gly	Ile	Thr	Arg	Glu	Gln	Ser	Gly	Arg	Tyr
				180					185					190	

Glu Cys Lys Ala Ala Asn Glu Val Ala Ser Ala Asp Val Lys Gln Val		
195	200	205
Arg Val Thr Val Asn Tyr Pro Pro Ile Ile Thr Glu Ser Lys Ser Asn		
210	215	220
Glu Ala Thr Thr Gly Lys Gln Ala Ile Leu Arg Cys Glu Ala Ser Ala		
225	230	235
Val Pro Ala Pro Asp Phe Glu Trp Tyr Lys Asp Asp Thr Arg Ile Asn		
	245	250
Ser Ala Gln Gly Leu Glu Ile Arg Asn Thr Gly Ser Arg Ser Val Leu		
	260	265
Met Val Ala Asn Val Thr Glu Glu His Tyr Gly Asn Tyr Thr Cys Val		
	275	280
Ala Ala Asn Lys Leu Gly Ile Thr Asn Thr Ser Leu Tyr Leu Tyr Ile		
	290	295
Gly Pro Gly Thr Pro Ile Asp Ser Ala Thr Ser Leu Ala Ala Ser Leu		
305	310	315
Trp Leu Met Ala Asn Leu Leu Phe Cys Leu Phe Cys Thr Cys		
	325	330

<210> 113

<211> 337

<212> PRT

<213> 罗非鱼 (*Oreochromis niloticus*)

<400> 113

Met Gln Val Gly Arg Lys Ser Cys Trp Arg Gln Leu Gln Ala Ser Phe		
1	5	10
Phe Arg Leu Leu Cys Leu Ile Pro Thr Gly Phe Pro Val Arg Ser Val		
	20	25
Asp Met Gln Arg Ala Thr Asp Asn Ile Thr Ile Arg Gln Gly Asp Thr		
	35	40
Ala Ile Ile Arg Cys Tyr Val Asp Asp Lys Val Ser Lys Val Ala Trp		
	50	55
Leu Asn Arg Ser Asn Ile Ile Phe Ala Gly Gln Asp Lys Trp Ser Leu		
65	70	75
Asp Pro Arg Val Asp Leu Val Thr Lys Gly Gln Leu Glu Tyr Ser Leu		
	85	90
Arg Ile Gln Lys Val Asp Val Tyr Asp Glu Gly Ser Tyr Thr Cys Ser		
	100	105
Ile Gln Thr Lys Gln Gln Pro Lys Thr Ser Gln Val Tyr Leu Ile Val		
	115	120

Gln Val Pro Ala Ser Ile Tyr Gln Val Ser Asn Asp Ile Thr Val Asn		
130	135	140
Glu Gly Ser Asn Val Thr Leu Ser Cys Leu Ala Asn Gly Arg Pro Asp		
145	150	155
Pro Ala Ile Thr Trp Arg Leu Leu Asn Pro Ser Ala Glu Pro Leu Asp		
	165	170
Gly Glu Glu Tyr Leu Asp Ile Ile Gly Ile Met Arg Thr Gln Ala Gly		
	180	185
Arg Tyr Glu Cys Lys Ala Ser Asn Asp Val Ala Thr Pro Asp Val Lys		
	195	200
Tyr Val Asn Val Ile Val Asn Tyr Pro Pro Thr Ile Lys Lys Thr Gln		
	210	215
Ser Ser Glu Thr Pro Val Gly Arg Asn Gly Thr Leu Arg Cys Glu Val		
225	230	235
Thr Ala Val Pro Thr Pro Glu Phe Glu Trp Tyr Arg Asp Asp Lys Arg		
	245	250
Leu Ala Asn Thr Gln Ser Ile Thr Ile Gln Thr Ser Gly Thr Thr Thr		
	260	265
Ser Leu Thr Ile Ala Asn Ile Thr Glu Glu Asp Tyr Gly Asn Tyr Thr		
	275	280
Cys Val Ala Ser Asn Arg Leu Gly Val Gln Asn Ala Ser Leu Phe Leu		
	290	295
Tyr Arg Pro Gly Thr Gly Arg Asp Ile Asn Gly Ser Ala Cys Val Ser		
305	310	315
Gln Ser Leu Trp Leu Leu Leu Ala Ser Phe Ala Cys Leu Phe Leu Lys		
	325	330

Cys

<210> 114

<211> 817

<212> PRT

<213> 梅克尔细胞多瘤病毒

<220>

<221> MISC_FEATURE

<223> 登记号YP_009111421

<400> 114

Met Asp Leu Val Leu Asn Arg Lys Glu Arg Glu Ala Leu Cys Lys Leu		
1	5	10
Leu Glu Ile Ala Pro Asn Cys Tyr Gly Asn Ile Pro Leu Met Lys Ala		
	20	30

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

340	345	350
Glu Lys Phe Lys Val Asp Phe Lys Ser Arg His Ala Cys Glu Leu Gly		
355	360	365
Cys Ile Leu Leu Phe Ile Thr Leu Ser Lys His Arg Val Ser Ala Ile		
370	375	380
Lys Asn Phe Cys Ser Thr Phe Cys Thr Ile Ser Phe Leu Ile Cys Lys		
385	390	395
Gly Val Asn Lys Met Pro Glu Met Tyr Asn Asn Leu Cys Lys Pro Pro		
405	410	415
Tyr Lys Leu Leu Gln Glu Asn Lys Pro Leu Leu Asn Tyr Glu Phe Gln		
420	425	430
Glu Lys Glu Lys Glu Ala Ser Cys Asn Trp Asn Leu Val Ala Glu Phe		
435	440	445
Ala Cys Glu Tyr Glu Leu Asp Asp His Phe Ile Ile Leu Ala His Tyr		
450	455	460
Leu Asp Phe Ala Lys Pro Phe Pro Cys Gln Lys Cys Glu Asn Arg Ser		
465	470	475
Arg Leu Lys Pro His Lys Ala His Glu Ala His His Ser Asn Ala Lys		
485	490	495
Leu Phe Tyr Glu Ser Lys Ser Gln Lys Thr Ile Cys Gln Gln Ala Ala		
500	505	510
Asp Thr Val Leu Ala Lys Arg Arg Leu Glu Met Leu Glu Met Thr Arg		
515	520	525
Thr Glu Met Leu Cys Lys Lys Phe Lys Lys His Leu Glu Arg Leu Arg		
530	535	540
Asp Leu Asp Thr Ile Asp Leu Leu Tyr Tyr Met Gly Gly Val Ala Trp		
545	550	555
Tyr Cys Cys Leu Phe Glu Glu Phe Glu Lys Lys Leu Gln Lys Ile Ile		
565	570	575
Gln Leu Leu Thr Glu Asn Ile Pro Lys Tyr Arg Asn Ile Trp Phe Lys		
580	585	590
Gly Pro Ile Asn Ser Gly Lys Thr Ser Phe Ala Ala Ala Leu Ile Asp		
595	600	605
Leu Leu Glu Gly Lys Ala Leu Asn Ile Asn Cys Pro Ser Asp Lys Leu		
610	615	620
Pro Phe Glu Leu Gly Cys Ala Leu Asp Lys Phe Met Val Val Phe Glu		
625	630	635
Asp Val Lys Gly Gln Asn Ser Leu Asn Lys Asp Leu Gln Pro Gly Gln		
645	650	655

Gly Ile Asn Asn Leu Asp Asn Leu Arg Asp His Leu Asp Gly Ala Val
 660 665 670
 Ala Val Ser Leu Glu Lys Lys His Val Asn Lys Lys His Gln Ile Phe
 675 680 685
 Pro Pro Cys Ile Val Thr Ala Asn Asp Tyr Phe Ile Pro Lys Thr Leu
 690 695 700
 Ile Ala Arg Phe Ser Tyr Thr Leu His Phe Ser Pro Lys Ala Asn Leu
 705 710 715 720
 Arg Asp Ser Leu Asp Gln Asn Met Glu Ile Arg Lys Arg Arg Ile Leu
 725 730 735
 Gln Ser Gly Thr Thr Leu Leu Leu Cys Leu Ile Trp Cys Leu Pro Asp
 740 745 750
 Thr Thr Phe Lys Pro Cys Leu Gln Glu Glu Ile Lys Asn Trp Lys Gln
 755 760 765
 Ile Leu Gln Ser Glu Ile Ser Tyr Gly Lys Phe Cys Gln Met Ile Glu
 770 775 780
 Asn Val Glu Ala Gly Gln Asp Pro Leu Leu Asn Ile Leu Ile Glu Glu
 785 790 795 800
 Glu Gly Pro Glu Glu Thr Glu Glu Thr Gln Asp Ser Gly Thr Phe Ser
 805 810 815

Gln

<210> 115

<211> 327

<212> PRT

<213> 梅克尔细胞多瘤病毒

<220>

<221> MISC_FEATURE

<222> (220) .. (220)

<223> Xaa可以是任何氨基酸,优选地其中Xaa是丙氨酸。

<400> 115

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

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

<210> 116

<211> 327

<212> PRT

<213> 梅克尔细胞多瘤病毒

<220>

<221> MISC_FEATURE

<223> 序列与SEQ ID NO:115相同,但第220位氨基酸被丙氨酸代替。

<400> 116

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

290	295	300
Lys Asn Arg Glu Thr Pro Val Pro Thr Asp Phe Pro Ile Asp Leu Ser		
305	310	315
Asp Tyr Leu Ser His Ala Val		320
	325	
<210> 117		
<211> 186		
<212> PRT		
<213> 梅克尔细胞多瘤病毒		
<400> 117		
Met Asp Leu Val Leu Asn Arg Lys Glu Arg Glu Ala Leu Cys Lys Leu		
1	5	10
Leu Glu Ile Ala Pro Asn Cys Tyr Gly Asn Ile Pro Leu Met Lys Ala		
	20	25
Ala Phe Lys Arg Ser Cys Leu Lys His His Pro Asp Lys Gly Gly Asn		30
	35	40
Pro Val Ile Met Met Glu Leu Asn Thr Leu Trp Ser Lys Phe Gln Gln		45
	50	55
Asn Ile His Lys Leu Arg Ser Asp Phe Ser Met Phe Asp Glu Val Ser		60
65	70	75
Thr Lys Phe Pro Trp Glu Glu Tyr Gly Thr Leu Lys Asp Tyr Met Gln		80
	85	90
Ser Gly Tyr Asn Ala Arg Phe Cys Arg Gly Pro Gly Cys Met Leu Lys		95
	100	105
Gln Leu Arg Asp Ser Lys Cys Ala Cys Ile Ser Cys Lys Leu Ser Arg		110
	115	120
Gln His Cys Ser Leu Lys Thr Leu Lys Gln Lys Asn Cys Leu Thr Trp		125
	130	135
Gly Glu Cys Phe Cys Tyr Gln Cys Phe Ile Leu Trp Phe Gly Phe Pro		140
145	150	155
Pro Thr Trp Glu Ser Phe Asp Trp Trp Gln Lys Thr Leu Glu Glu Thr		160
	165	170
Asp Tyr Cys Leu Leu His Leu His Leu Phe		175
	180	185
<210> 118		
<211> 369		
<212> PRT		
<213> 人工序列		
<220>		

<223> MAGE-A10__Homo_sapiens__A0A024RC14

<400> 118

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

290	295	300
Glu Ile Arg Lys Met Ser Leu Leu Lys Phe Leu Ala Lys Val Asn Gly		
305	310	315
Ser Asp Pro Arg Ser Phe Pro Leu Trp Tyr Glu Glu Ala Leu Lys Asp		320
	325	330
Glu Glu Glu Arg Ala Gln Asp Arg Ile Ala Thr Thr Asp Asp Thr Thr		335
	340	345
Ala Met Ala Ser Ala Ser Ser Ser Ala Thr Gly Ser Phe Ser Tyr Pro		350
355	360	365
Glu		
<210> 119		
<211> 314		
<212> PRT		
<213> 人工序列		
<220>		
<223> MAGE-A12__Homo_sapiens__P43365		
<400> 119		
Met Pro Leu Glu Gln Arg Ser Gln His Cys Lys Pro Glu Glu Gly Leu		
1	5	10
Glu Ala Gln Gly Glu Ala Leu Gly Leu Val Gly Ala Gln Ala Pro Ala		
20	25	30
Thr Glu Glu Gln Glu Thr Ala Ser Ser Ser Thr Leu Val Glu Val		
35	40	45
Thr Leu Arg Glu Val Pro Ala Ala Glu Ser Pro Ser Pro Pro His Ser		
50	55	60
Pro Gln Gly Ala Ser Thr Leu Pro Thr Thr Ile Asn Tyr Thr Leu Trp		
65	70	75
Ser Gln Ser Asp Glu Gly Ser Ser Asn Glu Glu Gln Glu Gly Pro Ser		
85	90	95
Thr Phe Pro Asp Leu Glu Thr Ser Phe Gln Val Ala Leu Ser Arg Lys		
100	105	110
Met Ala Glu Leu Val His Phe Leu Leu Leu Lys Tyr Arg Ala Arg Glu		
115	120	125
Pro Phe Thr Lys Ala Glu Met Leu Gly Ser Val Ile Arg Asn Phe Gln		
130	135	140
Asp Phe Phe Pro Val Ile Phe Ser Lys Ala Ser Glu Tyr Leu Gln Leu		
145	150	155
Val Phe Gly Ile Glu Val Val Glu Val Val Arg Ile Gly His Leu Tyr		
165	170	175

Ile Leu Val Thr Cys Leu Gly Leu Ser Tyr Asp Gly Leu Leu Gly Asp		
180	185	190
Asn Gln Ile Val Pro Lys Thr Gly Leu Leu Ile Ile Val Leu Ala Ile		
195	200	205
Ile Ala Lys Glu Gly Asp Cys Ala Pro Glu Glu Lys Ile Trp Glu Glu		
210	215	220
Leu Ser Val Leu Glu Ala Ser Asp Gly Arg Glu Asp Ser Val Phe Ala		
225	230	235
240		
His Pro Arg Lys Leu Leu Thr Gln Asp Leu Val Gln Glu Asn Tyr Leu		
245	250	255
Glu Tyr Arg Gln Val Pro Gly Ser Asp Pro Ala Cys Tyr Glu Phe Leu		
260	265	270
Trp Gly Pro Arg Ala Leu Val Glu Thr Ser Tyr Val Lys Val Leu His		
275	280	285
His Leu Leu Lys Ile Ser Gly Gly Pro His Ile Ser Tyr Pro Pro Leu		
290	295	300
His Glu Trp Ala Phe Arg Glu Gly Glu Glu		
305	310	
<210> 120		
<211> 309		
<212> PRT		
<213> 人工序列		
<220>		
<223> MAGE-A1__Homo_sapiens__P43355		
<400> 120		
Met Ser Leu Glu Gln Arg Ser Leu His Cys Lys Pro Glu Glu Ala Leu		
1	5	10
15		
Glu Ala Gln Gln Glu Ala Leu Gly Leu Val Cys Val Gln Ala Ala Thr		
20	25	30
Ser Ser Ser Ser Pro Leu Val Leu Gly Thr Leu Glu Glu Val Pro Thr		
35	40	45
Ala Gly Ser Thr Asp Pro Pro Gln Ser Pro Gln Gly Ala Ser Ala Phe		
50	55	60
Pro Thr Thr Ile Asn Phe Thr Arg Gln Arg Gln Pro Ser Glu Gly Ser		
65	70	75
80		
Ser Ser Arg Glu Glu Glu Gly Pro Ser Thr Ser Cys Ile Leu Glu Ser		
85	90	95
Leu Phe Arg Ala Val Ile Thr Lys Lys Val Ala Asp Leu Val Gly Phe		
100	105	110

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

Glu Glu Glu Gly Val

305

<210> 121

<211> 314

<212> PRT

<213> 人工序列

<220>

<223> MAGE-A2__Homo_sapiens__P43356

<400> 121

Met Pro Leu Glu Gln Arg Ser Gln His Cys Lys Pro Glu Glu Gly Leu
 1 5 10 15
 Glu Ala Arg Gly Glu Ala Leu Gly Leu Val Gly Ala Gln Ala Pro Ala
 20 25 30
 Thr Glu Glu Gln Gln Thr Ala Ser Ser Ser Ser Thr Leu Val Glu Val
 35 40 45

Thr	Leu	Gly	Glu	Val	Pro	Ala	Ala	Asp	Ser	Pro	Ser	Pro	Pro	His	Ser
50						55					60				
Pro	Gln	Gly	Ala	Ser	Ser	Phe	Ser	Thr	Thr	Ile	Asn	Tyr	Thr	Leu	Trp
65					70					75				80	
Arg	Gln	Ser	Asp	Glu	Gly	Ser	Ser	Asn	Gln	Glu	Glu	Glu	Gly	Pro	Arg
				85					90					95	
Met	Phe	Pro	Asp	Leu	Glu	Ser	Glu	Phe	Gln	Ala	Ala	Ile	Ser	Arg	Lys
				100					105					110	
Met	Val	Glu	Leu	Val	His	Phe	Leu	Leu	Leu	Lys	Tyr	Arg	Ala	Arg	Glu
				115					120					125	
Pro	Val	Thr	Lys	Ala	Glu	Met	Leu	Glu	Ser	Val	Leu	Arg	Asn	Cys	Gln
				130					135					140	
Asp	Phe	Phe	Pro	Val	Ile	Phe	Ser	Lys	Ala	Ser	Glu	Tyr	Leu	Gln	Leu
145					150					155					160
Val	Phe	Gly	Ile	Glu	Val	Val	Glu	Val	Val	Pro	Ile	Ser	His	Leu	Tyr
				165						170					175
Ile	Leu	Val	Thr	Cys	Leu	Gly	Leu	Ser	Tyr	Asp	Gly	Leu	Leu	Gly	Asp
				180						185					190
Asn	Gln	Val	Met	Pro	Lys	Thr	Gly	Leu	Leu	Ile	Ile	Val	Leu	Ala	Ile
				195						200					205
Ile	Ala	Ile	Glu	Gly	Asp	Cys	Ala	Pro	Glu	Glu	Lys	Ile	Trp	Glu	Glu
				210						215					220
Leu	Ser	Met	Leu	Glu	Val	Phe	Glu	Gly	Arg	Glu	Asp	Ser	Val	Phe	Ala
225					230					235					240
His	Pro	Arg	Lys	Leu	Leu	Met	Gln	Asp	Leu	Val	Gln	Glu	Asn	Tyr	Leu
				245						250					255
Glu	Tyr	Arg	Gln	Val	Pro	Gly	Ser	Asp	Pro	Ala	Cys	Tyr	Glu	Phe	Leu
				260						265					270
Trp	Gly	Pro	Arg	Ala	Leu	Ile	Glu	Thr	Ser	Tyr	Val	Lys	Val	Leu	His
				275						280					285
His	Thr	Leu	Lys	Ile	Gly	Gly	Glu	Pro	His	Ile	Ser	Tyr	Pro	Pro	Leu
				290						295					300
His	Glu	Arg	Ala	Leu	Arg	Glu	Gly	Glu	Glu						
305															310
<210> 122															
<211> 314															
<212> PRT															
<213> 人工序列															
<220>															

<223> MAGE-A3__Homo_sapiens__P43357

<400> 122

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

290	295	300
His Glu Trp Val Leu Arg Glu Gly Glu Glu		
305	310	
<210> 123		
<211> 317		
<212> PRT		
<213> 人工序列		
<220>		
<223> MAGE-A4__Homo_sapiens__A0A024RC12		
<400> 123		
Met Ser Ser Glu Gln Lys Ser Gln His Cys Lys Pro Glu Glu Gly Val		
1	5	10
Glu Ala Gln Glu Glu Ala Leu Gly Leu Val Gly Ala Gln Ala Pro Thr		
20	25	30
Thr Glu Glu Gln Glu Ala Ala Val Ser Ser Ser Ser Pro Leu Val Pro		
35	40	45
Gly Thr Leu Glu Glu Val Pro Ala Ala Glu Ser Ala Gly Pro Pro Gln		
50	55	60
Ser Pro Gln Gly Ala Ser Ala Leu Pro Thr Thr Ile Ser Phe Thr Cys		
65	70	75
Trp Arg Gln Pro Asn Glu Gly Ser Ser Ser Gln Glu Glu Glu Gly Pro		
85	90	95
Ser Thr Ser Pro Asp Ala Glu Ser Leu Phe Arg Glu Ala Leu Ser Asn		
100	105	110
Lys Val Asp Glu Leu Ala His Phe Leu Leu Arg Lys Tyr Arg Ala Lys		
115	120	125
Glu Leu Val Thr Lys Ala Glu Met Leu Glu Arg Val Ile Lys Asn Tyr		
130	135	140
Lys Arg Cys Phe Pro Val Ile Phe Gly Lys Ala Ser Glu Ser Leu Lys		
145	150	155
Met Ile Phe Gly Ile Asp Val Lys Glu Val Asp Pro Ala Ser Asn Thr		
165	170	175
Tyr Thr Leu Val Thr Cys Leu Gly Leu Ser Tyr Asp Gly Leu Leu Gly		
180	185	190
Asn Asn Gln Ile Phe Pro Lys Thr Gly Leu Leu Ile Ile Val Leu Gly		
195	200	205
Thr Ile Ala Met Glu Gly Asp Ser Ala Ser Glu Glu Glu Ile Trp Glu		
210	215	220
Glu Leu Gly Val Met Gly Val Tyr Asp Gly Arg Glu His Thr Val Tyr		

225	230	235	240
Gly Glu Pro Arg Lys Leu Leu Thr Gln Asp Trp Val Gln Glu Asn Tyr			
	245	250	255
Leu Glu Tyr Arg Gln Val Pro Gly Ser Asn Pro Ala Arg Tyr Glu Phe			
	260	265	270
Leu Trp Gly Pro Arg Ala Leu Ala Glu Thr Ser Tyr Val Lys Val Leu			
	275	280	285
Glu His Val Val Arg Val Asn Ala Arg Val Arg Ile Ala Tyr Pro Ser			
	290	295	300
Leu Arg Glu Ala Ala Leu Leu Glu Glu Glu Glu Gly Val			
305	310	315	
<210> 124			
<211> 317			
<212> PRT			
<213> 人工序列			
<220>			
<223> MAGE-A4__Homo_sapiens__P43358			
<400> 124			
Met Ser Ser Glu Gln Lys Ser Gln His Cys Lys Pro Glu Glu Gly Val			
1	5	10	15
Glu Ala Gln Glu Glu Ala Leu Gly Leu Val Gly Ala Gln Ala Pro Thr			
	20	25	30
Thr Glu Glu Gln Glu Ala Ala Val Ser Ser Ser Ser Pro Leu Val Pro			
	35	40	45
Gly Thr Leu Glu Glu Val Pro Ala Ala Glu Ser Ala Gly Pro Pro Gln			
	50	55	60
Ser Pro Gln Gly Ala Ser Ala Leu Pro Thr Thr Ile Ser Phe Thr Cys			
65	70	75	80
Trp Arg Gln Pro Asn Glu Gly Ser Ser Ser Gln Glu Glu Glu Gly Pro			
	85	90	95
Ser Thr Ser Pro Asp Ala Glu Ser Leu Phe Arg Glu Ala Leu Ser Asn			
	100	105	110
Lys Val Asp Glu Leu Ala His Phe Leu Leu Arg Lys Tyr Arg Ala Lys			
	115	120	125
Glu Leu Val Thr Lys Ala Glu Met Leu Glu Arg Val Ile Lys Asn Tyr			
	130	135	140
Lys Arg Cys Phe Pro Val Ile Phe Gly Lys Ala Ser Glu Ser Leu Lys			
145	150	155	160
Met Ile Phe Gly Ile Asp Val Lys Glu Val Asp Pro Ala Ser Asn Thr			

	165		170		175
Tyr Thr Leu Val Thr Cys Leu Gly Leu Ser Tyr Asp Gly Leu Leu Gly					
	180		185		190
Asn Asn Gln Ile Phe Pro Lys Thr Gly Leu Leu Ile Ile Val Leu Gly					
	195		200		205
Thr Ile Ala Met Glu Gly Asp Ser Ala Ser Glu Glu Glu Ile Trp Glu					
	210		215		220
Glu Leu Gly Val Met Gly Val Tyr Asp Gly Arg Glu His Thr Val Tyr					
225		230		235	240
Gly Glu Pro Arg Lys Leu Leu Thr Gln Asp Trp Val Gln Glu Asn Tyr					
	245		250		255
Leu Glu Tyr Arg Gln Val Pro Gly Ser Asn Pro Ala Arg Tyr Glu Phe					
	260		265		270
Leu Trp Gly Pro Arg Ala Leu Ala Glu Thr Ser Tyr Val Lys Val Leu					
	275		280		285
Glu His Val Val Arg Val Asn Ala Arg Val Arg Ile Ala Tyr Pro Ser					
	290		295		300
Leu Arg Glu Ala Ala Leu Leu Glu Glu Glu Glu Gly Val					
305		310		315	
<210> 125					
<211> 317					
<212> PRT					
<213> 人工序列					
<220>					
<223> MAGE-A4__Homo_sapiens__Q1RN33					
<400> 125					
Met Ser Ser Glu Gln Lys Ser Gln His Cys Lys Pro Glu Glu Gly Val					
1	5		10		15
Glu Ala Gln Glu Glu Ala Leu Gly Leu Val Gly Ala Gln Ala Pro Thr					
	20		25		30
Thr Glu Glu Gln Glu Ala Ala Val Ser Ser Ser Ser Pro Leu Val Pro					
	35		40		45
Gly Thr Leu Glu Glu Val Pro Ala Ala Glu Ser Ala Gly Pro Pro Gln					
	50		55		60
Ser Pro Gln Gly Ala Ser Ala Leu Pro Thr Thr Ile Ser Phe Thr Cys					
65		70		75	80
Trp Arg Gln Pro Asn Glu Gly Ser Ser Ser Gln Glu Glu Glu Gly Pro					
	85		90		95
Ser Thr Ser Pro Asp Ala Glu Ser Leu Phe Arg Glu Ala Leu Ser Asn					

100	105	110
Lys Val Asp Glu Leu Ala His Phe	Leu Leu Arg Lys Tyr Arg Ala Lys	
115	120	125
Glu Leu Val Thr Lys Ala Glu Met	Leu Glu Arg Val Ile Lys Asn Tyr	
130	135	140
Lys Arg Cys Phe Pro Val Ile Phe	Gly Lys Ala Ser Glu Ser Leu Lys	
145	150	155
Met Ile Phe Gly Ile Asp Val Lys	Glu Val Asp Pro Thr Ser Asn Thr	
165	170	175
Tyr Thr Leu Val Thr Cys Leu Gly	Leu Ser Tyr Asp Gly Leu Leu Gly	
180	185	190
Asn Asn Gln Ile Phe Pro Lys Thr	Gly Leu Leu Ile Ile Val Leu Gly	
195	200	205
Thr Ile Ala Met Glu Gly Asp Ser	Ala Ser Glu Glu Glu Ile Trp Glu	
210	215	220
Glu Leu Gly Val Met Gly Val Tyr	Asp Gly Arg Glu His Thr Val Tyr	
225	230	235
Gly Glu Pro Arg Lys Leu Leu Thr	Gln Asp Trp Val Gln Glu Asn Tyr	
245	250	255
Leu Glu Tyr Arg Gln Val Pro Gly	Ser Asn Pro Ala Arg Tyr Glu Phe	
260	265	270
Leu Trp Gly Pro Arg Ala Leu Ala	Glu Thr Ser Tyr Val Lys Val Leu	
275	280	285
Glu His Val Val Arg Val Asn Ala	Arg Val Arg Ile Ala Tyr Pro Ser	
290	295	300
Leu Arg Glu Ala Ala Leu Leu Glu	Glu Glu Gly Val	
305	310	315
<210>	126	
<211>	314	
<212>	PRT	
<213>	人工序列	
<220>		
<223>	MAGE-A6__Homo_sapiens__A8K072	
<400>	126	
Met Pro Leu Glu Gln Arg Ser Gln	His Cys Lys Pro Glu Glu Gly Leu	
1	5	10
Glu Ala Arg Gly Glu Ala Leu Gly	Leu Val Gly Ala Gln Ala Pro Ala	
20	25	30
Thr Glu Glu Gln Glu Ala Ala Ser	Ser Ser Ser Thr Leu Val Glu Val	

35	40	45
Thr Leu Gly Glu Val Pro Ala	Ala Glu Ser Pro Asp	Pro Pro Gln Ser
50	55	60
Pro Gln Gly Ala Ser Ser Leu	Pro Thr Thr Met Asn Tyr	Pro Leu Trp
65	70	75
Ser Gln Ser Tyr Glu Asp Ser	Ser Asn Gln Glu Glu Glu Gly	Pro Ser
85	90	95
Thr Phe Pro Asp Leu Glu Ser	Glu Phe Gln Ala Ala Leu	Ser Arg Lys
100	105	110
Leu Ala Lys Leu Val His Phe	Leu Leu Leu Lys Tyr Arg	Ala Arg Glu
115	120	125
Pro Val Thr Lys Ala Glu Met	Leu Gly Ser Val Val Gly	Asn Trp Gln
130	135	140
Tyr Phe Phe Pro Val Ile Phe	Ser Lys Ala Ser Asp Ser	Leu Gln Leu
145	150	155
Val Phe Gly Ile Glu Leu Met	Glu Val Asp Pro Ile Gly	His Val Tyr
165	170	175
Ile Phe Ala Thr Cys Leu Gly	Leu Ser Tyr Asp Gly Leu	Leu Gly Asp
180	185	190
Asn Gln Ile Met Pro Lys Thr	Gly Phe Leu Ile Ile Ile	Leu Ala Ile
195	200	205
Ile Ala Lys Glu Gly Asp Cys	Ala Pro Glu Glu Lys Ile	Trp Glu Glu
210	215	220
Leu Ser Val Leu Glu Val Phe	Glu Gly Arg Glu Asp Ile	Ile Phe Gly
225	230	235
Asp Pro Lys Lys Leu Leu Thr	Gln Tyr Phe Val Gln Glu	Asn Tyr Leu
245	250	255
Glu Tyr Arg Gln Val Pro Gly	Ser Asp Pro Ala Cys Tyr	Glu Phe Leu
260	265	270
Trp Gly Pro Arg Ala Leu Ile	Glu Thr Ser Tyr Val Lys	Val Leu His
275	280	285
His Met Val Lys Ile Ser Gly	Gly Pro Arg Ile Ser Tyr	Pro Leu Leu
290	295	300
His Glu Trp Ala Leu Arg Glu	Gly Glu Glu	
305	310	
<210> 127		
<211> 314		
<212> PRT		
<213> 人工序列		

<220>

<223> MAGE-A6__Homo_sapiens__P43360

<400> 127

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

His Met Val Lys Ile Ser Gly Gly Pro Arg Ile Ser Tyr Pro Leu Leu
 290 295 300
 His Glu Trp Ala Leu Arg Glu Gly Glu Glu
 305 310
 <210> 128
 <211> 314
 <212> PRT
 <213> 人工序列
 <220>
 <223> MAGE-A6__Homo_sapiens__Q6FHI5
 <400> 128
 Met Pro Leu Glu Gln Arg Ser Gln His Cys Lys Pro Glu Glu Gly Leu
 1 5 10 15
 Glu Ala Arg Gly Glu Ala Leu Gly Leu Val Gly Ala Gln Ala Pro Ala
 20 25 30
 Thr Glu Glu Gln Glu Ala Ala Ser Ser Ser Ser Thr Leu Val Glu Val
 35 40 45
 Thr Leu Gly Glu Val Pro Ala Ala Glu Ser Pro Asp Pro Pro Gln Ser
 50 55 60
 Pro Gln Gly Ala Ser Ser Leu Pro Thr Thr Met Asn Tyr Pro Leu Trp
 65 70 75 80
 Ser Gln Ser Tyr Glu Asp Ser Ser Asn Gln Glu Glu Glu Gly Pro Ser
 85 90 95
 Thr Phe Pro Asp Leu Glu Ser Glu Phe Gln Ala Ala Leu Ser Arg Lys
 100 105 110
 Val Ala Lys Leu Val His Phe Leu Leu Leu Lys Tyr Arg Ala Arg Glu
 115 120 125
 Pro Val Thr Lys Ala Glu Met Leu Gly Ser Val Val Gly Asn Trp Gln
 130 135 140
 Tyr Phe Phe Pro Val Ile Phe Ser Lys Ala Ser Asp Ser Leu Gln Leu
 145 150 155 160
 Val Phe Gly Ile Glu Leu Met Glu Val Asp Pro Ile Gly His Val Tyr
 165 170 175
 Ile Phe Ala Thr Cys Leu Gly Leu Ser Tyr Asp Gly Leu Leu Gly Asp
 180 185 190
 Asn Gln Ile Met Pro Lys Thr Gly Phe Leu Ile Ile Ile Leu Ala Ile
 195 200 205
 Ile Ala Lys Glu Gly Asp Cys Ala Pro Glu Glu Lys Ile Trp Glu Glu
 210 215 220

