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(73)专利权人 宾夕法尼亚大学托管会

地址 美国宾夕法尼亚州

(72)发明人 L·范登伯格 G·高

J·M·威尔森

(74)专利代理机构 上海专利商标事务所有限公司
31100

代理人 余颖

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审查员 刘苗

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(54)发明名称

增强腺相关病毒载体功能的方法

(57)摘要

本发明提供了一种在选定的腺相关病毒(AAV)序列中校正单现突变从而提高选定AAV的包装产量、转导效率和/或基因转移效率的方法。该方法包括改变亲代AAV衣壳中的一个或多个单现突变,使它们与用来比对的功能性AAV衣壳序列中相应位点上的氨基酸相一致。

1. 一种腺相关病毒载体,具有AAVrh32/33衣壳,所述衣壳的氨基酸序列如SEQ ID NO:2所示,所述病毒载体携有编码基因产物的转基因,所述转基因受指导其在宿主细胞内表达的调控序列的调控。
2. 如权利要求1所述的腺相关病毒载体,所述基因产物是免疫原或抗原。
3. 如权利要求1或2所述的腺相关病毒载体,所述基因产物源自病毒抗原或免疫原。
4. 如权利要求1至3中任一项所述的腺相关病毒载体,所述调控序列具有5' 和3' 反向末端重复序列。
5. 如权利要求4所述的腺相关病毒载体,所述反向末端重复序列来自与AAVrh32/33异源的AAV。
6. 如权利要求1至5中任一项所述的腺相关病毒载体,所述基因产物是免疫球蛋白。
7. 如权利要求1至5中任一项所述的腺相关病毒载体,所述转基因编码癌基因编码的多肽或产物。
8. 一种组合物,包含药学上认可的载体和权利要求1至7中任一项所述的腺相关病毒载体。
9. 一种宿主细胞,经权利要求1至7中任一项所述的腺相关病毒载体体外转染。
10. 一种核酸分子,包含编码AAVrh32/33衣壳的核酸序列,所述衣壳的氨基酸序列如SEQ ID NO:2所示。

增强腺相关病毒载体功能的方法

[0001] 本申请是国际申请PCT/US2006/013375,国际申请日2006年4月7日,中国国家阶段申请号200680010566.6,名称“增强腺相关病毒载体功能的方法”的发明专利申请的分案申请。

[0002] 发明背景

[0003] 腺相关病毒(AAV)是细小病毒科(Parvovirus)家族的一个成员,它是小的无包膜、二十面体病毒,具有4.7千碱基(kb)到6kb的单链线性DNA基因组。由于该病毒是作为纯化的腺病毒原种的污染物被发现的,AAV指定为依赖病毒属(Dependovirus)。AAV的生命周期包括潜伏期(AAV基因组在感染后位点特异性整合入宿主染色体),感染期(腺病毒或单纯疱疹病毒感染后,整合的基因组接着得到拯救、复制并包装入感染的病毒)。非致病性、宽宿主范围(包括非分裂细胞)感染性以及潜在的位点特异性染色体整合的特性使得AAV成为用于基因转移的有吸引力的工具。

[0004] 已经描述AAV载体用于治疗用和免疫原性分子的运载工具。迄今为止,已从人或非人灵长类(NHP)中分离了几种表征良好的不同AAV。

[0005] 最近,研究者描述了不同序列的大量AAV[G.Gao等人,Proc Natl Acad Sci USA, 100(10):6081-6086(2003年5月13日);US-2003-0138772-A1(2003年7月24日)],并且将这些AAV表征为不同的血清型和分化体[G.Gao等人,J.Virol.,78(12):6381-6388(2004年6月);国际专利公开号WO 2005/033321]。已报道不同的AAV表现出不同的转染效率,也表现出对不同细胞或组织的趋性。

[0006] 想要得到用于向不同细胞类型递送异源分子的基于AAV的构建体。

[0007] 发明概述

[0008] 本发明提供了一种用于改善无功能和/或功能弱的AAV载体的方法。

[0009] 一方面,该方法提供了一种在选定的腺相关病毒(AAV)序列中校正单现突变(singleton)以提高选定AAV的包装产量、转导效率和/或基因转移效率的方法。该方法包括改变亲代AAV衣壳中的一个或多个单现突变使所述单现突变与用来比对的功能性AAV衣壳序列中对应位点的氨基酸相一致。

[0010] 另一方面,本发明提供了经修正的AAV序列,即除去一个或多个单现突变的序列。

[0011] 又一方面,本发明提供了具有根据本发明修正的AAV衣壳的AAV载体。

[0012] 下述发明详述容易地表现出本发明的其他方面和优点。

[0013] 附图简述

[0014] 图1显示经单现突变校正的AAV载体的体外293转导。在载体名称之后标明了单现突变的校正(如果存在的话),数字表示突变的数目。

[0015] 图2A-2C显示用293细胞测定的AAV载体在感染复数范围为 10^1 到 10^4 的滴度,其中,图2A比较亲代rh.8和经单现突变校正的rh.8(rh.8R),图2B比较亲代rh.37和经修正的rh.37,图2C比较AAV2和AAV8。作为对照,还给出了AAV2和AAV2/8 eGFP表达载体的相似滴定的结果。Y轴表示以流式细胞计数法测定的eGFP阳性细胞百分比(%)。

[0016] 图3是AAV序列的系统发生树,显示了它们的系统发生关系和所属分化体。

[0017] 图4A-4L是AAV2 [SEQ ID NO:7]、cy.5 [SEQ ID NO:8]、rh.10 [SEQ ID NO:9]、rh.13 [SEQ ID NO:10]、AAV1 [SEQ ID NO:11]、AAV3 [SEQ ID NO:12]、AAV6 [SEQ ID NO:13]、AAV7 [SEQ ID NO:14]、AAV8 [SEQ ID NO:15]、hu.13 [SEQ ID NO:16]、hu.26 [SEQ ID NO:17]、hu.37 [SEQ ID NO:18]、hu.53 [SEQ ID NO:19]、rh.39 [SEQ ID NO:20]、rh.43 [SEQ ID NO:21] 和rh.46 [SEQ ID NO:22] 的衣壳蛋白 (vp1) 核酸序列的比对。

[0018] 图5A-5D是AAV2 [SEQ ID NO:23]、cy.5 [SEQ ID NO:24]、rh.10 [SEQ ID NO:25]、rh.13 [SEQ ID NO:26]、AAV1 [SEQ ID NO:27]、AAV3 [SEQ ID NO:28]、AAV6 [SEQ ID NO:29]、AAV7 [SEQ ID NO:30]、AAV8 [SEQ ID NO:31]、hu.13 [SEQ ID NO:32]、hu.26 [SEQ ID NO:33]、hu.37 [SEQ ID NO:34]、hu.53 [SEQ ID NO:35]、rh.39 [SEQ ID NO:36]、rh.43 [SEQ ID NO:37] 和rh.46 [SEQ ID NO:38] 的衣壳蛋白 (vp1) 氨基酸序列的比对。

[0019] 图6A-6B是rh.13 [SEQ ID NO:26]、rh.2 [SEQ ID NO:39]、rh.8 [SEQ ID NO:41]、hu.29 [SEQ ID NO:42] 和rh.64 [SEQ ID NO:43] 的衣壳蛋白 (vp1) 氨基酸序列的比对。

[0020] 发明详述

[0021] 本发明提供了一种改善AAV载体功能的方法。本发明尤其适合于改善衣壳含一个或多个单现突变的AAV载体的包装产量、转导效率和/或基因转移效率。本发明进一步提供了根据本发明的方法鉴定和制备的新AAV衣壳序列。

[0022] 本说明书与权利要求书使用的术语“包含/含有”和“包括”包括其他成分、元素、数值、步骤等等在内。相反，术语“由...组成”和其变体不包括其他成分、元素、数值、步骤等等在内。

[0023] 本发明的单现突变方法

[0024] 如本文中所述的术语“单现突变 (singleton)”指在选定的 (即亲代) AAV衣壳序列中的给定位点上的可变氨基酸。通过将亲代AAV衣壳序列与功能性AAV衣壳序列文库比对来确定可变氨基酸的存在。然后分析序列来确定亲代AAV衣壳中所有这样的可变氨基酸序列：功能性AAV文库中的AAV序列在此氨基酸位置完全保守。然后改变亲代AAV序列，将单现突变改变为经鉴定功能性AAV衣壳序列在该位点上的保守氨基酸。根据本发明，亲代AAV序列可能具有1-6、1-5、1-4、1-3或2个单现突变。亲代AAV序列也可能具有超过6个单现突变。

[0025] 一旦修正后，经修正的AAV衣壳可用于构建具有经修正衣壳的AAV载体。可使用本领域技术人员公知的技术来构建载体。

[0026] 根据本发明方法所选择的用于修正的AAV是想要与亲代AAV相比增强其下列三种功能特性之一或多种的AAV，所述的三种功能特性即：包装成具有选定AAV序列的衣壳的病毒粒子，提高转导效率或增加基因转移效率。例如，与密切相关的其他AAV相比，亲代AAV的特征可能在于具有较低的包装效率。在另一个实例中，与密切相关的AAV相比，亲代AAV可能具有较低的转导效率。在另一个实例中，与密切相关的AAV相比，亲代AAV可能具有较低的基因转移效率 (即：体内递送靶分子的能力较低)。在其他的实例中，亲代AAV的上述各项功能都合格，但有待进一步提高其中一项或多项功能。

[0027] 因此，本发明提供了一种功能性AAV的文库，其中AAV的序列与选定的 (亲代) AAV形成对照。适宜的是，该文库包含具有目标功能的AAV，该目标功能正是欲在选定亲代AAV实现的改善。换句话说，该功能性AAV文库的每一序列的特征在于具有目标水平的包装能力、目标水平的体外转导效率或目标水平的体内基因转移效率 (即：在对象中向选定靶组织或细

胞的递送能力)。组成文库的功能性AAV可分别具有这些功能性特征中的一种、两种或全部。本领域技术人员可容易地确定文库的其他目标功能。

[0028] 在一个实施方案中,功能性AAV是能产生具有与AAV1、AAV2、AAV7、AAV8或AAV9同等或更强包装和转导效率的病毒粒子的AAV。可用含AAV2 rep和AAV2 ITR的假型包装设定(pseudotype setting)来测评功能。因此,可使用常规技术构建改变的亲代AAV,并且,当与AAV2的产量相比,如果由所属亲代AAV产生病毒的滴度为至少50%时,则认为该AAV载体是功能性的。另外,本领域技术人员可容易地确定AAV转导细胞的能力。例如,可构建亲代AAV使其包含易于测知病毒的标记基因。例如,让AAV包含eGFP或另一可进行荧光检测的基因。如果AAV包含CMV-eGFP,当将由改变的亲代AAV衣壳产生的病毒以感染复数 10^4 转导293细胞时,转导效率大于全部细胞GFP荧光的5%时表示有功能,其中,所述细胞以感染复数20用野生型人5型腺病毒预处理2小时。

[0029] 适宜的是,文库由至少三种或至少四种功能性AAV衣壳序列组成,所述序列代表至少两种不同的分化体。优选地,文库包含各代表性分化体的至少两个序列。在某些实施方案中提供了三个、四个、五个、六个或更多的分化体。

[0030] “分化体”指基于AAV vp1氨基酸序列比对,经邻接算法、自展值(Bootstrap value)为至少75%(至少1000次复制)确定,并且泊松校正距离不大于0.05的在系统发生上彼此相关的一组AAV。

[0031] 文献中有关于邻接算法(Neighbor-joining algorithm)的详细描述。参见,例如:M.Nei与S.Kumar,《分子进化与系统发生学》(Molecular Evolution and Phylogenetics)(牛津大学出版社,纽约(2000))。已有现成用于执行该算法的计算机程序。例如,MEGA v2.1程序执行改进的Nci-Goibori方法。使用这些技术与计算机程序,以及AAV vp1衣壳蛋白序列,本领域的技术人员可容易地确定所选定的AAV是否包含在本文所鉴定的一个分化体内、另一个分化体内、或在这些分化体之外。

[0032] 虽然分化体主要基于天然存在的AAV vp1衣壳,但并不限于天然存在的AAV。分化体可包括非天然存在的AAV,包括但不限于重组、修饰或改变、嵌合、杂交、合成、人工即其他AAV,只要这些AAV是基于AAV vp1氨基酸序列比对、用邻接算法(自展值至少75%(至少1000次复制))确定且泊松校正距离测量值不大于0.05的系统发生上彼此相关的AAV。

[0033] 所描述的AAV分化体包括分化体A(以AAV1和AAV6为代表)、分化体B(以AAV2为代表)、分化体C(以AAV2-AAV3杂交体为代表)、分化体D(以AAV7为代表)、分化体E(以AAV8为代表)与分化体F(以人AAV9为代表)。这些分化体以各自的成员——一种已知AAV血清型——为代表。已知的AAV1和AAV6同属于一个分化体(分化体A),其中包括回收自3人的4种分离株。已知的AAV3和AAV5血清型彼此显著不同,但在本文所述的筛选中未检测到,没有包括于这些分化体中。

[0034] AAV分化体的进一步讨论可见于G.Gao等人,J.Virol.,78(12):6381-6388(2004年6月)和国际专利公开号WO 2004/028817和WO 2005/033321中。后一文件还提供了新的人AAV序列,此处引用作为参考。

[0035] 在一个实施方案中,用于本发明方法的文库不包括AAV5。在另一个实施方案中,用于本发明方法的文库不包括AAV4。然而,在某些实施方案中,例如:当亲代AAV类似于AAV5时,在比对中可能需要包括该序列。

[0036] 虽然可构建包含最小数目序列的文库,但是可通过利用包含较多序列的文库来优化鉴定单现突变的效率。适宜的是,所述文库包含最少四个序列,代表至少两个分化体。优选地,该文库中,各分化体各自有至少两种代表序列。在一个实施方案中,该文库包含超过100个AAV序列。在另一个实施方案中,该文库包含至少3到100个AAV序列。在又一个实施方案中,该文库包含至少6到50个AAV序列。

[0037] 适用于本发明功能性文库的AAV包含,例如:AAV1、AAV2、AAV6、AAV7、AAV8、AAV9及其他已描述的序列,[G.Gao等人,Proc Natl.Acad Sci.,100(10):6081-6086(2003年5月13日);国际专利公开号W0 2004/042397和W02005/033321]。本领域技术人员可以容易地选择其他AAV,例如:使用国际专利公开号W0 03/093460A1(2003年11月13日)和美国专利申请公开号2003-0138772A1(2003年7月24日)描述的方法所分离的AAV。

[0038] 根据本发明,所述文库内的所述至少三个序列在衣壳序列全长比对中至少有85%同一性。

[0039] 蛋白质全长或其片段的氨基酸序列的“同一性百分比(%)”可容易地确定。适宜的是,片段长度至少为大约8个氨基酸,也可长达大约700个氨基酸。通常,当提及两种不同的腺相关病毒之间的“同一性”、“同源性”或“相似性”时,“同一性”、“同源性”或“相似性”是参照进行“比对”的序列确定的。“比对”序列或“比对”指这样的多核酸序列或蛋白质(氨基酸)序列,它们与参考序列相比通常包含碱基或氨基酸缺失或增加的校正。

[0040] 可使用各种公知或市售的多序列比对程序进行比对。用于氨基酸序列比对的程序有例如:“Clustal X”、“MAP”、“PIMA”、“MSA”、“BLOCKMAKER”、“MEME”和“Match-Box”程序。虽然本领域技术人员可视需要改变设置,但通常这些程序都以默认设置使用。或者,本领域技术人员也可采用能够象上述算法和程序一样得出同一性述评或进行比对的其他算法和计算机程序。参见,例如:J.D.Thomson等人,Nucl.Acids.Res.,“多序列比对的综合比较(A comprehensive comparison of multiple sequence alignments)”,27(13):2682-2690(1999)。

[0041] 也有用于核酸序列的多序列比对程序。这种程序的实例包括通过因特网的网络服务器可得的“W串(Clustal W)”、“CAP序列组件”、“MAP”和“MEME”。这些程序的其他来源是本领域技术人员所已知的。或者,也可使用Vector NTI实用程序。还有许多本领域已知的算法也可用于测量核苷酸序列同一性,包括包含在上述程序中的算法。作为另一个实例,可使用GCG 6.1版中的程序Fasta™来比较多核苷酸序列。Fasta™可得出查询序列与检索序列之间最佳重叠区域的对比和序列同一性百分比。例如,可使用GCG 6.1版提供的默认参数(字长为6和用于计分矩阵的NOPAM系数)用Fasta™来确定核酸序列之间的序列同一性百分比,该程序此处引用作为参考。

[0042] 根据本发明,将被疑包含单现突变的靶或亲代AAV衣壳序列与文库的AAV衣壳序列进行比较。使用AAV衣壳的全长vp1蛋白序列比对进行该比较。

[0043] 当AAV序列对齐时,对于选定的氨基酸位点,如果文库中所有AAV在此具有相同的氨基酸残基(即:是完全保守的)而亲代AAV具有与此不同的氨基酸残基,则鉴定到单现突变。

[0044] 一般地,当以AAV衣壳vp1蛋白为基础来进行比对时,该比对包含了如此测得的与参比AAV序列(例如AAV2)相比的插入和缺失,氨基酸残基的编号是基于该比对产生的基准

标度(reference scale)。但是,任何给定的AAV序列都可能比基准标度少若干氨基酸残基。在本发明中,当描述亲代AAV和参考文库的序列时,术语“相同的位点”或“相应的位点”指相对于比对所用的基准标度,各序列氨基酸内相同编号残基处的氨基酸。但是,在比对之外,各AAV vp1蛋白质内的这些氨基酸可能在不同编号的残基处。

[0045] 可选地,可用核酸比对进行本发明方法,并将编码不同氨基酸的密码子(即非同义密码子)鉴定为单现突变。当亲代AAV中给定密码子的核酸序列虽然与文库中该密码子的序列不同,但编码的氨基酸相同时,这些不同的密码子序列是同义密码子而非单现突变。

[0046] 根据本发明,包含单现突变的亲代AAV被改变为其中的单现突变残基被替换为文库中AAV的保守氨基酸残基。

[0047] 可使用常规的定点诱变技术对可变氨基酸的密码子进行上述置换。一般地,使用仅包括必须步骤的定点诱变来获得想要的保守氨基酸残基的密码子。这样的方法是本领域技术人员已知的,并可使用公开的方法和/或市售的试剂盒来实行(例如:可以从Stratagene和Promega获得)。可在AAV基因组序列上实行定点诱变。为了方便起见可用载体(例如:质粒骨架)携带AAV序列。或者,本领域技术人员可使用本领域公知的其他技术来改变亲代AAV。

[0048] 亲代AAV可具有多于一个的单现突变,例如:两个、三个、四个、五个、六个或更多。但是,可能在一个单现突变校正之后就观察到功能上的改善。在亲代AAV携带多个单现突变的实施方案中,可以每次改变一个单现突变,随后测定修正AAV是否最强了想要的功能。或者,可在改变多个单现突变后测定想要的功能是否增强。

[0049] 当亲代AAV包含多个单现突变时,即使第一个单现突变改变后就观察到了功能的改善,仍可以通过改变其余的单现突变来优化功能。

[0050] 一般地,根据本发明的方法改变了一个或多个单现突变的亲代AAV通过将AAV包装成AAV颗粒来测定其功能。本领域技术人员熟知这些方法,参见,例如:如上引用的G.Gao等人,Proc Natl Acad Sci.;Sambrook等人,分子克隆:实验室手册(Molecular Cloning:A Laboratory Manual),冷泉港出版社(冷泉港,纽约)。

[0051] 这些改变的AAV具有根据本发明方法产生的新的衣壳,并就其功能接受测定。本文描述了测定AAV功能的适当方法,包括,例如:产生脱氧核糖核酸酶(DNase)保护颗粒能力、体外细胞转导效率和/或体内基因转移。适宜的是,与亲代AAV的功能相比,本发明改变的AAV具有足够数目的单现突变被改变从而增强了这些特征性功能中一项或全部。

[0052] II. 本发明的新AAV

[0053] 本发明进一步提供了预测新AAV是否有功能的方法。该方法包含使用本发明的单现突变方法和鉴定选定AAV序列中单现突变的缺失,即没有单现突变的AAV。

[0054] 因此,在一个实施方案中,本发明提供了选择AAV用于产生载体的方法。该方法包括选择待分析的亲代AAV衣壳序列,并在亲代AAV衣壳序列和功能性AAV衣壳序列文库的比对中鉴定亲代AAV衣壳上单现突变的缺失。一旦确定选定AAV衣壳没有单现突变,则该AAV可根据已知技术用来产生载体。

[0055] 当术语“基本同源性”或“基本相似性”用于核酸或其片段时意味着当与另一核酸(或其互补链)进行包含适当的核苷酸插入或缺失的最佳比对时,比对序列的至少约95%到99%具有核苷酸序同一性。优选在全长序列、或其开放读码框、或其他至少长15个核苷酸的

合适片段上具有上述同源性。本文描述了合适片段的实例。

[0056] 文中用于核酸序列时,术语“序列同一性”、“序列同一性百分比”或“同一性百分比”指在最佳匹配比对中,两条序列的残基相同。序列同一性比较的长度可以是基因组全长、基因编码序列的全长,或需要至少约500到5000个核苷酸的片段。然而,也可能要求较小片段之间的同一性,例如至少约9个核苷酸、通常至少约20到24个核苷酸、至少约28到32个核苷酸、至少约36或更多核苷酸的片段。

[0057] 当术语“基本同源性”或“基本相似性”用于描述氨基酸或其片段时意味着当与另一氨基酸(或其互补链)进行包含适当的氨基酸插入或缺失的最佳比对时,对比序列的至少约95%到99%具有氨基酸序列同一性,在某些实施方案中,对比序列中的约97%具有同一性。优选在全长序列,或其蛋白(例如, cap蛋白、rep蛋白)或其至少8个氨基酸、或更理想至少15个氨基酸长度的片段上具有上述同源性。本文描述了合适片段的实例。

[0058] 术语“高度保守的”表示至少80%的同一性,优选至少90%的同一性,更优选超过97%的同一性。本领域技术人员可根据本领域已知的算法和程序容易地确定同一性。

[0059] 术语“血清型”是指具有衣壳的AAV在血清学上不同于其他AAV血清型区别。血清学区别是基于该AAV的抗体与其他AAV没有交叉反应来确定的。交叉反应性通常用中和抗体试验测定。为了进行该试验,使用腺相关病毒在兔子或其他合适动物模型中产生抗特定AAV的多克隆血清。在该试验中,随后测试所产生的特定AAV的抗血清中和相同(同源)或异源AAV的能力。将达到50%中和作用的稀释度作为中和抗体滴度。如果就两种AAV而言,异源滴度除以同源滴度之商的倒数小于16,则此两种载体被认为是相同的血清型。相反,如果异源滴度与同源滴度之比的倒数是16或更大,则这两种AAV被认为是不同的血清型。

[0060] 在另外的的实施方案中,本发明提供了具有新的衣壳的AAV,包括rh.20、rh.32/33、rh.39、rh.46、rh.73和rh.74。rh.20的序列具有SEQ ID NO:1的氨基酸序列或与全长SEQ ID NO:1具有95-99%同一性的序列。rh.32/33的衣壳具有SEQ ID NO:2的氨基酸序列或与全长SEQ ID NO:2具有95-99%同一性的序列。rh.39的衣壳具有SEQ ID NO:3的氨基酸序列或与全长SEQ ID NO:3具有95-99%同一性的序列。rh.46的衣壳具有SEQ ID NO:4的氨基酸序列或与全长SEQ ID NO:4具有95-99%同一性的序列。rh.73的衣壳具有SEQ ID NO:5的氨基酸序列或与全长SEQ ID NO:5具有95-99%同一性的序列。rh.74的衣壳具有SEQ ID NO:6的氨基酸序列或与全长SEQ ID NO:6具有95-99%同一性的序列。优选地,这些新AAV衣壳序列的同一性达到使它们没有任何单现突变的程度。新AAV序列见序列表。

[0061] 在又一个实施方案中,本发明的新AAV序列包括经单现突变校正的AAV衣壳蛋白和编码这些衣壳蛋白的序列。适当的经单现突变校正的AAV序列的实例包括AAV6.1、AAV6.2、AAV6.1.2、rh.8R、rh.48.1、rh.48.2、rh.48.1.2、hu.44R1、hu.44R2、hu.44R3、hu.29R、ch.5R1、rh.67、rh.54、hu.48R1、hu.48R2和hu.48R3。例如,经单现突变校正的AAV6包括AAV6.1、AAV6.2和AAV6.12,它们显示了与亲代AAV6序列相比明显的功能改善。

[0062] 特别理想的蛋白质包括由如前所述鉴定的核苷酸序列所编码的AAV衣壳蛋白。所述AAV衣壳由vp1、vp2和vp3这三种蛋白质组成,它们互为剪接变体。衣壳蛋白的其他理想的片段包括位于高变区(HVR)之间的恒定区和可变区。衣壳蛋白的其他理想的片段包括HVR本身。

[0063] 一种开发用于确定AAV2中序列歧变区域的算法得出了12个高变区(HVR),其中的5

个与先前所述的四个可变区重叠或是其一部分 (Chiorini 等人, J. Virol., 73:1309-19 (1999); Rutledge 等人, J. Virol., 72:309-319)。使用该算法和/或本文所描述的比对技术, 确定了新 AAV 血清型的 HVR。例如, HVR 位于如下位置: HVR1, aa146-152; HVR2, aa182-186; HVR3, aa262-264; HVR4, aa381-383; HVR5, aa450-474; HVR6, aa490-495; HVR7, aa500-504; HVR8, aa514-522; HVR9, aa534-555; HVR10, aa581-594; HVR11, aa658-667; 以及 HVR12, aa705-719 [该编号系统是基于使用 AAV2 vp1 作为参考点的比对]。使用 Clustal X 程序及其默认设置, 或使用其他市售或公知的比对程序及其默认设置 (如本文所述的那些) 来进行本文的比对, 本领域技术人员可容易地确定本发明的新 AAV 衣壳的相应片段。

[0064] 适宜的是, 片段至少长 8 个氨基酸。但是, 也可方便地采用其他所需长度的片段。可通过重组或其他合适的方法例如化学合成来产生这样的片段。

[0065] 本发明进一步提供了使用本文所提供的序列信息鉴定的其他 AAV 序列。例如, 鉴于本文所提供的序列, 可使用基因组步移技术 (genome walking technology) (Siebert 等人, 1995, Nucleic Acid Research, 23:1087-1088, Friezner-Degen 等人, 1986, J. Biol. Chem. 261:6972-6985, BD Biosciences Clontech, Palo Alto, CA) 来分离感染性序列。基因组步移技术尤其适合于鉴定和分离与本发明方法所鉴定的新序列邻近的序列。基于本文所提供的新 AAV 衣壳序列和 rep 序列, 该技术还可用于分离新 AAV 的反向末端重复 (ITR)。

[0066] 可由本发明的 AAV 核酸序列来表达新的 AAV 氨基酸序列、肽和蛋白质。另外, 也可通过本领域已知的其他方法来产生这些氨基酸序列、肽和蛋白质, 所述方法包括例如化学合成、其他合成方法或其他方法。可使用多种方法容易地产生本文提供的任一 AAV 衣壳序列。

[0067] 合适的生产技术是本领域技术人员所熟知的。参见, 例如: Sambrook 等人, 分子克隆: 实验室手册 (Molecular Cloning: A Laboratory Manual), 冷泉港出版社 (冷泉港, 纽约)。或者, 还可通过众所周知的固相肽合成法 (Merrifield, J. Am. Chem. Soc., 85:2149 (1962); Stewart 和 Young, 固相肽合成 (Solid Phase Peptide Synthesis) (Freeman, 旧金山, 1969), 第 27-62 页) 来合成肽。这些及其他适当的生产方法是本领域技术人员已知的, 并且不构成对本发明的限定。

[0068] 可通过各种合适的方法生产本发明的序列、蛋白质和片段, 包括重组生产、化学合成或其他合成方法。这种生产方法是本领域技术人员已知的, 并且不构成对本发明的限定。

[0069] III. 具有新 AAV 衣壳的 rAAV 的生产

[0070] 本发明包括在按照本发明方法鉴定单现突变后通过突变产生的新的 AAV 衣壳序列。本发明进一步包括新的 AAV rh.20、rh.32/33、rh.39、rh.46、rh.73 和 rh.74 衣壳序列 (SEQ ID No:1-6)。

[0071] 在另一个方面, 本发明提供了利用了本发明的新 AAV 序列 (包括其片段) 的用于产生将异源基因或其他核酸序列递送至靶细胞的病毒载体的分子。

[0072] 本发明含有 AAV 序列的分子包括有可递送至宿主细胞的各种遗传元件 (载体), 例如: 能够传送所带序列的裸 DNA、质粒、噬菌体、转座子、粘粒、附加体、非病毒递送载体中的蛋白质 (如: 基于脂质的运载体)、病毒等。

[0073] 选定载体可通过各种合适的方法递送, 包括转染、电穿孔、脂质体递送、膜融合技术、高速 DNA 包被小球、病毒感染与原生质体融合。用于构建本发明这一方面实施方式的方

法是核酸操作领域(包括遗传工程、重组工程与合成技术)的技术人员已知的。参见,例如:Sambrook等,分子克隆:实验室手册(Molecular Cloning:A Laboratory Manual),冷泉港出版社,冷泉港,纽约。

[0074] 在一个实施方案中,本发明的载体含有编码本发明的AAV衣壳或其片段的序列及其他元件。在另一个实施方案中,本发明的载体至少含有编码AAV rep蛋白或其片段的序列。任选地,本发明的载体可含有AAV cap和rep蛋白。在既有AAV rep又有cap的载体中,AAV rep和AAV cap序列可来源于同一分化体的AAV。或者,本发明提供含有来自不同AAV的rep序列和cap序列载体。在一个实施方案中,rep和cap序列由彼此独立的来源(例如:分开的载体,或宿主细胞和载体)表达。在另一个实施方案中,rep序列与来自不同AAV的cap序列框内融合形成嵌合AAV载体。任选地,本发明的载体是包装在本发明的AAV衣壳中的载体。这些载体与本文所述的其他载体可进一步包含含有选定转基因的小基因,转基因两侧是AAV5' ITR和AAV3' ITR。

[0075] 因此,在一个实施方案中,本文所述的载体含有编码来自同一AAV序列的完整AAV衣壳的核酸序列。或者,这些载体含有编码人造衣壳的序列,所述人造衣壳含有与异源AAV或非AAV衣壳蛋白(或其片段)融合的经单现突变校正的AAV衣壳的一个或多个片段。这些人造衣壳蛋白选自经单现突变校正的衣壳的非连续部分或选自其他AAV衣壳。这些改变的目的是为了增加表达、产量和/或改善选定表达系统中的纯化,或为了其他目的(例如:改变趋性或修改中和抗体表位)。

[0076] 本文所描述的载体例如质粒可用于各种目的,但特别适用于产生含有衣壳的rAAV,所述衣壳包含AAV序列或其片段。本文详细描述了这些载体,包括rAAV、它们的元件、构建体和应用。

[0077] 在一方面,本发明提供了一种产生具有本发明新AAV衣壳的重组腺相关病毒(AAV)的方法。该方法涉及培养宿主细胞,该宿主细胞含有如本文所定义的编码本发明新AAV衣壳蛋白或其片段的核酸序列;功能性rep基因;至少由AAV反向末端重复(ITR)和转基因组成的小基因;与足够的辅助功能因子以将小基因包装进AAV衣壳蛋白。

[0078] 在宿主细胞内培养将AAV小基因包装进AAV衣壳所必需的成分可以瞬时性地(in transe)提供给宿主细胞。或者,由已经用本领域技术人员已知的方法改造而含有一种或多种必需成分的稳定宿主细胞来提供一种或多种必需成分(例如:小基因、rep序列、cap序列和/或辅助因子功能)。更适宜的是,这种稳定的宿主细胞含有在诱导型启动子控制下的所需成分。然而,必需成分也可在组成型启动子的控制下。在关于适合与转基因联用的调节元件的讨论中,本文提供了合适的诱导型和组成型启动子的实例。或者,选定的稳定宿主细胞可含有在组成型启动子控制下的选定成分和在一个或多个诱导型启动子控制下的其他选定成分。例如:可由293细胞(含有在组成型启动子控制下的E1辅助因子)制造稳定的宿主细胞,但所述稳定的宿主细胞含有在诱导型启动子控制下的rep和/或cap蛋白。本领域技术人员也可制备其他稳定的宿主细胞。

[0079] 产生本发明的rAAV所需的小基因、rep序列、cap序列和辅助因子可以各种能够传递所带序列的遗传元件的形式递送至包装宿主细胞。选定的遗传元件可通过任何适当的方法,包括本文所述的方法来递送。用于构建本发明这一方面的实施方案的方法是核酸操作(包括遗传工程、重组工程与合成技术)领域的技术人员已知的。参见,例如Sambrook等人,

分子克隆:实验室手册 (Molecular Cloning: A Laboratory Manual), 冷泉港出版社, 冷泉港, 纽约。类似地, 产生 AAV 病毒粒子的方法也是众所周知的, 并且适当方法的选择不限制本发明。参见, 例如: K. Fisher 等人, J. Virol., 70: 520-532 (1993) 与美国专利号 5,478,745。

[0080] 除非另有规定, 本文所述的 AAV ITR 与其他选定 AAV 成分可容易地选自任一 AAV, 所述 AAV 包括但不限于: AAV1、AAV2、AAV3、AAV4、AAV5、AAV6、AAV7、AAV9 和本发明的其他新 AAV 序列。可使用本领域技术人员已知的技术容易地从 AAV 序列中分离这些 ITR 或其他 AAV 成分。所述 AAV 可分离获得或得自学术、商业或公共来源 (例如: 美国典型培养物保藏中心 (ATCC), Manassas, VA)。或者, 所述 AAV 序列可参考例如文献或数据库 (例如, GenBank[®]、PubMed[®] 等) 中的已公开序列通过合成或其他适当的方法获得。

[0081] A、小基因

[0082] 小基因至少由转基因及其调节序列和 5' 和 3' 反向末端重复 (ITR) 组成。在一个理想的实施方案中, 使用了 AAV 血清型 2 的 ITR。然而, 也可选择其他适当来源的 ITR。正是该小基因将被包装进衣壳蛋白并递送至选定的宿主细胞。

[0083] 1. 转基因

[0084] 转基因是编码感兴趣的多肽、蛋白质或其他产物, 并与其侧翼的载体序列异源的核酸序列。核酸编码序列以允许转基因在宿主细胞中转录、翻译和/或表达的方式操作性地与调节组件相连。

[0085] 转基因序列的组成取决于所得到的载体的用途。例如: 一类转基因序列包含报道序列, 该序列在表达后产生可检测的信号。这种报道序列包括但不限于编码以下物质的 DNA 序列: β -内酰胺酶、 β -半乳糖苷酶 (LacZ)、碱性磷酸酶、胸腺激酶、绿色荧光蛋白 (GFP)、增强型 GFP (EGFP)、氯霉素乙酰转移酶 (CAT)、荧光素酶、膜结合蛋白 (如 CD2、CD4、CD8)、流感血凝素蛋白和本领域熟知的存在高亲和力抗体或可通过常规方法产生所述抗体的其他物质, 以及含有膜结合蛋白的融合蛋白, 该膜结合蛋白适当地与血凝素或 Myc 等物质的抗原标记区融合。

[0086] 当这些编码序列与驱动其表达的调节元件相关联时, 可提供由常规方法检测的信号, 所述常规方法包括酶法、放射显影法、比色法、荧光法或其他光谱测定、荧光激活细胞分选测定与免疫测定, 包括酶联免疫吸附测定 (ELISA)、放射性免疫测定 (RIA) 和免疫组织化学。例如: 当标记序列是 LacZ 基因时, 通过测定 β -半乳糖苷酶的活性来检测携带信号的载体的存在。当转基因是绿色荧光蛋白或荧光素酶时, 携带信号的载体可用光度计通过颜色或光的产生来观测。

[0087] 然而, 理想地, 转基因是编码具有生物或医药用途的产物的非标记序列, 所述产物例如蛋白质、肽、RNA、酶、显性阴性突变体或催化性 RNA。理想的 RNA 分子包括 tRNA、dsRNA、核糖体 RNA、催化性 RNA、siRNA、小发夹 RNA、反式剪接 RNA 和反义 RNA。有用的 RNA 序列的一个例子是抑制或消除靶核酸序列在经处理的动物中表达的序列。通常, 合适的靶序列包括肿瘤靶点和病毒疾病。例如后文免疫原部分所述的肿瘤靶点和病毒。

[0088] 转基因可用于校正或减少基因缺陷, 包括正常基因的表达低于正常水平的缺陷或功能基因产物不表达的缺陷。或者, 转基因可为细胞提供本来不在该细胞类型或该宿主中表达的产物。转基因序列的优选类型编码在宿主细胞中表达的治疗性蛋白质或多肽。本发明进一步包括使用多种转基因。在某些情况下, 可采用不同的转基因编码一个蛋白质的各

个亚基,或编码不同的肽或蛋白质。当编码蛋白质亚基的DNA很大时这尤其适合,所述蛋白质例如免疫球蛋白、血小板衍生的生长因子或抗肌萎缩蛋白。为使细胞产生多亚基蛋白质,用各自含有各不同亚基的重组病毒感染细胞。或者,蛋白质的不同亚基可由同一转基因编码。在这种情况下,单个转基因包含编码所有亚基的DNA,而各亚基的DNA由内部核糖体进入位点(IRES)隔开。当编码每个亚基的DNA较小时,例如编码亚基的DNA与IRES的总体积小于5千碱基对(5kb)时,这尤其适合。作为IRES的替代,DNA可用编码在翻译后阶段自我切割的2A肽的序列隔开。参见,例如:M.L.Donnelly等人,J.Gen.Virol.,78(第一部分):13-21(1997年1月);Furler,S.等人,Gene Ther.,8(11):864-873(2001年6月);Klump H.等人,Gene Ther.,8(10):811-817(2001年5月)。该2A肽明显小于IRES,使得其非常适合用于当空间成为制约因素的时候。更常见的是,当转基因较大、由多个亚基组成、或两个转基因共递送时,允许共用携带所需转基因或亚基的rAAV以使得它们在体内多联化形成单一的载体基因组。在这种实施方案中,第一AAV可携带表达一个转基因的表达盒,第二AAV可携带用于在宿主细胞中共表达的不同转基因的表达盒。然而,选定的转基因可编码任何生物活性产物或其他产物,例如:研究所需的产物。

[0089] 本领域技术人员可容易地选择适当的转基因。转基因的选择不限制本发明。

[0090] 2. 调节元件

[0091] 除了以上就小基因而言的主要元件以外,载体还包含常规控制元件,所述常规控制元件以允许转基因在以下所述细胞中转录、翻译和/或表达的方式操作性地与转基因相连,所述细胞为本发明产生的质粒载体转染或病毒所感染。本文的“操作性相连”的序列包括与感兴趣的基因毗连的表达控制序列和以反式(in trans)起作用或在一定距离开外控制感兴趣基因的表达的控制序列。

[0092] 表达控制序列包括适宜的转录起始子、终止子、启动子和增强子序列;有效的RNA加工信号,例如剪接和聚腺苷酸化(polyA)信号;稳定细胞质mRNA的序列;增强翻译效率的序列(即:Kozak共有序列);增强蛋白质稳定性的序列;以及在需要时增强编码产物分泌的序列。许多表达控制序列,包括天然的、组成型的、诱导型的和/或组织特异性的启动子是本领域已知并可利用的。

[0093] 组成型启动子的例子包括但不限于:逆转录病毒Rous肉瘤病毒(RSV)LTR启动子(任选连有RSV增强子)、巨细胞病毒(CMV)启动子(任选连有CMV增强子)[参见,例如:Boshart等人,Cell,41:521-530(1985)]、SV40启动子、二氢叶酸还原酶启动子、 β -肌动蛋白启动子、磷酸甘油激酶(PGK)启动子和EF1启动子(Invitrogen)。诱导型启动子能调节基因表达,并可由外源提供的化合物、环境因素(例如温度)、或特定生理状态调节,所述状态例如如急性期、细胞的特定分化状态,或仅在正在复制的细胞中起效。诱导型启动子和可诱导系统可从多种商业来源获得,包括但不限于Invitrogen、Clontech和Ariad。已知的还有许多其他系统,可由本领域技术人员容易地选择。受外源化合物调节的诱导型启动子的实例包括锌-诱导的金属硫蛋白(MT)启动子、地塞米松(Dex)-诱导的小鼠乳腺肿瘤病毒(MMTV)启动子、T7聚合酶启动子系统[国际专利公开号W0 98/10088]、蜕皮素昆虫启动子[No等人,Proc.Natl.Acad.Sci.美国,93:3346-3351(1996)]、四环素阻抑系统[Gossen等人,Proc.Natl.Acad.Sci.美国,89:5547-5551(1992)]、四环素诱导系统[Gossen等人,Science,268:1766-1769(1996)],也参见Harvey等人,Curr.Opin.Chem.Biol.,2:512-518

(1998)]、RU486-诱导系统[Wang等人,Nat.Biotech.,15:239-243(1997)与Wang等人,Gene Ther.,4:432-441(1997)]和雷帕霉素-诱导系统[Magari等人,J.Clin.Invest.,100:2856-2872(1997)]。可用于本发明的其他诱导型启动子类型是由特定的生理状态调节的那些,所述状态例如温度、急性期、细胞的特定分化状态,或仅在正在复制的细胞中起效。

[0094] 在另一个实施方案中使用了转基因的天然启动子。当需要转基因的表达模拟天然表达时,可优选天然启动子。当转基因的表达必须暂时性或发展性方式调节、或以组织特异性的方式调节或响应特定的转录刺激时,可使用天然启动子。在另外的实施方案中,也可使用其他天然表达控制元件,例如增强子元件、聚腺苷酸化位点或Kozak共有序列以模拟天然表达。

[0095] 转基因的另一实施方案包含操作性连接于组织特异性启动子的基因。例如,如果需要骨骼肌中表达,应该使用在肌肉中有活性的启动子。这包括编码以下产物的基因的启动子:骨骼 β -肌动蛋白、肌球蛋白轻链2A、抗肌萎缩蛋白、肌肉肌酸激酶以及活性高于天然启动子的合成肌肉启动子(参见:Li等人,Nat.Biotech.,17:241-245(1999))。已知的组织特异性启动子的实例有肝特异性的(白蛋白,Miyatake等人,J.Virol.,71:5124-32(1997);乙肝病毒核心启动子,Sandig等人,Gene Ther.,3:1002-9(1996); α -胎蛋白(AFP),Arbuthnot等人,Hum.GeneTher.,7:1503-14(1996))、骨的骨钙蛋白(Stein等人,Mol.Biol.Rep.,24:185-96(1997));骨唾液蛋白(Chen等人,J.Bone Miner.Res.,11:654-64(1996))、淋巴细胞特异性的(CD2,Hansal等人,J.Immunol.161:1063-8(1998);免疫球蛋白重链;T细胞受体链)、神经元特异性的(例如神经元-特异性烯醇酶(NSE)启动子(Andersen等人,Cell.Mol.Neurobiol.,13:503-15(1993))、神经丝轻链基因(Piccioli等人,Proc.Natl.Acad.Sci.,美国,88:5611-5(1991)),以及神经元-特异性vgf基因(Piccioli等人,Neuron,15:373-84(1995)))等。

[0096] 任选地,携带有治疗用途的转基因的质粒还可含有可选择标记基因或报道基因,例如编码遗传霉素抗性、潮霉素抗性 or 嘌呤霉素(purimycin)抗性等的序列。这种可选择性的报道基因或标记基因(优选位于有待本发明方法拯救的病毒基因组之外),例如氨苄青霉素抗性,可用来指示细菌细胞中存在质粒。质粒的其他成分可包括复制起点。可通过常规方法选择这些和其他启动子与载体元件,许多这种序列可获得[参见,例如:Sambrook等人,以及本文引用的参考文献]。

