(19)中华人民共和国国家知识产权局

(12)发明专利

(10)授权公告号 CN 107614534 B
(45)授权公告日 2021.03.09

(21)申请号 201680024623.X
(22)申请日 2016.04.28
(65)同一申请的已公布的文献号
申请公布号 CN 107614534 A
(43)申请公布日 2018.01.19
(85)PCT国际申请进入国家阶段日
2017.10.27
(86)PCT国际申请的申请数据
PCT/CN2016/080469 2016.04.28
(87)PCT国际申请的公布数据
WO2016/173504 ZH 2016.11.03
(73)专利权人 金协国际实业有限公司
地址 中国台湾台中市北区华美街二段82号8楼之4

(72)发明人 杨滢臻 郭村勇
(74)专利代理机构 北京天平专利商标代理有限公司 11239
代理人 孙刚
(51)Int.Cl.
C07K 19/00(2006.01)
C07K 14/36(2006.01)
C12N 15/62(2006.01)
C07K 16/12(2006.01)
A61K 39/02(2006.01)
A61P 31/04(2006.01)
G01N 33/53(2006.01)

审查员 梁亚茹

权利要求书1页 说明书17页
序列表56页 附图3页

(54)发明名称

猪胸膜肺炎放线杆菌重组毒素蛋白及其应用

(57)摘要

本发明提供了一种猪胸膜肺炎放线杆菌(Actinobacillus pleuropneumoniae)重组毒素蛋白,包括至少一个猪胸膜肺炎放线杆菌毒素蛋白的抗原决定位;当所述抗原决定位为复数个时,各抗原决定位之间可有连接子。所述重组蛋白可包含至少一个补体裂解片段C3d的氨基酸序列,且所述抗原决定位与C3d的氨基酸序列之间可有连接子。本发明还提供了编码所述蛋白的核苷酸序列,以及含有所述蛋白的免疫组合物。

CN 107614534 B

1.一种猪胸膜肺炎放线杆菌重组毒素蛋白,其特征在于,所述重组毒素蛋白的氨基酸序列如SEQ ID NO: 8、16、21或92所示。

2.一种编码根据权利要求1所述的猪胸膜肺炎放线杆菌重组毒素蛋白的核酸。

3.一种猪放线杆菌胸膜肺炎免疫组合物,其特征在于包含一根据权利要求1所述的猪胸膜肺炎放线杆菌重组毒素蛋白以及一药学上可接受的载体。

4.根据权利要求3所述的猪放线杆菌胸膜肺炎免疫组合物,其特征在于所述的猪胸膜肺炎放线杆菌重组毒素蛋白是选自由下列群组所组成的至少一者:氨基酸序列如SEQ ID NO: 8所示的猪胸膜肺炎放线杆菌重组毒素蛋白I、氨基酸序列如SEQ ID NO: 16所示的猪胸膜肺炎放线杆菌重组毒素蛋白II、氨基酸序列如SEQ ID NO: 21所示的猪胸膜肺炎放线杆菌重组毒素蛋白III,以及氨基酸序列如SEQ ID NO: 92所示的猪胸膜肺炎放线杆菌重组毒素蛋白IV。

5.根据权利要求3所述的猪放线杆菌胸膜肺炎免疫组合物,其特征在于进一步包含至少一个猪胸膜肺炎放线杆菌血清型全菌。

6.根据权利要求3所述的猪放线杆菌胸膜肺炎免疫组合物,其特征在于进一步包含其他病原抗原,所述病原抗原是选自由下列群组所组成者:猪第二型环状病毒抗原、猪流感病毒抗原、猪繁殖与呼吸症候群病毒抗原、猪支原体抗原、猪细小病毒抗原、猪丹毒杆菌抗原、支气管败血性博德氏杆菌抗原、败血性巴氏杆菌抗原,以及伪狂犬病毒抗原。

7.一种猪放线杆菌胸膜肺炎的检测试剂盒,其特征在于包含:一根据权利要求1所述的猪胸膜肺炎放线杆菌重组毒素蛋白。

猪胸膜肺炎放线杆菌重组毒素蛋白及其应用

技术领域

[0001] 本发明是关于猪胸膜肺炎放线杆菌重组蛋白的制备与应用,特别是关于使用猪胸膜肺炎放线杆菌重组毒素蛋白以预防猪只感染猪胸膜肺炎放线杆菌。

背景技术

[0002] 猪放线杆菌胸膜肺炎(porcine pleuropneumonia)是一种由猪胸膜肺炎放线杆菌(Actinobacillus pleuropneumoniae,App.)所造成的高感染性猪只呼吸疾病,其临床症状包括发烧、咳嗽、呕吐、呼吸困难、抑郁。感染本病后可能会引起急性肺炎造成骤死,或是慢性感染造成无症状出现的带原者。各种猪龄的猪只均会感染猪放线杆菌胸膜肺炎,尤其是6月龄以下的小猪发病率和死亡率最高。

[0003] 猪胸膜肺炎放线杆菌属于革兰氏阴性杆菌,具有二种生物型,生物型1需要β-烟碱酰胺腺二核苷酸(β-nicotinamide adenine dinucleotide,β-NAD),生物型2则不需要β-NAD。此外,根据荚膜多醣的差异,已有15种血清型的猪胸膜肺炎放线杆菌被确认,且所有的血清型皆具有致病能力。已知的毒力因子包括荚膜、脂多醣、外膜蛋白,以及最重要的细胞毒素(Apx)。

[0004] Apx毒素属于结构重复毒素家族(repeats in structural toxin,RTX)的成员。猪胸膜肺炎放线杆菌的15种血清型菌株共可产生四种不同的Apx毒素。每种血清型的菌株最多可产生3种Apx毒素。ApxI由1、5、9、10、11、14血清型菌株所分泌;ApxII除了第10、14血清型以外的其他血清型都可分泌;ApxIII由2、3、4、6、8、15血清型所分泌;ApxIV由所有的血清型所分泌,但只在感染时才会表现。

[0005] 猪放线杆菌胸膜肺炎在全世界的养猪业造成严重的经济损失。猪胸膜肺炎放线杆菌感染的治疗包括使用如阿莫西林(amoxicillin)、氨苄青霉素(ampicillin)、头孢噻呋(ceftiofur)、恩诺沙星(enrofloxacin)、泰妙菌素(tiamulin)、青霉素(penicillin)以及青霉素/链霉素(penicillin/streptomycin)等的抗生素。然而,因为对抗生素产生抗性的问题日益严重且消费者对食物安全的需求日益增加,以疫苗预防猪胸膜肺炎放线杆菌感染已变得重要。大部分市售猪胸膜肺炎放线杆菌疫苗为全菌疫苗,这些疫苗可降低猪只死亡率,但却无法预防最初的感染及带原状态的发生。因此,发展更有效的猪胸膜肺炎放线杆菌疫苗是重要的。

发明内容

[0006] 于一方面,本发明提供一种猪胸膜肺炎放线杆菌重组毒素蛋白(recombinant Apx toxins,re-Apx),是以下列式(I)表示:

[0007] $(A)_m$-(C3d片段)$_n$; 式(I);

[0008] 其中每一个A代表一个独立的猪胸膜肺炎放线杆菌毒素蛋白的抗原决定位;

[0009] 其中每一个C3d片段代表一个独立的补体裂解片段C3d的氨基酸序列,每一个C3d片段是各自独立选自于SEQ ID NOs:22、23、24及25所组成的群组;

[0010] 其中m是代表从1至约30的整数;以及

[0011] 其中n是代表从0至约10的整数。

[0012] 于另一方面,本发明提供一种编码所述猪胸膜肺炎放线杆菌重组毒素蛋白(re-Apx)的核苷酸序列。

[0013] 于另一方面,本发明提供一种猪放线杆菌胸膜肺炎免疫组合物,包含所述猪胸膜肺炎放线杆菌重组毒素蛋白(re-Apx)以及一药学上可接受的载体。

[0014] 于又一方面,本发明提供一种动物对抗猪放线杆菌胸膜肺炎的方法,包含使用有效量的上述免疫组合物以施予一动物,以增强所述动物对抗猪放线杆菌胸膜肺炎的免疫力。

[0015] 于再一方面,本发明提供一种抗猪胸膜肺炎放线杆菌毒素蛋白(Apx)的抗体,是藉由所述猪胸膜肺炎放线杆菌重组毒素蛋白(re-Apx)所制备或衍生而得。

[0016] 于另一方面,本发明提供一种猪放线杆菌胸膜肺炎的检测试剂盒。所述检测试剂盒是用以侦测检验样本中是否含有猪胸膜肺炎放线杆菌毒素蛋白(Apx),或侦测检验样本内是否含有抗猪胸膜肺炎放线杆菌毒素蛋白(Apx)的抗体。

[0017] 本发明所提供的猪放线杆菌胸膜肺炎免疫组合物,与其他习用技术相互比较时,更具有下列的优点:

[0018] 本发明所提供的猪放线杆菌胸膜肺炎免疫组合物含有一猪胸膜肺炎放线杆菌重组毒素蛋白(re-Apx)。所述猪胸膜肺炎放线杆菌重组毒素蛋白(re-Apx)包含至少一个猪胸膜肺炎放线杆菌毒素蛋白(Apx)的抗原决定位(epitopes)以及补体裂解片段C3d的部份氨基酸序列。所述猪胸膜肺炎放线杆菌重组毒素蛋白(re-Apx)远比猪胸膜肺炎放线杆菌毒素蛋白(Apx)的全长氨基酸序列短,在生物表现系统中较容易表达,且重组蛋白的产率较高,可降低制造疫苗的成本。

[0019] 此外,本发明所提供的猪放线杆菌胸膜肺炎免疫组合物所含的猪胸膜肺炎放线杆菌重组毒素蛋白(re-Apx)具有补体裂解片段C3d的部份氨基酸序列,因此可以增加特异性免疫反应,经试验结果显示,本发明所提供的猪放线杆菌胸膜肺炎免疫组合物可提高动物对抗猪胸膜肺炎放线杆菌感染的免疫性,显著增加受感染动物的存活率。

[0020] 本发明以下面的实施例予以示范阐明,但本发明不受下述实施例所限制。

附图说明

[0021] 图1所示为根据实施例一至四,以十二烷基硫酸钠聚丙烯酰胺凝胶电泳(sodium dodecyl sulfate polyacrylamide gel electrophoresis,SDS-PAGE)确认纯化的本发明猪胸膜肺炎放线杆菌重组毒素蛋白(re-Apx);M:蛋白质分子量标记;第1道:猪胸膜肺炎放线杆菌重组毒素蛋白I(re-ApxI);第2道:猪胸膜肺炎放线杆菌重组毒素蛋白II(re-ApxII);第3道:猪胸膜肺炎放线杆菌重组毒素蛋白III(re-ApxIII);第4道:猪胸膜肺炎放线杆菌重组毒素蛋白IV(re-ApxIV)。

[0022] 图2所示为根据实施例一至四,以西方墨点法确认纯化的本发明猪胸膜肺炎放线杆菌重组毒素蛋白(re-Apx);M:蛋白质分子量标记;第1道:猪胸膜肺炎放线杆菌重组毒素蛋白I(re-ApxI);第2道:猪胸膜肺炎放线杆菌重组毒素蛋白II(re-ApxII);第3道:猪胸膜肺炎放线杆菌重组毒素蛋白III(re-ApxIII);第4道:猪胸膜肺炎放线杆菌重组毒素蛋白IV

(re-ApxIV)；一级抗体为碱性磷酸酶缀合的小鼠抗His标记单株抗体(Alkaline phosphatase-conjugated mouse anti-His,Invitrogen)。

[0023] 图3为根据实施例九,以酵素连结免疫分析(ELISA)测定抗猪胸膜肺炎放线杆菌重组毒素蛋白II(re-ApxII)抗体效价的结果;第1组为负对照组(PBS组);第2组为含有实施例六所得的猪胸膜肺炎放线杆菌全菌多价疫苗(App 1,2,5组);第3组为实施例六所得的猪胸膜肺炎放线杆菌全菌及重组毒素蛋白混合多价疫苗(App 1,2,5+re-ApxI～III组);第4组为市售猪放线杆菌胸膜肺炎不活化疫苗,含有猪胸膜肺炎放线杆菌血清型第1,2,3,4,5,7型全菌(App 1,2,3,4,5,7组)。符号**代表所述组与负对照组之间具有显著差异($p<0.01$);符号##代表两组之间具有显著差异($p<0.01$)。

具体实施方式

[0024] 本发明提供一种猪胸膜肺炎放线杆菌重组毒素蛋白(re-Apx),包含至少一个猪胸膜肺炎放线杆菌毒素蛋白(Apx)的抗原决定位(epitopes),以诱导动物产生抗猪胸膜肺炎放线杆菌毒素蛋白(Apx)的抗体,并可进一步含补体裂解片段C3d的全长或部份氨基酸序列,以增加特异性免疫反应。本发明的猪胸膜肺炎放线杆菌重组毒素蛋白(re-Apx)是以下列式(I)表示:

[0025] (A)m-(C3d片段)n; 式(I);

[0026] 其中每一个A代表一个独立的猪胸膜肺炎放线杆菌毒素蛋白的抗原决定位;

[0027] 其中每一个C3d片段代表一个独立的补体裂解片段C3d的氨基酸序列;

[0028] 其中m是代表从1至约30的整数;以及

[0029] 其中n是代表从0至约10的整数。

[0030] 于一实施例中,所述补体裂解片段C3d的全长氨基酸序列为小鼠补体裂解片段C3d的全长序列(mC3d),具有如SEQ ID NO:25所示的氨基酸序列。于一较佳实施例中,所述补体裂解片段C3d的部份氨基酸序列为小鼠补体裂解片段C3d第211个氨基酸至第238个氨基酸片段序列(mC3d-p28),具有如SEQ ID NO:24所示的氨基酸序列。于另一实施例中,所述补体裂解片段C3d的全长氨基酸序列为猪补体裂解片段C3d的全长序列(pC3d),具有如SEQ ID NO:23所示的氨基酸序列。于另一较佳实施例中,所述补体裂解片段C3d的部份氨基酸序列为猪补体裂解片段C3d第201个氨基酸至第231个氨基酸片段序列(pC3d-p31),具有如SEQ ID NO:22所示的氨基酸序列。本发明所提供的猪胸膜肺炎放线杆菌重组毒素蛋白(re-Apx)具有0至10个单元重复的上述补体裂解片段C3d的全长或部份氨基酸序列,所述补体裂解片段C3d的全长或部份氨基酸序列较佳为1至重复10个单元,更佳为重复4至8个单元。

[0031] 于一实施例中,每一个A之间进一步以一个连接子连接,每一个连接子是各自独立选自于Gly-Gly、Gly-Ser及SEQ ID NOs:26、27、28、29、30、31、32、33、34、35及36。

[0032] 于一实施例中,每一个C3d片段之间进一步以一个连接子连接,每一个连接子是各自独立选自于Gly-Gly、Gly-Ser及SEQ ID NOs:26、27、28、29、30、31、32、33、34、35及36。

[0033] 于一实施例中,A与C3d片段之间进一步以一连接子连接,所述连接子是选自于Gly-Gly、Gly-Ser及SEQ ID NOs:26、27、28、29、30、31、32、33、34、35及36。

[0034] 于一实施例中,所述猪胸膜肺炎放线杆菌毒素蛋白为猪胸膜肺炎放线杆菌毒素蛋白I(ApxI),所述猪胸膜肺炎放线杆菌重组毒素蛋白为猪胸膜肺炎放线杆菌重组毒素蛋白I

(re-ApxI)，且每一个A是各自独立选自于SEQ ID NOs:37、4、39、40、41、42、43、44、45、46、47、48、49、50及51所示的氨基酸序列，所述猪胸膜肺炎放线杆菌毒素蛋白I(ApxI)的抗原决定位可为1至约30个，且各抗原决定位氨基酸序列自蛋白质N端到C端的排列顺序并不限于依照序列辨识号(SEQ ID NO)的顺序排列。于一较佳实施例中，分别以五段较长的抗原决定位氨基酸序列涵盖部分上述猪胸膜肺炎放线杆菌毒素蛋白I(ApxI)的抗原决定位，所述五段较长的抗原决定位氨基酸序列是分别如SEQ ID NOs:2、3、4、5、6所示。于一较佳实施例中，本发明的猪胸膜肺炎放线杆菌重组毒素蛋白I(re-ApxI)含有二个以上所述较长的抗原决定位氨基酸序列，且各抗原决定位氨基酸序列自蛋白质N端到C端的排列顺序并不限于依照序列辨识号(SEQ ID NO)的顺序排列。于一较佳实施例中，所述猪胸膜肺炎放线杆菌重组毒素蛋白I(re-ApxI)包含如SEQ ID NO:7或8所示的氨基酸序列。

[0035] 于一实施例中，所述猪胸膜肺炎放线杆菌毒素蛋白为猪胸膜肺炎放线杆菌毒素蛋白II(ApxII)，所述猪胸膜肺炎放线杆菌重组毒素蛋白为猪胸膜肺炎放线杆菌重组毒素蛋白II(re-ApxII)，且每一个A是各自独立选自于SEQ ID NOs:14、52、53、54、55、56、57、58、59、60、61、62、63、64、65、67及68所示的氨基酸序列，所述猪胸膜肺炎放线杆菌毒素蛋白II(ApxII)的抗原决定位可为1至约30个，且各抗原决定位氨基酸序列自蛋白质N端到C端的排列顺序并不限于依照序列辨识号(SEQ ID NO)的顺序排列。于一较佳实施例中，分别以五段较长的抗原决定位氨基酸序列涵盖部分上述猪胸膜肺炎放线杆菌毒素蛋白II(ApxII)的抗原决定位，所述五段较长的抗原决定位氨基酸序列是分别如SEQ ID NOs:10、11、12、13、14所示。于一较佳实施例中，本发明的猪胸膜肺炎放线杆菌重组毒素蛋白II(re-ApxII)含有二个以上所述较长的抗原决定位氨基酸序列，且各抗原决定位氨基酸序列自蛋白质N端到C端的排列顺序并不限于依照序列辨识号(SEQ ID NO)的顺序排列。于一较佳实施例中，所述猪胸膜肺炎放线杆菌重组毒素蛋白II(re-ApxII)包含如SEQ ID NO:15或16所示的氨基酸序列。

[0036] 于一实施例中，所述猪胸膜肺炎放线杆菌毒素蛋白为猪胸膜肺炎放线杆菌毒素蛋白III(ApxIII)，所述猪胸膜肺炎放线杆菌重组毒素蛋白为猪胸膜肺炎放线杆菌重组毒素蛋白III(re-ApxIII)，且每一个A是各自独立选自于SEQ ID NOs:69、70、71、72、73、74、75、76、77、78、79、80、81、82、83、84、85、86、87及88所示的氨基酸序列，所述猪胸膜肺炎放线杆菌毒素蛋白III(ApxIII)的抗原决定位可为1至约30个，且各抗原决定位氨基酸序列自蛋白质N端到C端的排列顺序并不限于依照序列辨识号(SEQ ID NO)的顺序排列。于一较佳实施例中，分别以二段较长的抗原决定位氨基酸序列涵盖部分上述猪胸膜肺炎放线杆菌毒素蛋白III(ApxIII)的抗原决定位，所述二段较长的抗原决定位氨基酸序列是分别如SEQ ID NOs:18、19所示。于一较佳实施例中，本发明的猪胸膜肺炎放线杆菌重组毒素蛋白III(re-ApxIII)含有所述二个所述较长的抗原决定位氨基酸序列，且各抗原决定位氨基酸序列自蛋白质N端到C端的排列顺序并不限于依照序列辨识号(SEQ ID NO)的顺序排列。于一较佳实施例中，所述猪胸膜肺炎放线杆菌重组毒素蛋白III(re-ApxIII)包含如SEQ ID NO:20或21所示的氨基酸序列。

[0037] 于一实施例中，所述猪胸膜肺炎放线杆菌毒素蛋白为猪胸膜肺炎放线杆菌毒素蛋白IV(ApxIV)，所述猪胸膜肺炎放线杆菌重组毒素蛋白为猪胸膜肺炎放线杆菌重组毒素蛋白IV(re-ApxIV)，且每一个A是各自独立选自于SEQ ID NOs:93、94、95、96、97、98、99、100、

101、102、103、104、105、106、107、108、109、110、111、112、113、114、115、116及117所示的氨基酸序列，所述猪胸膜肺炎放线杆菌毒素蛋白IV(ApxIV)的抗原决定位可为1至约30个，且各抗原决定位氨基酸序列自蛋白质N端到C端的排列顺序并不限于依照序列辨识号(SEQ ID NO)的顺序排列。于一较佳实施例中，分别以三段较长的抗原决定位氨基酸序列涵盖部分上述猪胸膜肺炎放线杆菌毒素蛋白IV(ApxIV)的抗原决定位，所述三段较长的抗原决定位氨基酸序列是分别如SEQ ID NOs:66、89、90所示。于一较佳实施例中，本发明的猪胸膜肺炎放线杆菌重组毒素蛋白IV(re-ApxIV)含有二个以上所述较长的抗原决定位氨基酸序列，且各抗原决定位氨基酸序列自蛋白质N端到C端的排列顺序并不限于依照序列辨识号(SEQ ID NO)的顺序排列。于一较佳实施例中，所述猪胸膜肺炎放线杆菌重组毒素蛋白IV(re-ApxIV)包含如SEQ ID NO:91或92所示的氨基酸序列。

[0038] 于部分实施态样中，本发明所提供的猪胸膜肺炎放线杆菌重组毒素蛋白(re-Apx)与上述式(I)所表示的氨基酸序列具有至少大约80％序列同源性，较佳者，具有大约85％序列同源性，更佳者，具有大约90％序列同源性，甚至是大约91％、大约92％、大约93％、大约94％、大约95％、大约96％、大约97％、大约98％、大约99％序列同源性。

[0039] 本发明亦提供一种编码猪胸膜肺炎放线杆菌重组毒素蛋白(re-Apx)的核苷酸序列。所述猪胸膜肺炎放线杆菌重组毒素蛋白(re-Apx)包含至少一个猪胸膜肺炎放线杆菌毒素蛋白(Apx)的抗原决定位，以及重复0至10个单元的补体裂解片段C3d的部份氨基酸序列。所述编码本发明的猪胸膜肺炎放线杆菌重组毒素蛋白(re-Apx)的核苷酸序列，是由本发明的猪胸膜肺炎放线杆菌重组毒素蛋白(re-Apx)的氨基酸序列衍生而来。将本发明的猪胸膜肺炎放线杆菌重组毒素蛋白(re-Apx)氨基酸序列上的各个氨基酸置换为遗传密码表(genetic code table)所列的编码所述氨基酸的核苷酸序列(包含各种简并密码子(degenerate codons，或称同义密码子，synonymous codons))，即可得到本发明所提供的所述核苷酸序列。例如，本发明的猪胸膜肺炎放线杆菌重组毒素蛋白(re-Apx)氨基酸序列上的丝胺酸(serine)可由TCT、TCC、TCA、TCG、AGT、AGC等核苷酸序列所编码。

[0040] 此外，本发明提供一种猪放线杆菌胸膜肺炎免疫组合物。所述猪放线杆菌胸膜肺炎免疫组合物包含本发明的猪胸膜肺炎放线杆菌重组毒素蛋白(re-Apx)以及一药学上可接受的载体。于一实施例中，所述猪胸膜肺炎放线杆菌重组毒素蛋白(re-Apx)为猪胸膜肺炎放线杆菌重组毒素蛋白I(re-ApxI)、猪胸膜肺炎放线杆菌重组毒素蛋白II(re-ApxII)、猪胸膜肺炎放线杆菌重组毒素蛋白III(re-ApxIII)、猪胸膜肺炎放线杆菌重组毒素蛋白IV(re-ApxIV)至少其中一种。于一较佳实施例中，所述猪放线杆菌胸膜肺炎免疫组合物包含猪胸膜肺炎放线杆菌重组毒素蛋白I(re-ApxI)、猪胸膜肺炎放线杆菌重组毒素蛋白II(re-ApxII)，与猪胸膜肺炎放线杆菌重组毒素蛋白III(re-ApxIII)，以及一药学上可接受的载体。于一较佳实施例中，所述猪放线杆菌胸膜肺炎免疫组合物包含猪胸膜肺炎放线杆菌重组毒素蛋白I(re-ApxI)、猪胸膜肺炎放线杆菌重组毒素蛋白II(re-ApxII)、猪胸膜肺炎放线杆菌重组毒素蛋白III(re-ApxIII)，与猪胸膜肺炎放线杆菌重组毒素蛋白IV(re-ApxIV)，以及一药学上可接受的载体。

[0041] 于一实施例中，所述猪放线杆菌胸膜肺炎免疫组合物可进一步包含至少一个猪胸膜肺炎放线杆菌血清型全菌。所述猪胸膜肺炎放线杆菌血清型全菌包括，但不限于，猪胸膜肺炎放线杆菌血清型1、2、3、4、5、6、7、8、9、10、11、12、13、14、15。于一较佳实施例中，所述猪

放线杆菌胸膜肺炎免疫组合物进一步包含猪胸膜肺炎放线杆菌血清型1、2、5三型。

[0042] 于一实施例中，本发明所提供的猪放线杆菌胸膜肺炎免疫组合物，进一步包含其他病原抗原，所述病原抗原包括，但不限于，猪环状病毒第二型(PCV2)抗原、猪流感病毒(SIV)抗原、猪繁殖与呼吸症候群病毒(PRRSV)抗原、猪支原体(Mycoplasma)、猪小病毒(Parvovirus，PPV)、猪丹毒(Erysipelas)、支气管败血性博德氏杆菌(Bordetella bronchiseptica)、败血性巴氏杆菌(Pasteurella multocida)，以及伪狂犬病(Aujeszky′s disease)。

[0043] 另，本发明所提供的猪放线杆菌胸膜肺炎免疫组合物可进一步包含一或多种选自于下列药学上可接受的载体，包括：溶剂、乳化剂、悬浮剂、分解剂、黏结剂、赋形剂、安定剂、螯合剂、稀释剂、胶凝剂、防腐剂、润滑剂、界面活性剂、佐剂、生物型载体等。

[0044] 所述药学上可接受的载体包含一或多种选自于下列的试剂：溶剂(solvent)、乳化剂(emulsifier)、悬浮剂(suspending agent)、分解剂(decomposer)、黏结剂(binding agent)、赋形剂(excipient)、安定剂(stabilizing agent)、螯合剂(chelating agent)、稀释剂(diluent)、胶凝剂(gelling agent)、防腐剂(preservative)、润滑剂(lubricant)、界面活性剂(surfactant)、佐剂(adjuvant)，及其他类似或适用本发明的载体。

