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(54)发明名称

包括TGFβ结合结构域的嵌合细胞因子受体

(57)摘要

本文提供了具有能够与TGF-β配体或TGF-β受体抗体结合的结合结构域的嵌合细胞因子受体。当此类受体存在于具有嵌合抗原受体(CAR)的免疫细胞(CAR-T细胞)上时,此类受体组成型地和/或通过TGF-β配体或TGF-β受体抗体的结合来使CAR-T细胞扩增、活性和持久性增加。本发明还提供了制备和使用本文所述的嵌合细胞因子受体的方法。

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1.一种嵌合细胞因子受体,其包括:

a.结合结构域,所述结合结构域包括TGF-β受体的细胞外部分或TGF-β抗原结合结构域;

b.跨膜结构域;

c.Janus激酶(JAK)结合结构域;以及

d.募集结构域。

2.根据权利要求1所述的嵌合细胞因子受体,其中所述募集结构域是STAT募集结构域。

3.根据权利要求1或2所述的嵌合细胞因子受体,其中所述募集结构域来自受体,任选地来自细胞因子受体。

4.根据权利要求1到3中任一项所述的嵌合细胞因子受体,其中所述嵌合细胞因子受体是成簇的。

5.根据权利要求1到3中任一项所述的嵌合细胞因子受体,其中所述嵌合细胞因子受体是二聚化的,并且每个单体包括:

a.结合结构域,所述结合结构域包括TGF-β受体的细胞外部分或TGF-β抗原结合结构域;

b.跨膜结构域;

c.Janus激酶(JAK)结合结构域;以及

d.募集结构域。

6.根据权利要求1到5中任一项所述的嵌合细胞因子受体,其中所述TGF-β抗原结合结构域是scFv。

7.根据权利要求1到5中任一项所述的嵌合细胞因子受体,其中所述结合结构域包括野生型TGF-β受体序列的细胞外部分。

8.根据权利要求1到5中任一项所述的嵌合细胞因子受体,其中所述结合结构域包括野生型TGF-β受体序列的细胞外部分的一个或多个突变。

9.根据权利要求1到5中任一项所述的嵌合细胞因子受体,其中所述结合结构域包括TGFβR2的细胞外部分。

10.根据权利要求1到5中任一项所述的嵌合细胞因子受体,其中所述结合结构域包括SEQ ID NO:2到SEQ ID NO:20以及SEQ ID NO:159中的任一个的氨基酸序列。

11.根据权利要求1到10中任一项所述的嵌合细胞因子受体,其中所述嵌合细胞因子受体具有组成型活性或在所述结合结构域与TGF-β配体结合时激活。

12.根据权利要求11所述的嵌合细胞因子受体,其中所述TGF-β配体是TGFβ-1、TGF-β2或TGF-β3中的任一个。

13.根据权利要求1到10中任一项所述的嵌合细胞因子受体,其中所述嵌合细胞因子受体具有组成型活性或在所述结合结构域与抗TGF-β受体抗体结合时激活。

14.根据权利要求1到13中任一项所述的嵌合细胞因子受体,其中所述JAK结合结构域是JAK1结合结构域、JAK2结合结构域、JAK3结合结构域或TYK2结合结构域。

15.根据权利要求1到14中任一项所述的嵌合细胞因子受体,其中所述跨膜结构域源自EpoR、GP130、PrlR、GHR、GCSFR或TPOR/MPLR受体。

16.根据权利要求1到15中任一项所述的嵌合细胞因子受体,其中所述跨膜结构域源自

TPOR/MPLR受体。

17.根据权利要求16所述的嵌合细胞因子受体，其中所述跨膜结构域和所述JAK结合结构域包括SEQ ID NO:26的天然存在的TPOR/MPLR受体的氨基酸478-582。根据权利要求17所述的嵌合细胞因子受体，其中所述跨膜结构域和所述JAK结合结构域进一步包括所述TPOR/MPLR受体的氨基酸位置H499、S505、W515、K553或K573处的至少一个取代。

18.根据权利要求17所述的嵌合细胞因子受体，其中所述跨膜结构域和所述JAK结合结构域包括选自H499L、S505N、W515K、K553R和K573R的至少一个氨基酸取代。

19.根据权利要求18所述的嵌合细胞因子受体，其中所述TPOR/MPLR受体的所述跨膜结构域和所述JAK结合结构域包括：(a)所述H499L取代；(b)所述S505N取代；(c)所述W515K取代；(d)所述S505N取代、所述W515K取代；或(e)所述H499L取代、所述S505N取代、所述W515K取代。

20.根据权利要求17到19中任一项所述的嵌合细胞因子受体，其中所述TPOR/MPLR受体的所述跨膜结构域和所述JAK结合结构域进一步包括所述K553R取代和/或所述K573R取代。

21.根据权利要求1到20中任一项所述的嵌合细胞因子受体，其中所述跨膜结构域和所述JAK结合结构域包括选自以下的氨基酸序列：SEQ ID NO:27到SEQ ID NO:79、SEQ ID NO:160以及SEQ ID NO:217到SEQ ID NO:234。

22.根据权利要求2到21中任一项所述的嵌合细胞因子受体，其中所述STAT募集结构域来自选自表4中所呈现的受体的受体。

23.根据权利要求2到22中任一项所述的嵌合细胞因子受体，其中所述募集结构域包括来自IL7Ra、IL12Rb2、EGFR、IL-21R或IL2Rb的一个或多个受体的STAT募集结构域。

24.根据权利要求2到23中任一项所述的嵌合细胞因子受体，其中所述STAT募集结构域包括SEQ ID NO:80到SEQ ID NO:122以及SEQ ID NO:161的氨基酸序列中的任一个氨基酸序列。

25.根据权利要求2到24中任一项所述的嵌合细胞因子受体，其中所述STAT募集结构域包括IL7Ra(316-459)(SEQ ID NO:80)、IL2Rb(339-379,393-433,518-551)(SEQ ID NO:112)、IL2Rb(393-433,518-551)(SEQ ID NO:111)、IL12Rb2(775-825)(SEQ ID NO:101)、IL12Rb2(714-862)(SEQ ID NO:120)、EGFR(1122-1165)(SEQ ID NO:99)或IL7Ra(316-459).IL12Rb2(775-825)(SEQ ID NO:161)。

26.根据权利要求1到25中任一项所述的嵌合细胞因子受体，其中所述嵌合细胞因子受体包括选自SEQ ID NO:123-151和SEQ ID NO:162-216的氨基酸序列。

27.根据权利要求1到26中任一项所述的嵌合细胞因子受体，其中所述嵌合细胞因子受体是诱导型的或具有组成型活性。

28.根据权利要求27所述的嵌合细胞因子受体，其中所述嵌合细胞因子受体能由TGFβ或抗TGFβR抗体诱导。

29.根据权利要求28所述的嵌合细胞因子受体，其中所述嵌合细胞因子受体具有组成型活性并且能在存在TGFβ或抗TGFβR抗体的情况下被进一步诱导或表现出进一步提高的活性。

30.根据权利要求1到29中任一项所述的嵌合细胞因子受体，其中所述嵌合细胞因子受体当在细胞中表达时能够抑制TGFbR2介导的信号转导和/或增强STAT介导的信号转导。

31.根据权利要求30所述的嵌合细胞因子受体,其中所述细胞是免疫细胞。

32.一种多核苷酸,其编码根据权利要求1到31中任一项所述的嵌合细胞因子受体。

33.一种表达载体,其包括根据权利要求32所述的多核苷酸。

34.根据权利要求33所述的表达载体,其进一步包括表达嵌合抗原受体(CAR)的多核苷酸。

35.根据权利要求34所述的表达载体,其中所述CAR与表8的靶标中的任何一个或多个靶标结合。

36.根据权利要求33到35中任一项所述的表达载体,其中所述载体是慢病毒载体。

37.一种工程化免疫细胞,其包括根据权利要求33到36中任一项所述的载体。

38.一种工程化免疫细胞,其表达根据权利要求1到31中任一项所述的嵌合细胞因子受体。

39.根据权利要求37或38所述的工程化免疫细胞,其进一步表达至少一个CAR。

40.根据权利要求39所述的工程化免疫细胞,其中所述CAR和所述嵌合细胞因子受体以化学计量上相等的量表达。

41.根据权利要求39或40所述的工程化免疫细胞,其中所述CAR与表8的靶标中的任何一个或多个靶标结合。

42.根据权利要求37到41中任一项所述的工程化免疫细胞,其中所述免疫细胞是同种异体免疫细胞。

43.根据权利要求37到41中任一项所述的工程化免疫细胞,其中所述免疫细胞是自体免疫细胞。

44.根据权利要求37到43中任一项所述的工程化免疫细胞,其中所述免疫细胞选自由以下组成的组:T细胞、树突状细胞、杀伤树突状细胞、肥大细胞、NK细胞、巨噬细胞、单核细胞、B细胞和源自干细胞的免疫细胞。

45.根据权利要求44所述的工程化免疫细胞,其中所述免疫细胞是T细胞。

46.根据权利要求37到45中任一项所述的工程化免疫细胞,其中与不表达嵌合细胞因子受体的免疫细胞相比,所述免疫细胞表现出降低的TGF-βR介导的信号转导和/或增强的Stat介导的信号转导。

47.根据权利要求37到46中任一项所述的工程化免疫细胞,其中当所述免疫细胞与TGF-β或抗TGF-βR抗体结合时,所述免疫细胞表现出降低的TGF-βR介导的信号转导和/或增强的Stat介导的信号转导。

48.一种调节根据权利要求37到47中任一项所述的工程化免疫细胞的活性的方法,所述方法包括使所述免疫细胞与TGF-β或抗TGF-β受体抗体接触。

49.一种制备工程化免疫细胞的方法,所述方法包括将根据权利要求32所述的多核苷酸或根据权利要求33到36中任一项所述的表达载体引入到免疫细胞中。

50.根据权利要求48或49所述的方法,其中所述免疫细胞选自由以下组成的组:T细胞、树突状细胞、杀伤树突状细胞、肥大细胞、NK细胞、巨噬细胞、单核细胞、B细胞和源自干细胞的免疫细胞。

51.一种药物组合物,其包括根据权利要求37到47中任一项所述的免疫细胞。

52.一种试剂盒,其包括根据权利要求37到47中任一项所述的免疫细胞或根据权利要

求51所述的药物组合物。

53.一种治疗受试者的癌症的方法,所述方法包括向所述受试者施用治疗有效量的根据权利要求37到47中任一项所述的工程化免疫细胞或根据权利要求51所述的药物组合物。

54.根据权利要求53所述的方法,其中所述癌症包括实体瘤。

55.根据权利要求53所述的方法,其中所述癌症包括液体瘤。

56.根据权利要求53到55中任一项所述的方法,其中所述肿瘤是TGFβ阳性肿瘤。

57.根据权利要求53到56中任一项所述的方法,其中所述受试者用抗TGF-β受体抗体进行治疗。

包括TGF B结合结构域的嵌合细胞因子受体

[0001] 相关申请的交叉引用

[0002] 本申请要求于2019年8月30日提交的美国临时申请第62/894,658号;以及于2020年7月17日提交的美国临时申请第63/053,322号的优先权的权益,所述两个美国临时申请的内容特此通过引用整体并入。

[0003] 序列表

[0004] 本申请经由EFS-Web电子申请并且包含呈.txt格式的电子提交的序列表。.txt文件含有2020年8月27日创建的名为“AT-030_03WO_SL.txt”的序列表,并且其大小为576,780字节。此.txt文件中含有的序列表是说明书的一部分,并且通过引用整体并入本文。

技术领域

背景技术

[0005] 经基因修饰以识别恶性肿瘤相关抗原的免疫细胞(例如,T细胞)的过继转移正在显示出作为治疗癌症的新方法的前景。例如,可以对T细胞进行基因修饰以表达嵌合抗原受体(CAR),所述嵌合抗原受体是包含抗原识别部分和T细胞激活结构域的融合蛋白。

[0006] T细胞增殖、细胞毒性效力和持久性由信号转导通路驱动。常规的CAR设计提供两种信号:CD3ζ激活(信号1)和共刺激(信号2,例如,通过4-1BB、OX40和/或CD28表达)。在一些情况下,第三种信号(信号3),细胞因子诱导的细胞因子受体信号传导(例如,用于免疫增强的细胞因子支持)可能是令人期望的。然而,提供信号3的方法已经受到显著的限制。

[0007] 提供细胞因子支持的一种方法包含将CAR-T细胞疗法与重组细胞因子/细胞因子模拟物的全身输注组合,以及对CAR-T细胞进行工程化以在细胞外分泌/表达细胞因子。由于细胞因子具有多效性作用并且也可以影响其它细胞类型的功能,CAR-T细胞的全身施用或产生免疫增强的细胞因子具有至少两个主要缺点:(i)这些方法可能导致人体全身毒性,以及(ii)在同种异体CAR-T细胞疗法的背景下,这些方法可能会导致旁观者宿主免疫激活,所述旁观者宿主免疫激活加速同种异体CAR-T细胞的排斥反应,从而影响治疗效果。提供细胞因子支持的另一种方法基于引入组成性激活的二聚化细胞因子受体IL-7Ra,这限制了信号传导输出的性质(仅IL-7信号传导)和量级。提供细胞因子支持的又一种方法涉及将信号3直接掺入到CAR分子中(《自然医学(Nat Med.)》2018年3月;24(3):352-359)。这种方法的限制在于信号3的强度取决于CAR激活的强度。在不存在靶标(和CAR激活)的情况下,信号3不会被转导。

[0008] 需要通过以背景相关的方式将细胞因子信号特异性靶向CAR-T细胞来规避这些缺点的解决方案,从而允许改善的安全性特征和治疗效果。本文提供了解决这种需要的组合物和方法。

发明内容

[0009] 本文提供了包括TGF-β结合结构域的嵌合细胞因子受体。本文提供了诱导型TGF-β

驱动的嵌合细胞因子受体，所述嵌合细胞因子受体当与转化生长因子β细胞因子家族的配体(TGF-β配体，例如，TGF-β1、TGF-β2和TGF-β3)结合时或用抗TGF-β受体抗体激活时是有活性的。当存在于具有嵌合抗原受体(CAR)的免疫细胞上并且与TGF-β配体结合和/或用抗TGF-βR抗体激活时，此类受体使细胞因子受体信号传导(信号3)增加，从而导致具有CAR的免疫细胞的免疫细胞激活、增殖、持久性和/或效力增加。因此，本公开的嵌合细胞因子受体允许细胞因子信号与内源性TGF-β配体一起被传递到免疫细胞中，从而阻断细胞因子信号的免疫抑制信号，并且将细胞因子信号转化成可以与CAR驱动的活性协同工作或协同作用的免疫增强信号。另外，由于临床批准的抗TGF-β受体抗体可以聚集和激活本公开的嵌合细胞因子受体，用抗TGF-β受体治疗的患者不仅可以受益于内源性TGF-β信号传导的阻断，而且还受益于具有嵌合细胞因子受体的细胞中细胞因子信号传导的激活。本文还提供了组成型活性TGF-β驱动的含TGF-β结合结构域的嵌合细胞因子受体；此类受体在不存在诱导剂的情况下继续发信号，但可以被进一步诱导或表现出进一步提高的性质或活性，例如，在存在TGF-β配体或抗TGF-βR抗体的情况下。在一些实施例中，TGF-βR是TGF-βR2，并且抗体是抗TGF-βR2抗体。如本文所使用的，“TGF-β(TGF-beta)”与“TGF-β”可互换使用。

[0010] 因此，一方面，本文提供了一种嵌合细胞因子受体，其包括：(a)结合结构域，所述结合结构域包括TGF-β受体的细胞外部分或TGF-β抗原结合结构域；(b)跨膜结构域；(c)Janus激酶(JAK)结合结构域；以及(d)募集结构域。如本文所使用的，“细胞外部分”是指TGF-β受体的细胞外结构域的任何部分。

[0011] 在相关方面，本文提供了一种编码本公开的嵌合细胞因子受体中的任何一个的多核苷酸，以及包括此类多核苷酸的表达载体。在一些实施例中，所述多核苷酸进一步编码嵌合抗原受体(CAR)，其中所述CAR与所关注靶标结合。所关注靶标可以是任何所关注分子，例如，包含但不限于表8中呈现的靶标中的任何一个或多个靶标。

[0012] 在另外的方面，本文提供了一种工程化免疫细胞，其包括本公开的至少一个嵌合细胞因子受体。在另一方面，本文提供了一种工程化免疫细胞，其包括本公开的至少一个嵌合抗原受体(CAR)和至少一个嵌合细胞因子受体。在一些实施例中，所述免疫细胞是T细胞。在一些实施例中，所述免疫细胞是同种异体免疫细胞。在其它实施例中，所述免疫细胞是自体免疫细胞。所述免疫细胞可以选自由以下组成的组：T细胞、树突状细胞、杀伤树突状细胞、肥大细胞、NK细胞、巨噬细胞、单核细胞、B细胞和源自干细胞的免疫细胞。在相关方面，本文提供了一种药物组合物，其包括本公开的工程化免疫细胞中的任何工程化免疫细胞；以及包括此类药物组合物的试剂盒。本文还提供了一种制备免疫细胞的方法。

[0013] 在另一方面，本文提供了一种治疗受试者的癌症的方法，所述方法包括向所述受试者施用治疗有效量的本文所述的工程化免疫细胞中的任何工程化免疫细胞。

附图说明

[0014] 图1示出了本公开的诱导型嵌合细胞因子受体的示意图。

[0015] 图2A示出了用于共表达TGFβR1或TGFβR2细胞因子受体与第2代EGFRvIII CAR的显性负性截短体的慢病毒载体的示意图。

[0016] 图2B示出了由TGFβR1 DN或TGFβR2 DN的表达对TGF-β信号传导的抑制。

[0017] 图3示出了用于共表达TGFβR2细胞因子受体与第2代EGFRvIII CAR的慢病毒载体

的总体示意图。

[0018] 图4A示出了所使用的具有IL7R(316-459)和IL12Rb2(775-825)募集结构域以模拟CAR-T细胞中的IL7和IL12信号传导的原型慢病毒载体的示意图。

[0019] 图4B示出了通过荧光素酶报告基因测定确定的TGF-β信号传导活性。

[0020] 图4C示出了在存在TGF-β的情况下,图4A的嵌合细胞因子受体的激活。

[0021] 图5A示出了所使用的在结合结构域中具有截短体的原型慢病毒载体的示意图。

[0022] 图5B示出了通过荧光素酶报告基因测定确定的TGF-β信号传导活性。

[0023] 图5C示出了在存在TGF-β的情况下,图5A的嵌合细胞因子受体的激活。

[0024] 图6A示出了引入到TGFβR2盒中的修饰的示意图。

[0025] 图6B示出了TGFβR2ΔN25嵌合细胞因子受体仍保留抑制TGF-β信号传导的能力。

[0026] 图6C示出了通过STAT报告基因活性评估的图6A的嵌合细胞因子受体的激活。

[0027] 图7示出了组成型活性嵌合细胞因子受体的示意图。

[0028] 图8A示出了引入到TGFβR2盒中的修饰的示意图。

[0029] 图8B示出了由图8A的嵌合细胞因子受体的表达对TGF-β信号传导的抑制。

[0030] 图8C示出了通过STAT5报告基因活性测量的经由图8A的嵌合细胞因子受体进行的细胞因子信号传导的激活。

[0031] 图9A-9B示出了野生型TPOR和各种跨膜缺失或插入变体的氨基酸序列。图9A-B按出现顺序分别公开了SEQ ID NO:235-246、235和247-254。

[0032] 图10A示出了野生型TPOR和另外的跨膜变体的氨基酸序列。图10B示出了在存在不同浓度的TGF-β的情况下,如通过荧光素酶测定确定的由图10A中所示的TGF-β驱动的嵌合细胞因子受体的过表达对内源性TGF-β信号传导的抑制。图10C示出了在存在各种浓度的TGF-β的情况下嵌合细胞因子受体的激活。图10A按出现顺序分别公开了SEQ ID NO:235和255-271。

[0033] 图11A示出了嵌合细胞因子受体(CCR)CAR表达构建体的示意图,其中CCR和EGFRvIII CAR的表达通过P2A肽连接。图11B-11C是描绘了表达各种CCR的CAR+T细胞的产率的条形图。图11D-11E示出了表达各种CCR或对照的CAR T细胞中的STAT5磷酸化的结果。图11F-11G描绘了在产生第14天时的CAR T细胞表型。图11H示出了CAR T细胞上的总TGF-βR2细胞外染色的结果。图11I描述了在存在不同浓度的TGF-β的情况下,在表达不同CCR的CAR T细胞中TGF-βR2信号传导的抑制结果。

[0034] 图12A展示了在不存在外源性TGFβ的情况下,表达各种CCR的CAR T细胞的针对U87-EGFRvIII细胞的细胞毒性测定的结果。图12B-12C示出了在不同浓度的TGFβ下表达各种CCR的CAR T细胞的细胞毒性测定的结果。

[0035] 图13A示出了STAT5磷酸化,并且图13B描绘了表达在TOPR/MPLR和JAK结合结构域中具有S505N/W515K并且具有或不具有K553R/K573R取代的CCR的CAR T细胞的T细胞表型。本实验中测试的所有TGFbR2嵌合细胞因子受体构建体含有S505N/W515K取代。标记为RR的构建体进一步含有另外的K553R/K573R取代。

[0036] 图14A-14B示出了在不存在(图14A)或存在(图14B)5ng/ml TGFβ的情况下,表达各种CCR的CAR T细胞的长期细胞杀伤测定的结果。

[0037] 图15A-15C示出了表达各种CCR的CAR T细胞的STAT5信号传导的激活(图15A)、TGF

β信号传导的抑制(图15B)和长期细胞杀伤测定(图15C)的结果,其中所述结果中的一些结果对TGFβ具有降低的亲和力(例如,在TGFβR2中的ECD中的D32A、E119A和/或I53A取代)。

[0038] 图16A-16B比较了具有或不具有降解抗性K533R/K573R取代的TGFβR2嵌合细胞因子受体对STAT5信号传导(图16A)和长期细胞杀伤(图16B)的作用。

具体实施方式

[0039] 本文提供了包括TGF-β结合结构域的嵌合细胞因子受体。本文提供了诱导型嵌合细胞因子受体,所述诱导型嵌合细胞因子受体当与TGF-B配体(例如,TGF-β1、TGF-β2和/或TGF-β3)结合时或用抗TGF-β受体抗体激活时是有活性的。本文还提供了包括TGF-β结合结构域的组成型活性嵌合细胞因子受体。本文还提供了具有嵌合抗原受体(CAR)的免疫细胞(CAR-I细胞,例如,CAR-T细胞),其表达本公开的嵌合细胞因子受体。在一些实施例中,与不具有TGF-β结合结构域的组成型活性嵌合细胞因子受体相比,当与TGF-β配体结合或用抗TGFβ受体抗体激活时,组成型活性嵌合细胞因子受体表现出提高的性质或活性。本文还提供了制备和使用嵌合细胞因子受体的方法。

[0040] I.具有TGF-β的嵌合细胞因子受体

[0041] 本公开的嵌合细胞因子受体在结合TGF-β配体(例如,TGF-β1、TGF-β2和/或TGF-β3)或抗TGF-β受体抗体时激活信号传导。当受体的单体聚集和/或二聚化时,这些受体激活信号传导。本公开的嵌合细胞因子受体是双功能嵌合细胞因子受体,所述双功能嵌合细胞因子受体可以同时中和TGF-β配体的免疫抑制作用,并且模拟免疫增强细胞因子信号的传递。

[0042] 在一些实施例中,本公开的嵌合细胞因子受体的单体包括:(a)结合结构域,所述结合结构域能够与TGF-β配体或抗TGF-β受体抗体结合;(b)跨膜结构域;(c)Janus激酶(JAK)结合结构域;以及;(d)STAT募集结构域(例如,来自受体的细胞质结构域;例如,来自细胞因子受体)。每个结构域可以直接连接或通过一个或多个肽连接子连接。在一些实施例中,本公开的嵌合细胞因子受体的单体包括:(a)结合结构域,所述结合结构域能够与TGF-β配体或抗TGF-β受体抗体结合;(b)跨膜结构域;(c)Janus激酶(JAK)结合结构域;以及;(d)募集结构域(例如,来自受体的细胞质结构域;例如,来自细胞因子受体)。募集结构域可以是STAT募集结构域、AP1募集结构域、Myc/Max募集结构域;或NFkB-募集结构域。在一些实施例中,在嵌合细胞因子受体与TGF-β配体结合时,所述嵌合细胞因子受体被聚集并激活,和/或所述嵌合细胞因子受体用抗TGF-β受体抗体聚集并激活。嵌合细胞因子受体在例如与TGF-β配体和/或TGF-β受体抗体结合时激活信号传导。在一些实施例中,TGF-β受体抗体是但不限于PF-03446962或LY3022859。在一些实施例中,嵌合细胞因子受体是组成性聚集或二聚化的。

[0043] 如本文所使用的,“TGF-β配体”是指TGF-β1、TGF-β2和TGF-β3及其同种型和衍生物。应理解,“TGF-β配体”和“TGF-β”在本文中可互换使用。

[0044] A.结合结构域

[0045] 本公开的嵌合细胞因子受体包括能够与TGF-β配体或抗TGF-β受体抗体结合的结合结构域。如本文所提及的,结合结构域是延伸到细胞外空间中的嵌合细胞因子受体的结构域。结合结构域结合并多价螯合TGF-β远离内源性TGF-β受体,由此防止或减少TGF-β诱导

的免疫抑制。本公开的结合结构域与TGF-β配体和抗TGF-β受体抗体结合，从而导致结合诱导的信号转导。

[0046] 在一些实施例中，结合结构域包括TGF-β受体的细胞外部分，例如TGFβR1或TGFβR2的细胞外部分。

[0047] 在一些实施例中，结合结构域包括野生型TGFβ受体的细胞外部分。在一些实施例中，TGF-β受体包括增强或改变对与TGFβ配体结合的亲和力的一个或多个突变。

[0048] 在一些实施例中，结合结构域包括野生型TGFβR1或TGFβR2的细胞外部分；在一些实施例中，结合结构域包括野生型TGFβR1或TGFβR2的细胞外部分并且分别包括SEQ ID NO:2或3的氨基酸序列。

[0049] 在一些实施例中，结合结构域包括野生型TGF-β受体的细胞外部分的突变。在一些实施例中，结合结构域包括野生型TGF-β受体的细胞外部分的突变并且包括SEQ ID NO:4到SEQ ID NO:20中的任一个的氨基酸序列。在一些实施例中，嵌合细胞因子受体包括与SEQ ID NO:4-20的氨基酸序列中的任一个具有至少80％、85％、90％、95％、98％或99％或100％相同的结合结构域。在一些实施例中，结合结构域不包括信号序列。

[0050] 表1示出了本公开的示例性结合结构域氨基酸序列。应注意，如TGF-β受体氨基酸序列等示例性结合结构域序列的表达和细胞外定位可以通过使用信号序列来实现。在示例性实施例中，利用CD8信号序列(CD8SS)MALPVTALLLPLALLLHAARP(SEQ ID NO:1)。在一些实施例中，结合结构域包括野生型TGFβR2的包括SEQ ID NO:159的氨基酸序列的细胞外结构域。在一些实施例中，信号序列是人TGF-βR2的内源性信号序列。

[0051] 表1:示例性结合结构域序列

[0052]

结合结构域	氨基酸序列	SEQ ID NO:
TGFβR1 (1-126)	MEAAVAAPRPRLLLLVLAAAAAAAAALLPGATALQCF CHLCTKDNFTCVTDGLCFVSVTETTDKVIHNSMCIAEI DLIPRDRPFVCAPSSKTGSVTTTYCCNQDHCNKIELPT TVKSSPGLGPVEL	2
TGFβR2 (1-166) 加下划线的TGFβR2信号序列	MGRGLLRGLWPLHIVLWTRIASTIPPHVQKSVNNDMI VTDNNGAVKFPQLCKFCDVRFSTCDNQKSCMSNCSIT SICEKPQEVCVAVWRKNDENITLETVCHDPKLPYHDFI LEDAASPKCIMKEKKKPGETFFMCSCSSDECNDNIIFS EEYNTSNPDLLLVIFQ	3
TGFβR2ΔN25	QLCKFCDVRFSTCDNQKSCMSNCSITSICEKPQEVCVA	4

[0053]

结合结构域	氨基酸序列	SEQ ID NO:
	VWRKNDENITLETVCHDPKLPYHDFILEDAASPKCIM KEKKKPGETFFMCSCSSDECNDNIIFSEEYNTSNPDLL LVIFQ	
TGFβR2ΔN25 FSE-N8	QLCKFCDVRFSTCDNQKSCMSNCSITSICEKPQEVCVA VWRKNDENITLETVCHDPKLPYHDFILEDAASPKCIM KEKKKPGETFFMCSCSSDECNDNIIFSELLLVIFQ	5
TGFβR2ΔN25 FSE-N6	QLCKFCDVRFSTCDNQKSCMSNCSITSICEKPQEVCVA VWRKNDENITLETVCHDPKLPYHDFILEDAASPKCIM KEKKKPGETFFMCSCSSDECNDNIIFSEPDLLLVIFQ	6
TGFβR2ΔN25 FSE-N5	QLCKFCDVRFSTCDNQKSCMSNCSITSICEKPQEVCVA VWRKNDENITLETVCHDPKLPYHDFILEDAASPKCIM KEKKKPGETFFMCSCSSDECNDNIIFSEEPDLLLVIFQ	7
TGFβR2ΔN25 FSE-N4	QLCKFCDVRFSTCDNQKSCMSNCSITSICEKPQEVCVA VWRKNDENITLETVCHDPKLPYHDFILEDAASPKCIM KEKKKPGETFFMCSCSSDECNDNIIFSEEYPDLLLVIFQ	8
TGFβR2ΔN25 FSE-N3	QLCKFCDVRFSTCDNQKSCMSNCSITSICEKPQEVCVA VWRKNDENITLETVCHDPKLPYHDFILEDAASPKCIM KEKKKPGETFFMCSCSSDECNDNIIFSEEYNPDLLLVIF Q	9
TGFβR2ΔN25. Glyc33	QLCKFCD**NRT**STCDNQKSCMSNCSITSICEKPQEVCVA VWRKNDENITLETVCHDPKLPYHDFILEDAASPKCIM KEKKKPGETFFMCSCSSDECNDNIIFSEEYNTSNPDLL LVIFQ	10
TGFβR2ΔN25. Glyc40	QLCKFCDVRFSTCD**NQT**SCMSNCSITSICEKPQEVCVA VWRKNDENITLETVCHDPKLPYHDFILEDAASPKCIM KEKKKPGETFFMCSCSSDECNDNIIFSEEYNTSNPDLL LVIFQ	11
TGFβR2ΔN25. Glyc56	QLCKFCDVRFSTCDNQKSCMSNCSITSICE**N**P**T**EVCVA VWRKNDENITLETVCHDPKLPYHDFILEDAASPKCIM KEKKKPGETFFMCSCSSDECNDNIIFSEEYNTSNPDLL LVIFQ	12
TGFβR2ΔN25. Glyc58	QLCKFCDVRFSTCDNQKSCMSNCSITSICEKP**N**E**T**CVA VWRKNDENITLETVCHDPKLPYHDFILEDAASPKCIM KEKKKPGETFFMCSCSSDECNDNIIFSEEYNTSNPDLL LVIFQ	13
TGFβR2ΔN25. V33K	QLCKFCD**K**RFSTCDNQKSCMSNCSITSICEKPQEVCVA VWRKNDENITLETVCHDPKLPYHDFILEDAASPKCIM KEKKKPGETFFMCSCSSDECNDNIIFSEEYNTSNPDLL LVIFQ	14
TGFβR2ΔN25. E70K	QLCKFCDVRFSTCDNQKSCMSNCSITSICEKPQEVCVA VWRKND**K**NITLETVCHDPKLPYHDFILEDAASPKCIM KEKKKPGETFFMCSCSSDECNDNIIFSEEYNTSNPDLL LVIFQ	15
TGFβR2ΔN25. Glyc87	QLCKFCDVRFSTCDNQKSCMSNCSITSICEKPQEVCVA VWRKNDENITLETVCHDPKLPYH**NFT**LEDAASPKCIM KEKKKPGETFFMCSCSSDECNDNIIF	16
TGFβR2ΔN25.	QLCKFCDVRFSTCDNQKSCMSNCSITSICEKPQEVCVA	17

[0054]

结合结构域	氨基酸序列	SEQ ID NO:
Glyc89	VWRKNDENITLETVCHDPKLPYHDF**NLT**DAASPKCI MKEKKKPGETFFMCSCSSDECNDNIIF	
TGFβR2ΔN25. Glyc102	QLCKFCDVRFSTCDNQKSCMSNCSITSICEKPQEVCVA VWRKNDENITLETVCHDPKLPYHDFILEDAASPKCIM K**NKT**KPGETFFMCSCSSDECNDNIIF	18
TGFβR2ΔN25. Glyc123	QLCKFCDVRFSTCDNQKSCMSNCSITSICEKPQEVCVA VWRKNDENITLETVCHDPKLPYHDFILEDAASPKCIM KEKKKPGETFFMCSCSSDECNDNI**T**F	19
TGFβR2ΔN25. I89E	QLCKFCDVRFSTCDNQKSCMSNCSITSICEKPQEVCVA VWRKNDENITLETVCHDPKLPYHDF**E**LEDAASPKCIM KEKKKPGETFFMCSCSSDECNDNIIF	20
TGFβR2（不具有信号序列）	IPPHVQKSVNNDMIVTDNNGAVKFPQLCKFCDVRFST CDNQKSCMSNCSITSICEKPQEVCVAVWRKNDENITL ETVCHDPKLPYHDFILEDAASPKCIMKEKKKPGETFF MCSCSSDECNDNIIFSEEYNTSNPDLLLVIFQ	159

[0055] 在一些实施例中，嵌合细胞因子受体是显性负性(DN)，其中表达TGF-β受体的结合结构域，但嵌合细胞因子受体不包括细胞内信号传导结构域，即嵌合细胞因子受体可以与TGF-β结合但不传递阳性信号(DN嵌合细胞因子受体)。在一些实施例中，TGF-β受体是TGFβR1(显性负性TGFβR1或TGFβR1 DN)，并且包括SEQ ID NO:2的氨基酸序列。在一些实施例中，TGF-β受体是TGFβR2(显性负性TGFβR2或TGFβR2 DN)，并且包括SEQ ID NO:3的氨基酸序列。TGF-β受体显性负性序列可以在信号序列的帮助下表达，例如SEQ ID NO:1的CD8SS信号序列。图2A中示出了DN嵌合细胞因子受体的示例性示意图。

[0056] 在其它实施例中，结合结构域包括TGF-β抗原结合结构域。此类抗原结合结构域包含但不限于可以与TGF-β配体结合的单链可变片段(scFv)和单结构域抗体(纳米抗体)。这些scFv和单结构域抗体可以包含可商购获得的scFv和单结构域抗体，以及源自例如骆驼和鲨鱼抗体的scFv和单结构域抗体。

[0057] 在其它实施例中，结合结构域包括TGF-β抗原结合结构域，其中抗原结合结构域包括Fab片段。

[0058] B.跨膜结构域

[0059] 本公开的嵌合细胞因子受体包括跨膜结构域。此类跨膜结构域与N端上的细胞外结合结构域和C端上的另外的细胞内/细胞质结构域偶联。在一些实施例中，偶联任选地是通过连接子实现的。

[0060] 如本文所使用的，跨膜结构域能够插入到细胞的膜中，在所述细胞中，所述跨膜结构域被表达。在一些实施例中，本公开的跨膜结构域跨越细胞膜，并且包括细胞外部分和/或细胞内部分。

[0061] 在一些实施例中，本公开的跨膜结构域是工程化的并且不类似于任何天然存在的跨膜结构域，例如本公开的跨膜结构域是非天然存在的。

[0062] 在其它实施例中，本公开的跨膜结构域源自天然存在的受体。

[0063] 在一些实施例中，本公开的跨膜和/或JAK结构域源自例如以下受体的一个或多个：促红细胞生成素受体(EpoR)、白介素6信号转导因子(GP130或IL6ST)、催乳素受体

(PrlR)、生长激素受体(GHR)、粒细胞集落-刺激因子受体(GCSFR)和血小板生成素受体/骨髓增生性白血病蛋白受体(TPOR/MPLR)。当源自天然存在的受体时,整个受体或受体的整个跨膜序列可能不是实现细胞内部分上的组成型激活和组成型JAK结合/激活所必需的。因此可以利用天然存在的受体的片段。此外,可以将某些突变引入到源自天然受体的跨膜结构域中,以进一步调整下游JAK依赖性信号传导。在一些实施例中,本公开的嵌合细胞因子受体包括天然存在的受体的一部分或片段,例如天然存在的受体的跨膜和/或JAK结合/激活结构域,任选地在其中包括一个或多个突变(例如,一个或多个缺失、插入和/或取代)。

[0064] 在一些实施例中,本公开的跨膜和/或JAK结构域源自天然存在的EpoR受体。

[0065] 在一些实施例中,本公开的跨膜和/或JAK结构域源自天然存在的GP130受体。

[0066] 在一些实施例中,本公开的跨膜和/或JAK结构域源自天然存在的PrlR受体。

[0067] 在一些实施例中,本公开的跨膜和/或JAK结构域源自天然存在的GHR受体。

[0068] 在一些实施例中,本公开的跨膜和/或JAK结构域源自天然存在的GCSF受体。

[0069] 在一些实施例中,本公开的跨膜和/或JAK结构域源自天然存在的TPOR受体。当TPOR跨膜结构域呈现允许的同型二聚体构象时,如响应于配体或由引入工程化修饰所引起的强制激活,所述跨膜结构域能够以JAK2依赖性方式激活下游细胞因子信号传导。对TPOR跨膜结构域引入各种修饰可能导致以下:免疫增强细胞因子信号可以是(a)静止的,直到在存在细胞外TGF-β的情况下诱导激活;或(b)具有组成型活性,而不管TGF-β可用性如何。

[0070] 表2提供了本公开中提供的天然存在的受体的示例性全长序列,跨膜和/或JAK结构域源自所述全长序列。

[0071] 表2:示例性天然存在的受体

[0072]

天然存在的受体名称	SEQ ID NO:
>AAI12154.1 促红细胞生成素受体[智人] MDHLGASLWPQVGSLCLLLAGAAWAPPPNLPDPKFESKAALLAARGP EELLCFTERLEDLVCFWEEAASAGVGPGNYSFSYQLEDEPWKLCRLH QAPTARGAVRFWCSLPTADTSSFVPLELRVTAASGAPRYHRVIHINEV VLLDAPVGLVARLADESGHVVLRWLPPPETPMTSHIRYEVDVSAGNG AGSVQRVEILEGRTECVLSNLRGRTRYTFAVRARMAEPSFGGFWSAW SEPVSLLTPSDLDPLILTLSLILVVILVLLTVLALLSHRRALKQKIWPGIP SPESEFEGLFTTHKGNFQLWLYQNDGCLWWSPCTPFTEDPPASLEVLS ERCWGTMQAVEPGTDDEGPLLEPVGSEHAQDTYLVLDKWLLPRNPP SEDLPGPGGSVDIVAMDEGSEASSCSSALASKPSPEGASAASFEYTILD PSSQLLRPWTLCPELPPTPPHLKYLYLVVSDSGISTDYSSGDSQGAQGG LSDGPYSNPYENSLIPAAEPLPPSYVACS	**21**
>AAI17403.1 白介素 6 信号转导因子（GP130，制瘤素 M 受体）[智人] MLTLQTWLVQALFIFLTTESTGELLDPCGYISPESPVVQLHSNFTAVCV LKEKCMDYFHVNANYIVWKTNHFTIPKEQYTIINRTASSVTFTDIASL NIQLTCNILTFGQLEQNVYGITIISGLPPEKPKNLSCIVNEGKKMRCEW DRGRETHLETNFTLKSEWATHKFADCKAKRDTPTSCTVDYSTVYFVN IEVWVEAENALGKVTSDHINFDPVYKVKPNPPHNLSVINSEELSSILKL TWTNPSIKSVIILKYNIQYRTKDASTWSQIPPEDTASTRSSFTVQDLKPF TEYVFRIRCMKEDGKGYWSDWSEEASGITYEDRPSKAPSFWYKIDPS HTQGYRTVQLVWKTLPPFEANGKILDYEVTLTRWKSHLQNYTVNATK LTVNLTNDRYVATLTVRNLVGKSDAAVLTIPACDFQATHPVMDLKAFP KDNMLWVEWTTPRESVKKYILEWCVLSDKAPCITDWQQEDGTVHRT YLRGNLAESKCYLITVTPVYADGPGSPESIKAYLKQAPPSKGPTVRTK KVGKNEAVLEWDQLPVDVQNGFIRNYTIFYRT IIGNETAVNVDSSHTEYTLSSLTSDTLYMVRMAAYTDEGGKDGPEFTF TTPKFAQGEIEAIVVPVCLAFLLTTLLGVLFCFNKRDLIKKHIWPNVPD PSKSHIAQWSPHTPPRHNFNSKDQMYSDGNFTDVSVVEIEANDKKPF PEDLKSLDLFKKEKINTEGHSSGIGGSSCMSSSRPSISSSDENESSQNTS STVQYSTVVHSGYRHQVPSVQVFSRSESTQPLLDSEERPEDLQLVDHV DGGDGILPRQQYFKQNCSQHESSPDISHFERSKQVSSVNEEDFVRLKQ QISDHISQSCGSGQMKMFQEVSAADAFGPGTEGQVERFETVGMEAAT DEGMPKSYLPQTVRQGGYMPQ	**22**
>XP_011512371.1 催乳素受体同种型 X2[智人] MKENVASATVFTLLLFLNTCLLNGQLPPGKPEIFKCRSPNKETFTCWW RPGTDGGLPTNYSLTYHREGETLMHECPDYITGGPNSCHFGKQYTSM WRTYIMMVNATNQMGSSFSDELYVDVTYIVQPDPPLELAVEVKQPED RKPYLWIKWSPPTLIDLKTGWFTLLYEIRLKPEKAAEWEIHFAGQQTE FKILSLHPGQKYLVQVRCKPDHGYWSAWSPATFIQIPSDFTMNDTTV WISVAVLSAVICLIIVWAVALKGYSMVTCIFPPVPGPKIKGFDAHLLEK	**23**

[0073]

天然存在的受体名称	SEQ ID NO:
GKSEELLSALGCQDFPPTSDYEDLLVEYLEVDDSEDQHLMSVHSKEH PSQGMKPTYLDPDTDSGRGSCDSPSLLSEKCEEPQANPSTFYDPEVIE KPENPETTHTWDPQCISMEGKIPYFHAGGSKCSTWPLPQPSQHNPRSS YHNITDVCELAVGPAGAPATLLNEAGKDALKSSQTIKSREEGKATQQR EVESFHSETDQDTPWLLPQEKTPFGSAKPLDYVEIHKVNKDGALSLLP KQRENSGKPKKPGTPENNKEYAKVSGVMDNNILVLVPDPHAKNVACF EESAKEAPPSLEQNQAEKALANFTATSSKCRLQLGGLDYLDPACFTHS FH	
>NP_000154.1 生长激素受体同种型 1 前体[智人] MDLWQLLLTLALAGSSDAFSGSEATAAILSRAPWSLQSVNPGLKTNSS KEPKFTKCRSPERETFSCHWTDEVHHGTKNLGPIQLFYTRRNTQEWT QEWKECPDYVSAGENSCYFNSSFTSIWIPYCIKLTSNGGTVDEKCFSV DEIVQPDPPIALNWTLLNVSLTGIHADIQVRWEAPRNADIQKGWMVL EYELQYKEVNETKWKMMDPILTTSVPVYSLKVDKEYEVRVRSKQRN SGNYGEFSEVLYVTLPQMSQFTCEEDFYFPWLLIIIFGIFGLTVMLFVFL FSKQQRIKMLILPPVPVPKIKGIDPDLLKEGKLEEVNTILAIHDSYKPEF HSDDSWVEFIELDIDEPDEKTEESDTDRLLSSDHEKSHSNLGVKDGDS GRTSCCEPDILETDFNANDIHEGTSEVAQPQRLKGEADLLCLDQKNQN NSPYHDACPATQQPSVIQAEKNKPQPLPTEGAESTHQAAHIQLSNPSSL SNIDFYAQVSDITPAGSVVLSPGQKNKAGMSQCDMHPEMVSLCQENF LMDNAYFCEADAKKCIPVAPHIKVESHIQPSLNQEDIYITTESLTTAAG RPGTGEHVPGSEMPVPDYTSIHIVQSPQGLILNATALPLPDKEFLSSCG YVSTDQLNKIMP	**24**
>XP_016855859.1 粒细胞集落-刺激因子受体同种型 X1[智人] MARLGNCSLTWAALIILLLPGSLEECGHISVSAPIVHLGDPITASCIIKQ NCSHLDPEPQILWRLGAELQPGGRQQRLSDGTQESIITLPHLNHTQAF LSCCLNWGNSLQILDQVELRAGYPPAIPHNLSCLMNLTTSSLICQWEP GPETHLPTSFTLKSFKSRGNCQTQGDSILDCVPKDGQSHCCIPRKHLLL YQNMGIWVQAENALGTSMSPQLCLDPMDVVKLEPPMLRTMDPSPEA APPQAGCLQLCWEPWQPGLHINQKCELRHKPQRGEASWALVGPLPLE ALQYELCGLLPATAYTLQIRCIRWPLPGHWSDWSPSLELRTTERAPTV RLDTWWRQRQLDPRTVQLFWKPVPLEEDSGRIQGYVVSWRPSGQAG AILPLCNTTELSCTFHLPSEAQEVALVAYNSAGTSRPTPVVFSESRGPAL TRLHAMARDPHSLWVGWEPPNPWPQGYVIEWGLGPPSASNSNKTWR MEQNGRATGFLLKENIRPFQLYEIIVTPLYQDTMGPSQHVYAYSQEMA PSHAPELHLKHIGKTWAQLEWVPEPPELGKSPLTHYTIFWTNAQNQSF SAILNASSRGFVLHGLEPASLYHIHLMAASQAGATNSTVLTLMTLTPE GSELHIILGLFGLLLLLTCLCGTAWLCCSPNRKNPLWPSVPDPAHSSLG SWVPTIMEELPGPRQGQWLGQTSEMSRALTPHPCVQDAFQLPGLGTP PITKLTVLEEDEKKPVPWESHNSSETCGLPTLVQTYVLQGDPRAVSTQ PQSQSGTSDQVLYGQLLGSPTSPGPGHYLRCDSTQPLLAGLTPSPKSY ENLWFQASPLGTLVTPAPSQEDDCVFGPLLNFPLLQGIRVHGMEALGS F	**25**
>NP_005364.1 血小板生成素受体前体[智人] MPSWALFMVTSCLLLAPQNLAQVSSQDVSLLASDSEPLKCFSRTFEDL TCFWDEEEAAPSGTYQLLYAYPREKPRACPLSSQSMPHFGTRYVCQFP DQEEVRLFFPLHLWVKNVFLNQTRTQRVLFVDSVGLPAPPSIIKAMGG	**26**

[0074]

天然存在的受体名称	SEQ ID NO:
SQPGELQISWEEPAPEISDFLRYELRYGPRDPKNSTGPTVIQLIATETCC PALQRPHSASALDQSPCAQPTMPWQDGPKQTSPSREASALTAEGGSC LISGLQPGNSYWLQLRSEPDGISLGGSWGSWSLPVTVDLPGDAVALGL QCFTLDLKNVTCQWQQQDHASSQGFFYHSRARCCPRDRYPIWENCE EEEKTNPGLQTPQFSRCHFKSRNDSIIHILVEVTTAPGTVHSYLGSPFWI HQAVRLPTPNLHWREISSGHLELEWQHPSSWAAQETCYQLRYTGEGH QDWKVLEPPLGARGGTLELRPRSRYRLQLRARLNGPTYQGPWSSWS DPTRVETATETAWISLVTALHLVLGLSAVLGLLLLRWQFPAHYRRLRH ALWPSLPDLHRVLGQYLRDTAALSPPKATVSDTCEEVEPSLLEILPKSS ERTPLPLCSSQAQMDYRRLQPSCLGTMPLSVCPPMAESGSCCTTHIAN HSYLPLSYWQQP	

[0075] 在一些实施例中,本公开的跨膜结构域源自表2中所示的天然存在的TPOR/MPLR受体的截短的或以其它方式修饰的版本。

[0076] 图9A-9B和10A示出了野生型TPOR和各种跨膜缺失(图9A、10A)或插入(图9B)变体的氨基酸序列。

[0077] 表3示出了与细胞内JAK2结合结构域序列偶联的示例性跨膜氨基酸序列。

[0078] 在一些实施例中,嵌合细胞因子受体的跨膜结构域包括SEQ ID NO:27的氨基酸序列。在一些实施例中,嵌合细胞因子受体的跨膜结构域包括SEQ ID NO:28的氨基酸序列。在一些实施例中,嵌合细胞因子受体的跨膜结构域包括SEQ ID NO:29的氨基酸序列。在一些实施例中,嵌合细胞因子受体的跨膜结构域包括SEQ ID NO:30的氨基酸序列。在一些实施例中,嵌合细胞因子受体的跨膜结构域包括SEQ ID NO:31的氨基酸序列。在一些实施例中,嵌合细胞因子受体的跨膜结构域包括SEQ ID NO:32的氨基酸序列。在一些实施例中,嵌合细胞因子受体的跨膜结构域包括SEQ ID NO:33的氨基酸序列。在一些实施例中,嵌合细胞因子受体的跨膜结构域包括SEQ ID NO:34的氨基酸序列。在一些实施例中,嵌合细胞因子受体的跨膜结构域包括SEQ ID NO:35的氨基酸序列。在一些实施例中,嵌合细胞因子受体的跨膜结构域包括SEQ ID NO:36的氨基酸序列。在一些实施例中,嵌合细胞因子受体的跨膜结构域包括SEQ ID NO:37的氨基酸序列。在一些实施例中,嵌合细胞因子受体的跨膜结构域包括SEQ ID NO:38的氨基酸序列。在一些实施例中,嵌合细胞因子受体的跨膜结构域包括SEQ ID NO:39的氨基酸序列。在一些实施例中,嵌合细胞因子受体的跨膜结构域包括SEQ ID NO:40的氨基酸序列。在一些实施例中,嵌合细胞因子受体的跨膜结构域包括SEQ ID NO:41的氨基酸序列。在一些实施例中,嵌合细胞因子受体的跨膜结构域包括SEQ ID NO:42的氨基酸序列。在一些实施例中,嵌合细胞因子受体的跨膜结构域包括SEQ ID NO:43的氨基酸序列。在一些实施例中,嵌合细胞因子受体的跨膜结构域包括SEQ ID NO:44的氨基酸序列。在一些实施例中,嵌合细胞因子受体的跨膜结构域包括SEQ ID NO:45的氨基酸序列。在一些实施例中,嵌合细胞因子受体的跨膜结构域包括SEQ ID NO:46的氨基酸序列。在一些实施例中,嵌合细胞因子受体的跨膜结构域包括SEQ ID NO:47的氨基酸序列。在一些实施例中,嵌合细胞因子受体的跨膜结构域包括SEQ ID NO:48的氨基酸序列。在一些实施例中,嵌合细胞因子受体的跨膜结构域包括SEQ ID NO:49的氨基酸序列。在一些实施例中,嵌合细胞因子受体的跨膜结构域包括SEQ ID NO:50的氨基酸序列。在一些实施例中,嵌合细胞因子受体的跨膜结构域包括SEQ ID NO:51的氨基酸序列。在一些实施例中,嵌合细

