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(54)发明名称

用于犬科动物中呼吸系统疾病控制的物质
和方法

(57)摘要

本发明涉及分离的流感病毒,其能够感染犬
科动物和在犬科动物中引起呼吸系统疾病。本发
明还涉及用于诱导针对本发明的流感病毒的免
疫应答的组合物和方法。本发明还涉及用于鉴定
本发明的病毒和诊断本发明病毒对动物的感染
的组合物和方法。

1. 分离的犬流感病毒,其能够感染犬科动物,其中所述流感病毒是甲型流感病毒,其中所述流感病毒包含编码氨基酸序列为SEQ ID NO:2、4、6、8、10、12、14和16;SEQ ID NO:2、4、6、8、10、12、14和33;SEQ ID NO:18、20、22、24、26、28、30和32;或SEQ ID NO:18、20、22、24、26、28、30和34的多肽的多核苷酸;或所述流感病毒包含氨基酸序列为SEQ ID NO:2、4、6、8、10、12、14和16;SEQ ID NO:2、4、6、8、10、12、14和33;SEQ ID NO:18、20、22、24、26、28、30和32;或SEQ ID NO:18、20、22、24、26、28、30和34的多肽。

2. 根据权利要求1的流感病毒,其中所述流感病毒包含核苷酸序列为SEQ ID NO:1、3、5、7、9、11、13、和15;或SEQ ID NO:17、19、21、23、25、27、29和31的多核苷酸。

3. 权利要求1—2任一项的流感病毒的分离的多核苷酸。

4. 根据权利要求3的多核苷酸,其中所述多核苷酸编码氨基酸序列为SEQ ID NO:2、4、6、8、10、12、14、16、18、20、22、24、26、28、30、32、33或34的任一个的多肽。

5. 根据权利要求3的多核苷酸,其中所述多核苷酸的核苷酸序列在SEQ ID NO:1、3、5、7、9、11、13、15、17、19、21、23、25、27、29或31的任一个中显示。

6. 多核苷酸表达构建体,其包含权利要求3—5任一项的多核苷酸。

7. 权利要求3到5任一项的多核苷酸编码的经分离的多肽。

8. 包含权利要求1到2任一项的流感病毒的免疫原的组合物,其中所述免疫原能够诱导针对流感病毒的免疫应答,所述流感病毒能够感染犬科动物。

9. 根据权利要求8的组合物,其中所述免疫原是病毒蛋白质、多肽或者肽并且所述病毒蛋白质、多肽或者肽的氨基酸序列为SEQ ID NO:2、4、6、8、10、12、14、16、18、20、22、24、26、28、30、32、33或34的任一个。

10. 根据权利要求8的组合物,其中所述病毒多核苷酸编码氨基酸序列为SEQ ID NO:2、4、6、8、10、12、14、16、18、20、22、24、26、28、30、32、33或34任一个的多肽。

11. 根据权利要求8—10任一项的组合物在制备用于在动物中诱导针对犬流感病毒的免疫应答的药物中的用途。

12. 根据权利要求11的用途,其中所述组合物包含病毒蛋白质、多肽或者肽,所述病毒蛋白质、多肽或者肽的氨基酸序列为SEQ ID NO:2、4、6、8、10、12、14、16、18、20、22、24、26、28、30、32、33或34任一个。

13. 根据权利要求11的用途,其中所述免疫应答是保护性免疫应答,其预防或者阻止流感病毒对所述动物的感染。

14. 根据权利要求11的用途,其中所述组合物还包含佐剂。

15. 根据权利要求11的用途,其中所述动物是犬科动物。

16. 根据权利要求15的用途,其中所述犬科动物是驯养的狗。

17. 根据权利要求11的用途,其中经鼻或者经口施用所述组合物。

18. 重排列病毒,其包含权利要求1—2任一项的流感病毒的基因组。

19. 疫苗,其包含权利要求1—2任一项的犬流感病毒。

20. 权利要求19的疫苗,其中所述流感病毒是失活的或减毒的。

21. 权利要求19的疫苗,其中所述流感病毒在可药用载体或稀释剂中提供。

22. 权利要求19的疫苗,其中所述流感病毒包含编码氨基酸序列为SEQ ID NO:33或SEQ ID NO:34的血凝素(HA)的多核苷酸,其中所述HA蛋白包含在氨基酸序列的82位的丝氨酸、

221位的亮氨酸、327位的苏氨酸和482位的苏氨酸。

23. 权利要求19的疫苗,其中所述流感病毒包含氨基酸序列为SEQ ID NO:33或SEQ ID NO:34的血凝素(HA),其中所述HA蛋白包含在氨基酸序列的82位的丝氨酸、221位的亮氨酸、327位的苏氨酸和482位的苏氨酸。

24. 权利要求19的疫苗,其中所述流感病毒包含编码氨基酸序列为SEQ ID NO:16或SEQ ID NO:32或其成熟形式的血凝素(HA)的多核苷酸。

25. 权利要求19的疫苗,其中所述多核苷酸的核苷酸序列为SEQ ID NO:15或SEQ ID NO:31。

26. 重组病毒载体或多核苷酸载体,其包含编码氨基酸序列为SEQ ID NOs:16和32任一项的多肽的多核苷酸。

27. 重组病毒载体或多核苷酸载体,其包含核苷酸序列为SEQ ID NOs:15和31任一项的多核苷酸。

28. 重组病毒载体或多核苷酸载体,其包含编码氨基酸序列为SEQ ID NO:33和34任一项的血凝素(HA)的多核苷酸,其中所述HA蛋白包含在氨基酸序列的82位的丝氨酸、221位的亮氨酸、327位的苏氨酸和482位的苏氨酸。

29. 权利要求28的载体,其中所述多核苷酸编码氨基酸序列为SEQ ID NO:16或SEQ ID NO:32的或其成熟形式的血凝素(HA)。

30. 权利要求28的载体,其中所述多核苷酸的核苷酸序列为SEQ ID NO:15和31任一项。

31. 权利要求26—30任一项的载体,其中所述重组病毒载体来自腺病毒、禽痘病毒、疱疹病毒、牛痘病毒、金丝雀痘、昆虫痘、猪痘或西尼罗病毒。

32. 权利要求26—30任一项的载体,其中所述重组病毒载体是金丝雀痘病毒载体。

33. 权利要求26—30任一项的载体,其中所述多核苷酸载体是病毒载体。

34. 权利要求1的流感病毒,其中所述流感病毒包含编码氨基酸序列为SEQ ID NO:33或SEQ ID NO:34的多肽的多核苷酸。

35. 权利要求1的流感病毒,其中所述流感病毒包含编码氨基酸序列为SEQ ID NO:33或SEQ ID NO:34的血凝素(HA)的多核苷酸,其中所述HA蛋白包含在氨基酸序列的82位的丝氨酸、221位的亮氨酸、327位的苏氨酸和482位的苏氨酸。

36. 权利要求1的流感病毒,其中所述流感病毒包含氨基酸序列为SEQ ID NO:33或SEQ ID NO:34的血凝素(HA),其中所述HA蛋白包含在氨基酸序列的82位的丝氨酸、221位的亮氨酸、327位的苏氨酸和482位的苏氨酸。

37. 权利要求1的流感病毒,其中所述多核苷酸编码氨基酸序列为SEQ ID NO:16或SEQ ID NO:32的或其成熟形式的血凝素(HA)。

38. 权利要求1的流感病毒,其中所述流感病毒的血凝素(HA)的氨基酸序列为SEQ ID NO:16或SEQ ID NO:32或其成熟形式。

39. 权利要求1的犬流感病毒,其中所述多核苷酸的核苷酸序列为SEQ ID NO:15或SEQ ID NO:31。

40. 权利要求3的多核苷酸,其中所述多核苷酸编码氨基酸序列为SEQ ID NO:33或SEQ ID NO:34的多肽。

41. 权利要求3的多核苷酸,其中所述多核苷酸编码氨基酸序列为SEQ ID NO:33或SEQ

ID NO:34的血凝素(HA),其中所述HA蛋白包含在氨基酸序列的82位的丝氨酸、221位的亮氨酸、327位的苏氨酸和482位的苏氨酸。

42.权利要求3的多核苷酸,其中所述多核苷酸编码氨基酸序列为SEQ ID NO:16或SEQ ID NO:32或其成熟形式的血凝素(HA)。

43.权利要求3的多核苷酸,其中所述多核苷酸的核苷酸序列为SEQ ID NO:15或SEQ ID NO:31。

44.权利要求6的多核苷酸表达构建体,其中所述多核苷酸编码氨基酸序列为SEQ ID NO:33或SEQ ID NO:34的多肽。

45.权利要求6的多核苷酸表达构建体,其中所述多核苷酸编码氨基酸序列为SEQ ID NO:33或SEQ ID NO:34的血凝素(HA),其中所述HA蛋白包含在氨基酸序列的82位的丝氨酸、221位的亮氨酸、327位的苏氨酸和482位的苏氨酸。

46.权利要求6的多核苷酸表达构建体,其中所述多核苷酸编码氨基酸序列为SEQ ID NO:16或SEQ ID NO:32或其成熟形式的血凝素(HA)。

47.权利要求6的多核苷酸表达构建体,其中所述多核苷酸的核苷酸序列为SEQ ID NO:15或SEQ ID NO:31。

48.权利要求7的多肽,其中所述多肽的氨基酸序列为SEQ ID NO:33或SEQ ID NO:34。

49.权利要求7的多肽,其中所述多肽是氨基酸序列为SEQ ID NO:33或SEQ ID NO:34的血凝素(HA),其中所述HA蛋白包含在氨基酸序列的82位的丝氨酸、221位的亮氨酸、327位的苏氨酸和482位的苏氨酸。

50.权利要求7的多肽,其中所述多肽的氨基酸序列为SEQ ID NO:16或SEQ ID NO:32或其成熟形式。

51.权利要求8的组合物,其中所述免疫原是编码氨基酸序列为SEQ ID NO:33或SEQ ID NO:34的多肽的多核苷酸。

52.权利要求8的组合物,其中所述免疫原是编码氨基酸序列为SEQ ID NO:33或SEQ ID NO:34的血凝素(HA)的多核苷酸,其中所述HA蛋白包含在氨基酸序列的82位的丝氨酸、221位的亮氨酸、327位的苏氨酸和482位的苏氨酸。

53.权利要求8的组合物,其中所述免疫原是氨基酸序列为SEQ ID NO:33或SEQ ID NO:34的血凝素(HA),其中所述HA蛋白包含在氨基酸序列的82位的丝氨酸、221位的亮氨酸、327位的苏氨酸和482位的苏氨酸。

54.权利要求8的组合物,其中所述免疫原是编码氨基酸序列为SEQ ID NO:16或SEQ ID NO:32或其成熟形式的血凝素(HA)的多核苷酸。

55.权利要求8的组合物,其中所述免疫原是血凝素(HA),其氨基酸序列为SEQ ID NO:16或SEQ ID NO:32或其成熟形式。

56.根据权利要求51-55任一项的组合物或权利要求19-25任一项的疫苗或权利要求26-33任一项的载体在制备用于在动物中诱导针对犬流感病毒的免疫应答的药物中的用途。

57.根据权利要求1,2,34,35,37和39中任一项所述的流感病毒,其中所述多核苷酸由核糖核酸(RNA)组成。

58.根据权利要求26-33中任一项所述的载体,其中所述多核苷酸由核糖核酸(RNA)组

成。

59. 疫苗,其包含权利要求34,38和57任一项的犬流感病毒。

用于犬科动物中呼吸系统疾病控制的物质和方法

[0001] 本申请是申请日为2006年4月21日、发明名称为“用于犬科动物中呼吸系统疾病控制的物质和方法”的中国专利申请200680018936.0 (国际申请号PCT/US2006/015090) 的分案申请。

[0002] 相关申请的参考

[0003] 本申请要求2005年4月21日申请的美国临时申请序号60/673,443的优先权,将该临时申请完整(包括任何附图、表、核酸序列、氨基酸序列和图)引入本文作为参考。

[0004] 发明背景

[0005] “狗舍咳嗽”或者感染性气管支气管炎(ITB)是狗中的急性、传染性呼吸系统感染,其特征主要是咳嗽(Ford et al,1998)。犬ITB被认为是世界上狗的最普遍的感染性呼吸系统疾病,并且当狗在高密度群体环境如狗舍中居住时,爆发可以达到流行性比例。多数爆发是由于直接的狗—狗接触或者呼吸系统分泌物的气雾化(Ford et al,1998)。临床病征由细菌和病毒的一种或者组合感染引起,所述细菌和病毒可以在上呼吸道和下呼吸道的上皮组织中建群。犬科动物副流感病毒(CPiV)和支气管博德特氏菌(*Bordetella bronchiseptica*)细菌是从受侵袭的狗分离的最常见的生物,但是几种其他病毒,如犬科动物瘟热病毒(CDV)和犬科动物腺病毒—1和—2(CAV-1,CAV-2),以及细菌如链球菌(*Streptococcus* sp.)、*Pasteurella multocida*和大肠杆菌(*Escherichia coli*)可以影响临床过程和结果(Ford et al,1998)。尽管在高密度群体中爆发最有效和快速发生,具有高的发病率,但是并发的呼吸系统感染和死亡是不常见的。尽管可以发生威胁生命的继发性细菌性肺炎,但是多数ITB病例是自身限制性的并且在没有任何治疗下消退(Ford et al,1998)。

[0006] 在1992年7月,推测为“狗舍咳嗽”的呼吸系统感染在新英格兰(New England)、佛罗里达(Florida)、西弗吉尼亚(West Virginia)、威斯康辛(Wisconsin)、堪萨斯(Kansas)、科罗拉多(Colorado)、俄克拉荷马(Oklahoma)和亚利桑那州(Arizona)的几个灵缇赛场(greyhound track)变得流行。从兽医了解到,多数受侵袭的狗具有后来消退的轻微咳嗽,但是一打以上的灵缇患上了急性出血性肺炎,接着快速死亡(Greyhound Daily News,1999)。

[0007] 在1998年下半年到1999年上半年,在美国的竞赛灵缇狗舍中发生了几次“狗舍咳嗽”爆发,导致强制关闭赛场和隔离美国的所有竞赛灵缇数周(Greyhound Daily News,1999)。在佛罗里达的一个赛场(Palm Beach Kennel Club),在一天中几乎40%的狗群体中记录到咳嗽(来自William Duggar博士的个人交流)。类似于1992年的爆发,该咳嗽在多数灵缇中消退,但是佛罗里达的10只狗死于“狗舍咳嗽”非特征性的出血性肺炎综合征(Putnam,1999)。

[0008] 在2003年3月—4月,在美国东部的灵缇赛场发生“狗舍咳嗽”的另一次爆发。认为该爆发在佛罗里达的四个赛场开始,并且因此几乎三周中止比赛和狗的隔离。在West Palm

Beach的赛场几乎25%的狗受到侵袭,而St.Petersburg的Derby Lane中1400条狗几乎50%发生咳嗽。再一次,多数狗恢复,但是一些狗死于呼吸系统感染。仅在Derby Lane的呼吸爆发的估计的经济影响为2百万美元。

[0009] 没有公开的报导记载在1992、1998-1999或2003年在竞赛灵~~灵~~狗舍中“狗舍咳嗽”流行的病因或者临床病理。假定该感染是由于CPiV和/或支气管博德特氏菌:狗舍咳嗽的两种最常见的病因。未证实的交流,如网站已经将在一些咳嗽的狗中报导的致命的出血性肺炎规因于 β -溶血性马链球菌兽瘟亚种(*Streptococcus equi subspecies zooepidemicus*),并且将该综合征称作“犬链球菌中毒性休克”。

[0010] 病毒从一个宿主物种传染到另一个是流感病毒的生态学和流行病学的关键特征(Webster,1998)。流感病毒的物种间传染的两个基本机制是可能的(Webster et al.,1992;Lipatov et al.,2004)。一种是基本上未变的病毒从一个物种直接转移到另一个物种。该机制的实例包括最近的家禽流感病毒的H5N1亚型对人的感染(Subbarao et al.,1998;Peiris et al.,2004;Guan et al.,2004)和可能地1918年的大流行,称作西班牙流感(Reid et al.,2004)。第二种机制是流感病毒基因组的区段化性质的结果。用来自不同物种的病毒共感染宿主可以导致区段化病毒基因的重排列,和产生能够感染其他物种的重组体。例如,鸟类和人流感病毒之间基因重排列产生的新的病毒在1957和1968年导致人类流感大流行(Webster et al.,1992;Lipatov et al.,2004;Kawaoka et al.,1989)。

[0011] 未改变的流感病毒从自然宿主物种向不同物种的多数直接传播是最终事件,因为在新物种的个体之间的持续传播不能发生。多种病毒-宿主相互作用是复制和水平传播所必须的并且为流感病毒在新的宿主中的永续性提供了强大的屏障(Webster et al.,2004)。因此,流感病毒的新的宿主特异性谱系的建立是不常见的并且仅仅在驯养的家禽、猪、马和人类中发生(Webster et al.,1992;Lipatov et al.,2004)。

[0012] 因为流感病毒感染的严重性质,所以仍然需要诊断、预防和治疗流感病毒感染的方法。

[0013] 发明概述

[0014] 本发明涉及分离的流感病毒,其能够感染犬科动物和在犬科动物中引起呼吸系统疾病。本发明还涉及用于诱导针对本发明的流感病毒的免疫应答的组合物和方法。本发明还涉及用于鉴定本发明的病毒和和诊断本发明的病毒对动物的感染的组合物和方法。

[0015] 附图简述

[0016] 本专利或者申请文件含有至少一副彩图。专利局将根据请求和在支付了必要的费用后提供具有彩图的本专利或专利申请公布的拷贝。

[0017] 图1A-1B显示了血凝素基因之间的系统发生关系。图1A显示了来自代表性犬、人、鸟类、猪和马分离群,包括作为外类群的A/Budgerigar/Hokkaido/1/77 (H4) 的HA基因树。图1B显示了使用A/Duck/Ukraine/63 (H3) 作为外类群,犬流感病毒HA基因与同一时期的和较老的马HA基因的树。通过近邻连接方法从核苷酸序列推论出系统树并且显示了 $\geq 90\%$ 的自展分析值。条形表示核苷酸改变数目/水平树枝的单位长度。

[0018] 图2A-2B显示了在肺中流感H3抗原的免疫组织化学检测。用针对HA血凝素的小鼠单克隆抗体检测肺组织切片并通过免疫过氧化物酶反应检测结合(褐色沉淀)。图2A显示了

来自具有自发疾病的灵猫的支气管上皮。检测支气管上皮细胞细胞质和呼吸道腔和肺泡腔中巨噬细胞中的病毒H3抗原。图2B显示了用A/canine/Florida/43/04 (H3N8) 接种后5天, 来自狗的支气管上皮。在支气管上皮细胞细胞质中检测到病毒H3抗原。比例尺, 66 μ m。

[0019] 图3显示了在死于与流感病毒感染有关的出血性肺炎的灵猫支气管中特征性组织学改变。对组织用H&E染色。上图: 具有纤毛上皮细胞、粘液细胞和基细胞的正常支气管。下图: 来自患有自发性流感的灵猫的支气管。支气管纤毛上皮细胞有坏死和糜烂。比例尺, 100 μ m。

[0020] 图4A-4B显示了在H3血凝素基因中的系统发生关系。图4A显示了犬科动物流感病毒HA基因与同一时期的和较老的马HA基因的系统树。图4B显示了犬科动物流感病毒HA蛋白质与同一时期的和较老的马HA基因的系统树。通过近邻连接方法从基因或者氨基酸序列推论出系统树并且显示了 $\geq 80\%$ 的自展分析值。条形表示氨基酸改变数目/水平树枝的单位长度。

[0021] 图5显示了在死于与流感病毒感染有关的肺炎的狗的肺中支气管和支气管腺的上皮细胞中流感病毒H3蛋白质。上图: 支气管中纤毛上皮细胞的糜烂。组织用H&E染色。下图: 在支气管(左)和支气管腺(右)上皮细胞的细胞质中流感病毒H3蛋白质。将组织用针对流感病毒H3的单克隆抗体染色, 通过免疫过氧化物酶反应检测(褐色沉淀)并用苏木精复染。

[0022] 图6A-6D显示了从扩增10倍连续体外稀释的转录的RNA标准得到的H3和基质基因(图6A和图6B)的扩增图。通过起始RNA浓度的对数值对从每次稀释得到的阈值循环数(Ct)作图, 构造H3和基质基因(图6C和图6D)的标准曲线。

[0023] 图7显示用10倍连续稀释的病毒原种(包括A/Wyoming/3/2003和A/canine/FL/242/2003)测试Directigen Flu A的灵敏性。紫色三角形指示阳性结果。

[0024] 序列简述

[0025] SEQ ID NO:1是可以根据本发明使用的编码PB2蛋白质的犬科动物流感病毒(Florida/43/04)的核苷酸序列。

[0026] SEQ ID NO:2是SEQ ID NO:1编码的氨基酸序列。

[0027] SEQ ID NO:3是可以根据本发明使用的编码PB1蛋白质的犬科动物流感病毒(Florida/43/04)的核苷酸序列。

[0028] SEQ ID NO:4是SEQ ID NO:3编码的氨基酸序列。

[0029] SEQ ID NO:5是可以根据本发明使用的编码PA蛋白质的犬科动物流感病毒(Florida/43/04)的核苷酸序列。

[0030] SEQ ID NO:6是SEQ ID NO:5编码的氨基酸序列。

[0031] SEQ ID NO:7是可以根据本发明使用的编码NS蛋白质的犬科动物流感病毒(Florida/43/04)的核苷酸序列。

[0032] SEQ ID NO:8是SEQ ID NO:7编码的氨基酸序列。

[0033] SEQ ID NO:9是可以根据本发明使用的编码NP蛋白质的犬科动物流感病毒(Florida/43/04)的核苷酸序列。

[0034] SEQ ID NO:10是SEQ ID NO:9编码的氨基酸序列。

[0035] SEQ ID NO:11是可以根据本发明使用的编码NA蛋白质的犬科动物流感病毒

(Florida/43/04)的核苷酸序列。

[0036] SEQ ID NO:12是SEQ ID NO:11编码的氨基酸序列。

[0037] SEQ ID NO:13是可以根据本发明使用的编码MA蛋白质的犬科动物流感病毒(Florida/43/04)的核苷酸序列。

[0038] SEQ ID NO:14是SEQ ID NO:13编码的氨基酸序列。

[0039] SEQ ID NO:15是可以根据本发明使用的编码HA蛋白质的犬科动物流感病毒(Florida/43/04)的核苷酸序列。

[0040] SEQ ID NO:16是SEQ ID NO:15编码的氨基酸序列。

[0041] SEQ ID NO:17是可以根据本发明使用的编码PB2蛋白质的犬科动物流感病毒(FL/242/03)的核苷酸序列。

[0042] SEQ ID NO:18是SEQ ID NO:17编码的氨基酸序列。

[0043] SEQ ID NO:19是可以根据本发明使用的编码PB1蛋白质的犬科动物流感病毒(FL/242/03)的核苷酸序列。

[0044] SEQ ID NO:20是SEQ ID NO:19编码的氨基酸序列。

[0045] SEQ ID NO:21是可以根据本发明使用的编码PA蛋白质的犬科动物流感病毒(FL/242/03)的核苷酸序列。

[0046] SEQ ID NO:22是SEQ ID NO:21编码的氨基酸序列。

[0047] SEQ ID NO:23是可以根据本发明使用的编码NS蛋白质的犬科动物流感病毒(FL/242/03)的核苷酸序列。

[0048] SEQ ID NO:24是SEQ ID NO:23编码的氨基酸序列。

[0049] SEQ ID NO:25是可以根据本发明使用的编码NP蛋白质的犬科动物流感病毒(FL/242/03)的核苷酸序列。

[0050] SEQ ID NO:26是SEQ ID NO:25编码的氨基酸序列。

[0051] SEQ ID NO:27是可以根据本发明使用的编码NA蛋白质的犬科动物流感病毒(FL/242/03)的核苷酸序列。

[0052] SEQ ID NO:28是SEQ ID NO:27编码的氨基酸序列。

[0053] SEQ ID NO:29是可以根据本发明使用的编码MA蛋白质的犬科动物流感病毒(FL/242/03)的核苷酸序列。

[0054] SEQ ID NO:30是SEQ ID NO:29编码的氨基酸序列。

[0055] SEQ ID NO:31是可以根据本发明使用的编码HA蛋白质的犬科动物流感病毒(FL/242/03)的核苷酸序列。

[0056] SEQ ID NO:32是SEQ ID NO:31编码的氨基酸序列。

[0057] SEQ ID NO:33是SEQ ID NO:16中显示的HA蛋白质的成熟形式,其中已经除去了N-末端16个氨基酸的信号序列。

[0058] SEQ ID NO:34是SEQ ID NO:32中显示的HA蛋白质的成熟形式,其中已经除去了N-末端16个氨基酸的信号序列。

[0059] SEQ ID NO:35是可以根据本发明使用的寡核苷酸。

[0060] SEQ ID NO:36是可以根据本发明使用的寡核苷酸。

[0061] SEQ ID NO:37是可以根据本发明使用的寡核苷酸。

- [0062] SEQ ID NO:38是可以根据本发明使用的寡核苷酸。
- [0063] SEQ ID NO:39是可以根据本发明使用的寡核苷酸。
- [0064] SEQ ID NO:40是可以根据本发明使用的寡核苷酸。
- [0065] SEQ ID NO:41是可以根据本发明使用的寡核苷酸。
- [0066] SEQ ID NO:42是可以根据本发明使用的寡核苷酸。
- [0067] SEQ ID NO:43是可以根据本发明使用的寡核苷酸。
- [0068] SEQ ID NO:44是可以根据本发明使用的寡核苷酸。
- [0069] SEQ ID NO:45是可以根据本发明使用的寡核苷酸。
- [0070] SEQ ID NO:46是可以根据本发明使用的寡核苷酸。
- [0071] SEQ ID NO:47是可以根据本发明使用的编码PB2蛋白质的犬科动物流感病毒(Miami/2005)的核苷酸序列。
- [0072] SEQ ID NO:48是SEQ ID NO:47编码的氨基酸序列。
- [0073] SEQ ID NO:49是可以根据本发明使用的编码PB1蛋白质的犬科动物流感病毒(Miami/2005)的核苷酸序列。
- [0074] SEQ ID NO:50是SEQ ID NO:49编码的氨基酸序列。
- [0075] SEQ ID NO:51是可以根据本发明使用的编码PA蛋白质的犬科动物流感病毒(Miami/2005)的核苷酸序列。
- [0076] SEQ ID NO:52是SEQ ID NO:51编码的氨基酸序列。
- [0077] SEQ ID NO:53是可以根据本发明使用的编码NS蛋白质的犬科动物流感病毒(Miami/2005)的核苷酸序列。
- [0078] SEQ ID NO:54是SEQ ID NO:53编码的氨基酸序列。
- [0079] SEQ ID NO:55是可以根据本发明使用的编码NP蛋白质的犬科动物流感病毒(Miami/2005)的核苷酸序列。
- [0080] SEQ ID NO:56是SEQ ID NO:55编码的氨基酸序列。
- [0081] SEQ ID NO:57是可以根据本发明使用的编码NA蛋白质的犬科动物流感病毒(Miami/2005)的核苷酸序列。
- [0082] SEQ ID NO:58是SEQ ID NO:57编码的氨基酸序列。
- [0083] SEQ ID NO:59是可以根据本发明使用的编码MA蛋白质的犬科动物流感病毒(Miami/2005)的核苷酸序列。
- [0084] SEQ ID NO:60是SEQ ID NO:59编码的氨基酸序列。
- [0085] SEQ ID NO:61是可以根据本发明使用的编码HA蛋白质的犬科动物流感病毒(Miami/2005)的核苷酸序列。
- [0086] SEQ ID NO:62是SEQ ID NO:61编码的氨基酸序列。
- [0087] SEQ ID NO:63是可以根据本发明使用的编码PB2蛋白质的犬科动物流感病毒(Jacksonville/2005)的核苷酸序列。
- [0088] SEQ ID NO:64是SEQ ID NO:63编码的氨基酸序列。
- [0089] SEQ ID NO:65是可以根据本发明使用的编码PB1蛋白质的犬科动物流感病毒(Jacksonville/2005)的核苷酸序列。
- [0090] SEQ ID NO:66是SEQ ID NO:65编码的氨基酸序列。

[0091] SEQ ID NO:67是可以根据本发明使用的编码PA蛋白质的犬科动物流感病毒(Jacksonville/2005)的核苷酸序列。

[0092] SEQ ID NO:68是SEQ ID NO:67编码的氨基酸序列。

[0093] SEQ ID NO:69是可以根据本发明使用的编码NS蛋白质的犬科动物流感病毒(Jacksonville/2005)的核苷酸序列。

[0094] SEQ ID NO:70是SEQ ID NO:69编码的氨基酸序列。

[0095] SEQ ID NO:71是可以根据本发明使用的编码NP蛋白质的犬科动物流感病毒(Jacksonville/2005)的核苷酸序列。

[0096] SEQ ID NO:72是SEQ ID NO:71编码的氨基酸序列。

[0097] SEQ ID NO:73是可以根据本发明使用的编码NA蛋白质的犬科动物流感病毒(Jacksonville/2005)的核苷酸序列。

[0098] SEQ ID NO:74是SEQ ID NO:73编码的氨基酸序列。

[0099] SEQ ID NO:75是可以根据本发明使用的编码MA蛋白质的犬科动物流感病毒(Jacksonville/2005)的核苷酸序列。

[0100] SEQ ID NO:76是SEQ ID NO:75编码的氨基酸序列。

[0101] SEQ ID NO:77是可以根据本发明使用的编码HA蛋白质的犬科动物流感病毒(Jacksonville/2005)的核苷酸序列。

[0102] SEQ ID NO:78是SEQ ID NO:77编码的氨基酸序列。

[0103] SEQ ID NO:79是可以根据本发明使用的寡核苷酸。

[0104] SEQ ID NO:80是可以根据本发明使用的寡核苷酸。

[0105] SEQ ID NO:81是可以根据本发明使用的寡核苷酸。

[0106] SEQ ID NO:82是可以根据本发明使用的寡核苷酸。

[0107] SEQ ID NO:83是可以根据本发明使用的寡核苷酸。

[0108] SEQ ID NO:84是可以根据本发明使用的寡核苷酸。

[0109] SEQ ID NO:85是可以根据本发明使用的寡核苷酸。

[0110] SEQ ID NO:86是可以根据本发明使用的寡核苷酸。

[0111] SEQ ID NO:87是可以根据本发明使用的寡核苷酸。

[0112] SEQ ID NO:88是可以根据本发明使用的寡核苷酸。

[0113] 发明详述

[0114] 本发明涉及分离的流感病毒,其能够感染犬科动物和引起呼吸系统疾病。在一个实施方案中,本发明的流感病毒包含编码具有SEQ ID NO:2、4、6、8、10、12、14、16、18、20、22、24、26、28、30、32、33、34、48、50、52、54、56、58、60、62、64、66、68、70、72、74、76或78任一个所示的氨基酸序列的蛋白质或者其功能和/或免疫原性片段或者变体的多核苷酸。在一个特定实施方案中,所述多核苷酸包含SEQ ID NO:1、3、5、7、9、11、13、15、17、19、21、23、25、27、29、31、47、49、51、53、55、57、59、61、63、65、67、69、71、73、75或77中任一个所示的核苷酸序列,或者其片段或者变体。在特定实施方案中,本发明的流感病毒是亚型H3。根据本文描述的方法,可以从受感染的狗分离病毒并在细胞或者蛋中培养。在示例的实施方案中,流感病毒是甲型流感病毒。

[0115] 本发明还涉及包含本发明的流感病毒的一种或多种基因或者基因组区段的全部

或者部分的多核苷酸。在一个实施方案中,本发明的多核苷酸包含流感血凝素(HA)基因、神经氨酸酶(NA)基因、核蛋白(NP)基因、基质蛋白(MA或者M)基因、聚合酶碱性(PB)蛋白基因、聚合酶酸性(PA)蛋白基因、非结构(NS)蛋白基因,或者这些基因任一种的功能片段或者变体。在特定实施方案中,本发明的多核苷酸包含血凝素(HA)基因或者其功能片段或者变体。在另一实施方案中,HA基因编码血凝素蛋白质,其与马H3共有序列的氨基酸序列相比,具有如下一个或多个:83位的丝氨酸;222位的亮氨酸;328位的苏氨酸;和/或483位的苏氨酸。在一个实施方案中,HA基因编码具有SEQ ID NO:16、32、62或78中所示的氨基酸序列的多肽,或者其功能和/或免疫原性片段或者变体。在一个特定实施方案中,HA基因包含SEQ ID NO:15、31、61或77中所示的核苷酸序列。

[0116] 在一个实施方案中,本发明的多核苷酸编码具有SEQ ID NO:2、4、6、8、10、12、14、16、18、20、22、24、26、28、30、32、33、34、48、50、52、54、56、58、60、62、64、66、68、70、72、74、76或78的任一个中所示的氨基酸序列的多肽,或者其功能和/或免疫原性片段或者变体。在特定实施方案中,编码SEQ ID NO:2、4、6、8、10、12、14、16、18、20、22、24、26、28、30、32、33、34、48、50、52、54、56、58、60、62、64、66、68、70、72、74、76或78中所示的氨基酸序列的多核苷酸分别包含SEQ ID NO:1、3、5、7、9、11、13、15、17、19、21、23、25、27、29、31、47、49、51、53、55、57、59、61、63、65、67、69、71、73、75或77中所示的核苷酸序列,或者编码SEQ ID NO:2、4、6、8、10、12、14、16、18、20、22、24、26、28、30、32、33、34、48、50、52、54、56、58、60、62、64、66、68、70、72、74、76或78的任一项的功能和/或免疫原性片段或者变体的序列。从而,本发明涉及多核苷酸序列,其包含SEQ ID NO:1、3、5、7、9、11、13、15、17、19、21、23、25、27、29、31、47、49、51、53、55、57、59、61、63、65、67、69、71、73、75或77的任一项中所示的核苷酸序列,或者SEQ ID NO:1、3、5、7、9、11、13、15、17、19、21、23、25、27、29、31、47、49、51、53、55、57、59、61、63、65、67、69、71、73、75或77的任一项的片段或者变体,包括简并变体。在一个特定实施方案中,本发明的多核苷酸可以包含:SEQ ID NO:3的核苷酸1-2271;SEQ ID NO:5的核苷酸1-2148;SEQ ID NO:7的核苷酸1-657;SEQ ID NO:9的核苷酸1-1494;SEQ ID NO:11的核苷酸1-1410;SEQ ID NO:13的核苷酸1-756;SEQ ID NO:15的核苷酸1-1695;SEQ ID NO:19的核苷酸1-2271;SEQ ID NO:21的核苷酸1-2148;SEQ ID NO:23的核苷酸1-657;SEQ ID NO:25的核苷酸1-1494;SEQ ID NO:29的核苷酸1-756;SEQ ID NO:31的核苷酸1-1695;SEQ ID NO:47的核苷酸1-2277;SEQ ID NO:49的核苷酸1-2271;SEQ ID NO:51的核苷酸1-2148;SEQ ID NO:53的核苷酸1-690;SEQ ID NO:55的核苷酸1-1494;SEQ ID NO:57的核苷酸1-1410;SEQ ID NO:59的核苷酸1-756;SEQ ID NO:61的核苷酸1-1695;SEQ ID NO:63的核苷酸1-2277;SEQ ID NO:65的核苷酸1-2271;SEQ ID NO:67的核苷酸1-2148;SEQ ID NO:69的核苷酸1-690;SEQ ID NO:71的核苷酸1-1494;SEQ ID NO:73的核苷酸1-1410;SEQ ID NO:75的核苷酸1-756;和SEQ ID NO:77的核苷酸1-1695。在本发明的范围内预期的病毒多核苷酸和多肽序列的核苷酸和氨基酸序列已经保存在GenBank,检索号为DQ124147到DQ124161和DQ124190,将其公开引入本文作为参考。

[0117] 本发明还涉及本发明的流感病毒的多核苷酸编码的多肽。本发明还涉及主题多肽的功能和/或免疫原性片段和变体。预期的多肽包括本发明的流感病毒的HA蛋白、NA蛋白、NS蛋白、核蛋白、聚合酶碱性蛋白、聚合酶酸性蛋白,和基质蛋白。在一个示例的实施方案中,本发明的多肽具有SEQ ID NO:2、4、6、8、10、12、14、16、18、20、22、24、26、28、30、32、33、

34、48、50、52、54、56、58、60、62、64、66、68、70、72、74、76或78任一项所示的氨基酸序列,或者其功能和/或免疫原性片段或变体。

[0118] 本发明还涉及包含本发明的多核苷酸序列的多核苷酸表达构建体。在一个实施方案中,本发明的表达构建体包含多核苷酸序列,该多核苷酸序列编码包含SEQ ID NO:2、4、6、8、10、12、14、16、18、20、22、24、26、28、30、32、33、34、48、50、52、54、56、58、60、62、64、66、68、70、72、74、76或78任一项所示的氨基酸序列的多肽,或者其功能和/或免疫原性片段或变体。在特定实施方案中,编码SEQ ID NO:2、4、6、8、10、12、14、16、18、20、22、24、26、28、30、32、33、34、48、50、52、54、56、58、60、62、64、66、68、70、72、74、76或78中所示的氨基酸序列的多核苷酸分别包含SEQ ID NO:1、3、5、7、9、11、13、15、17、19、21、23、25、27、29、31、47、49、51、53、55、57、59、61、63、65、67、69、71、73、75或77的任一个中所示的核苷酸序列,或者编码SEQ ID NO:2、4、6、8、10、12、14、16、18、20、22、24、26、28、30、32、33、34、48、50、52、54、56、58、60、62、64、66、68、70、72、74、76或78任一个的功能和/或免疫原性片段或变体的序列。从而,本发明涉及包含多核苷酸序列的表达构建体,所述多核苷酸序列包含SEQ ID NO:1、3、5、7、9、11、13、15、17、19、21、23、25、27、29、31、47、49、51、53、55、57、59、61、63、65、67、69、71、73、75或77的任一个中所示的核苷酸序列,或者SEQ ID NO:1、3、5、7、9、11、13、15、17、19、21、23、25、27、29、31、47、49、51、53、55、57、59、61、63、65、67、69、71、73、75或77任一个的片段或者变体,包括简并变体。在优选实施方案中,本发明的表达构建体提供了本发明的有效连接的多核苷酸的过表达。

[0119] 本发明的表达构建体一般包括在预计的宿主细胞中有功能的调节元件,在所述宿主细胞中将表达该表达构建体。从而,本领域技术人员可以选择用于例如人类宿主细胞、哺乳动物宿主细胞、昆虫宿主细胞、酵母宿主细胞、细菌宿主细胞、和植物宿主细胞的调节元件。在一个实施方案中,调节元件是在犬科动物细胞中有功能的调节元件。调节元件包括启动子、转录终止序列、翻译终止序列、增强子、和多聚腺苷酸化元件。如本文所用的,术语“表达构建体”指核酸序列的组合,其提供了有效连接的核酸序列的转录。如本文所用的,术语“有效连接”指所述的元件的并列,其中所述元件处于允许它们以它们预期的方式发挥功能的关系中。通常,有效连接的元件为邻接的关系。

[0120] 本发明的表达构建体可以包含有效连接到编码本发明多肽的多核苷酸序列的启动子序列。使用本领域中已知的标准技术,可以将启动子掺入多核苷酸中。在本发明的表达构建体中可以使用启动子的多个拷贝或者多个启动子。在优选实施方案中,启动子与表达构建体中转录起始位点的距离可以与它与天然遗传环境中转录起始位点的距离相同。在该距离中允许一定的变化而不实质性降低启动子活性。在表达构建体中通常包括转录起始位点。优选地,与本发明的表达构建体结合的启动子提供了本发明的有效连接的多核苷酸的过表达。

[0121] 与本发明的表达构建体用于真核细胞中的启动子可以是病毒或者细菌来源的。病毒启动子包括,但不限于,巨细胞病毒(CMV)基因启动子、SV40早期或者晚期启动子,或者劳斯肉瘤病毒(RSV)基因启动子。细胞来源的启动子包括,但不限于,结蛋白基因启动子和肌动蛋白基因启动子。适于与本发明的表达构建体用于酵母细胞的启动子包括,但不限于,3-磷酸甘油酸酯激酶启动子、甘油醛-3-磷酸脱氢酶启动子、金属硫蛋白启动子、醇脱氢酶-2启动子,和己糖激酶启动子。

[0122] 如果在植物细胞中提供或者向植物细胞中导入表达构建体,那么可以使用植物病毒启动子,如花椰菜花叶病毒(CaMV) 35S(包括增强的CaMV35S启动子(见,例如,美国专利号5,106,739和An,1997))或者CaMV19S启动子。可以用于植物中表达构建体的其他启动子包括,例如,prolifera启动子、Ap3启动子、热休克启动子、根癌农杆菌(*A. tumefaciens*)的T-DNA1'-或2'-启动子、多聚半乳糖醛酸酶启动子、来自牵牛花的查耳酮合酶A(CHS-A)启动子、烟草PR-1a启动子、泛蛋白启动子、肌动蛋白启动子、alcA基因启动子、pin2启动子(Xu et al.,1993)、玉米WipI启动子、玉米trpA基因启动子(美国专利号5,625,136)、玉米CDPK基因启动子、和RUBISCO SSU启动子(美国专利号5,034,322)。根特异的启动子,如美国专利号6,455,760或美国专利号6,696,623或公布的美国专利申请号20040078841;20040067506;20040019934;20030177536;20030084486;或20040123349中描述的任一种启动子序列可以用于本发明的表达构建体。组成性启动子(如CaMV、泛蛋白、肌动蛋白或者NOS启动子)、发育调节的启动子和诱导型启动子(如可以通过热、光、激素或者化学品诱导的那些启动子)也预期用于本发明的多核苷酸表达构建体。也可以使用组织特异性启动子,例如,果实特异性启动子,如番茄的E8启动子(检索号:AF515784;Good et al.(1994))。也可以使用种子特异性启动子,如来自 β -菜豆蛋白基因(例如,菜豆的)或者大豆球蛋白基因(例如,大豆的)的启动子,和其他启动子。

[0123] 对于在原核系统中表达,本发明的表达构建体可以包含启动子,如碱性磷酸酶启动子、色氨酸(trp)启动子、 λ PL启动子、 β -内酰胺酶启动子、乳糖启动子、phoA启动子、T3启动子、T7启动子、或者tac启动子(de Boer et al.,1983)。

[0124] 本发明的表达构建体可以任选含有转录终止序列、翻译终止序列、编码信号肽的序列,和/或增强子元件。转录终止区可以通常从真核生物或者病毒基因序列的3'非翻译区得到。转录终止序列可以位于编码区的下游以提供有效终止。信号肽序列是通常存在于蛋白质的氨基末端的短氨基酸序列,其负责有效连接的成熟多肽重定位到多种不同的翻译后细胞目的地,从特定细胞器隔室到蛋白质作用部位和细胞外环境。通过使用有效连接的信号肽序列将基因产物靶向预期的细胞和/或细胞外目的地预期用于本发明的多肽。典型的增强子是顺式作用元件,其增加基因转录并且可以包括在表达构建体中。典型的增强子元件是本领域中已知的,并且包括,但不限于,CaMV35S增强子元件、巨细胞病毒(CMV)早期启动子增强子元件,和SV40增强子元件。增强基因表达的内含子介导的增强子元件也是本领域中已知的。这些元件必须存在于转录区内并且是方向依赖性的。

[0125] 指导从表达构建体转录的mRNA的多聚腺苷酸化的DNA序列也可以包括在表达构建体中,并且包括,但不限于,章鱼碱合酶或者胭脂氨酸合酶信号。

[0126] 表达构建体还可以包括一种或多种显性选择标记基因,包括,例如,编码抗生素抗性和/或除草剂抗性用于选择转化细胞的基因。抗生素抗性基因可以提供对一种或多种下面的抗生素的抗性:潮霉素、卡那霉素、博来霉素、G418、链霉素、巴龙霉素、新霉素和大观霉素。通过新霉素磷酸转移酶(NPT II)可以提供卡那霉素抗性。除草剂抗性基因可以提供对膦丝菌素乙酰转移酶或者草甘膦的抗性。用于细胞转化筛选的其他标记包括,但不限于,编码 β -葡萄糖醛酸糖苷酶(GUS)、 β -半乳糖苷酶、萤光素酶、胭脂氨酸合成酶、氯霉素乙酰转移酶(CAT)、绿色荧光蛋白(GFP)或者增强的GFP的基因(Yang et al.,1996)。

[0127] 本发明还涉及包含编码本发明多肽的本发明的多核苷酸序列的多核苷酸载体。可

以在本发明的表达构建体或者多核苷酸的5'和3'末端包括独特的限制酶位点以允许插入到多核苷酸载体中。如本文所用的,术语“载体”指任一遗传元件,包括例如,质粒、粘粒、染色体、噬菌体、病毒等等,其当与适当的控制元件结合时能够复制并且可以在细胞之间转移多核苷酸序列。载体含有允许载体在所选的宿主细胞中复制的核苷酸序列。许多载体可以用于表达和/或克隆,并且包括,但不限于,pBR322、pUC系列、M13系列、pGEM系列、和pBLUESCRIPT载体(Stratagene,La Jolla,CA and Promega,Madison,WI)。

[0128] 本发明还涉及寡核苷酸探针和引物,如聚合酶链式反应(PCR)引物,其可以与本发明多核苷酸的编码或非编码序列杂交。本发明的寡核苷酸探针可以用于检测流感病毒核酸序列的方法中。本发明的寡核苷酸引物可以用于PCR方法和涉及核酸扩增的其他方法中。在优选实施方案中,本发明的探针或引物可以与本发明的多核苷酸在严格条件下杂交。本发明的探针和引物可以任选包含检测标记或者报道分子,如荧光分子、酶、放射性部分,等等。本发明的探针和引物对于使用它们的方法或测定法可以是任何合适的长度。通常,本发明的探针和引物将长为10到500个或者更多核苷酸。在本发明的范围内预期长为10到20、21到30、31到40、41到50、51到60、61到70、71到80、81到90、91到100或101个或更多核苷酸的探针和引物。在一个实施方案中,探针和引物长为9、10、11、12、13、14、15、16、17、18、19、20、21、22、23、24、25、26、27、28、29或30个核苷酸的任一个。本发明的探针和引物可以与所述多核苷酸序列具有完全(100%)的核苷酸序列同一性,或者序列同一性可以小于100%。例如,探针或引物和序列之间的序列同一性可以为99%、98%、97%、96%、95%、90%、85%、80%、75%、70%或者任一其他百分数序列同一性,只要该探针或引物可以在严格条件下与本发明的多核苷酸的核苷酸序列杂交。本发明的示例的探针和引物包括具有SEQ ID NO:35、SEQ ID NO:36、SEQ ID NO:37、SEQ ID NO:38、SEQ ID NO:39、SEQ ID NO:40、SEQ ID NO:41、SEQ ID NO:42、SEQ ID NO:43、SEQ ID NO:44、SEQ ID NO:45和SEQ ID NO:46的任一个中所示的核苷酸序列,或者SEQ ID NO:35-46的任一个的功能片段或者变体的那些探针和引物。

[0129] 如本文所用的,术语“核酸”、“多核苷酸”和“寡核苷酸”指单链或者双链形式的脱氧核糖核苷酸、核糖核苷酸或者混合的脱氧核糖核苷酸和核糖核苷酸聚合物,并且除非另外限制,将包括天然核苷酸的已知的类似物,其可以以类似于天然存在的核苷酸的方式发挥功能。多核苷酸序列包括可以转录成RNA的DNA链序列和可以翻译成蛋白质的RNA链。本发明的任一核酸、多核苷酸或者寡核苷酸的互补序列也预期在本发明的范围内。多核苷酸序列还包括全长序列以及衍生自全长序列的较短的序列。本发明还包括序列与本文公开的多核苷酸互补的那些多核苷酸。本发明的多核苷酸和多肽可以以纯化或者分离的形式提供。

[0130] 因为遗传密码的简并性,多种不同的多核苷酸序列可以编码本发明的多肽。在Lewin(1985)中描述了显示所有可能的三联体密码子(并且其中U也代表T)和每个密码子编码的氨基酸的表格。此外,本领域技术人员完全能够产生编码与本发明的多肽相同或者基本相同的多肽的备选的多核苷酸序列。这些简并变体和备选多核苷酸序列在本发明的范围内。如本文使用的,对“基本上相同”的序列的引用指编码氨基酸替代、缺失、添加或者插入的序列,其不实质上改变本发明的多核苷酸编码的多肽的功能和/或免疫原性活性。

[0131] 本发明还涉及编码本发明多肽的本发明的多核苷酸的变体。变体序列包括那些序列,其中该序列的一个或多个核苷酸已经被替代、缺失和/或插入。可以替代DNA的天然核苷酸的核苷酸具有碱基部分,其可以包括,但不限于,次黄苷、5-氟尿嘧啶、5-溴尿嘧啶、次黄

嘌呤、1-甲基鸟嘌呤、5-甲基胞嘧啶,和三苯甲基化碱基。序列中核苷酸的糖部分还可以是经修饰的并且包括,但不限于,阿拉伯糖、木酮糖和己糖。此外,可以用乙酰基、甲基和/或硫代基团修饰核苷酸的腺嘌呤、胞嘧啶、鸟嘌呤、胸腺嘧啶和尿嘧啶碱基。使用本领域中已知的标准技术可以制备和测试含有核苷酸替代、缺失、和/或插入的序列。

[0132] 本发明的范围内还预期与本发明的多肽中那些特别示例或者天然存在的氨基酸不同的氨基酸替代。例如,非天然氨基酸可以替代多肽的氨基酸,只要具有替代氨基酸的多肽基本上保留与没有替代的氨基酸的多肽相同的功能活性。非天然氨基酸的实例包括,但不限于,鸟氨酸、瓜氨酸、羟脯氨酸、高丝氨酸、苯基甘氨酸、牛磺酸、碘代酪氨酸、2,4-二氨基丁酸、 α -氨基异丁酸、4-氨基丁酸、2-氨基丁酸、 γ -氨基丁酸、 ϵ -氨基己酸、6-氨基己酸、2-氨基异丁酸、3-氨基丙酸、正亮氨酸、正缬氨酸、肌氨酸、高瓜氨酸、半胱磺酸、 τ -丁基甘氨酸、 τ -丁基丙氨酸、苯基甘氨酸、环己基丙氨酸、 β -丙氨酸、氟-氨基酸、设计者氨基酸,如 β -甲基氨基酸、C-甲基氨基酸、N-甲基氨基酸、和一般的氨基酸类似物。非天然氨基酸还包括具有衍生的侧基的氨基酸。此外,蛋白质中的任一氨基酸可以为D(右旋)型或者L(左旋)型。本发明的范围内还包括本发明多肽的蛋白质序列的等位基因变体。

[0133] 氨基酸可以一般以下面的类别分类:非极性的、不带电的极性的、碱性的和酸性的。保守替代(其中具有一个类别氨基酸的本发明的多肽用相同类别的另一氨基酸替代)落入本发明的范围内,只要具有替代的多肽仍然保留与不具有该替代的多肽基本上相同的功能活性。编码序列中具有一个或多个氨基酸替代的多肽的多核苷酸包括在本发明的范围内。下面的表11提供了属于每个类别的氨基酸的实例列表。在表12中定义了单字母氨基酸缩写。

[0134] 使用本领域中已知的标准方法可以产生本发明的流感病毒多肽的片段和变体并且使用本领域中已知的标准技术测试功能或者免疫原性的存在。例如,为了测试本发明的神经氨酸酶多肽的片段和/或变体,可以测定酶促活性。从而,普通技术人员可以容易制备和测试本发明多肽的片段和变体,并确定该片段或变体是否相对于全长或者非变异多肽保持活性。

[0135] 本发明范围内预期的多核苷酸和多肽也可以按照与本文特别示例的本发明的那些序列的更具体的同一性和/或相似性范围定义。序列同一性将通常大于60%,优选大于75%,更优选大于80%,甚至更优选大于90%,并且可以大于95%。与本文示例的序列相比,序列的同一性和/或相似性可以为49、50、51、52、53、54、55、56、57、58、59、60、61、62、63、64、65、66、67、68、69、70、71、72、73、74、75、76、77、78、79、80、81、82、83、84、85、86、87、88、89、90、91、92、93、94、95、96、97、98或99%。除非另外指出,如本文使用的,两个序列的百分比序列同一性和/或相似性可以使用Karlin和Altschul (1990)的,如在Karlin和Altschul (1993)中改进的算法确定。这种算法整合到Altschul et al. (1990)的NBLAST和XBLAST程序中。可以用NBLAST程序,得分=100,字长=12进行BLAST搜索,以得到具有所希望的百分比序列同一性的序列。为了得到用于比较目的的缺口比对,可以使用如Altschul et al. (1997)的Gapped BLAST。当利用BLAST和Gapped BLAST程序时,可以使用各自程序(NBLAST和XBLAST)的默认参数。见NCBI/NIH网站。

[0136] 本发明还预期这样的多核苷酸分子,其具有与本文示例的多核苷酸序列足够同源的序列,从而允许与该序列在标准的严格条件和标准方法 (Maniatis et al., 1982) 下杂

交。如本文使用的，杂交的“严格”条件指这样的条件，其中通常在6x SSPE, 5x Denhardt溶液, 0.1% SDS, 0.1mg/ml变性DNA中低于DNA杂交分子的解链温度(T_m) 20–25℃下过夜进行。通过下面的公式描述解链温度 T_m (Beltz et al., 1983)：

[0137] $T_m = 81.5C + 16.6 \log [Na^+] + 0.41 (\%G+C) - 0.61 (\% \text{甲酰胺}) - 600 / \text{双链体长度 (以碱基对计)}$ 。

[0138] 通常如下进行洗涤：

[0139] (1) 在1x SSPE, 0.1% SDS中室温下洗涤两次，每次15分钟 (低严格洗涤)。

[0140] (2) 在0.2x SSPE, 0.1% SDS中 $T_m - 20^\circ\text{C}$ 下洗涤一次15分钟 (中等严格洗涤)。

[0141] 本发明还涉及本发明的流感病毒的基因编码的病毒蛋白质和肽。在一个实施方案中，病毒蛋白是成熟HA蛋白。在特定实施方案中，成熟的HA蛋白包含下面的一个或多个：82位的丝氨酸；221位的亮氨酸；327位的苏氨酸；和/或482位的苏氨酸。在示例的实施方案中，成熟的HA蛋白质具有SEQ ID NO:33或SEQ ID NO:34中所示的氨基酸序列，或者SEQ ID NO:33或SEQ ID NO:34的功能和/或免疫原性片段或变体。在另一实施方案中，病毒蛋白是NA蛋白、NS蛋白、PB蛋白、PA蛋白、或者MA蛋白。本发明的病毒蛋白质和肽可以用于产生特异结合所述蛋白质或肽的抗体。本发明的病毒蛋白质和肽还可以用作疫苗组合物中的免疫原。

[0142] 本发明还涉及用于诱导针对流感病毒的免疫应答的组合物和方法，所述流感病毒能够感染易感的宿主动物和引起呼吸系统疾病。本发明可以用于在易感的宿主动物中诱导针对任一亚型的流感病毒的免疫应答。例如，流感病毒可以是H1、H2、H3、H4、H5、H6、H7、H8、H9、H10、H11、H12、H13、H14、H15或H16的HA亚型，和N1、N2、N3、N4、N5、N6、N7、N8或N9的NA亚型。在一个实施方案中，HA亚型是H3或者H5。在另一实施方案中，NA亚型是N7或者N8。在特定实施方案中，诱导针对亚型H3N8的流感病毒的免疫应答。在一个实施方案中，宿主动物是犬科动物。犬科动物包括野生的、动物园的和驯养的犬科动物，如狼、郊狼和狐狸。犬科动物还包括狗，尤其驯养的狗，如纯种和/或杂种陪伴狗、表演狗、役用狗、放牧狗、猎狗、守卫狗、警犬、赛犬和/或实验用狗。在特定实施方案中，宿主动物是驯养的狗，如灵缇。在一个实施方案中，对动物施用有效量的本发明的免疫原性组合物，其足以诱导针对本发明的流感病毒的免疫应答。免疫应答可以是体液和/或细胞免疫应答。在特定实施方案中，免疫应答是保护性免疫应答，其能够在免疫后在一定的时间段内预防或者减小受免疫的宿主动物中的病毒感染。从而，本发明还涉及疫苗组合物和方法，其为接种的动物提供了针对本发明病毒的保护性免疫应答。

[0143] 如本文所用的，本发明的疫苗或者免疫原性组合物可以包含无细胞的完整病毒，包括减毒的或者失活的病毒，或者病毒的部分，包括亚病毒颗粒 (包括“分离疫苗”，其中处理病毒体以除去一些或者全部病毒脂类)、病毒蛋白质 (包括个体蛋白质和多种蛋白质的大分子复合体)、多肽、和肽，以及病毒感染的细胞系，或者这些任一种的组合。包含病毒感染的细胞系的疫苗或者免疫原性组合物可以包含多种细胞系，每种用不同的病毒毒株感染。

[0144] 本发明的疫苗或者免疫原性组合物还包含重组的基于病毒载体的构建体，其可以包含例如编码本发明的流感病毒的HA蛋白、NA蛋白、核蛋白、聚合酶碱性蛋白、聚合酶酸性蛋白，和/或基质蛋白的基因。可以用于制备重组载体/病毒构建体的任何合适的病毒载体预期用于本发明。例如，来自腺病毒、禽痘、疱疹病毒、牛痘、金丝雀痘、昆虫痘、猪痘、西尼罗病毒和本领域已知的其他病毒的病毒载体可以用于本发明的组合物和方法中。可以使用本

领域中已知的标准遗传工程技术构建编码和表达组分的重组多核苷酸载体。此外,本文描述的多种疫苗组合物可以单独使用和相互组合使用。例如,动物的初次免疫可以使用重组的基于载体的构建体,其具有单个或者多个毒株组分,然后用包含失活病毒或者失活的病毒感染的细胞系的疫苗组合物二次加强。使用本发明的疫苗组合物的其他免疫方案是本领域技术人员显而易见的并且预计在本发明的范围内。

[0145] 本发明还涉及重排列病毒,其包含本发明的流感病毒的至少一种基因或者基因组区段和来自本发明的不同的流感病毒或者来自不同于本发明病毒的流感病毒的病毒基因或者基因组区段的剩余部分。通过本发明的供体流感病毒的核酸与受体流感病毒的核酸的遗传重排列,然后选择包含供体病毒的核酸的重排列病毒,可以产生重排列病毒。产生和分离重排列病毒的方法是本领域中公知的 (Fields et al., 1996)。在一个实施方案中,本发明的重排列病毒包含人类、鸟类、猪或者马流感病毒的基因或者基因组区段。本发明的重排列病毒可以包括来自供体和受体流感病毒的核酸的任一组合,只要重排列病毒包含来自本发明的供体流感病毒的至少一个基因或者基因组区段。在一个实施方案中,受体流感病毒可以是马流感病毒。

[0146] 病毒蛋白质的天然的、重组的或者合成的多肽,和其肽片段也可以用作根据本发明方法的疫苗组合物。在一个实施方案中,来自多种毒株的病毒多肽可以组合在疫苗组合物中并且用于接种宿主动物。例如,基于来自至少两种不同毒株的本发明的流感病毒的病毒HA蛋白质的多肽可以组合在疫苗中。该多肽可以与一种毒株同源或者可以包含“杂合”或“嵌合”多肽,其氨基酸序列来自结合或者连接来自至少两种不同毒株的多肽。制备病毒多肽的步骤是本领域公知的。例如,使用固相合成方法 (Merrifield, 1963) 可以合成病毒多肽和肽。使用重组DNA技术也可以产生病毒多肽和肽,其中编码病毒蛋白质或者肽的多核苷酸分子在宿主细胞,如细菌、酵母或者哺乳动物细胞系中表达,并且使用本领域的标准技术纯化表达的蛋白质。

[0147] 本发明的疫苗组合物还包括裸核酸组合物。在一个实施方案中,核酸可以包含编码本发明的流感病毒的HA和/或NA蛋白质的核苷酸序列。核酸接种的方法是本领域中已知的并且描述于例如美国专利号6,063,385和6,472,375。核酸可以为质粒或者基因表达盒的形式。在一个实施方案中,将核酸包裹在脂质体中提供,将所述脂质体施用于动物。

[0148] 可以为根据本发明使用的疫苗组合物和免疫原,如多肽和核酸提供可药用载体或者稀释剂。可以根据制备药学上有用的组合物的已知方法配制用于本发明的化合物和组合物。在本领域技术人员公知和容易得到的许多来源中详细描述了制剂。例如, E.W. Martin, Easton Pennsylvania, Mack Publishing Company, 19th ed., 1995的Remington's Pharmaceutical Science描述了可以用于本发明的制剂。通常,将配制本发明的组合物使得有效量的免疫原与合适的载体组合以便促进组合物的有效施用。用于本发明方法中的组合物还可以为多种形式。这些包括例如,固体、半固体和液体剂型,如片剂、丸剂、粉剂、液体溶液剂或混悬剂、栓剂、注射液和灌注液,和喷雾剂。优选的形式取决于预期的施用方式 and 治疗应用。组合物还优选包括本领域技术人员已知的常规的可药用载体和稀释剂。用于本发明肽模拟物的载体或稀释剂的实例包括,但不限于,水、盐水、油,包括矿物油、乙醇、二甲基亚砜、明胶、环糊精、硬脂酸镁、葡萄糖、纤维素、糖、碳酸钙、甘油、氧化铝、淀粉和等同的载体和稀释剂,或者这些任一种的混合物。本发明免疫原的制剂还可以包含悬浮剂、保护

剂、润滑剂、缓冲剂、防腐剂和稳定剂。为了提供施用此类剂量用于所希望的治疗性治疗,本发明的药物组合物将有利地包含基于包括载体或稀释剂的总组合物的重量按重量计约0.1%到45%,特别1到15%的一种或多种免疫原。

[0149] 通过本领域公知的方法可以制备本发明的疫苗和免疫原性组合物。例如,通常将疫苗或者免疫原制备为注射剂,例如,液体溶液剂或者混悬剂。以与剂量制剂相容的方式和在受体中治疗有效和免疫原性的量施用疫苗或者免疫原。本领域技术人员可以容易地确定具体疫苗或者免疫原制剂的最佳剂量和施用模式。

[0150] 还可以以多抗原肽(MAP)构建体的形式提供本发明的肽和/或多肽。已经在Tam (1988) 描述了MAP构建体的制备。MAP构建体利用赖氨酸残基的核心基质,其上合成多个拷贝的免疫原(Posnett et al., 1988)。可以根据本发明的方法制备并在疫苗组合物中施用多种MAP构建体,每种含有相同或者不同的免疫原。在一个实施方案中,为MAP构建体提供一种或多种佐剂和/或与一种或多种佐剂一起施用。还产生了本发明的流感多肽并且作为包含一种或多种多肽的大分子蛋白质结构施用。公布的美国专利申请US2005/0009008描述了产生作为流感病毒疫苗的病毒样颗粒的方法。

[0151] 根据本发明的方法,将本文描述的疫苗和免疫原性组合物施用于易感宿主,通常犬科动物,并且更通常为驯养的狗,以诱导保护性免疫以抵抗病毒对宿主随后的攻击或者感染的有效量和方式施用。在一个实施方案中,宿主动物是犬科动物。犬科动物包括野生的、动物园的和驯养的犬科动物,如狼、郊狼和狐狸。犬科动物还包括狗,尤其驯养的狗,如纯种和/或杂种陪伴狗、表演狗、役用狗、放牧狗、猎狗、守卫狗、警犬、赛犬和/或实验用狗。在特定实施方案中,宿主动物是驯养的狗,如灵~~猩~~。通常肠胃外、通过注射,例如皮下、腹膜内或者肌肉注射施用疫苗或者免疫原。其他合适的施用方式包括经口或者经鼻施用。通常,将疫苗或者免疫原施用于动物至少两次,每次施用之间为一周或多周的间隔。然而,设想用于初次和加强施用疫苗或者免疫原的其他方案,并且该方案可以取决于从业医生的判断和被治疗的具体宿主动物。

[0152] 使用本领域中已知的方法,可以将疫苗制剂中的病毒和病毒感染的细胞失活或者减毒。例如,通过暴露于低聚甲醛、福尔马林、苯酚、紫外线、高温等等可以失活或者减毒完整病毒和受感染的细胞。疫苗剂量中无细胞的完整病毒的量将通常为约0.1mg到约5mg,更通常约0.2mg到约2mg。包含病毒感染的细胞系的疫苗制剂的剂量将通常含有每剂约 10^6 到约 10^8 个细胞,更通常每剂约 5×10^6 到约 7.5×10^7 个细胞。用于动物的剂量中蛋白质或肽免疫原的量可以从约0.1 μ g到10000 μ g,或约1 μ g到5000 μ g,或约10 μ g到1000 μ g,或约25 μ g到750 μ g,或约50 μ g到500 μ g,或100 μ g到250 μ g,取决于接受剂量的动物的大小、年龄等等。

[0153] 本发明的免疫原性或者疫苗组合物,如病毒或者病毒感染的细胞或者病毒蛋白质或肽可以与佐剂组合,通常刚好在施用前组合。设想用于疫苗制剂的佐剂包括苏氨酸酰基胞壁酰二肽(MDP) (Byars et al., 1987)、皂苷、*Cornebacterium parvum*、弗氏完全佐剂和弗氏不完全佐剂、铝,或者这些任一种的混合物。适于用于本发明的方法和疫苗的多种其他佐剂,如明矾,是本领域中公知的,并且设想用于本发明。

[0154] 本发明还涉及特异结合本发明的蛋白质或者肽的抗体。本发明的抗体包括单克隆和多克隆抗体组合物。优选地,本发明的抗体是单克隆抗体。在本发明中设想完整抗体和其抗原结合片段。从而,例如,合适的抗原结合片段包括Fab₂、Fab和Fv抗体片段。本发明的抗

体可以用可检测部分,如荧光分子标记(例如,萤光素或者酶)。

[0155] 本发明还涉及用于检测和鉴定本发明的流感病毒和诊断本发明的流感病毒对动物的感染的方法和组合物。本发明的方法包括检测来自动物的生物样品中犬科动物流感的存在。样品中犬科动物流感的检测可用于诊断动物中的犬科动物流感。该信息又可以提供基于区分随时间存在的犬科动物流感的水平来预后动物的能力,并且可以帮助选择动物的治疗剂和治疗,和帮助监测疗法。该方法还提供了确立在测试的动物中不存在犬科动物流感的能力。

[0156] 检测动物中犬科动物流感的能力允许评估不同的地理位置中犬科动物流感的爆发。该信息还允许早期检测从而可以隔离受感染的动物,以限制疾病的传播,和允许早期干预治疗选择。此外,得到该信息可以为准备治疗许多患病动物的医学人员提供指导,包括装备药材供应,和如果可以得到,疫苗。

[0157] 在一个实施方案中,本发明的方法涉及从受试动物,如犬科动物收集生物样品。生物样品可以是任一种生物样品,包括细胞、组织、毛发、全血、血清、血浆、乳头抽吸物、肺灌洗液、脑脊液、唾液、汗液和泪液。

[0158] 动物受试样品可以来自怀疑具有犬科动物流感病毒的动物,无论该动物是否显示出疾病症状。还可以提供对照样品或者从已知没有犬科动物流感的动物收集。可以提供额外的对照例如,以减少假阳性和假阴性结果,和证实测定中的试剂主动检测犬科动物甲型流感病毒。

[0159] 除了检测生物样品中犬科动物流感的存在或不存在,本发明中使用的检测方法可以检测犬科动物流感病毒中的突变,如核酸序列的改变,其可以由环境、药物治疗、遗传操作或者突变、损伤、食物的改变、衰老或者动物的任何其他特征引起。突变还可以导致犬科动物甲型流感变得抵抗以前有效的药物,或者使得病毒感染和在不同物种的动物或者人类中繁殖。例如,已经表明鸟类甲型流感病毒感染其他动物和人。

[0160] 在用于检测动物中流感病毒的一个实施方案中,通过收集高质量的样品、它们快速运输到检测设施、和在实验室检验前合适的保存方便了诊断。在含有受感染的细胞和分泌物的样品中最佳地检测到病毒。在一个实施方案中,在临床症状发作后前3天内采集用于直接检测病毒抗原和/或核酸和/或病毒分离的样品。多种类型的样本适于诊断上呼吸道的病毒感染,包括,但不限于,鼻拭子、鼻咽拭子、鼻咽抽吸物、鼻洗液和喉咙拭子。除了拭子外,还可以采集组织或者血清的样品,并且还可以进行侵入性步骤。

[0161] 在一个实施方案中,收集呼吸系统样品并以1-5ml病毒运送培养基运输。满足多种病毒的回收的多种培养基可通过商业途径获得。向运送培养基中加入临床样品。还可以用病毒运送培养基运送鼻或者鼻咽拭子。运送培养基的一个实例是10克小牛肉浸汁和2克牛白蛋白级分V,加入到无菌蒸馏水至400ml。也可以加入抗生素,如0.8ml硫酸庆大霉素溶液(50mg/ml)和3.2ml两性霉素B(250µg/ml)。优选通过过滤消毒培养基。鼻洗液,如无菌盐水(0.85%NaCl)也可以用于收集呼吸系统病毒的样品。

[0162] 在一个实施方案中,在临床症状发生后不久,优选不迟于7天内,从急性期动物的1-5ml量的全血收集血清。还例如在症状发生后约14天收集恢复期血清样品。在中和试验中,血清样品可以用于检测抗呼吸系统病毒的抗体。

