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可活化细胞因子多肽及其使用方法

(57)摘要

本申请的特征在于作为感兴趣的细胞因子的条件活性变体的融合蛋白。在一个方面，即使本申请的全长多肽含有功能性细胞因子多肽，其具有降低或最小的细胞因子受体活化活性。活化后，例如通过裂解将例如空间阻断多肽的阻断部分按顺序连接到活性细胞因子的接头，所述细胞因子可结合其受体并影响信号传导。通常，所述融合蛋白还包含体内半衰期延长元件，其可在肿瘤微环境中从所述细胞因子裂解。

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1.一种融合多肽,所述融合多肽包含以下每一种中的至少一种:

a)细胞因子多肽[A];

b)细胞因子阻断部分[D];和

c)蛋白酶可裂解的多肽接头[L];

其中所述细胞因子多肽和所述细胞因子阻断部分通过所述蛋白酶可裂解的多肽接头可操作地连接,并且所述融合多肽具有减弱的细胞因子受体活化活性,其中所述融合多肽的所述细胞因子受体活化活性比含有通过裂解蛋白酶可裂解的接头而产生的细胞因子多肽的多肽的细胞因子受体活化活性小至少约10倍。

2.如权利要求错误!未找到引用源。所述的融合多肽,其中所述细胞因子多肽选自由以下组成的组:IL-2、IL-7、IL-12、IL-15、IL-18、IL-21、IL-23、TGFβ、IFNα、IFNβ、IFNγ、TNF、TGFβ、CXCL10、CCL19、CCL20、CCL21及其活性片段。

3.如权利要求1或2所述的融合多肽,其中所述细胞因子多肽为短半衰期细胞因子多肽。

4.如权利要求1至3中任一项所述的融合多肽,其中所述每种蛋白酶可裂解的接头多肽独立地包含能够被选自由以下组成的组的蛋白酶裂解的序列:激肽释放酶、凝血酶、糜酶、羧肽酶A、组织蛋白酶G、组织蛋白酶L、弹性蛋白酶、PR-3、颗粒酶M、钙蛋白酶、基质金属蛋白酶(MMP)、ADAM、FAP、组织蛋白酶L、纤溶酶原活化剂、组织蛋白酶、半胱天冬酶、类胰蛋白酶和肿瘤细胞表面蛋白酶。

5.如权利要求8所述的融合多肽,其中每种蛋白酶可裂解的多肽独立地包含同一蛋白酶的两个或更多个裂解位点或被不同蛋白酶裂解的两个或更多个裂解位点,或者所述蛋白酶可裂解的多肽中的至少一种包含两种或更多种不同蛋白酶的裂解位点。

6.如权利要求1至4中任一项所述的融合多肽,其中所述细胞因子阻断部分也是半衰期延长元件。

7.如权利要求1至5中任一项所述的融合多肽,其中所述细胞因子阻断部分在空间上阻断所述细胞因子的激动剂活性。

8.如权利要求5或6所述的融合多肽,其中所述细胞因子阻断部分为人血清白蛋白、抗原结合蛋白或结合人血清白蛋白的抗原结合多肽或其片段。

9.如权利要求错误!未找到引用源。至7中任一项所述的融合多肽,其中在所述蛋白酶可裂解的多肽接头被蛋白酶裂解后,所述细胞因子从所述细胞因子阻断部分自由解离。

10.如权利要求1至8中任一项所述的融合多肽,其中所述细胞因子阻断部分抑制所述细胞因子多肽活化其同源受体。

11.如权利要求1至9中任一项所述的融合多肽,其中所述融合多肽在裂解所述蛋白酶可裂解的接头之前结合所述细胞因子多肽的所述同源受体。

12.如权利要求1至10中任一项所述的融合多肽,其还包含至少一个半衰期延长元件。

13.如权利要求1至11中任一项所述的融合多肽,其中所述细胞因子阻断部分与所述细胞因子多肽非共价缔合,而与所述接头肽键无关。

14.如权利要求12所述的融合多肽,其中所述非共价缔合为pH依赖的。

15.如权利要求11所述的融合多肽,其中所述半衰期延长元件在空间上抑制或阻断所述细胞因子多肽对其同源受体的活化和/或所述细胞因子多肽与其同源受体的结合。

16.如权利要求14所述的融合多肽，其中所述半衰期延长元件为人血清白蛋白、人IgG、人源化IgG、scFv、Fab、sdAb或其片段。

17.如权利要求9所述的融合多肽，其中所述细胞因子阻断部分包含配体结合结构域、结合所述细胞因子多肽的单结构域抗体或scFv、或结合所述细胞因子多肽的受体的选自单结构域抗体和scFv的抗体或抗体片段。

18.如权利要求1至16中任一项所述的融合多肽，其中使用标准体外受体活化测定法以及以摩尔为基准的等量的所述细胞因子多肽和融合蛋白来确定所述细胞因子受体活化活性。

19.如权利要求10至17中任一项所述的融合多肽，其中在通过蛋白酶裂解所述蛋白酶可裂解的序列之后，细胞因子与所述细胞因子阻断部分和/或半衰期延长元件失去接触。

20.如权利要求1至18中任一项所述的融合多肽，其中所述融合多肽包含[A]、[D]和[L]每一种中的至少一种，呈以下取向中的任一种：

a)[A]-[L]-[D]；

b)[D]-[L]-[A]；

c)[D]-[L]-[A]-[L]-[D]-[L]-[A]；

d)[A]-[L]-[D]-[L]-[A]-[L]-[D]；

e)[D]-[L]-[A]-[L]-[D]；

f)[D]-[L]-[A]-[L]-[A]-[L]-[D]；

g)[D]-[L]-[A]-[L]-[D]-[L]-[A]-[L]-[D]；和

h)[D]-[L]-[A]-[A]-[L]-[D]。

21.如权利要求1至19中任一项所述的融合多肽，其中所述融合多肽包含两个细胞因子多肽。

22.如权利要求1所述的融合多肽，其具有式：

[A]-[L1]-[D]-[L2]-[A]-[L2]-[D]

其中，

A为细胞因子多肽；

L1和L2各自独立地为蛋白酶可裂解的多肽接头；

D为任选地能够延长血清半衰期的细胞因子阻断部分；并且

其中L1为第一蛋白酶的底物，并且其中L2为第二蛋白酶的底物。

23.如权利要求11中任一项所述的融合多肽，其中所述至少一个半衰期延长元件为一个半衰期延长元件、两个半衰期延长元件或三个半衰期延长元件。

24.如权利要求错误!未找到引用源。至22中任一项所述的融合多肽，其包含一个蛋白酶可裂解的接头、两个蛋白酶可裂解的接头、三个蛋白酶可裂解的接头、四个蛋白酶可裂解的接头、五个蛋白酶可裂解的接头、六个蛋白酶可裂解的接头或七个蛋白酶可裂解的接头。

25.如权利要求错误!未找到引用源。至23中任一项所述的融合多肽，其还包含肿瘤特异性抗原结合肽。

26.如权利要求错误!未找到引用源。所述的融合多肽，其中所述肿瘤特异性抗原结合肽通过不可裂解的接头可操作地连接到所述细胞因子多肽。

27.如权利要求错误!未找到引用源。所述的融合多肽，其中所述肿瘤特异性抗原结合

肽通过可裂解的接头可操作地连接到所述细胞因子多肽。

28.如权利要求1至26中任一项所述的融合多肽,其中所述细胞因子多肽的血清半衰期与相应的天然存在的细胞因子相当。

29.如权利要求1至26中任一项所述的融合多肽,其中含有通过裂解所述融合蛋白产生的所述细胞因子多肽的所述多肽的血清半衰期与相应的天然存在的细胞因子相当。

30.如权利要求1至26中任一项所述的融合多肽,其中所述细胞因子多肽为突变蛋白,其具有较短的血清半衰期并且在裂解所述融合多肽后迅速清除。

31.一种融合多肽,所述融合多肽包含以下每一种中的至少一种:

a)干扰素多肽[A];

b)干扰素阻断部分[D];和

c)蛋白酶可裂解的多肽接头[L];并且

其中所述干扰素多肽和所述干扰素阻断部分通过所述蛋白酶可裂解的多肽接头可操作地连接,所述融合多肽具有减弱的干扰素受体活化活性,其中所述融合多肽的所述干扰素受体活化活性比通过裂解所述蛋白酶可裂解的接头而产生的所述干扰素多肽的所述干扰素受体活化活性小至少约10倍。

32.如权利要求错误!未找到引用源。所述的融合多肽,其具有式:

[D]-[L1]-[A]-[L2]-[D];

其中,

A为干扰素α(IFNα)多肽;

L1和L2各自独立地为蛋白酶可裂解的多肽接头;

D为也能够延长体内半衰期的IFNα阻断部分;并且

其中所述干扰素α多肽和所述干扰素α阻断部分通过所述蛋白酶可裂解的多肽接头可操作地连接,所述融合多肽具有减弱的干扰素α受体活化活性,其中所述融合多肽的所述干扰素α受体活化活性比通过裂解所述蛋白酶可裂解的接头而产生的所述干扰素α多肽的所述干扰素受体活化活性小至少约10倍,并且其中当两个接头发生裂解时,所述干扰素α多肽的体内半衰期基本上与天然存在的干扰素α的半衰期相似。

33.如权利要求错误!未找到引用源。所述的融合多肽,其具有式:

[D]-[L1]-[A]-[L2]-[D]-[L3]-[A]-[L4]-[D];

其中,

A为干扰素γ(IFNγ)多肽;

L1、L2、L3和L4各自独立地为蛋白酶可裂解的多肽接头;

D为能够延长血清半衰期的IFNγ阻断部分;并且

其中所述干扰素γ多肽和所述干扰素γ阻断部分通过所述蛋白酶可裂解的多肽接头可操作地连接,所述融合多肽具有减弱的干扰素γ受体活化活性,其中所述融合多肽的所述干扰素γ受体活化活性比通过裂解所述蛋白酶可裂解的接头而产生的所述干扰素γ多肽的所述干扰素γ受体活化活性小至少约10倍,并且其中当两个接头发生裂解时,所述干扰素γ多肽的体内半衰期基本上与天然存在的干扰素γ的半衰期相似。

34.如权利要求27至29中任一项所述的融合多肽,其中所述蛋白酶可裂解的接头多肽包含能够被选自由以下组成的组的蛋白酶裂解的序列:激肽释放酶、凝血酶、糜酶、羧肽酶

A、组织蛋白酶G、组织蛋白酶L、弹性蛋白酶、PR-3、颗粒酶M、钙蛋白酶、基质金属蛋白酶(MMP)、ADAM、FAP、组织蛋白酶L、纤溶酶原活化剂、组织蛋白酶、半胱天冬酶、类胰蛋白酶和肿瘤细胞表面蛋白酶。

35.如权利要求34所述的融合多肽,其中每种蛋白酶可裂解的多肽独立地包含同一蛋白酶的两个或更多个裂解位点或被不同蛋白酶裂解的两个或更多个裂解位点,或者所述蛋白酶可裂解的多肽中的至少一种包含两种或更多种不同蛋白酶的裂解位点。

36.如权利要求错误!未找到引用源。或30所述的融合多肽,其中所述干扰素为干扰素α或干扰素γ。

37.如权利要求错误!未找到引用源。所述的融合多肽,其具有式:

[A]-[L1]-[D]-[L2]-[A]-[L2]-[D]

其中,

A为干扰素多肽;

L1和L2各自独立地为蛋白酶可裂解的多肽接头;

D为任选地能够延长血清半衰期的干扰素阻断部分;并且

其中L1为第一蛋白酶的底物,并且其中L2为第二蛋白酶的底物。

38.如权利要求27至32中任一项所述的融合多肽,其中所述干扰素阻断部分也是半衰期延长元件。

39.如权利要求27至33中任一项所述的融合多肽,其中所述干扰素阻断部分在空间上阻断所述细胞因子的激动剂活性。

40.如权利要求34所述的融合多肽,其中所述干扰素阻断部分为人血清白蛋白或结合人血清白蛋白的抗原结合多肽。

41.如权利要求27至35中任一项所述的融合多肽,其中在所述蛋白酶可裂解的多肽接头被蛋白酶裂解后,所述干扰素从所述干扰素阻断部分自由解离。

42.如权利要求27至36中任一项所述的融合多肽,其中所述干扰素阻断部分抑制所述干扰素多肽活化其同源受体。

43.如权利要求至错误!未找到引用源。错误!未找到引用源。中任一项所述的融合多肽,其中所述融合多肽在裂解所述蛋白酶可裂解的接头之前结合所述干扰素多肽的所述同源受体。

44.如权利要求错误!未找到引用源。中任一项所述的融合多肽,其还包含至少一个半衰期延长元件。

45.如权利要求错误!未找到引用源。中任一项所述的融合多肽,其中所述干扰素阻断部分与所述干扰素多肽非共价缔合。

46.如权利要求27至错误!未找到引用源。中任一项所述的融合多肽,其中所述非共价缔合为pH依赖的。

47.如权利要求错误!未找到引用源。所述的融合多肽,其中所述半衰期延长元件在空间上抑制或阻断所述干扰素多肽对其同源受体的活化和/或所述干扰素多肽与其同源受体的结合。

48.如权利要求错误!未找到引用源。所述的融合多肽,其中所述半衰期延长元件为人血清白蛋白、人IgG或其片段。

49.如权利要求错误!未找到引用源。至错误!未找到引用源。所述的融合多肽,其中所述半衰期延长元件不结合所述干扰素多肽。

50.如权利要求错误!未找到引用源。所述的融合多肽,其中所述干扰素阻断部分包含所述干扰素的同源受体的配体结合结构域或片段、结合所述干扰素多肽的单结构域抗体或scFv、或结合所述干扰素的受体的抗体或抗体片段(例如,单结构域抗体、scFv)。

51.如权利要求27至45错误!未找到引用源。中任一项所述的融合多肽,其中使用标准体外受体活化测定法以及以摩尔为基准的等量的所述融合多肽和干扰素多肽来确定所述同源干扰素受体活化活性。

52.如权利要求错误!未找到引用源。至错误!未找到引用源。中任一项所述的融合多肽,其中在通过蛋白酶裂解所述蛋白酶可裂解的序列之后,干扰素与所述干扰素阻断部分和/或半衰期延长元件自由解离。

53.如权利要求错误!未找到引用源。至错误!未找到引用源。中任一项所述的融合多肽,其中所述融合多肽包含[A]、[B]和[L]每一种中的至少一种,呈以下取向中的任一种:

a)[A]-[L]-[D];

b)[D]-[L]-[A];

c)[D]-[L]-[A]-[L]-[D]-[L]-[A];

d)[A]-[L]-[D]-[L]-[A]-[L]-[D];

e)[D]-[L]-[A]-[L]-[D];

f)[D]-[L]-[A]-[L]-[A]-[L]-[D];

g)[D]-[L]-[A]-[L]-[D]-[L]-[A]-[L]-[D];和

h)[D]-[L]-[A]-[A]-[L]-[D]。

54.如权利要求错误!未找到引用源。至48中任一项所述的融合多肽,其中所述融合多肽包含两个细胞因子肽。

55.如权利要求错误!未找到引用源。所述的融合多肽,其中所述两个细胞因子多肽是两个不同的细胞因子肽。

56.如权利要求39至50错误!未找到引用源。中任一项所述的融合多肽,其中所述至少一个半衰期延长元件为一个半衰期延长元件或两个半衰期延长元件。

57.如权利要求错误!未找到引用源。中任一项所述的融合多肽,其包含一个蛋白酶可裂解的多肽接头,所述一个蛋白酶可裂解的多肽接头为一个蛋白酶可裂解的接头、两个蛋白酶可裂解的接头、三个蛋白酶可裂解的接头、四个蛋白酶可裂解的接头、五个蛋白酶可裂解的接头、六个蛋白酶可裂解的接头或七个蛋白酶可裂解的接头。

58.如权利要求错误!未找到引用源。至错误!未找到引用源。中任一项所述的融合多肽,其还包含肿瘤特异性抗原结合肽。

59.如权利要求错误!未找到引用源。所述的融合多肽,其中所述肿瘤特异性抗原结合肽通过不可裂解的接头可操作地连接到所述干扰素多肽。

60.如权利要求错误!未找到引用源。所述的融合多肽,其中所述肿瘤特异性抗原结合肽通过可裂解的接头可操作地连接到所述干扰素多肽。

61.一种核酸,其编码如权利要求错误!未找到引用源。至60中任一项所述的融合多肽。

62.一种载体,其包含如权利要求61所述的核酸。

63.一种宿主细胞,其包含如权利要求62所述的载体或如权利要求61所述的核酸。

64.一种制备医药组成物的方法,所述方法包括在用于表达和收集所期望的多肽的合适条件下培养如权利要求63所述的宿主细胞。

65.一种医药组成物,其包含i)如权利要求错误!未找到引用源。至60中任一项所述的融合多肽和ii)药学上可接受的赋形剂。

66.一种用于治疗肿瘤的方法,所述方法包括向有此需要的受试者施用有效量的如权利要求错误!未找到引用源。至60中任一项所述的融合多肽。

67.如权利要求错误!未找到引用源。至60中任一项所述的融合多肽,其用作药物。

68.如权利要求错误!未找到引用源。至60中任一项所述的融合多肽,其用于治疗有此需要的受试者的肿瘤。

69.一种用于治疗有此需要的受试者的肿瘤的医药组成物,其包含作为活性成分的如权利要求错误!未找到引用源。至60中任一项所述的融合多肽。

可活化细胞因子多肽及其使用方法

[0001] 相关申请

[0002] 本申请要求2018年5月14日提交的美国临时申请62/671,225、2018年11月6日提交的美国临时申请号62/756,504、2018年11月6日提交的美国临时申请号62/756,515和2018年11月6日提交的美国临时申请号62/756,507的权益。以上申请的全部教义以引用的方式并入本文。

[0003] 序列表

[0004] 本申请含有以ASCII格式电子形式提交且以引用的方式整体并入本文的序列表。2019年5月14日创建的所述ASCII副本名为105365-0020_SL.txt且大小为866,384字节。

背景技术

[0005] 从较少定向分化的前体发育成成熟的免疫活性淋巴样细胞、其后续抗原驱动的免疫应答以及对这些和不必要的自身反应性应答的抑制高度依赖于细胞因子并受其调节,所述细胞因子(包括白介素-2[IL-2]、IL-4、IL-7、IL-9、IL-15和IL-21)利用共同γ链(γc)家族中的受体(Rochman等人,2009)以及包括IL-12、18和23的家族成员。IL-2为Treg细胞的胸腺发育所必要,并且严格调节成熟外周Treg和抗原活化的常规T细胞的几个关键方面。由于IL-2在体外具有强大的T细胞生长因子活性,所以已对其进行了广泛的研究,部分原因是这种活性提供了一种直接增强例如癌症和AIDS-HIV患者中的免疫力的潜在手段,或提供了一种对抗不必要的应答(例如移植排斥和自身免疫性疾病)的靶标。虽然用IL-2进行的体外研究为这些研究提供了有力的依据,但是IL-2在体内的功能显然要复杂得多,如在IL-2缺陷型小鼠中首次说明的那样,其中在不缺乏免疫力的情况下观察到快速致死性自身免疫综合征(Sadlack等人,1993,1995)。后来在分别消融编码IL-2Rα(Il2ra)和IL-2Rβ(Il2rb)的基因时,得到了类似的观察(Suzuki等人,1995;Willerford等人,1995)。

[0006] 本申请涉及用于治疗癌症和其他依赖于免疫上调或下调的疾病的条件活性和/或靶向细胞因子。例如,一些细胞因子的抗肿瘤活性是熟知且已描述的,并且一些细胞因子已经在人体内用于治疗目的。诸如白介素-2(IL-2)和干扰素α(IFNα)的细胞因子在患有不同类型肿瘤的患者中表现出了积极的抗肿瘤活性,所述肿瘤诸如肾转移癌、毛细胞白血病、卡波西氏肉瘤(Kaposi sarcoma)、黑色素瘤、多发性骨髓瘤等。其他细胞因子如IFNβ、肿瘤坏死因子(TNF)α、TNFβ、IL-1、4、6、12、15和CSF对一些类型的肿瘤表现出了一定的抗肿瘤活性,并因此成为进一步研究的对象。

发明内容

[0007] 本文提供了治疗性蛋白、编码所述蛋白的核酸以及使用所述蛋白和核酸治疗疾病或病症的组合物和方法,所述疾病或病症诸如增殖性疾病、肿瘤性疾病、炎性疾病、免疫性病症、自身免疫性疾病、感染性疾病、病毒性疾病、过敏反应、寄生虫反应、移植物抗宿主疾病等。

[0008] 本申请的特征在于作为目标细胞因子的条件活性变体的融合蛋白。在一个方面,

即使本申请的全长多肽含有功能性细胞因子多肽，其具有降低或最小的细胞因子受体活化活性。在例如通过裂解将阻断部分(例如空间阻断多肽)依次连接到活性细胞因子的接头来活化后，细胞因子(例如IL-2、IL-7、IL-12、IL-15、IL-18、IL-21、IL-23、IFNα、IFNβ、IFNγ、TNFα、淋巴毒素、TGF-β1、TGFβ2、TGFβ3、GM-CSF、CXCL10、CCL19、CCL20、CCL21或前述任一种的功能片段或突变蛋白)可结合其受体并影响信号传导。如果需要的话，全长多肽可包括还可提供额外有利特性的阻断多肽部分。例如，全长多肽可含有还可延长血清半衰期和/或将全长多肽靶向所期望细胞因子活性位点的阻断多肽部分。或者，全长融合多肽可含有与阻断多肽部分不同的血清半衰期延长元件和/或靶向结构域。优选地，融合蛋白含有至少一种能够延长体内循环半衰期的元件或结构域。优选地，在所期望体内位置酶促去除此元件(例如，肿瘤微环境中的蛋白酶裂解)，从而恢复与天然存在的有效载荷分子基本类似的有效载荷分子(例如IL2或IFNa)的药代动力学特性。融合蛋白可靶向所期望细胞或组织。如本文所述，通过还与所期望靶标结合的阻断多肽部分的作用或通过靶向结构域来实现靶向。识别优选靶标上的靶标抗原(例如，肿瘤特异性抗原)的结构域可通过可裂解或不可裂解的接头连接到细胞因子。如果通过不可裂解的接头连接，则靶向结构域可进一步有助于将细胞因子保留在肿瘤中，并且可将其视为保留结构域。靶向结构域不一定需要直接连接至有效载荷分子，但可直接连接至融合蛋白的另一个元件。如果靶向结构域通过可裂解的接头连接，则这点尤其正确。

[0009] 在一个方面，提供了一种融合多肽，其包含细胞因子多肽或其功能片段或突变蛋白；以及阻断部分，例如空间阻断结构域。阻断部分直接或通过接头融合至细胞因子多肽，并且可通过在融合位点或接头处或附近或在阻断部分中裂解(例如，蛋白酶介导的裂解)融合多肽来与细胞因子多肽分离。例如，当细胞因子多肽通过含有蛋白酶裂解位点的接头融合到阻断部分时，细胞因子多肽在蛋白酶介导的接头裂解后从阻断部分释放并可结合其受体。接头被设计成例如在肿瘤微环境中在所期望细胞因子活性的位点处裂解，从而避免脱靶细胞因子活性并降低细胞因子治疗的总体毒性。

[0010] 阻断部分还可用作血清半衰期延长元件。在一些实施方案中，融合多肽还包含单独的血清半衰期延长元件。在一些实施方案中，融合多肽还包含靶向结构域。在各种实施方案中，血清半衰期延长元件为水溶性多肽，诸如任选的分支或多臂聚乙二醇(PEG)、全长人血清白蛋白(HSA)或保留与FcRn结合的片段、Fc片段或直接结合到FcRn或结合到人血清白蛋白的纳米抗体。

[0011] 除了血清半衰期延长元件外，本文所述的医药组成物优选地包含至少一个或多个靶向结构域，所述靶向结构域与一个或多个靶抗原或单个靶抗原上的一个或多个区域结合。本文设想，本申请的多肽构建体例如在疾病特异性微环境中或在受试者的血液中在蛋白酶裂解位点处裂解，并且一个或多个靶向结构域将结合至靶细胞上的靶抗原。至少一种靶抗原涉及疾病、病症或病状和/或与疾病、病症或病状相关。示例性靶抗原包括与增殖性疾病、肿瘤性疾病、炎性疾病、免疫性病症、自身免疫性疾病、感染性疾病、病毒性疾病、过敏反应、寄生虫反应、移植物抗宿主疾病或宿主抗移植物疾病相关的那些抗原。

[0012] 在一些实施方案中，靶抗原为细胞表面分子，诸如蛋白质、脂质或多糖。在一些实施方案中，靶抗原是在肿瘤细胞、病毒感染的细胞、细菌感染的细胞、受损的红细胞、动脉斑块细胞或纤维化组织细胞上。

[0013] 在一些情况下，靶抗原在病变细胞或组织(例如肿瘤或癌细胞)的表面上表达。肿瘤的靶抗原包括但不限于成纤维细胞活化蛋白α(FAPa)、滋养层细胞糖蛋白(5T4)、肿瘤相关钙信号转导蛋白2(Trop2)、纤连蛋白EDB(EDB-FN)、纤连蛋白EIIIB结构域、CGS-2、EpCAM、EGFR、HER-2、HER-3、c-Met、FOLR1、FAP和CEA。本文所公开的医药组成物还包括包含两个抗原结合结构域的蛋白质，所述两个抗原结合结构域与已知在病变细胞或组织上表达的两个不同靶抗原结合。示例性抗原结合结构域对包括但不限于EGFR/CEA、EpCAM/CEA和HER-2/HER-3。

[0014] 在一些实施方案中，靶向多肽独立地包含scFv、VH结构域、VL结构域、非Ig结构域或特异性结合至靶抗原的配体。在一些实施方案中，靶向多肽特异性结合至细胞表面分子。在一些实施方案中，靶向多肽特异性结合至肿瘤抗原。在一些实施方案中，靶向多肽特异性地且独立地结合至选自EpCAM、EGFR、HER-2、HER-3、cMet、CEA和FOLR1中的至少一个的肿瘤抗原。在一些实施方案中，靶向多肽特异性地且独立地结合两个不同的抗原，其中抗原中的至少一个为选自EpCAM、EGFR、HER-2、HER-3、cMet、CEA和FOLR1的肿瘤抗原。在一些实施方案中，靶向多肽用作保留结构域，并通过不可裂解的接头连接至细胞因子。

[0015] 如本文所述，细胞因子阻断部分可结合至细胞因子，并由此阻断细胞因子的同源受体的活化。

[0016] 本申请还涉及编码本文所述的条件活性蛋白的核酸，例如DNA、RNA、mRNA，以及含有此类核酸的载体和宿主细胞。

[0017] 本申请还涉及含有条件活性蛋白、编码条件活性蛋白的核酸以及含有此类核酸的载体和宿主细胞的医药组成物。通常，医药组成物含有一种或多种生理上可接受的载剂和/或赋形剂。

[0018] 本申请还涉及治疗方法，所述治疗方法包括向有此需要的受试者施用有效量的条件活性蛋白、编码条件活性蛋白的核酸、含有此种核酸的载体或宿主细胞以及前述任一种的医药组成物。通常，受试者患有增殖性疾病、肿瘤性疾病、炎性疾病、免疫性病症、自身免疫性疾病、感染性疾病、病毒性疾病、过敏反应、寄生虫反应、移植物抗宿主疾病或宿主抗移植物疾病或处于发展所述疾病的风险下。

[0019] 本申请还涉及条件活性蛋白、编码条件活性蛋白的核酸、含有此种核酸的载体或宿主细胞以及前述任一种的医药组成物用于治疗有此需要的受试者的用途。通常，受试者患有增殖性疾病、肿瘤性疾病、炎性疾病、免疫性病症、自身免疫性疾病、感染性疾病、病毒性疾病、过敏反应、寄生虫反应、移植物抗宿主疾病或宿主抗移植物疾病或处于发展所述疾病的风险下。

[0020] 本申请还涉及条件活性蛋白、编码条件活性蛋白的核酸、含有此种核酸的载体或宿主细胞用于制造用于治疗疾病的药物的用途，所述疾病诸如增殖性疾病、肿瘤性疾病、炎性疾病、免疫性病症、自身免疫性疾病、感染性疾病、病毒性疾病、过敏反应、寄生虫反应、移植物抗宿主疾病或宿主抗移植物疾病。

附图说明

[0021] 图1A是示出包含阻断部分的蛋白酶活化的细胞因子或趋化因子的示意图。阻断部分可任选地用作血清半衰期延长结构域。箭头左侧的图显示细胞因子通过蛋白酶可裂解的

接头连接到阻断部分，从而阻断其与受体结合的能力。箭头右侧的图显示在炎性或肿瘤环境中，蛋白酶在接头上的蛋白酶裂解位点裂解，从而释放阻断部分并允许细胞因子与其受体结合。

[0022] 图1B是示出蛋白酶活化的细胞因子或趋化因子的示意图，其中HSA(阻断部分)直接结合至目标细胞因子或趋化因子，其中蛋白酶裂解位点在HSA与目标细胞因子或趋化因子之间。箭头左侧的图显示细胞因子通过蛋白酶可裂解的接头连接到阻断部分，从而阻断其与受体结合的能力。箭头右侧的图显示在炎性或肿瘤环境中，蛋白酶在接头上的蛋白酶裂解位点处裂解，从而释放阻断部分并允许细胞因子与其受体结合。

[0023] 图1C是示出蛋白酶活化的细胞因子或趋化因子的示意图，其中多于一个HSA(阻断部分)直接结合到目标分子上。如果需要的话，HSA中的一个或多个可通过接头(诸如含有蛋白酶裂解位点的接头)与细胞因子或趋化因子结合。箭头左侧的图显示细胞因子通过蛋白酶可裂解的接头连接到阻断部分，从而阻断其与受体结合的能力。箭头右侧的图显示在炎性或肿瘤环境中，蛋白酶在接头上的蛋白酶裂解位点处裂解，从而释放阻断部分并允许细胞因子结合受体。与天然细胞因子相比，所述细胞因子现在具有类似的pK特性(例如，具有较短的半衰期)。

[0024] 图1D是示出包含多于一个相同类型或不同类型细胞因子的蛋白酶活化的细胞因子或趋化因子的示意图，所述细胞因子各自通过蛋白酶可裂解的接头与结合结构域结合。箭头左侧的图显示细胞因子通过蛋白酶可裂解的接头连接到阻断部分，从而阻断其与受体结合的能力。箭头右侧的图显示在炎性或肿瘤环境中，蛋白酶在接头上的蛋白酶裂解位点处裂解，从而释放阻断部分并允许细胞因子与其受体结合。

[0025] 图2是示出蛋白酶活化的细胞因子或趋化因子的示意图，所述蛋白酶活化的细胞因子或趋化因子包含细胞因子或趋化因子多肽、阻断部分和通过至少一个蛋白酶可裂解的接头连接的血清半衰期延长结构域。箭头左侧的图显示细胞因子通过蛋白酶可裂解的接头连接到阻断部分，从而阻断其与受体结合的能力。所述接头还与单独的半衰期延长元件结合，这延长了血清的半衰期。箭头右侧的图显示在炎性或肿瘤环境中，蛋白酶在接头上的蛋白酶裂解位点处裂解，从而释放血清半衰期延长元件和阻断部分并允许细胞因子与其受体结合。与天然细胞因子相比，所述细胞因子现在具有类似的pK特性(例如，较短的半衰期)。

[0026] 图3是示出蛋白酶活化的细胞因子或趋化因子的示意图，所述蛋白酶活化的细胞因子或趋化因子包含细胞因子或趋化因子多肽、阻断部分和通过至少一个蛋白酶可裂解的接头连接的靶向结构域。箭头左侧的图显示细胞因子通过蛋白酶可裂解的接头连接到阻断部分和靶向结构域，从而阻断其与受体结合的能力。箭头右侧的图显示在炎性或肿瘤微环境中，蛋白酶在接头中的蛋白酶裂解位点处裂解，从而释放靶向结构域和阻断部分并允许细胞因子与其受体结合。

[0027] 图4A是示出蛋白酶活化的细胞因子或趋化因子的示意图，所述蛋白酶活化的细胞因子或趋化因子包含细胞因子或趋化因子多肽、阻断部分、靶向结构域和通过至少一个蛋白酶可裂解的接头连接的血清半衰期延长结构域，其中细胞因子多肽和靶向结构域通过蛋白酶可裂解的接头连接。箭头左侧的图显示细胞因子通过一个或多个蛋白酶可裂解的接头连接到靶向结构域、阻断部分和半衰期延长元件，从而阻断其与受体结合的能力。箭头右侧的图显示在炎性或肿瘤环境中，蛋白酶在一个或多个接头上的蛋白酶裂解位点处裂解，从

而释放半衰期延长元件、靶向结构域和阻断部分并允许细胞因子与其受体结合。与天然细胞因子相比，所述细胞因子现在具有类似的pK特性(例如，较短的半衰期)。

[0028] 图4B是示出蛋白酶活化的细胞因子或趋化因子的示意图，所述蛋白酶活化的细胞因子或趋化因子包含细胞因子或趋化因子多肽、阻断部分、靶向结构域和通过至少一个蛋白酶可裂解的接头连接的血清半衰期延长结构域。箭头左侧的图显示细胞因子通过一个或多个蛋白酶可裂解的接头连接到靶向结构域、阻断部分和半衰期延长元件，从而阻断其与受体结合的能力。箭头右侧的图显示在炎性或肿瘤环境中，蛋白酶在一个或多个接头上的蛋白酶裂解位点处裂解，从而释放半衰期延长元件和阻断部分并允许细胞因子与受体结合。靶向部分保持结合，从而使细胞因子保持在肿瘤微环境中。与天然细胞因子相比，所述细胞因子现在具有类似的pK特性(例如，较短的半衰期)。

[0029] 图5是示出免疫球蛋白分子可变结构域的结构的示意图。轻免疫球蛋白链和重免疫球蛋白链的可变结构域含有三个高变环或互补决定区(CDR)。V结构域的三个CDR(CDR1、CDR2、CDR3)在β桶的一端聚簇。CDR是连接免疫球蛋白折叠的β链B-C、C’-C”和F-G的环，而连接免疫球蛋白折叠的β链AB、CC’、C”-D和E-F的底部环和连接免疫球蛋白折叠的D-E链的顶部环是非CDR环。

[0030] 图6是示出蛋白酶活化的细胞因子或趋化因子的示意图，所述蛋白酶活化的细胞因子或趋化因子包含细胞因子或趋化因子多肽、为血清白蛋白结合结构域的阻断部分(例如，dAb)和蛋白酶可裂解的接头。在所示实例中，血清白蛋白结合结构域(例如，sdAb)中的非CDR环可形成细胞因子IL-2的结合位点。在此实例中，血清白蛋白的结合位点可由血清白蛋白结合结构域的CDR形成。

[0031] 图7A至图7H是示出示例性IL-2融合蛋白在IL-2依赖性细胞毒性T淋巴细胞的细胞系CTLL-2中的活性的一系列曲线图。每个曲线图示出了通过基于CellTiter-Glo®(Promega)发光的细胞活力测定所量化的IL-2增殖测定的结果。在使用HSA(图7B、7D、7E、7G)或不使用HSA(图7A、7C、7F、7H)的情况下进行每个增殖测定。每个融合蛋白包含抗HSA结合物，并且每次测定使用融合蛋白的未裂解和MMP9蛋白酶裂解形式。

[0032] 图8A至图8F是示出示例性IL-2融合蛋白在IL-2依赖性细胞毒性T淋巴细胞的细胞系CTLL-2中的活性的一系列曲线图。每个曲线图示出了通过基于CellTiter-Glo(Promega)发光的细胞活力测定所量化的IL-2增殖测定的结果。每次测定使用融合蛋白的未裂解和MMP9蛋白酶裂解形式。

[0033] 图9A至图9Z是示出示例性IL-2融合蛋白在IL-2依赖性细胞毒性T淋巴细胞的细胞系CTLL-2中的活性的一系列曲线图。每个曲线图示出了通过基于CellTiter-Glo(Promega)发光的细胞活力测定所量化的IL-2增殖测定的结果。每次测定使用融合蛋白的未裂解和MMP9蛋白酶裂解形式。

[0034] 图10示出蛋白裂解测定的结果。融合蛋白ACP16以裂解和未裂解形式在SDS-PAGE凝胶上运行。如在凝胶中可以看出的那样，裂解已完成。

[0035] 图11是描绘在蛋白酶裂解之前和之后对人p40/鼠p35 IL12融合蛋白进行的HEK-Blue IL-12报告基因测定的结果的曲线图。基于使用试剂QUANTI-Blue®(InvivoGen)对分泌型碱性磷酸酶(SEAP)活性进行定量来进行分析。结果证实IL12蛋白融合蛋白具有活性。

[0036] 图12A至图12F示出了描述四种IL-12融合蛋白在通过MMP9裂解之前和之后的HEK-blue测定结果的一系列曲线图。基于使用试剂QUANTI-Blue(InvivoGen)对分泌型碱性磷酸酶(SEAP)活性进行定量来进行分析。数据显示,裂解的IL12中的活性大于完整融合蛋白中的活性。所测试的构建体为ACP06(图12A)、ACP07(图12B)、ACP08(图12C)、ACP09(图12D)、ACP10(图12E)、ACP11(图12F)。

[0037] 图13示出蛋白裂解测定的结果。融合蛋白ACP11以裂解和未裂解形式在SDS-PAGE凝胶上运行。如在凝胶中可以看出的那样,裂解已完成。

[0038] 图14是描绘诱导型细胞因子蛋白的非限制性实例的示意图,其中构建体在蛋白酶裂解连接在细胞因子的两个亚基之间的接头时被活化。

[0039] 图15A至图15D是描绘在蛋白酶裂解之前和之后对人p40/鼠p35IL12融合蛋白进行的HEK-Blue测定的结果的曲线图。进行测定。结果证实IL12蛋白融合蛋白具有活性。在使用HSA或不使用HSA的情况下进行每个增殖测定。

[0040] 图16A至图16F是示出使用WEHI 279细胞存活测定法得到的与小鼠IFNγ对照的活性相比的示例性IFNγ融合蛋白的活性的一系列曲线图。使用含有HSA(+HSA)或不含HSA(-HSA)的培养基进行每次测定。每个融合蛋白包含抗HSA结合物,并且每次测定使用融合蛋白的未裂解和MMP9蛋白酶裂解形式。

[0041] 图17A至图17F是示出使用B16报告基因测定法得到的与小鼠IFNγ对照的活性相比的示例性IFNγ融合蛋白的活性的一系列曲线图。使用含有HSA(+HSA)或不含HSA(-HSA)的培养基进行每次测定。每个融合蛋白包含抗HSA结合物,并且每次测定使用融合蛋白的未裂解和MMP9蛋白酶裂解形式。

[0042] 图18A和图18B示出如实施例2中所述的蛋白质裂解测定的结果。两种构建体ACP31(IFN-a融合蛋白;9A)和ACP55(IFN-g融合蛋白;9B)在SDS-PAGE凝胶上以裂解和未裂解形式运行。如在凝胶中可以看出的那样,裂解已完成。

[0043] 图19A和图19B是示出使用B16报告基因测定法得到的在蛋白酶裂解之前和之后示例性IFNγ融合蛋白的活性的一系列曲线图(11A和11B)。使用含有HSA的培养基进行每次测定,并且每个融合蛋白包含抗HSA结合物。每次测定使用融合蛋白的未裂解和MMP9蛋白酶裂解形式。

[0044] 图20A和图20B是示出使用B16报告基因测定法得到的在裂解之前和之后示例性IFNa融合蛋白的活性的一系列图(12A和12B)。使用含有HSA的培养基进行每次测定,并且每个融合蛋白包含抗HSA结合物。每次测定使用融合蛋白的未裂解和MMP9蛋白酶裂解形式。

[0045] 图21A至图21D是描绘使用MC38细胞系进行的肿瘤生长研究的结果的一系列曲线图。图21A至图21C示出当使用不同给药水平和方案(ug=微克,BID=每天两次,BIW=每周两次,QW=每周)腹腔注射(IP)时,IFNγ和IFNγ融合蛋白对肿瘤生长的影响。图21D示出瘤内(IT)注射IFNγ和IL-2对肿瘤生长的影响。

[0046] 图22A和图22B是示出使用B16报告基因测定法得到的与未裂解融合蛋白的活性相比的MMP9蛋白酶裂解的示例性IFNγ融合蛋白(ACP51、ACP52和ACP62)的活性的一系列曲线图。每个融合蛋白包含抗HSA结合物和肿瘤靶向结构域。

[0047] 图23A和图23B是示出使用B16报告基因测定法得到的与未裂解融合蛋白的活性相比的MMP9蛋白酶裂解的示例性IFNγ融合蛋白(ACP53和ACP54)的活性的一系列曲线图。每

个融合蛋白包含直接融合至白蛋白的IFNγ。

[0048] 图24A至图24D是描绘对IL-2融合蛋白和重组人IL2(Rec hIL-2)进行的HEK-Blue IL-2报告基因测定的结果的曲线图。基于使用试剂QUANTI-Blue(InvivoGen)对分泌型碱性磷酸酶(SEAP)活性进行定量来进行分析。

[0049] 图25A和图25B是示出在HSA存在下在HEKBlue IL-2报告基因测定中对ACP16(25A)和ACP124(25B)进行的分析的两个曲线图。圆形描绘未切割多肽的活性,正方形描绘切割多肽的活性。图25C是示出CTLL-2增殖测定的结果的曲线图。将CTLL2细胞(ATCC)以500,000个细胞/孔的浓度的悬浮液接种在含有或不含40mg/ml人血清白蛋白(HSA)的培养基中,并在37℃和5％CO_2下用系列稀释的可活化hIL2刺激72小时。测试未裂解和裂解的可活化ACP16的活性。通过用活性MMP9孵育产生裂解的可活化hIL2。使用基于CellTiter-Glo(Promega)发光的细胞活力测定评定细胞活性。圆形描绘完整的融合蛋白,并且正方形描绘蛋白酶裂解的融合蛋白。

[0050] 图26A至图26C是示出融合蛋白在HEKBlue IL-12报告基因测定中的活性的一系列曲线图。图26A描绘在ACP11(人p40/鼠p35 IL12融合蛋白)与ACP04(阴性对照)的比较中的IL-12/STAT4活化。图26B是示出ACP91(嵌合IL-12融合蛋白)的分析的曲线图。圆形描绘对照多肽ACP04的活性,正方形描绘未切割ACP91多肽的活性,并且三角形描绘切割多肽(ACP91+MMP9)的活性。表中示出每个多肽的EC50值。图26C是示出ACP136(嵌合IL-12融合蛋白)的分析的曲线图。圆形描绘对照多肽ACP04的活性,正方形描绘未切割ACP136多肽的活性,并且三角形描绘切割多肽(ACP136+MMP9)的活性。插入表中示出每个多肽的EC50值。

[0051] 图27A至图27F是显示在HEKBlue报告基因测定中裂解的IL-12多肽具有活性的一系列曲线图。左上图显示鼠IL-12在此测定中具有活性(阳性对照)。左下图和右下图分别示出未切割(正方形)和切割(三角形)的活性。插入表(右上图)中示出每个抗体的EC50值。

[0052] 图28A至图28N是描绘APC56(图28A)、APC57(图8B)、APC58(图28C)、APC59(图28D)、APC60(图28E)、APC61+HSA(图28F)、ACP30+HSA(图28G)、ACP73(图28H)、ACP70+HSA(图28I)、ACP71(图28J)、ACO 72(图28K)、ACP 73(图28L)、ACP74(图28M)和ACP75(图28N)在B16 IFNα报告基因测定中的活性的一系列曲线图。测试每种融合物当切割(正方形)和未切割(圆形)时的活性。每个曲线图中包括对鼠IFNγ的分析作为比较。

[0053] 图29A和图29B是示出在肿瘤异种移植模型中分析ACP31(小鼠IFNα1融合蛋白)和ACP11(人p40/鼠p35 IL12融合蛋白)的结果的两个曲线图。图29A示出用30μg ACP31(圆形)、110μg ACP31(三角形)、330μg ACP31(菱形)以及作为对照的1μg鼠野生型IFNa1(虚线,正方形)和10μg mIFNa1(虚线,小圆)处理的小鼠随时间推移的肿瘤体积。大空心圆指示单独的媒介物。数据显示,在用ACP31治疗的小鼠中,肿瘤体积随时间推移呈剂量依赖性减少。图29B示出用17.5μg ACP11(正方形)、175μg ACP31(三角形)、525μg ACP31(圆形)以及作为对照的2μg ACP04(虚线,三角形)和10μg ACP04(虚线,菱形)处理的小鼠随时间推移的肿瘤体积。大空心圆指示单独的媒介物。数据显示,在用ACP11和ACP04(人p40/鼠p35 IL12融合蛋白)治疗的小鼠中,肿瘤体积随时间推移以剂量依赖性方式减少。

[0054] 图30是示出在小鼠中的小鼠异种移植肿瘤模型中随时间推移的肿瘤体积的一系列意大利面图,每只小鼠分别用单独的媒介物(左上图)、2μg ACP04(中上图)、10μg ACP04(右上图)、17.5μg ACP11(左下图)、175μg ACP11(中下图)和525μg ACP11(右下图)处理。每

条线代表单只小鼠。

[0055] 图31A至图31C是示出分析肿瘤异种移植模型中的ACP16、ACP124的结果的三个曲线图。图31A示出在用4.4μg ACP16(正方形)、17μg ACP16(三角形)、70μg ACP16(倒三角形)、232μg ACP16(黑色圆)以及作为比较的12μg野生型IL-2(虚线,三角形)和36μg野生型IL-2(虚线,菱形)处理的小鼠中随时间推移的肿瘤体积。大空心圆指示单独的媒介物。数据显示,在用更高浓度的ACP16治疗的小鼠中,肿瘤体积随时间推移以剂量依赖性方式减少。图31B示出在用17μg ACP124(正方形)、70μg ACP124(三角形)、230μg ACP124(倒三角形)和700μg ACP124处理的小鼠中随时间推移的肿瘤体积。大空心圆指示单独的媒介物。图31C示出在用17μg ACP16(三角形)、70μg ACP16(圆形)、232μg ACP16(黑色圆)以及作为比较的17μg ACP124(虚线,三角形)、70μg ACP124(虚线,菱形)、230μg ACP124(虚线,菱形)处理的小鼠中随时间推移的肿瘤体积。黑色倒三角形指示单独的媒介物。数据显示,在用ACP16而不是ACP124治疗的小鼠中,肿瘤体积随时间推移以剂量依赖性方式减少。

[0056] 图32A至图32C是示出在MC38小鼠异种移植模型中融合蛋白的活性的一系列意大利面图,这对应于图31中所示的数据。图中的每条线都是单只小鼠。

[0057] 图33是示出在小鼠异种移植模型中随时间推移的肿瘤体积的曲线图,其示出了对照小鼠(空心圆)和AP16处理的小鼠(正方形)中的肿瘤生长。

[0058] 图34A至图34D是示出用可裂解的融合蛋白处理后小鼠随时间推移的存活的一系列存活图。图34A示出用单独的媒介物(灰色线)、17μg ACP16(深色线)和1μg ACP124(虚线)处理的小鼠的数据。图34B示出用单独的媒介物(灰色线)、70μg ACP16(深色线)和70μg ACP124(虚线)处理的小鼠的数据。图34C示出用单独的媒介物(灰色线)、232μg ACP16(深色线)和230μg ACP124(虚线)处理的小鼠的数据。图34D示出用单独的媒介物(灰色线)、232μg ACP16(深色线)和700μg ACP124(虚线)处理的小鼠的数据。

[0059] 图35是示出在MC38小鼠异种移植模型中融合蛋白的活性的一系列意大利面图。除了APC132的最高三个剂量外,向所有小鼠组给予总共四个剂量,其中在1周/2个剂量后检测到致命毒性。示出了单独的媒介物(顶部)、17μg、55μg、70μg和230μg ACP16(顶部整行)、9μg、38μg、36μg和119μg ACP132(中间整行)以及13μg、42μg、54μg和177μg ACP21(底部整行)。图中的每条线代表单独的动物。

[0060] 图36至图41示出了TriTac多肽的特性,其用作示例性蛋白酶可裂解的融合蛋白。

具体实施方式

[0061] 本文公开了将包含诱导型细胞因子的构建体工程化并使用所述构建体的方法和组合物。细胞因子是有效的免疫激动剂,这导致它们被认为是有前途的肿瘤治疗剂。然而,细胞因子被证明具有非常狭窄的治疗窗。细胞因子的血清半衰期短,并且也被认为是高效的。因此,细胞因子的治疗性施用产生了不期望的全身作用和毒性。为了在预期的细胞因子作用位点(例如,肿瘤)处达到所期望细胞因子水平需要施用大量细胞因子,这加剧了这些问题。不幸的是,由于细胞因子的生物学特性以及不能有效地靶向并控制其活性,因此细胞因子在肿瘤的治疗中未达到所希望的临床优势。

[0062] 本文公开了克服毒性和半衰期短的问题的融合蛋白,所述问题严重限制了细胞因子在肿瘤学中的临床应用。融合蛋白含有具有受体激动剂活性的细胞因子多肽。但是在融

合蛋白的情况下，细胞因子受体激动剂的活性减弱并且循环半衰期延长。融合蛋白包含蛋白酶裂解位点，所述位点由与所期望细胞因子活性位点(例如，肿瘤)相关的蛋白酶裂解，并且通常富集于或选择性地存在于具有所期望活性的位点。因此，在所期望活性位点处优先(或选择性)且有效地裂解融合蛋白，以将细胞因子的活性基本上限制在所期望活性位点，诸如肿瘤微环境。蛋白酶在所期望活性位点(诸如肿瘤微环境中)的裂解从融合蛋白中释放出一种形式的细胞因子，所述细胞因子作为细胞因子受体激动剂的活性远大于融合蛋白(通常比融合蛋白大至少约100倍的活性)。在裂解融合蛋白时释放的细胞因子形式通常具有较短的半衰期，所述半衰期通常基本上相似于天然存在的细胞因子的半衰期，从而将细胞因子活性进一步限制到肿瘤微环境。即使融合蛋白的半衰期延长，但是因为循环融合蛋白减弱并且活性细胞因子靶向肿瘤微环境，所以毒性显著降低或消除。本文所述的融合蛋白首次使得能够施用有效治疗剂量的细胞因子来治疗肿瘤，其中细胞因子的活性基本上限制到肿瘤微环境，并且显著降低或消除细胞因子的不需要的全身作用和毒性。

[0063] 除非另外定义，否则本文使用的所有技术术语、符号和其他科学术语均意图具有本申请所属的领域的技术人员通常所理解的含义。在一些情况下，为了清楚和/或易于参考，本文定义了具有通常理解的含义的术语，并且本文中包括此类定义不一定应被解释为表示与本领域通常理解的内容的区别。本领域技术人员通常很好地理解本文所述或参考的技术和程序并通常使用常规方法来应用所述技术和程序，所述方法诸如Sambrook等人，Molecular Cloning:A Laboratory Manual第4版(2012)Cold Spring Harbor Laboratory Press,Cold Spring Harbor,NY中所述的广泛应用的分子克隆方法。适当地，除非另外说明，否则通常根据制造商定义的方案和条件进行涉及使用可商购获得的试剂盒和试剂的程序。

[0064] “细胞因子”是熟知的技术术语，是指由细胞(尤其是免疫系统的细胞)分泌的并且是免疫系统的调节剂的任何一类免疫调节蛋白(诸如白介素或干扰素)。可用于本文所公开的融合蛋白中的细胞因子多肽包括但不限于转化生长因子，诸如TGF-α和TGF-β(例如，TGFβ1、TGFβ2、TGFβ3)；干扰素，诸如干扰素-α、干扰素-β、干扰素-γ、干扰素-κ和干扰素-ω；白介素，诸如IL-1、IL-1α、IL-2、IL-3、IL-4、IL-5、IL-6、IL-7、IL-8、IL-9、IL-10、IL-11、IL-12、IL-13、IL-14、IL-15、IL-16、IL-17、IL-18、IL-21和IL-25；肿瘤坏死因子，诸如肿瘤坏死因子α和淋巴毒素；趋化因子(例如，C-X-C基序趋化因子10(CXCL10)、CCL19、CCL20、CCL21)和粒细胞巨噬细胞集落刺激因子(GM-CS)，以及活化细胞因子同源受体的此类多肽的片段(即前述功能片段)。“趋化因子”是本领域的术语，是指具有诱导附近的反应性细胞定向趋化的能力的任何小细胞因子家族。

[0065] 众所周知，细胞因子的血清半衰期较短，经常只有几分钟或几小时。即使已经改变旨在延长血清半衰期但保留受体激动剂活性的氨基酸序列的细胞因子形式也通常具有较短的血清半衰期。如本文所用，“半衰期细胞因子”是指在受试者的血清中具有基本上短暂的半衰期循环的细胞因子，诸如小于10分钟、小于15分钟、小于30分钟、小于60分钟、小于90分钟、小于120分钟、小于240分钟或小于480分钟的血清半衰期。如本文所用，半衰期短的细胞因子包括其序列尚未修饰来在受试者体内实现比正常半衰期更长的半衰期的细胞因子，以及已经改变旨在延长血清半衰期但保留受体激动剂活性的氨基酸序列的多肽。后一种情况并不意味着包括添加异源蛋白结构域，诸如真正的半衰期延长元件，诸如血清白蛋白。

[0066] “分选酶”是通过识别并裂解嵌入或末端连接于靶蛋白或肽的羧基端分选信号来修饰蛋白质的转肽酶。分选酶A催化靶蛋白上的Thr和Gly残基之间的LPXTG基序(其中X为任何标准氨基酸)的裂解,其中Thr残基短暂连接到所述酶上的活性位点Cys残基,从而形成酶硫酰基中间体。为了完成转肽作用并创建肽-单体缀合物,具有N端亲核基团(通常为寡甘氨酸基序)的生物分子攻击中间体,从而替代分选酶A并连接两个分子。

[0067] 如本文所用,术语“空间阻断剂”是指可通过诸如接头的其他部分(例如呈嵌合多肽(融合蛋白)形式)直接或间接地共价键合到细胞因子多肽但不以其他方式共价键合到细胞因子多肽的多肽或多肽部分。空间阻断剂可例如通过静电键合、疏水键合、离子键合或氢键键合来非共价键合到细胞因子多肽。空间阻断剂通常由于其靠近细胞因子部分和相对大小而抑制或阻断细胞因子部分的活性。空间阻断剂还可通过募集大蛋白结合配偶体来阻断。空间阻断剂的实例是与血清白蛋白结合的抗体;虽然抗体本身可能足够大或可能不足以大到自行阻止活化或结合,但白蛋白募集允许足够的空间阻断。

[0068] 如本文所用和描述的,“半衰期延长元件”是嵌合多肽的一部分,其例如通过改变其大小(例如,使其高于肾脏滤过界限)、形状、流体动力学半径、电荷、或吸收、生物分布、代谢和消除的参数来增加血清半衰期并改善pK。

[0069] 如本文所用,术语“可活化的”、“活化”、“诱导”和“可诱导的”是指作为融合蛋白的一部分的蛋白质(即细胞因子)结合其受体并在从融合蛋白裂解其他元件时实现活性的能力。

[0070] 如本文所用,“质粒”或“病毒载体”是将所公开的核酸运输到细胞中而不降解的剂,并且包含核酸分子和/或多肽在其所递送到的细胞中产生表达的启动子。

[0071] 如本文所用,术语“肽”、“多肽”或“蛋白质”广泛地用于指由肽键连接的两个或更多个氨基酸。蛋白质、肽和多肽在本文中也可互换使用,以指示氨基酸序列。应当认识到,术语多肽在本文中并不用于暗示构成所述分子的氨基酸的特定大小或数量,并且本申请的肽可含有至多几个氨基酸残基或更多。

[0072] 如通篇所用,“受试者”可为脊椎动物,更具体地为哺乳动物(例如人、马、猫、狗、牛、猪、绵羊、山羊、小鼠、兔、大鼠和豚鼠)、鸟类、爬行动物、两栖动物、鱼类和其他任何动物。术语不表示特定的年龄或性别。因此,旨在涵盖无论雄性还是雌性的成年和新生受试者。

[0073] 如本文所用,“患者”或“受试者”可互换使用,并且可指患有疾病或病症(例如癌症)的受试者。术语患者或受试者包括人和兽医学受试者。

[0074] 如本文所用,术语“治疗(treatment\treat\treating)”是指减少疾病或病状的作用或者疾病或病状的症状的方法。因此,在所公开的方法中,治疗可指确立的疾病或病状或疾病或病状的症状的严重程度至少约10%、至少约20%、至少约30%、至少约40%、至少约50%、至少约60%、至少约70%、至少约80%、至少约90%或基本上完全减少。例如,如果与对照相比,受试者疾病的一个或多个症状减少10%,则认为用于治疗疾病的方法是一种治疗。因此,与天然或对照水平相比,减少可为10%、20%、30%、40%、50%、60%、70%、80%、90%、100%或10%与100%之间的任何减少百分比。应理解,治疗不必指治愈或完全消除疾病、病状或者疾病或病状的症状。

[0075] 如本文所用,术语“预防(prevent\preventing\prevention)”疾病或病症是指例

如在受试者开始显示疾病或病症的一种或多种症状之前或大约同时发生的施用嵌合多肽或编码嵌合多肽的核酸序列的作用，其抑制或延迟疾病或病症的一种或多种症状的发作或加剧。

[0076] 如本文所用，对“降低”、“减少”或“抑制”的提及包括与合适的对照水平相比，至少约10％、至少约20％、至少约30％、至少约40％、至少约50％、至少约60％、至少约70％、至少约80％、至少约90％或更大的变化。此类术语可包括但不一定包括完全消除功能或特性，诸如激动剂活性。

[0077] “减弱的细胞因子受体激动剂”是与细胞因子受体的天然存在的激动剂相比，具有降低的受体激动剂活性的细胞因子受体激动剂。与受体的天然存在的激动剂相比，减弱的细胞因子激动剂可具有至少约10倍、至少约50倍、至少约100倍、至少约250倍、至少约500倍、至少约1000倍或更低的激动剂活性。当含有如本文所述的细胞因子多肽的融合蛋白被描述为“减弱的”或具有“减弱的活性”时，意指融合蛋白是减弱的细胞因子受体激动剂。

[0078] “完整融合蛋白”是其中结构域没有经例如通过蛋白酶裂解去除的融合蛋白。结构域可通过蛋白酶裂解或其他酶活性去除，但是当融合蛋白为“完整的”时，这并不会发生。

[0079] 如本文所用，“部分”是指分子的在该分子内具有不同功能的部分，并且该功能可在另一分子的情况下由该部分来执行。部分可为具有特定功能的化学实体，或具有特定功能的生物分子的一部分。例如，融合蛋白内的“阻断部分”是融合蛋白的能够阻断一些或所有融合多肽的活性的部分。这可能是蛋白质结构域，诸如血清白蛋白。阻断可通过空间阻断剂或特定阻断剂来完成。空间阻断剂通过大小和位置而不是基于特定结合来阻断；一个实例是血清白蛋白。特定的阻断剂通过与待阻断部分发生特定相互作用来阻断。必须针对具体细胞因子或活性结构域来调整特定阻断剂；无论有效载荷如何，都可使用空间阻断剂，只要其足够大。

[0080] 一般来讲，细胞因子的治疗应用受到其全身毒性的强烈限制。例如，最初发现TNF具有诱导一些肿瘤的出血性坏死的能力，并且对不同肿瘤细胞系具有体外细胞毒性作用，但它后来被证明具有很强的促炎活性，这可在过度产生的情况下对人体产生危险的影响。由于全身毒性是在人体中使用药物活性量的细胞因子的基本问题，因此目前正在评估新型衍生物和治疗策略，旨在降低此类生物效应物的毒性作用，同时保持其治疗功效。

[0081] IL-2在免疫系统中发挥刺激和调节功能，并且与共同γ链(γc)细胞因子家族的其他成员一起对免疫稳态起至关重要的作用。IL-2通过结合IL-2受体(IL-2R)来介导其作用，所述IL-2受体由以IL-2Rα(CD25)、IL-2Rβ(CD122)和IL-2Rγ(γc,CD132)链制成的三聚体受体IL-2或二聚体βγIL-2R(1,3)组成。两种IL-2R变体都能够在IL-2结合后传输信号。然而，三聚体αβγIL-2R对IL-2的亲和力比二聚体βγIL-2R(3)高约10至100倍，这暗示CD25赋予IL-2与其受体高亲和力结合，但对信号转导不重要。在活化的T细胞和CD4+叉头框P3(FoxP3)+T调节细胞(Treg)上发现三聚体IL-2R，它们在体外和体内对IL-2敏感。相反，抗原刺激过的(记忆)CD8+、CD44高记忆表型(MP)CD8+和自然杀伤(NK)细胞被赋予高水平的二聚体βγIL-2R，并且这些细胞也在体外和体内对IL-2作出有力反应。

[0082] 高亲和力IL-2R的表达对于赋予T细胞对体内瞬时可用的低浓度IL-2的反应至关重要。IL-2Rα表达在原初和记忆T细胞上不存在，但在抗原活化后被诱导。IL-2Rβ由NK、NKT和记忆CD8+ T细胞组成性表达，但在抗原活化后也在原初T细胞上被诱导。γc的调节不那

么严格，并且由所有淋巴样细胞组成性表达。一旦抗原诱导高亲和力IL-2R后，IL-2R信号传导就部分通过Stat5依赖性调节I12ra转录来上调IL-2Rα的表达(Kim等人，2001)。此过程代表了维持高亲和力IL-2R表达并保持IL-2信号传导，同时仍保留IL-2的来源的机制。

[0083] IL-2Rα通过被极性周边包围的大的疏水性结合表面捕获IL-2，从而导致相对较弱的相互作用(Kd 10-8M)和快速开关的结合动力学。然而，IL-2Rα-IL-2二元复合物导致IL-2的构象变化非常小，从而通过IL-2和IL-2Rβ之间明显的极性相互作用促进与IL-2Rβ的缔合。IL2/α/β三聚体复合物的假高亲和力(即Kd约300pM)清楚地指示，三聚体复合物比单独与α链(Kd＝10nM)或单独与β链(Kd＝450nM)结合的IL2更稳定，如Ciardelli的数据所示。无论如何，IL2/α/β三聚体接着将γ链募集到能够进行信号传导的四元复合物中，这通过γ链在IL2结合的β链上的大复合结合位点所促进。

[0084] 换句话讲，三元IL-2Rα-IL-2Rβ-IL-2复合物接着通过与IL-2的弱相互作用和与IL-2Rβ的强相互作用而募集γc，以产生稳定的四元高亲和力IL-2R(Kd 10-11M，即10pM)。高亲和力的四元IL-2-IL-2R复合物的形成导致通过酪氨酸激酶Jak1和Jak3进行信号转导，所述酪氨酸激酶分别与IL-2Rβ和γc缔合(Nelson和Willerford，1998)。四元IL-2-IL-2R复合物被快速内在化，其中IL-2、IL-2Rβ和γc迅速降解，但IL-2Rα循环到细胞表面(Hémar等人，1995；Yu和Malek，2001)。因此，需要持续的IL-2R信号传导的那些功能性活动需要持续的IL-2来源来与IL-2Rα接合并形成额外IL-2-IL-2R信号传导复合物。

[0085] 细胞因子4-α-螺旋束家族的另一个成员白介素-15(IL-15)也已作为用于治疗癌症的免疫调节剂出现。IL-15最初通过IL-15Rα捕获，所述IL-15Rα在抗原呈递的树突状细胞、单核细胞和巨噬细胞上表达。IL-15表现出广泛的活性，并经由通过IL-15/IL-2-R-β(CD122)和共同γ链(CD132)进行信号传导来诱导T细胞、B细胞和自然杀伤(NK)细胞的分化和增殖。IL-15还增强$CD8^+$ T细胞的细胞溶解活性，并诱导持久的抗原刺激过的$CD8^+$CD44记忆T细胞。IL-15刺激B细胞进行分化和免疫球蛋白合成，并诱导树突状细胞成熟。它不会刺激免疫抑制性T调节细胞(Treg)。因此，在肿瘤微环境中选择性地增强IL-15活性可增强先天免疫和特异性免疫并对抗肿瘤(Waldmann等人，2012)。最初鉴定出IL-15以IL-2样方式通过共同受体组分(IL-2R/15Rβ-γc)刺激T细胞增殖并通过JAK1/JAK3和STAT3/STAT5进行信号传导的能力。像IL-2一样，IL-15已显示刺激活化的CD4-CD8-、CD4+CD8+、CD4+和CD8+ T细胞增殖，并且促进细胞毒性T淋巴细胞的诱导以及NK细胞的生成、增殖和活化(Waldmann等人，1999)。然而，与维持表达叉头框P3(FOXP3)的CD4+CD25+Treg细胞并将这些细胞保留在外周所需的IL-2不同，IL-15对Treg几乎没有影响(Berger等人，2009)。这很重要，因为表达FOXP3的CD4+CD25+Treg抑制效应T细胞，从而抑制免疫应答，包括针对肿瘤的免疫应答。IL-2在启动活化诱导的细胞死亡(AICD)中也起至关重要的作用，所述细胞死亡是导致消除自身反应性T细胞的过程，而IL-15是T细胞的抗凋亡因子(Marks-Konczalik等人，2000)。与HIV肽疫苗共递送的IL-15已显示出通过提高抗原特异性CD8+ T细胞的寿命并阻断TRAIL介导的细胞凋亡来克服CD4+ T细胞缺乏症(Oh等人，2008)。此外，IL-15促进CD8+CD44hi记忆T细胞的长期维持(Kanegane等人，1996)。

[0086] 通过IL-15Rα$^{-/-}$和IL-15$^{-/-}$小鼠的表型进一步突显IL-15和IL-15Rα对T细胞和NK细胞发育的重要性。敲除小鼠表明CD8+ T细胞总数减少，并且缺乏记忆表型CD8+ T细胞、NK细胞、NK/T细胞和肠上皮内淋巴细胞的某些亚群，这指示IL-15为这些细胞亚群提供了必要的

正稳态功能(Lodolce等人,1996;Kennedy等人,1998)。这两个品系的敲除小鼠的表型相似性表明IL-15Rα在维持生理相关性IL-15信号中的重要性。

[0087] IL-15通过IL-15受体α链反式呈现到T细胞和自然杀伤(NK)细胞表面上展示的IL-15Rβγc复合物(Han等人,2011)。IL-15Ra链起伴侣蛋白的作用,稳定并增加IL-15的活性(Desbois等人,2016)。已显示出外源性IL-15可能对患有癌症的患者的影响有限,这是由于其对IL-15Ra的依赖性在癌症患者中经常下调。因此,已经提出由通过接头与IL-15偶合的IL15Ra的sushi+结构域组成的融合蛋白RLI作为IL15治疗的替代方法(Bessard等人,2009)。发现施用可溶性IL-15/IL-15Rα复合物极大地增强IL-15血清半衰期和体内生物利用度(Stoklasek等人,2010)。

[0088] 除了对T细胞和NK细胞的影响外,IL-15还对免疫系统的其他组分具有多种影响。IL-15保护中性粒细胞使其免于细胞凋亡,调节吞噬作用并刺激IL-8和IL-1R拮抗剂的分泌。IL-15通过活化JAK2、p38和ERK1/2MAPK、Syk激酶和NF-kB转录因子来起作用(Pelletier等人,2002)。在肥大细胞中,IL-15可充当生长因子和细胞凋亡抑制剂。在这些细胞中,IL-15活化JAK2/STAT5途径,而无需γc结合(Tagaya等人,1996)。IL-15还诱导B淋巴细胞增殖和分化,并增加免疫球蛋白分泌(Armitage等人,1995)。IL-15还预防Fas介导的细胞凋亡,并允许部分独立于CD4辅助而诱导抗体应答(Demerci等人,2004;Steel等人,2010)。单核细胞、巨噬细胞和树突状细胞有效地转录并翻译IL-15。它们还对IL-15刺激产生反应。巨噬细胞通过增加吞噬作用,诱导IL-8、IL-12和MCP-1表达并分泌IL-6、IL-8和TNFα来作出反应(Budagian等人,2006)。用IL-15孵育的树突状细胞表明,其中CD83、CD86、CD40和MHC II类表达增加的成熟也对细胞凋亡有抗性,并显示出增强的干扰素-γ分泌(Anguille等人,2009)。

[0089] IL-15还显示对非血液细胞具有影响,所述非血液细胞包括肌细胞、脂肪细胞、内皮细胞和神经细胞。IL-15对肌肉具有合成代谢作用,并且可支持肌肉细胞分化(Quinn等人,1995)。IL-15刺激肌细胞和肌肉纤维以积累收缩蛋白,并能够减慢患有癌症相关恶病质的大鼠的肌肉萎缩(Figueras等人,2004)。IL-15还显示刺激血管生成(Angiolillo等人,1997)并诱导小神经胶质细胞生长和存活(Hanisch等人,1997)。

[0090] 白介素-7(IL-7)也属于IL-2/IL-15家族,是明确表征的多效细胞因子,并且由基质细胞、上皮细胞、内皮细胞、成纤维细胞、平滑肌细胞和角质形成细胞表达,并且在活化后由树突状细胞标度(Alpdogan等人,2005)。虽然最初将其描述为前体B淋巴细胞的生长和分化因子,但后续研究显示IL-7关键性地参与T淋巴细胞的发育和分化。白介素-7信号传导对于最佳的CD8 T细胞功能、体内稳态和记忆的建立至关重要(Schluns等人,2000);它是大多数T细胞亚群的存活所需要的,并且其表达被认为对于调节T细胞数量很重要。

[0091] IL-7与二聚体受体(包括IL-7Rα和γ_c)结合以形成在T细胞和B细胞的细胞外基质重塑、发育和体内稳态中起基本作用的三元复合物(Mazzucchelli和Durum,2007)。IL-7Rα还与胸腺基质淋巴细胞生成素(TSLP)及其受体(TSLPR)交叉反应形成三元复合物,并活化TSLP途径,从而导致人的T细胞和树突状细胞增殖以及小鼠的B细胞进一步发育(Leonard,2002)。因此,由复合物活化的信号传导级联的严格调节对于正常细胞功能至关重要。由IL-7Rα胞外结构域突变引起的IL-7途径刺激不足会抑制T细胞和B细胞发育,从而导致患者患有重症综合性免疫缺陷(SCID)形式(Giliani等人,2005;Puel等人,1998)。

[0092] IL-7在细胞毒性化学疗法后增强癌症患者的免疫重建中具有潜在作用。IL-7治疗增强免疫重建,并且可通过促进甚至少量的近期胸腺移植物(emigrant)的外周扩张来增强甚至有限的胸腺功能。因此,IL-7治疗可潜在地修复已因细胞毒性化学疗法衰竭的患者的免疫系统(Capitini等人,2010)。

[0093] 白介素-12(IL-12)是两个单独编码的亚基(p35和p40)的二硫键连接的异源二聚体,所述亚基共价连接以产生所谓的生物活性异源二聚体(p70)分子(Lieschke等人,1997;Jana等人,2014)。除了形成异源二聚体(IL-12和IL-23)外,p40亚基还作为单体(p40)和同源二聚体($p40_2$)分泌出来。本领域已知合成异源二聚体作为具有将p35连接到p40亚基的接头的单链,保留了异源二聚体的全部生物学活性。IL-12在感染的早期炎症应答和Th1细胞的生成中起着关键作用,这有利于细胞介导的免疫。已发现,IL-12的过量产生对宿主可能存在危险,因为它涉及许多自身免疫性炎性疾病(例如MS、关节炎、1型糖尿病)的发病机制。

[0094] IL-12受体(IL-12R)是由在活化T细胞和自然杀伤细胞表面上表达的IL-12Rβ1和IL-12Rβ2链组成的异源二聚体复合物(Trinchieri等人,2003)。IL-12Rβ1链与IL-12p40亚基结合,而与IL-12Rβ2缔合的IL-12p35具有细胞内信号传导能力(Benson等人,2011)。通过IL-12R进行信号转导诱导了Janus激酶(Jak2)和酪氨酸激酶(Tyk2)磷酸化,从而使信号转导及转录活化蛋白(STAT)1、STAT3、STAT4和STAT5磷酸化和活化。IL-12的特定细胞作用主要是由于STAT4的活化。IL-12诱导自然杀伤细胞和T细胞产生细胞因子,特别是干扰素(IFN)γ,所述细胞因子介导IL-12的许多促炎活性,包括CD4+ T细胞向Th1表型分化(Montepaone等人,2014)。

[0095] 调节性T细胞主动抑制免疫系统的活化,并预防病理性自身反应和随后的自身免疫性疾病。开发选择性地活化调节性T细胞以治疗自身免疫性疾病的药物和方法是热门研究的主题,并且在很大程度上是不成功的,直到能够在炎症部位选择性地递送活性白介素的本申请的发展。调节性T细胞(Treg)是一类抑制其他免疫细胞活性的CD4+CD25+T细胞。Treg是免疫系统稳态的关键,并且在维持对自身抗原的耐受性和调节对外来抗原的免疫应答方面起主要作用。多种自身免疫性和炎性疾病,包括1型糖尿病(T1D)、系统性红斑狼疮(SLE)和移植物抗宿主病(GVHD),已显示出缺乏Treg细胞数量或Treg功能。

[0096] 因此,人们对开发增强Treg细胞数量和/或功能的疗法非常感兴趣。一种正在研究的针对自身免疫性疾病的治疗方法是移植自体、离体扩增的Treg细胞(Tang,Q.等人,2013,Cold Spring Harb.Perspect.Med.,3:1-15)。虽然这种方法在治疗动物疾病模型和多个早期人类临床试验方面具有前景,但它需要使用患者自身的T细胞进行个性化治疗,具有侵入性并且技术复杂。另一种方法是用低剂量白介素-2(IL-2)治疗。Treg细胞特征性表达高组成性水平的高亲和力IL-2受体IL2Rαβγ,所述受体由亚基IL2Rα(CD25)、IL2Rβ(CD122)和IL2Rγ(CD132)组成,并且已显示出Treg细胞的生长依赖于IL-2(Malek,T.R.等人,2010,Immunity,33:153-65)。

[0097] 相反,也使用IL-2来实现免疫活化,并且已批准重组IL-2(Proleukin®)用于治疗某些癌症。高剂量IL-2用于治疗患有转移性黑色素瘤和转移性肾细胞癌的患者,这对总体存活率有长期影响。

[0098] 低剂量IL-2治疗慢性GVHD(Koreth,J.等人,2011,N Engl J Med.,365:2055-66)和HCV相关性自身免疫性血管炎患者(Saadoun,D.等人,2011,N Engl J Med.,365:2067-

77)的临床试验已证明Treg水平的增加和临床功效的迹象。已开始研究IL-2在多种其他自身免疫性和炎性疾病中的功效的新临床试验。使用所谓的低剂量IL-2的基本原理是利用在Treg上组成性表达的三聚体IL-2受体的高IL-2亲和力,同时使其他不表达高亲和力受体的T细胞处于失活状态。这些试验中使用的IL-2的重组形式阿地白介素(Aldesleukin)(由Prometheus Laboratories,San Diego,CA以Proleukin®出售)与高毒性有关。已批准高剂量的阿地白介素用于治疗转移性黑色素瘤和转移性肾癌,但其副作用非常严重,以至仅建议在有重症监护室的医院中使用(网址:www.proleukin.com/assets/pdf/proleukin.pdf)。

[0099] IL-2在自身免疫性疾病中的临床试验采用了较低剂量的IL-2来靶向Treg细胞,因为Treg细胞由于表达IL2Rα而与许多其他免疫细胞类型相比,对更低浓度的IL-2作出反应(Klatzmann D,2015 Nat Rev Immunol.15:283-94)。然而,即使这些较低的剂量也会导致安全性和耐受性问题,并且所使用的治疗方法长期地或在间歇性5天疗程中采用每天皮下注射。因此,对增强Treg细胞数量和功能、比IL-2更特异性地靶向Treg细胞、更安全且更耐受、并且施用频率更低的自身免疫性疾病疗法存在需要。

[0100] 已提出一种用于改善基于IL-2的疗法的自身免疫性疾病治疗指数的方法是使用相对于其他免疫细胞对Treg细胞具有选择性的IL-2变体。IL-2受体表达于多种不同的免疫细胞上,所述细胞包括T细胞、NK细胞、嗜酸性粒细胞和单核细胞,并且这种广泛的表达模式可能有助于其对免疫系统的多效作用和高全身毒性。特别地,活化的T效应细胞与肺上皮细胞一样表达IL2Rαβγ。但是,活化T效应细胞与下调并控制免疫应答的目标直接相反,并且活化肺上皮细胞会导致已知的IL-2剂量限制性副作用,包括肺水肿。事实上,高剂量IL-2免疫疗法的主要副作用是血管渗漏综合征(VLS),它导致血管内流体在诸如肺和肝的器官中积聚,随后引起肺水肿和肝细胞损伤。除了停用IL-2外,没有其他治疗VLS的方法。已在患者中测试了低剂量IL-2方案以避免VLS,然而,这是以次最佳治疗结果为代价。

[0101] 根据文献,VLS被认为是由IL-2活化的NK细胞释放促炎性细胞因子引起的。然而,有一些证据表明,肺水肿是由IL-2与表达低至中等水平的功能性αβγIL-2R的肺内皮细胞的直接结合引起的。并且,通过在CD25缺陷型宿主小鼠中用抗CD25单克隆抗体(mAb)阻断与CD25的结合或通过使用CD122特异性IL-2/抗IL-2mAb(IL-2/mAb)复合物来消除与IL-2和肺内皮细胞相互作用相关联的肺水肿,从而预防VLS。

[0102] 用除IL-2以外的白介素细胞因子进行治疗受到更多的限制。IL-15表现出与IL-2相似的免疫细胞刺激活性,但没有相同的抑制作用,因此使其成为有前景的免疫治疗候选物。重组人IL-15治疗转移性恶性黑色素瘤或肾细胞癌的临床试验表明免疫细胞分布、增殖和活化发生了明显变化,并暗示潜在的抗肿瘤活性(Conlon等人,2014)。IL-15目前正在临床试验中,以治疗各种形式的癌症。然而,已知IL-15治疗与不期望和毒性作用,诸如加剧某些白血病、移植物抗宿主病、低血压、血小板减少和肝损伤相关联。(Mishra A.等人,Cance Cell,2012,22(5):645-55;Alpdogan O.等人,Blood,2005,105(2):866-73;Conlon KC等人,J Clin Oncol,2015,33(1):74-82。)

[0103] IL-7促进胸腺中淋巴细胞的发育,并维持外周原初和记忆T细胞稳态的存活。此外,其对于淋巴结(LN)的器官发生和维持募集入次级淋巴器官(SLO)的活化T细胞也很重要(Gao等人,2015)。在IL-7的临床试验中,接受IL-7的患者显示CD4+和CD8+ T细胞均增加,而

通过FoxP3表达监测的调节性T细胞数量没有显著增加(Sportes等人,2008)。在2006年、2008年和2010年报告的临床试验中,对患有不同类型的癌症诸如转移性黑色素瘤或肉瘤的患者皮下注射不同剂量的IL-7。除短暂发热和轻度红斑外,几乎未见毒性。CD4+和CD8+ T细胞的循环水平显著增加,并且Treg的数量减少。IL-7治疗后,TCR库多样性增加。然而,IL-7的抗肿瘤活性没有得到很好的评估(Gao等人,2015)。结果表明IL-7治疗可增强并扩大免疫应答。

[0104] IL-12是多效性细胞因子,其作用在先天性免疫与适应性免疫之间建立了联系。IL-12首先被描述为由PMA诱导的EBV转化的B细胞系分泌的因子。根据其作用,IL-12已被指定为细胞毒性淋巴细胞成熟因子和自然杀伤细胞刺激因子。由于IL-12桥接先天性免疫和适应性免疫并有效刺激协调自然抗癌防御机制的细胞因子IFNγ的产生,所以它似乎是人肿瘤免疫治疗的理想候选物。然而,在临床研究中与全身施用IL-12相关联的严重副作用以及此细胞因子的非常狭窄的治疗指数显著降低了在癌症患者中使用此细胞因子的热情(Lasek等人,2014)。以肿瘤为靶点递送细胞因子的IL-12治疗的方法目前正在癌症的临床试验中,所述方法可减少IL-12治疗的一些先前问题。

[0105] 由于IL-2具有充分证明的治疗风险,例如其血清半衰期短且毒性高,因此直接使用IL-2作为激动剂来结合IL-2R并治疗性地调节免疫应答一直存在问题。这些风险也限制了其他细胞因子的治疗开发和使用。需要降低这些风险的新形式的细胞因子。本文公开了包含IL-2和IL-15和其他细胞因子、细胞因子的功能片段和突变蛋白以及被设计为解决这些风险并提供所需免疫调节治疗剂的条件活性细胞因子的组合物和方法。

[0106] 本申请被设计为解决直接IL-2疗法和使用其他细胞因子的疗法的缺点,例如使用细胞因子阻断部分,例如空间阻断多肽、血清半衰期延长多肽、靶向多肽、连接多肽(包含蛋白酶可裂解的接头)及其组合。细胞因子当施用于患者时具有很高的效力,所述细胞因子包括白介素(例如IL-2、IL-7、IL-12、IL-15、IL-18、IL-21、IL-23)、干扰素(IFN,包括IFNα、IFNβ和IFNγ)、肿瘤坏死因子(例如,TNFα、淋巴毒素)、转化生长因子(例如,TGFβ1、TGFβ2、TGFβ3)、趋化因子(C-X-C基序趋化因子10(CXCL10)、CCL19、CCL20、CCL21)以及粒细胞-巨噬细胞集落刺激因子(GM-CS)。如本文所用,“趋化因子”意指具有诱导邻近反应性细胞中定向趋化能力的小细胞因子家族。细胞因子可提供有力的治疗,但伴随着临床上难以控制且限制细胞因子的临床使用的不期望的作用。本申请涉及可在不期望作用减少或消除的情况下在患者中使用的新形式的细胞因子。特别地,本申请涉及医药组成物,其包含嵌合多肽(融合蛋白)、编码融合蛋白的核酸的医药组成物和它们的药物制剂,其含有与相应细胞因子相比细胞因子受体活化活性降低的细胞因子或细胞因子的活性片段或突变蛋白。然而,在选定条件下或在选定生物环境中,嵌合多肽常常以与相应天然存在的细胞因子相同或更高的效力活化其同源受体。如本文所述,这通常使用细胞因子阻断部分来实现,所述细胞因子阻断部分在一般条件下而不是在选定条件下阻断或抑制细胞因子、其活性片段或突变蛋白(诸如在所期望细胞因子活性位点(例如,炎症位点或肿瘤)处存在的那些)的受体活化功能。

[0107] 嵌合多肽和编码嵌合多肽的核酸可使用任何合适的方法来制备。例如,编码嵌合多肽的核酸可使用重组DNA技术、合成化学或这些技术的组合来制备,并在合适的表达系统诸如CHO细胞中表达。可类似地制备嵌合多肽,例如通过使用合成或半合成化学技术等表达合适的核酸来制备。在一些实施方案中,可通过分选酶介导的缀合将阻断部分连接到细胞

因子多肽。“分选酶”是通过识别并裂解嵌入或末端连接于靶蛋白或肽的羧基端分选信号来修饰蛋白质的转肽酶。分选酶A催化靶蛋白上Thr和Gly残基之间的LPXTG基序(SEQ ID No.:193)(其中X为任何标准氨基酸)的裂解,其中Thr残基与酶上的活性位点Cys残基短暂连接,从而形成酶-硫酰基中间体。为了完成转肽作用并创建肽-单体缀合物,具有N端亲核基团(通常为寡甘氨酸基序)的生物分子攻击中间体,从而替代分选酶A并连接两个分子。

[0108] 为了形成细胞因子-阻断部分融合蛋白,首先在N端用聚甘氨酸序列标记细胞因子多肽,或可替代地在C端用LPXTG基序(SEQ ID NO.:193)标记细胞因子多肽。阻断部分或其他元件具有连接的用作标记多肽的受体位点的相应肽。对于与通过其N端连接的携带LPXTG(SEQ ID NO.:193)受体肽的结构域的缀合,多肽将标记有N端聚甘氨酸拉伸物。对于与通过其C端连接的携带聚甘氨酸肽的结构域的缀合,多肽将在其C端用LPXTG(SEQ ID NO.:193)分选酶识别序列进行标记。识别聚甘氨酸和LPXTG(SEQ ID NO.:193)序列,分选酶将在聚合物多肽和标记多肽之间形成肽键。分选酶反应裂解甘氨酸残基作为中间体,并在室温下发生。

[0109] 可利用多种机制来去除或减少由阻断部分引起的抑制。例如,医药组成物可包含具有蛋白酶可裂解的接头的细胞因子部分和阻断部分,例如空间阻断部分,所述蛋白酶可裂解的接头包含位于细胞因子和细胞因子阻断部分之间或细胞因子阻断部分内的蛋白酶裂解位点。当蛋白酶裂解位点被裂解时,阻断部分可与细胞因子解离,并且然后细胞因子可活化细胞因子受体。细胞因子部分也可通过结合在相关细胞因子上发现的表位的特定阻断部分(诸如抗体)阻断。

[0110] 可使用任何合适的接头。例如,接头可包含甘氨酸-甘氨酸、分选酶识别基序或分选酶识别基序和肽序列$(Gly_4Ser)_n$(SEQ ID NO.:195)或$(Gly_3Ser)_n$(SEQ ID NO.:196),其中n为1、2、3、4或5。通常,分选酶识别基序包含肽序列LPXTG(SEQ ID NO.:193),其中X为任何氨基酸。在一些实施方案中,共价键是在连接到细胞因子多肽的C端的反应性赖氨酸残基与连接到阻断剂或其他结构域的N端的反应性天冬氨酸之间。在其他实施方案中,共价键是在连接到细胞因子多肽的N端的反应性天冬氨酸残基与连接到所述阻断剂或其他结构域的C端的反应性赖氨酸残基之间。

[0111] 因此,如本文中详细描述的,所使用的细胞因子阻断部分可为空间阻断剂。如本文所用,“空间阻断剂”是指可直接或通过诸如接头的其他部分(例如呈嵌合多肽(融合蛋白)的形式)间接地共价键合到细胞因子多肽但不以其他方式共价键合到细胞因子多肽的多肽或多肽部分。空间阻断剂可例如通过静电键合、疏水键合、离子键合或氢键键合来非共价键合到细胞因子多肽。空间阻断剂通常由于其靠近细胞因子部分和相对大小而抑制或阻断细胞因子部分的活性。可通过在空间上分离细胞因子部分与空间阻断剂,诸如通过在空间阻断剂和细胞因子多肽之间的位点处酶促裂解包含空间阻断剂和细胞因子多肽的融合蛋白来去除细胞因子部分的空间抑制作用。

[0112] 如本文中更详细描述的,阻断功能可与医药组成物中的额外功能性组分(诸如靶向结构域、血清半衰期延长元件和蛋白酶可裂解的连接多肽)组合或由于所述组分存在。例如,血清半衰期延长多肽也可为空间阻断剂。

[0113] 为了呈现本申请的完整范围的简要公开,使用细胞因子IL-2作为示例性细胞因子详细描述本申请的方面。然而,本申请和本申请不限于IL-2。对于本领域技术人员将清楚的

是,包括所公开的方法、多肽和核酸的本申请充分地描述并使得能够使用其他细胞因子、片段和突变蛋白,诸如IL-2、IL-7、IL-12、IL-15、IL-18、IL-21、IL-23、IFNα、IFNβ、IFNγ、TNFα、淋巴毒素、TGF-β1、TGFβ2、TGFβ3、GM-CSF、CXCL10、CCL19、CCL20、CCL21和前述中任一者的功能片段或突变蛋白。

[0114] 各种元件确保IL-2在所期望IL-2活性位点的优先递送和活性,并通过优先与血清半衰期延长策略相关的阻断和/或靶向策略严重限制对白介素的全身暴露。在此血清半衰期延长策略中,白介素的阻断版本的循环时间延长(优选地1至2周或更多周),但活化版本具有典型的白介素血清半衰期。

[0115] 与血清半衰期延长版本相比,静脉内施用IL-2的血清半衰期仅为约10分钟,这是由于其分布在全身细胞外空间中,所述空间很大,在平均体型的成年人中为约15L。随后,IL-2被肾脏代谢,其半衰期为约2.5小时。(Smith,K."Interleukin 2 immunotherapy." Therapeutic Immunology 240(2001))。通过其他测量,IL-2具有非常短的血浆半衰期,对于静脉内施用为85分钟,并且对于皮下施用为3.3小时(Kirchner,G.I.等人,1998,Br J Clin Pharmacol.46:5-10)。在本申请的一些实施方案中,半衰期延长元件通过接头连接到白介素,所述接头在作用位点被裂解(例如通过炎症特异性或肿瘤特异性蛋白酶),从而在所期望位点释放白介素的全部活性,并还将其与未裂解版本的半衰期延长分离。在此类实施方案中,完全活性和游离白介素将具有非常不同的药代动力学(pK)特性,半衰期为数小时而不是数周。此外,暴露于活性细胞因子仅限于所期望的细胞因子活性位点(例如,炎症位点或肿瘤)以及全身暴露于活性细胞因子及相关毒性和副作用降低。

[0116] 本申请中设想的其他细胞因子(例如,由Blood 2011 117:4787-4795;doi:doi.org/10.1182/blood-2010-10-311456报告的IL-15)具有与IL-2类似的药理学,并且因此,本申请的设计解决了直接使用这些剂的缺点,并提供了可具有延长的半衰期和/或靶向所期望活性位点(例如,炎症位点或肿瘤)的嵌合多肽。

[0117] 如果需要的话,可将IL-2工程化来以与相应野生型IL-2不同的亲和力特异性结合通常为IL-2R复合物或三个IL-2R亚基中的一个,以例如选择性地活化Treg或Teff。例如,与野生型IL-2相比,被认为相对于Il-2受体的二聚体β/γ形式,对IL-2受体的三聚体形式具有更高亲和力的IL-2多肽可具有氨基酸序列,所述氨基酸序列包含相对于SEQ ID NO:1(成熟IL-2蛋白,其包含人IL-2的氨基酸21-153,具有Uniprot登录号P60568-1)的以下突变组中的一组:(a)K64R、V69A和Q74P;(b)V69A、Q74P和T101A;(c)V69A、Q74P和I128T;(d)N30D、V69A、Q74P和F103S;(e)K49E、V69A、A73V和K76E;(f)V69A、Q74P、T101A和T133N;(g)N30S、V69A、Q74P和I128A;(h)V69A、Q74P、N88D和S99P;(i)N30S、V69A、Q74P和I128T;(j)K9T、Q11R、K35R、V69A和Q74P;(k)A1T、M46L、K49R、E61D、V69A和H79R;(l)K48E、E68D、N71T、N90H、F103S和I114V;(m)S4P、T10A、Q11R、V69A、Q74P、N88D和T133A;(n)E15K、N30S Y31H、K35R、K48E、V69A、Q74P和I92T;(o)N30S、E68D、V69A、N71A、Q74P、S75P、K76R和N90H;(p)N30S、Y31C、T37A、V69A、A73V、Q74P、H79R和I128T;(q)N26D、N29S、N30S、K54R、E67G、V69A、Q74P和I92T;(r)K8R、Q13R、N26D、N30T、K35R、T37R、V69A、Q74P和I92T;以及(s)N29S、Y31H、K35R、T37A、K48E、V69A、N71R、Q74P、N88D和I89V。这种方法也可用于制备其他细胞因子的突变蛋白,所述细胞因子包括白介素(例如,IL-2、IL-7、IL-12、IL-15、IL-18、IL-23)、干扰素(IFN,包括IFNα、IFNβ和IFNγ)、肿瘤坏死因子(例如,TNFα、淋巴毒素)、转化生长因子(例如,TGFβ

1、TGFβ2、TGFβ3)和粒细胞-巨噬细胞集落刺激因子(GM-CS)。例如,可制备对同源受体具有所期望的结合亲和力的突变蛋白。

[0118] 如上文所述,本文所公开的任何突变体IL-2多肽都可包含所述序列;它们也可限于所述序列并另外与SEQ ID NO:1相同。此外,本文所公开的任何突变体IL-2多肽可任选地包含用另一个残基(例如,丝氨酸)取代位置125处的半胱氨酸残基和/或可任选地包含在SEQ ID NO:1的位置1处的丙氨酸残基的缺失。

[0119] 改善基于IL-2的疗法的治疗指数的另一种方法是优化所述分子的药代动力学以最大程度地活化Treg细胞。早期对IL-2作用的研究表明,IL-2在体外刺激人T细胞增殖需要至少5至6小时暴露于有效浓度的IL-2(Cantrell,D.A.等人,1984,Science,224:1312-1316)。当向人患者施用时,IL-2具有非常短的血浆半衰期,对于静脉内施用为85分钟,并且对于皮下施用为3.3小时(Kirchner,G.I.等人,1998,Br J Clin Pharmacol.46:5-10)。由于IL-2半衰期短,因此持续必要的时间段将循环IL-2维持在或高于刺激T细胞增殖所必需的水平需要高剂量来使IL-2峰值水平显著高于Treg细胞的EC50或将需要频繁施用。这些高IL-2峰值水平可活化IL2Rβγ受体并产生其他意外或不利影响,例如如上文所述的VLS。其中循环半衰期比IL-2长的IL-2类似物或的多功能蛋白(其中IL-2连接到能够与FcRn受体结合的结构域)可持续指定的时间段以低于IL-2的剂量达到目标药物浓度,并且其峰值水平更低。因此,此种IL-2类似物将需要比IL-2更低剂量或更低施用频率来有效地刺激Treg细胞。更低频率地皮下施用IL-2药物也将使患者更耐受。具有这些特征的治疗剂将在临床上转化为改善的药理功效、降低的毒性以及改善的患者对治疗的依从性。可替代地,IL-2或IL-2的突变蛋白(在本文中为"IL-2*")可选择性地靶向预期的作用位点(例如炎症位点或肿瘤)。可通过若干种策略中的一种,包括将结构域添加到包含被裂解的IL-2(或突变蛋白)的阻断剂的所施用剂上,或通过靶向结构域或两者组合来实现这种靶向。

[0120] 在一些实施方案中,可根据期望的靶标将IL-2*部分激动剂调整为以更高或更低的亲和力结合;例如,可将IL-2*工程化为以增强的亲和力与受体亚基中的一个结合而不与其他亚基结合。与完全激动剂或完全拮抗剂不同,这些类型的部分激动剂提供了将信号传导特性调整至引起所期望功能特性的幅度,同时不满足不期望特性的阈值的能力。鉴于部分激动剂的活性不同,可将一系列IL-2变体工程化以表现出甚至更好的独特信号传导活性,范围从几乎完全激动到部分激动到完全拮抗。

[0121] 在一些实施方案中,IL-2*改变了对IL-2Rα的亲和力。在一些实施方案中,与野生型IL-2相比,IL-2*对IL-2Rα的亲和力更高。在其他实施方案中,IL-2*改变了对IL-2Rβ的亲和力。在一个实施方案中,IL-2*对IL-2Rβ(例如IL-2Rβ的N端)具有增强的结合亲和力,这消除了对IL-2Rα的功能需求。在另一个实施方案中,生成的IL-2*对IL-2Rβ具有增加的结合亲和力但表现出与IL-2Rγ的结合降低,并且因此是缺陷型IL-2Rβγ异源二聚体和信号传导。

[0122] 在下文进一步详细描述的阻断部分也可用于促进与一种或多种受体的结合或所述受体的活化。在一个实施方案中,添加阻断部分,使得IL-2Rβγ结合或活化被阻断,但IL-2Rα结合或活化不改变。在另一个实施方案中,添加阻断部分,使得IL-2Rα结合或活化减少。在另一个实施方案中,添加阻断部分,使得与所有三个受体的结合和或所述受体的活化均受到抑制。可通过去除特定环境中的阻断部分,例如通过对将一个或多个阻断部分连接至细胞因子的接头进行蛋白水解裂解来消除这种阻断。

[0123] 可应用类似方法来改善其他细胞因子，特别是用作免疫刺激剂，例如用于治疗癌症。例如，在此方面，可调整细胞因子(例如，IL-2、IL-7、IL-12、IL-15、IL-18、IL-21、IL-23、IFNα、IFNβ和IFNγ、TNFα、淋巴毒素、TGFβ1、TGFβ2、TGFβ3、GM-CSF、CXCL10、CCL19、CCL20和CCL21)的药代动力学和/或药效动力学以在所期望活性的位点(诸如肿瘤中，但优选不是全身性)处最大程度地活化效应细胞(例如，效应T细胞、NK细胞)和/或细胞毒性免疫应答促进细胞(例如，诱导树突状细胞成熟)。

[0124] 因此，本文所提供的医药组成物包含至少一种细胞因子多肽，诸如白介素(例如，IL-2、IL-7、IL-12、IL-15、IL-18、IL-21、IL-23)、干扰素(IFN，包括IFNα、IFNβ和IFNγ)、肿瘤坏死因子(例如，TNFα、淋巴毒素)、转化生长因子(例如，TGFβ1、TGFβ2、TGFβ3)、趋化因子(例如CXCL10、CCL19、CCL20、CCL21)和粒细胞-巨噬细胞集落刺激因子(GM-CS)或前述任一种的功能片段或突变蛋白。多肽通常还包含至少一个接头氨基酸序列，其中在某些实施方案中，氨基酸序列能够被内源蛋白酶裂解。在一个实施方案中，接头包含有包含HSSKLQ(SEQ ID NO.:25)、GPLGVRG(SEQ ID NO.:197)、IPVSLRSG(SEQ ID NO.:198)、VPLSLYSG(SEQ ID NO.199)或SGESPAYYTA(SEQ ID NO.200)的氨基酸序列。在其他实施方案中，嵌合多肽还含有能够阻断白介素多肽活性的阻断部分，例如空间阻断多肽部分。例如，阻断部分可包含人血清白蛋白(HSA)结合结构域或任选地分支或多臂的聚乙二醇(PEG)。可替代地，医药组成物包含第一细胞因子多肽或其片段以及阻断部分，例如空间阻断多肽部分，其中阻断部分阻断在细胞因子受体上的细胞因子多肽的活性，并且其中在某些实施方案中，阻断部分包含蛋白酶可裂解的结构域。在一些实施方案中，仅通过将具有非常短的接头的额外结构域连接到白介素结构域的N端或C端来实现细胞因子活性的阻断和降低。在此类实施方案中，预期通过蛋白酶消化阻断部分或将阻断剂连接至白介素的短接头来减轻阻断。一旦结构域被剪断或释放，它将不再能够实现细胞因子活性的阻断。

[0125] 医药组成物例如嵌合多肽可包含两种或更多种细胞因子，其可为相同的细胞因子多肽或不同的细胞因子多肽。例如，两种或更多种不同类型的细胞因子具有互补功能。在一些实例中，第一细胞因子为IL-2，并且第二细胞因子为IL-12。在一些实施方案中，两种或更多种不同类型的细胞因子多肽中的每一种都具有调节其他细胞因子多肽活性的活性。在含有两个细胞因子多肽的嵌合多肽的一些实例中，第一细胞因子多肽为T细胞活化的，并且第二细胞因子多肽为非T细胞活化的。在含有两个细胞因子多肽的嵌合多肽的一些实例中，第一细胞因子为趋化剂，例如CXCL10，并且第二细胞因子为免疫细胞活化剂。

[0126] 优选地，本文所公开的融合蛋白中所包含的细胞因子多肽(包括功能片段)未经突变或工程化来改变天然存在的细胞因子的特性，包括受体结合亲和力和特异性或血清半衰期。然而，可接受天然存在的(包括野生型)细胞因子的氨基酸序列的改变，以例如促进克隆和实现所期望的表达水平。

[0127] 阻断部分

[0128] 阻断部分可为抑制细胞因子结合和/或活化其受体的能力的任何部分。阻断部分可抑制细胞因子结合和/或活化其受体从而在空间上阻断和/或通过非共价结合至细胞因子的能力。合适的阻断部分的实例包括细胞因子同源受体的全长或细胞因子结合片段或突变蛋白。也可使用结合细胞因子的抗体及其片段，包括多克隆抗体、重组抗体、人抗体、人源化抗体、单链可变片段(scFv)、单结构域抗体(诸如重链可变结构域(VH)、轻链可变结构域

(VL)和骆驼型纳米抗体的可变结构域(VHH))、dAb等。也可使用结合细胞因子的其他合适的抗原结合结构域，包括模拟抗体结合和/或结构的非免疫球蛋白蛋白，诸如anticalin、affilin、affibody分子、affimer、affitin、alphabody、avimer、DARPin、fynomer、库尼茨型(kunitz)结构域多肽、单体(monobody)，以及基于其他工程化支架诸如SpA、GroEL、纤维连接蛋白、脂质体和CTLA4支架的结合结构域。合适的阻断多肽的其他实例包括在空间上抑制或阻断细胞因子与其同源受体的结合的多肽。有利地，此类部分还可用作半衰期延长元件。例如，通过与水溶性聚合物诸如PEG缀合而修饰的肽可在空间上抑制或阻止细胞因子与其受体的结合。也可使用具有较长血清半衰期的多肽或其片段，诸如血清白蛋白(人血清白蛋白)、免疫球蛋白Fc、转铁蛋白等，以及此类多肽的片段和突变蛋白。

[0129] 与例如具有较长血清半衰期的蛋白质(诸如HSA、免疫球蛋白或转铁蛋白)结合或与循环到质膜的受体(诸如FcRn或转铁蛋白受体)结合的抗体和抗原结合结构域也可抑制细胞因子，特别是当结合其抗原时。此类抗原结合多肽的实例包括单链可变片段(scFv)、单结构域抗体(诸如重链可变结构域(VH)、轻链可变结构域(VL)和骆驼型纳米抗体的可变结构域(VHH))、dAb等。也可使用结合细胞因子的其他合适的抗原结合结构域，包括模拟抗体结合和/或结构的非免疫球蛋白蛋白，诸如anticalin、affilin、affibody分子、affimer、affitin、alphabody、avimer、DARPin、fynomer、库尼茨型结构域多肽、单体，以及基于其他工程化支架诸如SpA、GroEL、纤维连接蛋白、脂质体和CTLA4支架的结合结构域。

[0130] 在示例性实例中，当IL-2为嵌合多肽中的细胞因子时，阻断部分可为IL-2受体的α链(IL-2Rα)或IL-2受体的β链(IL-2Rβ)或γ链(IL-2Rγ)的全长或片段或突变蛋白、抗IL-2单结构域抗体(dAb)或scFv、Fab、抗CD25抗体或其片段以及抗HAS dAb或scFv等。

[0131] 本申请的额外方面

[0132] 1.一种融合蛋白，所述融合蛋白包含与结合部分可操作地连接的细胞因子部分，所述结合部分包含非CDR环和可裂解的接头，其中所述结合部分能够掩蔽所述细胞因子与其受体的结合和/或所述细胞因子对所述受体的活化。

[0133] 2.如方面1所述的融合蛋白，其中所述结合部分为天然肽、合成肽、工程化支架或工程化大血清蛋白。

[0134] 3.如方面1或2所述的融合蛋白，其中所述工程化支架包括sdAb、scFv、Fab、VHH、纤连蛋白III型结构域、免疫球蛋白样支架、DARPin、胱氨酸结肽、脂质运载蛋白、三螺旋束支架、蛋白G相关白蛋白结合模块、或DNA或RNA适体支架。

[0135] 4.如方面1至2中任一项所述的融合蛋白，其中所述结合部分能够结合大血清蛋白。

[0136] 5.如方面1至3中任一项所述的融合蛋白，其中所述非CDR环来自可变结构域、恒定结构域、C1组结构域、C2组结构域、I结构域或其任何组合。

[0137] 6.如方面1至4中任一项所述的融合蛋白，其中所述结合部分还包含互补决定区(CDR)。

[0138] 7.如方面5所述的融合蛋白，其中所述结合部分能够结合大血清蛋白。

[0139] 8.如方面6所述的融合蛋白，其中所述大血清蛋白为半衰期延长蛋白。

[0140] 9.如方面6或7所述的融合蛋白，其中所述大血清蛋白为白蛋白、转铁蛋白、XIII因子或纤维蛋白原。

[0141] 10.如方面5至8中任一项所述的融合蛋白,其中所述CDR环提供对大血清蛋白或免疫球蛋白轻链或其任何组合具有特异性的结合位点。

[0142] 11.如方面1至9中任一项所述的融合蛋白,其中所述可裂解的接头包含裂解位点。

[0143] 12.如方面10所述的融合蛋白,其中所述裂解位点由蛋白酶识别。

[0144] 13.如方面11所述的融合蛋白,其中所述结合部分结合至所述细胞因子。

[0145] 14.如方面11或11所述的融合蛋白,其中所述结合部分与所述细胞因子共价连接。

[0146] 15.如方面11、11或14所述的融合蛋白,其中所述结合部分能够通过所述结合部分和所述细胞因子之间的特异性分子间相互作用来掩蔽所述细胞因子与其靶标的结合。

[0147] 16.如方面11至14中任一项所述的融合蛋白,其中所述非CDR环提供对所述部分和所述细胞因子的结合具有特异性的结合位点。

[0148] 17.如方面11至15中任一项所述的融合蛋白,其中在裂解所述可裂解的接头后,所述结合部分与所述细胞因子分离,并且所述细胞因子与其靶标结合。

[0149] 18.如方面1至16中任一项所述的融合蛋白,其中所述细胞因子结合细胞因子受体。

[0150] 19.如方面17所述的融合蛋白,其中所述细胞因子受体包括I型细胞因子受体、I型IL受体、II型IL受体、趋化因子受体或肿瘤坏死受体超家族受体。

[0151] 20.如方面1至18中任一项所述的融合蛋白,其中所述可裂解的接头包含裂解位点。

[0152] 21.如方面20所述的融合蛋白,其中所述裂解位点由蛋白酶识别。

[0153] 22.如方面21所述的融合蛋白,其中所述蛋白酶裂解位点由丝氨酸蛋白酶、半胱氨酸蛋白酶、天冬氨酸蛋白酶、苏氨酸蛋白酶、谷氨酸蛋白酶、金属蛋白酶、明胶酶或天冬酰胺肽裂解酶识别。

[0154] 23.如方面21所述的融合蛋白,其中所述蛋白酶裂解位点由以下蛋白酶识别:组织蛋白酶B、组织蛋白酶C、组织蛋白酶D、组织蛋白酶E、组织蛋白酶K、组织蛋白酶L、激肽释放酶、hK1、hK10、hK15、纤溶酶(plasmin)、胶原酶、IV型胶原酶、溶基质素、Xa因子、糜蛋白酶样蛋白酶、胰蛋白酶样蛋白酶、弹性蛋白酶样蛋白酶、枯草杆菌蛋白酶样蛋白酶、猕猴桃蛋白酶、菠萝蛋白酶、钙蛋白酶、半胱天冬酶、半胱天冬酶-3、Mir1-CP、木瓜蛋白酶、HIV-1蛋白酶、HSV蛋白酶、CMV蛋白酶、凝乳酶、肾素、胃蛋白酶、蛋白裂解酶、豆荚蛋白、纤溶酶(plasmepsin)、猪笼草蛋白酶、金属外肽酶、金属内肽酶、基质金属蛋白酶(MMP)、MMP1、MMP2、MMP3、MMP8、MMP9、MMP10、MMP11、MMP12、MMP13、MMP14、ADAM10、ADAM17、ADAM12、尿激酶纤溶酶原活化剂(uPA)、肠激酶、前列腺特异性靶标(PSA、hK3)、白介素-1β转化酶、凝血酶、FAP(FAP-α)、二肽基肽酶或二肽基肽酶IV(DPPIV/CD26)、II型跨膜丝氨酸蛋白酶(TTSP)、中性粒细胞弹性蛋白酶、组织蛋白酶G、蛋白酶3、中性粒细胞丝氨酸蛋白酶4、肥大细胞糜酶、肥大细胞类胰蛋白酶、二肽基肽酶和二肽基肽酶IV(DPPIV/CD26)。

[0155] 24.一种条件活性结合蛋白,其包含结合部分(M),所述结合部分包含非CDR环、细胞因子和可裂解的接头(L),其中所述非CDR环能够结合所述细胞因子,并且其中所述结合部分能够抑制所述细胞因子与其受体的结合和/或抑制所述细胞因子对所述受体的活化。

[0156] 25.如方面24所述的条件活性结合蛋白,其中所述结合部分能够结合半衰期延长蛋白。

[0157] 26.如方面24或25所述的条件活性结合蛋白，其中所述结合部分为天然肽、合成肽、工程化支架或工程化大血清蛋白。

[0158] 27.如方面26所述的条件活性结合蛋白，其中所述工程化支架包括sdAb、scFv、Fab、VHH、纤连蛋白III型结构域、免疫球蛋白样支架、DARPin、胱氨酸结肽、脂质运载蛋白、三螺旋束支架、蛋白G相关白蛋白结合模块、或DNA或RNA适体支架。

[0159] 28.如方面24至27中任一项所述的条件活性结合蛋白，其中所述非CDR环来自可变结构域、恒定结构域、C1组结构域、C2组结构域、I结构域或其任何组合。

[0160] 29.如方面24至28中任一项所述的条件活性结合蛋白，其中所述结合部分还包含互补决定区(CDR)。

[0161] 30.如方面24至29中任一项所述的条件活性结合蛋白，其中所述结合部分包含对大血清蛋白具有特异性的结合位点。

[0162] 31.如方面30所述的条件活性结合蛋白，其中所述大血清蛋白为白蛋白、转铁蛋白、XIII因子或纤维蛋白原。

[0163] 32.如方面29至31中任一项所述的条件活性结合蛋白，其中所述CDR提供对大血清蛋白或免疫球蛋白轻链或其任何组合具有特异性的结合位点。

[0164] 33.如方面29至32中任一项所述的条件活性结合蛋白，其中所述结合部分能够通过结合部分和细胞因子之间的特异性分子间相互作用来掩蔽细胞因子与其靶标的结合。

[0165] 34.如方面29至33中任一项所述的条件活性结合蛋白，其中所述非CDR环提供对结合部分和细胞因子的结合具有特异性的结合位点。

[0166] 35.如方面24至34中任一项所述的条件活性结合蛋白，其中所述细胞因子结合细胞因子受体。

[0167] 36.如方面35所述的条件活性结合蛋白，其中所述细胞因子受体包含I型细胞因子受体、I型IL受体、II型IL受体、趋化因子受体或肿瘤坏死受体超家族受体。

[0168] 37.如方面24至36中任一项所述的条件活性结合蛋白，其中所述可裂解的接头包含裂解位点。

[0169] 38.如方面37所述的条件活性结合蛋白，其中所述裂解位点由蛋白酶识别。

[0170] 39.如方面38所述的条件活性结合蛋白，其中所述蛋白酶裂解位点由丝氨酸蛋白酶、半胱氨酸蛋白酶、天冬氨酸蛋白酶、苏氨酸蛋白酶、谷氨酸蛋白酶、金属蛋白酶、明胶酶或天冬酰胺肽裂解酶识别。

[0171] 40.如方面38所述的条件活性结合蛋白，其中所述蛋白酶裂解位点由以下蛋白酶识别:组织蛋白酶B、组织蛋白酶C、组织蛋白酶D、组织蛋白酶E、组织蛋白酶K、组织蛋白酶L、激肽释放酶、hK1、hK10、hK15、纤溶酶、胶原酶、IV型胶原酶、溶基质素、Xa因子、糜蛋白酶样蛋白酶、胰蛋白酶样蛋白酶、弹性蛋白酶样蛋白酶、枯草杆菌蛋白酶样蛋白酶、猕猴桃蛋白酶、菠萝蛋白酶、钙蛋白酶、半胱天冬酶、半胱天冬酶-3、Mir1-CP、木瓜蛋白酶、HIV-1蛋白酶、HSV蛋白酶、CMV蛋白酶、凝乳酶、肾素、胃蛋白酶、蛋白裂解酶、豆荚蛋白、纤溶酶、猪笼草蛋白酶、金属外肽酶、金属内肽酶、基质金属蛋白酶(MMP)、MMP1、MMP2、MMP3、MMP8、MMP9、MMP10、MMP11、MMP12、MMP13、MMP14、ADAM10、ADAM17、ADAM12、尿激酶纤溶酶原活化剂(uPA)、肠激酶、前列腺特异性靶标(PSA、hK3)、白介素-1β转化酶、凝血酶、FAP(FAP-α)、二肽基肽酶或二肽基肽酶IV(DPPIV/CD26)、II型跨膜丝氨酸蛋白酶(TTSP)、中性粒细胞弹性蛋白酶、组

织蛋白酶G、蛋白酶3、中性粒细胞丝氨酸蛋白酶4、肥大细胞糜酶、肥大细胞类胰蛋白酶、二肽基肽酶和二肽基肽酶IV(DPPIV/CD26)。

[0172] 41.如方面24所述的条件活性结合蛋白,其还包含结合至所述结合部分的半衰期延长结构域,其中所述半衰期延长结构域为结合蛋白提供安全开关,并且其中在所述接头裂解时,通过分离所述结合部分和所述半衰期延长结构域与所述细胞因子来活化所述结合蛋白,并且由此将所述结合蛋白与所述安全开关分离。

[0173] 42.如方面41所述的条件活性结合蛋白,其中所述接头的裂解位于肿瘤微环境中。

[0174] 43.一种条件活性结合蛋白,其包含通过结合部分内的非CDR环与细胞因子结合的结合部分,其中所述结合部分进一步连接至半衰期延长结构域并包含可裂解的接头,其中所述结合蛋白在其通过裂解接头而活化之前具有延长的半衰期,并且其中在活化时,所述结合部分和所述半衰期延长结构域与所述细胞因子分离,并且其中所述结合蛋白在活化状态下不具有延长的半衰期。

[0175] 44.如方面43所述的条件活性结合蛋白,其中所述接头的裂解位于肿瘤微环境中。

[0176] 体内半衰期延长元件

[0177] 优选地,嵌合多肽包含体内半衰期延长元件。增加天然地具有短半衰期的治疗分子的体内半衰期允许更可接受且可管理的给药方案而不牺牲有效性。如本文所用,"半衰期延长元件"是嵌合多肽的一部分,其例如通过改变其大小(例如,使其高于肾脏滤过界限)、形状、流体动力学半径、电荷、或吸收、生物分布、代谢和消除的参数来增加体内半衰期并改善pK。改善多肽pK的示例性方式是通过在多肽链中表达与受体结合的元件,所述受体再循环到细胞质膜而不是在溶酶体中降解,诸如内皮细胞上的FcRn受体和转铁蛋白受体。三种类型的蛋白质(例如人IgG、HSA(或片段)和转铁蛋白)在人血清中的存留时间比仅由其大小预测的时间长得多,这是它们与再循环而不是在溶酶体中降解的受体结合的能力的功能。保留FcRn结合的这些蛋白质或它们的片段通常与其他多肽连接,以延长其血清半衰期。在一个实施方案中,半衰期延长元件为人血清白蛋白(HSA)结合结构域。HSA(SEQ ID NO:2)也可直接结合至医药组成物或通过短接头结合。也可使用HSA的片段。HSA及其片段可用作阻断部分和半衰期延长元件。人IgG和Fc片段也可执行类似的功能。

[0178] 血清半衰期延长元件也可为与具有较长血清半衰期的蛋白质诸如血清白蛋白、转铁蛋白等结合的抗原结合多肽。此类多肽的实例包括抗体及其片段,包括多克隆抗体、重组抗体、人抗体、人源化抗体、单链可变片段(scFv)、单结构域抗体(诸如重链可变结构域(VH)、轻链可变结构域(VL)和骆驼型纳米抗体的可变结构域(VHH))、dAb等。其他合适的抗原结合结构域包括模拟抗体结合和/或结构的非免疫球蛋白蛋白,诸如anticalin、affilin、affibody分子、affimer、affitin、alphabody、avimer、DARPin、fynomer、库尼茨型(kunitz)结构域多肽、单体,以及基于诸如SpA、GroEL、纤维连接蛋白、脂质体和CTLA4支架的其他工程化支架的结合结构域。抗原结合多肽的其他实例包括所期望受体的配体、受体的配体结合部分、凝集素和与一种或多种靶抗原结合或缔合的肽。

[0179] 一些优选的血清半衰期延长元件是包含互补决定区(CDR)和任选地非CDR环的多肽。有利地,此类血清半衰期延长元件可延长细胞因子的血清半衰期,并且还用作细胞因子的抑制剂(例如,通过空间阻断、非共价相互作用或其组合)和/或作为靶向结构域。在一些情况下,血清半衰期延长元件是衍生自免疫球蛋白分子(Ig分子)或模拟抗体结构和/或结

合活性的工程化蛋白支架的结构域。Ig可为任何类别或子类(IgG1、IgG2、IgG3、IgG4、IgA、IgE、IgM等)。Ig分子的多肽链折叠成一系列由环连接的平行β链。在可变区中,三个环构成确定分子的抗原结合特异性的“互补决定区”(CDR)。IgG分子包含通过二硫键相互连接的至少两条重(H)链和两条轻(L)链或其抗原结合片段。每条重链由重链可变区(本文中缩写为VH)和重链恒定区构成。重链恒定区包含三个结构域CH1、CH2和CH3。每条轻链由轻链可变区(本文中缩写为VL)和轻链恒定区构成。轻链恒定区包含一个结构域CL。VH和VL区可进一步细分为高变区,称为互补决定区(CDR),其在序列上具有高变异性和/或参与抗原识别和/或通常形成结构明确的环,中间穿插有更保守的区域,称为框架区(FR)。每个VH和VL由三个CDR和四个FR构成,以下列顺序由氨基端至羧基端排列:FR1、CDR1、FR2、CDR2、FR3、CDR3、FR4。在本申请的一些实施方案中,FR1、FR2、FR3和FR4的氨基酸序列中的至少一些或所有是本文所述的结合部分的“非CDR环”的一部分。如图5所示,免疫球蛋白分子的可变结构域具有排列成两股的几条β链。轻免疫球蛋白链和重免疫球蛋白链的可变结构域含有三个高变环或互补决定区(CDR)。V结构域的三个CDR(CDR1、CDR2、CDR3)在β桶的一端聚簇。CDR是连接免疫球蛋白折叠的β链B-C、C’-C”和F-G的环,而连接免疫球蛋白折叠的β链AB、CC’、C”-D和E-F的底部环和连接免疫球蛋白折叠的D-E链的顶部环是非CDR环。在本申请的一些实施方案中,恒定结构域、CH1、CH2或CH3的至少一些氨基酸残基是本文所述的结合部分的“非CDR环”的一部分。在一些实施方案中,非CDR环包含Ig或Ig样分子的C1组结构域的AB、CD、EF和DE环中的一个或多个;Ig或Ig样分子的C2组结构域的AB、CC’、EF、FG、BC和EC’环;Ig或Ig样分子的I(中间)组结构域的DE、BD、GF、A(A1A2)B和EF环。

[0180] 在可变结构域内,CDR被认为负责抗原识别和结合,而FR残基被认为是CDR的支架。然而,在某些情况下,一些FR残基在抗原识别和结合中起重要作用。影响Ag结合的框架区残基分为两类。第一类是与抗原接触的FR残基,因此是结合位点的一部分,并且这些残基中的一些在序列上与CDR接近。其他残基是在序列上远离CDR但在分子的3-D结构中与其紧邻的残基,例如重链中的环。血清半衰期延长结构域(例如,包含CDR的结构域)可包含至少一个非CDR环。在一些实施方案中,非CDR环提供用于结合细胞因子、大血清蛋白或其他靶抗原的结合位点。

[0181] 除含有CDR之外或可替代地含有CDR,血清半衰期延长元件还包含非CDR环。在一些实施方案中,修饰非CDR环以产生对所期望靶抗原(诸如大血清蛋白,诸如白蛋白)或对细胞因子部分或其他靶向抗原具有特异性的抗原结合位点。设想可使用各种技术来修饰非CDR环,例如定点诱变、随机诱变、插入非CDR环氨基酸序列外来的至少一个氨基酸、氨基酸取代。在一些实例中,抗原肽被插入非CDR环。在一些实例中,抗原性肽取代非CDR环。在一些情况下,仅产生一个非CDR环的修饰以产生抗原结合位点。在其他情况下,对多于一个非CDR环进行修饰。例如,修饰在图5所示的非CDR环(即AB、CC’、C”D、EF和D-E)中的任一个。在一些情况下,修饰DE环。在其他情况下,修饰AB、CC’、C”-D、E-F环中的所有四个。

[0182] 在一些实例中,血清半衰期延长元件具有双重结合特异性,并含有特异性结合大血清蛋白(诸如血清白蛋白)的CDR和特异性结合并阻断细胞因子结构域的非CDR环。在其他实例中,血清半衰期延长元件含有特异性结合靶抗原诸如细胞因子结构域或其他靶抗原的CDR和特异性结合大血清蛋白诸如血清白蛋白的非CDR环。优选地,血清半衰期延长元件例如通过空间闭塞、通过特定分子间相互作用或两者的组合来抑制细胞因子结构域与同源细

胞因子受体的结合。

[0183] 在一些实施方案中，血清半衰期延长元件非共价地直接结合细胞因子并抑制其活性。

[0184] 在某些实例中，结合部分通过AB、CC'、C"D和E-F环中的一个或多个与细胞因子结合，并通过BC、C'C"和FG中的一个或多个与大血清蛋白诸如白蛋白结合。在某些实例中，结合部分通过其AB、CC'、C"D或EF环与大血清蛋白诸如白蛋白结合，并通过其BC、C'C"或FG环与细胞因子结合。在某些实例中，结合部分通过其AB、CC'、C"D和EF环与大血清蛋白诸如白蛋白结合，并通过其BC、C'C"和FG环与细胞因子结合。在某些实例中，结合部分通过AB、CC'、C"D和E-F环中的一个或多个与大血清蛋白诸如白蛋白结合，并通过BC、C'C"和FG中的一个或多个与细胞因子结合。

[0185] 结合部分为任何种类的多肽。例如，在某些情况下，结合部分为天然肽、合成肽或纤连蛋白支架或工程大血清蛋白。大血清蛋白包括例如白蛋白、纤维蛋白原或球蛋白。在一些实施方案中，结合部分为工程化支架。工程化支架包括例如sdAb、scFv、Fab、VHH、III型纤连蛋白结构域、免疫球蛋白样支架(如Halaby等人，1999 Prot Eng 12(7):563-571中提出的那样)、DARPin、胱氨酸结肽、脂质运载蛋白、三螺旋束支架、蛋白G相关白蛋白结合模块、或DNA或RNA适体支架。

[0186] 在一些情况下，血清半衰期延长元件通过其非CDR环结合细胞因子结构域，并且如本文所述，细胞因子结构域进一步连接至靶向结构域。在一些情况下，血清半衰期延长元件包含大血清蛋白的结合位点。在一些实施方案中，CDR提供大血清蛋白的结合位点。在一些实例中，大血清蛋白为球蛋白、白蛋白、转铁蛋白、IgG1、IgG2、IgG4、IgG3、IgA单体、XIII因子、纤维蛋白原、IgE或五聚体IgM。在一些实施方案中，CDR形成免疫球蛋白轻链(诸如Igκ游离轻链或Igλ游离轻链)的结合位点。

[0187] 一种示例性条件活性蛋白在图6中示出。在所示实例中，血清白蛋白结合结构域(例如dAb)中的非CDR环可形成细胞因子IL-2的结合位点。在此实例中，血清白蛋白的结合位点可由血清白蛋白结合结构域的CDR形成。

[0188] 血清半衰期延长元件可为任何类型的结合结构域，包括但不限于来自单克隆抗体、多克隆抗体、重组抗体、人抗体、人源化抗体的结构域。在一些实施方案中，结合部分为单链可变片段(scFv)、单结构域抗体，诸如重链可变结构域(VH)、轻链可变结构域(VL)和骆驼衍生纳米抗体的可变结构域(VHH)。在其他实施方案中，结合部分为非Ig结合结构域，即抗体模拟物，诸如anticalin、affilin、affibody分子、affimer、affitin、alphabody、avimer、DARPin、fynomer、库尼茨型结构域多肽和单体。

[0189] 在其他实施方案中，血清半衰期延长元件可为水溶性聚合物或与水溶性聚合物(诸如PEG)缀合的肽。如本文所用，“PEG”、“聚乙二醇”和“聚(乙二醇)”是可互换的，并包含任何非肽水溶性聚(环氧乙烷)。术语“PEG”也意指含有大部分，即大于50％的$-OCH_2CH_2-$重复亚基的聚合物。关于特定形式，PEG可采用多种分子量中的任何数量，以及将在下文更详细描述的结构或几何形状，诸如“分支”、“线性”、“叉状”、“多功能”等。PEG不限于特定的结构，并且可为线性的(例如，封端的，例如，烷氧基PEG或双官能PEG)、分支或多臂的(例如，叉状PEG或与多元醇核连接的PEG)、树突状(或星形)结构，每个结构具有或不具有一个或多个可降解的连接部分。此外，PEG的内部结构可以任何数量的不同重复模式来组织，并且可选自

由均聚物、交替共聚物、无规共聚物、嵌段共聚物、交替三元共聚物、无规三元共聚物和嵌段三元共聚物组成的组。PEG可通过任何合适的方法与多肽和肽缀合。通常，使反应性PEG衍生物(诸如N-羟基琥珀酰亚胺酯PEG)与包含具有侧链的氨基酸的肽或多肽反应，所述侧链含有胺、巯基、羧酸或羟基官能团，所述氨基酸诸如半胱氨酸、赖氨酸、天冬酰胺、谷氨酰胺、苏氨酸、酪氨酸、丝氨酸、天冬氨酸和谷氨酸。

[0190] 靶向结构域和保留结构域

[0191] 对于某些应用，可能需要使构建体在其体内期望位置存在的时间最大化。这可通过在嵌合多肽(融合蛋白)中包含另一个结构域以影响其在体内的运动来实现。例如，嵌合核酸可编码将多肽引导至体内某个位置(例如肿瘤细胞或炎症位点)的结构域；此结构域被称为“靶向结构域”和/或编码将多肽保留在体内某个位置(例如肿瘤细胞或炎症位点)的结构域；此结构域称为“保留结构域”。在一些实施方案中，结构域可用作靶向结构域和保留结构域。在一些实施方案中，靶向结构域和/或保留结构域对富含蛋白酶的环境具有特异性。在一些实施方案中，编码的靶向结构域和/或保留结构域对调节性T细胞(Treg)具有特异性，例如靶向CCR4或CD39受体。其他合适的靶向和/或保留结构域包括具有在炎症组织中过表达的同源配体的那些，例如IL-1受体或IL-6受体。在其他实施方案中，合适的靶向和/或保留结构域包括具有在肿瘤组织中过表达的同源配体的那些，例如Epcam、CEA或间皮素。在一些实施方案中，靶向结构域通过接头与白介素连接，所述接头在作用位点被裂解(例如通过炎症或癌症特异性蛋白酶)，从而在期望的位点释放白介素的全部活性。在一些实施方案中，靶向和/或保留结构域通过接头与白介素连接，所述接头不在作用位点被裂解(例如通过炎症或癌症特异性蛋白酶)，从而使细胞因子保留在所期望位点。

[0192] 在一些情况下，选择的抗原在病变细胞或组织(例如肿瘤或癌细胞)的表面上表达。可用于肿瘤靶向和保留的抗原包括但不限于EpCAM、EGFR、HER-2、HER-3、c-Met、FOLR1和CEA。本文所公开的医药组成物还包含含有两个靶向和/或保留结构域的蛋白质，所述两个靶向和/或保留结构域与已知在病变细胞或组织上表达的两个不同靶抗原结合。示例性抗原结合结构域对包括但不限于EGFR/CEA、EpCAM/CEA和HER-2/HER-3。

[0193] 合适的靶向和/或保留结构域包括抗原结合结构域，诸如抗体及其片段，包括多克隆抗体、重组抗体、人抗体、人源化抗体、单链可变片段(scFv)、单结构域抗体(诸如重链可变结构域(VH)、轻链可变结构域(VL)和骆驼型纳米抗体的可变结构域(VHH))、dAb等。其他合适的抗原结合结构域包括模拟抗体结合和/或结构的非免疫球蛋白蛋白，诸如anticalin、affilin、affibody分子、affimer、affitin、alphabody、avimer、DARPin、fynomer、库尼茨型结构域多肽、单体，以及基于其他工程化支架诸如SpA、GroEL、纤维连接蛋白、脂质体和CTLA4支架的结合结构域。抗原结合多肽的其他实例包括所期望受体的配体、受体的配体结合部分、凝集素和与一种或多种靶抗原结合或缔合的肽。

[0194] 在一些实施方案中，靶向和/或保留结构域特异性结合细胞表面分子。在一些实施方案中，靶向和/或保留结构域特异性结合肿瘤抗原。在一些实施方案中，靶向多肽特异性地且独立地结合选自以下至少一种的肿瘤抗原：成纤维细胞活化蛋白α(FAPa)、滋养层细胞糖蛋白(5T4)、肿瘤相关钙信号转导子2(Trop2)、纤连蛋白EDB(EDB-FN)、纤连蛋白EIIIB结构域、CGS-2、EpCAM、EGFR、HER-2、HER-3、cMet、CEA和FOLR1。在一些实施方案中，靶向多肽特异性地且独立地结合两个不同的抗原，其中抗原中的至少一个为选自EpCAM、EGFR、HER-2、

HER-3、cMet、CEA和FOLR1的肿瘤抗原。

[0195] 靶向和/或保留抗原可为在肿瘤细胞上表达的肿瘤抗原。肿瘤抗原是本领域中熟知的，并且包括例如EpCAM、EGFR、HER-2、HER-3、c-Met、FOLR1、PSMA、CD38、BCMA和CEA、5T4、AFP、B7-H3、钙粘蛋白-6、CAIX、CD117、CD123、CD138、CD166、CD19、CD20、CD205、CD22、CD30、CD33、CD352、CD37、CD44、CD52、CD56、CD70、CD71、CD74、CD79b、DLL3、EphA2、FAP、FGFR2、FGFR3、GPC3、gpA33、FLT-3、gpNMB、HPV-16E6、HPV-16E7、ITGA2、ITGA3、SLC39A6、MAGE、间皮素、Muc1、Muc16、NaPi2b、连接素-4、P-钙粘蛋白、NY-ESO-1、PRLR、PSCA、PTK7、ROR1、SLC44A4、SLTRK5、SLTRK6、STEAP1、TIM1、Trop2、WT1。

[0196] 靶向和/或保留抗原可为免疫检查点蛋白。免疫检查点蛋白的实例包括但不限于CD27、CD137、2B4、TIGIT、CD155、ICOS、HVEM、CD40L、LIGHT、TIM-1、OX40、DNAM-1、PD-L1、PD1、PD-L2、CTLA-4、CD8、CD40、CEACAM1、CD48、CD70、A2AR、CD39、CD73、B7-H3、B7-H4、BTLA、IDO1、IDO2、TDO、KIR、LAG-3、TIM-3或VISTA。

[0197] 靶向和/或保留抗原可为细胞表面分子，诸如蛋白质、脂质或多糖。在一些实施方案中，靶向和/或保留抗原是在肿瘤细胞、病毒感染的细胞、细菌感染的细胞、受损的红细胞、动脉斑块细胞、发炎或纤维化组织细胞上。靶向和/或保留抗原可包含免疫应答调节剂。免疫应答调节剂的实例包括但不限于粒细胞-巨噬细胞集落刺激因子(GM-CSF)、巨噬细胞集落刺激因子(M-CSF)、粒细胞集落刺激因子(G-CSF)、白介素2(IL-2)、白介素3(IL-3)、白介素12(IL-12)、白介素15(IL-15)、B7-1(CD80)、B7-2(CD86)、GITRL、CD3或GITR。

[0198] 靶向和/或保留抗原可为细胞因子受体。细胞因子受体的实例包括但不限于I型细胞因子受体，诸如GM-CSF受体、G-CSF受体、I型IL受体、Epo受体、LIF受体、CNTF受体、TPO受体；II型细胞因子受体，诸如IFN-α受体(IFNAR1、IFNAR2)、IFB-β受体、IFN-γ受体(IFNGR1、IFNGR2)、II型IL受体；趋化因子受体，诸如CC趋化因子受体、CXC趋化因子受体、CX3C趋化因子受体、XC趋化因子受体；肿瘤坏死受体超家族受体，诸如TNFRSF5/CD40、TNFRSF8/CD30、TNFRSF7/CD27、TNFRSF1A/TNFR1/CD120a、TNFRSF1B/TNFR2/CD120b；TGF-β受体，诸如TGF-β受体1、TGF-β受体2；Ig超家族受体，诸如IL-1受体、CSF-1R、PDGFR(PDGFRA、PDGFRB)、SCFR。

[0199] 接头

[0200] 如上文所述，医药组成物包含一个或多个接头序列。接头序列用于提供多肽之间的柔性，使得例如阻断部分能够抑制细胞因子多肽的活性。接头序列可位于细胞因子多肽、血清半衰期延长元件和/或阻断部分中的任何或所有之间。如本文所述，接头中的至少一个为蛋白酶可裂解的，并且含有(一种或多种)所期望蛋白酶的(一个或多个)裂解位点。优选地，所期望蛋白酶在所期望的细胞因子活性位点(例如肿瘤微环境)富集或选择性表达。因此，融合蛋白在所期望细胞因子活性的位点被优选地或选择性地裂解。

[0201] 合适的接头可具有不同的长度，诸如1个氨基酸(例如，Gly)至20个氨基酸、2个氨基酸至15个氨基酸、3个氨基酸至12个氨基酸，包括4个氨基酸至10个氨基酸、5个氨基酸至9个氨基酸、6个氨基酸至8个氨基酸或7个氨基酸至8个氨基酸，并且可为1、2、3、4、5、6、7、8、9、10、11、12、13、14、15、16、17、18、19、20、21、22、23、24、25、26、27、28、29、30、31、32、33、34、35、36、37、38、39、40、41、42、43、44、45、46、47、48、49、50、51、52、53、54、55、56、57、58、59或60个氨基酸。

[0202] 医药组成物的组分的取向在很大程度上是设计选择的问题，并且已经认识到多种

取向是可能的，并且所有取向都旨在由本申请涵盖。例如，阻断部分可位于细胞因子多肽的C端或N端。

[0203] 已知与患病细胞或组织相关的蛋白酶包括但不限于丝氨酸蛋白酶、半胱氨酸蛋白酶、天冬氨酸蛋白酶、苏氨酸蛋白酶、谷氨酸蛋白酶、金属蛋白酶、天冬酰胺肽裂解酶、血清蛋白酶、组织蛋白酶、组织蛋白酶B、组织蛋白酶C、组织蛋白酶D、组织蛋白酶E、组织蛋白酶K、组织蛋白酶L、激肽释放酶、hK1、hK10、hK15、纤溶酶、胶原酶、IV型胶原酶、溶基质素、Xa因子、糜蛋白酶样蛋白酶、胰蛋白酶样蛋白酶、弹性蛋白酶样蛋白酶、枯草杆菌蛋白酶样蛋白酶、猕猴桃蛋白酶、菠萝蛋白酶、钙蛋白酶、半胱天冬酶、半胱天冬酶-3、Mir1-CP、木瓜蛋白酶、HIV-1蛋白酶、HSV蛋白酶、CMV蛋白酶、凝乳酶、肾素、胃蛋白酶、蛋白裂解酶、豆荚蛋白、纤溶酶、猪笼草蛋白酶、金属外肽酶、金属内肽酶、基质金属蛋白酶(MMP)、MMP1、MMP2、MMP3、MMP8、MMP9、MMP13、MMP11、MMP14、尿激酶纤溶酶原活化剂(uPA)、肠激酶、前列腺特异性靶标(PSA，hK3)、白介素-1β转化酶、凝血酶、FAP(FAP-a)、二肽基肽酶、跨膜肽酶、颗粒酶和二肽基肽酶IV(DPPIV/CD26)。能够裂解由本文所提供的嵌合核酸序列编码的氨基酸序列的蛋白酶可例如选自由以下组成的组：前列腺特异性抗原(PSA)、基质金属蛋白酶(MMP)、A双歧蛋白和金属蛋白酶(ADAM)、纤溶酶原活化剂、组织蛋白酶、半胱天冬酶、肿瘤细胞表面蛋白酶和弹性蛋白酶。MMP可为例如基质金属蛋白酶2(MMP2)或基质金属蛋白酶9(MMP9)。

[0204] 表1列出了可用于本文所公开的方法的蛋白酶，并且表1a列出了示例性蛋白酶及其裂解位点：

[0205] 表1.与炎症和癌症相关的蛋白酶

[0206]

蛋白酶	特异性	其他方面
由杀伤 T 细胞分泌：		
颗粒酶 B（grB）	在 Asp 残基后裂解（asp-ase）	丝氨酸蛋白酶类型；强烈牵涉于诱导穿孔素依赖性靶细胞凋亡
颗粒酶 A（grA）	胰蛋白酶样，在碱性残基后裂解	丝氨酸蛋白酶类型；
颗粒酶 H（grH）	未知的底物特异性	丝氨酸蛋白酶类型； 其他颗粒酶也由杀伤 T 细胞分泌，但并非所有都存在于人中
半胱天冬酶-8	在 Asp 残基后裂解	半胱氨酸蛋白酶类型；在 TCR 诱导的细胞扩增中起重要作用，确切的分子作用尚不清楚
粘膜相关淋巴组织（MALT1）	在精氨酸残基后裂解	半胱氨酸蛋白酶类型；可能在 CBM 依赖性信号传导途径中充当支架和蛋白水解活性酶
类胰蛋白酶	靶标：血管紧张素 I、纤维蛋白原、尿激酶原、 TGF β；优选地在赖氨酸或精氨酸残基后裂解蛋白质	肥大细胞特异性丝氨酸蛋白酶类型；胰蛋白酶样；由于其四聚体结构，其中所有位点面向狭窄的中心孔，因此对哺乳动物中表达的大分子蛋白酶抑制剂的抑制具有抗性；还与炎症相关联
与炎症相关联：		