胞因子受体的跨膜结构域包括SEQ ID NO:52的氨基酸序列。在一些实施例中,嵌合细胞因子受体的跨膜结构域包括SEQ ID NO:53的氨基酸序列。在一些实施例中,嵌合细胞因子受体的跨膜结构域包括SEQ ID NO:54的氨基酸序列。在一些实施例中,嵌合细胞因子受体的跨膜结构域包括SEQ ID NO:55的氨基酸序列。在一些实施例中,嵌合细胞因子受体的跨膜结构域包括SEQ ID NO:56的氨基酸序列。在一些实施例中,嵌合细胞因子受体的跨膜结构域包括SEQ ID NO:57的氨基酸序列。在一些实施例中,嵌合细胞因子受体的跨膜结构域包括SEQ ID NO:58的氨基酸序列。在一些实施例中,嵌合细胞因子受体的跨膜结构域包括SEQ ID NO:59的氨基酸序列。在一些实施例中,嵌合细胞因子受体的跨膜结构域包括SEQ ID NO:60的氨基酸序列。在一些实施例中,嵌合细胞因子受体的跨膜结构域包括SEQ ID NO:61的氨基酸序列。在一些实施例中,嵌合细胞因子受体的跨膜结构域包括SEQ ID NO:62的氨基酸序列。在一些实施例中,嵌合细胞因子受体的跨膜结构域包括SEQ ID NO:63的氨基酸序列。在一些实施例中,嵌合细胞因子受体的跨膜结构域包括SEQ ID NO:64的氨基酸序列。在一些实施例中,嵌合细胞因子受体的跨膜结构域包括SEQ ID NO:65的氨基酸序列。在一些实施例中,嵌合细胞因子受体的跨膜结构域包括SEQ ID NO:66的氨基酸序列。在一些实施例中,嵌合细胞因子受体的跨膜结构域包括SEQ ID NO:67的氨基酸序列。在一些实施例中,嵌合细胞因子受体的跨膜结构域包括SEQ ID NO:68的氨基酸序列。在一些实施例中,嵌合细胞因子受体的跨膜结构域包括SEQ ID NO:69的氨基酸序列。在一些实施例中,嵌合细胞因子受体的跨膜结构域包括SEQ ID NO:70的氨基酸序列。在一些实施例中,嵌合细胞因子受体的跨膜结构域包括SEQ ID NO:71的氨基酸序列。在一些实施例中,嵌合细胞因子受体的跨膜结构域包括SEQ ID NO:72的氨基酸序列。在一些实施例中,嵌合细胞因子受体的跨膜结构域包括SEQ ID NO:73的氨基酸序列。在一些实施例中,嵌合细胞因子受体的跨膜结构域包括SEQ ID NO:74的氨基酸序列。在一些实施例中,嵌合细胞因子受体的跨膜结构域包括SEQ ID NO:75的氨基酸序列。在一些实施例中,嵌合细胞因子受体的跨膜结构域包括SEQ ID NO:76的氨基酸序列。在一些实施例中,嵌合细胞因子受体的跨膜结构域包括SEQ ID NO:77的氨基酸序列。在一些实施例中,嵌合细胞因子受体的跨膜结构域包括SEQ ID NO:78的氨基酸序列。在一些实施例中,嵌合细胞因子受体的跨膜结构域包括SEQ ID NO:79的氨基酸序列。在一些实施例中,嵌合细胞因子受体的跨膜结构域包括SEQ ID NO:160的氨基酸序列。在一些实施例中,嵌合细胞因子受体的跨膜结构域包括SEQ ID NO:217的氨基酸序列。在一些实施例中,嵌合细胞因子受体的跨膜结构域包括以下的氨基酸序列:SEQ ID NO:218、SEQ ID NO:219、SEQ ID NO:220、SEQ ID NO:221、SEQ ID NO:222、SEQ ID NO:223、SEQ ID NO:224、SEQ ID NO:225、SEQ ID NO:226、SEQ ID NO:227、SEQ ID NO:228、SEQ ID NO:229、SEQ ID NO:230、SEQ ID NO:231、SEQ ID NO:232、SEQ ID NO:233或SEQ ID NO:234。在一些实施例中,嵌合细胞因子受体的跨膜结构域包括与SEQ ID NO:27-79、160和217-234中的任一个的氨基酸序列具有至少80%、85%、90%、95%、98%或99%或100%相同的氨基酸序列。

[0079] 在一些实施例中,嵌合细胞因子受体(CCR)包括结合结构域以及跨膜结构域和JAK2结合结构域,所述结合结构域包括SEQ ID NO:3、4或159的氨基酸序列,所述结合结构域包括SEQ ID NO:64、69或70的氨基酸序列。在一些实施例中,CCR是诱导型的。在一些实施例中,CCR包括结合结构域以及跨膜结构域和JAK2结合结构域,所述结合结构域包括SEQ ID

NO:3、4或159的氨基酸序列，所述跨膜结构域和JAK2结合结构域包括SEQ ID NO:38、39、40或53的氨基酸序列。在一些实施例中，CCR包括结合结构域以及跨膜结构域和JAK2结合结构域，所述结合结构域包括SEQ ID NO:3、4或159的氨基酸序列，所述跨膜结构域和JAK2结合结构域包括SEQ ID NO:59、60、160或217的氨基酸序列。在一些实施例中，CCR具有组成型活性。在一些实施例中，在不具有TGF-β配体的情况下，使本公开的组成型活性CCR二聚化。

[0080] 表3:示例性跨膜+JAK2结合结构域序列

跨膜结构域和 JAK2 结合结构域	氨基酸序列	SEQ ID NO:
GCSFR(614-710)	LTLMTLTPEGSELHIILGLFGLLLLLTCLCGTA WLCCSPNRKNPLWPSVPDPAHSSLGSWVPTIM EEDAFQLPGLGTPPITKLTVLEEDEKKPVPWE	27
GP130(609-700)	TTPKFAQGEIEAIVVPVCLAFLLTTLLGVLFCF NKRDLIKKHIWPNVPDPSKSHIAQWSPHTPPR HNFNSKDQMYSDGNFTDVSVVEIEAND	28
TPOR/MPLR(478-582)	SDPTRVETATETAWISLVTALHLVLGLSAVLGL LLLRWQFPAHYRRLRHALWPSLPDLHRVLGQ YLRDTAALSPPKATVSDTCEEVEPSLLEILPKS SERTPLPL	29
TPOR/MPLR(N-1)	SDPTRVETATETWISLVTALHLVLGLSAVLGLL LLRWQFPAHYRRLRHALWPSLPDLHRVLGQY LRDTAALSPPKATVSDTCEEVEPSLLEILPKSSE RTPLPL	30
TPOR/MPLR(N-2)	SDPTRVETATETISLVTALHLVLGLSAVLGLLLL RWQFPAHYRRLRHALWPSLPDLHRVLGQYLR DTAALSPPKATVSDTCEEVEPSLLEILPKSSERT PLPL	31
TPOR/MPLR(N-2+1)	SDPTRVETATETLISLVTALHLVLGLSAVLGLLL LRWQFPAHYRRLRHALWPSLPDLHRVLGQYL RDTAALSPPKATVSDTCEEVEPSLLEILPKSSER TPLPL	32
TPOR/MPLR(N-3)	SDPTRVETATETSLVTALHLVLGLSAVLGLLLL RWQFPAHYRRLRHALWPSLPDLHRVLGQYLR DTAALSPPKATVSDTCEEVEPSLLEILPKSSERT PLPL	33
TPOR/MPLR(N-4)	SDPTRVETATETLVTALHLVLGLSAVLGLLLLR WQFPAHYRRLRHALWPSLPDLHRVLGQYLRD TAALSPPKATVSDTCEEVEPSLLEILPKSSERTP LPL	34
TPOR/MPLR(N-4+1)	SDPTRVETATETILVTALHLVLGLSAVLGLLLLR WQFPAHYRRLRHALWPSLPDLHRVLGQYLRD TAALSPPKATVSDTCEEVEPSLLEILPKSSERTP LPL	35
TPOR/MPLR(N-5)	SDPTRVETATETVTALHLVLGLSAVLGLLLLR WQFPAHYRRLRHALWPSLPDLHRVLGQYLRD TAALSPPKATVSDTCEEVEPSLLEILPKSSERTP LPL	36
TPOR/MPLR(N-6)	SDPTRVETATETTALHLVLGLSAVLGLLLLRW	37

[0081]

[0082]

跨膜结构域和 JAK2 结合结构域	氨基酸序列	SEQ ID NO:
	QFPAHYRRLRHALWPSLPDLHRVLGQYLRDTAALSPPKATVSDTCEEVEPSLLEILPKSSERTPLPL	
TPOR/MPLR(N-7)	SDPTRVETATETALHLVLGLSAVLGLLLLRWQFPAHYRRLRHALWPSLPDLHRVLGQYLRDTAALSPPKATVSDTCEEVEPSLLEILPKSSERTPLPL	38
TPOR/MPLR(N-8)	SDPTRVETATETLHLVLGLSAVLGLLLLRWQFPAHYRRLRHALWPSLPDLHRVLGQYLRDTAALSPPKATVSDTCEEVEPSLLEILPKSSERTPLPL	39
TPOR/MPLR(N-9)	SDPTRVETATETHLVLGLSAVLGLLLLRWQFPAHYRRLRHALWPSLPDLHRVLGQYLRDTAALSPPKATVSDTCEEVEPSLLEILPKSSERTPLPL	40
TPOR/MPLR(N-10)	SDPTRVETATETLVLGLSAVLGLLLLRWQFPAHYRRLRHALWPSLPDLHRVLGQYLRDTAALSPPKATVSDTCEEVEPSLLEILPKSSERTPLPL	41
TPOR/MPLR(N-11)	SDPTRVETATETVLGLSAVLGLLLLRWQFPAHYRRLRHALWPSLPDLHRVLGQYLRDTAALSPPKATVSDTCEEVEPSLLEILPKSSERTPLPL	42
TPOR/MPLR(N-12)	SDPTRVETATETLGLSAVLGLLLLRWQFPAHYRRLRHALWPSLPDLHRVLGQYLRDTAALSPPKATVSDTCEEVEPSLLEILPKSSERTPLPL	43
TPOR/MPLR(N-13)	SDPTRVETATETGLSAVLGLLLLRWQFPAHYRRLRHALWPSLPDLHRVLGQYLRDTAALSPPKATVSDTCEEVEPSLLEILPKSSERTPLPL	44
TPOR/MPLR(N-14)	SDPTRVETATETLSAVLGLLLLRWQFPAHYRRLRHALWPSLPDLHRVLGQYLRDTAALSPPKATVSDTCEEVEPSLLEILPKSSERTPLPL	45
TPOR/MPLR(N-15)	SDPTRVETATETSAVLGLLLLRWQFPAHYRRLRHALWPSLPDLHRVLGQYLRDTAALSPPKATVSDTCEEVEPSLLEILPKSSERTPLPL	46
TPOR/MPLR(N-16)	SDPTRVETATETAVLGLLLLRWQFPAHYRRLRHALWPSLPDLHRVLGQYLRDTAALSPPKATVSDTCEEVEPSLLEILPKSSERTPLPL	47
TPOR/MPLR(N-17)	SDPTRVETATETVLGLLLLRWQFPAHYRRLRHALWPSLPDLHRVLGQYLRDTAALSPPKATVSDTCEEVEPSLLEILPKSSERTPLPL	48
TPOR/MPLR(N-18)	SDPTRVETATETLGLLLLRWQFPAHYRRLRHALWPSLPDLHRVLGQYLRDTAALSPPKATVSDTCEEVEPSLLEILPKSSERTPLPL	49
TPOR/MPLR(N+1)	SDPTRVETATETAWLISLVTALHLVLGLSAVLGLLLLRWQFPAHYRRLRHALWPSLPDLHRVLGQYLRDTAALSPPKATVSDTCEEVEPSLLEILPKSSERTPLPL	50
TPOR/MPLR(N+2)	SDPTRVETATETAWVLISLVTALHLVLGLSAVLGLLLLRWQFPAHYRRLRHALWPSLPDLHRVLGQYLRDTAALSPPKATVSDTCEEVEPSLLEILPKSSERTPLPL	51

[0083]

跨膜结构域和 JAK2 结合结构域	氨基酸序列	SEQ ID NO:
TPOR/MPLR(N+3)	SDPTRVETATETAWLVLISLVTALHLVLGLSAV LGLLLLRWQFPAHYRRLRHALWPSLPDLHRV LGQYLRDTAALSPPKATVSDTCEEVEPSLLEIL PKSSERTPLPL	52
TPOR/MPLR(N+4)	SDPTRVETATETAWILVLISLVTALHLVLGLSAV LGLLLLRWQFPAHYRRLRHALWPSLPDLHRV LGQYLRDTAALSPPKATVSDTCEEVEPSLLEIL PKSSERTPLPL	53
TPOR/MPLR(N+5)	SDPTRVETATETAWLILVLISLVTALHLVLGLSA VLGLLLLRWQFPAHYRRLRHALWPSLPDLHR VLGQYLRDTAALSPPKATVSDTCEEVEPSLLEI LPKSSERTPLPL	54
TPOR/MPLR(N+6)	SDPTRVETATETAWLLILVLISLVTALHLVLGLS AVLGLLLLRWQFPAHYRRLRHALWPSLPDLHR VLGQYLRDTAALSPPKATVSDTCEEVEPSLLEI LPKSSERTPLPL	55
TPOR/MPLR(N+7)	SDPTRVETATETAWVLLILVLISLVTALHLVLGL SAVLGLLLLRWQFPAHYRRLRHALWPSLPDLH RVLGQYLRDTAALSPPKATVSDTCEEVEPSLL EILPKSSERTPLPL	56
TPOR/MPLR(N+8)	SDPTRVETATETAWLVLLILVLISLVTALHLVLG LSAVLGLLLLRWQFPAHYRRLRHALWPSLPDL HRVLGQYLRDTAALSPPKATVSDTCEEVEPSL LEILPKSSERTPLPL	57
TPOR/MPLR(478-582; W515K)	SDPTRVETATETAWISLVTALHLVLGLSAVLGL LLLR**K**QFPAHYRRLRHALWPSLPDLHRVLGQ YLRDTAALSPPKATVSDTCEEVEPSLLEILPKS SERTPLPL	58
TPOR/MPLR(478-582; H499L,S505N,W515K)	SDPTRVETATETAWISLVTAL**L**LVLGL**N**AVLGL LLLR**K**QFPAHYRRLRHALWPSLPDLHRVLGQ YLRDTAALSPPKATVSDTCEEVEPSLLEILPKS SERTPLPL	59
TPOR/MPLR(478-582; S505N,W515K)	SDPTRVETATETAWISLVTALHLVLGL**N**AVLGL LLLR**K**QFPAHYRRLRHALWPSLPDLHRVLGQ YLRDTAALSPPKATVSDTCEEVEPSLLEILPKS SERTPLPL	60
TPOR/MPLR(N-9-1)	SDPTRVETATEHLVLGLSAVLGLLLLRWQFPA HYRRLRHALWPSLPDLHRVLGQYLRDTAALS PPKATVSDTCEEVEPSLLEILPKSSERTPLPL	61
TPOR/MPLR(N-9-2)	SDPTRVETATHLVLGLSAVLGLLLLRWQFPAH YRRLRHALWPSLPDLHRVLGQYLRDTAALSPP KATVSDTCEEVEPSLLEILPKSSERTPLPL	62
TPOR/MPLR(N-9-3)	SDPTRVETAHLVLGLSAVLGLLLLRWQFPAHY RRLRHALWPSLPDLHRVLGQYLRDTAALSPPK ATVSDTCEEVEPSLLEILPKSSERTPLPL	63
TPOR/MPLR(N-9-4)	SDPTRVETHLVLGLSAVLGLLLLRWQFPAHYR RLRHALWPSLPDLHRVLGQYLRDTAALSPPKA	64

[0084]

跨膜结构域和 JAK2 结合结构域	氨基酸序列	SEQ ID NO:
	TVSDTCEEVEPSLLEILPKSSERTPLPL	
TPOR/MPLR(N-9-5)	SDPTRVEHLVLGLSAVLGLLLLRWQFPAHYRRLRHALWPSLPDLHRVLGQYLRDTAALSPPKATVSDTCEEVEPSLLEILPKSSERTPLPL	65
TPOR/MPLR(N-9-6)	SDPTRVHLVLGLSAVLGLLLLRWQFPAHYRRLRHALWPSLPDLHRVLGQYLRDTAALSPPKATVSDTCEEVEPSLLEILPKSSERTPLPL	66
TPOR/MPLR(N-9-7)	SDPTRHLVLGLSAVLGLLLLRWQFPAHYRRLRHALWPSLPDLHRVLGQYLRDTAALSPPKATVSDTCEEVEPSLLEILPKSSERTPLPL	67
TPOR/MPLR(N-9-8)	SDPTHLVLGLSAVLGLLLLRWQFPAHYRRLRHALWPSLPDLHRVLGQYLRDTAALSPPKATVSDTCEEVEPSLLEILPKSSERTPLPL	68
TPOR/MPLR(N-9-9)	SDPHLVLGLSAVLGLLLLRWQFPAHYRRLRHALWPSLPDLHRVLGQYLRDTAALSPPKATVSDTCEEVEPSLLEILPKSSERTPLPL	69
TPOR/MPLR(N-9-10)	SDHLVLGLSAVLGLLLLRWQFPAHYRRLRHALWPSLPDLHRVLGQYLRDTAALSPPKATVSDTCEEVEPSLLEILPKSSERTPLPL	70
TPOR/MPLR(N-9-11)	SHLVLGLSAVLGLLLLRWQFPAHYRRLRHALWPSLPDLHRVLGQYLRDTAALSPPKATVSDTCEEVEPSLLEILPKSSERTPLPL	71
TPOR/MPLR(N-9-12)	HLVLGLSAVLGLLLLRWQFPAHYRRLRHALWPSLPDLHRVLGQYLRDTAALSPPKATVSDTCEEVEPSLLEILPKSSERTPLPL	72
TPOR/MPLR(N-C3)	SDPTRVETATETAWISLVHLVLGLSAVLGLLLLRWQFPAHYRRLRHALWPSLPDLHRVLGQYLRDTAALSPPKATVSDTCEEVEPSLLEILPKSSERTPLPL	73
TPOR/MPLR(N-C5)	SDPTRVETATETAWISHLVLGLSAVLGLLLLRWQFPAHYRRLRHALWPSLPDLHRVLGQYLRDTAALSPPKATVSDTCEEVEPSLLEILPKSSERTPLPL	74
TPOR/MPLR(N-C5P)	SDPTRVETATETAWISPHLVLGLSAVLGLLLLRWQFPAHYRRLRHALWPSLPDLHRVLGQYLRDTAALSPPKATVSDTCEEVEPSLLEILPKSSERTPLPL	75
TPOR/MPLR(N-C5PP)	SDPTRVETATETAWISPPHLVLGLSAVLGLLLLRWQFPAHYRRLRHALWPSLPDLHRVLGQYLRDTAALSPPKATVSDTCEEVEPSLLEILPKSSERTPLPL	76
TPOR/MPLR(N-C6)	SDPTRVETATETAWIHLVLGLSAVLGLLLLRWQFPAHYRRLRHALWPSLPDLHRVLGQYLRDTAALSPPKATVSDTCEEVEPSLLEILPKSSERTPLPL	77
TPOR/MPLR(N-C6P)	SDPTRVETATETAWIPHLVLGLSAVLGLLLLRWQFPAHYRRLRHALWPSLPDLHRVLGQYLRDT	78

[0085]

跨膜结构域和 JAK2 结合结构域	氨基酸序列	SEQ ID NO:
	AALSPPKATVSDTCEEVEPSLLEILPKSSERTPLPL	
TPOR/MPLR(N-C6PP)	SDPTRVETATETAWIPPHLVLGLSAVLGLLLLRWQFPAHYRRLRHALWPSLPDLHRVLGQYLRDTAALSPPKATVSDTCEEVEPSLLEILPKSSERTPLPL	79
TPOR/MPLR(478-582; H499L,S505N,W515K, K553R,K573R)	SDPTRVETATETAWISLVTALLLVLGLNAVLGLLLLRKQFPAHYRRLRHALWPSLPDLHRVLGQYLRDTAALSPPRATVSDTCEEVEPSLLEILPRSSERTPLPL	217
TPOR/MPLR(478-582) S505N.W515K. K553R.K573R	SDPTRVETATETAWISLVTALHLVLGL**N**AVLGLLLLR**K**QFPAHYRRLRHALWPSLPDLHRVLGQYLRDTAALSPP**R**ATVSDTCEEVEPSLLEILP**R**SSERTPLPL	160
TPOR/MPLR(478-582) K553R.K573R	SDPTRVETATETAWISLVTALHLVLGLSAVLGLLLLRWQFPAHYRRLRHALWPSLPDLHRVLGQYLRDTAALSPP**R**ATVSDTCEEVEPSLLEILP**R**SSERTPLPL	218
TPOR/MPLR(N-7) S505N.W515K	SDPTRVETATETALHLVLGL**N**AVLGLLLLR**K**QFPAHYRRLRHALWPSLPDLHRVLGQYLRDTAALSPPKATVSDTCEEVEPSLLEILPKSSERTPLPL	219
TPOR/MPLR(N-7) S505N.W515K. K553R,K573R	SDPTRVETATETALHLVLGL**N**AVLGLLLLR**K**QFPAHYRRLRHALWPSLPDLHRVLGQYLRDTAALSPP**R**ATVSDTCEEVEPSLLEILP**R**SSERTPLPL	220
TPOR/MPLR(N-8) S505N.W515K	SDPTRVETATETLHLVLGL**N**AVLGLLLLR**K**QFPAHYRRLRHALWPSLPDLHRVLGQYLRDTAALSPPKATVSDTCEEVEPSLLEILPKSSERTPLPL	221
TPOR/MPLR(N-8) S505N.W515K. K553R,K573R	SDPTRVETATETLHLVLGL**N**AVLGLLLLR**K**QFPAHYRRLRHALWPSLPDLHRVLGQYLRDTAALSPP**R**ATVSDTCEEVEPSLLEILP**R**SSERTPLPL	222
TPOR/MPLR(N-9) S505N.W515K	SDPTRVETATETHLVLGL**N**AVLGLLLLR**K**QFPAHYRRLRHALWPSLPDLHRVLGQYLRDTAALSPPKATVSDTCEEVEPSLLEILPKSSERTPLPL	223
TPOR/MPLR(N-9) S505N.W515K. K553R,K573R	SDPTRVETATETHLVLGL**N**AVLGLLLLR**K**QFPAHYRRLRHALWPSLPDLHRVLGQYLRDTAALSPP**R**ATVSDTCEEVEPSLLEILP**R**SSERTPLPL	224
TPOR/MPLR(N+4) S505N.W515K	SDPTRVETATETAWILVLISLVTALHLVLGL**N**AVLGLLLLR**K**QFPAHYRRLRHALWPSLPDLHRVLGQYLRDTAALSPPKATVSDTCEEVEPSLLEILPKSSERTPLPL	225
TPOR/MPLR(N+4) S505N.W515K. K553R,K573R	SDPTRVETATETAWILVLISLVTALHLVLGL**N**AVLGLLLLR**K**QFPAHYRRLRHALWPSLPDLHRVLGQYLRDTAALSPP**R**ATVSDTCEEVEPSLLEILP**R**SSERTPLPL	226
TPOR/MPLR(N-9-1)	SDPTRVETATEHLVLGL**N**AVLGLLLLR**K**QFPA	227

[0086]

跨膜结构域和JAK2结合结构域	氨基酸序列	SEQ ID NO:
S505N.W515K	HYRRLRHALWPSLPDLHRVLGQYLRDTAALS PPKATVSDTCEEVEPSLLEILPKSSERTPLPL	
TPOR/MPLR(N-9-1) S505N.W515K. K553R,K573R	SDPTRVETATEHLVLGL**N**AVLGLLLLR**K**QFPA HYRRLRHALWPSLPDLHRVLGQYLRDTAALS PP**R**ATVSDTCEEVEPSLLEILP**R**SSERTPLPL	228
TPOR/MPLR(N-9-4) S505N.W515K	SDPTRVETHLVLGL**N**AVLGLLLLR**K**QFPAHYR RLRHALWPSLPDLHRVLGQYLRDTAALSPPKA TVSDTCEEVEPSLLEILPKSSERTPLPL	229
TPOR/MPLR(N-9-4) S505N.W515K. K553R,K573R	SDPTRVETHLVLGL**N**AVLGLLLLR**K**QFPAHYR RLRHALWPSLPDLHRVLGQYLRDTAALSPP**R**A TVSDTCEEVEPSLLEILP**R**SSERTPLPL	230
TPOR/MPLR(N-9-9) S505N.W515K	SDPHLVLGL**N**AVLGLLLLR**K**QFPAHYRRLRHA LWPSLPDLHRVLGQYLRDTAALSPPKATVSDT CEEVEPSLLEILPKSSERTPLPL	231
TPOR/MPLR(N-9-9) S505N.W515K. K553R,K573R	SDPHLVLGL**N**AVLGLLLLR**K**QFPAHYRRLRHA LWPSLPDLHRVLGQYLRDTAALSPP**R**ATVSDT CEEVEPSLLEILP**R**SSERTPLPL	232
TPOR/MPLR(N-9-10) S505N.W515K	SDHLVLGL**N**AVLGLLLLR**K**QFPAHYRRLRHAL WPSLPDLHRVLGQYLRDTAALSPPKATVSDTC EEVEPSLLEILPKSSERTPLPL	233
TPOR/MPLR(N-9-10) S505N.W515K. K553R,K573R	SDHLVLGL**N**AVLGLLLLR**K**QFPAHYRRLRHAL WPSLPDLHRVLGQYLRDTAALSPP**R**ATVSDTC EEVEPSLLEILP**R**SSERTPLPL	234

[0087] C.Janus激酶(JAK)结合结构域

[0088] 本公开的嵌合细胞因子受体包括细胞内JAK结合结构域。JAK结合结构域直接或通过连接子与跨膜结构域的C端偶联。JAK结合结构域与嵌合细胞因子受体的细胞内侧上的跨膜结构域偶联。

[0089] 在一些实施例中,JAK结合结构域是JAK-1结合结构域、JAK-2结合结构域、JAK-3结合结构域或TYK2结合结构域。

[0090] 在一些实施例中,本公开的嵌合细胞因子受体的JAK结合结构域是天然存在的,并且源自天然存在的受体。

[0091] 在一些实施例中,本公开的嵌合细胞因子受体的JAK结合结构域是合成的。

[0092] 在一些实施例中,嵌合细胞因子受体包括与SEQ ID NO:27-79、160和217-234的氨基酸序列中的任一个具有至少80%、85%、90%、95%、98%或99%或100%相同的跨膜结构域和JAK2结合结构域。

[0093] 表3提供了用于本公开的跨膜结构域和JAK2结合结构域的示例性氨基酸序列。在一些实施例中,跨膜结构域和JAK2结合结构域包括一个或多个突变,例如野生型序列的一个或多个缺失、插入和/或取代。在一些实施例中,跨膜结构域和JAK2结合结构域包括在野生型TPOR/MPLR序列的氨基酸位置H499、S505和W515处的一个或多个替代。参见表3。在一些实施例中,跨膜结构域和JAK2结合结构域包括野生型TPOR/MPLR序列的氨基酸位置K533和K573处的一个或多个取代。在一些实施例中,例如如表3中所示的跨膜结构域和JAK2结合结构域可以与例如表1中的如本文所公开的TGFβR2胞外域或PD-1胞外域(如高亲和力PD-1胞外域,如表6中的SEQ ID NO:274或275所指示的)和募集结构域组合,以形成嵌合细胞因子受体。在一些实施例中,跨膜结构域和JAK2结合结构域可以与募集结构域组合,以形成无胞

外域的嵌合细胞因子受体,参见例如SEQ ID NO:272或273。还参见于2020年2月28日提交的USSN 16/804,917和于2020年2月28日提交的USSN 16/804,545,所述两个文献均通过引用整体并入本文。

[0094] D.募集结构域

[0095] 本公开的嵌合细胞因子受体包括细胞质结构域,所述细胞质结构域包括募集结构域(其也可以被称为"信号传导结构域")。募集结构域可以是STAT募集结构域、AP1募集结构域、Myc/Max募集结构域;或NFkB募集结构域。在一些实施例中,募集结构域是来自受体尾区(细胞尾(cytotail))或来自细胞因子受体尾区的信号转导因子和转录激活子(STAT)--募集(Stat激活)结构域。本公开的嵌合细胞因子受体的这些细胞内募集结构域允许信号3在包括CAR和嵌合细胞因子受体的免疫细胞(例如,具有本公开的嵌合细胞因子受体的CAR-T细胞)中传播。通过Stat募集结构域传播的细胞因子信号传导允许细胞的基于细胞因子的免疫增强。在一些实施例中,免疫增强是稳态的,例如信号传导导致具有CAR的免疫细胞增加。在一些实施例中,免疫增强是炎性的,例如信号传导导致具有CAR的免疫细胞的效力增加。在一些实施例中,免疫增强防止衰竭,例如信号传导保持具有CAR的免疫细胞的长期功能性。

[0096] 在一些实施例中,本公开的募集结构域是合成的并且不类似于任何天然存在的受体片段。

[0097] 在一些实施例中,本公开的Stat募集结构域是合成的并且不类似于任何天然存在的受体片段。

[0098] 在其它实施例中,本公开的Stat募集结构域源自天然存在的受体的细胞质尾区,例如源自天然存在的细胞因子受体。在一些实施例中,嵌合细胞因子受体包括天然存在的受体的一部分或片段,例如天然存在的受体的细胞内Stat募集结构域,任选地在其中具有一个或多个突变(例如,一个或多个缺失、插入和/或取代)。天然存在的受体的这些细胞质尾区可能是位于受体的跨膜结构域的JAK激活结构域下游的区域。嵌合细胞因子受体的Stat募集结构域包括来自至少一个受体的至少一个STAT募集结构域。在一些实施例中,Stat募集结构域包括至少一个STAT1募集结构域。在一些实施例中,Stat募集结构域包括至少一个STAT2募集结构域。在一些实施例中,Stat募集结构域包括至少一个STAT3募集结构域。在一些实施例中,Stat募集结构域包括至少一个STAT4募集结构域。在一些实施例中,Stat募集结构域包括至少一个STAT5募集结构域。在一些实施例中,Stat募集结构域包括至少一个STAT6募集结构域。在一些实施例中,Stat募集结构域包括至少一个STAT7募集结构域。

[0099] 在一些实施例中,STAT募集结构域所源自的天然存在的受体不是细胞因子受体。

[0100] 在一些实施例中,Stat-募集结构域所源自的天然存在的受体是细胞因子受体。T细胞免疫增强细胞因子通过其发出信号的示例性细胞因子受体包含但不限于IL-2受体、IL-7受体、IL-15受体、IL12受体和IL-21受体。在一些实施例中,STAT募集结构域所源自的细胞因子受体含有位于同源JAK结合基序下游的可磷酸化酪氨酸残基,并且一个或多个所关注信号传导结构域可以融合在跨膜结构域下游以产生单个或多个信号传导输出。在替代性实施例中,Stat募集结构域所源自的受体不是细胞因子受体。通过选择嵌合细胞因子受体的Stat募集结构域,可以将受体重新定向到选择的信号传导。在一些实施例中,嵌合细胞

因子受体包括来自多于一个受体的两个或更多个Stat募集结构域。在一些实施例中,所述两个或更多个Stat募集结构域用或不用肽连接子连接。

[0101] 表4提供了示例性受体,本公开的嵌合细胞因子受体的Stat募集结构域(信号传导结构域)源自所述示例性受体。表5a提供了本公开的募集结构域的示例性氨基酸序列。

[0102] 在一些实施例中,本公开的嵌合细胞因子受体包括SEQ ID NO:80的STAT募集结构域的氨基酸序列。在一些实施例中,本公开的嵌合细胞因子受体包括SEQ ID NO:81的STAT募集结构域的氨基酸序列。在一些实施例中,本公开的嵌合细胞因子受体包括SEQ ID NO:82的STAT募集结构域的氨基酸序列。在一些实施例中,本公开的嵌合细胞因子受体包括SEQ ID NO:83的STAT募集结构域的氨基酸序列。在一些实施例中,本公开的嵌合细胞因子受体包括SEQ ID NO:84的STAT募集结构域的氨基酸序列。在一些实施例中,本公开的嵌合细胞因子受体包括SEQ ID NO:85的STAT募集结构域的氨基酸序列。在一些实施例中,本公开的嵌合细胞因子受体包括SEQ ID NO:86的STAT募集结构域的氨基酸序列。在一些实施例中,本公开的嵌合细胞因子受体包括SEQ ID NO:87的STAT募集结构域的氨基酸序列。在一些实施例中,本公开的嵌合细胞因子受体包括SEQ ID NO:88的STAT募集结构域的氨基酸序列。在一些实施例中,本公开的嵌合细胞因子受体包括SEQ ID NO:89的STAT募集结构域的氨基酸序列。在一些实施例中,本公开的嵌合细胞因子受体包括SEQ ID NO:90的STAT募集结构域的氨基酸序列。在一些实施例中,本公开的嵌合细胞因子受体包括SEQ ID NO:91的STAT募集结构域的氨基酸序列。在一些实施例中,本公开的嵌合细胞因子受体包括SEQ ID NO:92的STAT募集结构域的氨基酸序列。在一些实施例中,本公开的嵌合细胞因子受体包括SEQ ID NO:93的STAT募集结构域的氨基酸序列。在一些实施例中,本公开的嵌合细胞因子受体包括SEQ ID NO:94的STAT募集结构域的氨基酸序列。在一些实施例中,本公开的嵌合细胞因子受体包括SEQ ID NO:95的STAT募集结构域的氨基酸序列。在一些实施例中,本公开的嵌合细胞因子受体包括SEQ ID NO:96的STAT募集结构域的氨基酸序列。在一些实施例中,本公开的嵌合细胞因子受体包括SEQ ID NO:97的STAT募集结构域的氨基酸序列。在一些实施例中,本公开的嵌合细胞因子受体包括SEQ ID NO:98的STAT募集结构域的氨基酸序列。在一些实施例中,本公开的嵌合细胞因子受体包括SEQ ID NO:99的STAT募集结构域的氨基酸序列。在一些实施例中,本公开的嵌合细胞因子受体包括SEQ ID NO:100的STAT募集结构域的氨基酸序列。在一些实施例中,本公开的嵌合细胞因子受体包括SEQ ID NO:101的STAT募集结构域的氨基酸序列。在一些实施例中,本公开的嵌合细胞因子受体包括SEQ ID NO:102的STAT募集结构域的氨基酸序列。在一些实施例中,本公开的嵌合细胞因子受体包括SEQ ID NO:103的STAT募集结构域的氨基酸序列。在一些实施例中,本公开的嵌合细胞因子受体包括SEQ ID NO:104的STAT募集结构域的氨基酸序列。在一些实施例中,本公开的嵌合细胞因子受体包括SEQ ID NO:105的STAT募集结构域的氨基酸序列。在一些实施例中,本公开的嵌合细胞因子受体包括SEQ ID NO:106的STAT募集结构域的氨基酸序列。在一些实施例中,本公开的嵌合细胞因子受体包括SEQ ID NO:107的STAT募集结构域的氨基酸序列。在一些实施例中,本公开的嵌合细胞因子受体包括SEQ ID NO:108的STAT募集结构域的氨基酸序列。在一些实施例中,本公开的嵌合细胞因子受体包括SEQ ID NO:109的STAT募集结构域的氨基酸序列。在一些实施例中,本公开的嵌合细胞因子受体包括SEQ ID NO:110的STAT募集结构域的氨基酸序列。在一些实施例中,本公开的嵌合细胞因子受体包括SEQ ID NO:

111的STAT募集结构域的氨基酸序列。在一些实施例中，本公开的嵌合细胞因子受体包括SEQ ID NO:112的STAT募集结构域的氨基酸序列。在一些实施例中，本公开的嵌合细胞因子受体包括SEQ ID NO:113的STAT募集结构域的氨基酸序列。在一些实施例中，本公开的嵌合细胞因子受体包括SEQ ID NO:114的STAT募集结构域的氨基酸序列。在一些实施例中，本公开的嵌合细胞因子受体包括SEQ ID NO:115的STAT募集结构域的氨基酸序列。在一些实施例中，本公开的嵌合细胞因子受体包括SEQ ID NO:116的STAT募集结构域的氨基酸序列。在一些实施例中，本公开的嵌合细胞因子受体包括SEQ ID NO:117的STAT募集结构域的氨基酸序列。在一些实施例中，本公开的嵌合细胞因子受体包括SEQ ID NO:118的STAT募集结构域的氨基酸序列。在一些实施例中，本公开的嵌合细胞因子受体包括SEQ ID NO:119的STAT募集结构域的氨基酸序列。在一些实施例中，本公开的嵌合细胞因子受体包括SEQ ID NO:120的STAT募集结构域的氨基酸序列。在一些实施例中，本公开的嵌合细胞因子受体包括SEQ ID NO:121的STAT募集结构域的氨基酸序列。在一些实施例中，本公开的嵌合细胞因子受体包括SEQ ID NO:122的STAT募集结构域的氨基酸序列。在一些实施例中，本公开的嵌合细胞因子受体包括SEQ ID NO:161的STAT募集结构域的氨基酸序列。在一些实施例中，嵌合细胞因子受体包括募集结构域，所述募集结构域包括与SEQ ID NO:80-122和SEQ ID NO:161的氨基酸序列中的任一个具有至少80％、85％、90％、95％、98％或99％或100％相同的氨基酸序列。

[0103] 表4:募集结构域来源

[0104]

募集结构域的来源
BLNK
IL2RG

[0105]

募集结构域的来源
EGFR
EpoR
GHR
IFNAR1
IFNAR2
IFNAR1/2
IFNLR1
IL10R1
IL12Rb1
IL12Rb2
IL21R
IL2Rb
IL2small
IL7R
IL7Ra
IL9R
IL15R
IL21R

[0106] 表5a:募集结构域序列(细胞尾序列)

[0107]

募集结构域	氨基酸序列	SEQ ID NO:
IL7R(316-459)	ARDEVEGFLQDTFPQQLEESEKQRLGGDVQSP NCPSEDVVITPESFGRDSSLTCLAGNVSACDAP ILSSSRSLDCRESGKNGPHVYQDLLLSLGTTNS TLPPPFSLQSGILTLNPVAQGQPILTSLGSNQEEA YVTMSSFYQNQ	80
IL2Rb(333-551)	VTQLLLQQDKVPEPASLSSNHSLTSCFTNQGYF FFHLPDALEIEACQVYFTYDPYSEEDPDEGVAG APTGSSPQPLQPLSGEDDAYCTFPSRDDLLLFS PSLLGGPSPPSTAPGGSGAGEERMPPSLQERVP RDWDPQPLGPPTPGVPDLVDFQPPPELVLREA GEEVPDAGPREGVSFPWSRPPGQGEFRALNAR LPLNTDAYLSLQELQGQDPTHLV	81
IFNAR1(508-557)	ISTIATVEETNQTDEDHKKYSSQTSQDSGNYSN EDESESKTSEELQQDFV	82
IFNAR2(310-515)	KKKVWDYNYDDESDSDTEAAPRTSGGGYTM HGLTVRPLGQASATSTESQLIDPESEEEPDLPEV DVELPTMPKDSPQQLELLSGPCERRKSPLQDPF PEEDYSSTEGSGGRITFNVDLNSVFLRVLDDED SDDLEAPLMLSSHLEEMVDPEDPDNVQSNHLL ASGEGTQPTFPSPSSEGLWSEDAPSDQSDTSES DVDLGDGYIMR	83
IFNAR1/2(IFNAR1 残基 508-557-IFNAR2 残基 310-515)	ISTIATVEETNQTDEDHKKYSSQTSQDSGNYSN EDESESKTSEELQQDFVKKKVWDYNYDDESD SDTEAAPRTSGGGYTMHGLTVRPLGQASATST ESQLIDPESEEEPDLPEVDVELPTMPKDSPQQL	84

[0108]

募集结构域	氨基酸序列	SEQ ID NO:
	ELLSGPCERRKSPLQDPFPEEDYSSTEGSGGRIT FNVDLNSVFLRVLDDEDSDDLEAPLMLSSHLE EMVDPEDPDNVQSNHLLASGEGTQPTFPSPSSE GLWSEDAPSDQSDTSESDVDLGDGYIMR	
IFNLR1(300-520)	RGVRPTPRVRAPATQQTRWKKDLAEDEEEEDE EDTEDGVSFQPYIEPPSFLGQEHQAPGHSEAGG VDSGRPRAPLVPSEGSSAWDSSDRSWASTVDS SWDRAGSSGYLAEKGPGQGPGGDGHQESLPP PEFSKDSGFLEELPEDNLSSWATWGTLPPEPNL VPGGPPVSLQTLTFCWESSPEEEEEARESEIEDS DAGSWGAESTQRTEDRGRTLGHYMAR	85
共有γ链(335-369)	IPPKGGALGEGPGASPCNQHSPYWAPPCYTLK PET	86
IL9R(356-521)	TALLTCGPARPWKSVALEEEQEGPGTRLPGNLS SEDVLPAGCTEWRVQTLAYLPQEDWAPTSLTR PAPPDSEGSRSSSSSSSSNNNNYCALGCYGGW HLSALPGNTQSSGPIPALACGLSCDHQGLETQQ GVAWVLAGHCQRPGLHEDLQGMLLPSVLSKA RSWTF	87
IL21R(322-538)	PRSPAKRLQLTELQEPAELVESDGVPKPSFWPT AQNSGGSAYSEERDRPYGLVSIDTVTVLDAEG PCTWPCSCEDDGYPALDLDAGLEPSPGLEDPL LDAGTTVLSCGCVSAGSPGLGGPLGSLLDRLK PPLADGEDWAGGLPWGGRSPGGVSESEAGSPL AGLDMDTFDSGFVGSDCSSPVECDFTSPGDEG PPRSYLRQWVVIPPPLSSPGPQAS	88
GHR(353-638)	PDEKTEESDTDRLLSSDHEKSHSNLGVKDGDS GRTSCCEPDILETDFNANDIHEGTSEVAQPQRL KGEADLLCLDQKNQNNSPYHDACPATQQPSVI QAEKNKPQPLPTEGAESTHQAAHIQLSNPSSLS NIDFYAQVSDITPAGSVVLSPGQKNKAGMSQC DMHPEMVSLCQENFLMDNAYFCEADAKKCIP VAPHIKVESHIQPSLNQEDIYITTESLTTAAGRP GTGEHVPGSEMPVPDYTSIHIVQSPQGLILNAT ALPLPDKEFLSSCGYVSTDQLNKIMP	89
EpoR(339-508)	WGTMQAVEPGTDDEGPLLEPVGSEHAQDTYL VLDKWLLPRNPPSEDLPGPGGSVDIVAMDEGS EASSCSSALASKPSPEGASAASFEYTILDPSSQL LRPWTLCPELPPTPPHLKYLYLVVSDSGISTDY SSGDSQGAQGGLSDGPYSNPYENSLIPAAEPLP PSYVACS	90
鼠 IL2Rb(337-539)	AVQLLLLQKDSAPLPSPSGHSQASCFTNQGYFF FHLPNALEIESCQVYFTYDPCVEEEVEEDGSRL PEGSPHPPLLPLAGEQDDYCAFPPRDDLLLFSP SLSTPNTAYGGSRAPEERSPLSLHEGLPSLASRD LMGLQRPLERMPEGDGEGLSANSSGEQASVPE GNLHGQDQDRGQGPILTLNTDAYLSLQELQAQ DSVHLI	91

[0109]

募集结构域	氨基酸序列	SEQ ID NO:
鼠 IL7Ra(316-459)	ARDEVESFLPNDLPAQPEELETQGHRAAVHSANRSPETSVSPPETVRRESPLRCLARNLSTCNAPPLLSSRSPDYRDGDRNRPPVYQDLLPNSGNTNVPVPVPQPLPFQSGILIPVSQRQPISTSSVLNQEEAYVTMSSFYQNK	92
EGFR(955-1186)	VIQGDERMHLPSPTDSNFYRALMDEEDMDDVVDADEYLIPQQGFFSSPSTSRTPLLSSLSATSNNSTVACIDRNGLQSCPIKEDSFLQRYSSDPTGALTEDSIDDTFLPVPEYINQSVPKRPAGSVQNPVYHNQPLNPAPSRDPHYQDPHSTAVGNPEYLNTVQPTCVNSTFDSPAHWAQKGSHQISLDNPDYQQDFFPKEAKPNGIFKGSTAENAEYLRVAPQSSEFIGA	93
EGFR(955-1186;Y974F,d1045-1057)	VIQGDERMHLPSPTDSNFFRALMDEEDMDDVVDADEYLIPQQGFFSSPSTSRTPLLSSLSATSNNSTVACIDRNGLQSCPIKEDSFLQRIDDTFLPVPEYINQSVPKRPAGSVQNPVYHNQPLNPAPSRDPHYQDPHSTAVGNPEYLNTVQPTCVNSTFDSPAHWAQKGSHQISLDNPDYQQDFFPKEAKPNGIFKGSTAENAEYLRVAPQSSEFIGA	94
EGFR(955-1009;Y974F)	VIQGDERMHLPSPTDSNFFRALMDEEDMDDVVDADEYLIPQQGFFSSPSTSRTP	95
EGFR(1019-1085)	NNSTVACIDRNGLQSCPIKEDSFLQRIDDTFLPVPEYINQSVPKRPAGSVQNPV	96
EGFR(1037-1103;Y1068/1101F,d1045-1057)	KEDSFLQRIDDTFLPVPEFINQSVPKRPAGSVQNPVYHNQPLNPAPSRDPHFQD	97
EGFR(1066-1118;Y1068/1086F)	VPEFINQSVPKRPAGSVQNPVFHNQPLNPAPSRDPHYQDPHSTAVGNPEYLNTV	98
EGFR(1122-1165)	PEYLNTVQPTCVNSTFDSPAHWAQKGSHQISLDNPDYQQDFFPKEAKPNGIFKG	99
EGFR(1133-1186;Y1148F)	WAQKGSHQISLDNPDFQQDFFPKEAKPNGIFKGSTAENAEYLRVAPQSSEFIGA	100
IL12Rb2(775-825)	SDPKPENPACPWTVLPAGDLPTHDGYLPSNIDDLPSHEAPLADSLEELEPQ	101
IL7R(376-416)	ACDAPILSSSRSLDCRESGKNGPHVYQDLLLSLGTTNSTLP	102
IL7R(424-459)	GILTLNPVAQGQPILTSLGSNQEEAYVTMSSFYQNQ	103
IL7R(376-416,424-459)	ACDAPILSSSRSLDCRESGKNGPHVYQDLLLSLGTTNSTLPQGQPILTSLGSNQEEAYVTMSSFYQNQ	104
IL7R(424-459;Y456F)	GILTLNPVAQGQPILTSLGSNQEEAYVTMSSFFQNQ	105
IL7R(376-416,424-459,Y456F)	ACDAPILSSSRSLDCRESGKNGPHVYQDLLLSLGTTNSTLPQGQPILTSLGSNQEEAYVTMSSFFQNQ	106
IL2Rbsmall(393-433)	DEGVAGAPTGSSPQPLQPLSGEDDAYCTFPSRD	107

[0110]

募集结构域	氨基酸序列	SEQ ID NO:
	DLLLFSPS	
IL2Rbsmall(518-551)	GQGEFRALNARLPLNTDAYLSLQELQGQDPTH LV	108
IL2Rbsmall(339-379,393 -433)	QQDKVPEPASLSSNHSLTSCFTNQGYFFFHLPD ALEIEACQDEGVAGAPTGSSPQPLQPLSGEDDA YCTFPSRDDLLLFSPS	109
IL2Rbsmall(339-379,518 -551)	QQDKVPEPASLSSNHSLTSCFTNQGYFFFHLPD ALEIEACQ GQGEFRALNARLPLNTDAYLSLQELQGQDPTH LV	110
IL2Rbsmall(393-433,518 -551)	DEGVAGAPTGSSPQPLQPLSGEDDAYCTFPSRD DLLLFSPSGQGEFRALNARLPLNTDAYLSLQEL QGQDPTHLV	111
IL2Rbsmall(339-379,393 -433,518-551)	QQDKVPEPASLSSNHSLTSCFTNQGYFFFHLPD ALEIEACQDEGVAGAPTGSSPQPLQPLSGEDDA YCTFPSRDDLLLFSPSGQGEFRALNARLPLNTD AYLSLQELQGQDPTHLV	112
IFNAR2small(310-352)	KKKVWDYNYDDESDSDTEAAPRTSGGGYTM HGLTVRPLGQASA	113
IFNAR2small(486-515)	EGLWSEDAPSDQSDTSESDVDLGDGYIMR	114
IFNAR2small(310-352,4 86-515)	KKKVWDYNYDDESDSDTEAAPRTSGGGYTM HGLTVRPLGQASAEGLWSEDAPSDQSDTSESD VDLGDGYIMR	115
BLNK(53-208)	ASESPADEEEQWSDDFDSDYENPDEHSDSEMY VMPAEENADDSYEPPPVEQETRPVHPALPFAR GEYIDNRSSQRHSPPFSKTLPSKPSWPSEKARL TSTLPALTALQKPQVPPKPKGLLEDEADYVVPV EDNDENYIHPTESSSPPPEKAPMVNR	116
BLNK(53-208;Y72F)	ASESPADEEEQWSDDFDSDFENPDEHSDSEMY VMPAEENADDSYEPPPVEQETRPVHPALPFAR GEYIDNRSSQRHSPPFSKTLPSKPSWPSEKARL TSTLPALTALQKPQVPPKPKGLLEDEADYVVPV EDNDENYIHPTESSSPPPEKAPMVNR	117
BLNK(53-208;Y72F,Y96 F)	ASESPADEEEQWSDDFDSDFENPDEHSDSEMY VMPAEENADDSFEPPPVEQETRPVHPALPFARG EYIDNRSSQRHSPPFSKTLPSKPSWPSEKARLTS TLPALTALQKPQVPPKPKGLLEDEADYVVPVE DNDENYIHPTESSSPPPEKAPMVNR	118
EpoR(339-508)	WGTMQAVEPGTDDEGPLLEPVGSEHAQDTYL VLDKWLLPRNPPSEDLPGPGGSVDIVAMDEGS EASSCSSALASKPSPEGASAASFEYTILDPSSQL LRPWTLCPELPPTPPHLKYLYLVVSDSGISTDY SSGDSQGAQGGLSDGPYSNPYENSLIPAAEPLP PSYVACS	119
IL12Rb2(714-862)	VTPVFRHPPCSNWPQREKGIQGHQASEKDMM HSASSPPPPRALQAESRQLVDLYKVLESRGSDP KPENPACPWTVLPAGDLPTHDGYLPSNIDDLPS HEAPLADSLEELEPQHISLSVFPSSSLHPLTFSC	120

[0111]

募集结构域	氨基酸序列	SEQ ID NO:
	GDKLTLDQLKMRCDSLML	
IL12Rb1(622-662)	WDKGERTEPLEKTELPEGAPELALDTELSLED GDRCKAKM	121
IL10R1(304-578)	VSPELKNLDLHGSTDSGFGSTKPSLQTEEPQFL LPDPHPQADRTLGNREPPVLGDSCSSGSSNSTD SGICLQEPSLSPSTGPTWEQQVGSNSRGQDDSG IDLVQNSEGRAGDTQGGSALGHHSPPEPEVPG EEDPAAVAFQGYLRQTRCAEEKATKTGCLEEE SPLTDGLGPKFGRCLVDEAGLHPPALAKGYLK QDPLEMTLASSGAPTGQWNQPTEEWSLLALSS CSDLGISDWSFAHDLAPLGCVAAPGGLLGSFN SDLVTLPLISSLQSSE	122
IL7Ra(316-459).IL12Rb 2(775-825)	ARDEVEGFLQDTFPQQLEESEKQRLGGDVQSP NCPSEDVVITPESFGRDSSLTCLAGNVSACDAP ILSSSRSLDCRESGKNGPHVYQDLLLSLGTTNS TLPPPFSLQSGILTLNPVAQGQPILTSLGSNQEEA YVTMSSFYQNQSRSDPKPENPACPWTVLPAGD LPTHDGYLPSNIDDLPSHEAPLADSLEELEPQ	161

[0112] *SR指示示例性肽连接子

[0113] 在一些实施例中,本公开的嵌合细胞因子受体的Stat募集结构域包括来自一个受体的STAT募集结构域。

[0114] 为了生成多个输出,一个或多个STAT募集结构域可以串联连接以模拟来自一个或多个细胞因子的信号传导。

[0115] 在一些实施例中,STAT募集结构域包括多于一个受体的部分,例如包括多于一个STAT募集结构域。在此类实施例中,提供串联的细胞因子信号传导结构域,从而允许增强的信号传导。因此,在一些实施例中,本公开的嵌合细胞因子受体的单体的STAT募集结构域包括来自多于一个受体的STAT募集结构域,例如包括来自两个、三个、四个、五个或甚至六个受体的STAT募集结构域。例如,在一些实施例中,STAT募集结构域可以串联连接以刺激多种途径(例如,用于促持续性STAT5和促炎性STAT4的IL7R(316-459)-IL12Rb2(775-825)片段融合;用于促持续性IL7R(316-459)-IL2Rbsmall(393-433,518-551);用于促持续性和抗衰竭的IL7R(316-459)-EGFR(1122-1165);用于促持续性和抗衰竭的IL2Rbsmall(393-433,518-551)-EGFR(1122-1165))。