Leu Ser Val Leu Glu Val Phe Glu Gly Arg Glu Asp Ser Ile Phe Gly
 225 230 235 240
 Asp Pro Lys Lys Leu Leu Thr Gln Tyr Phe Val Gln Glu Asn Tyr Leu
 245 250 255
 Glu Tyr Arg Gln Val Pro Gly Ser Asp Pro Ala Cys Tyr Glu Phe Leu
 260 265 270
 Trp Gly Pro Arg Ala Leu Ile Glu Thr Ser Tyr Val Lys Val Leu His
 275 280 285
 His Met Val Lys Ile Ser Gly Gly Pro Arg Ile Ser Tyr Pro Leu Leu
 290 295 300
 His Glu Trp Ala Phe Arg Glu Gly Glu Glu
 305 310
 <210> 129
 <211> 315
 <212> PRT
 <213> 人工序列
 <220>
 <223> MAGE-A9__Homo_sapiens__P43362
 <400> 129
 Met Ser Leu Glu Gln Arg Ser Pro His Cys Lys Pro Asp Glu Asp Leu
 1 5 10 15
 Glu Ala Gln Gly Glu Asp Leu Gly Leu Met Gly Ala Gln Glu Pro Thr
 20 25 30
 Gly Glu Glu Glu Glu Thr Thr Ser Ser Ser Asp Ser Lys Glu Glu Glu
 35 40 45
 Val Ser Ala Ala Gly Ser Ser Ser Pro Pro Gln Ser Pro Gln Gly Gly
 50 55 60
 Ala Ser Ser Ser Ile Ser Val Tyr Tyr Thr Leu Trp Ser Gln Phe Asp
 65 70 75 80
 Glu Gly Ser Ser Ser Gln Glu Glu Glu Glu Pro Ser Ser Ser Val Asp
 85 90 95
 Pro Ala Gln Leu Glu Phe Met Phe Gln Glu Ala Leu Lys Leu Lys Val
 100 105 110
 Ala Glu Leu Val His Phe Leu Leu His Lys Tyr Arg Val Lys Glu Pro
 115 120 125
 Val Thr Lys Ala Glu Met Leu Glu Ser Val Ile Lys Asn Tyr Lys Arg
 130 135 140
 Tyr Phe Pro Val Ile Phe Gly Lys Ala Ser Glu Phe Met Gln Val Ile
 145 150 155 160

Phe Gly Thr Asp Val Lys Glu Val Asp Pro Ala Gly His Ser Tyr Ile		
165	170	175
Leu Val Thr Ala Leu Gly Leu Ser Cys Asp Ser Met Leu Gly Asp Gly		
180	185	190
His Ser Met Pro Lys Ala Ala Leu Leu Ile Ile Val Leu Gly Val Ile		
195	200	205
Leu Thr Lys Asp Asn Cys Ala Pro Glu Glu Val Ile Trp Glu Ala Leu		
210	215	220
Ser Val Met Gly Val Tyr Val Gly Lys Glu His Met Phe Tyr Gly Glu		
225	230	235
Pro Arg Lys Leu Leu Thr Gln Asp Trp Val Gln Glu Asn Tyr Leu Glu		
245	250	255
Tyr Arg Gln Val Pro Gly Ser Asp Pro Ala His Tyr Glu Phe Leu Trp		
260	265	270
Gly Ser Lys Ala His Ala Glu Thr Ser Tyr Glu Lys Val Ile Asn Tyr		
275	280	285
Leu Val Met Leu Asn Ala Arg Glu Pro Ile Cys Tyr Pro Ser Leu Tyr		
290	295	300
Glu Glu Val Leu Gly Glu Glu Gln Glu Gly Val		
305	310	315
<210> 130		
<211> 347		
<212> PRT		
<213> 人工序列		
<220>		
<223> MAGE-B10__Homo_sapiens__Q96LZ2		
<400> 130		
Met Pro Arg Gly Gln Lys Ser Lys Leu Arg Ala Arg Glu Lys Arg Arg		
1	5	10
Gln Ala Arg Gly Gly Leu Glu Asp Leu Ile Asp Ala Leu Asp Ile Leu		
20	25	30
Glu Glu Glu Glu Glu Ser Pro Pro Ser Ala Ser Ala Cys Leu Lys Asp		
35	40	45
Val Phe Gln Ser Ser Leu Asp Gly Ala Ser Asn Asn Pro His Gly Leu		
50	55	60
Arg Glu Ala Gln Ser Thr Ser Thr Ser Ala Thr Ala Ala Ser His Thr		
65	70	75
Arg His Pro Glu Gly Val Asn Asp Gln Met Glu Glu Arg Pro Ile Cys		
85	90	95

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

<210> 131

<211> 324

<212> PRT

<213> 人工序列

<220>

<223> MAGE-B16__Homo_sapiens__A2A368

<400> 131

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

305	310	315	320
Arg Ala Arg Ile			
<210> 132			
<211> 336			
<212> PRT			
<213> 人工序列			
<220>			
<223> MAGE-B17__Homo_sapiens__A8MXT2			
<400> 132			
Met Pro Arg Gly Gln Ala Ser Lys Arg Arg Ala Arg Glu Lys Arg Arg			
1 5 10 15			
Gln Ala Arg Gly Glu Asp Gln Cys Leu Gly Gly Ala Gln Ala Thr Ala			
20 25 30			
Ala Glu Lys Glu Lys Leu Pro Ser Ser Ser Ser Pro Ala Cys Gln Ser			
35 40 45			
Pro Pro Gln Ser Phe Pro Asn Ala Gly Ile Pro Gln Glu Ser Gln Arg			
50 55 60			
Ala Ser Tyr Pro Ser Ser Pro Ala Ser Ala Val Ser Leu Thr Ser Ser			
65 70 75 80			
Asp Glu Gly Ala Lys Gly Gln Lys Gly Glu Ser Pro Asn Ser Phe His			
85 90 95			
Gly Pro Ser Ser Ser Glu Ser Thr Gly Arg Asp Leu Leu Asn Thr Lys			
100 105 110			
Thr Gly Glu Leu Val Gln Phe Leu Leu Asn Lys Tyr Ile Arg Lys Glu			
115 120 125			
Pro Ile Thr Arg Glu Ala Met Leu Lys Val Ile Asn Arg Lys Tyr Lys			
130 135 140			
Gln His Phe Pro Glu Ile Leu Arg Arg Ser Thr Glu Asn Val Glu Val			
145 150 155 160			
Val Phe Gly Leu Tyr Leu Lys Glu Met Asp Pro Ser Arg Gln Ser Tyr			
165 170 175			
Val Leu Val Gly Lys Leu Asp Phe Pro Asn Gln Gly Ser Leu Ser Asp			
180 185 190			
Gly Gly Gly Phe Pro Leu Ser Gly Leu Leu Met Val Leu Leu Ser Thr			
195 200 205			
Ile Phe Met His Gly Asn Arg Ala Thr Glu Glu Glu Met Trp Glu Cys			
210 215 220			
Leu Asn Ala Leu Gly Met Tyr Lys Gly Arg Lys His Phe Ile Tyr Gly			
225 230 235 240			

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

Phe Gly Leu Asp Leu Lys Glu Asp Asn Pro Ser Ser His Thr Tyr Thr		
165	170	175
Leu Val Ser Lys Leu Asn Leu Thr Asn Asp Gly Asn Leu Ser Asn Asp		
180	185	190
Trp Asp Phe Pro Arg Asn Gly Leu Leu Met Pro Leu Leu Gly Val Ile		
195	200	205
Phe Leu Lys Gly Asn Ser Ala Thr Glu Glu Glu Ile Trp Lys Phe Met		
210	215	220
Asn Val Leu Gly Ala Tyr Asp Gly Glu Glu His Leu Ile Tyr Gly Glu		
225	230	235
Pro Arg Lys Phe Ile Thr Gln Asp Leu Val Gln Glu Lys Tyr Leu Lys		
245	250	255
Tyr Glu Gln Val Pro Asn Ser Asp Pro Pro Arg Tyr Gln Phe Leu Trp		
260	265	270
Gly Pro Arg Ala Tyr Ala Glu Thr Thr Lys Met Lys Val Leu Glu Phe		
275	280	285
Leu Ala Lys Met Asn Gly Ala Thr Pro Arg Asp Phe Pro Ser His Tyr		
290	295	300
Glu Glu Ala Leu Arg Asp Glu Glu Glu Arg Ala Gln Val Arg Ser Ser		
305	310	315
Val Arg Ala Arg Arg Arg Thr Thr Ala Thr Thr Phe Arg Ala Arg Ser		
325	330	335
Arg Ala Pro Phe Ser Arg Ser Ser His Pro Met		
340	345	

<210> 134

<211> 319

<212> PRT

<213> 人工序列

<220>

<223> MAGE-B2__Homo_sapiens__015479

<400> 134

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

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

<210> 135
 <211> 346
 <212> PRT
 <213> 人工序列
 <220>
 <223> MAGE-B3__Homo_sapiens__015480
 <400> 135

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

305	310	315	320
Ala Ala Met Leu Asn Asp Gly Ser Ser Ala Met Gly Arg Lys Cys Ser			
	325	330	335
Lys Ala Lys Ala Ser Ser Ser Ser His Ala			
	340	345	
<210> 136			
<211> 346			
<212> PRT			
<213> 人工序列			
<220>			
<223> MAGE-B4__Homo_sapiens__015481			
<400> 136			
Met Pro Arg Gly Gln Lys Ser Lys Leu Arg Ala Arg Glu Lys Arg Gln			
1	5	10	15
Arg Thr Arg Gly Gln Thr Gln Asp Leu Lys Val Gly Gln Pro Thr Ala			
	20	25	30
Ala Glu Lys Glu Glu Ser Pro Ser Ser Ser Ser Val Leu Arg Asp			
	35	40	45
Thr Ala Ser Ser Ser Leu Ala Phe Gly Ile Pro Gln Glu Pro Gln Arg			
	50	55	60
Glu Pro Pro Thr Thr Ser Ala Ala Ala Ala Met Ser Cys Thr Gly Ser			
65	70	75	80
Asp Lys Gly Asp Glu Ser Gln Asp Glu Glu Asn Ala Ser Ser Ser Gln			
	85	90	95
Ala Ser Thr Ser Thr Glu Arg Ser Leu Lys Asp Ser Leu Thr Arg Lys			
	100	105	110
Thr Lys Met Leu Val Gln Phe Leu Leu Tyr Lys Tyr Lys Met Lys Glu			
	115	120	125
Pro Thr Thr Lys Ala Glu Met Leu Lys Ile Ile Ser Lys Lys Tyr Lys			
	130	135	140
Glu His Phe Pro Glu Ile Phe Arg Lys Val Ser Gln Arg Thr Glu Leu			
145	150	155	160
Val Phe Gly Leu Ala Leu Lys Glu Val Asn Pro Thr Thr His Ser Tyr			
	165	170	175
Ile Leu Val Ser Met Leu Gly Pro Asn Asp Gly Asn Gln Ser Ser Ala			
	180	185	190
Trp Thr Leu Pro Arg Asn Gly Leu Leu Met Pro Leu Leu Ser Val Ile			
	195	200	205
Phe Leu Asn Gly Asn Cys Ala Arg Glu Glu Glu Ile Trp Glu Phe Leu			

210	215	220
Asn Met Leu Gly Ile Tyr Asp Gly Lys Arg His Leu Ile Phe Gly Glu		
225	230	235
Pro Arg Lys Leu Ile Thr Gln Asp Leu Val Gln Glu Lys Tyr Leu Glu		
245	250	255
Tyr Gln Gln Val Pro Asn Ser Asp Pro Pro Arg Tyr Gln Phe Leu Trp		
260	265	270
Gly Pro Arg Ala His Ala Glu Thr Ser Lys Met Lys Val Leu Glu Phe		
275	280	285
Leu Ala Lys Val Asn Asp Thr Thr Pro Asn Asn Phe Pro Leu Leu Tyr		
290	295	300
Glu Glu Ala Leu Arg Asp Glu Glu Glu Arg Ala Gly Ala Arg Pro Arg		
305	310	315
Val Ala Ala Arg Arg Gly Thr Thr Ala Met Thr Ser Ala Tyr Ser Arg		
325	330	335
Ala Thr Ser Ser Ser Ser Ser Gln Pro Met		
340	345	

<210> 137

<211> 275

<212> PRT

<213> 人工序列

<220>

<223> MAGE-B5__Homo_sapiens__Q9BZ81

<400> 137

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

115	120	125
Lys Thr Gly Leu Leu Met Thr Phe Leu Val Val Ile Phe Leu Lys Gly		
130	135	140
Asn Cys Ala Asn Lys Glu Asp Thr Trp Lys Phe Leu Asp Met Met Gln		
145	150	155
Ile Tyr Asp Gly Lys Lys Tyr Tyr Ile Tyr Gly Glu Pro Arg Lys Leu		
165	170	175
Ile Thr Gln Asp Phe Val Arg Leu Thr Tyr Leu Glu Tyr His Gln Val		
180	185	190
Pro Cys Ser Tyr Pro Ala His Tyr Gln Phe Leu Trp Gly Pro Arg Ala		
195	200	205
Tyr Thr Glu Thr Ser Lys Met Lys Val Leu Glu Tyr Leu Ala Lys Val		
210	215	220
Asn Asp Ile Ala Pro Gly Ala Phe Ser Ser Gln Tyr Glu Glu Ala Leu		
225	230	235
Gln Asp Glu Glu Glu Ser Pro Ser Gln Arg Cys Ser Arg Asn Trp His		
245	250	255
Tyr Cys Ser Gly Gln Asp Cys Leu Arg Ala Lys Phe Ser Ser Phe Ser		
260	265	270
Gln Pro Tyr		
275		
<210> 138		
<211> 407		
<212> PRT		
<213> 人工序列		
<220>		
<223> MAGE-B6__Homo_sapiens__Q8N7X4		
<400> 138		
Met Pro Arg Gly His Lys Ser Lys Leu Arg Thr Cys Glu Lys Arg Gln		
1	5	10
Glu Thr Asn Gly Gln Pro Gln Gly Leu Thr Gly Pro Gln Ala Thr Ala		
20	25	30
Glu Lys Gln Glu Glu Ser His Ser Ser Ser Ser Ser Ser Arg Ala Cys		
35	40	45
Leu Gly Asp Cys Arg Arg Ser Ser Asp Ala Ser Ile Pro Gln Glu Ser		
50	55	60
Gln Gly Val Ser Pro Thr Gly Ser Pro Asp Ala Val Val Ser Tyr Ser		
65	70	75
Lys Ser Asp Val Ala Ala Asn Gly Gln Asp Glu Lys Ser Pro Ser Thr		

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

Arg Ala Leu Arg Leu Arg Ala

405

<210> 139

<211> 1142

<212> PRT

<213> 人工序列

<220>

<223> MAGE-C1__Homo_sapiens__060732

<400> 139

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

1 5 10 15

Ser Ser Ser Glu Ser Pro Gln Ser Cys Pro Glu Gly Glu Asp Ser Gln

20 25 30

Ser Pro Leu Gln Ile Pro Gln Ser Ser Pro Glu Ser Asp Asp Thr Leu

35 40 45

Tyr Pro Leu Gln Ser Pro Gln Ser Arg Ser Glu Gly Glu Asp Ser Ser

50 55 60

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

65 70 75 80

Gln Ile Pro Gln Ser Ser Pro Glu Gly Asp Asp Thr Gln Ser Pro Leu

85 90 95

Gln Asn Ser Gln Ser Ser Pro Glu Gly Lys Asp Ser Leu Ser Pro Leu

100 105 110

Glu Ile Ser Gln Ser Pro Pro Glu Gly Glu Asp Val Gln Ser Pro Leu

115 120 125

Gln Asn Pro Ala Ser Ser Phe Phe Ser Ser Ala Leu Leu Ser Ile Phe

130 135 140

Gln Ser Ser Pro Glu Ser Thr Gln Ser Pro Phe Glu Gly Phe Pro Gln

145 150 155 160

Ser Val Leu Gln Ile Pro Val Ser Ala Ala Ser Ser Ser Thr Leu Val

165 170 175

Ser Ile Phe Gln Ser Ser Pro Glu Ser Thr Gln Ser Pro Phe Glu Gly

180 185 190

Phe Pro Gln Ser Pro Leu Gln Ile Pro Val Ser Arg Ser Phe Ser Ser

195 200 205

Thr Leu Leu Ser Ile Phe Gln Ser Ser Pro Glu Arg Thr Gln Ser Thr

210 215 220

Phe Glu Gly Phe Ala Gln Ser Pro Leu Gln Ile Pro Val Ser Pro Ser

225 230 235 240

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

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

Ser Pro Phe Ser Glu Glu Ser Ser Ser Pro Val Asp Glu Tyr Thr Ser			
865	870	875	880
Ser Ser Asp Thr Leu Leu Glu Ser Asp Ser Leu Thr Asp Ser Glu Ser			
	885	890	895
Leu Ile Glu Ser Glu Pro Leu Phe Thr Tyr Thr Leu Asp Glu Lys Val			
	900	905	910
Asp Glu Leu Ala Arg Phe Leu Leu Leu Lys Tyr Gln Val Lys Gln Pro			
	915	920	925
Ile Thr Lys Ala Glu Met Leu Thr Asn Val Ile Ser Arg Tyr Thr Gly			
	930	935	940
Tyr Phe Pro Val Ile Phe Arg Lys Ala Arg Glu Phe Ile Glu Ile Leu			
945	950	955	960
Phe Gly Ile Ser Leu Arg Glu Val Asp Pro Asp Asp Ser Tyr Val Phe			
	965	970	975
Val Asn Thr Leu Asp Leu Thr Ser Glu Gly Cys Leu Ser Asp Glu Gln			
	980	985	990
Gly Met Ser Gln Asn Arg Leu Leu Ile Leu Ile Leu Ser Ile Ile Phe			
	995	1000	1005
Ile Lys Gly Thr Tyr Ala Ser Glu Glu Val Ile Trp Asp Val Leu			
	1010	1015	1020
Ser Gly Ile Gly Val Arg Ala Gly Arg Glu His Phe Ala Phe Gly			
	1025	1030	1035
Glu Pro Arg Glu Leu Leu Thr Lys Val Trp Val Gln Glu His Tyr			
	1040	1045	1050
Leu Glu Tyr Arg Glu Val Pro Asn Ser Ser Pro Pro Arg Tyr Glu			
	1055	1060	1065
Phe Leu Trp Gly Pro Arg Ala His Ser Glu Val Ile Lys Arg Lys			
	1070	1075	1080
Val Val Glu Phe Leu Ala Met Leu Lys Asn Thr Val Pro Ile Thr			
	1085	1090	1095
Phe Pro Ser Ser Tyr Lys Asp Ala Leu Lys Asp Val Glu Glu Arg			
	1100	1105	1110
Ala Gln Ala Ile Ile Asp Thr Thr Asp Asp Ser Thr Ala Thr Glu			
	1115	1120	1125
Ser Ala Ser Ser Ser Val Met Ser Pro Ser Phe Ser Ser Glu			
	1130	1135	1140
<210> 140			
<211> 373			
<212> PRT			

<213> 人工序列

<220>

<223> MAGE-C2__Homo_sapiens__Q9UBF1

<400> 140

```

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

```

275	280	285
Val Pro His Ser Ser Pro Pro Tyr Tyr Glu Phe Leu Trp Gly Pro Arg		
290	295	300
Ala His Ser Glu Ser Ile Lys Lys Lys Val Leu Glu Phe Leu Ala Lys		
305	310	315
Leu Asn Asn Thr Val Pro Ser Ser Phe Pro Ser Trp Tyr Lys Asp Ala		
325	330	335
Leu Lys Asp Val Glu Glu Arg Val Gln Ala Thr Ile Asp Thr Ala Asp		
340	345	350
Asp Ala Thr Val Met Ala Ser Glu Ser Leu Ser Val Met Ser Ser Asn		
355	360	365
Val Ser Phe Ser Glu		
370		
<210> 141		
<211> 643		
<212> PRT		
<213> 人工序列		
<220>		
<223> MAGE-C3__Homo_sapiens__Q8TD91		
<400> 141		
Met Leu Leu Pro Cys His Trp Val Leu Asp Ala Thr Phe Ser Asp Gly		
1	5	10
Ser Leu Gly Gln Trp Val Lys Asn Thr Cys Ala Thr Tyr Ala Leu Ser		
20	25	30
Pro Val Val Leu Pro Pro Gln Pro Gln Pro Arg Lys Lys Ala Thr Asp		
35	40	45
Lys Asp Tyr Ser Ala Phe His Leu Gly His Leu Arg Glu Val Arg Leu		
50	55	60
Phe Leu Arg Gly Gly Thr Ser Asp Gln Arg Met Asp Ser Leu Val Leu		
65	70	75
Cys Pro Thr Tyr Phe Lys Leu Trp Arg Thr Leu Ser Gly Ser Pro Gly		
85	90	95
Leu Gln Leu Ser Asp Leu His Phe Gly Ser Gln Pro Glu Gly Lys Phe		
100	105	110
Ser Leu Arg Arg Ala Val Ser Val Lys Gln Arg Glu Glu Pro Gln Asp		
115	120	125
Trp Pro Leu Asn Glu Lys Arg Thr Leu Trp Lys Asp Ser Asp Leu Pro		
130	135	140
Thr Trp Arg Arg Gly Thr Gly Tyr Thr Leu Ser Leu Pro Ala Val Ser		

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

Gln Phe Leu Leu Leu Lys Tyr Gln Thr Lys Glu Pro Val Thr Lys Ala
 465 470 475 480
 Glu Met Leu Thr Thr Val Ile Lys Lys Tyr Lys Asp Tyr Phe Pro Met
 485 490 495
 Ile Phe Gly Lys Ala His Glu Phe Ile Glu Leu Ile Phe Gly Ile Ala
 500 505 510
 Leu Thr Asp Met Asp Pro Asp Asn His Ser Tyr Phe Phe Glu Asp Thr
 515 520 525
 Leu Asp Leu Thr Tyr Glu Gly Ser Leu Ile Asp Asp Gln Gly Met Pro
 530 535 540
 Lys Asn Cys Leu Leu Ile Leu Ile Leu Ser Met Ile Phe Ile Lys Gly
 545 550 555 560
 Ser Cys Val Pro Glu Glu Val Ile Trp Glu Val Leu Ser Ala Ile Gly
 565 570 575
 Pro Ile Gln Arg Pro Ala Arg Glu Val Leu Glu Phe Leu Ser Lys Leu
 580 585 590
 Ser Ser Ile Ile Pro Ser Ala Phe Pro Ser Trp Tyr Met Asp Ala Leu
 595 600 605
 Lys Asp Met Glu Asp Arg Ala Gln Ala Ile Ile Asp Thr Thr Asp Asp
 610 615 620
 Ala Thr Ala Met Ala Ser Ala Ser Pro Ser Val Met Ser Thr Asn Phe
 625 630 635 640
 Cys Pro Glu
 <210> 142
 <211> 778
 <212> PRT
 <213> 人工序列
 <220>
 <223> MAGE-D1__Homo_sapiens__Q9Y5V3
 <400> 142
 Met Ala Gln Lys Met Asp Cys Gly Ala Gly Leu Leu Gly Phe Gln Ala
 1 5 10 15
 Glu Ala Ser Val Glu Asp Ser Ala Leu Leu Met Gln Thr Leu Met Glu
 20 25 30
 Ala Ile Gln Ile Ser Glu Ala Pro Pro Thr Asn Gln Ala Thr Ala Ala
 35 40 45
 Ala Ser Pro Gln Ser Ser Gln Pro Pro Thr Ala Asn Glu Met Ala Asp
 50 55 60
 Ile Gln Val Ser Ala Ala Ala Ala Arg Pro Lys Ser Ala Phe Lys Val

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

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

690	695	700
Trp Ser Trp Asp Asp Ile Glu Phe Glu Leu Leu Thr Trp Asp Glu Glu		
705	710	715
Gly Asp Phe Gly Asp Pro Trp Ser Arg Ile Pro Phe Thr Phe Trp Ala		720
	725	730
Arg Tyr His Gln Asn Ala Arg Ser Arg Phe Pro Gln Thr Phe Ala Gly		735
	740	745
Pro Ile Ile Gly Pro Gly Gly Thr Ala Ser Ala Asn Phe Ala Ala Asn		750
	755	760
Phe Gly Ala Ile Gly Phe Phe Trp Val Glu		765
770	775	
<210> 143		
<211> 606		
<212> PRT		
<213> 人工序列		
<220>		
<223> MAGE-D2__Homo_sapiens__Q9UNF1		
<400> 143		
Met Ser Asp Thr Ser Glu Ser Gly Ala Gly Leu Thr Arg Phe Gln Ala		
1	5	10
Glu Ala Ser Glu Lys Asp Ser Ser Ser Met Met Gln Thr Leu Leu Thr		15
	20	25
Val Thr Gln Asn Val Glu Val Pro Glu Thr Pro Lys Ala Ser Lys Ala		30
	35	40
Leu Glu Val Ser Glu Asp Val Lys Val Ser Lys Ala Ser Gly Val Ser		45
	50	55
Lys Ala Thr Glu Val Ser Lys Thr Pro Glu Ala Arg Glu Ala Pro Ala		60
65	70	75
Thr Gln Ala Ser Ser Thr Thr Gln Leu Thr Asp Thr Gln Val Leu Ala		80
	85	90
Ala Glu Asn Lys Ser Leu Ala Ala Asp Thr Lys Lys Gln Asn Ala Asp		95
	100	105
Pro Gln Ala Val Thr Met Pro Ala Thr Glu Thr Lys Lys Val Ser His		110
	115	120
Val Ala Asp Thr Lys Val Asn Thr Lys Ala Gln Glu Thr Glu Ala Ala		125
	130	135
Pro Ser Gln Ala Pro Ala Asp Glu Pro Glu Pro Glu Ser Ala Ala Ala		140
145	150	155
Gln Ser Gln Glu Asn Gln Asp Thr Arg Pro Lys Val Lys Ala Lys Lys		160

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

Ala Asp Leu Lys	Ala Ala Ala Glu	Ala Ala Ala Glu	Ala Lys Ala Arg
485		490	495
Ala Glu Ile Arg	Ala Arg Met Gly	Ile Gly Leu Gly	Ser Glu Asn Ala
500		505	510
Ala Gly Pro Cys	Asn Trp Asp Glu	Ala Asp Ile Gly	Pro Trp Ala Lys
515		520	525
Ala Arg Ile Gln	Ala Gly Ala Glu	Ala Lys Ala Lys	Ala Gln Glu Ser
530		535	540
Gly Ser Ala Ser	Thr Gly Ala Ser	Thr Ser Thr Asn	Asn Ser Ala Ser
545		550	555
Ala Ser Ala Ser	Thr Ser Gly Gly	Phe Ser Ala Gly	Ala Ser Leu Thr
	565	570	575
Ala Thr Leu Thr	Phe Gly Leu Phe	Ala Gly Leu Gly	Gly Ala Gly Ala
	580	585	590
Ser Thr Ser Gly	Ser Ser Gly Ala	Cys Gly Phe Ser	Tyr Lys
595		600	605

<210> 144
 <211> 741
 <212> PRT
 <213> 人工序列
 <220>
 <223> MAGE-D4__Homo_sapiens__Q96JG8
 <400> 144

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

Ser Gln Val Val Ala Ser His Arg Val Ala Thr Pro Gln Val Ser Gly		
130	135	140
Glu Asp Thr Gln Pro Thr Thr Tyr Ala Ala Glu Ala Gln Gly Pro Thr		
145	150	155
Pro Glu Pro Pro Leu Ala Ser Pro Gln Thr Ser Gln Met Leu Val Thr		
	165	170
Ser Lys Met Ala Ala Pro Glu Ala Pro Ala Thr Ser Ala Gln Ser Gln		
	180	185
Thr Gly Ser Pro Ala Gln Glu Ala Ala Thr Glu Gly Pro Ser Ser Ala		
	195	200
Cys Ala Phe Ser Gln Ala Pro Cys Ala Arg Glu Val Asp Ala Asn Arg		
	210	215
Pro Ser Thr Ala Phe Leu Gly Gln Asn Asp Val Phe Asp Phe Thr Gln		
	225	230
Pro Ala Gly Val Ser Gly Met Ala Phe Pro Arg Pro Lys Arg Pro Ala		
	245	250
Pro Ala Gln Glu Ala Ala Thr Glu Gly Pro Ser Ala Ala Ser Gly Val		
	260	265
Pro Gln Thr Gly Pro Gly Arg Glu Val Ala Ala Thr Arg Pro Lys Thr		
	275	280
Thr Lys Ser Gly Lys Ala Leu Ala Lys Thr Arg Trp Val Glu Pro Gln		
	290	295
Asn Val Val Ala Ala Ala Ala Lys Ala Lys Met Ala Thr Ser Ile		
	305	310
Pro Glu Pro Glu Gly Ala Ala Ala Ala Thr Ala Gln His Ser Ala Glu		
	325	330
Pro Trp Ala Arg Met Gly Gly Lys Arg Thr Lys Lys Ser Lys His Leu		
	340	345
Asp Asp Glu Tyr Glu Ser Ser Glu Glu Glu Arg Glu Thr Pro Ala Val		
	355	360
Pro Pro Thr Trp Arg Ala Ser Gln Pro Ser Leu Thr Val Arg Ala Gln		
	370	375
Leu Ala Pro Arg Pro Pro Met Ala Pro Arg Ser Gln Ile Pro Ser Arg		
	385	390
His Val Leu Cys Leu Pro Pro Arg Asn Val Thr Leu Leu Gln Glu Arg		
	405	410
Ala Asn Lys Leu Val Lys Tyr Leu Met Ile Lys Asp Tyr Lys Lys Ile		
	420	425
Pro Ile Lys Arg Ala Asp Met Leu Lys Asp Val Ile Arg Glu Tyr Asp		

435	440	445
Glu His Phe Pro Glu Ile Ile	Glu Arg Ala Thr Tyr Thr	Leu Glu Lys
450	455	460
Lys Phe Gly Ile His Leu Lys	Glu Ile Asp Lys Glu Glu	His Leu Tyr
465	470	475
Ile Leu Val Cys Thr Arg Asp	Ser Ser Ala Arg Leu Leu	Gly Lys Thr
485	490	495
Lys Asp Thr Pro Arg Leu Ser	Leu Leu Val Ile Leu Gly	Val Ile
500	505	510
Phe Met Asn Gly Asn Arg Ala	Ser Glu Ala Val Leu Trp	Glu Ala Leu
515	520	525
Arg Lys Met Gly Leu Arg Pro	Gly Val Arg His Pro Phe	Leu Gly Asp
530	535	540
Leu Arg Lys Leu Ile Thr Asp	Asp Phe Val Lys Gln Lys	Tyr Leu Glu
545	550	555
Tyr Lys Lys Ile Pro Asn Ser	Asn Pro Pro Glu Tyr Glu	Phe Leu Trp
565	570	575
Gly Leu Arg Ala Arg His Glu	Thr Ser Lys Met Arg Val	Leu Arg Phe
580	585	590
Ile Ala Gln Asn Gln Asn Arg	Asp Pro Arg Glu Trp Lys	Ala His Phe
595	600	605
Leu Glu Ala Val Asp Asp Ala	Phe Lys Thr Met Asp Val	Asp Met Ala
610	615	620
Glu Glu His Ala Arg Ala Gln	Met Arg Ala Gln Met Asn	Ile Gly Asp
625	630	635
Glu Ala Leu Ile Gly Arg Trp	Ser Trp Asp Asp Ile Gln	Val Glu Leu
645	650	655
Leu Thr Trp Asp Glu Asp Gly	Asp Phe Gly Asp Ala Trp	Ala Arg Ile
660	665	670
Pro Phe Ala Phe Trp Ala Arg	Tyr His Gln Tyr Ile Leu	Asn Ser Asn
675	680	685
Arg Ala Asn Arg Arg Ala Thr	Trp Arg Ala Gly Val Ser	Ser Gly Thr
690	695	700
Asn Gly Gly Ala Ser Thr Ser	Val Leu Asp Gly Pro Ser	Thr Ser Ser
705	710	715
Thr Ile Arg Thr Arg Asn Ala	Ala Arg Ala Gly Ala Ser	Phe Phe Ser
725	730	735
Trp Ile Gln His Arg		
740		