[0207]

凝血酶	靶标：FGF-2、HB-EGF、骨桥蛋白、PDGF、VEGF	丝氨酸蛋白酶类型；调节血管生长因子、趋化因子和细胞外蛋白的活性；增强 VEGF 诱导的增殖；诱导细胞迁移；血管生成因子；调节止血
糜酶	表现出糜蛋白酶样特异性，在芳香族氨基酸残基后裂解蛋白质	肥大细胞特异性丝氨酸蛋白酶类型
羧肽酶 A（MC-CPA）	从肽和蛋白质的 C 末端裂解氨基酸残基	锌依赖性金属蛋白酶类型
激肽释放酶	靶标：高分子量激肽原、尿激酶原	丝氨酸蛋白酶类型；调节松弛应答；促进炎症应答；纤维蛋白降解
弹性蛋白酶	靶标：E-钙粘蛋白、GM-CSF、IL-1、IL-2、IL-6、IL8、$p38^{MAPK}$、TNFα、VE-钙粘蛋白	中性粒细胞丝氨酸蛋白酶类型；降解 ECM 组分；调节炎症应答；活化促凋亡信号传导
组织蛋白酶 G	靶标：EGF、ENA-78、IL-8、MCP-1、MMP-2、MT1-MMP、PAI-1 、 RANTES 、TGFβ、TNFα	丝氨酸蛋白酶类型；降解 ECM 组分；白细胞化学引诱物；调节炎症应答；促进细胞凋亡
PR-3	靶标：ENA-78、IL-8、IL-18、JNK、$p38^{MAPK}$、TNFα	丝氨酸蛋白酶类型；促进炎症应答；活化促凋亡信号传导
颗粒酶 M （grM）	在 Met 和其他长的无分支疏水残基后裂解	丝氨酸蛋白酶类型；仅在 NK 细胞中表达
钙蛋白酶	在 Arg 和 Gly 之间裂解	半胱氨酸蛋白酶家族；钙依赖性；活化涉及许多炎症相关疾病的过程

[0208] 表1a：示例性蛋白酶和蛋白酶识别序列

[0209]

蛋白酶	裂解结构域序列	SEQ ID NO:
MMP7	KRALGLPG	3
MMP7	$(DE)_8$RPLALWRS$(DR)_8$	4
MMP9	PR(S/T)(L/I)(S/T)	5

[0210]

MMP9	LEATA	6
MMP11	GGAANLVRGG	7
MMP14	SGRIGFLRTA	8
MMP	PLGLAG	9
MMP	PLGLAX	10
MMP	PLGC(me)AG	11
MMP	ESPAYYTA	12
MMP	RLQLKL	13
MMP	RLQLKAC	14
MMP2、MMP9、MMP14	EP(Cit)G(Hof)YL	15
尿激酶型纤溶酶原活化物(uPA)	SGRSA	16
尿激酶型纤溶酶原活化物(uPA)	DAFK	17
尿激酶型纤溶酶原活化物(uPA)	GGGRR	18
溶酶体酶	GFLG	19
溶酶体酶	ALAL	20
溶酶体酶	FK	21
组织蛋白酶 B	NLL	22
组织蛋白酶 D	PIC(Et)FF	23
组织蛋白酶 K	GGPRGLPG	24
前列腺特异性抗原	HSSKLQ	25
前列腺特异性抗原	HSSKLQL	26
前列腺特异性抗原	HSSKLQEDA	27
单纯疱疹病毒蛋白酶	LVLASSSFGY	28
HIV 蛋白酶	GVSQNYPIVG	29
CMV 蛋白酶	GVVQASCRLA	30
凝血酶	F(Pip)RS	31
凝血酶	DPRSFL	32
凝血酶	PPRSFL	33
半胱天冬酶-3	DEVD	34
半胱天冬酶-3	DEVDP	35
半胱天冬酶-3	KGSGDVEG	36
白介素 1β 转换酶	GWEHDG	37
肠激酶	EDDDDKA	38
FAP	KQEQNPGST	39
激肽释放酶 2	GKAFRR	40

[0211]

纤溶酶	DAFK	41
纤溶酶	DVLK	42
纤溶酶	DAFK	43
TOP	ALLLALL	44

[0212] 本文提供包含多肽序列的医药组成物。与所有肽、多肽和蛋白质(包括其片段)一样,应当理解,嵌合多肽的氨基酸序列中可能发生另外的修饰(氨基酸序列变体),但这些修饰不会改变肽、多肽或蛋白质的性质或功能。此类修饰包括保守性氨基酸取代,并在下文更详细地讨论。

[0213] 本文提供的组合物具有所期望的功能。组合物至少包含细胞因子多肽,诸如IL-2、IL-7、IL-12、IL-15、IL-18、IL-21、IFNa或IFNg;或趋化因子,诸如CXCL10、CCL19、CCL20、CCL21;阻断部分,例如空间阻断多肽;和任选的血清半衰期延长元件,以及任选的靶向多肽,其中一个或多个接头连接组合物中的每个多肽。提供第一多肽(例如IL-2突变蛋白)作为活性剂。提供阻断部分以阻断白介素的活性。提供接头多肽,例如蛋白酶可裂解多肽,以被在活性剂的预期靶标上特异性表达的蛋白酶裂解。任选地,阻断部分通过结合白介素多肽来阻断第一多肽的活性。在一些实施方案中,阻断部分(例如空间阻断肽)通过蛋白酶可裂解的接头与白介素连接,所述蛋白酶可裂解的接头在作用位点被裂解(例如通过炎症特异性或肿瘤特异性蛋白酶),从而在所期望位点释放细胞因子的全部活性。

[0214] 蛋白酶裂解位点可为天然存在的蛋白酶裂解位点或人工工程化的蛋白酶裂解位点。人工工程化的蛋白酶裂解位点可被多于一种对将发生裂解的所期望环境(例如肿瘤)具有特异性的蛋白酶裂解。蛋白酶裂解位点可被至少一种蛋白酶、至少两种蛋白酶、至少三种蛋白酶或至少四种蛋白酶裂解。

[0215] 在一些实施方案中,接头包含甘氨酸-甘氨酸、分选酶识别基序或分选酶识别基序和肽序列$(Gly_4Ser)_n$(SEQ ID NO.:195)或$(Gly_3Ser)_n$(SEQ ID NO.:196),其中n为1、2、3、4或5。在一个实施方案中,分选酶识别基序包含肽序列LPXTG(SEQ ID NO.:193),其中X为任何氨基酸。在一个实施方案中,共价键是在连接到细胞因子多肽的C端的反应性赖氨酸残基与连接到阻断部分或其他部分的N端的反应性天冬氨酸之间。在一个实施方案中,共价键是在连接到细胞因子多肽的N端的反应性天冬氨酸残基与连接到阻断部分或其他部分的C端的反应性赖氨酸残基之间。

[0216] 裂解和诱导性

[0217] 如本文所述,在融合蛋白的情况下,细胞因子多肽的活性减弱,并且在所期望的活性位点(诸如在肿瘤微环境中)进行蛋白酶裂解,从融合蛋白中释放出一种形式的细胞因子,所述细胞因子作为细胞因子受体激动剂比融合蛋白的活性高得多。例如,融合多肽的细胞因子-受体活化(激动剂)活性可比作为单独的分子实体的细胞因子多肽的细胞因子受体活化活性低至少约10倍、至少约50倍、至少约100倍、至少约250倍、至少约500倍或至少约1000倍。当作为融合蛋白的一部分的细胞因子多肽含有与细胞因子多肽基本相同且基本上不包含额外氨基酸并且不与其他分子缔合(通过共价或非共价键)的氨基酸时,则作为单独的分子实体存在。如果必要的话,作为单独的分子实体的细胞因子多肽可包含一些额外氨基酸序列,诸如标签或短序列,以帮助表达和/或纯化。

[0218] 在其他实例中，融合多肽的细胞因子-受体活化(激动剂)活性比含有通过裂解融合蛋白中的蛋白酶可裂解的接头而产生的细胞因子多肽的多肽的细胞因子受体活化活性低至少约10倍、至少约50倍、至少约100倍、至少约250倍、至少约500倍或约1000倍。换句话讲，含有通过裂解融合蛋白中的蛋白酶可裂解的接头而产生的细胞因子多肽的多肽的细胞因子受体活化(激动剂)活性比融合蛋白的细胞因子受体活化活性高至少约10倍、至少约50倍、至少约100倍、至少约250倍、至少约500倍或至少约1000倍。

[0219] 多肽取代

[0220] 本文所述的多肽可包含具有与相应天然存在的蛋白质(例如，IL-2、IL-15、HSA)相同的氨基酸序列或只要保持所期望的功能可具有不同于天然存在的蛋白质的氨基酸序列的组分(例如，细胞因子、阻断部分)。应当理解，对所公开的蛋白质和编码它们的核酸的任何已知修饰和衍生物或可能出现的修饰和衍生物进行定义的一种方式是通过根据与特定已知参考序列的同一性来定义序列变体。具体公开的多肽和核酸与本文所提供的嵌合多肽具有至少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％、99％同一性。例如，提供的多肽或核酸与本文所述的任何核酸或多肽的序列具有至少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％、99％同一性。本领域技术人员容易理解如何确定两个多肽或两个核酸的同一性。例如，可在比对两个序列之后计算同一性，以使同一性处于其最高水平。

[0221] 计算同一性的另一种方式可通过公布的算法执行。用于比较的最佳序列比对可通过以下方法进行：Smith和Waterman Adv.Appl.Math.2:482(1981)的局部同一性算法；Needleman和Wunsch,J.Mol.Biol.48:443(1970)的同一性比对算法；Pearson和Lipman,Proc.Natl.Acad.Sci.USA 85:2444(1988)的相似性探索方法；这些算法的计算机化实现(在Wisconsin Genetics软件包中的GAP、BESTFIT、FASTA和TFASTA，Genetics Computer Group,575Science Dr.,Madison,Wis.)；或检查。

[0222] 对于核酸，相同类型的同一性可通过例如Zuker,Science 244:48-52(1989)；Jaeger等人,Proc.Natl.Acad.Sci.USA 86:7706-7710(1989)；Jaeger等人,Methods Enzymol.183:281-306(1989)中公开的算法获得，所述文献中关于至少与核酸比对相关的材料以引用的方式并入本文。应当理解，通常可使用任何方法，并且在某些情况下，这些各种方法的结果可能不同，但是技术人员理解，如果使用这些方法中的至少一种发现同一性，则可认为序列具有所述同一性，并在本文中公开。

[0223] 蛋白质修饰包括氨基酸序列修饰。氨基酸序列的修饰可能自然出现为等位基因变异(例如，由于遗传多态性)，可能由于环境影响(例如，通过暴露于紫外线)而出现，或可能由人为干预(例如，通过诱变克隆的DNA序列)产生，诸如诱导点、缺失、插入和取代突变体。这些修饰可导致氨基酸序列发生变化，提供沉默突变，修饰限制性位点或提供其他特异性突变。氨基酸序列修饰通常属于三种类别中的一种或多种：取代、插入或缺失修饰。插入包括氨基和/或羧基端融合以及单个或多个氨基酸残基的序列内插入。插入通常将比氨基或羧基端融合的插入小，例如约一至四个残基。缺失的特征在于从蛋白质序列中去除一个或多个氨基酸残基。通常，在蛋白质分子内的任一位点处缺失不超过约2至6个残基。氨基酸取

代通常是单个残基,但是也可同时在多个不同位置处出现;插入通常为约1至10个氨基酸残基;并且缺失的范围是约1至30个残基。缺失或插入优选在相邻对中进行,即2个残基缺失或2个残基插入。取代、缺失、插入或其任何组合可以进行组合以得到最终构建体。突变不能将序列置于阅读框外,并且优选地将不创建可以产生二级mRNA结构的互补区。取代修饰是其中至少一个残基已被去除并且在其位置插入不同残基的修饰。此类取代通常根据下表2进行,并将其称为保守取代。

[0224] 表2.示例性氨基酸取代

[0225]

氨基酸	示例性取代
Ala	Ser、Gly、Cys
Arg	Lys、Gln、Met、Ile
Asn	Gln、His、Glu、Asp
Asp	Glu、Asn、Gln
Cys	Ser、Met、Thr
Gln	Asn、Lys、Glu、Asp
Glu	Asp、Asn、Gln
Gly	Pro、Ala
His	Asn、Gln
Ile	Leu、Val、Met
Leu	Ile、Val、Met
Lys	Arg、Gln、Met、Ile
Met	Leu、Ile、Val
Phe	Met、Leu、Tyr、Trp、His
Ser	Thr、Met、Cys

[0226]

Thr	Ser、Met、Val
Trp	Tyr、Phe
Tyr	Trp、Phe、His
Val	Ile、Leu、Met

[0227] 通过已知方法进行修饰,包括特定氨基酸取代。例如,通过对编码多肽的DNA中的核苷酸进行位点特异性诱变来进行修饰,从而产生编码所述修饰的DNA,并随后在重组细胞培养物中表达DNA。用于在具有已知序列的DNA的预先确定位点处进行取代突变的技术是熟知的,例如M13引物诱变和PCR诱变。

[0228] 可选择修饰以优化结合。例如,亲和力成熟技术可用于通过在互补决定区(CDR)内引入随机突变来改变scFv的结合。可使用多种技术引入此类随机突变,所述技术包括放射、

化学诱变剂或易错PCR。可使用例如噬菌体展示进行多轮突变和选择。

[0229] 本申请还涉及编码本文所述的嵌合多肽的核酸，并且涉及此类核酸产生嵌合多肽以及用于治疗目的的用途。例如，本申请包括编码嵌合多肽的DNA和RNA分子(例如，mRNA、自我复制RNA)，以及此类DNA和RNA分子的治疗用途。

[0230] 示例性组合物

[0231] 本申请的示例性融合蛋白以多种取向组合上文所述的元件。本节中描述的取向仅作为实例，并且不应视为限制性的。

[0232] 在一些实施方案中，融合蛋白包含细胞因子、阻断部分和半衰期延长元件。在一些实施方案中，细胞因子位于半衰期延长元件和阻断部分之间。在一些实施方案中，细胞因子位于阻断部分和半衰期延长元件的N端。在一些此类实施方案中，细胞因子位于阻断部分近端；在一些此类实施方案中，细胞因子位于半衰期延长元件近端。在所有实施方案中必须包括至少一种蛋白酶可裂解的接头，使得细胞因子可在裂解时具有活性。在一些实施方案中，细胞因子位于阻断部分和半衰期延长元件的C端。额外元件可通过可裂解的接头、不可裂解的接头或通过直接融合来彼此连接。

[0233] 在一些实施方案中，所使用的阻断结构域能够延长半衰期，并且细胞因子位于两个此类阻断结构域之间。在一些实施方案中，细胞因子位于两个阻断结构域之间，其中一个能够延长半衰期。

[0234] 在一些实施方案中，两种细胞因子包含在同一构建体中。在一些实施方案中，细胞因子各自连接到两个阻断结构域(一个分子中总共三个)，其中阻断结构域位于两个细胞因子结构域之间。在一些实施方案中，可包括一个或多个额外半衰期延长结构域来优化药代动力学特性。在一些情况下，有益的是包含两个相同的细胞因子以促进二聚化。充当二聚体的细胞因子的实例为IFNγ。

[0235] 在一些实施方案中，三种细胞因子包含在同一构建体中。在一些实施方案中，第三种细胞因子可代替其他两种细胞因子之间的阻断结构域来起到阻断其他两种细胞因子的作用。

[0236] 用于融合蛋白的优选的半衰期延长元件为人血清白蛋白(HSA)、结合血清白蛋白的抗体或抗体片段(例如scFV、dAb)、人或人源化IgG、或前述任一种的片段。在一些优选的实施方案中，阻断部分为人血清白蛋白(HSA)、或结合血清白蛋白的抗体或抗体片段、结合细胞因子并阻止结合活化或细胞因子受体即另一种细胞因子活化的抗体、或前述任一种的片段。在包含额外靶向结构域的优选的实施方案中，靶向结构域为结合富集在癌细胞表面上的细胞表面蛋白(诸如EpCAM、FOLR1和纤连蛋白)的抗体。

[0237] 治疗方法和医药组成物

[0238] 还提供了治疗患有疾病或病症或处于发展所述疾病或病症的风险下的受试者的方法，所述疾病或病症诸如增殖性疾病、肿瘤性疾病、炎性疾病、免疫性病症、自身免疫性疾病、感染性疾病、病毒性疾病、过敏反应、寄生虫反应或移植物抗宿主疾病。所述方法向有此需要的受试者施用有效量的如本文所公开的融合蛋白，所述融合蛋白通常作为医药组成物施用。在一些实施方案中，所述方法还包括选择患有此种疾病或病症或处于发展所述疾病或病症的风险下的受试者。医药组成物优选地包含在炎症或肿瘤位点处活化的阻断的细胞因子、其片段或突变蛋白。在一个实施方案中，嵌合多肽包含细胞因子多肽、其片段或突变

蛋白以及血清半衰期延长元件。在另一个实施方案中，嵌合多肽包含细胞因子多肽、其片段或突变蛋白以及阻断部分，例如空间阻断多肽，其中空间阻断多肽能够在空间上阻断细胞因子多肽、其片段或突变蛋白的活性。在另一个实施方案中，嵌合多肽包含细胞因子多肽、其片段或突变蛋白、阻断部分以及血清半衰期延长元件。

[0239] 炎症是人体组织对有害刺激(诸如病原体、受损细胞或刺激物)的复杂生物应答的一部分，并且是涉及免疫细胞、血管和分子介质的保护性应答。炎症的功能是消除细胞损伤的初始原因，清除最初损伤和炎症过程中受损的坏死细胞和组织，并开始组织修复。炎症可由感染引起，作为症状或疾病出现，例如癌症、动脉粥样硬化、过敏、肌病、HIV、肥胖症或自身免疫性疾病。自身免疫性疾病是由对自身抗原的异常免疫应答引起的慢性病状。可用本文所公开的多肽治疗的自身免疫性疾病包括但不限于狼疮、腹腔疾病、1型糖尿病、格雷氏病(Graves disease)、炎性肠病、多发性硬化、牛皮癣、类风湿性关节炎和系统性红斑狼疮。

[0240] 医药组成物可包含一种或多种蛋白酶可裂解的接头序列。接头序列用于提供多肽之间的柔性，使得每个多肽能够抑制第一多肽的活性。接头序列可位于细胞因子多肽、其片段或突变蛋白、阻断部分和血清半衰期延长元件中的任何或所有之间。任选地，组合物包含两个、三个、四个或五个接头序列。所述接头序列即两个、三个或四个接头序列可为相同或不同的接头序列。在一个实施方案中，接头序列包含GGGGS(SEQ ID NO.:201)、GSGSGS(SEQ ID NO.:202)或G(SGGG)$_2$SGGT(SEQ ID NO.:203)。在另一个实施方案中，接头包含选自由以下组成的组的蛋白酶可裂解的序列:HSSKLQ(SEQ ID NO.:25)、GPLGVRG(SEQ ID NO.:197)、IPVSLRSG(SEQ ID NO.:198)、VPLSLYSG(SEQ ID NO.:199)和SGESPAYYTA(SEQ ID NO.:200)。

[0241] 在一些实施方案中，接头被选自由以下组成的组的蛋白酶裂解:激肽释放酶、凝血酶、糜酶、羧肽酶A、组织蛋白酶G、弹性蛋白酶、PR-3、颗粒酶M、钙蛋白酶、基质金属蛋白酶(MMP)、纤溶酶原活化剂、组织蛋白酶、半胱天冬酶、类胰蛋白酶或肿瘤细胞表面蛋白酶。

[0242] 合适的接头可具有不同的长度，诸如1个氨基酸(例如，Gly)至20个氨基酸、2个氨基酸至15个氨基酸、3个氨基酸至12个氨基酸，包括4个氨基酸至10个氨基酸、5个氨基酸至9个氨基酸、6个氨基酸至8个氨基酸或7个氨基酸至8个氨基酸，并且可为1、2、3、4、5、6、7、8、9、10、11、12、13、14、15、16、17、18、19、20、21、22、23、24、25、26、27、28、29、30、31、32、33、34、35、36、37、38、39、40、41、42、43、44、45、46、47、48、49、50、51、52、53、54、55、56、57、58、59或60个氨基酸。

[0243] 还提供了治疗患有癌症或处于发展癌症的风险下的受试者的方法。所述方法包括向有此需要的受试者施用有效量的如本文所公开的嵌合多肽(融合蛋白)，所述嵌合多肽通常作为医药组成物施用。在一些实施方案中，所述方法还包括选择患有癌症或处于发展癌症的风险下的受试者。医药组成物优选地包含在肿瘤位点处活化的阻断的细胞因子、其片段或突变蛋白。优选地，肿瘤为实体肿瘤。癌症可以是但不限于结肠癌、肺癌、黑色素瘤、肉瘤、肾细胞癌和乳腺癌。

[0244] 所述方法还可包括施用一种或多种额外剂来治疗癌症，所述一种或多种额外剂诸如化学治疗剂(例如，阿霉素(Adriamycin)、柔红霉素(Cerubidine)、博莱霉素(Bleomycin)、马法兰(Alkeran)、长春碱(Velban)、长春新碱(Oncovin)、氟尿嘧啶、噻替派、甲氨蝶呤、比生群、米托蒽醌(Noantrone)、硫鸟嘌呤(Thiguanine)、阿糖胞苷

(Cytaribine)、丙卡巴肼(Procarabizine))、免疫肿瘤剂(例如,抗PD-L1、抗CTLA4、抗PD-1、抗CD47、抗GD2)、细胞疗法(例如,CAR-T、T细胞疗法)、溶瘤病毒等。

[0245] 本文提供含有嵌合多肽和药学上可接受的载剂的药物制剂或组合物。本文所提供的组合物适合于体外或体内施用。药学上可接受的载剂意指不为在生物学上或另外不合需要的材料,即所述材料向受试者施用而不引起不期望的生物作用或以有害方式与含有所述材料的药物制剂或组合物的其他组分相互作用。选择载剂以使活性成分的降解最小化并使受试者的不良副作用最小化。

[0246] 合适的载剂及其制剂描述于Remington:The Science and Practice of Pharmacy,第21版,David B.Troy编,Lippicott Williams&Wilkins(2005)中。通常,在制剂中使用适当量的药学上可接受的盐以使制剂等渗,尽管在需要时制剂可为高渗或低渗的。药学上可接受的载剂的实例包括但不限于无菌水、盐水、缓冲溶液(如林格氏溶液)和右旋糖溶液。溶液的pH通常为约5至约8或约7至7.5。其他载剂包括持续释放制剂,诸如含有免疫原性多肽的固体疏水性聚合物的半透性基质。基质呈成形制品的形式,例如膜、脂质体或微粒。根据例如施用途径和所施用组合物的浓度,某些制剂可能为更优选的。载剂是适合于将嵌合多肽或编码嵌合多肽的核酸序列施用于人或其他受试者的那些载剂。

[0247] 药物制剂或组合物根据是需要局部治疗或全身治疗以及待治疗的区域来以多种方式施用。通过若干种施用途径中的任一种施用组合物,所述施用途径包括局部、口服、肠胃外、静脉内、关节内、腹膜内、肌肉内、皮下、腔内、经皮、肝内、颅内、雾化/吸入或通过经由支气管镜检安装。在一些实施方案中,组合物局部(非全身性)施用,包括肿瘤内、关节内、鞘内等。

[0248] 用于肠胃外施用的制剂包括无菌水性或非水性溶液、悬浮液以及乳液。非水性溶剂的实例为丙二醇、聚乙二醇、植物油(诸如橄榄油)和可注射有机酯(诸如油酸乙酯)。水性载剂包括水、醇/水性溶液、乳液或悬浮液,包括盐水和缓冲介质。肠胃外媒介物包括氯化钠溶液、林格氏右旋糖、右旋糖和氯化钠、乳酸化林格氏溶液或不挥发性油。静脉内媒介物包括流体和营养补充剂、电解质补充剂(如基于林格氏右旋糖的那些)等。任选地存在防腐剂和其他添加剂,诸如例如抗微生物剂、抗氧化剂、螯合剂和惰性气体等。

[0249] 局部施用的制剂包括软膏、洗剂、乳膏、凝胶、滴剂、栓剂、喷雾剂、液体和粉末。常规药物载剂、水性、粉末或油性基质、增稠剂等任选地为必需或期望的。

[0250] 用于口服施用的组合物包括粉末或颗粒、水或非水性介质中的悬浮液或溶液、胶囊、囊剂或片剂。增稠剂、调味料、稀释剂、乳化剂、分散助剂或结合剂任选地为期望的。

[0251] 任选地,嵌合多肽或编码嵌合多肽的核酸序列由载体施用。有许多组合物和方法可用于通过例如表达载体在体外或体内将核酸分子和/或多肽递送至细胞。这些方法和组合物主要可分为两类:基于病毒的递送系统和基于非病毒的递送系统。此类方法为本领域中熟知的,并且易于适用于本文所述的组合物和方法。此类组合物和方法可用于体外或体内转染或转导细胞,以例如产生表达并优选地分泌编码的嵌合多肽的细胞系或将核酸治疗性地递送至受试者。本文所公开的嵌合核酸的组分通常在框架内可操作地连接以编码融合蛋白。

[0252] 如本文所用,质粒或病毒载体是将所公开的核酸运输到细胞中而不降解的剂,并且包括使核酸分子和/或多肽在其所递送到的细胞中产生表达的启动子。病毒载体为例如

腺病毒、腺相关病毒、疱疹病毒、痘苗病毒、脊髓灰质炎病毒、辛德毕斯(Sindbis)和其他RNA病毒,包括具有HIV骨架的这些病毒。还优选共享这些病毒的特性而使其适合用作载体的任何病毒家族。逆转录病毒载体通常由Coffin等人,Retroviruses,Cold Spring Harbor Laboratory Press(1997)描述,其中载体及其制备方法以引用的方式并入本文。已经描述了复制缺陷型腺病毒的构建(Berkner等人,J.Virol.61:1213-20(1987);Massie等人,Mol.Cell.Biol.6:2872-83(1986);Haj-Ahmad等人,J.Virol.57:267-74(1986);Davidson等人,J.Virol.61:1226-39(1987);Zhang等人,BioTechniques 15:868-72(1993))。这些病毒作为载体的益处和用途是它们可扩散到其他细胞类型上的程度受到限制,因为它们可以在初始感染的细胞内复制,但不能形成新的感染性病毒颗粒。重组腺病毒已显示在直接体内递送至气道上皮、肝细胞、血管内皮、CNS实质和许多其他组织位点之后实现高效率。其他有用的系统包括例如复制型和宿主限制性非复制型痘苗病毒载体。

[0253] 所提供的多肽和/或核酸分子可通过病毒样颗粒递送。病毒样颗粒(VLP)由衍生自病毒结构蛋白的一种或多种病毒蛋白组成。用于制备和使用病毒样颗粒的方法描述于例如Garcea和Gissmann,Current Opinion in Biotechnology 15:513-7(2004)。

[0254] 所提供的多肽可通过亚病毒致密体(DB)递送。DB通过膜融合将蛋白质运输到靶细胞中。用于制备和使用DB的方法描述于例如Pepperl-Klindworth等人,Gene Therapy 10:278-84(2003)。

[0255] 所提供的多肽可通过外皮聚集体递送。用于制备和使用外皮聚集体的方法描述于国际公布号WO 2006/110728中。

[0256] 基于非病毒的递送方法可包括含有核酸分子和编码多肽的核酸序列的表达载体,其中核酸可操作地连接到表达控制序列。合适的载体骨架包括例如本领域常规使用的那些,诸如质粒、人工染色体、BAC、YAC或PAC。许多载体和表达系统可从诸如Novagen(Madison,Wis.)、Clonetech(Pal Alto,Calif.)、Stratagene(La Jolla,Calif.)和Invitrogen/Life Technologies(Carlsbad,Calif.)的公司商购获得。载体通常含有一个或多个调节区。调节区包括但不限于启动子序列、增强子序列、应答元件、蛋白质识别位点、诱导因子、蛋白质结合序列、5'和3'非翻译区(UTR)、转录起始位点、末端序列、聚腺苷酸化序列和内含子。此类载体还可用于通过在合适宿主细胞诸如CHO细胞中表达来制备嵌合多肽。

[0257] 控制哺乳动物宿主细胞中载体转录的优选启动子可获自各种来源,例如病毒的基因组,诸如多瘤病毒、猿猴病毒40(SV40)、腺病毒、逆转录病毒、乙型肝炎病毒和最优选的巨细胞病毒(CMV);或获自异源哺乳动物启动子,例如β-肌动蛋白启动子或EF1α启动子;或获自杂合或嵌合启动子(例如,融合至β-肌动蛋白启动子的CMV启动子)。当然,来自宿主细胞或相关物种的启动子也可用于本文。

[0258] 增强子通常是指DNA中距转录起始位点不固定距离处起作用的序列,并且可位于转录单元的5'或3'。此外,增强子可位于内含子内以及在编码序列本身内。它们的长度通常在10个与300个碱基对(bp)之间,并且它们以顺式起作用。增强子通常起到增加附近启动子转录的作用。增强子还可含有介导转录调节的应答元件。虽然已知许多增强子序列来自哺乳动物基因(球蛋白、弹性蛋白酶、白蛋白、甲胎蛋白和胰岛素),但人们通常将使用来自真核细胞病毒的增强子进行一般表达。优选的实例为复制起点后侧上的SV40增强子、巨细胞

病毒早期启动子增强子、复制起点后侧上的多瘤增强子以及腺病毒增强子。

[0259] 启动子和/或增强子可为可诱导型的(例如化学或物理调节的)。化学调节的启动子和/或增强子可例如通过醇、四环素、类固醇或金属的存在来调节。物理调节的启动子和/或增强子可例如由环境因素诸如温度和光来调节。任选地,启动子和/或增强子区可充当组成型启动子和/或增强子,以最大化待转录的转录单元区的表达。在某些载体中,启动子和/或增强子区域可以细胞类型特异性方式具有活性。任选地,在某些载体中,启动子和/或增强子区域可在所有真核细胞中具有活性,而与细胞类型无关。这种类型的优选启动子为CMV启动子、SV40启动子、β-肌动蛋白启动子、EF1α启动子和逆转录病毒长末端重复序列(LTR)。

[0260] 载体还可包含例如复制起点和/或标记。标记基因可在细胞上赋予可选择表型,例如抗生素抗性。标记产物用于确定载体是否已被递送至细胞,并且一旦递送就被表达。哺乳动物细胞的可选择标记的实例为二氢叶酸还原酶(DHFR)、胸苷激酶、新霉素、新霉素类似物G418、潮霉素、嘌呤霉素和杀稻瘟菌素。当此类可选择标记成功地转移到哺乳动物宿主细胞中时,如果置于选择压力下,则转化的哺乳动物宿主细胞可存活。其他标记的实例包括例如大肠杆菌(E.coli)lacZ基因、绿色荧光蛋白(GFP)和荧光素酶。另外,表达载体可包括被设计为促进表达的多肽的操纵或检测(例如,纯化或定位)的标签序列。标签序列诸如GFP、谷胱甘肽S-转移酶(GST)、聚组氨酸、c-myc、血凝素或FLAG™标签(Kodak;New Haven,Conn.)序列通常表达为与编码的多肽的融合物。此类标签可插入多肽内的任何位置,包括羧基端或氨基端。

[0261] 如本文所用,术语肽、多肽或蛋白质广泛地用于指由肽键连接的两个或更多个氨基酸。蛋白质、肽和多肽在本文中也可互换使用,以指氨基酸序列。应当认识到,术语多肽在本文中并不用于暗示构成所述分子的氨基酸的特定大小或数量,并且本申请的肽可含有至多几个氨基酸残基或更多。如通篇所用,受试者可为脊椎动物,更具体地为哺乳动物(例如人、马、猫、狗、牛、猪、绵羊、山羊、小鼠、兔、大鼠和豚鼠)、鸟类、爬行动物、两栖动物、鱼类和其他任何动物。术语不表示特定的年龄或性别。因此,旨在涵盖无论雄性还是雌性的成年和新生受试者。如本文所用,患者或受试者可互换使用,并且可指患有疾病或病症(例如癌症)的受试者。术语患者或受试者包括人和兽医学受试者。

[0262] 处于发展疾病或病症的风险下的受试者可能在遗传上易患所述疾病或病症,例如具有家族史或具有引起所述疾病或病症的基因的突变,或表现出所述疾病或病症的早期体征或症状。当前患有疾病或病症的受试者具有疾病或病症的一种或多于一种症状,并且可能已诊断为患有所述疾病或病症。

[0263] 如本文所述的方法和剂可用于预防性治疗和治疗性治疗。为了预防性应用,在发作之前(例如,在癌症或炎症的明显体征之前)或在早发期间(例如,在癌症或炎症的早期体征和症状时)向受试者施用治疗有效量的本文所述的嵌合多肽或编码所述嵌合多肽的嵌合核酸序列。预防性施用可在表现癌症或炎症症状之前发生若干天至若干年。例如,预防性施用可用于预防性治疗诊断为患有癌症遗传倾向的受试者。治疗性治疗涉及在诊断或发展为癌症或炎症(例如,自身免疫性疾病)后,向受试者施用治疗有效量的本文所述的嵌合多肽或编码所述嵌合多肽的核酸序列。当患者正在接受预期会发炎的治疗(例如,化学疗法)时,也可使用预防性应用。

[0264] 根据本文教导的方法,向受试者施用有效量的剂(例如,嵌合多肽)。术语有效量和

有效剂量可互换使用。术语有效量定义为产生所期望的生理应答所必需的任何量。可凭经验确定施用所述剂的有效量和方案，并且进行此类确定是在本领域技术范围内的。施用的剂量范围是足够大以产生所期望的效果的剂量范围，其中疾病或病症的一种或多种症状受到影响(例如，减少或延迟)。剂量不应大到导致严重的不良副作用，诸如不需要的交叉反应、过敏反应等。一般来讲，剂量随着年龄、病状、性别、疾病类型、疾病或病症程度、施用途径或方案中是否包含其他药物而变化，并且可由本领域技术人员确定。在任何禁忌症的情况下，可由个体医师调节剂量。剂量可变化，并且可以每日一个或多个剂量施用来施用，历时一天或几天。关于给定类别药物产品的适当剂量，指导可发现于文献中。

[0265] 如本文所用，术语治疗(treatment、treat或treating)是指减少疾病或病状的作用或者疾病或病状的症状的方法。因此，在公开的方法中，治疗可指确立的疾病或病状或者疾病或病状的症状的严重程度的10％、20％、30％、40％、50％、60％、70％、80％、90％或100％减少。例如，如果与对照相比，受试者疾病的一个或多个症状减少10％，则认为用于治疗疾病的方法是一种治疗。因此，与天然或对照水平相比，减少可为10％、20％、30％、40％、50％、60％、70％、80％、90％、100％或10％与100％之间的任何减少百分比。应理解，治疗不必指治愈或完全消除疾病、病状或者疾病或病状的症状。

[0266] 如本文所用，术语疾病或病症的预防(prevent、preventing和prevention)是指例如在受试者开始显示疾病或病症的一种或多种症状之前或大约同时发生的施用嵌合多肽或编码嵌合多肽的核酸序列的作用，其抑制或延迟疾病或病症的一个或多个症状的发作或加剧。如本文所用，对降低、减少或抑制的提及包括与对照水平相比10％、20％、30％、40％、50％、60％、70％、80％、90％或更大的变化。此类术语可包括但不一定包括完全消除。

[0267] 已经开发了相对于IL2Rβγ对IL2Rαβγ具有选择性的IL-2变体(Shanafelt,A.B.等人,2000,Nat Biotechnol.18:1197-202;Cassell,D.J.等人,2002,Curr Pharm Des.,8:2171-83)。这些变体具有氨基酸取代，这降低了它们对IL2RB的亲和力。由于IL-2对IL2RG具有无法检测到的亲和力，因此这些变体降低了对IL2Rβγ受体复合物的亲和力，并且降低了活化IL2Rβγ表达细胞的能力，但保留了结合IL2RA的能力以及结合并活化IL2Rαβγ受体复合物的能力。

[0268] 基于表达IL2Rβγ的NK细胞是导致毒性的主要因素的假说，这些变体中的一种IL2/N88R(Bay 50-4798)作为免疫系统刺激物的IL-2低毒版本进行临床测试。Bay 50-4798已显示选择性地刺激活化的T细胞相对于NK细胞的增殖，并在癌症患者(Margolin,K.等人,2007,Clin Cancer Res.,13:3312-9)和HIV患者(Davey,R.T.等人,2008,J Interferon Cytokine Res.,28:89-100)的I/II期临床试验中进行评估。这些临床试验表明，Bay 50-4798比阿地白介素更安全且更耐受，并且还表明它增加了CD4+CD25+ T细胞(富含Treg细胞的细胞群)的水平。在这些试验之后，本领域的研究更充分地确立了Treg细胞的身份，并证明Treg细胞选择性表达IL2Rαβγ(回顾于Malek,T.R.等人,2010,Immunity,33:153-65中)。

[0269] 另外，可制备相对于天然IL-2选择性地改变对CD25链的亲和力的突变体。

[0270] IL-2可被工程化以产生通常结合IL-2R复合物或特异性结合IL-2Rα亚基的突变体，其亲和力不同于相应的野生型IL-2或目前可用的突变体(称为C125S，因为位置125处的半胱氨酸残基被丝氨酸残基替代)的亲和力。

[0271] 因此，本申请的特征在于突变体白介素-2(IL-2*)多肽，其包括与野生型IL-2具有

至少80％同一性(例如,85％、87％、90％、95％、97％、98％或99％同一性)的氨基酸序列,并且与WT IL-2相比,其与IL-2三聚体受体的结合相对于二聚体IL-2受体更高。通常,突变蛋白还将以比野生型IL-2结合IL-2Rα的亲和力更大的亲和力结合IL-2受体α亚基(IL-2Rα)。由于含有(或仅含有)一个或多个氨基酸取代(其可视为保守或非保守取代),突变体IL-2多肽内的氨基酸序列可与SEQ ID NO:1(UniProtKB登录号P60568)不同。也可并入非天然存在的氨基酸。可替代地或另外,由于含有和添加和/或缺失一个或多个氨基酸残基,氨基酸序列可与SEQ ID NO:1(其可视为“参考”序列)不同。更具体地,氨基酸序列可由于SEQ ID NO:1的以下位置中的至少一个位置处的突变而不同于SEQ ID NO:1:1、4、8、9、10、11、13、15、26、29、30、31、35、37、46、48、49、54、61、64、67、68、69、71、73、74、75、76、79、88、89、90、92、99、101、103、114、125、128或133(或其组合)。如所指出的,可能这些位置中只有一个可改变,可能位置中的两个、三个、四个、五个、六个、七个、八个、九个、十个或11个或更多个(包括至多所有)可改变。例如,氨基酸序列可在位置69和74以及进一步在位置30、35和128中的一个或多个处不同于SEQ ID NO:1。氨基酸序列也可在以下组的位置中的一组处不同于SEQ ID NO:2(如US 7569215中所公开的,所述专利以引用的方式并入本文):(a)位置64、69和74;(b)位置69、74和101;(c)位置69、74和128;(d)位置30、69、74和103;(e)位置49、69、73和76;(f)位置69、74、101和133;(g)位置30、69、74和128;(h)位置69、74、88和99;(i)位置30、69、74和128;(j)位置9、11、35、69和74;(k)位置1、46、49、61、69和79;(l)位置48、68、71、90、103和114;(m)位置4、10、11、69、74、88和133;(n)位置15、3031、35、48、69、74和92;(O)位置30、68、69、71、74、75、76和90;(p)位置30、31、37、69、73、74、79和128;(q)位置26、29、30、54、67、69、74和92;(r)位置8、13、26、30、35、37、69、74和92;和(s)位置29、31、35、37、48、69、71、74、88和89。除了这些位置的突变之外,突变体IL-2多肽的氨基酸序列可以在其他方面与SEQ ID NO:1相同。关于特异性取代,由于具有以下突变中的一种或多种,所述氨基酸序列可不同于SEQ ID NO:1:A1T、S4P、K8R、K9T、T10A、Q11R、Q13R、E15K、N26D、N29S、N30S、N30D、N30T、Y31H、Y31C、K35R、T37A、T37R、M46L、K48E、K49R、K49E、K54R、E61D、K64R、E67G、E68D、V69A、N71T、N71A、N71R、A73V、Q74P、S75P、K76E、K76R、H79R、N88D、I89V、N90H、I92T、S99P、T101A、F103S、I114V、I128T、I128A、T133A或T133N。我们的命名法与科学文献的命名法一致,其中野生型或参考序列中氨基酸的单字母代码紧接其在序列中的位置,然后紧接替代它的氨基酸的单字母代码。因此,A1T表示用苏氨酸取代位置1的丙氨酸残基。本申请范围内的其他突变体多肽包括那些包括在V69(例如A)和Q74(例如P)处具有取代的突变体SEQ ID NO:2的突变体多肽。例如,氨基酸序列可包含相对于SEQ ID NO:2的以下组突变中的一组:(a)K64R、V69A和Q74P;(b)V69A、Q74P和T101A;(c)V69A、Q74P和I128T;(d)N30D、V69A、Q74P和F103S;(e)K49E、V69A、A73V和K76E;(f)V69A、Q74P、T101A和T133N;(g)N30S、V69A、Q74P和I128A;(h)V69A、Q74P、N88D和S99P;(i)N30S、V69A、Q74P和I128T;(j)K9T、Q11R、K35R、V69A和Q74P;(k)A1T、M46L、K49R、E61D、V69A和H79R;(l)K48E、E68D、N71T、N90H、F103S和I114V;(m)S4P、T10A、Q11R、V69A、Q74P、N88D和T133A;(n)E15K、N30S Y31H、K35R、K48E、V69A、Q74P和I92T;(o)N30S、E68D、V69A、N71A、Q74P、S75P、K76R和N90H;(p)N30S、Y31C、T37A、V69A、A73V、Q74P、H79R和I128T;(q)N26D、N29S、N30S、K54R、E67G、V69A、Q74P和I92T;(r)K8R、Q13R、N26D、N30T、K35R、T37R、V69A、Q74P和I92T;以及(s)N29S、Y31H、K35R、T37A、K48E、V69A、N71R、Q74P、N88D和I89V。SEQ ID NO:2作为可用于本申请的示例性IL-2多肽序列公开

于US 7569215中,所述专利以引用的方式并入本文。

[0272] 如上文所述,本文所公开的任何突变体IL-2多肽都可包含所述序列;它们也可限于所述序列并在其他方面与SEQ ID NO:1相同。此外,本文所描述的任何突变体IL-2多肽可任选地包含用另一个残基(例如,丝氨酸)取代位置125处的半胱氨酸残基和/或可任选地包含在SEQ ID NO:1的位置1处的丙氨酸残基的缺失。

[0273] 本文所公开的突变体IL-2多肽可以结合至IL-2Rα亚基的K_d小于约28nM(例如,小于约25nM;小于约5nM;约1nM;小于约500pM;或小于约100pM)。更具体地,突变体IL-2多肽可具有小于1.0nM(例如,约0.8nM、0.6nM、0.4nM或0.2nM)的亲和力平衡常数。亲和力也可表示为与IL-2Rα亚基或IL-2受体复合物(例如,在细胞表面表达或以其他方式结合膜的复合物)解离的相对速率。例如,相对于野生型多肽或基于IL-2的治疗剂例如IL-2*,突变体IL-2多肽与例如IL-2Rα解离的速率降低。可替代地,亲和力可表征为IL-2*多肽在例如表达IL-2R的细胞表面上持续存在的时间或平均时间。例如,IL-2*多肽可在受体上持续存在至少约2、5、10、50、100或250次(或更多)。

[0274] 所公开的材料、组合物以及组分可用于所公开的方法和组合物,可与所公开的方法和组合物联用,可用来制备所公开的组合物,或者是所公开的方法和组合物的产品。本文公开了这些材料及其他材料,并且应理解,在公开了这些材料的组合、子组、相互作用、群组等,而没有明确地具体提及各种个体和集体组合的每一种组合以及这些化合物的排列方式时,每种情况均具体地涵盖并描述在本文中。例如,如果公开并讨论了方法并且讨论了可对多个分子(包括所述方法)进行的多种修改,除非明确地相反指示,否则明确涵盖了所述方法的每一种组合和排列以及可能的修改。同样,还特别预期并公开这些的任何子集或组合。这个概念适用于本申请的所有方面,包括但不限于使用所公开的组合物的方法中的步骤。因此,如果有多种附加步骤可进行,那么应理解,这些附加步骤中的每一个可与所公开的方法的任何具体方法步骤或方法步骤的组合一起实施,并且每种此类组合或组合的子集都在本申请的预想之中并应视为得到公开。

[0275] 本文引用的出版物和引用它们的材料特此以引用的方式整体明确地并入。

[0276] 实施例

[0277] 以下是本申请的方法和组合物的实例。应理解,鉴于本文所提供的一般描述,可实施各种其他实施方案。

[0278] 实施例1:通过ELISA检测融合蛋白中的IL-2、IL-2突变蛋白、IL-2Rα和IL-2Rγ

[0279] 用可商购获得的抗体(例如抗IL-2单克隆抗体(JES6-1A12)(BD Pharmingen;San Jose,Calif.))检测IL-2突变蛋白。阳性对照用于显示单克隆抗体是否识别细胞因子或突变蛋白。还使用针对IL-2Rα和IL-2Rγ链的抗体。使用PBS中的抗体(2.5μg/ml)涂覆96孔板的孔。用具有0.2%Tween®20的PBS中的5%脱脂牛奶(PBS-M-Tw)阻断孔,并在37℃下添加融合蛋白1至2小时。洗涤后,添加抗IL-2生物素标记的抗体,例如JES5H4(BD Pharmingen),并使用Strepavidin HRP(Southern Biotechnology Associates;Birmingham,Ala.)检测结合。通过在0.1M柠檬酸盐pH 4.5和0.04%H_2O_2中添加50μl邻苯二胺(OPD)(Sigma-Aldrich)来使ELISA板显影,通过添加50μl/孔2N H_2SO_4停止ELISA,并在490nm处读取吸光度。

[0280] 实施例2:通过MMP9蛋白酶对融合蛋白进行蛋白酶裂解

[0281] 本领域技术人员将熟悉建立蛋白质裂解测定的方法。用1ug活性MMP9(Sigma目录号SAE0078-50或Enzo目录BML-SE360)裂解1xPBS pH7.4中的100ug蛋白质,并在室温下孵育至多16小时。随后将消化的蛋白质用于功能测定或在测试之前储存于-80℃下。使用本领域中熟知的方法通过SDS PAGE监测裂解的程度。如图10、13、18A、18B、24B、24C和27A所示,查看MMP9蛋白酶完全裂解融合蛋白。

[0282] 实施例3:CTLL-2测定

[0283] 将CTLL2细胞(ATCC)以500,000个细胞/孔的浓度的悬浮液接种在含有或不含40mg/ml人血清白蛋白(HSA)的培养基中,并在37℃和5%CO_2下用系列稀释的重组hIL2或可活化hIL2刺激72小时。测试未裂解和裂解的可活化hIL2的活性。通过用活性MMP9孵育产生裂解的可活化hIL2。使用基于CellTiter-Glo(Promega)发光的细胞活力测定评定细胞活力。结果在图8、9和25中示出。

[0284] 实施例4:IL-2/IL-2Rα/IL-2Rγ嵌合多肽的蛋白酶裂解导致对抗体和生物活性IL-2突变蛋白的可及性增加。

[0285] 在用蛋白酶(例如PSA)裂解之前和之后,对IL-2突变蛋白融合蛋白进行生物化学表征。免疫印迹分析将显示融合蛋白可被PSA裂解,并且在用PSA处理样品后,约20kDa预测的低分子量裂解产物与抗IL-2抗体反应的强度增加。裂解程度取决于PSA的量以及孵育时间。有趣的是,当在PSA处理之前和之后通过ELISA对融合蛋白进行分析时,发现在PSA裂解后IL-2的表观量增加。在此实验中,根据构建体的不同,使用这种夹心ELISA检测到的IL-2表观量增加约2或4倍,这表明抗体结合在完整融合蛋白中受到部分阻碍。在PSA处理后,还使用CTLL-2细胞系(其生长和存活需要IL-2)对相同样品的等分试样进行分析,并且可使用比色MTT测定法确定细胞的活力。在此测定中,可稀释上清液越多,其所含的生物活性IL-2越多,并且PSA裂解后生物活性IL-2的数量会增加。IL-2突变蛋白的量增加将表明,在PSA裂解后,与抗IL-2抗体反应的约20kDa预测的低分子量裂解片段增加,抗体可及性增加,并且最重要的是,生物活性IL-2突变蛋白的数量增加。

[0286] 实施例5.蛋白酶活化的融合蛋白的体内递送导致肿瘤生长减少

[0287] 检查嵌合多肽以确定其在体内是否可具有生物作用。对于这些实验,使用一种系统,其中腹膜内注射的肿瘤细胞快速且优先附着于乳白色斑点并在其上开始生长,所述乳白色斑点是在网膜上发现的一系列有组织的免疫聚集体(Gerber等人,Am.J.Pathol.169:1739-52(2006))。这种系统提供了一种方便的方式来检查融合蛋白治疗对肿瘤生长的影响,因为融合蛋白可多次经腹膜内递送,并且可通过检查解离的网膜细胞来分析肿瘤生长。对于这些实验,可使用在体外表达MMP2和MMP9的快速生长的肿瘤细胞系结肠38细胞系。网膜组织通常表达相对少量的MMP2和MMP9,但是当网膜上出现结肠38肿瘤时,MMP水平升高。使用此肿瘤模型,检查IL-2突变蛋白融合蛋白影响肿瘤生长的能力。腹膜内注射结肠38细胞,使其附着并生长1天,并且然后每天用融合蛋白腹膜内处理。在第7天,处死动物,并且使用流式细胞术并通过集落形成测定法检查网膜的肿瘤生长。

[0288] 实施例6:靶向CD20的示例性可活化IL2蛋白的构建

[0289] 产生可活化IL2结构域

[0290] 如下产生能够与存在于肿瘤中或肿瘤细胞上的CD20多肽结合的IL-2多肽。产生含有以下核酸序列的核酸:(1)编码IFNg多肽序列和(2)一个或多个多肽接头。可活化的白介

素质粒构建体可具有任选的Flag、His或其他亲和标签，并且被电穿孔到HEK293或其他合适的人或哺乳动物细胞系中并被纯化。验证测定包括使用在蛋白酶存在下对IFNg刺激产生反应的T细胞进行的T细胞活化测定。

[0291] 产生scFv CD20结合结构域

[0292] CD20是存在于B淋巴细胞上的细胞表面蛋白中的一种。CD20抗原存在于正常和恶性的前B和成熟B淋巴细胞中，包括超过90％的B细胞非霍奇金氏淋巴瘤(NHL)中的那些。抗原在造血干细胞、活化的B淋巴细胞(浆细胞)和正常组织中不存在。这样，已经描述了几种主要来源于鼠类的抗体：1F5、2B8/C2B8、2H7和1H4。

[0293] 因此，人或人源化抗CD20抗体用于产生可活化白介素蛋白的CD20结合结构域的scFv序列。获得编码人或人源化VL和VH结构域的DNA序列，并且任选地优化构建体的密码子以在智人的细胞中表达。VL和VH结构域在scFv中出现的顺序是变化的(即VL-VH或VH-VL取向)，并且“G4S”(SEQ ID NO.:201)或“G_4S”(SEQ ID NO.:201)亚基$(G_4S)_3$(SEQ ID NO.:204)的三个拷贝连接可变结构域以创建scFv结构域。抗CD20 scFv质粒构建体可具有任选的Flag、His或其他亲和标签，并且被电穿孔到HEK293或其他合适的人或哺乳动物细胞系中并被纯化。验证测定包括通过FACS进行的结合分析、使用Proteon进行的动力学分析和对CD20表达细胞进行的染色。

[0294] 克隆编码可活化IL2蛋白的DNA表达构建体

[0295] 具有蛋白酶裂解位点结构域的可活化IL2构建体用于构建可活化白介素蛋白与抗CD20 scFv结构域和血清半衰期延长元件(例如，HSA结合肽或VH结构域)的组合，其中所组织的结构域如图11所示。为了在CHO细胞中表达可活化白介素蛋白，将所有蛋白结构域的编码序列克隆到哺乳动物表达载体系统中。简言之，单独合成并亚克隆编码可活化白介素结构域的基因序列、血清半衰期延长元件和CD20结合结构域以及肽接头L1和L2。然后将所得构建体按CD20结合结构域-L1-IL2亚基1-L2-蛋白酶裂解结构域-L3-IL2亚基2-L4-抗CD20 scFv-L5-血清半衰期延长元件的顺序连接在一起，以产生最终构建体。所有表达构建体被设计为含有N端信号肽和C端六聚组氨酸(6xHis)标签的编码序列(SEQ ID NO.205)，以分别促进蛋白质分泌和纯化。

[0296] 在稳定转染的CHO细胞中表达可活化IL2蛋白

[0297] 使用CHO-K1中国仓鼠卵巢细胞(ATCC，CCL-61)的衍生物CHO细胞表达系统((Flp-In®,Life Technologies)(Kao和Puck,Proc.Natl.Acad Sci USA 1968;60(4):1275-81)。根据Life Technologies提供的标准细胞培养方案对贴壁细胞进行传代培养。

[0298] 为了适应悬浮液中的生长，将细胞与组织培养瓶分离，并将其置于无血清培养基中。将悬浮液适应的细胞冷冻保存在含10％DMSO的培养基中。

[0299] 通过转染悬浮液适应的细胞来产生稳定表达分泌的可活化白介素蛋白的重组CHO细胞系。在用抗生素潮霉素B进行选择期间，每周两次测量活细胞密度，并且将细胞离心分离并以$0.1x10^6$个活细胞/mL的最大密度悬浮于新鲜的选择培养基中。选择2至3周后，回收稳定表达可活化白介素蛋白的细胞库，此时将细胞转移至摇瓶中的标准培养基中。通过进行蛋白凝胶电泳或流式细胞术来确认重组分泌蛋白的表达。将稳定的细胞库冷冻保存在含有DMSO的培养基中。

[0300] 在稳定转染的CHO细胞系的10天分批补料培养中通过分泌到细胞培养上清液中产

生可活化IL2蛋白。10天后以通常>75％培养活力收获细胞培养上清液。每隔一天从生产培养物中收集样品，并评定细胞密度和活力。在收获当天，通过离心和真空过滤清除细胞培养上清液，之后进一步使用。

[0301] 通过SDS-PAGE分析细胞培养上清液中的蛋白质表达滴度和产物完整性。

[0302] 纯化可活化IL2蛋白

[0303] 以两步程序从CHO细胞培养上清液中纯化可活化IL2蛋白。在第一步中对构建体进行亲和色谱，之后在第二步中在Superdex 200上进行制备性尺寸排阻色谱法(SEC)。对样品进行缓冲液交换，并通过超滤浓缩至>1mg/mL的典型浓度。通过在还原和非还原条件下进行SDS PAGE来评定最终样品的纯度和均质性(通常>90％)，之后分别通过使用抗HSA或抗独特型抗体进行免疫印迹以及通过分析型SEC来评定。纯化的蛋白质以等分形式储存于-80℃下直至使用。

[0304] 实施例7:通过流式细胞术确定抗原亲和力

[0305] 测试实施例1的可活化白介素蛋白与人$CD20^+$细胞和食蟹猴$CD20^+$细胞的结合亲和力。

[0306] 将$CD20^+$细胞与100μL实施例1的可活化白介素蛋白的连续稀释液和至少一种蛋白酶一起孵育。用FACS缓冲液洗涤三次后，将细胞与0.1mL的10μg/mL小鼠单克隆抗独特型抗体一起在同一缓冲液中于冰上孵育45min。在第二次洗涤循环后，将细胞与0.1mL的15μg/mL FITC缀合的山羊抗小鼠IgG抗体一起在与之前相同的条件下孵育。作为对照，将细胞与抗His IgG一起孵育，之后与不含可活化IL2蛋白的FITC缀合的山羊抗小鼠IgG抗体一起孵育。然后将细胞再次洗涤，并重悬于含有2μg/mL碘化丙啶(PI)的0.2mL FACS缓冲液中，以便排除死细胞。用使用MXP软件(Beckman-Coulter,Krefeld,Germany)的Beckman-Coulter FC500 MPL流式细胞仪或用使用Incyte软件(Merck Millipore,Schwalbach,Germany)的Millipore Guava EasyCyte流式细胞仪测量$1x10^4$个活细胞的荧光。使用CXP软件(Beckman-Coulter,Krefeld,Germany)或Incyte软件(Merck Millipore,Schwalbach,Germany)计算细胞样品的平均荧光强度。在减去仅用二级和三级试剂染色的细胞的荧光强度值之后，然后将这些值用于利用GraphPad Prism(Windows版本6.00,GraphPad软件,La Jolla California USA)的单点结合(双曲线)方程计算K_D值。

[0307] 评定在人$CD20^+$肿瘤细胞系上的CD20结合和交叉反应性。使用在表达重组人或重组食蟹猴抗原的CHO细胞系上确定的K_D值计算交叉反应性的K_D比。

[0308] 实施例8:细胞毒性测定

[0309] 体外评估实施例1的可活化白介素蛋白对$CD20^+$靶细胞的免疫应答的调节。

[0310] 将荧光标记的$CD20^+$REC-1细胞(被套细胞淋巴瘤细胞系,ATCC CRL-3004)与随机供体的分离的PBMC或作为效应细胞的CB15 T细胞(标准化T细胞系)一起在实施例5的可活化IL2蛋白和至少一种蛋白酶的存在下孵育。在湿润的培养箱中于37℃下孵育4h后，在荧光分光光度计中测定荧光染料从靶细胞到上清液中的释放。在不使用实施例1的可活化IL2蛋白的情况下孵育的靶细胞和在孵育结束时通过添加皂苷完全溶解的靶细胞分别充当阴性和阳性对照。

[0311] 基于测量的剩余活靶细胞，根据以下公式计算特定细胞裂解的百分比：[1-(活靶$_{(样品)}$数目/活靶$_{(自发)}$数目)]×100％。使用GraphPad软件通过非线性回归/4参数逻辑拟合

计算S型剂量应答曲线和EC_{50}值。使用对于给定的抗体浓度所获得的裂解值，以通过使用Prism软件的4参数对数拟合分析来计算S型剂量应答曲线。

[0312] 实施例9:可活化白介素蛋白的药代动力学

[0313] 在动物研究中评估实施例5的可活化白介素蛋白的半衰期消除。

[0314] 将可活化IL2蛋白以0.5mg/kg团注到隐静脉以施用于食蟹猴。另一个食蟹猴组接受大小相当的IL2构建体，但缺少血清半衰期延长元件。第三组和第四组分别接受具有血清半衰期延长元件的IL2构建体和具有CD20和血清半衰期延长元件的细胞因子，并且两者的大小均与可活化白介素蛋白相当。每个测试组由5只猴子组成。在指定的时间点采集血清样品，进行连续稀释，并使用CD20的结合ELISA测定蛋白质的浓度。

[0315] 使用测试制品的血浆浓度进行药代动力学分析。当针对给药后的时间作图时，每个测试制品的组平均血浆数据符合多指数曲线。数据通过具有用于分布阶段和消除阶段的团注输入和一级速率常数的标准两室模型拟合。静脉内施用数据的最佳拟合的一般方程为:$c(t)=Ae^{-\alpha t}+Be^{-\beta t}$，其中c(t)是时间t时的血浆浓度，A和B是Y轴上的截距，并且α和β分别是分布阶段和消除阶段的表观一级速率常数。α阶段是初始清除阶段并且反映蛋白质在动物所有细胞外流体中的分布，而衰减曲线的第二或β阶段代表真正的血浆清除。用于拟合此类方程的方法是本领域中熟知的。例如，$A=D/V(\alpha-k21)/(\alpha-\beta)$，$B=D/V(\beta-k21)/(\alpha-\beta)$，并且α和β(对于α>β)是二次方程的根$r^2+(k12+k21+k10)r+k21k10=0$，其使用以下估计参数:V＝分布体积，k10＝消除速率，k12＝从房室1到房室2的传输速率，k21＝从房室2到房室1的传输速率，以及D＝施用的剂量。

[0316] 数据分析:使用KaleidaGraph(KaleidaGraph™ V.3.09 Copyright 1986-1997 Synergy Software.Reading,Pa.)制得浓度相对于时间曲线的曲线图。报告为小于可报告(LTR)的值不包括在PK分析中，并且不以图形表示。使用WinNonlin软件(WinNonlin® Professional V.3.1 WinNonlin™ Copyright 1998-1999.Pharsight Corporation.Mountain View,Calif.)通过房室分析确定药代动力学参数。药代动力学参数的计算如Ritschel W A和Kearns G L,1999的Handbook Of Basic Pharmacokinetics Including Clinical Applications,第5版,American Pharmaceutical Assoc.,Washington,D.C中所述。

[0317] 预期与缺乏血清半衰期延长元件的蛋白质相比，实施例5的可活化白介素蛋白具有改善的药代动力学参数，诸如消除半衰期增加。

[0318] 实施例10:异种移植肿瘤模型

[0319] 在异种移植模型中评估实施例5的可活化IL2蛋白。

[0320] 雌性免疫缺陷型NOD/scid小鼠经亚致死性照射(2Gy)，并且在右背侧皮下接种$4x10^6$个Ramos RA1细胞。当肿瘤达到100至200mm^3时，将动物分为3个处理组。将第2组和第3组(每组8只动物)腹膜内注射$1.5x10^7$个活化的人T细胞。三天后，随后用总共9个50μg静脉内剂量的实施例1的可活化白介素蛋白(qdx9d)处理第3组的动物。第1组和第2组仅使用载体处理。持续30天测定体重和肿瘤体积。

[0321] 预期与相应载体处理的对照组相比，用实施例5的可活化白介素蛋白处理的动物在肿瘤生长上具有统计学上显著的延迟。

[0322] 尽管本文已示出并描述了本申请的优选实施方案，但对于本领域技术人员来说将

显而易见的是,此类实施方案仅作为实例提供。本领域技术人员现在将想到许多变化、改变和替换而不偏离本申请。应理解,本文所述的本申请的实施方案的各种替代方案可用于实行本申请。所意图的是,以下权利要求限定本申请的范围以及由此涵盖这些权利要求及其等同物范围内的方法和结构。

[0323] 实施例11:小鼠IFNg WEHI细胞存活测定

[0324] 将WEHI279细胞(ATCC)以25,000个细胞/孔浓度的悬浮液接种在含有或不含1.5%人血清白蛋白(HSA)的培养基中,并在37℃和5%的CO_2下用系列稀释的重组mIFNg或可诱导mIFNg刺激72小时。测试未裂解和裂解的可诱导mIFNg的活性。通过用活性MMP9孵育产生裂解的可诱导mIFNg。使用基于CellTiter-Glo(Promega)发光的细胞活力测定评定细胞存活。裂解的可诱导mIFNg分子的EC50值比未裂解的可诱导mIFNg分子更高效至少100倍。如图16所示,在培养基含有人血清白蛋白的测定中观察到更大的诱导性。

[0325] 实施例12:小鼠IFNg B16报告细胞测定

[0326] 将B16-Blue IFNg细胞(InvivoGen)以75,000个细胞/孔的浓度的接种在含有或不含1.5%人血清白蛋白(HSA)的培养基中,并在37℃和5%的CO_2下用系列稀释的重组mIFNg或可诱导mIFNg刺激24小时。测试未裂解和裂解的可诱导mIFNg的活性。通过用活性MMP9孵育产生裂解的可诱导mIFNg。收获上清液,并且通过添加QUANTI-Blue试剂(InvivoGen)、在37℃下孵育2小时并测量620nm处的吸光度来评定SEAP活化。结果在图17、19、22、23和28中示出。使用B16-Blue IFNa/b细胞对IFNa融合蛋白重复此实验。裂解的可诱导mIFNa分子的EC50值比未裂解的可诱导mIFNa分子更高效至少100倍。结果在图12中示出。

[0327] 实施例13.蛋白酶活化的融合蛋白的体内递送导致肿瘤生长减少

[0328] 检查嵌合多肽以确定其在体内是否可具有生物作用。对于这些实验,使用一种系统,其中腹膜内注射的肿瘤细胞快速且优先附着于乳白色斑点并在其上开始生长,所述乳白色斑点是在网膜上发现的一系列有组织的免疫聚集体(Gerber等人,Am.J.Pathol.169:1739-52(2006))。这种系统提供了一种方便的方式来检查融合蛋白治疗对肿瘤生长的影响,因为融合蛋白可多次经腹膜内递送,并且可通过检查解离的网膜细胞来分析肿瘤生长。对于这些实验,可使用在体外表达MMP2和MMP9的快速生长的肿瘤细胞系结肠38细胞系。网膜组织通常表达相对少量的MMP2和MMP9,但是当网膜上出现结肠38肿瘤时,MMP水平升高。使用此肿瘤模型,检查IFN融合蛋白影响肿瘤生长的能力。腹膜内注射结肠38细胞,使其附着并生长1天,并且然后每天用融合蛋白腹膜内处理。在第7天,处死动物,并且使用流式细胞术并通过集落形成测定法检查网膜的肿瘤生长。

[0329] 实施例13B:检查嵌合多肽以确定其在体内的生物学作用。

[0330] 使用在体外表达MMP9的快速生长的结肠腺癌细胞系MC38细胞系。使用此肿瘤模型,检查IFNγ融合蛋白影响肿瘤生长的能力。皮下注射MC38细胞,使其生长10至14天,并且然后每周两次腹膜内用融合蛋白处理,共四个剂量,其水平如图21所示。作为比较,野生型mIFNγ以指定的剂量水平施用,每天两次,连续2周,按施用5天/停用2天的方案(共10个剂量)。大约每周两次监测肿瘤生长和体重,持续两周。

[0331] 实施例14:靶向CD20的示例性IFNg蛋白的构建

[0332] 产生可活化细胞因子结构域

[0333] 能够与存在于肿瘤中或肿瘤细胞上的CD20多肽结合的IFNg多肽如下产生。产生含

有以下核酸序列的核酸：(1)编码IFNg多肽序列和(2)一个或多个多肽接头。可活化的IFNg质粒构建体可具有任选的Flag、His或其他亲和标签，并且被电穿孔到HEK293或其他合适的人或哺乳动物细胞系中并被纯化。验证测定包括使用在蛋白酶存在下对IFNg刺激产生反应的T细胞进行的T细胞活化测定。

[0334] 产生scFv CD20结合结构域

[0335] CD20是存在于B淋巴细胞上的细胞表面蛋白中的一种。CD20抗原存在于正常和恶性的前B和成熟B淋巴细胞中，包括超过90％的B细胞非霍奇金氏淋巴瘤(NHL)中的那些。抗原在造血干细胞、活化的B淋巴细胞(浆细胞)和正常组织中不存在。这样，已经描述了几种主要来源于鼠类的抗体：1F5、2B8/C2B8、2H7和1H4。

[0336] 因此，人或人源化抗CD20抗体用于产生可活化IFNg蛋白的CD20结合结构域的scFv序列。获得编码人或人源化VL和VH结构域的DNA序列，并且任选地优化构建体的密码子以在智人的细胞中表达。VL和VH结构域在scFv中出现的顺序是变化的(即VL-VH或VH-VL取向)，并且“G4S”(SEQ ID NO.:201)或“G_4S”(SEQ ID NO.:201)亚基$(G_4S)_3$(SEQ ID NO.:204)的三个拷贝连接可变结构域以创建scFv结构域。抗CD20 scFv质粒构建体可具有任选的Flag、His或其他亲和标签，并且被电穿孔到HEK293或其他合适的人或哺乳动物细胞系中并被纯化。验证测定包括通过FACS进行的结合分析、使用Proteon进行的动力学分析和对CD20表达细胞进行的染色。

[0337] 克隆编码可活化IFNg蛋白的DNA表达构建体

[0338] 具有蛋白酶裂解位点结构域的可活化IFNg构建体用于构建可活化IFNg蛋白与抗CD20 scFv结构域和血清半衰期延长元件(例如，HSA结合肽或VH结构域)的组合，其中所组织的结构域如图14所示。为了在CHO细胞中表达可活化IFNg蛋白，将所有蛋白结构域的编码序列克隆到哺乳动物表达载体系统中。简言之，单独合成并亚克隆编码可活化IFNg结构域的基因序列、血清半衰期延长元件和CD20结合结构域以及肽接头L1和L2。然后将所得构建体按CD20结合结构域-L1-IFNg亚基1-L2-蛋白酶裂解结构域-L3-IFNg亚基2-L4-抗CD20scFv-L5-血清半衰期延长元件的顺序连接在一起，以产生最终构建体。所有表达构建体被设计为含有N端信号肽和C端六聚组氨酸(6xHis)标签的编码序列(SEQ ID NO.:205)，以分别促进蛋白质分泌和纯化。

[0339] 可活化IFNg蛋白在稳定转染的CHO细胞中表达

[0340] 使用CHO-K1中国仓鼠卵巢细胞(ATCC，CCL-61)的衍生物CHO细胞表达系统((Flp-In®,Life Technologies)(Kao和Puck,Proc.Natl.Acad Sci USA 1968;60(4):1275-81)。根据Life Technologies提供的标准细胞培养方案对贴壁细胞进行传代培养。

[0341] 为了适应悬浮液中的生长，将细胞与组织培养瓶分离，并将其置于无血清培养基中。将悬浮液适应的细胞冷冻保存在含10％DMSO的培养基中。

[0342] 通过转染悬浮液适应的细胞来产生稳定表达分泌的可活化IFNg蛋白的重组CHO细胞系。在用抗生素潮霉素B进行选择期间，每周两次测量活细胞密度，并且将细胞离心分离并以$0.1x10^6$个活细胞/mL的最大密度悬浮于新鲜的选择培养基中。选择2至3周后，回收稳定表达可活化IFNg蛋白的细胞库，此时将细胞转移至摇瓶中的标准培养基中。通过进行蛋白凝胶电泳或流式细胞术来确认重组分泌蛋白的表达。将稳定的细胞库冷冻保存在含有DMSO的培养基中。

[0343] 在稳定转染的CHO细胞系的10天分批补料培养中通过分泌到细胞培养上清液中产生可活化IFNg蛋白。10天后以通常>75％培养活力收获细胞培养上清液。每隔一天从生产培养物中收集样品，并评定细胞密度和活力。在收获当天，通过离心和真空过滤清除细胞培养上清液，之后进一步使用。

[0344] 通过SDS-PAGE分析细胞培养上清液中的蛋白质表达滴度和产物完整性。

[0345] 纯化可活化IFNg蛋白

[0346] 以两步程序从CHO细胞培养上清液中纯化可活化IFNg蛋白。在第一步中对构建体进行亲和色谱，之后在第二步中在Superdex 200上进行制备性尺寸排阻色谱法(SEC)。对样品进行缓冲液交换，并通过超滤浓缩至>1mg/mL的典型浓度。通过在还原和非还原条件下进行SDS PAGE来评定最终样品的纯度和均质性(通常>90％)，之后分别通过使用抗HSA或抗独特型抗体进行免疫印迹以及通过分析型SEC来评定。纯化的蛋白质以等分形式储存于-80℃下直至使用。

[0347] 实施例15:通过流式细胞术确定抗原亲和力

[0348] 测试实施例1的可活化IFNg蛋白与人$CD20^+$细胞和食蟹猴$CD20^+$细胞的结合亲和力。

[0349] 将$CD20^+$细胞与100μL实施例1的可活化IFNg蛋白的连续稀释液和至少一种蛋白酶一起孵育。用FACS缓冲液洗涤三次后，将细胞与0.1mL的10μg/mL小鼠单克隆抗独特型抗体一起在同一缓冲液中于冰上孵育45min。在第二次洗涤循环后，将细胞与0.1mL的15μg/mL FITC缀合的山羊抗小鼠IgG抗体一起在与之前相同的条件下孵育。作为对照，将细胞与抗His IgG一起孵育，之后与不含可活化IFNg蛋白的FITC缀合的山羊抗小鼠IgG抗体一起孵育。然后将细胞再次洗涤，并重悬于含有2μg/mL碘化丙啶(PI)的0.2mL FACS缓冲液中，以便排除死细胞。用使用MXP软件(Beckman-Coulter,Krefeld,Germany)的Beckman-Coulter FC500 MPL流式细胞仪或用使用Incyte软件(Merck Millipore,Schwalbach,Germany)的Millipore Guava EasyCyte流式细胞仪测量$1x10^4$个活细胞的荧光。使用CXP软件(Beckman-Coulter,Krefeld,Germany)或Incyte软件(Merck Millipore,Schwalbach,Germany)计算细胞样品的平均荧光强度。在减去仅用二级和三级试剂染色的细胞的荧光强度值之后，然后将这些值用于利用GraphPad Prism(Windows版本6.00,GraphPad软件,La Jolla California USA)的单点结合(双曲线)方程计算K_D值。

[0350] 评定在人$CD20^+$肿瘤细胞系上的CD20结合和交叉反应性。使用在表达重组人或重组食蟹猴抗原的CHO细胞系上确定的K_D值计算交叉反应性的K_D比。

[0351] 实施例16:细胞毒性测定

[0352] 体外评估实施例5的可活化IFNg蛋白对$CD20^+$靶细胞的免疫应答的调节。

[0353] 将荧光标记的$CD20^+$REC-1细胞(被套细胞淋巴瘤细胞系,ATCC CRL-3004)与随机供体的分离的PBMC或作为效应细胞的CB15 T细胞(标准化T细胞系)一起在实施例5的可活化IFNg蛋白和至少一种蛋白酶的存在下孵育。在湿润的培养箱中于37℃下孵育4h后，在荧光分光光度计中测定荧光染料从靶细胞到上清液中的释放。在不使用实施例5的可活化IFNg蛋白的情况下孵育的靶细胞和在孵育结束时通过添加皂苷完全溶解的靶细胞分别充当阴性和阳性对照。

[0354] 基于测量的剩余活靶细胞，根据以下公式计算特定细胞裂解的百分比：[1-(活靶$_{(样品)}$数目/活靶$_{(自发)}$数目)]×100％。使用GraphPad软件通过非线性回归/4参数逻辑拟合

计算S型剂量应答曲线和EC_{50}值。使用对于给定的抗体浓度所获得的裂解值，以通过使用Prism软件的4参数对数拟合分析来计算S型剂量应答曲线。

[0355] 实施例17:可活化IFNg蛋白的药代动力学

[0356] 在动物研究中评估实施例5的可活化IFNg蛋白的半衰期消除。

[0357] 将可活化IFNg蛋白以0.5mg/kg团注入隐静脉以施用于食蟹猴。另一食蟹猴组接受大小相当的细胞因子，但缺少血清半衰期延长元件。第三和第四组分别接受具有血清半衰期延长元件的细胞因子和具有CD20和血清半衰期延长元件的细胞因子，并且两者的大小均与可活化IFNg蛋白相当。每个测试组由5只猴子组成。在指定的时间点采集血清样品，进行连续稀释，并使用CD20的结合ELISA测定蛋白质的浓度。

[0358] 使用测试制品的血浆浓度进行药代动力学分析。当针对给药后的时间作图时，每个测试制品的组平均血浆数据符合多指数曲线。数据通过具有用于分布阶段和消除阶段的团注输入和一级速率常数的标准两室模型拟合。静脉内施用数据的最佳拟合的一般方程为:$c(t)=Ae^{-\alpha t}+Be^{-\beta t}$，其中c(t)是时间t时的血浆浓度，A和B是Y轴上的截距，并且α和β分别是分布阶段和消除阶段的表观一级速率常数。α阶段是初始清除阶段并且反映蛋白质在动物所有细胞外流体中的分布，而衰减曲线的第二或β阶段代表真正的血浆清除。用于拟合此类方程的方法是本领域中熟知的。例如，$A=D/V(\alpha-k21)/(\alpha-\beta)$，$B=D/V(\beta-k21)/(\alpha-\beta)$，并且α和β(对于α>β)是二次方程的根$r^2+(k12+k21+k10)r+k21k10=0$，其使用以下估计参数:V＝分布体积，k10＝消除速率，k12＝从房室1到房室2的传输速率，k21＝从房室2到房室1的传输速率，以及D＝施用的剂量。

[0359] 数据分析:使用KaleidaGraph(KaleidaGraph™ V.3.09 Copyright 1986-1997 Synergy Software.Reading,Pa.)制得浓度相对于时间曲线的曲线图。报告为小于可报告(LTR)的值不包括在PK分析中，并且不以图形表示。使用WinNonlin软件(WinNonlin® Professional V.3.1 WinNonlin™ Copyright 1998-1999.Pharsight Corporation.Mountain View,Calif.)通过房室分析确定药代动力学参数。药代动力学参数的计算如Ritschel W A和Kearns G L,1999的Handbook Of Basic Pharmacokinetics Including Clinical Applications,第5版,American Pharmaceutical Assoc.,Washington,D.C中所述。

[0360] 预期与缺乏血清半衰期延长元件的蛋白质相比，实施例5的可活化IFNg蛋白具有改善的药代动力学参数，诸如消除半衰期增加。

[0361] 实施例18:异种移植肿瘤模型

[0362] 在异种移植模型中评估实施例5的可活化IFNg蛋白。

[0363] 雌性免疫缺陷型NOD/scid小鼠经亚致死性照射(2Gy)，并且在右背侧皮下接种$4x10^6$个Ramos RA1细胞。当肿瘤达到100至200mm^3时，将动物分为3个处理组。将第2组和第3组(每组8只动物)腹膜内注射$1.5x10^7$个活化的人T细胞。三天后，随后用总共9个50μg静脉内剂量的实施例5的可活化IFNg蛋白(qdx9d)处理第3组的动物。第1组和第2组仅使用载体处理。持续30天测定体重和肿瘤体积。

[0364] 预期与相应载体处理的对照组相比，用实施例5的可活化IFNg蛋白处理的动物在肿瘤生长上具有统计学上显著的延迟。

[0365] 尽管本文已示出并描述了本申请的优选实施方案，但对于本领域技术人员来说将

显而易见的是，此类实施方案仅作为实例提供。本领域技术人员现在将想到许多变化、改变和替换而不偏离本申请。应理解，本文所述的本申请的实施方案的各种替代方案可用于实行本申请。所意图的是，以下权利要求限定本申请的范围以及由此涵盖这些权利要求及其等同物范围内的方法和结构。

[0366] 实施例19:HEK Blue测定

[0367] 将HEK-Blue IL12细胞(InvivoGen)以250,000个细胞/孔的浓度的悬浮液接种在含有或不含40mg/ml人血清白蛋白(HSA)的培养基中，并在37℃和5％的CO_2下用系列稀释的重组hIL12、嵌合IL12(小鼠p35/人p40)或可活化hIL12刺激24小时。测试未裂解和裂解的可活化hIL12的活性。通过用活性MMP9孵育产生裂解的可诱导hIL12。通过使用试剂QUANTI-Blue(InvivoGen)对分泌型碱性磷酸酶(SEAP)活性进行定量(即基于比色的测定)来评定IL12活性。结果在图11、12、15、26和27中示出。

[0368] 将HEK-Blue IL2细胞(InvivoGen)以50,000个细胞/孔浓度的悬浮液接种在含有或不含15mg/ml至40mg/ml人血清白蛋白(HSA)的培养基中，并在37℃和5％的CO_2下用系列稀释的重组hIL2或可活化hIL2刺激24小时。测试未裂解和裂解的可活化hIL2的活性。通过用活性MMP9孵育产生裂解的可诱导hIL2。通过使用试剂QUANTI-Blue(InvivoGen)对分泌型碱性磷酸酶(SEAP)活性进行定量(即基于比色的测定)来评定IL12活性。结果在图24中示出。

[0369] 实施例20:脾细胞T-Blast测定

[0370] 用PHA孵育6天并用重组hIL12孵育24小时，从鼠脾细胞中诱导出T-Blast。然后将Tblast以200,000个细胞/孔的浓度的悬浮液接种在含有或不含40mg/ml人血清白蛋白(HSA)的培养基中，并在37℃和5％的CO_2下用系列稀释的重组hIL12或嵌合IL12(小鼠p35/人p40)或可活化IL12刺激72小时。测试未裂解和裂解的IL12的活性。通过用活性MMP9孵育产生裂解的可诱导hIL12。通过使用mIFNγαLISA下游定量IFNγ产生来评定IL12活性。

[0371] 实施例21:蛋白酶活化的融合蛋白的体内递送导致肿瘤生长减少

[0372] 检查嵌合多肽以确定其在体内是否可具有生物作用。对于这些实验，使用一种系统，其中腹膜内注射的肿瘤细胞快速且优先附着于乳白色斑点并在其上开始生长，所述乳白色斑点是在网膜上发现的一系列有组织的免疫聚集体(Gerber等人，Am.J.Pathol.169:1739-52(2006))。这种系统提供了一种方便的方式来检查融合蛋白治疗对肿瘤生长的影响，因为融合蛋白可多次经腹膜内递送，并且可通过检查解离的网膜细胞来分析肿瘤生长。对于这些实验，可使用在体外表达MMP2和MMP9的快速生长的肿瘤细胞系结肠38细胞系。网膜组织通常表达相对少量的MMP2和MMP9，但是当网膜上出现结肠38肿瘤时，MMP水平升高。使用此肿瘤模型，检查IL-2突变蛋白融合蛋白影响肿瘤生长的能力。腹膜内注射结肠38细胞，使其附着并生长1天，并且然后每天用融合蛋白腹膜内处理。在第7天，处死动物，并且使用流式细胞术并通过集落形成测定法检查网膜的肿瘤生长。

[0373] 实施例22:靶向CD20的示例性可活化白介素蛋白的构建

[0374] 产生可活化白介素结构域

[0375] 人IL-12p35链的标准序列为Uniprot登录号P29459。人IL-12p40链的标准序列为Uniprot登录号P29460。将IL-12p35和IL-12p40克隆到表达构建体中。蛋白酶裂解位点包含在IL-12p35和IL-12p40结构域之间。能够与存在于肿瘤中或肿瘤细胞上的CD20多肽结合的

IL-12多肽如下产生。产生含有以下核酸序列的核酸：(1)编码IFNg多肽序列和(2)一个或多个多肽接头。可活化的白介素质粒构建体可具有任选的Flag、His或其他亲和标签，并且被电穿孔到HEK293或其他合适的人或哺乳动物细胞系中并被纯化。验证测定包括使用在蛋白酶存在下对IL-12刺激产生反应的T细胞进行的T细胞活化测定。

[0376] 产生scFv CD20结合结构域

[0377] CD20是存在于B淋巴细胞上的细胞表面蛋白中的一种。CD20抗原存在于正常和恶性的前B和成熟B淋巴细胞中，包括超过90％的B细胞非霍奇金氏淋巴瘤(NHL)中的那些。抗原在造血干细胞、活化的B淋巴细胞(浆细胞)和正常组织中不存在。这样，已经描述了几种主要来源于鼠类的抗体：1F5、2B8/C2B8、2H7和1H4。

[0378] 因此，人或人源化抗CD20抗体用于产生可活化白介素蛋白的CD20结合结构域的scFv序列。获得编码人或人源化VL和VH结构域的DNA序列，并且任选地优化构建体的密码子以在智人的细胞中表达。VL和VH结构域在scFv中出现的顺序是变化的(即VL-VH或VH-VL取向)，并且“G4S”(SEQ ID NO.:201)或“G_4S”(SEQ ID NO.:201)亚基$(G_4S)_3$(SEQ ID NO.:204)的三个拷贝连接可变结构域以创建scFv结构域。抗CD20 scFv质粒构建体可具有任选的Flag、His或其他亲和标签，并且被电穿孔到HEK293或其他合适的人或哺乳动物细胞系中并被纯化。验证测定包括通过FACS进行的结合分析、使用Proteon进行的动力学分析和对CD20表达细胞进行的染色。

[0379] 克隆编码可活化白介素蛋白的DNA表达构建体

[0380] 具有蛋白酶裂解位点结构域的可活化白介素构建体用于构建可活化白介素蛋白与抗CD20 scFv结构域和血清半衰期延长元件(例如，HSA结合肽或VH结构域)的组合。为了在CHO细胞中表达可活化白介素蛋白，将所有蛋白结构域的编码序列克隆到哺乳动物表达载体系统中。简言之，单独合成并亚克隆编码可活化白介素结构域的基因序列、血清半衰期延长元件和CD20结合结构域以及肽接头L1和L2。然后将所得构建体按CD20结合结构域-L1-IL-12p35-L2-蛋白酶裂解结构域-L3-IL-12p40-L4-抗CD20 scFv-L5-血清半衰期延长元件的顺序连接在一起，以产生最终构建体。所有表达构建体被设计为含有N端信号肽和C端六聚组氨酸(6xHis)标签的编码序列(SEQ ID NO.:205)，以分别促进蛋白质分泌和纯化。

[0381] 可活化白介素蛋白在稳定转染的CHO细胞中表达

[0382] 使用CHO-K1中国仓鼠卵巢细胞(ATCC，CCL-61)的衍生物CHO细胞表达系统((Flp-In®,Life Technologies)(Kao和Puck,Proc.Natl.Acad Sci USA 1968;60(4):1275-81)。根据Life Technologies提供的标准细胞培养方案对贴壁细胞进行传代培养。

[0383] 为了适应悬浮液中的生长，将细胞与组织培养瓶分离，并将其置于无血清培养基中。将悬浮液适应的细胞冷冻保存在含10％DMSO的培养基中。

[0384] 通过转染悬浮液适应的细胞来产生稳定表达分泌的可活化白介素蛋白的重组CHO细胞系。在用抗生素潮霉素B进行选择期间，每周两次测量活细胞密度，并且将细胞离心分离并以$0.1x10^6$个活细胞/mL的最大密度悬浮于新鲜的选择培养基中。选择2至3周后，回收稳定表达可活化白介素蛋白的细胞库，此时将细胞转移至摇瓶中的标准培养基中。通过进行蛋白凝胶电泳或流式细胞术来确认重组分泌蛋白的表达。将稳定的细胞库冷冻保存在含有DMSO的培养基中。

[0385] 在稳定转染的CHO细胞系的10天分批补料培养中通过分泌到细胞培养上清液中产

生可活化白介素蛋白。10天后以通常>75％培养活力收获细胞培养上清液。每隔一天从生产培养物中收集样品，并评定细胞密度和活力。在收获当天，通过离心和真空过滤清除细胞培养上清液，之后进一步使用。

[0386] 通过SDS-PAGE分析细胞培养上清液中的蛋白质表达滴度和产物完整性。

[0387] 纯化可活化白介素蛋白

[0388] 以两步程序从CHO细胞培养上清液中纯化可活化白介素蛋白。在第一步中对构建体进行亲和色谱，之后在第二步中在Superdex 200上进行制备性尺寸排阻色谱法(SEC)。对样品进行缓冲液交换，并通过超滤浓缩至>1mg/mL的典型浓度。通过在还原和非还原条件下进行SDS PAGE来评定最终样品的纯度和均质性(通常>90％)，之后分别通过使用抗HSA或抗独特型抗体进行免疫印迹以及通过分析型SEC来评定。纯化的蛋白质以等分形式储存于-80℃下直至使用。

[0389] 实施例23:通过流式细胞术确定抗原亲和力

[0390] 测试实施例5的可活化白介素蛋白与人$CD20^+$细胞和食蟹猴$CD20^+$细胞的结合亲和力。

[0391] 将$CD20^+$细胞与100μL实施例5的可活化白介素蛋白的连续稀释液和至少一种蛋白酶一起孵育。用FACS缓冲液洗涤三次后，将细胞与0.1mL的10μg/mL小鼠单克隆抗独特型抗体一起在同一缓冲液中于冰上孵育45min。在第二次洗涤循环后，将细胞与0.1mL的15μg/mL FITC缀合的山羊抗小鼠IgG抗体一起在与之前相同的条件下孵育。作为对照，将细胞与抗His IgG一起孵育，之后与不含可活化白介素蛋白的FITC缀合的山羊抗小鼠IgG抗体一起孵育。然后将细胞再次洗涤，并重悬于含有2μg/mL碘化丙啶(PI)的0.2mL FACS缓冲液中，以便排除死细胞。用使用MXP软件(Beckman-Coulter,Krefeld,Germany)的Beckman-Coulter FC500 MPL流式细胞仪或用使用Incyte软件(Merck Millipore,Schwalbach,Germany)的Millipore Guava EasyCyte流式细胞仪测量$1x10^4$个活细胞的荧光。使用CXP软件(Beckman-Coulter,Krefeld,Germany)或Incyte软件(Merck Millipore,Schwalbach,Germany)计算细胞样品的平均荧光强度。在减去仅用二级和三级试剂染色的细胞的荧光强度值之后，然后将这些值用于利用GraphPad Prism(Windows版本6.00,GraphPad软件,La Jolla California USA)的单点结合(双曲线)方程计算K_D值。

[0392] 评定在人$CD20^+$肿瘤细胞系上的CD20结合和交叉反应性。使用在表达重组人或重组食蟹猴抗原的CHO细胞系上确定的K_D值计算交叉反应性的K_D比。

[0393] 实施例24:细胞毒性测定

[0394] 体外评估实施例5的可活化白介素蛋白对$CD20^+$靶细胞的免疫应答的调节。

[0395] 将荧光标记的$CD20^+$REC-1细胞(被套细胞淋巴瘤细胞系,ATCC CRL-3004)与随机供体的分离的PBMC或作为效应细胞的CB15 T细胞(标准化T细胞系)一起在实施例5的可活化白介素蛋白和至少一种蛋白酶的存在下孵育。在湿润的培养箱中于37℃下孵育4h后，在荧光分光光度计中测定荧光染料从靶细胞到上清液中的释放。在不使用实施例5的可活化白介素蛋白的情况下孵育的靶细胞和在孵育结束时通过添加皂苷完全溶解的靶细胞分别充当阴性和阳性对照。

[0396] 基于测量的剩余活靶细胞，根据以下公式计算特定细胞裂解的百分比：[1-(活靶$_{(样品)}$数目/活靶$_{(自发)}$数目)]×100％。使用GraphPad软件通过非线性回归/4参数逻辑拟合

计算S型剂量应答曲线和EC_{50}值。使用对于给定的抗体浓度所获得的裂解值，以通过使用Prism软件的4参数对数拟合分析来计算S型剂量应答曲线。

[0397] 实施例25:可活化白介素蛋白的药代动力学

[0398] 在动物研究中评估实施例5的可活化白介素蛋白的半衰期消除。

[0399] 将可活化白介素蛋白以0.5mg/kg团注入隐静脉以施用于食蟹猴。另一食蟹猴组接受大小相当的细胞因子，但缺少血清半衰期延长元件。第三和第四组分别接受具有血清半衰期延长元件的细胞因子和具有CD20和血清半衰期延长元件的细胞因子，并且两者的大小均与可活化白介素蛋白相当。每个测试组由5只猴子组成。在指定的时间点采集血清样品，进行连续稀释，并使用CD20的结合ELISA测定蛋白质的浓度。

[0400] 使用测试制品的血浆浓度进行药代动力学分析。当针对给药后的时间作图时，每个测试制品的组平均血浆数据符合多指数曲线。数据通过具有用于分布阶段和消除阶段的团注输入和一级速率常数的标准两室模型拟合。静脉内施用数据的最佳拟合的一般方程为:$c(t)=Ae^{-\alpha t}+Be^{-\beta t}$，其中c(t)是时间t时的血浆浓度，A和B是Y轴上的截距，并且α和β分别是分布阶段和消除阶段的表观一级速率常数。α阶段是初始清除阶段并且反映蛋白质在动物所有细胞外流体中的分布，而衰减曲线的第二或β阶段代表真正的血浆清除。用于拟合此类方程的方法是本领域中熟知的。例如，$A=D/V(\alpha-k21)/(\alpha-\beta)$，$B=D/V(\beta-k21)/(\alpha-\beta)$，并且α和β(对于α>β)是二次方程的根$r^2+(k12+k21+k10)r+k21k10=0$，其使用以下估计参数:V＝分布体积，k10＝消除速率，k12＝从房室1到房室2的传输速率，k21＝从房室2到房室1的传输速率，以及D＝施用的剂量。

[0401] 数据分析:使用KaleidaGraph(KaleidaGraph™ V.3.09 Copyright 1986-1997 Synergy Software.Reading,Pa.)制得浓度相对于时间曲线的曲线图。报告为小于可报告(LTR)的值不包括在PK分析中，并且不以图形表示。使用WinNonlin软件(WinNonlin® Professional V.3.1WinNonlin™ Copyright 1998-1999.Pharsight Corporation.Mountain View,Calif.)通过房室分析确定药代动力学参数。药代动力学参数的计算如Ritschel W A和Kearns G L,1999的Handbook Of Basic Pharmacokinetics Including Clinical Applications,第5版,American Pharmaceutical Assoc.,Washington,D.C中所述。

[0402] 预期与缺乏血清半衰期延长元件的蛋白质相比，实施例5的可活化白介素蛋白具有改善的药代动力学参数，诸如消除半衰期增加。

[0403] 实施例26:异种移植肿瘤模型

[0404] 在异种移植模型中评估实施例5的可活化白介素蛋白。

[0405] 雌性免疫缺陷型NOD/scid小鼠经亚致死性照射(2Gy)，并且在右背侧皮下接种$4x10^6$个Ramos RA1细胞。当肿瘤达到100至200mm^3时，将动物分为3个处理组。将第2组和第3组(每组8只动物)腹膜内注射$1.5x10^7$个活化的人T细胞。三天后，随后用总共9个50μg静脉内剂量的实施例5的可活化白介素蛋白(qdx9d)处理第3组的动物。第1组和第2组仅使用载体处理。持续30天测定体重和肿瘤体积。

[0406] 预期与相应载体处理的对照组相比，用实施例5的可活化白介素蛋白处理的动物在肿瘤生长上具有统计学上显著的延迟。

[0407] 尽管本文已示出并描述了本申请的优选实施方案，但对于本领域技术人员来说将

显而易见的是，此类实施方案仅作为实例提供。本领域技术人员现在将想到许多变化、改变和替换而不偏离本申请。应理解，本文所述的本申请的实施方案的各种替代方案可用于实行本申请。所意图的是，以下权利要求限定本申请的范围以及由此涵盖这些权利要求及其等同物范围内的方法和结构。

[0408] 实施例27:MC38实验

[0409] 使用在体外表达MMP9的快速生长的结肠腺癌细胞系MC38细胞系。使用此肿瘤模型，检查融合蛋白影响肿瘤生长的能力。

[0410] 实施例27a:MC38 IL-2POC

[0411] 剂和处理：

[0412]

组	N	剂	制剂剂量	途径	方案
1#	10	载体	-	ip	biwk x 3
2	7	ACP16	700 μg/动物	ip	biwk x 3
3	7	ACP16	230 μg/动物	ip	biwk x 3
4	7	ACP16	70 μg/动物	ip	biwk x 3
5	7	ACP16	55 ug/动物	ip	biwk x 3
6	7	ACP16	17 μg/动物	ip	biwk x 3
7	7	ACP132	361 μg/动物	ip	biwk x 3
8	7	ACP132	119 μg/动物	ip	biwk x 3
9	7	ACP132	36 μg/动物	ip	biwk x 3
10	7	ACP132	28 μg/动物	ip	biwk x 3
11	7	ACP132	9 μg/动物	ip	biwk x 3
12	7	ACP21	540 μg/动物	ip	biwk x 3
13	7	ACP21	177 μg/动物	ip	biwk x 3
14	7	ACP21	54 μg/动物	ip	biwk x 3
15	7	ACP21	42 μg/动物	ip	biwk x 3
16	7	ACP21	13 μg/动物	ip	biwk x 3

[0413]

17	7	ACP133	210 μg/动物	ip	bid x 5，然后暂停2天，然后bid x 5，然后暂停2天
18	7	ACP133	105 μg/动物	ip	bid x 5，然后暂停2天，然后bid x 5，然后暂停2天
19	7	ACP133	40 μg/动物	ip	bid x 5，然后暂停2天，然后bid x 5，然后暂停2天
20	7	ACP133	3 μg/动物	ip	bid x 5，然后暂停2天，然后bid x 5，然后暂停2天

[0414] #-对照组

[0415] 实施例27b:MC38 IL-2

[0416] 剂和处理:

[0417]

组	N	剂	制剂剂量	途径	方案
1#	12	载体	-	ip	biwk x 2
2	8	ACP16	4.4 μg/动物	ip	biwk x 2
3	8	ACP16	17 μg/动物	ip	biwk x 2
4	8	ACP16	70 μg/动物	ip	biwk x 2
5	8	ACP16	232 μg/动物	ip	biwk x 2
6	8	ACP130	19 μg/动物	ip	biwk x 2
7	8	ACP130	45 μg/动物	ip	biwk x 2
8	8	ACP130	180 μg/动物	ip	biwk x 2
9	8	ACP130	600 μg/动物	ip	biwk x 1
12	8	ACP124	17 μg/动物	ip	biwk x 2
13	8	ACP124	70 μg/动物	ip	biwk x 2
14	8	ACP124	230 μg/动物	ip	biwk x 2
15	8	ACP124	700 μg/动物	ip	biwk x 2
16	8	IL-2-WTI	12 μg/动物	ip	bid x 5，然后暂停 2 天，然后 bid x 5，然后暂停 2 天

[0418]

17	8	IL-2-WTI	36 μg/动物	ip	bid x 5，然后暂停 2 天，然后 bid x 5，然后暂停 2 天

[0419] #-对照组

[0420] 程序:

[0421] 用异氟烷麻醉小鼠以植入细胞以减少溃疡。将308只CR雌性C57BL/6小鼠的侧腹皮下建立有0%Matrigel中的$5x10^5$个MC38肿瘤细胞。细胞注射体积为0.1mL/小鼠。在开始日期时小鼠年龄为8至12周。当肿瘤的平均大小达到100-150mm^3并开始治疗时,进行配对。在开始时测量体重,并且然后每两周测量一次直到结束。每两周进行一次卡尺测量直到结束。任何不良反应都应立即报告。对单次观察体重减轻超过30%或连续三次体重减轻超过25%的任何个体动物实施安乐死。平均体重减轻>20%或死亡率>10%的任何组均停止给药;此组并不实施安乐死,并且使其恢复。在体重减轻>20%的组中,对达到体重减轻终点的个体实施安乐死。如果与组治疗相关的体重减轻恢复到原始体重的10%以内,则以较低剂量或较不频繁的给药方案恢复给药。非治疗体重%恢复的例外在个案基础上是允许的。终点是肿瘤生长延迟(TGD)。单独地监测动物。实验的终点是肿瘤体积达到1500mm^3或45天,以先到者为准。响应者的追踪时间更长。当达到终点时,将对动物实施安乐死。

[0422]

[0423] 结果在图31A至图31C和图32A至图32C中示出。存活曲线在图34A至图34D中示出。

[0424] 实施例27c:MC38 IFNa和IL-12

[0425] 剂和处理：

[0426]

组	N	剂	制剂剂量	途径	方案
1#	12	载体	-	ip	biwk x 3
2	8	ACP11	17.5 μg/动物	ip	biwk x 3
3	8	ACP11	175 μg/动物	ip	biwk x 3
4	8	ACP11	525 μg/动物	ip	biwk x 3
5	8	ACP31	33 μg/动物	ip	biwk x 3
6	8	ACP31	110 μg/动物	ip	biwk x 3
7	8	ACP31	330 μg/动物	ip	biwk x 3
8	8	ACP131	1 μg/动物	ip	bid x 5，然后暂停 2 天，然后 bid x 5，然后暂停 2 天
9	8	ACP131	10 μg/动物	ip	bid x 5，然后暂停 2 天，然后 bid x 5，然后暂停 2 天
10	8	ACP131	30 μg/动物	ip	bid x 5，然后暂停 2 天，然后 bid x 5，然后暂停 2 天
11	8	mIFNa1-WTI	1 μg/动物	ip	bid x 5，然后暂停 2 天，然后 bid x 5，然后暂停 2 天
12	8	mIFNa1-WTI	10 μg/动物	ip	bid x 5，然后暂停 2 天，然后 bid x 5，然后暂停 2 天
13	8	IL-12-HM-WTI	2 μg/动物	ip	bid x 5，然后暂停 2 天，然后 bid x 5，然后暂停 2 天
14	8	IL-12-HM-WTI	10 μg/动物	ip	bid x 5，然后暂停 2 天，然后 bid x 5，然后暂停 2 天
15	8	ACP131	5 μg/动物	itu	bid x 5，然后暂停 2 天，然后 bid x 5，然后暂停 2 天

[0427]

[0428] #-对照组

[0429] 程序：

[0430] 用异氟烷麻醉小鼠以植入细胞以减少溃疡。将308只CR雌性C57BL/6小鼠的侧腹皮下建立有0%Matrigel中的$5x10^5$个MC38肿瘤细胞。细胞注射体积为0.1mL/小鼠。在开始日期时小鼠年龄为8至12周。当肿瘤的平均大小达到100-150mm^3并开始治疗时，进行配对。在开始时测量体重，并且然后每两周测量一次直到结束。每两周进行一次卡尺测量直到结束。

任何不良反应都应立即报告。对单次观察体重减轻超过30％或连续三次体重减轻超过25％的任何个体动物实施安乐死。平均体重减轻>20％或死亡率>10％的任何组均停止给药;此组并不实施安乐死,并且使其恢复。在体重减轻>20％的组中,对达到体重减轻终点的个体实施安乐死。如果与组治疗相关的体重减轻恢复到原始体重的10％以内,则以较低剂量或较不频繁的给药方案恢复给药。非治疗体重％恢复的例外在个案基础上是允许的。终点是肿瘤生长延迟(TGD)。单独地监测动物。实验的终点是肿瘤体积达到1500mm^{3}或45天,以先到者为准。响应者的追踪时间更长。当达到终点时,将对动物实施安乐死。结果在图29B、29C和30中示出。

[0431] 实施例27d:用ACP16、ACP132和ACP21处理

[0432] 用异氟烷麻醉小鼠以植入细胞以减少溃疡将CR雌性C57BL/6小鼠的侧腹皮下建立有0％Matrigel中的5x10^{5}个MC38肿瘤细胞。细胞注射体积为0.1mL/小鼠。在开始日期时小鼠年龄为8至12周。当肿瘤的平均大小达到100-150mm^{3}并开始治疗时,进行配对。ACP16以17、55、70或230ug/动物给药;ACP132以9、28、36或119ug/动物给药;ACP21以13、42、54或177ug/动物给药。体重在开始时测量,并且然后每两周测量一次直到结束。每两周进行一次卡尺测量直到结束。任何不良反应都应立即报告。对单次观察体重减轻超过30％或连续三次体重减轻超过25％的任何个体动物实施安乐死。平均体重减轻>20％或死亡率>10％的任何组均停止给药;此组并不实施安乐死,并且使其恢复。在体重减轻>20％的组中,对达到体重减轻终点的个体实施安乐死。如果与组治疗相关的体重减轻恢复到原始体重的10％以内,则以较低剂量或较不频繁的给药方案恢复给药。非治疗体重％恢复的例外在个案基础上是允许的。终点是肿瘤生长延迟(TGD)。单独地监测动物。实验的终点是肿瘤体积达到1500mm^{3}或45天,以先到者为准。响应者的追踪时间更长。当达到终点时,将对动物实施安乐死。结果在图35中示出。

[0433] 实施例27e:MC38再激发

[0434] 通过肿瘤植入再激发实施例27b的治愈的小鼠(经ACP16处理的),以确定是否从初始处理建立了抗肿瘤记忆。

[0435] 剂和处理:

[0436]

组	N	剂	制剂剂量	途径	方案
1#	33	未处理	-	-	-
2	7	ACP16	70 μg/动物	ip	(ACP16 biwkx2)

[0437]

3	8	ACP16	232 μg/动物	ip	(ACP16 biwkx2)
5	5	IL-2-WTI	12 μg/动物	ip	(IL-2-WTI bid x 5，然后暂停 2 天，然后 bid x 5，然后暂停 2 天)
6	7	IL-2-WTI	36 μg/动物	ip	(IL-2-WTI bid x 5，然后暂停 2 天，然后 bid x 5，然后暂停 2 天)

[0438] #-对照组

[0439] 程序：

[0440] 用异氟烷麻醉小鼠以植入细胞以减少溃疡研究的这一部分开始于植入当天(第1天)。将由33只CR雌性C57BL/6小鼠组成的第1组的侧腹皮下建立有0％Matrigel中的$5x10^5$个MC38肿瘤细胞。将由33只CR雌性C57BL/6小鼠组成的第2组至第6组的左侧腹皮下建立有0％Matrigel中的$5x10^5$个MC38肿瘤细胞。将先前的MC38实验(实施例27b)的肿瘤植入每只动物的右侧腹。细胞注射体积为0.1mL/小鼠。在开始时对照小鼠的年龄为14至17周。这些小鼠与先前的MC38实验(实施例27b)的小鼠年龄匹配。再激发期间未发生活性剂给药。每两周测量一次体重直到结束，卡尺测量也一样。立即报告任何不良反应或死亡。对单次观察体重减轻超过30％或连续三次体重减轻超过25％的任何个体动物实施安乐死。终点是肿瘤生长延迟(TGD)。单独地监测动物。实验的终点是肿瘤体积达到$1000mm^3$或45天，以先到者为准。在可能的情况下，响应者的追踪时间更长。当达到终点时，对动物实施安乐死。结果在图33中示出。

[0441] 实施例28.条件活性融合蛋白含有作为血清白蛋白结合结构域的阻断部分

[0442] 此实施例描述了通常通过在阻断部分和活性部分之间的接头裂解后将阻断部分从活性部分中分离出来而具有可诱导活性(即它们在被诱导之前是无活性的)的融合蛋白(优选细胞因子)的产生和活性。融合蛋白含有单个抗体可变结构域(dAb)，其通过CDR环结合血清白蛋白，并通过一个或多个非CDR环(例如C环)结合到活性部分(此处为抗CD3scFV)。血清白蛋白结合阻断部分通过蛋白酶可裂解的接头可操作地连接到活性部分，并且活性部分通过非蛋白酶可裂解的接头可操作地连接到靶向结构域(此处为抗表皮生长因子受体(EGFR)dAb或抗前列腺特异性膜抗原(PSMA)dAb)。这些融合蛋白可作为非活性蛋白施用，所述非活性蛋白在裂解蛋白酶可裂解的接头并随后释放抑制性白蛋白结合结构域时被活化。融合蛋白中的抗CD3 scFV是本申请中描述的融合蛋白中所期望的细胞因子的替代物。可使用本文描述和例证的方法制备含有所期望的细胞因子(例如IL-2、IL-12、干扰素)或其功能片段或突变蛋白、靶向结构域和白蛋白结合dAb(也结合并抑制细胞因子或其功能片段或突变蛋白)的类似融合蛋白。结合并抑制所期望的细胞因子或其功能片段或突变蛋白的活性的抗血清白蛋白dAb可提供细胞因子的空间掩蔽(通过接近结合血清白蛋白的细胞因子)和细胞因子的特异性掩蔽(通过经由非CDR环(例如，C环)结合细胞因子))。可使用合适的方法获得结合并抑制所期望的细胞因子或其功能片段或突变蛋白活性的抗血清白蛋白dAb，所述方法诸如通过将氨基酸序列多样性引入到抗血清白蛋白结合dAb的非CDR环(例如，C环)中并筛选与所期望的细胞因子的结合。任何合适的方法都可用于选择，诸如噬菌体展示。例

如,可使用的示例性抗血清白蛋白dab具有以下序列,并且C环中的氨基酸序列(加粗下划线)可多样化(例如,随机化),并且筛选通过CDR相互作用与血清白蛋白结合和通过非CDR环相互作用与细胞因子结合的所得dAb。如果需要的话,可将已知细胞因子结合肽的氨基酸序列移植到C环中。

[0443] EVQLVESGGGLVQPGNSLRLSCAASGFTFSKFGMSWVRQ**GGGGGLDGNEEPGG**LEWVSSISGSGRDTLYADSVKGRFTISRDNAKTTLYLQMNSLRPEDTAVYYCTIGGSLSVSSQGTLVTVSS(SEQ ID NO.:194)

[0444] A.蛋白酶活化ProTriTAC导致体外活性显著增强

[0445] 测试纯化的ProTriTAC(前药)、不可裂解的ProTriTAC[前药(不可裂解)]和模仿蛋白酶活化的ProTriTAC(活性药物)的重组活性药物片段在ELISA测定中与重组人CD3的结合,在流式细胞术测定中与纯化的人原代T细胞的结合,以及在T细胞依赖性细胞毒性测定中的功能效价。

[0446] 对于ELISA,将指定浓度的可溶性ProTriTAC蛋白与固定化的重组人CD3e(R&D Systems)一起在室温下在补充有15mg/ml人血清白蛋白的PBS中孵育1h。使用SuperBlock(Thermo Fisher)阻断板,使用具有0.05%Tween-20的PBS洗涤,并使用非竞争性抗CD3独特型单克隆抗体11D3,之后使用过氧化物酶标记的二抗和TMB-ELISA底物溶液(Thermo Fisher)进行检测。

[0447] 对于流式细胞术,将指定浓度的可溶性ProTriTAC蛋白与纯化的人原代T细胞一起在具有2%胎牛血清和15mg/ml人血清白蛋白的PBS存在下于4℃下孵育1h。用具有2%胎牛血清的PBS洗涤板,使用AlexaFluor 647标记的非竞争性抗CD3独特型单克隆抗体11D3检测,并使用FlowJo 10(FlowJo,LLC)分析数据。

[0448] 对于在T细胞依赖性细胞毒性测定中的功能效价,将指定浓度的可溶性ProTriTAC蛋白与纯化的静息人T细胞(效应细胞)和HCT116癌细胞(靶细胞)一起以10:1的效应子:靶细胞比例在37℃下孵育48h。HCT116靶细胞系已被荧光素酶报告基因稳定转染,从而允许通过ONE-Glo(Promega)测量特异性T细胞介导的细胞杀伤。

[0449] B.ProTriTAC在啮齿动物肿瘤异种移植模型中表现出强大的蛋白酶依赖性抗肿瘤活性

[0450] 在免疫受损的NCG小鼠中,在与扩增的人T细胞混合的HCT116皮下异种移植肿瘤中评估ProTriTAC的体内抗肿瘤活性。具体地,在第0天将每只小鼠的5x106个HCT116细胞与2.5x106个扩增的T细胞混合。从第二天开始,通过腹膜内注射以q.d.x 10方案进行ProTriTAC的给药。使用卡尺测量确定肿瘤体积测量,并在指定时间使用公式V=(长度x宽度x宽度)/2计算。

[0451] C.示例性ProTriTAC三特异性分子的表达、纯化和稳定性蛋白质生产

[0452] 将编码诱导型融合蛋白分子的序列克隆到哺乳动物表达载体pcDNA 3.4(Invitrogen)中,在这之前是前导序列,并且之后是6x组氨酸标签(SEQ ID NO.:205)。将Expi293F细胞(Life Technologies A14527)以0.2至8x 1e6个细胞/ml之间的悬浮液保持在Expi 293培养基中的Optimum Growth Flasks(Thomson)中。按照Expi293表达系统试剂盒(Life Technologies,A14635)的方案将纯化的质粒DNA转染到Expi293细胞中,并将其在转染后保持4至6天。可替代地,将编码融合蛋白分子的序列克隆到转染到CHO-DG44 dhfr-细胞中的哺乳动物表达载体pDEF38(CMC ICOS)中,产生稳定的库,并在纯化之前在生产培

养基中培养多达12天。使用具有蛋白A尖端((ForteBio/Pall)的Octet RED 96仪器,使用标准曲线的对照融合蛋白对条件培养基中示例性融合蛋白的量进行定量。过滤来自任一宿主细胞的条件培养基,并通过亲和和脱盐色谱法进行部分纯化。随后通过离子交换对融合蛋白进行抛光,并在级分合并后配制成含有赋形剂的中性缓冲液。通过使用溶解于水/有机流动相中的Acquity BEH SEC 200 1.7u 4.6x150mm柱(Waters Corporation)的SDS-PAGE和分析SEC评定最终纯度,其中赋形剂在1290LC系统上的中性pH条件下,并且峰集成有Chemstation CDS软件(Agilent)。从CHO宿主细胞纯化的融合蛋白在以下描述的SDS-PAGE中示出。

[0453] 稳定性评定

[0454] 将两种制剂中纯化的融合蛋白再分装到无菌管中,并通过五个冻融循环施加压力,每个循环包括在-80℃和室温下超过1小时或在37℃下孵育1周。通过使用UV透明96孔板(Corning 3635)使用SpectraMax M2和SoftMaxPro软件(Molecular Devices)进行的UV光谱法、SDS-PAGE和分析SEC来对应力样品的浓度和浊度进行评估,并与对照的非应力样品的相同分析进行比较。下文描述了从293个宿主细胞纯化的单个示例性ProTriTAC分子的对照样品和应力样品的分析SEC色谱图的覆盖图。

[0455] 结果表明,ProTriTAC的产量与CHO稳定库中的常规TriTAC的产量相当;并且在反复冻融并在37℃下1周后,蛋白质是稳定的。

[0456] D.在三周食蟹猴药代动力学研究中证明ProTriTAC在体内的功能性掩蔽和稳定性

[0457] 将单剂量靶向PSMA的ProTriTAC(SEQ ID C1872)、不可裂解的ProTriTAC(SEQ ID NO.:187)、不可掩蔽/不可裂解的TriTAC(SEQ IDNO.:190)和模仿蛋白酶活化的ProTriTAC(SEQ IDNO.:188)的活性药物以0.1mg/kg的剂量通过静脉内注射到食蟹猴中。在指定时间点收集血浆样品。使用利用生物素化重组人PSMA(R&D systems)和MSD测定(Meso Scale Diagnostic,LLC)中磺基标记的抗CD3独特型抗体克隆11D3的配体结合测定来确定ProTriTAC浓度。使用Phoenix WinNonlin药代动力学软件,使用与静脉推注施用途径一致的非房室方法,估计药代动力学参数。

[0458] 为了计算体内前药转化率,通过求解以下微分方程组来估计循环中的活性药物浓度,其中P为前药的浓度,A为活性药物的浓度,k_a为循环中前药活化率,$k_{c,P}$为前药的清除率,并且$k_{c,A}$为活性药物的清除率。

[0459] $$\frac{dP}{dt} = -k_{c,P}P$$

[0460] $$\frac{dA}{dt} = k_aP - k_{c,A}A$$

[0461] 凭经验确定食蟹猴的前药、活性药物和不可裂解的前药对照($k_{c,NCLV}$)的清除率。为了估计循环中前药活化率,假设可裂解前药和不可裂解前药的清除率之间的差异仅源于循环中的非特异性活化。因此,通过从不可裂解前药中减去可裂解前药的清除率来估计前药在循环中转化为活性药物的比率。

[0462] $k_a = k_{c,NCLV} - k_{c,P}$

[0463] 凭经验确定循环中前药的初始浓度,并假设活性药物的初始浓度为零。

[0464] 结果和讨论

[0465] 实施例28的结果表明,可制备包含具有所期望治疗活性的多肽的融合蛋白,诸如细胞因子或其功能片段或突变蛋白或抗CD3 scFV,其中治疗活性被结合血清白蛋白和活性多肽的掩蔽结构域掩蔽。掩蔽结构域通过蛋白酶可裂解的接头可操作地连接到活性结构域。结果表明,此类型的融合蛋白可作为失活蛋白施用,所述失活蛋白在所期望的治疗活性位置诸如肿瘤处被蛋白酶裂解后被活化。

[0466] 实施例28中使用的融合蛋白的氨基酸序列以SEQ ID NO:183-190给出。

[0467] 表3中详细描述了样品融合蛋白构建体。在表3中,“L”为“接头”的缩写,并且“cleav.link.”为“可裂解的接头”的缩写。其他缩写“mIFNg”指示小鼠干扰素γ(IFNg);“hAlbumin”指示人血清白蛋白(HSA);“mAlbumin”指示小鼠血清白蛋白。

[0468] 表3:构建体置换表

[0469]

构建体名称	构建体说明
ACP01	(抗 HSA)-(可裂解的接头)-小鼠 IFNg-(可裂解的接头)-(抗 HSA)-6xHis
ACP02	(抗 HSA)-(可裂解的接头)-小鼠 IFNg-(可裂解的接头)-小鼠 IFNg-(可裂解的接头)-(抗 HSA)-6xHis
ACP03	(抗 HSA)-(可裂解的接头)-小鼠 IFNg-小鼠 IFNg-(可裂解的接头)-(抗 HSA)-6xHis
ACP50	(抗 EpCAM)-(抗 HSA)-(可裂解的接头)-小鼠 IFNg-小鼠 IFNg-(可裂解的接头)-(抗 HSA)-6xHis
ACP51	(抗 EpCAM)-接头-(抗 HSA)-(可裂解的接头)- mIFNg-(可裂解的接头)-(抗 HSA)-6xHis
ACP52	(抗 HSA)-(可裂解的接头)-mIFNg-(可裂解的接头)-(抗 HSA)-接头-(抗 EpCAM)-6xHis
ACP53	mAlbumin-(可裂解的接头)-mIFNg-(可裂解的接头)-mAlbumin-6xHis
ACP54	mAlbumin-(可裂解的接头)-mIFNg-接头-mIFNg-(可裂解的接头)-mAlbumin-6xHis
ACP30	(抗 HSA)-(可裂解的接头)-小鼠 IFNg-(可裂解的接头)-(抗 HSA)-(可裂解的接头)-小鼠 IFNg-(可裂解的接头)-(抗 HSA)-6xHis
ACP55	(抗 HSA)-(可裂解的接头)-小鼠 IFNg-(可裂解的接头)-(抗 HSA)-(可裂解的接头)-小鼠 IFNg-(可裂解的接头)-(抗 HSA)-6xHis-C-标签
ACP56	(抗 FOLR1)-接头-(抗 HSA)-(可裂解的接头)-mIFNg-(可裂解的接头)-(抗 HSA)-6xHis

[0470]

ACP57	(抗 HSA)-(可裂解的接头)-mIFNg-(可裂解的接头)-(抗 HSA)-接头-(抗 FOLR1)-6xHis
ACP58	(抗 HSA)-(可裂解的接头)-mIFNg-(可裂解的接头)-mIFNg-(可裂解的接头)-(抗 HSA)-接头-(抗 EpCAM)-6xHis
ACP59	(抗 FOLR1)-接头-(抗 HSA)-(可裂解的接头)- mIFNg-(可裂解的接头)-mIFNg-(可裂解的接头)-(抗 HSA)-6xHis
ACP60	(抗 HSA)-(可裂解的接头)-mIFNg-(可裂解的接头)-mIFNg-(可裂解的接头)-(抗 HSA)-接头-(抗 FOLR1)-6xHis
ACP61	(抗 HSA)-(可裂解的接头)-mIFNg-(可裂解的接头)-mIFNg-(可裂解的接头)-(抗 HSA)-接头-FN(CGS-2)-6xHis
ACP63	抗 FN CGS-2 scFv (Vh/Vl)-6xHis
ACP69	(抗 HSA)-(可裂解的接头)-小鼠 IFNg-(可裂解的接头)-(抗 HSA)-(可裂解的接头)-小鼠 IFNg
ACP70	小鼠 IFNg-(可裂解的接头)-(抗 HSA)-(可裂解的接头)-小鼠 IFNg-(可裂解的接头)-(抗 HSA)
ACP71	小鼠 IFNg-(可裂解的接头)-mAlbumin-(可裂解的接头)-小鼠 IFNg-(可裂解的接头)-mAlbumin
ACP72	mAlbumin-(可裂解的接头)-小鼠 IFNg-(可裂解的接头)-mAlbumin-(可裂解的接头)-小鼠 IFNg
ACP73	mAlbumin-(可裂解的接头)-小鼠 IFNg-(可裂解的接头)-mAlbumin-(可裂解的接头)-小鼠 IFNg-(可裂解的接头)-mAlbumin
ACP74	mAlbumin-(可裂解的接头)-小鼠 IFNg-(可裂解的接头)-5mer 接头-mAlbumin-5mer 接头-(可裂解的接头)-小鼠 IFNg-(可裂解的接头)-mAlbumin
ACP75	mAlbumin-(可裂解的接头)-小鼠 IFNg-(可裂解的接头)-10mer 接头-mAlbumin-10mer 接头-(可裂解的接头)-

[0471]

	小鼠 IFNg-(可裂解的接头)-mAlbumin
ACP78	(抗 HSA)-接头-小鼠 IFNg-接头-(抗 HSA)-接头-小鼠 IFNg-接头-(抗 HSA)_(不可裂解的对照组)
ACP134	抗 HSA-(可裂解的接头)-小鼠 IFNg-(可裂解的接头)-抗 HSA-(可裂解的接头)-小鼠 IFNg-(可裂解的接头)-抗 HSA-L-抗 FOLR1
ACP135	抗 FOLR1-L-HSA-(可裂解的接头)-小鼠 IFNg-(可裂解的接头)-HSA-(可裂解的接头)-小鼠 IFNg-(可裂解的接头)-HSA
ACP04	人 p40-鼠 p35-6xHis
ACP05	人 p40-人 p35-6xHis
ACP34	小鼠 p35-(可裂解的接头)-小鼠 p40-6xHis
ACP35	小鼠 p35-GS-(可裂解的接头)-GS-小鼠 p40-6xHis
ACP36	(抗 HSA)-(可裂解的接头)-小鼠 p40-小鼠 p35-(可裂解的接头)-(抗 HSA)-6xHis
ACP37	(抗 EpCAM)-(抗 HSA)-(可裂解的接头)-小鼠 p40-小鼠 p35-(可裂解的接头)-(抗 HSA)-6xHis
ACP79	(抗 EpCAM)-接头-(抗 HSA)-(可裂解的接头)-mIL12-(可裂解的接头)-(抗 HSA)-6xHis
ACP80	(抗 HSA)-(可裂解的接头)-mIL12-(可裂解的接头)-(抗 HSA)-接头-(抗 EpCAM)-6xHis
ACP06	阻断剂 12-接头-(可裂解的接头)-人 p40-接头-小鼠 p35-(可裂解的接头)-(抗 HSA)-6xHis
ACP07	阻断剂 12-接头-(可裂解的接头)-人 p40-接头-小鼠 p35-(可裂解的接头)-(抗 HSA)-接头-(抗 FOLR1)-6xHis
ACP08	(抗 FOLR1)-接头-阻断剂 12-接头-(可裂解的接头)-人 p40-接头-小鼠 p35-(可裂解的接头)-(抗 HSA)-6xHis
ACP09	(抗 HSA)-接头-阻断剂 12-接头-(可裂解的接头)-人 p40-接头-小鼠 p35-6xHis
ACP10	(抗 HSA)-(可裂解的接头)-人 p40-L-小鼠 p35-(可裂解的

	接头)-接头-阻断剂 12-6xHis
ACP11	人 p40-接头-小鼠 p35-(可裂解的接头)-接头-阻断剂 12-接头-(抗 HSA)-6xHis
ACP91	人 p40-接头-小鼠 p35-接头-接头-阻断剂-接头-(抗 HSA)_(不可裂解的对照组)
ACP136	人 p40-L-小鼠 p35-(可裂解的接头)-阻断剂
ACP138	人 p40-L-小鼠 p35-(可裂解的接头)-阻断剂-L-(抗 HSA)-L-FOLR1
ACP139	抗 FOLR1-L-人 p40-L-小鼠 p35-(可裂解的接头)-阻断剂 12-L-(抗 HSA)
ACP140	抗 FOLR1-(可裂解的接头)-人 p40-L-小鼠 p35-(可裂解的接头)-阻断剂 12-L-(抗 HSA)
ACP12	(抗 EpCAM)-IL2-(可裂解的接头)-(抗 HSA)-阻断剂 2-6xHis
ACP13	(抗 EpCAM)-阻断剂 2-(抗 HSA)-(可裂解的接头)-IL2-6xHis
ACP14	阻断剂 2-接头-(可裂解的接头)-IL2-(可裂解的接头)-(抗 HSA)-6xHis
ACP15	阻断剂 2-接头-(抗 HSA)-接头-(可裂解的接头)-IL2-6xHis
ACP16	IL2-(可裂解的接头)-(抗 HSA)-接头-(可裂解的接头)-阻断剂 2-6xHis
ACP17	(抗 EpCAM)-接头-IL2-(可裂解的接头)-(抗 HSA)-接头-(可裂解的接头)-阻断剂 2-6xHis
ACP18	(抗 EpCAM)-接头-IL2-(可裂解的接头)-(抗 HSA)-接头-vh(可裂解的接头)vl-6xHis
ACP19	IL2-(可裂解的接头)-接头-阻断剂 2-接头-(抗 HSA)-接头-(抗 EpCAM) -6xHis
ACP20	IL2-(可裂解的接头)-阻断剂 2-6xHis
ACP21	IL2-(可裂解的接头)-接头-阻断剂 2-6xHis

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[0473]

ACP22	IL2-(可裂解的接头)-接头-阻断剂-(可裂解的接头)-(抗HSA)-接头-(抗 EpCAM)-6xHis
ACP23	(抗 FOLR1)-(可裂解的接头)-阻断剂 2-接头-(可裂解的接头)-(抗 HSA)-(可裂解的接头)-IL2-6xHis
ACP24	(阻断剂 2)-(可裂解的接头)-(IL2)-6xHis
ACP25	阻断剂 2-接头-(可裂解的接头)-IL2-6xHis
ACP26	(抗 EpCAM)-接头-IL2-(可裂解的接头)-(抗 HSA)-接头-阻断剂(NARA1 Vh/Vl)
ACP27	(抗 EpCAM)-接头-IL2-(可裂解的接头)-(抗 HSA)-接头-阻断剂(NARA1 Vl/Vh)
ACP28	IL2-(可裂解的接头)-接头-阻断剂 2-(NARA1 Vh/Vl)-接头-(抗 HSA)-接头-(抗 EpCAM)
ACP29	IL2-(可裂解的接头)-接头-阻断剂 2-(NARA1 Vl/Vh)-接头-(抗 HSA)-接头-(抗 EpCAM)
ACP38	IL2-(可裂解的接头)-阻断剂-(抗 HSA)-(抗 EpCAM)-6xHis
ACP39	(抗 EpCAM)-(可裂解的接头)-(抗 HSA)-(可裂解的接头)-阻断剂 2-(可裂解的接头)-IL-2-6xHis
ACP40	CD25ecd-接头-(可裂解的接头)-IL2-6xHis
ACP41	IL2-(可裂解的接头)-接头-CD25ecd-6xHis
ACP42	(抗 HSA)-接头-CD25ecd-接头-(可裂解的接头)-IL2-6xHis
ACP43	IL2-(可裂解的接头)-接头-CD25ecd-接头-(抗 HSA)-6xHis
ACP44	IL2-(可裂解的接头)-接头-CD25ecd-(可裂解的接头)-(抗 HSA)-6xHis
ACP45	(抗 HSA)-(可裂解的接头)-阻断剂 2-接头-(可裂解的接头)-IL2-6xHis
ACP46	IL2-(可裂解的接头)-接头 L-vh(可裂解的接头)vl-接头-(抗 HSA)-L-(抗 EpCAM)-6xHis

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ACP47	(抗 EpCAM)-接头-IL2-(可裂解的接头)-(抗 HSA)-接头-阻断剂 2-6xHis
ACP48	IL2-(可裂解的接头)-阻断剂 2-接头-(抗 HSA)-6xHis
ACP49	IL2-(可裂解的接头)-接头-阻断剂 2-接头-(抗 HSA)-6xHis
ACP92	(抗 HSA)-(16mer 可裂解的接头)-IL2-(16mer 可裂解的接头)-(抗 HSA)-6XHis
ACP93	(抗 EpCAM)-(抗 HSA)-(抗 EpCAM)-阻断剂 2-(可裂解的接头)-IL2-6xHis
ACP94	(抗 EpCAM)-(抗 HSA)-阻断剂 2-(可裂解的接头)-IL2-6xHis
ACP95	(抗 EpCAM)-(抗 HSA)-(可裂解的接头)-IL2-6xHis
ACP96	(抗 EpCAM)-(16 聚体可裂解的接头)-IL2-(16 聚体可裂解的接头)-(抗 HSA)
ACP97	(抗 EpCAM)-(抗 HSA)-(可裂解的接头)-IL2-(可裂解的接头)-(抗 HSA)-6xHis
ACP99	(抗 EpCAM)-接头-IL2-(可裂解的接头)-(抗 HSA)-6xHis
ACP100	(抗 EpCAM)-接头-IL2-6xHis
ACP101	IL2-(可裂解的接头)-(抗 HSA)-6xHis
ACP102	(抗 EpCAM)-(可裂解的接头)-IL2-(可裂解的接头)-(抗 HSA)-接头-阻断剂-6xHis
ACP103	IL2-(可裂解的接头)-接头-阻断剂 2-接头-(抗 HSA)-接头-(抗 FOLR1)-6xHis
ACP104	(抗 FOLR1)-IL2-(可裂解的接头)-(抗 HSA)-接头-阻断剂 2-6xHis
ACP105	阻断剂 2-接头-(可裂解的接头)-IL2-(可裂解的接头)-(抗 HSA)-接头-(抗 FOLR1)-6xHis
ACP106	(抗 FOLR1)-接头-(抗 HSA)-(可裂解的接头)-阻断剂-接头-(可裂解的接头)-IL2-6xHis
ACP107	阻断剂 2-接头-(抗 HSA)-(可裂解的接头)-IL2-接头-(抗

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	FOLR1)-6xHis
ACP108	(抗 EpCAM)-IL2-(双重可裂解的接头)-(抗 HSA)-接头-阻断剂-6xHis
ACP117	抗 FN CGS-2 scFv (Vh/Vl)-6xHis
ACP118	NARA1 Vh/Vl 不可裂解
ACP119	NARA1 Vh/Vl 可裂解
ACP120	NARA1 Vl/Vh 不可裂解
ACP121	NARA1 Vl/Vh 可裂解
ACP124	IL2-接头-(抗 HSA)-接头-接头-阻断剂_(不可裂解的对照组)
ACP132	IL2-L-HSA
ACP141	IL2-L-人白蛋白
ACP142	IL2-(可裂解的接头)-人白蛋白
ACP144	IL2-(可裂解的接头)-HSA-(可裂解的接头)阻断剂-L-(抗 FOLR1)
ACP145	抗 FOLR1-L-IL2-(可裂解的接头)-HSA-接头-(可裂解的接头)-阻断剂 2
ACP146	抗 FOLR1-(可裂解的接头)-IL2-(可裂解的接头)-HSA-接头-(可裂解的接头)-阻断剂 2
ACP133	IL2-6x His
ACP147	IL2-(可裂解的接头)-(抗 HSA)-接头-(可裂解的接头)-阻断剂 2-L-(抗 EpCAM)
ACP148	(抗 EpCAM)-L-IL2-(可裂解的接头)-(抗 HSA)-L-(可裂解的接头)-阻断剂 2
ACP149	(抗 EpCAM)-(可裂解的接头)-IL2-(可裂解的接头)-(抗 HSA)-L-(可裂解的接头)-阻断剂 2
ACP31	(抗 HSA)-(可裂解的接头)-mIFNa1-(可裂解的接头)-(抗 HSA)
ACP32	(抗 HSA)-(可裂解的接头)-mIFNa1(N+C trunc)-(可裂解的接头)-(抗 HSA)

[0476]

ACP33	(抗 HSA)-(可裂解的接头)-mIFNa1(C trunc)-(可裂解的接头)-(抗 HSA)
ACP131	mIFNa1
ACP125	抗 HSA-(可裂解的接头)-mIFNa1
ACP126	mIFNa1-(可裂解的接头)-(抗 HSA)
ACP127	小鼠白蛋白-(可裂解的接头)-mIFNa1-(可裂解的接头)-小鼠白蛋白
ACP128	小鼠白蛋白-(可裂解的接头)-mIFNa1
ACP129	mIFNa1-(可裂解的接头)-mA1b
ACP150	(抗 FOLR1)-L-(抗 HSA)-(可裂解的接头)- mIFNa1-(可裂解的接头)-(抗 HSA)
ACP151	抗 FOLR1-L-(抗 HSA)-(可裂解的接头)-mIFNa1-(可裂解的接头)-(抗 HSA)-L-(抗 FOLR1)
ACP152	(抗 HSA)-L-mIFNa1-L-(抗 HSA)_(不可裂解的对照组)
ACP153	IL2-(可裂解的接头)-(抗 HSA)-接头(可裂解的接头)-阻断剂 2
ACP154	IL2-(可裂解的接头)-(抗 HSA)-接头(可裂解的接头)-阻断剂 2
ACP155	IL2-(可裂解的接头)-(抗 HSA)-接头(可裂解的接头)-阻断剂 2
ACP156	IL2-(可裂解的接头)-(抗 HSA)-接头(可裂解的接头)-阻断剂 2
ACP157	IL2-(可裂解的接头)-(抗 HSA)-接头(可裂解的接头)-阻断剂 2

[0477] 序列表

[0478]

SEQ ID NO.	名称	序列			
1	人 IL-2	MYRMQLLSCI	ALSLALVTNS	APTSSSTKKT	QLQLEHLLLD
		LQMILNGINN	YKNPKLTRML	TFKFYMPKKA	TELKHLQCLE

[0479]

		EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR WITFCQSIISTLT
2	人血清白蛋白	MKWVTFISLL FLFSSAYSRG VFRRDAHKSE VAHRFKDLGE ENFKALVLIA FAQYLQQCPF EDHVKLVNEV TEFAKTCVAD ESAENCDKSL HTLFGDKLCT VATLRETYGE MADCCAKQEP ERNECFLQHK DDNPNLPRLV RPEVDVMCTA FHDNEETFLK KYLYEIARRH PYFYAPELLF FAKRYKAAFT ECCQAADKAA CLLPKLDELR DEGKASSAKQ GLKCASLQKF GERAFKAWAV ARLSQRFPKA EFAEVSKLVT DLTKVHTECC HGDLLECADD RADLAKYICE NQDSISSKLK ECCEKPLLEK SHCIAEVEND EMPADLPSLA ADFVGSKDVC KNYAEAKDVF LGMFLYEYAR RHPDYSVVLL LRLAKTYETT LEKCCAAADP HECYAKVFDE FKPLVEEPQN LIKQNCELFE QLGEYKFQNA LLVRYTKKVP QVSTPTLVEV SRNLGKVGSK CCKHPEAKRM PCAEDCLSVF LNQLCVLHEK TPVSDRVTKC CTESLVNGRPCFSALEVDETYVPKEFNAETFTFHADICTLSEKERQIKK QTALV ELVKHK PKATKEQLKAVMDDFAAFVEKCCKADDKET CFAEEGKKLVAASQAALGL
45	ACP12（IL2 融合蛋白）	QVQLQESGGGLVQAGGSLRLSCAASGRIFSIDIMSWYRQAPGKQRELVA RITRGGTISYDDSVKGRFTISRDNAKNTVYLQMNSLKPEDTGVYYCNAL YGTDYWGKGTQVTVSSggggsggggsggggsaptssstkktqlqlehll ldlqmilnginnyknpkltrmltfkfympkkatelkhlqcleeelkple evlnlaqsknfhlrprdlisninvivlelkgsettfmceyadetative flnrwitfcqsiistltSGGPGPAGMKGLPGSEVQLVESGGGLVQPGNS LRLSCAASGFTFSKFGMSWVRQAPGKGLEWVSSISGSGRDTLYAESVKG RFTISRDNAKTTLYLQMNSLRPEDTAVYYCTIGGSLSVSSQGTLVTVSS ggggsggggsggggsEVQLVESGGGLVQPGGSLRLSCAASGFTFSSYTL AWVRQAPGKGLEWVAAIDSSSYTYSPDTVRGRFTISRDNAKNSLYLQMN SLRAEDTAVYYCARDSNWDALDYWGQGTTVTVSSGGGGSGGGGSGGGGS DIQMTQSPSSLSASVGDRVTITCKASQNVGTNVGWYQQKPGKAPKALIY SASFRYSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQYYTYPYTF GGGTKVEIKHHHHHH
46	ACP13（IL2 融合蛋白）	QVQLQESGGGLVQAGGSLRLSCAASGRIFSIDIMSWYRQAPGKQRELVA RITRGGTISYDDSVKGRFTISRDNAKNTVYLQMNSLKPEDTGVYYCNAL YGTDYWGKGTQVTVSSggggsggggsggggsEVQLVESGGGLVQPGGSL

[0480]