[0163] 在一个实例中,可以在一定期限内(例如,每天一次,每周一次,每月一次,每半年

一次或者每年一次)从个体动物收集样品。在一定时期内从个体动物得到多个样品可以用于验证来自更早检测的结果,和/或鉴定对特定治疗,例如,对所选的治疗药物的应答或者抗性。

[0164] 本发明的方法可以用于检测来自动物的受试样品中一种或多种病理物质的存在,和每种病理物质的水平。可以使用用于检测病理物质的任何方法,包括但不限于,抗体测定法,包括酶联免疫吸附测定(ELISA)、间接荧光抗体(IFA)检测、血细胞凝集,和血细胞凝集抑制(HI)测定法,和蛋白质印迹。也可以使用已知的细胞培养方法。使用细胞培养物的免疫荧光或者细胞培养基(上清液)的HI测定法,可以进一步鉴定阳性培养物。

[0165] 此外,可以使用检测核酸(DNA或者RNA)或者蛋白质的方法。此类方法包括,但不限于,聚合酶链式反应(PCR)和逆转录酶(RT)PCR测试和实时测试,和定量核酸酶保护测定法。可利用通过商业途径可获得的测试试剂盒用于进行这些测定法。例如,QIAGEN (Valencia, CA)出售一步RT-PCR试剂盒,和病毒RNA提取试剂盒。

[0166] 在一个实施方案中,该方法利用对本发明的病毒或病毒蛋白质特异的抗体。在特定实施方案中,利用对本发明病毒的HA蛋白质特异的抗体。在一个实施方案中,使用对本发明病毒的NP蛋白质特异的抗体。从动物得到合适的样品,如来自鼻或者鼻咽区域的样品,并从中分离病毒或者病毒蛋白质。然后对病毒组分筛选对蛋白质,如本发明病毒的HA或者NP特异的抗体的结合。在另一实施方案中,从动物得到血清样品(或者其他含有抗体的样品)并对血清筛选结合本发明病毒的蛋白质的抗体的存在。例如,可以进行ELISA测定,其中平板壁具有结合到壁的HA和/或NP蛋白质,或者其肽片段。然后将平板壁与来自受试动物的血清或者抗体接触。动物中特异结合HA和/或NP蛋白质的抗体的存在表明该受试动物受到或者已经受到本发明的流感病毒的感染。

[0167] 在一个实施方案中,通过测定生物样品中抗病理物质的抗体的存在或不存在,检测病理物质的存在。在动物受感染后可以在血液检验中检测到抗体之前,需要一定的时间(例如,数月)。抗体一旦形成,通常持续许多年,甚至在成功地治疗该疾病之后。发现针对犬科动物甲型流感病毒的抗体不能指出感染是最近的还是在过去的某个时间。

[0168] 还可以用液体进行抗体测试。抗体测定法包括酶联免疫吸附测定(ELISA)、间接荧光抗体(IFA)测定法,和蛋白质印迹。优选地,使用多种测定法,如ELISA或者IFA,接着通过蛋白质印迹进行抗体测试。在两步方法中,使用ELISA或者IFA测定法,接着通过蛋白质印迹进行抗体测定法。认为ELISA是比IFA更可靠和更准确的测定法,但是如果不能利用EILSA,那么可以使用IFA。蛋白质印迹测试(其是更特异的测试)也可以在所有动物中进行,尤其在那些在ELISA或者IFA测定中检测为阳性或者临界阳性(含糊的)的动物中进行。

[0169] 可以用于检测流感病毒的其他基于抗体的测试包括血细胞凝集抑制测定法。如所述的使用鸡或者火鸡红细胞(Burleson et al.,1992)和Kendal et al.,1982),可以检测来自动物的生物样品中的血细胞凝集活性。在一个实施方案中,将本发明的流感或者HA蛋白或者肽与含有血清或者抗体的测试样品接触。然后加入来自动物如鸟的红细胞(RBC)。如果存在抗HA的抗体,那么RBC将不凝集。如果不存在抗HA的抗体,那么在HA存在下,RBC将凝集。对标准血细胞凝集抑制测定法的变更和修改是本领域中已知的并且设想在本发明的范围内。

[0170] 通过从样品如鼻或者鼻咽拭子分离病毒,可以确定动物的感染。使用标准方法,包

括细胞培养和鸡胚接种,可以进行病毒分离。

[0171] 在进一步的实施方案中,可以用基于核酸的测定法检测本发明的病毒。在一个实施方案中,从动物得到核酸样品并将该核酸进行PCR,如果该核酸含有对本发明的流感病毒特异的序列,那么使用的引物将产生扩增产物。在特定实施方案中,在测定中将RT-PCR用于本发明病毒。在示例的实施方案中,用实时RT-PCR测定本发明的流感病毒。PCR、RT-PCR和实时PCR方法是本领域中已知的并且已经在美国专利号4,683,202;4,683,195;4,800,159;4,965,188;5,994,056;6,814,934;和Saiki et al. (1985);Sambrook et al. (1989);Lee et al. (1993);和Livak et al. (1995)中。在一个实施方案中,PCR测定法使用对流感基质(MA)基因和/或HA基因特异的寡核苷酸。还可以对扩增产物测序以确定该产物是否具有本发明的流感病毒的序列。其他基于核酸的测定法可以用于检测和诊断本发明病毒的病毒感染并且设想此类测定法在本发明的范围内。在一个实施方案中,将含有核酸的样品进行基于PCR的扩增,使用正向和反向引物,其中所述引物对病毒多核苷酸或者基因序列特异。如果样品中的核酸是RNA,那么可以进行RT-PCR。对于实时PCR,将可检测的探针与引物一起使用。

[0172] 对许多循环流感病毒的血凝素(HA)基因特异的引物组是已知,并且正在被不断开发出来。流感病毒基因组是单链RNA,并且必须使用逆转录酶(RT)聚合酶进行DNA拷贝(cDNA)。例如,使用RT-PCR对RNA基因组的扩增需要一对寡核苷酸引物,其通常基于甲型流感病毒亚型的已知的HA序列和神经氨酸酶(NM)-1设计。可以选择引物使得它们将特异扩增仅一种病毒亚型的RNA。使用亚型特异的引物产生的DNA可以通过分子遗传学技术如测序进一步分析。试验优选阳性对照进行,或者产物通过测序并与已知序列比较来验证。不存在目标PCR产物(即,“阴性”结果)不能排除病毒的存在。然后可以在几小时内从临床拭子或者感染的细胞培养物得到结果。甲型流感病毒的PCR和RT-PCR试验由Fouchier et al.,2000和Maertzdorf et al.,2004描述。

[0173] 本发明还涉及筛选对本发明的病毒具有抗病毒活性的化合物或药物的方法。在一个实施方案中,将本发明的病毒感染的细胞与受试化合物或者药物接触。然后测定接触后病毒的量或者病毒活性。可以选择显示出抗病毒活性的那些化合物或者药物用于进一步评估。

[0174] 本发明还涉及用本发明的流感病毒感染的分离的细胞。在一个实施方案中,所述细胞是犬科动物细胞,如犬科动物肾上皮细胞。

[0175] 本发明还涉及用编码本发明多肽的本发明多核苷酸转化的细胞。优选地,在本发明的表达构建体中提供所述多核苷酸序列。更优选地,所述表达构建体提供了在细胞中过表达有效连接的本发明的多核苷酸。在一个实施方案中,用多核苷酸序列转化细胞,所述多核苷酸序列包含编码SEQ ID NO:2、4、6、8、10、12、14、16、18、20、22、24、26、28、30、32、33、34、48、50、52、54、56、58、60、62、64、66、68、70、72、74、76或78的任一个中显示的氨基酸序列,或者其功能片段或者变体的序列。在特定实施方案中,用编码SEQ ID NO:2、4、6、8、10、12、14、16、18、20、22、24、26、28、30、32、33、34、48、50、52、54、56、58、60、62、64、66、68、70、72、74、76或78中所示的氨基酸序列的多核苷酸转化的细胞分别包含SEQ ID NO:1、3、5、7、9、11、13、15、17、19、21、23、25、27、29、31、47、49、51、53、55、57、59、61、63、65、67、69、71、73、75或77中所示的核苷酸序列,或者编码SEQ ID NO:2、4、6、8、10、12、14、16、18、20、22、24、26、28、30、32、33、34、48、50、52、54、56、58、60、62、64、66、68、70、72、74、76或78的任一个的

功能片段或者变体的序列。从而,本发明涉及用包含SEQ ID NO:1、3、5、7、9、11、13、15、17、19、21、23、25、27、29、31、47、49、51、53、55、57、59、61、63、65、67、69、71、73、75或77的任一个中所示的核苷酸序列或者SEQ ID NO:1、3、5、7、9、11、13、15、17、19、21、23、25、27、29、31、47、49、51、53、55、57、59、61、63、65、67、69、71、73、75或77的任一个的片段或者变体,包括简并变体的多核苷酸序列转化的细胞。

[0176] 所转化的细胞可以是真核细胞,例如,植物细胞,包括原生质体,或者转化的细胞可以是原核细胞,例如,细菌细胞,如大肠杆菌或者枯草芽孢杆菌。动物细胞包括人细胞,哺乳动物细胞,部分犬科动物细胞、鸟类细胞和昆虫细胞。植物细胞包括,但不限于,双子叶植物细胞、单子叶植物细胞和针叶树细胞。

[0177] 本发明还涉及表达和产生本发明的病毒蛋白或者多肽的转基因植物。本发明设想用本发明的多核苷酸转化或者经育种而含有本发明的多核苷酸的植物、植物组织和植物细胞。优选地,在植物、植物组织或者植物细胞中过表达本发明的多核苷酸。植物可以用于产生本发明的流感疫苗组合物并且可以通过植物的消费施用疫苗(见,例如,美国专利号5,484,719和6,136,320)。

[0178] 本发明还涉及用于检测病毒或者诊断本发明的病毒感染的试剂盒。在一个实施方案中,试剂盒包含本发明的抗体,其特异结合本发明的流感病毒,或者其抗原性部分。在另一实施方案中,试剂盒包含本发明的一种或多种多肽或者肽。在特定实施方案中,所述多肽具有SEQ ID NO.2、4、6、8、10、12、14、16、18、20、22、24、26、28、30、32、33、34、48、50、52、54、56、58、60、62、64、66、68、70、72、74、76或78任一个中所示的氨基酸序列,或者其功能和/或免疫原性片段或变体。在另一实施方案中,试剂盒包含一种或多种本发明的多核苷酸或者寡核苷酸。在特定实施方案中,所述多核苷酸具有SEQ ID NO.1、3、5、7、9、11、13、15、17、19、21、23、25、27、29、31、47、49、51、53、55、57、59、61、63、65、67、69、71、73、75或77任一个中所示的核苷酸序列,或者其片段或者变体。试剂盒可以任选包含一种或多种对照抗体、对照多肽或者肽,和/或对照多核苷酸或者寡核苷酸。试剂盒的抗体、多肽、肽、多核苷酸和/或寡核苷酸可以在合适的容器或者包装中提供。

[0179] 本申请还涉及杂种狗作为流感病毒感染和发病机理模型的用途。在一个实施方案中,对杂种狗接种本发明的流感病毒,如犬科动物流感病毒。任选地,接种后可以对狗施用治疗剂。在用病毒接种之前,还可以对狗施用组合物用于产生针对流感病毒的免疫应答。可以在接种之前和/或之后得到组织、血液、血清和其他生物样品并使用本领域中已知的方法检查病毒的存在和组织的发病机理,所述方法包括,但不限于,PCR、RT-PCR、核酸测序,和免疫组织化学。

[0180] 本文公开的任一实施方案的任一元素可以与本文的任何其他元素或者实施方案组合,并且特别设想此类组合在本发明的范围内。

[0181] 本文提及或者引用的所有专利、专利申请、临时申请和出版物都完整(包括所有图和表)引入本文作为参考,直到它们与本说明书的明确教导不一致的程度。

[0182] 实施例1—6的材料和方法

[0183] 从灵~~猩~~收集血液和鼻拭子

[0184] 从在赛跑狗舍中经历呼吸系统疾病爆发的临床上患病的或者正常的灵~~猩~~通过颈

静脉穿刺收集急性和恢复期血液样品。在急性样品后4到12周收集恢复期样品。收获血清并在-80℃保存。收集鼻拭子并在递交用于细菌分离之前置于具有炭的Amies运送培养基(Becton Dickinson Biosciences)中。

[0185] 灵类的尸体剖检

[0186] 由佛罗里达大学兽医学院(University of Florida College of Veterinary Medicine(UF CVM))的解剖病理学处(Anatomic Pathology Service)对2004年1月在佛罗里达赛场的爆发中死亡的8只灵类的5只进行完全的尸体剖检。另一只狗的尸体剖检在私立的兽医诊所进行,将组织递交到UF CVM用于组织病理学诊断。将组织用10%中性缓冲福尔马林固定,包埋在石蜡中,并对5-μm切片用苏木精和伊红染色用于组织病理学诊断或者处理用于如下述的免疫组织化学。递交未固定的组织用于细菌培养并且也保存在-80℃。

[0187] 犬科动物呼吸系统病原体的血清学试验

[0188] 将配对的急性和恢复期血清样品递交给康耐尔大学兽医学院(Cornell University College of Veterinary Medicine)的动物健康诊断实验室(Animal Health Diagnostic Laboratory(AHDL)),对犬瘟热病毒、2型腺病毒和副流感病毒进行血清中和测定。抗体效价表达为抑制细胞培养物的病毒感染的血清的最终稀释度。血清转变表明病毒感染,将血清转变定义为急性和恢复期样品之间抗体效价升高 ≥ 4 倍。没有检测到对这些病毒病原体的血清转变。

[0189] 犬科动物细菌呼吸系统病原体的微生物试验

[0190] 将配对的鼻拭子和死后组织递交给UF CVM的诊断临床微生物学/寄生虫学/血清学处(Diagnostic Clinical Microbiology/Parasitology/Serology Service)用于细菌分离和鉴定。在非选择培养基以及选择博德特氏菌(*Bordetella*)种(Regan-Lowe;Remel)和支原体(*Mycoplasma*)种(Remel)的培养基上培养样品。在没有报告生长前,保持所有培养物21天。还将一些灵的鼻拭子递交给堪萨斯州立大学兽医学院(Kansas State University College of Veterinary Medicine)的诊断医学/病理生物学系(Department of Diagnostic Medicine/Pathobiology)用于细菌培养。在所检验的70只临床上患病的狗中,从1只狗的鼻腔分离支气管博德特氏菌(*Bordetella bronchiseptica*),而从33只狗的鼻腔回收支原体。通常用化脓性鼻涕从狗的鼻腔回收出血败血性巴斯德氏菌(*Pasteurella multocida*)。在2004年1月的爆发中死亡的两只狗在死亡后肺中具有大肠杆菌的不足的生长,一只狗具有大肠杆菌和犬链球菌(*Streptococcus canis*)的不足的生长,另一只具有铜绿假单胞菌(*Pseudomonas aeruginosa*)和酵母的不足的生长。从死亡狗的气管或者肺中没有分离到支气管博德特氏菌或者支原体。

[0191] 从死后组织分离病毒

[0192] 将冷冻的组织解冻并在10倍体积的补充0.5%牛血清白蛋白(BSA)和抗生素的极限必需培养基(MEM)中匀浆。通过离心除去固体碎片并将上清液接种到培养的细胞或者10天龄的含胚的鸡蛋中。将来自死亡灵类的组织匀浆物接种到不同的细胞培养物中,该培养物支持多种病毒病原体的复制。细胞培养物包括Vero(非洲绿猴肾上皮细胞,ATCC No.CCL-81)、A-72(犬肿瘤成纤维细胞,CRL-1542)、HRT-18(人直肠上皮细胞,CRL-11663)、MDCK(犬肾上皮细胞,CCL-34)、原代犬肾上皮细胞(AHDL,Cornell University)、原代犬肺上皮细胞

(AHD) 和原代牛睾丸细胞 (AHD)。在补充 2.5 µg/mL TPCK-处理的胰蛋白酶 (Sigma) 的 MEM 中培养 MDCK 和 HRT 细胞; 在补充 10% 胎牛血清和抗生素的 MEM 中培养剩余的细胞系。在 25 cm² 瓶中 37°C 下在含有 5% CO₂ 的增湿空气中培养细胞。用经补充的 MEM 接种对照培养物。每天观察培养物的形态改变并在接种后 5 天收获。将收获的液体和细胞通过离心澄清并如最初接种所描述的接种在新鲜细胞上; 进行两次盲法传代。使用鸡或者火鸡血红细胞如所述的 (Burleson et al., 1992; Kendal et al., 1982) 测定澄清的上清液中的血细胞凝集活性。对于鸡胚中的病毒分离, 将 0.1 mL 组织匀浆物接种在尿膜囊中并在 35°C 下培养 48 小时。两次盲法传代后, 如所述的测定尿囊液中的血细胞凝集活性 (Burleson et al., 1992; Kendal et al., 1982)。

[0193] RT-PCR、核苷酸测序和系统进化分析

[0194] 使用 RNeasy 试剂盒 (Qiagen, Valencia, CA) 根据生产商的使用说明, 从组织培养物上清液或者尿囊液提取总 RNA。使用一步 RT-PCR 试剂盒 (Qiagen, Valencia, CA) 根据生产商的使用说明将总 RNA (10 ng) 逆转录成 cDNA。如以前描述的 (Klimov et al., 1992a), 使用通用的基因特异性引物组进行 cDNA 中 8 种流感病毒基因的编码区的 PCR 扩增。所得 DNA 扩增产子用作 Applied Biosystems 3100 自动化 DNA 测序仪上的自动化测序的模板, 使用循环测序染料终止化学 (ABI)。用 GCG **Package**[®], 版本 10.0 (Accelrys) (Womble, 2000) 分析核苷酸序列。用 Phylogeny Inference **Package**[®] 版本 3.5 估计系统发生和从核苷酸序列计算自展值 (Felsenstein, 1989)。使用 **MEGA**[®] 程序 (Kumar et al., 2004) 中实现的 Tamura-Nei gamma 模型, 将系统树与近邻连接分析产生的那些系统树比较, 并通过 **PAUP**[®] 4.0 Beta 程序 (Sinauer Associates) 证实。

[0195] 狗的实验接种

[0196] 使用四只 6 个月龄的特定无病原体的小猎兔犬 [2 只雄性和 2 只雌性 (Liberty Research)]。体检和基线血试验, 包括全血细胞计数/微分、血清化学小组和尿分析确定动物是健康的。将它们养在试验动物照料评估和认证协会 (Association for Assessment and Accreditation of Laboratory Animal Care) 认证的 BSL2-增强型设施中。每天两次持续 7 天记录基线直肠温度。通过异丙酚 (**Diprivan**[®], Zeneca Pharmaceuticals, 0.4 mg/kg 体重以生效) 的静脉内注射麻醉狗用于用气管内插管进行插管法。每只狗接种总剂量为 10^{6.6} 半数组织培养感染量 (TCID₅₀) 的 A/Canine/Florida/43/2004 (Canine/FL/04) (H3N8) 病毒, 将一半的剂量通过气管内插管施用于远端气管并将另一半剂量通过导管施用于鼻道深处。接种后 (p.i.) 14 天, 每天两次进行体检和直肠温度记录。通过颈静脉穿刺在接种后 0、3、5、7、10 和 14 天收集血样 (4 mL)。在接种后 0 到 5、7、10 和 14 天用聚酯拭子 (Fisher Scientific) 从每只狗收集鼻和鼻咽样品。将拭子置于病毒运送培养基 (Remel) 中并保存在 -80°C。通过在接种后 5 天静脉内接种 Beuthanasia-D[®] 溶液 (1 mL/5 kg 体重; Schering-Plough Animal Health Corp) 对两只狗实施安乐死 (1 只雄性和 1 只雌性) 并在第 14 天对剩下的 2 只狗进行尸体剖检。如所述的处理用于组织学分析的组织。用于病毒培养的组织在 -80°C 保存。该研究得到佛罗里达大学机构动物管理和使用委员会 (University of Florida Institutional Animal Care and Use Committee) 的批准。

[0197] 病毒从实验接种的狗的脱落

[0198] 通过离心澄清拭子运送培养基制备的肺匀浆物和拭子提取物的连续稀释液用补充0.5%BSA和抗生素的MEM建立。如所述的 (Burleson et al., 1992) 使用单层MDCK细胞在6孔组织培养板中进行噬菌斑测定。用含有0.8%琼脂糖和1.5ug/mL TPCK-胰蛋白酶的补充的MEM覆盖接种的细胞单层。在固定和用结晶紫染色前,在含有5%CO₂的增湿的空气中37℃下培养细胞72小时。病毒浓度表达为每克组织或者每个拭子的噬斑形成单位 (PFU)。

[0199] 免疫组织化学

[0200] 在Bond-Rite™载玻片 (Richard-Allan Scientific, Kalamazoo, MI) 上封固来自灵~~捷~~和小猎兔犬的脱蜡和再水化的5-μm肺组织切片并随后用蛋白酶K (DakoCytomation, Carpinteria, CA) 接着用过氧化物酶封闭试剂 (**Dako®** EnVision™Peroxidase Kit, Dako Corp.) 处理。将切片与抗犬瘟热病毒 (VMRD, Inc.)、犬2型腺病毒 (VMRD, Inc.)、犬副流感病毒 (VMRD, Inc.) 或者甲型流感H3 (Chemicon International, Inc.) 的单克隆抗体的1:500稀释液在室温下温育2小时。对照包括用小鼠IgG (1mg/mL, Serotec, Inc.) 温育相同的切片,并温育单克隆抗体与正常的犬肺切片。用一级抗体处理后,用二级免疫过氧化物酶和过氧化物酶底物试剂 (**Dako®** EnVision™Peroxidase Kit, Dako Corp.) 根据生产商的使用说明温育切片。将切片用苏木精复染,用Clarifier#2和Bluing Reagent (Richard-Allan Scientific, Kalamazoo, MI) 处理,脱水,并用Permunt (ProSciTech) 盖片。

[0201] 血细胞凝集抑制 (HI) 测定法

[0202] 在37℃下用受体破坏酶 (RDE, Denka) (1份血清:3份RDE) 温育血清样品16小时,然后在56℃热失活60分钟。在37℃下在MDCK细胞中培养Influenza A/Canine/FL/04 (H3N8) 病毒36-48小时。收获病毒培养上清液,通过离心澄清,并在-80℃保存。如以前描述的进行HI测定法 (Kendal et al., 1982)。简言之,将25μl中的4血凝单位病毒加入微量滴定孔中等体积的连续稀释的血清,并在室温温育30分钟。加入等体积的0.5%v/v火鸡红细胞并在30分钟后通过视觉评估血细胞凝集效价。将终点HI效价定义为完全抑制血细胞凝集的血清的最后稀释度。将血清转变定义为配对的急性和恢复期样品之间的HI效价≥4倍增加。将单个样品的血清阳性定义为≥1:32的HI抗体效价。

[0203] 微量中和 (MN) 测定

[0204] 通过如以前描述的MN测定法 (Rowe et al., 1999) 检测对A/Canine/FL/04 (H3N8) 的中和血清抗体应答,只是在测定前对犬血清进行如上述的RDE处理。将终点效价定义为得到病毒的100TCID₅₀50%中和的血清的最高稀释度。将血清转变定义为配对的急性和恢复期样品之间MN效价≥4-倍增加。将单个样品的血清阳性定义为MN效价≥1:80。

[0205] 下面是阐明实施本发明方法的实例。不应该将这些实施例理解为限制。除非另外指出,所有百分数都是按重量计并且所有溶剂混合物比例都是按体积计。

[0206] 实施例1

[0207] 在2004年1月,在Florida赛场的2个狗舍中喂养的22只竞赛灵~~捷~~和为这些狗舍提供狗的当地农场中发生了呼吸系统疾病的爆发。在每个狗舍建筑中有约60只狗,农场中约300只狗。在6天内发生了爆发,之后没有鉴定到新的病例。22只狗的14只具有39.5到41.5℃的发热,发热的作呕性咳嗽10到14天,并且最终恢复。在剩余的8只狗中,6只明显健康的狗

出乎意料地死亡,具有口和鼻出血。两只其他狗由于快速恶化,在发生口鼻出血的24小时内实施安乐死。这些狗都具有41℃发热。8例死亡中4例在狗舍建筑物中发生,4例在农场发生。50%的死亡发生在爆发的第3天。22只狗的年龄为17个月到4岁,但是73%的为17到33个月龄。

[0208] 两种临床综合征是明显的:较轻微的病,其特征是最初的发热和然后咳嗽10—14天(14只狗),随后恢复,或者过急性死亡,伴随着呼吸道中的出血(8只狗,死亡率为36%)。对8个死亡病例的6例进行了尸体剖检。所有狗都在肺、纵隔和胸膜腔中具有广泛的出血。对呼吸道的组织学检查揭示除了肺部出血外,所有狗都具有气管炎、支气管炎、细支气管炎和化脓性支气管肺炎(图3)。这些组织中上皮层和气道腔中浸润嗜中性粒细胞和巨噬细胞。将从这些狗制备的肺匀浆物接种到多种猴、人、牛和犬细胞系用于病毒培养。来自一条狗的肺匀浆物在胰蛋白酶存在下在培养的Madin-Darby犬肾上皮细胞(MDCK)中引起细胞病变效应,并且细胞培养上清液凝集了鸡红细胞。通过商业ELISA检测甲型和乙型流感病毒的核蛋白,和通过使用对甲型流感病毒的基质基因特异的引物进行PCR分析,提供甲型流感病毒的初步证据。此外,通过针对马甲型流感H3亚型的参照抗血清抑制了血细胞凝集活性,但是通过对人甲型流感亚型H1-H11和H13特异的抗血清没有抑制血细胞凝集活性(表3)。为了表征病毒的分子性质,我们测定了病毒基因组的8个RNA区段的核苷酸序列。与已知的流感病毒基因的序列比较和系统进化分析表明犬分离群的8种基因与来自同时代的马甲型流感(H3N8)病毒最相似,它们与所述病毒的基因共有 $\geq 96-97\%$ 的序列同一性(图1A,表4)。相比,来自鸟类、猪和人甲型流感分离株的代表性基因与犬分离群具有 $\leq 94\%$ 同一性(表4)。这些数据将犬分离群A/Canine/Florida/43/04(Canine/FL/04)鉴定为与马流感病毒的同时代谱系密切相关的甲型流感H3N8病毒。因为犬分离群的所有基因都是马流感病毒来源的,所以我们推断马流感病毒的整个基因组已经转移到狗。

[0209] 实施例2

[0210] 为了研究Canine/FL/04在灵~~猴~~中的临床和病理学观察中的作用,我们使用抗甲型流感H3的单克隆抗体对肺组织进行了免疫组织化学染色(IHC)。在支气管和细支气管上皮细胞的细胞质、支气管腺上皮细胞和气道腔和肺泡腔的巨噬细胞中总是检测到病毒H3抗原(图2A)。这些数据支持在多只狗中H3亚型流感病毒的肺部感染的诊断。

[0211] 实施例3

[0212] 为了确定Canine/FL/04-样病毒参与呼吸系统疾病爆发的病因,我们通过血细胞凝集抑制(HI)和微量中和法(MN)分析了来自11只病狗和16只无症状接触狗的急性和恢复期血清。在两种测定法中,在11只中的8只(73%)病狗中发生了血清转变,其定义为对Canine/FL/04的抗体效价从急性到恢复期升高 ≥ 4 -倍(表1)。在HI测定中,16只中的6只(38%)无症状接触狗中发生血清转变,而在MN测定法中,16只中的8只(50%)血清转变(表1)。血清转变数据表明Canine/FL/04-样病毒对狗的感染,其与多数动物中呼吸系统疾病的发作在时间上吻合。

[0213] 在与病狗一起喂养的额外的46只无症状狗的爆发后3个月,收集单个血清样品。其中,在两种测定法中43只(93%)为血清阳性。对于所测试的73只狗的总群体中,93%的在两种测定中为血清阳性,包括82%(9/11)只病狗和95%(59/62)健康接触狗。没有呼吸系统疾病史的狗中的高血清阳性率表明犬科动物流感病毒的多数感染是亚临床的并且提示病毒在

狗中的有效传播。亚临床感染是否促进病毒的传播还是未知的。

[0214] 实施例4

[0215] 为了更好地理解Canine/FL/04病毒感染狗的能力,用 $10^{6.6}$ 半数组织培养感染量(TCID₅₀)通过气管内和鼻内途径接种四只6月龄purpose-品种的小猎兔犬的每一只。所有狗在接种后前2天(p.i.)都发生发热(直肠温度 $\geq 39^{\circ}\text{C}$),但是在14天的观察期内没有一只显示出呼吸症状,如咳嗽或者鼻涕。通过用鼻或者口咽拭子定量病毒检查病毒脱落。4只狗的仅仅两只脱落可检测量的病毒。一只狗在接种后1和2天脱落病毒(每个拭子 $1.0-2.5\log_{10}\text{PFU}$),而另一只狗在接种后连续四天脱落病毒(每个拭子 $1.4-4.5\log_{10}\text{PFU}$)。在5p.i.对两只狗的尸体剖检揭示了类似于在灵~~猩~~中的自发疾病中发现的坏死和增生性气管炎、支气管炎和细支气管炎,但是没有肺出血或者支气管肺炎。通过IHC在支气管、细支气管和支气管腺的上皮细胞的细胞质中检测到病毒H3抗原(图2B)。从一只狗的肺组织回收感染性病毒。在接种后14天对剩下两只狗的尸体剖检显示了呼吸系统组织中最小的组织学改变,通过IHC没有检测到病毒H3抗原,从肺匀浆物没有回收病毒。到接种后第7天用MN测定法检测到后两只狗中的血清转变,到第14天抗体效价进一步增加2到3倍。这些结果确定狗对Canine/FL/04感染的易感性,如通过发热反应、在肺实质中存在病毒抗原和感染性病毒、流感的典型组织学发现,和血清转变所证实。在实验接种的小猎兔犬中不能再现严重疾病和死亡并不令人惊奇,因为大部分的天然感染的灵~~猩~~是无症状的。

[0216] 实施例5

[0217] 为了研究在2004年1月爆发前,Canine/FL/04-样流感病毒是否已经在佛罗里达的灵~~猩~~群体中传播,使用HI和MN测定法对来自65只竞赛灵~~猩~~的存档血清测试抗Canine/FL/04的抗体。在来自1996到1999年的33个狗样品中没有检测到抗体。在2000到2003年间的32个狗样品中,9个样品在两种测定法中都是血清阳性的—1个在2000年,2个在2002年,6个在2003年(表5)。血清阳性狗位于佛罗里达赛场,这些赛场与从1999到2003年未知病因的呼吸系统疾病爆发有关,提示Canine/FL/04-样病毒可能是那些爆发的致病因子。为了进一步研究该可能性,我们检查了来自2003年3月死于出血性支气管肺炎的灵~~猩~~的存档组织。接种到MDCK细胞和鸡胚的来自一只狗的肺匀浆物产生了H3N8流感病毒,称作A/Canine/Florida/242/2003(Canine/FL/03)。对Canine/FL/03的完整基因组的序列分析揭示与Canine/FL/04的 $>99\%$ 同一性(表4),表明Canine/FL/04-样病毒在2004年前已经感染了灵~~猩~~。

[0218] 实施例6

[0219] 从2004年6月到8月,在佛罗里达、德克萨斯、阿拉巴马、阿肯色、西佛吉尼亚和堪萨斯州的14个赛场的几千只竞赛灵~~猩~~中发生了呼吸系统疾病爆发。

[0220] 一些赛场的官员估计他们至少80%的狗群体患有临床疾病。多数狗具有与2004年1月爆发中的狗类似的发热($\geq 39^{\circ}\text{C}$)和咳嗽的临床病征,但是许多狗也具有粘液脓性鼻涕。报导了多例死亡,但是不能确定准确的死亡率。

[0221] 我们收集了位于4佛罗里达赛场的94只狗的配对的急性和恢复期血清:56%的这些狗对Canine/FL/04的抗体效价升高 ≥ 4 倍,100%为血清阳性的(表6)。来自西佛吉尼亚和

堪萨斯州的29只狗的恢复期血清也具有抗Canine/FL/04的抗体。我们从德克萨斯赛场的死于出血性支气管肺炎的灵~~猩~~的肺分离了甲型流感(H3N8)病毒。该分离群(称作A/Canine/Texas/1/2004(Canine/TX/04))的完整基因组的序列分析揭示与Canine/FL/04 $\geq 99\%$ 的同一性(表4)。在13个月期间内和从不同的地理位置从致死的犬病例分离出三种密切相关的流感病毒,以及在竞赛灵~~猩~~中普遍感染的实质性血清学证据,提示Canine/FL/04-样病毒在狗群体中的持续传播。

[0222] Canine/FL/03、Canine/FL/04和Canine/TX/04的HA基因的系统进化分析表明它们组成单源群,具有有力的自引支持度,其与2002和2003年分离的马病毒的同时代H3基因明显不同(图1B)。其他7种基因组区段的系统发生分析和逐对核苷酸序列比较提示犬基因隔离为与马病毒谱系最密切相关的不同的亚谱系(数据未显示,和表4)。在HA中存在4个标记氨基酸改变也支持犬流感基因聚类为与马流感分离的单源群(表2)。与来自2003和2004年的血清学结果一起,这些数据与如下相一致:从马到狗的单个病毒传播事件和随后该病毒在灵~~猩~~群体中的水平扩散。然而,不能正式排除来自未鉴定的储存物种的流感病毒的该独特谱系的重复导入,虽然这无论如何不太可能。

[0223] 病毒HA是流感病毒的宿主物种特异性的关键决定子(Suzuki et al., 2000)。为了鉴定HA内可能与对犬科动物宿主的适应有关的残基,我们比较了犬HA的推导的氨基酸序列与同时代马病毒的那些氨基酸序列。在马和犬成熟HA共有氨基酸序列中有四个氨基酸不同:N83S、W222L、I328T和N483T(见表2)。犬病毒当与共有的马序列比较时具有氨基酸缺失。因此,HA马序列中的氨基酸位置7是HA犬序列中的位置6,HA马序列中的氨基酸位置29是HA犬序列中的位置28,HA马序列中的氨基酸位置82是HA犬序列中的位置82,等等。从而,四个替代的氨基酸在SEQ ID NO:33和SEQ ID NO:34中所示氨基酸序列的位置82、221、327和482。在共有序列位置83上丝氨酸对天冬酰胺的替代是未知功能重要性的改变,因为在来自其他物种的H3分子中发现多种极性残基。在接近H3HA的切割位点的共有序列位置328上的严格保守的异亮氨酸已经被苏氨酸替代。发病机理中宿主蛋白酶对HA切割的重要作用提示该改变值得进一步研究。在共有序列位置222上亮氨酸对色氨酸的替代是相当值得注意的,因为它代表与唾液酸结合口袋相邻的非保守改变,其可以调节受体功能(Weis et al., 1988)。有趣的是,在222位的亮氨酸不是犬H3HA特有的,因为它通常被发现于H4、H8、H9和H12HA亚型中(Nobusawa et al., 1991; Kovacova et al., 2002)。亮氨酸替代与对哺乳动物宿主的病毒特异性可能更相容,因为已经报导了亚型H4病毒对猪的感染(Karasin et al., 2000)和亚型H9病毒对人和猪的感染(Peirisi et al., 1999)。在共有序列483位上天冬酰胺对苏氨酸的替代导致在HA2亚基中糖基化位点的丧失,该位点在所有HA亚型中保守(Wagner et al., 2002)。尽管HA中这些氨基酸改变对于马病毒对狗的适应性的的重要性还有待确定,但是以前已经观察到与物种间转移有关的类似的氨基酸改变(Vines et al., 1998; Matrosovich et al., 2000)。在表19到25中显示了本发明的其他流感病毒蛋白质和马共有序列之间的氨基酸差异。

[0224] 最初感染竞赛灵~~猩~~的马流感病毒的来源仍然是推测性的。在灵~~猩~~竞赛场的狗舍不位于附近的马或者马赛场,提示该灵~~猩~~和脱落病毒的马之间的接触不能充分解释2004

年在不同州的多处爆发。接触马病毒的潜在来源是对灵~~灵~~喂饲马肉,所述灵~~灵~~的食物被补充食品加工厂的生肉,食品加工厂提供可能携带流感的尸体,包括马。该感染方式的先例包括H5N1禽流感病毒向进食受感染的鸡尸体的猪和动物园猫科动物的种间传播(Webster, 1998;Keawcharoen et al.,2004;Kuiken et al.,2004)。尽管这是马流感向狗的最初引入的似乎合理的途径,但是它不能解释最近在不同州的几千只狗中的多次流感爆发。我们的实验接种研究表明在狗的鼻道和口咽中存在病毒,尽管处于适度的滴度。然而,这些结果表明脱落是可能的,并且通过大滴气溶胶、污染物进行的病毒的狗-狗传播或者间接粘膜接触可以在该疾病的动物流行病学中起作用。

[0225] 全部哺乳动物流感病毒向不相关的哺乳动物物种的种间转移是罕见的事件。以前的研究已经提供了狗与人甲型流感(H3N2)病毒的暂时感染的有限的血清学或者病毒学证据,但不是血清学和病毒学证据两者(Nikitin et al.,1972,Kilbourne,et al.,1975;Chang et al.,1976;Houser et al.,1980)。然而,没有犬科动物宿主中持续传播的证据。尽管充分记载了猪流感病毒从猪向人的直接转移(Dacso et al.,1984;Kimura et al.,1998;Patriarca et al.,1984;Top et al.,1977),但是没有猪病毒在人宿主中适应的证据。在该报导中,我们提供了完整马甲型流感(H3N8)病毒向另一种哺乳动物物种狗的种间传播。犬病毒HA中独特的氨基酸替代,以及美国多个州中狗感染的血清学证据,提示该病毒适应了犬科动物宿主。因为狗是人类的主要陪伴动物,所以这些发现具有公共健康的牵连;狗可能提供新的甲型流感病毒向人类传播的新的来源。

[0226]

表 1.对 A/Canine/Florida/43/04 (H3N8)的抗体应答				
	病狗(11) ^a		健康接触者(16) ^b	
应答	HI ^c	SN ^d	HI	SN
血清转变 (%) ^e	73	73	38	50
血清阳性 (%) ^f	82	82	100	100
几何平均效价 ^g	329	424	268	431

[0227] ^a具有疾病的临床病征的狗的数目。

[0228] ^b与临床上患病狗接触喂养的无症状狗的数目。

[0229] ^c使用A/Canine/Florida/43/04病毒的血细胞凝集抑制(HI)测定法。

[0230] ^d使用A/Canine/Florida/43/04病毒的微量中和(MN)测定法。

[0231] ^e具有配对的急性和恢复期血清中抗体效价增加至少4倍的狗的百分比。

[0232] ^f在恢复期血清中具有阳性抗体效价(HI效价 $\geq$ 32;MN效价 $\geq$ 80)的狗的百分比。

[0233] ^g恢复期血清的几何平均抗体效价。

[0234]

表 2. 犬和马 H3 血凝素之间的氨基酸差异				
马 H3 共有序 列	Can/FL/03	Can/FL/04	Can/TX/04	潜在的功能重要性
G7*	D	- [†]	-	D 也在鸭和人 H3 HA 中发现
I29	-	M	M	I 在来自所有物种的 H3 HA 中保守
N83	S	S	S	在其他物种的 H3 HA 中该位置上存在的多种极性氨基酸
S92	-	N	-	N 存在于一些鸭 H3 HA 中
L118	-	-	V	L 在所有 H3 HA 中保守
W222	L	L	L	W 在所有物种的多数 H3 HA 中保守; 位于受体结合部位附近
A272	V	A	V	V 存在于一些最近的马分离群中
I328	T	T	T	T 在所有鸟类、猪或者人 H3 HA 中严格保守
N483	T	T	T	N 发生在所有 H3 和其他 HA 亚型中。替代导致失去糖基化位点。
K541	-	R	-	碱性氨基酸保守改变

[0235] *成熟H3HA中的氨基酸残基(单字母代码)和位置。氨基酸代码是:A=丙氨酸,D=天冬氨酸,G=甘氨酸,I=异亮氨酸,K=赖氨酸,L=亮氨酸,M=甲硫氨酸,N=天冬酰胺,R=精氨酸,S=丝氨酸,T=苏氨酸,V=缬氨酸,W=色氨酸。

[0236] [†]表示没有从共有马H3HA的改变。

[0237]

表 3. 通过针对不同 HA 亚型的参考血清对病毒分离群的血细胞凝集抑制		
参考抗血清	HA 特异性	HI 效价 ^a
Puerto Rico/8/34	H1	5
Swine/Iowa15/30	H1	5
Singapore/01/57	H2	5
Shanghai/11/87	H3 ^b	5
Equine/Miami/1/63	H3	160
Duck/Czechoslovakia/56	H4	5
Tern/South Africa/61	H5	5
Turkey/Massachussetts/65	H6	5
Fowl Plague/Dutch/27	H7	5
Fowl Plague/Rostock/34	H7	5
Equine/Prague/1/56	H7	5
Turkey/Ontario/6118/68	H8	5
Quail/Hong Kong/G1/97	H9 ^b	5
Chicken/Hong Kong/G9/97	H9 ^b	5
Chicken/Germany/49	H10	5
Duck/England/56	H11	5
Gull/Maryland/704/77	H13	5
正常绵羊血清	-	5
正常白鼬血清	-	5

[0238] ^a对来自#43狗的病毒分离群的血细胞凝集抑制滴定度。[0239] ^b在白鼬中产生多克隆抗血清,而在绵羊或山羊中产生所有其他抗血清。

[0240]

表 4. A/Canine/Florida/43/04 (H3N8)基因与马、鸟类、猪和人的甲型流感毒株的序列同源性				
基因	马	鸟类	猪	人
PB2 DQ1241 47	96.9 (98.7)^a Eq/Kentucky/2/8 M73526	88.6 (96.8) Mall/Alberta/98 /85 AY633315	87.9 (96.8) Sw/Ontario/ 01911-1/99 AF285892	86.2 (96.4) PR/8/34 (HK/213/ 03) AF38911 5 (AY57638 1)
PB1 DQ1241 48	97.1 (98.8) Eq/Tennessee 5/86 M25929	83.9 (97.1) Ck/British Columbia/04 (Gull/Md/704/77) AY61675 (M25933)	83.9 (97.1) Sw/Korea/S109 /04 (Sw/Saskatchewan/ 18789/02) AY790287 (AY619955)	83.9 (97.1) WSN/33 (Sing/1/57) J02178 (M25924)
PA DQ1241 49	96.3 (97.5) M26082 Eq/Tennessee /5/86	87.0 (94.3) Ck/Chile/4591/0 2 (Ostrich/SA/081 03/95) AY303660(AF5 08662)	84.3 (94.6) Sw/Hong Kong/ 126/02 M26081	83.8 (93.4) Taiwan/2/ 70 (Viet Nam/ 1203/04) AY21019 9 (AY81813 2)

[0241]

HA (H3) DQ1241 90	97.4 (97.1) Eq/FL/1/93 L39916	80.7 (89.0) Dk/Norway/1/03 AJ841293	80.0 (87.7) Sw/Ontario/427 29a/01 AY619977	81.8 (87.9) HK/1/68 AF34817 6
NP DQ1241 50	96.6 (97.9) Eq/Tennessee /5/86 M30758	87.9 (95.1) Ck/Chile/17682 2/02 AY303658	85.4 (93.5) Sw/Ontario/427 29a/01 (Sw/Fujian/1/2 003) AY619974 (AY747611)	84.7 (93.0) HK/1073/ 99 (Hong Kong /538/97) AF25574 2 (AF25575 1)
NA (N8) DQ1241 51	96.8 (97.0) Eq/Tennessee /5/86 L06583	84.0 (85.2) Dk/NJ/2000 L06583	na^b	na^b
M DQ1241 52	97.9 (95.7) Eq/Tennessee /5/86 (Eq/Kentuck y/92) M63529 (AF001683)	94.1 (94.0) Tky/Mn/833/80 AF001683	93.7 (93.5) Sw/Saskatchew an/ 18789/02 M63527	91.2 (95.4) WSN/33 (Hong Kong/ 1073/99) J02177 (AJ27864 6)
NS DQ1241	97.5 (95.7) Eq/Tn/5/86	92.0 (90.4) Mal/NY/6750/78	91.1 (89.1) Sw/China/8/78	91.4 (90.0)

[0242]

53	(Eq/Kentucky/92) M80973 (AF001671)	M80945	(Sw/Korea/s452/04) M80968 (AY790309)	Brevig Mission/1/18 AF333238
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[0243] ^a A/Canine/Florida/43/04 (H3N8) 基因与来自所述物种的流感病毒分离群的多数同源基因的百分比核苷酸和氨基酸(括号内)序列同一性,接着是它们的Genbank序列数据库检索号。

[0244] ^b不可应用:在人或者猪病毒中从没有报道N8神经氨酸酶。

[0245]

表 5. 对 1996 到 2003 年收集的灵缇血清中 A/canine/Florida/43/04 (H3N8) 的抗体效价

	年 ^a					
	1996	1997	1998	2000	2002	2003
测试的狗的数目	8	6	19	4	6	22
血清阳性狗的数目	0	0	0	1	2	6
抗体效价 ^b				512	232, 524	280-2242

[0246] ^a从佛罗里达竞赛灵缇收集血清样品年份。

[0247] ^b血清阳性狗的微量中和测定抗体效价,包括6只2003年血清阳性狗。

[0248]

表 6. 2004 年 6 月在佛罗里达赛场的竞赛灵缇中对 A/canine/Florida/43/04 (H3N8)的抗体应答				
应答	赛场 A	赛场 B	赛场 C	赛场 D
测试的狗的数目 ^a	37	10	22	25
血清转变(%) ^b	46	90	100	64
血清阳性 (%) ^c	100	100	100	100
几何平均效价 ^d	401	512	290	446

[0249] ^a使用A/canine/Florida/43/04 (H3N8) 通过HI测试的临床患病狗的数目。

[0250] ^b在急性和恢复期血清之间抗体效价升高 ≥ 4 倍的狗的百分比。

[0251] ^c在恢复期血清中具有阳性抗体效价 (HI效价 >16) 的狗的百分比。

[0252] ^d恢复期血清的几何平均抗体效价。

[0253] 实施例7-11的材料和方法

[0254] 犬组织

[0255] 由佛罗里达大学兽医学院的解剖病理学处对6只杂种狗和一只宠物Yorkshire Terrier狗进行尸体剖检,所述杂种狗在2005年4月/5月流感爆发期间在佛罗里达东北部的收容所死亡,所述Yorkshire Terrier狗在2005年5月流感病毒爆发期间在佛罗里达东南部的兽医诊所中死亡。将组织用10%中性缓冲福尔马林固定,包埋在石蜡中,并用苏木精和伊红染色5- μm 的切片用于组织病理学诊断。在病毒学分析之前,未固定的组织在 -80°C 保存。

[0256] 从犬组织样品提取RNA

[0257] 将来自7只狗的每一只的冷冻的肺组织解冻并在补充0.5%牛血清白蛋白 (BSA) (Kendall, Lifeline Medical Inc., Danbury, CT) 和抗生素 (庆大霉素和环丙沙星) 的极限必需培养基 (MEM) 中用一次性组织研磨机匀浆。使用商业试剂盒 (**RNeasy**[®] Mini Kit, QIAGEN Inc., Valencia, CA) 根据生产商的使用说明提取总的RNA并用60 μL 最终体积的缓冲液洗脱。还从自没有呼吸系统疾病的狗收集的肺组织提取总RNA。

[0258] 实时RT-PCR

[0259] 使用含有ROX作为被动参考染料的 **QuantiTect**[®] Probe RT-PCR试剂盒 (QIAGEN Inc., Valencia, CA), 对从犬组织样品提取的总RNA进行一步定量实时RT-PCR。简言之, 两个引物-探针组用于检测每种样品中的甲型流感序列 (表7)。一个引物-探针组对于犬血凝素 (H3) 基因序列是选择性的。另一个引物-探针组靶定甲型流感病毒的基质 (M) 基因的高度保守区。对于每个实时RT-PCR反应, 向含有12.5 μL 2X **QuantiTech**[®] Probe RT-PCR Master Mix, 0.25 μL **QuantiTech**[®] RT Mix, 正向和反向引物 (每种0.4 μM 终浓度), 探针 (0.1 μM 终浓度) 和无RNA酶的水的反应混合物中加入5 μL 提取的总RNA, 最终体积为25 μL 。根据生产商的使用说明, 用 **TaqMan**[®] Ribosomal RNA Control Reagents (Applied

Biosystems, Foster City, CA) 检测18S rRNA, 其作为从犬组织样品提取的RNA的存在的内源性内部对照。

[0260] 在**Mx3000P**[®] QPCR系统 (Stratagene, La Jolla, CA) 中对反应混合物进行定量一步实时RT-PCR。循环条件包括50℃ 30分钟的逆转录步骤, 95℃ 15分钟以激活**HotStarTaq**[®] DNA聚合酶的最初变性步骤, 和40个循环的扩增。每个扩增循环包括94℃ 变性15秒, 接着60℃下退火/延伸1分钟。在每个循环结束时记录FAM (发射波长518nm) 和VIC (发射波长554nm) 荧光信号。通过在每个单独的实验中设置阈值荧光 (dR) 为1000, 确定阈值循环数 (Ct)。用**Mx3000P**[®] 版本2.0软件程序 (Stratagene, La Jolla, CA) 进行数据采集和分析。当H3或者M基因的阈值循环 (Ct) 比来自没有呼吸系统疾病的狗的肺组织的Ct小3个单位时, 认为样品是甲型流感病毒阳性的。阳性对照由从A/canine/FL/242/03 (H3N8) 病毒提取的RNA的扩增组成。

[0261] MDCK细胞中的病毒分离

[0262] 解冻来自7只狗的每一只的冷冻的肺组织并在10倍体积的补充0.5% (BSA) 和抗生素 (庆大霉素和环丙沙星) 的Dulbecco改良的Eagle培养基 (DMEM) 中匀浆。离心除去固体残渣并将上清液接种到在补充1μg/mL TPCK-处理的胰蛋白酶 (Sigma-Aldrich Corp., St. Louis, MO) 和抗生素 (庆大霉素和环丙沙星) 的DMEM中培养的Madin-Darby犬肾 (MDCK) 细胞上。细胞在含有5%CO₂的湿润空气中37℃下在25cm²瓶中生长。每天观察培养物的形态学改变并在接种后5天收获。通过离心澄清收获的培养物并如对于最初接种所述的将上清液接种到新鲜的MDCK细胞上; 对通过血细胞凝集或者RT-PCR没有显示流感病毒证据的样品进行两次额外的传代。使用0.5%火鸡细胞如以前描述 (Burleson, F. et al., 1992; Kendal, P. et al., 1982) 的测定澄清的上清液中的血细胞凝集活性。如下述进行RT-PCR。

[0263] 含胚的鸡蛋中的病毒分离

[0264] 如上文关于MDCK细胞的接种所述的从冷冻的肺组织制备匀浆。将匀浆 (0.2mL) 接种到10天龄含胚的鸡蛋的尿膜囊中。在35℃培育48小时后, 在4℃过夜冷冻鸡蛋, 然后收获尿囊液。使用0.5%火鸡血红细胞如以前描述的 (Burleson, F. et al., 1992; Kendal, P. et al., 1982) 测定澄清的上清液中的血细胞凝集活性。如下文描述的进行RT-PCR。对最初接种后没有显示出流感病毒证据的样品用含胚的蛋进行两次额外传代。

[0265] RT-PCR、核苷酸测序和系统进化分析

[0266] 使用**QIAamp**[®] Viral RNA Mini试剂盒 (QIAGEN Inc., Valencia, CA) 根据生产商的使用说明从MDCK上清液或者尿囊液提取病毒RNA。使用**QIAGEN**[®] OneStep RT-PCR试剂盒 (QIAGEN Inc., Valencia, CA) 根据生产商的使用说明将病毒RNA反转录成cDNA。如以前描述的 (Klimov, A. et al., 1992b), 使用通用的基因特异性引物组 (根据请求可以得到引物序列) 进行cDNA中8种流感病毒基因的编码区的PCR扩增。所得的DNA扩增子用作ABI**PRISM**[®] 3100自动化DNA测序仪中自动化测序的模板, 使用循环测序染料终止化学 (Applied Biosystems, Foster City, CA)。使用Lasergene6**Package**[®] (DNASTAR, Inc.,

Madison, WI) 分析核苷酸序列。用PHYLIP版本 3.5[®] 软件程序从核苷酸序列估计系统发生和计算自展值 (Felsenstein, J., 1989)。将系统树与用 MEGA[®] 程序 (Kumar, S. et al., 2004) 中实现的 Tamura-Nei 模型进行的近邻连接分析产生的系统树相比较, 并通过 PAUP[®] 4.0Beta 程序 (Sinauer Associates, Inc., Sunderland, MA) 证实。

[0267] 血细胞凝集抑制 (HI) 测定

[0268] 将血清样品与受体破坏酶 (RDE, DENKA SEIKEN Co., Ltd., Tokyo, Japan) (1份血清:3份RDE) 在37℃温育16小时, 然后在56℃热失活30分钟。流感A/Canine/Jacksonville/05 (H3N8) 病毒在37℃下5%CO₂中在MDCK细胞中生长72小时。收获病毒培养上清液, 通过离心澄清, 并在-80℃保存。HI测定中使用的所有其他病毒都生长在10天龄的含胚的鸡蛋中, 从其收集尿囊液并在-80℃保存。如以前描述的 (Kendal, P. et al., 1982) 进行HI测定。简言之, 向96孔塑料板中等体积的连续稀释的血清中加入25μl 4凝血单位的病毒并在室温下温育30分钟。加入等体积的0.5%火鸡红细胞并在30分钟后通过视觉估计血细胞凝集效价。将终点HI效价定义为完全抑制血细胞凝集的血清的最后稀释度。

[0269] 实施例7—临床病例

[0270] 在2005年4月和5月, 在佛罗里达东北部的收容所中喂养的狗中发生了以前描述的呼吸系统疾病爆发 (Crawford, P. C. et al., 2005)。该爆发涉及3个月至9岁年龄的至少58条狗, 并且包括纯种狗以及杂种狗。最常见的临床病征是脓性鼻分泌物和咳嗽7到21天。在具有临床疾病≥7天的43条狗中, 41条对canine/FL/04 (H3N8) 的HI抗体效价为32到>1024。至少10条狗发展成肺炎, 其中6条被实施安乐死。这6条杂种狗包括3条雄性和3条雌性, 年龄为4个月到3岁。在安乐死时临床病征的持续时间为2到10天。在尸体剖检时, 这些狗具有肺充血和水肿。对呼吸道的组织学检查揭示了鼻炎、气管炎、支气管炎、细支气管炎和化脓性支气管肺炎。在气管、支气管、细支气管和支气管腺中存在上皮细胞坏死和糜烂。呼吸系统组织被嗜中性粒细胞和巨噬细胞浸润。

[0271] 在2005年5月, 在佛罗里达东南部的一个兽医诊所中40条宠物狗中发生呼吸系统疾病爆发。最常见的临床病征是脓性鼻分泌物和咳嗽10到30天。在40条狗中, 17条对于canine/FL/04 (H3N8) 是血清阳性的, HI抗体效价范围为32到>1024。在可以得到配对的急性和恢复期血清的10条狗中发生了血清转变。三条狗发展为肺炎。一条狗为9岁的雄性 Yorkshire Terrier, 在临床病征发作后3天死亡。该狗具有气管支气管炎、肺水肿和充血, 和严重的支气管肺炎。类似于6条收容所的狗, 在组织中有上皮细胞坏死和气道糜烂和嗜中性粒细胞浸润。

[0272] 实施例8—实时RT-PCR和病毒分离

[0273] 通过定量实时RT-PCR测定法分析来自7条狗的肺组织, 所述测定法检测甲型流感的M基因和犬H3N8甲型流感病毒的H3基因。来自所有7条狗的肺对于甲型流感M基因和犬流感H3基因都是阳性的 (表8)。在MDCK细胞中传代3次后, 从在肺炎3天后死亡的收容所狗的肺分离亚型H3N8病毒。该病毒称作A/canine/Jacksonville/05 (H3N8) (canine/Jax/05)。在含胚的鸡蛋中传代2次后, 从肺炎3天后也死亡的宠物狗的肺回收甲型流感亚型H3N8病毒。将该病毒称作A/canine/Miami//05 (H3N8) (canine/Miami/05)。

[0274] 实施例9—犬甲型流感H3N8分离群的遗传学分析

[0275] canine/Jax/05和canine/Miami/05的序列分析揭示它们的血凝素(HA)基因与从2004和2005年赛场的流感爆发期间死于肺炎的竞赛灵~~猴~~的肺回收的canine/FL/04、canine/TX/04和canine/Iowa/05分离群具有98%同一性(Crawford,P.C.et al.,2005;Yoon K-Y.et al.,2005)。此外,canine/Jax/05和canine/Miami/05的HA基因与2000年后分离的同时代马流感病毒有98%同一性。HA基因的系统发生比较表明canine/Jax/05和canine/Miami/05病毒与canine/FL/04、canine/TX/04和canine/Iowa/05灵~~猴~~分离群和同时代的马分离群聚类,形成与20世纪90年代早期分离的较早的马病毒不同的组(图4)。此外,canine/Jax/05、canine/Miami/05和canine/Iowa/05分离群与canine/Tx/04比对canine/FL/04或canine/FL/03更接近。2005年分离群形成了一个亚组,其似乎与较早的2003和2004犬病毒分叉,在约10个简约信息位点具有差异。这些差异支持如下假说,即犬流感病毒在狗与狗之间水平传播,而不是从外部来源定期地再次输入。从2003到2005年的突变积累表明病毒被传播到新的宿主后必须经历的正在进行的适应过程,如对犬流感病毒预期已经发生。

[0276] 实施例10—犬甲型流感病毒H3N8分离群的氨基酸分析

[0277] 在所有6种犬分离群中都有保守氨基酸替代,其使得它们与同时代的马流感病毒不同(表9)。这些保守替代是I15M、N83S、W222L、I328T和N483T。成熟HA蛋白质的系统发生比较表明canine/Jax/05、canine/Miami/05和canine/Iowa/05病毒与canine/TX/04分离群形成一个亚组(图4)。有3个氨基酸改变(L118V、K261N和G479E)使得该亚组与其他犬病毒不同(表9)。有两个氨基酸改变(F79L和G218E),其使得2005分离群与它们的canine/TX/04根不同。此外,来自非灵~~猴~~狗的2005分离群canine/Jax/05和canine/Miami/05与canine/Iowa/05灵~~猴~~分离群有一个氨基酸改变R492K而不同。最后,canine/Jax/05与canine/Miami/05的差别是一个氨基酸S107P。在所有其他H3N8马和犬病毒中,S在107位保守,但是A/Equine/Jilin/1/89除外,其具有T(Guo Y.et al.,1992)。

[0278] 实施例11—犬甲型流感H3N8分离群的抗原分析

[0279] 使用较早的和同时代的马流感病毒和犬流感病毒的血清组,和在2005年从感染流感病毒的马和狗收集的血清进行血细胞凝集抑制(HI)试验(表10)。在该分析中还包括来自对canine/FL/04免疫的白鼬的血清。当用同时代的马病毒测试时,马血清中HI抗体效价比以前的分离群高8到16倍,但是当用犬病毒测试时降低至少4倍。犬血清不与较早的马病毒反应,但是当用同时代的马分离群和犬分离群测试时,抗体效价增加4倍。该结果也在来自对犬流感病毒免疫的白鼬的血清中观察到。这些血清反应性模式表明犬流感病毒和同时代的马流感病毒之间的抗原相似性,并且与系统发生分析相一致。抗canine/Miami/05分离群的马、犬和白鼬血清中的抗体效价与2003和2004白鼬分离群的那些相似。然而,canine/Jax/05分离群的效价低2到4倍。这提示canine/Jax/05在抗原上与其他犬分离群不同,这可能与成熟HA中107位的单个氨基酸改变部分有关。

[0280]

引物	靶标	序列	应用
Ca-H3-F387	H3 (nt 387-406)	5'-tatgcatcgctccgatccat-3' (SEQ ID NO: 79)	H3 的正向引物
Ca-H3-R487	H3 (nt 487-467)	5'-gctecacttcttcgtttga-3' (SEQ ID NO: 80)	H3 的反向引物
Ca-H3-P430	H3 (nt 430-459)	FAM-aattcacagcagagggattcacatggacag-BHQ1 (SEQ ID NO: 81)	TaqMan® 探针
FluA-M-F151	M (nt 151-174)	5'-catggartggctaagacaagacc-3' ^a (SEQ ID NO: 82)	M 的正向引物
FluA-M-R276	M (nt 276-253)	5'-aggcattttggacaaaakegtcta-3' (SEQ ID NO: 83)	M 的反向引物
FluA-M-P218	M (nt 218-235)	FAM-acgcTcaccgTgcccAgt-BHQ1 ^b (SEQ ID NO: 84)	TaqMan® 探针

^a 加下划线的字母 r 代表核苷酸 a 或者 g, 加下划线的字母 k 代表核苷酸 g 或者 t。
^b 大写字母代表锁定核酸残基。

[0281]

表 8. 对呼吸系统疾病爆发期间, 在佛罗里达的收容所和兽医诊所死于肺炎的狗的肺组织进行的定量实时 RT-PCR 和病毒分离

狗 ID	位置	临床疾病的持续时间	实时 RT-PCR		病毒分离
			M (Ct)	HA (Ct)	
A/canine/FL/242/03	阳性对照		28.15	27.36	
1079	收容所 (NE FL)	2 天	29.81	28.84	无
1078	收容所 (NE FL)	3 天	30.37	29.71	MDCK 第三代
318	收容所 (NE FL)	9 天	33.89	32.97	无
320	收容所 (NE FL)	10 天	39.44	37.09	无
319	收容所 (NE FL)	6 天	33.87	32.23	无
1080	收容所 (NE FL)	6 天	38.87	38.23	无
374	兽医诊所 (SE FL)	3 天	24.05	22.65	蛋 第二代

[0282]

表 9. 犬流感病毒和同时代的马流感病毒的成熟 HA 的氨基酸比较																			
		氨基酸																	
		7	15	54	78	79	83	92	107	118	159	218	222	261	328	479	483	492	541
A/equine/KY/5/02	G	I	N	V	F	N	S	S	S	L	N	G	W	K	I	G	N	R	K
A/equine/MA/213/03	.	.	.	A	.	.	.	.	.	.	S	.	.	.	.	.	.	.	.
A/equine/OH/1/03	D	.	K	A	.	.	.	.	.	.	S	.	.	.	.	.	.	.	.
A/canine/FL/242/03	.	M	K	A	.	S	.	.	.	.	S	.	L	.	T	.	T	.	.
A/canine/FL/43/04	.	M	K	A	.	S	N	.	.	.	S	.	L	.	T	.	T	.	R
A/canine/TX/1/04	.	M	K	A	.	S	.	.	.	V	S	.	L	N	T	E	T	.	.
A/canine/Iowa/05	.	M	K	A	L	S	.	.	.	V	S	E	L	N	T	E	T	.	.
A/canine/Miami/05	.	M	K	A	L	S	.	.	.	V	S	E	L	N	T	E	T	K	.
A/canine/Jacksonville/05	.	M	K	A	L	S	.	.	P	V	S	E	L	N	T	E	T	K	.