[0045] 所述药学上可接受的赋形剂可为适合于肠外、肠内或滴鼻施用的药学上可接受的有机或无机载体物质，且所述赋形剂不会与活性组合物产生有害的反应。适合的赋形剂包含但不限于水、盐类溶液、蔬菜油、聚乙二醇、明胶、直链淀粉、乳糖、硬脂酸镁、滑石、硅酸、黏性石蜡、脂肪酸单甘酯和甘油、脂肪酸酯、羟甲基纤维素、聚乙烯吡咯烷酮等。

[0046] 所述药学上可接受的佐剂包含但不限于水性氢氧化铝胶、明矾、Freund氏不完全佐剂、油质佐剂、水溶性佐剂、或水包油包水双相佐剂(water-in-oil-in-water，W/O/W)；于一实施例中，所述佐剂为水性氢氧化铝胶。

[0047] 进一步地，本发明提供一种动物对抗猪放线杆菌胸膜肺炎的方法，包含使用有效量的上述免疫组合物以施予一动物，以增强所述动物对抗猪放线杆菌胸膜肺炎的免疫力，增加感染后的存活率。

[0048] 本发明并提供一种抗猪胸膜肺炎放线杆菌毒素蛋白(Apx)的抗体，是藉由本发明所提供的猪胸膜肺炎放线杆菌重组毒素蛋白(re-Apx)所制备或衍生而得；所述抗体包括但不限于：单株抗体、多株抗体，以及经基因重组的抗体。于一实施例中，所述抗体是为经由将本发明所提供的猪胸膜肺炎放线杆菌重组毒素蛋白(re-Apx)施打于一动物体内而得到的多株抗体。

[0049] 于另一方面，本发明提供一种猪放线杆菌胸膜肺炎的检测试剂盒。所述检测试剂盒是用以侦测检验样本中是否含有猪胸膜肺炎放线杆菌毒素蛋白(Apx)，或侦测检验样本内是否含有抗猪胸膜肺炎放线杆菌毒素蛋白(Apx)的抗体。所述检测试剂盒包含但不限于：(1)一抗原，所述抗原是为本发明所提供的猪胸膜肺炎放线杆菌重组毒素蛋白(re-Apx)，于一实施例中，所述抗原是置于一抗原盘上；及/或(2)一抗体，所述抗体是由所述本发明所提供的猪胸膜肺炎放线杆菌重组毒素蛋白(re-Apx)所衍生、制备而得的单株抗体或多株抗体。

[0050] 所述检测试剂盒的形式包含但不限于：酵素连结免疫分析(enzyme-linked immunosorbent assay，ELISA)试剂盒、微晶片检验试剂盒(Microchip kit)、免疫萤光分析

法(immuno fluorescent assay,IFA)检测试剂盒、或其他藉由所述猪胸膜肺炎放线杆菌重组毒素蛋白(re-Apx)所制得的检测试剂盒。于一实施例中,所述检测试剂盒至少包含一含有本发明所提供的猪胸膜肺炎放线杆菌重组毒素蛋白(re-Apx)的抗原盘,可用以检验样本中是否含有抗猪胸膜肺炎放线杆菌毒素蛋白(Apx)的抗体。

[0051] 于本发明中所使用的单数形式「一」、及「所述」包含复数形式,除非文中另有清楚指明者。因此,例如,当提及「一样本」时,包含复数个所述等样本及对所述领域具有通常技艺者所知的同等物。

[0052] 本文所使用的「约」、「大约」或「近乎」一词实质上代表所述的数值或范围位于20%以内,较佳为于10%以内,以及更佳者为于5%以内。于本文所提供的数字化的量为近似值,意旨若术语「约」、「大约」或「近乎」没有被使用时亦可被推得。

[0053] 本说明书中所述的所有技术性及科学术语,除非另外有所定义,皆为所述所属领域具有通常技艺者可共同了解的意义。

[0054] 本发明是以下面的实施例予以示范阐明,但本发明不受下述实施例所限制。

[0055] 实施例一 猪胸膜肺炎放线杆菌重组毒素蛋白I(re-ApxI)的构筑

[0056] 自猪胸膜肺炎放线杆菌毒素蛋白I(ApxI)全长氨基酸序列(如SEQ ID NO:1所示)选出5个抗原决定位(epitopes)片段,分别为:

[0057] 抗原决定位片段ApxI-1:ELAGITRKGADAKSGK(SEQ ID NO:2);

[0058] 抗原决定位片段ApxI-2:PAGVGAAA(SEQ ID NO:3);

[0059] 抗原决定位片段ApxI-3:DILYGSDGTNLFDGGVGNDKIYGG(SEQ ID NO:4);

[0060] 抗原决定位片段ApxI-4:EHGQVLVGAGGPLAYSNSPNSIPNAF(SEQ ID NO:5);

[0061] 抗原决定位片段ApxI-5:

[0062] RAKDELHSVEEIIGSNRKDKFFGSRFTDIFHGAKGDDEIYGNDGHDILYGDDGNDVIHGGDGNDHLVGGNGNDRLIGGKGNNFLNGGDGDDELLQVFE(SEQ ID NO:6);

[0063] 这些抗原决定位片段中包含,但不限于,以下抗原决定位:

RKGADAKSGK (SEQ ID NO: 37);

DILYGSDGTNLFDGGVGNDKIYGG (SEQ ID NO: 4);

GGPLAYSNSPNSIPNA (SEQ ID NO: 39);

GAGGPLAYSNSPNS (SEQ ID NO: 40);

LVGAGGPLAYSNSPNSIPNA (SEQ ID NO: 41);

GSNRKD (SEQ ID NO: 42);

GAKGDDEIYGNDGHDILYGDDGNDVIHGGDGNDHLVGGNGNDRLIGG (SEQ ID NO: 43;

[0064] NNFLNGGDGDDEL (SEQ ID NO: 44);

GSRFTDIFHGAKGDDEIYGN (SEQ ID NO: 45);

DVIHGGDGNDHLVGGNGNDR (SEQ ID NO: 46);

IGGKGNNFLNGGDGDDELQV (SEQ ID NO: 47);

HGAKGDDEIYGNDG (SEQ ID NO: 48);

GGKGNNFLNGGDGD (SEQ ID NO: 49);

DGHDILYGDDGNDVIHGGDG (SEQ ID NO: 50);

RLIGGKGNNFLNGGDGDDEL (SEQ ID NO: 51)。

[0065] 由N端至C端依序连接抗原决定位片段ApxI-1、抗原决定位片段ApxI-2、抗原决定位片段ApxI-3、抗原决定位片段ApxI-4、抗原决定位片段ApxI-5，且分别在各抗原决定位片段之间以一个以上的连接子连接，所述连接子具有如SEQ ID NO:26所示的氨基酸序列；并且在抗原决定位片段ApxI-5的C端加上6个pC3d-p31生物佐剂(bioadjuvant)序列(如SEQ ID NO:22所示)，每个pC3d-p31生物佐剂序列皆以一个以上的连接子(SEQ ID NO:26)连接；得到的猪胸膜肺炎放线杆菌重组毒素蛋白I(re-ApxI)氨基酸序列如SEQ ID NO:7所示。所述氨基酸序列可以合成仪合成。或者，先合成编码所述氨基酸序列的核酸序列，并将所述核酸序列选殖至表现载体中，于生物表现宿主中表现所述氨基酸序列并纯化。

[0066] 此外，亦可以基因选殖方式构筑编码猪胸膜肺炎放线杆菌重组毒素蛋白I(re-ApxI)的核酸序列，以限制酶切位连接DNA片段，并将所述核酸序列选殖至表现载体中，于生物表现宿主中表现所述氨基酸序列并纯化。于本实施例中，以HindIII限制酶切位连接编码猪胸膜肺炎放线杆菌毒素蛋白I的抗原决定位片段的DNA序列以及编码pC3d-p31生物佐剂片段的DNA序列，经过选殖后得到的猪胸膜肺炎放线杆菌重组毒素蛋白I(re-ApxI)的氨基酸序列如SEQ ID NO:8所示。以镍亲和管柱(nickel affinity chromatography)以及离子交换层析管柱(ion exchange chromatography)纯化后的猪胸膜肺炎放线杆菌重组毒素蛋白I(re-ApxI)再以十二烷基硫酸钠聚丙烯酰胺凝胶电泳(sodium dodecyl sulfate polyacrylamide gel electrophoresis,SDS-PAGE)以及西方墨点法(western blot)确认，结果分别如图1(第1道)及图2(第2道)所示。猪胸膜肺炎放线杆菌重组毒素蛋白I(re-ApxI)的分子量如预期的为约46kDa。

[0067] 实施例二 猪胸膜肺炎放线杆菌重组毒素蛋白II(re-ApxII)的构筑

[0068] 自猪胸膜肺炎放线杆菌毒素蛋白II(ApxII)全长氨基酸序列(如SEQ ID NO:9所示)选出5个抗原决定位片段，分别为：

[0069] 抗原决定位片段ApxII-1：

[0070] GNGVDTIDGNDGDDHLFGGAGDDVIDGGNGNNFLVGGTGNDIISGGKDNDIYVHKTGDGND SITDSGGQDKL(SEQ ID NO:10)；

[0071] 抗原决定位片段ApxII-2:KVGNDYNTSKDRQNV(SEQ ID NO:11)；

[0072] 抗原决定位片段ApxII-3:LTPGEENRERIQEGKNSYITKLHIQRVDSWTVTDGDASSSV(SEQ ID NO:12)；

[0073] 抗原决定位片段ApxII-4:ILYIPQGYDSGQGNGVQDLV(SEQ ID NO:13)；

[0074] 抗原决定位片段ApxII-5:ATHPTNVGNREEKIEYRREDDRFH(SEQ ID NO:14)；

[0075] 这些抗原决定位片段中包含,但不限于,以下抗原决定位：

GTGNDIISGGKDNDI(SEQ ID NO:52)；

HKTGDGNDSITDSGGQDKL(SEQ ID NO:53)；

FGGAGDDVIDGGNGNNFLVG(SEQ ID NO:54)；

YVHKTGDGNDSITDSGGQDK(SEQ ID NO:55)；

GGAGDDVIDGGNGN(SEQ ID NO:56)；

GGTGNDIISGGKDN(SEQ ID NO:57)；

KTGDGNDSITDSGG(SEQ ID NO:58)；

[0076] AGDDVIDGGNGNNFLVGGTG(SEQ ID NO:59)；

DIYVHKTGDGNDSITDSGGQ(SEQ ID NO:60)；

LTPGEENRERIQEGKNS(SEQ ID NO:61)；

WTVTDGDASSSV(SEQ ID NO:62)；

TPGEENRERIQEGKNSYITK(SEQ ID NO:63)；

LFRTPLLTPGEENR(SEQ ID NO:64)；

QGYDSGQGNGVQ(SEQ ID NO:65)；

ATHPTNVGNREEKIEYRREDDRFH(SEQ ID NO:14)；

NREEKIEYRREDDR(SEQ ID NO:67)；

[0077] PTNVGNREEKIEYRREDDRF(SEQ ID NO:68)。

[0078] 由N端至C端依序连接抗原决定位片段ApxII-1、抗原决定位片段ApxII-2、抗原决定位片段ApxII-3、抗原决定位片段ApxII-4、抗原决定位片段ApxII-5,且分别在各抗原决定位片段之间以一个以上的连接子连接,所述连接子具有如SEQ ID NO:26所示的氨基酸序列;并且在抗原决定位片段ApxII-5的C端加上6个pC3d-p31生物佐剂序列(如SEQ ID NO:22所示),每个pC3d-p31生物佐剂序列皆以一个以上的连接子(SEQ ID NO:26)连接;得到的猪胸膜肺炎放线杆菌重组毒素蛋白II(re-ApxII)氨基酸序列如SEQ ID NO:15所示。所述氨基酸序列可以合成仪合成。或者,先合成编码所述氨基酸序列的核酸序列,并将所述核酸序列选殖至表现载体中,于生物表现宿主中表现所述氨基酸序列并纯化。

[0079] 此外,亦可以基因选殖方式构筑编码猪胸膜肺炎放线杆菌重组毒素蛋白II(re-ApxII)的核酸序列,以限制酶切位连接DNA片段,并将所述核酸序列选殖至表现载体中,于

生物表现宿主中表现所述氨基酸序列并纯化。于本实施例中，以HindIII限制酶切位连接编码猪胸膜肺炎放线杆菌毒素蛋白II的抗原决定位片段的DNA序列以及编码pC3d-p31生物佐剂片段的DNA序列，经过选殖后得到的猪胸膜肺炎放线杆菌重组毒素蛋白I(re-ApxII)的氨基酸序列如SEQ ID NO:16所示。以镍亲和管柱(nickel affinity chromatography)以及离子交换层析管柱(ion exchange chromatography)纯化后的猪胸膜肺炎放线杆菌重组毒素蛋白II(re-ApxII)再以十二烷基硫酸钠聚丙烯酰胺凝胶电泳(SDS-PAGE)以及西方墨点法(western blot)确认，结果分别如图1(第2道)及图2(第3道)所示。猪胸膜肺炎放线杆菌重组毒素蛋白II(re-ApxII)的分子量如预期的为约47kDa。

[0080] 实施例三 猪胸膜肺炎放线杆菌重组毒素蛋白III(re-ApxIII)的构筑

[0081] 自猪胸膜肺炎放线杆菌毒素蛋白III(ApxIII)全长氨基酸序列(如SEQ ID NO:17所示)选出2个抗原决定位片段，分别为：

[0082] 抗原决定位片段ApxIII-1：

[0083] ADGDDLLNGNDGDDILYGDKGNDELRGDNGNDQLYGGEGNDKLLGGNGNNYLSGGDGNDELQVLGNGFNVLRAGKGDDKLYGSSGSDLLDGGEGNDYLEGGDGSDFYVYRSTSGNHTIYDQGKSSDL (SEQ ID NO: 18);

[0084] 抗原决定位片段ApxIII-2：

[0085] GELAGITGKGDKLSSGKAYVDYFQEGKLLEKKPDDFSKVVFDPTKGEIDISNSQTSTLLKFVTPLLTPGTESRERTQTGK (SEQ ID NO: 19);

[0086] 这些抗原决定位片段中包含，但不限于，以下抗原决定位：

[0087] GADGDDLLNGNDGDDILYGDKGNDELRGDNGNDQLYGGEGNDKLLGGNGNNYLSGGDGNDEL (SEQ ID NO: 69);

AGKGDDKLYGSSGSDLLDGGEGNDYLEGGDGSD (SEQ ID NO: 70);

STSGNHTIYDQGKSSD (SEQ ID NO: 71);

GDKGNDELRGDNGNDQLYGG (SEQ ID NO: 72);

LLGGNGNNYLSGGDGNDELQ (SEQ ID NO: 73);

GDKGNDELRGDNGN (SEQ ID NO: 74);

GGNGNNYLSGGDGN (SEQ ID NO: 75);

DGDDILYGDKGNDELRGDNG (SEQ ID NO: 76);

LLGGNGNNYLSGGDGNDELQ (SEQ ID NO: 77);

NGFNVLRAGKGDDKLYGSSG (SEQ ID NO: 78);

GITGKGDKLSSGKA (SEQ ID NO: 79);

[0088] LLEKKPDDF (SEQ ID NO: 80);

FDPTKGEIDISNSQT (SEQ ID NO: 81);

GITGKGDKLSSGKAYVDYFQ (SEQ ID NO: 82);

VFDPTKGEIDISNSQTSTLL (SEQ ID NO: 83);

KGDKLSSGKAYVDY (SEQ ID NO: 84);

EKKPDDFSKVVFDP (SEQ ID NO: 85);

FVTPLLTPGTESRE (SEQ ID NO: 86);

ELAGITGKGDKLSSGKAYVD (SEQ ID NO: 87);

TLLKFVTPLLTPGTESRERT (SEQ ID NO: 88)。

[0089] 由N端至C端依序连接抗原决定位片段ApxIII-1与抗原决定位片段ApxIII-2,且分别在各抗原决定位片段之间以一个以上的连接子连接,所述连接子具有如SEQ ID NO:26所示的氨基酸序列;并且在抗原决定位片段ApxIII-2的C端加上6个pC3d-p31生物佐剂序列(如SEQ ID NO:22所示),每个pC3d-p31生物佐剂序列皆以一个以上的连接子(SEQ ID NO:26)连接;得到的猪胸膜肺炎放线杆菌重组毒素蛋白III(re-ApxIII)氨基酸序列如SEQ ID NO:20所示。所述氨基酸序列可以合成仪合成。或者,先合成编码所述氨基酸序列的核酸序列,并将所述核酸序列选殖至表现载体中,于生物表现宿主中表现所述氨基酸序列并纯化。

[0090] 此外,亦可以基因选殖方式构筑编码猪胸膜肺炎放线杆菌重组毒素蛋白III(re-ApxIII)的核酸序列,以限制酶切位连接DNA片段,并将所述核酸序列选殖至表现载体中,于生物表现宿主中表现所述氨基酸序列并纯化。于本实施例中,以HindIII限制酶切位连接编码猪胸膜肺炎放线杆菌毒素蛋白III的抗原决定位片段的DNA序列以及编码pC3d-p31生物佐剂片段的DNA序列,经过选殖后得到的猪胸膜肺炎放线杆菌重组毒素蛋白III(re-ApxIII)的氨基酸序列如SEQ ID NO:21所示。以镍亲和管柱(nickel affinity chromatography)以及离子交换层析管柱(ion exchange chromatography)纯化后的猪胸膜肺炎放线杆菌重组毒素蛋白III(re-ApxIII)再以十二烷基硫酸钠聚丙烯酰胺凝胶电泳(SDS-PAGE)以及西方墨点法(western blot)确认,结果分别如图1(第3道)及图2(第4道)所示。猪胸膜肺炎放线杆菌重组毒素蛋白III(re-ApxIII)的分子量如预期的为约49kDa。

[0091] 实施例四 猪胸膜肺炎放线杆菌重组毒素蛋白IV(re-ApxIV)的构筑

[0092] 自猪胸膜肺炎放线杆菌毒素蛋白IV(ApxIV)全长氨基酸序列(如SEQ ID NO:38所示)选出3个抗原决定位片段,分别为:

[0093] 抗原决定位片段ApxIV-1:

[0094] VIDAGAGNDTVNGGNGDDTLIGGKGNDILRGGYGADTYIFSKGHGQDIVYEDTNNDNRAR (SEQ ID NO: 66);

[0095] 抗原决定位片段ApxIV-2:

[0096] EGKDTGFYGHAFYIERKNGGGSKNNSSGAGNSKDWGGNGHGNHRNNASDLNKPDGNNGN NQNNGSNQDNNSDVNAPNNPGRNYD (SEQ ID NO: 89);

[0097] 抗原决定位片段ApxIV-3:

[0098] VIDAGAGNDTINGGYGDDTLIGGKGNDILKGSYGADTYIFSKGHGQDIVYEDTNNDNRARDI DTLK (SEQ ID NO: 90);

[0099] 这些抗原决定位片段中包含,但不限于,以下抗原决定位:

[0100] VIDAGAGNDTVNGGNGDDTLIGGKGNDILR (SEQ ID NO: 93);

GYGA (SEQ ID NO: 94);

AGAGNDTVNGGNGDDTLIGG (SEQ ID NO: 95);

SKGHGQDIVYEDTNNDNRAR (SEQ ID NO: 96);

DAGAGNDTVNGGNG (SEQ ID NO: 97);

DIVYEDTNNDNRAR (SEQ ID NO: 98);

SKGHGQDIVYEDTNNDNRAR (SEQ ID NO: 99);

KNGGGSKNNSSGAGNSKDWG (SEQ ID NO: 100);

HRNNASDLNKPDGNNGNNQN (SEQ ID NO: 101);

GSNQDNNSDVNAPNNPGRNY (SEQ ID NO: 102);

ERKNGGGSKNNSSG (SEQ ID NO: 103);

GNSKDWGGNGHGNH (SEQ ID NO: 104);

KPDGNNGNNQNNGS (SEQ ID NO: 105);

DNNSDVNAPNNPGR (SEQ ID NO: 106);

NGGGSKNNSSGAGNSKDWGG (SEQ ID NO: 107);

NQNNGSNQDNNSDVNAPNNP (SEQ ID NO: 108);

VIDAGAGNDTINGGYGDDTLIGGKGNDILK (SEQ ID NO: 109);

SYGA (SEQ ID NO: 110);

GHGQDIVYEDTNNDNRARD (SEQ ID NO: 111);

DAGAGNDTINGGYGDDTLIG (SEQ ID NO: 112);

SKGHGQDIVYEDTNNDNRAR (SEQ ID NO: 113);

DAGAGNDTINGGYG (SEQ ID NO: 114);

[0101] DIVYEDTNNDNRAR (SEQ ID NO: 115);

NGGYGDDTLIGGKGNDILKG (SEQ ID NO: 116);

SKGHGQDIVYEDTNNDNRAR (SEQ ID NO: 117)。

[0102] 由N端至C端依序连接抗原决定位片段ApxIV-1、抗原决定位片段ApxIV-2、抗原决定位片段ApxIV-3，且分别在各抗原决定位片段之间以一个以上的连接子连接，所述连接子具有如SEQ ID NO:26所示的氨基酸序列；并且在抗原决定位片段ApxIV-3的C端加上6个pC3d-p31生物佐剂序列(如SEQ ID NO:22所示)，每个pC3d-p31生物佐剂序列皆以一个以上的连接子(SEQ ID NO:26)连接；得到的猪胸膜肺炎放线杆菌重组毒素蛋白IV(re-ApxIV)氨基酸序列如SEQ ID NO:91所示。所述氨基酸序列可以合成仪合成。或者，先合成编码所述氨基酸序列的核酸序列，并将所述核酸序列选殖至表现载体中，于生物表现宿主中表现所述氨基酸序列并纯化。

[0103] 此外，亦可以基因选殖方式构筑编码猪胸膜肺炎放线杆菌重组毒素蛋白IV(re-ApxIV)的核酸序列，以限制酶切位连接DNA片段，并将所述核酸序列选殖至表现载体中，于生物表现宿主中表现所述氨基酸序列并纯化。于本实施例中，以HindIII限制酶切位连接编码猪胸膜肺炎放线杆菌毒素蛋白IV的抗原决定位片段的DNA序列以及编码pC3d-p31生物佐剂片段的DNA序列，经过选殖后得到的猪胸膜肺炎放线杆菌重组毒素蛋白IV(re-ApxIV)的氨基酸序列如SEQ ID NO:92所示。以镍亲和管柱(nickel affinity chromatography)以及离子交换层析管柱(ion exchange chromatography)纯化后的猪胸膜肺炎放线杆菌重组毒素蛋白IV(re-ApxIV)再以十二烷基硫酸钠聚丙烯酰胺凝胶电泳(SDS-PAGE)以及西方墨点法(western blot)确认，结果分别如图1(第4道)及图2(第5道)所示。猪胸膜肺炎放线杆菌重组毒素蛋白IV(re-ApxIV)的分子量如预期的为约50kDa。

[0104] 实施例五 猪胸膜肺炎放线杆菌毒素萃取

[0105] 1.猪胸膜肺炎放线杆菌的培养

[0106] 将具有生产毒素能力的猪胸膜肺炎放线杆菌血清型第1型(台湾野外分离株，分泌ApxI、ApxII、ApxIV毒素)、第2型(台湾野外分离株，分泌ApxII、ApxIII、ApxIV毒素)全菌接种于含有0.01％(v/v)烟酰胺腺嘌呤二核苷酸(β-Nicotinamide adenine dinucleotide，β-NAD)以及10％(v/v)马血清的脑心浸出液(BHI)液体培养基内(BD公司，美国)，于37℃、5％CO2下培养隔夜。

[0107] 2.猪胸膜肺炎放线杆菌毒素的制备

[0108] 将上述猪胸膜肺炎放线杆菌血清型第1、2型菌液以超音波振荡器(SONOPULS，Bandelin公司，德国)处理以将细菌击碎，再以高速离心机(KUBOTA公司，日本)离心后，取上清液以0.22μm孔径过滤膜(Millipore公司，美国)过滤后，此过滤液即为猪胸膜肺炎放线杆菌粗萃毒素蛋白ApxI～IV(crude extracted ApxI～IV)，分装后保存于-80℃备用。

[0109] 3.不活化猪胸膜肺炎放线杆菌的制备

[0110] 将具有生产毒素能力的猪胸膜肺炎放线杆菌血清型第1型(台湾野外分离株)、第2型(台湾野外分离株)、第5型(台湾野外分离株)全菌接种于含有0.01％(v/v)烟酰胺腺嘌呤

二核苷酸(β-NAD)以及10％(v/v)马血清的脑心浸出液(BHI)液体培养基内(BD公司,美国),于37℃、5％CO_2下培养至少隔夜,接着加入甲醛以进行灭活作用,得到灭活猪胸膜肺炎放线杆菌。

[0111] 实施例六 猪胸膜肺炎放线杆菌疫苗的配制

[0112] 1.猪胸膜肺炎放线杆菌重组毒素蛋白亚单位疫苗(re-ApxI、re-ApxII、re-ApxIII、re-ApxIV)的配制

[0113] 分别将实施例一至实施例四所得到的猪胸膜肺炎放线杆菌重组毒素蛋白re-ApxI(SEQ ID NO:8)(最终浓度为500μg/ml)、re-ApxII(SEQ ID NO:16)(最终浓度为500μg/ml)、re-ApxIII(SEQ ID NO:21)(最终浓度为500μg/ml)、re-ApxIV(SEQ ID NO:92)(最终浓度为500μg/ml)以磷酸盐缓冲溶液(phosphate buffered solution,PBS)混和均匀,并加入铝胶[最终浓度为30％(v/v)]作为佐剂,以配制成为猪胸膜肺炎放线杆菌重组蛋白亚单位疫苗。

[0114] 2.猪胸膜肺炎放线杆菌全菌多价疫苗(App 1,2,5)的配制

[0115] 将实施例五所得到的灭活猪胸膜肺炎放线杆菌血清型第1,2,5型全菌(各菌株最终浓度皆为1x 10^9cfu/ml)以及磷酸盐缓冲溶液(PBS)混和均匀,并加入铝胶[最终浓度为30％(v/v)]作为佐剂,以配制成为猪胸膜肺炎放线杆菌全菌多价疫苗(App 1,2,5)。