<210> 145

<211> 373

<212> PRT

<213> 人工序列

<220>

<223> MAGE-_E1__Homo_sapiens__Q6IAI7

<400> 145

```

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

```

Gly Val Tyr Ala Gly Arg Glu His Phe Val Tyr Gly Glu Pro Arg Glu
 260 265 270
 Leu Leu Thr Lys Val Trp Val Gln Gly His Tyr Leu Glu Tyr Arg Glu
 275 280 285
 Val Pro His Ser Ser Pro Pro Tyr Tyr Glu Phe Leu Trp Gly Pro Arg
 290 295 300
 Ala His Ser Glu Ser Ile Lys Lys Lys Val Leu Glu Phe Leu Ala Lys
 305 310 315 320
 Leu Asn Asn Thr Val Pro Ser Ser Phe Pro Ser Trp Tyr Lys Asp Ala
 325 330 335
 Leu Lys Asp Val Glu Glu Arg Val Gln Ala Thr Ile Asp Thr Ala Asp
 340 345 350
 Asp Ala Thr Val Met Ala Ser Glu Ser Leu Ser Val Met Ser Ser Asn
 355 360 365
 Val Ser Phe Ser Asp
 370
 <210> 146
 <211> 957
 <212> PRT
 <213> 人工序列
 <220>
 <223> MAGE-E1_(MAGE1) __Homo_sapiens__Q9HCI5
 <400> 146
 Met Ser Leu Val Ser Gln Asn Ser Arg Arg Arg Arg Arg Val Ala
 1 5 10 15
 Lys Ala Thr Ala His Asn Ser Ser Trp Gly Glu Met Gln Ala Pro Asn
 20 25 30
 Ala Pro Gly Leu Pro Ala Asp Val Pro Gly Ser Asp Val Pro Gln Gly
 35 40 45
 Pro Ser Asp Ser Gln Ile Leu Gln Gly Leu Cys Ala Ser Glu Gly Pro
 50 55 60
 Ser Thr Ser Val Leu Pro Thr Ser Ala Glu Gly Pro Ser Thr Phe Val
 65 70 75 80
 Pro Pro Thr Ile Ser Glu Ala Ser Ser Ala Ser Gly Gln Pro Thr Ile
 85 90 95
 Ser Glu Gly Pro Gly Thr Ser Val Leu Pro Thr Pro Ser Glu Gly Leu
 100 105 110
 Ser Thr Ser Gly Pro Pro Thr Ile Ser Lys Gly Leu Cys Thr Ser Val
 115 120 125

Thr	Leu	Ala	Ala	Ser	Glu	Gly	Arg	Asn	Thr	Ser	Arg	Pro	Pro	Thr	Ser
130						135					140				
Ser	Glu	Glu	Pro	Ser	Thr	Ser	Val	Pro	Pro	Thr	Ala	Ser	Glu	Val	Pro
145					150					155					160
Ser	Thr	Ser	Leu	Pro	Pro	Thr	Pro	Gly	Glu	Gly	Thr	Ser	Thr	Ser	Val
				165						170					175
Pro	Pro	Thr	Ala	Tyr	Glu	Gly	Pro	Ser	Thr	Ser	Val	Val	Pro	Thr	Pro
			180							185					190
Asp	Glu	Gly	Pro	Ser	Thr	Ser	Val	Leu	Pro	Thr	Pro	Gly	Glu	Gly	Pro
			195							200					205
Gly	Thr	Ser	Val	Pro	Leu	Ala	Ala	Thr	Glu	Gly	Leu	Ser	Thr	Ser	Val
			210							215					220
Gln	Ala	Thr	Pro	Asp	Glu	Gly	Pro	Ser	Thr	Ser	Val	Pro	Pro	Thr	Ala
225					230						235				240
Thr	Glu	Gly	Leu	Ser	Thr	Pro	Val	Pro	Pro	Thr	Arg	Asp	Glu	Gly	Pro
					245						250				255
Ser	Thr	Ser	Val	Pro	Ala	Thr	Pro	Gly	Glu	Gly	Pro	Ser	Thr	Ser	Val
			260								265				270
Leu	Pro	Ala	Ala	Ser	Asp	Gly	Gln	Ser	Ile	Ser	Leu	Val	Pro	Thr	Arg
			275												285
Gly	Lys	Gly	Ser	Ser	Thr	Ser	Val	Pro	Pro	Thr	Ala	Thr	Glu	Gly	Leu
			290												300
Ser	Thr	Ser	Val	Gln	Pro	Thr	Ala	Gly	Glu	Gly	Ser	Ser	Thr	Ser	Val
305					310						315				320
Pro	Pro	Thr	Pro	Gly	Gly	Gly	Leu	Ser	Thr	Ser	Val	Pro	Pro	Thr	Ala
				325							330				335
Thr	Glu	Glu	Leu	Ser	Thr	Ser	Val	Pro	Pro	Thr	Pro	Gly	Glu	Gly	Pro
			340												350
Ser	Thr	Ser	Val	Leu	Pro	Ile	Pro	Gly	Glu	Gly	Leu	Ser	Thr	Ser	Val
			355												365
Pro	Pro	Thr	Ala	Ser	Asp	Gly	Ser	Asp	Thr	Ser	Val	Pro	Pro	Thr	Pro
			370												380
Gly	Glu	Gly	Ala	Ser	Thr	Leu	Val	Gln	Pro	Thr	Ala	Pro	Asp	Gly	Pro
385					390						395				400
Gly	Ser	Ser	Val	Leu	Pro	Asn	Pro	Gly	Glu	Gly	Pro	Ser	Thr	Leu	Phe
				405							410				415
Ser	Ser	Ser	Ala	Ser	Val	Asp	Arg	Asn	Pro	Ser	Lys	Cys	Ser	Leu	Val
			420												430
Leu	Pro	Ser	Pro	Arg	Val	Thr	Lys	Ala	Ser	Val	Asp	Ser	Asp	Ser	Glu

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

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

<210> 147

<211> 523

<212> PRT

<213> 人工序列

<220>

<223> MAGE-E2__Homo_sapiens__Q8TD90

<400> 147

Met Ser Leu Val Ser Gln Asn Ala Arg His Cys Ser Ala Glu Ile Thr		
1	5	10
Ala Asp Tyr Gly Asp Gly Arg Gly Glu Ile Gln Ala Thr Asn Ala Ser		
20	25	30
Gly Ser Pro Thr Ser Met Leu Val Val Asp Ala Pro Gln Cys Pro Gln		
35	40	45

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

355	360	365
Ile Glu Val Asp Thr Ser Glu His Ile Tyr Leu Leu Val Gln Gln Pro		
370	375	380
Glu Ser Glu Glu Glu Gln Val Met Leu Glu Ser Leu Gly Arg Pro Thr		
385	390	395
Gln Glu Tyr Val Met Pro Ile Leu Gly Leu Ile Phe Leu Met Gly Asn		400
405	410	415
Arg Val Lys Glu Ala Asn Val Trp Asn Leu Leu Arg Arg Phe Ser Val		
420	425	430
Asp Val Gly Arg Lys His Ser Ile Thr Arg Lys Leu Met Arg Gln Arg		
435	440	445
Tyr Leu Glu Cys Arg Pro Leu Ser Tyr Ser Asn Pro Val Glu Tyr Glu		
450	455	460
Leu Leu Trp Gly Pro Arg Ala His His Glu Thr Ile Lys Met Lys Val		
465	470	475
Leu Glu Tyr Met Ala Arg Leu Tyr Arg Lys Arg Pro Gln Asn Trp Pro		480
485	490	495
Glu Gln Tyr Arg Glu Ala Val Glu Asp Glu Glu Ala Arg Ala Lys Ser		
500	505	510
Glu Ala Thr Ile Met Phe Phe Leu Asp Pro Thr		
515	520	
<210> 148		
<211> 307		
<212> PRT		
<213> 人工序列		
<220>		
<223> MAGE-F1__Homo_sapiens__Q9HAY2		
<400> 148		
Met Leu Gln Thr Pro Glu Ser Arg Gly Leu Pro Val Pro Gln Ala Glu		
1	5	10
Gly Glu Lys Asp Gly Gly His Asp Gly Glu Thr Arg Ala Pro Thr Ala		
20	25	30
Ser Gln Glu Arg Pro Lys Glu Glu Leu Gly Ala Gly Arg Glu Glu Gly		
35	40	45
Ala Ala Glu Pro Ala Leu Thr Arg Lys Gly Ala Arg Ala Leu Ala Ala		
50	55	60
Lys Ala Leu Ala Arg Arg Arg Ala Tyr Arg Arg Leu Asn Arg Thr Val		
65	70	75
Ala Glu Leu Val Gln Phe Leu Leu Val Lys Asp Lys Lys Lys Ser Pro		80

	85		90		95
Ile Thr Arg Ser Glu Met Val Lys Tyr Val Ile Gly Asp Leu Lys Ile					
100		105		110	
Leu Phe Pro Asp Ile Ile Ala Arg Ala Ala Glu His Leu Arg Tyr Val					
115		120		125	
Phe Gly Phe Glu Leu Lys Gln Phe Asp Arg Lys His His Thr Tyr Ile					
130		135		140	
Leu Ile Asn Lys Leu Lys Pro Leu Glu Glu Glu Glu Glu Glu Asp Leu					
145		150		155	160
Gly Gly Asp Gly Pro Arg Leu Gly Leu Leu Met Met Ile Leu Gly Leu					
165		170		175	
Ile Tyr Met Arg Gly Asn Ser Ala Arg Glu Ala Gln Val Trp Glu Met					
180		185		190	
Leu Arg Arg Leu Gly Val Gln Pro Ser Lys Tyr His Phe Leu Phe Gly					
195		200		205	
Tyr Pro Lys Arg Leu Ile Met Glu Asp Phe Val Gln Gln Arg Tyr Leu					
210		215		220	
Ser Tyr Arg Arg Val Pro His Thr Asn Pro Pro Glu Tyr Glu Phe Ser					
225		230		235	240
Trp Gly Pro Arg Ser Asn Leu Glu Ile Ser Lys Met Glu Val Leu Gly					
245		250		255	
Phe Val Ala Lys Leu His Lys Lys Glu Pro Gln His Trp Pro Val Gln					
260		265		270	
Tyr Arg Glu Ala Leu Ala Asp Glu Ala Asp Arg Ala Arg Ala Lys Ala					
275		280		285	
Arg Ala Glu Ala Ser Met Arg Ala Arg Ala Ser Ala Arg Ala Gly Ile					
290		295		300	
His Leu Trp					
305					
<210> 149					
<211> 219					
<212> PRT					
<213> 人工序列					
<220>					
<223> MAGE-H1__Homo_sapiens__Q9H213					
<400> 149					
Met Pro Arg Gly Arg Lys Ser Arg Arg Arg Asn Ala Arg Ala Ala					
1	5	10	15		
Glu Glu Asn Arg Asn Asn Arg Lys Ile Gln Ala Ser Glu Ala Ser Glu					

			20				25				30					
Thr	Pro	Met	Ala	Ala	Ser	Val	Val	Ala	Ser	Thr	Pro	Glu	Asp	Asp	Leu	
			35				40				45					
Ser	Gly	Pro	Glu	Glu	Asp	Pro	Ser	Thr	Pro	Glu	Glu	Ala	Ser	Thr	Thr	
			50				55				60					
Pro	Glu	Glu	Ala	Ser	Ser	Thr	Ala	Gln	Ala	Gln	Lys	Pro	Ser	Val	Pro	
65							70				75				80	
Arg	Ser	Asn	Phe	Gln	Gly	Thr	Lys	Lys	Ser	Leu	Leu	Met	Ser	Ile	Leu	
			85				90				95					
Ala	Leu	Ile	Phe	Ile	Met	Gly	Asn	Ser	Ala	Lys	Glu	Ala	Leu	Val	Trp	
			100				105				110					
Lys	Val	Leu	Gly	Lys	Leu	Gly	Met	Gln	Pro	Gly	Arg	Gln	His	Ser	Ile	
			115				120				125					
Phe	Gly	Asp	Pro	Lys	Lys	Ile	Val	Thr	Glu	Glu	Phe	Val	Arg	Arg	Gly	
130							135				140					
Tyr	Leu	Ile	Tyr	Lys	Pro	Val	Pro	Arg	Ser	Ser	Pro	Val	Glu	Tyr	Glu	
145							150				155				160	
Phe	Phe	Trp	Gly	Pro	Arg	Ala	His	Val	Glu	Ser	Ser	Lys	Leu	Lys	Val	
			165				170				175					
Met	His	Phe	Val	Ala	Arg	Val	Arg	Asn	Arg	Cys	Ser	Lys	Asp	Trp	Pro	
			180				185				190					
Cys	Asn	Tyr	Asp	Trp	Asp	Ser	Asp	Asp	Asp	Ala	Glu	Val	Glu	Ala	Ile	
			195				200				205					
Leu	Asn	Ser	Gly	Ala	Arg	Gly	Tyr	Ser	Ala	Pro						
210							215									
<210> 150																
<211> 1249																
<212> PRT																
<213> 人工序列																
<220>																
<223> MAGEL2__Homo_sapiens__Q9UJ55																
<400> 150																
Met	Ser	Gln	Leu	Ser	Lys	Asn	Leu	Gly	Asp	Ser	Ser	Pro	Pro	Ala	Glu	
1				5				10				15				
Ala	Pro	Lys	Pro	Pro	Val	Tyr	Ser	Arg	Pro	Thr	Val	Leu	Met	Arg	Ala	
			20				25				30					
Pro	Pro	Ala	Ser	Ser	Arg	Ala	Pro	Pro	Val	Pro	Trp	Asp	Pro	Pro	Pro	
			35				40				45					
Ile	Asp	Leu	Gln	Ala	Ser	Leu	Ala	Ala	Trp	Gln	Ala	Pro	Gln	Pro	Ala	

50	55	60
Trp Glu Ala Pro Gln Gly	Gln Leu Pro Ala Pro	Val Val Pro Met Thr
65	70	75
Gln Pro Pro Ala Leu Gly	Gly Pro Ile Val Pro	Ala Pro Pro Leu Gly
85	90	95
Gly Pro Met Gly Lys Pro	Pro Thr Pro Gly Val	Leu Met Val His Pro
100	105	110
Pro Pro Pro Gly Ala Pro	Met Ala Gln Pro Pro	Thr Pro Gly Val Leu
115	120	125
Met Val His Pro Ser Ala	Pro Gly Ala Pro Met	Ala His Pro Pro Pro
130	135	140
Pro Gly Thr Pro Met Ser	His Pro Pro Pro Gly	Thr Pro Met Ala
145	150	155
His Pro Pro Pro Pro Gly	Thr Pro Met Ala His	Pro Pro Pro Pro Gly
165	170	175
Thr Pro Met Val His Pro	Pro Pro Pro Gly Thr	Pro Met Ala His Pro
180	185	190
Pro Pro Pro Gly Thr Pro	Met Ala His Pro Pro	Pro Pro Gly Thr Pro
195	200	205
Met Ala His Pro Pro Pro	Pro Gly Thr Pro Met	Ala His Pro Pro Pro
210	215	220
Pro Gly Thr Pro Met Ala	Gln Pro Pro Ala Pro	Gly Val Leu Met Ala
225	230	235
Gln Pro Leu Thr Pro Gly	Val Leu Met Val Gln	Pro Ala Ala Pro Gly
245	250	255
Ala Pro Met Val Gln Pro	Pro Pro Ala Ala Met	Met Thr Gln Pro Gln
260	265	270
Pro Ser Gly Ala Pro Met	Ala Lys Pro Pro Gly	Pro Gly Val Leu Met
275	280	285
Ile His Pro Pro Gly Ala	Arg Ala Pro Met Thr	Gln Pro Pro Ala Ser
290	295	300
Gly Ala Pro Met Ala Gln	Pro Ala Ala Pro Pro	Ala Gln Pro Met Ala
305	310	315
Pro Pro Ala Gln Pro Met	Ala Ser Trp Ala Pro	Gln Ala Gln Pro Leu
325	330	335
Ile Leu Gln Ile Gln Ser	Gln Val Ile Arg Ala	Pro Pro Gln Val Pro
340	345	350
Gln Gly Pro Gln Ala Pro	Pro Ala Gln Leu Ala	Thr Pro Pro Gly Trp
355	360	365

Gln Ala Thr Ser Pro Gly Trp Gln Ala Thr Gln Gln Gly Trp Gln Ala		
370	375	380
Thr Pro Leu Thr Trp Gln Thr Thr Gln Val Thr Trp Gln Ala Pro Ala		
385	390	395 400
Val Thr Trp Gln Val Pro Pro Pro Met Arg Gln Gly Pro Pro Pro Ile		
405	410	415
Arg Pro Gly Pro Pro Pro Ile Arg Pro Gly Pro Pro Pro Val Arg Gln		
420	425	430
Ala Pro Pro Leu Ile Arg Gln Ala Pro Pro Val Ile Arg Gln Ala Pro		
435	440	445
Pro Val Ile Arg Gln Ala Pro Pro Val Ile Arg Gln Ala Pro Ala Val		
450	455	460
Ile Arg Gln Ala Pro Pro Val Ile Arg Gln Ala Pro Pro Val Ile Arg		
465	470	475 480
Gln Ala Pro Pro Val Ile Arg Gln Ala Pro Pro Leu Ile Arg Gln Ala		
485	490	495
Pro Pro Pro Ile Arg Pro Ala Pro Gln Val Leu Ala Thr Gln Pro Pro		
500	505	510
Leu Trp Gln Ala Leu Pro Pro Pro Pro Pro Leu Arg Gln Ala Pro Gln		
515	520	525
Ala Arg Leu Pro Ala Pro Gln Val Gln Ala Ala Pro Gln Val Pro Thr		
530	535	540
Ala Pro Pro Ala Thr Gln Val Pro Ala Ala Pro Pro Ala Gly Pro Gln		
545	550	555 560
Val Pro Gln Pro Val Leu Pro Ala Pro Leu Ser Ala Pro Leu Ser Ala		
565	570	575
Pro Gln Ala Val His Cys Pro Ser Ile Ile Trp Gln Ala Pro Lys Gly		
580	585	590
Gln Pro Pro Val Pro His Glu Ile Pro Thr Ser Met Glu Phe Gln Glu		
595	600	605
Val Gln Gln Thr Gln Ala Leu Ala Trp Gln Ala Gln Lys Ala Pro Thr		
610	615	620
His Ile Trp Gln Pro Leu Pro Ala Gln Glu Ala Gln Arg Gln Ala Pro		
625	630	635 640
Pro Leu Val Gln Leu Glu Gln Pro Phe Gln Gly Ala Pro Pro Ser Gln		
645	650	655
Lys Ala Val Gln Ile Gln Leu Pro Pro Gln Gln Ala Gln Ala Ser Gly		
660	665	670
Pro Gln Ala Glu Val Pro Thr Leu Pro Leu Gln Pro Ser Trp Gln Ala		

675	680	685
Pro Pro Ala Val Leu Gln Ala Gln Pro Gly Pro Pro Val Ala Ala Ala		
690	695	700
Asn Phe Pro Leu Gly Ser Ala Lys Ser Leu Met Thr Pro Ser Gly Glu		
705	710	715
Cys Arg Ala Ser Ser Ile Asp Arg Arg Gly Ser Ser Lys Glu Arg Arg		
725	730	735
Thr Ser Ser Lys Glu Arg Arg Ala Pro Ser Lys Asp Arg Met Ile Phe		
740	745	750
Ala Ala Thr Phe Cys Ala Pro Lys Ala Val Ser Ala Ala Arg Ala His		
755	760	765
Leu Pro Ala Ala Trp Lys Asn Leu Pro Ala Thr Pro Glu Thr Phe Ala		
770	775	780
Pro Ser Ser Ser Val Phe Pro Ala Thr Ser Gln Phe Gln Pro Ala Ser		
785	790	795
Leu Asn Ala Phe Lys Gly Pro Ser Ala Ala Ser Glu Thr Pro Lys Ser		
805	810	815
Leu Pro Tyr Ala Leu Gln Asp Pro Phe Ala Cys Val Glu Ala Leu Pro		
820	825	830
Ala Val Pro Trp Val Pro Gln Pro Asn Met Asn Ala Ser Lys Ala Ser		
835	840	845
Gln Ala Val Pro Thr Phe Leu Met Ala Thr Ala Ala Ala Pro Gln Ala		
850	855	860
Thr Ala Thr Thr Gln Glu Ala Ser Lys Thr Ser Val Glu Pro Pro Arg		
865	870	875
Arg Ser Gly Lys Ala Thr Arg Lys Lys Lys His Leu Glu Ala Gln Glu		
885	890	895
Asp Ser Arg Gly His Thr Leu Ala Phe His Asp Trp Gln Gly Pro Arg		
900	905	910
Pro Trp Glu Asn Leu Asn Leu Ser Asp Trp Glu Val Gln Ser Pro Ile		
915	920	925
Gln Val Ser Gly Asp Trp Glu His Pro Asn Thr Pro Arg Gly Leu Ser		
930	935	940
Gly Trp Glu Gly Pro Ser Thr Ser Arg Ile Leu Ser Gly Trp Glu Gly		
945	950	955
Pro Ser Ala Ser Trp Ala Leu Ser Ala Trp Glu Gly Pro Ser Thr Ser		
965	970	975
Arg Ala Leu Gly Leu Ser Glu Ser Pro Gly Ser Ser Leu Pro Val Val		
980	985	990

Val Ser Glu Val Ala Ser Val Ser Pro Gly Ser Ser Ala Thr Gln Asp		
995	1000	1005
Asn Ser Lys Val Glu Ala Gln Pro Leu Ser Pro Leu Asp Glu Arg		
1010	1015	1020
Ala Asn Ala Leu Val Gln Phe Leu Leu Val Lys Asp Gln Ala Lys		
1025	1030	1035
Val Pro Val Gln Arg Ser Glu Met Val Lys Val Ile Leu Arg Glu		
1040	1045	1050
Tyr Lys Asp Glu Cys Leu Asp Ile Ile Asn Arg Ala Asn Asn Lys		
1055	1060	1065
Leu Glu Cys Ala Phe Gly Tyr Gln Leu Lys Glu Ile Asp Thr Lys		
1070	1075	1080
Asn His Ala Tyr Ile Ile Ile Asn Lys Leu Gly Tyr His Thr Gly		
1085	1090	1095
Asn Leu Val Ala Ser Tyr Leu Asp Arg Pro Lys Phe Gly Leu Leu		
1100	1105	1110
Met Val Val Leu Ser Leu Ile Phe Met Lys Gly Asn Cys Val Arg		
1115	1120	1125
Glu Asp Leu Ile Phe Asn Phe Leu Phe Lys Leu Gly Leu Asp Val		
1130	1135	1140
Arg Glu Thr Asn Gly Leu Phe Gly Asn Thr Lys Lys Leu Ile Thr		
1145	1150	1155
Glu Val Phe Val Arg Gln Lys Tyr Leu Glu Tyr Arg Arg Ile Pro		
1160	1165	1170
Tyr Thr Glu Pro Ala Glu Tyr Glu Phe Leu Trp Gly Pro Arg Ala		
1175	1180	1185
Phe Leu Glu Thr Ser Lys Met Leu Val Leu Arg Phe Leu Ala Lys		
1190	1195	1200
Leu His Lys Lys Asp Pro Gln Ser Trp Pro Phe His Tyr Leu Glu		
1205	1210	1215
Ala Leu Ala Glu Cys Glu Trp Glu Asp Thr Asp Glu Asp Glu Pro		
1220	1225	1230
Asp Thr Gly Asp Ser Ala His Gly Pro Thr Ser Arg Pro Pro Pro		
1235	1240	1245
Arg		
<210> 151		
<211> 712		
<212> PRT		
<213> 人工序列		

<220>

<223> 具有大T抗原S220A替换的ILC-4

<400> 151

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	Leu	Glu	Met	Asp	Leu	Val	Leu	Asn	Arg	Lys	Glu	Arg	Glu	Ala	Leu
	195					200					205				
Cys	Lys	Leu	Leu	Glu	Ile	Ala	Pro	Asn	Cys	Tyr	Gly	Asn	Ile	Pro	Leu
	210					215					220				
Met	Lys	Ala	Ala	Phe	Lys	Arg	Ser	Cys	Leu	Lys	His	His	Pro	Asp	Lys
225					230				235					240	
Gly	Gly	Asn	Pro	Val	Ile	Met	Met	Glu	Leu	Asn	Thr	Leu	Trp	Ser	Lys
			245					250					255		
Phe	Gln	Gln	Asn	Ile	His	Lys	Leu	Arg	Ser	Asp	Phe	Ser	Met	Phe	Asp
		260						265					270		
Glu	Val	Asp	Glu	Ala	Pro	Ile	Tyr	Gly	Thr	Thr	Lys	Phe	Lys	Glu	Trp
	275						280					285			

Trp	Arg	Ser	Gly	Gly	Phe	Ser	Phe	Gly	Lys	Ala	Tyr	Glu	Tyr	Gly	Pro
290						295				300					
Asn	Pro	His	Gly	Thr	Asn	Ser	Arg	Ser	Arg	Lys	Pro	Ser	Ser	Asn	Ala
305					310					315					320
Ser	Arg	Gly	Ala	Pro	Ser	Gly	Ser	Ser	Pro	Pro	His	Ser	Gln	Ser	Ser
				325					330					335	
Ser	Ser	Gly	Tyr	Gly	Ser	Phe	Ser	Ala	Ser	Gln	Ala	Ser	Asp	Ser	Gln
			340					345					350		
Ser	Arg	Gly	Pro	Asp	Ile	Pro	Pro	Glu	His	His	Glu	Glu	Pro	Thr	Ser
		355				360					365				
Ser	Ser	Gly	Ser	Ser	Ser	Arg	Glu	Glu	Thr	Thr	Asn	Ser	Gly	Arg	Glu
		370				375					380				
Ser	Ser	Thr	Pro	Asn	Gly	Thr	Ser	Val	Pro	Arg	Asn	Ser	Ser	Arg	Thr
385				390						395					400
Asp	Gly	Thr	Trp	Glu	Asp	Leu	Phe	Cys	Asp	Glu	Ser	Leu	Ser	Ala	Pro
				405					410					415	
Glu	Pro	Pro	Ser	Ser	Ser	Glu	Glu	Pro	Glu	Glu	Pro	Pro	Ser	Ser	Arg
			420					425					430		
Ser	Ser	Pro	Arg	Gln	Pro	Pro	Ser	Ser	Ser	Ala	Glu	Glu	Ala	Ser	Ser
		435					440				445				
Ser	Gln	Phe	Thr	Asp	Glu	Glu	Tyr	Arg	Ser	Ser	Ser	Phe	Thr	Thr	Pro
450					455						460				
Lys	Thr	Pro	Pro	Pro	Phe	Ser	Arg	Lys	Arg	Lys	Phe	Gly	Gly	Ser	Arg
465					470					475					480
Ser	Ser	Ala	Ser	Ser	Ala	Ser	Ser	Ala	Ser	Phe	Thr	Ser	Thr	Pro	Pro
				485					490					495	
Lys	Pro	Lys	Lys	Asn	Arg	Glu	Thr	Pro	Val	Pro	Thr	Asp	Phe	Pro	Ile
			500					505					510		
Asp	Leu	Ser	Asp	Tyr	Leu	Ser	His	Ala	Val	Glu	Phe	Thr	Cys	Leu	Leu
		515					520					525			
Ala	Ser	Met	Gly	Leu	Gln	Leu	Asn	Leu	Thr	Tyr	Glu	Arg	Lys	Asp	Asn
		530					535				540				
Thr	Thr	Val	Thr	Arg	Leu	Leu	Asn	Ile	Asn	Pro	Asn	Lys	Thr	Ser	Ala
545					550					555					560
Ser	Gly	Ser	Cys	Gly	Ala	His	Leu	Val	Thr	Leu	Glu	Leu	His	Ser	Glu
				565					570					575	
Gly	Thr	Thr	Val	Leu	Leu	Phe	Gln	Phe	Gly	Met	Asn	Ala	Ser	Ser	Ser
			580					585				590			
Arg	Phe	Phe	Leu	Gln	Gly	Ile	Gln	Leu	Asn	Thr	Ile	Leu	Pro	Asp	Ala

595	600	605
Arg Asp Pro Ala Phe Lys Ala Ala Asn Gly Ser Leu Arg Ala Leu Gln		
610	615	620
Ala Thr Val Gly Asn Ser Tyr Lys Cys Asn Ala Glu Glu His Val Arg		
625	630	635
Val Thr Lys Ala Phe Ser Val Asn Ile Phe Lys Val Trp Val Gln Ala		
645	650	655
Phe Lys Val Glu Gly Gly Gln Phe Gly Ser Val Glu Glu Cys Leu Leu		
660	665	670
Asp Glu Asn Ser Met Leu Ile Pro Ile Ala Val Gly Gly Ala Leu Ala		
675	680	685
Gly Leu Val Leu Ile Val Leu Ile Ala Tyr Leu Val Gly Arg Lys Arg		
690	695	700
Ser His Ala Gly Tyr Gln Thr Ile		
705	710	

<210> 152

<211> 5

<212> PRT

<213> 人工序列

<220>

<223> 示例性连接物1

<400> 152

Gly Pro Gly Pro Gly

1 5

<210> 153

<211> 5

<212> PRT

<213> 人工序列

<220>

<223> 示例性连接物No. 2

<400> 153

Pro Met Gly Leu Pro

1 5

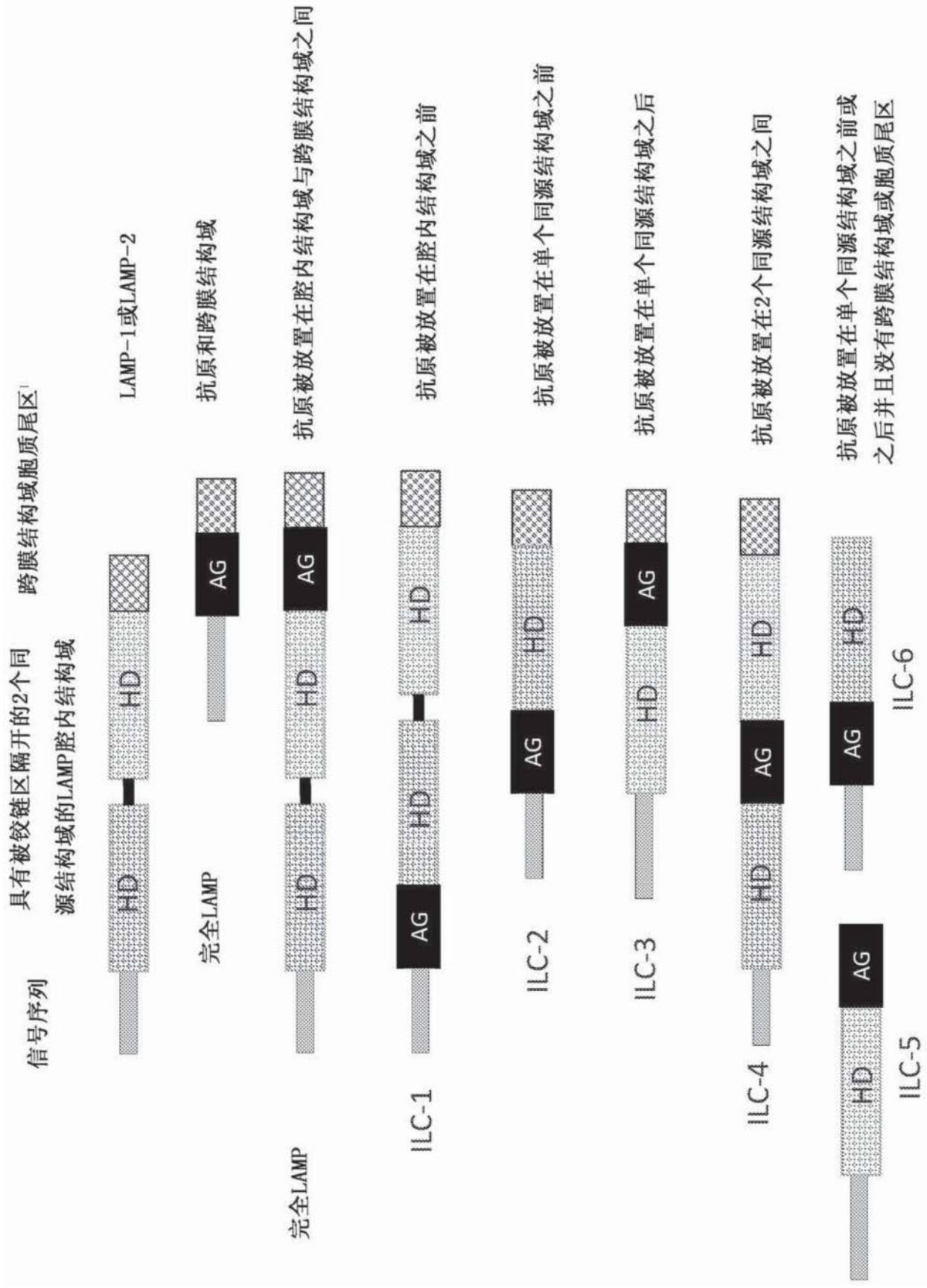


图1

基因名称 登记号	替代名称	SEQ ID NO.	直系同源物	信号 序列	腔内结构域			跨膜结构域	胞质尾区
					第一同源 结构域	铰链区	第二同源 结构域		
h. LAMP-1 NP_005552.3	CD107a; LAMPA; LGP120	1	SEQ ID NO: 6-24	1-28	29-194	195-227	第228位至第 381或382位	第382或383位 至第405位	406-417
h. LAMP-2 NP_002285.1	CD107b; LAMPB; LGP110	2	SEQ ID NO:25-43	1-28	29-192	193-228	229-375	376-399	400-410
h. LAMP-3 NP_055213.2	CD208; DC LAMP; DC- LAMP; DCLAMP; TSC403	3	SEQ ID NO:44-55	1-27	28-219	220-234	235-381	382-402	403-416
LIMP-2 Q14108	AMRF; EPM4; LGP85; CD36L2; HLGP85; LIMP1I; SR-BII; SCARB2	4	SEQ ID NO:56-66	*5-27 跨膜 *不可 切割的	28-433			434-459	460-478
h. Endolyn NP_006007.2	唾液黏蛋白 CD164 MUC-24	5	SEQ ID NO:73-79	1-23	24-162			163-183	184-197
Macrosalain NP_001242.2	CD68	80	SEQ ID NO: 81-92	1-21	22-319			320-344	345-354