[0097] 为援引方便,转基因、启动子/增强子与5'和3'AAV ITR的组合在此称为“小基因”。鉴于本发明的教导,凭借常规技术即可设计这种小基因。

[0098] 3. 将小基因递送至包装宿主细胞

[0099] 可用任何递送至宿主细胞的适当载体例如质粒来携带小基因。用于本发明的质粒可改造为适合于在原核细胞、哺乳动物细胞或这二种细胞中复制和整合(任选)的质粒。这些质粒(或其他携带5'AAV ITR-异源分子-3'AAV ITR的载体)含有允许小基因在真核细胞和/或原核细胞中复制的序列和用于这些系统的选择标记。可选择标记基因或报道基因可包括编码遗传霉素抗性、潮霉素抗性 or 嘌呤霉素抗性等的序列。这些质粒还可含有可用来指示细菌细胞中存在载体的某些可选择报道基因或标记基因,例如氨苄青霉素抗性。质粒的其他成分可包括复制起点和扩增子,例如使用Epstein Barr病毒核抗原的扩增子系统。该扩增子系统或其他类似的扩增子成分允许细胞中高拷贝附加型复制。携带小基因

优选转染入其可暂时存在的细胞中。或者,小基因(携带5'AAV ITR-异源分子-3'AAV ITR)可稳定地整合进宿主细胞的基因组,或进入染色体或作为附加体。在某些实施方案中,小基因可以任选地以头-对-头、头-对-尾或尾-对-尾的多联体形式多拷贝存在。合适的转染技术是已知的,并可容易地用于将小基因递送至宿主细胞。

[0100] 通常,当通过转染递送含有小基因的载体时,通常将约5 μ g-100 μ g DNA、约10 μ g-50 μ g DNA递送约 1×10^4 - 1×10^{13} 个细胞或约 1×10^5 个细胞。然而,考虑到诸如所选择的载体、递送方法和所选择的宿主细胞等因素,本领域技术人员可调整载体DNA量与宿主细胞之比。

[0101] B. Rep与Cap序列

[0102] 除了小基因以外,宿主细胞还含有在宿主细胞中驱动本发明的新AAV衣壳蛋白(或含有其片段的衣壳蛋白)表达的序列和与小基因中的AAV ITR相同来源或来自交叉互补来源的rep序列。AAV cap和rep序列可彼此独立地由前述AAV源获得,并可以前述本领域人员已知的任何方式引入宿主细胞。此外,在进行AAV载体假型包装时,可用不同的AAV来源(例如:AAV1、AAV2、AAV3、AAV4、AAV5、AAV6、AAV7、AAV8、AAV9)提供编码各种主要rep蛋白的序列。例如:rep78/68序列得自AAV2,而rep52/40序列得自AAV8。

[0103] 在一个实施方案中,宿主细胞稳定地含有在合适的启动子(例如前文所述)控制下的衣壳蛋白。在该实施方案中,衣壳蛋白最好在诱导型启动子的控制下表达。在另一个实施方案中,衣壳蛋白以转入方式(in trans)提供至宿主细胞。当以转入方式递送至宿主细胞时,衣壳蛋白可通过含有指导选定衣壳蛋白在宿主细胞中表达所需序列的质粒递送。当以转入方式递送至宿主细胞时,携带衣壳蛋白的质粒最好还携带包装rAAV所需的其他序列,例如rep序列。

[0104] 在另一个实施方案中,宿主细胞稳定地含有在合适的启动子(如前文所述)控制下的rep序列。在该实施方案中,主要rep蛋白最好在诱导型启动子的控制下表达。在另一个实施方案中,rep蛋白以转入方式(in trans)提供至宿主细胞。当以转入方式递送至宿主细胞时,rep蛋白可通过含有指导选定的rep蛋白在宿主细胞中表达所需序列的质粒递送。当以转入方式递送至宿主细胞时,携带衣壳蛋白的质粒也最好携带包装rAAV所需的其他序列,例如rep和cap序列。

[0105] 因此,在一个实施方案中,rep和cap序列可以位于一个核酸分子上转染入宿主细胞,并且作为附加体稳定地存在于细胞中。在另一个实施方案中,rep和cap序列稳定地整合进细胞的染色体。在另一个实施方案中,rep和cap序列在宿主细胞中瞬时表达。例如,用于这种转染的有用核酸分子从5'到3'含有启动子、插在启动子与rep基因序列起始位点之间可选的间隔子、AAV rep基因序列和AAV cap基因序列。

[0106] 任选地,rep和/或cap序列可提供于载体上,该载体含有待引入宿主细胞的其他DNA序列。例如:载体可含有包含小基因的rAAV构建体。载体可含有一个或多个编码辅助因子功能例如腺病毒蛋白E1、E2a和E4 ORF6的基因与VAI RNA的基因。

[0107] 用于该构建体的启动子优选本领域技术人员已知的或前文所述的特征组成型、诱导型或天然启动子。在一个实施方案中,使用AAV P5启动子序列。选择AAV来提供这些序列不是对本发明的限制。

[0108] 在另一个优选的实施方案中,rep的启动子是诱导型启动子,例如前文就转基因调节元件所述的那些。Rep表达的优选的启动子之一是T7启动子。用包含由T7启动子调节的

rep基因和cap基因的载体转染或转化组成性或诱导性表达T7聚合酶的细胞。参见1998年3月12日公开的国际专利公开号W0 98/10088。

[0109] 在设计载体中,间隔子是可选元件。间隔子是插在启动子和rep基因的ATG起始位点间的DNA序列。间隔子可具有任何所需的设计;即,它可是随机的核苷酸序列,或者可编码一个基因产物,例如标记基因。间隔子可含有通常包括起始/终止和polyA位点的基因。间隔子可以是来自原核生物或真核生物的非编码DNA序列、重复非编码序列、无转录控制的编码序列或有转录控制的编码序列。间隔子序列的两个典型来源是噬菌体梯序列或酵母梯序列,二者可购自例如Gibco或Invitrogen等。间隔子可是任何大小的,只要足以降低rep78和rep68基因产物的表达,使rep52、rep40和cap基因产物的表达处于正常水平。因此,间隔子的长度范围约为10bp-10.0kbp,优选约100bp-8.0kbp。为减少重组的可能性,间隔子长度优选小于2kbp;然而,本发明不限于此。

[0110] 虽然提供rep和cap的分子可能瞬时(即通过转染)存在于宿主细胞中,但优选rep和cap蛋白之一或二者与控制其表达的启动子在宿主细胞中稳定地表达,例如作为附加体或通过整合进宿主细胞染色体。用于构建本发明这方面内容的实施方案的方法是常规遗传工程或重组工程技术,例如前文参考文献所述的技术。虽然本说明书提供了具体的构建体的说明性实例,但本领域技术人员可使用本文提供的信息来选择间隔子、P5启动子和其他元件(包括至少一个翻译起始和终止信号)和任选加入的聚腺苷酸化位点,从而可选择和设计其他合适的构建体。

[0111] 在本发明的另一个实施方案中,可由宿主细胞稳定地提供rep或cap蛋白。

[0112] C. 辅助因子功能

[0113] 为包装本发明的rAAV,包装宿主细胞还需要辅助因子功能。任选地,这些功能可由疱疹病毒提供。所需的辅助功能物最好分别由人或非人灵长类腺病毒源提供,例如前文所述的和/或得自各种来源的(包括美国典型培养物保藏中心(ATCC),Manassas,VA(美国))。在一个目前优选的实施方案中,向宿主细胞提供和/或宿主细胞含有E1a基因产物、E1b基因产物、E2a基因产物和/或E4 ORF6基因产物。宿主细胞可含有其他腺病毒基因,例如VAI RNA,但这些基因不是必需的。在优选的实施方案中,宿主细胞中不存在其他腺病毒基因或基因功能。

[0114] “表达E1a基因产物的腺病毒DNA”表示编码E1a或其功能性部分的各种腺病毒序列。表达E2a基因产物的腺病毒DNA和表达E4 ORF6基因产物的腺病毒DNA的定义类似。腺病毒基因或其功能部分的各等位基因或其他修饰形式也包括在内。所述修饰既包括借助常规遗传工程或诱变技术特地引入从而以某种方式增强腺病毒功能的那些,也包括天然存在的等位变体。这些用来通过DNA操作获得腺病毒基因功能的修饰和方法是本领域技术人员已知的。

[0115] 腺病毒E1a、E1b、E2a和/或E4 ORF6基因产物以及各种其他需要的辅助因子功能可使用各种使其在细胞中表达的方法提供。各条编码这些产物的序列可各自位于单独的载体上,或者一个或多个基因可位于同一载体上。载体可以是本领域已知的或前文所述的各种载体,包括质粒、粘粒和病毒。载体可通过本领域已知或前文所述的各种方法引入宿主细胞,所述方法包括转染、感染、电穿孔、脂质体递送、膜融合技术、高速DNA-包被小球、病毒感染与原生质体融合等。一个或多个腺病毒基因可稳定地整合入宿主细胞基因组,作为附加

体稳定表达,或者瞬时表达。基因产物可全部瞬时表达,包含在附加体上或稳定整合;或者,一些基因产物可稳定地表达,而另一些瞬时表达。此外,各腺病毒基因的启动子可彼此独立地选自组成型启动子、诱导型启动子或天然腺病毒启动子。启动子可由生物体或细胞的特定生理状态调节(即,分化状态或复制或静息细胞)或由其他方法例如外源添加因子调节。

[0116] D. 宿主细胞和包装细胞系

[0117] 宿主细胞本身可选自各种生物体,包括原核(例如:细菌)细胞和真核细胞,包括昆虫细胞、酵母细胞和哺乳动物细胞。特别理想的宿主细胞选自特征哺乳动物种类,包括,不限于以下细胞:A549、WEHI、3T3、10T1/2、BHK、MDCK、COS1、COS7、BSC1、BSC40、BMT10、VERO、W138、HeLa、293细胞(表达功能性腺病毒E1)、Saos、C2C12、L细胞、HT1080、HepG2和来源于哺乳动物(包括人、猴、小鼠、大鼠、兔子和仓鼠)的初级成纤维细胞、肝细胞和成肌细胞。选择细胞的哺乳动物来源和哺乳动物细胞的类型(即成纤维细胞、肝细胞、肿瘤细胞等)不限制本发明。对所使用细胞的要求是:它不携带任何除E1、E2a和/或E4 ORF6以外的腺病毒基因;它不含有在rAAV产生过程中可导致污染病毒的同源重组的任何其他病毒基因;并且,它能被DNA感染或转染并表达所转染的DNA。在优选的实施方案中,宿主细胞是在包含稳定转染的rep和cap的细胞。

[0118] 用于本发明的宿主细胞之一是用编码rep和cap的序列稳定转化,并用腺病毒E1、E2a和E4 ORF6 DNA和携带有前文所述小基因的构建体转染的宿主细胞。也可类似地使用稳定的rep和/或cap表达细胞系,例如B-50(国际专利申请公开号W099/15685),或美国专利号5,658,785所述的细胞系。另一种理想的宿主细胞含有表达E4 ORF6所需的基本腺病毒DNA。使用本发明的新经单现突变校正的AAVcap序列还可构建出其他细胞系。

[0119] 本发明制备宿主细胞涉及诸如装配选定的DNA序列等技术。可使用常规技术实现这种装配。这种技术包括公知的且描述于前文引用的Sambrook等人的著作中的cDNA和基因组克隆、使用腺病毒和AAV基因组的重叠寡核苷酸序列,结合聚合酶链式反应、合成方法以及提供所需核苷酸序列的其他合适方法。

[0120] 也可使用技术人员已知和本说明书中讨论的技术将这些分子(如质粒或病毒)引入宿主细胞。在优选的实施方案中,使用标准转染技术,例如:CaPO₄转染或电穿孔,和/或用杂交腺病毒/AAV载体感染细胞系,所述细胞系例如人胚胎肾细胞系HEK293(一种人肾细胞系,含功能性腺病毒E1基因,该基因提供反式作用的E1蛋白)。

[0121] 本领域技术人员易于理解的是,本发明的新AAV序列可容易地经调整而适用在上述及其他表达载体系统中用于体外、离体或体内的基因递送。类似地,本领域技术人员可容易地选择本发明的其他AAV基因组片段用于各种rAAV和非rAAV载体系统。这些载体系统包括例如:慢病毒、逆转录病毒、痘病毒、牛痘病毒和腺病毒系统等。这些载体系统的选择不限制本发明。

[0122] 因此,本发明进一步提供了使用本发明的新AAV的核酸与氨基酸序列产生的载体。这种载体可用于多种目的,包括递送治疗性分子和用在疫苗给药方案(vaccine regimens)中。含有本发明的新AAV衣壳的重组AAV对递送治疗性分子特别理想。含有本发明的新AAV序列的这些或其他载体构建体可用于疫苗给药方案,例如:用于共同递送细胞因子,或用于递送免疫原本身。

[0123] IV. 重组病毒及其应用

[0124] 本领域技术人员可使用本文所述的技术来产生rAAV,该rAAV具有本发明AAV的衣壳或其衣壳含有本发明AAV的一个或多个片段。在一个实施方案中,使用来自经单现突变校正的AAV的全长衣壳。

[0125] A.病毒的递送

[0126] 另一方面,本发明提供了一种将转基因递送至宿主的方法,该方法涉及利用本发明经单现突变校正的AAV(或其功能性片段)产生的重组病毒载体转染或感染所选宿主细胞。用于递送的方法是本领域技术人员公知的,并不限制本发明。

[0127] 在一个理想的实施方案中,本发明提供了一种用于AAV-介导递送转基因至宿主的方法。该方法涉及利用含有所选转基因和修正衣壳蛋白的重组病毒载体转染或感染所选宿主细胞,该转基因在指导其表达的序列的控制下。

[0128] 任选地,来自宿主的样品可首先测定其是否含有所选AAV源(例如:某血清型)的抗体。用于检测中和抗体的各种测定方式已为本领域技术人员所熟知。这种测定的选择不限制本发明。参见,例如:Fisher等人,Nature Med.,3(3):306-312(1997年3月)和W.C.Manning等人,Human Gene Therapy,9:477-485(1998年3月1日)。该测定的结果,例如没有某衣壳来源的特异性中和抗体,可用于确定哪种含有特定来源的衣壳蛋白的AAV载体是递送所优选的。

[0129] 该方法的一方面,可在递送具有本发明AAV衣壳蛋白的载体之前或之后递送具有另一不同AAV衣壳蛋白的载体。因此,通过rAAV载体的基因递送可用于重复地将基因递送至所选定的宿主细胞中。理想地,在后给予的rAAV载体携带与第一rAAV载体中相同的转基因,但在后给予的载体含有的衣壳蛋白的来源不同于第一载体(并且优选不同的血清型)。例如:如果第一载体具有经单现突变校正的衣壳蛋白,在后给予的载体可具有选自其他AAV的衣壳蛋白,例如可以是另一血清型或另一分化体的AAV。

[0130] 任选地,多个rAAV载体可通过共同给予多个rAAV载体用于递送大的转基因或多个转基因,在体内多联化成单个载体基因组。在这种实施方案中,第一AAV可携带表达单个转基因(或其亚基)的表达盒,第二AAV可携带在宿主细胞中共表达的表达式第二转基因(或不同亚基)的表达盒。第一AAV可携带多顺反子构建体的第一部分(例如:启动子和转基因,或亚基)的表达盒,第二AAV可携带多顺反子构建体的第二部分(例如:转基因或亚基和polyA序列)的表达盒。多顺反子构建体的这两个部分在体内多联化成共表达由第一和第二AAV递送的转基因的单个载体基因组。在这种实施方案中,携带第一表达盒的rAAV载体和携带第二表达盒的rAAV载体可以包含在单个药物组合物中来递送。在其他实施方案中,两个或多个rAAV载体以分开的药物组合物来递送,这些药物组合物可基本上同时给药或略有先后。

[0131] 上述重组载体可按照公开的方法递送至宿主细胞中。可将rAAV,优选悬浮在生理相容载体中的rAAV,给予人或非人哺乳动物患者。本领域技术人员可依据病毒递送所针对的适应症容易地选择适当的载体。例如,适当的载体包括可用各种缓冲液配制的盐水(例如:磷酸缓冲盐水)。其他的载体例子包括无菌盐水、乳糖、蔗糖、磷酸钙、明胶、葡萄糖、琼脂、果胶、花生油、芝麻油和水。载体的选择不限制本发明。

[0132] 任选地,除rAAV和载体以外,本发明的组合物还可含有其他常规药物组分,例如防腐剂或化学稳定剂。适当的防腐剂例如氯代丁醇、山梨酸钾、山梨酸、二氧化硫、没食子酸丙酯、对羟基苯甲酸酯类、乙基香草醛、甘油、苯酚与对氯苯酚。适当的化学稳定剂包括明胶和

白蛋白。

[0133] 载体的给予量应满足转染细胞所需并应提供足够的基因传送和表达水平以提供疗效而无副作用,或有医学上可接受的生理作用,这可由医学领域技术人员确定。常规的和药学上可接受的给药途径包括但不限于:直接递送至目标器官(例如,肝(任选经肝动脉)或肺)、口服、吸入、鼻内、气管内、动脉内、眼内、静脉内、肌肉内、皮下、真皮内和其他胃肠外给药途径。如果需要,可多种给药途径联用。

[0134] 病毒载体的剂量主要取决于以下因素,例如治疗的病症、患者的年龄、体重和健康状况,因此可依患者而改变。例如,病毒载体的人用治疗有效剂量一般约为含有浓度约 1×10^9 – 1×10^{16} 个基因组病毒载体的0.1mL–100mL溶液。递送至大器官(例如:肝、肌肉、心脏和肺)的优选的人用剂量可约为 5×10^{10} – 5×10^{13} 个AAV基因组/kg,体积约为1–100mL。递送至眼的优选剂量约为 5×10^9 – 5×10^{12} 份基因组拷贝,体积约为0.1mL–1mL。可调整剂量以平衡副作用和疗效,并且这种剂量可根据重组载体的具体治疗性用途而改变。可监测转基因的表达水平来确定给药频率,以获得病毒载体,优选含有小基因的AAV载体。任选地,可按照类似于就治疗性目所述的给药方案用本发明的组合物来免疫接种。

[0135] 后文提供了用本发明的含AAV载体进行递送的治疗性产物和免疫原性产物的实例。这些载体可用于本文所述的各种治疗性或接种方案。此外,按照治疗性和/或接种方案所需,这些载体可联合一种或多种其他载体或活性成分用于递送。

[0136] B. 治疗性转基因

[0137] 转基因编码的有用的治疗性产物包括激素与生长因子和分化因子,包括但不限于:胰岛素、胰高血糖素、生长激素(GH)、甲状旁腺激素(PTH)、生长激素释放因子(GRF)、卵泡刺激素(FSH)、黄体激素(LH)、人绒毛膜促性腺激素(hCG)、血管内皮生长因子(VEGF)、促血管生成素、血管抑制素、粒细胞集落刺激因子(GCSF)、促红细胞生成素(EPO)、结缔组织生长因子(CTGF)、碱性成纤维细胞生长因子(bFGF)、酸性成纤维细胞生长因子(aFGF)、表皮生长因子(EGF)、血小板衍生的生长因子(PDGF)、胰岛素生长因子I和II(IGF-I和IGF-II)、转化生长因子 α 超家族中的任一个(包括TGF α 、活化素、抑制素)、或骨形态发生蛋白(BMP) BMP1–15中的任一个、生长因子中的调蛋白/神经调节蛋白/ARIA/neu分化因子(NDF)家族的任一个、神经生长因子(NGF)、脑源性神经营养因子(BDNF)、神经营养蛋白NT-3和NT-4/5、睫状神经营养因子(CNTF)、胶质细胞系衍生神经营养因子(GDNF)、neurturin、聚集蛋白、脑信号蛋白/瓦解蛋白家族的任一个、导蛋白-1和导蛋白-2、肝细胞生长因子(HGF)、肝配蛋白、头蛋白、sonic hedgehog蛋白和酪氨酸羟化酶。

[0138] 其他有用的转基因产物包括调节免疫系统的蛋白质,包括但不限于:细胞因子和淋巴因子,例如血小板生成素(TPO)、白介素(IL) IL-1到IL-25(包括,例如:IL-2、IL-4、IL-12和IL-18)、单核细胞化学诱导蛋白、白血病抑制因子、粒细胞-巨噬细胞集落刺激因子、Fas配体、肿瘤坏死因子 α 和 β 、干扰素 α 、 β 和 γ 、干细胞因子、flk-2/flt3配体。免疫系统产生的基因产物也可用于本发明。这些产物包括但不限于:免疫球蛋白IgG、IgM、IgA、IgD和IgE、嵌合免疫球蛋白、人源化抗体、单链抗体、T细胞受体、嵌合T细胞受体、单链T细胞受体、I类和II类MHC分子,以及经改造的免疫球蛋白和MHC分子。有用的基因产物还包括补体调节蛋白质,例如补体调节蛋白、膜辅因子蛋白(MCP)、衰变加速因子(DAF)、CR1、CF2和CD59。

[0139] 其他有用的基因产物包括激素受体、生长因子、细胞因子、淋巴因子、调节蛋白质

和免疫系统蛋白质的任一种。本发明包括胆固醇调节和/或脂质调节的受体,包括低密度脂蛋白(LDL)受体、高密度脂蛋白(HDL)受体、极低密度脂蛋白(VLDL)受体和清除受体。本发明也包括以下基因产物:例如类固醇激素受体超家族的成员,包括糖皮质激素受体和雌激素受体、维生素D受体和其他核受体。此外,有用的基因产物包括转录因子,例如jun、fos、max、mad、血清效应因子(SRF)、AP-1、AP2、myb、MyoD和肌细胞生成蛋白、含有蛋白质的ETS-盒、TFE3、E2F、ATF1、ATF2、ATF3、ATF4、ZF5、NFAT、CREB、HNF-4、C/EBP、SP1、CCAAT-盒结合蛋白、干扰素调节因子(IRF-1)、Wilms肿瘤蛋白、ETS-结合蛋白、STAT、GATA-盒结合蛋白,例如GATA-3和翼状螺旋蛋白的叉头蛋白家族。

[0140] 其他有用的基因产物包括氨甲酰合成酶I、鸟氨酸转氨甲酰酶、精氨基琥珀酸合成酶、精氨基琥珀酸裂合酶、精氨酸酶、延胡索酰乙酰乙酸水解酶、苯丙氨酸羟化酶、 α -1抗胰蛋白酶、葡萄糖-6-磷酸酶、胆色素原脱氨酶、胱硫醚 β -合成酶、支链酮酸脱羧酶、白蛋白、异戊酰-CoA脱氢酶、丙酰-CoA羧化酶、甲基丙二酰CoA变位酶、戊二酰-CoA脱氢酶、胰岛素、 β -葡糖苷酶、丙酮酸羧酸盐、肝磷酸化酶、磷酸化酶激酶、甘氨酸脱羧酶、H-蛋白、T-蛋白、囊性纤维化跨膜传导调节蛋白(CFTR)序列和抗肌萎缩蛋白基因产物[例如:小-或微-抗肌萎缩蛋白]。其他有用的基因产物包括可用于酶活性缺乏所导致的各种病症例如可用于酶替代治疗的酶。例如,含有甘露糖-6-磷酸的酶可用于治疗溶菌酶储存疾病(例如编码 β -葡糖醛酸糖苷酶(GUSB)的基因)。

[0141] 其他有用的基因产物包括用于治疗血友病的产物,包括B型血友病(包括因子IX)和A型血友病(包括因子VIII及其变体,例如异二聚体的轻链和重链和B-缺失结构域;美国专利号6,200,560和美国专利号6,221,349)。因子VIII基因编码2351个氨基酸,该蛋白具有六个结构域,从氨基向羧基端依次指定为A1-A2-B-A3-C1-C2 [Wood等人, *Nature*, 312:330 (1984); Vehar等人, *Nature*, 312:337 (1984); 以及Toole等人, *Nature*, 342:337 (1984)]。人因子VIII在细胞内经加工产生主要含有重链和轻链的异二聚体,所述重链含有A1、A2和B结构域,所述轻链含有A3、C1和C2结构域。单链多肽与异二聚体作为无活性的前体在血浆中循环,直至在A2和B结构域之间被凝血酶切割而激活,由此释放出B结构域并形成由A1和A2结构域组成的重链。该蛋白质激活的前凝血质形式不含B结构域。此外,在天然蛋白中,B结构域之侧的两条多肽链(“a”和“b”)与二价钙阳离子结合。

[0142] 在一些实施方案中,小基因含有编码10个氨基酸信号序列的因子VIII重链的前57个碱基对和人生长激素(hGH)聚腺苷酸化序列。在另一实施方案中,小基因进一步含有A1和A2结构域,以及B结构域N-末端的5个氨基酸,和/或B结构域C-末端的85个氨基酸,以及A3、C1和C2结构域。在另外的实施方案中,编码因子VIII重链和轻链的核酸被编码B结构域的14个氨基酸的42个核酸隔开并包含在单个小基因中[美国专利号6,200,560]。

[0143] 本文使用的治疗上的有效量指可产生足够量的因子VIII以降低受试对象血液凝结所需时间的AAV载体的量。通常,因子VIII水平低于正常水平的1%的严重血友病患者的全血凝时间大于60分钟,而非血友病患者约为10分钟。

[0144] 本发明不限于任何具体的因子VIII序列。已经分离和产生了许多因子VIII的天然和重组形式。因子VIII的天然形式和重组形式的实例见专利和科学文献,包括美国专利号5,563,045;5,451,521;5,422,260;5,004,803;4,757,006;5,661,008;5,789,203;5,681,746;5,595,886;5,045,455;5,668,108;5,633,150;5,693,499;5,587,310;5,171,844;5,

149,637;5,112,950;4,886,876;国际专利公开号WO 94/11503,WO 87/07144,WO 92/16557,WO 91/09122,WO 97/03195,W096/21035和WO 91/07490;欧洲专利申请号EP 0 672 138,EP 0 270 618,EP 0 182448,EP 0 162 067,EP 0 786 474,EP 0 533 862,EP 0 506 757,EP 0 874 057,EP 0 795 021,EP 0 670 332,EP 0 500 734;EP 0 232 112和EP 0 160 457;Sanberg等人,世界血友病联合会第20届国际会议(XXth Int.Congress of the World Fed.Of Hemophilia),(1992)和Lind等人,Eur.J.Biochem.,232:19(1995)。

[0145] 编码上述因子VIII的核酸序列可使用重组方法获得或从已知包含该序列的载体得到。此外,也可使用标准技术直接从含有该序列的细胞和组织中分离所需序列,所述标准技术例如酚提取与cDNA或基因组DNA的PCR[参见,例如: Sambrook等人]。除了克隆以外,核苷酸序列也可合成产生。可用标准方法制备重叠的寡核苷酸,从重叠的寡核苷酸装配成完整的编码序列中[参见,例如: Edge, Nature, 292:757(1981); Nambari等人, Science, 223: 1299(1984)和Jay等人, J. Biol. Chem., 259:6311(1984)]。

[0146] 此外,本发明不限于人因子VIII。实际上,本发明意在包括来自除人以外的动物的因子VIII,所述动物包括但不限于宠物动物(例如:狗、猫和马)、牲畜(例如:牛、山羊和绵羊)、实验室动物、海生动物、大型猫科动物(large cat)等。

[0147] AAV载体可含有编码因子VIII片段的核酸,该片段本身无生物活性,但当给予受试对象时则能改善或恢复血凝时间。例如,如前所述,因子VIII蛋白含有两条多肽链:由B结构域隔开的重链和轻链,B结构域将在加工过程中被切除。如本发明所证明的,用因子VIII的重链和轻链共转导受体细胞导致生物活性因子VIII的表达。由于大多数血友病患者仅在一条链(例如:重链或轻链)中含有突变或缺失,这就有可能仅给予患者有缺陷的那条链来与另一条链互补。

[0148] 其他有用的基因产物包括非天然存在的多肽,例如具有非天然存在的氨基酸序列的嵌合或杂交多肽,所述非天然存在的氨基酸序列含有插入、缺失或氨基酸取代。例如,经单链改造的免疫球蛋白可用在某些免疫低下患者中。其他类型的非天然存在的基因序列包括反义分子和催化性核酸,例如核酶,可用于降低靶的过度表达。

[0149] 降低和/或调节基因表达对治疗以细胞过度增殖为特征的过度增殖性疾病,例如癌症和银屑病,尤其理想。靶多肽包括,与正常细胞相比,仅在过度增殖细胞中产生或在过度增殖细胞中以更高水平产生的多肽。靶抗原包括癌基因和易位基因编码的多肽,所述癌基因编码的多肽例如myb、myc、fyn,所述易位基因编码的多肽如bcr/abl、ras、src、P53、neu、trk和EGFR。除了作为靶抗原的癌基因产物,用于抗癌治疗和保护性治疗方案的靶多肽包括B细胞淋巴瘤产生的抗体的可变区和T细胞淋巴瘤的T细胞受体的可变区,在某些些实施方案中,它们也用作自身免疫疾病的靶抗原。其他肿瘤相关多肽也可用作靶多肽,例如在肿瘤细胞中处于较高水平的多肽,包括单克隆抗体17-1A所识别的多肽和叶酸结合多肽。

[0150] 其他合适的治疗性多肽和蛋白质包括通过赋予抗自身免疫相关靶的广谱基础保护性免疫应答来治疗患自身免疫疾病和紊乱的个体的多肽和蛋白,所述自身免疫相关靶包括细胞受体和产生“自我”定向抗体的细胞。T细胞介导的自身免疫疾病包括类风湿性关节炎(RA)、多发性硬化症(MS)、Sjögren氏综合征、结节病、胰岛素依赖型糖尿病(IDDM)、自身免疫甲状腺炎、反应性关节炎、强直性脊柱炎、硬皮病、多肌炎、皮肌炎、银屑病、脉管炎、韦格纳肉芽肿病、克罗恩病和溃疡性结肠炎。这些疾病均以结合内源性抗原并引发自身免疫

疾病相关炎性级联反应的T细胞受体(TCR)为特征。

[0151] C.免疫原性转基因

[0152] 本发明的AAV载体以避免产生针对包含于载体的AAV序列的免疫应答为宜。然而,这些载体配制成使得载体携带的转基因得以表达从而诱导对选定抗原的免疫应答。例如,为促进免疫应答,可由组成型启动子控制转基因的表达,如本文所述将载体与佐剂组合,和/或可将载体引入退化组织中。

[0153] 适当的免疫原性转基因的实例可包括选自各种病毒科的免疫原性转基因。需要免疫应答来抵御的病毒科的实例包括:小RNA病毒科,其包括导致约50%普通感冒病例的鼻病毒属;肠病毒属,其包括脊髓灰质炎病毒、柯萨奇病毒、艾柯病毒和人肠病毒(例如甲肝病毒);以及口疮病毒属,其主要在非人动物中导致口蹄疫。在小RNA病毒科内,靶抗原包括VP1、VP2、VP3、VP4和VPG。其他病毒科包括星状病毒和杯状病毒科。杯状病毒科包括视为流行性肠胃炎重要病因的诺瓦克组病毒。另一种有望用于靶抗原在人或非人动物中诱导免疫应答的病毒科是披膜病毒科,该科包括甲型病毒属,该甲型病毒属包括辛德毕斯病毒、罗斯河病毒、和委内瑞拉、东部和西部马脑炎病毒和风疹病毒属,包括风疹病毒。黄病毒科包括登革热、黄热、日本脑炎、圣路易斯脑炎和蜱传性脑炎病毒。其他靶抗原可从丙型肝炎或冠状病毒科产生,其中包括许多非人病毒,例如感染性支气管炎病毒(家禽)、猪传染性胃肠病毒(猪)、猪凝血性脑脊髓炎病毒(猪)、猫感染性腹膜炎病毒(猫)、猫肠冠状病毒(猫)、狗冠状病毒(狗)和可导致普通感冒和/或非-甲型、乙型或丙型肝炎的人呼吸冠状病毒,该科病毒还可能是严重急性呼吸道综合症(SARS)的病因。在冠状病毒科内,靶抗原包括E1(也称为M或基质蛋白)、E2(也称为S或刺蛋白)、E3(也称为HE或血凝素-依尔替糖)、糖蛋白(并非所有冠状病毒中都有)或N(核衣壳)。他抗原还可以是针对动脉炎病毒科和弹状病毒科的。弹状病毒科包括水疱病毒属(例如:疱疹口炎病毒)和狂犬病病毒属(例如:狂犬病)。在弹状病毒科内,适当的抗原可源于G蛋白或N蛋白。包括出血热病毒例如马尔堡和埃博拉病毒的丝状病毒科可能是合适的抗原来源。副黏病毒科包括1型副流感病毒、3型副流感病毒、3型牛副流感病毒、腮腺炎病毒(流行性腮腺炎病毒)、2型副流感病毒、4型副流感病毒、新城疫病毒(小鸡)、牛瘟病毒、麻疹病毒(其包括麻疹和犬瘟热),以及肺病毒(其包括呼吸道合胞病毒)。流感病毒被分在正黏病毒科内,并且是抗原(例如:HA蛋白、N1蛋白)的合适来源。布尼亚病毒科包括布尼亚病毒属(加利福尼亚脑炎,拉克罗斯脑炎)、白蛉热病毒属(裂谷热)、汉坦病毒属(普马拉是hemahagin热病毒)、内罗毕病毒属(内罗毕绵羊病)和各种未命名的银环蛇病毒(bungaviruse)。沙粒病毒科提供抗LCM和拉沙热病毒的抗原来源。抗原的另一来源是博内病毒科。呼肠孤病毒科包括呼肠孤病毒属、轮状病毒属(其导致儿童急性肠胃炎)、环状病毒属和科罗拉多蜱热病毒属(科罗拉多蜱热病毒属、Lebombo病毒属(人)、马变性脑病病毒属、蓝舌病病毒属)。逆转录病毒科包括致肿瘤RNA病毒亚科,该亚科包括人和兽医疾病,例如猫白血病病毒、HTLVI和HTLVII、慢病毒亚科(包括HIV、猿免疫缺陷病毒、猫免疫缺陷病毒、犬感染性贫血病毒和泡沫病毒亚科)。

[0154] 就HIV和SIV而言,已经描述了许多合适的抗原,并可以容易地选择。合适的HIV和SIV抗原的实例包括但不限于gag、pol、Vif、Vpx、VPR、Env、Tat和Rev蛋白,及其各种片段。例如,适当的被膜(env)蛋白的片段包括,例如:gp41、gp140和gp120。另外,已经描述了对于这些及其他HIV和SIV抗原的各种修饰。用于该用途的合适抗原是本领域技术人员所知的。例

如,可从其他蛋白中选择编码gag、pol、Vif以及Vpr、Env、Tat和Rev的序列。参见,例如:在美国专利5,972,596中描述了修饰的gag蛋白。同时参见,在D.H.Barouch等人,J.Virol.,75(5):2462-2467(2001年3月)和R.R.Amara等人,Science,292:69-74(2001年4月6日)中所描述的HIV和SIV蛋白。这些蛋白质或其亚基可经由多个载体或由单个载体单独或组合递送。

[0155] 乳多空病毒科包括多瘤病毒亚科(BKU和JCU病毒)和乳头瘤病毒亚科(与癌症或乳头的恶性进展有关)。腺病毒科包括导致呼吸疾病和/或肠炎的病毒(EX、AD7、ARD、O.B.)。细小病毒科包括猫细小病毒(猫肠炎)、猫全白细胞减少病病毒、狗细小病毒和猪细小病毒科。疱疹病毒科包括疱疹病毒亚科,该亚科包括单纯疱疹病毒属(HSVI、HSVII)、水痘病毒属(假狂犬病、水痘带状疱疹);以及 β 疱疹病毒亚科,该亚科包括巨细胞病毒属(HCMV,鼠巨细胞病毒属);和 γ 疱疹病毒亚科,该亚科包括淋巴潜伏病毒属、EBV(伯基特淋巴瘤)、人疱疹病毒6A、6B和7、卡波西肉瘤相关疱疹病毒与弥猴疱疹病毒(B病毒)、传染性鼻气管炎病毒属、马雷克病病毒属和细长病毒属。痘病毒科包括脊椎动物痘病毒亚科,包括正痘病毒属(大天花(天花)和牛痘(牛痘))、副痘病毒属、禽痘病毒属、山羊痘病毒属、兔痘病毒属、猪痘病毒属和昆虫痘病毒亚科。嗜肝DNA病毒科包括乙肝病毒。可作为抗原的合适来源的一种未归类病毒是肝炎 δ 病毒、戊肝病毒和朊病毒。另一种作为抗原来源的病毒是Nipah病毒。其他的病毒来源包括鸟感染性粘液囊病病毒和猪呼吸和生殖综合征病毒。甲型病毒科包括马动脉炎病毒和各种脑炎病毒。

[0156] 本发明还包括用于免疫人或非人动物抗其他病原体的免疫原,所述病原体包括感染人和非人脊椎动物的细菌、真菌、寄生微生物或多细胞寄生虫,或来自癌细胞或肿瘤细胞的病原体。细菌病原体的实例包括致病性革兰氏阳性球菌,其包括肺炎球菌、葡萄球菌(及其产生的毒素,例如:肠毒素B)和链球菌。致病性革兰氏阴性球菌包括脑膜炎球菌、淋球菌。致病性肠革兰氏阴性杆菌包括肠杆菌科;假单胞菌属、不动杆菌属和埃肯菌属;类鼻疽假单胞菌属;沙门氏菌属;志贺氏菌属;嗜血杆菌属;莫拉氏菌属;杜克雷嗜血杆菌(*H. ducreyi*)(其导致软下疳);布鲁杆菌(布鲁杆菌病);野兔热弗朗西丝菌(*Francisella tularensis*)(其导致兔热病);鼠疫耶尔森菌(鼠疫)和其他耶尔森菌属(巴斯德菌属);念珠状链杆菌和螺菌属;革兰氏阳性杆菌,其包括单核细胞增多李斯特菌;红斑丹毒丝菌;白喉棒状杆菌(*Corynebacterium diphtheria*)(白喉);霍乱;炭疽杆菌(*B. anthracis*)(炭疽);多诺万病(腹股沟肉芽肿)和巴尔通体病。致病性厌氧细菌导致的疾病包括破伤风;肉毒中毒(肉毒梭菌(*Clostridium botulinum*)及其毒素);产气荚膜梭菌(*Clostridium perfringens*)及其 ϵ 毒素;其他梭菌属;结核病;麻风和其他分枝杆菌属。致病性螺旋体疾病包括梅毒;密螺旋体病:雅司病、品他病和地方性梅毒;以及钩端螺旋体病。较高致病性细菌和致病性真菌导致的其他感染包括鼻疽(鼻疽伯克霍尔德氏菌(*Burkholderia mallei*));放线菌病;诺卡菌病;隐球菌病、芽生菌病、组织胞浆菌病和球孢子菌病;念珠菌病、曲霉病和毛霉病;孢子丝菌病;副球孢子菌病、石样真菌病、球拟酵母病、足分枝菌病和着色真菌病;以及皮真菌病。立克次体感染包括斑疹伤寒热、落矶山斑疹热、Q热(伯内特科克斯立克次体(*Coxiella burnetii*)) and 立克次氏体痘。支原体和衣原体感染的实例包括:支原体肺炎、性病性淋巴肉芽肿、鹦鹉热和围产期衣原体感染。致病性真核细胞包括致病性原生动物和蠕虫,并且由其产生的感染包括:阿米巴病、疟疾、利什曼病、锥虫病、弓形体病、卡氏肺囊虫(*Pneumocystis carinii*)、Trichans、鼠弓形体(*Toxoplasma gondii*)、巴贝虫病、贾第虫病、旋毛虫病、丝虫

病、血吸虫病、线虫、吸虫 (trematode) 或吸虫 (fluke) 感染和绦虫 (绦虫) 感染。

[0157] 这些生物体和/或其产生的毒素中有许多已被疾病控制中心 [(CDC), 健康与人类服务部 (Department of Health and Human Services), 美国] 认定为是可用于生物攻击的物质。例如, 某些此类生物物质包括目前分类为A类物质的炭疽杆菌 (*Bacillus anthracis*) (炭疽)、肉毒梭菌 (*Clostridium botulinum*) 及其毒素 (肉毒杆菌毒素)、鼠疫耶尔森菌 (*Yersinia pestis*) (鼠疫)、大天花 (天花)、野兔热弗朗西丝菌 (*Francisella tularensis*) (兔热病) 和病毒性出血热 [丝状病毒 (例如: 埃博拉病毒、马尔堡病毒) 和沙粒病毒 [例如: 拉沙病毒、马丘博病毒]; 目前分类为B类物质的伯内特科克斯立克次体 (*Coxiella burnetii*) (Q热)、布鲁杆菌 (布鲁杆菌病)、鼻疽伯克霍尔德氏菌 (*Burkholderia mallei*) (鼻疽)、假鼻疽伯克霍尔德氏菌 (*Burkholderia pseudomallei*) (类鼻疽)、蓖麻 (*Ricinus communis*) 及其毒素 (蓖麻蛋白毒素)、产气荚膜梭菌 (*Clostridium perfringens*) 及其毒素 (ϵ 毒素)、葡萄球菌 (*Staphylococcus*) 及其毒素 (肠毒素B)、鹦鹉热衣原体 (*Chlamydia psittaci*) (鹦鹉热)、水上安全威胁 (water safety threat) (例如: 霍乱弧菌 (*Vibrio cholerae*)、小隐孢子虫 (*Cryptosporidium parvum*)、斑疹伤寒热 (普氏立克次体 (*Rickettsia prowazekii*) 和病毒性脑炎 (甲型病毒, 例如: 委内瑞拉马脑炎、东部马脑炎、西部马脑炎); 以及目前分类为C类物质的Nipah病毒和汉坦病毒。此外, 其他如此分类或不同分类的生物体也可能在将来可被鉴定和/或用于这种目的。容易理解的是, 本文所述的病毒载体和其他构建体可用于传递来自这些生物体的抗原、病毒、其毒素或其他副产物, 这可预防和/或治疗这些生物物质引起的感染或其他不良反应。

[0158] 施用本发明的载体来递送抗T细胞可变区的免疫原引发包括CTL在内的免疫应答来消除T细胞。在类风湿性关节炎 (RA) 中, 已鉴定了参与该疾病的数种特定TCR可变区。这些TCR包括V-3、V-14、V-17和V-17。因此, 递送编码这些多肽中至少一种的核酸序列将引发以参与RA的T细胞为目标的免疫应答。在多发性硬化症 (MS) 中, 已鉴定了参与该疾病的数种特定TCR可变区。这些TCR包括V-7和V-10。因此, 递送编码这些多肽中至少一种的核酸序列将引发以参与MS的T细胞为目标的免疫应答。在硬皮病中, 已鉴定了参与该疾病的数种特定TCR可变区。这些TCR包括V-6、V-8、V-14和V-16、V-3C、V-7、V-14、V-15、V-16、V-28和V-12。因此, 递送编码这些多肽中至少一种的核酸分子将引发以参与硬皮病的T细胞为目标的免疫应答。

[0159] 因此, 本发明的rAAV衍生的重组病毒载体提供了一种有效的基因转送载体, 它们能在体内或体外将选定转基因递送至选定宿主细胞中, 即使该生物体具有针对一种或多种AAV源的中和抗体。在一个实施方案中, rAAV与细胞体外混合, 使用常规方法培养被感染的细胞, 并将被转导细胞回输给患者。

[0160] 这些组合物尤其适用于治疗目的和免疫接种目的的基因递送, 所述免疫接种包括诱导保护性免疫。本发明的AAV和包含本发明的AAV的组合物还可以用于免疫疗法, 例如在为本申请申请人所共有的、2004年4月28日递交的“致免疫分子的连续的腺病毒和AAV介导的传递”的美国专利申请号60/565,936。