表 10. 抗早期和同时代的马流感病毒和犬流感病毒的马、犬和白鼬血清中的抗体效价

	血清	抗体	效价 ^a
抗原	马	犬	白鼬 ^b
equine/Miami/63	40	<10	16
equine/Ky/86	40	40	32
equine/KY/92	40	<10	32
equine/NY/99	320	40	128
equine/KY/05/02	320	160	256
equine/MA/213/03	640	160	512
equine/OH/01/03	640	160	512
canine/FL/03	160	160	512
canine/FL/04	160	80	512
canine/Tx/04	160	160	512
canine/Miami/05	160	80	256
canine/Jax/05	40	40	128

[0284] ^a在用抗原栏中所列出的马、犬或者白鼬血清和病毒进行的血细胞凝集抑制测定中测定的抗体效价。

[0285] ^b来自用canine/FL/04病毒免疫的血清。

[0286] 实施例12-15的材料和方法

[0287] 犬流感病毒接种物

[0288] 通过用代表以前描述的 (Crawford et al., 2005) 最初分离群的第3代的A/canine/FL/43/04 (H3N8) 原种接种Madin-Darby犬肾 (MDCK) 上皮细胞, 制备病毒接种物。在补充1μg/mL TPCK-处理的胰蛋白酶 (Sigma-Aldrich Corp., St. Louis, MO) 和抗生素 (庆大霉素和环丙沙星) 的Dulbecco极限必需培养基 (DMEM) 中接种的MDCK细胞在含有5%CO₂的湿润空气中37℃下生长在250cm²培养瓶中。每天观察培养物的形态改变并在接种后5天收获。通过离心澄清收获的培养物并在接种狗之前将上清液在-80℃保存。用上清液的等分试样通过Reed和Muench方法测定病毒效价。效价为10⁷半数组织培养感染量 (TCID₅₀) 的A/canine/Florida/43/04 (canine/FL/04) /mL。

[0289] 实验接种

[0290] 8条4个月龄的colony品种的杂种狗 (Marshall BioResources, North Rose, NY) (4

条雄性和4条雌性)用于佛罗里达大学机构动物管理和使用委员会批准的实验接种研究。狗的体重为13到17kg。在接种前,根据体检、基线血试验和记录体温两周,发现狗是健康的。根据对在到达实验室之时和2周后收集的配对血清样品进行的血清学试验,所有狗以前都没有接触犬流感病毒。通过静脉内注射异丙酚(**Diprivan®**, Zeneca Pharmaceuticals, 0.4mg/kg体重以生效)麻醉狗以用气管内管插管。6条狗(3条雄性和3条雌性)每条接种5mL 无菌盐水中的 10^7 TCID₅₀ canine/FL/04病毒,通过插入到气管内插管的小直径橡胶导管将所述病毒施用于气管远端。两条狗(1条雄性和1条雌性)用等体积的无菌盐水假接种。假接种的对照狗与接种病毒的狗关在不同的房间内并且由不同的工作人员照料。每天进行两次体检和直肠温度记录,直到接种后6天(p.i.)。

[0291] 咽和直肠拭子采集

[0292] 为了监视病毒脱落,在接种后0到6天,使用聚酯拭子(Fisher Scientific International Inc., Pittsburgh, PA)从每条狗每天两次收集口咽样品。将拭子置于含有0.5%牛血清白蛋白(BSA)的1mL无菌磷酸缓冲盐水(PBS)中。从第0到6天每天从每条狗收集直肠拭子。通过离心澄清拭子运送培养液,制备拭子提取物。使用Directigen™商业免疫测定试剂盒(BD, Franklin Lakes, NJ)根据生产商的使用说明,对拭子提取物的等分试样立即测试甲型流感病毒核蛋白。剩余的提取物在-80℃保存备用其他的病毒学测定。

[0293] 尸体剖检

[0294] 在接种后第1天,通过静脉内接种**Beuthanasia-D®**溶液(1mL/5kg体重; Schering-Plough Animal Health Corp),对一条假接种的狗和一条病毒接种的狗实施安乐死。从接种后第2到第5天,每天对一条病毒接种的狗类似地实施安乐死。在接种后第6天,对剩下的假接种的和病毒接种的狗实施安乐死。由研究人员(WLC)之一进行完全的尸体剖检。将组织用10%中性缓冲的福尔马林固定,石蜡包埋,并对5-μm切片用苏木精和伊红染色用于组织病理学诊断或者处理用于如下文所述的免疫组织化学。将未固定的肺组织送到佛罗里达大学兽医学院的诊断临床微生物学/寄生虫学/血清学处(Diagnostic Clinical Microbiology/Parasitology/Serology Service)用于细菌分离和鉴定。在非选择性培养基以及选择博德特氏菌(*Bordetella*)种(Regan-Lowe; Remel, Lenexa, KS)和支原体(*Mycoplasma*)种(Remel)的培养基上培养样品。在报告无生长前,所有培养物都保持了21天。在病毒学分析之前,未固定的组织也在-80℃保存。

[0295] 免疫组织化学

[0296] 将脱石蜡并再水化的5-μm气管和肺组织切片封固在Bond-Rite™载玻片(Richard-Allan Scientific, Kalamazoo, MI)上并随后用蛋白酶K(DAKOCytomation Inc., Carpinteria, CA)处理,接着用过氧化物酶封闭试剂(**DAKO®** EnVision™ Peroxidase Kit, DAKO Corp., Carpinteria, CA)处理。将切片用抗甲型流感H3的单克隆抗体(Chemicon International, Inc., Temecula, CA)的1:500稀释液在室温下温育2小时。对照包括用小鼠IgG(1mg/mL, Serotec, Inc. Raleigh, NC)温育相同的切片,和使用正常的犬肺切片与单克隆抗体温育。用一级抗体处理后,将切片与二级免疫过氧化物酶和过氧化物酶底物试剂(**Dako®** EnVision™ Peroxidase Kit, Dako Corp.)根据生产商的使用说明处理。将切片用苏木精复染,用Clarifier#2和Bluing试剂(Richard-Allan Scientific, Kalamazoo, MI)处

理,脱水,并用Permout (ProSciTech,Queensland,Australia) 盖片。

[0297] 来自拭子和组织的RNA提取物

[0298] 将来自每条狗的肺和气管组织解冻并在补充0.5%牛血清白蛋白 (BSA) 和抗生素 (庆大霉素和环丙沙星) 的极限必需培养基 (MEM) 中,使用一次性组织研磨机 (Kendall, Lifeline Medical Inc.,Danbury,CT) 匀浆。使用商业试剂盒 (**RNeasy**[®] Mini Kit, QIAGEN Inc.,Valencia,CA), 根据生产商的使用说明从组织匀浆以及咽和直肠拭子提取物提取总RNA并用最终体积60μL的缓冲液洗脱。

[0299] 实时RT-PCR

[0300] 使用 **QuantiTect**[®] Probe RT-PCR试剂盒 (QIAGEN Inc.,Valencia,CA) 和引物一探针组对总的RNA进行一步定量实时RT-PCR,该试剂盒含有作为被动参照染料的ROX, 所述引物一探针组靶定甲型流感病毒的基质 (M) 基因的高度保守区 (Payungporn S.et al.,2006a;Payungporn S.et al.,2006b)。对于每次实时RT-PCR反应,向含有12.5μL2X **QuantiTect**[®] Probe RT-PCR Master Mix,0.25μL **QuantiTect**[®] RT Mix,正向和反向引物 (每种终浓度0.4μM), 探针 (0.1μM终浓度) 和无RNA酶的水的反应混合物中加入5μL提取的总RNA,终体积为25μL。使用 **TaqMan**[®] GAPDH Control Reagents (Applied Biosystems,Foster City,CA) 根据生产商的使用说明检测GAPDH,其作为从拭子和组织样品提取的RNA存在的内源性内部对照和作为归一化对照。

[0301] 对 **Mx3000P**[®] QPCR系统 (Stratagene,La Jolla,CA) 中的反应混合物进行定量一步实时RT-PCR。循环条件包括50℃30分钟的反转录步骤,95℃15分钟以活化 **HotStarTaq**[®] DNA聚合酶的最初变性步骤,和40个循环的扩增。每个扩增循环包括94℃变性15秒,接着60℃下退火/延伸1分钟。在每个循环结束时记录FAM (发射波长518nm) 和VIC (发射波长554nm) 荧光信号。通过在每个单独的实验中设置阈值荧光 (dR) 为1000,确定阈值循环数 (Ct)。用 **Mx3000P**[®] 版本2.0软件程序 (Stratagene,La Jolla,CA) 进行数据采集和分析。阳性对照由从A/canine/FL/242/03 (H3N8) 病毒提取的RNA的扩增组成。对于每个样品,通过将M Ct值除以对应的GAPDH Ct值对结果归一化。

[0302] 从组织再次分离病毒

[0303] 解冻来自接种病毒的狗的冷冻的肺和气管组织并在10倍体积的补充0.5% (BSA) 和抗生素的DMEM中匀浆。离心除去固体残渣并将上清液接种到在补充1μg/mL TPCK-处理的胰蛋白酶 (Sigma-Aldrich Corp.,St.Louis,MO) 和如上述抗生素的DMEM中培养的MDCK细胞上。细胞在含有5%CO₂的湿润空气中37℃下在25cm²瓶中生长。每天观察培养物的形态学改变并在接种后5天收获。通过离心澄清收获的培养物并如对于最初接种所述的将上清液接种到新鲜的MDCK细胞上;对通过血细胞凝集或者RT-PCR没有显示流感病毒证据的样品进行两次额外的传代。使用0.5%火鸡细胞如以前描述 (Crawford et al.,2005) 的测定经澄清的上清液中的血细胞凝集活性。如下述进行RT-PCR。

[0304] RT-PCR、核苷酸测序和系统进化分析

[0305] 使用**QIAamp**[®] Viral RNA Mini试剂盒(QIAGEN Inc.,Valencia,CA)根据生产商的使用说明从MDCK上清液提取病毒RNA。使用**QIAGEN**[®] OneStep RT-PCR试剂盒(QIAGEN Inc.,Valencia,CA)根据生产商的使用说明将病毒RNA反转录成cDNA。如以前描述的(Crawford et al.,2005),使用通用的基因特异性引物组(根据请求可以得到引物序列)进行cDNA中8种流感病毒基因的编码区的PCR扩增。所得的DNA扩增子用作ABI **PRISM**[®] 3100自动化DNA测序仪中自动化测序的模板,使用循环测序染料终止化学(Applied Biosystems,Foster City,CA)。使用Lasergene6 **Package**[®] (DNASTAR,Inc.,Madison,WI)分析核苷酸序列。将从受感染的狗回收的病毒的核苷酸序列与接种物中病毒的序列比较以确定在呼吸道中复制期间是否已经发生了改变。

[0306] 实施例12—临床疾病

[0307] 所有6条接种病毒的狗在接种后前2天都产生了暂时发热(直肠温度 $\geq 39^{\circ}\text{C}$),但是没有一只在6天的观察期内显示出呼吸系统病征如咳嗽或者鼻涕。假接种的狗保持临床上健康。

[0308] 实施例13—病毒脱落

[0309] 对接种后24小时从一条接种病毒的狗收集的口咽拭子检测甲型流感核蛋白。通过定量实时RT-PCR,在接种后72、84和120小时从一条狗和接种后108、120和132小时从另一条狗收集的口咽拭子是病毒阳性的(表11)。每 μL 拭子提取物中流感M基因拷贝的绝对数目从接种后第3天到第6天随时间增加。在直肠拭子中没有检测到病毒。

[0310] 实施例14—尸体剖检

[0311] 与以前使用特定无病原体的小猎兔犬的实验感染(Crawford et al.,2005)相比,接种病毒的杂种狗患有肺炎,如通过来自接种后1到6天的肺的总体的和组织学分析所证明。除了肺炎外,狗还患有类似于自然感染的狗中所描述的鼻炎、气管炎、支气管炎和细支气管炎(Crawford et al.,2005)。在呼吸道和支气管腺层中存在上皮坏死和糜烂,在粘膜下层组织中有嗜酸性粒细胞和巨噬细胞浸润(图5,上图)。免疫组织化学在支气管、细支气管和支气管腺的上皮细胞中检测到病毒H3抗原(图5,下图)。不存在细菌超感染。来自2条假接种的狗的呼吸系统组织是正常的。

[0312] 实施例15—气管和肺中的病毒复制

[0313] 通过定量实时RT-PCR,从接种后第1天到第6天,所有狗中的气管和肺都是病毒阳性的(表12)。每 μL 气管匀浆的流感M基因拷贝的绝对数目从接种后第1天到第5天增加,然后在第6天下降。每 μL 肺匀浆的M基因拷贝的绝对数目从接种后第1天到第6天下降。通常,在接种后6天的每天,气管含有比肺多 $\geq 11\log_{10}$ 的病毒。

[0314]

表 11. 通过定量实时 RT-PCR 检测用犬流感病毒接种的杂种狗的口咽中的病毒脱落			
狗 ID	接种后时间 (小时) ^a	M/GAPDH 比 ^b	基质基因 (拷贝 / μ L) ^c
860	72	1.20	1.57E+02
	84	1.30	8.25E+02
	120	1.23	1.47E+03
894	108	1.17	1.17E+02
	120	1.41	1.37E+02
	132	1.27	3.74E+02

[0315] ^a用A/canine/FL/43/04 (H3N8) 病毒接种后从狗收集口咽拭子的时间。[0316] ^b通过将M (Ct) 除以每个拭子提取物的GAPDH (Ct) 计算归一化比。[0317] ^c每 μ L拭子提取物的基质基因拷贝的绝对数目。

[0318]

表 12. 通过定量实时 RT-PCR 检测用犬流感病毒接种的杂种狗的气管和肺中病毒复制					
狗 ID	接种后时间 (小时) ^a	M/GAPDH 比 ^b		基质基因(拷贝 / μ L) ^c	
		肺	气管	肺	气管
797	24	1.20	1.43	8.22E+05	3.11E+04
801	48	1.33	0.99	1.15E+05	6.52E+06
789	72	1.44	1.12	2.39E+04	1.56E+05
819	96	1.40	1.27	3.19E+04	1.43E+05

[0319]

860	120	1.59	1.04	3.48E+03	1.17E+06
894	144	1.70	1.15	4.78E+02	1.50E+03

[0320] ^a用A/canine/FL/43/04 (H3N8) 病毒接种后从狗收集组织的时间。[0321] ^b通过将M (Ct) 除以每个组织匀浆的GAPDH (Ct) 计算归一化比。[0322] ^c每 μ L组织匀浆的基质基因拷贝的绝对数目。

[0323] 实施例16的材料和实施例方法

[0324] 病毒毒株

[0325] 在含胚的卵或者MDCK细胞中增殖犬流感病毒毒株以及鸟、马和人来源的那些流感病毒毒株(表15中所列),并通过鸡胚中的终点稀释或者噬斑测定法滴定它们的感染力。使用火鸡血红细胞通过血细胞凝集测定法进行快速病毒定量。

[0326] 诊断样品

[0327] 对2005年期间病毒呼吸系统疾病的疑似病例收集的共60条犬的肺组织测试犬流感病毒的存在。

[0328] 从犬组织样品提取RNA

[0329] 将重量为20到30mg的肺组织块在一次性组织研磨机(Kendal)中匀浆。按照生产商的推荐,使用商业试剂盒(RNeasy Mini Kit, Qiagen, Valencia, CA)提取总RNA并用终体积60μL稀释。

[0330] 引物和探针设计

[0331] 使用CLUSTAL X程序(版本1.8)进行来自多种亚型和来自多种物种的H3和M基因的多序列比对。从对应于甲型流感病毒的不同亚型的已知序列的保守区选择基质(M)引物和探针,而选择H3血凝素基因特异引物和探针组以特别匹配马和犬甲型流感病毒基因和错配同源的鸟和人基因(表13)。用引物设计软件(OLIGOS版本9.1)和EXIQON(<http://lnatools.com>)提供的基于网络的分析工具进行T_m计算和预测二级结构以及自身杂交。18S rRNA基因的保守区用作从犬组织样品的提取的RNA的存在的内源性内部对照。Pre-Developed **TaqMan®** Assay Reagents for Eukaryotic 18S rRNA (VIC/TAMRA) (Applied Biosystems)用于实时检测组织样品中的18S rRNA。

[0332] 实时RT-PCR条件

[0333] 通过使用含有作为被动参照染料的ROX的Quantitect Probe RT-PCR试剂盒(Qiagen, Valencia, CA)进行一步实时RT-PCR。在每次实时RT-PCR反应中,5μL RNA样品用作模板与反应混合物组合,所述反应混合物含有10μL 2X QuantiTech Probe RT-PCR Master Mix, 0.2μL QuantiTech RT Mix, 引物(0.4μM终浓度的H3基因或者0.6μM终浓度的M基因), 探针(0.1μM终浓度的H3基因或者0.2μM终浓度的M基因)和无RNA酶的水,最终体积为20μL。在Mx3005P Real-Time QPCR系统(Stratagene)中进行一步实时RT-PCR。循环条件包括50℃ 30分钟的反转录步骤。95℃ 15分钟以便活化HotStarTaq DNA聚合酶的初步变性步骤后,在40个循环中进行扩增,每个循环包括变性(94℃ 15秒)和退火/延伸(60℃ 30秒)。在每个循环延伸步骤结束时得到FAM(发射波长516nm,用于H3和M检测)和VIC(发射波长555nm,用于18S rRNA检测)荧光信号一次。使用Mx3005P软件版本2.02(Stratagene)进行实时PCR测定的数据采集和分析。

[0334] H3引物/探针组对于犬流感(H3N8)的特异性和M引物/探针组对于甲型流感病毒的通用性

[0335] 为了测试每种引物/探针组的特异性,从甲型流感病毒的几种已知的亚型提取的RNA用作实时RT-PCR测定中的模板(表15)。

[0336] 用于确定实时RT-PCR性能的RNA标准

[0337] 通过使用与T7启动子连接的引物,用犬甲型流感病毒(A/canine/Florida/242/2003(H3N8))的基因产生H3(nt1-487)和M(nt1-276)的PCR扩增子(表13)。然后通过使用

Riboprobe体外转录系统-T7 (Promega),按照生产商的推荐,将H3和M基因的纯化的PCR扩增子用作体外转录的模板。通过测量260nm的吸光度计算所转录的RNA的浓度。然后将RNA连续稀释10倍,从 10^8 到10个拷贝/ μL 以进行灵敏度测试。此外,通过将最初的RNA模板浓度(拷贝/ μL)的对数对为每次稀释得到的阈值循环数(C_t)作图产生标准曲线,以便确定实时RT-PCR的总体性能。

[0338] 实时RT-PCR和Directigen Flu A测试试剂盒之间的比较灵敏度测试

[0339] 将包括 $10^{6.67}\text{EID}_{50}/\text{mL}$ (HA=64) 的A/Wyoming/3/2003 (H3N2) 和 $10^{7.17}\text{EID}_{50}/\text{mL}$ (HA=16) 的A/canine/Florida/242/2003 (H3N8) 的两种病毒毒株的原种病毒用于检测阈值测定法。按照生产商的使用说明,在快速甲型流感病毒抗原检测试剂盒Directigen Flu A, (Becton,Dickinson and Company) 中使用磷酸缓冲盐水(PBS) (125 μL) 中样品的对数稀释度。每个DirectigenFlu A测试装置在膜中央具有一个H1N1流感抗原点,其显影为紫色点并且指出该测试的完整性,该测试是基于抗核蛋白(NP)的单克隆抗体。在所述点周围紫色三角形的显影表明在测试的样品中存在流感NP。将来自三角形的紫色信号的强度打分为+ (三角形轮廓),++ (浅色三角形),+++ (深紫色三角形) 和++++ (极深紫色三角形)。使用QIAamp Viral RNA Mini试剂盒(Qiagen,Valencia,CA)从每种病毒稀释液的125 μL 等分试样提取病毒RNA并以最终体积50 μL 稀释。通过实时RT-PCR测试5 μL 体积提取的病毒RNA用于与Directigen Flu A试剂盒的比较灵敏度测试。

[0340] 实施例16

[0341] 犬流感病毒的实时RT-PCR测定依赖于来自三种分子探针的信息,所述探针靶定来自宿主细胞的18S rRNA以及来自甲型流感病毒基因组的M和H3(表14)。宿主基因的扩增报告样品质量和完整性。预期含有犬流感(H3N8)病毒的临床的、尸体剖检或实验室样品用三种探针产生扩增信号。用M和18S rRNA探针产生扩增信号但是对于H3阴性的样品将表明来自人、猪或者鸟来源的流感病毒亚型H3或者来自非H3亚型的流感病毒。这些罕见的情况可以通过RT-PCR解决,其使用HA通用引物以产生扩增子cDNA,可以通过测序分析所述cDNA。适当收集和处理的缺少甲型流感病毒的样品仅仅产生18S rRNA扩增信号。仅仅18S rRNA探针和H3探针产生扩增信号的情况表明有缺点的技术,除非证明相反;需要阐明使用M探针的假阴性或者对于H3的假阳性。最后,用这三种探针不能产生扩增信号的样品表明有缺陷的样品收集、降解、错误的RNA提取或者存在PCR中使用的聚合酶的抑制剂。

[0342] 为了测试犬甲型流感病毒(H3N8)的H3引物/探针组的特异性和甲型流感的M引物/探针组的通用性,通过实时RT-PCR测试甲型流感病毒的几种亚型。结果表明H3引物/探针组仅仅用犬流感(H3N8)产生阳性扩增信号。在其他亚型或者人H3毒株中没有观察到显著的假阳性或者非特异性扩增信号。M引物/探针组对测试的所有毒株产生了阳性扩增信号(表15)。这些结果表明H3引物/探针特异检测犬甲型流感病毒(H3N8),而M引物/探针检测甲型流感病毒的多种亚型。

[0343] 通过M和H3体外转录的RNA的终点稀释评估实时RT-PCR测定法的性能。如所预期的,阈值循环数(C_t)与RNA标准品的稀释度以正相关增加。可以在M和H3的分别低至 10^3 和 10^2 个拷贝/ μL 的RNA标准品稀释度下检测到荧光信号(图6A和6B)。通过将起始RNA浓度的对数对从每个稀释度得到的阈值循环数(C_t)作图,构建M和H3基因的标准曲线(图6C和6D)。用标准曲线的斜率确定PCR反应效率,其在理论上是指数的;100%扩增效率将意味着每个循环

的扩增子浓度的加倍。具有约-3.1到-3.6之间斜率的标准曲线通常适于多数需要准确定量的应用(90-110%反应效率)。Rs_q值是所有数据对标准曲线图的拟合。如果所有数据都精确地位于曲线上,那么Rs_q将为1.00。随着数据从该曲线进一步下降,Rs_q降低。Rs_q≥0.985是多数测定法可接受的。M标准曲线揭示了-3.576的斜率(效率=90.4%)和Rs_q=1.00,而H3标准曲线产生了-3.423的斜率(效率=95.9%)和Rs_q=0.999。这些值表明实时RT-PCR测定法的满意的扩增效率和总体性能。我们将M引物/探针组与H3引物/探针组相比较低的效率和灵敏度规因于M引物序列的N倍简并性,需要该简并性来确保M基因序列变异性在多种亚型、宿主和谱系的病毒之间的宽覆盖度。

[0344] 还将实时RT-PCR测定法的灵敏度与商业的快速抗原检测测定法(Directigen Flu A)相比较。用Directigen Flu A和通过实时RT-PCR分析了A/Wyoming/3/2003(H3N2)和A/canine/Florida/242/2003(H3N8)的对数稀释度。Directigen Flu A的结果表明对两种病毒毒株的灵敏度为用于这些实验的原种病毒的约100倍稀释度(图7)。犬病毒(A/canine/Florida/242/2003:10^{6.5} PFU/ml)样品产生的信号(紫色)比在人病毒(A/Wyoming/3/2003:10^{7.5} PFU/ml)中发现的弱得多,与这些样品中较低的病毒浓度相一致。备选地,犬流感的较低信号可以规因于单克隆抗体对NP的分子特异性;即在犬甲型流感病毒的NP表位中氨基酸的保守性很差。

[0345] A/canine/Florida/242/2003和A/Wyoming/3/2003的每次反应分别使用病毒10和30PFU当量,M基因的实时RT-PCR产生了高于阈值的C_t值(表16)。两种病毒毒株的灵敏度值的差异是因为最初的病毒滴定度的不同。没有进行犬和人流感病毒之间的H3基因检测比较,是因为我们的实时RT-PCR测定中的H3引物/探针唯一地扩增犬甲型流感病毒。RT-PCR比快速抗原检测试剂盒灵敏10⁵倍。

[0346] 为了评估RT-PCR测试在来自患有急性呼吸系统疾病的狗的尸体剖检样品中的性能,通过实时RT-PCR测试了在2005年送交的60个犬肺组织样品中犬甲型流感病毒的存在。60个样品中总共12个(20%)对于M和H3基因是阳性的,而剩下的48个样品对于M和H3基因都产生了阴性结果。通过蛋和MDCK细胞接种进行病毒分离尝试,以评估实时测定法的特异性;根据RT-PCR,12个样品中对犬流感阳性的两个样品产生了犬流感病毒(数据未显示,手稿准备中)。尽管所有组织都从具有严重呼吸系统疾病史的狗中收集,但是通过实时PCR或者常规分离,多数样品都没有产生犬流感病毒,提示其他呼吸系统病原体如支气管博德特氏菌(*Bordetella bronchiseptica*)、犬瘟热或者副流感病毒的高发生率。本文的一步实时RT-PCR测定法提供了犬甲型流感病毒(H3N8)检测的快速、灵敏和划算的方法。该疾病的早期中,犬甲型流感病毒(H3N8)感染的快速实验室诊断可以得到与临床患者和设施管理相关的信息。

[0347]

表 13: 用于实时 RT-PCR 检测和体外转录的引物和探针					应用
Oligo 名称	类型	靶标	序列 *		
Ca-H3-F387	正向引物	H3 (nt 387-406)	5'-tatgcatcgcctccatcat-3' (SEQ ID NO: 79)		
Ca-H3-R487	反向引物	H3 (nt 487-467)	5'-gcctccactctctcgttttga-3' (SEQ ID NO: 80)		
Ca-H3-P430	TaqMan 探 针	H3 (nt 430-459)	FAM-aattcacagcagagggttcacatggacag-BHQ1 (SEQ ID NO: 81)		
FluA-M-F151	正向引物	M (nt 151-174)	5'-catggartggctaaagacaagacc-3' (SEQ ID NO: 82)		
FluA-M-R276	反向引物	M (nt 276-253)	5'-agggcattttggacaacacgtcta-3' (SEQ ID NO: 83)		
FluA-M-P218	LNA TaqMan 探针	M (nt 218-235)	FAM-acgcTcaccgTgccCAgt-BHQ1 (SEQ ID NO: 84)		
H3-F1	正向引物	H3 (nt 1-14)	5'-tatcgtctcaggaggcaaaagcagggg-3' (SEQ ID NO: 85)		
T7/H3-R490	反向引物	T7 / H3 (nt 487-467)	5'-tgtaatacgaactcactatagggtccactctctcgttttga-3' (SEQ ID NO: 86)		

体外转录

[0348]

M-F1	正向引物	M (nt 1-15)	5'-gategctcttcaggaggcaaaagcaggtag-3' (SEQ ID NO: 87)	体外转录
T7/M-R276	反向引物	M (nt 276-253)	5'-tgtaatacgaactcactatagggcattttggacaaagcgtc-3' (SEQ ID NO: 88)	

* 注释: 大写 = LNA (锁定核酸) 残基, r = a 或 g, k= g 或 t, 下划线= T7 启动子序列

[0349]

表 14:实时 RT-PCR 测定法的解释			
解释	结果		
	M	H3	18S rRNA
犬甲型流感病毒(H3N8)阳性	+	+	+
甲型流感病毒(未知亚型)阳性	+	-	+
甲型流感病毒阴性	-	-	+
RNA 提取错误或存在 PCR 抑制剂	-	-	-

[0350]

表 15:用甲型流感病毒的几种亚型对犬 H3 引物/探针组的 特异性测试和 M 引物/探针组的通用性测试				
亚 型	毒株名称	宿主	实时 RT-PCR 检 测	
			H3 基 因 (Ct)	M 基因 (Ct)
H1	A/Ohio/1983	人	无 Ct	15.40
	A/WSN/1933	人	无 Ct	20.09
H3	A/Wyoming/3/2003	人	无 Ct	28.85
	A/Victoria/3/1975	人	无 Ct	16.62
	A/canine/FL/242/2003	犬	28.43	29.25
H4	Turkey/MN/1066/1980	鸟	无 Ct	17.49
	临床样品*	鸟	无 Ct	20.87
H5	AChicken/Thailand/CUK2/2004	鸟	无 Ct	20.13
	A/Pheasant/NJ/1335/1998	鸟	无 Ct	16.64
H6	临床样品*	鸟	无 Ct	19.52
H10	临床样品*	鸟	无 Ct	25.64
	临床样品*	鸟	无 Ct	19.59
H11	临床样品*	鸟	无 Ct	15.72
	临床样品*	鸟	无 Ct	24.55

[0351] *注意通过核苷酸测序证实临床样品的亚型。

[0352]

表 16: 实时 RT-PCR 和 Directigen Flu A 之间对甲型流感病毒检测的 比较灵敏度测试				
病毒 稀释 度	Directigen Flu A		M (Ct)的实时 RT-PCR	
	A/canine/242/03	A/Wyoming/3/03	A/canine/242/03	A/Wyoming/3/2003
10^{-1}	++	++++	22.42	19.48
10^{-2}	+	+++	25.85	22.66
10^{-3}	-	-	29.27	25.76
10^{-4}	未做	未做	32.66	28.66
10^{-5}	未做	未做	35.48	33.14
10^{-6}	未做	未做	37.51	35.06
10^{-7}	未做	未做	39.09	36.44
10^{-8}	未做	未做	无 Ct	38.93

[0353]

表 17.	
氨基酸类型	氨基酸的例子
非极性的	Ala, Val, Leu, Ile, Pro, Met, Phe, Trp
不带电极性的	Gly, Ser, Thr, Cys, Tyr, Asn, Gln
酸性的	Asp, Glu
碱性的	Lys, Arg, His

[0354]

表 18.			
字母符号	氨基酸	字母符号	氨基酸
A	丙氨酸	M	甲硫氨酸
B	天冬酰胺或天冬氨酸	N	天冬酰胺
C	半胱氨酸	P	脯氨酸
D	天冬氨酸	Q	谷氨酰胺
E	谷氨酸	R	精氨酸
F	苯丙氨酸	S	丝氨酸
G	甘氨酸	T	苏氨酸
H	组氨酸	V	缬氨酸
I	异亮氨酸	W	色氨酸
K	赖氨酸	Y	酪氨酸
L	亮氨酸	Z	谷氨酰胺或谷氨酸

[0355]

表 19. H3N8 马和犬流感病毒的 PB2 蛋白质之间的氨基酸差异			
位置	马共有的 *	Canine/FL/03	Canine/FL/04
5	K	K	E
12	S	L	L
37	G	G	E
175	R	R	I
374	L	I	I
375	R	R	K
447	Q	Q	H

[0356]

表 20. H3N8 马和犬流感病毒的 PB1 蛋白质之间的氨基酸差异			
位置	马共有的*	Canine/FL/03	Canine/FL/04
114	V	I	I
154	D	G	G
221	A	T	T
317	M	I	I
459	I	I	V
682	I	I	V

[0357]

表 21. H3N8 马和犬流感病毒的 PA 蛋白质之间的氨基酸差异			
位置	马共有的*	Canine/FL/03	Canine/FL/04
27	D	N	N
62	I	V	V
213	R	K	K
337	A	T	T
343	A	E	E
345	L	I	I
353	K	R	R
400	T	T	A
450	V	I	I
460	M	M	I
673	R	R	K
675	N	D	D

[0358] *基于1963和1998年间分离的病毒的可利用的基因。

[0359]

表 22. H3N8 马和犬流感病毒的 NP 蛋白质之间的氨基酸差异			
位置	马共有的*	Canine/FL/03	Canine/FL/04
16	G	D	D
157	A	T	T
214	R	R	K
285	V	V	I
286	A	T	T
359	A	T	T
375	D	D	N
384	R	K	K
452	R	K	K

[0360]

表 23. H3N8 马和犬流感病毒的 NA 蛋白质之间的氨基酸差异			
位置	马共有的*	Canine/FL/03	Canine/FL/04
9	A/T	T	A
12	S	F	F
20	L	I	I
40	G	R	R
42	G	D	D
46	N	K	K
52	E	E	K
61	R	K	K
69	N	S	S
72	E	K	K
201	V	I	I
261	I	V	V
301	I	I	V
396	N	D	D
397	L	P	P

[0361]

表 24. H3N8 马和犬流感病毒的 M1 蛋白质之间的氨基酸差异			
位置	马共有的*	Canine/FL/03	Canine/FL/04
M1 161	S	S	A
M1 208	K/Q	R	R

[0362] *基于1963和1998年间分离的病毒的可利用的基因。

[0363]

表 25. H3N8 马和犬流感病毒的 NS1 蛋白质之间的氨基酸差异			
位置	马共有的*	Canine/FL/03	Canine/FL/04
44	K	R	R
59	R	H	H
71	E	K	K
86	A	T	T
88	R	R	L
140	R	G	G
216	P	S	S

[0364] *基于1963和1998年间分离的病毒的可利用的基因。

[0365] 应该理解本文描述的实施例和实施方案仅用于阐明目的,并且参照其的多种修饰或更改将是本领域技术人员可以想到的,并且包括在本申请的精神和范围内。

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序 列 表

- <110> 佛罗里达大学研究基金公司
 <120> 用于犬科动物中呼吸系统疾病控制的物质和方法
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 tgg atg atg gca atg aaa tac cca att aca gca gat aag agg ata atg 192
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Lys Ile Arg Val His Glu Gly Tyr Glu Glu Phe Thr Met Val Gly Arg	355	360	365	
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Arg Ala Thr Ala Ile Ile Lys Lys Ala Thr Arg Arg Leu Ile Gln Leu	370	375	380	
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	agc ggt ttc gta aga acc ctg ttt cag caa atg cga gat gta ctt gga	1824

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[0006]

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Thr Val Leu Gly Val Ser Ile Leu Asn Leu Gly Gln Arg Lys Tyr Thr				
	420	425	430	
aag acc aca tac tgg tgg gat ggt ctg caa tca tcc gat gac ttt gct				1344
Lys Thr Thr Tyr Trp Trp Asp Gly Leu Gln Ser Ser Asp Asp Phe Ala				
	435	440	445	
ttg ata gtg aat gcg cct aat cat gaa gga gta caa get gga gta gac				1392
Leu Ile Val Asn Ala Pro Asn His Glu Gly Val Gln Ala Gly Val Asp				
	450	455	460	
aga ttc tat aga act tgc aaa ctg gtc ggg atc aac atg agc aaa aag				1440
Arg Phe Tyr Arg Thr Cys Lys Leu Val Gly Ile Asn Met Ser Lys Lys				
	465	470	475	480
[0013]				
aag tcc tac ata aat aga act gga aca ttc gaa ttc aca agc ttt ttc				1488
Lys Ser Tyr Ile Asn Arg Thr Gly Thr Phe Glu Phe Thr Ser Phe Phe				
	485	490	495	
tac egg tat ggt ttt gta gcc aat ttc agc atg gaa cta ccc agt ttt				1536
Tyr Arg Tyr Gly Phe Val Ala Asn Phe Ser Met Glu Leu Pro Ser Phe				
	500	505	510	
ggg gtt tcc gga ata aat gaa tct gca gac atg agc att gga gtg aca				1584
Gly Val Ser Gly Ile Asn Glu Ser Ala Asp Met Ser Ile Gly Val Thr				
	515	520	525	
gtc atc aaa aac aac atg ata aat aat gat ctc ggt cct gcc acg gca				1632
Val Ile Lys Asn Asn Met Ile Asn Asn Asp Leu Gly Pro Ala Thr Ala				
	530	535	540	
caa atg gca ctc caa ctc ttc att aag gat tat egg tac aca tac egg				1680
Gln Met Ala Leu Gln Leu Phe Ile Lys Asp Tyr Arg Tyr Thr Tyr Arg				
	545	550	555	560
tgc cat aga ggt gat acc cag ata caa acc aga aga tct ttt gag ttg				1728
Cys His Arg Gly Asp Thr Gln Ile Gln Thr Arg Arg Ser Phe Glu Leu				

	565	570	575	
	aag aaa ctg tgg gaa cag act cga tca aag act ggt cta ctg gta tca			1776
	Lys Lys Leu Trp Glu Gln Thr Arg Ser Lys Thr Gly Leu Leu Val Ser			
	580	585	590	
	gat ggg ggt cca aac cta tat aac atc aga aac cta cac atc ccg gaa			1824
	Asp Gly Gly Pro Asn Leu Tyr Asn Ile Arg Asn Leu His Ile Pro Glu			
	595	600	605	
	gtc tgt tta aaa tgg gag cta atg gat gaa gat tat aag ggg agg cta			1872
	Val Cys Leu Lys Trp Glu Leu Met Asp Glu Asp Tyr Lys Gly Arg Leu			
	610	615	620	
	tgc aat cca ttg aat cct ttc gtt agt cac aaa gaa att gaa tca gtc			1920
	Cys Asn Pro Leu Asn Pro Phe Val Ser His Lys Glu Ile Glu Ser Val			
	625	630	635	640
	aac agt gca gta gta atg cct geg cat ggc cct gcc aaa agc atg gag			1968
	Asn Ser Ala Val Val Met Pro Ala His Gly Pro Ala Lys Ser Met Glu			
	645	650	655	
[0014]	tat gat gct gtt gca aca aca cat tet tgg atc ccc aag agg aac egg			2016
	Tyr Asp Ala Val Ala Thr Thr His Ser Trp Ile Pro Lys Arg Asn Arg			
	660	665	670	
	tec ata ttg aac aca agc caa agg gga gta ctc gaa gat gag cag atg			2064
	Ser Ile Leu Asn Thr Ser Gln Arg Gly Val Leu Glu Asp Glu Gln Met			
	675	680	685	
	tat cag aaa tgc tgc aac ctg ttt gaa aaa ttc ttc ccc agc agc tca			2112
	Tyr Gln Lys Cys Cys Asn Leu Phe Glu Lys Phe Phe Pro Ser Ser Ser			
	690	695	700	
	tac aga aga cca gtc gga att tet agt atg gtt gag gcc atg gtg tcc			2160
	Tyr Arg Arg Pro Val Gly Ile Ser Ser Met Val Glu Ala Met Val Ser			
	705	710	715	720
	agg gcc cgc att gat gca cga att gac ttc gaa tct gga cgg ata aag			2208
	Arg Ala Arg Ile Asp Ala Arg Ile Asp Phe Glu Ser Gly Arg Ile Lys			
	725	730	735	
	aag gat gag ttc gct gag atc atg aag atc tgt tcc acc att gaa gag			2256
	Lys Asp Glu Phe Ala Glu Ile Met Lys Ile Cys Ser Thr Ile Glu Glu			

	740	745	750	
	etc aga egg caa aaa tag			2274
	Leu Arg Arg Gln Lys			
	755			
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<213>	流感病毒			
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	Met Asp Val Asn Pro Thr Leu Leu Phe Leu Lys Val Pro Ala Gln Asn			
	1 5 10 15			
	Ala Ile Ser Thr Thr Phe Pro Tyr Thr Gly Asp Pro Pro Tyr Ser His			
	20 25 30			
[0015]	Gly Thr Gly Thr Gly Tyr Thr Met Asp Thr Val Asn Arg Thr His Gln			
	35 40 45			
	Tyr Ser Glu Lys Gly Lys Trp Thr Thr Asn Thr Glu Ile Gly Ala Pro			
	50 55 60			
	Gln Leu Asn Pro Ile Asp Gly Pro Leu Pro Glu Asp Asn Glu Pro Ser			
	65 70 75 80			
	Gly Tyr Ala Gln Thr Asp Cys Val Leu Glu Ala Met Ala Phe Leu Glu			
	85 90 95			
	Glu Ser His Pro Gly Ile Phe Glu Asn Ser Cys Leu Glu Thr Met Glu			
	100 105 110			
	Val Ile Gln Gln Thr Arg Val Asp Lys Leu Thr Gln Gly Arg Gln Thr			
	115 120 125			

	Tyr	Asp	Trp	Thr	Leu	Asn	Arg	Asn	Gln	Pro	Ala	Ala	Thr	Ala	Leu	Ala
	130						135						140			
	Asn	Thr	Ile	Glu	Val	Phe	Arg	Ser	Asn	Gly	Leu	Thr	Ser	Asn	Glu	Ser
	145					150					155				160	
	Gly	Arg	Leu	Met	Asp	Phe	Leu	Lys	Asp	Val	Met	Glu	Ser	Met	Asn	Lys
					165					170					175	
	Glu	Glu	Met	Glu	Ile	Thr	Thr	His	Phe	Gln	Arg	Lys	Arg	Arg	Val	Arg
				180						185					190	
	Asp	Asn	Met	Thr	Lys	Arg	Met	Val	Thr	Gln	Arg	Thr	Ile	Gly	Lys	Lys
		195						200						205		
[0016]	Lys	Gln	Arg	Leu	Asn	Arg	Lys	Ser	Tyr	Leu	Ile	Arg	Thr	Leu	Thr	Leu
	210						215						220			
	Asn	Thr	Met	Thr	Lys	Asp	Ala	Glu	Arg	Gly	Lys	Leu	Lys	Arg	Arg	Ala
	225					230					235				240	
	Ile	Ala	Thr	Pro	Gly	Met	Gln	Ile	Arg	Gly	Phe	Val	Tyr	Phe	Val	Glu
					245					250					255	
	Thr	Leu	Ala	Arg	Arg	Ile	Cys	Glu	Lys	Leu	Glu	Gln	Ser	Gly	Leu	Pro
				260						265					270	
	Val	Gly	Gly	Asn	Glu	Lys	Lys	Ala	Lys	Leu	Ala	Asn	Val	Val	Arg	Lys
			275					280					285			
	Met	Met	Thr	Asn	Ser	Gln	Asp	Thr	Glu	Leu	Ser	Phe	Thr	Ile	Thr	Gly
	290						295						300			

Asp Asn Thr Lys Trp Asn Glu Asn Gln Asn Pro Arg Ile Phe Leu Ala
305 310 315 320

Met Ile Thr Tyr Ile Thr Arg Asn Gln Pro Glu Trp Phe Arg Asn Val
325 330 335

Leu Ser Ile Ala Pro Ile Met Phe Ser Asn Lys Met Ala Arg Leu Gly
340 345 350

Lys Gly Tyr Met Phe Glu Ser Lys Ser Met Lys Leu Arg Thr Gln Ile
355 360 365

Pro Ala Glu Met Leu Ala Ser Ile Asp Leu Lys Tyr Phe Asn Asp Ser
370 375 380

[0017]

Thr Lys Lys Lys Ile Glu Lys Ile Arg Pro Leu Leu Val Asp Gly Thr
385 390 395 400

Ala Ser Leu Ser Pro Gly Met Met Met Gly Met Phe Asn Met Leu Ser
405 410 415

Thr Val Leu Gly Val Ser Ile Leu Asn Leu Gly Gln Arg Lys Tyr Thr
420 425 430

Lys Thr Thr Tyr Trp Trp Asp Gly Leu Gln Ser Ser Asp Asp Phe Ala
435 440 445

Leu Ile Val Asn Ala Pro Asn His Glu Gly Val Gln Ala Gly Val Asp
450 455 460

Arg Phe Tyr Arg Thr Cys Lys Leu Val Gly Ile Asn Met Ser Lys Lys
465 470 475 480

	Lys Ser Tyr Ile Asn Arg Thr Gly Thr Phe Glu Phe Thr Ser Phe Phe	
	485	490 495
	Tyr Arg Tyr Gly Phe Val Ala Asn Phe Ser Met Glu Leu Pro Ser Phe	
	500	505 510
	Gly Val Ser Gly Ile Asn Glu Ser Ala Asp Met Ser Ile Gly Val Thr	
	515	520 525
	Val Ile Lys Asn Asn Met Ile Asn Asn Asp Leu Gly Pro Ala Thr Ala	
	530	535 540
	Gln Met Ala Leu Gln Leu Phe Ile Lys Asp Tyr Arg Tyr Thr Tyr Arg	
	545	550 555 560
[0018]	Cys His Arg Gly Asp Thr Gln Ile Gln Thr Arg Arg Ser Phe Glu Leu	
	565	570 575
	Lys Lys Leu Trp Glu Gln Thr Arg Ser Lys Thr Gly Leu Leu Val Ser	
	580	585 590
	Asp Gly Gly Pro Asn Leu Tyr Asn Ile Arg Asn Leu His Ile Pro Glu	
	595	600 605
	Val Cys Leu Lys Trp Glu Leu Met Asp Glu Asp Tyr Lys Gly Arg Leu	
	610	615 620
	Cys Asn Pro Leu Asn Pro Phe Val Ser His Lys Glu Ile Glu Ser Val	
	625	630 635 640
	Asn Ser Ala Val Val Met Pro Ala His Gly Pro Ala Lys Ser Met Glu	
	645	650 655

Tyr Asp Ala Val Ala Thr Thr His Ser Trp Ile Pro Lys Arg Asn Arg
660 665 670

Ser Ile Leu Asn Thr Ser Gln Arg Gly Val Leu Glu Asp Glu Gln Met
675 680 685

Tyr Gln Lys Cys Cys Asn Leu Phe Glu Lys Phe Phe Pro Ser Ser Ser
690 695 700

Tyr Arg Arg Pro Val Gly Ile Ser Ser Met Val Glu Ala Met Val Ser
705 710 715 720

Arg Ala Arg Ile Asp Ala Arg Ile Asp Phe Glu Ser Gly Arg Ile Lys
725 730 735

[0019] Lys Asp Glu Phe Ala Glu Ile Met Lys Ile Cys Ser Thr Ile Glu Glu
740 745 750

Leu Arg Arg Gln Lys
755

<210> 5

<211> 2151

<212> DNA

<213> 流感病毒

<220>

<221> CDS

<222> (1).. (2151)

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Met Glu Asp Phe Val Arg Gln Cys Phe Asn Pro Met Ile Val Glu Leu
1 5 10 15

48

	gcg gaa aag gca atg aaa gaa tat gga gag aac ceg aaa atc gaa aca	96
	Ala Glu Lys Ala Met Lys Glu Tyr Gly Glu Asn Pro Lys Ile Glu Thr	
	20 25 30	
	aac aaa ttt gca gca ata tgc act cac ttg gaa gtc tgc ttc atg tac	144
	Asn Lys Phe Ala Ala Ile Cys Thr His Leu Glu Val Cys Phe Met Tyr	
	35 40 45	
	tcg gat ttt cac ttt att aat gaa ctg ggt gag tca gtg gtc ata gag	192
	Ser Asp Phe His Phe Ile Asn Glu Leu Gly Glu Ser Val Val Ile Glu	
	50 55 60	
	tct ggt gac cca aat get ctt ttg aaa cac aga ttt gaa atc att gag	240
	Ser Gly Asp Pro Asn Ala Leu Leu Lys His Arg Phe Glu Ile Ile Glu	
	65 70 75 80	
	ggg aga gat cga aca atg gca tgg aca gta gta aac agc atc tgc aac	288
	Gly Arg Asp Arg Thr Met Ala Trp Thr Val Val Asn Ser Ile Cys Asn	
	85 90 95	
[0020]	acc aca aga get gaa aaa cct aaa ttt ctt cca gat tta tac gac tat	336
	Thr Thr Arg Ala Glu Lys Pro Lys Phe Leu Pro Asp Leu Tyr Asp Tyr	
	100 105 110	
	aag gag aac aga ttt gtt gaa att ggt gtg aca agg aga gaa gtt cac	384
	Lys Glu Asn Arg Phe Val Glu Ile Gly Val Thr Arg Arg Glu Val His	
	115 120 125	
	ata tac tac ctg gag aag gcc aac aaa ata aag tct gag aaa aca cat	432
	Ile Tyr Tyr Leu Glu Lys Ala Asn Lys Ile Lys Ser Glu Lys Thr His	
	130 135 140	
	atc cac att ttc tca ttt aca gga gag gaa atg get aca aaa gcg gac	480
	Ile His Ile Phe Ser Phe Thr Gly Glu Glu Met Ala Thr Lys Ala Asp	
	145 150 155 160	
	tat act ctt gat gaa gag agt aga gcc agg atc aag acc aga cta ttc	528
	Tyr Thr Leu Asp Glu Glu Ser Arg Ala Arg Ile Lys Thr Arg Leu Phe	
	165 170 175	
	acc ata aga caa gaa atg gcc agt aga gcc ctc tgg gat tcc ttt cgt	576
	Thr Ile Arg Gln Glu Met Ala Ser Arg Gly Leu Trp Asp Ser Phe Arg	
	180 185 190	

	cag tcc gag aga ggc gaa gag aca att gaa gaa aga ttt gaa ata aca Gln Ser Glu Arg Gly Glu Glu Thr Ile Glu Glu Arg Phe Glu Ile Thr 195 200 205	624
	ggg acg atg cgc aag ctt gcc aat tac agt ctc cca ccg aac ttc tcc Gly Thr Met Arg Lys Leu Ala Asn Tyr Ser Leu Pro Pro Asn Phe Ser 210 215 220	672
	age ctt gaa aat ttt aga gtc tat gtg gat gga ttc gaa ccg aac ggc Ser Leu Glu Asn Phe Arg Val Tyr Val Asp Gly Phe Glu Pro Asn Gly 225 230 235 240	720
	tgc att gag agt aag ctt tct caa atg tcc aaa gaa gta aat gcc aga Cys Ile Glu Ser Lys Leu Ser Gln Met Ser Lys Glu Val Asn Ala Arg 245 250 255	768
	atc gaa cca ttt tca aag aca aca ccc cga cca ctc aaa atg cca ggt Ile Glu Pro Phe Ser Lys Thr Thr Pro Arg Pro Leu Lys Met Pro Gly 260 265 270	816
[0021]	ggt cca ccc tgc cat cag cga tct aaa ttc ttg cta atg gat gct ctg Gly Pro Pro Cys His Gln Arg Ser Lys Phe Leu Leu Met Asp Ala Leu 275 280 285	864
	aaa ctg agc att gag gac cca agt cac gag gga gag gga ata cca cta Lys Leu Ser Ile Glu Asp Pro Ser His Glu Gly Glu Gly Ile Pro Leu 290 295 300	912
	tat gat gca atc aaa tgc atg aaa act ttc ttt gga tgg aaa gag ccc Tyr Asp Ala Ile Lys Cys Met Lys Thr Phe Phe Gly Trp Lys Glu Pro 305 310 315 320	960
	agt att gtt aaa cca cat gaa aag ggt ata aac ccg aac tat ctc caa Ser Ile Val Lys Pro His Glu Lys Gly Ile Asn Pro Asn Tyr Leu Gln 325 330 335	1008
	act tgg aag caa gta tta gaa gaa ata caa gac ctt gag aac gaa gaa Thr Trp Lys Gln Val Leu Glu Glu Ile Gln Asp Leu Glu Asn Glu Glu 340 345 350	1056
	agg acc ccc aag acc aag aat atg aaa aaa aca age caa ttg aaa tgg Arg Thr Pro Lys Thr Lys Asn Met Lys Lys Thr Ser Gln Leu Lys Trp 355 360 365	1104

	gea cta ggt gaa aat atg gca cca gag aaa gtg gat ttt gag gat tgt	1152
	Ala Leu Gly Glu Asn Met Ala Pro Glu Lys Val Asp Phe Glu Asp Cys	
	370 375 380	
	aaa gac atc aat gat tta aaa caa tat gac agt gat gag cca gaa gca	1200
	Lys Asp Ile Asn Asp Leu Lys Gln Tyr Asp Ser Asp Glu Pro Glu Ala	
	385 390 395 400	
	agg tct ctt gca agt tgg att caa agt gag ttc aac aaa gct tgt gag	1248
	Arg Ser Leu Ala Ser Trp Ile Gln Ser Glu Phe Asn Lys Ala Cys Glu	
	405 410 415	
	ctg aca gat tca agc tgg ata gag ctc gat gaa att ggg gag gat gtc	1296
	Leu Thr Asp Ser Ser Trp Ile Glu Leu Asp Glu Ile Gly Glu Asp Val	
	420 425 430	
	gcc cca ata gaa tac att ggc agc atg agg agu aat tat ttt act gct	1344
	Ala Pro Ile Glu Tyr Ile Ala Ser Met Arg Arg Asn Tyr Phe Thr Ala	
	435 440 445	
[0022]	gag att tcc cat tgt aga gca aca gaa tat ata ata aaa gga gtg tac	1392
	Glu Ile Ser His Cys Arg Ala Thr Glu Tyr Ile Ile Lys Gly Val Tyr	
	450 455 460	
	atc aac act gct cta ctc aat gca tcc tgt gct ggc atg gat gaa ttt	1440
	Ile Asn Thr Ala Leu Leu Asn Ala Ser Cys Ala Ala Met Asp Glu Phe	
	465 470 475 480	
	caa tta att ccg atg ata agt aaa tgc agg acc aaa gaa ggg aga agg	1488
	Gln Leu Ile Pro Met Ile Ser Lys Cys Arg Thr Lys Glu Gly Arg Arg	
	485 490 495	
	aaa aca aat tta tat gga ttc ata ata aag gga agg tcc cat tta aga	1536
	Lys Thr Asn Leu Tyr Gly Phe Ile Ile Lys Gly Arg Ser His Leu Arg	
	500 505 510	
	aat gat act gac gtg gtg aac ttt gta agt atg gaa ttt tct ctc act	1584
	Asn Asp Thr Asp Val Val Asn Phe Val Ser Met Glu Phe Ser Leu Thr	
	515 520 525	
	gat cca aga ttt gag cca cac aaa tgg gaa aaa tac tgc gtt cta gaa	1632
	Asp Pro Arg Phe Glu Pro His Lys Trp Glu Lys Tyr Cys Val Leu Glu	
	530 535 540	

	att gga gac atg ctt cta aga acf gct gta ggt caa gtg tca aga ccc	1680
	Ile Gly Asp Met Leu Leu Arg Thr Ala Val Gly Gln Val Ser Arg Pro	
	545 550 555 560	
	atg ttt ttg tat gta agg aca aat gga acc tct aaa att aaa atg aaa	1728
	Met Phe Leu Tyr Val Arg Thr Asn Gly Thr Ser Lys Ile Lys Met Lys	
	565 570 575	
	tgg gga atg gaa atg agg cgc tgc ctc ctt cag tct ctg caa cag att	1776
	Trp Gly Met Glu Met Arg Arg Cys Leu Leu Gln Ser Leu Gln Gln Ile	
	580 585 590	
	gaa agc atg atc gaa gct gag tcc tca gtc aaa gaa aag gac atg acc	1824
	Glu Ser Met Ile Glu Ala Glu Ser Ser Val Lys Glu Lys Asp Met Thr	
	595 600 605	
	aaa gaa ttt ttt gag aac aaa tca gag aca tgg cct ata gga gag tcc	1872
	Lys Glu Phe Phe Glu Asn Lys Ser Glu Thr Trp Pro Ile Gly Glu Ser	
	610 615 620	
[0023]	ccc aaa gga gtg gaa gag ggc tca atc ggg aag gtt tgc agg acc tta	1920
	Pro Lys Gly Val Glu Glu Gly Ser Ile Gly Lys Val Cys Arg Thr Leu	
	625 630 635 640	
	tta gca aaa tct gtg ttt aac agt tta tat gca tct cca caa ctg gaa	1968
	Leu Ala Lys Ser Val Phe Asn Ser Leu Tyr Ala Ser Pro Gln Leu Glu	
	645 650 655	
	ggg ttt tca gct gaa tct agg aaa tta ctt ctc att gtt cag gct ctt	2016
	Gly Phe Ser Ala Glu Ser Arg Lys Leu Leu Leu Ile Val Gln Ala Leu	
	660 665 670	
	aag gat gac ctg gaa cct gga acc ttt gat att ggg ggg tta tat gaa	2064
	Lys Asp Asp Leu Glu Pro Gly Thr Phe Asp Ile Gly Gly Leu Tyr Glu	
	675 680 685	
	tca att gag gag tgc ctg att aat gat ccc tgg gtt ttg ctt aat gca	2112
	Ser Ile Glu Glu Cys Leu Ile Asn Asp Pro Trp Val Leu Leu Asn Ala	
	690 695 700	
	tct tgg ttc aac tcc ttc ctt aca cat gca ctg aag tag	2151
	Ser Trp Phe Asn Ser Phe Leu Thr His Ala Leu Lys	
	705 710 715	

<210> 6

<211> 716

<212> PRT

<213> 流感病毒

<400> 6

Met	Glu	Asp	Phe	Val	Arg	Gln	Cys	Phe	Asn	Pro	Met	Ile	Val	Glu	Leu
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Ala	Glu	Lys	Ala	Met	Lys	Glu	Tyr	Gly	Glu	Asn	Pro	Lys	Ile	Glu	Thr
			20					25					30		

Asn	Lys	Phe	Ala	Ala	Ile	Cys	Thr	His	Leu	Glu	Val	Cys	Phe	Met	Tyr
			35					40					45		

Ser	Asp	Phe	His	Phe	Ile	Asn	Glu	Leu	Gly	Glu	Ser	Val	Val	Ile	Glu
[0024]			50				55				60				

Ser	Gly	Asp	Pro	Asn	Ala	Leu	Leu	Lys	His	Arg	Phe	Glu	Ile	Ile	Glu
65					70					75				80	

Gly	Arg	Asp	Arg	Thr	Met	Ala	Trp	Thr	Val	Val	Asn	Ser	Ile	Cys	Asn
				85					90					95	

Thr	Thr	Arg	Ala	Glu	Lys	Pro	Lys	Phe	Leu	Pro	Asp	Leu	Tyr	Asp	Tyr
			100					105					110		

Lys	Glu	Asn	Arg	Phe	Val	Glu	Ile	Gly	Val	Thr	Arg	Arg	Glu	Val	His
			115					120					125		

Ile	Tyr	Tyr	Leu	Glu	Lys	Ala	Asn	Lys	Ile	Lys	Ser	Glu	Lys	Thr	His
			130				135				140				

	Ile His Ile Phe Ser Phe Thr Gly Glu Glu Met Ala Thr Lys Ala Asp	
	145	150 155 160
	Tyr Thr Leu Asp Glu Glu Ser Arg Ala Arg Ile Lys Thr Arg Leu Phe	
		165 170 175
	Thr Ile Arg Gln Glu Met Ala Ser Arg Gly Leu Trp Asp Ser Phe Arg	
		180 185 190
	Gln Ser Glu Arg Gly Glu Glu Thr Ile Glu Glu Arg Phe Glu Ile Thr	
		195 200 205
	Gly Thr Met Arg Lys Leu Ala Asn Tyr Ser Leu Pro Pro Asn Phe Ser	
		210 215 220
[0025]	Ser Leu Glu Asn Phe Arg Val Tyr Val Asp Gly Phe Glu Pro Asn Gly	
	225	230 235 240
	Cys Ile Glu Ser Lys Leu Ser Gln Met Ser Lys Glu Val Asn Ala Arg	
		245 250 255
	Ile Glu Pro Phe Ser Lys Thr Thr Pro Arg Pro Leu Lys Met Pro Gly	
		260 265 270
	Gly Pro Pro Cys His Gln Arg Ser Lys Phe Leu Leu Met Asp Ala Leu	
		275 280 285
	Lys Leu Ser Ile Glu Asp Pro Ser His Glu Gly Glu Gly Ile Pro Leu	
		290 295 300
	Tyr Asp Ala Ile Lys Cys Met Lys Thr Phe Phe Gly Trp Lys Glu Pro	
	305	310 315 320

Ser Ile Val Lys Pro His Glu Lys Gly Ile Asn Pro Asn Tyr Leu Gln
325 330 335

Thr Trp Lys Gln Val Leu Glu Glu Ile Gln Asp Leu Glu Asn Glu Glu
340 345 350

Arg Thr Pro Lys Thr Lys Asn Met Lys Lys Thr Ser Gln Leu Lys Trp
355 360 365

Ala Leu Gly Glu Asn Met Ala Pro Glu Lys Val Asp Phe Glu Asp Cys
370 375 380

Lys Asp Ile Asn Asp Leu Lys Gln Tyr Asp Ser Asp Glu Pro Glu Ala
385 390 395 400

[0026] Arg Ser Leu Ala Ser Trp Ile Gln Ser Glu Phe Asn Lys Ala Cys Glu
405 410 415

Leu Thr Asp Ser Ser Trp Ile Glu Leu Asp Glu Ile Gly Glu Asp Val
420 425 430

Ala Pro Ile Glu Tyr Ile Ala Ser Met Arg Arg Asn Tyr Phe Thr Ala
435 440 445

Glu Ile Ser His Cys Arg Ala Thr Glu Tyr Ile Ile Lys Gly Val Tyr
450 455 460

Ile Asn Thr Ala Leu Leu Asn Ala Ser Cys Ala Ala Met Asp Glu Phe
465 470 475 480

Gln Leu Ile Pro Met Ile Ser Lys Cys Arg Thr Lys Glu Gly Arg Arg
485 490 495

Lys Thr Asn Leu Tyr Gly Phe Ile Ile Lys Gly Arg Ser His Leu Arg
500 505 510

Asn Asp Thr Asp Val Val Asn Phe Val Ser Met Glu Phe Ser Leu Thr
515 520 525

Asp Pro Arg Phe Glu Pro His Lys Trp Glu Lys Tyr Cys Val Leu Glu
530 535 540

Ile Gly Asp Met Leu Leu Arg Thr Ala Val Gly Gln Val Ser Arg Pro
545 550 555 560

Met Phe Leu Tyr Val Arg Thr Asn Gly Thr Ser Lys Ile Lys Met Lys
565 570 575

[0027]

Trp Gly Met Glu Met Arg Arg Cys Leu Leu Gln Ser Leu Gln Gln Ile
580 585 590

Glu Ser Met Ile Glu Ala Glu Ser Ser Val Lys Glu Lys Asp Met Thr
595 600 605

Lys Glu Phe Phe Glu Asn Lys Ser Glu Thr Trp Pro Ile Gly Glu Ser
610 615 620

Pro Lys Gly Val Glu Glu Gly Ser Ile Gly Lys Val Cys Arg Thr Leu
625 630 635 640

Leu Ala Lys Ser Val Phe Asn Ser Leu Tyr Ala Ser Pro Gln Leu Glu
645 650 655

Gly Phe Ser Ala Glu Ser Arg Lys Leu Leu Leu Ile Val Gln Ala Leu
660 665 670

Lys Asp Asp Leu Glu Pro Gly Thr Phe Asp Ile Gly Gly Leu Tyr Glu
675 680 685

Ser Ile Glu Glu Cys Leu Ile Asn Asp Pro Trp Val Leu Leu Asn Ala
690 695 700

Ser Trp Phe Asn Ser Phe Leu Thr His Ala Leu Lys
705 710 715

<210> 7

<211> 838

<212> DNA

<213> 流感病毒

<220>

<221> CDS

<222> (1)..(657)

[0028]

<400> 7

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cat gtc cgc aaa cga ttc gca gac caa gaa ctg ggt gat gcc cca ttc 96
His Val Arg Lys Arg Phe Ala Asp Gln Glu Leu Gly Asp Ala Pro Phe
20 25 30

ctt gac cgg ctt cgc cga gac cag aag tcc cta agg gga aga ggt agc 144
Leu Asp Arg Leu Arg Arg Asp Gln Lys Ser Leu Arg Gly Arg Gly Ser
35 40 45

act ctt ggt ctg gac atc gaa aca gcc act cat gca gga aag cag ata 192
Thr Leu Gly Leu Asp Ile Glu Thr Ala Thr His Ala Gly Lys Gln Ile
50 55 60

gtg gag cag att ctg gaa aag gaa tca gat gag gca ctt aaa atg acc 240
Val Glu Gln Ile Leu Glu Lys Glu Ser Asp Glu Ala Leu Lys Met Thr
65 70 75 80

[0029]	att gcc tct gtt cct act tca ctc tac tta act gac atg act ctt gat	288
	Ile Ala Ser Val Pro Thr Ser Leu Tyr Leu Thr Asp Met Thr Leu Asp	
	85 90 95	
	gag atg tca aga gac tgg ttc atg ctc atg ccc aag caa aaa gta aca	336
	Glu Met Ser Arg Asp Trp Phe Met Leu Met Pro Lys Gln Lys Val Thr	
	100 105 110	
	ggc tcc cta tgt ata aga atg gac cag gca atc atg gat aag aac atc	384
	Gly Ser Leu Cys Ile Arg Met Asp Gln Ala Ile Met Asp Lys Asn Ile	
	115 120 125	
	ata ctt aaa gca aac ttt agt gtg att ttc gaa ggg ctg gaa aca cta	432
	Ile Leu Lys Ala Asn Phe Ser Val Ile Phe Glu Gly Leu Glu Thr Leu	
	130 135 140	
	ata cta ctt aga gcc ttc acc gaa gaa gga gca gtc gtt ggc gaa att	480
	Ile Leu Leu Arg Ala Phe Thr Glu Glu Gly Ala Val Val Gly Glu Ile	
	145 150 155 160	
	tca cca tta cct tct ctt cca gga cat act aat gag gat gtc aaa aat	528
	Ser Pro Leu Pro Ser Leu Pro Gly His Thr Asn Glu Asp Val Lys Asn	
	165 170 175	
	gca att ggg gtc ctc atc gga gga ctt aaa tgg aat gat aat acg gtt	576
	Ala Ile Gly Val Leu Ile Gly Gly Leu Lys Trp Asn Asp Asn Thr Val	
	180 185 190	
	aga atc tct gaa act cta cag aga ttc get tgg aga agc agt cat gag	624
	Arg Ile Ser Glu Thr Leu Gln Arg Phe Ala Trp Arg Ser Ser His Glu	
	195 200 205	
	aat ggg aga cct tca ttc cct tca aag cag aaa tgaaaaatgg agagaacaat	677
	Asn Gly Arg Pro Ser Phe Pro Ser Lys Gln Lys	
	210 215	
	taagccagaa atttgaagaa ataagatggt tgattgaaga agtgcgacat agattgaaaa	737
	atcacagaaa tagttttgaa caaataacat ttatgaagc cttacaacta ttgettgaag	797
	tagaacaaga gataagaact ttctcgtttc agcttattta a	838

<210> 8

<211> 219

<212> PRT

<213> 流感病毒

<400> 8

Met	Asp	Ser	Asn	Thr	Val	Ser	Ser	Phe	Gln	Val	Asp	Cys	Phe	Leu	Trp
1				5					10					15	

His	Val	Arg	Lys	Arg	Phe	Ala	Asp	Gln	Glu	Leu	Gly	Asp	Ala	Pro	Phe
			20					25					30		

Leu	Asp	Arg	Leu	Arg	Arg	Asp	Gln	Lys	Ser	Leu	Arg	Gly	Arg	Gly	Ser
		35					40					45			

Thr	Leu	Gly	Leu	Asp	Ile	Glu	Thr	Ala	Thr	His	Ala	Gly	Lys	Gln	Ile
	50					55						60			

[0030]

Val	Glu	Gln	Ile	Leu	Glu	Lys	Glu	Ser	Asp	Glu	Ala	Leu	Lys	Met	Thr
65				70						75				80	

Ile	Ala	Ser	Val	Pro	Thr	Ser	Leu	Tyr	Leu	Thr	Asp	Met	Thr	Leu	Asp
			85						90				95		

Glu	Met	Ser	Arg	Asp	Trp	Phe	Met	Leu	Met	Pro	Lys	Gln	Lys	Val	Thr
			100					105					110		

Gly	Ser	Leu	Cys	Ile	Arg	Met	Asp	Gln	Ala	Ile	Met	Asp	Lys	Asn	Ile
			115					120					125		

Ile	Leu	Lys	Ala	Asn	Phe	Ser	Val	Ile	Phe	Glu	Gly	Leu	Glu	Thr	Leu
	130						135					140			

Ile	Leu	Leu	Arg	Ala	Phe	Thr	Glu	Glu	Gly	Ala	Val	Val	Gly	Glu	Ile
145					150					155					160

Ser Pro Leu Pro Ser Leu Pro Gly His Thr Asn Glu Asp Val Lys Asn
 165 170 175

Ala Ile Gly Val Leu Ile Gly Gly Leu Lys Trp Asn Asp Asn Thr Val
 180 185 190

Arg Ile Ser Glu Thr Leu Gln Arg Phe Ala Trp Arg Ser Ser His Glu
 195 200 205

Asn Gly Arg Pro Ser Phe Pro Ser Lys Gln Lys
 210 215

<210> 9
 <211> 1497
 <212> DNA
 <213> 流感病毒

[0031]

<220>
 <221> CDS
 <222> (1).. (1497)

<400> 9
 atg gcg tct caa ggc acc aaa cga tcc tat gaa cag atg gaa act gat 48
 Met Ala Ser Gln Gly Thr Lys Arg Ser Tyr Glu Gln Met Glu Thr Asp
 1 5 10 15
 ggg gaa cgc cag aat gca act gaa atc aga gca tct gtc gga agg atg 96
 Gly Glu Arg Gln Asn Ala Thr Glu Ile Arg Ala Ser Val Gly Arg Met
 20 25 30
 gtg gga gga atc ggc cga ttt tat gtt cag atg tgt act gag ctt aaa 144
 Val Gly Gly Ile Gly Arg Phe Tyr Val Gln Met Cys Thr Glu Leu Lys
 35 40 45
 cta aac gac cat gaa ggg cgg ctg att cag aac age ata aca ata gaa 192
 Leu Asn Asp His Glu Gly Arg Leu Ile Gln Asn Ser Ile Thr Ile Glu
 50 55 60

	agg atg gta ctt tgc gca ttc gac gaa aga aga aac aag tat etc gag	240
	Arg Met Val Leu Ser Ala Phe Asp Glu Arg Arg Asn Lys Tyr Leu Glu	
	65 70 75 80	
	gag cat ccc agt gct ggg aaa gac cct aag aaa acg gga ggc ccg ata	288
	Glu His Pro Ser Ala Gly Lys Asp Pro Lys Lys Thr Gly Gly Pro Ile	
	85 90 95	
	tac aga agg aaa gat ggg aaa tgg atg agg gaa etc atc etc cat gat	336
	Tyr Arg Arg Lys Asp Gly Lys Trp Met Arg Glu Leu Ile Leu His Asp	
	100 105 110	
	aaa gaa gaa atc atg aga atc tgg cgt cag gcc aac aat ggt gaa gac	384
	Lys Glu Glu Ile Met Arg Ile Trp Arg Gln Ala Asn Asn Gly Glu Asp	
	115 120 125	
	gct act gct ggt ctt act cat atg atg atc tgg cac tcc aat etc aat	432
	Ala Thr Ala Gly Leu Thr His Met Met Ile Trp His Ser Asn Leu Asn	
	130 135 140	
[0032]	gac acc aca tac caa aga aca agg gct ctt gtt cgg act ggg atg gat	480
	Asp Thr Thr Tyr Gln Arg Thr Arg Ala Leu Val Arg Thr Gly Met Asp	
	145 150 155 160	
	ccc aga atg tgc tct ctg atg caa ggc tea acc etc cca egg aga tct	528
	Pro Arg Met Cys Ser Leu Met Gln Gly Ser Thr Leu Pro Arg Arg Ser	
	165 170 175	
	gga gcc gct ggt gct gca gta aaa ggt gtt gga aca atg gta atg gaa	576
	Gly Ala Ala Gly Ala Ala Val Lys Gly Val Gly Thr Met Val Met Glu	
	180 185 190	
	etc atc aga atg atc aaa cgc gga ata aat gat cgg aat ttc tgg aga	624
	Leu Ile Arg Met Ile Lys Arg Gly Ile Asn Asp Arg Asn Phe Trp Arg	
	195 200 205	
	ggt gaa aat ggt cga aaa acc aga att gct tat gaa aga atg tgc aat	672
	Gly Glu Asn Gly Arg Lys Thr Arg Ile Ala Tyr Glu Arg Met Cys Asn	
	210 215 220	
	atc etc aaa ggg aaa ttt cag aca gca gca caa cgg gct atg atg gac	720
	Ile Leu Lys Gly Lys Phe Gln Thr Ala Ala Gln Arg Ala Met Met Asp	
	225 230 235 240	

	cag gtg agg gaa ggc cgc aat cct gga aac gct gag att gag gat etc	768
	Gln Val Arg Glu Gly Arg Asn Pro Gly Asn Ala Glu Ile Glu Asp Leu	
	245 250 255	
	att ttc ttg gca cga tca gca ctt att ttg aga gga tca gta gcc cat	816
	Ile Phe Leu Ala Arg Ser Ala Leu Ile Leu Arg Gly Ser Val Ala His	
	260 265 270	
	aaa tca tgc cta cct gcc tgt gtt tat ggc ctt gca ata acc agt ggg	864
	Lys Ser Cys Leu Pro Ala Cys Val Tyr Gly Leu Ala Ile Thr Ser Gly	
	275 280 285	
	tat gac ttt gag aag gaa gga tac tct ctg gtt gga att gat cct ttc	912
	Tyr Asp Phe Glu Lys Glu Gly Tyr Ser Leu Val Gly Ile Asp Pro Phe	
	290 295 300	
	aaa cta ctc cag aac agt caa att ttc agt cta atc aga cca aaa gaa	960
	Lys Leu Leu Gln Asn Ser Gln Ile Phe Ser Leu Ile Arg Pro Lys Glu	
	305 310 315 320	
[0033]	aac cca gca cac aag agc cag ttg gtg tgg atg gca tgc cat tct gca	1008
	Asn Pro Ala His Lys Ser Gln Leu Val Trp Met Ala Cys His Ser Ala	
	325 330 335	
	gca ttt gag gac ctg aga gtt tta aat ttc att aga gga acc aaa gta	1056
	Ala Phe Glu Asp Leu Arg Val Leu Asn Phe Ile Arg Gly Thr Lys Val	
	340 345 350	
	atc cca aga gga cag tta aca acc aga gga gtt caa att gct tca aat	1104
	Ile Pro Arg Gly Gln Leu Thr Thr Arg Gly Val Gln Ile Ala Ser Asn	
	355 360 365	
	gaa aac atg gag aca ata aat tct agc aca ctt gaa ctg aga agc aaa	1152
	Glu Asn Met Glu Thr Ile Asn Ser Ser Thr Leu Glu Leu Arg Ser Lys	
	370 375 380	
	tat tgg gca ata agg acc aga agc gga gga aac acc agt caa cag aga	1200
	Tyr Trp Ala Ile Arg Thr Arg Ser Gly Gly Asn Thr Ser Gln Gln Arg	
	385 390 395 400	
	gca tct gca gga cag ata agt gtg caa cct act ttc tca gta cag aga	1248
	Ala Ser Ala Gly Gln Ile Ser Val Gln Pro Thr Phe Ser Val Gln Arg	
	405 410 415	

	aat cta ccc ttt gag aga gcg acc att atg get gca ttc act ggt aac	1296
	Asn Leu Pro Phe Glu Arg Ala Thr Ile Met Ala Ala Phe Thr Gly Asn	
	420 425 430	
	act gaa ggg agg act tcc gac atg aga acg gaa atc ata agg atg atg	1344
	Thr Glu Gly Arg Thr Ser Asp Met Arg Thr Glu Ile Ile Arg Met Met	
	435 440 445	
	gaa aat gcc aaa tca gaa gat gtg tct ttc cag ggg egg gga gtc ttc	1392
	Glu Asn Ala Lys Ser Glu Asp Val Ser Phe Gln Gly Arg Gly Val Phe	
	450 455 460	
	gag ctc teg gac gaa aag gca acg aac ccg atc gtg cct tcc ttt gac	1440
	Glu Leu Ser Asp Glu Lys Ala Thr Asn Pro Ile Val Pro Ser Phe Asp	
	465 470 475 480	
	atg agc aat gaa ggg tct tat ttc ttc gga gac aat get gag gag ttt	1488
	Met Ser Asn Glu Gly Ser Tyr Phe Phe Gly Asp Asn Ala Glu Glu Phe	
	485 490 495	
[0034]	gac agt taa	1497
	Asp Ser	