[0116] 当生成多个输出时,单个STAT募集结构域与细胞膜的接近度可以影响其相应的信号传导输出的强度。表5b示出了具有双输出的嵌合细胞因子受体的实例,其中每个输出可以放置在细胞膜的近端或远端。

[0117] 表5b:具有双输出的嵌合细胞因子受体的实例

[0118]

双输出 STAT 募集结构域	膜近端	膜远端
IL2Rbsmall(393-433,518-551)/IL21R(322-538)	IL2Rbsmall(393-433,518-551)	IL21R(322-538)
IL21R(322-538)/IL2Rbsmall(393-433,518-551)	IL21R(322-538)	IL2Rbsmall(393-433,518-551)
IL2Rbsmall(339-379,393-433,518-551)/IL21R(322-538)	IL2Rbsmall(339-379,393-433,518-551)	IL21R(322-538)
IL21R(322-538)/IL2Rbsmall(339-379,393-433,518-551)	IL21R(322-538)	IL2Rbsmall(339-379,393-433,518-551)
IL7R(316-459)/IL21R(322-538)	IL7R (316-459)	IL21R(322-538)
IL7R (316-459)/IL12Rb2(775-825)	IL7R (316-459)	IL12Rb2(775-825)
IL21R(322-538)/IL7R(316-459)	IL21R(322-538)	IL7R (316-459)

[0119] 不受理论或机制的束缚，在一些实施例中，JAK蛋白(JAK1、JAK2、JAK3或TYK2)与本公开的嵌合细胞因子受体(包括结合结构域、跨膜结构域、JAK结合结构域和募集结构域)结合。在一些实施例中，在存在(例如，结合)TGF-β配体或抗TGF-β受体抗体的情况下，嵌合细胞因子受体聚集并允许两种结合的JAK蛋白被激活，这进而使嵌合受体的募集结构域上的酪氨酸残基磷酸化。然后，磷酸化募集结构域能够与募集的蛋白质结合(例如，磷酸化STAT募集结构域与STAT蛋白结合)，这进而在细胞核中实现转录事件。

[0120] E.示例性TGF-β驱动嵌合细胞因子受体

[0121] 本公开的背景依赖性嵌合细胞因子受体可以用信号序列表达，例如SEQ ID NO:1的CD8SS。表6示出了本公开的示例性背景依赖性细胞因子受体序列。受体可以用信号序列表达，例如SEQ ID NO:1的CD8SS。

[0122] 在一些实施例中，本公开的嵌合细胞因子受体包括TGF-β结合结构域，其包括SEQ ID NO:3-20和159中的任一个的氨基酸序列；跨膜和JAK2结合结构域，其包括SEQ ID NO:27-79、160和217-234中的任一个的氨基酸序列；以及募集结构域，其包括SEQ ID NO:80-122和161中的任一个的氨基酸序列。在一些实施例中，嵌合细胞因子受体不包括信号序列。

[0123] 在一些实施例中，本公开的嵌合细胞因子受体包括TGF-β结合结构域，其包括选自由以下组成的组的氨基酸序列：SEQ ID NO:3、4和159；TPOR/MPLR跨膜结构域和JAK2结合结构域，其包括选自由以下组成的组的氨基酸序列：SEQ ID NO:38、39、40、53、59、60、61、64、69、70、160和217-234；以及募集结构域，其包括选自由以下组成的组的氨基酸序列：SEQ ID NO:80、99、111、112和161。任选地，嵌合细胞因子受体包括信号序列，所述信号序列包括例如SEQ ID NO:1的氨基酸序列。

[0124] 在一些实施例中，嵌合细胞因子受体包括结合结构域、跨膜结构域和JAK2结合结构域以及募集结构域，所述结合结构域包括SEQ ID NO:3、4或159的氨基酸序列，所述跨膜结构域和所述JAK2结合结构域包括SEQ ID NO:64、69或70的氨基酸序列，并且所述募集结构域包括SEQ ID NO:80、99、111、112或161的氨基酸序列。在一些实施例中，嵌合细胞因子受体是诱导型的。在一些实施例中，嵌合细胞因子受体结合结构域、跨膜结构域和JAK2结合结构域以及募集结构域，所述结合结构域包括SEQ ID NO:3、4或159的氨基酸序列，所述跨膜结构域和JAK2结合结构域包括SEQ ID NO:38、39、40或53的氨基酸序列，并且所述募集结构域包括SEQ ID NO:80、99、111、112或161的氨基酸序列。在一些实施例中，嵌合细胞因子受体结合结构域、跨膜结构域和JAK2结合结构域以及募集结构域，所述结合结构域包括SEQ

ID NO:3、4或159的氨基酸序列，所述跨膜结构域和JAK2结合结构域包括SEQ ID NO:59、60、160或217的氨基酸序列，并且所述募集结构域包括SEQ ID NO:80、99、111、112或161的氨基酸序列。在一些实施例中，嵌合细胞因子受体具有组成型活性。在一些实施例中，在不与TGFβ配体或抗TGFβR抗体结合的情况下，使本公开的组成型活性嵌合细胞因子受体二聚化。在一些实施例中，本公开的嵌合细胞因子受体组成型地或由TGF-β或抗TGFβR抗体诱导地抑制TGFβR介导的信号传导和/或激活STAT介导的信号传导。在一些实施例中，嵌合细胞因子受体在存在TGF-βR配体，例如TGF-β或抗TGF-βR抗体的情况下具有组成型活性和/或表现出进一步增强的活性或性质。在一些实施例中，TGF-βR是TGF-βR2，并且抗体是抗TGF-βR2抗体。

[0125] 在一些实施例中，嵌合细胞因子受体不包括信号序列。在一些实施例中，嵌合细胞因子受体包括TGFβR2内源性信号序列或包括例如SEQ ID NO:1的氨基酸序列的信号序列。

[0126] 在一些实施例中，本公开的嵌合细胞因子受体包括SEQ ID NO:123的氨基酸序列。在一些实施例中，本公开的嵌合细胞因子受体包括SEQ ID NO:124的氨基酸序列。在一些实施例中，本公开的嵌合细胞因子受体包括SEQ ID NO:125的氨基酸序列。在一些实施例中，本公开的嵌合细胞因子受体包括SEQ ID NO:126的氨基酸序列。在一些实施例中，本公开的嵌合细胞因子受体包括SEQ ID NO:127的氨基酸序列。在一些实施例中，本公开的嵌合细胞因子受体包括SEQ ID NO:128的氨基酸序列。在一些实施例中，本公开的嵌合细胞因子受体包括SEQ ID NO:129的氨基酸序列。在一些实施例中，本公开的嵌合细胞因子受体包括SEQ ID NO:130的氨基酸序列。在一些实施例中，本公开的嵌合细胞因子受体包括SEQ ID NO:131的氨基酸序列。在一些实施例中，本公开的嵌合细胞因子受体包括SEQ ID NO:132的氨基酸序列。在一些实施例中，本公开的嵌合细胞因子受体包括SEQ ID NO:133的氨基酸序列。在一些实施例中，本公开的嵌合细胞因子受体包括SEQ ID NO:134的氨基酸序列。在一些实施例中，本公开的嵌合细胞因子受体包括SEQ ID NO:135的氨基酸序列。在一些实施例中，本公开的嵌合细胞因子受体包括SEQ ID NO:136的氨基酸序列。在一些实施例中，本公开的嵌合细胞因子受体包括SEQ ID NO:137的氨基酸序列。在一些实施例中，本公开的嵌合细胞因子受体包括SEQ ID NO:138的氨基酸序列。在一些实施例中，本公开的嵌合细胞因子受体包括SEQ ID NO:139的氨基酸序列。在一些实施例中，本公开的嵌合细胞因子受体包括SEQ ID NO:140的氨基酸序列。在一些实施例中，本公开的嵌合细胞因子受体包括SEQ ID NO:141的氨基酸序列。在一些实施例中，本公开的嵌合细胞因子受体包括SEQ ID NO:142的氨基酸序列。在一些实施例中，本公开的嵌合细胞因子受体包括SEQ ID NO:143的氨基酸序列。在一些实施例中，本公开的嵌合细胞因子受体包括SEQ ID NO:144的氨基酸序列。在一些实施例中，本公开的嵌合细胞因子受体包括SEQ ID NO:145的氨基酸序列。在一些实施例中，本公开的嵌合细胞因子受体包括SEQ ID NO:146的氨基酸序列。在一些实施例中，本公开的嵌合细胞因子受体包括SEQ ID NO:147的氨基酸序列。在一些实施例中，本公开的嵌合细胞因子受体包括SEQ ID NO:148的氨基酸序列。在一些实施例中，本公开的嵌合细胞因子受体包括SEQ ID NO:149的氨基酸序列。在一些实施例中，本公开的嵌合细胞因子受体包括SEQ ID NO:150的氨基酸序列。在一些实施例中，本公开的嵌合细胞因子受体包括SEQ ID NO:151的氨基酸序列。在一些实施例中，本公开的嵌合细胞因子受体包括SEQ ID NO:162的氨基酸序列。在一些实施例中，本公开的嵌合细胞因子受体包括SEQ ID NO:163的氨基酸序列。在一些实施例中，本公开的嵌合细胞因子受体包括SEQ ID NO:164的氨基酸序列。在一

些实施例中，本公开的嵌合细胞因子受体包括SEQ ID NO:165的氨基酸序列。在一些实施例中，本公开的嵌合细胞因子受体包括SEQ ID NO:166的氨基酸序列。在一些实施例中，本公开的嵌合细胞因子受体包括SEQ ID NO:167的氨基酸序列。在一些实施例中，本公开的嵌合细胞因子受体包括SEQ ID NO:168的氨基酸序列。在一些实施例中，本公开的嵌合细胞因子受体包括SEQ ID NO:169的氨基酸序列。在一些实施例中，本公开的嵌合细胞因子受体包括SEQ ID NO:170的氨基酸序列。在一些实施例中，本公开的嵌合细胞因子受体包括SEQ ID NO:171的氨基酸序列。在一些实施例中，本公开的嵌合细胞因子受体包括SEQ ID NO:172的氨基酸序列。在一些实施例中，本公开的嵌合细胞因子受体包括SEQ ID NO:173的氨基酸序列。在一些实施例中，本公开的嵌合细胞因子受体包括SEQ ID NO:174的氨基酸序列。在一些实施例中，本公开的嵌合细胞因子受体包括SEQ ID NO:175的氨基酸序列。在一些实施例中，本公开的嵌合细胞因子受体包括SEQ ID NO:176的氨基酸序列。在一些实施例中，本公开的嵌合细胞因子受体包括SEQ ID NO:177的氨基酸序列。在一些实施例中，本公开的嵌合细胞因子受体包括SEQ ID NO:178的氨基酸序列。在一些实施例中，本公开的嵌合细胞因子受体包括SEQ ID NO:179的氨基酸序列。在一些实施例中，本公开的嵌合细胞因子受体包括SEQ ID NO:180的氨基酸序列。在一些实施例中，本公开的嵌合细胞因子受体包括SEQ ID NO:181的氨基酸序列。在一些实施例中，本公开的嵌合细胞因子受体包括SEQ ID NO:182的氨基酸序列。在一些实施例中，本公开的嵌合细胞因子受体包括SEQ ID NO:183的氨基酸序列。在一些实施例中，本公开的嵌合细胞因子受体包括SEQ ID NO:184的氨基酸序列。在一些实施例中，本公开的嵌合细胞因子受体包括SEQ ID NO:185的氨基酸序列。在一些实施例中，本公开的嵌合细胞因子受体包括SEQ ID NO:186的氨基酸序列。在一些实施例中，本公开的嵌合细胞因子受体包括SEQ ID NO:187的氨基酸序列。在一些实施例中，本公开的嵌合细胞因子受体包括SEQ ID NO:188的氨基酸序列。在一些实施例中，本公开的嵌合细胞因子受体包括SEQ ID NO:189的氨基酸序列。在一些实施例中，本公开的嵌合细胞因子受体包括SEQ ID NO:190的氨基酸序列。在一些实施例中，本公开的嵌合细胞因子受体包括SEQ ID NO:191的氨基酸序列。在一些实施例中，本公开的嵌合细胞因子受体包括SEQ ID NO:192的氨基酸序列。在一些实施例中，本公开的嵌合细胞因子受体包括SEQ ID NO:193的氨基酸序列。在一些实施例中，本公开的嵌合细胞因子受体包括SEQ ID NO:194的氨基酸序列。在一些实施例中，本公开的嵌合细胞因子受体包括SEQ ID NO:195的氨基酸序列。在一些实施例中，本公开的嵌合细胞因子受体包括SEQ ID NO:196的氨基酸序列。在一些实施例中，本公开的嵌合细胞因子受体包括SEQ ID NO:197的氨基酸序列。在一些实施例中，本公开的嵌合细胞因子受体包括SEQ ID NO:198的氨基酸序列。在一些实施例中，本公开的嵌合细胞因子受体包括SEQ ID NO:199的氨基酸序列。在一些实施例中，本公开的嵌合细胞因子受体包括SEQ ID NO:200的氨基酸序列。在一些实施例中，本公开的嵌合细胞因子受体包括SEQ ID NO:201的氨基酸序列。在一些实施例中，本公开的嵌合细胞因子受体包括SEQ ID NO:202的氨基酸序列。在一些实施例中，本公开的嵌合细胞因子受体包括SEQ ID NO:203的氨基酸序列。在一些实施例中，本公开的嵌合细胞因子受体包括SEQ ID NO:204的氨基酸序列。在一些实施例中，本公开的嵌合细胞因子受体包括SEQ ID NO:205的氨基酸序列。在一些实施例中，本公开的嵌合细胞因子受体包括SEQ ID NO:206的氨基酸序列。在一些实施例中，本公开的嵌合细胞因子受体包括SEQ ID NO:207的氨基酸序列。在一些实施例中，本公开的嵌合

细胞因子受体包括SEQ ID NO:208的氨基酸序列。在一些实施例中,本公开的嵌合细胞因子受体包括SEQ ID NO:209的氨基酸序列。在一些实施例中,本公开的嵌合细胞因子受体包括SEQ ID NO:210的氨基酸序列。在一些实施例中,本公开的嵌合细胞因子受体包括SEQ ID NO:211的氨基酸序列。在一些实施例中,本公开的嵌合细胞因子受体包括SEQ ID NO:212的氨基酸序列。在一些实施例中,本公开的嵌合细胞因子受体包括SEQ ID NO:213的氨基酸序列。在一些实施例中,本公开的嵌合细胞因子受体包括SEQ ID NO:214的氨基酸序列。在一些实施例中,本公开的嵌合细胞因子受体包括SEQ ID NO:215的氨基酸序列。在一些实施例中,本公开的嵌合细胞因子受体包括SEQ ID NO:216的氨基酸序列。

[0127] 在一些实施例中,嵌合细胞因子受体(CCR)包括结合结构域、跨膜结构域和JAK2结合结构域以及募集结构域,所述结合结构域包括SEQ ID NO:159的氨基酸序列,所述跨膜结构域和JAK2结合结构域包括SEQ ID NO:40的氨基酸序列,并且所述募集结构域包括SEQ ID NO:80、99、111、112或161的氨基酸序列。在一些实施例中,CCR包括结合结构域、跨膜结构域和JAK2结合结构域以及募集结构域,所述结合结构域包括SEQ ID NO:159的氨基酸序列,所述跨膜结构域和JAK2结合结构域包括SEQ ID NO:53的氨基酸序列,并且所述募集结构域包括SEQ ID NO:80、99、111、112或161的氨基酸序列。在一些实施例中,CCR包括结合结构域、跨膜结构域和JAK2结合结构域以及募集结构域,所述结合结构域包括SEQ ID NO:4的氨基酸序列,所述跨膜结构域和JAK2结合结构域包括SEQ ID NO:38的氨基酸序列,并且所述募集结构域包括SEQ ID NO:80、99、111、112或161的氨基酸序列。在一些实施例中,CCR包括结合结构域、跨膜结构域和JAK2结合结构域以及募集结构域,所述结合结构域包括SEQ ID NO:4的氨基酸序列,所述跨膜结构域和JAK2结合结构域包括SEQ ID NO:39的氨基酸序列,并且所述募集结构域包括SEQ ID NO:80、99、111、112或161的氨基酸序列。在一些实施例中,CCR包括结合结构域、跨膜结构域和JAK2结合结构域以及募集结构域,所述结合结构域包括SEQ ID NO:4的氨基酸序列,所述跨膜结构域和JAK2结合结构域包括SEQ ID NO:40的氨基酸序列,并且所述募集结构域包括SEQ ID NO:80、99、111、112或161的氨基酸序列。在一些实施例中,CCR包括结合结构域、跨膜结构域和JAK2结合结构域以及募集结构域,所述结合结构域包括SEQ ID NO:4的氨基酸序列,所述跨膜结构域和JAK2结合结构域包括SEQ ID NO:53的氨基酸序列,并且所述募集结构域包括SEQ ID NO:80、99、111、112或161的氨基酸序列。在一些实施例中,CCR包括结合结构域、跨膜结构域和JAK2结合结构域以及募集结构域,所述结合结构域包括SEQ ID NO:159的氨基酸序列,所述跨膜结构域和JAK2结合结构域包括SEQ ID NO:70的氨基酸序列,并且所述募集结构域包括SEQ ID NO:80、99、111、112或161的氨基酸序列。在一些实施例中,CCR包括结合结构域、跨膜结构域和JAK2结合结构域以及募集结构域,所述结合结构域包括SEQ ID NO:159的氨基酸序列,所述跨膜结构域和JAK2结合结构域包括SEQ ID NO:69的氨基酸序列,并且所述募集结构域包括SEQ ID NO:80、99、111、112或161的氨基酸序列。在一些实施例中,CCR包括结合结构域、跨膜结构域和JAK2结合结构域以及募集结构域,所述结合结构域包括SEQ ID NO:4的氨基酸序列,所述跨膜结构域和JAK2结合结构域包括SEQ ID NO:64的氨基酸序列,并且所述募集结构域包括SEQ ID NO:80、99、111、112或161的氨基酸序列。在一些实施例中,CCR包括结合结构域、跨膜结构域和JAK2结合结构域以及募集结构域,所述结合结构域包括SEQ ID NO:4的氨基酸序列,所述跨膜结构域和JAK2结合结构域包括SEQ ID NO:69的氨基酸序列,并且所述募集

结构域包括SEQ ID NO:80、99、111、112或161的氨基酸序列。在一些实施例中,CCR包括结合结构域、跨膜结构域和JAK2结合结构域以及募集结构域,所述结合结构域包括SEQ ID NO:4的氨基酸序列,所述跨膜结构域和JAK2结合结构域包括SEQ ID NO:70的氨基酸序列,并且所述募集结构域包括SEQ ID NO:80、99、111、112或161的氨基酸序列。在一些实施例中,CCR包括结合结构域、跨膜结构域和JAK2结合结构域以及募集结构域,所述结合结构域包括SEQ ID NO:159的氨基酸序列,所述跨膜结构域和JAK2结合结构域包括SEQ ID NO:160或219的氨基酸序列,并且所述募集结构域包括SEQ ID NO:80、99、111、112或161的氨基酸序列。在一些实施例中,CCR包括结合结构域、跨膜结构域和JAK2结合结构域以及募集结构域,所述结合结构域包括SEQ ID NO:159的氨基酸序列,所述跨膜结构域和JAK2结合结构域包括SEQ ID NO:223、224的氨基酸序列,并且所述募集结构域包括SEQ ID NO:80、99、111、112或161的氨基酸序列。在一些实施例中,CCR包括结合结构域、跨膜结构域和JAK2结合结构域以及募集结构域,所述结合结构域包括SEQ ID NO:159的氨基酸序列,所述跨膜结构域和JAK2结合结构域包括SEQ ID NO:225或226的氨基酸序列,并且所述募集结构域包括SEQ ID NO:80、99、111、112或161的氨基酸序列。在一些实施例中,CCR包括结合结构域、跨膜结构域和JAK2结合结构域以及募集结构域,所述结合结构域包括SEQ ID NO:4的氨基酸序列,所述跨膜结构域和JAK2结合结构域包括SEQ ID NO:60或160的氨基酸序列,并且所述募集结构域包括SEQ ID NO:80、99、111、112或161的氨基酸序列。在一些实施例中,CCR包括结合结构域、跨膜结构域和JAK2结合结构域以及募集结构域,所述结合结构域包括SEQ ID NO:4的氨基酸序列,所述跨膜结构域和JAK2结合结构域包括SEQ ID NO:223、224的氨基酸序列,并且所述募集结构域包括SEQ ID NO:80、99、111、112或161的氨基酸序列。在一些实施例中,CCR包括结合结构域、跨膜结构域和JAK2结合结构域以及募集结构域,所述结合结构域包括SEQ ID NO:4的氨基酸序列,所述跨膜结构域和JAK2结合结构域包括SEQ ID NO:225或226的氨基酸序列,并且所述募集结构域包括SEQ ID NO:80、99、111、112或161的氨基酸序列。

[0128] 在一些实施例中,本公开的嵌合细胞因子受体包括SEQ ID NO:272、SEQ ID NO:273、SEQ ID NO:274或SEQ ID NO:275的氨基酸序列。在一些实施例中,嵌合细胞因子受体包括与SEQ ID NO:123-216和SEQ ID NO:272-275的氨基酸序列中的任一个具有至少80%、85%、90%、95%、98%或99%或100%相同的氨基酸序列。

[0129] 表6:示例性嵌合细胞因子受体序列(组装的诱导型或组成型活性TGF-β受体嵌合细胞因子受体):

[0130]

受体	氨基酸序列	SEQ ID NO:
CD8SS-TGFbR2(1-166).TPOR/MPLR(478-582).IL7Ra(316-459).IL12Rb2(775-825) 下划线表示 CD8SS	MALPVTALLLPLALLLHAARPMGRGLLRGLWP LHIVLWTRIASTIPPHVQKSVNNDMIVTDNNGA VKFPQLCKFCDVRFSTCDNQKSCMSNCSITSICE KPQEVCVAVWRKNDENITLETVCHDPKLPYHDF ILEDAASPKCIMKEKKKPGETFFMCSCSSDECN DNIIFSEEYNTSNPDLLLVIFQSDPTRVETATETA WISLVTALHLVLGLSAVLGLLLLRWQFPAHYRR LRHALWPSLPDLHRVLGQYLRDTAALSPPKATV SDTCEEVEPSLLEILPKSSERTPLPLARDEVEGFL QDTFPQQLEESEKQRLGGDVQSPNCPSEDVVIT PESFGRDSSLTCLAGNVSACDAPILSSSRSLDCR ESGKNGPHVYQDLLLSLGTTNSTLPPPFSLQSGI LTLNPVAQGQPILTSLGSNQEEAYVTMSSFYQNQ SDPKPENPACPWTVLPAGDLPTHDGYLPSNIDD LPSHEAPLADSLEELEPQ	123
CD8SS-TGFbR2(1-166).TPOR/MPLR(478-582;N-1).IL7Ra(316-459).IL12Rb2(775-825) 下划线表示 CD8SS	MALPVTALLLPLALLLHAARPMGRGLLRGLWP LHIVLWTRIASTIPPHVQKSVNNDMIVTDNNGA VKFPQLCKFCDVRFSTCDNQKSCMSNCSITSICE KPQEVCVAVWRKNDENITLETVCHDPKLPYHDF ILEDAASPKCIMKEKKKPGETFFMCSCSSDECN DNIIFSEEYNTSNPDLLLVIFQSDPTRVETATETWI SLVTALHLVLGLSAVLGLLLLRWQFPAHYRRLR HALWPSLPDLHRVLGQYLRDTAALSPPKATVSD TCEEVEPSLLEILPKSSERTPLPLARDEVEGFLQD TFPQQLEESEKQRLGGDVQSPNCPSEDVVITPES FGRDSSLTCLAGNVSACDAPILSSSRSLDCRESG KNGPHVYQDLLLSLGTTNSTLPPPFSLQSGILTL NPVAQGQPILTSLGSNQEEAYVTMSSFYQNQSD PKPENPACPWTVLPAGDLPTHDGYLPSNIDDLPS HEAPLADSLEELEPQ	124
CD8SS-TGFbR2(1-166).TPOR/MPLR(478-582;N-2).IL7Ra(316-459).IL12Rb2(775-825) 下划线表示 CD8SS	MALPVTALLLPLALLLHAARPMGRGLLRGLWP LHIVLWTRIASTIPPHVQKSVNNDMIVTDNNGA VKFPQLCKFCDVRFSTCDNQKSCMSNCSITSICE KPQEVCVAVWRKNDENITLETVCHDPKLPYHDF ILEDAASPKCIMKEKKKPGETFFMCSCSSDECN DNIIFSEEYNTSNPDLLLVIFQSDPTRVETATETIS LVTALHLVLGLSAVLGLLLLRWQFPAHYRRLRH	125

[0131]

	ALWPSLPDLHRVLGQYLRDTAALSPPKATVSDT CEEVEPSLLEILPKSSERTPLPLARDEVEGFLQDT FPQQLEESEKQRLGGDVQSPNCPSEDVVITPESF GRDSSLTCLAGNVSACDAPILSSSRSLDCRESGK NGPHVYQDLLLSLGTTNSTLPPPFSLQSGILTLN PVAQGQPILTSLGSNQEEAYVTMSSFYQNQSDP KPENPACPWTVLPAGDLPTHDGYLPSNIDDLPS HEAPLADSLEELEPQ	
CD8SS-TGFbR2(1-166). TPOR/MPLR(478-582;N -2+1).IL7Ra(316-459).IL 12Rb2(775-825) 下划线表示 CD8SS	MALPVTALLLPLALLLHAARPMGRGLLRGLWP LHIVLWTRIASTIPPHVQKSVNNDMIVTDNNGA VKFPQLCKFCDVRFSTCDNQKSCMSNCSITSICE KPQEVCVAVWRKNDENITLETVCHDPKLPYHDF ILEDAASPKCIMKEKKKPGETFFMCSCSSDECN DNIIFSEEYNTSNPDLLLVIFQSDPTRVETATETLI SLVTALHLVLGLSAVLGLLLLRWQFPAHYRRLR HALWPSLPDLHRVLGQYLRDTAALSPPKATVSD TCEEVEPSLLEILPKSSERTPLPLARDEVEGFLQD TFPQQLEESEKQRLGGDVQSPNCPSEDVVITPES FGRDSSLTCLAGNVSACDAPILSSSRSLDCRESG KNGPHVYQDLLLSLGTTNSTLPPPFSLQSGILTL NPVAQGQPILTSLGSNQEEAYVTMSSFYQNQSD PKPENPACPWTVLPAGDLPTHDGYLPSNIDDLPS HEAPLADSLEELEPQ	126
CD8SS-TGFbR2(1-166). TPOR/MPLR(478-582;N -3).IL7Ra(316-459).IL12 Rb2(775-825) 下划线表示 CD8SS	MALPVTALLLPLALLLHAARPMGRGLLRGLWP LHIVLWTRIASTIPPHVQKSVNNDMIVTDNNGA VKFPQLCKFCDVRFSTCDNQKSCMSNCSITSICE KPQEVCVAVWRKNDENITLETVCHDPKLPYHDF ILEDAASPKCIMKEKKKPGETFFMCSCSSDECN DNIIFSEEYNTSNPDLLLVIFQSDPTRVETATETSL VTALHLVLGLSAVLGLLLLRWQFPAHYRRLRHA LWPSLPDLHRVLGQYLRDTAALSPPKATVSDTC EEVEPSLLEILPKSSERTPLPLARDEVEGFLQDTF PQQLEESEKQRLGGDVQSPNCPSEDVVITPESFG RDSSLTCLAGNVSACDAPILSSSRSLDCRESGKN GPHVYQDLLLSLGTTNSTLPPPFSLQSGILTLNPV AQGQPILTSLGSNQEEAYVTMSSFYQNQSDPKP ENPACPWTVLPAGDLPTHDGYLPSNIDDLPSHE APLADSLEELEPQ	127
CD8SS-TGFbR2(1-166). TPOR/MPLR(478-582;N -4).IL7Ra(316-459).IL12 Rb2(775-825) 下划线表示 CD8SS	MALPVTALLLPLALLLHAARPMGRGLLRGLWP LHIVLWTRIASTIPPHVQKSVNNDMIVTDNNGA VKFPQLCKFCDVRFSTCDNQKSCMSNCSITSICE KPQEVCVAVWRKNDENITLETVCHDPKLPYHDF ILEDAASPKCIMKEKKKPGETFFMCSCSSDECN DNIIFSEEYNTSNPDLLLVIFQSDPTRVETATETLV TALHLVLGLSAVLGLLLLRWQFPAHYRRLRHAL WPSLPDLHRVLGQYLRDTAALSPPKATVSDTCE EVEPSLLEILPKSSERTPLPLARDEVEGFLQDTFP QQLEESEKQRLGGDVQSPNCPSEDVVITPESFGR DSSLTCLAGNVSACDAPILSSSRSLDCRESGKNG PHVYQDLLLSLGTTNSTLPPPFSLQSGILTLNPVA	128

[0132]

	QGQPILTSLGSNQEEAYVTMSSFYQNQSDPKPE NPACPWTVLPAGDLPTHDGYLPSNIDDLPSHEA PLADSLEELEPQ	
CD8SS-TGFbR2(1-166). TPOR/MPLR(478-582;N -4+1).IL7Ra(316-459).IL 12Rb2(775-825) 下划线表示 CD8SS	MALPVTALLLPLALLLHAARPMGRGLLRGLWP LHIVLWTRIASTIPPHVQKSVNNDMIVTDNNGA VKFPQLCKFCDVRFSTCDNQKSCMSNCSITSICE KPQEVCVAVWRKNDENITLETVCHDPKLPYHDF ILEDAASPKCIMKEKKKPGETFFMCSCSSDECN DNIIFSEEYNTSNPDLLLVIFQSDPTRVETATETIL VTALHLVLGLSAVLGLLLLRWQFPAHYRRLRHA LWPSLPDLHRVLGQYLRDTAALSPPKATVSDTC EEVEPSLLEILPKSSERTPLPLARDEVEGFLQDTF PQQLEESEKQRLGGDVQSPNCPSEDVVITPESFG RDSSLTCLAGNVSACDAPILSSSRSLDCRESGKN GPHVYQDLLLSLGTTNSTLPPPFSLQSGILTLNPV AQGQPILTSLGSNQEEAYVTMSSFYQNQSDPKP ENPACPWTVLPAGDLPTHDGYLPSNIDDLPSHE APLADSLEELEPQ	129
CD8SS-TGFbR2(1-166). TPOR/MPLR(478-582;N -5).IL7Ra(316-459).IL12 Rb2(775-825) 下划线表示 CD8SS	MALPVTALLLPLALLLHAARPMGRGLLRGLWP LHIVLWTRIASTIPPHVQKSVNNDMIVTDNNGA VKFPQLCKFCDVRFSTCDNQKSCMSNCSITSICE KPQEVCVAVWRKNDENITLETVCHDPKLPYHDF ILEDAASPKCIMKEKKKPGETFFMCSCSSDECN DNIIFSEEYNTSNPDLLLVIFQSDPTRVETATETVT ALHLVLGLSAVLGLLLLRWQFPAHYRRLRHAL WPSLPDLHRVLGQYLRDTAALSPPKATVSDTCE EVEPSLLEILPKSSERTPLPLARDEVEGFLQDTFP QQLEESEKQRLGGDVQSPNCPSEDVVITPESFGR DSSLTCLAGNVSACDAPILSSSRSLDCRESGKNG PHVYQDLLLSLGTTNSTLPPPFSLQSGILTLNPVA QGQPILTSLGSNQEEAYVTMSSFYQNQSDPKPE NPACPWTVLPAGDLPTHDGYLPSNIDDLPSHEA PLADSLEELEPQ	130
CD8SS-TGFbR2(1-166). TPOR/MPLR(478-582;N -6).IL7Ra(316-459).IL12 Rb2(775-825) 下划线表示 CD8SS	MALPVTALLLPLALLLHAARPMGRGLLRGLWP LHIVLWTRIASTIPPHVQKSVNNDMIVTDNNGA VKFPQLCKFCDVRFSTCDNQKSCMSNCSITSICE KPQEVCVAVWRKNDENITLETVCHDPKLPYHDF ILEDAASPKCIMKEKKKPGETFFMCSCSSDECN DNIIFSEEYNTSNPDLLLVIFQSDPTRVETATETTA LHLVLGLSAVLGLLLLRWQFPAHYRRLRHALWP SLPDLHRVLGQYLRDTAALSPPKATVSDTCEEV EPSLLEILPKSSERTPLPLARDEVEGFLQDTFPQQ LEESEKQRLGGDVQSPNCPSEDVVITPESFGRDS SLTCLAGNVSACDAPILSSSRSLDCRESGKNGPH VYQDLLLSLGTTNSTLPPPFSLQSGILTLNPVAQ GQPILTSLGSNQEEAYVTMSSFYQNQSDPKPENP ACPWTVLPAGDLPTHDGYLPSNIDDLPSHEAPL ADSLEELEPQ	131
CD8SS-TGFbR2(1-166). TPOR/MPLR(478-582;N	MALPVTALLLPLALLLHAARPMGRGLLRGLWP LHIVLWTRIASTIPPHVQKSVNNDMIVTDNNGA	132

[0133]

-7).IL7Ra(316-459).IL12Rb2(775-825) 下划线表示 CD8SS	VKFPQLCKFCDVRFSTCDNQKSCMSNCSITSICEKPQEVCVAVWRKNDENITLETVCHDPKLPYHDFILEDAASPKCIMKEKKKPGETFFMCSCSSDECNDNIIFSEEYNTSNPDLLLVIFQSDPTRVETATETALHLVLGLSAVLGLLLLRWQFPAHYRRLRHALWPSLPDLHRVLGQYLRDTAALSPPKATVSDTCEEVEPSLLEILPKSSERTPLPLARDEVEGFLQDTFPQQLEESEKQRLGGDVQSPNCPSEDVVITPESFGRDSSLTCLAGNVSACDAPILSSSRSLDCRESGKNGPHVYQDLLLSLGTTNSTLPPPFSLQSGILTLNPVAQGQPILTSLGSNQEEAYVTMSSFYQNQSDPKPENPACPWTVLPAGDLPTHDGYLPSNIDDLPSHEAPLADSLEELEPQ	
CD8SS-TGFbR2(1-166).TPOR/MPLR(478-582;N-8).IL7Ra(316-459).IL12Rb2(775-825) 下划线表示 CD8SS	MALPVTALLLPLALLLHAARPMGRGLLRGLWPLHIVLWTRIASTIPPHVQKSVNNDMIVTDNNGAVKFPQLCKFCDVRFSTCDNQKSCMSNCSITSICEKPQEVCVAVWRKNDENITLETVCHDPKLPYHDFILEDAASPKCIMKEKKKPGETFFMCSCSSDECNDNIIFSEEYNTSNPDLLLVIFQSDPTRVETATETLHLVLGLSAVLGLLLLRWQFPAHYRRLRHALWPSLPDLHRVLGQYLRDTAALSPPKATVSDTCEEVEPSLLEILPKSSERTPLPLARDEVEGFLQDTFPQQLEESEKQRLGGDVQSPNCPSEDVVITPESFGRDSSLTCLAGNVSACDAPILSSSRSLDCRESGKNGPHVYQDLLLSLGTTNSTLPPPFSLQSGILTLNPVAQGQPILTSLGSNQEEAYVTMSSFYQNQSDPKPENPACPWTVLPAGDLPTHDGYLPSNIDDLPSHEAPLADSLEELEPQ	133
CD8SS-TGFbR2(1-166).TPOR/MPLR(478-582;N-9).IL7Ra(316-459).IL12Rb2(775-825) 下划线表示 CD8SS	MALPVTALLLPLALLLHAARPMGRGLLRGLWPLHIVLWTRIASTIPPHVQKSVNNDMIVTDNNGAVKFPQLCKFCDVRFSTCDNQKSCMSNCSITSICEKPQEVCVAVWRKNDENITLETVCHDPKLPYHDFILEDAASPKCIMKEKKKPGETFFMCSCSSDECNDNIIFSEEYNTSNPDLLLVIFQSDPTRVETATETHLVLGLSAVLGLLLLRWQFPAHYRRLRHALWPSLPDLHRVLGQYLRDTAALSPPKATVSDTCEEVEPSLLEILPKSSERTPLPLARDEVEGFLQDTFPQQLEESEKQRLGGDVQSPNCPSEDVVITPESFGRDSSLTCLAGNVSACDAPILSSSRSLDCRESGKNGPHVYQDLLLSLGTTNSTLPPPFSLQSGILTLNPVAQGQPILTSLGSNQEEAYVTMSSFYQNQSDPKPENPACPWTVLPAGDLPTHDGYLPSNIDDLPSHEAPLADSLEELEPQ	134
CD8SS-TGFbR2(1-166).TPOR/MPLR(478-582;N-10).IL7Ra(316-459).IL12Rb2(775-825) 下划线表示 CD8SS	MALPVTALLLPLALLLHAARPMGRGLLRGLWPLHIVLWTRIASTIPPHVQKSVNNDMIVTDNNGAVKFPQLCKFCDVRFSTCDNQKSCMSNCSITSICEKPQEVCVAVWRKNDENITLETVCHDPKLPYHDFILEDAASPKCIMKEKKKPGETFFMCSCSSDECNDNIIFSEEYNTSNPDLLLVIFQSDPTRVETATETLVLGLSAVLGLLLLRWQFPAHYRRLRHALWPSLPD	135

[0134]

	LHRVLGQYLRDTAALSPPKATVSDTCEEVEPSL LEILPKSSERTPLPLARDEVEGFLQDTFPQQLEES EKQRLGGDVQSPNCPSEDVVITPESFGRDSSLTC LAGNVSACDAPILSSSRSLDCRESGKNGPHVYQ DLLLSLGTTNSTLPPPFSLQSGILTLNPVAQGQPI LTSLGSNQEEAYVTMSSFYQNQSDPKPENPACP WTVLPAGDLPTHDGYLPSNIDDLPSHEAPLADS LEELEPQ	
CD8SS-TGFbR2(1-166). TPOR/MPLR(478-582;N -11).IL7Ra(316-459).IL1 2Rb2(775-825) 下划线表示 CD8SS	MALPVTALLLPLALLLHAARPMGRGLLRGLWP LHIVLWTRIASTIPPHVQKSVNNDMIVTDNNGA VKFPQLCKFCDVRFSTCDNQKSCMSNCSITSICE KPQEVCVAVWRKNDENITLETVCHDPKLPYHDF ILEDAASPKCIMKEKKKPGETFFMCSCSSDECN DNIIFSEEYNTSNPDLLLVIFQSDPTRVETATETV LGLSAVLGLLLLRWQFPAHYRRLRHALWPSLPD LHRVLGQYLRDTAALSPPKATVSDTCEEVEPSL LEILPKSSERTPLPLARDEVEGFLQDTFPQQLEES EKQRLGGDVQSPNCPSEDVVITPESFGRDSSLTC LAGNVSACDAPILSSSRSLDCRESGKNGPHVYQ DLLLSLGTTNSTLPPPFSLQSGILTLNPVAQGQPI LTSLGSNQEEAYVTMSSFYQNQSDPKPENPACP WTVLPAGDLPTHDGYLPSNIDDLPSHEAPLADS LEELEPQ	136
CD8SS-TGFbR2(1-166). TPOR/MPLR(478-582;N -12).IL7Ra(316-459).IL1 2Rb2(775-825) 下划线表示 CD8SS	MALPVTALLLPLALLLHAARPMGRGLLRGLWP LHIVLWTRIASTIPPHVQKSVNNDMIVTDNNGA VKFPQLCKFCDVRFSTCDNQKSCMSNCSITSICE KPQEVCVAVWRKNDENITLETVCHDPKLPYHDF ILEDAASPKCIMKEKKKPGETFFMCSCSSDECN DNIIFSEEYNTSNPDLLLVIFQSDPTRVETATETL GLSAVLGLLLLRWQFPAHYRRLRHALWPSLPDL HRVLGQYLRDTAALSPPKATVSDTCEEVEPSLL EILPKSSERTPLPLARDEVEGFLQDTFPQQLEESE KQRLGGDVQSPNCPSEDVVITPESFGRDSSLTCL AGNVSACDAPILSSSRSLDCRESGKNGPHVYQD LLLSLGTTNSTLPPPFSLQSGILTLNPVAQGQPILT SLGSNQEEAYVTMSSFYQNQSDPKPENPACPWT VLPAGDLPTHDGYLPSNIDDLPSHEAPLADSLEE LEPQ	137
CD8SS-TGFbR2(1-166). TPOR/MPLR(478-582;N -13).IL7Ra(316-459).IL1 2Rb2(775-825) 下划线表示 CD8SS	MALPVTALLLPLALLLHAARPMGRGLLRGLWP LHIVLWTRIASTIPPHVQKSVNNDMIVTDNNGA VKFPQLCKFCDVRFSTCDNQKSCMSNCSITSICE KPQEVCVAVWRKNDENITLETVCHDPKLPYHDF ILEDAASPKCIMKEKKKPGETFFMCSCSSDECN DNIIFSEEYNTSNPDLLLVIFQSDPTRVETATETG LSAVLGLLLLRWQFPAHYRRLRHALWPSLPDLH RVLGQYLRDTAALSPPKATVSDTCEEVEPSLLEI LPKSSERTPLPLARDEVEGFLQDTFPQQLEESEK QRLGGDVQSPNCPSEDVVITPESFGRDSSLTCLA GNVSACDAPILSSSRSLDCRESGKNGPHVYQDL LLSLGTTNSTLPPPFSLQSGILTLNPVAQGQPILTS	138

[0135]

	LGSNQEEAYVTMSSFYQNQSDPKPENPACPWT VLPAGDLPTHDGYLPSNIDDLPSHEAPLADSLEE LEPQ	
CD8SS-TGFbR2(1-166).TPOR/MPLR(478-582;N-14).IL7Ra(316-459).IL12Rb2(775-825) 下划线表示 CD8SS	MALPVTALLLPLALLLHAARPMGRGLLRGLWP LHIVLWTRIASTIPPHVQKSVNNDMIVTDNNGA VKFPQLCKFCDVRFSTCDNQKSCMSNCSITSICE KPQEVCVAVWRKNDENITLETVCHDPKLPYHDF ILEDAASPKCIMKEKKKPGETFFMCSCSSDECN DNIIFSEEYNTSNPDLLLVIFQSDPTRVETATETLS AVLGLLLLRWQFPAHYRRLRHALWPSLPDLHRV LGQYLRDTAALSPPKATVSDTCEEVEPSLLEILP KSSERTPLPLARDEVEGFLQDTFPQQLEESEKQR LGGDVQSPNCPSEDVVITPESFGRDSSLTCLAGN VSACDAPILSSSRSLDCRESGKNGPHVYQDLLLS LGTTNSTLPPPFSLQSGILTLNPVAQGQPILTSLGS NQEEAYVTMSSFYQNQSDPKPENPACPWTVLPA GDLPTHDGYLPSNIDDLPSHEAPLADSLEELEPQ	139
CD8SS-TGFbR2(1-166).TPOR/MPLR(478-582;N-15).IL7Ra(316-459).IL12Rb2(775-825) 下划线表示 CD8SS	MALPVTALLLPLALLLHAARPMGRGLLRGLWP LHIVLWTRIASTIPPHVQKSVNNDMIVTDNNGA VKFPQLCKFCDVRFSTCDNQKSCMSNCSITSICE KPQEVCVAVWRKNDENITLETVCHDPKLPYHDF ILEDAASPKCIMKEKKKPGETFFMCSCSSDECN DNIIFSEEYNTSNPDLLLVIFQSDPTRVETATETSA VLGLLLLRWQFPAHYRRLRHALWPSLPDLHRVL GQYLRDTAALSPPKATVSDTCEEVEPSLLEILPK SSERTPLPLARDEVEGFLQDTFPQQLEESEKQRL GGDVQSPNCPSEDVVITPESFGRDSSLTCLAGNV SACDAPILSSSRSLDCRESGKNGPHVYQDLLLSL GTTNSTLPPPFSLQSGILTLNPVAQGQPILTSLGS NQEEAYVTMSSFYQNQSDPKPENPACPWTVLPA GDLPTHDGYLPSNIDDLPSHEAPLADSLEELEPQ	140
CD8SS-TGFbR2(1-166).TPOR/MPLR(478-582;N-16).IL7Ra(316-459).IL12Rb2(775-825) 下划线表示 CD8SS	MALPVTALLLPLALLLHAARPMGRGLLRGLWP LHIVLWTRIASTIPPHVQKSVNNDMIVTDNNGA VKFPQLCKFCDVRFSTCDNQKSCMSNCSITSICE KPQEVCVAVWRKNDENITLETVCHDPKLPYHDF ILEDAASPKCIMKEKKKPGETFFMCSCSSDECN DNIIFSEEYNTSNPDLLLVIFQSDPTRVETATETAV LGLLLLRWQFPAHYRRLRHALWPSLPDLHRVLG QYLRDTAALSPPKATVSDTCEEVEPSLLEILPKSS ERTPLPLARDEVEGFLQDTFPQQLEESEKQRLG GDVQSPNCPSEDVVITPESFGRDSSLTCLAGNVS ACDAPILSSSRSLDCRESGKNGPHVYQDLLLSL GTTNSTLPPPFSLQSGILTLNPVAQGQPILTSLGS NQEEAYVTMSSFYQNQSDPKPENPACPWTVLPA GDLPTHDGYLPSNIDDLPSHEAPLADSLEELEPQ	141
CD8SS-TGFbR2(1-166).TPOR/MPLR(478-582;N-17).IL7Ra(316-459).IL12Rb2(775-825) 下划线表示 CD8SS	MALPVTALLLPLALLLHAARPMGRGLLRGLWP LHIVLWTRIASTIPPHVQKSVNNDMIVTDNNGA VKFPQLCKFCDVRFSTCDNQKSCMSNCSITSICE KPQEVCVAVWRKNDENITLETVCHDPKLPYHDF ILEDAASPKCIMKEKKKPGETFFMCSCSSDECN	142

[0136]

	DNIIFSEEYNTSNPDLLLVIFQSDPTRVETATETV LGLLLLRWQFPAHYRRLRHALWPSLPDLHRVLG QYLRDTAALSPPKATVSDTCEEVEPSLLEILPKSS ERTPLPLARDEVEGFLQDTFPQQLEESEKQRLG GDVQSPNCPSEDVVITPESFGRDSSLTCLAGNVS ACDAPILSSSRSLDCRESGKNGPHVYQDLLLSL GTTNSTLPPPFSLQSGILTLNPVAQGQPILTSLGS NQEEAYVTMSSFYQNQSDPKPENPACPWTVLPA GDLPTHDGYLPSNIDDLPSHEAPLADSLEELEPQ	
CD8SS-TGFbR2(1-166).TPOR/MPLR(478-582;N-18).IL7Ra(316-459).IL12Rb2(775-825) 下划线表示 CD8SS	MALPVTALLLPLALLLHAARPMGRGLLRGLWP LHIVLWTRIASTIPPHVQKSVNNDMIVTDNNGA VKFPQLCKFCDVRFSTCDNQKSCMSNCSITSICE KPQEVCVAVWRKNDENITLETVCHDPKLPYHDF ILEDAASPKCIMKEKKKPGETFFMCSCSSDECN DNIIFSEEYNTSNPDLLLVIFQSDPTRVETATETL GLLLLRWQFPAHYRRLRHALWPSLPDLHRVLG QYLRDTAALSPPKATVSDTCEEVEPSLLEILPKSS ERTPLPLARDEVEGFLQDTFPQQLEESEKQRLG GDVQSPNCPSEDVVITPESFGRDSSLTCLAGNVS ACDAPILSSSRSLDCRESGKNGPHVYQDLLLSL GTTNSTLPPPFSLQSGILTLNPVAQGQPILTSLGS NQEEAYVTMSSFYQNQSDPKPENPACPWTVLPA GDLPTHDGYLPSNIDDLPSHEAPLADSLEELEPQ	143
CD8SS-TGFbR2(1-166).TPOR/MPLR(478-582;N+1).IL7Ra(316-459).IL12Rb2(775-825) 下划线表示 CD8SS	MALPVTALLLPLALLLHAARPMGRGLLRGLWP LHIVLWTRIASTIPPHVQKSVNNDMIVTDNNGA VKFPQLCKFCDVRFSTCDNQKSCMSNCSITSICE KPQEVCVAVWRKNDENITLETVCHDPKLPYHDF ILEDAASPKCIMKEKKKPGETFFMCSCSSDECN DNIIFSEEYNTSNPDLLLVIFQSDPTRVETATETA WLISLVTALHLVLGLSAVLGLLLLRWQFPAHYR RLRHALWPSLPDLHRVLGQYLRDTAALSPPKAT VSDTCEEVEPSLLEILPKSSERTPLPLARDEVEGF LQDTFPQQLEESEKQRLGGDVQSPNCPSEDVVI TPESFGRDSSLTCLAGNVSACDAPILSSSRSLDC RESGKNGPHVYQDLLLSLGTTNSTLPPPFSLQSG ILTLNPVAQGQPILTSLGSNQEEAYVTMSSFYQN QSDPKPENPACPWTVLPAGDLPTHDGYLPSNID DLPSHEAPLADSLEELEPQ	144
CD8SS-TGFbR2(1-166).TPOR/MPLR(478-582;N+2).IL7Ra(316-459).IL12Rb2(775-825) 下划线表示 CD8SS	MALPVTALLLPLALLLHAARPMGRGLLRGLWP LHIVLWTRIASTIPPHVQKSVNNDMIVTDNNGA VKFPQLCKFCDVRFSTCDNQKSCMSNCSITSICE KPQEVCVAVWRKNDENITLETVCHDPKLPYHDF ILEDAASPKCIMKEKKKPGETFFMCSCSSDECN DNIIFSEEYNTSNPDLLLVIFQSDPTRVETATETA WVLISLVTALHLVLGLSAVLGLLLLRWQFPAHY RRLRHALWPSLPDLHRVLGQYLRDTAALSPPKA TVSDTCEEVEPSLLEILPKSSERTPLPLARDEVEG FLQDTFPQQLEESEKQRLGGDVQSPNCPSEDVV ITPESFGRDSSLTCLAGNVSACDAPILSSSRSLDC RESGKNGPHVYQDLLLSLGTTNSTLPPPFSLQSG	145

[0137]