[0161] 此外, 本发明的组合物也可用于体外生产所需基因产物。就体外生产而言, 可如下获得所需产物 (例如: 蛋白质): 用含有编码所需产物的分子的rAAV转染宿主细胞, 并在允许表达的条件下培养细胞培养物, 然后从培养物中获得所需产物。然后, 可视需要纯化和分离

该表达产物。合适的转染、细胞培养、纯化和分离技术是本领域技术人员已知的。

[0162] 以下实施例阐述了本发明的几个方面与实施方案。

[0163] 实施例1

[0164] 根据本发明的方法,将AAV序列与包含分化体A、B、C、D、E和F(由AAV9代表)各自代表性序列的文库比对时,确定了其具有单现突变。下列表格显示了有待改变为保守序列的衣壳序列和单现突变。为表示某些突变,单现突变后面有*,再后面是用于取代它的氨基酸残基。为表示其他有些突变,单现突变后面是其氨基酸位置和用来取代它的残基。

[0165] 氨基酸编号是基于这些AAV衣壳各自的已公开序列。参见,例如:G.Gao等人,J.Virol.,78(12):6381-6388(2004年6月)和国际专利公开号W0 2004/042397[其中的全部序列存放在GenBank中],以及2004年9月30日提交的国际专利公开号W02005/033321,其引用作为参考。

[0166] 例如,就下表而言,各名称应如下理解。Cy5R1指氨基酸残基位点13处为天冬氨酸(D)的经修正氨基酸序列SEQ ID NO:24;cy5天然氨基酸序列的第13位残基处是甘氨酸。Cy5R2指氨基酸残基位点13处(在天然序列中为甘氨酸)为天冬氨酸且在氨基酸残基位点403处(在天然序列中为天冬氨酸)为天冬酰胺的经修正氨基酸序列SEQ ID NO:24。Cy5R3具有经修正的氨基酸序列SEQ ID NO:24,具有与Cy5R2相同的改变,此外,在位点158处为赖氨酸(在天然序列中为天冬酰胺),在位点161处为谷氨酰胺(在天然序列中为脯氨酸)。鉴于以上信息,本领域技术人员可容易地确定在下表中所列的其他单现突变改变。

[0167]

名称	SEQ ID NO: (亲代 AAV)	突变的位点				分化体
Cy5	24					
Cy5R1		G13D				D
Cy5R2		G13D	D403N			D
Cy5R3		G13D	D403N	R51K		D
Cy5R4		G13D	D403N	R51K	N158K+P161Q	D
rh.13	26					D
Rh.13R		E538K				D
Rh37	40					D
Rh37R2		E634K	T207M			D
Rh.2	39					E
rh.2R		V651I				E
Rh.8	41					
rh.8R		D531E				
Rh.48	44					
Rh.48.1		K217E				B
Rh.48.2		S304N				B
Rh.48.1.2		K217E	S304N			B
Hu.44	45					A
Hu.44R1		E137K				A
Hu.44R2		E137K	P446L			A

[0168]

Hu.44R3		E137K	P446L	G609D		A
Rh32/33	2					
Hu.29	42					B
Hu.29R		G396E				B
Ch.5	46					
Ch.5R1		T611I				
rh.67	47					D
rh.58	48			S653N		E
Rh.64	43					E
Rh64R1		R697W				E
Rh64R2		R697W	V686E			E
AAV6	29					A
AAV6.2		F129L				A
AAV6.1		K531E				A
AAV6.12		F129L	K531E			A
rh.54	49	V404M				D
hu.48	50					A
hu.48R1		G277S				A
hu.48R2		G277S	E322K			A
hu.48R3		G277S	E322K	S552N		A

[0169] 实施例2

[0170] 在初步研究中,选择五个克隆来试验本发明的单现突变方法。下表提供了这5个克隆的表型描述。在预测单现突变数目之外还列明了所属分化体和血清型分类。

[0171] 当其滴度低于 1×10^{11} GC时,包装表型认定为不足;当低于 1×10^{12} GC时,认定为低;当低于 1×10^{13} GC时,认为是好;更高则认为是优良。

[0172] 通过CB.A1AT基因表达来确定基因转移表型,并且表示如下:“+++”表示比靶组织的首选候选物更好,“++”、“+”和“-”分别表示与首选候选物(肌肉:AAV1,肝:AAV8,肺:AAV9)的A1AT血清浓度水平相比超过该水平的50%、相当于该水平的10-50%,低于该水平的10%。“n/a”表明不能产生用于体内基因转移研究的足够水平的载体。

[0173] 单现突变校正克隆如下进行。对原包装质粒进行定点诱变。在此之后,通过Pst1消化测定载体骨架的完整性,并通过测序确认单现突变的校正。然后在12-孔板上一式三份产生EGFP-表达载体,与包含单现突变的亲代载体、AAV2和AAV2/8阳性对照生产以及作为阴性对照的不存在包装质粒情况下的生产并列。在 $3 \times$ 冷冻之后,将等量的收获的裂解物培养于293细胞。在转导后72小时,通过流式细胞计数法检测eGFP表达。

[0174] 在克隆rh.37、rh.2、ch.5、rh.13和rh.8中进行单现突变的定位诱变。选择这些特定的序列来代表以前文献中记载的各种表型。

	克隆	包装	基因转移表型			#单现突变	分化体(血清型)
		表型	肺	肝	肌肉		
[0175]	Rh.37	不足	N/a	N/a	N/a	2	D(AAV7)
	Rh.2	低	++	+	+++	1	E(AAV8)
	Ch.5	好	-	-	-	1	Ch.5
	Rh.13	优良	+	+	+	1	D(AAV7)
	Rh.8	好	-	+	++	1	Rh.8

[0176] 在5个克隆中的4个中观察到载体表达的增加。以前显示低包装产量的rh.37和rh.2的增加最为显著。这些载体产生颗粒的生产水平可满足检测所需。载体rh.8和rh.13显示了转导率提高。

[0177] 为了区分单现突变对转导的作用与对包装和装配的作用,制备小量的载体制剂,并通过定量PCR进行耐Dnase颗粒滴定。就rh.37可观察到载体产量的两倍对数(two-log)增加。rh.8显示滴度的5倍增加,而rh.13表现不变。与AAV2和AAV2/8产物相比,并且在推广到大量制备时,经单现突变校正的克隆的滴度全都在可接受的范围内。没有对rh.2进行滴定测定。

[0178] 随后在每一细胞相等颗粒数的转导环境中体外监测单现突变改变的作用。对rh.8和rh.13用293细胞进行滴定。全部感染复数(MOI)的转导效率的都适中增加。

[0179] 这最初5个克隆的亚组中,3个能够转导细胞并具有生产能力。两个克隆在该试验设定的环境中不能产生任何eGFP表达。这很可能是由于某种无法由单现突变方法预知的载体包装缺陷所致。

[0180] 使用本发明的方法来校正AAV克隆hu.46中的四个预计单现突变位点:P156S R362C S393F A676。但是,这些修正没有产生可回复其活性的AAV,这表明了在hu.46序列中有其他类型的致死错误。

[0181] 实施例3—具有改变衣壳的病毒载体的体外分析

[0182] 使用本发明的方法,改变rh.64和hu.29的衣壳蛋白,然后如实施例2和G.Gao等人,Proc Natl Acad Sci美国,99,11854-9(2002年9月3日)所述通过假型包装构建具有改变衣壳的病毒载体。

[0183] 简短地说,用表达强化绿色荧光蛋白(EGFP)的载体体外检测载体在人内皮肾细胞(293细胞)中的转导效率。在与wtAd5一起短暂预孵育之后,在有 10^4 GC/细胞的假型AAVCMVeGFP颗粒存在下孵育这些293细胞。通过检测灵敏度为5细胞/10K的FACS分析测定每10,000个细胞中eGFP阳性细胞的数目。

[0184] 在R697W改变之后,按本发明修正Rh.64衣壳提供了效率提高100-倍的修正rh.64颗粒。随后的V686E突变将包装能力提高了两倍。

[0185] 按本发明修正Hu.29衣壳,通过G396E这一改变提供了包装能力缺陷获得修复的rh.64病毒颗粒。据观察,病毒生产的提高超过1000倍。

[0186] 20多个修正AAV病毒颗粒中许多显示表达增强,这些病毒颗粒包括AAV6.1、hu.48R1、hu.48R2、hu.44R2、hu.44R3、rh.48.2、rh.48.2、rh.48.2.1。

[0187] 实施例4—在体内基因转移应用中单现突变的效应

[0188] 在体内环境设定中研究了单现突变体的效应。已开始用C57B/6小鼠对许多按照本发明方法修正的载体进行了基因转移研究。开始了肌肉定向和肝定向的研究,并且以目前用于特定应用的首选候选物为基准进行了比较。

[0189] 选择人的 α -抗胰蛋白酶(A1AT)作为载体中的敏感定量报告基因,并使其在CMV-增强鸡 β -肌动蛋白启动子控制下表达。使用CB启动子能够实现高水平的非组织特异性和组成性的A1AT基因转移,并容许在任何感兴趣组织中使用相同的载体制剂来研究基因转移。

[0190] 选择肌肉作为第一个靶组织。将40种不同的新载体(基于各含相应单现突变体的24个不同克隆)肌内注射到C57B/6小鼠的后肢中。用CB.A1AT转基因盒,以 1×10^{11} GC/动物来进行全部试验。每一分化体的每组每鼠每次使用等量的载体(50 μ l)。每个独立研究包括一个或两个分化体和对照组,所述对照组包括分化体的代表性血清型,AAV2/8和AAV2/1,以它们为基准来研究定向于肌肉的基因转移。在注射之后的第7、14、28和63天检测转基因的表达,并用特异性的hA1AT ELISA来评定。

[0191] 获得了几种分离株和单现突变校正入门内(intraportal)肝定向注射之后的性能数据。初步结果表明大部分校正克隆的表现与原分离株相当或更好。

[0192] 就一种特定的克隆即cy.5而言,单现突变校正看来对肌肉转导具有有益的作用。携带4个单现突变校正的克隆cy.5R4,与原始分离株已有的适当的肌肉趋性相比,基因转移的效率进一步提高。cy.5R4的表现等同于或稍好于作为基准对照的AAV2/1和AAV2/7。

[0193] 以前应过低滴度而无法进一步测评的分离株rh.64,在对一个单现突变进行校正之后在肌肉中表现特别好。Rh.64R1表现好于rh.64.2,其产生的hA1AT水平高于其最近的相关血清型AAV2/8,并且高于AAV2/7。

[0194] 在其他的研究中,给小鼠注射基于分化体分组的载体。用表达CB.hA1AT的载体按照 1×10^{11} GC/小鼠给药。用特异性的hA1AT ELISA测定hA1AT的血清浓度水平。

[0195] 单现突变在体内对基因转移的作用看来取决于分离株和靶组织。有数项观测结果是有意义的。

[0196] 就某些单现突变克隆而言,定性地说,单现突变的作用在肌肉中和在肝中类似(例如:rh.2、rh.13或cy.5)。分离株hu.48和rh.48显示,在肌肉中,随着回复的单现突变数目的增加,表达也增加。

[0197] 其他克隆,如rh.64和laav6,显示了特定的表达特征。以分离株hu.48R2为例,其包装效率比hu.48R3大约低10倍它的,但后者转导肌肉的效率大约低5倍。AAV6包含两个单现突变。它们对于包装都具有中等强度的作用,它们的组合使AAV6包装达到了基准水平。体外,亲代克隆和各不同克隆之间差别小得几乎难以察觉。体内,在肌肉中,AAV6.1和AAV6.1.2减弱基因转移,而AAV6.2则中等强度地增强转移。

[0198] 实施例5—在肺和肝中单现突变一校正的AAV的评定

[0199] 在肺和肝中进一步评定了就包装和基因转移效率通过单现突变残基回复突变而优化的AAV载体。给出了不含单现突变载体和单现突变残基被回复为保守氨基酸的载体的数据。

[0200] A. 气管内注射之后,pi2、rh32.33、AAV2/9、AAV2/5、rh.2R、ch5R介导的CB.A1AT AAV基因的肺转移鉴定

[0201] 比较了数种AAV衣壳进入目标即肺的能力。测定了血清中CB.A1AT的水平。接受评定的AAV无单现突变(pi2、rh32.33、AAV2/9、AAV2/5、rh.2R、ch5R)或包含一个单现突变(rh.2、rh.8)。AAV2/5和AAV2/9被作为基准。

[0202] 使用携带有包含在上述衣壳中的CB.A1AT表达盒(即:AAV25' ITR、鸡 β -肌动蛋白启动子(CB)、人 α 1-抗胰蛋白酶(A1AT)、AAV23' ITR)或CB.nLacZ表达盒(即:AAV25' ITR、核定位 β -半乳糖苷酶(nLacZ)、AAV23' ITR)的载体在C57B/6小鼠(雄性、每组5只)中进行基因转移研究。简短地说,将50 μ L的单现突变一校正的或无单现突变的载体与携带A1AT的载体和携带nLacZ(1×10^{11} GC)的载体进行气管内共灌输(1×10^{11} 基因组拷贝(GC))。

[0203] 在第12天和第20天,采集了20份血液,并测定了A1AT的血清浓度水平(ngAAT/mL血清)。数据显示:在 1×10^{11} GC气管内(IT)注射之后,rh.2到rh.2R在肺中使人 α 1-抗胰蛋白酶的表达显著增加。另外,还鉴定了一批无单现突变残基的AAV载体。全部载体显示了在肺中可接受的表达水平。

[0204] B. 与AAV2/5和AAV2/9相比,AAV6单现突变载体的评定

[0205] 评定单现突变校正克隆AAV6。使用本发明的单现突变校正法和本文所描述的假型包装技术来制备修正AAV6(AAV6.2)。如实施例5所述制备携带A1AT和LacZ表达盒的AAV6.2颗粒,同时鼻内(1×10^{11} GC)和气管内感染。用ELISA评定血清和支气管肺泡液(BAL)中的AAT表达。根据总蛋白的表达水平进行归一。用ELISA检测肺组织匀浆中的 β -半乳糖苷酶来测定LacZ表达。在第21天进行尸检。

[0206] 在采用C57B1/6小鼠(雄性,n=8/组)的研究中将这载体与AAV2/6、AAV2/5和AAV2/9相比较,所述AAV2/6是目前肺基因转移的临床候选载体。

[0207] 在血清A1AT分泌方面,AAV6.2与AAV6相比存在统计上的显著改善。AAV6.2与其他载体(包括AAV2/9和AAV2/5)相比,还显示了较高的A1AT水平。在BAL中,略有改善,肺组织匀浆中的LacZ表达亦是如此。然而,由于动物与动物间差异巨大,所以从LacZ定量中得不出结论。

[0208] 当测定AAV基因表达的定位时,与AAV2/6相比,观察到在AAV2/6.2组中,核定位LacZ着色较深。在囊肿性纤维化等疾病的主要目标肺气管上皮中,观察到了与AAV2/6和AAV2/5相比明显的改进。

[0209] C. 用分化体B和分化体C的AAV成员在C57B1/6小鼠中进行AAV.CB.A1AT(1×10^{11} GC)的静脉内(iv)注射

[0210] 所用的全部载体都不含来自分离物(AAV2/8、AAV2.hu.13、hu.51、hu.11、hu.53)或通过突变(hu.29R)形成的单现突变残基。将全部载体与作为基准的AAV2/8(分化体E)相比较。

[0211] D. 分化体E的AVV成员静脉注射。成员rh.64R1、rh.64R2、rh.2R的是单现突变优化的。其他载体都是无单现突变的。

[0212] 发现,AAV分化体B和C的成员,包括单现突变优化克隆hu.29R,它们的表达彼此近似至相当。hu.29R由hu.29重构而成,回复了其包装能力,现在,其表现出与该病毒家族其他成员近似的基因转移功能。

[0213] 就接受测定的分化体E载体而言,不论是天然无单现突变载体还是经单现突变校正的载体,表现都与目前肝定向基因转移的最佳载体AAV2/8近似。尤其值得注意的是AAV

rh64R1和rh.64R2。rh.64曾被认为有包装缺陷,但现在,在一个(rh.64R1)或两个(rh.64R2)单现突变转变之后,其肝定向基因转移同样良好。就rh.2而言,对单现突变校正相对应的是基因运送效率超过10倍的显著提高。

[0214] 本说明书中引用的所有出版物,包括专利都在此处引用作为参考。尽管参考特别优选的实施方式描述了本发明,但应该理解的是可作出改进而不脱离本发明的精神。

<110> 宾夕法尼亚州立大学托管会
 <120> 增强腺相关病毒载体功能的方法
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 <150> US 60/733,497
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[0001]

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[0006]

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Gly Tyr Lys Tyr Leu Gly Pro Phe Asn Gly Leu Asp Lys Gly Glu Pro
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Val Asn Ala Ala Asp Ala Ala Ala Leu Glu His Asp Lys Ala Tyr Asp
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Gln Gln Leu Lys Ala Gly Asp Asn Pro Tyr Leu Arg Tyr Asn His Ala
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Asp Ala Glu Phe Gln Glu Arg Leu Gln Glu Asp Thr Ser Phe Gly Gly
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Asn Leu Gly Arg Ala Val Phe Gln Ala Lys Lys Arg Val Leu Glu Pro
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Thr Gly Asp Ser Glu Ser Val Pro Asp Pro Gln Pro Ile Gly Glu Pro
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Pro Ala Gly Pro Ser Gly Leu Gly Ser Gly Thr Met Ala Ala Gly Gly
195 200 205

Gly Ala Pro Met Ala Asp Asn Asn Glu Gly Ala Asp Gly Val Gly Ser
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Ser Ser Gly Asn Trp His Cys Asp Ser Thr Trp Leu Gly Asp Arg Val
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Ile Thr Thr Ser Thr Arg Thr Trp Ala Leu Pro Thr Tyr Asn Asn His
245 250 255

Leu Tyr Lys Gln Ile Ser Asn Gly Thr Ser Gly Gly Ser Thr Asn Asp

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	Asn Thr Tyr Phe Gly Tyr Ser Thr Pro Trp Gly Tyr Phe Asp Phe Asn 275	280	285
	Arg Phe His Cys His Phe Ser Pro Arg Asp Trp Gln Arg Leu Ile Asn 290	295	300
	Asn Asn Trp Gly Phe Arg Pro Lys Arg Leu Ser Phe Lys Leu Phe Asn 305	310	315 320
	Ile Gln Val Lys Glu Val Thr Gln Asn Glu Gly Thr Lys Thr Ile Ala 325	330	335
	Asn Asn Leu Thr Ser Thr Ile Gln Val Phe Thr Asp Ser Glu Tyr Gln 340	345	350
	Leu Pro Tyr Val Leu Gly Ser Ala His Gln Gly Cys Leu Pro Pro Phe 355	360	365
	Pro Ala Asp Val Phe Met Ile Pro Gln Tyr Gly Tyr Leu Thr Leu Asn 370	375	380
	Asn Gly Ser Gln Ala Val Gly Arg Ser Ser Phe Tyr Cys Leu Glu Tyr 385	390	395 400
[0008]	Phe Pro Ser Gln Met Leu Arg Thr Gly Asn Asn Phe Glu Phe Ser Tyr 405	410	415
	Thr Phe Glu Asp Val Pro Phe His Ser Ser Tyr Ala His Ser Gln Ser 420	425	430
	Leu Asp Arg Leu Met Asn Pro Leu Ile Asp Gln Tyr Leu Tyr Tyr Leu 435	440	445
	Ser Arg Thr Gln Ser Thr Gly Gly Thr Gln Gly Thr Gln Gln Leu Leu 450	455	460
	Phe Ser Gln Ala Gly Pro Ala Asn Met Ser Ala Gln Ala Lys Asn Trp 465	470	475 480
	Leu Pro Gly Pro Cys Tyr Arg Gln Gln Arg Val Ser Thr Thr Leu Ser 485	490	495
	Gln Asn Asn Asn Ser Asn Phe Ala Trp Thr Gly Ala Thr Lys Tyr His 500	505	510
	Leu Asn Gly Arg Asp Ser Leu Val Asn Pro Gly Val Ala Met Ala Thr 515	520	525
	His Lys Asp Asp Glu Glu Arg Phe Phe Pro Ser Ser Gly Val Leu Met		

530	535	540
Phe Gly Lys Gln Gly Ala Gly Arg Asp Asn Val Asp Tyr Ser Ser Val		
545	550	555 560
Met Leu Thr Ser Glu Glu Glu Ile Lys Thr Thr Asn Pro Val Ala Thr		
	565	570 575
Glu Gln Tyr Gly Val Val Ala Asp Asn Leu Gln Gln Thr Asn Thr Gly		
	580	585 590
Pro Ile Val Gly Asn Val Asn Ser Gln Gly Ala Leu Pro Gly Met Val		
	595	600 605
Trp Gln Asn Arg Asp Val Tyr Leu Gln Gly Pro Ile Trp Ala Lys Ile		
	610	615 620
Pro His Thr Asp Gly Asn Phe His Pro Ser Pro Leu Met Gly Gly Phe		
	625	630 635 640
Gly Leu Lys His Pro Pro Pro Gln Ile Leu Ile Lys Asn Thr Pro Val		
	645	650 655
Pro Ala Asp Pro Pro Thr Thr Phe Ser Gln Ala Lys Leu Ala Ser Phe		
	660	665 670
Ile Thr Gln Tyr Ser Thr Gly Gln Val Ser Val Glu Ile Glu Trp Glu		
	675	680 685
Leu Gln Lys Glu Asn Ser Lys Arg Trp Asn Pro Glu Ile Gln Tyr Thr		
	690	695 700
Ser Asn Tyr Tyr Lys Ser Thr Asn Val Asp Phe Ala Val Asn Thr Glu		
	705	710 715 720
Gly Thr Tyr Ser Glu Pro Arg Pro Ile Gly Thr Arg Tyr Leu Thr Arg		
	725	730 735

Asn Leu

<210> 4
 <211> 738
 <212> PRT
 <213> 猕猴腺相关病毒克隆 46衣壳蛋白
 <400> 4

Met Ala Ala Asp Gly Tyr Leu Pro Asp Trp Leu Glu Asp Asn Leu Ser
1 5 10 15

Glu Gly Ile Arg Glu Trp Trp Asp Leu Lys Pro Gly Ala Pro Lys Pro
20 25 30

	Lys	Ala	Asn	Gln	Gln	Lys	Gln	Asp	Asp	Gly	Arg	Gly	Leu	Val	Leu	Pro	
		35						40					45				
	Gly	Tyr	Lys	Tyr	Leu	Gly	Pro	Phe	Asn	Gly	Leu	Asp	Lys	Gly	Glu	Pro	
		50					55					60					
	Val	Asn	Ala	Ala	Asp	Ala	Ala	Ala	Leu	Glu	His	Asp	Lys	Ala	Tyr	Asp	
	65				70						75					80	
	Gln	Gln	Leu	Lys	Ala	Gly	Asp	Asn	Pro	Tyr	Leu	Arg	Tyr	Asn	His	Ala	
				85						90					95		
	Asp	Ala	Glu	Phe	Gln	Glu	Arg	Leu	Gln	Glu	Asp	Thr	Ser	Phe	Gly	Gly	
				100					105						110		
	Asn	Leu	Gly	Arg	Ala	Val	Phe	Gln	Ala	Lys	Lys	Arg	Val	Leu	Glu	Pro	
		115						120					125				
	Leu	Gly	Leu	Val	Glu	Glu	Gly	Ala	Lys	Thr	Ala	Pro	Gly	Lys	Lys	Arg	
		130					135					140					
	Pro	Val	Glu	Pro	Ser	Pro	Gln	Arg	Ser	Pro	Asp	Ser	Ser	Thr	Gly	Ile	
	145				150						155					160	
[0010]	Gly	Lys	Lys	Gly	Gln	Gln	Pro	Ala	Arg	Lys	Arg	Leu	Asn	Phe	Gly	Gln	
					165					170					175		
	Thr	Gly	Asp	Ser	Glu	Ser	Val	Pro	Asp	Pro	Gln	Pro	Ile	Gly	Glu	Pro	
			180						185					190			
	Pro	Ala	Ala	Pro	Ser	Ser	Val	Gly	Ser	Gly	Thr	Met	Ala	Ala	Gly	Gly	
			195					200					205				
	Gly	Ala	Pro	Met	Ala	Asp	Asn	Asn	Glu	Gly	Ala	Asp	Gly	Val	Gly	Ser	
		210					215					220					
	Ser	Ser	Gly	Asn	Trp	His	Cys	Asp	Ser	Thr	Trp	Leu	Gly	Asp	Arg	Val	
	225				230						235					240	
	Ile	Thr	Thr	Ser	Thr	Arg	Thr	Trp	Ala	Leu	Pro	Thr	Tyr	Asn	Asn	His	
					245					250					255		
	Leu	Tyr	Lys	Gln	Ile	Ser	Asn	Gly	Thr	Ser	Gly	Gly	Ser	Thr	Asn	Asp	
				260					265					270			
	Asn	Thr	Tyr	Phe	Gly	Tyr	Ser	Thr	Pro	Trp	Gly	Tyr	Phe	Asp	Phe	Asn	
		275						280					285				
	Arg	Phe	His	Cys	His	Phe	Ser	Pro	Arg	Asp	Trp	Gln	Arg	Leu	Ile	Asn	
		290					295					300					

	Asn	Asn	Trp	Gly	Phe	Arg	Pro	Lys	Arg	Leu	Ser	Phe	Lys	Leu	Phe	Asn
	305					310					315					320
	Ile	Gln	Val	Lys	Glu	Val	Thr	Gln	Asn	Glu	Gly	Thr	Lys	Thr	Ile	Ala
					325					330					335	
	Asn	Asn	Leu	Thr	Ser	Thr	Ile	Gln	Val	Phe	Thr	Asp	Ser	Glu	Tyr	Gln
				340					345					350		
	Leu	Pro	Tyr	Val	Leu	Gly	Ser	Ala	His	Gln	Gly	Cys	Leu	Pro	Pro	Phe
			355					360					365			
	Pro	Ala	Asp	Val	Phe	Met	Ile	Pro	Gln	Tyr	Gly	Tyr	Leu	Thr	Leu	Asn
		370					375					380				
	Asn	Gly	Ser	Gln	Ala	Val	Gly	Arg	Ser	Ser	Phe	Tyr	Cys	Leu	Glu	Tyr
	385					390					395					400
	Phe	Pro	Ser	Gln	Met	Leu	Arg	Thr	Gly	Asn	Asn	Phe	Ser	Phe	Ser	Tyr
					405					410					415	
	Thr	Phe	Glu	Asp	Val	Pro	Phe	His	Ser	Ser	Tyr	Ala	His	Ser	Gln	Ser
				420					425					430		
[0011]	Leu	Asp	Arg	Leu	Met	Asn	Pro	Leu	Ile	Asp	Gln	Tyr	Leu	Tyr	Tyr	Leu
			435					440					445			
	Ser	Arg	Thr	Gln	Ser	Thr	Gly	Gly	Thr	Ala	Gly	Thr	Gln	Gln	Leu	Leu
		450					455					460				
	Phe	Ser	Gln	Ala	Gly	Pro	Ser	Asn	Met	Ser	Ala	Gln	Ala	Arg	Asn	Trp
	465					470					475					480
	Leu	Pro	Gly	Pro	Cys	Tyr	Arg	Gln	Gln	Arg	Val	Ser	Thr	Thr	Leu	Ser
					485					490					495	
	Gln	Asn	Asn	Asn	Ser	Asn	Phe	Ala	Trp	Thr	Gly	Ala	Thr	Lys	Tyr	His
				500					505					510		
	Leu	Asn	Gly	Arg	Asp	Ser	Leu	Val	Asn	Pro	Gly	Val	Ala	Met	Ala	Thr
			515					520					525			
	Asn	Lys	Asp	Asp	Glu	Asp	Arg	Phe	Phe	Pro	Ser	Ser	Gly	Ile	Leu	Met
		530					535					540				
	Phe	Gly	Lys	Gln	Gly	Ala	Gly	Lys	Asp	Asn	Val	Asp	Tyr	Ser	Asn	Val
	545					550				555						560
	Met	Leu	Thr	Ser	Glu	Glu	Glu	Ile	Lys	Ala	Thr	Asn	Pro	Val	Ala	Thr
					565					570					575	

Glu Gln Tyr Gly Val Val Ala Asp Asn Leu Gln Gln Gln Asn Thr Ala
580 585 590

Pro Ile Val Gly Ala Val Asn Ser Gln Gly Ala Leu Pro Gly Met Val
595 600 605

Trp Gln Asn Arg Asp Val Tyr Leu Gln Gly Pro Ile Trp Ala Lys Ile
610 615 620

Pro His Thr Asp Gly Asn Phe His Pro Ser Pro Leu Met Gly Gly Phe
625 630 635 640

Gly Leu Lys His Pro Pro Pro Gln Ile Leu Ile Lys Asn Thr Pro Val
645 650 655

Pro Ala Asp Pro Pro Thr Ala Phe Asn Gln Ala Lys Leu Asn Ser Phe
660 665 670

Ile Thr Gln Tyr Ser Thr Gly Gln Val Ser Val Glu Ile Glu Trp Glu
675 680 685

Leu Gln Lys Glu Asn Ser Lys Arg Trp Asn Pro Glu Ile Gln Tyr Thr
690 695 700

[0012] Ser Asn Tyr Tyr Lys Ser Thr Asn Val Asp Phe Ala Val Asn Thr Glu
705 710 715 720

Gly Val Tyr Ser Glu Pro Arg Pro Ile Gly Thr Arg Tyr Leu Thr Arg
725 730 735

Asn Leu

<210> 5

<211> 738

<212> PRT

<213> 猕猴腺相关病毒克隆 73 衣壳

<400> 5

Met Ala Ala Asp Gly Tyr Leu Pro Asp Trp Leu Glu Asp Asn Leu Ser
1 5 10 15

Glu Gly Ile Arg Glu Trp Trp Asp Leu Lys Pro Gly Ala Pro Lys Pro
20 25 30

Lys Ala Asn Gln Gln Lys Gln Asp Asp Gly Arg Gly Leu Val Leu Pro
35 40 45

Gly Tyr Lys Tyr Leu Gly Pro Phe Asn Gly Leu Asp Lys Gly Glu Pro
50 55 60

	Val	Asn	Ala	Ala	Asp	Ala	Ala	Ala	Leu	Glu	His	Asp	Lys	Ala	Tyr	Asp
	65					70					75					80
	Gln	Gln	Leu	Lys	Ala	Gly	Asp	Asn	Pro	Tyr	Leu	Arg	Tyr	Asn	His	Ala
				85						90					95	
	Asp	Ala	Glu	Phe	Gln	Glu	Arg	Leu	Gln	Glu	Asp	Thr	Ser	Phe	Gly	Gly
				100					105						110	
	Asn	Leu	Gly	Arg	Ala	Val	Phe	Gln	Ala	Lys	Lys	Arg	Val	Leu	Glu	Pro
			115					120					125			
	Leu	Gly	Leu	Val	Glu	Glu	Gly	Ala	Lys	Thr	Ala	Pro	Gly	Lys	Lys	Arg
		130					135					140				
	Pro	Val	Glu	Pro	Ser	Pro	Gln	Arg	Ser	Pro	Asp	Ser	Ser	Thr	Gly	Ile
	145					150					155					160
	Gly	Lys	Lys	Gly	Gln	Gln	Pro	Ala	Arg	Lys	Arg	Leu	Asn	Phe	Gly	Gln
				165						170					175	
	Thr	Gly	Asp	Ser	Glu	Ser	Val	Pro	Asp	Pro	Gln	Pro	Leu	Gly	Glu	Pro
				180					185						190	
[0013]	Pro	Ala	Ala	Pro	Ser	Ser	Val	Gly	Ser	Gly	Thr	Met	Ala	Ala	Gly	Gly
			195					200					205			
	Gly	Ala	Pro	Met	Ala	Asp	Asn	Asn	Glu	Gly	Ala	Asp	Gly	Val	Gly	Ser
		210					215					220				
	Ser	Ser	Gly	Asn	Trp	His	Cys	Asp	Ser	Thr	Trp	Leu	Gly	Asp	Arg	Val
	225					230					235					240
	Ile	Thr	Thr	Ser	Thr	Arg	Thr	Trp	Ala	Leu	Pro	Thr	Tyr	Asn	Asn	His
				245						250					255	
	Leu	Tyr	Lys	Gln	Ile	Ser	Asn	Gly	Thr	Ser	Gly	Gly	Ser	Thr	Asn	Asp
			260					265						270		
	Asn	Thr	Tyr	Phe	Gly	Tyr	Ser	Thr	Pro	Trp	Gly	Tyr	Phe	Asp	Phe	Asn
		275						280					285			
	Arg	Phe	His	Cys	His	Phe	Ser	Pro	Arg	Asp	Trp	Gln	Arg	Leu	Ile	Asn
		290					295					300				
	Asn	Asn	Trp	Gly	Phe	Arg	Pro	Lys	Arg	Leu	Ser	Phe	Lys	Leu	Phe	Asn
	305					310					315					320
	Ile	Gln	Val	Lys	Glu	Val	Thr	Gln	Asn	Glu	Gly	Thr	Lys	Thr	Ile	Ala
				325						330					335	

	Asn	Asn	Leu	Thr	Ser	Thr	Ile	Gln	Val	Phe	Thr	Asp	Ser	Glu	Tyr	Gln	
			340						345					350			
	Leu	Pro	Tyr	Val	Leu	Gly	Ser	Ala	His	Gln	Gly	Cys	Leu	Pro	Pro	Phe	
			355					360					365				
	Pro	Ala	Asp	Val	Phe	Met	Ile	Pro	Gln	Tyr	Gly	Tyr	Leu	Thr	Leu	Asn	
		370					375					380					
	Asn	Gly	Ser	Gln	Ala	Val	Gly	Arg	Ser	Ser	Phe	Tyr	Cys	Leu	Glu	Tyr	
	385					390					395					400	
	Phe	Pro	Ser	Gln	Met	Leu	Arg	Thr	Gly	Asn	Asn	Phe	Ser	Phe	Ser	Tyr	
					405					410					415		
	Thr	Phe	Glu	Asp	Val	Pro	Phe	His	Ser	Ser	Tyr	Ala	His	Ser	Gln	Ser	
			420						425					430			
	Leu	Asp	Arg	Leu	Met	Asn	Pro	Leu	Ile	Asp	Gln	Tyr	Leu	Tyr	Tyr	Leu	
		435						440					445				
	Ser	Arg	Thr	Gln	Ser	Thr	Gly	Gly	Thr	Ala	Gly	Thr	Gln	Gln	Leu	Leu	
		450					455					460					
[0014]	Phe	Ser	Gln	Ala	Gly	Pro	Ser	Asn	Met	Ser	Ala	Gln	Ala	Arg	Asn	Trp	
	465					470					475				480		
	Leu	Pro	Gly	Pro	Cys	Tyr	Arg	Gln	Gln	Arg	Val	Ser	Thr	Thr	Leu	Ser	
					485					490					495		
	Gln	Asn	Asn	Asn	Ser	Asn	Phe	Ala	Trp	Thr	Gly	Ala	Thr	Lys	Tyr	His	
				500					505					510			
	Leu	Asn	Gly	Arg	Asp	Ser	Leu	Val	Asn	Pro	Gly	Val	Ala	Met	Ala	Thr	
		515						520					525				
	Asn	Lys	Asp	Asp	Glu	Asp	Arg	Phe	Phe	Pro	Ser	Ser	Gly	Ile	Leu	Met	
		530					535					540					
	Phe	Gly	Lys	Gln	Gly	Ala	Gly	Lys	Asp	Asn	Val	Asp	Tyr	Ser	Asn	Val	
	545					550					555					560	
	Met	Leu	Thr	Ser	Glu	Glu	Glu	Ile	Lys	Thr	Thr	Asn	Pro	Val	Ala	Thr	
				565						570					575		
	Glu	Gln	Tyr	Gly	Val	Val	Ala	Asp	Asn	Leu	Gln	Arg	Gln	Asn	Thr	Ala	
				580					585					590			
	Pro	Ile	Val	Gly	Ala	Val	Asn	Ser	Gln	Gly	Ala	Leu	Pro	Gly	Met	Val	
			595					600					605				

Trp Gln Asn Arg Asp Val Tyr Leu Gln Gly Pro Ile Trp Ala Lys Ile
610 615 620

Pro His Thr Asp Gly Asn Phe His Pro Ser Pro Leu Met Gly Gly Phe
625 630 635 640

Gly Leu Lys His Pro Pro Pro Gln Ile Leu Ile Lys Asn Thr Pro Val
645 650 655

Pro Ala Asp Pro Pro Thr Ala Phe Asn Gln Ala Lys Leu Asn Ser Phe
660 665 670

Ile Thr Gln Tyr Ser Thr Gly Gln Val Ser Val Glu Ile Glu Trp Glu
675 680 685

Leu Gln Lys Glu Asn Ser Lys Arg Trp Asn Pro Glu Ile Gln Tyr Thr
690 695 700

Ser Asn Tyr Tyr Lys Ser Thr Asn Val Asp Phe Ala Val Asn Thr Glu
705 710 715 720

Gly Val Tyr Ser Glu Pro Arg Pro Ile Gly Thr Arg Tyr Leu Thr Arg
725 730 735

[0015] Asn Leu

<210> 6

<211> 736

<212> PRT

<213> 猕猴腺相关病毒克隆 74 衣壳

<400> 6

Met Ala Ala Asp Gly Tyr Leu Pro Asp Trp Leu Glu Asp Asn Leu Ser
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Glu Gly Ile Arg Glu Trp Leu Asn Leu Lys Pro Gly Ala Pro Gln Pro
20 25 30

Lys Ala Asn Gln Gln Lys Gln Asp Asn Ala Arg Gly Leu Val Leu Pro
35 40 45

Gly Tyr Lys Tyr Leu Gly Pro Phe Asn Gly Leu Asp Lys Gly Asp Pro
50 55 60

Val Asn Glu Ala Asp Ala Ala Ala Leu Glu His Asp Lys Ala Tyr Gly
65 70 75 80

Gln Gln Leu Lys Ala Gly Asp Asn Pro Tyr Leu Lys Tyr Asn His Ala
85 90 95

	Asp	Ala	Glu	Phe	Gln	Glu	Arg	Leu	Gln	Lys	Asp	Thr	Ser	Phe	Gly	Gly	
				100					105							110	
	Asn	Leu	Gly	Lys	Ala	Val	Phe	Gln	Ala	Lys	Lys	Arg	Ile	Leu	Glu	Pro	
			115					120					125				
	Leu	Gly	Leu	Val	Glu	Thr	Pro	Ala	Lys	Thr	Ala	Pro	Gly	Lys	Lys	Arg	
		130					135					140					
	Pro	Val	Asp	Pro	Ser	Pro	Gln	Arg	Ser	Pro	Asp	Ser	Ser	Ser	Gly	Ile	
	145					150					155					160	
	Gly	Lys	Lys	Ser	Pro	His	Pro	Ala	Arg	Lys	Arg	Leu	Asn	Phe	Gly	Gln	
					165					170					175		
	Thr	Gly	Glu	Ala	Glu	Ser	Val	Pro	Asp	Pro	Gln	Pro	Ile	Gly	Glu	Pro	
				180					185					190			
	Pro	Ser	Asp	Pro	Ser	Ser	Val	Gly	Ser	Gly	Thr	Met	Ala	Ala	Gly	Gly	
			195					200					205				
	Gly	Ala	Pro	Met	Ala	Asp	Asn	Asn	Glu	Gly	Ala	Asp	Gly	Val	Gly	Asn	
		210					215					220					
[0016]	Ser	Ser	Gly	Asn	Trp	His	Cys	Asp	Ser	Thr	Trp	Leu	Gly	Asp	Arg	Val	
	225					230					235					240	
	Ile	Thr	Thr	Ser	Thr	Arg	Thr	Trp	Ala	Leu	Pro	Thr	Tyr	Asn	Asn	His	
					245					250				255			
	Leu	Tyr	Lys	Gln	Ile	Ser	Ser	Gln	Ser	Gly	Ala	Thr	Asn	Asp	Asn	His	
				260					265					270			
	Tyr	Phe	Gly	Tyr	Ser	Thr	Pro	Trp	Gly	Tyr	Phe	Asp	Phe	Asn	Arg	Phe	
			275					280					285				
	His	Cys	His	Phe	Ser	Pro	Arg	Asp	Trp	Gln	Arg	Leu	Ile	Asn	Asn	Asn	
		290					295					300					
	Trp	Gly	Phe	Arg	Pro	Lys	Arg	Leu	Ser	Phe	Lys	Leu	Phe	Asn	Ile	Gln	
	305					310					315					320	
	Val	Lys	Glu	Val	Thr	Gln	Asn	Asp	Gly	Thr	Thr	Thr	Ile	Ala	Asn	Asn	
					325					330					335		
	Leu	Thr	Ser	Thr	Val	Gln	Val	Phe	Thr	Asp	Ser	Glu	Tyr	Gln	Leu	Pro	
					340				345					350			
	Tyr	Val	Leu	Gly	Ser	Ala	His	Gln	Gly	Cys	Leu	Pro	Pro	Phe	Pro	Ala	
			355					360					365				

Asp Val Phe Met Ile Pro Gln Tyr Gly Tyr Leu Thr Leu Asn Asn Gly
 370 375 380
 Ser Gln Ala Val Gly Arg Ser Ser Phe Tyr Cys Leu Glu Tyr Phe Pro
 385 390 395 400
 Ser Gln Met Leu Arg Thr Gly Asn Asn Phe Gln Phe Ser Tyr Thr Phe
 405 410 415
 Glu Asp Val Pro Phe His Ser Ser Tyr Ala His Ser Gln Ser Leu Asp
 420 425 430
 Arg Leu Met Asn Pro Leu Ile Asp Gln Tyr Leu Tyr Tyr Leu Ser Lys
 435 440 445
 Thr Gln Gly Thr Asn Ala Thr Val Gln Gly Ala Lys Leu Gln Phe Ser
 450 455 460
 Gln Ala Gly Pro Ser Asn Met Arg Asp Gln Ala Arg Asn Trp Leu Pro
 465 470 475 480
 Gly Pro Cys Tyr Arg Gln Gln Arg Val Ser Lys Thr Ala Asn Asp Asn
 485 490 495
 [0017] Asn Asn Ser Glu Tyr Ala Trp Thr Gly Ala Thr Lys Tyr His Leu Asn
 500 505 510
 Gly Arg Asp Ser Leu Val Asn Pro Gly Pro Ala Met Ala Ser His Lys
 515 520 525
 Asp Asp Glu Glu Lys Phe Phe Pro Met Asn Gly Thr Leu Val Phe Gly
 530 535 540
 Lys Asn Gly Ala Gly Asn Ser Asn Val Asp Ile Glu Asn Val Met Ile
 545 550 555 560
 Thr Asp Glu Glu Glu Ile Arg Thr Thr Asn Pro Val Ala Thr Glu Gln
 565 570 575
 Tyr Gly Val Val Ser Asp Asn Leu Gln Ser Ser Asn Thr Arg Pro Ile
 580 585 590
 Thr Gly Asp Val Asp Ser Gln Gly Val Leu Pro Gly Met Val Trp Gln
 595 600 605
 Asp Arg Asp Val Tyr Leu Gln Gly Pro Ile Trp Ala Lys Ile Pro His
 610 615 620
 Thr Asp Gly His Phe His Pro Ser Pro Leu Met Gly Gly Phe Gly Leu
 625 630 635 640