[0116] 3.猪胸膜肺炎放线杆菌全菌及重组毒素蛋白混合多价疫苗(App 1,2,5+re-ApxI～III)的配制

[0117] 将实施例一至实施例三所得到的猪胸膜肺炎放线杆菌重组毒素蛋白re-ApxI(SEQ ID NO:8)(最终浓度为20μg/ml)、re-ApxII(SEQ ID NO:16)(最终浓度为20μg/ml)、re-ApxIII(SEQ ID NO:21)(最终浓度为20μg/ml)、实施例五所得到的灭活猪胸膜肺炎放线杆菌血清型第1,2,5型全菌(各菌株最终浓度皆为1 x 10^9cfu/ml)以及磷酸盐缓冲溶液(PBS)混和均匀,并加入铝胶[最终浓度为30％(v/v)]作为佐剂,以配制成为猪胸膜肺炎放线杆菌全菌及重组毒素蛋白混合多价疫苗(App 1,2,5+re-ApxI～III)。

[0118] 实施例七 猪胸膜肺炎放线杆菌重组毒素蛋白疫苗有效性分析

[0119] 1.小鼠免疫及以猪胸膜肺炎放线杆菌粗萃毒素蛋白攻毒试验

[0120] 取猪胸膜肺炎放线杆菌抗体阴性的3～4周龄健康ICR小鼠(国家实验动物中心,台湾)60只,随机分为6组,每组10只;第1组为负对照组,第2～6组为免疫试验组;各组每只小鼠分别以腹腔注射(ip.)0.2ml的以下物质:

[0121] 第1组:含30％(v/v)铝胶的PBS缓冲溶液(PBS组);

[0122] 第2组:含实施例一所得的猪胸膜肺炎放线杆菌重组毒素蛋白I(re-ApxI)(SEQ ID NO:8)的亚单位疫苗(re-ApxI组);

[0123] 第3组:含实施例二所得的猪胸膜肺炎放线杆菌重组毒素蛋白II(re-ApxII)(SEQ ID NO:16)的亚单位疫苗(re-ApxII组);

[0124] 第4组:含实施例三所得的猪胸膜肺炎放线杆菌重组毒素蛋白III(re-ApxIII)(SEQ ID NO:21)的亚单位疫苗(re-ApxIII组);

[0125] 第5组:含实施例四所得的猪胸膜肺炎放线杆菌重组毒素蛋白IV(re-ApxIV)(SEQ ID NO:92)的亚单位疫苗(re-ApxIV组);以及

[0126] 第6组:含实施例六所得的猪胸膜肺炎放线杆菌全菌多价疫苗(App 1,2,5组)。

[0127] 每只小鼠第一次免疫后第14天以相同免疫剂量再进行第二次免疫,第二次免疫后

第10天再对每只小鼠注射0.1ml的实施例五所得的猪胸膜肺炎放线杆菌粗萃毒素蛋白ApxI～IV以进行攻毒。以所述全菌粗萃毒素蛋白的LD_{90}剂量(萃取APP1菌量$6.5x10^9$cfu/ml及APP2菌量$9.65x10^{10}$cfu/ml)进行攻毒,十天后纪录小鼠死亡数,以计算各组存活率。

[0128] 2.统计方法

[0129] 小鼠存活率以Kaplan-Meier存活分析(Kaplan-Meier Survival Analysis:Log-Rank test)进行统计,并以$p<0.05$视为具有统计上的显著差异。

[0130] 3.结果

[0131] 小鼠攻毒试验结果如表1所示,各别含有猪胸膜肺炎放线杆菌重组毒素蛋白re-ApxI、re-ApxII、re-ApxIII、re-ApxIV的亚单位疫苗(即第2～5组)相较于负对照组(第1组,存活率0%)确实能诱发小鼠产生保护效力,并耐过猪胸膜肺炎放线杆菌粗萃毒素蛋白ApxI～IV的攻毒,提高存活率并且具有统计上的显著差异。

[0132] 表1小鼠攻毒试验存活率

[0133]

试验组别	小鼠数目	存活率
第1组(PBS组)	10	0%
第2组(re-ApxI组)	10	50%*
第3组(re-ApxII组)	10	50%*
第4组(re-ApxIII组)	10	50%**
第5组(re-ApxIV组)	10	30%*
第6组(App 1,2,5组)	10	20%

[0134] *表示相对于负对照组有统计上的显著差异($p<0.05$)。

[0135] **表示相对于负对照组有统计上的显著差异($p<0.01$)。

[0136] 实施例八 猪胸膜肺炎放线杆菌多价疫苗对猪胸膜肺炎放线杆菌血清型第2型菌株(App 2)的保护效力的分析

[0137] 1.小鼠免疫及以猪胸膜肺炎放线杆菌血清型第2型菌株(App2)攻毒试验

[0138] 取猪胸膜肺炎放线杆菌抗体阴性3～4周龄健康的ICR小鼠(国家实验动物中心,台湾)40只,随机分为4组,每组10只;第1组为负对照组,第2～4组为免疫试验组;各组每只小鼠分别以腹腔注射(ip.)注射0.2ml的以下物质:

[0139] 第1组:含30%(v/v)铝胶的PBS缓冲溶液(PBS组);

[0140] 第2组:实施例六所得的猪胸膜肺炎放线杆菌全菌多价疫苗(App 1,2,5组);

[0141] 第3组:实施例六所得的猪胸膜肺炎放线杆菌全菌及重组毒素蛋白混合多价疫苗(App 1,2,5+re-ApxI～III组);以及

[0142] 第4组:市售猪放线杆菌胸膜肺炎灭活疫苗,含有猪胸膜肺炎放线杆菌血清型第1,2,3,4,5,7型全菌(App 1,2,3,4,5,7组)。

[0143] 每只小鼠第一次免疫后第14天以相同免疫剂量再进行第二次免疫,第二次免疫后第10天再对每只小鼠注射0.1ml的LD_{90}剂量($7.5x10^8$cfu/ml)的猪胸膜肺炎放线杆菌血清型第2型全菌(App 2)以进行攻毒,观察小鼠10天并纪录死亡数,以计算各组存活率。

[0144] 2.统计方法同实施例七所述。

[0145] 3.结果

[0146] 小鼠攻毒试验结果如表2所示,相较于负对照组(第1组,存活率为20%),各免疫试

验组的存活率皆显著增加,并具有统计上的差异。尤其是含有本发明重组毒素蛋白re-ApxI～III的多价疫苗(App 1,2,5+re-ApxI～III组)对小鼠的保护效果最好,存活率最高。

[0147] 表2以猪胸膜肺炎放线杆菌血清型第2型菌株(App 2)对小鼠攻毒试验的存活率

[0148]

试验组别	小鼠数目	存活率
第1组(PBS组)	10	20%
第2组(App 1,2,5组)	10	70%**
第3组(App 1,2,5+re-ApxI～III组)	10	80%**
第4组(市售App 1,2,3,4,5,7组)	10	60%*

[0149] *表示相对于负对照组有统计上的显著差异(p＜0.05)。

[0150] **表示相对于负对照组有统计上的显著差异(p＜0.01)。

[0151] 实施例九 猪胸膜肺炎放线杆菌多价疫苗对猪胸膜肺炎放线杆菌血清型第5型菌株(App 5)的保护效力的分析

[0152] 1.小鼠免疫及以猪胸膜肺炎放线杆菌血清型第5型菌株(App5)攻毒试验

[0153] 取猪胸膜肺炎放线杆菌抗体阴性3～4周龄健康的ICR小鼠(国家实验动物中心,台湾)50只,随机分为4组;第1组为负对照组,第2～4组为免疫试验组;各组每只小鼠分别以腹腔注射(ip.)注射0.2ml的以下物质:

[0154] 第1组:含30%(v/v)铝胶的PBS缓冲溶液(PBS组)(n＝15);

[0155] 第2组:实施例六所得的猪胸膜肺炎放线杆菌全菌多价疫苗(App 1,2,5组)(n＝15);

[0156] 第3组:实施例六所得的猪胸膜肺炎放线杆菌全菌及重组毒素蛋白混合多价疫苗(APp 1,2,5+re-ApxI～III组)(n＝10);以及

[0157] 第4组:市售猪放线杆菌胸膜肺炎灭活疫苗,含有猪胸膜肺炎放线杆菌血清型第1,2,3,4,5,7型全菌(App 1,2,3,4,5,7组)(n＝10)。

[0158] 每只小鼠分别于第一次免疫前24小时采血保存,第一次免疫后第14天以相同免疫剂量再进行第二次免疫,第二次免疫后第10天采血,并分离血液样本中的血清,以进行毒素抗体的酵素连结免疫分析(ELISA);采血后,对每只小鼠注射0.1ml的LD_{90}剂量($7.32x10^8$cfu/ml)的猪胸膜肺炎放线杆菌血清型第5型全菌(App 5)以进行攻毒,观察小鼠10天并纪录死亡数,以计算各组存活率。

[0159] 2.毒素抗体的酵素连结免疫分析(ELISA)

[0160] 以猪胸膜肺炎放线杆菌重组毒素蛋白II(re-ApxII,SEQ ID NO:16)作为抗原,并将抗原涂布(coating)于ELISA用96孔盘(Thermo公司,美国)(100ng/孔),于4℃下静置16小时。去除多余抗原后加入清洗缓冲液(wash buffer;0.9%NaCl;0.1%Tween20),清洗3次后倒干。接着加入阻隔缓冲液(blocking buffer;含有1%BSA的wash buffer),于室温下静置1小时后,以清洗缓冲液清洗,接着将上述各组小鼠采集到的血清样品以PBS缓冲溶液稀释后,每孔加入稀释(1:100)的小鼠血清,于室温下静置1小时后,去除血清样品,并以清洗缓冲液清洗,然后加入辣根过氧化酵素(Horseradish peroxidase,HRP)标定的山羊抗小鼠的二级抗体(goat anti-mouse conjugated HRP,Gene Tex公司,美国),所述二级抗体先以阻隔缓冲液稀释5,000倍后再加入96孔盘(100μl/孔),于室温下静置1小时后,去除二级抗体,并以清洗缓冲液清洗后,每孔加入100μl 3,3',5,5'-四甲基联苯胺二盐酸(3,3',5,5'-

tetramethylbenzidine,TMB,KPL公司,美国)溶液避光呈色10分钟,并以酵素连结免疫分析测读仪(SpectraMax®M2/M2 ELISA Reader,Molecular Devices公司,美国)读取波长650nm的吸光值(OD_{650nm})。

[0161] 3.统计方法

[0162] 小鼠存活率以Kaplan-Meier存活分析(Kaplan-Meier Survival Analysis:Log-Rank test)进行统计,并以$p<0.05$视为具有统计上的显著差异。酵素连结免疫分析(ELISA)结果以Student Newman-Keuls Method方法进行统计,并以$p<0.05$视为具有统计上的显著差异。

[0163] 4.结果

[0164] 小鼠攻毒试验结果如表3所示,相较于负对照组(第1组,存活率为6.7%),各免疫试验组的存活率皆显著增加,并具有统计上的差异。尤其是含有本发明重组毒素蛋白re-ApxI～III的多价疫苗(App 1,2,5+re-ApxI～III组)对小鼠的保护效果最好,存活率最高。

[0165] 表3以猪胸膜肺炎放线杆菌血清型第5型菌株(App 5)对小鼠攻毒试验的存活率

[0166]

试验组别	小鼠数目	存活率
第1组(PBS组)	15	6.7%
第2组(App 1,2,5组)	15	26.7%*
第3组(App 1,2,5+re-ApxI～III组)	10	70%**
第4组(市售App 1,2,3,4,5,7组)	10	60%*

[0167] *表示相对于负对照组有统计上的显著差异($p<0.05$)。

[0168] **表示相对于负对照组有统计上的显著差异($p<0.01$)。

[0169] 酵素连结免疫分析(ELISA)结果如图3所示,免疫含有本发明的猪胸膜肺炎放线杆菌全菌及重组蛋白混合多价疫苗的小鼠(第3组,即App 1,2,5+ApxI～III组),在第二次免疫第10天后,其血清中的抗猪胸膜肺炎放线杆菌毒素蛋白抗体效价显著高于负对照组小鼠(第1组,即PBS组,$p<0.01$)、免疫猪胸膜肺炎放线杆菌全菌多价疫苗(第2组,即App 1,2,5组,$p<0.01$)、免疫市售猪放线杆菌胸膜肺炎灭活疫苗(第4组,即市售App 1,2,3,4,5,7组,$p<0.01$)的小鼠的抗体效价。由此可知,本发明所提供的猪胸膜肺炎放线杆菌全菌及重组蛋白混合多价疫苗可以在动物体内有效地诱导出抗猪胸膜肺炎放线杆菌毒素蛋白抗体,具免疫原性,且效果显著优于习知疫苗。

[0170] 实施例十 抗猪胸膜肺炎放线杆菌毒素I～IV(ApxI～IV)多株抗体的制备

[0171] 分别将实施例一至实施例四所得到的猪胸膜肺炎放线杆菌重组蛋白re-ApxI(SEQ ID NO:8)、re-ApxII(SEQ ID NO:16)、re-ApxIII(SEQ ID NO:21)、re-ApxIV(SEQ ID NO:92)与佛氏完全佐剂(Freund's complete adjuvant,FCA,Sigma)充分混合乳化后,再以腹腔注射方式施与Balb/c小鼠(0.2ml/只)以进行初级免疫,3周后以相同方式进行第二次免疫,隔周采集免疫小鼠的血清,即制得抗猪胸膜肺炎放线杆菌毒素I～IV(ApxI～IV)的多株抗体,所述多株抗体是用于西方墨点法进行抗原分析。

[0172] 上列详细说明系针对本发明的一可行实施例的具体说明,惟该实施例并非用以限制本发明的专利范围,凡未脱离本发明技艺精神所为的等效实施或变更,均应包含于本案的专利范围中。

[0001] 序列表

[0002] <110> 金协国际实业有限公司

[0003] <120> 猪胸膜肺炎放线杆菌重组毒素蛋白及其应用

[0004] <130> P16-0075

[0005] <150> US 62/153711

[0006] <151> 2015-04-28

[0007] <160> 117

[0008] <170> PatentIn version 3.5

[0009] <210> 1

[0010] <211> 1022

[0011] <212> PRT

[0012] <213> 猪胸膜肺炎放线杆菌(Actinobacillus pleuropneumoniae)

[0013] <400> 1

[0014] Met Ala Asn Ser Gln Leu Asp Arg Val Lys Gly Leu Ile Asp Ser Leu

[0015] 1 5 10 15

[0016] Asn Gln His Thr Lys Ser Ala Ala Lys Ser Gly Ala Gly Ala Leu Lys

[0017] 20 25 30

[0018] Asn Gly Leu Gly Gln Val Lys Gln Ala Gly Gln Lys Leu Ile Leu Tyr

[0019] 35 40 45

[0020] Ile Pro Lys Asp Tyr Gln Ala Ser Thr Gly Ser Ser Leu Asn Asp Leu

[0021] 50 55 60

[0022] Val Lys Ala Ala Glu Ala Leu Gly Ile Glu Val His Arg Ser Glu Lys

[0023] 65 70 75 80

[0024] Asn Gly Thr Ala Leu Ala Lys Glu Leu Phe Gly Thr Thr Glu Lys Leu

[0025] 85 90 95

[0026] Leu Gly Phe Ser Glu Arg Gly Ile Ala Leu Phe Ala Pro Gln Phe Asp

[0027] 100 105 110

[0028] Lys Leu Leu Asn Lys Asn Gln Lys Leu Ser Lys Ser Leu Gly Gly Ser

[0029] 115 120 125

[0030] Ser Glu Ala Leu Gly Gln Arg Leu Asn Lys Thr Gln Thr Ala Leu Ser

[0031] 130 135 140

[0032] Ala Leu Gln Ser Phe Leu Gly Thr Ala Ile Ala Gly Met Asp Leu Asp

[0033] 145 150 155 160

[0034] Ser Leu Leu Arg Arg Arg Arg Asn Gly Glu Asp Val Ser Gly Ser Glu

[0035] 165 170 175

[0036] Leu Ala Lys Ala Gly Val Asp Leu Ala Ala Gln Leu Val Asp Asn Ile

[0037] 180 185 190

[0038] Ala Ser Ala Thr Gly Thr Val Asp Ala Phe Ala Glu Gln Leu Gly Lys

[0039] 195 200 205

[0040] Leu Gly Asn Ala Leu Ser Asn Thr Arg Leu Ser Gly Leu Ala Ser Lys

[0041] 210 215 220

[0042] Leu Asn Asn Leu Pro Asp Leu Ser Leu Ala Gly Pro Gly Phe Asp Ala

[0043] 225 230 235 240

[0044] Val Ser Gly Ile Leu Ser Val Val Ser Ala Ser Phe Ile Leu Ser Asn

[0045] 245 250 255

[0046] Lys Asp Ala Asp Ala Gly Thr Lys Ala Ala Ala Gly Ile Glu Ile Ser

[0047] 260 265 270

[0048] Thr Lys Ile Leu Gly Asn Ile Gly Lys Ala Val Ser Gln Tyr Ile Ile

[0049] 275 280 285

[0050] Ala Gln Arg Val Ala Ala Gly Leu Ser Thr Thr Ala Ala Thr Arg Trp

[0051] 290 295 300

[0052] Phe Asn Arg Ser Val Val Ala Leu Ala Ile Ser Pro Leu Ser Phe Leu

[0053] 305 310 315 320

[0054] Asn Val Ala Asp Lys Phe Glu Arg Ala Lys Gln Leu Glu Gln Tyr Ser

[0055] 325 330 335

[0056] Glu Arg Phe Lys Lys Phe Gly Tyr Glu Gly Asp Ser Leu Leu Ala Ser

[0057] 340 345 350

[0058] Phe Tyr Arg Glu Thr Gly Ala Ile Glu Ala Ala Leu Thr Thr Ile Asn

[0059] 355 360 365

[0060] Ser Val Leu Ser Ala Ala Pro Ala Gly Val Gly Ala Ala Ala Thr Gly

[0061] 370 375 380

[0062] Ser Leu Val Gly Ala Pro Val Ala Ala Leu Val Ser Ala Ile Thr Gly

[0063] 385 390 395 400

[0064] Ile Ile Ser Gly Ile Leu Asp Ala Ser Lys Gln Ala Ile Phe Glu Arg

[0065] 405 410 415

[0066] Val Ala Thr Lys Leu Ala Asn Lys Ile Asp Glu Trp Glu Lys Lys His

[0067] 420 425 430

[0068] Gly Lys Asn Tyr Phe Glu Asn Gly Tyr Asp Ala Arg His Ser Ala Phe

[0069] 435 440 445

[0070] Leu Glu Asp Thr Phe Glu Leu Leu Ser Gln Tyr Asn Lys Glu Tyr Ser

[0071] 450 455 460

[0072] Val Glu Arg Val Val Ala Ile Thr Gln Gln Arg Trp Asp Val Asn Ile

[0073] 465 470 475 480

[0074] Gly Glu Leu Ala Gly Ile Thr Arg Lys Gly Ala Asp Ala Lys Ser Gly

[0075] 485 490 495

[0076] Lys Ala Tyr Val Asp Phe Phe Glu Glu Gly Lys Leu Leu Glu Lys Asp

[0077] 500 505 510

[0078] Pro Asp Arg Phe Asp Lys Lys Val Phe Asp Pro Leu Glu Gly Lys Ile
[0079] 515 520 525
[0080] Asp Leu Ser Ser Ile Asn Lys Thr Thr Leu Leu Lys Phe Ile Thr Pro
[0081] 530 535 540
[0082] Ala Phe Thr Ala Gly Glu Glu Ile Arg Glu Arg Lys Gln Thr Gly Lys
[0083] 545 550 555 560
[0084] Tyr Glu Tyr Met Thr Glu Leu Phe Val Lys Gly Lys Glu Lys Trp Val
[0085] 565 570 575
[0086] Val Thr Gly Val Gln Ser His Asn Ala Ile Tyr Asp Tyr Thr Asn Leu
[0087] 580 585 590
[0088] Ile Gln Leu Ala Ile Asp Lys Lys Gly Glu Lys Arg Gln Val Thr Ile
[0089] 595 600 605
[0090] Glu Ser His Leu Gly Glu Lys Asn Asp Arg Ile Tyr Leu Ser Ser Gly
[0091] 610 615 620
[0092] Ser Ser Ile Glu Tyr Ala Gly Asn Gly His Asp Val Ala Tyr Tyr Asp
[0093] 625 630 635 640
[0094] Lys Thr Asp Thr Gly Tyr Leu Thr Phe Asp Gly Gln Ser Ala Gln Lys
[0095] 645 650 655
[0096] Ala Gly Glu Tyr Ile Val Thr Lys Glu Leu Lys Ala Asp Val Lys Val
[0097] 660 665 670
[0098] Leu Lys Glu Val Val Lys Thr Gln Asp Ile Ser Val Gly Lys Arg Ser
[0099] 675 680 685
[0100] Glu Lys Leu Glu Tyr Arg Asp Tyr Glu Leu Ser Pro Phe Glu Leu Gly
[0101] 690 695 700
[0102] Asn Gly Ile Arg Ala Lys Asp Glu Leu His Ser Val Glu Glu Ile Ile
[0103] 705 710 715 720
[0104] Gly Ser Asn Arg Lys Asp Lys Phe Phe Gly Ser Arg Phe Thr Asp Ile
[0105] 725 730 735
[0106] Phe His Gly Ala Lys Gly Asp Asp Glu Ile Tyr Gly Asn Asp Gly His
[0107] 740 745 750
[0108] Asp Ile Leu Tyr Gly Asp Asp Gly Asn Asp Val Ile His Gly Gly Asp
[0109] 755 760 765
[0110] Gly Asn Asp His Leu Val Gly Gly Asn Gly Asn Asp Arg Leu Ile Gly
[0111] 770 775 780
[0112] Gly Lys Gly Asn Asn Phe Leu Asn Gly Gly Asp Gly Asp Asp Glu Leu
[0113] 785 790 795 800
[0114] Gln Val Phe Glu Cys Gln Tyr Asn Val Leu Leu Gly Gly Ala Gly Asn
[0115] 805 810 815
[0116] Asp Ile Leu Tyr Gly Ser Asp Gly Thr Asn Leu Phe Asp Gly Gly Val

[0117] 820 825 830

[0118] Gly Asn Asp Lys Ile Tyr Gly Gly Leu Gly Lys Asp Ile Tyr Arg Tyr

[0119] 835 840 845

[0120] Ser Lys Glu Tyr Gly Arg His Ile Ile Ile Glu Lys Gly Gly Asp Asp

[0121] 850 855 860

[0122] Asp Thr Leu Leu Leu Ser Asp Leu Ser Phe Lys Asp Val Gly Phe Ile

[0123] 865 870 875 880

[0124] Arg Ile Gly Asp Asp Leu Leu Val Asn Lys Arg Ile Gly Gly Thr Leu

[0125] 885 890 895

[0126] Tyr Tyr His Glu Asp Tyr Asn Gly Asn Ala Leu Thr Ile Lys Asp Trp

[0127] 900 905 910

[0128] Phe Lys Glu Gly Lys Glu Gly Gln Asn Asn Lys Val Glu Lys Ile Val

[0129] 915 920 925

[0130] Asp Lys Asp Gly Ala Tyr Val Leu Ser Gln Tyr Leu Thr Glu Leu Thr

[0131] 930 935 940

[0132] Ala Pro Gly Arg Gly Ile Asn Tyr Phe Asn Gly Leu Glu Glu Lys Leu

[0133] 945 950 955 960

[0134] Tyr Tyr Gly Glu Gly Tyr Asn Ala Leu Pro Gln Leu Arg Lys Asp Ile

[0135] 965 970 975

[0136] Glu Gln Ile Ile Ser Ser Thr Gly Ala Leu Thr Gly Glu His Gly Gln

[0137] 980 985 990

[0138] Val Leu Val Gly Ala Gly Gly Pro Leu Ala Tyr Ser Asn Ser Pro Asn

[0139] 995 1000 1005

[0140] Ser Ile Pro Asn Ala Phe Ser Asn Tyr Leu Thr Gln Ser Ala

[0141] 1010 1015 1020

[0142] <210> 2

[0143] <211> 16

[0144] <212> PRT

[0145] <213> 猪胸膜肺炎放线杆菌(Actinobacillus pleuropneumoniae)

[0146] <400> 2

[0147] Glu Leu Ala Gly Ile Thr Arg Lys Gly Ala Asp Ala Lys Ser Gly Lys

[0148] 1 5 10 15

[0149] <210> 3

[0150] <211> 8

[0151] <212> PRT

[0152] <213> 猪胸膜肺炎放线杆菌(Actinobacillus pleuropneumoniae)

[0153] <400> 3

[0154] Pro Ala Gly Val Gly Ala Ala Ala

[0155] 1 5

[0156] <210> 4

[0157] <211> 24

[0158] <212> PRT

[0159] <213> 猪胸膜肺炎放线杆菌(Actinobacillus pleuropneumoniae)

[0160] <400> 4

[0161] Asp Ile Leu Tyr Gly Ser Asp Gly Thr Asn Leu Phe Asp Gly Gly Val

[0162] 1 5 10 15

[0163] Gly Asn Asp Lys Ile Tyr Gly Gly

[0164] 20

[0165] <210> 5

[0166] <211> 26

[0167] <212> PRT

[0168] <213> 猪胸膜肺炎放线杆菌(Actinobacillus pleuropneumoniae)

[0169] <400> 5

[0170] Glu His Gly Gln Val Leu Val Gly Ala Gly Gly Pro Leu Ala Tyr Ser

[0171] 1 5 10 15

[0172] Asn Ser Pro Asn Ser Ile Pro Asn Ala Phe

[0173] 20 25

[0174] <210> 6

[0175] <211> 97

[0176] <212> PRT

[0177] <213> 猪胸膜肺炎放线杆菌(Actinobacillus pleuropneumoniae)