	ILTLNPVAQGQPILTSLGSNQEEAYVTMSSFYQN QSDPKPENPACPWTVLPAGDLPTHDGYLPSNID DLPSHEAPLADSLEELEPQ	
CD8SS-TGFbR2(1-166). TPOR/MPLR(478-582;N +3).IL7Ra(316-459).IL1 2Rb2(775-825) 下划线表示 CD8SS	MALPVTALLLPLALLLHAARPMGRGLLRGLWP LHIVLWTRIASTIPPHVQKSVNNDMIVTDNNGA VKFPQLCKFCDVRFSTCDNQKSCMSNCSITSICE KPQEVCVAVWRKNDENITLETVCHDPKLPYHDF ILEDAASPKCIMKEKKKPGETFFMCSCSSDECN DNIIFSEEYNTSNPDLLLVIFQSDPTRVETATETA WLVLISLVTALHLVLGLSAVLGLLLLRWQFPAH YRRLRHALWPSLPDLHRVLGQYLRDTAALSPPK ATVSDTCEEVEPSLLEILPKSSERTPLPLARDEVE GFLQDTFPQQLEESEKQRLGGDVQSPNCPSEDV VITPESFGRDSSLTCLAGNVSACDAPILSSSRSLD CRESGKNGPHVYQDLLLSLGTTNSTLPPPFSLQS GILTLNPVAQGQPILTSLGSNQEEAYVTMSSFYQ NQSDPKPENPACPWTVLPAGDLPTHDGYLPSNI DDLPSHEAPLADSLEELEPQ	146
CD8SS-TGFbR2(1-166). TPOR/MPLR(478-582;N +4).IL7Ra(316-459).IL1 2Rb2(775-825) 下划线表示 CD8SS	MALPVTALLLPLALLLHAARPMGRGLLRGLWP LHIVLWTRIASTIPPHVQKSVNNDMIVTDNNGA VKFPQLCKFCDVRFSTCDNQKSCMSNCSITSICE KPQEVCVAVWRKNDENITLETVCHDPKLPYHDF ILEDAASPKCIMKEKKKPGETFFMCSCSSDECN DNIIFSEEYNTSNPDLLLVIFQSDPTRVETATETA WILVLISLVTALHLVLGLSAVLGLLLLRWQFPAH YRRLRHALWPSLPDLHRVLGQYLRDTAALSPPK ATVSDTCEEVEPSLLEILPKSSERTPLPLARDEVE GFLQDTFPQQLEESEKQRLGGDVQSPNCPSEDV VITPESFGRDSSLTCLAGNVSACDAPILSSSRSLD CRESGKNGPHVYQDLLLSLGTTNSTLPPPFSLQS GILTLNPVAQGQPILTSLGSNQEEAYVTMSSFYQ NQSDPKPENPACPWTVLPAGDLPTHDGYLPSNI DDLPSHEAPLADSLEELEPQ	147
CD8SS-TGFbR2(1-166). TPOR/MPLR(478-582;N +5).IL7Ra(316-459).IL1 2Rb2(775-825) 下划线表示 CD8SS	MALPVTALLLPLALLLHAARPMGRGLLRGLWP LHIVLWTRIASTIPPHVQKSVNNDMIVTDNNGA VKFPQLCKFCDVRFSTCDNQKSCMSNCSITSICE KPQEVCVAVWRKNDENITLETVCHDPKLPYHDF ILEDAASPKCIMKEKKKPGETFFMCSCSSDECN DNIIFSEEYNTSNPDLLLVIFQSDPTRVETATETA WLILVLISLVTALHLVLGLSAVLGLLLLRWQFPA HYRRLRHALWPSLPDLHRVLGQYLRDTAALSPP KATVSDTCEEVEPSLLEILPKSSERTPLPLARDEV EGFLQDTFPQQLEESEKQRLGGDVQSPNCPSED VVITPESFGRDSSLTCLAGNVSACDAPILSSSRSL DCRESGKNGPHVYQDLLLSLGTTNSTLPPPFSL QSGILTLNPVAQGQPILTSLGSNQEEAYVTMSSF YQNQSDPKPENPACPWTVLPAGDLPTHDGYLPS NIDDLPSHEAPLADSLEELEPQ	148
CD8SS-TGFbR2(1-166). TPOR/MPLR(478-582;N	MALPVTALLLPLALLLHAARPMGRGLLRGLWP LHIVLWTRIASTIPPHVQKSVNNDMIVTDNNGA	149

[0138]

+6).IL7Ra(316-459).IL12Rb2(775-825) 下划线表示 CD8SS	VKFPQLCKFCDVRFSTCDNQKSCMSNCSITSICEKPQEVCVAVWRKNDENITLETVCHDPKLPYHDFILEDAASPKCIMKEKKKPGETFFMCSCSSDECNDNIIFSEEYNTSNPDLLLVIFQSDPTRVETATETAWLLILVLISLVTALHLVLGLSAVLGLLLLRWQFPAHYRRLRHALWPSLPDLHRVLGQYLRDTAALSPPKATVSDTCEEVEPSLLEILPKSSERTPLPLARDEVEGFLQDTFPQQLEESEKQRLGGDVQSPNCPSEDVVITPESFGRDSSLTCLAGNVSACDAPILSSSRSLDCRESGKNGPHVYQDLLLSLGTTNSTLPPPFSLQSGILTLNPVAQGQPILTSLGSNQEEAYVTMSSFYQNQSDPKPENPACPWTVLPAGDLPTHDGYLPSNIDDLPSHEAPLADSLEELEPQ	
CD8SS-TGFbR2(1-166).TPOR/MPLR(478-582;N+7).IL7Ra(316-459).IL12Rb2(775-825) 下划线表示 CD8SS	MALPVTALLLPLALLLHAARPMGRGLLRGLWPLHIVLWTRIASTIPPHVQKSVNNDMIVTDNNGAVKFPQLCKFCDVRFSTCDNQKSCMSNCSITSICEKPQEVCVAVWRKNDENITLETVCHDPKLPYHDFILEDAASPKCIMKEKKKPGETFFMCSCSSDECNDNIIFSEEYNTSNPDLLLVIFQSDPTRVETATETAWVLLILVLISLVTALHLVLGLSAVLGLLLLRWQFPAHYRRLRHALWPSLPDLHRVLGQYLRDTAALSPPKATVSDTCEEVEPSLLEILPKSSERTPLPLARDEVEGFLQDTFPQQLEESEKQRLGGDVQSPNCPSEDVVITPESFGRDSSLTCLAGNVSACDAPILSSSRSLDCRESGKNGPHVYQDLLLSLGTTNSTLPPPFSLQSGILTLNPVAQGQPILTSLGSNQEEAYVTMSSFYQNQSDPKPENPACPWTVLPAGDLPTHDGYLPSNIDDLPSHEAPLADSLEELEPQ	150
CD8SS-TGFbR2(1-166).TPOR/MPLR(478-582;N+8).IL7Ra(316-459).IL12Rb2(775-825) 下划线表示 CD8SS	MALPVTALLLPLALLLHAARPMGRGLLRGLWPLHIVLWTRIASTIPPHVQKSVNNDMIVTDNNGAVKFPQLCKFCDVRFSTCDNQKSCMSNCSITSICEKPQEVCVAVWRKNDENITLETVCHDPKLPYHDFILEDAASPKCIMKEKKKPGETFFMCSCSSDECNDNIIFSEEYNTSNPDLLLVIFQSDPTRVETATETAWLVLLILVLISLVTALHLVLGLSAVLGLLLLRWQFPAHYRRLRHALWPSLPDLHRVLGQYLRDTAALSPPKATVSDTCEEVEPSLLEILPKSSERTPLPLARDEVEGFLQDTFPQQLEESEKQRLGGDVQSPNCPSEDVVITPESFGRDSSLTCLAGNVSACDAPILSSSRSLDCRESGKNGPHVYQDLLLSLGTTNSTLPPPFSLQSGILTLNPVAQGQPILTSLGSNQEEAYVTMSSFYQNQSDPKPENPACPWTVLPAGDLPTHDGYLPSNIDDLPSHEAPLADSLEELEPQ	151
CD8SS-TGFbR2(1-166).TPOR/MPLR(478-582).IL7Ra(316-459).IL12Rb2(775-825) 下划线表示 CD8SS	MALPVTALLLPLALLLHAARPMGRGLLRGLWPLHIVLWTRIASTIPPHVQKSVNNDMIVTDNNGAVKFPQLCKFCDVRFSTCDNQKSCMSNCSITSICEKPQEVCVAVWRKNDENITLETVCHDPKLPYHDFILEDAASPKCIMKEKKKPGETFFMCSCSSDECNDNIIFSEEYNTSNPDLLLVIFQSDPTRVETATETAWISLVTALHLVLGLSAVLGLLLLRWQFPAHYRR	162

[0139]

	LRHALWPSLPDLHRVLGQYLRDTAALSPPKATV SDTCEEVEPSLLEILPKSSERTPLPLLEARDEVEG FLQDTFPQQLEESEKQRLGGDVQSPNCPSEDVV ITPESFGRDSSLTCLAGNVSACDAPILSSSRSLDC RESGKNGPHVYQDLLLSLGTTNSTLPPPFSLQSG ILTLNPVAQGQPILTSLGSNQEEAYVTMSSFYQN QSRSDPKPENPACPWTVLPAGDLPTHDGYLPSNI DDLPSHEAPLADSLEELEPQ	
CD8SS-TGFbR2(1-166). TPOR/MPLR(478-582) S505N.W515K.IL7Ra(31 6-459).IL12Rb2(775-825) 下划线表示 CD8SS	MALPVTALLLPLALLLHAARPMGRGLLRGLWP LHIVLWTRIASTIPPHVQKSVNNDMIVTDNNGA VKFPQLCKFCDVRFSTCDNQKSCMSNCSITSICE KPQEVCVAVWRKNDENITLETVCHDPKLPYHDF ILEDAASPKCIMKEKKKPGETFFMCSCSSDECN DNIIFSEEYNTSNPDLLLVIFQSDPTRVETATETA WISLVTALHLVLGLNAVLGLLLLRKQFPAHYRR LRHALWPSLPDLHRVLGQYLRDTAALSPPKATV SDTCEEVEPSLLEILPKSSERTPLPL*LE*ARDEVEG FLQDTFPQQLEESEKQRLGGDVQSPNCPSEDVV ITPESFGRDSSLTCLAGNVSACDAPILSSSRSLDC RESGKNGPHVYQDLLLSLGTTNSTLPPPFSLQSG ILTLNPVAQGQPILTSLGSNQEEAYVTMSSFYQN Q*SR*SDPKPENPACPWTVLPAGDLPTHDGYLPSNI DDLPSHEAPLADSLEELEPQ	163
CD8SS-TGFbR2(1-166). TPOR/MPLR(478-582) S505N.W515K.IL2Rbsm all(393-433,518-551) 下划线表示 CD8SS	MALPVTALLLPLALLLHAARPMGRGLLRGLWP LHIVLWTRIASTIPPHVQKSVNNDMIVTDNNGA VKFPQLCKFCDVRFSTCDNQKSCMSNCSITSICE KPQEVCVAVWRKNDENITLETVCHDPKLPYHDF ILEDAASPKCIMKEKKKPGETFFMCSCSSDECN DNIIFSEEYNTSNPDLLLVIFQSDPTRVETATETA WISLVTALHLVLGLNAVLGLLLLRKQFPAHYRR LRHALWPSLPDLHRVLGQYLRDTAALSPPKATV SDTCEEVEPSLLEILPKSSERTPLPLLEDEGVAGA PTGSSPQPLQPLSGEDDAYCTFPSRDDLLLFSPS GQGEFRALNARLPLNTDAYLSLQELQGQDPTHL V	164
CD8SS-TGFbR2(1-166). TPOR/MPLR(478-582) S505N.W515K. K553R.K573R.IL7Ra(31 6-459).IL12Rb2(775-825) 下划线表示 CD8SS	MALPVTALLLPLALLLHAARPMGRGLLRGLWP LHIVLWTRIASTIPPHVQKSVNNDMIVTDNNGA VKFPQLCKFCDVRFSTCDNQKSCMSNCSITSICE KPQEVCVAVWRKNDENITLETVCHDPKLPYHDF ILEDAASPKCIMKEKKKPGETFFMCSCSSDECN DNIIFSEEYNTSNPDLLLVIFQSDPTRVETATETA WISLVTALHLVLGLNAVLGLLLLRKQFPAHYRR LRHALWPSLPDLHRVLGQYLRDTAALSPPRATV SDTCEEVEPSLLEILPRSSERTPLPL*LE*ARDEVEG FLQDTFPQQLEESEKQRLGGDVQSPNCPSEDVV ITPESFGRDSSLTCLAGNVSACDAPILSSSRSLDC RESGKNGPHVYQDLLLSLGTTNSTLPPPFSLQSG ILTLNPVAQGQPILTSLGSNQEEAYVTMSSFYQN Q*SR*SDPKPENPACPWTVLPAGDLPTHDGYLPSNI DDLPSHEAPLADSLEELEPQ	165

[0140]

CD8SS-TGFbR2(1-166).TPOR/MPLR(478-582)S505N.W515K.K553R.K573R.IL2Rbsmall(393-433,518-551) 下划线表示 CD8SS	MALPVTALLLPLALLLHAARPMGRGLLRGLWPLHIVLWTRIASTIPPHVQKSVNNDMIVTDNNGAVKFPQLCKFCDVRFSTCDNQKSCMSNCSITSICEKPQEVCVAVWRKNDENITLETVCHDPKLPYHDFILEDAASPKCIMKEKKKPGETFFMCSCSSDECNDNIIFSEEYNTSNPDLLLVIFQSDPTRVETATETAWISLVTALHLVLGLNAVLGLLLLRKQFPAHYRRLRHALWPSLPDLHRVLGQYLRDTAALSPPRATVSDTCEEVEPSLLEILPRSSERTPLPLLEDEGVAGAPTGSSPQPLQPLSGEDDAYCTFPSRDDLLLFSPSGQGEFRALNARLPLNTDAYLSLQELQGQDPTHLV	166
TGFbR2(1-166).TPOR/MPLR(478-582)S505N.W515K.IL2Rbsmall(393-433,518-551)	MGRGLLRGLWPLHIVLWTRIASTIPPHVQKSVNNDMIVTDNNGAVKFPQLCKFCDVRFSTCDNQKSCMSNCSITSICEKPQEVCVAVWRKNDENITLETVCHDPKLPYHDFILEDAASPKCIMKEKKKPGETFFMCSCSSDECNDNIIFSEEYNTSNPDLLLVIFQSDPTRVETATETAWISLVTALHLVLGLNAVLGLLLLRKQFPAHYRRLRHALWPSLPDLHRVLGQYLRDTAALSPPKATVSDTCEEVEPSLLEILPKSSERTPLPLLEDEGVAGAPTGSSPQPLQPLSGEDDAYCTFPSRDDLLLFSPSGQGEFRALNARLPLNTDAYLSLQELQGQDPTHLV	167
TGFbR2(1-166).TPOR/MPLR(478-582)S505N.W515K.K553R.K573R.IL2Rbsmall(393-433,518-551)	MGRGLLRGLWPLHIVLWTRIASTIPPHVQKSVNNDMIVTDNNGAVKFPQLCKFCDVRFSTCDNQKSCMSNCSITSICEKPQEVCVAVWRKNDENITLETVCHDPKLPYHDFILEDAASPKCIMKEKKKPGETFFMCSCSSDECNDNIIFSEEYNTSNPDLLLVIFQSDPTRVETATETAWISLVTALHLVLGLNAVLGLLLLRKQFPAHYRRLRHALWPSLPDLHRVLGQYLRDTAALSPPRATVSDTCEEVEPSLLEILPRSSERTPLPLLEDEGVAGAPTGSSPQPLQPLSGEDDAYCTFPSRDDLLLFSPSGQGEFRALNARLPLNTDAYLSLQELQGQDPTHLV	168
CD8SS-TGFbR2(1-166).TPOR/MPLR(478-582)S505N.W515K.IL7Ra(316-459) 下划线表示 CD8SS	MALPVTALLLPLALLLHAARPMGRGLLRGLWPLHIVLWTRIASTIPPHVQKSVNNDMIVTDNNGAVKFPQLCKFCDVRFSTCDNQKSCMSNCSITSICEKPQEVCVAVWRKNDENITLETVCHDPKLPYHDFILEDAASPKCIMKEKKKPGETFFMCSCSSDECNDNIIFSEEYNTSNPDLLLVIFQSDPTRVETATETAWISLVTALHLVLGLNAVLGLLLLRKQFPAHYRRLRHALWPSLPDLHRVLGQYLRDTAALSPPKATVSDTCEEVEPSLLEILPKSSERTPLPLLEARDEVEGFLQDTFPQQLEESEKQRLGGDVQSPNCPSEDVVITPESFGRDSSLTCLAGNVSACDAPILSSSRSLDCRESGKNGPHVYQDLLLSLGTTNSTLPPPFSLQSGILTLNPVAQGQPILTSLGSNQEEAYVTMSSFYQNQ	169
CD8SS-TGFbR2(1-166).TPOR/MPLR(478-582)	MALPVTALLLPLALLLHAARPMGRGLLRGLWPLHIVLWTRIASTIPPHVQKSVNNDMIVTDNNGA	170

[0141]

S505N.W515K.K553R.K573R.IL7Ra(316-459) 下划线表示 CD8SS	VKFPQLCKFCDVRFSTCDNQKSCMSNCSITSICE KPQEVCVAVWRKNDENITLETVCHDPKLPYHDF ILEDAASPKCIMKEKKKPGETFFMCSCSSDECN DNIIFSEEYNTSNPDLLLVIFQSDPTRVETATETA WISLVTALHLVLGLNAVLGLLLLRKQFPAHYRR LRHALWPSLPDLHRVLGQYLRDTAALSPPRATV SDTCEEVEPSLLEILPRSSERTPLPLLEARDEVEG FLQDTFPQQLEESEKQRLGGDVQSPNCPSEDVV ITPESFGRDSSLTCLAGNVSACDAPILSSSRSLDC RESGKNGPHVYQDLLLSLGTTNSTLPPPFSLQSG ILTLNPVAQGQPILTSLGSNQEEAYVTMSSFYQN Q	
CD8SS-TGFbR2(1-166).TPOR/MPLR(478-582)S505N.W515K.IL2Rbsmall(339-379,393-433,518-551) 下划线表示 CD8SS	MALPVTALLLPLALLLHAARPMGRGLLRGLWP LHIVLWTRIASTIPPHVQKSVNNDMIVTDNNGA VKFPQLCKFCDVRFSTCDNQKSCMSNCSITSICE KPQEVCVAVWRKNDENITLETVCHDPKLPYHDF ILEDAASPKCIMKEKKKPGETFFMCSCSSDECN DNIIFSEEYNTSNPDLLLVIFQSDPTRVETATETA WISLVTALLLVLGLNAVLGLLLLRKQFPAHYRR LRHALWPSLPDLHRVLGQYLRDTAALSPPKATV SDTCEEVEPSLLEILPKSSERTPLPLLEQQDKVPE PASLSSNHSLTSCFTNQGYFFFHLPDALEIEACQ DEGVAGAPTGSSPQPLQPLSGEDDAYCTFPSRD DLLLFSPSGQGEFRALNARLPLNTDAYLSLQEL QGQDPTHLV	171
CD8SS-TGFbR2(1-166).TPOR/MPLR(478-582;N-1).IL7Ra(316-459).IL12Rb2(775-825) 下划线表示 CD8SS	MALPVTALLLPLALLLHAARPMGRGLLRGLWP LHIVLWTRIASTIPPHVQKSVNNDMIVTDNNGA VKFPQLCKFCDVRFSTCDNQKSCMSNCSITSICE KPQEVCVAVWRKNDENITLETVCHDPKLPYHDF ILEDAASPKCIMKEKKKPGETFFMCSCSSDECN DNIIFSEEYNTSNPDLLLVIFQSDPTRVETATETWI SLVTALHLVLGLSAVLGLLLLRWQFPAHYRRLR HALWPSLPDLHRVLGQYLRDTAALSPPKATVSD TCEEVEPSLLEILPKSSERTPLPLLEARDEVEGFL QDTFPQQLEESEKQRLGGDVQSPNCPSEDVVIT PESFGRDSSLTCLAGNVSACDAPILSSSRSLDCR ESGKNGPHVYQDLLLSLGTTNSTLPPPFSLQSGI LTLNPVAQGQPILTSLGSNQEEAYVTMSSFYQNQ SRSDPKPENPACPWTVLPAGDLPTHDGYLPSNID DLPSHEAPLADSLEELEPQ	172
CD8SS-TGFbR2(1-166).TPOR/MPLR(478-582;N-2).IL7Ra(316-459).IL12Rb2(775-825) 下划线表示 CD8SS	MALPVTALLLPLALLLHAARPMGRGLLRGLWP LHIVLWTRIASTIPPHVQKSVNNDMIVTDNNGA VKFPQLCKFCDVRFSTCDNQKSCMSNCSITSICE KPQEVCVAVWRKNDENITLETVCHDPKLPYHDF ILEDAASPKCIMKEKKKPGETFFMCSCSSDECN DNIIFSEEYNTSNPDLLLVIFQSDPTRVETATETIS LVTALHLVLGLSAVLGLLLLRWQFPAHYRRLRH ALWPSLPDLHRVLGQYLRDTAALSPPKATVSDT CEEVEPSLLEILPKSSERTPLPLLEARDEVEGFLQ DTFPQQLEESEKQRLGGDVQSPNCPSEDVVITPE	173

[0142]

	SFGRDSSLTCLAGNVSACDAPILSSSRSLDCRES GKNGPHVYQDLLLSLGTTNSTLPPPFSLQSGILT LNPVAQGQPILTSLGSNQEEAYVTMSSFYQNQ*SR* SDPKPENPACPWTVLPAGDLPTHDGYLPSNIDD LPSHEAPLADSLEELEPQ	
CD8SS-TGFbR2(1-166).TPOR/MPLR(478-582;N-2+1).IL7Ra(316-459).IL12Rb2(775-825)	MALPVTALLLPLALLLHAARPMGRGLLRGLWP LHIVLWTRIASTIPPHVQKSVNNDMIVTDNNGA VKFPQLCKFCDVRFSTCDNQKSCMSNCSITSICE KPQEVCVAVWRKNDENITLETVCHDPKLPYHDF ILEDAASPKCIMKEKKKPGETFFMCSCSSDECN DNIIFSEEYNTSNPDLLLVIFQSDPTRVETATETLI SLVTALHLVLGLSAVLGLLLLRWQFPAHYRRLR HALWPSLPDLHRVLGQYLRDTAALSPPKATVSD TCEEVEPSLLEILPKSSERTPLPL*LE*ARDEVEGFL QDTFPQQLEESEKQRLGGDVQSPNCPSEDVVIT PESFGRDSSLTCLAGNVSACDAPILSSSRSLDCR ESGKNGPHVYQDLLLSLGTTNSTLPPPFSLQSGI LTLNPVAQGQPILTSLGSNQEEAYVTMSSFYQNQ *SR*SDPKPENPACPWTVLPAGDLPTHDGYLPSNID DLPSHEAPLADSLEELEPQ	174
CD8SS-TGFbR2(1-166).TPOR/MPLR(478-582;N-3).IL7Ra(316-459).IL12Rb2(775-825)	MALPVTALLLPLALLLHAARPMGRGLLRGLWP LHIVLWTRIASTIPPHVQKSVNNDMIVTDNNGA VKFPQLCKFCDVRFSTCDNQKSCMSNCSITSICE KPQEVCVAVWRKNDENITLETVCHDPKLPYHDF ILEDAASPKCIMKEKKKPGETFFMCSCSSDECN DNIIFSEEYNTSNPDLLLVIFQSDPTRVETATETSL VTALHLVLGLSAVLGLLLLRWQFPAHYRRLRHA LWPSLPDLHRVLGQYLRDTAALSPPKATVSDTC EEVEPSLLEILPKSSERTPLPL*LE*ARDEVEGFLQD TFPQQLEESEKQRLGGDVQSPNCPSEDVVITPES FGRDSSLTCLAGNVSACDAPILSSSRSLDCRESG KNGPHVYQDLLLSLGTTNSTLPPPFSLQSGILTL NPVAQGQPILTSLGSNQEEAYVTMSSFYQNQ*SR*S DPKPENPACPWTVLPAGDLPTHDGYLPSNIDDL PSHEAPLADSLEELEPQ	175
CD8SS-TGFbR2(1-166).TPOR/MPLR(478-582;N-4).IL7Ra(316-459).IL12Rb2(775-825) 下划线表示 CD8SS	MALPVTALLLPLALLLHAARPMGRGLLRGLWP LHIVLWTRIASTIPPHVQKSVNNDMIVTDNNGA VKFPQLCKFCDVRFSTCDNQKSCMSNCSITSICE KPQEVCVAVWRKNDENITLETVCHDPKLPYHDF ILEDAASPKCIMKEKKKPGETFFMCSCSSDECN DNIIFSEEYNTSNPDLLLVIFQSDPTRVETATETLV TALHLVLGLSAVLGLLLLRWQFPAHYRRLRHAL WPSLPDLHRVLGQYLRDTAALSPPKATVSDTCE EVEPSLLEILPKSSERTPLPL*LE*ARDEVEGFLQDT FPQQLEESEKQRLGGDVQSPNCPSEDVVITPESF GRDSSLTCLAGNVSACDAPILSSSRSLDCRESGK NGPHVYQDLLLSLGTTNSTLPPPFSLQSGILTLN PVAQGQPILTSLGSNQEEAYVTMSSFYQNQ*SR*SD PKPENPACPWTVLPAGDLPTHDGYLPSNIDDLPS HEAPLADSLEELEPQ	176

[0143]

CD8SS-TGFbR2(1-166).TPOR/MPLR(478-582;N-4+1).IL7Ra(316-459).IL12Rb2(775-825) 下划线表示 CD8SS	MALPVTALLLPLALLLHAARPMGRGLLRGLWPLHIVLWTRIASTIPPHVQKSVNNDMIVTDNNGAVKFPQLCKFCDVRFSTCDNQKSCMSNCSITSICEKPQEVCVAVWRKNDENITLETVCHDPKLPYHDFILEDAASPKCIMKEKKKPGETFFMCSCSSDECNDNIIFSEEYNTSNPDLLLVIFQSDPTRVETATETILVTALHLVLGLSAVLGLLLLRWQFPAHYRRLRHALWPSLPDLHRVLGQYLRDTAALSPPKATVSDTCEEVEPSLLEILPKSSERTPLPLLEARDEVEGFLQDTFPQQLEESEKQRLGGDVQSPNCPSEDVVITPESFGRDSSLTCLAGNVSACDAPILSSSRSLDCRESGKNGPHVYQDLLLSLGTTNSTLPPPFSLQSGILTLNPVAQGQPILTSLGSNQEEAYVTMSSFYQNQSRSDPKPENPACPWTVLPAGDLPTHDGYLPSNIDDLPSHEAPLADSLEELEPQ	177
CD8SS-TGFbR2(1-166).TPOR/MPLR(478-582;N-5).IL7Ra(316-459).IL12Rb2(775-825)	MALPVTALLLPLALLLHAARPMGRGLLRGLWPLHIVLWTRIASTIPPHVQKSVNNDMIVTDNNGAVKFPQLCKFCDVRFSTCDNQKSCMSNCSITSICEKPQEVCVAVWRKNDENITLETVCHDPKLPYHDFILEDAASPKCIMKEKKKPGETFFMCSCSSDECNDNIIFSEEYNTSNPDLLLVIFQSDPTRVETATETVTALHLVLGLSAVLGLLLLRWQFPAHYRRLRHALWPSLPDLHRVLGQYLRDTAALSPPKATVSDTCEEVEPSLLEILPKSSERTPLPLLEARDEVEGFLQDTFPQQLEESEKQRLGGDVQSPNCPSEDVVITPESFGRDSSLTCLAGNVSACDAPILSSSRSLDCRESGKNGPHVYQDLLLSLGTTNSTLPPPFSLQSGILTLNPVAQGQPILTSLGSNQEEAYVTMSSFYQNQSRSDPKPENPACPWTVLPAGDLPTHDGYLPSNIDDLPSHEAPLADSLEELEPQ	178
CD8SS-TGFbR2(1-166).TPOR/MPLR(478-582;N-6).IL7Ra(316-459).IL12Rb2(775-825) 下划线表示 CD8SS	MALPVTALLLPLALLLHAARPMGRGLLRGLWPLHIVLWTRIASTIPPHVQKSVNNDMIVTDNNGAVKFPQLCKFCDVRFSTCDNQKSCMSNCSITSICEKPQEVCVAVWRKNDENITLETVCHDPKLPYHDFILEDAASPKCIMKEKKKPGETFFMCSCSSDECNDNIIFSEEYNTSNPDLLLVIFQSDPTRVETATETTALHLVLGLSAVLGLLLLRWQFPAHYRRLRHALWPSLPDLHRVLGQYLRDTAALSPPKATVSDTCEEVEPSLLEILPKSSERTPLPLLEARDEVEGFLQDTFPQQLEESEKQRLGGDVQSPNCPSEDVVITPESFGRDSSLTCLAGNVSACDAPILSSSRSLDCRESGKNGPHVYQDLLLSLGTTNSTLPPPFSLQSGILTLNPVAQGQPILTSLGSNQEEAYVTMSSFYQNQSRSDPKPENPACPWTVLPAGDLPTHDGYLPSNIDDLPSHEAPLADSLEELEPQ	179
CD8SS-TGFbR2(1-166).TPOR/MPLR(478-582;N-7).IL7Ra(316-459).IL12Rb2(775-825)	MALPVTALLLPLALLLHAARPMGRGLLRGLWPLHIVLWTRIASTIPPHVQKSVNNDMIVTDNNGAVKFPQLCKFCDVRFSTCDNQKSCMSNCSITSICEKPQEVCVAVWRKNDENITLETVCHDPKLPYHDFILEDAASPKCIMKEKKKPGETFFMCSCSSDECN	180

[0144]

	DNIIFSEEYNTSNPDLLLVIFQSDPTRVETATETAL HLVLGLSAVLGLLLLRWQFPAHYRRLRHALWPS LPDLHRVLGQYLRDTAALSPPKATVSDTCEEVE PSLLEILPKSSERTPLPL*LE*ARDEVEGFLQDTFPQ QLEESEKQRLGGDVQSPNCPSEDVVITPESFGRD SSLTCLAGNVSACDAPILSSSRSLDCRESGKNGP HVYQDLLLSLGTTNSTLPPPFSLQSGILTLNPVA QGQPILTSLGSNQEEAYVTMSSFYQNQ*SR*SDPKP ENPACPWTVLPAGDLPTHDGYLPSNIDDLPSHE APLADSLEELEPQ	
CD8SS-TGFbR2(1-166). TPOR/MPLR(478-582;N -8).IL7Ra(316-459).IL12 Rb2(775-825) 下划线表示 CD8SS	MALPVTALLLPLALLLHAARPMGRGLLRGLWP LHIVLWTRIASTIPPHVQKSVNNDMIVTDNNGA VKFPQLCKFCDVRFSTCDNQKSCMSNCSITSICE KPQEVCVAVWRKNDENITLETVCHDPKLPYHDF ILEDAASPKCIMKEKKKPGETFFMCSCSSDECN DNIIFSEEYNTSNPDLLLVIFQSDPTRVETATETL HLVLGLSAVLGLLLLRWQFPAHYRRLRHALWPS LPDLHRVLGQYLRDTAALSPPKATVSDTCEEVE PSLLEILPKSSERTPLPL*LE*ARDEVEGFLQDTFPQ QLEESEKQRLGGDVQSPNCPSEDVVITPESFGRD SSLTCLAGNVSACDAPILSSSRSLDCRESGKNGP HVYQDLLLSLGTTNSTLPPPFSLQSGILTLNPVA QGQPILTSLGSNQEEAYVTMSSFYQNQ*SR*SDPKP ENPACPWTVLPAGDLPTHDGYLPSNIDDLPSHE APLADSLEELEPQ	181
CD8SS-TGFbR2(1-166). TPOR/MPLR(478-582;N -9).IL7Ra(316-459).IL12 Rb2(775-825) 下划线表示 CD8SS	MALPVTALLLPLALLLHAARPMGRGLLRGLWP LHIVLWTRIASTIPPHVQKSVNNDMIVTDNNGA VKFPQLCKFCDVRFSTCDNQKSCMSNCSITSICE KPQEVCVAVWRKNDENITLETVCHDPKLPYHDF ILEDAASPKCIMKEKKKPGETFFMCSCSSDECN DNIIFSEEYNTSNPDLLLVIFQSDPTRVETATETHL VLGLSAVLGLLLLRWQFPAHYRRLRHALWPSLP DLHRVLGQYLRDTAALSPPKATVSDTCEEVEPS LLEILPKSSERTPLPL*LE*ARDEVEGFLQDTFPQQL EESEKQRLGGDVQSPNCPSEDVVITPESFGRDSS LTCLAGNVSACDAPILSSSRSLDCRESGKNGPH VYQDLLLSLGTTNSTLPPPFSLQSGILTLNPVAQ GQPILTSLGSNQEEAYVTMSSFYQNQ*SR*SDPKPE NPACPWTVLPAGDLPTHDGYLPSNIDDLPSHEA PLADSLEELEPQ	182
CD8SS-TGFbR2(1-166). TPOR/MPLR(478-582;N -10).IL7Ra(316-459).IL1 2Rb2(775-825) 下划线表示 CD8SS	MALPVTALLLPLALLLHAARPMGRGLLRGLWP LHIVLWTRIASTIPPHVQKSVNNDMIVTDNNGA VKFPQLCKFCDVRFSTCDNQKSCMSNCSITSICE KPQEVCVAVWRKNDENITLETVCHDPKLPYHDF ILEDAASPKCIMKEKKKPGETFFMCSCSSDECN DNIIFSEEYNTSNPDLLLVIFQSDPTRVETATETLV LGLSAVLGLLLLRWQFPAHYRRLRHALWPSLPD LHRVLGQYLRDTAALSPPKATVSDTCEEVEPSL LEILPKSSERTPLPL*LE*ARDEVEGFLQDTFPQQLE ESEKQRLGGDVQSPNCPSEDVVITPESFGRDSSL	183

[0145]

	TCLAGNVSACDAPILSSSRSLDCRESGKNGPHV YQDLLLSLGTTNSTLPPPFSLQSGILTLNPVAQG QPILTSLGSNQEEAYVTMSSFYQNQ*SR*SDPKPEN PACPWTVLPAGDLPTHDGYLPSNIDDLPSHEAPL ADSLEELEPQ	
CD8SS-TGFbR2(1-166).TPOR/MPLR(478-582;N-11).IL7Ra(316-459).IL12Rb2(775-825) 下划线表示 CD8SS	MALPVTALLLPLALLLHAARPMGRGLLRGLWP LHIVLWTRIASTIPPHVQKSVNNDMIVTDNNGA VKFPQLCKFCDVRFSTCDNQKSCMSNCSITSICE KPQEVCVAVWRKNDENITLETVCHDPKLPYHDF ILEDAASPKCIMKEKKKPGETFFMCSCSSDECN DNIIFSEEYNTSNPDLLLVIFQSDPTRVETATETV LGLSAVLGLLLLRWQFPAHYRRLRHALWPSLPD LHRVLGQYLRDTAALSPPKATVSDTCEEVEPSL LEILPKSSERTPLPL*LE*ARDEVEGFLQDTFPQQLE ESEKQRLGGDVQSPNCPSEDVVITPESFGRDSSL TCLAGNVSACDAPILSSSRSLDCRESGKNGPHV YQDLLLSLGTTNSTLPPPFSLQSGILTLNPVAQG QPILTSLGSNQEEAYVTMSSFYQNQ*SR*SDPKPEN PACPWTVLPAGDLPTHDGYLPSNIDDLPSHEAPL ADSLEELEPQ	184
CD8SS-TGFbR2(1-166).TPOR/MPLR(478-582;N-12).IL7Ra(316-459).IL12Rb2(775-825) 下划线表示 CD8SS	MALPVTALLLPLALLLHAARPMGRGLLRGLWP LHIVLWTRIASTIPPHVQKSVNNDMIVTDNNGA VKFPQLCKFCDVRFSTCDNQKSCMSNCSITSICE KPQEVCVAVWRKNDENITLETVCHDPKLPYHDF ILEDAASPKCIMKEKKKPGETFFMCSCSSDECN DNIIFSEEYNTSNPDLLLVIFQSDPTRVETATETL GLSAVLGLLLLRWQFPAHYRRLRHALWPSLPDL HRVLGQYLRDTAALSPPKATVSDTCEEVEPSLL EILPKSSERTPLPL*LE*ARDEVEGFLQDTFPQQLEE SEKQRLGGDVQSPNCPSEDVVITPESFGRDSSLT CLAGNVSACDAPILSSSRSLDCRESGKNGPHVY QDLLLSLGTTNSTLPPPFSLQSGILTLNPVAQGQP ILTSLGSNQEEAYVTMSSFYQNQ*SR*SDPKPENPA CPWTVLPAGDLPTHDGYLPSNIDDLPSHEAPLA DSLEELEPQ	185
CD8SS-TGFbR2(1-166).TPOR/MPLR(478-582;N-13).IL7Ra(316-459).IL12Rb2(775-825) 下划线表示 CD8SS	MALPVTALLLPLALLLHAARPMGRGLLRGLWP LHIVLWTRIASTIPPHVQKSVNNDMIVTDNNGA VKFPQLCKFCDVRFSTCDNQKSCMSNCSITSICE KPQEVCVAVWRKNDENITLETVCHDPKLPYHDF ILEDAASPKCIMKEKKKPGETFFMCSCSSDECN DNIIFSEEYNTSNPDLLLVIFQSDPTRVETATETG LSAVLGLLLLRWQFPAHYRRLRHALWPSLPDLH RVLGQYLRDTAALSPPKATVSDTCEEVEPSLLEI LPKSSERTPLPL*LE*ARDEVEGFLQDTFPQQLEES EKQRLGGDVQSPNCPSEDVVITPESFGRDSSLTC LAGNVSACDAPILSSSRSLDCRESGKNGPHVYQ DLLLSLGTTNSTLPPPFSLQSGILTLNPVAQGQPI LTSLGSNQEEAYVTMSSFYQNQ*SR*SDPKPENPAC PWTVLPAGDLPTHDGYLPSNIDDLPSHEAPLAD SLEELEPQ	186

[0146]

CD8SS-TGFbR2(1-166).TPOR/MPLR(478-582;N-14).IL7Ra(316-459).IL12Rb2(775-825) 下划线表示 CD8SS	MALPVTALLLPLALLLHAARPMGRGLLRGLWPLHIVLWTRIASTIPPHVQKSVNNDMIVTDNNGAVKFPQLCKFCDVRFSTCDNQKSCMSNCSITSICEKPQEVCVAVWRKNDENITLETVCHDPKLPYHDFILEDAASPKCIMKEKKKPGETFFMCSCSSDECNDNIIFSEEYNTSNPDLLLVIFQSDPTRVETATETLSAVLGLLLLRWQFPAHYRRLRHALWPSLPDLHRVLGQYLRDTAALSPPKATVSDTCEEVEPSLLEILPKSSERTPLPL*LE*ARDEVEGFLQDTFPQQLEESEKQRLGGDVQSPNCPSEDVVITPESFGRDSSLTCLAGNVSACDAPILSSSRSLDCRESGKNGPHVYQDLLLSLGTTNSTLPPPFSLQSGILTLNPVAQGQPILTSLGSNQEEAYVTMSSFYQNQ*SR*SDPKPENPACPWTVLPAGDLPTHDGYLPSNIDDLPSHEAPLADSLEELEPQ	187
CD8SS-TGFbR2(1-166).TPOR/MPLR(478-582;N-15).IL7Ra(316-459).IL12Rb2(775-825) 下划线表示 CD8SS	MALPVTALLLPLALLLHAARPMGRGLLRGLWPLHIVLWTRIASTIPPHVQKSVNNDMIVTDNNGAVKFPQLCKFCDVRFSTCDNQKSCMSNCSITSICEKPQEVCVAVWRKNDENITLETVCHDPKLPYHDFILEDAASPKCIMKEKKKPGETFFMCSCSSDECNDNIIFSEEYNTSNPDLLLVIFQSDPTRVETATETSAVLGLLLLRWQFPAHYRRLRHALWPSLPDLHRVLGQYLRDTAALSPPKATVSDTCEEVEPSLLEILPKSSERTPLPL*LE*ARDEVEGFLQDTFPQQLEESEKQRLGGDVQSPNCPSEDVVITPESFGRDSSLTCLAGNVSACDAPILSSSRSLDCRESGKNGPHVYQDLLLSLGTTNSTLPPPFSLQSGILTLNPVAQGQPILTSLGSNQEEAYVTMSSFYQNQ*SR*SDPKPENPACPWTVLPAGDLPTHDGYLPSNIDDLPSHEAPLADSLEELEPQ	188
CD8SS-TGFbR2(1-166).TPOR/MPLR(478-582;N-16).IL7Ra(316-459).IL12Rb2(775-825) 下划线表示 CD8SS	MALPVTALLLPLALLLHAARPMGRGLLRGLWPLHIVLWTRIASTIPPHVQKSVNNDMIVTDNNGAVKFPQLCKFCDVRFSTCDNQKSCMSNCSITSICEKPQEVCVAVWRKNDENITLETVCHDPKLPYHDFILEDAASPKCIMKEKKKPGETFFMCSCSSDECNDNIIFSEEYNTSNPDLLLVIFQSDPTRVETATETAVLGLLLLRWQFPAHYRRLRHALWPSLPDLHRVLGQYLRDTAALSPPKATVSDTCEEVEPSLLEILPKSSERTPLPL*LE*ARDEVEGFLQDTFPQQLEESEKQRLGGDVQSPNCPSEDVVITPESFGRDSSLTCLAGNVSACDAPILSSSRSLDCRESGKNGPHVYQDLLLSLGTTNSTLPPPFSLQSGILTLNPVAQGQPILTSLGSNQEEAYVTMSSFYQNQ*SR*SDPKPENPACPWTVLPAGDLPTHDGYLPSNIDDLPSHEAPLADSLEELEPQ	189
CD8SS-TGFbR2(1-166).TPOR/MPLR(478-582;N-17).IL7Ra(316-459).IL12Rb2(775-825) 下划线表示 CD8SS	MALPVTALLLPLALLLHAARPMGRGLLRGLWPLHIVLWTRIASTIPPHVQKSVNNDMIVTDNNGAVKFPQLCKFCDVRFSTCDNQKSCMSNCSITSICEKPQEVCVAVWRKNDENITLETVCHDPKLPYHDFILEDAASPKCIMKEKKKPGETFFMCSCSSDECN	190

[0147]

	DNIIFSEEYNTSNPDLLLVIFQSDPTRVETATETV LGLLLLRWQFPAHYRRLRHALWPSLPDLHRVLG QYLRDTAALSPPKATVSDTCEEVEPSLLEILPKSS ERTPLPL*LE*ARDEVEGFLQDTFPQQLEESEKQRL GGDVQSPNCPSEDVVITPESFGRDSSLTCLAGNV SACDAPILSSSRSLDCRESGKNGPHVYQDLLLSL GTTNSTLPPPFSLQSGILTLNPVAQGQPILTSLGS NQEEAYVTMSSFYQNQ*SR*SDPKPENPACPWTVL PAGDLPTHDGYLPSNIDDLPSHEAPLADSLEELE PQ	
CD8SS-TGFbR2(1-166). TPOR/MPLR(478-582;N -18).IL7Ra(316-459).IL1 2Rb2(775-825) 下划线表示 CD8SS	MALPVTALLLPLALLLHAARPMGRGLLRGLWP LHIVLWTRIASTIPPHVQKSVNNDMIVTDNNGA VKFPQLCKFCDVRFSTCDNQKSCMSNCSITSICE KPQEVCVAVWRKNDENITLETVCHDPKLPYHDF ILEDAASPKCIMKEKKKPGETFFMCSCSSDECN DNIIFSEEYNTSNPDLLLVIFQSDPTRVETATETL GLLLLRWQFPAHYRRLRHALWPSLPDLHRVLG QYLRDTAALSPPKATVSDTCEEVEPSLLEILPKSS ERTPLPL*LE*ARDEVEGFLQDTFPQQLEESEKQRL GGDVQSPNCPSEDVVITPESFGRDSSLTCLAGNV SACDAPILSSSRSLDCRESGKNGPHVYQDLLLSL GTTNSTLPPPFSLQSGILTLNPVAQGQPILTSLGS NQEEAYVTMSSFYQNQ*SR*SDPKPENPACPWTVL PAGDLPTHDGYLPSNIDDLPSHEAPLADSLEELE PQ	191
CD8SS-TGFbR2(1-166). TPOR/MPLR(478-582;N +1).IL7Ra(316-459).IL1 2Rb2(775-825) 下划线表示 CD8SS	MALPVTALLLPLALLLHAARPMGRGLLRGLWP LHIVLWTRIASTIPPHVQKSVNNDMIVTDNNGA VKFPQLCKFCDVRFSTCDNQKSCMSNCSITSICE KPQEVCVAVWRKNDENITLETVCHDPKLPYHDF ILEDAASPKCIMKEKKKPGETFFMCSCSSDECN DNIIFSEEYNTSNPDLLLVIFQSDPTRVETATETA WLISLVTALHLVLGLSAVLGLLLLRWQFPAHYR RLRHALWPSLPDLHRVLGQYLRDTAALSPPKAT VSDTCEEVEPSLLEILPKSSERTPLPL*LE*ARDEVE GFLQDTFPQQLEESEKQRLGGDVQSPNCPSEDV VITPESFGRDSSLTCLAGNVSACDAPILSSSRSLD CRESGKNGPHVYQDLLLSLGTTNSTLPPPFSLQS GILTLNPVAQGQPILTSLGSNQEEAYVTMSSFYQ NQ*SR*SDPKPENPACPWTVLPAGDLPTHDGYLPS NIDDLPSHEAPLADSLEELEPQ	192
CD8SS-TGFbR2(1-166). TPOR/MPLR(478-582;N +2).IL7Ra(316-459).IL1 2Rb2(775-825) 下划线表示 CD8SS	MALPVTALLLPLALLLHAARPMGRGLLRGLWP LHIVLWTRIASTIPPHVQKSVNNDMIVTDNNGA VKFPQLCKFCDVRFSTCDNQKSCMSNCSITSICE KPQEVCVAVWRKNDENITLETVCHDPKLPYHDF ILEDAASPKCIMKEKKKPGETFFMCSCSSDECN DNIIFSEEYNTSNPDLLLVIFQSDPTRVETATETA WVLISLVTALHLVLGLSAVLGLLLLRWQFPAHY RRLRHALWPSLPDLHRVLGQYLRDTAALSPPKA TVSDTCEEVEPSLLEILPKSSERTPLPL*LE*ARDEV EGFLQDTFPQQLEESEKQRLGGDVQSPNCPSED	193

[0148]

	VVITPESFGRDSSLTCLAGNVSACDAPILSSSRSL DCRESGKNGPHVYQDLLLSLGTTNSTLPPPFSL QSGILTLNPVAQGQPILTSLGSNQEEAYVTMSSF YQNQ*SR*SDPKPENPACPWTVLPAGDLPTHDGYL PSNIDDLPSHEAPLADSLEELEPQ	
CD8SS-TGFbR2(1-166). TPOR/MPLR(478-582;N +3).IL7Ra(316-459).IL1 2Rb2(775-825) 下划线表示 CD8SS	MALPVTALLLPLALLLHAARPMGRGLLRGLWP LHIVLWTRIASTIPPHVQKSVNNDMIVTDNNGA VKFPQLCKFCDVRFSTCDNQKSCMSNCSITSICE KPQEVCVAVWRKNDENITLETVCHDPKLPYHDF ILEDAASPKCIMKEKKKPGETFFMCSCSSDECN DNIIFSEEYNTSNPDLLLVIFQSDPTRVETATETA WLVLISLVTALHLVLGLSAVLGLLLLRWQFPAH YRRLRHALWPSLPDLHRVLGQYLRDTAALSPPK ATVSDTCEEVEPSLLEILPKSSERTPLPL*LE*ARDE VEGFLQDTFPQQLEESEKQRLGGDVQSPNCPSE DVVITPESFGRDSSLTCLAGNVSACDAPILSSSRS LDCRESGKNGPHVYQDLLLSLGTTNSTLPPPFSL QSGILTLNPVAQGQPILTSLGSNQEEAYVTMSSF YQNQ*SR*SDPKPENPACPWTVLPAGDLPTHDGYL PSNIDDLPSHEAPLADSLEELEPQ	194
CD8SS-TGFbR2(1-166). TPOR/MPLR(478-582;N +4).IL7Ra(316-459).IL1 2Rb2(775-825) 下划线表示 CD8SS	MALPVTALLLPLALLLHAARPMGRGLLRGLWP LHIVLWTRIASTIPPHVQKSVNNDMIVTDNNGA VKFPQLCKFCDVRFSTCDNQKSCMSNCSITSICE KPQEVCVAVWRKNDENITLETVCHDPKLPYHDF ILEDAASPKCIMKEKKKPGETFFMCSCSSDECN DNIIFSEEYNTSNPDLLLVIFQSDPTRVETATETA WILVLISLVTALHLVLGLSAVLGLLLLRWQFPAH YRRLRHALWPSLPDLHRVLGQYLRDTAALSPPK ATVSDTCEEVEPSLLEILPKSSERTPLPL*LE*ARDE VEGFLQDTFPQQLEESEKQRLGGDVQSPNCPSE DVVITPESFGRDSSLTCLAGNVSACDAPILSSSRS LDCRESGKNGPHVYQDLLLSLGTTNSTLPPPFSL QSGILTLNPVAQGQPILTSLGSNQEEAYVTMSSF YQNQ*SR*SDPKPENPACPWTVLPAGDLPTHDGYL PSNIDDLPSHEAPLADSLEELEPQ	195
CD8SS-TGFbR2(1-166). TPOR/MPLR(478-582;N +5).IL7Ra(316-459).IL1 2Rb2(775-825) 下划线表示 CD8SS	MALPVTALLLPLALLLHAARPMGRGLLRGLWP LHIVLWTRIASTIPPHVQKSVNNDMIVTDNNGA VKFPQLCKFCDVRFSTCDNQKSCMSNCSITSICE KPQEVCVAVWRKNDENITLETVCHDPKLPYHDF ILEDAASPKCIMKEKKKPGETFFMCSCSSDECN DNIIFSEEYNTSNPDLLLVIFQSDPTRVETATETA WLILVLISLVTALHLVLGLSAVLGLLLLRWQFPA HYRRLRHALWPSLPDLHRVLGQYLRDTAALSPP KATVSDTCEEVEPSLLEILPKSSERTPLPL*LE*ARD EVEGFLQDTFPQQLEESEKQRLGGDVQSPNCPS EDVVITPESFGRDSSLTCLAGNVSACDAPILSSSR SLDCRESGKNGPHVYQDLLLSLGTTNSTLPPPFS LQSGILTLNPVAQGQPILTSLGSNQEEAYVTMSS FYQNQ*SR*SDPKPENPACPWTVLPAGDLPTHDGY LPSNIDDLPSHEAPLADSLEELEPQ	196

[0149]

CD8SS-TGFbR2(1-166).TPOR/MPLR(478-582;N+6).IL7Ra(316-459).IL12Rb2(775-825) 下划线表示 CD8SS	MALPVTALLLPLALLLHAARPMGRGLLRGLWP LHIVLWTRIASTIPPHVQKSVNNDMIVTDNNGA VKFPQLCKFCDVRFSTCDNQKSCMSNCSITSICE KPQEVCVAVWRKNDENITLETVCHDPKLPYHDF ILEDAASPKCIMKEKKKPGETFFMCSCSSDECN DNIIFSEEYNTSNPDLLLVIFQSDPTRVETATETA WLLILVLISLVTALHLVLGLSAVLGLLLLRWQFP AHYRRLRHALWPSLPDLHRVLGQYLRDTAALS PPKATVSDTCEEVEPSLLEILPKSSERTPLPL*LE*A RDEVEGFLQDTFPQQLEESEKQRLGGDVQSPNC PSEDVVITPESFGRDSSLTCLAGNVSACDAPILSS SRSLDCRESGKNGPHVYQDLLLSLGTTNSTLPPP FSLQSGILTLNPVAQGQPILTSLGSNQEEAYVTM SSFYQNQ*SR*SDPKPENPACPWTVLPAGDLPTHD GYLPSNIDDLPSHEAPLADSLEELEPQ	197
CD8SS-TGFbR2(1-166).TPOR/MPLR(478-582;N+7).IL7Ra(316-459).IL12Rb2(775-825) 下划线表示 CD8SS	MALPVTALLLPLALLLHAARPMGRGLLRGLWP LHIVLWTRIASTIPPHVQKSVNNDMIVTDNNGA VKFPQLCKFCDVRFSTCDNQKSCMSNCSITSICE KPQEVCVAVWRKNDENITLETVCHDPKLPYHDF ILEDAASPKCIMKEKKKPGETFFMCSCSSDECN DNIIFSEEYNTSNPDLLLVIFQSDPTRVETATETA WVLLILVLISLVTALHLVLGLSAVLGLLLLRWQF PAHYRRLRHALWPSLPDLHRVLGQYLRDTAALS PPKATVSDTCEEVEPSLLEILPKSSERTPLPL*LE*A RDEVEGFLQDTFPQQLEESEKQRLGGDVQSPNC PSEDVVITPESFGRDSSLTCLAGNVSACDAPILSS SRSLDCRESGKNGPHVYQDLLLSLGTTNSTLPPP FSLQSGILTLNPVAQGQPILTSLGSNQEEAYVTM SSFYQNQ*SR*SDPKPENPACPWTVLPAGDLPTHD GYLPSNIDDLPSHEAPLADSLEELEPQ	198
CD8SS-TGFbR2(1-166).TPOR/MPLR(478-582;N+8).IL7Ra(316-459).IL12Rb2(775-825) 下划线表示 CD8SS	MALPVTALLLPLALLLHAARPMGRGLLRGLWP LHIVLWTRIASTIPPHVQKSVNNDMIVTDNNGA VKFPQLCKFCDVRFSTCDNQKSCMSNCSITSICE KPQEVCVAVWRKNDENITLETVCHDPKLPYHDF ILEDAASPKCIMKEKKKPGETFFMCSCSSDECN DNIIFSEEYNTSNPDLLLVIFQSDPTRVETATETA WLVLLILVLISLVTALHLVLGLSAVLGLLLLRWQ FPAHYRRLRHALWPSLPDLHRVLGQYLRDTAAL SPPKATVSDTCEEVEPSLLEILPKSSERTPLPL*LE* ARDEVEGFLQDTFPQQLEESEKQRLGGDVQSPN CPSEDVVITPESFGRDSSLTCLAGNVSACDAPILS SSRSLDCRESGKNGPHVYQDLLLSLGTTNSTLPP PFSLQSGILTLNPVAQGQPILTSLGSNQEEAYVT MSSFYQNQ*SR*SDPKPENPACPWTVLPAGDLPTH DGYLPSNIDDLPSHEAPLADSLEELEPQ	199
CD8SS-TGFbR2(1-166).TPOR/MPLR(478-582;N-9-1).IL7Ra(316-459).IL12Rb2(775-825) 下划线表示 CD8SS	MALPVTALLLPLALLLHAARPMGRGLLRGLWP LHIVLWTRIASTIPPHVQKSVNNDMIVTDNNGA VKFPQLCKFCDVRFSTCDNQKSCMSNCSITSICE KPQEVCVAVWRKNDENITLETVCHDPKLPYHDF ILEDAASPKCIMKEKKKPGETFFMCSCSSDECN	200