Lys His Pro Pro Pro Gln Ile Leu Ile Lys Asn Thr Pro Val Pro Ala
645 650 655

Asn Pro Ala Thr Thr Phe Thr Pro Gly Lys Phe Ala Ser Phe Ile Thr
660 665 670

Gln Tyr Ser Thr Gly Gln Val Ser Val Gln Ile Glu Trp Glu Leu Gln
675 680 685

Lys Glu Asn Ser Lys Arg Trp Asn Pro Glu Ile Gln Tyr Thr Ser Asn
690 695 700

Tyr Asn Lys Ser Val Asn Val Asp Phe Thr Val Asp Thr Asn Gly Val
705 710 715 720

Tyr Ser Glu Pro Arg Pro Ile Gly Thr Arg Tyr Leu Thr Arg Asn Leu
725 730 735

<210> 7

<211> 2208

<212> DNA

<213> 腺相关病毒 血清型2

<400> 7

[0018]

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atggetgecg atggttatet tccagattgg ctcgaggaca ctctctctga aggaataaga      60
cagtgggtgga agctcaaacc tggcccacca ccaccaaaage ccgcagagcg gcataaggac      120
gacagcagggg gtcttgtgtct tectgggtac aagtaccteg gaccttcaa cggactcgac      180
aaggagagagc cggtaacga ggcagagccg geggcctcg agcacgacaa agcctacgac      240
cggcagctcg acageggaga caacccttac ctcaagtaca accacgcga cgcggagttt      300
caggagcgcc ttaaagaaga tacgtctttt gggggcaacc tcggacgagc agtcttcag      360
gcgaaaaaga gggttcttga acctctgggc ctggttgagg aacctgttaa gacggctccg      420
ggaaaaaaga ggccggtaga gcactctctt gtggagccag actcctctc gggaaccgga      480
aaggcgggcc agcagcctgc aagaaaaaga ttgaattttg gtcagactgg agacgcagac      540
tcagtacctg acccccagcc tctcgacag ccaccagcag cccctctgg tctgggaact      600
aatacgatgg ctacaggcag tggcgacca atggcagaca ataacgagg cgccgacgga      660
gtgggtaatt cctcgggaaa ttggcattgc gattccacat ggatgggca cagagtcac      720
accaccagca cccgaacctg ggccctgccc acctacaaca accaccteta caaacaatt      780
tecagccaat caggagcctc gaacgacaat cactactttg gtacagcac ccttggggg      840
tattttgact tcaacagatt ccactgcac ttttcaccac gtgactggca aagactcac      900
aacaacaact ggggattccg acccaagaga ctcaacttca agctctttaa cattcaagtc      960
aaagaggtea cgcagaatga cggtagcag acgattgcca ataacctac cagcacggtt     1020
cagggttita ctgactegga gtaccagct cgtacgtcc tcggtctegge gcataagga     1080
tgctctccgc cgttccagc agacgtcttc atggtgccac agtatggata cctcaccctg     1140

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	cagatgctgc gtaccggaaa caactttacc ttcagetaca ettttgagga cgttccttct	1260
	cacagcagct acgtcacag ccagagctcg gaccgtctca tgaatcctct cctcgaccag	1320
	tacctgtatt acttgagcag aacaaacact ccaagtggaa ccaccacgca gtcaaggett	1380
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[0033]

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tccaaactaca acaaatctgt taatgtggac tttactgtgg acactaatgg tgtgtattca 2160
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 <211> 2217
 <212> DNA
 <213> 猕猴腺相关病毒, rh. 39

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gacggccggg gtctgggtgt tctgggtac aagtacctcg gaccttcaa cggactcgac 180

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	caggagcgtc tgcaagaaga tacgtctttt gggggcaacc tgggcgagc agtcttcag	360
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	atatccaatg ggacatcgga aggaagcacc aacgacaaca cctacttcgg ctacagcacc	840
	ccctgggggt attttgactt caacagattc caetgccact tctcaccag tgaetggcag	900
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	agcagattc aggtatttac ggaactggaa taccagctgc cgtacgtctt cggctccgcg	1080
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	ccaacaacgt tcagccagc gaaattggct tcttcatta cgcagtacag caccggacag	2040
	gtcagcgttg aaatcgagt ggagctgcag aaggagaaca gcaaacgtg gaaccagag	2100
	attcagtaca cttcaaaact ctacaaatct acaaatgtgg actttgtgt caatacagag	2160
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	<213>	猕猴腺相关病毒, rh. 43	
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	gacggccggg gcctgggtgt tcttggtac aagtacctcg gaccttcaa cggactcgac	180	
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	caggagcgtc tgcaagaaga tacgtctttt gggggcaacc tcgggcgagc agtcttccag	360	
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	aagaaaggcc aacagccgc cagaaaaaga ctcaattttg gccagactgg cgactcagag	540	
	tcagttccag acctcaacc tctcgagaa cctccagcag cggcctcigg tglgggacct	600	
	aatacaatgg ctgcaggcgg tggcgacca atggcagaca ataacgaagg cgccgacgga	660	
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	ctcatcaaca acaactgggg attccggccc aagagactca gcttcaaget ctccaacatc	960	
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	accatccagg tgtttacgga ctcgagtagc cagctgcctg acgtttctcg ctctgccac	1080	
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<210> 23
 <211> 735
 <212> PRT
 <213> 腺相关病毒血清型2的衣壳蛋白

<400> 23

[0037]

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Met Ala Ala Asp Gly Tyr Leu Pro Asp Trp Leu Glu Asp Thr Leu Ser
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Glu Gly Ile Arg Gln Trp Trp Lys Leu Lys Pro Gly Pro Pro Pro Pro
20           25           30

Lys Pro Ala Glu Arg His Lys Asp Asp Ser Arg Gly Leu Val Leu Pro
35           40           45

Gly Tyr Lys Tyr Leu Gly Pro Phe Asn Gly Leu Asp Lys Gly Glu Pro
50           55           60

Val Asn Glu Ala Asp Ala Ala Ala Leu Glu His Asp Lys Ala Tyr Asp
65           70           75           80

Arg Gln Leu Asp Ser Gly Asp Asn Pro Tyr Leu Lys Tyr Asn His Ala
85           90           95

Asp Ala Glu Phe Gln Glu Arg Leu Lys Glu Asp Thr Ser Phe Gly Gly
100          105          110

Asn Leu Gly Arg Ala Val Phe Gln Ala Lys Lys Arg Val Leu Glu Pro
115          120          125

Leu Gly Leu Val Glu Glu Pro Val Lys Thr Ala Pro Gly Lys Lys Arg

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

[0038]

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

[0039]

	675	680	685
	Glu Asn Ser Lys Arg Trp	Asn Pro Glu Ile Gln Tyr Thr Ser Asn Tyr	
	690	695	700
	Asn Lys Ser Val Asn Val Asp Phe Thr Val Asp Thr Asn Gly Val Tyr		
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	Ser Glu Pro Arg Pro Ile Gly Thr Arg Tyr Leu Thr Arg Asn Leu		
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<213>	cy. 5的衣壳蛋白		
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Glu Gly Ile Arg Glu Trp Trp Asp Leu Lys Pro Gly Ala Pro Lys Pro			
	20	25	30
Lys Ala Asn Gln Gln Lys Gln Asp Asp Gly Arg Gly Leu Val Leu Pro			
	35	40	45
[0040]	Gly Tyr Arg Tyr Leu Gly Pro Phe Asn Gly Leu Asp Lys Gly Glu Pro		
	50	55	60
Val Asn Glu Ala Asp Ala Ala Ala Leu Glu His Asp Lys Ala Tyr Asp			
65	70	75	80
Lys Gln Leu Glu Gln Gly Asp Asn Pro Tyr Leu Lys Tyr Asn His Ala			
	85	90	95
Asp Ala Glu Phe Gln Glu Arg Leu Gln Glu Asp Thr Ser Phe Gly Gly			
	100	105	110
Asn Leu Gly Arg Ala Val Phe Gln Ala Lys Lys Arg Val Leu Glu Pro			
	115	120	125
Leu Gly Leu Val Glu Glu Gly Ala Lys Thr Ala Pro Gly Lys Lys Arg			
	130	135	140
Pro Ile Glu Ser Pro Asp Ser Ser Thr Gly Ile Gly Lys Asn Gly Gln			
145	150	155	160
Pro Pro Ala Lys Lys Lys Leu Asn Phe Gly Gln Thr Gly Asp Ser Glu			
	165	170	175
Ser Val Pro Asp Pro Gln Pro Leu Gly Glu Pro Pro Ala Ala Pro Ser			
	180	185	190

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

Ala Glu Gln Ser Lys Asn Trp Leu Pro Gly Pro Cys Tyr Arg Gln Gln
 465 470 475 480
 Arg Leu Ser Lys Asn Ile Asp Ser Asn Asn Asn Ser Asn Phe Ala Trp
 485 490 495
 Thr Gly Ala Thr Lys Tyr His Leu Asn Gly Arg Asn Ser Leu Thr Asn
 500 505 510
 Pro Gly Val Ala Met Ala Thr Asn Lys Asp Asp Glu Asp Gln Phe Phe
 515 520 525
 Pro Ile Asn Gly Val Leu Val Phe Gly Lys Thr Gly Ala Ala Asn Lys
 530 535 540
 Thr Thr Leu Glu Asn Val Leu Met Thr Ser Glu Glu Glu Ile Lys Thr
 545 550 555 560
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 580 585 590
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 610 615 620
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 Ile Lys Asn Thr Pro Val Pro Ala Asn Pro Pro Glu Val Phe Thr Pro
 645 650 655
 Ala Lys Phe Ala Ser Phe Ile Thr Gln Tyr Ser Thr Gly Gln Val Ser
 660 665 670
 Val Glu Ile Glu Trp Glu Leu Gln Lys Glu Asn Ser Lys Arg Trp Asn
 675 680 685
 Pro Glu Ile Gln Tyr Thr Ser Asn Tyr Ala Lys Ser Asn Asn Val Glu
 690 695 700
 Phe Ala Val Asn Asn Glu Gly Val Tyr Thr Glu Pro Arg Pro Ile Gly
 705 710 715 720
 Thr Arg Tyr Leu Thr Arg Asn Leu
 725

<210> 25
 <211> 738
 <212> PRT
 <213> 猕猴腺相关病毒, rh.10的衣壳蛋白

<400> 25

Met Ala Ala Asp Gly Tyr Leu Pro Asp Trp Leu Glu Asp Asn Leu Ser
 1 5 10 15

Glu Gly Ile Arg Glu Trp Trp Asp Leu Lys Pro Gly Ala Pro Lys Pro
 20 25 30

Lys Ala Asn Gln Gln Lys Gln Asp Asp Gly Arg Gly Leu Val Leu Pro
 35 40 45

Gly Tyr Lys Tyr Leu Gly Pro Phe Asn Gly Leu Asp Lys Gly Glu Pro
 50 55 60

Val Asn Ala Ala Asp Ala Ala Ala Leu Glu His Asp Lys Ala Tyr Asp
 65 70 75 80

Gln Gln Leu Lys Ala Gly Asp Asn Pro Tyr Leu Arg Tyr Asn His Ala
 85 90 95

[0043]

Asp Ala Glu Phe Gln Glu Arg Leu Gln Glu Asp Thr Ser Phe Gly Gly
 100 105 110

Asn Leu Gly Arg Ala Val Phe Gln Ala Lys Lys Arg Val Leu Glu Pro
 115 120 125

Leu Gly Leu Val Glu Glu Gly Ala Lys Thr Ala Pro Gly Lys Lys Arg
 130 135 140

Pro Val Glu Pro Ser Pro Gln Arg Ser Pro Asp Ser Ser Thr Gly Ile
 145 150 155 160

Gly Lys Lys Gly Gln Gln Pro Ala Lys Lys Arg Leu Asn Phe Gly Gln
 165 170 175

Thr Gly Asp Ser Glu Ser Val Pro Asp Pro Gln Pro Ile Gly Glu Pro
 180 185 190

Pro Ala Gly Pro Ser Gly Leu Gly Ser Gly Thr Met Ala Ala Gly Gly
 195 200 205

Gly Ala Pro Met Ala Asp Asn Asn Glu Gly Ala Asp Gly Val Gly Ser
 210 215 220

Ser Ser Gly Asn Trp His Cys Asp Ser Thr Trp Leu Gly Asp Arg Val
 225 230 235 240

	Ile	Thr	Thr	Ser	Thr	Arg	Thr	Trp	Ala	Leu	Pro	Thr	Tyr	Asn	Asn	His	
					245					250					255		
	Leu	Tyr	Lys	Gln	Ile	Ser	Asn	Gly	Thr	Ser	Gly	Gly	Ser	Thr	Asn	Asp	
			260						265					270			
	Asn	Thr	Tyr	Phe	Gly	Tyr	Ser	Thr	Pro	Trp	Gly	Tyr	Phe	Asp	Phe	Asn	
		275						280					285				
	Arg	Phe	His	Cys	His	Phe	Ser	Pro	Arg	Asp	Trp	Gln	Arg	Leu	Ile	Asn	
	290						295					300					
	Asn	Asn	Trp	Gly	Phe	Arg	Pro	Lys	Arg	Leu	Asn	Phe	Lys	Leu	Phe	Asn	
	305					310					315					320	
	Ile	Gln	Val	Lys	Glu	Val	Thr	Gln	Asn	Glu	Gly	Thr	Lys	Thr	Ile	Ala	
				325						330					335		
	Asn	Asn	Leu	Thr	Ser	Thr	Ile	Gln	Val	Phe	Thr	Asp	Ser	Glu	Tyr	Gln	
			340						345					350			
	Leu	Pro	Tyr	Val	Leu	Gly	Ser	Ala	His	Gln	Gly	Cys	Leu	Pro	Pro	Phe	
		355						360					365				
[0044]	Pro	Ala	Asp	Val	Phe	Met	Ile	Pro	Gln	Tyr	Gly	Tyr	Leu	Thr	Leu	Asn	
		370					375					380					
	Asn	Gly	Ser	Gln	Ala	Val	Gly	Arg	Ser	Ser	Phe	Tyr	Cys	Leu	Glu	Tyr	
	385					390					395					400	
	Phe	Pro	Ser	Gln	Met	Leu	Arg	Thr	Gly	Asn	Asn	Phe	Glu	Phe	Ser	Tyr	
				405						410					415		
	Gln	Phe	Glu	Asp	Val	Pro	Phe	His	Ser	Ser	Tyr	Ala	His	Ser	Gln	Ser	
			420					425						430			
	Leu	Asp	Arg	Leu	Met	Asn	Pro	Leu	Ile	Asp	Gln	Tyr	Leu	Tyr	Tyr	Leu	
		435					440						445				
	Ser	Arg	Thr	Gln	Ser	Thr	Gly	Gly	Thr	Ala	Gly	Thr	Gln	Gln	Leu	Leu	
		450					455					460					
	Phe	Ser	Gln	Ala	Gly	Pro	Asn	Asn	Met	Ser	Ala	Gln	Ala	Lys	Asn	Trp	
	465					470					475					480	
	Leu	Pro	Gly	Pro	Cys	Tyr	Arg	Gln	Gln	Arg	Val	Ser	Thr	Thr	Leu	Ser	
				485					490						495		
	Gln	Asn	Asn	Asn	Ser	Asn	Phe	Ala	Trp	Thr	Gly	Ala	Thr	Lys	Tyr	His	
			500						505					510			

	Leu	Asn	Gly	Arg	Asp	Ser	Leu	Val	Asn	Pro	Gly	Val	Ala	Met	Ala	Thr	
		515						520					525				
	His	Lys	Asp	Asp	Glu	Glu	Arg	Phe	Phe	Pro	Ser	Ser	Gly	Val	Leu	Met	
		530					535					540					
	Phe	Gly	Lys	Gln	Gly	Ala	Gly	Lys	Asp	Asn	Val	Asp	Tyr	Ser	Ser	Val	
	545					550					555					560	
	Met	Leu	Thr	Ser	Glu	Glu	Glu	Ile	Lys	Thr	Thr	Asn	Pro	Val	Ala	Thr	
				565						570					575		
	Glu	Gln	Tyr	Gly	Val	Val	Ala	Asp	Asn	Leu	Gln	Gln	Gln	Asn	Ala	Ala	
			580						585					590			
	Pro	Ile	Val	Gly	Ala	Val	Asn	Ser	Gln	Gly	Ala	Leu	Pro	Gly	Met	Val	
		595						600					605				
	Trp	Gln	Asn	Arg	Asp	Val	Tyr	Leu	Gln	Gly	Pro	Ile	Trp	Ala	Lys	Ile	
	610						615					620					
	Pro	His	Thr	Asp	Gly	Asn	Phe	His	Pro	Ser	Pro	Leu	Met	Gly	Gly	Phe	
	625					630					635					640	
[0045]	Gly	Leu	Lys	His	Pro	Pro	Pro	Gln	Ile	Leu	Ile	Lys	Asn	Thr	Pro	Val	
				645					650					655			
	Pro	Ala	Asp	Pro	Pro	Thr	Thr	Phe	Ser	Gln	Ala	Lys	Leu	Ala	Ser	Phe	
			660					665					670				
	Ile	Thr	Gln	Tyr	Ser	Thr	Gly	Gln	Val	Ser	Val	Glu	Ile	Glu	Trp	Glu	
		675					680					685					
	Leu	Gln	Lys	Glu	Asn	Ser	Lys	Arg	Trp	Asn	Pro	Glu	Ile	Gln	Tyr	Thr	
	690						695				700						
	Ser	Asn	Tyr	Tyr	Lys	Ser	Thr	Asn	Val	Asp	Phe	Ala	Val	Asn	Thr	Asp	
	705					710				715					720		
	Gly	Thr	Tyr	Ser	Glu	Pro	Arg	Pro	Ile	Gly	Thr	Arg	Tyr	Leu	Thr	Arg	
				725					730					735			
	Asn	Leu															
	<210>	26															
	<211>	728															
	<212>	PRT															
	<213>	猕猴腺相关病毒, rh. 13的衣壳蛋白															
	<400>	26															

Met Ala Ala Asp Gly Tyr Leu Pro Asp Trp Leu Glu Asp Asn Leu Ser
 1 5 10 15
 Glu Gly Ile Arg Glu Trp Trp Asp Leu Lys Pro Gly Ala Pro Lys Pro
 20 25 30
 Lys Ala Asn Gln Gln Lys Gln Asp Asp Gly Arg Gly Leu Val Leu Pro
 35 40 45
 Gly Tyr Lys Tyr Leu Gly Pro Phe Asn Gly Leu Asp Lys Gly Glu Pro
 50 55 60
 Val Asn Glu Ala Asp Ala Ala Ala Leu Glu His Asp Lys Ala Tyr Asp
 65 70 75 80
 Lys Gln Leu Glu Gln Gly Asp Asn Pro Tyr Leu Lys Tyr Asn His Ala
 85 90 95
 Asp Ala Glu Phe Gln Glu Arg Leu Gln Glu Asp Thr Ser Phe Gly Gly
 100 105 110
 Asn Leu Gly Arg Ala Val Phe Gln Ala Lys Lys Arg Val Leu Glu Pro
 115 120 125
 [0046] Leu Gly Leu Val Glu Glu Gly Ala Lys Thr Ala Pro Gly Lys Lys Arg
 130 135 140
 Pro Ile Glu Ser Pro Asp Ser Ser Thr Gly Ile Gly Lys Lys Gly Gln
 145 150 155 160
 Gln Pro Ala Lys Lys Lys Leu Asn Phe Gly Gln Thr Gly Asp Ser Glu
 165 170 175
 Ser Val Pro Asp Pro Gln Pro Leu Gly Glu Pro Pro Ala Ala Pro Ser
 180 185 190
 Gly Leu Gly Ser Gly Thr Met Ala Ala Gly Gly Gly Ala Pro Met Ala
 195 200 205
 Asp Asn Asn Glu Gly Ala Asp Gly Val Gly Asn Ala Ser Gly Asn Trp
 210 215 220
 His Cys Asp Ser Thr Trp Leu Gly Asp Arg Val Ile Thr Thr Ser Thr
 225 230 235 240
 Arg Thr Trp Ala Leu Pro Thr Tyr Asn Asn His Leu Tyr Lys Gln Ile
 245 250 255
 Ser Ser Gln Ser Gly Ala Thr Asn Asp Asn His Phe Phe Gly Tyr Ser
 260 265 270

Thr Pro Trp Gly Tyr Phe Asp Phe Asn Arg Phe His Cys His Phe Ser
 275 280 285
 Pro Arg Asp Trp Gln Arg Leu Ile Asn Asn Asn Trp Gly Phe Arg Pro
 290 295 300
 Arg Lys Leu Arg Phe Lys Leu Phe Asn Ile Gln Val Lys Glu Val Thr
 305 310 315 320
 Thr Asn Asp Gly Val Thr Thr Ile Ala Asn Asn Leu Thr Ser Thr Ile
 325 330 335
 Gln Val Phe Ser Asp Ser Glu Tyr Gln Leu Pro Tyr Val Leu Gly Ser
 340 345 350
 Ala His Gln Gly Cys Leu Pro Pro Phe Pro Ala Asp Val Phe Met Ile
 355 360 365
 Pro Gln Tyr Gly Tyr Leu Thr Leu Asn Asn Gly Ser Gln Ser Val Gly
 370 375 380
 Arg Ser Ser Phe Tyr Cys Leu Glu Tyr Phe Pro Ser Gln Met Leu Arg
 385 390 395 400
 [0047] Thr Gly Asn Asn Phe Glu Phe Ser Tyr Thr Phe Glu Glu Val Pro Phe
 405 410 415
 His Ser Ser Tyr Ala His Ser Gln Ser Leu Asp Arg Leu Met Asn Pro
 420 425 430
 Leu Ile Asp Gln Tyr Leu Tyr Tyr Leu Ala Arg Thr Gln Ser Thr Thr
 435 440 445
 Gly Ser Thr Arg Glu Leu Gln Phe His Gln Ala Gly Pro Asn Thr Met
 450 455 460
 Ala Glu Gln Ser Lys Asn Trp Leu Pro Gly Pro Cys Tyr Arg Gln Gln
 465 470 475 480
 Arg Leu Ser Lys Asn Ile Asp Ser Asn Asn Asn Ser Asn Phe Ala Trp
 485 490 495
 Thr Gly Ala Thr Lys Tyr His Leu Asn Gly Arg Asn Ser Leu Thr Asn
 500 505 510
 Pro Gly Val Ala Met Ala Thr Asn Lys Asp Asp Glu Asp Gln Phe Phe
 515 520 525
 Pro Ile Asn Gly Val Leu Val Phe Gly Glu Thr Gly Ala Ala Asn Lys
 530 535 540

Thr Thr Leu Glu Asn Val Leu Met Thr Ser Glu Glu Glu Ile Lys Thr
545 550 555 560

Thr Asn Pro Val Ala Thr Glu Glu Tyr Gly Val Val Ser Ser Asn Leu
565 570 575

Gln Ser Ser Thr Ala Gly Pro Gln Thr Gln Thr Val Asn Ser Gln Gly
580 585 590

Ala Leu Pro Gly Met Val Trp Gln Asn Arg Asp Val Tyr Leu Gln Gly
595 600 605

Pro Ile Trp Ala Lys Ile Pro His Thr Asp Gly Asn Phe His Pro Ser
610 615 620

Pro Leu Met Gly Gly Phe Gly Leu Lys His Pro Pro Pro Gln Ile Leu
625 630 635 640

Ile Lys Asn Thr Pro Val Pro Ala Asn Pro Pro Glu Val Phe Thr Pro
645 650 655

Ala Lys Phe Ala Ser Phe Ile Thr Gln Tyr Ser Thr Gly Gln Val Ser
660 665 670

Val Glu Ile Glu Trp Glu Leu Gln Lys Glu Asn Ser Lys Arg Trp Asn
675 680 685

[0048]

Pro Glu Ile Gln Tyr Thr Ser Asn Tyr Ala Lys Ser Asn Asn Val Glu
690 695 700

Phe Ala Val Asn Asn Glu Gly Val Tyr Thr Glu Pro Arg Pro Ile Gly
705 710 715 720

Thr Arg Tyr Leu Thr Arg Asn Leu
725

<210> 27

<211> 736

<212> PRT

<213> 腺相关病毒血清型1的衣壳蛋白

<400> 27

Met Ala Ala Asp Gly Tyr Leu Pro Asp Trp Leu Glu Asp Asn Leu Ser
1 5 10 15

Glu Gly Ile Arg Glu Trp Trp Asp Leu Lys Pro Gly Ala Pro Lys Pro
20 25 30

Lys Ala Asn Gln Gln Lys Gln Asp Asp Gly Arg Gly Leu Val Leu Pro
35 40 45

Gly Tyr Lys Tyr Leu Gly Pro Phe Asn Gly Leu Asp Lys Gly Glu Pro

50	55	60
Val Asn Ala Ala Asp 65	Ala Ala Leu Glu 70	His Asp Lys Ala Tyr Asp 75 80
Gln Gln Leu Lys Ala Gly 85	Asp Asn Pro Tyr Leu Arg Tyr Asn His Ala 90 95	
Asp Ala Glu Phe Gln Glu Arg Leu Gln Glu Asp Thr Ser Phe Gly Gly 100 105 110		
Asn Leu Gly Arg Ala Val Phe Gln Ala Lys Lys Arg Val Leu Glu Pro 115 120 125		
Leu Gly Leu Val Glu Glu Gly Ala Lys Thr Ala Pro Gly Lys Lys Arg 130 135 140		
Pro Val Glu Gln Ser Pro Gln Glu Pro Asp Ser Ser Ser Gly Ile Gly 145 150 155 160		
Lys Thr Gly Gln Gln Pro Ala Lys Lys Arg Leu Asn Phe Gly Gln Thr 165 170 175		
Gly Asp Ser Glu Ser Val Pro Asp Pro Gln Pro Leu Gly Glu Pro Pro 180 185 190		
[0049]		
Ala Thr Pro Ala Ala Val Gly Pro Thr Thr Met Ala Ser Gly Gly Gly 195 200 205		
Ala Pro Met Ala Asp Asn Asn Glu Gly Ala Asp Gly Val Gly Asn Ala 210 215 220		
Ser Gly Asn Trp His Cys Asp Ser Thr Trp Leu Gly Asp Arg Val Ile 225 230 235 240		
Thr Thr Ser Thr Arg Thr Trp Ala Leu Pro Thr Tyr Asn Asn His Leu 245 250 255		
Tyr Lys Gln Ile Ser Ser Ala Ser Thr Gly Ala Ser Asn Asp Asn His 260 265 270		
Tyr Phe Gly Tyr Ser Thr Pro Trp Gly Tyr Phe Asp Phe Asn Arg Phe 275 280 285		
His Cys His Phe Ser Pro Arg Asp Trp Gln Arg Leu Ile Asn Asn Asn 290 295 300		
Trp Gly Phe Arg Pro Lys Arg Leu Asn Phe Lys Leu Phe Asn Ile Gln 305 310 315 320		
Val Lys Glu Val Thr Thr Asn Asp Gly Val Thr Thr Ile Ala Asn Asn		

	325		330		335
Leu Thr Ser Thr Val Gln Val Phe Ser Asp Ser Glu Tyr Gln Leu Pro	340		345		350
Tyr Val Leu Gly Ser Ala His Gln Gly Cys Leu Pro Pro Phe Pro Ala	355		360		365
Asp Val Phe Met Ile Pro Gln Tyr Gly Tyr Leu Thr Leu Asn Asn Gly	370		375		380
Ser Gln Ala Val Gly Arg Ser Ser Phe Tyr Cys Leu Glu Tyr Phe Pro	385		390		395
Ser Gln Met Leu Arg Thr Gly Asn Asn Phe Thr Phe Ser Tyr Thr Phe	405		410		415
Glu Glu Val Pro Phe His Ser Ser Tyr Ala His Ser Gln Ser Leu Asp	420		425		430
Arg Leu Met Asn Pro Leu Ile Asp Gln Tyr Leu Tyr Tyr Leu Asn Arg	435		440		445
Thr Gln Asn Gln Ser Gly Ser Ala Gln Asn Lys Asp Leu Leu Phe Ser	450		455		460
[0050]					
Arg Gly Ser Pro Ala Gly Met Ser Val Gln Pro Lys Asn Trp Leu Pro	465		470		475
Gly Pro Cys Tyr Arg Gln Gln Arg Val Ser Lys Thr Lys Thr Asp Asn	485		490		495
Asn Asn Ser Asn Phe Thr Trp Thr Gly Ala Ser Lys Tyr Asn Leu Asn	500		505		510
Gly Arg Glu Ser Ile Ile Asn Pro Gly Thr Ala Met Ala Ser His Lys	515		520		525
Asp Asp Glu Asp Lys Phe Phe Pro Met Ser Gly Val Met Ile Phe Gly	530		535		540
Lys Glu Ser Ala Gly Ala Ser Asn Thr Ala Leu Asp Asn Val Met Ile	545		550		555
Thr Asp Glu Glu Glu Ile Lys Ala Thr Asn Pro Val Ala Thr Glu Arg	565		570		575
Phe Gly Thr Val Ala Val Asn Phe Gln Ser Ser Ser Thr Asp Pro Ala	580		585		590
Thr Gly Asp Val His Ala Met Gly Ala Leu Pro Gly Met Val Trp Gln					

595	600	605
Asp Arg Asp Val Tyr Leu Gln Gly Pro Ile Trp Ala Lys Ile Pro His		
610	615	620
Thr Asp Gly His Phe His Pro Ser Pro Leu Met Gly Gly Phe Gly Leu		
625	630	635
Lys Asn Pro Pro Pro Gln Ile Leu Ile Lys Asn Thr Pro Val Pro Ala		
	645	650
		655
Asn Pro Pro Ala Glu Phe Ser Ala Thr Lys Phe Ala Ser Phe Ile Thr		
	660	665
		670
Gln Tyr Ser Thr Gly Gln Val Ser Val Glu Ile Glu Trp Glu Leu Gln		
	675	680
		685
Lys Glu Asn Ser Lys Arg Trp Asn Pro Glu Val Gln Tyr Thr Ser Asn		
	690	695
		700
Tyr Ala Lys Ser Ala Asn Val Asp Phe Thr Val Asp Asn Asn Gly Leu		
705	710	715
		720
Tyr Thr Glu Pro Arg Pro Ile Gly Thr Arg Tyr Leu Thr Arg Pro Leu		
	725	730
		735

[0051]

<210> 28
 <211> 736
 <212> PRT
 <213> 腺相关病毒血清型3的衣壳蛋白

<400> 28

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

	Asn	Leu	Gly	Arg	Ala	Val	Phe	Gln	Ala	Lys	Lys	Arg	Ile	Leu	Glu	Pro	
	115							120					125				
	Leu	Gly	Leu	Val	Glu	Glu	Ala	Ala	Lys	Thr	Ala	Pro	Gly	Lys	Lys	Gly	
	130						135					140					
	Ala	Val	Asp	Gln	Ser	Pro	Gln	Glu	Pro	Asp	Ser	Ser	Ser	Gly	Val	Gly	
	145					150					155					160	
	Lys	Ser	Gly	Lys	Gln	Pro	Ala	Arg	Lys	Arg	Leu	Asn	Phe	Gly	Gln	Thr	
					165					170					175		
	Gly	Asp	Ser	Glu	Ser	Val	Pro	Asp	Pro	Gln	Pro	Leu	Gly	Glu	Pro	Pro	
				180					185					190			
	Ala	Ala	Pro	Thr	Ser	Leu	Gly	Ser	Asn	Thr	Met	Ala	Ser	Gly	Gly	Gly	
		195						200					205				
	Ala	Pro	Met	Ala	Asp	Asn	Asn	Glu	Gly	Ala	Asp	Gly	Val	Gly	Asn	Ser	
	210						215					220					
	Ser	Gly	Asn	Trp	His	Cys	Asp	Ser	Gln	Trp	Leu	Gly	Asp	Arg	Val	Ile	
	225					230					235					240	
[0052]	Thr	Thr	Ser	Thr	Arg	Thr	Trp	Ala	Leu	Pro	Thr	Tyr	Asn	Asn	His	Leu	
					245					250					255		
	Tyr	Lys	Gln	Ile	Ser	Ser	Gln	Ser	Gly	Ala	Ser	Asn	Asp	Asn	His	Tyr	
				260					265					270			
	Phe	Gly	Tyr	Ser	Thr	Pro	Trp	Gly	Tyr	Phe	Asp	Phe	Asn	Arg	Phe	His	
		275						280					285				
	Cys	His	Phe	Ser	Pro	Arg	Asp	Trp	Gln	Arg	Leu	Ile	Asn	Asn	Asn	Trp	
	290						295					300					
	Gly	Phe	Arg	Pro	Lys	Lys	Leu	Ser	Phe	Lys	Leu	Phe	Asn	Ile	Gln	Val	
	305					310					315					320	
	Arg	Gly	Val	Thr	Gln	Asn	Asp	Gly	Thr	Thr	Thr	Ile	Ala	Asn	Asn	Leu	
					325					330					335		
	Thr	Ser	Thr	Val	Gln	Val	Phe	Thr	Asp	Ser	Glu	Tyr	Gln	Leu	Pro	Tyr	
				340					345					350			
	Val	Leu	Gly	Ser	Ala	His	Gln	Gly	Cys	Leu	Pro	Pro	Phe	Pro	Ala	Asp	
		355						360					365				
	Val	Phe	Met	Val	Pro	Gln	Tyr	Gly	Tyr	Leu	Thr	Leu	Asn	Asn	Gly	Ser	
	370						375					380					

Gln Ala Val Gly Arg Ser Ser Phe Tyr Cys Leu Glu Tyr Phe Pro Ser
 385 390 395 400
 Gln Met Leu Arg Thr Gly Asn Asn Phe Gln Phe Ser Tyr Thr Phe Glu
 405 410 415
 Asp Val Pro Phe His Ser Ser Tyr Ala His Ser Gln Ser Leu Asp Arg
 420 425 430
 Leu Met Asn Pro Leu Ile Asp Gln Tyr Leu Tyr Tyr Leu Asn Arg Thr
 435 440 445
 Gln Gly Thr Thr Ser Gly Thr Thr Asn Gln Ser Arg Leu Leu Phe Ser
 450 455 460
 Gln Ala Gly Pro Gln Ser Met Ser Leu Gln Ala Arg Asn Trp Leu Pro
 465 470 475 480
 Gly Pro Cys Tyr Arg Gln Gln Arg Leu Ser Lys Thr Ala Asn Asp Asn
 485 490 495
 Asn Asn Ser Asn Phe Pro Trp Thr Ala Ala Ser Lys Tyr His Leu Asn
 500 505 510
 [0053] Gly Arg Asp Ser Leu Val Asn Pro Gly Pro Ala Met Ala Ser His Lys
 515 520 525
 Asp Asp Glu Glu Lys Phe Phe Pro Met His Gly Asn Leu Ile Phe Gly
 530 535 540
 Lys Glu Gly Thr Thr Ala Ser Asn Ala Glu Leu Asp Asn Val Met Ile
 545 550 555 560
 Thr Asp Glu Glu Glu Ile Arg Thr Thr Asn Pro Val Ala Thr Glu Gln
 565 570 575
 Tyr Gly Thr Val Ala Asn Asn Leu Gln Ser Ser Asn Thr Ala Pro Thr
 580 585 590
 Thr Gly Thr Val Asn His Gln Gly Ala Leu Pro Gly Met Val Trp Gln
 595 600 605
 Asp Arg Asp Val Tyr Leu Gln Gly Pro Ile Trp Ala Lys Ile Pro His
 610 615 620
 Thr Asp Gly His Phe His Pro Ser Pro Leu Met Gly Gly Phe Gly Leu
 625 630 635 640
 Lys His Pro Pro Pro Gln Ile Met Ile Lys Asn Thr Pro Val Pro Ala
 645 650 655

Asn Pro Pro Thr Thr Phe Ser Pro Ala Lys Phe Ala Ser Phe Ile Thr
660 665 670

Gln Tyr Ser Thr Gly Gln Val Ser Val Glu Ile Glu Trp Glu Leu Gln
675 680 685

Lys Glu Asn Ser Lys Arg Trp Asn Pro Glu Ile Gln Tyr Thr Ser Asn
690 695 700

Tyr Asn Lys Ser Val Asn Val Asp Phe Thr Val Asp Thr Asn Gly Val
705 710 715 720

Tyr Ser Glu Pro Arg Pro Ile Gly Thr Arg Tyr Leu Thr Arg Asn Leu
725 730 735

<210> 29

<211> 736

<212> PRT

<213> 腺相关病毒血清型6的衣壳蛋白

<400> 29

Met Ala Ala Asp Gly Tyr Leu Pro Asp Trp Leu Glu Asp Asn Leu Ser
1 5 10 15

[0054]

Glu Gly Ile Arg Glu Trp Trp Asp Leu Lys Pro Gly Ala Pro Lys Pro
20 25 30

Lys Ala Asn Gln Gln Lys Gln Asp Asp Gly Arg Gly Leu Val Leu Pro
35 40 45

Gly Tyr Lys Tyr Leu Gly Pro Phe Asn Gly Leu Asp Lys Gly Glu Pro
50 55 60

Val Asn Ala Ala Asp Ala Ala Ala Leu Glu His Asp Lys Ala Tyr Asp
65 70 75 80

Gln Gln Leu Lys Ala Gly Asp Asn Pro Tyr Leu Arg Tyr Asn His Ala
85 90 95

Asp Ala Glu Phe Gln Glu Arg Leu Gln Glu Asp Thr Ser Phe Gly Gly
100 105 110

Asn Leu Gly Arg Ala Val Phe Gln Ala Lys Lys Arg Val Leu Glu Pro
115 120 125

Phe Gly Leu Val Glu Glu Gly Ala Lys Thr Ala Pro Gly Lys Lys Arg
130 135 140

Pro Val Glu Gln Ser Pro Gln Glu Pro Asp Ser Ser Ser Gly Ile Gly
145 150 155 160

	Lys	Thr	Gly	Gln	Gln	Pro	Ala	Lys	Lys	Arg	Leu	Asn	Phe	Gly	Gln	Thr	
				165						170					175		
	Gly	Asp	Ser	Glu	Ser	Val	Pro	Asp	Pro	Gln	Pro	Leu	Gly	Glu	Pro	Pro	
			180						185					190			
	Ala	Thr	Pro	Ala	Ala	Val	Gly	Pro	Thr	Thr	Met	Ala	Ser	Gly	Gly	Gly	
			195					200					205				
	Ala	Pro	Met	Ala	Asp	Asn	Asn	Glu	Gly	Ala	Asp	Gly	Val	Gly	Asn	Ala	
		210					215					220					
	Ser	Gly	Asn	Trp	His	Cys	Asp	Ser	Thr	Trp	Leu	Gly	Asp	Arg	Val	Ile	
	225					230					235					240	
	Thr	Thr	Ser	Thr	Arg	Thr	Trp	Ala	Leu	Pro	Thr	Tyr	Asn	Asn	His	Leu	
					245					250					255		
	Tyr	Lys	Gln	Ile	Ser	Ser	Ala	Ser	Thr	Gly	Ala	Ser	Asn	Asp	Asn	His	
			260						265					270			
	Tyr	Phe	Gly	Tyr	Ser	Thr	Pro	Trp	Gly	Tyr	Phe	Asp	Phe	Asn	Arg	Phe	
			275					280					285				
[0055]	His	Cys	His	Phe	Ser	Pro	Arg	Asp	Trp	Gln	Arg	Leu	Ile	Asn	Asn	Asn	
		290					295					300					
	Trp	Gly	Phe	Arg	Pro	Lys	Arg	Leu	Asn	Phe	Lys	Leu	Phe	Asn	Ile	Gln	
	305					310					315					320	
	Val	Lys	Glu	Val	Thr	Thr	Asn	Asp	Gly	Val	Thr	Thr	Ile	Ala	Asn	Asn	
				325						330					335		
	Leu	Thr	Ser	Thr	Val	Gln	Val	Phe	Ser	Asp	Ser	Glu	Tyr	Gln	Leu	Pro	
				340					345					350			
	Tyr	Val	Leu	Gly	Ser	Ala	His	Gln	Gly	Cys	Leu	Pro	Pro	Phe	Pro	Ala	
		355						360					365				
	Asp	Val	Phe	Met	Ile	Pro	Gln	Tyr	Gly	Tyr	Leu	Thr	Leu	Asn	Asn	Gly	
		370					375					380					
	Ser	Gln	Ala	Val	Gly	Arg	Ser	Ser	Phe	Tyr	Cys	Leu	Glu	Tyr	Phe	Pro	
	385					390					395					400	
	Ser	Gln	Met	Leu	Arg	Thr	Gly	Asn	Asn	Phe	Thr	Phe	Ser	Tyr	Thr	Phe	
				405						410					415		
	Glu	Asp	Val	Pro	Phe	His	Ser	Ser	Tyr	Ala	His	Ser	Gln	Ser	Leu	Asp	
			420						425					430			

	Arg Leu Met Asn Pro Leu Ile Asp Gln Tyr Leu Tyr Tyr Leu Asn Arg	
	435	440 445
	Thr Gln Asn Gln Ser Gly Ser Ala Gln Asn Lys Asp Leu Leu Phe Ser	
	450	455 460
	Arg Gly Ser Pro Ala Gly Met Ser Val Gln Pro Lys Asn Trp Leu Pro	
	465	470 475 480
	Gly Pro Cys Tyr Arg Gln Gln Arg Val Ser Lys Thr Lys Thr Asp Asn	
		485 490 495
	Asn Asn Ser Asn Phe Thr Trp Thr Gly Ala Ser Lys Tyr Asn Leu Asn	
		500 505 510
	Gly Arg Glu Ser Ile Ile Asn Pro Gly Thr Ala Met Ala Ser His Lys	
		515 520 525
	Asp Asp Lys Asp Lys Phe Phe Pro Met Ser Gly Val Met Ile Phe Gly	
		530 535 540
	Lys Glu Ser Ala Gly Ala Ser Asn Thr Ala Leu Asp Asn Val Met Ile	
		545 550 555 560
[0056]	Thr Asp Glu Glu Glu Ile Lys Ala Thr Asn Pro Val Ala Thr Glu Arg	
		565 570 575
	Phe Gly Thr Val Ala Val Asn Leu Gln Ser Ser Ser Thr Asp Pro Ala	
		580 585 590
	Thr Gly Asp Val His Val Met Gly Ala Leu Pro Gly Met Val Trp Gln	
		595 600 605
	Asp Arg Asp Val Tyr Leu Gln Gly Pro Ile Trp Ala Lys Ile Pro His	
		610 615 620
	Thr Asp Gly His Phe His Pro Ser Pro Leu Met Gly Gly Phe Gly Leu	
		625 630 635 640
	Lys His Pro Pro Pro Gln Ile Leu Ile Lys Asn Thr Pro Val Pro Ala	
		645 650 655
	Asn Pro Pro Ala Glu Phe Ser Ala Thr Lys Phe Ala Ser Phe Ile Thr	
		660 665 670
	Gln Tyr Ser Thr Gly Gln Val Ser Val Glu Ile Glu Trp Glu Leu Gln	
		675 680 685
	Lys Glu Asn Ser Lys Arg Trp Asn Pro Glu Val Gln Tyr Thr Ser Asn	
		690 695 700

Tyr Ala Lys Ser Ala Asn Val Asp Phe Thr Val Asp Asn Asn Gly Leu
705 710 715 720

Tyr Thr Glu Pro Arg Pro Ile Gly Thr Arg Tyr Leu Thr Arg Pro Leu
725 730 735

<210> 30

<211> 737

<212> PRT

<213> 腺相关病毒血清型7的衣壳蛋白

<400> 30

Met Ala Ala Asp Gly Tyr Leu Pro Asp Trp Leu Glu Asp Asn Leu Ser
1 5 10 15

Glu Gly Ile Arg Glu Trp Trp Asp Leu Lys Pro Gly Ala Pro Lys Pro
20 25 30

Lys Ala Asn Gln Gln Lys Gln Asp Asn Gly Arg Gly Leu Val Leu Pro
35 40 45

Gly Tyr Lys Tyr Leu Gly Pro Phe Asn Gly Leu Asp Lys Gly Glu Pro
50 55 60

[0057]