		RLSCAASGFTFSSYTLAWVRQAPGKGLEWVAAIDSSSYTYSPDTVRGRF TISRDNAKNSLYLQMNSLRAEDTAVYYCARDSNWDALDYWGQGTTVTVS SGGGGSGGGGSGGGGSDIQMTQSPSSLSASVGDRVTITCKASQNVGTNV GWYQQKPGKAPKALIYSASFRYSGVPSRFSGSGSGTDFTLTISSLQPED FATYYCQQYYTYPYTFGGGTKVEIKggggsggggsggggsEVQLVESGG GLVQPGNSLRLSCAASGFTFSKFGMSWVRQAPGKGLEWVSSISGSGRDT LYAESVKGRFTISRDNAKTTLYLQMNSLRPEDTAVYYCTIGGSLSVSSQ GTLVTVSSSGGPGPAGMKGLPGSaptssstkktqlqlehlllldlqmiln ginnyknpkltrmltfkfympkkatelkhlqcleeelkpleevlnlaqs knfhlrprdlisninvivlelkgsettfmceyadetativeflnrwitf cqsiistltHHHHHH
47	ACP14 (IL2 融 合蛋白)	EVQLVESGGGLVQPGGSLRLSCAASGFTFSSYTLAWVRQAPGKGLEWVA AIDSSSYTYSPDTVRGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARD SNWDALDYWGQGTTVTVSSGGGGSGGGGSGGGGSDIQMTQSPSSLSASV GDRVTITCKASQNVGTNVGWYQQKPGKAPKALIYSASFRYSGVPSRFSG SGSGTDFTLTISSLQPEDFATYYCQQYYTYPYTFGGGTKVEIKggggsg gggsggggsggggsggggsggggsSGGPGPAGMKGLPGSaptssstkkt qlqlehlllldlqmilnginnyknpkltrmltfkfympkkatelkhlqcl eeelkpleevlnlaqsknfhlrprdlisninvivlelkgsettfmceya detativeflnrwitfcqsiistltSGGPGPAGMKGLPGSEVQLVESGG GLVQPGNSLRLSCAASGFTFSKFGMSWVRQAPGKGLEWVSSISGSGRDT LYAESVKGRFTISRDNAKTTLYLQMNSLRPEDTAVYYCTIGGSLSVSSQ GTLVTVSSHHHHHH
48	ACP15 (IL2 融 合蛋白)	EVQLVESGGGLVQPGGSLRLSCAASGFTFSSYTLAWVRQAPGKGLEWVA AIDSSSYTYSPDTVRGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARD SNWDALDYWGQGTTVTVSSGGGGSGGGGSGGGGSDIQMTQSPSSLSASV GDRVTITCKASQNVGTNVGWYQQKPGKAPKALIYSASFRYSGVPSRFSG SGSGTDFTLTISSLQPEDFATYYCQQYYTYPYTFGGGTKVEIKggggsg gggsggggsggggsggggsggggsEVQLVESGGGLVQPGNSLRLSCAAS GFTFSKFGMSWVRQAPGKGLEWVSSISGSGRDTLYAESVKGRFTISRDN AKTTLYLQMNSLRPEDTAVYYCTIGGSLSVSSQGTLVTVSSggggsggg gsggggsSGGPGPAGMKGLPGSaptssstkktqlqlehlllldlqmilng innyknpkltrmltfkfympkkatelkhlqcleeelkpleevlnlaqsk nfhlrprdlisninvivlelkgsettfmceyadetativeflnrwitfc qsiistltHHHHHH
49	ACP16	aptssstkktqlqlehlllldlqmilnginnyknpkltrmltfkfympkk

[0481]

	(IL2 融合蛋白)	atelkhlqcleeelkpleevlnlaqsknfhlrprdlisninvivlelkg settfmceyadetativeflnrwitfcqsiistltSGGPGPAGMKGLPG SEVQLVESGGGLVQPGNSLRLSCAASGFTFSKFGMSWVRQAPGKGLEWV SSISGSGRDTLYAESVKGRFTISRDNAKTTLYLQMNSLRPEDTAVYYCT IGGSLSVSSQGTLVTVSSggggsggggsggggsggggsggggsggggsS GGPGPAGMKGLPGSEVQLVESGGGLVQPGGSLRLSCAASGFTFSSYTLA WVRQAPGKGLEWVAAIDSSSYTYSPDTVRGRFTISRDNAKNSLYLQMNS LRAEDTAVYYCARDSNWDALDYWGQGTTVTVSSGGGGSGGGGSGGGGSD IQMTQSPSSLSASVGDRVTITCKASQNVGTNVGWYQQKPGKAPKALIYS ASFRYSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQYYTYPYTFG GGTKVEIKHHHHHH
50	ACP17 (IL2 融合蛋白)	QVQLQESGGGLVQAGGSLRLSCAASGRIFSIDIMSWYRQAPGKQRELVA RITRGGTISYDDSVKGRFTISRDNAKNTVYLQMNSLKPEDTGVYYCNAL YGTDYWGKGTQVTVSSggggsggggsggggsaptssstkktqlqlehll ldlqmilnginnyknpkltrmltfkfympkkatelkhlqcleeelkple evlnlaqsknfhlrprdlisninvivlelkgsettfmceyadetative flnrwitfcqsiistltSGGPGPAGMKGLPGSEVQLVESGGGLVQPGNS LRLSCAASGFTFSKFGMSWVRQAPGKGLEWVSSISGSGRDTLYAESVKG RFTISRDNAKTTLYLQMNSLRPEDTAVYYCTIGGSLSVSSQGTLVTVSS ggggsggggsggggsggggsggggsggggsSGGPGPAGMKGLPGSEVQL VESGGGLVQPGGSLRLSCAASGFTFSSYTLAWVRQAPGKGLEWVAAIDS SSYTYSPDTVRGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARDSNWD ALDYWGQGTTVTVSSGGGGSGGGGSGGGGSDIQMTQSPSSLSASVGDRV TITCKASQNVGTNVGWYQQKPGKAPKALIYSASFRYSGVPSRFSGSGSG TDFTLTISSLQPEDFATYYCQQYYTYPYTFGGGTKVEIKHHHHHH
51	ACP18 (IL2 融合蛋白)	QVQLQESGGGLVQAGGSLRLSCAASGRIFSIDIMSWYRQAPGKQRELVA RITRGGTISYDDSVKGRFTISRDNAKNTVYLQMNSLKPEDTGVYYCNAL YGTDYWGKGTQVTVSSggggsggggsggggsaptssstkktqlqlehll ldlqmilnginnyknpkltrmltfkfympkkatelkhlqcleeelkple evlnlaqsknfhlrprdlisninvivlelkgsettfmceyadetative flnrwitfcqsiistltSGGPGPAGMKGLPGSEVQLVESGGGLVQPGNS LRLSCAASGFTFSKFGMSWVRQAPGKGLEWVSSISGSGRDTLYAESVKG RFTISRDNAKTTLYLQMNSLRPEDTAVYYCTIGGSLSVSSQGTLVTVSS ggggsggggsggggsggggsggggsggggsEVQLVESGGGLVQPGGSLR LSCAASGFTFSSYTLAWVRQAPGKGLEWVAAIDSSSYTYSPDTVRGRFT ISRDNAKNSLYLQMNSLRAEDTAVYYCARDSNWDALDYWGQGTTVTVSS

[0482]

		sggpgpagmkglpgsDIQMTQSPSSLSASVGDRVTITCKASQNVGTNVG WYQQKPGKAPKALIYSASFRYSGVPSRFSGSGSGTDFTLTISSLQPEDF ATYYCQQYYTYPYTFGGGTKVEIKHHHHHH
52	ACP19 (IL2 融合蛋白)	aptssstkktqlqlehlllqmilnginnyknpkltrmltfkfympkk atelkhlqcleeelkpleevlnlaqsknfhlrprdlisninvivlelkg settfmceyadetativeflnrwitfcqsiistltSGGPGPAGMKGLPG SggggsggggsggggsggggsggggsggggsEVQLVESGGGLVQPGGSL RLSCAASGFTFSSYTLAWVRQAPGKGLEWVAAIDSSSYTYSPDTVRGRF TISRDNAKNSLYLQMNSLRAEDTAVYYCARDSNWDALDYWGQGTTVTVS SGGGGSGGGGSGGGGSDIQMTQSPSSLSASVGDRVTITCKASQNVGTNV GWYQQKPGKAPKALIYSASFRYSGVPSRFSGSGSGTDFTLTISSLQPED FATYYCQQYYTYPYTFGGGTKVEIKggggsggggsggggsEVQLVESGG GLVQPGNSLRLSCAASGFTFSKFGMSWVRQAPGKGLEWVSSISGSGRDT LYAESVKGRFTISRDNAKTTLYLQMNSLRPEDTAVYYCTIGGSLSVSSQ GTLVTVSSggggsggggsggggsQVQLQESGGGLVQAGGSLRLSCAASG RIFSIDIMSWYRQAPGKQRELVARITRGGTISYDDSVKGRFTISRDNAK NTVYLQMNSLKPEDTGVYYCNALYGTDYWGKGTQVTVSSHHHHHH**
53	ACP20 (IL2 融合蛋白)	aptssstkktqlqlehlllqmilnginnyknpkltrmltfkfympkk atelkhlqcleeelkpleevlnlaqsknfhlrprdlisninvivlelkg settfmceyadetativeflnrwitfcqsiistltSGGPGPAGMKGLPG SEVQLVESGGGLVQPGGSLRLSCAASGFTFSSYTLAWVRQAPGKGLEWV AAIDSSSYTYSPDTVRGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCAR DSNWDALDYWGQGTTVTVSSGGGGSGGGGSGGGGSGGGGSDIQMTQSPSSLSAS VGDRVTITCKASQNVGTNVGWYQQKPGKAPKALIYSASFRYSGVPSRFS GSGSGTDFTLTISSLQPEDFATYYCQQYYTYPYTFGGGTKVEIKHHHHHH H
54	ACP21 (IL2 融合蛋白)	aptssstkktqlqlehlllqmilnginnyknpkltrmltfkfympkk atelkhlqcleeelkpleevlnlaqsknfhlrprdlisninvivlelkg settfmceyadetativeflnrwitfcqsiistltSGGPGPAGMKGLPG SggggsggggsggggsggggsggggsggggsEVQLVESGGGLVQPGGSL RLSCAASGFTFSSYTLAWVRQAPGKGLEWVAAIDSSSYTYSPDTVRGRF TISRDNAKNSLYLQMNSLRAEDTAVYYCARDSNWDALDYWGQGTTVTVS SGGGGSGGGGSGGGGSDIQMTQSPSSLSASVGDRVTITCKASQNVGTNV GWYQQKPGKAPKALIYSASFRYSGVPSRFSGSGSGTDFTLTISSLQPED FATYYCQQYYTYPYTFGGGTKVEIKHHHHHH
55	ACP22	aptssstkktqlqlehlllqmilnginnyknpkltrmltfkfympkk

[0483]

	(IL2 融合蛋白)	atelkhlqcleeelkpleevlnlaqsknfhlrprdlisninvivlelkg settfmceyadetativeflnrwitfcqsiistltSGGPGPAGMKGLPG SggggsggggsggggsggggsggggsggggsEVQLVESGGGLVQPGGSL RLSCAASGFTFSSYTLAWVRQAPGKGLEWVAAIDSSSYTYSPDTVRGRF TISRDNAKNSLYLQMNSLRAEDTAVYYCARDSNWDALDYWGQGTTVTVS SGGGGSGGGGSGGGGSDIQMTQSPSSLSASVGDRVTITCKASQNVGTNV GWYQQKPGKAPKALIYSASFRYSGVPSRFSGSGSGTDFTLTISSLQPED FATYYCQQYYTYPYTFGGGTKVEIKSGGPGPAGMKGLPGSEVQLVESGG GLVQPGNSLRLSCAASGFTFSKFGMSWVRQAPGKGLEWVSSISGSGRDT LYAESVKGRFTISRDNAKTTLYLQMNSLRPEDTAVYYCTIGGSLSVSSQ GTLVTVSSggggsggggsggggsQVQLQESGGGLVQAGGSLRLSCAASG RIFSIDIMSWYRQAPGKQRELVARITRGGTISYDDSVKGRFTISRDNAK NTVYLQMNSLKPEDTGVYYCNALYGTDYWGKGTQVTVSSHHHHHH
56	ACP23 (IL2 融合蛋白)	QVQLQESGGGLAQAGGSLSLSCAASGFTVSNSVMAWYRQTPGKQREFVA IINSVGSTNYADSVKGRFTISRDNAKNTVYLQMNNLKPEDTAVYVCNRN FDRIYWGQGTQVTVSSSGGPGPAGMKGLPGSEVQLVESGGGLVQPGGSL RLSCAASGFTFSSYTLAWVRQAPGKGLEWVAAIDSSSYTYSPDTVRGRF TISRDNAKNSLYLQMNSLRAEDTAVYYCARDSNWDALDYWGQGTTVTVS SGGGGSGGGGSGGGGSDIQMTQSPSSLSASVGDRVTITCKASQNVGTNV GWYQQKPGKAPKALIYSASFRYSGVPSRFSGSGSGTDFTLTISSLQPED FATYYCQQYYTYPYTFGGGTKVEIKggggsggggsggggsggggsgggg sggggsSGGPGPAGMKGLPGSEVQLVESGGGLVQPGNSLRLSCAASGFT FSKFGMSWVRQAPGKGLEWVSSISGSGRDTLYAESVKGRFTISRDNAKT TLYLQMNSLRPEDTAVYYCTIGGSLSVSSQGTLVTVSSSGGPGPAGMKG LPGSaptssstkktqlqlehlllldlqmilnginnyknpkltrmltfkfy mpkkatelkhlqcleeelkpleevlnlaqsknfhlrprdlisninvivl elkgsettfmceyadetativeflnrwitfcqsiistltHHHHHH
57	ACP24 (IL2 融合蛋白)	EVQLVESGGGLVQPGGSLRLSCAASGFTFSSYTLAWVRQAPGKGLEWVA AIDSSSYTYSPDTVRGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARD SNWDALDYWGQGTTVTVSSGGGGSGGGGSGGGGSDIQMTQSPSSLSASV GDRVTITCKASQNVGTNVGWYQQKPGKAPKALIYSASFRYSGVPSRFSG SGSGTDFTLTISSLQPEDFATYYCQQYYTYPYTFGGGTKVEIKSGGPGP AGMKGLPGSaptssstkktqlqlehlllldlqmilnginnyknpkltrml tfkfympkkatelkhlqcleeelkpleevlnlaqsknfhlrprdlisni nvivlelkgsettfmceyadetativeflnrwitfcqsiistltHHHHH H

[0484]

58	ACP25（IL2 融合蛋白）	EVQLVESGGGLVQPGGSLRLSCAASGFTFSSYTLAWVRQAPGKGLEWVA AIDSSSYTYSPDTVRGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARD SNWDALDYWGQGTTVTVSSGGGGSGGGGSGGGGSDIQMTQSPSSLSASV GDRVTITCKASQNVGTNVGWYQQKPGKAPKALIYSASFRYSGVPSRFSG SGSGTDFTLTISSLQPEDFATYYCQQYYTYPYTFGGGTKVEIKggggsg gggsggggsggggsggggsggggsSGGPGPAGMKGLPGSaptssstkkt qlqlehlllldlqmilnginnyknpkltrmltfkfympkkatelkhlqcl eeelkpleevlnlaqsknfhlrprdlisninvivlelkgsettfmceya detativeflnrwitfcqsiistltHHHHHH
59	ACP26（IL2 融合蛋白）	QVQLQESGGGLVQAGGSLRLSCAASGRIFSIDIMSWYRQAPGKQRELVA RITRGGTISYDDSVKGRFTISRDNAKNTVYLQMNSLKPEDTGVYYCNAL YGTDYWGKGTQVTVSSggggsggggsggggsaptssstkktqlqlehll ldlqmilnginnyknpkltrmltfkfympkkatelkhlqcleeelkple evlnlaqsknfhlrprdlisninvivlelkgsettfmceyadetative flnrwitfcqsiistltSGGPGPAGMKGLPGSEVQLVESGGGLVQPGNS LRLSCAASGFTFSKFGMSWVRQAPGKGLEWVSSISGSGRDTLYAESVKG RFTISRDNAKTTLYLQMNSLRPEDTAVYYCTIGGSLSVSSQGTLVTVSS ggggsggggsggggsggggsQVQLQQSGAELVRPGTSVKVSCKASGYAF TNYLIEWVKQRPGQGLEWIGVINPGSGGTNYNEKFKGKATLTADKSSST AYMQLSSLTSDDSAVYFCARWRGDGYYAYFDVWGAGTTVTVSSggggsg gggsggggsDIVLTQSPASLAVSLGQRATISCKASQSVDYDGDSYMNWY QQKPGQPPKLLIYAASNLESGIPARFSGSGSGTDFTLNIHPVEEEDAAT YYCQQSNEDPYTFGGGTKLEIKHHHHHHHEPEA
60	ACP27（IL2 融合蛋白）	QVQLQESGGGLVQAGGSLRLSCAASGRIFSIDIMSWYRQAPGKQRELVA RITRGGTISYDDSVKGRFTISRDNAKNTVYLQMNSLKPEDTGVYYCNAL YGTDYWGKGTQVTVSSggggsggggsggggsaptssstkktqlqlehll ldlqmilnginnyknpkltrmltfkfympkkatelkhlqcleeelkple evlnlaqsknfhlrprdlisninvivlelkgsettfmceyadetative flnrwitfcqsiistltSGGPGPAGMKGLPGSEVQLVESGGGLVQPGNS LRLSCAASGFTFSKFGMSWVRQAPGKGLEWVSSISGSGRDTLYAESVKG RFTISRDNAKTTLYLQMNSLRPEDTAVYYCTIGGSLSVSSQGTLVTVSS ggggsggggsggggsggggsDIVLTQSPASLAVSLGQRATISCKASQSV DYDGDSYMNWYQQKPGQPPKLLIYAASNLESGIPARFSGSGSGTDFTLN IHPVEEEDAATYYCQQSNEDPYTFGGGTKLEIKggggsggggsggggsQ VQLQQSGAELVRPGTSVKVSCKASGYAFTNYLIEWVKQRPGQGLEWIGV INPGSGGTNYNEKFKGKATLTADKSSSTAYMQLSSLTSDDSAVYFCARW

[0485]

		RGDGYYAYFDVWGAGTTVTVSSHHHHHHHEPEA
61	ACP28（IL2 融合蛋白）	aptssstkktqlqlehlllldlqmilnginnyknpkltrmltfkfympkk atelkhlqcleeelkpleevlnlaqsknfhlrprdlisninvivlelkg settfmceyadetativeflnrwitfcqsiistltSGGPGPAGMKGLPG SggggsggggsggggsggggsggggsQVQLQQSGAELVRPGTSVKVSCK ASGYAFTNYLIEWVKQRPGQGLEWIGVINPGSGGTNYNEKFKGKATLTA DKSSSTAYMQLSSLTSDDSAVYFCARWRGDGYYAYFDVWGAGTTVTVSS ggggsggggsggggsDIVLTQSPASLAVSLGQRATISCKASQSVDYDGD SYMNWYQQKPGQPPKLLIYAASNLESGIPARFSGSGSGTDFTLNIHPVE EEDAATYYCQQSNEDPYTFGGGTKLEIKggggsggggsggggsEVQLVE SGGGLVQPGNSLRLSCAASGFTFSKFGMSWVRQAPGKGLEWVSSISGSG RDTLYAESVKGRFTISRDNAKTTLYLQMNSLRPEDTAVYYCTIGGSLSV SSQGTLVTVSSggggsggggsggggsQVQLQESGGGLVQAGGSLRLSCA ASGRIFSIDIMSWYRQAPGKQRELVARITRGGTISYDDSVKGRFTISRD NAKNTVYLQMNSLKPEDTGVYYCNALYGTDYWGKGTQVTVSSHHHHHHE PEA
62	ACP29（IL2 融合蛋白）	aptssstkktqlqlehlllldlqmilnginnyknpkltrmltfkfympkk atelkhlqcleeelkpleevlnlaqsknfhlrprdlisninvivlelkg settfmceyadetativeflnrwitfcqsiistltSGGPGPAGMKGLPG SggggsggggsggggsggggsggggsDIVLTQSPASLAVSLGQRATISC KASQSVDYDGDSYMNWYQQKPGQPPKLLIYAASNLESGIPARFSGSGSG TDFTLNIHPVEEEDAATYYCQQSNEDPYTFGGGTKLEIKggggsggggs ggggsQVQLQQSGAELVRPGTSVKVSCKASGYAFTNYLIEWVKQRPGQG LEWIGVINPGSGGTNYNEKFKGKATLTADKSSSTAYMQLSSLTSDDSAV YFCARWRGDGYYAYFDVWGAGTTVTVSSggggsggggsggggsEVQLVE SGGGLVQPGNSLRLSCAASGFTFSKFGMSWVRQAPGKGLEWVSSISGSG RDTLYAESVKGRFTISRDNAKTTLYLQMNSLRPEDTAVYYCTIGGSLSV SSQGTLVTVSSggggsggggsggggsQVQLQESGGGLVQAGGSLRLSCA ASGRIFSIDIMSWYRQAPGKQRELVARITRGGTISYDDSVKGRFTISRD NAKNTVYLQMNSLKPEDTGVYYCNALYGTDYWGKGTQVTVSSHHHHHHE PEA

[0486]

63	IL2Ra	10 20 30 40 50 MDSYLLMWGL LTFIMVPGCQ AELCDDDPPE IPHATFKAMA YKEGTMLNCE 60 70 80 90 100 CKRGFRRIKS GSLYMLCTGN SSHSSWDNQC QCTSSATRNT TKQVTPQPEE 110 120 130 140 150 QKERKTTEMQ SPMQPVDQAS LPGHCREPPP WENEATERIY HFVVGQMVYY 160 170 180 190 200 QCVQGYRALH RGPAESVCKM THGKTRWTQP QLICTGEMET SQFPGEEKPQ 210 220 230 240 250 ASPEGRPESE TSCLVTTTDF QIQTEMAATM ETSIFTTEYQ VAVAGCVFLL 260 270 ISVLLLSGLT WQRRQRKSRR TI
64	IL2Rb	10 20 30 40 50 MAAPALSWRL PLLILLLPLA TSWASAAVNG TSQFTCFYNS RANISCVWSQ 60 70 80 90 100 DGALQDTSCQ VHAWPDRRRW NQTCELLPVS QASWACNLIL GAPDSQKLTT 110 120 130 140 150 VDIVTLRVLC REGVRWRVMA IQDFKPFENL RLMAPISLQV VHVETHRCNI 160 170 180 190 200 SWEISQASHY FERHLEFEAR TLSPGHTWEE APLLTLKQKQ EWICLETLTP 210 220 230 240 250 DTQYEFQVRV KPLQGEFTTW SPWSQPLAFR TKPAALGKDT IPWLGHLLVG 260 270 280 290 300 LSGAFGFIIL VYLLINCRNT GPWLKKVLKC NTPDPSKFFS QLSSEHGGDV 310 320 330 340 350 QKWLSSPFPS SSFSPGGLAP EISPLEVLER DKVTQLLLQQ DKVPEPASLS 360 370 380 390 400 SNHSLTSCFT NQGYFFFHLP DALEIEACQV YFTYDPYSEE DPDEGVAGAP 410 420 430 440 450 TGSSPQPLQP LSGEDDAYCT FPSRDDLLLF SPSLLGGPSP PSTAPGGSGA 460 470 480 490 500 GEERMPPSLQ ERVPRDWDPQ PLGPPTPGVP DLVDFQPPPE LVLREAGEEV 510 520 530 540 550 PDAGPREGVS FPWSRPPGQG EFRALNARLP LNTDAYLSLQ ELQGQDPTHL V
65	IL2Rg	10 20 30 40 50 MLKPSLPFTS LLFLQLPLLG VGLNTTILTP NGNEDTTADF FLTTMPTDSL 60 70 80 90 100 SVSTLPLPEV QCFVFNVEYM NCTWNSSSEP QPTNLTLHYW YKNSDNDKVQ 110 120 130 140 150 KCSHYLFSEE ITSGCQLQKK EIHLYQTFVV QLQDPREPRR QATQMLKLQN 160 170 180 190 200 LVIPWAPENL TLHKLSESQL ELNWNNRFLN HCLEHLVQYR TDWDHSWTEQ 210 220 230 240 250 SVDYRHKFSL PSVDGQKRYT FRVRSRFNPL CGSAQHWSEW SHPIHWGSNT 260 270 280 290 300 SKENPFLFAL EAVVISVGSM GLIISLLCVY FWLERTMPRI PTLKNLEDLV 310 320 330 340 350 TEYHGNFSAW SGVSKGLAES LQPDYSERLC LVSEIPPKGG ALGEGPGASP 360 CNQHSPYWAP PCYTLKPET
66	ACP04（人 p40/鼠 p35 IL12 融合蛋白）	iwelkkdvyvveldwypdapgemvvltcdtpeedgitwtldqssevlgs gktltiqvkefgdagqytchkggevlshsllllhkkedgiwstdilkdq kepknktflrceaknysgrftcwwlttistdltfsvkssrgssdpqgvt cgaatlsaervrgdnkeyeysvecqedsacpaaeeslpievmvdavhkl kyenytssffirdiikpdppknlqlkplknsrqvevsweypdtwstphs yfsltfcvqvqgkskrekkdrvftdktsatvicrknasisvraqdryys

		sswsewasvpcsggggsggggsggggsrvipvsgparclsqsrnllktt ddmvktareklkhysctaedidheditrdqtstlktclplelhknescl atretssttrgsclppqktslmmtlclgsiyedlkmyqtefqainaalq nhnhqqiildkgmlvaidelmqslnhngetlrqkppvgeadpyrvkmkl cillhafstrvvtinrvmgylssaHHHHHH
67	ACP05 (人 p40/ 鼠 p35 IL12 融 合蛋白)	iwelkkdvyvveldwypdapgemvvltcdtpeedgitwtldqssevlgs gktltiqvkefgdagqytchkggevlshsllllhkkedgiwstdilkdq kepknktflrceaknysgrftcwwlttistdltfsvkssrgssdpqgvt cgaatlsaervrgdnkeyeysvecqedsacpaaeeslpievmvdavhkl kyenytssffirdiikpdppknlqlkplknsrqvevsweypdtwstphs yfsltfcvqvqgkskrekkdrvftdktsatvicrknasisvraqdryys sswsewasvpcsggggsggggsggggsrnlpvatpdpgmfpclhhsqnl lravsnmlqkarqtlefypctseeidheditkdktstveaclpleltkn esclnsretsfitngsclasrktsfmmalclssiyedlkmyqvefktmn akllmdpkrqifldqnmlavidelmqalnfnsetvpqkssleepdfykt kiklcillhafriravtidrvmsylnasHHHHHH
68	ACP06 (人 p40/ 鼠 p35 IL12 融 合蛋白)	QSVLTQPPSVSGAPGQRVTISCSGSRSNIGSNTVKWYQQLPGTAPKLLI YYNDQRPSGVPDRFSGSKSGTSASLAITGLQAEDEADYYCQSYDRYTHP ALLFGTGTKVTVLggggsggggsggggsQVQLVESGGGVVQPGRSLRLS CAASGFTFSSYGMHWVRQAPGKGLEWVAFIRYDGSNKYYADSVKGRFTI SRDNSKNTLYLQMNSLRAEDTAVYYCKTHGSHDNWGQGTMVTVSSgggg sggggsggggsggggsggggsggggsSGGPGPAGMKGLPGSiwelkkdv yvveldwypdapgemvvltcdtpeedgitwtldqssevlgsgktltiqv kefgdagqytchkggevlshsllllhkkedgiwstdilkdqkepknktf lrceaknysgrftcwwlttistdltfsvkssrgssdpqgvtcgaatlsa ervrgdnkeyeysvecqedsacpaaeeslpievmvdavhklkyenytss ffirdiikpdppknlqlkplknsrqvevsweypdtwstphsyfsltfcv qvqgkskrekkdrvftdktsatvicrknasisvraqdryyssswsewas vpcsggggsggggsggggsrvipvsgparclsqsrnllkttddmvktar eklkhysctaedidheditrdqtstlktclplelhknesclatretsst trgsclppqktslmmtlclgsiyedlkmyqtefqainaalqnhnhqqii ldkgmlvaidelmqslnhngetlrqkppvgeadpyrvkmklcillhafs trvvtinrvmgylssaSGGPGPAGMKGLPGSEVQLVESGGGLVQPGNSL RLSCAASGFTFSKFGMSWVRQAPGKGLEWVSSISGSGRDTLYAESVKGR FTISRDNAKTTLYLQMNSLRPEDTAVYYCTIGGSLSVSSQGTLVTVSSH HHHHHEPEA

[0487]

[0488]

69	ACP07（人 p40/鼠 p35 IL12 融合蛋白）	QSVLTQPPSVSGAPGQRVTISCSGSRSNIGSNTVKWYQQLPGTAPKLLI YYNDQRPSGVPDRFSGSKSGTSASLAITGLQAEDEADYYCQSYDRYTHP ALLFGTGTKVTVLggggsggggsggggsQVQLVESGGGVVQPGRSLRLS CAASGFTFSSYGMHWVRQAPGKGLEWVAFIRYDGSNKYYADSVKGRFTI SRDNSKNTLYLQMNSLRAEDTAVYYCKTHGSHDNWGQGTMVTVSSgggg sggggsggggsggggsggggsggggsSGGPGPAGMKGLPGSiwelkkdv yvveldwypdapgemvvltcdtpeedgitwtldqssevlgsgktltiqv kefgdagqytchkggevlshsllllhkkedgiwstdilkdqkepknktf lrceaknysgrftcwwlttistdltfsvkssrgssdpqgvtcgaatlsa ervrgdnkeyeysvecqedsacpaaeeslpievmvdavhklkyenytss ffirdiikpdppknlqlkplknsrqvevsweypdtwstphsyfsltfcv qvqgkskrekkdrvftdktsatvicrknasisvraqdryyssswsewas vpcsggggsggggsggggsrvipvsgparclsqsrnllkttddmvktar eklkhysctaedidheditrdqtstlktclplelhknesclatretsst trgsclppqktslmmtlclgsiyedlkmyqtefqainaalqnhnhqqii ldkgmlvaidelmqslnhngetlrqkppvgeadpyrvkmklcillhafs trvvtinrvmgylssaSGGPGPAGMKGLPGSEVQLVESGGGLVQPGNSL RLSCAASGFTFSKFGMSWVRQAPGKGLEWVSSISGSGRDTLYAESVKGR FTISRDNAKTTLYLQMNSLRPEDTAVYYCTIGGSLSVSSQGTLVTVSSg gggsggggsggggsQVQLQESGGGLAQAGGSLSLSCAASGFTVSNSVMA WYRQTPGKQREFVAIINSVGSTNYADSVKGRFTISRDNAKNTVYLQMNN LKPEDTAVYVCNRNFDRIYWGQGTQVTVSSHHHHHHEPEA
70	ACP08（人 p40/鼠 p35 IL12 融合蛋白）	QVQLQESGGGLAQAGGSLSLSCAASGFTVSNSVMAWYRQTPGKQREFVA IINSVGSTNYADSVKGRFTISRDNAKNTVYLQMNNLKPEDTAVYVCNRN FDRIYWGQGTQVTVSSggggsggggsggggsQSVLTQPPSVSGAPGQRV TISCSGSRSNIGSNTVKWYQQLPGTAPKLLIYYNDQRPSGVPDRFSGSK SGTSASLAITGLQAEDEADYYCQSYDRYTHPALLFGTGTKVTVLggggs ggggsggggsQVQLVESGGGVVQPGRSLRLSCAASGFTFSSYGMHWVRQ APGKGLEWVAFIRYDGSNKYYADSVKGRFTISRDNSKNTLYLQMNSLRA EDTAVYYCKTHGSHDNWGQGTMVTVSSggggsggggsggggsggggsgg ggsggggsSGGPGPAGMKGLPGSiwelkkdvyvveldwypdapgemvvl tcdtpeedgitwtldqssevlgsgktltiqvkefgdagqytchkggevl shsllllhkkedgiwstdilkdqkepknktflrceaknysgrftcwwlt tistdltfsvkssrgssdpqgvtcgaatlsaervrgdnkeyeysvecqe dsacpaaeeslpievmvdavhklkyenytssffirdiikpdppknlqlk plknsrqvevsweypdtwstphsyfsltfcvqvqgkskrekkdrvftdk

[0489]

		tsatvicrknasisvraqdryyssswsewasvpcsggggsggggsgggg srvipvsgparclsqsrnllkttddmvktareklkhysctaedidhedi trdqtstlktclplelhknesclatretssttrgsclppqktslmmtlc lgsiyedlkmyqtefqainaalqnhnhqqiildkgmlvaidelmqslnh ngetlrqkppvgeadpyrvkmklcillhafstrvvtinrvmgylssaSG GPGPAGMKGLPGSEVQLVESGGGLVQPGNSLRLSCAASGFTFSKFGMSW VRQAPGKGLEWVSSISGSGRDTLYAESVKGRFTISRDNAKTTLYLQMNS LRPEDTAVYYCTIGGSLSVSSQGTLVTVSSHHHHHHEPEA
71	ACP09 (人 p40/ 鼠 p35 IL12 融 合蛋白)	EVQLVESGGGLVQPGNSLRLSCAASGFTFSKFGMSWVRQAPGKGLEWVS SISGSGRDTLYAESVKGRFTISRDNAKTTLYLQMNSLRPEDTAVYYCTI GGSLSVSSQGTLVTVSSggggsggggsggggsQSVLTQPPSVSGAPGQR VTISCSGSRSNIGSNTVKWYQQLPGTAPKLLIYYNDQRPSGVPDRFSGS KSGTSASLAITGLQAEDEADYYCQSYDRYTHPALLFGTGTKVTVLgggg sggggsggggsQVQLVESGGGVVQPGRSLRLSCAASGFTFSSYGMHWVR QAPGKGLEWVAFIRYDGSNKYYADSVKGRFTISRDNSKNTLYLQMNSLR AEDTAVYYCKTHGSHDNWGQGTMVTVSSggggsggggsggggsggggsg gggsggggsSGGPGPAGMKGLPGSiwelkkdvyvveldwypdapgemvv ltcdtpeedgitwtldqssevlgsgktltiqvkefgdagqytchkggev lshslllhkkedgiwstdilkdqkepknktflrceaknysgrftcwwl ttistdltfsvkssrgssdpqgvtcgaatlsaervrgdnkeyeysvecq edsacpaaeeslpievmvdavhklkyenytssffirdiikpdppknlql kplknsrqvevsweypdtwstphsyfsltfcvqvqgkskrekkdrvftd ktsatvicrknasisvraqdryyssswsewasvpcsggggsggggsgggg gsrvipvsgparclsqsrnllkttddmvktareklkhysctaedidhed itrdqtstlktclplelhknesclatretssttrgsclppqktslmmtl clgsiyedlkmyqtefqainaalqnhnhqqiildkgmlvaidelmqsln hngetlrqkppvgeadpyrvkmklcillhafstrvvtinrvmgylssaH HHHHHEPEA
72	ACP10 (人 p40/ 鼠 p35 IL12 融 合蛋白)	EVQLVESGGGLVQPGNSLRLSCAASGFTFSKFGMSWVRQAPGKGLEWVS SISGSGRDTLYAESVKGRFTISRDNAKTTLYLQMNSLRPEDTAVYYCTI GGSLSVSSQGTLVTVSSSGGPGPAGMKGLPGSiwelkkdvyvveldwyp dapgemvvltcdtpeedgitwtldqssevlgsgktltiqvkefgdagqy tchkggevlshslllhkkedgiwstdilkdqkepknktflrceaknys grftcwwlttistdltfsvkssrgssdpqgvtcgaatlsaervrgdnke yeysvecqedsacpaaeeslpievmvdavhklkyenytssffirdiikp dppknlqlkplknsrqvevsweypdtwstphsyfsltfcvqvqgkskre

		kkdrvftdktsatvicrknasisvraqdryyssswsewasvpcsggggs ggggsggggsrvipvsgparclsqsrnllkttddmvktareklkhysct aedidheditrdqtstlktclplelhknesclatretssttrgsclppq ktslmmtlclgsiyedlkmyqtefqainaalqnhnhqqiildkgmlvai delmqslnhngetlrqkppvgeadpyrvkmklcillhafstrvvtinrv mgylssaSGGPGPAGMKGLPGSggggsggggsggggsggggsggggsgg ggsQSVLTQPPSVSGAPGQRVTISCSGSRSNIGSNTVKWYQQLPGTAPK LLIYYNDQRPSGVPDRFSGSKSGTSASLAITGLQAEDEADYYCQSYDRY THPALLFGTGTKVTVLggggsggggsggggsQVQLVESGGGVVQPGRSL RLSCAASGFTFSSYGMHWVRQAPGKGLEWVAFIRYDGSNKYYADSVKGR FTISRDNSKNTLYLQMNSLRAEDTAVYYCKTHGSHDNWGQGTMVTVSSH HHHHHEPEA
73	ACP11（人 p40/鼠 p35 IL12 融合蛋白）	iwelkkdvyvveldwypdapgemvvltcdtpeedgitwtldqssevlgs gktltiqvkefgdagqytchkggevlshsllllhkkedgiwstdilkdq kepknktflrceaknysgrftcwwlttistdltfsvkssrgssdpqgvt cgaatlsaervrgdnkeyeysvecqedsacpaaeeslpievmvdavhkl kyenytssffirdiikpdppknlqlkplknsrqvevsweypdtwstphs yfsltfcvqvqgkskrekkdrvftdktsatvicrknasisvraqdryys sswsewasvpcsggggsggggsggggsrvipvsgparclsqsrnllktt ddmvktareklkhysctaedidheditrdqtstlktclplelhknescl atretssttrgsclppqktslmmtlclgsiyedlkmyqtefqainaalq nhnhqqiildkgmlvaidelmqslnhngetlrqkppvgeadpyrvkmkl cillhafstrvvtinrvmgylssaSGGPGPAGMKGLPGSggggsggggs ggggsggggsggggsggggsQSVLTQPPSVSGAPGQRVTISCSGSRSNI GSNTVKWYQQLPGTAPKLLIYYNDQRPSGVPDRFSGSKSGTSASLAITG LQAEDEADYYCQSYDRYTHPALLFGTGTKVTVLggggsggggsggggsQ VQLVESGGGVVQPGRSLRLSCAASGFTFSSYGMHWVRQAPGKGLEWVAF IRYDGSNKYYADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCKTH GSHDNWGQGTMVTVSSggggsggggsggggsEVQLVESGGGLVQPGNSL RLSCAASGFTFSKFGMSWVRQAPGKGLEWVSSISGSGRDTLYAESVKGR FTISRDNAKTTLYLQMNSLRPEDTAVYYCTIGGSLSVSSQGTLVTVSSH HHHHHEPEA

[0490]

[0491]

74	IL12 p40 人 (Uniprot 登录号 P29460)	10 20 30 40 50 MCHQQLVISW FSLVFLASPL VAIWELKKDV YVVELDWYPD APGEMVVLTC 60 70 80 90 100 DTPEEDGITW TLDQSSEVLG SGKTLTIQVK EFGDAGQYTC HKGGEVLSHS 110 120 130 140 150 LLLLHKKEDG IWSTDILKDQ KEPKNKTFLR CEAKNYSGRF TCWWLTTIST 160 170 180 190 200 DLTFSVKSSR GSSDPQGVTC GAATLSAERV RGDNKEYEYS VECQEDSACP 210 220 230 240 250 AAEESLPIEV MVDAVHKLKY ENYTSSFFIR DIIKPDPPKN LQLKPLKNSR 260 270 280 290 300 QVEVSWEYPD TWSTPHSYFS LTFCVQVQGK SKREKKDRVF TDKTSATVIC 310 320 RKNASISVRA QDRYYSSSWS EWASVPCS
75	IL12 p35 小鼠 (Uniprot 登录号 P43431)	10 20 30 40 50 MCQSRYLLFL ATLALLNHLS LARVIPVSGP ARCLSQSRNL LKTTDDMVKT 60 70 80 90 100 AREKLKHYSC TAEDIDHEDI TRDQTSTLKT CLPLELHKNE SCLATRETSS 110 120 130 140 150 TTRGSCLPPQ KTSLMMTLCL GSIYEDLKMY QTEFQAINAA LQNHNHQQII 160 170 180 190 200 LDKGMLVAID ELMQSLNHNG ETLRQKPPVG EADPYRVKMK LCILLHAFST 210 RVVTINRVMG YLSSA
76	IL12Rb-2	10 20 30 40 50 MRWIFRGCSL AFMFIINWL IFAKLDACKA GPNIYKPDNV IILGSEIVIII 60 70 80 90 100 CSLKPRQGCF HVSRDWKLIL IKFDARINFH HGHSLNSQVI GLRLGTLLEV 110 120 130 140 150 CKLACINSDR IQICGAEIFV GVAPEQRQNL SCIQKGRQGT VACTWERGRD 160 170 180 190 200 THLYTFYILQ LSGPKNLTNQ KQCKDIKGDV LDEGINLTRE SPESNFIAKV 210 220 230 240 250 TAVNSLGSRS SLPSTFTFLD IVRPLRPMDI PIKFQKASVS SCTLVKPDRG 260 270 280 290 300 LVLLWRLRVR RSNSRLWNSV NVIKAKGRHD LLDLKPFTEY EFQISSKLHL 310 320 330 340 350 YKGSESDMSE SLRAQIPREE PTGMLDVNKM KRHIDVSRQQ ISLFNKVLSV 360 370 380 390 400 SRARGKILHY QVTLQELTGG KANIQNIIGH ISKFTVIRRI GNAAVAVSAA 410 420 430 440 450 NSKGASLRTR INIMNLCRAG LIAPRQVSAN SRGMSNILVT WQPPRKDRSA 460 470 480 490 500 VQEYVVERWR LHRGGDTQVP LWWLRSRFVN VSALISEWIK SYICYRIDVY 510 520 530 540 550 ALSGRQGSCS SILGNSKHKA PLSGPHINAI IEEKGSILIS WNSIPVQEQM 560 570 580 590 600 GCLLHYRIKN KERDSNSQRQ LCEIFKRVSQ NSHPINSLQR EVTVVLWNTA 610 620 630 640 650 LTAAGRSSHG WERFFCLQGK ANRMAFVAPS ICIAIIMVGI FSTHYFQQNV 660 670 680 690 700 FVLLAALRPQ WCSREIPDPA NSTCAKKYPI AEEKTQLPLD RLLIDWPTPE 710 720 730 740 750 DPEPLVISEV LHQVTPVFRH PPCSNWPQRE KGIQGHQASE KDMMHSASSP 760 770 780 790 800 PPPPALQAES RQLVDLYKVL ESRGSDPKPE NPACPWTVLP AGDLPTHDGY 810 820 830 840 850 LPSNIDDLPS HEAPLADSLE ELEPQHISLS VFPSSSLHPL TFSCGDKLTL 860 DQLKMRCDSL ML

[0492]

77	IL12Rb-1	10 20 30 40 50 MEPLVTWVVP LLFLFLLSRQ GAACRTSECC FQDPPYPDAD SGSASGPRDL 60 70 80 90 100 RCYRISSDRY ECSWQYEGPT AGVSHFLRCC LSSGRCCYFA AGSATRLQFS 110 120 130 140 150 DQAGVSVLYT VTLWVESWAR NQTEKSPEVT LQLYNSVKYE PPLGDIKVSK 160 170 180 190 200 LAGQLRMEWE TPDNQVGAEV QFRHRTPSSP WKLGDCGPQD DDTESCLCPL 210 220 230 240 250 EMNVAQEFQL RRRQLGSQGS SWSKWSSPVC VPPENPPQPQ VRFSVEQLGQ 260 270 280 290 300 DGRRRLTLKE QPTQLELPEG CQGLAPGTEV TYRLQLHMLS CPCKAKATRT 310 320 330 340 350 LHLGKMPYLS GAAYNVAVIS SNQFGPGLNQ TWHIPADTHT EPVALNISVG 360 370 380 390 400 TNGTTMYWPA RAQSMTYCIE WQPVGQDGGL ATCSLTAPQD PDPAGMATYS 410 420 430 440 450 WSRESGAMGQ EKCYYITIFA SAHPEKLTLW STVLSTYHFG GNASAAGTPH 460 470 480 490 500 HVSVKNHSLD SVSVDWAPSL LSTCPGVLKE YVVRCRDEDS KQVSEHPVQP 510 520 530 540 550 TETQVTLSGL RAGVAYTVQV RADTAWLRGV WSQPQRFSIE VQVSDWLIFF 560 570 580 590 600 ASLGSFLSIL LVGVLGYLGL NRAARHLCPP LPTPCASSAI EFPGGKETWQ 610 620 630 640 650 WINPVDFQEE ASLQEALVVE MSWDKGERTE PLEKTELPEG APELALDTEL 660 SLEDGDRCKA KM
78	IL-12 p35 人 (Uniprot 登录号 P29459)	10 20 30 40 50 MCHQQLVISW FSLVFLASPL VAIWELKKDV YVVELDWYPD APGEMVVLTC 60 70 80 90 100 DTPEEDGITW TLDQSSEVLG SGKTLTIQVK EFGDAGQYTC HKGGEVLSHS 110 120 130 140 150 LLLLHKKEDG IWSTDILKDQ KEPKNKTFLR CEAKNYSGRF TCWWLTTIST 160 170 180 190 200 DLTFSVKSSR GSSDPQGVTC GAATLSAERV RGDNKEYEYS VECQEDSACP 210 220 230 240 250 AAEESLPIEV MVDAVHKLKY ENYTSSFFIR DIIKPDPPKN LQLKPLKNSR 260 270 280 290 300 QVEVSWEYPD TWSTPHSYFS LTFCVQVQGK SKREKKDRVF TDKTSATVIC 310 320 RKNASISVRA QDRYYSSSWS EWASVPCS
79	IL-12 p40 小鼠 (Uniprot 登录号 P43432)	10 20 30 40 50 MCPQKLTISW FAIVLLVSPL MAMWELEKDV YVVEVDWTPD APGETVNLTC 60 70 80 90 100 DTPEEDDITW TSDQRHGVIG SGKTLTITVK EFLDAGQYTC HKGGETLSHS 110 120 130 140 150 HLLLHKKENG IWSTEILKNF KNKTFLKCEA PNYSGRFTCS WLVQRNMDLK 160 170 180 190 200 FNIKSSSSSP DSRAVTCGMA SLSAEKVTLD QRDYEKYSVS CQEDVTCPTA 210 220 230 240 250 EETLPIELAL EARQQNKYEN YSTSFFIRDI IKPDPPKNLQ MKPLKNSQVE 260 270 280 290 300 VSWEYPDSWS TPHSYFSLKF FVRIQRKKEK MKETEEGCNQ KGAFLVEKTS 310 320 330 TEVQCKGGNV CVQAQDRYYN SSCSKWACVP CRVRS

[0493]

80	ACP01（小鼠IFNg融合蛋白）	EVQLVESGGGLVQPGNSLRLSCAASGFTFSKFGMSWVRQAPGKGLEWVSSISGSGRDTLYAESVKGRFTISRDNAKTTLYLQMNSLRPEDTAVYYCTIGGSLSVSSQGTLVTVSSSGGPGPAGMKGLPGShgtviesleslnnyfnssgidveekslfldiwrnwqkdgdmkilqsqiisfylrlfevlkdnqaisnnisvieshlittffsnskakkdafmsiakfevnnpqvqrqafnelirvvhqllpesslrkrkrsrcSGGPGPAGMKGLPGSEVQLVESGGGLVQPGNSLRLSCAASGFTFSKFGMSWVRQAPGKGLEWVSSISGSGRDTLYAESVKGRFTISRDNAKTTLYLQMNSLRPEDTAVYYCTIGGSLSVSSQGTLVTVSSHHHHHH
81	ACP02（小鼠IFNg融合蛋白）	EVQLVESGGGLVQPGNSLRLSCAASGFTFSKFGMSWVRQAPGKGLEWVSSISGSGRDTLYAESVKGRFTISRDNAKTTLYLQMNSLRPEDTAVYYCTIGGSLSVSSQGTLVTVSSSGGPGPAGMKGLPGShgtviesleslnnyfnssgidveekslfldiwrnwqkdgdmkilqsqiisfylrlfevlkdnqaisnnisvieshlittffsnskakkdafmsiakfevnnpqvqrqafnelirvvhqllpesslrkrkrsrcSGGPGPAGMKGLPGShgtviesleslnnyfnssgidveekslfldiwrnwqkdgdmkilqsqiisfylrlfevlkdnqaisnnisvieshlittffsnskakkdafmsiakfevnnpqvqrqafnelirvvhqllpesslrkrkrsrcSGGPGPAGMKGLPGSEVQLVESGGGLVQPGNSLRLSCAASGFTFSKFGMSWVRQAPGKGLEWVSSISGSGRDTLYAESVKGRFTISRDNAKTTLYLQMNSLRPEDTAVYYCTIGGSLSVSSQGTLVTVSSHHHHHH
82	ACP03（小鼠IFNg融合蛋白）	EVQLVESGGGLVQPGNSLRLSCAASGFTFSKFGMSWVRQAPGKGLEWVSSISGSGRDTLYAESVKGRFTISRDNAKTTLYLQMNSLRPEDTAVYYCTIGGSLSVSSQGTLVTVSSSGGPGPAGMKGLPGShgtviesleslnnyfnssgidveekslfldiwrnwqkdgdmkilqsqiisfylrlfevlkdnqaisnnisvieshlittffsnskakkdafmsiakfevnnpqvqrqafnelirvvhqllpesslrkrkrsrcggggsggggsggggshgtviesleslnnyfnssgidveekslfldiwrnwqkdgdmkilqsqiisfylrlfevlkdnqaisnnisvieshlittffsnskakkdafmsiakfevnnpqvqrqafnelirvvhqllpesslrkrkrsrcSGGPGPAGMKGLPGSEVQLVESGGGLVQPGNSLRLSCAASGFTFSKFGMSWVRQAPGKGLEWVSSISGSGRDTLYAESVKGRFTISRDNAKTTLYLQMNSLRPEDTAVYYCTIGGSLSVSSQGTLVTVSSHHHHHH

[0494]

83	人 IFN-g (Uniprot 登录号 P01579)	10 20 30 40 50 MKYTSYILAF QLCIVLGSLG CYCQDPYVKE AENLKKYFNA GHSDVADNGT 60 70 80 90 100 LFLGILKNWK EESDRKIMQS QIVSFYFKLF KNFKDDQSIQ KSVETIKEDM 110 120 130 140 150 NVKFFNSNKK KRDDFEKLTN YSVTDLNVQR KAIHELIQVM AELSPAAKTG 160 KRKRSQMLFR GRRASQ
84	小鼠 IFN-g (Uniprot 登录号 P01580)	10 20 30 40 50 MNATHCILAL QLFLMAVSGC YCHGTVIESL ESLNNYFNSS GIDVEEKSLF 60 70 80 90 100 LDIWRNWQKD GDMKILQSQI ISFYLRLFEV LKDNQAISNN ISVIESHLIT 110 120 130 140 150 TFFSNSKAKK DAFMSIAKFE VNNPQVQRQA FNELIRVVHQ LLPESSLRKR KRSRC
85	ACP30 (小鼠 IFNg 融合蛋白)	mdmrvpaqllgllllwlrgarcEVQLVESGGGLVQPGNSLRLSCAASGF TFSKFGMSWVRQAPGKGLEWVSSISGSGRDTLYAESVKGRFTISRDNAK TTLYLQMNSLRPEDTAVYYCTIGGSLSVSSQGTLVTVSSSGGPGPAGMK GLPGShgtviesleslnnyfnssgidveekslfldiwrnwqkdgdmkil qsqiisfylrlfevlkdnqaisnnisvieshlittffsnskakkdafms iakfevnnpqvqrqafnelirvvhqllpesslrkrkrsrcSGGPGPAGM KGLPGSEVQLVESGGGLVQPGNSLRLSCAASGFTFSKFGMSWVRQAPGK GLEWVSSISGSGRDTLYAESVKGRFTISRDNAKTTLYLQMNSLRPEDTA VYYCTIGGSLSVSSQGTLVTVSSSGGPGPAGMKGLPGShgtvieslesl nnyfnssgidveekslfldiwrnwqkdgdmkilqsqiisfylrlfevlk dnqaisnnisvieshlittffsnskakkdafmsiakfevnnpqvqrqaf nelirvvhqllpesslrkrkrsrcSGGPGPAGMKGLPGSEVQLVESGGG LVQPGNSLRLSCAASGFTFSKFGMSWVRQAPGKGLEWVSSISGSGRDTL YAESVKGRFTISRDNAKTTLYLQMNSLRPEDTAVYYCTIGGSLSVSSQG TLVTVSSHHHHHH
86	ACP31 (小鼠 IFNa1 融合蛋白)	EVQLVESGGGLVQPGNSLRLSCAASGFTFSKFGMSWVRQAPGKGLEWVS SISGSGRDTLYAESVKGRFTISRDNAKTTLYLQMNSLRPEDTAVYYCTI GGSLSVSSQGTLVTVSSSGGPGPAGMKGLPGScdlpqthnlrnkraltl lvqmrrlsplsclkdrkdfgfpqekvdaqqikkaqaipvlseltqqiln iftskdssaawnttlldsfcndlhqqlndlqgclmqqvgvqefpltqed allavrkyfhritvylrekkhspcawevvraevwralsssanvlgrlre ekSGGPGPAGMKGLPGSEVQLVESGGGLVQPGNSLRLSCAASGFTFSKF GMSWVRQAPGKGLEWVSSISGSGRDTLYAESVKGRFTISRDNAKTTLYL

[0495]

		QMNSLRPEDTAVYYCTIGGSLSVSSQGTLVTVSSHHHHHHHEPEA
87	ACP32（小鼠IFNa1融合蛋白）	EVQLVESGGGLVQPGNSLRLSCAASGFTFSKFGMSWVRQAPGKGLEWVS SISGSGRDTLYAESVKGRFTISRDNAKTTLYLQMNSLRPEDTAVYYCTI GGSLSVSSQGTLVTVSSSGGPGPAGMKGLPGScdlpqthnlrnkraltl lvqmrrlsplsclkdrkdfgfpqekvdaqqikkaqaipvlseltqqiln iftskdssaawnttlldsfcndlhqqlndlqgclmqqvgvqefpltqed allavrkyfhritvylrekkhspcawevvraevwralsssanvSGGPGP AGMKGLPGSEVQLVESGGGLVQPGNSLRLSCAASGFTFSKFGMSWVRQA PGKGLEWVSSISGSGRDTLYAESVKGRFTISRDNAKTTLYLQMNSLRPE DTAVYYCTIGGSLSVSSQGTLVTVSSHHHHHHHEPEA
88	IFNgR1	10 20 30 40 50 MALLFLLPLV MQGVSRAEMG TADLGPSSVP TPTNVTIESY NMNPIVYWEY 60 70 80 90 100 QIMPQVPVFT VEVKNYGVKN SEWIDACINI SHHYCNISDH VGDPSNSLWV 110 120 130 140 150 RVKARVGQKE SAYAKSEEFA VCRDGKIGPP KLDIRKEEKQ IMIDIFHPSV 160 170 180 190 200 FVNGDEQEVD YDPETTCYIR VYNVYVRMNG SEIQYKILTQ KEDDCDEIQC 210 220 230 240 250 QLAIPVSSLN SQYCVSAEGV LHVWGVTTEK SKEVCITIFN SSIKGSLWIP 260 270 280 290 300 VVAALLLFLV LSLVFICFYI KKINPLKEKS IILPKSLISV VRSATLETKP 310 320 330 340 350 ESKYVSLITS YQPFSLEKEV VCEEPLSPAT VPGMHTEDNP GKVEHTEELS 360 370 380 390 400 SITEVVTTEE NIPDVVPGSH LTPIERESSS PLSSNQSEPG SIALNSYHSR 410 420 430 440 450 NCSESDHSRN GFDTDSSCLE SHSSLSDSEF PPNNKGEIKT EGQELITVIK 460 470 480 APTSFGYDKP HVLVDLLVDD SGKESLIGYR PTEDSKEFS
89	IFNgR2	10 20 30 40 50 MRPTLLWSLL LLLGVFAAAA AAPPDPLSQL PAPQHPKIRL YNAEQVLSWE 60 70 80 90 100 PVALSNSTRP VVYQVQFKYT DSKWFTADIM SIGVNCTQIT ATECDFTAAS 110 120 130 140 150 PSAGFPMDFN VTLRLRAELG ALHSAWVTMP WFQHYRNVTV GPPENIEVTP 160 170 180 190 200 GEGSLIIRFS SPFDIADTST AFFCYYVHYW EKGGIQQVKG PFRSNSISLD 210 220 230 240 250 NLKPSRVYCL QVQAQLLWNK SNIFRVGHLS NISCYETMAD ASTELQQVIL 260 270 280 290 300 ISVGTFSLLS VLAGACFFLV LKYRGLIKYW FHTPPSIPLQ IEEYLKDPTQ 310 320 330 PILEALDKDS SPKDDVWDSV SIISFPEKEQ EDVLQTL
90	ACP51小鼠IFG融合蛋白	QVQLQESGGGLVQAGGSLRLSCAASGRIFSIDIMSWYRQAPGKQRELVA RITRGGTISYDDSVKGRFTISRDNAKNTVYLQMNSLKPEDTGVYYCNAL YGTDYWGKGTQVTVSSggggsggggsggggsEVQLVESGGGLVQPGNSL RLSCAASGFTFSKFGMSWVRQAPGKGLEWVSSISGSGRDTLYAESVKGR FTISRDNAKTTLYLQMNSLRPEDTAVYYCTIGGSLSVSSQGTLVTVSSS GGPGPAGMKGLPGShgtviesleslnnyfnssgidveekslfldiwrnw qkdgdmkilqsqiisfylrlfevlkdnqaisnnisvieshlittffsns

[0496]

		kakkdafmsiakfevnnpqvqrqafnelirvvhqllpesslrkrkrsrc SGGPGPAGMKGLPGSEVQLVESGGGLVQPGNSLRLSCAASGFTFSKFGM SWVRQAPGKGLEWVSSISGSGRDTLYAESVKGRFTISRDNAKTTLYLQM NSLRPEDTAVYYCTIGGSLSVSSQGTLVTVSSHHHHHH
91	ACP52 小鼠 IFG 融合蛋 白	EVQLVESGGGLVQPGNSLRLSCAASGFTFSKFGMSWVRQAPGKGLEWVS SISGSGRDTLYAESVKGRFTISRDNAKTTLYLQMNSLRPEDTAVYYCTI GGSLSVSSQGTLVTVSSSGGPGPAGMKGLPGShgtviesleslnnyfns sgidveekslfldiwrnwqkdgdmkilqsqiisfylrlfevlkdnqais nnisvieshlittffsnskakkdafmsiakfevnnpqvqrqafnelirv vhqllpesslrkrkrsrcSGGPGPAGMKGLPGSEVQLVESGGGLVQPGN SLRLSCAASGFTFSKFGMSWVRQAPGKGLEWVSSISGSGRDTLYAESVK GRFTISRDNAKTTLYLQMNSLRPEDTAVYYCTIGGSLSVSSQGTLVTVS SSGGPGPAGMKGLPGSEVQLVESGGGLVQPGNSLRLSCAASGFTFSKFG MSWVRQAPGKGLEWVSSISGSGRDTLYAESVKGRFTISRDNAKTTLYLQ MNSLRPEDTAVYYCTIGGSLSVSSQGTLVTVSSggggsggggsggggsQ VQLQESGGGLVQAGGSLRLSCAASGRIFSIDIMSWYRQAPGKQRELVAR ITRGGTISYDDSVKGRFTISRDNAKNTVYLQMNSLKPEDTGVYYCNALY GTDYWGKGTQVTVSSHHHHHH
92	ACP53 小鼠 IFG 融合蛋 白	eahkseiahryndlgeqhfkglvliafsqylqkcsydehaklvqevtdf aktcvadesaancdkslhtlfgdklcaipnlrenygeladcctkqeper necflqhkddnpslppferpeaeamctsfkenpttfmghylhevarrhp yfyapellyyaeqyneiltqccaeadkescltpkldgvkekalvssvrq rmkcssmqkfgerafkawavarlsqtfpnadfaeitklatdltkvnkec chgdllecaddraelakymcenqatisskl qtccdkpllkkahclseve hdtmpadlpaiaadfvedqevcknyaeakdvflgtflyeysrrhpdysv slllrlakkyeatlekccaeanppacygtvlaefqplveepknlvktnc dlyeklgeygfqnailvrytqkapqvstptlveaarnlgrvgtkcctlp edqrlpcvedylsailnrvcllhektpvsehvtkccsgslverrpcfsa ltvdetyvpkefkaetftfhsdictlpekekqikkqtalaelvkhkpka taeqlktvmddfaqfldtcckaadkdtcfstegpnlvtrckdalaSGGP GPAGMKGLPGShgtviesleslnnyfnssgidveekslfldiwrnwqkd gdmkilqsqiisfylrlfevlkdnqaisnnisvieshlittffsnskak kdafmsiakfevnnpqvqrqafnelirvvhqllpesslrkrkrsrcSGG PGPAGMKGLPGSeahkseiahryndlgeqhfkglvliafsqylqkcsyd ehaklvqevtdfaktcvadesaancdkslhtlfgdklcaipnlrenyge ladcctkqepernecflqhkddnpslppferpeaeamctsfkenpttfm

[0497]

		ghylhevarrhpyfyapellyyaeqyneiltqccaeadkescltpkldg vkekalvssvrqrmkcssmqkfgerafkawavarlsqtfpnadfaeitk latdltkvnkecchgdllecaddraelakymcenqatissklqtccdkp llkkahclsevehdtmpadlpaiaadfvedqevcknyaeakdvflgtfl yeysrrhpdysvslllrlakkyeatlekccaeanppacygtvlaefqpl veepknlvktncdlyeklgeygfqnailvrytqkapqvstptlveaarn lgrvgtkcctlpedqrlpcvedylsailnrvcllhektpvsehvtkccs gslverrpcfsaltvdetyvpkefkaetftfhsdictlpekekqikkqt alaelvkhkpkataeqlktvmddfaqfldtcckaadkdtcfstegpnlv trckdalaHHHHHH
93	ACP54 小鼠 IFG 融合蛋 白	eahkseiahryndlgeqhfkglvliafsqylqkcsydehaklvqevtdf aktcvadesaancdkslhtlfgdklcaipnlrenygeladcctkqeper necflqhkddnpslppferpeaeamctsfkenpttfmghylhevarrhp yfyapellyyaeqyneiltqccaeadkescltpkldgvkekalvssvrq rmkcssmqkfgerafkawavarlsqtfpnadfaeitklatdltkvnkec chgdllecaddraelakymcenqatissklqtccdkpllkkahclseve hdtmpadlpaiaadfvedqevcknyaeakdvflgtflyeysrrhpdysv slllrlakkyeatlekccaeanppacygtvlaefqplveepknlvktnc dlyeklgeygfqnailvrytqkapqvstptlveaarnlgrvgtkcctlp edqrlpcvedylsailnrvcllhektpvsehvtkccsgslverrpcfsa ltvdetyvpkefkaetftfhsdictlpekekqikkqtalaelvkhkpka taeqlktvmddfaqfldtcckaadkdtcfstegpnlvtrckdalaSGGP GPAGMKGLPGShgtviesleslnnyfnssgidveekslfldiwrnwqkd gdmkilqsqiisfylrlfevlkdnqaisnnisvieshlittffsnskak kdafmsiakfevnnpqvqrqafnelirvvhqllpesslrkrkrsrcggg gsggggsggggshgtviesleslnnyfnssgidveekslfldiwrnwqk dgdmkilqsqiisfylrlfevlkdnqaisnnisvieshlittffsnska kkdafmsiakfevnnpqvqrqafnelirvvhqllpesslrkrkrsrcSG GPGPAGMKGLPGSeahkseiahryndlgeqhfkglvliafsqylqkcsy dehaklvqevtdfaktcvadesaancdkslhtlfgdklcaipnlrenyg eladcctkqepernecflqhkddnpslppferpeaeamctsfkenpttf mghylhevarrhpyfyapellyyaeqyneiltqccaeadkescltpkld gvkekalvssvrqrmkcssmqkfgerafkawavarlsqtfpnadfaeit klatdltkvnkecchgdllecaddraelakymcenqatissklqtccdk pllkkahclsevehdtmpadlpaiaadfvedqevcknyaeakdvflgtf lyeysrrhpdysvslllrlakkyeatlekccaeanppacygtvlaefqp

[0498]

		lveepknlvktncdlyeklgeygfqnailvrytqkapqvstptlveaar nlgrvgtkcctlpedqrlpcvedylsailnrvcllhektpvsehvtkcc sgslverrpcfsaltvdetyvpkefkaetftfhsdictlpekekqikkq talaelvkhkpkataeqlktvmddfaqfldtcckaadkdtcfstegpnl vtrckdalaHHHHHH
94	ACP50 小鼠 IFG 融合蛋白	mdmrvpaqllgllllwlrgarcQVQLQESGGGLVQAGGSLRLSCAASGR IFSIDIMSWYRQAPGKQRELVARITRGGTISYDDSVKGRFTISRDNAKN TVYLQMNSLKPEDTGVYYCNALYGTDYWGKGTQVTVSSggggsggggsg gggsEVQLVESGGGLVQPGNSLRLSCAASGFTFSKFGMSWVRQAPGKGL EWVSSISGSGRDTLYAESVKGRFTISRDNAKTTLYLQMNSLRPEDTAVY YCTIGGSLSVSSQGTLVTVSSSGGPGPAGMKGLPGShgtviesleslnn yfnssgidveekslfldiwrnwqkdgdmkilqsqiisfylrlfevlkdn qaisnnisvieshlittffsnskakkdafmsiakfevnnpqvqrqafne lirvvhqllpesslrkrkrsrcggggsggggsggggshgtvieslesln nyfnssgidveekslfldiwrnwqkdgdmkilqsqiisfylrlfevlkd nqaisnnisvieshlittffsnskakkdafmsiakfevnnpqvqrqafn elirvvhqllpesslrkrkrsrcSGGPGPAGMKGLPGSEVQLVESGGGL VQPGNSLRLSCAASGFTFSKFGMSWVRQAPGKGLEWVSSISGSGRDTLY AESVKGRFTISRDNAKTTLYLQMNSLRPEDTAVYYCTIGGSLSVSSQGT LVTVSSHHHHHH
95	ACP55 小鼠 IFG 融合蛋白	mdmrvpaqllgllllwlrgarcEVQLVESGGGLVQPGNSLRLSCAASGF TFSKFGMSWVRQAPGKGLEWVSSISGSGRDTLYAESVKGRFTISRDNAK TTLYLQMNSLRPEDTAVYYCTIGGSLSVSSQGTLVTVSSSGGPGPAGMK GLPGShgtviesleslnnyfnssgidveekslfldiwrnwqkdgdmkil qsqiisfylrlfevlkdnqaisnnisvieshlittffsnskakkdafms iakfevnnpqvqrqafnelirvvhqllpesslrkrkrsrcSGGPGPAGM KGLPGSEVQLVESGGGLVQPGNSLRLSCAASGFTFSKFGMSWVRQAPGK GLEWVSSISGSGRDTLYAESVKGRFTISRDNAKTTLYLQMNSLRPEDTA VYYCTIGGSLSVSSQGTLVTVSSSGGPGPAGMKGLPGShgtviesleslnnyfnssgidveekslfldiwrnwqkdgdmkilqsqiisfylrlfevlk dnqaisnnisvieshlittffsnskakkdafmsiakfevnnpqvqrqaf nelirvvhqllpesslrkrkrsrcSGGPGPAGMKGLPGSEVQLVESGGG LVQPGNSLRLSCAASGFTFSKFGMSWVRQAPGKGLEWVSSISGSGRDTL YAESVKGRFTISRDNAKTTLYLQMNSLRPEDTAVYYCTIGGSLSVSSQG TLVTVSSHHHHHH
96	ACP56	mdmrvpaqllgllllwlrgarcQVQLQESGGGLAQAGGSLSLSCAASGF

[0499]

	小鼠 IFG 融合蛋白	TVSNSVMAWYRQTPGKQREFVAIINSVGSTNYADSVKGRFTISRDNAKN TVYLQMNNLKPEDTAVYVCNRNFDRIYWGQGTQVTVSSggggsggggsg gggsEVQLVESGGGLVQPGNSLRLSCAASGFTFSKFGMSWVRQAPGKGL EWVSSISGSGRDTLYAESVKGRFTISRDNAKTTLYLQMNSLRPEDTAVY YCTIGGSLSVSSQGTLVTVSSSGGPGPAGMKGLPGShgtvieslesln nyfnssgidveekslfldiwrnwqkdgdmkilqsqiisfylrlfevlkdn qaisnnisvieshlittffsnskakkdafmsiakfevnnpqvqrqafne lirvvhqllpesslrkrkrsrcSGGPGPAGMKGLPGSEVQLVESGGGLV QPGNSLRLSCAASGFTFSKFGMSWVRQAPGKGLEWVSSISGSGRDTLYA ESVKGRFTISRDNAKTTLYLQMNSLRPEDTAVYYCTIGGSLSVSSQGTL VTVSSHHHHHHEPEA
97	ACP57 小鼠 IFG 融合蛋白	mdmrvpaqllgllllwlrgarcEVQLVESGGGLVQPGNSLRLSCAASGF TFSKFGMSWVRQAPGKGLEWVSSISGSGRDTLYAESVKGRFTISRDNAK TTLYLQMNSLRPEDTAVYYCTIGGSLSVSSQGTLVTVSSSGGPGPAGMK GLPGShgtviesleslnnyfnssgidveekslfldiwrnwqkdgdmkil qsqiisfylrlfevlkdnqaisnnisvieshlittffsnskakkdafms iakfevnnpqvqrqafnelirvvhqllpesslrkrkrsrcSGGPGPAGM KGLPGSEVQLVESGGGLVQPGNSLRLSCAASGFTFSKFGMSWVRQAPGK GLEWVSSISGSGRDTLYAESVKGRFTISRDNAKTTLYLQMNSLRPEDTA VYYCTIGGSLSVSSQGTLVTVSSggggsggggsggggsQVQLQESGGGL AQAGGSLSLSCAASGFTVSNSVMAWYRQTPGKQREFVAIINSVGSTNYA DSVKGRFTISRDNAKNTVYLQMNNLKPEDTAVYVCNRNFDRIYWGQGTQ VTVSSHHHHHHEPEA
98	ACP58 小鼠 IFG 融合蛋白	mdmrvpaqllgllllwlrgarcEVQLVESGGGLVQPGNSLRLSCAASGF TFSKFGMSWVRQAPGKGLEWVSSISGSGRDTLYAESVKGRFTISRDNAK TTLYLQMNSLRPEDTAVYYCTIGGSLSVSSQGTLVTVSSSGGPGPAGMK GLPGShgtviesleslnnyfnssgidveekslfldiwrnwqkdgdmkil qsqiisfylrlfevlkdnqaisnnisvieshlittffsnskakkdafms iakfevnnpqvqrqafnelirvvhqllpesslrkrkrsrcSGGPGPAGM KGLPGShgtviesleslnnyfnssgidveekslfldiwrnwqkdgdmki lqsqiisfylrlfevlkdnqaisnnisvieshlittffsnskakkdafm siakfevnnpqvqrqafnelirvvhqllpesslrkrkrsrcSGGPGPAG MKGLPGSEVQLVESGGGLVQPGNSLRLSCAASGFTFSKFGMSWVRQAPG KGLEWVSSISGSGRDTLYAESVKGRFTISRDNAKTTLYLQMNSLRPEDT AVYYCTIGGSLSVSSQGTLVTVSSggggsggggsggggsQVQLQESGGG LVQAGGSLRLSCAASGRIFSIDIMSWYRQAPGKQRELVARITRGGTISY

		DDSVKGRFTISRDNAKNTVYLQMNSLKPEDTGVYYCNALYGTDYWGKGT QVTVSSHHHHHHEPEA
99	ACP59 小鼠 IFG 融合蛋 白	mdmrvpaqllgllllwlrgarcQVQLQESGGGLAQAGGSLSLSCAASGF TVSNSVMAWYRQTPGKQREFVAIINSVGSTNYADSVKGRFTISRDNAKN TVYLQMNNLKPEDTAVYVCNRNFDRIYWGQGTQVTVSSggggsggggsg gggsEVQLVESGGGLVQPGNSLRLSCAASGFTFSKFGMSWVRQAPGKGL EWVSSISGSGRDTLYAESVKGRFTISRDNAKTTLYLQMNSLRPEDTAVY YCTIGGSLSVSSQGTLVTVSSSGGPGPAGMKGLPGShgtvieslesln yfnssgidveekslfldiwrnwqkdgdmkilqsqiisfylrlfevlkdn qaisnnisvieshlittffsnskakkdafmsiakfevnnpqvqrqafne lirvvhqllpesslrkrkrsrcSGGPGPAGMKGLPGShgtvieslesln nyfnssgidveekslfldiwrnwqkdgdmkilqsqiisfylrlfevlkd nqaisnnisvieshlittffsnskakkdafmsiakfevnnpqvqrqafn elirvvhqllpesslrkrkrsrcSGGPGPAGMKGLPGSEVQLVESGGGL VQPGNSLRLSCAASGFTFSKFGMSWVRQAPGKGLEWVSSISGSGRDTLY AESVKGRFTISRDNAKTTLYLQMNSLRPEDTAVYYCTIGGSLSVSSQGT LVTVSSHHHHHHEPEA
100	ACP60 小鼠 IFG 融合蛋 白	mdmrvpaqllgllllwlrgarcEVQLVESGGGLVQPGNSLRLSCAASGF TFSKFGMSWVRQAPGKGLEWVSSISGSGRDTLYAESVKGRFTISRDNAK TTLYLQMNSLRPEDTAVYYCTIGGSLSVSSQGTLVTVSSSGGPGPAGMK GLPGShgtviesleslnnyfnssgidveekslfldiwrnwqkdgdmkil qsqiisfylrlfevlkdnqaisnnisvieshlittffsnskakkdafms iakfevnnpqvqrqafnelirvvhqllpesslrkrkrsrcSGGPGPAGM KGLPGShgtviesleslnnyfnssgidveekslfldiwrnwqkdgdmki lqsqiisfylrlfevlkdnqaisnnisvieshlittffsnskakkdafm siakfevnnpqvqrqafnelirvvhqllpesslrkrkrsrcSGGPGPAG MKGLPGSEVQLVESGGGLVQPGNSLRLSCAASGFTFSKFGMSWVRQAPG KGLEWVSSISGSGRDTLYAESVKGRFTISRDNAKTTLYLQMNSLRPEDT AVYYCTIGGSLSVSSQGTLVTVSSggggsggggsggggsQVQLQESGGG LAQAGGSLSLSCAASGFTVSNSVMAWYRQTPGKQREFVAIINSVGSTNY ADSVKGRFTISRDNAKNTVYLQMNNLKPEDTAVYVCNRNFDRIYWGQGT QVTVSSHHHHHHEPEA
101	ACP61 小鼠 IFG 融合蛋 白	mdmrvpaqllgllllwlrgarcEVQLVESGGGLVQPGNSLRLSCAASGF TFSKFGMSWVRQAPGKGLEWVSSISGSGRDTLYAESVKGRFTISRDNAK TTLYLQMNSLRPEDTAVYYCTIGGSLSVSSQGTLVTVSSSGGPGPAGMK GLPGShgtviesleslnnyfnssgidveekslfldiwrnwqkdgdmkil

[0500]

[0501]

		qsqiisfylrlfevlkdnqaisnnisvieshlittffsnskakkdafms iakfevnnpqvqrqafnelirvvhqllpesslrkrkrsrcSGGPGPAGM KGLPGShgtviesleslnnyfnssgidveekslfldiwrnwqkdgdmki lqsqiisfylrlfevlkdnqaisnnisvieshlittffsnskakkdafm siakfevnnpqvqrqafnelirvvhqllpesslrkrkrsrcSGGPGPAG MKGLPGSEVQLVESGGGLVQPGNSLRLSCAASGFTFSKFGMSWVRQAPG KGLEWVSSISGSGRDTLYAESVKGRFTISRDNAKTTLYLQMNSLRPEDT AVYYCTIGGSLSVSSQGTLVTVSSggggsggggsggggsEVQLVESGGG LVQPGGSLRLSCAASGFTFSSYAMSWVRQAPGKGLEWVSAISGSGGSTY YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARGVGAFRPYRK HEWGQGTLVTVSRggggsggggsggggsSSELTQDPAVSVALGQTVRIT CQGDSLRSYYASWYQQKPGQAPVLVIYGKNNRPSGIPDRFSGSSSGNTA SLTTTGAQAEDEADYYCNSSPFEHNLVVFGGGTKLTVLHHHHHHEPEA
102	ACP63 抗 FN CGS-2 scFv	mdmrvpaqllgllllwlrgarcEVQLVESGGGLVQPGGSLRLSCAASGF TFSSYAMSWVRQAPGKGLEWVSAISGSGGSTYYADSVKGRFTISRDNSK NTLYLQMNSLRAEDTAVYYCARGVGAFRPYRKHEWGQGTLVTVSRgggg sggggsggggsSSELTQDPAVSVALGQTVRITCQGDSLRSYYASWYQQK PGQAPVLVIYGKNNRPSGIPDRFSGSSSGNTASLTTTGAQAEDEADYYC NSSPFEHNLVVFGGGTKLTVLHHHHHHEPEA
103	ACP69 小鼠 IFG 融合蛋 白	mdmrvpaqllgllllwlrgarcEVQLVESGGGLVQPGNSLRLSCAASGF TFSKFGMSWVRQAPGKGLEWVSSISGSGRDTLYAESVKGRFTISRDNAK TTLYLQMNSLRPEDTAVYYCTIGGSLSVSSQGTLVTVSSSGGPGPAGMK GLPGShgtviesleslnnyfnssgidveekslfldiwrnwqkdgdmkil qsqiisfylrlfevlkdnqaisnnisvieshlittffsnskakkdafms iakfevnnpqvqrqafnelirvvhqllpesslrkrkrsrcSGGPGPAGM KGLPGSEVQLVESGGGLVQPGNSLRLSCAASGFTFSKFGMSWVRQAPGK GLEWVSSISGSGRDTLYAESVKGRFTISRDNAKTTLYLQMNSLRPEDTA VYYCTIGGSLSVSSQGTLVTVSSSGGPGPAGMKGLPGShgtviesles nnyfnssgidveekslfldiwrnwqkdgdmkilqsqiisfylrlfevlk dnqaisnnisvieshlittffsnskakkdafmsiakfevnnpqvqrqaf nelirvvhqllpesslrkrkrsrcHHHHHHEPEA
104	ACP70 小鼠 IFG 融合蛋 白	mdmrvpaqllgllllwlrgarchgtviesleslnnyfnssgidveeksl fldiwrnwqkdgdmkilqsqiisfylrlfevlkdnqaisnnisvieshl ittffsnskakkdafmsiakfevnnpqvqrqafnelirvvhqllpessl rkrkrsrcSGGPGPAGMKGLPGSEVQLVESGGGLVQPGNSLRLSCAASG FTFSKFGMSWVRQAPGKGLEWVSSISGSGRDTLYAESVKGRFTISRDNA

		KTTLYLQMNSLRPEDTAVYYCTIGGSLSVSSQGTLVTVSSSGGPGPAGM KGLPGShgtviesleslnnyfnssgidveekslfldiwrnwqkdgdmki lqsqiisfylrlfevlkdnqaisnnisvieshlittffsnskakkdafm siakfevnnpqvqrqafnelirvvhqllpesslrkrkrsrcSGGPGPAG MKGLPGSEVQLVESGGGLVQPGNSLRLSCAASGFTFSKFGMSWVRQAPG KGLEWVSSISGSGRDTLYAESVKGRFTISRDNAKTTLYLQMNSLRPEDT AVYYCTIGGSLSVSSQGTLVTVSSHHHHHHEPEA
105	ACP71 小鼠 IFG 融合蛋 白	mdmrvpaqllgllllwlrgarchgtviesleslnnyfnssgidveeksl fldiwrnwqkdgdmkilqsqiisfylrlfevlkdnqaisnnisvieshl ittffsnskakkdafmsiakfevnnpqvqrqafnelirvvhqllpessl rkrkrsrcSGGPGPAGMKGLPGSEAHKSEIAHRYNDLGEQHFKGLVLIA FSQYLQKCSYDEHAKLVQEVTDFAKTCVADESAANCDKSLHTLFGDKLC AIPNLRENYGELADCCTKQEPERNECFLQHKDDNPSLPPFERPEAEAMC TSFKENPTTFMGHYLHEVARRHPYFYAPELLYYAEQYNEILTQCCAEAD KESCLTPKLDGVKEKALVSSVRQRMKCSSMQKFGERAFKAWAVARLSQT FPNADFAEITKLATDLTKVNKECCHGDLLECADDRAELAKYMCENQATI SSKLQTCCDKPLLKKAHCLSEVEHDTMPADLPAIAADFVEDQEVCKNYA EAKDVFLGTFLYEYSRRHPDYSVSLLLRLAKKYEATLEKCCAEANPPAC YGTVLAEFQPLVEEPKNLVKTNCDLYEKLGEYGFQNAILVRYTQKAPQV STPTLVEAARNLGRVGTKCCTLPEDQRLPCVEDYLSAILNRVCLLHEKT PVSEHVTKCCSGSLVERRPCFSALTVDETYVPKEFKAETFTFHSDICTL PEKEKQIKKQTALAELVKHKPKATAEQLKTVMDDFAQFLDTCCKAADKD TCFSTEGPNLVTRCKDALASGGPGPAGMKGLPGShgtviesleslnnyf nssgidveekslfldiwrnwqkdgdmkilqsqiisfylrlfevlkdnqa isnnisvieshlittffsnskakkdafmsiakfevnnpqvqrqafneli rvvhqllpesslrkrkrsrcSGGPGPAGMKGLPGSEAHKSEIAHRYNDL GEQHFKGLVLIAFSQYLQKCSYDEHAKLVQEVTDFAKTCVADESAANCD KSLHTLFGDKLCAIPNLRENYGELADCCTKQEPERNECFLQHKDDNPSL PPFERPEAEAMCTSFKENPTTFMGHYLHEVARRHPYFYAPELLYYAEQY NEILTQCCAEADKESCLTPKLDGVKEKALVSSVRQRMKCSSMQKFGERA FKAWAVARLSQTFPNADFAEITKLATDLTKVNKECCHGDLLECADDRAE LAKYMCENQATISSKLQTCCDKPLLKKAHCLSEVEHDTMPADLPAIAAD FVEDQEVCKNYAEAKDVFLGTFLYEYSRRHPDYSVSLLLRLAKKYEATL EKCCAEANPPACYGTVLAEFQPLVEEPKNLVKTNCDLYEKLGEYGFQNA ILVRYTQKAPQVSTPTLVEAARNLGRVGTKCCTLPEDQRLPCVEDYLSA ILNRVCLLHEKTPVSEHVTKCCSGSLVERRPCFSALTVDETYVPKEFKA

[0502]

[0503]

		ETFTFHSDICTLPEKEKQIKKQTALAELVKHKPKATAEQLKTVMDDFAQ FLDTCCKAADKDTCFSTEGPNLVTRCKDALAHHHHHHEPEA
106	ACP72 小鼠 IFG 融合蛋 白	mdmrvpaqllgllllwlrgarcEAHKSEIAHRYNDLGEQHFKGLVLIAF SQYLQKCSYDEHAKLVQEVTDFAKTCVADESAANCDKSLHTLFGDKLCA IPNLRENYGELADCCTKQEPERNECFLQHKDDNPSLPPFERPEAEAMCT SFKENPTTFMGHYLHEVARRHPYFYAPELLYYAEQYNEILTQCCAEADK ESCLTPKLDGVKEKALVSSVRQRMKCSSMQKFGERAFKAWAVARLSQTF PNADFAEITKLATDLTKVNKECCHGDLLECADDRAELAKYMCENQATIS SKLQTCCDKPLLKKAHCLSEVEHDTMPADLPAIAADFVEDQEVCKNYAE AKDVFLGTFLYEYSRRHPDYSVSLLLRLAKKYEATLEKCCAEANPPACY GTVLAEFQPLVEEPKNLVKTNCDLYEKLGEYGFQNAILVRYTQKAPQVS TPTLVEAARNLGRVGTKCCTLPEDQRLPCVEDYLSAILNRVCLLHEKTP VSEHVTKCCSGSLVERRPCFSALTVDETYVPKEFKAETFTFHSDICTLP EKEKQIKKQTALAELVKHKPKATAEQLKTVMDDFAQFLDTCCKAADKDT CFSTEGPNLVTRCKDALASGGPGPAGMKGLPGShgtviesleslnnyfn ssgidveekslfldiwrnwqkdgdmkilqsqiisfylrlfevlkdnqai snnisvieshlittffsnskakkdafmsiakfevnnpqvqrqafnelir vvhqllpesslrkrkrsrcSGGPGPAGMKGLPGSEAHKSEIAHRYNDLG EQHFKGLVLIAFSQYLQKCSYDEHAKLVQEVTDFAKTCVADESAANCDK SLHTLFGDKLCAIPNLRENYGELADCCTKQEPERNECFLQHKDDNPSLP PFERPEAEAMCTSFKENPTTFMGHYLHEVARRHPYFYAPELLYYAEQYN EILTQCCAEADKESCLTPKLDGVKEKALVSSVRQRMKCSSMQKFGERAF KAWAVARLSQTFPNADFAEITKLATDLTKVNKECCHGDLLECADDRAEL AKYMCENQATISSKLQTCCDKPLLKKAHCLSEVEHDTMPADLPAIAADF VEDQEVCKNYAEAKDVFLGTFLYEYSRRHPDYSVSLLLRLAKKYEATLE KCCAEANPPACYGTVLAEFQPLVEEPKNLVKTNCDLYEKLGEYGFQNAI LVRYTQKAPQVSTPTLVEAARNLGRVGTKCCTLPEDQRLPCVEDYLSAI LNRVCLLHEKTPVSEHVTKCCSGSLVERRPCFSALTVDETYVPKEFKAE TFTFHSDICTLPEKEKQIKKQTALAELVKHKPKATAEQLKTVMDDFAQF LDTCCKAADKDTCFSTEGPNLVTRCKDALASGGPGPAGMKGLPGShgtv iesleslnnyfnssgidveekslfldiwrnwqkdgdmkilqsqiisfyl rlfevlkdnqaisnnisvieshlittffsnskakkdafmsiakfevnnp qvqrqafnelirvvhqllpesslrkrkrsrcHHHHHHHEPEA
107	ACP73 小鼠 IFG 融合蛋	mdmrvpaqllgllllwlrgarcEAHKSEIAHRYNDLGEQHFKGLVLIAF SQYLQKCSYDEHAKLVQEVTDFAKTCVADESAANCDKSLHTLFGDKLCA IPNLRENYGELADCCTKQEPERNECFLQHKDDNPSLPPFERPEAEAMCT

[0504]

	白	SFKENPTTFMGHYLHEVARRHPYFYAPELLYYAEQYNEILTQCCAEADK ESCLTPKLDGVKEKALVSSVRQRMKCSSMQKFGERAFKAWAVARLSQTF PNADFAEITKLATDLTKVNKECCHGDLLECADDRAELAKYMCENQATIS SKLQTCCDKPLLKKAHCLSEVEHDTMPADLPAIAADFVEDQEVCKNYAE AKDVFLGTFLYEYSRRHPDYSVSLLLRLAKKYEATLEKCCAEANPPACY GTVLAEFQPLVEEPKNLVKTNCDLYEKLGEYGFQNAILVRYTQKAPQVS TPTLVEAARNLGRVGTKCCTLPEDQRLPCVEDYLSAILNRVCLLHEKTP VSEHVTKCCSGSLVERRPCFSALTVDETYVPKEFKAETFTFHSDICTLP EKEKQIKKQTALAELVKHKPKATAEQLKTVMDDFAQFLDTCCKAADKDT CFSTEGPNLVTRCKDALASGGPGPAGMKGLPGShgtviesleslnnyfn ssgidveekslfldiwrnwqkdgdmkilqsqiisfylrlfevlkdnqai snnisvieshlittffsnskakkdafmsiakfevnnpqvqrqafnelir vvhqllpesslrkrkrsrcSGGPGPAGMKGLPGSEAHKSEIAHRYNDLG EQHFKGLVLIAFSQYLQKCSYDEHAKLVQEVTDFAKTCVADESAANCDK SLHTLFGDKLCAIPNLRENYGELADCCTKQEPERNECFLQHKDDNPSLP PFERPEAEAMCTSFKENPTTFMGHYLHEVARRHPYFYAPELLYYAEQYN EILTQCCAEADKESCLTPKLDGVKEKALVSSVRQRMKCSSMQKFGERAF KAWAVARLSQTFPNADFAEITKLATDLTKVNKECCHGDLLECADDRAEL AKYMCENQATISSKLQTCCDKPLLKKAHCLSEVEHDTMPADLPAIAADF VEDQEVCKNYAEAKDVFLGTFLYEYSRRHPDYSVSLLLRLAKKYEATLE KCCAEANPPACYGTVLAEFQPLVEEPKNLVKTNCDLYEKLGEYGFQNAI LVRYTQKAPQVSTPTLVEAARNLGRVGTKCCTLPEDQRLPCVEDYLSAI LNRVCLLHEKTPVSEHVTKCCSGSLVERRPCFSALTVDETYVPKEFKAE TFTFHSDICTLPEKEKQIKKQTALAELVKHKPKATAEQLKTVMDDFAQF LDTCCKAADKDTCFSTEGPNLVTRCKDALASGGPGPAGMKGLPGShgtv iesleslnnyfnssgidveekslfldiwrnwqkdgdmkilqsqiisfyl rlfevlkdnqaisnnisvieshlittffsnskakkdafmsiakfevnnp qvqrqafnelirvvhqllpesslrkrkrsrcSGGPGPAGMKGLPGSEAH KSEIAHRYNDLGEQHFKGLVLIAFSQYLQKCSYDEHAKLVQEVTDFAKT CVADESAANCDKSLHTLFGDKLCAIPNLRENYGELADCCTKQEPERNEC FLQHKDDNPSLPPFERPEAEAMCTSFKENPTTFMGHYLHEVARRHPYFY APELLYYAEQYNEILTQCCAEADKESCLTPKLDGVKEKALVSSVRQRMK CSSMQKFGERAFKAWAVARLSQTFPNADFAEITKLATDLTKVNKECCHG DLLECADDRAELAKYMCENQATISSKLQTCCDKPLLKKAHCLSEVEHDT MPADLPAIAADFVEDQEVCKNYAEAKDVFLGTFLYEYSRRHPDYSVSLL LRLAKKYEATLEKCCAEANPPACYGTVLAEFQPLVEEPKNLVKTNCDLY

[0505]

		EKLGEYGFQNAILVRYTQKAPQVSTPTLVEAARNLGRVGTKCCTLPEDQ RLPCVEDYLSAILNRVCLLHEKTPVSEHVTKCCSGSLVERRPCFSALTV DETYVPKEFKAETFTFHSDICTLPEKEKQIKKQTALAELVKHKPKATAE QLKTVMDDFAQFLDTCCKAADKDTCFSTEGPNLVTRCKDALAHHHHHHE PEA
108	ACP74 小鼠 IFG 融合蛋 白	mdmrvpaqllgllllwlrgarcEAHKSEIAHRYNDLGEQHFKGLVLIAF SQYLQKCSYDEHAKLVQEVTDFAKTCVADESAANCDKSLHTLFGDKLCA IPNLRENYGELADCCTKQEPERNECFLQHKDDNPSLPPFERPEAEAMCT SFKENPTTFMGHYLHEVARRHPYFYAPELLYYAEQYNEILTQCCAEADK ESCLTPKLDGVKEKALVSSVRQRMKCSSMQKFGERAFKAWAVARLSQTF PNADFAEITKLATDLTKVNKECCHGDLLECADDRAELAKYMCENQATIS SKLQTCCDKPLLKKAHCLSEVEHDTMPADLPAIAADFVEDQEVCKNYAE AKDVFLGTFLYEYSRRHPDYSVSLLLRLAKKYEATLEKCCAEANPPACY GTVLAEFQPLVEEPKNLVKTNCDLYEKLGEYGFQNAILVRYTQKAPQVS TPTLVEAARNLGRVGTKCCTLPEDQRLPCVEDYLSAILNRVCLLHEKTP VSEHVTKCCSGSLVERRPCFSALTVDETYVPKEFKAETFTFHSDICTLP EKEKQIKKQTALAELVKHKPKATAEQLKTVMDDFAQFLDTCCKAADKDT CFSTEGPNLVTRCKDALASGGPGPAGMKGLPGShgtviesleslnnyfn ssgidveekslfldiwrnwqkdgdmkilqsqiisfylrlfevlkdnqai snnisvieshlittffsnskakkdafmsiakfevnnpqvqrqafnelir vvhqllpesslrkrkrsrcSGGPGPAGMKGLPGSggggsEAHKSEIAHR YNDLGEQHFKGLVLIAFSQYLQKCSYDEHAKLVQEVTDFAKTCVADESA ANCDKSLHTLFGDKLCAIPNLRENYGELADCCTKQEPERNECFLQHKDD NPSLPPFERPEAEAMCTSFKENPTTFMGHYLHEVARRHPYFYAPELLYY AEQYNEILTQCCAEADKESCLTPKLDGVKEKALVSSVRQRMKCSSMQKF GERAFKAWAVARLSQTFPNADFAEITKLATDLTKVNKECCHGDLLECAD DRAELAKYMCENQATISSKLQTCCDKPLLKKAHCLSEVEHDTMPADLPA IAADFVEDQEVCKNYAEAKDVFLGTFLYEYSRRHPDYSVSLLLRLAKKY EATLEKCCAEANPPACYGTVLAEFQPLVEEPKNLVKTNCDLYEKLGEYG FQNAILVRYTQKAPQVSTPTLVEAARNLGRVGTKCCTLPEDQRLPCVED YLSAILNRVCLLHEKTPVSEHVTKCCSGSLVERRPCFSALTVDETYVPK EFKAETFTFHSDICTLPEKEKQIKKQTALAELVKHKPKATAEQLKTVMD DFAQFLDTCCKAADKDTCFSTEGPNLVTRCKDALAggggsSGGPGPAGM KGLPGShgtviesleslnnyfnssgidveekslfldiwrnwqkdgdmki lqsqiisfylrlfevlkdnqaisnnisvieshlittffsnskakkdafm siakfevnnpqvqrqafnelirvvhqllpesslrkrkrsrcSGGPGPAG

		MKGLPGSEAHKSEIAHRYNDLGEQHFKGLVLIAFSQYLQKCSYDEHAKL VQEVTDFAKTCVADESAANCDKSLHTLFGDKLCAIPNLRENYGELADCC TKQEPERNECFLQHKDDNPSLPPFERPEAEAMCTSFKENPTTFMGHYLH EVARRHPYFYAPELLYYAEQYNEILTQCCAEADKESCLTPKLDGVKEKA LVSSVRQRMKCSSMQKFGERAFKAWAVARLSQTFPNADFAEITKLATDL TKVNKECCHGDLLECADDRAELAKYMCENQATISSKLQTCCDKPLLKKA HCLSEVEHDTMPADLPAIAADFVEDQEVCKNYAEAKDVFLGTFLYEYSR RHPDYSVSLLLRLAKKYEATLEKCCAEANPPACYGTVLAEFQPLVEEPK NLVKTNCDLYEKLGEYGFQNAILVRYTQKAPQVSTPTLVEAARNLGRVG TKCCTLPEDQRLPCVEDYLSAILNRVCLLHEKTPVSEHVTKCCSGSLVE RRPCFSALTVDETYVPKEFKAETFTFHSDICTLPEKEKQIKKQTALAEL VKHKPKATAEQLKTVMDDFAQFLDTCCKAADKDTCFSTEGPNLVTRCKD ALAHHHHHHEPEA
109	ACP75 小鼠 IFG 融合蛋 白	mdmrvpaqllgllllwlrgarcEAHKSEIAHRYNDLGEQHFKGLVLIAF SQYLQKCSYDEHAKLVQEVTDFAKTCVADESAANCDKSLHTLFGDKLCA IPNLRENYGELADCCTKQEPERNECFLQHKDDNPSLPPFERPEAEAMCT SFKENPTTFMGHYLHEVARRHPYFYAPELLYYAEQYNEILTQCCAEADK ESCLTPKLDGVKEKALVSSVRQRMKCSSMQKFGERAFKAWAVARLSQTF PNADFAEITKLATDLTKVNKECCHGDLLECADDRAELAKYMCENQATIS SKLQTCCDKPLLKKAHCLSEVEHDTMPADLPAIAADFVEDQEVCKNYAE AKDVFLGTFLYEYSRRHPDYSVSLLLRLAKKYEATLEKCCAEANPPACY GTVLAEFQPLVEEPKNLVKTNCDLYEKLGEYGFQNAILVRYTQKAPQVS TPTLVEAARNLGRVGTKCCTLPEDQRLPCVEDYLSAILNRVCLLHEKTP VSEHVTKCCSGSLVERRPCFSALTVDETYVPKEFKAETFTFHSDICTLP EKEKQIKKQTALAELVKHKPKATAEQLKTVMDDFAQFLDTCCKAADKDT CFSTEGPNLVTRCKDALASGGPGPAGMKGLPGShgtviesleslnnyfn ssgidveekslfldiwrnwqkdgdmkilqsqiisfylrlfevlkdnqai snnisvieshlittffsnskakkdafmsiakfevnnpqvqrqafnelir vvhqllpesslrkrkrsrcSGGPGPAGMKGLPGSggggsggggsEAHKS EIAHRYNDLGEQHFKGLVLIAFSQYLQKCSYDEHAKLVQEVTDFAKTCV ADESAANCDKSLHTLFGDKLCAIPNLRENYGELADCCTKQEPERNECFL QHKDDNPSLPPFERPEAEAMCTSFKENPTTFMGHYLHEVARRHPYFYAP ELLYYAEQYNEILTQCCAEADKESCLTPKLDGVKEKALVSSVRQRMKCS SMQKFGERAFKAWAVARLSQTFPNADFAEITKLATDLTKVNKECCHGDL LECADDRAELAKYMCENQATISSKLQTCCDKPLLKKAHCLSEVEHDTMP ADLPAIAADFVEDQEVCKNYAEAKDVFLGTFLYEYSRRHPDYSVSLLLR

[0506]

[0507]

		LAKKYEATLEKCCAEANPPACYGTVLAEFQPLVEEPKNLVKTNCDLYEK LGEYGFQNAILVRYTQKAPQVSTPTLVEAARNLGRVGTKCCTLPEDQRL PCVEDYLSAILNRVCLLHEKTPVSEHVTKCCSGSLVERRPCFSALTVDE TYVPKEFKAETFTFHSDICTLPEKEKQIKKQTALAELVKHKPKATAEQL KTVMDDFAQFLDTCCKAADKDTCFSTEGPNLVTRCKDALAggggsgggg sSGGPGPAGMKGLPGShgtviesleslnnyfnssgidveekslfldiwr nwqkdgdmkilqsqiisfylrlfevlkdnqaisnnisvieshlittffs nskakkdafmsiakfevnnpqvqrqafnelirvvhqllpesslrkrkrs rcSGGPGPAGMKGLPGSEAHKSEIAHRYNDLGEQHFKGLVLIAFSQYLQ KCSYDEHAKLVQEVTDFAKTCVADESAANCDKSLHTLFGDKLCAIPNLR ENYGELADCCTKQEPERNECFLQHKDDNPSLPPFERPEAEAMCTSFKEN PTTFMGHYLHEVARRHPYFYAPELLYYAEQYNEILTQCCAEADKESCLT PKLDGVKEKALVSSVRQRMKCSSMQKFGERAFKAWAVARLSQTFPNADF AEITKLATDLTKVNKECCHGDLLECADDRAELAKYMCENQATISSKLQT CCDKPLLKKAHCLSEVEHDTMPADLPAIAADFVEDQEVCKNYAEAKDVF LGTFLYEYSRRHPDYSVSLLLRLAKKYEATLEKCCAEANPPACYGTVLA EFQPLVEEPKNLVKTNCDLYEKLGEYGFQNAILVRYTQKAPQVSTPTLV EAARNLGRVGTKCCTLPEDQRLPCVEDYLSAILNRVCLLHEKTPVSEHV TKCCSGSLVERRPCFSALTVDETYVPKEFKAETFTFHSDICTLPEKEKQ IKKQTALAELVKHKPKATAEQLKTVMDDFAQFLDTCCKAADKDTCFSTE GPNLVTRCKDALAHHHHHHHEPEA
110	ACP78 小鼠 IFG 融合蛋 白	mdmrvpaqllgllllwlrgarcEVQLVESGGGLVQPGNSLRLSCAASGF TFSKFGMSWVRQAPGKGLEWVSSISGSGRDTLYAESVKGRFTISRDNAK TTLYLQMNSLRPEDTAVYYCTIGGSLSVSSQGTLVTVSSggggsggggs ggggshgtviesleslnnyfnssgidveekslfldiwrnwqkdgdmkil qsqiisfylrlfevlkdnqaisnnisvieshlittffsnskakkdafms iakfevnnpqvqrqafnelirvvhqllpesslrkrkrsrcggggsgggg sggggsEVQLVESGGGLVQPGNSLRLSCAASGFTFSKFGMSWVRQAPGK GLEWVSSISGSGRDTLYAESVKGRFTISRDNAKTTLYLQMNSLRPEDTA VYYCTIGGSLSVSSQGTLVTVSSggggsggggsggggshgtviesles nnyfnssgidveekslfldiwrnwqkdgdmkilqsqiisfylrlfevlk dnqaisnnisvieshlittffsnskakkdafmsiakfevnnpqvqrqaf nelirvvhqllpesslrkrkrsrcggggsggggsggggsEVQLVESGGG LVQPGNSLRLSCAASGFTFSKFGMSWVRQAPGKGLEWVSSISGSGRDTL YAESVKGRFTISRDNAKTTLYLQMNSLRPEDTAVYYCTIGGSLSVSSQG TLVTVSSHHHHHHHEPEA

[0508]

111	ACP134 小鼠 IFG 融合蛋 白	mdmrvpaqllgllllwlrgarcEVQLVESGGGLVQPGNSLRLSCAASGF TFSKFGMSWVRQAPGKGLEWVSSISGSGRDTLYAESVKGRFTISRDNAK TTLYLQMNSLRPEDTAVYYCTIGGSLSVSSQGTLVTVSSSGGPGPAGMK GLPGShgtviesleslnnyfnssgidveekslfldiwrnwqkdgdmkil qsqiisfylrlfevlkdnqaisnnisvieshlittffsnskakkdafms iakfevnnpqvqrqafnelirvvhqllpesslrkrkrsrcSGGPGPAGM KGLPGSEVQLVESGGGLVQPGNSLRLSCAASGFTFSKFGMSWVRQAPGK GLEWVSSISGSGRDTLYAESVKGRFTISRDNAKTTLYLQMNSLRPEDTA VYYCTIGGSLSVSSQGTLVTVSSSGGPGPAGMKGLPGShgtviesles l nnyfnssgidveekslfldiwrnwqkdgdmkilqsqiisfylrlfevlk dnqaisnnisvieshlittffsnskakkdafmsiakfevnnpqvqrqaf nelirvvhqllpesslrkrkrsrcSGGPGPAGMKGLPGSEVQLVESGGG LVQPGNSLRLSCAASGFTFSKFGMSWVRQAPGKGLEWVSSISGSGRDTL YAESVKGRFTISRDNAKTTLYLQMNSLRPEDTAVYYCTIGGSLSVSSQG TLVTVSSggggsggggsggggsQVQLQESGGGLAQAGGSLSLSCAASGF TVSNSVMAWYRQTPGKQREFVAIINSVGSTNYADSVKGRFTISRDNAKN TVYLQMNNLKPEDTAVYVCNRNFDRIYWGQGTQVTVSSHHHHHHEPEA
112	ACP135 小鼠 IFG 融合蛋 白	mdmrvpaqllgllllwlrgarcQVQLQESGGGLAQAGGSLSLSCAASGF TVSNSVMAWYRQTPGKQREFVAIINSVGSTNYADSVKGRFTISRDNAKN TVYLQMNNLKPEDTAVYVCNRNFDRIYWGQGTQVTVSSggggsggggsg gggsEVQLVESGGGLVQPGNSLRLSCAASGFTFSKFGMSWVRQAPGKGL EWVSSISGSGRDTLYAESVKGRFTISRDNAKTTLYLQMNSLRPEDTAVY YCTIGGSLSVSSQGTLVTVSSSGGPGPAGMKGLPGShgtviesleslnn yfnssgidveekslfldiwrnwqkdgdmkilqsqiisfylrlfevlkdn qaisnnisvieshlittffsnskakkdafmsiakfevnnpqvqrqafne lirvvhqllpesslrkrkrsrcSGGPGPAGMKGLPGSEVQLVESGGGLV QPGNSLRLSCAASGFTFSKFGMSWVRQAPGKGLEWVSSISGSGRDTLYA ESVKGRFTISRDNAKTTLYLQMNSLRPEDTAVYYCTIGGSLSVSSQGTL VTVSSSGGPGPAGMKGLPGShgtviesleslnnyfnssgidveekslfl diwrnwqkdgdmkilqsqiisfylrlfevlkdnqaisnnisvieshlit tffsnskakkdafmsiakfevnnpqvqrqafnelirvvhqllpesslrk rkrsrcSGGPGPAGMKGLPGSEVQLVESGGGLVQPGNSLRLSCAASGFT FSKFGMSWVRQAPGKGLEWVSSISGSGRDTLYAESVKGRFTISRDNAKT TLYLQMNSLRPEDTAVYYCTIGGSLSVSSQGTLVTVSSHHHHHHEPEA
113	ACP34 小鼠	mdmrvpaqllgllllwlrgarcrvipvsgparclsqsrnllkttddmvk tareklkhysctaedidheditrdqtstlktclplelhknesclatret

[0509]

	IL-12 融合蛋白	ssttrgsclppqktslmmtlclgsiyedlkmyqtefqainaalqnhnhq qiildkgmlvaidelmqslnhngetlrqkppvgeadpyrvkmklcillh afstrvvtinrvmgylssaSGGPGPAGMKGLPGSmwelekdvyvvevdw tpdapgetvnltcdtpeedditwtsdqrhgvigsgktltitvkefldag qytchkggetlshshlllhkkengiwsteilknfknktflkceapnysg rftcswlvqrnmdlkfnikssssspdsravtcgmaslsaekvtldqrdy ekysvscqedvtcptaeetlpielalearqqnkyenystsffirdiikp dppknlqmkplknsqvevsweypdswstphsyfslkffvriqrkkekmk eteegcnqkgaflvektstevqckggnvcvqaqdryynsscskwacvpc rvrsHHHHHH
114	ACP35 小鼠 IL-12 融合蛋白	mdmrvpaqllgllllwlrgarcrvipvsgparclsqsrnllkttddmvk tareklkhysctaedidheditrdqtstlktclplelhknesclatret ssttrgsclppqktslmmtlclgsiyedlkmyqtefqainaalqnhnhq qiildkgmlvaidelmqslnhngetlrqkppvgeadpyrvkmklcillh afstrvvtinrvmgylssaggggsggggsggggsSGGPGPAGMKGLPGS ggggsggggsggggsmwelekdvyvvevdwtpdapgetvnltcdtpeed ditwtsdqrhgvigsgktltitvkefldagqytchkggetlshshlllh kkengiwsteilknfknktflkceapnysgrftcswlvqrnmdlkfnik sssssspdsravtcgmaslsaekvtldqrdyekysvscqedvtcptaeet lpielalearqqnkyenystsffirdiikpdppknlqmkplknsqvevs weypdswstphsyfslkffvriqrkkekmketeegcnqkgaflvektst evqckggnvcvqaqdryynsscskwacvpcrvrsHHHHHH
115	ACP36 小鼠 IL-12 融合蛋白	mdmrvpaqllgllllwlrgarcEVQLVESGGGLVQPGNSLRLSCAASGF TFSKFGMSWVRQAPGKGLEWVSSISGSGRDTLYAESVKGRFTISRDNAK TTLYLQMNSLRPEDTAVYYCTIGGSLSVSSQGTLVTVSSSGGPGPAGMK GLPGSmwelekdvyvvevdwtpdapgetvnltcdtpeedditwtsdqrh gvigsgktltitvkefldagqytchkggetlshshlllhkkengiwste ilknfknktflkceapnysgrftcswlvqrnmdlkfnikssssspdsra vtcgmaslsaekvtldqrdyekysvscqedvtcptaeetlpielalear qqnkyenystsffirdiikpdppknlqmkplknsqvevsweypdswstp hsyfslkffvriqrkkekmketeegcnqkgaflvektstevqckggnvc vqaqdryynsscskwacvpcrvrsggggsggggsggggsrvipvsgpar clsqsrnllkttddmvktareklkhysctaedidheditrdqtstlktc lplelhknesclatretssttrgsclppqktslmmtlclgsiyedlkmy qtefqainaalqnhnhqqiildkgmlvaidelmqslnhngetlrqkppv geadpyrvkmklcillhafstrvvtinrvmgylssaSGGPGPAGMKGLP

[0510]

		GSEVQLVESGGGLVQPGNSLRLSCAASGFTFSKFGMSWVRQAPGKGLEW VSSISGSGRDTLYAESVKGRFTISRDNAKTTLYLQMNSLRPEDTAVYYC TIGGSLSVSSQGTLVTVSSHHHHHH
116	ACP37 小鼠 IL-12 融合蛋白	mdmrvpaqllgllllwlrgarcQVQLQESGGGLVQAGGSLRLSCAASGR IFSIDIMSWYRQAPGKQRELVARITRGGTISYDDSVKGRFTISRDNAKN TVYLQMNSLKPEDTGVYYCNALYGTDYWGKGTQVTVSSggggsggggsg gggsEVQLVESGGGLVQPGNSLRLSCAASGFTFSKFGMSWVRQAPGKGL EWVSSISGSGRDTLYAESVKGRFTISRDNAKTTLYLQMNSLRPEDTAVY YCTIGGSLSVSSQGTLVTVSSSGGPGPAGMKGLPGSmwelekdvyvvev dwtpdapgetvnltcdtpeedditwtsdqrhgvigsgktltitvkefld agqytchkggetlshshlllhkkengiwsteilknfknktflkceapny sgrftcswlvqrnmdlkfnikssssspdsravtcgmaslsaekvtldqr dyekysvscqedvtcptaeetlpielalearqqnkyenystsffirdii kpdppknlqmkplknsqvevsweypdswstphsyfslkffvriqrkkek mketeegcnqkgaflvektstevqckggnvcvqaqdryynsscskwacv pcrvrsggggsggggsggggsrvipvsgparclsqsrnllkttddmvkt areklkhysctaedidheditrdqtstlktclplelhknesclatrets sttrgsclppqktslmmtlclgsiyedlkmyqtefqainaalqnhnhqq iildkgmlvaidelmqslnhngetlrqkppvgeadpyrvkmklcillha fstrvvtinrvmgylssaSGGPGPAGMKGLPGSEVQLVESGGGLVQPGN SLRLSCAASGFTFSKFGMSWVRQAPGKGLEWVSSISGSGRDTLYAESVK GRFTISRDNAKTTLYLQMNSLRPEDTAVYYCTIGGSLSVSSQGTLVTVS SHHHHHH
117	ACP79 小鼠 IL-12 融合蛋白	mdmrvpaqllgllllwlrgarcQVQLQESGGGLVQAGGSLRLSCAASGR IFSIDIMSWYRQAPGKQRELVARITRGGTISYDDSVKGRFTISRDNAKN TVYLQMNSLKPEDTGVYYCNALYGTDYWGKGTQVTVSSggggsggggsg gggsEVQLVESGGGLVQPGNSLRLSCAASGFTFSKFGMSWVRQAPGKGL EWVSSISGSGRDTLYAESVKGRFTISRDNAKTTLYLQMNSLRPEDTAVY YCTIGGSLSVSSQGTLVTVSSSGGPGPAGMKGLPGSmwelekdvyvvev dwtpdapgetvnltcdtpeedditwtsdqrhgvigsgktltitvkefld agqytchkggetlshshlllhkkengiwsteilknfknktflkceapny sgrftcswlvqrnmdlkfnikssssspdsravtcgmaslsaekvtldqr dyekysvscqedvtcptaeetlpielalearqqnkyenystsffirdii kpdppknlqmkplknsqvevsweypdswstphsyfslkffvriqrkkek mketeegcnqkgaflvektstevqckggnvcvqaqdryynsscskwacv pcrvrsggggsggggsggggsrvipvsgparclsqsrnllkttddmvkt

[0511]

		areklkhysctaedidheditrdqtstlktclplelhknesclatrets sttrgsclppqktslmmtlclgsiyedlkmyqtefqainaalqnhnhqq iildkgmlvaidelmqslnhngetlrqkppvgeadpyrvkmklcillha fstrvvtinrvmgylssaSGGPGPAGMKGLPGSEVQLVESGGGLVQPGN SLRLSCAASGFTFSKFGMSWVRQAPGKGLEWVSSISGSGRDTLYAESVK GRFTISRDNAKTTLYLQMNSLRPEDTAVYYCTIGGSLSVSSQGTLVTVS SHHHHHH
118	ACP80 小鼠 IL-12 融合蛋白	mdmrvpaqllgllllwlrgarcEVQLVESGGGLVQPGNSLRLSCAASGF TFSKFGMSWVRQAPGKGLEWVSSISGSGRDTLYAESVKGRFTISRDNAK TTLYLQMNSLRPEDTAVYYCTIGGSLSVSSQGTLVTVSSSGGPGPAGMK GLPGSmwelekdvyvvevdwtpdapgetvnltcdtpeedditwtsdqrh gvigsgktltitvkefldagqytchkggetlshshlllhkkengiwste ilknfknktflkceapnysgrftcswlvqrnmdlkfnikssssspdsra vtcgmaslsaekvtldqrdyekysvscqedvtcptaeetlpielalear qqnkyenystsffirdiikpdppknlqmkplknsqvevsweypdswstp hsyfslkffvriqrkkekmketeegcnqkgaflvektstevqckggnvc vqaqdryynsscskwacvpcrvrsggggsggggsggggsrvipvsgpar clsqsrnllkttddmvktareklkhysctaedidheditrdqtstlktc lplelhknesclatretssttrgsclppqktslmmtlclgsiyedlkmy qtefqainaalqnhnhqqiildkgmlvaidelmqslnhngetlrqkppv geadpyrvkmklcillhafstrvvtinrvmgylssaSGGPGPAGMKGLP GSEVQLVESGGGLVQPGNSLRLSCAASGFTFSKFGMSWVRQAPGKGLEW VSSISGSGRDTLYAESVKGRFTISRDNAKTTLYLQMNSLRPEDTAVYYC TIGGSLSVSSQGTLVTVSSggggsggggsggggsQVQLQESGGGLVQAG GSLRLSCAASGRIFSIDIMSWYRQAPGKQRELVARITRGGTISYDDSVK GRFTISRDNAKNTVYLQMNSLKPEDTGVYYCNALYGTDYWGKGTQVTVS SHHHHHH
119	ACP91 嵌合 IL-12 融合蛋白	mdmrvpaqllgllllwlrgarciwelkkdvyvveldwypdapgemvvlt cdtpeedgitwtldqssevlgsgktltiqvkefgdagqytchkggevls hslllhkkedgiwstdilkdqkepknktflrceaknysgrftcwwltt istdltfsvkssrgssdpqgvtcgaatlsaervrgdnkeyeysvecqed sacpaaeeslpievmvdavhklkyenytssffirdiikpdppknlqlkp lknsrqvevsweypdtwstphsyfsltfcvqvqgkskrekkdrvftdkt satvicrknasisvraqdryyssswsewasvpcsggggsggggsggggs rvipvsgparclsqsrnllkttddmvktareklkhysctaedidhedit rdqtstlktclplelhknesclatretssttrgsclppqktslmmtlcl

[0512]

		gsiyedlkmyqtefqainaalqnhnhqqiildkgmlvaidelmqslnhn getlrqkppvgeadpyrvkmklcillhafstrvvtinrvmgylssaggg gsggggsggggsggggsggggsggggsggggsggggsQSVLTQP PSVSGAPGQRVTISCSGSRSNIGSNTVKWYQQLPGTAPKLLIYYNDQRP SGVPDRFSGSKSGTSASLAITGLQAEDEADYYCQSYDRYTHPALLFGTG TKVTVLggggsggggsggggsQVQLVESGGGVVQPGRSLRLSCAASGFT FSSYGMHWVRQAPGKGLEWVAFIRYDGSNKYYADSVKGRFTISRDNSKN TLYLQMNSLRAEDTAVYYCKTHGSHDNWGQGTMVTVSSggggsggggsg gggsEVQLVESGGGLVQPGNSLRLSCAASGFTFSKFGMSWVRQAPGKGL EWVSSISGSGRDTLYAESVKGRFTISRDNAKTTLYLQMNSLRPEDTAVY YCTIGGSLSVSSQGTLVTVSSHHHHHHHEPEA
120	ACP136 嵌合 IL-12 融 合蛋白	mdmrvpaqllgllllwlrgarciwelkkdvyvveldwypdapgemvvlt cdtpeedgitwtldqssevlgsgktltiqvkefgdagqytchkggevls hslllhkkedgiwstdilkdqkepknktflrceaknysgrftcwwltt istdltfsvkssrgssdpqgvtcgaatlsaervrgdnkeyeysvecqed sacpaaeeslpievmvdavhklkyenytssffirdiikpdppknlqlkp lknsrqvevsweypdtwstphsyfsltfcvqvqgkskrekkdrvftdkt satvicrknasisvraqdryyssswsewasvpcsggggsggggsggggs rvipvsgparclsqsrnllkttddmvktareklkhysctaedidhedit rdqtstlktclplelhknesclatretssttrgsclppqktslmmtlcl gsiyedlkmyqtefqainaalqnhnhqqiildkgmlvaidelmqslnhn getlrqkppvgeadpyrvkmklcillhafstrvvtinrvmgylssaSGG PGPAGMKGLPGSggggsggggsggggsggggsggggsggggsQSVLTQP PSVSGAPGQRVTISCSGSRSNIGSNTVKWYQQLPGTAPKLLIYYNDQRP SGVPDRFSGSKSGTSASLAITGLQAEDEADYYCQSYDRYTHPALLFGTG TKVTVLggggsggggsggggsQVQLVESGGGVVQPGRSLRLSCAASGFT FSSYGMHWVRQAPGKGLEWVAFIRYDGSNKYYADSVKGRFTISRDNSKN TLYLQMNSLRAEDTAVYYCKTHGSHDNWGQGTMVTVSSHHHHHHHEPEA
121	ACP138 嵌合 IL-12 融 合蛋白	mdmrvpaqllgllllwlrgarciwelkkdvyvveldwypdapgemvvlt cdtpeedgitwtldqssevlgsgktltiqvkefgdagqytchkggevls hslllhkkedgiwstdilkdqkepknktflrceaknysgrftcwwltt istdltfsvkssrgssdpqgvtcgaatlsaervrgdnkeyeysvecqed sacpaaeeslpievmvdavhklkyenytssffirdiikpdppknlqlkp lknsrqvevsweypdtwstphsyfsltfcvqvqgkskrekkdrvftdkt satvicrknasisvraqdryyssswsewasvpcsggggsggggsggggs rvipvsgparclsqsrnllkttddmvktareklkhysctaedidhedit

		rdqtstlktclplelhknesclatretssttrgsclppqktslmmtlcl gsiyedlkmyqtefqainaalqnhnhqqiildkgmlvaidelmqslnhn getlrqkppvgeadpyrvkmklcillhafstrvvtinrvmgylssaSGG PGPAGMKGLPGSggggsggggsggggsggggsggggsggggsQSVLTQP PSVSGAPGQRVTISCSGSRSNIGSNTVKWYQQLPGTAPKLLIYYNDQRP SGVPDRFSGSKSGTSASLAITGLQAEDEADYYCQSYDRYTHPALLFGTG TKVTVLggggsggggsggggsQVQLVESGGGVVQPGRSLRLSCAASGFT FSSYGMHWVRQAPGKGLEWVAFIRYDGSNKYYADSVKGRFTISRDNSKN TLYLQMNSLRAEDTAVYYCKTHGSHDNWGQGTMVTVSSggggsggggsg gggsEVQLVESGGGLVQPGNSLRLSCAASGFTFSKFGMSWVRQAPGKGL EWVSSISGSGRDTLYAESVKGRFTISRDNAKTTLYLQMNSLRPEDTAVY YCTIGGSLSVSSQGTLVTVSSggggsggggsggggsQVQLQESGGGLAQ AGGSLSLSCAASGFTVSNSVMAWYRQTPGKQREFVAIINSVGSTNYADS VKGRFTISRDNAKNTVYLQMNNLKPEDTAVYVCNRNFDRIYWGQGTQVT VSSHHHHHHEPEA
122	ACP139 嵌合 IL-12 融 合蛋白	mdmrvpaqllgllllwlrgarcQVQLQESGGGLAQAGGSLSLSCAASGF TVSNSVMAWYRQTPGKQREFVAIINSVGSTNYADSVKGRFTISRDNAKN TVYLQMNNLKPEDTAVYVCNRNFDRIYWGQGTQVTVSSggggsggggsg gggsiwelkkdvyvveldwypdapgemvvltcdtpeedgitwtldqsse vlgsgktltiqvkefgdagqytchkggevlshslllhkkedgiwstdi lkdqkepknktflrceaknysgrftcwwlttistdltfsvkssrgssdp qgvtcgaatlsaervrgdnkeyeysvecqedsacpaaeeslpievmvda vhklkyenytssffirdiikpdppknlqlkplknsrqvevsweypdtws tphsyfsltfcvqvqgkskrekkdrvftdktsatvicrknasisvraqd ryyssswsewasvpcsggggsggggsggggsrvipvsgparclsqsrnl lkttddmvktareklkhysctaedidheditrdqtstlktclplelhkn esclatretssttrgsclppqktslmmtlclgsiyedlkmyqtefqain aalqnhnhqqiildkgmlvaidelmqslnhngetlrqkppvgeadpyrv kmklcillhafstrvvtinrvmgylssaSGGPGPAGMKGLPGSggggsg gggsggggsggggsggggsggggsQSVLTQPPSVSGAPGQRVTISCSGS RSNIGSNTVKWYQQLPGTAPKLLIYYNDQRPSGVPDRFSGSKSGTSASL AITGLQAEDEADYYCQSYDRYTHPALLFGTGTKVTVLggggsggggsgg ggsQVQLVESGGGVVQPGRSLRLSCAASGFTFSSYGMHWVRQAPGKGLE WVAFIRYDGSNKYYADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYY CKTHGSHDNWGQGTMVTVSSggggsggggsggggsEVQLVESGGGLVQP GNSLRLSCAASGFTFSKFGMSWVRQAPGKGLEWVSSISGSGRDTLYAES

[0513]

[0514]

		VKGRFTISRDNAKTTLYLQMNSLRPEDTAVYYCTIGGSLSVSSQGTLVT VSSHHHHHHEPEA
123	ACP140 嵌合 IL-12 融合蛋白	mdmrvpaqllgllllwlrgarcQVQLQESGGGLAQAGGSLSLSCAASGF TVSNSVMAWYRQTPGKQREFVAIINSVGSTNYADSVKGRFTISRDNAKN TVYLQMNNLKPEDTAVYVCNRNFDRIYWGQGTQVTVSSSGGPGPAGMKG LPGSiwelkkdvyvveldwypdapgemvvltcdtpeedgitwtldqsse vlgsgktltiqvkefgdagqytchkggevlshsllllhkkedgiwstdi lkdqkepknktflrceaknysgrftcwwlttistdltfsvkssrgssdp qgvtcgaatlsaervrgdnkeyeysvecqedsacpaaeeslpievmvda vhklkyenytssffirdiikpdppknlqlkplknsrqvevsweypdtws tphsyfsltfcvqvqgkskrekkdrvftdktsatvicrknasisvraqd ryyssswsewasvpcsggggsggggsggggsrvipvsgparclsqsrnl lkttddmvktareklkhysctaedidheditrdqtstlktclplelhkn esclatretssttrgsclppqktslmmtlclgsiyedlkmyqtefqain aalqnhnhqqiildkgmlvaidelmqslnhngetlrqkppvgeadpyrv kmklcillhafstrvvtinrvmgylssaSGGPGPAGMKGLPGSggggsg gggsggggsggggsggggsggggsQSVLTQPPSVSGAPGQRVTISCSGS RSNIGSNTVKWYQQLPGTAPKLLIYYNDQRPSGVPDRFSGSKSGTSASL AITGLQAEDEADYYCQSYDRYTHPALLFGTGTKVTVLggggsggggsgg ggsQVQLVESGGGVVQPGRSLRLSCAASGFTFSSYGMHWVRQAPGKGLE WVAFIRYDGSNKYYADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYY CKTHGSHDNWGQGTMVTVSSggggsggggsggggsEVQLVESGGGLVQP GNSLRLSCAASGFTFSKFGMSWVRQAPGKGLEWVSSISGSGRDTLYAES VKGRFTISRDNAKTTLYLQMNSLRPEDTAVYYCTIGGSLSVSSQGTLVT VSSHHHHHHEPEA
124	ACP38 IL-2 融合蛋白	mdmrvpaqllgllllwlrgarcaptssstkktqlqlehlllqlqmilng innyknpkltrmltfkfympkkatelkhlqcleeelkpleevlnlaqsk nfhlrprdlisninvivlelkgsettfmceyadetativeflnrwitfc qsiistltSGGPGPAGMKGLPGSEVQLVESGGGLVQPGGSLRLSCAASG FTFSSYTLAWVRQAPGKGLEWVAAIDSSSYTYSPDTVRGRFTISRDNAK NSLYLQMNSLRAEDTAVYYCARDSNWDALDYWGQGTTVTVSSGGGGSGG GGSGGGGSDIQMTQSPSSLSASVGDRVTITCKASQNVGTNVGWYQQKPG KAPKALIYSASFRYSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQ YYTYPYTFGGGTKVEIKggggsggggsggggsEVQLVESGGGLVQPGNS LRLSCAASGFTFSKFGMSWVRQAPGKGLEWVSSISGSGRDTLYAESVKG RFTISRDNAKTTLYLQMNSLRPEDTAVYYCTIGGSLSVSSQGTLVTVSS

		ggggsggggsggggsQVQLQESGGGLVQAGGSLRLSCAASGRIFSIDIMSWYRQAPGKQRELVARITRGGTISYDDSVKGRFTISRDNAKNTVYLQMNSLKPEDTGVYYCNALYGTDYWGKGTQVTVSSHHHHHH
125	ACP39 IL-2 融合蛋白	mdmrvpaqllgllllwlrgarcQVQLQESGGGLVQAGGSLRLSCAASGRIFSIDIMSWYRQAPGKQRELVARITRGGTISYDDSVKGRFTISRDNAKNTVYLQMNSLKPEDTGVYYCNALYGTDYWGKGTQVTVSSSGGPGPAGMKGLPGSEVQLVESGGGLVQPGNSLRLSCAASGFTFSKFGMSWVRQAPGKGLEWVSSISGSGRDTLYAESVKGRFTISRDNAKTTLYLQMNSLRPEDTAVYYCTIGGSLSVSSQGTLVTVSSSGGPGPAGMKGLPGSEVQLVESGGGLVQPGGSLRLSCAASGFTFSSYTLAWVRQAPGKGLEWVAAIDSSSYTYSPDTVRGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARDSNWDALDYWGQGTTVTVSSGGGGSGGGGSGGGGSDIQMTQSPSSLSASVGDRVTITCKASQNVGTNVGWYQQKPGKAPKALIYSASFRYSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQYYTYPYTFGGGTKVEIKSGGPGPAGMKGLPGSaptssstkktqlqlehlllldlqmilnginnyknpkltrmltfkfympkkatelkhlqcleeelkpleevlnlaqsknfhlrprdlisninvivlelkgsettfmceyadetativeflnrwitfcqsiistltHHHHHH**
126	ACP40 IL-2 融合蛋白	mdmrvpaqllgllllwlrgarcelcdddppeiphatfkamaykegtmlnceckrgfrriksgslymlctgnsshsswdnqcqctssatrnttkqvtpqpeeqkerkttemqspmqpvdqaslpghcrepppweneateriyhfvvgqmvyyqcvqgyralhrgpaesvckmthgktrwtqpqlictgemetsqfpgeekpqaspegrpesetsclvtttdfqiqtemaatmetsiftteyqggggsggggsggggsggggsggggsSGGPGPAGMKGLPGSaptssstkktqlqlehlllldlqmilnginnyknpkltrmltfkfympkkatelkhlqcleeelkpleevlnlaqsknfhlrprdlisninvivlelkgsettfmceyadetativeflnrwitfcqsiistltHHHHHH
127	ACP41 IL-2 融合蛋白	mdmrvpaqllgllllwlrgarcaptssstkktqlqlehlllldlqmilnginnyknpkltrmltfkfympkkatelkhlqcleeelkpleevlnlaqsknfhlrprdlisninvivlelkgsettfmceyadetativeflnrwitfcqsiistltSGGPGPAGMKGLPGSggggsggggsggggsggggsggggsggggsggggselcdddppeiphatfkamaykegtmlnceckrgfrriksgslymlctgnsshsswdnqcqctssatrnttkqvtpqpeeqkerkttemqspmqpvdqaslpghcrepppweneateriyhfvvgqmvyyqcvqgyralhrgpaesvckmthgktrwtqpqlictgemetsqfpgeekpqaspegrpesetsclvtttdfqiqtemaatmetsiftteyqHHHHHH
128	ACP42	mdmrvpaqllgllllwlrgarcEVQLVESGGGLVQPGNSLRLSCAASGF

[0515]

[0516]

	IL-2 融合蛋白	TFSKFGMSWVRQAPGKGLEWVSSISGSGRDTLYAESVKGRFTISRDNAKTTLYLQMNSLRPEDTAVYYCTIGGSLSVSSQGTLVTVSSggggsggggsggggselcdddppeiphatfkamaykegtmlnceckrgfrriksgslymlctgnsshsswdnqcqctssatrnttkqvtpqpeeqkerkttemqspmqpvdqaslpghcrepppweneateriyhfvvgqmvyyqcvqgyralhrgpaesvckmthgktrwtqpqlictgemetsqfpgeekpqaspegrpesetsclvtttdfqiqtemaatmetsiftteyqggggsggggsggggsggggsggggsSGGPGPAGMKGLPGSaptssstkktqlqlehlllldlqmilnginnyknpkltrmltfkfympkkatelkhlqcleeelkpleevlnlaqsknfhlrprdlisninvivlelkgsettfmceyadetativeflnrwitfcqsiistltHHHHHH
129	ACP43 IL-2 融合蛋白	mdmrvpaqllgllllwlrgarcaptssstkktqlqlehlllldlqmilnginnyknpkltrmltfkfympkkatelkhlqcleeelkpleevlnlaqsknfhlrprdlisninvivlelkgsettfmceyadetativeflnrwitfcqsiistltSGGPGPAGMKGLPGSggggsggggsggggsggggsggggsggggselcdddppeiphatfkamaykegtmlnceckrgfrriksgslymlctgnsshsswdnqcqctssatrnttkqvtpqpeeqkerkttemqspmqpvdqaslpghcrepppweneateriyhfvvgqmvyyqcvqgyralhrgpaesvckmthgktrwtqpqlictgemetsqfpgeekpqaspegrpesetsclvtttdfqiqtemaatmetsiftteyqggggsggggsggggsEVQLVESGGGLVQPGNSLRLSCAASGFTFSKFGMSWVRQAPGKGLEWVSSISGSGRDTLYAESVKGRFTISRDNAKTTLYLQMNSLRPEDTAVYYCTIGGSLSVSSQGTLVTVSSHHHHHH
130	ACP44 IL-2 融合蛋白	mdmrvpaqllgllllwlrgarcaptssstkktqlqlehlllldlqmilnginnyknpkltrmltfkfympkkatelkhlqcleeelkpleevlnlaqsknfhlrprdlisninvivlelkgsettfmceyadetativeflnrwitfcqsiistltSGGPGPAGMKGLPGSggggsggggsggggsggggsggggsggggselcdddppeiphatfkamaykegtmlnceckrgfrriksgslymlctgnsshsswdnqcqctssatrnttkqvtpqpeeqkerkttemqspmqpvdqaslpghcrepppweneateriyhfvvgqmvyyqcvqgyralhrgpaesvckmthgktrwtqpqlictgemetsqfpgeekpqaspegrpesetsclvtttdfqiqtemaatmetsiftteyqSGGPGPAGMKGLPGSEVQLVESGGGLVQPGNSLRLSCAASGFTFSKFGMSWVRQAPGKGLEWVSSISGSGRDTLYAESVKGRFTISRDNAKTTLYLQMNSLRPEDTAVYYCTIGGSLSVSSQGTLVTVSSHHHHHH
131	ACP45	mdmrvpaqllgllllwlrgarcEVQLVESGGGLVQPGNSLRLSCAASGF

[0517]

	IL-2 融合蛋白	TFSKFGMSWVRQAPGKGLEWVSSISGSGRDTLYAESVKGRFTISRDNAKTTLYLQMNSLRPEDTAVYYCTIGGSLSVSSQGTLVTVSSSGGPGPAGMKGLPGSEVQLVESGGGLVQPGGSLRLSCAASGFTFSSYTLAWVRQAPGKGLEWVAAIDSSSYTYSPDTVRGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARDSNWDALDYWGQGTTVTVSSGGGGSGGGGSGGGGSDIQMTQSPSSLSASVGDRVTITCKASQNVGTNVGWYQQKPGKAPKALIYSASFRYSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQYYTYPYTFGGGTKVEIKggggsggggsggggsggggsggggsSGGPGPAGMKGLPGSaptsstkktqlqlehlldlqmilnginnyknpkltrmltfkfympkkatelkhlqcleeelkpleevlnlaqsknfhlrprdlisninvivlelkgsettfmceyadetativeflnrwitfcqsiistltHHHHHH
132	ACP46 IL-2 融合蛋白	mdmrvpaqllgllllwlrgarcaptssstkktqlqlehlldlqmilnginnyknpkltrmltfkfympkkatelkhlqcleeelkpleevlnlaqsknfhlrprdlisninvivlelkgsettfmceyadetativeflnrwitfcqsiistltSGGPGPAGMKGLPGSggggsggggsggggsggggsggggsgggsEVQLVESGGGLVQPGGSLRLSCAASGFTFSSYTLAWVRQAPGKGLEWVAAIDSSSYTYSPDTVRGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARDSNWDALDYWGQGTTVTVSSsggpgpagmkglpgsDIQMTQSPSSLSASVGDRVTITCKASQNVGTNVGWYQQKPGKAPKALIYSASFRYSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQYYTYPYTFGGGTKVEIKggggsggggsggggsEVQLVESGGGLVQPGNSLRLSCAASGFTFSKFGMSWVRQAPGKGLEWVSSISGSGRDTLYAESVKGRFTISRDNAKTTLYLQMNSLRPEDTAVYYCTIGGSLSVSSQGTLVTVSSggggsggggsggggsQVQLQESGGGLVQAGGSLRLSCAASGRIFSIDIMSWYRQAPGKQRELVARITRGGTISYDDSVKGRFTISRDNAKNTVYLQMNSLKPEDTGVYYCNALYGTDYWGKGTQVTVSSHHHHHH
133	ACP47 IL-2 融合蛋白	mdmrvpaqllgllllwlrgarcQVQLQESGGGLVQAGGSLRLSCAASGRIFSIDIMSWYRQAPGKQRELVARITRGGTISYDDSVKGRFTISRDNAKNTVYLQMNSLKPEDTGVYYCNALYGTDYWGKGTQVTVSSggggsggggsggggsaptssstkktqlqlehlldlqmilnginnyknpkltrmltfkfympkkatelkhlqcleeelkpleevlnlaqsknfhlrprdlisninvivlelkgsettfmceyadetativeflnrwitfcqsiistltSGGPGPAGMKGLPGSEVQLVESGGGLVQPGNSLRLSCAASGFTFSKFGMSWVRQAPGKGLEWVSSISGSGRDTLYAESVKGRFTISRDNAKTTLYLQMNSLRPEDTAVYYCTIGGSLSVSSQGTLVTVSSggggsggggsggggsggggsggggsggggsEVQLVESGGGLVQPGGSLRLSCAASGFTFSSYTLAWVRQAPGKGLE

[0518]

		WVAAIDSSSYTYSPDTVRGRFTISRDNAKNSLYLQMNSLRAEDTAVYYC ARDSNWDALDYWGQGTTVTVSSGGGGSGGGGSGGGGSDIQMTQSPSSLS ASVGDRVTITCKASQNVGTNVGWYQQKPGKAPKALIYSASFRYSGVPSR FSGSGSGTDFTLTISSLQPEDFATYYCQQYYTYPYTFGGGTKVEIKHHH HHH
134	ACP48 IL-2 融 合蛋白	mdmrvpaqllgllllwlrgarcaptssstkktqlqlehlllqmilng innyknpkltrmltfkfympkkatelkhlqcleeelkpleevlnlaqsk nfhlrprdlisninvivlelkgsettfmceyadetativeflnrwitfc qsiistltSGGPGPAGMKGLPGSEVQLVESGGGLVQPGGSLRLSCAASG FTFSSYTLAWVRQAPGKGLEWVAAIDSSSYTYSPDTVRGRFTISRDNAK NSLYLQMNSLRAEDTAVYYCARDSNWDALDYWGQGTTVTVSSGGGGSGG GGSGGGGSDIQMTQSPSSLSASVGDRVTITCKASQNVGTNVGWYQQKPG KAPKALIYSASFRYSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQ YYTYPYTFGGGTKVEIKggggsggggsggggsEVQLVESGGGLVQPGNS LRLSCAASGFTFSKFGMSWVRQAPGKGLEWVSSISGSGRDTLYAESVKG RFTISRDNAKTTLYLQMNSLRPEDTAVYYCTIGGSLSVSSQGTLVTVSS HHHHHH
135	ACP49 IL-2 融 合蛋白	mdmrvpaqllgllllwlrgarcaptssstkktqlqlehlllqmilng innyknpkltrmltfkfympkkatelkhlqcleeelkpleevlnlaqsk nfhlrprdlisninvivlelkgsettfmceyadetativeflnrwitfc qsiistltSGGPGPAGMKGLPGSggggsggggsggggsggggsggggsg gggsEVQLVESGGGLVQPGGSLRLSCAASGFTFSSYTLAWVRQAPGKGL EWVAAIDSSSYTYSPDTVRGRFTISRDNAKNSLYLQMNSLRAEDTAVYY CARDSNWDALDYWGQGTTVTVSSGGGGSGGGGSGGGGSDIQMTQSPSSL SASVGDRVTITCKASQNVGTNVGWYQQKPGKAPKALIYSASFRYSGVPS RFSGSGSGTDFTLTISSLQPEDFATYYCQQYYTYPYTFGGGTKVEIKgg ggsggggsggggsEVQLVESGGGLVQPGNSLRLSCAASGFTFSKFGMSW VRQAPGKGLEWVSSISGSGRDTLYAESVKGRFTISRDNAKTTLYLQMNS LRPEDTAVYYCTIGGSLSVSSQGTLVTVSSHHHHHH
136	ACP92 IL-2 融 合蛋白	mdmrvpaqllgllllwlrgarcEVQLVESGGGLVQPGNSLRLSCAASGF TFSKFGMSWVRQAPGKGLEWVSSISGSGRDTLYAESVKGRFTISRDNAK TTLYLQMNSLRPEDTAVYYCTIGGSLSVSSQGTLVTVSSSGGPGPAGMK GLPGSaptssstkktqlqlehlllqmilnginnyknpkltrmltfkf ympkkatelkhlqcleeelkpleevlnlaqsknfhlrprdlisninviv lelkgsettfmceyadetativeflnrwitfcqsiistltSGGPGPAGM KGLPGSEVQLVESGGGLVQPGNSLRLSCAASGFTFSKFGMSWVRQAPGK