图2A

LAMP5 NP_036393	BD-LAMP	93	SEQ ID NO: 94-101	1-29	30-235	236-256	257-280
h. LIMBIC NP_002329.2	LSAMP IGLON3	67	SEQ ID NO: 68-72 和 102-113	1-28	29-315	316-338	无尾区

图2A续

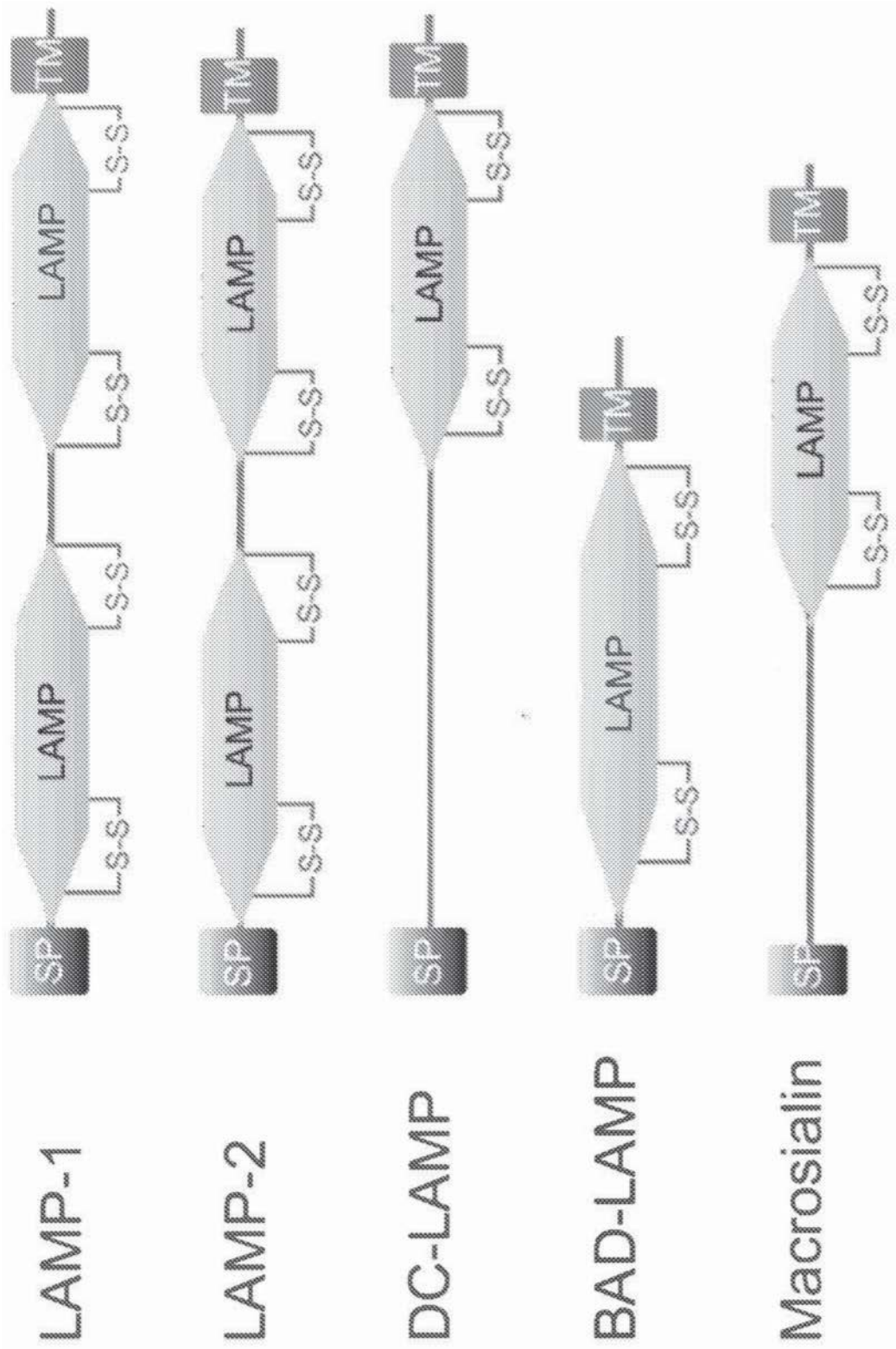


图2B

人类LAMP-1与直系同源序列的比对

信号序列	LAMP同源结构域1	
	1	
SEQIDNO:1	MAAPGSARRPLLLLLLLLLGLMH-CASAAMFMVKNNGN-GTACIMANFSAAFSVNYDTKS	58
SEQIDNO:6	MAAPGAR-RPLL---LLLLAGLAH--GASALFEVK-NN-GTTCIMASFSASFLTYYETAN	52
SEQIDNO:7	-----MARAAG-VCWTLMLGCVFA-AHAVTFEVT DGN--STCIKGELNASFSISYNTTN	50
SEQIDNO:8	--MSWRQVKMPVYWMVMLLIGVVQ--VATAVQFEVKDGKTNITCILADLSINFSVSYNVSS	58
SEQIDNO:9	MAAPGSARRPLLLLLLLLLGLVH-CASAAMFMVKNNGN-GTACIMANFSASFSVNYDTKS	58
SEQIDNO:10	MAAPGSARRSLLL-LLLLLGLTH-CASAAMFIVKNNGN-GTACIMANFSAAFSVNYDTKS	57
SEQIDNO:11	MAAPGGARPRPL--LLLLLAGLVH--GAAAVFVVKDAN-GTACIMANFSAAFLASYETRS	55
SEQIDNO:12	MEAPGGARRPLLLL---LLGLVH--GASAVFVVRNSN-GTACIMANFSAVFSVIYESKS	54
SEQIDNO:13	MAAPGGARRRPLL--LLFAGLVH--GASAVFVKNNGN-GTACIMADFSATFLT SYDTRS	55
SEQIDNO:14	MAAPGAR-RPLL--LLLLAGLAH--SAPALFEVKDNN-GTACIMASFSASFLT TYDAGH	53
SEQIDNO:15	-----MGGAA--RAVLLGFL---QASSSFDVRDST-GKVCIIANLTVAFSVEYKSSG	46
SEQIDNO:16	MAAPGGAWRRPLLLL-LLLLGLAR--GASAVFVSDGN-GTACIMADFAAAFEISYDSRS	56
SEQIDNO:17	MAEPGGARTPQRLL--LLLLGLIH--VASSIFVVKNGT-GTACIMANFSATFSMNYTTKS	55
SEQIDNO:18	-----MARALL--AAVLLGFL---QASSSFDVRDST-GKVCIIANLTVAFSVEYKSNG	47
SEQIDNO:19	-----MARGLLA--AAALLGFL---QASSSFEVKDSS-GKVCIIADLTVAFSVEYKTNV	48
SEQIDNO:20	MVSSSSCRRLLL--AAVLLGFL---QASSTFEVRDST-GKICILANFSAEFTVDYSTKA	54
SEQIDNO:21	MKSFPSPFVALFI-VCSAVLADT---QAVVTLEVKEGN--STCIKAESAVFSITYNTTN	53
SEQIDNO:22	MKRSHALVVL-I-IAWFSLSGC---IQAVSLEVKEGN--STCIKANLSAYFSITYNTSS	52
SEQIDNO:23	MTRTCPFVVG-I-AC-FAILGCVTVVQSQVTLVTEGN--STCIKAELSASFSITYDTAN	55
SEQIDNO:24	-----	0
LAMP同源结构域1		
	2	
SEQIDNO:1	GPKNMTFDLPSDATVVLNRSSCGKENTSDPSLVIAFGRGH--TLTLNFTRNATRYSVQLM	116
SEQIDNO:6	GSQIVNISLPASAEVLKNGSSCGKENVSDPSLTITFGRGY--LLTLNFTKNTRYSVQHM	110
SEQIDNO:7	GTSVSVFALPASASVSE-RSSCGS-AAVPELALVFGDTHHTLSLLFSRDQRLYRVSN	108
SEQIDNO:8	KMELATFVLPSEAVTNINKSSCGVENTTAPVLAIQFGSNH--SLSIHFARNNTRYEVAEL	116
SEQIDNO:9	GPKNMTFDLPSDATVVLNRSSCGKENTSDPSLVIAFGRGH--TLTLNFTRNATRYSVQLM	116
SEQIDNO:10	GPKNMTFDLPSDAKVVLNRSSCGKENTSDPSLVIAFGRGQ--TLTLNFTRNATRYSVQLM	115
SEQIDNO:11	GPKNMTFDLPSDA-VVLNRSSCGKENTSDPSLMIAFGKGH--GLTLNFTRNATRYSVQLM	112
SEQIDNO:12	GYKNASFELPATA-EVQNTSSCGRENTSNPSLQIAFGRGH--VLALNFTRNATLYSVPLL	111
SEQIDNO:13	GPQNKSFELPAGA-EVSNSSSCGKENASDSSLVITFGRGH--TLTLNFTRNATRYEVQLM	112
SEQIDNO:14	VSKVSNMTLPASAEVLKNSSSCGEKNASEPTLAITFGEY--LLKLTFTKNTRYSVQHM	111
SEQIDNO:15	QKQFAHFFLPQNATSQ-SHSSCGEGNTSHPILALSFGAGH--LISLNFSKTLDKYQVEEL	103
SEQIDNO:16	GAKNTTFLPASA-QVLNRSSCGKENTSDSSLVIAFGRGH--TLTLNFTRNATRYSVQLM	113
SEQIDNO:17	GLESTTFRLPQNA-SVMNSSSCGKENTSNPILEIGFGGGH--TLTMNFSSTTQSYQVELL	112
SEQIDNO:18	QKQFAHFFLPQNATSQ-SHSSCGEGNTSHPILALSFGAGH--LLSLNFSKTLDKYQVEEL	104
SEQIDNO:19	QKEFVHFFLPQNASVD-SQSSCGKDNASHPILVLDGFGGH--SLSLNFSSESADKYQVEEL	105
SEQIDNO:20	KVERKTFQLPSSAHINKESSSCGKEKETSQVLVVEFGTGN--SLTFTFEKSNDFFYHVSNL	112
SEQIDNO:21	DTRTVSVFLPNSTTVDSANSSCGS-NGSTPGLMAKFGPGH--YFGMNFSTNGSLYSVDTL	110
SEQIDNO:22	STRTAQFILPDSATVDPDSSCTCGG-NGSPWLVAVFGAGH--ALGLGFSTNGSFYSVANL	109
SEQIDNO:23	GTRTMVPLPGSAVVG-ASSCGG-DGRSPWLVALFGDGH--ALGLGFSSNDSLYSVAKL	111
SEQIDNO:24	-----	0

图3

LAMP同源结构域1

	3	
SEQIDNO:1	SFVYNLSDTHLFPNASSK-EIKT-VESITDIRADIDKKYRCVSGTQVHMNN-VTVTLHDA	173
SEQIDNO:6	YFTYNLSDTEHFPNAISK-EIYT-MDSTTDIKADINKAYRCVSDIRVYMKN-VTVVLRDA	167
SEQIDNO:7	SLQYNLSDGDIFFQSSSAGVQSVMASVSELSARLNSTYRCVSSSSISLSAAVNLTLSGV	168
SEQIDNO:8	VMSYNLSDKIIFFPNASENGTKTV-STNKTAVLAENDTVYKCMNPHLIRMDN-ANATFHD	174
SEQIDNO:9	SFVYNLSDTHLFPNASSK-EIKT-VESITDIRADIDKKYRCVSGTQVHMNN-VTVTLHDA	173
SEQIDNO:10	SFVYNLSDTHLFPNASSK-EIKT-VESITDIRADIDKKYRCVSGTQVHMNN-VTVTLHDA	172
SEQIDNO:11	SFIYNLSDTQIFPNASSK-ETKT-VESATDIRADINKKYRCVSNQIHMHN-VTVTFHDV	169
SEQIDNO:12	SFVYNLSDSDLFPNASSK-DIKT-VGSTTDIKADIDKRYRCVSDSKVPMGN-VTVTLQDA	168
SEQIDNO:13	RFAYNLSDTDTFPNSSST-GVKT-VESATDIKADINKTYRCVSETQVNMDN-VTVTLRDA	169
SEQIDNO:14	YFTYNLSDTQFFPNASSK-GPDT-VDSTTDIKADINKTYRCVSDIRVYMKN-VTIVLWDA	168
SEQIDNO:15	TFHYNLSDETLFPNATEG-KVMV-ATQKSVIQARIGTEYRCINSKYVRMKH-VNITFSNV	160
SEQIDNO:16	TLVYNLSDAEFFPSASSK-GTKT-VAASDIRADLNTKYRCVSNQVHLLN-VTVTLGNA	170
SEQIDNO:17	SFSYNLSDATLFPNASKGSEESS-VKSKTDIQADIHKYRCVSSNRITMSN-VTIVLSDV	170
SEQIDNO:18	TFHYNLSDETLFPNASEG-KVME-VTQKSVIQARIGTEYRCINSKYIYIRH-VNITFSNV	161
SEQIDNO:19	VFHYNLSDATLFPNSSSTG-GMKT-VSHKSIIQAHMGTQYRCINSKHINMKN-VNVTFSNV	162
SEQIDNO:20	TFSYNLSDSSFFPNSSG--GQRE-VSRAGDIQANINTTYRCRSNHRVNMTN-VTVLFSNV	168
SEQIDNO:21	FLRYNLSDASLFPEANSSGPVDFELSASVGIWAPTNTTYRCLSPPTITITR-PSVTFSEM	169
SEQIDNO:22	TLQYNLSDASVFPDANSSGVTV-VSSSVGIWAAVNTTYRCLSSVLFQVGG-ATVTFSDM	167
SEQIDNO:23	TLQYNLSDVSNFPEANSTDVVTVE-TTSVGMVARVNTTYRCISASPVIVGG-ATVTFSNV	169
SEQIDNO:24	-----	0

LAMP同源结构域1

铰链区

	4	
SEQIDNO:1	TIQAYLSNSSFSGETRCEQDRPSPTTAPPAP-----PSP-SP---SPVPKSPS	218
SEQIDNO:6	TIQAYLSSGNFSKEETHCTQDGPSTTGP-----PSP-SP---PLVPTNPT	209
SEQIDNO:7	QMEAYMSSANLSADESVCSADQPSTTVAPPPSTT-----TSPPPIPPVPE	213
SEQIDNO:8	RLEAYLKQSNFSQKVSTCSEDITPTSAPA-FV--T-----T-----TAPVPAP-VPDPP	219
SEQIDNO:9	TIQAYLSNSSFSGETRCEQDRPSPTTAPPAP-----PSP-SP---SPVPESPS	218
SEQIDNO:10	TIQAYLSNSSFSGRETRCEQDRPSPTTAPPAP-----PSP-SP---SPVPESPS	217
SEQIDNO:11	TIQAYLANSNFSKEETRCEQDGFPTTAPPPP-----PHP-SP---SPAPESPS	214
SEQIDNO:12	TIQAYLWNNFSQAESRCRQDMPSTTAPPAPPVP-----PSPPSP-SP---PPKPESPS	219
SEQIDNO:13	AIQAYLSSSNFSREETRCEQDLPT-----P-----TTPPQP-AP---TPAPASPA	210
SEQIDNO:14	TIQAYLPSSNFSKEETRCPODQPSPTTGP-----PSP-SP---PLVPTNPS	210
SEQIDNO:15	TLEAYPTNDTFSANKTECREDMVSTTTVAPTTPKH-----ATSQVPTTSPAPTAAPSSPA	215
SEQIDNO:16	TIQAYLANNSFSQETRCEQDKPSP-----PTP-----TAPPTP-TP---TPAPTSVP	214
SEQIDNO:17	TIQAYLSNNTFSKEETRCSDTPSPSPVPTTHPTT-----IPVPTP-TPTRPPTPAEIPP	224
SEQIDNO:18	TLEAYPTNGTFTSNKTECEDMVSTTTVAPTTPKH-----ITSQVPATSPAPTAAPSNPA	216
SEQIDNO:19	TLEAYLTNGTSLVNKTECAEDRVSTTTMVPTTPKQ-----TTSQSPTTGAPTS-PPNPT	216
SEQIDNO:20	TLEAYLPNNAFKNDSVCAEDKTSTVA--PPITTH-----IPTTSLAPPT-PPPTDTPK	220
SEQIDNO:21	KLEAYMPGNDFSPAERVCAADQTTGAPTTTT-----SAATP-TT-PSPTPAGTPE	218
SEQIDNO:22	RLEAYMPGNDLSPRESFCAADQTTAPPTTTAAP---TTTAATM-AP-PAPTPPGTPV	221
SEQIDNO:23	TMEAFMTGEDLSPNESVCTADQSFTTAPPPPPS-----TTTAA-PA-PVPTPPGTPS	219
SEQIDNO:24	-----MVQICRVQSWFVGVTPLLI FATVLHQGFATVAP-PTPAPHKEPGRPE	46

* ; *

图3续

LAMP同源结构域2

	1	2
SEQIDNO:1	VDKYNVSGTNGT-CLLASMGQLNLITYE-RKDNTTVTRLLNINPNKTSASGSCGAHLVTL	276
SEQIDNO:6	VSKYNVTGNNGT-CLLASMALQLNITYL-KKDNTVTTRAFNISPNDT-SSGSCGINLVTL	266
SEQIDNO:7	RGNYSVTDENGTVCVLALMGLQLNITHY-TTQNQSVSELMLNLPNQTTVSGSCGVTESSL	272
SEQIDNO:8	VVQYSVNRSSEP-CLLAKVGLQMNITYT-TKDGKNGSYVFNIESKGVTVDGNCTNTTAYL	277
SEQIDNO:9	VDKYNVSGTNGT-CLLASMGQLNLITYE-RKDNTTVTRLLNINPNKTSASGSCGAHLVTL	276
SEQIDNO:10	VDKYNVSGTNGT-CLLASMGQLNLITYE-RKDNTTVTRLLNINPNKTLASGSCGAHLVTL	275
SEQIDNO:11	VHKYNVSGANGT-CLLASMGQLNLVITYK-KKDNTTVVKVVSINPNKTTAGGSCGAQLVTL	272
SEQIDNO:12	VSRYNVSDGNAT-CLLASMGQLNLITYV-HRDNATVTRVFNINPNKTKPSGHCGAQQVTL	277
SEQIDNO:13	VFRYNVSGSNGT-CLLASMGQLNLVITYR-RVDNKTVTREFNVNPNKTTFGGNCSATLATL	268
SEQIDNO:14	VSKYNVTGDNGT-CLLASMALQLNITYM-KKDNTTVTRAFNINPSDK-YSGTGCAQLVTL	267
SEQIDNO:15	VGKYNVTGANGT-CVLASMGQLNLITYV-KKDEKMGLDLLNFIPHNTSASGMCESTSAFL	273
SEQIDNO:16	VSRYNVSGANGT-CLLASMGQLNLVITYR-TKDNTTVTRGLNINPNKTTFGGSCSAQLVTL	272
SEQIDNO:17	IFKYNVSDANGT-CLLASMGQLNLITYA-KKDNSSARIWININPNKTVAGGSCSPQVAIL	282
SEQIDNO:18	VGKYNVTGANGT-CVLASMGQLNLITYL-KKDGTGLDLLNFVPHNTNAGSCTCENTSAFL	274
SEQIDNO:19	VGKYNVTGPNGT-CVLAYMGLQLNLITYQ-QKDEKMGLDLLNFVPHNTTSSGRCDNTSALL	274
SEQIDNO:20	IGRYNVTGLHGI-CLLATMGLQVNVITYS-TKNKTSKSELLNLPP-TAEVSGTCENSSITL	277
SEQIDNO:21	QGSYSVKNASGTVCCLMAKMGVQLNVSYFSQSQNKTQVQELLNLTPNLNLTSSSGLCGGTNATL	278
SEQIDNO:22	RGTYSVVNGNDTTCLLAQMGLQLNVSYFSRSQNKTQVQSLVNLTPNLNLTSTGSCCKGSATL	281
SEQIDNO:23	QGSYSVSNNGTVCCLLARMALQLNISHFSASQNKTQEVVNLFPNQTTSSGSCDPTSATL	279
SEQIDNO:24	RGYYNVNTNHNGTICLMAYMGLQLNISYNSTSQKKVVQDVMMNLQPNLTKHSLGCDSDIASL	106
	* * * * *	

SEQIDNO:1	ELHS-EGTTVLLLFQFGMNASSSRFFLQGIQLNTILP-DARDPAFKAANGSLRALQATVGN	334
SEQIDNO:6	KVEN-K-NRALELQFGMNASSSLFFLQGVRLNMTLP-DALVPTFSISNHSILKALQATVGN	323
SEQIDNO:7	RLSD--ETTNLTFSTMTNSTTQKYLSAVSVSALWP-DMS-VVEAGNTSLSALQCSVGR	328
SEQIDNO:8	SLST-GS-IDLRFNFTLNSSLEVFYLDGVSLSSTGLPADANDTHFEAANSSLNMQTNVHK	335
SEQIDNO:9	ELHS-EGSTVLLFLFQFGMNASSSRFFLQGIQLNTTLP-DARDPAFKAANGSLRALQATVGN	334
SEQIDNO:10	ELHS-EGSTVLLFQFGMNASSSRFFLQGIQLNTTLP-DARDPAFKAANGSLRALQATVGN	333
SEQIDNO:11	ELRS-EVSTLLAFQFGMNASTSRFFLQGIQLNMTLP-DARDPTFKAGNNSLRALQATIGN	330
SEQIDNO:12	ELQS-ERSTVLVFQFGMNASSGQYFLQGVLLNTTLP-DAREPAFSASNSSLRALQATLGN	335
SEQIDNO:13	ELHS-ENLLLLALQFVMNESSSRVFLQGVQLNLTLP-DAKEGSFTATNSSLRALQATAGN	326
SEQIDNO:14	KVGN-K-SRVLELQFGMNATSSSLFFLQGVQLNMTLP-DAIEPTFSTSNYSLKALQASVGN	324
SEQIDNO:15	NLAF-EK-TKITTFHFVLNASSEKFFLQGVNVSTTLPSEAKAPTFEASNDMSSESRA TVGN	331
SEQIDNO:16	ELQG-ESLRLALQFALNTSSSRVFLQGVQLNMTLP-DARDPSFSAANSSLRALQATAGN	330
SEQIDNO:17	ELQT-EN-STLAFSGFMNATTSKFFLRERIRFKHFFP-DAKDPAGAVNSSLKELQATVGN	339
SEQIDNO:18	NLAF-EK-TKITTFHFVLNASSEKFFLQGVNVSTTLPSEAKAPFEASNDMSSELRA TVGN	332
SEQIDNO:19	NLTF-EK-TRVIFQFALNATAEKFFLQGVSVSTTLPSEAKNPKFEATNNSMSELRASVGN	332
SEQIDNO:20	NLTS-ES-TSLSFQFSQNTSTKEYFLQGIIVTANLPPEATEKNISYSNHTLNALKTSVGK	335
SEQIDNO:21	VLAQ-EETTVLSELFETVNSTSNKYHLSGITLQANWT-DMM-SFSAASNTSLDYLRSSLGH	335
SEQIDNO:22	ILTQ-Q-TTILIFTFSLNSTSSKYHLSGLSLQANWS-DMA-AAFSAASNASLSYLRSTFGH	337
SEQIDNO:23	VLTQ-ANATNLSFLFTLNSTSNRYHLTGLSVVAAWS-DMT-APFNTSNSSLDYQRGSLGR	336
SEQIDNO:24	NLTVDAVKTNLTFTVFTMNSTSNKYHLSSEVTVSAAWP-EMK-EPVSVHNSSLDYLRGTGVY	164

279

LAMP同源结构域2		跨膜结构域
	3	4
SEQIDNO:1	SYKCNAAEEHVRVTKAFSVNIFKVVVQAFKVEGGQFGSVEECILLDENSM	LIPIAVGGALAG 394
SEQIDNO:6	SYKCNTTEHIFVSKMLSLNVFSVQVQAFKVDSDRFGSVEECVQDGNM	LIPIAVGGALAG 383
SEQIDNO:7	SYVCSAQQMLSVTPVFSINTFRLQLQPFNITANRFSTAEECRVDQEN	MPIIIVGAALAG 388
SEQIDNO:8	SFKCNSKQTLQITDPFTVNTYHLQVQAFNSD-NTFASAVECSLDENG	MVPIVVGALAG 394
SEQIDNO:9	SYKCNAAEEHVRVTKAFSVNIFKVVVQAFKVEGGQFGSVEECVLDEN	NMPIIPIAVGGALAG 394
SEQIDNO:10	SYKCNAAEEHVRVTKAFSVNIFKVVVQAFKVEGGQFGSVEECVLDEN	NMPIIPIAVGGALAG 393
SEQIDNO:11	SYKCNAGEHVQVTEAFSVNIIKVVVQAFQVQGDKFGSVEECQLDEN	SMLPIPIAVGGALAG 390
SEQIDNO:12	SYKCNSEEHVRVTPAFSLSIFKVVVQAFQVKGDKFGSVEECVLDQD	SMLPIPIAVGGALAG 395
SEQIDNO:13	SYKCNAEQRLRVTSFSLNMFVRVWLQAFRVDGDKFGPVEECQLDEN	SMLPIPIAVGGALAG 386
SEQIDNO:14	SYKCNSEEHIFVSKALALNVFSVQVQAFRVESDRFGSVEECVQDGN	NMPIIPIAVGGALAG 384
SEQIDNO:15	SYKCSAEENFQVTDKALNVFNQVQAFKVDGDKFGAMEECQLDEN	NMPIIIVGAALAG 391
SEQIDNO:16	SYKCRSEQRLQVTEAFALNVFQVRVQAFRVDGDKFGPAEECQLDEN	SMLPIPIAVGGALAG 390
SEQIDNO:17	SYKCNAAEENVHVTDGFSVNI FRVRVQAFKVEGDKFGSVEECVLDEN	NMPIIPIAVGGALAG 399
SEQIDNO:18	SYKCSAEENLQVTDKALNVFNQVQAFKVDGDKFGAVEECQLDEN	NMPIIIVGAALAG 392
SEQIDNO:19	SYKCSSEENLQVTDQALNVFNQVQVQIFKIDGDKFGPVEECQLDEN	NMPIIIVGAALAG 392
SEQIDNO:20	SYKCIAEESIWIISGKAAVNIFNIQLQAFKIPGDKFGAVEECQLDEN	NMPIIIVGAALAG 395
SEQIDNO:21	SYMCNAEQTLFVVSTFSINMFELQVQPFPGVTSTQFASAEEVCQIDQ	QMLPIIIVGAALAG 395
SEQIDNO:22	SYMCNAEQILAVTPVFSLNTFSLQIQPFPGVTTNQFAAAEECQMDQ	QMLPIIIVGASLAG 397
SEQIDNO:23	SYMCISEQTLVVDQNFSLNTFQLQVQPFGITRGQFAQAEECQLDQ	NMPIIIVGAALAG 396
SEQIDNO:24	SYFCRDEQTLNVAQNLSINTFQLQVQPFQFAVKGQDQFGAAEECQL	DEDDMLPIIVVGALAG 224
	* : * : . : : : : * * * * : * : * : * : * : *	
胞质尾区		
SEQIDNO:1	LVLIVLIAYLIVGRKRSHAGYQTI	417
SEQIDNO:6	LVLIVLIAYLIGRKRSHAGYQTI	406
SEQIDNO:7	LVLIVLVAYLIGRKRTHAGYQTI	411
SEQIDNO:8	LVLIVLIAYLIGRKRSHAGYQTI	417
SEQIDNO:9	LVLIVLIAYLIVGRKRSHAGYQTI	417
SEQIDNO:10	LVLIVLIAYLIVGRKRSHAGYQT-	415
SEQIDNO:11	LVLIVLIAYLIGRKRSHAGYQTI	413
SEQIDNO:12	LVLVLIAYLIGRKRSHAGYQT-	417
SEQIDNO:13	LVLIVLLAYLIGRKRSHAGYQTI	409
SEQIDNO:14	LVLIVLIAYLIGRKRSHAGYQTI	407
SEQIDNO:15	LVLIVLIAYLIGRKRSHAGYQTI	414
SEQIDNO:16	LVLVVLIMAYLIVGRKRSHAGYQTI	413
SEQIDNO:17	LVLIVLIAYLIGRKRSHAGYQTI	422
SEQIDNO:18	LVLIVLIAYLIGRKRSHAGYQTI	415
SEQIDNO:19	LVLIVLIAYLIGRKRSHAGYQTI	415
SEQIDNO:20	LVLIVLIAYLIGRKRSHAGYQTI	418
SEQIDNO:21	LVLIVLIAYLIGRKRSHAGYQTI	418
SEQIDNO:22	LVLIVLIAYLIGRKRSHAGYQTI	420
SEQIDNO:23	LVLIVLIAYLIGRKRSHAGYQTI	419
SEQIDNO:24	LVLIVLLAYLIGRKRSHAGYQSI	247
	** : ** : ** : ** : ** : ** :	

图3续

LAMP-1					
登记号	物种	SEQ ID NO:	登记号	物种	SEQ ID NO:
NP_005552.3	智人 (<i>H. sapiens</i>)	1	NP_990614.1	原鸡 (<i>G. gallus</i>)	15
NP_034814.2	小鼠 (<i>M. musculus</i>)	6	NP_001011507.1	野猪 (<i>S. scrofa</i>)	16
NP_955996.1	斑马鱼 (<i>D. rerio</i>)	7	XP_001374132.1	短尾负鼠 (<i>M. domestica</i>)	17
NP_001087042.1	非洲爪蟾 (<i>X. laevis</i>)	8	XP_003203252.1	火鸡 (<i>M. gallopavo</i>)	18
NP_001233491.1	黑猩猩 (<i>P. troglodytes</i>)	9	XP_002191607.2	斑胸草雀 (<i>T. guttata</i>)	19
XP_001087801.1	猕猴 (<i>M. mulatta</i>)	10	XP_003218797.1	变色蜥 (<i>A. carolinensis</i>)	20
XP_534193.2	家犬 (<i>C. lupus familiaris</i>)	11	XP_004067118.1	青鳉 (<i>O. latipes</i>)	21
XP_002723509.1	家兔 (<i>O. cuniculus</i>)	12	XP_003969941.1	红鳍东方鲀 (<i>T. rubripes</i>)	22
NP_001068592.1	家牛 (<i>B. taurus</i>)	13	NP_001158846.1	安大略鲑 (<i>S. salar</i>)	23
NP_036989.1	褐家鼠 (<i>R. norvegicus</i>)	14	XP_003452974.1	罗非鱼 (<i>O. niloticus</i>)	24

图3续

人类LAMP-2与直系同源序列的比对

SEQIDNO:2	-----	0
SEQIDNO:25	-----	0
SEQIDNO:26	-----	0
SEQIDNO:27	-----	0
SEQIDNO:28	-----	0
SEQIDNO:29	-----	0
SEQIDNO:30	-----	0
SEQIDNO:31	-----	0
SEQIDNO:32	-----	0
SEQIDNO:33	-----	0
SEQIDNO:34	-----	0
SEQIDNO:35	-----	0
SEQIDNO:36	-----	0
SEQIDNO:37	MAMKNFTLQQERDTSVALIIRTYVRAFLKVYTKVPKPQRCHNQW---QSLNIEGIEGIEI	57
SEQIDNO:38	-----	0
SEQIDNO:39	-----MECREGEVTRCKQKNNLFSGIN-DDISGAKQ	30
SEQIDNO:40	-----	0
SEQIDNO:41	-----	0
SEQIDNO:42	-----	0
SEQIDNO:43	-----	0

SEQIDNO:2	-----	0
SEQIDNO:25	-----	0
SEQIDNO:26	-----	0
SEQIDNO:27	-----	0
SEQIDNO:28	-----	0
SEQIDNO:29	-----	0
SEQIDNO:30	-----	0
SEQIDNO:31	-----	0
SEQIDNO:32	-----	0
SEQIDNO:33	-----	0
SEQIDNO:34	-----	0
SEQIDNO:35	-----	0
SEQIDNO:36	-----	0
SEQIDNO:37	VKGSKWR---SALETIITIIVKPK-----SQVQKYHPFSLHSECQKTNQE	99
SEQIDNO:38	-----	0
SEQIDNO:39	AKQRQCTPQKPPKRAATLPLQRPPRGIPGPAPAAVAAVAADRITPSGSHQTRPPEAAR	90
SEQIDNO:40	-----	0
SEQIDNO:41	-----	0
SEQIDNO:42	-----	0
SEQIDNO:43	-----	0