Val Asn Ala Ala Asp Ala Ala Ala Leu Glu His Asp Lys Ala Tyr Asp
65 70 75 80

Gln Gln Leu Lys Ala Gly Asp Asn Pro Tyr Leu Arg Tyr Asn His Ala
85 90 95

Asp Ala Glu Phe Gln Glu Arg Leu Gln Glu Asp Thr Ser Phe Gly Gly
100 105 110

Asn Leu Gly Arg Ala Val Phe Gln Ala Lys Lys Arg Val Leu Glu Pro
115 120 125

Leu Gly Leu Val Glu Glu Gly Ala Lys Thr Ala Pro Ala Lys Lys Arg
130 135 140

Pro Val Glu Pro Ser Pro Gln Arg Ser Pro Asp Ser Ser Thr Gly Ile
145 150 155 160

Gly Lys Lys Gly Gln Gln Pro Ala Arg Lys Arg Leu Asn Phe Gly Gln
165 170 175

Thr Gly Asp Ser Glu Ser Val Pro Asp Pro Gln Pro Leu Gly Glu Pro
180 185 190

Pro Ala Ala Pro Ser Ser Val Gly Ser Gly Thr Val Ala Ala Gly Gly
195 200 205

Gly Ala Pro Met Ala Asp Asn Asn Glu Gly Ala Asp Gly Val Gly Asn
 210 215 220
 Ala Ser Gly Asn Trp His Cys Asp Ser Thr Trp Leu Gly Asp Arg Val
 225 230 235 240
 Ile Thr Thr Ser Thr Arg Thr Trp Ala Leu Pro Thr Tyr Asn Asn His
 245 250 255
 Leu Tyr Lys Gln Ile Ser Ser Glu Thr Ala Gly Ser Thr Asn Asp Asn
 260 265 270
 Thr Tyr Phe Gly Tyr Ser Thr Pro Trp Gly Tyr Phe Asp Phe Asn Arg
 275 280 285
 Phe His Cys His Phe Ser Pro Arg Asp Trp Gln Arg Leu Ile Asn Asn
 290 295 300
 Asn Trp Gly Phe Arg Pro Lys Lys Leu Arg Phe Lys Leu Phe Asn Ile
 305 310 315 320
 Gln Val Lys Glu Val Thr Thr Asn Asp Gly Val Thr Thr Ile Ala Asn
 325 330 335
 [0058] Asn Leu Thr Ser Thr Ile Gln Val Phe Ser Asp Ser Glu Tyr Gln Leu
 340 345 350
 Pro Tyr Val Leu Gly Ser Ala His Gln Gly Cys Leu Pro Pro Phe Pro
 355 360 365
 Ala Asp Val Phe Met Ile Pro Gln Tyr Gly Tyr Leu Thr Leu Asn Asn
 370 375 380
 Gly Ser Gln Ser Val Gly Arg Ser Ser Phe Tyr Cys Leu Glu Tyr Phe
 385 390 395 400
 Pro Ser Gln Met Leu Arg Thr Gly Asn Asn Phe Glu Phe Ser Tyr Ser
 405 410 415
 Phe Glu Asp Val Pro Phe His Ser Ser Tyr Ala His Ser Gln Ser Leu
 420 425 430
 Asp Arg Leu Met Asn Pro Leu Ile Asp Gln Tyr Leu Tyr Tyr Leu Ala
 435 440 445
 Arg Thr Gln Ser Asn Pro Gly Gly Thr Ala Gly Asn Arg Glu Leu Gln
 450 455 460
 Phe Tyr Gln Gly Gly Pro Ser Thr Met Ala Glu Gln Ala Lys Asn Trp
 465 470 475 480

	Leu	Pro	Gly	Pro	Cys	Phe	Arg	Gln	Gln	Arg	Val	Ser	Lys	Thr	Leu	Asp	
					485					490						495	
	Gln	Asn	Asn	Asn	Ser	Asn	Phe	Ala	Trp	Thr	Gly	Ala	Thr	Lys	Tyr	His	
				500					505						510		
	Leu	Asn	Gly	Arg	Asn	Ser	Leu	Val	Asn	Pro	Gly	Val	Ala	Met	Ala	Thr	
			515					520					525				
	His	Lys	Asp	Asp	Glu	Asp	Arg	Phe	Phe	Pro	Ser	Ser	Gly	Val	Leu	Ile	
		530					535					540					
	Phe	Gly	Lys	Thr	Gly	Ala	Thr	Asn	Lys	Thr	Thr	Leu	Glu	Asn	Val	Leu	
	545					550					555					560	
	Met	Thr	Asn	Glu	Glu	Glu	Ile	Arg	Pro	Thr	Asn	Pro	Val	Ala	Thr	Glu	
					565					570						575	
	Glu	Tyr	Gly	Ile	Val	Ser	Ser	Asn	Leu	Gln	Ala	Ala	Asn	Thr	Ala	Ala	
				580					585					590			
	Gln	Thr	Gln	Val	Val	Asn	Asn	Gln	Gly	Ala	Leu	Pro	Gly	Met	Val	Trp	
			595					600					605				
[0059]	Gln	Asn	Arg	Asp	Val	Tyr	Leu	Gln	Gly	Pro	Ile	Trp	Ala	Lys	Ile	Pro	
		610					615					620					
	His	Thr	Asp	Gly	Asn	Phe	His	Pro	Ser	Pro	Leu	Met	Gly	Gly	Phe	Gly	
	625					630					635					640	
	Leu	Lys	His	Pro	Pro	Pro	Gln	Ile	Leu	Ile	Lys	Asn	Thr	Pro	Val	Pro	
					645					650					655		
	Ala	Asn	Pro	Pro	Glu	Val	Phe	Thr	Pro	Ala	Lys	Phe	Ala	Ser	Phe	Ile	
				660					665					670			
	Thr	Gln	Tyr	Ser	Thr	Gly	Gln	Val	Ser	Val	Glu	Ile	Glu	Trp	Glu	Leu	
			675					680					685				
	Gln	Lys	Glu	Asn	Ser	Lys	Arg	Trp	Asn	Pro	Glu	Ile	Gln	Tyr	Thr	Ser	
		690					695					700					
	Asn	Phe	Glu	Lys	Gln	Thr	Gly	Val	Asp	Phe	Ala	Val	Asp	Ser	Gln	Gly	
	705					710					715					720	
	Val	Tyr	Ser	Glu	Pro	Arg	Pro	Ile	Gly	Thr	Arg	Tyr	Leu	Thr	Arg	Asn	
					725					730					735		
	Leu																

<210> 31
 <211> 738
 <212> PRT
 <213> 腺相关病毒血清型8的衣壳蛋白

<400> 31

Met Ala Ala Asp Gly Tyr Leu Pro Asp Trp Leu Glu Asp Asn Leu Ser
 1 5 10 15

Glu Gly Ile Arg Glu Trp Trp Ala Leu Lys Pro Gly Ala Pro Lys Pro
 20 25 30

Lys Ala Asn Gln Gln Lys Gln Asp Asp Gly Arg Gly Leu Val Leu Pro
 35 40 45

Gly Tyr Lys Tyr Leu Gly Pro Phe Asn Gly Leu Asp Lys Gly Glu Pro
 50 55 60

Val Asn Ala Ala Asp Ala Ala Ala Leu Glu His Asp Lys Ala Tyr Asp
 65 70 75 80

Gln Gln Leu Gln Ala Gly Asp Asn Pro Tyr Leu Arg Tyr Asn His Ala
 85 90 95

Asp Ala Glu Phe Gln Glu Arg Leu Gln Glu Asp Thr Ser Phe Gly Gly
 100 105 110

[0060]

Asn Leu Gly Arg Ala Val Phe Gln Ala Lys Lys Arg Val Leu Glu Pro
 115 120 125

Leu Gly Leu Val Glu Glu Gly Ala Lys Thr Ala Pro Gly Lys Lys Arg
 130 135 140

Pro Val Glu Pro Ser Pro Gln Arg Ser Pro Asp Ser Ser Thr Gly Ile
 145 150 155 160

Gly Lys Lys Gly Gln Gln Pro Ala Arg Lys Arg Leu Asn Phe Gly Gln
 165 170 175

Thr Gly Asp Ser Glu Ser Val Pro Asp Pro Gln Pro Leu Gly Glu Pro
 180 185 190

Pro Ala Ala Pro Ser Gly Val Gly Pro Asn Thr Met Ala Ala Gly Gly
 195 200 205

Gly Ala Pro Met Ala Asp Asn Asn Glu Gly Ala Asp Gly Val Gly Ser
 210 215 220

Ser Ser Gly Asn Trp His Cys Asp Ser Thr Trp Leu Gly Asp Arg Val
 225 230 235 240

Ile Thr Thr Ser Thr Arg Thr Trp Ala Leu Pro Thr Tyr Asn Asn His

[0061]

515	520	525
His Lys Asp Asp Glu Glu Arg Phe Phe Pro Ser Asn Gly Ile Leu Ile		
530	535	540
Phe Gly Lys Gln Asn Ala Ala Arg Asp Asn Ala Asp Tyr Ser Asp Val		
545	550	555
Met Leu Thr Ser Glu Glu Glu Ile Lys Thr Thr Asn Pro Val Ala Thr		
	565	570
		575
Glu Glu Tyr Gly Ile Val Ala Asp Asn Leu Gln Gln Gln Asn Thr Ala		
	580	585
		590
Pro Gln Ile Gly Thr Val Asn Ser Gln Gly Ala Leu Pro Gly Met Val		
	595	600
		605
Trp Gln Asn Arg Asp Val Tyr Leu Gln Gly Pro Ile Trp Ala Lys Ile		
	610	615
		620
Pro His Thr Asp Gly Asn Phe His Pro Ser Pro Leu Met Gly Gly Phe		
625	630	635
		640
Gly Leu Lys His Pro Pro Pro Gln Ile Leu Ile Lys Asn Thr Pro Val		
	645	650
		655
Pro Ala Asp Pro Pro Thr Thr Phe Asn Gln Ser Lys Leu Asn Ser Phe		
	660	665
		670
Ile Thr Gln Tyr Ser Thr Gly Gln Val Ser Val Glu Ile Glu Trp Glu		
	675	680
		685
Leu Gln Lys Glu Asn Ser Lys Arg Trp Asn Pro Glu Ile Gln Tyr Thr		
	690	695
		700
Ser Asn Tyr Tyr Lys Ser Thr Ser Val Asp Phe Ala Val Asn Thr Glu		
705	710	715
		720
Gly Val Tyr Ser Glu Pro Arg Pro Ile Gly Thr Arg Tyr Leu Thr Arg		
	725	730
		735
Asn Leu		
<210> 32		
<211> 735		
<212> PRT		
<213> 腺相关病毒, hu, 13的衣壳蛋白		
<400> 32		
Met Ala Ala Asp Gly Tyr Leu Pro Asp Trp Leu Glu Asp Thr Leu Ser		
1	5	10
		15

	Glu	Gly	Ile	Arg	Gln	Trp	Trp	Lys	Leu	Lys	Pro	Gly	Pro	Pro	Pro	Pro	
				20					25					30			
	Lys	Pro	Ala	Glu	Arg	His	Lys	Asp	Asp	Ser	Arg	Gly	Leu	Val	Leu	Pro	
		35						40					45				
	Gly	Tyr	Lys	Tyr	Leu	Gly	Pro	Phe	Asn	Gly	Leu	Asp	Lys	Gly	Glu	Pro	
		50					55					60					
	Val	Asn	Glu	Ala	Asp	Ala	Ala	Ala	Leu	Glu	His	Asp	Lys	Ala	Tyr	Asp	
	65					70					75					80	
	Arg	Gln	Leu	Asp	Ser	Gly	Asp	Asn	Pro	Tyr	Leu	Lys	Tyr	Asn	His	Ala	
				85						90					95		
	Asp	Ala	Glu	Phe	Gln	Glu	Arg	Leu	Lys	Glu	Asp	Thr	Ser	Phe	Gly	Gly	
			100						105					110			
	Asn	Leu	Gly	Arg	Ala	Val	Phe	Gln	Ala	Lys	Lys	Arg	Val	Leu	Glu	Pro	
		115						120					125				
	Leu	Gly	Leu	Val	Glu	Glu	Pro	Val	Lys	Thr	Ala	Pro	Gly	Lys	Lys	Arg	
		130					135					140					
[0063]	Pro	Val	Glu	His	Ser	Pro	Ala	Glu	Pro	Asp	Ser	Ser	Ser	Gly	Thr	Gly	
	145					150					155					160	
	Lys	Ala	Gly	Gln	Gln	Pro	Ala	Arg	Lys	Arg	Leu	Asn	Phe	Gly	Gln	Thr	
				165						170					175		
	Gly	Asp	Ala	Asp	Ser	Val	Pro	Asp	Pro	Gln	Pro	Leu	Gly	Gln	Pro	Pro	
			180						185					190			
	Ala	Ala	Pro	Ser	Gly	Leu	Gly	Thr	Asn	Thr	Met	Ala	Ser	Gly	Ser	Gly	
		195						200					205				
	Ala	Pro	Met	Ala	Asp	Asn	Asn	Glu	Gly	Ala	Asp	Gly	Val	Gly	Asn	Ser	
		210					215					220					
	Ser	Gly	Asn	Trp	His	Cys	Asp	Ser	Thr	Trp	Met	Gly	Asp	Arg	Val	Ile	
	225					230					235					240	
	Thr	Thr	Ser	Thr	Arg	Thr	Trp	Ala	Leu	Pro	Thr	Tyr	Asn	Asn	His	Leu	
					245					250					255		
	Tyr	Lys	Gln	Ile	Ser	Ser	Gln	Ser	Gly	Ala	Ser	Asn	Asp	Asn	His	Tyr	
			260						265					270			
	Phe	Gly	Tyr	Ser	Thr	Pro	Trp	Gly	Tyr	Phe	Asp	Phe	Asn	Arg	Phe	His	
		275						280					285				

	Cys	His	Phe	Ser	Pro	Arg	Asp	Trp	Gln	Arg	Leu	Ile	Asn	Asn	Asn	Trp
	290						295					300				
	Gly	Phe	Arg	Pro	Lys	Arg	Leu	Asn	Phe	Lys	Leu	Phe	Asn	Ile	Gln	Val
	305					310					315					320
	Lys	Glu	Val	Thr	Gln	Asn	Asp	Gly	Thr	Thr	Thr	Ile	Ala	Asn	Asn	Leu
					325					330					335	
	Thr	Ser	Thr	Val	Gln	Val	Phe	Thr	Asp	Ser	Glu	Tyr	Gln	Leu	Pro	Tyr
				340					345						350	
	Val	Leu	Gly	Ser	Ala	His	Gln	Gly	Cys	Leu	Pro	Pro	Phe	Pro	Ala	Asp
			355					360					365			
	Val	Phe	Met	Val	Pro	Gln	Tyr	Gly	Tyr	Leu	Thr	Leu	Asn	Asn	Gly	Ser
	370						375					380				
	Gln	Ala	Val	Gly	Arg	Ser	Ser	Phe	Tyr	Cys	Leu	Glu	Tyr	Phe	Pro	Ser
	385					390					395					400
	Gln	Met	Leu	Arg	Thr	Gly	Asn	Asn	Phe	Thr	Phe	Ser	Tyr	Thr	Phe	Glu
					405					410					415	
[0064]	Asp	Val	Pro	Phe	His	Ser	Ser	Tyr	Ala	His	Ser	Gln	Ser	Leu	Asp	Arg
				420					425					430		
	Leu	Met	Asn	Pro	Leu	Ile	Asp	Gln	Tyr	Leu	Tyr	Tyr	Leu	Ser	Arg	Thr
			435					440					445			
	Asn	Thr	Pro	Ser	Gly	Thr	Thr	Thr	Gln	Ser	Arg	Leu	Gln	Phe	Ser	Gln
	450						455					460				
	Ala	Gly	Ala	Ser	Asp	Ile	Arg	Asp	Gln	Ser	Arg	Asn	Trp	Leu	Pro	Gly
	465					470					475					480
	Pro	Cys	Tyr	Arg	Gln	Gln	Arg	Val	Ser	Lys	Thr	Ser	Ala	Asp	Asn	Asn
					485					490				495		
	Asn	Ser	Glu	Tyr	Ser	Trp	Thr	Gly	Ala	Thr	Lys	Tyr	His	Leu	Asn	Gly
			500						505					510		
	Arg	Asp	Ser	Leu	Val	Asn	Pro	Gly	Pro	Ala	Met	Ala	Ser	His	Lys	Asp
			515					520					525			
	Asp	Glu	Glu	Lys	Phe	Phe	Pro	Gln	Ser	Gly	Val	Leu	Ile	Phe	Gly	Lys
	530						535					540				
	Gln	Gly	Ser	Glu	Lys	Thr	Asn	Val	Asp	Ile	Glu	Lys	Val	Met	Ile	Thr
	545					550					555				560	

Asp Glu Glu Glu Ile Arg Thr Thr Asn Pro Val Ala Thr Glu Gln Tyr
565 570 575

Gly Ser Val Ser Thr Asn Leu Gln Gly Gly Asn Thr Gln Ala Ala Thr
580 585 590

Ala Asp Val Asn Thr Gln Gly Val Leu Pro Gly Met Val Trp Gln Asp
595 600 605

Arg Asp Val Tyr Leu Gln Gly Pro Ile Trp Ala Lys Ile Pro His Thr
610 615 620

Asp Gly His Phe His Pro Ser Pro Leu Met Gly Gly Phe Gly Leu Lys
625 630 635 640

His Pro Pro Pro Gln Ile Leu Ile Lys Asn Thr Pro Val Pro Ala Asn
645 650 655

Pro Ser Thr Thr Phe Ser Ala Ala Lys Phe Ala Ser Phe Ile Thr Gln
660 665 670

Tyr Ser Thr Gly Gln Val Ser Val Glu Ile Glu Trp Glu Leu Gln Lys
675 680 685

[0065] Glu Asn Ser Lys Arg Trp Asn Pro Glu Ile Gln Tyr Thr Ser Asn Tyr
690 695 700

Asn Lys Ser Val Asn Val Asp Phe Thr Val Asp Thr Asn Gly Val Tyr
705 710 715 720

Ser Glu Pro Arg Pro Ile Gly Thr Arg Tyr Leu Thr Arg Asn Leu
725 730 735

<210> 33

<211> 735

<212> PRT

<213> 腺相关病毒, hu. 26的衣壳蛋白

<400> 33

Met Ala Ala Asp Gly Tyr Leu Pro Asp Trp Leu Glu Asp Thr Leu Ser
1 5 10 15

Glu Gly Ile Arg Gln Trp Trp Lys Leu Lys Pro Gly Pro Pro Pro Pro
20 25 30

Lys Pro Ala Glu Arg His Lys Asp Asp Ser Arg Gly Leu Val Leu Pro
35 40 45

Gly Tyr Lys Tyr Leu Gly Pro Phe Asn Gly Leu Asp Lys Gly Glu Pro
50 55 60

	Val	Asn	Glu	Ala	Asp	Ala	Ala	Ala	Leu	Glu	His	Asp	Lys	Ala	Tyr	Asp	
	65					70					75					80	
	Arg	Gln	Leu	Asp	Ser	Gly	Asp	Asn	Pro	Tyr	Leu	Lys	Tyr	Asn	His	Ala	
				85						90					95		
	Asp	Ala	Glu	Phe	Gln	Glu	Arg	Leu	Lys	Glu	Asp	Thr	Ser	Phe	Gly	Gly	
				100					105						110		
	Asn	Leu	Gly	Arg	Ala	Val	Phe	Gln	Ala	Lys	Lys	Arg	Ile	Leu	Glu	Pro	
			115					120					125				
	Leu	Gly	Leu	Val	Glu	Glu	Pro	Val	Lys	Thr	Ala	Pro	Gly	Lys	Lys	Arg	
		130					135					140					
	Pro	Val	Glu	His	Ser	Pro	Ala	Glu	Pro	Asp	Ser	Ser	Ser	Gly	Thr	Gly	
	145					150				155						160	
	Lys	Ala	Gly	Gln	Gln	Pro	Ala	Arg	Lys	Arg	Leu	Asn	Phe	Gly	Gln	Thr	
				165					170						175		
	Gly	Asp	Ala	Asp	Ser	Val	Pro	Asp	Pro	Gln	Pro	Leu	Gly	Gln	Pro	Pro	
				180				185						190			
[0066]	Ala	Ala	Pro	Ser	Gly	Leu	Gly	Thr	Asn	Thr	Met	Ala	Ser	Gly	Ser	Gly	
			195					200					205				
	Ala	Pro	Met	Ala	Asp	Asn	Asn	Glu	Gly	Ala	Asp	Gly	Val	Gly	Asn	Ser	
		210					215					220					
	Ser	Gly	Asn	Trp	His	Cys	Asp	Ser	Thr	Trp	Met	Gly	Asp	Arg	Val	Ile	
	225					230					235					240	
	Thr	Thr	Ser	Thr	Arg	Thr	Trp	Ala	Leu	Pro	Thr	Tyr	Asn	Asn	His	Leu	
					245					250					255		
	Tyr	Lys	Gln	Ile	Ser	Ser	Gln	Ser	Gly	Ala	Ser	Asn	Asp	Asn	His	Tyr	
				260					265						270		
	Phe	Gly	Tyr	Ser	Thr	Pro	Trp	Gly	Tyr	Phe	Asp	Phe	Asn	Arg	Phe	His	
		275						280					285				
	Cys	His	Phe	Ser	Pro	Arg	Asp	Trp	Gln	Arg	Leu	Ile	Asn	Asn	Asn	Trp	
		290					295					300					
	Gly	Phe	Arg	Pro	Lys	Arg	Leu	Ser	Phe	Lys	Leu	Phe	Asn	Ile	Gln	Val	
	305					310					315					320	
	Lys	Glu	Val	Thr	Gln	Asn	Asp	Gly	Thr	Thr	Thr	Ile	Ala	Asn	Asn	Leu	
					325					330					335		

Thr Ser Thr Val Gln Val Phe Thr Asp Ser Glu Tyr Gln Leu Pro Tyr
 340 345 350
 Val Leu Gly Ser Ala His Gln Gly Cys Leu Pro Pro Phe Pro Ala Asp
 355 360 365
 Val Phe Met Val Pro Gln Tyr Gly Tyr Leu Thr Leu Asn Asn Gly Ser
 370 375 380
 Gln Ala Val Gly Arg Ser Ser Phe Tyr Cys Leu Glu Tyr Phe Pro Ser
 385 390 395 400
 Gln Met Leu Arg Thr Gly Asn Asn Phe Thr Phe Ser Tyr Thr Phe Glu
 405 410 415
 Asp Val Pro Phe His Ser Ser Tyr Ala His Ser Gln Ser Leu Asp Arg
 420 425 430
 Leu Met Asn Pro Leu Ile Asp Gln Tyr Leu Tyr Tyr Leu Ser Arg Thr
 435 440 445
 Asn Thr Pro Ser Gly Thr Thr Thr Met Ser Arg Leu Gln Phe Ser Gln
 450 455 460
 [0067] Ala Gly Ala Ser Asp Ile Arg Asp Gln Ser Arg Asn Trp Leu Pro Gly
 465 470 475 480
 Pro Cys Tyr Arg Gln Gln Arg Val Ser Lys Thr Ala Ala Asp Asn Asn
 485 490 495
 Asn Ser Asp Tyr Ser Trp Thr Gly Ala Thr Lys Tyr His Leu Asn Gly
 500 505 510
 Arg Asp Ser Leu Val Asn Pro Gly Pro Ala Met Ala Ser His Lys Asp
 515 520 525
 Asp Glu Glu Lys Tyr Phe Pro Gln Ser Gly Val Leu Ile Phe Gly Lys
 530 535 540
 Gln Asp Ser Gly Lys Thr Asn Val Asp Ile Glu Lys Val Met Ile Thr
 545 550 555 560
 Asp Glu Glu Glu Ile Arg Thr Thr Asn Pro Val Ala Thr Glu Gln Tyr
 565 570 575
 Gly Ser Val Ser Thr Asn Leu Gln Ser Gly Asn Thr Gln Ala Ala Thr
 580 585 590
 Ser Asp Val Asn Thr Gln Gly Val Leu Pro Gly Met Val Trp Gln Asp
 595 600 605

Arg Asp Val Tyr Leu Gln Gly Pro Ile Trp Ala Lys Ile Pro His Thr
610 615 620

Asp Gly His Phe His Pro Ser Pro Leu Met Gly Gly Phe Gly Leu Lys
625 630 635 640

His Pro Pro Pro Gln Ile Leu Ile Lys Asn Thr Pro Val Pro Ala Asn
645 650 655

Pro Ser Thr Thr Phe Ser Ala Ala Lys Phe Ala Ser Phe Ile Thr Gln
660 665 670

Tyr Ser Thr Gly Gln Val Ser Val Glu Ile Glu Trp Glu Leu Gln Lys
675 680 685

Glu Asn Ser Lys Arg Trp Asn Pro Glu Ile Gln Tyr Thr Ser Asn Tyr
690 695 700

Asn Lys Ser Val Asn Val Asp Phe Thr Val Asp Thr Asn Gly Val Tyr
705 710 715 720

Ser Glu Pro Arg Pro Ile Gly Thr Arg Tyr Leu Thr Arg Asn Leu
725 730 735

[0068]

<210> 34

<211> 738

<212> PRT

<213> 腺相关病毒, hu. 37的衣壳蛋白

<400> 34

Met Ala Ala Asp Gly Tyr Leu Pro Asp Trp Leu Glu Asp Asn Leu Ser
1 5 10 15

Glu Gly Ile Arg Glu Trp Trp Asp Leu Lys Pro Gly Ala Pro Lys Pro
20 25 30

Lys Ala Asn Gln Gln Lys Gln Asp Asp Gly Arg Gly Leu Val Leu Pro
35 40 45

Gly Tyr Lys Tyr Leu Gly Pro Phe Asn Gly Leu Asp Lys Gly Glu Pro
50 55 60

Val Asn Ala Ala Asp Ala Ala Ala Leu Glu His Asp Lys Ala Tyr Asp
65 70 75 80

Gln Gln Leu Lys Ala Gly Asp Asn Pro Tyr Leu Arg Tyr Asn His Ala
85 90 95

Asp Ala Glu Phe Gln Glu Arg Leu Gln Glu Asp Thr Ser Phe Gly Gly
100 105 110

Asn	Leu	Gly	Arg	Ala	Val	Phe	Gln	Ala	Lys	Lys	Arg	Val	Leu	Glu	Pro		
	115						120					125					
Leu	Gly	Leu	Val	Glu	Glu	Ala	Ala	Lys	Thr	Ala	Pro	Gly	Lys	Lys	Arg		
	130					135					140						
Pro	Val	Glu	Pro	Ser	Pro	Gln	Arg	Ser	Pro	Asp	Ser	Ser	Thr	Gly	Ile		
	145				150					155					160		
Gly	Lys	Lys	Gly	Gln	Gln	Pro	Ala	Lys	Lys	Arg	Leu	Asn	Phe	Gly	Gln		
				165					170					175			
Thr	Gly	Asp	Ser	Glu	Ser	Val	Pro	Asp	Pro	Gln	Pro	Ile	Gly	Glu	Pro		
			180					185					190				
Pro	Ala	Gly	Pro	Ser	Gly	Leu	Gly	Ser	Gly	Thr	Met	Ala	Ala	Gly	Gly		
		195					200					205					
Gly	Ala	Pro	Met	Ala	Asp	Asn	Asn	Glu	Gly	Ala	Asp	Gly	Val	Gly	Ser		
	210					215					220						
Ser	Ser	Gly	Asn	Trp	His	Cys	Asp	Ser	Thr	Trp	Leu	Gly	Asp	Arg	Val		
	225				230					235					240		
[0069]	Ile	Thr	Thr	Ser	Thr	Arg	Thr	Trp	Ala	Leu	Pro	Thr	Tyr	Asn	Asn	His	
					245					250				255			
Leu	Tyr	Lys	Gln	Ile	Ser	Asn	Gly	Thr	Ser	Gly	Gly	Ser	Thr	Asn	Asp		
			260					265					270				
Asn	Thr	Tyr	Phe	Gly	Tyr	Ser	Thr	Pro	Trp	Gly	Tyr	Phe	Asp	Phe	Asn		
		275					280					285					
Arg	Phe	His	Cys	His	Phe	Ser	Pro	Arg	Asp	Trp	Gln	Arg	Leu	Ile	Asn		
	290					295					300						
Asn	Asn	Trp	Gly	Phe	Arg	Pro	Lys	Arg	Leu	Ser	Phe	Lys	Leu	Phe	Asn		
	305				310					315				320			
Ile	Gln	Val	Lys	Glu	Val	Thr	Gln	Asn	Glu	Gly	Thr	Lys	Thr	Ile	Ala		
				325					330					335			
Asn	Asn	Leu	Thr	Ser	Thr	Ile	Gln	Val	Phe	Thr	Asp	Ser	Glu	Tyr	Gln		
			340				345						350				
Leu	Pro	Tyr	Val	Leu	Gly	Ser	Ala	His	Gln	Gly	Cys	Leu	Pro	Pro	Phe		
		355					360					365					
Pro	Ala	Asp	Val	Phe	Met	Ile	Pro	Gln	Tyr	Gly	Tyr	Leu	Thr	Leu	Asn		
	370					375					380						

	Asn Gly Ser Gln Ala Val Gly Arg Ser Ser Phe Tyr Cys Leu Glu Tyr	
	385 390 395 400	
	Phe Pro Ser Gln Met Leu Arg Thr Gly Asn Asn Phe Glu Phe Ser Tyr	
	405 410 415	
	Thr Phe Glu Asp Val Pro Phe His Ser Ser Tyr Ala His Ser Gln Ser	
	420 425 430	
	Leu Asp Arg Leu Met Asn Pro Leu Ile Asp Gln Tyr Leu Tyr Tyr Leu	
	435 440 445	
	Ser Arg Thr Gln Ser Thr Gly Gly Thr Gln Gly Thr Gln Gln Leu Leu	
	450 455 460	
	Phe Ser Gln Ala Gly Pro Ala Asn Met Ser Ala Gln Ala Lys Asn Trp	
	465 470 475 480	
	Leu Pro Gly Pro Cys Tyr Arg Gln Gln Arg Val Ser Thr Thr Leu Ser	
	485 490 495	
	Gln Asn Asn Asn Ser Asn Phe Ala Trp Thr Gly Ala Thr Lys Tyr His	
	500 505 510	
[0070]	Leu Asn Gly Arg Asp Ser Leu Val Asn Pro Gly Val Ala Met Ala Thr	
	515 520 525	
	His Lys Asp Asp Glu Glu Arg Phe Phe Pro Ser Ser Gly Val Leu Met	
	530 535 540	
	Phe Gly Lys Gln Gly Ala Gly Arg Asp Asn Val Asp Tyr Ser Ser Val	
	545 550 555 560	
	Met Leu Thr Ser Glu Glu Glu Ile Lys Thr Thr Asn Pro Val Ala Thr	
	565 570 575	
	Glu Gln Tyr Gly Val Val Ala Asp Asn Leu Gln Gln Thr Asn Thr Gly	
	580 585 590	
	Pro Ile Val Gly Asn Val Asn Ser Gln Gly Ala Leu Pro Gly Met Val	
	595 600 605	
	Trp Gln Asn Arg Asp Val Tyr Leu Gln Gly Pro Ile Trp Ala Lys Ile	
	610 615 620	
	Pro His Thr Asp Gly Asn Phe His Pro Ser Pro Leu Met Gly Gly Phe	
	625 630 635 640	
	Gly Leu Lys His Pro Pro Pro Gln Ile Leu Ile Lys Asn Thr Pro Val	
	645 650 655	

Pro Ala Asp Pro Pro Thr Thr Phe Ser Gln Ala Lys Leu Ala Ser Phe
660 665 670

Ile Thr Gln Tyr Ser Thr Gly Gln Val Ser Val Glu Ile Glu Trp Glu
675 680 685

Leu Gln Lys Glu Asn Ser Lys Arg Trp Asn Pro Glu Ile Gln Tyr Thr
690 695 700

Ser Asn Tyr Tyr Lys Ser Thr Asn Val Asp Phe Ala Val Asn Thr Glu
705 710 715 720

Gly Thr Tyr Ser Glu Pro Arg Pro Ile Gly Thr Arg Tyr Leu Thr Arg
725 730 735

Asn Leu

<210> 35

<211> 734

<212> PRT

<213> 腺相关病毒, hu. 53的衣壳蛋白

<400> 35

Met Ala Ala Asp Gly Tyr Leu Pro Asp Trp Leu Glu Asp Thr Leu Ser
1 5 10 15

[0071]

Glu Gly Ile Arg Gln Trp Trp Lys Leu Lys Pro Gly Pro Pro Pro Pro
20 25 30

Lys Pro Ala Glu Arg His Lys Asp Asp Ser Arg Gly Leu Val Leu Pro
35 40 45

Gly Tyr Lys Tyr Leu Gly Pro Phe Asn Gly Leu Asp Lys Gly Glu Pro
50 55 60

Val Asn Glu Ala Asp Ala Ala Ala Leu Glu His Asp Lys Ala Tyr Asp
65 70 75 80

Arg Gln Leu Asp Ser Gly Asp Asn Pro Tyr Leu Lys Tyr Asn His Ala
85 90 95

Asp Ala Glu Phe Gln Glu Arg Leu Lys Glu Asp Thr Ser Phe Gly Gly
100 105 110

Asn Leu Gly Arg Ala Val Phe Gln Ala Lys Lys Arg Val Leu Glu Pro
115 120 125

Leu Gly Leu Val Glu Glu Pro Val Lys Thr Ala Pro Gly Lys Lys Arg
130 135 140

Pro Val Glu His Ser Pro Ala Glu Pro Asp Ser Ser Ser Gly Thr Gly

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

[0072]

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

[0073]

690	695	700
Lys Ser Val Asn Val Asp Phe Thr Val Asp Thr Asn Gly Val Tyr Ser 705 710 715 720		
Glu Pro Arg Pro Ile Gly Thr Arg Tyr Leu Thr Arg Asn Leu 725 730		
<210> 36 <211> 738 <212> PRT <213> 猕猴腺相关病毒, rh. 39的衣壳蛋白 <400> 36		
Met Ala Ala Asp Gly Tyr Leu Pro Asp Trp Leu Glu Asp Asn Leu Ser 1 5 10 15		
Glu Gly Ile Arg Glu Trp Trp Asp Leu Lys Pro Gly Ala Pro Lys Pro 20 25 30		
Lys Ala Asn Gln Gln Lys Gln Asp Asp Gly Arg Gly Leu Val Leu Pro 35 40 45		
Gly Tyr Lys Tyr Leu Gly Pro Phe Asn Gly Leu Asp Lys Gly Glu Pro 50 55 60		
Val Asn Ala Ala Asp Ala Ala Ala Leu Glu His Asp Lys Ala Tyr Asp 65 70 75 80		
Gln Gln Leu Lys Ala Gly Asp Asn Pro Tyr Leu Arg Tyr Asn His Ala 85 90 95		
Asp Ala Glu Phe Gln Glu Arg Leu Gln Glu Asp Thr Ser Phe Gly Gly 100 105 110		
Asn Leu Gly Arg Ala Val Phe Gln Ala Lys Lys Arg Val Leu Glu Pro 115 120 125		
Leu Gly Leu Val Glu Glu Ala Ala Lys Thr Ala Pro Gly Lys Lys Arg 130 135 140		
Pro Val Glu Pro Ser Pro Gln Arg Ser Pro Asp Ser Ser Thr Gly Ile 145 150 155 160		
Gly Lys Lys Gly Gln Gln Pro Ala Lys Lys Arg Leu Asn Phe Gly Gln 165 170 175		
Thr Gly Asp Ser Glu Ser Val Pro Asp Pro Gln Pro Ile Gly Glu Pro 180 185 190		
Pro Ala Gly Pro Ser Gly Leu Gly Ser Gly Thr Met Ala Ala Gly Gly 195 200 205		

[0074]

Gly Ala Pro Met Ala Asp Asn Asn Glu Gly Ala Asp Gly Val Gly Ser
 210 215 220
 Ser Ser Gly Asn Trp His Cys Asp Ser Thr Trp Leu Gly Asp Arg Val
 225 230 235 240
 Ile Thr Thr Ser Thr Arg Thr Trp Ala Leu Pro Thr Tyr Asn Asn His
 245 250 255
 Leu Tyr Lys Gln Ile Ser Asn Gly Thr Ser Gly Gly Ser Thr Asn Asp
 260 265 270
 Asn Thr Tyr Phe Gly Tyr Ser Thr Pro Trp Gly Tyr Phe Asp Phe Asn
 275 280 285
 Arg Phe His Cys His Phe Ser Pro Arg Asp Trp Gln Arg Leu Ile Asn
 290 295 300
 Asn Asn Trp Gly Phe Arg Pro Lys Arg Leu Ser Phe Lys Leu Phe Asn
 305 310 315 320
 Ile Gln Val Lys Glu Val Thr Gln Asn Glu Gly Thr Lys Thr Ile Ala
 325 330 335
 [0075] Asn Asn Leu Thr Ser Thr Ile Gln Val Phe Thr Asp Ser Glu Tyr Gln
 340 345 350
 Leu Pro Tyr Val Leu Gly Ser Ala His Gln Gly Cys Leu Pro Pro Phe
 355 360 365
 Pro Ala Asp Val Phe Met Ile Pro Gln Tyr Gly Tyr Leu Thr Leu Asn
 370 375 380
 Asn Gly Ser Gln Ala Val Gly Arg Ser Ser Phe Tyr Cys Leu Glu Tyr
 385 390 395 400
 Phe Pro Ser Gln Met Leu Arg Thr Gly Asn Asn Phe Glu Phe Ser Tyr
 405 410 415
 Thr Phe Glu Asp Val Pro Phe His Ser Ser Tyr Ala His Ser Gln Ser
 420 425 430
 Leu Asp Arg Leu Met Asn Pro Leu Ile Asp Gln Tyr Leu Tyr Tyr Leu
 435 440 445
 Ser Arg Thr Gln Ser Thr Gly Gly Thr Gln Gly Thr Gln Gln Leu Leu
 450 455 460
 Phe Ser Gln Ala Gly Pro Ala Asn Met Ser Ala Gln Ala Lys Asn Trp
 465 470 475 480

Leu Pro Gly Pro Cys Tyr Arg Gln Gln Arg Val Ser Thr Thr Leu Ser
 485 490 495

Gln Asn Asn Asn Ser Asn Phe Ala Trp Thr Gly Ala Thr Lys Tyr His
 500 505 510

Leu Asn Gly Arg Asp Ser Leu Val Asn Pro Gly Val Ala Met Ala Thr
 515 520 525

His Lys Asp Asp Glu Glu Arg Phe Phe Pro Ser Ser Gly Val Leu Met
 530 535 540

Phe Gly Lys Gln Gly Ala Gly Arg Asp Asn Val Asp Tyr Ser Ser Val
 545 550 555 560

Met Leu Thr Ser Glu Glu Glu Ile Lys Thr Thr Asn Pro Val Ala Thr
 565 570 575

Glu Gln Tyr Gly Val Val Ala Asp Asn Leu Gln Gln Thr Asn Thr Gly
 580 585 590

Pro Ile Val Gly Asn Val Asn Ser Gln Gly Ala Leu Pro Gly Met Val
 595 600 605

[0076] Trp Gln Asn Arg Asp Val Tyr Leu Gln Gly Pro Ile Trp Ala Lys Ile
 610 615 620

Pro His Thr Asp Gly Asn Phe His Pro Ser Pro Leu Met Gly Gly Phe
 625 630 635 640

Gly Leu Lys His Pro Pro Pro Gln Ile Leu Ile Lys Asn Thr Pro Val
 645 650 655

Pro Ala Asp Pro Pro Thr Thr Phe Ser Gln Ala Lys Leu Ala Ser Phe
 660 665 670

Ile Thr Gln Tyr Ser Thr Gly Gln Val Ser Val Glu Ile Glu Trp Glu
 675 680 685

Leu Gln Lys Glu Asn Ser Lys Arg Trp Asn Pro Glu Ile Gln Tyr Thr
 690 695 700

Ser Asn Tyr Tyr Lys Ser Thr Asn Val Asp Phe Ala Val Asn Thr Glu
 705 710 715 720

Gly Thr Tyr Ser Glu Pro Arg Pro Ile Gly Thr Arg Tyr Leu Thr Arg
 725 730 735

Asn Leu

<210> 37
 <211> 736
 <212> PRT
 <213> 猕猴腺相关病毒, rh. 43的衣壳蛋白

<400> 37

Met Ala Ala Asp Gly Tyr Leu Pro Asp Trp Leu Glu Asp Asn Leu Ser
 1 5 10 15

Glu Gly Ile Arg Glu Trp Trp Asp Leu Lys Pro Gly Ala Pro Lys Pro
 20 25 30

Lys Ala Asn Gln Gln Lys Gln Asp Asp Gly Arg Gly Leu Val Leu Pro
 35 40 45

Gly Tyr Lys Tyr Leu Gly Pro Phe Asn Gly Leu Asp Lys Gly Glu Pro
 50 55 60

Val Asn Ala Ala Asp Ala Ala Ala Leu Glu His Asp Lys Ala Tyr Asp
 65 70 75 80

Gln Gln Leu Glu Ala Gly Asp Asn Pro Tyr Leu Arg Tyr Asn His Ala
 85 90 95

[0077]