[0519]

		GLEWVSSISGSGRDTLYAESVKGRFTISRDNAKTTLYLQMNSLRPEDTA VYYCTIGGSLSVSSQGTLVTVSSHHHHHH
137	ACP93 IL-2 融合蛋白	mdmrvpaqllgllllwlrgarcQVQLQESGGGLVQAGGSLRLSCAASGR IFSIDIMSWYRQAPGKQRELVARITRGGTISYDDSVKGRFTISRDNAKN TVYLQMNSLKPEDTGVYYCNALYGTDYWGKGTQVTVSSgsgsgsgsgsg sgsgsEVQLVESGGGLVQPGNSLRLSCAASGFTFSKFGMSWVRQAPGKG LEWVSSISGSGRDTLYAESVKGRFTISRDNAKTTLYLQMNSLRPEDTAV YYCTIGGSLSVSSQGTLVTVSSgsgsgsgsgsgsgsgsQVQLQESGGGL VQAGGSLRLSCAASGRIFSIDIMSWYRQAPGKQRELVARITRGGTISYD DSVKGRFTISRDNAKNTVYLQMNSLKPEDTGVYYCNALYGTDYWGKGTQ VTVSSgsgsgsgsgsgsgsgsEVQLVESGGGLVQPGGSLRLSCAASGFT FSSYTLAWVRQAPGKGLEWVAAIDSSSYTYSPDTVRGRFTISRDNAKNS LYLQMNSLRAEDTAVYYCARDSNWDALDYWGQGTTVTVSSGGGGSGGGG SGGGGSDIQMTQSPSSLSASVGDRVTITCKASQNVGTNVGWYQQKPGKA PKALIYSASFRYSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQYY TYPYTFGGGTKVEIKSGGPGPAGMKGLPGSaptssstkktqlqlehlll dlqmilnginnyknpkltrmltfkfympkkatelkhlqcleeelkplee vlnlaqsknfhlrprdlisninvivlelkgsettfmceyadetativef lnrwitfcqsiistltHHHHHH
138	ACP94 IL-2 融合蛋白	mdmrvpaqllgllllwlrgarcQVQLQESGGGLVQAGGSLRLSCAASGR IFSIDIMSWYRQAPGKQRELVARITRGGTISYDDSVKGRFTISRDNAKN TVYLQMNSLKPEDTGVYYCNALYGTDYWGKGTQVTVSSgsgsgsgsgsg sgsgsEVQLVESGGGLVQPGNSLRLSCAASGFTFSKFGMSWVRQAPGKG LEWVSSISGSGRDTLYAESVKGRFTISRDNAKTTLYLQMNSLRPEDTAV YYCTIGGSLSVSSQGTLVTVSSgsgsgsgsgsgsgsgsEVQLVESGGGL VQPGGSLRLSCAASGFTFSSYTLAWVRQAPGKGLEWVAAIDSSSYTYSP DTVRGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARDSNWDALDYWGQ GTTVTVSSGGGGSGGGGSGGGGSDIQMTQSPSSLSASVGDRVTITCKAS QNVGTNVGWYQQKPGKAPKALIYSASFRYSGVPSRFSGSGSGTDFTLTI SSLQPEDFATYYCQQYYTYPYTFGGGTKVEIKSGGPGPAGMKGLPGSap tssstkktqlqlehlllldlqmilnginnyknpkltrmltfkfympkkat elkhlqcleeelkpleevlnlaqsknfhlrprdlisninvivlelkgse ttfmceyadetativeflnrwitfcqsiistltHHHHHH
139	ACP95 IL-2 融合蛋白	mdmrvpaqllgllllwlrgarcQVQLQESGGGLVQAGGSLRLSCAASGR IFSIDIMSWYRQAPGKQRELVARITRGGTISYDDSVKGRFTISRDNAKN TVYLQMNSLKPEDTGVYYCNALYGTDYWGKGTQVTVSSgsgsgsgsgsg

		sgsgsEVQLVESGGGLVQPGNSLRLSCAASGFTFSKFGMSWVRQAPGKG LEWVSSISGSGRDTLYAESVKGRFTISRDNAKTTLYLQMNSLRPEDTAV YYCTIGGSLSVSSQGTLVTVSSSGGPGPAGMKGLPGSaptssstkktql qlehlllldlqmilnginnyknpkltrmltfkfympkkatelkhlqclee elkpleevlnlaqsknfhlrprdlisninvivlelkgsettfmceyade tativeflnrwitfcqsiistltHHHHHH
140	ACP96 IL-2 融 合蛋白	mdmrvpaqllgllllwlrgarcQVQLQESGGGLVQAGGSLRLSCAASGR IFSIDIMSWYRQAPGKQRELVARITRGGTISYDDSVKGRFTISRDNAKN TVYLQMNSLKPEDTGVYYCNALYGTDYWGKGTQVTVSSSGGPGPAGMKG LPGSaptssstkktqlqlehlllldlqmilnginnyknpkltrmltfkfy mpkkatelkhlqcleeelkpleevlnlaqsknfhlrprdlisninvivl elkgsettfmceyadetativeflnrwitfcqsiistltSGGPGPAGMK GLPGSEVQLVESGGGLVQPGNSLRLSCAASGFTFSKFGMSWVRQAPGKG LEWVSSISGSGRDTLYAESVKGRFTISRDNAKTTLYLQMNSLRPEDTAV YYCTIGGSLSVSSQGTLVTVSSHHHHHH
141	ACP97 IL-2 融 合蛋白	mdmrvpaqllgllllwlrgarcQVQLQESGGGLVQAGGSLRLSCAASGR IFSIDIMSWYRQAPGKQRELVARITRGGTISYDDSVKGRFTISRDNAKN TVYLQMNSLKPEDTGVYYCNALYGTDYWGKGTQVTVSSggggsggggsg gggsEVQLVESGGGLVQPGNSLRLSCAASGFTFSKFGMSWVRQAPGKGL EWVSSISGSGRDTLYAESVKGRFTISRDNAKTTLYLQMNSLRPEDTAVY YCTIGGSLSVSSQGTLVTVSSSGGPGPAGMKGLPGSaptssstkktqlq lehlllldlqmilnginnyknpkltrmltfkfympkkatelkhlqcleee lkpleevlnlaqsknfhlrprdlisninvivlelkgsettfmceyadet ativeflnrwitfcqsiistltSGGPGPAGMKGLPGSEVQLVESGGGLV QPGNSLRLSCAASGFTFSKFGMSWVRQAPGKGLEWVSSISGSGRDTLYA ESVKGRFTISRDNAKTTLYLQMNSLRPEDTAVYYCTIGGSLSVSSQGTL VTVSSHHHHHH
142	ACP99 IL-2 融 合蛋白	mdmrvpaqllgllllwlrgarcQVQLQESGGGLVQAGGSLRLSCAASGR IFSIDIMSWYRQAPGKQRELVARITRGGTISYDDSVKGRFTISRDNAKN TVYLQMNSLKPEDTGVYYCNALYGTDYWGKGTQVTVSSggggsggggsg gggsaptssstkktqlqlehlllldlqmilnginnyknpkltrmltfkfy mpkkatelkhlqcleeelkpleevlnlaqsknfhlrprdlisninvivl elkgsettfmceyadetativeflnrwitfcqsiistltSGGPGPAGMK GLPGSEVQLVESGGGLVQPGNSLRLSCAASGFTFSKFGMSWVRQAPGKG LEWVSSISGSGRDTLYAESVKGRFTISRDNAKTTLYLQMNSLRPEDTAV YYCTIGGSLSVSSQGTLVTVSSHHHHHH

[0520]

[0521]

143	ACP100 IL-2 融合蛋白	mdmrvpaqllgllllwlrgarcQVQLQESGGGLVQAGGSLRLSCAASGR IFSIDIMSWYRQAPGKQRELVARITRGGTISYDDSVKGRFTISRDNAKN TVYLQMNSLKPEDTGVYYCNALYGTDYWGKGTQVTVSSggggsggggsg gggsaptssstkktqlqlehlldlqmilnginnyknpkltrmltfkfy mpkkatelkhlqcleeelkpleevlnlaqsknfhlrprdlisninvivl elkgsettfmceyadetativeflnrwitfcqsiistltHHHHHH
144	ACP101 IL-2 融合蛋白	mdmrvpaqllgllllwlrgarcaptssstkktqlqlehlldlqmilng innyknpkltrmltfkfympkkatelkhlqcleeelkpleevlnlaqsk nfhlrprdlisninvivlelkgsettfmceyadetativeflnrwitfc qsiistltSGGPGPAGMKGLPGSEVQLVESGGGLVQPGNSLRLSCAASG FTFSKFGMSWVRQAPGKGLEWVSSISGSGRDTLYAESVKGRFTISRDNA KTTLYLQMNSLRPEDTAVYYCTIGGSLSVSSQGTLVTVSSHHHHHH
145	ACP102 IL-2 融合蛋白	mdmrvpaqllgllllwlrgarcQVQLQESGGGLVQAGGSLRLSCAASGR IFSIDIMSWYRQAPGKQRELVARITRGGTISYDDSVKGRFTISRDNAKN TVYLQMNSLKPEDTGVYYCNALYGTDYWGKGTQVTVSSSGGPGPAGMKG LPGSaptssstkktqlqlehlldlqmilnginnyknpkltrmltfkfy mpkkatelkhlqcleeelkpleevlnlaqsknfhlrprdlisninvivl elkgsettfmceyadetativeflnrwitfcqsiistltSGGPGPAGMK GLPGSEVQLVESGGGLVQPGNSLRLSCAASGFTFSKFGMSWVRQAPGKG LEWVSSISGSGRDTLYAESVKGRFTISRDNAKTTLYLQMNSLRPEDTAV YYCTIGGSLSVSSQGTLVTVSSggggsggggsggggsggggsggggsgg ggsEVQLVESGGGLVQPGGSLRLSCAASGFTFSSYTLAWVRQAPGKGLE WVAAIDSSSYTYSPDTVRGRFTISRDNAKNSLYLQMNSLRAEDTAVYYC ARDSNWDALDYWGQGTTVTVSSGGGGSGGGGSGGGGSDIQMTQSPSSLS ASVGDRVTITCKASQNVGTNVGWYQQKPGKAPKALIYSASFRYSGVPSR FSGSGSGTDFTLTISSLQPEDFATYYCQQYYTYPYTFGGGTKVEIKHHH HHH
146	ACP103 IL-2 融合蛋白	mdmrvpaqllgllllwlrgarcaptssstkktqlqlehlldlqmilng innyknpkltrmltfkfympkkatelkhlqcleeelkpleevlnlaqsk nfhlrprdlisninvivlelkgsettfmceyadetativeflnrwitfc qsiistltSGGPGPAGMKGLPGSggggsggggsggggsggggsggggsg ggggsEVQLVESGGGLVQPGGSLRLSCAASGFTFSSYTLAWVRQAPGKGL EWVAAIDSSSYTYSPDTVRGRFTISRDNAKNSLYLQMNSLRAEDTAVYY CARDSNWDALDYWGQGTTVTVSSGGGGSGGGGSGGGGSDIQMTQSPSSL SASVGDRVTITCKASQNVGTNVGWYQQKPGKAPKALIYSASFRYSGVPS RFSGSGSGTDFTLTISSLQPEDFATYYCQQYYTYPYTFGGGTKVEIKgg

[0522]

		ggsggggsggggsEVQLVESGGGLVQPGNSLRLSCAASGFTFSKFGMSW VRQAPGKGLEWVSSISGSGRDTLYAESVKGRFTISRDNAKTTLYLQMNS LRPEDTAVYYCTIGGSLSVSSQGTLVTVSSggggsggggsggggsQVQL QESGGGLAQAGGSLSLSCAASGFTVSNSVMAWYRQTPGKQREFVAIINS VGSTNYADSVKGRFTISRDNAKNTVYLQMNNLKPEDTAVYVCNRNFDRI YWGQGTQVTVSSHHHHHH
147	ACP104 IL-2 融 合蛋白	mdmrvpaqllgllllwlrgarcQVQLQESGGGLAQAGGSLSLSCAASGF TVSNSVMAWYRQTPGKQREFVAIINSVGSTNYADSVKGRFTISRDNAKN TVYLQMNNLKPEDTAVYVCNRNFDRIYWGQGTQVTVSSaptssstkktq lqlehlllldlqmilnginnyknpkltrmltfkfympkkatelkhlqcle eelkpleevlnlaqsknfhlrprdlisninvivlelkgsettfmceyad etativeflnrwitfcqsiistltSGGPGPAGMKGLPGSEVQLVESGGG LVQPGNSLRLSCAASGFTFSKFGMSWVRQAPGKGLEWVSSISGSGRDTL YAESVKGRFTISRDNAKTTLYLQMNSLRPEDTAVYYCTIGGSLSVSSQG TLVTVSSggggsggggsggggsggggsggggsggggsEVQLVESGGGLV QPGGSLRLSCAASGFTFSSYTLAWVRQAPGKGLEWVAAIDSSSYTYSPD TVRGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARDSNWDALDYWGQG TTVTVSSGGGGSGGGGSGGGGSDIQMTQSPSSLSASVGDRVTITCKASQ NVGTNVGWYQQKPGKAPKALIYSASFRYSGVPSRFSGSGSGTDFTLTIS SLQPEDFATYYCQQYYTYPYTFGGGTKVEIKHHHHHH
148	ACP105 IL-2 融 合蛋白	mdmrvpaqllgllllwlrgarcEVQLVESGGGLVQPGGSLRLSCAASGF TFSSYTLAWVRQAPGKGLEWVAAIDSSSYTYSPDTVRGRFTISRDNAKN SLYLQMNSLRAEDTAVYYCARDSNWDALDYWGQGTTVTVSSGGGGSGGG GSGGGGSDIQMTQSPSSLSASVGDRVTITCKASQNVGTNVGWYQQKPGK APKALIYSASFRYSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQY YTYPYTFGGGTKVEIKggggsggggsggggsggggsggggsggggsSGG PGPAGMKGLPGSaptssstkktqlqlehlllldlqmilnginnyknpklt rmltfkfympkkatelkhlqcleeelkpleevlnlaqsknfhlrprdli sninvivlelkgsettfmceyadetativeflnrwitfcqsiistltSG GPGPAGMKGLPGSEVQLVESGGGLVQPGNSLRLSCAASGFTFSKFGMSW VRQAPGKGLEWVSSISGSGRDTLYAESVKGRFTISRDNAKTTLYLQMNS LRPEDTAVYYCTIGGSLSVSSQGTLVTVSSggggsggggsggggsQVQL QESGGGLAQAGGSLSLSCAASGFTVSNSVMAWYRQTPGKQREFVAIINS VGSTNYADSVKGRFTISRDNAKNTVYLQMNNLKPEDTAVYVCNRNFDRI YWGQGTQVTVSSHHHHHH
149	ACP106	mdmrvpaqllgllllwlrgarcQVQLQESGGGLAQAGGSLSLSCAASGF

[0523]

	IL-2 融合蛋白	TVSNSVMAWYRQTPGKQREFVAIINSVGSTNYADSVKGRFTISRDNAKNTVYLQMNNLKPEDTAVYVCNRNFDRIYWGQGTQVTVSSggggsggggsggggsEVQLVESGGGLVQPGNSLRLSCAASGFTFSKFGMSWVRQAPGKGLEWVSSISGSGRDTLYAESVKGRFTISRDNAKTTLYLQMNSLRPEDTAVYYCTIGGSLSVSSQGTLVTVSSSGGPGPAGMKGLPGSEVQLVESGGGLVQPGGSLRLSCAASGFTFSSYTLAWVRQAPGKGLEWVAAIDSSSYTYSPDTVRGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARDSNWDALDYWGQGTTVTVSSGGGGSGGGGSGGGGSDIQMTQSPSSLSASVGDRVTITCKASQNVGTNVGWYQQKPGKAPKALIYSASFRYSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQYYTYPYTFGGGTKVEIKggggsggggsggggsggggsggggsggggsSGGPGPAGMKGLPGSaptssstkktqlqlehlllldlqmilnginnyknpkltrmltfkfympkkatelkhlqcleeelkpleevlnlaqsknfhlrprdlisninvivlelkgsettfmceyadetativeflnrwitfcqsiistltHHHHHH
150	ACP107 IL-2 融合蛋白	mdmrvpaqllgllllwlrgarcEVQLVESGGGLVQPGGSLRLSCAASGFTFSSYTLAWVRQAPGKGLEWVAAIDSSSYTYSPDTVRGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARDSNWDALDYWGQGTTVTVSSGGGGSGGGGSGGGGSDIQMTQSPSSLSASVGDRVTITCKASQNVGTNVGWYQQKPGKAPKALIYSASFRYSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQYYTYPYTFGGGTKVEIKggggsggggsggggsggggsggggsggggsEVQLVESGGGLVQPGNSLRLSCAASGFTFSKFGMSWVRQAPGKGLEWVSSISGSGRDTLYAESVKGRFTISRDNAKTTLYLQMNSLRPEDTAVYYCTIGGSLSVSSQGTLVTVSSSGGPGPAGMKGLPGSaptssstkktqlqlehlllldlqmilnginnyknpkltrmltfkfympkkatelkhlqcleeelkpleevlnlaqsknfhlrprdlisninvivlelkgsettfmceyadetativeflnrwitfcqsiistltggggsggggsggggsQVQLQESGGGLAQAGGSLSLSCAASGFTVSNSVMAWYRQTPGKQREFVAIINSVGSTNYADSVKGRFTISRDNAKNTVYLQMNNLKPEDTAVYVCNRNFDRIYWGQGTQVTVSSHHHHHHH
151	ACP108 IL-2 融合蛋白	mdmrvpaqllgllllwlrgarcQVQLQESGGGLVQAGGSLRLSCAASGRIFSIDIMSWYRQAPGKQRELVARITRGGTISYDDSVKGRFTISRDNAKNTVYLQMNSLKPEDTGVYYCNALYGTDYWGKGTQVTVSSggggsggggsggggsaptssstkktqlqlehlllldlqmilnginnyknpkltrmltfkfympkkatelkhlqcleeelkpleevlnlaqsknfhlrprdlisninvivlelkgsettfmceyadetativeflnrwitfcqsiistltSGGPGPAGMKGLPGSrgetgpaaPGSEVQLVESGGGLVQPGNSLRLSCAASGFTFSKFG

[0524]

		MSWVRQAPGKGLEWVSSISGSGRDTLYAESVKGRFTISRDNAKTTLYLQMNSLRPEDTAVYYCTIGGSLSVSSQGTLVTVSSggggsggggsggggsggggsgggsggggsggggsEVQLVESGGGLVQPGGSLRLSCAASGFTFSSYTLAWVRQAPGKGLEWVAAIDSSSYTYSPDTVRGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARDSNWDALDYWGQGTTVTVSSGGGGSGGGGSGGGGSDIQMTQSPSSLSASVGDRVTITCKASQNVGTNVGWYQQKPGKAPKALIYSASFRYSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQYYTYPYTFGGGTKVEIKHHHHHH
152	ACP117 抗 FN CGS-2 scFv	mdmrvpaqllgllllwlrgarcEVQLVESGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPGKGLEWVSAISGSGGSTYYADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARGVGAFRPYRKHEWGQGTLVTVSRggggsggggsggggsSSELTQDPAVSVALGQTVRITCQGDSLRSYYASWYQQKPGQAPVLVIYGKNNRPSGIPDRFSGSSSGNTASLTTTGAQAEDEADYYCNSSPFEHNLVVFGGGTKLTVLHHHHHHHEPEA
153	ACP118 NARA1 Vh/V1 不可裂解	mdmrvpaqllgllllwlrgarcQVQLQQSGAELVRPGTSVKVSCKASGYAFTNYLIEWVKQRPGQGLEWIGVINPGSGGTNYNEKFKGKATLTADKSSSTAYMQLSSLTSDDSAVYFCARWRGDGYYAYFDVWGAGTTVTVSSggggsggggsggggsDIVLTQSPASLAVSLGQRATISCKASQSVDYDGDSYMNWYQQKPGQPPKLLIYAASNLESGIPARFSGSGSGTDFTLNIHPVEEEDAATYYCQQSNEDPYTFGGGTKLEIKHHHHHHHEPEA
154	ACP119 NARA1 Vh/V1 可裂解	mdmrvpaqllgllllwlrgarcQVQLQQSGAELVRPGTSVKVSCKASGYAFTNYLIEWVKQRPGQGLEWIGVINPGSGGTNYNEKFKGKATLTADKSSSTAYMQLSSLTSDDSAVYFCARWRGDGYYAYFDVWGAGTTVTVSSSGGPGPAGMKGLPGSDIVLTQSPASLAVSLGQRATISCKASQSVDYDGDSYMNWYQQKPGQPPKLLIYAASNLESGIPARFSGSGSGTDFTLNIHPVEEEDAATYYCQQSNEDPYTFGGGTKLEIKHHHHHHHEPEA
155	ACP120 NARA1 V1/Vh 不可裂解	mdmrvpaqllgllllwlrgarcDIVLTQSPASLAVSLGQRATISCKASQSVDYDGDSYMNWYQQKPGQPPKLLIYAASNLESGIPARFSGSGSGTDFTLNIHPVEEEDAATYYCQQSNEDPYTFGGGTKLEIKggggsggggsggggsQVQLQQSGAELVRPGTSVKVSCKASGYAFTNYLIEWVKQRPGQGLEWIGVINPGSGGTNYNEKFKGKATLTADKSSSTAYMQLSSLTSDDSAVYFCARWRGDGYYAYFDVWGAGTTVTVSSHHHHHHHEPEA
156	ACP121 NARA1 V1/Vh 可裂解	mdmrvpaqllgllllwlrgarcDIVLTQSPASLAVSLGQRATISCKASQSVDYDGDSYMNWYQQKPGQPPKLLIYAASNLESGIPARFSGSGSGTDFTLNIHPVEEEDAATYYCQQSNEDPYTFGGGTKLEIKSGGPGPAGMKGLPGSQVQLQQSGAELVRPGTSVKVSCKASGYAFTNYLIEWVKQRPGQGLEWI

[0525]

		GVINPGSGGTNYNEKFKGKATLTADKSSSTAYMQLSSLTSDDSAVYFCA RWRGDGYYAYFDVWGAGTTVTVSSHHHHHHHEPEA
157	ACP124 IL-2 融合蛋白	mdmrvpaqllgllllwlrgarcaptssstkktqlqlehlldlqmilng innyknpkltrmltfkfympkkatelkhlqcleeelkpleevlnlaqsk nfhlrprdlisninvivlelkgsettfmceyadetativeflnrwitfc qsiistltggggsggggsggggsEVQLVESGGGLVQPGNSLRLSCAASG FTFSKFGMSWVRQAPGKGLEWVSSISGSGRDTLYAESVKGRFTISRDNA KTTLYLQMNSLRPEDTAVYYCTIGGSLSVSSQGTLVTVSSHHHHHHEPE A
158	ACP132 IL-2 融合蛋白	mdmrvpaqllgllllwlrgarcaptssstkktqlqlehlldlqmilng innyknpkltrmltfkfympkkatelkhlqcleeelkpleevlnlaqsk nfhlrprdlisninvivlelkgsettfmceyadetativeflnrwitfc qsiistltggggsggggsggggsdahksevahrfkdlgeenfkalvlia faqylqqcpfedhvklvnevtefaktcvadesaencdkslhtlfgdklc tvatlretygemadccakqepernecflqhkddnpnlprlvrpevdvmc tafhdneetflkkylyeiarrhpyfyapellffakrykaafteccqaad kaacllpkldelrdegkassakqrlkcaslqkfgerafkawavarlsqr fpkaefaevsklvtdltkvhtecchgdllecaddradlakyicenqdsi ssklkeccekpllekshciaevendempadlpslaadfveskdvcknya eakdvflgmflyeyarrhpdysvvlllrlaktyettlekccaaadphec yakvfdefkplveepqnlikqncelfeqlgeykfqnallvrytkkvpqv stptlvevsrnlgkvgskcckhpeakrmpcaedylsvvlnqlcvlhekt pvsdrvtkccteslvnrrpcfsalevdetyvpkefnaetftfhadictl sekerqikkqtalvelvkhkpkatkeqlkavmddfaafvekcckaddke tcfaeegkklvaasqaalglHHHHHHHEPEA
159	ACP141 IL-2 融合蛋白	mdmrvpaqllgllllwlrgarcaptssstkktqlqlehlldlqmilng innyknpkltrmltfkfympkkatelkhlqcleeelkpleevlnlaqsk nfhlrprdlisninvivlelkgsettfmceyadetativeflnrwitfc qsiistltggggsggggsggggsdahksevahrfkdlgeenfkalvlia faqylqqcpfedhvklvnevtefaktcvadesaencdkslhtlfgdklc tvatlretygemadccakqepernecflqhkddnpnlprlvrpevdvmc tafhdneetflkkylyeiarrhpyfyapellffakrykaafteccqaad kaacllpkldelrdegkassakqrlkcaslqkfgerafkawavarlsqr fpkaefaevsklvtdltkvhtecchgdllecaddradlakyicenqdsi ssklkeccekpllekshciaevendempadlpslaadfveskdvcknya eakdvflgmflyeyarrhpdysvvlllrlaktyettlekccaaadphec

[0526]

		yakvfdefkplveepqnlikqncelfeqlgeykfqnallvrytkkvpqv stptlvevsrnlgkvgskcckhpeakrmpcaedylsvvlnqlcvlhekt pvsdrvtkccteslvnrrpcfsalevdetyvpkefnaetftfhadictl sekerqikkqtalvelvkhkpkatkeqlkavmddfaafvekcckaddke tcfaeegkklvaasqaalglHHHHHHHEPEA
160	ACP142 IL-2 融 合蛋白	mdmrvpaqllgllllwlrgarcaptssstkktqlqlehlldlqmilng innyknpkltrmltfkfympkkatelkhlqcleeelkpleevlnlaqsk nfhlrprdlisninvivlelkgsettfmceyadetativeflnrwitfc qsiistltSGGPGPAGMKGLPGSdahksevahrfkdlgeenfkalvlia faqylqqcpfedhvklvnevtefaktcvadesaencdkslhtlfgdklc tvatlretygemadccakqepernecflqhkddnpnlprlvrpevdvmc tafhdneetflkkylyeiarrhpyfyapellffakrykaafteccqaad kaacllpkldelrdegkassakqrlkcaslqkfgerafkawavarlsqr fpkaefaevsklvtdltkvhtecchgdllecaddradlakyicenqdsi ssklkeccekpllekshciaevendempadlpslaadfveskdvcknya eakdvflgmflyeyarrhpdysvvlllrlaktyettlekccaaadphec yakvfdefkplveepqnlikqncelfeqlgeykfqnallvrytkkvpqv stptlvevsrnlgkvgskcckhpeakrmpcaedylsvvlnqlcvlhekt pvsdrvtkccteslvnrrpcfsalevdetyvpkefnaetftfhadictl sekerqikkqtalvelvkhkpkatkeqlkavmddfaafvekcckaddke tcfaeegkklvaasqaalglHHHHHHHEPEA
161	ACP144 IL-2 融 合蛋白	mdmrvpaqllgllllwlrgarcaptssstkktqlqlehlldlqmilng innyknpkltrmltfkfympkkatelkhlqcleeelkpleevlnlaqsk nfhlrprdlisninvivlelkgsettfmceyadetativeflnrwitfc qsiistltSGGPGPAGMKGLPGSEVQLVESGGGLVQPGNSLRLSCAASG FTFSKFGMSWVRQAPGKGLEWVSSISGSGRDTLYAESVKGRFTISRDNA KTTLYLQMNSLRPEDTAVYYCTIGGSLSVSSQGTLVTVSSggggsgggg sggggsggggsggggsggggsSGGPGPAGMKGLPGSEVQLVESGGGLVQ PGGSLRLSCAASGFTFSSYTLAWVRQAPGKGLEWVAAIDSSSYTYSPDT VRGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARDSNWDALDYWGQGT TVTVSSGGGGSGGGGSGGGGSDIQMTQSPSSLSASVGDRVTITCKASQN VGTNVGWYQQKPGKAPKALIYSASFRYSGVPSRFSGSGSGTDFTLTISS LQPEDFATYYCQQYYTYPYTFGGGTKVEIKggggsggggsggggsQVQL QESGGGLAQAGGSLSLSCAASGFTVSNSVMAWYRQTPGKQREFVAIINS VGSTNYADSVKGRFTISRDNAKNTVYLQMNNLKPEDTAVYVCNRNFDRI YWGQGTQVTVSSHHHHHHHEPEA

[0527]

162	ACP145 IL-2 融合蛋白	mdmrvpaqllgllllwlrgarcQVQLQESGGGLAQAGGSLSLSCAASGF TVSNSVMAWYRQTPGKQREFVAIINSVGSTNYADSVKGRFTISRDNAKN TVYLQMNNLKPEDTAVYVCNRNFDRIYWGQGTQVTVSSggggsggggsg gggsaptssstkktqlqlehlldlqmilnginnyknpkltrmltfkfy mpkkatelkhlqcleeelkpleevlnlaqsknfhlrprdlisninvivl elkgsettfmceyadetativeflnrwitfcqsiistltSGGPGPAGMK GLPGSEVQLVESGGGLVQPGNSLRLSCAASGFTFSKFGMSWVRQAPGKG LEWVSSISGSGRDTLYAESVKGRFTISRDNAKTTLYLQMNSLRPEDTAV YYCTIGGSLSVSSQGTLVTVSSggggsggggsggggsggggsggggsgg ggsSGGPGPAGMKGLPGSEVQLVESGGGLVQPGGSLRLSCAASGFTFSS YTLAWVRQAPGKGLEWVAAIDSSSYTYSPDTVRGRFTISRDNAKNSLYL QMNSLRAEDTAVYYCARDSNWDALDYWGQGTTVTVSSGGGGSGGGGSGG GGSDIQMTQSPSSLSASVGDRVTITCKASQNVGTNVGWYQQKPGKAPKA LIYSASFRYSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQYYTYP YTFGGGTKVEIKHHHHHHHEPEA
163	ACP146 IL-2 融合蛋白	mdmrvpaqllgllllwlrgarcQVQLQESGGGLAQAGGSLSLSCAASGF TVSNSVMAWYRQTPGKQREFVAIINSVGSTNYADSVKGRFTISRDNAKN TVYLQMNNLKPEDTAVYVCNRNFDRIYWGQGTQVTVSSSGGPGPAGMKG LPGSaptssstkktqlqlehlldlqmilnginnyknpkltrmltfkfy mpkkatelkhlqcleeelkpleevlnlaqsknfhlrprdlisninvivl elkgsettfmceyadetativeflnrwitfcqsiistltSGGPGPAGMK GLPGSEVQLVESGGGLVQPGNSLRLSCAASGFTFSKFGMSWVRQAPGKG LEWVSSISGSGRDTLYAESVKGRFTISRDNAKTTLYLQMNSLRPEDTAV YYCTIGGSLSVSSQGTLVTVSSggggsggggsggggsggggsggggsgg ggsSGGPGPAGMKGLPGSEVQLVESGGGLVQPGGSLRLSCAASGFTFSS YTLAWVRQAPGKGLEWVAAIDSSSYTYSPDTVRGRFTISRDNAKNSLYL QMNSLRAEDTAVYYCARDSNWDALDYWGQGTTVTVSSGGGGSGGGGSGG GGSDIQMTQSPSSLSASVGDRVTITCKASQNVGTNVGWYQQKPGKAPKA LIYSASFRYSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQYYTYP YTFGGGTKVEIKHHHHHHHEPEA
164	ACP133 IL-2-6x His（“6xHis”公开为 SEQ	mdmrvpaqllgllllwlrgarcaptssstkktqlqlehlldlqmilng innyknpkltrmltfkfympkkatelkhlqcleeelkpleevlnlaqsk nfhlrprdlisninvivlelkgsettfmceyadetativeflnrwitfc qsiistltHHHHHH

	ID NO.：205)	
165	ACP147 IL-2 融合蛋白	mdmrvpaqllgllllwlrgarcaptssstkktqlqlehlldlqmilng innyknpkltrmltfkfympkkatelkhlqcleeelkpleevlnlaqsk nfhlrprdlisninvivlelkgsettfmceyadetativeflnrwitfc qsiistltSGGPGPAGMKGLPGSEVQLVESGGGLVQPGNSLRLSCAASG FTFSKFGMSWVRQAPGKGLEWVSSISGSGRDTLYAESVKGRFTISRDNA KTTLYLQMNSLRPEDTAVYYCTIGGSLSVSSQGTLVTVSSggggsgggg sggggsggggsggggsggggsSGGPGPAGMKGLPGSEVQLVESGGGLVQ PGGSLRLSCAASGFTFSSYTLAWVRQAPGKGLEWVAAIDSSSYTYSPDT VRGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARDSNWDALDYWGQGT TVTVSSGGGGSGGGGSGGGGSDIQMTQSPSSLSASVGDRVTITCKASQN VGTNVGWYQQKPGKAPKALIYSASFRYSGVPSRFSGSGSGTDFTLTISS LQPEDFATYYCQQYYTYPYTFGGGTKVEIKggggsggggsggggsQVQL QESGGGLVQAGGSLRLSCAASGRIFSIDIMSWYRQAPGKQRELVARITR GGTISYDDSVKGRFTISRDNAKNTVYLQMNSLKPEDTGVYYCNALYGTD YWGKGTQVTVSSHHHHHHHEPEA
166	ACP148 IL-2 融合蛋白	mdmrvpaqllgllllwlrgarcQVQLQESGGGLVQAGGSLRLSCAASGR IFSIDIMSWYRQAPGKQRELVARITRGGTISYDDSVKGRFTISRDNAKN TVYLQMNSLKPEDTGVYYCNALYGTDYWGKGTQVTVSSggggsggggsg gggsaptssstkktqlqlehlldlqmilnginnyknpkltrmltfkfy mpkkatelkhlqcleeelkpleevlnlaqsknfhlrprdlisninvivl elkgsettfmceyadetativeflnrwitfcqsiistltSGGPGPAGMK GLPGSEVQLVESGGGLVQPGNSLRLSCAASGFTFSKFGMSWVRQAPGKG LEWVSSISGSGRDTLYAESVKGRFTISRDNAKTTLYLQMNSLRPEDTAV YYCTIGGSLSVSSQGTLVTVSSggggsggggsggggsggggsggggsgg ggsSGGPGPAGMKGLPGSEVQLVESGGGLVQPGGSLRLSCAASGFTFSS YTLAWVRQAPGKGLEWVAAIDSSSYTYSPDTVRGRFTISRDNAKNSLYL QMNSLRAEDTAVYYCARDSNWDALDYWGQGTTVTVSSGGGGSGGGGSGG GGSDIQMTQSPSSLSASVGDRVTITCKASQNVGTNVGWYQQKPGKAPKA LIYSASFRYSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQYYTYP YTFGGGTKVEIKHHHHHHHEPEA
167	ACP149 IL-2 融合蛋白	mdmrvpaqllgllllwlrgarcQVQLQESGGGLVQAGGSLRLSCAASGR IFSIDIMSWYRQAPGKQRELVARITRGGTISYDDSVKGRFTISRDNAKN TVYLQMNSLKPEDTGVYYCNALYGTDYWGKGTQVTVSSSGGPGPAGMKG LPGSaptssstkktqlqlehlldlqmilnginnyknpkltrmltfkfy

[0528]

[0529]

		mpkkatelkhlqcleeelkpleevlnlaqsknfhlrprdlisninvivl elkgsettfmceyadetativeflnrwitfcqsiistltSGGPGPAGMK GLPGSEVQLVESGGGLVQPGNSLRLSCAASGFTFSKFGMSWVRQAPGKG LEWVSSISGSGRDTLYAESVKGRFTISRDNAKTTLYLQMNSLRPEDTAV YYCTIGGSLSVSSQGTLVTVSSggggsggggsggggsggggsggggsgg ggsSGGPGPAGMKGLPGSEVQLVESGGGLVQPGGSLRLSCAASGFTFSS YTLAWVRQAPGKGLEWVAAIDSSSYTYSPDTVRGRFTISRDNAKNSLYL QMNSLRAEDTAVYYCARDSNWDALDYWGQGTTVTVSSGGGGSGGGGSGG GGSDIQMTQSPSSLSASVGDRVTITCKASQNVGTNVGWYQQKPGKAPKA LIYSASFRYSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQYYTYP YTFGGGTKVEIKHHHHHHHEPEA
168	ACP33 小鼠 IFNa 融合蛋白	mdmrvpaqllgllllwlrgarcEVQLVESGGGLVQPGNSLRLSCAASGF TFSKFGMSWVRQAPGKGLEWVSSISGSGRDTLYAESVKGRFTISRDNAK TTLYLQMNSLRPEDTAVYYCTIGGSLSVSSQGTLVTVSSSGGPGPAGMK GLPGScdlpqthnlrnkraltllvqmrrlsplsclkdrkdfgfpqekvd aqqikkaqaipvlseltqqilniftskdssaawnttlldsfcndlhqql ndlqgclmqqvgvqefpltqedallavrkyfhritvylrekkhspcawe vvraevwralsssanvSGGPGPAGMKGLPGSEVQLVESGGGLVQPGNSL RLSCAASGFTFSKFGMSWVRQAPGKGLEWVSSISGSGRDTLYAESVKGR FTISRDNAKTTLYLQMNSLRPEDTAVYYCTIGGSLSVSSQGTLVTVSSH HHHHHEPEA
169	ACP131 小鼠 IFNa	mdmrvpaqllgllllwlrgarccdlpqthnlrnkraltllvqmrrlspl sclkdrkdfgfpqekvdaqqikkaqaipvlseltqqilniftskdssaa wnttlldsfcndlhqqlndlqgclmqqvgvqefpltqedallavrkyfh ritvylrekkhspcawevvraevwralsssanvlgrlreekHHHHHHHEP EA
170	ACP125 小鼠 IFNa 融合蛋白	mdmrvpaqllgllllwlrgarcEVQLVESGGGLVQPGNSLRLSCAASGF TFSKFGMSWVRQAPGKGLEWVSSISGSGRDTLYAESVKGRFTISRDNAK TTLYLQMNSLRPEDTAVYYCTIGGSLSVSSQGTLVTVSSSGGPGPAGMK GLPGScdlpqthnlrnkraltllvqmrrlsplsclkdrkdfgfpqekvd aqqikkaqaipvlseltqqilniftskdssaawnttlldsfcndlhqql ndlqgclmqqvgvqefpltqedallavrkyfhritvylrekkhspcawe vvraevwralsssanvlgrlreekHHHHHHHEPEA
171	ACP126 小鼠 IFNa 融	mdmrvpaqllgllllwlrgarccdlpqthnlrnkraltllvqmrrlspl sclkdrkdfgfpqekvdaqqikkaqaipvlseltqqilniftskdssaa wnttlldsfcndlhqqlndlqgclmqqvgvqefpltqedallavrkyfh

[0530]

	合蛋白	ritvylrekkhspcawevvraevwralsssanvlgrlreekSGGPGPAG MKGLPGSEVQLVESGGGLVQPGNSLRLSCAASGFTFSKFGMSWVRQAPG KGLEWVSSISGSGRDTLYAESVKGRFTISRDNAKTTLYLQMNSLRPEDT AVYYCTIGGSLSVSSQGTLVTVSSHHHHHHHEPEA
172	ACP127 小鼠 IFNa 融 合蛋白	mdmrvpaqllgllllwlrgarcEAHKSEIAHRYNDLGEQHFKGLVLIAF SQYLQKCSYDEHAKLVQEVTDFAKTCVADESAANCDKSLHTLFGDKLCA IPNLRENYGELADCCTKQEPERNECFLQHKDDNPSLPPFERPEAEAMCT SFKENPTTFMGHYLHEVARRHPYFYAPELLYYAEQYNEILTQCCAEADK ESCLTPKLDGVKEKALVSSVRQRMKCSSMQKFGERAFKAWAVARLSQTF PNADFAEITKLATDLTKVNKECCHGDLLECADDRAELAKYMCENQATIS SKLQTCCDKPLLKKAHCLSEVEHDTMPADLPAIAADFVEDQEVCKNYAE AKDVFLGTFLYEYSRRHPDYSVSLLLRLAKKYEATLEKCCAEANPPACY GTVLAEFQPLVEEPKNLVKTNCDLYEKLGEYGFQNAILVRYTQKAPQVS TPTLVEAARNLGRVGTKCCTLPEDQRLPCVEDYLSAILNRVCLLHEKTP VSEHVTKCCSGSLVERRPCFSALTVDETYVPKEFKAETFTFHSDICTLP EKEKQIKKQTALAELVKHKPKATAEQLKTVMDDFAQFLDTCCKAADKDT CFSTEGPNLVTRCKDALASGGPGPAGMKGLPGScdlpqthnlrnkralt llvqmrrlsplsclkdrkdfgfpqekvdaqqikkaqaipvlseltqqil niftskdssaawnttlldsfcndlhqqlndlqgclmqqvgvqefpltqe dallavrkyfhritvylrekkhspcawevvraevwralsssanvlgrlr eekSGGPGPAGMKGLPGSEAHKSEIAHRYNDLGEQHFKGLVLIAFSQYL QKCSYDEHAKLVQEVTDFAKTCVADESAANCDKSLHTLFGDKLCAIPNL RENYGELADCCTKQEPERNECFLQHKDDNPSLPPFERPEAEAMCTSFKE NPTTFMGHYLHEVARRHPYFYAPELLYYAEQYNEILTQCCAEADKESCL TPKLDGVKEKALVSSVRQRMKCSSMQKFGERAFKAWAVARLSQTFPNAD FAEITKLATDLTKVNKECCHGDLLECADDRAELAKYMCENQATISSKLQ TCCDKPLLKKAHCLSEVEHDTMPADLPAIAADFVEDQEVCKNYAEAKDV FLGTFLYEYSRRHPDYSVSLLLRLAKKYEATLEKCCAEANPPACYGTVL AEFQPLVEEPKNLVKTNCDLYEKLGEYGFQNAILVRYTQKAPQVSTPTL VEAARNLGRVGTKCCTLPEDQRLPCVEDYLSAILNRVCLLHEKTPVSEH VTKCCSGSLVERRPCFSALTVDETYVPKEFKAETFTFHSDICTLPEKEK QIKKQTALAELVKHKPKATAEQLKTVMDDFAQFLDTCCKAADKDTCFST EGPNLVTRCKDALAHHHHHHHEPEA
173	ACP128 小鼠 IFNa 融	mdmrvpaqllgllllwlrgarcEAHKSEIAHRYNDLGEQHFKGLVLIAF SQYLQKCSYDEHAKLVQEVTDFAKTCVADESAANCDKSLHTLFGDKLCA IPNLRENYGELADCCTKQEPERNECFLQHKDDNPSLPPFERPEAEAMCT

[0531]

	合蛋白	SFKENPTTFMGHYLHEVARRHPYFYAPELLYYAEQYNEILTQCCAEADK ESCLTPKLDGVKEKALVSSVRQRMKCSSMQKFGERAFKAWAVARLSQTF PNADFAEITKLATDLTKVNKECCHGDLLECADDRAELAKYMCENQATIS SKLQTCCDKPLLKKAHCLSEVEHDTMPADLPAIAADFVEDQEVCKNYAE AKDVFLGTFLYEYSRRHPDYSVSLLLRLAKKYEATLEKCCAEANPPACY GTVLAEFQPLVEEPKNLVKTNCDLYEKLGEYGFQNAILVRYTQKAPQVS TPTLVEAARNLGRVGTKCCTLPEDQRLPCVEDYLSAILNRVCLLHEKTP VSEHVTKCCSGSLVERRPCFSALTVDETYVPKEFKAETFTFHSDICTLP EKEKQIKKQTALAELVKHKPKATAEQLKTVMDDFAQFLDTCCKAADKDT CFSTEGPNLVTRCKDALASGGPGPAGMKGLPGScdlpqthnlrnkralt llvqmrrlsplsclkdrkdfgfpqekvdaqqikkaqaipvlseltqqil niftskdssaawnttlldsfcndlhqqlndlqgclmqqvgvqefpltqe dallavrkyfhritvylrekkhspcawevvraevwralsssanvlgrlr eekHHHHHHHEPEA
174	ACP129 小鼠 IFNa 融 合蛋白	mdmrvpaqllgllllwlrgarccdlpqthnlrnkraltllvqmrrlspl sclkdrkdfgfpqekvdaqqikkaqaipvlseltqqilniftskdssaa wnttlldsfcndlhqqlndlqgclmqqvgvqefpltqedallavrkyfh ritvylrekkhspcawevvraevwralsssanvlgrlreekSGGPGPAG MKGLPGSEAHKSEIAHRYNDLGEQHFKGLVLIAFSQYLQKCSYDEHAKL VQEVTDFAKTCVADESAANCDKSLHTLFGDKLCAIPNLRENYGELADCC TKQEPERNECFLQHKDDNPSLPPFERPEAEAMCTSFKENPTTFMGHYLH EVARRHPYFYAPELLYYAEQYNEILTQCCAEADKESCLTPKLDGVKEKA LVSSVRQRMKCSSMQKFGERAFKAWAVARLSQTFPNADFAEITKLATDL TKVNKECCHGDLLECADDRAELAKYMCENQATISSKLQTCCDKPLLKKA HCLSEVEHDTMPADLPAIAADFVEDQEVCKNYAEAKDVFLGTFLYEYSR RHPDYSVSLLLRLAKKYEATLEKCCAEANPPACYGTVLAEFQPLVEEPK NLVKTNCDLYEKLGEYGFQNAILVRYTQKAPQVSTPTLVEAARNLGRVG TKCCTLPEDQRLPCVEDYLSAILNRVCLLHEKTPVSEHVTKCCSGSLVE RRPCFSALTVDETYVPKEFKAETFTFHSDICTLPEKEKQIKKQTALAEL VKHKPKATAEQLKTVMDDFAQFLDTCCKAADKDTCFSTEGPNLVTRCKD ALAHHHHHHEPEA
175	ACP150 小鼠 IFNa 融 合蛋白	mdmrvpaqllgllllwlrgarcQVQLQESGGGLAQAGGSLSLSCAASGF TVSNSVMAWYRQTPGKQREFVAIINSVGSTNYADSVKGRFTISRDNAKN TVYLQMNNLKPEDTAVYVCNRNFDRIYWGQGTQVTVSSggggsggggsg gggsEVQLVESGGGLVQPGNSLRLSCAASGFTFSKFGMSWVRQAPGKGL EWVSSISGSGRDTLYAESVKGRFTISRDNAKTTLYLQMNSLRPEDTAVY

[0532]

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176	ACP151 小鼠 IFNa 融合蛋白	mdmrvpaqllgllllwlrgarcEVQLVESGGGLVQPGNSLRLSCAASGF TFSKFGMSWVRQAPGKGLEWVSSISGSGRDTLYAESVKGRFTISRDNAK TTLYLQMNSLRPEDTAVYYCTIGGSLSVSSQGTLVTVSSSGGPGPAGMK GLPGScdlpqthnlrnkraltllvqmrrlsplsclkdrkdfgfpqekvd aqqikkaqaipvlseltqqilniftskdssaawnttlldsfcndlhqql ndlqgclmqqvgvqefpltqedallavrkyfhritvylrekkhspcawe vvraevwralsssanvlgrlreekSGGPGPAGMKGLPGSEVQLVESGGG LVQPGNSLRLSCAASGFTFSKFGMSWVRQAPGKGLEWVSSISGSGRDTL YAESVKGRFTISRDNAKTTLYLQMNSLRPEDTAVYYCTIGGSLSVSSQG TLVTVSSggggsggggsggggsQVQLQESGGGLAQAGGSLSLSCAASGF TVSNSVMAWYRQTPGKQREFVAIINSVGSTNYADSVKGRFTISRDNAKN TVYLQMNNLKPEDTAVYVCNRNFDRIYWGQGTQVTVSSHHHHHHHEPEA
177	ACP152 小鼠 IFNa 融合蛋白	mdmrvpaqllgllllwlrgarcEVQLVESGGGLVQPGNSLRLSCAASGF TFSKFGMSWVRQAPGKGLEWVSSISGSGRDTLYAESVKGRFTISRDNAK TTLYLQMNSLRPEDTAVYYCTIGGSLSVSSQGTLVTVSSggggsggggs ggggscdlpqthnlrnkraltllvqmrrlsplsclkdrkdfgfpqekvd aqqikkaqaipvlseltqqilniftskdssaawnttlldsfcndlhqql ndlqgclmqqvgvqefpltqedallavrkyfhritvylrekkhspcawe vvraevwralsssanvlgrlreekggggsggggsggggsEVQLVESGGG LVQPGNSLRLSCAASGFTFSKFGMSWVRQAPGKGLEWVSSISGSGRDTL YAESVKGRFTISRDNAKTTLYLQMNSLRPEDTAVYYCTIGGSLSVSSQG TLVTVSSHHHHHHHEPEA
178	ACP153 (IL-2 缀合门)	mdmrvpaqllgllllwlrgarcaptssstkktqlqlehlllqlqmilng innyknpkltrmltfkfympkkatelkhlqcleeelkpleevlnlaqsk nfhlrprdlisninvivlelkgsettfmceyadetativeflnrwitfc qsiistltsggpGPAGLYAQpgsEVQLVESGGGLVQPGNSLRLSCAASG FTFSKFGMSWVRQAPGKGLEWVSSISGSGRDTLYAESVKGRFTISRDNA KTTLYLQMNSLRPEDTAVYYCTIGGSLSVSSQGTLVTVSSggggsggggs sggggsggggsggggsggggsggggsggpGPAGLYAQpgsEVQLVESGGGLVQ

		PGGSLRLSCAASGFTFSSYTLAWVRQAPGKGLEWVAAIDSSSYTYSPDT VRGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARDSNWDALDYWGQGT TVTVSSGGGGSGGGGSGGGGSDIQMTQSPSSLSASVGDRVTITCKASQN VGTNVGWYQQKPGKAPKALIYSASFRYSGVPSRFSGSGSGTDFTLTISS LQPEDFATYYCQQYYTYPYTFGGGTKVEIKHHHHHHHEPEA
179	ACP154 (IL-2 缀合门)	mdmrvpaqllgllllwlrgarcaptssstkktqlqlehlldlqmilng innyknpkltrmltfkfympkkatelkhlqcleeelkpleevlnlaqsk nfhlrprdlisninvivlelkgsettfmceyadetativeflnrwitfc qsiistltsggpPGGPAGIGpgsEVQLVESGGGLVQPGNSLRLSCAASG FTFSKFGMSWVRQAPGKGLEWVSSISGSGRDTLYAESVKGRFTISRDNA KTTLYLQMNSLRPEDTAVYYCTIGGSLSVSSQGTLVTVSSggggsgggg sggggsggggsggggsggggssggpPGGPAGIGpgsEVQLVESGGGLVQ PGGSLRLSCAASGFTFSSYTLAWVRQAPGKGLEWVAAIDSSSYTYSPDT VRGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARDSNWDALDYWGQGT TVTVSSGGGGSGGGGSGGGGSDIQMTQSPSSLSASVGDRVTITCKASQN VGTNVGWYQQKPGKAPKALIYSASFRYSGVPSRFSGSGSGTDFTLTISS LQPEDFATYYCQQYYTYPYTFGGGTKVEIKHHHHHHHEPEA
180	ACP155 (IL-2 缀合门)	mdmrvpaqllgllllwlrgarcaptssstkktqlqlehlldlqmilng innyknpkltrmltfkfympkkatelkhlqcleeelkpleevlnlaqsk nfhlrprdlisninvivlelkgsettfmceyadetativeflnrwitfc qsiistltsggpALFKSSFPpgsEVQLVESGGGLVQPGNSLRLSCAASG FTFSKFGMSWVRQAPGKGLEWVSSISGSGRDTLYAESVKGRFTISRDNA KTTLYLQMNSLRPEDTAVYYCTIGGSLSVSSQGTLVTVSSggggsgggg sggggsggggsggggsggggssggpALFKSSFPpgsEVQLVESGGGLVQ PGGSLRLSCAASGFTFSSYTLAWVRQAPGKGLEWVAAIDSSSYTYSPDT VRGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARDSNWDALDYWGQGT TVTVSSGGGGSGGGGSGGGGSDIQMTQSPSSLSASVGDRVTITCKASQN VGTNVGWYQQKPGKAPKALIYSASFRYSGVPSRFSGSGSGTDFTLTISS LQPEDFATYYCQQYYTYPYTFGGGTKVEIKHHHHHHHEPEA
181	ACP156 (IL-2 缀合门)	mdmrvpaqllgllllwlrgarcaptssstkktqlqlehlldlqmilng innyknpkltrmltfkfympkkatelkhlqcleeelkpleevlnlaqsk nfhlrprdlisninvivlelkgsettfmceyadetativeflnrwitfc qsiistltsggpPLAQKLKSSpgsEVQLVESGGGLVQPGNSLRLSCAAS GFTFSKFGMSWVRQAPGKGLEWVSSISGSGRDTLYAESVKGRFTISRDN AKTTLYLQMNSLRPEDTAVYYCTIGGSLSVSSQGTLVTVSSggggsggg gsggggsggggsggggsggggssggpPLAQKLKSSpgsEVQLVESGGGL

[0533]

[0534]

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182	ACP157 (IL-2 缀 合门)	mdmrvpaqllgllllwlrgarcaptssstkktqlqlehlldlqmilng innyknpkltrmltfkfympkkatelkhlqcleeelkpleevlnlaqsk nfhlrprdlisninvivlelkgsettfmceyadetativeflnrwitfc qsiistltsggpPGGPAGIGalfkssfpPLAQKLKSSpgsEVQLVESGG GLVQPGNSLRLSCAASGFTFSKFGMSWVRQAPGKGLEWVSSISGSGRDT LYAESVKGRFTISRDNAKTTLYLQMNSLRPEDTAVYYCTIGGSLSVSSQ GTLVTVSSggggsggggsggggsggggsggggsggggsggpPGGPAGI GalfkssfpPLAQKLKSSpgsEVQLVESGGGLVQPGGSLRLSCAASGFT FSSYTLAWVRQAPGKGLEWVAAIDSSSYTYSPDTVRGRFTISRDNAKNS LYLQMNSLRAEDTAVYYCARDSNWDALDYWGQGTTVTVSSGGGGSGGGG SGGGGSDIQMTQSPSSLSASVGDRVTITCKASQNVGTNVGWYQQKPGKA PKALIYSASFRYSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQYY TYPYTFGGGTKVEIKHHHHHHHEPEA
183	EGFR (G8)前 药 C1486	EVQLVESGGGLVQPGNSLRLSCAASGFTFSKFGMSWVRQGGGGGLDGNE EPGGLEWVSSISGSGRDTLYADSVKGRFTISRDNAKTTLYLQMNSLRPE DTAVYYCTIGGSLSVSSQGTLVTVSSGGGGKPLGLQARVVGGGGTQTVV TQEPSLTVSPGGTVTLTCASSTGAVTSGNYPNWVQQKPGQAPRGLIGGT KFLVPGTPARFSGSLLGGKAALTLSGVQPEDEAEYYCTLWYSNRWVFGG GTKLTVLGGGGSGGGGSGGGGSEVQLVESGGGLVQPGGSLKLSCAASGF TFNKYAINWVRQAPGKGLEWVARIRSKYNNYATYYADQVKDRFTISRDD SKNTAYLQMNNLKTEDTAVYYCVRHANFGNSYISYWAYWGQGTLVTVSS GGGGSGGGS*EVQLVESGGGLVQPGGSLTLSCAASGRTFSSYAMGWFRQA* *PGKEREFVVAINWASGSTYYADSVKGRFTISRDNSKNTLYLQMNSLRAE* *DTAVYYCAAGYQINSGNYNFKDYEYDYWGQGTLVTVSS*HHHHHH
184	EGFR (G8)不 可裂解 前药 C1756	EVQLVESGGGLVQPGNSLRLSCAASGFTFSKFGMSWVRQGGGGGLDGNE EPGGLEWVSSISGSGRDTLYADSVKGRFTISRDNAKTTLYLQMNSLRPE DTAVYYCTIGGSLSVSSQGTLVTVSSGGGGSGGGGSGGVVGGGGTQTVV TQEPSLTVSPGGTVTLTCASSTGAVTSGNYPNWVQQKPGQAPRGLIGGT KFLVPGTPARFSGSLLGGKAALTLSGVQPEDEAEYYCTLWYSNRWVFGG GTKLTVLGGGGSGGGGSGGGGSEVQLVESGGGLVQPGGSLKLSCAASGF TFNKYAINWVRQAPGKGLEWVARIRSKYNNYATYYADQVKDRFTISRDD

[0535]

		SKNTAYLQMNNLKTEDTAVYYCVRHANFGNSYISYWAYWGQGTLVTVSS GGGGSGGGS*EVQLVESGGGLVQPGGSLTLSCAASGRTFSSYAMGWFRQA PGKEREFVVAINWASGSTYYADSVKGRFTISRDNSKNTLYLQMNSLRAE DTAVYYCAAGYQINSGNYNFKDYEYDYWGQGTLVTVSS*HHHHHH
185	EGFR (G8)活性药物C1300	VVGGGGTQTVVTQEPSLTVSPGGTVTLTCASSTGAVTSGNYPNWVQQKP GQAPRGLIGGTKFLVPGTPARFSGSLLGGKAALTLSGVQPEDEAEYYCT LWYSNRWVFGGGTKLTVLGGGGSGGGGSGGGGSEVQLVESGGGLVQPGG SLKLSCAASGFTFNKYAINWVRQAPGKGLEWVARIRSKYNNYATYYADQ VKDRFTISRDDSKNTAYLQMNNLKTEDTAVYYCVRHANFGNSYISYWAY WGQGTLVTVSSGGGGSGGGS*EVQLVESGGGLVQPGGSLTLSCAASGRTF SSYAMGWFRQAPGKEREFVVAINWASGSTYYADSVKGRFTISRDNSKNT LYLQMNSLRAEDTAVYYCAAGYQINSGNYNFKDYEYDYWGQGTLVTVSS* HHHHHH
186	PSMA 前药 C1872	EVQLVESGGGLVQPGNSLRLSCAASGFTFSKFGMSWVRQGGGGGLDGNE EPGGLEWVSSISGSGRDTLYADSVKGRFTISRDNAKTTLYLQMNSLRPE DTAVYYCTIGGSLSVSSQGTLVTVSSGGGGKPLGLQARVVGGGGTQTVV TQEPSLTVSPGGTVTLTCASSTGAVTSGNYPNWVQQKPGQAPRGLIGGT KFLVPGTPARFSGSLLGGKAALTLSGVQPEDEAEYYCTLWYSNRWVFGG GTKLTVLGGGGSGGGGSGGGGSEVQLVESGGGLVQPGGSLKLSCAASGF TFNKYAINWVRQAPGKGLEWVARIRSKYNNYATYYADQVKDRFTISRDD SKNTAYLQMNNLKTEDTAVYYCVRHANFGNSYISYWAYWGQGTLVTVSS GGGGSGGGS*EVQLVESGGGLVQPGGSLTLSCAASRFMISEYHMHWVRQA PGKGLEWVSTINPAGTTDYAESVKGRFTISRDNAKNTLYLQMNSLKPED TAVYYCDSYGYRGQGTQVTVSS*HHHHHH
187	PSMA 不可裂解前药 C1873	EVQLVESGGGLVQPGNSLRLSCAASGFTFSKFGMSWVRQGGGGGLDGNE EPGGLEWVSSISGSGRDTLYADSVKGRFTISRDNAKTTLYLQMNSLRPE DTAVYYCTIGGSLSVSSQGTLVTVSSGGGGSGGGGSGGVVGGGGTQTVV TQEPSLTVSPGGTVTLTCASSTGAVTSGNYPNWVQQKPGQAPRGLIGGT KFLVPGTPARFSGSLLGGKAALTLSGVQPEDEAEYYCTLWYSNRWVFGG GTKLTVLGGGGSGGGGSGGGGSEVQLVESGGGLVQPGGSLKLSCAASGF TFNKYAINWVRQAPGKGLEWVARIRSKYNNYATYYADQVKDRFTISRDD SKNTAYLQMNNLKTEDTAVYYCVRHANFGNSYISYWAYWGQGTLVTVSS GGGGSGGGS*EVQLVESGGGLVQPGGSLTLSCAASRFMISEYHMHWVRQA PGKGLEWVSTINPAGTTDYAESVKGRFTISRDNAKNTLYLQMNSLKPED TAVYYCDSYGYRGQGTQVTVSS*HHHHHH
188	PSMA 活	VVGGGGTQTVVTQEPSLTVSPGGTVTLTCASSTGAVTSGNYPNWVQQKP

[0536]

	性药物 C1875	GQAPRGLIGGTKFLVPGTPARFSGSLLGGKAALTLSGVQPEDEAEYYCT LWYSNRWVFGGGTKLTVLGGGGSGGGGSGGGGSEVQLVESGGGLVQPGG SLKLSCAASGFTFNKYAINWVRQAPGKGLEWVARIRSKYNNYATYYADQ VKDRFTISRDDSKNTAYLQMNNLKTEDTAVYYCVRHANFGNSYISYWAY WGQGTLVTVSSGGGGSGGGS*EVQLVESGGGLVQPGGSLTLSCAASRFMI SEYHMHWVRQAPGKGLEWVSTINPAGTTDYAESVKGRFTISRDNAKNTL YLQMNSLKPEDTAVYYCDSYGYRGQGTQVTVSS*HHHHHH
189	GFP TriTAC C646	*QVQLVESGGALVQPGGSLRLSCAASGFPVNRYSMRWYRQAPGKEREWVA GMSSAGDRSSYEDSVKGRFTISRDDARNTVYLQMNSLKPEDTAVYYCNV NVGFEYWGQGTQVTVSS*GGGGSGGGSEVQLVESGGGLVQPGNSLRLSCA ASGFTFSKFGMSWVRQAPGKGLEWVSSISGSGRDTLYADSVKGRFTISR DNAKTTLYLQMNSLRPEDTAVYYCTIGGSLSVSSQGTLVTVSSGGGGSG GGSEVQLVESGGGLVQPGGSLKLSCAASGFTFNKYAINWVRQAPGKGLE WVARIRSKYNNYATYYADQVKDRFTISRDDSKNTAYLQMNNLKTEDTAV YYCVRHANFGNSYISYWAYWGQGTLVTVSSGGGGSGGGGSGGGGSQTVV TQEPSLTVSPGGTVTLTCASSTGAVTSGNYPNWVQQKPGQAPRGLIGGT KFLVPGTPARFSGSLLGGKAALTLSGVQPEDEAEYYCTLWYSNRWVFGG GTKLTVLHHHHHH
190	不可掩蔽/不可裂解的 TriTAC C1874	EVQLVESGGGLVQPGNSLRLSCAASGFTFSKFGMSWVRQAPGKGLEWVS SISGSGRDTLYADSVKGRFTISRDNAKTTLYLQMNSLRPEDTAVYYCTI GGSLSVSSQGTLVTVSSGGGGSGGGGSGGVVGGGGTQTVVTQEPSLTVS PGGTVTLTCASSTGAVTSGNYPNWVQQKPGQAPRGLIGGTKFLVPGTPA RFSGSLLGGKAALTLSGVQPEDEAEYYCTLWYSNRWVFGGGTKLTVLGG GGSGGGGSGGGGSEVQLVESGGGLVQPGGSLKLSCAASGFTFNKYAINW VRQAPGKGLEWVARIRSKYNNYATYYADQVKDRFTISRDDSKNTAYLQM NNLKTEDTAVYYCVRHANFGNSYISYWAYWGQGTLVTVSSGGGGSGGGS EVQLVESGGGLVQPGGSLTLSCAASRFMISEYHMHWVRQAPGKGLEWVS TINPAGTTDYAESVKGRFTISRDNAKNTLYLQMNSLKPEDTAVYYCDSY GYRGQGTQVTVSSHHHHHH
191	阻断剂 2 (IL2 阻断剂)	mdmrvpaqllgllllwlrgarcEVQLVESGGGLVQPGGSLRLSCAASGF TFSSYTLAWVRQAPGKGLEWVAAIDSSSYTYSPDTVRGRFTISRDNAKN SLYLQMNSLRAEDTAVYYCARDSNWDALDYWGQGTTVTVSSggggsggg gsggggsDIQMTQSPSSLSASVGDRVTITCKASQNVGTNVGWYQQKPGK APKALIYSASFRYSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQY YTYPYTFGGGTKVEIKHHHHHH
192	阻断剂	mdmrvpaqllgllllwlrgarcQSVLTQPPSVSGAPGQRVTISCSGSRS

[0537]

	12 (IL-12 阻断剂)	NIGSNTVKWYQQLPGTAPKLLIYYNDQRPSGVPDRFSGSKSGTSASLAI TGLQAEDEADYYCQSYDRYTHPALLFGTGTKVTVLggggsggggsgggg sQVQLVESGGGVVQPGRSLRLSCAASGFTFSSYGMHWVRQAPGKGLEWV AFIRYDGSNKYYADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCK THGSHDNWGQGTMVTVSSHHHHHH

[0538] 以引用的方式并入

[0539] 本文引用的所有专利和非专利出版物的全部公开内容各自出于所有目的以引用的方式整体并入本文。

[0540] 其他实施方案

[0541] 上文阐述的公开内容可包括具有独立效用的多种不同的发明。虽然已经以其一个或多个优选的形式公开了这些发明中的每一种,但是本文公开并例示的特定实施方案不应被认为是限制意义的,因为多种变化是可能的。本申请的主题包括本文所公开的各种元件、特征、功能和/或性质的全部新颖的和不明显的组合和子组合。以下权利要求特别指出被视为新颖的和不明显的某些组合和子组合。在本申请中、在要求本申请优先权的申请中或在相关申请中,可要求保护以特征、功能、元件和/或特性的其他组合和子组合体现的发明。此类权利要求与原始权利要求相比无论是针对不同的发明还是相同的发明,以及无论在范围上更宽、更窄、等同或不同都被认为包括在本申请的发明主题内。

序列表

<110> 狼人治疗公司

<120> 可活化细胞因子多肽及其使用方法

<130> 105365-0020

<140>

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<150> 62/756,507

<151> 2018-11-06

<150> 62/756,515

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<151> 2018-05-14

<160> 205

<170> PatentIn version 3.5

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<212> PRT

<213> 智人(Homo sapiens)

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50 55 60
Tyr Met Pro Lys Lys Ala Thr Glu Leu Lys His Leu Gln Cys Leu Glu
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85 90 95
Asn Phe His Leu Arg Pro Arg Asp Leu Ile Ser Asn Ile Asn Val Ile
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Val Leu Glu Leu Lys Gly Ser Glu Thr Thr Phe Met Cys Glu Tyr Ala
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130 135 140

Cys Gln Ser Ile Ile Ser Thr Leu Thr
145 150

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<211> 609
<212> PRT
<213> 智人(Homo sapiens)
<400> 2

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

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Lys Leu Val Thr Asp Leu Thr Lys Val His Thr Glu Cys Cys His Gly
260 265 270
Asp Leu Leu Glu Cys Ala Asp Asp Arg Ala Asp Leu Ala Lys Tyr Ile
275 280 285
Cys Glu Asn Gln Asp Ser Ile Ser Ser Lys Leu Lys Glu Cys Cys Glu
290 295 300
Lys Pro Leu Leu Glu Lys Ser His Cys Ile Ala Glu Val Glu Asn Asp
305 310 315 320
Glu Met Pro Ala Asp Leu Pro Ser Leu Ala Ala Asp Phe Val Gly Ser
325 330 335
Lys Asp Val Cys Lys Asn Tyr Ala Glu Ala Lys Asp Val Phe Leu Gly
340 345 350
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Val Arg Tyr Thr Lys Lys Val Pro Gln Val Ser Thr Pro Thr Leu Val
435 440 445
Glu Val Ser Arg Asn Leu Gly Lys Val Gly Ser Lys Cys Cys Lys His
450 455 460
Pro Glu Ala Lys Arg Met Pro Cys Ala Glu Asp Cys Leu Ser Val Phe
465 470 475 480
Leu Asn Gln Leu Cys Val Leu His Glu Lys Thr Pro Val Ser Asp Arg
485 490 495
Val Thr Lys Cys Cys Thr Glu Ser Leu Val Asn Gly Arg Pro Cys Phe
500 505 510
Ser Ala Leu Glu Val Asp Glu Thr Tyr Val Pro Lys Glu Phe Asn Ala
515 520 525
Glu Thr Phe Thr Phe His Ala Asp Ile Cys Thr Leu Ser Glu Lys Glu
530 535 540
Arg Gln Ile Lys Lys Gln Thr Ala Leu Val Glu Leu Val Lys His Lys
545 550 555 560

Pro Lys Ala Thr Lys Glu Gln Leu Lys Ala Val Met Asp Asp Phe Ala
565 570 575
Ala Phe Val Glu Lys Cys Cys Lys Ala Asp Asp Lys Glu Thr Cys Phe
580 585 590
Ala Glu Glu Gly Lys Lys Leu Val Ala Ala Ser Gln Ala Ala Leu Gly
595 600 605
Leu

<210> 3
<211> 8
<212> PRT
<213> 未知(Unknown)
<220>
<221> 来源
<223> /注释="未知描述：
MMP7裂解结构域序列"
<400> 3
Lys Arg Ala Leu Gly Leu Pro Gly
1 5

<210> 4
<211> 40
<212> PRT
<213> 未知(Unknown)
<220>
<221> 来源
<223> /注释="未知描述：
MMP7裂解结构域序列"
<400> 4
Asp Glu Asp Glu Asp Glu Asp Glu Asp Glu Asp Glu Asp Glu Asp Glu
1 5 10 15
Arg Pro Leu Ala Leu Trp Arg Ser Asp Arg Asp Arg Asp Arg Asp Arg
20 25 30
Asp Arg Asp Arg Asp Arg Asp Arg
35 40

<210> 5
<211> 5
<212> PRT
<213> 未知(Unknown)
<220>
<221> 来源

<223> /注释="未知描述：
MMP9裂解结构域序列"
<220>
<221> 变体
<222> (3)..(3)
<223> /置换="Thr"
<220>
<221> 变体
<222> (4)..(4)
<223> /置换="Ile"
<220>
<221> 变体
<222> (5)..(5)
<223> /置换="Thr"
<220>
<221> 位点
<222> (1)..(5)
<223> /注释="序列中给出的变体残基相对于变体位置的注释中的那些残基没有偏好"
<400> 5
Pro Arg Ser Leu Ser
1 5
<210> 6
<211> 5
<212> PRT
<213> 未知(Unknown)
<220>
<221> 来源
<223> /注释="未知描述：
MMP9裂解结构域序列"
<400> 6
Leu Glu Ala Thr Ala
1 5
<210> 7
<211> 10
<212> PRT
<213> 未知(Unknown)
<220>
<221> 来源

<223> /注释="未知描述：
MMP11裂解结构域序列"
<400> 7
Gly Gly Ala Ala Asn Leu Val Arg Gly Gly
1 5 10
<210> 8
<211> 10
<212> PRT
<213> 未知(Unknown)
<220>
<221> 来源
<223> /注释="未知描述：
MMP14裂解结构域序列"
<400> 8
Ser Gly Arg Ile Gly Phe Leu Arg Thr Ala
1 5 10
<210> 9
<211> 6
<212> PRT
<213> 未知(Unknown)
<220>
<221> 来源
<223> /注释="未知描述：
MMP裂解结构域序列"
<400> 9
Pro Leu Gly Leu Ala Gly
1 5
<210> 10
<211> 6
<212> PRT
<213> 未知(Unknown)
<220>
<221> 来源
<223> /注释="未知描述：
MMP裂解结构域序列"
<220>
<221> MOD_RES
<222> (6)..(6)
<223> 任何氨基酸

<400> 10
Pro Leu Gly Leu Ala Xaa
1 5
<210> 11
<211> 6
<212> PRT
<213> 未知(Unknown)
<220>
<221> 来源
<223> /注释="未知描述：
MMP裂解结构域序列"
<220>
<221> MOD_RES
<222> (4)..(4)
<223> Cys(me)
<400> 11
Pro Leu Gly Xaa Ala Gly
1 5
<210> 12
<211> 8
<212> PRT
<213> 未知(Unknown)
<220>
<221> 来源
<223> /注释="未知描述：
MMP裂解结构域序列"
<400> 12
Glu Ser Pro Ala Tyr Tyr Thr Ala
1 5
<210> 13
<211> 6
<212> PRT
<213> 未知(Unknown)
<220>
<221> 来源
<223> /注释="未知描述：
MMP裂解结构域序列"
<400> 13
Arg Leu Gln Leu Lys Leu

1 5

<210> 14

<211> 7

<212> PRT

<213> 未知(Unknown)

<220>

<221> 来源

<223> /注释="未知描述：
MMP裂解结构域序列"

<400> 14

Arg Leu Gln Leu Lys Ala Cys

1 5

<210> 15

<211> 7

<212> PRT

<213> 未知(Unknown)

<220>

<221> 来源

<223> /注释="未知描述：
MMP2、MMP9、MMP14裂解结构域序列"

<220>

<221> MOD_RES

<222> (3)..(3)

<223> Cit

<220>

<221> MOD_RES

<222> (5)..(5)

<223> Hof

<400> 15

Glu Pro Xaa Gly Xaa Tyr Leu

1 5

<210> 16

<211> 5

<212> PRT

<213> 未知(Unknown)

<220>

<221> 来源

<223> /注释="未知描述：
尿激酶纤溶酶原活化物(uPA)裂解结构域序列"

<400> 16
Ser Gly Arg Ser Ala
1 5
<210> 17
<211> 4
<212> PRT
<213> 未知(Unknown)
<220>
<221> 来源
<223> /注释="未知描述：
尿激酶纤溶酶原活化物(uPA)裂解结构域序列"
<400> 17
Asp Ala Phe Lys
1
<210> 18
<211> 5
<212> PRT
<213> 未知(Unknown)
<220>
<221> 来源
<223> /注释="未知描述：
尿激酶纤溶酶原活化物(uPA)裂解结构域序列"
<400> 18
Gly Gly Gly Arg Arg
1 5
<210> 19
<211> 4
<212> PRT
<213> 未知(Unknown)
<220>
<221> 来源
<223> /注释="未知描述：
溶酶体酶裂解结构域序列"
<400> 19
Gly Phe Leu Gly
1
<210> 20
<211> 4
<212> PRT

<213> 未知(Unknown)
<220>
<221> 来源
<223> /注释="未知描述：
溶酶体酶裂解结构域序列"
<400> 20
Ala Leu Ala Leu
1
<210> 21
<211> 2
<212> PRT
<213> 未知(Unknown)
<220>
<221> 来源
<223> /注释="未知描述：
溶酶体酶裂解结构域序列"
<400> 21
Phe Lys
1
<210> 22
<211> 3
<212> PRT
<213> 未知(Unknown)
<220>
<221> 来源
<223> /注释="未知描述：
组织蛋白酶B裂解结构域序列"
<400> 22
Asn Leu Leu
1
<210> 23
<211> 5
<212> PRT
<213> 未知(Unknown)
<220>
<221> 来源
<223> /注释="未知描述：
组织蛋白酶D裂解结构域序列"
<220>

<221> MOD_RES
<222> (3)..(3)
<223> Cys(Et)
<400> 23
Pro Ile Xaa Phe Phe
1 5
<210> 24
<211> 8
<212> PRT
<213> 未知(Unknown)
<220>
<221> 来源
<223> /注释="未知描述：
组织蛋白酶K裂解结构域序列"
<400> 24
Gly Gly Pro Arg Gly Leu Pro Gly
1 5
<210> 25
<211> 6
<212> PRT
<213> 未知(Unknown)
<220>
<221> 来源
<223> /注释="未知描述：
前列腺特异性抗原裂解结构域序列"
<400> 25
His Ser Ser Lys Leu Gln
1 5
<210> 26
<211> 7
<212> PRT
<213> 未知(Unknown)
<220>
<221> 来源
<223> /注释="未知描述：
前列腺特异性抗原裂解结构域序列"
<400> 26
His Ser Ser Lys Leu Gln Leu
1 5

<210> 27
<211> 9
<212> PRT
<213> 未知(Unknown)
<220>
<221> 来源
<223> /注释="未知描述：
前列腺特异性抗原裂解结构域序列"
<400> 27
His Ser Ser Lys Leu Gln Glu Asp Ala
1 5
<210> 28
<211> 10
<212> PRT
<213> 未知(Unknown)
<220>
<221> 来源
<223> /注释="未知描述：
单纯疱疹病毒蛋白酶裂解结构域序列"
<400> 28
Leu Val Leu Ala Ser Ser Ser Phe Gly Tyr
1 5 10
<210> 29
<211> 10
<212> PRT
<213> 未知(Unknown)
<220>
<221> 来源
<223> /注释="未知描述：
HIV蛋白酶裂解结构域序列"
<400> 29
Gly Val Ser Gln Asn Tyr Pro Ile Val Gly
1 5 10
<210> 30
<211> 10
<212> PRT
<213> 未知(Unknown)
<220>
<221> 来源

<223> /注释="未知描述：
CMV蛋白酶裂解结构域序列"
<400> 30
Gly Val Val Gln Ala Ser Cys Arg Leu Ala
1 5 10
<210> 31
<211> 4
<212> PRT
<213> 未知(Unknown)
<220>
<221> 来源
<223> /注释="未知描述：
凝血酶裂解结构域序列"
<220>
<221> MOD_RES
<222> (2)..(2)
<223> 2-羧基哌啶
<400> 31
Phe Xaa Arg Ser
1
<210> 32
<211> 6
<212> PRT
<213> 未知(Unknown)
<220>
<221> 来源
<223> /注释="未知描述：
凝血酶裂解结构域序列"
<400> 32
Asp Pro Arg Ser Phe Leu
1 5
<210> 33
<211> 6
<212> PRT
<213> 未知(Unknown)
<220>
<221> 来源
<223> /注释="未知描述：
凝血酶裂解结构域序列"

<400> 33
Pro Pro Arg Ser Phe Leu
1 5
<210> 34
<211> 4
<212> PRT
<213> 未知(Unknown)
<220>
<221> 来源
<223> /注释="未知描述：
半胱天冬酶-3裂解结构域序列"
<400> 34
Asp Glu Val Asp
1
<210> 35
<211> 5
<212> PRT
<213> 未知(Unknown)
<220>
<221> 来源
<223> /注释="未知描述：
半胱天冬酶-3裂解结构域序列"
<400> 35
Asp Glu Val Asp Pro
1 5
<210> 36
<211> 8
<212> PRT
<213> 未知(Unknown)
<220>
<221> 来源
<223> /注释="未知描述：
半胱天冬酶-3裂解结构域序列"
<400> 36
Lys Gly Ser Gly Asp Val Glu Gly
1 5
<210> 37
<211> 6
<212> PRT

<213> 未知(Unknown)
<220>
<221> 来源
<223> /注释="未知描述：
白介素1β转化酶裂解结构域序列"
<400> 37
Gly Trp Glu His Asp Gly
1 5
<210> 38
<211> 7
<212> PRT
<213> 未知(Unknown)
<220>
<221> 来源
<223> /注释="未知描述：
肠激酶裂解结构域序列"
<400> 38
Glu Asp Asp Asp Asp Lys Ala
1 5
<210> 39
<211> 9
<212> PRT
<213> 未知(Unknown)
<220>
<221> 来源
<223> /注释="未知描述：
FAP裂解结构域序列"
<400> 39
Lys Gln Glu Gln Asn Pro Gly Ser Thr
1 5
<210> 40
<211> 6
<212> PRT
<213> 未知(Unknown)
<220>
<221> 来源
<223> /注释="未知描述：
激肽释放酶2裂解结构域序列"
<400> 40

Gly Lys Ala Phe Arg Arg
1 5
<210> 41
<211> 4
<212> PRT
<213> 未知(Unknown)
<220>
<221> 来源
<223> /注释="未知描述：
纤溶酶裂解结构域序列"
<400> 41
Asp Ala Phe Lys
1
<210> 42
<211> 4
<212> PRT
<213> 未知(Unknown)
<220>
<221> 来源
<223> /注释="未知描述：
纤溶酶裂解结构域序列"
<400> 42
Asp Val Leu Lys
1
<210> 43
<211> 4
<212> PRT
<213> 未知(Unknown)
<220>
<221> 来源
<223> /注释="未知描述：
纤溶酶裂解结构域序列"
<400> 43
Asp Ala Phe Lys
1
<210> 44
<211> 7
<212> PRT
<213> 未知(Unknown)

<220>
<221> 来源
<223> /注释="未知描述：
TOP裂解结构域序列"
<400> 44
Ala Leu Leu Leu Ala Leu Leu
1 5
<210> 45
<211> 652
<212> PRT
<213> 人工序列(Artificial Sequence)
<220>
<221> 来源
<223> /注释="人工序列描述:合成多肽"
<400> 45
Gln Val Gln Leu Gln Glu Ser Gly Gly Gly Leu Val Gln Ala Gly Gly
1 5 10 15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Arg Ile Phe Ser Ile Asp
20 25 30
Ile Met Ser Trp Tyr Arg Gln Ala Pro Gly Lys Gln Arg Glu Leu Val
35 40 45
Ala Arg Ile Thr Arg Gly Gly Thr Ile Ser Tyr Asp Asp Ser Val Lys
50 55 60
Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Thr Val Tyr Leu
65 70 75 80
Gln Met Asn Ser Leu Lys Pro Glu Asp Thr Gly Val Tyr Tyr Cys Asn
85 90 95
Ala Leu Tyr Gly Thr Asp Tyr Trp Gly Lys Gly Thr Gln Val Thr Val
100 105 110
Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly
115 120 125
Ser Ala Pro Thr Ser Ser Ser Thr Lys Lys Thr Gln Leu Gln Leu Glu
130 135 140
His Leu Leu Leu Asp Leu Gln Met Ile Leu Asn Gly Ile Asn Asn Tyr
145 150 155 160
Lys Asn Pro Lys Leu Thr Arg Met Leu Thr Phe Lys Phe Tyr Met Pro
165 170 175
Lys Lys Ala Thr Glu Leu Lys His Leu Gln Cys Leu Glu Glu Glu Leu
180 185 190

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

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

<210> 46
<211> 652
<212> PRT
<213> 人工序列(Artificial Sequence)
<220>
<221> 来源
<223> /注释="人工序列描述:合成多肽"
<400> 46
Gln Val Gln Leu Gln Glu Ser Gly Gly Gly Leu Val Gln Ala Gly Gly
1 5 10 15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Arg Ile Phe Ser Ile Asp
20 25 30
Ile Met Ser Trp Tyr Arg Gln Ala Pro Gly Lys Gln Arg Glu Leu Val
35 40 45
Ala Arg Ile Thr Arg Gly Gly Thr Ile Ser Tyr Asp Asp Ser Val Lys
50 55 60
Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Thr Val Tyr Leu
65 70 75 80
Gln Met Asn Ser Leu Lys Pro Glu Asp Thr Gly Val Tyr Tyr Cys Asn
85 90 95

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

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

<210> 47
<211> 553
<212> PRT
<213> 人工序列(Artificial Sequence)
<220>
<221> 来源
<223> /注释="人工序列描述:合成多肽"
<400> 47

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

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

<210> 48
<211> 553
<212> PRT
<213> 人工序列(Artificial Sequence)
<220>
<221> 来源
<223> /注释="人工序列描述:合成多肽"
<400> 48

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

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

<210> 49
<211> 553
<212> PRT
<213> 人工序列(Artificial Sequence)
<220>
<221> 来源
<223> /注释="人工序列描述:合成多肽"
<400> 49

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

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

<210> 50
<211> 682
<212> PRT
<213> 人工序列(Artificial Sequence)
<220>
<221> 来源
<223> /注释="人工序列描述:合成多肽"
<400> 50

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

305 310 315 320
Gly Leu Glu Trp Val Ser Ser Ile Ser Gly Ser Gly Arg Asp Thr Leu
325 330 335
Tyr Ala Glu Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala
340 345 350
Lys Thr Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Pro Glu Asp Thr
355 360 365
Ala Val Tyr Tyr Cys Thr Ile Gly Gly Ser Leu Ser Val Ser Ser Gln
370 375 380
Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly
385 390 395 400
Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly
405 410 415
Ser Gly Gly Gly Gly Ser Ser Gly Gly Pro Gly Pro Ala Gly Met Lys
420 425 430
Gly Leu Pro Gly Ser Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu
435 440 445
Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe
450 455 460
Thr Phe Ser Ser Tyr Thr Leu Ala Trp Val Arg Gln Ala Pro Gly Lys
465 470 475 480
Gly Leu Glu Trp Val Ala Ala Ile Asp Ser Ser Ser Tyr Thr Tyr Ser
485 490 495
Pro Asp Thr Val Arg Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys
500 505 510
Asn Ser Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala
515 520 525
Val Tyr Tyr Cys Ala Arg Asp Ser Asn Trp Asp Ala Leu Asp Tyr Trp
530 535 540
Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly
545 550 555 560
Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Gln Met Thr Gln Ser
565 570 575
Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys
580 585 590
Lys Ala Ser Gln Asn Val Gly Thr Asn Val Gly Trp Tyr Gln Gln Lys
595 600 605
Pro Gly Lys Ala Pro Lys Ala Leu Ile Tyr Ser Ala Ser Phe Arg Tyr
610 615 620

Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe
625 630 635 640
Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr
645 650 655
Cys Gln Gln Tyr Tyr Thr Tyr Pro Tyr Thr Phe Gly Gly Gly Thr Lys
660 665 670
Val Glu Ile Lys His His His His His His
675 680

<210> 51
<211> 667
<212> PRT
<213> 人工序列(Artificial Sequence)
<220>
<221> 来源
<223> /注释="人工序列描述:合成多肽"
<400> 51
Gln Val Gln Leu Gln Glu Ser Gly Gly Gly Leu Val Gln Ala Gly Gly
1 5 10 15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Arg Ile Phe Ser Ile Asp
20 25 30
Ile Met Ser Trp Tyr Arg Gln Ala Pro Gly Lys Gln Arg Glu Leu Val
35 40 45
Ala Arg Ile Thr Arg Gly Gly Thr Ile Ser Tyr Asp Asp Ser Val Lys
50 55 60
Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Thr Val Tyr Leu
65 70 75 80
Gln Met Asn Ser Leu Lys Pro Glu Asp Thr Gly Val Tyr Tyr Cys Asn
85 90 95
Ala Leu Tyr Gly Thr Asp Tyr Trp Gly Lys Gly Thr Gln Val Thr Val
100 105 110
Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly
115 120 125
Ser Ala Pro Thr Ser Ser Ser Thr Lys Lys Thr Gln Leu Gln Leu Glu
130 135 140
His Leu Leu Leu Asp Leu Gln Met Ile Leu Asn Gly Ile Asn Asn Tyr
145 150 155 160
Lys Asn Pro Lys Leu Thr Arg Met Leu Thr Phe Lys Phe Tyr Met Pro
165 170 175
Lys Lys Ala Thr Glu Leu Lys His Leu Gln Cys Leu Glu Glu Glu Leu

180 185 190

Lys Pro Leu Glu Glu Val Leu Asn Leu Ala Gln Ser Lys Asn Phe His

195 200 205

Leu Arg Pro Arg Asp Leu Ile Ser Asn Ile Asn Val Ile Val Leu Glu

210 215 220

Leu Lys Gly Ser Glu Thr Thr Phe Met Cys Glu Tyr Ala Asp Glu Thr

225 230 235 240

Ala Thr Ile Val Glu Phe Leu Asn Arg Trp Ile Thr Phe Cys Gln Ser

245 250 255

Ile Ile Ser Thr Leu Thr Ser Gly Gly Pro Gly Pro Ala Gly Met Lys

260 265 270

Gly Leu Pro Gly Ser Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu

275 280 285

Val Gln Pro Gly Asn Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe

290 295 300

Thr Phe Ser Lys Phe Gly Met Ser Trp Val Arg Gln Ala Pro Gly Lys

305 310 315 320

Gly Leu Glu Trp Val Ser Ser Ile Ser Gly Ser Gly Arg Asp Thr Leu

325 330 335

Tyr Ala Glu Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala

340 345 350

Lys Thr Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Pro Glu Asp Thr

355 360 365

Ala Val Tyr Tyr Cys Thr Ile Gly Gly Ser Leu Ser Val Ser Ser Gln

370 375 380

Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly

385 390 395 400

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly

405 410 415

Ser Gly Gly Gly Gly Ser Glu Val Gln Leu Val Glu Ser Gly Gly Gly

420 425 430

Leu Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly

435 440 445

Phe Thr Phe Ser Ser Tyr Thr Leu Ala Trp Val Arg Gln Ala Pro Gly

450 455 460

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

465 470 475 480

Ser Pro Asp Thr Val Arg Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala

485 490 495

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

<210> 52
<211> 682
<212> PRT
<213> 人工序列(Artificial Sequence)
<220>
<221> 来源
<223> /注释="人工序列描述:合成多肽"
<400> 52
Ala Pro Thr Ser Ser Ser Thr Lys Lys Thr Gln Leu Gln Leu Glu His
1 5 10 15
Leu Leu Leu Asp Leu Gln Met Ile Leu Asn Gly Ile Asn Asn Tyr Lys
20 25 30
Asn Pro Lys Leu Thr Arg Met Leu Thr Phe Lys Phe Tyr Met Pro Lys
35 40 45
Lys Ala Thr Glu Leu Lys His Leu Gln Cys Leu Glu Glu Glu Leu Lys
50 55 60
Pro Leu Glu Glu Val Leu Asn Leu Ala Gln Ser Lys Asn Phe His Leu

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

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

<210> 53

<211> 393
<212> PRT
<213> 人工序列(Artificial Sequence)
<220>
<221> 来源
<223> /注释="人工序列描述:合成多肽"
<400> 53

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

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

<210> 54
<211> 423
<212> PRT
<213> 人工序列(Artificial Sequence)
<220>
<221> 来源
<223> /注释="人工序列描述:合成多肽"
<400> 54
Ala Pro Thr Ser Ser Ser Thr Lys Lys Thr Gln Leu Gln Leu Glu His
1 5 10 15
Leu Leu Leu Asp Leu Gln Met Ile Leu Asn Gly Ile Asn Asn Tyr Lys
20 25 30
Asn Pro Lys Leu Thr Arg Met Leu Thr Phe Lys Phe Tyr Met Pro Lys
35 40 45
Lys Ala Thr Glu Leu Lys His Leu Gln Cys Leu Glu Glu Glu Leu Lys
50 55 60
Pro Leu Glu Glu Val Leu Asn Leu Ala Gln Ser Lys Asn Phe His Leu
65 70 75 80
Arg Pro Arg Asp Leu Ile Ser Asn Ile Asn Val Ile Val Leu Glu Leu
85 90 95
Lys Gly Ser Glu Thr Thr Phe Met Cys Glu Tyr Ala Asp Glu Thr Ala

100 105 110

Thr Ile Val Glu Phe Leu Asn Arg Trp Ile Thr Phe Cys Gln Ser Ile

115 120 125

Ile Ser Thr Leu Thr Ser Gly Gly Pro Gly Pro Ala Gly Met Lys Gly

130 135 140

Leu Pro Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly

145 150 155 160

Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly

165 170 175

Gly Ser Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro

180 185 190

Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser

195 200 205

Ser Tyr Thr Leu Ala Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu

210 215 220

Trp Val Ala Ala Ile Asp Ser Ser Ser Tyr Thr Tyr Ser Pro Asp Thr

225 230 235 240

Val Arg Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu

245 250 255

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

260 265 270

Cys Ala Arg Asp Ser Asn Trp Asp Ala Leu Asp Tyr Trp Gly Gln Gly

275 280 285

Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly

290 295 300

Ser Gly Gly Gly Gly Ser Asp Ile Gln Met Thr Gln Ser Pro Ser Ser

305 310 315 320

Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Lys Ala Ser

325 330 335

Gln Asn Val Gly Thr Asn Val Gly Trp Tyr Gln Gln Lys Pro Gly Lys

340 345 350

Ala Pro Lys Ala Leu Ile Tyr Ser Ala Ser Phe Arg Tyr Ser Gly Val

355 360 365

Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr

370 375 380

Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln

385 390 395 400

Tyr Tyr Thr Tyr Pro Tyr Thr Phe Gly Gly Gly Thr Lys Val Glu Ile

405 410 415

Lys His His His His His His
420

<210> 55
<211> 682
<212> PRT
<213> 人工序列(Artificial Sequence)
<220>
<221> 来源
<223> /注释="人工序列描述:合成多肽"
<400> 55

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

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

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

<210> 56
<211> 682
<212> PRT
<213> 人工序列(Artificial Sequence)
<220>
<221> 来源
<223> /注释="人工序列描述:合成多肽"
<400> 56
Gln Val Gln Leu Gln Glu Ser Gly Gly Gly Leu Ala Gln Ala Gly Gly
1 5 10 15
Ser Leu Ser Leu Ser Cys Ala Ala Ser Gly Phe Thr Val Ser Asn Ser
20 25 30
Val Met Ala Trp Tyr Arg Gln Thr Pro Gly Lys Gln Arg Glu Phe Val
35 40 45
Ala Ile Ile Asn Ser Val Gly Ser Thr Asn Tyr Ala Asp Ser Val Lys
50 55 60
Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Thr Val Tyr Leu
65 70 75 80
Gln Met Asn Asn Leu Lys Pro Glu Asp Thr Ala Val Tyr Val Cys Asn
85 90 95
Arg Asn Phe Asp Arg Ile Tyr Trp Gly Gln Gly Thr Gln Val Thr Val

100 105 110
Ser Ser Ser Gly Gly Pro Gly Pro Ala Gly Met Lys Gly Leu Pro Gly
115 120 125
Ser Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly
130 135 140
Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser
145 150 155 160
Tyr Thr Leu Ala Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp
165 170 175
Val Ala Ala Ile Asp Ser Ser Ser Tyr Thr Tyr Ser Pro Asp Thr Val
180 185 190
Arg Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
195 200 205
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
210 215 220
Ala Arg Asp Ser Asn Trp Asp Ala Leu Asp Tyr Trp Gly Gln Gly Thr
225 230 235 240
Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
245 250 255
Gly Gly Gly Gly Ser Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu
260 265 270
Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Lys Ala Ser Gln
275 280 285
Asn Val Gly Thr Asn Val Gly Trp Tyr Gln Gln Lys Pro Gly Lys Ala
290 295 300
Pro Lys Ala Leu Ile Tyr Ser Ala Ser Phe Arg Tyr Ser Gly Val Pro
305 310 315 320
Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile
325 330 335
Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr
340 345 350
Tyr Thr Tyr Pro Tyr Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
355 360 365
Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
370 375 380
Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Ser Gly
385 390 395 400
Gly Pro Gly Pro Ala Gly Met Lys Gly Leu Pro Gly Ser Glu Val Gln
405 410 415

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

<210> 57
<211> 393
<212> PRT
<213> 人工序列(Artificial Sequence)
<220>

<221> 来源

<223> /注释="人工序列描述:合成多肽"

<400> 57

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

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

<210> 58
<211> 423
<212> PRT
<213> 人工序列(Artificial Sequence)
<220>
<221> 来源
<223> /注释="人工序列描述:合成多肽"
<400> 58
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20 25 30
Thr Leu Ala Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45
Ala Ala Ile Asp Ser Ser Ser Tyr Thr Tyr Ser Pro Asp Thr Val Arg
50 55 60
Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr Leu
65 70 75 80
Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala
85 90 95
Arg Asp Ser Asn Trp Asp Ala Leu Asp Tyr Trp Gly Gln Gly Thr Thr
100 105 110
Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
115 120 125
Gly Gly Gly Ser Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser

130 135 140

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

<210> 59
<211> 669

<212> PRT
<213> 人工序列(Artificial Sequence)
<220>
<221> 来源
<223> /注释="人工序列描述:合成多肽"
<400> 59

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

260 265 270

Gly Leu Pro Gly Ser Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu

275 280 285

Val Gln Pro Gly Asn Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe

290 295 300

Thr Phe Ser Lys Phe Gly Met Ser Trp Val Arg Gln Ala Pro Gly Lys

305 310 315 320

Gly Leu Glu Trp Val Ser Ser Ile Ser Gly Ser Gly Arg Asp Thr Leu

325 330 335

Tyr Ala Glu Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala

340 345 350

Lys Thr Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Pro Glu Asp Thr

355 360 365

Ala Val Tyr Tyr Cys Thr Ile Gly Gly Ser Leu Ser Val Ser Ser Gln

370 375 380

Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly

385 390 395 400

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Val Gln Leu

405 410 415

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

420 425 430

Ser Cys Lys Ala Ser Gly Tyr Ala Phe Thr Asn Tyr Leu Ile Glu Trp

435 440 445

Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile Gly Val Ile Asn

450 455 460

Pro Gly Ser Gly Gly Thr Asn Tyr Asn Glu Lys Phe Lys Gly Lys Ala

465 470 475 480

Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Ala Tyr Met Gln Leu Ser

485 490 495

Ser Leu Thr Ser Asp Asp Ser Ala Val Tyr Phe Cys Ala Arg Trp Arg

500 505 510

Gly Asp Gly Tyr Tyr Ala Tyr Phe Asp Val Trp Gly Ala Gly Thr Thr

515 520 525

Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly

530 535 540

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

545 550 555 560

Val Ser Leu Gly Gln Arg Ala Thr Ile Ser Cys Lys Ala Ser Gln Ser

565 570 575

Val Asp Tyr Asp Gly Asp Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro
580 585 590
Gly Gln Pro Pro Lys Leu Leu Ile Tyr Ala Ala Ser Asn Leu Glu Ser
595 600 605
Gly Ile Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr
610 615 620
Leu Asn Ile His Pro Val Glu Glu Glu Asp Ala Ala Thr Tyr Tyr Cys
625 630 635 640
Gln Gln Ser Asn Glu Asp Pro Tyr Thr Phe Gly Gly Gly Thr Lys Leu
645 650 655
Glu Ile Lys His His His His His His Glu Pro Glu Ala
660 665

<210> 60
<211> 669
<212> PRT
<213> 人工序列(Artificial Sequence)
<220>
<221> 来源
<223> /注释="人工序列描述:合成多肽"
<400> 60
Gln Val Gln Leu Gln Glu Ser Gly Gly Gly Leu Val Gln Ala Gly Gly
1 5 10 15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Arg Ile Phe Ser Ile Asp
20 25 30
Ile Met Ser Trp Tyr Arg Gln Ala Pro Gly Lys Gln Arg Glu Leu Val
35 40 45
Ala Arg Ile Thr Arg Gly Gly Thr Ile Ser Tyr Asp Asp Ser Val Lys
50 55 60
Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Thr Val Tyr Leu
65 70 75 80
Gln Met Asn Ser Leu Lys Pro Glu Asp Thr Gly Val Tyr Tyr Cys Asn
85 90 95
Ala Leu Tyr Gly Thr Asp Tyr Trp Gly Lys Gly Thr Gln Val Thr Val
100 105 110
Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly
115 120 125
Ser Ala Pro Thr Ser Ser Ser Thr Lys Lys Thr Gln Leu Gln Leu Glu
130 135 140
His Leu Leu Leu Asp Leu Gln Met Ile Leu Asn Gly Ile Asn Asn Tyr

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

Tyr Ala Ala Ser Asn Leu Glu Ser Gly Ile Pro Ala Arg Phe Ser Gly
465 470 475 480
Ser Gly Ser Gly Thr Asp Phe Thr Leu Asn Ile His Pro Val Glu Glu
485 490 495
Glu Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Ser Asn Glu Asp Pro Tyr
500 505 510
Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Gly Gly Gly Gly Ser
515 520 525
Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Val Gln Leu Gln Gln
530 535 540
Ser Gly Ala Glu Leu Val Arg Pro Gly Thr Ser Val Lys Val Ser Cys
545 550 555 560
Lys Ala Ser Gly Tyr Ala Phe Thr Asn Tyr Leu Ile Glu Trp Val Lys
565 570 575
Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile Gly Val Ile Asn Pro Gly
580 585 590
Ser Gly Gly Thr Asn Tyr Asn Glu Lys Phe Lys Gly Lys Ala Thr Leu
595 600 605
Thr Ala Asp Lys Ser Ser Ser Thr Ala Tyr Met Gln Leu Ser Ser Leu
610 615 620
Thr Ser Asp Asp Ser Ala Val Tyr Phe Cys Ala Arg Trp Arg Gly Asp
625 630 635 640
Gly Tyr Tyr Ala Tyr Phe Asp Val Trp Gly Ala Gly Thr Thr Val Thr
645 650 655
Val Ser Ser His His His His His His Glu Pro Glu Ala
660 665

<210> 61
<211> 689
<212> PRT
<213> 人工序列(Artificial Sequence)
<220>
<221> 来源
<223> /注释="人工序列描述:合成多肽"
<400> 61
Ala Pro Thr Ser Ser Ser Thr Lys Lys Thr Gln Leu Gln Leu Glu His
1 5 10 15
Leu Leu Leu Asp Leu Gln Met Ile Leu Asn Gly Ile Asn Asn Tyr Lys
20 25 30
Asn Pro Lys Leu Thr Arg Met Leu Thr Phe Lys Phe Tyr Met Pro Lys

35 40 45

Lys Ala Thr Glu Leu Lys His Leu Gln Cys Leu Glu Glu Glu Leu Lys
50 55 60

Pro Leu Glu Glu Val Leu Asn Leu Ala Gln Ser Lys Asn Phe His Leu
65 70 75 80

Arg Pro Arg Asp Leu Ile Ser Asn Ile Asn Val Ile Val Leu Glu Leu
85 90 95

Lys Gly Ser Glu Thr Thr Phe Met Cys Glu Tyr Ala Asp Glu Thr Ala
100 105 110

Thr Ile Val Glu Phe Leu Asn Arg Trp Ile Thr Phe Cys Gln Ser Ile
115 120 125

Ile Ser Thr Leu Thr Ser Gly Gly Pro Gly Pro Ala Gly Met Lys Gly
130 135 140

Leu Pro Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
145 150 155 160

Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Val Gln
165 170 175

Leu Gln Gln Ser Gly Ala Glu Leu Val Arg Pro Gly Thr Ser Val Lys
180 185 190

Val Ser Cys Lys Ala Ser Gly Tyr Ala Phe Thr Asn Tyr Leu Ile Glu
195 200 205

Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile Gly Val Ile
210 215 220

Asn Pro Gly Ser Gly Gly Thr Asn Tyr Asn Glu Lys Phe Lys Gly Lys
225 230 235 240

Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Ala Tyr Met Gln Leu
245 250 255

Ser Ser Leu Thr Ser Asp Asp Ser Ala Val Tyr Phe Cys Ala Arg Trp
260 265 270

Arg Gly Asp Gly Tyr Tyr Ala Tyr Phe Asp Val Trp Gly Ala Gly Thr
275 280 285

Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
290 295 300

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

Ala Val Ser Leu Gly Gln Arg Ala Thr Ile Ser Cys Lys Ala Ser Gln
325 330 335

Ser Val Asp Tyr Asp Gly Asp Ser Tyr Met Asn Trp Tyr Gln Gln Lys
340 345 350

Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr Ala Ala Ser Asn Leu Glu
355 360 365
Ser Gly Ile Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe
370 375 380
Thr Leu Asn Ile His Pro Val Glu Glu Glu Asp Ala Ala Thr Tyr Tyr
385 390 395 400
Cys Gln Gln Ser Asn Glu Asp Pro Tyr Thr Phe Gly Gly Gly Thr Lys
405 410 415
Leu Glu Ile Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
420 425 430
Gly Gly Ser Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln
435 440 445
Pro Gly Asn Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe
450 455 460
Ser Lys Phe Gly Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu
465 470 475 480
Glu Trp Val Ser Ser Ile Ser Gly Ser Gly Arg Asp Thr Leu Tyr Ala
485 490 495
Glu Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Thr
500 505 510
Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Val
515 520 525
Tyr Tyr Cys Thr Ile Gly Gly Ser Leu Ser Val Ser Ser Gln Gly Thr
530 535 540
Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
545 550 555 560
Gly Gly Gly Gly Ser Gln Val Gln Leu Gln Glu Ser Gly Gly Gly Leu
565 570 575
Val Gln Ala Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Arg
580 585 590
Ile Phe Ser Ile Asp Ile Met Ser Trp Tyr Arg Gln Ala Pro Gly Lys
595 600 605
Gln Arg Glu Leu Val Ala Arg Ile Thr Arg Gly Gly Thr Ile Ser Tyr
610 615 620
Asp Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys
625 630 635 640
Asn Thr Val Tyr Leu Gln Met Asn Ser Leu Lys Pro Glu Asp Thr Gly
645 650 655
Val Tyr Tyr Cys Asn Ala Leu Tyr Gly Thr Asp Tyr Trp Gly Lys Gly

660 665 670
Thr Gln Val Thr Val Ser Ser His His His His His His Glu Pro Glu
675 680 685
Ala
<210> 62
<211> 689
<212> PRT
<213> 人工序列(Artificial Sequence)
<220>
<221> 来源
<223> /注释="人工序列描述:合成多肽"
<400> 62
Ala Pro Thr Ser Ser Ser Thr Lys Lys Thr Gln Leu Gln Leu Glu His
1 5 10 15
Leu Leu Leu Asp Leu Gln Met Ile Leu Asn Gly Ile Asn Asn Tyr Lys
20 25 30
Asn Pro Lys Leu Thr Arg Met Leu Thr Phe Lys Phe Tyr Met Pro Lys
35 40 45
Lys Ala Thr Glu Leu Lys His Leu Gln Cys Leu Glu Glu Glu Leu Lys
50 55 60
Pro Leu Glu Glu Val Leu Asn Leu Ala Gln Ser Lys Asn Phe His Leu
65 70 75 80
Arg Pro Arg Asp Leu Ile Ser Asn Ile Asn Val Ile Val Leu Glu Leu
85 90 95
Lys Gly Ser Glu Thr Thr Phe Met Cys Glu Tyr Ala Asp Glu Thr Ala
100 105 110
Thr Ile Val Glu Phe Leu Asn Arg Trp Ile Thr Phe Cys Gln Ser Ile
115 120 125
Ile Ser Thr Leu Thr Ser Gly Gly Pro Gly Pro Ala Gly Met Lys Gly
130 135 140
Leu Pro Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
145 150 155 160
Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Val
165 170 175
Leu Thr Gln Ser Pro Ala Ser Leu Ala Val Ser Leu Gly Gln Arg Ala
180 185 190
Thr Ile Ser Cys Lys Ala Ser Gln Ser Val Asp Tyr Asp Gly Asp Ser
195 200 205
Tyr Met Asn Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro Lys Leu Leu

210 215 220

Ile Tyr Ala Ala Ser Asn Leu Glu Ser Gly Ile Pro Ala Arg Phe Ser
225 230 235 240

Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Asn Ile His Pro Val Glu
245 250 255

Glu Glu Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Ser Asn Glu Asp Pro
260 265 270

Tyr Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Gly Gly Gly Gly
275 280 285

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Val Gln Leu Gln
290 295 300

Gln Ser Gly Ala Glu Leu Val Arg Pro Gly Thr Ser Val Lys Val Ser
305 310 315 320

Cys Lys Ala Ser Gly Tyr Ala Phe Thr Asn Tyr Leu Ile Glu Trp Val
325 330 335

Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile Gly Val Ile Asn Pro
340 345 350

Gly Ser Gly Gly Thr Asn Tyr Asn Glu Lys Phe Lys Gly Lys Ala Thr
355 360 365

Leu Thr Ala Asp Lys Ser Ser Ser Thr Ala Tyr Met Gln Leu Ser Ser
370 375 380

Leu Thr Ser Asp Asp Ser Ala Val Tyr Phe Cys Ala Arg Trp Arg Gly
385 390 395 400

Asp Gly Tyr Tyr Ala Tyr Phe Asp Val Trp Gly Ala Gly Thr Thr Val
405 410 415

Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
420 425 430

Gly Gly Ser Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln
435 440 445

Pro Gly Asn Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe
450 455 460

Ser Lys Phe Gly Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu
465 470 475 480

Glu Trp Val Ser Ser Ile Ser Gly Ser Gly Arg Asp Thr Leu Tyr Ala
485 490 495

Glu Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Thr
500 505 510

Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Val
515 520 525

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

<210> 63
<211> 272
<212> PRT
<213> 未知(Unknown)
<220>
<221> 来源
<223> /注释="未知描述：
IL2Ra序列"
<400> 63

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

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

<210> 64
<211> 551
<212> PRT
<213> 未知(Unknown)
<220>
<221> 来源
<223> /注释="未知描述：
IL2Rb序列"
<400> 64

Met Ala Ala Pro Ala Leu Ser Trp Arg Leu Pro Leu Leu Ile Leu Leu
1 5 10 15
Leu Pro Leu Ala Thr Ser Trp Ala Ser Ala Ala Val Asn Gly Thr Ser
20 25 30
Gln Phe Thr Cys Phe Tyr Asn Ser Arg Ala Asn Ile Ser Cys Val Trp

35 40 45

Ser Gln Asp Gly Ala Leu Gln Asp Thr Ser Cys Gln Val His Ala Trp
50 55 60

Pro Asp Arg Arg Arg Trp Asn Gln Thr Cys Glu Leu Leu Pro Val Ser
65 70 75 80

Gln Ala Ser Trp Ala Cys Asn Leu Ile Leu Gly Ala Pro Asp Ser Gln
85 90 95

Lys Leu Thr Thr Val Asp Ile Val Thr Leu Arg Val Leu Cys Arg Glu
100 105 110

Gly Val Arg Trp Arg Val Met Ala Ile Gln Asp Phe Lys Pro Phe Glu
115 120 125

Asn Leu Arg Leu Met Ala Pro Ile Ser Leu Gln Val Val His Val Glu
130 135 140

Thr His Arg Cys Asn Ile Ser Trp Glu Ile Ser Gln Ala Ser His Tyr
145 150 155 160

Phe Glu Arg His Leu Glu Phe Glu Ala Arg Thr Leu Ser Pro Gly His
165 170 175

Thr Trp Glu Glu Ala Pro Leu Leu Thr Leu Lys Gln Lys Gln Glu Trp
180 185 190

Ile Cys Leu Glu Thr Leu Thr Pro Asp Thr Gln Tyr Glu Phe Gln Val
195 200 205

Arg Val Lys Pro Leu Gln Gly Glu Phe Thr Thr Trp Ser Pro Trp Ser
210 215 220

Gln Pro Leu Ala Phe Arg Thr Lys Pro Ala Ala Leu Gly Lys Asp Thr
225 230 235 240

Ile Pro Trp Leu Gly His Leu Leu Val Gly Leu Ser Gly Ala Phe Gly
245 250 255

Phe Ile Ile Leu Val Tyr Leu Leu Ile Asn Cys Arg Asn Thr Gly Pro
260 265 270

Trp Leu Lys Lys Val Leu Lys Cys Asn Thr Pro Asp Pro Ser Lys Phe
275 280 285

Phe Ser Gln Leu Ser Ser Glu His Gly Gly Asp Val Gln Lys Trp Leu
290 295 300

Ser Ser Pro Phe Pro Ser Ser Ser Phe Ser Pro Gly Gly Leu Ala Pro
305 310 315 320

Glu Ile Ser Pro Leu Glu Val Leu Glu Arg Asp Lys Val Thr Gln Leu
325 330 335

Leu Leu Gln Gln Asp Lys Val Pro Glu Pro Ala Ser Leu Ser Ser Asn
340 345 350

His Ser Leu Thr Ser Cys Phe Thr Asn Gln Gly Tyr Phe Phe Phe His
355 360 365
Leu Pro Asp Ala Leu Glu Ile Glu Ala Cys Gln Val Tyr Phe Thr Tyr
370 375 380
Asp Pro Tyr Ser Glu Glu Asp Pro Asp Glu Gly Val Ala Gly Ala Pro
385 390 395 400
Thr Gly Ser Ser Pro Gln Pro Leu Gln Pro Leu Ser Gly Glu Asp Asp
405 410 415
Ala Tyr Cys Thr Phe Pro Ser Arg Asp Asp Leu Leu Leu Phe Ser Pro
420 425 430
Ser Leu Leu Gly Gly Pro Ser Pro Pro Ser Thr Ala Pro Gly Gly Ser
435 440 445
Gly Ala Gly Glu Glu Arg Met Pro Pro Ser Leu Gln Glu Arg Val Pro
450 455 460
Arg Asp Trp Asp Pro Gln Pro Leu Gly Pro Pro Thr Pro Gly Val Pro
465 470 475 480
Asp Leu Val Asp Phe Gln Pro Pro Pro Glu Leu Val Leu Arg Glu Ala
485 490 495
Gly Glu Glu Val Pro Asp Ala Gly Pro Arg Glu Gly Val Ser Phe Pro
500 505 510
Trp Ser Arg Pro Pro Gly Gln Gly Glu Phe Arg Ala Leu Asn Ala Arg
515 520 525
Leu Pro Leu Asn Thr Asp Ala Tyr Leu Ser Leu Gln Glu Leu Gln Gly
530 535 540
Gln Asp Pro Thr His Leu Val
545 550

<210> 65
<211> 369
<212> PRT
<213> 未知(Unknown)
<220>
<221> 来源
<223> /注释="未知描述：
IL2Rg序列"
<400> 65

Met Leu Lys Pro Ser Leu Pro Phe Thr Ser Leu Leu Phe Leu Gln Leu
1 5 10 15
Pro Leu Leu Gly Val Gly Leu Asn Thr Thr Ile Leu Thr Pro Asn Gly
20 25 30

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

340 345 350
Gln His Ser Pro Tyr Trp Ala Pro Pro Cys Tyr Thr Leu Lys Pro Glu
355 360 365
Thr
<210> 66
<211> 520
<212> PRT
<213> 人工序列(Artificial Sequence)
<220>
<221> 来源
<223> /注释="人工序列描述:合成多肽"
<400> 66
Ile Trp Glu Leu Lys Lys Asp Val Tyr Val Val Glu Leu Asp Trp Tyr
1 5 10 15
Pro Asp Ala Pro Gly Glu Met Val Val Leu Thr Cys Asp Thr Pro Glu
20 25 30
Glu Asp Gly Ile Thr Trp Thr Leu Asp Gln Ser Ser Glu Val Leu Gly
35 40 45
Ser Gly Lys Thr Leu Thr Ile Gln Val Lys Glu Phe Gly Asp Ala Gly
50 55 60
Gln Tyr Thr Cys His Lys Gly Gly Glu Val Leu Ser His Ser Leu Leu
65 70 75 80
Leu Leu His Lys Lys Glu Asp Gly Ile Trp Ser Thr Asp Ile Leu Lys
85 90 95
Asp Gln Lys Glu Pro Lys Asn Lys Thr Phe Leu Arg Cys Glu Ala Lys
100 105 110
Asn Tyr Ser Gly Arg Phe Thr Cys Trp Trp Leu Thr Thr Ile Ser Thr
115 120 125
Asp Leu Thr Phe Ser Val Lys Ser Ser Arg Gly Ser Ser Asp Pro Gln
130 135 140
Gly Val Thr Cys Gly Ala Ala Thr Leu Ser Ala Glu Arg Val Arg Gly
145 150 155 160
Asp Asn Lys Glu Tyr Glu Tyr Ser Val Glu Cys Gln Glu Asp Ser Ala
165 170 175
Cys Pro Ala Ala Glu Glu Ser Leu Pro Ile Glu Val Met Val Asp Ala
180 185 190
Val His Lys Leu Lys Tyr Glu Asn Tyr Thr Ser Ser Phe Phe Ile Arg
195 200 205
Asp Ile Ile Lys Pro Asp Pro Pro Lys Asn Leu Gln Leu Lys Pro Leu

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

<210> 67
<211> 524
<212> PRT
<213> 人工序列(Artificial Sequence)
<220>
<221> 来源
<223> /注释="人工序列描述:合成多肽"
<400> 67

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

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

<210> 68
<211> 940
<212> PRT
<213> 人工序列(Artificial Sequence)

<220>

<221> 来源

<223> /注释="人工序列描述:合成多肽"

<400> 68

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

275 280 285

Glu Leu Lys Lys Asp Val Tyr Val Val Glu Leu Asp Trp Tyr Pro Asp

290 295 300

Ala Pro Gly Glu Met Val Val Leu Thr Cys Asp Thr Pro Glu Glu Asp

305 310 315 320

Gly Ile Thr Trp Thr Leu Asp Gln Ser Ser Glu Val Leu Gly Ser Gly

325 330 335

Lys Thr Leu Thr Ile Gln Val Lys Glu Phe Gly Asp Ala Gly Gln Tyr

340 345 350

Thr Cys His Lys Gly Gly Glu Val Leu Ser His Ser Leu Leu Leu Leu

355 360 365

His Lys Lys Glu Asp Gly Ile Trp Ser Thr Asp Ile Leu Lys Asp Gln

370 375 380

Lys Glu Pro Lys Asn Lys Thr Phe Leu Arg Cys Glu Ala Lys Asn Tyr

385 390 395 400

Ser Gly Arg Phe Thr Cys Trp Trp Leu Thr Thr Ile Ser Thr Asp Leu

405 410 415

Thr Phe Ser Val Lys Ser Ser Arg Gly Ser Ser Asp Pro Gln Gly Val

420 425 430

Thr Cys Gly Ala Ala Thr Leu Ser Ala Glu Arg Val Arg Gly Asp Asn

435 440 445

Lys Glu Tyr Glu Tyr Ser Val Glu Cys Gln Glu Asp Ser Ala Cys Pro

450 455 460

Ala Ala Glu Glu Ser Leu Pro Ile Glu Val Met Val Asp Ala Val His

465 470 475 480

Lys Leu Lys Tyr Glu Asn Tyr Thr Ser Ser Phe Phe Ile Arg Asp Ile

485 490 495

Ile Lys Pro Asp Pro Pro Lys Asn Leu Gln Leu Lys Pro Leu Lys Asn

500 505 510

Ser Arg Gln Val Glu Val Ser Trp Glu Tyr Pro Asp Thr Trp Ser Thr

515 520 525

Pro His Ser Tyr Phe Ser Leu Thr Phe Cys Val Gln Val Gln Gly Lys

530 535 540

Ser Lys Arg Glu Lys Lys Asp Arg Val Phe Thr Asp Lys Thr Ser Ala

545 550 555 560

Thr Val Ile Cys Arg Lys Asn Ala Ser Ile Ser Val Arg Ala Gln Asp

565 570 575

Arg Tyr Tyr Ser Ser Ser Trp Ser Glu Trp Ala Ser Val Pro Cys Ser

580 585 590

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Arg
595 600 605
Val Ile Pro Val Ser Gly Pro Ala Arg Cys Leu Ser Gln Ser Arg Asn
610 615 620
Leu Leu Lys Thr Thr Asp Asp Met Val Lys Thr Ala Arg Glu Lys Leu
625 630 635 640
Lys His Tyr Ser Cys Thr Ala Glu Asp Ile Asp His Glu Asp Ile Thr
645 650 655
Arg Asp Gln Thr Ser Thr Leu Lys Thr Cys Leu Pro Leu Glu Leu His
660 665 670
Lys Asn Glu Ser Cys Leu Ala Thr Arg Glu Thr Ser Ser Thr Thr Arg
675 680 685
Gly Ser Cys Leu Pro Pro Gln Lys Thr Ser Leu Met Met Thr Leu Cys
690 695 700
Leu Gly Ser Ile Tyr Glu Asp Leu Lys Met Tyr Gln Thr Glu Phe Gln
705 710 715 720
Ala Ile Asn Ala Ala Leu Gln Asn His Asn His Gln Gln Ile Ile Leu
725 730 735
Asp Lys Gly Met Leu Val Ala Ile Asp Glu Leu Met Gln Ser Leu Asn
740 745 750
His Asn Gly Glu Thr Leu Arg Gln Lys Pro Pro Val Gly Glu Ala Asp
755 760 765
Pro Tyr Arg Val Lys Met Lys Leu Cys Ile Leu Leu His Ala Phe Ser
770 775 780
Thr Arg Val Val Thr Ile Asn Arg Val Met Gly Tyr Leu Ser Ser Ala
785 790 795 800
Ser Gly Gly Pro Gly Pro Ala Gly Met Lys Gly Leu Pro Gly Ser Glu
805 810 815
Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Asn Ser
820 825 830
Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Lys Phe Gly
835 840 845
Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ser
850 855 860
Ser Ile Ser Gly Ser Gly Arg Asp Thr Leu Tyr Ala Glu Ser Val Lys
865 870 875 880
Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Thr Thr Leu Tyr Leu
885 890 895
Gln Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Val Tyr Tyr Cys Thr

900 905 910
Ile Gly Gly Ser Leu Ser Val Ser Ser Gln Gly Thr Leu Val Thr Val
915 920 925
Ser Ser His His His His His His Glu Pro Glu Ala
930 935 940
<210> 69
<211> 1069
<212> PRT
<213> 人工序列(Artificial Sequence)
<220>
<221> 来源
<223> /注释="人工序列描述:合成多肽"
<400> 69
Gln Ser Val Leu Thr Gln Pro Pro Ser Val Ser Gly Ala Pro Gly Gln
1 5 10 15
Arg Val Thr Ile Ser Cys Ser Gly Ser Arg Ser Asn Ile Gly Ser Asn
20 25 30
Thr Val Lys Trp Tyr Gln Gln Leu Pro Gly Thr Ala Pro Lys Leu Leu
35 40 45
Ile Tyr Tyr Asn Asp Gln Arg Pro Ser Gly Val Pro Asp Arg Phe Ser
50 55 60
Gly Ser Lys Ser Gly Thr Ser Ala Ser Leu Ala Ile Thr Gly Leu Gln
65 70 75 80
Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Gln Ser Tyr Asp Arg Tyr Thr
85 90 95
His Pro Ala Leu Leu Phe Gly Thr Gly Thr Lys Val Thr Val Leu Gly
100 105 110
Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Val
115 120 125
Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg Ser Leu
130 135 140
Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr Gly Met
145 150 155 160
His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala Phe
165 170 175
Ile Arg Tyr Asp Gly Ser Asn Lys Tyr Tyr Ala Asp Ser Val Lys Gly
180 185 190
Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr Leu Gln
195 200 205

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

515 520 525

Pro His Ser Tyr Phe Ser Leu Thr Phe Cys Val Gln Val Gln Gly Lys
530 535 540

Ser Lys Arg Glu Lys Lys Asp Arg Val Phe Thr Asp Lys Thr Ser Ala
545 550 555 560

Thr Val Ile Cys Arg Lys Asn Ala Ser Ile Ser Val Arg Ala Gln Asp
565 570 575

Arg Tyr Tyr Ser Ser Ser Trp Ser Glu Trp Ala Ser Val Pro Cys Ser
580 585 590

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Arg
595 600 605

Val Ile Pro Val Ser Gly Pro Ala Arg Cys Leu Ser Gln Ser Arg Asn
610 615 620

Leu Leu Lys Thr Thr Asp Asp Met Val Lys Thr Ala Arg Glu Lys Leu
625 630 635 640

Lys His Tyr Ser Cys Thr Ala Glu Asp Ile Asp His Glu Asp Ile Thr
645 650 655

Arg Asp Gln Thr Ser Thr Leu Lys Thr Cys Leu Pro Leu Glu Leu His
660 665 670

Lys Asn Glu Ser Cys Leu Ala Thr Arg Glu Thr Ser Ser Thr Thr Arg
675 680 685

Gly Ser Cys Leu Pro Pro Gln Lys Thr Ser Leu Met Met Thr Leu Cys
690 695 700

Leu Gly Ser Ile Tyr Glu Asp Leu Lys Met Tyr Gln Thr Glu Phe Gln
705 710 715 720

Ala Ile Asn Ala Ala Leu Gln Asn His Asn His Gln Gln Ile Ile Leu
725 730 735

Asp Lys Gly Met Leu Val Ala Ile Asp Glu Leu Met Gln Ser Leu Asn
740 745 750

His Asn Gly Glu Thr Leu Arg Gln Lys Pro Pro Val Gly Glu Ala Asp
755 760 765

Pro Tyr Arg Val Lys Met Lys Leu Cys Ile Leu Leu His Ala Phe Ser
770 775 780

Thr Arg Val Val Thr Ile Asn Arg Val Met Gly Tyr Leu Ser Ser Ala
785 790 795 800

Ser Gly Gly Pro Gly Pro Ala Gly Met Lys Gly Leu Pro Gly Ser Glu
805 810 815

Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Asn Ser
820 825 830

Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Lys Phe Gly
835 840 845
Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ser
850 855 860
Ser Ile Ser Gly Ser Gly Arg Asp Thr Leu Tyr Ala Glu Ser Val Lys
865 870 875 880
Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Thr Thr Leu Tyr Leu
885 890 895
Gln Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Val Tyr Tyr Cys Thr
900 905 910
Ile Gly Gly Ser Leu Ser Val Ser Ser Gln Gly Thr Leu Val Thr Val
915 920 925
Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly
930 935 940
Ser Gln Val Gln Leu Gln Glu Ser Gly Gly Gly Leu Ala Gln Ala Gly
945 950 955 960
Gly Ser Leu Ser Leu Ser Cys Ala Ala Ser Gly Phe Thr Val Ser Asn
965 970 975
Ser Val Met Ala Trp Tyr Arg Gln Thr Pro Gly Lys Gln Arg Glu Phe
980 985 990
Val Ala Ile Ile Asn Ser Val Gly Ser Thr Asn Tyr Ala Asp Ser Val
995 1000 1005
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Thr Val
1010 1015 1020
Tyr Leu Gln Met Asn Asn Leu Lys Pro Glu Asp Thr Ala Val Tyr
1025 1030 1035
Val Cys Asn Arg Asn Phe Asp Arg Ile Tyr Trp Gly Gln Gly Thr
1040 1045 1050
Gln Val Thr Val Ser Ser His His His His His His Glu Pro Glu
1055 1060 1065
Ala

<210> 70
<211> 1069
<212> PRT
<213> 人工序列(Artificial Sequence)
<220>
<221> 来源
<223> /注释="人工序列描述:合成多肽"
<400> 70

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

305 310 315 320
Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr Leu
325 330 335
Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Lys
340 345 350
Thr His Gly Ser His Asp Asn Trp Gly Gln Gly Thr Met Val Thr Val
355 360 365
Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly
370 375 380
Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
385 390 395 400
Ser Gly Gly Pro Gly Pro Ala Gly Met Lys Gly Leu Pro Gly Ser Ile
405 410 415
Trp Glu Leu Lys Lys Asp Val Tyr Val Val Glu Leu Asp Trp Tyr Pro
420 425 430
Asp Ala Pro Gly Glu Met Val Val Leu Thr Cys Asp Thr Pro Glu Glu
435 440 445
Asp Gly Ile Thr Trp Thr Leu Asp Gln Ser Ser Glu Val Leu Gly Ser
450 455 460
Gly Lys Thr Leu Thr Ile Gln Val Lys Glu Phe Gly Asp Ala Gly Gln
465 470 475 480
Tyr Thr Cys His Lys Gly Gly Glu Val Leu Ser His Ser Leu Leu Leu
485 490 495
Leu His Lys Lys Glu Asp Gly Ile Trp Ser Thr Asp Ile Leu Lys Asp
500 505 510
Gln Lys Glu Pro Lys Asn Lys Thr Phe Leu Arg Cys Glu Ala Lys Asn
515 520 525
Tyr Ser Gly Arg Phe Thr Cys Trp Trp Leu Thr Thr Ile Ser Thr Asp
530 535 540
Leu Thr Phe Ser Val Lys Ser Ser Arg Gly Ser Ser Asp Pro Gln Gly
545 550 555 560
Val Thr Cys Gly Ala Ala Thr Leu Ser Ala Glu Arg Val Arg Gly Asp
565 570 575
Asn Lys Glu Tyr Glu Tyr Ser Val Glu Cys Gln Glu Asp Ser Ala Cys
580 585 590
Pro Ala Ala Glu Glu Ser Leu Pro Ile Glu Val Met Val Asp Ala Val
595 600 605
His Lys Leu Lys Tyr Glu Asn Tyr Thr Ser Ser Phe Phe Ile Arg Asp
610 615 620

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

930 935 940
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Asn
945 950 955 960
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Lys Phe
965 970 975
Gly Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
980 985 990
Ser Ser Ile Ser Gly Ser Gly Arg Asp Thr Leu Tyr Ala Glu Ser Val
995 1000 1005
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Thr Thr Leu
1010 1015 1020
Tyr Leu Gln Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Val Tyr
1025 1030 1035
Tyr Cys Thr Ile Gly Gly Ser Leu Ser Val Ser Ser Gln Gly Thr
1040 1045 1050
Leu Val Thr Val Ser Ser His His His His His His Glu Pro Glu
1055 1060 1065
Ala

<210> 71
<211> 940
<212> PRT
<213> 人工序列(Artificial Sequence)
<220>
<221> 来源
<223> /注释="人工序列描述:合成多肽"
<400> 71
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Asn
1 5 10 15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Lys Phe
20 25 30
Gly Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45
Ser Ser Ile Ser Gly Ser Gly Arg Asp Thr Leu Tyr Ala Glu Ser Val
50 55 60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Thr Thr Leu Tyr
65 70 75 80
Leu Gln Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95
Thr Ile Gly Gly Ser Leu Ser Val Ser Ser Gln Gly Thr Leu Val Thr

100 105 110

Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly

115 120 125

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

130 135 140

Gly Gln Arg Val Thr Ile Ser Cys Ser Gly Ser Arg Ser Asn Ile Gly

145 150 155 160

Ser Asn Thr Val Lys Trp Tyr Gln Gln Leu Pro Gly Thr Ala Pro Lys

165 170 175

Leu Leu Ile Tyr Tyr Asn Asp Gln Arg Pro Ser Gly Val Pro Asp Arg

180 185 190

Phe Ser Gly Ser Lys Ser Gly Thr Ser Ala Ser Leu Ala Ile Thr Gly

195 200 205

Leu Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Gln Ser Tyr Asp Arg

210 215 220

Tyr Thr His Pro Ala Leu Leu Phe Gly Thr Gly Thr Lys Val Thr Val

225 230 235 240

Leu Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser

245 250 255

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

260 265 270

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr

275 280 285

Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val

290 295 300

Ala Phe Ile Arg Tyr Asp Gly Ser Asn Lys Tyr Tyr Ala Asp Ser Val

305 310 315 320

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr

325 330 335

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys

340 345 350

Lys Thr His Gly Ser His Asp Asn Trp Gly Gln Gly Thr Met Val Thr

355 360 365

Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly

370 375 380

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly

385 390 395 400

Ser Ser Gly Gly Pro Gly Pro Ala Gly Met Lys Gly Leu Pro Gly Ser

405 410 415

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

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

<210> 72
<211> 940
<212> PRT
<213> 人工序列(Artificial Sequence)
<220>
<221> 来源
<223> /注释="人工序列描述:合成多肽"
<400> 72
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Asn
1 5 10 15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Lys Phe
20 25 30

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

340 345 350

Pro Leu Lys Asn Ser Arg Gln Val Glu Val Ser Trp Glu Tyr Pro Asp
355 360 365

Thr Trp Ser Thr Pro His Ser Tyr Phe Ser Leu Thr Phe Cys Val Gln
370 375 380

Val Gln Gly Lys Ser Lys Arg Glu Lys Lys Asp Arg Val Phe Thr Asp
385 390 395 400

Lys Thr Ser Ala Thr Val Ile Cys Arg Lys Asn Ala Ser Ile Ser Val
405 410 415

Arg Ala Gln Asp Arg Tyr Tyr Ser Ser Ser Trp Ser Glu Trp Ala Ser
420 425 430

Val Pro Cys Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
435 440 445

Gly Gly Ser Arg Val Ile Pro Val Ser Gly Pro Ala Arg Cys Leu Ser
450 455 460

Gln Ser Arg Asn Leu Leu Lys Thr Thr Asp Asp Met Val Lys Thr Ala
465 470 475 480

Arg Glu Lys Leu Lys His Tyr Ser Cys Thr Ala Glu Asp Ile Asp His
485 490 495

Glu Asp Ile Thr Arg Asp Gln Thr Ser Thr Leu Lys Thr Cys Leu Pro
500 505 510

Leu Glu Leu His Lys Asn Glu Ser Cys Leu Ala Thr Arg Glu Thr Ser
515 520 525

Ser Thr Thr Arg Gly Ser Cys Leu Pro Pro Gln Lys Thr Ser Leu Met
530 535 540

Met Thr Leu Cys Leu Gly Ser Ile Tyr Glu Asp Leu Lys Met Tyr Gln
545 550 555 560

Thr Glu Phe Gln Ala Ile Asn Ala Ala Leu Gln Asn His Asn His Gln
565 570 575

Gln Ile Ile Leu Asp Lys Gly Met Leu Val Ala Ile Asp Glu Leu Met
580 585 590

Gln Ser Leu Asn His Asn Gly Glu Thr Leu Arg Gln Lys Pro Pro Val
595 600 605

Gly Glu Ala Asp Pro Tyr Arg Val Lys Met Lys Leu Cys Ile Leu Leu
610 615 620

His Ala Phe Ser Thr Arg Val Val Thr Ile Asn Arg Val Met Gly Tyr
625 630 635 640

Leu Ser Ser Ala Ser Gly Gly Pro Gly Pro Ala Gly Met Lys Gly Leu
645 650 655

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

<210> 73
<211> 940
<212> PRT

<213> 人工序列(Artificial Sequence)
<220>
<221> 来源
<223> /注释="人工序列描述:合成多肽"
<400> 73

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

Ser Ala Thr Val Ile Cys Arg Lys Asn Ala Ser Ile Ser Val Arg Ala
275 280 285
Gln Asp Arg Tyr Tyr Ser Ser Ser Trp Ser Glu Trp Ala Ser Val Pro
290 295 300
Cys Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly
305 310 315 320
Ser Arg Val Ile Pro Val Ser Gly Pro Ala Arg Cys Leu Ser Gln Ser
325 330 335
Arg Asn Leu Leu Lys Thr Thr Asp Asp Met Val Lys Thr Ala Arg Glu
340 345 350
Lys Leu Lys His Tyr Ser Cys Thr Ala Glu Asp Ile Asp His Glu Asp
355 360 365
Ile Thr Arg Asp Gln Thr Ser Thr Leu Lys Thr Cys Leu Pro Leu Glu
370 375 380
Leu His Lys Asn Glu Ser Cys Leu Ala Thr Arg Glu Thr Ser Ser Thr
385 390 395 400
Thr Arg Gly Ser Cys Leu Pro Pro Gln Lys Thr Ser Leu Met Met Thr
405 410 415
Leu Cys Leu Gly Ser Ile Tyr Glu Asp Leu Lys Met Tyr Gln Thr Glu
420 425 430
Phe Gln Ala Ile Asn Ala Ala Leu Gln Asn His Asn His Gln Gln Ile
435 440 445
Ile Leu Asp Lys Gly Met Leu Val Ala Ile Asp Glu Leu Met Gln Ser
450 455 460
Leu Asn His Asn Gly Glu Thr Leu Arg Gln Lys Pro Pro Val Gly Glu
465 470 475 480
Ala Asp Pro Tyr Arg Val Lys Met Lys Leu Cys Ile Leu Leu His Ala
485 490 495
Phe Ser Thr Arg Val Val Thr Ile Asn Arg Val Met Gly Tyr Leu Ser
500 505 510
Ser Ala Ser Gly Gly Pro Gly Pro Ala Gly Met Lys Gly Leu Pro Gly
515 520 525
Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
530 535 540
Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln
545 550 555 560
Ser Val Leu Thr Gln Pro Pro Ser Val Ser Gly Ala Pro Gly Gln Arg
565 570 575
Val Thr Ile Ser Cys Ser Gly Ser Arg Ser Asn Ile Gly Ser Asn Thr

580 585 590

Val Lys Trp Tyr Gln Gln Leu Pro Gly Thr Ala Pro Lys Leu Leu Ile

595 600 605

Tyr Tyr Asn Asp Gln Arg Pro Ser Gly Val Pro Asp Arg Phe Ser Gly

610 615 620

Ser Lys Ser Gly Thr Ser Ala Ser Leu Ala Ile Thr Gly Leu Gln Ala

625 630 635 640

Glu Asp Glu Ala Asp Tyr Tyr Cys Gln Ser Tyr Asp Arg Tyr Thr His

645 650 655

Pro Ala Leu Leu Phe Gly Thr Gly Thr Lys Val Thr Val Leu Gly Gly

660 665 670

Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Val Gln

675 680 685

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

690 695 700

Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr Gly Met His

705 710 715 720

Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala Phe Ile

725 730 735

Arg Tyr Asp Gly Ser Asn Lys Tyr Tyr Ala Asp Ser Val Lys Gly Arg

740 745 750

Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr Leu Gln Met

755 760 765

Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Lys Thr His

770 775 780

Gly Ser His Asp Asn Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser

785 790 795 800

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu

805 810 815

Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Asn Ser

820 825 830

Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Lys Phe Gly

835 840 845

Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ser

850 855 860

Ser Ile Ser Gly Ser Gly Arg Asp Thr Leu Tyr Ala Glu Ser Val Lys

865 870 875 880

Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Thr Thr Leu Tyr Leu

885 890 895

Gln Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Val Tyr Tyr Cys Thr
900 905 910
Ile Gly Gly Ser Leu Ser Val Ser Ser Gln Gly Thr Leu Val Thr Val
915 920 925
Ser Ser His His His His His His Glu Pro Glu Ala
930 935 940