图4

SEQIDNO:2	-----MVCF	4
SEQIDNO:25	-----M	1
SEQIDNO:26	-----MGDT	4
SEQIDNO:27	-----	0
SEQIDNO:28	-----MVCF	4
SEQIDNO:29	-----MVCF	4
SEQIDNO:30	-----MVCF	4
SEQIDNO:31	-----MVCF	4
SEQIDNO:32	-----MVCF	4
SEQIDNO:33	-----MVCF	4
SEQIDNO:34	-----MVCF	4
SEQIDNO:35	-----MVCF	4
SEQIDNO:36	-----MR	2
SEQIDNO:37	G---TGGVATVIADDECLLWPSIPFSTLAQKVNLGSCFAFSIIIGYSVFALFIYLPKPNMLDF	156
SEQIDNO:38	-----	0
SEQIDNO:39	DERPVRDPRNRAAAPSGHWRRAAGGPRHR-----HHR-----HRRHGAPAPLRR	133
SEQIDNO:40	-----	0
SEQIDNO:41	-----	0
SEQIDNO:42	-----	0
SEQIDNO:43	-----	0

信号序列

LAMP同源结构域1

	1	
SEQIDNO:2	-RL---FPVPGSGLVLVCLVLGAVR--SYALELNLTDSENATCLYAKWQMNFTVRYETT	57
SEQIDNO:25	-CL---SPVKGAKLILIFLFLGAVQ--SNALIVNLTDS-KGTCLYAEWEMNFTITYETT	53
SEQIDNO:26	GAM---ERCACPAAVLLLSLVL---MG---ATAFEVEIKDDKNATCIYAKLSVNITVQYETD	57
SEQIDNO:27	-----MAVRGFLPLLFIILLSGIVHADDMMTSPLPS-----TAELEK	35
SEQIDNO:28	-RL---FPVPGSGLVLVCLVLGAVQ--SYALELNLTDSGKATCLYAKWQMNFTVRYETT	57
SEQIDNO:29	-RL---FPVPGSGLVLVCLVLGAVQ--SYALELNLTDSGKATCLYAKWQMNFTVRYETT	57
SEQIDNO:30	-RL---FPVPGSGLVLVCLVLGAVR--SHALELNEDSAIN-----	39
SEQIDNO:31	-RL---SPAPGSGLVLLCLVLGAVS--SYALEVNVTDSKATCLYAKWQMNFTIQYNTT	57
SEQIDNO:32	-RL---SPVPGSGLVLLCLVLGAVS--SYALELNLTDSKALCLYAKWQMNFTIPYETT	57
SEQIDNO:33	-RL---APVPGSGFLLLCVLGAVS--SYALELNLTDSNATCLYAKWQMNFTIRYETT	57
SEQIDNO:34	-RL---APVPGSGLMLCLVLGAVS--SYALELNLTNSEKATCLYAKWQMNFTIRYETT	57
SEQIDNO:35	-RL---APVPGCGFLLFCLVLGTVS--SYALELNLTDSKATCLYAKWQMNFTIRYETT	57
SEQIDNO:36	-LL---SPVTGSKLVLLFLFLGAVR--SDALKNLNLTDS-KGTCLYAEWEMNFTITYEAL	54
SEQIDNO:37	IELAELMLSTETQLLEPTRVCCGICQ--SYALELNLTDSKNATCLYSKWQMTFTINYETT	214
SEQIDNO:38	--MAPPRCPAGLALLLLLLGACGFFQ--SYAVEVDVKDASNFTCLYAQWMMKFLIKYETN	56
SEQIDNO:39	LLLRPPP-PAA-----AAARFLGFFQ--SYAVEVDIKDASNATCLYADWMMRFLIKYESN	185
SEQIDNO:40	--M---ERCACPAALLLSLVL---MG---AMAFDVEIKDDKNATCIYAKLSVNVTVQYETN	51
SEQIDNO:41	-----MF-RCAFLILFLALGNEHLHSHGTEVSVNNTENKLCLYANLMVNFSVTYEVG	51
SEQIDNO:42	-----MKVSHATAGLVVWFVVLGCIDAVT---L-EVKESNTTCIKADLSASFIIYNTT	50
SEQIDNO:43	-----	0

图4续

LAMP同源结构域1

2

SEQIDNO:2	NKTYKTVTISDH--GTVTYNGSICGDDQNGPKIAVQFGPGFS-WIANFTKAA---STYSI	111
SEQIDNO:25	NQTNKTITIAVP--DKATHDGSSCGDDRNSAKIMIQFGFAVS-WAVNFTKEA---SHYSI	107
SEQIDNO:26	TSSSKNITFPVP--SDVTNNGSSCGSDGKAPLLVINFGNSQS-WSLNFTRRN---STYSG	111
SEQIDNO:27	---T---ANLP--LVIQTTSSTSTTTT-SRP--SSTSTHSTLTTEPAA-----	73
SEQIDNO:28	NKTYKTVTISDR--GTVTYNGSICGDDQNGPKIAVQFGPGFS-WIANFSKAA---STYSI	111
SEQIDNO:29	NKTYKTVTISDR--GTVTYNGSICGDDQNGPKIAVQFGPGFS-WIANFSKAA---STYSI	111
SEQIDNO:30	CSKCKTVTISDH--GTVTYNGSICGDDQNGPKIAVQFGPGFS-WIANFTKAA---STYSI	93
SEQIDNO:31	SKNFKTATISDF--STATYNGSVCNDQNNPKIVVQFGSGFS-WIVNFTKKE---SAYLI	111
SEQIDNO:32	SKSYKTVTISNF--GTPYNGSICGDNQNGSRIAVQFGSGFS-WIVNFTKSV---SVYSI	111
SEQIDNO:33	DKHNKTVPISDL--GAATYNGSFCGDDQNGPKIAVQFGSGFS-WIVNFTKEAASPSTYLV	114
SEQIDNO:34	NNSHKTVSISDF--GAATYNGSFCGDDHNDPQIVMQFGSGFS-WIVNFAKES---SSYLI	111
SEQIDNO:35	DKHNKTVTISDF--DAAAYNGSVCGDDQNGPKIAVQFGSGFS-WIVNFTKEASSTSTYLV	114
SEQIDNO:36	K-VNETVTITVP--DKVTYNGSSCGDDKNGAKIMIQYGSTLS-WAVNFTKEA---SQYFI	107
SEQIDNO:37	GNETKNVTITVP--ENVTYDNGSSCGDNQTVPQIAVQFGLGYS-WHLNFTKKN--NSYSF	269
SEQIDNO:38	SSDYKNASLDLT--STVTHNGSICGSDTQAALLAVQFGDGHS-WSINFTKNN---ETYRA	110
SEQIDNO:39	SGDYKTTTLNLS--SSVTHNGSVCNDTQAALVAVQFGEGHS-WSINFTKNN---ETYQG	239
SEQIDNO:40	TSSTKNVTFVSP--SEVTNNGSSCGSNGKAPILVINFGNGHS-WSLNFTRRND---SMYSG	105
SEQIDNO:41	VNKNETVIFVLP--ENVTEGSTCDNTTSTLKL--SFGHGHS-WTVEFTKKN---KTYQV	103
SEQIDNO:42	HAER-TVQVLLPNSTTVDTANSTCGKDGSSPRLVAVFGSGY-TLGLNFSTNG---TLYQV	105
SEQIDNO:43	-----	0

LAMP同源结构域1

3

SEQIDNO:2	DSVSFSYNTGDNTTFPDAEDKGI-LTVDELLAIRIPLNDLFRCNLSLSTLEKNDVVQHYWD	170
SEQIDNO:25	HDIVLSYNTSDSTVFPGAVAKGV-HTVKNPENFKVPLDVIFKCNVLTYNLTPVVQKYWG	166
SEQIDNO:26	SALIFTYNTNDTILFPDALRKGLIS-STAMFLGPVPLNSTYKCISEVVVSENVQTIIYD	170
SEQIDNO:27	-----KTTTARTTVTTSA---PTSTQSTSSSSTSATVTTLAP	107
SEQIDNO:28	DSISFSYNTGDNTTFPDAEDKGI-ITVDELLAIKIPLNDLFRCNLSLSTLEKNDVVQNYWD	170
SEQIDNO:29	DSISFSYNTGDNTTFPDAEDKGI-ITVDELLAIKIPLNDLFRCNLSLSTLEKNDVVQNYWD	170
SEQIDNO:30	DSISFSYNTGDNTTFPDAEDKGI-LTVDELLAIKIPLNDLFRCNLSLSTLEKNDVVQHYWD	152
SEQIDNO:31	DSISFSYNLSDNATFPDAKEKGI-LTVHDLVGFRIPLNNIFRCNSLSTLEKNGVVQYYWD	170
SEQIDNO:32	DSISFSYNTGDNTTFPDAKEKGI-LTVNESVAFKIPLNDIFRCNSLSSLVKNGVVQNYWD	170
SEQIDNO:33	DTISFSYNTNDNKTFPDAKEKEV-FTVNNRVALKIPLNDIFRCNSLSTLENRDVVQHYWD	173
SEQIDNO:34	NSISFSYNTSDTTTFPDAKKGV-LTVNDSVGFQVPLNDIFRCNSLSTLEKDNVVQHYWD	170
SEQIDNO:35	DSISFSYNTNDNATFPDAKEKGV-FTVNNRVALKIPLNDIFRCNSLSTLEKSDVVQHYWD	173
SEQIDNO:36	NNITLSYNTNDTKTFPGAVPKGI-LTVIIPVGSQPLPLGVIFKCSSVLTFFNLSPVVQHYWG	166
SEQIDNO:37	DTIVFTYNTSDNETFPFAKEKGQVLSVFREFRYARIPLNKIFRCHSEESLIGDKATHHYWE	329
SEQIDNO:38	EFITFTYNTNDTAVFPDARRQGPVTIVVKDAMHPIQLNNVVFVCHHTTSLEAENVQTIFWN	170
SEQIDNO:39	DFITLTNTNDTAVFPDAKRGPITVLVRDPSRPIQLNTVFVCHNSFVIEAENTTQIFWN	299
SEQIDNO:40	GALIFTYNTNDSTLFPDALKEGLIS-STAAFLGPIPLNSTYKCISEVVVSENVQTIIISD	164
SEQIDNO:41	DTIVFSYNLNDSSVFPNSTSKETKFVTVKSIITNVSVDTYYSCKSENVLTVESVIQTLYD	163
SEQIDNO:42	SSLTLQYNLSDTSVFPNATISGVVTLVSASVGIEANVNTTYKASPTVIDVATAKVNFTD	165
SEQIDNO:43	-----MTQIGGVQPVFLA	13

图4续

LAMP同源结构域1		铰链区
	4	
SEQIDNO:2	VLVQAFVQNGTVSTNEFLCDKDKTS---TVAPTIHTTVPS-----PTTTPT--PKEKPE	219
SEQIDNO:25	IHLQAFVQNGTVSKNEQVCEEDQTP--TTVAPIIHTTAPSTTTTLTPTSTPTPTPTPT	224
SEQIDNO:26	VKLEAFMANGTLGK-EIICDADKPS--PVPSPTQPST-----TASTAIPAPTSKPLDKPT	222
SEQIDNO:27	TTTGHNTTNSTTEPPTTGHNTTNS--TTDAPTTHTTNAT----VAPTPTPTTSPVPKPT	161
SEQIDNO:28	VLVQAFVQNGTVSTNEFLCDEDEKTS---TVAPTIHTTVPS-----PTTTPT--PKEKPE	219
SEQIDNO:29	VLVQAFVQNGTVSTNEFLCDEDEKTS---TVAPTIHTTVPS-----PTTTPT--PKEKPE	219
SEQIDNO:30	VLVQAFVQNGTVSTNEFLCDEDEKTS---TVAPTIHTTVPS-----PTTTPT--RIP---	198
SEQIDNO:31	VHVQAFVQNGTVSTKEFLCEKDKTS--TTVVPTISTTTPS-----PTTTPT--PKEKPE	220
SEQIDNO:32	VHVQAFVQNGTVSTNEYLCEKDNTT--TTVAPIVPTTVPSPTTSSPTTTPS--PKEKPD	226
SEQIDNO:33	VHVQAFVQNGTVSTTEFLCDKDKTV--TTAVPIVPTTLPS-----PT-----KPV	216
SEQIDNO:34	VHVQAFVQNGTVSTKEFLCDKDKTL--TTTVPIPTSVPS-----PTTTPT--PKEKPE	220
SEQIDNO:35	VHVQAFVQNGTVSTTEFLCDKDKTV--TTAMPVPTTAPS-----PT-----KPV	216
SEQIDNO:36	IHLQAFVQNGTVSKHEQVCKEDKTA--TTVAPIIHTTVPSPTTTTLPTSI----PVPTPT	220
SEQIDNO:37	TVVQAFIQNGTISKKEFICSKDRAS--TTVAPVTTQVPS-----TTATPVPQDKPY	379
SEQIDNO:38	VTMQPFVQNGTISKKESRCYADTPTAAPTVLPTVANVTAS-TTISPAPTAPKPAENPV	229
SEQIDNO:39	VTMQAFVQNGTVSKKESRCPADTPTSEPTVPPTIANVTASTTTLSPAPTAPKPVENPV	359
SEQIDNO:40	VKLEAFMQNGTLGK-EVSCDADKPS--PTPT-TNPST-----TASTTTPTPTSKPLDNPT	215
SEQIDNO:41	VALQAFVINGSKSDTDVCSADMTS--TTVAPTT---TV----TSTAAPTSTPTLPTPT	213
SEQIDNO:42	MRLEAYMPGNELSPNETVCFADQTS--TTPSPTTVSTTAV----PTQT----P--PGTPQ	213
SEQIDNO:43	VTVHLIL-----ATV--LHQTF--AT---VTPPVTTA----VPHK----E--PGRPD	48
铰链		LAMP同源结构域2
	1	2
SEQIDNO:2	AGTYSVNNG--NDTCLLATMGLQLNITQ-----DKVASVININPNTTHSTGSCRSHAL	271
SEQIDNO:25	VGNYSIRNG--NTTCLLATMGLQLNITE-----EKVPFIFNINPATNFTGSCQPQSAQ	276
SEQIDNO:26	MGNYSVSDA--SGICLLASMGQLINTSLL--SEGKNIWRPFNIDPLGIKTNGTCTNQTGT	278
SEQIDNO:27	VGNYSVKTD--NVSDCLLAKMGLQFSFKIS---GNASLQTVNLDPNVTKVNGTCGSGGSD	216
SEQIDNO:28	AGTYSVNNG--NDTCLLATMGLQLNITQ-----DKVASVININPNTTHSTGSCRSHAL	271
SEQIDNO:29	AGTYSVNNG--NETCLLATMGLQLNITQ-----DKVASVININPNTTHSTGSCRSHAL	271
SEQIDNO:30	-----PKVASVININPNTTHSTGSCRSHAL	224
SEQIDNO:31	VGSYSVNNS--NGTCLLATMGLQLNITH-----NKVASVININPNTDFTGSCQPQTAL	272
SEQIDNO:32	VGSYLVKNG--SDTCLLATMGLQLNVTH-----DKVASVININPNVTGYSGSCHPQTAL	278
SEQIDNO:33	VGSYSVNNS--NGTCLLATMGLQLNITH-----DKVASVFNINPNTTNATGSCQPQTAL	268
SEQIDNO:34	TGSYSVTSS--NGTCLLANMGLQLNITQ-----DKVASVININPNTTNATGNCHSKTAL	272
SEQIDNO:35	VGSYSVNNS--NGTCLLATMGLQLNITH-----DKVASVFNINPNTTNATGSCQPQTAL	268
SEQIDNO:36	VGNYSISNG--NATCLLATMGLQLNITE-----EKVPFIFNINPATNFTGSCQPQTAQ	272
SEQIDNO:37	PGKYAVKNG--NDTCLLATMGLQLNVTQ-----NKVNSVININPNVTDFTGSCSNETA	431
SEQIDNO:38	TGNYSLKTG--NKTCLLATVGLQLNISQ-----DK-PLLINIDPKTTHADGTCGNTSAT	280
SEQIDNO:39	TGNYSLKSG--NKTCLLATVGLQLNVSQ-----EK-PLLININPKTTVADGACGNTTAT	410
SEQIDNO:40	TGNYSVSDV--NGTCLLASMGQLINTSLL--SEGKNIWTA FNIDPTAMSKNGTCSNQTGT	271
SEQIDNO:41	TGKYSIAPDVNSTACLMATFGLQIGYKQG----D--KEETINLVPNITEVGGACGANSS-	266
SEQIDNO:42	QGNYSVKDA--NDTICLLAKMGLQLNVSYT--SQNKTVQDVLNLPNVNTSTGSCGASSAT	270
SEQIDNO:43	QGDYQVTSS--NGTVCFLLASMGQLNITFNSTSQNKTLQEVINIQPNTKSSGSCDTSSAL	107
. * : * * * *		

图4续

LAMP同源结构域2

```

SEQIDNO:2      LRLNS-STIKYLDVFAVKNE----NRFYLKEVNISMV-LVNGSV-FSIANNNLSYWDAP 324
SEQIDNO:25     LRLNN-SQIKYLDVFAVKNE----KRFYLKEVNVSMY-LANGSA-FNISNKNLSFWDAP 329
SEQIDNO:26     LILTE--NRTIEFTFALKNK----NHFYLEEVNITLI---NGSAFSSRQNLSTWEAS 329
SEQIDNO:27     SSLFLTS--KDITVHFVFTNDS---QKFLRLHALTLTVD-LGNG-NIFNDSNTNLSLWEAS 269
SEQIDNO:28     LRLNS-STIKYLDVFAVKNE----NRFYLKEVNVSMY-LVNGSV-FSIANNNLSYWDAP 324
SEQIDNO:29     LRLNS-STIKYLDVFAVKNE----NRFYLKEVNVSMY-LVNGSV-FSIANNNLSYWDAP 324
SEQIDNO:30     LRLNS-STIKYLDVFAVKNE----NRFYLKEVNISMV-LVNGSV-FSIANNNLSYWDAP 277
SEQIDNO:31     LRLNS-SNIKYLDVFAVKNE----NRFYLKEVNVSMY-LVNGSV-FSIANNNLSYWDAP 325
SEQIDNO:32     LRLNS-SNIKYLDVFAVKNE----NRFYLKEVNVSMY-LANGSV-FSFANNNLSYWDAP 331
SEQIDNO:33     LRLSS-SNIKYLDVFAVKNE----NRFYLKEVNVSMI-LVNGSV-YSISNTNLSYWDAP 321
SEQIDNO:34     LRLSG-SNIKYLDVFAVKND----NRFYLKEVNVSMY-LVNGSV-FSIANNNLSYWDAP 325
SEQIDNO:35     LRLSS-SNIKYLDVFAVKNE----NRFYLKEVNVSMI-LVNGSV-YSISNTNLSYWDAP 321
SEQIDNO:36     LRLNN-SQIKYLDVFAVKNE----KRFYLKEVNVSMY-LANGSA-FHVSNNNLSFWDAP 325
SEQIDNO:37     LRLSG-SNVKYIDVFAVKNG----NRFYLKEVNVSMI-LVNGSV-YSISNTNLSYWDAP 484
SEQIDNO:38     LKLND-GNRTLIDFTFIV-NASASVQKFLREVNTLLNYQNGSVILSADNNNLSKWDAS 338
SEQIDNO:39     LKLND-GNSTLIGFTFAVKNTSASVQKFLREVNTLLNRLNGSVISSADNLSKWDAS 469
SEQIDNO:40     LILTD--NSTVIEFTLALKNK----NHFYLKEVNVALI---NGSASSTRQNLSTWEAS 322
SEQIDNO:41     -DLILTS--DTITIMFTFSNDG---KKFHLHALKVTVK-PATG-DPVIANNNLSIWAAA 318
SEQIDNO:42     LVLTQ-TQSTILTFTNFTLNSTT---NKYHLSGVTLIAN-WFDS-AHFSMSNNLSNYLRST 324
SEQIDNO:43     LTLTTDAEKTNLTFVFALNTTS---NKYHLSEVSLSAA-LSDMKETFVAQNHSLDYLRGT 163
      *           : . : . .           ::: *   :.:           * .:. .

```

LAMP同源结构域2

跨膜结构域

```

      3                                     4
SEQIDNO:2      LGSSYMCNKEQTVSVSGAFQINTFDLRVQPFNVTVQGYSTAQDCSADD-DNFLVPIAVGA 383
SEQIDNO:25     LGSSYMCNKEQVLSVSRFQINTFNLKVQPFNVTKGQYSTAQECSLDDD-TILIPPIVGA 388
SEQIDNO:26     VDSSYMCHKEQQIKVSEDLFINAFDVRVQPFVNGGTFAAEDCFAD-Q-NFIVPIVGA 387
SEQIDNO:27     VGSSYMCNKEQSYNISDKLTNTFELQVQPFVKKNSFSTAHECSLDDT-SLLIPPIVGA 328
SEQIDNO:28     LGSSYMCNKEQTVSVSGAFQINTFDLRVQPFNVTVQGYSTAEECSADSDNLFIPVAVGV 384
SEQIDNO:29     LGSSYMCNKEQTVSVSGAFQINTFDLRVQPFNVTVQGYSTAQDCSADD-DNFLVPIAVGA 383
SEQIDNO:30     LGSSYMCNKEQTVSVSGAFQINTFDLRVQPFNVTVQGYSTAEECSADSDNLFIPVAVGV 337
SEQIDNO:31     LGSSYMCNKEQTVSVSGAFQINTFDLRVQPFNVMEGKYSTAQECSLDDD-TILIPPIVGA 384
SEQIDNO:32     LGSSYMCNKEQTVSVSGEFQINTFDLRVQPFNVKDGKYSTAQDCRADD-DNFLVPIAVGA 390
SEQIDNO:33     LGSSYMCNKEQTVSVSGAFQINTFDLRVQPFVTEGKYSTAQECSLDDD-TILIPPIVGA 380
SEQIDNO:34     LGSSYMCNKEQTVSVSGAFQINTFNLRVQPFVMEGKYSTAQDCSADD-DNFIVPIAVGA 384
SEQIDNO:35     LGSSYMCNKEQTVSVSGALQINTFDLRVQPFVTEGKYSTAEECSADSDNLFIPVAVGV 381
SEQIDNO:36     LGSSYMCNKEQVSVSRTFQINTFNLKVQPFNVTKGEYSTAQDCSADD-NFLVPIAVGA 384
SEQIDNO:37     LGSSYMCNKEQTLALADSLQINTFNLRVQPFVSVAGKYSTAEDCSADDD-NFIVPIAVGA 543
SEQIDNO:38     LGNSYMCNKEQTLINENLQVHTFNLVQPFVVKENKFSIAEECFADSDNLFIPVAVGM 398
SEQIDNO:39     LGSSYMCNKEQTLQINENVQVHTFNLWIQPFVLEANKFATAEECIADSDNLFIPVAVGV 529
SEQIDNO:40     VGSSYMCNKEQQIKVSEDLVINSFDVRVQLFGVKNETFATAQQCSLDDD-SIVIPVGA 381
SEQIDNO:41     VGSSYMCNKEQTLNVTDTLTLYTFELRVQPFVVKGEFATAHECSLDDT-SILIPPIVGA 377
SEQIDNO:42     LGSYMCNKEQTLFVTPSFLNTFDLQVQPFVVKSGRFATAEECQMDQN-QMIIPPIVGA 383
SEQIDNO:43     LGFSYMCNKEQTLGVTPDFAINTFQVQVQPFVGTGQFAAAEECQLDKD-DMLIPPIVGA 222
      :. ****. . *   : . : : : : : * * *   : : * . : * *   : : : : : *

```

图4续

胞质尾区

```

SEQIDNO:2      ALAGVLILVLLAYFIGLKHHH-AGYEQF  410
SEQIDNO:25     GLSGLIIVIVIAAYLIGRRKTY-AGYQTL  415
SEQIDNO:26     ALGVLVVLVMVAYFIGRRKQSSAGYEQM  415
SEQIDNO:27     ALAGLIFIVVIAYVIGRRRTY-VGYQTL  355
SEQIDNO:28     ALGFLIIVVFISYMIGRRKSR-TGYQSV  411
SEQIDNO:29     ALAGVLILVLLAYFIGLKRRH-AGYEQF  410
SEQIDNO:30     ALGFLIIVVFISYMIGRRKSR-TGYQSV  364
SEQIDNO:31     GLSGLIIVIVIAAYLIGRRKSY-AGYQTL  411
SEQIDNO:32     ALAGVLILVLLAYFIGLKRRH-AGYEQF  417
SEQIDNO:33     GLSGLIIVIVIAAYLIGRRKSY-AGYQTL  407
SEQIDNO:34     ALAGVLILVLLAYFIGLKRRH-AGYEQF  411
SEQIDNO:35     ALGFLIIVVFISYMIGRRKSR-TGYQSV  408
SEQIDNO:36     ALGGVLILVLLAYFIGLKRRH-TGYEQF  411
SEQIDNO:37     ALGGLVILVLMAYFVGRKRRA-TGYEQF  570
SEQIDNO:38     ALGFLIILVFISYIIGRRKSR-TGYQSV  425
SEQIDNO:39     ALGFLIILVFISYIIGRRKSR-TGYQSV  556
SEQIDNO:40     ALAGLIVIVIAAYLIGRRKGY-SGYQTL  408
SEQIDNO:41     ALAGLILIVVIAYVIGRRKTY-VGYQTL  404
SEQIDNO:42     ALAGLVLTITLIAYLIGRRSH-AGYQAI  410
SEQIDNO:43     ALAALVLIVLSAYLIGRRSH-AGYQSI  249
.*. :.:. . :*.:* :. **:.

```

LAMP-2					
登记号	物种	SEQ ID NO:	登记号	物种	SEQ ID NO:
NP_002285.1	智人 (<i>H. sapiens</i>)	2	NP_001231184.1	野猪 (<i>S. scrofa</i>)	34
NP_034815.2	小鼠 (<i>M. musculus</i>)	25	XP_004022401.1	绵羊 (<i>O. aries</i>)	35
NP_001087881.1	非洲爪蟾 (<i>X. laevis</i>)	26	NP_058764.2	褐家鼠 (<i>R. norvegicus</i>)	36
NP_001013551.1	斑马鱼 (<i>D. rerio</i>)	27	XP_001510101.2	鸭嘴兽 (<i>O. anatinus</i>)	37
XP_003918270.1	东非狒狒 (<i>P. Anubis</i>)	28	NP_001001749.1	原鸡 (<i>G. gallus</i>)	38
XP_001084005.2	猕猴 (<i>M. mulatta</i>)	29	XP_002191794.1	斑胸草雀 (<i>T. guttata</i>)	39
XP_003317709.1	黑猩猩 (<i>P. troglodytes</i>)	30	NP_001116192.2	热带爪蟾 (<i>X. tropicalis</i>)	40
XP_005641822.1	家犬 (<i>C. lupus familiaris</i>)	31	NP_001133282.1	安大略鲑 (<i>S. salar</i>)	41
XP_001493687.3	家马 (<i>E. caballus</i>)	32	XP_003445830.1	罗非鱼 (<i>O. niloticus</i>)	42
NP_001029742.1	家牛 (<i>B. taurus</i>)	33	XP_003961835.1	红鳍东方鲀 (<i>T. rubripes</i>)	43

图4续

人类LAMP-3与直系同源序列的比对

信号序列	LAMP同源结构域1	
SEQIDNO:3	MPRQLSAAAAALFASLAVILHD----GSQMRKAKAFPETRDYSQPTAAATVQDIKKPV-QQP	55
SEQIDNO:44	MPRQLSAAAAALFASLAVILHD----GSQMRKAKAFPETRDYSQPSAAATVQDIKKPV-QQP	55
SEQIDNO:45	MPRQLSAAAVLFASLAVILHD----GSQMRKAKFPKTRDYSQPTAAATGQDIAPV-QQP	55
SEQIDNO:46	MPRQLSAAAVLFASLAVILHD----GSQMRKAKFPKTRDYSQPTAAATGQDIAPV-QQP	55
SEQIDNO:47	MSWQLSAAVALFVSLALILHY----GSQIRAKMFPETVDFQ-PTTAATVRATAKPFLL-HL	54
SEQIDNO:48	MSWRLSAVILVSFVSLAVFLHY----GHHMKAKVFPEITDSSSPTTAATVQATAEPSLWKP	56
SEQIDNO:49	-----	0
SEQIDNO:50	MAWQLSAVVVLFVSLAVILYY----GSHVRANVFPEITDYSQPTTAATIQTARQPSLSQP	56
SEQIDNO:51	MSWQIPAVVMSEFMAVIAIYYDSHYNSHMQAQVFPEITGYSSPTTG---QATVKPSLLQP	57
SEQIDNO:52	MSWQISAVVLFVSLAVIYYDS----HMKANVFPEITGYSSPTTG---QATVKPSLLQP	53
SEQIDNO:53	MPGQTSAAVAL-LCLAVILH----GYQIREKEFPEARGYLQYTATTTEQITAKPPL-PL	53
SEQIDNO:54	MPGQISAAVALFLSLTVILH----GYQIREKEFPKARGYLQYTATSAEQITTKPLL-QL	54
SEQIDNO:55	-----	0

LAMP同源结构域1

SEQIDNO:3	AKQAPHQTLAARFMDGHITFQTAATVKIP-----TTTPATTKNTATTSPITY	102
SEQIDNO:44	AKQAPHQTLAARFMDGHITFQTAATVKTP-----TTTPATTKNTATTSPITY	102
SEQIDNO:45	ANQAPHQTLAARLMDGHITFQTAATIKTP-----TTTPVTTKNTPTTSPIIY	102
SEQIDNO:46	ANQAPHQTLAARLMDGHITFQTAATIKTP-----TTTPVTTKNTPTTSPIIY	102
SEQIDNO:47	TNQVPSQTLAARSMGDGHIASTTSSSEPPTTHTTVKTLVTTSLVTANSTPSSSPIIY	114
SEQIDNO:48	TNHTPHKTLAAKSTDGHVTSQIATTVTDSETLTTHTTITTLAATSLAATNSTPSTSPTH	116
SEQIDNO:49	-----	0
SEQIDNO:50	TNQVPHKTLATRSMDGQVTSQTAATTVNPETPVTHTTIKTAAATSLVTNSTLSTSPITN	116
SEQIDNO:51	TNYVPHKTAAARSTDGHVTSQTVAKTSSSETLTNTTIDVLATTSPVTTKSTLPTTPTTH	117
SEQIDNO:52	TNHVPCNTAAAKSTDGHVTSQTVAKTSSPETLTNTTIEVLVTTSPVTTQSTLPTTPTTH	113
SEQIDNO:53	TNQTSHATLASRSKDDYIQTAAETS--TFE---DTAHITMKTAPVTTKSLLPISSTSY	107
SEQIDNO:54	INQRSHITLASRFKDDYIQMAAETS--AIE---NTAHITMKTVPVTTKSLPPISSASY	108
SEQIDNO:55	-----MDRVSLSTILLY	14

LAMP同源结构域1

SEQIDNO:3	TLVT-----TQATPNNSHTAPPVTEVTVGPSLAPYSLPPTI--TPPAHTTGTSSTV	152
SEQIDNO:44	TLVT-----TQATPNNSHTAPPVTEVTVGPSLVPYSLPPTI--TPPAHTTGTSSTV	152
SEQIDNO:45	TLVT-----TQATSNNSHTAPPLTKVTVGPSLAPYSLPPTI--TPPAHTTGTSSTV	152
SEQIDNO:46	TLVT-----TQATSNNSHTAPPLTKVTVGPSLAPYSLPPTI--TPPAHTTGTSSTV	152
SEQIDNO:47	TLVT-----TIVTPNNSNTAAPVTEATIGPSADPGSLPTTS--TFLAHTTRTNPSTL	164
SEQIDNO:48	TLFT-----TLATPNTSHMAAPVTEAAISPSAGLSSLLPTI--IPPAHTTGTRSSTL	166
SEQIDNO:49	-----	0
SEQIDNO:50	TLLT-----TLATPDNTHTTTPVTEATIGPSAGPGSPPTTIITTTSSAYTTGTRSSTV	168
SEQIDNO:51	TLVT-----TLATPNKSHVTFPVTEAKVGLSVGPSSPPVTV--NPTAHTTGNRPSTA	167
SEQIDNO:52	TLVT-----TLATPSKSHVTFPVTEAKAGLSIGPSSPPVTI--NPAAHTTGNRPSTA	163
SEQIDNO:53	TFV-----RTNNSHMTASSTEDTIGSGSITHL-----FPPTTRASLAIV	146
SEQIDNO:54	TFV-----RSNNAHMTASSTDDTIGSGSIAHL-----FVPTTRASLAIV	147
SEQIDNO:55	GLLYINDAYSSENTFAQPSNTTTPAPNTTTTHVTSNTTTLAP-----NTTT	59