Asp Ala Glu Phe Gln Glu Arg Leu Gln Glu Asp Thr Ser Phe Gly Gly
 100 105 110

Asn Leu Gly Arg Ala Val Phe Gln Ala Lys Lys Arg Val Leu Glu Pro
 115 120 125

Leu Gly Leu Val Glu Glu Gly Ala Lys Thr Ala Pro Gly Lys Lys Arg
 130 135 140

Pro Val Glu Gln Ser Pro Gln Glu Pro Asp Ser Ser Ser Gly Ile Gly
 145 150 155 160

Lys Lys Gly Gln Gln Pro Ala Arg Lys Arg Leu Asn Phe Gly Gln Thr
 165 170 175

Gly Asp Ser Glu Ser Val Pro Asp Pro Gln Pro Leu Gly Glu Pro Pro
 180 185 190

Ala Ala Pro Ser Gly Val Gly Pro Asn Thr Met Ala Ala Gly Gly Gly
 195 200 205

Ala Pro Met Ala Asp Asn Asn Glu Gly Ala Asp Gly Val Gly Ser Ser
 210 215 220

Ser Gly Asn Trp His Cys Asp Ser Thr Trp Leu Gly Asp Arg Val Ile
 225 230 235 240

	Thr	Thr	Ser	Thr	Arg	Thr	Trp	Ala	Leu	Pro	Thr	Tyr	Asn	Asn	His	Leu	
					245					250					255		
	Tyr	Lys	Gln	Ile	Ser	Asn	Gly	Thr	Ser	Gly	Gly	Ala	Thr	Asn	Asp	Asn	
				260					265					270			
	Thr	Tyr	Phe	Gly	Tyr	Ser	Thr	Pro	Trp	Gly	Tyr	Phe	Asp	Phe	Asn	Arg	
			275					280					285				
	Phe	His	Cys	His	Phe	Ser	Pro	Arg	Asp	Trp	Gln	Arg	Leu	Ile	Asn	Asn	
	290						295				300						
	Asn	Trp	Gly	Phe	Arg	Pro	Lys	Arg	Leu	Ser	Phe	Lys	Leu	Phe	Asn	Ile	
	305				310					315						320	
	Gln	Val	Lys	Glu	Val	Thr	Gln	Asn	Glu	Gly	Thr	Lys	Thr	Ile	Ala	Asn	
				325						330					335		
	Asn	Leu	Thr	Ser	Thr	Ile	Gln	Val	Phe	Thr	Asp	Ser	Glu	Tyr	Gln	Leu	
				340					345					350			
	Pro	Tyr	Val	Leu	Gly	Ser	Ala	His	Gln	Gly	Cys	Leu	Pro	Pro	Phe	Pro	
			355				360					365					
[0078]	Ala	Asp	Val	Phe	Met	Ile	Pro	Gln	Tyr	Gly	Tyr	Leu	Thr	Leu	Asn	Asn	
	370					375						380					
	Gly	Ser	Gln	Ala	Val	Gly	Arg	Ser	Ser	Phe	Tyr	Cys	Leu	Glu	Tyr	Phe	
	385					390				395						400	
	Pro	Ser	Gln	Met	Leu	Arg	Thr	Gly	Asn	Asn	Phe	Gln	Phe	Thr	Tyr	Thr	
				405					410						415		
	Phe	Glu	Asp	Val	Pro	Phe	His	Ser	Ser	Tyr	Ala	His	Ser	Gln	Ser	Leu	
				420				425						430			
	Asp	Arg	Leu	Met	Asn	Pro	Leu	Ile	Asp	Gln	Tyr	Leu	Tyr	Tyr	Leu	Ser	
			435				440					445					
	Arg	Thr	Gln	Thr	Thr	Gly	Gly	Thr	Ala	Asn	Thr	Gln	Thr	Leu	Gly	Phe	
	450					455						460					
	Ser	Gln	Gly	Gly	Pro	Asn	Thr	Met	Ala	Asn	Gln	Ala	Lys	Asn	Trp	Leu	
	465				470					475						480	
	Pro	Gly	Pro	Cys	Tyr	Arg	Gln	Gln	Arg	Val	Ser	Thr	Thr	Thr	Gly	Gln	
				485					490						495		
	Asn	Asn	Asn	Ser	Asn	Phe	Ala	Trp	Thr	Ala	Gly	Thr	Lys	Tyr	His	Leu	
				500				505						510			

Asn Gly Arg Asn Ser Leu Ala Asn Pro Gly Ile Ala Met Ala Thr His
515 520 525

Lys Asp Asp Glu Glu Arg Phe Phe Pro Val Thr Gly Ser Cys Phe Trp
530 535 540

Gln Gln Asn Ala Ala Arg Asp Asn Ala Asp Tyr Ser Asp Val Met Leu
545 550 555 560

Thr Ser Glu Glu Glu Ile Lys Thr Thr Asn Pro Val Ala Thr Glu Glu
565 570 575

Tyr Gly Ile Val Ala Asp Asn Leu Gln Gln Gln Asn Thr Ala Pro Gln
580 585 590

Ile Gly Thr Val Asn Ser Gln Gly Ala Leu Pro Gly Met Val Trp Gln
595 600 605

Asn Arg Asp Val Tyr Leu Gln Gly Pro Ile Trp Ala Lys Ile Pro His
610 615 620

Thr Asp Gly Asn Phe His Pro Ser Pro Leu Met Gly Gly Phe Gly Leu
625 630 635 640

[0079] Lys His Pro Pro Pro Gln Ile Leu Ile Lys Asn Thr Pro Val Pro Ala
645 650 655

Asp Pro Pro Thr Thr Phe Asn Gln Ser Lys Leu Asn Ser Phe Ile Thr
660 665 670

Gln Tyr Ser Thr Gly Gln Val Ser Val Glu Ile Glu Trp Glu Leu Gln
675 680 685

Lys Glu Asn Ser Lys Arg Trp Asn Pro Glu Ile Gln Tyr Thr Ser Asn
690 695 700

Tyr Tyr Lys Ser Thr Ser Val Asp Phe Ala Val Asn Thr Glu Gly Val
705 710 715 720

Tyr Ser Glu Pro Arg Pro Ile Gly Thr Arg Tyr Leu Thr Arg Asn Leu
725 730 735

<210> 38

<211> 738

<212> PRT

<213> 猕猴腺相关病毒, rh.46的衣壳蛋白

<400> 38

Met Ala Ala Asp Gly Tyr Leu Pro Asp Trp Leu Glu Asp Asn Leu Ser
1 5 10 15

Glu Gly Ile Arg Glu Trp Trp Asp Leu Lys Pro Gly Ala Pro Lys Pro
 20 25 30
 Lys Ala Asn Gln Gln Lys Gln Asp Asp Gly Arg Gly Leu Val Leu Pro
 35 40 45
 Gly Tyr Lys Tyr Leu Gly Pro Phe Asn Gly Leu Asp Lys Gly Glu Pro
 50 55 60
 Val Asn Ala Ala Asp Ala Ala Ala Leu Glu His Asp Lys Ala Tyr Asp
 65 70 75 80
 Gln Gln Leu Lys Ala Gly Asp Asn Pro Tyr Leu Arg Tyr Asn His Ala
 85 90 95
 Asp Ala Glu Phe Gln Glu Arg Leu Gln Glu Asp Thr Ser Phe Gly Gly
 100 105 110
 Asn Leu Gly Arg Ala Val Phe Gln Ala Lys Lys Arg Val Leu Glu Pro
 115 120 125
 Leu Gly Leu Val Glu Glu Gly Ala Lys Thr Ala Pro Gly Lys Lys Arg
 130 135 140
 [0080] Pro Val Glu Pro Ser Pro Gln Arg Ser Pro Asp Ser Ser Thr Gly Ile
 145 150 155 160
 Gly Lys Lys Gly Gln Gln Pro Ala Arg Lys Arg Leu Asn Phe Gly Gln
 165 170 175
 Thr Gly Asp Ser Glu Ser Val Pro Asp Pro Gln Pro Ile Gly Glu Pro
 180 185 190
 Pro Ala Ala Pro Ser Ser Val Gly Ser Gly Thr Met Ala Ala Gly Gly
 195 200 205
 Gly Ala Pro Met Ala Asp Asn Asn Glu Gly Ala Asp Gly Val Gly Ser
 210 215 220
 Ser Ser Gly Asn Trp His Cys Asp Ser Thr Trp Leu Gly Asp Arg Val
 225 230 235 240
 Ile Thr Thr Ser Thr Arg Thr Trp Ala Leu Pro Thr Tyr Asn Asn His
 245 250 255
 Leu Tyr Lys Gln Ile Ser Asn Gly Thr Ser Gly Gly Ser Thr Asn Asp
 260 265 270
 Asn Thr Tyr Phe Gly Tyr Ser Thr Pro Trp Gly Tyr Phe Asp Phe Asn
 275 280 285

	Arg	Phe	His	Cys	His	Phe	Ser	Pro	Arg	Asp	Trp	Gln	Arg	Leu	Ile	Asn	
	290						295					300					
	Asn	Asn	Trp	Gly	Phe	Arg	Pro	Lys	Arg	Leu	Ser	Phe	Lys	Leu	Phe	Asn	
	305					310					315					320	
	Ile	Gln	Val	Lys	Glu	Val	Thr	Gln	Asn	Glu	Gly	Thr	Lys	Thr	Ile	Ala	
					325					330					335		
	Asn	Asn	Leu	Thr	Ser	Thr	Ile	Gln	Val	Phe	Thr	Asp	Ser	Glu	Tyr	Gln	
				340					345					350			
	Leu	Pro	Tyr	Val	Leu	Gly	Ser	Ala	His	Gln	Gly	Cys	Leu	Pro	Pro	Phe	
			355					360					365				
	Pro	Ala	Asp	Val	Phe	Met	Ile	Pro	Gln	Tyr	Gly	Tyr	Leu	Thr	Leu	Asn	
	370						375					380					
	Asn	Gly	Ser	Gln	Ala	Val	Gly	Arg	Ser	Ser	Phe	Tyr	Cys	Leu	Glu	Tyr	
	385					390					395					400	
	Phe	Pro	Ser	Gln	Met	Leu	Arg	Thr	Gly	Asn	Asn	Phe	Ser	Phe	Ser	Tyr	
					405					410					415		
[0081]	Thr	Phe	Glu	Asp	Val	Pro	Phe	His	Ser	Ser	Tyr	Ala	His	Ser	Gln	Ser	
				420					425					430			
	Leu	Asp	Arg	Leu	Met	Asn	Pro	Leu	Ile	Asp	Gln	Tyr	Leu	Tyr	Tyr	Leu	
			435					440					445				
	Ser	Arg	Thr	Gln	Ser	Thr	Gly	Gly	Thr	Ala	Gly	Thr	Gln	Gln	Leu	Leu	
		450					455					460					
	Phe	Ser	Gln	Ala	Gly	Pro	Ser	Asn	Met	Ser	Ala	Gln	Ala	Arg	Asn	Trp	
	465					470					475					480	
	Leu	Pro	Gly	Pro	Cys	Tyr	Arg	Gln	Gln	Arg	Val	Ser	Thr	Thr	Leu	Ser	
					485					490					495		
	Gln	Asn	Asn	Asn	Ser	Asn	Phe	Ala	Trp	Thr	Gly	Ala	Thr	Lys	Tyr	His	
					500				505					510			
	Leu	Asn	Gly	Arg	Asp	Ser	Leu	Val	Asn	Pro	Gly	Val	Ala	Met	Ala	Thr	
		515						520					525				
	Asn	Lys	Asp	Asp	Glu	Asp	Arg	Phe	Phe	Pro	Ser	Ser	Gly	Ile	Leu	Met	
		530					535					540					
	Phe	Gly	Lys	Gln	Gly	Ala	Gly	Lys	Asp	Asn	Val	Asp	Tyr	Ser	Asn	Val	
	545					550					555					560	

Met Leu Thr Ser Glu Glu Glu Ile Lys Ala Thr Asn Pro Val Ala Thr
565 570 575

Glu Gln Tyr Gly Val Val Ala Asp Asn Leu Gln Gln Gln Asn Thr Ala
580 585 590

Pro Ile Val Gly Ala Val Asn Ser Gln Gly Ala Leu Pro Gly Met Val
595 600 605

Trp Gln Asn Arg Asp Val Tyr Leu Gln Gly Pro Ile Trp Ala Lys Ile
610 615 620

Pro His Thr Asp Gly Asn Phe His Pro Ser Pro Leu Met Gly Gly Phe
625 630 635 640

Gly Leu Lys His Pro Pro Pro Gln Ile Leu Ile Lys Asn Thr Pro Val
645 650 655

Pro Ala Asp Pro Pro Thr Ala Phe Asn Gln Ala Lys Leu Asn Ser Phe
660 665 670

Ile Thr Gln Tyr Ser Thr Gly Gln Val Ser Val Glu Ile Glu Trp Glu
675 680 685

Leu Gln Lys Glu Asn Ser Lys Arg Trp Asn Pro Glu Ile Gln Tyr Thr
690 695 700

[0082]

Ser Asn Tyr Tyr Lys Ser Thr Asn Val Asp Phe Ala Val Asn Thr Glu
705 710 715 720

Gly Val Tyr Ser Glu Pro Arg Pro Ile Gly Thr Arg Tyr Leu Thr Arg
725 730 735

Asn Leu

<210> 39

<211> 738

<212> PRT

<213> 猕猴腺相关病毒, rh. 2的衣壳蛋白

<400> 39

Met Ala Ala Asp Gly Tyr Leu Pro Asp Trp Leu Glu Asp Asn Leu Ser
1 5 10 15

Glu Gly Ile Arg Glu Trp Trp Asp Leu Lys Pro Gly Ala Pro Lys Pro
20 25 30

Lys Ala Asn Gln Gln Lys Gln Asp Asp Gly Arg Gly Leu Val Leu Pro
35 40 45

Gly Tyr Lys Tyr Leu Gly Pro Phe Asn Gly Leu Asp Lys Gly Glu Pro

50	55	60
Val Asn Ala Ala Asp	Ala Ala Ala Leu Glu His Asp Lys Ala Tyr Asp	
65	70	75
Gln Gln Leu Lys Ala Gly Asp Asn Pro Tyr Leu Arg Tyr Asn His Ala		
	85	90
Asp Ala Glu Phe Gln Glu Arg Leu Gln Glu Asp Thr Ser Phe Gly Gly		
	100	105
Asn Leu Gly Arg Ala Val Phe Gln Ala Lys Lys Arg Val Leu Glu Pro		
	115	120
Leu Gly Leu Val Glu Glu Gly Ala Lys Thr Ala Pro Gly Lys Lys Arg		
	130	135
Pro Val Glu Pro Ser Pro Gln Arg Ser Pro Asp Ser Ser Thr Gly Ile		
	145	150
Gly Lys Lys Gly His Gln Pro Ala Arg Lys Arg Leu Asn Phe Gly Gln		
	165	170
Thr Gly Asp Ser Glu Ser Val Pro Asp Pro Gln Pro Ile Gly Glu Pro		
	180	185
Pro Ala Gly Pro Ser Gly Leu Gly Ser Gly Thr Met Ala Ala Gly Gly		
	195	200
Gly Ala Pro Met Ala Asp Asn Asn Glu Gly Ala Asp Gly Val Gly Ser		
	210	215
Ser Ser Gly Asn Trp His Cys Asp Ser Thr Trp Leu Gly Asp Arg Val		
	225	230
Ile Thr Thr Ser Thr Arg Thr Trp Ala Leu Pro Thr Tyr Asn Asn His		
	245	250
Leu Tyr Lys Gln Ile Ser Asn Gly Thr Ser Gly Gly Ser Thr Asn Asp		
	260	265
Asn Thr Tyr Phe Gly Tyr Ser Thr Pro Trp Gly Tyr Phe Asp Phe Asn		
	275	280
Arg Phe His Cys His Phe Ser Pro Arg Asp Trp Gln Arg Leu Ile Asn		
	290	295
Asn Asn Trp Gly Phe Arg Pro Lys Arg Leu Asn Phe Lys Leu Phe Asn		
	305	310
Ile Gln Val Lys Glu Val Thr Gln Asn Glu Gly Thr Lys Thr Ile Ala		

[0083]

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

[0084]

595	600	605
Trp Gln Asn Arg Asp Val Tyr Leu Gln Gly Pro Ile Trp Ala Lys Ile		
610	615	620
Pro His Thr Asp Gly Asn Phe His Pro Ser Pro Leu Met Gly Gly Phe		
625	630	635
Gly Leu Lys His Pro Pro Pro Gln Ile Leu Val Lys Asn Thr Pro Val		
	645	650
		655
Pro Ala Asp Pro Pro Thr Thr Phe Ser Gln Ala Lys Leu Ala Ser Phe		
	660	665
		670
Ile Thr Gln Tyr Ser Thr Gly Gln Val Ser Val Glu Ile Glu Trp Glu		
	675	680
		685
Leu Gln Lys Glu Asn Ser Lys Arg Trp Asn Pro Glu Ile Gln Tyr Thr		
	690	695
		700
Ser Asn Tyr Tyr Lys Ser Thr Asn Val Asp Phe Ala Val Asn Thr Glu		
705	710	715
		720
Gly Thr Tyr Ser Glu Pro Arg Pro Ile Gly Thr Arg Tyr Leu Thr Arg		
	725	730
		735

[0085]

Asn Leu

<210> 40
 <211> 729
 <212> PRT
 <213> 猕猴腺相关病毒, rh.37的衣壳蛋白

<400> 40

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

Ile Pro Gln Tyr Gly Tyr Leu Thr Leu Asn Asn Gly Ser Gln Ser Val
 370 375 380
 Gly Arg Ser Ser Phe Tyr Cys Leu Glu Tyr Phe Pro Ser Gln Met Leu
 385 390 395 400
 Arg Thr Gly Asn Asn Phe Glu Phe Ser Tyr Ser Phe Glu Asp Val Pro
 405 410 415
 Phe His Ser Ser Tyr Ala His Ser Gln Ser Leu Asp Arg Leu Met Asn
 420 425 430
 Pro Leu Ile Asp Gln Tyr Leu Tyr Tyr Leu Ala Arg Thr Gln Ser Thr
 435 440 445
 Thr Gly Ser Thr Arg Glu Leu Gln Phe His Gln Ala Gly Pro Asn Thr
 450 455 460
 Met Ala Glu Gln Ser Lys Asn Trp Leu Pro Gly Pro Cys Tyr Arg Gln
 465 470 475 480
 Gln Arg Leu Ser Lys Asn Leu Asp Phe Asn Asn Asn Ser Asn Phe Ala
 485 490 495
 [0087] Trp Thr Ala Ala Thr Lys Tyr His Leu Asn Gly Arg Asn Ser Leu Thr
 500 505 510
 Asn Pro Gly Ile Pro Met Ala Thr Asn Lys Asp Asp Glu Asp Gln Phe
 515 520 525
 Phe Pro Ile Asn Gly Val Leu Val Phe Gly Lys Thr Gly Ala Ala Asn
 530 535 540
 Lys Thr Thr Leu Glu Asn Val Leu Met Thr Ser Glu Glu Glu Ile Lys
 545 550 555 560
 Thr Thr Asn Pro Val Ala Thr Glu Glu Tyr Gly Val Val Ser Ser Asn
 565 570 575
 Leu Gln Ser Ser Thr Ala Gly Pro Gln Ser Gln Thr Ile Asn Ser Gln
 580 585 590
 Gly Ala Leu Pro Gly Met Val Trp Gln Asn Arg Asp Val Tyr Leu Gln
 595 600 605
 Gly Pro Ile Trp Ala Lys Ile Pro His Thr Asp Gly Asn Phe His Pro
 610 615 620
 Ser Pro Leu Met Gly Gly Phe Gly Leu Glu His Pro Pro Pro Gln Ile
 625 630 635 640

Leu Ile Lys Asn Thr Pro Val Pro Ala Asn Pro Pro Glu Val Phe Thr
645 650 655

Pro Ala Lys Phe Ala Ser Phe Ile Thr Gln Tyr Ser Thr Gly Gln Val
660 665 670

Ser Val Glu Ile Glu Trp Glu Leu Gln Lys Glu Asn Ser Lys Arg Trp
675 680 685

Asn Pro Glu Ile Gln Tyr Thr Ser Asn Tyr Ala Lys Ser Asn Asn Val
690 695 700

Glu Phe Ala Val Asn Pro Asp Gly Val Tyr Thr Glu Pro Arg Pro Ile
705 710 715 720

Gly Thr Arg Tyr Leu Thr Arg Asn Leu
725

<210> 41

<211> 736

<212> PRT

<213> 猕猴腺相关病毒, rh. 8的衣壳蛋白

<400> 41

[0088]

Met Ala Ala Asp Gly Tyr Leu Pro Asp Trp Leu Glu Asp Asn Leu Ser
1 5 10 15

Glu Gly Ile Arg Glu Trp Trp Asp Leu Lys Pro Gly Ala Pro Lys Pro
20 25 30

Lys Ala Asn Gln Gln Lys Gln Asp Asp Gly Arg Gly Leu Val Leu Pro
35 40 45

Gly Tyr Lys Tyr Leu Gly Pro Phe Asn Gly Leu Asp Lys Gly Glu Pro
50 55 60

Val Asn Ala Ala Asp Ala Ala Ala Leu Glu His Asp Lys Ala Tyr Asp
65 70 75 80

Gln Gln Leu Lys Ala Gly Asp Asn Pro Tyr Leu Arg Tyr Asn His Ala
85 90 95

Asp Ala Glu Phe Gln Glu Arg Leu Gln Glu Asp Thr Ser Phe Gly Gly
100 105 110

Asn Leu Gly Arg Ala Val Phe Gln Ala Lys Lys Arg Val Leu Glu Pro
115 120 125

Leu Gly Leu Val Glu Glu Gly Ala Lys Thr Ala Pro Gly Lys Lys Arg
130 135 140

	Pro	Val	Glu	Gln	Ser	Pro	Gln	Glu	Pro	Asp	Ser	Ser	Ser	Gly	Ile	Gly	
	145					150					155					160	
	Lys	Thr	Gly	Gln	Gln	Pro	Ala	Lys	Lys	Arg	Leu	Asn	Phe	Gly	Gln	Thr	
				165						170					175		
	Gly	Asp	Ser	Glu	Ser	Val	Pro	Asp	Pro	Gln	Pro	Leu	Gly	Glu	Pro	Pro	
				180					185					190			
	Ala	Ala	Pro	Ser	Gly	Leu	Gly	Pro	Asn	Thr	Met	Ala	Ser	Gly	Gly	Gly	
			195					200					205				
	Ala	Pro	Met	Ala	Asp	Asn	Asn	Glu	Gly	Ala	Asp	Gly	Val	Gly	Asn	Ser	
		210				215						220					
	Ser	Gly	Asn	Trp	His	Cys	Asp	Ser	Thr	Trp	Leu	Gly	Asp	Arg	Val	Ile	
	225					230					235					240	
	Thr	Thr	Ser	Thr	Arg	Thr	Trp	Ala	Leu	Pro	Thr	Tyr	Asn	Asn	His	Leu	
					245					250					255		
	Tyr	Lys	Gln	Ile	Ser	Asn	Gly	Thr	Ser	Gly	Gly	Ser	Thr	Asn	Asp	Asn	
				260					265					270			
[0089]	Thr	Tyr	Phe	Gly	Tyr	Ser	Thr	Pro	Trp	Gly	Tyr	Phe	Asp	Phe	Asn	Arg	
			275					280					285				
	Phe	His	Cys	His	Phe	Ser	Pro	Arg	Asp	Trp	Gln	Arg	Leu	Ile	Asn	Asn	
		290					295					300					
	Asn	Trp	Gly	Phe	Arg	Pro	Lys	Arg	Leu	Asn	Phe	Lys	Leu	Phe	Asn	Ile	
	305					310					315					320	
	Gln	Val	Lys	Glu	Val	Thr	Thr	Asn	Glu	Gly	Thr	Lys	Thr	Ile	Ala	Asn	
				325						330					335		
	Asn	Leu	Thr	Ser	Thr	Val	Gln	Val	Phe	Thr	Asp	Ser	Glu	Tyr	Gln	Leu	
				340					345					350			
	Pro	Tyr	Val	Leu	Gly	Ser	Ala	His	Gln	Gly	Cys	Leu	Pro	Pro	Phe	Pro	
			355					360					365				
	Ala	Asp	Val	Phe	Met	Val	Pro	Gln	Tyr	Gly	Tyr	Leu	Thr	Leu	Asn	Asn	
		370					375					380					
	Gly	Ser	Gln	Ala	Leu	Gly	Arg	Ser	Ser	Phe	Tyr	Cys	Leu	Glu	Tyr	Phe	
	385					390					395					400	
	Pro	Ser	Gln	Met	Leu	Arg	Thr	Gly	Asn	Asn	Phe	Gln	Phe	Ser	Tyr	Thr	
				405						410					415		

	Phe	Glu	Asp	Val	Pro	Phe	His	Ser	Ser	Tyr	Ala	His	Ser	Gln	Ser	Leu	
				420					425						430		
	Asp	Arg	Leu	Met	Asn	Pro	Leu	Ile	Asp	Gln	Tyr	Leu	Tyr	Tyr	Leu	Val	
			435					440					445				
	Arg	Thr	Gln	Thr	Thr	Gly	Thr	Gly	Gly	Thr	Gln	Thr	Leu	Ala	Phe	Ser	
		450					455					460					
	Gln	Ala	Gly	Pro	Ser	Ser	Met	Ala	Asn	Gln	Ala	Arg	Asn	Trp	Val	Pro	
	465					470					475					480	
	Gly	Pro	Cys	Tyr	Arg	Gln	Gln	Arg	Val	Ser	Thr	Thr	Thr	Asn	Gln	Asn	
					485					490					495		
	Asn	Asn	Ser	Asn	Phe	Ala	Trp	Thr	Gly	Ala	Ala	Lys	Phe	Lys	Leu	Asn	
				500					505					510			
	Gly	Arg	Asp	Ser	Leu	Met	Asn	Pro	Gly	Val	Ala	Met	Ala	Ser	His	Lys	
			515					520					525				
	Asp	Asp	Asp	Asp	Arg	Phe	Phe	Pro	Ser	Ser	Gly	Val	Leu	Ile	Phe	Gly	
		530					535					540					
[0090]	Lys	Gln	Gly	Ala	Gly	Asn	Asp	Gly	Val	Asp	Tyr	Ser	Gln	Val	Leu	Ile	
	545					550				555						560	
	Thr	Asp	Glu	Glu	Glu	Ile	Lys	Ala	Thr	Asn	Pro	Val	Ala	Thr	Glu	Glu	
					565					570					575		
	Tyr	Gly	Ala	Val	Ala	Ile	Asn	Asn	Gln	Ala	Ala	Asn	Thr	Gln	Ala	Gln	
				580					585					590			
	Thr	Gly	Leu	Val	His	Asn	Gln	Gly	Val	Ile	Pro	Gly	Met	Val	Trp	Gln	
		595						600					605				
	Asn	Arg	Asp	Val	Tyr	Leu	Gln	Gly	Pro	Ile	Trp	Ala	Lys	Ile	Pro	His	
		610					615					620					
	Thr	Asp	Gly	Asn	Phe	His	Pro	Ser	Pro	Leu	Met	Gly	Gly	Phe	Gly	Leu	
	625					630					635					640	
	Lys	His	Pro	Pro	Pro	Gln	Ile	Leu	Ile	Lys	Asn	Thr	Pro	Val	Pro	Ala	
					645					650					655		
	Asp	Pro	Pro	Leu	Thr	Phe	Asn	Gln	Ala	Lys	Leu	Asn	Ser	Phe	Ile	Thr	
				660					665					670			
	Gln	Tyr	Ser	Thr	Gly	Gln	Val	Ser	Val	Glu	Ile	Glu	Trp	Glu	Leu	Gln	
			675					680					685				

Lys Glu Asn Ser Lys Arg Trp Asn Pro Glu Ile Gln Tyr Thr Ser Asn
690 695 700

Tyr Tyr Lys Ser Thr Asn Val Asp Phe Ala Val Asn Thr Glu Gly Val
705 710 715 720

Tyr Ser Glu Pro Arg Pro Ile Gly Thr Arg Tyr Leu Thr Arg Asn Leu
725 730 735

<210> 42

<211> 735

<212> PRT

<213> 腺相关病毒, hu. 29的衣壳蛋白

<400> 42

Met Ala Ala Asp Gly Tyr Leu Pro Asp Trp Leu Glu Asp Thr Leu Ser
1 5 10 15

Glu Gly Ile Arg Gln Trp Trp Lys Leu Lys Pro Gly Pro Pro Pro Pro
20 25 30

Lys Pro Ala Glu Arg His Lys Asp Asp Ser Arg Gly Leu Val Leu Pro
35 40 45

[0091]

Gly Tyr Lys Tyr Leu Gly Pro Phe Asn Gly Leu Asp Lys Gly Glu Pro
50 55 60

Val Asn Glu Ala Asp Ala Ala Ala Leu Glu His Asp Lys Ala Tyr Asp
65 70 75 80

Arg Gln Leu Asp Ser Gly Asp Asn Pro Tyr Leu Lys Tyr Asn His Ala
85 90 95

Asp Ala Glu Phe Gln Glu Arg Leu Lys Glu Asp Thr Ser Phe Gly Gly
100 105 110

Asn Leu Gly Arg Ala Val Phe Gln Ala Lys Lys Arg Val Leu Glu Pro
115 120 125

Leu Gly Leu Val Glu Glu Pro Val Lys Thr Ala Pro Gly Lys Lys Arg
130 135 140

Pro Val Glu His Ser Pro Ala Glu Pro Asp Ser Ser Ser Gly Thr Gly
145 150 155 160

Lys Ser Gly Asn Gln Pro Ala Arg Lys Arg Leu Asn Phe Gly Gln Thr
165 170 175

Gly Asp Ser Asp Ser Val Pro Asp Pro Gln Pro Leu Gly Gln Pro Pro
180 185 190

	Ala	Ala	Pro	Ser	Gly	Leu	Gly	Thr	Asn	Thr	Met	Ala	Thr	Gly	Ser	Gly	
			195					200						205			
	Ala	Pro	Met	Ala	Asp	Asn	Asn	Glu	Gly	Ala	Asp	Gly	Val	Gly	Asn	Ser	
		210					215					220					
	Ser	Gly	Asn	Trp	His	Cys	Asp	Ser	Thr	Trp	Met	Gly	Asp	Arg	Val	Ile	
	225					230					235					240	
	Thr	Thr	Ser	Thr	Arg	Thr	Trp	Ala	Leu	Pro	Thr	Tyr	Asn	Asn	His	Leu	
					245					250					255		
	Tyr	Lys	Gln	Ile	Ser	Ser	Gln	Ser	Gly	Ala	Ser	Asn	Asp	Asn	His	Tyr	
			260						265					270			
	Phe	Gly	Tyr	Ser	Thr	Pro	Trp	Gly	Tyr	Phe	Asp	Phe	Asn	Arg	Phe	His	
			275					280						285			
	Cys	His	Phe	Ser	Pro	Arg	Asp	Trp	Gln	Arg	Leu	Ile	Asn	Asn	Asn	Trp	
		290					295					300					
	Gly	Phe	Arg	Pro	Lys	Arg	Leu	Asn	Phe	Lys	Leu	Phe	Asn	Ile	Gln	Val	
	305					310					315					320	
[0092]	Lys	Glu	Val	Thr	Gln	Asn	Asp	Gly	Thr	Thr	Thr	Ile	Ala	Asn	Asn	Leu	
					325					330					335		
	Thr	Ser	Thr	Val	Gln	Val	Phe	Thr	Asp	Ser	Glu	Tyr	Gln	Leu	Pro	Tyr	
				340					345					350			
	Val	Leu	Gly	Ser	Ala	His	Gln	Gly	Cys	Leu	Pro	Pro	Phe	Pro	Ala	Asp	
			355					360					365				
	Val	Phe	Met	Val	Pro	Gln	Tyr	Gly	Tyr	Leu	Thr	Leu	Asn	Asn	Gly	Ser	
		370					375					380					
	Gln	Ala	Val	Gly	Arg	Ser	Ser	Phe	Tyr	Cys	Leu	Gly	Tyr	Phe	Pro	Ser	
	385					390					395					400	
	Gln	Met	Leu	Arg	Thr	Gly	Asn	Asn	Phe	Thr	Phe	Ser	Tyr	Thr	Phe	Glu	
					405					410					415		
	Asp	Val	Pro	Phe	His	Ser	Ser	Tyr	Ala	His	Ser	Gln	Ser	Leu	Asp	Arg	
				420					425					430			
	Leu	Met	Asn	Pro	Leu	Ile	Asp	Gln	Tyr	Leu	Tyr	Tyr	Leu	Ser	Arg	Thr	
			435					440					445				
	Asn	Thr	Pro	Ser	Gly	Thr	Thr	Thr	Gln	Ser	Arg	Leu	Gln	Phe	Ser	Gln	
		450					455					460					

Ala Gly Ala Ser Asp Ile Arg Asp Gln Ser Arg Asn Trp Leu Pro Gly
 465 470 475 480
 Pro Cys Tyr Arg Gln Gln Arg Val Ser Lys Thr Ser Ala Asp Asn Asn
 485 490 495
 Asn Ser Glu Tyr Ser Trp Thr Gly Ala Thr Lys Tyr His Leu Asn Gly
 500 505 510
 Arg Asp Ser Leu Val Asn Pro Gly Pro Ala Met Ala Ser His Lys Asp
 515 520 525
 Asp Glu Glu Lys Phe Phe Pro Gln Ser Gly Val Leu Ile Phe Gly Lys
 530 535 540
 Gln Gly Pro Glu Lys Thr Asn Val Asp Ile Glu Lys Val Met Ile Thr
 545 550 555 560
 Asp Glu Glu Glu Ile Arg Thr Thr Asn Pro Val Ala Thr Glu Gln Tyr
 565 570 575
 Gly Ser Val Ser Thr Asn Leu Gln Ser Gly Asn Thr Gln Ala Ala Thr
 580 585 590
 [0093] Ala Asp Val Asn Thr Gln Gly Val Leu Pro Gly Met Val Trp Gln Asp
 595 600 605
 Arg Asp Val Tyr Leu Gln Gly Pro Ile Trp Ala Lys Ile Pro His Thr
 610 615 620
 Asp Gly His Phe His Pro Ser Pro Leu Met Gly Gly Phe Gly Leu Lys
 625 630 635 640
 His Pro Pro Pro Gln Ile Leu Ile Lys Asn Thr Pro Val Pro Ala Asn
 645 650 655
 Pro Ser Thr Thr Phe Ser Ala Ala Lys Phe Ala Ser Phe Ile Thr Gln
 660 665 670
 Tyr Ser Thr Gly Gln Val Ser Val Glu Ile Glu Trp Glu Leu Gln Lys
 675 680 685
 Glu Asn Ser Lys Arg Trp Asn Pro Glu Ile Gln Tyr Thr Ser Asn Tyr
 690 695 700
 Asn Lys Ser Val Asn Val Asp Phe Thr Val Asp Thr Asn Gly Val Tyr
 705 710 715 720
 Ser Glu Pro Arg Pro Ile Gly Thr Arg Tyr Leu Thr Arg Asn Leu
 725 730 735

<210> 43
 <211> 738
 <212> PRT
 <213> 猕猴腺相关病毒, rh. 64的衣壳蛋白
 <400> 43
 Met Ala Ala Asp Gly Tyr Leu Pro Asp Trp Leu Glu Asp Asn Leu Ser
 1 5 10 15
 Glu Gly Ile Arg Glu Trp Trp Asp Leu Lys Pro Gly Ala Pro Lys Pro
 20 25 30
 Lys Ala Asn Gln Gln Lys Gln Asp Asp Gly Arg Gly Leu Val Leu Pro
 35 40 45
 Gly Tyr Lys Tyr Leu Gly Pro Phe Asn Gly Leu Asp Lys Gly Glu Pro
 50 55 60
 Val Asn Ala Ala Asp Ala Ala Ala Leu Glu His Asp Lys Ala Tyr Asp
 65 70 75 80
 Gln Gln Leu Lys Ala Gly Asp Asn Pro Tyr Leu Arg Tyr Asn His Ala
 85 90 95
 Asp Ala Glu Phe Gln Glu Arg Leu Gln Glu Asp Thr Ser Phe Gly Gly
 100 105 110
 [0094]
 Asn Leu Gly Arg Ala Val Phe Gln Ala Lys Lys Arg Val Leu Glu Pro
 115 120 125
 Leu Gly Leu Val Glu Glu Gly Ala Lys Thr Ala Pro Gly Lys Lys Arg
 130 135 140
 Pro Val Glu Pro Ser Pro Gln Arg Ser Pro Asp Ser Ser Thr Gly Ile
 145 150 155 160
 Gly Lys Lys Gly Gln Gln Pro Ala Arg Lys Arg Leu Asn Phe Gly Gln
 165 170 175
 Thr Gly Asp Ser Glu Ser Val Pro Asp Pro Gln Pro Ile Gly Glu Pro
 180 185 190
 Pro Ala Ala Pro Ser Ser Val Gly Ser Gly Thr Met Ala Ala Gly Gly
 195 200 205
 Gly Ala Pro Met Ala Asp Asn Asn Glu Gly Ala Asp Gly Val Gly Ser
 210 215 220
 Ser Ser Gly Asn Trp His Cys Asp Ser Thr Trp Leu Gly Asp Arg Val
 225 230 235 240
 Ile Thr Thr Ser Thr Arg Thr Trp Ala Leu Pro Thr Tyr Asn Asn His

[0095]

515	520	525
Asn Lys Asp Asp Glu Asp Arg Phe Phe Pro Ser Ser Gly Ile Leu Met		
530	535	540
Phe Gly Lys Gln Gly Ala Gly Lys Asp Asn Val Asp Tyr Ser Asn Val		
545	550	555 560
Met Leu Thr Ser Glu Glu Glu Ile Lys Thr Thr Asn Pro Val Ala Thr		
	565	570 575
Glu Gln Tyr Gly Val Val Ala Asp Asn Leu Gln Gln Gln Asn Thr Ala		
	580	585 590
Pro Ile Val Gly Ala Val Asn Ser Gln Gly Ala Leu Pro Gly Met Val		
	595	600 605
Trp Gln Asn Arg Asp Val Tyr Leu Gln Gly Pro Ile Trp Ala Lys Ile		
	610	615 620
Pro His Thr Asp Gly Asn Phe His Pro Ser Pro Leu Met Gly Gly Phe		
625	630	635 640
Gly Leu Lys His Pro Pro Pro Gln Ile Leu Ile Lys Asn Thr Pro Val		
	645	650 655
Pro Ala Asp Pro Pro Thr Ala Phe Asn Gln Ala Lys Leu Asn Ser Phe		
	660	665 670
Ile Thr Gln Tyr Ser Thr Gly Gln Val Ser Val Glu Ile Val Trp Glu		
	675	680 685
Leu Gln Lys Glu Asn Ser Lys Arg Arg Asn Pro Glu Ile Gln Tyr Thr		
	690	695 700
Ser Asn Tyr Tyr Lys Ser Thr Asn Val Asp Phe Ala Val Asn Thr Glu		
705	710	715 720
Gly Val Tyr Ser Glu Pro Arg Pro Ile Gly Thr Arg Tyr Leu Thr Arg		
	725	730 735
Asn Leu		
<210> 44		
<211> 737		
<212> PRT		
<213> 猕猴腺相关病毒, rh. 48的衣壳蛋白		
<400> 44		
Met Ala Ala Asp Gly Tyr Leu Pro Asp Trp Leu Glu Asp Asn Leu Ser		
1	5	10 15

Glu Gly Ile Arg Glu Trp Trp Asp Leu Lys Pro Gly Ala Pro Lys Pro
 20 25 30
 Lys Ala Asn Gln Gln Lys Gln Asp Asp Gly Arg Gly Leu Val Leu Pro
 35 40 45
 Gly Tyr Lys Tyr Leu Gly Pro Phe Asn Gly Leu Asp Lys Gly Glu Pro
 50 55 60
 Val Asn Ala Ala Asp Ala Ala Ala Leu Glu His Asp Lys Ala Tyr Asp
 65 70 75 80
 Gln Gln Leu Lys Ala Gly Asp Asn Pro Tyr Leu Arg Tyr Asn His Ala
 85 90 95
 Asp Ala Glu Phe Gln Glu Arg Leu Gln Glu Asp Thr Ser Phe Gly Gly
 100 105 110
 Asn Leu Gly Arg Ala Val Phe Gln Ala Lys Lys Arg Val Leu Glu Pro
 115 120 125
 Leu Gly Leu Val Glu Glu Ala Ala Lys Thr Ala Pro Gly Lys Lys Arg
 130 135 140
 [0097] Pro Val Glu Pro Ser Pro Gln Arg Ser Pro Asp Ser Ser Thr Gly Ile
 145 150 155 160
 Gly Lys Lys Gly Gln Gln Pro Ala Arg Lys Arg Leu Asn Phe Gly Gln
 165 170 175
 Thr Gly Asp Ser Glu Ser Val Pro Asp Pro Gln Pro Ile Gly Glu Pro
 180 185 190
 Pro Ala Gly Pro Ser Gly Leu Gly Ser Gly Thr Met Ala Ala Gly Gly
 195 200 205
 Gly Ala Pro Met Ala Asp Asn Asn Lys Gly Ala Asp Gly Val Gly Asn
 210 215 220
 Ala Ser Gly Asn Trp His Cys Asp Ser Thr Trp Leu Gly Asp Arg Val
 225 230 235 240
 Ile Thr Thr Ser Thr Arg Thr Trp Ala Leu Pro Thr Tyr Asn Asn His
 245 250 255
 Leu Tyr Lys Gln Ile Ser Ser Gln Ser Ala Gly Ser Thr Asn Asp Asn
 260 265 270
 Val Tyr Phe Gly Tyr Ser Thr Pro Trp Gly Tyr Phe Asp Phe Asn Arg
 275 280 285

	Phe	His	Cys	His	Phe	Ser	Pro	Arg	Asp	Trp	Gln	Arg	Leu	Ile	Asn	Ser	
	290						295				300						
	Asn	Trp	Gly	Phe	Arg	Pro	Lys	Lys	Leu	Asn	Phe	Lys	Leu	Phe	Asn	Ile	
	305					310				315					320		
	Gln	Val	Lys	Glu	Val	Thr	Thr	Asn	Asp	Gly	Val	Thr	Thr	Ile	Ala	Asn	
				325						330					335		
	Asn	Leu	Thr	Ser	Thr	Val	Gln	Val	Phe	Ser	Asp	Ser	Glu	Tyr	Gln	Leu	
				340					345					350			
	Pro	Tyr	Val	Leu	Gly	Ser	Ala	His	Gln	Gly	Cys	Leu	Pro	Pro	Phe	Pro	
			355					360					365				
	Ala	Asp	Val	Phe	Met	Ile	Pro	Gln	Tyr	Gly	Tyr	Leu	Thr	Leu	Asn	Asn	
		370					375					380					
	Gly	Ser	Gln	Ser	Val	Gly	Arg	Ser	Ser	Phe	Tyr	Cys	Leu	Glu	Tyr	Phe	
	385					390				395						400	
	Pro	Ser	Gln	Met	Leu	Arg	Thr	Gly	Asn	Asn	Phe	Thr	Phe	Ser	Tyr	Thr	
				405					410						415		
[0098]	Phe	Glu	Asp	Val	Pro	Phe	His	Ser	Ser	Tyr	Ala	His	Ser	Gln	Ser	Leu	
				420				425						430			
	Asp	Arg	Leu	Met	Asn	Pro	Leu	Ile	Asp	Gln	Tyr	Leu	Tyr	Tyr	Leu	Ala	
			435					440					445				
	Arg	Thr	Gln	Ser	Asn	Ala	Gly	Gly	Thr	Ala	Gly	Asn	Arg	Glu	Leu	Gln	
		450					455					460					
	Phe	Tyr	Gln	Gly	Gly	Pro	Thr	Thr	Met	Ala	Glu	Gln	Ala	Lys	Asn	Trp	
	465					470				475						480	
	Leu	Pro	Gly	Pro	Cys	Phe	Arg	Gln	Gln	Arg	Val	Ser	Lys	Thr	Leu	Asp	
					485					490					495		
	Gln	Asn	Asn	Asn	Ser	Asn	Phe	Ala	Trp	Thr	Gly	Ala	Thr	Lys	Tyr	His	
				500					505					510			
	Leu	Asn	Gly	Arg	Asn	Ser	Leu	Val	Asn	Pro	Gly	Val	Ala	Met	Ala	Thr	
		515						520					525				
	His	Lys	Asp	Asp	Glu	Glu	Arg	Phe	Phe	Pro	Ser	Ser	Gly	Val	Leu	Ile	
		530					535					540					
	Phe	Gly	Lys	Thr	Gly	Ala	Ala	Asn	Lys	Thr	Thr	Leu	Glu	Asn	Val	Leu	
	545					550					555					560	

Met Thr Asn Glu Glu Glu Ile Arg Pro Thr Asn Pro Val Ala Thr Glu
565 570 575

Glu Tyr Gly Thr Val Ser Ser Asn Leu Gln Ala Ala Asn Thr Ala Ala
580 585 590

Gln Thr Gln Val Val Asn Asn Gln Gly Ala Leu Pro Gly Met Val Trp
595 600 605

Gln Asn Arg Asp Val Tyr Leu Gln Gly Pro Ile Trp Ala Lys Ile Pro
610 615 620

His Thr Asp Gly Asn Phe His Pro Ser Pro Leu Met Gly Gly Phe Gly
625 630 635 640

Leu Lys His Pro Pro Pro Gln Ile Leu Ile Lys Asn Thr Pro Val Pro
645 650 655

Ala Asn Pro Pro Glu Val Phe Thr Pro Ala Lys Phe Ala Ser Phe Ile
660 665 670

Thr Gln Tyr Ser Thr Gly Gln Val Ser Val Glu Ile Glu Trp Glu Leu
675 680 685

[0099] Gln Lys Glu Asn Ser Lys Arg Trp Asn Pro Glu Ile Gln Tyr Thr Ser
690 695 700