[0150]

	DNIIFSEEYNTSNPDLLLVIFQSDPTRVETATEHL VLGLSAVLGLLLLRWQFPAHYRRLRHALWPSLP DLHRVLGQYLRDTAALSPPKATVSDTCEEVEPS LLEILPKSSERTPLPL*LE*ARDEVEGFLQDTFPQQL EESEKQRLGGDVQSPNCPSEDVVITPESFGRDSS LTCLAGNVSACDAPILSSSRSLDCRESGKNGPH VYQDLLLSLGTTNSTLPPPFSLQSGILTLNPVAQ GQPILTSLGSNQEEAYVTMSSFYQNQ*SR*SDPKPE NPACPWTVLPAGDLPTHDGYLPSNIDDLPSHEA PLADSLEELEPQ	
CD8SS-TGFbR2(1-166). TPOR/MPLR(478-582;N -9-2).IL7Ra(316-459).IL 12Rb2(775-825) 下划线表示 CD8SS	MALPVTALLLPLALLLHAARPMGRGLLRGLWP LHIVLWTRIASTIPPHVQKSVNNDMIVTDNNGA VKFPQLCKFCDVRFSTCDNQKSCMSNCSITSICE KPQEVCVAVWRKNDENITLETVCHDPKLPYHDF ILEDAASPKCIMKEKKKPGETFFMCSCSSDECN DNIIFSEEYNTSNPDLLLVIFQSDPTRVETATHLV LGLSAVLGLLLLRWQFPAHYRRLRHALWPSLPD LHRVLGQYLRDTAALSPPKATVSDTCEEVEPSL LEILPKSSERTPLPL*LE*ARDEVEGFLQDTFPQQLE ESEKQRLGGDVQSPNCPSEDVVITPESFGRDSSL TCLAGNVSACDAPILSSSRSLDCRESGKNGPHV YQDLLLSLGTTNSTLPPPFSLQSGILTLNPVAQG QPILTSLGSNQEEAYVTMSSFYQNQ*SR*SDPKPEN PACPWTVLPAGDLPTHDGYLPSNIDDLPSHEAPL ADSLEELEPQ	201
CD8SS-TGFbR2(1-166). TPOR/MPLR(478-582;N -9-3).IL7Ra(316-459).IL 12Rb2(775-825) 下划线表示 CD8SS	MALPVTALLLPLALLLHAARPMGRGLLRGLWP LHIVLWTRIASTIPPHVQKSVNNDMIVTDNNGA VKFPQLCKFCDVRFSTCDNQKSCMSNCSITSICE KPQEVCVAVWRKNDENITLETVCHDPKLPYHDF ILEDAASPKCIMKEKKKPGETFFMCSCSSDECN DNIIFSEEYNTSNPDLLLVIFQSDPTRVETAHLVL GLSAVLGLLLLRWQFPAHYRRLRHALWPSLPDL HRVLGQYLRDTAALSPPKATVSDTCEEVEPSLL EILPKSSERTPLPL*LE*ARDEVEGFLQDTFPQQLEE SEKQRLGGDVQSPNCPSEDVVITPESFGRDSSLT CLAGNVSACDAPILSSSRSLDCRESGKNGPHVY QDLLLSLGTTNSTLPPPFSLQSGILTLNPVAQGQP ILTSLGSNQEEAYVTMSSFYQNQ*SR*SDPKPENPA CPWTVLPAGDLPTHDGYLPSNIDDLPSHEAPLA DSLEELEPQ	202
CD8SS-TGFbR2(1-166). TPOR/MPLR(478-582;N -9-4).IL7Ra(316-459).IL 12Rb2(775-825) 下划线表示 CD8SS	MALPVTALLLPLALLLHAARPMGRGLLRGLWP LHIVLWTRIASTIPPHVQKSVNNDMIVTDNNGA VKFPQLCKFCDVRFSTCDNQKSCMSNCSITSICE KPQEVCVAVWRKNDENITLETVCHDPKLPYHDF ILEDAASPKCIMKEKKKPGETFFMCSCSSDECN DNIIFSEEYNTSNPDLLLVIFQSDPTRVETHLVLG LSAVLGLLLLRWQFPAHYRRLRHALWPSLPDLH RVLGQYLRDTAALSPPKATVSDTCEEVEPSLLEI LPKSSERTPLPL*LE*ARDEVEGFLQDTFPQQLEES EKQRLGGDVQSPNCPSEDVVITPESFGRDSSLTC	203

[0151]

	LAGNVSACDAPILSSSRSLDCRESGKNGPHVYQ DLLLSLGTTNSTLPPPFSLQSGILTLNPVAQGQPI LTSLGSNQEEAYVTMSSFYQNQ*SR*SDPKPENPAC PWTVLPAGDLPTHDGYLPSNIDDLPSHEAPLAD SLEELEPQ	
CD8SS-TGFbR2(1-166).TPOR/MPLR(478-582;N-9-5).IL7Ra(316-459).IL12Rb2(775-825) 下划线表示 CD8SS	MALPVTALLLPLALLLHAARPMGRGLLRGLWP LHIVLWTRIASTIPPHVQKSVNNDMIVTDNNGA VKFPQLCKFCDVRFSTCDNQKSCMSNCSITSICE KPQEVCVAVWRKNDENITLETVCHDPKLPYHDF ILEDAASPKCIMKEKKKPGETFFMCSCSSDECN DNIIFSEEYNTSNPDLLLVIFQSDPTRVEHLVLGL SAVLGLLLLRWQFPAHYRRLRHALWPSLPDLHR VLGQYLRDTAALSPPKATVSDTCEEVEPSLLEIL PKSSERTPLPL*LE*ARDEVEGFLQDTFPQQLEESE KQRLGGDVQSPNCPSEDVVITPESFGRDSSLTCL AGNVSACDAPILSSSRSLDCRESGKNGPHVYQD LLLSLGTTNSTLPPPFSLQSGILTLNPVAQGQPILT SLGSNQEEAYVTMSSFYQNQ*SR*SDPKPENPACP WTVLPAGDLPTHDGYLPSNIDDLPSHEAPLADS LEELEPQ	204
CD8SS-TGFbR2(1-166).TPOR/MPLR(478-582;N-9-6).IL7Ra(316-459).IL12Rb2(775-825) 下划线表示 CD8SS	MALPVTALLLPLALLLHAARPMGRGLLRGLWP LHIVLWTRIASTIPPHVQKSVNNDMIVTDNNGA VKFPQLCKFCDVRFSTCDNQKSCMSNCSITSICE KPQEVCVAVWRKNDENITLETVCHDPKLPYHDF ILEDAASPKCIMKEKKKPGETFFMCSCSSDECN DNIIFSEEYNTSNPDLLLVIFQSDPTRVHLVLGLS AVLGLLLLRWQFPAHYRRLRHALWPSLPDLHRV LGQYLRDTAALSPPKATVSDTCEEVEPSLLEILP KSSERTPLPL*LE*ARDEVEGFLQDTFPQQLEESEK QRLGGDVQSPNCPSEDVVITPESFGRDSSLTCLA GNVSACDAPILSSSRSLDCRESGKNGPHVYQDL LLSLGTTNSTLPPPFSLQSGILTLNPVAQGQPILTS LGSNQEEAYVTMSSFYQNQ*SR*SDPKPENPACPW TVLPAGDLPTHDGYLPSNIDDLPSHEAPLADSLE ELEPQ	205
CD8SS-TGFbR2(1-166).TPOR/MPLR(478-582;N-9-7).IL7Ra(316-459).IL12Rb2(775-825) 下划线表示 CD8SS	MALPVTALLLPLALLLHAARPMGRGLLRGLWP LHIVLWTRIASTIPPHVQKSVNNDMIVTDNNGA VKFPQLCKFCDVRFSTCDNQKSCMSNCSITSICE KPQEVCVAVWRKNDENITLETVCHDPKLPYHDF ILEDAASPKCIMKEKKKPGETFFMCSCSSDECN DNIIFSEEYNTSNPDLLLVIFQSDPTRHLVLGLSA VLGLLLLRWQFPAHYRRLRHALWPSLPDLHRVL GQYLRDTAALSPPKATVSDTCEEVEPSLLEILPK SSERTPLPL*LE*ARDEVEGFLQDTFPQQLEESEKQ RLGGDVQSPNCPSEDVVITPESFGRDSSLTCLAG NVSACDAPILSSSRSLDCRESGKNGPHVYQDLL LSLGTTNSTLPPPFSLQSGILTLNPVAQGQPILTSL GSNQEEAYVTMSSFYQNQ*SR*SDPKPENPACPWT VLPAGDLPTHDGYLPSNIDDLPSHEAPLADSLEE LEPQ	206

[0152]

CD8SS-TGFbR2(1-166).TPOR/MPLR(478-582;N-9-8).IL7Ra(316-459).IL12Rb2(775-825) 下划线表示 CD8SS	MALPVTALLLPLALLLHAARPMGRGLLRGLWPLHIVLWTRIASTIPPHVQKSVNNDMIVTDNNGAVKFPQLCKFCDVRFSTCDNQKSCMSNCSITSICEKPQEVCVAVWRKNDENITLETVCHDPKLPYHDFILEDAASPKCIMKEKKKPGETFFMCSCSSDECNDNIIFSEEYNTSNPDLLLVIFQSDPTHLVLGLSAVLGLLLLRWQFPAHYRRLRHALWPSLPDLHRVLGQYLRDTAALSPPKATVSDTCEEVEPSLLEILPKSSERTPLPLLEARDEVEGFLQDTFPQQLEESEKQRLGGDVQSPNCPSEDVVITPESFGRDSSLTCLAGNVSACDAPILSSSRSLDCRESGKNGPHVYQDLLLSLGTTNSTLPPPFSLQSGILTLNPVAQGQPILTSLGSNQEEAYVTMSSFYQNQSRSDPKPENPACPWTVLPAGDLPTHDGYLPSNIDDLPSHEAPLADSLEELEPQ	207
CD8SS-TGFbR2(1-166).TPOR/MPLR(478-582;N-9-9).IL7Ra(316-459).IL12Rb2(775-825) 下划线表示 CD8SS	MALPVTALLLPLALLLHAARPMGRGLLRGLWPLHIVLWTRIASTIPPHVQKSVNNDMIVTDNNGAVKFPQLCKFCDVRFSTCDNQKSCMSNCSITSICEKPQEVCVAVWRKNDENITLETVCHDPKLPYHDFILEDAASPKCIMKEKKKPGETFFMCSCSSDECNDNIIFSEEYNTSNPDLLLVIFQSDPHLVLGLSAVLGLLLLRWQFPAHYRRLRHALWPSLPDLHRVLGQYLRDTAALSPPKATVSDTCEEVEPSLLEILPKSSERTPLPLLEARDEVEGFLQDTFPQQLEESEKQRLGGDVQSPNCPSEDVVITPESFGRDSSLTCLAGNVSACDAPILSSSRSLDCRESGKNGPHVYQDLLLSLGTTNSTLPPPFSLQSGILTLNPVAQGQPILTSLGSNQEEAYVTMSSFYQNQSRSDPKPENPACPWTVLPAGDLPTHDGYLPSNIDDLPSHEAPLADSLEELEPQ	208
CD8SS-TGFbR2(1-166).TPOR/MPLR(478-582;N-9-10).IL7Ra(316-459).IL12Rb2(775-825) 下划线表示 CD8SS	MALPVTALLLPLALLLHAARPMGRGLLRGLWPLHIVLWTRIASTIPPHVQKSVNNDMIVTDNNGAVKFPQLCKFCDVRFSTCDNQKSCMSNCSITSICEKPQEVCVAVWRKNDENITLETVCHDPKLPYHDFILEDAASPKCIMKEKKKPGETFFMCSCSSDECNDNIIFSEEYNTSNPDLLLVIFQSDPHLVLGLSAVLGLLLLRWQFPAHYRRLRHALWPSLPDLHRVLGQYLRDTAALSPPKATVSDTCEEVEPSLLEILPKSSERTPLPLLEARDEVEGFLQDTFPQQLEESEKQRLGGDVQSPNCPSEDVVITPESFGRDSSLTCLAGNVSACDAPILSSSRSLDCRESGKNGPHVYQDLLLSLGTTNSTLPPPFSLQSGILTLNPVAQGQPILTSLGSNQEEAYVTMSSFYQNQSRSDPKPENPACPWTVLPAGDLPTHDGYLPSNIDDLPSHEAPLADSLEELEPQ	209
CD8SS-TGFbR2(1-166).TPOR/MPLR(478-582;N-9-11).IL7Ra(316-459).IL12Rb2(775-825) 下划线表示 CD8SS	MALPVTALLLPLALLLHAARPMGRGLLRGLWPLHIVLWTRIASTIPPHVQKSVNNDMIVTDNNGAVKFPQLCKFCDVRFSTCDNQKSCMSNCSITSICEKPQEVCVAVWRKNDENITLETVCHDPKLPYHDFILEDAASPKCIMKEKKKPGETFFMCSCSSDECN	210

[0153]

	DNIIFSEEYNTSNPDLLLVIFQSHLVLGLSAVLGL LLLRWQFPAHYRRLRHALWPSLPDLHRVLGQY LRDTAALSPPKATVSDTCEEVEPSLLEILPKSSER TPLPL*LE*ARDEVEGFLQDTFPQQLEESEKQRLG GDVQSPNCPSEDVVITPESFGRDSSLTCLAGNVS ACDAPILSSSRSLDCRESGKNGPHVYQDLLLSL GTTNSTLPPPFSLQSGILTLNPVAQGQPILTSLGS NQEEAYVTMSSFYQNQ*SR*SDPKPENPACPWTVL PAGDLPTHDGYLPSNIDDLPSHEAPLADSLEELE PQ	
CD8SS-TGFbR2(1-166).TPOR/MPLR(478-582;N-9-12).IL7Ra(316-459).IL12Rb2(775-825) 下划线表示 CD8SS	MALPVTALLLPLALLLHAARPMGRGLLRGLWP LHIVLWTRIASTIPPHVQKSVNNDMIVTDNNGA VKFPQLCKFCDVRFSTCDNQKSCMSNCSITSICE KPQEVCVAVWRKNDENITLETVCHDPKLPYHDF ILEDAASPKCIMKEKKKPGETFFMCSCSSDECN DNIIFSEEYNTSNPDLLLVIFQHLVLGLSAVLGLL LLRWQFPAHYRRLRHALWPSLPDLHRVLGQYL RDTAALSPPKATVSDTCEEVEPSLLEILPKSSERT PLPL*LE*ARDEVEGFLQDTFPQQLEESEKQRLGG DVQSPNCPSEDVVITPESFGRDSSLTCLAGNVSA CDAPILSSSRSLDCRESGKNGPHVYQDLLLSLGT TNSTLPPPFSLQSGILTLNPVAQGQPILTSLGSNQ EEAYVTMSSFYQNQ*SR*SDPKPENPACPWTVLPA GDLPTHDGYLPSNIDDLPSHEAPLADSLEELEPQ	211
CD8SS-TGFbR2▲N25.TPOR/MPLR(478-582;N-9).IL7Ra(316-459).IL12Rb2(775-825) 下划线表示 CD8SS	MALPVTALLLPLALLLHAARPQLCKFCDVRFST CDNQKSCMSNCSITSICEKPQEVCVAVWRKNDE NITLETVCHDPKLPYHDFILEDAASPKCIMKEKK KPGETFFMCSCSSDECNDNIIFSEEYNTSNPDLLL VIFQSDPTRVETATETHLVLGLSAVLGLLLLRWQ FPAHYRRLRHALWPSLPDLHRVLGQYLRDTAAL SPPKATVSDTCEEVEPSLLEILPKSSERTPLPL*LE* ARDEVEGFLQDTFPQQLEESEKQRLGGDVQSPN CPSEDVVITPESFGRDSSLTCLAGNVSACDAPILS SSRSLDCRESGKNGPHVYQDLLLSLGTTNSTLPP PFSLQSGILTLNPVAQGQPILTSLGSNQEEAYVT MSSFYQNQ*SR*SDPKPENPACPWTVLPAGDLPTH DGYLPSNIDDLPSHEAPLADSLEELEPQ	212
CD8SS-TGFbR2▲N25.TPOR/MPLR(478-582;N+4).IL7Ra(316-459).IL12Rb2(775-825) 下划线表示 CD8SS	MALPVTALLLPLALLLHAARPQLCKFCDVRFST CDNQKSCMSNCSITSICEKPQEVCVAVWRKNDE NITLETVCHDPKLPYHDFILEDAASPKCIMKEKK KPGETFFMCSCSSDECNDNIIFSEEYNTSNPDLLL VIFQSDPTRVETATETAWILVLISLVTALHLVLGL SAVLGLLLLRWQFPAHYRRLRHALWPSLPDLHR VLGQYLRDTAALSPPKATVSDTCEEVEPSLLEIL PKSSERTPLPL*LE*ARDEVEGFLQDTFPQQLEESE KQRLGGDVQSPNCPSEDVVITPESFGRDSSLTCL AGNVSACDAPILSSSRSLDCRESGKNGPHVYQD LLLSLGTTNSTLPPPFSLQSGILTLNPVAQGQPILT SLGSNQEEAYVTMSSFYQNQ*SR*SDPKPENPACP WTVLPAGDLPTHDGYLPSNIDDLPSHEAPLADS	213

[0154]

	LEELEPQ	
CD8SS-TGFbR2▲N25.TPOR/MPLR(478-582;N-9-4).IL7Ra(316-459).IL12Rb2(775-825) 下划线表示 CD8SS	MALPVTALLLPLALLLHAARPQLCKFCDVRFSTCDNQKSCMSNCSITSICEKPQEVCVAVWRKNDENITLETVCHDPKLPYHDFILEDAASPKCIMKEKKKPGETFFMCSCSSDECNDNIIFSEEYNTSNPDLLLVIFQSDPTRVETHLVLGLSAVLGLLLLRWQFPAHYRRLRHALWPSLPDLHRVLGQYLRDTAALSPPKATVSDTCEEVEPSLLEILPKSSERTPLPL*LE*ARDEVEGFLQDTFPQQLEESEKQRLGGDVQSPNCPSEDVVITPESFGRDSSLTCLAGNVSACDAPILSSSRSLDCRESGKNGPHVYQDLLLSLGTTNSTLPPPFSLQSGILTLNPVAQGQPILTSLGSNQEEAYVTMSSFYQNQ*SR*SDPKPENPACPWTVLPAGDLPTHDGYLPSNIDDLPSHEAPLADSLEELEPQ	214
CD8SS-TGFbR2▲N25.TPOR/MPLR(478-582;N-9-9).IL7Ra(316-459).IL12Rb2(775-825) 下划线表示 CD8SS	MALPVTALLLPLALLLHAARPQLCKFCDVRFSTCDNQKSCMSNCSITSICEKPQEVCVAVWRKNDENITLETVCHDPKLPYHDFILEDAASPKCIMKEKKKPGETFFMCSCSSDECNDNIIFSEEYNTSNPDLLLVIFQSDPHLVLGLSAVLGLLLLRWQFPAHYRRLRHALWPSLPDLHRVLGQYLRDTAALSPPKATVSDTCEEVEPSLLEILPKSSERTPLPL*LE*ARDEVEGFLQDTFPQQLEESEKQRLGGDVQSPNCPSEDVVITPESFGRDSSLTCLAGNVSACDAPILSSSRSLDCRESGKNGPHVYQDLLLSLGTTNSTLPPPFSLQSGILTLNPVAQGQPILTSLGSNQEEAYVTMSSFYQNQ*SR*SDPKPENPACPWTVLPAGDLPTHDGYLPSNIDDLPSHEAPLADSLEELEPQ	215
CD8SS-TGFbR2▲N25.TPOR/MPLR(478-582;N-9-10).IL7Ra(316-459).IL12Rb2(775-825) 下划线表示 CD8SS	MALPVTALLLPLALLLHAARPQLCKFCDVRFSTCDNQKSCMSNCSITSICEKPQEVCVAVWRKNDENITLETVCHDPKLPYHDFILEDAASPKCIMKEKKKPGETFFMCSCSSDECNDNIIFSEEYNTSNPDLLLVIFQSDPHLVLGLSAVLGLLLLRWQFPAHYRRLRHALWPSLPDLHRVLGQYLRDTAALSPPKATVSDTCEEVEPSLLEILPKSSERTPLPL*LE*ARDEVEGFLQDTFPQQLEESEKQRLGGDVQSPNCPSEDVVITPESFGRDSSLTCLAGNVSACDAPILSSSRSLDCRESGKNGPHVYQDLLLSLGTTNSTLPPPFSLQSGILTLNPVAQGQPILTSLGSNQEEAYVTMSSFYQNQ*SR*SDPKPENPACPWTVLPAGDLPTHDGYLPSNIDDLPSHEAPLADSLEELEPQ	216
CD8SS-TPOR/MPLR(478-582;H499L,S505N,W515K,K553R,K573R).IL2Rb(339-379,393-433,518-551) 下划线表示 CD8SS	MALPVTALLLPLALLLHAARPSDPTRVETATETAWISLVTAL**L**LVLGL**N**AVLGLLLLR**K**QFPAHYRRLRHALWPSLPDLHRVLGQYLRDTAALSPP**R**ATVSDTCEEVEPSLLEILP**R**SSERTPLPL*LE*QQDKVPEPASLSSNHSLTSCFTNQGYFFFHLPDALEIEACQDEGVAGAPTGSSPQPLQPLSGEDDAYCTFPSRDDLLLFSPSGQGEFRALNARLPLNTDAYLSLQELQGQDPTHLV	272
CD8SS-TPOR/MPLR(478-582;S505N,W515K,K5	MALPVTALLLPLALLLHAARPSDPTRVETATETAWISLVTALHLVLGL**N**AVLGLLLLR**K**QFPAHYRR	273

[0155]

53R,K573R).IL2Rb(393-433,518-551) 下划线表示 CD8SS	LRHALWPSLPDLHRVLGQYLRDTAALSPP**R**ATV SDTCEEVEPSLLEILP**R**SSERTPLPL*LE*DEGVAGA PTGSSPQPLQPLSGEDDAYCTFPSRDDLLLFSPS GQGEFRALNARLPLNTDAYLSLQELQGQDPTHL V	
CD8SS-HAPD1.TPOR/MPLR(478-582;H499L,S505N,W515K,K553R,K573R).IL2Rb(339-379,393-433,518-551) 下划线表示 CD8SS 斜体标记高亲和力 PD-1 胞外域	MALPVTALLLPLALLLHAARP*PGWFLDSPDRPW* *NPPTFSPALLVVTEGDNATFTCSFSNTSESFHVIWH* *RESPSGQTDTLAAFPEDRSQPGQDCRFRVTQLPN* *GRDFHMSVVRARRNDSGTYVCGVISLAPKIQIKESL* *RAELRVTERRAEVPTAHPSPSPRPAGQFQTLV*SDPT RVETATETAWISLVTAL**L**LVLGL**N**AVLGLLLLR**K** QFPAHYRRLRHALWPSLPDLHRVLGQYLRDTA ALSPP**R**ATVSDTCEEVEPSLLEILP**R**SSERTPLPL *LE*QQDKVPEPASLSSNHSLTSCFTNQGYFFFHLP DALEIEACQDEGVAGAPTGSSPQPLQPLSGEDD AYCTFPSRDDLLLFSPSGQGEFRALNARLPLNTD AYLSLQELQGQDPTHLV	274
CD8SS-HAPD1.TPOR/MPLR(478-582;S505N,W515K,K553R,K573R).IL2Rb(393-433,518-551) 下划线表示 CD8SSItalicized 标记高亲和力 PD-1 胞外域	MALPVTALLLPLALLLHAARP*PGWFLDSPDRPW* *NPPTFSPALLVVTEGDNATFTCSFSNTSESFHVIWH* *RESPSGQTDTLAAFPEDRSQPGQDCRFRVTQLPN* *GRDFHMSVVRARRNDSGTYVCGVISLAPKIQIKESL* *RAELRVTERRAEVPTAHPSPSPRPAGQFQTLV*SDPT RVETATETAWISLVTALHLVLGL**N**AVLGLLLLR**K** QFPAHYRRLRHALWPSLPDLHRVLGQYLRDTA ALSPP**R**ATVSDTCEEVEPSLLEILP**R**SSERTPLPL *LE*DEGVAGAPTGSSPQPLQPLSGEDDAYCTFPSR DDLLLFSPSGQGEFRALNARLPLNTDAYLSLQE LQGQDPTHLV	275

[0156] *下划线LE和SR表示示例性肽连接子。

[0157] F.嵌合细胞因子受体的表达

[0158] 本文提供了编码本文提供的嵌合细胞因子受体中的任何一个的多核苷酸。同样，本文提供了包括此类多核苷酸的表达载体。在一些实施例中，载体是病毒载体。在一些实施例中，载体不是病毒载体。

[0159] 在一些实施例中，载体包括编码嵌合细胞因子受体的多核苷酸和表达嵌合抗原受体(CAR)的多核苷酸。

[0160] 在一些实施例中，嵌合细胞因子受体和CAR的表达被表达为由连接子分开的单个多肽链。图2A、3、4A、5A、6A、8A和11A示出了可用于共表达本公开的嵌合细胞因子受体和CAR的载体的示意图。一个或多个STAT募集结构域可以串联连接，以模拟来自一个或多个细胞因子的信号传导。

[0161] II.具有CAR的免疫细胞

[0162] 本文提供了包括编码本公开的嵌合抗原受体和嵌合细胞因子受体的多核苷酸的工程化免疫细胞；并且本文提供了表达本公开的嵌合抗原受体(CAR-I细胞)和嵌合细胞因子受体的工程化免疫细胞。免疫细胞的实例包含T细胞，例如，α/βT细胞和γ/δT细胞、B细胞、自然杀伤(NK)细胞、自然杀伤T(NKT)细胞、不变NKT细胞、肥大细胞、髓源性吞噬细胞、树突状细胞、杀伤树突状细胞、巨噬细胞和单核细胞。免疫细胞还指源自，例如但不限于，干细胞的细胞。干细胞可以是成体干细胞、非人胚胎干细胞，更具体地非人干细胞、脐带血干细胞、祖细胞、骨髓干细胞、诱导多能干细胞、全能干细胞或造血干细胞。

[0163] 因此，在一些实施例中，本文提供了包括本公开的嵌合细胞因子受体的CAR-T细胞。

[0164] 在一些实施例中，CAR可以包括细胞外配体结合结构域(例如，单链可变片段(scFv))、跨膜结构域和细胞内信号传导结构域。在一些实施例中，细胞外配体结合结构域、跨膜结构域和细胞内信号传导结构域在一个多肽中，即在单链中。本文还提供了多链CAR和多肽。在一些实施例中，多链CAR包括：第一多肽，所述第一多肽包括跨膜结构域和至少一个细胞外配体结合结构域；以及第二多肽，所述第二多肽包括跨膜结构域和至少一个细胞内信号传导结构域，其中所述多肽组装在一起以形成多链CAR。

[0165] CAR的细胞外配体结合结构域与所关注靶标特异性结合。所关注靶标可以是任何所关注分子，例如，包含但不限于表8中呈现的靶标中的任何一个或多个靶标。

[0166] 表8：所关注靶标的列表

[0167]

BCMA
EGFRvIII
Flt-3
WT-1
CD20
CD23
CD30
CD38
CD70
CD33
CD133
MHC- WT1
TSPAN10
MHC-PRAME
Liv1
ADAM10

[0168]

CHRNA2
LeY
NKG2D
CS1
CD44v6
ROR1
CD19
密封蛋白-18.2（密封蛋白-18A2 或密封蛋白 18 同种型 2）
DLL3（δ样蛋白 3、果蝇 δ 同源物 3、δ3）
Muc17（粘蛋白 17、Muc3、Muc3）
FAP α（成纤维细胞激活蛋白 α）
Ly6G6D（淋巴细胞抗原 6 复合物基因座蛋白 G6d）
c6orf23
G6D
MEGT1
NG25)
RNF43（E3 泛素蛋白连接酶 RNF43、环指蛋白 43）
ErbB2（HER2/neu）
癌胚抗原（CEA）
上皮细胞粘附分子（EpCAM）
表皮生长因子受体（EGFR）
CD40
双唾液酸神经节苷脂 GD2
GD3
C 型凝集素样分子 1（CLL-1）
导管上皮粘蛋白
gp36
TAG-72
鞘糖脂
神经胶质瘤相关抗原
β 人绒毛膜促性腺激素
甲胎蛋白（AFP）
凝集素反应性 AFP
甲状腺球蛋白
RAGE-1
MN-CA IX
人端粒酶逆转录酶
RU1
RU2 (AS)
肠羧基酯酶
mut hsp70-2
M-CSF
前列腺酶
前列腺酶特异性抗原（PSA）
PAP

[0169]

NY-ESO-1
LAGA-la
p53
前列腺素
PSMA
存活蛋白和端粒酶
前列腺癌肿瘤抗原 1（PCTA-1）
MAGE
ELF2M
中性粒细胞弹性蛋白酶
肝配蛋白 B2
CD22
胰岛素生长因子（IGF1）-1
IGF-II
IGFI 受体
间皮素
呈现肿瘤特异性肽表位的主要组织相容性复合物（MHC）分子
5T4
O 1
Nkp30
肿瘤基质抗原
纤连蛋白的额外结构域 A（EDA）和额外结构域 B（EDB）以及腱生蛋白-C 的 AI 结构域（TnC AI）和成纤维细胞相关蛋白（fap）
LRP6
黑素瘤相关硫酸软骨素蛋白多糖（MCSP）
MARTI
MUC1
LMP2
独特型
NY-ESO-1
Ras 突变体
gp100
蛋白酶 3
bcr-abl
酪氨酸酶
hTERT
EphA2
ML-TAP
ERG
NA17
PAX3
ALK
雄激素受体
谱系特异性或组织特异性抗原，如 CD3
CD4
CD8

[0170]

CD24
CD25
CD34
CD79
CD116
CD117
CD135
CD123
CD138
CTLA-4
B7-1 (CD80)
B7-2 (CD86)
内皮糖蛋白
主要组织相容性复合物（MHC）分子
MUC16
PSCA
Trop2
CD171 (L1CAM)
CA9
STEAP1
VEGFR2

[0171] 在一些实施例中,CAR的细胞外配体结合结构域包括scFv,所述scFv包括通过柔性连接子连接的靶抗原特异性单克隆抗体的轻链可变(VL)区和重链可变(VH)区。单链可变区片段是通过使用短连接肽(Bird等人,《科学(Science)》242:423-426,1988)(例如,含有甘氨酸-丝氨酸的连接子)连接轻链和/或重链可变区来制备的。通常,连接子可以是短的柔性多肽并且通常包含约20个或更少的氨基酸残基。连接子可以进而被修饰以实现另外的功能,如附着药物或附着在固体支持物上。单链变体可以通过重组或合成产生。对于scFv的合成生产,可以使用自动合成仪。对于scFv的重组产生,可以将含有编码scFv的多核苷酸的合适质粒引入到合适的宿主细胞(如酵母、植物、昆虫或哺乳动物细胞等真核细胞或如大肠杆菌等原核细胞)中。编码所关注scFv的多核苷酸可以通过如多核苷酸的连接等常规操作来制备。可以使用本领域已知的标准蛋白质纯化技术分离所得scFv。

[0172] 根据本发明的CAR的细胞内信号传导结构域负责在细胞外配体结合结构域与靶标结合之后产生细胞内信号传导,从而导致免疫细胞的激活和免疫应答(信号1和/或2)。细胞内信号传导结构域能够激活表达CAR的免疫细胞的至少一种正常效应子功能。例如,T细胞的效应子功能可以是细胞溶解活性或辅助活性(包含细胞因子的分泌)。

[0173] 在一些实施例中,用于CAR的细胞内信号传导结构域可以是例如但不限于T细胞受体和共受体的细胞质序列,所述受体在抗原受体结合后协同作用以启动信号转导,以及这些序列的任何衍生物或变体以及具有相同功能能力的任何合成序列。细胞内信号传导结构域包括两种不同类别的细胞质信号传导序列:启动抗原依赖性初级激活的细胞质信号传导序列,以及以抗原非依赖性方式起作用以提供次级或共刺激信号的细胞质信号传导序列。初级细胞质信号传导序列可以包括被称为ITAM的基于免疫受体酪氨酸的激活基序的信号传导基序。ITAM是在充当syk/zap70类酪氨酸激酶的结合位点的各种受体的胞质内尾区发现的明确定义的信号传导基序。本发明中使用的ITAM的实例可以包含作为非限制性实例的源自TCRζ、FcRγ、FcRβ、FcRε、CD3γ、CD3δ、CD3ε、CD5、CD22、CD79a、CD79b和CD66d的那些。在

一些实施例中，CAR的细胞内信号传导结构域可以包括CD3ζ信号传导结构域。在一些实施例中，本发明的CAR的细胞内信号传导结构域包括共刺激分子的结构域。

[0174] 在一些实施例中，本发明的CAR的细胞内信号传导结构域包括选自由41BB(GenBank:AAA53133.)和CD28(NP_006130.1)的片段组成的组的共刺激分子的一部分。

[0175] CAR在细胞的表面膜上表达。因此，CAR包括跨膜结构域。本文所公开的CAR的合适跨膜结构域具有以下能力:(a)在细胞表面表达，优选地在免疫细胞表面表达，所述免疫细胞如例如但不限于淋巴细胞或自然杀伤(NK)细胞;以及(b)与配体结合结构域和细胞内信号传导结构域相互作用，以指导免疫细胞对预定靶细胞的细胞应答。跨膜结构域可以源自天然的或合成的来源。跨膜结构域可以源自任何膜结合蛋白或跨膜蛋白。作为非限制性实例，跨膜多肽可以是T细胞受体的亚基，如α、β、γ或δ;构成CD3复合物的多肽;IL-2受体p55(a链)、p75(β链)或γ链;Fc受体，具体地Fcγ受体III，的亚基链;或CD蛋白。可替代地，跨膜结构域可以是合成的并且可以主要包括疏水残基，如亮氨酸和缬氨酸。在一些实施例中，所述跨膜结构域源自人类CD8α链(例如，NP_001139345.1)。跨膜结构域可以进一步包括位于细胞外配体结合结构域和所述跨膜结构域之间的茎结构域。茎结构域可以包括多达300个氨基酸，优选地10到100个氨基酸，并且最优选地25到50个氨基酸。茎区域可以源自天然存在的分子的全部或部分，如源自CD8、CD4或CD28的细胞外区域的全部或部分，或源自抗体恒定区的全部或部分。可替代地，茎结构域可以是对应于天然存在的茎序列的合成序列，或者可以是完全合成的茎序列。在一些实施例中，所述茎结构域是人CD8α链的一部分(例如，NP_001139345.1)。在另一个特定的实施例中，所述跨膜和铰链结构域包括人CD8α链的一部分。在一些实施例中，本文所公开的CAR可以包括与BCMA、CD8α人铰链特异性结合的细胞外配体结合结构域以及跨膜结构域、CD3ζ信号传导结构域和4-1BB信号传导结构域。

[0176] 在一些实施例中，CAR可以作为转基因通过质粒载体被引入到免疫细胞中。在一些实施例中，质粒载体还可以含有，例如，提供用于鉴定和/或选择接受载体的细胞的选择标志物。

[0177] 表7提供了可以用于本文所公开的CAR中的CAR组分的示例性序列。

[0178] 表7:示例性序列

[0179]

结构域	氨基酸序列	SEQ ID NO:
V5 表位标签	KPIPNPLLGLDST	152
2173 scFv	EIQLVQSGAEVKKPGESLRISCKGSGFNIEDYYIH WVRQMPGKGLEWMGRIDPENDETKYGPIFQGHV TISADTSINTVYLQWSSLKASDTAMYYCAFRGGV YWGQGTTVTVSSGGGGSGGGGSGGGGSGGGGSD VVMTQSPDSLAVSLGERATINCKSSQSLLDSDGKT YLNWLQQKPGQPPKRLISLVSKLDSGVPDRFSGSG SGTDFTLTISSLQAEDVAVYYCWQGTHFPGTFGGG TKVEIK	153
CD8 铰链和跨膜	TTTPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVH TRGLDFACDIYIWAPLAGTCGVLLLSLVITLYC	154
4-1BB 细胞内信号传导	KRGRKKLLYIFKQPFMRPVQTTQEEDGCSCRFPEE EEGGCEL	155
CD3z 细胞内信号传导	RVKFSRSADAPAYQQGQNQLYNELNLGRREEYDV LDKRRGRDPEMGGKPRRKNPQEGLYNELQKDKM AEAYSEIGMKGERRRGKGHDGLYQGLSTATKDTY DALHMQALPPR	156
BFP（蓝色荧光蛋白）	MSELIKENMHMKLYMEGTVDNHHFKCTSEGEGK PYEGTQTMRIKVVEGGPLPFAFDILATSFLYGSKTF INHTQGIPDFFKQSFPEGFTWERVTTYEDGGVLTA TQDTSLQDGCLIYNVKIRGVNFTSNGPVMQKKTL GWEAFTETLYPADGGLEGRNDMALKLVGGSHLIA NIKTTYRSKKPAKNLKMPGVYYVDYRLERIKEAN NETYVEQHEVAVARYCDLPSKLGHKLN	157
P2A	GSGATNFSLLKQAGDVEENPGP	158

[0180] 在一些实施例中，本公开的CAR免疫细胞（例如，CAR-T细胞）包括编码自杀多肽，例如RQR8的多核苷酸。参见，例如WO2013153391A，所述文献特此通过引用整体并入本文。在一些实施例中，自杀多肽在细胞表面上表达。在一些实施例中，自杀多肽包含在CAR构建体中。在一些实施例中，自杀多肽不是CAR构建体的一部分。

[0181] 在一些实施例中，本文所公开的CAR中的任何一个的细胞外结构域可以包括对单克隆抗体具有特异性（被单克隆抗体特异性识别）的一个或多个表位。这些表位在本文中也被称为mAb特异性表位。在国际专利公开第WO 2016/120216号中公开了示例性mAb特异性表位，所述国际专利以其整体并入本文。在这些实施例中，CAR的细胞外结构域包括与所关注靶标特异性结合的抗原结合结构域和与一个或多个单克隆抗体（mAb）结合的一个或多个表位。包括mAb特异性表位的CAR可以是单链或多链的。

[0182] 在本文所述的CAR的细胞外结构域中包含对单克隆抗体具有特异性的表位允许分选和耗竭表达CAR的工程化免疫细胞。在一些实施例中，允许耗竭在有害影响的情况下，例如在施用于受试者时提供安全开关。

[0183] 本文还提供了制备用于免疫疗法的免疫细胞的方法。在一些实施例中，所述方法包括将嵌合细胞因子受体和CAR引入到免疫细胞中以及使细胞扩增。在一些实施例中，本发明涉及一种工程化免疫细胞的方法，所述方法包括：提供细胞；以及表达嵌合细胞因子受体；以及在细胞表面处表达至少一个CAR。在一些实施例中，所述方法包括：用编码嵌合细胞因子受体的至少一个多核苷酸和编码CAR的至少一个多核苷酸转染细胞；以及在细胞中表达多核苷酸。在一些实施例中，所述方法包括：用编码嵌合细胞因子受体的至少一个多核苷酸、编码CAR的至少一个多核苷酸转染细胞；以及在细胞中表达多核苷酸。在一些实施例中，

嵌合细胞因子受体和CAR存在于一个多核苷酸上。

[0184] 在一些实施例中，编码嵌合细胞因子受体和CAR的所述一个或多个多核苷酸存在于一种或多种表达载体中，以在细胞中稳定表达。在一些实施例中，多核苷酸存在于病毒载体中，以在细胞中稳定表达。在一些实施例中，所述一个或多个多核苷酸通过随机整合插入到细胞基因组中，并且在其它实施例中，所述一个或多个多核苷酸通过位点特异性整合插入到细胞基因组的特定位置中。在一些实施例中，病毒载体可以是例如慢病毒载体或腺病毒载体。在一些实施例中，所述一个或多个多核苷酸存在于非病毒载体中。

[0185] 在一些实施例中，编码根据本公开的多肽的多核苷酸可以是例如通过电穿孔被直接引入到细胞中的mRNA。在一些实施例中，如PulseAgile等CytoPulse电穿孔技术可以用于瞬时渗透活细胞以将材料递送到细胞中(例如，US 6,078,490；PCT/US2011/000827；和PCT/US2004/005237)。可以修改参数以确定高转染效率和最低死亡率的条件。

[0186] 本文还提供了转染免疫细胞，例如T细胞的方法。在一些实施例中，所述方法包括：使T细胞与RNA接触；以及向T细胞施加敏捷脉冲序列(agile pulse sequence)。在一些实施例中，包括使免疫细胞与RNA接触以及向细胞施加敏捷脉冲序列的转染免疫细胞(例如，T细胞)的方法。

[0187] 在一些实施例中，所述方法可以进一步包括以下步骤：通过使表达例如但不限于TCR的组分、免疫抑制剂的靶标、HLA基因和/或免疫检查点蛋白(如例如PDCD1或CTLA-4)的至少一个基因灭活来对细胞进行基因修饰。使基因灭活旨在使所关注基因不以功能性蛋白质形式表达。在一些实施例中，待灭活的基因选自由以下组成的组：例如但不限于，TCRα、TCRβ、CD52、GR、脱氧胞苷激酶(DCK)、TGF-B和CTLA-4。在一些实施例中，所述方法包括通过将能够通过选择性DNA切割选择性灭活基因的稀切核酸内切酶引入细胞来使一个或多个基因灭活。在一些实施例中，稀切核酸内切酶可以是例如转录激活因子样效应物核酸酶(TALE-核酸酶)或基于CRISPR的核酸内切酶(例如，Cas-9或Cas12a)。

[0188] 在另一方面，对细胞进行基因修饰的步骤可以包括：通过使表达免疫抑制剂的靶标的至少一个基因灭活来修饰免疫细胞(例如，T细胞)；以及任选地在存在免疫抑制剂的情况下，使细胞扩增。

[0189] 在一些实施例中，相对于不表达嵌合细胞因子受体的工程化免疫细胞，本文所提供的工程化免疫细胞(例如，T细胞)在与结合到嵌合细胞因子受体的结合结构域的TGF-β配体或抗TGF-β受体抗体接触时表现出改善的细胞毒性、增加的扩增和/或增加的记忆表型标志物水平。

[0190] 在一些实施例中，相对于不表达嵌合细胞因子受体的工程化免疫细胞，本文所提供的工程化免疫细胞(例如，T细胞)在与结合到嵌合细胞因子受体的结合结构域的TGF-β配体或抗TGF-β受体抗体接触时表现出(i)增加的体内持久性、(ii)增加的STAT激活、(iii)增加的细胞毒性、(iv)增加的记忆表型标志物水平、(v)增加的扩增(增殖)或这些功能特征的组合。在一些实施例中，本文所述的一个或多个功能特征的改善是剂量依赖性的，即，包括嵌合细胞因子受体的免疫细胞的功能活性在与增加剂量的PD-L1/PD-L2/TGF-β或相应受体的抗体接触时增加。在一些实施例中，被包括所公开的一个或多个嵌合细胞因子受体的工程化免疫细胞激活的STAT是STAT1、STAT2、STAT3、STAT4、STAT5、STAT6或其组合。在一个实施例中，由包括本公开的嵌合细胞因子受体的免疫细胞增加或维持的记忆表型标志物包含

干细胞记忆(Tscm)标志物和中央记忆(Tcm)标志物。

[0191] 在一些实施例中,与不表达嵌合细胞因子受体的免疫细胞相比,包括本文所提供的嵌合细胞因子受体的工程化免疫细胞所表现出的一个或多个功能特征的改善是至少约2倍、2.5倍、3倍、3.5倍、4倍、4.5倍、5倍、6倍、7倍、8倍、9倍、10倍、15倍、20倍、25倍、30倍、40倍、50倍、60倍、70倍、80倍、90倍、100倍、125倍、150倍、200倍、250倍、300倍、350倍、400倍、450倍或甚至约10-500倍,包含其间的值和范围。

[0192] 在一些实施例中,与不表达嵌合细胞因子受体的工程化免疫细胞相比,包括本文所提供的嵌合细胞因子受体的工程化免疫细胞所表现出的一个或多个功能特征的改善是至少约10%、20%、25%、30%、35%、40%、45%、50%、55%、60%、70%、75%、80%、90%、100%、125%、150%、200%、250%、300%、350%、400%或甚至约80%-500%,包含其间的值和范围。

[0193] III.治疗方法

[0194] 本文提供了包括具有本公开的嵌合细胞因子受体和CAR的细胞的药物组合物。

[0195] 通过上述方法获得的具有工程化嵌合细胞因子受体和具有CAR的免疫细胞(例如,T细胞)或源自此类工程化免疫细胞的细胞系可以用作药物。在一些实施例中,此类药物可以用于治疗病症,例如病毒性疾病、细菌性疾病、癌症、炎性疾病、免疫疾病或衰老相关疾病。在一些实施例中,癌症是实体癌。在一些实施例中,癌症是液体癌。癌症可以选自由以下组成的组:胃癌(gastric cancer)、肉瘤、淋巴瘤、白血病、头颈癌、胸腺癌、上皮癌、唾液癌、肝癌、胃癌(stomach cancer)、甲状腺癌、肺癌、小细胞肺癌、卵巢癌、乳腺癌、前列腺癌、食管癌、胰腺癌、神经胶质瘤、成胶质细胞瘤、白血病、多发性骨髓瘤、肾细胞癌、膀胱癌、宫颈癌、绒毛膜癌、结肠癌、口腔癌、皮肤癌和黑素瘤。在一些实施例中,受试者是先前经治疗的患有局部晚期或转移性黑素瘤、鳞状细胞头颈癌(SCHNC)、卵巢癌、肉瘤或复发性或难治性经典霍奇金氏淋巴瘤(classic Hodgkin's Lymphoma,cHL)的成年受试者。

[0196] 在一些实施例中,工程化免疫细胞或源自工程化免疫细胞的细胞系可以用于制造用于治疗有需要的受试者的病症的药物。在一些实施例中,病症可以是例如癌症、自身免疫病症或感染。

[0197] 本文还提供了用于治疗需要这种治疗的受试者的方法。

[0198] 如本文所使用的,术语"受试者"是指任何脊椎动物,所述任何脊椎动物包含但不限于人和其它灵长类动物(例如,黑猩猩、食蟹猴和其它猿和猴物种)、农场动物(例如,牛、绵羊、猪、山羊和马)、家养哺乳动物(例如,狗和猫)、实验室动物(例如,兔、啮齿动物,如小鼠、大鼠和豚鼠)和鸟类(例如,家禽、野禽和猎禽,如鸡、火鸡以及其它鸡类鸟类、鸭、鹅等)。在一些实施例中,受试者是哺乳动物。在示例性实施例中,受试者是人。

[0199] 在一些实施例中,所述方法包括向有需要的受试者提供具有本文所述的嵌合细胞因子受体和CAR的本公开的免疫细胞。

[0200] 在一些实施例中,本发明的具有嵌合细胞因子受体和CAR的T细胞可以经历强大的体内T细胞扩增并且可以持续延长的时间量。

[0201] 本发明的治疗方法可以是改善、治愈或预防。本发明的方法可以是自体免疫疗法的一部分或同种异体免疫疗法治疗的一部分。

[0202] 在另一方面,本发明提供了一种抑制患有肿瘤的受试者的肿瘤生长或进展的方

法,所述方法包括向所述受试者施用有效量的如本文所述的表达嵌合细胞因子受体和表达CAR的免疫细胞。在另一方面,本发明提供了一种抑制或预防受试者的癌细胞的转移的方法,所述方法包括包括向有需要的受试者施用有效量的如本文所述的工程化免疫细胞。在另一方面,本发明提供了一种诱导患有肿瘤的受试者的肿瘤消退的方法,所述方法包括向所述受试者施用有效量的如本文所述的工程化免疫细胞。在一些实施例中,向受试者进一步施用抗TGF-βR抗体,具体地抗TGF-βR2抗体。

[0203] 在一些实施例中,本文中的工程化T细胞可以肠胃外施用于受试者。在一些实施例中,本文所公开的工程化T细胞可以静脉内施用于受试者。

[0204] 还提供了本文所提供的工程化T细胞中的任何工程化T细胞在制备用于治疗癌症或用于抑制有需要的受试者的肿瘤生长或进展的药物中的用途。

[0205] 在一些实施例中,治疗可以施用于经历免疫抑制性治疗的受试者。实际上,本发明优选地依赖于由于编码此类免疫抑制剂的受体的基因失活而对至少一种免疫抑制剂产生抗性的细胞或细胞群。在这方面,免疫抑制性治疗应该有助于在受试者体内选择和扩增根据本发明的T细胞。根据本发明的细胞或细胞群的施用可以以任何方便的方式进行,所述方式包含气溶胶吸入、注射、摄取、输血、植入或移植。可以将本文所述的组合物皮下、皮内、瘤内、结内、髓内、肌内、通过静脉内或淋巴管内注射或腹膜内施用于受试者。具有本公开的嵌合细胞因子受体和/或CAR或其药物组合物的细胞可以通过以下施用途径中的一个或多个施用途径进行施用:静脉内、眼内、玻璃体内、肌内、皮下、局部、口服、透皮、腹膜内、眶内、通过植入、通过吸入、鞘内、心室内、经由耳或鼻内。

[0206] 在一些实施例中,细胞或细胞群(具有本公开的嵌合细胞因子受体和CAR的细胞或细胞群)的施用可以包括施用,例如,每kg体重约10^4到约10^9个细胞,包含这些范围内的细胞数的所有整数值。在一些实施例中,细胞或细胞群的施用可以包括施用约每kg体重10^4到10^5个细胞、每kg体重10^5到10^6个细胞、每kg体重10^6到10^7个细胞、每kg体重10^7到10^8个细胞或每kg体重10^8到10^9个细胞。细胞或细胞群可以按一个或多个剂量施用。在一些实施例中,所述有效量的细胞可以作为单剂量施用。在一些实施例中,所述有效量的细胞可以在一段时间内作为多于一个剂量施用。施用时间在主治医师的判断范围内并且取决于受试者的临床状况。细胞或细胞群可以从任何来源获得,如血库或供体。虽然个体需求不同,但对于特定疾病或病状的给定细胞类型的有效量的最佳范围的确定在本领域的技术范围内。有效量意指提供治疗或预防益处的量。所施用的剂量将取决于接受者的年龄、健康状况和体重、同期治疗(如果有的话)的种类、治疗频率以及所期望的效果的性质。在一些实施例中,肠胃外施用有效量的细胞或包括那些细胞的组合物。在一些实施例中,施用可以是静脉内施用。在一些实施例中,施用可以通过注射到肿瘤内直接进行。