<210> 10

<211> 498

<212> PRT

<213> 流感病毒

<400> 10

Met Ala Ser Gln Gly Thr Lys Arg Ser Tyr Glu Gln Met Glu Thr Asp
1 5 10 15

Gly Glu Arg Gln Asn Ala Thr Glu Ile Arg Ala Ser Val Gly Arg Met
20 25 30

Val Gly Gly Ile Gly Arg Phe Tyr Val Gln Met Cys Thr Glu Leu Lys
35 40 45

Leu Asn Asp His Glu Gly Arg Leu Ile Gln Asn Ser Ile Thr Ile Glu
50 55 60

Arg Met Val Leu Ser Ala Phe Asp Glu Arg Arg Asn Lys Tyr Leu Glu
65 70 75 80

Glu His Pro Ser Ala Gly Lys Asp Pro Lys Lys Thr Gly Gly Pro Ile
85 90 95

Tyr Arg Arg Lys Asp Gly Lys Trp Met Arg Glu Leu Ile Leu His Asp
100 105 110

Lys Glu Glu Ile Met Arg Ile Trp Arg Gln Ala Asn Asn Gly Glu Asp
115 120 125

[0035]

Ala Thr Ala Gly Leu Thr His Met Met Ile Trp His Ser Asn Leu Asn
130 135 140

Asp Thr Thr Tyr Gln Arg Thr Arg Ala Leu Val Arg Thr Gly Met Asp
145 150 155 160

Pro Arg Met Cys Ser Leu Met Gln Gly Ser Thr Leu Pro Arg Arg Ser
165 170 175

Gly Ala Ala Gly Ala Ala Val Lys Gly Val Gly Thr Met Val Met Glu
180 185 190

Leu Ile Arg Met Ile Lys Arg Gly Ile Asn Asp Arg Asn Phe Trp Arg
195 200 205

Gly Glu Asn Gly Arg Lys Thr Arg Ile Ala Tyr Glu Arg Met Cys Asn
210 215 220

	Ile	Leu	Lys	Gly	Lys	Phe	Gln	Thr	Ala	Ala	Gln	Arg	Ala	Met	Met	Asp	
	225					230					235					240	
	Gln	Val	Arg	Glu	Gly	Arg	Asn	Pro	Gly	Asn	Ala	Glu	Ile	Glu	Asp	Leu	
					245					250					255		
	Ile	Phe	Leu	Ala	Arg	Ser	Ala	Leu	Ile	Leu	Arg	Gly	Ser	Val	Ala	His	
					260					265					270		
	Lys	Ser	Cys	Leu	Pro	Ala	Cys	Val	Tyr	Gly	Leu	Ala	Ile	Thr	Ser	Gly	
			275					280							285		
	Tyr	Asp	Phe	Glu	Lys	Glu	Gly	Tyr	Ser	Leu	Val	Gly	Ile	Asp	Pro	Phe	
	290						295					300					
[0036]	Lys	Leu	Leu	Gln	Asn	Ser	Gln	Ile	Phe	Ser	Leu	Ile	Arg	Pro	Lys	Glu	
	305					310					315					320	
	Asn	Pro	Ala	His	Lys	Ser	Gln	Leu	Val	Trp	Met	Ala	Cys	His	Ser	Ala	
					325					330					335		
	Ala	Phe	Glu	Asp	Leu	Arg	Val	Leu	Asn	Phe	Ile	Arg	Gly	Thr	Lys	Val	
					340					345					350		
	Ile	Pro	Arg	Gly	Gln	Leu	Thr	Thr	Arg	Gly	Val	Gln	Ile	Ala	Ser	Asn	
					355					360					365		
	Glu	Asn	Met	Glu	Thr	Ile	Asn	Ser	Ser	Thr	Leu	Glu	Leu	Arg	Ser	Lys	
					370					375					380		
	Tyr	Trp	Ala	Ile	Arg	Thr	Arg	Ser	Gly	Gly	Asn	Thr	Ser	Gln	Gln	Arg	
	385									390					395		400

Ala Ser Ala Gly Gln Ile Ser Val Gln Pro Thr Phe Ser Val Gln Arg
405 410 415

Asn Leu Pro Phe Glu Arg Ala Thr Ile Met Ala Ala Phe Thr Gly Asn
420 425 430

Thr Glu Gly Arg Thr Ser Asp Met Arg Thr Glu Ile Ile Arg Met Met
435 440 445

Glu Asn Ala Lys Ser Glu Asp Val Ser Phe Gln Gly Arg Gly Val Phe
450 455 460

Glu Leu Ser Asp Glu Lys Ala Thr Asn Pro Ile Val Pro Ser Phe Asp
465 470 475 480

[0037] Met Ser Asn Glu Gly Ser Tyr Phe Phe Gly Asp Asn Ala Glu Glu Phe
485 490 495

Asp Ser

<210> 11

<211> 1413

<212> DNA

<213> 流感病毒

<220>

<221> CDS

<222> (1).. (1413)

<400> 11

atg aat cca aat caa aag ata ata gca att gga ttt gea tca ttg ggg
Met Asn Pro Asn Gln Lys Ile Ile Ala Ile Gly Phe Ala Ser Leu Gly
1 5 10 15

48

	ata tta atc att aat gtc att ctc cat gta gtc agc att ata gta aca Ile Leu Ile Ile Asn Val Ile Leu His Val Val Ser Ile Ile Val Thr 20 25 30	96
	gta ctg gtc ctc aat aac aat aga aca gat ctg aac tgc aaa ggg acg Val Leu Val Leu Asn Asn Asn Arg Thr Asp Leu Asn Cys Lys Gly Thr 35 40 45	144
	atc ata aga aag tac aat gaa aca gta aga gta gaa aaa att act caa Ile Ile Arg Lys Tyr Asn Glu Thr Val Arg Val Glu Lys Ile Thr Gln 50 55 60	192
	tgg tat aat acc agt aca att aag tac ata gag aga cct tca aat gaa Trp Tyr Asn Thr Ser Thr Ile Lys Tyr Ile Glu Arg Pro Ser Asn Glu 65 70 75 80	240
	tac tac atg aac aac act gaa cca ctt tgt gag gcc caa ggc ttt gca Tyr Tyr Met Asn Asn Thr Glu Pro Leu Cys Glu Ala Gln Gly Phe Ala 85 90 95	288
[0038]	cca ttt tcc aaa gat aat gga ata cga att ggg teg aga ggc cat gtt Pro Phe Ser Lys Asp Asn Gly Ile Arg Ile Gly Ser Arg Gly His Val 100 105 110	336
	ttt gtg ata aga gaa cct ttt gta tca tgt teg ccc tca gaa tgt aga Phe Val Ile Arg Glu Pro Phe Val Ser Cys Ser Pro Ser Glu Cys Arg 115 120 125	384
	acc ttt ttc ctc aca cag ggc tca tta ctc aat gac aaa cat tct aac Thr Phe Phe Leu Thr Gln Gly Ser Leu Leu Asn Asp Lys His Ser Asn 130 135 140	432
	ggc aca gta aag gac cga agt ccg tat agg act ttg atg agt gtc aaa Gly Thr Val Lys Asp Arg Ser Pro Tyr Arg Thr Leu Met Ser Val Lys 145 150 155 160	480
	ata ggg caa tca cct aat gta tat caa gct aga ttt gaa teg gta gca Ile Gly Gln Ser Pro Asn Val Tyr Gln Ala Arg Phe Glu Ser Val Ala 165 170 175	528
	tgg tca gca aca gca tgc cat gat gga aaa aaa tgg atg aca gtt gga Trp Ser Ala Thr Ala Cys His Asp Gly Lys Lys Trp Met Thr Val Gly 180 185 190	576

[0039]	gtc aca ggg ccc gac aat caa gca att gca gta gtg aac tat gga ggt	624
	Val Thr Gly Pro Asp Asn Gln Ala Ile Ala Val Val Asn Tyr Gly Gly	
	195 200 205	
	ggt ccg gtt gat att att aat tca tgg gca ggg gat att tta aga acc	672
	Val Pro Val Asp Ile Ile Asn Ser Trp Ala Gly Asp Ile Leu Arg Thr	
	210 215 220	
	caa gaa tca tca tgc acc tgc att aaa gga gac tgt tat tgg gta atg	720
	Gln Glu Ser Ser Cys Thr Cys Ile Lys Gly Asp Cys Tyr Trp Val Met	
	225 230 235 240	
	act gat gga ccg gca aat agg caa gct aaa tat agg ata ttc aaa gca	768
	Thr Asp Gly Pro Ala Asn Arg Gln Ala Lys Tyr Arg Ile Phe Lys Ala	
	245 250 255	
	aaa gat gga aga gta att gga cag act gat ata agt ttc aat ggg gga	816
	Lys Asp Gly Arg Val Ile Gly Gln Thr Asp Ile Ser Phe Asn Gly Gly	
	260 265 270	
	cac ata gag gag tgt tct tgt tac ccc aat gaa ggg aag gtg gaa tgc	864
	His Ile Glu Glu Cys Ser Cys Tyr Pro Asn Glu Gly Lys Val Glu Cys	
	275 280 285	
	ata tgc agg gac aat tgg act gga aca aat aga cca gtt ctg gta ata	912
	Ile Cys Arg Asp Asn Trp Thr Gly Thr Asn Arg Pro Val Leu Val Ile	
	290 295 300	
	tct tct gat cta tgc tac aca gtt gga tat ttg tgt gct ggc att ccc	960
	Ser Ser Asp Leu Ser Tyr Thr Val Gly Tyr Leu Cys Ala Gly Ile Pro	
	305 310 315 320	
	act gac act cct agg gga gag gat agt caa ttc aca ggc tca tgt aca	1008
	Thr Asp Thr Pro Arg Gly Glu Asp Ser Gln Phe Thr Gly Ser Cys Thr	
	325 330 335	
	agt cct ttg gga aat aaa gga tac ggt gta aaa ggt ttc ggg ttt cga	1056
	Ser Pro Leu Gly Asn Lys Gly Tyr Gly Val Lys Gly Phe Gly Phe Arg	
	340 345 350	
	caa gga act gac gta tgg gcc gga agg aca att agt agg act tca aga	1104
	Gln Gly Thr Asp Val Trp Ala Gly Arg Thr Ile Ser Arg Thr Ser Arg	
	355 360 365	

	tca gga ttc gaa ata ata aaa atc agg aat ggt tgg aca cag aac agt	1152
	Ser Gly Phe Glu Ile Ile Lys Ile Arg Asn Gly Trp Thr Gln Asn Ser	
	370 375 380	
	aaa gac caa atc agg agg caa gtg att atc gat gac cca aat tgg tca	1200
	Lys Asp Gln Ile Arg Arg Gln Val Ile Ile Asp Asp Pro Asn Trp Ser	
	385 390 395 400	
	gga tat agc ggt tct ttc aca ttg ccg gtt gaa cta aca aaa aag gga	1248
	Gly Tyr Ser Gly Ser Phe Thr Leu Pro Val Glu Leu Thr Lys Lys Gly	
	405 410 415	
	tgt ttg gtc ccc tgt ttc tgg gtt gaa atg att aga ggt aaa cct gaa	1296
	Cys Leu Val Pro Cys Phe Trp Val Glu Met Ile Arg Gly Lys Pro Glu	
	420 425 430	
	gaa aca aca ata tgg acc tct agt agc tcc att gtg atg tgt gga gta	1344
	Glu Thr Thr Ile Trp Thr Ser Ser Ser Ile Val Met Cys Gly Val	
	435 440 445	
[0040]	gat cat aaa att gcc agt tgg tca tgg cac gat gga get att ctt ccc	1392
	Asp His Lys Ile Ala Ser Trp Ser Trp His Asp Gly Ala Ile Leu Pro	
	450 455 460	
	ttt gac atc gat aag atg taa	1413
	Phe Asp Ile Asp Lys Met	
	465 470	
	<210> 12	
	<211> 470	
	<212> PRT	
	<213> 流感病毒	
	<400> 12	
	Met Asn Pro Asn Gln Lys Ile Ile Ala Ile Gly Phe Ala Ser Leu Gly	
	1 5 10 15	
	Ile Leu Ile Ile Asn Val Ile Leu His Val Val Ser Ile Ile Val Thr	
	20 25 30	

Val Pro Val Asp Ile Ile Asn Ser Trp Ala Gly Asp Ile Leu Arg Thr
210 215 220

Gln Glu Ser Ser Cys Thr Cys Ile Lys Gly Asp Cys Tyr Trp Val Met
225 230 235 240

Thr Asp Gly Pro Ala Asn Arg Gln Ala Lys Tyr Arg Ile Phe Lys Ala
245 250 255

Lys Asp Gly Arg Val Ile Gly Gln Thr Asp Ile Ser Phe Asn Gly Gly
260 265 270

His Ile Glu Glu Cys Ser Cys Tyr Pro Asn Glu Gly Lys Val Glu Cys
275 280 285

[0042]

Ile Cys Arg Asp Asn Trp Thr Gly Thr Asn Arg Pro Val Leu Val Ile
290 295 300

Ser Ser Asp Leu Ser Tyr Thr Val Gly Tyr Leu Cys Ala Gly Ile Pro
305 310 315 320

Thr Asp Thr Pro Arg Gly Glu Asp Ser Gln Phe Thr Gly Ser Cys Thr
325 330 335

Ser Pro Leu Gly Asn Lys Gly Tyr Gly Val Lys Gly Phe Gly Phe Arg
340 345 350

Gln Gly Thr Asp Val Trp Ala Gly Arg Thr Ile Ser Arg Thr Ser Arg
355 360 365

Ser Gly Phe Glu Ile Ile Lys Ile Arg Asn Gly Trp Thr Gln Asn Ser
370 375 380

Lys Asp Gln Ile Arg Arg Gln Val Ile Ile Asp Asp Pro Asn Trp Ser
385 390 395 400

Gly Tyr Ser Gly Ser Phe Thr Leu Pro Val Glu Leu Thr Lys Lys Gly
405 410 415

Cys Leu Val Pro Cys Phe Trp Val Glu Met Ile Arg Gly Lys Pro Glu
420 425 430

Glu Thr Thr Ile Trp Thr Ser Ser Ser Ser Ile Val Met Cys Gly Val
435 440 445

Asp His Lys Ile Ala Ser Trp Ser Trp His Asp Gly Ala Ile Leu Pro
450 455 460

Phe Asp Ile Asp Lys Met
465 470

[0043]

<210> 13

<211> 982

<212> DNA

<213> 流感病毒

<220>

<221> CDS

<222> (1)...(756)

<400> 13

atg agt ctt cta acc gag gtc gaa acg tac gtt ctc tet atc gta cca 48
Met Ser Leu Leu Thr Glu Val Glu Thr Tyr Val Leu Ser Ile Val Pro
1 5 10 15

tca ggc ccc ctc aaa gcc gag atc geg cag aga ctt gaa gat gtc ttt 96
Ser Gly Pro Leu Lys Ala Glu Ile Ala Gln Arg Leu Glu Asp Val Phe
20 25 30

gca gga aag aac acc gat ctt gag gca ctc atg gaa tgg cta aag aca 144

[0044]	Ala Gly Lys Asn Thr Asp Leu Glu Ala Leu Met Glu Trp Leu Lys Thr	
	35 40 45	
	aga cca atc ctg tca cct ctg act aaa ggg att tta gga ttt gta ttc	192
	Arg Pro Ile Leu Ser Pro Leu Thr Lys Gly Ile Leu Gly Phe Val Phe	
	50 55 60	
	acg ctc acc gtg ccc agt gag cga gga ctg cag cgt aga cgc ttt gtc	240
	Thr Leu Thr Val Pro Ser Glu Arg Gly Leu Gln Arg Arg Arg Phe Val	
	65 70 75 80	
	caa aat gcc ctt agt gga aac gga gat cca aac aac atg gac aga gca	288
	Gln Asn Ala Leu Ser Gly Asn Gly Asp Pro Asn Asn Met Asp Arg Ala	
	85 90 95	
	gta aaa ctg tac agg aag ctt aaa aga gaa ata aca ttc cat ggg gea	336
	Val Lys Leu Tyr Arg Lys Leu Lys Arg Glu Ile Thr Phe His Gly Ala	
	100 105 110	
	aaa gag gta gea ctc agc tat tcc act ggt gea cta gcc agc tgc atg	384
	Lys Glu Val Ala Leu Ser Tyr Ser Thr Gly Ala Leu Ala Ser Cys Met	
	115 120 125	
	gga ctc ata tac aac aga atg gga act gtt aca acc gaa gtg gea ttt	432
	Gly Leu Ile Tyr Asn Arg Met Gly Thr Val Thr Thr Glu Val Ala Phe	
	130 135 140	
	ggc ctg gta tgc gcc aca tgt gaa cag att get gat tcc cag cat cga	480
	Gly Leu Val Cys Ala Thr Cys Glu Gln Ile Ala Asp Ser Gln His Arg	
	145 150 155 160	
	get cac agg cag atg gtg aca aca acc aac cca ttg atc aga cat gaa	528
	Ala His Arg Gln Met Val Thr Thr Thr Asn Pro Leu Ile Arg His Glu	
	165 170 175	
	aac aga atg gta tta gcc agt acc acg get aaa gcc atg gaa cag atg	576
	Asn Arg Met Val Leu Ala Ser Thr Thr Ala Lys Ala Met Glu Gln Met	
	180 185 190	
	gea gga teg agt gag cag gca gea gag gcc atg gag gtt get agt agg	624
	Ala Gly Ser Ser Glu Gln Ala Ala Glu Ala Met Glu Val Ala Ser Arg	
	195 200 205	
	get agg cag atg gta cag gca atg aga acc att ggg acc cac cct agc	672

Ala Arg Gln Met Val Gln Ala Met Arg Thr Ile Gly Thr His Pro Ser
 210 215 220

tec agt gcc ggt ttg aaa gat gat etc ctt gaa aat tta cag gcc tac 720
 Ser Ser Ala Gly Leu Lys Asp Asp Leu Leu Glu Asn Leu Gln Ala Tyr
 225 230 235 240

cag aaa cgg atg gga gtg caa atg cag cga ttc aag tgatcctetc 766
 Gln Lys Arg Met Gly Val Gln Met Gln Arg Phe Lys
 245 250

gttatcgcag caagtatcat tgggatcttg caattgatat tgtggattct tgategtett 826

ttcttcaaat tcatttatcg tcgctttaa tacgggttga aaagagggcc ttctacggaa 886

ggagtacctg agtctatgag ggaagaatat cggcagggaac agcagaatgc tgtggatgtt 946

gacgatggtc attttgtcaa catagagctg gagtaa 982

[0045]

<210> 14
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<400> 14

Met Ser Leu Leu Thr Glu Val Glu Thr Tyr Val Leu Ser Ile Val Pro
 1 5 10 15

Ser Gly Pro Leu Lys Ala Glu Ile Ala Gln Arg Leu Glu Asp Val Phe
 20 25 30

Ala Gly Lys Asn Thr Asp Leu Glu Ala Leu Met Glu Trp Leu Lys Thr
 35 40 45

Arg Pro Ile Leu Ser Pro Leu Thr Lys Gly Ile Leu Gly Phe Val Phe
 50 55 60

Thr Leu Thr Val Pro Ser Glu Arg Gly Leu Gln Arg Arg Arg Phe Val

65	70	75	80
Gln Asn Ala Leu Ser Gly Asn Gly Asp Pro Asn Asn Met Asp Arg Ala			
85	90	95	
Val Lys Leu Tyr Arg Lys Leu Lys Arg Glu Ile Thr Phe His Gly Ala			
100	105	110	
Lys Glu Val Ala Leu Ser Tyr Ser Thr Gly Ala Leu Ala Ser Cys Met			
115	120	125	
Gly Leu Ile Tyr Asn Arg Met Gly Thr Val Thr Thr Glu Val Ala Phe			
130	135	140	
Gly Leu Val Cys Ala Thr Cys Glu Gln Ile Ala Asp Ser Gln His Arg			
145	150	155	160
[0046]			
Ala His Arg Gln Met Val Thr Thr Thr Asn Pro Leu Ile Arg His Glu			
165	170	175	
Asn Arg Met Val Leu Ala Ser Thr Thr Ala Lys Ala Met Glu Gln Met			
180	185	190	
Ala Gly Ser Ser Glu Gln Ala Ala Glu Ala Met Glu Val Ala Ser Arg			
195	200	205	
Ala Arg Gln Met Val Gln Ala Met Arg Thr Ile Gly Thr His Pro Ser			
210	215	220	
Ser Ser Ala Gly Leu Lys Asp Asp Leu Leu Glu Asn Leu Gln Ala Tyr			
225	230	235	240
Gln Lys Arg Met Gly Val Gln Met Gln Arg Phe Lys			

245

250

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<211> 1698

<212> DNA

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<220>

<221> CDS

<222> (1)..(1698)

<400> 15

atg aag aca acc att att ttg ata cta cta acc cat tgg gcc tac agt	48
Met Lys Thr Thr Ile Ile Leu Ile Leu Leu Thr His Trp Ala Tyr Ser	
1 5 10 15	

caa aac cca atc agt ggc aac aac aca gcc aca ctg tgt ctg gga cac	96
Gln Asn Pro Ile Ser Gly Asn Asn Thr Ala Thr Leu Cys Leu Gly His	
20 25 30	

[0047]

cat gea gta gea aat gga aca ttg gta aaa aca atg agt gat gat caa	144
His Ala Val Ala Asn Gly Thr Leu Val Lys Thr Met Ser Asp Asp Gln	
35 40 45	

att gag gtg aca aat get aca gaa tta gtt cag age att tca atg ggg	192
Ile Glu Val Thr Asn Ala Thr Glu Leu Val Gln Ser Ile Ser Met Gly	
50 55 60	

aaa ata tgc aac aaa tca tat aga att cta gat gga aga aat tgc aca	240
Lys Ile Cys Asn Lys Ser Tyr Arg Ile Leu Asp Gly Arg Asn Cys Thr	
65 70 75 80	

tta ata gat gea atg cta gga gac ecc cac tgt gac gcc ttt cag tat	288
Leu Ile Asp Ala Met Leu Gly Asp Pro His Cys Asp Ala Phe Gln Tyr	
85 90 95	

gag agt tgg gac ctc ttc ata gaa aga age aac got ttc agc aat tgc	336
Glu Ser Trp Asp Leu Phe Ile Glu Arg Ser Asn Ala Phe Ser Asn Cys	
100 105 110	

tac cca tat gac atc cct gac tat gca teg ctc cga tcc att gta gea	384
Tyr Pro Tyr Asp Ile Pro Asp Tyr Ala Ser Leu Arg Ser Ile Val Ala	

115	120	125	
tcc tca gga aca ttg gaa ttc aca gca gag gga ttc aca tgg aca ggt			432
Ser Ser Gly Thr Leu Glu Phe Thr Ala Glu Gly Phe Thr Trp Thr Gly			
130	135	140	
gtc act caa aac gga aga agt gga gcc tgc aaa agg gga tca gcc gat			480
Val Thr Gln Asn Gly Arg Ser Gly Ala Cys Lys Arg Gly Ser Ala Asp			
145	150	155	160
agt ttc ttt agc cga ctg aat tgg cta aca aaa tct gga agc tct tac			528
Ser Phe Phe Ser Arg Leu Asn Trp Leu Thr Lys Ser Gly Ser Ser Tyr			
165	170	175	
ccc aca ttg aat gtg aca atg cct aac aat aaa aat ttc gac aag cta			576
Pro Thr Leu Asn Val Thr Met Pro Asn Asn Lys Asn Phe Asp Lys Leu			
180	185	190	
tac atc tgg ggg att cat cac ccg agc tca aat caa gag cag aca aaa			624
Tyr Ile Trp Gly Ile His His Pro Ser Ser Asn Gln Glu Gln Thr Lys			
195	200	205	
[0048]			
ttg tac atc caa gaa tca gga cga gta aca gtc tca aca aaa aga agt			672
Leu Tyr Ile Gln Glu Ser Gly Arg Val Thr Val Ser Thr Lys Arg Ser			
210	215	220	
caa caa aca ata atc cct aac atc gga tct aga ccg ttg gtc aga ggt			720
Gln Gln Thr Ile Ile Pro Asn Ile Gly Ser Arg Pro Leu Val Arg Gly			
225	230	235	240
caa tca ggc agg ata agc ata tac tgg acc att gta aaa cct gga gat			768
Gln Ser Gly Arg Ile Ser Ile Tyr Trp Thr Ile Val Lys Pro Gly Asp			
245	250	255	
atc cta atg ata aac agt aat ggc aac ita gtt gca ccg cgg gga tat			816
Ile Leu Met Ile Asn Ser Asn Gly Asn Leu Val Ala Pro Arg Gly Tyr			
260	265	270	
ttt aaa ttg aaa aca ggg aaa agc tct gta atg aga tca gat gca ccc			864
Phe Lys Leu Lys Thr Gly Lys Ser Ser Val Met Arg Ser Asp Ala Pro			
275	280	285	
ata gac att tgt gtg tct gaa tgt att aca cca aat gga agc atc tcc			912
Ile Asp Ile Cys Val Ser Glu Cys Ile Thr Pro Asn Gly Ser Ile Ser			

290	295	300	
aac gac aag cca ttc caa aat gtg aac aaa gtt aca tat gga aaa tgc			960
Asn Asp Lys Pro Phe Gln Asn Val Asn Lys Val Thr Tyr Gly Lys Cys			
305	310	315	320
ect aag tat atc agg caa aac act tta aag ctg gcc act ggg atg agg			1008
Pro Lys Tyr Ile Arg Gln Asn Thr Leu Lys Leu Ala Thr Gly Met Arg			
325	330	335	
aat gta cca gaa aag caa acc aga gga atc ttt gga gca ata gcg gga			1056
Asn Val Pro Glu Lys Gln Thr Arg Gly Ile Phe Gly Ala Ile Ala Gly			
340	345	350	
ttc atc gaa aac ggc tgg gaa gga atg gtt gat ggg tgg tat ggg ttc			1104
Phe Ile Glu Asn Gly Trp Glu Gly Met Val Asp Gly Trp Tyr Gly Phe			
355	360	365	
cga tat caa aac tct gaa gga aca ggg caa gct gca gat cta aag ago			1152
Arg Tyr Gln Asn Ser Glu Gly Thr Gly Gln Ala Ala Asp Leu Lys Ser			
370	375	380	
[0049]			
act caa gca gcc atc gac cag att aat gga aag tta aac aga gtg att			1200
Thr Gln Ala Ala Ile Asp Gln Ile Asn Gly Lys Leu Asn Arg Val Ile			
385	390	395	400
gaa aga acc aat gag aaa ttc cat caa ata gag aag gaa ttc tca gaa			1248
Glu Arg Thr Asn Glu Lys Phe His Gln Ile Glu Lys Glu Phe Ser Glu			
405	410	415	
gta gaa gga aga att cag gac ctg gag aaa tat gta gaa gac acc aaa			1296
Val Glu Gly Arg Ile Gln Asp Leu Glu Lys Tyr Val Glu Asp Thr Lys			
420	425	430	
ata gac cta tgg tcc tac aat gca gaa itg ctg gtg gct cta gaa aat			1344
Ile Asp Leu Trp Ser Tyr Asn Ala Glu Leu Leu Val Ala Leu Glu Asn			
435	440	445	
caa cat aca att gac tta aca gat gca gaa atg aat aaa tta ttt gag			1392
Gln His Thr Ile Asp Leu Thr Asp Ala Glu Met Asn Lys Leu Phe Glu			
450	455	460	
aag act aga cgc cag tta aga gaa aac gca gaa gac atg gga ggt gga			1440
Lys Thr Arg Arg Gln Leu Arg Glu Asn Ala Glu Asp Met Gly Gly Gly			

465	470	475	480	
tgt ttc aag att tac cac aaa tgt gat aat gca tgc att gga tca ata				1488
Cys Phe Lys Ile Tyr His Lys Cys Asp Asn Ala Cys Ile Gly Ser Ile				
485	490	495		
aga act ggg aca tat gac cat tac ata tac aga gat gaa gca tta aac				1536
Arg Thr Gly Thr Tyr Asp His Tyr Ile Tyr Arg Asp Glu Ala Leu Asn				
500	505	510		
aac cga ttt cag atc aaa ggt gta gag ttg aaa tca ggc tac aaa gat				1584
Asn Arg Phe Gln Ile Lys Gly Val Glu Leu Lys Ser Gly Tyr Lys Asp				
515	520	525		
tgg ata ttg tgg att tca ttc gcc ata tca tgc ttc tta att tgc gtt				1632
Trp Ile Leu Trp Ile Ser Phe Ala Ile Ser Cys Phe Leu Ile Cys Val				
530	535	540		
gtt cta ttg ggt ttc att atg tgg gct tgc caa aga ggc aac atc aga				1680
Val Leu Leu Gly Phe Ile Met Trp Ala Cys Gln Arg Gly Asn Ile Arg				
545	550	555	560	
[0050]				
tgc aac att tgc att tga				1698
Cys Asn Ile Cys Ile				
565				
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Met Lys Thr Thr Ile Ile Leu Ile Leu Leu Thr His Trp Ala Tyr Ser				
1	5	10	15	
Gln Asn Pro Ile Ser Gly Asn Asn Thr Ala Thr Leu Cys Leu Gly His				
20	25	30		
His Ala Val Ala Asn Gly Thr Leu Val Lys Thr Met Ser Asp Asp Gln				
35	40	45		

	Ile	Glu	Val	Thr	Asn	Ala	Thr	Glu	Leu	Val	Gln	Ser	Ile	Ser	Met	Gly	
	50						55					60					
	Lys	Ile	Cys	Asn	Lys	Ser	Tyr	Arg	Ile	Leu	Asp	Gly	Arg	Asn	Cys	Thr	
	65				70					75					80		
	Leu	Ile	Asp	Ala	Met	Leu	Gly	Asp	Pro	His	Cys	Asp	Ala	Phe	Gln	Tyr	
					85				90						95		
	Glu	Ser	Trp	Asp	Leu	Phe	Ile	Glu	Arg	Ser	Asn	Ala	Phe	Ser	Asn	Cys	
			100						105					110			
	Tyr	Pro	Tyr	Asp	Ile	Pro	Asp	Tyr	Ala	Ser	Leu	Arg	Ser	Ile	Val	Ala	
		115						120					125				
[0051]	Ser	Ser	Gly	Thr	Leu	Glu	Phe	Thr	Ala	Glu	Gly	Phe	Thr	Trp	Thr	Gly	
	130						135					140					
	Val	Thr	Gln	Asn	Gly	Arg	Ser	Gly	Ala	Cys	Lys	Arg	Gly	Ser	Ala	Asp	
	145					150					155				160		
	Ser	Phe	Phe	Ser	Arg	Leu	Asn	Trp	Leu	Thr	Lys	Ser	Gly	Ser	Ser	Tyr	
					165					170					175		
	Pro	Thr	Leu	Asn	Val	Thr	Met	Pro	Asn	Asn	Lys	Asn	Phe	Asp	Lys	Leu	
				180						185					190		
	Tyr	Ile	Trp	Gly	Ile	His	His	Pro	Ser	Ser	Asn	Gln	Glu	Gln	Thr	Lys	
		195						200					205				
	Leu	Tyr	Ile	Gln	Glu	Ser	Gly	Arg	Val	Thr	Val	Ser	Thr	Lys	Arg	Ser	
	210						215						220				

Gln Gln Thr Ile Ile Pro Asn Ile Gly Ser Arg Pro Leu Val Arg Gly
225 230 235 240

Gln Ser Gly Arg Ile Ser Ile Tyr Trp Thr Ile Val Lys Pro Gly Asp
245 250 255

Ile Leu Met Ile Asn Ser Asn Gly Asn Leu Val Ala Pro Arg Gly Tyr
260 265 270

Phe Lys Leu Lys Thr Gly Lys Ser Ser Val Met Arg Ser Asp Ala Pro
275 280 285

Ile Asp Ile Cys Val Ser Glu Cys Ile Thr Pro Asn Gly Ser Ile Ser
290 295 300

[0052]

Asn Asp Lys Pro Phe Gln Asn Val Asn Lys Val Thr Tyr Gly Lys Cys
305 310 315 320

Pro Lys Tyr Ile Arg Gln Asn Thr Leu Lys Leu Ala Thr Gly Met Arg
325 330 335

Asn Val Pro Glu Lys Gln Thr Arg Gly Ile Phe Gly Ala Ile Ala Gly
340 345 350

Phe Ile Glu Asn Gly Trp Glu Gly Met Val Asp Gly Trp Tyr Gly Phe
355 360 365

Arg Tyr Gln Asn Ser Glu Gly Thr Gly Gln Ala Ala Asp Leu Lys Ser
370 375 380

Thr Gln Ala Ala Ile Asp Gln Ile Asn Gly Lys Leu Asn Arg Val Ile
385 390 395 400

	Glu Arg Thr Asn Glu Lys Phe His Gln Ile Glu Lys Glu Phe Ser Glu	
	405	410 415
	Val Glu Gly Arg Ile Gln Asp Leu Glu Lys Tyr Val Glu Asp Thr Lys	
	420	425 430
	Ile Asp Leu Trp Ser Tyr Asn Ala Glu Leu Leu Val Ala Leu Glu Asn	
	435	440 445
	Gln His Thr Ile Asp Leu Thr Asp Ala Glu Met Asn Lys Leu Phe Glu	
	450	455 460
	Lys Thr Arg Arg Gln Leu Arg Glu Asn Ala Glu Asp Met Gly Gly Gly	
	465	470 475 480
[0053]	Cys Phe Lys Ile Tyr His Lys Cys Asp Asn Ala Cys Ile Gly Ser Ile	
	485	490 495
	Arg Thr Gly Thr Tyr Asp His Tyr Ile Tyr Arg Asp Glu Ala Leu Asn	
	500	505 510
	Asn Arg Phe Gln Ile Lys Gly Val Glu Leu Lys Ser Gly Tyr Lys Asp	
	515	520 525
	Trp Ile Leu Trp Ile Ser Phe Ala Ile Ser Cys Phe Leu Ile Cys Val	
	530	535 540
	Val Leu Leu Gly Phe Ile Met Trp Ala Cys Gln Arg Gly Asn Ile Arg	
	545	550 555 560
	Cys Asn Ile Cys Ile	
	565	

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	1 5 10 15		
	cgc gag ata cta aca aaa act act gtg gac cac atg gcc ata atc aag	96	
	Arg Glu Ile Leu Thr Lys Thr Thr Val Asp His Met Ala Ile Ile Lys		
	20 25 30		
	aaa tac aca tca gga aga caa gag aag aac cct gca ctt agg atg aaa	144	
[0054]	Lys Tyr Thr Ser Gly Arg Gln Glu Lys Asn Pro Ala Leu Arg Met Lys		
	35 40 45		
	tgg atg atg gca atg aaa tac cca att aca gca gat aag agg ata atg	192	
	Trp Met Met Ala Met Lys Tyr Pro Ile Thr Ala Asp Lys Arg Ile Met		
	50 55 60		
	gag atg att cct gag aga aat gaa cag gga caa acc ctt tgg agc aaa	240	
	Glu Met Ile Pro Glu Arg Asn Glu Gln Gly Gln Thr Leu Trp Ser Lys		
	65 70 75 80		
	acg aac gat gct ggc tca gac cgc gta atg gta tca cct ctg gca gtg	288	
	Thr Asn Asp Ala Gly Ser Asp Arg Val Met Val Ser Pro Leu Ala Val		
	85 90 95		
	aca tgg tgg aat agg aat gga cca aca acg agc aca att cat tat cca	336	
	Thr Trp Trp Asn Arg Asn Gly Pro Thr Thr Ser Thr Ile His Tyr Pro		
	100 105 110		
	aaa gtc tac aaa act tat ttt gaa aag gtt gaa aga ttg aaa cac gga	384	
	Lys Val Tyr Lys Thr Tyr Phe Glu Lys Val Glu Arg Leu Lys His Gly		
	115 120 125		

	acc ttt ggc ccc gtt cat ttt agg aat caa gtc aag ata aga cga aga	432
	Thr Phe Gly Pro Val His Phe Arg Asn Gln Val Lys Ile Arg Arg Arg	
	130 135 140	
	gtt gat gta aac cct ggt cac ggc gac ctc agt gcc aaa gaa gca caa	480
	Val Asp Val Asn Pro Gly His Ala Asp Leu Ser Ala Lys Glu Ala Gln	
	145 150 155 160	
	gat gtg atc atg gaa gtt gtt ttc cca aat gaa gtg gga gcc aga att	528
	Asp Val Ile Met Glu Val Val Phe Pro Asn Glu Val Gly Ala Arg Ile	
	165 170 175	
	cta aca tcg gaa tca caa cta aca ata acc aaa gag aaa aag gaa gaa	576
	Leu Thr Ser Glu Ser Gln Leu Thr Ile Thr Lys Glu Lys Lys Glu Glu	
	180 185 190	
	ctt cag gac tgc aaa att get ccc ttg atg gta gca tac atg cta gaa	624
	Leu Gln Asp Cys Lys Ile Ala Pro Leu Met Val Ala Tyr Met Leu Glu	
	195 200 205	
[0055]	aga gag ttg gtc cga aaa aca agg ttc ctc cca gta gca ggc gga aca	672
	Arg Glu Leu Val Arg Lys Thr Arg Phe Leu Pro Val Ala Gly Gly Thr	
	210 215 220	
	agc agt gta tac att gaa gtg ttg cat ctg act cag gga aca tgc tgg	720
	Ser Ser Val Tyr Ile Glu Val Leu His Leu Thr Gln Gly Thr Cys Trp	
	225 230 235 240	
	gag caa atg tac acc cca gga gga gaa gtt aga aac gat gat att gat	768
	Glu Gln Met Tyr Thr Pro Gly Gly Glu Val Arg Asn Asp Asp Ile Asp	
	245 250 255	
	caa agt tta att att gca gcc cgg aac ata gtg aga aga gcg aca gta	816
	Gln Ser Leu Ile Ile Ala Ala Arg Asn Ile Val Arg Arg Ala Thr Val	
	260 265 270	
	tca gca gat cca cta gca tcc cta ctg gaa atg tgc cac agt aca cag	864
	Ser Ala Asp Pro Leu Ala Ser Leu Leu Glu Met Cys His Ser Thr Gln	
	275 280 285	
	att ggt gga ata agg atg gta gac atc ctt aag cag aat cca aca gag	912
	Ile Gly Gly Ile Arg Met Val Asp Ile Leu Lys Gln Asn Pro Thr Glu	
	290 295 300	

	gaa caa gct gtg gat ata tgc aaa gca gca atg gga ttg aga att agc	960
	Glu Gln Ala Val Asp Ile Cys Lys Ala Ala Met Gly Leu Arg Ile Ser	
	305 310 315 320	
	tca tca ttc agc ttt ggt gga ttc acc ttc aaa aga aca agt gga tca	1008
	Ser Ser Phe Ser Phe Gly Gly Phe Thr Phe Lys Arg Thr Ser Gly Ser	
	325 330 335	
	tca gtc aag aga gaa gaa gaa atg ctt acg ggc aac ctt caa aca ttg	1056
	Ser Val Lys Arg Glu Glu Glu Met Leu Thr Gly Asn Leu Gln Thr Leu	
	340 345 350	
	aaa ata aga gtg cat gag ggc tat gaa gaa ttc aca atg gtc gga aga	1104
	Lys Ile Arg Val His Glu Gly Tyr Glu Glu Phe Thr Met Val Gly Arg	
	355 360 365	
	aga gca aca gcc att atc aga aag gca acc aga aga ttg att caa ttg	1152
	Arg Ala Thr Ala Ile Ile Arg Lys Ala Thr Arg Arg Leu Ile Gln Leu	
	370 375 380	
[0056]	ata gta agt ggg aga gat gaa caa tca att gct gaa gca ata att gta	1200
	Ile Val Ser Gly Arg Asp Glu Gln Ser Ile Ala Glu Ala Ile Ile Val	
	385 390 395 400	
	gcc atg gtg ttt tcg caa gaa gat tgc atg ata aaa gca gtt cga ggc	1248
	Ala Met Val Phe Ser Gln Glu Asp Cys Met Ile Lys Ala Val Arg Gly	
	405 410 415	
	gat ttg aac ttt gtt aat aga gca aat cag cgt ttg aac ccc atg cat	1296
	Asp Leu Asn Phe Val Asn Arg Ala Asn Gln Arg Leu Asn Pro Met His	
	420 425 430	
	caa ctc ttg agg cat ttc caa aaa gat gca aaa gtg ctt ttc caa aat	1344
	Gln Leu Leu Arg His Phe Gln Lys Asp Ala Lys Val Leu Phe Gln Asn	
	435 440 445	
	tgg gga att gaa ccc atc gac aat gta atg ggg atg att gga ata ttg	1392
	Trp Gly Ile Glu Pro Ile Asp Asn Val Met Gly Met Ile Gly Ile Leu	
	450 455 460	
	cct gac atg acc cca agc acc gag atg tca ttg aga gga gtg aga gtc	1440
	Pro Asp Met Thr Pro Ser Thr Glu Met Ser Leu Arg Gly Val Arg Val	
	465 470 475 480	

	agc aaa atg gga gtg gat gag tac tcc agc act gag aga gtg gtg gtg	1488
	Ser Lys Met Gly Val Asp Glu Tyr Ser Ser Thr Glu Arg Val Val Val	
	485 490 495	
	agc att gac cgt ttt tta aga gtt cgg gat caa agg gga aac ata cta	1536
	Ser Ile Asp Arg Phe Leu Arg Val Arg Asp Gln Arg Gly Asn Ile Leu	
	500 505 510	
	ctg tcc cct gaa gaa gtc agt gaa aca caa gga acg gaa aag ctg aca	1584
	Leu Ser Pro Glu Glu Val Ser Glu Thr Gln Gly Thr Glu Lys Leu Thr	
	515 520 525	
	ata att tat teg tca tca atg atg tgg gag att aat ggt ccc gaa tca	1632
	Ile Ile Tyr Ser Ser Ser Met Met Trp Glu Ile Asn Gly Pro Glu Ser	
	530 535 540	
	gtg ttg gtc aat act tat caa tgg atc atc agg aac tgg gaa att gta	1680
	Val Leu Val Asn Thr Tyr Gln Trp Ile Ile Arg Asn Trp Glu Ile Val	
	545 550 555 560	
[0057]	aaa att cag tgg tca cag gac ccc aca atg tta tac aat aag ata gaa	1728
	Lys Ile Gln Trp Ser Gln Asp Pro Thr Met Leu Tyr Asn Lys Ile Glu	
	565 570 575	
	ttt gag cca ttc caa tcc ctg gtc cct agg gcc acc aga agc caa tac	1776
	Phe Glu Pro Phe Gln Ser Leu Val Pro Arg Ala Thr Arg Ser Gln Tyr	
	580 585 590	
	agc ggt ttc gta aga acc ctg ttt cag caa atg cga gat gta ctt gga	1824
	Ser Gly Phe Val Arg Thr Leu Phe Gln Gln Met Arg Asp Val Leu Gly	
	595 600 605	
	aca ttt gat act get caa ata ata aaa ctc ctc cct ttt gcc get get	1872
	Thr Phe Asp Thr Ala Gln Ile Ile Lys Leu Leu Pro Phe Ala Ala Ala	
	610 615 620	
	cct ccg gaa cag agt agg atg cag ttc tct tet ttg act gtt aat gta	1920
	Pro Pro Glu Gln Ser Arg Met Gln Phe Ser Ser Leu Thr Val Asn Val	
	625 630 635 640	
	aga ggt teg gga atg agg ata ctt gta aga ggc aat tcc cca gtg ttc	1968
	Arg Gly Ser Gly Met Arg Ile Leu Val Arg Gly Asn Ser Pro Val Phe	
	645 650 655	

	aac tac aat aaa gcc act aaa agg ctc aca gtc ctc gga aag gat gca	2016
	Asn Tyr Asn Lys Ala Thr Lys Arg Leu Thr Val Leu Gly Lys Asp Ala	
	660 665 670	
	ggt gcg ctt act gag gac cca gat gaa ggt acg gct gga gta gaa tct	2064
	Gly Ala Leu Thr Glu Asp Pro Asp Glu Gly Thr Ala Gly Val Glu Ser	
	675 680 685	
	gct gtt cta aga ggg ttt ctc att tta ggt aaa gaa aac aag aga tat	2112
	Ala Val Leu Arg Gly Phe Leu Ile Leu Gly Lys Glu Asn Lys Arg Tyr	
	690 695 700	
	ggc cca gca cta agc atc aat gaa cta agc aaa ctt gca aaa ggg gag	2160
	Gly Pro Ala Leu Ser Ile Asn Glu Leu Ser Lys Leu Ala Lys Gly Glu	
	705 710 715 720	
	aaa gcc aat gta cta att ggg caa ggg gac rta gtg ttg gta atg aaa	2208
	Lys Ala Asn Val Leu Ile Gly Gln Gly Asp Xaa Val Leu Val Met Lys	
	725 730 735	
[0058]	cgg aaa cgt gac tct agc ata ctt act gac agc cag aca gcg acc aaa	2256
	Arg Lys Arg Asp Ser Ser Ile Leu Thr Asp Ser Gln Thr Ala Thr Lys	
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	agg att cgg atg gcc atc aat	2277
	Arg Ile Arg Met Ala Ile Asn	
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<211> 759

<212> PRT

<213> 流感病毒

<220>

<221> misc_feature

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<223> 731 位的' Xaa' 代表 Val 或者 Ile。

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1

5

10

15

Arg Glu Ile Leu Thr Lys Thr Thr Val Asp His Met Ala Ile Ile Lys
20 25 30

Lys Tyr Thr Ser Gly Arg Gln Glu Lys Asn Pro Ala Leu Arg Met Lys
35 40 45

Trp Met Met Ala Met Lys Tyr Pro Ile Thr Ala Asp Lys Arg Ile Met
50 55 60

Glu Met Ile Pro Glu Arg Asn Glu Gln Gly Gln Thr Leu Trp Ser Lys
65 70 75 80

Thr Asn Asp Ala Gly Ser Asp Arg Val Met Val Ser Pro Leu Ala Val
85 90 95

[0059]

Thr Trp Trp Asn Arg Asn Gly Pro Thr Thr Ser Thr Ile His Tyr Pro
100 105 110

Lys Val Tyr Lys Thr Tyr Phe Glu Lys Val Glu Arg Leu Lys His Gly
115 120 125

Thr Phe Gly Pro Val His Phe Arg Asn Gln Val Lys Ile Arg Arg Arg
130 135 140

Val Asp Val Asn Pro Gly His Ala Asp Leu Ser Ala Lys Glu Ala Gln
145 150 155 160

Asp Val Ile Met Glu Val Val Phe Pro Asn Glu Val Gly Ala Arg Ile
165 170 175

Leu Thr Ser Glu Ser Gln Leu Thr Ile Thr Lys Glu Lys Lys Glu Glu
180 185 190

Leu Gln Asp Cys Lys Ile Ala Pro Leu Met Val Ala Tyr Met Leu Glu
195 200 205

Arg Glu Leu Val Arg Lys Thr Arg Phe Leu Pro Val Ala Gly Gly Thr
210 215 220

Ser Ser Val Tyr Ile Glu Val Leu His Leu Thr Gln Gly Thr Cys Trp
225 230 235 240

Glu Gln Met Tyr Thr Pro Gly Gly Glu Val Arg Asn Asp Asp Ile Asp
245 250 255

Gln Ser Leu Ile Ile Ala Ala Arg Asn Ile Val Arg Arg Ala Thr Val
260 265 270

[0060]

Ser Ala Asp Pro Leu Ala Ser Leu Leu Glu Met Cys His Ser Thr Gln
275 280 285

Ile Gly Gly Ile Arg Met Val Asp Ile Leu Lys Gln Asn Pro Thr Glu
290 295 300

Glu Gln Ala Val Asp Ile Cys Lys Ala Ala Met Gly Leu Arg Ile Ser
305 310 315 320

Ser Ser Phe Ser Phe Gly Gly Phe Thr Phe Lys Arg Thr Ser Gly Ser
325 330 335

Ser Val Lys Arg Glu Glu Glu Met Leu Thr Gly Asn Leu Gln Thr Leu
340 345 350

Lys Ile Arg Val His Glu Gly Tyr Glu Glu Phe Thr Met Val Gly Arg
355 360 365

Arg Ala Thr Ala Ile Ile Arg Lys Ala Thr Arg Arg Leu Ile Gln Leu
370 375 380

Ile Val Ser Gly Arg Asp Glu Gln Ser Ile Ala Glu Ala Ile Ile Val
385 390 395 400

Ala Met Val Phe Ser Gln Glu Asp Cys Met Ile Lys Ala Val Arg Gly
405 410 415

Asp Leu Asn Phe Val Asn Arg Ala Asn Gln Arg Leu Asn Pro Met His
420 425 430

Gln Leu Leu Arg His Phe Gln Lys Asp Ala Lys Val Leu Phe Gln Asn
435 440 445

[0061]

Trp Gly Ile Glu Pro Ile Asp Asn Val Met Gly Met Ile Gly Ile Leu
450 455 460

Pro Asp Met Thr Pro Ser Thr Glu Met Ser Leu Arg Gly Val Arg Val
465 470 475 480

Ser Lys Met Gly Val Asp Glu Tyr Ser Ser Thr Glu Arg Val Val Val
485 490 495

Ser Ile Asp Arg Phe Leu Arg Val Arg Asp Gln Arg Gly Asn Ile Leu
500 505 510

Leu Ser Pro Glu Glu Val Ser Glu Thr Gln Gly Thr Glu Lys Leu Thr
515 520 525

Ile Ile Tyr Ser Ser Ser Met Met Trp Glu Ile Asn Gly Pro Glu Ser
530 535 540

Val Leu Val Asn Thr Tyr Gln Trp Ile Ile Arg Asn Trp Glu Ile Val
545 550 555 560

Lys Ile Gln Trp Ser Gln Asp Pro Thr Met Leu Tyr Asn Lys Ile Glu
565 570 575

Phe Glu Pro Phe Gln Ser Leu Val Pro Arg Ala Thr Arg Ser Gln Tyr
580 585 590

Ser Gly Phe Val Arg Thr Leu Phe Gln Gln Met Arg Asp Val Leu Gly
595 600 605

Thr Phe Asp Thr Ala Gln Ile Ile Lys Leu Leu Pro Phe Ala Ala Ala
610 615 620

[0062]

Pro Pro Glu Gln Ser Arg Met Gln Phe Ser Ser Leu Thr Val Asn Val
625 630 635 640

Arg Gly Ser Gly Met Arg Ile Leu Val Arg Gly Asn Ser Pro Val Phe
645 650 655

Asn Tyr Asn Lys Ala Thr Lys Arg Leu Thr Val Leu Gly Lys Asp Ala
660 665 670

Gly Ala Leu Thr Glu Asp Pro Asp Glu Gly Thr Ala Gly Val Glu Ser
675 680 685

Ala Val Leu Arg Gly Phe Leu Ile Leu Gly Lys Glu Asn Lys Arg Tyr
690 695 700

Gly Pro Ala Leu Ser Ile Asn Glu Leu Ser Lys Leu Ala Lys Gly Glu
705 710 715 720

Lys Ala Asn Val Leu Ile Gly Gln Gly Asp Xaa Val Leu Val Met Lys
 725 730 735

Arg Lys Arg Asp Ser Ser Ile Leu Thr Asp Ser Gln Thr Ala Thr Lys
 740 745 750

Arg Ile Arg Met Ala Ile Asn
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<210> 19

<211> 2274

<212> DNA

<213> 流感病毒

<220>

<221> CDS

<222> (1)..(2274)

[0063]

<400> 19

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 Met Asp Val Asn Pro Thr Leu Leu Phe Leu Lys Val Pro Ala Gln Asn
 1 5 10 15

gct ata agc aca aca ttc cct tat act gga gat cct ccc tac agt cat 96
 Ala Ile Ser Thr Thr Phe Pro Tyr Thr Gly Asp Pro Pro Tyr Ser His
 20 25 30

gga aca ggg aca gga tac acc atg gat act gtc aac aga aca cae caa 144
 Gly Thr Gly Thr Gly Tyr Thr Met Asp Thr Val Asn Arg Thr His Gln
 35 40 45

tat tca gaa aaa ggg aaa tgg aca aca aac act gag att gga gca cca 192
 Tyr Ser Glu Lys Gly Lys Trp Thr Thr Asn Thr Glu Ile Gly Ala Pro
 50 55 60

caa ctt aat cca atc gat gga cca ctt cct gaa gac aat gaa cca agt 240
 Gln Leu Asn Pro Ile Asp Gly Pro Leu Pro Glu Asp Asn Glu Pro Ser
 65 70 75 80

[0064]	ggg tac gcc caa aca gat tgt gta ttg gaa gca atg gct ttc ctt gaa	288
	Gly Tyr Ala Gln Thr Asp Cys Val Leu Glu Ala Met Ala Phe Leu Glu	
	85 90 95	
	gaa tcc cat ccc gga atc ttt gaa aat tcc tgt ctt gaa acg atg gag	336
	Glu Ser His Pro Gly Ile Phe Glu Asn Ser Cys Leu Glu Thr Met Glu	
	100 105 110	
	gtg att cag cag aca aga gtg gac aaa cta aca caa ggc cga caa act	384
	Val Ile Gln Gln Thr Arg Val Asp Lys Leu Thr Gln Gly Arg Gln Thr	
	115 120 125	
	tat gat tgg acc ttg aat agg aat caa cct gcc gca aca gca ctt gct	432
	Tyr Asp Trp Thr Leu Asn Arg Asn Gln Pro Ala Ala Thr Ala Leu Ala	
	130 135 140	
[0064]	aat acg att gaa gta ttc aga tca aat ggt ctg act tcc aat gaa tcc	480
	Asn Thr Ile Glu Val Phe Arg Ser Asn Gly Leu Thr Ser Asn Glu Ser	
	145 150 155 160	
	ggg aga ttg atg gac ttc ctc aaa gat gtc atg gag tcc atg aac aag	528
	Gly Arg Leu Met Asp Phe Leu Lys Asp Val Met Glu Ser Met Asn Lys	
	165 170 175	
	gaa gaa atg gaa ata aca aca cac ttc caa cgg aag aga aga gta aga	576
	Glu Glu Met Glu Ile Thr Thr His Phe Gln Arg Lys Arg Arg Val Arg	
	180 185 190	
	gac aac atg aca aag aga atg gta aca cag aga acc ata ggg aag aaa	624
	Asp Asn Met Thr Lys Arg Met Val Thr Gln Arg Thr Ile Gly Lys Lys	
	195 200 205	
[0064]	aaa caa cga tta aac aga aag agc tat cta atc aga aca tta acc cta	672
	Lys Gln Arg Leu Asn Arg Lys Ser Tyr Leu Ile Arg Thr Leu Thr Leu	
	210 215 220	
	aac aca atg acc aag gac gct gag aga ggg aaa ttg aaa cga cga gca	720
	Asn Thr Met Thr Lys Asp Ala Glu Arg Gly Lys Leu Lys Arg Arg Ala	
	225 230 235 240	
	atc gct acc cca ggg atg cag ata aga ggg ttt gta tat ttt gtt gaa	768
	Ile Ala Thr Pro Gly Met Gln Ile Arg Gly Phe Val Tyr Phe Val Glu	
	245 250 255	

	aca cta gcc cga aga ata tgt gaa aag ctt gaa caa tca gga ttg cca	816
	Thr Leu Ala Arg Arg Ile Cys Glu Lys Leu Glu Gln Ser Gly Leu Pro	
	260 265 270	
	gtt ggc ggt aat gag aaa aag gcc aaa ctg gct aat gtc gtc aga aaa	864
	Val Gly Gly Asn Glu Lys Lys Ala Lys Leu Ala Asn Val Val Arg Lys	
	275 280 285	
	atg atg act aat tcc caa gac act gaa ctc tcc ttc acc atc act ggg	912
	Met Met Thr Asn Ser Gln Asp Thr Glu Leu Ser Phe Thr Ile Thr Gly	
	290 295 300	
	gac aat acc aaa tgg aat gaa aat cag aac cca cgc ata ttc ctg gca	960
	Asp Asn Thr Lys Trp Asn Glu Asn Gln Asn Pro Arg Ile Phe Leu Ala	
	305 310 315 320	
	atg atc aca tac ata act aga aac cag cca gaa tgg ttc aga aat gtt	1008
	Met Ile Thr Tyr Ile Thr Arg Asn Gln Pro Glu Trp Phe Arg Asn Val	
	325 330 335	
[0065]	cta agc att gca ccg att atg ttc tca aat aaa atg gca aga ctg ggg	1056
	Leu Ser Ile Ala Pro Ile Met Phe Ser Asn Lys Met Ala Arg Leu Gly	
	340 345 350	
	aaa gga tat atg ttt gaa agc aaa agt atg aaa ttg aga act caa ata	1104
	Lys Gly Tyr Met Phe Glu Ser Lys Ser Met Lys Leu Arg Thr Gln Ile	
	355 360 365	
	cca gca gaa atg cta gca agc att gac cta aaa tat ttc aat gat tca	1152
	Pro Ala Glu Met Leu Ala Ser Ile Asp Leu Lys Tyr Phe Asn Asp Ser	
	370 375 380	
	aca aaa aag aaa att gaa aag ata cga cca ctt ctg gtt gac ggg act	1200
	Thr Lys Lys Lys Ile Glu Lys Ile Arg Pro Leu Leu Val Asp Gly Thr	
	385 390 395 400	
	gct tca ctg agt cct ggc atg atg atg gga atg ttc aac atg ttg age	1248
	Ala Ser Leu Ser Pro Gly Met Met Met Gly Met Phe Asn Met Leu Ser	
	405 410 415	
	act gtg ctg ggt gta tcc ata tta aac ctg ggc cag agg aaa tac aca	1296
	Thr Val Leu Gly Val Ser Ile Leu Asn Leu Gly Gln Arg Lys Tyr Thr	
	420 425 430	

	aag acc aca tac tgg tgg gat ggt ctg caa tea tcc gat gac ttt gct	1344
	Lys Thr Thr Tyr Trp Trp Asp Gly Leu Gln Ser Ser Asp Asp Phe Ala	
	435 440 445	
	ttg ata gtg aat gcg cct aat cat gaa gga ata caa gct gga gta gac	1392
	Leu Ile Val Asn Ala Pro Asn His Glu Gly Ile Gln Ala Gly Val Asp	
	450 455 460	
	aga ttc tat aga act tgc aaa ctg gtc ggg atc aac atg agc aaa aag	1440
	Arg Phe Tyr Arg Thr Cys Lys Leu Val Gly Ile Asn Met Ser Lys Lys	
	465 470 475 480	
	aaa tcc tac ata aat aga act gga aca ttc gaa ttc aca agc ttt ttc	1488
	Lys Ser Tyr Ile Asn Arg Thr Gly Thr Phe Glu Phe Thr Ser Phe Phe	
	485 490 495	
	tac cgg tat ggt ttt gta gcc aat ttc agc atg gaa cta ccc agt ttt	1536
	Tyr Arg Tyr Gly Phe Val Ala Asn Phe Ser Met Glu Leu Pro Ser Phe	
	500 505 510	
[0066]	ggg gtt tcc gga ata aat gaa tct gca gac atg agc att gga gtg aca	1584
	Gly Val Ser Gly Ile Asn Glu Ser Ala Asp Met Ser Ile Gly Val Thr	
	515 520 525	
	gtc atc aaa aac aac atg ata aat aat gat ctc ggt cct gcc acg gca	1632
	Val Ile Lys Asn Asn Met Ile Asn Asn Asp Leu Gly Pro Ala Thr Ala	
	530 535 540	
	caa atg gca ctc caa ctc ttc att aag gat tat cgg tac aca tac cgg	1680
	Gln Met Ala Leu Gln Leu Phe Ile Lys Asp Tyr Arg Tyr Thr Tyr Arg	
	545 550 555 560	
	tgc cat aga ggt gat acc cag ata caa acc aga aga tct ttt gag ttg	1728
	Cys His Arg Gly Asp Thr Gln Ile Gln Thr Arg Arg Ser Phe Glu Leu	
	565 570 575	
	aag aaa ctg tgg gaa cag act cga tca aag act ggt cta ctg gta tca	1776
	Lys Lys Leu Trp Glu Gln Thr Arg Ser Lys Thr Gly Leu Leu Val Ser	
	580 585 590	
	gat ggg ggt cca aac cta tat aac atc aga aac cta cac atc ceg gaa	1824
	Asp Gly Gly Pro Asn Leu Tyr Asn Ile Arg Asn Leu His Ile Pro Glu	
	595 600 605	

	gtc tgt tta aaa tgg gag cta atg gat gaa gat tat aag ggg agg cta	1872
	Val Cys Leu Lys Trp Glu Leu Met Asp Glu Asp Tyr Lys Gly Arg Leu	
	610 615 620	
	tgc aat cca ttg aat cct ttc gtt agt cac aaa gaa att gaa tca gtc	1920
	Cys Asn Pro Leu Asn Pro Phe Val Ser His Lys Glu Ile Glu Ser Val	
	625 630 635 640	
	aac agt gca gta gta atg cct gcg cat ggc cct gcc aaa age atg gag	1968
	Asn Ser Ala Val Val Met Pro Ala His Gly Pro Ala Lys Ser Met Glu	
	645 650 655	
	tat gat get gtt gca aca aca cat tct tgg atc ccc aag agg aac cgg	2016
	Tyr Asp Ala Val Ala Thr Thr His Ser Trp Ile Pro Lys Arg Asn Arg	
	660 665 670	
	tcc ata ttg aac aca age caa agg gga ata ctc gaa gat gag cag atg	2064
	Ser Ile Leu Asn Thr Ser Gln Arg Gly Ile Leu Glu Asp Glu Gln Met	
	675 680 685	
[0067]	tat cag aaa tgc tgc aac ctg ttt gaa aaa ttc ttc ccc age age tca	2112
	Tyr Gln Lys Cys Cys Asn Leu Phe Glu Lys Phe Phe Pro Ser Ser Ser	
	690 695 700	
	tac aga aga cca gtc gga att tct agt atg gtt gag gcc atg gtg tcc	2160
	Tyr Arg Arg Pro Val Gly Ile Ser Ser Met Val Glu Ala Met Val Ser	
	705 710 715 720	
	agg gcc cgc att gat gca cga att gac ttc gaa tct gga cgg ata aag	2208
	Arg Ala Arg Ile Asp Ala Arg Ile Asp Phe Glu Ser Gly Arg Ile Lys	
	725 730 735	
	aag gat gag ttc get gag atc atg aag atc tgt tcc acc att gaa gag	2256
	Lys Asp Glu Phe Ala Glu Ile Met Lys Ile Cys Ser Thr Ile Glu Glu	
	740 745 750	
	ctc aga cgg caa aaa tag	2274
	Leu Arg Arg Gln Lys	
	755	
	<210> 20	
	<211> 757	

<212> PRT

<213> 流感病毒

<400> 20

Met	Asp	Val	Asn	Pro	Thr	Leu	Leu	Phe	Leu	Lys	Val	Pro	Ala	Gln	Asn
1				5					10					15	

Ala	Ile	Ser	Thr	Thr	Phe	Pro	Tyr	Thr	Gly	Asp	Pro	Pro	Tyr	Ser	His
			20					25					30		

Gly	Thr	Gly	Thr	Gly	Tyr	Thr	Met	Asp	Thr	Val	Asn	Arg	Thr	His	Gln
		35					40					45			

Tyr	Ser	Glu	Lys	Gly	Lys	Trp	Thr	Thr	Asn	Thr	Glu	Ile	Gly	Ala	Pro
	50					55					60				

[0068] Gln Leu Asn Pro Ile Asp Gly Pro Leu Pro Glu Asp Asn Glu Pro Ser

65					70					75					80
----	--	--	--	--	----	--	--	--	--	----	--	--	--	--	----

Gly	Tyr	Ala	Gln	Thr	Asp	Cys	Val	Leu	Glu	Ala	Met	Ala	Phe	Leu	Glu
				85					90					95	

Glu	Ser	His	Pro	Gly	Ile	Phe	Glu	Asn	Ser	Cys	Leu	Glu	Thr	Met	Glu
			100					105					110		

Val	Ile	Gln	Gln	Thr	Arg	Val	Asp	Lys	Leu	Thr	Gln	Gly	Arg	Gln	Thr
				115				120					125		

Tyr	Asp	Trp	Thr	Leu	Asn	Arg	Asn	Gln	Pro	Ala	Ala	Thr	Ala	Leu	Ala
	130					135					140				

Asn	Thr	Ile	Glu	Val	Phe	Arg	Ser	Asn	Gly	Leu	Thr	Ser	Asn	Glu	Ser
145						150				155				160	

Gly Arg Leu Met Asp Phe Leu Lys Asp Val Met Glu Ser Met Asn Lys
165 170 175

Glu Glu Met Glu Ile Thr Thr His Phe Gln Arg Lys Arg Arg Val Arg
180 185 190

Asp Asn Met Thr Lys Arg Met Val Thr Gln Arg Thr Ile Gly Lys Lys
195 200 205

Lys Gln Arg Leu Asn Arg Lys Ser Tyr Leu Ile Arg Thr Leu Thr Leu
210 215 220

Asn Thr Met Thr Lys Asp Ala Glu Arg Gly Lys Leu Lys Arg Arg Ala
225 230 235 240

[0069]

Ile Ala Thr Pro Gly Met Gln Ile Arg Gly Phe Val Tyr Phe Val Glu
245 250 255

Thr Leu Ala Arg Arg Ile Cys Glu Lys Leu Glu Gln Ser Gly Leu Pro
260 265 270

Val Gly Gly Asn Glu Lys Lys Ala Lys Leu Ala Asn Val Val Arg Lys
275 280 285

Met Met Thr Asn Ser Gln Asp Thr Glu Leu Ser Phe Thr Ile Thr Gly
290 295 300

Asp Asn Thr Lys Trp Asn Glu Asn Gln Asn Pro Arg Ile Phe Leu Ala
305 310 315 320

Met Ile Thr Tyr Ile Thr Arg Asn Gln Pro Glu Trp Phe Arg Asn Val
325 330 335

Leu Ser Ile Ala Pro Ile Met Phe Ser Asn Lys Met Ala Arg Leu Gly
340 345 350

Lys Gly Tyr Met Phe Glu Ser Lys Ser Met Lys Leu Arg Thr Gln Ile
355 360 365

Pro Ala Glu Met Leu Ala Ser Ile Asp Leu Lys Tyr Phe Asn Asp Ser
370 375 380

Thr Lys Lys Lys Ile Glu Lys Ile Arg Pro Leu Leu Val Asp Gly Thr
385 390 395 400

Ala Ser Leu Ser Pro Gly Met Met Met Gly Met Phe Asn Met Leu Ser
405 410 415

[0070]

Thr Val Leu Gly Val Ser Ile Leu Asn Leu Gly Gln Arg Lys Tyr Thr
420 425 430

Lys Thr Thr Tyr Trp Trp Asp Gly Leu Gln Ser Ser Asp Asp Phe Ala
435 440 445

Leu Ile Val Asn Ala Pro Asn His Glu Gly Ile Gln Ala Gly Val Asp
450 455 460

Arg Phe Tyr Arg Thr Cys Lys Leu Val Gly Ile Asn Met Ser Lys Lys
465 470 475 480

Lys Ser Tyr Ile Asn Arg Thr Gly Thr Phe Glu Phe Thr Ser Phe Phe
485 490 495

Tyr Arg Tyr Gly Phe Val Ala Asn Phe Ser Met Glu Leu Pro Ser Phe
500 505 510

	Gly Val Ser Gly Ile Asn Glu Ser Ala Asp Met Ser Ile Gly Val Thr	
	515	520 525
	Val Ile Lys Asn Asn Met Ile Asn Asn Asp Leu Gly Pro Ala Thr Ala	
	530	535 540
	Gln Met Ala Leu Gln Leu Phe Ile Lys Asp Tyr Arg Tyr Thr Tyr Arg	
	545	550 555 560
	Cys His Arg Gly Asp Thr Gln Ile Gln Thr Arg Arg Ser Phe Glu Leu	
	565	570 575
	Lys Lys Leu Trp Glu Gln Thr Arg Ser Lys Thr Gly Leu Leu Val Ser	
	580	585 590
[0071]	Asp Gly Gly Pro Asn Leu Tyr Asn Ile Arg Asn Leu His Ile Pro Glu	
	595	600 605
	Val Cys Leu Lys Trp Glu Leu Met Asp Glu Asp Tyr Lys Gly Arg Leu	
	610	615 620
	Cys Asn Pro Leu Asn Pro Phe Val Ser His Lys Glu Ile Glu Ser Val	
	625	630 635 640
	Asn Ser Ala Val Val Met Pro Ala His Gly Pro Ala Lys Ser Met Glu	
	645	650 655
	Tyr Asp Ala Val Ala Thr Thr His Ser Trp Ile Pro Lys Arg Asn Arg	
	660	665 670
	Ser Ile Leu Asn Thr Ser Gln Arg Gly Ile Leu Glu Asp Glu Gln Met	
	675	680 685