Asn Phe Asp Lys Gln Thr Gly Val Asp Phe Ala Val Asp Ser Gln Gly
705 710 715 720

Val Tyr Ser Glu Pro Arg Pro Ile Gly Thr Arg Tyr Leu Thr Arg Asn
725 730 735

Leu

<210> 45

<211> 736

<212> PRT

<213> 腺相关病毒, hu. 44的衣壳蛋白

<400> 45

Met Ala Ala Asp Gly Tyr Leu Pro Asp Trp Leu Glu Asp Thr Leu Ser
1 5 10 15

Glu Gly Ile Arg Gln Trp Trp Lys Leu Arg Pro Gly Pro Pro Pro Pro
20 25 30

Lys Pro Ala Glu Arg His Lys Asp Asp Ser Arg Gly Leu Val Leu Pro
35 40 45

	Gly	Tyr	Lys	Tyr	Leu	Gly	Pro	Phe	Asn	Gly	Leu	Asp	Lys	Gly	Glu	Pro	
	50						55					60					
	Val	Asn	Glu	Ala	Asp	Ala	Ala	Ala	Leu	Glu	His	Asp	Lys	Ala	Tyr	Asp	
	65				70					75					80		
	Arg	Gln	Leu	Asp	Ser	Gly	Asp	Asn	Pro	Tyr	Leu	Lys	Tyr	Asn	His	Ala	
				85					90					95			
	Asp	Ala	Glu	Phe	Gln	Glu	Arg	Leu	Lys	Glu	Asp	Thr	Ser	Phe	Gly	Gly	
				100				105						110			
	Asn	Leu	Gly	Arg	Ala	Val	Phe	Gln	Ala	Lys	Lys	Arg	Val	Leu	Glu	Pro	
		115					120						125				
	Leu	Gly	Leu	Val	Glu	Glu	Gly	Ala	Glu	Thr	Ala	Pro	Gly	Lys	Lys	Arg	
	130						135					140					
	Pro	Val	Glu	Gln	Ser	Pro	Gln	Gly	Pro	Asp	Ser	Ser	Ser	Gly	Ile	Gly	
	145					150				155						160	
	Lys	Thr	Gly	Gln	Gln	Pro	Ala	Lys	Lys	Arg	Leu	Asn	Phe	Gly	Gln	Thr	
				165						170					175		
[0100]	Gly	Asp	Ser	Glu	Ser	Val	Pro	Asp	Pro	Gln	Pro	Leu	Gly	Glu	Pro	Pro	
			180					185					190				
	Ala	Thr	Pro	Ala	Ala	Val	Gly	Pro	Thr	Thr	Met	Ala	Ser	Gly	Gly	Gly	
		195						200				205					
	Ala	Pro	Met	Ala	Asp	Asn	Asn	Glu	Gly	Ala	Asp	Gly	Val	Gly	Asn	Ala	
		210					215					220					
	Ser	Gly	Asn	Trp	His	Cys	Asp	Ser	Thr	Trp	Leu	Gly	Asp	Arg	Val	Ile	
	225				230					235					240		
	Thr	Thr	Ser	Thr	Arg	Thr	Trp	Ala	Leu	Pro	Thr	Tyr	Asn	Asn	His	Leu	
				245					250					255			
	Tyr	Lys	Gln	Ile	Ser	Ser	Ala	Ser	Thr	Gly	Ala	Ser	Asn	Asp	Asn	His	
			260						265				270				
	Tyr	Phe	Gly	Tyr	Ser	Thr	Pro	Trp	Gly	Tyr	Phe	Asp	Phe	Asn	Arg	Phe	
		275					280						285				
	His	Cys	His	Phe	Ser	Pro	Arg	Asp	Trp	Gln	Arg	Leu	Ile	Asn	Asn	Asn	
		290					295					300					
	Trp	Gly	Phe	Arg	Pro	Lys	Arg	Leu	Asn	Phe	Lys	Leu	Phe	Asn	Ile	Gln	
	305					310				315					320		

	Val	Lys	Glu	Val	Thr	Thr	Asn	Asp	Gly	Val	Thr	Thr	Ile	Ala	Asn	Asn	
					325					330					335		
	Leu	Thr	Ser	Thr	Val	Gln	Val	Phe	Ser	Asp	Ser	Glu	Tyr	Gln	Leu	Pro	
				340					345					350			
	Tyr	Val	Leu	Gly	Ser	Ala	His	Gln	Gly	Cys	Leu	Pro	Pro	Phe	Pro	Ala	
			355					360					365				
	Asp	Val	Phe	Met	Ile	Pro	Gln	Tyr	Gly	Tyr	Leu	Thr	Leu	Asn	Asn	Gly	
		370					375					380					
	Ser	Gln	Ala	Val	Gly	Arg	Ser	Ser	Phe	Tyr	Cys	Leu	Glu	Tyr	Phe	Pro	
	385					390					395					400	
	Ser	Gln	Met	Leu	Arg	Thr	Gly	Asn	Asn	Phe	Thr	Phe	Ser	Tyr	Thr	Phe	
				405						410					415		
	Glu	Glu	Val	Pro	Phe	His	Ser	Ser	Tyr	Ala	His	Ser	Gln	Ser	Leu	Asp	
				420					425					430			
	Arg	Leu	Met	Asn	Pro	Leu	Ile	Asp	Gln	Tyr	Leu	Tyr	Tyr	Pro	Asn	Arg	
		435						440					445				
[0101]	Thr	Gln	Asn	Gln	Ser	Gly	Ser	Ala	Gln	Asn	Lys	Asp	Leu	Leu	Phe	Ser	
		450				455						460					
	Arg	Gly	Ser	Pro	Ala	Gly	Met	Ser	Val	Gln	Pro	Lys	Asn	Trp	Leu	Pro	
	465					470					475					480	
	Gly	Pro	Cys	Tyr	Arg	Gln	Gln	Arg	Val	Ser	Lys	Thr	Lys	Thr	Asp	Asn	
					485					490					495		
	Asn	Asn	Ser	Asn	Phe	Thr	Trp	Thr	Gly	Ala	Ser	Lys	Tyr	Asn	Leu	Asn	
				500					505					510			
	Gly	Arg	Glu	Ser	Ile	Ile	Asn	Pro	Gly	Thr	Ala	Met	Ala	Ser	His	Lys	
			515				520						525				
	Asp	Asp	Glu	Asp	Lys	Phe	Phe	Pro	Met	Ser	Gly	Val	Met	Ile	Phe	Gly	
		530					535					540					
	Lys	Glu	Ser	Ala	Gly	Ala	Ser	Asn	Thr	Ala	Leu	Asp	Asn	Val	Met	Ile	
	545					550					555					560	
	Thr	Asp	Glu	Glu	Glu	Ile	Lys	Ala	Thr	Asn	Pro	Val	Ala	Thr	Glu	Arg	
					565					570					575		
	Phe	Gly	Thr	Val	Ala	Val	Asn	Phe	Gln	Ser	Ser	Ser	Thr	Asp	Pro	Ala	
				580					585					590			

Thr Gly Asp Val His Ala Met Gly Ala Leu Pro Gly Met Val Trp Gln
595 600 605

Gly Arg Asp Val Tyr Leu Gln Gly Pro Ile Trp Ala Lys Ile Pro His
610 615 620

Thr Asp Gly His Phe His Pro Ser Pro Leu Met Gly Gly Phe Gly Leu
625 630 635 640

Lys Asn Pro Pro Pro Gln Ile Leu Ile Lys Asn Thr Pro Val Pro Ala
645 650 655

Asn Pro Pro Ala Glu Phe Ser Ala Thr Lys Phe Ala Ser Phe Ile Thr
660 665 670

Gln Tyr Ser Thr Gly Gln Val Ser Val Glu Ile Glu Trp Glu Leu Gln
675 680 685

Lys Glu Asn Ser Lys Arg Trp Asn Pro Glu Val Gln Tyr Thr Ser Asn
690 695 700

Tyr Ala Lys Ser Ala Asn Val Asp Phe Thr Val Asp Asn Asn Gly Leu
705 710 715 720

[0102] Tyr Thr Glu Pro Arg Pro Ile Gly Thr Arg Tyr Leu Thr Arg Pro Leu
725 730 735

<210> 46

<211> 735

<212> PRT

<213> ch. 5的衣壳蛋白

<400> 46

Met Ala Ala Asp Gly Tyr Leu Pro Asp Trp Leu Glu Asp Thr Leu Ser
1 5 10 15

Glu Gly Ile Arg Gln Trp Trp Lys Leu Lys Pro Gly Pro Pro Pro Pro
20 25 30

Lys Pro Asn Gln Gln His Arg Asp Asp Ser Arg Gly Leu Val Leu Pro
35 40 45

Gly Tyr Lys Tyr Leu Gly Pro Phe Asn Gly Leu Asp Lys Gly Glu Pro
50 55 60

Val Asn Glu Ala Asp Ala Ala Ala Leu Glu His Asp Lys Ala Tyr Asp
65 70 75 80

His Gln Leu Lys Gln Gly Asp Asn Pro Tyr Leu Lys Tyr Asn His Ala
85 90 95

	Asp	Ala	Glu	Phe	Gln	Glu	Arg	Leu	Gln	Glu	Asp	Thr	Ser	Phe	Gly	Gly	
				100					105							110	
	Asn	Leu	Gly	Arg	Ala	Val	Phe	Gln	Ala	Lys	Lys	Arg	Val	Leu	Glu	Pro	
			115					120					125				
	Leu	Gly	Leu	Val	Glu	Glu	Ala	Val	Lys	Thr	Ala	Pro	Gly	Lys	Lys	Arg	
		130						135					140				
	Pro	Ile	Glu	Gln	Ser	Pro	Ala	Glu	Pro	Asp	Ser	Ser	Ser	Gly	Ile	Gly	
	145					150					155					160	
	Lys	Ser	Gly	Gln	Gln	Pro	Ala	Lys	Lys	Arg	Leu	Asn	Phe	Gly	Gln	Thr	
					165					170					175		
	Gly	Asp	Thr	Glu	Ser	Val	Pro	Asp	Pro	Gln	Pro	Ile	Gly	Glu	Pro	Pro	
				180					185					190			
	Ala	Ala	Pro	Ser	Gly	Val	Gly	Ser	Asn	Thr	Met	Ala	Ser	Gly	Gly	Gly	
			195					200					205				
	Ala	Pro	Met	Ala	Asp	Asn	Asn	Glu	Gly	Ala	Asp	Gly	Val	Gly	Asn	Ser	
		210					215					220					
[0103]	Ser	Gly	Asn	Trp	His	Cys	Asp	Ser	Thr	Trp	Met	Gly	Asp	Arg	Val	Ile	
	225					230					235					240	
	Thr	Thr	Ser	Thr	Arg	Thr	Trp	Ala	Leu	Pro	Thr	Tyr	Asn	Asn	His	Leu	
					245					250					255		
	Tyr	Lys	Gln	Ile	Ser	Ser	Glu	Ser	Gly	Ala	Thr	Asn	Asp	Asn	His	Tyr	
			260						265					270			
	Phe	Gly	Tyr	Ser	Thr	Pro	Trp	Gly	Tyr	Phe	Asp	Phe	Asn	Arg	Phe	His	
		275						280					285				
	Cys	His	Phe	Ser	Pro	Arg	Asp	Trp	Gln	Arg	Leu	Ile	Asn	Asn	Asn	Trp	
		290					295					300					
	Gly	Phe	Arg	Pro	Lys	Lys	Leu	Asn	Phe	Lys	Leu	Phe	Asn	Ile	Gln	Val	
	305					310					315					320	
	Lys	Glu	Val	Thr	Gln	Asn	Asp	Gly	Thr	Thr	Thr	Ile	Ala	Asn	Asn	Leu	
					325					330					335		
	Thr	Ser	Thr	Val	Gln	Val	Phe	Thr	Asp	Ser	Glu	Tyr	Gln	Leu	Pro	Tyr	
				340					345					350			
	Val	Leu	Gly	Ser	Ala	His	Gln	Gly	Cys	Leu	Pro	Pro	Phe	Pro	Ala	Asp	
		355						360					365				

	Val	Phe	Met	Ile	Pro	Gln	Tyr	Gly	Tyr	Leu	Thr	Leu	Asn	Asn	Gly	Ser	
	370						375					380					
	Gln	Ala	Val	Gly	Arg	Ser	Ser	Phe	Tyr	Cys	Leu	Glu	Tyr	Phe	Pro	Ser	
	385					390					395					400	
	Gln	Met	Leu	Arg	Thr	Gly	Asn	Asn	Phe	Thr	Phe	Ser	Tyr	Thr	Phe	Glu	
					405					410					415		
	Asp	Val	Pro	Phe	His	Ser	Ser	Tyr	Ala	His	Ser	Gln	Ser	Leu	Asp	Arg	
				420					425					430			
	Leu	Met	Asn	Pro	Leu	Ile	Asp	Gln	Tyr	Leu	Tyr	Tyr	Leu	Ser	Lys	Thr	
		435						440					445				
	Gln	Gly	Thr	Ser	Gly	Thr	Thr	Gln	Gln	Ser	Arg	Leu	Gln	Phe	Ser	Gln	
	450						455					460					
	Ala	Gly	Pro	Ser	Ser	Met	Ala	Gln	Gln	Ala	Lys	Asn	Trp	Leu	Pro	Gly	
	465					470					475					480	
	Pro	Ser	Tyr	Arg	Gln	Gln	Arg	Met	Ser	Lys	Thr	Ala	Asn	Asp	Asn	Asn	
					485					490					495		
[0104]	Asn	Ser	Glu	Phe	Ala	Trp	Thr	Ala	Ala	Thr	Lys	Tyr	Tyr	Leu	Asn	Gly	
				500				505						510			
	Arg	Asn	Ser	Leu	Val	Asn	Pro	Gly	Pro	Pro	Met	Ala	Ser	His	Lys	Asp	
			515					520					525				
	Asp	Glu	Glu	Lys	Tyr	Phe	Pro	Met	His	Gly	Asn	Leu	Ile	Phe	Gly	Lys	
	530						535					540					
	Gln	Gly	Thr	Gly	Thr	Thr	Asn	Val	Asp	Ile	Glu	Ser	Val	Leu	Ile	Thr	
	545					550				555					560		
	Asp	Glu	Glu	Glu	Ile	Arg	Thr	Thr	Asn	Pro	Val	Ala	Thr	Glu	Gln	Tyr	
					565				570					575			
	Gly	Gln	Val	Ala	Thr	Asn	His	Gln	Ser	Gln	Asn	Thr	Thr	Ala	Ser	Tyr	
				580				585						590			
	Gly	Ser	Val	Asp	Ser	Gln	Gly	Ile	Leu	Pro	Gly	Met	Val	Trp	Gln	Asp	
		595					600						605				
	Arg	Asp	Val	Tyr	Leu	Gln	Gly	Pro	Ile	Trp	Ala	Lys	Ile	Pro	His	Thr	
	610						615					620					
	Asp	Gly	His	Phe	His	Pro	Ser	Pro	Leu	Met	Gly	Gly	Phe	Gly	Leu	Lys	
	625					630					635				640		

His Pro Pro Pro Gln Ile Leu Ile Lys Asn Thr Pro Val Pro Ala Asn
645 650 655

Pro Ala Thr Thr Phe Thr Pro Gly Lys Phe Ala Ser Phe Ile Thr Gln
660 665 670

Tyr Ser Thr Gly Gln Val Ser Val Glu Ile Glu Trp Glu Leu Gln Lys
675 680 685

Glu Asn Ser Lys Arg Trp Asn Pro Glu Ile Gln Tyr Thr Ser Asn Tyr
690 695 700

Asn Lys Ser Val Asn Val Glu Phe Thr Val Asp Ala Asn Gly Val Tyr
705 710 715 720

Ser Glu Pro Arg Pro Ile Gly Thr Arg Tyr Leu Thr Arg Asn Leu
725 730 735

<210> 47

<211> 737

<212> PRT

<213> 猕猴腺相关病毒, rh. 67的衣壳蛋白

<400> 47

Met Ala Ala Asp Gly Tyr Leu Pro Asp Trp Leu Glu Asp Asn Leu Ser
1 5 10 15

[0105]

Glu Gly Ile Arg Glu Trp Trp Asp Leu Lys Pro Gly Ala Pro Lys Pro
20 25 30

Lys Ala Asn Gln Gln Lys Gln Asp Asp Gly Arg Gly Leu Val Leu Pro
35 40 45

Gly Tyr Lys Tyr Leu Gly Pro Phe Asn Gly Leu Asp Lys Gly Glu Pro
50 55 60

Val Asn Ala Ala Asp Ala Ala Ala Leu Glu His Asp Lys Ala Tyr Asp
65 70 75 80

Gln Gln Leu Lys Ala Gly Asp Asn Pro Tyr Leu Arg Tyr Asn His Ala
85 90 95

Asp Ala Glu Phe Gln Glu Arg Leu Gln Glu Asp Thr Ser Phe Gly Gly
100 105 110

Asn Leu Gly Arg Ala Val Leu Gln Ala Lys Lys Arg Val Leu Glu Pro
115 120 125

Leu Gly Leu Val Glu Glu Ala Ala Lys Thr Ala Pro Gly Lys Lys Arg
130 135 140

Pro Val Glu Pro Ser Pro Gln Arg Ser Pro Asp Ser Ser Thr Gly Ile

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

[0106]

	420	425	430
	Asp Arg Leu Met Asn Pro Leu Ile Asp Gln Tyr Leu Tyr Tyr Leu Ala		
	435	440	445
	Arg Thr Gln Ser Asn Ala Gly Gly Thr Ala Gly Asn Arg Glu Leu Gln		
	450	455	460
	Phe Tyr Gln Gly Gly Pro Thr Thr Met Ala Glu Gln Ala Lys Asn Trp		
	465	470	475 480
	Leu Pro Gly Pro Cys Phe Arg Gln Gln Arg Val Ser Lys Thr Leu Asp		
	485	490	495
	Gln Asn Asn Asn Ser Asn Phe Ala Trp Thr Gly Ala Thr Lys Tyr His		
	500	505	510
	Leu Asn Gly Arg Asn Ser Leu Val Asn Pro Gly Val Ala Met Ala Thr		
	515	520	525
	His Lys Asp Asp Glu Glu Arg Phe Phe Pro Ser Ser Gly Val Leu Ile		
	530	535	540
	Phe Gly Lys Thr Gly Ala Ala Asn Lys Thr Thr Leu Glu Asn Val Leu		
	545	550	555 560
[0107]	Met Thr Asn Glu Glu Glu Ile Arg Pro Thr Asn Pro Val Ala Thr Glu		
	565	570	575
	Glu Tyr Gly Thr Val Ser Ser Asn Leu Gln Ala Ala Asn Thr Ala Ala		
	580	585	590
	Gln Thr Gln Val Val Asn Asn Gln Gly Ala Leu Pro Gly Met Val Trp		
	595	600	605
	Gln Asn Arg Asp Val Tyr Leu Gln Gly Pro Ile Trp Ala Lys Ile Pro		
	610	615	620
	His Thr Asp Gly Asn Phe His Pro Ser Pro Leu Met Gly Gly Phe Gly		
	625	630	635 640
	Leu Lys His Pro Pro Pro Gln Ile Leu Ile Lys Asn Thr Pro Val Pro		
	645	650	655
	Ala Asn Pro Pro Glu Val Phe Thr Pro Ala Lys Phe Ala Ser Phe Ile		
	660	665	670
	Thr Gln Tyr Ser Thr Gly Gln Val Ser Val Glu Ile Glu Trp Glu Leu		
	675	680	685
	Gln Lys Glu Asn Ser Lys Arg Trp Asn Pro Glu Ile Gln Tyr Thr Ser		

690	695	700
Asn Phe Asp Lys Gln Thr Gly Val Asp Phe Ala Val Asp Ser Gln Gly 705 710 715 720		
Val Tyr Ser Glu Pro Arg Pro Ile Gly Thr Arg Tyr Leu Thr Arg Asn 725 730 735		
Leu		
<210> 48		
<211> 738		
<212> PRT		
<213> 猕猴腺相关病毒, rh. 58 的衣壳蛋白		
<400> 48		
Met Ala Ala Asp Gly Tyr Leu Pro Asp Trp Leu Glu Asp Asn Leu Ser 1 5 10 15		
Glu Gly Ile Arg Glu Trp Trp Asp Leu Lys Pro Gly Ala Pro Lys Pro 20 25 30		
Lys Ala Asn Gln Gln Lys Gln Asp Asp Gly Arg Gly Leu Val Leu Pro 35 40 45		
[0108] Gly Tyr Lys Tyr Leu Gly Pro Phe Asn Gly Leu Asp Lys Gly Glu Pro 50 55 60		
Val Asn Ala Ala Asp Ala Ala Ala Leu Glu His Asp Lys Ala Tyr Asp 65 70 75 80		
Gln Gln Leu Lys Ala Gly Asp Asn Pro Tyr Leu Arg Tyr Asn His Ala 85 90 95		
Asp Ala Glu Phe Gln Glu Arg Leu Gln Glu Asp Thr Ser Phe Gly Gly 100 105 110		
Asn Leu Gly Arg Ala Val Phe Gln Ala Lys Lys Arg Val Leu Glu Pro 115 120 125		
Leu Gly Leu Val Glu Glu Ala Ala Lys Thr Ala Pro Gly Lys Lys Arg 130 135 140		
Pro Val Glu Pro Ser Pro Gln Arg Ser Pro Asp Ser Ser Thr Gly Ile 145 150 155 160		
Gly Lys Lys Gly Gln Gln Pro Ala Arg Lys Arg Leu Asn Phe Gly Gln 165 170 175		
Thr Gly Asp Ser Gln Ser Val Pro Asp Pro Gln Pro Ile Gly Glu Pro 180 185 190		

Pro Ala Ala Pro Ser Ser Val Gly Ser Gly Thr Met Ala Ala Gly Gly
 195 200 205
 Gly Ala Pro Met Ala Asp Asn Asn Glu Gly Ala Asp Gly Val Gly Ser
 210 215 220
 Ser Ser Gly Asn Trp His Cys Asp Ser Thr Trp Leu Gly Asp Arg Val
 225 230 235 240
 Ile Thr Thr Ser Thr Arg Thr Trp Ala Leu Pro Thr Tyr Asn Asn His
 245 250 255
 Leu Tyr Lys Gln Ile Ser Asn Gly Thr Ser Gly Gly Ser Thr Asn Asp
 260 265 270
 Asn Thr Tyr Phe Gly Tyr Ser Thr Pro Trp Gly Tyr Phe Asp Phe Asn
 275 280 285
 Arg Phe His Cys His Phe Ser Pro Arg Asp Trp Gln Arg Leu Ile Asn
 290 295 300
 Asn Asn Trp Gly Phe Arg Pro Lys Arg Leu Ser Phe Lys Leu Phe Asn
 305 310 315 320
 [0109] Ile Gln Val Lys Glu Val Thr Gln Asn Glu Gly Thr Lys Thr Ile Ala
 325 330 335
 Asn Asn Leu Thr Ser Thr Ile Gln Val Phe Thr Asp Ser Glu Tyr Gln
 340 345 350
 Leu Pro Tyr Val Leu Gly Ser Ala His Gln Gly Cys Leu Pro Pro Phe
 355 360 365
 Pro Ala Asp Val Phe Met Ile Pro Gln Tyr Gly Tyr Leu Thr Leu Asn
 370 375 380
 Asn Gly Ser Gln Ala Val Gly Arg Ser Ser Phe Tyr Cys Leu Glu Tyr
 385 390 395 400
 Phe Pro Ser Gln Met Leu Arg Thr Gly Asn Asn Phe Ser Phe Ser Tyr
 405 410 415
 Thr Phe Glu Asp Val Pro Phe His Ser Ser Tyr Ala His Ser Gln Ser
 420 425 430
 Leu Asp Arg Leu Met Asn Pro Leu Ile Asp Gln Tyr Leu Tyr Tyr Leu
 435 440 445
 Ser Arg Thr Gln Ser Thr Gly Gly Thr Ala Gly Thr Gln Gln Leu Leu
 450 455 460

	Phe	Ser	Gln	Ala	Gly	Pro	Ser	Asn	Met	Ser	Ala	Gln	Ala	Arg	Asn	Trp
	465					470					475					480
	Leu	Pro	Gly	Pro	Cys	Tyr	Arg	Gln	Gln	Arg	Val	Ser	Thr	Thr	Leu	Ser
					485					490						495
	Gln	Asn	Asn	Asn	Ser	Asn	Phe	Ala	Trp	Thr	Gly	Ala	Thr	Lys	Tyr	His
				500					505					510		
	Leu	Asn	Gly	Arg	Asp	Ser	Leu	Val	Asn	Pro	Gly	Val	Ala	Met	Ala	Thr
			515					520					525			
	Asn	Lys	Asp	Asp	Glu	Asp	Arg	Phe	Phe	Pro	Ser	Ser	Gly	Ile	Leu	Met
		530					535					540				
	Phe	Gly	Lys	Gln	Gly	Ala	Gly	Lys	Asp	Asn	Val	Asp	Tyr	Ser	Asn	Val
	545					550					555					560
	Met	Leu	Thr	Ser	Glu	Glu	Glu	Ile	Lys	Thr	Thr	Asn	Pro	Val	Ala	Thr
					565					570						575
	Glu	Gln	Tyr	Gly	Val	Val	Ala	Asp	Asn	Leu	Gln	Gln	Gln	Asn	Thr	Ala
				580					585							590
[0110]	Pro	Ile	Val	Gly	Ala	Val	Asn	Ser	Gln	Gly	Ala	Leu	Pro	Gly	Met	Val
			595					600					605			
	Trp	Gln	Asn	Arg	Asp	Val	Tyr	Leu	Gln	Gly	Pro	Ile	Trp	Ala	Lys	Ile
		610					615					620				
	Pro	His	Thr	Asp	Gly	Asn	Phe	His	Pro	Ser	Pro	Leu	Met	Gly	Gly	Phe
	625					630					635					640
	Gly	Leu	Lys	His	Pro	Pro	Pro	Gln	Ile	Leu	Ile	Lys	Ser	Thr	Pro	Val
					645					650					655	
	Pro	Ala	Asp	Pro	Pro	Thr	Ala	Phe	Asn	Gln	Ala	Lys	Leu	Asn	Ser	Phe
				660					665					670		
	Ile	Thr	Gln	Tyr	Ser	Thr	Gly	Gln	Val	Ser	Val	Glu	Ile	Glu	Trp	Glu
			675					680					685			
	Leu	Gln	Lys	Glu	Asn	Ser	Lys	Cys	Trp	Asn	Pro	Glu	Ile	Gln	Tyr	Thr
		690					695					700				
	Ser	Asn	Tyr	Tyr	Lys	Ser	Thr	Asn	Val	Asp	Phe	Ala	Val	Asn	Thr	Glu
	705					710					715					720
	Gly	Val	Tyr	Ser	Glu	Pro	Arg	Pro	Ile	Gly	Thr	Arg	Tyr	Leu	Thr	Arg
					725					730					735	

Asn Leu

<210> 49

<211> 737

<212> PRT

<213> 猕猴腺相关病毒, rh. 54的衣壳蛋白

<400> 49

Met Ala Ala Asp Gly Tyr Leu Pro Asp Trp Leu Glu Asp Asn Leu Ser
1 5 10 15

Glu Gly Ile Arg Glu Trp Trp Asp Leu Lys Pro Gly Ala Pro Lys Pro
20 25 30

Lys Ala Asn Gln Gln Lys Gln Asp Asp Gly Arg Gly Leu Val Leu Pro
35 40 45

Gly Tyr Lys Tyr Leu Gly Pro Phe Asn Gly Leu Asp Lys Gly Glu Pro
50 55 60

Val Asn Ala Ala Asp Ala Ala Ala Leu Glu His Asp Lys Ala Tyr Asp
65 70 75 80

[0111]

Gln Gln Leu Lys Ala Gly Asp Asn Pro Tyr Leu Arg Tyr Asn His Ala
85 90 95

Asp Ala Glu Phe Gln Glu Arg Leu Gln Glu Asp Thr Ser Phe Gly Gly
100 105 110

Asn Leu Gly Arg Ala Val Phe Gln Ala Lys Lys Arg Val Leu Glu Pro
115 120 125

Leu Gly Leu Val Glu Glu Ala Ala Lys Thr Ala Pro Gly Lys Lys Arg
130 135 140

Pro Val Glu Pro Ser Pro Gln Arg Ser Pro Asp Ser Ser Thr Gly Ile
145 150 155 160

Gly Lys Lys Gly Gln Gln Pro Ala Arg Lys Arg Leu Asn Phe Gly Gln
165 170 175

Thr Gly Asp Ser Glu Ser Val Pro Asp Pro Gln Pro Leu Gly Glu Pro
180 185 190

Pro Ala Gly Pro Ser Gly Leu Gly Ser Gly Thr Met Ala Ala Gly Gly
195 200 205

Gly Ala Pro Met Ala Asp Asn Asn Glu Gly Ala Asp Gly Val Gly Asn
210 215 220

	Ala	Ser	Gly	Asn	Trp	His	Cys	Asp	Ser	Thr	Trp	Leu	Gly	Asp	Arg	Val
	225				230						235					240
	Ile	Thr	Thr	Ser	Thr	Arg	Thr	Trp	Ala	Leu	Pro	Thr	Tyr	Asn	Asn	His
				245						250					255	
	Leu	Tyr	Lys	Gln	Ile	Ser	Ser	Gln	Ser	Ala	Gly	Ser	Thr	Asn	Asp	Asn
			260					265						270		
	Val	Tyr	Phe	Gly	Tyr	Ser	Thr	Pro	Trp	Gly	Tyr	Phe	Asp	Phe	Asn	Arg
			275					280					285			
	Phe	His	Cys	His	Phe	Ser	Pro	Arg	Asp	Trp	Gln	Arg	Leu	Ile	Asn	Asn
		290					295					300				
	Asn	Trp	Gly	Phe	Arg	Pro	Lys	Lys	Leu	Asn	Phe	Lys	Leu	Phe	Asn	Ile
	305					310					315					320
	Gln	Val	Lys	Glu	Val	Thr	Thr	Asn	Asp	Gly	Val	Thr	Thr	Ile	Ala	Asn
				325						330					335	
	Asn	Leu	Thr	Ser	Thr	Val	Gln	Val	Phe	Ser	Asp	Ser	Glu	Tyr	Gln	Leu
			340						345					350		
[0112]	Pro	Tyr	Val	Leu	Gly	Ser	Ala	His	Gln	Gly	Cys	Leu	Pro	Pro	Phe	Pro
			355					360					365			
	Ala	Asp	Val	Phe	Met	Ile	Pro	Gln	Tyr	Gly	Tyr	Leu	Thr	Leu	Asn	Asn
		370					375					380				
	Gly	Ser	Gln	Ser	Val	Gly	Arg	Ser	Ser	Phe	Tyr	Cys	Leu	Glu	Tyr	Phe
	385				390						395					400
	Pro	Ser	Gln	Val	Leu	Arg	Thr	Gly	Asn	Asn	Phe	Thr	Phe	Ser	Tyr	Thr
				405						410					415	
	Phe	Glu	Asp	Val	Pro	Phe	His	Ser	Ser	Tyr	Ala	His	Ser	Gln	Ser	Leu
			420					425						430		
	Asp	Arg	Leu	Met	Asn	Pro	Leu	Ile	Asp	Gln	Tyr	Leu	Tyr	Tyr	Leu	Ala
			435				440						445			
	Arg	Thr	Gln	Ser	Asn	Pro	Gly	Gly	Thr	Ser	Gly	Asn	Arg	Glu	Leu	Gln
		450					455					460				
	Phe	Tyr	Gln	Gly	Gly	Pro	Ser	Thr	Met	Ala	Glu	Gln	Ala	Lys	Asn	Trp
	465					470					475					480
	Leu	Pro	Gly	Pro	Cys	Phe	Arg	Gln	Gln	Arg	Val	Ser	Lys	Thr	Leu	Asp
				485					490						495	

	Gln	Asn	Asn	Asn	Ser	Asn	Phe	Ala	Trp	Thr	Gly	Ala	Thr	Lys	Tyr	His	
				500					505					510			
	Leu	Asn	Gly	Arg	Asn	Ser	Leu	Val	Asn	Pro	Gly	Val	Ala	Met	Ala	Thr	
		515					520					525					
	His	Lys	Asp	Asp	Glu	Asp	Arg	Phe	Phe	Pro	Ser	Ser	Gly	Val	Leu	Ile	
		530					535					540					
	Phe	Gly	Lys	Thr	Gly	Ala	Thr	Asn	Lys	Thr	Thr	Leu	Glu	Asn	Val	Leu	
	545					550				555						560	
	Met	Thr	Asn	Glu	Glu	Glu	Ile	Arg	Pro	Thr	Asn	Pro	Val	Ala	Thr	Glu	
				565					570						575		
	Glu	Tyr	Gly	Ile	Val	Ser	Ser	Asn	Leu	Gln	Ala	Ala	Asn	Thr	Ala	Ala	
			580					585					590				
	Gln	Thr	Gln	Val	Val	Asn	Asn	Gln	Gly	Ala	Leu	Pro	Gly	Met	Val	Trp	
		595					600					605					
	Gln	Asn	Arg	Asp	Val	Tyr	Leu	Gln	Gly	Pro	Ile	Trp	Ala	Lys	Ile	Pro	
		610					615				620						
[0113]	His	Thr	Asp	Gly	Asn	Phe	His	Pro	Ser	Pro	Leu	Met	Gly	Gly	Phe	Gly	
	625					630					635					640	
	Leu	Lys	His	Pro	Pro	Pro	Gln	Ile	Leu	Ile	Lys	Asn	Thr	Pro	Val	Pro	
				645					650						655		
	Ala	Asn	Pro	Pro	Glu	Val	Phe	Thr	Pro	Ala	Lys	Phe	Ala	Ser	Phe	Ile	
			660					665					670				
	Thr	Gln	Tyr	Ser	Thr	Gly	Gln	Val	Ser	Val	Glu	Ile	Glu	Trp	Glu	Leu	
		675					680					685					
	Gln	Lys	Glu	Asn	Ser	Lys	Arg	Trp	Asn	Pro	Glu	Ile	Gln	Tyr	Thr	Ser	
		690					695				700						
	Asn	Phe	Asp	Lys	Gln	Thr	Gly	Val	Asp	Phe	Ala	Val	Asp	Ser	Gln	Gly	
	705					710				715						720	
	Val	Tyr	Ser	Glu	Pro	Arg	Pro	Ile	Gly	Thr	Arg	Tyr	Leu	Thr	Arg	Asn	
				725				730						735			
	Leu																
	<210>	50															
	<211>	736															
	<212>	PRT															

<213> 腺相关病毒, hu, 48的衣壳蛋白

<400> 50

Met Ala Ala Asp Gly Tyr Leu Pro Asp Trp Leu Glu Asp Asn Leu Ser
1 5 10 15

Glu Gly Ile Arg Glu Trp Trp Asp Leu Lys Pro Gly Ala Pro Lys Pro
20 25 30

Lys Ala Asn Gln Gln Lys Gln Asp Asp Gly Arg Gly Leu Val Leu Pro
35 40 45

Gly Tyr Lys Tyr Leu Gly Pro Phe Asn Gly Leu Asp Lys Gly Glu Pro
50 55 60

Val Asn Ala Ala Asp Ala Ala Ala Leu Glu His Asp Lys Ala Tyr Asp
65 70 75 80

Gln Gln Leu Lys Ala Gly Asp Asn Pro Tyr Leu Arg Tyr Asn His Ala
85 90 95

Asp Ala Glu Phe Gln Glu Arg Leu Gln Glu Asp Thr Ser Phe Gly Gly
100 105 110

[0114]

Asn Leu Gly Arg Ala Val Phe Gln Ala Lys Lys Arg Val Leu Glu Pro
115 120 125

Leu Gly Leu Val Glu Glu Gly Ala Lys Thr Ala Pro Gly Lys Lys Arg
130 135 140

Pro Val Glu Gln Ser Pro Gln Glu Pro Asp Ser Ser Ser Gly Ile Gly
145 150 155 160

Lys Thr Gly Gln Gln Pro Ala Lys Lys Arg Leu Asn Phe Gly Gln Thr
165 170 175

Gly Asp Ser Glu Ser Val Pro Asp Pro Gln Pro Leu Gly Glu Pro Pro
180 185 190

Ala Thr Pro Ala Ala Val Gly Pro Thr Thr Met Ala Ser Gly Gly Gly
195 200 205

Ala Pro Met Ala Asp Asn Asn Glu Gly Ala Asp Gly Val Gly Asn Ala
210 215 220

Ser Gly Asn Trp His Cys Asp Ser Thr Trp Leu Gly Asp Arg Val Ile
225 230 235 240

Thr Thr Ser Thr Arg Thr Trp Ala Leu Pro Thr Tyr Asn Asn His Leu
245 250 255

	Tyr	Lys	Gln	Ile	Ser	Ser	Thr	Ser	Thr	Gly	Ala	Ser	Asn	Asp	Asn	His	
				260						265					270		
	Tyr	Phe	Gly	Tyr	Gly	Thr	Pro	Trp	Gly	Tyr	Phe	Asp	Phe	Asn	Arg	Phe	
			275					280					285				
	His	Cys	His	Phe	Ser	Pro	Arg	Asp	Trp	Gln	Arg	Leu	Ile	Asn	Asn	Asn	
		290					295					300					
	Trp	Gly	Phe	Arg	Pro	Lys	Arg	Leu	Asn	Phe	Lys	Leu	Phe	Asn	Ile	Gln	
	305					310				315						320	
	Val	Glu	Glu	Val	Thr	Thr	Asn	Asp	Gly	Val	Thr	Thr	Ile	Ala	Asn	Asn	
				325						330					335		
	Leu	Thr	Ser	Thr	Val	Gln	Val	Phe	Ser	Asp	Ser	Glu	Tyr	Gln	Leu	Pro	
				340					345					350			
	Tyr	Val	Leu	Gly	Ser	Ala	His	Gln	Gly	Cys	Leu	Pro	Pro	Phe	Pro	Ala	
		355						360					365				
	Asp	Val	Phe	Met	Ile	Pro	Gln	Tyr	Gly	Tyr	Leu	Thr	Leu	Asn	Asn	Gly	
		370					375					380					
[0115]	Ser	Gln	Ala	Val	Gly	Arg	Ser	Ser	Phe	Tyr	Cys	Leu	Glu	Tyr	Phe	Pro	
	385					390					395					400	
	Ser	Gln	Met	Leu	Arg	Thr	Gly	Asn	Asn	Phe	Thr	Phe	Ser	Tyr	Thr	Phe	
				405						410					415		
	Glu	Glu	Val	Pro	Phe	His	Ser	Ser	Tyr	Ala	His	Ser	Gln	Ser	Leu	Asp	
				420					425					430			
	Arg	Leu	Met	Asn	Pro	Leu	Ile	Asp	Gln	Tyr	Leu	Tyr	Tyr	Leu	Asn	Arg	
		435					440						445				
	Thr	Gln	Asn	Gln	Ser	Gly	Ser	Ala	Gln	Asn	Lys	Asp	Leu	Leu	Phe	Ser	
		450				455						460					
	Arg	Gly	Ser	Pro	Ala	Gly	Met	Ser	Val	Gln	Pro	Lys	Asn	Trp	Leu	Pro	
	465					470					475					480	
	Gly	Pro	Cys	Tyr	Arg	Gln	Gln	Arg	Val	Ser	Lys	Thr	Lys	Thr	Asp	Asn	
				485					490						495		
	Asn	Asn	Ser	Asn	Phe	Thr	Trp	Thr	Gly	Ala	Ser	Lys	Tyr	Asn	Leu	Asn	
				500					505					510			
	Gly	Arg	Glu	Ser	Ile	Ile	Asn	Pro	Gly	Thr	Ala	Val	Ala	Ser	His	Lys	
		515					520						525				

	Asp	Asp	Glu	Asp	Lys	Phe	Phe	Pro	Met	Ser	Gly	Val	Met	Ile	Phe	Gly
	530							535				540				
	Lys	Glu	Ser	Ala	Gly	Ala	Ser	Ser	Thr	Ala	Leu	Asp	Asn	Val	Met	Ile
	545					550					555				560	
	Thr	Asp	Glu	Glu	Glu	Ile	Lys	Ala	Thr	Asn	Pro	Val	Ala	Thr	Glu	Arg
					565					570					575	
	Phe	Gly	Thr	Val	Ala	Val	Asn	Phe	Gln	Ser	Ser	Ser	Thr	Asp	Pro	Ala
				580					585					590		
	Thr	Gly	Asp	Val	His	Ala	Met	Gly	Ala	Leu	Pro	Gly	Met	Val	Trp	Gln
		595						600					605			
	Asp	Arg	Asp	Val	Tyr	Leu	Gln	Gly	Pro	Ile	Trp	Ala	Lys	Ile	Pro	His
	610						615					620				
[0116]	Thr	Asp	Gly	His	Phe	His	Pro	Ser	Pro	Leu	Met	Gly	Gly	Phe	Gly	Leu
	625					630					635					640
	Lys	Asn	Pro	Pro	Pro	Gln	Ile	Leu	Ile	Lys	Asn	Thr	Pro	Val	Pro	Ala
					645					650					655	
	Asn	Pro	Pro	Ala	Glu	Phe	Ser	Ala	Thr	Lys	Phe	Ala	Ser	Phe	Ile	Thr
				660					665					670		
	Gln	Tyr	Ser	Thr	Gly	Gln	Val	Ser	Val	Glu	Ile	Glu	Trp	Glu	Leu	Gln
		675					680						685			
	Lys	Glu	Asn	Ser	Lys	Arg	Trp	Asn	Pro	Glu	Val	Gln	Tyr	Thr	Ser	Asn
	690						695					700				
	Tyr	Ala	Lys	Ser	Ala	Asn	Val	Asp	Phe	Thr	Val	Asp	Asn	Asn	Gly	Leu
	705					710					715				720	
	Tyr	Thr	Glu	Pro	Arg	Pro	Ile	Gly	Thr	Arg	Tyr	Leu	Thr	Arg	Pro	Leu
					725					730					735	