[0207] 所述方法可以进一步包括在施用具有本文所提供的CAR和嵌合细胞因子受体的工程化免疫细胞之前向受试者施用一种或多种药剂。在某些实施例中,药剂是淋巴细胞清除(预调节)方案。例如,淋巴细胞清除需要这种疗法的受试者的方法包括向所述受试者施用指定的有益剂量的环磷酰胺(在200mg/m^2/天与2000mg/m^2/天之间、约100mg/m^2/天与约2000mg/m^2/天;例如,约100mg/m^2/天、约200mg/m^2/天、约300mg/m^2/天、约400mg/m^2/天、约500mg/m^2/天、约600mg/m^2/天、约700mg/m^2/天、约800mg/m^2/天、约900mg/m^2/天、约1000mg/m^2/天、约1500mg/m^2/天或约2000mg/m^2/天);以及指定剂量的氟达拉滨(在20mg/m^2/天与

900mg/m^2/天之间、在约10mg/m^2/天与约900mg/m^2/天之间;例如,约10mg/m^2/天、约20mg/m^2/天、约30mg/m^2/天、约40mg/m^2/天、约40mg/m^2/天、约50mg/m^2/天、约60mg/m^2/天、约70mg/m^2/天、约80mg/m^2/天、约90mg/m^2/天、约100mg/m^2/天、约500mg/m^2/天或约900mg/m^2/天)。示例性给药方案涉及治疗受试者,其包括:在向患者施用治疗有效量的工程化免疫细胞之前三天,组合地或在施用约30mg/m^2/天的氟达拉滨之前或之后,每天向患者施用约300mg/m^2/天的环磷酰胺。

[0208] 在一些实施例中,特别是在本文所提供的工程化细胞已被基因编辑以消除或最小化CD52的表面表达的情况下,淋巴细胞清除进一步包括施用抗CD52抗体,如阿仑单抗。在一些实施例中,以约1-20毫克/天(例如,约13毫克/天)的剂量IV施用CD52抗体,持续1天、2天、3天或更多天。抗体可以与淋巴细胞清除方案的其它要素(例如,环磷酰胺和/或氟达拉滨)组合施用、在施用所述其它要素之前或之后施用。

[0209] 在某些实施例中,包括本文所公开的表达CAR的免疫效应细胞的组合物可以与任何数量的化学治疗剂联合施用。

[0210] IV.试剂盒和制品

[0211] 本公开提供了包括本文所述的嵌合细胞因子受体和具有嵌合细胞因子受体的细胞中的任何一种或多种,及其药物组合物的试剂盒。本公开还提供了包括本文所述的嵌合细胞因子受体和具有嵌合细胞因子受体的CAR-I细胞中的任何一种或多种、其药物组合物和本文所述的试剂盒的制品。

[0212] 以下实例被包含用于说明性目的,并且不旨在限制本公开的范围。

[0213] 贯穿本公开引用的所有专利和非专利文件出于所有目的通过引用整体并入本文。

[0214] 实例

[0215] 实例1:具有TGFβR1或TGFβR2显性负性截短体的嵌合细胞因子受体-CAR构建体的构建和测试

[0216] 图1示出了本公开的诱导型嵌合细胞因子受体的示意图。为了将同时的TGF-β结合与细胞因子信号传导偶联,构建由以下模块构成的嵌合细胞因子受体:(i)结合结构域,所述结合结构域包括TGF-β受体的细胞外部分或TGF-β抗原结合结构域;(ii)跨膜结构域,所述跨膜结构域具有细胞内部分,所述细胞内部分具有JAK2激活结构域;以及(iii)STAT募集结构域,所述STAT募集结构域包括来自细胞因子受体尾区(细胞尾)的Stat募集(Stat激活)结构域。如图1中作为实例示出的,结合结构域包括TGFβR2的细胞外结构域。

[0217] 使用HEK293T细胞报告基因测定,通过使用嵌合细胞因子受体中和TGF-β信号传导或激活STAT应答来测试细胞因子信号传导的可诱导性和量值,所述可诱导性和量值可以用作细胞因子ICD激活和细胞因子信号传导的替代测量。简言之,将20,000个HEK293T细胞铺板到聚-L-赖氨酸-包被的96孔平底板的每个孔中,并且在37℃下用5%CO_2培养过夜。将嵌合细胞因子受体-CAR构建体(2.5ng)、驱动萤火虫荧光素酶的TGF-β或STAT应答元件(100ng;普洛麦格(Promega))以及海肾荧光素酶对照报告基因载体(1ng;普洛麦格)在Opti-MEM(Gibco)(“DNA混合物”)中混合到5μl的最终体积。

[0218] 用BFP-EGFRvIII CAR构建体转染细胞,其中BFP基因代替嵌合细胞因子受体作为阴性对照。还构建TGFβR2的显性负性截短体(“TGFβR2 DN”)和TGFβ1的显性负性截短体(“TGFβR1 DN”)作为另外的对照,以检查在不存在细胞内细胞因子信号的情况下的显性负

效应(dominant negative effect)。在将DNA混合物与预混合的0.3μlLipofectamine 2000(英杰公司(Invitrogen))和5μl Opti-MEM在室温下温育20分钟后,将总体积为10μl的混合物添加到含有HEK293T细胞的每个孔中。在转染后一天,将可商购获得的TGF-β1配体(百进公司(BioLegend),在下文实例1-4中称为"TGF-β")添加到培养物中进行刺激至各种最终浓度。在刺激20-24小时后,使用双Glo荧光素酶测定系统(普洛麦格)评估TGF-β或STAT5报告基因活性。将TGF-β或STAT5报告基因活性的诱导倍数归一化为仅用报告基因载体转染并且不进行处理的HEK293T细胞的诱导倍数。

[0219] 图2A示出了用于共表达TGFβR1或TGFβR2嵌合细胞因子受体与第2代EGFRvIII CAR的显性负性截短体的慢病毒载体的示意图。

[0220] 图2B示出了由TGFβR1 DN或TGFβR2 DN的表达对TGF-β信号传导的抑制(由图2A示出,并且分别包括SEQ ID NO:2和3的氨基酸序列)。所示的数据表明,TGFβR2 DN嵌合细胞因子受体抑制由TGF-β配体诱导的TGF-β信号传导(高达100ng/ml),其中功效高于TGFβR1 DN。这可能是由于与TGFβR1与TGF-β配体结合的亲和力相比,TGFβR2与TGF-β配体结合的亲和力更高(在Groppe等人,2008,《分子细胞(Mol.Cell)》,29(2):157-68中描述的)。因此,以下实例的设计集中在具有TGFβR2的结合结构域的嵌合细胞因子受体上。

[0221] 实例2:使用TGFβR2设计和测试诱导型嵌合细胞因子受体

[0222] 如参考图1简要描述的,构建嵌合细胞因子受体,所述嵌合细胞因子受体具有源自TGFβR2的结合结构域("TGFβR2嵌合细胞因子受体")。为了研究TGFβR2嵌合细胞因子受体在CAR-T细胞的背景下的效用,构建TGFβR2细胞外结构域(ECD)的变体和TPOR跨膜(TM)结构域的变体。将每个TGFβR2 ECD变体、每个TPOR TM结构域变体和所期望的细胞因子受体的细胞内结构域(ICD)的融合克隆到编码第2代EGFRvIII特异性CAR的慢病毒载体中(2173scFv;在《科学转化医学(Sci TranslMed)》,2015年2月18日;7(275):275ra22中描述的),并且测试这些受体变体的活性。为了允许嵌合细胞因子受体和CAR的化学计量共表达,将这两个基因通过P2A肽("嵌合细胞因子受体-CAR构建体")连接。为了促进经转导细胞的检测,在scFv与CD8铰链结构域之间插入v5表位标签(SEQ ID NO:152)。

[0223] 图3示出了用于共表达TGFβR2嵌合细胞因子受体与第2代EGFRvIII CAR的慢病毒载体的总体示意图。一个或多个细胞尾或募集结构域可以串联连接以模拟来自一个或多个细胞因子的信号传导。

[0224] 图4A-4C示出了由使用TGFβR2构建的嵌合细胞因子受体的过表达对TGF-β信号传导的抑制。以与如实例1描述的方式类似的方式构建所使用的慢病毒载体。图4A示出了所使用的具有IL7R(316-459)和IL12Rb2(775-825)细胞尾或募集结构域以模拟CAR-T细胞中的IL7和IL12信号传导的原型慢病毒载体的示意图。设计了TpoR盒的跨膜结构域中的各种截短体(如表3所示)。确定了这些截短体调节细胞因子信号传导的能力。图4B示出了通过荧光素酶报告基因测定确定的TGF-β信号传导活性。显示使用TGFβR2构建的所有所测试的嵌合细胞因子受体能够抑制TGF-β信号传导,因为所述嵌合细胞因子受体在这些工程化细胞因子受体中竞争通过TGFβR2的细胞外结构域的结合。图4C示出了在存在TGF-β的情况下,图4A的嵌合细胞因子受体的激活。嵌合细胞因子受体的激活是通过STAT报告基因活性来测量的。鉴定出若干变体具有通过TGF-β配体诱导细胞因子信号传导的能力。图4B-4C的X轴中列出的跨膜结构域的氨基酸序列是表3中呈现的SEQ ID NO:29到SEQ ID NO:40以及SEQ ID

NO:50到SEQ ID NO:57。

[0225] 图5A-5C示出了由使用TGFβR2构建的另外的嵌合细胞因子受体的过表达对TGF-β信号传导的抑制。以与参考图4A-4C和实例1描述的方式类似的方式构建所使用的慢病毒载体。图5A示出了所使用的在结合结构域中具有截短体的原型慢病毒载体的示意图。

[0226] 再次,设计了TpoR盒的TM结构域中的另外的截短体(N-10、N-11、N-12等)(如表3中所示),并且确定了所述截短体调节细胞因子信号传导的能力。图5B示出了通过荧光素酶报告基因测定确定的TGF-β信号传导活性。显示所测试的大多数嵌合细胞因子受体能够抑制TGF-β信号传导(除了N-12、N-13、N-14TM截短体之外,其显示出较低的抑制程度)。图5C示出了在存在TGF-β的情况下,图5A的嵌合细胞因子受体的激活。嵌合细胞因子受体的激活是通过STAT报告基因活性来测量的。鉴定出若干变体具有通过TGF-β配体诱导细胞因子信号传导的能力。图5B-5C的X轴中列出的跨膜结构域的氨基酸序列是表3中呈现的SEQ ID NO:29、38、53、SEQ ID NO:40到SEQ ID NO:44以及SEQ ID NO:61到SEQ ID NO:72。

[0227] 实例3:嵌合细胞因子受体结合结构域的修饰和所构建的嵌合细胞因子受体的测试

[0228] 在不存在TGFβR2的情况下,TGFβR1以非常低的亲和力与TGF-β配体相互作用。一旦TGFβR2的ECD与TGF-β配体结合,二元复合物就具有延伸界面以有效地募集TGFβR1,从而形成三元复合物。工程化TGFβR2嵌合细胞因子受体也可以与内源性TGFβR1结合,所述内源性TGFβR1可以通过细胞因子受体ICD在空间上干扰预期的信号传导。为了消除TGFβR2嵌合细胞因子受体与TGFβR1之间的相互作用,设计了TGFβR1盒的若干变体,并且鉴定了可以增强细胞因子信号传导同时抑制TGF-β信号传导的修饰。

[0229] 图6A-6C示出了通过由具有修饰的TGFβR2构建的嵌合细胞因子受体的表达对TGF-β信号传导的抑制。图6A示出了引入到TGFβR2盒中的修饰的示意图。以与如实例1描述的方式类似的方式构建所使用的慢病毒载体。为了消除TGFβR1的结合,基于参考图6A-6C描述的先前构建体(“TGFβR2ΔN25”),将截短体(ΔN25)引入到TGFβR2结合结构域中,并且通过TGF-β报告基因测定测试TGF-β信号传导的抑制。图6B示出了TGFβR2ΔN25嵌合细胞因子受体仍保留抑制TGF-β信号传导的能力。图6C示出了通过STAT报告基因活性评估的图6A的嵌合细胞因子受体的激活。图6B-6C的X轴中列出的跨膜结构域的氨基酸序列是表1和3中呈现的SEQ ID NO:29、38、39、40和53,其中结合结构域序列为SEQ ID NO:4或SEQ ID NO:3。

[0230] 已经确定,即使在不存在TGF-β配体的情况下,TGFβR2结合结构域中的截短体使细胞因子信号传导增强5到10倍。有趣的是,ΔN25截短体能够协同增强与TpoR TM截短体(例如,N-7、N-8、N-9和N+4)的信号传导。TGFβR2结合结构域和TpoR TM截短体突变体的这种组合使用代表了用于同时地抑制免疫抑制性TGF-β信号传导同时传递免疫增强细胞因子信号传导的新颖方法。

[0231] 实例4:组成型活性嵌合细胞因子受体的设计和测试

[0232] 图7示出了组成型活性嵌合细胞因子受体的示意图。为了实现细胞因子细胞内结构域的组成型活性信号传导,在TPOR跨膜结构域中引入固有地使TPOR跨膜结构域二聚化并且激活JAK-STAT通路的双突变。如图7作为示例性构建体示出的,结合结构域包括TGFβR2的细胞外部分;示例性跨膜结构域可以包括SEQ ID NO:29、40、53或60。

[0233] 图8A-8C示出了组成型活性的嵌合细胞因子受体的设计和测试功能。以与如实例1

描述的方式类似的方式构建所使用的慢病毒载体。将双突变体(S505N,W515K)与已经显示出最有前景的功能性的变体(例如,TPOR盒中的TGFβR2ΔN25、N-9和N+4截短体)组合引入到TPOR盒中以加强受体的二聚化和激活。图8A示出了引入到TGFβR2盒中的修饰的示意图。图8B示出了由图8A的嵌合细胞因子受体的表达对TGF-β信号传导的抑制。图8C示出了通过293个细胞中的STAT5报告基因活性测量的经由图8A的嵌合细胞因子受体进行的细胞因子信号传导的激活。与亲本设计(TGFβR2_TpoR、TGFβR2_TpoR_N-9和TGFβR2_TpoR_N+4)相比,具有S505N和W515K突变的受体显示出显著的细胞因子信号传导(例如,TGFβR2_TpoR.S505.W515K、TGFβR2_TpoR_N-9.S505N.W515K)。图8B-8C的X轴中列出的跨膜结构域的序列包括表1和3中呈现的SEQ ID NO:40、53、59和60,其中结合结构域序列为SEQ ID NO:4或SEQ ID NO:3。

[0234] 实例5:对另外的嵌合细胞因子受体的测试

[0235] 图10A示出了诱导型TGF-β驱动的嵌合细胞因子受体的另外的设计。制备在跨膜结构域中具有另外的截短体以降低ECD与细胞内信号传导结构域之间的柔性的构建体。图10B示出了在293细胞中,在存在不同浓度的TGF-β的情况下,如通过荧光素酶测定确定的由图10A中所示的TGF-β驱动的嵌合细胞因子受体的过表达对内源性TGF-β信号传导的抑制。所述构建体中的一些构建体还在ECD结构域中具有ΔN25缺失(“TGF-βR2ΔN25”)。图10B中的所有TGF-β驱动的嵌合细胞因子受体抑制内源性TGF-β信号传导,但具有ΔN25缺失的克隆显示出对TGF-β信号传导的略微降低的抑制。图10C中的数据示出了在存在各种浓度的TGF-β的情况下嵌合细胞因子受体的激活。在存在的情况下,具有跨膜结构域中的缺失和ΔN25缺失的嵌合受体诱导STAT5信号传导。

[0236] 接下来测试CAR T细胞中的组成型嵌合受体。图11-16中测试的所有构建体在TPOR/MPLR跨膜结构域中含有S505N和W515K取代。图11A示出了用于在CAR T细胞中共表达TGF-βR2嵌合细胞因子受体与EGFRvIII特异性CAR(2173scFv)的慢病毒载体的示意图。所有嵌合细胞因子受体在TPOR/MPLR的跨膜结构域中具有二聚化突变(S505N,W515K,参见SEQ ID NO:60),并且一个或多个细胞因子受体募集结构域串联连接以模拟来自一个或多个细胞因子的信号传导。“IL2YY”是指IL2Rb(393-433,518-551),并且“IL7IL12”是指串联连接的IL7R(316-459)和IL12Rb2(775-825)。作为对照,还产生了CAR T细胞,其表达TGF-βR2的显性负性截短体(“TGF-βR2.DN”)、不具有TGF-βR2 ECD(“IL7IL12”、“IL2YY”)的组成型嵌合细胞因子受体或BFP蛋白。用于产生CAR T细胞的方法如以下文献所述:Sommer C等人,靶向BCMA的同种异体CAR T细胞的临床前评估用于治疗多发性骨髓瘤(Preclinical Evaluation of Allogeneic CAR T Cells Targeting BCMA for the Treatment ofMultiple Myeloma)《分子疗法(Mol Ther)》2019.doi:10.1016/j.ymthe.2019.04.001以及Sommer C等人,具有关闭-切换的同种异体FLT3 CAR T细胞表现出抗AML的有效活性并且可以被耗竭以加速骨髓恢复(Allogeneic FLT3 CAR T Cells with an Off-Switch Exhibit Potent Activity against AML and Can Be Depleted to Expedite Bone Marrow Recovery)《分子疗法》2020.doi:10.1016/j.ymthe.2020.06.022。简言之,将来自健康供体的原代T细胞用表达CAR的慢病毒以及每种TGFβR2嵌合细胞因子受体或对照在MOI为5下进行转导。图11B示出了在CAR T细胞产生期间第7、9和14天时的CAR+T细胞的百分比。与单独的BFP相比,在产生时段内,具有如所指示的组成型嵌合细胞因子受体(“TGF-β

R2.IL7IL12”、“TGF-βR2.IL2YY”、“IL7IL12”或“IL2YY”)的CAR T细胞显示出更高的增殖和富集。因此,与单独表达BFP而不具有嵌合细胞因子受体的CAR T相比,随时间推移获得了更多的EGFRvIII CAR+T细胞(图11C)。

[0237] 图11D和11E示出了评估共表达各种嵌合细胞因子受体或对照的CAR T细胞中的STAT 5磷酸化的结果。用于检测磷酸化STAT5的抗体来自BD生物科学公司(BD Biosciences)(BDB612599)。与IL2YY和IL7IL12(即,不具有TGF-βR2 ECD的组成型嵌合细胞因子受体)相比,具有TGF-βR2 ECD的组成型嵌合细胞因子受体(即,TGF-βR2.IL7IL12或TGF-βR2.IL2YY)的CAR T细胞表现出更高水平的STAT5磷酸化,即使在不存在TGFβ的情况下,这指示具有TGF-βR2ECD结构域的细胞因子信号传导更强。数据表明,TGF-βR2 ECD改善了CAR T细胞中的细胞间募集结构域信号传导。

[0238] 图11F和11G中的数据示出了嵌合细胞因子受体在CAR T产生的第14天调节CAR T细胞的分化。分别使用来自BioLegned公司(编号:304822)和BioLegand公司(编号:304234)的抗体进行CD62L和CD45RO染色。值得注意的是,表达TGF-βR2.IL7IL12嵌合细胞因子受体的CAR T细胞大部分分化为中央记忆T细胞($CD62L^{hi}CD45RO^{hi}$)——这一结果可能是由于强IL12Rb信号传导导致的,而表达TGFbR2.IL2YY或IL2YY嵌合细胞因子受体的CAR T细胞表现出干细胞样(干细胞)记忆T细胞($CD62L^{hi}CD45RO^{low}$)的富集群体,这是与更好的临床结果相关的令人期望的T细胞表型。

[0239] 接下来,通过使用抗人TGF-βR2多克隆抗体(R&D系统公司(R&DSystems),FAB2411A100)通过流式细胞术测量总表面ECD,将TGF-βR2嵌合细胞因子受体的表达与内源性TGF-βR2的表达进行比较。图11H中的结果示出了在约1400-2300处,在表达IL7IL12或IL2YY嵌合细胞因子受体的CAR T细胞和表达BFP的CAR T细胞中由内源性TGF-βR2产生的ECD染色的MFI。表达TGF-βR2嵌合细胞因子受体(TGF-βR2.IL7IL12和TGF-βR2.IL2YY)的CAR T细胞显示出2-3倍的过量MFI值,这表明TGF-βR2 ECD染色水平比内源性TGF-βR2受体的水平高2-3倍。图11I示出了当暴露于各种浓度的TGFβ时,表达不同嵌合细胞因子受体或对照的CAR T细胞内的SMAD磷酸化的水平。用于检测磷酸化的SMAD的抗体来自BD生物科学公司(BDB562586)。结果显示,与分别表达不具有TGF-βR2胞外域的IL7IL12和IL2YY嵌合细胞因子受体的CAR T细胞相比,表达TGF-βR2.IL7IL12和TGF-βR2.IL2YY嵌合细胞因子受体的CAR T细胞表现出降低的SMAD磷酸化。

[0240] 接下来,评估了表达不同嵌合细胞因子受体或对照的EGFRvIII CAR T细胞对靶细胞U87-EGFRvIII细胞的抗肿瘤活性。简言之,将CAR T细胞与10,000个靶细胞以1:2的E:T比率在200ul的含10%FBS以及0ng/ml、5ng/ml和20ng/ml的各种浓度的TGF-β的RPMI培养基中温育。在与靶细胞共培养一周之后,将100ul上清液中的CAR T细胞转移到具有与前一周相同的TGFβ浓度的新靶细胞(10,000个)中。评估在没有添加TGF-β的第二周内CAR T细胞的细胞毒性,并且图12A中示出了结果。在不存在外源性TGFβ的情况下,表达TGF-βR2嵌合细胞因子受体(TGF-βR2.IL7IL12和TGF-βR2.IL2YY)的CAR T细胞显示出最持久的细胞毒性,其中大多数靶细胞被CAR T细胞杀伤。表达不具有TGF-βR2 ECD(IL7IL12和IL2YY)的嵌合细胞因子受体的CAR T细胞还表现出相当大的细胞毒性并且抑制U87细胞的生长直到第二周。相比之下,具有BFP或TGF-βR2.DN的CART细胞丧失活性并且未能抑制U87细胞的生长(图12A)。数据表明,TGF-βR2嵌合细胞因子受体能够对靶细胞产生更持久的细胞毒性。在存在TGFβ的情

况下,没有表达具有TGFbR2 ECD的嵌合细胞因子受体的CAR T细胞的活性被TGF-β抑制到各种水平,这很可能是通过内源性TGF-β受体的信号转导的作用(图12B-12C)。相比之下,表达TGF-βR2嵌合细胞因子受体的CAR T细胞对TGF-β抑制具有抗性,并且能够在高达20ng/mLTGF-β的条件下维持强细胞毒性(图12B、12C)。

[0241] 接下来,评估了CAR T细胞中的另外的经修饰的组成型TGF-βR2嵌合细胞因子受体。如上文所示,在TPOR/MPLR跨膜结构域和IL7Ra/IL12Rb募集结构域(例如,SEQ ID NO:163)中具有S505N/W515K取代的组成型TGFβR2.IL7IL12嵌合细胞因子受体增加了STAT5磷酸化并且导致中央记忆T细胞的实质性分化。由于IL12细胞因子信号传导已经涉及记忆T细胞的分化,设计了消除IL12信号传导的TGF-βR2.IL7嵌合细胞因子受体。另外,在TpoR JAK结合结构域K553R和K573R(命名为"RR",例如,SEQ ID NO:165和170)中引入两个突变,以减少泛素诱导的受体降解。参见Saur SJ、Sangkhae V、Geddis AE、Kaushansky K、Hitchcock IS,血小板生成素受体c-Mpl的泛素化和降解(Ubiquitination and degradation of the thrombopoietin receptor c-Mpl)《血液学(Blood)》2010.doi:10.1182/blood-2009-06-227033。产生表达嵌合细胞因子受体的CAR T细胞,并且评估STAT5磷酸化和T细胞分化。与先前类似,这些另外的经修饰的TGF-βR2嵌合细胞因子受体显示出比不具有TGF-βR2ECD结构域(IL7IL12和IL7嵌合细胞因子受体构建体两者均含有S505N/W515K取代)的嵌合细胞因子受体更高水平的STAT5信号传导(如通过STAT5磷酸化确定的)(图13A)。在T细胞分化的评估中,表达不具有IL12R募集结构域(TGF-βR2.IL7,TGF-βR2.IL7_RR和IL7)的嵌合细胞因子受体的CAR T细胞显示出与具有IL12R募集结构域的其对应物相比,干记忆T细胞的比例增加(图13B)。这些数据证明,通过选择不同的细胞因子受体基序,可以调节TGF-βR2嵌合细胞因子受体信号传导和T细胞分化。

[0242] 为了评估TGF-βR2嵌合细胞因子受体如何影响T细胞功能,在长期杀伤测定中评估CART细胞。简言之,将表达不同嵌合细胞因子受体的CAR T细胞与10,000个U87-EGFRvIII癌细胞以1:1的E:T比率在200ul的含10%FBS、具有或不具有5ng/ml TGFβ的RPMI培养基中混合。每两天或三天,将100ul的具有CAR T细胞的上清液转移到10,000个新鲜靶细胞上,至最终体积为200ul的含10%FBS和5ng/ml的TGFβ的RPMI培养基中,并且对老的靶细胞的存活率进行定量。图14A-B总结了具有不同TGF-βR2嵌合细胞因子受体的CART细胞的长期细胞毒性。在不存在外源性TGFβ的情况下,具有各种募集结构域的TGF-βR2嵌合细胞因子受体(例如,TGF-βR2.IL2YY、TGF-βR2.IL7或TGF-βR2.IL2YYY(IL2Rb(339-379,393-433,518-551)))与表达不具有TGF-βR2 ECD的嵌合细胞因子受体的CAR T细胞相比,全部赋予更有效且持久的细胞毒性,这证实了先前观察结果:TGF-βR2 ECD结构域增强了嵌合细胞因子受体信号传导(图14A)。在存在5ng/ml TGFβ的情况下,表达TGF-βR2嵌合细胞因子受体的CAR T细胞维持比表达或不表达不具有TGF-βR2 ECD的嵌合细胞因子受体的CAR T细胞更有效且持久的细胞毒性(图14B)。所测试的嵌合细胞因子受体全部含有S505N/W515K取代,并且TGFbR2.IL2YYY和IL2YYY构建体在TOPR/MPLR跨膜结构域中具有另外的H499L取代。

[0243] 为了进一步评估TGF-βR2嵌合细胞因子受体对TGFβ信号传导的抑制及其对CAR T细胞的功能性的影响,分析了TGF-βR2.IL2YY_RR嵌合细胞因子受体(SEQ ID NO:166),其在TM区(S505N,W515K)中具有二聚化突变并且在JAK结合结构域中具有抗降解突变(K553R和K573R)。设计了在TGF-βR2 ECD中具有突变的两种另外的变体(D32A.E119A和

D32A.E119A.I53A)，所述两种另外的变体消除了受体结合TGFβ配体的能力。产生表达指定的嵌合细胞因子受体的CAR T细胞，并且评估细胞因子信号传导(pSTAT5)、TGFβ信号传导(pSMAD)和针对U87-EGFRvIII靶细胞的细胞毒性的持久性。图15A示出了CAR T细胞中的STAT5信号传导的分析，其中与仅表达CAR的T细胞相比，所有TGF-βR2嵌合细胞因子受体导致CAR T细胞中的强STAT5磷酸化。当CAR T细胞暴露于5ng/ml TGFβ配体时，观察到各种水平的SMAD磷酸化。与具有结合丧失突变体的TGF-βR2嵌合细胞因子受体相比，具有野生型TGFβ结合结构域的TGF-βR2.IL2YY_RR表现出降低的SMAD磷酸化水平，这表明具有野生型功能性配体结合结构域的TGF-βR2嵌合细胞因子受体成功地抑制了内源性TGFβ信号传导(图15B)。

[0244] 图15C示出了在存在5ng/ml TGFβ的情况下，表达不同的TGF-βR2嵌合细胞因子受体的CAR T细胞针对癌细胞的长期细胞毒性。与在第8天时快速丧失杀伤靶细胞的活性的对照CAR T细胞相比，具有TGF-βR2嵌合细胞因子受体的CAR T细胞赋予更持久的活性。与表达具有野生型TGFβ结合ECD的TGF-βR2.IL2YY_RR嵌合细胞因子受体的CAR T细胞相比，具有与TGFβ结合的能力受损的TGF-βR2嵌合细胞因子受体(D32A.E119A和D32A.E119A.I53A)在细胞毒性测定中还显示出更快的下降。这些数据证明，细胞因子信号传导和抑制内源性TGFβ信号传导的能力两者对于CAR T细胞的长期活性都很重要。

[0245] 图16A-B中的结果示出了抗降解突变K553R和K573R可以进一步改善组成型TGF-βR2嵌合细胞因子受体的功能性。在此实验中，在具有5ng/ml TGFβ配体的培养基中，对表达具有或不具有抗降解突变(命名为“RR”)的TGF-βR2嵌合细胞因子受体的CAR T细胞的细胞因子信号传导的强度以及针对U87-EGFRvIII的长期细胞毒性测定进行评估。具有K533R和K573R取代的TGF-βR2嵌合细胞因子受体一致地显示出更强的STAT5磷酸化(图16A)和更持久的杀伤靶细胞的能力(图16B)。

序列表

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Pro Gly Glu Thr Phe Phe Met Cys Ser Cys Ser Ser Asp Glu Cys Asn
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<223> /注释 = “人工序列的描述：合成多肽”
<400> 19
Gln Leu Cys Lys Phe Cys Asp Val Arg Phe Ser Thr Cys Asp Asn Gln
1 5 10 15
[0009] Lys Ser Cys Met Ser Asn Cys Ser Ile Thr Ser Ile Cys Glu Lys Pro
20 25 30
Gln Glu Val Cys Val Ala Val Trp Arg Lys Asn Asp Glu Asn Ile Thr
35 40 45
Leu Glu Thr Val Cys His Asp Pro Lys Leu Pro Tyr His Asp Phe Ile
50 55 60
Leu Glu Asp Ala Ala Ser Pro Lys Cys Ile Met Lys Glu Lys Lys Lys
65 70 75 80
Pro Gly Glu Thr Phe Phe Met Cys Ser Cys Ser Ser Asp Glu Cys Asn
85 90 95
Asp Asn Ile Thr Phe
100
<210> 20
<211> 101
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 20
Gln Leu Cys Lys Phe Cys Asp Val Arg Phe Ser Thr Cys Asp Asn Gln
1 5 10 15
Lys Ser Cys Met Ser Asn Cys Ser Ile Thr Ser Ile Cys Glu Lys Pro
20 25 30
Gln Glu Val Cys Val Ala Val Trp Arg Lys Asn Asp Glu Asn Ile Thr
35 40 45

Leu Glu Thr Val Cys His Asp Pro Lys Leu Pro Tyr His Asp Phe Glu
50 55 60
Leu Glu Asp Ala Ala Ser Pro Lys Cys Ile Met Lys Glu Lys Lys Lys
65 70 75 80
Pro Gly Glu Thr Phe Phe Met Cys Ser Cys Ser Ser Asp Glu Cys Asn
85 90 95
Asp Asn Ile Ile Phe
100

<210> 21
<211> 508
<212> PRT
<213> 智人 (Homo sapiens)
<400> 21
Met Asp His Leu Gly Ala Ser Leu Trp Pro Gln Val Gly Ser Leu Cys
1 5 10 15
Leu Leu Leu Ala Gly Ala Ala Trp Ala Pro Pro Pro Asn Leu Pro Asp
20 25 30
Pro Lys Phe Glu Ser Lys Ala Ala Leu Leu Ala Ala Arg Gly Pro Glu
35 40 45
Glu Leu Leu Cys Phe Thr Glu Arg Leu Glu Asp Leu Val Cys Phe Trp
50 55 60
Glu Glu Ala Ala Ser Ala Gly Val Gly Pro Gly Asn Tyr Ser Phe Ser
65 70 75 80
Tyr Gln Leu Glu Asp Glu Pro Trp Lys Leu Cys Arg Leu His Gln Ala
85 90 95
[0010] Pro Thr Ala Arg Gly Ala Val Arg Phe Trp Cys Ser Leu Pro Thr Ala
100 105 110
Asp Thr Ser Ser Phe Val Pro Leu Glu Leu Arg Val Thr Ala Ala Ser
115 120 125
Gly Ala Pro Arg Tyr His Arg Val Ile His Ile Asn Glu Val Val Leu
130 135 140
Leu Asp Ala Pro Val Gly Leu Val Ala Arg Leu Ala Asp Glu Ser Gly
145 150 155 160
His Val Val Leu Arg Trp Leu Pro Pro Pro Glu Thr Pro Met Thr Ser
165 170 175
His Ile Arg Tyr Glu Val Asp Val Ser Ala Gly Asn Gly Ala Gly Ser
180 185 190
Val Gln Arg Val Glu Ile Leu Glu Gly Arg Thr Glu Cys Val Leu Ser
195 200 205
Asn Leu Arg Gly Arg Thr Arg Tyr Thr Phe Ala Val Arg Ala Arg Met
210 215 220
Ala Glu Pro Ser Phe Gly Gly Phe Trp Ser Ala Trp Ser Glu Pro Val
225 230 235 240
Ser Leu Leu Thr Pro Ser Asp Leu Asp Pro Leu Ile Leu Thr Leu Ser
245 250 255
Leu Ile Leu Val Val Ile Leu Val Leu Leu Thr Val Leu Ala Leu Leu
260 265 270
Ser His Arg Arg Ala Leu Lys Gln Lys Ile Trp Pro Gly Ile Pro Ser
275 280 285
Pro Glu Ser Glu Phe Glu Gly Leu Phe Thr Thr His Lys Gly Asn Phe
290 295 300

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

<210> 22
<211> 918
<212> PRT
<213> 智人 (Homo sapiens)
<400> 22
Met Leu Thr Leu Gln Thr Trp Leu Val Gln Ala Leu Phe Ile Phe Leu
1 5 10 15
Thr Thr Glu Ser Thr Gly Glu Leu Leu Asp Pro Cys Gly Tyr Ile Ser
20 25 30
Pro Glu Ser Pro Val Val Gln Leu His Ser Asn Phe Thr Ala Val Cys
35 40 45
Val Leu Lys Glu Lys Cys Met Asp Tyr Phe His Val Asn Ala Asn Tyr
50 55 60
Ile Val Trp Lys Thr Asn His Phe Thr Ile Pro Lys Glu Gln Tyr Thr
65 70 75 80
Ile Ile Asn Arg Thr Ala Ser Ser Val Thr Phe Thr Asp Ile Ala Ser
85 90 95
Leu Asn Ile Gln Leu Thr Cys Asn Ile Leu Thr Phe Gly Gln Leu Glu
100 105 110
Gln Asn Val Tyr Gly Ile Thr Ile Ile Ser Gly Leu Pro Pro Glu Lys
115 120 125
Pro Lys Asn Leu Ser Cys Ile Val Asn Glu Gly Lys Lys Met Arg Cys
130 135 140
Glu Trp Asp Arg Gly Arg Glu Thr His Leu Glu Thr Asn Phe Thr Leu
145 150 155 160

[0012]

```
Lys Ser Glu Trp Ala Thr His Lys Phe Ala Asp Cys Lys Ala Lys Arg
                165                 170                 175
Asp Thr Pro Thr Ser Cys Thr Val Asp Tyr Ser Thr Val Tyr Phe Val
            180                 185                 190
Asn Ile Glu Val Trp Val Glu Ala Glu Asn Ala Leu Gly Lys Val Thr
        195                 200                 205
Ser Asp His Ile Asn Phe Asp Pro Val Tyr Lys Val Lys Pro Asn Pro
    210                 215                 220
Pro His Asn Leu Ser Val Ile Asn Ser Glu Glu Leu Ser Ser Ile Leu
225                 230                 235                 240
Lys Leu Thr Trp Thr Asn Pro Ser Ile Lys Ser Val Ile Ile Leu Lys
                245                 250                 255
Tyr Asn Ile Gln Tyr Arg Thr Lys Asp Ala Ser Thr Trp Ser Gln Ile
            260                 265                 270
Pro Pro Glu Asp Thr Ala Ser Thr Arg Ser Ser Phe Thr Val Gln Asp
        275                 280                 285
Leu Lys Pro Phe Thr Glu Tyr Val Phe Arg Ile Arg Cys Met Lys Glu
    290                 295                 300
Asp Gly Lys Gly Tyr Trp Ser Asp Trp Ser Glu Glu Ala Ser Gly Ile
305                 310                 315                 320
Thr Tyr Glu Asp Arg Pro Ser Lys Ala Pro Ser Phe Trp Tyr Lys Ile
                325                 330                 335
Asp Pro Ser His Thr Gln Gly Tyr Arg Thr Val Gln Leu Val Trp Lys
            340                 345                 350
Thr Leu Pro Pro Phe Glu Ala Asn Gly Lys Ile Leu Asp Tyr Glu Val
        355                 360                 365
Thr Leu Thr Arg Trp Lys Ser His Leu Gln Asn Tyr Thr Val Asn Ala
    370                 375                 380
Thr Lys Leu Thr Val Asn Leu Thr Asn Asp Arg Tyr Val Ala Thr Leu
385                 390                 395                 400
Thr Val Arg Asn Leu Val Gly Lys Ser Asp Ala Ala Val Leu Thr Ile
                405                 410                 415
Pro Ala Cys Asp Phe Gln Ala Thr His Pro Val Met Asp Leu Lys Ala
            420                 425                 430
Phe Pro Lys Asp Asn Met Leu Trp Val Glu Trp Thr Thr Pro Arg Glu
        435                 440                 445
Ser Val Lys Lys Tyr Ile Leu Glu Trp Cys Val Leu Ser Asp Lys Ala
    450                 455                 460
Pro Cys Ile Thr Asp Trp Gln Gln Glu Asp Gly Thr Val His Arg Thr
465                 470                 475                 480
Tyr Leu Arg Gly Asn Leu Ala Glu Ser Lys Cys Tyr Leu Ile Thr Val
                485                 490                 495
Thr Pro Val Tyr Ala Asp Gly Pro Gly Ser Pro Glu Ser Ile Lys Ala
            500                 505                 510
Tyr Leu Lys Gln Ala Pro Pro Ser Lys Gly Pro Thr Val Arg Thr Lys
        515                 520                 525
Lys Val Gly Lys Asn Glu Ala Val Leu Glu Trp Asp Gln Leu Pro Val
    530                 535                 540
Asp Val Gln Asn Gly Phe Ile Arg Asn Tyr Thr Ile Phe Tyr Arg Thr
545                 550                 555                 560
Ile Ile Gly Asn Glu Thr Ala Val Asn Val Asp Ser Ser His Thr Glu
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565 570 575
Tyr Thr Leu Ser Ser Leu Thr Ser Asp Thr Leu Tyr Met Val Arg Met
580 585 590
Ala Ala Tyr Thr Asp Glu Gly Gly Lys Asp Gly Pro Glu Phe Thr Phe
595 600 605
Thr Thr Pro Lys Phe Ala Gln Gly Glu Ile Glu Ala Ile Val Val Pro
610 615 620
Val Cys Leu Ala Phe Leu Leu Thr Thr Leu Leu Gly Val Leu Phe Cys
625 630 635 640
Phe Asn Lys Arg Asp Leu Ile Lys Lys His Ile Trp Pro Asn Val Pro
645 650 655
Asp Pro Ser Lys Ser His Ile Ala Gln Trp Ser Pro His Thr Pro Pro
660 665 670
Arg His Asn Phe Asn Ser Lys Asp Gln Met Tyr Ser Asp Gly Asn Phe
675 680 685
Thr Asp Val Ser Val Val Glu Ile Glu Ala Asn Asp Lys Lys Pro Phe
690 695 700
Pro Glu Asp Leu Lys Ser Leu Asp Leu Phe Lys Lys Glu Lys Ile Asn
705 710 715 720
Thr Glu Gly His Ser Ser Gly Ile Gly Gly Ser Ser Cys Met Ser Ser
725 730 735
Ser Arg Pro Ser Ile Ser Ser Ser Asp Glu Asn Glu Ser Ser Gln Asn
740 745 750
Thr Ser Ser Thr Val Gln Tyr Ser Thr Val Val His Ser Gly Tyr Arg
755 760 765

[0013] His Gln Val Pro Ser Val Gln Val Phe Ser Arg Ser Glu Ser Thr Gln
770 775 780
Pro Leu Leu Asp Ser Glu Glu Arg Pro Glu Asp Leu Gln Leu Val Asp
785 790 795 800
His Val Asp Gly Gly Asp Gly Ile Leu Pro Arg Gln Gln Tyr Phe Lys
805 810 815
Gln Asn Cys Ser Gln His Glu Ser Ser Pro Asp Ile Ser His Phe Glu
820 825 830
Arg Ser Lys Gln Val Ser Ser Val Asn Glu Glu Asp Phe Val Arg Leu
835 840 845
Lys Gln Gln Ile Ser Asp His Ile Ser Gln Ser Cys Gly Ser Gly Gln
850 855 860
Met Lys Met Phe Gln Glu Val Ser Ala Ala Asp Ala Phe Gly Pro Gly
865 870 875 880
Thr Glu Gly Gln Val Glu Arg Phe Glu Thr Val Gly Met Glu Ala Ala
885 890 895
Thr Asp Glu Gly Met Pro Lys Ser Tyr Leu Pro Gln Thr Val Arg Gln
900 905 910
Gly Gly Tyr Met Pro Gln
915

<210> 23
<211> 622
<212> PRT
<213> 智人 (Homo sapiens)
<400> 23
Met Lys Glu Asn Val Ala Ser Ala Thr Val Phe Thr Leu Leu Leu Phe

```
1               5                   10                  15
Leu Asn Thr Cys Leu Leu Asn Gly Gln Leu Pro Pro Gly Lys Pro Glu
            20                  25                  30
Ile Phe Lys Cys Arg Ser Pro Asn Lys Glu Thr Phe Thr Cys Trp Trp
        35                  40                  45
Arg Pro Gly Thr Asp Gly Gly Leu Pro Thr Asn Tyr Ser Leu Thr Tyr
    50                  55                  60
His Arg Glu Gly Glu Thr Leu Met His Glu Cys Pro Asp Tyr Ile Thr
65                  70                  75                  80
Gly Gly Pro Asn Ser Cys His Phe Gly Lys Gln Tyr Thr Ser Met Trp
                85                  90                  95
Arg Thr Tyr Ile Met Met Val Asn Ala Thr Asn Gln Met Gly Ser Ser
            100                 105                 110
Phe Ser Asp Glu Leu Tyr Val Asp Val Thr Tyr Ile Val Gln Pro Asp
        115                 120                 125
Pro Pro Leu Glu Leu Ala Val Glu Val Lys Gln Pro Glu Asp Arg Lys
    130                 135                 140
Pro Tyr Leu Trp Ile Lys Trp Ser Pro Pro Thr Leu Ile Asp Leu Lys
145                 150                 155                 160
Thr Gly Trp Phe Thr Leu Leu Tyr Glu Ile Arg Leu Lys Pro Glu Lys
                165                 170                 175
Ala Ala Glu Trp Glu Ile His Phe Ala Gly Gln Gln Thr Glu Phe Lys
            180                 185                 190
Ile Leu Ser Leu His Pro Gly Gln Lys Tyr Leu Val Gln Val Arg Cys
        195                 200                 205
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[0014]

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

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

[0015] 610 615 620

<210> 24
<211> 638
<212> PRT
<213> 智人 (Homo sapiens)
<400> 24
Met Asp Leu Trp Gln Leu Leu Leu Thr Leu Ala Leu Ala Gly Ser Ser
1 5 10 15
Asp Ala Phe Ser Gly Ser Glu Ala Thr Ala Ala Ile Leu Ser Arg Ala
20 25 30
Pro Trp Ser Leu Gln Ser Val Asn Pro Gly Leu Lys Thr Asn Ser Ser
35 40 45
Lys Glu Pro Lys Phe Thr Lys Cys Arg Ser Pro Glu Arg Glu Thr Phe
50 55 60
Ser Cys His Trp Thr Asp Glu Val His His Gly Thr Lys Asn Leu Gly
65 70 75 80
Pro Ile Gln Leu Phe Tyr Thr Arg Arg Asn Thr Gln Glu Trp Thr Gln
85 90 95
Glu Trp Lys Glu Cys Pro Asp Tyr Val Ser Ala Gly Glu Asn Ser Cys
100 105 110
Tyr Phe Asn Ser Ser Phe Thr Ser Ile Trp Ile Pro Tyr Cys Ile Lys
115 120 125
Leu Thr Ser Asn Gly Gly Thr Val Asp Glu Lys Cys Phe Ser Val Asp
130 135 140
Glu Ile Val Gln Pro Asp Pro Pro Ile Ala Leu Asn Trp Thr Leu Leu
145 150 155 160

Asn Val Ser Leu Thr Gly Ile His Ala Asp Ile Gln Val Arg Trp Glu
165 170 175
Ala Pro Arg Asn Ala Asp Ile Gln Lys Gly Trp Met Val Leu Glu Tyr
180 185 190
Glu Leu Gln Tyr Lys Glu Val Asn Glu Thr Lys Trp Lys Met Met Asp
195 200 205
Pro Ile Leu Thr Thr Ser Val Pro Val Tyr Ser Leu Lys Val Asp Lys
210 215 220
Glu Tyr Glu Val Arg Val Arg Ser Lys Gln Arg Asn Ser Gly Asn Tyr
225 230 235 240
Gly Glu Phe Ser Glu Val Leu Tyr Val Thr Leu Pro Gln Met Ser Gln
245 250 255
Phe Thr Cys Glu Glu Asp Phe Tyr Phe Pro Trp Leu Leu Ile Ile Ile
260 265 270
Phe Gly Ile Phe Gly Leu Thr Val Met Leu Phe Val Phe Leu Phe Ser
275 280 285
Lys Gln Gln Arg Ile Lys Met Leu Ile Leu Pro Pro Val Pro Val Pro
290 295 300
Lys Ile Lys Gly Ile Asp Pro Asp Leu Leu Lys Glu Gly Lys Leu Glu
305 310 315 320
Glu Val Asn Thr Ile Leu Ala Ile His Asp Ser Tyr Lys Pro Glu Phe
325 330 335
His Ser Asp Asp Ser Trp Val Glu Phe Ile Glu Leu Asp Ile Asp Glu
340 345 350
Pro Asp Glu Lys Thr Glu Glu Ser Asp Thr Asp Arg Leu Leu Ser Ser
[0016] 355 360 365
Asp His Glu Lys Ser His Ser Asn Leu Gly Val Lys Asp Gly Asp Ser
370 375 380
Gly Arg Thr Ser Cys Cys Glu Pro Asp Ile Leu Glu Thr Asp Phe Asn
385 390 395 400
Ala Asn Asp Ile His Glu Gly Thr Ser Glu Val Ala Gln Pro Gln Arg
405 410 415
Leu Lys Gly Glu Ala Asp Leu Leu Cys Leu Asp Gln Lys Asn Gln Asn
420 425 430
Asn Ser Pro Tyr His Asp Ala Cys Pro Ala Thr Gln Gln Pro Ser Val
435 440 445
Ile Gln Ala Glu Lys Asn Lys Pro Gln Pro Leu Pro Thr Glu Gly Ala
450 455 460
Glu Ser Thr His Gln Ala Ala His Ile Gln Leu Ser Asn Pro Ser Ser
465 470 475 480
Leu Ser Asn Ile Asp Phe Tyr Ala Gln Val Ser Asp Ile Thr Pro Ala
485 490 495
Gly Ser Val Val Leu Ser Pro Gly Gln Lys Asn Lys Ala Gly Met Ser
500 505 510
Gln Cys Asp Met His Pro Glu Met Val Ser Leu Cys Gln Glu Asn Phe
515 520 525
Leu Met Asp Asn Ala Tyr Phe Cys Glu Ala Asp Ala Lys Lys Cys Ile
530 535 540
Pro Val Ala Pro His Ile Lys Val Glu Ser His Ile Gln Pro Ser Leu
545 550 555 560
Asn Gln Glu Asp Ile Tyr Ile Thr Thr Glu Ser Leu Thr Thr Ala Ala

565 570 575
Gly Arg Pro Gly Thr Gly Glu His Val Pro Gly Ser Glu Met Pro Val
580 585 590
Pro Asp Tyr Thr Ser Ile His Ile Val Gln Ser Pro Gln Gly Leu Ile
595 600 605
Leu Asn Ala Thr Ala Leu Pro Leu Pro Asp Lys Glu Phe Leu Ser Ser
610 615 620
Cys Gly Tyr Val Ser Thr Asp Gln Leu Asn Lys Ile Met Pro
625 630 635

<210> 25
<211> 863
<212> PRT
<213> 智人 (Homo sapiens)
<400> 25

Met Ala Arg Leu Gly Asn Cys Ser Leu Thr Trp Ala Ala Leu Ile Ile
1 5 10 15
Leu Leu Leu Pro Gly Ser Leu Glu Glu Cys Gly His Ile Ser Val Ser
20 25 30
Ala Pro Ile Val His Leu Gly Asp Pro Ile Thr Ala Ser Cys Ile Ile
35 40 45
Lys Gln Asn Cys Ser His Leu Asp Pro Glu Pro Gln Ile Leu Trp Arg
50 55 60
Leu Gly Ala Glu Leu Gln Pro Gly Gly Arg Gln Gln Arg Leu Ser Asp
65 70 75 80
Gly Thr Gln Glu Ser Ile Ile Thr Leu Pro His Leu Asn His Thr Gln
[0017] 85 90 95
Ala Phe Leu Ser Cys Cys Leu Asn Trp Gly Asn Ser Leu Gln Ile Leu
100 105 110
Asp Gln Val Glu Leu Arg Ala Gly Tyr Pro Pro Ala Ile Pro His Asn
115 120 125
Leu Ser Cys Leu Met Asn Leu Thr Thr Ser Ser Leu Ile Cys Gln Trp
130 135 140
Glu Pro Gly Pro Glu Thr His Leu Pro Thr Ser Phe Thr Leu Lys Ser
145 150 155 160
Phe Lys Ser Arg Gly Asn Cys Gln Thr Gln Gly Asp Ser Ile Leu Asp
165 170 175
Cys Val Pro Lys Asp Gly Gln Ser His Cys Cys Ile Pro Arg Lys His
180 185 190
Leu Leu Leu Tyr Gln Asn Met Gly Ile Trp Val Gln Ala Glu Asn Ala
195 200 205
Leu Gly Thr Ser Met Ser Pro Gln Leu Cys Leu Asp Pro Met Asp Val
210 215 220
Val Lys Leu Glu Pro Pro Met Leu Arg Thr Met Asp Pro Ser Pro Glu
225 230 235 240
Ala Ala Pro Pro Gln Ala Gly Cys Leu Gln Leu Cys Trp Glu Pro Trp
245 250 255
Gln Pro Gly Leu His Ile Asn Gln Lys Cys Glu Leu Arg His Lys Pro
260 265 270
Gln Arg Gly Glu Ala Ser Trp Ala Leu Val Gly Pro Leu Pro Leu Glu
275 280 285
Ala Leu Gln Tyr Glu Leu Cys Gly Leu Leu Pro Ala Thr Ala Tyr Thr

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

[0018] Phe Gln Leu Tyr Glu Ile Ile Val Thr Pro Leu Tyr Gln Asp Thr Met
500 505 510
Gly Pro Ser Gln His Val Tyr Ala Tyr Ser Gln Glu Met Ala Pro Ser
515 520 525
His Ala Pro Glu Leu His Leu Lys His Ile Gly Lys Thr Trp Ala Gln
530 535 540
Leu Glu Trp Val Pro Glu Pro Pro Glu Leu Gly Lys Ser Pro Leu Thr
545 550 555 560
His Tyr Thr Ile Phe Trp Thr Asn Ala Gln Asn Gln Ser Phe Ser Ala
565 570 575
Ile Leu Asn Ala Ser Ser Arg Gly Phe Val Leu His Gly Leu Glu Pro
580 585 590
Ala Ser Leu Tyr His Ile His Leu Met Ala Ala Ser Gln Ala Gly Ala
595 600 605
Thr Asn Ser Thr Val Leu Thr Leu Met Thr Leu Thr Pro Glu Gly Ser
610 615 620
Glu Leu His Ile Ile Leu Gly Leu Phe Gly Leu Leu Leu Leu Leu Thr
625 630 635 640
Cys Leu Cys Gly Thr Ala Trp Leu Cys Cys Ser Pro Asn Arg Lys Asn
645 650 655
Pro Leu Trp Pro Ser Val Pro Asp Pro Ala His Ser Ser Leu Gly Ser
660 665 670
Trp Val Pro Thr Ile Met Glu Glu Leu Pro Gly Pro Arg Gln Gly Gln
675 680 685
Trp Leu Gly Gln Thr Ser Glu Met Ser Arg Ala Leu Thr Pro His Pro
690 695 700