<210> 74
<211> 328
<212> PRT
<213> 智人(Homo sapiens)
<400> 74

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

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

<210> 75
<211> 215
<212> PRT
<213> 小家鼠(Mus musculus)
<400> 75
Met Cys Gln Ser Arg Tyr Leu Leu Phe Leu Ala Thr Leu Ala Leu Leu
1 5 10 15
Asn His Leu Ser Leu Ala Arg Val Ile Pro Val Ser Gly Pro Ala Arg
20 25 30
Cys Leu Ser Gln Ser Arg Asn Leu Leu Lys Thr Thr Asp Asp Met Val
35 40 45
Lys Thr Ala Arg Glu Lys Leu Lys His Tyr Ser Cys Thr Ala Glu Asp
50 55 60
Ile Asp His Glu Asp Ile Thr Arg Asp Gln Thr Ser Thr Leu Lys Thr
65 70 75 80
Cys Leu Pro Leu Glu Leu His Lys Asn Glu Ser Cys Leu Ala Thr Arg
85 90 95
Glu Thr Ser Ser Thr Thr Arg Gly Ser Cys Leu Pro Pro Gln Lys Thr
100 105 110
Ser Leu Met Met Thr Leu Cys Leu Gly Ser Ile Tyr Glu Asp Leu Lys
115 120 125
Met Tyr Gln Thr Glu Phe Gln Ala Ile Asn Ala Ala Leu Gln Asn His
130 135 140
Asn His Gln Gln Ile Ile Leu Asp Lys Gly Met Leu Val Ala Ile Asp
145 150 155 160

Glu Leu Met Gln Ser Leu Asn His Asn Gly Glu Thr Leu Arg Gln Lys
165 170 175
Pro Pro Val Gly Glu Ala Asp Pro Tyr Arg Val Lys Met Lys Leu Cys
180 185 190
Ile Leu Leu His Ala Phe Ser Thr Arg Val Val Thr Ile Asn Arg Val
195 200 205
Met Gly Tyr Leu Ser Ser Ala
210 215

<210> 76
<211> 862
<212> PRT
<213> 未知(Unknown)
<220>
<221> 来源
<223> /注释="未知描述：
IL12Rb-2序列"
<400> 76

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

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

485 490 495

Ile Arg Val Tyr Ala Leu Ser Gly Asp Gln Gly Gly Cys Ser Ser Ile

500 505 510

Leu Gly Asn Ser Lys His Lys Ala Pro Leu Ser Gly Pro His Ile Asn

515 520 525

Ala Ile Thr Glu Glu Lys Gly Ser Ile Leu Ile Ser Trp Asn Ser Ile

530 535 540

Pro Val Gln Glu Gln Met Gly Cys Leu Leu His Tyr Arg Ile Tyr Trp

545 550 555 560

Lys Glu Arg Asp Ser Asn Ser Gln Pro Gln Leu Cys Glu Ile Pro Tyr

565 570 575

Arg Val Ser Gln Asn Ser His Pro Ile Asn Ser Leu Gln Pro Arg Val

580 585 590

Thr Tyr Val Leu Trp Met Thr Ala Leu Thr Ala Ala Gly Glu Ser Ser

595 600 605

His Gly Asn Glu Arg Glu Phe Cys Leu Gln Gly Lys Ala Asn Trp Met

610 615 620

Ala Phe Val Ala Pro Ser Ile Cys Ile Ala Ile Ile Met Val Gly Ile

625 630 635 640

Phe Ser Thr His Tyr Phe Gln Gln Lys Val Phe Val Leu Leu Ala Ala

645 650 655

Leu Arg Pro Gln Trp Cys Ser Arg Glu Ile Pro Asp Pro Ala Asn Ser

660 665 670

Thr Cys Ala Lys Lys Tyr Pro Ile Ala Glu Glu Lys Thr Gln Leu Pro

675 680 685

Leu Asp Arg Leu Leu Ile Asp Trp Pro Thr Pro Glu Asp Pro Glu Pro

690 695 700

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

705 710 715 720

Pro Pro Cys Ser Asn Trp Pro Gln Arg Glu Lys Gly Ile Gln Gly His

725 730 735

Gln Ala Ser Glu Lys Asp Met Met His Ser Ala Ser Ser Pro Pro Pro

740 745 750

Pro Arg Ala Leu Gln Ala Glu Ser Arg Gln Leu Val Asp Leu Tyr Lys

755 760 765

Val Leu Glu Ser Arg Gly Ser Asp Pro Lys Pro Glu Asn Pro Ala Cys

770 775 780

Pro Trp Thr Val Leu Pro Ala Gly Asp Leu Pro Thr His Asp Gly Tyr

785 790 795 800

Leu Pro Ser Asn Ile Asp Asp Leu Pro Ser His Glu Ala Pro Leu Ala
805 810 815
Asp Ser Leu Glu Glu Leu Glu Pro Gln His Ile Ser Leu Ser Val Phe
820 825 830
Pro Ser Ser Ser Leu His Pro Leu Thr Phe Ser Cys Gly Asp Lys Leu
835 840 845
Thr Leu Asp Gln Leu Lys Met Arg Cys Asp Ser Leu Met Leu
850 855 860

<210> 77
<211> 662
<212> PRT
<213> 未知(Unknown)
<220>
<221> 来源
<223> /注释="未知描述：
IL12Rb-1序列"
<400> 77

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

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

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

<210> 78
<211> 328
<212> PRT
<213> 智人(Homo sapiens)
<400> 78
Met Cys His Gln Gln Leu Val Ile Ser Trp Phe Ser Leu Val Phe Leu
1 5 10 15
Ala Ser Pro Leu Val Ala Ile Trp Glu Leu Lys Lys Asp Val Tyr Val
20 25 30
Val Glu Leu Asp Trp Tyr Pro Asp Ala Pro Gly Glu Met Val Val Leu
35 40 45
Thr Cys Asp Thr Pro Glu Glu Asp Gly Ile Thr Trp Thr Leu Asp Gln
50 55 60
Ser Ser Glu Val Leu Gly Ser Gly Lys Thr Leu Thr Ile Gln Val Lys
65 70 75 80
Glu Phe Gly Asp Ala Gly Gln Tyr Thr Cys His Lys Gly Gly Glu Val

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

<210> 79
<211> 335
<212> PRT
<213> 小家鼠(Mus musculus)
<400> 79
Met Cys Pro Gln Lys Leu Thr Ile Ser Trp Phe Ala Ile Val Leu Leu
1 5 10 15
Val Ser Pro Leu Met Ala Met Trp Glu Leu Glu Lys Asp Val Tyr Val

20 25 30

Val Glu Val Asp Trp Thr Pro Asp Ala Pro Gly Glu Thr Val Asn Leu
35 40 45

Thr Cys Asp Thr Pro Glu Glu Asp Asp Ile Thr Trp Thr Ser Asp Gln
50 55 60

Arg His Gly Val Ile Gly Ser Gly Lys Thr Leu Thr Ile Thr Val Lys
65 70 75 80

Glu Phe Leu Asp Ala Gly Gln Tyr Thr Cys His Lys Gly Gly Glu Thr
85 90 95

Leu Ser His Ser His Leu Leu Leu His Lys Lys Glu Asn Gly Ile Trp
100 105 110

Ser Thr Glu Ile Leu Lys Asn Phe Lys Asn Lys Thr Phe Leu Lys Cys
115 120 125

Glu Ala Pro Asn Tyr Ser Gly Arg Phe Thr Cys Ser Trp Leu Val Gln
130 135 140

Arg Asn Met Asp Leu Lys Phe Asn Ile Lys Ser Ser Ser Ser Ser Pro
145 150 155 160

Asp Ser Arg Ala Val Thr Cys Gly Met Ala Ser Leu Ser Ala Glu Lys
165 170 175

Val Thr Leu Asp Gln Arg Asp Tyr Glu Lys Tyr Ser Val Ser Cys Gln
180 185 190

Glu Asp Val Thr Cys Pro Thr Ala Glu Glu Thr Leu Pro Ile Glu Leu
195 200 205

Ala Leu Glu Ala Arg Gln Gln Asn Lys Tyr Glu Asn Tyr Ser Thr Ser
210 215 220

Phe Phe Ile Arg Asp Ile Ile Lys Pro Asp Pro Pro Lys Asn Leu Gln
225 230 235 240

Met Lys Pro Leu Lys Asn Ser Gln Val Glu Val Ser Trp Glu Tyr Pro
245 250 255

Asp Ser Trp Ser Thr Pro His Ser Tyr Phe Ser Leu Lys Phe Phe Val
260 265 270

Arg Ile Gln Arg Lys Lys Glu Lys Met Lys Glu Thr Glu Glu Gly Cys
275 280 285

Asn Gln Lys Gly Ala Phe Leu Val Glu Lys Thr Ser Thr Glu Val Gln
290 295 300

Cys Lys Gly Gly Asn Val Cys Val Gln Ala Gln Asp Arg Tyr Tyr Asn
305 310 315 320

Ser Ser Cys Ser Lys Trp Ala Cys Val Pro Cys Arg Val Arg Ser
325 330 335

<210> 80
<211> 399
<212> PRT
<213> 人工序列(Artificial Sequence)
<220>
<221> 来源
<223> /注释="人工序列描述:合成多肽"
<400> 80

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

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

<210> 81
<211> 547
<212> PRT
<213> 人工序列(Artificial Sequence)
<220>
<221> 来源
<223> /注释="人工序列描述:合成多肽"
<400> 81
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Asn
1 5 10 15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Lys Phe
20 25 30
Gly Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45
Ser Ser Ile Ser Gly Ser Gly Arg Asp Thr Leu Tyr Ala Glu Ser Val
50 55 60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Thr Thr Leu Tyr
65 70 75 80
Leu Gln Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

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

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

<210> 82
<211> 547
<212> PRT
<213> 人工序列(Artificial Sequence)
<220>
<221> 来源
<223> /注释="人工序列描述:合成多肽"
<400> 82
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Asn
1 5 10 15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Lys Phe
20 25 30
Gly Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45
Ser Ser Ile Ser Gly Ser Gly Arg Asp Thr Leu Tyr Ala Glu Ser Val
50 55 60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Thr Thr Leu Tyr
65 70 75 80
Leu Gln Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

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

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

<210> 83
<211> 166
<212> PRT
<213> 智人(Homo sapiens)
<400> 83
Met Lys Tyr Thr Ser Tyr Ile Leu Ala Phe Gln Leu Cys Ile Val Leu
1 5 10 15
Gly Ser Leu Gly Cys Tyr Cys Gln Asp Pro Tyr Val Lys Glu Ala Glu
20 25 30
Asn Leu Lys Lys Tyr Phe Asn Ala Gly His Ser Asp Val Ala Asp Asn
35 40 45
Gly Thr Leu Phe Leu Gly Ile Leu Lys Asn Trp Lys Glu Glu Ser Asp
50 55 60
Arg Lys Ile Met Gln Ser Gln Ile Val Ser Phe Tyr Phe Lys Leu Phe
65 70 75 80
Lys Asn Phe Lys Asp Asp Gln Ser Ile Gln Lys Ser Val Glu Thr Ile
85 90 95
Lys Glu Asp Met Asn Val Lys Phe Phe Asn Ser Asn Lys Lys Lys Arg
100 105 110
Asp Asp Phe Glu Lys Leu Thr Asn Tyr Ser Val Thr Asp Leu Asn Val

115 120 125
Gln Arg Lys Ala Ile His Glu Leu Ile Gln Val Met Ala Glu Leu Ser
130 135 140
Pro Ala Ala Lys Thr Gly Lys Arg Lys Arg Ser Gln Met Leu Phe Arg
145 150 155 160
Gly Arg Arg Ala Ser Gln
165

<210> 84
<211> 155
<212> PRT
<213> 小家鼠(Mus musculus)
<400> 84
Met Asn Ala Thr His Cys Ile Leu Ala Leu Gln Leu Phe Leu Met Ala
1 5 10 15
Val Ser Gly Cys Tyr Cys His Gly Thr Val Ile Glu Ser Leu Glu Ser
20 25 30
Leu Asn Asn Tyr Phe Asn Ser Ser Gly Ile Asp Val Glu Glu Lys Ser
35 40 45
Leu Phe Leu Asp Ile Trp Arg Asn Trp Gln Lys Asp Gly Asp Met Lys
50 55 60
Ile Leu Gln Ser Gln Ile Ile Ser Phe Tyr Leu Arg Leu Phe Glu Val
65 70 75 80
Leu Lys Asp Asn Gln Ala Ile Ser Asn Asn Ile Ser Val Ile Glu Ser
85 90 95
His Leu Ile Thr Thr Phe Phe Ser Asn Ser Lys Ala Lys Lys Asp Ala
100 105 110
Phe Met Ser Ile Ala Lys Phe Glu Val Asn Asn Pro Gln Val Gln Arg
115 120 125
Gln Ala Phe Asn Glu Leu Ile Arg Val Val His Gln Leu Leu Pro Glu
130 135 140
Ser Ser Leu Arg Lys Arg Lys Arg Ser Arg Cys
145 150 155

<210> 85
<211> 699
<212> PRT
<213> 人工序列(Artificial Sequence)
<220>
<221> 来源
<223> /注释="人工序列描述:合成多肽"

<400> 85

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

Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Asn Ser Leu Arg Leu
305 310 315 320
Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Lys Phe Gly Met Ser Trp
325 330 335
Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ser Ser Ile Ser
340 345 350
Gly Ser Gly Arg Asp Thr Leu Tyr Ala Glu Ser Val Lys Gly Arg Phe
355 360 365
Thr Ile Ser Arg Asp Asn Ala Lys Thr Thr Leu Tyr Leu Gln Met Asn
370 375 380
Ser Leu Arg Pro Glu Asp Thr Ala Val Tyr Tyr Cys Thr Ile Gly Gly
385 390 395 400
Ser Leu Ser Val Ser Ser Gln Gly Thr Leu Val Thr Val Ser Ser Ser
405 410 415
Gly Gly Pro Gly Pro Ala Gly Met Lys Gly Leu Pro Gly Ser His Gly
420 425 430
Thr Val Ile Glu Ser Leu Glu Ser Leu Asn Asn Tyr Phe Asn Ser Ser
435 440 445
Gly Ile Asp Val Glu Glu Lys Ser Leu Phe Leu Asp Ile Trp Arg Asn
450 455 460
Trp Gln Lys Asp Gly Asp Met Lys Ile Leu Gln Ser Gln Ile Ile Ser
465 470 475 480
Phe Tyr Leu Arg Leu Phe Glu Val Leu Lys Asp Asn Gln Ala Ile Ser
485 490 495
Asn Asn Ile Ser Val Ile Glu Ser His Leu Ile Thr Thr Phe Phe Ser
500 505 510
Asn Ser Lys Ala Lys Lys Asp Ala Phe Met Ser Ile Ala Lys Phe Glu
515 520 525
Val Asn Asn Pro Gln Val Gln Arg Gln Ala Phe Asn Glu Leu Ile Arg
530 535 540
Val Val His Gln Leu Leu Pro Glu Ser Ser Leu Arg Lys Arg Lys Arg
545 550 555 560
Ser Arg Cys Ser Gly Gly Pro Gly Pro Ala Gly Met Lys Gly Leu Pro
565 570 575
Gly Ser Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro
580 585 590
Gly Asn Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser
595 600 605
Lys Phe Gly Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu

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

<210> 86
<211> 436
<212> PRT
<213> 人工序列(Artificial Sequence)
<220>
<221> 来源
<223> /注释="人工序列描述:合成多肽"
<400> 86
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Asn
1 5 10 15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Lys Phe
20 25 30
Gly Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45
Ser Ser Ile Ser Gly Ser Gly Arg Asp Thr Leu Tyr Ala Glu Ser Val
50 55 60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Thr Thr Leu Tyr
65 70 75 80
Leu Gln Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95
Thr Ile Gly Gly Ser Leu Ser Val Ser Ser Gln Gly Thr Leu Val Thr
100 105 110
Val Ser Ser Ser Gly Gly Pro Gly Pro Ala Gly Met Lys Gly Leu Pro
115 120 125
Gly Ser Cys Asp Leu Pro Gln Thr His Asn Leu Arg Asn Lys Arg Ala
130 135 140
Leu Thr Leu Leu Val Gln Met Arg Arg Leu Ser Pro Leu Ser Cys Leu
145 150 155 160

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

<210> 87
<211> 428
<212> PRT

<213> 人工序列(Artificial Sequence)
<220>
<221> 来源
<223> /注释="人工序列描述:合成多肽"
<400> 87

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Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Asn
1               5                  10                  15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Lys Phe
            20                  25                  30
Gly Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45
Ser Ser Ile Ser Gly Ser Gly Arg Asp Thr Leu Tyr Ala Glu Ser Val
    50                  55                  60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Thr Thr Leu Tyr
65                  70                  75                  80
Leu Gln Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95
Thr Ile Gly Gly Ser Leu Ser Val Ser Ser Gln Gly Thr Leu Val Thr
            100                 105                 110
Val Ser Ser Ser Gly Gly Pro Gly Pro Ala Gly Met Lys Gly Leu Pro
        115                 120                 125
Gly Ser Cys Asp Leu Pro Gln Thr His Asn Leu Arg Asn Lys Arg Ala
    130                 135                 140
Leu Thr Leu Leu Val Gln Met Arg Arg Leu Ser Pro Leu Ser Cys Leu
145                 150                 155                 160
Lys Asp Arg Lys Asp Phe Gly Phe Pro Gln Glu Lys Val Asp Ala Gln
                165                 170                 175
Gln Ile Lys Lys Ala Gln Ala Ile Pro Val Leu Ser Glu Leu Thr Gln
            180                 185                 190
Gln Ile Leu Asn Ile Phe Thr Ser Lys Asp Ser Ser Ala Ala Trp Asn
        195                 200                 205
Thr Thr Leu Leu Asp Ser Phe Cys Asn Asp Leu His Gln Gln Leu Asn
    210                 215                 220
Asp Leu Gln Gly Cys Leu Met Gln Gln Val Gly Val Gln Glu Phe Pro
225                 230                 235                 240
Leu Thr Gln Glu Asp Ala Leu Leu Ala Val Arg Lys Tyr Phe His Arg
                245                 250                 255
Ile Thr Val Tyr Leu Arg Glu Lys Lys His Ser Pro Cys Ala Trp Glu
            260                 265                 270
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Val Val Arg Ala Glu Val Trp Arg Ala Leu Ser Ser Ser Ala Asn Val
275 280 285
Ser Gly Gly Pro Gly Pro Ala Gly Met Lys Gly Leu Pro Gly Ser Glu
290 295 300
Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Asn Ser
305 310 315 320
Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Lys Phe Gly
325 330 335
Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ser
340 345 350
Ser Ile Ser Gly Ser Gly Arg Asp Thr Leu Tyr Ala Glu Ser Val Lys
355 360 365
Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Thr Thr Leu Tyr Leu
370 375 380
Gln Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Val Tyr Tyr Cys Thr
385 390 395 400
Ile Gly Gly Ser Leu Ser Val Ser Ser Gln Gly Thr Leu Val Thr Val
405 410 415
Ser Ser His His His His His His Glu Pro Glu Ala
420 425

<210> 88
<211> 489
<212> PRT
<213> 未知(Unknown)
<220>
<221> 来源
<223> /注释="未知描述：
IFNgR1序列"
<400> 88
Met Ala Leu Leu Phe Leu Leu Pro Leu Val Met Gln Gly Val Ser Arg
1 5 10 15
Ala Glu Met Gly Thr Ala Asp Leu Gly Pro Ser Ser Val Pro Thr Pro
20 25 30
Thr Asn Val Thr Ile Glu Ser Tyr Asn Met Asn Pro Ile Val Tyr Trp
35 40 45
Glu Tyr Gln Ile Met Pro Gln Val Pro Val Phe Thr Val Glu Val Lys
50 55 60
Asn Tyr Gly Val Lys Asn Ser Glu Trp Ile Asp Ala Cys Ile Asn Ile
65 70 75 80

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

385 390 395 400
Asn Cys Ser Glu Ser Asp His Ser Arg Asn Gly Phe Asp Thr Asp Ser
405 410 415
Ser Cys Leu Glu Ser His Ser Ser Leu Ser Asp Ser Glu Phe Pro Pro
420 425 430
Asn Asn Lys Gly Glu Ile Lys Thr Glu Gly Gln Glu Leu Ile Thr Val
435 440 445
Ile Lys Ala Pro Thr Ser Phe Gly Tyr Asp Lys Pro His Val Leu Val
450 455 460
Asp Leu Leu Val Asp Asp Ser Gly Lys Glu Ser Leu Ile Gly Tyr Arg
465 470 475 480
Pro Thr Glu Asp Ser Lys Glu Phe Ser
485

<210> 89
<211> 337
<212> PRT
<213> 未知(Unknown)
<220>
<221> 来源
<223> /注释="未知描述：
IFNgR2序列"
<400> 89
Met Arg Pro Thr Leu Leu Trp Ser Leu Leu Leu Leu Leu Gly Val Phe
1 5 10 15
Ala Ala Ala Ala Ala Ala Pro Pro Asp Pro Leu Ser Gln Leu Pro Ala
20 25 30
Pro Gln His Pro Lys Ile Arg Leu Tyr Asn Ala Glu Gln Val Leu Ser
35 40 45
Trp Glu Pro Val Ala Leu Ser Asn Ser Thr Arg Pro Val Val Tyr Gln
50 55 60
Val Gln Phe Lys Tyr Thr Asp Ser Lys Trp Phe Thr Ala Asp Ile Met
65 70 75 80
Ser Ile Gly Val Asn Cys Thr Gln Ile Thr Ala Thr Glu Cys Asp Phe
85 90 95
Thr Ala Ala Ser Pro Ser Ala Gly Phe Pro Met Asp Phe Asn Val Thr
100 105 110
Leu Arg Leu Arg Ala Glu Leu Gly Ala Leu His Ser Ala Trp Val Thr
115 120 125
Met Pro Trp Phe Gln His Tyr Arg Asn Val Thr Val Gly Pro Pro Glu

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

<210> 90
<211> 528
<212> PRT
<213> 人工序列(Artificial Sequence)
<220>
<221> 来源
<223> /注释="人工序列描述:合成多肽"
<400> 90
Gln Val Gln Leu Gln Glu Ser Gly Gly Gly Leu Val Gln Ala Gly Gly
1 5 10 15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Arg Ile Phe Ser Ile Asp
20 25 30
Ile Met Ser Trp Tyr Arg Gln Ala Pro Gly Lys Gln Arg Glu Leu Val

35 40 45

Ala Arg Ile Thr Arg Gly Gly Thr Ile Ser Tyr Asp Asp Ser Val Lys
50 55 60

Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Thr Val Tyr Leu
65 70 75 80

Gln Met Asn Ser Leu Lys Pro Glu Asp Thr Gly Val Tyr Tyr Cys Asn
85 90 95

Ala Leu Tyr Gly Thr Asp Tyr Trp Gly Lys Gly Thr Gln Val Thr Val
100 105 110

Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly
115 120 125

Ser Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly
130 135 140

Asn Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Lys
145 150 155 160

Phe Gly Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp
165 170 175

Val Ser Ser Ile Ser Gly Ser Gly Arg Asp Thr Leu Tyr Ala Glu Ser
180 185 190

Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Thr Thr Leu
195 200 205

Tyr Leu Gln Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Val Tyr Tyr
210 215 220

Cys Thr Ile Gly Gly Ser Leu Ser Val Ser Ser Gln Gly Thr Leu Val
225 230 235 240

Thr Val Ser Ser Ser Gly Gly Pro Gly Pro Ala Gly Met Lys Gly Leu
245 250 255

Pro Gly Ser His Gly Thr Val Ile Glu Ser Leu Glu Ser Leu Asn Asn
260 265 270

Tyr Phe Asn Ser Ser Gly Ile Asp Val Glu Glu Lys Ser Leu Phe Leu
275 280 285

Asp Ile Trp Arg Asn Trp Gln Lys Asp Gly Asp Met Lys Ile Leu Gln
290 295 300

Ser Gln Ile Ile Ser Phe Tyr Leu Arg Leu Phe Glu Val Leu Lys Asp
305 310 315 320

Asn Gln Ala Ile Ser Asn Asn Ile Ser Val Ile Glu Ser His Leu Ile
325 330 335

Thr Thr Phe Phe Ser Asn Ser Lys Ala Lys Lys Asp Ala Phe Met Ser
340 345 350

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

<210> 91
<211> 658
<212> PRT
<213> 人工序列(Artificial Sequence)
<220>
<221> 来源
<223> /注释="人工序列描述:合成多肽"
<400> 91

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

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

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

<210> 92
<211> 1337
<212> PRT
<213> 人工序列(Artificial Sequence)

<220>

<221> 来源

<223> /注释="人工序列描述:合成多肽"

<400> 92

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

275 280 285

Cys Leu Ser Glu Val Glu His Asp Thr Met Pro Ala Asp Leu Pro Ala

290 295 300

Ile Ala Ala Asp Phe Val Glu Asp Gln Glu Val Cys Lys Asn Tyr Ala

305 310 315 320

Glu Ala Lys Asp Val Phe Leu Gly Thr Phe Leu Tyr Glu Tyr Ser Arg

325 330 335

Arg His Pro Asp Tyr Ser Val Ser Leu Leu Leu Arg Leu Ala Lys Lys

340 345 350

Tyr Glu Ala Thr Leu Glu Lys Cys Cys Ala Glu Ala Asn Pro Pro Ala

355 360 365

Cys Tyr Gly Thr Val Leu Ala Glu Phe Gln Pro Leu Val Glu Glu Pro

370 375 380

Lys Asn Leu Val Lys Thr Asn Cys Asp Leu Tyr Glu Lys Leu Gly Glu

385 390 395 400

Tyr Gly Phe Gln Asn Ala Ile Leu Val Arg Tyr Thr Gln Lys Ala Pro

405 410 415

Gln Val Ser Thr Pro Thr Leu Val Glu Ala Ala Arg Asn Leu Gly Arg

420 425 430

Val Gly Thr Lys Cys Cys Thr Leu Pro Glu Asp Gln Arg Leu Pro Cys

435 440 445

Val Glu Asp Tyr Leu Ser Ala Ile Leu Asn Arg Val Cys Leu Leu His

450 455 460

Glu Lys Thr Pro Val Ser Glu His Val Thr Lys Cys Cys Ser Gly Ser

465 470 475 480

Leu Val Glu Arg Arg Pro Cys Phe Ser Ala Leu Thr Val Asp Glu Thr

485 490 495

Tyr Val Pro Lys Glu Phe Lys Ala Glu Thr Phe Thr Phe His Ser Asp

500 505 510

Ile Cys Thr Leu Pro Glu Lys Glu Lys Gln Ile Lys Lys Gln Thr Ala

515 520 525

Leu Ala Glu Leu Val Lys His Lys Pro Lys Ala Thr Ala Glu Gln Leu

530 535 540

Lys Thr Val Met Asp Asp Phe Ala Gln Phe Leu Asp Thr Cys Cys Lys

545 550 555 560

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

565 570 575

Thr Arg Cys Lys Asp Ala Leu Ala Ser Gly Gly Pro Gly Pro Ala Gly

580 585 590

Met Lys Gly Leu Pro Gly Ser His Gly Thr Val Ile Glu Ser Leu Glu
595 600 605
Ser Leu Asn Asn Tyr Phe Asn Ser Ser Gly Ile Asp Val Glu Glu Lys
610 615 620
Ser Leu Phe Leu Asp Ile Trp Arg Asn Trp Gln Lys Asp Gly Asp Met
625 630 635 640
Lys Ile Leu Gln Ser Gln Ile Ile Ser Phe Tyr Leu Arg Leu Phe Glu
645 650 655
Val Leu Lys Asp Asn Gln Ala Ile Ser Asn Asn Ile Ser Val Ile Glu
660 665 670
Ser His Leu Ile Thr Thr Phe Phe Ser Asn Ser Lys Ala Lys Lys Asp
675 680 685
Ala Phe Met Ser Ile Ala Lys Phe Glu Val Asn Asn Pro Gln Val Gln
690 695 700
Arg Gln Ala Phe Asn Glu Leu Ile Arg Val Val His Gln Leu Leu Pro
705 710 715 720
Glu Ser Ser Leu Arg Lys Arg Lys Arg Ser Arg Cys Ser Gly Gly Pro
725 730 735
Gly Pro Ala Gly Met Lys Gly Leu Pro Gly Ser Glu Ala His Lys Ser
740 745 750
Glu Ile Ala His Arg Tyr Asn Asp Leu Gly Glu Gln His Phe Lys Gly
755 760 765
Leu Val Leu Ile Ala Phe Ser Gln Tyr Leu Gln Lys Cys Ser Tyr Asp
770 775 780
Glu His Ala Lys Leu Val Gln Glu Val Thr Asp Phe Ala Lys Thr Cys
785 790 795 800
Val Ala Asp Glu Ser Ala Ala Asn Cys Asp Lys Ser Leu His Thr Leu
805 810 815
Phe Gly Asp Lys Leu Cys Ala Ile Pro Asn Leu Arg Glu Asn Tyr Gly
820 825 830
Glu Leu Ala Asp Cys Cys Thr Lys Gln Glu Pro Glu Arg Asn Glu Cys
835 840 845
Phe Leu Gln His Lys Asp Asp Asn Pro Ser Leu Pro Pro Phe Glu Arg
850 855 860
Pro Glu Ala Glu Ala Met Cys Thr Ser Phe Lys Glu Asn Pro Thr Thr
865 870 875 880
Phe Met Gly His Tyr Leu His Glu Val Ala Arg Arg His Pro Tyr Phe
885 890 895
Tyr Ala Pro Glu Leu Leu Tyr Tyr Ala Glu Gln Tyr Asn Glu Ile Leu

900 905 910
Thr Gln Cys Cys Ala Glu Ala Asp Lys Glu Ser Cys Leu Thr Pro Lys
915 920 925
Leu Asp Gly Val Lys Glu Lys Ala Leu Val Ser Ser Val Arg Gln Arg
930 935 940
Met Lys Cys Ser Ser Met Gln Lys Phe Gly Glu Arg Ala Phe Lys Ala
945 950 955 960
Trp Ala Val Ala Arg Leu Ser Gln Thr Phe Pro Asn Ala Asp Phe Ala
965 970 975
Glu Ile Thr Lys Leu Ala Thr Asp Leu Thr Lys Val Asn Lys Glu Cys
980 985 990
Cys His Gly Asp Leu Leu Glu Cys Ala Asp Asp Arg Ala Glu Leu Ala
995 1000 1005
Lys Tyr Met Cys Glu Asn Gln Ala Thr Ile Ser Ser Lys Leu Gln
1010 1015 1020
Thr Cys Cys Asp Lys Pro Leu Leu Lys Lys Ala His Cys Leu Ser
1025 1030 1035
Glu Val Glu His Asp Thr Met Pro Ala Asp Leu Pro Ala Ile Ala
1040 1045 1050
Ala Asp Phe Val Glu Asp Gln Glu Val Cys Lys Asn Tyr Ala Glu
1055 1060 1065
Ala Lys Asp Val Phe Leu Gly Thr Phe Leu Tyr Glu Tyr Ser Arg
1070 1075 1080
Arg His Pro Asp Tyr Ser Val Ser Leu Leu Leu Arg Leu Ala Lys
1085 1090 1095
Lys Tyr Glu Ala Thr Leu Glu Lys Cys Cys Ala Glu Ala Asn Pro
1100 1105 1110
Pro Ala Cys Tyr Gly Thr Val Leu Ala Glu Phe Gln Pro Leu Val
1115 1120 1125
Glu Glu Pro Lys Asn Leu Val Lys Thr Asn Cys Asp Leu Tyr Glu
1130 1135 1140
Lys Leu Gly Glu Tyr Gly Phe Gln Asn Ala Ile Leu Val Arg Tyr
1145 1150 1155
Thr Gln Lys Ala Pro Gln Val Ser Thr Pro Thr Leu Val Glu Ala
1160 1165 1170
Ala Arg Asn Leu Gly Arg Val Gly Thr Lys Cys Cys Thr Leu Pro
1175 1180 1185
Glu Asp Gln Arg Leu Pro Cys Val Glu Asp Tyr Leu Ser Ala Ile
1190 1195 1200

Leu Asn Arg Val Cys Leu Leu His Glu Lys Thr Pro Val Ser Glu
1205 1210 1215
His Val Thr Lys Cys Cys Ser Gly Ser Leu Val Glu Arg Arg Pro
1220 1225 1230
Cys Phe Ser Ala Leu Thr Val Asp Glu Thr Tyr Val Pro Lys Glu
1235 1240 1245
Phe Lys Ala Glu Thr Phe Thr Phe His Ser Asp Ile Cys Thr Leu
1250 1255 1260
Pro Glu Lys Glu Lys Gln Ile Lys Lys Gln Thr Ala Leu Ala Glu
1265 1270 1275
Leu Val Lys His Lys Pro Lys Ala Thr Ala Glu Gln Leu Lys Thr
1280 1285 1290
Val Met Asp Asp Phe Ala Gln Phe Leu Asp Thr Cys Cys Lys Ala
1295 1300 1305
Ala Asp Lys Asp Thr Cys Phe Ser Thr Glu Gly Pro Asn Leu Val
1310 1315 1320
Thr Arg Cys Lys Asp Ala Leu Ala His His His His His His
1325 1330 1335

<210> 93
<211> 1485
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<213> 人工序列(Artificial Sequence)
<220>
<221> 来源
<223> /注释="人工序列描述:合成多肽"
<400> 93

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

100 105 110

Pro Pro Phe Glu Arg Pro Glu Ala Glu Ala Met Cys Thr Ser Phe Lys
115 120 125

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

Arg His Pro Tyr Phe Tyr Ala Pro Glu Leu Leu Tyr Tyr Ala Glu Gln
145 150 155 160

Tyr Asn Glu Ile Leu Thr Gln Cys Cys Ala Glu Ala Asp Lys Glu Ser
165 170 175

Cys Leu Thr Pro Lys Leu Asp Gly Val Lys Glu Lys Ala Leu Val Ser
180 185 190

Ser Val Arg Gln Arg Met Lys Cys Ser Ser Met Gln Lys Phe Gly Glu
195 200 205

Arg Ala Phe Lys Ala Trp Ala Val Ala Arg Leu Ser Gln Thr Phe Pro
210 215 220

Asn Ala Asp Phe Ala Glu Ile Thr Lys Leu Ala Thr Asp Leu Thr Lys
225 230 235 240

Val Asn Lys Glu Cys Cys His Gly Asp Leu Leu Glu Cys Ala Asp Asp
245 250 255

Arg Ala Glu Leu Ala Lys Tyr Met Cys Glu Asn Gln Ala Thr Ile Ser
260 265 270

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

Cys Leu Ser Glu Val Glu His Asp Thr Met Pro Ala Asp Leu Pro Ala
290 295 300

Ile Ala Ala Asp Phe Val Glu Asp Gln Glu Val Cys Lys Asn Tyr Ala
305 310 315 320

Glu Ala Lys Asp Val Phe Leu Gly Thr Phe Leu Tyr Glu Tyr Ser Arg
325 330 335

Arg His Pro Asp Tyr Ser Val Ser Leu Leu Leu Arg Leu Ala Lys Lys
340 345 350

Tyr Glu Ala Thr Leu Glu Lys Cys Cys Ala Glu Ala Asn Pro Pro Ala
355 360 365

Cys Tyr Gly Thr Val Leu Ala Glu Phe Gln Pro Leu Val Glu Glu Pro
370 375 380

Lys Asn Leu Val Lys Thr Asn Cys Asp Leu Tyr Glu Lys Leu Gly Glu
385 390 395 400

Tyr Gly Phe Gln Asn Ala Ile Leu Val Arg Tyr Thr Gln Lys Ala Pro
405 410 415

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

725 730 735
Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser His Gly Thr Val Ile
740 745 750
Glu Ser Leu Glu Ser Leu Asn Asn Tyr Phe Asn Ser Ser Gly Ile Asp
755 760 765
Val Glu Glu Lys Ser Leu Phe Leu Asp Ile Trp Arg Asn Trp Gln Lys
770 775 780
Asp Gly Asp Met Lys Ile Leu Gln Ser Gln Ile Ile Ser Phe Tyr Leu
785 790 795 800
Arg Leu Phe Glu Val Leu Lys Asp Asn Gln Ala Ile Ser Asn Asn Ile
805 810 815
Ser Val Ile Glu Ser His Leu Ile Thr Thr Phe Phe Ser Asn Ser Lys
820 825 830
Ala Lys Lys Asp Ala Phe Met Ser Ile Ala Lys Phe Glu Val Asn Asn
835 840 845
Pro Gln Val Gln Arg Gln Ala Phe Asn Glu Leu Ile Arg Val Val His
850 855 860
Gln Leu Leu Pro Glu Ser Ser Leu Arg Lys Arg Lys Arg Ser Arg Cys
865 870 875 880
Ser Gly Gly Pro Gly Pro Ala Gly Met Lys Gly Leu Pro Gly Ser Glu
885 890 895
Ala His Lys Ser Glu Ile Ala His Arg Tyr Asn Asp Leu Gly Glu Gln
900 905 910
His Phe Lys Gly Leu Val Leu Ile Ala Phe Ser Gln Tyr Leu Gln Lys
915 920 925
Cys Ser Tyr Asp Glu His Ala Lys Leu Val Gln Glu Val Thr Asp Phe
930 935 940
Ala Lys Thr Cys Val Ala Asp Glu Ser Ala Ala Asn Cys Asp Lys Ser
945 950 955 960
Leu His Thr Leu Phe Gly Asp Lys Leu Cys Ala Ile Pro Asn Leu Arg
965 970 975
Glu Asn Tyr Gly Glu Leu Ala Asp Cys Cys Thr Lys Gln Glu Pro Glu
980 985 990
Arg Asn Glu Cys Phe Leu Gln His Lys Asp Asp Asn Pro Ser Leu Pro
995 1000 1005
Pro Phe Glu Arg Pro Glu Ala Glu Ala Met Cys Thr Ser Phe Lys
1010 1015 1020
Glu Asn Pro Thr Thr Phe Met Gly His Tyr Leu His Glu Val Ala
1025 1030 1035

Arg Arg His Pro Tyr Phe Tyr Ala Pro Glu Leu Leu Tyr Tyr Ala
1040 1045 1050
Glu Gln Tyr Asn Glu Ile Leu Thr Gln Cys Cys Ala Glu Ala Asp
1055 1060 1065
Lys Glu Ser Cys Leu Thr Pro Lys Leu Asp Gly Val Lys Glu Lys
1070 1075 1080
Ala Leu Val Ser Ser Val Arg Gln Arg Met Lys Cys Ser Ser Met
1085 1090 1095
Gln Lys Phe Gly Glu Arg Ala Phe Lys Ala Trp Ala Val Ala Arg
1100 1105 1110
Leu Ser Gln Thr Phe Pro Asn Ala Asp Phe Ala Glu Ile Thr Lys
1115 1120 1125
Leu Ala Thr Asp Leu Thr Lys Val Asn Lys Glu Cys Cys His Gly
1130 1135 1140
Asp Leu Leu Glu Cys Ala Asp Asp Arg Ala Glu Leu Ala Lys Tyr
1145 1150 1155
Met Cys Glu Asn Gln Ala Thr Ile Ser Ser Lys Leu Gln Thr Cys
1160 1165 1170
Cys Asp Lys Pro Leu Leu Lys Lys Ala His Cys Leu Ser Glu Val
1175 1180 1185
Glu His Asp Thr Met Pro Ala Asp Leu Pro Ala Ile Ala Ala Asp
1190 1195 1200
Phe Val Glu Asp Gln Glu Val Cys Lys Asn Tyr Ala Glu Ala Lys
1205 1210 1215
Asp Val Phe Leu Gly Thr Phe Leu Tyr Glu Tyr Ser Arg Arg His
1220 1225 1230
Pro Asp Tyr Ser Val Ser Leu Leu Leu Arg Leu Ala Lys Lys Tyr
1235 1240 1245
Glu Ala Thr Leu Glu Lys Cys Cys Ala Glu Ala Asn Pro Pro Ala
1250 1255 1260
Cys Tyr Gly Thr Val Leu Ala Glu Phe Gln Pro Leu Val Glu Glu
1265 1270 1275
Pro Lys Asn Leu Val Lys Thr Asn Cys Asp Leu Tyr Glu Lys Leu
1280 1285 1290
Gly Glu Tyr Gly Phe Gln Asn Ala Ile Leu Val Arg Tyr Thr Gln
1295 1300 1305
Lys Ala Pro Gln Val Ser Thr Pro Thr Leu Val Glu Ala Ala Arg
1310 1315 1320
Asn Leu Gly Arg Val Gly Thr Lys Cys Cys Thr Leu Pro Glu Asp

1325 1330 1335
Gln Arg Leu Pro Cys Val Glu Asp Tyr Leu Ser Ala Ile Leu Asn
1340 1345 1350
Arg Val Cys Leu Leu His Glu Lys Thr Pro Val Ser Glu His Val
1355 1360 1365
Thr Lys Cys Cys Ser Gly Ser Leu Val Glu Arg Arg Pro Cys Phe
1370 1375 1380
Ser Ala Leu Thr Val Asp Glu Thr Tyr Val Pro Lys Glu Phe Lys
1385 1390 1395
Ala Glu Thr Phe Thr Phe His Ser Asp Ile Cys Thr Leu Pro Glu
1400 1405 1410
Lys Glu Lys Gln Ile Lys Lys Gln Thr Ala Leu Ala Glu Leu Val
1415 1420 1425
Lys His Lys Pro Lys Ala Thr Ala Glu Gln Leu Lys Thr Val Met
1430 1435 1440
Asp Asp Phe Ala Gln Phe Leu Asp Thr Cys Cys Lys Ala Ala Asp
1445 1450 1455
Lys Asp Thr Cys Phe Ser Thr Glu Gly Pro Asn Leu Val Thr Arg
1460 1465 1470
Cys Lys Asp Ala Leu Ala His His His His His His
1475 1480 1485

<210> 94
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<220>
<221> 来源
<223> /注释="人工序列描述:合成多肽"
<400> 94

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

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

385 390 395 400
Leu Pro Glu Ser Ser Leu Arg Lys Arg Lys Arg Ser Arg Cys Gly Gly
405 410 415
Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser His Gly Thr
420 425 430
Val Ile Glu Ser Leu Glu Ser Leu Asn Asn Tyr Phe Asn Ser Ser Gly
435 440 445
Ile Asp Val Glu Glu Lys Ser Leu Phe Leu Asp Ile Trp Arg Asn Trp
450 455 460
Gln Lys Asp Gly Asp Met Lys Ile Leu Gln Ser Gln Ile Ile Ser Phe
465 470 475 480
Tyr Leu Arg Leu Phe Glu Val Leu Lys Asp Asn Gln Ala Ile Ser Asn
485 490 495
Asn Ile Ser Val Ile Glu Ser His Leu Ile Thr Thr Phe Phe Ser Asn
500 505 510
Ser Lys Ala Lys Lys Asp Ala Phe Met Ser Ile Ala Lys Phe Glu Val
515 520 525
Asn Asn Pro Gln Val Gln Arg Gln Ala Phe Asn Glu Leu Ile Arg Val
530 535 540
Val His Gln Leu Leu Pro Glu Ser Ser Leu Arg Lys Arg Lys Arg Ser
545 550 555 560
Arg Cys Ser Gly Gly Pro Gly Pro Ala Gly Met Lys Gly Leu Pro Gly
565 570 575
Ser Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly
580 585 590
Asn Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Lys
595 600 605
Phe Gly Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp
610 615 620
Val Ser Ser Ile Ser Gly Ser Gly Arg Asp Thr Leu Tyr Ala Glu Ser
625 630 635 640
Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Thr Thr Leu
645 650 655
Tyr Leu Gln Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Val Tyr Tyr
660 665 670
Cys Thr Ile Gly Gly Ser Leu Ser Val Ser Ser Gln Gly Thr Leu Val
675 680 685
Thr Val Ser Ser His His His His His His
690 695

<210> 95
<211> 699
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<400> 95

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

245 250 255

Gln Arg Gln Ala Phe Asn Glu Leu Ile Arg Val Val His Gln Leu Leu
260 265 270

Pro Glu Ser Ser Leu Arg Lys Arg Lys Arg Ser Arg Cys Ser Gly Gly
275 280 285

Pro Gly Pro Ala Gly Met Lys Gly Leu Pro Gly Ser Glu Val Gln Leu
290 295 300

Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Asn Ser Leu Arg Leu
305 310 315 320

Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Lys Phe Gly Met Ser Trp
325 330 335

Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ser Ser Ile Ser
340 345 350

Gly Ser Gly Arg Asp Thr Leu Tyr Ala Glu Ser Val Lys Gly Arg Phe
355 360 365

Thr Ile Ser Arg Asp Asn Ala Lys Thr Thr Leu Tyr Leu Gln Met Asn
370 375 380

Ser Leu Arg Pro Glu Asp Thr Ala Val Tyr Tyr Cys Thr Ile Gly Gly
385 390 395 400

Ser Leu Ser Val Ser Ser Gln Gly Thr Leu Val Thr Val Ser Ser Ser
405 410 415

Gly Gly Pro Gly Pro Ala Gly Met Lys Gly Leu Pro Gly Ser His Gly
420 425 430

Thr Val Ile Glu Ser Leu Glu Ser Leu Asn Asn Tyr Phe Asn Ser Ser
435 440 445

Gly Ile Asp Val Glu Glu Lys Ser Leu Phe Leu Asp Ile Trp Arg Asn
450 455 460

Trp Gln Lys Asp Gly Asp Met Lys Ile Leu Gln Ser Gln Ile Ile Ser
465 470 475 480

Phe Tyr Leu Arg Leu Phe Glu Val Leu Lys Asp Asn Gln Ala Ile Ser
485 490 495

Asn Asn Ile Ser Val Ile Glu Ser His Leu Ile Thr Thr Phe Phe Ser
500 505 510

Asn Ser Lys Ala Lys Lys Asp Ala Phe Met Ser Ile Ala Lys Phe Glu
515 520 525

Val Asn Asn Pro Gln Val Gln Arg Gln Ala Phe Asn Glu Leu Ile Arg
530 535 540

Val Val His Gln Leu Leu Pro Glu Ser Ser Leu Arg Lys Arg Lys Arg
545 550 555 560

Ser Arg Cys Ser Gly Gly Pro Gly Pro Ala Gly Met Lys Gly Leu Pro
565 570 575
Gly Ser Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro
580 585 590
Gly Asn Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser
595 600 605
Lys Phe Gly Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu
610 615 620
Trp Val Ser Ser Ile Ser Gly Ser Gly Arg Asp Thr Leu Tyr Ala Glu
625 630 635 640
Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Thr Thr
645 650 655
Leu Tyr Leu Gln Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Val Tyr
660 665 670
Tyr Cys Thr Ile Gly Gly Ser Leu Ser Val Ser Ser Gln Gly Thr Leu
675 680 685
Val Thr Val Ser Ser His His His His His His
690 695

<210> 96
<211> 554
<212> PRT
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<400> 96
Met Asp Met Arg Val Pro Ala Gln Leu Leu Gly Leu Leu Leu Leu Trp
1 5 10 15
Leu Arg Gly Ala Arg Cys Gln Val Gln Leu Gln Glu Ser Gly Gly Gly
20 25 30
Leu Ala Gln Ala Gly Gly Ser Leu Ser Leu Ser Cys Ala Ala Ser Gly
35 40 45
Phe Thr Val Ser Asn Ser Val Met Ala Trp Tyr Arg Gln Thr Pro Gly
50 55 60
Lys Gln Arg Glu Phe Val Ala Ile Ile Asn Ser Val Gly Ser Thr Asn
65 70 75 80
Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala
85 90 95
Lys Asn Thr Val Tyr Leu Gln Met Asn Asn Leu Lys Pro Glu Asp Thr

100 105 110

Ala Val Tyr Val Cys Asn Arg Asn Phe Asp Arg Ile Tyr Trp Gly Gln
115 120 125

Gly Thr Gln Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly
130 135 140

Gly Ser Gly Gly Gly Gly Ser Glu Val Gln Leu Val Glu Ser Gly Gly
145 150 155 160

Gly Leu Val Gln Pro Gly Asn Ser Leu Arg Leu Ser Cys Ala Ala Ser
165 170 175

Gly Phe Thr Phe Ser Lys Phe Gly Met Ser Trp Val Arg Gln Ala Pro
180 185 190

Gly Lys Gly Leu Glu Trp Val Ser Ser Ile Ser Gly Ser Gly Arg Asp
195 200 205

Thr Leu Tyr Ala Glu Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp
210 215 220

Asn Ala Lys Thr Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Pro Glu
225 230 235 240

Asp Thr Ala Val Tyr Tyr Cys Thr Ile Gly Gly Ser Leu Ser Val Ser
245 250 255

Ser Gln Gly Thr Leu Val Thr Val Ser Ser Ser Gly Gly Pro Gly Pro
260 265 270

Ala Gly Met Lys Gly Leu Pro Gly Ser His Gly Thr Val Ile Glu Ser
275 280 285

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

Glu Lys Ser Leu Phe Leu Asp Ile Trp Arg Asn Trp Gln Lys Asp Gly
305 310 315 320

Asp Met Lys Ile Leu Gln Ser Gln Ile Ile Ser Phe Tyr Leu Arg Leu
325 330 335

Phe Glu Val Leu Lys Asp Asn Gln Ala Ile Ser Asn Asn Ile Ser Val
340 345 350

Ile Glu Ser His Leu Ile Thr Thr Phe Phe Ser Asn Ser Lys Ala Lys
355 360 365

Lys Asp Ala Phe Met Ser Ile Ala Lys Phe Glu Val Asn Asn Pro Gln
370 375 380

Val Gln Arg Gln Ala Phe Asn Glu Leu Ile Arg Val Val His Gln Leu
385 390 395 400

Leu Pro Glu Ser Ser Leu Arg Lys Arg Lys Arg Ser Arg Cys Ser Gly
405 410 415

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

<210> 97
<211> 554
<212> PRT
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<220>
<221> 来源
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<400> 97
Met Asp Met Arg Val Pro Ala Gln Leu Leu Gly Leu Leu Leu Leu Trp
1 5 10 15
Leu Arg Gly Ala Arg Cys Glu Val Gln Leu Val Glu Ser Gly Gly Gly
20 25 30
Leu Val Gln Pro Gly Asn Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly
35 40 45
Phe Thr Phe Ser Lys Phe Gly Met Ser Trp Val Arg Gln Ala Pro Gly
50 55 60
Lys Gly Leu Glu Trp Val Ser Ser Ile Ser Gly Ser Gly Arg Asp Thr
65 70 75 80
Leu Tyr Ala Glu Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn
85 90 95
Ala Lys Thr Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Pro Glu Asp

100 105 110

Thr Ala Val Tyr Tyr Cys Thr Ile Gly Gly Ser Leu Ser Val Ser Ser
115 120 125

Gln Gly Thr Leu Val Thr Val Ser Ser Ser Gly Gly Pro Gly Pro Ala
130 135 140

Gly Met Lys Gly Leu Pro Gly Ser His Gly Thr Val Ile Glu Ser Leu
145 150 155 160

Glu Ser Leu Asn Asn Tyr Phe Asn Ser Ser Gly Ile Asp Val Glu Glu
165 170 175

Lys Ser Leu Phe Leu Asp Ile Trp Arg Asn Trp Gln Lys Asp Gly Asp
180 185 190

Met Lys Ile Leu Gln Ser Gln Ile Ile Ser Phe Tyr Leu Arg Leu Phe
195 200 205

Glu Val Leu Lys Asp Asn Gln Ala Ile Ser Asn Asn Ile Ser Val Ile
210 215 220

Glu Ser His Leu Ile Thr Thr Phe Phe Ser Asn Ser Lys Ala Lys Lys
225 230 235 240

Asp Ala Phe Met Ser Ile Ala Lys Phe Glu Val Asn Asn Pro Gln Val
245 250 255

Gln Arg Gln Ala Phe Asn Glu Leu Ile Arg Val Val His Gln Leu Leu
260 265 270

Pro Glu Ser Ser Leu Arg Lys Arg Lys Arg Ser Arg Cys Ser Gly Gly
275 280 285

Pro Gly Pro Ala Gly Met Lys Gly Leu Pro Gly Ser Glu Val Gln Leu
290 295 300

Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Asn Ser Leu Arg Leu
305 310 315 320

Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Lys Phe Gly Met Ser Trp
325 330 335

Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ser Ser Ile Ser
340 345 350

Gly Ser Gly Arg Asp Thr Leu Tyr Ala Glu Ser Val Lys Gly Arg Phe
355 360 365

Thr Ile Ser Arg Asp Asn Ala Lys Thr Thr Leu Tyr Leu Gln Met Asn
370 375 380

Ser Leu Arg Pro Glu Asp Thr Ala Val Tyr Tyr Cys Thr Ile Gly Gly
385 390 395 400

Ser Leu Ser Val Ser Ser Gln Gly Thr Leu Val Thr Val Ser Ser Gly
405 410 415

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

<210> 98
<211> 702
<212> PRT
<213> 人工序列(Artificial Sequence)
<220>
<221> 来源
<223> /注释="人工序列描述:合成多肽"
<400> 98
Met Asp Met Arg Val Pro Ala Gln Leu Leu Gly Leu Leu Leu Leu Trp
1 5 10 15
Leu Arg Gly Ala Arg Cys Glu Val Gln Leu Val Glu Ser Gly Gly Gly
20 25 30
Leu Val Gln Pro Gly Asn Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly
35 40 45
Phe Thr Phe Ser Lys Phe Gly Met Ser Trp Val Arg Gln Ala Pro Gly
50 55 60
Lys Gly Leu Glu Trp Val Ser Ser Ile Ser Gly Ser Gly Arg Asp Thr
65 70 75 80
Leu Tyr Ala Glu Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn
85 90 95
Ala Lys Thr Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Pro Glu Asp

100 105 110

Thr Ala Val Tyr Tyr Cys Thr Ile Gly Gly Ser Leu Ser Val Ser Ser
115 120 125

Gln Gly Thr Leu Val Thr Val Ser Ser Ser Gly Gly Pro Gly Pro Ala
130 135 140

Gly Met Lys Gly Leu Pro Gly Ser His Gly Thr Val Ile Glu Ser Leu
145 150 155 160

Glu Ser Leu Asn Asn Tyr Phe Asn Ser Ser Gly Ile Asp Val Glu Glu
165 170 175

Lys Ser Leu Phe Leu Asp Ile Trp Arg Asn Trp Gln Lys Asp Gly Asp
180 185 190

Met Lys Ile Leu Gln Ser Gln Ile Ile Ser Phe Tyr Leu Arg Leu Phe
195 200 205

Glu Val Leu Lys Asp Asn Gln Ala Ile Ser Asn Asn Ile Ser Val Ile
210 215 220

Glu Ser His Leu Ile Thr Thr Phe Phe Ser Asn Ser Lys Ala Lys Lys
225 230 235 240

Asp Ala Phe Met Ser Ile Ala Lys Phe Glu Val Asn Asn Pro Gln Val
245 250 255

Gln Arg Gln Ala Phe Asn Glu Leu Ile Arg Val Val His Gln Leu Leu
260 265 270

Pro Glu Ser Ser Leu Arg Lys Arg Lys Arg Ser Arg Cys Ser Gly Gly
275 280 285

Pro Gly Pro Ala Gly Met Lys Gly Leu Pro Gly Ser His Gly Thr Val
290 295 300

Ile Glu Ser Leu Glu Ser Leu Asn Asn Tyr Phe Asn Ser Ser Gly Ile
305 310 315 320

Asp Val Glu Glu Lys Ser Leu Phe Leu Asp Ile Trp Arg Asn Trp Gln
325 330 335

Lys Asp Gly Asp Met Lys Ile Leu Gln Ser Gln Ile Ile Ser Phe Tyr
340 345 350

Leu Arg Leu Phe Glu Val Leu Lys Asp Asn Gln Ala Ile Ser Asn Asn
355 360 365

Ile Ser Val Ile Glu Ser His Leu Ile Thr Thr Phe Phe Ser Asn Ser
370 375 380

Lys Ala Lys Lys Asp Ala Phe Met Ser Ile Ala Lys Phe Glu Val Asn
385 390 395 400

Asn Pro Gln Val Gln Arg Gln Ala Phe Asn Glu Leu Ile Arg Val Val
405 410 415

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

<210> 99
<211> 702
<212> PRT

<213> 人工序列(Artificial Sequence)
<220>
<221> 来源
<223> /注释="人工序列描述:合成多肽"
<400> 99

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Met Asp Met Arg Val Pro Ala Gln Leu Leu Gly Leu Leu Leu Leu Trp
1               5                  10                  15
Leu Arg Gly Ala Arg Cys Gln Val Gln Leu Gln Glu Ser Gly Gly Gly
            20                  25                  30
Leu Ala Gln Ala Gly Gly Ser Leu Ser Leu Ser Cys Ala Ala Ser Gly
        35                  40                  45
Phe Thr Val Ser Asn Ser Val Met Ala Trp Tyr Arg Gln Thr Pro Gly
    50                  55                  60
Lys Gln Arg Glu Phe Val Ala Ile Ile Asn Ser Val Gly Ser Thr Asn
65                  70                  75                  80
Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala
                85                  90                  95
Lys Asn Thr Val Tyr Leu Gln Met Asn Asn Leu Lys Pro Glu Asp Thr
            100                 105                 110
Ala Val Tyr Val Cys Asn Arg Asn Phe Asp Arg Ile Tyr Trp Gly Gln
        115                 120                 125
Gly Thr Gln Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly
    130                 135                 140
Gly Ser Gly Gly Gly Gly Ser Glu Val Gln Leu Val Glu Ser Gly Gly
145                 150                 155                 160
Gly Leu Val Gln Pro Gly Asn Ser Leu Arg Leu Ser Cys Ala Ala Ser
                165                 170                 175
Gly Phe Thr Phe Ser Lys Phe Gly Met Ser Trp Val Arg Gln Ala Pro
            180                 185                 190
Gly Lys Gly Leu Glu Trp Val Ser Ser Ile Ser Gly Ser Gly Arg Asp
        195                 200                 205
Thr Leu Tyr Ala Glu Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp
    210                 215                 220
Asn Ala Lys Thr Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Pro Glu
225                 230                 235                 240
Asp Thr Ala Val Tyr Tyr Cys Thr Ile Gly Gly Ser Leu Ser Val Ser
                245                 250                 255
Ser Gln Gly Thr Leu Val Thr Val Ser Ser Ser Gly Gly Pro Gly Pro
            260                 265                 270
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Ala Gly Met Lys Gly Leu Pro Gly Ser His Gly Thr Val Ile Glu Ser
275 280 285
Leu Glu Ser Leu Asn Asn Tyr Phe Asn Ser Ser Gly Ile Asp Val Glu
290 295 300
Glu Lys Ser Leu Phe Leu Asp Ile Trp Arg Asn Trp Gln Lys Asp Gly
305 310 315 320
Asp Met Lys Ile Leu Gln Ser Gln Ile Ile Ser Phe Tyr Leu Arg Leu
325 330 335
Phe Glu Val Leu Lys Asp Asn Gln Ala Ile Ser Asn Asn Ile Ser Val
340 345 350
Ile Glu Ser His Leu Ile Thr Thr Phe Phe Ser Asn Ser Lys Ala Lys
355 360 365
Lys Asp Ala Phe Met Ser Ile Ala Lys Phe Glu Val Asn Asn Pro Gln
370 375 380
Val Gln Arg Gln Ala Phe Asn Glu Leu Ile Arg Val Val His Gln Leu
385 390 395 400
Leu Pro Glu Ser Ser Leu Arg Lys Arg Lys Arg Ser Arg Cys Ser Gly
405 410 415
Gly Pro Gly Pro Ala Gly Met Lys Gly Leu Pro Gly Ser His Gly Thr
420 425 430
Val Ile Glu Ser Leu Glu Ser Leu Asn Asn Tyr Phe Asn Ser Ser Gly
435 440 445
Ile Asp Val Glu Glu Lys Ser Leu Phe Leu Asp Ile Trp Arg Asn Trp
450 455 460
Gln Lys Asp Gly Asp Met Lys Ile Leu Gln Ser Gln Ile Ile Ser Phe
465 470 475 480
Tyr Leu Arg Leu Phe Glu Val Leu Lys Asp Asn Gln Ala Ile Ser Asn
485 490 495
Asn Ile Ser Val Ile Glu Ser His Leu Ile Thr Thr Phe Phe Ser Asn
500 505 510
Ser Lys Ala Lys Lys Asp Ala Phe Met Ser Ile Ala Lys Phe Glu Val
515 520 525
Asn Asn Pro Gln Val Gln Arg Gln Ala Phe Asn Glu Leu Ile Arg Val
530 535 540
Val His Gln Leu Leu Pro Glu Ser Ser Leu Arg Lys Arg Lys Arg Ser
545 550 555 560
Arg Cys Ser Gly Gly Pro Gly Pro Ala Gly Met Lys Gly Leu Pro Gly
565 570 575
Ser Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly

580 585 590
Asn Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Lys
595 600 605
Phe Gly Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp
610 615 620
Val Ser Ser Ile Ser Gly Ser Gly Arg Asp Thr Leu Tyr Ala Glu Ser
625 630 635 640
Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Thr Thr Leu
645 650 655
Tyr Leu Gln Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Val Tyr Tyr
660 665 670
Cys Thr Ile Gly Gly Ser Leu Ser Val Ser Ser Gln Gly Thr Leu Val
675 680 685
Thr Val Ser Ser His His His His His His Glu Pro Glu Ala
690 695 700

<210> 100
<211> 702
<212> PRT
<213> 人工序列(Artificial Sequence)
<220>
<221> 来源
<223> /注释="人工序列描述:合成多肽"
<400> 100
Met Asp Met Arg Val Pro Ala Gln Leu Leu Gly Leu Leu Leu Leu Trp
1 5 10 15
Leu Arg Gly Ala Arg Cys Glu Val Gln Leu Val Glu Ser Gly Gly Gly
20 25 30
Leu Val Gln Pro Gly Asn Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly
35 40 45
Phe Thr Phe Ser Lys Phe Gly Met Ser Trp Val Arg Gln Ala Pro Gly
50 55 60
Lys Gly Leu Glu Trp Val Ser Ser Ile Ser Gly Ser Gly Arg Asp Thr
65 70 75 80
Leu Tyr Ala Glu Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn
85 90 95
Ala Lys Thr Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Pro Glu Asp
100 105 110
Thr Ala Val Tyr Tyr Cys Thr Ile Gly Gly Ser Leu Ser Val Ser Ser
115 120 125

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

435 440 445

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Asn
450 455 460

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Lys Phe
465 470 475 480

Gly Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
485 490 495

Ser Ser Ile Ser Gly Ser Gly Arg Asp Thr Leu Tyr Ala Glu Ser Val
500 505 510

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Thr Thr Leu Tyr
515 520 525

Leu Gln Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Val Tyr Tyr Cys
530 535 540

Thr Ile Gly Gly Ser Leu Ser Val Ser Ser Gln Gly Thr Leu Val Thr
545 550 555 560

Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly
565 570 575

Gly Ser Gln Val Gln Leu Gln Glu Ser Gly Gly Gly Leu Ala Gln Ala
580 585 590

Gly Gly Ser Leu Ser Leu Ser Cys Ala Ala Ser Gly Phe Thr Val Ser
595 600 605

Asn Ser Val Met Ala Trp Tyr Arg Gln Thr Pro Gly Lys Gln Arg Glu
610 615 620

Phe Val Ala Ile Ile Asn Ser Val Gly Ser Thr Asn Tyr Ala Asp Ser
625 630 635 640

Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Thr Val
645 650 655

Tyr Leu Gln Met Asn Asn Leu Lys Pro Glu Asp Thr Ala Val Tyr Val
660 665 670

Cys Asn Arg Asn Phe Asp Arg Ile Tyr Trp Gly Gln Gly Thr Gln Val
675 680 685

Thr Val Ser Ser His His His His His His Glu Pro Glu Ala
690 695 700

<210> 101
<211> 832
<212> PRT
<213> 人工序列(Artificial Sequence)
<220>
<221> 来源

<223> /注释="人工序列描述:合成多肽"

<400> 101

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

290 295 300
Ile Glu Ser Leu Glu Ser Leu Asn Asn Tyr Phe Asn Ser Ser Gly Ile
305 310 315 320
Asp Val Glu Glu Lys Ser Leu Phe Leu Asp Ile Trp Arg Asn Trp Gln
325 330 335
Lys Asp Gly Asp Met Lys Ile Leu Gln Ser Gln Ile Ile Ser Phe Tyr
340 345 350
Leu Arg Leu Phe Glu Val Leu Lys Asp Asn Gln Ala Ile Ser Asn Asn
355 360 365
Ile Ser Val Ile Glu Ser His Leu Ile Thr Thr Phe Phe Ser Asn Ser
370 375 380
Lys Ala Lys Lys Asp Ala Phe Met Ser Ile Ala Lys Phe Glu Val Asn
385 390 395 400
Asn Pro Gln Val Gln Arg Gln Ala Phe Asn Glu Leu Ile Arg Val Val
405 410 415
His Gln Leu Leu Pro Glu Ser Ser Leu Arg Lys Arg Lys Arg Ser Arg
420 425 430
Cys Ser Gly Gly Pro Gly Pro Ala Gly Met Lys Gly Leu Pro Gly Ser
435 440 445
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Asn
450 455 460
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Lys Phe
465 470 475 480
Gly Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
485 490 495
Ser Ser Ile Ser Gly Ser Gly Arg Asp Thr Leu Tyr Ala Glu Ser Val
500 505 510
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Thr Thr Leu Tyr
515 520 525
Leu Gln Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Val Tyr Tyr Cys
530 535 540
Thr Ile Gly Gly Ser Leu Ser Val Ser Ser Gln Gly Thr Leu Val Thr
545 550 555 560
Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly
565 570 575
Gly Ser Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro
580 585 590
Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser
595 600 605

Ser Tyr Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu
610 615 620
Trp Val Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp
625 630 635 640
Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr
645 650 655
Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr
660 665 670
Tyr Cys Ala Arg Gly Val Gly Ala Phe Arg Pro Tyr Arg Lys His Glu
675 680 685
Trp Gly Gln Gly Thr Leu Val Thr Val Ser Arg Gly Gly Gly Gly Ser
690 695 700
Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Ser Ser Glu Leu Thr Gln
705 710 715 720
Asp Pro Ala Val Ser Val Ala Leu Gly Gln Thr Val Arg Ile Thr Cys
725 730 735
Gln Gly Asp Ser Leu Arg Ser Tyr Tyr Ala Ser Trp Tyr Gln Gln Lys
740 745 750
Pro Gly Gln Ala Pro Val Leu Val Ile Tyr Gly Lys Asn Asn Arg Pro
755 760 765
Ser Gly Ile Pro Asp Arg Phe Ser Gly Ser Ser Ser Gly Asn Thr Ala
770 775 780
Ser Leu Thr Thr Thr Gly Ala Gln Ala Glu Asp Glu Ala Asp Tyr Tyr
785 790 795 800
Cys Asn Ser Ser Pro Phe Glu His Asn Leu Val Val Phe Gly Gly Gly
805 810 815
Thr Lys Leu Thr Val Leu His His His His His His Glu Pro Glu Ala
820 825 830

<210> 102
<211> 276
<212> PRT
<213> 人工序列(Artificial Sequence)
<220>
<221> 来源
<223> /注释="人工序列描述:合成多肽"
<400> 102
Met Asp Met Arg Val Pro Ala Gln Leu Leu Gly Leu Leu Leu Leu Trp
1 5 10 15
Leu Arg Gly Ala Arg Cys Glu Val Gln Leu Val Glu Ser Gly Gly Gly

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

<210> 103
<211> 573
<212> PRT
<213> 人工序列(Artificial Sequence)
<220>
<221> 来源

<223> /注释="人工序列描述:合成多肽"

<400> 103

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

290 295 300

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

<210> 104
<211> 573
<212> PRT
<213> 人工序列(Artificial Sequence)

<220>

<221> 来源

<223> /注释="人工序列描述:合成多肽"

<400> 104

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

275 280 285

Pro Gly Pro Ala Gly Met Lys Gly Leu Pro Gly Ser His Gly Thr Val

290 295 300

Ile Glu Ser Leu Glu Ser Leu Asn Asn Tyr Phe Asn Ser Ser Gly Ile

305 310 315 320

Asp Val Glu Glu Lys Ser Leu Phe Leu Asp Ile Trp Arg Asn Trp Gln

325 330 335

Lys Asp Gly Asp Met Lys Ile Leu Gln Ser Gln Ile Ile Ser Phe Tyr

340 345 350

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

355 360 365

Ile Ser Val Ile Glu Ser His Leu Ile Thr Thr Phe Phe Ser Asn Ser

370 375 380

Lys Ala Lys Lys Asp Ala Phe Met Ser Ile Ala Lys Phe Glu Val Asn

385 390 395 400

Asn Pro Gln Val Gln Arg Gln Ala Phe Asn Glu Leu Ile Arg Val Val

405 410 415

His Gln Leu Leu Pro Glu Ser Ser Leu Arg Lys Arg Lys Arg Ser Arg

420 425 430

Cys Ser Gly Gly Pro Gly Pro Ala Gly Met Lys Gly Leu Pro Gly Ser

435 440 445

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Asn

450 455 460

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Lys Phe

465 470 475 480

Gly Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val

485 490 495

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

500 505 510

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Thr Thr Leu Tyr

515 520 525

Leu Gln Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Val Tyr Tyr Cys

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Thr Ile Gly Gly Ser Leu Ser Val Ser Ser Gln Gly Thr Leu Val Thr

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Val Ser Ser His His His His His His Glu Pro Glu Ala

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

260 265 270

Leu Gln His Lys Asp Asp Asn Pro Ser Leu Pro Pro Phe Glu Arg Pro
275 280 285

Glu Ala Glu Ala Met Cys Thr Ser Phe Lys Glu Asn Pro Thr Thr Phe
290 295 300

Met Gly His Tyr Leu His Glu Val Ala Arg Arg His Pro Tyr Phe Tyr
305 310 315 320

Ala Pro Glu Leu Leu Tyr Tyr Ala Glu Gln Tyr Asn Glu Ile Leu Thr
325 330 335

Gln Cys Cys Ala Glu Ala Asp Lys Glu Ser Cys Leu Thr Pro Lys Leu
340 345 350

Asp Gly Val Lys Glu Lys Ala Leu Val Ser Ser Val Arg Gln Arg Met
355 360 365

Lys Cys Ser Ser Met Gln Lys Phe Gly Glu Arg Ala Phe Lys Ala Trp
370 375 380

Ala Val Ala Arg Leu Ser Gln Thr Phe Pro Asn Ala Asp Phe Ala Glu
385 390 395 400

Ile Thr Lys Leu Ala Thr Asp Leu Thr Lys Val Asn Lys Glu Cys Cys
405 410 415

His Gly Asp Leu Leu Glu Cys Ala Asp Asp Arg Ala Glu Leu Ala Lys
420 425 430

Tyr Met Cys Glu Asn Gln Ala Thr Ile Ser Ser Lys Leu Gln Thr Cys
435 440 445

Cys Asp Lys Pro Leu Leu Lys Lys Ala His Cys Leu Ser Glu Val Glu
450 455 460

His Asp Thr Met Pro Ala Asp Leu Pro Ala Ile Ala Ala Asp Phe Val
465 470 475 480

Glu Asp Gln Glu Val Cys Lys Asn Tyr Ala Glu Ala Lys Asp Val Phe
485 490 495

Leu Gly Thr Phe Leu Tyr Glu Tyr Ser Arg Arg His Pro Asp Tyr Ser
500 505 510

Val Ser Leu Leu Leu Arg Leu Ala Lys Lys Tyr Glu Ala Thr Leu Glu
515 520 525

Lys Cys Cys Ala Glu Ala Asn Pro Pro Ala Cys Tyr Gly Thr Val Leu
530 535 540

Ala Glu Phe Gln Pro Leu Val Glu Glu Pro Lys Asn Leu Val Lys Thr
545 550 555 560

Asn Cys Asp Leu Tyr Glu Lys Leu Gly Glu Tyr Gly Phe Gln Asn Ala
565 570 575

Ile Leu Val Arg Tyr Thr Gln Lys Ala Pro Gln Val Ser Thr Pro Thr
580 585 590
Leu Val Glu Ala Ala Arg Asn Leu Gly Arg Val Gly Thr Lys Cys Cys
595 600 605
Thr Leu Pro Glu Asp Gln Arg Leu Pro Cys Val Glu Asp Tyr Leu Ser
610 615 620
Ala Ile Leu Asn Arg Val Cys Leu Leu His Glu Lys Thr Pro Val Ser
625 630 635 640
Glu His Val Thr Lys Cys Cys Ser Gly Ser Leu Val Glu Arg Arg Pro
645 650 655
Cys Phe Ser Ala Leu Thr Val Asp Glu Thr Tyr Val Pro Lys Glu Phe
660 665 670
Lys Ala Glu Thr Phe Thr Phe His Ser Asp Ile Cys Thr Leu Pro Glu
675 680 685
Lys Glu Lys Gln Ile Lys Lys Gln Thr Ala Leu Ala Glu Leu Val Lys
690 695 700
His Lys Pro Lys Ala Thr Ala Glu Gln Leu Lys Thr Val Met Asp Asp
705 710 715 720
Phe Ala Gln Phe Leu Asp Thr Cys Cys Lys Ala Ala Asp Lys Asp Thr
725 730 735
Cys Phe Ser Thr Glu Gly Pro Asn Leu Val Thr Arg Cys Lys Asp Ala
740 745 750
Leu Ala Ser Gly Gly Pro Gly Pro Ala Gly Met Lys Gly Leu Pro Gly
755 760 765
Ser His Gly Thr Val Ile Glu Ser Leu Glu Ser Leu Asn Asn Tyr Phe
770 775 780
Asn Ser Ser Gly Ile Asp Val Glu Glu Lys Ser Leu Phe Leu Asp Ile
785 790 795 800
Trp Arg Asn Trp Gln Lys Asp Gly Asp Met Lys Ile Leu Gln Ser Gln
805 810 815
Ile Ile Ser Phe Tyr Leu Arg Leu Phe Glu Val Leu Lys Asp Asn Gln
820 825 830
Ala Ile Ser Asn Asn Ile Ser Val Ile Glu Ser His Leu Ile Thr Thr
835 840 845
Phe Phe Ser Asn Ser Lys Ala Lys Lys Asp Ala Phe Met Ser Ile Ala
850 855 860
Lys Phe Glu Val Asn Asn Pro Gln Val Gln Arg Gln Ala Phe Asn Glu
865 870 875 880
Leu Ile Arg Val Val His Gln Leu Leu Pro Glu Ser Ser Leu Arg Lys

885 890 895

Arg Lys Arg Ser Arg Cys Ser Gly Gly Pro Gly Pro Ala Gly Met Lys

900 905 910

Gly Leu Pro Gly Ser Glu Ala His Lys Ser Glu Ile Ala His Arg Tyr

915 920 925

Asn Asp Leu Gly Glu Gln His Phe Lys Gly Leu Val Leu Ile Ala Phe

930 935 940

Ser Gln Tyr Leu Gln Lys Cys Ser Tyr Asp Glu His Ala Lys Leu Val

945 950 955 960

Gln Glu Val Thr Asp Phe Ala Lys Thr Cys Val Ala Asp Glu Ser Ala

965 970 975

Ala Asn Cys Asp Lys Ser Leu His Thr Leu Phe Gly Asp Lys Leu Cys

980 985 990

Ala Ile Pro Asn Leu Arg Glu Asn Tyr Gly Glu Leu Ala Asp Cys Cys

995 1000 1005

Thr Lys Gln Glu Pro Glu Arg Asn Glu Cys Phe Leu Gln His Lys

1010 1015 1020

Asp Asp Asn Pro Ser Leu Pro Pro Phe Glu Arg Pro Glu Ala Glu

1025 1030 1035

Ala Met Cys Thr Ser Phe Lys Glu Asn Pro Thr Thr Phe Met Gly

1040 1045 1050

His Tyr Leu His Glu Val Ala Arg Arg His Pro Tyr Phe Tyr Ala

1055 1060 1065

Pro Glu Leu Leu Tyr Tyr Ala Glu Gln Tyr Asn Glu Ile Leu Thr

1070 1075 1080

Gln Cys Cys Ala Glu Ala Asp Lys Glu Ser Cys Leu Thr Pro Lys

1085 1090 1095

Leu Asp Gly Val Lys Glu Lys Ala Leu Val Ser Ser Val Arg Gln

1100 1105 1110

Arg Met Lys Cys Ser Ser Met Gln Lys Phe Gly Glu Arg Ala Phe

1115 1120 1125

Lys Ala Trp Ala Val Ala Arg Leu Ser Gln Thr Phe Pro Asn Ala

1130 1135 1140

Asp Phe Ala Glu Ile Thr Lys Leu Ala Thr Asp Leu Thr Lys Val

1145 1150 1155

Asn Lys Glu Cys Cys His Gly Asp Leu Leu Glu Cys Ala Asp Asp

1160 1165 1170

Arg Ala Glu Leu Ala Lys Tyr Met Cys Glu Asn Gln Ala Thr Ile

1175 1180 1185

Ser Ser Lys Leu Gln Thr Cys Cys Asp Lys Pro Leu Leu Lys Lys
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1205 1210 1215
Leu Pro Ala Ile Ala Ala Asp Phe Val Glu Asp Gln Glu Val Cys
1220 1225 1230
Lys Asn Tyr Ala Glu Ala Lys Asp Val Phe Leu Gly Thr Phe Leu
1235 1240 1245
Tyr Glu Tyr Ser Arg Arg His Pro Asp Tyr Ser Val Ser Leu Leu
1250 1255 1260
Leu Arg Leu Ala Lys Lys Tyr Glu Ala Thr Leu Glu Lys Cys Cys
1265 1270 1275
Ala Glu Ala Asn Pro Pro Ala Cys Tyr Gly Thr Val Leu Ala Glu
1280 1285 1290
Phe Gln Pro Leu Val Glu Glu Pro Lys Asn Leu Val Lys Thr Asn
1295 1300 1305
Cys Asp Leu Tyr Glu Lys Leu Gly Glu Tyr Gly Phe Gln Asn Ala
1310 1315 1320
Ile Leu Val Arg Tyr Thr Gln Lys Ala Pro Gln Val Ser Thr Pro
1325 1330 1335
Thr Leu Val Glu Ala Ala Arg Asn Leu Gly Arg Val Gly Thr Lys
1340 1345 1350
Cys Cys Thr Leu Pro Glu Asp Gln Arg Leu Pro Cys Val Glu Asp
1355 1360 1365
Tyr Leu Ser Ala Ile Leu Asn Arg Val Cys Leu Leu His Glu Lys
1370 1375 1380
Thr Pro Val Ser Glu His Val Thr Lys Cys Cys Ser Gly Ser Leu
1385 1390 1395
Val Glu Arg Arg Pro Cys Phe Ser Ala Leu Thr Val Asp Glu Thr
1400 1405 1410
Tyr Val Pro Lys Glu Phe Lys Ala Glu Thr Phe Thr Phe His Ser
1415 1420 1425
Asp Ile Cys Thr Leu Pro Glu Lys Glu Lys Gln Ile Lys Lys Gln
1430 1435 1440
Thr Ala Leu Ala Glu Leu Val Lys His Lys Pro Lys Ala Thr Ala
1445 1450 1455
Glu Gln Leu Lys Thr Val Met Asp Asp Phe Ala Gln Phe Leu Asp
1460 1465 1470
Thr Cys Cys Lys Ala Ala Asp Lys Asp Thr Cys Phe Ser Thr Glu

1475 1480 1485
Gly Pro Asn Leu Val Thr Arg Cys Lys Asp Ala Leu Ala His His
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<210> 106
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<400> 106

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

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

515 520 525

Phe Thr Phe His Ser Asp Ile Cys Thr Leu Pro Glu Lys Glu Lys Gln

530 535 540

Ile Lys Lys Gln Thr Ala Leu Ala Glu Leu Val Lys His Lys Pro Lys

545 550 555 560

Ala Thr Ala Glu Gln Leu Lys Thr Val Met Asp Asp Phe Ala Gln Phe

565 570 575

Leu Asp Thr Cys Cys Lys Ala Ala Asp Lys Asp Thr Cys Phe Ser Thr

580 585 590

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

595 600 605

Gly Pro Gly Pro Ala Gly Met Lys Gly Leu Pro Gly Ser His Gly Thr

610 615 620

Val Ile Glu Ser Leu Glu Ser Leu Asn Asn Tyr Phe Asn Ser Ser Gly

625 630 635 640

Ile Asp Val Glu Glu Lys Ser Leu Phe Leu Asp Ile Trp Arg Asn Trp

645 650 655

Gln Lys Asp Gly Asp Met Lys Ile Leu Gln Ser Gln Ile Ile Ser Phe

660 665 670

Tyr Leu Arg Leu Phe Glu Val Leu Lys Asp Asn Gln Ala Ile Ser Asn

675 680 685

Asn Ile Ser Val Ile Glu Ser His Leu Ile Thr Thr Phe Phe Ser Asn

690 695 700

Ser Lys Ala Lys Lys Asp Ala Phe Met Ser Ile Ala Lys Phe Glu Val

705 710 715 720

Asn Asn Pro Gln Val Gln Arg Gln Ala Phe Asn Glu Leu Ile Arg Val

725 730 735

Val His Gln Leu Leu Pro Glu Ser Ser Leu Arg Lys Arg Lys Arg Ser

740 745 750

Arg Cys Ser Gly Gly Pro Gly Pro Ala Gly Met Lys Gly Leu Pro Gly

755 760 765

Ser Glu Ala His Lys Ser Glu Ile Ala His Arg Tyr Asn Asp Leu Gly

770 775 780

Glu Gln His Phe Lys Gly Leu Val Leu Ile Ala Phe Ser Gln Tyr Leu

785 790 795 800

Gln Lys Cys Ser Tyr Asp Glu His Ala Lys Leu Val Gln Glu Val Thr

805 810 815

Asp Phe Ala Lys Thr Cys Val Ala Asp Glu Ser Ala Ala Asn Cys Asp

820 825 830

Lys Ser Leu His Thr Leu Phe Gly Asp Lys Leu Cys Ala Ile Pro Asn
835 840 845
Leu Arg Glu Asn Tyr Gly Glu Leu Ala Asp Cys Cys Thr Lys Gln Glu
850 855 860
Pro Glu Arg Asn Glu Cys Phe Leu Gln His Lys Asp Asp Asn Pro Ser
865 870 875 880
Leu Pro Pro Phe Glu Arg Pro Glu Ala Glu Ala Met Cys Thr Ser Phe
885 890 895
Lys Glu Asn Pro Thr Thr Phe Met Gly His Tyr Leu His Glu Val Ala
900 905 910
Arg Arg His Pro Tyr Phe Tyr Ala Pro Glu Leu Leu Tyr Tyr Ala Glu
915 920 925
Gln Tyr Asn Glu Ile Leu Thr Gln Cys Cys Ala Glu Ala Asp Lys Glu
930 935 940
Ser Cys Leu Thr Pro Lys Leu Asp Gly Val Lys Glu Lys Ala Leu Val
945 950 955 960
Ser Ser Val Arg Gln Arg Met Lys Cys Ser Ser Met Gln Lys Phe Gly
965 970 975
Glu Arg Ala Phe Lys Ala Trp Ala Val Ala Arg Leu Ser Gln Thr Phe
980 985 990
Pro Asn Ala Asp Phe Ala Glu Ile Thr Lys Leu Ala Thr Asp Leu Thr
995 1000 1005
Lys Val Asn Lys Glu Cys Cys His Gly Asp Leu Leu Glu Cys Ala
1010 1015 1020
Asp Asp Arg Ala Glu Leu Ala Lys Tyr Met Cys Glu Asn Gln Ala
1025 1030 1035
Thr Ile Ser Ser Lys Leu Gln Thr Cys Cys Asp Lys Pro Leu Leu
1040 1045 1050
Lys Lys Ala His Cys Leu Ser Glu Val Glu His Asp Thr Met Pro
1055 1060 1065
Ala Asp Leu Pro Ala Ile Ala Ala Asp Phe Val Glu Asp Gln Glu
1070 1075 1080
Val Cys Lys Asn Tyr Ala Glu Ala Lys Asp Val Phe Leu Gly Thr
1085 1090 1095
Phe Leu Tyr Glu Tyr Ser Arg Arg His Pro Asp Tyr Ser Val Ser
1100 1105 1110
Leu Leu Leu Arg Leu Ala Lys Lys Tyr Glu Ala Thr Leu Glu Lys
1115 1120 1125
Cys Cys Ala Glu Ala Asn Pro Pro Ala Cys Tyr Gly Thr Val Leu

1130 1135 1140

Ala Glu Phe Gln Pro Leu Val Glu Glu Pro Lys Asn Leu Val Lys
1145 1150 1155

Thr Asn Cys Asp Leu Tyr Glu Lys Leu Gly Glu Tyr Gly Phe Gln
1160 1165 1170

Asn Ala Ile Leu Val Arg Tyr Thr Gln Lys Ala Pro Gln Val Ser
1175 1180 1185

Thr Pro Thr Leu Val Glu Ala Ala Arg Asn Leu Gly Arg Val Gly
1190 1195 1200

Thr Lys Cys Cys Thr Leu Pro Glu Asp Gln Arg Leu Pro Cys Val
1205 1210 1215

Glu Asp Tyr Leu Ser Ala Ile Leu Asn Arg Val Cys Leu Leu His
1220 1225 1230

Glu Lys Thr Pro Val Ser Glu His Val Thr Lys Cys Cys Ser Gly
1235 1240 1245

Ser Leu Val Glu Arg Arg Pro Cys Phe Ser Ala Leu Thr Val Asp
1250 1255 1260

Glu Thr Tyr Val Pro Lys Glu Phe Lys Ala Glu Thr Phe Thr Phe
1265 1270 1275

His Ser Asp Ile Cys Thr Leu Pro Glu Lys Glu Lys Gln Ile Lys
1280 1285 1290

Lys Gln Thr Ala Leu Ala Glu Leu Val Lys His Lys Pro Lys Ala
1295 1300 1305

Thr Ala Glu Gln Leu Lys Thr Val Met Asp Asp Phe Ala Gln Phe
1310 1315 1320

Leu Asp Thr Cys Cys Lys Ala Ala Asp Lys Asp Thr Cys Phe Ser
1325 1330 1335

Thr Glu Gly Pro Asn Leu Val Thr Arg Cys Lys Asp Ala Leu Ala
1340 1345 1350

Ser Gly Gly Pro Gly Pro Ala Gly Met Lys Gly Leu Pro Gly Ser
1355 1360 1365

His Gly Thr Val Ile Glu Ser Leu Glu Ser Leu Asn Asn Tyr Phe
1370 1375 1380

Asn Ser Ser Gly Ile Asp Val Glu Glu Lys Ser Leu Phe Leu Asp
1385 1390 1395

Ile Trp Arg Asn Trp Gln Lys Asp Gly Asp Met Lys Ile Leu Gln
1400 1405 1410

Ser Gln Ile Ile Ser Phe Tyr Leu Arg Leu Phe Glu Val Leu Lys
1415 1420 1425

Asp Asn Gln Ala Ile Ser Asn Asn Ile Ser Val Ile Glu Ser His
1430 1435 1440
Leu Ile Thr Thr Phe Phe Ser Asn Ser Lys Ala Lys Lys Asp Ala
1445 1450 1455
Phe Met Ser Ile Ala Lys Phe Glu Val Asn Asn Pro Gln Val Gln
1460 1465 1470
Arg Gln Ala Phe Asn Glu Leu Ile Arg Val Val His Gln Leu Leu
1475 1480 1485
Pro Glu Ser Ser Leu Arg Lys Arg Lys Arg Ser Arg Cys His His
1490 1495 1500
His His His His Glu Pro Glu Ala
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Tyr Asn Asp Leu Gly Glu Gln His Phe Lys Gly Leu Val Leu Ile Ala
35 40 45
Phe Ser Gln Tyr Leu Gln Lys Cys Ser Tyr Asp Glu His Ala Lys Leu
50 55 60
Val Gln Glu Val Thr Asp Phe Ala Lys Thr Cys Val Ala Asp Glu Ser
65 70 75 80
Ala Ala Asn Cys Asp Lys Ser Leu His Thr Leu Phe Gly Asp Lys Leu
85 90 95
Cys Ala Ile Pro Asn Leu Arg Glu Asn Tyr Gly Glu Leu Ala Asp Cys
100 105 110
Cys Thr Lys Gln Glu Pro Glu Arg Asn Glu Cys Phe Leu Gln His Lys
115 120 125
Asp Asp Asn Pro Ser Leu Pro Pro Phe Glu Arg Pro Glu Ala Glu Ala
130 135 140
Met Cys Thr Ser Phe Lys Glu Asn Pro Thr Thr Phe Met Gly His Tyr

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

Asp Gln Arg Leu Pro Cys Val Glu Asp Tyr Leu Ser Ala Ile Leu Asn
465 470 475 480
Arg Val Cys Leu Leu His Glu Lys Thr Pro Val Ser Glu His Val Thr
485 490 495
Lys Cys Cys Ser Gly Ser Leu Val Glu Arg Arg Pro Cys Phe Ser Ala
500 505 510
Leu Thr Val Asp Glu Thr Tyr Val Pro Lys Glu Phe Lys Ala Glu Thr
515 520 525
Phe Thr Phe His Ser Asp Ile Cys Thr Leu Pro Glu Lys Glu Lys Gln
530 535 540
Ile Lys Lys Gln Thr Ala Leu Ala Glu Leu Val Lys His Lys Pro Lys
545 550 555 560
Ala Thr Ala Glu Gln Leu Lys Thr Val Met Asp Asp Phe Ala Gln Phe
565 570 575
Leu Asp Thr Cys Cys Lys Ala Ala Asp Lys Asp Thr Cys Phe Ser Thr
580 585 590
Glu Gly Pro Asn Leu Val Thr Arg Cys Lys Asp Ala Leu Ala Ser Gly
595 600 605
Gly Pro Gly Pro Ala Gly Met Lys Gly Leu Pro Gly Ser His Gly Thr
610 615 620
Val Ile Glu Ser Leu Glu Ser Leu Asn Asn Tyr Phe Asn Ser Ser Gly
625 630 635 640
Ile Asp Val Glu Glu Lys Ser Leu Phe Leu Asp Ile Trp Arg Asn Trp
645 650 655
Gln Lys Asp Gly Asp Met Lys Ile Leu Gln Ser Gln Ile Ile Ser Phe
660 665 670
Tyr Leu Arg Leu Phe Glu Val Leu Lys Asp Asn Gln Ala Ile Ser Asn
675 680 685
Asn Ile Ser Val Ile Glu Ser His Leu Ile Thr Thr Phe Phe Ser Asn
690 695 700
Ser Lys Ala Lys Lys Asp Ala Phe Met Ser Ile Ala Lys Phe Glu Val
705 710 715 720
Asn Asn Pro Gln Val Gln Arg Gln Ala Phe Asn Glu Leu Ile Arg Val
725 730 735
Val His Gln Leu Leu Pro Glu Ser Ser Leu Arg Lys Arg Lys Arg Ser
740 745 750
Arg Cys Ser Gly Gly Pro Gly Pro Ala Gly Met Lys Gly Leu Pro Gly
755 760 765
Ser Glu Ala His Lys Ser Glu Ile Ala His Arg Tyr Asn Asp Leu Gly

770 775 780
Glu Gln His Phe Lys Gly Leu Val Leu Ile Ala Phe Ser Gln Tyr Leu
785 790 795 800
Gln Lys Cys Ser Tyr Asp Glu His Ala Lys Leu Val Gln Glu Val Thr
805 810 815
Asp Phe Ala Lys Thr Cys Val Ala Asp Glu Ser Ala Ala Asn Cys Asp
820 825 830
Lys Ser Leu His Thr Leu Phe Gly Asp Lys Leu Cys Ala Ile Pro Asn
835 840 845
Leu Arg Glu Asn Tyr Gly Glu Leu Ala Asp Cys Cys Thr Lys Gln Glu
850 855 860
Pro Glu Arg Asn Glu Cys Phe Leu Gln His Lys Asp Asp Asn Pro Ser
865 870 875 880
Leu Pro Pro Phe Glu Arg Pro Glu Ala Glu Ala Met Cys Thr Ser Phe
885 890 895
Lys Glu Asn Pro Thr Thr Phe Met Gly His Tyr Leu His Glu Val Ala
900 905 910
Arg Arg His Pro Tyr Phe Tyr Ala Pro Glu Leu Leu Tyr Tyr Ala Glu
915 920 925
Gln Tyr Asn Glu Ile Leu Thr Gln Cys Cys Ala Glu Ala Asp Lys Glu
930 935 940
Ser Cys Leu Thr Pro Lys Leu Asp Gly Val Lys Glu Lys Ala Leu Val
945 950 955 960
Ser Ser Val Arg Gln Arg Met Lys Cys Ser Ser Met Gln Lys Phe Gly
965 970 975
Glu Arg Ala Phe Lys Ala Trp Ala Val Ala Arg Leu Ser Gln Thr Phe
980 985 990
Pro Asn Ala Asp Phe Ala Glu Ile Thr Lys Leu Ala Thr Asp Leu Thr
995 1000 1005
Lys Val Asn Lys Glu Cys Cys His Gly Asp Leu Leu Glu Cys Ala
1010 1015 1020
Asp Asp Arg Ala Glu Leu Ala Lys Tyr Met Cys Glu Asn Gln Ala
1025 1030 1035
Thr Ile Ser Ser Lys Leu Gln Thr Cys Cys Asp Lys Pro Leu Leu
1040 1045 1050
Lys Lys Ala His Cys Leu Ser Glu Val Glu His Asp Thr Met Pro
1055 1060 1065
Ala Asp Leu Pro Ala Ile Ala Ala Asp Phe Val Glu Asp Gln Glu
1070 1075 1080

Val Cys Lys Asn Tyr Ala Glu Ala Lys Asp Val Phe Leu Gly Thr
1085 1090 1095
Phe Leu Tyr Glu Tyr Ser Arg Arg His Pro Asp Tyr Ser Val Ser
1100 1105 1110
Leu Leu Leu Arg Leu Ala Lys Lys Tyr Glu Ala Thr Leu Glu Lys
1115 1120 1125
Cys Cys Ala Glu Ala Asn Pro Pro Ala Cys Tyr Gly Thr Val Leu
1130 1135 1140
Ala Glu Phe Gln Pro Leu Val Glu Glu Pro Lys Asn Leu Val Lys
1145 1150 1155
Thr Asn Cys Asp Leu Tyr Glu Lys Leu Gly Glu Tyr Gly Phe Gln
1160 1165 1170
Asn Ala Ile Leu Val Arg Tyr Thr Gln Lys Ala Pro Gln Val Ser
1175 1180 1185
Thr Pro Thr Leu Val Glu Ala Ala Arg Asn Leu Gly Arg Val Gly
1190 1195 1200
Thr Lys Cys Cys Thr Leu Pro Glu Asp Gln Arg Leu Pro Cys Val
1205 1210 1215
Glu Asp Tyr Leu Ser Ala Ile Leu Asn Arg Val Cys Leu Leu His
1220 1225 1230
Glu Lys Thr Pro Val Ser Glu His Val Thr Lys Cys Cys Ser Gly
1235 1240 1245
Ser Leu Val Glu Arg Arg Pro Cys Phe Ser Ala Leu Thr Val Asp
1250 1255 1260
Glu Thr Tyr Val Pro Lys Glu Phe Lys Ala Glu Thr Phe Thr Phe
1265 1270 1275
His Ser Asp Ile Cys Thr Leu Pro Glu Lys Glu Lys Gln Ile Lys
1280 1285 1290
Lys Gln Thr Ala Leu Ala Glu Leu Val Lys His Lys Pro Lys Ala
1295 1300 1305
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1310 1315 1320
Leu Asp Thr Cys Cys Lys Ala Ala Asp Lys Asp Thr Cys Phe Ser
1325 1330 1335
Thr Glu Gly Pro Asn Leu Val Thr Arg Cys Lys Asp Ala Leu Ala
1340 1345 1350
Ser Gly Gly Pro Gly Pro Ala Gly Met Lys Gly Leu Pro Gly Ser
1355 1360 1365
His Gly Thr Val Ile Glu Ser Leu Glu Ser Leu Asn Asn Tyr Phe

1370 1375 1380

Asn Ser Ser Gly Ile Asp Val Glu Glu Lys Ser Leu Phe Leu Asp

1385 1390 1395

Ile Trp Arg Asn Trp Gln Lys Asp Gly Asp Met Lys Ile Leu Gln

1400 1405 1410

Ser Gln Ile Ile Ser Phe Tyr Leu Arg Leu Phe Glu Val Leu Lys

1415 1420 1425

Asp Asn Gln Ala Ile Ser Asn Asn Ile Ser Val Ile Glu Ser His

1430 1435 1440

Leu Ile Thr Thr Phe Phe Ser Asn Ser Lys Ala Lys Lys Asp Ala

1445 1450 1455

Phe Met Ser Ile Ala Lys Phe Glu Val Asn Asn Pro Gln Val Gln

1460 1465 1470

Arg Gln Ala Phe Asn Glu Leu Ile Arg Val Val His Gln Leu Leu

1475 1480 1485

Pro Glu Ser Ser Leu Arg Lys Arg Lys Arg Ser Arg Cys Ser Gly

1490 1495 1500

Gly Pro Gly Pro Ala Gly Met Lys Gly Leu Pro Gly Ser Glu Ala

1505 1510 1515

His Lys Ser Glu Ile Ala His Arg Tyr Asn Asp Leu Gly Glu Gln

1520 1525 1530

His Phe Lys Gly Leu Val Leu Ile Ala Phe Ser Gln Tyr Leu Gln

1535 1540 1545

Lys Cys Ser Tyr Asp Glu His Ala Lys Leu Val Gln Glu Val Thr

1550 1555 1560

Asp Phe Ala Lys Thr Cys Val Ala Asp Glu Ser Ala Ala Asn Cys

1565 1570 1575

Asp Lys Ser Leu His Thr Leu Phe Gly Asp Lys Leu Cys Ala Ile

1580 1585 1590

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

1595 1600 1605

Lys Gln Glu Pro Glu Arg Asn Glu Cys Phe Leu Gln His Lys Asp

1610 1615 1620

Asp Asn Pro Ser Leu Pro Pro Phe Glu Arg Pro Glu Ala Glu Ala

1625 1630 1635

Met Cys Thr Ser Phe Lys Glu Asn Pro Thr Thr Phe Met Gly His

1640 1645 1650

Tyr Leu His Glu Val Ala Arg Arg His Pro Tyr Phe Tyr Ala Pro

1655 1660 1665

Glu Leu Leu Tyr Tyr Ala Glu Gln Tyr Asn Glu Ile Leu Thr Gln
1670 1675 1680
Cys Cys Ala Glu Ala Asp Lys Glu Ser Cys Leu Thr Pro Lys Leu
1685 1690 1695
Asp Gly Val Lys Glu Lys Ala Leu Val Ser Ser Val Arg Gln Arg
1700 1705 1710
Met Lys Cys Ser Ser Met Gln Lys Phe Gly Glu Arg Ala Phe Lys
1715 1720 1725
Ala Trp Ala Val Ala Arg Leu Ser Gln Thr Phe Pro Asn Ala Asp
1730 1735 1740
Phe Ala Glu Ile Thr Lys Leu Ala Thr Asp Leu Thr Lys Val Asn
1745 1750 1755
Lys Glu Cys Cys His Gly Asp Leu Leu Glu Cys Ala Asp Asp Arg
1760 1765 1770
Ala Glu Leu Ala Lys Tyr Met Cys Glu Asn Gln Ala Thr Ile Ser
1775 1780 1785
Ser Lys Leu Gln Thr Cys Cys Asp Lys Pro Leu Leu Lys Lys Ala
1790 1795 1800
His Cys Leu Ser Glu Val Glu His Asp Thr Met Pro Ala Asp Leu
1805 1810 1815
Pro Ala Ile Ala Ala Asp Phe Val Glu Asp Gln Glu Val Cys Lys
1820 1825 1830
Asn Tyr Ala Glu Ala Lys Asp Val Phe Leu Gly Thr Phe Leu Tyr
1835 1840 1845
Glu Tyr Ser Arg Arg His Pro Asp Tyr Ser Val Ser Leu Leu Leu
1850 1855 1860
Arg Leu Ala Lys Lys Tyr Glu Ala Thr Leu Glu Lys Cys Cys Ala
1865 1870 1875
Glu Ala Asn Pro Pro Ala Cys Tyr Gly Thr Val Leu Ala Glu Phe
1880 1885 1890
Gln Pro Leu Val Glu Glu Pro Lys Asn Leu Val Lys Thr Asn Cys
1895 1900 1905
Asp Leu Tyr Glu Lys Leu Gly Glu Tyr Gly Phe Gln Asn Ala Ile
1910 1915 1920
Leu Val Arg Tyr Thr Gln Lys Ala Pro Gln Val Ser Thr Pro Thr
1925 1930 1935
Leu Val Glu Ala Ala Arg Asn Leu Gly Arg Val Gly Thr Lys Cys
1940 1945 1950
Cys Thr Leu Pro Glu Asp Gln Arg Leu Pro Cys Val Glu Asp Tyr

1955 1960 1965
Leu Ser Ala Ile Leu Asn Arg Val Cys Leu Leu His Glu Lys Thr
1970 1975 1980
Pro Val Ser Glu His Val Thr Lys Cys Cys Ser Gly Ser Leu Val
1985 1990 1995
Glu Arg Arg Pro Cys Phe Ser Ala Leu Thr Val Asp Glu Thr Tyr
2000 2005 2010
Val Pro Lys Glu Phe Lys Ala Glu Thr Phe Thr Phe His Ser Asp
2015 2020 2025
Ile Cys Thr Leu Pro Glu Lys Glu Lys Gln Ile Lys Lys Gln Thr
2030 2035 2040
Ala Leu Ala Glu Leu Val Lys His Lys Pro Lys Ala Thr Ala Glu
2045 2050 2055
Gln Leu Lys Thr Val Met Asp Asp Phe Ala Gln Phe Leu Asp Thr
2060 2065 2070
Cys Cys Lys Ala Ala Asp Lys Asp Thr Cys Phe Ser Thr Glu Gly
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His His His Glu Pro Glu Ala
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35 40 45
Phe Ser Gln Tyr Leu Gln Lys Cys Ser Tyr Asp Glu His Ala Lys Leu
50 55 60
Val Gln Glu Val Thr Asp Phe Ala Lys Thr Cys Val Ala Asp Glu Ser
65 70 75 80

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

385 390 395 400
Pro Leu Val Glu Glu Pro Lys Asn Leu Val Lys Thr Asn Cys Asp Leu
405 410 415
Tyr Glu Lys Leu Gly Glu Tyr Gly Phe Gln Asn Ala Ile Leu Val Arg
420 425 430
Tyr Thr Gln Lys Ala Pro Gln Val Ser Thr Pro Thr Leu Val Glu Ala
435 440 445
Ala Arg Asn Leu Gly Arg Val Gly Thr Lys Cys Cys Thr Leu Pro Glu
450 455 460
Asp Gln Arg Leu Pro Cys Val Glu Asp Tyr Leu Ser Ala Ile Leu Asn
465 470 475 480
Arg Val Cys Leu Leu His Glu Lys Thr Pro Val Ser Glu His Val Thr
485 490 495
Lys Cys Cys Ser Gly Ser Leu Val Glu Arg Arg Pro Cys Phe Ser Ala
500 505 510
Leu Thr Val Asp Glu Thr Tyr Val Pro Lys Glu Phe Lys Ala Glu Thr
515 520 525
Phe Thr Phe His Ser Asp Ile Cys Thr Leu Pro Glu Lys Glu Lys Gln
530 535 540
Ile Lys Lys Gln Thr Ala Leu Ala Glu Leu Val Lys His Lys Pro Lys
545 550 555 560
Ala Thr Ala Glu Gln Leu Lys Thr Val Met Asp Asp Phe Ala Gln Phe
565 570 575
Leu Asp Thr Cys Cys Lys Ala Ala Asp Lys Asp Thr Cys Phe Ser Thr
580 585 590
Glu Gly Pro Asn Leu Val Thr Arg Cys Lys Asp Ala Leu Ala Ser Gly
595 600 605
Gly Pro Gly Pro Ala Gly Met Lys Gly Leu Pro Gly Ser His Gly Thr
610 615 620
Val Ile Glu Ser Leu Glu Ser Leu Asn Asn Tyr Phe Asn Ser Ser Gly
625 630 635 640
Ile Asp Val Glu Glu Lys Ser Leu Phe Leu Asp Ile Trp Arg Asn Trp
645 650 655
Gln Lys Asp Gly Asp Met Lys Ile Leu Gln Ser Gln Ile Ile Ser Phe
660 665 670
Tyr Leu Arg Leu Phe Glu Val Leu Lys Asp Asn Gln Ala Ile Ser Asn
675 680 685
Asn Ile Ser Val Ile Glu Ser His Leu Ile Thr Thr Phe Phe Ser Asn
690 695 700

Ser Lys Ala Lys Lys Asp Ala Phe Met Ser Ile Ala Lys Phe Glu Val
705 710 715 720
Asn Asn Pro Gln Val Gln Arg Gln Ala Phe Asn Glu Leu Ile Arg Val
725 730 735
Val His Gln Leu Leu Pro Glu Ser Ser Leu Arg Lys Arg Lys Arg Ser
740 745 750
Arg Cys Ser Gly Gly Pro Gly Pro Ala Gly Met Lys Gly Leu Pro Gly
755 760 765
Ser Gly Gly Gly Gly Ser Glu Ala His Lys Ser Glu Ile Ala His Arg
770 775 780
Tyr Asn Asp Leu Gly Glu Gln His Phe Lys Gly Leu Val Leu Ile Ala
785 790 795 800
Phe Ser Gln Tyr Leu Gln Lys Cys Ser Tyr Asp Glu His Ala Lys Leu
805 810 815
Val Gln Glu Val Thr Asp Phe Ala Lys Thr Cys Val Ala Asp Glu Ser
820 825 830
Ala Ala Asn Cys Asp Lys Ser Leu His Thr Leu Phe Gly Asp Lys Leu
835 840 845
Cys Ala Ile Pro Asn Leu Arg Glu Asn Tyr Gly Glu Leu Ala Asp Cys
850 855 860
Cys Thr Lys Gln Glu Pro Glu Arg Asn Glu Cys Phe Leu Gln His Lys
865 870 875 880
Asp Asp Asn Pro Ser Leu Pro Pro Phe Glu Arg Pro Glu Ala Glu Ala
885 890 895
Met Cys Thr Ser Phe Lys Glu Asn Pro Thr Thr Phe Met Gly His Tyr
900 905 910
Leu His Glu Val Ala Arg Arg His Pro Tyr Phe Tyr Ala Pro Glu Leu
915 920 925
Leu Tyr Tyr Ala Glu Gln Tyr Asn Glu Ile Leu Thr Gln Cys Cys Ala
930 935 940
Glu Ala Asp Lys Glu Ser Cys Leu Thr Pro Lys Leu Asp Gly Val Lys
945 950 955 960
Glu Lys Ala Leu Val Ser Ser Val Arg Gln Arg Met Lys Cys Ser Ser
965 970 975
Met Gln Lys Phe Gly Glu Arg Ala Phe Lys Ala Trp Ala Val Ala Arg
980 985 990
Leu Ser Gln Thr Phe Pro Asn Ala Asp Phe Ala Glu Ile Thr Lys Leu
995 1000 1005
Ala Thr Asp Leu Thr Lys Val Asn Lys Glu Cys Cys His Gly Asp

1010 1015 1020

Leu Leu Glu Cys Ala Asp Asp Arg Ala Glu Leu Ala Lys Tyr Met
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Cys Glu Asn Gln Ala Thr Ile Ser Ser Lys Leu Gln Thr Cys Cys
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Asp Lys Pro Leu Leu Lys Lys Ala His Cys Leu Ser Glu Val Glu
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His Asp Thr Met Pro Ala Asp Leu Pro Ala Ile Ala Ala Asp Phe
1070 1075 1080

Val Glu Asp Gln Glu Val Cys Lys Asn Tyr Ala Glu Ala Lys Asp
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Val Phe Leu Gly Thr Phe Leu Tyr Glu Tyr Ser Arg Arg His Pro
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Asp Tyr Ser Val Ser Leu Leu Leu Arg Leu Ala Lys Lys Tyr Glu
1115 1120 1125

Ala Thr Leu Glu Lys Cys Cys Ala Glu Ala Asn Pro Pro Ala Cys
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Tyr Gly Thr Val Leu Ala Glu Phe Gln Pro Leu Val Glu Glu Pro
1145 1150 1155

Lys Asn Leu Val Lys Thr Asn Cys Asp Leu Tyr Glu Lys Leu Gly
1160 1165 1170

Glu Tyr Gly Phe Gln Asn Ala Ile Leu Val Arg Tyr Thr Gln Lys
1175 1180 1185

Ala Pro Gln Val Ser Thr Pro Thr Leu Val Glu Ala Ala Arg Asn
1190 1195 1200

Leu Gly Arg Val Gly Thr Lys Cys Cys Thr Leu Pro Glu Asp Gln
1205 1210 1215

Arg Leu Pro Cys Val Glu Asp Tyr Leu Ser Ala Ile Leu Asn Arg
1220 1225 1230

Val Cys Leu Leu His Glu Lys Thr Pro Val Ser Glu His Val Thr
1235 1240 1245

Lys Cys Cys Ser Gly Ser Leu Val Glu Arg Arg Pro Cys Phe Ser
1250 1255 1260

Ala Leu Thr Val Asp Glu Thr Tyr Val Pro Lys Glu Phe Lys Ala
1265 1270 1275

Glu Thr Phe Thr Phe His Ser Asp Ile Cys Thr Leu Pro Glu Lys
1280 1285 1290

Glu Lys Gln Ile Lys Lys Gln Thr Ala Leu Ala Glu Leu Val Lys
1295 1300 1305

His Lys Pro Lys Ala Thr Ala Glu Gln Leu Lys Thr Val Met Asp
1310 1315 1320
Asp Phe Ala Gln Phe Leu Asp Thr Cys Cys Lys Ala Ala Asp Lys
1325 1330 1335
Asp Thr Cys Phe Ser Thr Glu Gly Pro Asn Leu Val Thr Arg Cys
1340 1345 1350
Lys Asp Ala Leu Ala Gly Gly Gly Gly Ser Ser Gly Gly Pro Gly
1355 1360 1365
Pro Ala Gly Met Lys Gly Leu Pro Gly Ser His Gly Thr Val Ile
1370 1375 1380
Glu Ser Leu Glu Ser Leu Asn Asn Tyr Phe Asn Ser Ser Gly Ile
1385 1390 1395
Asp Val Glu Glu Lys Ser Leu Phe Leu Asp Ile Trp Arg Asn Trp
1400 1405 1410
Gln Lys Asp Gly Asp Met Lys Ile Leu Gln Ser Gln Ile Ile Ser
1415 1420 1425
Phe Tyr Leu Arg Leu Phe Glu Val Leu Lys Asp Asn Gln Ala Ile
1430 1435 1440
Ser Asn Asn Ile Ser Val Ile Glu Ser His Leu Ile Thr Thr Phe
1445 1450 1455
Phe Ser Asn Ser Lys Ala Lys Lys Asp Ala Phe Met Ser Ile Ala
1460 1465 1470
Lys Phe Glu Val Asn Asn Pro Gln Val Gln Arg Gln Ala Phe Asn
1475 1480 1485
Glu Leu Ile Arg Val Val His Gln Leu Leu Pro Glu Ser Ser Leu
1490 1495 1500
Arg Lys Arg Lys Arg Ser Arg Cys Ser Gly Gly Pro Gly Pro Ala
1505 1510 1515
Gly Met Lys Gly Leu Pro Gly Ser Glu Ala His Lys Ser Glu Ile
1520 1525 1530
Ala His Arg Tyr Asn Asp Leu Gly Glu Gln His Phe Lys Gly Leu
1535 1540 1545
Val Leu Ile Ala Phe Ser Gln Tyr Leu Gln Lys Cys Ser Tyr Asp
1550 1555 1560
Glu His Ala Lys Leu Val Gln Glu Val Thr Asp Phe Ala Lys Thr
1565 1570 1575
Cys Val Ala Asp Glu Ser Ala Ala Asn Cys Asp Lys Ser Leu His
1580 1585 1590
Thr Leu Phe Gly Asp Lys Leu Cys Ala Ile Pro Asn Leu Arg Glu

1595 1600 1605

Asn Tyr Gly Glu Leu Ala Asp Cys Cys Thr Lys Gln Glu Pro Glu

1610 1615 1620

Arg Asn Glu Cys Phe Leu Gln His Lys Asp Asp Asn Pro Ser Leu

1625 1630 1635

Pro Pro Phe Glu Arg Pro Glu Ala Glu Ala Met Cys Thr Ser Phe

1640 1645 1650

Lys Glu Asn Pro Thr Thr Phe Met Gly His Tyr Leu His Glu Val

1655 1660 1665

Ala Arg Arg His Pro Tyr Phe Tyr Ala Pro Glu Leu Leu Tyr Tyr

1670 1675 1680

Ala Glu Gln Tyr Asn Glu Ile Leu Thr Gln Cys Cys Ala Glu Ala

1685 1690 1695

Asp Lys Glu Ser Cys Leu Thr Pro Lys Leu Asp Gly Val Lys Glu

1700 1705 1710

Lys Ala Leu Val Ser Ser Val Arg Gln Arg Met Lys Cys Ser Ser

1715 1720 1725

Met Gln Lys Phe Gly Glu Arg Ala Phe Lys Ala Trp Ala Val Ala

1730 1735 1740

Arg Leu Ser Gln Thr Phe Pro Asn Ala Asp Phe Ala Glu Ile Thr

1745 1750 1755

Lys Leu Ala Thr Asp Leu Thr Lys Val Asn Lys Glu Cys Cys His

1760 1765 1770

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

1775 1780 1785

Tyr Met Cys Glu Asn Gln Ala Thr Ile Ser Ser Lys Leu Gln Thr

1790 1795 1800

Cys Cys Asp Lys Pro Leu Leu Lys Lys Ala His Cys Leu Ser Glu

1805 1810 1815

Val Glu His Asp Thr Met Pro Ala Asp Leu Pro Ala Ile Ala Ala

1820 1825 1830

Asp Phe Val Glu Asp Gln Glu Val Cys Lys Asn Tyr Ala Glu Ala

1835 1840 1845

Lys Asp Val Phe Leu Gly Thr Phe Leu Tyr Glu Tyr Ser Arg Arg

1850 1855 1860

His Pro Asp Tyr Ser Val Ser Leu Leu Leu Arg Leu Ala Lys Lys

1865 1870 1875

Tyr Glu Ala Thr Leu Glu Lys Cys Cys Ala Glu Ala Asn Pro Pro

1880 1885 1890

Ala Cys Tyr Gly Thr Val Leu Ala Glu Phe Gln Pro Leu Val Glu
1895 1900 1905
Glu Pro Lys Asn Leu Val Lys Thr Asn Cys Asp Leu Tyr Glu Lys
1910 1915 1920
Leu Gly Glu Tyr Gly Phe Gln Asn Ala Ile Leu Val Arg Tyr Thr
1925 1930 1935
Gln Lys Ala Pro Gln Val Ser Thr Pro Thr Leu Val Glu Ala Ala
1940 1945 1950
Arg Asn Leu Gly Arg Val Gly Thr Lys Cys Cys Thr Leu Pro Glu
1955 1960 1965
Asp Gln Arg Leu Pro Cys Val Glu Asp Tyr Leu Ser Ala Ile Leu
1970 1975 1980
Asn Arg Val Cys Leu Leu His Glu Lys Thr Pro Val Ser Glu His
1985 1990 1995
Val Thr Lys Cys Cys Ser Gly Ser Leu Val Glu Arg Arg Pro Cys
2000 2005 2010
Phe Ser Ala Leu Thr Val Asp Glu Thr Tyr Val Pro Lys Glu Phe
2015 2020 2025
Lys Ala Glu Thr Phe Thr Phe His Ser Asp Ile Cys Thr Leu Pro
2030 2035 2040
Glu Lys Glu Lys Gln Ile Lys Lys Gln Thr Ala Leu Ala Glu Leu
2045 2050 2055
Val Lys His Lys Pro Lys Ala Thr Ala Glu Gln Leu Lys Thr Val
2060 2065 2070
Met Asp Asp Phe Ala Gln Phe Leu Asp Thr Cys Cys Lys Ala Ala
2075 2080 2085
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Glu Ala
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35 40 45
Phe Ser Gln Tyr Leu Gln Lys Cys Ser Tyr Asp Glu His Ala Lys Leu
50 55 60
Val Gln Glu Val Thr Asp Phe Ala Lys Thr Cys Val Ala Asp Glu Ser
65 70 75 80
Ala Ala Asn Cys Asp Lys Ser Leu His Thr Leu Phe Gly Asp Lys Leu
85 90 95
Cys Ala Ile Pro Asn Leu Arg Glu Asn Tyr Gly Glu Leu Ala Asp Cys
100 105 110
Cys Thr Lys Gln Glu Pro Glu Arg Asn Glu Cys Phe Leu Gln His Lys
115 120 125
Asp Asp Asn Pro Ser Leu Pro Pro Phe Glu Arg Pro Glu Ala Glu Ala
130 135 140
Met Cys Thr Ser Phe Lys Glu Asn Pro Thr Thr Phe Met Gly His Tyr
145 150 155 160
Leu His Glu Val Ala Arg Arg His Pro Tyr Phe Tyr Ala Pro Glu Leu
165 170 175
Leu Tyr Tyr Ala Glu Gln Tyr Asn Glu Ile Leu Thr Gln Cys Cys Ala
180 185 190
Glu Ala Asp Lys Glu Ser Cys Leu Thr Pro Lys Leu Asp Gly Val Lys
195 200 205
Glu Lys Ala Leu Val Ser Ser Val Arg Gln Arg Met Lys Cys Ser Ser
210 215 220
Met Gln Lys Phe Gly Glu Arg Ala Phe Lys Ala Trp Ala Val Ala Arg
225 230 235 240
Leu Ser Gln Thr Phe Pro Asn Ala Asp Phe Ala Glu Ile Thr Lys Leu
245 250 255
Ala Thr Asp Leu Thr Lys Val Asn Lys Glu Cys Cys His Gly Asp Leu
260 265 270
Leu Glu Cys Ala Asp Asp Arg Ala Glu Leu Ala Lys Tyr Met Cys Glu
275 280 285
Asn Gln Ala Thr Ile Ser Ser Lys Leu Gln Thr Cys Cys Asp Lys Pro
290 295 300

Leu Leu Lys Lys Ala His Cys Leu Ser Glu Val Glu His Asp Thr Met
305 310 315 320
Pro Ala Asp Leu Pro Ala Ile Ala Ala Asp Phe Val Glu Asp Gln Glu
325 330 335
Val Cys Lys Asn Tyr Ala Glu Ala Lys Asp Val Phe Leu Gly Thr Phe
340 345 350
Leu Tyr Glu Tyr Ser Arg Arg His Pro Asp Tyr Ser Val Ser Leu Leu
355 360 365
Leu Arg Leu Ala Lys Lys Tyr Glu Ala Thr Leu Glu Lys Cys Cys Ala
370 375 380
Glu Ala Asn Pro Pro Ala Cys Tyr Gly Thr Val Leu Ala Glu Phe Gln
385 390 395 400
Pro Leu Val Glu Glu Pro Lys Asn Leu Val Lys Thr Asn Cys Asp Leu
405 410 415
Tyr Glu Lys Leu Gly Glu Tyr Gly Phe Gln Asn Ala Ile Leu Val Arg
420 425 430
Tyr Thr Gln Lys Ala Pro Gln Val Ser Thr Pro Thr Leu Val Glu Ala
435 440 445
Ala Arg Asn Leu Gly Arg Val Gly Thr Lys Cys Cys Thr Leu Pro Glu
450 455 460
Asp Gln Arg Leu Pro Cys Val Glu Asp Tyr Leu Ser Ala Ile Leu Asn
465 470 475 480
Arg Val Cys Leu Leu His Glu Lys Thr Pro Val Ser Glu His Val Thr
485 490 495
Lys Cys Cys Ser Gly Ser Leu Val Glu Arg Arg Pro Cys Phe Ser Ala
500 505 510
Leu Thr Val Asp Glu Thr Tyr Val Pro Lys Glu Phe Lys Ala Glu Thr
515 520 525
Phe Thr Phe His Ser Asp Ile Cys Thr Leu Pro Glu Lys Glu Lys Gln
530 535 540
Ile Lys Lys Gln Thr Ala Leu Ala Glu Leu Val Lys His Lys Pro Lys
545 550 555 560
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565 570 575
Leu Asp Thr Cys Cys Lys Ala Ala Asp Lys Asp Thr Cys Phe Ser Thr
580 585 590
Glu Gly Pro Asn Leu Val Thr Arg Cys Lys Asp Ala Leu Ala Ser Gly
595 600 605
Gly Pro Gly Pro Ala Gly Met Lys Gly Leu Pro Gly Ser His Gly Thr

610 615 620
Val Ile Glu Ser Leu Glu Ser Leu Asn Asn Tyr Phe Asn Ser Ser Gly
625 630 635 640
Ile Asp Val Glu Glu Lys Ser Leu Phe Leu Asp Ile Trp Arg Asn Trp
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Gln Lys Asp Gly Asp Met Lys Ile Leu Gln Ser Gln Ile Ile Ser Phe
660 665 670
Tyr Leu Arg Leu Phe Glu Val Leu Lys Asp Asn Gln Ala Ile Ser Asn
675 680 685
Asn Ile Ser Val Ile Glu Ser His Leu Ile Thr Thr Phe Phe Ser Asn
690 695 700
Ser Lys Ala Lys Lys Asp Ala Phe Met Ser Ile Ala Lys Phe Glu Val
705 710 715 720
Asn Asn Pro Gln Val Gln Arg Gln Ala Phe Asn Glu Leu Ile Arg Val
725 730 735
Val His Gln Leu Leu Pro Glu Ser Ser Leu Arg Lys Arg Lys Arg Ser
740 745 750
Arg Cys Ser Gly Gly Pro Gly Pro Ala Gly Met Lys Gly Leu Pro Gly
755 760 765
Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Ala His Lys Ser
770 775 780
Glu Ile Ala His Arg Tyr Asn Asp Leu Gly Glu Gln His Phe Lys Gly
785 790 795 800
Leu Val Leu Ile Ala Phe Ser Gln Tyr Leu Gln Lys Cys Ser Tyr Asp
805 810 815
Glu His Ala Lys Leu Val Gln Glu Val Thr Asp Phe Ala Lys Thr Cys
820 825 830
Val Ala Asp Glu Ser Ala Ala Asn Cys Asp Lys Ser Leu His Thr Leu
835 840 845
Phe Gly Asp Lys Leu Cys Ala Ile Pro Asn Leu Arg Glu Asn Tyr Gly
850 855 860
Glu Leu Ala Asp Cys Cys Thr Lys Gln Glu Pro Glu Arg Asn Glu Cys
865 870 875 880
Phe Leu Gln His Lys Asp Asp Asn Pro Ser Leu Pro Pro Phe Glu Arg
885 890 895
Pro Glu Ala Glu Ala Met Cys Thr Ser Phe Lys Glu Asn Pro Thr Thr
900 905 910
Phe Met Gly His Tyr Leu His Glu Val Ala Arg Arg His Pro Tyr Phe
915 920 925

Tyr Ala Pro Glu Leu Leu Tyr Tyr Ala Glu Gln Tyr Asn Glu Ile Leu
930 935 940
Thr Gln Cys Cys Ala Glu Ala Asp Lys Glu Ser Cys Leu Thr Pro Lys
945 950 955 960
Leu Asp Gly Val Lys Glu Lys Ala Leu Val Ser Ser Val Arg Gln Arg
965 970 975
Met Lys Cys Ser Ser Met Gln Lys Phe Gly Glu Arg Ala Phe Lys Ala
980 985 990
Trp Ala Val Ala Arg Leu Ser Gln Thr Phe Pro Asn Ala Asp Phe Ala
995 1000 1005
Glu Ile Thr Lys Leu Ala Thr Asp Leu Thr Lys Val Asn Lys Glu
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1070 1075 1080
Ile Ala Ala Asp Phe Val Glu Asp Gln Glu Val Cys Lys Asn Tyr
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Ala Glu Ala Lys Asp Val Phe Leu Gly Thr Phe Leu Tyr Glu Tyr
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1115 1120 1125
Ala Lys Lys Tyr Glu Ala Thr Leu Glu Lys Cys Cys Ala Glu Ala
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1160 1165 1170
Tyr Glu Lys Leu Gly Glu Tyr Gly Phe Gln Asn Ala Ile Leu Val
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Arg Tyr Thr Gln Lys Ala Pro Gln Val Ser Thr Pro Thr Leu Val
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1205 1210 1215
Leu Pro Glu Asp Gln Arg Leu Pro Cys Val Glu Asp Tyr Leu Ser

1220 1225 1230

Ala Ile Leu Asn Arg Val Cys Leu Leu His Glu Lys Thr Pro Val
1235 1240 1245

Ser Glu His Val Thr Lys Cys Cys Ser Gly Ser Leu Val Glu Arg
1250 1255 1260

Arg Pro Cys Phe Ser Ala Leu Thr Val Asp Glu Thr Tyr Val Pro
1265 1270 1275

Lys Glu Phe Lys Ala Glu Thr Phe Thr Phe His Ser Asp Ile Cys
1280 1285 1290

Thr Leu Pro Glu Lys Glu Lys Gln Ile Lys Lys Gln Thr Ala Leu
1295 1300 1305

Ala Glu Leu Val Lys His Lys Pro Lys Ala Thr Ala Glu Gln Leu
1310 1315 1320

Lys Thr Val Met Asp Asp Phe Ala Gln Phe Leu Asp Thr Cys Cys
1325 1330 1335

Lys Ala Ala Asp Lys Asp Thr Cys Phe Ser Thr Glu Gly Pro Asn
1340 1345 1350

Leu Val Thr Arg Cys Lys Asp Ala Leu Ala Gly Gly Gly Gly Ser
1355 1360 1365

Gly Gly Gly Gly Ser Ser Gly Gly Pro Gly Pro Ala Gly Met Lys
1370 1375 1380

Gly Leu Pro Gly Ser His Gly Thr Val Ile Glu Ser Leu Glu Ser
1385 1390 1395

Leu Asn Asn Tyr Phe Asn Ser Ser Gly Ile Asp Val Glu Glu Lys
1400 1405 1410

Ser Leu Phe Leu Asp Ile Trp Arg Asn Trp Gln Lys Asp Gly Asp
1415 1420 1425

Met Lys Ile Leu Gln Ser Gln Ile Ile Ser Phe Tyr Leu Arg Leu
1430 1435 1440

Phe Glu Val Leu Lys Asp Asn Gln Ala Ile Ser Asn Asn Ile Ser
1445 1450 1455

Val Ile Glu Ser His Leu Ile Thr Thr Phe Phe Ser Asn Ser Lys
1460 1465 1470

Ala Lys Lys Asp Ala Phe Met Ser Ile Ala Lys Phe Glu Val Asn
1475 1480 1485

Asn Pro Gln Val Gln Arg Gln Ala Phe Asn Glu Leu Ile Arg Val
1490 1495 1500

Val His Gln Leu Leu Pro Glu Ser Ser Leu Arg Lys Arg Lys Arg
1505 1510 1515

Ser Arg Cys Ser Gly Gly Pro Gly Pro Ala Gly Met Lys Gly Leu
1520 1525 1530
Pro Gly Ser Glu Ala His Lys Ser Glu Ile Ala His Arg Tyr Asn
1535 1540 1545
Asp Leu Gly Glu Gln His Phe Lys Gly Leu Val Leu Ile Ala Phe
1550 1555 1560
Ser Gln Tyr Leu Gln Lys Cys Ser Tyr Asp Glu His Ala Lys Leu
1565 1570 1575
Val Gln Glu Val Thr Asp Phe Ala Lys Thr Cys Val Ala Asp Glu
1580 1585 1590
Ser Ala Ala Asn Cys Asp Lys Ser Leu His Thr Leu Phe Gly Asp
1595 1600 1605
Lys Leu Cys Ala Ile Pro Asn Leu Arg Glu Asn Tyr Gly Glu Leu
1610 1615 1620
Ala Asp Cys Cys Thr Lys Gln Glu Pro Glu Arg Asn Glu Cys Phe
1625 1630 1635
Leu Gln His Lys Asp Asp Asn Pro Ser Leu Pro Pro Phe Glu Arg
1640 1645 1650
Pro Glu Ala Glu Ala Met Cys Thr Ser Phe Lys Glu Asn Pro Thr
1655 1660 1665
Thr Phe Met Gly His Tyr Leu His Glu Val Ala Arg Arg His Pro
1670 1675 1680
Tyr Phe Tyr Ala Pro Glu Leu Leu Tyr Tyr Ala Glu Gln Tyr Asn
1685 1690 1695
Glu Ile Leu Thr Gln Cys Cys Ala Glu Ala Asp Lys Glu Ser Cys
1700 1705 1710
Leu Thr Pro Lys Leu Asp Gly Val Lys Glu Lys Ala Leu Val Ser
1715 1720 1725
Ser Val Arg Gln Arg Met Lys Cys Ser Ser Met Gln Lys Phe Gly
1730 1735 1740
Glu Arg Ala Phe Lys Ala Trp Ala Val Ala Arg Leu Ser Gln Thr
1745 1750 1755
Phe Pro Asn Ala Asp Phe Ala Glu Ile Thr Lys Leu Ala Thr Asp
1760 1765 1770
Leu Thr Lys Val Asn Lys Glu Cys Cys His Gly Asp Leu Leu Glu
1775 1780 1785
Cys Ala Asp Asp Arg Ala Glu Leu Ala Lys Tyr Met Cys Glu Asn
1790 1795 1800
Gln Ala Thr Ile Ser Ser Lys Leu Gln Thr Cys Cys Asp Lys Pro

1805 1810 1815
Leu Leu Lys Lys Ala His Cys Leu Ser Glu Val Glu His Asp Thr
1820 1825 1830
Met Pro Ala Asp Leu Pro Ala Ile Ala Ala Asp Phe Val Glu Asp
1835 1840 1845
Gln Glu Val Cys Lys Asn Tyr Ala Glu Ala Lys Asp Val Phe Leu
1850 1855 1860
Gly Thr Phe Leu Tyr Glu Tyr Ser Arg Arg His Pro Asp Tyr Ser
1865 1870 1875
Val Ser Leu Leu Leu Arg Leu Ala Lys Lys Tyr Glu Ala Thr Leu
1880 1885 1890
Glu Lys Cys Cys Ala Glu Ala Asn Pro Pro Ala Cys Tyr Gly Thr
1895 1900 1905
Val Leu Ala Glu Phe Gln Pro Leu Val Glu Glu Pro Lys Asn Leu
1910 1915 1920
Val Lys Thr Asn Cys Asp Leu Tyr Glu Lys Leu Gly Glu Tyr Gly
1925 1930 1935
Phe Gln Asn Ala Ile Leu Val Arg Tyr Thr Gln Lys Ala Pro Gln
1940 1945 1950
Val Ser Thr Pro Thr Leu Val Glu Ala Ala Arg Asn Leu Gly Arg
1955 1960 1965
Val Gly Thr Lys Cys Cys Thr Leu Pro Glu Asp Gln Arg Leu Pro
1970 1975 1980
Cys Val Glu Asp Tyr Leu Ser Ala Ile Leu Asn Arg Val Cys Leu
1985 1990 1995
Leu His Glu Lys Thr Pro Val Ser Glu His Val Thr Lys Cys Cys
2000 2005 2010
Ser Gly Ser Leu Val Glu Arg Arg Pro Cys Phe Ser Ala Leu Thr
2015 2020 2025
Val Asp Glu Thr Tyr Val Pro Lys Glu Phe Lys Ala Glu Thr Phe
2030 2035 2040
Thr Phe His Ser Asp Ile Cys Thr Leu Pro Glu Lys Glu Lys Gln
2045 2050 2055
Ile Lys Lys Gln Thr Ala Leu Ala Glu Leu Val Lys His Lys Pro
2060 2065 2070
Lys Ala Thr Ala Glu Gln Leu Lys Thr Val Met Asp Asp Phe Ala
2075 2080 2085
Gln Phe Leu Asp Thr Cys Cys Lys Ala Ala Asp Lys Asp Thr Cys
2090 2095 2100

Phe Ser Thr Glu Gly Pro Asn Leu Val Thr Arg Cys Lys Asp Ala
2105 2110 2115
Leu Ala His His His His His His Glu Pro Glu Ala
2120 2125 2130

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

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

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

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

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

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

690 695 700

Gly Gly Gly Ser Gln Val Gln Leu Gln Glu Ser Gly Gly Gly Leu Ala
705 710 715 720
Gln Ala Gly Gly Ser Leu Ser Leu Ser Cys Ala Ala Ser Gly Phe Thr
725 730 735
Val Ser Asn Ser Val Met Ala Trp Tyr Arg Gln Thr Pro Gly Lys Gln
740 745 750
Arg Glu Phe Val Ala Ile Ile Asn Ser Val Gly Ser Thr Asn Tyr Ala
755 760 765
Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn
770 775 780
Thr Val Tyr Leu Gln Met Asn Asn Leu Lys Pro Glu Asp Thr Ala Val
785 790 795 800
Tyr Val Cys Asn Arg Asn Phe Asp Arg Ile Tyr Trp Gly Gln Gly Thr
805 810 815
Gln Val Thr Val Ser Ser His His His His His His Glu Pro Glu Ala
820 825 830

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

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

420 425 430

Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Asn Ser Leu Arg

435 440 445

Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Lys Phe Gly Met Ser

450 455 460

Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ser Ser Ile

465 470 475 480

Ser Gly Ser Gly Arg Asp Thr Leu Tyr Ala Glu Ser Val Lys Gly Arg

485 490 495

Phe Thr Ile Ser Arg Asp Asn Ala Lys Thr Thr Leu Tyr Leu Gln Met

500 505 510

Asn Ser Leu Arg Pro Glu Asp Thr Ala Val Tyr Tyr Cys Thr Ile Gly

515 520 525

Gly Ser Leu Ser Val Ser Ser Gln Gly Thr Leu Val Thr Val Ser Ser

530 535 540

Ser Gly Gly Pro Gly Pro Ala Gly Met Lys Gly Leu Pro Gly Ser His

545 550 555 560

Gly Thr Val Ile Glu Ser Leu Glu Ser Leu Asn Asn Tyr Phe Asn Ser

565 570 575

Ser Gly Ile Asp Val Glu Glu Lys Ser Leu Phe Leu Asp Ile Trp Arg

580 585 590

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

595 600 605

Ser Phe Tyr Leu Arg Leu Phe Glu Val Leu Lys Asp Asn Gln Ala Ile

610 615 620

Ser Asn Asn Ile Ser Val Ile Glu Ser His Leu Ile Thr Thr Phe Phe

625 630 635 640

Ser Asn Ser Lys Ala Lys Lys Asp Ala Phe Met Ser Ile Ala Lys Phe

645 650 655

Glu Val Asn Asn Pro Gln Val Gln Arg Gln Ala Phe Asn Glu Leu Ile

660 665 670

Arg Val Val His Gln Leu Leu Pro Glu Ser Ser Leu Arg Lys Arg Lys

675 680 685

Arg Ser Arg Cys Ser Gly Gly Pro Gly Pro Ala Gly Met Lys Gly Leu

690 695 700

Pro Gly Ser Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln

705 710 715 720

Pro Gly Asn Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe

725 730 735

Ser Lys Phe Gly Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu
740 745 750
Glu Trp Val Ser Ser Ile Ser Gly Ser Gly Arg Asp Thr Leu Tyr Ala
755 760 765
Glu Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Thr
770 775 780
Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Val
785 790 795 800
Tyr Tyr Cys Thr Ile Gly Gly Ser Leu Ser Val Ser Ser Gln Gly Thr
805 810 815
Leu Val Thr Val Ser Ser His His His His His His Glu Pro Glu Ala
820 825 830

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<400> 113

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Leu Arg Gly Ala Arg Cys Arg Val Ile Pro Val Ser Gly Pro Ala Arg
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Cys Leu Ser Gln Ser Arg Asn Leu Leu Lys Thr Thr Asp Asp Met Val
35 40 45
Lys Thr Ala Arg Glu Lys Leu Lys His Tyr Ser Cys Thr Ala Glu Asp
50 55 60
Ile Asp His Glu Asp Ile Thr Arg Asp Gln Thr Ser Thr Leu Lys Thr
65 70 75 80
Cys Leu Pro Leu Glu Leu His Lys Asn Glu Ser Cys Leu Ala Thr Arg
85 90 95
Glu Thr Ser Ser Thr Thr Arg Gly Ser Cys Leu Pro Pro Gln Lys Thr
100 105 110
Ser Leu Met Met Thr Leu Cys Leu Gly Ser Ile Tyr Glu Asp Leu Lys
115 120 125
Met Tyr Gln Thr Glu Phe Gln Ala Ile Asn Ala Ala Leu Gln Asn His
130 135 140
Asn His Gln Gln Ile Ile Leu Asp Lys Gly Met Leu Val Ala Ile Asp