单现突变体外裂解物的转导

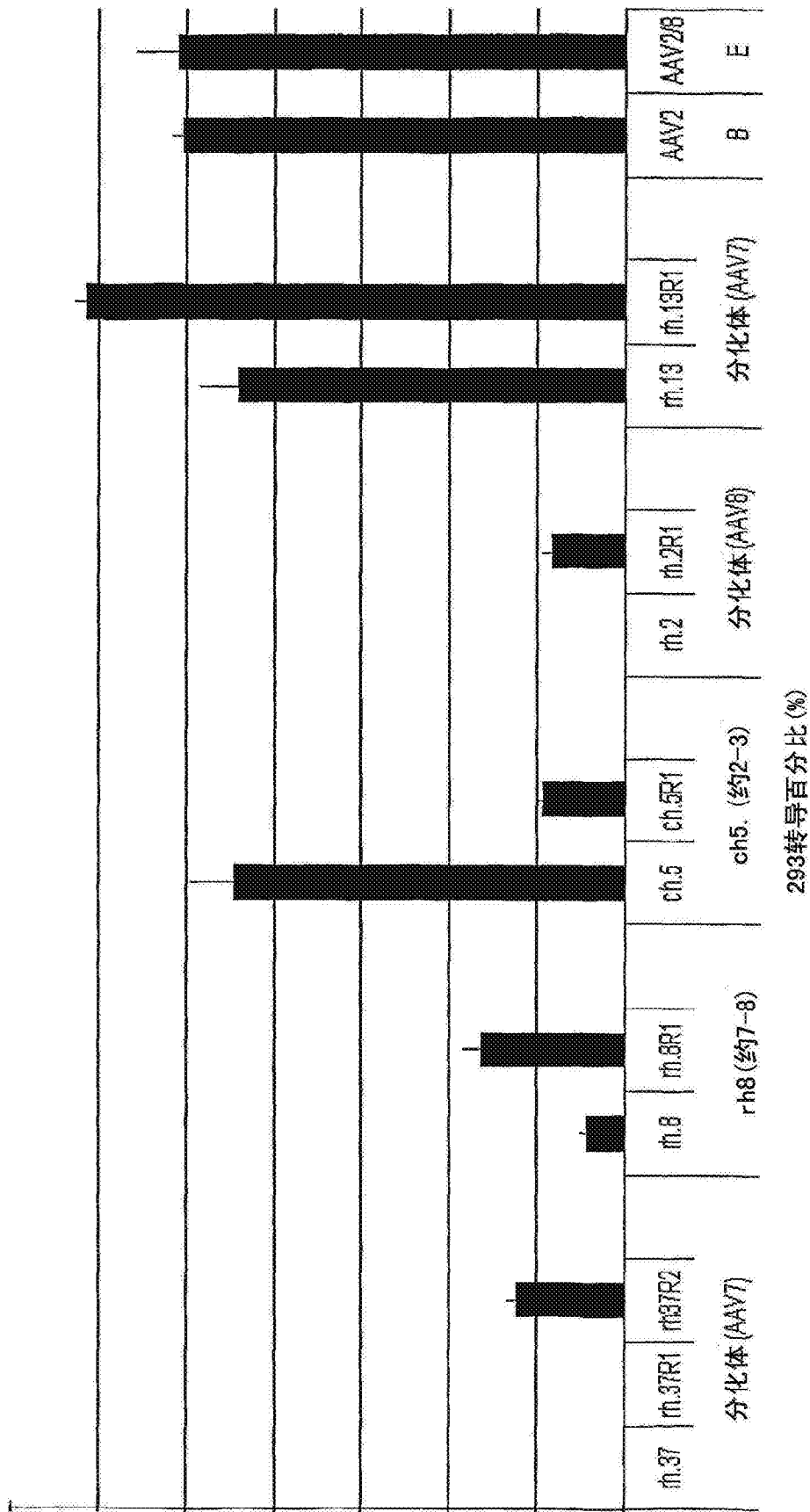


图1

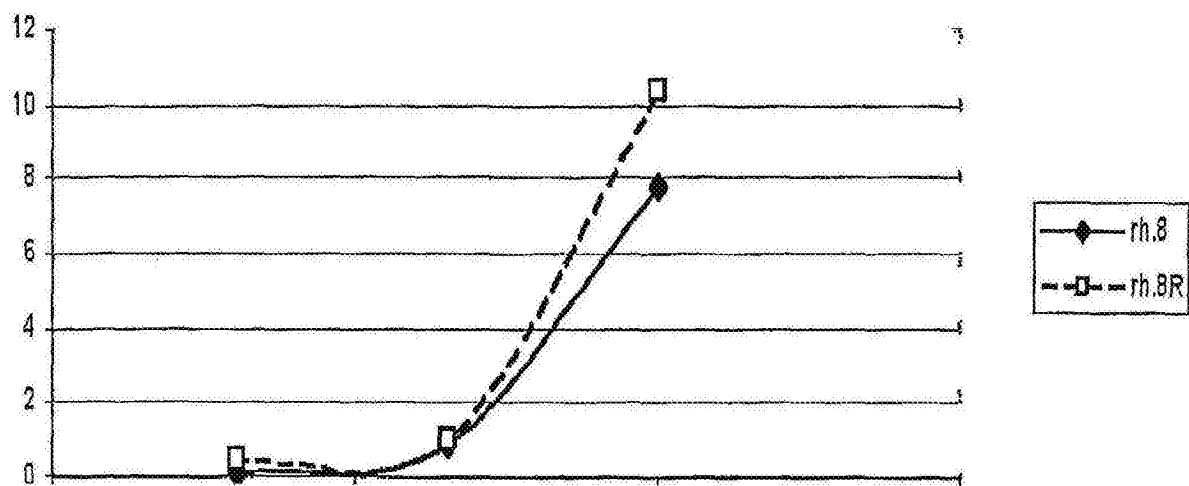


图2A

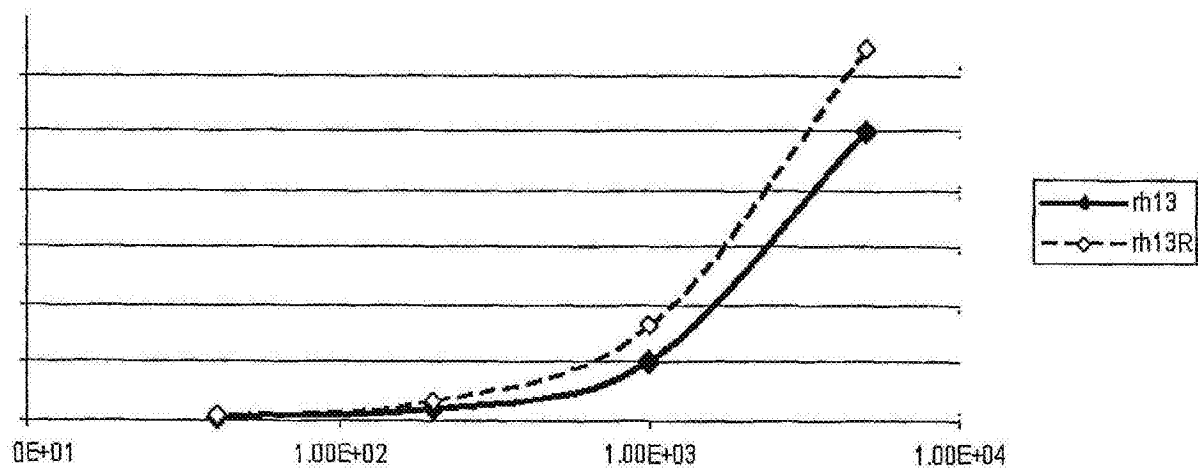


图2B

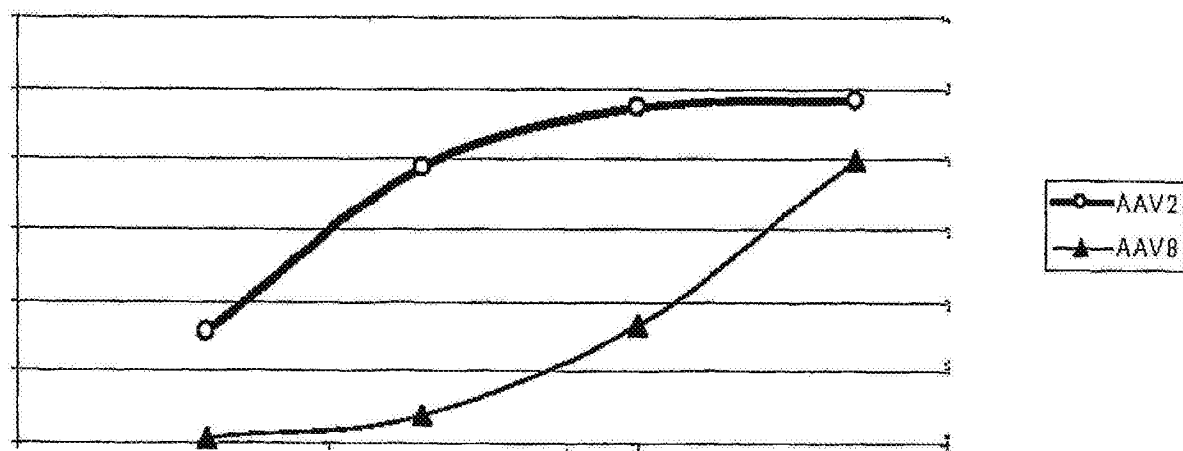


图2C

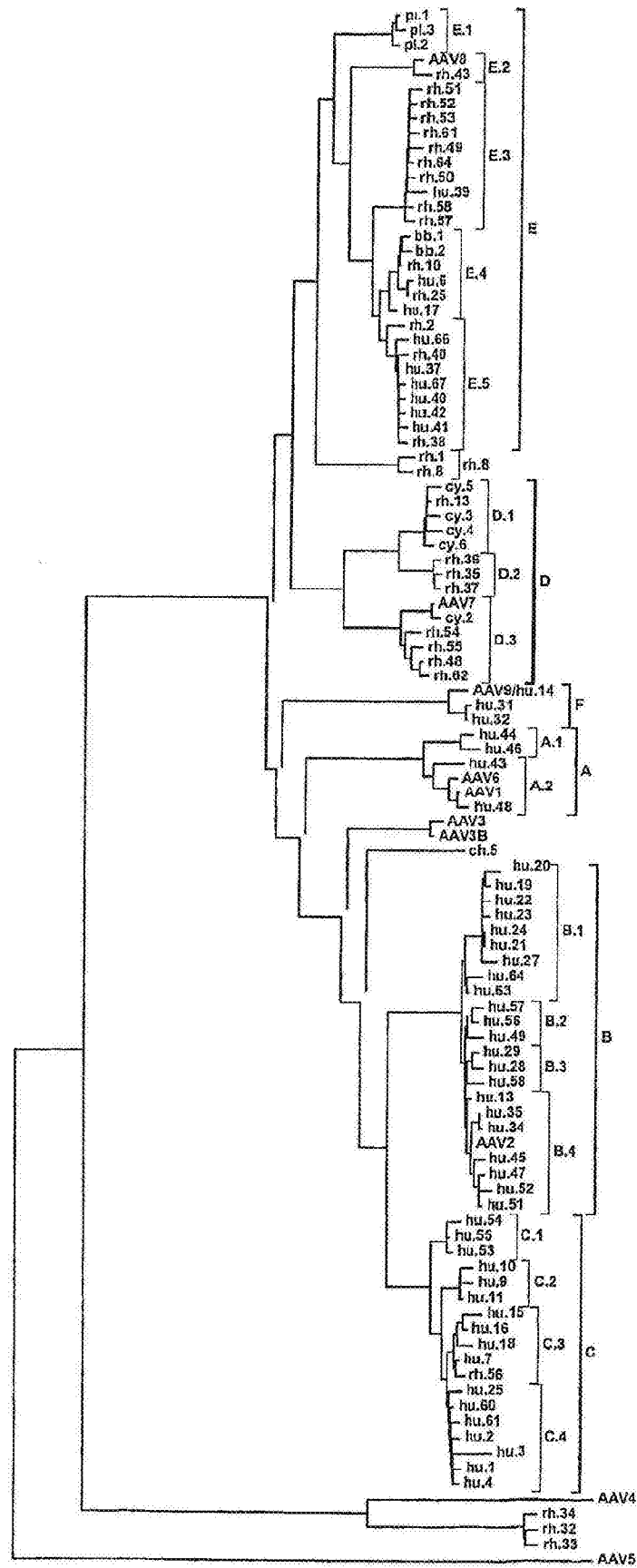


图3

图4A

	210	220	230	240	250	260	270	280	290	300
AAV2	g	g	g	g	g	g	g	g	g	g
cy.5	g	g	g	g	g	g	g	g	g	g
rh.10	g	g	g	g	g	g	g	g	g	g
rh.13	g	g	g	g	g	g	g	g	g	g
AAV1	g	g	g	g	g	g	g	g	g	g
AAV3	g	g	g	g	g	g	g	g	g	g
AAV6	g	g	g	g	g	g	g	g	g	g
AAV7	g	g	g	g	g	g	g	g	g	g
AAV8	g	g	g	g	g	g	g	g	g	g
hu.13	g	g	g	g	g	g	g	g	g	g
hu.26	g	g	g	g	g	g	g	g	g	g
hu.37	g	g	g	g	g	g	g	g	g	g
hu.53	g	g	g	g	g	g	g	g	g	g
rh.39	g	g	g	g	g	g	g	g	g	g
rh.43	g	g	g	g	g	g	g	g	g	g
rh.46	g	g	g	g	g	g	g	g	g	g

	310	320	330	340	350	360	370	380	390	400
AAV2	c	c	c	c	c	c	c	c	c	c
cy.5	c	c	c	c	c	c	c	c	c	c
rh.10	c	c	c	c	c	c	c	c	c	c
rh.13	c	c	c	c	c	c	c	c	c	c
AAV1	c	c	c	c	c	c	c	c	c	c
AAV3	c	c	c	c	c	c	c	c	c	c
AAV6	c	c	c	c	c	c	c	c	c	c
AAV7	c	c	c	c	c	c	c	c	c	c
AAV8	c	c	c	c	c	c	c	c	c	c
hu.13	c	c	c	c	c	c	c	c	c	c
hu.26	c	c	c	c	c	c	c	c	c	c
hu.37	c	c	c	c	c	c	c	c	c	c
hu.53	c	c	c	c	c	c	c	c	c	c
rh.39	c	c	c	c	c	c	c	c	c	c
rh.43	c	c	c	c	c	c	c	c	c	c
rh.46	c	c	c	c	c	c	c	c	c	c

图4B

	410	420	430	440	450	460	470	480	490	500
AAV2	aac	ctgt	taag	acg	ctc	cgga	aaag	ggc	ggg	taag
cy.5	ggc	c	t	g	a	ca	a	g	a	g
rh.10	ggc	c	t	g	a	ca	a	g	a	g
rh.13	ggc	c	t	g	a	ca	a	g	a	g
AAV1	ggc	c	t	g	a	ca	a	g	a	g
AAV3	g	a	c	a	t	g	a	c	a	a
AAV6	gg	c	t	g	a	c	a	t	g	a
AAV7	ggc	c	t	g	a	ca	cg	ttcc	c	a
AAV8	ggc	c	t	g	a	ca	cg	ttct	c	a
hu.13	g	a	c	a	t	g	a	c	a	a
hu.26	g	a	c	a	t	g	a	c	a	a
hu.37	g	a	c	a	t	g	a	c	a	a
hu.53	g	a	c	a	t	g	a	c	a	a
rh.39	ggc	c	t	g	a	ca	cg	ttcc	c	a
rh.43	ggc	c	t	g	a	ca	cg	ttcc	c	a
rh.46	ggc	c	t	g	a	ca	cg	ttcc	c	a
	510	520	530	540	550	560	570	580	590	600
AAV2	tg	ca	g	a	a	a	a	a	a	a
cy.5	c	t	a	g	a	c	c	c	c	c
rh.10	c	g	a	g	a	c	c	c	c	c
rh.13	c	t	a	g	a	c	c	c	c	c
AAV1	c	t	a	g	a	c	c	c	c	c
AAV3	c	t	a	g	a	c	c	c	c	c
AAV6	c	t	a	g	a	c	c	c	c	c
AAV7	c	t	a	g	a	c	c	c	c	c
AAV8	c	t	a	g	a	c	c	c	c	c
hu.13	c	t	a	g	a	c	c	c	c	c
hu.26	c	t	a	g	a	c	c	c	c	c
hu.37	c	t	a	g	a	c	c	c	c	c
hu.53	c	t	a	g	a	c	c	c	c	c
rh.39	c	t	a	g	a	c	c	c	c	c
rh.43	c	t	a	g	a	c	c	c	c	c
rh.46	c	t	a	g	a	c	c	c	c	c

图4C

	610	620	630	640	650	660	670	680	690	700
AAV2	actaatacga	tggtacag	gcagtg	gcacga	taacag	ggggcc	gcagga	gtgggt	aatctc	tcctcg
cy.5	tgga	ga	ga	ga	ga	ga	ga	ga	ga	ga
rh.10	tgga	ga	ga	ga	ga	ga	ga	ga	ga	ga
rh.13	tgga	ga	ga	ga	ga	ga	ga	ga	ga	ga
AAV1	ctc	ctc	ctc	ctc	ctc	ctc	ctc	ctc	ctc	ctc
AAV3	ctc	ctc	ctc	ctc	ctc	ctc	ctc	ctc	ctc	ctc
AAV6	ctc	ctc	ctc	ctc	ctc	ctc	ctc	ctc	ctc	ctc
AAV7	ctc	ctc	ctc	ctc	ctc	ctc	ctc	ctc	ctc	ctc
AAV8	ctc	ctc	ctc	ctc	ctc	ctc	ctc	ctc	ctc	ctc
hu.13	ctc	ctc	ctc	ctc	ctc	ctc	ctc	ctc	ctc	ctc
hu.26	ctc	ctc	ctc	ctc	ctc	ctc	ctc	ctc	ctc	ctc
hu.37	ctc	ctc	ctc	ctc	ctc	ctc	ctc	ctc	ctc	ctc
hu.53	ctc	ctc	ctc	ctc	ctc	ctc	ctc	ctc	ctc	ctc
rh.39	ctc	ctc	ctc	ctc	ctc	ctc	ctc	ctc	ctc	ctc
rh.43	ctc	ctc	ctc	ctc	ctc	ctc	ctc	ctc	ctc	ctc
rh.46	ctc	ctc	ctc	ctc	ctc	ctc	ctc	ctc	ctc	ctc

	710	720	730	740	750	760	770	780	790	800
AAV2	catggatgg	gcagag	tcattc	accacg	acccga	acccgt	ggccct	ggccac	ctacac	caacaa
cy.5	ctc	ctc	ctc	ctc	ctc	ctc	ctc	ctc	ctc	ctc
rh.10	ctc	ctc	ctc	ctc	ctc	ctc	ctc	ctc	ctc	ctc
rh.13	ctc	ctc	ctc	ctc	ctc	ctc	ctc	ctc	ctc	ctc
AAV1	ctc	ctc	ctc	ctc	ctc	ctc	ctc	ctc	ctc	ctc
AAV3	ctc	ctc	ctc	ctc	ctc	ctc	ctc	ctc	ctc	ctc
AAV6	ctc	ctc	ctc	ctc	ctc	ctc	ctc	ctc	ctc	ctc
AAV7	ctc	ctc	ctc	ctc	ctc	ctc	ctc	ctc	ctc	ctc
AAV8	ctc	ctc	ctc	ctc	ctc	ctc	ctc	ctc	ctc	ctc
hu.13	ctc	ctc	ctc	ctc	ctc	ctc	ctc	ctc	ctc	ctc
hu.26	ctc	ctc	ctc	ctc	ctc	ctc	ctc	ctc	ctc	ctc
hu.37	ctc	ctc	ctc	ctc	ctc	ctc	ctc	ctc	ctc	ctc
rh.39	ctc	ctc	ctc	ctc	ctc	ctc	ctc	ctc	ctc	ctc
rh.43	ctc	ctc	ctc	ctc	ctc	ctc	ctc	ctc	ctc	ctc
rh.46	ctc	ctc	ctc	ctc	ctc	ctc	ctc	ctc	ctc	ctc

图4D

[illegible]

图4E

	1010	1020	1030	1040	1050	1060	1070	1080	1090	1100
AAV2	cgattgccaataac	cttaccagcacggt	tcagggtgtttact	gactgactggagta	ccagctcccgta	ccgtacgtccctgg	ctcctggcgaat	caaggatgcctcc	ccgc	
cy.5	.c.c.t.	.a.a.a.	.c.ct.g.	.a.g.	.t.	.c.g.c.	.g.c.	.g.c.	.g.c.	.t.
rh.10	.c.c.t.	.a.a.a.	.c.ct.g.	.a.g.	.t.	.c.g.c.	.g.c.	.g.c.	.g.c.	.t.
rh.13	.c.c.t.	.a.a.a.	.c.ct.g.	.a.g.	.t.	.c.g.c.	.g.c.	.g.c.	.g.c.	.t.
AAV1	.c.c.t.	.a.a.a.	.c.ct.g.	.a.g.	.t.	.c.g.c.	.g.c.	.g.c.	.g.c.	.t.
AAV3	.t.	.a.a.a.	.c.ct.g.	.a.g.	.t.	.c.g.c.	.g.c.	.g.c.	.g.c.	.t.
AAV6	.c.c.t.	.a.a.a.	.c.ct.g.	.a.g.	.t.	.c.g.c.	.g.c.	.g.c.	.g.c.	.t.
AAV7	.c.c.t.	.a.a.a.	.c.ct.g.	.a.g.	.t.	.c.g.c.	.g.c.	.g.c.	.g.c.	.t.
AAV8	.c.c.c.	.c.ca.c.	.c.g.	.g.	.t.	.c.c.c.	.g.c.	.g.c.	.g.c.	.t.
hu.13										
hu.26	.c.c.	.a.a.g.	.a.g.	.g.	.c.g.c.	.g.c.	.g.c.	.g.c.	.g.c.	.t.
hu.37	.c.c.	.a.a.g.	.a.g.	.g.	.c.g.c.	.g.c.	.g.c.	.g.c.	.g.c.	.t.
hu.53	.c.c.	.a.a.g.	.a.g.	.g.	.c.g.c.	.g.c.	.g.c.	.g.c.	.g.c.	.t.
rh.39	.c.c.	.ca.c.	.c.g.	.g.	.t.	.c.c.c.	.g.c.	.g.c.	.g.c.	.t.
rh.43	.c.c.	.ca.c.	.c.g.	.g.	.t.	.c.c.c.	.g.c.	.g.c.	.g.c.	.t.
rh.46	.c.c.	.ca.c.	.c.g.	.g.	.t.	.c.c.c.	.g.c.	.g.c.	.g.c.	.t.

	1110	1120	1130	1140	1150	1160	1170	1180	1190	1200
AAV2	gttcccagcagcgt	cttctcatggtg	ccacagtatgg	atacctcaccct	gaacaacggg	agtcaggcagtc	agtaggacgct	cttctcattt	actgctggag	tac
cy.5	.t.g.	.g.	.a.t.t.	.c.c.t.	.g.t.a.	.c.c.c.	.t.g.	.c.c.c.	.c.c.	.t.
rh.10	.g.g.	.a.t.t.	.c.c.g.	.g.t.	.t.a.	.c.c.c.	.c.g.	.c.c.c.	.c.c.	.t.
rh.13	.t.g.	.g.	.a.t.t.	.c.c.t.	.g.t.a.	.c.c.c.	.t.g.	.c.c.c.	.c.c.	.t.
AAV1	.g.g.	.g.	.a.t.t.	.c.c.c.	.g.g.c.	.t.c.c.a.c.g.	.t.a.c.	.c.c.	.c.c.	.t.
AAV3	.t.	.c.t.	.c.c.	.t.	.a.a.g.g.	.a.a.c.	.a.c.	.a.c.	.a.c.	.t.
AAV6	.g.g.	.g.	.a.t.g.	.c.c.c.	.a.g.c.	.t.c.c.	.g.g.	.a.c.	.a.c.	.t.
AAV7	.g.g.	.a.t.t.	.c.c.c.	.g.t.c.	.t.c.	.t.c.	.t.g.	.c.c.c.	.c.c.	.t.
AAV8	.g.g.	.g.	.a.t.c.	.c.c.c.	.a.a.c.	.t.c.c.	.c.g.	.c.c.c.	.c.c.	.t.
hu.13										
hu.26	.g.g.	.a.t.c.	.c.c.c.	.t.a.	.t.a.	.c.c.c.	.c.g.	.c.c.c.	.c.c.	.t.
hu.37	.t.g.	.c.c.	.c.c.c.	.t.a.	.t.a.	.c.c.c.	.g.g.	.c.c.	.c.c.	.t.
hu.53	.g.g.	.a.t.c.	.c.c.c.	.t.a.	.t.a.	.c.c.c.	.c.g.	.c.c.c.	.c.c.	.t.
rh.39	.g.g.	.a.t.c.	.c.c.c.	.a.a.c.	.t.c.c.	.t.c.c.	.c.g.	.c.c.c.	.c.c.	.t.
rh.43	.g.g.	.a.t.t.	.c.c.c.	.g.t.c.	.t.c.c.	.t.c.c.	.c.g.	.c.c.c.	.c.c.	.t.
rh.46	.g.g.	.a.t.t.	.c.c.c.	.g.t.c.	.t.c.c.	.t.c.c.	.c.g.	.c.c.c.	.c.c.	.t.

图4F

图4G

图4H

	1610	1620	1630	1640	1650	1660	1670	1680	1690	1700
AAV2										
cy.5	aagaaaagtttttctcagagcggggttctcatcttttgggaagcaggctcagagaacacaatgttgacattgaaaggtcatgtattacagacgaaga									
rh.10	.g..cc.....c..catc.a...a..g..gg.t.....c..aacg..gg.t.cc..c---.gacaacgc.g.....c..gc.a..g..cag...g..									
rh.13	..gcca.....gtcc.....a..ct.a..g.....a..g..ag.t.ga...gac..C.....ta.agc.gc..t...c.a..cagt...g..									
AAV1	.g..cc.....c..catc.a...a..g..gg.t.....cg.aacg..gg.t.cc..c---.gacaacgc.g.....c..gc.a..g..cag...g..									
AAV3	..c.....c.....cat.....t..ca.g.t.....a..ag.ga..g..c.gagctt...cact.cat.g..c..t.....g..t.....									
AAV6	a.....c.....at.ca...caa...a.....c..ag...ga...ac.gc..gt..c.ca..at.a..t..t..a.....g..t.....									
AAV7	..c.....c.....cat.....t..ca.g.t.....a.....g.ga..g..c.gagctt...cact.cat.g..c..t.....c.....									
AAV8	.g..ccgc.....c..atcc.....a..C..g.t.....a..aact..ag..act..c---.aactacat.g.....t..gt.a..g...a.t.....									
hu.13	.g..gcgt.....cagct.a...a..c..g.t.....c..a..aatg.t.cc.g.gac...c..ttacagcg.t.....c..c.c.cag...g..									
hu.26	a.....a.....a.....a.....a.....a.....a.....a.....a.....a.....a.....a.....a.....a.....a.....									
hu.37	.g...cgc..C..C..gtc...t..a..C..g..g..C..a..a..g..tg.t.ga.g.gac.....tacagc.gc..t...c..a..cag.....									
hu.53	c.....c.....cat.cat..aacc..a..a.....t..ag...aa..a.tgct...c..c..c...at.g.....t.....t.....									
rh.39	.g...cgc...c..c..gtc...t..a..c..g..g...a..a..g..tg.t.ga.g.gac.....tacagc.gc..t...c..a..cag.....									
rh.43	.g..gcgt.....c..agta.cg..a---tc.tgt...t..c..a..aatg.t.cc.g.gac...c..ttacagcg.t.....c..c.c.cag...g..									
rh.46	.g...cgc..C..C..atcc.....ca.C.....c.....g..ag.t.ga...gac..C.....ta.agc..c..g...c..a..cag...g..									
AAV2										
cy.5	ggaatcaggacaacccaatcccggtggctacggagcagtatggttctgtatctaccacccctccagagagggccaacagcagcagctaccgcagatgtcaac									
rh.10	a.....t..aa..C.....C..a.....C..a..a.....C..gtg..c..c..g.....g...atcgctc.cggcgg.c.ccag..acagac.....									
rh.13	..g.....aa..C.....C..a.....C..a..a.....C..gtg..c..c..g.....g...atcgctc.cggcgg.c.ccag..acagac.....									
AAV1	t..aag.C..t..c..t.....C..C..aaga.t...ga.C..gg.agt...tt.....ca...g..c.g.cc.t..g...g...gc.t									
AAV3	a..g..tc.t..C.....t.....t.....a.....a.....gg.a.at...t.g.....ctca...t.c.gctc.ca.g..t.g.ac...t									
AAV6	aag.C..t..c.....C..C..aaga.t...ga...gg.agt...t.....Ca...g..c.g.cc.t..g...g...gc.t									
AAV7	a.....tc.tc.t..t.....t..a..C.....ag.a..C..gata..cagc.g...t..a..agcg.ct...t.ctgc...ccag..aca..t.....									
AAV8	a.....aa..C..t..c..t.....a.....g.a..C...atc..gg.agat...t.g...cagcaa...cggctc.tcaa.tt.g.ac.....									
hu.13	C.....C.....C.....C.....C.....C.....C.....C.....C.....C.....C.....C.....C.....C.....									
hu.26	t..aa..C..t..c.....a.....C..a..a..a..C...gtg..gg..ga...t.g...ca.ac...t.c.gggc.tat.gtg.g.a.....									
hu.37	C.....C.....C.....C.....C.....C.....C.....C.....C.....C.....C.....C.....C.....C.....									
hu.53	t..aa..C..t..c..t.....a.....C..a..a..a..C...gtg..gg..gat...t.g...ca.ac...t.cggggc.tat.gtg.g.a.....									
rh.39	a.....aa..C..t..c..t.....a.....g.a..C...atc..gg.agat...t.g...cagcaa...cggctc.tcaa.tt.g.ac.....									
rh.43	a.g.c.....C.....C.....C.....C.....C.....C.....C.....C.....C.....C.....C.....C.....C.....									
rh.46	a.g.c.....C.....C.....C.....C.....C.....C.....C.....C.....C.....C.....C.....C.....C.....									

图41

	2010	2020	2030	2040	2050	2060	2070	2080	2090	2100
AAV2	g	g	g	g	g	g	g	g	g	g
cy.5	t	t	t	t	t	t	t	t	t	t
rh.10	a	a	a	a	a	a	a	a	a	a
rh.13	t	t	t	t	t	t	t	t	t	t
AAV1	ta	ta	ta	ta	ta	ta	ta	ta	ta	ta
AAV3	ta	ta	ta	ta	ta	ta	ta	ta	ta	ta
AAV6	ta	ta	ta	ta	ta	ta	ta	ta	ta	ta
AAV7	t	t	t	t	t	t	t	t	t	t
AAV8	t	t	t	t	t	t	t	t	t	t
hu.13	t	t	t	t	t	t	t	t	t	t
hu.26	t	t	t	t	t	t	t	t	t	t
hu.37	t	t	t	t	t	t	t	t	t	t
hu.53	t	t	t	t	t	t	t	t	t	t
rh.39	t	t	t	t	t	t	t	t	t	t
rh.43	t	t	t	t	t	t	t	t	t	t
rh.46	t	t	t	t	t	t	t	t	t	t
AAV2	g	g	g	g	g	g	g	g	g	g
cy.5	t	t	t	t	t	t	t	t	t	t
rh.10	a	a	a	a	a	a	a	a	a	a
rh.13	t	t	t	t	t	t	t	t	t	t
AAV1	ta	ta	ta	ta	ta	ta	ta	ta	ta	ta
AAV3	ta	ta	ta	ta	ta	ta	ta	ta	ta	ta
AAV6	ta	ta	ta	ta	ta	ta	ta	ta	ta	ta
AAV7	t	t	t	t	t	t	t	t	t	t
AAV8	t	t	t	t	t	t	t	t	t	t
hu.13	t	t	t	t	t	t	t	t	t	t
hu.26	t	t	t	t	t	t	t	t	t	t
hu.37	t	t	t	t	t	t	t	t	t	t
hu.53	t	t	t	t	t	t	t	t	t	t
rh.39	t	t	t	t	t	t	t	t	t	t
rh.43	t	t	t	t	t	t	t	t	t	t
rh.46	t	t	t	t	t	t	t	t	t	t

图4K

	2210	2220
AAV2	...l...l...l...l	...l...l...l...l
cy.5	acctgactcgtaatactgtaa	
rh.10	...c...c...c...c	
rh.13	...c...c...c...c	
AAV1	...c...c...c...c	
AAV3	...t...c...c...c	
AAV6	...t...c...a...a...ct...	
AAV7	...c...c...c...c...c...c	
AAV8	...c...c...c...c...c...c	
hu.13	...	
hu.26	...	
hu.37	...c...c...c...c	
hu.53	...c...c...c...c	
rh.39	...c...c...c...c	
rh.43	...c...c...c...c	
rh.46	...c...c...c...c	

图4L

	10	20	30	40	50	60	70	80	90	100													
AAV2	MAADG	YLPD	WLED	TLSE	GIRQ	WKLK	PGPP	PKPA	ERHK	DSRGL	VLPG	YKYL	GPFG	NGLD	KGEP	NEAD	AAALE	HDKAY	DRQLD	SCDN	PYLK	YNHDA	EAEF
CY.5	GN	E.D.	A.K.	ANQKQ	G	R														K.EQ			
rh.10	N	E.D.	A.K.	ANQKQ	G															Q.KA			
rh.13	N	E.D.	A.K.	ANQKQ	G															K.EQ			
AAV1	N	E.D.	A.K.	ANQKQ	G															Q.KA			
AAV3	N	E.A.	V.Q.	ANQKQ	Q.NR	G														Q.KA			
AAV6	N	E.D.	A.K.	ANQKQ	G															Q.KA			
AAV7	N	E.D.	A.K.	ANQKQ	NG															Q.KA			
AAV8	N	E.A.	A.K.	ANQKQ	G															Q.QA			
hu.13																							
hu.26																							
hu.37	N	E.D.	A.K.	ANQKQ	G															Q.KA			
hu.53																							
rh.39	N	E.D.	A.K.	ANQKQ	G															Q.KA			
rh.43	N	E.D.	A.K.	ANQKQ	G															Q.EA			
rh.46	N	E.D.	A.K.	ANQKQ	G															Q.KA			
AAV2	QERL	KEDT	SFGN	LGRA	VFOA	KRVLEP	LGVEE	VPKTA	PGKRP	VEHSPV	EPDSS	SGTGKAG	QOPAR	KRLN	FGQT	GDAD	SVDP	QDQ	LCOP	PAAP	SGLG		
CY.5	Q																						
rh.10	Q																						
rh.13	Q																						
AAV1	Q																						
AAV3	Q																						
AAV6	Q																						
AAV7	Q																						
AAV8	Q																						
hu.13																							
hu.26																							
hu.37	Q																						
hu.53																							
rh.39	Q																						
rh.43	Q																						
rh.46	Q																						

图5A

[illegible]

	510	520	530	540	550	560	570	580	590	600												
AAV2	NSEYSW	GATKYH	NGRDSL	VNPG	AMASHK	DEEKFF	QSGV	LIEFK	QSGSEK	TNV	IEKVM	ITDEE	IRTTN	PVATE	QYGSV	STNL	QRN	QAATAD	VN			
cy 5	NFA	N	T	V	DN	Q	IN	V	T	AAN	KITL	N	LM	S	K	E	V	S	SSTAGPQ	QT		
rh 10	NFA		V	T	R	S	M	AG	D	YSS	I	S	K		V	AD	QQ	AAPIVGA				
rh 13	NFA	N	T	V	DN	Q	IN	V	ET	AAN	KITL	N	LM	S	K	E	V	S	SSTAGPQ	QT		
AAV1	NFT	S	N	E	II	T	D	M	M	ESAGAS	TALDN				KA	RE	T	AV	F	SSSTDP	G	H
AAV3	NFP	A	S					MH	N	E	TTAS	AELDN				T	AN	SS	TAPT	GT		
AAV6	NFT	S	N	E	II	T	KD	M	M	ESAGAS	TALDN				KA	RF	T	AV	SSSTDP	G	H	
AAV7	NFA		N	V	T	DR	S	T	ATN	KITL	N	LM	N		P	E	I	S	AA	TA	Q	QV
AAV8	NFA	AG	N	A	I	T	R	SN	I	NAARD	A	YSD	I	S	K	E	I	AD	QQ	TAPQIGT		
hu 13	D																					
hu 26	D																					
hu 37	NFA		V	T	R	S	M	AGRD	YSS	I	S	K				V	AD	QT	TGPIVGN			
hu 53	NFP	Y			MH	T	E	TNA	AELN							Y	N	NS	TA	S	ET	
rh 39	NFA		V	T	R	S	M	AGRD	YSS	I	S	K				V	AD	QT	TGPIVGN			
rh 43	NFA	AG	N	A	I	T	R	VT	SC	WQ	NAARD	A	YSD	I	S	K	E	I	AD	QQ	TAPQIGT	
rh 46	NFA		V	TN	DR	S	I	M	AG	D	YSN	I	S	K		V	AD	QQ	TAPIVGA			

图5C

	610	620	630	640	650	660	670	680	690	700
AAV2	TQGVLP	GMVWQDRD	VYLOGP	PIWAKIPHT	DGHEHP	SPIMG	CGFLKH	PPQI	LKNTFP	PANPST
cy.5	S..A..	N..N..	N..N..	N..N..	N..N..	N..N..	N..N..	N..N..	N..N..	N..N..
rh.10	S..A..	N..N..	N..N..	N..N..	N..N..	N..N..	N..N..	N..N..	N..N..	N..N..
rh.13	S..A..	N..N..	N..N..	N..N..	N..N..	N..N..	N..N..	N..N..	N..N..	N..N..
AAV1	AM..A..	N..N..	N..N..	N..N..	N..N..	N..N..	N..N..	N..N..	N..N..	N..N..
AAV3	H..A..	N..N..	N..N..	N..N..	N..N..	N..N..	N..N..	N..N..	N..N..	N..N..
AAV6	VM..A..	N..N..	N..N..	N..N..	N..N..	N..N..	N..N..	N..N..	N..N..	N..N..
AAV7	N..A..	N..N..	N..N..	N..N..	N..N..	N..N..	N..N..	N..N..	N..N..	N..N..
AAV8	S..A..	N..N..	N..N..	N..N..	N..N..	N..N..	N..N..	N..N..	N..N..	N..N..
hu.13										
hu.26										
hu.37	S..A..	N..N..	N..N..	N..N..	N..N..	N..N..	N..N..	N..N..	N..N..	N..N..
hu.53	H..A..	N..N..	N..N..	N..N..	N..N..	N..N..	N..N..	N..N..	N..N..	N..N..
rh.39	S..A..	N..N..	N..N..	N..N..	N..N..	N..N..	N..N..	N..N..	N..N..	N..N..
rh.43	S..A..	N..N..	N..N..	N..N..	N..N..	N..N..	N..N..	N..N..	N..N..	N..N..
rh.46	S..A..	N..N..	N..N..	N..N..	N..N..	N..N..	N..N..	N..N..	N..N..	N..N..
AAV2	EIQYTS	NYNKS	WVDF	TVD	NGVY	SEPR	PIG	TRY	LTR	NL*
cy.5	..	..	..	..	..	..	..	..	..	..
rh.10	..	..	..	..	..	..	..	..	..	..
rh.13	..	..	..	..	..	..	..	..	..	..
AAV1	..	..	..	..	..	..	..	..	..	..
AAV3	..	..	..	..	..	..	..	..	..	..
AAV6	..	..	..	..	..	..	..	..	..	..
AAV7	..	..	..	..	..	..	..	..	..	..
AAV8	..	..	..	..	..	..	..	..	..	..
hu.13	..	..	..	..	..	..	..	..	..	..
hu.26	..	..	..	..	..	..	..	..	..	..
hu.37	..	..	..	..	..	..	..	..	..	..
hu.53	..	..	..	..	..	..	..	..	..	..
rh.39	..	..	..	..	..	..	..	..	..	..
rh.43	..	..	..	..	..	..	..	..	..	..
rh.46	..	..	..	..	..	..	..	..	..	..

图5D

rh.13	10	20	30	40	50	60	70	80	90	100
rh.2	MAADG	YLPD	WLED	NLSE	GIRE	WDLK	PGAP	KPKAN	QKQD	DGRGL
rh.37	VP	GYK	YLG	PF	NG	LK	GE	PN	EA	AA
rh.8	LE	Q	KA	Q	KA	Q	KA	Q	KA	Q
hu.29	KA	Q	KA	Q	KA	Q	KA	Q	KA	Q
rh.64	KA	Q	KA	Q	KA	Q	KA	Q	KA	Q
rh.13	110	120	130	140	150	160	170	180	190	200
rh.2	QER	LQED	TS	FG	CN	LG	RA	VF	QA	KK
rh.37	RV	FA	QK	RV	LE	PL	GL	VE	GA	KT
rh.8	AP	KG	KR	PI	E	SP	DS	TG	IG	KK
hu.29	Q	KA	Q	KA	Q	KA	Q	KA	Q	KA
rh.64	Q	KA	Q	KA	Q	KA	Q	KA	Q	KA
rh.13	210	220	230	240	250	260	270	280	290	300
rh.2	SGT	MA	AC	GA	PM	AD	NE	GA	DG	VG
rh.37	NA	SG	NH	CD	ST	WL	GR	VT	TS	TR
rh.8	WA	LE	PT	YN	NH	LY	KQ	IS	SG	S
hu.29	Q	KA	Q	KA	Q	KA	Q	KA	Q	KA
rh.64	Q	KA	Q	KA	Q	KA	Q	KA	Q	KA
rh.13	310	320	330	340	350	360	370	380	390	400
rh.2	RL	NN	WG	ER	PK	LR	KL	RE	KN	IQ
rh.37	VE	NI	QV	KE	NT	ND	GV	TT	AN	LT
rh.8	SI	TI	QV	ES	DS	SE	YQ	LP	VL	GS
hu.29	A	HA	QC	LP	FP	AD	VM	IP	QY	LT
rh.64	A	HA	QC	LP	FP	AD	VM	IP	QY	LT

图6A

	410	420	430	440	450	460	470	480	490	500
rh.13	FPQMLRTGNNEFSYTFEEVPHSSVAHSQSILDRIMNPLIDQYLARTQSTT--GSTRLEQFHQAQCPNTMAEQSKNWLPGPCYRQORLSKNIDSNNN									
rh.2	S.D.	D.	D.	D.	S	GQTQG.QQ.L.S	AN.SA.A.		V.TTTSQ.	
rh.37	S.D.	S.D.							L.F.	
rh.8	Q.	D.	D.	D.	V.	T.G-T.G.QT.A.S.	SS.N.AR.V.		V.TTNQ.	
hu.29	T.	D.	D.	D.	S.	NTPSGTTQSR..S.	ASDIRD.R.		V.TSAD.	
rh.64	S.	D.	D.	D.	S.	GGTAG.QQ.L.S.	SN.SA.AR.		V.TTTSQ.	
	510	520	530	540	550	560	570	580	590	600
rh.13	SNEAWTGATKYHLNGRNSLTNPGVAMATNKDEDDQFFPINGVLVFGETGAAN-KTTLENVMTSEEEIKTNPVATEEYGVVSSNLQSSTAGPOTQTVNS									
rh.2	D.V.	D.V.	H.	ER..SS..M.KQ.	GKDNVDYS.ML.		.Q.	AD..QTNGA.IVG.		
rh.37	A.	IP			K.				S.I.	
rh.8	A.FK.	D.M.	SH.	D.R.	SS.	I.KQ.G.DGVDSQ.I.D.	A.	A.AI.N.AANTQA.	GL.HN	
hu.29	EYS.	D.V.	P.SH.	EK.	QS.	I.KQ.PEKTNVDI.K.MI.D.	R.	Q.S.T.	GNTQAA.AD.T	
rh.64	D.V.	D.V.	R.	SS.I.M.KQ.	GKONVDYS.ML.		Q.	AD..QONTA.IVGA.		
	610	620	630	640	650	660	670	680	690	700
rh.13	QCALPGMVWQNORDVYLOGPPIWAKIPHITDCNHSPIMGFGFLKHPPQIILIKNTPVPANPEVETPAKFASFITQYSTGQVSVEIEWELOKENSKRWNPE									
rh.2					V	D.TT.SQ.L.				
rh.37					E.					
rh.8	VI.					D.LT.NQ.IN.				
hu.29	V.	D.	H.			STT.SA.				
rh.64						D.TA.NQ.IN.		V.		R.
	710	720	730							
rh.13	IQYTSNYAKSNVEFAVNNEGVTTEPRIGTRYLTRNL*									
rh.2	Y.T.D.	T.T.S.	*							
rh.37		PD.	*							
rh.8	Y.T.D.	T.S.	*							
hu.29	N.V.D.	T.DTN.	*							
rh.64	Y.T.D.	T.S.	*							

图6B