Cys Val Gln Asp Ala Phe Gln Leu Pro Gly Leu Gly Thr Pro Pro Ile
705 710 715 720
Thr Lys Leu Thr Val Leu Glu Glu Asp Glu Lys Lys Pro Val Pro Trp
725 730 735
Glu Ser His Asn Ser Ser Glu Thr Cys Gly Leu Pro Thr Leu Val Gln
740 745 750
Thr Tyr Val Leu Gln Gly Asp Pro Arg Ala Val Ser Thr Gln Pro Gln
755 760 765
Ser Gln Ser Gly Thr Ser Asp Gln Val Leu Tyr Gly Gln Leu Leu Gly
770 775 780
Ser Pro Thr Ser Pro Gly Pro Gly His Tyr Leu Arg Cys Asp Ser Thr
785 790 795 800
Gln Pro Leu Leu Ala Gly Leu Thr Pro Ser Pro Lys Ser Tyr Glu Asn
805 810 815
Leu Trp Phe Gln Ala Ser Pro Leu Gly Thr Leu Val Thr Pro Ala Pro
820 825 830
Ser Gln Glu Asp Asp Cys Val Phe Gly Pro Leu Leu Asn Phe Pro Leu
835 840 845
Leu Gln Gly Ile Arg Val His Gly Met Glu Ala Leu Gly Ser Phe
850 855 860

<210> 26
<211> 635
<212> PRT
<213> 智人 (Homo sapiens)
<400> 26

[0019]
Met Pro Ser Trp Ala Leu Phe Met Val Thr Ser Cys Leu Leu Leu Ala
1 5 10 15
Pro Gln Asn Leu Ala Gln Val Ser Ser Gln Asp Val Ser Leu Leu Ala
20 25 30
Ser Asp Ser Glu Pro Leu Lys Cys Phe Ser Arg Thr Phe Glu Asp Leu
35 40 45
Thr Cys Phe Trp Asp Glu Glu Glu Ala Ala Pro Ser Gly Thr Tyr Gln
50 55 60
Leu Leu Tyr Ala Tyr Pro Arg Glu Lys Pro Arg Ala Cys Pro Leu Ser
65 70 75 80
Ser Gln Ser Met Pro His Phe Gly Thr Arg Tyr Val Cys Gln Phe Pro
85 90 95
Asp Gln Glu Glu Val Arg Leu Phe Phe Pro Leu His Leu Trp Val Lys
100 105 110
Asn Val Phe Leu Asn Gln Thr Arg Thr Gln Arg Val Leu Phe Val Asp
115 120 125
Ser Val Gly Leu Pro Ala Pro Pro Ser Ile Ile Lys Ala Met Gly Gly
130 135 140
Ser Gln Pro Gly Glu Leu Gln Ile Ser Trp Glu Glu Pro Ala Pro Glu
145 150 155 160
Ile Ser Asp Phe Leu Arg Tyr Glu Leu Arg Tyr Gly Pro Arg Asp Pro
165 170 175
Lys Asn Ser Thr Gly Pro Thr Val Ile Gln Leu Ile Ala Thr Glu Thr
180 185 190
Cys Cys Pro Ala Leu Gln Arg Pro His Ser Ala Ser Ala Leu Asp Gln
195 200 205

Ser Pro Cys Ala Gln Pro Thr Met Pro Trp Gln Asp Gly Pro Lys Gln
210 215 220
Thr Ser Pro Ser Arg Glu Ala Ser Ala Leu Thr Ala Glu Gly Gly Ser
225 230 235 240
Cys Leu Ile Ser Gly Leu Gln Pro Gly Asn Ser Tyr Trp Leu Gln Leu
245 250 255
Arg Ser Glu Pro Asp Gly Ile Ser Leu Gly Gly Ser Trp Gly Ser Trp
260 265 270
Ser Leu Pro Val Thr Val Asp Leu Pro Gly Asp Ala Val Ala Leu Gly
275 280 285
Leu Gln Cys Phe Thr Leu Asp Leu Lys Asn Val Thr Cys Gln Trp Gln
290 295 300
Gln Gln Asp His Ala Ser Ser Gln Gly Phe Phe Tyr His Ser Arg Ala
305 310 315 320
Arg Cys Cys Pro Arg Asp Arg Tyr Pro Ile Trp Glu Asn Cys Glu Glu
325 330 335
Glu Glu Lys Thr Asn Pro Gly Leu Gln Thr Pro Gln Phe Ser Arg Cys
340 345 350
His Phe Lys Ser Arg Asn Asp Ser Ile Ile His Ile Leu Val Glu Val
355 360 365
Thr Thr Ala Pro Gly Thr Val His Ser Tyr Leu Gly Ser Pro Phe Trp
370 375 380
Ile His Gln Ala Val Arg Leu Pro Thr Pro Asn Leu His Trp Arg Glu
385 390 395 400
Ile Ser Ser Gly His Leu Glu Leu Glu Trp Gln His Pro Ser Ser Trp
[0020] 405 410 415
Ala Ala Gln Glu Thr Cys Tyr Gln Leu Arg Tyr Thr Gly Glu Gly His
420 425 430
Gln Asp Trp Lys Val Leu Glu Pro Pro Leu Gly Ala Arg Gly Gly Thr
435 440 445
Leu Glu Leu Arg Pro Arg Ser Arg Tyr Arg Leu Gln Leu Arg Ala Arg
450 455 460
Leu Asn Gly Pro Thr Tyr Gln Gly Pro Trp Ser Ser Trp Ser Asp Pro
465 470 475 480
Thr Arg Val Glu Thr Ala Thr Glu Thr Ala Trp Ile Ser Leu Val Thr
485 490 495
Ala Leu His Leu Val Leu Gly Leu Ser Ala Val Leu Gly Leu Leu Leu
500 505 510
Leu Arg Trp Gln Phe Pro Ala His Tyr Arg Arg Leu Arg His Ala Leu
515 520 525
Trp Pro Ser Leu Pro Asp Leu His Arg Val Leu Gly Gln Tyr Leu Arg
530 535 540
Asp Thr Ala Ala Leu Ser Pro Pro Lys Ala Thr Val Ser Asp Thr Cys
545 550 555 560
Glu Glu Val Glu Pro Ser Leu Leu Glu Ile Leu Pro Lys Ser Ser Glu
565 570 575
Arg Thr Pro Leu Pro Leu Cys Ser Ser Gln Ala Gln Met Asp Tyr Arg
580 585 590
Arg Leu Gln Pro Ser Cys Leu Gly Thr Met Pro Leu Ser Val Cys Pro
595 600 605
Pro Met Ala Glu Ser Gly Ser Cys Cys Thr Thr His Ile Ala Asn His

610 615 620
Ser Tyr Leu Pro Leu Ser Tyr Trp Gln Gln Pro
625 630 635
<210> 27
<211> 97
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 27
Leu Thr Leu Met Thr Leu Thr Pro Glu Gly Ser Glu Leu His Ile Ile
1 5 10 15
Leu Gly Leu Phe Gly Leu Leu Leu Leu Leu Thr Cys Leu Cys Gly Thr
20 25 30
Ala Trp Leu Cys Cys Ser Pro Asn Arg Lys Asn Pro Leu Trp Pro Ser
35 40 45
Val Pro Asp Pro Ala His Ser Ser Leu Gly Ser Trp Val Pro Thr Ile
50 55 60
Met Glu Glu Asp Ala Phe Gln Leu Pro Gly Leu Gly Thr Pro Pro Ile
65 70 75 80
Thr Lys Leu Thr Val Leu Glu Glu Asp Glu Lys Lys Pro Val Pro Trp
85 90 95
Glu

[0021] <210> 28
<211> 92
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 28
Thr Thr Pro Lys Phe Ala Gln Gly Glu Ile Glu Ala Ile Val Val Pro
1 5 10 15
Val Cys Leu Ala Phe Leu Leu Thr Thr Leu Leu Gly Val Leu Phe Cys
20 25 30
Phe Asn Lys Arg Asp Leu Ile Lys Lys His Ile Trp Pro Asn Val Pro
35 40 45
Asp Pro Ser Lys Ser His Ile Ala Gln Trp Ser Pro His Thr Pro Pro
50 55 60
Arg His Asn Phe Asn Ser Lys Asp Gln Met Tyr Ser Asp Gly Asn Phe
65 70 75 80
Thr Asp Val Ser Val Val Glu Ile Glu Ala Asn Asp
85 90
<210> 29
<211> 105
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
<221> source

<223> /注释 = “人工序列的描述：合成多肽”
<400> 29
Ser Asp Pro Thr Arg Val Glu Thr Ala Thr Glu Thr Ala Trp Ile Ser
1 5 10 15
Leu Val Thr Ala Leu His Leu Val Leu Gly Leu Ser Ala Val Leu Gly
20 25 30
Leu Leu Leu Leu Arg Trp Gln Phe Pro Ala His Tyr Arg Arg Leu Arg
35 40 45
His Ala Leu Trp Pro Ser Leu Pro Asp Leu His Arg Val Leu Gly Gln
50 55 60
Tyr Leu Arg Asp Thr Ala Ala Leu Ser Pro Pro Lys Ala Thr Val Ser
65 70 75 80
Asp Thr Cys Glu Glu Val Glu Pro Ser Leu Leu Glu Ile Leu Pro Lys
85 90 95
Ser Ser Glu Arg Thr Pro Leu Pro Leu
100 105
<210> 30
<211> 104
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 30
Ser Asp Pro Thr Arg Val Glu Thr Ala Thr Glu Thr Trp Ile Ser Leu
[0022] 1 5 10 15
Val Thr Ala Leu His Leu Val Leu Gly Leu Ser Ala Val Leu Gly Leu
20 25 30
Leu Leu Leu Arg Trp Gln Phe Pro Ala His Tyr Arg Arg Leu Arg His
35 40 45
Ala Leu Trp Pro Ser Leu Pro Asp Leu His Arg Val Leu Gly Gln Tyr
50 55 60
Leu Arg Asp Thr Ala Ala Leu Ser Pro Pro Lys Ala Thr Val Ser Asp
65 70 75 80
Thr Cys Glu Glu Val Glu Pro Ser Leu Leu Glu Ile Leu Pro Lys Ser
85 90 95
Ser Glu Arg Thr Pro Leu Pro Leu
100
<210> 31
<211> 103
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 31
Ser Asp Pro Thr Arg Val Glu Thr Ala Thr Glu Thr Ile Ser Leu Val
1 5 10 15
Thr Ala Leu His Leu Val Leu Gly Leu Ser Ala Val Leu Gly Leu Leu
20 25 30
Leu Leu Arg Trp Gln Phe Pro Ala His Tyr Arg Arg Leu Arg His Ala

35 40 45
Leu Trp Pro Ser Leu Pro Asp Leu His Arg Val Leu Gly Gln Tyr Leu
50 55 60
Arg Asp Thr Ala Ala Leu Ser Pro Pro Lys Ala Thr Val Ser Asp Thr
65 70 75 80
Cys Glu Glu Val Glu Pro Ser Leu Leu Glu Ile Leu Pro Lys Ser Ser
85 90 95
Glu Arg Thr Pro Leu Pro Leu
100

<210> 32
<211> 104
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 32
Ser Asp Pro Thr Arg Val Glu Thr Ala Thr Glu Thr Leu Ile Ser Leu
1 5 10 15
Val Thr Ala Leu His Leu Val Leu Gly Leu Ser Ala Val Leu Gly Leu
20 25 30
Leu Leu Leu Arg Trp Gln Phe Pro Ala His Tyr Arg Arg Leu Arg His
35 40 45
Ala Leu Trp Pro Ser Leu Pro Asp Leu His Arg Val Leu Gly Gln Tyr
50 55 60

[0023]
Leu Arg Asp Thr Ala Ala Leu Ser Pro Pro Lys Ala Thr Val Ser Asp
65 70 75 80
Thr Cys Glu Glu Val Glu Pro Ser Leu Leu Glu Ile Leu Pro Lys Ser
85 90 95
Ser Glu Arg Thr Pro Leu Pro Leu
100

<210> 33
<211> 102
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 33
Ser Asp Pro Thr Arg Val Glu Thr Ala Thr Glu Thr Ser Leu Val Thr
1 5 10 15
Ala Leu His Leu Val Leu Gly Leu Ser Ala Val Leu Gly Leu Leu Leu
20 25 30
Leu Arg Trp Gln Phe Pro Ala His Tyr Arg Arg Leu Arg His Ala Leu
35 40 45
Trp Pro Ser Leu Pro Asp Leu His Arg Val Leu Gly Gln Tyr Leu Arg
50 55 60
Asp Thr Ala Ala Leu Ser Pro Pro Lys Ala Thr Val Ser Asp Thr Cys
65 70 75 80
Glu Glu Val Glu Pro Ser Leu Leu Glu Ile Leu Pro Lys Ser Ser Glu
85 90 95

Arg Thr Pro Leu Pro Leu
100

<210> 34
<211> 101
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 34

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

<210> 35
[0024] <211> 102
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 35

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

<210> 36
<211> 100
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>

<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 36
Ser Asp Pro Thr Arg Val Glu Thr Ala Thr Glu Thr Val Thr Ala Leu
1 5 10 15
His Leu Val Leu Gly Leu Ser Ala Val Leu Gly Leu Leu Leu Leu Arg
20 25 30
Trp Gln Phe Pro Ala His Tyr Arg Arg Leu Arg His Ala Leu Trp Pro
35 40 45
Ser Leu Pro Asp Leu His Arg Val Leu Gly Gln Tyr Leu Arg Asp Thr
50 55 60
Ala Ala Leu Ser Pro Pro Lys Ala Thr Val Ser Asp Thr Cys Glu Glu
65 70 75 80
Val Glu Pro Ser Leu Leu Glu Ile Leu Pro Lys Ser Ser Glu Arg Thr
85 90 95
Pro Leu Pro Leu
100
<210> 37
<211> 99
<212> PRT
<213> 人工序列（Artificial Sequence）
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 37

[0025]
Ser Asp Pro Thr Arg Val Glu Thr Ala Thr Glu Thr Thr Ala Leu His
1 5 10 15
Leu Val Leu Gly Leu Ser Ala Val Leu Gly Leu Leu Leu Leu Arg Trp
20 25 30
Gln Phe Pro Ala His Tyr Arg Arg Leu Arg His Ala Leu Trp Pro Ser
35 40 45
Leu Pro Asp Leu His Arg Val Leu Gly Gln Tyr Leu Arg Asp Thr Ala
50 55 60
Ala Leu Ser Pro Pro Lys Ala Thr Val Ser Asp Thr Cys Glu Glu Val
65 70 75 80
Glu Pro Ser Leu Leu Glu Ile Leu Pro Lys Ser Ser Glu Arg Thr Pro
85 90 95
Leu Pro Leu

<210> 38
<211> 98
<212> PRT
<213> 人工序列（Artificial Sequence）
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 38
Ser Asp Pro Thr Arg Val Glu Thr Ala Thr Glu Thr Ala Leu His Leu
1 5 10 15
Val Leu Gly Leu Ser Ala Val Leu Gly Leu Leu Leu Leu Arg Trp Gln
20 25 30

Phe Pro Ala His Tyr Arg Arg Leu Arg His Ala Leu Trp Pro Ser Leu
35 40 45
Pro Asp Leu His Arg Val Leu Gly Gln Tyr Leu Arg Asp Thr Ala Ala
50 55 60
Leu Ser Pro Pro Lys Ala Thr Val Ser Asp Thr Cys Glu Glu Val Glu
65 70 75 80
Pro Ser Leu Leu Glu Ile Leu Pro Lys Ser Ser Glu Arg Thr Pro Leu
85 90 95
Pro Leu

<210> 39
<211> 97
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 39
Ser Asp Pro Thr Arg Val Glu Thr Ala Thr Glu Thr Leu His Leu Val
1 5 10 15
Leu Gly Leu Ser Ala Val Leu Gly Leu Leu Leu Leu Arg Trp Gln Phe
20 25 30
Pro Ala His Tyr Arg Arg Leu Arg His Ala Leu Trp Pro Ser Leu Pro
35 40 45
Asp Leu His Arg Val Leu Gly Gln Tyr Leu Arg Asp Thr Ala Ala Leu
[0026] 50 55 60
Ser Pro Pro Lys Ala Thr Val Ser Asp Thr Cys Glu Glu Val Glu Pro
65 70 75 80
Ser Leu Leu Glu Ile Leu Pro Lys Ser Ser Glu Arg Thr Pro Leu Pro
85 90 95
Leu

<210> 40
<211> 96
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 40
Ser Asp Pro Thr Arg Val Glu Thr Ala Thr Glu Thr His Leu Val Leu
1 5 10 15
Gly Leu Ser Ala Val Leu Gly Leu Leu Leu Leu Arg Trp Gln Phe Pro
20 25 30
Ala His Tyr Arg Arg Leu Arg His Ala Leu Trp Pro Ser Leu Pro Asp
35 40 45
Leu His Arg Val Leu Gly Gln Tyr Leu Arg Asp Thr Ala Ala Leu Ser
50 55 60
Pro Pro Lys Ala Thr Val Ser Asp Thr Cys Glu Glu Val Glu Pro Ser
65 70 75 80
Leu Leu Glu Ile Leu Pro Lys Ser Ser Glu Arg Thr Pro Leu Pro Leu

85 90 95

<210> 41
<211> 95
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 41

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

<210> 42
<211> 94
<212> PRT
<213> 人工序列 (Artificial Sequence)

[0027]

<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 42

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

<210> 43
<211> 93
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 43

Ser Asp Pro Thr Arg Val Glu Thr Ala Thr Glu Thr Leu Gly Leu Ser
1 5 10 15

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

<210> 44
<211> 92
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 44
Ser Asp Pro Thr Arg Val Glu Thr Ala Thr Glu Thr Gly Leu Ser Ala
1 5 10 15
Val Leu Gly Leu Leu Leu Leu Arg Trp Gln Phe Pro Ala His Tyr Arg
20 25 30
Arg Leu Arg His Ala Leu Trp Pro Ser Leu Pro Asp Leu His Arg Val
35 40 45
Leu Gly Gln Tyr Leu Arg Asp Thr Ala Ala Leu Ser Pro Pro Lys Ala
[0028] 50 55 60
Thr Val Ser Asp Thr Cys Glu Glu Val Glu Pro Ser Leu Leu Glu Ile
65 70 75 80
Leu Pro Lys Ser Ser Glu Arg Thr Pro Leu Pro Leu
85 90

<210> 45
<211> 91
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 45
Ser Asp Pro Thr Arg Val Glu Thr Ala Thr Glu Thr Leu Ser Ala Val
1 5 10 15
Leu Gly Leu Leu Leu Leu Arg Trp Gln Phe Pro Ala His Tyr Arg Arg
20 25 30
Leu Arg His Ala Leu Trp Pro Ser Leu Pro Asp Leu His Arg Val Leu
35 40 45
Gly Gln Tyr Leu Arg Asp Thr Ala Ala Leu Ser Pro Pro Lys Ala Thr
50 55 60
Val Ser Asp Thr Cys Glu Glu Val Glu Pro Ser Leu Leu Glu Ile Leu
65 70 75 80
Pro Lys Ser Ser Glu Arg Thr Pro Leu Pro Leu
85 90

<210> 46

<210> 90
<211> PRT
<212> 人工序列 (Artificial Sequence)
<213>
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 46
Ser Asp Pro Thr Arg Val Glu Thr Ala Thr Glu Thr Ser Ala Val Leu
1 5 10 15
Gly Leu Leu Leu Leu Arg Trp Gln Phe Pro Ala His Tyr Arg Arg Leu
20 25 30
Arg His Ala Leu Trp Pro Ser Leu Pro Asp Leu His Arg Val Leu Gly
35 40 45
Gln Tyr Leu Arg Asp Thr Ala Ala Leu Ser Pro Pro Lys Ala Thr Val
50 55 60
Ser Asp Thr Cys Glu Glu Val Glu Pro Ser Leu Leu Glu Ile Leu Pro
65 70 75 80
Lys Ser Ser Glu Arg Thr Pro Leu Pro Leu
85 90
<210> 47
<211> 89
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
<221> source
[0029] <223> /注释 = “人工序列的描述：合成多肽”
<400> 47
Ser Asp Pro Thr Arg Val Glu Thr Ala Thr Glu Thr Ala Val Leu Gly
1 5 10 15
Leu Leu Leu Leu Arg Trp Gln Phe Pro Ala His Tyr Arg Arg Leu Arg
20 25 30
His Ala Leu Trp Pro Ser Leu Pro Asp Leu His Arg Val Leu Gly Gln
35 40 45
Tyr Leu Arg Asp Thr Ala Ala Leu Ser Pro Pro Lys Ala Thr Val Ser
50 55 60
Asp Thr Cys Glu Glu Val Glu Pro Ser Leu Leu Glu Ile Leu Pro Lys
65 70 75 80
Ser Ser Glu Arg Thr Pro Leu Pro Leu
85
<210> 48
<211> 88
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 48
Ser Asp Pro Thr Arg Val Glu Thr Ala Thr Glu Thr Val Leu Gly Leu
1 5 10 15
Leu Leu Leu Arg Trp Gln Phe Pro Ala His Tyr Arg Arg Leu Arg His
20 25 30

Ala Leu Trp Pro Ser Leu Pro Asp Leu His Arg Val Leu Gly Gln Tyr
35 40 45
Leu Arg Asp Thr Ala Ala Leu Ser Pro Pro Lys Ala Thr Val Ser Asp
50 55 60
Thr Cys Glu Glu Val Glu Pro Ser Leu Leu Glu Ile Leu Pro Lys Ser
65 70 75 80
Ser Glu Arg Thr Pro Leu Pro Leu
85

<210> 49
<211> 87
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 49
Ser Asp Pro Thr Arg Val Glu Thr Ala Thr Glu Thr Leu Gly Leu Leu
1 5 10 15
Leu Leu Arg Trp Gln Phe Pro Ala His Tyr Arg Arg Leu Arg His Ala
20 25 30
Leu Trp Pro Ser Leu Pro Asp Leu His Arg Val Leu Gly Gln Tyr Leu
35 40 45
Arg Asp Thr Ala Ala Leu Ser Pro Pro Lys Ala Thr Val Ser Asp Thr
50 55 60
Cys Glu Glu Val Glu Pro Ser Leu Leu Glu Ile Leu Pro Lys Ser Ser
[0030] 65 70 75 80
Glu Arg Thr Pro Leu Pro Leu
85

<210> 50
<211> 106
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 50
Ser Asp Pro Thr Arg Val Glu Thr Ala Thr Glu Thr Ala Trp Leu Ile
1 5 10 15
Ser Leu Val Thr Ala Leu His Leu Val Leu Gly Leu Ser Ala Val Leu
20 25 30
Gly Leu Leu Leu Leu Arg Trp Gln Phe Pro Ala His Tyr Arg Arg Leu
35 40 45
Arg His Ala Leu Trp Pro Ser Leu Pro Asp Leu His Arg Val Leu Gly
50 55 60
Gln Tyr Leu Arg Asp Thr Ala Ala Leu Ser Pro Pro Lys Ala Thr Val
65 70 75 80
Ser Asp Thr Cys Glu Glu Val Glu Pro Ser Leu Leu Glu Ile Leu Pro
85 90 95
Lys Ser Ser Glu Arg Thr Pro Leu Pro Leu
100 105

<210> 51

<211> 107
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 51
Ser Asp Pro Thr Arg Val Glu Thr Ala Thr Glu Thr Ala Trp Val Leu
1 5 10 15
Ile Ser Leu Val Thr Ala Leu His Leu Val Leu Gly Leu Ser Ala Val
20 25 30
Leu Gly Leu Leu Leu Leu Arg Trp Gln Phe Pro Ala His Tyr Arg Arg
35 40 45
Leu Arg His Ala Leu Trp Pro Ser Leu Pro Asp Leu His Arg Val Leu
50 55 60
Gly Gln Tyr Leu Arg Asp Thr Ala Ala Leu Ser Pro Pro Lys Ala Thr
65 70 75 80
Val Ser Asp Thr Cys Glu Glu Val Glu Pro Ser Leu Leu Glu Ile Leu
85 90 95
Pro Lys Ser Ser Glu Arg Thr Pro Leu Pro Leu
100 105
<210> 52
<211> 108
<212> PRT
<213> 人工序列 (Artificial Sequence)
[0031] <220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 52
Ser Asp Pro Thr Arg Val Glu Thr Ala Thr Glu Thr Ala Trp Leu Val
1 5 10 15
Leu Ile Ser Leu Val Thr Ala Leu His Leu Val Leu Gly Leu Ser Ala
20 25 30
Val Leu Gly Leu Leu Leu Leu Arg Trp Gln Phe Pro Ala His Tyr Arg
35 40 45
Arg Leu Arg His Ala Leu Trp Pro Ser Leu Pro Asp Leu His Arg Val
50 55 60
Leu Gly Gln Tyr Leu Arg Asp Thr Ala Ala Leu Ser Pro Pro Lys Ala
65 70 75 80
Thr Val Ser Asp Thr Cys Glu Glu Val Glu Pro Ser Leu Leu Glu Ile
85 90 95
Leu Pro Lys Ser Ser Glu Arg Thr Pro Leu Pro Leu
100 105
<210> 53
<211> 109
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 53

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

<210> 54
<211> 110
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 54

[0032]

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

<210> 55
<211> 111
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 55
Ser Asp Pro Thr Arg Val Glu Thr Ala Thr Glu Thr Ala Trp Leu Leu
1 5 10 15
Ile Leu Val Leu Ile Ser Leu Val Thr Ala Leu His Leu Val Leu Gly
20 25 30
Leu Ser Ala Val Leu Gly Leu Leu Leu Leu Arg Trp Gln Phe Pro Ala
35 40 45
His Tyr Arg Arg Leu Arg His Ala Leu Trp Pro Ser Leu Pro Asp Leu

50 55 60
His Arg Val Leu Gly Gln Tyr Leu Arg Asp Thr Ala Ala Leu Ser Pro
65 70 75 80
Pro Lys Ala Thr Val Ser Asp Thr Cys Glu Glu Val Glu Pro Ser Leu
85 90 95
Leu Glu Ile Leu Pro Lys Ser Ser Glu Arg Thr Pro Leu Pro Leu
100 105 110

<210> 56
<211> 112
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 56
Ser Asp Pro Thr Arg Val Glu Thr Ala Thr Glu Thr Ala Trp Val Leu
1 5 10 15
Leu Ile Leu Val Leu Ile Ser Leu Val Thr Ala Leu His Leu Val Leu
20 25 30
Gly Leu Ser Ala Val Leu Gly Leu Leu Leu Leu Arg Trp Gln Phe Pro
35 40 45
Ala His Tyr Arg Arg Leu Arg His Ala Leu Trp Pro Ser Leu Pro Asp
50 55 60
Leu His Arg Val Leu Gly Gln Tyr Leu Arg Asp Thr Ala Ala Leu Ser
65 70 75 80
[0033] Pro Pro Lys Ala Thr Val Ser Asp Thr Cys Glu Glu Val Glu Pro Ser
85 90 95
Leu Leu Glu Ile Leu Pro Lys Ser Ser Glu Arg Thr Pro Leu Pro Leu
100 105 110

<210> 57
<211> 113
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 57
Ser Asp Pro Thr Arg Val Glu Thr Ala Thr Glu Thr Ala Trp Leu Val
1 5 10 15
Leu Leu Ile Leu Val Leu Ile Ser Leu Val Thr Ala Leu His Leu Val
20 25 30
Leu Gly Leu Ser Ala Val Leu Gly Leu Leu Leu Leu Arg Trp Gln Phe
35 40 45
Pro Ala His Tyr Arg Arg Leu Arg His Ala Leu Trp Pro Ser Leu Pro
50 55 60
Asp Leu His Arg Val Leu Gly Gln Tyr Leu Arg Asp Thr Ala Ala Leu
65 70 75 80
Ser Pro Pro Lys Ala Thr Val Ser Asp Thr Cys Glu Glu Val Glu Pro
85 90 95
Ser Leu Leu Glu Ile Leu Pro Lys Ser Ser Glu Arg Thr Pro Leu Pro
100 105 110

Leu

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

<210> 59
[0034] <211> 105
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 59
Ser Asp Pro Thr Arg Val Glu Thr Ala Thr Glu Thr Ala Trp Ile Ser
1 5 10 15
Leu Val Thr Ala Leu Leu Leu Val Leu Gly Leu Asn Ala Val Leu Gly
20 25 30
Leu Leu Leu Leu Arg Lys Gln Phe Pro Ala His Tyr Arg Arg Leu Arg
35 40 45
His Ala Leu Trp Pro Ser Leu Pro Asp Leu His Arg Val Leu Gly Gln
50 55 60
Tyr Leu Arg Asp Thr Ala Ala Leu Ser Pro Pro Lys Ala Thr Val Ser
65 70 75 80
Asp Thr Cys Glu Glu Val Glu Pro Ser Leu Leu Glu Ile Leu Pro Lys
85 90 95
Ser Ser Glu Arg Thr Pro Leu Pro Leu
100 105

<210> 60
<211> 105
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>

<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 60
Ser Asp Pro Thr Arg Val Glu Thr Ala Thr Glu Thr Ala Trp Ile Ser
1 5 10 15
Leu Val Thr Ala Leu His Leu Val Leu Gly Leu Asn Ala Val Leu Gly
20 25 30
Leu Leu Leu Leu Arg Lys Gln Phe Pro Ala His Tyr Arg Arg Leu Arg
35 40 45
His Ala Leu Trp Pro Ser Leu Pro Asp Leu His Arg Val Leu Gly Gln
50 55 60
Tyr Leu Arg Asp Thr Ala Ala Leu Ser Pro Pro Lys Ala Thr Val Ser
65 70 75 80
Asp Thr Cys Glu Glu Val Glu Pro Ser Leu Leu Glu Ile Leu Pro Lys
85 90 95
Ser Ser Glu Arg Thr Pro Leu Pro Leu
100 105
<210> 61
<211> 95
<212> PRT
<213> 人工序列（Artificial Sequence）
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 61
[0035] Ser Asp Pro Thr Arg Val Glu Thr Ala Thr Glu His Leu Val Leu Gly
1 5 10 15
Leu Ser Ala Val Leu Gly Leu Leu Leu Leu Arg Trp Gln Phe Pro Ala
20 25 30
His Tyr Arg Arg Leu Arg His Ala Leu Trp Pro Ser Leu Pro Asp Leu
35 40 45
His Arg Val Leu Gly Gln Tyr Leu Arg Asp Thr Ala Ala Leu Ser Pro
50 55 60
Pro Lys Ala Thr Val Ser Asp Thr Cys Glu Glu Val Glu Pro Ser Leu
65 70 75 80
Leu Glu Ile Leu Pro Lys Ser Ser Glu Arg Thr Pro Leu Pro Leu
85 90 95
<210> 62
<211> 94
<212> PRT
<213> 人工序列（Artificial Sequence）
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 62
Ser Asp Pro Thr Arg Val Glu Thr Ala Thr His Leu Val Leu Gly Leu
1 5 10 15
Ser Ala Val Leu Gly Leu Leu Leu Leu Arg Trp Gln Phe Pro Ala His
20 25 30
Tyr Arg Arg Leu Arg His Ala Leu Trp Pro Ser Leu Pro Asp Leu His
35 40 45

Arg Val Leu Gly Gln Tyr Leu Arg Asp Thr Ala Ala Leu Ser Pro Pro
50 55 60
Lys Ala Thr Val Ser Asp Thr Cys Glu Glu Val Glu Pro Ser Leu Leu
65 70 75 80
Glu Ile Leu Pro Lys Ser Ser Glu Arg Thr Pro Leu Pro Leu
85 90

<210> 63
<211> 93
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 63
Ser Asp Pro Thr Arg Val Glu Thr Ala His Leu Val Leu Gly Leu Ser
1 5 10 15
Ala Val Leu Gly Leu Leu Leu Leu Arg Trp Gln Phe Pro Ala His Tyr
20 25 30
Arg Arg Leu Arg His Ala Leu Trp Pro Ser Leu Pro Asp Leu His Arg
35 40 45
Val Leu Gly Gln Tyr Leu Arg Asp Thr Ala Ala Leu Ser Pro Pro Lys
50 55 60
Ala Thr Val Ser Asp Thr Cys Glu Glu Val Glu Pro Ser Leu Leu Glu
65 70 75 80
Ile Leu Pro Lys Ser Ser Glu Arg Thr Pro Leu Pro Leu
85 90

[0036]

<210> 64
<211> 92
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 64
Ser Asp Pro Thr Arg Val Glu Thr His Leu Val Leu Gly Leu Ser Ala
1 5 10 15
Val Leu Gly Leu Leu Leu Leu Arg Trp Gln Phe Pro Ala His Tyr Arg
20 25 30
Arg Leu Arg His Ala Leu Trp Pro Ser Leu Pro Asp Leu His Arg Val
35 40 45
Leu Gly Gln Tyr Leu Arg Asp Thr Ala Ala Leu Ser Pro Pro Lys Ala
50 55 60
Thr Val Ser Asp Thr Cys Glu Glu Val Glu Pro Ser Leu Leu Glu Ile
65 70 75 80
Leu Pro Lys Ser Ser Glu Arg Thr Pro Leu Pro Leu
85 90

<210> 65
<211> 91
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>

<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 65
Ser Asp Pro Thr Arg Val Glu His Leu Val Leu Gly Leu Ser Ala Val
1 5 10 15
Leu Gly Leu Leu Leu Leu Arg Trp Gln Phe Pro Ala His Tyr Arg Arg
20 25 30
Leu Arg His Ala Leu Trp Pro Ser Leu Pro Asp Leu His Arg Val Leu
35 40 45
Gly Gln Tyr Leu Arg Asp Thr Ala Ala Leu Ser Pro Pro Lys Ala Thr
50 55 60
Val Ser Asp Thr Cys Glu Glu Val Glu Pro Ser Leu Leu Glu Ile Leu
65 70 75 80
Pro Lys Ser Ser Glu Arg Thr Pro Leu Pro Leu
85 90
<210> 66
<211> 90
<212> PRT
<213> 人工序列（Artificial Sequence）
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 66
Ser Asp Pro Thr Arg Val His Leu Val Leu Gly Leu Ser Ala Val Leu
1 5 10 15
[0037] Gly Leu Leu Leu Leu Arg Trp Gln Phe Pro Ala His Tyr Arg Arg Leu
20 25 30
Arg His Ala Leu Trp Pro Ser Leu Pro Asp Leu His Arg Val Leu Gly
35 40 45
Gln Tyr Leu Arg Asp Thr Ala Ala Leu Ser Pro Pro Lys Ala Thr Val
50 55 60
Ser Asp Thr Cys Glu Glu Val Glu Pro Ser Leu Leu Glu Ile Leu Pro
65 70 75 80
Lys Ser Ser Glu Arg Thr Pro Leu Pro Leu
85 90
<210> 67
<211> 89
<212> PRT
<213> 人工序列（Artificial Sequence）
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 67
Ser Asp Pro Thr Arg His Leu Val Leu Gly Leu Ser Ala Val Leu Gly
1 5 10 15
Leu Leu Leu Leu Arg Trp Gln Phe Pro Ala His Tyr Arg Arg Leu Arg
20 25 30
His Ala Leu Trp Pro Ser Leu Pro Asp Leu His Arg Val Leu Gly Gln
35 40 45
Tyr Leu Arg Asp Thr Ala Ala Leu Ser Pro Pro Lys Ala Thr Val Ser
50 55 60

Asp Thr Cys Glu Glu Val Glu Pro Ser Leu Leu Glu Ile Leu Pro Lys
65 70 75 80
Ser Ser Glu Arg Thr Pro Leu Pro Leu
85

<210> 68
<211> 88
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 68
Ser Asp Pro Thr His Leu Val Leu Gly Leu Ser Ala Val Leu Gly Leu
1 5 10 15
Leu Leu Leu Arg Trp Gln Phe Pro Ala His Tyr Arg Arg Leu Arg His
20 25 30
Ala Leu Trp Pro Ser Leu Pro Asp Leu His Arg Val Leu Gly Gln Tyr
35 40 45
Leu Arg Asp Thr Ala Ala Leu Ser Pro Pro Lys Ala Thr Val Ser Asp
50 55 60
Thr Cys Glu Glu Val Glu Pro Ser Leu Leu Glu Ile Leu Pro Lys Ser
65 70 75 80
Ser Glu Arg Thr Pro Leu Pro Leu
85

<210> 69
[0038] <211> 87
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 69
Ser Asp Pro His Leu Val Leu Gly Leu Ser Ala Val Leu Gly Leu Leu
1 5 10 15
Leu Leu Arg Trp Gln Phe Pro Ala His Tyr Arg Arg Leu Arg His Ala
20 25 30
Leu Trp Pro Ser Leu Pro Asp Leu His Arg Val Leu Gly Gln Tyr Leu
35 40 45
Arg Asp Thr Ala Ala Leu Ser Pro Pro Lys Ala Thr Val Ser Asp Thr
50 55 60
Cys Glu Glu Val Glu Pro Ser Leu Leu Glu Ile Leu Pro Lys Ser Ser
65 70 75 80
Glu Arg Thr Pro Leu Pro Leu
85

<210> 70
<211> 86
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”

<400> 70
Ser Asp His Leu Val Leu Gly Leu Ser Ala Val Leu Gly Leu Leu Leu
1 5 10 15
Leu Arg Trp Gln Phe Pro Ala His Tyr Arg Arg Leu Arg His Ala Leu
20 25 30
Trp Pro Ser Leu Pro Asp Leu His Arg Val Leu Gly Gln Tyr Leu Arg
35 40 45
Asp Thr Ala Ala Leu Ser Pro Pro Lys Ala Thr Val Ser Asp Thr Cys
50 55 60
Glu Glu Val Glu Pro Ser Leu Leu Glu Ile Leu Pro Lys Ser Ser Glu
65 70 75 80
Arg Thr Pro Leu Pro Leu
85
<210> 71
<211> 85
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 71
Ser His Leu Val Leu Gly Leu Ser Ala Val Leu Gly Leu Leu Leu Leu
1 5 10 15
Arg Trp Gln Phe Pro Ala His Tyr Arg Arg Leu Arg His Ala Leu Trp
20 25 30
[0039] Pro Ser Leu Pro Asp Leu His Arg Val Leu Gly Gln Tyr Leu Arg Asp
35 40 45
Thr Ala Ala Leu Ser Pro Pro Lys Ala Thr Val Ser Asp Thr Cys Glu
50 55 60
Glu Val Glu Pro Ser Leu Leu Glu Ile Leu Pro Lys Ser Ser Glu Arg
65 70 75 80
Thr Pro Leu Pro Leu
85
<210> 72
<211> 84
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 72
His Leu Val Leu Gly Leu Ser Ala Val Leu Gly Leu Leu Leu Leu Arg
1 5 10 15
Trp Gln Phe Pro Ala His Tyr Arg Arg Leu Arg His Ala Leu Trp Pro
20 25 30
Ser Leu Pro Asp Leu His Arg Val Leu Gly Gln Tyr Leu Arg Asp Thr
35 40 45
Ala Ala Leu Ser Pro Pro Lys Ala Thr Val Ser Asp Thr Cys Glu Glu
50 55 60
Val Glu Pro Ser Leu Leu Glu Ile Leu Pro Lys Ser Ser Glu Arg Thr
65 70 75 80

Pro Leu Pro Leu

<210> 73
<211> 102
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 73
Ser Asp Pro Thr Arg Val Glu Thr Ala Thr Glu Thr Ala Trp Ile Ser
1 5 10 15
Leu Val His Leu Val Leu Gly Leu Ser Ala Val Leu Gly Leu Leu Leu
20 25 30
Leu Arg Trp Gln Phe Pro Ala His Tyr Arg Arg Leu Arg His Ala Leu
35 40 45
Trp Pro Ser Leu Pro Asp Leu His Arg Val Leu Gly Gln Tyr Leu Arg
50 55 60
Asp Thr Ala Ala Leu Ser Pro Pro Lys Ala Thr Val Ser Asp Thr Cys
65 70 75 80
Glu Glu Val Glu Pro Ser Leu Leu Glu Ile Leu Pro Lys Ser Ser Glu
85 90 95
Arg Thr Pro Leu Pro Leu
100

[0040]
<210> 74
<211> 100
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 74
Ser Asp Pro Thr Arg Val Glu Thr Ala Thr Glu Thr Ala Trp Ile Ser
1 5 10 15
His Leu Val Leu Gly Leu Ser Ala Val Leu Gly Leu Leu Leu Leu Arg
20 25 30
Trp Gln Phe Pro Ala His Tyr Arg Arg Leu Arg His Ala Leu Trp Pro
35 40 45
Ser Leu Pro Asp Leu His Arg Val Leu Gly Gln Tyr Leu Arg Asp Thr
50 55 60
Ala Ala Leu Ser Pro Pro Lys Ala Thr Val Ser Asp Thr Cys Glu Glu
65 70 75 80
Val Glu Pro Ser Leu Leu Glu Ile Leu Pro Lys Ser Ser Glu Arg Thr
85 90 95
Pro Leu Pro Leu
100

<210> 75
<211> 101
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>

<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 75
Ser Asp Pro Thr Arg Val Glu Thr Ala Thr Glu Thr Ala Trp Ile Ser
1 5 10 15
Pro His Leu Val Leu Gly Leu Ser Ala Val Leu Gly Leu Leu Leu Leu
20 25 30
Arg Trp Gln Phe Pro Ala His Tyr Arg Arg Leu Arg His Ala Leu Trp
35 40 45
Pro Ser Leu Pro Asp Leu His Arg Val Leu Gly Gln Tyr Leu Arg Asp
50 55 60
Thr Ala Ala Leu Ser Pro Pro Lys Ala Thr Val Ser Asp Thr Cys Glu
65 70 75 80
Glu Val Glu Pro Ser Leu Leu Glu Ile Leu Pro Lys Ser Ser Glu Arg
85 90 95
Thr Pro Leu Pro Leu
100
<210> 76
<211> 102
<212> PRT
<213> 人工序列（Artificial Sequence）
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 76

[0041]

Ser Asp Pro Thr Arg Val Glu Thr Ala Thr Glu Thr Ala Trp Ile Ser
1 5 10 15
Pro Pro His Leu Val Leu Gly Leu Ser Ala Val Leu Gly Leu Leu Leu
20 25 30
Leu Arg Trp Gln Phe Pro Ala His Tyr Arg Arg Leu Arg His Ala Leu
35 40 45
Trp Pro Ser Leu Pro Asp Leu His Arg Val Leu Gly Gln Tyr Leu Arg
50 55 60
Asp Thr Ala Ala Leu Ser Pro Pro Lys Ala Thr Val Ser Asp Thr Cys
65 70 75 80
Glu Glu Val Glu Pro Ser Leu Leu Glu Ile Leu Pro Lys Ser Ser Glu
85 90 95
Arg Thr Pro Leu Pro Leu
100
<210> 77
<211> 99
<212> PRT
<213> 人工序列（Artificial Sequence）
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 77
Ser Asp Pro Thr Arg Val Glu Thr Ala Thr Glu Thr Ala Trp Ile His
1 5 10 15
Leu Val Leu Gly Leu Ser Ala Val Leu Gly Leu Leu Leu Leu Arg Trp
20 25 30

Gln Phe Pro Ala His Tyr Arg Arg Leu Arg His Ala Leu Trp Pro Ser
35 40 45
Leu Pro Asp Leu His Arg Val Leu Gly Gln Tyr Leu Arg Asp Thr Ala
50 55 60
Ala Leu Ser Pro Pro Lys Ala Thr Val Ser Asp Thr Cys Glu Glu Val
65 70 75 80
Glu Pro Ser Leu Leu Glu Ile Leu Pro Lys Ser Ser Glu Arg Thr Pro
85 90 95
Leu Pro Leu

<210> 78
<211> 100
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 78
Ser Asp Pro Thr Arg Val Glu Thr Ala Thr Glu Thr Ala Trp Ile Pro
1 5 10 15
His Leu Val Leu Gly Leu Ser Ala Val Leu Gly Leu Leu Leu Leu Arg
20 25 30
Trp Gln Phe Pro Ala His Tyr Arg Arg Leu Arg His Ala Leu Trp Pro
35 40 45
Ser Leu Pro Asp Leu His Arg Val Leu Gly Gln Tyr Leu Arg Asp Thr
[0042] 50 55 60
Ala Ala Leu Ser Pro Pro Lys Ala Thr Val Ser Asp Thr Cys Glu Glu
65 70 75 80
Val Glu Pro Ser Leu Leu Glu Ile Leu Pro Lys Ser Ser Glu Arg Thr
85 90 95
Pro Leu Pro Leu
100
<210> 79
<211> 101
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 79
Ser Asp Pro Thr Arg Val Glu Thr Ala Thr Glu Thr Ala Trp Ile Pro
1 5 10 15
Pro His Leu Val Leu Gly Leu Ser Ala Val Leu Gly Leu Leu Leu Leu
20 25 30
Arg Trp Gln Phe Pro Ala His Tyr Arg Arg Leu Arg His Ala Leu Trp
35 40 45
Pro Ser Leu Pro Asp Leu His Arg Val Leu Gly Gln Tyr Leu Arg Asp
50 55 60
Thr Ala Ala Leu Ser Pro Pro Lys Ala Thr Val Ser Asp Thr Cys Glu
65 70 75 80
Glu Val Glu Pro Ser Leu Leu Glu Ile Leu Pro Lys Ser Ser Glu Arg

85 90 95
Thr Pro Leu Pro Leu
100
<210> 80
<211> 144
<212> PRT
<213> 人工序列（Artificial Sequence）
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 80
Ala Arg Asp Glu Val Glu Gly Phe Leu Gln Asp Thr Phe Pro Gln Gln
1 5 10 15
Leu Glu Glu Ser Glu Lys Gln Arg Leu Gly Gly Asp Val Gln Ser Pro
20 25 30
Asn Cys Pro Ser Glu Asp Val Val Ile Thr Pro Glu Ser Phe Gly Arg
35 40 45
Asp Ser Ser Leu Thr Cys Leu Ala Gly Asn Val Ser Ala Cys Asp Ala
50 55 60
Pro Ile Leu Ser Ser Ser Arg Ser Leu Asp Cys Arg Glu Ser Gly Lys
65 70 75 80
Asn Gly Pro His Val Tyr Gln Asp Leu Leu Leu Ser Leu Gly Thr Thr
85 90 95
Asn Ser Thr Leu Pro Pro Pro Phe Ser Leu Gln Ser Gly Ile Leu Thr
100 105 110
[0043] Leu Asn Pro Val Ala Gln Gly Gln Pro Ile Leu Thr Ser Leu Gly Ser
115 120 125
Asn Gln Glu Glu Ala Tyr Val Thr Met Ser Ser Phe Tyr Gln Asn Gln
130 135 140
<210> 81
<211> 219
<212> PRT
<213> 人工序列（Artificial Sequence）
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 81
Val Thr Gln Leu Leu Leu Gln Gln Asp Lys Val Pro Glu Pro Ala Ser
1 5 10 15
Leu Ser Ser Asn His Ser Leu Thr Ser Cys Phe Thr Asn Gln Gly Tyr
20 25 30
Phe Phe Phe His Leu Pro Asp Ala Leu Glu Ile Glu Ala Cys Gln Val
35 40 45
Tyr Phe Thr Tyr Asp Pro Tyr Ser Glu Glu Asp Pro Asp Glu Gly Val
50 55 60
Ala Gly Ala Pro Thr Gly Ser Ser Pro Gln Pro Leu Gln Pro Leu Ser
65 70 75 80
Gly Glu Asp Asp Ala Tyr Cys Thr Phe Pro Ser Arg Asp Asp Leu Leu
85 90 95
Leu Phe Ser Pro Ser Leu Leu Gly Gly Pro Ser Pro Pro Ser Thr Ala
100 105 110

Pro Gly Gly Ser Gly Ala Gly Glu Glu Arg Met Pro Pro Ser Leu Gln
115 120 125
Glu Arg Val Pro Arg Asp Trp Asp Pro Gln Pro Leu Gly Pro Pro Thr
130 135 140
Pro Gly Val Pro Asp Leu Val Asp Phe Gln Pro Pro Pro Glu Leu Val
145 150 155 160
Leu Arg Glu Ala Gly Glu Glu Val Pro Asp Ala Gly Pro Arg Glu Gly
165 170 175
Val Ser Phe Pro Trp Ser Arg Pro Pro Gly Gln Gly Glu Phe Arg Ala
180 185 190
Leu Asn Ala Arg Leu Pro Leu Asn Thr Asp Ala Tyr Leu Ser Leu Gln
195 200 205
Glu Leu Gln Gly Gln Asp Pro Thr His Leu Val
210 215

<210> 82
<211> 50
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 82
Ile Ser Thr Ile Ala Thr Val Glu Glu Thr Asn Gln Thr Asp Glu Asp
1 5 10 15
His Lys Lys Tyr Ser Ser Gln Thr Ser Gln Asp Ser Gly Asn Tyr Ser
20 25 30

[0044]

Asn Glu Asp Glu Ser Glu Ser Lys Thr Ser Glu Glu Leu Gln Gln Asp
35 40 45
Phe Val
50

<210> 83
<211> 206
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 83
Lys Lys Lys Val Trp Asp Tyr Asn Tyr Asp Asp Glu Ser Asp Ser Asp
1 5 10 15
Thr Glu Ala Ala Pro Arg Thr Ser Gly Gly Gly Tyr Thr Met His Gly
20 25 30
Leu Thr Val Arg Pro Leu Gly Gln Ala Ser Ala Thr Ser Thr Glu Ser
35 40 45
Gln Leu Ile Asp Pro Glu Ser Glu Glu Glu Pro Asp Leu Pro Glu Val
50 55 60
Asp Val Glu Leu Pro Thr Met Pro Lys Asp Ser Pro Gln Gln Leu Glu
65 70 75 80
Leu Leu Ser Gly Pro Cys Glu Arg Arg Lys Ser Pro Leu Gln Asp Pro
85 90 95
Phe Pro Glu Glu Asp Tyr Ser Ser Thr Glu Gly Ser Gly Gly Arg Ile

100 105 110
Thr Phe Asn Val Asp Leu Asn Ser Val Phe Leu Arg Val Leu Asp Asp
115 120 125
Glu Asp Ser Asp Asp Leu Glu Ala Pro Leu Met Leu Ser Ser His Leu
130 135 140
Glu Glu Met Val Asp Pro Glu Asp Pro Asp Asn Val Gln Ser Asn His
145 150 155 160
Leu Leu Ala Ser Gly Glu Gly Thr Gln Pro Thr Phe Pro Ser Pro Ser
165 170 175
Ser Glu Gly Leu Trp Ser Glu Asp Ala Pro Ser Asp Gln Ser Asp Thr
180 185 190
Ser Glu Ser Asp Val Asp Leu Gly Asp Gly Tyr Ile Met Arg
195 200 205
<210> 84
<211> 256
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 84
Ile Ser Thr Ile Ala Thr Val Glu Glu Thr Asn Gln Thr Asp Glu Asp
1 5 10 15
His Lys Lys Tyr Ser Ser Gln Thr Ser Gln Asp Ser Gly Asn Tyr Ser
20 25 30
[0045] Asn Glu Asp Glu Ser Glu Ser Lys Thr Ser Glu Glu Leu Gln Gln Asp
35 40 45
Phe Val Lys Lys Lys Val Trp Asp Tyr Asn Tyr Asp Asp Glu Ser Asp
50 55 60
Ser Asp Thr Glu Ala Ala Pro Arg Thr Ser Gly Gly Gly Tyr Thr Met
65 70 75 80
His Gly Leu Thr Val Arg Pro Leu Gly Gln Ala Ser Ala Thr Ser Thr
85 90 95
Glu Ser Gln Leu Ile Asp Pro Glu Ser Glu Glu Glu Pro Asp Leu Pro
100 105 110
Glu Val Asp Val Glu Leu Pro Thr Met Pro Lys Asp Ser Pro Gln Gln
115 120 125
Leu Glu Leu Leu Ser Gly Pro Cys Glu Arg Arg Lys Ser Pro Leu Gln
130 135 140
Asp Pro Phe Pro Glu Glu Asp Tyr Ser Ser Thr Glu Gly Ser Gly Gly
145 150 155 160
Arg Ile Thr Phe Asn Val Asp Leu Asn Ser Val Phe Leu Arg Val Leu
165 170 175
Asp Asp Glu Asp Ser Asp Asp Leu Glu Ala Pro Leu Met Leu Ser Ser
180 185 190
His Leu Glu Glu Met Val Asp Pro Glu Asp Pro Asp Asn Val Gln Ser
195 200 205
Asn His Leu Leu Ala Ser Gly Glu Gly Thr Gln Pro Thr Phe Pro Ser
210 215 220
Pro Ser Ser Glu Gly Leu Trp Ser Glu Asp Ala Pro Ser Asp Gln Ser
225 230 235 240