[0178] <400> 6

[0179] Arg Ala Lys Asp Glu Leu His Ser Val Glu Glu Ile Ile Gly Ser Asn

[0180] 1 5 10 15

[0181] Arg Lys Asp Lys Phe Phe Gly Ser Arg Phe Thr Asp Ile Phe His Gly

[0182] 20 25 30

[0183] Ala Lys Gly Asp Asp Glu Ile Tyr Gly Asn Asp Gly His Asp Ile Leu

[0184] 35 40 45

[0185] Tyr Gly Asp Asp Gly Asn Asp Val Ile His Gly Gly Asp Gly Asn Asp

[0186] 50 55 60

[0187] His Leu Val Gly Gly Asn Gly Asn Asp Arg Leu Ile Gly Gly Lys Gly

[0188] 65 70 75 80

[0189] Asn Asn Phe Leu Asn Gly Gly Asp Gly Asp Asp Glu Leu Gln Val Phe

[0190] 85 90 95

[0191] Glu

[0192] <210> 7

[0193] <211> 410

[0194] <212> PRT

[0195] <213> 人工序列

[0196] <220>

[0197] <223> 重组ApxI毒素

[0198] <400> 7

[0199] Glu Leu Ala Gly Ile Thr Arg Lys Gly Ala Asp Ala Lys Ser Gly Lys

[0200] 1 5 10 15

[0201] Gly Ser Thr Ala Pro Ala Gly Val Gly Ala Ala Ala Gly Ser Thr Ala

[0202] 20 25 30

[0203] Gly Ser Thr Ala Asp Ile Leu Tyr Gly Ser Asp Gly Thr Asn Leu Phe

[0204] 35 40 45

[0205] Asp Gly Gly Val Gly Asn Asp Lys Ile Tyr Gly Gly Gly Ser Thr Ala

[0206] 50 55 60

[0207] Glu His Gly Gln Val Leu Val Gly Ala Gly Gly Pro Leu Ala Tyr Ser

[0208] 65 70 75 80

[0209] Asn Ser Pro Asn Ser Ile Pro Asn Ala Phe Gly Ser Thr Ala Arg Ala

[0210] 85 90 95

[0211] Lys Asp Glu Leu His Ser Val Glu Glu Ile Ile Gly Ser Asn Arg Lys

[0212] 100 105 110

[0213] Asp Lys Phe Phe Gly Ser Arg Phe Thr Asp Ile Phe His Gly Ala Lys

[0214] 115 120 125

[0215] Gly Asp Asp Glu Ile Tyr Gly Asn Asp Gly His Asp Ile Leu Tyr Gly

[0216] 130 135 140

[0217] Asp Asp Gly Asn Asp Val Ile His Gly Gly Asp Gly Asn Asp His Leu

[0218] 145 150 155 160

[0219] Val Gly Gly Asn Gly Asn Asp Arg Leu Ile Gly Gly Lys Gly Asn Asn

[0220] 165 170 175

[0221] Phe Leu Asn Gly Gly Asp Gly Asp Asp Glu Leu Leu Gln Val Phe Glu

[0222] 180 185 190

[0223] Gly Ser Thr Ala Gly Ser Thr Ala Phe Leu Asn Lys Leu Leu Ser Thr

[0224] 195 200 205

[0225] Ala Lys Glu Arg Asn Arg Trp Glu Glu Pro Gly Gln Lys Leu Tyr Asn

[0226] 210 215 220

[0227] Val Glu Ala Thr Ser Tyr Ala Gly Ser Thr Ala Phe Leu Asn Lys Leu

[0228] 225 230 235 240

[0229] Leu Ser Thr Ala Lys Glu Arg Asn Arg Trp Glu Glu Pro Gly Gln Lys

[0230] 245 250 255

[0231] Leu Tyr Asn Val Glu Ala Thr Ser Tyr Ala Gly Ser Thr Ala Phe Leu

[0232] 260 265 270

[0233] Asn Lys Leu Leu Ser Thr Ala Lys Glu Arg Asn Arg Trp Glu Glu Pro

[0234] 275 280 285

[0235] Gly Gln Lys Leu Tyr Asn Val Glu Ala Thr Ser Tyr Ala Gly Ser Thr

[0236] 290 295 300

[0237] Ala Phe Leu Asn Lys Leu Leu Ser Thr Ala Lys Glu Arg Asn Arg Trp

[0238] 305 310 315 320

[0239] Glu Glu Pro Gly Gln Lys Leu Tyr Asn Val Glu Ala Thr Ser Tyr Ala

[0240] 325 330 335

[0241] Gly Ser Thr Ala Phe Leu Asn Lys Leu Leu Ser Thr Ala Lys Glu Arg

[0242] 340 345 350

[0243] Asn Arg Trp Glu Glu Pro Gly Gln Lys Leu Tyr Asn Val Glu Ala Thr

[0244] 355 360 365

[0245] Ser Tyr Ala Gly Ser Thr Ala Phe Leu Asn Lys Leu Leu Ser Thr Ala

[0246] 370 375 380

[0247] Lys Glu Arg Asn Arg Trp Glu Glu Pro Gly Gln Lys Leu Tyr Asn Val

[0248] 385 390 395 400

[0249] Glu Ala Thr Ser Tyr Ala Gly Ser Thr Ala

[0250] 405 410

[0251] <210> 8

[0252] <211> 412

[0253] <212> PRT

[0254] <213> 人工序列

[0255] <220>

[0256] <223> 带有一个HindIII切位的重组ApxI毒素

[0257] <400> 8

[0258] Glu Leu Ala Gly Ile Thr Arg Lys Gly Ala Asp Ala Lys Ser Gly Lys

[0259] 1 5 10 15

[0260] Gly Ser Thr Ala Pro Ala Gly Val Gly Ala Ala Ala Gly Ser Thr Ala

[0261] 20 25 30

[0262] Gly Ser Thr Ala Asp Ile Leu Tyr Gly Ser Asp Gly Thr Asn Leu Phe

[0263] 35 40 45

[0264] Asp Gly Gly Val Gly Asn Asp Lys Ile Tyr Gly Gly Gly Ser Thr Ala

[0265] 50 55 60

[0266] Glu His Gly Gln Val Leu Val Gly Ala Gly Gly Pro Leu Ala Tyr Ser

[0267] 65 70 75 80

[0268] Asn Ser Pro Asn Ser Ile Pro Asn Ala Phe Gly Ser Thr Ala Arg Ala

[0269] 85 90 95

[0270] Lys Asp Glu Leu His Ser Val Glu Glu Ile Ile Gly Ser Asn Arg Lys

[0271] 100 105 110

[0272] Asp Lys Phe Phe Gly Ser Arg Phe Thr Asp Ile Phe His Gly Ala Lys

[0273] 115 120 125

[0274] Gly Asp Asp Glu Ile Tyr Gly Asn Asp Gly His Asp Ile Leu Tyr Gly

[0275] 130 135 140

[0276] Asp Asp Gly Asn Asp Val Ile His Gly Gly Asp Gly Asn Asp His Leu

[0277] 145 150 155 160

[0278] Val Gly Gly Asn Gly Asn Asp Arg Leu Ile Gly Gly Lys Gly Asn Asn

[0279] 165 170 175

[0280] Phe Leu Asn Gly Gly Asp Gly Asp Asp Glu Leu Leu Gln Val Phe Glu

[0281] 180 185 190

[0282] Gly Ser Thr Ala Lys Leu Gly Ser Thr Ala Phe Leu Asn Lys Leu Leu

[0283] 195 200 205

[0284] Ser Thr Ala Lys Glu Arg Asn Arg Trp Glu Glu Pro Gly Gln Lys Leu

[0285] 210 215 220

[0286] Tyr Asn Val Glu Ala Thr Ser Tyr Ala Gly Ser Thr Ala Phe Leu Asn

[0287] 225 230 235 240

[0288] Lys Leu Leu Ser Thr Ala Lys Glu Arg Asn Arg Trp Glu Glu Pro Gly

[0289] 245 250 255

[0290] Gln Lys Leu Tyr Asn Val Glu Ala Thr Ser Tyr Ala Gly Ser Thr Ala

[0291] 260 265 270

[0292] Phe Leu Asn Lys Leu Leu Ser Thr Ala Lys Glu Arg Asn Arg Trp Glu

[0293] 275 280 285

[0294] Glu Pro Gly Gln Lys Leu Tyr Asn Val Glu Ala Thr Ser Tyr Ala Gly

[0295] 290 295 300

[0296] Ser Thr Ala Phe Leu Asn Lys Leu Leu Ser Thr Ala Lys Glu Arg Asn

[0297] 305 310 315 320

[0298] Arg Trp Glu Glu Pro Gly Gln Lys Leu Tyr Asn Val Glu Ala Thr Ser

[0299] 325 330 335

[0300] Tyr Ala Gly Ser Thr Ala Phe Leu Asn Lys Leu Leu Ser Thr Ala Lys

[0301] 340 345 350

[0302] Glu Arg Asn Arg Trp Glu Glu Pro Gly Gln Lys Leu Tyr Asn Val Glu

[0303] 355 360 365

[0304] Ala Thr Ser Tyr Ala Gly Ser Thr Ala Phe Leu Asn Lys Leu Leu Ser

[0305] 370 375 380

[0306] Thr Ala Lys Glu Arg Asn Arg Trp Glu Glu Pro Gly Gln Lys Leu Tyr

[0307] 385 390 395 400

[0308] Asn Val Glu Ala Thr Ser Tyr Ala Gly Ser Thr Ala

[0309] 405 410

[0310] <210> 9

[0311] <211> 956

[0312] <212> PRT

[0313] <213> 猪胸膜肺炎放线杆菌(Actinobacillus pleuropneumoniae)

[0314] <400> 9

[0315] Met Ser Lys Ile Thr Leu Ser Ser Leu Lys Ser Ser Leu Gln Gln Gly

[0316] 1 5 10 15

[0317] Leu Lys Asn Gly Lys Asn Lys Leu Asn Gln Ala Gly Thr Thr Leu Lys

[0318] 20 25 30

[0319] Asn Gly Leu Thr Gln Thr Gly His Ser Leu Gln Asn Gly Ala Lys Lys

[0320] 35 40 45

[0321] Leu Ile Leu Tyr Ile Pro Gln Gly Tyr Asp Ser Gly Gln Gly Asn Gly

[0322] 50 55 60

[0323] Val Gln Asp Leu Val Lys Ala Ala Asn Asp Leu Gly Ile Glu Val Trp

[0324] 65 70 75 80

[0325] Arg Glu Glu Arg Ser Asn Leu Asp Ile Ala Lys Thr Ser Phe Asp Thr

[0326] 85 90 95

[0327] Thr Gln Lys Ile Leu Gly Phe Thr Asp Arg Gly Ile Val Leu Phe Ala

[0328] 100 105 110

[0329] Pro Gln Leu Asp Asn Leu Leu Lys Lys Asn Pro Lys Ile Gly Asn Thr

[0330] 115 120 125

[0331] Leu Gly Ser Ala Ser Ser Ile Ser Gln Asn Ile Gly Lys Ala Asn Thr

[0332] 130 135 140

[0333] Val Leu Gly Gly Ile Gln Ser Ile Leu Gly Ser Val Leu Ser Gly Val

[0334] 145 150 155 160

[0335] Asn Leu Asn Glu Leu Leu Gln Asn Lys Asp Pro Asn Gln Leu Glu Leu

[0336] 165 170 175

[0337] Ala Lys Ala Gly Leu Glu Leu Thr Asn Glu Leu Val Gly Asn Ile Ala

[0338] 180 185 190

[0339] Ser Ser Val Gln Thr Val Asp Ala Phe Ala Glu Gln Ile Ser Lys Leu

[0340] 195 200 205

[0341] Gly Ser His Leu Gln Asn Val Lys Gly Leu Gly Gly Leu Ser Asn Lys

[0342] 210 215 220

[0343] Leu Gln Asn Leu Pro Asp Leu Gly Lys Ala Ser Leu Gly Leu Asp Ile

[0344] 225 230 235 240

[0345] Ile Ser Gly Leu Leu Ser Gly Ala Ser Ala Gly Leu Ile Leu Ala Asp

[0346] 245 250 255

[0347] Lys Glu Ala Ser Thr Glu Lys Lys Ala Ala Ala Gly Val Glu Phe Ala

[0348] 260 265 270

[0349] Asn Gln Ile Ile Gly Asn Val Thr Lys Ala Val Ser Ser Tyr Ile Leu

[0350] 275 280 285

[0351] Ala Gln Arg Val Ala Ser Gly Leu Ser Ser Thr Gly Pro Val Ala Ala
[0352] 290 295 300
[0353] Leu Ile Ala Ser Thr Val Ala Leu Ala Val Ser Pro Leu Ser Phe Leu
[0354] 305 310 315 320
[0355] Asn Val Ala Asp Lys Phe Lys Gln Ala Asp Leu Ile Lys Ser Tyr Ser
[0356] 325 330 335
[0357] Glu Arg Phe Gln Lys Leu Gly Tyr Asp Gly Asp Arg Leu Leu Ala Asp
[0358] 340 345 350
[0359] Phe His Arg Glu Thr Gly Thr Ile Asp Ala Ser Val Thr Thr Ile Asn
[0360] 355 360 365
[0361] Thr Ala Leu Ala Ala Ile Ser Gly Gly Val Gly Ala Ala Ser Ala Gly
[0362] 370 375 380
[0363] Ser Leu Val Gly Ala Pro Val Ala Leu Leu Val Ala Gly Val Thr Gly
[0364] 385 390 395 400
[0365] Leu Ile Thr Thr Ile Leu Glu Tyr Ser Lys Gln Ala Met Phe Glu His
[0366] 405 410 415
[0367] Val Ala Asn Lys Val His Asp Arg Ile Val Glu Trp Glu Lys Lys His
[0368] 420 425 430
[0369] Asn Lys Asn Tyr Phe Glu Gln Gly Tyr Asp Ser Arg His Leu Ala Asp
[0370] 435 440 445
[0371] Leu Gln Asp Asn Met Lys Phe Leu Ile Asn Leu Asn Lys Glu Leu Gln
[0372] 450 455 460
[0373] Ala Glu Arg Val Val Ala Ile Thr Gln Gln Arg Trp Asp Asn Gln Ile
[0374] 465 470 475 480
[0375] Gly Asp Leu Ala Ala Ile Ser Arg Arg Thr Asp Lys Ile Ser Ser Gly
[0376] 485 490 495
[0377] Lys Ala Tyr Val Asp Ala Phe Glu Glu Gly Gln His Gln Ser Tyr Asp
[0378] 500 505 510
[0379] Ser Ser Val Gln Leu Asp Asn Lys Asn Gly Ile Ile Asn Ile Ser Asn
[0380] 515 520 525
[0381] Thr Asn Arg Lys Thr Gln Ser Val Leu Phe Arg Thr Pro Leu Leu Thr
[0382] 530 535 540
[0383] Pro Gly Glu Glu Asn Arg Glu Arg Ile Gln Glu Gly Lys Asn Ser Tyr
[0384] 545 550 555 560
[0385] Ile Thr Lys Leu His Ile Gln Arg Val Asp Ser Trp Thr Val Thr Asp
[0386] 565 570 575
[0387] Gly Asp Ala Ser Ser Ser Val Asp Phe Thr Asn Val Val Gln Arg Ile
[0388] 580 585 590
[0389] Ala Val Lys Phe Asp Asp Ala Gly Asn Ile Ile Glu Ser Lys Asp Thr

[0390] 595 600 605

[0391] Lys Ile Ile Ala Asn Leu Gly Ala Gly Asn Asp Asn Val Phe Val Gly

[0392] 610 615 620

[0393] Ser Ser Thr Thr Val Ile Asp Gly Gly Asp Gly His Asp Arg Val His

[0394] 625 630 635 640

[0395] Tyr Ser Arg Gly Glu Tyr Gly Ala Leu Val Ile Asp Ala Thr Ala Glu

[0396] 645 650 655

[0397] Thr Glu Lys Gly Ser Tyr Ser Val Lys Arg Tyr Val Gly Asp Ser Lys

[0398] 660 665 670

[0399] Ala Leu His Glu Thr Ile Ala Thr His Pro Thr Asn Val Gly Asn Arg

[0400] 675 680 685

[0401] Glu Glu Lys Ile Glu Tyr Arg Arg Glu Asp Asp Arg Phe His Thr Gly

[0402] 690 695 700

[0403] Tyr Thr Val Thr Asp Ser Leu Lys Ser Val Glu Glu Ile Ile Gly Ser

[0404] 705 710 715 720

[0405] Gln Phe Asn Asp Ile Phe Lys Gly Ser Gln Phe Asp Asp Val Phe His

[0406] 725 730 735

[0407] Gly Gly Asn Gly Val Asp Thr Ile Asp Gly Asn Asp Gly Asp Asp His

[0408] 740 745 750

[0409] Leu Phe Gly Gly Ala Gly Asp Asp Val Ile Asp Gly Gly Asn Gly Asn

[0410] 755 760 765

[0411] Asn Phe Leu Val Gly Gly Thr Gly Asn Asp Ile Ile Ser Gly Gly Lys

[0412] 770 775 780

[0413] Asp Asn Asp Ile Tyr Val His Lys Thr Gly Asp Gly Asn Asp Ser Ile

[0414] 785 790 795 800

[0415] Thr Asp Ser Gly Gly Gln Asp Lys Leu Ala Phe Ser Asp Val Asn Leu

[0416] 805 810 815

[0417] Lys Asp Leu Thr Phe Lys Lys Val Asp Ser Ser Leu Glu Ile Ile Asn

[0418] 820 825 830

[0419] Gln Lys Gly Glu Lys Val Arg Ile Gly Asn Trp Phe Leu Lys Asn Asp

[0420] 835 840 845

[0421] Leu Ala Ser Thr Val Ala Asn Tyr Lys Ala Thr Asn Asp Arg Lys Ile

[0422] 850 855 860

[0423] Glu Glu Ile Ile Gly Lys Gly Gly Glu Arg Ile Thr Ser Lys Gln Val

[0424] 865 870 875 880

[0425] Asp Lys Leu Ile Lys Glu Gly Asn Asn Gln Ile Ser Ala Lys Ala Leu

[0426] 885 890 895

[0427] Ser Lys Val Gly Asn Asp Tyr Asn Thr Ser Lys Asp Arg Gln Asn Val

[0428] 900 905 910

[0429] Ser Asn Ser Leu Ala Lys Leu Ile Ser Ser Val Glu Ser Phe Thr Ser
[0430] 915 920 925
[0431] Ser Ser Asn Phe Arg Asn Asn Leu Gly Ala Tyr Val Pro Ser Ser Ile
[0432] 930 935 940
[0433] Asn Val Ser Asn Asn Ile Gln Leu Ala Arg Ala Ala
[0434] 945 950 955
[0435] <210> 10
[0436] <211> 72
[0437] <212> PRT
[0438] <213> 猪胸膜肺炎放线杆菌(Actinobacillus pleuropneumoniae)
[0439] <400> 10
[0440] Gly Asn Gly Val Asp Thr Ile Asp Gly Asn Asp Gly Asp Asp His Leu
[0441] 1 5 10 15
[0442] Phe Gly Gly Ala Gly Asp Asp Val Ile Asp Gly Gly Asn Gly Asn Asn
[0443] 20 25 30
[0444] Phe Leu Val Gly Gly Thr Gly Asn Asp Ile Ile Ser Gly Gly Lys Asp
[0445] 35 40 45
[0446] Asn Asp Ile Tyr Val His Lys Thr Gly Asp Gly Asn Asp Ser Ile Thr
[0447] 50 55 60
[0448] Asp Ser Gly Gly Gln Asp Lys Leu
[0449] 65 70
[0450] <210> 11
[0451] <211> 15
[0452] <212> PRT
[0453] <213> 猪胸膜肺炎放线杆菌(Actinobacillus pleuropneumoniae)
[0454] <400> 11
[0455] Lys Val Gly Asn Asp Tyr Asn Thr Ser Lys Asp Arg Gln Asn Val
[0456] 1 5 10 15
[0457] <210> 12
[0458] <211> 41
[0459] <212> PRT
[0460] <213> 猪胸膜肺炎放线杆菌(Actinobacillus pleuropneumoniae)
[0461] <400> 12
[0462] Leu Thr Pro Gly Glu Glu Asn Arg Glu Arg Ile Gln Glu Gly Lys Asn
[0463] 1 5 10 15
[0464] Ser Tyr Ile Thr Lys Leu His Ile Gln Arg Val Asp Ser Trp Thr Val
[0465] 20 25 30
[0466] Thr Asp Gly Asp Ala Ser Ser Ser Val
[0467] 35 40

[0468] <210> 13

[0469] <211> 20

[0470] <212> PRT

[0471] <213> 猪胸膜肺炎放线杆菌(Actinobacillus pleuropneumoniae)

[0472] <400> 13

[0473] Ile Leu Tyr Ile Pro Gln Gly Tyr Asp Ser Gly Gln Gly Asn Gly Val

[0474] 1 5 10 15

[0475] Gln Asp Leu Val

[0476] 20

[0477] <210> 14

[0478] <211> 24

[0479] <212> PRT

[0480] <213> 猪胸膜肺炎放线杆菌(Actinobacillus pleuropneumoniae)

[0481] <400> 14

[0482] Ala Thr His Pro Thr Asn Val Gly Asn Arg Glu Glu Lys Ile Glu Tyr

[0483] 1 5 10 15

[0484] Arg Arg Glu Asp Asp Arg Phe His

[0485] 20

[0486] <210> 15

[0487] <211> 410

[0488] <212> PRT

[0489] <213> 人工序列

[0490] <220>

[0491] <223> 重组ApxII毒素

[0492] <400> 15

[0493] Gly Asn Gly Val Asp Thr Ile Asp Gly Asn Asp Gly Asp Asp His Leu

[0494] 1 5 10 15

[0495] Phe Gly Gly Ala Gly Asp Asp Val Ile Asp Gly Gly Asn Gly Asn Asn

[0496] 20 25 30

[0497] Phe Leu Val Gly Gly Thr Gly Asn Asp Ile Ile Ser Gly Gly Lys Asp

[0498] 35 40 45

[0499] Asn Asp Ile Tyr Val His Lys Thr Gly Asp Gly Asn Asp Ser Ile Thr

[0500] 50 55 60

[0501] Asp Ser Gly Gly Gln Asp Lys Leu Gly Ser Thr Ala Lys Val Gly Asn

[0502] 65 70 75 80

[0503] Asp Tyr Asn Thr Ser Lys Asp Arg Gln Asn Val Gly Ser Thr Ala Gly

[0504] 85 90 95

[0505] Ser Thr Ala Leu Thr Pro Gly Glu Glu Asn Arg Glu Arg Ile Gln Glu

[0506] 100 105 110

[0507] Gly Lys Asn Ser Tyr Ile Thr Lys Leu His Ile Gln Arg Val Asp Ser
[0508] 115 120 125
[0509] Trp Thr Val Thr Asp Gly Asp Ala Ser Ser Ser Val Gly Ser Thr Ala
[0510] 130 135 140
[0511] Ile Leu Tyr Ile Pro Gln Gly Tyr Asp Ser Gly Gln Gly Asn Gly Val
[0512] 145 150 155 160
[0513] Gln Asp Leu Val Gly Ser Thr Ala Ala Thr His Pro Thr Asn Val Gly
[0514] 165 170 175
[0515] Asn Arg Glu Glu Lys Ile Glu Tyr Arg Arg Glu Asp Asp Arg Phe His
[0516] 180 185 190
[0517] Gly Ser Thr Ala Gly Ser Thr Ala Phe Leu Asn Lys Leu Leu Ser Thr
[0518] 195 200 205
[0519] Ala Lys Glu Arg Asn Arg Trp Glu Glu Pro Gly Gln Lys Leu Tyr Asn
[0520] 210 215 220
[0521] Val Glu Ala Thr Ser Tyr Ala Gly Ser Thr Ala Phe Leu Asn Lys Leu
[0522] 225 230 235 240
[0523] Leu Ser Thr Ala Lys Glu Arg Asn Arg Trp Glu Glu Pro Gly Gln Lys
[0524] 245 250 255
[0525] Leu Tyr Asn Val Glu Ala Thr Ser Tyr Ala Gly Ser Thr Ala Phe Leu
[0526] 260 265 270
[0527] Asn Lys Leu Leu Ser Thr Ala Lys Glu Arg Asn Arg Trp Glu Glu Pro
[0528] 275 280 285
[0529] Gly Gln Lys Leu Tyr Asn Val Glu Ala Thr Ser Tyr Ala Gly Ser Thr
[0530] 290 295 300
[0531] Ala Phe Leu Asn Lys Leu Leu Ser Thr Ala Lys Glu Arg Asn Arg Trp
[0532] 305 310 315 320
[0533] Glu Glu Pro Gly Gln Lys Leu Tyr Asn Val Glu Ala Thr Ser Tyr Ala
[0534] 325 330 335
[0535] Gly Ser Thr Ala Phe Leu Asn Lys Leu Leu Ser Thr Ala Lys Glu Arg
[0536] 340 345 350
[0537] Asn Arg Trp Glu Glu Pro Gly Gln Lys Leu Tyr Asn Val Glu Ala Thr
[0538] 355 360 365
[0539] Ser Tyr Ala Gly Ser Thr Ala Phe Leu Asn Lys Leu Leu Ser Thr Ala
[0540] 370 375 380
[0541] Lys Glu Arg Asn Arg Trp Glu Glu Pro Gly Gln Lys Leu Tyr Asn Val
[0542] 385 390 395 400
[0543] Glu Ala Thr Ser Tyr Ala Gly Ser Thr Ala
[0544] 405 410
[0545] <210> 16