图5

LAMP同源结构域1

SEQIDNO:3	SHTTGNTTQPSNQTTLPATLSIALHKSTTGQKPVQP---THAPGTTAAAHNTTTRTAAPAS	209
SEQIDNO:44	SHTTGNTTQPSNQTTLPATLSIALHKSTTGQKPVQP---THAPGTTAAAHNTTTRTAAPAS	209
SEQIDNO:45	NHTTGNATQPSNQTTLPATLSIALHKSTTGQKPVQP---THAPGTTAAAHNTTTRTAAPAS	209
SEQIDNO:46	NHTTGNATQPSNQTTLPATLSIALHKSTTGQKPVQP---THAPGTTAAAHNTTTRTAAPAS	209
SEQIDNO:47	SHKTRKTTTFGNQTTLPATLSTSTHKSTSSHKSAQS---THAPGTTAAAHNTTQTASPAT	221
SEQIDNO:48	SPTAGKTTQPSNQTTLPATLSTSPHNSTASQKPTHF---NHTPGPTTGAHNTTQTASPAT	223
SEQIDNO:49	-----MTQSSRSVLLMLSSLHCLGSSLESNPKDPSVLAEAPGQN-----KRDSDISL	48
SEQIDNO:50	SHTTGKTTQLSNQTTLPATLSTSPHNSTTSQNPAHS---THTPGPTTGTCTNTTQTASPTT	225
SEQIDNO:51	SHTTGKTTQLSNQTTLPATLSTSPHNITTSQKPTQP---THTPGPTTATYNTTQTASPAT	224
SEQIDNO:52	SHTTGKTTQLSNQTTLPATLSTSPHNITTSQKPTQP---THTPGPTTAAAHNTTHTASPAT	220
SEQIDNO:53	NHITGRSTQLGGQTTLPKALFTPSHESTTTQRPTLS---TI-VSELTPTGKDRSTTSSVP	202
SEQIDNO:54	NYITGRATQLGGQTTLPKFTTASHKSTTNQRPTLS---TNVLGTSTPTHKDRSTTSPVP	204
SEQIDNO:55	THVTSNTTTLA-----PNTTTHITSNTTTTLAPNTT---TTLAPNTTTTHSVTTTKTAST	111

* . :

铰链

LAMP同源结构域2

SEQIDNO:3	TVPGPTLAPQPSVKTGIYQVLN-GSRLCIKAEMGIQLIVQDKESVFSPPRYFNIDPNAT	268
SEQIDNO:44	TVPGPTLAPQPSVKTGIYQVLN-GSRLCIKAEMGIQLIVQDKESVSWGHRTITLSS--K	266
SEQIDNO:45	TVPGSTLAPQPSVKTGIYQVLN-GSRLCIKAEMGIQLIVQDKESVFSPPRYFNLDPNAT	268
SEQIDNO:46	TVPGSTLAPQPSIKTGIYQVLN-GSRLCIKAEMGIQLIVQDKESVFSPPRYFNLDPNAT	268
SEQIDNO:47	PASGPTLAPQPSPKTGIYQVLN-GSRLCIKAEMGIELMVQDTKSQVFSPPRYFNIDPNAT	280
SEQIDNO:48	IAPGPTLAPQPSAKTGIYQVLN-GSKLCIKAEMGIELTVQDTQSVFSPPRYFNIDPNAT	282
SEQIDNO:49	VPQMPVLQPKETAPPLVTYTIIRNPQGVKVCVRASFGVEFVVREN----KKKYFNLTPNSA	104
SEQIDNO:50	TAPGPTLAPQPSAKTGMQIILN-GSKLCIKAEMGIQLTVQDTKSASPPQGYFNIDPNAT	284
SEQIDNO:51	IAPRPTLAPQPLSPKTGIYQVHN-GSKLCIKAEMGIQLTVQDSVSVFSPPQKYFNIDPNAT	283
SEQIDNO:52	IAPRPTLAPQPLSPKTGLYQVHN-GSKLCIKAEMGIQLTVQDSVSVFSPPQKYFNIDPNAT	279
SEQIDNO:53	LVRPPTLVTWSSPAKIGTYEVLN-GSRLCIKAEMGLALIVQEKGLDSATQRYFNIDPSLT	261
SEQIDNO:54	LVRPPTLVTWSSPAKIGTYEVLN-GSRLCIKAEMGLALIVQEKGLDSATQRYFNIDPSLT	263
SEQIDNO:55	TTPTPTLEPKPSPPETGNYTVKI-KNEFCIEALMGLELELTNS---TKTQQYFNIVPSQI	167

.: * : ...*:* :*: : : : : : : : :

LAMP同源结构域2

SEQIDNO:3	QASGNCGRK---SNLLLNFGGGFVNLTFTKDEESYYIIEVGAYLTVS-----DPETIY	319
SEQIDNO:44	SLSGGCLARNEHSPHPLFLFFFEKGPPSVTQAEDEESYYIIEVGAYLTVS-----DPETIY	321
SEQIDNO:45	QASGNCGRN---SNLLLNFGGGFVNLTFTKDEGSYYIIEVGACLTVS-----DPETIY	319
SEQIDNO:46	QASGNCGRN---SNLLLNFGGGFVNLTFTKDEGSYYIIEVGACLTVS-----DPETIY	319
SEQIDNO:47	QTSNGCSQK---SNLLLNFGGGFVNLTFLKDENSYYINEVGAYLTVS-----NPEKIY	331
SEQIDNO:48	QASGNCGRK---SKLLLNFGGGFVNLTFTKDENSYYVSGVGAYLTVS-----NPEKVV	333
SEQIDNO:49	RATGYCANQK---TVLSLEFSGGNLEFTFIKDGDSYVKTVKGSLRAAPPCKNCPSKIY	160
SEQIDNO:50	QVSGICGRK---SNLLLNFGGGFVNLTFTKDENSYYIIEVGAYLTVS-----NPEKTY	335
SEQIDNO:51	QASGNCGRK---SNLLLNFGGGFVNLTFTKGEKSYIIEVEAYLTVS-----NPAKVV	334
SEQIDNO:52	QASGNCGRK---SNLLLNFGGGFVNLTFTKDENSYYIIEVEAYLTVS-----NPAKVV	330
SEQIDNO:53	HASGKCGSQN---SNLFLNFQGGSVNVTFTKEENLYYVSEVGAYLTIS-----NTEKTY	312
SEQIDNO:54	HASGKCDQK---SNLFLNFQGGSVNITFTKEENLYYIIEVGAYLTIS-----NTEKTY	314
SEQIDNO:55	NSNGTCEKSK---ANLNLTFANSYINVFQAQDDNSYYLDNVTYFNLTVYFNLT-----RSESWY	218

.* * : * * * . . . : * : * : : . *

图5续

LAMP同源结构域2

	3	4	
SEQIDN0:3	QGIIKHAVVMFQTAVGHSFKCVSEQSIQLSAHLQVKTTDVQLQAFDFEDDHFGNVDECSSD		379
SEQIDN0:44	QGIIKHAVVMFQTAVGHSFKCVSEQSIQLSAHLQVKTTDVQLQAFDFEDDHFGNVDECSSD		381
SEQIDN0:45	QGMKHAVVMFQTAVGHSFKCVSEQSIQLSAHLQVKTTNVQLQAFDFEDDHFGNVDECSSD		379
SEQIDN0:46	QGMKHAVVMFQTVVGHSFKCVSEQSIQLSAHLQVKTTNVQLQAFDFEDDHFGNVDECSSD		379
SEQIDN0:47	QGMKSSVVMFETGVGHSFKCVSEQSIQLSTHLQKTMNVQFQAFDFEDDHFGNVDECSSD		391
SEQIDN0:48	QGMKNAVVMFETMIGHSFKCVSEQSIQLSPHLQKTMNVQLQAFDFEDDHFGNVDECSSD		393
SEQIDN0:49	VGLVDNEKLKFAKNGLSFNCKSETMLILADYFRLKLVPLQIQAFDLVNGAFGKEVECWAD		220
SEQIDN0:50	QGMKSPVVMFETVIGHSFKCVSEQSIQLSTHLQKTMNVQLQAFDFEDDHFGNVDECSSD		395
SEQIDN0:51	QGLKHAMMMFETVVGHSFKCVSEQSIQLSTYLQKTMNVQLQAFDFEDDHFGNADECISD		394
SEQIDN0:52	QGMKYAMMMFETVVGHSFKCVSEQSIQLSNHLQKTMNVQLQAFDFEDDHFGNADECISD		390
SEQIDN0:53	QGKS-TMMMFETVVGHSFKCVSEQSIQLSAQLQMKTMNIHLQAFDFEGDSFGIVDECLSD		371
SEQIDN0:54	QGKKNLTMMFETVVGHSFKCVSEQSIQLSAQLQMKTMNIHLQAFDFEGDSFGNVNECLSD		374
SEQIDN0:55	GNAT-NQKLLKTENGYSVKCKNTPKIQLGDTMNLVMTNVKLQVFNFKDNSFGKETTCKYD		277
	. : : : * * . : : : : : : : : : * * * *		

跨膜

胞质尾区

SEQIDN0:3	YIV-LPV-IGAIIVGLCLMGMGVYKIRLRCSGGYQRI	416
SEQIDN0:44	YTIV-LPV-IGAIIVGLCLMGMGVYKIRLRCSGGYQRI	418
SEQIDN0:45	YTIV-LPV-IGAIIVGLCLVGIGVYKIRLRCSGGYQRI	416
SEQIDN0:46	YTIV-LPV-IGAIIVGLCLVGMGVYKIRLRCSGGYQRI	416
SEQIDN0:47	YTVV-LPV-IGAIIVGLCAVGLIVYGIHLRRESSGYQRI	428
SEQIDN0:48	YTIV-LPV-IGAIIVGLCAVGLIVYGIHLKRESSEYQRI	430
SEQIDN0:49	YNKRMIPIILGAVAAAICLIAILTYVLVREHRNQGYEQL	259
SEQIDN0:50	YTVV-LPV-IGAIIVGLFAVGLIVYGVVRREASGYQRI	432
SEQIDN0:51	RNRREIPVAVGLSIAVLLAVLLTACLVTTRKRPSRGYERM	433
SEQIDN0:52	RNRREIPVAVGLSIAVLLAVLLTACLVTTRKRPSRGYERM	429
SEQIDN0:53	YTVV-LPV-VGIIVVLCVVGGLGIYKIRQRQSSAYQRI	408
SEQIDN0:54	YTVV-LPM-VAIIVVICVVGGLSVYKIRQRHQSAYQRI	411
SEQIDN0:55	HNFG-LMI-AGIVIVVIVVGLVVIYFIWHKRKSSGYQRI	314
	. : : . : : : : : * : : :	

LAMP-3					
登记号	物种	SEQ ID NO:	登记号	物种	SEQ ID NO:
NP_055213.2	智人 (H. sapiens)	3	XP_001496333.1	家马 (E. caballus)	50
XP_001155195.3	黑猩猩 (P. troglodytes)	44	NP_001095605.1	家牛 (B. taurus)	51
XP_003894825.1	东非狒狒 (P. Anubis)	45	XP_004003158.1	绵羊 (O. aries)	52
NP_001028044.1	猕猴 (M. mulatta)	46	NP_001012015.1	褐家鼠 (R. norvegicus)	53
XP_848889.2	家犬 (C. lupus familiaris)	47	NP_796330.2	小鼠 (M. musculus)	54
XP_003358746.1	野猪 (S. scrofa)	48	XP_002936919.2	热带爪蟾 (X. tropicalis)	55
XP_001342688.2	斑马鱼 (D. rerio)	49			

图5续

人类LIMP-2与直系同源序列的比对

信号序列

```

SEQIDNO:4      -----MGRCCFYTAGTLS 13
SEQIDNO:56     -----MGRCCFYTAGTLS 13
SEQIDNO:57     -----MGRCCFYTAGTLS 13
SEQIDNO:58     -----MGRCCFYTAGTLS 13
SEQIDNO:59     -----MGRCCFYTAGTLS 13
SEQIDNO:60     -----MGRCCFYTAGTLS 13
SEQIDNO:61     -----MTRRSCTIYATGIVC 15
SEQIDNO:62     -----MARCCFYTAGTLS 13
SEQIDNO:63     -----MRSLCLVTVGVLIA 13
SEQIDNO:64     -----MVKWAVFGTAAVS 13
SEQIDNO:65     MQLDDILHINNCKADCSSLSTTPNPKTDLVNMNGPKHKFCTKLSSTYLRKWWITIV--VA 58
SEQIDNO:66     -----MYGRSNRLCAKLSSAFLRKWWFVIA--FA 27

```

* * *

LAMP同源结构域

```

SEQIDNO:4      LLLLVTSVTLLVARVFQKAVDQSIEKKIVLRNGTEAFDSWEKPPPLPVYTQFYFFNVTNPE 73
SEQIDNO:56     LLLLVTSVTLLVARVFQKAVDQSIEKKIVLRNGTEAFDSWEKPPPLPVYTQFYFFNVTNPE 73
SEQIDNO:57     LLLLVTSVTLLVARVFQKAVDQSIEKKIVLRNGTEAFDSWEKPPPLPVYTQFYFFNVTNPE 73
SEQIDNO:58     LLLLVTSLALLVARVFQKAVDQTEKNIVLRNGSETFDSWKKPPLPVYAQFYFFNVTNPE 73
SEQIDNO:59     LLLLVTSLITLLVARVFQKAVDQTEKNIVLRNGSETFDSWKKPPLPVYTQFYFFNVTNPE 73
SEQIDNO:60     LLLLVTSVTLLVARVFQKAVDQTEKNMVLQNGTKVFNSWEKPPPLPVYIQFYFFNVTNPE 73
SEQIDNO:61     AHLLILGIALLLAQVFQTMQIERIKKEITLAENSRVLDGWINPPPPVYMQFYFFNVTNPD 75
SEQIDNO:62     LLLLVTSVTLLVARVFQKAVDQTEKNMVLQNGTKVFDSWEKPPPLPVYIQFYFFNVTNPE 73
SEQIDNO:63     LTLLIASISLLVAHVQTVVDLQVKQGTVLKNGTETFEAWEDPPPPVYMQFYFFNVTNPL 73
SEQIDNO:64     VTLLIVSIVLLTHTFMDIVEGQVKQAIVLKNESEVFEDWANPPPPVYMQFYFFNVTNPL 73
SEQIDNO:65     AALIIG--GIVVACEFTVLIDAVVDRMVALRPGAKTFGWAKPPVEPRISLYIYNVTNAD 116
SEQIDNO:66     LSLVL--GALVTFGTAFIRTIIDHQVALRVGGQSFGWWSRPPVEPIIRIFVYNVTNAD 85

```

*:: ::: * : ::: .* . : * ** :::****

LAMP同源结构域

```

SEQIDNO:4      EILRGE-TPRVEEVGPYTYRELRNKANIQFGDNGTTISAVSNKAYVFERDQSVGDPKIDL 132
SEQIDNO:56     EILRGE-TPRVEEVGPYTYRELRNKANIQFGDNGTTISAVSNKAYVFERDQSVGDPKIDL 132
SEQIDNO:57     EILRGE-TPRVEEVGPYTYRELRNKANVQFGDNGTTISAVSNKAYVFERDQSVGDPKIDL 132
SEQIDNO:58     EILRGE-IPRLEEVGPYTYRELRDKADIQFGDNGTTISAVSNKAYVFERNQSVGDPKTDL 132
SEQIDNO:59     EILNGE-TPRLEEVGPYTYRELRNKDDIQFGDNGTTISAVSNKAYVFERDKSVGDPKIDL 132
SEQIDNO:60     EILQGE-IPLLEEVGPYTYRELRNKANIQFGENGTTISAVTNKAYVFERNQSVGDPNVDL 132
SEQIDNO:61     EFLAGKEKAKVTQMGPYTYREYRPRENVTYLENGTKIFATNPKSFVFLRNMSAGDPEVDR 135
SEQIDNO:62     EILQGE-IPLLEEVGPYTYRELRNKANVQFGENGTTISAVTNKAYIFERNQSVGDPTVDL 132
SEQIDNO:63     EVLQGA-TPLVEEKGPYTYREYRPRVHVQFLDNGTKVSALNPKTYVFEPEKSVGNPEVDL 132
SEQIDNO:64     EVLSGE-KPFVDEIGPYTYREYRPRENITFSVNGTEVS AVTPKTYVFEPEKSIGDPKVDL 132
SEQIDNO:65     DFLSNGSKAIVDEVGPYVYSETWEKVNIVENDNGTL--SYNLRKIYSFREDLSVG--PEDDV 174
SEQIDNO:66     EFLNNGTKPILDELGPYVYVQVQTEWEKVNIVENPNTI--SYNQKRVYIFNEDLSGG--LEDDV 143

```

:.* . : : ***.* : : : *** : : * : * *

图6

LAMP同源结构域

```

SEQIDNO:4      IRTLNIPLVLTVIEWSQ-V-HFLREIEAMLKAYQQKLFVTHTVDELLWGYKDEILSLIHV 190
SEQIDNO:56     IRTLNIPLVLTVIEWSQ-V-RFLREIEAMLKAYQQKLFVTHTVDELLWGYKDEILSLIHV 190
SEQIDNO:57     IRTLNIPLVLTVIEWSQ-V-HFLREIEAMLKAYQQKLFVTHTVDELLWGYKDEILSLIHV 190
SEQIDNO:58     IRTLNIPLVLTVIEWSQ-V-HFLREIEAMLKAYQQKLFVTHTVDELLWGYKDEILSLIHV 190
SEQIDNO:59     LRTLNIPLVLTVIEWSQ-V-HFLREIEAMLKAYQQKLFVTHTVDELLWGYKDEILSLIHV 190
SEQIDNO:60     IRTINIPALTAMETWQ-L-PLLRDIEAMLKAYQQKLFVTHTVDELLWGYKDEILSLIHV 190
SEQIDNO:61     VTTVNIPMIAMNENLSYSFFVRTAVSMYMGSMGMGLFMNRTVHEILWGFKDPPLTKLHA 195
SEQIDNO:62     IRTINIPALTAMETWQ-L-PLLRDIEAMLKAYQQKLFVTHTVDELLWGYKDEILSLIHV 190
SEQIDNO:63     IRTINIPALTAMETWQ-L-PLLRDIEAMLKAYQQKLFVTHTVDELLWGYKDEILSLIHV 190
SEQIDNO:64     IRTINIPALTAMETWQ-L-PLLRDIEAMLKAYQQKLFVTHTVDELLWGYKDEILSLIHV 190
SEQIDNO:65     VIVPNIPMLSATSSQSKHAARFLRLAMASIMDILKIKPFVQVSVGQLLWGYEDPLLKLAKD 234
SEQIDNO:66     VIVPNIPMLSATSSQSKHAARFLRLAMASIMDILKIKPFVQVSVGQLLWGYEDPLLKLAKD 203
                : . * : * : : . . . : : * : * : : * : * : :

```

LAMP同源结构域

```

SEQIDNO:4      FRPDI----SPYFGLFYEKNGTNDGDYVFLTGEDSYLNFTKIVEWNGKTSLDWWITDKCN 246
SEQIDNO:56     FRPDI----SPYFGLFYEKNGTNDGDYVFLTGEDSYLNFTKIVEWNGKTSLDWWITDKCN 246
SEQIDNO:57     FRPDI----SPYFGLFYEKNGTNDGDYVFLTGEDSYLNFTKIVEWNGKTSLDWWITDKCN 246
SEQIDNO:58     FKPEI----SPYFGLFYEKNGTNDGDYVFLTGEDSYLNFTKIVEWNGKTSLDWWITDKCN 246
SEQIDNO:59     FKHDV----SPYFGLFYEKNGTNDGDYVFLTGEDSYLNFTKIVEWNGKTSLDWWITDKCN 246
SEQIDNO:60     FKPDV----SPNFGFLFYERNGTNDGEYVFLTGEDSYLNFTKIVEWNGKTSLDWWITDKCN 246
SEQIDNO:61     MRPEV----DEHFGMLYNKNGTHEGEFVFHTGEKNYMNNGKIDTWNIGSQMNWSSNQSN 251
SEQIDNO:62     FRPDV----SPNFGFLFYERNGTNDGEYVFLTGEDSYLNFTKIVEWNGKTSLDWWITDKCN 246
SEQIDNO:63     LHPEI----DPVFGFENKMGNTDDGEYVFLSGEMNYLNFSRIVEWNGKTSLDWWITDKCN 246
SEQIDNO:64     FKKNI----SDTFGLFYKMNNTDDGEYVFLSGEKDYLEFTQIAEWKQKALNWWTTETCN 247
SEQIDNO:65     VVPKEQKLPYEEFGLLYGKNGTSSDRVTVNTGVDDIRRYGIIDNFNGRTHLPHWTTDACN 294
SEQIDNO:66     VVPKEQKLPYEEFGLMYGKNSTSKDVTVTWTVGVDDITQYGIIDKYNGRSHQTHWLSEQCN 263
                . . . ** : * * . . . : * . . : * : * * : * . . *

```

LAMP同源结构域

```

SEQIDNO:4      MINGTDGDSFHPLITKDEVLYVFPSEDFCRSVYITFSDYES-VQGLPAFRYKVP AEILANT 305
SEQIDNO:56     MINGTDGDSFHPLITKDEVLYVFPSEDFCRSVYITFSDYES-VQGLPAFRYKVP AEILANT 305
SEQIDNO:57     MINGTDGDSFHPLITKDEVLYVFPSEDFCRSVYITFSDYES-VQGLPAFRYKVP AEILANT 305
SEQIDNO:58     MINGTDGDSFHPLITKDEVLYVFPSEDFCRSVYITFSDYES-VQGLPAFRYKVP AEILANT 305
SEQIDNO:59     MINGTDGDSFHPLITKDEVLYVFPSEDFCRSVYITFSDYES-VQGLPAFRYKVP AEILANT 305
SEQIDNO:60     MINGTDGDSFHPLITKDEVLYVFPSEDFCRSVYITFSDYES-VQGLPAFRYKVP AEILANT 305
SEQIDNO:61     MINGTDGDSFHPLITKDEVLYVFPSEDFCRSVYITFSDYES-VQGLPAFRYKVP AEILANT 305
SEQIDNO:62     MINGTDGDSFHPLITKDEVLYVFPSEDFCRSVYITFSDYES-VQGLPAFRYKVP AEILANT 305
SEQIDNO:63     MINGTDGDSFHPLITKDEVLYVFPSEDFCRSVYITFSDYES-VQGLPAFRYKVP AEILANT 305
SEQIDNO:64     MINGTDGDSFHPLITKDEVLYVFPSEDFCRSVYITFSDYES-VQGLPAFRYKVP AEILANT 305
SEQIDNO:65     TLAGTDGDSIFPPHIDHDLRLHVDKDLRLPLVFEKEVMTSNEVPGYRFTPEWVFADV 354
SEQIDNO:66     RLNGTDGDSIFPPRITKNSTLHVYEKDLRLPLVFEKEVMTSNEVPGYRFTPEWVFADV 323
                : **** * : : . : : : : : : : : : : : : : :

```

图6续

LAMP同源结构域

```

          3       4       5
SEQIDNO:4  ---SDNAGFCIPE-GNCLGSGVLNVSICKNGAPIIMSFPHFYQADERFVSAIEGMHP-NQ 360
SEQIDNO:56 ---SDNAGFCIPE-GNCLGSGVLNVSICKNGAPIIMSFPHFYQADERFVSAIEGMHP-NK 360
SEQIDNO:57 ---SDNAGFCIPE-GNCLGSGVLNVSICKNGAPIIMSFPHFYQADERFVSAIEGMHP-NK 360
SEQIDNO:58 ---SDNAGFCVPE-GNCLGSGVLNVSICKNGAPIIMSFPHFYQADERFVSAIDGMHP-NK 360
SEQIDNO:59 ---SDNAGFCIPK-GNCLGSGVLNVSICKNGAPIIMSFPHFYQADERFVSAIGGMHP-NK 360
SEQIDNO:60 ---SENAGFCIPE-GNCMDSGVLNVSICKNGAPIIMSFPHFYQADERFVSAIKGMHP-NK 360
SEQIDNO:61 DENPANAGFCVPA-GDCLGKGVLVSVCRQGAPIVVSFPHFYQADERYINAIEGMNP-NE 368
SEQIDNO:62 ---SENAGFCIPE-GNCMDAGVLNVSICKNGAPIIMSFPHFYQADERFVSAIKGMHP-NK 360
SEQIDNO:63 TVNPDNAGFCVPP-GNCPGAGVLNVSICKQGAPIFLSAPHFYQADQKFVSDIEGMHP-TK 363
SEQIDNO:64 SVNPNQKGFVPE-GNCLPSGLLNVSICKGAPIVLSSPHFYQADENVINSIRGMKP-VK 364
SEQIDNO:65 DSHPDNMCFCPAGKPCSPNGLFNVSLCQYDSPIMLSFPHFYLADES LRTQVEGISPPMK 414
SEQIDNO:66 DKNPNMCMCYCPAG-PPCAPHGLFNVSLCQYDSPILLSFPHFYMAQT LRTAVEGISPPEK 382
          * : *      * : : : : * : : : : * : : : : * : : : :

```

LAMP同源结构域

```

SEQIDNO:4  EDHETFVDINPLTGIILKAAKRFQINIYVKKLDDFVETGDIRTMVFPVMYLNESVHIDKE 420
SEQIDNO:56 EDHETFVDINPLTGIILKAAKRFQINIYVKKLDDFVETGDIRTMVFPVMYLNESVHIDKE 420
SEQIDNO:57 EDHETFVDINPLTGIILKAAKRFQINIYVKKLDDFVETGDIRTMVFPVMYLNESVHIDKE 420
SEQIDNO:58 DYHETFVDINPLTGIILRAAKRFQINVYVKKLDDFIETGNIRTMVFPVMYINESVLIDKD 420
SEQIDNO:59 EYHETFVDINPLTGIILRAAKRFQINVYVKKLDDFVETGNIQTLVFPVMYINESVLIDKE 420
SEQIDNO:60 EEHESFVDINPLTGIILRGAKRFQINTYVRKLDDFVETGDIRTMVFPVMYLNESVLIDKE 420
SEQIDNO:61 EEHETYLDINPTTGVPPIRACKRAQLNIILKRVRGFPNTKFLNETIFPIMYVNETATIDDE 428
SEQIDNO:62 EEHESFVDINPLTGIILRGAKRFQINTYVKKLDDFVETGNIRTMVFPVMYLNESVLIDKE 420
SEQIDNO:63 EYHETFVDINPLTGLVLQAARKMQINIHVRKLPEFFETGNIRTLIFPVMYINESVLIDEA 423
SEQIDNO:64 EHHMTFLDLNPLTGLTILQAARKIQNVYVRKINVYLITQDIQTLFFPVMHNLNESVLIDDK 424
SEQIDNO:65 EKHQFFFDVQPKMGTTLVRARIQINLAVSQVFDIKQVANFPDIIFPILWFEEGIDNLPD 474
SEQIDNO:66 DKHQFLFDVQPDMTALRPARARIQINLAVSQVVDIKQVANFPDIVFPILWFEEGIDSLPD 442
          : * : : : * : : : * : : : * : : : * : : : * : : :

```

跨膜结构域

胞质尾区

```

SEQIDNO:4  TASRLKSMINTTTLITNI----PYIIMALGVFFGLVFTWLACKGQGSMDDEGTADERAPLI 476
SEQIDNO:56 TASRLKSMINTTTLITNI----PYIIMALGVFFGLVFTWLACKGQGSMDDEGTADERAPLI 476
SEQIDNO:57 TASRLKSVINTTTLITNI----PYIIMALGVFFGLVFTWLACKGQGSMDDEGTADERAPLI 476
SEQIDNO:58 TASRLKSVINTTTLITNI----PYIIMALGVFFGLVFTWLACRGQGSMDDEGTADERAPLI 476
SEQIDNO:59 TASRLKSVINTTTLITNI----PYIIMALGVFFGLVFTWLACRGQGSMDDEGTADERAPLI 476
SEQIDNO:60 TANQLKSVINTTTLIVTNI----PYIIMALGVFFGLVFTWLACRGQGSMDDEGTADERAPLI 476
SEQIDNO:61 SAAQMRMLLLIVTVVSNF----PVIILALGVILLVLI FLVCRNRQRKNEVKRIDFTEAF 484
SEQIDNO:62 TASQLKSVINTTTLIVTNI----PYIIMALGVFFGLVFTWLACRGQGSMDDEGTADERAPLI 476
SEQIDNO:63 SANKLKHVLEASVVTGI----PFVIMAIGIVFGIVSVLVCRAQGAREESTEEERSPLI 479
SEQIDNO:64 SAGRLRSILFQGRVANI----PFIIMGLGIIILAFLETTLSCLQKRSRDEGTEEEERGPII 480
SEQIDNO:65 EVTDL--MRAEQVPPKIRVALIVGLCALGVILLLLSTF--CLIRNSHRQSTLHLEGSNY 530
SEQIDNO:66 EILD--MKVATNIPPRAKFI LIALFGLGGFLFVAVI--CLVRKSHRQSTLHLEGSNY 498
          : : : : : : : : : : : : : : : :

```

图6续

```

SEQIDNO:4      RT----- 478
SEQIDNO:56     RT----- 478
SEQIDNO:57     RT----- 478
SEQIDNO:58     RT----- 478
SEQIDNO:59     RT----- 478
SEQIDNO:60     RT----- 478
SEQIDNO:61     HSFATTKDEYATQVSNQAEDSPENRNNQPLRNGSYIAMSPVEAQKC 531
SEQIDNO:62     RT----- 478
SEQIDNO:63     RT----- 481
SEQIDNO:64     RAS----- 483
SEQIDNO:65     LATA-----QVDMNKKQNKDNQPARY----- 551
SEQIDNO:66     LATA-----SVDQAKKKAKMDNGMSSKSN----- 522
                :

```

LIMP-2					
登记号	物种	SEQ ID NO:	登记号	物种	SEQ ID NO:
NP_005497.1	智人 (<i>H. sapiens</i>)	4	NP_775366.1	斑马鱼 (<i>D. rerio</i>)	61
XP_517214.2	黑猩猩 (<i>P. troglodytes</i>)	56	NP_446453.1	褐家鼠 (<i>R. norvegicus</i>)	62
XP_001096458.1	猕猴 (<i>M. mulatta</i>)	57	XP_420593.1	原鸡 (<i>G. gallus</i>)	63
XP_005639134.1	家犬 (<i>C. lupus familiaris</i>)	58	NP_001016557.1	热带爪哇 (<i>X. tropicalis</i>)	64
NP_001095623.1	家牛 (<i>B. Taurus</i>)	59	NP_726504.2	黑腹果蝇 (<i>D. Melanogaster</i>)	65
NP_031670.1	小鼠 (<i>M. musculus</i>)	60	XP_314345.2	冈比亚按蚊 (<i>A. gambiae</i>)	66

图6续

人类LIMBIC/SLAMP与直系同源序列的比对

信号序列	LAMP同源结构域	
		1
SEQIDNO:67	-MVRVQPDQRKQLPLV-LLRLCL-LPTGLPVRSDVDFNRGTDNITVRQGDTAILRCVVED	57
SEQIDNO:68	-MVRVQPDQRKQLPLV-LLRLCL-LPTGLPVRSDVDFNRGTDNITVRQGDTAILRCVVED	57
SEQIDNO:69	-MGARVQPDQRKQLPLV-LLRLCL-LPTGLPVRSDVDFNRGTDNITVRQGDTAILRCVVED	57
SEQIDNO:70	-MVGRVQPDQRKQLPLV-LLRLCL-LPTGLPVRSDVDFNRGTDNITVRQGDTAILRCVVED	57
SEQIDNO:71	-MVGRSQSDRNQPLPLF-LLRLCL-LPTGLPVRSGDFNRSTDNMTVRQGDTAILRCFVED	57
SEQIDNO:72	----MSCLWIHSVFIPGFF--LLF-GFEGFPVISVESQRSTDNITVRQGDITVIRCYVDD	53
SEQIDNO:102	-MVGRVQPDQRKQLPLV-LLRLCL-LPTGLPVRSDVDFNRGTDNITVRQGDTAILRCVVED	57
SEQIDNO:103	-MVGRVQPDQRKQLPLV-LLRLCL-LPTGLPVRSDVDFNRGTDNITVRQGDTAILRCVVED	57
SEQIDNO:104	-MVARVQPDQRKQLPLV-LLRLCL-LPTGLPVRSDVDFNRGTDNITVRQGDTAILRCVVED	57
SEQIDNO:105	-MVARVQPDQRKQLPLV-LLRLCL-LPTGLPVRSDVDFNRGTDNITVRQGDTAILRCVVED	57
SEQIDNO:106	-----MSFAGEAA-----SQILNKAEPFI SRSEAFKFAVGDTITLPCEVAS	42
SEQIDNO:107	-----MRPCLLHSIWMLGFVLCCLSLQGLPVRSGDFNRSTDNITVRQGDTAILRCFVED	54
SEQIDNO:108	-MLGARRPPRSQPLPLV-LLRLCL-LPTGLPVRSDVDFNRGTDNITVRQGDTAILRCVVED	57
SEQIDNO:109	-MVGRVHPDRKQLPLV-LLRLCL-LPTGLPVRGVDFTRGTDNITVRQGDTAILRCYVED	57
SEQIDNO:110	-MVARQPDQRKQLPLV-LLRLCL-LPTGLPVRSDVDFNRGTDNITVRQGDTAILRCFVED	57
SEQIDNO:111	----MPTYW-LHSIWVL-GFFLSLF-SLQGLPVRSDVDFNRGTDNITVRQGDTAILRCYVED	54
SEQIDNO:112	-----MRPCLLHSIWMLGFVLCCLSLQGLPVRSGDFNRSTDNITVRQGDTAILRCFVED	54
SEQIDNO:113	MQVGRKSCWRQ--LQASFRLCL-IPTGFVRSVDMQRATDNITVRQGDTAILRCYVDD	57
	:	:: :.. *** : * * .