Tyr Gln Lys Cys Cys Asn Leu Phe Glu Lys Phe Phe Pro Ser Ser Ser
690 695 700

Tyr Arg Arg Pro Val Gly Ile Ser Ser Met Val Glu Ala Met Val Ser
705 710 715 720

Arg Ala Arg Ile Asp Ala Arg Ile Asp Phe Glu Ser Gly Arg Ile Lys
725 730 735

Lys Asp Glu Phe Ala Glu Ile Met Lys Ile Cys Ser Thr Ile Glu Glu
740 745 750

Leu Arg Arg Gln Lys
755

[0072]

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<211> 2151

<212> DNA

<213> 流感病毒

<220>

<221> CDS

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1 5 10 15

gcg gaa aag gca atg aaa gaa tat gga gag aac ccg aaa atc gaa aca 96

Ala Glu Lys Ala Met Lys Glu Tyr Gly Glu Asn Pro Lys Ile Glu Thr

20 25 30

aac aaa ttt gca gca ata tgc act cac ttg gaa gtc tgc ttc atg tac 144

Asn Lys Phe Ala Ala Ile Cys Thr His Leu Glu Val Cys Phe Met Tyr

35 40 45

	tgc gat ttt cac ttt att aat gaa ctg ggt gag tca gtg gtc ata gag	192
	Ser Asp Phe His Phe Ile Asn Glu Leu Gly Glu Ser Val Val Ile Glu	
	50 55 60	
	tct ggt gac cca aat get ctt ttg aaa cac aga ttt gaa atc att gag	240
	Ser Gly Asp Pro Asn Ala Leu Leu Lys His Arg Phe Glu Ile Ile Glu	
	65 70 75 80	
	ggg aga gat cga aca atg gca tgg aca gta gta aac agc atc tgc aac	288
	Gly Arg Asp Arg Thr Met Ala Trp Thr Val Val Asn Ser Ile Cys Asn	
	85 90 95	
	acc aca aga get gaa aaa cct aaa ttt ctt cca gat tta tac gac tat	336
	Thr Thr Arg Ala Glu Lys Pro Lys Phe Leu Pro Asp Leu Tyr Asp Tyr	
	100 105 110	
	aag gag aac aga ttt gtt gaa att ggt gtg aca agg aga gaa gtt cac	384
	Lys Glu Asn Arg Phe Val Glu Ile Gly Val Thr Arg Arg Glu Val His	
	115 120 125	
[0073]	ata tac tac ctg gag aag gcc aac aaa ata aag tct gag aaa aca cat	432
	Ile Tyr Tyr Leu Glu Lys Ala Asn Lys Ile Lys Ser Glu Lys Thr His	
	130 135 140	
	atc cac att ttc tca ttt aca gga gag gaa atg gct aca aaa geg gac	480
	Ile His Ile Phe Ser Phe Thr Gly Glu Glu Met Ala Thr Lys Ala Asp	
	145 150 155 160	
	tat act ctt gat gaa gag agt aga gcc agg atc aag acc aga cta ttc	528
	Tyr Thr Leu Asp Glu Glu Ser Arg Ala Arg Ile Lys Thr Arg Leu Phe	
	165 170 175	
	act ata aga caa gaa atg gcc agt aga ggc ctc tgg gat tcc ttt cgt	576
	Thr Ile Arg Gln Glu Met Ala Ser Arg Gly Leu Trp Asp Ser Phe Arg	
	180 185 190	
	cag tcc gag aga ggc gaa gag aca att gaa gaa aga ttt gaa atc aca	624
	Gln Ser Glu Arg Gly Glu Glu Thr Ile Glu Glu Arg Phe Glu Ile Thr	
	195 200 205	
	ggg acg atg cgc aag ctt gcc aat tac agt ctc cca ccg aac ttc tcc	672
	Gly Thr Met Arg Lys Leu Ala Asn Tyr Ser Leu Pro Pro Asn Phe Ser	
	210 215 220	

	agc ett gaa aat ttt aga gtc tat gtg gat gga ttc gaa ccg aac ggc	720
	Ser Leu Glu Asn Phe Arg Val Tyr Val Asp Gly Phe Glu Pro Asn Gly	
	225 230 235 240	
	tgc att gag agt aag ett tct caa atg tcc aaa gaa gta aat gcc aga	768
	Cys Ile Glu Ser Lys Leu Ser Gln Met Ser Lys Glu Val Asn Ala Arg	
	245 250 255	
	atc gaa cca ttt tca aag aca aca ccc cga cca ctc aaa atg cca ggt	816
	Ile Glu Pro Phe Ser Lys Thr Thr Pro Arg Pro Leu Lys Met Pro Gly	
	260 265 270	
	ggc cca ccc tgc cat cag cga tct aaa ttc ttg cta atg gat get ctg	864
	Gly Pro Pro Cys His Gln Arg Ser Lys Phe Leu Leu Met Asp Ala Leu	
	275 280 285	
	aaa ctg agc att gag gac cca agt cac gag gga gag gga ata cca cta	912
	Lys Leu Ser Ile Glu Asp Pro Ser His Glu Gly Glu Gly Ile Pro Leu	
	290 295 300	
[0074]	tat gat gca atc aaa tgc atg aaa act ttc ttt gga tgg aaa gag ccc	960
	Tyr Asp Ala Ile Lys Cys Met Lys Thr Phe Phe Gly Trp Lys Glu Pro	
	305 310 315 320	
	agt att gtt aaa cca cat gaa aag ggt ata aac ccg aac tat ctc caa	1008
	Ser Ile Val Lys Pro His Glu Lys Gly Ile Asn Pro Asn Tyr Leu Gln	
	325 330 335	
	act tgg aag caa gta tta gaa gaa ata caa gac ctt gag aac gaa gaa	1056
	Thr Trp Lys Gln Val Leu Glu Glu Ile Gln Asp Leu Glu Asn Glu Glu	
	340 345 350	
	agg acc ccc aag acc aag aat atg aaa aaa aca agc caa ttg aaa tgg	1104
	Arg Thr Pro Lys Thr Lys Asn Met Lys Lys Thr Ser Gln Leu Lys Trp	
	355 360 365	
	gca cta ggt gaa aat atg gca cca gag aaa gtg gat ttt gag gat tgt	1152
	Ala Leu Gly Glu Asn Met Ala Pro Glu Lys Val Asp Phe Glu Asp Cys	
	370 375 380	
	aaa gac atc aat gat tta aaa caa tat gac agt gat gag cca gaa aca	1200
	Lys Asp Ile Asn Asp Leu Lys Gln Tyr Asp Ser Asp Glu Pro Glu Thr	
	385 390 395 400	

	agg tct ett gca agt tgg att caa agt gag ttc aac aaa gct tgt gag	1248
	Arg Ser Leu Ala Ser Trp Ile Gln Ser Glu Phe Asn Lys Ala Cys Glu	
	405 410 415	
	ctg aca gat tca agc tgg ata gag ctc gat gaa att ggg gag gat gtc	1296
	Leu Thr Asp Ser Ser Trp Ile Glu Leu Asp Glu Ile Gly Glu Asp Val	
	420 425 430	
	gcc cca ata gaa tac att geg agc atg agg aga aat tat ttt act gct	1344
	Ala Pro Ile Glu Tyr Ile Ala Ser Met Arg Arg Asn Tyr Phe Thr Ala	
	435 440 445	
	gag att tcc cat tgt aga gca aca gaa tat ata atg aaa gga gtg tac	1392
	Glu Ile Ser His Cys Arg Ala Thr Glu Tyr Ile Met Lys Gly Val Tyr	
	450 455 460	
	atc aac act gct cta ctc aat gca tcc tgt gct geg atg gat gaa ttt	1440
	Ile Asn Thr Ala Leu Leu Asn Ala Ser Cys Ala Ala Met Asp Glu Phe	
	465 470 475 480	
[0075]	caa tta att ccg atg ata agt aaa tgc agg acc aaa gaa ggg aga agg	1488
	Gln Leu Ile Pro Met Ile Ser Lys Cys Arg Thr Lys Glu Gly Arg Arg	
	485 490 495	
	aaa aca aat tta tat gga ttc ata ata aag gga agg tcc cat tta aga	1536
	Lys Thr Asn Leu Tyr Gly Phe Ile Ile Lys Gly Arg Ser His Leu Arg	
	500 505 510	
	aat gat act gac gtg gtg aac ttt gta agt atg gaa ttt tct ctc act	1584
	Asn Asp Thr Asp Val Val Asn Phe Val Ser Met Glu Phe Ser Leu Thr	
	515 520 525	
	gat cca aga ttt gag cca cac aaa tgg gaa aaa tac tgc gtt cta gaa	1632
	Asp Pro Arg Phe Glu Pro His Lys Trp Glu Lys Tyr Cys Val Leu Glu	
	530 535 540	
	att gga gac atg ett cta aga act gct gta ggt caa gtg tca aga ccc	1680
	Ile Gly Asp Met Leu Leu Arg Thr Ala Val Gly Gln Val Ser Arg Pro	
	545 550 555 560	
	atg ttt ttg tat gta agg aca aat gga acc tct aaa att aaa atg aaa	1728
	Met Phe Leu Tyr Val Arg Thr Asn Gly Thr Ser Lys Ile Lys Met Lys	
	565 570 575	

	tgg gga atg gaa atg agg cgc tgc ctc ctt cag tct ctg caa cag att	1776
	Trp Gly Met Glu Met Arg Arg Cys Leu Leu Gln Ser Leu Gln Gln Ile	
	580 585 590	
	gaa agc atg atc gaa get gag tcc tca gtc aaa gaa aag gac atg acc	1824
	Glu Ser Met Ile Glu Ala Glu Ser Ser Val Lys Glu Lys Asp Met Thr	
	595 600 605	
	aaa gaa ttt ttt gag aac aaa tca gag aca tgg cct ata gga gag tcc	1872
	Lys Glu Phe Phe Glu Asn Lys Ser Glu Thr Trp Pro Ile Gly Glu Ser	
	610 615 620	
	ccc aaa gga gtg gaa gag ggc tca atc ggg aag gtt tgc agg acc tta	1920
	Pro Lys Gly Val Glu Glu Gly Ser Ile Gly Lys Val Cys Arg Thr Leu	
	625 630 635 640	
	tta gca aaa tct gtg ttt aac agt tta tat gca tct cca caa ctg gaa	1968
	Leu Ala Lys Ser Val Phe Asn Ser Leu Tyr Ala Ser Pro Gln Leu Glu	
	645 650 655	
[0076]	ggg ttt tca gct gaa tct agg aaa tta ctt ctc att gtt cag gct ctt	2016
	Gly Phe Ser Ala Glu Ser Arg Lys Leu Leu Leu Ile Val Gln Ala Leu	
	660 665 670	
	agg gat gac ctg gaa cct gga acc ttt gat att ggg ggg tta tat gaa	2064
	Arg Asp Asp Leu Glu Pro Gly Thr Phe Asp Ile Gly Gly Leu Tyr Glu	
	675 680 685	
	tca att gag gag tgc ctg att aat gat ccc tgg gtt ttg ctt aat gca	2112
	Ser Ile Glu Glu Cys Leu Ile Asn Asp Pro Trp Val Leu Leu Asn Ala	
	690 695 700	
	tct tgg ttc aac tcc ttc ctt aca cat gca ctg aag tag	2151
	Ser Trp Phe Asn Ser Phe Leu Thr His Ala Leu Lys	
	705 710 715	
	<210> 22	
	<211> 716	
	<212> PRT	
	<213> 流感病毒	
	<400> 22	

Met Glu Asp Phe Val Arg Gln Cys Phe Asn Pro Met Ile Val Glu Leu
1 5 10 15

Ala Glu Lys Ala Met Lys Glu Tyr Gly Glu Asn Pro Lys Ile Glu Thr
20 25 30

Asn Lys Phe Ala Ala Ile Cys Thr His Leu Glu Val Cys Phe Met Tyr
35 40 45

Ser Asp Phe His Phe Ile Asn Glu Leu Gly Glu Ser Val Val Ile Glu
50 55 60

Ser Gly Asp Pro Asn Ala Leu Leu Lys His Arg Phe Glu Ile Ile Glu
65 70 75 80

[0077]

Gly Arg Asp Arg Thr Met Ala Trp Thr Val Val Asn Ser Ile Cys Asn
85 90 95

Thr Thr Arg Ala Glu Lys Pro Lys Phe Leu Pro Asp Leu Tyr Asp Tyr
100 105 110

Lys Glu Asn Arg Phe Val Glu Ile Gly Val Thr Arg Arg Glu Val His
115 120 125

Ile Tyr Tyr Leu Glu Lys Ala Asn Lys Ile Lys Ser Glu Lys Thr His
130 135 140

Ile His Ile Phe Ser Phe Thr Gly Glu Glu Met Ala Thr Lys Ala Asp
145 150 155 160

Tyr Thr Leu Asp Glu Glu Ser Arg Ala Arg Ile Lys Thr Arg Leu Phe
165 170 175

	Thr	Ile	Arg	Gln	Glu	Met	Ala	Ser	Arg	Gly	Leu	Trp	Asp	Ser	Phe	Arg	
						180				185					190		
	Gln	Ser	Glu	Arg	Gly	Glu	Glu	Thr	Ile	Glu	Glu	Arg	Phe	Glu	Ile	Thr	
			195					200					205				
	Gly	Thr	Met	Arg	Lys	Leu	Ala	Asn	Tyr	Ser	Leu	Pro	Pro	Asn	Phe	Ser	
		210					215					220					
	Ser	Leu	Glu	Asn	Phe	Arg	Val	Tyr	Val	Asp	Gly	Phe	Glu	Pro	Asn	Gly	
	225				230					235						240	
	Cys	Ile	Glu	Ser	Lys	Leu	Ser	Gln	Met	Ser	Lys	Glu	Val	Asn	Ala	Arg	
					245				250					255			
[0078]	Ile	Glu	Pro	Phe	Ser	Lys	Thr	Thr	Pro	Arg	Pro	Leu	Lys	Met	Pro	Gly	
					260				265					270			
	Gly	Pro	Pro	Cys	His	Gln	Arg	Ser	Lys	Phe	Leu	Leu	Met	Asp	Ala	Leu	
		275					280						285				
	Lys	Leu	Ser	Ile	Glu	Asp	Pro	Ser	His	Glu	Gly	Glu	Gly	Ile	Pro	Leu	
		290					295					300					
	Tyr	Asp	Ala	Ile	Lys	Cys	Met	Lys	Thr	Phe	Phe	Gly	Trp	Lys	Glu	Pro	
	305				310					315					320		
	Ser	Ile	Val	Lys	Pro	His	Glu	Lys	Gly	Ile	Asn	Pro	Asn	Tyr	Leu	Gln	
					325				330					335			
	Thr	Trp	Lys	Gln	Val	Leu	Glu	Glu	Ile	Gln	Asp	Leu	Glu	Asn	Glu	Glu	
			340						345					350			

	Arg Thr Pro Lys Thr Lys Asn Met Lys Lys Thr Ser Gln Leu Lys Trp	
	355	360 365
	Ala Leu Gly Glu Asn Met Ala Pro Glu Lys Val Asp Phe Glu Asp Cys	
	370	375 380
	Lys Asp Ile Asn Asp Leu Lys Gln Tyr Asp Ser Asp Glu Pro Glu Thr	
	385	390 395 400
	Arg Ser Leu Ala Ser Trp Ile Gln Ser Glu Phe Asn Lys Ala Cys Glu	
	405	410 415
	Leu Thr Asp Ser Ser Trp Ile Glu Leu Asp Glu Ile Gly Glu Asp Val	
	420	425 430
[0079]	Ala Pro Ile Glu Tyr Ile Ala Ser Met Arg Arg Asn Tyr Phe Thr Ala	
	435	440 445
	Glu Ile Ser His Cys Arg Ala Thr Glu Tyr Ile Met Lys Gly Val Tyr	
	450	455 460
	Ile Asn Thr Ala Leu Leu Asn Ala Ser Cys Ala Ala Met Asp Glu Phe	
	465	470 475 480
	Gln Leu Ile Pro Met Ile Ser Lys Cys Arg Thr Lys Glu Gly Arg Arg	
	485	490 495
	Lys Thr Asn Leu Tyr Gly Phe Ile Ile Lys Gly Arg Ser His Leu Arg	
	500	505 510
	Asn Asp Thr Asp Val Val Asn Phe Val Ser Met Glu Phe Ser Leu Thr	
	515	520 525

Asp Pro Arg Phe Glu Pro His Lys Trp Glu Lys Tyr Cys Val Leu Glu
530 535 540

Ile Gly Asp Met Leu Leu Arg Thr Ala Val Gly Gln Val Ser Arg Pro
545 550 555 560

Met Phe Leu Tyr Val Arg Thr Asn Gly Thr Ser Lys Ile Lys Met Lys
565 570 575

Trp Gly Met Glu Met Arg Arg Cys Leu Leu Gln Ser Leu Gln Gln Ile
580 585 590

Glu Ser Met Ile Glu Ala Glu Ser Ser Val Lys Glu Lys Asp Met Thr
595 600 605

[0080]

Lys Glu Phe Phe Glu Asn Lys Ser Glu Thr Trp Pro Ile Gly Glu Ser
610 615 620

Pro Lys Gly Val Glu Glu Gly Ser Ile Gly Lys Val Cys Arg Thr Leu
625 630 635 640

Leu Ala Lys Ser Val Phe Asn Ser Leu Tyr Ala Ser Pro Gln Leu Glu
645 650 655

Gly Phe Ser Ala Glu Ser Arg Lys Leu Leu Leu Ile Val Gln Ala Leu
660 665 670

Arg Asp Asp Leu Glu Pro Gly Thr Phe Asp Ile Gly Gly Leu Tyr Glu
675 680 685

Ser Ile Glu Glu Cys Leu Ile Asn Asp Pro Trp Val Leu Leu Asn Ala
690 695 700

Ser Trp Phe Asn Ser Phe Leu Thr His Ala Leu Lys
705 710 715

<210> 23

<211> 838

<212> DNA

<213> 流感病毒

<220>

<221> CDS

<222> (1)..(657)

<400> 23

atg gat tcc aac act gtg tca agc ttt cag gta gac tgt ttt ctt tgg 48

Met Asp Ser Asn Thr Val Ser Ser Phe Gln Val Asp Cys Phe Leu Trp

1 5 10 15

cat gtc cgc aaa cga ttc gca gac caa gaa ctg ggt gat gcc cca ttc 96

His Val Arg Lys Arg Phe Ala Asp Gln Glu Leu Gly Asp Ala Pro Phe

20 25 30

[0081]

ctt gac egg ctt cgc cga gac cag aag tcc cta agg gga aga ggt agc 144

Leu Asp Arg Leu Arg Arg Asp Gln Lys Ser Leu Arg Gly Arg Gly Ser

35 40 45

act ctt ggt ctg gac atc gaa aca gcc act cat gca gga aag cag ata 192

Thr Leu Gly Leu Asp Ile Glu Thr Ala Thr His Ala Gly Lys Gln Ile

50 55 60

gtg gag cag att ctg gaa aag gaa tca gat gag gca ctt aaa atg acc 240

Val Glu Gln Ile Leu Glu Lys Glu Ser Asp Glu Ala Leu Lys Met Thr

65 70 75 80

att gcc tct gtt cct act tca cgc tac tta act gac atg act ctt gat 288

Ile Ala Ser Val Pro Thr Ser Arg Tyr Leu Thr Asp Met Thr Leu Asp

85 90 95

gag atg tca aga gac tgg ttc atg ctc atg ccc aag caa aaa gta aca 336

Glu Met Ser Arg Asp Trp Phe Met Leu Met Pro Lys Gln Lys Val Thr

100 105 110

ggc tcc cta tgt ata aga atg gac cag gca atc atg gat aag aac atc 384

	Gly Ser Leu Cys Ile Arg Met Asp Gln Ala Ile Met Asp Lys Asn Ile	
	115 120 125	
	ata ctt aaa gca aac ttt agt gtg att ttc gaa ggg ctg gaa aca cta	432
	Ile Leu Lys Ala Asn Phe Ser Val Ile Phe Glu Gly Leu Glu Thr Leu	
	130 135 140	
	ata cta ctt aga gcc ttc acc gaa gaa gga gca gtc gtt ggc gaa att	480
	Ile Leu Leu Arg Ala Phe Thr Glu Glu Gly Ala Val Val Gly Glu Ile	
	145 150 155 160	
	tca cca tta cct tct ctt cca gga cat act aat gag gat gtc aaa aat	528
	Ser Pro Leu Pro Ser Leu Pro Gly His Thr Asn Glu Asp Val Lys Asn	
	165 170 175	
	gca att ggg gtc ctc atc gga gga ctt aaa tgg aat gat aat acg gtt	576
	Ala Ile Gly Val Leu Ile Gly Gly Leu Lys Trp Asn Asp Asn Thr Val	
	180 185 190	
	aga atc tct gaa act cta cag aga ttc gct tgg aga agc agt cat gag	624
	Arg Ile Ser Glu Thr Leu Gln Arg Phe Ala Trp Arg Ser Ser His Glu	
[0082]	195 200 205	
	aat ggg aga cct tca ttc cct tca aag cag aaa tgaaaaatgg agagaacaat	677
	Asn Gly Arg Pro Ser Phe Pro Ser Lys Gln Lys	
	210 215	
	taagccagaa atttgaagaa ataagatggt tgattgaaga agtgcgacat agattgaaaa	737
	atacagaaaa tagtttigaa caaataacat ttaigcaagc cttacaacta ttgettgaag	797
	tagaacaaga gataagaact ttctcgtttc agcttattta a	838
	<210> 24	
	<211> 219	
	<212> PRT	
	<213> 流感病毒	
	<400> 24	
	Met Asp Ser Asn Thr Val Ser Ser Phe Gln Val Asp Cys Phe Leu Trp	
	1 5 10 15	

	His	Val	Arg	Lys	Arg	Phe	Ala	Asp	Gln	Glu	Leu	Gly	Asp	Ala	Pro	Phe	
				20					25					30			
	Leu	Asp	Arg	Leu	Arg	Arg	Asp	Gln	Lys	Ser	Leu	Arg	Gly	Arg	Gly	Ser	
		35						40					45				
	Thr	Leu	Gly	Leu	Asp	Ile	Glu	Thr	Ala	Thr	His	Ala	Gly	Lys	Gln	Ile	
		50					55					60					
	Val	Glu	Gln	Ile	Leu	Glu	Lys	Glu	Ser	Asp	Glu	Ala	Leu	Lys	Met	Thr	
	65				70					75					80		
	Ile	Ala	Ser	Val	Pro	Thr	Ser	Arg	Tyr	Leu	Thr	Asp	Met	Thr	Leu	Asp	
				85					90					95			
[0083]	Glu	Met	Ser	Arg	Asp	Trp	Phe	Met	Leu	Met	Pro	Lys	Gln	Lys	Val	Thr	
				100					105					110			
	Gly	Ser	Leu	Cys	Ile	Arg	Met	Asp	Gln	Ala	Ile	Met	Asp	Lys	Asn	Ile	
		115						120					125				
	Ile	Leu	Lys	Ala	Asn	Phe	Ser	Val	Ile	Phe	Glu	Gly	Leu	Glu	Thr	Leu	
		130					135					140					
	Ile	Leu	Leu	Arg	Ala	Phe	Thr	Glu	Glu	Gly	Ala	Val	Val	Gly	Glu	Ile	
	145				150					155					160		
	Ser	Pro	Leu	Pro	Ser	Leu	Pro	Gly	His	Thr	Asn	Glu	Asp	Val	Lys	Asn	
				165					170					175			
	Ala	Ile	Gly	Val	Leu	Ile	Gly	Gly	Leu	Lys	Trp	Asn	Asp	Asn	Thr	Val	
			180					185					190				

Arg Ile Ser Glu Thr Leu Gln Arg Phe Ala Trp Arg Ser Ser His Glu
 195 200 205

Asn Gly Arg Pro Ser Phe Pro Ser Lys Gln Lys
 210 215

<210> 25

<211> 1497

<212> DNA

<213> 流感病毒

<220>

<221> CDS

<222> (1).. (1497)

<400> 25

[0084] atg gcg tct caa ggc acc aaa cga tcc tat gaa cag atg gaa act gat 48
 Met Ala Ser Gln Gly Thr Lys Arg Ser Tyr Glu Gln Met Glu Thr Asp
 1 5 10 15

ggg gaa cgc cag aat gca act gaa atc aga gca tct gtc gga agg atg 96
 Gly Glu Arg Gln Asn Ala Thr Glu Ile Arg Ala Ser Val Gly Arg Met
 20 25 30

gtg gga gga atc ggc cgg ttt tat gtt cag atg tgt act gag ctt aaa 144
 Val Gly Gly Ile Gly Arg Phe Tyr Val Gln Met Cys Thr Glu Leu Lys
 35 40 45

cta aac gac cat gaa ggg cgg ctg att cag aac age ata aca ata gaa 192
 Leu Asn Asp His Glu Gly Arg Leu Ile Gln Asn Ser Ile Thr Ile Glu
 50 55 60

agg atg gta ctt tcg gca ttc gac gaa aga aga aac aag tat ctc gag 240
 Arg Met Val Leu Ser Ala Phe Asp Glu Arg Arg Asn Lys Tyr Leu Glu
 65 70 75 80

gag cat ccc agt gct ggg aaa gac cct aag aaa acg gga ggc cgg ata 288
 Glu His Pro Ser Ala Gly Lys Asp Pro Lys Lys Thr Gly Gly Pro Ile
 85 90 95

	tac aga agg aaa gat ggg aaa tgg atg agg gaa ctc atc ctc cat gat	336
	Tyr Arg Arg Lys Asp Gly Lys Trp Met Arg Glu Leu Ile Leu His Asp	
	100 105 110	
	aaa gaa gaa atc atg aga atc tgg cgt cag gcc aac aat ggt gaa gac	384
	Lys Glu Glu Ile Met Arg Ile Trp Arg Gln Ala Asn Asn Gly Glu Asp	
	115 120 125	
	get act get ggt ctt act cat atg atg atc tgg cac tcc aat ctc aat	432
	Ala Thr Ala Gly Leu Thr His Met Met Ile Trp His Ser Asn Leu Asn	
	130 135 140	
	gac acc aca tac caa aga aca agg get ctt gtt cgg act ggg atg gat	480
	Asp Thr Thr Tyr Gln Arg Thr Arg Ala Leu Val Arg Thr Gly Met Asp	
	145 150 155 160	
	ccc aga atg tgc tct ctg atg caa gcc tca acc ctc cca cgg aga tct	528
	Pro Arg Met Cys Ser Leu Met Gln Gly Ser Thr Leu Pro Arg Arg Ser	
	165 170 175	
[0085]	gga gcc get ggt get gca gta aaa ggt gtt gga aca atg gta atg gaa	576
	Gly Ala Ala Gly Ala Ala Val Lys Gly Val Gly Thr Met Val Met Glu	
	180 185 190	
	ctc atc aga atg atc aaa cgc gga ata aat gat cgg aat ttc tgg aga	624
	Leu Ile Arg Met Ile Lys Arg Gly Ile Asn Asp Arg Asn Phe Trp Arg	
	195 200 205	
	ggt gaa aat ggt cga aga acc aga att get tat gaa aga atg tgc aat	672
	Gly Glu Asn Gly Arg Arg Thr Arg Ile Ala Tyr Glu Arg Met Cys Asn	
	210 215 220	
	atc ctc aaa ggg aaa ttt cag aca gca gca caa cgg get atg atg gac	720
	Ile Leu Lys Gly Lys Phe Gln Thr Ala Ala Gln Arg Ala Met Met Asp	
	225 230 235 240	
	cag gtg agg gaa gcc cgc aat cct gga aac get gag att gag gat ctc	768
	Gln Val Arg Glu Gly Arg Asn Pro Gly Asn Ala Glu Ile Glu Asp Leu	
	245 250 255	
	att ttc ttg gca cga tca gca ctt att ttg aga gga tca gta gcc cat	816
	Ile Phe Leu Ala Arg Ser Ala Leu Ile Leu Arg Gly Ser Val Ala His	
	260 265 270	

	aaa tca tgc cta cct gcc tgt gtt tat ggc ctt gea gta acc agt ggg	864
	Lys Ser Cys Leu Pro Ala Cys Val Tyr Gly Leu Ala Val Thr Ser Gly	
	275 280 285	
	tat gac ttt gag aag gaa gga tac tct ctg gtt gga att gat cct ttc	912
	Tyr Asp Phe Glu Lys Glu Gly Tyr Ser Leu Val Gly Ile Asp Pro Phe	
	290 295 300	
	aaa cta ctc cag aac agt caa att ttc agt cta atc aga cca aaa gaa	960
	Lys Leu Leu Gln Asn Ser Gln Ile Phe Ser Leu Ile Arg Pro Lys Glu	
	305 310 315 320	
	aac cca gea cac aag agc cag ttg gtg tgg atg gea tgc cat tct gea	1008
	Asn Pro Ala His Lys Ser Gln Leu Val Trp Met Ala Cys His Ser Ala	
	325 330 335	
	gea ttt gag gac ctg aga gtt tta aat ttc att aga gga acc aaa gta	1056
	Ala Phe Glu Asp Leu Arg Val Leu Asn Phe Ile Arg Gly Thr Lys Val	
	340 345 350	
[0086]	atc cca aga gga cag tta aca acc aga gga gtt caa att gct tca aat	1104
	Ile Pro Arg Gly Gln Leu Thr Thr Arg Gly Val Gln Ile Ala Ser Asn	
	355 360 365	
	gaa aac atg gag aca ata gat tct agc aca ctt gaa ctg aga agc aaa	1152
	Glu Asn Met Glu Thr Ile Asp Ser Ser Thr Leu Glu Leu Arg Ser Lys	
	370 375 380	
	tat tgg gea ata agg acc aga agc gga gga aac acc agt caa cag aga	1200
	Tyr Trp Ala Ile Arg Thr Arg Ser Gly Gly Asn Thr Ser Gln Gln Arg	
	385 390 395 400	
	gea tct gea gga cag ata agt gtg caa cct act ttc tca gta cag aga	1248
	Ala Ser Ala Gly Gln Ile Ser Val Gln Pro Thr Phe Ser Val Gln Arg	
	405 410 415	
	aat ctt ccc ttt gag aga gea acc att atg get gea ttc act ggt aac	1296
	Asn Leu Pro Phe Glu Arg Ala Thr Ile Met Ala Ala Phe Thr Gly Asn	
	420 425 430	
	act gaa ggg agg act tcc gac atg aga acg gaa atc ata agg atg atg	1344
	Thr Glu Gly Arg Thr Ser Asp Met Arg Thr Glu Ile Ile Arg Met Met	
	435 440 445	

gaa aat gcc aaa tca gaa gat gtg tet ttc cag ggg egg gga gtc ttc 1392
 Glu Asn Ala Lys Ser Glu Asp Val Ser Phe Gln Gly Arg Gly Val Phe
 450 455 460

gag ctc teg gac gaa aag gca acg aac ccg atc gtg cct tcc ttt gac 1440
 Glu Leu Ser Asp Glu Lys Ala Thr Asn Pro Ile Val Pro Ser Phe Asp
 465 470 475 480

atg agc aat gaa ggg tet tat ttc ttc gga gac aat gct gag gag ttt 1488
 Met Ser Asn Glu Gly Ser Tyr Phe Phe Gly Asp Asn Ala Glu Glu Phe
 485 490 495

gac agt taa 1497
 Asp Ser

<210> 26

<211> 498

<212> PRT

<213> 流感病毒

[0087]

<400> 26

Met Ala Ser Gln Gly Thr Lys Arg Ser Tyr Glu Gln Met Glu Thr Asp
 1 5 10 15

Gly Glu Arg Gln Asn Ala Thr Glu Ile Arg Ala Ser Val Gly Arg Met
 20 25 30

Val Gly Gly Ile Gly Arg Phe Tyr Val Gln Met Cys Thr Glu Leu Lys
 35 40 45

Leu Asn Asp His Glu Gly Arg Leu Ile Gln Asn Ser Ile Thr Ile Glu
 50 55 60

Arg Met Val Leu Ser Ala Phe Asp Glu Arg Arg Asn Lys Tyr Leu Glu
 65 70 75 80

	Glu	His	Pro	Ser	Ala	Gly	Lys	Asp	Pro	Lys	Lys	Thr	Gly	Gly	Pro	Ile	
						85				90					95		
	Tyr	Arg	Arg	Lys	Asp	Gly	Lys	Trp	Met	Arg	Glu	Leu	Ile	Leu	His	Asp	
				100				105						110			
	Lys	Glu	Glu	Ile	Met	Arg	Ile	Trp	Arg	Gln	Ala	Asn	Asn	Gly	Glu	Asp	
				115				120						125			
	Ala	Thr	Ala	Gly	Leu	Thr	His	Met	Met	Ile	Trp	His	Ser	Asn	Leu	Asn	
				130				135						140			
	Asp	Thr	Thr	Tyr	Gln	Arg	Thr	Arg	Ala	Leu	Val	Arg	Thr	Gly	Met	Asp	
	145					150					155					160	
[0088]	Pro	Arg	Met	Cys	Ser	Leu	Met	Gln	Gly	Ser	Thr	Leu	Pro	Arg	Arg	Ser	
				165						170					175		
	Gly	Ala	Ala	Gly	Ala	Ala	Val	Lys	Gly	Val	Gly	Thr	Met	Val	Met	Glu	
				180						185					190		
	Leu	Ile	Arg	Met	Ile	Lys	Arg	Gly	Ile	Asn	Asp	Arg	Asn	Phe	Trp	Arg	
				195					200					205			
	Gly	Glu	Asn	Gly	Arg	Arg	Thr	Arg	Ile	Ala	Tyr	Glu	Arg	Met	Cys	Asn	
				210				215					220				
	Ile	Leu	Lys	Gly	Lys	Phe	Gln	Thr	Ala	Ala	Gln	Arg	Ala	Met	Met	Asp	
	225					230					235					240	
	Gln	Val	Arg	Glu	Gly	Arg	Asn	Pro	Gly	Asn	Ala	Glu	Ile	Glu	Asp	Leu	
						245				250					255		

Ile Phe Leu Ala Arg Ser Ala Leu Ile Leu Arg Gly Ser Val Ala His
260 265 270

Lys Ser Cys Leu Pro Ala Cys Val Tyr Gly Leu Ala Val Thr Ser Gly
275 280 285

Tyr Asp Phe Glu Lys Glu Gly Tyr Ser Leu Val Gly Ile Asp Pro Phe
290 295 300

Lys Leu Leu Gln Asn Ser Gln Ile Phe Ser Leu Ile Arg Pro Lys Glu
305 310 315 320

Asn Pro Ala His Lys Ser Gln Leu Val Trp Met Ala Cys His Ser Ala
325 330 335

[0089] Ala Phe Glu Asp Leu Arg Val Leu Asn Phe Ile Arg Gly Thr Lys Val
340 345 350

Ile Pro Arg Gly Gln Leu Thr Thr Arg Gly Val Gln Ile Ala Ser Asn
355 360 365

Glu Asn Met Glu Thr Ile Asp Ser Ser Thr Leu Glu Leu Arg Ser Lys
370 375 380

Tyr Trp Ala Ile Arg Thr Arg Ser Gly Gly Asn Thr Ser Gln Gln Arg
385 390 395 400

Ala Ser Ala Gly Gln Ile Ser Val Gln Pro Thr Phe Ser Val Gln Arg
405 410 415

Asn Leu Pro Phe Glu Arg Ala Thr Ile Met Ala Ala Phe Thr Gly Asn
420 425 430

Thr Glu Gly Arg Thr Ser Asp Met Arg Thr Glu Ile Ile Arg Met Met
435 440 445

Glu Asn Ala Lys Ser Glu Asp Val Ser Phe Gln Gly Arg Gly Val Phe
450 455 460

Glu Leu Ser Asp Glu Lys Ala Thr Asn Pro Ile Val Pro Ser Phe Asp
465 470 475 480

Met Ser Asn Glu Gly Ser Tyr Phe Phe Gly Asp Asn Ala Glu Glu Phe
485 490 495

Asp Ser

[0090]

<210> 27

<211> 1410

<212> DNA

<213> 流感病毒

<220>

<221> CDS

<222> (1)..(1410)

<400> 27

atg aat cca aat caa aag ata ata aca att gga ttt gca tca ttg ggg 48
Met Asn Pro Asn Gln Lys Ile Ile Thr Ile Gly Phe Ala Ser Leu Gly
1 5 10 15

ata tta atc att aat gtc att ctc cat gta gtc agc att ata gta aca 96
Ile Leu Ile Ile Asn Val Ile Leu His Val Val Ser Ile Ile Val Thr
20 25 30

gta ctg gtc ctc aat aac aat aga aca gat ctg aac tgc aaa ggg acg 144
Val Leu Val Leu Asn Asn Asn Arg Thr Asp Leu Asn Cys Lys Gly Thr
35 40 45

atc ata aga gag tac aat gaa aca gta aga gta gaa aaa att act caa 192

Ile Ile Arg Glu Tyr Asn Glu Thr Val Arg Val Glu Lys Ile Thr Gln	
50 55 60	
tgg tat aat acc agt aca att aag tac ata gag aga cct tca aat gaa	240
Trp Tyr Asn Thr Ser Thr Ile Lys Tyr Ile Glu Arg Pro Ser Asn Glu	
65 70 75 80	
tac tac atg aac aac act gaa cca ctt tgt gag gcc caa ggc ttt gea	288
Tyr Tyr Met Asn Asn Thr Glu Pro Leu Cys Glu Ala Gln Gly Phe Ala	
85 90 95	
cca ttt tcc aaa gat aat gga ata cga att ggg teg aga ggc cat gtt	336
Pro Phe Ser Lys Asp Asn Gly Ile Arg Ile Gly Ser Arg Gly His Val	
100 105 110	
ttt gtg ata aga gaa cct ttt gta tca tgt teg ccc tca gaa tgt aga	384
Phe Val Ile Arg Glu Pro Phe Val Ser Cys Ser Pro Ser Glu Cys Arg	
115 120 125	
acc ttt ttc ctc aca cag ggc tca tta ctc aat gac aaa cat tct aac	432
Thr Phe Phe Leu Thr Gln Gly Ser Leu Leu Asn Asp Lys His Ser Asn	
130 135 140	
[0091]	
ggc aca gta aag gac cga agt ccg tat agg act ttg atg agt gtc aaa	480
Gly Thr Val Lys Asp Arg Ser Pro Tyr Arg Thr Leu Met Ser Val Lys	
145 150 155 160	
ata ggg caa tca cct aat gta tat caa gct agg ttt gaa teg gtg gea	528
Ile Gly Gln Ser Pro Asn Val Tyr Gln Ala Arg Phe Glu Ser Val Ala	
165 170 175	
tgg tca gea aca gea tgc cat gat gga aaa aaa tgg atg aca gtt gga	576
Trp Ser Ala Thr Ala Cys His Asp Gly Lys Lys Trp Met Thr Val Gly	
180 185 190	
gtc aca ggg ccc gac aat caa gea att gea gta gtg aac tat gga ggt	624
Val Thr Gly Pro Asp Asn Gln Ala Ile Ala Val Val Asn Tyr Gly Gly	
195 200 205	
gtt ccg gtt gat att att aat tca tgg gea ggg gat att tta aga acc	672
Val Pro Val Asp Ile Ile Asn Ser Trp Ala Gly Asp Ile Leu Arg Thr	
210 215 220	
caa gaa tca tca tgc acc tgc att aaa gga gac tgt tat tgg gta atg	720

[0092]

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

Gly Tyr Ser Gly Ser Phe Thr Leu Pro Val Glu Leu Thr Lys Lys Gly	
405 410 415	
tgt ttg gtc ccc tgt ttc tgg gtt gaa atg att aga ggt aaa cct gaa	1296
Cys Leu Val Pro Cys Phe Trp Val Glu Met Ile Arg Gly Lys Pro Glu	
420 425 430	
gaa aca aca ata tgg acc tct agc agc tcc att gtg atg tgt gga gta	1344
Glu Thr Thr Ile Trp Thr Ser Ser Ser Ser Ile Val Met Cys Gly Val	
435 440 445	
gat cat aaa att gcc agt tgg tca tgg cac gat gga gct att ctt ccc	1392
Asp His Lys Ile Ala Ser Trp Ser Trp His Asp Gly Ala Ile Leu Pro	
450 455 460	
ttt gac atc gat aag atg	1410
Phe Asp Ile Asp Lys Met	
465 470	
<210> 28	
<211> 470	
<212> PRT	
<213> 流感病毒	
<400> 28	
Met Asn Pro Asn Glu Lys Ile Ile Thr Ile Gly Phe Ala Ser Leu Gly	
1 5 10 15	
Ile Leu Ile Ile Asn Val Ile Leu His Val Val Ser Ile Ile Val Thr	
20 25 30	
Val Leu Val Leu Asn Asn Asn Arg Thr Asp Leu Asn Cys Lys Gly Thr	
35 40 45	
Ile Ile Arg Glu Tyr Asn Glu Thr Val Arg Val Glu Lys Ile Thr Glu	
50 55 60	
Trp Tyr Asn Thr Ser Thr Ile Lys Tyr Ile Glu Arg Pro Ser Asn Glu	

[0093]

65	70	75	80
Tyr Tyr Met Asn Asn Thr Glu Pro Leu Cys Glu Ala Gln Gly Phe Ala			
	85	90	95
Pro Phe Ser Lys Asp Asn Gly Ile Arg Ile Gly Ser Arg Gly His Val			
	100	105	110
Phe Val Ile Arg Glu Pro Phe Val Ser Cys Ser Pro Ser Glu Cys Arg			
	115	120	125
Thr Phe Phe Leu Thr Gln Gly Ser Leu Leu Asn Asp Lys His Ser Asn			
	130	135	140
Gly Thr Val Lys Asp Arg Ser Pro Tyr Arg Thr Leu Met Ser Val Lys			
145	150	155	160
[0094]			
Ile Gly Gln Ser Pro Asn Val Tyr Gln Ala Arg Phe Glu Ser Val Ala			
	165	170	175
Trp Ser Ala Thr Ala Cys His Asp Gly Lys Lys Trp Met Thr Val Gly			
	180	185	190
Val Thr Gly Pro Asp Asn Gln Ala Ile Ala Val Val Asn Tyr Gly Gly			
	195	200	205
Val Pro Val Asp Ile Ile Asn Ser Trp Ala Gly Asp Ile Leu Arg Thr			
	210	215	220
Gln Glu Ser Ser Cys Thr Cys Ile Lys Gly Asp Cys Tyr Trp Val Met			
225	230	235	240
Thr Asp Gly Pro Ala Asn Arg Gln Ala Lys Tyr Arg Ile Phe Lys Ala			

	245	250	255
Lys Asp Gly Arg Val Ile Gly Gln Thr Asp Ile Ser Phe Asn Gly Gly			
	260	265	270
His Ile Glu Glu Cys Ser Cys Tyr Pro Asn Glu Gly Lys Val Glu Cys			
	275	280	285
Ile Cys Arg Asp Asn Trp Thr Gly Thr Asn Arg Pro Ile Leu Val Ile			
	290	295	300
Ser Ser Asp Leu Ser Tyr Thr Val Gly Tyr Leu Cys Ala Gly Ile Pro			
305	310	315	320
Thr Asp Thr Pro Arg Gly Glu Asp Ser Gln Phe Thr Gly Ser Cys Thr			
	325	330	335
[0095]			
Ser Pro Leu Gly Asn Lys Gly Tyr Gly Val Lys Gly Phe Gly Phe Arg			
	340	345	350
Gln Gly Thr Asp Val Trp Ala Gly Arg Thr Ile Ser Arg Thr Ser Arg			
	355	360	365
Ser Gly Phe Glu Ile Ile Lys Ile Arg Asn Gly Trp Thr Gln Asn Ser			
	370	375	380
Lys Asp Gln Ile Arg Arg Gln Val Ile Ile Asp Asp Pro Asn Trp Ser			
	385	390	395
Gly Tyr Ser Gly Ser Phe Thr Leu Pro Val Glu Leu Thr Lys Lys Gly			
	405	410	415
Cys Leu Val Pro Cys Phe Trp Val Glu Met Ile Arg Gly Lys Pro Glu			

	420	425	430
Glu Thr Thr Ile Trp Thr Ser Ser Ser Ser Ile Val Met Cys Gly Val			
435	440	445	
Asp His Lys Ile Ala Ser Trp Ser Trp His Asp Gly Ala Ile Leu Pro			
450	455	460	
Phe Asp Ile Asp Lys Met			
465	470		

<210> 29
 <211> 982
 <212> DNA
 <213> 流感病毒

[0096]

<220>
 <221> CDS
 <222> (1)..(756)

<400> 29	
atg agt ctt cta acc gag gtc gaa acg tac gtt ctc tet atc gta cca	48
Met Ser Leu Leu Thr Glu Val Glu Thr Tyr Val Leu Ser Ile Val Pro	
1 5 10 15	
tea ggc ccc ctc aaa gcc gag atc gcg cag aga ctt gaa gat gtc ttt	96
Ser Gly Pro Leu Lys Ala Glu Ile Ala Gln Arg Leu Glu Asp Val Phe	
20 25 30	
gea ggg aag aac acc gat ctt gag gca ctc atg gaa tgg cta aag aca	144
Ala Gly Lys Asn Thr Asp Leu Glu Ala Leu Met Glu Trp Leu Lys Thr	
35 40 45	
aga cca atc ctg tca cct ctg act aaa ggg att tta gga ttt gta ttc	192
Arg Pro Ile Leu Ser Pro Leu Thr Lys Gly Ile Leu Gly Phe Val Phe	
50 55 60	
acg ctc acc gtg ccc agt gag cga gga ctg cag cgt aga cgc ttt gtc	240
Thr Leu Thr Val Pro Ser Glu Arg Gly Leu Gln Arg Arg Arg Phe Val	

65	70	75	80	
caa aat gcc ctt agt gga aac gga gat cca aac aac atg gac aga gea				288
Gln Asn Ala Leu Ser Gly Asn Gly Asp Pro Asn Asn Met Asp Arg Ala				
85	90	95		
gta aaa ctg tac agg aag ctt aaa aga gaa ata aca ttc cat ggg gea				336
Val Lys Leu Tyr Arg Lys Leu Lys Arg Glu Ile Thr Phe His Gly Ala				
100	105	110		
aaa gag gtg gca ctc agc tat tcc act ggt gea cta gcc agc tgc atg				384
Lys Glu Val Ala Leu Ser Tyr Ser Thr Gly Ala Leu Ala Ser Cys Met				
115	120	125		
gga ctc ata tac aac aga atg gga act gtt aca acc gaa gtg gea ttt				432
Gly Leu Ile Tyr Asn Arg Met Gly Thr Val Thr Thr Glu Val Ala Phe				
130	135	140		
ggc ctg gta tgc gcc aca tgt gaa cag att get gat tcc cag cat cga				480
Gly Leu Val Cys Ala Thr Cys Glu Gln Ile Ala Asp Ser Gln His Arg				
145	150	155	160	
[0097] tct cac agg cag atg gtg aca aca acc aac cea tta atc aga cat gaa				528
Ser His Arg Gln Met Val Thr Thr Thr Asn Pro Leu Ile Arg His Glu				
165	170	175		
aac aga atg gta tta gcc agt acc acg get aaa gcc atg gaa cag atg				576
Asn Arg Met Val Leu Ala Ser Thr Thr Ala Lys Ala Met Glu Gln Met				
180	185	190		
gea gga teg agt gag cag gea gea gag gcc atg gag gtt get agt agg				624
Ala Gly Ser Ser Glu Gln Ala Ala Glu Ala Met Glu Val Ala Ser Arg				
195	200	205		
get agg cag atg gta cag gea atg aga acc att ggg acc cac cct agc				672
Ala Arg Gln Met Val Gln Ala Met Arg Thr Ile Gly Thr His Pro Ser				
210	215	220		
tcc agt gcc ggt ttg aaa gat gat ctc ctt gaa aat tta cag gcc tac				720
Ser Ser Ala Gly Leu Lys Asp Asp Leu Leu Glu Asn Leu Gln Ala Tyr				
225	230	235	240	
cag aaa cgg atg gga gtg caa atg cag cga ttc aag tgatcctctc				766
Gln Lys Arg Met Gly Val Gln Met Gln Arg Phe Lys				

Val Lys Leu Tyr Arg Lys Leu Lys Arg Glu Ile Thr Phe His Gly Ala
100 105 110

Lys Glu Val Ala Leu Ser Tyr Ser Thr Gly Ala Leu Ala Ser Cys Met
115 120 125

Gly Leu Ile Tyr Asn Arg Met Gly Thr Val Thr Thr Glu Val Ala Phe
130 135 140

Gly Leu Val Cys Ala Thr Cys Glu Gln Ile Ala Asp Ser Gln His Arg
145 150 155 160

Ser His Arg Gln Met Val Thr Thr Thr Asn Pro Leu Ile Arg His Glu
165 170 175

Asn Arg Met Val Leu Ala Ser Thr Thr Ala Lys Ala Met Glu Gln Met
180 185 190

[0099]

Ala Gly Ser Ser Glu Gln Ala Ala Glu Ala Met Glu Val Ala Ser Arg
195 200 205

Ala Arg Gln Met Val Gln Ala Met Arg Thr Ile Gly Thr His Pro Ser
210 215 220

Ser Ser Ala Gly Leu Lys Asp Asp Leu Leu Glu Asn Leu Gln Ala Tyr
225 230 235 240

Gln Lys Arg Met Gly Val Gln Met Gln Arg Phe Lys
245 250

<210> 31

<211> 1698

<212> DNA

<213> 流感病毒

<220>			
<221> CDS			
<222> (1)..(1698)			
<400> 31			
atg aag aca acc att att ttg ata cta ctg acc cat tgg gcc tac agt		48	
Met Lys Thr Thr Ile Ile Leu Ile Leu Leu Thr His Trp Ala Tyr Ser			
1 5 10 15			
caa aac cca atc agt gac aac aac aca gcc aca ctg tgt ctg gga cac		96	
Gln Asn Pro Ile Ser Asp Asn Asn Thr Ala Thr Leu Cys Leu Gly His			
20 25 30			
cat gca gta gca aat gga aca ttg gta aaa aca ata agt gat gat caa		144	
His Ala Val Ala Asn Gly Thr Leu Val Lys Thr Ile Ser Asp Asp Gln			
35 40 45			
att gag gtg aca aat gct aca gaa tta gtt cag agc att tca atg ggg		192	
Ile Glu Val Thr Asn Ala Thr Glu Leu Val Gln Ser Ile Ser Met Gly			
50 55 60			
[0100]	aaa ata tgc aac aaa tca tat aga att cta gat gga aga aat tgc aca	240	
	Lys Ile Cys Asn Lys Ser Tyr Arg Ile Leu Asp Gly Arg Asn Cys Thr		
	65 70 75 80		
	tta ata gat gca atg cta gga gac ccc cac tgt gac gcc ttt cag tat	288	
	Leu Ile Asp Ala Met Leu Gly Asp Pro His Cys Asp Ala Phe Gln Tyr		
	85 90 95		
	gag agt tgg gac ctc ttt ata gaa aga agc agc gct ttc agc aat tgc	336	
	Glu Ser Trp Asp Leu Phe Ile Glu Arg Ser Ser Ala Phe Ser Asn Cys		
	100 105 110		
	tac cca tat gac atc cct gac tat gca tgc ctc cga tcc att gta gca	384	
	Tyr Pro Tyr Asp Ile Pro Asp Tyr Ala Ser Leu Arg Ser Ile Val Ala		
	115 120 125		
	tcc tca gga aca ttg gaa ttc aca gca gag gga ttc aca tgg aca ggt	432	
	Ser Ser Gly Thr Leu Glu Phe Thr Ala Glu Gly Phe Thr Trp Thr Gly		
	130 135 140		
	gtc act caa aac gga aga agt gga gcc tgc aaa agg gga tca gcc gat	480	
	Val Thr Gln Asn Gly Arg Ser Gly Ala Cys Lys Arg Gly Ser Ala Asp		
	145 150 155 160		

	agt ttc ttt agc cga ctg aat tgg cta aca aaa tct gga agc tct tac	528
	Ser Phe Phe Ser Arg Leu Asn Trp Leu Thr Lys Ser Gly Ser Ser Tyr	
	165 170 175	
	ccc aca ttg aat gtg aca atg cct aac aat aaa aat ttc gac aag cta	576
	Pro Thr Leu Asn Val Thr Met Pro Asn Asn Lys Asn Phe Asp Lys Leu	
	180 185 190	
	tac atc tgg ggg att cat cac ccg agc tca aat caa gag cag aca aaa	624
	Tyr Ile Trp Gly Ile His His Pro Ser Ser Asn Gln Glu Gln Thr Lys	
	195 200 205	
	ttg tac atc caa gaa tca gga cga gta aca gtc tca aca aaa aga agt	672
	Leu Tyr Ile Gln Glu Ser Gly Arg Val Thr Val Ser Thr Lys Arg Ser	
	210 215 220	
	caa caa aca ata atc cct aac atc gga tct aga ccg ttg gtc aga ggt	720
	Gln Gln Thr Ile Ile Pro Asn Ile Gly Ser Arg Pro Leu Val Arg Gly	
	225 230 235 240	
[0101]	caa tca ggc agg ata agc ata tac tgg acc att gta aaa cct gga gat	768
	Gln Ser Gly Arg Ile Ser Ile Tyr Trp Thr Ile Val Lys Pro Gly Asp	
	245 250 255	
	atc cta atg ata aac agt aat ggc aac tta gtt gca ccg cgg gga tat	816
	Ile Leu Met Ile Asn Ser Asn Gly Asn Leu Val Ala Pro Arg Gly Tyr	
	260 265 270	
	ttt aaa ttg aaa aca ggg aaa agc tct gta atg aga tca gat gta ccc	864
	Phe Lys Leu Lys Thr Gly Lys Ser Ser Val Met Arg Ser Asp Val Pro	
	275 280 285	
	ata gac att tgt gtg tct gaa tgt att aca cca aat gga agc atc tcc	912
	Ile Asp Ile Cys Val Ser Glu Cys Ile Thr Pro Asn Gly Ser Ile Ser	
	290 295 300	
	aac gac aag cca ttc caa aat gtg aac aaa gtt aca tat gga aaa tgc	960
	Asn Asp Lys Pro Phe Gln Asn Val Asn Lys Val Thr Tyr Gly Lys Cys	
	305 310 315 320	
	ccc aag tat atc agg caa aac act tta aag ctg gcc act ggg atg agg	1008
	Pro Lys Tyr Ile Arg Gln Asn Thr Leu Lys Leu Ala Thr Gly Met Arg	
	325 330 335	

	aat gta cca gaa aag caa acc aga gga atc ttt gga gca ata geg gga	1056
	Asn Val Pro Glu Lys Gln Thr Arg Gly Ile Phe Gly Ala Ile Ala Gly	
	340 345 350	
	ttc atc gaa aac ggc tgg gaa gga atg gtt gat ggg tgg tat ggg ttc	1104
	Phe Ile Glu Asn Gly Trp Glu Gly Met Val Asp Gly Trp Tyr Gly Phe	
	355 360 365	
	cga tat caa aac tct gaa gga aca ggg caa get gca gat cta aag agc	1152
	Arg Tyr Gln Asn Ser Glu Gly Thr Gly Gln Ala Ala Asp Leu Lys Ser	
	370 375 380	
	act caa gca gcc atc gac cag att aat gga aag tta aac aga gtg att	1200
	Thr Gln Ala Ala Ile Asp Gln Ile Asn Gly Lys Leu Asn Arg Val Ile	
	385 390 395 400	
	gaa aga acc aat gag aaa ttc cat cua ata gag aag gaa ttc tca gaa	1248
	Glu Arg Thr Asn Glu Lys Phe His Gln Ile Glu Lys Glu Phe Ser Glu	
	405 410 415	
[0102]	gta gaa gga aga att cag gac ttg gag aaa tat gta gaa gac acc aaa	1296
	Val Glu Gly Arg Ile Gln Asp Leu Glu Lys Tyr Val Glu Asp Thr Lys	
	420 425 430	
	ata gac cta tgg tcc tac aat gca gaa ttg ctg gtg get cta gaa aat	1344
	Ile Asp Leu Trp Ser Tyr Asn Ala Glu Leu Leu Val Ala Leu Glu Asn	
	435 440 445	
	caa cat aca att gac tta aca gat gca gaa atg aat aaa tta ttt gag	1392
	Gln His Thr Ile Asp Leu Thr Asp Ala Glu Met Asn Lys Leu Phe Glu	
	450 455 460	
	aag act aga cgc cag tta aga gaa aac gca gaa gac atg gga ggt gga	1440
	Lys Thr Arg Arg Gln Leu Arg Glu Asn Ala Glu Asp Met Gly Gly Gly	
	465 470 475 480	
	tgt ttc aag att tac cac aaa tgt gat aat gca tgc att gga tca ata	1488
	Cys Phe Lys Ile Tyr His Lys Cys Asp Asn Ala Cys Ile Gly Ser Ile	
	485 490 495	
	aga act ggg aca tat gac cat tac ata tac aga gat gaa gca tta aac	1536
	Arg Thr Gly Thr Tyr Asp His Tyr Ile Tyr Arg Asp Glu Ala Leu Asn	
	500 505 510	

aac cga ttt cag atc aaa ggt gta gag ttg aaa tca ggc tac aaa gat 1584
 Asn Arg Phe Gln Ile Lys Gly Val Glu Leu Lys Ser Gly Tyr Lys Asp
 515 520 525

tgg ata ctg tgg att tca ttc gcc ata tca tgc ttc tta att tgc gtt 1632
 Trp Ile Leu Trp Ile Ser Phe Ala Ile Ser Cys Phe Leu Ile Cys Val
 530 535 540

gtt cta ttg ggt ttc att atg tgg gct tgc caa aaa ggc aac atc aga 1680
 Val Leu Leu Gly Phe Ile Met Trp Ala Cys Gln Lys Gly Asn Ile Arg
 545 550 555 560

tgc aac att tgc att tga 1698
 Cys Asn Ile Cys Ile
 565

<210> 32

<211> 565

<212> PRT

<213> 流感病毒

[0103]

<400> 32

Met Lys Thr Thr Ile Ile Leu Ile Leu Leu Thr His Trp Ala Tyr Ser
 1 5 10 15

Gln Asn Pro Ile Ser Asp Asn Asn Thr Ala Thr Leu Cys Leu Gly His
 20 25 30

His Ala Val Ala Asn Gly Thr Leu Val Lys Thr Ile Ser Asp Asp Gln
 35 40 45

Ile Glu Val Thr Asn Ala Thr Glu Leu Val Gln Ser Ile Ser Met Gly
 50 55 60

Lys Ile Cys Asn Lys Ser Tyr Arg Ile Leu Asp Gly Arg Asn Cys Thr
 65 70 75 80

Leu Ile Asp Ala Met Leu Gly Asp Pro His Cys Asp Ala Phe Gln Tyr
85 90 95

Glu Ser Trp Asp Leu Phe Ile Glu Arg Ser Ser Ala Phe Ser Asn Cys
100 105 110

Tyr Pro Tyr Asp Ile Pro Asp Tyr Ala Ser Leu Arg Ser Ile Val Ala
115 120 125

Ser Ser Gly Thr Leu Glu Phe Thr Ala Glu Gly Phe Thr Trp Thr Gly
130 135 140

Val Thr Gln Asn Gly Arg Ser Gly Ala Cys Lys Arg Gly Ser Ala Asp
145 150 155 160

[0104]

Ser Phe Phe Ser Arg Leu Asn Trp Leu Thr Lys Ser Gly Ser Ser Tyr
165 170 175

Pro Thr Leu Asn Val Thr Met Pro Asn Asn Lys Asn Phe Asp Lys Leu
180 185 190

Tyr Ile Trp Gly Ile His His Pro Ser Ser Asn Gln Glu Gln Thr Lys
195 200 205

Leu Tyr Ile Gln Glu Ser Gly Arg Val Thr Val Ser Thr Lys Arg Ser
210 215 220

Gln Gln Thr Ile Ile Pro Asn Ile Gly Ser Arg Pro Leu Val Arg Gly
225 230 235 240

Gln Ser Gly Arg Ile Ser Ile Tyr Trp Thr Ile Val Lys Pro Gly Asp
245 250 255

Ile Leu Met Ile Asn Ser Asn Gly Asn Leu Val Ala Pro Arg Gly Tyr
260 265 270

Phe Lys Leu Lys Thr Gly Lys Ser Ser Val Met Arg Ser Asp Val Pro
275 280 285

Ile Asp Ile Cys Val Ser Glu Cys Ile Thr Pro Asn Gly Ser Ile Ser
290 295 300

Asn Asp Lys Pro Phe Gln Asn Val Asn Lys Val Thr Tyr Gly Lys Cys
305 310 315 320

Pro Lys Tyr Ile Arg Gln Asn Thr Leu Lys Leu Ala Thr Gly Met Arg
325 330 335

[0105]

Asn Val Pro Glu Lys Gln Thr Arg Gly Ile Phe Gly Ala Ile Ala Gly
340 345 350

Phe Ile Glu Asn Gly Trp Glu Gly Met Val Asp Gly Trp Tyr Gly Phe
355 360 365

Arg Tyr Gln Asn Ser Glu Gly Thr Gly Gln Ala Ala Asp Leu Lys Ser
370 375 380

Thr Gln Ala Ala Ile Asp Gln Ile Asn Gly Lys Leu Asn Arg Val Ile
385 390 395 400

Glu Arg Thr Asn Glu Lys Phe His Gln Ile Glu Lys Glu Phe Ser Glu
405 410 415

Val Glu Gly Arg Ile Gln Asp Leu Glu Lys Tyr Val Glu Asp Thr Lys
420 425 430

Ile Asp Leu Trp Ser Tyr Asn Ala Glu Leu Leu Val Ala Leu Glu Asn
435 440 445

Gln His Thr Ile Asp Leu Thr Asp Ala Glu Met Asn Lys Leu Phe Glu
450 455 460

Lys Thr Arg Arg Gln Leu Arg Glu Asn Ala Glu Asp Met Gly Gly Gly
465 470 475 480

Cys Phe Lys Ile Tyr His Lys Cys Asp Asn Ala Cys Ile Gly Ser Ile
485 490 495

Arg Thr Gly Thr Tyr Asp His Tyr Ile Tyr Arg Asp Glu Ala Leu Asn
500 505 510

[0106]

Asn Arg Phe Gln Ile Lys Gly Val Glu Leu Lys Ser Gly Tyr Lys Asp
515 520 525

Trp Ile Leu Trp Ile Ser Phe Ala Ile Ser Cys Phe Leu Ile Cys Val
530 535 540

Val Leu Leu Gly Phe Ile Met Trp Ala Cys Gln Lys Gly Asn Ile Arg
545 550 555 560

Cys Asn Ile Cys Ile
565

<210> 33

<211> 549

<212> PRT

<213> 流感病毒

<400> 33

Gln Asn Pro Ile Ser Gly Asn Asn Thr Ala Thr Leu Cys Leu Gly His
1 5 10 15

His Ala Val Ala Asn Gly Thr Leu Val Lys Thr Met Ser Asp Asp Gln
20 25 30

Ile Glu Val Thr Asn Ala Thr Glu Leu Val Gln Ser Ile Ser Met Gly
35 40 45

Lys Ile Cys Asn Lys Ser Tyr Arg Ile Leu Asp Gly Arg Asn Cys Thr
50 55 60

Leu Ile Asp Ala Met Leu Gly Asp Pro His Cys Asp Ala Phe Gln Tyr
65 70 75 80

[0107]

Glu Ser Trp Asp Leu Phe Ile Glu Arg Ser Asn Ala Phe Ser Asn Cys
85 90 95

Tyr Pro Tyr Asp Ile Pro Asp Tyr Ala Ser Leu Arg Ser Ile Val Ala
100 105 110

Ser Ser Gly Thr Leu Glu Phe Thr Ala Glu Gly Phe Thr Trp Thr Gly
115 120 125

Val Thr Gln Asn Gly Arg Ser Gly Ala Cys Lys Arg Gly Ser Ala Asp
130 135 140

Ser Phe Phe Ser Arg Leu Asn Trp Leu Thr Lys Ser Gly Ser Ser Tyr
145 150 155 160

Pro Thr Leu Asn Val Thr Met Pro Asn Asn Lys Asn Phe Asp Lys Leu
165 170 175

	Arg Tyr Gln Asn Ser Glu Gly Thr Gly Gln Ala Ala Asp Leu Lys Ser	
	355	360 365
	Thr Gln Ala Ala Ile Asp Gln Ile Asn Gly Lys Leu Asn Arg Val Ile	
	370	375 380
	Glu Arg Thr Asn Glu Lys Phe His Gln Ile Glu Lys Glu Phe Ser Glu	
	385	390 395 400
	Val Glu Gly Arg Ile Gln Asp Leu Glu Lys Tyr Val Glu Asp Thr Lys	
		405 410 415
	Ile Asp Leu Trp Ser Tyr Asn Ala Glu Leu Leu Val Ala Leu Glu Asn	
		420 425 430
[0109]	Gln His Thr Ile Asp Leu Thr Asp Ala Glu Met Asn Lys Leu Phe Glu	
	435	440 445
	Lys Thr Arg Arg Gln Leu Arg Glu Asn Ala Glu Asp Met Gly Gly Gly	
	450	455 460
	Cys Phe Lys Ile Tyr His Lys Cys Asp Asn Ala Cys Ile Gly Ser Ile	
	465	470 475 480
	Arg Thr Gly Thr Tyr Asp His Tyr Ile Tyr Arg Asp Glu Ala Leu Asn	
		485 490 495
	Asn Arg Phe Gln Ile Lys Gly Val Glu Leu Lys Ser Gly Tyr Lys Asp	
		500 505 510
	Trp Ile Leu Trp Ile Ser Phe Ala Ile Ser Cys Phe Leu Ile Cys Val	
	515	520 525

Val Leu Leu Gly Phe Ile Met Trp Ala Cys Gln Arg Gly Asn Ile Arg
530 535 540

Cys Asn Ile Cys Ile
545

<210> 34

<211> 549

<212> PRT

<213> 流感病毒

<400> 34

Gln Asn Pro Ile Ser Asp Asn Asn Thr Ala Thr Leu Cys Leu Gly His
1 5 10 15

His Ala Val Ala Asn Gly Thr Leu Val Lys Thr Ile Ser Asp Asp Gln
20 25 30

[0110]

Ile Glu Val Thr Asn Ala Thr Glu Leu Val Gln Ser Ile Ser Met Gly
35 40 45

Lys Ile Cys Asn Lys Ser Tyr Arg Ile Leu Asp Gly Arg Asn Cys Thr
50 55 60

Leu Ile Asp Ala Met Leu Gly Asp Pro His Cys Asp Ala Phe Gln Tyr
65 70 75 80

Glu Ser Trp Asp Leu Phe Ile Glu Arg Ser Ser Ala Phe Ser Asn Cys
85 90 95

Tyr Pro Tyr Asp Ile Pro Asp Tyr Ala Ser Leu Arg Ser Ile Val Ala
100 105 110

Ser Ser Gly Thr Leu Glu Phe Thr Ala Glu Gly Phe Thr Trp Thr Gly

115	120	125
Val Thr Gln Asn Gly Arg Ser Gly Ala Cys Lys Arg Gly Ser Ala Asp		
130	135	140
Ser Phe Phe Ser Arg Leu Asn Trp Leu Thr Lys Ser Gly Ser Ser Tyr		
145	150	155 160
Pro Thr Leu Asn Val Thr Met Pro Asn Asn Lys Asn Phe Asp Lys Leu		
165	170	175
Tyr Ile Trp Gly Ile His His Pro Ser Ser Asn Gln Glu Gln Thr Lys		
180	185	190
Leu Tyr Ile Gln Glu Ser Gly Arg Val Thr Val Ser Thr Lys Arg Ser		
195	200	205
[0111]		
Gln Gln Thr Ile Ile Pro Asn Ile Gly Ser Arg Pro Leu Val Arg Gly		
210	215	220
Gln Ser Gly Arg Ile Ser Ile Tyr Trp Thr Ile Val Lys Pro Gly Asp		
225	230	235 240
Ile Leu Met Ile Asn Ser Asn Gly Asn Leu Val Ala Pro Arg Gly Tyr		
245	250	255
Phe Lys Leu Lys Thr Gly Lys Ser Ser Val Met Arg Ser Asp Val Pro		
260	265	270
Ile Asp Ile Cys Val Ser Glu Cys Ile Thr Pro Asn Gly Ser Ile Ser		
275	280	285
Asn Asp Lys Pro Phe Gln Asn Val Asn Lys Val Thr Tyr Gly Lys Cys		

290	295	300
Pro Lys Tyr Ile Arg Gln Asn Thr Leu Lys Leu Ala Thr Gly Met Arg		
305	310	315 320
Asn Val Pro Glu Lys Gln Thr Arg Gly Ile Phe Gly Ala Ile Ala Gly		
325	330	335
Phe Ile Glu Asn Gly Trp Glu Gly Met Val Asp Gly Trp Tyr Gly Phe		
340	345	350
Arg Tyr Gln Asn Ser Glu Gly Thr Gly Gln Ala Ala Asp Leu Lys Ser		
355	360	365
Thr Gln Ala Ala Ile Asp Gln Ile Asn Gly Lys Leu Asn Arg Val Ile		
370	375	380
[0112]		
Glu Arg Thr Asn Glu Lys Phe His Gln Ile Glu Lys Glu Phe Ser Glu		
385	390	395 400
Val Glu Gly Arg Ile Gln Asp Leu Glu Lys Tyr Val Glu Asp Thr Lys		
405	410	415
Ile Asp Leu Trp Ser Tyr Asn Ala Glu Leu Leu Val Ala Leu Glu Asn		
420	425	430
Gln His Thr Ile Asp Leu Thr Asp Ala Glu Met Asn Lys Leu Phe Glu		
435	440	445
Lys Thr Arg Arg Gln Leu Arg Glu Asn Ala Glu Asp Met Gly Gly Gly		
450	455	460
Cys Phe Lys Ile Tyr His Lys Cys Asp Asn Ala Cys Ile Gly Ser Ile		