[0546] <211> 412

[0547] <212> PRT

[0548] <213> 人工序列

[0549] <220>

[0550] <223> 带有一个HindIII切位的重组ApxII毒素

[0551] <400> 16

[0552] Gly Asn Gly Val Asp Thr Ile Asp Gly Asn Asp Gly Asp Asp His Leu

[0553] 1 5 10 15

[0554] Phe Gly Gly Ala Gly Asp Asp Val Ile Asp Gly Gly Asn Gly Asn Asn

[0555] 20 25 30

[0556] Phe Leu Val Gly Gly Thr Gly Asn Asp Ile Ile Ser Gly Gly Lys Asp

[0557] 35 40 45

[0558] Asn Asp Ile Tyr Val His Lys Thr Gly Asp Gly Asn Asp Ser Ile Thr

[0559] 50 55 60

[0560] Asp Ser Gly Gly Gln Asp Lys Leu Gly Ser Thr Ala Lys Val Gly Asn

[0561] 65 70 75 80

[0562] Asp Tyr Asn Thr Ser Lys Asp Arg Gln Asn Val Gly Ser Thr Ala Gly

[0563] 85 90 95

[0564] Ser Thr Ala Leu Thr Pro Gly Glu Glu Asn Arg Glu Arg Ile Gln Glu

[0565] 100 105 110

[0566] Gly Lys Asn Ser Tyr Ile Thr Lys Leu His Ile Gln Arg Val Asp Ser

[0567] 115 120 125

[0568] Trp Thr Val Thr Asp Gly Asp Ala Ser Ser Ser Val Gly Ser Thr Ala

[0569] 130 135 140

[0570] Ile Leu Tyr Ile Pro Gln Gly Tyr Asp Ser Gly Gln Gly Asn Gly Val

[0571] 145 150 155 160

[0572] Gln Asp Leu Val Gly Ser Thr Ala Ala Thr His Pro Thr Asn Val Gly

[0573] 165 170 175

[0574] Asn Arg Glu Glu Lys Ile Glu Tyr Arg Arg Glu Asp Asp Arg Phe His

[0575] 180 185 190

[0576] Gly Ser Thr Ala Lys Leu Gly Ser Thr Ala Phe Leu Asn Lys Leu Leu

[0577] 195 200 205

[0578] Ser Thr Ala Lys Glu Arg Asn Arg Trp Glu Glu Pro Gly Gln Lys Leu

[0579] 210 215 220

[0580] Tyr Asn Val Glu Ala Thr Ser Tyr Ala Gly Ser Thr Ala Phe Leu Asn

[0581] 225 230 235 240

[0582] Lys Leu Leu Ser Thr Ala Lys Glu Arg Asn Arg Trp Glu Glu Pro Gly

[0583] 245 250 255

[0584] Gln Lys Leu Tyr Asn Val Glu Ala Thr Ser Tyr Ala Gly Ser Thr Ala

[0585] 260 265 270

[0586] Phe Leu Asn Lys Leu Leu Ser Thr Ala Lys Glu Arg Asn Arg Trp Glu

[0587] 275 280 285

[0588] Glu Pro Gly Gln Lys Leu Tyr Asn Val Glu Ala Thr Ser Tyr Ala Gly

[0589] 290 295 300

[0590] Ser Thr Ala Phe Leu Asn Lys Leu Leu Ser Thr Ala Lys Glu Arg Asn

[0591] 305 310 315 320

[0592] Arg Trp Glu Glu Pro Gly Gln Lys Leu Tyr Asn Val Glu Ala Thr Ser

[0593] 325 330 335

[0594] Tyr Ala Gly Ser Thr Ala Phe Leu Asn Lys Leu Leu Ser Thr Ala Lys

[0595] 340 345 350

[0596] Glu Arg Asn Arg Trp Glu Glu Pro Gly Gln Lys Leu Tyr Asn Val Glu

[0597] 355 360 365

[0598] Ala Thr Ser Tyr Ala Gly Ser Thr Ala Phe Leu Asn Lys Leu Leu Ser

[0599] 370 375 380

[0600] Thr Ala Lys Glu Arg Asn Arg Trp Glu Glu Pro Gly Gln Lys Leu Tyr

[0601] 385 390 395 400

[0602] Asn Val Glu Ala Thr Ser Tyr Ala Gly Ser Thr Ala

[0603] 405 410

[0604] <210> 17

[0605] <211> 1052

[0606] <212> PRT

[0607] <213> 猪胸膜肺炎放线杆菌(Actinobacillus pleuropneumoniae)

[0608] <400> 17

[0609] Met Ser Thr Trp Ser Ser Met Leu Ala Asp Leu Lys Lys Arg Ala Glu

[0610] 1 5 10 15

[0611] Glu Ala Lys Arg Gln Ala Lys Lys Gly Tyr Asp Val Thr Lys Asn Gly

[0612] 20 25 30

[0613] Leu Gln Tyr Gly Val Ser Gln Ala Lys Leu Gln Ala Leu Ala Ala Gly

[0614] 35 40 45

[0615] Lys Ala Val Gln Lys Tyr Gly Asn Lys Leu Val Leu Val Ile Pro Lys

[0616] 50 55 60

[0617] Glu Tyr Asp Gly Ser Val Gly Asn Gly Phe Phe Asp Leu Val Lys Ala

[0618] 65 70 75 80

[0619] Ala Glu Glu Leu Gly Ile Gln Val Lys Tyr Val Asn Arg Asn Glu Leu

[0620] 85 90 95

[0621] Glu Val Ala His Lys Ser Leu Gly Thr Ala Asp Gln Phe Leu Gly Leu

[0622] 100 105 110

[0623] Thr Glu Arg Gly Leu Thr Leu Ser Ala Pro Gln Leu Asp Gln Phe Leu

[0624] 115 120 125

[0625] Gln Lys His Ser Lys Ile Ser Asn Val Val Gly Ser Ser Thr Gly Asp

[0626] 130 135 140

[0627] Ala Val Ser Lys Leu Ala Lys Ser Gln Thr Ile Ile Ser Gly Ile Gln

[0628] 145 150 155 160

[0629] Ser Val Leu Gly Thr Val Leu Ala Gly Ile Asn Leu Asn Glu Ala Ile

[0630] 165 170 175

[0631] Ile Ser Gly Gly Ser Glu Leu Glu Leu Ala Glu Ala Gly Val Ser Leu

[0632] 180 185 190

[0633] Ala Ser Glu Leu Val Ser Asn Ile Ala Lys Gly Thr Thr Thr Ile Asp

[0634] 195 200 205

[0635] Ala Phe Thr Thr Gln Ile Gln Asn Phe Gly Lys Leu Val Glu Asn Ala

[0636] 210 215 220

[0637] Lys Gly Leu Gly Gly Val Gly Arg Gln Leu Gln Asn Ile Ser Gly Ser

[0638] 225 230 235 240

[0639] Ala Leu Ser Lys Thr Gly Leu Gly Leu Asp Ile Ile Ser Ser Leu Leu

[0640] 245 250 255

[0641] Ser Gly Val Thr Ala Ser Phe Ala Leu Ala Asn Lys Asn Ala Ser Thr

[0642] 260 265 270

[0643] Ser Thr Lys Val Ala Ala Gly Phe Glu Leu Ser Asn Gln Val Ile Gly

[0644] 275 280 285

[0645] Gly Ile Thr Lys Ala Val Ser Ser Tyr Ile Leu Ala Gln Arg Leu Ala

[0646] 290 295 300

[0647] Ala Gly Leu Ser Thr Thr Gly Pro Ala Ala Ala Leu Ile Ala Ser Ser

[0648] 305 310 315 320

[0649] Ile Ser Leu Ala Ile Ser Pro Leu Ala Phe Leu Arg Val Ala Asp Asn

[0650] 325 330 335

[0651] Phe Asn Arg Ser Lys Glu Ile Gly Glu Phe Ala Glu Arg Phe Lys Lys

[0652] 340 345 350

[0653] Leu Gly Tyr Asp Gly Asp Lys Leu Leu Ser Glu Phe Tyr His Glu Ala

[0654] 355 360 365

[0655] Gly Thr Ile Asp Ala Ser Ile Thr Thr Ile Ser Thr Ala Leu Ser Ala

[0656] 370 375 380

[0657] Ile Ala Ala Gly Thr Ala Ala Ala Ser Ala Gly Ala Leu Val Gly Ala

[0658] 385 390 395 400

[0659] Pro Ile Thr Leu Leu Val Thr Gly Ile Thr Gly Leu Ile Ser Gly Ile

[0660] 405 410 415

[0661] Leu Glu Phe Ser Lys Gln Pro Met Leu Asp His Val Ala Ser Lys Ile

[0662] 420 425 430

[0663] Gly Asn Lys Ile Asp Glu Trp Glu Lys Lys Tyr Gly Lys Asn Tyr Phe
[0664] 435 440 445
[0665] Glu Asn Gly Tyr Asp Ala Arg His Lys Ala Phe Leu Glu Asp Ser Phe
[0666] 450 455 460
[0667] Ser Leu Leu Ser Ser Phe Asn Lys Gln Tyr Glu Thr Glu Arg Ala Val
[0668] 465 470 475 480
[0669] Leu Ile Thr Gln Gln Arg Trp Asp Glu Tyr Ile Gly Glu Leu Ala Gly
[0670] 485 490 495
[0671] Ile Thr Gly Lys Gly Asp Lys Leu Ser Ser Gly Lys Ala Tyr Val Asp
[0672] 500 505 510
[0673] Tyr Phe Gln Glu Gly Lys Leu Leu Glu Lys Lys Pro Asp Asp Phe Ser
[0674] 515 520 525
[0675] Lys Val Val Phe Asp Pro Thr Lys Gly Glu Ile Asp Ile Ser Asn Ser
[0676] 530 535 540
[0677] Gln Thr Ser Thr Leu Leu Lys Phe Val Thr Pro Leu Leu Thr Pro Gly
[0678] 545 550 555 560
[0679] Thr Glu Ser Arg Glu Arg Thr Gln Thr Gly Lys Tyr Glu Tyr Ile Thr
[0680] 565 570 575
[0681] Lys Leu Val Val Lys Gly Lys Asp Lys Trp Val Val Asn Gly Val Lys
[0682] 580 585 590
[0683] Asp Lys Gly Ala Val Tyr Asp Tyr Thr Asn Leu Ile Gln His Ala His
[0684] 595 600 605
[0685] Ile Ser Ser Ser Val Ala Arg Gly Glu Glu Tyr Arg Glu Val Arg Leu
[0686] 610 615 620
[0687] Val Ser His Leu Gly Asn Gly Asn Asp Lys Val Phe Leu Ala Ala Gly
[0688] 625 630 635 640
[0689] Ser Ala Glu Ile His Ala Gly Glu Gly His Asp Val Val Tyr Tyr Asp
[0690] 645 650 655
[0691] Lys Thr Asp Thr Gly Leu Leu Val Ile Asp Gly Thr Lys Ala Thr Glu
[0692] 660 665 670
[0693] Gln Gly Arg Tyr Ser Val Thr Arg Glu Leu Ser Gly Ala Thr Lys Ile
[0694] 675 680 685
[0695] Leu Arg Glu Val Ile Lys Asn Gln Lys Ser Ala Val Gly Lys Arg Glu
[0696] 690 695 700
[0697] Glu Thr Leu Glu Tyr Arg Asp Tyr Glu Leu Thr Gln Ser Gly Asn Ser
[0698] 705 710 715 720
[0699] Asn Leu Lys Ala His Asp Glu Leu His Ser Val Glu Glu Ile Ile Gly
[0700] 725 730 735
[0701] Ser Asn Gln Arg Asp Glu Phe Lys Gly Ser Lys Phe Arg Asp Ile Phe

[0702] 740 745 750

[0703] His Gly Ala Asp Gly Asp Asp Leu Leu Asn Gly Asn Asp Gly Asp Asp

[0704] 755 760 765

[0705] Ile Leu Tyr Gly Asp Lys Gly Asn Asp Glu Leu Arg Gly Asp Asn Gly

[0706] 770 775 780

[0707] Asn Asp Gln Leu Tyr Gly Gly Glu Gly Asn Asp Lys Leu Leu Gly Gly

[0708] 785 790 795 800

[0709] Asn Gly Asn Asn Tyr Leu Ser Gly Gly Asp Gly Asn Asp Glu Leu Gln

[0710] 805 810 815

[0711] Val Leu Gly Asn Gly Phe Asn Val Leu Arg Ala Gly Lys Gly Asp Asp

[0712] 820 825 830

[0713] Lys Leu Tyr Gly Ser Ser Gly Ser Asp Leu Leu Asp Gly Gly Glu Gly

[0714] 835 840 845

[0715] Asn Asp Tyr Leu Glu Gly Gly Asp Gly Ser Asp Phe Tyr Val Tyr Arg

[0716] 850 855 860

[0717] Ser Thr Ser Gly Asn His Thr Ile Tyr Asp Gln Gly Lys Ser Ser Asp

[0718] 865 870 875 880

[0719] Leu Asp Lys Leu Tyr Leu Ser Asp Phe Ser Phe Asp Arg Leu Leu Val

[0720] 885 890 895

[0721] Glu Lys Val Asp Asp Asn Leu Val Leu Arg Ser Asn Glu Ser Ser His

[0722] 900 905 910

[0723] Asn Asn Arg Val Leu Thr Ile Lys Asp Trp Phe Lys Glu Gly Asn Lys

[0724] 915 920 925

[0725] Tyr Asn His Lys Ile Glu Gln Ile Val Asp Lys Asn Gly Arg Lys Leu

[0726] 930 935 940

[0727] Thr Ala Glu Asn Leu Gly Thr Tyr Phe Lys Asn Ala Pro Lys Ala Asp

[0728] 945 950 955 960

[0729] Asn Leu Leu Asn Tyr Ala Thr Lys Glu Asp Gln Asn Glu Ser Asn Leu

[0730] 965 970 975

[0731] Ser Ser Leu Lys Thr Glu Leu Ser Lys Ile Ile Thr Asn Ala Gly Asn

[0732] 980 985 990

[0733] Phe Gly Val Ala Lys Gln Gly Asn Thr Gly Ile Asn Thr Ala Ala Leu

[0734] 995 1000 1005

[0735] Asn Asn Glu Val Asn Lys Ile Ile Ser Ser Ala Asn Thr Phe Ala

[0736] 1010 1015 1020

[0737] Thr Ser Gln Leu Gly Gly Ser Gly Met Gly Thr Leu Pro Ser Thr

[0738] 1025 1030 1035

[0739] Asn Val Asn Ser Met Met Leu Gly Asn Leu Ala Arg Ala Ala

[0740] 1040 1045 1050

[0741] <210> 18

[0742] <211> 127

[0743] <212> PRT

[0744] <213> 猪胸膜肺炎放线杆菌(Actinobacillus pleuropneumoniae)

[0745] <400> 18

[0746] Ala Asp Gly Asp Asp Leu Leu Asn Gly Asn Asp Gly Asp Asp Ile Leu

[0747] 1 5 10 15

[0748] Tyr Gly Asp Lys Gly Asn Asp Glu Leu Arg Gly Asp Asn Gly Asn Asp

[0749] 20 25 30

[0750] Gln Leu Tyr Gly Gly Glu Gly Asn Asp Lys Leu Leu Gly Gly Asn Gly

[0751] 35 40 45

[0752] Asn Asn Tyr Leu Ser Gly Gly Asp Gly Asn Asp Glu Leu Gln Val Leu

[0753] 50 55 60

[0754] Gly Asn Gly Phe Asn Val Leu Arg Ala Gly Lys Gly Asp Asp Lys Leu

[0755] 65 70 75 80

[0756] Tyr Gly Ser Ser Gly Ser Asp Leu Leu Asp Gly Gly Glu Gly Asn Asp

[0757] 85 90 95

[0758] Tyr Leu Glu Gly Gly Asp Gly Ser Asp Phe Tyr Val Tyr Arg Ser Thr

[0759] 100 105 110

[0760] Ser Gly Asn His Thr Ile Tyr Asp Gln Gly Lys Ser Ser Asp Leu

[0761] 115 120 125

[0762] <210> 19

[0763] <211> 80

[0764] <212> PRT

[0765] <213> 猪胸膜肺炎放线杆菌(Actinobacillus pleuropneumoniae)

[0766] <400> 19

[0767] Gly Glu Leu Ala Gly Ile Thr Gly Lys Gly Asp Lys Leu Ser Ser Gly

[0768] 1 5 10 15

[0769] Lys Ala Tyr Val Asp Tyr Phe Gln Glu Gly Lys Leu Leu Glu Lys Lys

[0770] 20 25 30

[0771] Pro Asp Asp Phe Ser Lys Val Val Phe Asp Pro Thr Lys Gly Glu Ile

[0772] 35 40 45

[0773] Asp Ile Ser Asn Ser Gln Thr Ser Thr Leu Leu Lys Phe Val Thr Pro

[0774] 50 55 60

[0775] Leu Leu Thr Pro Gly Thr Glu Ser Arg Glu Arg Thr Gln Thr Gly Lys

[0776] 65 70 75 80

[0777] <210> 20

[0778] <211> 433

[0779] <212> PRT

[0780] <213> 人工序列

[0781] <220>

[0782] <223> 重组ApxIII毒素

[0783] <400> 20

[0784] Ala Asp Gly Asp Asp Leu Leu Asn Gly Asn Asp Gly Asp Asp Ile Leu

[0785] 1 5 10 15

[0786] Tyr Gly Asp Lys Gly Asn Asp Glu Leu Arg Gly Asp Asn Gly Asn Asp

[0787] 20 25 30

[0788] Gln Leu Tyr Gly Gly Glu Gly Asn Asp Lys Leu Leu Gly Gly Asn Gly

[0789] 35 40 45

[0790] Asn Asn Tyr Leu Ser Gly Gly Asp Gly Asn Asp Glu Leu Gln Val Leu

[0791] 50 55 60

[0792] Gly Asn Gly Phe Asn Val Leu Arg Ala Gly Lys Gly Asp Asp Lys Leu

[0793] 65 70 75 80

[0794] Tyr Gly Ser Ser Gly Ser Asp Leu Leu Asp Gly Gly Glu Gly Asn Asp

[0795] 85 90 95

[0796] Tyr Leu Glu Gly Gly Asp Gly Ser Asp Phe Tyr Val Tyr Arg Ser Thr

[0797] 100 105 110

[0798] Ser Gly Asn His Thr Ile Tyr Asp Gln Gly Lys Ser Ser Asp Leu Gly

[0799] 115 120 125

[0800] Ser Thr Ala Gly Ser Thr Ala Gly Glu Leu Ala Gly Ile Thr Gly Lys

[0801] 130 135 140

[0802] Gly Asp Lys Leu Ser Ser Gly Lys Ala Tyr Val Asp Tyr Phe Gln Glu

[0803] 145 150 155 160

[0804] Gly Lys Leu Leu Glu Lys Lys Pro Asp Asp Phe Ser Lys Val Val Phe

[0805] 165 170 175

[0806] Asp Pro Thr Lys Gly Glu Ile Asp Ile Ser Asn Ser Gln Thr Ser Thr

[0807] 180 185 190

[0808] Leu Leu Lys Phe Val Thr Pro Leu Leu Thr Pro Gly Thr Glu Ser Arg

[0809] 195 200 205

[0810] Glu Arg Thr Gln Thr Gly Lys Gly Ser Thr Ala Gly Ser Thr Ala Phe

[0811] 210 215 220

[0812] Leu Asn Lys Leu Leu Ser Thr Ala Lys Glu Arg Asn Arg Trp Glu Glu

[0813] 225 230 235 240

[0814] Pro Gly Gln Lys Leu Tyr Asn Val Glu Ala Thr Ser Tyr Ala Gly Ser

[0815] 245 250 255

[0816] Thr Ala Phe Leu Asn Lys Leu Leu Ser Thr Ala Lys Glu Arg Asn Arg

[0817] 260 265 270

[0818] Trp Glu Glu Pro Gly Gln Lys Leu Tyr Asn Val Glu Ala Thr Ser Tyr

[0819] 275 280 285

[0820] Ala Gly Ser Thr Ala Phe Leu Asn Lys Leu Leu Ser Thr Ala Lys Glu

[0821] 290 295 300

[0822] Arg Asn Arg Trp Glu Glu Pro Gly Gln Lys Leu Tyr Asn Val Glu Ala

[0823] 305 310 315 320

[0824] Thr Ser Tyr Ala Gly Ser Thr Ala Phe Leu Asn Lys Leu Leu Ser Thr

[0825] 325 330 335

[0826] Ala Lys Glu Arg Asn Arg Trp Glu Glu Pro Gly Gln Lys Leu Tyr Asn

[0827] 340 345 350

[0828] Val Glu Ala Thr Ser Tyr Ala Gly Ser Thr Ala Phe Leu Asn Lys Leu

[0829] 355 360 365

[0830] Leu Ser Thr Ala Lys Glu Arg Asn Arg Trp Glu Glu Pro Gly Gln Lys

[0831] 370 375 380

[0832] Leu Tyr Asn Val Glu Ala Thr Ser Tyr Ala Gly Ser Thr Ala Phe Leu

[0833] 385 390 395 400

[0834] Asn Lys Leu Leu Ser Thr Ala Lys Glu Arg Asn Arg Trp Glu Glu Pro

[0835] 405 410 415

[0836] Gly Gln Lys Leu Tyr Asn Val Glu Ala Thr Ser Tyr Ala Gly Ser Thr

[0837] 420 425 430

[0838] Ala

[0839] <210> 21

[0840] <211> 435

[0841] <212> PRT

[0842] <213> 人工序列

[0843] <220>

[0844] <223> 带有一个HindIII切位的重组ApxIII毒素

[0845] <400> 21

[0846] Ala Asp Gly Asp Asp Leu Leu Asn Gly Asn Asp Gly Asp Asp Ile Leu

[0847] 1 5 10 15

[0848] Tyr Gly Asp Lys Gly Asn Asp Glu Leu Arg Gly Asp Asn Gly Asn Asp

[0849] 20 25 30

[0850] Gln Leu Tyr Gly Gly Glu Gly Asn Asp Lys Leu Leu Gly Gly Asn Gly

[0851] 35 40 45

[0852] Asn Asn Tyr Leu Ser Gly Gly Asp Gly Asn Asp Glu Leu Gln Val Leu

[0853] 50 55 60

[0854] Gly Asn Gly Phe Asn Val Leu Arg Ala Gly Lys Gly Asp Asp Lys Leu

[0855] 65 70 75 80

[0856] Tyr Gly Ser Ser Gly Ser Asp Leu Leu Asp Gly Gly Glu Gly Asn Asp

[0857] 85 90 95

[0858] Tyr Leu Glu Gly Gly Asp Gly Ser Asp Phe Tyr Val Tyr Arg Ser Thr
[0859] 100 105 110
[0860] Ser Gly Asn His Thr Ile Tyr Asp Gln Gly Lys Ser Ser Asp Leu Gly
[0861] 115 120 125
[0862] Ser Thr Ala Gly Ser Thr Ala Gly Glu Leu Ala Gly Ile Thr Gly Lys
[0863] 130 135 140
[0864] Gly Asp Lys Leu Ser Ser Gly Lys Ala Tyr Val Asp Tyr Phe Gln Glu
[0865] 145 150 155 160
[0866] Gly Lys Leu Leu Glu Lys Lys Pro Asp Asp Phe Ser Lys Val Val Phe
[0867] 165 170 175
[0868] Asp Pro Thr Lys Gly Glu Ile Asp Ile Ser Asn Ser Gln Thr Ser Thr
[0869] 180 185 190
[0870] Leu Leu Lys Phe Val Thr Pro Leu Leu Thr Pro Gly Thr Glu Ser Arg
[0871] 195 200 205
[0872] Glu Arg Thr Gln Thr Gly Lys Gly Ser Thr Ala Lys Leu Gly Ser Thr
[0873] 210 215 220
[0874] Ala Phe Leu Asn Lys Leu Leu Ser Thr Ala Lys Glu Arg Asn Arg Trp
[0875] 225 230 235 240
[0876] Glu Glu Pro Gly Gln Lys Leu Tyr Asn Val Glu Ala Thr Ser Tyr Ala
[0877] 245 250 255
[0878] Gly Ser Thr Ala Phe Leu Asn Lys Leu Leu Ser Thr Ala Lys Glu Arg
[0879] 260 265 270
[0880] Asn Arg Trp Glu Glu Pro Gly Gln Lys Leu Tyr Asn Val Glu Ala Thr
[0881] 275 280 285
[0882] Ser Tyr Ala Gly Ser Thr Ala Phe Leu Asn Lys Leu Leu Ser Thr Ala
[0883] 290 295 300
[0884] Lys Glu Arg Asn Arg Trp Glu Glu Pro Gly Gln Lys Leu Tyr Asn Val
[0885] 305 310 315 320
[0886] Glu Ala Thr Ser Tyr Ala Gly Ser Thr Ala Phe Leu Asn Lys Leu Leu
[0887] 325 330 335
[0888] Ser Thr Ala Lys Glu Arg Asn Arg Trp Glu Glu Pro Gly Gln Lys Leu
[0889] 340 345 350
[0890] Tyr Asn Val Glu Ala Thr Ser Tyr Ala Gly Ser Thr Ala Phe Leu Asn
[0891] 355 360 365
[0892] Lys Leu Leu Ser Thr Ala Lys Glu Arg Asn Arg Trp Glu Glu Pro Gly
[0893] 370 375 380
[0894] Gln Lys Leu Tyr Asn Val Glu Ala Thr Ser Tyr Ala Gly Ser Thr Ala
[0895] 385 390 395 400
[0896] Phe Leu Asn Lys Leu Leu Ser Thr Ala Lys Glu Arg Asn Arg Trp Glu

[0897] 405 410 415

[0898] Glu Pro Gly Gln Lys Leu Tyr Asn Val Glu Ala Thr Ser Tyr Ala Gly

[0899] 420 425 430

[0900] Ser Thr Ala

[0901] 435

[0902] <210> 22

[0903] <211> 31

[0904] <212> PRT

[0905] <213> 猪(Sus scrofa)

[0906] <300>

[0907] <308> GenBank: ADG26759

[0908] <309> 2010-05-08

[0909] <313> (201)..(231)

[0910] <400> 22

[0911] Phe Leu Asn Lys Leu Leu Ser Thr Ala Lys Glu Arg Asn Arg Trp Glu

[0912] 1 5 10 15

[0913] Glu Pro Gly Gln Lys Leu Tyr Asn Val Glu Ala Thr Ser Tyr Ala

[0914] 20 25 30

[0915] <210> 23

[0916] <211> 296

[0917] <212> PRT

[0918] <213> 猪(Sus scrofa)

[0919] <300>

[0920] <308> GenBank: ADG26759

[0921] <309> 2010-05-08

[0922] <313> (1)..(296)