LAMP同源结构域

		2
SEQIDNO:67	KN-SKVAWLNRSGIIFAGHDKWSDPRVELEKRHSLEYSRLRIQKVDVYDEGSYTCVQTQ	116
SEQIDNO:68	KN-SKVAWLNRSGIIFAGHDKWSDPRVELEKRHSLEYSRLRIQKVDVYDEGSYTCVQTQ	116
SEQIDNO:69	KN-SKVAWLNRSGIIFAGHDKWSDPRVELEKRHSLEYSRLRIQKVDVYDEGSYTCVQTQ	116
SEQIDNO:70	KN-SKVAWLNRSGIIFAGHDKWSDPRVELEKRHALEYSLRIQKVDVYDEGSYTCVQTQ	116
SEQIDNO:71	KS-SKVAWLNRSGIIFAVDDKWSDPRVELEKRSPFEYSRLRIQKVDVSDGEPYICVQTN	116
SEQIDNO:72	KV-SKVAWLNRSGIIFAGEDKWSDPRVELVTQGGLEYSLRIQKVDVDEGPYTCVQTK	112
SEQIDNO:102	KN-SKVAWLNRSGIIFAGHDKWSDPRVELEKRHALEYSLRIQKVDVYDEGSYTCVQTQ	116
SEQIDNO:103	KN-SKVAWLNRSGIIFAGHDKWSDPRVELEKRHSLEYSRLRIQKVDVYDEGSYTCVQTQ	116
SEQIDNO:104	KN-SKVAWLNRSGIIFAGHDKWSDPRVELEKRHSLEYSRLRIQKVDVYDEGSYTCVQTQ	116
SEQIDNO:105	KN-SKVAWLNRSGIIFAGHDKWSDPRVELEKRHSLEYSRLRIQKVDVYDEGSYTCVQTQ	116
SEQIDNO:106	PGTYVLAWKRGIAILTAGSVKVTDPVRVLVN---GYSLQIRDAVPQDAGDYICQIAML	98
SEQIDNO:107	RS-SRVAWLNRSGIIFAGDDKWSDPRVELEKRSLLEYSLRIQKVDVSDGEPYTCVQTK	113
SEQIDNO:108	KN-SKVAWLNRSGIIFAGHDKWSDPRVELEKRHSLEYSRLRIQKVDVYDEGSYTCVQTQ	116
SEQIDNO:109	KS-SKVAWLNRSGIIFAGHDKWSDPRVELEKRRTALEYSRLRIQKVDVYDEGSYTCVQTQ	116
SEQIDNO:110	RS-SKVAWLNRSGIIFAGEDKWSDPRVELEKRSPLEYSLRIQKVDVYDEGSYTCVQTQ	116
SEQIDNO:111	RS-SKVAWLNRSGIIFAGEDKWSDPRVELEKRNPLEYSLRIQKVDVYDEGSYTCVQTQ	113
SEQIDNO:112	RS-SRVAWLNRSGIIFAGDDKWSDPRVELEKRSLLEYSLRIQKVDVSDGEPYTCVQTK	113
SEQIDNO:113	KV-SKVAWLNRSGIIFAGQDKWSDPRVDLVTKGLEYSLRIQKVDVYDEGSYTCVQTK	116
	: ** . * : * * : * * * * . * * * : * : . * * * * . :	

图7

LAMP同源结构域

3

```

SEQIDNO:67 HEPKTSQVYLVQVPPKISNISS--DVTVNEGSNVTLVCMANGRPEPVITWRHLTP---T 171
SEQIDNO:68 HEPKTSQVYLVQVPPKISNISS--DVTVNEGSNVTLVCMANGRPEPVITWRHLTP---T 171
SEQIDNO:69 HEPKTSQVYLVQVPPKISNISS--DVTVNEGSNVTLVCMANGRPEPVITWRHLTP---T 171
SEQIDNO:70 HEPKTSQVYLVQVPPKISNISS--DVTVNEGSNVTLVCMANGRPEPVITWRHLTP---L 171
SEQIDNO:71 QHTKTMQVYLVQVPPKISNISA--DITVNEGSNVTLMCIAYGRPEPMITWRHLTP---T 171
SEQIDNO:72 QQSKTSQVYLVQVPAIIYKVSE--DITVNEGSNVALTCLANGRPDPAITWRLLNP---S 167
SEQIDNO:102 HEPKTSQVYLVQVPPKISNISS--DVTVNEGSNVTLVCMANGRPEPVITWRHLTP---L 171
SEQIDNO:103 HEPKTSQVYLVQVPPKISNISS--DVTVNEGSNVTLVCMANGRPEPVITWRHLTP---T 171
SEQIDNO:104 HEPKTSQVYLVQVPPKISNISS--DVTVNEGSNVTLVCMANGRPEPVITWRHLTP---T 171
SEQIDNO:105 HEPKTSQVYLVQVPPKISNISS--DVTVNEGSNVTLVCMANGRPEPVITWRHLTP---T 171
SEQIDNO:106 DPR-EITHSVEILVPPKITHVTSGGHLQVRKGSFVRLECSATGNPMPNITWRKNNLLPN 157
SEQIDNO:107 QHTKTTQVYLVQVPPKISNISA--DITVNEGSNVTLMCIAYGRPEPMITWRHLTP---T 168
SEQIDNO:108 HEPKTSQVYLVQVPPKISNISS--DVTVNEGSNVTLVCMANGRPEPVITWRHLTP---T 171
SEQIDNO:109 HQPKTSQVYLVQVPPKISNISS--DVTVNEGSNVTLVCMANGRPEPVITWRHLTP---T 171
SEQIDNO:110 HHPKTSQVYLVQVPPKISNISS--DITVNEGSNVTLVCMANGRPEPVITWRHLTP---T 171
SEQIDNO:111 HHPKTSQVYLVQVPPKISNISS--DITVNEGSNVTLVCMANGRPEPVITWRHLTP---T 168
SEQIDNO:112 QHTKTTQVYLVQVPPKISNISA--DITVNEGSNVTLMCIAYGRPEPMITWRHLTP---T 168
SEQIDNO:113 QQPKTSQVYLVQVPASIVQVSN--DITVNEGSNVTLSCLANGRPDPAITWRLLNP---S 171
. : * * * : : . : * : * * * * * * * * * * *

```

LAMP同源结构域

4

```

SEQIDNO:67 GREFEGEEYLEILGITREQSGKYECKAANEVSSADVQVKVTVNYPPTITESKS 230
SEQIDNO:68 GREFEGEEYLEILGITREQSGKYECKAANEVSSADVQVKVTVNYPPTITESKS-NEAT 230
SEQIDNO:69 GREFEGEEYLEILGITREQSGKYECKAANEVSSADVQVKVTVNYPPTITESKS-NEAT 230
SEQIDNO:70 GREFEGEEYLEILGITREQSGKYECKAANEVSSADVQVKVTVNYPPTITESKS-NEAT 230
SEQIDNO:71 ARDFEGEEEFLEIQGITREQSGRYECKAANEVASADVQVRVTVNYPPIITESNS-NEAT 230
SEQIDNO:72 AEALDV-GEYLEISGVVRSQAGRYECKASNDVSTPDVKYVNVVNVNYPPIKDVRS-SETA 225
SEQIDNO:102 GREFEGEEYLEILGITREQSGKYECKAANEVSSADVQVKVTVNYPPTITESKS-NEAT 230
SEQIDNO:103 GREFEGEEYLEILGITREQSGKYECKAANEVSSADVQVKVTVNYPPTITESKS-NEAT 230
SEQIDNO:104 GRELEGEYLEILGITREQSGKYECKAANEVSSADVQVKVTVNYPPTITESKS-NEAT 230
SEQIDNO:105 GREFEGEEYLEILGITREQSGKYECKAANEVSSADVQVKVTVNYPPTITESKS-NEAT 230
SEQIDNO:106 GEEQFT-NPVYVIENMDRHKGTYICTANNGVGQVATSQIILHVLYPEISVENPTVYSG 216
SEQIDNO:107 ARDFEGEEEFLEIQGITREQSGRYECKAANEVASADVQVRVTVNYPPIITESKS-NEAT 227
SEQIDNO:108 GREFEGEEYLEILGITREQSGKYECKAANEVSSADVQVKVTVNYPPTITESKS-NEAT 230
SEQIDNO:109 GREFEGEEYLEILGITREQSGKYECKAANEVSSADVQVKVTVNYPPTITESKS-NEAT 230
SEQIDNO:110 GKEFEGEEYLEILGITREQSGKYECKAANEVASADVQVRVTVNYPPTITESKS-NEAA 230
SEQIDNO:111 GKEFEGEEYLEILGITREQSGKYECKAANEVASADVQVRVTVNYPPTITESKS-NEAA 227
SEQIDNO:112 ARDFEGEEEFLEIQGITREQSGRYECKAANEVASADVQVRVTVNYPPIITESKS-NEAT 227
SEQIDNO:113 AEPLDG-EEYLDIIGIMRTQAGRYECKASNDVATPDVKYVNVVNVNYPPTIKKTQS-SETP 229
.. * . : * : * * * * * * * * . : : * * * * * . :

```

图7续


```

SEQIDNO:67 ----- 338
SEQIDNO:68 ----- 338
SEQIDNO:69 ----- 338
SEQIDNO:70 ----- 341
SEQIDNO:71 ----- 337
SEQIDNO:72 ----- 333
SEQIDNO:102 ----- 338
SEQIDNO:103 ----- 338
SEQIDNO:104 ----- 338
SEQIDNO:105 ----- 338
SEQIDNO:106 MTFSIGQLQLQTDWRDIVLPAPFPYSHHYTQGMSYLRGLEDQDQYQEARVQSRNRYGWS 393
SEQIDNO:107 ----- 334
SEQIDNO:108 ----- 338
SEQIDNO:109 ----- 338
SEQIDNO:110 ----- 338
SEQIDNO:111 ----- 335
SEQIDNO:112 ----- 334
SEQIDNO:113 ----- 337

SEQIDNO:67 ----- 338
SEQIDNO:68 ----- 338
SEQIDNO:69 ----- 338
SEQIDNO:70 ----- 341
SEQIDNO:71 ----- 337
SEQIDNO:72 ----- 333
SEQIDNO:102 ----- 338
SEQIDNO:103 ----- 338
SEQIDNO:104 ----- 338
SEQIDNO:105 ----- 338
SEQIDNO:106 FSESFLFTTSNTGKWMGQCCTNPG 417
SEQIDNO:107 ----- 334
SEQIDNO:108 ----- 338
SEQIDNO:109 ----- 338
SEQIDNO:110 ----- 338
SEQIDNO:111 ----- 335
SEQIDNO:112 ----- 334
SEQIDNO:113 ----- 337

```

LIMBIC/LSAMP					
登记号	物种	SEQ ID NO:	登记号	物种	SEQ ID NO:
NP_002329.2	智人 (<i>H. sapiens</i>)	67	NP_001192297.1	家牛 (<i>B. Taurus</i>)	105
XP_516662.2	黑猩猩 (<i>P. troglodytes</i>)	68	XP_312298.5	冈比亚按蚊 (<i>A. gambiae</i>)	106
XP_002716722.1	家兔 (<i>O. cuniculus</i>)	69	NP_001096385.1	热带爪蟾 (<i>X. tropicalis</i>)	107
NP_780757.1	小鼠 (<i>M. musculus</i>)	70	XP_003434117.1	家犬 (<i>C. lupus familiaris</i>)	108
NP_001086181.1	非洲爪蟾 (<i>X. laevis</i>)	71	XP_001362972.1	短尾负鼠 (<i>M. domestica</i>)	109
NP_001034921.1	斑马鱼 (<i>D. rerio</i>)	72	NP_990205.1	原鸡 (<i>G. gallus</i>)	110
NP_058938.1	褐家鼠 (<i>R. norvegicus</i>)	102	XP_002190582.1	斑胸草雀 (<i>T. guttata</i>)	111
XP_001502710.1	家马 (<i>E. caballus</i>)	103	NP_001096385.1	热带爪蟾 (<i>X. tropicalis</i>)	112
NP_001231626.1	野猪 (<i>S. scrofa</i>)	104	XP_003449349.1	罗非鱼 (<i>O. niloticus</i>)	113

图7续

Endolyn					
登记号	物种	SEQ ID NO:	登记号	物种	SEQ ID NO:
NP_006007.2	智人 (H. sapiens)	5	NP_001039506.1	家牛 (B. taurus)	76
NP_058594.1	小鼠 (M. musculus)	73	XP_004011265.1	绵羊 (O. aries)	77
XP_001091286.1	猕猴 (M. mulatta)	74	XP_532256.2	家犬 (C. lupus familiaris)	78
XP_001924661.2	野猪 (S. scrofa)	75	NP_114000.1	褐家鼠 (R. norvegicus)	79

图8续

人类MACROSAILIN与直系同源序列的比对

信号序列

LAMP同源结构域 1

1

```

SEQIDNO:80  MRLAVLFSGALLGL-LAAQGTGNDCPHKKSATLLPSFTVTPTVTEST----GTTSHRRTK 55
SEQIDNO:81  MRLAVLFSGALLGL-LAAQGTGNDCPHKKSATLLPSFTVTPTVTEST----GTTSHRRTK 55
SEQIDNO:82  MRLAVFFSGALLGL-LAAQGTGNDCPHKKSATLLPSFTVTPTATESTPS-PGTTSHRRTK 58
SEQIDNO:83  MRLPVCL--ILLGP-LIAQGTEDDCPHKKAVTLLPSFTMTPTATESTAS-PTTSHRPTTT 56
SEQIDNO:84  MRLAVLFLGALLGL-LAAQGTGNDCPHKKSATLLPSFTVTPTATEST----GTTSHRRTK 55
SEQIDNO:85  MRFPVCL--TLLVL-LVAQGTGKDCPHKKAATLLPSFTETPTTTGSTAS-PTTTHRPPTT 56
SEQIDNO:86  MRPAVFFLGALVGL-LAAQGTGNDCPHKKSATLLPSFTVTPTATESTGS-PGTTSHSTTT 58
SEQIDNO:87  MRLAVLFSGALLGL-LAAQGTGNDCPHKKSATLLPSFTVTPTATESTAS-PGTTSHQTTQ 58
SEQIDNO:88  MRLPVFLFLA-LLGL-HAA-----S-SGTTSHRRTK 27
SEQIDNO:89  MTLAVLFLGALLGL-LAESTTSH-----22
SEQIDNO:90  MRLAVLFSGALLGL-LAAQGTGNDCPHKKSATLLPSFTVTPTATEST----GTTSHRRTK 55
SEQIDNO:91  MRLSLLSGILLGL-LAEQGAGDKCPQEKSVTLVPSFTVTTIATERSTTSPETTTSSGS- 58
SEQIDNO:92  -----MGLTLPLPAQGSQCRANCPHKKSATLVPSFTVTPTATSG----PTTTAHQTTT 49

```

LAMP同源结构域 1

```

SEQIDNO:80  SHKTTTHRRTT-----TGTTSHGPTTATHNPPTTSHGNVTVHPTSNSTATSQGPSTAT 108
SEQIDNO:81  SHKTTTHRRTT-----TGTASHGPTTATHNPPTTSHGNVTVHPTSNSTATSQGPSTAT 108
SEQIDNO:82  SHRTTWRISTTHTTNTTGTSSSESPTATHSPA-----92
SEQIDNO:83  SHGNVTVH-----T-----SSGPTTVTHNPA-----77
SEQIDNO:84  SHKTTTHRRTT-----TGTTSHRPTTATHNPPTTSHRNATVHPTSNSTATSQGPSTAT 108
SEQIDNO:85  SHRPTTTS-----HRPTTSHRPTTSHRPT-----TTS 85
SEQIDNO:86  AETT-----SHAPNTTTHQ-----72
SEQIDNO:87  SHRTTTT-----GTTSDHPTTATHNP-----79
SEQIDNO:88  NPHTT-----SHSTATPGTTSRPTTAT-----50
SEQIDNO:89  --RTTTPR-----TTTTGTSHGPTTVTHNPA-----47
SEQIDNO:90  SHKTTTHRRTT-----TGTTSHRPTTATHNPNTTSHRNATVHPTSNSTATSQGPSTAT 108
SEQIDNO:91  --TATTYRTS-----TAATTPHS-----NSTATS-----80
SEQIDNO:92  DHGTTTSHETTTSQGTSTHGTSPTHTTTTGHGTT-TGHQN-----TSH-----91

```

LAMP同源结构域 1

```

SEQIDNO:80  HSPATTSHGNATVHPT-SNSTATSPG-----F-T--SSAHPEPPPPSPSPSPTSK 154
SEQIDNO:81  HSPATTSHGNATVHPT-SNSTATSPG-----F-T--SSAHPEPPPPSPSPSPTSK 154
SEQIDNO:82  ---TTTSHQNTTVHPT-SNITATSPG-----PST--RSPHPEP-PPSPSPSPGSK 135
SEQIDNO:83  ---TTTSHGNATISHATVSPTT-----NG-TATSPRSST--VGPHPGPPPPSP--SPRSK 124
SEQIDNO:84  HRPATTSHGNATVHPT-SNSTATSPG-----L-T--SSAHPGPPPPSPSPSPASK 154
SEQIDNO:85  HRPTTSHGNATV-----SP-----TTNSPGFST--VGPHPGPPPPSPSPSPSST 128
SEQIDNO:86  -APTTPGHRNTTIHPTTSNSTSNTTGTGTGKPHSTSY--TQPGPGPRPPPPSPGPGPQ 129
SEQIDNO:87  ---TTTSHGNTTVHPTTSNSTVTSPT-----SAS--SSPHRPPPPSPSPSPGSK 124
SEQIDNO:88  ---PTTGHGNVTVHPTTSNTTSNTTTTGTGTS---PGFST--STPHPGPPPPPPSPSPGSR 102
SEQIDNO:89  ---TTTSHGNATVHPT-SSSTATSPG-----SST--RPPHPGPPPPSPSPSPGSQ 91
SEQIDNO:90  HRPATTSHGNATVHPT-SNSTATSPG-----L-T--SSAHPGPPPPSPSPSPASK 154
SEQIDNO:91  --YSTTSEGTAVTHGTTSPRN-----TSTT--STSQSVFPVPPSPQFTSSPS 123
SEQIDNO:92  --STTTSHGTSTPHKTTTRHPTTSHGTTTSHGTSTGHWTARPTIRGPPPPPP-----SPG 145

```

* . . . *

* * * *

图9

跨膜结构域		胞质尾区
SEQIDNO:80	-SILLPLIIGLILLGLLALVLI	AFCIIRRRPSAYQAL 354
SEQIDNO:81	-SILLPLIIGLILLGLLALVLI	AFCIIRRRPSAYQAL 354
SEQIDNO:82	-SILLPLIIGLILLGLLTLVLT	FCIIRRRPPTYQPL 335
SEQIDNO:83	-SLLLPLIIGLVLLGLLTLVLT	AFCITRRRQSTYQPL 335
SEQIDNO:84	-SILLPLIIGLVLLGLLALVLI	AFCIVRRRPSAYQAL 354
SEQIDNO:85	-SLLLPLIIGLVLLGLLTLVLT	AFCVTRRRQSTYQPL 330
SEQIDNO:86	-FNLLPLIVGVISLGLLALALV	TFCIIRRRPPTYQPL 329
SEQIDNO:87	-SILLPLIIGLILLGLFALVLT	FCVIRRRPPTYQAL 322
SEQIDNO:88	PSILVPLIIGLILVGLLALVLV	AFCIARRRPSAYQAL 305
SEQIDNO:89	-TILLPLIIGLIFLGLLILVLT	FCIIRRRPPAYQPL 291
SEQIDNO:90	-SILLPLIIGLVLLGLLALVLI	AFCIVRRRPSAYQAL 354
SEQIDNO:91	-NILVPLVVGLVLLTLILLVL	SAFCISRRRPPAYQPL 323
SEQIDNO:92	-----	263

Macrosailin					
登记号	物种	SEQ ID NO:	登记号	物种	SEQ ID NO:
NP_001242.2	智人 (H. sapiens)	80	XP_849733.1	家犬 (C. lupus familiaris)	86
XP_003315403.1	黑猩猩 (P. troglodytes)	81	NP_001093232.1	家马 (E. caballus)	87
NP_001039367.1	家牛 (B. taurus)	82	XP_002719034.1	绵羊 (O. aries)	88
BAA23738.1	小鼠 (M. musculus)	83	XP_003131995.1	野猪 (S. scrofa)	89
XP_014974003.1	猕猴 (M. mulatta)	84	XP_003912313.1	东非狒狒 (P. anubis)	90
NP_001026808.1	褐家鼠 (R. norvegicus)	85	XP_001369761.1	短尾鱼鼠 (M. domestica)	91
			XP_001517723.2	鸭嘴兽 (O. anatinus)	92

图9续

LAMP同源结构域

3

```

SEQIDNO:93      KDAVSAGKHTANSHHLSALVTPAGKSYECQAQQTISLASSDPQKVTMILSAVHIQPFDI 213
SEQIDNO:94      KDAVSAGKHTANSHHLSALVTPAGKSYECQAQQTISLASSDLQKVTMILSAVHIQPFDI 213
SEQIDNO:95      KDAVSAGKHTANSHHLSALVTPAGKSYECQAQQTISLASSDPQKVTMILSAVHIQPFDI 213
SEQIDNO:96      KDAVSAGKHTANSHRLSALVTPAGKSYECQAQQTISLASSDPQKVTMILSAVHIQPFDI 213
SEQIDNO:97      KDAVSAGKHTANSHHLSALVTPAGKSYECQAQQTISLASSDPQKVTMILSAVHIQPFDI 213
SEQIDNO:98      KAPVKVNKYIASSHLSALVTPAGMSYECQAQQTISLASSDPQKVTMILSAVHIQPFDI 213
SEQIDNO:99      KDAVSAGKHTANSHHLSALVTPAGMSYECQAQQTISLASSDPQKVTMILSAVHIQPFDI 213
SEQIDNO:100     KDAVSPGKHTASSHRLSALVTPAGKSYECQAQQTISLISSDHQKSVQLLLSEVRIQPFDI 232
SEQIDNO:101     KSGARPGRHTANSHHLSLMVTPAGMSYECEATQRISLTSTDHQQIVVLYLSEVHLQPFDI 209

```

```

* . .:: *.**:* :***** ***:* * ** *:* * * * : * * *:*****

```

跨膜结构域

胞质尾区

4

```

SEQIDNO:93      ISDFVFSEEHKCPVDEREQLEETLPLILGLILGLVIMVTLAIYHVHHKMTANQVQIPRDR 273
SEQIDNO:94      ISDFVFSEEHKCPVDEREQLEETLPLILGLILGLVIMVTLAIYHVHHKMTANQVQIPRDR 273
SEQIDNO:95      ISDFVFSEEHKCPVDEREQLEETLPLILGLILGLVIMVTLAIYHVHHKMTANQVQIPRDR 273
SEQIDNO:96      ISDFVFSEEHKCPVDEREQLEETLPLILGLILGLVIMVTLAIYHIIHKMTANQVQIPRDR 273
SEQIDNO:97      ISDFVFSEEHKCPVDEREQLEETLPLILGLILGLVIMVTLVIYHIIHKMTANQVQIPRDR 273
SEQIDNO:98      ISDFVFSEEHKCPVDEQELEETLPLILGLILGLVIVITLVIYHIIHKMTANQVQIPRDR 273
SEQIDNO:99      ISDFVFSEEHKCPVDEREQLEETLPLILGLILGLVIVITLVIYHIIHKMTANQVQIPRDR 273
SEQIDNO:100     TADFVFSEEHKCPVDQRELEETLPLILGLILGLVIVITLCVYHIIHKMTANQVQIPRDR 292
SEQIDNO:101     KSDFVYSEYKCPDQKQLEETLPLILGLTLGVAILIIVAVYHIIHKMTANQVQIPRDR 269

```

```

:***:***:***.***:***** ***:**:: : ***:***:*****

```

```

SEQIDNO:93      SQYKHM 280
SEQIDNO:94      SQYKHM 280
SEQIDNO:95      SQYKHM 280
SEQIDNO:96      SQYKHM 280
SEQIDNO:97      SQYKHM 280
SEQIDNO:98      SQYKHM 280
SEQIDNO:99      SQYKHM 280
SEQIDNO:100     SQYKHM 299
SEQIDNO:101     SLYKHM 276

```

```

* *****

```

LAMP5					
登记号	物种	SEQ ID NO:	登记号	物种	SEQ ID NO:
NP_036393.1	智人 (<i>H. sapiens</i>)	93	NP_001076887.1	家牛 (<i>B. taurus</i>)	97
XP_514512.3	黑猩猩 (<i>P. troglodytes</i>)	94	NP_083806.2	小鼠 (<i>M. musculus</i>)	98
NP_001181627.1	猕猴 (<i>M. mulatta</i>)	95	NP_001014205.1	褐家鼠 (<i>R. norvegicus</i>)	99
XP_850634.1	家犬 (<i>C. lupus familiaris</i>)	96	XP_004935300.1	原鸡 (<i>G. gallus</i>)	100
			NP_001090781.1	热带爪哇 (<i>X. tropicalis</i>)	101

图10续

SEQ ID NO:114

基因座 YP_009111421 817 aa 线性 VRL 13-AUG-2018
 定义 大T抗原[梅克尔细胞多瘤病毒]
 登记号 YP_009111421
 版本 YP_009111421.1

```

1   mdlvlnrker ealcklleia pncygniplt kaafkrscik hhpdkggnpv immelntlws
61  kfqqnihklr sdfsmfdevd eapiygttkf kewwrsaggfs fgkayeygpn phgtnsrsrk
121 pssnasrgap sgsspphsqs sssgygsfss sqasdsqsrq pdippehhee ptsssgsssr
181 eettmsgres stpngtsvpr nssrtdgtwe dlfcdeslss peppsseep eeppssrssp
241 rqpsssaee asssqftdee yrsssfthpk tpppfsrkrk fggsrssass assasftstp
301 pkpkknretp vptdfpidls dylshavysn ktvscfaiyt tsdkaielyd kiekfkvdfk
361 srhacelgci llfitlskhr vsaiknfcst fctisflick gvnkmpemyn nlckppykll
421 qenkpllnye fqekekeasc nwnlvaefac eyelddhfii lahyldefakp fpcqkcenrs
481 rlkphkahea hhsnaklfye sksqkticqk aadtvlakrr lemlemtrte mlckkfkkhl
541 erlrdldtid llyymggvaw yccifeefek klqkiiqlt enipkyrniw fkgpinsgtk
601 sfaaalidll egkalnincp sdklpfelgc aldkfmvffe dvkgqnslnk dlqpggginn
661 ldnlrhdldg avavslekkh vnkkhqifpp civtandyfi pktliarfsy tlhfspkanl
721 rdsldqnmel rkrrilqsgt tlllcliwcl pdttfkpcld eeiknwqkil qseisylgkfc
781 qmienveagq dpllniliee egpeeteetq dsqtfsq

```

截短的大T (LT) 220A (SEQ ID NO: 115和116)

```

MDLVLNKEREALCKLLEIAPNICYGNIPLMKAFAKRSCLKHHPDKGGNPVIMMELNTLWSKFQQNIHK
LRSDFSMFDEVDEAPIYGTTFKEWWRSAGGFSFGKAYEYGNPHGTNSRSRKPSSNASRGAPSGSSPE
HSQSSSSSGYGSFSASQASDSQSRGPDIPPEHHEEPTSSSGSSSREETTNSGRESSTPNGTSVPRNSSR
TDGTWEDLFCDESLXSPEPPSSSEEPPEPPSSRSPRQPPSSSAEEASSSQFTDEEYRSSSFTHPKTP
PPFSFSGGSRSSASSASSASFTSTPPKPKKNRETPVPTDFPIDLSYLSHAV

```

X可以是任何氨基酸。在优选实施方式中，X是丙氨酸 (S220A)。

红色本文是细胞增殖活性必需的RB结合基序

紫色加深是核定位信号

已知不与蛋白质功能相关的区域用灰色示出

图11A

MAPRSARRPLLLLLLLLLGLMHCAAMFMVKNNGTACIMANFSAAFSVNYDTKSGPKNMTLDLPSDATVV
 LNRSSCGKENTSDPSLVIAFGRGHTLTlnFTRNATRYSVQLMSFVYNLSDTHLFPNASSKEIKTVESITDIRADIDK
 KYRCVSGTQVHMNNVTVTLHDATIQAAYLSNSSFSRGETRCEQDLEMDLVLNKEREALCKLEIAPNCYGNIPLM
 KAAFKRSLKHHPDKGGNPVIMMELNTLWSKFQQNIHKLRSDFSMFDEVDEAPIYGTTKFKEWWRSGGFSFGKA
 YEYGNPHGHTNSRSRKPSSNASRGAPSGSSPPHSQSSSSGYGSFSASQASDSQSRGPDIPPEHHEPTSSSGSSSREE
 TTNSGRESSTPNGTSVPRNSSRTDGTWEDLFCDESLSAPEPPSSSEEPPEPPSSRSPRQPPSSSAEEASSSQFTDEEY
 RSSFTTPKTPPPFSRKRKFGGSRSSASSASSASFTSTPPKPKKNRETVPVPTDFPIDLSDYLSHAFEFTCLLASMGQLQ
 NLTYERKDNTTVTRLLNINPNKTSASGSCGAHLVTLELHSEGTTVLLFQFGMNASSSRFFLQGIQLNTILPDARDP
 AFKAANGSLRALQATVGNSYKCAEEHVRVTKAFSVNIFKVWVQAFKVEGGQFGSVEECLLDENSM~~LIPIAVGG~~
 ALAGLVLIYLVGRKRSHAGYQTI