465	470	475	480
Arg Thr Gly Thr Tyr Asp His Tyr Ile Tyr Arg Asp Glu Ala Leu Asn			
485	490	495	
Asn Arg Phe Gln Ile Lys Gly Val Glu Leu Lys Ser Gly Tyr Lys Asp			
500	505	510	
Trp Ile Leu Trp Ile Ser Phe Ala Ile Ser Cys Phe Leu Ile Cys Val			
515	520	525	
Val Leu Leu Gly Phe Ile Met Trp Ala Cys Gln Lys Gly Asn Ile Arg			
530	535	540	
Cys Asn Ile Cys Ile			
545			

[0113]

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9

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<400> 36
ccgttggtc

9

<210> 37
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<212> DNA

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	<210> 38	
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	<400> 38	
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	<400> 39	
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	<400> 41	
	aagcaaacca gagga	15
	<210> 42	
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	<400> 42	
	ataagaactg ggaca	15
	<210> 43	
	<211> 9	
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	<400> 43	
	acaatgagt	9
	<210> 44	
	<211> 15	
	<212> DNA	
	<213> 流感病毒	
[0115]	<400> 44	
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	<210> 45	
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	<400> 45	
	gatgtaccc	9
	<210> 46	
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	<400> 46	
	tcagatgtac ccata	15
	<210> 47	

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 Met Glu Arg Ile Lys Glu Leu Arg Asp Leu Met Leu Gln Ser Arg Thr
 1 5 10 15

cgc gag ata cta aca aaa act act gtg gac cac atg gcc ata atc aag 96
 Arg Glu Ile Leu Thr Lys Thr Thr Val Asp His Met Ala Ile Ile Lys
 20 25 30

aaa tac aca tca gga aga caa gag aag aac cct gca ctt agg atg aaa 144
 Lys Tyr Thr Ser Gly Arg Gln Glu Lys Asn Pro Ala Leu Arg Met Lys
 35 40 45

[0116]

tgg atg atg gca atg aaa tac cca att aca gca gat aag agg ata atg 192
 Trp Met Met Ala Met Lys Tyr Pro Ile Thr Ala Asp Lys Arg Ile Met
 50 55 60

gag atg att cct gag aga aat gaa cag gga caa acc ctt tgg agc aaa 240
 Glu Met Ile Pro Glu Arg Asn Glu Gln Gly Gln Thr Leu Trp Ser Lys
 65 70 75 80

aeg aac gat gct ggc tca gac cgc gta atg gta tca cct ctg gca gtg 288
 Thr Asn Asp Ala Gly Ser Asp Arg Val Met Val Ser Pro Leu Ala Val
 85 90 95

aca tgg tgg aat agg aat gga cca aca aeg aac aca att cat tat cca 336
 Thr Trp Trp Asn Arg Asn Gly Pro Thr Thr Asn Thr Ile His Tyr Pro
 100 105 110

aaa gtc tac aaa act tat ttt gaa aag gtt gaa aga ttg aaa cac gga 384
 Lys Val Tyr Lys Thr Tyr Phe Glu Lys Val Glu Arg Leu Lys His Gly
 115 120 125

acc ttt ggc ccc gtt cat ttt agg aat caa gtc aag ata aga cga aga 432
 Thr Phe Gly Pro Val His Phe Arg Asn Gln Val Lys Ile Arg Arg Arg

130	135	140	
gtt gat gta aac cct ggt cac gcg gac ctc agt gct aaa gaa gca caa			480
Val Asp Val Asn Pro Gly His Ala Asp Leu Ser Ala Lys Glu Ala Glu			
145	150	155	160
gat gtg atc atg gaa gtt gtt ttc cca aat gaa gtg gga gcc aga att			528
Asp Val Ile Met Glu Val Val Phe Pro Asn Glu Val Gly Ala Arg Ile			
165	170	175	
cta aca tca gaa tca caa cta aca ata acc aaa gag aaa aag gaa gaa			576
Leu Thr Ser Glu Ser Gln Leu Thr Ile Thr Lys Glu Lys Lys Glu Glu			
180	185	190	
ctt eag gac tgc aaa att gct ccc ttg atg gta gca tac atg cta gaa			624
Leu Gln Asp Cys Lys Ile Ala Pro Leu Met Val Ala Tyr Met Leu Glu			
195	200	205	
aga gag ttg gtc cga aaa aca agg ttc ctc cca gta gta ggc gga aca			672
Arg Glu Leu Val Arg Lys Thr Arg Phe Leu Pro Val Val Gly Gly Thr			
210	215	220	
[0117]			
agc agt gta tac att gaa gtg ttg cat ctg act cag gga aca tgc tgg			720
Ser Ser Val Tyr Ile Glu Val Leu His Leu Thr Gln Gly Thr Cys Trp			
225	230	235	240
gag caa atg tac acc cca gga gga aaa gtt aga aac gat gat att gat			768
Glu Gln Met Tyr Thr Pro Gly Gly Lys Val Arg Asn Asp Asp Ile Asp			
245	250	255	
caa agt tta att att gca gcc cgg aac ata gtg aga aga gca aca gta			816
Gln Ser Leu Ile Ile Ala Ala Arg Asn Ile Val Arg Arg Ala Thr Val			
260	265	270	
tca gca gat cca cta gca tcc cta ctg gaa atg tgc cac agt aca cag			864
Ser Ala Asp Pro Leu Ala Ser Leu Leu Glu Met Cys His Ser Thr Gln			
275	280	285	
att ggt gga aca agg atg gta gac atc ctt aag cag aac cca aca gag			912
Ile Gly Gly Thr Arg Met Val Asp Ile Leu Lys Gln Asn Pro Thr Glu			
290	295	300	
gaa caa gct gtg gat ata tgc aaa gca gca atg gga ttg aga att agc			960
Glu Gln Ala Val Asp Ile Cys Lys Ala Ala Met Gly Leu Arg Ile Ser			

305	310	315	320	
tca tca ttc agc ttt ggt gga ttc acc ttc aaa agg aca agt gga tca				1008
Ser Ser Phe Ser Phe Gly Gly Phe Thr Phe Lys Arg Thr Ser Gly Ser				
325	330	335		
tca gtc aag aga gaa gaa gaa atg ctt acg ggc aac ctt caa aca ttg				1056
Ser Val Lys Arg Glu Glu Glu Met Leu Thr Gly Asn Leu Gln Thr Leu				
340	345	350		
aaa ata aga gtg cat gag ggc tat gaa gaa ttc aca atg gtc gga aga				1104
Lys Ile Arg Val His Glu Gly Tyr Glu Glu Phe Thr Met Val Gly Arg				
355	360	365		
aga gca aca gcc att atc aga aag gca acc aga aga ttg att caa ttg				1152
Arg Ala Thr Ala Ile Ile Arg Lys Ala Thr Arg Arg Leu Ile Gln Leu				
370	375	380		
ata gta agt ggg aga gat gaa caa tca att gct gaa gca ata att gta				1200
Ile Val Ser Gly Arg Asp Glu Gln Ser Ile Ala Glu Ala Ile Ile Val				
385	390	395	400	
[0118]				
gcc atg gtg ttt tcg caa gaa gat tgc atg ata aaa gca gtt cga ggc				1248
Ala Met Val Phe Ser Gln Glu Asp Cys Met Ile Lys Ala Val Arg Gly				
405	410	415		
gat ttg aac ttt gtt aat aga gca aat cag cgt ttg aac ccc atg cat				1296
Asp Leu Asn Phe Val Asn Arg Ala Asn Gln Arg Leu Asn Pro Met His				
420	425	430		
caa ctc ttg agg cat ttc caa aaa gat gca aaa gtg ctt ttc caa aat				1344
Gln Leu Leu Arg His Phe Gln Lys Asp Ala Lys Val Leu Phe Gln Asn				
435	440	445		
tgg gga att gaa ccc atc gac aat gta atg ggg atg att gga ata ttg				1392
Trp Gly Ile Glu Pro Ile Asp Asn Val Met Gly Met Ile Gly Ile Leu				
450	455	460		
cct gac atg acc cca agc acc gag atg tca ttg aga gga gtg aga gtc				1440
Pro Asp Met Thr Pro Ser Thr Glu Met Ser Leu Arg Gly Val Arg Val				
465	470	475	480	
agc aaa atg gga gtg gat gag tac tcc agc act gag aga gtg gtg gtg				1488
Ser Lys Met Gly Val Asp Glu Tyr Ser Ser Thr Glu Arg Val Val Val				

	485	490	495	
	agc att gac cgt ttt tta aga gtt cgg gat caa agg gga aac ata cta			1536
	Ser Ile Asp Arg Phe Leu Arg Val Arg Asp Gln Arg Gly Asn Ile Leu			
	500	505	510	
	ctg tcc cct gaa gaa gtc agt gaa aca caa gga acg gaa aag ctg aca			1584
	Leu Ser Pro Glu Glu Val Ser Glu Thr Gln Gly Thr Glu Lys Leu Thr			
	515	520	525	
	ata att tat tcg tca tca atg atg tgg gag att aat ggt ccc gaa tca			1632
	Ile Ile Tyr Ser Ser Ser Met Met Trp Glu Ile Asn Gly Pro Glu Ser			
	530	535	540	
	gtg ttg gtc aat act tat caa tgg atc atc aga aac tgg gaa att gta			1680
	Val Leu Val Asn Thr Tyr Gln Trp Ile Ile Arg Asn Trp Glu Ile Val			
	545	550	555	560
	aaa att cag tgg tca cag gac ccc aca atg tta tac aat aag ata gaa			1728
	Lys Ile Gln Trp Ser Gln Asp Pro Thr Met Leu Tyr Asn Lys Ile Glu			
	565	570	575	
[0119]	ttt gaa cca ttc caa tcc ctg gtc cct agg gcc acc aga agc caa tac			1776
	Phe Glu Pro Phe Gln Ser Leu Val Pro Arg Ala Thr Arg Ser Gln Tyr			
	580	585	590	
	agc ggt ttc gta aga acc ctg ttt cag caa atg cga gat gta ctt gga			1824
	Ser Gly Phe Val Arg Thr Leu Phe Gln Gln Met Arg Asp Val Leu Gly			
	595	600	605	
	aca ttt gat act gct caa ata ata aaa etc etc cct ttt gcc get get			1872
	Thr Phe Asp Thr Ala Gln Ile Ile Lys Leu Leu Pro Phe Ala Ala Ala			
	610	615	620	
	cct ccg gaa cag agt agg atg cag ttc tct tct ttg act gtt aat gta			1920
	Pro Pro Glu Gln Ser Arg Met Gln Phe Ser Ser Leu Thr Val Asn Val			
	625	630	635	640
	aga ggt tcg gga atg agg ata ctt gta aga ggc aat tcc cca gtg ttc			1968
	Arg Gly Ser Gly Met Arg Ile Leu Val Arg Gly Asn Ser Pro Val Phe			
	645	650	655	
	aac tac aat aaa gtc act aaa agg etc aca gtc etc gga aag gat gca			2016
	Asn Tyr Asn Lys Val Thr Lys Arg Leu Thr Val Leu Gly Lys Asp Ala			

	660	665	670	
	ggt gcg ctt act gag gac cca gat gaa ggt acg gct gga gta gag tct			2064
	Gly Ala Leu Thr Glu Asp Pro Asp Glu Gly Thr Ala Gly Val Glu Ser			
	675	680	685	
	gct gtt cta aga ggg ttt ctc att tta ggt aaa gaa aac aag aga tat			2112
	Ala Val Leu Arg Gly Phe Leu Ile Leu Gly Lys Glu Asn Lys Arg Tyr			
	690	695	700	
	ggc cca gca cta agc atc aat gaa ctt agc aaa ctt gca aaa ggg gag			2160
	Gly Pro Ala Leu Ser Ile Asn Glu Leu Ser Lys Leu Ala Lys Gly Glu			
	705	710	715	720
	aaa gcc aat gta cta att ggg caa ggg gac gta gtg ttg gta atg aaa			2208
	Lys Ala Asn Val Leu Ile Gly Gln Gly Asp Val Val Leu Val Met Lys			
	725	730	735	
	cgg aaa cgt gac tct agc ata ctt act gac agc cag aca geg acc aaa			2256
	Arg Lys Arg Asp Ser Ser Ile Leu Thr Asp Ser Gln Thr Ala Thr Lys			
	740	745	750	
[0120]	agg att cgg atg gcc atc aat tag			2280
	Arg Ile Arg Met Ala Ile Asn			
	755			
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<400>	48			
	Met Glu Arg Ile Lys Glu Leu Arg Asp Leu Met Leu Gln Ser Arg Thr			
	1	5	10	15
	Arg Glu Ile Leu Thr Lys Thr Thr Val Asp His Met Ala Ile Ile Lys			
	20	25	30	
	Lys Tyr Thr Ser Gly Arg Gln Glu Lys Asn Pro Ala Leu Arg Met Lys			
	35	40	45	

	Trp	Met	Met	Ala	Met	Lys	Tyr	Pro	Ile	Thr	Ala	Asp	Lys	Arg	Ile	Met	
	50					55					60						
	Glu	Met	Ile	Pro	Glu	Arg	Asn	Glu	Gln	Gly	Gln	Thr	Leu	Trp	Ser	Lys	
	65				70					75					80		
	Thr	Asn	Asp	Ala	Gly	Ser	Asp	Arg	Val	Met	Val	Ser	Pro	Leu	Ala	Val	
				85					90					95			
	Thr	Trp	Trp	Asn	Arg	Asn	Gly	Pro	Thr	Thr	Asn	Thr	Ile	His	Tyr	Pro	
				100				105						110			
	Lys	Val	Tyr	Lys	Thr	Tyr	Phe	Glu	Lys	Val	Glu	Arg	Leu	Lys	His	Gly	
				115				120					125				
[0121]	Thr	Phe	Gly	Pro	Val	His	Phe	Arg	Asn	Gln	Val	Lys	Ile	Arg	Arg	Arg	
	130						135					140					
	Val	Asp	Val	Asn	Pro	Gly	His	Ala	Asp	Leu	Ser	Ala	Lys	Glu	Ala	Gln	
	145					150					155				160		
	Asp	Val	Ile	Met	Glu	Val	Val	Phe	Pro	Asn	Glu	Val	Gly	Ala	Arg	Ile	
				165						170					175		
	Leu	Thr	Ser	Glu	Ser	Gln	Leu	Thr	Ile	Thr	Lys	Glu	Lys	Lys	Glu	Glu	
				180					185					190			
	Leu	Gln	Asp	Cys	Lys	Ile	Ala	Pro	Leu	Met	Val	Ala	Tyr	Met	Leu	Glu	
				195				200					205				
	Arg	Glu	Leu	Val	Arg	Lys	Thr	Arg	Phe	Leu	Pro	Val	Val	Gly	Gly	Thr	
	210					215						220					

	Ser	Ser	Val	Tyr	Ile	Glu	Val	Leu	His	Leu	Thr	Gln	Gly	Thr	Cys	Trp
	225					230					235					240
	Glu	Gln	Met	Tyr	Thr	Pro	Gly	Gly	Lys	Val	Arg	Asn	Asp	Asp	Ile	Asp
					245					250					255	
	Gln	Ser	Leu	Ile	Ile	Ala	Ala	Arg	Asn	Ile	Val	Arg	Arg	Ala	Thr	Val
				260					265						270	
	Ser	Ala	Asp	Pro	Leu	Ala	Ser	Leu	Leu	Glu	Met	Cys	His	Ser	Thr	Gln
			275					280						285		
	Ile	Gly	Gly	Thr	Arg	Met	Val	Asp	Ile	Leu	Lys	Gln	Asn	Pro	Thr	Glu
	290						295					300				
[0122]	Glu	Gln	Ala	Val	Asp	Ile	Cys	Lys	Ala	Ala	Met	Gly	Leu	Arg	Ile	Ser
	305					310					315					320
	Ser	Ser	Phe	Ser	Phe	Gly	Gly	Phe	Thr	Phe	Lys	Arg	Thr	Ser	Gly	Ser
					325					330					335	
	Ser	Val	Lys	Arg	Glu	Glu	Glu	Met	Leu	Thr	Gly	Asn	Leu	Gln	Thr	Leu
				340					345					350		
	Lys	Ile	Arg	Val	His	Glu	Gly	Tyr	Glu	Glu	Phe	Thr	Met	Val	Gly	Arg
			355					360					365			
	Arg	Ala	Thr	Ala	Ile	Ile	Arg	Lys	Ala	Thr	Arg	Arg	Leu	Ile	Gln	Leu
	370						375					380				
	Ile	Val	Ser	Gly	Arg	Asp	Glu	Gln	Ser	Ile	Ala	Glu	Ala	Ile	Ile	Val
	385					390					395					400

	Ala Met Val Phe Ser Gln Glu Asp Cys Met Ile Lys Ala Val Arg Gly	
	405	410 415
	Asp Leu Asn Phe Val Asn Arg Ala Asn Gln Arg Leu Asn Pro Met His	
	420	425 430
	Gln Leu Leu Arg His Phe Gln Lys Asp Ala Lys Val Leu Phe Gln Asn	
	435	440 445
	Trp Gly Ile Glu Pro Ile Asp Asn Val Met Gly Met Ile Gly Ile Leu	
	450	455 460
	Pro Asp Met Thr Pro Ser Thr Glu Met Ser Leu Arg Gly Val Arg Val	
	465	470 475 480
[0123]	Ser Lys Met Gly Val Asp Glu Tyr Ser Ser Thr Glu Arg Val Val Val	
	485	490 495
	Ser Ile Asp Arg Phe Leu Arg Val Arg Asp Gln Arg Gly Asn Ile Leu	
	500	505 510
	Leu Ser Pro Glu Glu Val Ser Glu Thr Gln Gly Thr Glu Lys Leu Thr	
	515	520 525
	Ile Ile Tyr Ser Ser Ser Met Met Trp Glu Ile Asn Gly Pro Glu Ser	
	530	535 540
	Val Leu Val Asn Thr Tyr Gln Trp Ile Ile Arg Asn Trp Glu Ile Val	
	545	550 555 560
	Lys Ile Gln Trp Ser Gln Asp Pro Thr Met Leu Tyr Asn Lys Ile Glu	
	565	570 575

Arg Ile Arg Met Ala Ile Asn
755

<210> 49
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<213> 流感病毒

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1 5 10 15

[0125] get ata agc aca aca ttc cct tat act gga gat cct ccc tac agt cat 96
Ala Ile Ser Thr Thr Phe Pro Tyr Thr Gly Asp Pro Pro Tyr Ser His
20 25 30

gga aca ggg aca gga tac acc atg gat act gtc aac aga aca cae caa 144
Gly Thr Gly Thr Gly Tyr Thr Met Asp Thr Val Asn Arg Thr His Gln
35 40 45

tat tca gaa aaa ggg aaa tgg aca aca aac act gag att gga gca cca 192
Tyr Ser Glu Lys Gly Lys Trp Thr Thr Asn Thr Glu Ile Gly Ala Pro
50 55 60

caa ctt aat cca atc gat gga cca ctt cct gaa gac aat gaa cca agt 240
Gln Leu Asn Pro Ile Asp Gly Pro Leu Pro Glu Asp Asn Glu Pro Ser
65 70 75 80

ggg tac gcc caa aca gat tgt gta ttg gaa gca atg gct ttc ctt gaa 288
Gly Tyr Ala Gln Thr Asp Cys Val Leu Glu Ala Met Ala Phe Leu Glu
85 90 95

gaa tcc cat ccc gga atc ttt gaa aat tcg tgt ctt gaa acg atg gag 336
Glu Ser His Pro Gly Ile Phe Glu Asn Ser Cys Leu Glu Thr Met Glu
100 105 110

	gtg att cag cag aca aga gtg gac aaa cta aca caa ggc cga caa act	384
	Val Ile Gln Gln Thr Arg Val Asp Lys Leu Thr Gln Gly Arg Gln Thr	
	115 120 125	
	tat gat tgg acc ttg aat agg aat caa cct gcc gca aca gca ctt get	432
	Tyr Asp Trp Thr Leu Asn Arg Asn Gln Pro Ala Ala Thr Ala Leu Ala	
	130 135 140	
	aat acg att gaa gta ttc aga tca aat ggt ctg acc tcc aat gaa tgc	480
	Asn Thr Ile Glu Val Phe Arg Ser Asn Gly Leu Thr Ser Asn Glu Ser	
	145 150 155 160	
	ggg aga ttg atg gac ttc ctc aaa gat gtc atg gag tcc atg aac aag	528
	Gly Arg Leu Met Asp Phe Leu Lys Asp Val Met Glu Ser Met Asn Lys	
	165 170 175	
	gag gaa atg gaa ata aca aca cac ttc caa cgg aag aga aga gta aga	576
	Glu Glu Met Glu Ile Thr Thr His Phe Gln Arg Lys Arg Arg Val Arg	
	180 185 190	
[0126]	gac aac atg aca aag aga atg ata aca cag aga acc ata gga aag aaa	624
	Asp Asn Met Thr Lys Arg Met Ile Thr Gln Arg Thr Ile Gly Lys Lys	
	195 200 205	
	aaa caa cga tta agc aga aag agc tat cta atc aga aca tta acc cta	672
	Lys Gln Arg Leu Ser Arg Lys Ser Tyr Leu Ile Arg Thr Leu Thr Leu	
	210 215 220	
	aac aca atg acc aag gac gct gag aga ggg aaa ttg aaa cga cga gca	720
	Asn Thr Met Thr Lys Asp Ala Glu Arg Gly Lys Leu Lys Arg Arg Ala	
	225 230 235 240	
	atc get acc cca ggg atg cag ata aga gga ttt gta tat ttt gtt gaa	768
	Ile Ala Thr Pro Gly Met Gln Ile Arg Gly Phe Val Tyr Phe Val Glu	
	245 250 255	
	aca cta get cga aga ata tgt gaa aag ctt gaa caa tca gga ttg cca	816
	Thr Leu Ala Arg Arg Ile Cys Glu Lys Leu Glu Gln Ser Gly Leu Pro	
	260 265 270	
	gtt gcc ggt aat gag aaa aag gcc aaa ctg get aat gtc gtc aga aaa	864
	Val Gly Gly Asn Glu Lys Lys Ala Lys Leu Ala Asn Val Val Arg Lys	
	275 280 285	

	atg atg act aat tcc caa gac acf gaa ctc tcc ttc acc atc aet ggg	912
	Met Met Thr Asn Ser Gln Asp Thr Glu Leu Ser Phe Thr Ile Thr Gly	
	290 295 300	
	gac aat acc aaa tgg aat gaa aat cag aac cca cgc ata ttc ctg gca	960
	Asp Asn Thr Lys Trp Asn Glu Asn Gln Asn Pro Arg Ile Phe Leu Ala	
	305 310 315 320	
	atg atc aca tac ata act aga gat cag cca gaa tgg ttc aga aat gtt	1008
	Met Ile Thr Tyr Ile Thr Arg Asp Gln Pro Glu Trp Phe Arg Asn Val	
	325 330 335	
	cta agc att gea ccc att atg ttc tca aat aaa atg gea aga ctg ggg	1056
	Leu Ser Ile Ala Pro Ile Met Phe Ser Asn Lys Met Ala Arg Leu Gly	
	340 345 350	
	aaa gga tat atg ttt gaa agc aaa agt atg aaa ttg aga acf caa ata	1104
	Lys Gly Tyr Met Phe Glu Ser Lys Ser Met Lys Leu Arg Thr Gln Ile	
	355 360 365	
[0127]	cca gea gaa atg cta gea agc att gac cta aaa tat ttc aat gat tca	1152
	Pro Ala Glu Met Leu Ala Ser Ile Asp Leu Lys Tyr Phe Asn Asp Ser	
	370 375 380	
	aca aaa aag aaa att gaa aag ata cga cca ctc ctg gtt gac ggg act	1200
	Thr Lys Lys Lys Ile Glu Lys Ile Arg Pro Leu Leu Val Asp Gly Thr	
	385 390 395 400	
	get tca ctg agt cct ggc atg atg atg gga atg ttc aac atg ttg agc	1248
	Ala Ser Leu Ser Pro Gly Met Met Met Gly Met Phe Asn Met Leu Ser	
	405 410 415	
	act gtg ctg ggt gta tcc ata tta aac ctg ggc cag agg aaa tat aca	1296
	Thr Val Leu Gly Val Ser Ile Leu Asn Leu Gly Gln Arg Lys Tyr Thr	
	420 425 430	
	aag acc aca tac tgg tgg gat ggt ctg caa tca tcc gat gac tit get	1344
	Lys Thr Thr Tyr Trp Trp Asp Gly Leu Gln Ser Ser Asp Asp Phe Ala	
	435 440 445	
	ttg ata gtg aat ggc cct aat cat gaa gga ata caa get gga gta gac	1392
	Leu Ile Val Asn Ala Pro Asn His Glu Gly Ile Gln Ala Gly Val Asp	
	450 455 460	

	aga ttc tat aga act tgc aaa ctg gtc ggg atc aac atg agc aaa aag	1440
	Arg Phe Tyr Arg Thr Cys Lys Leu Val Gly Ile Asn Met Ser Lys Lys	
	465 470 475 480	
	aag tcc tac ata aat aga act gga aca ttc gaa ttc aca agc ttt ttc	1488
	Lys Ser Tyr Ile Asn Arg Thr Gly Thr Phe Glu Phe Thr Ser Phe Phe	
	485 490 495	
	tac egg tat ggt ttt gta gcc aat ttc agc atg gaa cta ccc agt ttt	1536
	Tyr Arg Tyr Gly Phe Val Ala Asn Phe Ser Met Glu Leu Pro Ser Phe	
	500 505 510	
	ggg gtt tcc gga ata aat gaa tct gca gac atg agc att gga gtg aca	1584
	Gly Val Ser Gly Ile Asn Glu Ser Ala Asp Met Ser Ile Gly Val Thr	
	515 520 525	
	gtc atc aaa aac aac atg ata aat aat gat ctc ggt cct gcc acg gca	1632
	Val Ile Lys Asn Asn Met Ile Asn Asn Asp Leu Gly Pro Ala Thr Ala	
	530 535 540	
[0128]	caa atg gca ctc caa ctc ttc att aag gat tat cgg tac aca tac cgg	1680
	Gln Met Ala Leu Gln Leu Phe Ile Lys Asp Tyr Arg Tyr Thr Tyr Arg	
	545 550 555 560	
	tgc cat aga ggt gat acc cag ata caa acc aga aga tct ttt gag ttg	1728
	Cys His Arg Gly Asp Thr Gln Ile Gln Thr Arg Arg Ser Phe Glu Leu	
	565 570 575	
	aag aaa ctg tgg gaa cag act cga tca aag act ggt cta ctg gta tca	1776
	Lys Lys Leu Trp Glu Gln Thr Arg Ser Lys Thr Gly Leu Leu Val Ser	
	580 585 590	
	gat ggg ggt cca aac cta tat aac atc aga aac cta cac atc ccg gaa	1824
	Asp Gly Gly Pro Asn Leu Tyr Asn Ile Arg Asn Leu His Ile Pro Glu	
	595 600 605	
	gtc tgt tta aaa tgg gag cta atg gat gaa gat tat aag ggg agg cta	1872
	Val Cys Leu Lys Trp Glu Leu Met Asp Glu Asp Tyr Lys Gly Arg Leu	
	610 615 620	
	tgc aat cca ttg aat cct ttc gtt agt cac aaa gaa att gaa tca gtc	1920
	Cys Asn Pro Leu Asn Pro Phe Val Ser His Lys Glu Ile Glu Ser Val	
	625 630 635 640	

	aac agt gca gta gta atg cct gct cat ggc cct gcc aaa agc atg gag	1968
	Asn Ser Ala Val Val Met Pro Ala His Gly Pro Ala Lys Ser Met Glu	
	645 650 655	
	tat gat get gtt gca aca aca cat tet tgg atc ccc aag agg aac egg	2016
	Tyr Asp Ala Val Ala Thr Thr His Ser Trp Ile Pro Lys Arg Asn Arg	
	660 665 670	
	tcc ata ttg aac aca agc caa agg gga ata cta gaa gat gag cag atg	2064
	Ser Ile Leu Asn Thr Ser Gln Arg Gly Ile Leu Glu Asp Glu Gln Met	
	675 680 685	
	tat cag aaa tgc tgc aac ctg ttt gaa aaa ttc ttc ccc agc agc tca	2112
	Tyr Gln Lys Cys Cys Asn Leu Phe Glu Lys Phe Phe Pro Ser Ser Ser	
	690 695 700	
	tac aga aga cca gtc gga att tet agt atg gtt gag gcc atg gta tcc	2160
	Tyr Arg Arg Pro Val Gly Ile Ser Ser Met Val Glu Ala Met Val Ser	
	705 710 715 720	
[0129]	agg gcc cgc att gat gca cga att gac ttc gaa tet gga cgg ata aag	2208
	Arg Ala Arg Ile Asp Ala Arg Ile Asp Phe Glu Ser Gly Arg Ile Lys	
	725 730 735	
	aag gat gag ttc gct gag atc atg aag atc tgt tcc acc att gaa gag	2256
	Lys Asp Glu Phe Ala Glu Ile Met Lys Ile Cys Ser Thr Ile Glu Glu	
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	ctc aga cgg caa aaa tag	2274
	Leu Arg Arg Gln Lys	
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Asp Asn Met Thr Lys Arg Met Ile Thr Gln Arg Thr Ile Gly Lys Lys
 195 200 205

Lys Gln Arg Leu Ser Arg Lys Ser Tyr Leu Ile Arg Thr Leu Thr Leu
 210 215 220

Asn Thr Met Thr Lys Asp Ala Glu Arg Gly Lys Leu Lys Arg Arg Ala
 225 230 235 240

Ile Ala Thr Pro Gly Met Gln Ile Arg Gly Phe Val Tyr Phe Val Glu
 245 250 255

Thr Leu Ala Arg Arg Ile Cys Glu Lys Leu Glu Gln Ser Gly Leu Pro
 260 265 270

[0131]

Val Gly Gly Asn Glu Lys Lys Ala Lys Leu Ala Asn Val Val Arg Lys
 275 280 285

Met Met Thr Asn Ser Gln Asp Thr Glu Leu Ser Phe Thr Ile Thr Gly
 290 295 300

Asp Asn Thr Lys Trp Asn Glu Asn Gln Asn Pro Arg Ile Phe Leu Ala
 305 310 315 320

Met Ile Thr Tyr Ile Thr Arg Asp Gln Pro Glu Trp Phe Arg Asn Val
 325 330 335

Leu Ser Ile Ala Pro Ile Met Phe Ser Asn Lys Met Ala Arg Leu Gly
 340 345 350

Lys Gly Tyr Met Phe Glu Ser Lys Ser Met Lys Leu Arg Thr Gln Ile
 355 360 365

Pro Ala Glu Met Leu Ala Ser Ile Asp Leu Lys Tyr Phe Asn Asp Ser
370 375 380

Thr Lys Lys Lys Ile Glu Lys Ile Arg Pro Leu Leu Val Asp Gly Thr
385 390 395 400

Ala Ser Leu Ser Pro Gly Met Met Met Gly Met Phe Asn Met Leu Ser
405 410 415

Thr Val Leu Gly Val Ser Ile Leu Asn Leu Gly Gln Arg Lys Tyr Thr
420 425 430

Lys Thr Thr Tyr Trp Trp Asp Gly Leu Gln Ser Ser Asp Asp Phe Ala
435 440 445

[0132]

Leu Ile Val Asn Ala Pro Asn His Glu Gly Ile Gln Ala Gly Val Asp
450 455 460

Arg Phe Tyr Arg Thr Cys Lys Leu Val Gly Ile Asn Met Ser Lys Lys
465 470 475 480

Lys Ser Tyr Ile Asn Arg Thr Gly Thr Phe Glu Phe Thr Ser Phe Phe
485 490 495

Tyr Arg Tyr Gly Phe Val Ala Asn Phe Ser Met Glu Leu Pro Ser Phe
500 505 510

Gly Val Ser Gly Ile Asn Glu Ser Ala Asp Met Ser Ile Gly Val Thr
515 520 525

Val Ile Lys Asn Asn Met Ile Asn Asn Asp Leu Gly Pro Ala Thr Ala
530 535 540

Gln Met Ala Leu Gln Leu Phe Ile Lys Asp Tyr Arg Tyr Thr Tyr Arg
545 550 555 560

Cys His Arg Gly Asp Thr Gln Ile Gln Thr Arg Arg Ser Phe Glu Leu
565 570 575

Lys Lys Leu Trp Glu Gln Thr Arg Ser Lys Thr Gly Leu Leu Val Ser
580 585 590

Asp Gly Gly Pro Asn Leu Tyr Asn Ile Arg Asn Leu His Ile Pro Glu
595 600 605

Val Cys Leu Lys Trp Glu Leu Met Asp Glu Asp Tyr Lys Gly Arg Leu
610 615 620

[0133]

Cys Asn Pro Leu Asn Pro Phe Val Ser His Lys Glu Ile Glu Ser Val
625 630 635 640

Asn Ser Ala Val Val Met Pro Ala His Gly Pro Ala Lys Ser Met Glu
645 650 655

Tyr Asp Ala Val Ala Thr Thr His Ser Trp Ile Pro Lys Arg Asn Arg
660 665 670

Ser Ile Leu Asn Thr Ser Gln Arg Gly Ile Leu Glu Asp Glu Gln Met
675 680 685

Tyr Gln Lys Cys Cys Asn Leu Phe Glu Lys Phe Phe Pro Ser Ser Ser
690 695 700

Tyr Arg Arg Pro Val Gly Ile Ser Ser Met Val Glu Ala Met Val Ser
705 710 715 720

Arg Ala Arg Ile Asp Ala Arg Ile Asp Phe Glu Ser Gly Arg Ile Lys
 725 730 735

Lys Asp Glu Phe Ala Glu Ile Met Lys Ile Cys Ser Thr Ile Glu Glu
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Leu Arg Arg Gln Lys
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gcg gaa aag gca atg aaa gaa tat gga gag aac ccg aaa atc gaa aca 96
 Ala Glu Lys Ala Met Lys Glu Tyr Gly Glu Asn Pro Lys Ile Glu Thr
 20 25 30

aac aaa ttt gca gca ata tgc act cac ttg gaa gtc tgc ttc atg tac 144
 Asn Lys Phe Ala Ala Ile Cys Thr His Leu Glu Val Cys Phe Met Tyr
 35 40 45

teg gat ttc cac ttt ata aat gaa ctg ggt gag tca gtg gtc ata gag 192
 Ser Asp Phe His Phe Ile Asn Glu Leu Gly Glu Ser Val Val Ile Glu
 50 55 60

tct ggt gac cca aat gct ctt ttg aaa cac aga ttt gaa atc att gag 240
 Ser Gly Asp Pro Asn Ala Leu Leu Lys His Arg Phe Glu Ile Ile Glu
 65 70 75 80

	ggg aga gat cga aca atg gca tgg aca gta gta aac agc atc tgc aac	288
	Gly Arg Asp Arg Thr Met Ala Trp Thr Val Val Asn Ser Ile Cys Asn	
	85 90 95	
	acc aca aga gct gaa aaa cct aaa ttt ctt cca gat tta tac gac tat	336
	Thr Thr Arg Ala Glu Lys Pro Lys Phe Leu Pro Asp Leu Tyr Asp Tyr	
	100 105 110	
	aaa gag aac aga ttt gtt gaa att ggt gtg aca agg aga gaa gtt cac	384
	Lys Glu Asn Arg Phe Val Glu Ile Gly Val Thr Arg Arg Glu Val His	
	115 120 125	
	ata tac tac ctg gag aag gcc aac aaa ata aag tct gag aaa aca cat	432
	Ile Tyr Tyr Leu Glu Lys Ala Asn Lys Ile Lys Ser Glu Lys Thr His	
	130 135 140	
	atc cac att ttc tca ttt aca gga gaa gaa atg gct aca aaa gcg gac	480
	Ile His Ile Phe Ser Phe Thr Gly Glu Glu Met Ala Thr Lys Ala Asp	
	145 150 155 160	
[0135]	tat act ctt gat gaa gag agt aga gcc agg atc aag acc aga cta ttc	528
	Tyr Thr Leu Asp Glu Glu Ser Arg Ala Arg Ile Lys Thr Arg Leu Phe	
	165 170 175	
	act ata aga caa gaa atg gcc agt aga ggc ctc tgg gat tcc ttt cgt	576
	Thr Ile Arg Gln Glu Met Ala Ser Arg Gly Leu Trp Asp Ser Phe Arg	
	180 185 190	
	cag tcc gag aga ggc gaa gag aca att gaa gaa aga ttt gaa atc aca	624
	Gln Ser Glu Arg Gly Glu Glu Thr Ile Glu Glu Arg Phe Glu Ile Thr	
	195 200 205	
	ggg acg atg cgc aag ctt gcc aat tac agt ctc cca ccg aac ttc tcc	672
	Gly Thr Met Arg Lys Leu Ala Asn Tyr Ser Leu Pro Pro Asn Phe Ser	
	210 215 220	
	agc ctt gaa aat ttt aga gtc tat ata gat gga ttc gaa ccg aac ggc	720
	Ser Leu Glu Asn Phe Arg Val Tyr Ile Asp Gly Phe Glu Pro Asn Gly	
	225 230 235 240	
	tgc att gag agt aag ctt tct caa atg tcc aaa gaa gta aat gcc aaa	768
	Cys Ile Glu Ser Lys Leu Ser Gln Met Ser Lys Glu Val Asn Ala Lys	
	245 250 255	

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

	gcc cca ata gaa tac att gcg agc atg agg aga aat tat ttt act gct	1344
	Ala Pro Ile Glu Tyr Ile Ala Ser Met Arg Arg Asn Tyr Phe Thr Ala	
	435 440 445	
	gag att tcc cat tgt aga gca aca gaa tat ata atg aaa gga gtg tac	1392
	Glu Ile Ser His Cys Arg Ala Thr Glu Tyr Ile Met Lys Gly Val Tyr	
	450 455 460	
	atc aac act get cta ctc aat gea tcc tgt get gcg atg gat gaa ttt	1440
	Ile Asn Thr Ala Leu Leu Asn Ala Ser Cys Ala Ala Met Asp Glu Phe	
	465 470 475 480	
	caa tta att ccg atg ata agt aaa igc agg acc aaa gaa ggg aga agg	1488
	Gln Leu Ile Pro Met Ile Ser Lys Cys Arg Thr Lys Glu Gly Arg Arg	
	485 490 495	
	aaa aca aat tta tat gga ttc ata ata aag gga agg tcc cat tta aga	1536
	Lys Thr Asn Leu Tyr Gly Phe Ile Ile Lys Gly Arg Ser His Leu Arg	
	500 505 510	
[0137]	aat gat act gac gtg gtg aac ttt gta agt atg gaa ttt tct etc act	1584
	Asn Asp Thr Asp Val Val Asn Phe Val Ser Met Glu Phe Ser Leu Thr	
	515 520 525	
	gat cca aga ttt gag cca cac aaa tgg gaa aaa tac tgc gtt cta gaa	1632
	Asp Pro Arg Phe Glu Pro His Lys Trp Glu Lys Tyr Cys Val Leu Glu	
	530 535 540	
	att gga gac atg ctt tta aga act get gta ggt caa gtg tca aga ccc	1680
	Ile Gly Asp Met Leu Leu Arg Thr Ala Val Gly Gln Val Ser Arg Pro	
	545 550 555 560	
	atg ttt ttg tat gta agg aca aat gga acc tct aaa att aaa atg aaa	1728
	Met Phe Leu Tyr Val Arg Thr Asn Gly Thr Ser Lys Ile Lys Met Lys	
	565 570 575	
	tgg gga atg gaa atg agg cgc tgc etc ctt cag tct ctg caa cag att	1776
	Trp Gly Met Glu Met Arg Arg Cys Leu Leu Gln Ser Leu Gln Gln Ile	
	580 585 590	
	gaa age atg atc gaa get gag tcc tca gtc aaa gaa aag gac atg acc	1824
	Glu Ser Met Ile Glu Ala Glu Ser Ser Val Lys Glu Lys Asp Met Thr	
	595 600 605	

	aaa gaa ttt ttt gag aac aaa tca gag aca tgg cct ata gga gag tcc	1872
	Lys Glu Phe Phe Glu Asn Lys Ser Glu Thr Trp Pro Ile Gly Glu Ser	
	610 615 620	
	ccc aaa gga gtg gaa gag ggc tca atc ggg aag gtt tgc agg acc tta	1920
	Pro Lys Gly Val Glu Glu Gly Ser Ile Gly Lys Val Cys Arg Thr Leu	
	625 630 635 640	
	tta gca aaa tct gtg ttt aac agt tta tat gca tct cca eaa ctg gaa	1968
	Leu Ala Lys Ser Val Phe Asn Ser Leu Tyr Ala Ser Pro Gln Leu Glu	
	645 650 655	
	gga ttt tca gct gaa tct agg aaa tta ctt ctc att gtt cag gct ctt	2016
	Gly Phe Ser Ala Glu Ser Arg Lys Leu Leu Leu Ile Val Gln Ala Leu	
	660 665 670	
	aga gat gac ctg gaa cct gga acc ttt gat att ggg ggg tta tat gaa	2064
	Arg Asp Asp Leu Glu Pro Gly Thr Phe Asp Ile Gly Gly Leu Tyr Glu	
	675 680 685	
[0138]	tca att gag gag tgc ctg att aat gat ccc tgg gtt ttg ctt aat gca	2112
	Ser Ile Glu Glu Cys Leu Ile Asn Asp Pro Trp Val Leu Leu Asn Ala	
	690 695 700	
	tct tgg ttc aac tcc ttc ctc aca cat gca ctg aag tag	2151
	Ser Trp Phe Asn Ser Phe Leu Thr His Ala Leu Lys	
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Asn Lys Phe Ala Ala Ile Cys Thr His Leu Glu Val Cys Phe Met Tyr
35 40 45

Ser Asp Phe His Phe Ile Asn Glu Leu Gly Glu Ser Val Val Ile Glu
50 55 60

Ser Gly Asp Pro Asn Ala Leu Leu Lys His Arg Phe Glu Ile Ile Glu
65 70 75 80

Gly Arg Asp Arg Thr Met Ala Trp Thr Val Val Asn Ser Ile Cys Asn
85 90 95

Thr Thr Arg Ala Glu Lys Pro Lys Phe Leu Pro Asp Leu Tyr Asp Tyr
100 105 110

[0139]

Lys Glu Asn Arg Phe Val Glu Ile Gly Val Thr Arg Arg Glu Val His
115 120 125

Ile Tyr Tyr Leu Glu Lys Ala Asn Lys Ile Lys Ser Glu Lys Thr His
130 135 140

Ile His Ile Phe Ser Phe Thr Gly Glu Glu Met Ala Thr Lys Ala Asp
145 150 155 160

Tyr Thr Leu Asp Glu Glu Ser Arg Ala Arg Ile Lys Thr Arg Leu Phe
165 170 175

Thr Ile Arg Gln Glu Met Ala Ser Arg Gly Leu Trp Asp Ser Phe Arg
180 185 190

Gln Ser Glu Arg Gly Glu Glu Thr Ile Glu Glu Arg Phe Glu Ile Thr
195 200 205

	Gly Thr Met Arg Lys Leu Ala Asn Tyr Ser Leu Pro Pro Asn Phe Ser	
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	Ser Leu Glu Asn Phe Arg Val Tyr Ile Asp Gly Phe Glu Pro Asn Gly	
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	Cys Ile Glu Ser Lys Leu Ser Gln Met Ser Lys Glu Val Asn Ala Lys	
		245 250 255
	Ile Glu Pro Phe Ser Lys Thr Thr Pro Arg Pro Leu Lys Met Pro Gly	
		260 265 270
	Gly Pro Pro Cys His Gln Arg Ser Lys Phe Leu Leu Met Asp Ala Leu	
		275 280 285
[0140]	Lys Leu Ser Ile Glu Asp Pro Ser His Glu Gly Glu Gly Ile Pro Leu	
	290	295 300
	Tyr Asp Ala Ile Lys Cys Met Lys Thr Phe Phe Gly Trp Lys Glu Pro	
	305	310 315 320
	Ser Ile Val Lys Pro His Lys Lys Gly Ile Asn Pro Asn Tyr Leu Gln	
		325 330 335
	Thr Trp Lys Gln Val Leu Glu Glu Ile Gln Asp Leu Glu Asn Glu Glu	
		340 345 350
	Arg Thr Pro Lys Thr Lys Asn Met Lys Lys Thr Ser Gln Leu Lys Trp	
		355 360 365
	Ala Leu Gly Glu Asn Met Ala Pro Glu Lys Val Asp Phe Glu Asp Cys	
	370	375 380

	Lys Asp Ile Asn Asp Leu Lys Gln Tyr Asp Ser Asp Glu Pro Glu Ala	
	385 390 395 400	
	Arg Ser Leu Ala Ser Trp Ile Gln Ser Glu Phe Asn Lys Ala Cys Glu	
	405 410 415	
	Leu Thr Asp Ser Ser Trp Ile Glu Leu Asp Glu Ile Gly Glu Asp Val	
	420 425 430	
	Ala Pro Ile Glu Tyr Ile Ala Ser Met Arg Arg Asn Tyr Phe Thr Ala	
	435 440 445	
	Glu Ile Ser His Cys Arg Ala Thr Glu Tyr Ile Met Lys Gly Val Tyr	
	450 455 460	
[0141]	Ile Asn Thr Ala Leu Leu Asn Ala Ser Cys Ala Ala Met Asp Glu Phe	
	465 470 475 480	
	Gln Leu Ile Pro Met Ile Ser Lys Cys Arg Thr Lys Glu Gly Arg Arg	
	485 490 495	
	Lys Thr Asn Leu Tyr Gly Phe Ile Ile Lys Gly Arg Ser His Leu Arg	
	500 505 510	
	Asn Asp Thr Asp Val Val Asn Phe Val Ser Met Glu Phe Ser Leu Thr	
	515 520 525	
	Asp Pro Arg Phe Glu Pro His Lys Trp Glu Lys Tyr Cys Val Leu Glu	
	530 535 540	
	Ile Gly Asp Met Leu Leu Arg Thr Ala Val Gly Gln Val Ser Arg Pro	
	545 550 555 560	

Met Phe Leu Tyr Val Arg Thr Asn Gly Thr Ser Lys Ile Lys Met Lys
565 570 575

Trp Gly Met Glu Met Arg Arg Cys Leu Leu Gln Ser Leu Gln Gln Ile
580 585 590

Glu Ser Met Ile Glu Ala Glu Ser Ser Val Lys Glu Lys Asp Met Thr
595 600 605

Lys Glu Phe Phe Glu Asn Lys Ser Glu Thr Trp Pro Ile Gly Glu Ser
610 615 620

Pro Lys Gly Val Glu Glu Gly Ser Ile Gly Lys Val Cys Arg Thr Leu
625 630 635 640

Leu Ala Lys Ser Val Phe Asn Ser Leu Tyr Ala Ser Pro Gln Leu Glu
645 650 655

[0142]

Gly Phe Ser Ala Glu Ser Arg Lys Leu Leu Leu Ile Val Gln Ala Leu
660 665 670

Arg Asp Asp Leu Glu Pro Gly Thr Phe Asp Ile Gly Gly Leu Tyr Glu
675 680 685

Ser Ile Glu Glu Cys Leu Ile Asn Asp Pro Trp Val Leu Leu Asn Ala
690 695 700

Ser Trp Phe Asn Ser Phe Leu Thr His Ala Leu Lys
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<210> 53

<211> 844

<212> DNA

<213> 流感病毒

$\langle 220 \rangle$

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〈222〉 (1) .. (690)

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cat gtc cgt aaa cga ttc gca gac caa gaa ctg ggt gat gcc cca ttc 96

His Val Arg Lys Arg Phe Ala Asp Gln Glu Leu Gly Asp Ala Pro Phe

20 25 30

ctt gac cgg ctt cgc cga gac cag aag tcc cta agg gga aga ggt agc 144

Leu Asp Arg Leu Arg Arg Asp Gln Lys Ser Leu Arg Gly Arg Gly Ser

35 40 45

act ctt ggt ctg gac atc gaa aca gcc act cat gca gga aag cag ata 192

Thr Leu Gly Leu Asp Ile Glu Thr Ala Thr His Ala Gly Lys Gln Ile

50 55 60

[0143]

gtg gag cag att ctg gaa aag gaa tea gat gag gca ctt aaa atg ace 240

Val Glu Gln Ile Leu Glu Lys Glu Ser Asp Glu Ala Leu Lys Met Thr

65 70 75 80

att gcc tct gtt cct get tca cgc tac tta act gac atg act ctt gat 288

Ile Ala Ser Val Pro Ala Ser Arg Tyr Leu Thr Asp Met Thr Leu Asp

85 90 95

gag atg tca aga gac tgg ttc atg ctc atg ccc aag caa aaa gta aca 336

Glu Met Ser Arg Asp Trp Phe Met Leu Met Pro Lys Gln Lys Val Thr

100 105 110

ggc tcc cta tgt ata aga atg gac cag gca atc atg gat aag aac atc 384

Gly Ser Leu Cys Ile Arg Met Asp Gln Ala Ile Met Asp Lys Asn Ile

115 120 125

ata ctt aaa gca aac ttt agt gtg att tte gaa agg ctg gaa aca cta 432

Ile Leu Lys Ala Asn Phe Ser Val Ile Phe Glu Arg Leu Glu Thr Leu

130 135 140

ata cta ctt aga gcc ttc ace gaa gaa gga gca gtc gtt ggc gaa att 480

	Ile Leu Leu Arg Ala Phe Thr Glu Glu Gly Ala Val Val Gly Glu Ile	
	145 150 155 160	
	tea cca tta cct tct ctt cca gga cat act aat gag gat gtc aaa aat	528
	Ser Pro Leu Pro Ser Leu Pro Gly His Thr Asn Glu Asp Val Lys Asn	
	165 170 175	
	gea att ggg gtc ctc atc gga gga ctt aaa tgg aat gat aat acg gtt	576
	Ala Ile Gly Val Leu Ile Gly Gly Leu Lys Trp Asn Asp Asn Thr Val	
	180 185 190	
	aga atc tct gaa act cta cag aga ttc gct tgg aga agc agt cat gaa	624
	Arg Ile Ser Glu Thr Leu Gln Arg Phe Ala Trp Arg Ser Ser His Glu	
	195 200 205	
	aat ggg aga cct tca ttc cct tca aaa cag aaa cga aaa atg gag aga	672
	Asn Gly Arg Pro Ser Phe Pro Ser Lys Gln Lys Arg Lys Met Glu Arg	
	210 215 220	
	aca att aag cca gaa att tgaagaaata agatgggtga ttgaagaagt	720
	Thr Ile Lys Pro Glu Ile	
[0144]	225 230	
	ggcacaataga ttgaaaaata cagaaaatag ttttgaacaa ataacattta tgcaagcctt	780
	acaactatttg cttgaagtag aacaagagat aagaacttgc tegtttcage ttattttaatg	840
	ataa	844
	<210> 54	
	<211> 230	
	<212> PRT	
	<213> 流感病毒	
	<400> 54	
	Met Asp Ser Asn Thr Val Ser Ser Phe Gln Val Asp Cys Phe Leu Trp	
	1 5 10 15	
	His Val Arg Lys Arg Phe Ala Asp Gln Glu Leu Gly Asp Ala Pro Phe	
	20 25 30	

	Leu	Asp	Arg	Leu	Arg	Arg	Asp	Gln	Lys	Ser	Leu	Arg	Gly	Arg	Gly	Ser	
		35						40					45				
	Thr	Leu	Gly	Leu	Asp	Ile	Glu	Thr	Ala	Thr	His	Ala	Gly	Lys	Gln	Ile	
		50					55					60					
	Val	Glu	Gln	Ile	Leu	Glu	Lys	Glu	Ser	Asp	Glu	Ala	Leu	Lys	Met	Thr	
	65					70					75				80		
	Ile	Ala	Ser	Val	Pro	Ala	Ser	Arg	Tyr	Leu	Thr	Asp	Met	Thr	Leu	Asp	
					85					90					95		
	Glu	Met	Ser	Arg	Asp	Trp	Phe	Met	Leu	Met	Pro	Lys	Gln	Lys	Val	Thr	
				100					105					110			
[0145]	Gly	Ser	Leu	Cys	Ile	Arg	Met	Asp	Gln	Ala	Ile	Met	Asp	Lys	Asn	Ile	
			115					120					125				
	Ile	Leu	Lys	Ala	Asn	Phe	Ser	Val	Ile	Phe	Glu	Arg	Leu	Glu	Thr	Leu	
		130						135					140				
	Ile	Leu	Leu	Arg	Ala	Phe	Thr	Glu	Glu	Gly	Ala	Val	Val	Gly	Glu	Ile	
	145				150						155				160		
	Ser	Pro	Leu	Pro	Ser	Leu	Pro	Gly	His	Thr	Asn	Glu	Asp	Val	Lys	Asn	
					165					170					175		
	Ala	Ile	Gly	Val	Leu	Ile	Gly	Gly	Leu	Lys	Trp	Asn	Asp	Asn	Thr	Val	
				180					185					190			
	Arg	Ile	Ser	Glu	Thr	Leu	Gln	Arg	Phe	Ala	Trp	Arg	Ser	Ser	His	Glu	
		195						200					205				

Asn Gly Arg Pro Ser Phe Pro Ser Lys Gln Lys Arg Lys Met Glu Arg
 210 215 220

Thr Ile Lys Pro Glu Ile
 225 230

<210> 55
 <211> 1497
 <212> DNA
 <213> 流感病毒

<220>
 <221> CDS
 <222> (1).. (1497)

<400> 55
 atg gcg tct caa ggc acc aaa cga tcc tat gaa cag atg gaa act gat 48
 Met Ala Ser Gln Gly Thr Lys Arg Ser Tyr Glu Gln Met Glu Thr Asp
 [0146] 1 5 10 15

ggg gaa cgc cag aat gca act gaa atc aga gca tct gtc gga agg atg 96
 Gly Glu Arg Gln Asn Ala Thr Glu Ile Arg Ala Ser Val Gly Arg Met
 20 25 30

gtg gga gga atc gga cgg ttt tat gtc cag atg tgt act gag ctt aaa 144
 Val Gly Gly Ile Gly Arg Phe Tyr Val Gln Met Cys Thr Glu Leu Lys
 35 40 45

cta aac gac cat gaa ggg cgg ctg att cag aac age ata aca ata gaa 192
 Leu Asn Asp His Glu Gly Arg Leu Ile Gln Asn Ser Ile Thr Ile Glu
 50 55 60

agg atg gtg ctt tcg gca ttc gac gaa aga aga aac aag tat ctc gag 240
 Arg Met Val Leu Ser Ala Phe Asp Glu Arg Arg Asn Lys Tyr Leu Glu
 65 70 75 80

gag cat ccc agt gct ggg aaa gac cct aag aaa acg gga ggc cgg ata 288
 Glu His Pro Ser Ala Gly Lys Asp Pro Lys Lys Thr Gly Gly Pro Ile
 85 90 95

	tac aga aga aaa gat ggg aaa tgg atg agg gaa ctc atc ctc cat gat	336
	Tyr Arg Arg Lys Asp Gly Lys Trp Met Arg Glu Leu Ile Leu His Asp	
	100 105 110	
	aaa gaa gaa atc atg aga atc tgg cgt cag gcc aac aat ggt gaa gac	384
	Lys Glu Glu Ile Met Arg Ile Trp Arg Gln Ala Asn Asn Gly Glu Asp	
	115 120 125	
	get act get ggt ctt act cat atg atg atc tgg cac tcc aat ctc aat	432
	Ala Thr Ala Gly Leu Thr His Met Met Ile Trp His Ser Asn Leu Asn	
	130 135 140	
	gac acc aca tac caa aga aca agg get ctt gtt cgg act ggg atg gat	480
	Asp Thr Thr Tyr Gln Arg Thr Arg Ala Leu Val Arg Thr Gly Met Asp	
	145 150 155 160	
	ccc aga atg tgc tct ctg atg caa ggc tca acc ctc cca cgg aga tct	528
	Pro Arg Met Cys Ser Leu Met Gln Gly Ser Thr Leu Pro Arg Arg Ser	
	165 170 175	
[0147]	gga gcc get ggt get gca gta aaa ggc gtt gga aca atg gta atg gaa	576
	Gly Ala Ala Gly Ala Ala Val Lys Gly Val Gly Thr Met Val Met Glu	
	180 185 190	
	ctc atc aga atg atc aag cgc gga ata aat gat cgg aat ttc tgg aga	624
	Leu Ile Arg Met Ile Lys Arg Gly Ile Asn Asp Arg Asn Phe Trp Arg	
	195 200 205	
	ggt gaa aat ggt cga aga acc aga att get tat gaa aga atg tgc aat	672
	Gly Glu Asn Gly Arg Arg Thr Arg Ile Ala Tyr Glu Arg Met Cys Asn	
	210 215 220	
	atc ctc aaa ggg aaa ttt cag aca gca gca caa cgg get atg atg gac	720
	Ile Leu Lys Gly Lys Phe Gln Thr Ala Ala Gln Arg Ala Met Met Asp	
	225 230 235 240	
	cag gtg agg gaa ggc cgc aat cct gga aac get gag att gag gat ctc	768
	Gln Val Arg Glu Gly Arg Asn Pro Gly Asn Ala Glu Ile Glu Asp Leu	
	245 250 255	
	att ttc ttg gca cga tca gca ctt att ttg aga gga tca gta gcc cat	816
	Ile Phe Leu Ala Arg Ser Ala Leu Ile Leu Arg Gly Ser Val Ala His	
	260 265 270	

	aaa tca tgc cta cct gcc tgt gtt tat ggc ctt gca gta acc agt ggg	864
	Lys Ser Cys Leu Pro Ala Cys Val Tyr Gly Leu Ala Val Thr Ser Gly	
	275 280 285	
	tat gac ttt gag aag gaa gga tac tct ctg gtt gga att gat cct ttc	912
	Tyr Asp Phe Glu Lys Glu Gly Tyr Ser Leu Val Gly Ile Asp Pro Phe	
	290 295 300	
	aaa cta ctc cag aac agt caa att ttc agt cta atc aga cca aaa gaa	960
	Lys Leu Leu Gln Asn Ser Gln Ile Phe Ser Leu Ile Arg Pro Lys Glu	
	305 310 315 320	
	aac cca gca cac aaa agc cag ttg gtg tgg atg gca tgc cat tct gca	1008
	Asn Pro Ala His Lys Ser Gln Leu Val Trp Met Ala Cys His Ser Ala	
	325 330 335	
	gca ttt gag gat ctg aga gtt tta aat ttc att aga gga acc aaa gta	1056
	Ala Phe Glu Asp Leu Arg Val Leu Asn Phe Ile Arg Gly Thr Lys Val	
	340 345 350	
[0148]	atc cca aga gga cag tta aca acc aga gga gtt caa att gct tca aat	1104
	Ile Pro Arg Gly Gln Leu Thr Thr Arg Gly Val Gln Ile Ala Ser Asn	
	355 360 365	
	gaa aac atg gag aca ata aat tct agc aca ctt gaa ctg aga agc aaa	1152
	Glu Asn Met Glu Thr Ile Asn Ser Ser Thr Leu Glu Leu Arg Ser Lys	
	370 375 380	
	tat tgg gca ata agg acc aga agc gga gga aac acc agt caa cag aga	1200
	Tyr Trp Ala Ile Arg Thr Arg Ser Gly Gly Asn Thr Ser Gln Gln Arg	
	385 390 395 400	
	gca tct gca gga cag ata agt gtg caa cct act ttc tca gta cag aga	1248
	Ala Ser Ala Gly Gln Ile Ser Val Gln Pro Thr Phe Ser Val Gln Arg	
	405 410 415	
	aat ctt ccc ttt gag aga gca acc att atg get gca ttc act ggt aac	1296
	Asn Leu Pro Phe Glu Arg Ala Thr Ile Met Ala Ala Phe Thr Gly Asn	
	420 425 430	
	act gaa gga agg act tcc gac atg aga acg gaa atc ata agg atg atg	1344
	Thr Glu Gly Arg Thr Ser Asp Met Arg Thr Glu Ile Ile Arg Met Met	
	435 440 445	

gaa aat gcc aaa tca gaa gat gtg tet ttc cag ggg egg gga gtc ttc 1392
 Glu Asn Ala Lys Ser Glu Asp Val Ser Phe Gln Gly Arg Gly Val Phe
 450 455 460

gag ctc teg gac gaa aag gca acg aac ccg atc gtg cct tcc ttt gac 1440
 Glu Leu Ser Asp Glu Lys Ala Thr Asn Pro Ile Val Pro Ser Phe Asp
 465 470 475 480

atg agc aat gaa ggg tet tat ttc ttc gga gac aat gct gag gag ttt 1488
 Met Ser Asn Glu Gly Ser Tyr Phe Phe Gly Asp Asn Ala Glu Glu Phe
 485 490 495

gac agt taa 1497
 Asp Ser

<210> 56

<211> 498

<212> PRT

<213> 流感病毒

[0149]

<400> 56

Met Ala Ser Gln Gly Thr Lys Arg Ser Tyr Glu Gln Met Glu Thr Asp
 1 5 10 15

Gly Glu Arg Gln Asn Ala Thr Glu Ile Arg Ala Ser Val Gly Arg Met
 20 25 30

Val Gly Gly Ile Gly Arg Phe Tyr Val Gln Met Cys Thr Glu Leu Lys
 35 40 45

Leu Asn Asp His Glu Gly Arg Leu Ile Gln Asn Ser Ile Thr Ile Glu
 50 55 60

Arg Met Val Leu Ser Ala Phe Asp Glu Arg Arg Asn Lys Tyr Leu Glu
 65 70 75 80

	Glu	His	Pro	Ser	Ala	Gly	Lys	Asp	Pro	Lys	Lys	Thr	Gly	Gly	Pro	Ile	
						85				90					95		
	Tyr	Arg	Arg	Lys	Asp	Gly	Lys	Trp	Met	Arg	Glu	Leu	Ile	Leu	His	Asp	
				100				105					110				
	Lys	Glu	Glu	Ile	Met	Arg	Ile	Trp	Arg	Gln	Ala	Asn	Asn	Gly	Glu	Asp	
				115				120					125				
	Ala	Thr	Ala	Gly	Leu	Thr	His	Met	Met	Ile	Trp	His	Ser	Asn	Leu	Asn	
		130					135					140					
	Asp	Thr	Thr	Tyr	Gln	Arg	Thr	Arg	Ala	Leu	Val	Arg	Thr	Gly	Met	Asp	
	145					150					155					160	
[0150]	Pro	Arg	Met	Cys	Ser	Leu	Met	Gln	Gly	Ser	Thr	Leu	Pro	Arg	Arg	Ser	
				165						170					175		
	Gly	Ala	Ala	Gly	Ala	Ala	Val	Lys	Gly	Val	Gly	Thr	Met	Val	Met	Glu	
				180						185				190			
	Leu	Ile	Arg	Met	Ile	Lys	Arg	Gly	Ile	Asn	Asp	Arg	Asn	Phe	Trp	Arg	
		195						200					205				
	Gly	Glu	Asn	Gly	Arg	Arg	Thr	Arg	Ile	Ala	Tyr	Glu	Arg	Met	Cys	Asn	
		210					215					220					
	Ile	Leu	Lys	Gly	Lys	Phe	Gln	Thr	Ala	Ala	Gln	Arg	Ala	Met	Met	Asp	
	225					230					235					240	
	Gln	Val	Arg	Glu	Gly	Arg	Asn	Pro	Gly	Asn	Ala	Glu	Ile	Glu	Asp	Leu	
				245						250					255		

Ile Phe Leu Ala Arg Ser Ala Leu Ile Leu Arg Gly Ser Val Ala His
260 265 270

Lys Ser Cys Leu Pro Ala Cys Val Tyr Gly Leu Ala Val Thr Ser Gly
275 280 285

Tyr Asp Phe Glu Lys Glu Gly Tyr Ser Leu Val Gly Ile Asp Pro Phe
290 295 300

Lys Leu Leu Gln Asn Ser Gln Ile Phe Ser Leu Ile Arg Pro Lys Glu
305 310 315 320

Asn Pro Ala His Lys Ser Gln Leu Val Trp Met Ala Cys His Ser Ala
325 330 335

[0151]

Ala Phe Glu Asp Leu Arg Val Leu Asn Phe Ile Arg Gly Thr Lys Val
340 345 350

Ile Pro Arg Gly Gln Leu Thr Thr Arg Gly Val Gln Ile Ala Ser Asn
355 360 365

Glu Asn Met Glu Thr Ile Asn Ser Ser Thr Leu Glu Leu Arg Ser Lys
370 375 380

Tyr Trp Ala Ile Arg Thr Arg Ser Gly Gly Asn Thr Ser Gln Gln Arg
385 390 395 400

Ala Ser Ala Gly Gln Ile Ser Val Gln Pro Thr Phe Ser Val Gln Arg
405 410 415

Asn Leu Pro Phe Glu Arg Ala Thr Ile Met Ala Ala Phe Thr Gly Asn
420 425 430

Thr Glu Gly Arg Thr Ser Asp Met Arg Thr Glu Ile Ile Arg Met Met
435 440 445

Glu Asn Ala Lys Ser Glu Asp Val Ser Phe Gln Gly Arg Gly Val Phe
450 455 460

Glu Leu Ser Asp Glu Lys Ala Thr Asn Pro Ile Val Pro Ser Phe Asp
465 470 475 480

Met Ser Asn Glu Gly Ser Tyr Phe Phe Gly Asp Asn Ala Glu Glu Phe
485 490 495

Asp Ser

[0152]

<210> 57

<211> 1413

<212> DNA

<213> 流感病毒

<220>

<221> CDS

<222> (1)..(1413)

<400> 57

atg aat cca aat caa aag ata ata gca att gga ttt gca tca ttg ggg 48
Met Asn Pro Asn Gln Lys Ile Ile Ala Ile Gly Phe Ala Ser Leu Gly
1 5 10 15

ata tta atc att aat gtc att ctc cat gta gtc age att ata gta aca 96
Ile Leu Ile Ile Asn Val Ile Leu His Val Val Ser Ile Ile Val Thr
20 25 30

gta ctg gtc ctc aat aac aat aga aca gat ctg aac tgc aaa ggg acg 144
Val Leu Val Leu Asn Asn Asn Arg Thr Asp Leu Asn Cys Lys Gly Thr
35 40 45

atc ata aga gaa tac aat gaa aca gta aga gta gaa aaa ctt act caa 192

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

[0154]

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

Gly Tyr Ser Gly Ser Phe Thr Leu Pro Val Glu Leu Thr Lys Lys Gly
 405 410 415
 tgt ttg gtc ccc tgt ttc tgg gtt gaa atg att aga ggt aaa cct gaa 1296
 Cys Leu Val Pro Cys Phe Trp Val Glu Met Ile Arg Gly Lys Pro Glu
 420 425 430
 gaa aca aca ata tgg acc tct agc agc tcc att gtg atg tgt gga gta 1344
 Glu Thr Thr Ile Trp Thr Ser Ser Ser Ser Ile Val Met Cys Gly Val
 435 440 445
 gat cat aaa att gcc agt tgg tca tgg cac gat gga gct att ctt ccc 1392
 Asp His Lys Ile Ala Ser Trp Ser Trp His Asp Gly Ala Ile Leu Pro
 450 455 460
 ttt gac atc gat aag atg taa 1413
 Phe Asp Ile Asp Lys Met
 465 470
 <210> 58
 <211> 470
 [0155] <212> PRT
 <213> 流感病毒
 <400> 58
 Met Asn Pro Asn Gln Lys Ile Ile Ala Ile Gly Phe Ala Ser Leu Gly
 1 5 10 15
 Ile Leu Ile Ile Asn Val Ile Leu His Val Val Ser Ile Ile Val Thr
 20 25 30
 Val Leu Val Leu Asn Asn Asn Arg Thr Asp Leu Asn Cys Lys Gly Thr
 35 40 45
 Ile Ile Arg Glu Tyr Asn Glu Thr Val Arg Val Glu Lys Leu Thr Gln
 50 55 60
 Trp Tyr Asn Thr Ser Thr Ile Lys Tyr Ile Glu Arg Pro Ser Asn Glu