[0923] <400> 23

[0924] Thr Pro Ser Gly Cys Gly Lys Gln Asn Met Ile Gly Met Thr Pro Thr

[0925] 1 5 10 15

[0926] Val Ile Ala Val His Tyr Leu Asp Ser Thr Glu Gln Trp Glu Lys Phe

[0927] 20 25 30

[0928] Gly Leu Glu Lys Arg Gln Glu Ala Leu Glu Leu Ile Lys Lys Gly Tyr

[0929] 35 40 45

[0930] Thr Gln Gln Leu Ala Phe Arg Gln Lys Asn Ser Ala Phe Ala Ala Phe

[0931] 50 55 60

[0932] Gln Asp Arg Leu Ser Ser Thr Trp Leu Thr Ala Tyr Val Val Lys Val

[0933] 65 70 75 80

[0934] Phe Ala Met Ala Ala Asn Leu Ile Ala Ile Asp Ser Gln Val Leu Cys

[0935] 85 90 95

[0936] Gly Ala Val Lys Trp Leu Ile Leu Glu Lys Gln Lys Pro Asp Gly Val
[0937] 100 105 110
[0938] Phe Glu Glu Asn Gly Pro Val Ile His Gln Glu Met Ile Gly Gly Phe
[0939] 115 120 125
[0940] Lys Asn Thr Glu Glu Lys Asp Val Ser Leu Thr Ala Phe Val Leu Ile
[0941] 130 135 140
[0942] Ala Leu Gln Glu Ala Lys Asp Ile Cys Glu Pro Gln Val Asn Ser Leu
[0943] 145 150 155 160
[0944] Leu Arg Ser Ile Asn Lys Ala Arg Asp Phe Leu Ala Asp Tyr Tyr Leu
[0945] 165 170 175
[0946] Glu Leu Lys Arg Pro Tyr Thr Val Ala Ile Ala Gly Tyr Ala Leu Ala
[0947] 180 185 190
[0948] Leu Ser Asp Lys Leu Asp Glu Pro Phe Leu Asn Lys Leu Leu Ser Thr
[0949] 195 200 205
[0950] Ala Lys Glu Arg Asn Arg Trp Glu Glu Pro Gly Gln Lys Leu Tyr Asn
[0951] 210 215 220
[0952] Val Glu Ala Thr Ser Tyr Ala Leu Leu Ala Leu Leu Val Val Lys Asp
[0953] 225 230 235 240
[0954] Phe Asp Ser Val Pro Pro Ile Val Arg Trp Leu Asn Glu Gln Arg Tyr
[0955] 245 250 255
[0956] Tyr Gly Gly Gly Tyr Gly Ser Thr Gln Ala Thr Phe Met Val Phe Gln
[0957] 260 265 270
[0958] Ala Leu Ala Gln Tyr Gln Lys Asp Val Pro Asp His Lys Asp Leu Asn
[0959] 275 280 285
[0960] Leu Asp Val Ser Ile His Leu Pro
[0961] 290 295
[0962] <210> 24
[0963] <211> 28
[0964] <212> PRT
[0965] <213> 小鼠(Mus musculus)
[0966] <300>
[0967] <308> GenBank: ADL70201
[0968] <309> 2010-08-18
[0969] <313> (211)..(238)
[0970] <400> 24
[0971] Lys Phe Leu Asn Thr Ala Lys Asp Arg Asn Arg Trp Glu Glu Pro Asp
[0972] 1 5 10 15
[0973] Gln Gln Leu Tyr Asn Val Glu Ala Thr Ser Tyr Ala
[0974] 20 25

[0975] <210> 25

[0976] <211> 312

[0977] <212> PRT

[0978] <213> 小鼠(Mus musculus)

[0979] <300>

[0980] <308> GenBank: ADL70201

[0981] <309> 2010-08-18

[0982] <313> (1)..(312)

[0983] <400> 25

[0984] Arg Leu Lys His Leu Ile Val Thr Pro Ala Gly Cys Gly Glu Gln Asn

[0985] 1 5 10 15

[0986] Met Ile Gly Met Thr Pro Thr Val Ile Ala Val His Tyr Leu Asp Gln

[0987] 20 25 30

[0988] Thr Glu Gln Trp Glu Lys Phe Gly Ile Glu Lys Arg Gln Glu Ala Leu

[0989] 35 40 45

[0990] Glu Leu Ile Lys Lys Gly Tyr Thr Gln Gln Leu Ala Phe Lys Gln Pro

[0991] 50 55 60

[0992] Ser Ser Ala Tyr Ala Ala Phe Asn Asn Arg Pro Pro Ser Thr Trp Leu

[0993] 65 70 75 80

[0994] Thr Ala Tyr Val Val Lys Val Phe Ser Leu Ala Ala Asn Leu Ile Ala

[0995] 85 90 95

[0996] Ile Asp Ser His Val Leu Cys Gly Ala Val Lys Trp Leu Ile Leu Glu

[0997] 100 105 110

[0998] Lys Gln Lys Pro Asp Gly Val Phe Gln Glu Asp Gly Pro Val Ile His

[0999] 115 120 125

[1000] Gln Glu Met Ile Gly Gly Phe Arg Asn Ala Lys Glu Ala Asp Val Ser

[1001] 130 135 140

[1002] Leu Thr Ala Phe Val Leu Ile Ala Leu Gln Glu Ala Arg Asp Ile Cys

[1003] 145 150 155 160

[1004] Glu Gly Gln Val Asn Ser Leu Pro Gly Ser Ile Asn Lys Ala Gly Glu

[1005] 165 170 175

[1006] Tyr Ile Glu Ala Ser Tyr Met Asn Leu Gln Arg Pro Tyr Thr Val Ala

[1007] 180 185 190

[1008] Ile Ala Gly Tyr Ala Leu Ala Leu Met Asn Lys Leu Glu Glu Pro Tyr

[1009] 195 200 205

[1010] Leu Gly Lys Phe Leu Asn Thr Ala Lys Asp Arg Asn Arg Trp Glu Glu

[1011] 210 215 220

[1012] Pro Asp Gln Gln Leu Tyr Asn Val Glu Ala Thr Ser Tyr Ala Leu Leu

[1013] 225 230 235 240

[1014] Ala Leu Leu Leu Leu Lys Asp Phe Asp Ser Val Pro Pro Val Val Arg
[1015] 245 250 255
[1016] Trp Leu Asn Glu Gln Arg Tyr Tyr Gly Gly Gly Tyr Gly Ser Thr Gln
[1017] 260 265 270
[1018] Ala Thr Phe Met Val Phe Gln Ala Leu Ala Gln Tyr Gln Thr Asp Val
[1019] 275 280 285
[1020] Pro Asp His Lys Asp Leu Asn Met Asp Val Ser Phe His Leu Pro Ser
[1021] 290 295 300
[1022] Cys Ser Ser Ala Thr Thr Phe Arg
[1023] 305 310
[1024] <210> 26
[1025] <211> 4
[1026] <212> PRT
[1027] <213> 人工序列
[1028] <220>
[1029] <223> GSTA连接子的氨基酸序列
[1030] <400> 26
[1031] Gly Ser Thr Ala
[1032] 1
[1033] <210> 27
[1034] <211> 9
[1035] <212> PRT
[1036] <213> 人工序列
[1037] <220>
[1038] <223> GS连接子的氨基酸序列
[1039] <400> 27
[1040] Gly Gly Gly Gly Ser Gly Gly Gly Gly
[1041] 1 5
[1042] <210> 28
[1043] <211> 14
[1044] <212> PRT
[1045] <213> 人工序列
[1046] <220>
[1047] <223> GSGGG连接子的氨基酸序列
[1048] <400> 28
[1049] Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Ser
[1050] 1 5 10
[1051] <210> 29
[1052] <211> 6

[1053] <212> PRT
[1054] <213> 人工序列
[1055] <220>
[1056] <223> (GS)3连接子的氨基酸序列
[1057] <400> 29
[1058] Gly Ser Gly Ser Gly Ser
[1059] 1 5
[1060] <210> 30
[1061] <211> 15
[1062] <212> PRT
[1063] <213> 人工序列
[1064] <220>
[1065] <223> (GGGGS)3连接子的氨基酸序列
[1066] <400> 30
[1067] Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
[1068] 1 5 10 15
[1069] <210> 31
[1070] <211> 4
[1071] <212> PRT
[1072] <213> 人工序列
[1073] <220>
[1074] <223> GGSG连接子的氨基酸序列
[1075] <400> 31
[1076] Gly Gly Ser Gly
[1077] 1
[1078] <210> 32
[1079] <211> 8
[1080] <212> PRT
[1081] <213> 人工序列
[1082] <220>
[1083] <223> (GGSG)2连接子的氨基酸序列
[1084] <400> 32
[1085] Gly Gly Ser Gly Gly Gly Ser Gly
[1086] 1 5
[1087] <210> 33
[1088] <211> 12
[1089] <212> PRT
[1090] <213> 人工序列
[1091] <220>

[1092] <223> (GGSG)3连接子的氨基酸序列
[1093] <400> 33
[1094] Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly
[1095] 1 5 10
[1096] <210> 34
[1097] <211> 10
[1098] <212> PRT
[1099] <213> 人工序列
[1100] <220>
[1101] <223> GENLYFQSGG连接子的氨基酸序列
[1102] <400> 34
[1103] Gly Glu Asn Leu Tyr Phe Gln Ser Gly Gly
[1104] 1 5 10
[1105] <210> 35
[1106] <211> 36
[1107] <212> PRT
[1108] <213> 人工序列
[1109] <220>
[1110] <223> GAST连接子的氨基酸序列
[1111] <400> 35
[1112] Gly Gly Ser Ala Gly Gly Ser Gly Ser Gly Ser Ser Gly Gly Ser Ser
[1113] 1 5 10 15
[1114] Gly Ala Ser Gly Thr Gly Thr Ala Gly Gly Thr Gly Ser Gly Ser Gly
[1115] 20 25 30
[1116] Thr Gly Ser Gly
[1117] 35
[1118] <210> 36
[1119] <211> 36
[1120] <212> PRT
[1121] <213> 人工序列
[1122] <220>
[1123] <223> SEG连接子的氨基酸序列
[1124] <400> 36
[1125] Gly Gly Ser Gly Gly Gly Ser Glu Gly Gly Gly Ser Glu Gly Gly Gly
[1126] 1 5 10 15
[1127] Ser Glu Gly Gly Gly Ser Glu Gly Gly Gly Ser Glu Gly Gly Gly Ser
[1128] 20 25 30
[1129] Gly Gly Gly Ser
[1130] 35

[1131] <210> 37

[1132] <211> 10

[1133] <212> PRT

[1134] <213> 猪胸膜肺炎放线杆菌(Actinobacillus pleuropneumoniae)

[1135] <400> 37

[1136] Arg Lys Gly Ala Asp Ala Lys Ser Gly Lys

[1137] 1 5 10

[1138] <210> 38

[1139] <211> 1951

[1140] <212> PRT

[1141] <213> 猪胸膜肺炎放线杆菌(Actinobacillus pleuropneumoniae)

[1142] <400> 38

[1143] Met Thr Lys Leu Thr Met Gln Asp Val Thr Asn Leu Tyr Leu Tyr Lys

[1144] 1 5 10 15

[1145] Thr Lys Thr Leu Pro Lys Asp Arg Leu Asp Asp Ser Leu Ile Ser Glu

[1146] 20 25 30

[1147] Ile Gly Lys Gly Asp Asp Asp Ile Asp Arg Lys Glu Phe Met Val Gly

[1148] 35 40 45

[1149] Pro Gly Arg Phe Val Thr Ala Asp Asn Phe Ser Val Val Arg Asp Phe

[1150] 50 55 60

[1151] Phe Asn Ala Gly Lys Ser Arg Ile Ile Ala Pro Gln Val Pro Pro Ile

[1152] 65 70 75 80

[1153] Arg Ser Gln Gln Glu Lys Ile Leu Val Gly Leu Lys Pro Gly Lys Tyr

[1154] 85 90 95

[1155] Ser Lys Ala Gln Ile Leu Glu Met Leu Gly Tyr Thr Lys Gly Gly Glu

[1156] 100 105 110

[1157] Val Val Asn Gly Met Phe Ala Gly Glu Val Gln Thr Leu Gly Phe Tyr

[1158] 115 120 125

[1159] Asp Asp Gly Lys Gly Asp Leu Leu Glu Arg Ala Tyr Ile Trp Asn Thr

[1160] 130 135 140

[1161] Thr Gly Phe Lys Met Ser Asp Asn Ala Phe Phe Val Ile Glu Glu Ser

[1162] 145 150 155 160

[1163] Gly Lys Arg Tyr Ile Glu Asn Phe Gly Ile Glu Pro Leu Gly Lys Gln

[1164] 165 170 175

[1165] Glu Asp Phe Asp Phe Val Gly Gly Phe Trp Ser Asn Leu Val Asn Arg

[1166] 180 185 190

[1167] Gly Leu Glu Ser Ile Ile Asp Pro Ser Gly Ile Gly Gly Thr Val Asn

[1168] 195 200 205

[1169] Leu Asn Phe Thr Gly Glu Val Glu Thr Tyr Thr Leu Asp Glu Thr Arg

[1170] 210 215 220

[1171] Phe Lys Ala Glu Ala Ala Lys Lys Ser His Trp Ser Leu Val Asn Ala

[1172] 225 230 235 240

[1173] Ala Lys Val Tyr Gly Gly Leu Asp Gln Ile Ile Lys Lys Leu Trp Asp

[1174] 245 250 255

[1175] Ser Gly Ser Ile Lys His Leu Tyr Gln Asp Lys Asp Thr Gly Lys Leu

[1176] 260 265 270

[1177] Lys Pro Ile Ile Tyr Gly Thr Ala Gly Asn Asp Ser Lys Ile Glu Gly

[1178] 275 280 285

[1179] Thr Lys Ile Thr Arg Arg Ile Ala Gly Lys Glu Val Thr Leu Asp Ile

[1180] 290 295 300

[1181] Ala Asn Gln Lys Ile Glu Lys Gly Val Leu Glu Lys Leu Gly Leu Ser

[1182] 305 310 315 320

[1183] Val Ser Gly Ser Asp Ile Ile Lys Leu Leu Phe Gly Ala Leu Thr Pro

[1184] 325 330 335

[1185] Thr Leu Asn Arg Met Leu Leu Ser Gln Leu Ile Gln Ser Phe Ser Asp

[1186] 340 345 350

[1187] Ser Leu Ala Lys Leu Asp Asn Pro Leu Ala Pro Tyr Thr Lys Asn Gly

[1188] 355 360 365

[1189] Val Val Tyr Val Thr Gly Lys Gly Asn Asp Val Leu Lys Gly Thr Glu

[1190] 370 375 380

[1191] His Glu Asp Leu Phe Leu Gly Gly Glu Gly Asn Asp Thr Tyr Tyr Ala

[1192] 385 390 395 400

[1193] Arg Val Gly Asp Thr Ile Glu Asp Ala Asp Gly Lys Gly Lys Val Tyr

[1194] 405 410 415

[1195] Phe Val Arg Glu Lys Gly Val Pro Lys Ala Asp Pro Lys Arg Val Glu

[1196] 420 425 430

[1197] Phe Ser Glu Tyr Ile Thr Lys Glu Glu Ile Lys Glu Val Glu Lys Gly

[1198] 435 440 445

[1199] Leu Leu Thr Tyr Ala Val Leu Glu Asn Tyr Asn Trp Glu Glu Lys Thr

[1200] 450 455 460

[1201] Ala Thr Phe Ala His Ala Thr Met Leu Asn Glu Leu Phe Thr Asp Tyr

[1202] 465 470 475 480

[1203] Thr Asn Tyr Arg Tyr Glu Val Lys Gly Leu Lys Leu Pro Ala Val Lys

[1204] 485 490 495

[1205] Lys Leu Lys Ser Pro Leu Val Glu Phe Thr Ala Asp Leu Leu Thr Val

[1206] 500 505 510

[1207] Thr Pro Ile Asp Glu Asn Gly Lys Ala Leu Ser Glu Lys Ser Ile Thr

[1208] 515 520 525

[1209] Val Lys Asn Phe Lys Asn Gly Asp Leu Gly Ile Arg Leu Leu Asp Pro
[1210] 530 535 540
[1211] Asn Ser Tyr Tyr Tyr Phe Leu Glu Gly Lys Asp Thr Gly Phe Tyr Gly
[1212] 545 550 555 560
[1213] His Ala Phe Tyr Ile Glu Arg Lys Asn Gly Gly Gly Ser Lys Asn Asn
[1214] 565 570 575
[1215] Ser Ser Gly Ala Gly Asn Ser Lys Asp Trp Gly Gly Asn Gly His Gly
[1216] 580 585 590
[1217] Asn His Arg Asn Asn Ala Ser Asp Leu Asn Lys Pro Asp Gly Asn Asn
[1218] 595 600 605
[1219] Gly Asn Asn Gln Asn Asn Gly Ser Asn Gln Asp Asn Asn Ser Asp Val
[1220] 610 615 620
[1221] Asn Ala Pro Asn Asn Pro Gly Arg Asn Tyr Asp Ile Tyr Asp Pro Leu
[1222] 625 630 635 640
[1223] Ala Leu Asp Leu Asp Gly Asp Gly Leu Glu Thr Val Ser Met Asn Gly
[1224] 645 650 655
[1225] Arg Gln Gly Ala Leu Phe Asp His Glu Gly Lys Gly Ile Arg Thr Ala
[1226] 660 665 670
[1227] Thr Gly Trp Leu Ala Ala Asp Asp Gly Phe Leu Val Leu Asp Arg Asn
[1228] 675 680 685
[1229] Gln Asp Gly Ile Ile Asn Asp Ile Ser Glu Leu Phe Ser Asn Lys Asn
[1230] 690 695 700
[1231] Gln Leu Ser Asp Gly Ser Ile Ser Ala His Gly Phe Ala Ala Leu Ala
[1232] 705 710 715 720
[1233] Asp Leu Asp Thr Asn Gln Asp Gln Arg Ile Asp Gln Asn Asp Lys Leu
[1234] 725 730 735
[1235] Phe Ser Lys Leu Gln Ile Trp Arg Asp Leu Asn Gln Asn Gly Phe Ser
[1236] 740 745 750
[1237] Glu Ala Asn Glu Leu Phe Ser Leu Glu Ser Leu Asn Ile Lys Ser Leu
[1238] 755 760 765
[1239] His Thr Ala Tyr Glu Glu Arg Asn Asp Phe Leu Ala Gly Asn Asn Ile
[1240] 770 775 780
[1241] Leu Ala Gln Leu Gly Lys Tyr Glu Lys Thr Asp Gly Thr Phe Ala Gln
[1242] 785 790 795 800
[1243] Met Gly Asp Leu Asn Phe Ser Phe Asn Pro Phe Tyr Ser Arg Phe Thr
[1244] 805 810 815
[1245] Glu Ala Leu Asn Leu Thr Glu Gln Gln Arg Arg Thr Ile Asn Leu Thr
[1246] 820 825 830
[1247] Gly Thr Gly Arg Val Arg Asp Leu Arg Glu Ala Ala Ala Leu Ser Glu

[1248] 835 840 845
[1249] Glu Leu Ala Ala Leu Leu Gln Gln Tyr Thr Lys Ala Ser Asp Phe Gln
[1250] 850 855 860
[1251] Ala Gln Arg Glu Leu Leu Pro Ala Ile Leu Asp Lys Trp Ala Ala Thr
[1252] 865 870 875 880
[1253] Asp Leu Gln Tyr Gln His Tyr Asp Lys Thr Leu Leu Lys Thr Leu Glu
[1254] 885 890 895
[1255] Ser Thr Asp Ser Ser Ala Ser Val Val Arg Val Thr Pro Ser Gln Leu
[1256] 900 905 910
[1257] Ser Ser Ile Arg Asn Val Lys His Asp Pro Thr Val Met Gln Asn Phe
[1258] 915 920 925
[1259] Glu Gln Ser Lys Ala Lys Ile Ala Thr Leu Asn Ser Leu Tyr Gly Leu
[1260] 930 935 940
[1261] Asn Ile Asp Gln Leu Tyr Tyr Thr Thr Asp Lys Asp Ile Arg Tyr Ile
[1262] 945 950 955 960
[1263] Thr Asp Lys Val Asn Asn Met Tyr Gln Thr Thr Val Glu Leu Ala Tyr
[1264] 965 970 975
[1265] Arg Ser Leu Leu Leu Gln Thr Arg Leu Lys Lys Tyr Val Tyr Ser Val
[1266] 980 985 990
[1267] Asn Ala Lys Gln Phe Glu Gly Lys Trp Val Ala Asp Tyr Ser Arg Thr
[1268] 995 1000 1005
[1269] Glu Ala Leu Phe Asn Ser Thr Phe Lys Gln Ser Pro Glu Asn Ala
[1270] 1010 1015 1020
[1271] Leu Tyr Asp Leu Ser Glu Tyr Leu Ser Phe Phe Asn Asp Pro Thr
[1272] 1025 1030 1035
[1273] Glu Trp Lys Glu Gly Leu Leu Leu Leu Ser Arg Tyr Ile Asp Tyr
[1274] 1040 1045 1050
[1275] Ala Lys Ala Gln Gly Phe Tyr Glu Asn Trp Ala Thr Thr Ser Asn
[1276] 1055 1060 1065
[1277] Leu Thr Ile Ala Arg Leu Arg Glu Ala Gly Val Ile Phe Ala Glu
[1278] 1070 1075 1080
[1279] Ser Thr Asp Leu Lys Gly Asp Glu Lys Asn Asn Ile Leu Leu Gly
[1280] 1085 1090 1095
[1281] Ser Gln Lys Asp Asn Asn Leu Ser Gly Ser Ala Gly Asp Asp Leu
[1282] 1100 1105 1110
[1283] Leu Ile Gly Gly Glu Gly Asn Asp Thr Leu Lys Gly Ser Tyr Gly
[1284] 1115 1120 1125
[1285] Ala Asp Thr Tyr Leu Phe Ser Lys Gly His Gly Gln Asp Val Ile
[1286] 1130 1135 1140

[1287] Tyr Glu Tyr Ser Asp Ser Ala Asn Ser Lys Ser Asp Ile Asp Thr
[1288] 1145 1150 1155
[1289] Leu Lys Phe Thr Asp Ile Asn Tyr Ala Glu Val Lys Phe Arg Arg
[1290] 1160 1165 1170
[1291] Val Gly Asp Asp Leu Met Leu Phe Gly Tyr His Asp Thr Asp Ser
[1292] 1175 1180 1185
[1293] Val Thr Val Lys Ser Phe Tyr Asn His Glu Tyr Tyr Gln Phe Glu
[1294] 1190 1195 1200
[1295] Lys Leu Glu Phe Ala Asp Arg Ser Ile Thr Arg Asp Glu Leu Gly
[1296] 1205 1210 1215
[1297] Lys Gln Gly Met Ala Leu Phe Gly Thr Asp Gly Asp Asp Asp Ile
[1298] 1220 1225 1230
[1299] Asn Asp Trp Gly Arg Asn Ser Val Ile Asp Ala Gly Ala Gly Asn
[1300] 1235 1240 1245
[1301] Asp Thr Ile Asn Gly Ser Tyr Gly Asp Asp Thr Leu Ile Gly Gly
[1302] 1250 1255 1260
[1303] Thr Gly Asn Asp Ile Leu Lys Gly Ser Tyr Gly Ala Asp Thr Tyr
[1304] 1265 1270 1275
[1305] Leu Phe Ser Lys Gly His Gly Gln Asp Val Ile Tyr Glu Tyr Ser
[1306] 1280 1285 1290
[1307] Asp Ser Ala Asn Ser Lys Arg Asp Ile Asp Thr Leu Lys Phe Thr
[1308] 1295 1300 1305
[1309] Asp Val Asn Tyr Ala Glu Val Lys Phe Arg Arg Val Gly Asp Asp
[1310] 1310 1315 1320
[1311] Leu Met Leu Phe Gly Tyr His Asp Thr Asp Ser Val Thr Val Lys
[1312] 1325 1330 1335
[1313] Ser Phe Tyr Asp His Glu Tyr Tyr Gln Phe Glu Lys Leu Glu Phe
[1314] 1340 1345 1350
[1315] Ala Asp Arg Ser Ile Ser Arg Asp Glu Leu Ile Lys Ala Gly Leu
[1316] 1355 1360 1365
[1317] His Leu Tyr Gly Thr Asp Gly Asn Asp Glu Ile Asn Asp His Ala
[1318] 1370 1375 1380
[1319] Asp Trp Asp Ser Ile Leu Glu Gly Gly Lys Gly Asn Asp Ile Leu
[1320] 1385 1390 1395
[1321] Arg Gly Ser Tyr Gly Ala Asp Thr Tyr Ile Phe Ser Lys Gly His
[1322] 1400 1405 1410
[1323] Gly Gln Asp Val Ile Tyr Glu Tyr Ser Asp Ser Ala Asn Ser Lys
[1324] 1415 1420 1425
[1325] Arg Asp Ile Asp Thr Leu Lys Phe Thr Asp Val Asn Tyr Ala Glu