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

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

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Cys Leu Ser Gln Ser Arg Asn Leu Leu Lys Thr Thr Asp Asp Met Val
35 40 45
Lys Thr Ala Arg Glu Lys Leu Lys His Tyr Ser Cys Thr Ala Glu Asp
50 55 60
Ile Asp His Glu Asp Ile Thr Arg Asp Gln Thr Ser Thr Leu Lys Thr
65 70 75 80
Cys Leu Pro Leu Glu Leu His Lys Asn Glu Ser Cys Leu Ala Thr Arg
85 90 95
Glu Thr Ser Ser Thr Thr Arg Gly Ser Cys Leu Pro Pro Gln Lys Thr
100 105 110
Ser Leu Met Met Thr Leu Cys Leu Gly Ser Ile Tyr Glu Asp Leu Lys
115 120 125
Met Tyr Gln Thr Glu Phe Gln Ala Ile Asn Ala Ala Leu Gln Asn His
130 135 140
Asn His Gln Gln Ile Ile Leu Asp Lys Gly Met Leu Val Ala Ile Asp

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

Ile Arg Asp Ile Ile Lys Pro Asp Pro Pro Lys Asn Leu Gln Met Lys
465 470 475 480
Pro Leu Lys Asn Ser Gln Val Glu Val Ser Trp Glu Tyr Pro Asp Ser
485 490 495
Trp Ser Thr Pro His Ser Tyr Phe Ser Leu Lys Phe Phe Val Arg Ile
500 505 510
Gln Arg Lys Lys Glu Lys Met Lys Glu Thr Glu Glu Gly Cys Asn Gln
515 520 525
Lys Gly Ala Phe Leu Val Glu Lys Thr Ser Thr Glu Val Gln Cys Lys
530 535 540
Gly Gly Asn Val Cys Val Gln Ala Gln Asp Arg Tyr Tyr Asn Ser Ser
545 550 555 560
Cys Ser Lys Trp Ala Cys Val Pro Cys Arg Val Arg Ser His His His
565 570 575
His His His

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

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

435 440 445

Tyr Asn Ser Ser Cys Ser Lys Trp Ala Cys Val Pro Cys Arg Val Arg

450 455 460

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser

465 470 475 480

Arg Val Ile Pro Val Ser Gly Pro Ala Arg Cys Leu Ser Gln Ser Arg

485 490 495

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

500 505 510

Leu Lys His Tyr Ser Cys Thr Ala Glu Asp Ile Asp His Glu Asp Ile

515 520 525

Thr Arg Asp Gln Thr Ser Thr Leu Lys Thr Cys Leu Pro Leu Glu Leu

530 535 540

His Lys Asn Glu Ser Cys Leu Ala Thr Arg Glu Thr Ser Ser Thr Thr

545 550 555 560

Arg Gly Ser Cys Leu Pro Pro Gln Lys Thr Ser Leu Met Met Thr Leu

565 570 575

Cys Leu Gly Ser Ile Tyr Glu Asp Leu Lys Met Tyr Gln Thr Glu Phe

580 585 590

Gln Ala Ile Asn Ala Ala Leu Gln Asn His Asn His Gln Gln Ile Ile

595 600 605

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

610 615 620

Asn His Asn Gly Glu Thr Leu Arg Gln Lys Pro Pro Val Gly Glu Ala

625 630 635 640

Asp Pro Tyr Arg Val Lys Met Lys Leu Cys Ile Leu Leu His Ala Phe

645 650 655

Ser Thr Arg Val Val Thr Ile Asn Arg Val Met Gly Tyr Leu Ser Ser

660 665 670

Ala Ser Gly Gly Pro Gly Pro Ala Gly Met Lys Gly Leu Pro Gly Ser

675 680 685

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Asn

690 695 700

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Lys Phe

705 710 715 720

Gly Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val

725 730 735

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

740 745 750

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Thr Thr Leu Tyr
755 760 765
Leu Gln Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Val Tyr Tyr Cys
770 775 780
Thr Ile Gly Gly Ser Leu Ser Val Ser Ser Gln Gly Thr Leu Val Thr
785 790 795 800
Val Ser Ser His His His His His His
805

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

180 185 190

Gly Lys Gly Leu Glu Trp Val Ser Ser Ile Ser Gly Ser Gly Arg Asp

195 200 205

Thr Leu Tyr Ala Glu Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp

210 215 220

Asn Ala Lys Thr Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Pro Glu

225 230 235 240

Asp Thr Ala Val Tyr Tyr Cys Thr Ile Gly Gly Ser Leu Ser Val Ser

245 250 255

Ser Gln Gly Thr Leu Val Thr Val Ser Ser Ser Gly Gly Pro Gly Pro

260 265 270

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

275 280 285

Val Tyr Val Val Glu Val Asp Trp Thr Pro Asp Ala Pro Gly Glu Thr

290 295 300

Val Asn Leu Thr Cys Asp Thr Pro Glu Glu Asp Asp Ile Thr Trp Thr

305 310 315 320

Ser Asp Gln Arg His Gly Val Ile Gly Ser Gly Lys Thr Leu Thr Ile

325 330 335

Thr Val Lys Glu Phe Leu Asp Ala Gly Gln Tyr Thr Cys His Lys Gly

340 345 350

Gly Glu Thr Leu Ser His Ser His Leu Leu Leu His Lys Lys Glu Asn

355 360 365

Gly Ile Trp Ser Thr Glu Ile Leu Lys Asn Phe Lys Asn Lys Thr Phe

370 375 380

Leu Lys Cys Glu Ala Pro Asn Tyr Ser Gly Arg Phe Thr Cys Ser Trp

385 390 395 400

Leu Val Gln Arg Asn Met Asp Leu Lys Phe Asn Ile Lys Ser Ser Ser

405 410 415

Ser Ser Pro Asp Ser Arg Ala Val Thr Cys Gly Met Ala Ser Leu Ser

420 425 430

Ala Glu Lys Val Thr Leu Asp Gln Arg Asp Tyr Glu Lys Tyr Ser Val

435 440 445

Ser Cys Gln Glu Asp Val Thr Cys Pro Thr Ala Glu Glu Thr Leu Pro

450 455 460

Ile Glu Leu Ala Leu Glu Ala Arg Gln Gln Asn Lys Tyr Glu Asn Tyr

465 470 475 480

Ser Thr Ser Phe Phe Ile Arg Asp Ile Ile Lys Pro Asp Pro Pro Lys

485 490 495

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

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

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<223> /注释="人工序列描述:合成多肽"
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Leu Arg Gly Ala Arg Cys Gln Val Gln Leu Gln Glu Ser Gly Gly Gly
20 25 30
Leu Val Gln Ala Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly
35 40 45
Arg Ile Phe Ser Ile Asp Ile Met Ser Trp Tyr Arg Gln Ala Pro Gly
50 55 60
Lys Gln Arg Glu Leu Val Ala Arg Ile Thr Arg Gly Gly Thr Ile Ser
65 70 75 80
Tyr Asp Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala
85 90 95
Lys Asn Thr Val Tyr Leu Gln Met Asn Ser Leu Lys Pro Glu Asp Thr
100 105 110

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

420 425 430

Ala Glu Lys Val Thr Leu Asp Gln Arg Asp Tyr Glu Lys Tyr Ser Val

435 440 445

Ser Cys Gln Glu Asp Val Thr Cys Pro Thr Ala Glu Glu Thr Leu Pro

450 455 460

Ile Glu Leu Ala Leu Glu Ala Arg Gln Gln Asn Lys Tyr Glu Asn Tyr

465 470 475 480

Ser Thr Ser Phe Phe Ile Arg Asp Ile Ile Lys Pro Asp Pro Pro Lys

485 490 495

Asn Leu Gln Met Lys Pro Leu Lys Asn Ser Gln Val Glu Val Ser Trp

500 505 510

Glu Tyr Pro Asp Ser Trp Ser Thr Pro His Ser Tyr Phe Ser Leu Lys

515 520 525

Phe Phe Val Arg Ile Gln Arg Lys Lys Glu Lys Met Lys Glu Thr Glu

530 535 540

Glu Gly Cys Asn Gln Lys Gly Ala Phe Leu Val Glu Lys Thr Ser Thr

545 550 555 560

Glu Val Gln Cys Lys Gly Gly Asn Val Cys Val Gln Ala Gln Asp Arg

565 570 575

Tyr Tyr Asn Ser Ser Cys Ser Lys Trp Ala Cys Val Pro Cys Arg Val

580 585 590

Arg Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly

595 600 605

Ser Arg Val Ile Pro Val Ser Gly Pro Ala Arg Cys Leu Ser Gln Ser

610 615 620

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

625 630 635 640

Lys Leu Lys His Tyr Ser Cys Thr Ala Glu Asp Ile Asp His Glu Asp

645 650 655

Ile Thr Arg Asp Gln Thr Ser Thr Leu Lys Thr Cys Leu Pro Leu Glu

660 665 670

Leu His Lys Asn Glu Ser Cys Leu Ala Thr Arg Glu Thr Ser Ser Thr

675 680 685

Thr Arg Gly Ser Cys Leu Pro Pro Gln Lys Thr Ser Leu Met Met Thr

690 695 700

Leu Cys Leu Gly Ser Ile Tyr Glu Asp Leu Lys Met Tyr Gln Thr Glu

705 710 715 720

Phe Gln Ala Ile Asn Ala Ala Leu Gln Asn His Asn His Gln Gln Ile

725 730 735

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

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Leu Arg Gly Ala Arg Cys Glu Val Gln Leu Val Glu Ser Gly Gly Gly
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Leu Val Gln Pro Gly Asn Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly

35 40 45

Phe Thr Phe Ser Lys Phe Gly Met Ser Trp Val Arg Gln Ala Pro Gly
50 55 60

Lys Gly Leu Glu Trp Val Ser Ser Ile Ser Gly Ser Gly Arg Asp Thr
65 70 75 80

Leu Tyr Ala Glu Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn
85 90 95

Ala Lys Thr Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Pro Glu Asp
100 105 110

Thr Ala Val Tyr Tyr Cys Thr Ile Gly Gly Ser Leu Ser Val Ser Ser
115 120 125

Gln Gly Thr Leu Val Thr Val Ser Ser Ser Gly Gly Pro Gly Pro Ala
130 135 140

Gly Met Lys Gly Leu Pro Gly Ser Met Trp Glu Leu Glu Lys Asp Val
145 150 155 160

Tyr Val Val Glu Val Asp Trp Thr Pro Asp Ala Pro Gly Glu Thr Val
165 170 175

Asn Leu Thr Cys Asp Thr Pro Glu Glu Asp Asp Ile Thr Trp Thr Ser
180 185 190

Asp Gln Arg His Gly Val Ile Gly Ser Gly Lys Thr Leu Thr Ile Thr
195 200 205

Val Lys Glu Phe Leu Asp Ala Gly Gln Tyr Thr Cys His Lys Gly Gly
210 215 220

Glu Thr Leu Ser His Ser His Leu Leu Leu His Lys Lys Glu Asn Gly
225 230 235 240

Ile Trp Ser Thr Glu Ile Leu Lys Asn Phe Lys Asn Lys Thr Phe Leu
245 250 255

Lys Cys Glu Ala Pro Asn Tyr Ser Gly Arg Phe Thr Cys Ser Trp Leu
260 265 270

Val Gln Arg Asn Met Asp Leu Lys Phe Asn Ile Lys Ser Ser Ser Ser
275 280 285

Ser Pro Asp Ser Arg Ala Val Thr Cys Gly Met Ala Ser Leu Ser Ala
290 295 300

Glu Lys Val Thr Leu Asp Gln Arg Asp Tyr Glu Lys Tyr Ser Val Ser
305 310 315 320

Cys Gln Glu Asp Val Thr Cys Pro Thr Ala Glu Glu Thr Leu Pro Ile
325 330 335

Glu Leu Ala Leu Glu Ala Arg Gln Gln Asn Lys Tyr Glu Asn Tyr Ser
340 345 350

Thr Ser Phe Phe Ile Arg Asp Ile Ile Lys Pro Asp Pro Pro Lys Asn
355 360 365
Leu Gln Met Lys Pro Leu Lys Asn Ser Gln Val Glu Val Ser Trp Glu
370 375 380
Tyr Pro Asp Ser Trp Ser Thr Pro His Ser Tyr Phe Ser Leu Lys Phe
385 390 395 400
Phe Val Arg Ile Gln Arg Lys Lys Glu Lys Met Lys Glu Thr Glu Glu
405 410 415
Gly Cys Asn Gln Lys Gly Ala Phe Leu Val Glu Lys Thr Ser Thr Glu
420 425 430
Val Gln Cys Lys Gly Gly Asn Val Cys Val Gln Ala Gln Asp Arg Tyr
435 440 445
Tyr Asn Ser Ser Cys Ser Lys Trp Ala Cys Val Pro Cys Arg Val Arg
450 455 460
Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
465 470 475 480
Arg Val Ile Pro Val Ser Gly Pro Ala Arg Cys Leu Ser Gln Ser Arg
485 490 495
Asn Leu Leu Lys Thr Thr Asp Asp Met Val Lys Thr Ala Arg Glu Lys
500 505 510
Leu Lys His Tyr Ser Cys Thr Ala Glu Asp Ile Asp His Glu Asp Ile
515 520 525
Thr Arg Asp Gln Thr Ser Thr Leu Lys Thr Cys Leu Pro Leu Glu Leu
530 535 540
His Lys Asn Glu Ser Cys Leu Ala Thr Arg Glu Thr Ser Ser Thr Thr
545 550 555 560
Arg Gly Ser Cys Leu Pro Pro Gln Lys Thr Ser Leu Met Met Thr Leu
565 570 575
Cys Leu Gly Ser Ile Tyr Glu Asp Leu Lys Met Tyr Gln Thr Glu Phe
580 585 590
Gln Ala Ile Asn Ala Ala Leu Gln Asn His Asn His Gln Gln Ile Ile
595 600 605
Leu Asp Lys Gly Met Leu Val Ala Ile Asp Glu Leu Met Gln Ser Leu
610 615 620
Asn His Asn Gly Glu Thr Leu Arg Gln Lys Pro Pro Val Gly Glu Ala
625 630 635 640
Asp Pro Tyr Arg Val Lys Met Lys Leu Cys Ile Leu Leu His Ala Phe
645 650 655
Ser Thr Arg Val Val Thr Ile Asn Arg Val Met Gly Tyr Leu Ser Ser

660 665 670

Ala Ser Gly Gly Pro Gly Pro Ala Gly Met Lys Gly Leu Pro Gly Ser
675 680 685

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Asn
690 695 700

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Lys Phe
705 710 715 720

Gly Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
725 730 735

Ser Ser Ile Ser Gly Ser Gly Arg Asp Thr Leu Tyr Ala Glu Ser Val
740 745 750

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Thr Thr Leu Tyr
755 760 765

Leu Gln Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Val Tyr Tyr Cys
770 775 780

Thr Ile Gly Gly Ser Leu Ser Val Ser Ser Gln Gly Thr Leu Val Thr
785 790 795 800

Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly
805 810 815

Gly Ser Gln Val Gln Leu Gln Glu Ser Gly Gly Gly Leu Val Gln Ala
820 825 830

Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Arg Ile Phe Ser
835 840 845

Ile Asp Ile Met Ser Trp Tyr Arg Gln Ala Pro Gly Lys Gln Arg Glu
850 855 860

Leu Val Ala Arg Ile Thr Arg Gly Gly Thr Ile Ser Tyr Asp Asp Ser
865 870 875 880

Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Thr Val
885 890 895

Tyr Leu Gln Met Asn Ser Leu Lys Pro Glu Asp Thr Gly Val Tyr Tyr
900 905 910

Cys Asn Ala Leu Tyr Gly Thr Asp Tyr Trp Gly Lys Gly Thr Gln Val
915 920 925

Thr Val Ser Ser His His His His His His
930 935

<210> 119

<211> 962

<212> PRT

<213> 人工序列(Artificial Sequence)

<220>

<221> 来源

<223> /注释="人工序列描述:合成多肽"

<400> 119

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

275 280 285

Val Phe Thr Asp Lys Thr Ser Ala Thr Val Ile Cys Arg Lys Asn Ala

290 295 300

Ser Ile Ser Val Arg Ala Gln Asp Arg Tyr Tyr Ser Ser Ser Trp Ser

305 310 315 320

Glu Trp Ala Ser Val Pro Cys Ser Gly Gly Gly Gly Ser Gly Gly Gly

325 330 335

Gly Ser Gly Gly Gly Gly Ser Arg Val Ile Pro Val Ser Gly Pro Ala

340 345 350

Arg Cys Leu Ser Gln Ser Arg Asn Leu Leu Lys Thr Thr Asp Asp Met

355 360 365

Val Lys Thr Ala Arg Glu Lys Leu Lys His Tyr Ser Cys Thr Ala Glu

370 375 380

Asp Ile Asp His Glu Asp Ile Thr Arg Asp Gln Thr Ser Thr Leu Lys

385 390 395 400

Thr Cys Leu Pro Leu Glu Leu His Lys Asn Glu Ser Cys Leu Ala Thr

405 410 415

Arg Glu Thr Ser Ser Thr Thr Arg Gly Ser Cys Leu Pro Pro Gln Lys

420 425 430

Thr Ser Leu Met Met Thr Leu Cys Leu Gly Ser Ile Tyr Glu Asp Leu

435 440 445

Lys Met Tyr Gln Thr Glu Phe Gln Ala Ile Asn Ala Ala Leu Gln Asn

450 455 460

His Asn His Gln Gln Ile Ile Leu Asp Lys Gly Met Leu Val Ala Ile

465 470 475 480

Asp Glu Leu Met Gln Ser Leu Asn His Asn Gly Glu Thr Leu Arg Gln

485 490 495

Lys Pro Pro Val Gly Glu Ala Asp Pro Tyr Arg Val Lys Met Lys Leu

500 505 510

Cys Ile Leu Leu His Ala Phe Ser Thr Arg Val Val Thr Ile Asn Arg

515 520 525

Val Met Gly Tyr Leu Ser Ser Ala Gly Gly Gly Gly Ser Gly Gly Gly

530 535 540

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly

545 550 555 560

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser

565 570 575

Gly Gly Gly Gly Ser Gln Ser Val Leu Thr Gln Pro Pro Ser Val Ser

580 585 590

Gly Ala Pro Gly Gln Arg Val Thr Ile Ser Cys Ser Gly Ser Arg Ser
595 600 605
Asn Ile Gly Ser Asn Thr Val Lys Trp Tyr Gln Gln Leu Pro Gly Thr
610 615 620
Ala Pro Lys Leu Leu Ile Tyr Tyr Asn Asp Gln Arg Pro Ser Gly Val
625 630 635 640
Pro Asp Arg Phe Ser Gly Ser Lys Ser Gly Thr Ser Ala Ser Leu Ala
645 650 655
Ile Thr Gly Leu Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Gln Ser
660 665 670
Tyr Asp Arg Tyr Thr His Pro Ala Leu Leu Phe Gly Thr Gly Thr Lys
675 680 685
Val Thr Val Leu Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
690 695 700
Gly Gly Ser Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln
705 710 715 720
Pro Gly Arg Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe
725 730 735
Ser Ser Tyr Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu
740 745 750
Glu Trp Val Ala Phe Ile Arg Tyr Asp Gly Ser Asn Lys Tyr Tyr Ala
755 760 765
Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn
770 775 780
Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val
785 790 795 800
Tyr Tyr Cys Lys Thr His Gly Ser His Asp Asn Trp Gly Gln Gly Thr
805 810 815
Met Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
820 825 830
Gly Gly Gly Gly Ser Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu
835 840 845
Val Gln Pro Gly Asn Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe
850 855 860
Thr Phe Ser Lys Phe Gly Met Ser Trp Val Arg Gln Ala Pro Gly Lys
865 870 875 880
Gly Leu Glu Trp Val Ser Ser Ile Ser Gly Ser Gly Arg Asp Thr Leu
885 890 895
Tyr Ala Glu Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala

900 905 910
Lys Thr Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Pro Glu Asp Thr
915 920 925
Ala Val Tyr Tyr Cys Thr Ile Gly Gly Ser Leu Ser Val Ser Ser Gln
930 935 940
Gly Thr Leu Val Thr Val Ser Ser His His His His His His Glu Pro
945 950 955 960
Glu Ala

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<211> 832
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<220>
<221> 来源
<223> /注释="人工序列描述:合成多肽"
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Leu Arg Gly Ala Arg Cys Ile Trp Glu Leu Lys Lys Asp Val Tyr Val
20 25 30
Val Glu Leu Asp Trp Tyr Pro Asp Ala Pro Gly Glu Met Val Val Leu
35 40 45
Thr Cys Asp Thr Pro Glu Glu Asp Gly Ile Thr Trp Thr Leu Asp Gln
50 55 60
Ser Ser Glu Val Leu Gly Ser Gly Lys Thr Leu Thr Ile Gln Val Lys
65 70 75 80
Glu Phe Gly Asp Ala Gly Gln Tyr Thr Cys His Lys Gly Gly Glu Val
85 90 95
Leu Ser His Ser Leu Leu Leu Leu His Lys Lys Glu Asp Gly Ile Trp
100 105 110
Ser Thr Asp Ile Leu Lys Asp Gln Lys Glu Pro Lys Asn Lys Thr Phe
115 120 125
Leu Arg Cys Glu Ala Lys Asn Tyr Ser Gly Arg Phe Thr Cys Trp Trp
130 135 140
Leu Thr Thr Ile Ser Thr Asp Leu Thr Phe Ser Val Lys Ser Ser Arg
145 150 155 160
Gly Ser Ser Asp Pro Gln Gly Val Thr Cys Gly Ala Ala Thr Leu Ser
165 170 175
Ala Glu Arg Val Arg Gly Asp Asn Lys Glu Tyr Glu Tyr Ser Val Glu

180 185 190

Cys Gln Glu Asp Ser Ala Cys Pro Ala Ala Glu Glu Ser Leu Pro Ile
195 200 205

Glu Val Met Val Asp Ala Val His Lys Leu Lys Tyr Glu Asn Tyr Thr
210 215 220

Ser Ser Phe Phe Ile Arg Asp Ile Ile Lys Pro Asp Pro Pro Lys Asn
225 230 235 240

Leu Gln Leu Lys Pro Leu Lys Asn Ser Arg Gln Val Glu Val Ser Trp
245 250 255

Glu Tyr Pro Asp Thr Trp Ser Thr Pro His Ser Tyr Phe Ser Leu Thr
260 265 270

Phe Cys Val Gln Val Gln Gly Lys Ser Lys Arg Glu Lys Lys Asp Arg
275 280 285

Val Phe Thr Asp Lys Thr Ser Ala Thr Val Ile Cys Arg Lys Asn Ala
290 295 300

Ser Ile Ser Val Arg Ala Gln Asp Arg Tyr Tyr Ser Ser Ser Trp Ser
305 310 315 320

Glu Trp Ala Ser Val Pro Cys Ser Gly Gly Gly Gly Ser Gly Gly Gly
325 330 335

Gly Ser Gly Gly Gly Gly Ser Arg Val Ile Pro Val Ser Gly Pro Ala
340 345 350

Arg Cys Leu Ser Gln Ser Arg Asn Leu Leu Lys Thr Thr Asp Asp Met
355 360 365

Val Lys Thr Ala Arg Glu Lys Leu Lys His Tyr Ser Cys Thr Ala Glu
370 375 380

Asp Ile Asp His Glu Asp Ile Thr Arg Asp Gln Thr Ser Thr Leu Lys
385 390 395 400

Thr Cys Leu Pro Leu Glu Leu His Lys Asn Glu Ser Cys Leu Ala Thr
405 410 415

Arg Glu Thr Ser Ser Thr Thr Arg Gly Ser Cys Leu Pro Pro Gln Lys
420 425 430

Thr Ser Leu Met Met Thr Leu Cys Leu Gly Ser Ile Tyr Glu Asp Leu
435 440 445

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

His Asn His Gln Gln Ile Ile Leu Asp Lys Gly Met Leu Val Ala Ile
465 470 475 480

Asp Glu Leu Met Gln Ser Leu Asn His Asn Gly Glu Thr Leu Arg Gln
485 490 495

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

805 810 815
Met Val Thr Val Ser Ser His His His His His His Glu Pro Glu Ala
820 825 830

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<211> 1091
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<220>
<221> 来源
<223> /注释="人工序列描述:合成多肽"
<400> 121
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Leu Arg Gly Ala Arg Cys Ile Trp Glu Leu Lys Lys Asp Val Tyr Val
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Val Glu Leu Asp Trp Tyr Pro Asp Ala Pro Gly Glu Met Val Val Leu
35 40 45
Thr Cys Asp Thr Pro Glu Glu Asp Gly Ile Thr Trp Thr Leu Asp Gln
50 55 60
Ser Ser Glu Val Leu Gly Ser Gly Lys Thr Leu Thr Ile Gln Val Lys
65 70 75 80
Glu Phe Gly Asp Ala Gly Gln Tyr Thr Cys His Lys Gly Gly Glu Val
85 90 95
Leu Ser His Ser Leu Leu Leu Leu His Lys Lys Glu Asp Gly Ile Trp
100 105 110
Ser Thr Asp Ile Leu Lys Asp Gln Lys Glu Pro Lys Asn Lys Thr Phe
115 120 125
Leu Arg Cys Glu Ala Lys Asn Tyr Ser Gly Arg Phe Thr Cys Trp Trp
130 135 140
Leu Thr Thr Ile Ser Thr Asp Leu Thr Phe Ser Val Lys Ser Ser Arg
145 150 155 160
Gly Ser Ser Asp Pro Gln Gly Val Thr Cys Gly Ala Ala Thr Leu Ser
165 170 175
Ala Glu Arg Val Arg Gly Asp Asn Lys Glu Tyr Glu Tyr Ser Val Glu
180 185 190
Cys Gln Glu Asp Ser Ala Cys Pro Ala Ala Glu Glu Ser Leu Pro Ile
195 200 205
Glu Val Met Val Asp Ala Val His Lys Leu Lys Tyr Glu Asn Tyr Thr
210 215 220

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

530 535 540

Met Lys Gly Leu Pro Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly
545 550 555 560

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
565 570 575

Gly Gly Gly Gly Ser Gln Ser Val Leu Thr Gln Pro Pro Ser Val Ser
580 585 590

Gly Ala Pro Gly Gln Arg Val Thr Ile Ser Cys Ser Gly Ser Arg Ser
595 600 605

Asn Ile Gly Ser Asn Thr Val Lys Trp Tyr Gln Gln Leu Pro Gly Thr
610 615 620

Ala Pro Lys Leu Leu Ile Tyr Tyr Asn Asp Gln Arg Pro Ser Gly Val
625 630 635 640

Pro Asp Arg Phe Ser Gly Ser Lys Ser Gly Thr Ser Ala Ser Leu Ala
645 650 655

Ile Thr Gly Leu Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Gln Ser
660 665 670

Tyr Asp Arg Tyr Thr His Pro Ala Leu Leu Phe Gly Thr Gly Thr Lys
675 680 685

Val Thr Val Leu Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
690 695 700

Gly Gly Ser Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln
705 710 715 720

Pro Gly Arg Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe
725 730 735

Ser Ser Tyr Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu
740 745 750

Glu Trp Val Ala Phe Ile Arg Tyr Asp Gly Ser Asn Lys Tyr Tyr Ala
755 760 765

Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn
770 775 780

Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val
785 790 795 800

Tyr Tyr Cys Lys Thr His Gly Ser His Asp Asn Trp Gly Gln Gly Thr
805 810 815

Met Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
820 825 830

Gly Gly Gly Gly Ser Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu
835 840 845

Val Gln Pro Gly Asn Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe
850 855 860
Thr Phe Ser Lys Phe Gly Met Ser Trp Val Arg Gln Ala Pro Gly Lys
865 870 875 880
Gly Leu Glu Trp Val Ser Ser Ile Ser Gly Ser Gly Arg Asp Thr Leu
885 890 895
Tyr Ala Glu Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala
900 905 910
Lys Thr Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Pro Glu Asp Thr
915 920 925
Ala Val Tyr Tyr Cys Thr Ile Gly Gly Ser Leu Ser Val Ser Ser Gln
930 935 940
Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly
945 950 955 960
Gly Ser Gly Gly Gly Gly Ser Gln Val Gln Leu Gln Glu Ser Gly Gly
965 970 975
Gly Leu Ala Gln Ala Gly Gly Ser Leu Ser Leu Ser Cys Ala Ala Ser
980 985 990
Gly Phe Thr Val Ser Asn Ser Val Met Ala Trp Tyr Arg Gln Thr Pro
995 1000 1005
Gly Lys Gln Arg Glu Phe Val Ala Ile Ile Asn Ser Val Gly Ser
1010 1015 1020
Thr Asn Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg
1025 1030 1035
Asp Asn Ala Lys Asn Thr Val Tyr Leu Gln Met Asn Asn Leu Lys
1040 1045 1050
Pro Glu Asp Thr Ala Val Tyr Val Cys Asn Arg Asn Phe Asp Arg
1055 1060 1065
Ile Tyr Trp Gly Gln Gly Thr Gln Val Thr Val Ser Ser His His
1070 1075 1080
His His His His Glu Pro Glu Ala
1085 1090

<210> 122
<211> 1091
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<213> 人工序列(Artificial Sequence)
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<221> 来源
<223> /注释="人工序列描述:合成多肽"

<400> 122

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

Ser Ala Glu Arg Val Arg Gly Asp Asn Lys Glu Tyr Glu Tyr Ser Val
305 310 315 320
Glu Cys Gln Glu Asp Ser Ala Cys Pro Ala Ala Glu Glu Ser Leu Pro
325 330 335
Ile Glu Val Met Val Asp Ala Val His Lys Leu Lys Tyr Glu Asn Tyr
340 345 350
Thr Ser Ser Phe Phe Ile Arg Asp Ile Ile Lys Pro Asp Pro Pro Lys
355 360 365
Asn Leu Gln Leu Lys Pro Leu Lys Asn Ser Arg Gln Val Glu Val Ser
370 375 380
Trp Glu Tyr Pro Asp Thr Trp Ser Thr Pro His Ser Tyr Phe Ser Leu
385 390 395 400
Thr Phe Cys Val Gln Val Gln Gly Lys Ser Lys Arg Glu Lys Lys Asp
405 410 415
Arg Val Phe Thr Asp Lys Thr Ser Ala Thr Val Ile Cys Arg Lys Asn
420 425 430
Ala Ser Ile Ser Val Arg Ala Gln Asp Arg Tyr Tyr Ser Ser Ser Trp
435 440 445
Ser Glu Trp Ala Ser Val Pro Cys Ser Gly Gly Gly Gly Ser Gly Gly
450 455 460
Gly Gly Ser Gly Gly Gly Gly Ser Arg Val Ile Pro Val Ser Gly Pro
465 470 475 480
Ala Arg Cys Leu Ser Gln Ser Arg Asn Leu Leu Lys Thr Thr Asp Asp
485 490 495
Met Val Lys Thr Ala Arg Glu Lys Leu Lys His Tyr Ser Cys Thr Ala
500 505 510
Glu Asp Ile Asp His Glu Asp Ile Thr Arg Asp Gln Thr Ser Thr Leu
515 520 525
Lys Thr Cys Leu Pro Leu Glu Leu His Lys Asn Glu Ser Cys Leu Ala
530 535 540
Thr Arg Glu Thr Ser Ser Thr Thr Arg Gly Ser Cys Leu Pro Pro Gln
545 550 555 560
Lys Thr Ser Leu Met Met Thr Leu Cys Leu Gly Ser Ile Tyr Glu Asp
565 570 575
Leu Lys Met Tyr Gln Thr Glu Phe Gln Ala Ile Asn Ala Ala Leu Gln
580 585 590
Asn His Asn His Gln Gln Ile Ile Leu Asp Lys Gly Met Leu Val Ala
595 600 605
Ile Asp Glu Leu Met Gln Ser Leu Asn His Asn Gly Glu Thr Leu Arg

610 615 620
Gln Lys Pro Pro Val Gly Glu Ala Asp Pro Tyr Arg Val Lys Met Lys
625 630 635 640
Leu Cys Ile Leu Leu His Ala Phe Ser Thr Arg Val Val Thr Ile Asn
645 650 655
Arg Val Met Gly Tyr Leu Ser Ser Ala Ser Gly Gly Pro Gly Pro Ala
660 665 670
Gly Met Lys Gly Leu Pro Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly
675 680 685
Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly
690 695 700
Ser Gly Gly Gly Gly Ser Gln Ser Val Leu Thr Gln Pro Pro Ser Val
705 710 715 720
Ser Gly Ala Pro Gly Gln Arg Val Thr Ile Ser Cys Ser Gly Ser Arg
725 730 735
Ser Asn Ile Gly Ser Asn Thr Val Lys Trp Tyr Gln Gln Leu Pro Gly
740 745 750
Thr Ala Pro Lys Leu Leu Ile Tyr Tyr Asn Asp Gln Arg Pro Ser Gly
755 760 765
Val Pro Asp Arg Phe Ser Gly Ser Lys Ser Gly Thr Ser Ala Ser Leu
770 775 780
Ala Ile Thr Gly Leu Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Gln
785 790 795 800
Ser Tyr Asp Arg Tyr Thr His Pro Ala Leu Leu Phe Gly Thr Gly Thr
805 810 815
Lys Val Thr Val Leu Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
820 825 830
Gly Gly Gly Ser Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val
835 840 845
Gln Pro Gly Arg Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr
850 855 860
Phe Ser Ser Tyr Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly
865 870 875 880
Leu Glu Trp Val Ala Phe Ile Arg Tyr Asp Gly Ser Asn Lys Tyr Tyr
885 890 895
Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys
900 905 910
Asn Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala
915 920 925

Val Tyr Tyr Cys Lys Thr His Gly Ser His Asp Asn Trp Gly Gln Gly
930 935 940
Thr Met Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly
945 950 955 960
Ser Gly Gly Gly Gly Ser Glu Val Gln Leu Val Glu Ser Gly Gly Gly
965 970 975
Leu Val Gln Pro Gly Asn Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly
980 985 990
Phe Thr Phe Ser Lys Phe Gly Met Ser Trp Val Arg Gln Ala Pro Gly
995 1000 1005
Lys Gly Leu Glu Trp Val Ser Ser Ile Ser Gly Ser Gly Arg Asp
1010 1015 1020
Thr Leu Tyr Ala Glu Ser Val Lys Gly Arg Phe Thr Ile Ser Arg
1025 1030 1035
Asp Asn Ala Lys Thr Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg
1040 1045 1050
Pro Glu Asp Thr Ala Val Tyr Tyr Cys Thr Ile Gly Gly Ser Leu
1055 1060 1065
Ser Val Ser Ser Gln Gly Thr Leu Val Thr Val Ser Ser His His
1070 1075 1080
His His His His Glu Pro Glu Ala
1085 1090

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<211> 1091
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<221> 来源
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Leu Arg Gly Ala Arg Cys Gln Val Gln Leu Gln Glu Ser Gly Gly Gly
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Leu Ala Gln Ala Gly Gly Ser Leu Ser Leu Ser Cys Ala Ala Ser Gly
35 40 45
Phe Thr Val Ser Asn Ser Val Met Ala Trp Tyr Arg Gln Thr Pro Gly
50 55 60
Lys Gln Arg Glu Phe Val Ala Ile Ile Asn Ser Val Gly Ser Thr Asn

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

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

690 695 700

Ser Gly Gly Gly Gly Ser Gln Ser Val Leu Thr Gln Pro Pro Ser Val
705 710 715 720
Ser Gly Ala Pro Gly Gln Arg Val Thr Ile Ser Cys Ser Gly Ser Arg
725 730 735
Ser Asn Ile Gly Ser Asn Thr Val Lys Trp Tyr Gln Gln Leu Pro Gly
740 745 750
Thr Ala Pro Lys Leu Leu Ile Tyr Tyr Asn Asp Gln Arg Pro Ser Gly
755 760 765
Val Pro Asp Arg Phe Ser Gly Ser Lys Ser Gly Thr Ser Ala Ser Leu
770 775 780
Ala Ile Thr Gly Leu Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Gln
785 790 795 800
Ser Tyr Asp Arg Tyr Thr His Pro Ala Leu Leu Phe Gly Thr Gly Thr
805 810 815
Lys Val Thr Val Leu Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
820 825 830
Gly Gly Gly Ser Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val
835 840 845
Gln Pro Gly Arg Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr
850 855 860
Phe Ser Ser Tyr Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly
865 870 875 880
Leu Glu Trp Val Ala Phe Ile Arg Tyr Asp Gly Ser Asn Lys Tyr Tyr
885 890 895
Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys
900 905 910
Asn Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala
915 920 925
Val Tyr Tyr Cys Lys Thr His Gly Ser His Asp Asn Trp Gly Gln Gly
930 935 940
Thr Met Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly
945 950 955 960
Ser Gly Gly Gly Gly Ser Glu Val Gln Leu Val Glu Ser Gly Gly Gly
965 970 975
Leu Val Gln Pro Gly Asn Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly
980 985 990
Phe Thr Phe Ser Lys Phe Gly Met Ser Trp Val Arg Gln Ala Pro Gly
995 1000 1005

Lys Gly Leu Glu Trp Val Ser Ser Ile Ser Gly Ser Gly Arg Asp
1010 1015 1020
Thr Leu Tyr Ala Glu Ser Val Lys Gly Arg Phe Thr Ile Ser Arg
1025 1030 1035
Asp Asn Ala Lys Thr Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg
1040 1045 1050
Pro Glu Asp Thr Ala Val Tyr Tyr Cys Thr Ile Gly Gly Ser Leu
1055 1060 1065
Ser Val Ser Ser Gln Gly Thr Leu Val Thr Val Ser Ser His His
1070 1075 1080
His His His His Glu Pro Glu Ala
1085 1090

<210> 124
<211> 674
<212> PRT
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<220>
<221> 来源
<223> /注释="人工序列描述:合成多肽"
<400> 124

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

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

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

<210> 125
<211> 674
<212> PRT
<213> 人工序列(Artificial Sequence)
<220>
<221> 来源
<223> /注释="人工序列描述:合成多肽"
<400> 125
Met Asp Met Arg Val Pro Ala Gln Leu Leu Gly Leu Leu Leu Leu Trp
1 5 10 15
Leu Arg Gly Ala Arg Cys Gln Val Gln Leu Gln Glu Ser Gly Gly Gly
20 25 30

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

340 345 350

Asp Asn Ala Lys Asn Ser Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala
355 360 365

Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Asp Ser Asn Trp Asp Ala
370 375 380

Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly
385 390 395 400

Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Gln
405 410 415

Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val
420 425 430

Thr Ile Thr Cys Lys Ala Ser Gln Asn Val Gly Thr Asn Val Gly Trp
435 440 445

Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Ala Leu Ile Tyr Ser Ala
450 455 460

Ser Phe Arg Tyr Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser
465 470 475 480

Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe
485 490 495

Ala Thr Tyr Tyr Cys Gln Gln Tyr Tyr Thr Tyr Pro Tyr Thr Phe Gly
500 505 510

Gly Gly Thr Lys Val Glu Ile Lys Ser Gly Gly Pro Gly Pro Ala Gly
515 520 525

Met Lys Gly Leu Pro Gly Ser Ala Pro Thr Ser Ser Ser Thr Lys Lys
530 535 540

Thr Gln Leu Gln Leu Glu His Leu Leu Leu Asp Leu Gln Met Ile Leu
545 550 555 560

Asn Gly Ile Asn Asn Tyr Lys Asn Pro Lys Leu Thr Arg Met Leu Thr
565 570 575

Phe Lys Phe Tyr Met Pro Lys Lys Ala Thr Glu Leu Lys His Leu Gln
580 585 590

Cys Leu Glu Glu Glu Leu Lys Pro Leu Glu Glu Val Leu Asn Leu Ala
595 600 605

Gln Ser Lys Asn Phe His Leu Arg Pro Arg Asp Leu Ile Ser Asn Ile
610 615 620

Asn Val Ile Val Leu Glu Leu Lys Gly Ser Glu Thr Thr Phe Met Cys
625 630 635 640

Glu Tyr Ala Asp Glu Thr Ala Thr Ile Val Glu Phe Leu Asn Arg Trp
645 650 655

Ile Thr Phe Cys Gln Ser Ile Ile Ser Thr Leu Thr His His His His
660 665 670

His His

<210> 126

<211> 425

<212> PRT

<213> 人工序列(Artificial Sequence)

<220>

<221> 来源

<223> /注释="人工序列描述:合成多肽"

<400> 126

Met Asp Met Arg Val Pro Ala Gln Leu Leu Gly Leu Leu Leu Leu Trp
1 5 10 15

Leu Arg Gly Ala Arg Cys Glu Leu Cys Asp Asp Asp Pro Pro Glu Ile
20 25 30

Pro His Ala Thr Phe Lys Ala Met Ala Tyr Lys Glu Gly Thr Met Leu
35 40 45

Asn Cys Glu Cys Lys Arg Gly Phe Arg Arg Ile Lys Ser Gly Ser Leu
50 55 60

Tyr Met Leu Cys Thr Gly Asn Ser Ser His Ser Ser Trp Asp Asn Gln
65 70 75 80

Cys Gln Cys Thr Ser Ser Ala Thr Arg Asn Thr Thr Lys Gln Val Thr
85 90 95

Pro Gln Pro Glu Glu Gln Lys Glu Arg Lys Thr Thr Glu Met Gln Ser
100 105 110

Pro Met Gln Pro Val Asp Gln Ala Ser Leu Pro Gly His Cys Arg Glu
115 120 125

Pro Pro Pro Trp Glu Asn Glu Ala Thr Glu Arg Ile Tyr His Phe Val
130 135 140

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

His Arg Gly Pro Ala Glu Ser Val Cys Lys Met Thr His Gly Lys Thr
165 170 175

Arg Trp Thr Gln Pro Gln Leu Ile Cys Thr Gly Glu Met Glu Thr Ser
180 185 190

Gln Phe Pro Gly Glu Glu Lys Pro Gln Ala Ser Pro Glu Gly Arg Pro
195 200 205

Glu Ser Glu Thr Ser Cys Leu Val Thr Thr Thr Asp Phe Gln Ile Gln
210 215 220

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

<210> 127
<211> 425
<212> PRT
<213> 人工序列(Artificial Sequence)
<220>
<221> 来源
<223> /注释="人工序列描述:合成多肽"
<400> 127
Met Asp Met Arg Val Pro Ala Gln Leu Leu Gly Leu Leu Leu Leu Trp
1 5 10 15
Leu Arg Gly Ala Arg Cys Ala Pro Thr Ser Ser Ser Thr Lys Lys Thr
20 25 30
Gln Leu Gln Leu Glu His Leu Leu Leu Asp Leu Gln Met Ile Leu Asn

35 40 45

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

Lys Thr Arg Trp Thr Gln Pro Gln Leu Ile Cys Thr Gly Glu Met Glu
355 360 365
Thr Ser Gln Phe Pro Gly Glu Glu Lys Pro Gln Ala Ser Pro Glu Gly
370 375 380
Arg Pro Glu Ser Glu Thr Ser Cys Leu Val Thr Thr Thr Asp Phe Gln
385 390 395 400
Ile Gln Thr Glu Met Ala Ala Thr Met Glu Thr Ser Ile Phe Thr Thr
405 410 415
Glu Tyr Gln His His His His His His
420 425

<210> 128
<211> 555
<212> PRT
<213> 人工序列(Artificial Sequence)
<220>
<221> 来源
<223> /注释="人工序列描述:合成多肽"
<400> 128
Met Asp Met Arg Val Pro Ala Gln Leu Leu Gly Leu Leu Leu Leu Trp
1 5 10 15
Leu Arg Gly Ala Arg Cys Glu Val Gln Leu Val Glu Ser Gly Gly Gly
20 25 30
Leu Val Gln Pro Gly Asn Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly
35 40 45
Phe Thr Phe Ser Lys Phe Gly Met Ser Trp Val Arg Gln Ala Pro Gly
50 55 60
Lys Gly Leu Glu Trp Val Ser Ser Ile Ser Gly Ser Gly Arg Asp Thr
65 70 75 80
Leu Tyr Ala Glu Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn
85 90 95
Ala Lys Thr Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Pro Glu Asp
100 105 110
Thr Ala Val Tyr Tyr Cys Thr Ile Gly Gly Ser Leu Ser Val Ser Ser
115 120 125
Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly
130 135 140
Gly Gly Ser Gly Gly Gly Gly Ser Glu Leu Cys Asp Asp Asp Pro Pro
145 150 155 160
Glu Ile Pro His Ala Thr Phe Lys Ala Met Ala Tyr Lys Glu Gly Thr

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

Pro Leu Glu Glu Val Leu Asn Leu Ala Gln Ser Lys Asn Phe His Leu
485 490 495
Arg Pro Arg Asp Leu Ile Ser Asn Ile Asn Val Ile Val Leu Glu Leu
500 505 510
Lys Gly Ser Glu Thr Thr Phe Met Cys Glu Tyr Ala Asp Glu Thr Ala
515 520 525
Thr Ile Val Glu Phe Leu Asn Arg Trp Ile Thr Phe Cys Gln Ser Ile
530 535 540
Ile Ser Thr Leu Thr His His His His His His
545 550 555

<210> 129
<211> 555
<212> PRT
<213> 人工序列(Artificial Sequence)
<220>
<221> 来源
<223> /注释="人工序列描述:合成多肽"
<400> 129

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

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

Trp Val Ser Ser Ile Ser Gly Ser Gly Arg Asp Thr Leu Tyr Ala Glu
485 490 495
Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Thr Thr
500 505 510
Leu Tyr Leu Gln Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Val Tyr
515 520 525
Tyr Cys Thr Ile Gly Gly Ser Leu Ser Val Ser Ser Gln Gly Thr Leu
530 535 540
Val Thr Val Ser Ser His His His His His His
545 550 555

<210> 130
<211> 555
<212> PRT
<213> 人工序列(Artificial Sequence)
<220>
<221> 来源
<223> /注释="人工序列描述:合成多肽"
<400> 130

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

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

Trp Val Ser Ser Ile Ser Gly Ser Gly Arg Asp Thr Leu Tyr Ala Glu
485 490 495
Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Thr Thr
500 505 510
Leu Tyr Leu Gln Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Val Tyr
515 520 525
Tyr Cys Thr Ile Gly Gly Ser Leu Ser Val Ser Ser Gln Gly Thr Leu
530 535 540
Val Thr Val Ser Ser His His His His His His
545 550 555

<210> 131
<211> 575
<212> PRT
<213> 人工序列(Artificial Sequence)
<220>
<221> 来源
<223> /注释="人工序列描述:合成多肽"
<400> 131

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

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

Tyr Met Pro Lys Lys Ala Thr Glu Leu Lys His Leu Gln Cys Leu Glu
485 490 495
Glu Glu Leu Lys Pro Leu Glu Glu Val Leu Asn Leu Ala Gln Ser Lys
500 505 510
Asn Phe His Leu Arg Pro Arg Asp Leu Ile Ser Asn Ile Asn Val Ile
515 520 525
Val Leu Glu Leu Lys Gly Ser Glu Thr Thr Phe Met Cys Glu Tyr Ala
530 535 540
Asp Glu Thr Ala Thr Ile Val Glu Phe Leu Asn Arg Trp Ile Thr Phe
545 550 555 560
Cys Gln Ser Ile Ile Ser Thr Leu Thr His His His His His His
565 570 575

<210> 132
<211> 704
<212> PRT
<213> 人工序列(Artificial Sequence)
<220>
<221> 来源
<223> /注释="人工序列描述:合成多肽"
<400> 132

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

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

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

<210> 133
<211> 689
<212> PRT
<213> 人工序列(Artificial Sequence)
<220>
<221> 来源
<223> /注释="人工序列描述:合成多肽"
<400> 133
Met Asp Met Arg Val Pro Ala Gln Leu Leu Gly Leu Leu Leu Leu Trp

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

Cys Ala Ala Ser Gly Phe Thr Phe Ser Lys Phe Gly Met Ser Trp Val
325 330 335
Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ser Ser Ile Ser Gly
340 345 350
Ser Gly Arg Asp Thr Leu Tyr Ala Glu Ser Val Lys Gly Arg Phe Thr
355 360 365
Ile Ser Arg Asp Asn Ala Lys Thr Thr Leu Tyr Leu Gln Met Asn Ser
370 375 380
Leu Arg Pro Glu Asp Thr Ala Val Tyr Tyr Cys Thr Ile Gly Gly Ser
385 390 395 400
Leu Ser Val Ser Ser Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly
405 410 415
Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly
420 425 430
Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Val Gln Leu
435 440 445
Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Leu Arg Leu
450 455 460
Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr Thr Leu Ala Trp
465 470 475 480
Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala Ala Ile Asp
485 490 495
Ser Ser Ser Tyr Thr Tyr Ser Pro Asp Thr Val Arg Gly Arg Phe Thr
500 505 510
Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr Leu Gln Met Asn Ser
515 520 525
Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Asp Ser Asn
530 535 540
Trp Asp Ala Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser
545 550 555 560
Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
565 570 575
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
580 585 590
Asp Arg Val Thr Ile Thr Cys Lys Ala Ser Gln Asn Val Gly Thr Asn
595 600 605
Val Gly Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Ala Leu Ile
610 615 620
Tyr Ser Ala Ser Phe Arg Tyr Ser Gly Val Pro Ser Arg Phe Ser Gly

625 630 635 640
Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
645 650 655
Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Tyr Thr Tyr Pro Tyr
660 665 670
Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys His His His His His
675 680 685
His

<210> 134
<211> 545
<212> PRT
<213> 人工序列(Artificial Sequence)
<220>
<221> 来源
<223> /注释="人工序列描述:合成多肽"
<400> 134
Met Asp Met Arg Val Pro Ala Gln Leu Leu Gly Leu Leu Leu Leu Trp
1 5 10 15
Leu Arg Gly Ala Arg Cys Ala Pro Thr Ser Ser Ser Thr Lys Lys Thr
20 25 30
Gln Leu Gln Leu Glu His Leu Leu Leu Asp Leu Gln Met Ile Leu Asn
35 40 45
Gly Ile Asn Asn Tyr Lys Asn Pro Lys Leu Thr Arg Met Leu Thr Phe
50 55 60
Lys Phe Tyr Met Pro Lys Lys Ala Thr Glu Leu Lys His Leu Gln Cys
65 70 75 80
Leu Glu Glu Glu Leu Lys Pro Leu Glu Glu Val Leu Asn Leu Ala Gln
85 90 95
Ser Lys Asn Phe His Leu Arg Pro Arg Asp Leu Ile Ser Asn Ile Asn
100 105 110
Val Ile Val Leu Glu Leu Lys Gly Ser Glu Thr Thr Phe Met Cys Glu
115 120 125
Tyr Ala Asp Glu Thr Ala Thr Ile Val Glu Phe Leu Asn Arg Trp Ile
130 135 140
Thr Phe Cys Gln Ser Ile Ile Ser Thr Leu Thr Ser Gly Gly Pro Gly
145 150 155 160
Pro Ala Gly Met Lys Gly Leu Pro Gly Ser Glu Val Gln Leu Val Glu
165 170 175
Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys

180 185 190

Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr Thr Leu Ala Trp Val Arg

195 200 205

Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala Ala Ile Asp Ser Ser

210 215 220

Ser Tyr Thr Tyr Ser Pro Asp Thr Val Arg Gly Arg Phe Thr Ile Ser

225 230 235 240

Arg Asp Asn Ala Lys Asn Ser Leu Tyr Leu Gln Met Asn Ser Leu Arg

245 250 255

Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Asp Ser Asn Trp Asp

260 265 270

Ala Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly

275 280 285

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile

290 295 300

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

305 310 315 320

Val Thr Ile Thr Cys Lys Ala Ser Gln Asn Val Gly Thr Asn Val Gly

325 330 335

Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Ala Leu Ile Tyr Ser

340 345 350

Ala Ser Phe Arg Tyr Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly

355 360 365

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

370 375 380

Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Tyr Thr Tyr Pro Tyr Thr Phe

385 390 395 400

Gly Gly Gly Thr Lys Val Glu Ile Lys Gly Gly Gly Gly Ser Gly Gly

405 410 415

Gly Gly Ser Gly Gly Gly Gly Ser Glu Val Gln Leu Val Glu Ser Gly

420 425 430

Gly Gly Leu Val Gln Pro Gly Asn Ser Leu Arg Leu Ser Cys Ala Ala

435 440 445

Ser Gly Phe Thr Phe Ser Lys Phe Gly Met Ser Trp Val Arg Gln Ala

450 455 460

Pro Gly Lys Gly Leu Glu Trp Val Ser Ser Ile Ser Gly Ser Gly Arg

465 470 475 480

Asp Thr Leu Tyr Ala Glu Ser Val Lys Gly Arg Phe Thr Ile Ser Arg

485 490 495

Asp Asn Ala Lys Thr Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Pro
500 505 510
Glu Asp Thr Ala Val Tyr Tyr Cys Thr Ile Gly Gly Ser Leu Ser Val
515 520 525
Ser Ser Gln Gly Thr Leu Val Thr Val Ser Ser His His His His His
530 535 540
His
545

<210> 135
<211> 575
<212> PRT
<213> 人工序列(Artificial Sequence)
<220>
<221> 来源
<223> /注释="人工序列描述:合成多肽"
<400> 135

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

180 185 190

Gly Gly Ser Gly Gly Gly Gly Ser Glu Val Gln Leu Val Glu Ser Gly

195 200 205

Gly Gly Leu Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala

210 215 220

Ser Gly Phe Thr Phe Ser Ser Tyr Thr Leu Ala Trp Val Arg Gln Ala

225 230 235 240

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

245 250 255

Thr Tyr Ser Pro Asp Thr Val Arg Gly Arg Phe Thr Ile Ser Arg Asp

260 265 270

Asn Ala Lys Asn Ser Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu

275 280 285

Asp Thr Ala Val Tyr Tyr Cys Ala Arg Asp Ser Asn Trp Asp Ala Leu

290 295 300

Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly

305 310 315 320

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Gln Met

325 330 335

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

340 345 350

Ile Thr Cys Lys Ala Ser Gln Asn Val Gly Thr Asn Val Gly Trp Tyr

355 360 365

Gln Gln Lys Pro Gly Lys Ala Pro Lys Ala Leu Ile Tyr Ser Ala Ser

370 375 380

Phe Arg Tyr Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly

385 390 395 400

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

405 410 415

Thr Tyr Tyr Cys Gln Gln Tyr Tyr Thr Tyr Pro Tyr Thr Phe Gly Gly

420 425 430

Gly Thr Lys Val Glu Ile Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly

435 440 445

Ser Gly Gly Gly Gly Ser Glu Val Gln Leu Val Glu Ser Gly Gly Gly

450 455 460

Leu Val Gln Pro Gly Asn Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly

465 470 475 480

Phe Thr Phe Ser Lys Phe Gly Met Ser Trp Val Arg Gln Ala Pro Gly

485 490 495

Lys Gly Leu Glu Trp Val Ser Ser Ile Ser Gly Ser Gly Arg Asp Thr
500 505 510
Leu Tyr Ala Glu Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn
515 520 525
Ala Lys Thr Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Pro Glu Asp
530 535 540
Thr Ala Val Tyr Tyr Cys Thr Ile Gly Gly Ser Leu Ser Val Ser Ser
545 550 555 560
Gln Gly Thr Leu Val Thr Val Ser Ser His His His His His His
565 570 575

<210> 136
<211> 421
<212> PRT
<213> 人工序列(Artificial Sequence)
<220>
<221> 来源
<223> /注释="人工序列描述:合成多肽"
<400> 136
Met Asp Met Arg Val Pro Ala Gln Leu Leu Gly Leu Leu Leu Leu Trp
1 5 10 15
Leu Arg Gly Ala Arg Cys Glu Val Gln Leu Val Glu Ser Gly Gly Gly
20 25 30
Leu Val Gln Pro Gly Asn Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly
35 40 45
Phe Thr Phe Ser Lys Phe Gly Met Ser Trp Val Arg Gln Ala Pro Gly
50 55 60
Lys Gly Leu Glu Trp Val Ser Ser Ile Ser Gly Ser Gly Arg Asp Thr
65 70 75 80
Leu Tyr Ala Glu Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn
85 90 95
Ala Lys Thr Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Pro Glu Asp
100 105 110
Thr Ala Val Tyr Tyr Cys Thr Ile Gly Gly Ser Leu Ser Val Ser Ser
115 120 125
Gln Gly Thr Leu Val Thr Val Ser Ser Ser Gly Gly Pro Gly Pro Ala
130 135 140
Gly Met Lys Gly Leu Pro Gly Ser Ala Pro Thr Ser Ser Ser Thr Lys
145 150 155 160
Lys Thr Gln Leu Gln Leu Glu His Leu Leu Leu Asp Leu Gln Met Ile

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

<210> 137
<211> 806
<212> PRT
<213> 人工序列(Artificial Sequence)
<220>
<221> 来源

<223> /注释="人工序列描述:合成多肽"

<400> 137

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

290 295 300

Cys Ala Ala Ser Gly Arg Ile Phe Ser Ile Asp Ile Met Ser Trp Tyr
305 310 315 320

Arg Gln Ala Pro Gly Lys Gln Arg Glu Leu Val Ala Arg Ile Thr Arg
325 330 335

Gly Gly Thr Ile Ser Tyr Asp Asp Ser Val Lys Gly Arg Phe Thr Ile
340 345 350

Ser Arg Asp Asn Ala Lys Asn Thr Val Tyr Leu Gln Met Asn Ser Leu
355 360 365

Lys Pro Glu Asp Thr Gly Val Tyr Tyr Cys Asn Ala Leu Tyr Gly Thr
370 375 380

Asp Tyr Trp Gly Lys Gly Thr Gln Val Thr Val Ser Ser Gly Ser Gly
385 390 395 400

Ser Gly Ser Gly Ser Gly Ser Gly Ser Gly Ser Gly Ser Glu Val Gln
405 410 415

Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Leu Arg
420 425 430

Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr Thr Leu Ala
435 440 445

Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala Ala Ile
450 455 460

Asp Ser Ser Ser Tyr Thr Tyr Ser Pro Asp Thr Val Arg Gly Arg Phe
465 470 475 480

Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr Leu Gln Met Asn
485 490 495

Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Asp Ser
500 505 510

Asn Trp Asp Ala Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val
515 520 525

Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly
530 535 540

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

Gly Asp Arg Val Thr Ile Thr Cys Lys Ala Ser Gln Asn Val Gly Thr
565 570 575

Asn Val Gly Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Ala Leu
580 585 590

Ile Tyr Ser Ala Ser Phe Arg Tyr Ser Gly Val Pro Ser Arg Phe Ser
595 600 605

Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln
610 615 620
Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Tyr Thr Tyr Pro
625 630 635 640
Tyr Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Ser Gly Gly Pro
645 650 655
Gly Pro Ala Gly Met Lys Gly Leu Pro Gly Ser Ala Pro Thr Ser Ser
660 665 670
Ser Thr Lys Lys Thr Gln Leu Gln Leu Glu His Leu Leu Leu Asp Leu
675 680 685
Gln Met Ile Leu Asn Gly Ile Asn Asn Tyr Lys Asn Pro Lys Leu Thr
690 695 700
Arg Met Leu Thr Phe Lys Phe Tyr Met Pro Lys Lys Ala Thr Glu Leu
705 710 715 720
Lys His Leu Gln Cys Leu Glu Glu Glu Leu Lys Pro Leu Glu Glu Val
725 730 735
Leu Asn Leu Ala Gln Ser Lys Asn Phe His Leu Arg Pro Arg Asp Leu
740 745 750
Ile Ser Asn Ile Asn Val Ile Val Leu Glu Leu Lys Gly Ser Glu Thr
755 760 765
Thr Phe Met Cys Glu Tyr Ala Asp Glu Thr Ala Thr Ile Val Glu Phe
770 775 780
Leu Asn Arg Trp Ile Thr Phe Cys Gln Ser Ile Ile Ser Thr Leu Thr
785 790 795 800
His His His His His His
805

<210> 138
<211> 676
<212> PRT
<213> 人工序列(Artificial Sequence)
<220>
<221> 来源
<223> /注释="人工序列描述:合成多肽"
<400> 138
Met Asp Met Arg Val Pro Ala Gln Leu Leu Gly Leu Leu Leu Leu Trp
1 5 10 15
Leu Arg Gly Ala Arg Cys Gln Val Gln Leu Gln Glu Ser Gly Gly Gly
20 25 30
Leu Val Gln Ala Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly

35 40 45

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

Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr Leu Gln Met Asn Ser Leu
355 360 365
Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Asp Ser Asn Trp
370 375 380
Asp Ala Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
385 390 395 400
Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp
405 410 415
Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp
420 425 430
Arg Val Thr Ile Thr Cys Lys Ala Ser Gln Asn Val Gly Thr Asn Val
435 440 445
Gly Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Ala Leu Ile Tyr
450 455 460
Ser Ala Ser Phe Arg Tyr Ser Gly Val Pro Ser Arg Phe Ser Gly Ser
465 470 475 480
Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu
485 490 495
Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Tyr Thr Tyr Pro Tyr Thr
500 505 510
Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Ser Gly Gly Pro Gly Pro
515 520 525
Ala Gly Met Lys Gly Leu Pro Gly Ser Ala Pro Thr Ser Ser Ser Thr
530 535 540
Lys Lys Thr Gln Leu Gln Leu Glu His Leu Leu Leu Asp Leu Gln Met
545 550 555 560
Ile Leu Asn Gly Ile Asn Asn Tyr Lys Asn Pro Lys Leu Thr Arg Met
565 570 575
Leu Thr Phe Lys Phe Tyr Met Pro Lys Lys Ala Thr Glu Leu Lys His
580 585 590
Leu Gln Cys Leu Glu Glu Glu Leu Lys Pro Leu Glu Glu Val Leu Asn
595 600 605
Leu Ala Gln Ser Lys Asn Phe His Leu Arg Pro Arg Asp Leu Ile Ser
610 615 620
Asn Ile Asn Val Ile Val Leu Glu Leu Lys Gly Ser Glu Thr Thr Phe
625 630 635 640
Met Cys Glu Tyr Ala Asp Glu Thr Ala Thr Ile Val Glu Phe Leu Asn
645 650 655
Arg Trp Ile Thr Phe Cys Gln Ser Ile Ile Ser Thr Leu Thr His His

660 665 670

His His His His
675

<210> 139
<211> 421
<212> PRT
<213> 人工序列(Artificial Sequence)
<220>
<221> 来源
<223> /注释="人工序列描述:合成多肽"
<400> 139

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

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

<210> 140
<211> 420
<212> PRT
<213> 人工序列(Artificial Sequence)
<220>
<221> 来源
<223> /注释="人工序列描述:合成多肽"
<400> 140
Met Asp Met Arg Val Pro Ala Gln Leu Leu Gly Leu Leu Leu Leu Trp
1 5 10 15
Leu Arg Gly Ala Arg Cys Gln Val Gln Leu Gln Glu Ser Gly Gly Gly
20 25 30
Leu Val Gln Ala Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly

35 40 45

Arg Ile Phe Ser Ile Asp Ile Met Ser Trp Tyr Arg Gln Ala Pro Gly
50 55 60

Lys Gln Arg Glu Leu Val Ala Arg Ile Thr Arg Gly Gly Thr Ile Ser
65 70 75 80

Tyr Asp Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala
85 90 95

Lys Asn Thr Val Tyr Leu Gln Met Asn Ser Leu Lys Pro Glu Asp Thr
100 105 110

Gly Val Tyr Tyr Cys Asn Ala Leu Tyr Gly Thr Asp Tyr Trp Gly Lys
115 120 125

Gly Thr Gln Val Thr Val Ser Ser Ser Gly Gly Pro Gly Pro Ala Gly
130 135 140

Met Lys Gly Leu Pro Gly Ser Ala Pro Thr Ser Ser Ser Thr Lys Lys
145 150 155 160

Thr Gln Leu Gln Leu Glu His Leu Leu Leu Asp Leu Gln Met Ile Leu
165 170 175

Asn Gly Ile Asn Asn Tyr Lys Asn Pro Lys Leu Thr Arg Met Leu Thr
180 185 190

Phe Lys Phe Tyr Met Pro Lys Lys Ala Thr Glu Leu Lys His Leu Gln
195 200 205

Cys Leu Glu Glu Glu Leu Lys Pro Leu Glu Glu Val Leu Asn Leu Ala
210 215 220

Gln Ser Lys Asn Phe His Leu Arg Pro Arg Asp Leu Ile Ser Asn Ile
225 230 235 240

Asn Val Ile Val Leu Glu Leu Lys Gly Ser Glu Thr Thr Phe Met Cys
245 250 255

Glu Tyr Ala Asp Glu Thr Ala Thr Ile Val Glu Phe Leu Asn Arg Trp
260 265 270

Ile Thr Phe Cys Gln Ser Ile Ile Ser Thr Leu Thr Ser Gly Gly Pro
275 280 285

Gly Pro Ala Gly Met Lys Gly Leu Pro Gly Ser Glu Val Gln Leu Val
290 295 300

Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Asn Ser Leu Arg Leu Ser
305 310 315 320

Cys Ala Ala Ser Gly Phe Thr Phe Ser Lys Phe Gly Met Ser Trp Val
325 330 335

Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ser Ser Ile Ser Gly
340 345 350

Ser Gly Arg Asp Thr Leu Tyr Ala Glu Ser Val Lys Gly Arg Phe Thr
355 360 365
Ile Ser Arg Asp Asn Ala Lys Thr Thr Leu Tyr Leu Gln Met Asn Ser
370 375 380
Leu Arg Pro Glu Asp Thr Ala Val Tyr Tyr Cys Thr Ile Gly Gly Ser
385 390 395 400
Leu Ser Val Ser Ser Gln Gly Thr Leu Val Thr Val Ser Ser His His
405 410 415
His His His His
420

<210> 141
<211> 550
<212> PRT
<213> 人工序列(Artificial Sequence)
<220>
<221> 来源
<223> /注释="人工序列描述:合成多肽"
<400> 141
Met Asp Met Arg Val Pro Ala Gln Leu Leu Gly Leu Leu Leu Leu Trp
1 5 10 15
Leu Arg Gly Ala Arg Cys Gln Val Gln Leu Gln Glu Ser Gly Gly Gly
20 25 30
Leu Val Gln Ala Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly
35 40 45
Arg Ile Phe Ser Ile Asp Ile Met Ser Trp Tyr Arg Gln Ala Pro Gly
50 55 60
Lys Gln Arg Glu Leu Val Ala Arg Ile Thr Arg Gly Gly Thr Ile Ser
65 70 75 80
Tyr Asp Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala
85 90 95
Lys Asn Thr Val Tyr Leu Gln Met Asn Ser Leu Lys Pro Glu Asp Thr
100 105 110
Gly Val Tyr Tyr Cys Asn Ala Leu Tyr Gly Thr Asp Tyr Trp Gly Lys
115 120 125
Gly Thr Gln Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly
130 135 140
Gly Ser Gly Gly Gly Gly Ser Glu Val Gln Leu Val Glu Ser Gly Gly
145 150 155 160
Gly Leu Val Gln Pro Gly Asn Ser Leu Arg Leu Ser Cys Ala Ala Ser

165 170 175

Gly Phe Thr Phe Ser Lys Phe Gly Met Ser Trp Val Arg Gln Ala Pro
180 185 190

Gly Lys Gly Leu Glu Trp Val Ser Ser Ile Ser Gly Ser Gly Arg Asp
195 200 205

Thr Leu Tyr Ala Glu Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp
210 215 220

Asn Ala Lys Thr Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Pro Glu
225 230 235 240

Asp Thr Ala Val Tyr Tyr Cys Thr Ile Gly Gly Ser Leu Ser Val Ser
245 250 255

Ser Gln Gly Thr Leu Val Thr Val Ser Ser Ser Gly Gly Pro Gly Pro
260 265 270

Ala Gly Met Lys Gly Leu Pro Gly Ser Ala Pro Thr Ser Ser Ser Thr
275 280 285

Lys Lys Thr Gln Leu Gln Leu Glu His Leu Leu Leu Asp Leu Gln Met
290 295 300

Ile Leu Asn Gly Ile Asn Asn Tyr Lys Asn Pro Lys Leu Thr Arg Met
305 310 315 320

Leu Thr Phe Lys Phe Tyr Met Pro Lys Lys Ala Thr Glu Leu Lys His
325 330 335

Leu Gln Cys Leu Glu Glu Glu Leu Lys Pro Leu Glu Glu Val Leu Asn
340 345 350

Leu Ala Gln Ser Lys Asn Phe His Leu Arg Pro Arg Asp Leu Ile Ser
355 360 365

Asn Ile Asn Val Ile Val Leu Glu Leu Lys Gly Ser Glu Thr Thr Phe
370 375 380

Met Cys Glu Tyr Ala Asp Glu Thr Ala Thr Ile Val Glu Phe Leu Asn
385 390 395 400

Arg Trp Ile Thr Phe Cys Gln Ser Ile Ile Ser Thr Leu Thr Ser Gly
405 410 415

Gly Pro Gly Pro Ala Gly Met Lys Gly Leu Pro Gly Ser Glu Val Gln
420 425 430

Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Asn Ser Leu Arg
435 440 445

Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Lys Phe Gly Met Ser
450 455 460

Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ser Ser Ile
465 470 475 480

Ser Gly Ser Gly Arg Asp Thr Leu Tyr Ala Glu Ser Val Lys Gly Arg
485 490 495
Phe Thr Ile Ser Arg Asp Asn Ala Lys Thr Thr Leu Tyr Leu Gln Met
500 505 510
Asn Ser Leu Arg Pro Glu Asp Thr Ala Val Tyr Tyr Cys Thr Ile Gly
515 520 525
Gly Ser Leu Ser Val Ser Ser Gln Gly Thr Leu Val Thr Val Ser Ser
530 535 540
His His His His His His
545 550

<210> 142
<211> 420
<212> PRT
<213> 人工序列(Artificial Sequence)
<220>
<221> 来源
<223> /注释="人工序列描述:合成多肽"
<400> 142

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

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

<210> 143
<211> 290
<212> PRT
<213> 人工序列(Artificial Sequence)
<220>
<221> 来源

<223> /注释="人工序列描述:合成多肽"

<400> 143

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

290

<210> 144

<211> 291

<212> PRT

<213> 人工序列(Artificial Sequence)

<220>

<221> 来源

<223> /注释="人工序列描述:合成多肽"

<400> 144

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

Ser Arg Asp Asn Ala Lys Thr Thr Leu Tyr Leu Gln Met Asn Ser Leu
245 250 255
Arg Pro Glu Asp Thr Ala Val Tyr Tyr Cys Thr Ile Gly Gly Ser Leu
260 265 270
Ser Val Ser Ser Gln Gly Thr Leu Val Thr Val Ser Ser His His His
275 280 285
His His His
290

<210> 145
<211> 689
<212> PRT
<213> 人工序列(Artificial Sequence)
<220>
<221> 来源
<223> /注释="人工序列描述:合成多肽"
<400> 145
Met Asp Met Arg Val Pro Ala Gln Leu Leu Gly Leu Leu Leu Leu Trp
1 5 10 15
Leu Arg Gly Ala Arg Cys Gln Val Gln Leu Gln Glu Ser Gly Gly Gly
20 25 30
Leu Val Gln Ala Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly
35 40 45
Arg Ile Phe Ser Ile Asp Ile Met Ser Trp Tyr Arg Gln Ala Pro Gly
50 55 60
Lys Gln Arg Glu Leu Val Ala Arg Ile Thr Arg Gly Gly Thr Ile Ser
65 70 75 80
Tyr Asp Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala
85 90 95
Lys Asn Thr Val Tyr Leu Gln Met Asn Ser Leu Lys Pro Glu Asp Thr
100 105 110
Gly Val Tyr Tyr Cys Asn Ala Leu Tyr Gly Thr Asp Tyr Trp Gly Lys
115 120 125
Gly Thr Gln Val Thr Val Ser Ser Ser Gly Gly Pro Gly Pro Ala Gly
130 135 140
Met Lys Gly Leu Pro Gly Ser Ala Pro Thr Ser Ser Ser Thr Lys Lys
145 150 155 160
Thr Gln Leu Gln Leu Glu His Leu Leu Leu Asp Leu Gln Met Ile Leu
165 170 175
Asn Gly Ile Asn Asn Tyr Lys Asn Pro Lys Leu Thr Arg Met Leu Thr

180 185 190

Phe Lys Phe Tyr Met Pro Lys Lys Ala Thr Glu Leu Lys His Leu Gln
195 200 205

Cys Leu Glu Glu Glu Leu Lys Pro Leu Glu Glu Val Leu Asn Leu Ala
210 215 220

Gln Ser Lys Asn Phe His Leu Arg Pro Arg Asp Leu Ile Ser Asn Ile
225 230 235 240

Asn Val Ile Val Leu Glu Leu Lys Gly Ser Glu Thr Thr Phe Met Cys
245 250 255

Glu Tyr Ala Asp Glu Thr Ala Thr Ile Val Glu Phe Leu Asn Arg Trp
260 265 270

Ile Thr Phe Cys Gln Ser Ile Ile Ser Thr Leu Thr Ser Gly Gly Pro
275 280 285

Gly Pro Ala Gly Met Lys Gly Leu Pro Gly Ser Glu Val Gln Leu Val
290 295 300

Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Asn Ser Leu Arg Leu Ser
305 310 315 320

Cys Ala Ala Ser Gly Phe Thr Phe Ser Lys Phe Gly Met Ser Trp Val
325 330 335

Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ser Ser Ile Ser Gly
340 345 350

Ser Gly Arg Asp Thr Leu Tyr Ala Glu Ser Val Lys Gly Arg Phe Thr
355 360 365

Ile Ser Arg Asp Asn Ala Lys Thr Thr Leu Tyr Leu Gln Met Asn Ser
370 375 380

Leu Arg Pro Glu Asp Thr Ala Val Tyr Tyr Cys Thr Ile Gly Gly Ser
385 390 395 400

Leu Ser Val Ser Ser Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly
405 410 415

Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly
420 425 430

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Val Gln Leu
435 440 445

Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Leu Arg Leu
450 455 460

Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr Thr Leu Ala Trp
465 470 475 480

Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala Ala Ile Asp
485 490 495

Ser Ser Ser Tyr Thr Tyr Ser Pro Asp Thr Val Arg Gly Arg Phe Thr
500 505 510
Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr Leu Gln Met Asn Ser
515 520 525
Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Asp Ser Asn
530 535 540
Trp Asp Ala Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser
545 550 555 560
Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
565 570 575
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
580 585 590
Asp Arg Val Thr Ile Thr Cys Lys Ala Ser Gln Asn Val Gly Thr Asn
595 600 605
Val Gly Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Ala Leu Ile
610 615 620
Tyr Ser Ala Ser Phe Arg Tyr Ser Gly Val Pro Ser Arg Phe Ser Gly
625 630 635 640
Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
645 650 655
Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Tyr Thr Tyr Pro Tyr
660 665 670
Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys His His His His His
675 680 685
His

<210> 146
<211> 704
<212> PRT
<213> 人工序列(Artificial Sequence)
<220>
<221> 来源
<223> /注释="人工序列描述:合成多肽"
<400> 146
Met Asp Met Arg Val Pro Ala Gln Leu Leu Gly Leu Leu Leu Leu Trp
1 5 10 15
Leu Arg Gly Ala Arg Cys Ala Pro Thr Ser Ser Ser Thr Lys Lys Thr
20 25 30
Gln Leu Gln Leu Glu His Leu Leu Leu Asp Leu Gln Met Ile Leu Asn
35 40 45

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

355 360 365

Gln Gln Lys Pro Gly Lys Ala Pro Lys Ala Leu Ile Tyr Ser Ala Ser

370 375 380

Phe Arg Tyr Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly

385 390 395 400

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

405 410 415

Thr Tyr Tyr Cys Gln Gln Tyr Tyr Thr Tyr Pro Tyr Thr Phe Gly Gly

420 425 430

Gly Thr Lys Val Glu Ile Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly

435 440 445

Ser Gly Gly Gly Gly Ser Glu Val Gln Leu Val Glu Ser Gly Gly Gly

450 455 460

Leu Val Gln Pro Gly Asn Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly

465 470 475 480

Phe Thr Phe Ser Lys Phe Gly Met Ser Trp Val Arg Gln Ala Pro Gly

485 490 495

Lys Gly Leu Glu Trp Val Ser Ser Ile Ser Gly Ser Gly Arg Asp Thr

500 505 510

Leu Tyr Ala Glu Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn

515 520 525

Ala Lys Thr Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Pro Glu Asp

530 535 540

Thr Ala Val Tyr Tyr Cys Thr Ile Gly Gly Ser Leu Ser Val Ser Ser

545 550 555 560

Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly

565 570 575

Gly Gly Ser Gly Gly Gly Gly Ser Gln Val Gln Leu Gln Glu Ser Gly

580 585 590

Gly Gly Leu Ala Gln Ala Gly Gly Ser Leu Ser Leu Ser Cys Ala Ala

595 600 605

Ser Gly Phe Thr Val Ser Asn Ser Val Met Ala Trp Tyr Arg Gln Thr

610 615 620

Pro Gly Lys Gln Arg Glu Phe Val Ala Ile Ile Asn Ser Val Gly Ser

625 630 635 640

Thr Asn Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp

645 650 655

Asn Ala Lys Asn Thr Val Tyr Leu Gln Met Asn Asn Leu Lys Pro Glu

660 665 670

Asp Thr Ala Val Tyr Val Cys Asn Arg Asn Phe Asp Arg Ile Tyr Trp
675 680 685
Gly Gln Gly Thr Gln Val Thr Val Ser Ser His His His His His His
690 695 700
<210> 147
<211> 674
<212> PRT
<213> 人工序列(Artificial Sequence)
<220>
<221> 来源
<223> /注释="人工序列描述:合成多肽"
<400> 147
Met Asp Met Arg Val Pro Ala Gln Leu Leu Gly Leu Leu Leu Leu Trp
1 5 10 15
Leu Arg Gly Ala Arg Cys Gln Val Gln Leu Gln Glu Ser Gly Gly Gly
20 25 30
Leu Ala Gln Ala Gly Gly Ser Leu Ser Leu Ser Cys Ala Ala Ser Gly
35 40 45
Phe Thr Val Ser Asn Ser Val Met Ala Trp Tyr Arg Gln Thr Pro Gly
50 55 60
Lys Gln Arg Glu Phe Val Ala Ile Ile Asn Ser Val Gly Ser Thr Asn
65 70 75 80
Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala
85 90 95
Lys Asn Thr Val Tyr Leu Gln Met Asn Asn Leu Lys Pro Glu Asp Thr
100 105 110
Ala Val Tyr Val Cys Asn Arg Asn Phe Asp Arg Ile Tyr Trp Gly Gln
115 120 125
Gly Thr Gln Val Thr Val Ser Ser Ala Pro Thr Ser Ser Ser Thr Lys
130 135 140
Lys Thr Gln Leu Gln Leu Glu His Leu Leu Leu Asp Leu Gln Met Ile
145 150 155 160
Leu Asn Gly Ile Asn Asn Tyr Lys Asn Pro Lys Leu Thr Arg Met Leu
165 170 175
Thr Phe Lys Phe Tyr Met Pro Lys Lys Ala Thr Glu Leu Lys His Leu
180 185 190
Gln Cys Leu Glu Glu Glu Leu Lys Pro Leu Glu Glu Val Leu Asn Leu
195 200 205
Ala Gln Ser Lys Asn Phe His Leu Arg Pro Arg Asp Leu Ile Ser Asn

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

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

<210> 148
<211> 704
<212> PRT
<213> 人工序列(Artificial Sequence)
<220>
<221> 来源
<223> /注释="人工序列描述:合成多肽"
<400> 148

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

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

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

<210> 149

<211> 704

<212> PRT
<213> 人工序列(Artificial Sequence)
<220>
<221> 来源
<223> /注释="人工序列描述:合成多肽"
<400> 149

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

260 265 270

Ala Gly Met Lys Gly Leu Pro Gly Ser Glu Val Gln Leu Val Glu Ser

275 280 285

Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala

290 295 300

Ala Ser Gly Phe Thr Phe Ser Ser Tyr Thr Leu Ala Trp Val Arg Gln

305 310 315 320

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

325 330 335

Tyr Thr Tyr Ser Pro Asp Thr Val Arg Gly Arg Phe Thr Ile Ser Arg

340 345 350

Asp Asn Ala Lys Asn Ser Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala

355 360 365

Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Asp Ser Asn Trp Asp Ala

370 375 380

Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly

385 390 395 400

Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Gln

405 410 415

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

420 425 430

Thr Ile Thr Cys Lys Ala Ser Gln Asn Val Gly Thr Asn Val Gly Trp

435 440 445

Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Ala Leu Ile Tyr Ser Ala

450 455 460

Ser Phe Arg Tyr Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser

465 470 475 480

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

485 490 495

Ala Thr Tyr Tyr Cys Gln Gln Tyr Tyr Thr Tyr Pro Tyr Thr Phe Gly

500 505 510

Gly Gly Thr Lys Val Glu Ile Lys Gly Gly Gly Gly Ser Gly Gly Gly

515 520 525

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly

530 535 540

Ser Gly Gly Gly Gly Ser Ser Gly Gly Pro Gly Pro Ala Gly Met Lys

545 550 555 560

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

565 570 575

Leu Gln Leu Glu His Leu Leu Leu Asp Leu Gln Met Ile Leu Asn Gly
580 585 590
Ile Asn Asn Tyr Lys Asn Pro Lys Leu Thr Arg Met Leu Thr Phe Lys
595 600 605
Phe Tyr Met Pro Lys Lys Ala Thr Glu Leu Lys His Leu Gln Cys Leu
610 615 620
Glu Glu Glu Leu Lys Pro Leu Glu Glu Val Leu Asn Leu Ala Gln Ser
625 630 635 640
Lys Asn Phe His Leu Arg Pro Arg Asp Leu Ile Ser Asn Ile Asn Val
645 650 655
Ile Val Leu Glu Leu Lys Gly Ser Glu Thr Thr Phe Met Cys Glu Tyr
660 665 670
Ala Asp Glu Thr Ala Thr Ile Val Glu Phe Leu Asn Arg Trp Ile Thr
675 680 685
Phe Cys Gln Ser Ile Ile Ser Thr Leu Thr His His His His His His
690 695 700

<210> 150
<211> 689
<212> PRT
<213> 人工序列(Artificial Sequence)
<220>
<221> 来源
<223> /注释="人工序列描述:合成多肽"
<400> 150

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

115 120 125

Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser

130 135 140

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Gln Met Thr Gln

145 150 155 160

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

165 170 175

Cys Lys Ala Ser Gln Asn Val Gly Thr Asn Val Gly Trp Tyr Gln Gln

180 185 190

Lys Pro Gly Lys Ala Pro Lys Ala Leu Ile Tyr Ser Ala Ser Phe Arg

195 200 205

Tyr Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp

210 215 220

Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr

225 230 235 240

Tyr Cys Gln Gln Tyr Tyr Thr Tyr Pro Tyr Thr Phe Gly Gly Gly Thr

245 250 255

Lys Val Glu Ile Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly

260 265 270

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly

275 280 285

Gly Gly Ser Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln

290 295 300

Pro Gly Asn Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe

305 310 315 320

Ser Lys Phe Gly Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu

325 330 335

Glu Trp Val Ser Ser Ile Ser Gly Ser Gly Arg Asp Thr Leu Tyr Ala

340 345 350

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

355 360 365

Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Val

370 375 380

Tyr Tyr Cys Thr Ile Gly Gly Ser Leu Ser Val Ser Ser Gln Gly Thr

385 390 395 400

Leu Val Thr Val Ser Ser Ser Gly Gly Pro Gly Pro Ala Gly Met Lys

405 410 415

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

420 425 430

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

<210> 151
<211> 700
<212> PRT
<213> 人工序列(Artificial Sequence)
<220>
<221> 来源

<223> /注释="人工序列描述:合成多肽"

<400> 151

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

290 295 300

Pro Ala Ala Pro Gly Ser Glu Val Gln Leu Val Glu Ser Gly Gly Gly
305 310 315 320

Leu Val Gln Pro Gly Asn Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly
325 330 335

Phe Thr Phe Ser Lys Phe Gly Met Ser Trp Val Arg Gln Ala Pro Gly
340 345 350

Lys Gly Leu Glu Trp Val Ser Ser Ile Ser Gly Ser Gly Arg Asp Thr
355 360 365

Leu Tyr Ala Glu Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn
370 375 380

Ala Lys Thr Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Pro Glu Asp
385 390 395 400

Thr Ala Val Tyr Tyr Cys Thr Ile Gly Gly Ser Leu Ser Val Ser Ser
405 410 415

Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly
420 425 430

Gly Gly Ser Gly Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly
435 440 445

Gly Ser Gly Gly Gly Gly Ser Glu Val Gln Leu Val Glu Ser Gly Gly
450 455 460

Gly Leu Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser
465 470 475 480

Gly Phe Thr Phe Ser Ser Tyr Thr Leu Ala Trp Val Arg Gln Ala Pro
485 490 495

Gly Lys Gly Leu Glu Trp Val Ala Ala Ile Asp Ser Ser Ser Tyr Thr
500 505 510

Tyr Ser Pro Asp Thr Val Arg Gly Arg Phe Thr Ile Ser Arg Asp Asn
515 520 525

Ala Lys Asn Ser Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp
530 535 540

Thr Ala Val Tyr Tyr Cys Ala Arg Asp Ser Asn Trp Asp Ala Leu Asp
545 550 555 560

Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly
565 570 575

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Gln Met Thr
580 585 590

Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile
595 600 605

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

<210> 152
<211> 276
<212> PRT
<213> 人工序列(Artificial Sequence)
<220>
<221> 来源
<223> /注释="人工序列描述:合成多肽"
<400> 152

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

145 150 155 160
Glu Leu Thr Gln Asp Pro Ala Val Ser Val Ala Leu Gly Gln Thr Val
165 170 175
Arg Ile Thr Cys Gln Gly Asp Ser Leu Arg Ser Tyr Tyr Ala Ser Trp
180 185 190
Tyr Gln Gln Lys Pro Gly Gln Ala Pro Val Leu Val Ile Tyr Gly Lys
195 200 205
Asn Asn Arg Pro Ser Gly Ile Pro Asp Arg Phe Ser Gly Ser Ser Ser
210 215 220
Gly Asn Thr Ala Ser Leu Thr Thr Thr Gly Ala Gln Ala Glu Asp Glu
225 230 235 240
Ala Asp Tyr Tyr Cys Asn Ser Ser Pro Phe Glu His Asn Leu Val Val
245 250 255
Phe Gly Gly Gly Thr Lys Leu Thr Val Leu His His His His His His
260 265 270
Glu Pro Glu Ala
275

<210> 153
<211> 279
<212> PRT
<213> 人工序列(Artificial Sequence)
<220>
<221> 来源
<223> /注释="人工序列描述:合成多肽"
<400> 153
Met Asp Met Arg Val Pro Ala Gln Leu Leu Gly Leu Leu Leu Leu Trp
1 5 10 15
Leu Arg Gly Ala Arg Cys Gln Val Gln Leu Gln Gln Ser Gly Ala Glu
20 25 30
Leu Val Arg Pro Gly Thr Ser Val Lys Val Ser Cys Lys Ala Ser Gly
35 40 45
Tyr Ala Phe Thr Asn Tyr Leu Ile Glu Trp Val Lys Gln Arg Pro Gly
50 55 60
Gln Gly Leu Glu Trp Ile Gly Val Ile Asn Pro Gly Ser Gly Gly Thr
65 70 75 80
Asn Tyr Asn Glu Lys Phe Lys Gly Lys Ala Thr Leu Thr Ala Asp Lys
85 90 95
Ser Ser Ser Thr Ala Tyr Met Gln Leu Ser Ser Leu Thr Ser Asp Asp
100 105 110

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

<210> 154
<211> 279
<212> PRT
<213> 人工序列(Artificial Sequence)
<220>
<221> 来源
<223> /注释="人工序列描述:合成多肽"
<400> 154
Met Asp Met Arg Val Pro Ala Gln Leu Leu Gly Leu Leu Leu Leu Trp
1 5 10 15
Leu Arg Gly Ala Arg Cys Gln Val Gln Leu Gln Gln Ser Gly Ala Glu
20 25 30
Leu Val Arg Pro Gly Thr Ser Val Lys Val Ser Cys Lys Ala Ser Gly
35 40 45
Tyr Ala Phe Thr Asn Tyr Leu Ile Glu Trp Val Lys Gln Arg Pro Gly
50 55 60
Gln Gly Leu Glu Trp Ile Gly Val Ile Asn Pro Gly Ser Gly Gly Thr

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

<210> 155
<211> 279
<212> PRT
<213> 人工序列(Artificial Sequence)
<220>
<221> 来源
<223> /注释="人工序列描述:合成多肽"
<400> 155
Met Asp Met Arg Val Pro Ala Gln Leu Leu Gly Leu Leu Leu Leu Trp
1 5 10 15
Leu Arg Gly Ala Arg Cys Asp Ile Val Leu Thr Gln Ser Pro Ala Ser
20 25 30

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

<210> 156
<211> 279
<212> PRT
<213> 人工序列(Artificial Sequence)
<220>
<221> 来源
<223> /注释="人工序列描述:合成多肽"

<400> 156

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

<210> 157

<211> 295

<212> PRT
<213> 人工序列(Artificial Sequence)
<220>
<221> 来源
<223> /注释="人工序列描述:合成多肽"
<400> 157

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

260 265 270

Ser Val Ser Ser Gln Gly Thr Leu Val Thr Val Ser Ser His His His

275 280 285

His His His Glu Pro Glu Ala

290 295

<210> 158

<211> 765

<212> PRT

<213> 人工序列(Artificial Sequence)

<220>

<221> 来源

<223> /注释="人工序列描述:合成多肽"

<400> 158

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Leu Arg Gly Ala Arg Cys Ala Pro Thr Ser Ser Ser Thr Lys Lys Thr

20 25 30

Gln Leu Gln Leu Glu His Leu Leu Leu Asp Leu Gln Met Ile Leu Asn

35 40 45

Gly Ile Asn Asn Tyr Lys Asn Pro Lys Leu Thr Arg Met Leu Thr Phe

50 55 60

Lys Phe Tyr Met Pro Lys Lys Ala Thr Glu Leu Lys His Leu Gln Cys

65 70 75 80

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

85 90 95

Ser Lys Asn Phe His Leu Arg Pro Arg Asp Leu Ile Ser Asn Ile Asn

100 105 110

Val Ile Val Leu Glu Leu Lys Gly Ser Glu Thr Thr Phe Met Cys Glu

115 120 125

Tyr Ala Asp Glu Thr Ala Thr Ile Val Glu Phe Leu Asn Arg Trp Ile

130 135 140

Thr Phe Cys Gln Ser Ile Ile Ser Thr Leu Thr Gly Gly Gly Gly Ser

145 150 155 160

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ala His Lys Ser Glu

165 170 175

Val Ala His Arg Phe Lys Asp Leu Gly Glu Glu Asn Phe Lys Ala Leu

180 185 190

Val Leu Ile Ala Phe Ala Gln Tyr Leu Gln Gln Cys Pro Phe Glu Asp

195 200 205

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

515 520 525

Lys Cys Cys Ala Ala Ala Asp Pro His Glu Cys Tyr Ala Lys Val Phe
530 535 540

Asp Glu Phe Lys Pro Leu Val Glu Glu Pro Gln Asn Leu Ile Lys Gln
545 550 555 560

Asn Cys Glu Leu Phe Glu Gln Leu Gly Glu Tyr Lys Phe Gln Asn Ala
565 570 575

Leu Leu Val Arg Tyr Thr Lys Lys Val Pro Gln Val Ser Thr Pro Thr
580 585 590

Leu Val Glu Val Ser Arg Asn Leu Gly Lys Val Gly Ser Lys Cys Cys
595 600 605

Lys His Pro Glu Ala Lys Arg Met Pro Cys Ala Glu Asp Tyr Leu Ser
610 615 620

Val Val Leu Asn Gln Leu Cys Val Leu His Glu Lys Thr Pro Val Ser
625 630 635 640

Asp Arg Val Thr Lys Cys Cys Thr Glu Ser Leu Val Asn Arg Arg Pro
645 650 655

Cys Phe Ser Ala Leu Glu Val Asp Glu Thr Tyr Val Pro Lys Glu Phe
660 665 670

Asn Ala Glu Thr Phe Thr Phe His Ala Asp Ile Cys Thr Leu Ser Glu
675 680 685

Lys Glu Arg Gln Ile Lys Lys Gln Thr Ala Leu Val Glu Leu Val Lys
690 695 700

His Lys Pro Lys Ala Thr Lys Glu Gln Leu Lys Ala Val Met Asp Asp
705 710 715 720

Phe Ala Ala Phe Val Glu Lys Cys Cys Lys Ala Asp Asp Lys Glu Thr
725 730 735

Cys Phe Ala Glu Glu Gly Lys Lys Leu Val Ala Ala Ser Gln Ala Ala
740 745 750

Leu Gly Leu His His His His His His Glu Pro Glu Ala
755 760 765

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<223> /注释="人工序列描述:合成多肽"
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Leu Arg Gly Ala Arg Cys Ala Pro Thr Ser Ser Ser Thr Lys Lys Thr
20 25 30
Gln Leu Gln Leu Glu His Leu Leu Leu Asp Leu Gln Met Ile Leu Asn
35 40 45
Gly Ile Asn Asn Tyr Lys Asn Pro Lys Leu Thr Arg Met Leu Thr Phe
50 55 60
Lys Phe Tyr Met Pro Lys Lys Ala Thr Glu Leu Lys His Leu Gln Cys
65 70 75 80
Leu Glu Glu Glu Leu Lys Pro Leu Glu Glu Val Leu Asn Leu Ala Gln
85 90 95
Ser Lys Asn Phe His Leu Arg Pro Arg Asp Leu Ile Ser Asn Ile Asn
100 105 110
Val Ile Val Leu Glu Leu Lys Gly Ser Glu Thr Thr Phe Met Cys Glu
115 120 125
Tyr Ala Asp Glu Thr Ala Thr Ile Val Glu Phe Leu Asn Arg Trp Ile
130 135 140
Thr Phe Cys Gln Ser Ile Ile Ser Thr Leu Thr Gly Gly Gly Gly Ser
145 150 155 160
Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ala His Lys Ser Glu
165 170 175
Val Ala His Arg Phe Lys Asp Leu Gly Glu Glu Asn Phe Lys Ala Leu
180 185 190
Val Leu Ile Ala Phe Ala Gln Tyr Leu Gln Gln Cys Pro Phe Glu Asp
195 200 205
His Val Lys Leu Val Asn Glu Val Thr Glu Phe Ala Lys Thr Cys Val
210 215 220
Ala Asp Glu Ser Ala Glu Asn Cys Asp Lys Ser Leu His Thr Leu Phe
225 230 235 240
Gly Asp Lys Leu Cys Thr Val Ala Thr Leu Arg Glu Thr Tyr Gly Glu
245 250 255
Met Ala Asp Cys Cys Ala Lys Gln Glu Pro Glu Arg Asn Glu Cys Phe
260 265 270
Leu Gln His Lys Asp Asp Asn Pro Asn Leu Pro Arg Leu Val Arg Pro
275 280 285
Glu Val Asp Val Met Cys Thr Ala Phe His Asp Asn Glu Glu Thr Phe
290 295 300
Leu Lys Lys Tyr Leu Tyr Glu Ile Ala Arg Arg His Pro Tyr Phe Tyr

305 310 315 320
Ala Pro Glu Leu Leu Phe Phe Ala Lys Arg Tyr Lys Ala Ala Phe Thr
325 330 335
Glu Cys Cys Gln Ala Ala Asp Lys Ala Ala Cys Leu Leu Pro Lys Leu
340 345 350
Asp Glu Leu Arg Asp Glu Gly Lys Ala Ser Ser Ala Lys Gln Arg Leu
355 360 365
Lys Cys Ala Ser Leu Gln Lys Phe Gly Glu Arg Ala Phe Lys Ala Trp
370 375 380
Ala Val Ala Arg Leu Ser Gln Arg Phe Pro Lys Ala Glu Phe Ala Glu
385 390 395 400
Val Ser Lys Leu Val Thr Asp Leu Thr Lys Val His Thr Glu Cys Cys
405 410 415
His Gly Asp Leu Leu Glu Cys Ala Asp Asp Arg Ala Asp Leu Ala Lys
420 425 430
Tyr Ile Cys Glu Asn Gln Asp Ser Ile Ser Ser Lys Leu Lys Glu Cys
435 440 445
Cys Glu Lys Pro Leu Leu Glu Lys Ser His Cys Ile Ala Glu Val Glu
450 455 460
Asn Asp Glu Met Pro Ala Asp Leu Pro Ser Leu Ala Ala Asp Phe Val
465 470 475 480
Glu Ser Lys Asp Val Cys Lys Asn Tyr Ala Glu Ala Lys Asp Val Phe
485 490 495
Leu Gly Met Phe Leu Tyr Glu Tyr Ala Arg Arg His Pro Asp Tyr Ser
500 505 510
Val Val Leu Leu Leu Arg Leu Ala Lys Thr Tyr Glu Thr Thr Leu Glu
515 520 525
Lys Cys Cys Ala Ala Ala Asp Pro His Glu Cys Tyr Ala Lys Val Phe
530 535 540
Asp Glu Phe Lys Pro Leu Val Glu Glu Pro Gln Asn Leu Ile Lys Gln
545 550 555 560
Asn Cys Glu Leu Phe Glu Gln Leu Gly Glu Tyr Lys Phe Gln Asn Ala
565 570 575
Leu Leu Val Arg Tyr Thr Lys Lys Val Pro Gln Val Ser Thr Pro Thr
580 585 590
Leu Val Glu Val Ser Arg Asn Leu Gly Lys Val Gly Ser Lys Cys Cys
595 600 605
Lys His Pro Glu Ala Lys Arg Met Pro Cys Ala Glu Asp Tyr Leu Ser
610 615 620

Val Val Leu Asn Gln Leu Cys Val Leu His Glu Lys Thr Pro Val Ser
625 630 635 640
Asp Arg Val Thr Lys Cys Cys Thr Glu Ser Leu Val Asn Arg Arg Pro
645 650 655
Cys Phe Ser Ala Leu Glu Val Asp Glu Thr Tyr Val Pro Lys Glu Phe
660 665 670
Asn Ala Glu Thr Phe Thr Phe His Ala Asp Ile Cys Thr Leu Ser Glu
675 680 685
Lys Glu Arg Gln Ile Lys Lys Gln Thr Ala Leu Val Glu Leu Val Lys
690 695 700
His Lys Pro Lys Ala Thr Lys Glu Gln Leu Lys Ala Val Met Asp Asp
705 710 715 720
Phe Ala Ala Phe Val Glu Lys Cys Cys Lys Ala Asp Asp Lys Glu Thr
725 730 735
Cys Phe Ala Glu Glu Gly Lys Lys Leu Val Ala Ala Ser Gln Ala Ala
740 745 750
Leu Gly Leu His His His His His His Glu Pro Glu Ala
755 760 765

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

100 105 110

Val Ile Val Leu Glu Leu Lys Gly Ser Glu Thr Thr Phe Met Cys Glu
115 120 125

Tyr Ala Asp Glu Thr Ala Thr Ile Val Glu Phe Leu Asn Arg Trp Ile
130 135 140

Thr Phe Cys Gln Ser Ile Ile Ser Thr Leu Thr Ser Gly Gly Pro Gly
145 150 155 160

Pro Ala Gly Met Lys Gly Leu Pro Gly Ser Asp Ala His Lys Ser Glu
165 170 175

Val Ala His Arg Phe Lys Asp Leu Gly Glu Glu Asn Phe Lys Ala Leu
180 185 190

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

His Val Lys Leu Val Asn Glu Val Thr Glu Phe Ala Lys Thr Cys Val
210 215 220

Ala Asp Glu Ser Ala Glu Asn Cys Asp Lys Ser Leu His Thr Leu Phe
225 230 235 240

Gly Asp Lys Leu Cys Thr Val Ala Thr Leu Arg Glu Thr Tyr Gly Glu
245 250 255

Met Ala Asp Cys Cys Ala Lys Gln Glu Pro Glu Arg Asn Glu Cys Phe
260 265 270

Leu Gln His Lys Asp Asp Asn Pro Asn Leu Pro Arg Leu Val Arg Pro
275 280 285

Glu Val Asp Val Met Cys Thr Ala Phe His Asp Asn Glu Glu Thr Phe
290 295 300

Leu Lys Lys Tyr Leu Tyr Glu Ile Ala Arg Arg His Pro Tyr Phe Tyr
305 310 315 320

Ala Pro Glu Leu Leu Phe Phe Ala Lys Arg Tyr Lys Ala Ala Phe Thr
325 330 335

Glu Cys Cys Gln Ala Ala Asp Lys Ala Ala Cys Leu Leu Pro Lys Leu
340 345 350

Asp Glu Leu Arg Asp Glu Gly Lys Ala Ser Ser Ala Lys Gln Arg Leu
355 360 365

Lys Cys Ala Ser Leu Gln Lys Phe Gly Glu Arg Ala Phe Lys Ala Trp
370 375 380

Ala Val Ala Arg Leu Ser Gln Arg Phe Pro Lys Ala Glu Phe Ala Glu
385 390 395 400

Val Ser Lys Leu Val Thr Asp Leu Thr Lys Val His Thr Glu Cys Cys
405 410 415

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

725 730 735
Cys Phe Ala Glu Glu Gly Lys Lys Leu Val Ala Ala Ser Gln Ala Ala
740 745 750
Leu Gly Leu His His His His His His Glu Pro Glu Ala
755 760 765
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Leu Arg Gly Ala Arg Cys Ala Pro Thr Ser Ser Ser Thr Lys Lys Thr
20 25 30
Gln Leu Gln Leu Glu His Leu Leu Leu Asp Leu Gln Met Ile Leu Asn
35 40 45
Gly Ile Asn Asn Tyr Lys Asn Pro Lys Leu Thr Arg Met Leu Thr Phe
50 55 60
Lys Phe Tyr Met Pro Lys Lys Ala Thr Glu Leu Lys His Leu Gln Cys
65 70 75 80
Leu Glu Glu Glu Leu Lys Pro Leu Glu Glu Val Leu Asn Leu Ala Gln
85 90 95
Ser Lys Asn Phe His Leu Arg Pro Arg Asp Leu Ile Ser Asn Ile Asn
100 105 110
Val Ile Val Leu Glu Leu Lys Gly Ser Glu Thr Thr Phe Met Cys Glu
115 120 125
Tyr Ala Asp Glu Thr Ala Thr Ile Val Glu Phe Leu Asn Arg Trp Ile
130 135 140
Thr Phe Cys Gln Ser Ile Ile Ser Thr Leu Thr Ser Gly Gly Pro Gly
145 150 155 160
Pro Ala Gly Met Lys Gly Leu Pro Gly Ser Glu Val Gln Leu Val Glu
165 170 175
Ser Gly Gly Gly Leu Val Gln Pro Gly Asn Ser Leu Arg Leu Ser Cys
180 185 190
Ala Ala Ser Gly Phe Thr Phe Ser Lys Phe Gly Met Ser Trp Val Arg
195 200 205

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

515 520 525
Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp
530 535 540
Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Tyr Thr Tyr Pro Tyr Thr Phe
545 550 555 560
Gly Gly Gly Thr Lys Val Glu Ile Lys Gly Gly Gly Gly Ser Gly Gly
565 570 575
Gly Gly Ser Gly Gly Gly Gly Ser Gln Val Gln Leu Gln Glu Ser Gly
580 585 590
Gly Gly Leu Ala Gln Ala Gly Gly Ser Leu Ser Leu Ser Cys Ala Ala
595 600 605
Ser Gly Phe Thr Val Ser Asn Ser Val Met Ala Trp Tyr Arg Gln Thr
610 615 620
Pro Gly Lys Gln Arg Glu Phe Val Ala Ile Ile Asn Ser Val Gly Ser
625 630 635 640
Thr Asn Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp
645 650 655
Asn Ala Lys Asn Thr Val Tyr Leu Gln Met Asn Asn Leu Lys Pro Glu
660 665 670
Asp Thr Ala Val Tyr Val Cys Asn Arg Asn Phe Asp Arg Ile Tyr Trp
675 680 685
Gly Gln Gly Thr Gln Val Thr Val Ser Ser His His His His His His
690 695 700
Glu Pro Glu Ala
705

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Leu Arg Gly Ala Arg Cys Gln Val Gln Leu Gln Glu Ser Gly Gly Gly
20 25 30
Leu Ala Gln Ala Gly Gly Ser Leu Ser Leu Ser Cys Ala Ala Ser Gly
35 40 45

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

355 360 365

Ile Ser Arg Asp Asn Ala Lys Thr Thr Leu Tyr Leu Gln Met Asn Ser

370 375 380

Leu Arg Pro Glu Asp Thr Ala Val Tyr Tyr Cys Thr Ile Gly Gly Ser

385 390 395 400

Leu Ser Val Ser Ser Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly

405 410 415

Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly

420 425 430

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Ser Gly Gly Pro

435 440 445

Gly Pro Ala Gly Met Lys Gly Leu Pro Gly Ser Glu Val Gln Leu Val

450 455 460

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

465 470 475 480

Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr Thr Leu Ala Trp Val

485 490 495

Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala Ala Ile Asp Ser

500 505 510

Ser Ser Tyr Thr Tyr Ser Pro Asp Thr Val Arg Gly Arg Phe Thr Ile

515 520 525

Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr Leu Gln Met Asn Ser Leu

530 535 540

Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Asp Ser Asn Trp

545 550 555 560

Asp Ala Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser

565 570 575

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp

580 585 590

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

595 600 605

Arg Val Thr Ile Thr Cys Lys Ala Ser Gln Asn Val Gly Thr Asn Val

610 615 620

Gly Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Ala Leu Ile Tyr

625 630 635 640

Ser Ala Ser Phe Arg Tyr Ser Gly Val Pro Ser Arg Phe Ser Gly Ser

645 650 655

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

660 665 670

Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Tyr Thr Tyr Pro Tyr Thr
675 680 685
Phe Gly Gly Gly Thr Lys Val Glu Ile Lys His His His His His His
690 695 700
Glu Pro Glu Ala
705

<210> 163
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Met Asp Met Arg Val Pro Ala Gln Leu Leu Gly Leu Leu Leu Leu Trp
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Leu Arg Gly Ala Arg Cys Gln Val Gln Leu Gln Glu Ser Gly Gly Gly
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Leu Ala Gln Ala Gly Gly Ser Leu Ser Leu Ser Cys Ala Ala Ser Gly
35 40 45
Phe Thr Val Ser Asn Ser Val Met Ala Trp Tyr Arg Gln Thr Pro Gly
50 55 60
Lys Gln Arg Glu Phe Val Ala Ile Ile Asn Ser Val Gly Ser Thr Asn
65 70 75 80
Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala
85 90 95
Lys Asn Thr Val Tyr Leu Gln Met Asn Asn Leu Lys Pro Glu Asp Thr
100 105 110
Ala Val Tyr Val Cys Asn Arg Asn Phe Asp Arg Ile Tyr Trp Gly Gln
115 120 125
Gly Thr Gln Val Thr Val Ser Ser Ser Gly Gly Pro Gly Pro Ala Gly
130 135 140
Met Lys Gly Leu Pro Gly Ser Ala Pro Thr Ser Ser Ser Thr Lys Lys
145 150 155 160
Thr Gln Leu Gln Leu Glu His Leu Leu Leu Asp Leu Gln Met Ile Leu
165 170 175
Asn Gly Ile Asn Asn Tyr Lys Asn Pro Lys Leu Thr Arg Met Leu Thr
180 185 190
Phe Lys Phe Tyr Met Pro Lys Lys Ala Thr Glu Leu Lys His Leu Gln

195 200 205

Cys Leu Glu Glu Glu Leu Lys Pro Leu Glu Glu Val Leu Asn Leu Ala
210 215 220

Gln Ser Lys Asn Phe His Leu Arg Pro Arg Asp Leu Ile Ser Asn Ile
225 230 235 240

Asn Val Ile Val Leu Glu Leu Lys Gly Ser Glu Thr Thr Phe Met Cys
245 250 255

Glu Tyr Ala Asp Glu Thr Ala Thr Ile Val Glu Phe Leu Asn Arg Trp
260 265 270

Ile Thr Phe Cys Gln Ser Ile Ile Ser Thr Leu Thr Ser Gly Gly Pro
275 280 285

Gly Pro Ala Gly Met Lys Gly Leu Pro Gly Ser Glu Val Gln Leu Val
290 295 300

Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Asn Ser Leu Arg Leu Ser
305 310 315 320

Cys Ala Ala Ser Gly Phe Thr Phe Ser Lys Phe Gly Met Ser Trp Val
325 330 335

Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ser Ser Ile Ser Gly
340 345 350

Ser Gly Arg Asp Thr Leu Tyr Ala Glu Ser Val Lys Gly Arg Phe Thr
355 360 365

Ile Ser Arg Asp Asn Ala Lys Thr Thr Leu Tyr Leu Gln Met Asn Ser
370 375 380

Leu Arg Pro Glu Asp Thr Ala Val Tyr Tyr Cys Thr Ile Gly Gly Ser
385 390 395 400

Leu Ser Val Ser Ser Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly
405 410 415

Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly
420 425 430

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Ser Gly Gly Pro
435 440 445

Gly Pro Ala Gly Met Lys Gly Leu Pro Gly Ser Glu Val Gln Leu Val
450 455 460

Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Leu Arg Leu Ser
465 470 475 480

Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr Thr Leu Ala Trp Val
485 490 495

Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala Ala Ile Asp Ser
500 505 510

Ser Ser Tyr Thr Tyr Ser Pro Asp Thr Val Arg Gly Arg Phe Thr Ile
515 520 525
Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr Leu Gln Met Asn Ser Leu
530 535 540
Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Asp Ser Asn Trp
545 550 555 560
Asp Ala Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
565 570 575
Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp
580 585 590
Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp
595 600 605
Arg Val Thr Ile Thr Cys Lys Ala Ser Gln Asn Val Gly Thr Asn Val
610 615 620
Gly Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Ala Leu Ile Tyr
625 630 635 640
Ser Ala Ser Phe Arg Tyr Ser Gly Val Pro Ser Arg Phe Ser Gly Ser
645 650 655
Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu
660 665 670
Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Tyr Thr Tyr Pro Tyr Thr
675 680 685
Phe Gly Gly Gly Thr Lys Val Glu Ile Lys His His His His His His
690 695 700
Glu Pro Glu Ala
705

<210> 164
<211> 161
<212> PRT
<213> 人工序列(Artificial Sequence)
<220>
<221> 来源
<223> /注释="人工序列描述:合成多肽"
<400> 164

Met Asp Met Arg Val Pro Ala Gln Leu Leu Gly Leu Leu Leu Leu Trp
1 5 10 15
Leu Arg Gly Ala Arg Cys Ala Pro Thr Ser Ser Ser Thr Lys Lys Thr
20 25 30
Gln Leu Gln Leu Glu His Leu Leu Leu Asp Leu Gln Met Ile Leu Asn

35 40 45

Gly Ile Asn Asn Tyr Lys Asn Pro Lys Leu Thr Arg Met Leu Thr Phe
50 55 60

Lys Phe Tyr Met Pro Lys Lys Ala Thr Glu Leu Lys His Leu Gln Cys
65 70 75 80

Leu Glu Glu Glu Leu Lys Pro Leu Glu Glu Val Leu Asn Leu Ala Gln
85 90 95

Ser Lys Asn Phe His Leu Arg Pro Arg Asp Leu Ile Ser Asn Ile Asn
100 105 110

Val Ile Val Leu Glu Leu Lys Gly Ser Glu Thr Thr Phe Met Cys Glu
115 120 125

Tyr Ala Asp Glu Thr Ala Thr Ile Val Glu Phe Leu Asn Arg Trp Ile
130 135 140

Thr Phe Cys Gln Ser Ile Ile Ser Thr Leu Thr His His His His His
145 150 155 160

His

<210> 165

<211> 708

<212> PRT

<213> 人工序列(Artificial Sequence)

<220>

<221> 来源

<223> /注释="人工序列描述:合成多肽"

<400> 165

Met Asp Met Arg Val Pro Ala Gln Leu Leu Gly Leu Leu Leu Leu Trp
1 5 10 15

Leu Arg Gly Ala Arg Cys Ala Pro Thr Ser Ser Ser Thr Lys Lys Thr
20 25 30

Gln Leu Gln Leu Glu His Leu Leu Leu Asp Leu Gln Met Ile Leu Asn
35 40 45

Gly Ile Asn Asn Tyr Lys Asn Pro Lys Leu Thr Arg Met Leu Thr Phe
50 55 60

Lys Phe Tyr Met Pro Lys Lys Ala Thr Glu Leu Lys His Leu Gln Cys
65 70 75 80

Leu Glu Glu Glu Leu Lys Pro Leu Glu Glu Val Leu Asn Leu Ala Gln
85 90 95

Ser Lys Asn Phe His Leu Arg Pro Arg Asp Leu Ile Ser Asn Ile Asn
100 105 110

Val Ile Val Leu Glu Leu Lys Gly Ser Glu Thr Thr Phe Met Cys Glu

115 120 125

Tyr Ala Asp Glu Thr Ala Thr Ile Val Glu Phe Leu Asn Arg Trp Ile
130 135 140

Thr Phe Cys Gln Ser Ile Ile Ser Thr Leu Thr Ser Gly Gly Pro Gly
145 150 155 160

Pro Ala Gly Met Lys Gly Leu Pro Gly Ser Glu Val Gln Leu Val Glu
165 170 175

Ser Gly Gly Gly Leu Val Gln Pro Gly Asn Ser Leu Arg Leu Ser Cys
180 185 190

Ala Ala Ser Gly Phe Thr Phe Ser Lys Phe Gly Met Ser Trp Val Arg
195 200 205

Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ser Ser Ile Ser Gly Ser
210 215 220

Gly Arg Asp Thr Leu Tyr Ala Glu Ser Val Lys Gly Arg Phe Thr Ile
225 230 235 240

Ser Arg Asp Asn Ala Lys Thr Thr Leu Tyr Leu Gln Met Asn Ser Leu
245 250 255

Arg Pro Glu Asp Thr Ala Val Tyr Tyr Cys Thr Ile Gly Gly Ser Leu
260 265 270

Ser Val Ser Ser Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly
275 280 285

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly
290 295 300

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Ser Gly Gly Pro Gly
305 310 315 320

Pro Ala Gly Met Lys Gly Leu Pro Gly Ser Glu Val Gln Leu Val Glu
325 330 335

Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys
340 345 350

Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr Thr Leu Ala Trp Val Arg
355 360 365

Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala Ala Ile Asp Ser Ser
370 375 380

Ser Tyr Thr Tyr Ser Pro Asp Thr Val Arg Gly Arg Phe Thr Ile Ser
385 390 395 400

Arg Asp Asn Ala Lys Asn Ser Leu Tyr Leu Gln Met Asn Ser Leu Arg
405 410 415

Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Asp Ser Asn Trp Asp
420 425 430

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

<210> 166
<211> 708
<212> PRT

<213> 人工序列(Artificial Sequence)
<220>
<221> 来源
<223> /注释="人工序列描述:合成多肽"
<400> 166

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

Ile Thr Phe Cys Gln Ser Ile Ile Ser Thr Leu Thr Ser Gly Gly Pro
275 280 285
Gly Pro Ala Gly Met Lys Gly Leu Pro Gly Ser Glu Val Gln Leu Val
290 295 300
Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Asn Ser Leu Arg Leu Ser
305 310 315 320
Cys Ala Ala Ser Gly Phe Thr Phe Ser Lys Phe Gly Met Ser Trp Val
325 330 335
Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ser Ser Ile Ser Gly
340 345 350
Ser Gly Arg Asp Thr Leu Tyr Ala Glu Ser Val Lys Gly Arg Phe Thr
355 360 365
Ile Ser Arg Asp Asn Ala Lys Thr Thr Leu Tyr Leu Gln Met Asn Ser
370 375 380
Leu Arg Pro Glu Asp Thr Ala Val Tyr Tyr Cys Thr Ile Gly Gly Ser
385 390 395 400
Leu Ser Val Ser Ser Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly
405 410 415
Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly
420 425 430
Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Ser Gly Gly Pro
435 440 445
Gly Pro Ala Gly Met Lys Gly Leu Pro Gly Ser Glu Val Gln Leu Val
450 455 460
Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Leu Arg Leu Ser
465 470 475 480
Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr Thr Leu Ala Trp Val
485 490 495
Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala Ala Ile Asp Ser
500 505 510
Ser Ser Tyr Thr Tyr Ser Pro Asp Thr Val Arg Gly Arg Phe Thr Ile
515 520 525
Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr Leu Gln Met Asn Ser Leu
530 535 540
Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Asp Ser Asn Trp
545 550 555 560
Asp Ala Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
565 570 575
Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp

580 585 590
Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp
595 600 605
Arg Val Thr Ile Thr Cys Lys Ala Ser Gln Asn Val Gly Thr Asn Val
610 615 620
Gly Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Ala Leu Ile Tyr
625 630 635 640
Ser Ala Ser Phe Arg Tyr Ser Gly Val Pro Ser Arg Phe Ser Gly Ser
645 650 655
Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu
660 665 670
Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Tyr Thr Tyr Pro Tyr Thr
675 680 685
Phe Gly Gly Gly Thr Lys Val Glu Ile Lys His His His His His His
690 695 700
Glu Pro Glu Ala
705

<210> 167
<211> 708
<212> PRT
<213> 人工序列(Artificial Sequence)
<220>
<221> 来源
<223> /注释="人工序列描述:合成多肽"
<400> 167
Met Asp Met Arg Val Pro Ala Gln Leu Leu Gly Leu Leu Leu Leu Trp
1 5 10 15
Leu Arg Gly Ala Arg Cys Gln Val Gln Leu Gln Glu Ser Gly Gly Gly
20 25 30
Leu Val Gln Ala Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly
35 40 45
Arg Ile Phe Ser Ile Asp Ile Met Ser Trp Tyr Arg Gln Ala Pro Gly
50 55 60
Lys Gln Arg Glu Leu Val Ala Arg Ile Thr Arg Gly Gly Thr Ile Ser
65 70 75 80
Tyr Asp Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala
85 90 95
Lys Asn Thr Val Tyr Leu Gln Met Asn Ser Leu Lys Pro Glu Asp Thr
100 105 110

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

420 425 430

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Ser Gly Gly Pro

435 440 445

Gly Pro Ala Gly Met Lys Gly Leu Pro Gly Ser Glu Val Gln Leu Val

450 455 460

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

465 470 475 480

Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr Thr Leu Ala Trp Val

485 490 495

Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala Ala Ile Asp Ser

500 505 510

Ser Ser Tyr Thr Tyr Ser Pro Asp Thr Val Arg Gly Arg Phe Thr Ile

515 520 525

Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr Leu Gln Met Asn Ser Leu

530 535 540

Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Asp Ser Asn Trp

545 550 555 560

Asp Ala Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser

565 570 575

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp

580 585 590

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

595 600 605

Arg Val Thr Ile Thr Cys Lys Ala Ser Gln Asn Val Gly Thr Asn Val

610 615 620

Gly Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Ala Leu Ile Tyr

625 630 635 640

Ser Ala Ser Phe Arg Tyr Ser Gly Val Pro Ser Arg Phe Ser Gly Ser

645 650 655

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

660 665 670

Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Tyr Thr Tyr Pro Tyr Thr

675 680 685

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys His His His His His His

690 695 700

Glu Pro Glu Ala

705

<210> 168

<211> 450

<212> PRT
<213> 人工序列(Artificial Sequence)
<220>
<221> 来源
<223> /注释="人工序列描述:合成多肽"
<400> 168

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

260 265 270
Arg Lys Tyr Phe His Arg Ile Thr Val Tyr Leu Arg Glu Lys Lys His
275 280 285
Ser Pro Cys Ala Trp Glu Val Val Arg Ala Glu Val Trp Arg Ala Leu
290 295 300
Ser Ser Ser Ala Asn Val Ser Gly Gly Pro Gly Pro Ala Gly Met Lys
305 310 315 320
Gly Leu Pro Gly Ser Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu
325 330 335
Val Gln Pro Gly Asn Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe
340 345 350
Thr Phe Ser Lys Phe Gly Met Ser Trp Val Arg Gln Ala Pro Gly Lys
355 360 365
Gly Leu Glu Trp Val Ser Ser Ile Ser Gly Ser Gly Arg Asp Thr Leu
370 375 380
Tyr Ala Glu Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala
385 390 395 400
Lys Thr Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Pro Glu Asp Thr
405 410 415
Ala Val Tyr Tyr Cys Thr Ile Gly Gly Ser Leu Ser Val Ser Ser Gln
420 425 430
Gly Thr Leu Val Thr Val Ser Ser His His His His His His Glu Pro
435 440 445
Glu Ala
450

<210> 169
<211> 198
<212> PRT
<213> 人工序列(Artificial Sequence)
<220>
<221> 来源
<223> /注释="人工序列描述:合成多肽"
<400> 169
Met Asp Met Arg Val Pro Ala Gln Leu Leu Gly Leu Leu Leu Leu Trp
1 5 10 15
Leu Arg Gly Ala Arg Cys Cys Asp Leu Pro Gln Thr His Asn Leu Arg
20 25 30
Asn Lys Arg Ala Leu Thr Leu Leu Val Gln Met Arg Arg Leu Ser Pro
35 40 45

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

<210> 170
<211> 328
<212> PRT
<213> 人工序列(Artificial Sequence)
<220>
<221> 来源
<223> /注释="人工序列描述:合成多肽"
<400> 170

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

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

<210> 171
<211> 328
<212> PRT
<213> 人工序列(Artificial Sequence)
<220>
<221> 来源
<223> /注释="人工序列描述:合成多肽"
<400> 171

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

305 310 315 320
His His His His Glu Pro Glu Ala
325

<210> 172
<211> 1396
<212> PRT
<213> 人工序列(Artificial Sequence)
<220>
<221> 来源
<223> /注释="人工序列描述:合成多肽"
<400> 172

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

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

530 535 540

Ile Lys Lys Gln Thr Ala Leu Ala Glu Leu Val Lys His Lys Pro Lys
545 550 555 560

Ala Thr Ala Glu Gln Leu Lys Thr Val Met Asp Asp Phe Ala Gln Phe
565 570 575

Leu Asp Thr Cys Cys Lys Ala Ala Asp Lys Asp Thr Cys Phe Ser Thr
580 585 590

Glu Gly Pro Asn Leu Val Thr Arg Cys Lys Asp Ala Leu Ala Ser Gly
595 600 605

Gly Pro Gly Pro Ala Gly Met Lys Gly Leu Pro Gly Ser Cys Asp Leu
610 615 620

Pro Gln Thr His Asn Leu Arg Asn Lys Arg Ala Leu Thr Leu Leu Val
625 630 635 640

Gln Met Arg Arg Leu Ser Pro Leu Ser Cys Leu Lys Asp Arg Lys Asp
645 650 655

Phe Gly Phe Pro Gln Glu Lys Val Asp Ala Gln Gln Ile Lys Lys Ala
660 665 670

Gln Ala Ile Pro Val Leu Ser Glu Leu Thr Gln Gln Ile Leu Asn Ile
675 680 685

Phe Thr Ser Lys Asp Ser Ser Ala Ala Trp Asn Thr Thr Leu Leu Asp
690 695 700

Ser Phe Cys Asn Asp Leu His Gln Gln Leu Asn Asp Leu Gln Gly Cys
705 710 715 720

Leu Met Gln Gln Val Gly Val Gln Glu Phe Pro Leu Thr Gln Glu Asp
725 730 735

Ala Leu Leu Ala Val Arg Lys Tyr Phe His Arg Ile Thr Val Tyr Leu
740 745 750

Arg Glu Lys Lys His Ser Pro Cys Ala Trp Glu Val Val Arg Ala Glu
755 760 765

Val Trp Arg Ala Leu Ser Ser Ser Ala Asn Val Leu Gly Arg Leu Arg
770 775 780

Glu Glu Lys Ser Gly Gly Pro Gly Pro Ala Gly Met Lys Gly Leu Pro
785 790 795 800

Gly Ser Glu Ala His Lys Ser Glu Ile Ala His Arg Tyr Asn Asp Leu
805 810 815

Gly Glu Gln His Phe Lys Gly Leu Val Leu Ile Ala Phe Ser Gln Tyr
820 825 830

Leu Gln Lys Cys Ser Tyr Asp Glu His Ala Lys Leu Val Gln Glu Val
835 840 845

Thr Asp Phe Ala Lys Thr Cys Val Ala Asp Glu Ser Ala Ala Asn Cys
850 855 860
Asp Lys Ser Leu His Thr Leu Phe Gly Asp Lys Leu Cys Ala Ile Pro
865 870 875 880
Asn Leu Arg Glu Asn Tyr Gly Glu Leu Ala Asp Cys Cys Thr Lys Gln
885 890 895
Glu Pro Glu Arg Asn Glu Cys Phe Leu Gln His Lys Asp Asp Asn Pro
900 905 910
Ser Leu Pro Pro Phe Glu Arg Pro Glu Ala Glu Ala Met Cys Thr Ser
915 920 925
Phe Lys Glu Asn Pro Thr Thr Phe Met Gly His Tyr Leu His Glu Val
930 935 940
Ala Arg Arg His Pro Tyr Phe Tyr Ala Pro Glu Leu Leu Tyr Tyr Ala
945 950 955 960
Glu Gln Tyr Asn Glu Ile Leu Thr Gln Cys Cys Ala Glu Ala Asp Lys
965 970 975
Glu Ser Cys Leu Thr Pro Lys Leu Asp Gly Val Lys Glu Lys Ala Leu
980 985 990
Val Ser Ser Val Arg Gln Arg Met Lys Cys Ser Ser Met Gln Lys Phe
995 1000 1005
Gly Glu Arg Ala Phe Lys Ala Trp Ala Val Ala Arg Leu Ser Gln
1010 1015 1020
Thr Phe Pro Asn Ala Asp Phe Ala Glu Ile Thr Lys Leu Ala Thr
1025 1030 1035
Asp Leu Thr Lys Val Asn Lys Glu Cys Cys His Gly Asp Leu Leu
1040 1045 1050
Glu Cys Ala Asp Asp Arg Ala Glu Leu Ala Lys Tyr Met Cys Glu
1055 1060 1065
Asn Gln Ala Thr Ile Ser Ser Lys Leu Gln Thr Cys Cys Asp Lys
1070 1075 1080
Pro Leu Leu Lys Lys Ala His Cys Leu Ser Glu Val Glu His Asp
1085 1090 1095
Thr Met Pro Ala Asp Leu Pro Ala Ile Ala Ala Asp Phe Val Glu
1100 1105 1110
Asp Gln Glu Val Cys Lys Asn Tyr Ala Glu Ala Lys Asp Val Phe
1115 1120 1125
Leu Gly Thr Phe Leu Tyr Glu Tyr Ser Arg Arg His Pro Asp Tyr
1130 1135 1140
Ser Val Ser Leu Leu Leu Arg Leu Ala Lys Lys Tyr Glu Ala Thr

1145 1150 1155
Leu Glu Lys Cys Cys Ala Glu Ala Asn Pro Pro Ala Cys Tyr Gly
1160 1165 1170
Thr Val Leu Ala Glu Phe Gln Pro Leu Val Glu Glu Pro Lys Asn
1175 1180 1185
Leu Val Lys Thr Asn Cys Asp Leu Tyr Glu Lys Leu Gly Glu Tyr
1190 1195 1200
Gly Phe Gln Asn Ala Ile Leu Val Arg Tyr Thr Gln Lys Ala Pro
1205 1210 1215
Gln Val Ser Thr Pro Thr Leu Val Glu Ala Ala Arg Asn Leu Gly
1220 1225 1230
Arg Val Gly Thr Lys Cys Cys Thr Leu Pro Glu Asp Gln Arg Leu
1235 1240 1245
Pro Cys Val Glu Asp Tyr Leu Ser Ala Ile Leu Asn Arg Val Cys
1250 1255 1260
Leu Leu His Glu Lys Thr Pro Val Ser Glu His Val Thr Lys Cys
1265 1270 1275
Cys Ser Gly Ser Leu Val Glu Arg Arg Pro Cys Phe Ser Ala Leu
1280 1285 1290
Thr Val Asp Glu Thr Tyr Val Pro Lys Glu Phe Lys Ala Glu Thr
1295 1300 1305
Phe Thr Phe His Ser Asp Ile Cys Thr Leu Pro Glu Lys Glu Lys
1310 1315 1320
Gln Ile Lys Lys Gln Thr Ala Leu Ala Glu Leu Val Lys His Lys
1325 1330 1335
Pro Lys Ala Thr Ala Glu Gln Leu Lys Thr Val Met Asp Asp Phe
1340 1345 1350
Ala Gln Phe Leu Asp Thr Cys Cys Lys Ala Ala Asp Lys Asp Thr
1355 1360 1365
Cys Phe Ser Thr Glu Gly Pro Asn Leu Val Thr Arg Cys Lys Asp
1370 1375 1380
Ala Leu Ala His His His His His His Glu Pro Glu Ala
1385 1390 1395

<210> 173
<211> 797
<212> PRT
<213> 人工序列(Artificial Sequence)
<220>
<221> 来源

<223> /注释="人工序列描述:合成多肽"

<400> 173

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

290 295 300

Leu Leu Lys Lys Ala His Cys Leu Ser Glu Val Glu His Asp Thr Met
305 310 315 320
Pro Ala Asp Leu Pro Ala Ile Ala Ala Asp Phe Val Glu Asp Gln Glu
325 330 335
Val Cys Lys Asn Tyr Ala Glu Ala Lys Asp Val Phe Leu Gly Thr Phe
340 345 350
Leu Tyr Glu Tyr Ser Arg Arg His Pro Asp Tyr Ser Val Ser Leu Leu
355 360 365
Leu Arg Leu Ala Lys Lys Tyr Glu Ala Thr Leu Glu Lys Cys Cys Ala
370 375 380
Glu Ala Asn Pro Pro Ala Cys Tyr Gly Thr Val Leu Ala Glu Phe Gln
385 390 395 400
Pro Leu Val Glu Glu Pro Lys Asn Leu Val Lys Thr Asn Cys Asp Leu
405 410 415
Tyr Glu Lys Leu Gly Glu Tyr Gly Phe Gln Asn Ala Ile Leu Val Arg
420 425 430
Tyr Thr Gln Lys Ala Pro Gln Val Ser Thr Pro Thr Leu Val Glu Ala
435 440 445
Ala Arg Asn Leu Gly Arg Val Gly Thr Lys Cys Cys Thr Leu Pro Glu
450 455 460
Asp Gln Arg Leu Pro Cys Val Glu Asp Tyr Leu Ser Ala Ile Leu Asn
465 470 475 480
Arg Val Cys Leu Leu His Glu Lys Thr Pro Val Ser Glu His Val Thr
485 490 495
Lys Cys Cys Ser Gly Ser Leu Val Glu Arg Arg Pro Cys Phe Ser Ala
500 505 510
Leu Thr Val Asp Glu Thr Tyr Val Pro Lys Glu Phe Lys Ala Glu Thr
515 520 525
Phe Thr Phe His Ser Asp Ile Cys Thr Leu Pro Glu Lys Glu Lys Gln
530 535 540
Ile Lys Lys Gln Thr Ala Leu Ala Glu Leu Val Lys His Lys Pro Lys
545 550 555 560
Ala Thr Ala Glu Gln Leu Lys Thr Val Met Asp Asp Phe Ala Gln Phe
565 570 575
Leu Asp Thr Cys Cys Lys Ala Ala Asp Lys Asp Thr Cys Phe Ser Thr
580 585 590
Glu Gly Pro Asn Leu Val Thr Arg Cys Lys Asp Ala Leu Ala Ser Gly
595 600 605

Gly Pro Gly Pro Ala Gly Met Lys Gly Leu Pro Gly Ser Cys Asp Leu
610 615 620
Pro Gln Thr His Asn Leu Arg Asn Lys Arg Ala Leu Thr Leu Leu Val
625 630 635 640
Gln Met Arg Arg Leu Ser Pro Leu Ser Cys Leu Lys Asp Arg Lys Asp
645 650 655
Phe Gly Phe Pro Gln Glu Lys Val Asp Ala Gln Gln Ile Lys Lys Ala
660 665 670
Gln Ala Ile Pro Val Leu Ser Glu Leu Thr Gln Gln Ile Leu Asn Ile
675 680 685
Phe Thr Ser Lys Asp Ser Ser Ala Ala Trp Asn Thr Thr Leu Leu Asp
690 695 700
Ser Phe Cys Asn Asp Leu His Gln Gln Leu Asn Asp Leu Gln Gly Cys
705 710 715 720
Leu Met Gln Gln Val Gly Val Gln Glu Phe Pro Leu Thr Gln Glu Asp
725 730 735
Ala Leu Leu Ala Val Arg Lys Tyr Phe His Arg Ile Thr Val Tyr Leu
740 745 750
Arg Glu Lys Lys His Ser Pro Cys Ala Trp Glu Val Val Arg Ala Glu
755 760 765
Val Trp Arg Ala Leu Ser Ser Ser Ala Asn Val Leu Gly Arg Leu Arg
770 775 780
Glu Glu Lys His His His His His His Glu Pro Glu Ala
785 790 795

<210> 174
<211> 797
<212> PRT
<213> 人工序列(Artificial Sequence)
<220>
<221> 来源
<223> /注释="人工序列描述:合成多肽"
<400> 174

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

50 55 60

Val Asp Ala Gln Gln Ile Lys Lys Ala Gln Ala Ile Pro Val Leu Ser
65 70 75 80

Glu Leu Thr Gln Gln Ile Leu Asn Ile Phe Thr Ser Lys Asp Ser Ser
85 90 95

Ala Ala Trp Asn Thr Thr Leu Leu Asp Ser Phe Cys Asn Asp Leu His
100 105 110

Gln Gln Leu Asn Asp Leu Gln Gly Cys Leu Met Gln Gln Val Gly Val
115 120 125

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

Tyr Phe His Arg Ile Thr Val Tyr Leu Arg Glu Lys Lys His Ser Pro
145 150 155 160

Cys Ala Trp Glu Val Val Arg Ala Glu Val Trp Arg Ala Leu Ser Ser
165 170 175

Ser Ala Asn Val Leu Gly Arg Leu Arg Glu Glu Lys Ser Gly Gly Pro
180 185 190

Gly Pro Ala Gly Met Lys Gly Leu Pro Gly Ser Glu Ala His Lys Ser
195 200 205

Glu Ile Ala His Arg Tyr Asn Asp Leu Gly Glu Gln His Phe Lys Gly
210 215 220

Leu Val Leu Ile Ala Phe Ser Gln Tyr Leu Gln Lys Cys Ser Tyr Asp
225 230 235 240

Glu His Ala Lys Leu Val Gln Glu Val Thr Asp Phe Ala Lys Thr Cys
245 250 255

Val Ala Asp Glu Ser Ala Ala Asn Cys Asp Lys Ser Leu His Thr Leu
260 265 270

Phe Gly Asp Lys Leu Cys Ala Ile Pro Asn Leu Arg Glu Asn Tyr Gly
275 280 285

Glu Leu Ala Asp Cys Cys Thr Lys Gln Glu Pro Glu Arg Asn Glu Cys
290 295 300

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

Pro Glu Ala Glu Ala Met Cys Thr Ser Phe Lys Glu Asn Pro Thr Thr
325 330 335

Phe Met Gly His Tyr Leu His Glu Val Ala Arg Arg His Pro Tyr Phe
340 345 350

Tyr Ala Pro Glu Leu Leu Tyr Tyr Ala Glu Gln Tyr Asn Glu Ile Leu
355 360 365

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

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

<210> 175
<211> 587
<212> PRT
<213> 人工序列(Artificial Sequence)
<220>
<221> 来源
<223> /注释="人工序列描述:合成多肽"
<400> 175
Met Asp Met Arg Val Pro Ala Gln Leu Leu Gly Leu Leu Leu Leu Trp
1 5 10 15
Leu Arg Gly Ala Arg Cys Gln Val Gln Leu Gln Glu Ser Gly Gly Gly
20 25 30
Leu Ala Gln Ala Gly Gly Ser Leu Ser Leu Ser Cys Ala Ala Ser Gly
35 40 45
Phe Thr Val Ser Asn Ser Val Met Ala Trp Tyr Arg Gln Thr Pro Gly
50 55 60
Lys Gln Arg Glu Phe Val Ala Ile Ile Asn Ser Val Gly Ser Thr Asn
65 70 75 80
Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala
85 90 95
Lys Asn Thr Val Tyr Leu Gln Met Asn Asn Leu Lys Pro Glu Asp Thr
100 105 110
Ala Val Tyr Val Cys Asn Arg Asn Phe Asp Arg Ile Tyr Trp Gly Gln
115 120 125

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

435 440 445

Gly Gly Pro Gly Pro Ala Gly Met Lys Gly Leu Pro Gly Ser Glu Val
450 455 460

Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Asn Ser Leu
465 470 475 480

Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Lys Phe Gly Met
485 490 495

Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ser Ser
500 505 510

Ile Ser Gly Ser Gly Arg Asp Thr Leu Tyr Ala Glu Ser Val Lys Gly
515 520 525

Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Thr Thr Leu Tyr Leu Gln
530 535 540

Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Val Tyr Tyr Cys Thr Ile
545 550 555 560

Gly Gly Ser Leu Ser Val Ser Ser Gln Gly Thr Leu Val Thr Val Ser
565 570 575

Ser His His His His His His Glu Pro Glu Ala
580 585

<210> 176
<211> 587
<212> PRT
<213> 人工序列(Artificial Sequence)
<220>
<221> 来源
<223> /注释="人工序列描述:合成多肽"
<400> 176

Met Asp Met Arg Val Pro Ala Gln Leu Leu Gly Leu Leu Leu Leu Trp
1 5 10 15

Leu Arg Gly Ala Arg Cys Glu Val Gln Leu Val Glu Ser Gly Gly Gly
20 25 30

Leu Val Gln Pro Gly Asn Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly
35 40 45