65	70	75	80
Tyr Tyr Met Asn Asn Thr Glu Pro Leu Cys Glu Ala Gln Gly Phe Ala			
	85	90	95
Pro Phe Ser Lys Asp Asn Gly Ile Arg Ile Gly Ser Arg Gly His Val			
	100	105	110
Phe Val Ile Arg Glu Pro Phe Val Ser Cys Ser Pro Ser Glu Cys Arg			
	115	120	125
Thr Phe Phe Leu Thr Gln Gly Ser Leu Leu Asn Asp Lys His Ser Asn			
	130	135	140
Gly Thr Ile Lys Asp Arg Ser Pro Tyr Arg Thr Leu Met Ser Val Lys			
145	150	155	160
[0156]			
Ile Gly Gln Ser Pro Asn Val Tyr Gln Ala Arg Phe Glu Ser Val Ala			
	165	170	175
Trp Ser Ala Thr Ala Cys His Asp Gly Lys Lys Trp Met Thr Val Gly			
	180	185	190
Val Thr Gly Pro Asp Asn Gln Ala Ile Ala Val Val Asn Tyr Gly Gly			
	195	200	205
Val Pro Val Asp Ile Ile Asn Ser Trp Ala Gly Asp Ile Leu Arg Thr			
	210	215	220
Gln Glu Ser Ser Cys Thr Cys Ile Lys Gly Asp Cys Tyr Trp Val Met			
225	230	235	240
Thr Asp Gly Pro Ala Asn Arg Gln Ala Lys Tyr Arg Ile Phe Lys Ala			

245	250	255
Lys Asp Gly Arg Val Ile Gly Gln Thr Asp Ile Ser Phe Asn Gly Gly		
260	265	270
His Ile Glu Glu Cys Ser Cys Tyr Pro Asn Glu Gly Lys Val Glu Cys		
275	280	285
Ile Cys Arg Asp Asn Trp Thr Gly Thr Asn Arg Pro Ile Leu Val Ile		
290	295	300
Ser Ser Asp Leu Ser Tyr Thr Val Gly Tyr Leu Cys Ala Gly Ile Pro		
305	310	315 320
Thr Asp Thr Pro Arg Gly Glu Asp Ser Gln Phe Thr Gly Ser Cys Thr		
325	330	335
[0157]		
Ser Pro Leu Gly Asn Lys Gly Tyr Gly Val Lys Gly Phe Gly Phe Arg		
340	345	350
Gln Gly Thr Asp Val Trp Ala Gly Arg Thr Ile Ser Arg Thr Ser Arg		
355	360	365
Ser Gly Phe Glu Ile Ile Lys Ile Arg Asn Gly Trp Thr Gln Asn Ser		
370	375	380
Lys Asp Gln Ile Arg Arg Gln Val Ile Ile Asp Asp Pro Asn Trp Ser		
385	390	395 400
Gly Tyr Ser Gly Ser Phe Thr Leu Pro Val Glu Leu Thr Lys Lys Gly		
405	410	415
Cys Leu Val Pro Cys Phe Trp Val Glu Met Ile Arg Gly Lys Pro Glu		

	420	425	430
Glu Thr Thr Ile Trp Thr Ser Ser Ser Ser Ile Val Met Cys Gly Val			
	435	440	445

Asp His Lys Ile Ala Ser Trp Ser Trp His Asp Gly Ala Ile Leu Pro			
	450	455	460

Phe Asp Ile Asp Lys Met		
	465	470

<210> 59
 <211> 981
 <212> DNA
 <213> 流感病毒

[0158]

<220>
 <221> CDS
 <222> (1)..(756)

<400> 59	
atg agt ctt cta acc gag gtc gaa acg tac gtt ctc tet atc gta cca	48
Met Ser Leu Leu Thr Glu Val Glu Thr Tyr Val Leu Ser Ile Val Pro	
1 5 10 15	
tea ggc ccc ctc aaa gcc gag atc geg cag aga ctt gaa gat gtc ttt	96
Ser Gly Pro Leu Lys Ala Glu Ile Ala Gln Arg Leu Glu Asp Val Phe	
20 25 30	
geg gga aag aac acc gat ctt gag gca ctc atg gaa tgg cta aag aca	144
Ala Gly Lys Asn Thr Asp Leu Glu Ala Leu Met Glu Trp Leu Lys Thr	
35 40 45	
aga cca atc ctg tca cct ctg act aaa ggg att tta gga ttt gta ttc	192
Arg Pro Ile Leu Ser Pro Leu Thr Lys Gly Ile Leu Gly Phe Val Phe	
50 55 60	
acg ctc acc gtg ccc agt gag cga gga ctg cag cgt aga cgc ttt gtc	240
Thr Leu Thr Val Pro Ser Glu Arg Gly Leu Gln Arg Arg Arg Phe Val	

65	70	75	80	
caa aat gcc ctt agt gga aac gga gat cca aac aac atg gac aga gea				288
Gln Asn Ala Leu Ser Gly Asn Gly Asp Pro Asn Asn Met Asp Arg Ala				
85	90	95		
gta aaa ctg tac agg aag ctt aaa aga gaa ata aca ttc cat ggg gea				336
Val Lys Leu Tyr Arg Lys Leu Lys Arg Glu Ile Thr Phe His Gly Ala				
100	105	110		
aaa gag gtg gca ctc agc tat tcc act ggt gea cta gcc agc tgc atg				384
Lys Glu Val Ala Leu Ser Tyr Ser Thr Gly Ala Leu Ala Ser Cys Met				
115	120	125		
gga ctc ata tac aac aga atg gga act gtt aca acc gaa gtg gea ttt				432
Gly Leu Ile Tyr Asn Arg Met Gly Thr Val Thr Thr Glu Val Ala Phe				
130	135	140		
ggc ctg gta tgc gcc aca tgt gaa cag att get gat tcc cag cat cga				480
Gly Leu Val Cys Ala Thr Cys Glu Gln Ile Ala Asp Ser Gln His Arg				
145	150	155	160	
[0159] tct cac agg cag atg gtg aca aca acc aac cea tta atc aga cat gaa				528
Ser His Arg Gln Met Val Thr Thr Thr Asn Pro Leu Ile Arg His Glu				
165	170	175		
aac aga atg gta tta gcc agt acc acg get aaa gcc atg gaa cag atg				576
Asn Arg Met Val Leu Ala Ser Thr Thr Ala Lys Ala Met Glu Gln Met				
180	185	190		
gea gga teg agt gag cag gea gea gag gcc atg gag gtt get agt agg				624
Ala Gly Ser Ser Glu Gln Ala Ala Glu Ala Met Glu Val Ala Ser Arg				
195	200	205		
get agg cag atg gta cag gea atg aga acc att ggg acc cac cct agc				672
Ala Arg Gln Met Val Gln Ala Met Arg Thr Ile Gly Thr His Pro Ser				
210	215	220		
tcc agt gcc ggt ttg aaa gat gat ctc ctt gaa aat tta cag gcc tac				720
Ser Ser Ala Gly Leu Lys Asp Asp Leu Leu Glu Asn Leu Gln Ala Tyr				
225	230	235	240	
cag aaa cgg atg gga gtg caa atg cag cga ttc aag tgatcctctc				766
Gln Lys Arg Met Gly Val Gln Met Gln Arg Phe Lys				

Val Lys Leu Tyr Arg Lys Leu Lys Arg Glu Ile Thr Phe His Gly Ala
100 105 110

Lys Glu Val Ala Leu Ser Tyr Ser Thr Gly Ala Leu Ala Ser Cys Met
115 120 125

Gly Leu Ile Tyr Asn Arg Met Gly Thr Val Thr Thr Glu Val Ala Phe
130 135 140

Gly Leu Val Cys Ala Thr Cys Glu Gln Ile Ala Asp Ser Gln His Arg
145 150 155 160

Ser His Arg Gln Met Val Thr Thr Thr Asn Pro Leu Ile Arg His Glu
165 170 175

Asn Arg Met Val Leu Ala Ser Thr Thr Ala Lys Ala Met Glu Gln Met
180 185 190

[0161]

Ala Gly Ser Ser Glu Gln Ala Ala Glu Ala Met Glu Val Ala Ser Arg
195 200 205

Ala Arg Gln Met Val Gln Ala Met Arg Thr Ile Gly Thr His Pro Ser
210 215 220

Ser Ser Ala Gly Leu Lys Asp Asp Leu Leu Glu Asn Leu Gln Ala Tyr
225 230 235 240

Gln Lys Arg Met Gly Val Gln Met Gln Arg Phe Lys
245 250

<210> 61

<211> 1698

<212> DNA

<213> 流感病毒

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<400> 61			
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Met Lys Thr Thr Ile Ile Leu Ile Leu Leu Thr His Trp Ala Tyr Ser			
1 5 10 15			
caa aac cca atc agt gcc aat aac aca gcc aca ctg tgt ctg gga cac			96
Gln Asn Pro Ile Ser Gly Asn Asn Thr Ala Thr Leu Cys Leu Gly His			
20 25 30			
cat gca gta gca aat gga aca ttg gta aaa aca atg agt gat gat caa			144
His Ala Val Ala Asn Gly Thr Leu Val Lys Thr Met Ser Asp Asp Gln			
35 40 45			
att gag gtg aca aat gct aca gaa tta gtt cag agc att tca atg ggg			192
Ile Glu Val Thr Asn Ala Thr Glu Leu Val Gln Ser Ile Ser Met Gly			
50 55 60			
[0162]	aaa ata tgc aac aaa tca tat aga att cta gat gga aga aat tgc aca		240
	Lys Ile Cys Asn Lys Ser Tyr Arg Ile Leu Asp Gly Arg Asn Cys Thr		
65 70 75 80			
	tta ata gat gca atg cta gga gac ccc cac tgt gac gcc ttt cag tat		288
	Leu Ile Asp Ala Met Leu Gly Asp Pro His Cys Asp Ala Phe Gln Tyr		
85 90 95			
	gag agt tgg gac ctc ttt ata gaa aga agc agc gct ttc agc aat tgc		336
	Glu Ser Trp Asp Leu Phe Ile Glu Arg Ser Ser Ala Phe Ser Asn Cys		
100 105 110			
	tac cca tat gac atc cct gac tat gca tgg ctc cga tcc att gta gca		384
	Tyr Pro Tyr Asp Ile Pro Asp Tyr Ala Ser Leu Arg Ser Ile Val Ala		
115 120 125			
	tcc tca ggg aca gtg gaa ttc aca gca gag gga ttc aca tgg aca ggt		432
	Ser Ser Gly Thr Val Glu Phe Thr Ala Glu Gly Phe Thr Trp Thr Gly		
130 135 140			
	gta act caa aac gga aga agt gga gcc tgc aaa agg gga tca gcc gat		480
	Val Thr Gln Asn Gly Arg Ser Gly Ala Cys Lys Arg Gly Ser Ala Asp		
145 150 155 160			

	agt ttc ttt agc cga ctg aat tgg cta aca aaa tct gga agc tct tac	528
	Ser Phe Phe Ser Arg Leu Asn Trp Leu Thr Lys Ser Gly Ser Ser Tyr	
	165 170 175	
	ccc aca ttg aat gtg aca atg cct aac aat aaa aat ttc gac aag cta	576
	Pro Thr Leu Asn Val Thr Met Pro Asn Asn Lys Asn Phe Asp Lys Leu	
	180 185 190	
	tac atc tgg ggg att cat cac ccg agc tca aat caa gag cag aca aaa	624
	Tyr Ile Trp Gly Ile His His Pro Ser Ser Asn Gln Glu Gln Thr Lys	
	195 200 205	
	ttg tac atc caa gaa tca gga cga gta aca gtc tca aca aaa aga agt	672
	Leu Tyr Ile Gln Glu Ser Gly Arg Val Thr Val Ser Thr Lys Arg Ser	
	210 215 220	
	caa caa aca ata atc cct aac atc gga tct aga ccg ttg gtc aga ggt	720
	Gln Gln Thr Ile Ile Pro Asn Ile Gly Ser Arg Pro Leu Val Arg Gly	
	225 230 235 240	
[0163]	caa tca ggc agg ata agc ata tac tgg acc att gta aaa cct gga gat	768
	Gln Ser Gly Arg Ile Ser Ile Tyr Trp Thr Ile Val Lys Pro Gly Asp	
	245 250 255	
	atc cta atg ata aac agt aat ggc aac tta gtt gca ccg cgg gga tat	816
	Ile Leu Met Ile Asn Ser Asn Gly Asn Leu Val Ala Pro Arg Gly Tyr	
	260 265 270	
	ttt aaa ttg aac aca ggg aaa agc tct gta atg aga tcc gat gta ccc	864
	Phe Lys Leu Asn Thr Gly Lys Ser Ser Val Met Arg Ser Asp Val Pro	
	275 280 285	
	ata gac att tgt gtg tct gaa tgt att aca cca aat gga agc atc tcc	912
	Ile Asp Ile Cys Val Ser Glu Cys Ile Thr Pro Asn Gly Ser Ile Ser	
	290 295 300	
	aac gac aag cca ttc caa aat gtg aac aaa gtt aca tat gga aaa tgc	960
	Asn Asp Lys Pro Phe Gln Asn Val Asn Lys Val Thr Tyr Gly Lys Cys	
	305 310 315 320	
	ccc aag tat atc agg caa aac act tta aag ctg gcc act ggg atg agg	1008
	Pro Lys Tyr Ile Arg Gln Asn Thr Leu Lys Leu Ala Thr Gly Met Arg	
	325 330 335	

	aat gta cca gaa aag caa acc aga gga atc ttt gga gca ata geg gga	1056
	Asn Val Pro Glu Lys Gln Thr Arg Gly Ile Phe Gly Ala Ile Ala Gly	
	340 345 350	
	ttc atc gaa aac ggc tgg gaa gga atg gtt gat ggg tgg tat ggg ttc	1104
	Phe Ile Glu Asn Gly Trp Glu Gly Met Val Asp Gly Trp Tyr Gly Phe	
	355 360 365	
	cga tat caa aac tct gaa gga aca ggg caa get gca gat cta aag agc	1152
	Arg Tyr Gln Asn Ser Glu Gly Thr Gly Gln Ala Ala Asp Leu Lys Ser	
	370 375 380	
	act caa gca gcc atc gac cag att aat gga aag tta aac aga gtg att	1200
	Thr Gln Ala Ala Ile Asp Gln Ile Asn Gly Lys Leu Asn Arg Val Ile	
	385 390 395 400	
	gaa aga acc aat gag aaa ttc cat cua ata gag aag gaa ttc tca gaa	1248
	Glu Arg Thr Asn Glu Lys Phe His Gln Ile Glu Lys Glu Phe Ser Glu	
	405 410 415	
[0164]	gta gaa gga aga att cag gac ttg gag aaa tat gta gaa gac acc aaa	1296
	Val Glu Gly Arg Ile Gln Asp Leu Glu Lys Tyr Val Glu Asp Thr Lys	
	420 425 430	
	ata gac cta tgg tcc tac aat gca gaa ttg ctg gtg get cta gaa aat	1344
	Ile Asp Leu Trp Ser Tyr Asn Ala Glu Leu Leu Val Ala Leu Glu Asn	
	435 440 445	
	caa cat aca att gac tta aca gat gca gaa atg aat aaa tta ttt gag	1392
	Gln His Thr Ile Asp Leu Thr Asp Ala Glu Met Asn Lys Leu Phe Glu	
	450 455 460	
	aag act aga cgc cag tta aga gaa aac gca gaa gac atg gga ggt gga	1440
	Lys Thr Arg Arg Gln Leu Arg Glu Asn Ala Glu Asp Met Gly Gly Gly	
	465 470 475 480	
	tgt ttc aag att tac cac aaa tgt gat aat gca tgc att gaa tca ata	1488
	Cys Phe Lys Ile Tyr His Lys Cys Asp Asn Ala Cys Ile Glu Ser Ile	
	485 490 495	
	aga act ggg aca tat gac cat tac ata tac aaa gat gaa gca tta aac	1536
	Arg Thr Gly Thr Tyr Asp His Tyr Ile Tyr Lys Asp Glu Ala Leu Asn	
	500 505 510	

aat cga ttt cag atc aaa ggt gta gag ttg aaa tca ggc tac aaa gat 1584
 Asn Arg Phe Gln Ile Lys Gly Val Glu Leu Lys Ser Gly Tyr Lys Asp
 515 520 525

tgg ata ctg tgg att tca ttc gcc ata tca tgc ttc tta att tgc gtt 1632
 Trp Ile Leu Trp Ile Ser Phe Ala Ile Ser Cys Phe Leu Ile Cys Val
 530 535 540

gtt cta ttg ggt ttc att atg tgg gct tgc caa aaa ggc aac atc aga 1680
 Val Leu Leu Gly Phe Ile Met Trp Ala Cys Gln Lys Gly Asn Ile Arg
 545 550 555 560

tgc aac att tgc att tga 1698
 Cys Asn Ile Cys Ile
 565

<210> 62

<211> 565

<212> PRT

<213> 流感病毒

[0165]

<400> 62

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Gln Asn Pro Ile Ser Gly Asn Asn Thr Ala Thr Leu Cys Leu Gly His
 20 25 30

His Ala Val Ala Asn Gly Thr Leu Val Lys Thr Met Ser Asp Asp Gln
 35 40 45

Ile Glu Val Thr Asn Ala Thr Glu Leu Val Gln Ser Ile Ser Met Gly
 50 55 60

Lys Ile Cys Asn Lys Ser Tyr Arg Ile Leu Asp Gly Arg Asn Cys Thr
 65 70 75 80

Leu Ile Asp Ala Met Leu Gly Asp Pro His Cys Asp Ala Phe Gln Tyr
85 90 95

Glu Ser Trp Asp Leu Phe Ile Glu Arg Ser Ser Ala Phe Ser Asn Cys
100 105 110

Tyr Pro Tyr Asp Ile Pro Asp Tyr Ala Ser Leu Arg Ser Ile Val Ala
115 120 125

Ser Ser Gly Thr Val Glu Phe Thr Ala Glu Gly Phe Thr Trp Thr Gly
130 135 140

Val Thr Gln Asn Gly Arg Ser Gly Ala Cys Lys Arg Gly Ser Ala Asp
145 150 155 160

[0166]

Ser Phe Phe Ser Arg Leu Asn Trp Leu Thr Lys Ser Gly Ser Ser Tyr
165 170 175

Pro Thr Leu Asn Val Thr Met Pro Asn Asn Lys Asn Phe Asp Lys Leu
180 185 190

Tyr Ile Trp Gly Ile His His Pro Ser Ser Asn Gln Glu Gln Thr Lys
195 200 205

Leu Tyr Ile Gln Glu Ser Gly Arg Val Thr Val Ser Thr Lys Arg Ser
210 215 220

Gln Gln Thr Ile Ile Pro Asn Ile Gly Ser Arg Pro Leu Val Arg Gly
225 230 235 240

Gln Ser Gly Arg Ile Ser Ile Tyr Trp Thr Ile Val Lys Pro Gly Asp
245 250 255

Ile Leu Met Ile Asn Ser Asn Gly Asn Leu Val Ala Pro Arg Gly Tyr
260 265 270

Phe Lys Leu Asn Thr Gly Lys Ser Ser Val Met Arg Ser Asp Val Pro
275 280 285

Ile Asp Ile Cys Val Ser Glu Cys Ile Thr Pro Asn Gly Ser Ile Ser
290 295 300

Asn Asp Lys Pro Phe Gln Asn Val Asn Lys Val Thr Tyr Gly Lys Cys
305 310 315 320

Pro Lys Tyr Ile Arg Gln Asn Thr Leu Lys Leu Ala Thr Gly Met Arg
325 330 335

[0167]

Asn Val Pro Glu Lys Gln Thr Arg Gly Ile Phe Gly Ala Ile Ala Gly
340 345 350

Phe Ile Glu Asn Gly Trp Glu Gly Met Val Asp Gly Trp Tyr Gly Phe
355 360 365

Arg Tyr Gln Asn Ser Glu Gly Thr Gly Gln Ala Ala Asp Leu Lys Ser
370 375 380

Thr Gln Ala Ala Ile Asp Gln Ile Asn Gly Lys Leu Asn Arg Val Ile
385 390 395 400

Glu Arg Thr Asn Glu Lys Phe His Gln Ile Glu Lys Glu Phe Ser Glu
405 410 415

Val Glu Gly Arg Ile Gln Asp Leu Glu Lys Tyr Val Glu Asp Thr Lys
420 425 430

Ile Asp Leu Trp Ser Tyr Asn Ala Glu Leu Leu Val Ala Leu Glu Asn
435 440 445

Gln His Thr Ile Asp Leu Thr Asp Ala Glu Met Asn Lys Leu Phe Glu
450 455 460

Lys Thr Arg Arg Gln Leu Arg Glu Asn Ala Glu Asp Met Gly Gly Gly
465 470 475 480

Cys Phe Lys Ile Tyr His Lys Cys Asp Asn Ala Cys Ile Glu Ser Ile
485 490 495

Arg Thr Gly Thr Tyr Asp His Tyr Ile Tyr Lys Asp Glu Ala Leu Asn
500 505 510

[0168] Asn Arg Phe Gln Ile Lys Gly Val Glu Leu Lys Ser Gly Tyr Lys Asp
515 520 525

Trp Ile Leu Trp Ile Ser Phe Ala Ile Ser Cys Phe Leu Ile Cys Val
530 535 540

Val Leu Leu Gly Phe Ile Met Trp Ala Cys Gln Lys Gly Asn Ile Arg
545 550 555 560

Cys Asn Ile Cys Ile
565

<210> 63

<211> 2280

<212> DNA

<213> 流感病毒

<220>

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	<222>	(1)..(2280)	
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	Met Glu Arg Ile Lys Glu Leu Arg Asp Leu Met Leu Gln Ser Arg Thr		
	1 5 10 15		
	cgc gag ata cta aca aaa act act gtg gac cac atg gcc ata atc aag	96	
	Arg Glu Ile Leu Thr Lys Thr Thr Val Asp His Met Ala Ile Ile Lys		
	20 25 30		
	aaa tac aca tca gga aga caa gag aag aac cct gca ctt agg atg aaa	144	
	Lys Tyr Thr Ser Gly Arg Gln Glu Lys Asn Pro Ala Leu Arg Met Lys		
	35 40 45		
	tgg atg atg gca atg aaa tac cca att aca gca gat aag agg ata atg	192	
	Trp Met Met Ala Met Lys Tyr Pro Ile Thr Ala Asp Lys Arg Ile Met		
	50 55 60		
[0169]	gag atg att cct gag aga aat gaa cag gga caa acc ctt tgg agc aaa	240	
	Glu Met Ile Pro Glu Arg Asn Glu Gln Gly Gln Thr Leu Trp Ser Lys		
	65 70 75 80		
	acg aac gat gct ggc tca gac cgc gta atg gta tca cct ctg gca gtg	288	
	Thr Asn Asp Ala Gly Ser Asp Arg Val Met Val Ser Pro Leu Ala Val		
	85 90 95		
	aca tgg tgg aat agg aat gga cca aca acg aac aca att cat tat cca	336	
	Thr Trp Trp Asn Arg Asn Gly Pro Thr Thr Asn Thr Ile His Tyr Pro		
	100 105 110		
	aaa gtc tac aaa act tat ttt gaa aag gtt gaa aga ttg aaa cac gga	384	
	Lys Val Tyr Lys Thr Tyr Phe Glu Lys Val Glu Arg Leu Lys His Gly		
	115 120 125		
	acc ttt ggc ccc gtt cat ttt agg aat caa gtc aag ata aga cga aga	432	
	Thr Phe Gly Pro Val His Phe Arg Asn Gln Val Lys Ile Arg Arg Arg		
	130 135 140		
	gtt gat gta aac cct ggt cac gcg gac ctc agt gct aaa gaa gca caa	480	
	Val Asp Val Asn Pro Gly His Ala Asp Leu Ser Ala Lys Glu Ala Gln		
	145 150 155 160		

	gat gtg atc atg gaa gtt gtt ttc cca aat gaa gtg gga gcc aga att	528
	Asp Val Ile Met Glu Val Val Phe Pro Asn Glu Val Gly Ala Arg Ile	
	165 170 175	
	cta aca tca gaa tca caa cta aca ata acc aaa gag aaa aag gaa gaa	576
	Leu Thr Ser Glu Ser Gln Leu Thr Ile Thr Lys Glu Lys Lys Glu Glu	
	180 185 190	
	ett cag gac tgc aaa att get ccc itg atg gta gca tac atg cta gaa	624
	Leu Gln Asp Cys Lys Ile Ala Pro Leu Met Val Ala Tyr Met Leu Glu	
	195 200 205	
	aga gag ttg gtc cga aaa aca agg ttc ctc cca gta gta ggc gga aca	672
	Arg Glu Leu Val Arg Lys Thr Arg Phe Leu Pro Val Val Gly Gly Thr	
	210 215 220	
	agc agt gta tac att gaa gtg ttg cat ctg act cag gga aca tgc tgg	720
	Ser Ser Val Tyr Ile Glu Val Leu His Leu Thr Gln Gly Thr Cys Trp	
	225 230 235 240	
[0170]	gag caa atg tac acc cca gga gga aaa gtt aga aac gat gat att gat	768
	Glu Gln Met Tyr Thr Pro Gly Gly Lys Val Arg Asn Asp Asp Ile Asp	
	245 250 255	
	caa agt tta att att gca gcc cgg aac ata gtg aga aga gca aca gta	816
	Gln Ser Leu Ile Ile Ala Ala Arg Asn Ile Val Arg Arg Ala Thr Val	
	260 265 270	
	tca gca gat cca cta gca tcc cta ctg gaa atg tgc cac agt aca cag	864
	Ser Ala Asp Pro Leu Ala Ser Leu Leu Glu Met Cys His Ser Thr Gln	
	275 280 285	
	att ggt gga aca agg atg gta gac atc ctt aag cag aac cca aca gag	912
	Ile Gly Gly Thr Arg Met Val Asp Ile Leu Lys Gln Asn Pro Thr Glu	
	290 295 300	
	gaa caa get gtg gat ata tgc aaa gca gca atg gga ttg aga att agc	960
	Glu Gln Ala Val Asp Ile Cys Lys Ala Ala Met Gly Leu Arg Ile Ser	
	305 310 315 320	
	tca tca ttc agc ttt ggt gga ttc acc ttc aaa agg aca agt gga tca	1008
	Ser Ser Phe Ser Phe Gly Gly Phe Thr Phe Lys Arg Thr Ser Gly Ser	
	325 330 335	

	tea gtc aag aga gaa gaa gaa atg ctt acg ggc aac ctt caa aca ttg	1056
	Ser Val Lys Arg Glu Glu Glu Met Leu Thr Gly Asn Leu Gln Thr Leu	
	340 345 350	
	aaa ata aga gtg cat gag ggc tat gaa gaa ttc aca atg gtc gga aga	1104
	Lys Ile Arg Val His Glu Gly Tyr Glu Glu Phe Thr Met Val Gly Arg	
	355 360 365	
	aga gca aca gcc att atc aga aag gca acc aga aga ttg att caa ttg	1152
	Arg Ala Thr Ala Ile Ile Arg Lys Ala Thr Arg Arg Leu Ile Gln Leu	
	370 375 380	
	ata gta agt ggg aga gat gaa caa tea att get gaa gca ata att gta	1200
	Ile Val Ser Gly Arg Asp Glu Gln Ser Ile Ala Glu Ala Ile Ile Val	
	385 390 395 400	
	gcc atg gtg ttt tcg caa gaa gat tgc atg ata aaa gca gtt cga ggc	1248
	Ala Met Val Phe Ser Gln Glu Asp Cys Met Ile Lys Ala Val Arg Gly	
	405 410 415	
[0171]	gat ttg aac ttt gtt aat aga gca aat cag cgt ttg aac ccc atg cat	1296
	Asp Leu Asn Phe Val Asn Arg Ala Asn Gln Arg Leu Asn Pro Met His	
	420 425 430	
	caa etc ttg agg cat ttc caa aaa gat gca aaa gtg ctt ttc caa aat	1344
	Gln Leu Leu Arg His Phe Gln Lys Asp Ala Lys Val Leu Phe Gln Asn	
	435 440 445	
	tgg gga att gaa ccc atc gac aat gta atg ggg atg att gga ata ttg	1392
	Trp Gly Ile Glu Pro Ile Asp Asn Val Met Gly Met Ile Gly Ile Leu	
	450 455 460	
	cct gac atg acc cca agc acc gag atg tea ttg aga gga gtg aga gtc	1440
	Pro Asp Met Thr Pro Ser Thr Glu Met Ser Leu Arg Gly Val Arg Val	
	465 470 475 480	
	agc aaa atg gga gtg gat gag tac tcc agc act gag aga gtg gtg gtg	1488
	Ser Lys Met Gly Val Asp Glu Tyr Ser Ser Thr Glu Arg Val Val Val	
	485 490 495	
	agc att gac cgt ttt tta aga gtt cgg gat caa agg gga aac ata cta	1536
	Ser Ile Asp Arg Phe Leu Arg Val Arg Asp Gln Arg Gly Asn Ile Leu	
	500 505 510	

	ctg tcc ect gaa gaa gtc agt gaa aca caa gga acg gaa aag ctg aca	1584
	Leu Ser Pro Glu Glu Val Ser Glu Thr Gln Gly Thr Glu Lys Leu Thr	
	515 520 525	
	ata att tat tgc tca tca atg atg tgg gag att aat ggt ccc gaa tca	1632
	Ile Ile Tyr Ser Ser Ser Met Met Trp Glu Ile Asn Gly Pro Glu Ser	
	530 535 540	
	gtg ttg gtc aat act tat caa tgg atc atc aga aac tgg gaa att gta	1680
	Val Leu Val Asn Thr Tyr Gln Trp Ile Ile Arg Asn Trp Glu Ile Val	
	545 550 555 560	
	aaa att cag tgg tca cag gac ccc aca atg tta tac aat aag ata gaa	1728
	Lys Ile Gln Trp Ser Gln Asp Pro Thr Met Leu Tyr Asn Lys Ile Glu	
	565 570 575	
	ttt gaa cca ttc caa tcc ctg gtc ect agg gcc acc aga agc caa tac	1776
	Phe Glu Pro Phe Gln Ser Leu Val Pro Arg Ala Thr Arg Ser Gln Tyr	
	580 585 590	
[0172]	agc ggt ttc gta aga acc ctg ttt cag caa atg cga gat gta ett gga	1824
	Ser Gly Phe Val Arg Thr Leu Phe Gln Gln Met Arg Asp Val Leu Gly	
	595 600 605	
	aca ttt gat act gct caa ata ata aaa ctc ctc cct ttt gcc gct gct	1872
	Thr Phe Asp Thr Ala Gln Ile Ile Lys Leu Leu Pro Phe Ala Ala Ala	
	610 615 620	
	ect ccg gaa cag agt agg atg cag ttc tet tet ttg act gtt aat gta	1920
	Pro Pro Glu Gln Ser Arg Met Gln Phe Ser Ser Leu Thr Val Asn Val	
	625 630 635 640	
	aga ggt tgc gga atg agg ata ctt gta aga gcc aat tcc cca gtg ttc	1968
	Arg Gly Ser Gly Met Arg Ile Leu Val Arg Gly Asn Ser Pro Val Phe	
	645 650 655	
	aac tac aat aaa gtc act aaa agg ctc aca gtc ctc gga aag gat gca	2016
	Asn Tyr Asn Lys Val Thr Lys Arg Leu Thr Val Leu Gly Lys Asp Ala	
	660 665 670	
	ggc ggc ctt act gag gac cca gat gaa ggt acg gct gga gta gag tet	2064
	Gly Ala Leu Thr Glu Asp Pro Asp Glu Gly Thr Ala Gly Val Glu Ser	
	675 680 685	

gct gtt cta aga ggg ttt ctc att tta ggt aaa gaa aac aag aga tat	2112
Ala Val Leu Arg Gly Phe Leu Ile Leu Gly Lys Glu Asn Lys Arg Tyr	
690 695 700	
ggc cca gca cta agc atc aat gaa ctt age aaa ctt gca aaa ggg gag	2160
Gly Pro Ala Leu Ser Ile Asn Glu Leu Ser Lys Leu Ala Lys Gly Glu	
705 710 715 720	
aaa gcc aat gta cta att ggg caa ggg gac gta gtg ttg gta atg aaa	2208
Lys Ala Asn Val Leu Ile Gly Gln Gly Asp Val Val Leu Val Met Lys	
725 730 735	
cgg aaa cgt gac tet agc ata ctt act gac agc cag aca gcg acc aaa	2256
Arg Lys Arg Asp Ser Ser Ile Leu Thr Asp Ser Gln Thr Ala Thr Lys	
740 745 750	
agg att cgg atg gcc atc aat tag	2280
Arg Ile Arg Met Ala Ile Asn	
755	

[0173]

<210> 64	
<211> 759	
<212> PRT	
<213> 流感病毒	
<400> 64	
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Arg Glu Ile Leu Thr Lys Thr Thr Val Asp His Met Ala Ile Ile Lys	
20 25 30	
Lys Tyr Thr Ser Gly Arg Gln Glu Lys Asn Pro Ala Leu Arg Met Lys	
35 40 45	
Trp Met Met Ala Met Lys Tyr Pro Ile Thr Ala Asp Lys Arg Ile Met	
50 55 60	

	Glu	Met	Ile	Pro	Glu	Arg	Asn	Glu	Gln	Gly	Gln	Thr	Leu	Trp	Ser	Lys
	65					70					75					80
	Thr	Asn	Asp	Ala	Gly	Ser	Asp	Arg	Val	Met	Val	Ser	Pro	Leu	Ala	Val
					85					90					95	
	Thr	Trp	Trp	Asn	Arg	Asn	Gly	Pro	Thr	Thr	Asn	Thr	Ile	His	Tyr	Pro
				100					105					110		
	Lys	Val	Tyr	Lys	Thr	Tyr	Phe	Glu	Lys	Val	Glu	Arg	Leu	Lys	His	Gly
			115					120					125			
	Thr	Phe	Gly	Pro	Val	His	Phe	Arg	Asn	Gln	Val	Lys	Ile	Arg	Arg	Arg
		130					135					140				
[0174]	Val	Asp	Val	Asn	Pro	Gly	His	Ala	Asp	Leu	Ser	Ala	Lys	Glu	Ala	Gln
	145					150					155					160
	Asp	Val	Ile	Met	Glu	Val	Val	Phe	Pro	Asn	Glu	Val	Gly	Ala	Arg	Ile
				165						170				175		
	Leu	Thr	Ser	Glu	Ser	Gln	Leu	Thr	Ile	Thr	Lys	Glu	Lys	Lys	Glu	Glu
			180						185					190		
	Leu	Gln	Asp	Cys	Lys	Ile	Ala	Pro	Leu	Met	Val	Ala	Tyr	Met	Leu	Glu
		195						200					205			
	Arg	Glu	Leu	Val	Arg	Lys	Thr	Arg	Phe	Leu	Pro	Val	Val	Gly	Gly	Thr
		210					215					220				
	Ser	Ser	Val	Tyr	Ile	Glu	Val	Leu	His	Leu	Thr	Gln	Gly	Thr	Cys	Trp
	225					230					235				240	

	Asp	Leu	Asn	Phe	Val	Asn	Arg	Ala	Asn	Gln	Arg	Leu	Asn	Pro	Met	His	
					420				425					430			
	Gln	Leu	Leu	Arg	His	Phe	Gln	Lys	Asp	Ala	Lys	Val	Leu	Phe	Gln	Asn	
					435				440					445			
	Trp	Gly	Ile	Glu	Pro	Ile	Asp	Asn	Val	Met	Gly	Met	Ile	Gly	Ile	Leu	
					450				455					460			
	Pro	Asp	Met	Thr	Pro	Ser	Thr	Glu	Met	Ser	Leu	Arg	Gly	Val	Arg	Val	
	465					470					475					480	
	Ser	Lys	Met	Gly	Val	Asp	Glu	Tyr	Ser	Ser	Thr	Glu	Arg	Val	Val	Val	
					485						490					495	
[0176]	Ser	Ile	Asp	Arg	Phe	Leu	Arg	Val	Arg	Asp	Gln	Arg	Gly	Asn	Ile	Leu	
					500						505					510	
	Leu	Ser	Pro	Glu	Glu	Val	Ser	Glu	Thr	Gln	Gly	Thr	Glu	Lys	Leu	Thr	
					515						520					525	
	Ile	Ile	Tyr	Ser	Ser	Ser	Met	Met	Trp	Glu	Ile	Asn	Gly	Pro	Glu	Ser	
					530						535					540	
	Val	Leu	Val	Asn	Thr	Tyr	Gln	Trp	Ile	Ile	Arg	Asn	Trp	Glu	Ile	Val	
	545						550					555				560	
	Lys	Ile	Gln	Trp	Ser	Gln	Asp	Pro	Thr	Met	Leu	Tyr	Asn	Lys	Ile	Glu	
					565						570					575	
	Phe	Glu	Pro	Phe	Gln	Ser	Leu	Val	Pro	Arg	Ala	Thr	Arg	Ser	Gln	Tyr	
					580						585					590	

	Ser Gly Phe Val Arg Thr Leu Phe Gln Gln Met Arg Asp Val Leu Gly	
	595	600 605
	Thr Phe Asp Thr Ala Gln Ile Ile Lys Leu Leu Pro Phe Ala Ala Ala	
	610	615 620
	Pro Pro Glu Gln Ser Arg Met Gln Phe Ser Ser Leu Thr Val Asn Val	
	625	630 635 640
	Arg Gly Ser Gly Met Arg Ile Leu Val Arg Gly Asn Ser Pro Val Phe	
		645 650 655
	Asn Tyr Asn Lys Val Thr Lys Arg Leu Thr Val Leu Gly Lys Asp Ala	
		660 665 670
[0177]	Gly Ala Leu Thr Glu Asp Pro Asp Glu Gly Thr Ala Gly Val Glu Ser	
	675	680 685
	Ala Val Leu Arg Gly Phe Leu Ile Leu Gly Lys Glu Asn Lys Arg Tyr	
	690	695 700
	Gly Pro Ala Leu Ser Ile Asn Glu Leu Ser Lys Leu Ala Lys Gly Glu	
	705	710 715 720
	Lys Ala Asn Val Leu Ile Gly Gln Gly Asp Val Val Leu Val Met Lys	
		725 730 735
	Arg Lys Arg Asp Ser Ser Ile Leu Thr Asp Ser Gln Thr Ala Thr Lys	
		740 745 750
	Arg Ile Arg Met Ala Ile Asn	
	755	

<210> 65

<211> 2274

<212> DNA

<213> 流感病毒

<220>

<221> CDS

<222> (1)..(2274)

<400> 65

atg gat gtc aat ccg act cta ctt ttc tta aag gtg cca gcg caa aat 48

Met Asp Val Asn Pro Thr Leu Leu Phe Leu Lys Val Pro Ala Gln Asn

1 5 10 15

gct ata agc aca aca ttc cct tat act gga gat cct ccc tac agt cat 96

Ala Ile Ser Thr Thr Phe Pro Tyr Thr Gly Asp Pro Pro Tyr Ser His

20 25 30

gga aca ggg aca gga tac acc atg gat act gtc aac aga aca cac caa 144

Gly Thr Gly Thr Gly Tyr Thr Met Asp Thr Val Asn Arg Thr His Gln

35 40 45

[0178]

tat tca gaa aaa ggg aaa tgg aca aca aac act gag att gga gca cca 192

Tyr Ser Glu Lys Gly Lys Trp Thr Thr Asn Thr Glu Ile Gly Ala Pro

50 55 60

caa ctt aat cca atc gat gga cca ctt cct gaa gac aat gaa cca agt 240

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

65 70 75 80

ggg tac gcc caa aca gat tgt gta ttg gaa gca atg gct ttc ctt gaa 288

Gly Tyr Ala Gln Thr Asp Cys Val Leu Glu Ala Met Ala Phe Leu Glu

85 90 95

gaa tcc cat ccc gga atc ttt gaa aat tcc tgt ctt gaa acg atg gag 336

Glu Ser His Pro Gly Ile Phe Glu Asn Ser Cys Leu Glu Thr Met Glu

100 105 110

gtg att cag cag aca aga gtg gac aaa cta aca caa ggc cga caa act 384

Val Ile Gln Gln Thr Arg Val Asp Lys Leu Thr Gln Gly Arg Gln Thr

115 120 125

tat gat tgg acc ttg aat agg aat caa cct gcc gca aca gca ctt gct 432

[0179]	Tyr Asp Trp Thr Leu Asn Arg Asn Gln Pro Ala Ala Thr Ala Leu Ala	
	130 135 140	
	aat aag att gaa gta ttc aga tca aat ggt ctg acc tcc aat gaa teg	480
	Asn Thr Ile Glu Val Phe Arg Ser Asn Gly Leu Thr Ser Asn Glu Ser	
	145 150 155 160	
	ggg aga ttg atg gac ttc ctc aaa gat gtc atg gag tcc atg aac aag	528
	Gly Arg Leu Met Asp Phe Leu Lys Asp Val Met Glu Ser Met Asn Lys	
	165 170 175	
	gag gaa atg gaa ata aca aca cac ttc caa cgg aag aga aga gta aga	576
	Glu Glu Met Glu Ile Thr Thr His Phe Gln Arg Lys Arg Arg Val Arg	
	180 185 190	
	gac aac atg aca aag aga atg ata aca cag aga acc ata gga aag aaa	624
	Asp Asn Met Thr Lys Arg Met Ile Thr Gln Arg Thr Ile Gly Lys Lys	
	195 200 205	
	aaa caa cga tta agc aga aag agc tat cta atc aga aca tta acc cta	672
	Lys Gln Arg Leu Ser Arg Lys Ser Tyr Leu Ile Arg Thr Leu Thr Leu	
	210 215 220	
	aac aca atg acc aag gac gct gag aga ggg aaa ttg aaa cga cga gea	720
	Asn Thr Met Thr Lys Asp Ala Glu Arg Gly Lys Leu Lys Arg Arg Ala	
	225 230 235 240	
	atc gct acc cca ggg atg cag ata aga gga ttt gta tat ttt gtt gaa	768
	Ile Ala Thr Pro Gly Met Gln Ile Arg Gly Phe Val Tyr Phe Val Glu	
	245 250 255	
	aca cta gct cga aga ata tgt gaa aag ctt gaa caa tca gga ttg cca	816
	Thr Leu Ala Arg Arg Ile Cys Glu Lys Leu Glu Gln Ser Gly Leu Pro	
	260 265 270	
	gtt ggc ggt aat gag aaa aag gcc aaa ctg gct aat gtc gtc aga aaa	864
	Val Gly Gly Asn Glu Lys Lys Ala Lys Leu Ala Asn Val Val Arg Lys	
	275 280 285	
	atg atg act aat tcc caa gac act gaa ctc tcc ttc acc atc act ggg	912
	Met Met Thr Asn Ser Gln Asp Thr Glu Leu Ser Phe Thr Ile Thr Gly	
	290 295 300	
	gac aat acc aaa tgg aat gaa aat cag aac cca cgc ata ttc ctg gea	960

	Asp Asn Thr Lys Trp Asn Glu Asn Gln Asn Pro Arg Ile Phe Leu Ala	
	305 310 315 320	
	atg atc aca tac ata act aga gat cag cca gaa tgg ttc aga aat gtt	1008
	Met Ile Thr Tyr Ile Thr Arg Asp Gln Pro Glu Trp Phe Arg Asn Val	
	325 330 335	
	cta agc att gea ccg att atg ttc tca aat aaa atg gea aga ctg ggg	1056
	Leu Ser Ile Ala Pro Ile Met Phe Ser Asn Lys Met Ala Arg Leu Gly	
	340 345 350	
	aaa gga tat atg ttt gaa agc aaa agt atg aaa ttg aga act caa ata	1104
	Lys Gly Tyr Met Phe Glu Ser Lys Ser Met Lys Leu Arg Thr Gln Ile	
	355 360 365	
	cca gea gaa atg cta gea agc att gac cta aaa tat ttc aat gat tca	1152
	Pro Ala Glu Met Leu Ala Ser Ile Asp Leu Lys Tyr Phe Asn Asp Ser	
	370 375 380	
	aca aaa aag aaa att gaa aag ata cga cca ctc ctg gtt gac ggg act	1200
	Thr Lys Lys Lys Ile Glu Lys Ile Arg Pro Leu Leu Val Asp Gly Thr	
[0180]	385 390 395 400	
	get tca ctg agt cct ggc atg atg atg gga atg ttc aac atg ttg agc	1248
	Ala Ser Leu Ser Pro Gly Met Met Met Gly Met Phe Asn Met Leu Ser	
	405 410 415	
	act gtg ctg ggt gta tcc ata tta aac ctg ggc cag agg aaa tat aca	1296
	Thr Val Leu Gly Val Ser Ile Leu Asn Leu Gly Gln Arg Lys Tyr Thr	
	420 425 430	
	aag acc aca tac tgg tgg gat ggt ctg caa tca tcc gat gac ttt get	1344
	Lys Thr Thr Tyr Trp Trp Asp Gly Leu Gln Ser Ser Asp Asp Phe Ala	
	435 440 445	
	ttg ata gtg aat gcg cct aat cat gaa gga ata caa get gga gta gac	1392
	Leu Ile Val Asn Ala Pro Asn His Glu Gly Ile Gln Ala Gly Val Asp	
	450 455 460	
	aga ttc tat aga act tgc aaa ctg gtc ggg atc aac atg agc aaa aag	1440
	Arg Phe Tyr Arg Thr Cys Lys Leu Val Gly Ile Asn Met Ser Lys Lys	
	465 470 475 480	
	aag tcc tac ata aat aga act gga aca ttc gaa ttc aca agc ttt ttc	1488

	Lys Ser Tyr Ile Asn Arg Thr Gly Thr Phe Glu Phe Thr Ser Phe Phe	
	485 490 495	
	tac egg tat ggt ttt gta gec aat ttc age atg gaa cta ccc agt ttt	1536
	Tyr Arg Tyr Gly Phe Val Ala Asn Phe Ser Met Glu Leu Pro Ser Phe	
	500 505 510	
	ggg gtt tcc gga ata aat gaa tct gca gac atg age att gga gtg aca	1584
	Gly Val Ser Gly Ile Asn Glu Ser Ala Asp Met Ser Ile Gly Val Thr	
	515 520 525	
	gtc atc aaa aac aac atg ata aat aat gat ctc ggt cct gec acg gca	1632
	Val Ile Lys Asn Asn Met Ile Asn Asn Asp Leu Gly Pro Ala Thr Ala	
	530 535 540	
	caa atg gca ctc caa ctc ttc att aag gat tat egg tac aca tac egg	1680
	Gln Met Ala Leu Gln Leu Phe Ile Lys Asp Tyr Arg Tyr Thr Tyr Arg	
	545 550 555 560	
	tgc cat aga ggt gat acc cag ata caa acc aga aga tct ttt gag ttg	1728
	Cys His Arg Gly Asp Thr Gln Ile Gln Thr Arg Arg Ser Phe Glu Leu	
[0181]	565 570 575	
	aag aaa ctg tgg gaa cag act cga tca aag act ggt cta ctg gta tca	1776
	Lys Lys Leu Trp Glu Gln Thr Arg Ser Lys Thr Gly Leu Leu Val Ser	
	580 585 590	
	gat ggg ggt cca aac cta tat aac atc aga aac cta cac atc ccg gaa	1824
	Asp Gly Gly Pro Asn Leu Tyr Asn Ile Arg Asn Leu His Ile Pro Glu	
	595 600 605	
	gtc tgt tta aaa tgg gag cta atg gat gaa gat tat aag ggg agg cta	1872
	Val Cys Leu Lys Trp Glu Leu Met Asp Glu Asp Tyr Lys Gly Arg Leu	
	610 615 620	
	tgc aat cca ttg aat cct ttc gtt agt cac aaa gaa att gaa tca gtc	1920
	Cys Asn Pro Leu Asn Pro Phe Val Ser His Lys Glu Ile Glu Ser Val	
	625 630 635 640	
	aac agt gca gta gta atg cct get cat ggc cct gec aaa age atg gag	1968
	Asn Ser Ala Val Val Met Pro Ala His Gly Pro Ala Lys Ser Met Glu	
	645 650 655	
	tat gat get gtt gca aca aca cat tet tgg atc ccc aag agg aac egg	2016

Tyr Asp Ala Val Ala Thr Thr His Ser Trp Ile Pro Lys Arg Asn Arg	
660 665 670	
tec ata ttg aac aca agc caa agg gga ata cta gaa gat gag cag atg	2064
Ser Ile Leu Asn Thr Ser Gln Arg Gly Ile Leu Glu Asp Glu Gln Met	
675 680 685	
tat cag aaa tgc tgc aac ctg ttt gaa aaa ttc ttc ccc age age tca	2112
Tyr Gln Lys Cys Cys Asn Leu Phe Glu Lys Phe Phe Pro Ser Ser Ser	
690 695 700	
tac aga aga cca gtc gga att tet agt atg gtt gag gcc atg gta tcc	2160
Tyr Arg Arg Pro Val Gly Ile Ser Ser Met Val Glu Ala Met Val Ser	
705 710 715 720	
agg gcc cgc att gat gca cga att gac ttc gaa tct gga cgg ata aag	2208
Arg Ala Arg Ile Asp Ala Arg Ile Asp Phe Glu Ser Gly Arg Ile Lys	
725 730 735	
aag gat gag ttc gct gag atc atg aag atc tgt tcc acc att gaa gag	2256
Lys Asp Glu Phe Ala Glu Ile Met Lys Ile Cys Ser Thr Ile Glu Glu	
740 745 750	
etc aga cgg caa aaa tag	2274
Leu Arg Arg Gln Lys	
755	

[0182]

<210> 66

<211> 757

<212> PRT

<213> 流感病毒

<400> 66

Met Asp Val Asn Pro Thr Leu Leu Phe Leu Lys Val Pro Ala Gln Asn
1 5 10 15

Ala Ile Ser Thr Thr Phe Pro Tyr Thr Gly Asp Pro Pro Tyr Ser His
20 25 30

Gly Thr Gly Thr Gly Tyr Thr Met Asp Thr Val Asn Arg Thr His Gln

[0183]

210	215	220
Asn Thr Met Thr Lys Asp Ala Glu Arg Gly Lys Leu Lys Arg Arg Ala		
225	230	235 240
Ile Ala Thr Pro Gly Met Gln Ile Arg Gly Phe Val Tyr Phe Val Glu		
245	250	255
Thr Leu Ala Arg Arg Ile Cys Glu Lys Leu Glu Gln Ser Gly Leu Pro		
260	265	270
Val Gly Gly Asn Glu Lys Lys Ala Lys Leu Ala Asn Val Val Arg Lys		
275	280	285
Met Met Thr Asn Ser Gln Asp Thr Glu Leu Ser Phe Thr Ile Thr Gly		
290	295	300
[0184]		
Asp Asn Thr Lys Trp Asn Glu Asn Gln Asn Pro Arg Ile Phe Leu Ala		
305	310	315 320
Met Ile Thr Tyr Ile Thr Arg Asp Gln Pro Glu Trp Phe Arg Asn Val		
325	330	335
Leu Ser Ile Ala Pro Ile Met Phe Ser Asn Lys Met Ala Arg Leu Gly		
340	345	350
Lys Gly Tyr Met Phe Glu Ser Lys Ser Met Lys Leu Arg Thr Gln Ile		
355	360	365
Pro Ala Glu Met Leu Ala Ser Ile Asp Leu Lys Tyr Phe Asn Asp Ser		
370	375	380
Thr Lys Lys Lys Ile Glu Lys Ile Arg Pro Leu Leu Val Asp Gly Thr		

385	390	395	400
Ala Ser Leu Ser Pro Gly Met Met Met Gly Met Phe Asn Met Leu Ser			
405	410	415	
Thr Val Leu Gly Val Ser Ile Leu Asn Leu Gly Gln Arg Lys Tyr Thr			
420	425	430	
Lys Thr Thr Tyr Trp Trp Asp Gly Leu Gln Ser Ser Asp Asp Phe Ala			
435	440	445	
Leu Ile Val Asn Ala Pro Asn His Glu Gly Ile Gln Ala Gly Val Asp			
450	455	460	
Arg Phe Tyr Arg Thr Cys Lys Leu Val Gly Ile Asn Met Ser Lys Lys			
465	470	475	480
[0185]			
Lys Ser Tyr Ile Asn Arg Thr Gly Thr Phe Glu Phe Thr Ser Phe Phe			
485	490	495	
Tyr Arg Tyr Gly Phe Val Ala Asn Phe Ser Met Glu Leu Pro Ser Phe			
500	505	510	
Gly Val Ser Gly Ile Asn Glu Ser Ala Asp Met Ser Ile Gly Val Thr			
515	520	525	
Val Ile Lys Asn Asn Met Ile Asn Asn Asp Leu Gly Pro Ala Thr Ala			
530	535	540	
Gln Met Ala Leu Gln Leu Phe Ile Lys Asp Tyr Arg Tyr Thr Tyr Arg			
545	550	555	560
Cys His Arg Gly Asp Thr Gln Ile Gln Thr Arg Arg Ser Phe Glu Leu			

	565	570	575
Lys Lys Leu Trp Glu Gln Thr Arg Ser Lys Thr Gly Leu Leu Val Ser			
580	585	590	
Asp Gly Gly Pro Asn Leu Tyr Asn Ile Arg Asn Leu His Ile Pro Glu			
595	600	605	
Val Cys Leu Lys Trp Glu Leu Met Asp Glu Asp Tyr Lys Gly Arg Leu			
610	615	620	
Cys Asn Pro Leu Asn Pro Phe Val Ser His Lys Glu Ile Glu Ser Val			
625	630	635	640
Asn Ser Ala Val Val Met Pro Ala His Gly Pro Ala Lys Ser Met Glu			
645	650	655	
[0186]			
Tyr Asp Ala Val Ala Thr Thr His Ser Trp Ile Pro Lys Arg Asn Arg			
660	665	670	
Ser Ile Leu Asn Thr Ser Gln Arg Gly Ile Leu Glu Asp Glu Gln Met			
675	680	685	
Tyr Gln Lys Cys Cys Asn Leu Phe Glu Lys Phe Phe Pro Ser Ser Ser			
690	695	700	
Tyr Arg Arg Pro Val Gly Ile Ser Ser Met Val Glu Ala Met Val Ser			
705	710	715	720
Arg Ala Arg Ile Asp Ala Arg Ile Asp Phe Glu Ser Gly Arg Ile Lys			
725	730	735	
Lys Asp Glu Phe Ala Glu Ile Met Lys Ile Cys Ser Thr Ile Glu Glu			

	740	745	750
	Leu Arg Arg Gln Lys		
	755		
<210>	67		
<211>	2151		
<212>	DNA		
<213>	流感病毒		
<220>			
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<222>	(1)..(2151)		
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	Met Glu Asp Phe Val Arg Gln Cys Phe Asn Pro Met Ile Val Glu Leu		
	1 5 10 15		
[0187]	gcg gaa aag gca atg aaa gaa tat gga gag aac ccg aaa atc gaa aca	96	
	Ala Glu Lys Ala Met Lys Glu Tyr Gly Glu Asn Pro Lys Ile Glu Thr		
	20 25 30		
	aac aaa ttt gca gca ata tgc act cac ttg gaa gtc tgc ttc atg tac	144	
	Asn Lys Phe Ala Ala Ile Cys Thr His Leu Glu Val Cys Phe Met Tyr		
	35 40 45		
	tcg gat ttc cac ttt ata aat gaa ctg ggt gag tca gtg gtc ata gag	192	
	Ser Asp Phe His Phe Ile Asn Glu Leu Gly Glu Ser Val Val Ile Glu		
	50 55 60		
	tct ggt gac cca aat gct ctt ttg aaa cac aga ttt gaa atc att gag	240	
	Ser Gly Asp Pro Asn Ala Leu Leu Lys His Arg Phe Glu Ile Ile Glu		
	65 70 75 80		
	ggg aga gat cga aca atg gca tgg aca gta gta aac agc atc tgc aac	288	
	Gly Arg Asp Arg Thr Met Ala Trp Thr Val Val Asn Ser Ile Cys Asn		
	85 90 95		
	acc aca aga gct gaa aaa cct aaa ttt ctt cca gat tta tac gac tat	336	
	Thr Thr Arg Ala Glu Lys Pro Lys Phe Leu Pro Asp Leu Tyr Asp Tyr		

	100	105	110	
	aaa gag aac aga ttt gtt gaa att ggt gig aca agg aga gaa gtt cac			384
	Lys Glu Asn Arg Phe Val Glu Ile Gly Val Thr Arg Arg Glu Val His			
	115	120	125	
	ata tac tac ctg gag aag gcc aac aaa ata aag tet gag aaa aca cat			432
	Ile Tyr Tyr Leu Glu Lys Ala Asn Lys Ile Lys Ser Glu Lys Thr His			
	130	135	140	
	atc cac att ttc tca ttt aca gga gaa gaa atg get aca aaa gcg gac			480
	Ile His Ile Phe Ser Phe Thr Gly Glu Glu Met Ala Thr Lys Ala Asp			
	145	150	155	160
	tat act ctt gat gaa gag agt aga gcc agg atc aag acc aga cta ttc			528
	Tyr Thr Leu Asp Glu Glu Ser Arg Ala Arg Ile Lys Thr Arg Leu Phe			
	165	170	175	
	act ata aga caa gaa atg gcc agt aga ggc etc tgg gat tcc ttt cgt			576
	Thr Ile Arg Gln Glu Met Ala Ser Arg Gly Leu Trp Asp Ser Phe Arg			
	180	185	190	
[0188]	cag tcc gag aga ggc gaa gag aca att gaa gaa aga ttt gaa atc aca			624
	Gln Ser Glu Arg Gly Glu Glu Thr Ile Glu Glu Arg Phe Glu Ile Thr			
	195	200	205	
	ggg acg atg cgc aag ctt gcc aat tac agt etc cca ccg aac ttc tcc			672
	Gly Thr Met Arg Lys Leu Ala Asn Tyr Ser Leu Pro Pro Asn Phe Ser			
	210	215	220	
	agc ctt gaa aat ttt aga gtc tat ata gat gga ttc gaa ccg aac ggc			720
	Ser Leu Glu Asn Phe Arg Val Tyr Ile Asp Gly Phe Glu Pro Asn Gly			
	225	230	235	240
	tgc att gag agt aag ctt tet caa atg tcc aaa gaa gta aat gcc aaa			768
	Cys Ile Glu Ser Lys Leu Ser Gln Met Ser Lys Glu Val Asn Ala Lys			
	245	250	255	
	ata gaa cca ttt tca aag aca aca ccc cga cca etc aaa atg cca ggt			816
	Ile Glu Pro Phe Ser Lys Thr Thr Pro Arg Pro Leu Lys Met Pro Gly			
	260	265	270	
	ggg cca ccc tgc cat cag cga tcc aaa ttc ttg cta atg gat get ctg			864
	Gly Pro Pro Cys His Gln Arg Ser Lys Phe Leu Leu Met Asp Ala Leu			

275	280	285	
aaa ctg agc att gag gac cca agt cac gag gga gag ggg ata cca cta			912
Lys Leu Ser Ile Glu Asp Pro Ser His Glu Gly Glu Gly Ile Pro Leu			
290	295	300	
tat gat gca atc aaa tgc atg aaa act ttc ttt gga tgg aaa gag ccc			960
Tyr Asp Ala Ile Lys Cys Met Lys Thr Phe Phe Gly Trp Lys Glu Pro			
305	310	315	320
agt att gtt aaa cca cat aaa aag ggt ata aac ccc aac tat ctc caa			1008
Ser Ile Val Lys Pro His Lys Lys Gly Ile Asn Pro Asn Tyr Leu Gln			
325	330	335	
act tgg aag caa gta tta gaa gaa ata caa gac ctt gag aac gaa gaa			1056
Thr Trp Lys Gln Val Leu Glu Glu Ile Gln Asp Leu Glu Asn Glu Glu			
340	345	350	
agg acc ccc aag acc aag aat atg aaa aaa aca age caa ttg aaa tgg			1104
Arg Thr Pro Lys Thr Lys Asn Met Lys Lys Thr Ser Gln Leu Lys Trp			
355	360	365	
[0189]			
gca cta ggt gaa aat atg gca cca gag aaa gtg gat ttt gag gat tgt			1152
Ala Leu Gly Glu Asn Met Ala Pro Glu Lys Val Asp Phe Glu Asp Cys			
370	375	380	
aaa gac atc aat gat tta aaa caa tat gac agt gat gag cca gaa gca			1200
Lys Asp Ile Asn Asp Leu Lys Gln Tyr Asp Ser Asp Glu Pro Glu Ala			
385	390	395	400
agg tct ctt gca agt tgg att caa agt gag ttc aac aag gct tgt gag			1248
Arg Ser Leu Ala Ser Trp Ile Gln Ser Glu Phe Asn Lys Ala Cys Glu			
405	410	415	
ctg aca gat tca agc tgg ata gag ctc gat gaa att ggg gag gat gtc			1296
Leu Thr Asp Ser Ser Trp Ile Glu Leu Asp Glu Ile Gly Glu Asp Val			
420	425	430	
gcc cca ata gaa tac att gcg agc atg agg aga aat tat ttt act gct			1344
Ala Pro Ile Glu Tyr Ile Ala Ser Met Arg Arg Asn Tyr Phe Thr Ala			
435	440	445	
gag att tcc cat tgt aga gca aca gaa tat ata atg aaa gga gtg tac			1392
Glu Ile Ser His Cys Arg Ala Thr Glu Tyr Ile Met Lys Gly Val Tyr			

450	455	460	
atc aac act gct cta ctc aat gca tcc tgt gct gcg atg gat gaa ttt			1440
Ile Asn Thr Ala Leu Leu Asn Ala Ser Cys Ala Ala Met Asp Glu Phe			
465	470	475	480
caa tta att ccg atg ata agt aaa tgc agg acc aaa gaa ggg aga agg			1488
Gln Leu Ile Pro Met Ile Ser Lys Cys Arg Thr Lys Glu Gly Arg Arg			
485	490	495	
aaa aca aat tta tat gga ttc ata ata aag gga agg tcc cat tta aga			1536
Lys Thr Asn Leu Tyr Gly Phe Ile Ile Lys Gly Arg Ser His Leu Arg			
500	505	510	
aat gat act gac gtg gtg aac ttt gta agt atg gaa ttt tct ctc act			1584
Asn Asp Thr Asp Val Val Asn Phe Val Ser Met Glu Phe Ser Leu Thr			
515	520	525	
gat cca aga ttt gag cca cac aaa tgg gaa aaa tac tgc gtt cta gaa			1632
Asp Pro Arg Phe Glu Pro His Lys Trp Glu Lys Tyr Cys Val Leu Glu			
530	535	540	
[0190] att gga gac atg ctt tta aga act gct gta ggt caa gtg tca aga ccc			1680
Ile Gly Asp Met Leu Leu Arg Thr Ala Val Gly Gln Val Ser Arg Pro			
545	550	555	560
atg ttt ttg tat gta agg aca aat gga acc tct aaa att aaa atg aaa			1728
Met Phe Leu Tyr Val Arg Thr Asn Gly Thr Ser Lys Ile Lys Met Lys			
565	570	575	
tgg gga atg gaa atg agg cgc tgc etc ctt cag tct ctg caa cag att			1776
Trp Gly Met Glu Met Arg Arg Cys Leu Leu Gln Ser Leu Gln Gln Ile			
580	585	590	
gaa agc atg atc gaa gct gag tcc tca gtc aaa gaa aag gac atg acc			1824
Glu Ser Met Ile Glu Ala Glu Ser Ser Val Lys Glu Lys Asp Met Thr			
595	600	605	
aaa gaa ttt ttt gag aac aaa tca gag aca tgg cct ata gga gag tcc			1872
Lys Glu Phe Phe Glu Asn Lys Ser Glu Thr Trp Pro Ile Gly Glu Ser			
610	615	620	
ccc aaa gga gtg gaa gag ggc tca atc ggg aag gtt tgc agg acc tta			1920
Pro Lys Gly Val Glu Glu Gly Ser Ile Gly Lys Val Cys Arg Thr Leu			

[0191]

255

Ser Gly Asp Pro Asn Ala Leu Leu Lys His Arg Phe Glu Ile Ile Glu
65 70 75 80

Gly Arg Asp Arg Thr Met Ala Trp Thr Val Val Asn Ser Ile Cys Asn
85 90 95

Thr Thr Arg Ala Glu Lys Pro Lys Phe Leu Pro Asp Leu Tyr Asp Tyr
100 105 110

Lys Glu Asn Arg Phe Val Glu Ile Gly Val Thr Arg Arg Glu Val His
115 120 125

Ile Tyr Tyr Leu Glu Lys Ala Asn Lys Ile Lys Ser Glu Lys Thr His
130 135 140

[0192]

Ile His Ile Phe Ser Phe Thr Gly Glu Glu Met Ala Thr Lys Ala Asp
145 150 155 160

Tyr Thr Leu Asp Glu Glu Ser Arg Ala Arg Ile Lys Thr Arg Leu Phe
165 170 175

Thr Ile Arg Gln Glu Met Ala Ser Arg Gly Leu Trp Asp Ser Phe Arg
180 185 190

Gln Ser Glu Arg Gly Glu Glu Thr Ile Glu Glu Arg Phe Glu Ile Thr
195 200 205

Gly Thr Met Arg Lys Leu Ala Asn Tyr Ser Leu Pro Pro Asn Phe Ser
210 215 220

Ser Leu Glu Asn Phe Arg Val Tyr Ile Asp Gly Phe Glu Pro Asn Gly
225 230 235 240

	Cys Ile Glu Ser Lys Leu Ser Gln Met Ser Lys Glu Val Asn Ala Lys	
	245	250 255
	Ile Glu Pro Phe Ser Lys Thr Thr Pro Arg Pro Leu Lys Met Pro Gly	
	260	265 270
	Gly Pro Pro Cys His Gln Arg Ser Lys Phe Leu Leu Met Asp Ala Leu	
	275	280 285
	Lys Leu Ser Ile Glu Asp Pro Ser His Glu Gly Glu Gly Ile Pro Leu	
	290	295 300
	Tyr Asp Ala Ile Lys Cys Met Lys Thr Phe Phe Gly Trp Lys Glu Pro	
	305	310 315 320
[0193]	Ser Ile Val Lys Pro His Lys Lys Gly Ile Asn Pro Asn Tyr Leu Gln	
	325	330 335
	Thr Trp Lys Gln Val Leu Glu Glu Ile Gln Asp Leu Glu Asn Glu Glu	
	340	345 350
	Arg Thr Pro Lys Thr Lys Asn Met Lys Lys Thr Ser Gln Leu Lys Trp	
	355	360 365
	Ala Leu Gly Glu Asn Met Ala Pro Glu Lys Val Asp Phe Glu Asp Cys	
	370	375 380
	Lys Asp Ile Asn Asp Leu Lys Gln Tyr Asp Ser Asp Glu Pro Glu Ala	
	385	390 395 400
	Arg Ser Leu Ala Ser Trp Ile Gln Ser Glu Phe Asn Lys Ala Cys Glu	
	405	410 415

Leu Thr Asp Ser Ser Trp Ile Glu Leu Asp Glu Ile Gly Glu Asp Val
420 425 430

Ala Pro Ile Glu Tyr Ile Ala Ser Met Arg Arg Asn Tyr Phe Thr Ala
435 440 445

Glu Ile Ser His Cys Arg Ala Thr Glu Tyr Ile Met Lys Gly Val Tyr
450 455 460

Ile Asn Thr Ala Leu Leu Asn Ala Ser Cys Ala Ala Met Asp Glu Phe
465 470 475 480

Gln Leu Ile Pro Met Ile Ser Lys Cys Arg Thr Lys Glu Gly Arg Arg
485 490 495

[0194] Lys Thr Asn Leu Tyr Gly Phe Ile Ile Lys Gly Arg Ser His Leu Arg
500 505 510

Asn Asp Thr Asp Val Val Asn Phe Val Ser Met Glu Phe Ser Leu Thr
515 520 525

Asp Pro Arg Phe Glu Pro His Lys Trp Glu Lys Tyr Cys Val Leu Glu
530 535 540

Ile Gly Asp Met Leu Leu Arg Thr Ala Val Gly Gln Val Ser Arg Pro
545 550 555 560

Met Phe Leu Tyr Val Arg Thr Asn Gly Thr Ser Lys Ile Lys Met Lys
565 570 575

Trp Gly Met Glu Met Arg Arg Cys Leu Leu Gln Ser Leu Gln Gln Ile
580 585 590

Glu Ser Met Ile Glu Ala Glu Ser Ser Val Lys Glu Lys Asp Met Thr
595 600 605

Lys Glu Phe Phe Glu Asn Lys Ser Glu Thr Trp Pro Ile Gly Glu Ser
610 615 620

Pro Lys Gly Val Glu Glu Gly Ser Ile Gly Lys Val Cys Arg Thr Leu
625 630 635 640

Leu Ala Lys Ser Val Phe Asn Ser Leu Tyr Ala Ser Pro Gln Leu Glu
645 650 655

Gly Phe Ser Ala Glu Ser Arg Lys Leu Leu Leu Ile Val Gln Ala Leu
660 665 670

[0195] Arg Asp Asp Leu Glu Pro Gly Thr Phe Asp Ile Gly Gly Leu Tyr Glu
675 680 685

Ser Ile Glu Glu Cys Leu Ile Asn Asp Pro Trp Val Leu Leu Asn Ala
690 695 700

Ser Trp Phe Asn Ser Phe Leu Thr His Ala Leu Lys
705 710 715

<210> 69

<211> 844

<212> DNA

<213> 流感病毒

<220>

<221> CDS

<222> (1).. (690)