SEQ ID NO: 151

灰色：腔内结构域1和2

下划线：LT^{S220A}

黑色斜体：LAMP TM/胞质

图11A-续

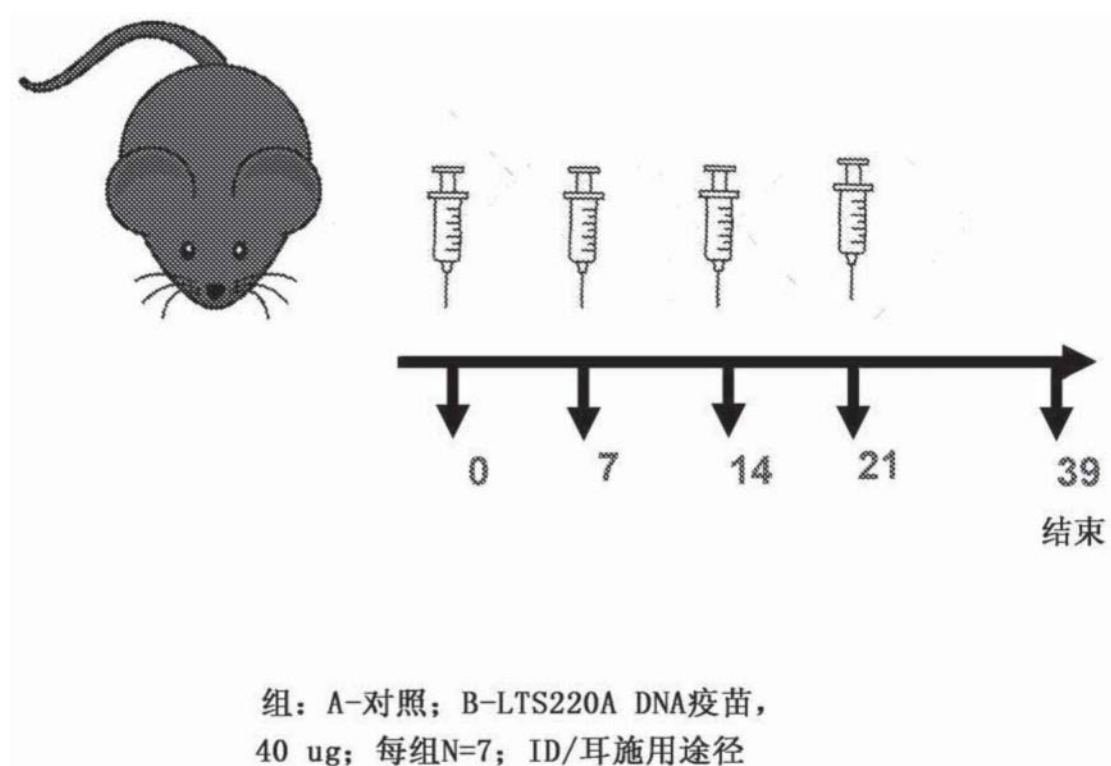


图11B

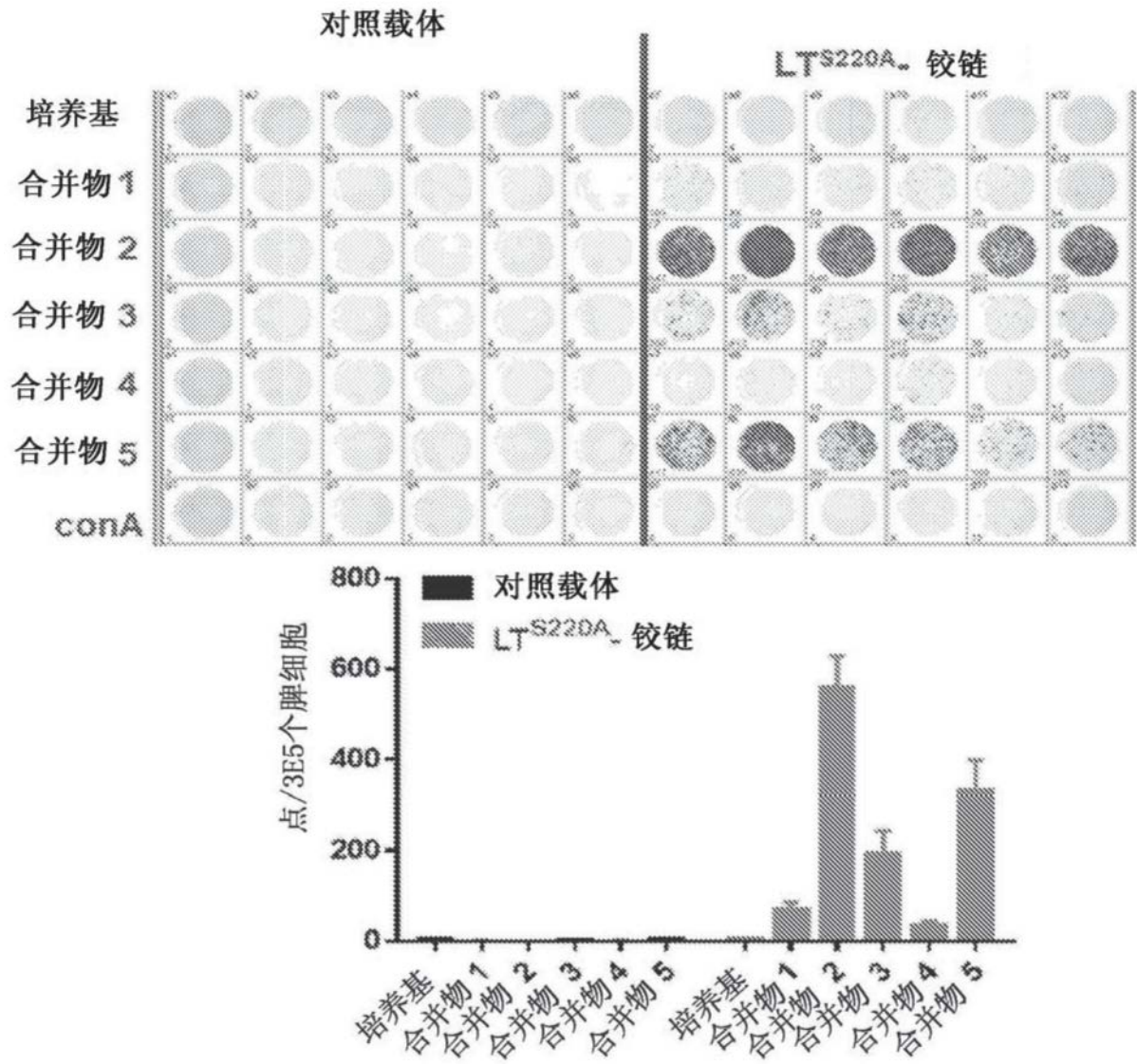


图11C

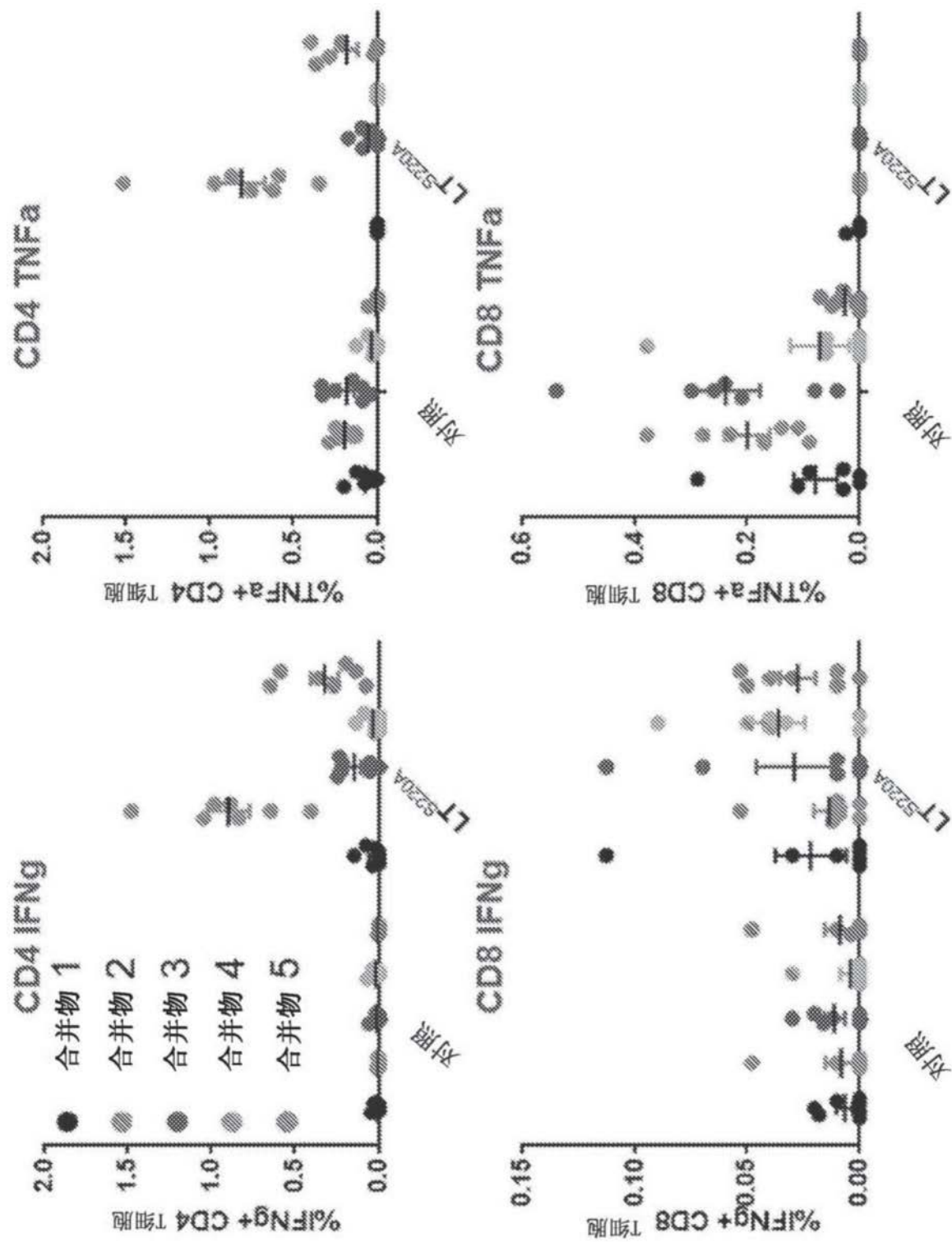


图11D

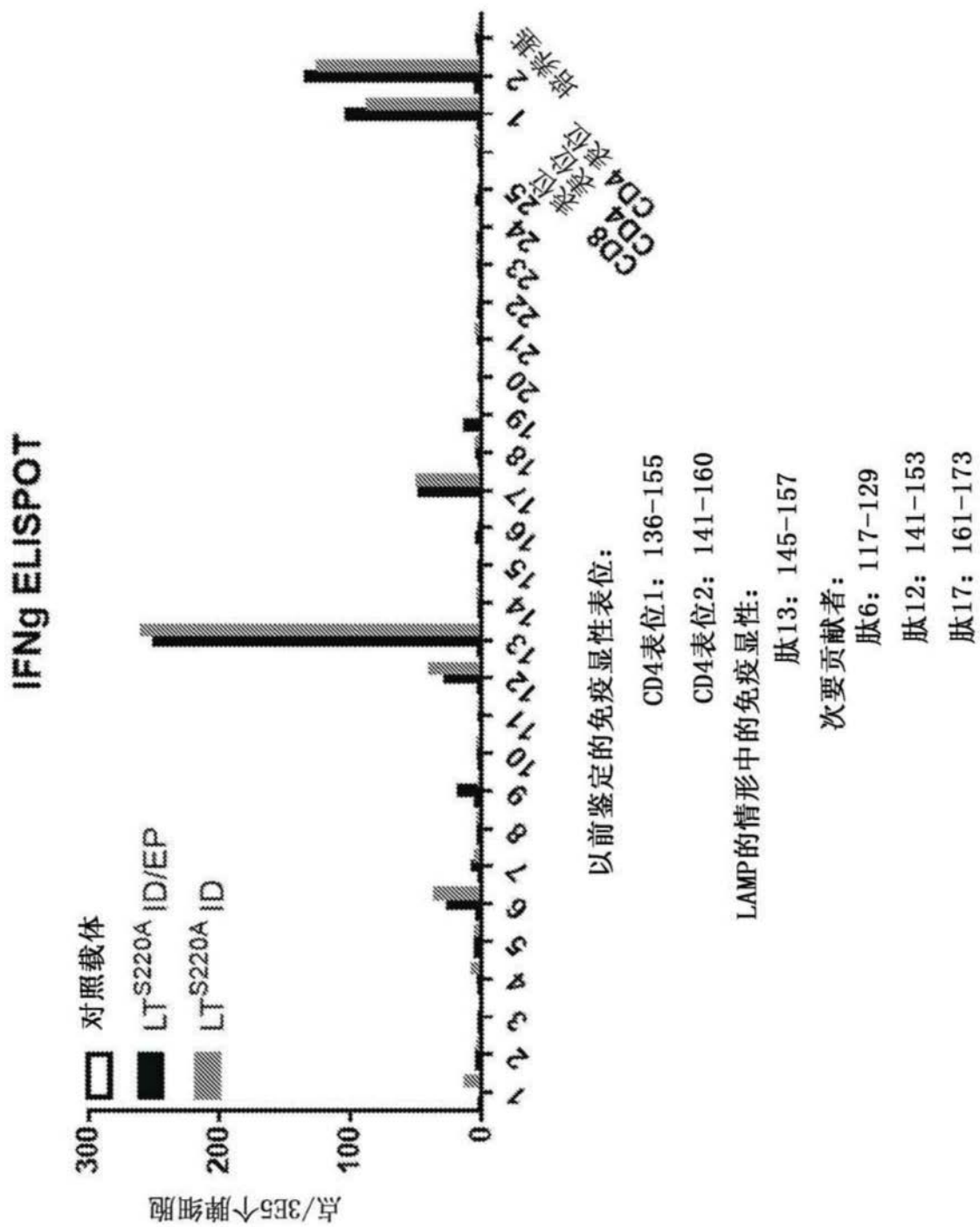


图11E

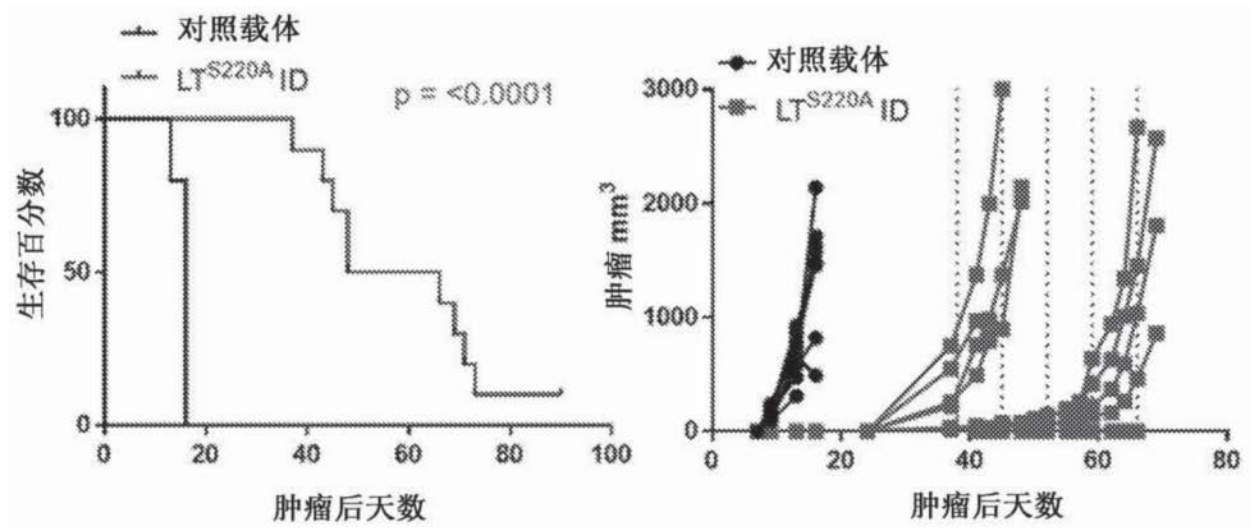


图12A

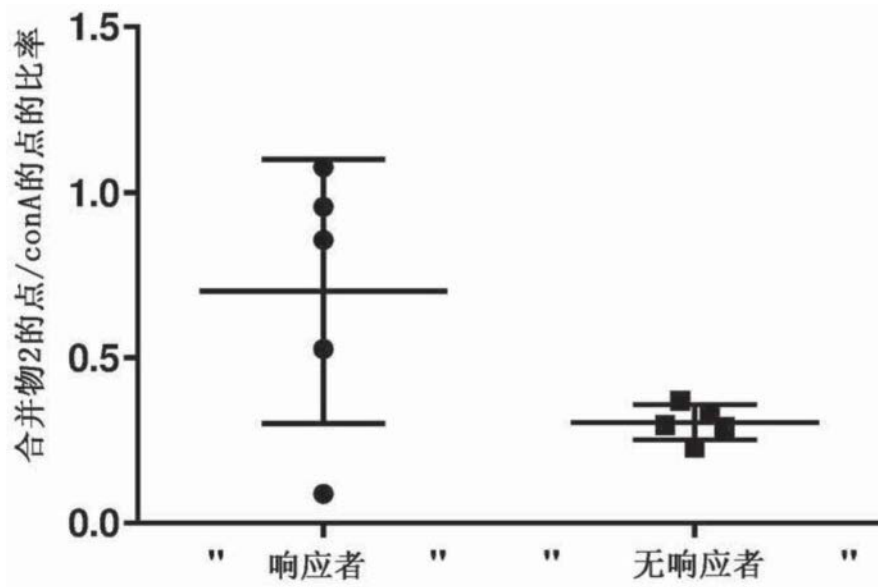


图12B

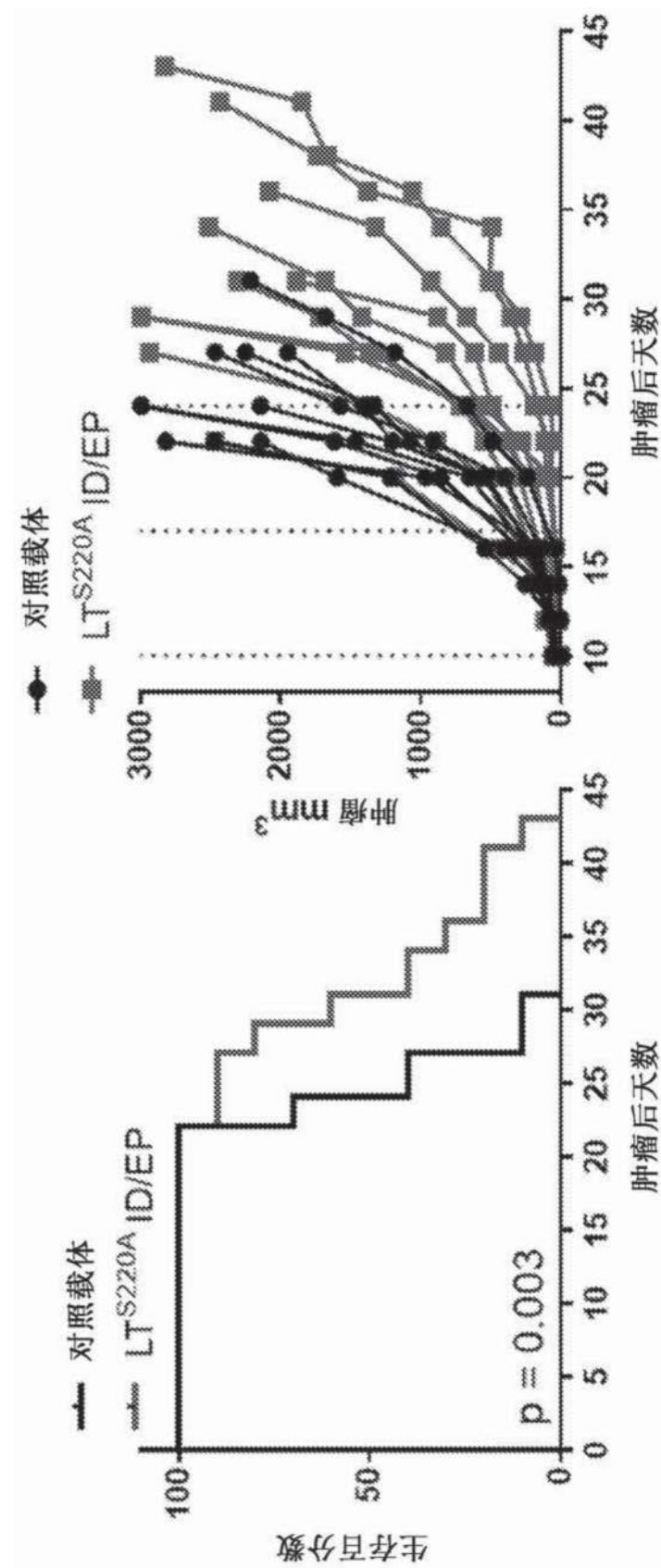


图13A

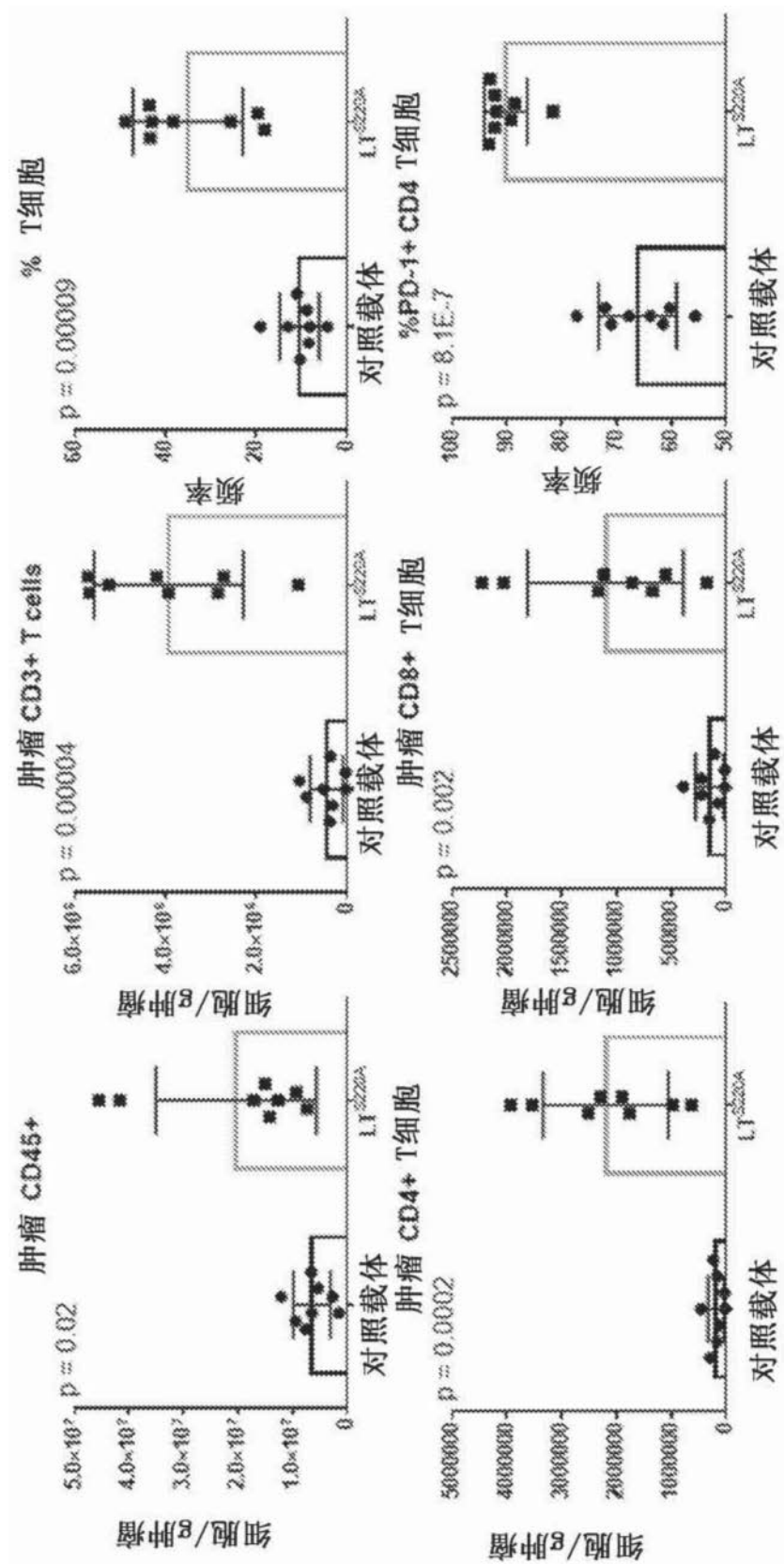


图13B

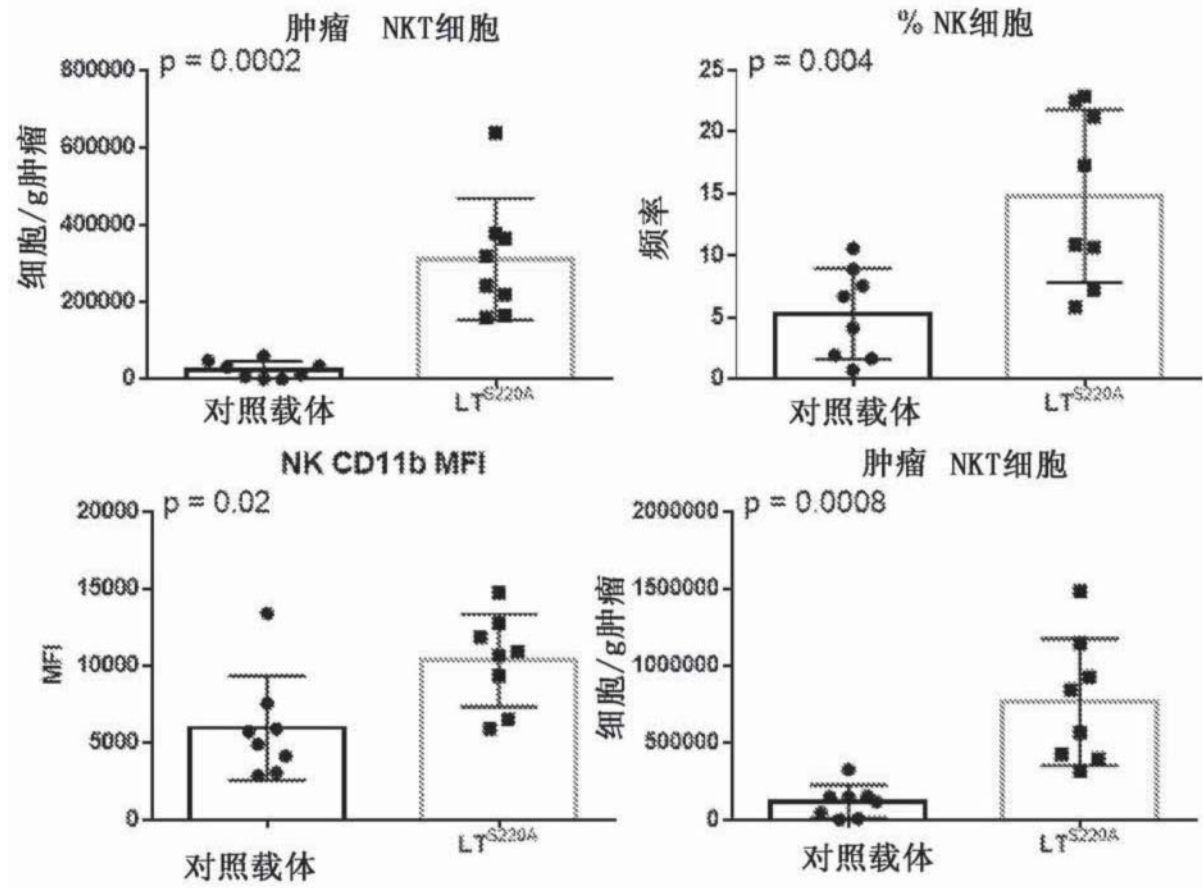


图13C

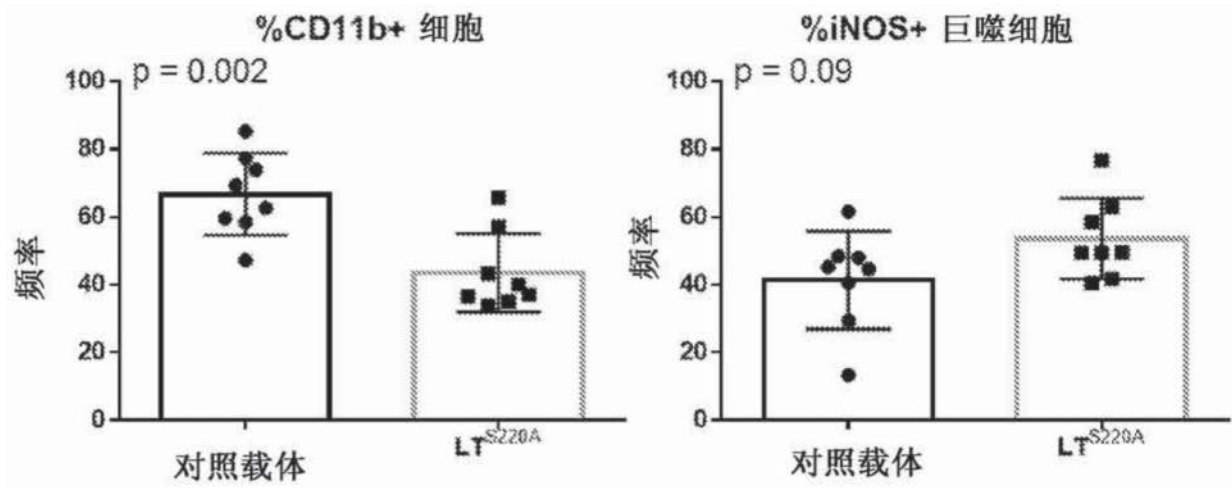


图13D

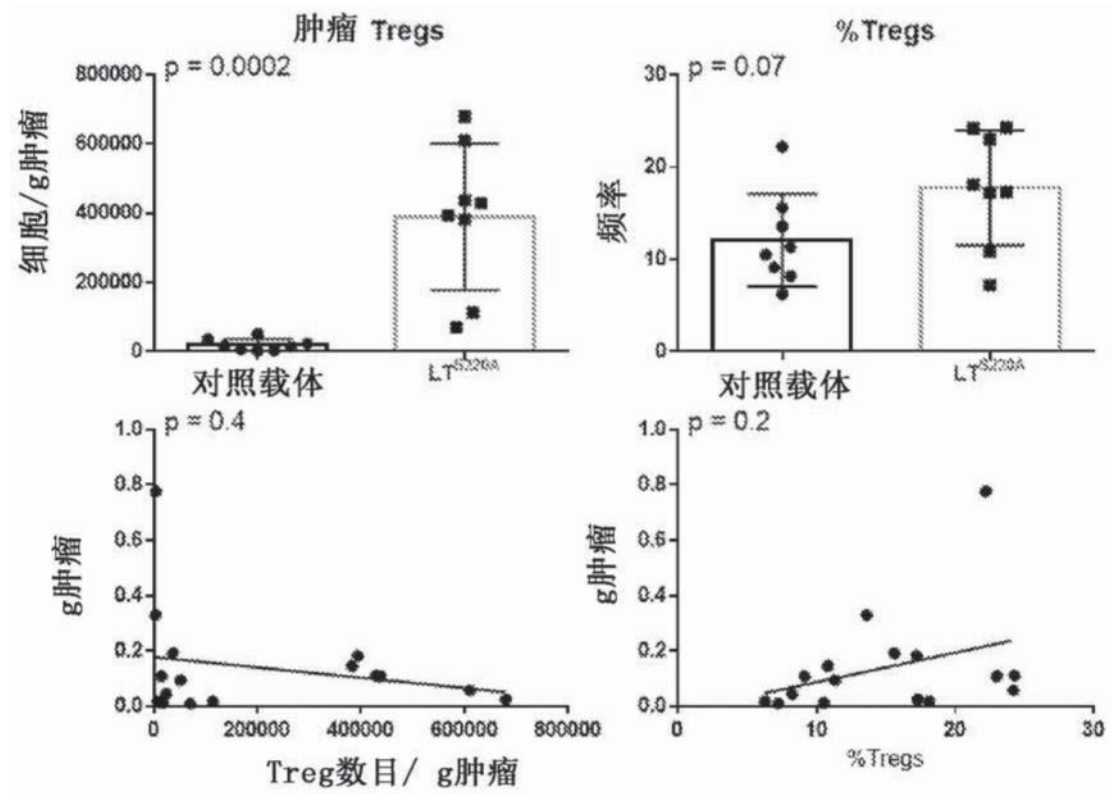


图13E

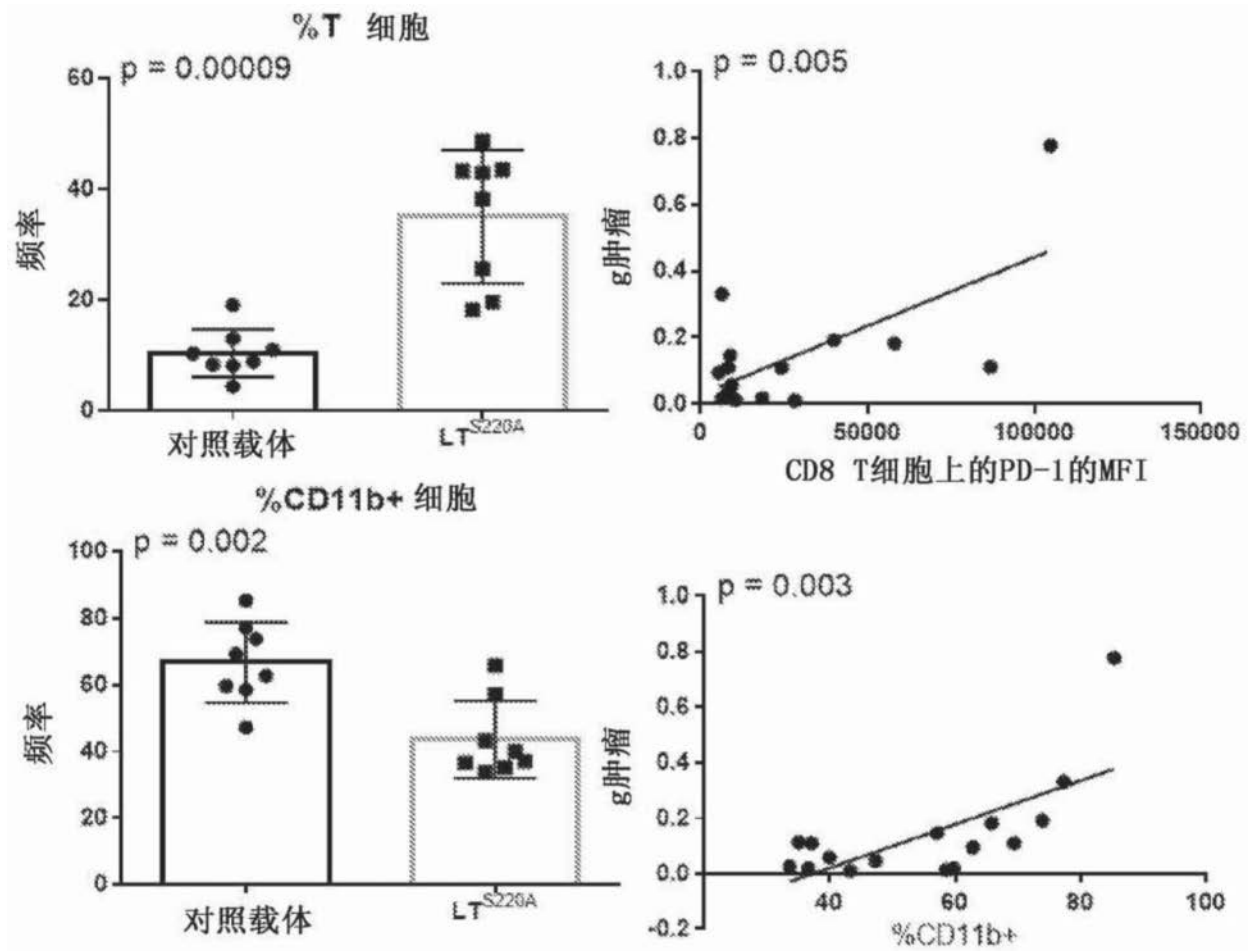


图13F