[1326] 1430 1435 1440

[1327] Val Lys Phe Arg Arg Val Asp Asp Asp Leu Met Leu Phe Gly Tyr

[1328] 1445 1450 1455

[1329] His Asp Thr Asp Ser Val Thr Val Lys Ser Phe Tyr Asp His Glu

[1330] 1460 1465 1470

[1331] Tyr Tyr Gln Phe Glu Lys Leu Glu Phe Ala Asp Arg Ser Ile Thr

[1332] 1475 1480 1485

[1333] Arg Asp Glu Leu Gly Lys Gln Gly Met Ala Leu Phe Gly Thr Asp

[1334] 1490 1495 1500

[1335] Gly Asp Asp Asp Ile Asn Asp Trp Gly Arg Asn Ser Val Ile Asp

[1336] 1505 1510 1515

[1337] Ala Gly Ala Gly Asn Asp Thr Ile Asn Gly Gly Tyr Gly Asp Asp

[1338] 1520 1525 1530

[1339] Thr Leu Ile Gly Gly Lys Gly Asn Asp Ile Leu Lys Gly Ser Tyr

[1340] 1535 1540 1545

[1341] Gly Ala Asp Thr Tyr Ile Phe Ser Lys Gly His Gly Gln Asp Ile

[1342] 1550 1555 1560

[1343] Val Tyr Glu Asp Thr Asn Asn Asp Asn Arg Ala Arg Asp Ile Asp

[1344] 1565 1570 1575

[1345] Thr Leu Lys Phe Thr Asp Val Asn Tyr Ala Glu Val Lys Phe Arg

[1346] 1580 1585 1590

[1347] Arg Val Asp Asn Asp Leu Met Leu Phe Gly Tyr His Asp Thr Asp

[1348] 1595 1600 1605

[1349] Ser Val Thr Val Lys Ser Phe Tyr Ser His Val Asp Tyr Gln Phe

[1350] 1610 1615 1620

[1351] Asp Lys Leu Glu Phe Ala Asp Arg Ser Ile Thr Arg Asp Glu Leu

[1352] 1625 1630 1635

[1353] Ile Lys Ala Gly Leu His Leu Tyr Gly Thr Asp Gly Asn Asp Asp

[1354] 1640 1645 1650

[1355] Ile Lys Asp His Ala Asp Trp Asp Ser Ile Leu Glu Gly Gly Lys

[1356] 1655 1660 1665

[1357] Gly Asn Asp Ile Leu Arg Gly Gly Tyr Gly Ala Asp Thr Tyr Ile

[1358] 1670 1675 1680

[1359] Phe Ser Lys Gly His Gly Gln Asp Ile Val Tyr Glu Asp Thr Asn

[1360] 1685 1690 1695

[1361] Asn Asp Asn Arg Ala Arg Asp Ile Asp Thr Leu Lys Phe Thr Asp

[1362] 1700 1705 1710

[1363] Val Asn Tyr Ala Glu Val Lys Phe Arg Arg Val Asp Asn Asp Leu

[1364] 1715 1720 1725

[1365] Met Leu Phe Gly Tyr His Asp Thr Asp Ser Val Thr Ile Lys Ser
[1366] 1730 1735 1740
[1367] Phe Tyr Asn His Val Asp Tyr Gln Phe Asp Lys Leu Asp Phe Ala
[1368] 1745 1750 1755
[1369] Asp Arg Ser Ile Thr Arg Asp Glu Leu Gly Lys Gln Gly Met Ala
[1370] 1760 1765 1770
[1371] Leu Phe Gly Thr Asp Gly Asp Asp Asn Ile Asn Asp Trp Gly Arg
[1372] 1775 1780 1785
[1373] Asn Ser Val Ile Asp Ala Gly Ala Gly Asn Asp Thr Val Asn Gly
[1374] 1790 1795 1800
[1375] Gly Asn Gly Asp Asp Thr Leu Ile Gly Gly Lys Gly Asn Asp Ile
[1376] 1805 1810 1815
[1377] Leu Arg Gly Gly Tyr Gly Ala Asp Thr Tyr Ile Phe Ser Lys Gly
[1378] 1820 1825 1830
[1379] His Gly Gln Asp Ile Val Tyr Glu Asp Thr Asn Asn Asp Asn Arg
[1380] 1835 1840 1845
[1381] Ala Arg Asp Ile Asp Thr Leu Lys Phe Thr Asp Ile Asn Leu Ser
[1382] 1850 1855 1860
[1383] Glu Leu Trp Phe Ser Arg Glu Asn Asn Asp Leu Ile Ile Lys Ser
[1384] 1865 1870 1875
[1385] Leu Leu Ser Glu Asp Lys Val Thr Val Gln Asn Trp Tyr Ser His
[1386] 1880 1885 1890
[1387] Gln Asp His Lys Ile Glu Asn Ile Arg Leu Ser Asn Glu Gln Thr
[1388] 1895 1900 1905
[1389] Leu Val Ser Thr Gln Val Glu Lys Met Val Glu Ser Met Ala Gly
[1390] 1910 1915 1920
[1391] Phe Ala Gln Lys His Gly Gly Glu Ile Ser Leu Ala Ser Pro Glu
[1392] 1925 1930 1935
[1393] Glu Val Lys Gln Tyr Ile Asn Ser Leu Thr Ala Ala Leu
[1394] 1940 1945 1950
[1395] <210> 39
[1396] <211> 16
[1397] <212> PRT
[1398] <213> 猪胸膜肺炎放线杆菌(Actinobacillus pleuropneumoniae)
[1399] <400> 39
[1400] Gly Gly Pro Leu Ala Tyr Ser Asn Ser Pro Asn Ser Ile Pro Asn Ala
[1401] 1 5 10 15
[1402] <210> 40
[1403] <211> 14

[1404] <212> PRT
[1405] <213> 猪胸膜肺炎放线杆菌(Actinobacillus pleuropneumoniae)
[1406] <400> 40
[1407] Gly Ala Gly Gly Pro Leu Ala Tyr Ser Asn Ser Pro Asn Ser
[1408] 1 5 10
[1409] <210> 41
[1410] <211> 20
[1411] <212> PRT
[1412] <213> 猪胸膜肺炎放线杆菌(Actinobacillus pleuropneumoniae)
[1413] <400> 41
[1414] Leu Val Gly Ala Gly Gly Pro Leu Ala Tyr Ser Asn Ser Pro Asn Ser
[1415] 1 5 10 15
[1416] Ile Pro Asn Ala
[1417] 20
[1418] <210> 42
[1419] <211> 6
[1420] <212> PRT
[1421] <213> 猪胸膜肺炎放线杆菌(Actinobacillus pleuropneumoniae)
[1422] <400> 42
[1423] Gly Ser Asn Arg Lys Asp
[1424] 1 5
[1425] <210> 43
[1426] <211> 47
[1427] <212> PRT
[1428] <213> 猪胸膜肺炎放线杆菌(Actinobacillus pleuropneumoniae)
[1429] <400> 43
[1430] Gly Ala Lys Gly Asp Asp Glu Ile Tyr Gly Asn Asp Gly His Asp Ile
[1431] 1 5 10 15
[1432] Leu Tyr Gly Asp Asp Gly Asn Asp Val Ile His Gly Gly Asp Gly Asn
[1433] 20 25 30
[1434] Asp His Leu Val Gly Gly Asn Gly Asn Asp Arg Leu Ile Gly Gly
[1435] 35 40 45
[1436] <210> 44
[1437] <211> 13
[1438] <212> PRT
[1439] <213> 猪胸膜肺炎放线杆菌(Actinobacillus pleuropneumoniae)
[1440] <400> 44
[1441] Asn Asn Phe Leu Asn Gly Gly Asp Gly Asp Asp Glu Leu
[1442] 1 5 10

[1443] <210> 45

[1444] <211> 20

[1445] <212> PRT

[1446] <213> 猪胸膜肺炎放线杆菌(Actinobacillus pleuropneumoniae)

[1447] <400> 45

[1448] Gly Ser Arg Phe Thr Asp Ile Phe His Gly Ala Lys Gly Asp Asp Glu

[1449] 1 5 10 15

[1450] Ile Tyr Gly Asn

[1451] 20

[1452] <210> 46

[1453] <211> 20

[1454] <212> PRT

[1455] <213> 猪胸膜肺炎放线杆菌(Actinobacillus pleuropneumoniae)

[1456] <400> 46

[1457] Asp Val Ile His Gly Gly Asp Gly Asn Asp His Leu Val Gly Gly Asn

[1458] 1 5 10 15

[1459] Gly Asn Asp Arg

[1460] 20

[1461] <210> 47

[1462] <211> 20

[1463] <212> PRT

[1464] <213> 猪胸膜肺炎放线杆菌(Actinobacillus pleuropneumoniae)

[1465] <400> 47

[1466] Ile Gly Gly Lys Gly Asn Asn Phe Leu Asn Gly Gly Asp Gly Asp Asp

[1467] 1 5 10 15

[1468] Glu Leu Gln Val

[1469] 20

[1470] <210> 48

[1471] <211> 14

[1472] <212> PRT

[1473] <213> 猪胸膜肺炎放线杆菌(Actinobacillus pleuropneumoniae)

[1474] <400> 48

[1475] His Gly Ala Lys Gly Asp Asp Glu Ile Tyr Gly Asn Asp Gly

[1476] 1 5 10

[1477] <210> 49

[1478] <211> 14

[1479] <212> PRT

[1480] <213> 猪胸膜肺炎放线杆菌(Actinobacillus pleuropneumoniae)

[1481] <400> 49

[1482] Gly Gly Lys Gly Asn Asn Phe Leu Asn Gly Gly Asp Gly Asp
[1483] 1 5 10
[1484] <210> 50
[1485] <211> 20
[1486] <212> PRT
[1487] <213> 猪胸膜肺炎放线杆菌(Actinobacillus pleuropneumoniae)
[1488] <400> 50
[1489] Asp Gly His Asp Ile Leu Tyr Gly Asp Asp Gly Asn Asp Val Ile His
[1490] 1 5 10 15
[1491] Gly Gly Asp Gly
[1492] 20
[1493] <210> 51
[1494] <211> 20
[1495] <212> PRT
[1496] <213> 猪胸膜肺炎放线杆菌(Actinobacillus pleuropneumoniae)
[1497] <400> 51
[1498] Arg Leu Ile Gly Gly Lys Gly Asn Asn Phe Leu Asn Gly Gly Asp Gly
[1499] 1 5 10 15
[1500] Asp Asp Glu Leu
[1501] 20
[1502] <210> 52
[1503] <211> 15
[1504] <212> PRT
[1505] <213> 猪胸膜肺炎放线杆菌(Actinobacillus pleuropneumoniae)
[1506] <400> 52
[1507] Gly Thr Gly Asn Asp Ile Ile Ser Gly Gly Lys Asp Asn Asp Ile
[1508] 1 5 10 15
[1509] <210> 53
[1510] <211> 19
[1511] <212> PRT
[1512] <213> 猪胸膜肺炎放线杆菌(Actinobacillus pleuropneumoniae)
[1513] <400> 53
[1514] His Lys Thr Gly Asp Gly Asn Asp Ser Ile Thr Asp Ser Gly Gly Gln
[1515] 1 5 10 15
[1516] Asp Lys Leu
[1517] <210> 54
[1518] <211> 20
[1519] <212> PRT
[1520] <213> 猪胸膜肺炎放线杆菌(Actinobacillus pleuropneumoniae)

[1521] <400> 54

[1522] Phe Gly Gly Ala Gly Asp Asp Val Ile Asp Gly Gly Asn Gly Asn Asn

[1523] 1 5 10 15

[1524] Phe Leu Val Gly

[1525] 20

[1526] <210> 55

[1527] <211> 20

[1528] <212> PRT

[1529] <213> 猪胸膜肺炎放线杆菌(Actinobacillus pleuropneumoniae)

[1530] <400> 55

[1531] Tyr Val His Lys Thr Gly Asp Gly Asn Asp Ser Ile Thr Asp Ser Gly

[1532] 1 5 10 15

[1533] Gly Gln Asp Lys

[1534] 20

[1535] <210> 56

[1536] <211> 14

[1537] <212> PRT

[1538] <213> 猪胸膜肺炎放线杆菌(Actinobacillus pleuropneumoniae)

[1539] <400> 56

[1540] Gly Gly Ala Gly Asp Asp Val Ile Asp Gly Gly Asn Gly Asn

[1541] 1 5 10

[1542] <210> 57

[1543] <211> 14

[1544] <212> PRT

[1545] <213> 猪胸膜肺炎放线杆菌(Actinobacillus pleuropneumoniae)

[1546] <400> 57

[1547] Gly Gly Thr Gly Asn Asp Ile Ile Ser Gly Gly Lys Asp Asn

[1548] 1 5 10

[1549] <210> 58

[1550] <211> 14

[1551] <212> PRT

[1552] <213> 猪胸膜肺炎放线杆菌(Actinobacillus pleuropneumoniae)

[1553] <400> 58

[1554] Lys Thr Gly Asp Gly Asn Asp Ser Ile Thr Asp Ser Gly Gly

[1555] 1 5 10

[1556] <210> 59

[1557] <211> 20

[1558] <212> PRT

[1559] <213> 猪胸膜肺炎放线杆菌(Actinobacillus pleuropneumoniae)

[1560] <400> 59

[1561] Ala Gly Asp Asp Val Ile Asp Gly Gly Asn Gly Asn Asn Phe Leu Val

[1562] 1 5 10 15

[1563] Gly Gly Thr Gly

[1564] 20

[1565] <210> 60

[1566] <211> 20

[1567] <212> PRT

[1568] <213> 猪胸膜肺炎放线杆菌(Actinobacillus pleuropneumoniae)

[1569] <400> 60

[1570] Asp Ile Tyr Val His Lys Thr Gly Asp Gly Asn Asp Ser Ile Thr Asp

[1571] 1 5 10 15

[1572] Ser Gly Gly Gln

[1573] 20

[1574] <210> 61

[1575] <211> 17

[1576] <212> PRT

[1577] <213> 猪胸膜肺炎放线杆菌(Actinobacillus pleuropneumoniae)

[1578] <400> 61

[1579] Leu Thr Pro Gly Glu Glu Asn Arg Glu Arg Ile Gln Glu Gly Lys Asn

[1580] 1 5 10 15

[1581] Ser

[1582] <210> 62

[1583] <211> 12

[1584] <212> PRT

[1585] <213> 猪胸膜肺炎放线杆菌(Actinobacillus pleuropneumoniae)

[1586] <400> 62

[1587] Trp Thr Val Thr Asp Gly Asp Ala Ser Ser Ser Val

[1588] 1 5 10

[1589] <210> 63

[1590] <211> 20

[1591] <212> PRT

[1592] <213> 猪胸膜肺炎放线杆菌(Actinobacillus pleuropneumoniae)

[1593] <400> 63

[1594] Thr Pro Gly Glu Glu Asn Arg Glu Arg Ile Gln Glu Gly Lys Asn Ser

[1595] 1 5 10 15

[1596] Tyr Ile Thr Lys

[1597] 20

[1598] <210> 64

[1599] <211> 14

[1600] <212> PRT

[1601] <213> 猪胸膜肺炎放线杆菌(Actinobacillus pleuropneumoniae)

[1602] <400> 64

[1603] Leu Phe Arg Thr Pro Leu Leu Thr Pro Gly Glu Glu Asn Arg

[1604] 1 5 10

[1605] <210> 65

[1606] <211> 12

[1607] <212> PRT

[1608] <213> 猪胸膜肺炎放线杆菌(Actinobacillus pleuropneumoniae)

[1609] <400> 65

[1610] Gln Gly Tyr Asp Ser Gly Gln Gly Asn Gly Val Gln

[1611] 1 5 10

[1612] <210> 66

[1613] <211> 60

[1614] <212> PRT

[1615] <213> 猪胸膜肺炎放线杆菌(Actinobacillus pleuropneumoniae)

[1616] <400> 66

[1617] Val Ile Asp Ala Gly Ala Gly Asn Asp Thr Val Asn Gly Gly Asn Gly

[1618] 1 5 10 15

[1619] Asp Asp Thr Leu Ile Gly Gly Lys Gly Asn Asp Ile Leu Arg Gly Gly

[1620] 20 25 30

[1621] Tyr Gly Ala Asp Thr Tyr Ile Phe Ser Lys Gly His Gly Gln Asp Ile

[1622] 35 40 45

[1623] Val Tyr Glu Asp Thr Asn Asn Asp Asn Arg Ala Arg

[1624] 50 55 60

[1625] <210> 67

[1626] <211> 14

[1627] <212> PRT

[1628] <213> 猪胸膜肺炎放线杆菌(Actinobacillus pleuropneumoniae)

[1629] <400> 67

[1630] Asn Arg Glu Glu Lys Ile Glu Tyr Arg Arg Glu Asp Asp Arg

[1631] 1 5 10

[1632] <210> 68

[1633] <211> 20

[1634] <212> PRT

[1635] <213> 猪胸膜肺炎放线杆菌(Actinobacillus pleuropneumoniae)

[1636] <400> 68

[1637] Pro Thr Asn Val Gly Asn Arg Glu Glu Lys Ile Glu Tyr Arg Arg Glu

[1638] 1 5 10 15
[1639] Asp Asp Arg Phe
[1640] 20
[1641] <210> 69
[1642] <211> 62
[1643] <212> PRT
[1644] <213> 猪胸膜肺炎放线杆菌(Actinobacillus pleuropneumoniae)
[1645] <400> 69
[1646] Gly Ala Asp Gly Asp Asp Leu Leu Asn Gly Asn Asp Gly Asp Asp Ile
[1647] 1 5 10 15
[1648] Leu Tyr Gly Asp Lys Gly Asn Asp Glu Leu Arg Gly Asp Asn Gly Asn
[1649] 20 25 30
[1650] Asp Gln Leu Tyr Gly Gly Glu Gly Asn Asp Lys Leu Leu Gly Gly Asn
[1651] 35 40 45
[1652] Gly Asn Asn Tyr Leu Ser Gly Gly Asp Gly Asn Asp Glu Leu
[1653] 50 55 60
[1654] <210> 70
[1655] <211> 33
[1656] <212> PRT
[1657] <213> 猪胸膜肺炎放线杆菌(Actinobacillus pleuropneumoniae)
[1658] <400> 70
[1659] Ala Gly Lys Gly Asp Asp Lys Leu Tyr Gly Ser Ser Gly Ser Asp Leu
[1660] 1 5 10 15
[1661] Leu Asp Gly Gly Glu Gly Asn Asp Tyr Leu Glu Gly Gly Asp Gly Ser
[1662] 20 25 30
[1663] Asp
[1664] <210> 71
[1665] <211> 16
[1666] <212> PRT
[1667] <213> 猪胸膜肺炎放线杆菌(Actinobacillus pleuropneumoniae)
[1668] <400> 71
[1669] Ser Thr Ser Gly Asn His Thr Ile Tyr Asp Gln Gly Lys Ser Ser Asp
[1670] 1 5 10 15
[1671] <210> 72
[1672] <211> 20
[1673] <212> PRT
[1674] <213> 猪胸膜肺炎放线杆菌(Actinobacillus pleuropneumoniae)
[1675] <400> 72
[1676] Gly Asp Lys Gly Asn Asp Glu Leu Arg Gly Asp Asn Gly Asn Asp Gln

[1677] 1 5 10 15

[1678] Leu Tyr Gly Gly

[1679] 20

[1680] <210> 73

[1681] <211> 20

[1682] <212> PRT

[1683] <213> 猪胸膜肺炎放线杆菌(Actinobacillus pleuropneumoniae)

[1684] <400> 73

[1685] Leu Leu Gly Gly Asn Gly Asn Asn Tyr Leu Ser Gly Gly Asp Gly Asn

[1686] 1 5 10 15

[1687] Asp Glu Leu Gln

[1688] 20

[1689] <210> 74

[1690] <211> 14

[1691] <212> PRT

[1692] <213> 猪胸膜肺炎放线杆菌(Actinobacillus pleuropneumoniae)

[1693] <400> 74

[1694] Gly Asp Lys Gly Asn Asp Glu Leu Arg Gly Asp Asn Gly Asn

[1695] 1 5 10

[1696] <210> 75

[1697] <211> 14

[1698] <212> PRT

[1699] <213> 猪胸膜肺炎放线杆菌(Actinobacillus pleuropneumoniae)

[1700] <400> 75

[1701] Gly Gly Asn Gly Asn Asn Tyr Leu Ser Gly Gly Asp Gly Asn

[1702] 1 5 10

[1703] <210> 76

[1704] <211> 20

[1705] <212> PRT

[1706] <213> 猪胸膜肺炎放线杆菌(Actinobacillus pleuropneumoniae)

[1707] <400> 76

[1708] Asp Gly Asp Asp Ile Leu Tyr Gly Asp Lys Gly Asn Asp Glu Leu Arg

[1709] 1 5 10 15

[1710] Gly Asp Asn Gly

[1711] 20

[1712] <210> 77

[1713] <211> 20

[1714] <212> PRT

[1715] <213> 猪胸膜肺炎放线杆菌(Actinobacillus pleuropneumoniae)

[1716] <400> 77

[1717] Leu Leu Gly Gly Asn Gly Asn Asn Tyr Leu Ser Gly Gly Asp Gly Asn

[1718] 1 5 10 15

[1719] Asp Glu Leu Gln

[1720] 20

[1721] <210> 78

[1722] <211> 20

[1723] <212> PRT

[1724] <213> 猪胸膜肺炎放线杆菌(Actinobacillus pleuropneumoniae)

[1725] <400> 78

[1726] Asn Gly Phe Asn Val Leu Arg Ala Gly Lys Gly Asp Asp Lys Leu Tyr

[1727] 1 5 10 15

[1728] Gly Ser Ser Gly

[1729] 20

[1730] <210> 79

[1731] <211> 14

[1732] <212> PRT

[1733] <213> 猪胸膜肺炎放线杆菌(Actinobacillus pleuropneumoniae)

[1734] <400> 79

[1735] Gly Ile Thr Gly Lys Gly Asp Lys Leu Ser Ser Gly Lys Ala

[1736] 1 5 10

[1737] <210> 80

[1738] <211> 9

[1739] <212> PRT

[1740] <213> 猪胸膜肺炎放线杆菌(Actinobacillus pleuropneumoniae)

[1741] <400> 80

[1742] Leu Leu Glu Lys Lys Pro Asp Asp Phe

[1743] 1 5

[1744] <210> 81

[1745] <211> 15

[1746] <212> PRT

[1747] <213> 猪胸膜肺炎放线杆菌(Actinobacillus pleuropneumoniae)

[1748] <400> 81

[1749] Phe Asp Pro Thr Lys Gly Glu Ile Asp Ile Ser Asn Ser Gln Thr

[1750] 1 5 10 15

[1751] <210> 82

[1752] <211> 20

[1753] <212> PRT

[1754] <213> 猪胸膜肺炎放线杆菌(Actinobacillus pleuropneumoniae)

[1755] <400> 82

[1756] Gly Ile Thr Gly Lys Gly Asp Lys Leu Ser Ser Gly Lys Ala Tyr Val

[1757] 1 5 10 15

[1758] Asp Tyr Phe Gln

[1759] 20

[1760] <210> 83

[1761] <211> 20

[1762] <212> PRT

[1763] <213> 猪胸膜肺炎放线杆菌(Actinobacillus pleuropneumoniae)

[1764] <400> 83

[1765] Val Phe Asp Pro Thr Lys Gly Glu Ile Asp Ile Ser Asn Ser Gln Thr

[1766] 1 5 10 15

[1767] Ser Thr Leu Leu

[1768] 20

[1769] <210> 84

[1770] <211> 14

[1771] <212> PRT

[1772] <213> 猪胸膜肺炎放线杆菌(Actinobacillus pleuropneumoniae)

[1773] <400> 84

[1774] Lys Gly Asp Lys Leu Ser Ser Gly Lys Ala Tyr Val Asp Tyr

[1775] 1 5 10

[1776] <210> 85

[1777] <211> 14

[1778] <212> PRT

[1779] <213> 猪胸膜肺炎放线杆菌(Actinobacillus pleuropneumoniae)

[1780] <400> 85

[1781] Glu Lys Lys Pro Asp Asp Phe Ser Lys Val Val Phe Asp Pro

[1782] 1 5 10

[1783] <210> 86

[1784] <211> 14

[1785] <212> PRT

[1786] <213> 猪胸膜肺炎放线杆菌(Actinobacillus pleuropneumoniae)

[1787] <400> 86

[1788] Phe Val Thr Pro Leu Leu Thr Pro Gly Thr Glu Ser Arg Glu

[1789] 1 5 10

[1790] <210> 87

[1791] <211> 20

[1792] <212> PRT

[1793] <213> 猪胸膜肺炎放线杆菌(Actinobacillus pleuropneumoniae)

[1794] <400> 87

[1795] Glu Leu Ala Gly Ile Thr Gly Lys Gly Asp Lys Leu Ser Ser Gly Lys

[1796] 1 5 10 15

[1797] Ala Tyr Val Asp

[1798] 20

[1799] <210> 88

[1800] <211> 20

[1801] <212> PRT

[1802] <213> 猪胸膜肺炎放线杆菌(Actinobacillus pleuropneumoniae)

[1803] <400> 88

[1804] Thr Leu Leu Lys Phe Val Thr Pro Leu Leu Thr Pro Gly Thr Glu Ser

[1805] 1 5 10 15

[1806] Arg Glu Arg Thr

[1807] 20

[1808] <210> 89

[1809] <211> 84

[1810] <212> PRT

[1811] <213> 猪胸膜肺炎放线杆菌(Actinobacillus pleuropneumoniae)

[1812] <400> 89

[1813] Glu Gly Lys Asp Thr Gly Phe Tyr Gly His Ala Phe Tyr Ile Glu Arg

[1814] 1 5 10 15

[1815] Lys Asn Gly Gly Gly Ser Lys Asn Asn Ser Ser Gly Ala Gly Asn Ser

[1816] 20 25 30

[1817] Lys Asp Trp Gly Gly Asn Gly His Gly Asn His Arg Asn Asn Ala Ser

[1818] 35 40 45

[1819] Asp Leu Asn Lys Pro Asp Gly Asn Asn Gly Asn Asn Gln Asn Asn Gly

[1820] 50 55 60

[1821] Ser Asn Gln Asp Asn Asn Ser Asp Val Asn Ala Pro Asn Asn Pro Gly

[1822] 65 70 75 80

[1823] Arg Asn Tyr Asp

[1824] <210> 90

[1825] <211> 66

[1826] <212> PRT

[1827] <213> 猪胸膜肺炎放线杆菌(Actinobacillus pleuropneumoniae)

[1828] <400> 90

[1829] Val Ile Asp Ala Gly Ala Gly Asn Asp Thr Ile Asn Gly Gly Tyr Gly

[1830] 1 5 10 15

[1831] Asp Asp Thr Leu Ile Gly Gly Lys Gly Asn Asp Ile Leu Lys Gly Ser

[1832] 20 25 30

[1833] Tyr Gly Ala Asp Thr Tyr Ile Phe Ser Lys Gly His Gly Gln Asp Ile
[1834] 35 40 45
[1835] Val Tyr Glu Asp Thr Asn Asn Asp Asn Arg Ala Arg Asp Ile Asp Thr
[1836] 50 55 60
[1837] Leu Lys
[1838] 65
[1839] <210> 91
[1840] <211> 440
[1841] <212> PRT
[1842] <213> 人工序列
[1843] <220>
[1844] <223> 重组ApxIV毒素
[1845] <400> 91
[1846] Val Ile Asp Ala Gly Ala Gly Asn Asp Thr Val Asn Gly Gly Asn Gly
[1847] 1 5 10 15
[1848] Asp Asp Thr Leu Ile Gly Gly Lys Gly Asn Asp Ile Leu Arg Gly Gly
[1849] 20 25 30
[1850] Tyr Gly Ala Asp Thr Tyr Ile Phe Ser Lys Gly His Gly Gln Asp Ile
[1851] 35 40 45
[1852] Val Tyr Glu Asp Thr Asn Asn Asp Asn Arg Ala Arg Gly Ser Thr Ala
[1853] 50 55 60
[1854] Glu Gly Lys Asp Thr Gly Phe Tyr Gly His Ala Phe Tyr Ile Glu Arg
[1855] 65 70 75 80
[1856] Lys Asn Gly Gly Gly Ser Lys Asn Asn Ser Ser Gly Ala Gly Asn Ser
[1857] 85 90 95
[1858] Lys Asp Trp Gly Gly Asn Gly His Gly Asn His Arg Asn Asn Ala Ser
[1859] 100 105 110
[1860] Asp Leu Asn Lys Pro Asp Gly Asn Asn Gly Asn Asn Gln Asn Asn Gly
[1861] 115 120 125
[1862] Ser Asn Gln Asp Asn Asn Ser Asp Val Asn Ala Pro Asn Asn Pro Gly
[1863] 130 135 140
[1864] Arg Asn Tyr Asp Gly Ser Thr Ala Gly Ser Thr Ala Val Ile Asp Ala
[1865] 145 150 155 160
[1866] Gly Ala Gly Asn Asp Thr Ile Asn Gly Gly Tyr Gly Asp Asp Thr Leu
[1867] 165 170 175
[1868] Ile Gly Gly Lys Gly Asn Asp Ile Leu Lys Gly Ser Tyr Gly Ala Asp
[1869] 180 185 190
[1870] Thr Tyr Ile Phe Ser Lys Gly His Gly Gln Asp Ile Val Tyr Glu Asp
[1871] 195 200 205