Phe Thr Phe Ser Lys Phe Gly Met Ser Trp Val Arg Gln Ala Pro Gly
50 55 60

Lys Gly Leu Glu Trp Val Ser Ser Ile Ser Gly Ser Gly Arg Asp Thr
65 70 75 80

Leu Tyr Ala Glu Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn
85 90 95

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

405 410 415
Asn Ser Leu Arg Pro Glu Asp Thr Ala Val Tyr Tyr Cys Thr Ile Gly
420 425 430
Gly Ser Leu Ser Val Ser Ser Gln Gly Thr Leu Val Thr Val Ser Ser
435 440 445
Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln
450 455 460
Val Gln Leu Gln Glu Ser Gly Gly Gly Leu Ala Gln Ala Gly Gly Ser
465 470 475 480
Leu Ser Leu Ser Cys Ala Ala Ser Gly Phe Thr Val Ser Asn Ser Val
485 490 495
Met Ala Trp Tyr Arg Gln Thr Pro Gly Lys Gln Arg Glu Phe Val Ala
500 505 510
Ile Ile Asn Ser Val Gly Ser Thr Asn Tyr Ala Asp Ser Val Lys Gly
515 520 525
Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Thr Val Tyr Leu Gln
530 535 540
Met Asn Asn Leu Lys Pro Glu Asp Thr Ala Val Tyr Val Cys Asn Arg
545 550 555 560
Asn Phe Asp Arg Ile Tyr Trp Gly Gln Gly Thr Gln Val Thr Val Ser
565 570 575
Ser His His His His His His Glu Pro Glu Ala
580 585

<210> 177
<211> 458
<212> PRT
<213> 人工序列(Artificial Sequence)
<220>
<221> 来源
<223> /注释="人工序列描述:合成多肽"
<400> 177
Met Asp Met Arg Val Pro Ala Gln Leu Leu Gly Leu Leu Leu Leu Trp
1 5 10 15
Leu Arg Gly Ala Arg Cys Glu Val Gln Leu Val Glu Ser Gly Gly Gly
20 25 30
Leu Val Gln Pro Gly Asn Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly
35 40 45
Phe Thr Phe Ser Lys Phe Gly Met Ser Trp Val Arg Gln Ala Pro Gly
50 55 60

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

370 375 380
Ser Gly Ser Gly Arg Asp Thr Leu Tyr Ala Glu Ser Val Lys Gly Arg
385 390 395 400
Phe Thr Ile Ser Arg Asp Asn Ala Lys Thr Thr Leu Tyr Leu Gln Met
405 410 415
Asn Ser Leu Arg Pro Glu Asp Thr Ala Val Tyr Tyr Cys Thr Ile Gly
420 425 430
Gly Ser Leu Ser Val Ser Ser Gln Gly Thr Leu Val Thr Val Ser Ser
435 440 445
His His His His His His Glu Pro Glu Ala
450 455

<210> 178
<211> 579
<212> PRT
<213> 人工序列(Artificial Sequence)
<220>
<221> 来源
<223> /注释="人工序列描述:合成多肽"
<400> 178
Met Asp Met Arg Val Pro Ala Gln Leu Leu Gly Leu Leu Leu Leu Trp
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Leu Arg Gly Ala Arg Cys Ala Pro Thr Ser Ser Ser Thr Lys Lys Thr
20 25 30
Gln Leu Gln Leu Glu His Leu Leu Leu Asp Leu Gln Met Ile Leu Asn
35 40 45
Gly Ile Asn Asn Tyr Lys Asn Pro Lys Leu Thr Arg Met Leu Thr Phe
50 55 60
Lys Phe Tyr Met Pro Lys Lys Ala Thr Glu Leu Lys His Leu Gln Cys
65 70 75 80
Leu Glu Glu Glu Leu Lys Pro Leu Glu Glu Val Leu Asn Leu Ala Gln
85 90 95
Ser Lys Asn Phe His Leu Arg Pro Arg Asp Leu Ile Ser Asn Ile Asn
100 105 110
Val Ile Val Leu Glu Leu Lys Gly Ser Glu Thr Thr Phe Met Cys Glu
115 120 125
Tyr Ala Asp Glu Thr Ala Thr Ile Val Glu Phe Leu Asn Arg Trp Ile
130 135 140
Thr Phe Cys Gln Ser Ile Ile Ser Thr Leu Thr Ser Gly Gly Pro Gly
145 150 155 160

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

465 470 475 480
Val Thr Ile Thr Cys Lys Ala Ser Gln Asn Val Gly Thr Asn Val Gly
485 490 495
Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Ala Leu Ile Tyr Ser
500 505 510
Ala Ser Phe Arg Tyr Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly
515 520 525
Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp
530 535 540
Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Tyr Thr Tyr Pro Tyr Thr Phe
545 550 555 560
Gly Gly Gly Thr Lys Val Glu Ile Lys His His His His His His Glu
565 570 575
Pro Glu Ala

<210> 179
<211> 579
<212> PRT
<213> 人工序列(Artificial Sequence)
<220>
<221> 来源
<223> /注释="人工序列描述:合成多肽"
<400> 179
Met Asp Met Arg Val Pro Ala Gln Leu Leu Gly Leu Leu Leu Leu Trp
1 5 10 15
Leu Arg Gly Ala Arg Cys Ala Pro Thr Ser Ser Ser Thr Lys Lys Thr
20 25 30
Gln Leu Gln Leu Glu His Leu Leu Leu Asp Leu Gln Met Ile Leu Asn
35 40 45
Gly Ile Asn Asn Tyr Lys Asn Pro Lys Leu Thr Arg Met Leu Thr Phe
50 55 60
Lys Phe Tyr Met Pro Lys Lys Ala Thr Glu Leu Lys His Leu Gln Cys
65 70 75 80
Leu Glu Glu Glu Leu Lys Pro Leu Glu Glu Val Leu Asn Leu Ala Gln
85 90 95
Ser Lys Asn Phe His Leu Arg Pro Arg Asp Leu Ile Ser Asn Ile Asn
100 105 110
Val Ile Val Leu Glu Leu Lys Gly Ser Glu Thr Thr Phe Met Cys Glu
115 120 125
Tyr Ala Asp Glu Thr Ala Thr Ile Val Glu Phe Leu Asn Arg Trp Ile

130 135 140
Thr Phe Cys Gln Ser Ile Ile Ser Thr Leu Thr Ser Gly Gly Pro Pro
145 150 155 160
Gly Gly Pro Ala Gly Ile Gly Pro Gly Ser Glu Val Gln Leu Val Glu
165 170 175
Ser Gly Gly Gly Leu Val Gln Pro Gly Asn Ser Leu Arg Leu Ser Cys
180 185 190
Ala Ala Ser Gly Phe Thr Phe Ser Lys Phe Gly Met Ser Trp Val Arg
195 200 205
Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ser Ser Ile Ser Gly Ser
210 215 220
Gly Arg Asp Thr Leu Tyr Ala Glu Ser Val Lys Gly Arg Phe Thr Ile
225 230 235 240
Ser Arg Asp Asn Ala Lys Thr Thr Leu Tyr Leu Gln Met Asn Ser Leu
245 250 255
Arg Pro Glu Asp Thr Ala Val Tyr Tyr Cys Thr Ile Gly Gly Ser Leu
260 265 270
Ser Val Ser Ser Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly
275 280 285
Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly
290 295 300
Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Ser Gly Gly Pro Pro
305 310 315 320
Gly Gly Pro Ala Gly Ile Gly Pro Gly Ser Glu Val Gln Leu Val Glu
325 330 335
Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys
340 345 350
Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr Thr Leu Ala Trp Val Arg
355 360 365
Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala Ala Ile Asp Ser Ser
370 375 380
Ser Tyr Thr Tyr Ser Pro Asp Thr Val Arg Gly Arg Phe Thr Ile Ser
385 390 395 400
Arg Asp Asn Ala Lys Asn Ser Leu Tyr Leu Gln Met Asn Ser Leu Arg
405 410 415
Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Asp Ser Asn Trp Asp
420 425 430
Ala Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly
435 440 445

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile
450 455 460
Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg
465 470 475 480
Val Thr Ile Thr Cys Lys Ala Ser Gln Asn Val Gly Thr Asn Val Gly
485 490 495
Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Ala Leu Ile Tyr Ser
500 505 510
Ala Ser Phe Arg Tyr Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly
515 520 525
Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp
530 535 540
Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Tyr Thr Tyr Pro Tyr Thr Phe
545 550 555 560
Gly Gly Gly Thr Lys Val Glu Ile Lys His His His His His His Glu
565 570 575
Pro Glu Ala

<210> 180
<211> 579
<212> PRT
<213> 人工序列(Artificial Sequence)
<220>
<221> 来源
<223> /注释="人工序列描述:合成多肽"
<400> 180
Met Asp Met Arg Val Pro Ala Gln Leu Leu Gly Leu Leu Leu Leu Trp
1 5 10 15
Leu Arg Gly Ala Arg Cys Ala Pro Thr Ser Ser Ser Thr Lys Lys Thr
20 25 30
Gln Leu Gln Leu Glu His Leu Leu Leu Asp Leu Gln Met Ile Leu Asn
35 40 45
Gly Ile Asn Asn Tyr Lys Asn Pro Lys Leu Thr Arg Met Leu Thr Phe
50 55 60
Lys Phe Tyr Met Pro Lys Lys Ala Thr Glu Leu Lys His Leu Gln Cys
65 70 75 80
Leu Glu Glu Glu Leu Lys Pro Leu Glu Glu Val Leu Asn Leu Ala Gln
85 90 95
Ser Lys Asn Phe His Leu Arg Pro Arg Asp Leu Ile Ser Asn Ile Asn
100 105 110

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

420 425 430

Ala Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly

435 440 445

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile

450 455 460

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

465 470 475 480

Val Thr Ile Thr Cys Lys Ala Ser Gln Asn Val Gly Thr Asn Val Gly

485 490 495

Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Ala Leu Ile Tyr Ser

500 505 510

Ala Ser Phe Arg Tyr Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly

515 520 525

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

530 535 540

Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Tyr Thr Tyr Pro Tyr Thr Phe

545 550 555 560

Gly Gly Gly Thr Lys Val Glu Ile Lys His His His His His His Glu

565 570 575

Pro Glu Ala

<210> 181

<211> 581

<212> PRT

<213> 人工序列(Artificial Sequence)

<220>

<221> 来源

<223> /注释="人工序列描述:合成多肽"

<400> 181

Met Asp Met Arg Val Pro Ala Gln Leu Leu Gly Leu Leu Leu Leu Trp

1 5 10 15

Leu Arg Gly Ala Arg Cys Ala Pro Thr Ser Ser Ser Thr Lys Lys Thr

20 25 30

Gln Leu Gln Leu Glu His Leu Leu Leu Asp Leu Gln Met Ile Leu Asn

35 40 45

Gly Ile Asn Asn Tyr Lys Asn Pro Lys Leu Thr Arg Met Leu Thr Phe

50 55 60

Lys Phe Tyr Met Pro Lys Lys Ala Thr Glu Leu Lys His Leu Gln Cys

65 70 75 80

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

85 90 95

Ser Lys Asn Phe His Leu Arg Pro Arg Asp Leu Ile Ser Asn Ile Asn
100 105 110

Val Ile Val Leu Glu Leu Lys Gly Ser Glu Thr Thr Phe Met Cys Glu
115 120 125

Tyr Ala Asp Glu Thr Ala Thr Ile Val Glu Phe Leu Asn Arg Trp Ile
130 135 140

Thr Phe Cys Gln Ser Ile Ile Ser Thr Leu Thr Ser Gly Gly Pro Pro
145 150 155 160

Leu Ala Gln Lys Leu Lys Ser Ser Pro Gly Ser Glu Val Gln Leu Val
165 170 175

Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Asn Ser Leu Arg Leu Ser
180 185 190

Cys Ala Ala Ser Gly Phe Thr Phe Ser Lys Phe Gly Met Ser Trp Val
195 200 205

Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ser Ser Ile Ser Gly
210 215 220

Ser Gly Arg Asp Thr Leu Tyr Ala Glu Ser Val Lys Gly Arg Phe Thr
225 230 235 240

Ile Ser Arg Asp Asn Ala Lys Thr Thr Leu Tyr Leu Gln Met Asn Ser
245 250 255

Leu Arg Pro Glu Asp Thr Ala Val Tyr Tyr Cys Thr Ile Gly Gly Ser
260 265 270

Leu Ser Val Ser Ser Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly
275 280 285

Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly
290 295 300

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Ser Gly Gly Pro
305 310 315 320

Pro Leu Ala Gln Lys Leu Lys Ser Ser Pro Gly Ser Glu Val Gln Leu
325 330 335

Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Leu Arg Leu
340 345 350

Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr Thr Leu Ala Trp
355 360 365

Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala Ala Ile Asp
370 375 380

Ser Ser Ser Tyr Thr Tyr Ser Pro Asp Thr Val Arg Gly Arg Phe Thr
385 390 395 400

Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr Leu Gln Met Asn Ser
405 410 415
Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Asp Ser Asn
420 425 430
Trp Asp Ala Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser
435 440 445
Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
450 455 460
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
465 470 475 480
Asp Arg Val Thr Ile Thr Cys Lys Ala Ser Gln Asn Val Gly Thr Asn
485 490 495
Val Gly Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Ala Leu Ile
500 505 510
Tyr Ser Ala Ser Phe Arg Tyr Ser Gly Val Pro Ser Arg Phe Ser Gly
515 520 525
Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
530 535 540
Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Tyr Thr Tyr Pro Tyr
545 550 555 560
Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys His His His His His
565 570 575
His Glu Pro Glu Ala
580

<210> 182
<211> 613
<212> PRT
<213> 人工序列(Artificial Sequence)
<220>
<221> 来源
<223> /注释="人工序列描述:合成多肽"
<400> 182
Met Asp Met Arg Val Pro Ala Gln Leu Leu Gly Leu Leu Leu Leu Trp
1 5 10 15
Leu Arg Gly Ala Arg Cys Ala Pro Thr Ser Ser Ser Thr Lys Lys Thr
20 25 30
Gln Leu Gln Leu Glu His Leu Leu Leu Asp Leu Gln Met Ile Leu Asn
35 40 45
Gly Ile Asn Asn Tyr Lys Asn Pro Lys Leu Thr Arg Met Leu Thr Phe

50 55 60

Lys Phe Tyr Met Pro Lys Lys Ala Thr Glu Leu Lys His Leu Gln Cys
65 70 75 80

Leu Glu Glu Glu Leu Lys Pro Leu Glu Glu Val Leu Asn Leu Ala Gln
85 90 95

Ser Lys Asn Phe His Leu Arg Pro Arg Asp Leu Ile Ser Asn Ile Asn
100 105 110

Val Ile Val Leu Glu Leu Lys Gly Ser Glu Thr Thr Phe Met Cys Glu
115 120 125

Tyr Ala Asp Glu Thr Ala Thr Ile Val Glu Phe Leu Asn Arg Trp Ile
130 135 140

Thr Phe Cys Gln Ser Ile Ile Ser Thr Leu Thr Ser Gly Gly Pro Pro
145 150 155 160

Gly Gly Pro Ala Gly Ile Gly Ala Leu Phe Lys Ser Ser Phe Pro Pro
165 170 175

Leu Ala Gln Lys Leu Lys Ser Ser Pro Gly Ser Glu Val Gln Leu Val
180 185 190

Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Asn Ser Leu Arg Leu Ser
195 200 205

Cys Ala Ala Ser Gly Phe Thr Phe Ser Lys Phe Gly Met Ser Trp Val
210 215 220

Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ser Ser Ile Ser Gly
225 230 235 240

Ser Gly Arg Asp Thr Leu Tyr Ala Glu Ser Val Lys Gly Arg Phe Thr
245 250 255

Ile Ser Arg Asp Asn Ala Lys Thr Thr Leu Tyr Leu Gln Met Asn Ser
260 265 270

Leu Arg Pro Glu Asp Thr Ala Val Tyr Tyr Cys Thr Ile Gly Gly Ser
275 280 285

Leu Ser Val Ser Ser Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly
290 295 300

Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly
305 310 315 320

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Ser Gly Gly Pro
325 330 335

Pro Gly Gly Pro Ala Gly Ile Gly Ala Leu Phe Lys Ser Ser Phe Pro
340 345 350

Pro Leu Ala Gln Lys Leu Lys Ser Ser Pro Gly Ser Glu Val Gln Leu
355 360 365

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

<210> 183
<211> 534
<212> PRT
<213> 人工序列(Artificial Sequence)
<220>
<221> 来源
<223> /注释="人工序列描述:合成多肽"

<400> 183

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

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

<210> 184
<211> 534
<212> PRT
<213> 人工序列(Artificial Sequence)
<220>
<221> 来源
<223> /注释="人工序列描述:合成多肽"
<400> 184
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Asn

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

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

<210> 185
<211> 398
<212> PRT
<213> 人工序列(Artificial Sequence)
<220>
<221> 来源
<223> /注释="人工序列描述:合成多肽"
<400> 185
Val Val Gly Gly Gly Gly Thr Gln Thr Val Val Thr Gln Glu Pro Ser
1 5 10 15
Leu Thr Val Ser Pro Gly Gly Thr Val Thr Leu Thr Cys Ala Ser Ser

20 25 30

Thr Gly Ala Val Thr Ser Gly Asn Tyr Pro Asn Trp Val Gln Gln Lys

35 40 45

Pro Gly Gln Ala Pro Arg Gly Leu Ile Gly Gly Thr Lys Phe Leu Val

50 55 60

Pro Gly Thr Pro Ala Arg Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala

65 70 75 80

Ala Leu Thr Leu Ser Gly Val Gln Pro Glu Asp Glu Ala Glu Tyr Tyr

85 90 95

Cys Thr Leu Trp Tyr Ser Asn Arg Trp Val Phe Gly Gly Gly Thr Lys

100 105 110

Leu Thr Val Leu Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly

115 120 125

Gly Gly Ser Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln

130 135 140

Pro Gly Gly Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe

145 150 155 160

Asn Lys Tyr Ala Ile Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu

165 170 175

Glu Trp Val Ala Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr

180 185 190

Tyr Ala Asp Gln Val Lys Asp Arg Phe Thr Ile Ser Arg Asp Asp Ser

195 200 205

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

210 215 220

Ala Val Tyr Tyr Cys Val Arg His Ala Asn Phe Gly Asn Ser Tyr Ile

225 230 235 240

Ser Tyr Trp Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser

245 250 255

Gly Gly Gly Gly Ser Gly Gly Gly Ser Glu Val Gln Leu Val Glu Ser

260 265 270

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

275 280 285

Ala Ser Gly Arg Thr Phe Ser Ser Tyr Ala Met Gly Trp Phe Arg Gln

290 295 300

Ala Pro Gly Lys Glu Arg Glu Phe Val Val Ala Ile Asn Trp Ala Ser

305 310 315 320

Gly Ser Thr Tyr Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser

325 330 335

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

<210> 186
<211> 518
<212> PRT
<213> 人工序列(Artificial Sequence)
<220>
<221> 来源
<223> /注释="人工序列描述:合成多肽"
<400> 186

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

180 185 190

Ile Gly Gly Thr Lys Phe Leu Val Pro Gly Thr Pro Ala Arg Phe Ser

195 200 205

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

210 215 220

Pro Glu Asp Glu Ala Glu Tyr Tyr Cys Thr Leu Trp Tyr Ser Asn Arg

225 230 235 240

Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly Gly Gly Gly

245 250 255

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Val Gln Leu Val

260 265 270

Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Leu Lys Leu Ser

275 280 285

Cys Ala Ala Ser Gly Phe Thr Phe Asn Lys Tyr Ala Ile Asn Trp Val

290 295 300

Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala Arg Ile Arg Ser

305 310 315 320

Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp Gln Val Lys Asp Arg

325 330 335

Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr Ala Tyr Leu Gln Met

340 345 350

Asn Asn Leu Lys Thr Glu Asp Thr Ala Val Tyr Tyr Cys Val Arg His

355 360 365

Ala Asn Phe Gly Asn Ser Tyr Ile Ser Tyr Trp Ala Tyr Trp Gly Gln

370 375 380

Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly

385 390 395 400

Ser Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly

405 410 415

Gly Ser Leu Thr Leu Ser Cys Ala Ala Ser Arg Phe Met Ile Ser Glu

420 425 430

Tyr His Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp

435 440 445

Val Ser Thr Ile Asn Pro Ala Gly Thr Thr Asp Tyr Ala Glu Ser Val

450 455 460

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Thr Leu Tyr

465 470 475 480

Leu Gln Met Asn Ser Leu Lys Pro Glu Asp Thr Ala Val Tyr Tyr Cys

485 490 495

Asp Ser Tyr Gly Tyr Arg Gly Gln Gly Thr Gln Val Thr Val Ser Ser
500 505 510
His His His His His His
515

<210> 187
<211> 518
<212> PRT
<213> 人工序列(Artificial Sequence)
<220>
<221> 来源
<223> /注释="人工序列描述:合成多肽"
<400> 187

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

210 215 220

Pro Glu Asp Glu Ala Glu Tyr Tyr Cys Thr Leu Trp Tyr Ser Asn Arg
225 230 235 240

Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly Gly Gly Gly
245 250 255

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Val Gln Leu Val
260 265 270

Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Leu Lys Leu Ser
275 280 285

Cys Ala Ala Ser Gly Phe Thr Phe Asn Lys Tyr Ala Ile Asn Trp Val
290 295 300

Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala Arg Ile Arg Ser
305 310 315 320

Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp Gln Val Lys Asp Arg
325 330 335

Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr Ala Tyr Leu Gln Met
340 345 350

Asn Asn Leu Lys Thr Glu Asp Thr Ala Val Tyr Tyr Cys Val Arg His
355 360 365

Ala Asn Phe Gly Asn Ser Tyr Ile Ser Tyr Trp Ala Tyr Trp Gly Gln
370 375 380

Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly
385 390 395 400

Ser Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly
405 410 415

Gly Ser Leu Thr Leu Ser Cys Ala Ala Ser Arg Phe Met Ile Ser Glu
420 425 430

Tyr His Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp
435 440 445

Val Ser Thr Ile Asn Pro Ala Gly Thr Thr Asp Tyr Ala Glu Ser Val
450 455 460

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Thr Leu Tyr
465 470 475 480

Leu Gln Met Asn Ser Leu Lys Pro Glu Asp Thr Ala Val Tyr Tyr Cys
485 490 495

Asp Ser Tyr Gly Tyr Arg Gly Gln Gly Thr Gln Val Thr Val Ser Ser
500 505 510

His His His His His His
515

<210> 188
<211> 382
<212> PRT
<213> 人工序列(Artificial Sequence)
<220>
<221> 来源
<223> /注释="人工序列描述:合成多肽"
<400> 188

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

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

<210> 189
<211> 503
<212> PRT
<213> 人工序列(Artificial Sequence)
<220>
<221> 来源
<223> /注释="人工序列描述:合成多肽"
<400> 189
Gln Val Gln Leu Val Glu Ser Gly Gly Ala Leu Val Gln Pro Gly Gly
1 5 10 15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Pro Val Asn Arg Tyr
20 25 30
Ser Met Arg Trp Tyr Arg Gln Ala Pro Gly Lys Glu Arg Glu Trp Val
35 40 45
Ala Gly Met Ser Ser Ala Gly Asp Arg Ser Ser Tyr Glu Asp Ser Val
50 55 60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ala Arg Asn Thr Val Tyr
65 70 75 80
Leu Gln Met Asn Ser Leu Lys Pro Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95
Asn Val Asn Val Gly Phe Glu Tyr Trp Gly Gln Gly Thr Gln Val Thr
100 105 110

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

420 425 430

Ala Pro Arg Gly Leu Ile Gly Gly Thr Lys Phe Leu Val Pro Gly Thr

435 440 445

Pro Ala Arg Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr

450 455 460

Leu Ser Gly Val Gln Pro Glu Asp Glu Ala Glu Tyr Tyr Cys Thr Leu

465 470 475 480

Trp Tyr Ser Asn Arg Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val

485 490 495

Leu His His His His His His

500

<210> 190

<211> 509

<212> PRT

<213> 人工序列(Artificial Sequence)

<220>

<221> 来源

<223> /注释="人工序列描述:合成多肽"

<400> 190

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Asn

1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Lys Phe

20 25 30

Gly Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val

35 40 45

Ser Ser Ile Ser Gly Ser Gly Arg Asp Thr Leu Tyr Ala Asp Ser Val

50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Thr Thr Leu Tyr

65 70 75 80

Leu Gln Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Val Tyr Tyr Cys

85 90 95

Thr Ile Gly Gly Ser Leu Ser Val Ser Ser Gln Gly Thr Leu Val Thr

100 105 110

Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Val

115 120 125

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

130 135 140

Thr Val Ser Pro Gly Gly Thr Val Thr Leu Thr Cys Ala Ser Ser Thr

145 150 155 160

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

465 470 475 480
Asp Thr Ala Val Tyr Tyr Cys Asp Ser Tyr Gly Tyr Arg Gly Gln Gly
485 490 495
Thr Gln Val Thr Val Ser Ser His His His His His His
500 505

<210> 191
<211> 267
<212> PRT
<213> 人工序列(Artificial Sequence)
<220>
<221> 来源
<223> /注释="人工序列描述:合成多肽"
<400> 191
Met Asp Met Arg Val Pro Ala Gln Leu Leu Gly Leu Leu Leu Leu Trp
1 5 10 15
Leu Arg Gly Ala Arg Cys Glu Val Gln Leu Val Glu Ser Gly Gly Gly
20 25 30
Leu Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly
35 40 45
Phe Thr Phe Ser Ser Tyr Thr Leu Ala Trp Val Arg Gln Ala Pro Gly
50 55 60
Lys Gly Leu Glu Trp Val Ala Ala Ile Asp Ser Ser Ser Tyr Thr Tyr
65 70 75 80
Ser Pro Asp Thr Val Arg Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala
85 90 95
Lys Asn Ser Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr
100 105 110
Ala Val Tyr Tyr Cys Ala Arg Asp Ser Asn Trp Asp Ala Leu Asp Tyr
115 120 125
Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser
130 135 140
Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Gln Met Thr Gln
145 150 155 160
Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr
165 170 175
Cys Lys Ala Ser Gln Asn Val Gly Thr Asn Val Gly Trp Tyr Gln Gln
180 185 190
Lys Pro Gly Lys Ala Pro Lys Ala Leu Ile Tyr Ser Ala Ser Phe Arg
195 200 205

Tyr Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp
210 215 220
Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr
225 230 235 240
Tyr Cys Gln Gln Tyr Tyr Thr Tyr Pro Tyr Thr Phe Gly Gly Gly Thr
245 250 255
Lys Val Glu Ile Lys His His His His His His
260 265

<210> 192
<211> 269
<212> PRT
<213> 人工序列(Artificial Sequence)
<220>
<221> 来源
<223> /注释="人工序列描述:合成多肽"
<400> 192
Met Asp Met Arg Val Pro Ala Gln Leu Leu Gly Leu Leu Leu Leu Trp
1 5 10 15
Leu Arg Gly Ala Arg Cys Gln Ser Val Leu Thr Gln Pro Pro Ser Val
20 25 30
Ser Gly Ala Pro Gly Gln Arg Val Thr Ile Ser Cys Ser Gly Ser Arg
35 40 45
Ser Asn Ile Gly Ser Asn Thr Val Lys Trp Tyr Gln Gln Leu Pro Gly
50 55 60
Thr Ala Pro Lys Leu Leu Ile Tyr Tyr Asn Asp Gln Arg Pro Ser Gly
65 70 75 80
Val Pro Asp Arg Phe Ser Gly Ser Lys Ser Gly Thr Ser Ala Ser Leu
85 90 95
Ala Ile Thr Gly Leu Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Gln
100 105 110
Ser Tyr Asp Arg Tyr Thr His Pro Ala Leu Leu Phe Gly Thr Gly Thr
115 120 125
Lys Val Thr Val Leu Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
130 135 140
Gly Gly Gly Ser Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val
145 150 155 160
Gln Pro Gly Arg Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr
165 170 175
Phe Ser Ser Tyr Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly

180 185 190
Leu Glu Trp Val Ala Phe Ile Arg Tyr Asp Gly Ser Asn Lys Tyr Tyr
195 200 205
Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys
210 215 220
Asn Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala
225 230 235 240
Val Tyr Tyr Cys Lys Thr His Gly Ser His Asp Asn Trp Gly Gln Gly
245 250 255
Thr Met Val Thr Val Ser Ser His His His His His His
260 265

<210> 193
<211> 5
<212> PRT
<213> 未知(Unknown)
<220>
<221> 来源
<223> /注释="未知描述：
分选酶A裂解位点"
<220>
<221> MOD_RES
<222> (3)..(3)
<223> 任何氨基酸
<400> 193
Leu Pro Xaa Thr Gly
1 5
<210> 194
<211> 124
<212> PRT
<213> 人工序列(Artificial Sequence)
<220>
<221> 来源
<223> /注释="人工序列描述:合成多肽"
<400> 194
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Asn
1 5 10 15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Lys Phe
20 25 30
Gly Met Ser Trp Val Arg Gln Gly Gly Gly Gly Gly Leu Asp Gly Asn

35 40 45

Glu Glu Pro Gly Gly Leu Glu Trp Val Ser Ser Ile Ser Gly Ser Gly
50 55 60

Arg Asp Thr Leu Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser
65 70 75 80

Arg Asp Asn Ala Lys Thr Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg
85 90 95

Pro Glu Asp Thr Ala Val Tyr Tyr Cys Thr Ile Gly Gly Ser Leu Ser
100 105 110

Val Ser Ser Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 195
<211> 25
<212> PRT
<213> 人工序列(Artificial Sequence)
<220>
<221> 来源
<223> /注释="人工序列描述:合成多肽"
<220>
<221> 位点
<222> (1)..(25)
<223> /注释="此序列可包含1-5 'Gly Gly Gly Gly Ser'重复单元"
<400> 195

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
1 5 10 15

Gly Gly Gly Ser Gly Gly Gly Gly Ser
20 25

<210> 196
<211> 20
<212> PRT
<213> 人工序列(Artificial Sequence)
<220>
<221> 来源
<223> /注释="人工序列描述:合成多肽"
<220>
<221> 位点
<222> (1)..(20)
<223> /注释="此序列可包含1-5 'Gly Gly Gly Ser'重复单元"
<400> 196

Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser
1 5 10 15
Gly Gly Gly Ser
20
<210> 197
<211> 7
<212> PRT
<213> 未知(Unknown)
<220>
<221> 来源
<223> /注释="未知描述：
蛋白酶裂解序列"
<400> 197
Gly Pro Leu Gly Val Arg Gly
1 5
<210> 198
<211> 8
<212> PRT
<213> 未知(Unknown)
<220>
<221> 来源
<223> /注释="未知描述：
蛋白酶裂解序列"
<400> 198
Ile Pro Val Ser Leu Arg Ser Gly
1 5
<210> 199
<211> 8
<212> PRT
<213> 未知(Unknown)
<220>
<221> 来源
<223> /注释="未知描述：
蛋白酶裂解序列"
<400> 199
Val Pro Leu Ser Leu Tyr Ser Gly
1 5
<210> 200
<211> 10

<212> PRT
<213> 未知(Unknown)
<220>
<221> 来源
<223> /注释="未知描述：
蛋白酶裂解序列"
<400> 200
Ser Gly Glu Ser Pro Ala Tyr Tyr Thr Ala
1 5 10
<210> 201
<211> 5
<212> PRT
<213> 人工序列(Artificial Sequence)
<220>
<221> 来源
<223> /注释="人工序列描述:合成多肽"
<400> 201
Gly Gly Gly Gly Ser
1 5
<210> 202
<211> 6
<212> PRT
<213> 人工序列(Artificial Sequence)
<220>
<221> 来源
<223> /注释="人工序列描述:合成多肽"
<400> 202
Gly Ser Gly Ser Gly Ser
1 5
<210> 203
<211> 13
<212> PRT
<213> 人工序列(Artificial Sequence)
<220>
<221> 来源
<223> /注释="人工序列描述:合成多肽"
<400> 203
Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Thr
1 5 10

<210> 204
<211> 15
<212> PRT
<213> 人工序列(Artificial Sequence)
<220>
<221> 来源
<223> /注释="人工序列描述:合成多肽"
<400> 204
Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
1 5 10 15
<210> 205
<211> 6
<212> PRT
<213> 人工序列(Artificial Sequence)
<220>
<221> 来源
<223> /注释="人工序列描述:合成6xHis标签"
<400> 205
His His His His His His
1 5

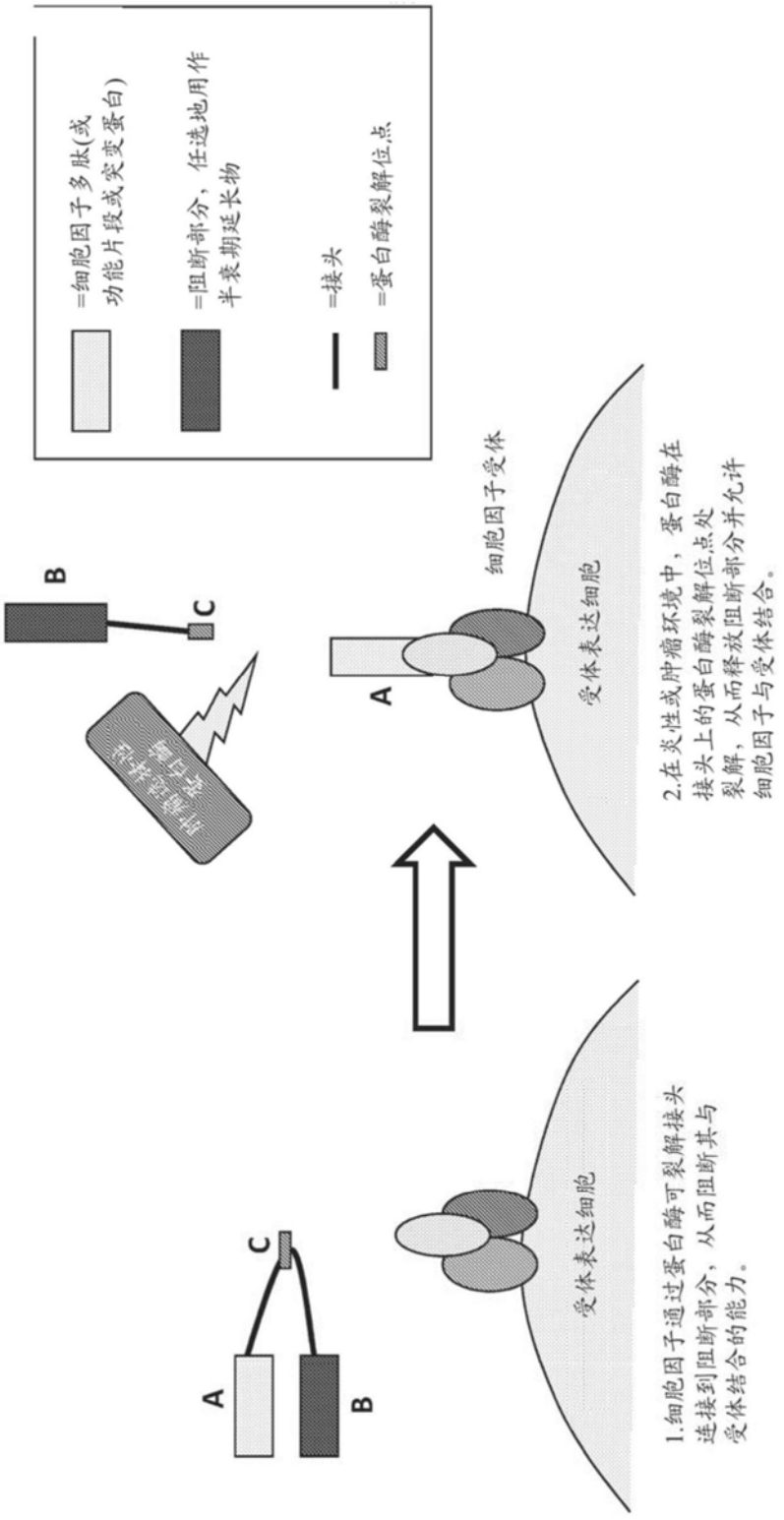

=细胞因子多肽(或
功能片段或突变蛋白)
=阻断部分，任选地用作
半衰期延长物
=接头
=蛋白酶裂解位点
A
B
C
细胞因子受体
受体表达细胞
1.细胞因子通过蛋白酶可裂解接头
连接到阻断部分，从而阻断其与
受体结合的能力。
2.在炎性或肿瘤环境中，蛋白酶在
接头上的蛋白酶裂解位点处
裂解，从而释放阻断部分并允许
细胞因子与受体结合。

图1A

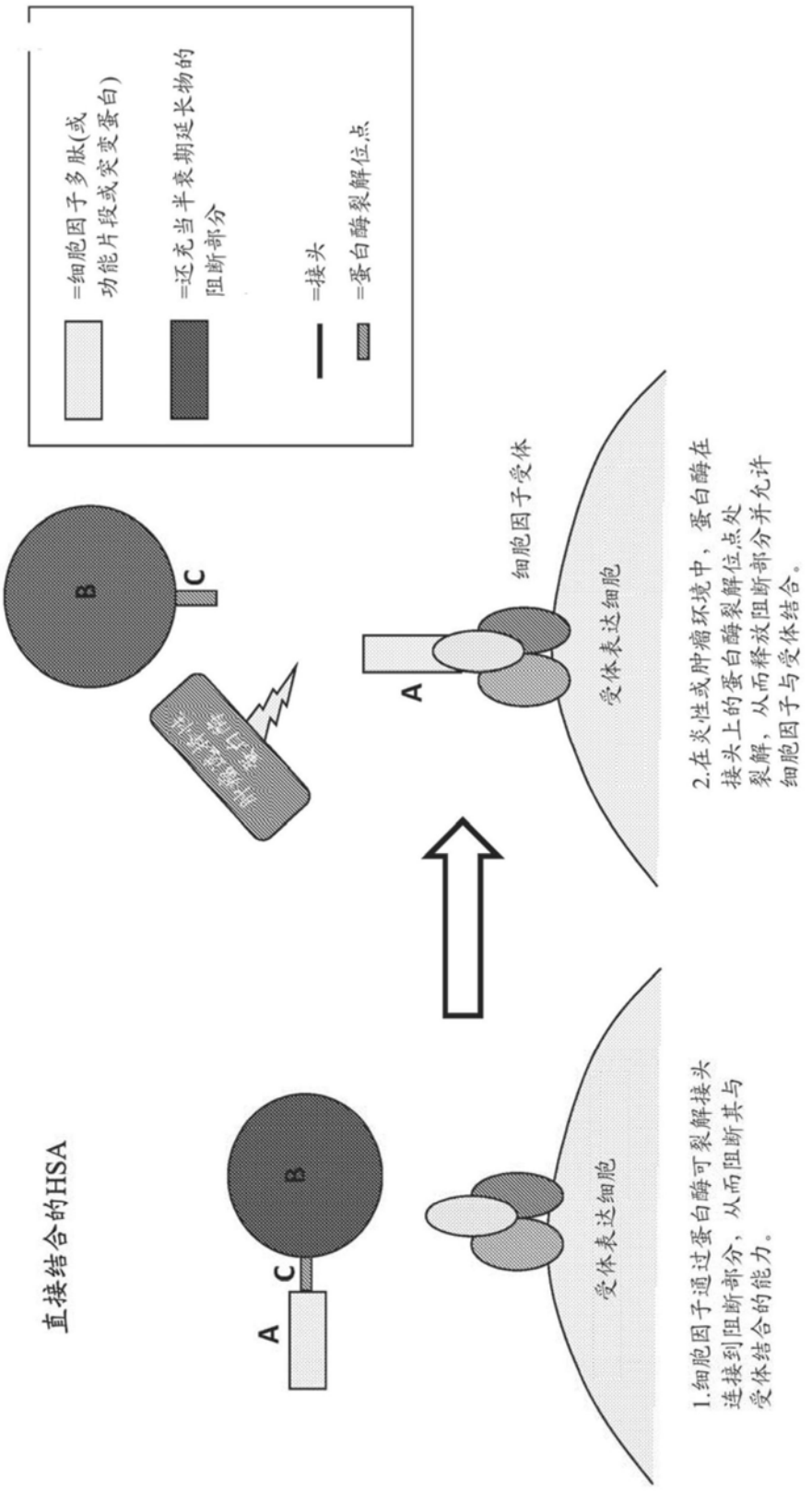

=细胞因子多肽(或
功能片段或突变蛋白)
=还充当半衰期延长物的
阻断部分
=接头
=蛋白酶裂解位点
直接结合的HSA
A
C
B
受体表达细胞
1.细胞因子通过蛋白酶可裂解接头
连接到阻断部分，从而阻断其与
受体结合的能力。
细胞因子受体
受体表达细胞
2.在炎性或肿瘤环境中，蛋白酶在
接头上的蛋白酶裂解位点处
裂解，从而释放阻断部分并允许
细胞因子与受体结合。

图1B

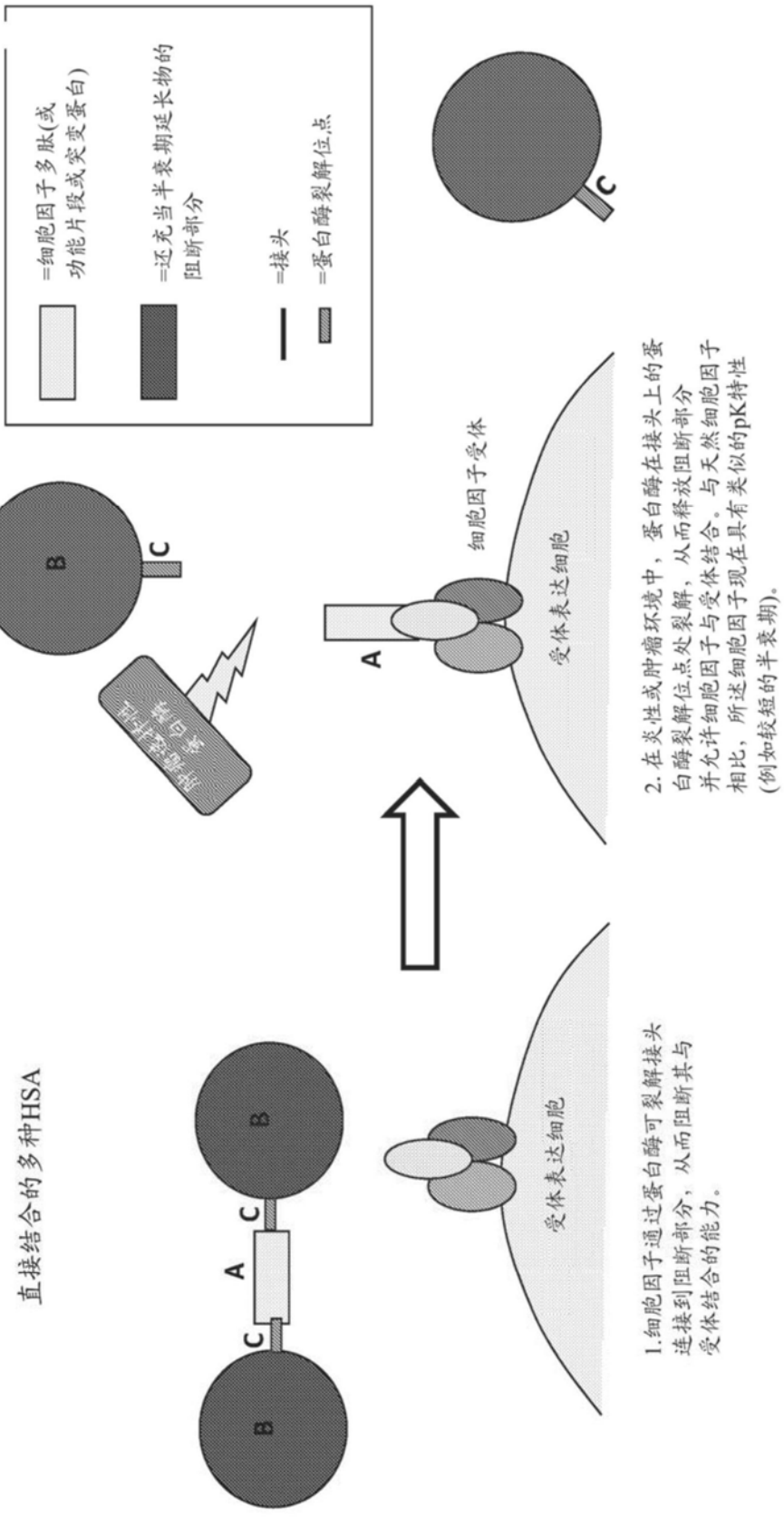

=细胞因子多肽(或
功能片段或突变蛋白)
=还充当半衰期延长物的
阻断部分
=接头
=蛋白酶裂解位点
直接结合的多种HSA
A
B
C
细胞因子受体
受体表达细胞
1.细胞因子通过蛋白酶可裂解接头
连接到阻断部分，从而阻断其与
受体结合的能力。
2.在炎性或肿瘤环境中，蛋白酶在接头上的蛋
白酶裂解位点处裂解，从而释放阻断部分
并允许细胞因子与受体结合。与天然细胞因子
相比，所述细胞因子现在具有类似的pK特性
(例如较短的半衰期)。

图1C

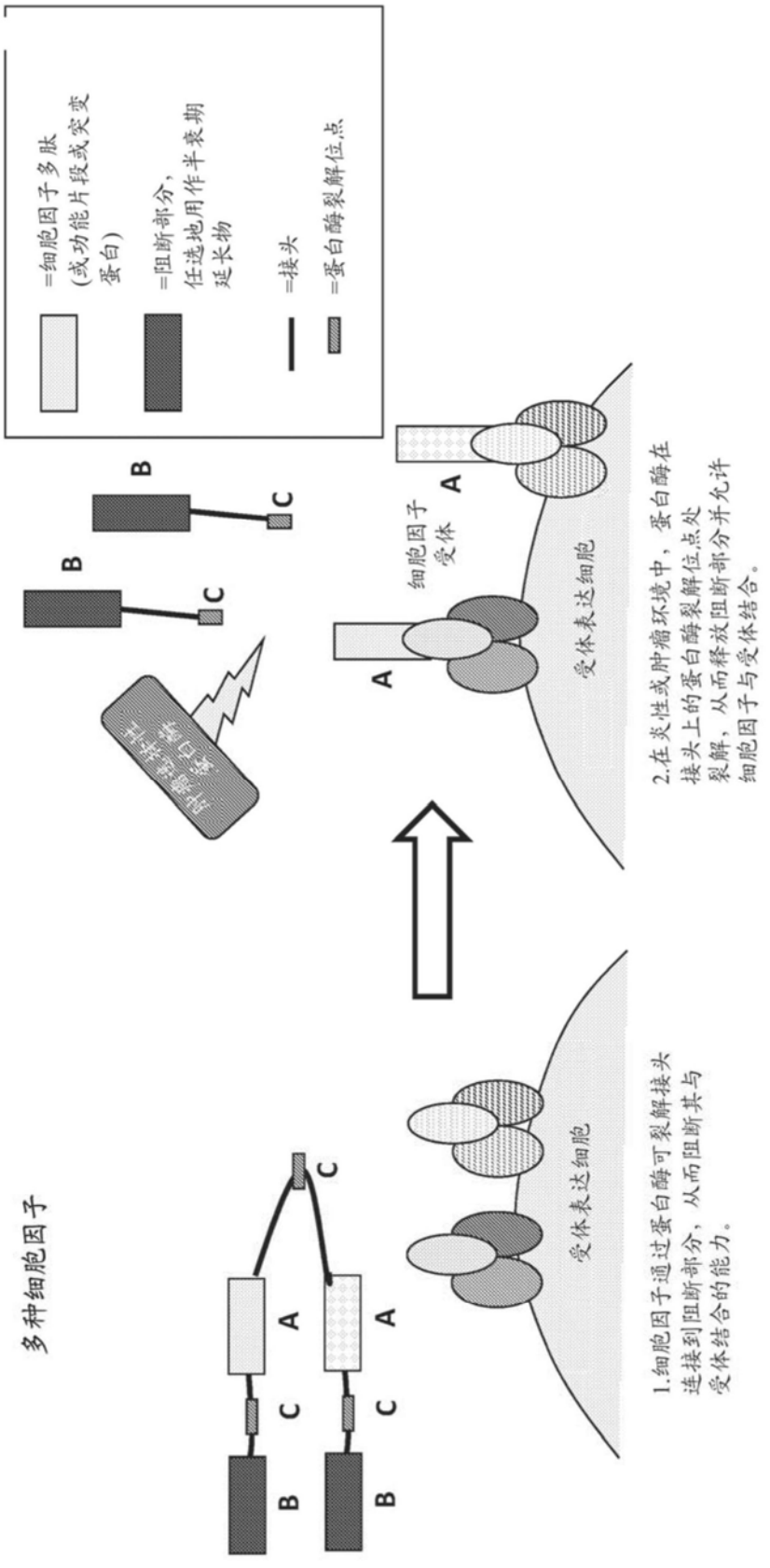

=细胞因子多肽
(或功能片段或突变
蛋白)
=阻断部分,
任选地用作半衰期
延长物
=接头
=蛋白酶裂解位点
多种细胞因子
A
B
C
受体表达细胞
细胞因子
受体
1.细胞因子通过蛋白酶可裂解接头
连接到阻断部分，从而阻断其与
受体结合的能力。
2.在炎性或肿瘤环境中，蛋白酶在
接头上的蛋白酶裂解位点处
裂解，从而释放阻断部分并允许
细胞因子与受体结合。

图1D

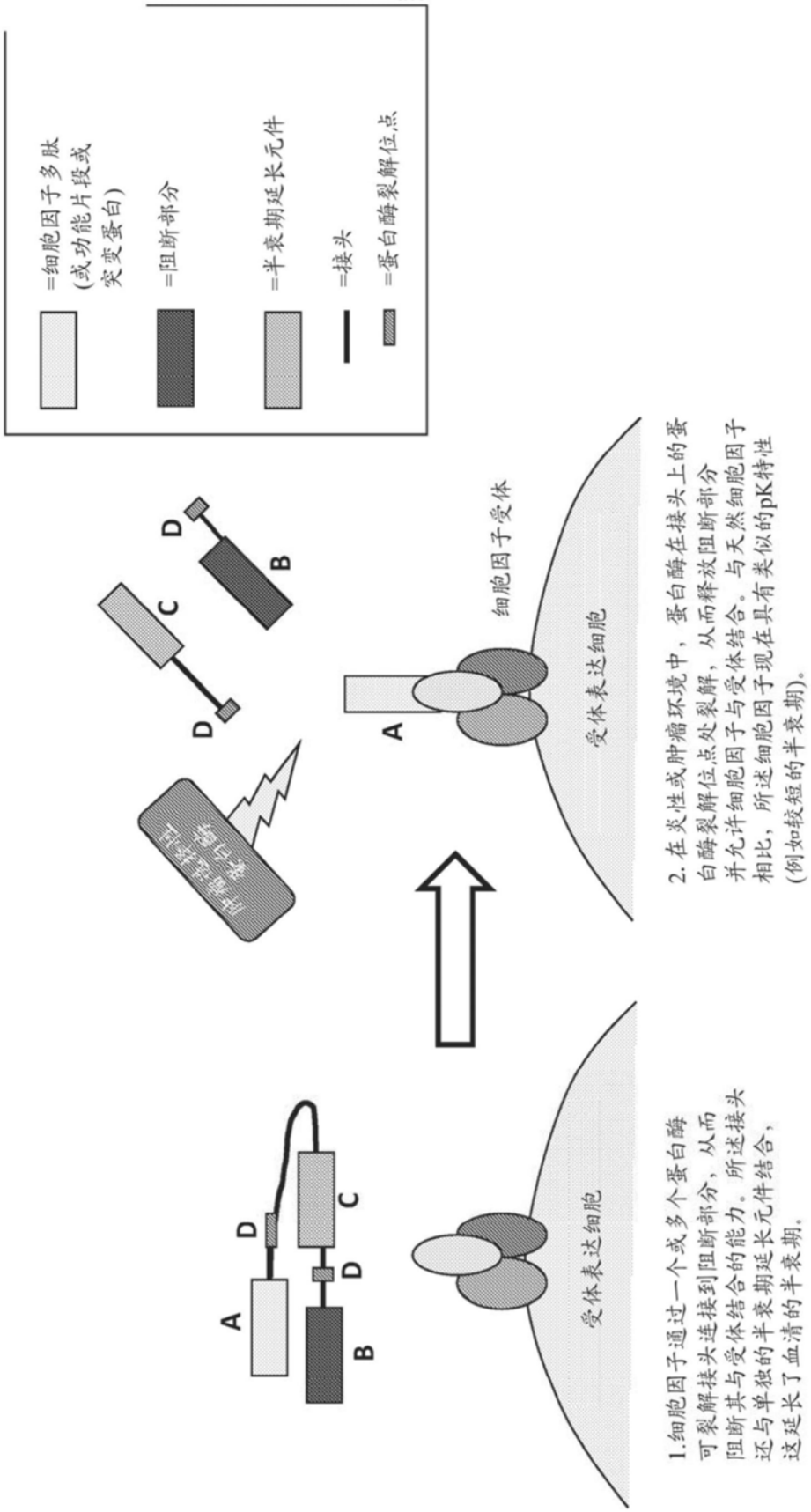

=细胞因子多肽
(或功能片段或
突变蛋白)
=阻断部分
=半衰期延长元件
=接头
=蛋白酶裂解位点
A
B
C
D
细胞因子受体
受体表达细胞
1.细胞因子通过一个或多个蛋白酶
可裂解接头连接到阻断部分，从而
阻断其与受体结合的能力。所述接头
还与单独的半衰期延长元件结合，
这延长了血清的半衰期。
2. 在炎性或肿瘤环境中，蛋白酶在接头上的蛋
白酶裂解位点处裂解，从而释放阻断部分
并允许细胞因子与受体结合。与天然细胞因子
相比，所述细胞因子现在具有类似的pK特性
(例如较短的半衰期)。

图2

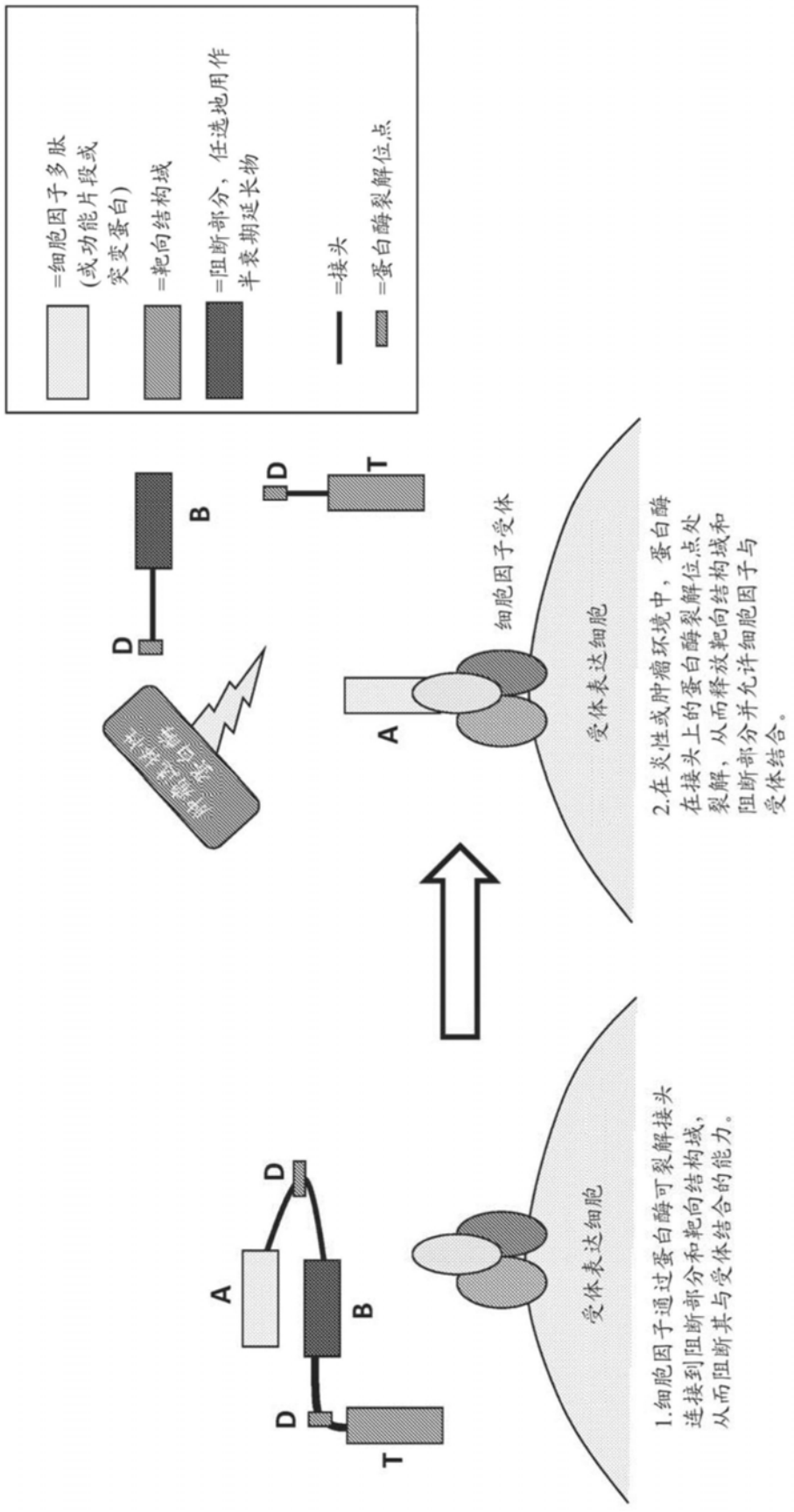

=细胞因子多肽
(或功能片段或
突变蛋白)
=靶向结构域
=阻断部分，任选地用作
半衰期延长物
=接头
=蛋白酶裂解位点
A
B
D
T
细胞因子受体
受体表达细胞
1.细胞因子通过蛋白酶可裂解接头
连接到阻断部分和靶向结构域，
从而阻断其与受体结合的能力。
2.在炎性或肿瘤环境中，蛋白酶
在接头上的蛋白酶裂解位点处
裂解，从而释放靶向结构域和
阻断部分并允许细胞因子与
受体结合。

图3

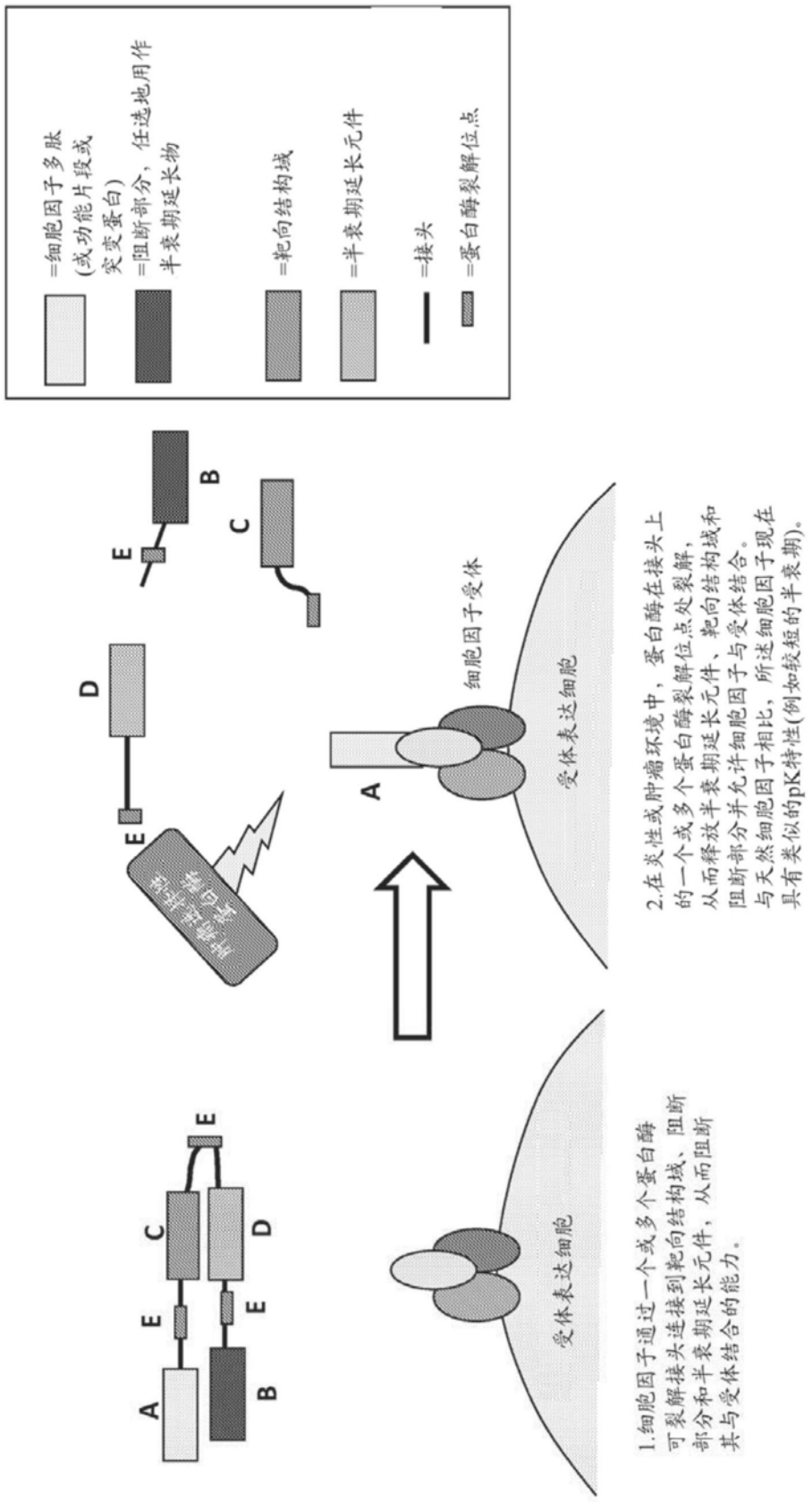

=细胞因子多肽
(或功能片段或
突变蛋白)
=阻断部分，任选地用作
半衰期延长物
=靶向结构域
=半衰期延长元件
=接头
=蛋白酶裂解位点
A
B
C
D
E
细胞因子受体
受体表达细胞
受体表达细胞
1.细胞因子通过一个或多个蛋白酶
可裂解接头连接到靶向结构域、阻断
部分和半衰期延长元件，从而阻断
其与受体结合的能力。
2.在炎性或肿瘤环境中，蛋白酶在接头上
的一个或多个蛋白酶裂解位点处裂解，
从而释放半衰期延长元件、靶向结构域和
阻断部分并允许细胞因子与受体结合。
与天然细胞因子相比，所述细胞因子现在
具有类似的pK特性(例如较短的半衰期)。

图4A

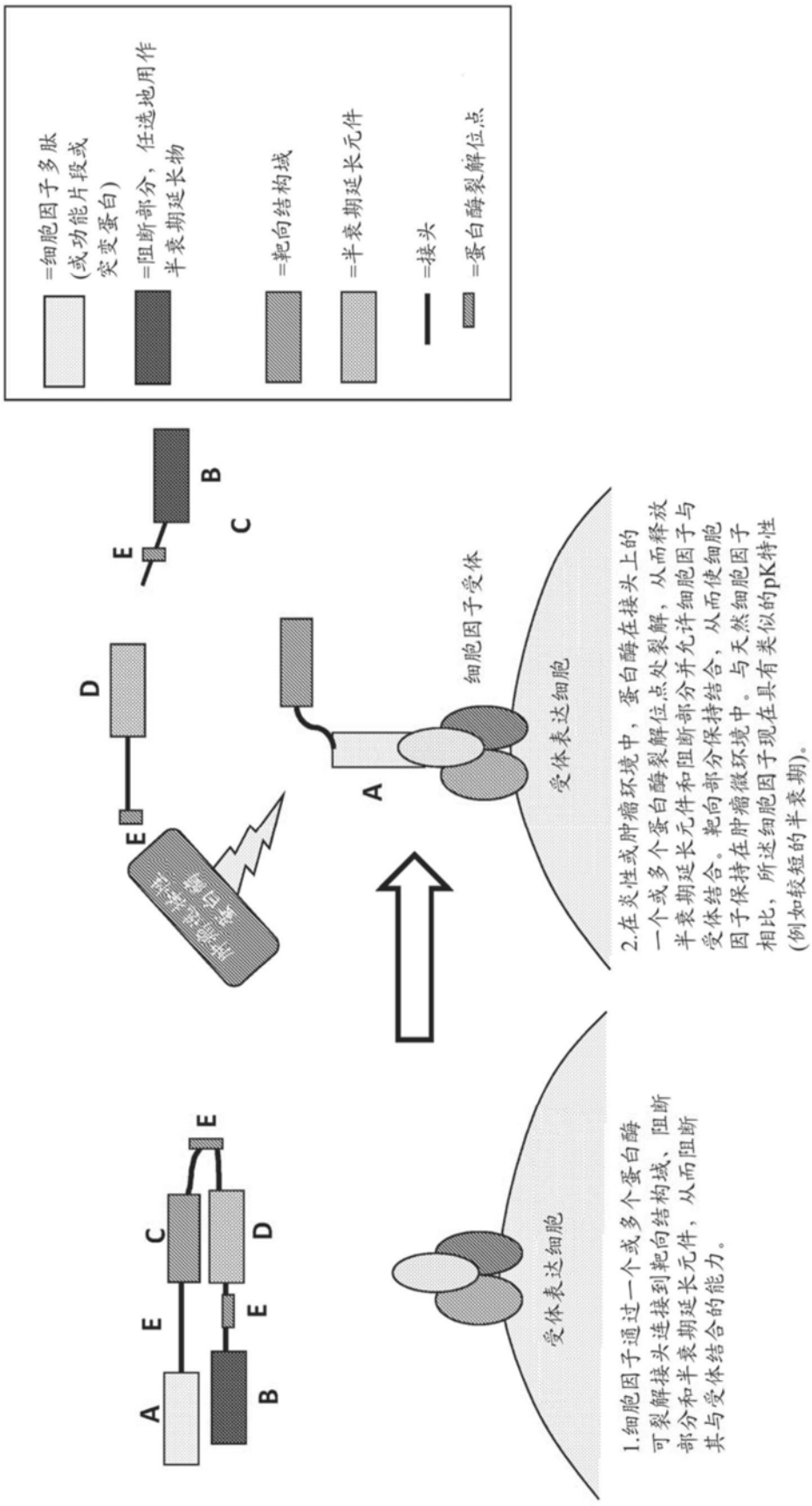

=细胞因子多肽
(或功能片段或
突变蛋白)
=阻断部分，任选地用作
半衰期延长物
=靶向结构域
=半衰期延长元件
=接头
=蛋白酶裂解位点
A
B
C
D
E
细胞因子受体
受体表达细胞
受体表达细胞
1.细胞因子通过一个或多个蛋白酶
可裂解接头连接到靶向结构域、阻断
部分和半衰期延长元件，从而阻断
其与受体结合的能力。
2.在炎性或肿瘤环境中，蛋白酶在接头上的
一个或多个蛋白酶裂解位点处裂解，从而释放
半衰期延长元件和阻断部分并允许细胞因子与
受体结合。靶向部分保持结合，从而使细胞
因子保持在肿瘤微环境中。与天然细胞因子
相比，所述细胞因子现在具有类似的pK特性
(例如较短的半衰期)。

图4B

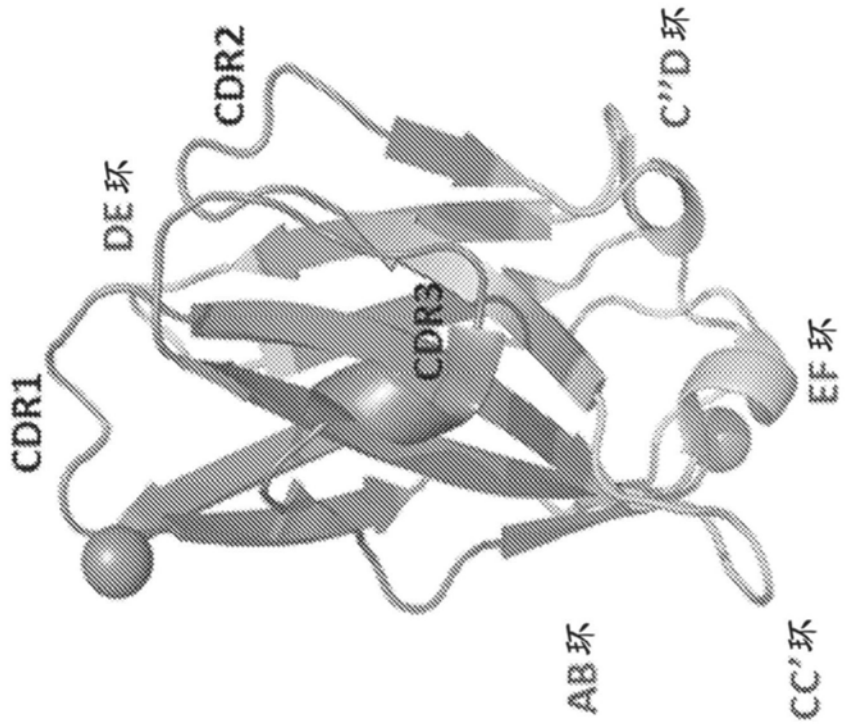


图5

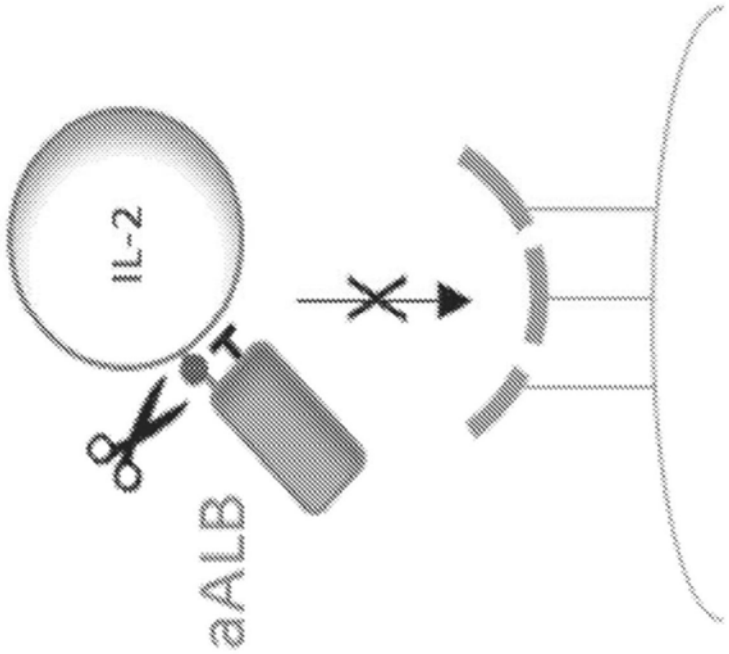


图6

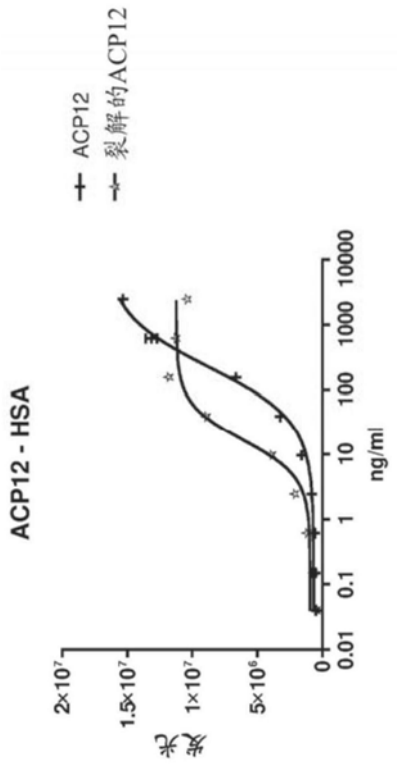

ACP12
裂解的ACP12
ACP12 - HSA
2×10^7
1.5×10^7
1×10^7
5×10^6
0
0.01
0.1
1
10
100
1000
10000
ng/ml

图7A

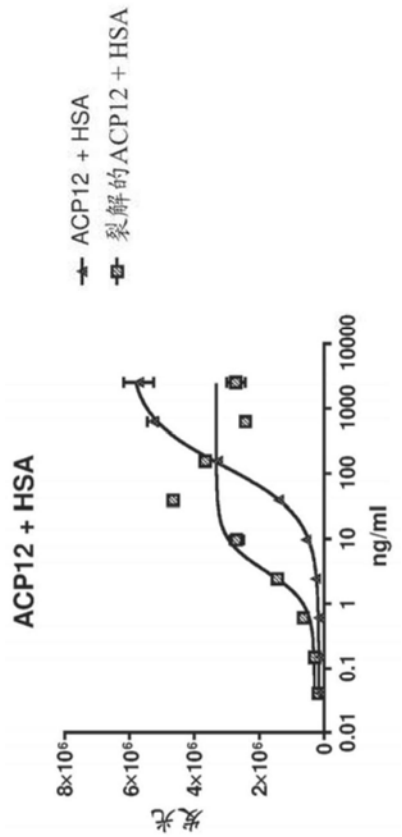

ACP12 + HSA
裂解的ACP12 + HSA
ACP12 + HSA
8×10⁶
6×10⁶
4×10⁶
2×10⁶
0
0.01
0.1
1
10
100
1000
10000
ng/ml

图7B

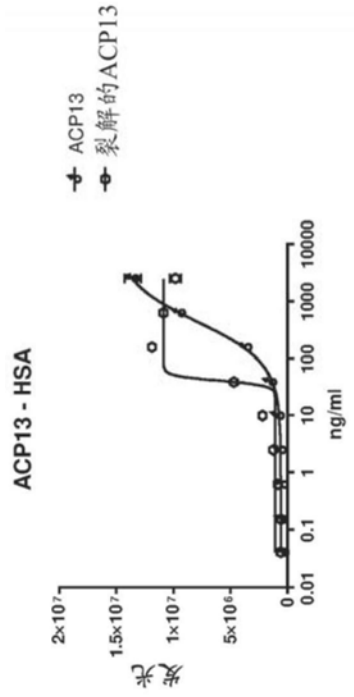

ACP13
裂解的ACP13
ACP13 - HSA
2×10⁷
1.5×10⁷
1×10⁷
5×10⁶
0
0.01
0.1
1
10
100
1000
10000
ng/ml

图7C

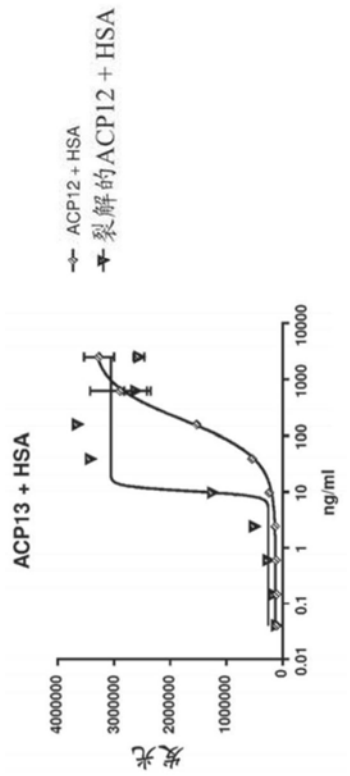

ACP12 + HSA
裂解的ACP12 + HSA
ACP13 + HSA
4000000
3000000
2000000
1000000
0
0.01
0.1
1
10
100
1000
10000
ng/ml

图7D

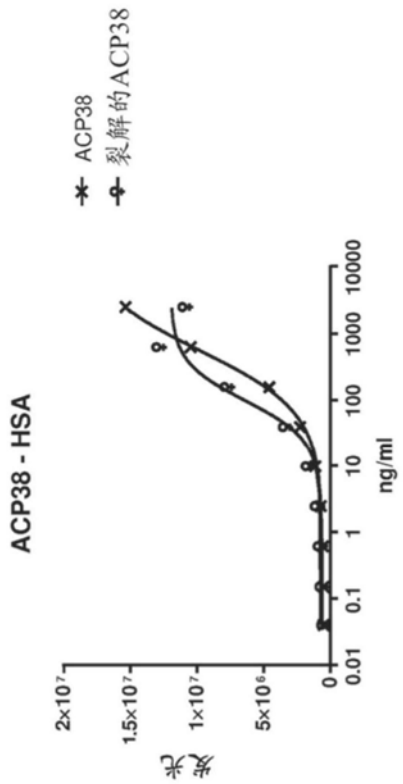

ACP38
裂解的ACP38
ACP38 - HSA
2×10⁷
1.5×10⁷
1×10⁷
5×10⁶
0
0.01
0.1
1
10
100
1000
10000
ng/ml

图7E

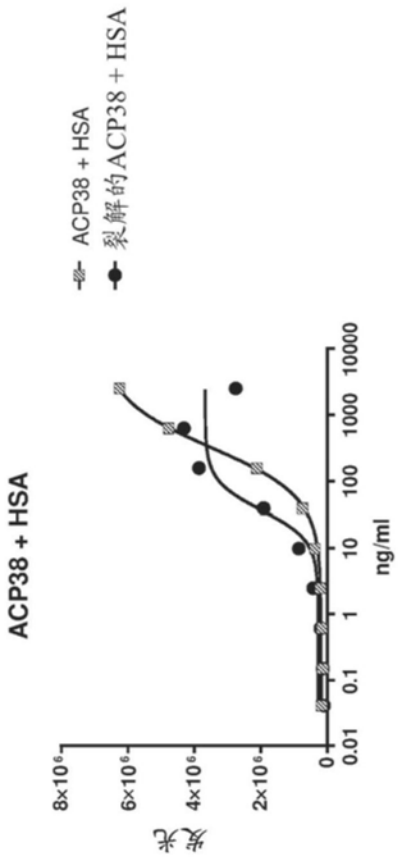

ACP38 + HSA
ACP38 + HSA
裂解的ACP38 + HSA
8×10⁶
6×10⁶
4×10⁶
2×10⁶
0
0.01
0.1
1
10
100
1000
10000
ng/ml

图7F

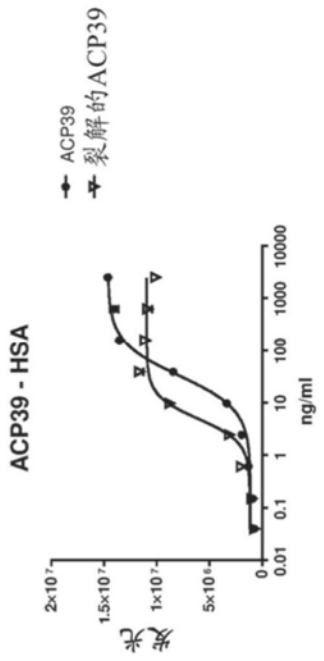

ACP39 - HSA
ACP39
裂解的ACP39
2×10⁷
1.5×10⁷
1×10⁷
5×10⁶
0
0.01
0.1
1
10
100
1000
10000
ng/ml

图7G

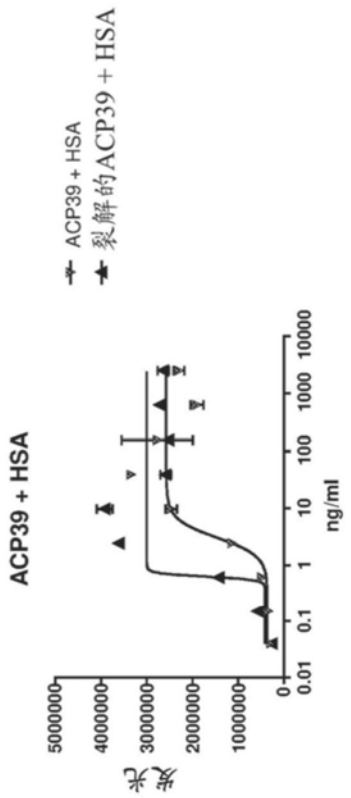

ACP39 + HSA
裂解的ACP39 + HSA
ACP39 + HSA
5000000
4000000
3000000
2000000
1000000
0
0.01
0.1
1
10
100
1000
10000
ng/ml

图7H

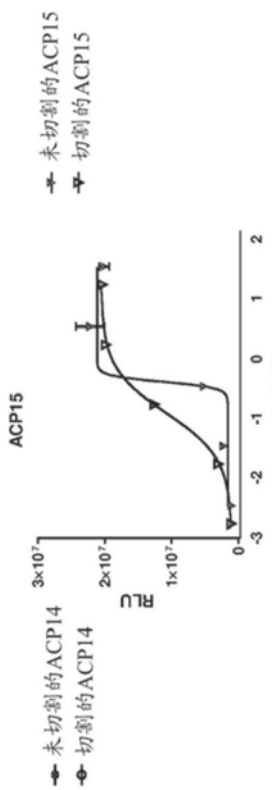

ACP14
RLU
log[nM]
未切割的ACP14
切割的ACP14
ACP15
RLU
log[nM]
未切割的ACP15
切割的ACP15

图 8A

图 8B

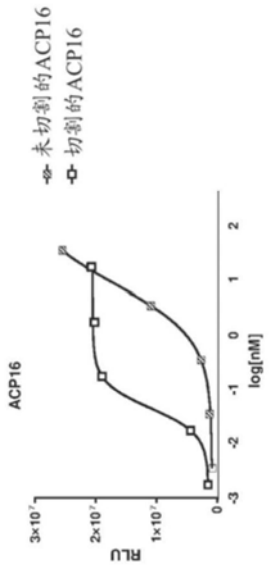


图8C

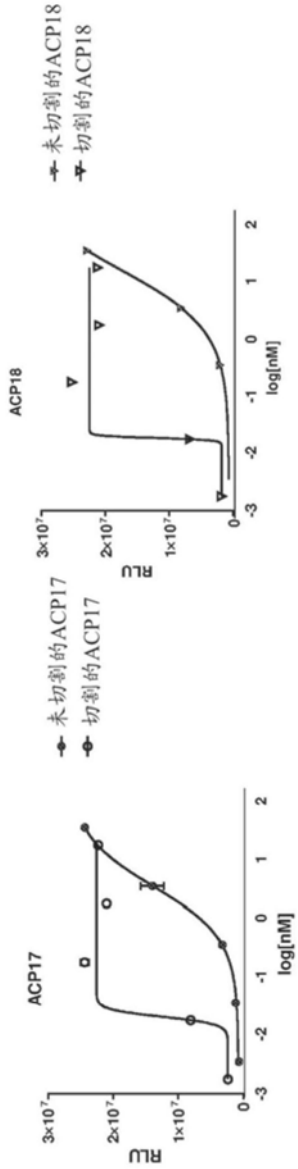

未切割的ACP17
切割的ACP17
ACP17
RLU
3×10^7
2×10^7
1×10^7
0
-3
-2
-1
0
1
2
log[nM]

图 8D

未切割的ACP18
切割的ACP18
ACP18
RLU
3×10^7
2×10^7
1×10^7
0
-3
-2
-1
0
1
2
log[nM]

图 8E

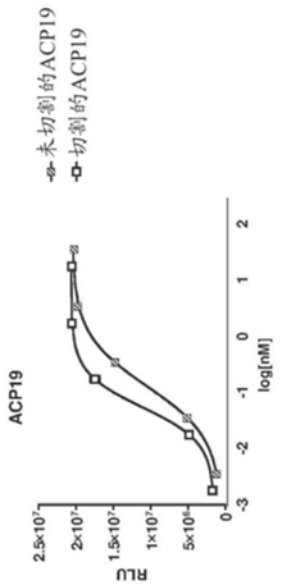

未切割的ACP19
切割的ACP19
ACP19
RLU
log[nM]

图8F

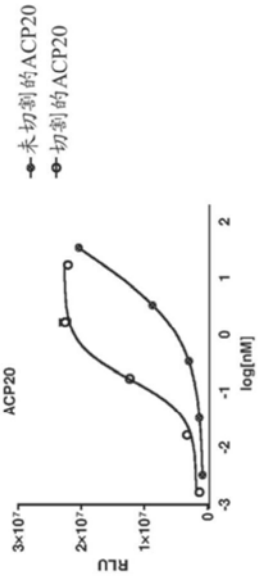

未切割的ACP20
切割的ACP20
ACP20
RLU
log[nM]

图9A

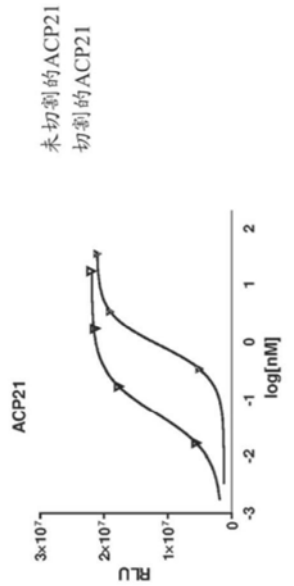

未切割的ACP21
切割的ACP21
ACP21
RLU
3x10^7
2x10^7
1x10^7
0
-3
-2
-1
0
1
2
log[nM]

图9B

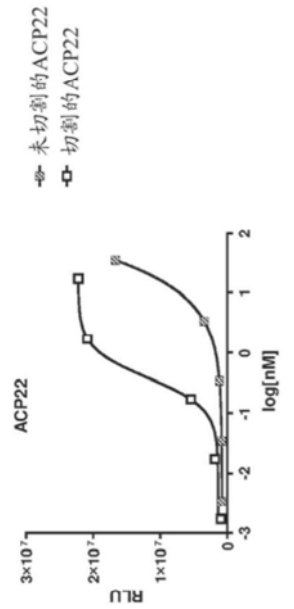

未切割的ACP22
切割的ACP22
ACP22
RLU
3x10^7
2x10^7
1x10^7
0
-3
-2
-1
0
1
2
log[nM]

图9C

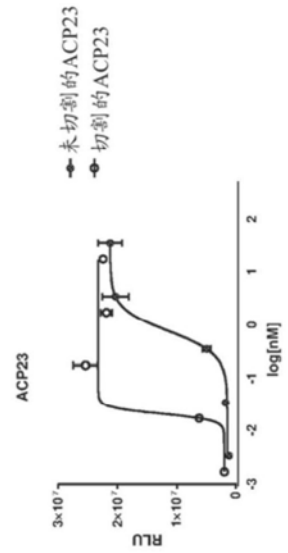

未切割的ACP23
切割的ACP23
ACP23
RLU
log[nM]

图9D

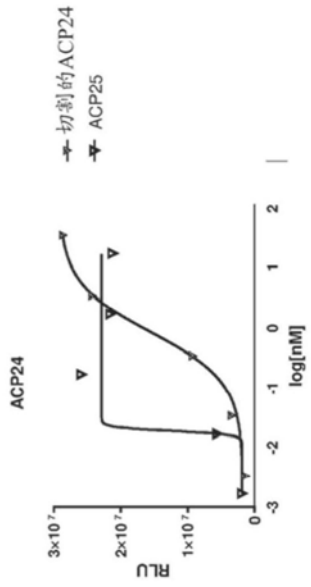

切割的ACP24
ACP25
ACP24
RLU
log[nM]

图9E

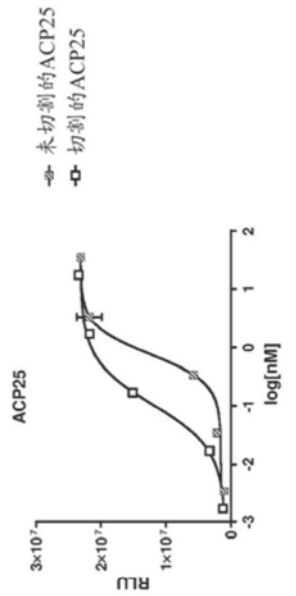

未切割的ACP25
切割的ACP25
ACP25
RLU
3×10^7
2×10^7
1×10^7
0
-3
-2
-1
0
1
2
log[nM]

图9F

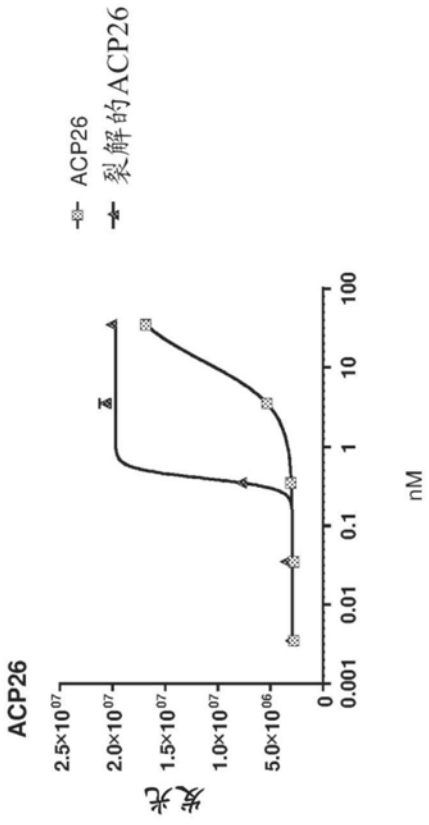

ACP26
裂解的ACP26
ACP26
发光
2.5×10^07
2.0×10^07
1.5×10^07
1.0×10^07
5.0×10^06
0
0.001
0.01
0.1
1
10
100
nM

图9G

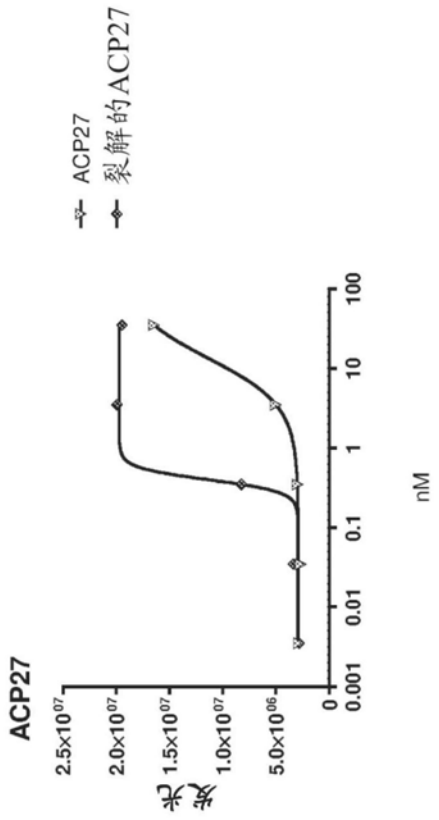

ACP27
裂解的ACP27
ACP27
2.5x10^07
2.0x10^07
1.5x10^07
1.0x10^07
5.0x10^06
0
0.001
0.01
0.1
1
10
100
nM

图9H

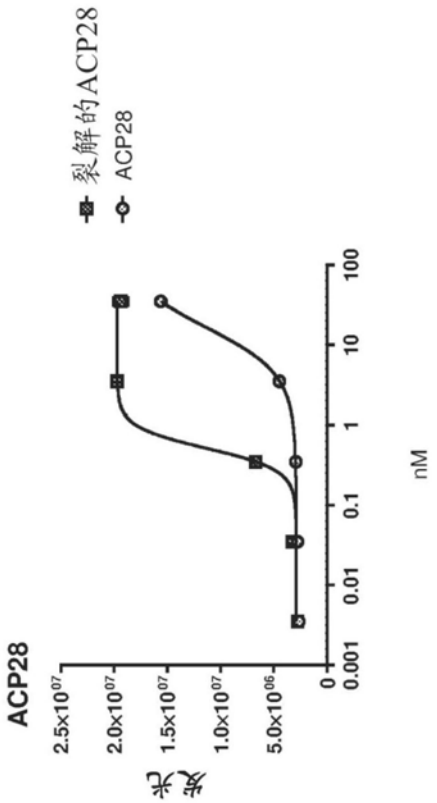

裂解的ACP28
ACP28
ACP28
2.5x10^07
2.0x10^07
1.5x10^07
1.0x10^07
5.0x10^06
0
0.001
0.01
0.1
1
10
100
nM

图9i

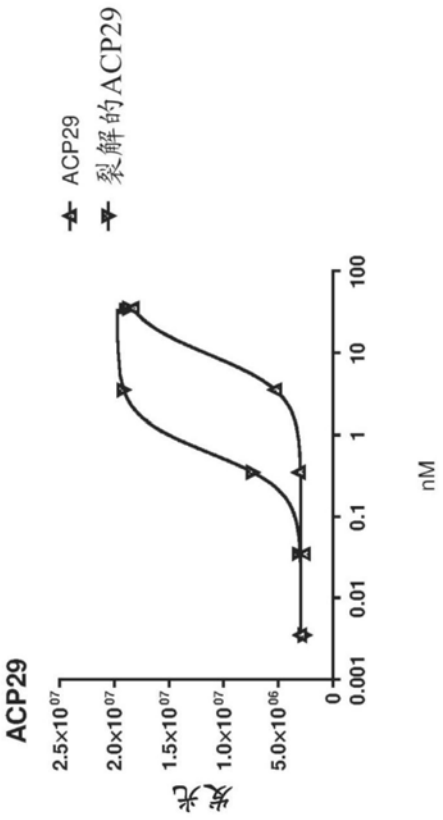

ACP29
裂解的ACP29
ACP29
2.5x10^07
2.0x10^07
1.5x10^07
1.0x10^07
5.0x10^06
0
0.001
0.01
0.1
1
10
100
nM

图9J

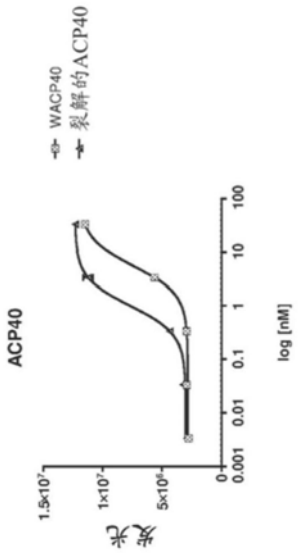

WACP40
裂解的ACP40
ACP40
1.5x10^7
1x10^7
5x10^6
0
0.001
0.01
0.1
1
10
100
log [nM]

图9K

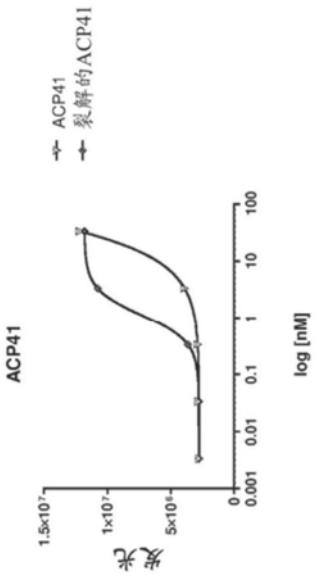

ACP41
裂解的ACP41
ACP41
log [nM]
1.5x10⁷
1x10⁷
5x10⁶
0
0.001
0.01
0.1
1
10
100

图9L

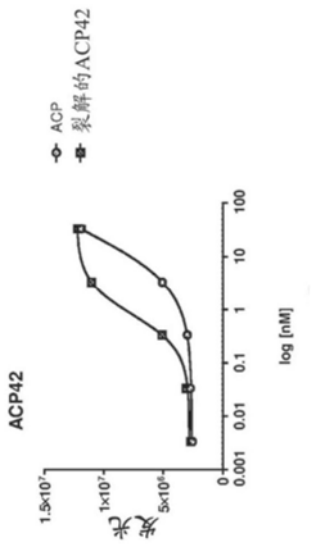

ACP
裂解的ACP42
ACP42
log [nM]
1.5x10⁷
1x10⁷
5x10⁶
0
0.001
0.01
0.1
1
10
100

图9M

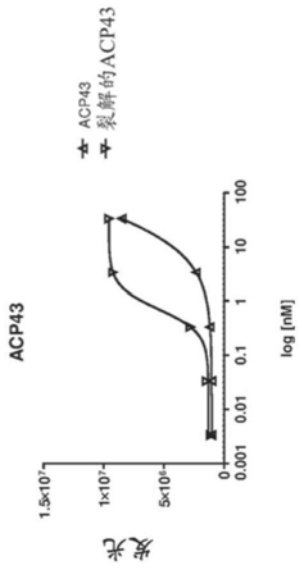

ACP43
ACP43
裂解的ACP43
1.5x10⁷
1x10⁷
5x10⁶
0
0.001
0.01
0.1
1
10
100
log [nM]
细胞

图9N

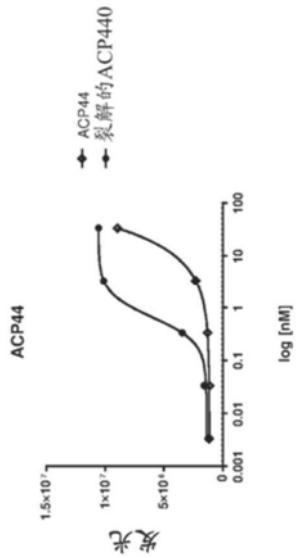

ACP44
ACP44
裂解的ACP440
1.5x10⁷
1x10⁷
5x10⁶
0
0.001
0.01
0.1
1
10
100
log [nM]
细胞

图90

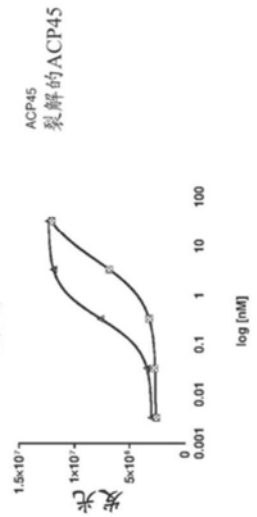

ACP45
裂解的ACP45
ACP45
1.5×10⁷
1×10⁷
5×10⁶
0
0.001
0.01
0.1
1
10
100
log [nM]
发光

图9P

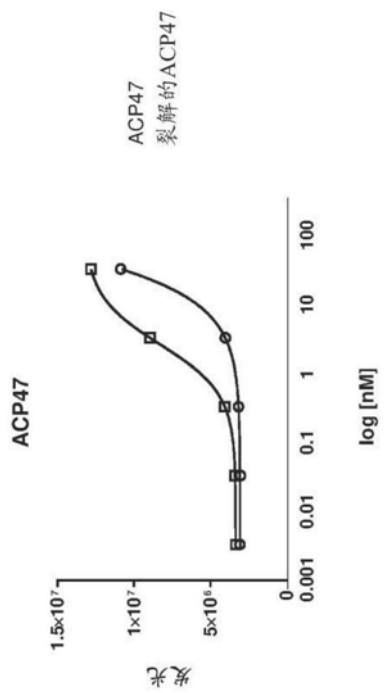

ACP47
裂解的ACP47
ACP47
1.5×10⁷
1×10⁷
5×10⁶
0
0.001
0.01
0.1
1
10
100
log [nM]
发光

图9Q

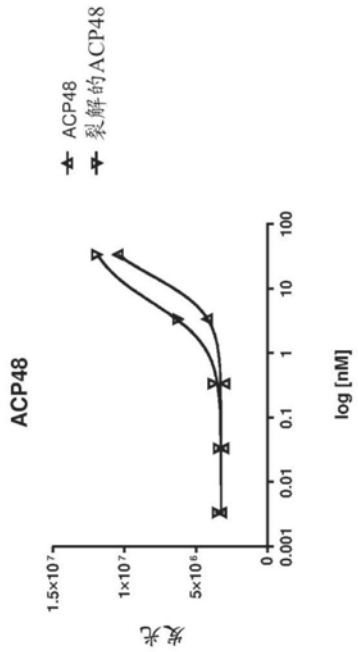

ACP48
裂解的ACP48
ACP48
1.5×10⁷
1×10⁷
5×10⁶
发光
0
0.001
0.01
0.1
1
10
100
log [nM]

图9R

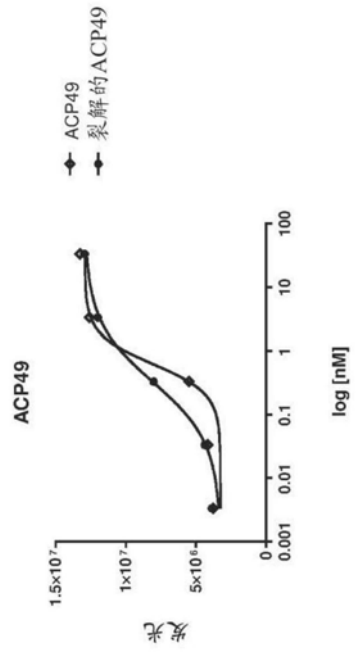

ACP49
裂解的ACP49
ACP49
1.5×10⁷
1×10⁷
5×10⁶
发光
0
0.001
0.01
0.1
1
10
100
log [nM]

图9S

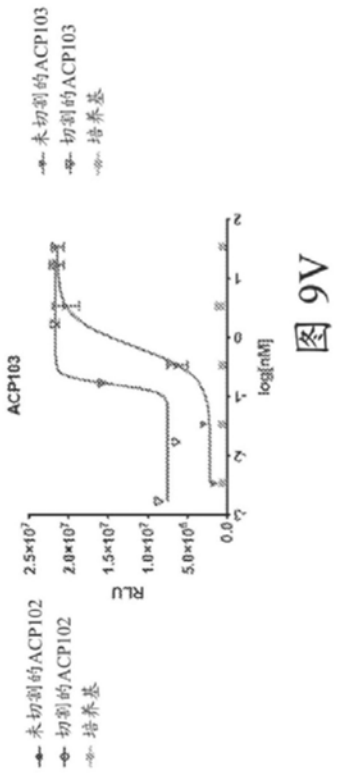

ACP103
RLU
log[nM]
未切割的ACP103
切割的ACP103
培养基

图 9V

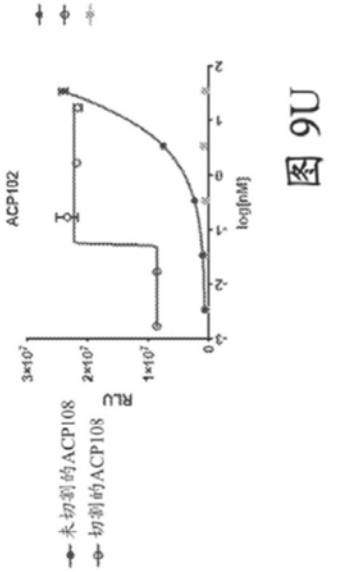

ACP102
RLU
log[nM]
未切割的ACP102
切割的ACP102
培养基

图 9U

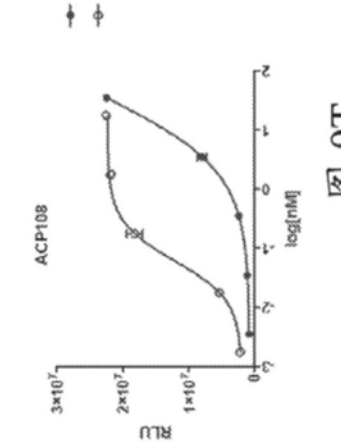

ACP108
RLU
log[nM]
未切割的ACP108
切割的ACP108

图 9T

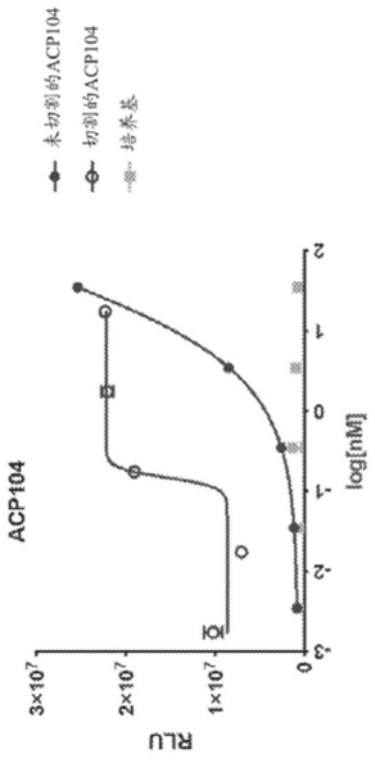

未切割的ACP104
切割的ACP104
培养基
ACP104
RLU
3×10^7
2×10^7
1×10^7
0
-3
-2
-1
0
1
2
log[nM]

图9W

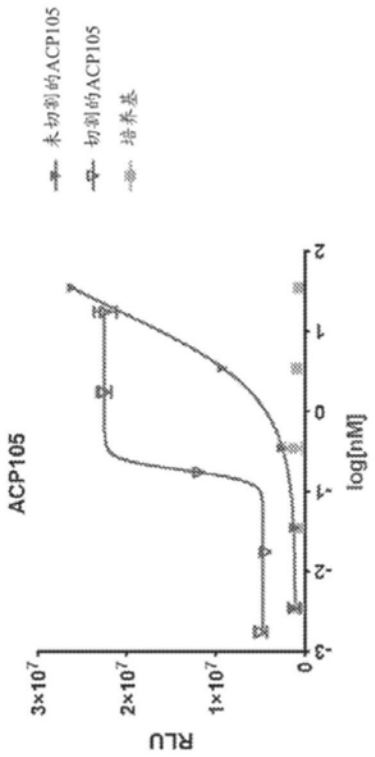

未切割的ACP105
切割的ACP105
培养基
ACP105
RLU
3×10^7
2×10^7
1×10^7
0
-3
-2
-1
0
1
2
log[nM]

图9X

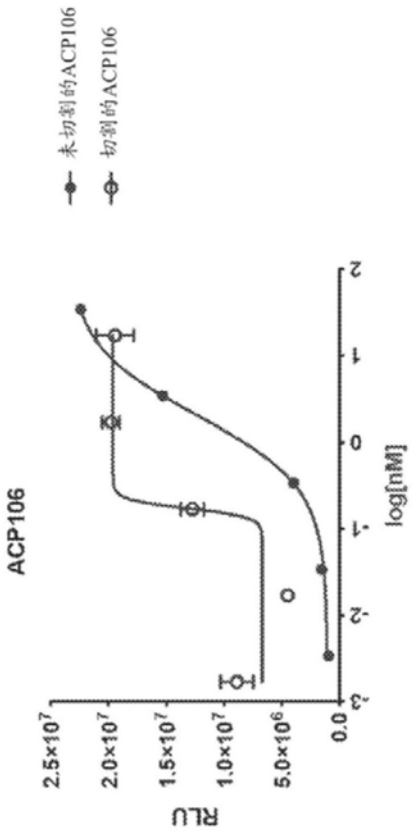

未切割的ACP106
切割的ACP106
ACP106
RLU
2.5×10^7
2.0×10^7
1.5×10^7
1.0×10^7
5.0×10^6
0.0
log[nM]

图9Y

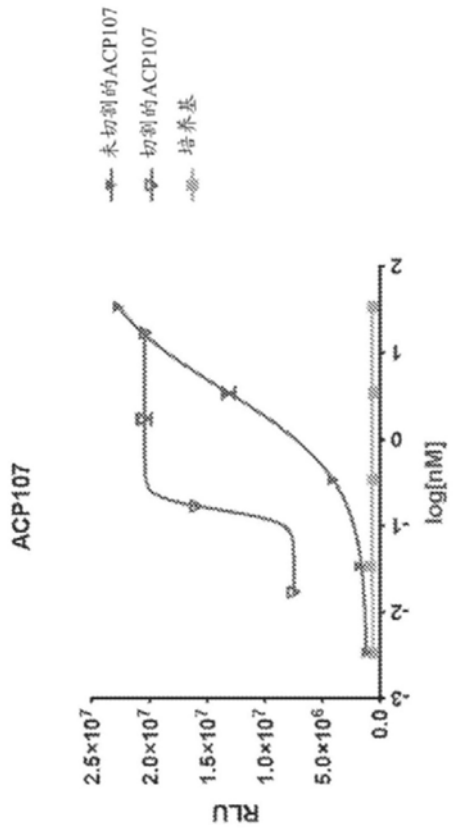

未切割的ACP107
切割的ACP107
培养基
ACP107
RLU
2.5×10^7
2.0×10^7
1.5×10^7
1.0×10^7
5.0×10^6
0.0
log[nM]

图9Z

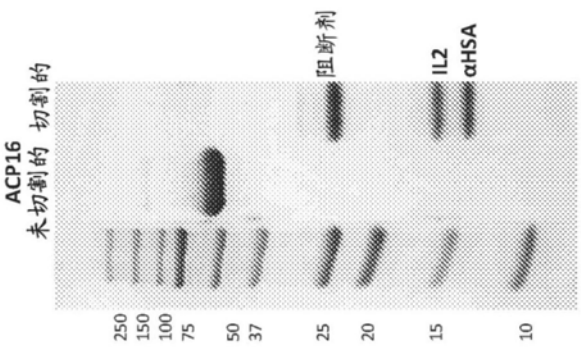

ACP16
未切割的
切割的
阻断剂
IL2
αHSA
250
150
100
75
50
37
25
20
15
10

图10

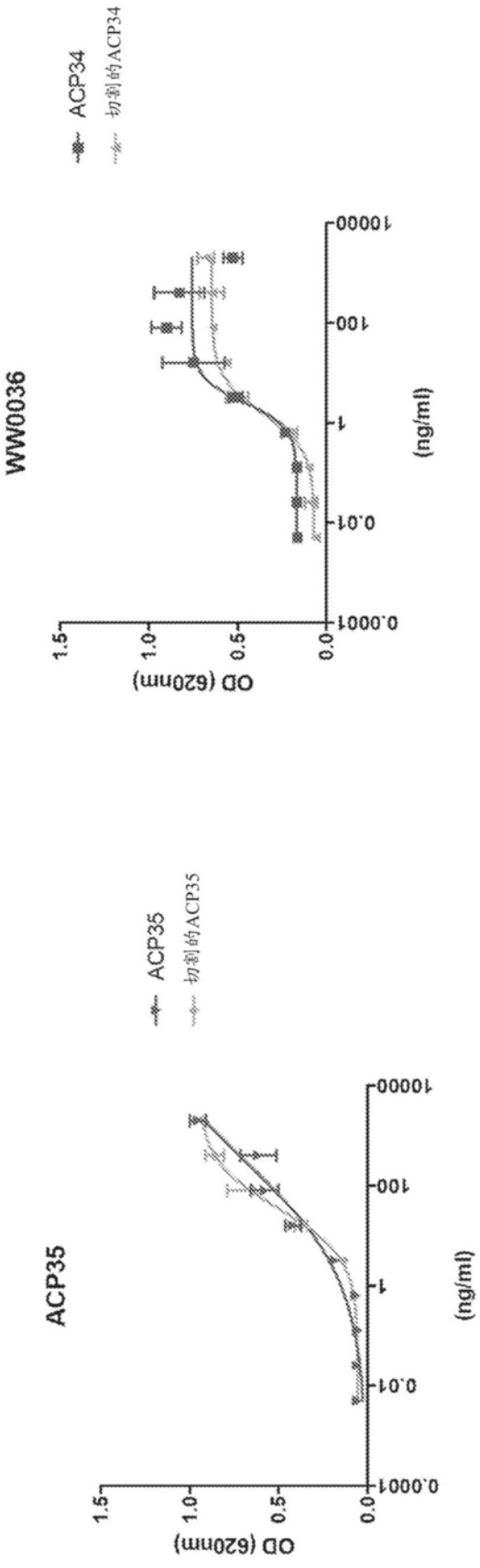

ACP34
切割的ACP34
WW0036
OD (620nm)
1.5
1.0
0.5
0.0
0.0001
0.01
1
100
10000
(ng/ml)
ACP35
切割的ACP35
ACP35
OD (620nm)
1.5
1.0
0.5
0.0
0.0001
0.01
1
100
10000
(ng/ml)

图11

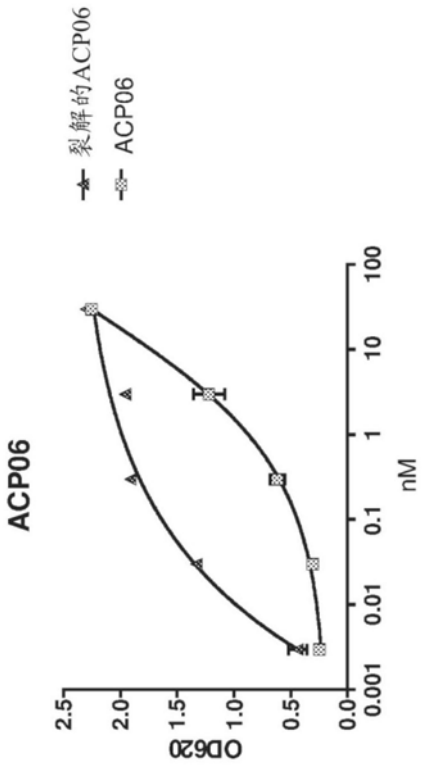

裂解的ACP06
ACP06
ACP06
OD620
2.5
2.0
1.5
1.0
0.5
0.0
0.001
0.01
0.1
1
10
100
nM

图12A

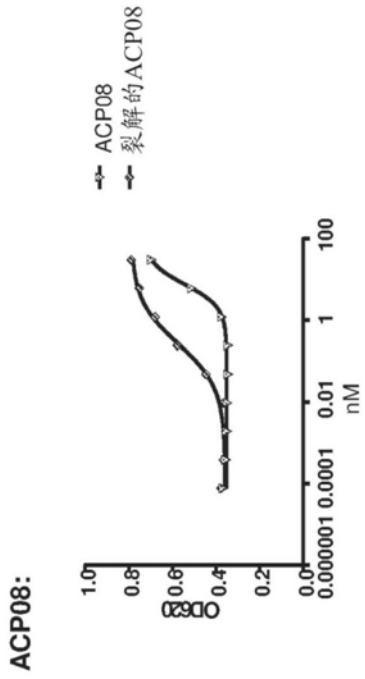

ACP08
裂解的ACP08
ACP08:
OD620
1.0
0.8
0.6
0.4
0.2
0.0
0.000001
0.0001
0.01
1
100
nM

图12B

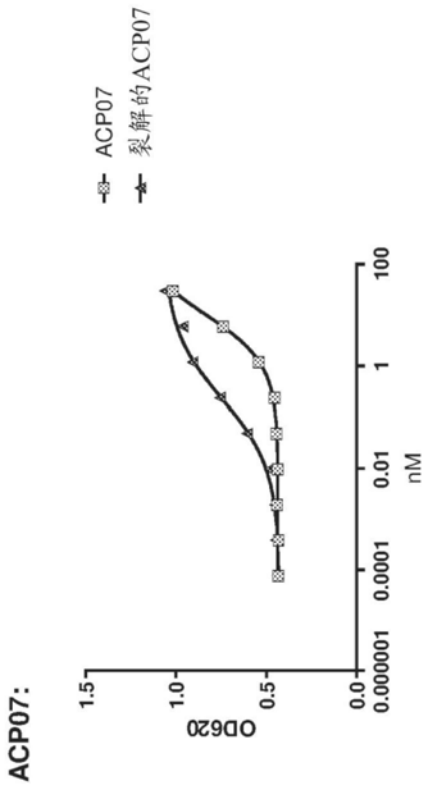

ACP07:
ACP07
裂解的ACP07
OD620
1.5
1.0
0.5
0.0
0.000001
0.0001
0.01
1
100
nM

图12C

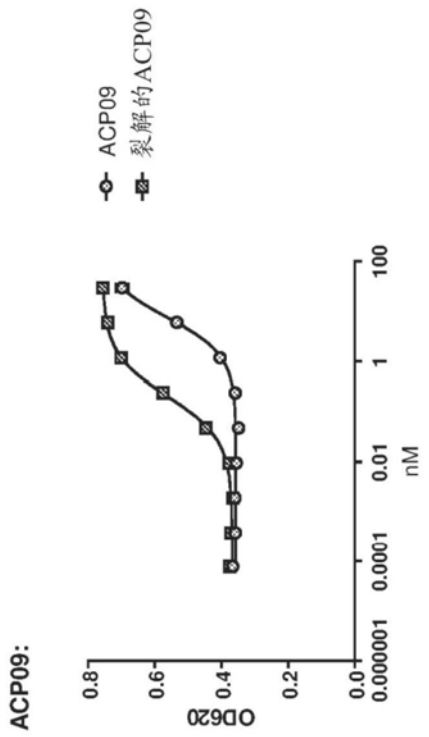

ACP09:
ACP09
裂解的ACP09
OD620
0.8
0.6
0.4
0.2
0.0
0.000001
0.0001
0.01
1
100
nM

图12D

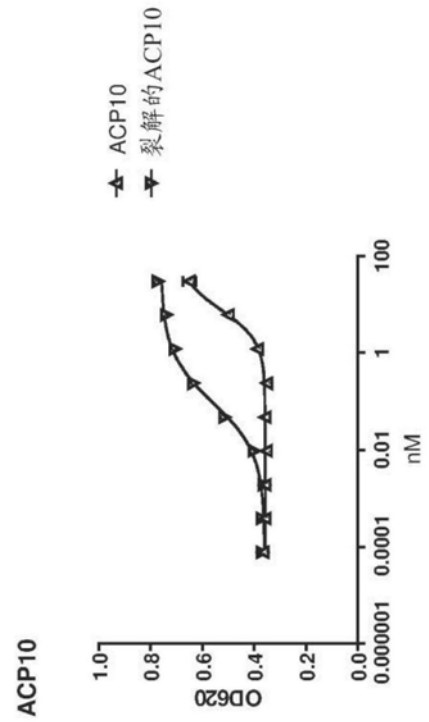

ACP10
ACP10
裂解的ACP10
OD620
1.0
0.8
0.6
0.4
0.2
0.0
0.000001
0.0001
0.01
1
100
nM

图12E

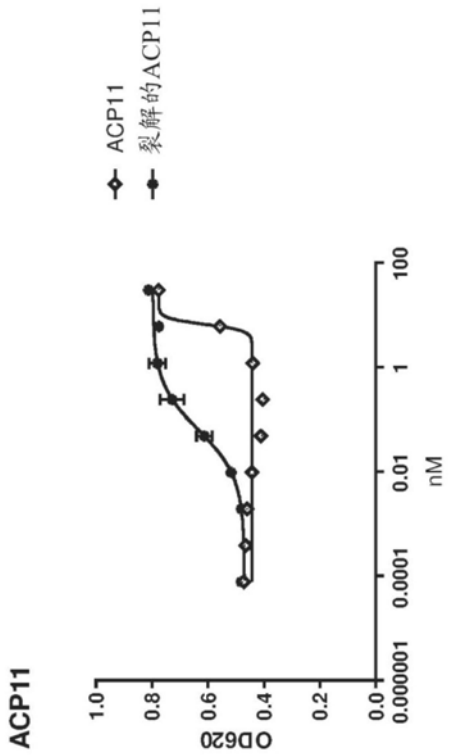

ACP11
ACP11
裂解的ACP11
OD620
1.0
0.8
0.6
0.4
0.2
0.0
0.000001
0.0001
0.01
1
100
nM

图12F

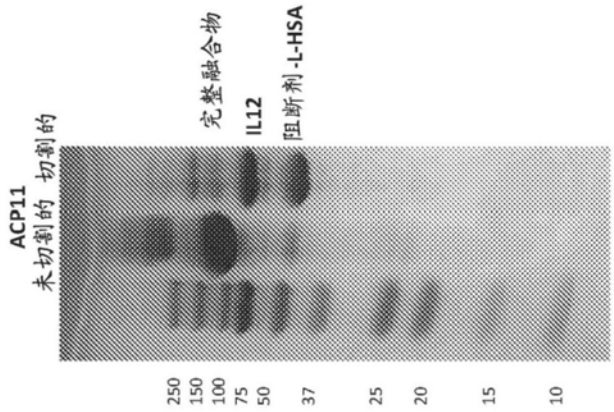

ACP11
未切割的
切割的
完整融合物
IL12
阻断剂-L-HSA
250
150
100
75
50
37
25
20
15
10

图13

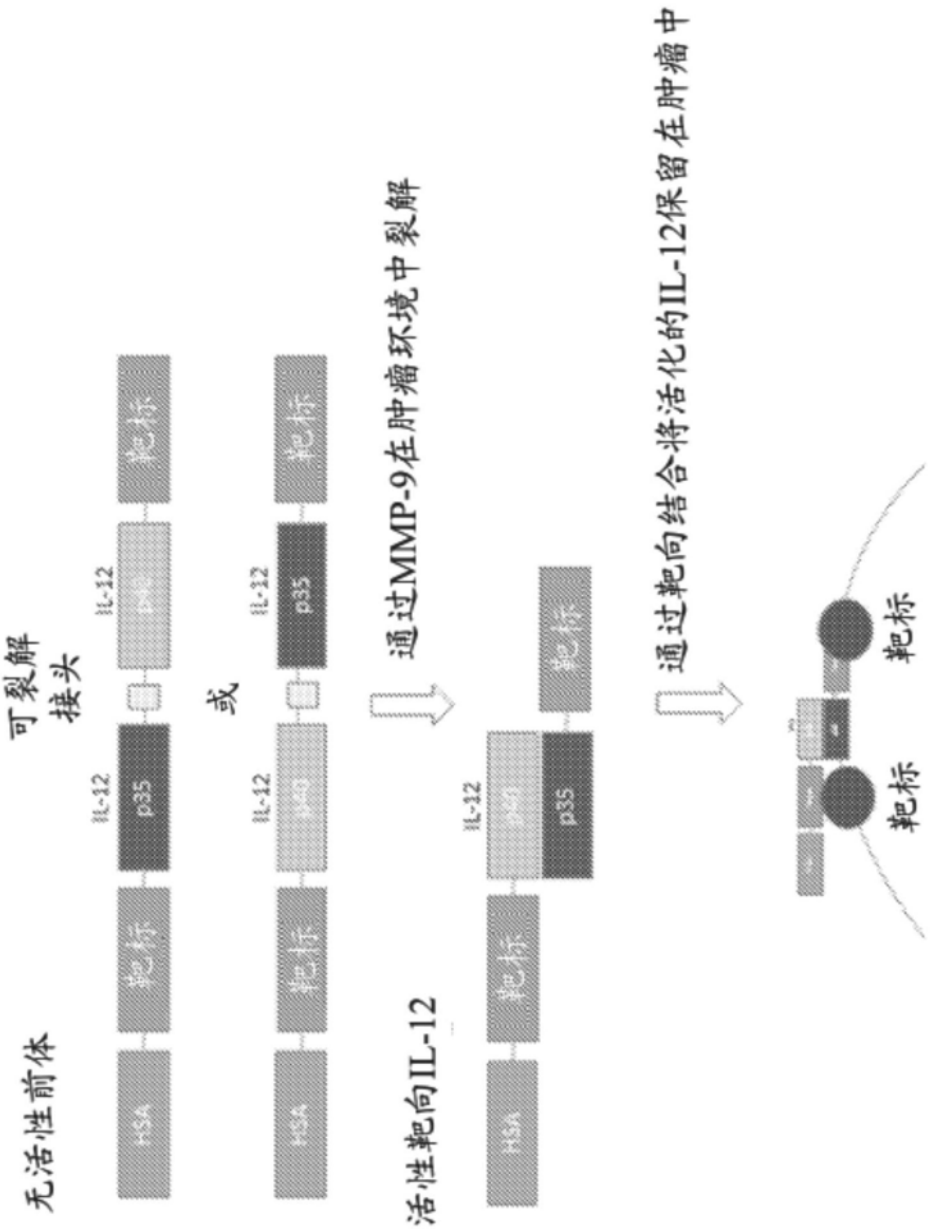

无活性前体
可裂解
接头
HSA
靶标
IL-12
p35
或
IL-12
p40
靶标
HSA
靶标
IL-12
p40
IL-12
p35
通过MMP-9在肿瘤环境中裂解
活性靶向IL-12
HSA
靶标
IL-12
p40
p35
靶标
通过靶向结合将活化的IL-12保留在肿瘤中
靶标
靶标

图14

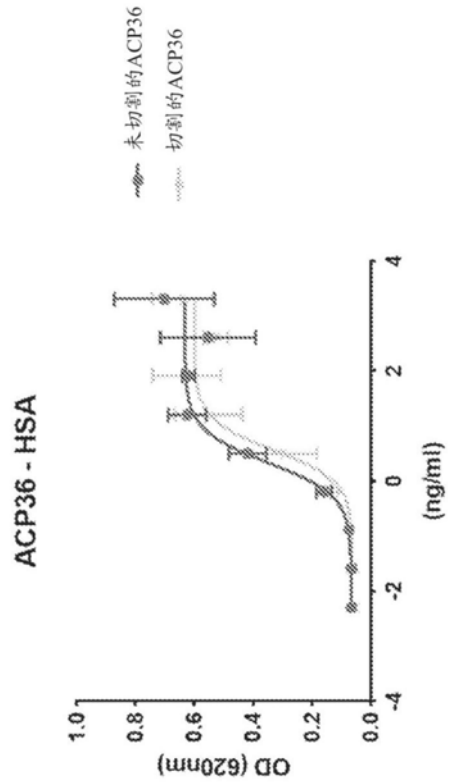

ACP36 - HSA
未切割的ACP36
切割的ACP36
OD (620nm)
1.0
0.8
0.6
0.4
0.2
0.0
-4
-2
0
2
4
(ng/ml)

图15A

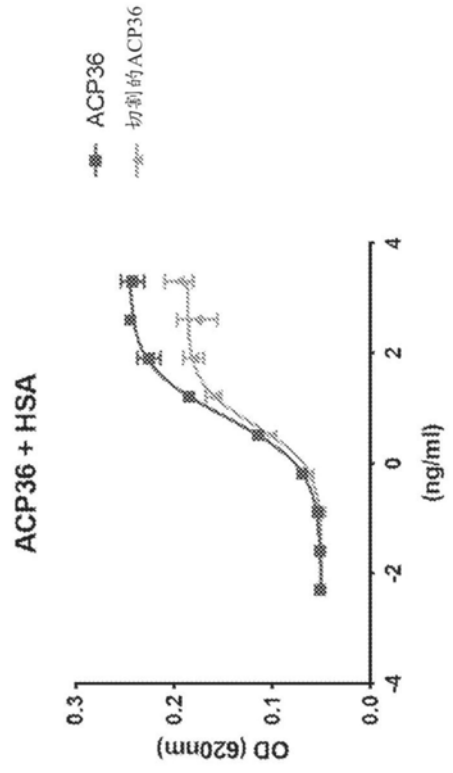

ACP36 + HSA
ACP36
切割的ACP36
OD (620nm)
0.3
0.2
0.1
0.0
-4
-2
0
2
4
(ng/ml)

图15B

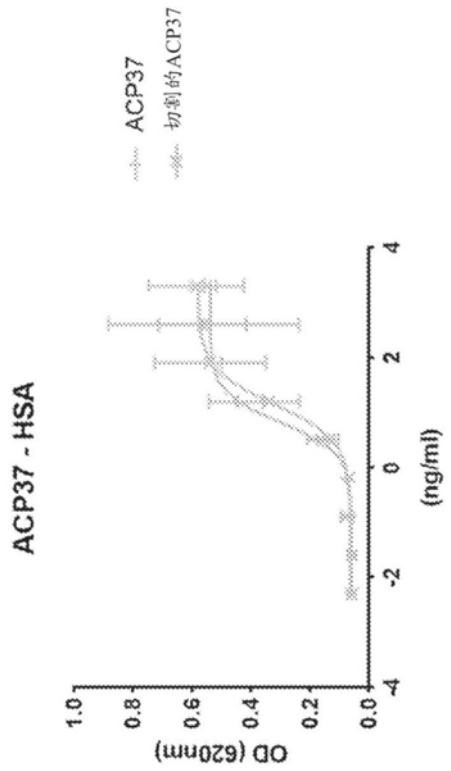

ACP37
切割的ACP37
ACP37 - HSA
OD (620nm)
1.0
0.8
0.6
0.4
0.2
0.0
-4
-2
0
2
4
(ng/ml)

图15C

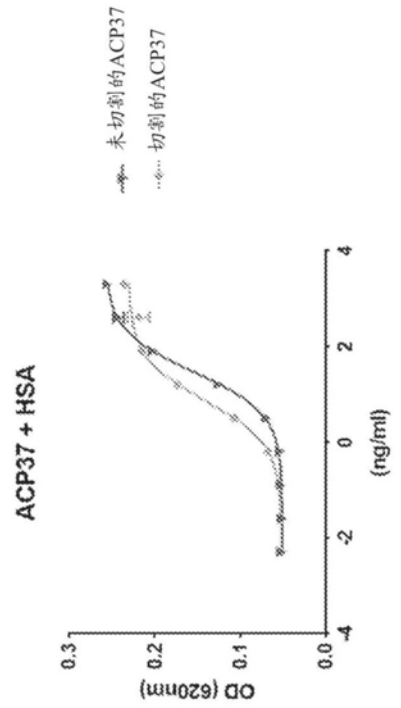
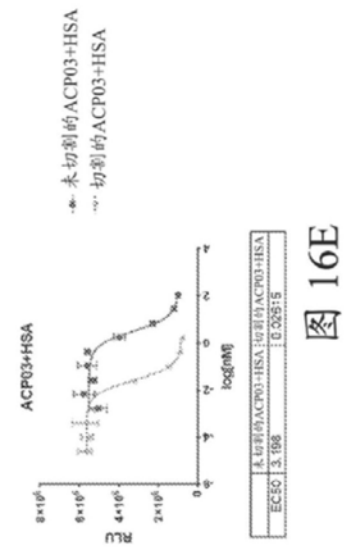
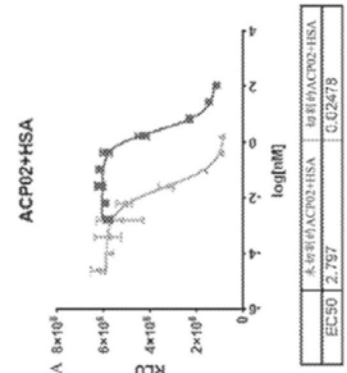

未切割的ACP37
切割的ACP37
ACP37 + HSA
OD (620nm)
0.3
0.2
0.1
0.0
-4
-2
0
2
4
(ng/ml)

图15D



	未切割的ACP01-HSA	切割的ACP01-HSA
EC50	153.4	0.2990

图 16A

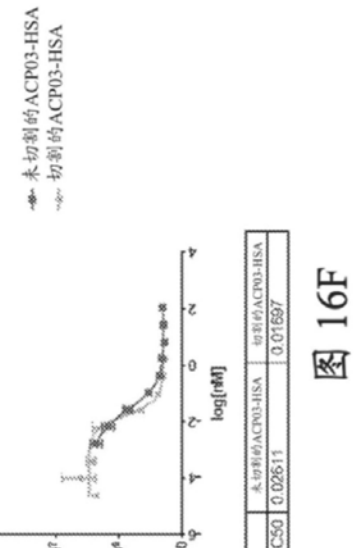


	未切割的ACP02-HSA	切割的ACP02-HSA
EC50	2.797	0.02479

图 16C

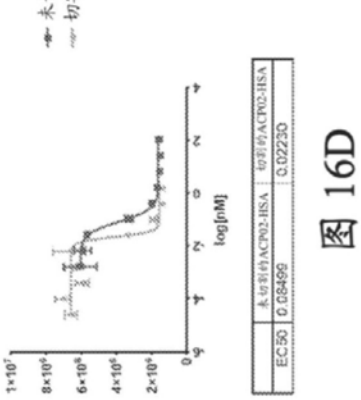
	未切割的ACP03-HSA	切割的ACP03-HSA
EC50	3.198	0.02615

图 16E



	未切割的ACP01-HSA	切割的ACP01-HSA
EC50	0.3787	0.1621

图 16B



	未切割的ACP02-HSA	切割的ACP02-HSA
EC50	0.08499	0.02230

图 16D

	未切割的ACP03-HSA	切割的ACP03-HSA
EC50	0.02611	0.01697

图 16F

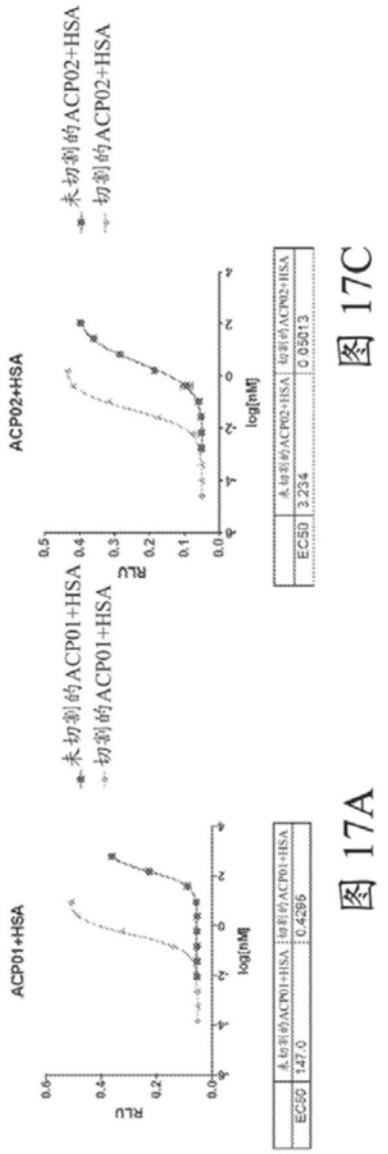


图 17A

图 17C

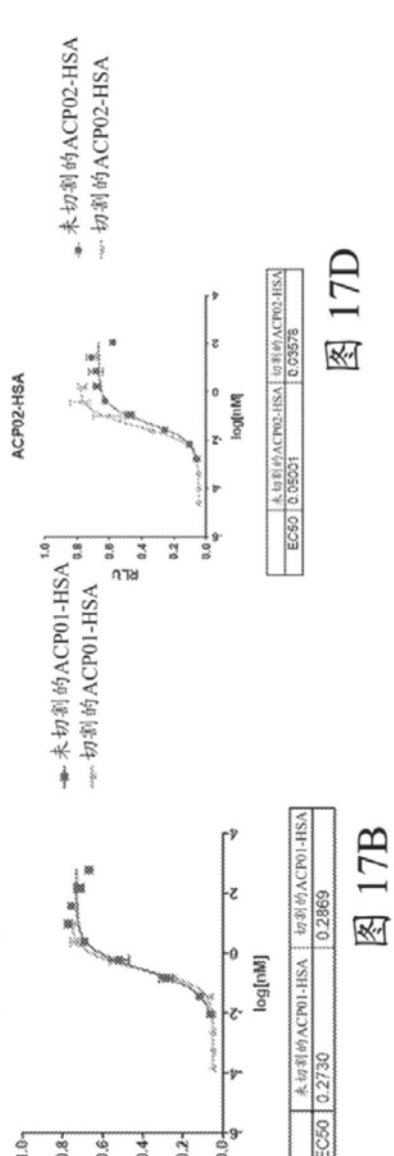


图 17B

图 17D

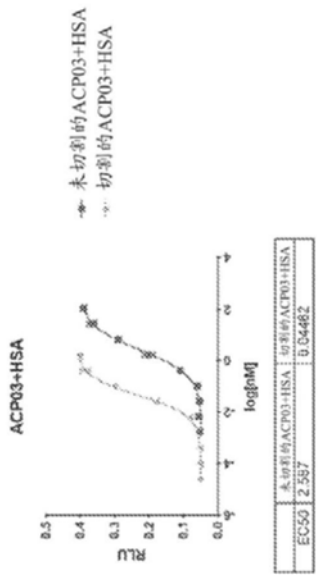

ACP03+HSA
RLU
log[pM]
未切割的ACP03+HSA
切割的ACP03+HSA
EC50
2.597
0.04482

图17E

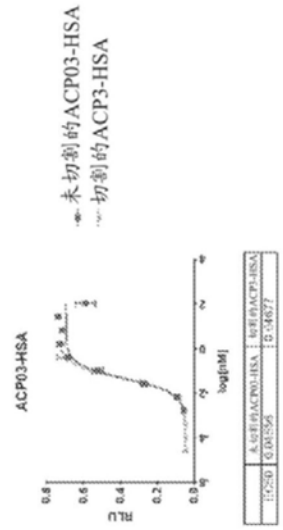

ACP03-HSA
RLU
log[pM]
未切割的ACP03-HSA
切割的ACP3-HSA

图17F

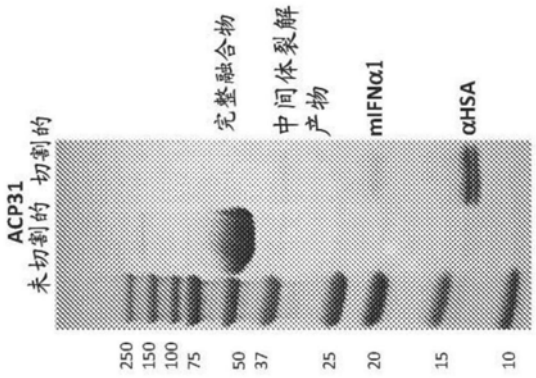

ACP31
未切割的
切割的
完整融合物
中间体裂解产物
mIFNα1
αHSA
250
150
100
75
50
37
25
20
15
10

图18A

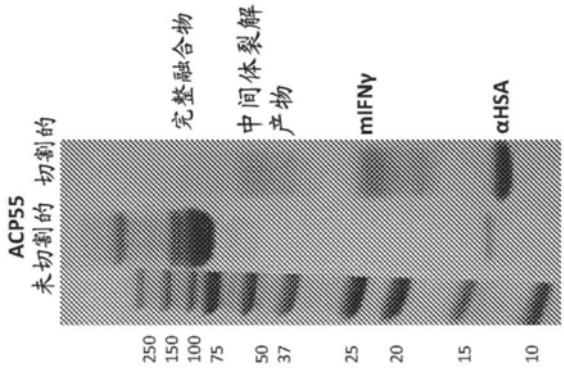

ACP55
未切割的
切割的
完整融合物
中间体裂解产物
mIFNγ
αHSA
250
150
100
75
50
37
25
20
15
10

图18B

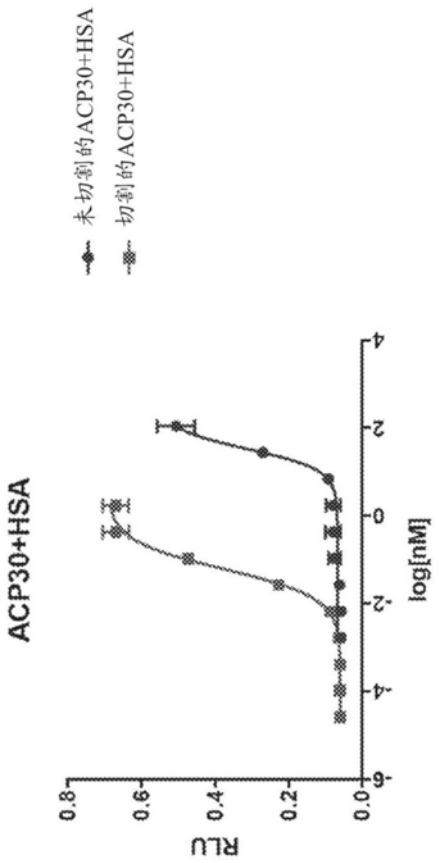

未切割的ACP30+HSA
切割的ACP30+HSA
ACP30+HSA
RLU
0.8
0.6
0.4
0.2
0.0
-6
-4
-2
0
2
4
log[nM]