[0196]	<400> 69	
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	Met Asp Ser Asn Thr Val Ser Ser Phe Gln Val Asp Cys Phe Leu Trp	
	1 5 10 15	
	cat gtc cgt aaa cga ttc gca gac caa gaa ctg ggt gat gcc cca ttc	96
	His Val Arg Lys Arg Phe Ala Asp Gln Glu Leu Gly Asp Ala Pro Phe	
	20 25 30	
	ctt gac cgg ctt cgc cga gac cag aag tcc cta agg gga aga ggt agc	144
	Leu Asp Arg Leu Arg Arg Asp Gln Lys Ser Leu Arg Gly Arg Gly Ser	
	35 40 45	
	act ctt ggt ctg gac atc gaa aca gcc act cat gca gga aag cag ata	192
	Thr Leu Gly Leu Asp Ile Glu Thr Ala Thr His Ala Gly Lys Gln Ile	
	50 55 60	
	gtg gag cag att ctg gaa aag gaa tca gat gag gca ctt aaa atg acc	240
	Val Glu Gln Ile Leu Glu Lys Glu Ser Asp Glu Ala Leu Lys Met Thr	
	65 70 75 80	
	att gcc tet gtt cct gct tca cgc tac tta act gac atg act ctt gat	288
	Ile Ala Ser Val Pro Ala Ser Arg Tyr Leu Thr Asp Met Thr Leu Asp	
	85 90 95	
	gag atg tca aga gac tgg ttc atg etc atg ccc aag caa aaa gta aca	336
	Glu Met Ser Arg Asp Trp Phe Met Leu Met Pro Lys Gln Lys Val Thr	
	100 105 110	
	ggc tcc cta tgt ata aga atg gac cag gca atc atg gat aag aac atc	384
	Gly Ser Leu Cys Ile Arg Met Asp Gln Ala Ile Met Asp Lys Asn Ile	
	115 120 125	
	ata ctt aaa gca aac ttt agt gtg att ttc gaa agg ctg gaa aca cta	432
	Ile Leu Lys Ala Asn Phe Ser Val Ile Phe Glu Arg Leu Glu Thr Leu	
	130 135 140	
	ata cta ctt aga gcc ttc acc gaa gaa gga gca gtc gtt ggc gaa att	480
	Ile Leu Leu Arg Ala Phe Thr Glu Glu Gly Ala Val Val Gly Glu Ile	
	145 150 155 160	
	tca cca tta cct tet ctt cca gga cat act aat gag gat gtc aaa aat	528
	Ser Pro Leu Pro Ser Leu Pro Gly His Thr Asn Glu Asp Val Lys Asn	
	165 170 175	

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gea att ggg gtc ctc atc gga gga ctt aaa tgg aat gat aat acg gtt      576
Ala Ile Gly Val Leu Ile Gly Gly Leu Lys Trp Asn Asp Asn Thr Val
      180              185              190

aga atc tct gaa act cta cag aga ttc get tgg aga agc agt cat gaa      624
Arg Ile Ser Glu Thr Leu Gln Arg Phe Ala Trp Arg Ser Ser His Glu
      195              200              205

aat ggg aga cct tca ttc cct tca aaa cag aaa cga aaa atg gag aga      672
Asn Gly Arg Pro Ser Phe Pro Ser Lys Gln Lys Arg Lys Met Glu Arg
      210              215              220

aca att aag cca gaa att tgaagaaata agatgggtga ttgaagaagt      720
Thr Ile Lys Pro Glu Ile
      225              230

gegacataga ttgaaaaata cagaaaatag ttttgaacaa ataacatita tgcaagcett      780

acaactattg ctggaagtag aacaagagat aagaacttic tcgtttcage ttattttaatg      840

ataa      844

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[0197]

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<210> 70
<211> 230
<212> PRT
<213> 流感病毒

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<400> 70

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Met Asp Ser Asn Thr Val Ser Ser Phe Gln Val Asp Cys Phe Leu Trp
1              5              10              15

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His Val Arg Lys Arg Phe Ala Asp Gln Glu Leu Gly Asp Ala Pro Phe
      20              25              30

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Leu Asp Arg Leu Arg Arg Asp Gln Lys Ser Leu Arg Gly Arg Gly Ser
      35              40              45

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Thr Leu Gly Leu Asp Ile Glu Thr Ala Thr His Ala Gly Lys Gln Ile

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

[0198]

Ile Leu Leu Arg Ala Phe Thr Glu Glu Gly Ala Val Val Gly Glu Ile		
145	150	155 160
Ser Pro Leu Pro Ser Leu Pro Gly His Thr Asn Glu Asp Val Lys Asn		
	165	170 175
Ala Ile Gly Val Leu Ile Gly Gly Leu Lys Trp Asn Asp Asn Thr Val		
	180	185 190
Arg Ile Ser Glu Thr Leu Gln Arg Phe Ala Trp Arg Ser Ser His Glu		
	195	200 205
Asn Gly Arg Pro Ser Phe Pro Ser Lys Gln Lys Arg Lys Met Glu Arg		
	210	215 220
Thr Ile Lys Pro Glu Ile		

225 230

<210> 71

<211> 1497

<212> DNA

<213> 流感病毒

<220>

<221> CDS

<222> (1)..(1497)

<400> 71

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Met Ala Ser Gln Gly Thr Lys Arg Ser Tyr Glu Gln Met Glu Thr Asp
1 5 10 15

ggg gaa cgc cag aat gca act gaa atc aga gca tct gtc gga agg atg 96
Gly Glu Arg Gln Asn Ala Thr Glu Ile Arg Ala Ser Val Gly Arg Met
20 25 30

[0199]

gtg gga gga atc gga cgg ttt tat gtc cag atg tgt act gag ctt aaa 144
Val Gly Gly Ile Gly Arg Phe Tyr Val Gln Met Cys Thr Glu Leu Lys
35 40 45

cta aac gac cat gaa ggg cgg ctg att cag aac agc ata aca ata gaa 192
Leu Asn Asp His Glu Gly Arg Leu Ile Gln Asn Ser Ile Thr Ile Glu
50 55 60

agg atg gtg ctt tcg gca ttc gac gaa aga aga aac aag tat ctc gag 240
Arg Met Val Leu Ser Ala Phe Asp Glu Arg Arg Asn Lys Tyr Leu Glu
65 70 75 80

gag cat ccc agt gct ggg aaa gac cct aag aaa acg gga ggc ccg ata 288
Glu His Pro Ser Ala Gly Lys Asp Pro Lys Lys Thr Gly Gly Pro Ile
85 90 95

tac aga aga aaa gat ggg aaa tgg atg agg gaa etc atc etc cat gat 336
Tyr Arg Arg Lys Asp Gly Lys Trp Met Arg Glu Leu Ile Leu His Asp
100 105 110

aaa gaa gaa atc atg aga atc tgg cgt cag gcc aac aat ggt gaa gac 384
Lys Glu Glu Ile Met Arg Ile Trp Arg Gln Ala Asn Asn Gly Glu Asp

115	120	125	
gct act gct ggt ctt act cat atg atg atc tgg cac tcc aat ctc aat			432
Ala Thr Ala Gly Leu Thr His Met Met Ile Trp His Ser Asn Leu Asn			
130	135	140	
gac acc aca tac caa aga aca agg gct ctt gtt cgg act ggg atg gat			480
Asp Thr Thr Tyr Gln Arg Thr Arg Ala Leu Val Arg Thr Gly Met Asp			
145	150	155	160
ccc aga atg tgc tct ctg atg caa ggc tca acc ctc cca cgg aga tct			528
Pro Arg Met Cys Ser Leu Met Gln Gly Ser Thr Leu Pro Arg Arg Ser			
165	170	175	
gga gcc gct ggt gct gca gta aaa ggc gtt gga aca atg gta atg gaa			576
Gly Ala Ala Gly Ala Ala Val Lys Gly Val Gly Thr Met Val Met Glu			
180	185	190	
ctc atc aga atg atc aag cgc gga ata aat gat cgg aat ttc tgg aga			624
Leu Ile Arg Met Ile Lys Arg Gly Ile Asn Asp Arg Asn Phe Trp Arg			
195	200	205	
[0200]			
ggt gaa aat ggt cga aga acc aga att gct tat gaa aga atg tgc aat			672
Gly Glu Asn Gly Arg Arg Thr Arg Ile Ala Tyr Glu Arg Met Cys Asn			
210	215	220	
atc ctc aaa ggg aaa ttt cag aca gca gca caa cgg gct atg atg gac			720
Ile Leu Lys Gly Lys Phe Gln Thr Ala Ala Gln Arg Ala Met Met Asp			
225	230	235	240
cag gtg agg gaa ggc cgc aat cct gga aac gct gag att gag gat ctc			768
Gln Val Arg Glu Gly Arg Asn Pro Gly Asn Ala Glu Ile Glu Asp Leu			
245	250	255	
att ttc ttg gca cga tca gca ctt att itg aga gga tca gta gcc cat			816
Ile Phe Leu Ala Arg Ser Ala Leu Ile Leu Arg Gly Ser Val Ala His			
260	265	270	
aaa tca tgc cta cct gcc tgt gtt tat ggc ctt gca cta acc agt ggg			864
Lys Ser Cys Leu Pro Ala Cys Val Tyr Gly Leu Ala Leu Thr Ser Gly			
275	280	285	
tat gac ttt gag aag gaa gga tac tct ctg gtt gga att gat cct ttc			912
Tyr Asp Phe Glu Lys Glu Gly Tyr Ser Leu Val Gly Ile Asp Pro Phe			

290	295	300	
aaa cta ctc cag aac agt caa att ttc agt cta atc aga cca aaa gaa			960
Lys Leu Leu Gln Asn Ser Gln Ile Phe Ser Leu Ile Arg Pro Lys Glu			
305	310	315	320
aac cca gca cac aaa agc cag ttg gtg tgg atg gca tgc cat tet gea			1008
Asn Pro Ala His Lys Ser Gln Leu Val Trp Met Ala Cys His Ser Ala			
325	330	335	
gca ttt gag gat ctg aga gtt tta aat ttc att aga gga acc aaa gta			1056
Ala Phe Glu Asp Leu Arg Val Leu Asn Phe Ile Arg Gly Thr Lys Val			
340	345	350	
atc cca aga gga cag tta aca acc aga gga gtt caa att get tea aat			1104
Ile Pro Arg Gly Gln Leu Thr Thr Arg Gly Val Gln Ile Ala Ser Asn			
355	360	365	
gaa aac atg gag aca ata aat tet age aca ctt gaa ctg aga agc aaa			1152
Glu Asn Met Glu Thr Ile Asn Ser Ser Thr Leu Glu Leu Arg Ser Lys			
370	375	380	
[0201] tat tgg gca ata agg acc aga agc gga gga aac acc agt caa cag aga			1200
Tyr Trp Ala Ile Arg Thr Arg Ser Gly Gly Asn Thr Ser Gln Gln Arg			
385	390	395	400
gca tet gca gga cag ata agt gtg caa cct act ttc tea gta cag aga			1248
Ala Ser Ala Gly Gln Ile Ser Val Gln Pro Thr Phe Ser Val Gln Arg			
405	410	415	
aat ctt ccc ttt gag aga gca acc att atg get gca ttc act ggt aac			1296
Asn Leu Pro Phe Glu Arg Ala Thr Ile Met Ala Ala Phe Thr Gly Asn			
420	425	430	
act gaa gga agg act tcc gac atg aga acg gaa atc ata agg atg atg			1344
Thr Glu Gly Arg Thr Ser Asp Met Arg Thr Glu Ile Ile Arg Met Met			
435	440	445	
gaa aat gcc aaa tca gaa gat gtg tet ttc cag ggg cgg gga gtc ttc			1392
Glu Asn Ala Lys Ser Glu Asp Val Ser Phe Gln Gly Arg Gly Val Phe			
450	455	460	
gag ctc teg gac gaa aag gca acg aac cag atc gtg cct tcc ttt gac			1440
Glu Leu Ser Asp Glu Lys Ala Thr Asn Pro Ile Val Pro Ser Phe Asp			

465	470	475	480	
atg agc aat gaa ggg tct tat ttc ttc gga gac aat get gag gag ttt				1488
Met Ser Asn Glu Gly Ser Tyr Phe Phe Gly Asp Asn Ala Glu Glu Phe				
	485	490	495	
gac agt taa				1497
Asp Ser				
<210> 72				
<211> 498				
<212> PRT				
<213> 流感病毒				
<400> 72				
Met Ala Ser Gln Gly Thr Lys Arg Ser Tyr Glu Gln Met Glu Thr Asp				
1	5	10	15	
[0202]				
Gly Glu Arg Gln Asn Ala Thr Glu Ile Arg Ala Ser Val Gly Arg Met				
	20	25	30	
Val Gly Gly Ile Gly Arg Phe Tyr Val Gln Met Cys Thr Glu Leu Lys				
	35	40	45	
Leu Asn Asp His Glu Gly Arg Leu Ile Gln Asn Ser Ile Thr Ile Glu				
	50	55	60	
Arg Met Val Leu Ser Ala Phe Asp Glu Arg Arg Asn Lys Tyr Leu Glu				
	65	70	75	80
Glu His Pro Ser Ala Gly Lys Asp Pro Lys Lys Thr Gly Gly Pro Ile				
	85	90	95	
Tyr Arg Arg Lys Asp Gly Lys Trp Met Arg Glu Leu Ile Leu His Asp				
	100	105	110	

	Lys	Glu	Glu	Ile	Met	Arg	Ile	Trp	Arg	Gln	Ala	Asn	Asn	Gly	Glu	Asp	
	115				120				125								
	Ala	Thr	Ala	Gly	Leu	Thr	His	Met	Met	Ile	Trp	His	Ser	Asn	Leu	Asn	
	130				135				140								
	Asp	Thr	Thr	Tyr	Gln	Arg	Thr	Arg	Ala	Leu	Val	Arg	Thr	Gly	Met	Asp	
	145				150				155				160				
	Pro	Arg	Met	Cys	Ser	Leu	Met	Gln	Gly	Ser	Thr	Leu	Pro	Arg	Arg	Ser	
	165				170				175								
	Gly	Ala	Ala	Gly	Ala	Ala	Val	Lys	Gly	Val	Gly	Thr	Met	Val	Met	Glu	
	180				185				190								
[0203]	Leu	Ile	Arg	Met	Ile	Lys	Arg	Gly	Ile	Asn	Asp	Arg	Asn	Phe	Trp	Arg	
	195				200				205								
	Gly	Glu	Asn	Gly	Arg	Arg	Thr	Arg	Ile	Ala	Tyr	Glu	Arg	Met	Cys	Asn	
	210				215				220								
	Ile	Leu	Lys	Gly	Lys	Phe	Gln	Thr	Ala	Ala	Gln	Arg	Ala	Met	Met	Asp	
	225				230				235				240				
	Gln	Val	Arg	Glu	Gly	Arg	Asn	Pro	Gly	Asn	Ala	Glu	Ile	Glu	Asp	Leu	
	245				250				255								
	Ile	Phe	Leu	Ala	Arg	Ser	Ala	Leu	Ile	Leu	Arg	Gly	Ser	Val	Ala	His	
	260				265				270								
	Lys	Ser	Cys	Leu	Pro	Ala	Cys	Val	Tyr	Gly	Leu	Ala	Leu	Thr	Ser	Gly	
	275				280				285								

	Tyr	Asp	Phe	Glu	Lys	Glu	Gly	Tyr	Ser	Leu	Val	Gly	Ile	Asp	Pro	Phe	
	290						295					300					
	Lys	Leu	Leu	Gln	Asn	Ser	Gln	Ile	Phe	Ser	Leu	Ile	Arg	Pro	Lys	Glu	
	305					310					315				320		
	Asn	Pro	Ala	His	Lys	Ser	Gln	Leu	Val	Trp	Met	Ala	Cys	His	Ser	Ala	
					325					330					335		
	Ala	Phe	Glu	Asp	Leu	Arg	Val	Leu	Asn	Phe	Ile	Arg	Gly	Thr	Lys	Val	
				340					345					350			
	Ile	Pro	Arg	Gly	Gln	Leu	Thr	Thr	Arg	Gly	Val	Gln	Ile	Ala	Ser	Asn	
				355				360					365				
[0204]	Glu	Asn	Met	Glu	Thr	Ile	Asn	Ser	Ser	Thr	Leu	Glu	Leu	Arg	Ser	Lys	
	370						375					380					
	Tyr	Trp	Ala	Ile	Arg	Thr	Arg	Ser	Gly	Gly	Asn	Thr	Ser	Gln	Gln	Arg	
	385					390					395				400		
	Ala	Ser	Ala	Gly	Gln	Ile	Ser	Val	Gln	Pro	Thr	Phe	Ser	Val	Gln	Arg	
				405						410					415		
	Asn	Leu	Pro	Phe	Glu	Arg	Ala	Thr	Ile	Met	Ala	Ala	Phe	Thr	Gly	Asn	
				420						425					430		
	Thr	Glu	Gly	Arg	Thr	Ser	Asp	Met	Arg	Thr	Glu	Ile	Ile	Arg	Met	Met	
				435				440					445				
	Glu	Asn	Ala	Lys	Ser	Glu	Asp	Val	Ser	Phe	Gln	Gly	Arg	Gly	Val	Phe	
	450						455					460					

Glu Leu Ser Asp Glu Lys Ala Thr Asn Pro Ile Val Pro Ser Phe Asp
 465 470 475 480

Met Ser Asn Glu Gly Ser Tyr Phe Phe Gly Asp Asn Ala Glu Glu Phe
 485 490 495

Asp Ser

<210> 73
 <211> 1413
 <212> DNA
 <213> 流感病毒

<220>
 <221> CDS
 <222> (1)..(1413)

[0205]

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 Met Asn Pro Asn Gln Lys Ile Ile Ala Ile Gly Phe Ala Ser Leu Gly
 1 5 10 15
 ata tta atc att aat gtc att ctc cat gta gtc agc att ata gta aca 96
 Ile Leu Ile Ile Asn Val Ile Leu His Val Val Ser Ile Ile Val Thr
 20 25 30
 gta ctg gtc ctc aat aac aat aga aca gat ctg aac tgc aaa ggg acg 144
 Val Leu Val Leu Asn Asn Asn Arg Thr Asp Leu Asn Cys Lys Gly Thr
 35 40 45
 atc ata aga gaa tac aat gaa aca gta aga gta gaa aaa ctt act caa 192
 Ile Ile Arg Glu Tyr Asn Glu Thr Val Arg Val Glu Lys Leu Thr Gln
 50 55 60
 tgg tat aat acc agt aca att aag tac ata gag aga cct tca aat gaa 240
 Trp Tyr Asn Thr Ser Thr Ile Lys Tyr Ile Glu Arg Pro Ser Asn Glu
 65 70 75 80

	tac tac atg aat aac act gaa cca ctt tgt gag gcc caa ggc ttt gca	288
	Tyr Tyr Met Asn Asn Thr Glu Pro Leu Cys Glu Ala Gln Gly Phe Ala	
	85 90 95	
	cca ttt tcc aaa gat aat gga ata cga att ggg teg aga ggc cat gtt	336
	Pro Phe Ser Lys Asp Asn Gly Ile Arg Ile Gly Ser Arg Gly His Val	
	100 105 110	
	ttt gtg ata aga gaa cct ttt gta tca tgt teg ccc tca gaa tgt aga	384
	Phe Val Ile Arg Glu Pro Phe Val Ser Cys Ser Pro Ser Glu Cys Arg	
	115 120 125	
	acc ttt ttc ctc aca cag ggc tca tta ctc aat gac aaa cat tet aac	432
	Thr Phe Phe Leu Thr Gln Gly Ser Leu Leu Asn Asp Lys His Ser Asn	
	130 135 140	
	ggc aca ata aag gat cga agt ccg tat agg act ttg atg agt gtc aaa	480
	Gly Thr Ile Lys Asp Arg Ser Pro Tyr Arg Thr Leu Met Ser Val Lys	
	145 150 155 160	
[0206]	ata ggg caa tca cct aat gta tat caa gct agg ttt gaa teg gtg gca	528
	Ile Gly Gln Ser Pro Asn Val Tyr Gln Ala Arg Phe Glu Ser Val Ala	
	165 170 175	
	tgg tca gca aca gca tgc cat gat gga aaa aaa tgg atg aca gtt gga	576
	Trp Ser Ala Thr Ala Cys His Asp Gly Lys Lys Trp Met Thr Val Gly	
	180 185 190	
	gtc aca ggg ccc gac aat caa gca att gca gta gtg aac tat gga ggt	624
	Val Thr Gly Pro Asp Asn Gln Ala Ile Ala Val Val Asn Tyr Gly Gly	
	195 200 205	
	gtt ccg gtt gat att att aat tca tgg gca ggg gat att tta aga acc	672
	Val Pro Val Asp Ile Ile Asn Ser Trp Ala Gly Asp Ile Leu Arg Thr	
	210 215 220	
	caa gaa tca tca tgc acc tgc att aaa gga gac tgt tat tgg gta atg	720
	Gln Glu Ser Ser Cys Thr Cys Ile Lys Gly Asp Cys Tyr Trp Val Met	
	225 230 235 240	
	act gat gga ccg gca aat agg caa gct aaa tat agg ata ttc aaa gca	768
	Thr Asp Gly Pro Ala Asn Arg Gln Ala Lys Tyr Arg Ile Phe Lys Ala	
	245 250 255	

	aaa gat gga aga gta att gga caa act gat ata agt ttc aat ggg gga	816
	Lys Asp Gly Arg Val Ile Gly Gln Thr Asp Ile Ser Phe Asn Gly Gly	
	260 265 270	
	cac ata gag gag tgt tct tgt tac ccc aat gaa ggg aag gtg gaa tgc	864
	His Ile Glu Glu Cys Ser Cys Tyr Pro Asn Glu Gly Lys Val Glu Cys	
	275 280 285	
	ata tgc agg gac aat tgg act gga aca aat aga cca att ctg gta ata	912
	Ile Cys Arg Asp Asn Trp Thr Gly Thr Asn Arg Pro Ile Leu Val Ile	
	290 295 300	
	tct tct gat cta teg tac aca gtt gga tat ttg tgt get ggc att ccc	960
	Ser Ser Asp Leu Ser Tyr Thr Val Gly Tyr Leu Cys Ala Gly Ile Pro	
	305 310 315 320	
	act gac act cct agg gga gag gat agt caa ttc aca ggc tca tgt aca	1008
	Thr Asp Thr Pro Arg Gly Glu Asp Ser Gln Phe Thr Gly Ser Cys Thr	
	325 330 335	
[0207]	agt cct ttg gga aat aaa gga tac ggt gta aaa ggc ttc ggg ttt cga	1056
	Ser Pro Leu Gly Asn Lys Gly Tyr Gly Val Lys Gly Phe Gly Phe Arg	
	340 345 350	
	caa gga act gac gta tgg gcc gga agg aca att agt agg act tca aga	1104
	Gln Gly Thr Asp Val Trp Ala Gly Arg Thr Ile Ser Arg Thr Ser Arg	
	355 360 365	
	tca gga ttc gaa ata ata aaa atc agg aat ggt tgg aca cag aac agt	1152
	Ser Gly Phe Glu Ile Ile Lys Ile Arg Asn Gly Trp Thr Gln Asn Ser	
	370 375 380	
	aag gac caa atc agg agg caa gtg att atc gat gac cca aat tgg tca	1200
	Lys Asp Gln Ile Arg Arg Gln Val Ile Ile Asp Asp Pro Asn Trp Ser	
	385 390 395 400	
	gga tat agc ggt tct ttc aca ttg ccg gtt gaa ctg aca aaa aag gga	1248
	Gly Tyr Ser Gly Ser Phe Thr Leu Pro Val Glu Leu Thr Lys Lys Gly	
	405 410 415	
	tgt ttg gtc ccc tgt ttc tgg gtt gaa atg att aga ggt aaa cct gaa	1296
	Cys Leu Val Pro Cys Phe Trp Val Glu Met Ile Arg Gly Lys Pro Glu	
	420 425 430	

gaa aca aca ata tgg acc tct agc agc tcc att gtg atg tgt gga gta 1344
 Glu Thr Thr Ile Trp Thr Ser Ser Ser Ser Ile Val Met Cys Gly Val
 435 440 445

gat cat aaa att gcc agt tgg tca tgg cac gat gga get att ctt ccc 1392
 Asp His Lys Ile Ala Ser Trp Ser Trp His Asp Gly Ala Ile Leu Pro
 450 455 460

ttt gac atc gat aag atg taa 1413
 Phe Asp Ile Asp Lys Met
 465 470

<210> 74

<211> 470

<212> PRT

<213> 流感病毒

<400> 74

[0208]

Met Asn Pro Asn Gln Lys Ile Ile Ala Ile Gly Phe Ala Ser Leu Gly
 1 5 10 15

Ile Leu Ile Ile Asn Val Ile Leu His Val Val Ser Ile Ile Val Thr
 20 25 30

Val Leu Val Leu Asn Asn Asn Arg Thr Asp Leu Asn Cys Lys Gly Thr
 35 40 45

Ile Ile Arg Glu Tyr Asn Glu Thr Val Arg Val Glu Lys Leu Thr Gln
 50 55 60

Trp Tyr Asn Thr Ser Thr Ile Lys Tyr Ile Glu Arg Pro Ser Asn Glu
 65 70 75 80

Tyr Tyr Met Asn Asn Thr Glu Pro Leu Cys Glu Ala Gln Gly Phe Ala
 85 90 95

Pro Phe Ser Lys Asp Asn Gly Ile Arg Ile Gly Ser Arg Gly His Val
100 105 110

Phe Val Ile Arg Glu Pro Phe Val Ser Cys Ser Pro Ser Glu Cys Arg
115 120 125

Thr Phe Phe Leu Thr Gln Gly Ser Leu Leu Asn Asp Lys His Ser Asn
130 135 140

Gly Thr Ile Lys Asp Arg Ser Pro Tyr Arg Thr Leu Met Ser Val Lys
145 150 155 160

Ile Gly Gln Ser Pro Asn Val Tyr Gln Ala Arg Phe Glu Ser Val Ala
165 170 175

[0209] Trp Ser Ala Thr Ala Cys His Asp Gly Lys Lys Trp Met Thr Val Gly
180 185 190

Val Thr Gly Pro Asp Asn Gln Ala Ile Ala Val Val Asn Tyr Gly Gly
195 200 205

Val Pro Val Asp Ile Ile Asn Ser Trp Ala Gly Asp Ile Leu Arg Thr
210 215 220

Gln Glu Ser Ser Cys Thr Cys Ile Lys Gly Asp Cys Tyr Trp Val Met
225 230 235 240

Thr Asp Gly Pro Ala Asn Arg Gln Ala Lys Tyr Arg Ile Phe Lys Ala
245 250 255

Lys Asp Gly Arg Val Ile Gly Gln Thr Asp Ile Ser Phe Asn Gly Gly
260 265 270

His Ile Glu Glu Cys Ser Cys Tyr Pro Asn Glu Gly Lys Val Glu Cys
275 280 285

Ile Cys Arg Asp Asn Trp Thr Gly Thr Asn Arg Pro Ile Leu Val Ile
290 295 300

Ser Ser Asp Leu Ser Tyr Thr Val Gly Tyr Leu Cys Ala Gly Ile Pro
305 310 315 320

Thr Asp Thr Pro Arg Gly Glu Asp Ser Gln Phe Thr Gly Ser Cys Thr
325 330 335

Ser Pro Leu Gly Asn Lys Gly Tyr Gly Val Lys Gly Phe Gly Phe Arg
340 345 350

[0210]

Gln Gly Thr Asp Val Trp Ala Gly Arg Thr Ile Ser Arg Thr Ser Arg
355 360 365

Ser Gly Phe Glu Ile Ile Lys Ile Arg Asn Gly Trp Thr Gln Asn Ser
370 375 380

Lys Asp Gln Ile Arg Arg Gln Val Ile Ile Asp Asp Pro Asn Trp Ser
385 390 395 400

Gly Tyr Ser Gly Ser Phe Thr Leu Pro Val Glu Leu Thr Lys Lys Gly
405 410 415

Cys Leu Val Pro Cys Phe Trp Val Glu Met Ile Arg Gly Lys Pro Glu
420 425 430

Glu Thr Thr Ile Trp Thr Ser Ser Ser Ser Ile Val Met Cys Gly Val
435 440 445

Asp His Lys Ile Ala Ser Trp Ser Trp His Asp Gly Ala Ile Leu Pro
 450 455 460

Phe Asp Ile Asp Lys Met
 465 470

<210> 75
 <211> 981
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 <213> 流感病毒

<220>
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 <222> (1).. (756)

<400> 75
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 Met Ser Leu Leu Thr Glu Val Glu Thr Tyr Val Leu Ser Ile Val Pro
 [0211] 1 5 10 15

tca ggc ccc ctc aaa gcc gag atc gcg cag aga ctt gaa gat gtc ttt 96
 Ser Gly Pro Leu Lys Ala Glu Ile Ala Gln Arg Leu Glu Asp Val Phe
 20 25 30

gcg gga aag aac acc gat ctt gag gca ctc atg gaa tgg cta aag aca 144
 Ala Gly Lys Asn Thr Asp Leu Glu Ala Leu Met Glu Trp Leu Lys Thr
 35 40 45

aga cca atc ctg tca cct ctg act aaa ggg att tta gga ttt gta ttc 192
 Arg Pro Ile Leu Ser Pro Leu Thr Lys Gly Ile Leu Gly Phe Val Phe
 50 55 60

acg ctc acc gtg ccc agt gag cga gga ctg cag cgt aga cgc ttt gtc 240
 Thr Leu Thr Val Pro Ser Glu Arg Gly Leu Gln Arg Arg Arg Phe Val
 65 70 75 80

caa aat gcc ctt agt gga aac gga gat cca aac aac atg gac aga gca 288
 Gln Asn Ala Leu Ser Gly Asn Gly Asp Pro Asn Asn Met Asp Arg Ala
 85 90 95

	gta aaa ctg tac agg aag ctt aaa aga gaa ata aca ttc cat ggg gca	336
	Val Lys Leu Tyr Arg Lys Leu Lys Arg Glu Ile Thr Phe His Gly Ala	
	100 105 110	
	aaa gag gtg gca ctc agc tat tcc act ggt gca cta gcc agc tgc atg	384
	Lys Glu Val Ala Leu Ser Tyr Ser Thr Gly Ala Leu Ala Ser Cys Met	
	115 120 125	
	gga ctc ata tac aac aga atg gga act gtt aca acc gaa gtg gca ttt	432
	Gly Leu Ile Tyr Asn Arg Met Gly Thr Val Thr Thr Glu Val Ala Phe	
	130 135 140	
	ggc ctg gta tgc gcc aca tgt gaa cag att get gat tcc cag cat cga	480
	Gly Leu Val Cys Ala Thr Cys Glu Gln Ile Ala Asp Ser Gln His Arg	
	145 150 155 160	
	tct cac agg cag atg gtg aca aca acc aac cea tta atc aga cat gaa	528
	Ser His Arg Gln Met Val Thr Thr Thr Asn Pro Leu Ile Arg His Glu	
	165 170 175	
[0212]	aac aga atg gta tta gcc agt acc acg gct aaa gcc atg gaa cag atg	576
	Asn Arg Met Val Leu Ala Ser Thr Thr Ala Lys Ala Met Glu Gln Met	
	180 185 190	
	gca gga teg agt gag cag gca gca gag gcc atg gag gtt gct agt agg	624
	Ala Gly Ser Ser Glu Gln Ala Ala Glu Ala Met Glu Val Ala Ser Arg	
	195 200 205	
	gct agg cag atg gta cag gca atg aga acc att ggg acc cac cct agc	672
	Ala Arg Gln Met Val Gln Ala Met Arg Thr Ile Gly Thr His Pro Ser	
	210 215 220	
	tcc agt gcc ggt ttg aaa gat gat ctc ctt gaa aat tta cag gcc tac	720
	Ser Ser Ala Gly Leu Lys Asp Asp Leu Leu Glu Asn Leu Gln Ala Tyr	
	225 230 235 240	
	cag aaa cgg atg gga gtg caa atg cag cga ttc aag tgatcctctc	766
	Gln Lys Arg Met Gly Val Gln Met Gln Arg Phe Lys	
	245 250	
	gtcattgcag caagtatcat tgggatcttg cacttgatat tgtggattct tgaatgtctt	826
	ttcttcaaatt tcatttatcg tgccttaaa tacgggttga aaagagggcc ttctacggaa	886

ggagtaccctg agtctatgag ggaagaatat cggcaggaac agcagaatgc tgtggatgtt 946

gacgatggtc atttgtcaa catagagctg gagta 981

<210> 76

<211> 252

<212> PRT

<213> 流感病毒

<400> 76

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1 5 10 15

Ser Gly Pro Leu Lys Ala Glu Ile Ala Gln Arg Leu Glu Asp Val Phe
20 25 30

[0213] Ala Gly Lys Asn Thr Asp Leu Glu Ala Leu Met Glu Trp Leu Lys Thr
35 40 45

Arg Pro Ile Leu Ser Pro Leu Thr Lys Gly Ile Leu Gly Phe Val Phe
50 55 60

Thr Leu Thr Val Pro Ser Glu Arg Gly Leu Gln Arg Arg Arg Phe Val
65 70 75 80

Gln Asn Ala Leu Ser Gly Asn Gly Asp Pro Asn Asn Met Asp Arg Ala
85 90 95

Val Lys Leu Tyr Arg Lys Leu Lys Arg Glu Ile Thr Phe His Gly Ala
100 105 110

Lys Glu Val Ala Leu Ser Tyr Ser Thr Gly Ala Leu Ala Ser Cys Met
115 120 125

Gly Leu Ile Tyr Asn Arg Met Gly Thr Val Thr Thr Glu Val Ala Phe
130 135 140

Gly Leu Val Cys Ala Thr Cys Glu Gln Ile Ala Asp Ser Gln His Arg
145 150 155 160

Ser His Arg Gln Met Val Thr Thr Thr Asn Pro Leu Ile Arg His Glu
165 170 175

Asn Arg Met Val Leu Ala Ser Thr Thr Ala Lys Ala Met Glu Gln Met
180 185 190

Ala Gly Ser Ser Glu Gln Ala Ala Glu Ala Met Glu Val Ala Ser Arg
195 200 205

Ala Arg Gln Met Val Gln Ala Met Arg Thr Ile Gly Thr His Pro Ser
210 215 220

[0214]

Ser Ser Ala Gly Leu Lys Asp Asp Leu Leu Glu Asn Leu Gln Ala Tyr
225 230 235 240

Gln Lys Arg Met Gly Val Gln Met Gln Arg Phe Lys
245 250

<210> 77

<211> 1698

<212> DNA

<213> 流感病毒

<220>

<221> CDS

<222> (1)..(1698)

<400> 77

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48

Met Lys Thr Thr Ile Ile Leu Ile Leu Leu Thr His Trp Ala Tyr Ser	
1 5 10 15	
caa aac cca atc agt ggc aat aac aca gcc aca ctg tgt ctg gga cac	96
Gln Asn Pro Ile Ser Gly Asn Asn Thr Ala Thr Leu Cys Leu Gly His	
20 25 30	
cat gca gta gca aat gga aca ttg gta aaa aca atg agt gat gat caa	144
His Ala Val Ala Asn Gly Thr Leu Val Lys Thr Met Ser Asp Asp Gln	
35 40 45	
att gag gtg aca aat gct aca gaa tta gtt cag age att tca atg ggg	192
Ile Glu Val Thr Asn Ala Thr Glu Leu Val Gln Ser Ile Ser Met Gly	
50 55 60	
aaa ata tgc aac aaa tca tat aga att cta gat gga aga aat tgc aca	240
Lys Ile Cys Asn Lys Ser Tyr Arg Ile Leu Asp Gly Arg Asn Cys Thr	
65 70 75 80	
tta ata gat gca atg cta gga gac ccc cac tgt gac gcc ttt cag tat	288
Leu Ile Asp Ala Met Leu Gly Asp Pro His Cys Asp Ala Phe Gln Tyr	
85 90 95	
[0215]	
gag agt tgg gac ctg ttt ata gaa aga age age gct ttc age aat tgc	336
Glu Ser Trp Asp Leu Phe Ile Glu Arg Ser Ser Ala Phe Ser Asn Cys	
100 105 110	
tac cca tat gac atc cct gac tat gca ccg ctg cga tcc att gta gca	384
Tyr Pro Tyr Asp Ile Pro Asp Tyr Ala Pro Leu Arg Ser Ile Val Ala	
115 120 125	
tcc tca ggg aca gtg gaa ttc aca gca gag gga ttc aca tgg aca ggt	432
Ser Ser Gly Thr Val Glu Phe Thr Ala Glu Gly Phe Thr Trp Thr Gly	
130 135 140	
gta act caa aac gga aga agt gga gcc tgc aaa agg gga tca gcc gat	480
Val Thr Gln Asn Gly Arg Ser Gly Ala Cys Lys Arg Gly Ser Ala Asp	
145 150 155 160	
agt ttc ttt age cga ctg aat tgg cta aca aaa tct gga age tct tac	528
Ser Phe Phe Ser Arg Leu Asn Trp Leu Thr Lys Ser Gly Ser Ser Tyr	
165 170 175	
ccc aca ttg aat gtg aca atg cct aac aat aaa aat ttc gac aag cta	576

[0216]

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

[0217]	Phe Ile Glu Asn Gly Trp Glu Gly Met Val Asp Gly Trp Tyr Gly Phe 355 360 365	
	ega tat caa aac tet gaa gga aca ggg caa got gca gat cta aag agc Arg Tyr Gln Asn Ser Glu Gly Thr Gly Gln Ala Ala Asp Leu Lys Ser 370 375 380	1152
	act caa gca gcc atc gac cag att aat gga aag tta aac aga gtg att Thr Gln Ala Ala Ile Asp Gln Ile Asn Gly Lys Leu Asn Arg Val Ile 385 390 395 400	1200
	gaa aga acc aat gag aaa ttc cat caa ata gag aag gaa ttc tca gaa Glu Arg Thr Asn Glu Lys Phe His Gln Ile Glu Lys Glu Phe Ser Glu 405 410 415	1248
	gta gaa gga aga att cag gac ttg gag aaa tat gta gaa gac acc aaa Val Glu Gly Arg Ile Gln Asp Leu Glu Lys Tyr Val Glu Asp Thr Lys 420 425 430	1296
	ata gac cta tgg tcc tac aat gca gaa ttg ctg gtg got cta gaa aat Ile Asp Leu Trp Ser Tyr Asn Ala Glu Leu Leu Val Ala Leu Glu Asn 435 440 445	1344
	caa cat aca att gac tta aca gat gca gaa atg aat aaa tta ttt gag Gln His Thr Ile Asp Leu Thr Asp Ala Glu Met Asn Lys Leu Phe Glu 450 455 460	1392
	aag act aga cgc cag tta aga gaa aac gca gaa gac atg gga ggt gga Lys Thr Arg Arg Gln Leu Arg Glu Asn Ala Glu Asp Met Gly Gly Gly 465 470 475 480	1440
	tgt ttc aag att tac cac aaa tgt gat aat gca tgc att gaa tca ata Cys Phe Lys Ile Tyr His Lys Cys Asp Asn Ala Cys Ile Glu Ser Ile 485 490 495	1488
	aga act ggg aca tat gac cat tac ata tac aaa gat gaa gca tta aac Arg Thr Gly Thr Tyr Asp His Tyr Ile Tyr Lys Asp Glu Ala Leu Asn 500 505 510	1536
	aat cga ttt cag atc aaa ggt gta gag ttg aaa tca ggc tac aaa gat Asn Arg Phe Gln Ile Lys Gly Val Glu Leu Lys Ser Gly Tyr Lys Asp 515 520 525	1584
	tgg ata ctg tgg att tca ttc gcc ata tca tgc ttc tta att tgc gtt	1632

Trp Ile Leu Trp Ile Ser Phe Ala Ile Ser Cys Phe Leu Ile Cys Val
530 535 540

ggt cta ttt ggt ttc att atg tgg gct tgc caa aaa ggc aac atc aga 1680
Val Leu Leu Gly Phe Ile Met Trp Ala Cys Gln Lys Gly Asn Ile Arg
545 550 555 560

tgc aac att tgc att tga 1698
Cys Asn Ile Cys Ile
565

<210> 78

<211> 565

<212> PRT

<213> 流感病毒

<400> 78

Met Lys Thr Thr Ile Ile Leu Ile Leu Leu Thr His Trp Ala Tyr Ser
1 5 10 15

[0218]

Gln Asn Pro Ile Ser Gly Asn Asn Thr Ala Thr Leu Cys Leu Gly His
20 25 30

His Ala Val Ala Asn Gly Thr Leu Val Lys Thr Met Ser Asp Asp Gln
35 40 45

Ile Glu Val Thr Asn Ala Thr Glu Leu Val Gln Ser Ile Ser Met Gly
50 55 60

Lys Ile Cys Asn Lys Ser Tyr Arg Ile Leu Asp Gly Arg Asn Cys Thr
65 70 75 80

Leu Ile Asp Ala Met Leu Gly Asp Pro His Cys Asp Ala Phe Gln Tyr
85 90 95

Glu Ser Trp Asp Leu Phe Ile Glu Arg Ser Ser Ala Phe Ser Asn Cys

	100		105		110
Tyr Pro Tyr Asp Ile Pro Asp Tyr Ala Pro Leu Arg Ser Ile Val Ala					
	115		120		125
Ser Ser Gly Thr Val Glu Phe Thr Ala Glu Gly Phe Thr Trp Thr Gly					
	130		135		140
Val Thr Gln Asn Gly Arg Ser Gly Ala Cys Lys Arg Gly Ser Ala Asp					
145		150		155	160
Ser Phe Phe Ser Arg Leu Asn Trp Leu Thr Lys Ser Gly Ser Ser Tyr					
	165		170		175
Pro Thr Leu Asn Val Thr Met Pro Asn Asn Lys Asn Phe Asp Lys Leu					
	180		185		190
[0219]					
Tyr Ile Trp Gly Ile His His Pro Ser Ser Asn Gln Glu Gln Thr Lys					
	195		200		205
Leu Tyr Ile Gln Glu Ser Gly Arg Val Thr Val Ser Thr Lys Arg Ser					
210		215		220	
Gln Gln Thr Ile Ile Pro Asn Ile Gly Ser Arg Pro Leu Val Arg Gly					
225		230		235	240
Gln Ser Gly Arg Ile Ser Ile Tyr Trp Thr Ile Val Lys Pro Gly Asp					
	245		250		255
Ile Leu Met Ile Asn Ser Asn Gly Asn Leu Val Ala Pro Arg Gly Tyr					
260		265		270	
Phe Lys Leu Asn Thr Gly Lys Ser Ser Val Met Arg Ser Asp Val Pro					

275	280	285
Ile Asp Ile Cys Val Ser Glu Cys Ile Thr Pro Asn Gly Ser Ile Ser		
290	295	300
Asn Asp Lys Pro Phe Gln Asn Val Asn Lys Val Thr Tyr Gly Lys Cys		
305	310	315 320
Pro Lys Tyr Ile Arg Gln Asn Thr Leu Lys Leu Ala Thr Gly Met Arg		
	325	330 335
Asn Val Pro Glu Lys Gln Thr Arg Gly Ile Phe Gly Ala Ile Ala Gly		
	340	345 350
Phe Ile Glu Asn Gly Trp Glu Gly Met Val Asp Gly Trp Tyr Gly Phe		
	355	360 365
[0220]		
Arg Tyr Gln Asn Ser Glu Gly Thr Gly Gln Ala Ala Asp Leu Lys Ser		
370	375	380
Thr Gln Ala Ala Ile Asp Gln Ile Asn Gly Lys Leu Asn Arg Val Ile		
385	390	395 400
Glu Arg Thr Asn Glu Lys Phe His Gln Ile Glu Lys Glu Phe Ser Glu		
	405	410 415
Val Glu Gly Arg Ile Gln Asp Leu Glu Lys Tyr Val Glu Asp Thr Lys		
	420	425 430
Ile Asp Leu Trp Ser Tyr Asn Ala Glu Leu Leu Val Ala Leu Glu Asn		
	435	440 445
Gln His Thr Ile Asp Leu Thr Asp Ala Glu Met Asn Lys Leu Phe Glu		

450	455	460
Lys Thr Arg Arg Gln Leu Arg Glu Asn Ala Glu Asp Met Gly Gly Gly		
465	470	475 480
Cys Phe Lys Ile Tyr His Lys Cys Asp Asn Ala Cys Ile Glu Ser Ile		
485	490	495
Arg Thr Gly Thr Tyr Asp His Tyr Ile Tyr Lys Asp Glu Ala Leu Asn		
500	505	510
Asn Arg Phe Gln Ile Lys Gly Val Glu Leu Lys Ser Gly Tyr Lys Asp		
515	520	525
Trp Ile Leu Trp Ile Ser Phe Ala Ile Ser Cys Phe Leu Ile Cys Val		
530	535	540

[0221]

Val Leu Leu Gly Phe Ile Met Trp Ala Cys Gln Lys Gly Asn Ile Arg		
545	550	555 560
Cys Asn Ile Cys Ile		
565		

<210> 79
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<400> 79
tatgeategc tccgatccat

20

<210> 80
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	<400> 80 gtctccacttc ttccgttttg a	21
	<210> 81 <211> 30 <212> DNA <213> 流感病毒	
	<400> 81 aattcacagc agagggattc acatggacag	30
	<210> 82 <211> 24 <212> DNA <213> 流感病毒	
[0222]	<220> <221> variation <222> (7).. (7) <223> r = a or g	
	<400> 82 catggartgg ctaaagacaa gacc	24
	<210> 83 <211> 24 <212> DNA <213> 流感病毒	
	<220> <221> variation <222> (18).. (18) <223> k = g or t	
	<400> 83 agggcatttt ggacaaakeg teta	24

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	<211> 18	
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	<213> 流感病毒	
	<400> 84	
	acgctcaccg tgcceagt	18
	<210> 85	
	<211> 28	
	<212> DNA	
	<213> 流感病毒	
	<400> 85	
	tatttgtctc agggagcaaa agcagggg	28
	<210> 86	
	<211> 42	
	<212> DNA	
[0223]	<213> 流感病毒	
	<400> 86	
	tgtaatacga ctcactatag ggctccactt cttecgtttt ga	42
	<210> 87	
	<211> 30	
	<212> DNA	
	<213> 流感病毒	
	<400> 87	
	gatcgctctt cagggageaa aagcaggtag	30
	<210> 88	
	<211> 40	
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	<213> 流感病毒	
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	tgtaatacga ctcactatag ggcattttgg acaaagegtc	40

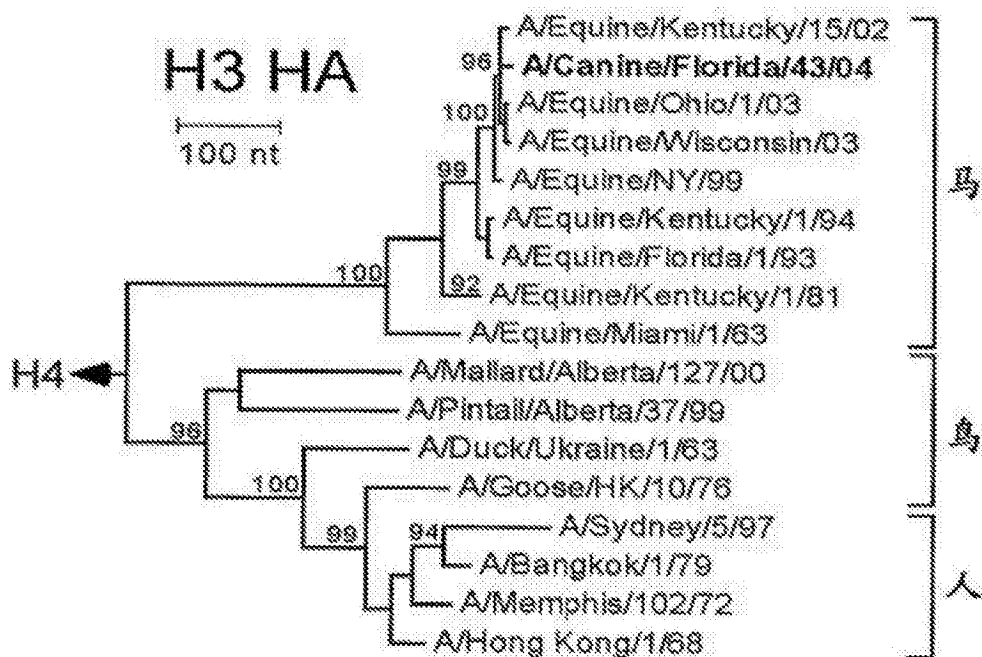


图1A

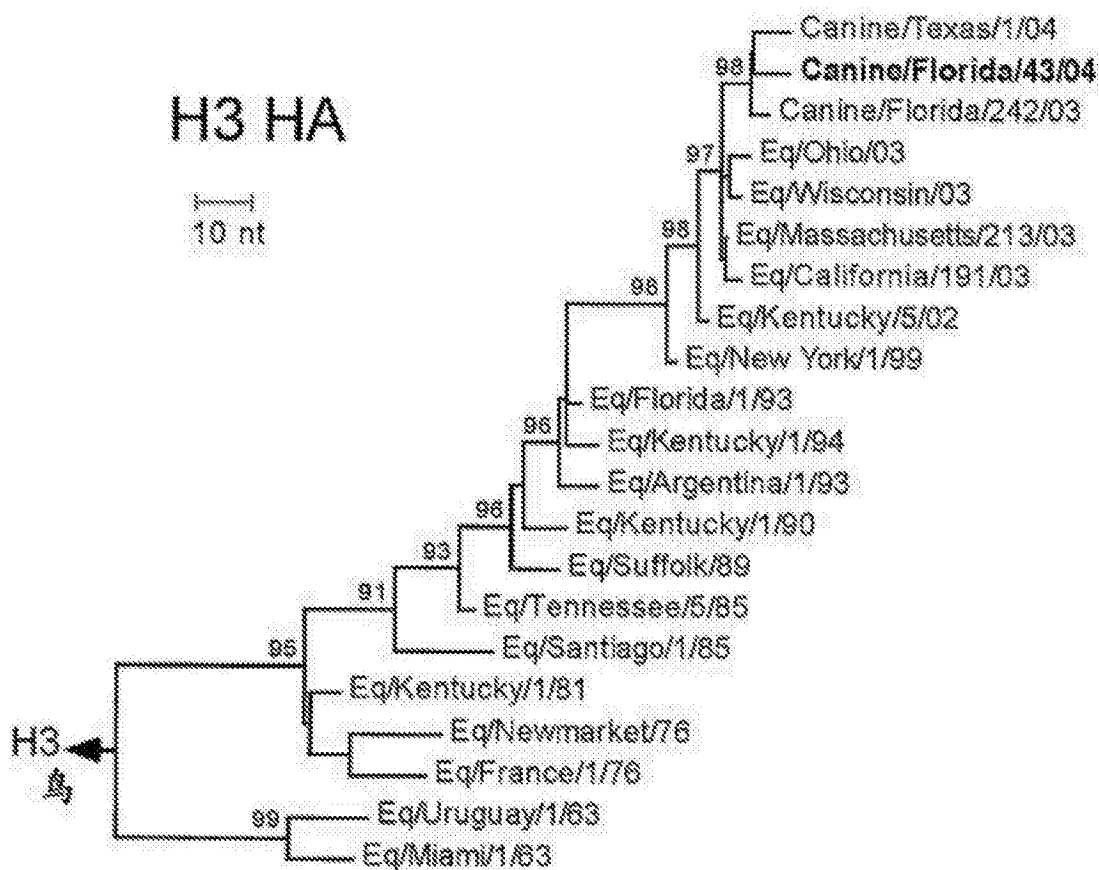


图1B

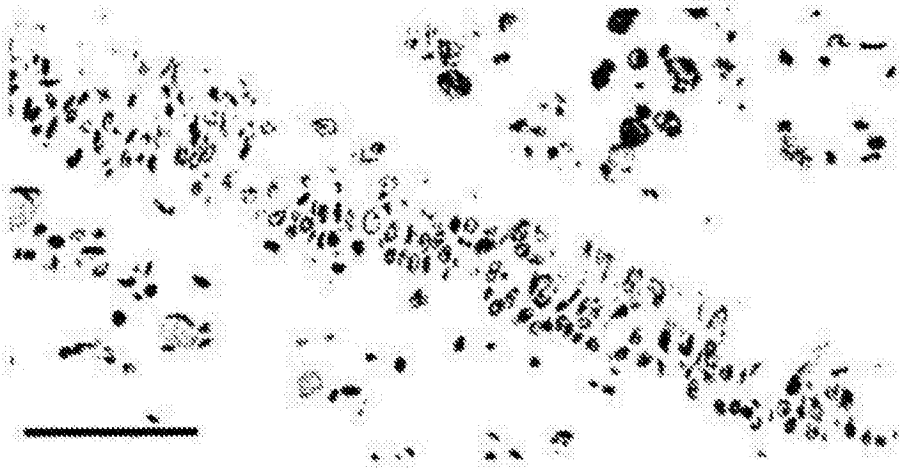


图2A

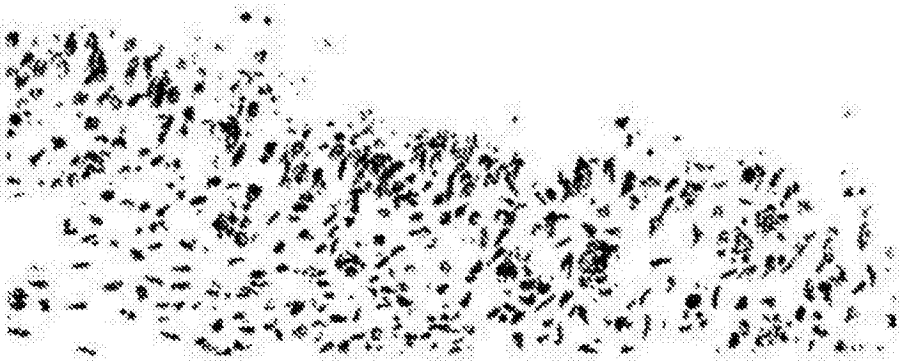


图2B



图3A



图3B

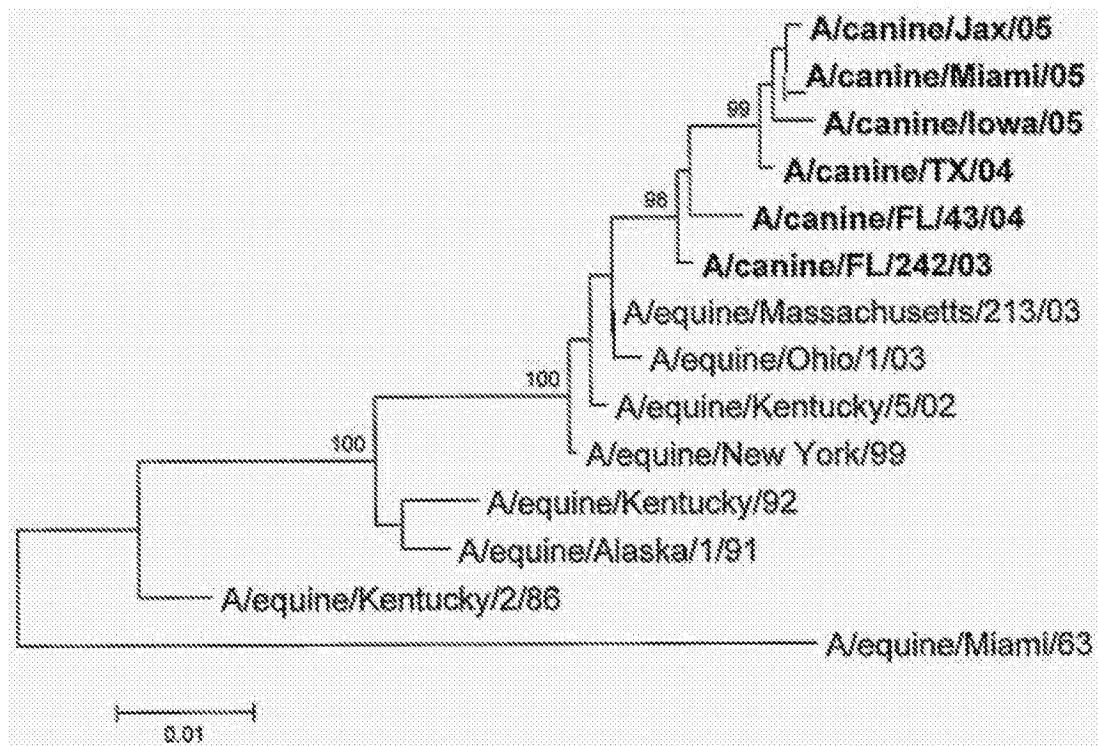


图4A

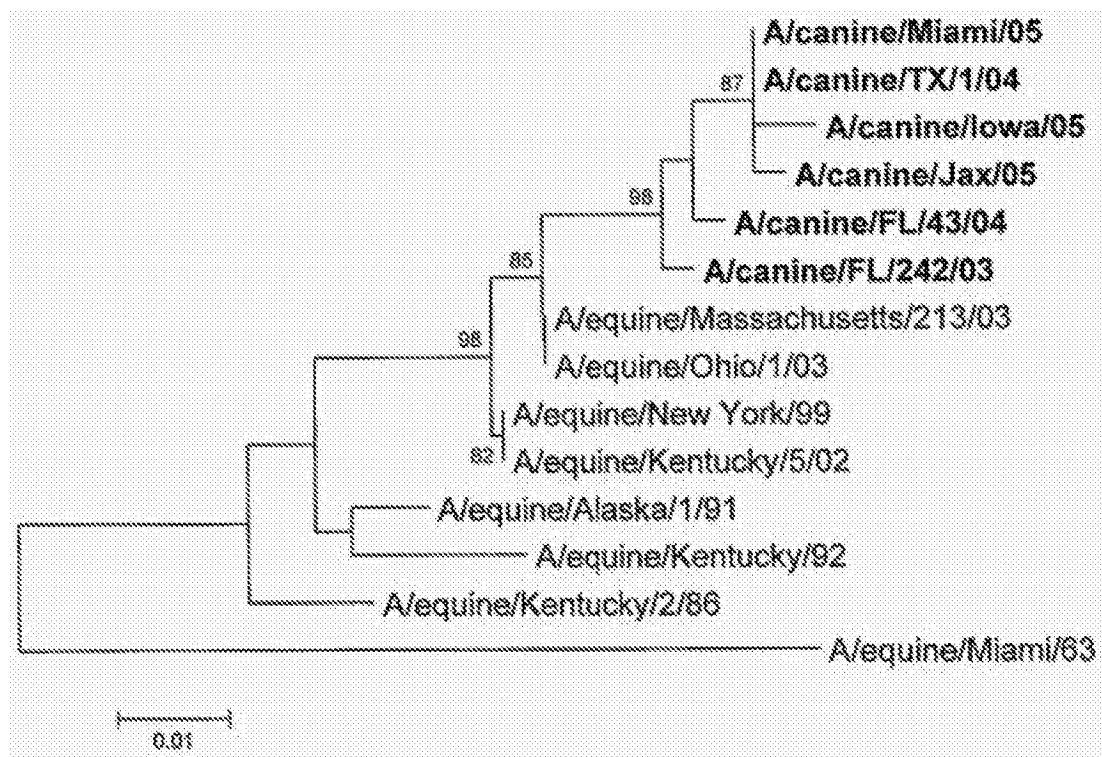


图4B

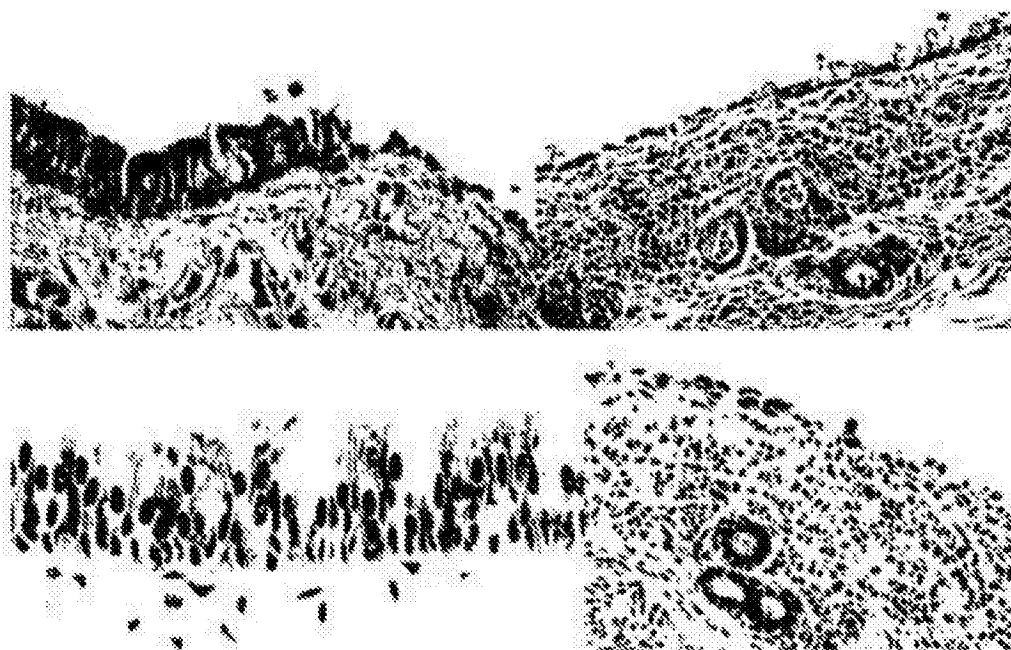


图5

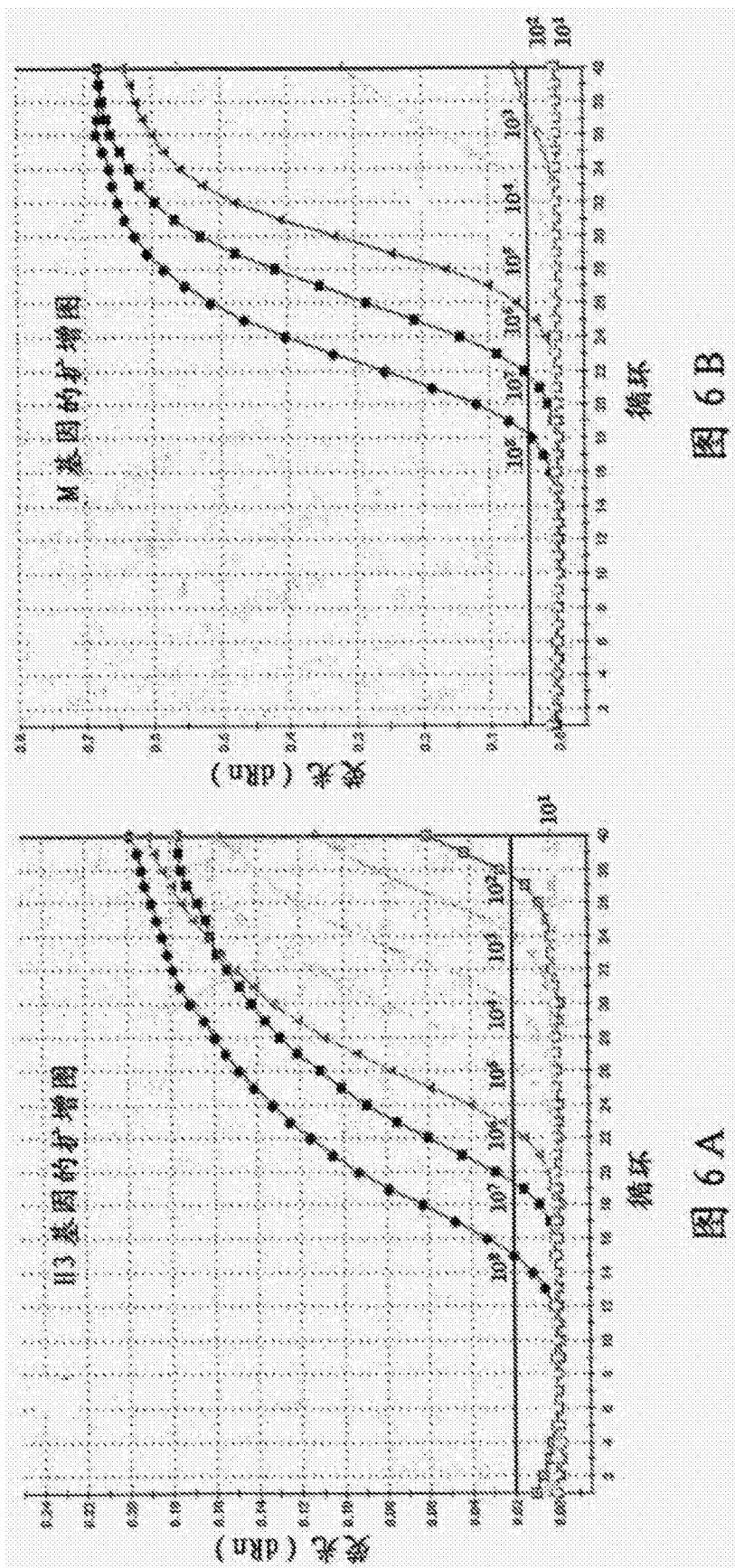


图 6 B

图 6 A

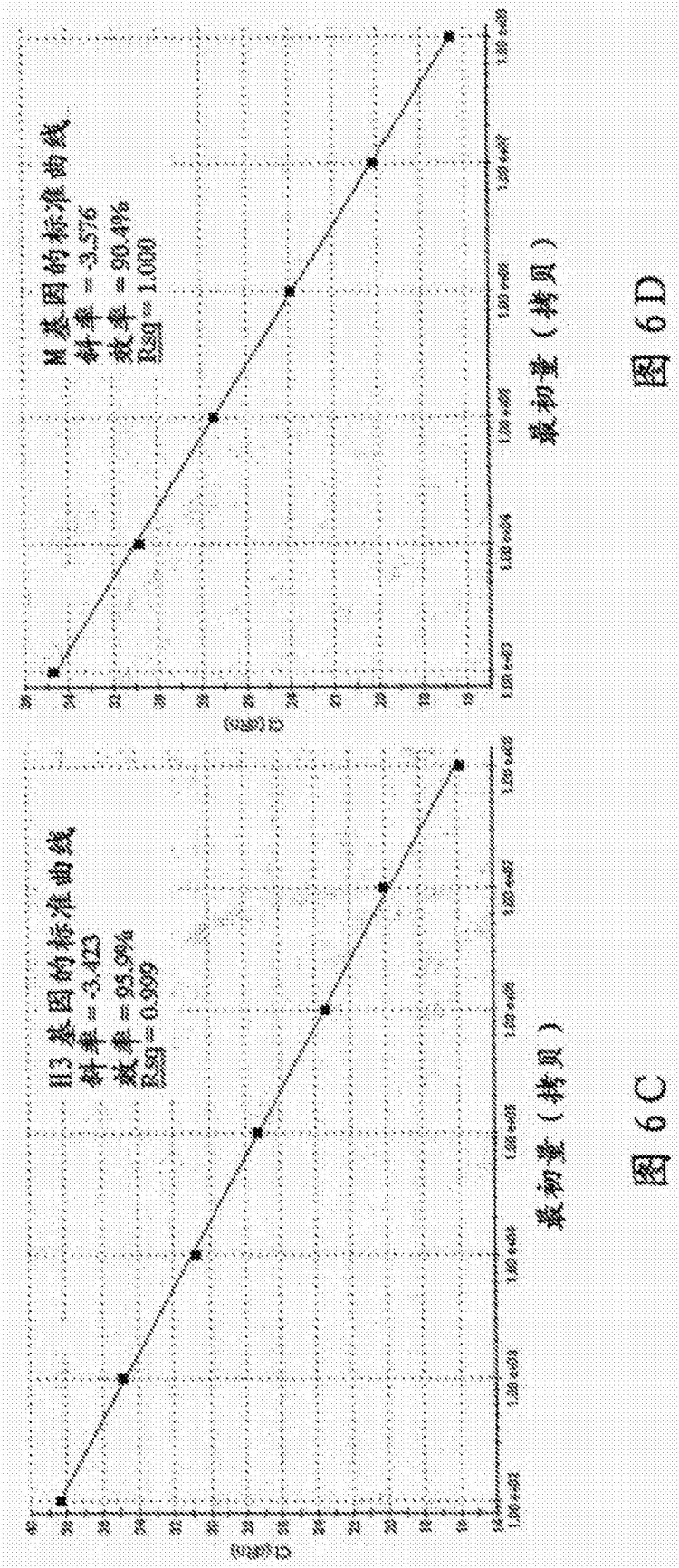


图 6D

图 6C

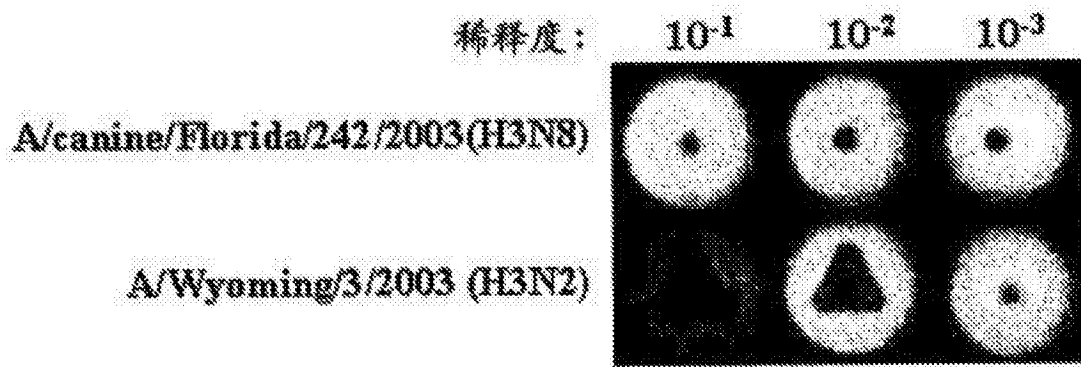


图7