[1872] Thr Asn Asn Asp Asn Arg Ala Arg Asp Ile Asp Thr Leu Lys Gly Ser
[1873] 210 215 220
[1874] Thr Ala Gly Ser Thr Ala Phe Leu Asn Lys Leu Leu Ser Thr Ala Lys
[1875] 225 230 235 240
[1876] Glu Arg Asn Arg Trp Glu Glu Pro Gly Gln Lys Leu Tyr Asn Val Glu
[1877] 245 250 255
[1878] Ala Thr Ser Tyr Ala Gly Ser Thr Ala Phe Leu Asn Lys Leu Leu Ser
[1879] 260 265 270
[1880] Thr Ala Lys Glu Arg Asn Arg Trp Glu Glu Pro Gly Gln Lys Leu Tyr
[1881] 275 280 285
[1882] Asn Val Glu Ala Thr Ser Tyr Ala Gly Ser Thr Ala Phe Leu Asn Lys
[1883] 290 295 300
[1884] Leu Leu Ser Thr Ala Lys Glu Arg Asn Arg Trp Glu Glu Pro Gly Gln
[1885] 305 310 315 320
[1886] Lys Leu Tyr Asn Val Glu Ala Thr Ser Tyr Ala Gly Ser Thr Ala Phe
[1887] 325 330 335
[1888] Leu Asn Lys Leu Leu Ser Thr Ala Lys Glu Arg Asn Arg Trp Glu Glu
[1889] 340 345 350
[1890] Pro Gly Gln Lys Leu Tyr Asn Val Glu Ala Thr Ser Tyr Ala Gly Ser
[1891] 355 360 365
[1892] Thr Ala Phe Leu Asn Lys Leu Leu Ser Thr Ala Lys Glu Arg Asn Arg
[1893] 370 375 380
[1894] Trp Glu Glu Pro Gly Gln Lys Leu Tyr Asn Val Glu Ala Thr Ser Tyr
[1895] 385 390 395 400
[1896] Ala Gly Ser Thr Ala Phe Leu Asn Lys Leu Leu Ser Thr Ala Lys Glu
[1897] 405 410 415
[1898] Arg Asn Arg Trp Glu Glu Pro Gly Gln Lys Leu Tyr Asn Val Glu Ala
[1899] 420 425 430
[1900] Thr Ser Tyr Ala Gly Ser Thr Ala
[1901] 435 440
[1902] <210> 92
[1903] <211> 442
[1904] <212> PRT
[1905] <213> 人工序列
[1906] <220>
[1907] <223> 带有一个HindIII切位的重组ApxIV毒素
[1908] <400> 92
[1909] Val Ile Asp Ala Gly Ala Gly Asn Asp Thr Val Asn Gly Gly Asn Gly
[1910] 1 5 10 15

[1911] Asp Asp Thr Leu Ile Gly Gly Lys Gly Asn Asp Ile Leu Arg Gly Gly
[1912] 20 25 30
[1913] Tyr Gly Ala Asp Thr Tyr Ile Phe Ser Lys Gly His Gly Gln Asp Ile
[1914] 35 40 45
[1915] Val Tyr Glu Asp Thr Asn Asn Asp Asn Arg Ala Arg Gly Ser Thr Ala
[1916] 50 55 60
[1917] Glu Gly Lys Asp Thr Gly Phe Tyr Gly His Ala Phe Tyr Ile Glu Arg
[1918] 65 70 75 80
[1919] Lys Asn Gly Gly Gly Ser Lys Asn Asn Ser Ser Gly Ala Gly Asn Ser
[1920] 85 90 95
[1921] Lys Asp Trp Gly Gly Asn Gly His Gly Asn His Arg Asn Asn Ala Ser
[1922] 100 105 110
[1923] Asp Leu Asn Lys Pro Asp Gly Asn Asn Gly Asn Asn Gln Asn Asn Gly
[1924] 115 120 125
[1925] Ser Asn Gln Asp Asn Asn Ser Asp Val Asn Ala Pro Asn Asn Pro Gly
[1926] 130 135 140
[1927] Arg Asn Tyr Asp Gly Ser Thr Ala Gly Ser Thr Ala Val Ile Asp Ala
[1928] 145 150 155 160
[1929] Gly Ala Gly Asn Asp Thr Ile Asn Gly Gly Tyr Gly Asp Asp Thr Leu
[1930] 165 170 175
[1931] Ile Gly Gly Lys Gly Asn Asp Ile Leu Lys Gly Ser Tyr Gly Ala Asp
[1932] 180 185 190
[1933] Thr Tyr Ile Phe Ser Lys Gly His Gly Gln Asp Ile Val Tyr Glu Asp
[1934] 195 200 205
[1935] Thr Asn Asn Asp Asn Arg Ala Arg Asp Ile Asp Thr Leu Lys Gly Ser
[1936] 210 215 220
[1937] Thr Ala Lys Leu Gly Ser Thr Ala Phe Leu Asn Lys Leu Leu Ser Thr
[1938] 225 230 235 240
[1939] Ala Lys Glu Arg Asn Arg Trp Glu Glu Pro Gly Gln Lys Leu Tyr Asn
[1940] 245 250 255
[1941] Val Glu Ala Thr Ser Tyr Ala Gly Ser Thr Ala Phe Leu Asn Lys Leu
[1942] 260 265 270
[1943] Leu Ser Thr Ala Lys Glu Arg Asn Arg Trp Glu Glu Pro Gly Gln Lys
[1944] 275 280 285
[1945] Leu Tyr Asn Val Glu Ala Thr Ser Tyr Ala Gly Ser Thr Ala Phe Leu
[1946] 290 295 300
[1947] Asn Lys Leu Leu Ser Thr Ala Lys Glu Arg Asn Arg Trp Glu Glu Pro
[1948] 305 310 315 320
[1949] Gly Gln Lys Leu Tyr Asn Val Glu Ala Thr Ser Tyr Ala Gly Ser Thr

[1950] 325 330 335
[1951] Ala Phe Leu Asn Lys Leu Leu Ser Thr Ala Lys Glu Arg Asn Arg Trp
[1952] 340 345 350
[1953] Glu Glu Pro Gly Gln Lys Leu Tyr Asn Val Glu Ala Thr Ser Tyr Ala
[1954] 355 360 365
[1955] Gly Ser Thr Ala Phe Leu Asn Lys Leu Leu Ser Thr Ala Lys Glu Arg
[1956] 370 375 380
[1957] Asn Arg Trp Glu Glu Pro Gly Gln Lys Leu Tyr Asn Val Glu Ala Thr
[1958] 385 390 395 400
[1959] Ser Tyr Ala Gly Ser Thr Ala Phe Leu Asn Lys Leu Leu Ser Thr Ala
[1960] 405 410 415
[1961] Lys Glu Arg Asn Arg Trp Glu Glu Pro Gly Gln Lys Leu Tyr Asn Val
[1962] 420 425 430
[1963] Glu Ala Thr Ser Tyr Ala Gly Ser Thr Ala
[1964] 435 440
[1965] <210> 93
[1966] <211> 30
[1967] <212> PRT
[1968] <213> 猪胸膜肺炎放线杆菌(Actinobacillus pleuropneumoniae)
[1969] <400> 93
[1970] Val Ile Asp Ala Gly Ala Gly Asn Asp Thr Val Asn Gly Gly Asn Gly
[1971] 1 5 10 15
[1972] Asp Asp Thr Leu Ile Gly Gly Lys Gly Asn Asp Ile Leu Arg
[1973] 20 25 30
[1974] <210> 94
[1975] <211> 4
[1976] <212> PRT
[1977] <213> 猪胸膜肺炎放线杆菌(Actinobacillus pleuropneumoniae)
[1978] <400> 94
[1979] Gly Tyr Gly Ala
[1980] 1
[1981] <210> 95
[1982] <211> 20
[1983] <212> PRT
[1984] <213> 猪胸膜肺炎放线杆菌(Actinobacillus pleuropneumoniae)
[1985] <400> 95
[1986] Ala Gly Ala Gly Asn Asp Thr Val Asn Gly Gly Asn Gly Asp Asp Thr
[1987] 1 5 10 15
[1988] Leu Ile Gly Gly

[1989] 20

[1990] <210> 96

[1991] <211> 20

[1992] <212> PRT

[1993] <213> 猪胸膜肺炎放线杆菌(Actinobacillus pleuropneumoniae)

[1994] <400> 96

[1995] Ser Lys Gly His Gly Gln Asp Ile Val Tyr Glu Asp Thr Asn Asn Asp

[1996] 1 5 10 15

[1997] Asn Arg Ala Arg

[1998] 20

[1999] <210> 97

[2000] <211> 14

[2001] <212> PRT

[2002] <213> 猪胸膜肺炎放线杆菌(Actinobacillus pleuropneumoniae)

[2003] <400> 97

[2004] Asp Ala Gly Ala Gly Asn Asp Thr Val Asn Gly Gly Asn Gly

[2005] 1 5 10

[2006] <210> 98

[2007] <211> 14

[2008] <212> PRT

[2009] <213> 猪胸膜肺炎放线杆菌(Actinobacillus pleuropneumoniae)

[2010] <400> 98

[2011] Asp Ile Val Tyr Glu Asp Thr Asn Asn Asp Asn Arg Ala Arg

[2012] 1 5 10

[2013] <210> 99

[2014] <211> 20

[2015] <212> PRT

[2016] <213> 猪胸膜肺炎放线杆菌(Actinobacillus pleuropneumoniae)

[2017] <400> 99

[2018] Ser Lys Gly His Gly Gln Asp Ile Val Tyr Glu Asp Thr Asn Asn Asp

[2019] 1 5 10 15

[2020] Asn Arg Ala Arg

[2021] 20

[2022] <210> 100

[2023] <211> 20

[2024] <212> PRT

[2025] <213> 猪胸膜肺炎放线杆菌(Actinobacillus pleuropneumoniae)

[2026] <400> 100

[2027] Lys Asn Gly Gly Gly Ser Lys Asn Asn Ser Ser Gly Ala Gly Asn Ser

[2028] 1 5 10 15

[2029] Lys Asp Trp Gly

[2030] 20

[2031] <210> 101

[2032] <211> 20

[2033] <212> PRT

[2034] <213> 猪胸膜肺炎放线杆菌(Actinobacillus pleuropneumoniae)

[2035] <400> 101

[2036] His Arg Asn Asn Ala Ser Asp Leu Asn Lys Pro Asp Gly Asn Asn Gly

[2037] 1 5 10 15

[2038] Asn Asn Gln Asn

[2039] 20

[2040] <210> 102

[2041] <211> 20

[2042] <212> PRT

[2043] <213> 猪胸膜肺炎放线杆菌(Actinobacillus pleuropneumoniae)

[2044] <400> 102

[2045] His Arg Asn Asn Ala Ser Asp Leu Asn Lys Pro Asp Gly Asn Asn Gly

[2046] 1 5 10 15

[2047] Asn Asn Gln Asn

[2048] 20

[2049] <210> 103

[2050] <211> 14

[2051] <212> PRT

[2052] <213> 猪胸膜肺炎放线杆菌(Actinobacillus pleuropneumoniae)

[2053] <400> 103

[2054] Glu Arg Lys Asn Gly Gly Gly Ser Lys Asn Asn Ser Ser Gly

[2055] 1 5 10

[2056] <210> 104

[2057] <211> 14

[2058] <212> PRT

[2059] <213> 猪胸膜肺炎放线杆菌(Actinobacillus pleuropneumoniae)

[2060] <400> 104

[2061] Gly Asn Ser Lys Asp Trp Gly Gly Asn Gly His Gly Asn His

[2062] 1 5 10

[2063] <210> 105

[2064] <211> 14

[2065] <212> PRT

[2066] <213> 猪胸膜肺炎放线杆菌(Actinobacillus pleuropneumoniae)

[2067] <400> 105

[2068] Lys Pro Asp Gly Asn Asn Gly Asn Asn Gln Asn Asn Gly Ser

[2069] 1 5 10

[2070] <210> 106

[2071] <211> 14

[2072] <212> PRT

[2073] <213> 猪胸膜肺炎放线杆菌(Actinobacillus pleuropneumoniae)

[2074] <400> 106

[2075] Asp Asn Asn Ser Asp Val Asn Ala Pro Asn Asn Pro Gly Arg

[2076] 1 5 10

[2077] <210> 107

[2078] <211> 20

[2079] <212> PRT

[2080] <213> 猪胸膜肺炎放线杆菌(Actinobacillus pleuropneumoniae)

[2081] <400> 107

[2082] Asn Gly Gly Gly Ser Lys Asn Asn Ser Ser Gly Ala Gly Asn Ser Lys

[2083] 1 5 10 15

[2084] Asp Trp Gly Gly

[2085] 20

[2086] <210> 108

[2087] <211> 20

[2088] <212> PRT

[2089] <213> 猪胸膜肺炎放线杆菌(Actinobacillus pleuropneumoniae)

[2090] <400> 108

[2091] Asn Gln Asn Asn Gly Ser Asn Gln Asp Asn Asn Ser Asp Val Asn Ala

[2092] 1 5 10 15

[2093] Pro Asn Asn Pro

[2094] 20

[2095] <210> 109

[2096] <211> 30

[2097] <212> PRT

[2098] <213> 猪胸膜肺炎放线杆菌(Actinobacillus pleuropneumoniae)

[2099] <400> 109

[2100] Val Ile Asp Ala Gly Ala Gly Asn Asp Thr Ile Asn Gly Gly Tyr Gly

[2101] 1 5 10 15

[2102] Asp Asp Thr Leu Ile Gly Gly Lys Gly Asn Asp Ile Leu Lys

[2103] 20 25 30

[2104] <210> 110

[2105] <211> 4

[2106] <212> PRT
[2107] <213> 猪胸膜肺炎放线杆菌(Actinobacillus pleuropneumoniae)
[2108] <400> 110
[2109] Ser Tyr Gly Ala
[2110] 1
[2111] <210> 111
[2112] <211> 19
[2113] <212> PRT
[2114] <213> 猪胸膜肺炎放线杆菌(Actinobacillus pleuropneumoniae)
[2115] <400> 111
[2116] Gly His Gly Gln Asp Ile Val Tyr Glu Asp Thr Asn Asn Asp Asn Arg
[2117] 1 5 10 15
[2118] Ala Arg Asp
[2119] <210> 112
[2120] <211> 20
[2121] <212> PRT
[2122] <213> 猪胸膜肺炎放线杆菌(Actinobacillus pleuropneumoniae)
[2123] <400> 112
[2124] Asp Ala Gly Ala Gly Asn Asp Thr Ile Asn Gly Gly Tyr Gly Asp Asp
[2125] 1 5 10 15
[2126] Thr Leu Ile Gly
[2127] 20
[2128] <210> 113
[2129] <211> 20
[2130] <212> PRT
[2131] <213> 猪胸膜肺炎放线杆菌(Actinobacillus pleuropneumoniae)
[2132] <400> 113
[2133] Ser Lys Gly His Gly Gln Asp Ile Val Tyr Glu Asp Thr Asn Asn Asp
[2134] 1 5 10 15
[2135] Asn Arg Ala Arg
[2136] 20
[2137] <210> 114
[2138] <211> 14
[2139] <212> PRT
[2140] <213> 猪胸膜肺炎放线杆菌(Actinobacillus pleuropneumoniae)
[2141] <400> 114
[2142] Asp Ala Gly Ala Gly Asn Asp Thr Ile Asn Gly Gly Tyr Gly
[2143] 1 5 10
[2144] <210> 115

[2145] <211> 14

[2146] <212> PRT

[2147] <213> 猪胸膜肺炎放线杆菌(Actinobacillus pleuropneumoniae)

[2148] <400> 115

[2149] Asp Ile Val Tyr Glu Asp Thr Asn Asn Asp Asn Arg Ala Arg

[2150] 1 5 10

[2151] <210> 116

[2152] <211> 20

[2153] <212> PRT

[2154] <213> 猪胸膜肺炎放线杆菌(Actinobacillus pleuropneumoniae)

[2155] <400> 116

[2156] Asn Gly Gly Tyr Gly Asp Asp Thr Leu Ile Gly Gly Lys Gly Asn Asp

[2157] 1 5 10 15

[2158] Ile Leu Lys Gly

[2159] 20

[2160] <210> 117

[2161] <211> 20

[2162] <212> PRT

[2163] <213> 猪胸膜肺炎放线杆菌(Actinobacillus pleuropneumoniae)

[2164] <400> 117

[2165] Ser Lys Gly His Gly Gln Asp Ile Val Tyr Glu Asp Thr Asn Asn Asp

[2166] 1 5 10 15

[2167] Asn Arg Ala Arg

[2168] 20

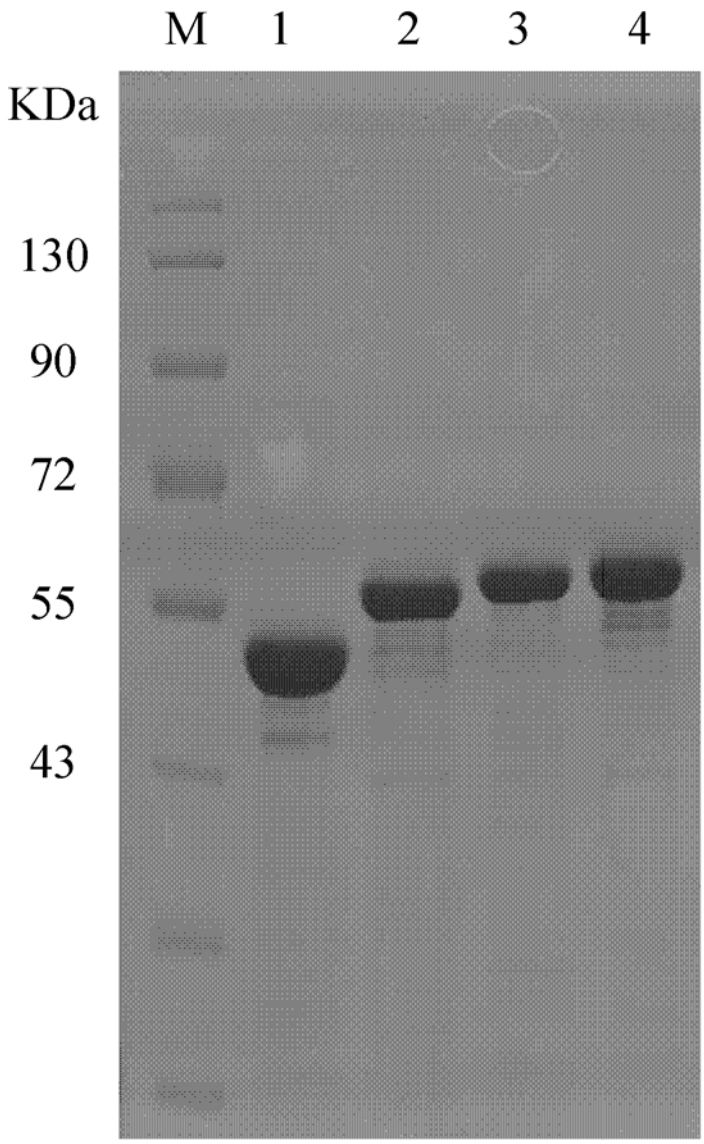

图1

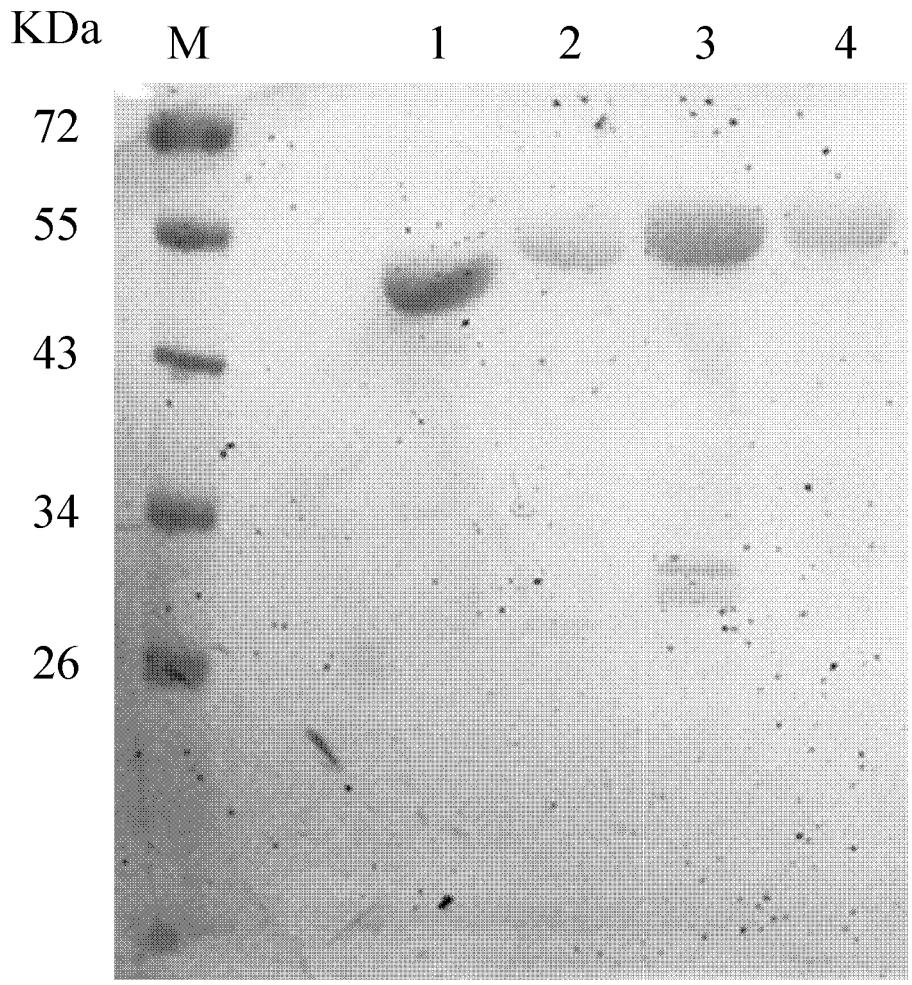

图2

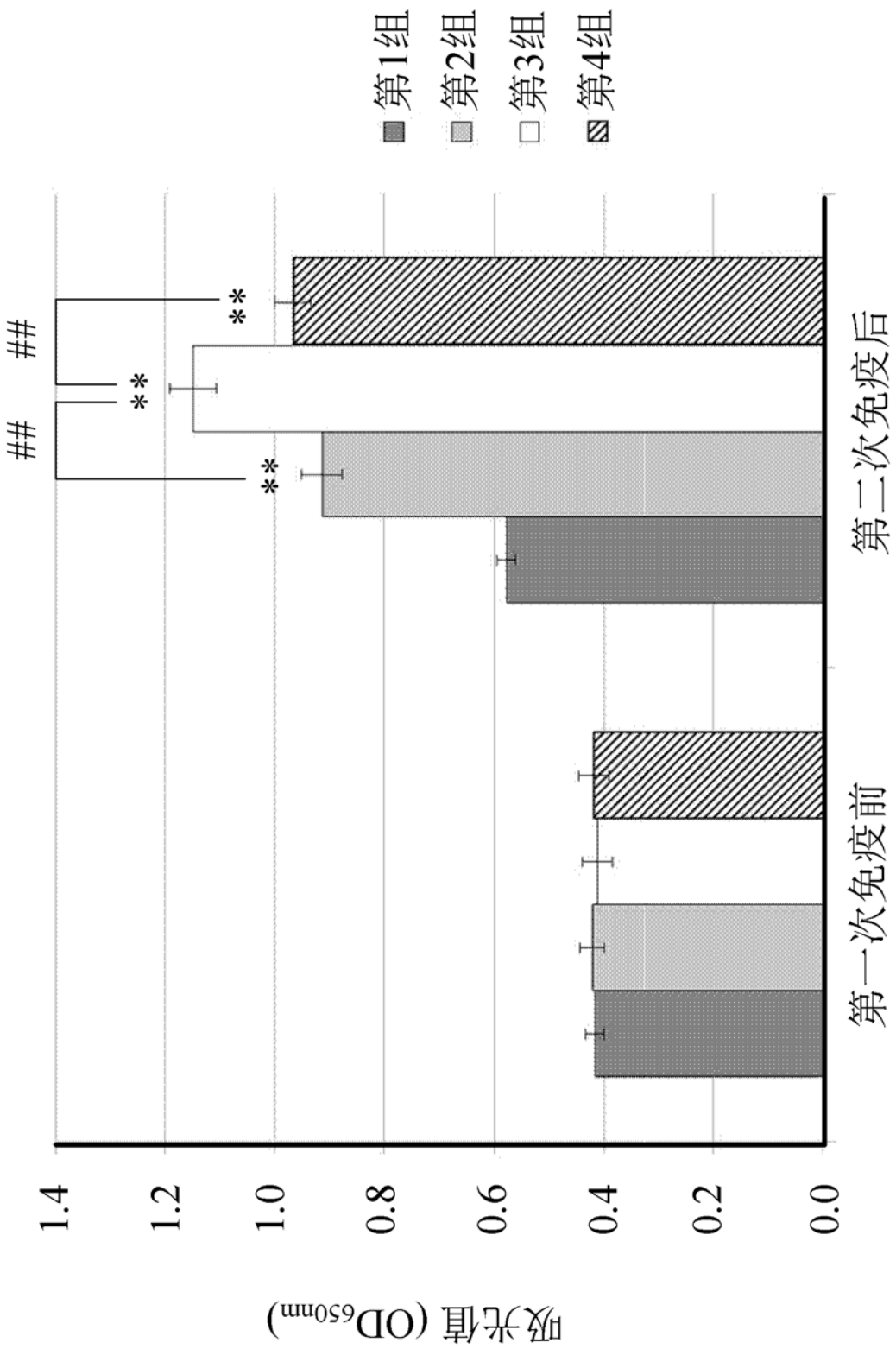
第1组
第2组
第3组
第4组
吸光值 (OD650nm)
1.4
1.2
1.0
0.8
0.6
0.4
0.2
0.0
第一次免疫前
第二次免疫后
**
**
**
##
##

图3