图19A

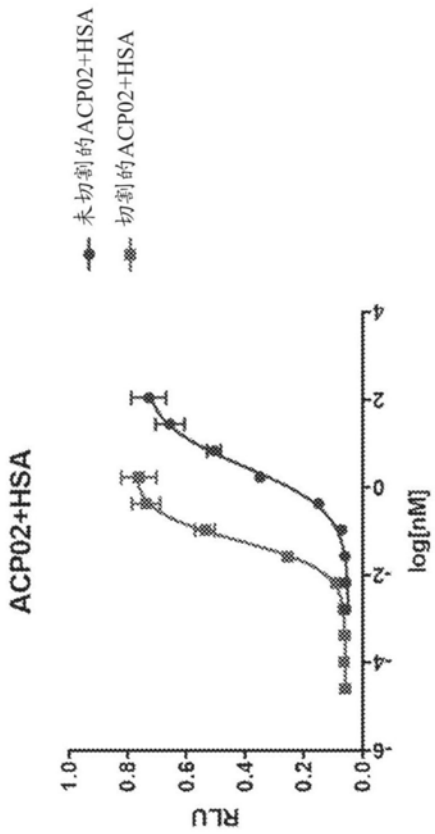

未切割的ACP02+HSA
切割的ACP02+HSA
ACP02+HSA
RLU
1.0
0.8
0.6
0.4
0.2
0.0
-6
-4
-2
0
2
4
log[nM]

图19B

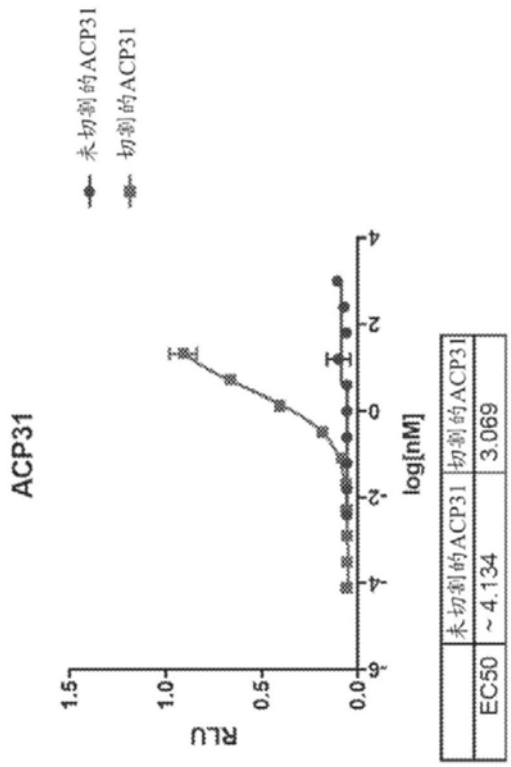

未切割的ACP31
切割的ACP31
ACP31
RLU
log[nM]
1.5
1.0
0.5
0.0
-6
-4
-2
0
2
4
EC50
~ 4.134
3.069

图20A

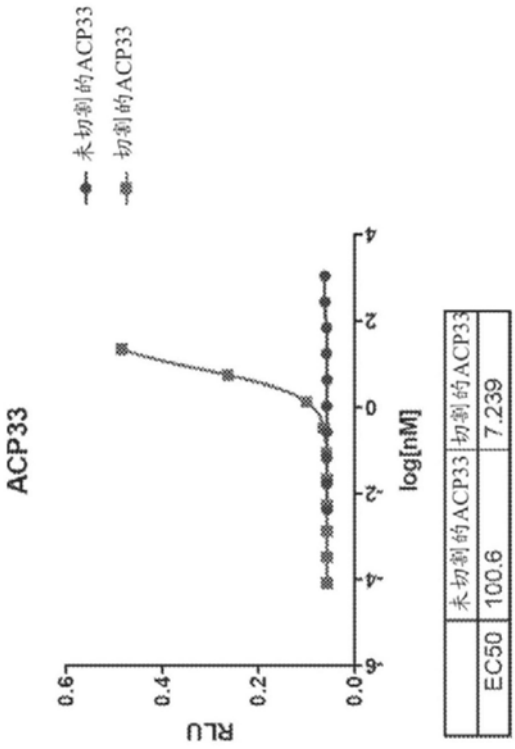

未切割的ACP33
切割的ACP33
ACP33
RLU
log[nM]
0.6
0.4
0.2
0.0
-6
-4
-2
0
2
4
EC50
100.6
7.239

图20B

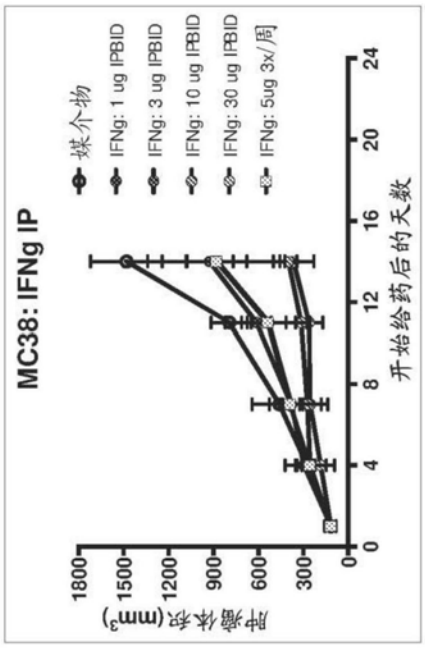

MC38: IFNg IP
媒介物
IFNg: 1 ug IPBID
IFNg: 3 ug IPBID
IFNg: 10 ug IPBID
IFNg: 30 ug IPBID
IFNg: 5ug 3x/周
肿瘤体积(mm³)
开始给药后的天数
0
300
600
900
1200
1500
1800
0
4
8
12
16
20
24

图21A

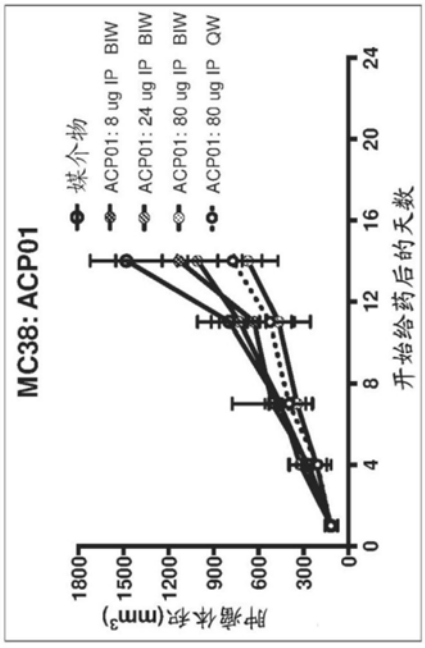

MC38: ACP01
媒介物
ACP01: 8 ug IP BIW
ACP01: 24 ug IP BIW
ACP01: 80 ug IP BIW
ACP01: 80 ug IP QW
肿瘤体积(mm³)
开始给药后的天数
0
300
600
900
1200
1500
1800
0
4
8
12
16
20
24

图21B

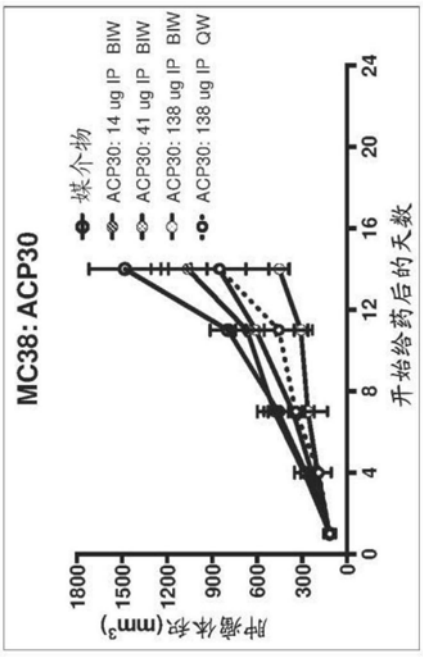

MC38: ACP30
媒介物
ACP30: 14 ug IP BIW
ACP30: 41 ug IP BIW
ACP30: 138 ug IP BIW
ACP30: 138 ug IP QW
肿瘤体积 (mm³)
开始给药后的天数
0
300
600
900
1200
1500
1800
0
4
8
12
16
20
24

图21C

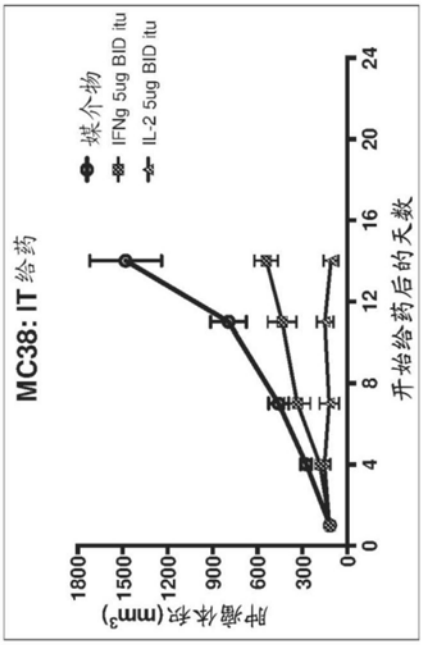
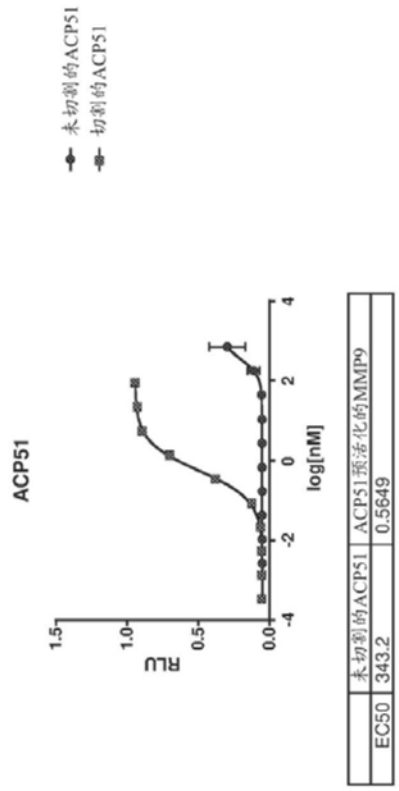
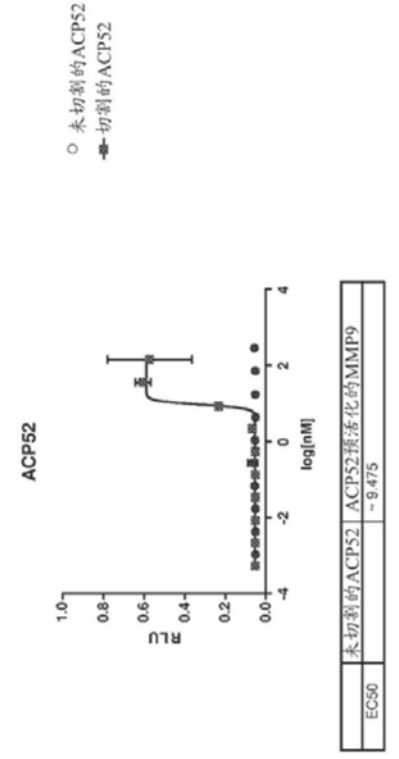

MC38: IT 给药
媒介物
IFNg 5ug BID itu
IL-2 5ug BID itu
肿瘤体积 (mm³)
开始给药后的天数
0
300
600
900
1200
1500
1800
0
4
8
12
16
20
24

图21D



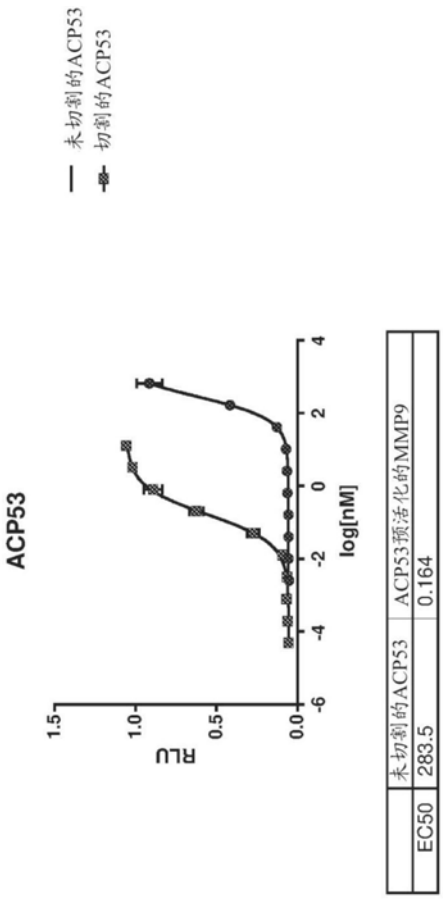
	未切割的ACP51	ACP51预活化的MMP9
EC50	343.2	0.5649

图22A



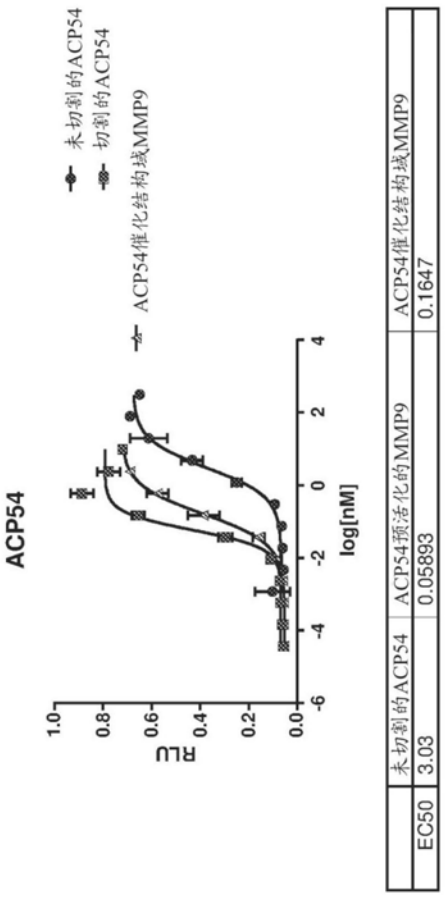
	未切割的ACP52	ACP52预活化的MMP9
EC50		~9.475

图22B



	未切割的ACP53	ACP53预活化的MMP9
EC50	283.5	0.164

图23A



	未切割的ACP54	ACP54预活化的MMP9	ACP54催化结构域MMP9
EC50	3.03	0.05893	0.1647

图23B

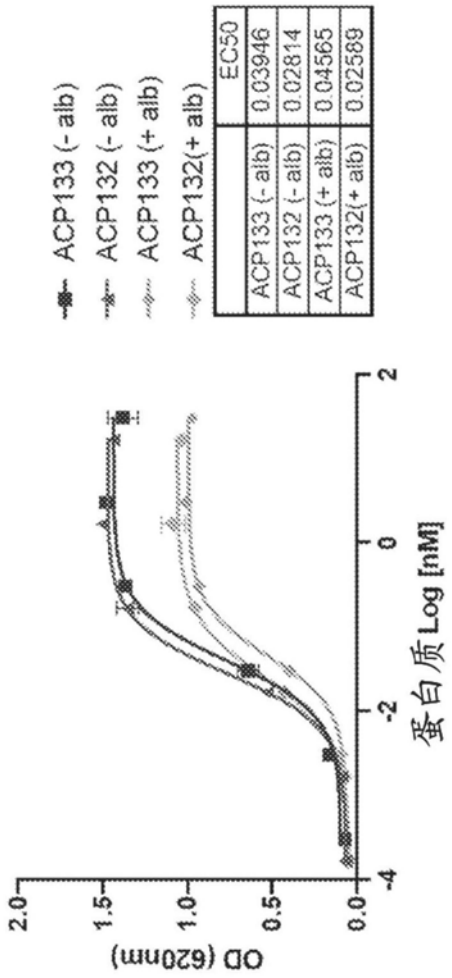

ACP133 (- alb)
ACP132 (- alb)
ACP133 (+ alb)
ACP132(+ alb)
EC50
ACP133 (- alb) 0.03946
ACP132 (- alb) 0.02814
ACP133 (+ alb) 0.04565
ACP132(+ alb) 0.02589
OD (620nm)
2.0
1.5
1.0
0.5
0.0
-4
-2
0
2
蛋白质Log [nM]

图24A

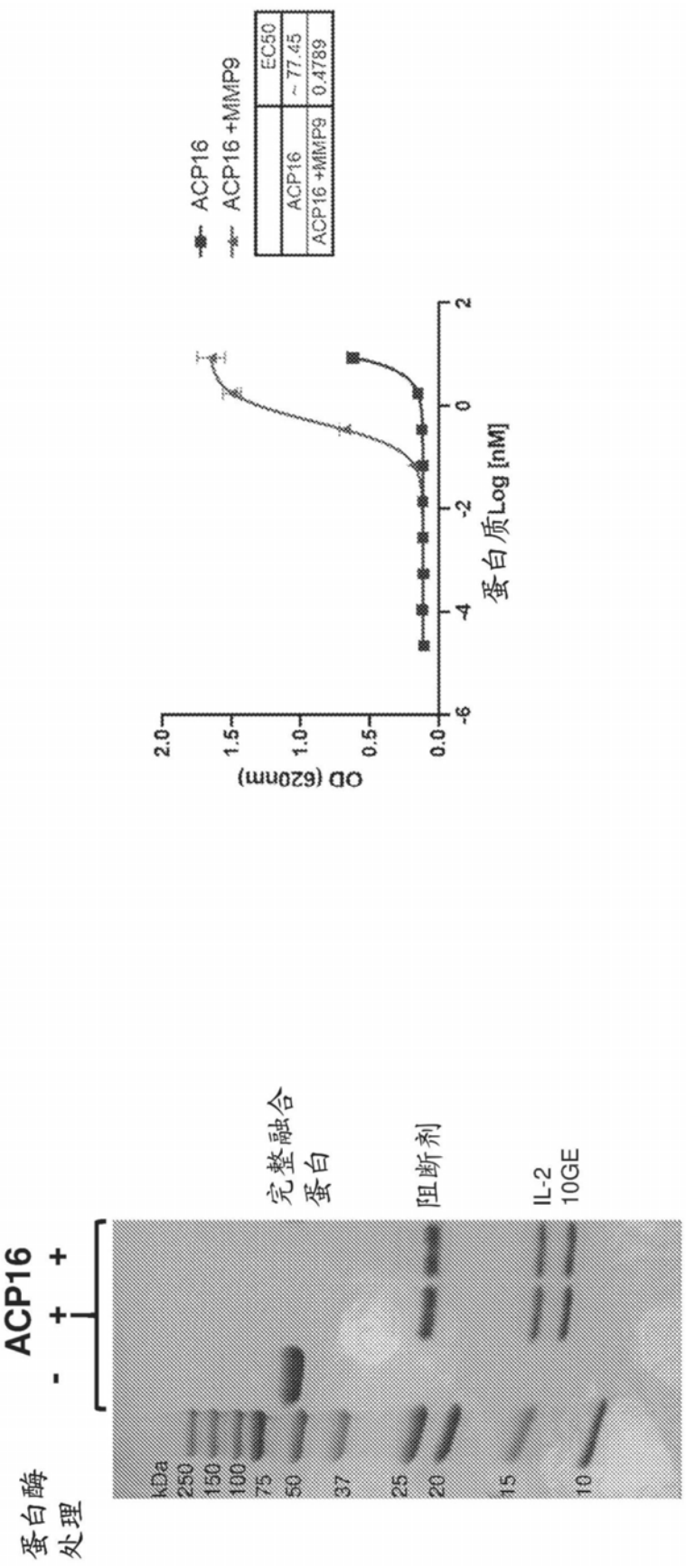

ACP16
ACP16 +MMP9
EC50
ACP16 ~ 77.45
ACP16 +MMP9 0.4789
OD (620nm)
蛋白质Log [nM]
蛋白酶处理
ACP16
kDa
250
150
100
75
50
37
25
20
15
10
完整融合蛋白
阻断剂
IL-2
10GE

图24B

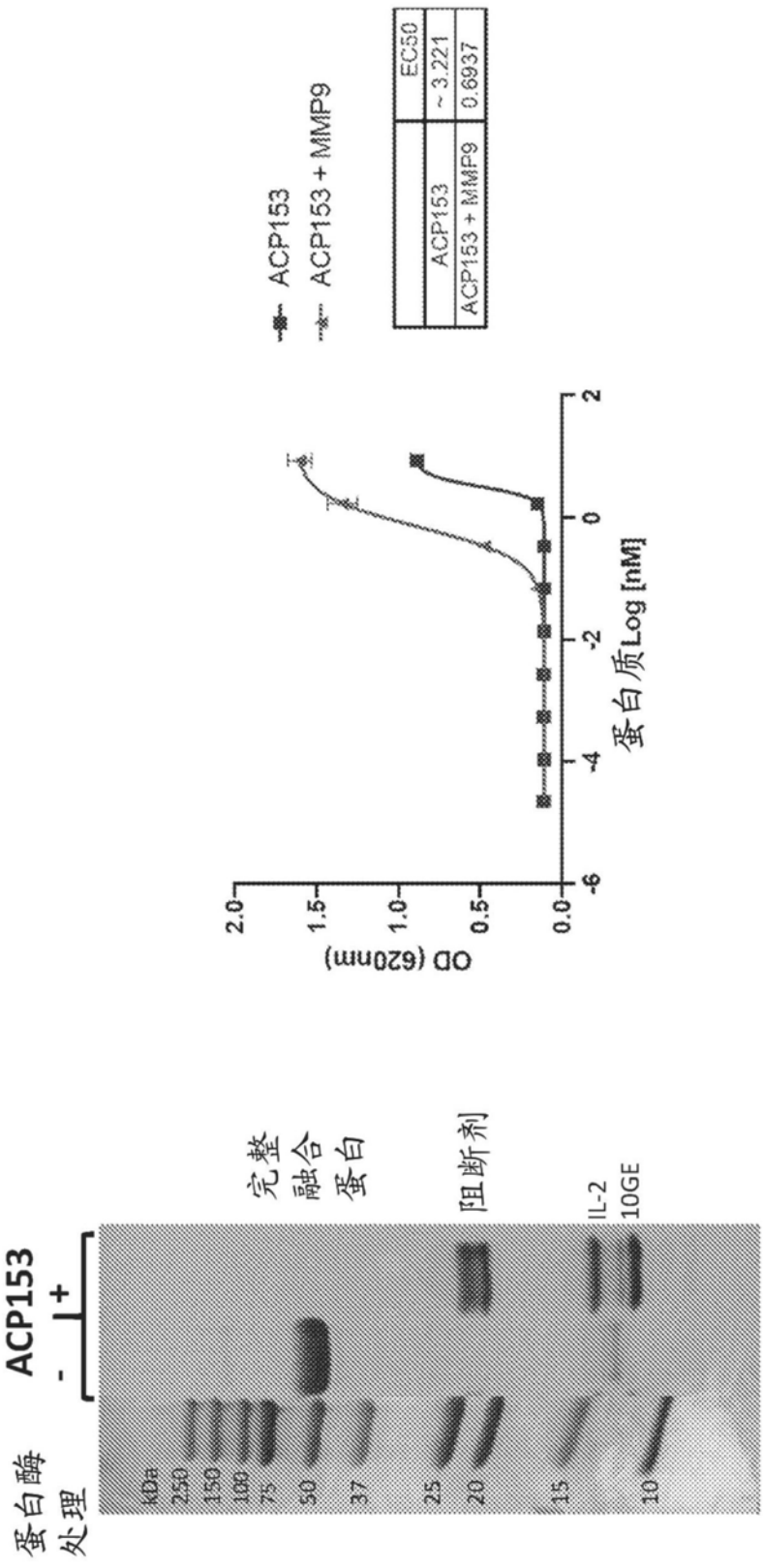
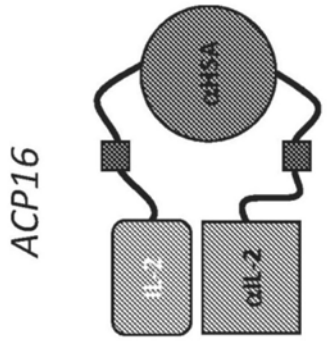

蛋白酶
处理
ACP153
-
+
kDa
250
150
100
75
50
37
25
20
15
10
完整
融合
蛋白
阻断剂
IL-2
10GE
ACP153
ACP153 + MMP9
EC50
ACP153
~ 3.221
ACP153 + MMP9
0.6937
OD (620nm)
2.0
1.5
1.0
0.5
0.0
-6
-4
-2
0
2
蛋白质Log [nM]

图24C


ACP16
IL-2
cIL-2
cHSA

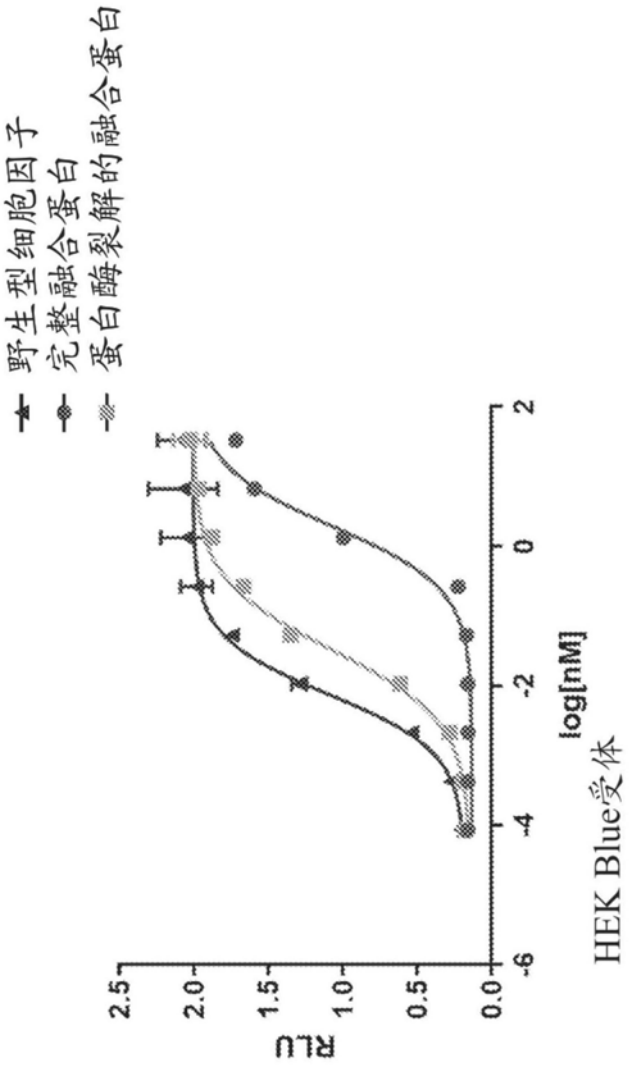
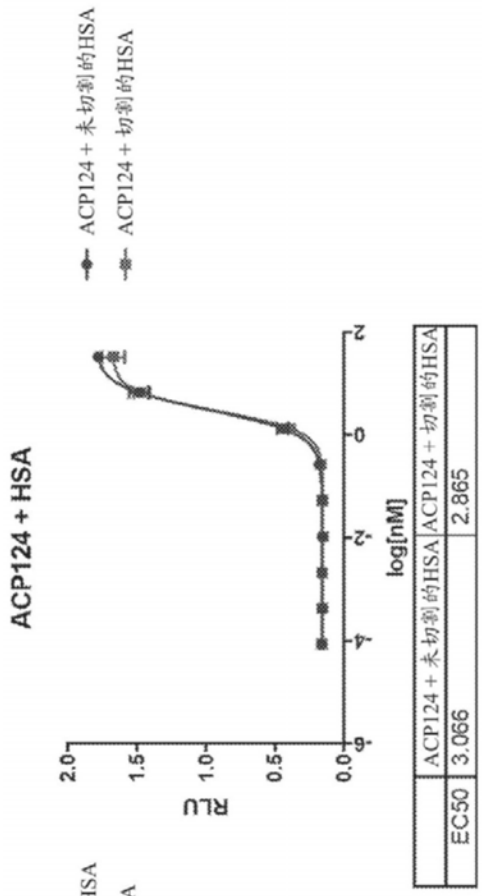

野生型细胞因子
完整融合蛋白
蛋白酶裂解的融合蛋白
RLU
2.5
2.0
1.5
1.0
0.5
0.0
-6
-4
-2
0
2
log[nM]
HEK Blue受体

图24D

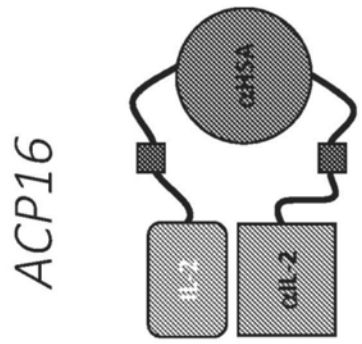


	未切割的ACP16+HSA	切割的ACP16+HSA
EC50	1.214	0.03146

图 25A

	ACP124 + 未切割的HSA	ACP124 + 切割的HSA
EC50	3.066	2.865

图 25B


ACP16
α-HSA
IL-2
cIL-2

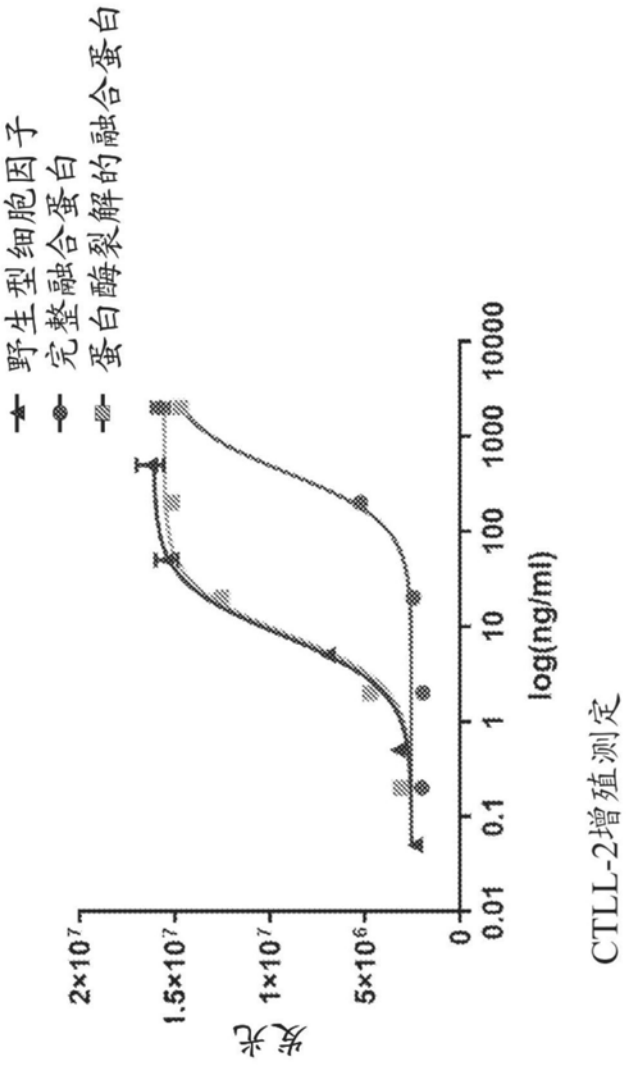
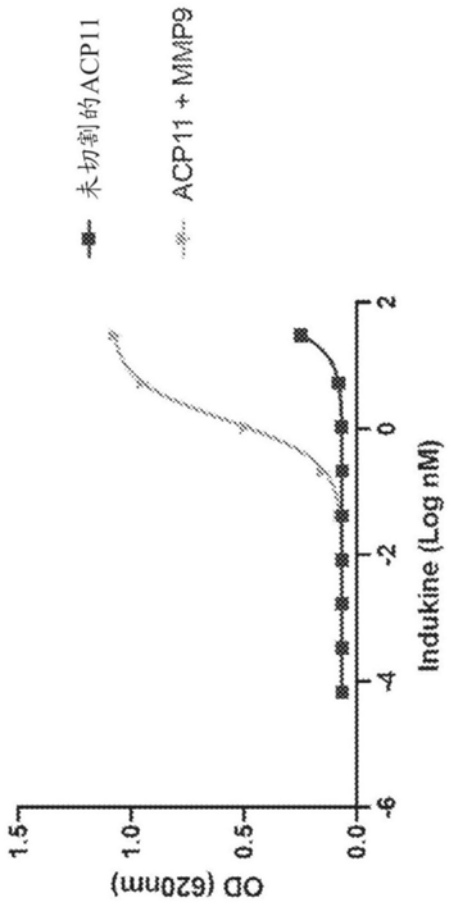

野生型细胞因子
完整融合蛋白
蛋白酶裂解的融合蛋白
2×10^7
1.5×10^7
1×10^7
5×10^6
0
0.01
0.1
1
10
100
1000
10000
log(ng/ml)
CTLL-2增殖测定

图25C



	未切割的ACP11	ACP11 + MMP9
EC50	~ 212.2	1.349

图26A

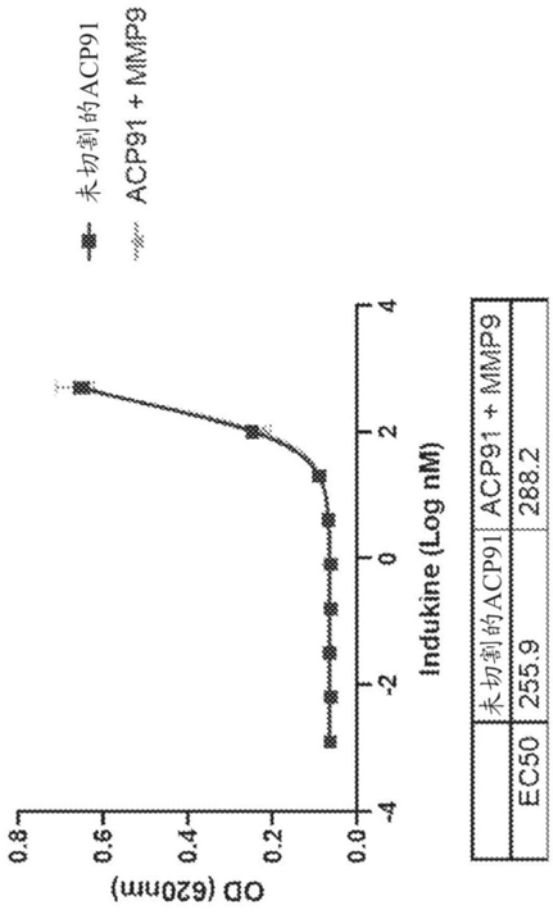

未切割的ACP91
ACP91 + MMP9
OD (620nm)
0.0
0.2
0.4
0.6
0.8
-4
-2
0
2
4
Indukine (Log nM)
未切割的ACP91
ACP91 + MMP9
EC50
255.9
288.2

图26B

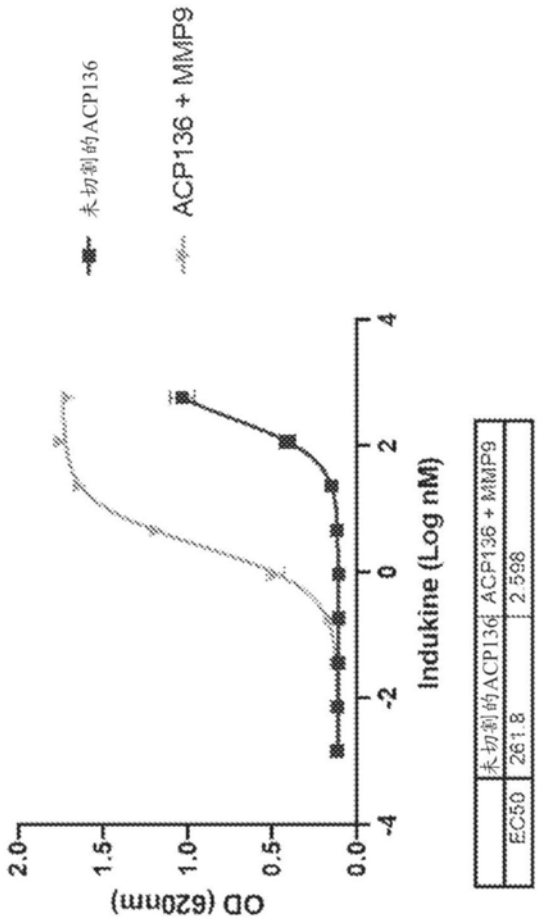
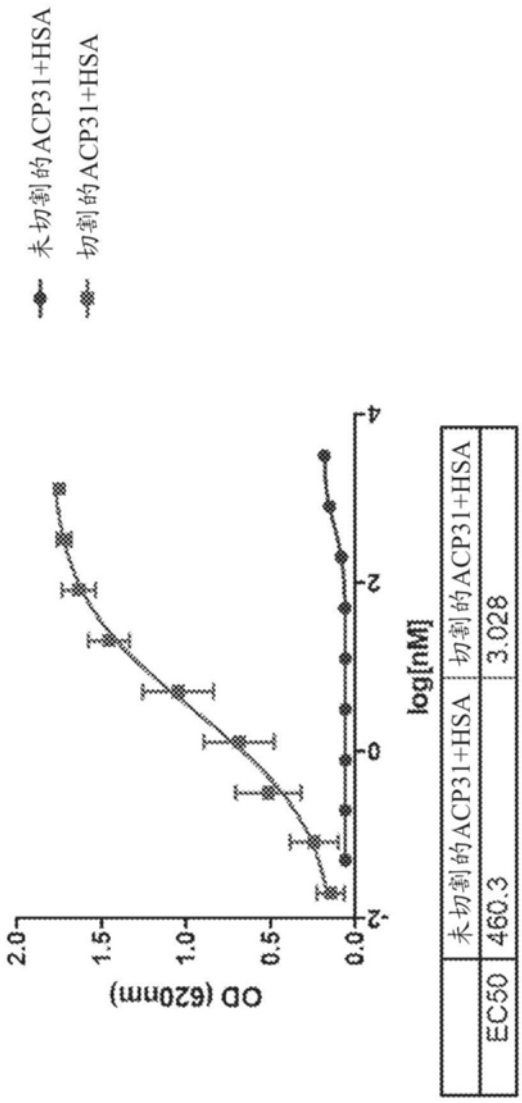

未切割的ACP136
ACP136 + MMP9
OD (620nm)
2.0
1.5
1.0
0.5
0.0
-4
-2
0
2
4
Indukine (Log nM)
未切割的ACP136
ACP136 + MMP9
EC50
261.8
2.598

图26C


未切割的ACP31+HSA
切割的ACP31+HSA
OD (620nm)
2.0
1.5
1.0
0.5
0.0
-2
0
2
4
log[nM]
未切割的ACP31+HSA
切割的ACP31+HSA
EC50
460.3
3.028

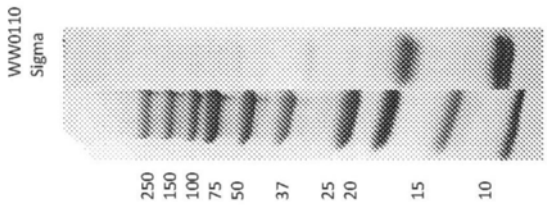
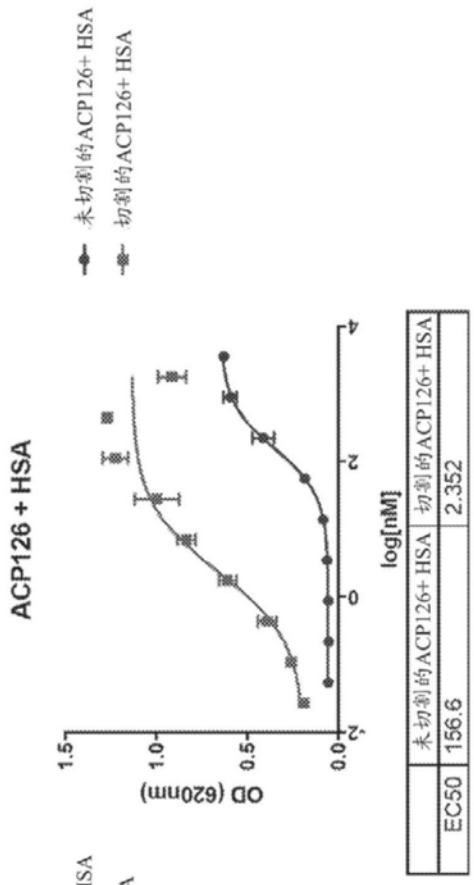

WW0110
Sigma
250
150
100
75
50
37
25
20
15
10

图27A



	ACPI25 +未切割的 HSA	ACPI25 +切割的 HSA
EC50	35.65	3.175

图 27B

	未切割的ACP126+ HSA	切割的ACP126+ HSA
EC50	156.6	2.352

图 27C

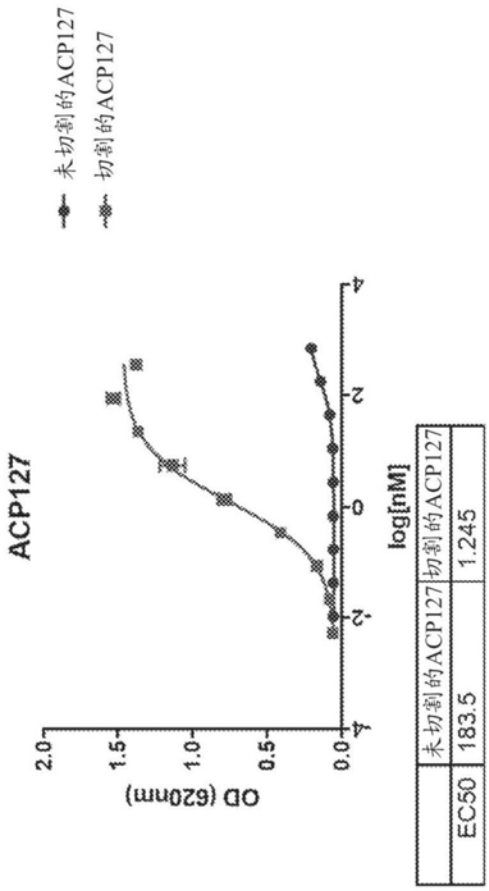

未切割的ACP127
切割的ACP127
ACP127
OD (620nm)
2.0
1.5
1.0
0.5
0.0
-4
-2
0
2
4
log[nM]
未切割的ACP127
切割的ACP127
EC50
183.5
1.245

图27D

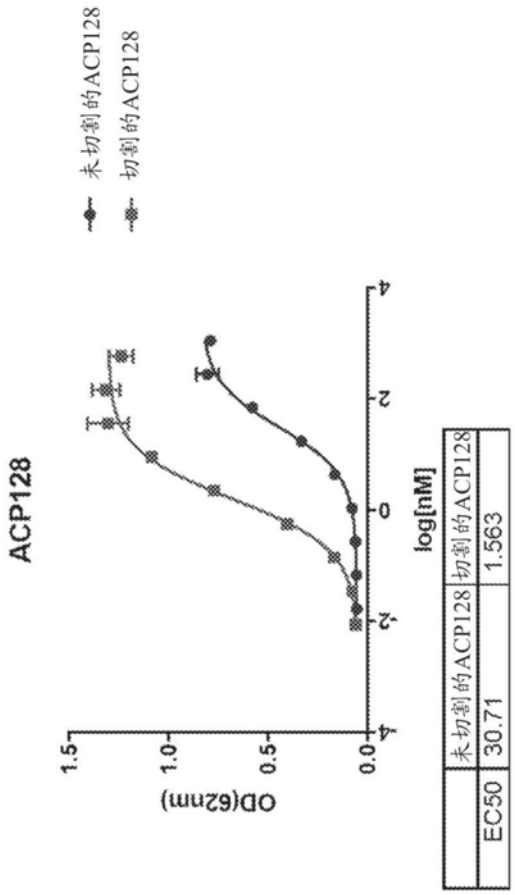

未切割的ACP128
切割的ACP128
ACP128
OD(62nm)
1.5
1.0
0.5
0.0
-4
-2
0
2
4
log[nM]
EC50
未切割的ACP128
30.71
切割的ACP128
1.563

图27E

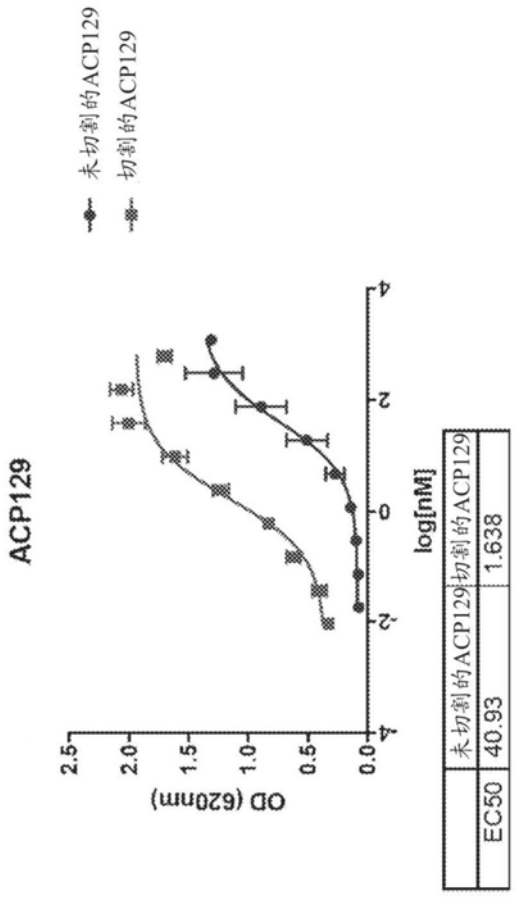

未切割的ACP129
切割的ACP129
ACP129
OD (620nm)
2.5
2.0
1.5
1.0
0.5
0.0
-4
-2
0
2
4
log[nM]
EC50
未切割的ACP129
40.93
切割的ACP129
1.638

图27F

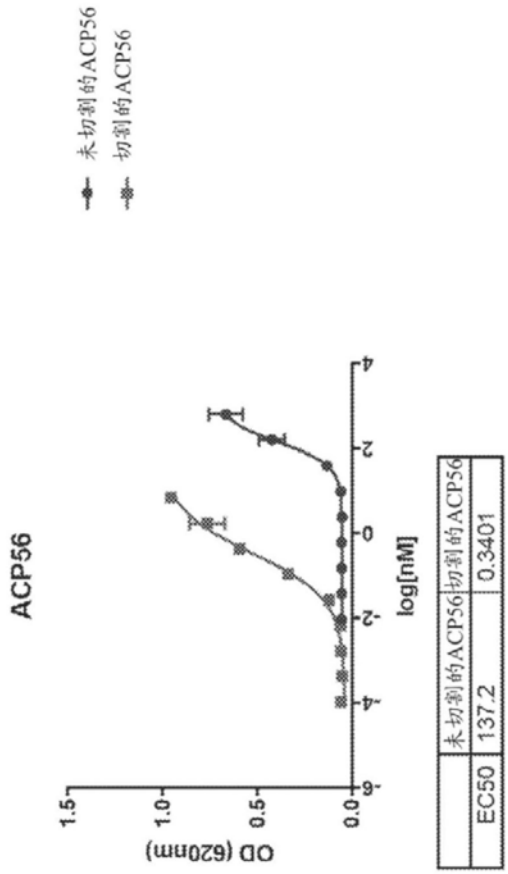

未切割的ACP56
切割的ACP56
ACP56
OD (620nm)
1.5
1.0
0.5
0.0
-6
-4
-2
0
2
4
log[nM]
未切割的ACP56
切割的ACP56
EC50
137.2
0.3401

图28A

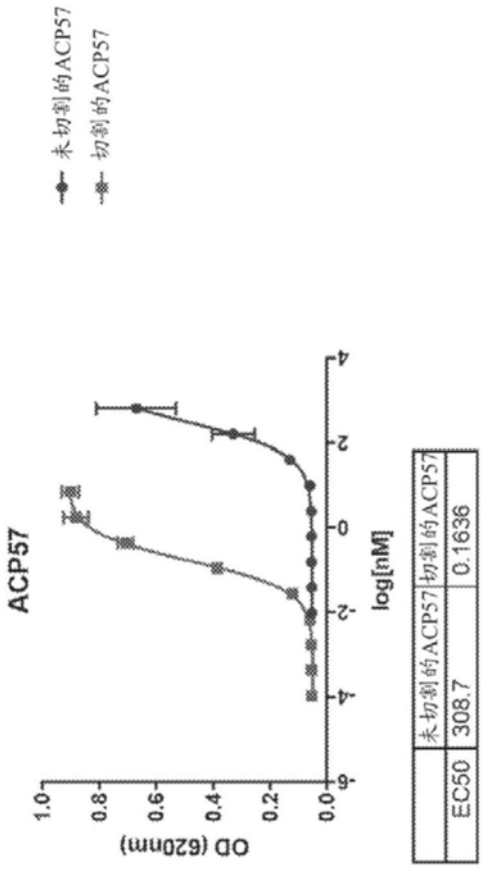

未切割的ACP57
切割的ACP57
ACP57
OD (620nm)
1.0
0.8
0.6
0.4
0.2
0.0
-6
-4
-2
0
2
4
log[nM]
未切割的ACP57
切割的ACP57
EC50
308.7
0.1636

图28B

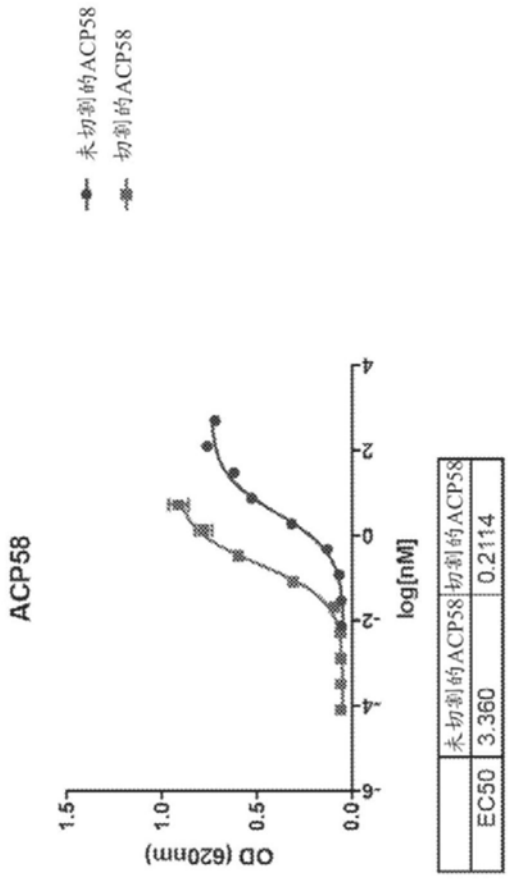

未切割的ACP58
切割的ACP58
ACP58
OD (620nm)
1.5
1.0
0.5
0.0
-6
-4
-2
0
2
4
log[nM]
未切割的ACP58
切割的ACP58
EC50
3.360
0.2114

图28C

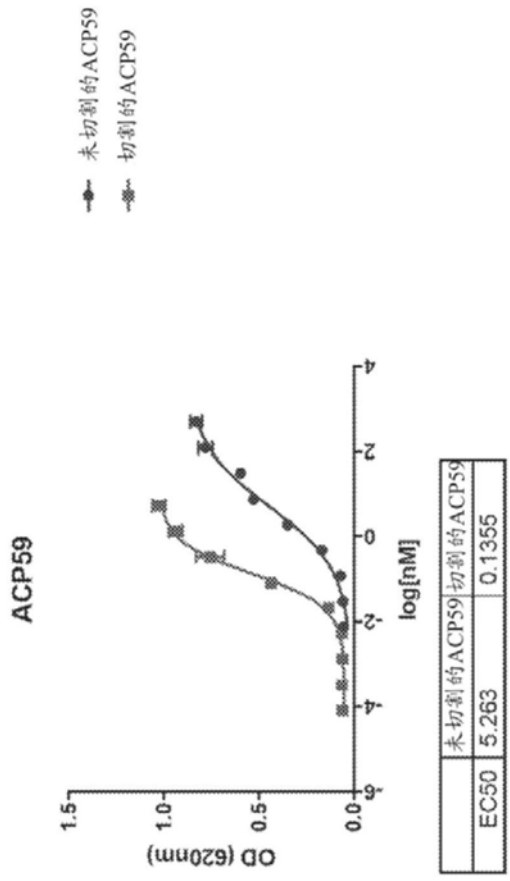
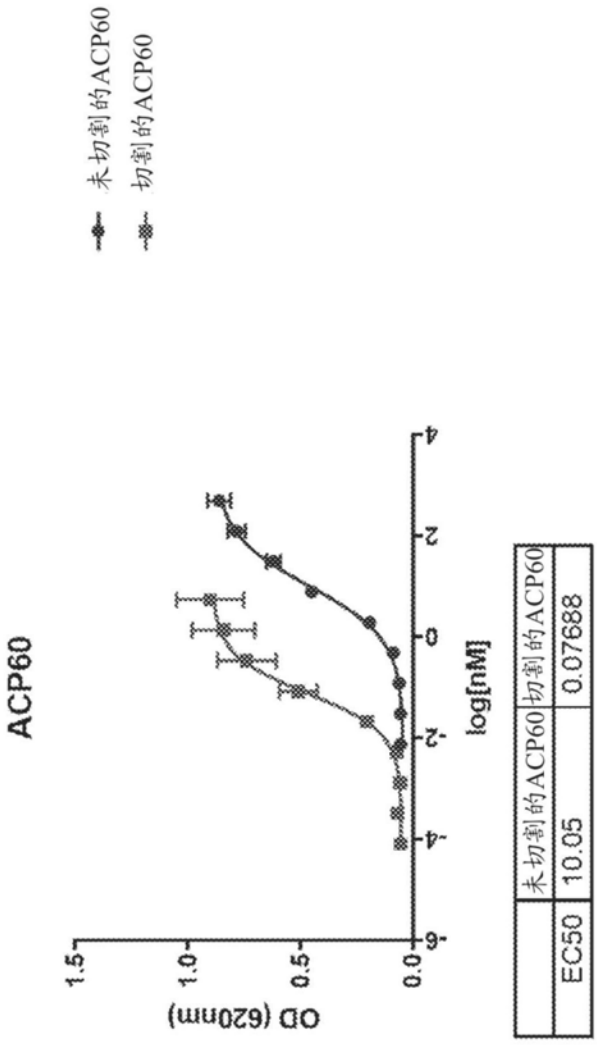

未切割的ACP59
切割的ACP59
ACP59
OD (620nm)
1.5
1.0
0.5
0.0
-6
-4
-2
0
2
4
log[nM]
未切割的ACP59 切割的ACP59
EC50 5.263 0.1355

图28D



	未切割的ACP60	切割的ACP60
EC50	10.05	0.07688

图28E

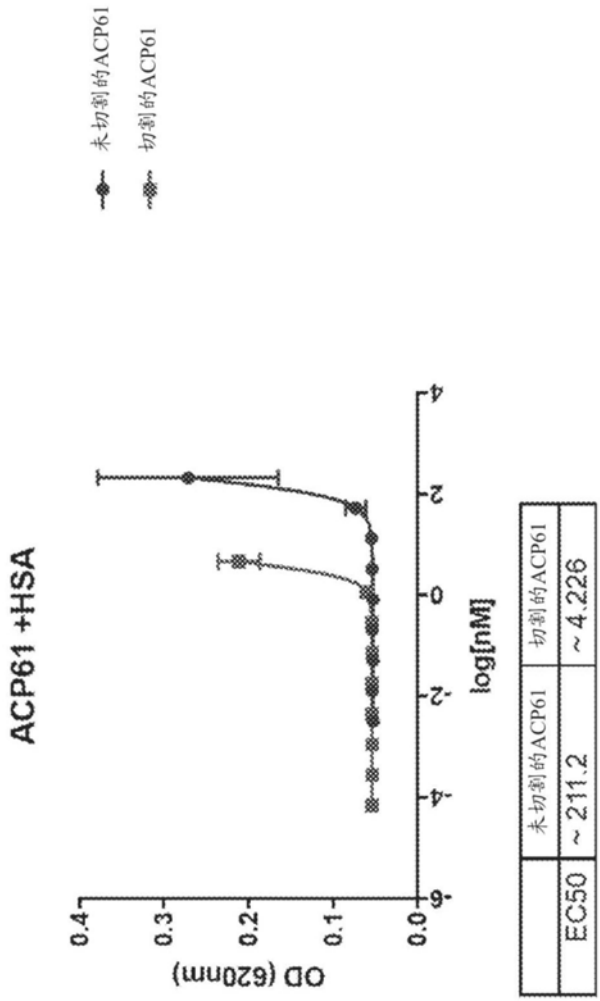
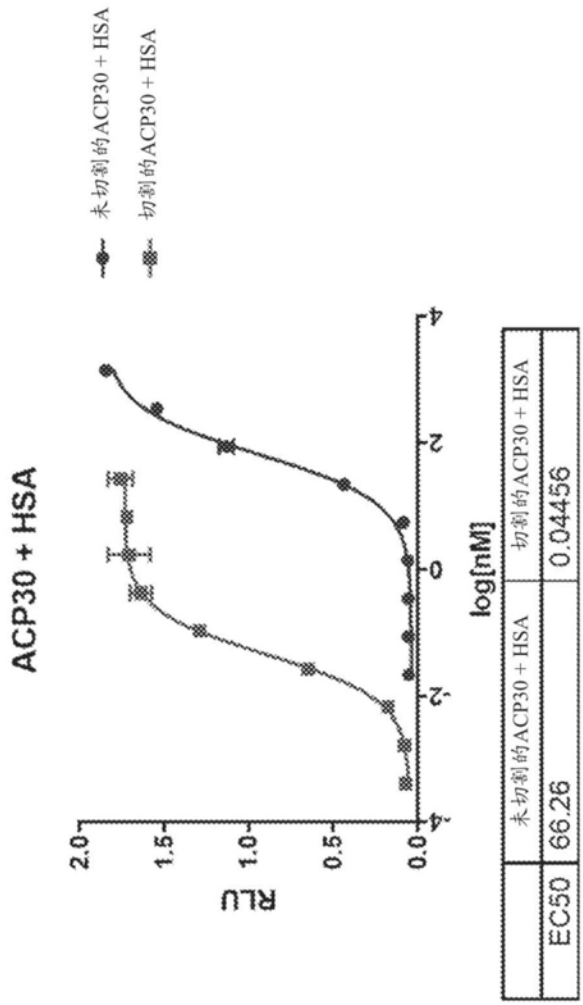

未切割的ACP61
切割的ACP61
ACP61 +HSA
OD (620nm)
0.4
0.3
0.2
0.1
0.0
-6
-4
-2
0
2
4
log[nM]
未切割的ACP61
切割的ACP61
EC50
~ 211.2
~ 4.226

图28F



	未切割的ACP30 + HSA	切割的ACP30 + HSA
EC50	66.26	0.04456

图28G

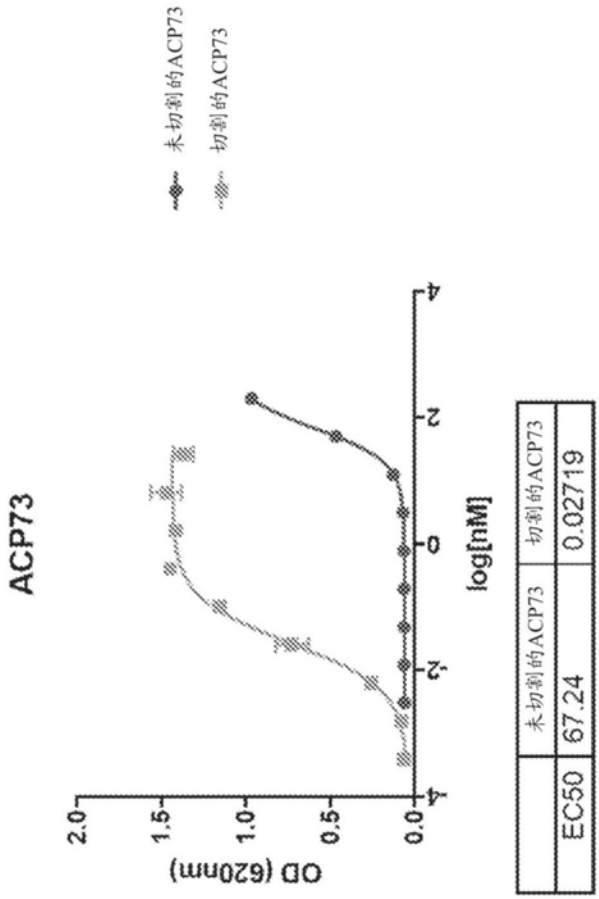
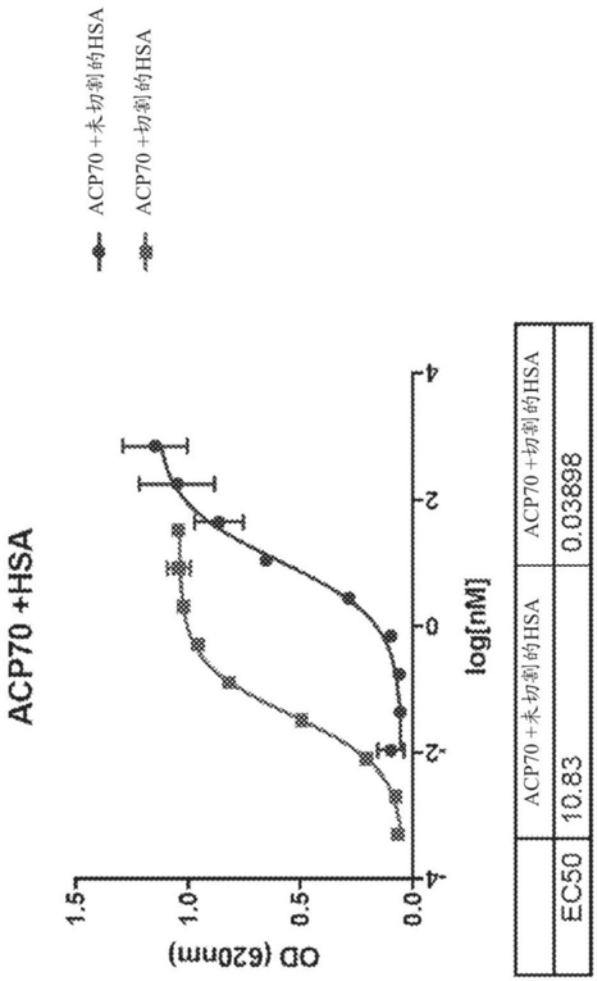

未切割的ACP73
切割的ACP73
ACP73
OD (620nm)
2.0
1.5
1.0
0.5
0.0
-4
-2
0
2
4
log[nM]
EC50
未切割的ACP73
67.24
切割的ACP73
0.02719

图28H



	ACP70 +未切割的HSA	ACP70 +切割的HSA
EC50	10.83	0.03898

图28i

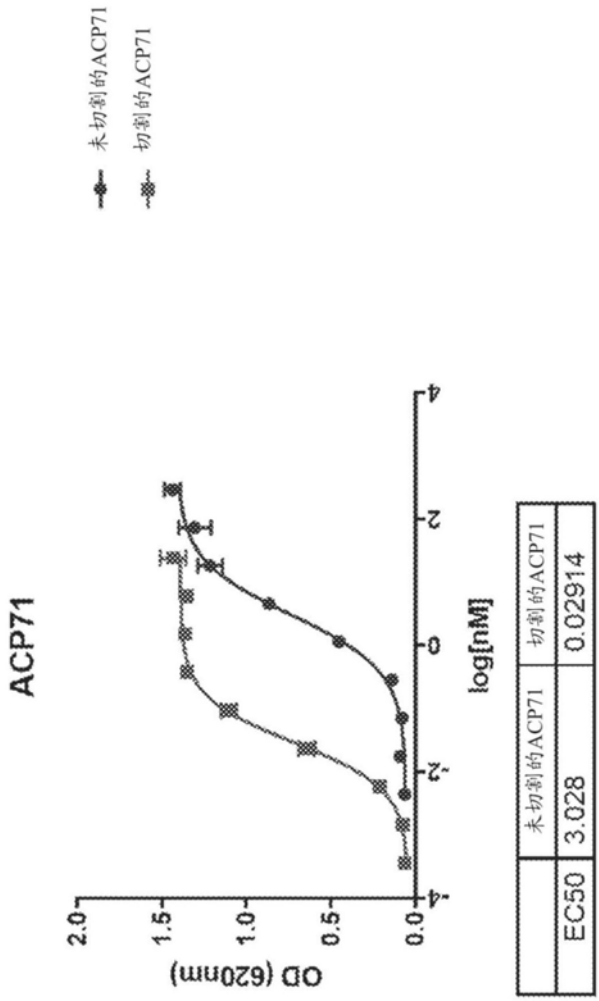

未切割的ACP71
切割的ACP71
ACP71
OD (620nm)
2.0
1.5
1.0
0.5
0.0
-4
-2
0
2
4
log[nM]
EC50
未切割的ACP71
3.028
切割的ACP71
0.02914

图28J

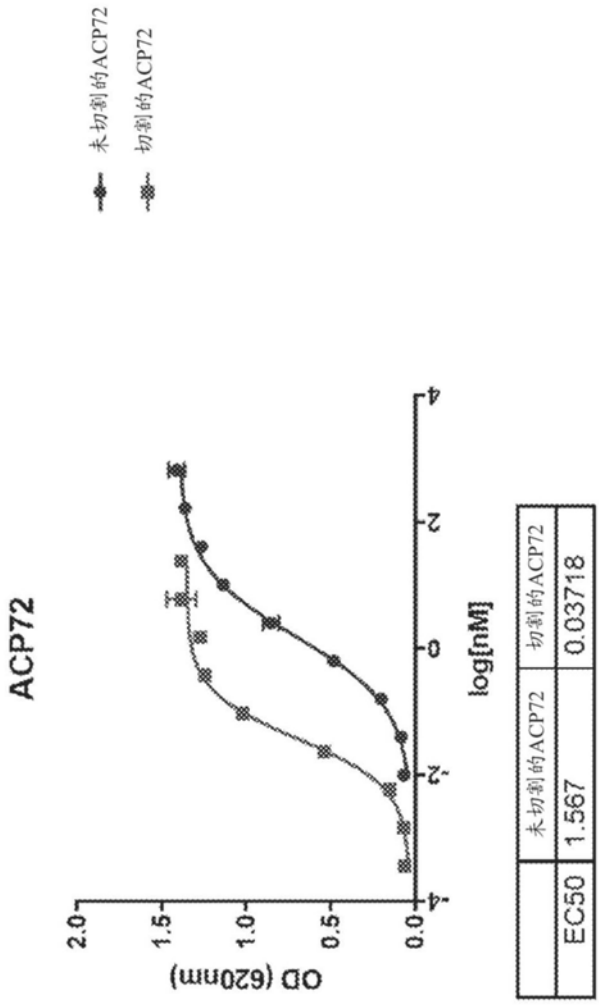

未切割的ACP72
切割的ACP72
ACP72
OD (620nm)
2.0
1.5
1.0
0.5
0.0
-4
-2
0
2
4
log[nM]
EC50
未切割的ACP72
1.567
切割的ACP72
0.03718

图28K

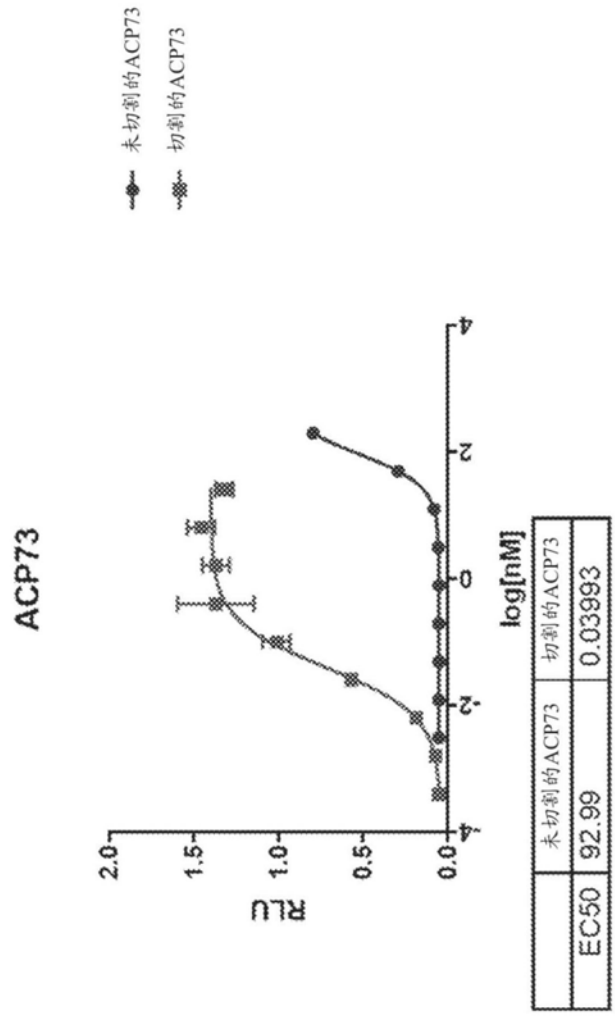

未切割的ACP73
切割的ACP73
ACP73
RLU
2.0
1.5
1.0
0.5
0.0
-4
-2
0
2
4
log[nM]
未切割的ACP73
切割的ACP73
EC50
92.99
0.03993

图28L

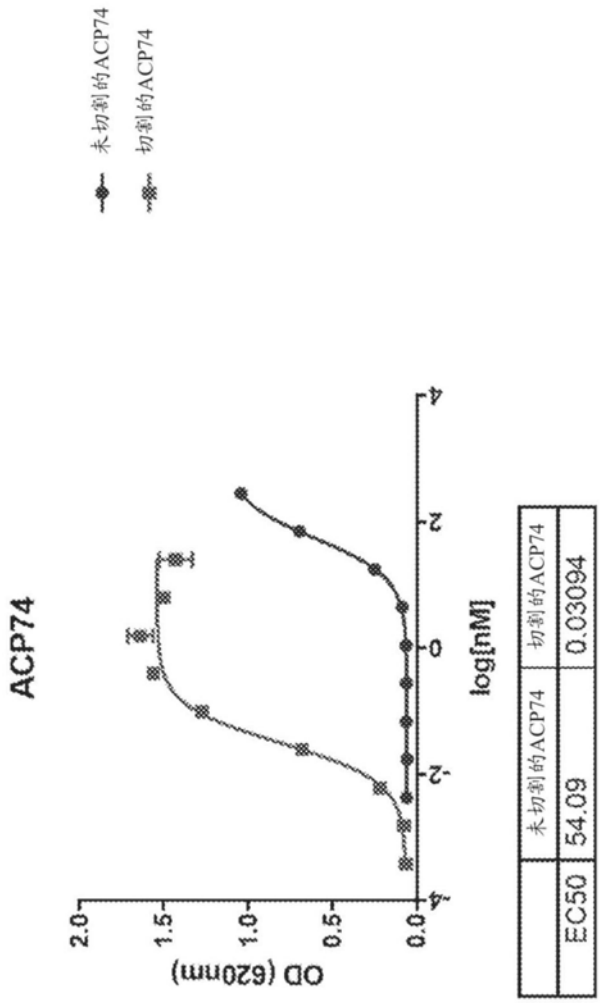
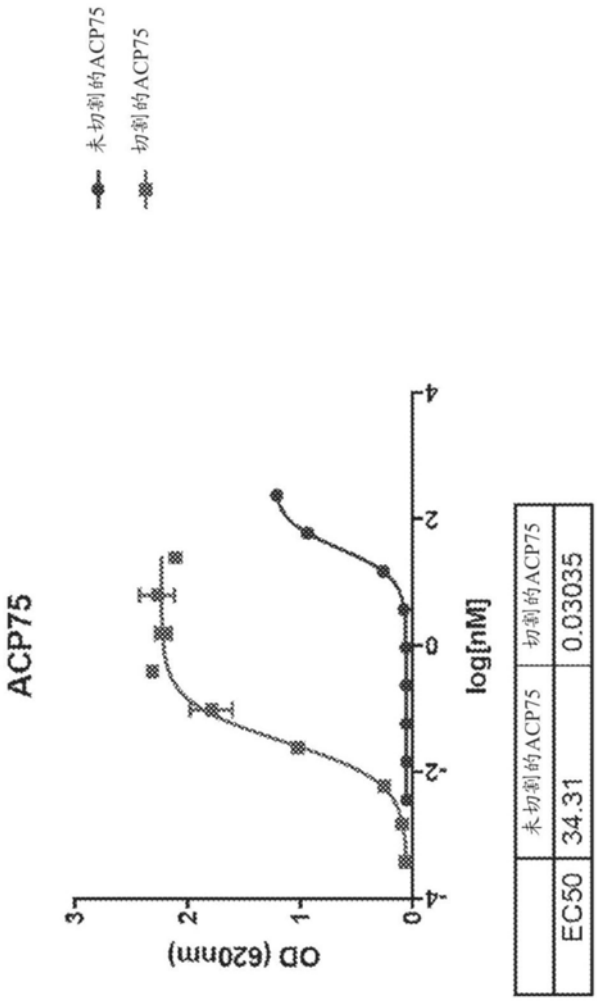

未切割的ACP74
切割的ACP74
ACP74
OD (620nm)
2.0
1.5
1.0
0.5
0.0
-4
-2
0
2
4
log[nM]
未切割的ACP74
切割的ACP74
EC50
54.09
0.03094

图28M



	未切割的ACP75	切割的ACP75
EC50	34.31	0.03035

图28N

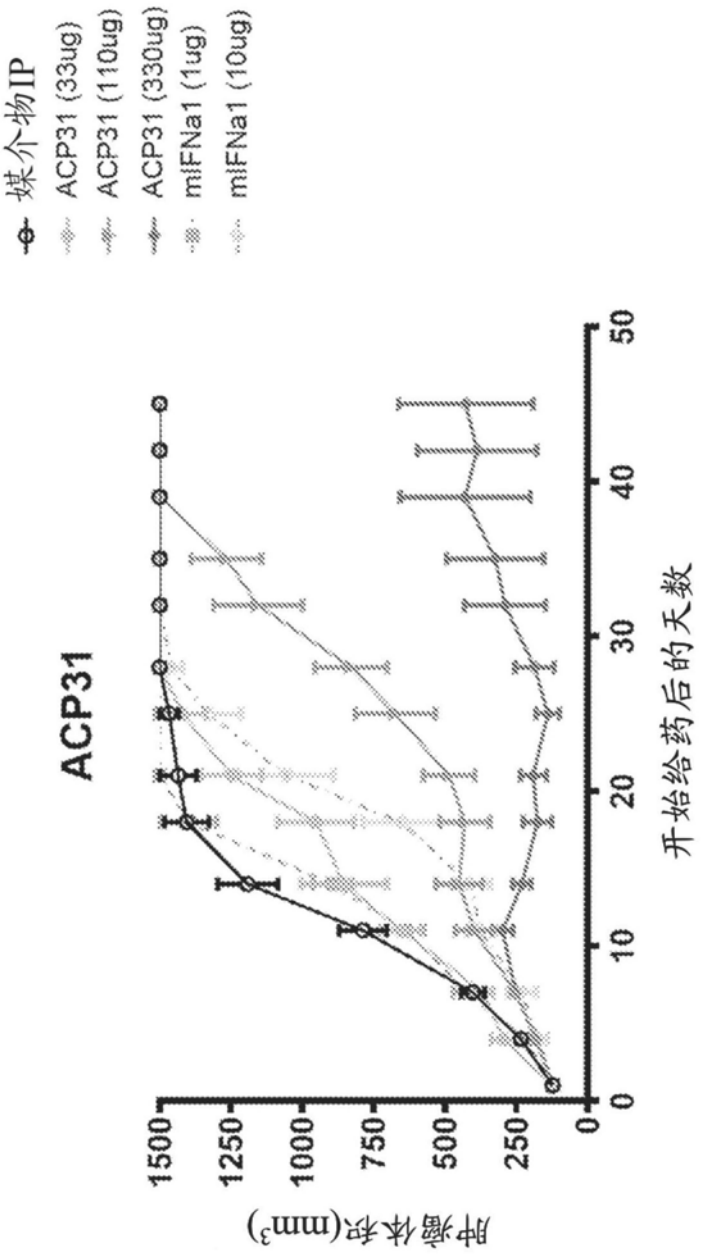

媒介物IP
ACP31 (33ug)
ACP31 (110ug)
ACP31 (330ug)
mIFNa1 (1ug)
mIFNa1 (10ug)
ACP31
肿瘤体积(mm³)
1500
1250
1000
750
500
250
0
0
10
20
30
40
50
开始给药后的天数

图29A

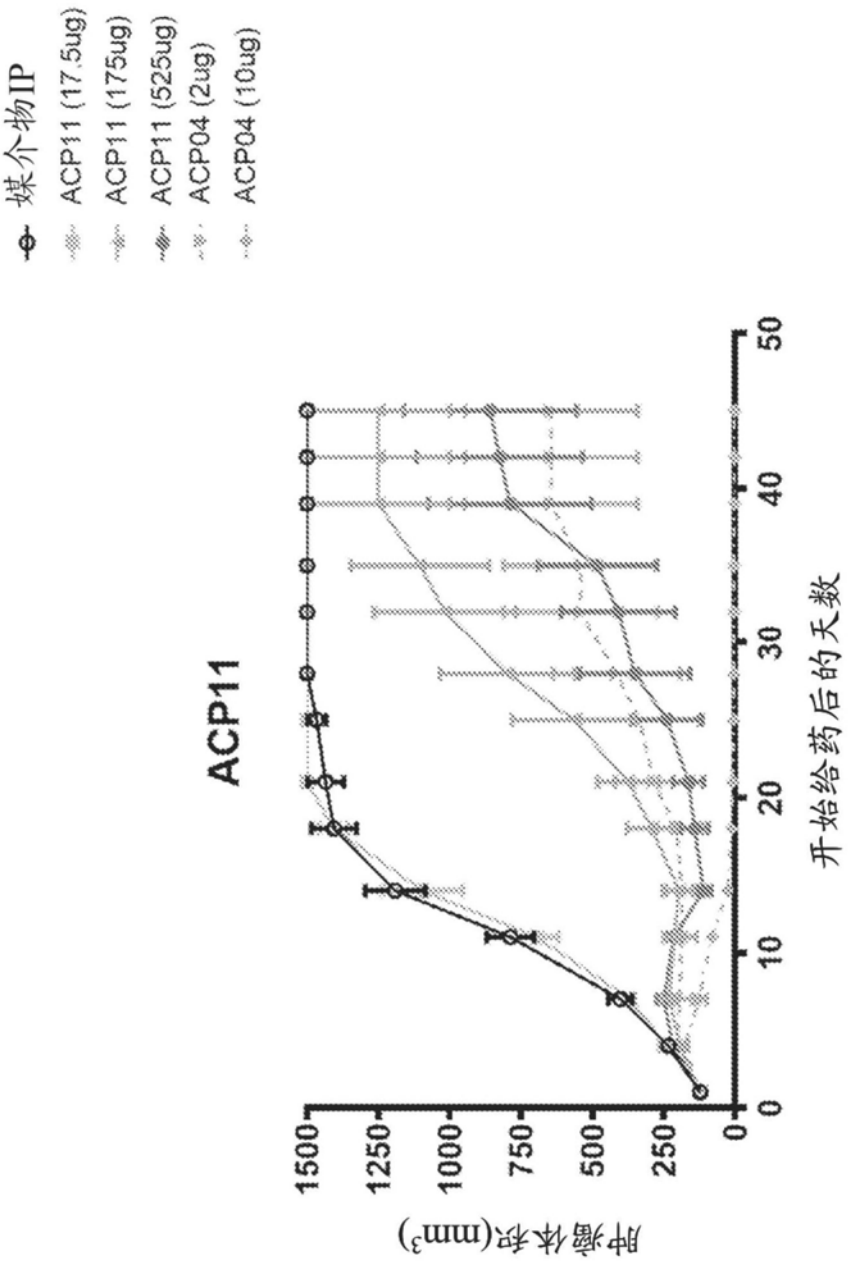

媒介物IP
ACP11 (17.5ug)
ACP11 (175ug)
ACP11 (525ug)
ACP04 (2ug)
ACP04 (10ug)
ACP11
肿瘤体积(mm³)
1500
1250
1000
750
500
250
0
0
10
20
30
40
50
开始给药后的天数

图29B

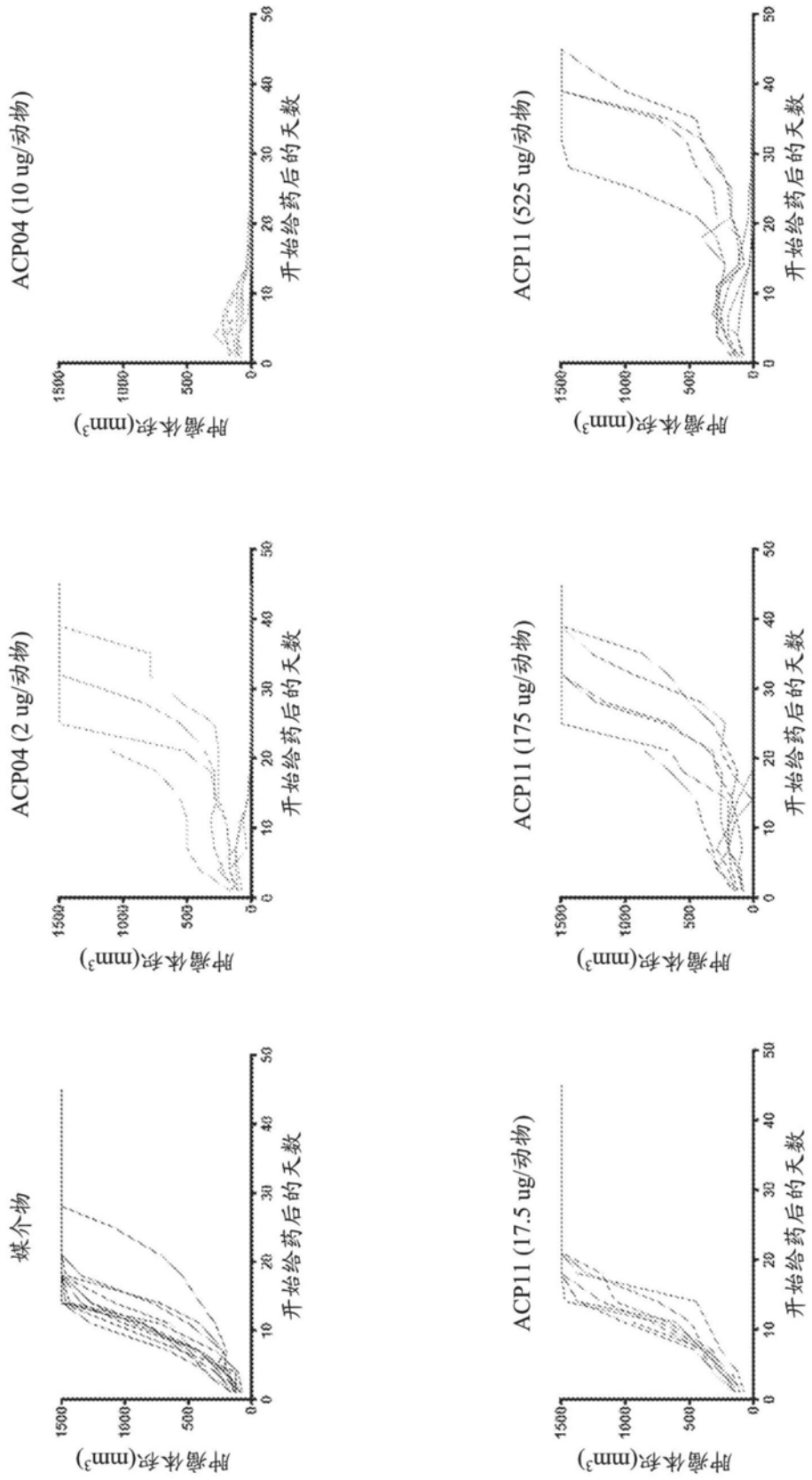

媒介物
ACP04 (2 ug/动物)
ACP04 (10 ug/动物)
ACP11 (17.5 ug/动物)
ACP11 (175 ug/动物)
ACP11 (525 ug/动物)
肿瘤体积(mm³)
开始给药后的天数
0
500
1000
1500
10
20
30
40
50

图30

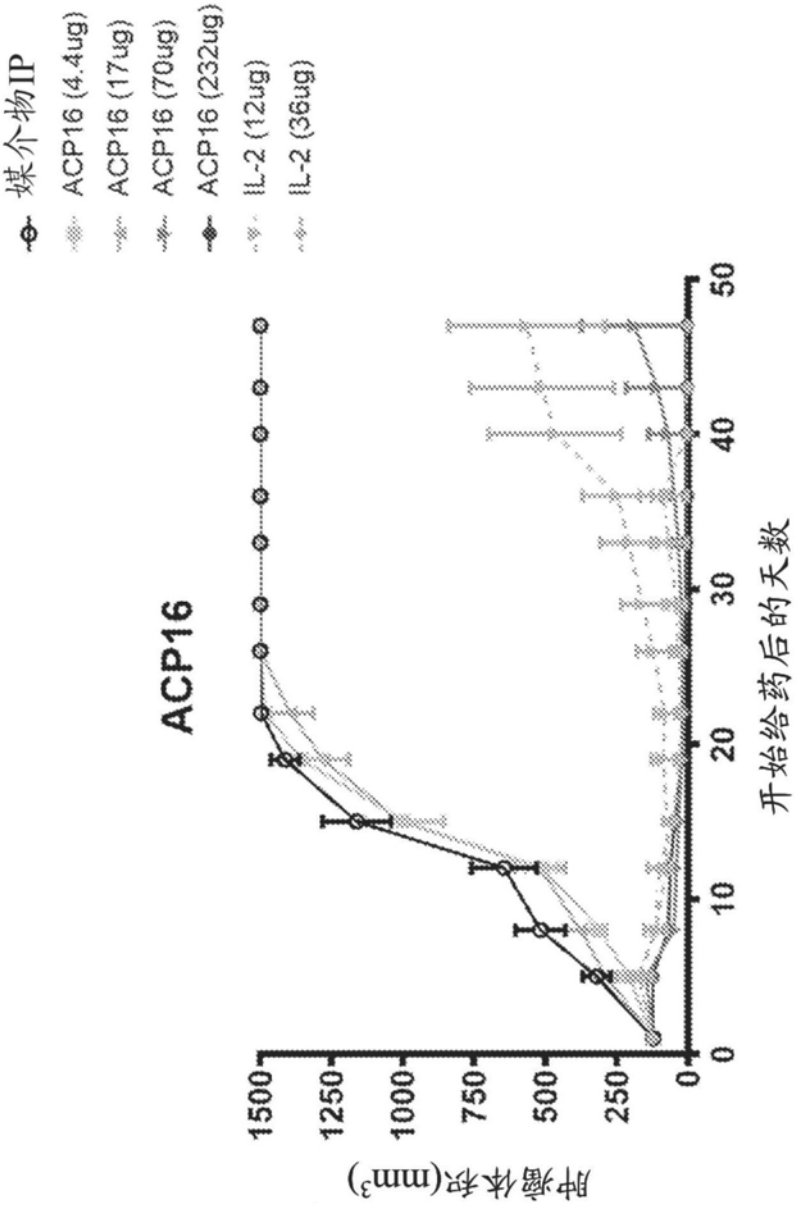

媒介物IP
ACP16 (4.4ug)
ACP16 (17ug)
ACP16 (70ug)
ACP16 (232ug)
IL-2 (12ug)
IL-2 (36ug)
ACP16
肿瘤体积(mm3)
1500
1250
1000
750
500
250
0
0
10
20
30
40
50
开始给药后的天数

图31A

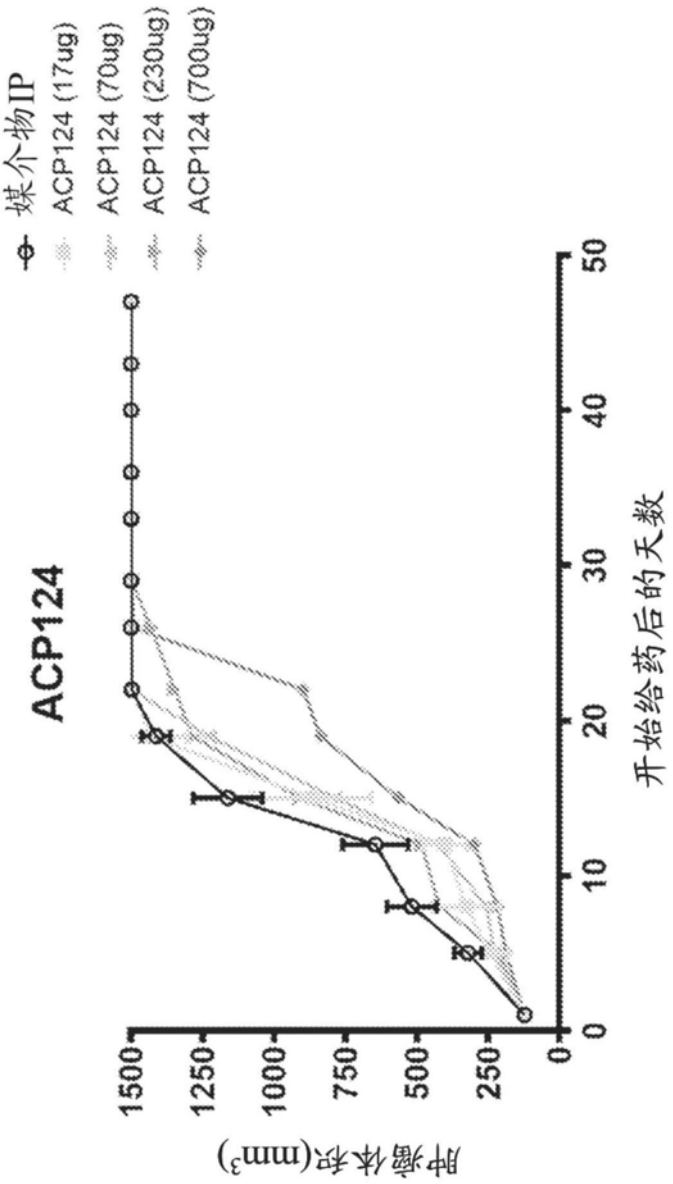

媒介物IP
ACP124 (17ug)
ACP124 (70ug)
ACP124 (230ug)
ACP124 (700ug)
ACP124
肿瘤体积(mm3)
1500
1250
1000
750
500
250
0
0
10
20
30
40
50
开始给药后的天数

图31B

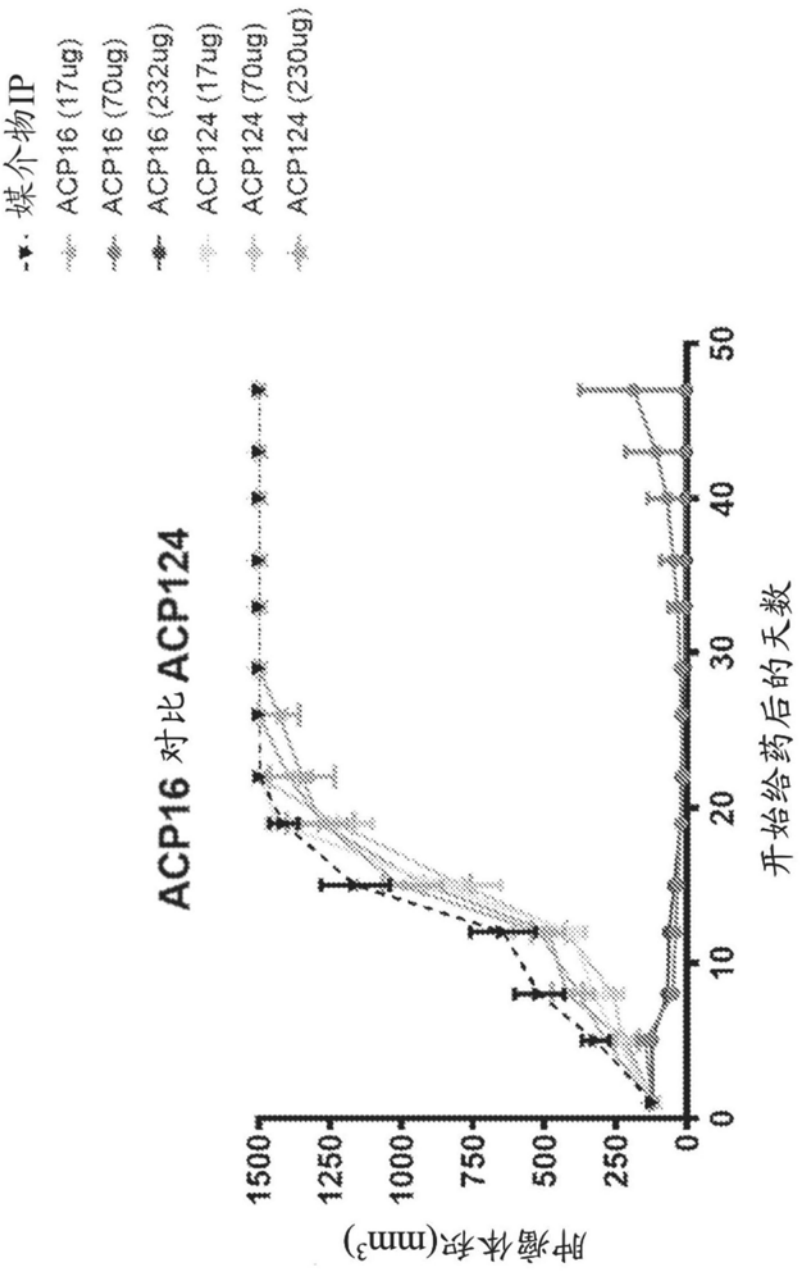

媒介物IP
ACP16 (17ug)
ACP16 (70ug)
ACP16 (232ug)
ACP124 (17ug)
ACP124 (70ug)
ACP124 (230ug)
ACP16 对比 ACP124
肿瘤体积(mm³)
1500
1250
1000
750
500
250
0
0
10
20
30
40
50
开始给药后的天数

图31C

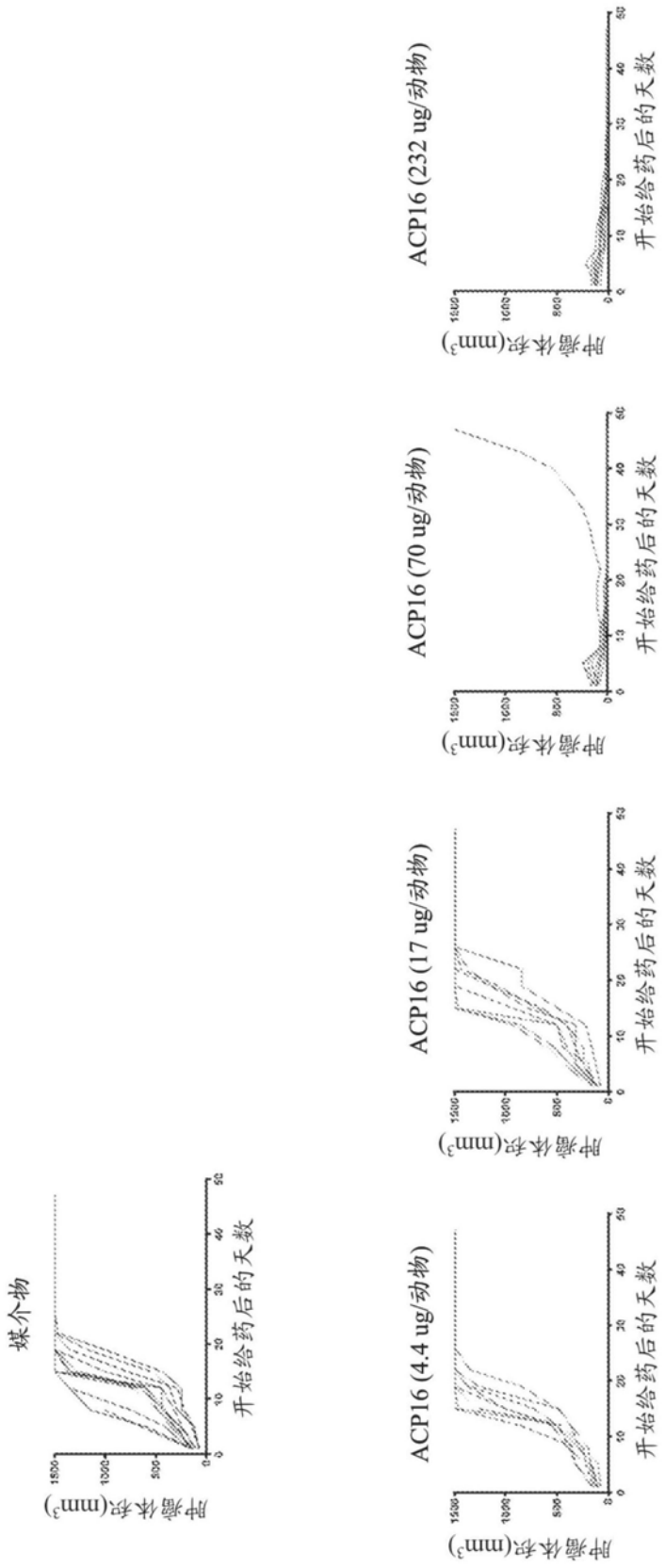

媒介物
ACP16 (4.4 ug/动物)
ACP16 (17 ug/动物)
ACP16 (70 ug/动物)
ACP16 (232 ug/动物)
肿瘤体积(mm³)
开始给药后的天数

图32A

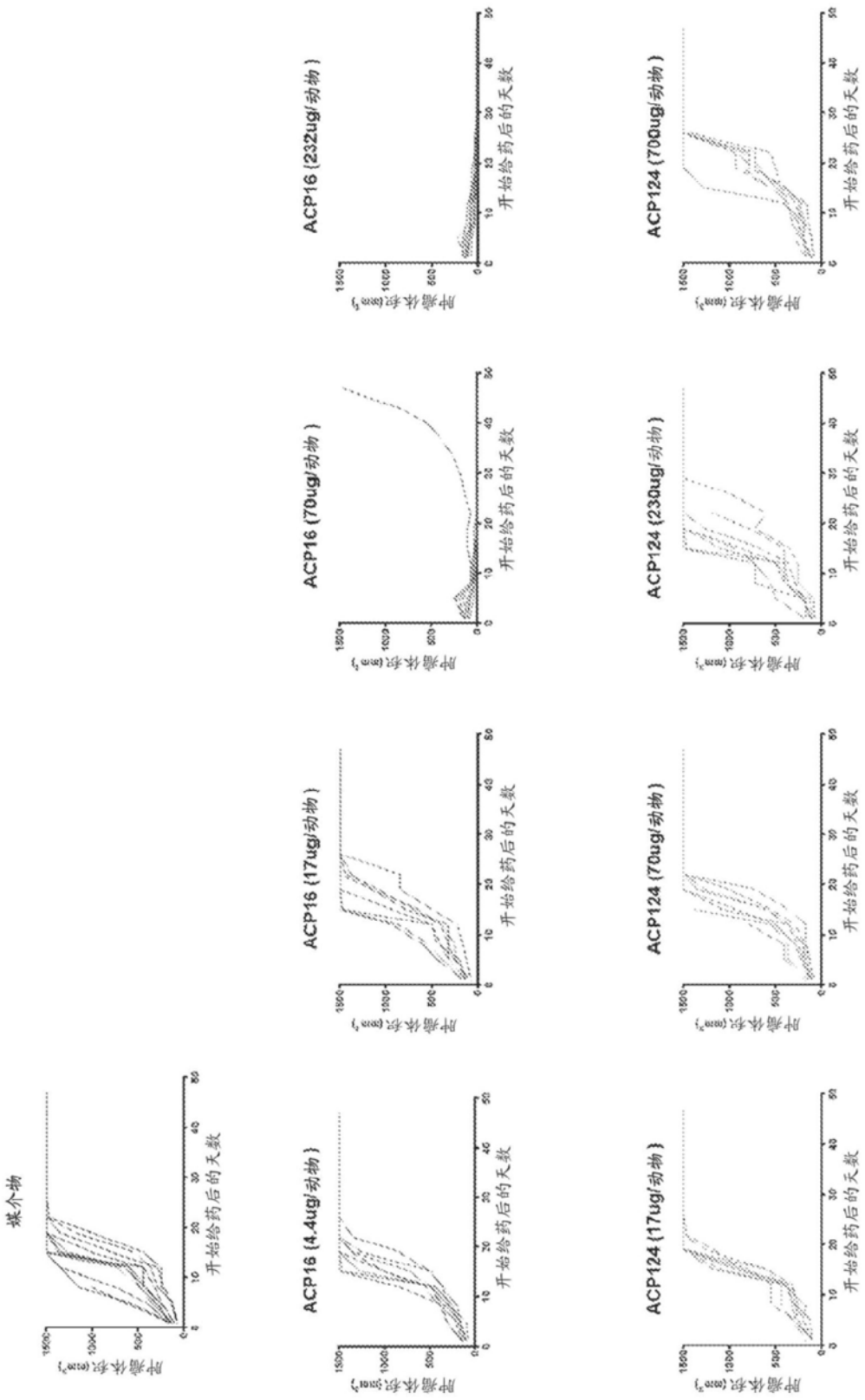

媒介物
ACP16 (4.4ug/动物)
ACP16 (17ug/动物)
ACP16 (70ug/动物)
ACP16 (232ug/动物)
ACP124 (17ug/动物)
ACP124 (70ug/动物)
ACP124 (230ug/动物)
ACP124 (700ug/动物)
开始给药后的天数

图32B

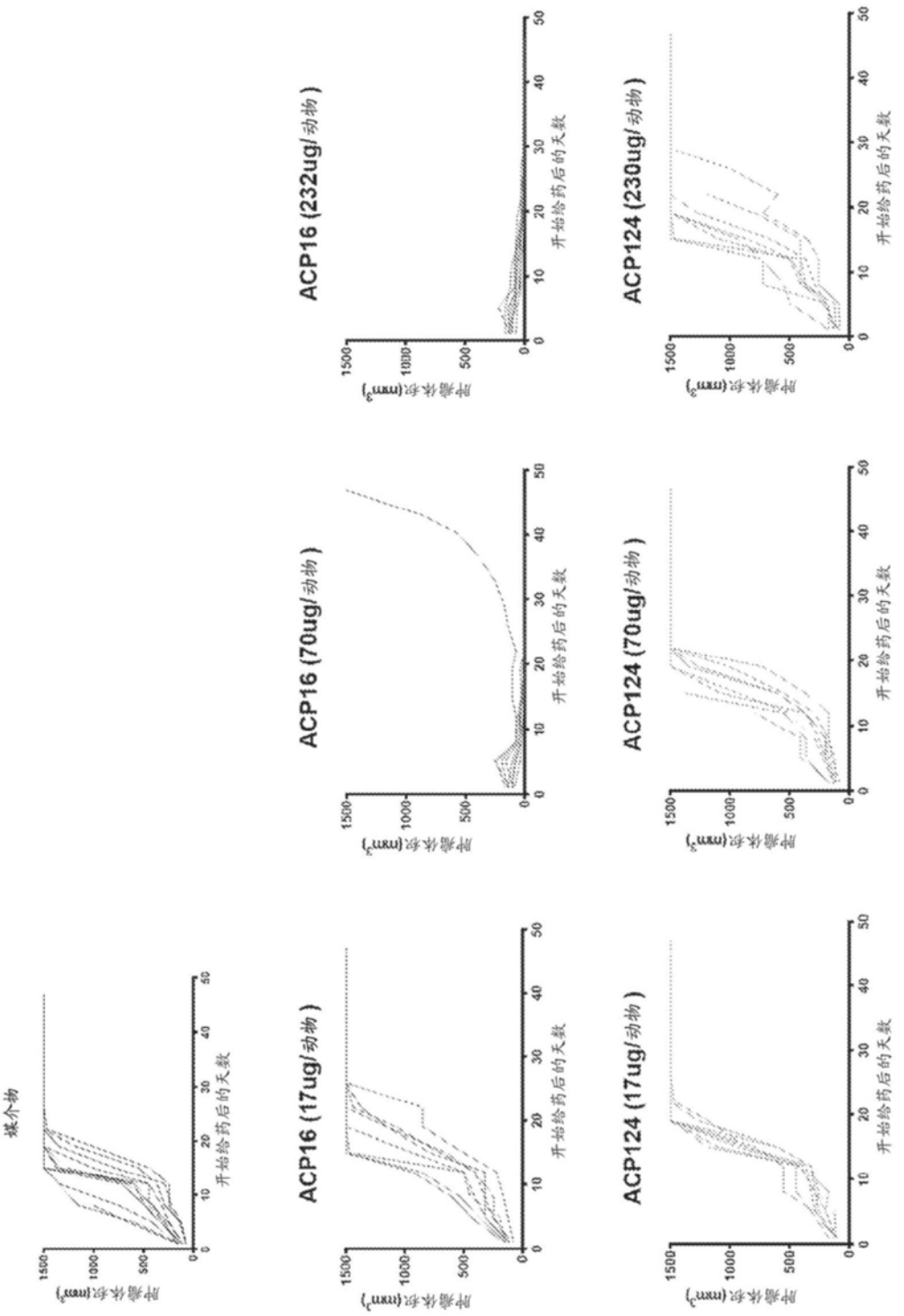

媒介物
ACP16 (17ug/动物)
ACP16 (70ug/动物)
ACP16 (232ug/动物)
ACP124 (17ug/动物)
ACP124 (70ug/动物)
ACP124 (230ug/动物)
平均体积 (mm³)
开始给药后的天数
0
500
1000
1500
10
20
30
40
50

图32C

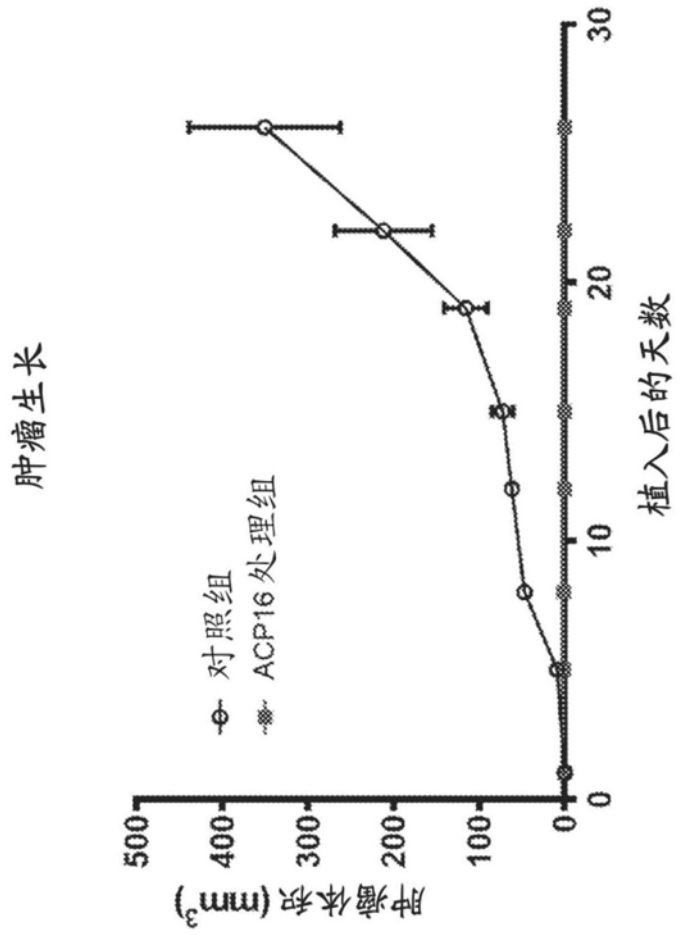

肿瘤生长
肿瘤体积 (mm³)
500
400
300
200
100
0
0
10
20
30
植入后的天数
对照组
ACP16处理组

图33

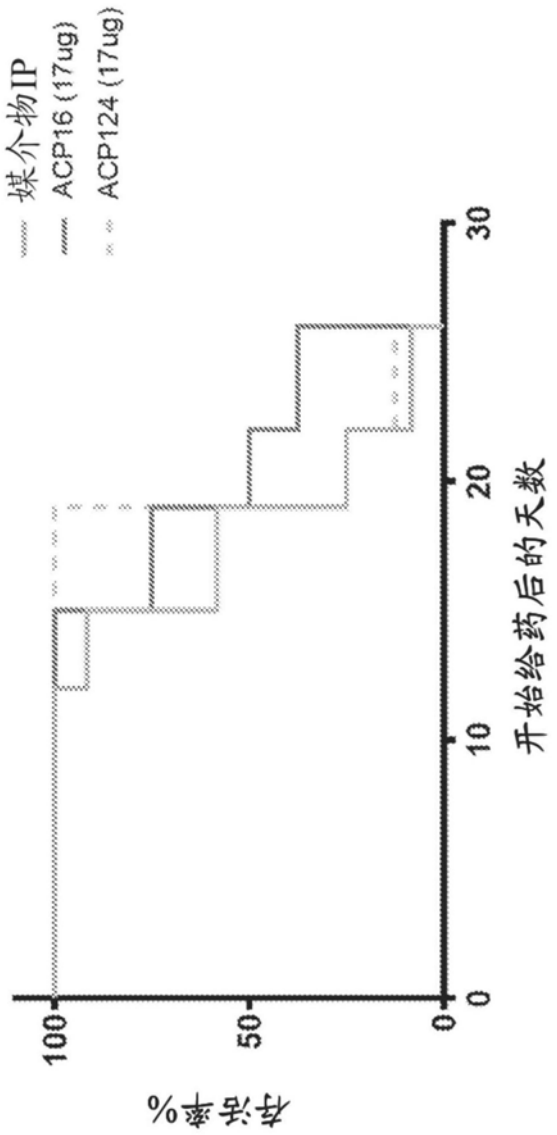


图34A

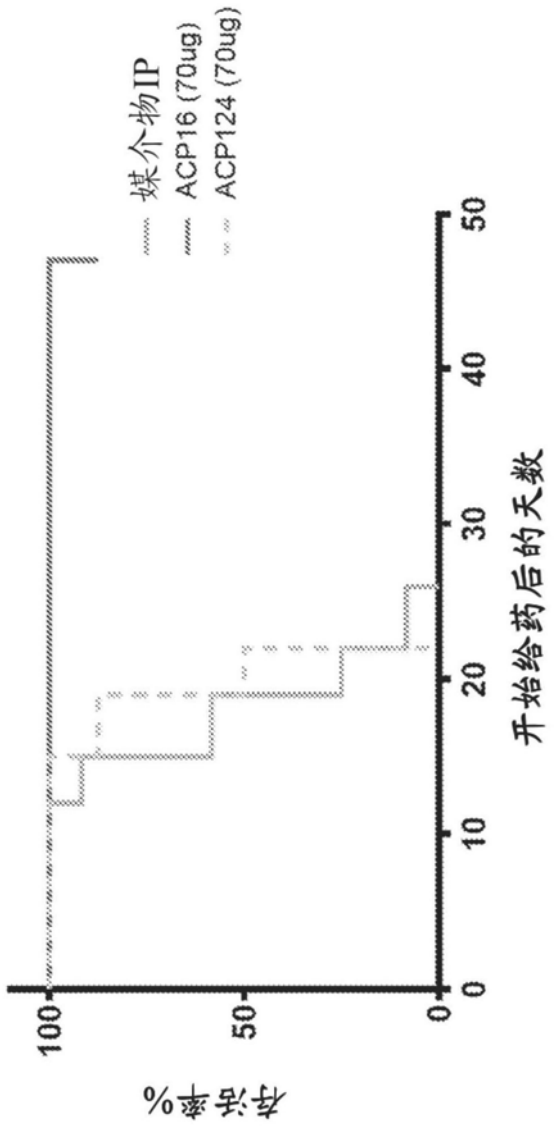

媒介物IP
ACP16 (70ug)
ACP124 (70ug)
存活率%
100
50
0
0
10
20
30
40
50
开始给药后的天数

图34B

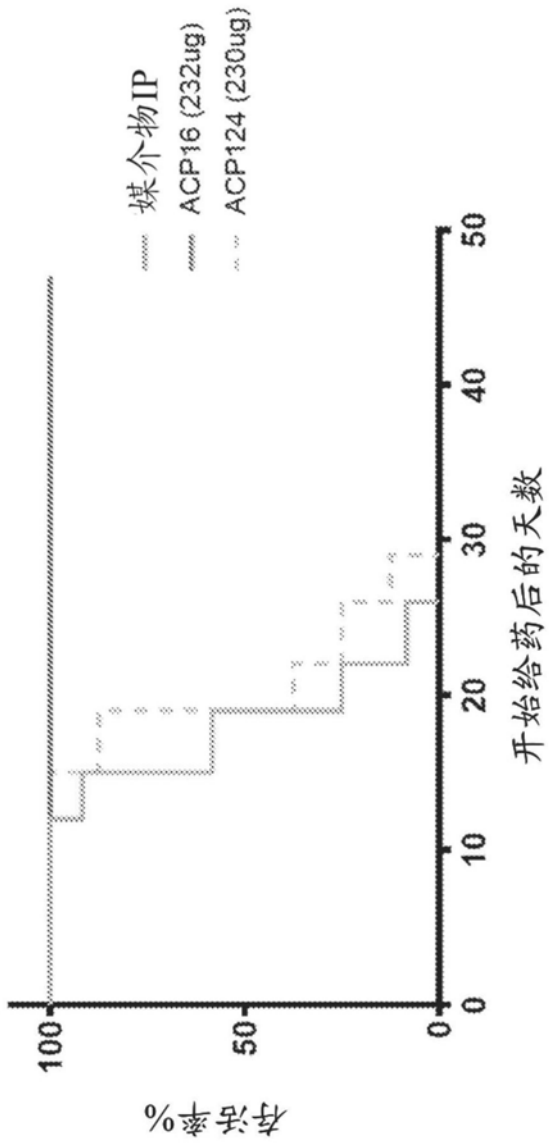

媒介物IP
ACP16 (232ug)
ACP124 (230ug)
存活率%
100
50
0
0
10
20
30
40
50
开始给药后的天数

图34C

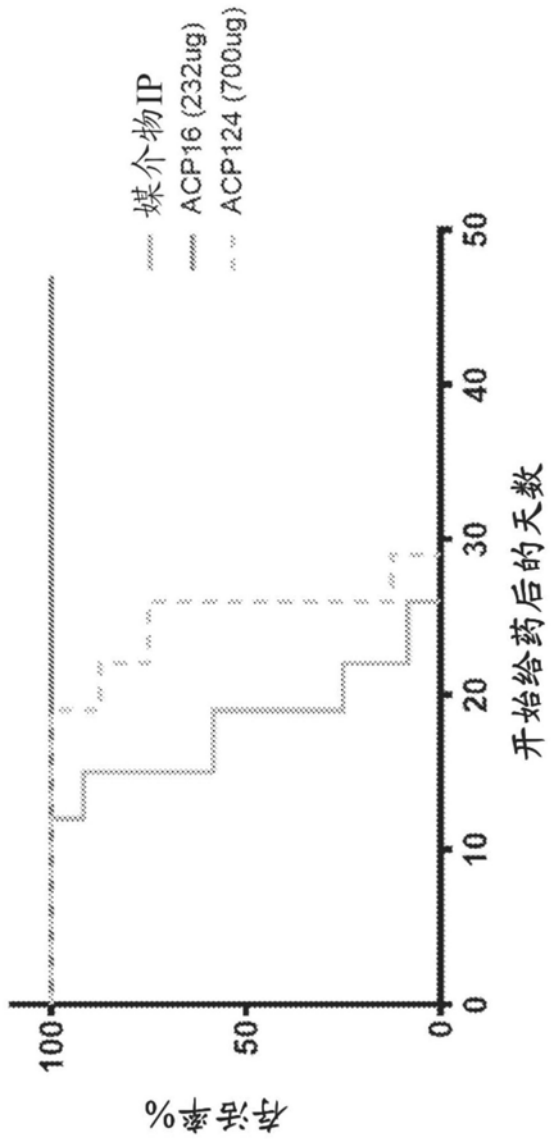

媒介物IP
ACP16 (232ug)
ACP124 (700ug)
存活率%
100
50
0
0
10
20
30
40
50
开始给药后的天数

图34D

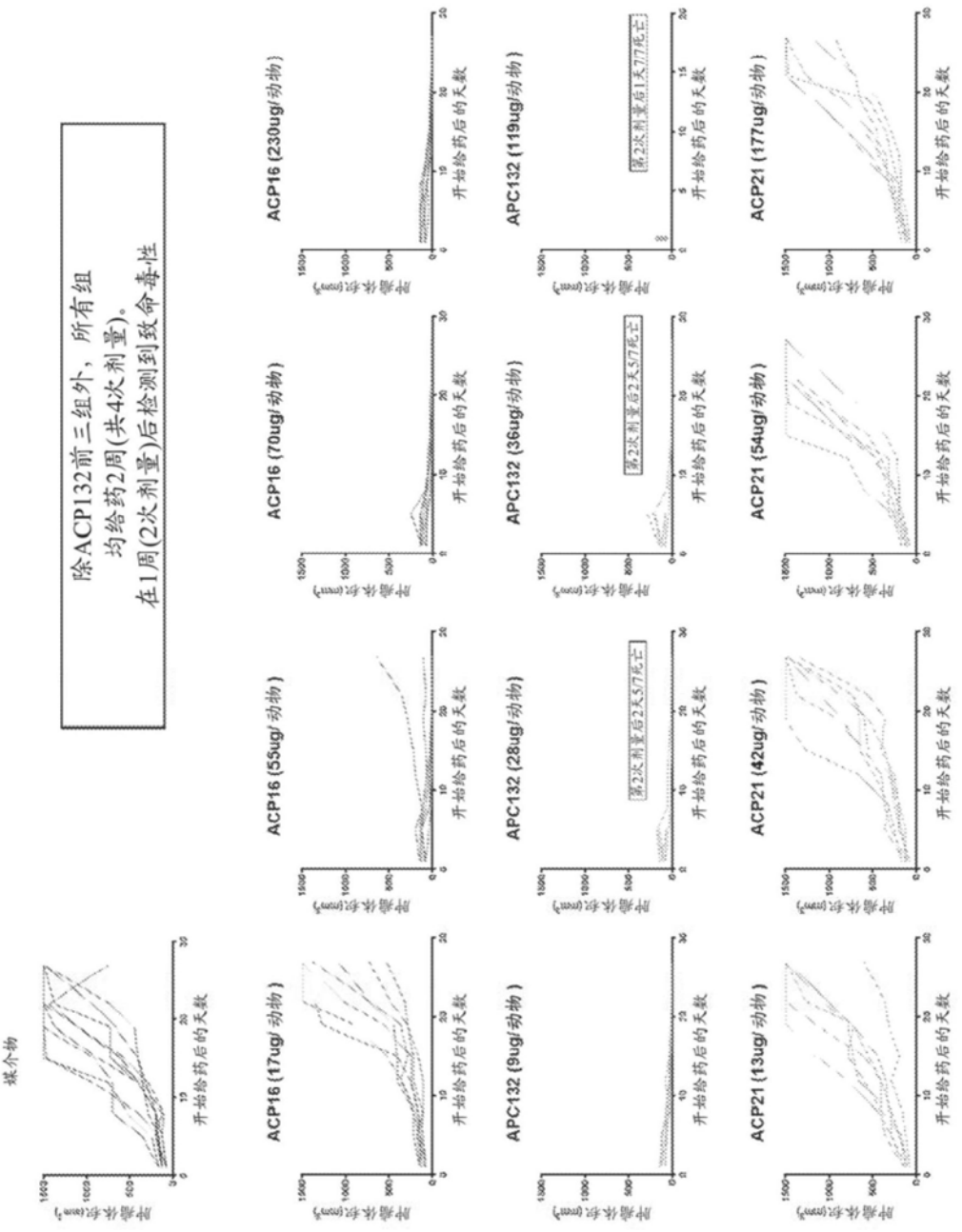

除ACP132前三组外，所有组
均给药2周(共4次剂量)。
在1周(2次剂量)后检测到致命毒性
媒介物
ACP16 (17ug/动物)
ACP16 (55ug/动物)
ACP16 (70ug/动物)
ACP16 (230ug/动物)
APC132 (9ug/动物)
APC132 (28ug/动物)
APC132 (36ug/动物)
APC132 (119ug/动物)
ACP21 (13ug/动物)
ACP21 (42ug/动物)
ACP21 (54ug/动物)
ACP21 (177ug/动物)
第2次剂量后2天5/7死亡
第2次剂量后1天7/7死亡
开始给药后的天数

图35

ProTriTAC可被肿瘤相关蛋白酶活化
αALB
蛋白酶可裂解接头
...GGGGXXXXXXXXGGGG...
蛋白酶A 蛋白酶B
αCD3
αEGFR
1 2 3
1. 单独的ProTriTAC
2. +蛋白酶B
3. +蛋白酶A
55 kD (前药)
42 kD (活性药物)
13 kD
SDS-PAGE凝胶
* 具有工程化的不同可裂解性的底物接头的专利库

图36

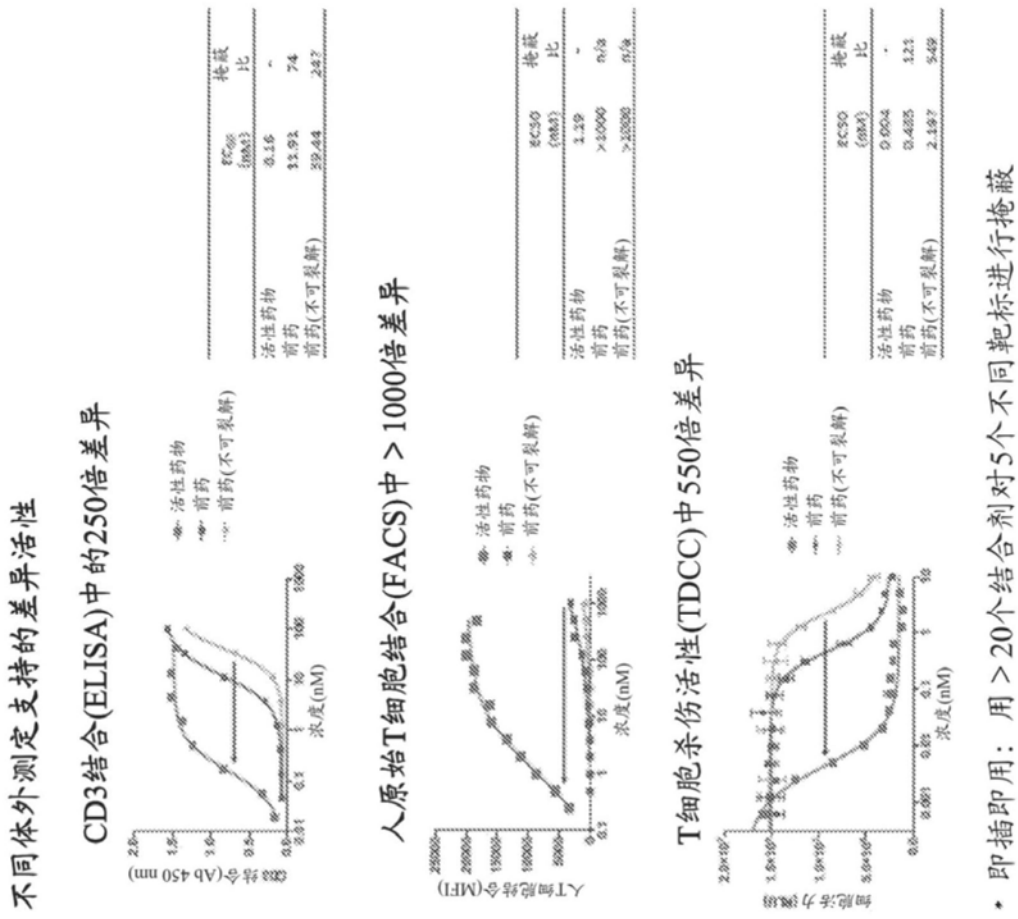

不同体外测定支持的差异活性
CD3结合(ELISA)中的250倍差异
活性药物
前药
前药(不可裂解)
浓度(nM)
活性药物 0.16 -
前药 13.92 74
前药(不可裂解) 39.44 247
人原始T细胞结合(FACS)中 > 1000倍差异
活性药物
前药
前药(不可裂解)
浓度(nM)
活性药物 1.29 -
前药 >1000 n/a
前药(不可裂解) >10000 n/a
T细胞杀伤活性(TDCC)中550倍差异
活性药物
前药
前药(不可裂解)
浓度(nM)
活性药物 0.004 -
前药 0.485 121
前药(不可裂解) 2.197 549
即插即用：用 > 20个结合剂对5个不同靶标进行掩蔽

图37

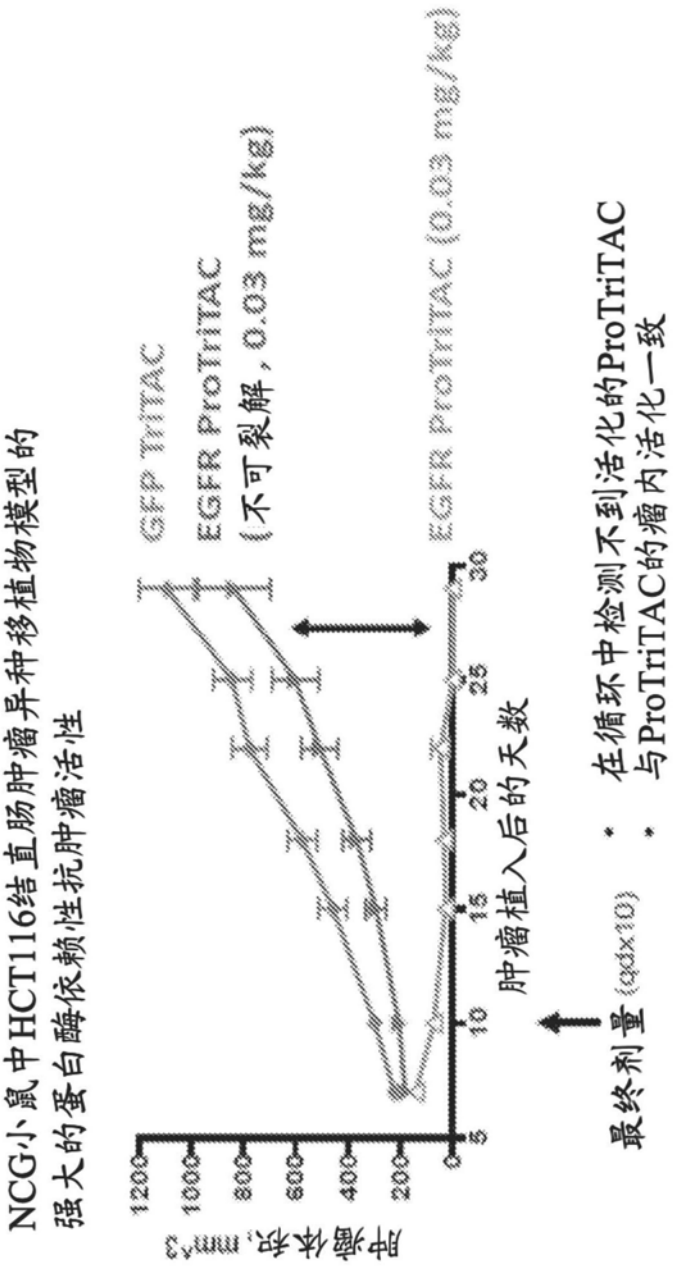

NCG小鼠中HCT116结直肠肿瘤异种移植物模型的
强大的蛋白酶依赖性抗肿瘤活性
肿瘤体积，mm³
1200
1000
800
600
400
200
0
5
10
15
20
25
30
肿瘤植入后的天数
GFP TriTAC
EGFR ProTriTAC
(不可裂解，0.03 mg/kg)
EGFR ProTriTAC (0.03 mg/kg)
最终剂量 (qdx10)
* 在循环中检测不到活化的ProTriTAC
* 与ProTriTAC的瘤内活化一致

图38

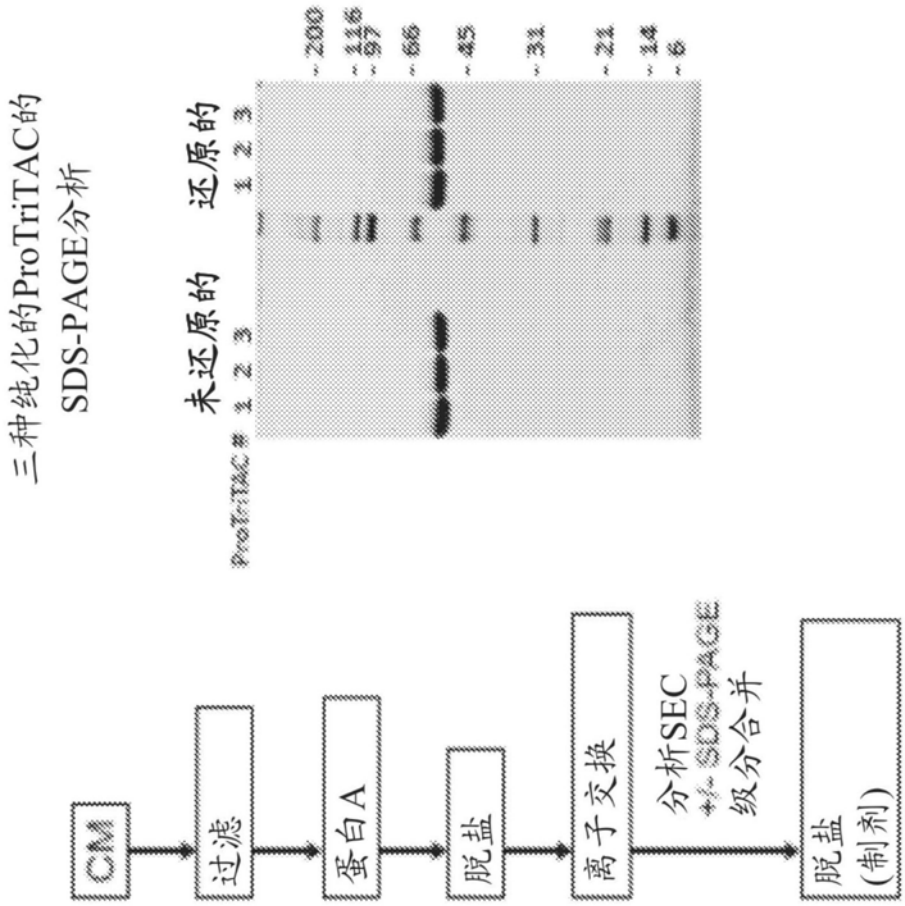
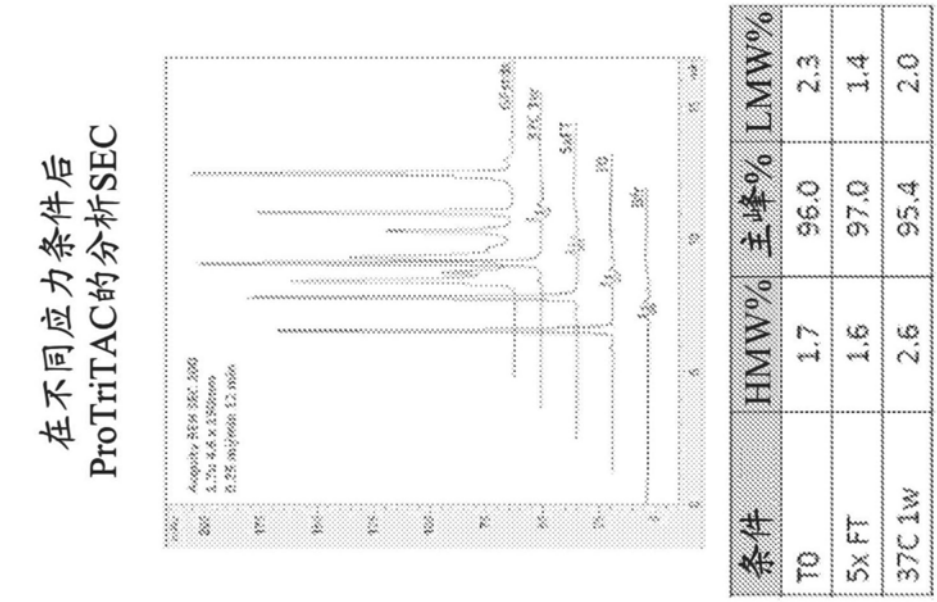


图39



条件	HMW%	主峰%	LMW%
T0	1.7	96.0	2.3
5x FT	1.6	97.0	1.4
37C 1w	2.6	95.4	2.0

图40

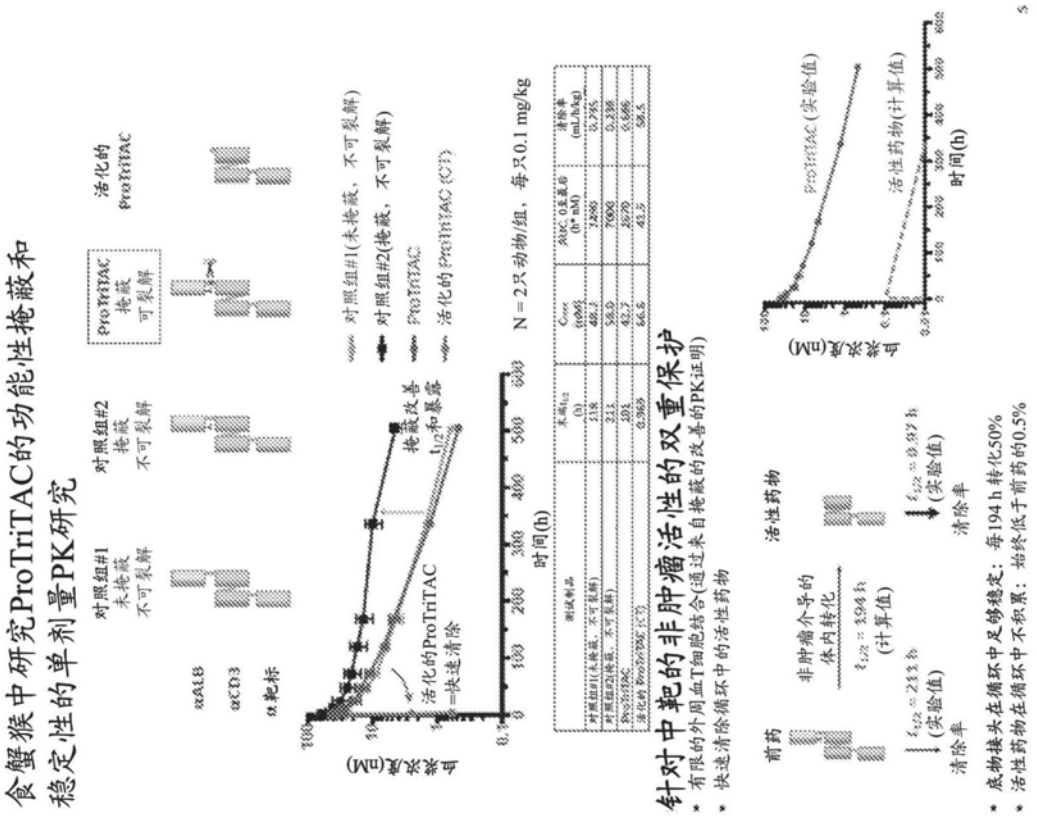

食蟹猴中研究ProTriTAC的功能性掩蔽和稳定性的单剂量PK研究
对照组#1 未掩蔽 不可裂解
对照组#2 掩蔽 不可裂解
ProTriTAC 掩蔽 可裂解
活化的 ProTriTAC
αALB
αCD3
α靶标
对照组#1(未掩蔽，不可裂解)
对照组#2(掩蔽，不可裂解)
ProTriTAC
活化的ProTriTAC (CT)
掩蔽改善 t1/2和暴露
=快速清除
时间(h)
N = 2只动物/组，每只0.1 mg/kg
测试物品
针对中靶的非肿瘤活性的双重保护
有限的外周血T细胞结合(通过来自掩蔽的改善的PK证明)
快速清除循环中的活性药物
前药
非肿瘤介导的体内转化
(计算值)
(实验值)
清除率
活性药物
ProTriTAC (实验值)
活性药物(计算值)
时间(h)
底物接头在循环中足够稳定：每194 h转化50%
活性药物在循环中不积累：始终低于前药的0.5%

图41