Asp Thr Ser Glu Ser Asp Val Asp Leu Gly Asp Gly Tyr Ile Met Arg
245 250 255

<210> 85
<211> 221
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 85

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

<210> 86
<211> 35
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 86

Ile Pro Pro Lys Gly Gly Ala Leu Gly Glu Gly Pro Gly Ala Ser Pro
1 5 10 15
Cys Asn Gln His Ser Pro Tyr Trp Ala Pro Pro Cys Tyr Thr Leu Lys
20 25 30
Pro Glu Thr

35

<210> 87
<211> 166
<212> PRT
<213> 人工序列（Artificial Sequence）
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 87

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

[0047]

Gln Gln Gly Val Ala Trp Val Leu Ala Gly His Cys Gln Arg Pro Gly
130 135 140
Leu His Glu Asp Leu Gln Gly Met Leu Leu Pro Ser Val Leu Ser Lys
145 150 155 160
Ala Arg Ser Trp Thr Phe
165

<210> 88
<211> 217
<212> PRT
<213> 人工序列（Artificial Sequence）
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 88

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

Leu Leu Asp Ala Gly Thr Thr Val Leu Ser Cys Gly Cys Val Ser Ala
100 105 110
Gly Ser Pro Gly Leu Gly Gly Pro Leu Gly Ser Leu Leu Asp Arg Leu
115 120 125
Lys Pro Pro Leu Ala Asp Gly Glu Asp Trp Ala Gly Gly Leu Pro Trp
130 135 140
Gly Gly Arg Ser Pro Gly Gly Val Ser Glu Ser Glu Ala Gly Ser Pro
145 150 155 160
Leu Ala Gly Leu Asp Met Asp Thr Phe Asp Ser Gly Phe Val Gly Ser
165 170 175
Asp Cys Ser Ser Pro Val Glu Cys Asp Phe Thr Ser Pro Gly Asp Glu
180 185 190
Gly Pro Pro Arg Ser Tyr Leu Arg Gln Trp Val Val Ile Pro Pro Pro
195 200 205
Leu Ser Ser Pro Gly Pro Gln Ala Ser
210 215

<210> 89
<211> 286
<212> PRT
<213> 人工序列（Artificial Sequence）
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 89

[0048]

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

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

<210> 90
<211> 170
<212> PRT
<213> 人工序列（Artificial Sequence）
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 90
Trp Gly Thr Met Gln Ala Val Glu Pro Gly Thr Asp Asp Glu Gly Pro
1 5 10 15
Leu Leu Glu Pro Val Gly Ser Glu His Ala Gln Asp Thr Tyr Leu Val
20 25 30
Leu Asp Lys Trp Leu Leu Pro Arg Asn Pro Pro Ser Glu Asp Leu Pro
35 40 45
Gly Pro Gly Gly Ser Val Asp Ile Val Ala Met Asp Glu Gly Ser Glu
50 55 60

[0049]
Ala Ser Ser Cys Ser Ser Ala Leu Ala Ser Lys Pro Ser Pro Glu Gly
65 70 75 80
Ala Ser Ala Ala Ser Phe Glu Tyr Thr Ile Leu Asp Pro Ser Ser Gln
85 90 95
Leu Leu Arg Pro Trp Thr Leu Cys Pro Glu Leu Pro Pro Thr Pro Pro
100 105 110
His Leu Lys Tyr Leu Tyr Leu Val Val Ser Asp Ser Gly Ile Ser Thr
115 120 125
Asp Tyr Ser Ser Gly Asp Ser Gln Gly Ala Gln Gly Gly Leu Ser Asp
130 135 140
Gly Pro Tyr Ser Asn Pro Tyr Glu Asn Ser Leu Ile Pro Ala Ala Glu
145 150 155 160
Pro Leu Pro Pro Ser Tyr Val Ala Cys Ser
165 170

<210> 91
<211> 203
<212> PRT
<213> 人工序列（Artificial Sequence）
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 91
Ala Val Gln Leu Leu Leu Leu Gln Lys Asp Ser Ala Pro Leu Pro Ser
1 5 10 15
Pro Ser Gly His Ser Gln Ala Ser Cys Phe Thr Asn Gln Gly Tyr Phe
20 25 30

Phe Phe His Leu Pro Asn Ala Leu Glu Ile Glu Ser Cys Gln Val Tyr
35 40 45
Phe Thr Tyr Asp Pro Cys Val Glu Glu Glu Val Glu Glu Asp Gly Ser
50 55 60
Arg Leu Pro Glu Gly Ser Pro His Pro Pro Leu Leu Pro Leu Ala Gly
65 70 75 80
Glu Gln Asp Asp Tyr Cys Ala Phe Pro Pro Arg Asp Asp Leu Leu Leu
85 90 95
Phe Ser Pro Ser Leu Ser Thr Pro Asn Thr Ala Tyr Gly Gly Ser Arg
100 105 110
Ala Pro Glu Glu Arg Ser Pro Leu Ser Leu His Glu Gly Leu Pro Ser
115 120 125
Leu Ala Ser Arg Asp Leu Met Gly Leu Gln Arg Pro Leu Glu Arg Met
130 135 140
Pro Glu Gly Asp Gly Glu Gly Leu Ser Ala Asn Ser Ser Gly Glu Gln
145 150 155 160
Ala Ser Val Pro Glu Gly Asn Leu His Gly Gln Asp Gln Asp Arg Gly
165 170 175
Gln Gly Pro Ile Leu Thr Leu Asn Thr Asp Ala Tyr Leu Ser Leu Gln
180 185 190
Glu Leu Gln Ala Gln Asp Ser Val His Leu Ile
195 200
<210> 92
<211> 144
<212> PRT
[0050] <213> 人工序列 (Artificial Sequence)
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 92
Ala Arg Asp Glu Val Glu Ser Phe Leu Pro Asn Asp Leu Pro Ala Gln
1 5 10 15
Pro Glu Glu Leu Glu Thr Gln Gly His Arg Ala Ala Val His Ser Ala
20 25 30
Asn Arg Ser Pro Glu Thr Ser Val Ser Pro Pro Glu Thr Val Arg Arg
35 40 45
Glu Ser Pro Leu Arg Cys Leu Ala Arg Asn Leu Ser Thr Cys Asn Ala
50 55 60
Pro Pro Leu Leu Ser Ser Arg Ser Pro Asp Tyr Arg Asp Gly Asp Arg
65 70 75 80
Asn Arg Pro Pro Val Tyr Gln Asp Leu Leu Pro Asn Ser Gly Asn Thr
85 90 95
Asn Val Pro Val Pro Val Pro Gln Pro Leu Pro Phe Gln Ser Gly Ile
100 105 110
Leu Ile Pro Val Ser Gln Arg Gln Pro Ile Ser Thr Ser Ser Val Leu
115 120 125
Asn Gln Glu Glu Ala Tyr Val Thr Met Ser Ser Phe Tyr Gln Asn Lys
130 135 140
<210> 93
<211> 231
<212> PRT

<213> 人工序列 (Artificial Sequence)
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 93

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

[0051]

```
Asn Thr Val Gln Pro Thr Cys Val Asn Ser Thr Phe Asp Ser Pro Ala
                165                 170                 175
His Trp Ala Gln Lys Gly Ser His Gln Ile Ser Leu Asp Asn Pro Asp
            180                 185                 190
Tyr Gln Gln Asp Phe Phe Pro Lys Glu Ala Lys Pro Asn Gly Ile Phe
        195                 200                 205
Lys Gly Ser Thr Ala Glu Asn Ala Glu Tyr Leu Arg Val Ala Pro Gln
    210                 215                 220
Ser Ser Glu Phe Ile Gly Ala
225                 230
```

<210> 94
<211> 218
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 94

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

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

<210> 95
<211> 54
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>

[0052]

<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 95
Val Ile Gln Gly Asp Glu Arg Met His Leu Pro Ser Pro Thr Asp Ser
1 5 10 15
Asn Phe Phe Arg Ala Leu Met Asp Glu Glu Asp Met Asp Asp Val Val
20 25 30
Asp Ala Asp Glu Tyr Leu Ile Pro Gln Gln Gly Phe Phe Ser Ser Pro
35 40 45
Ser Thr Ser Arg Thr Pro
50

<210> 96
<211> 54
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 96
Asn Asn Ser Thr Val Ala Cys Ile Asp Arg Asn Gly Leu Gln Ser Cys
1 5 10 15
Pro Ile Lys Glu Asp Ser Phe Leu Gln Arg Ile Asp Asp Thr Phe Leu
20 25 30
Pro Val Pro Glu Tyr Ile Asn Gln Ser Val Pro Lys Arg Pro Ala Gly
35 40 45
Ser Val Gln Asn Pro Val

50
<210> 97
<211> 54
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 97
Lys Glu Asp Ser Phe Leu Gln Arg Ile Asp Asp Thr Phe Leu Pro Val
1 5 10 15
Pro Glu Phe Ile Asn Gln Ser Val Pro Lys Arg Pro Ala Gly Ser Val
20 25 30
Gln Asn Pro Val Tyr His Asn Gln Pro Leu Asn Pro Ala Pro Ser Arg
35 40 45
Asp Pro His Phe Gln Asp
50
<210> 98
<211> 54
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 98

[0053]
Val Pro Glu Phe Ile Asn Gln Ser Val Pro Lys Arg Pro Ala Gly Ser
1 5 10 15
Val Gln Asn Pro Val Phe His Asn Gln Pro Leu Asn Pro Ala Pro Ser
20 25 30
Arg Asp Pro His Tyr Gln Asp Pro His Ser Thr Ala Val Gly Asn Pro
35 40 45
Glu Tyr Leu Asn Thr Val
50
<210> 99
<211> 54
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 99
Pro Glu Tyr Leu Asn Thr Val Gln Pro Thr Cys Val Asn Ser Thr Phe
1 5 10 15
Asp Ser Pro Ala His Trp Ala Gln Lys Gly Ser His Gln Ile Ser Leu
20 25 30
Asp Asn Pro Asp Tyr Gln Gln Asp Phe Phe Pro Lys Glu Ala Lys Pro
35 40 45
Asn Gly Ile Phe Lys Gly
50
<210> 100
<211> 54

<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 100
Trp Ala Gln Lys Gly Ser His Gln Ile Ser Leu Asp Asn Pro Asp Phe
1 5 10 15
Gln Gln Asp Phe Phe Pro Lys Glu Ala Lys Pro Asn Gly Ile Phe Lys
20 25 30
Gly Ser Thr Ala Glu Asn Ala Glu Tyr Leu Arg Val Ala Pro Gln Ser
35 40 45
Ser Glu Phe Ile Gly Ala
50
<210> 101
<211> 51
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 101
Ser Asp Pro Lys Pro Glu Asn Pro Ala Cys Pro Trp Thr Val Leu Pro
1 5 10 15
Ala Gly Asp Leu Pro Thr His Asp Gly Tyr Leu Pro Ser Asn Ile Asp
[0054] 20 25 30
Asp Leu Pro Ser His Glu Ala Pro Leu Ala Asp Ser Leu Glu Glu Leu
35 40 45
Glu Pro Gln
50
<210> 102
<211> 41
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 102
Ala Cys Asp Ala Pro Ile Leu Ser Ser Ser Arg Ser Leu Asp Cys Arg
1 5 10 15
Glu Ser Gly Lys Asn Gly Pro His Val Tyr Gln Asp Leu Leu Leu Ser
20 25 30
Leu Gly Thr Thr Asn Ser Thr Leu Pro
35 40
<210> 103
<211> 36
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”

<400> 103
Gly Ile Leu Thr Leu Asn Pro Val Ala Gln Gly Gln Pro Ile Leu Thr
1 5 10 15
Ser Leu Gly Ser Asn Gln Glu Glu Ala Tyr Val Thr Met Ser Ser Phe
20 25 30
Tyr Gln Asn Gln
35
<210> 104
<211> 68
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 104
Ala Cys Asp Ala Pro Ile Leu Ser Ser Ser Arg Ser Leu Asp Cys Arg
1 5 10 15
Glu Ser Gly Lys Asn Gly Pro His Val Tyr Gln Asp Leu Leu Leu Ser
20 25 30
Leu Gly Thr Thr Asn Ser Thr Leu Pro Gln Gly Gln Pro Ile Leu Thr
35 40 45
Ser Leu Gly Ser Asn Gln Glu Glu Ala Tyr Val Thr Met Ser Ser Phe
50 55 60
Tyr Gln Asn Gln
65

[0055]
<210> 105
<211> 36
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 105
Gly Ile Leu Thr Leu Asn Pro Val Ala Gln Gly Gln Pro Ile Leu Thr
1 5 10 15
Ser Leu Gly Ser Asn Gln Glu Glu Ala Tyr Val Thr Met Ser Ser Phe
20 25 30
Phe Gln Asn Gln
35
<210> 106
<211> 68
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 106
Ala Cys Asp Ala Pro Ile Leu Ser Ser Ser Arg Ser Leu Asp Cys Arg
1 5 10 15
Glu Ser Gly Lys Asn Gly Pro His Val Tyr Gln Asp Leu Leu Leu Ser
20 25 30

Leu Gly Thr Thr Asn Ser Thr Leu Pro Gln Gly Gln Pro Ile Leu Thr
35 40 45
Ser Leu Gly Ser Asn Gln Glu Glu Ala Tyr Val Thr Met Ser Ser Phe
50 55 60
Phe Gln Asn Gln
65

<210> 107
<211> 41
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 107
Asp Glu Gly Val Ala Gly Ala Pro Thr Gly Ser Ser Pro Gln Pro Leu
1 5 10 15
Gln Pro Leu Ser Gly Glu Asp Asp Ala Tyr Cys Thr Phe Pro Ser Arg
20 25 30
Asp Asp Leu Leu Leu Phe Ser Pro Ser
35 40

<210> 108
<211> 34
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
[0056] <221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 108
Gly Gln Gly Glu Phe Arg Ala Leu Asn Ala Arg Leu Pro Leu Asn Thr
1 5 10 15
Asp Ala Tyr Leu Ser Leu Gln Glu Leu Gln Gly Gln Asp Pro Thr His
20 25 30
Leu Val

<210> 109
<211> 82
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 109
Gln Gln Asp Lys Val Pro Glu Pro Ala Ser Leu Ser Ser Asn His Ser
1 5 10 15
Leu Thr Ser Cys Phe Thr Asn Gln Gly Tyr Phe Phe Phe His Leu Pro
20 25 30
Asp Ala Leu Glu Ile Glu Ala Cys Gln Asp Glu Gly Val Ala Gly Ala
35 40 45
Pro Thr Gly Ser Ser Pro Gln Pro Leu Gln Pro Leu Ser Gly Glu Asp
50 55 60
Asp Ala Tyr Cys Thr Phe Pro Ser Arg Asp Asp Leu Leu Leu Phe Ser

65 70 75 80
Pro Ser

<210> 110
<211> 75
<212> PRT
<213> 人工序列（Artificial Sequence）
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 110
Gln Gln Asp Lys Val Pro Glu Pro Ala Ser Leu Ser Ser Asn His Ser
1 5 10 15
Leu Thr Ser Cys Phe Thr Asn Gln Gly Tyr Phe Phe Phe His Leu Pro
20 25 30
Asp Ala Leu Glu Ile Glu Ala Cys Gln Gly Gln Gly Glu Phe Arg Ala
35 40 45
Leu Asn Ala Arg Leu Pro Leu Asn Thr Asp Ala Tyr Leu Ser Leu Gln
50 55 60
Glu Leu Gln Gly Gln Asp Pro Thr His Leu Val
65 70 75
<210> 111
<211> 75
<212> PRT
<213> 人工序列（Artificial Sequence）
[0057] <220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 111
Asp Glu Gly Val Ala Gly Ala Pro Thr Gly Ser Ser Pro Gln Pro Leu
1 5 10 15
Gln Pro Leu Ser Gly Glu Asp Asp Ala Tyr Cys Thr Phe Pro Ser Arg
20 25 30
Asp Asp Leu Leu Leu Phe Ser Pro Ser Gly Gln Gly Glu Phe Arg Ala
35 40 45
Leu Asn Ala Arg Leu Pro Leu Asn Thr Asp Ala Tyr Leu Ser Leu Gln
50 55 60
Glu Leu Gln Gly Gln Asp Pro Thr His Leu Val
65 70 75
<210> 112
<211> 116
<212> PRT
<213> 人工序列（Artificial Sequence）
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 112
Gln Gln Asp Lys Val Pro Glu Pro Ala Ser Leu Ser Ser Asn His Ser
1 5 10 15
Leu Thr Ser Cys Phe Thr Asn Gln Gly Tyr Phe Phe Phe His Leu Pro
20 25 30

Asp Ala Leu Glu Ile Glu Ala Cys Gln Asp Glu Gly Val Ala Gly Ala
35 40 45
Pro Thr Gly Ser Ser Pro Gln Pro Leu Gln Pro Leu Ser Gly Glu Asp
50 55 60
Asp Ala Tyr Cys Thr Phe Pro Ser Arg Asp Asp Leu Leu Leu Phe Ser
65 70 75 80
Pro Ser Gly Gln Gly Glu Phe Arg Ala Leu Asn Ala Arg Leu Pro Leu
85 90 95
Asn Thr Asp Ala Tyr Leu Ser Leu Gln Glu Leu Gln Gly Gln Asp Pro
100 105 110
Thr His Leu Val
115

<210> 113
<211> 43
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 113
Lys Lys Lys Val Trp Asp Tyr Asn Tyr Asp Asp Glu Ser Asp Ser Asp
1 5 10 15
Thr Glu Ala Ala Pro Arg Thr Ser Gly Gly Gly Tyr Thr Met His Gly
20 25 30
Leu Thr Val Arg Pro Leu Gly Gln Ala Ser Ala
35 40

[0058]

<210> 114
<211> 29
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
<221> source
<223> /注释 = “人工序列的描述：合成肽”
<400> 114
Glu Gly Leu Trp Ser Glu Asp Ala Pro Ser Asp Gln Ser Asp Thr Ser
1 5 10 15
Glu Ser Asp Val Asp Leu Gly Asp Gly Tyr Ile Met Arg
20 25

<210> 115
<211> 72
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 115
Lys Lys Lys Val Trp Asp Tyr Asn Tyr Asp Asp Glu Ser Asp Ser Asp
1 5 10 15
Thr Glu Ala Ala Pro Arg Thr Ser Gly Gly Gly Tyr Thr Met His Gly
20 25 30
Leu Thr Val Arg Pro Leu Gly Gln Ala Ser Ala Glu Gly Leu Trp Ser

35 40 45
Glu Asp Ala Pro Ser Asp Gln Ser Asp Thr Ser Glu Ser Asp Val Asp
50 55 60
Leu Gly Asp Gly Tyr Ile Met Arg
65 70
<210> 116
<211> 156
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 116
Ala Ser Glu Ser Pro Ala Asp Glu Glu Glu Gln Trp Ser Asp Asp Phe
1 5 10 15
Asp Ser Asp Tyr Glu Asn Pro Asp Glu His Ser Asp Ser Glu Met Tyr
20 25 30
Val Met Pro Ala Glu Glu Asn Ala Asp Asp Ser Tyr Glu Pro Pro Pro
35 40 45
Val Glu Gln Glu Thr Arg Pro Val His Pro Ala Leu Pro Phe Ala Arg
50 55 60
Gly Glu Tyr Ile Asp Asn Arg Ser Ser Gln Arg His Ser Pro Pro Phe
65 70 75 80
Ser Lys Thr Leu Pro Ser Lys Pro Ser Trp Pro Ser Glu Lys Ala Arg
85 90 95
[0059] Leu Thr Ser Thr Leu Pro Ala Leu Thr Ala Leu Gln Lys Pro Gln Val
100 105 110
Pro Pro Lys Pro Lys Gly Leu Leu Glu Asp Glu Ala Asp Tyr Val Val
115 120 125
Pro Val Glu Asp Asn Asp Glu Asn Tyr Ile His Pro Thr Glu Ser Ser
130 135 140
Ser Pro Pro Pro Glu Lys Ala Pro Met Val Asn Arg
145 150 155
<210> 117
<211> 156
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 117
Ala Ser Glu Ser Pro Ala Asp Glu Glu Glu Gln Trp Ser Asp Asp Phe
1 5 10 15
Asp Ser Asp Phe Glu Asn Pro Asp Glu His Ser Asp Ser Glu Met Tyr
20 25 30
Val Met Pro Ala Glu Glu Asn Ala Asp Asp Ser Tyr Glu Pro Pro Pro
35 40 45
Val Glu Gln Glu Thr Arg Pro Val His Pro Ala Leu Pro Phe Ala Arg
50 55 60
Gly Glu Tyr Ile Asp Asn Arg Ser Ser Gln Arg His Ser Pro Pro Phe
65 70 75 80

Ser Lys Thr Leu Pro Ser Lys Pro Ser Trp Pro Ser Glu Lys Ala Arg
85 90 95
Leu Thr Ser Thr Leu Pro Ala Leu Thr Ala Leu Gln Lys Pro Gln Val
100 105 110
Pro Pro Lys Pro Lys Gly Leu Leu Glu Asp Glu Ala Asp Tyr Val Val
115 120 125
Pro Val Glu Asp Asn Asp Glu Asn Tyr Ile His Pro Thr Glu Ser Ser
130 135 140
Ser Pro Pro Pro Glu Lys Ala Pro Met Val Asn Arg
145 150 155

<210> 118
<211> 156
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 118

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

[0060]

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

<210> 119
<211> 170
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 119

Trp Gly Thr Met Gln Ala Val Glu Pro Gly Thr Asp Asp Glu Gly Pro
1 5 10 15
Leu Leu Glu Pro Val Gly Ser Glu His Ala Gln Asp Thr Tyr Leu Val
20 25 30
Leu Asp Lys Trp Leu Leu Pro Arg Asn Pro Pro Ser Glu Asp Leu Pro

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

<210> 120
<211> 149
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 120

[0061]
Val Thr Pro Val Phe Arg His Pro Pro Cys Ser Asn Trp Pro Gln Arg
1 5 10 15
Glu Lys Gly Ile Gln Gly His Gln Ala Ser Glu Lys Asp Met Met His
20 25 30
Ser Ala Ser Ser Pro Pro Pro Pro Arg Ala Leu Gln Ala Glu Ser Arg
35 40 45
Gln Leu Val Asp Leu Tyr Lys Val Leu Glu Ser Arg Gly Ser Asp Pro
50 55 60
Lys Pro Glu Asn Pro Ala Cys Pro Trp Thr Val Leu Pro Ala Gly Asp
65 70 75 80
Leu Pro Thr His Asp Gly Tyr Leu Pro Ser Asn Ile Asp Asp Leu Pro
85 90 95
Ser His Glu Ala Pro Leu Ala Asp Ser Leu Glu Glu Leu Glu Pro Gln
100 105 110
His Ile Ser Leu Ser Val Phe Pro Ser Ser Ser Leu His Pro Leu Thr
115 120 125
Phe Ser Cys Gly Asp Lys Leu Thr Leu Asp Gln Leu Lys Met Arg Cys
130 135 140
Asp Ser Leu Met Leu
145

<210> 121
<211> 40
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
<221> source

<223> /注释 = “人工序列的描述：合成多肽”
<400> 121
Trp Asp Lys Gly Glu Arg Thr Glu Pro Leu Glu Lys Thr Glu Leu Pro
1 5 10 15
Glu Gly Ala Pro Glu Leu Ala Leu Asp Thr Glu Leu Ser Leu Glu Asp
20 25 30
Gly Asp Arg Cys Lys Ala Lys Met
35 40
<210> 122
<211> 275
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 122
Val Ser Pro Glu Leu Lys Asn Leu Asp Leu His Gly Ser Thr Asp Ser
1 5 10 15
Gly Phe Gly Ser Thr Lys Pro Ser Leu Gln Thr Glu Glu Pro Gln Phe
20 25 30
Leu Leu Pro Asp Pro His Pro Gln Ala Asp Arg Thr Leu Gly Asn Arg
35 40 45
Glu Pro Pro Val Leu Gly Asp Ser Cys Ser Ser Gly Ser Ser Asn Ser
50 55 60
Thr Asp Ser Gly Ile Cys Leu Gln Glu Pro Ser Leu Ser Pro Ser Thr
[0062] 65 70 75 80
Gly Pro Thr Trp Glu Gln Gln Val Gly Ser Asn Ser Arg Gly Gln Asp
85 90 95
Asp Ser Gly Ile Asp Leu Val Gln Asn Ser Glu Gly Arg Ala Gly Asp
100 105 110
Thr Gln Gly Gly Ser Ala Leu Gly His His Ser Pro Pro Glu Pro Glu
115 120 125
Val Pro Gly Glu Glu Asp Pro Ala Ala Val Ala Phe Gln Gly Tyr Leu
130 135 140
Arg Gln Thr Arg Cys Ala Glu Glu Lys Ala Thr Lys Thr Gly Cys Leu
145 150 155 160
Glu Glu Glu Ser Pro Leu Thr Asp Gly Leu Gly Pro Lys Phe Gly Arg
165 170 175
Cys Leu Val Asp Glu Ala Gly Leu His Pro Pro Ala Leu Ala Lys Gly
180 185 190
Tyr Leu Lys Gln Asp Pro Leu Glu Met Thr Leu Ala Ser Ser Gly Ala
195 200 205
Pro Thr Gly Gln Trp Asn Gln Pro Thr Glu Glu Trp Ser Leu Leu Ala
210 215 220
Leu Ser Ser Cys Ser Asp Leu Gly Ile Ser Asp Trp Ser Phe Ala His
225 230 235 240
Asp Leu Ala Pro Leu Gly Cys Val Ala Ala Pro Gly Gly Leu Leu Gly
245 250 255
Ser Phe Asn Ser Asp Leu Val Thr Leu Pro Leu Ile Ser Ser Leu Gln
260 265 270
Ser Ser Glu

275

<210> 123
<211> 487
<212> PRT
<213> 人工序列（Artificial Sequence）
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 123

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

[0063]

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

Ser Phe Gly Arg Asp Ser Ser Leu Thr Cys Leu Ala Gly Asn Val Ser
340 345 350
Ala Cys Asp Ala Pro Ile Leu Ser Ser Ser Arg Ser Leu Asp Cys Arg
355 360 365
Glu Ser Gly Lys Asn Gly Pro His Val Tyr Gln Asp Leu Leu Leu Ser
370 375 380
Leu Gly Thr Thr Asn Ser Thr Leu Pro Pro Pro Phe Ser Leu Gln Ser
385 390 395 400
Gly Ile Leu Thr Leu Asn Pro Val Ala Gln Gly Gln Pro Ile Leu Thr
405 410 415
Ser Leu Gly Ser Asn Gln Glu Glu Ala Tyr Val Thr Met Ser Ser Phe
420 425 430
Tyr Gln Asn Gln Ser Asp Pro Lys Pro Glu Asn Pro Ala Cys Pro Trp
435 440 445
Thr Val Leu Pro Ala Gly Asp Leu Pro Thr His Asp Gly Tyr Leu Pro
450 455 460
Ser Asn Ile Asp Asp Leu Pro Ser His Glu Ala Pro Leu Ala Asp Ser
465 470 475 480
Leu Glu Glu Leu Glu Pro Gln
485

<210> 124
<211> 486
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>

[0064] <221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 124
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15
His Ala Ala Arg Pro Met Gly Arg Gly Leu Leu Arg Gly Leu Trp Pro
20 25 30
Leu His Ile Val Leu Trp Thr Arg Ile Ala Ser Thr Ile Pro Pro His
35 40 45
Val Gln Lys Ser Val Asn Asn Asp Met Ile Val Thr Asp Asn Asn Gly
50 55 60
Ala Val Lys Phe Pro Gln Leu Cys Lys Phe Cys Asp Val Arg Phe Ser
65 70 75 80
Thr Cys Asp Asn Gln Lys Ser Cys Met Ser Asn Cys Ser Ile Thr Ser
85 90 95
Ile Cys Glu Lys Pro Gln Glu Val Cys Val Ala Val Trp Arg Lys Asn
100 105 110
Asp Glu Asn Ile Thr Leu Glu Thr Val Cys His Asp Pro Lys Leu Pro
115 120 125
Tyr His Asp Phe Ile Leu Glu Asp Ala Ala Ser Pro Lys Cys Ile Met
130 135 140
Lys Glu Lys Lys Lys Pro Gly Glu Thr Phe Phe Met Cys Ser Cys Ser
145 150 155 160
Ser Asp Glu Cys Asn Asp Asn Ile Ile Phe Ser Glu Glu Tyr Asn Thr
165 170 175
Ser Asn Pro Asp Leu Leu Leu Val Ile Phe Gln Ser Asp Pro Thr Arg

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

[0065]
Gly Thr Thr Asn Ser Thr Leu Pro Pro Pro Phe Ser Leu Gln Ser Gly
385 390 395 400
Ile Leu Thr Leu Asn Pro Val Ala Gln Gly Gln Pro Ile Leu Thr Ser
405 410 415
Leu Gly Ser Asn Gln Glu Glu Ala Tyr Val Thr Met Ser Ser Phe Tyr
420 425 430
Gln Asn Gln Ser Asp Pro Lys Pro Glu Asn Pro Ala Cys Pro Trp Thr
435 440 445
Val Leu Pro Ala Gly Asp Leu Pro Thr His Asp Gly Tyr Leu Pro Ser
450 455 460
Asn Ile Asp Asp Leu Pro Ser His Glu Ala Pro Leu Ala Asp Ser Leu
465 470 475 480
Glu Glu Leu Glu Pro Gln
485

<210> 125
<211> 485
<212> PRT
<213> 人工序列（Artificial Sequence）
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 125
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15
His Ala Ala Arg Pro Met Gly Arg Gly Leu Leu Arg Gly Leu Trp Pro
20 25 30

Leu His Ile Val Leu Trp Thr Arg Ile Ala Ser Thr Ile Pro Pro His
35 40 45
Val Gln Lys Ser Val Asn Asn Asp Met Ile Val Thr Asp Asn Asn Gly
50 55 60
Ala Val Lys Phe Pro Gln Leu Cys Lys Phe Cys Asp Val Arg Phe Ser
65 70 75 80
Thr Cys Asp Asn Gln Lys Ser Cys Met Ser Asn Cys Ser Ile Thr Ser
85 90 95
Ile Cys Glu Lys Pro Gln Glu Val Cys Val Ala Val Trp Arg Lys Asn
100 105 110
Asp Glu Asn Ile Thr Leu Glu Thr Val Cys His Asp Pro Lys Leu Pro
115 120 125
Tyr His Asp Phe Ile Leu Glu Asp Ala Ala Ser Pro Lys Cys Ile Met
130 135 140
Lys Glu Lys Lys Lys Pro Gly Glu Thr Phe Phe Met Cys Ser Cys Ser
145 150 155 160
Ser Asp Glu Cys Asn Asp Asn Ile Ile Phe Ser Glu Glu Tyr Asn Thr
165 170 175
Ser Asn Pro Asp Leu Leu Leu Val Ile Phe Gln Ser Asp Pro Thr Arg
180 185 190
Val Glu Thr Ala Thr Glu Thr Ile Ser Leu Val Thr Ala Leu His Leu
195 200 205
Val Leu Gly Leu Ser Ala Val Leu Gly Leu Leu Leu Leu Arg Trp Gln
210 215 220
Phe Pro Ala His Tyr Arg Arg Leu Arg His Ala Leu Trp Pro Ser Leu
[0066] 225 230 235 240
Pro Asp Leu His Arg Val Leu Gly Gln Tyr Leu Arg Asp Thr Ala Ala
245 250 255
Leu Ser Pro Pro Lys Ala Thr Val Ser Asp Thr Cys Glu Glu Val Glu
260 265 270
Pro Ser Leu Leu Glu Ile Leu Pro Lys Ser Ser Glu Arg Thr Pro Leu
275 280 285
Pro Leu Ala Arg Asp Glu Val Glu Gly Phe Leu Gln Asp Thr Phe Pro
290 295 300
Gln Gln Leu Glu Glu Ser Glu Lys Gln Arg Leu Gly Gly Asp Val Gln
305 310 315 320
Ser Pro Asn Cys Pro Ser Glu Asp Val Val Ile Thr Pro Glu Ser Phe
325 330 335
Gly Arg Asp Ser Ser Leu Thr Cys Leu Ala Gly Asn Val Ser Ala Cys
340 345 350
Asp Ala Pro Ile Leu Ser Ser Ser Arg Ser Leu Asp Cys Arg Glu Ser
355 360 365
Gly Lys Asn Gly Pro His Val Tyr Gln Asp Leu Leu Leu Ser Leu Gly
370 375 380
Thr Thr Asn Ser Thr Leu Pro Pro Pro Phe Ser Leu Gln Ser Gly Ile
385 390 395 400
Leu Thr Leu Asn Pro Val Ala Gln Gly Gln Pro Ile Leu Thr Ser Leu
405 410 415
Gly Ser Asn Gln Glu Glu Ala Tyr Val Thr Met Ser Ser Phe Tyr Gln
420 425 430
Asn Gln Ser Asp Pro Lys Pro Glu Asn Pro Ala Cys Pro Trp Thr Val

435 440 445
Leu Pro Ala Gly Asp Leu Pro Thr His Asp Gly Tyr Leu Pro Ser Asn
450 455 460
Ile Asp Asp Leu Pro Ser His Glu Ala Pro Leu Ala Asp Ser Leu Glu
465 470 475 480
Glu Leu Glu Pro Gln
485

<210> 126
<211> 486
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 126
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15
His Ala Ala Arg Pro Met Gly Arg Gly Leu Leu Arg Gly Leu Trp Pro
20 25 30
Leu His Ile Val Leu Trp Thr Arg Ile Ala Ser Thr Ile Pro Pro His
35 40 45
Val Gln Lys Ser Val Asn Asn Asp Met Ile Val Thr Asp Asn Asn Gly
50 55 60
Ala Val Lys Phe Pro Gln Leu Cys Lys Phe Cys Asp Val Arg Phe Ser
65 70 75 80
[0067] Thr Cys Asp Asn Gln Lys Ser Cys Met Ser Asn Cys Ser Ile Thr Ser
85 90 95
Ile Cys Glu Lys Pro Gln Glu Val Cys Val Ala Val Trp Arg Lys Asn
100 105 110
Asp Glu Asn Ile Thr Leu Glu Thr Val Cys His Asp Pro Lys Leu Pro
115 120 125
Tyr His Asp Phe Ile Leu Glu Asp Ala Ala Ser Pro Lys Cys Ile Met
130 135 140
Lys Glu Lys Lys Lys Pro Gly Glu Thr Phe Phe Met Cys Ser Cys Ser
145 150 155 160
Ser Asp Glu Cys Asn Asp Asn Ile Ile Phe Ser Glu Glu Tyr Asn Thr
165 170 175
Ser Asn Pro Asp Leu Leu Leu Val Ile Phe Gln Ser Asp Pro Thr Arg
180 185 190
Val Glu Thr Ala Thr Glu Thr Leu Ile Ser Leu Val Thr Ala Leu His
195 200 205
Leu Val Leu Gly Leu Ser Ala Val Leu Gly Leu Leu Leu Leu Arg Trp
210 215 220
Gln Phe Pro Ala His Tyr Arg Arg Leu Arg His Ala Leu Trp Pro Ser
225 230 235 240
Leu Pro Asp Leu His Arg Val Leu Gly Gln Tyr Leu Arg Asp Thr Ala
245 250 255
Ala Leu Ser Pro Pro Lys Ala Thr Val Ser Asp Thr Cys Glu Glu Val
260 265 270
Glu Pro Ser Leu Leu Glu Ile Leu Pro Lys Ser Ser Glu Arg Thr Pro
275 280 285

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

[0068]

<210> 127
<211> 484
<212> PRT
<213> 人工序列（Artificial Sequence）
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 127
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15
His Ala Ala Arg Pro Met Gly Arg Gly Leu Leu Arg Gly Leu Trp Pro
20 25 30
Leu His Ile Val Leu Trp Thr Arg Ile Ala Ser Thr Ile Pro Pro His
35 40 45
Val Gln Lys Ser Val Asn Asn Asp Met Ile Val Thr Asp Asn Asn Gly
50 55 60
Ala Val Lys Phe Pro Gln Leu Cys Lys Phe Cys Asp Val Arg Phe Ser
65 70 75 80
Thr Cys Asp Asn Gln Lys Ser Cys Met Ser Asn Cys Ser Ile Thr Ser
85 90 95
Ile Cys Glu Lys Pro Gln Glu Val Cys Val Ala Val Trp Arg Lys Asn
100 105 110
Asp Glu Asn Ile Thr Leu Glu Thr Val Cys His Asp Pro Lys Leu Pro
115 120 125
Tyr His Asp Phe Ile Leu Glu Asp Ala Ala Ser Pro Lys Cys Ile Met

130 135 140

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

[0069] Arg Asp Ser Ser Leu Thr Cys Leu Ala Gly Asn Val Ser Ala Cys Asp
340 345 350
Ala Pro Ile Leu Ser Ser Ser Arg Ser Leu Asp Cys Arg Glu Ser Gly
355 360 365
Lys Asn Gly Pro His Val Tyr Gln Asp Leu Leu Leu Ser Leu Gly Thr
370 375 380
Thr Asn Ser Thr Leu Pro Pro Pro Phe Ser Leu Gln Ser Gly Ile Leu
385 390 395 400
Thr Leu Asn Pro Val Ala Gln Gly Gln Pro Ile Leu Thr Ser Leu Gly
405 410 415
Ser Asn Gln Glu Glu Ala Tyr Val Thr Met Ser Ser Phe Tyr Gln Asn
420 425 430
Gln Ser Asp Pro Lys Pro Glu Asn Pro Ala Cys Pro Trp Thr Val Leu
435 440 445
Pro Ala Gly Asp Leu Pro Thr His Asp Gly Tyr Leu Pro Ser Asn Ile
450 455 460
Asp Asp Leu Pro Ser His Glu Ala Pro Leu Ala Asp Ser Leu Glu Glu
465 470 475 480
Leu Glu Pro Gln

<210> 128
<211> 483
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
<221> source

<223> /注释 = “人工序列的描述：合成多肽”

<400> 128

Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15
His Ala Ala Arg Pro Met Gly Arg Gly Leu Leu Arg Gly Leu Trp Pro
20 25 30
Leu His Ile Val Leu Trp Thr Arg Ile Ala Ser Thr Ile Pro Pro His
35 40 45
Val Gln Lys Ser Val Asn Asn Asp Met Ile Val Thr Asp Asn Asn Gly
50 55 60
Ala Val Lys Phe Pro Gln Leu Cys Lys Phe Cys Asp Val Arg Phe Ser
65 70 75 80
Thr Cys Asp Asn Gln Lys Ser Cys Met Ser Asn Cys Ser Ile Thr Ser
85 90 95
Ile Cys Glu Lys Pro Gln Glu Val Cys Val Ala Val Trp Arg Lys Asn
100 105 110
Asp Glu Asn Ile Thr Leu Glu Thr Val Cys His Asp Pro Lys Leu Pro
115 120 125
Tyr His Asp Phe Ile Leu Glu Asp Ala Ala Ser Pro Lys Cys Ile Met
130 135 140
Lys Glu Lys Lys Lys Pro Gly Glu Thr Phe Phe Met Cys Ser Cys Ser
145 150 155 160
Ser Asp Glu Cys Asn Asp Asn Ile Ile Phe Ser Glu Glu Tyr Asn Thr
165 170 175
Ser Asn Pro Asp Leu Leu Leu Val Ile Phe Gln Ser Asp Pro Thr Arg
[0070] 180 185 190
Val Glu Thr Ala Thr Glu Thr Leu Val Thr Ala Leu His Leu Val Leu
195 200 205
Gly Leu Ser Ala Val Leu Gly Leu Leu Leu Leu Arg Trp Gln Phe Pro
210 215 220
Ala His Tyr Arg Arg Leu Arg His Ala Leu Trp Pro Ser Leu Pro Asp
225 230 235 240
Leu His Arg Val Leu Gly Gln Tyr Leu Arg Asp Thr Ala Ala Leu Ser
245 250 255
Pro Pro Lys Ala Thr Val Ser Asp Thr Cys Glu Glu Val Glu Pro Ser
260 265 270
Leu Leu Glu Ile Leu Pro Lys Ser Ser Glu Arg Thr Pro Leu Pro Leu
275 280 285
Ala Arg Asp Glu Val Glu Gly Phe Leu Gln Asp Thr Phe Pro Gln Gln
290 295 300
Leu Glu Glu Ser Glu Lys Gln Arg Leu Gly Gly Asp Val Gln Ser Pro
305 310 315 320
Asn Cys Pro Ser Glu Asp Val Val Ile Thr Pro Glu Ser Phe Gly Arg
325 330 335
Asp Ser Ser Leu Thr Cys Leu Ala Gly Asn Val Ser Ala Cys Asp Ala
340 345 350
Pro Ile Leu Ser Ser Ser Arg Ser Leu Asp Cys Arg Glu Ser Gly Lys
355 360 365
Asn Gly Pro His Val Tyr Gln Asp Leu Leu Leu Ser Leu Gly Thr Thr
370 375 380
Asn Ser Thr Leu Pro Pro Pro Phe Ser Leu Gln Ser Gly Ile Leu Thr

385 390 395 400
Leu Asn Pro Val Ala Gln Gly Gln Pro Ile Leu Thr Ser Leu Gly Ser
405 410 415
Asn Gln Glu Glu Ala Tyr Val Thr Met Ser Ser Phe Tyr Gln Asn Gln
420 425 430
Ser Asp Pro Lys Pro Glu Asn Pro Ala Cys Pro Trp Thr Val Leu Pro
435 440 445
Ala Gly Asp Leu Pro Thr His Asp Gly Tyr Leu Pro Ser Asn Ile Asp
450 455 460
Asp Leu Pro Ser His Glu Ala Pro Leu Ala Asp Ser Leu Glu Glu Leu
465 470 475 480
Glu Pro Gln

<210> 129
<211> 484
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 129
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15
His Ala Ala Arg Pro Met Gly Arg Gly Leu Leu Arg Gly Leu Trp Pro
20 25 30
[0071] Leu His Ile Val Leu Trp Thr Arg Ile Ala Ser Thr Ile Pro Pro His
35 40 45
Val Gln Lys Ser Val Asn Asn Asp Met Ile Val Thr Asp Asn Asn Gly
50 55 60
Ala Val Lys Phe Pro Gln Leu Cys Lys Phe Cys Asp Val Arg Phe Ser
65 70 75 80
Thr Cys Asp Asn Gln Lys Ser Cys Met Ser Asn Cys Ser Ile Thr Ser
85 90 95
Ile Cys Glu Lys Pro Gln Glu Val Cys Val Ala Val Trp Arg Lys Asn
100 105 110
Asp Glu Asn Ile Thr Leu Glu Thr Val Cys His Asp Pro Lys Leu Pro
115 120 125
Tyr His Asp Phe Ile Leu Glu Asp Ala Ala Ser Pro Lys Cys Ile Met
130 135 140
Lys Glu Lys Lys Lys Pro Gly Glu Thr Phe Phe Met Cys Ser Cys Ser
145 150 155 160
Ser Asp Glu Cys Asn Asp Asn Ile Ile Phe Ser Glu Glu Tyr Asn Thr
165 170 175
Ser Asn Pro Asp Leu Leu Leu Val Ile Phe Gln Ser Asp Pro Thr Arg
180 185 190
Val Glu Thr Ala Thr Glu Thr Ile Leu Val Thr Ala Leu His Leu Val
195 200 205
Leu Gly Leu Ser Ala Val Leu Gly Leu Leu Leu Leu Arg Trp Gln Phe
210 215 220
Pro Ala His Tyr Arg Arg Leu Arg His Ala Leu Trp Pro Ser Leu Pro
225 230 235 240

Asp Leu His Arg Val Leu Gly Gln Tyr Leu Arg Asp Thr Ala Ala Leu
245 250 255
Ser Pro Pro Lys Ala Thr Val Ser Asp Thr Cys Glu Glu Val Glu Pro
260 265 270
Ser Leu Leu Glu Ile Leu Pro Lys Ser Ser Glu Arg Thr Pro Leu Pro
275 280 285
Leu Ala Arg Asp Glu Val Glu Gly Phe Leu Gln Asp Thr Phe Pro Gln
290 295 300
Gln Leu Glu Glu Ser Glu Lys Gln Arg Leu Gly Gly Asp Val Gln Ser
305 310 315 320
Pro Asn Cys Pro Ser Glu Asp Val Val Ile Thr Pro Glu Ser Phe Gly
325 330 335
Arg Asp Ser Ser Leu Thr Cys Leu Ala Gly Asn Val Ser Ala Cys Asp
340 345 350
Ala Pro Ile Leu Ser Ser Ser Arg Ser Leu Asp Cys Arg Glu Ser Gly
355 360 365
Lys Asn Gly Pro His Val Tyr Gln Asp Leu Leu Leu Ser Leu Gly Thr
370 375 380
Thr Asn Ser Thr Leu Pro Pro Pro Phe Ser Leu Gln Ser Gly Ile Leu
385 390 395 400
Thr Leu Asn Pro Val Ala Gln Gly Gln Pro Ile Leu Thr Ser Leu Gly
405 410 415
Ser Asn Gln Glu Glu Ala Tyr Val Thr Met Ser Ser Phe Tyr Gln Asn
420 425 430
Gln Ser Asp Pro Lys Pro Glu Asn Pro Ala Cys Pro Trp Thr Val Leu
[0072] 435 440 445
Pro Ala Gly Asp Leu Pro Thr His Asp Gly Tyr Leu Pro Ser Asn Ile
450 455 460
Asp Asp Leu Pro Ser His Glu Ala Pro Leu Ala Asp Ser Leu Glu Glu
465 470 475 480
Leu Glu Pro Gln

<210> 130
<211> 482
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 130
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15
His Ala Ala Arg Pro Met Gly Arg Gly Leu Leu Arg Gly Leu Trp Pro
20 25 30
Leu His Ile Val Leu Trp Thr Arg Ile Ala Ser Thr Ile Pro Pro His
35 40 45
Val Gln Lys Ser Val Asn Asn Asp Met Ile Val Thr Asp Asn Asn Gly
50 55 60
Ala Val Lys Phe Pro Gln Leu Cys Lys Phe Cys Asp Val Arg Phe Ser
65 70 75 80
Thr Cys Asp Asn Gln Lys Ser Cys Met Ser Asn Cys Ser Ile Thr Ser

[0073]

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                85                  90                  95
Ile Cys Glu Lys Pro Gln Glu Val Cys Val Ala Val Trp Arg Lys Asn
            100                 105                 110
Asp Glu Asn Ile Thr Leu Glu Thr Val Cys His Asp Pro Lys Leu Pro
        115                 120                 125
Tyr His Asp Phe Ile Leu Glu Asp Ala Ala Ser Pro Lys Cys Ile Met
    130                 135                 140
Lys Glu Lys Lys Lys Pro Gly Glu Thr Phe Phe Met Cys Ser Cys Ser
145                 150                 155                 160
Ser Asp Glu Cys Asn Asp Asn Ile Ile Phe Ser Glu Glu Tyr Asn Thr
                165                 170                 175
Ser Asn Pro Asp Leu Leu Leu Val Ile Phe Gln Ser Asp Pro Thr Arg
            180                 185                 190
Val Glu Thr Ala Thr Glu Thr Val Thr Ala Leu His Leu Val Leu Gly
        195                 200                 205
Leu Ser Ala Val Leu Gly Leu Leu Leu Leu Arg Trp Gln Phe Pro Ala
    210                 215                 220
His Tyr Arg Arg Leu Arg His Ala Leu Trp Pro Ser Leu Pro Asp Leu
225                 230                 235                 240
His Arg Val Leu Gly Gln Tyr Leu Arg Asp Thr Ala Ala Leu Ser Pro
                245                 250                 255
Pro Lys Ala Thr Val Ser Asp Thr Cys Glu Glu Val Glu Pro Ser Leu
            260                 265                 270
Leu Glu Ile Leu Pro Lys Ser Ser Glu Arg Thr Pro Leu Pro Leu Ala
        275                 280                 285
Arg Asp Glu Val Glu Gly Phe Leu Gln Asp Thr Phe Pro Gln Gln Leu
    290                 295                 300
Glu Glu Ser Glu Lys Gln Arg Leu Gly Gly Asp Val Gln Ser Pro Asn
305                 310                 315                 320
Cys Pro Ser Glu Asp Val Val Ile Thr Pro Glu Ser Phe Gly Arg Asp
                325                 330                 335
Ser Ser Leu Thr Cys Leu Ala Gly Asn Val Ser Ala Cys Asp Ala Pro
            340                 345                 350
Ile Leu Ser Ser Ser Arg Ser Leu Asp Cys Arg Glu Ser Gly Lys Asn
        355                 360                 365
Gly Pro His Val Tyr Gln Asp Leu Leu Leu Ser Leu Gly Thr Thr Asn
    370                 375                 380
Ser Thr Leu Pro Pro Pro Phe Ser Leu Gln Ser Gly Ile Leu Thr Leu
385                 390                 395                 400
Asn Pro Val Ala Gln Gly Gln Pro Ile Leu Thr Ser Leu Gly Ser Asn
                405                 410                 415
Gln Glu Glu Ala Tyr Val Thr Met Ser Ser Phe Tyr Gln Asn Gln Ser
            420                 425                 430
Asp Pro Lys Pro Glu Asn Pro Ala Cys Pro Trp Thr Val Leu Pro Ala
        435                 440                 445
Gly Asp Leu Pro Thr His Asp Gly Tyr Leu Pro Ser Asn Ile Asp Asp
    450                 455                 460
Leu Pro Ser His Glu Ala Pro Leu Ala Asp Ser Leu Glu Glu Leu Glu
465                 470                 475                 480
Pro Gln
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<210> 131
<211> 481
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 131

Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15
His Ala Ala Arg Pro Met Gly Arg Gly Leu Leu Arg Gly Leu Trp Pro
20 25 30
Leu His Ile Val Leu Trp Thr Arg Ile Ala Ser Thr Ile Pro Pro His
35 40 45
Val Gln Lys Ser Val Asn Asn Asp Met Ile Val Thr Asp Asn Asn Gly
50 55 60
Ala Val Lys Phe Pro Gln Leu Cys Lys Phe Cys Asp Val Arg Phe Ser
65 70 75 80
Thr Cys Asp Asn Gln Lys Ser Cys Met Ser Asn Cys Ser Ile Thr Ser
85 90 95
Ile Cys Glu Lys Pro Gln Glu Val Cys Val Ala Val Trp Arg Lys Asn
100 105 110
Asp Glu Asn Ile Thr Leu Glu Thr Val Cys His Asp Pro Lys Leu Pro
115 120 125
Tyr His Asp Phe Ile Leu Glu Asp Ala Ala Ser Pro Lys Cys Ile Met
[0074] 130 135 140
Lys Glu Lys Lys Lys Pro Gly Glu Thr Phe Phe Met Cys Ser Cys Ser
145 150 155 160
Ser Asp Glu Cys Asn Asp Asn Ile Ile Phe Ser Glu Glu Tyr Asn Thr
165 170 175
Ser Asn Pro Asp Leu Leu Leu Val Ile Phe Gln Ser Asp Pro Thr Arg
180 185 190
Val Glu Thr Ala Thr Glu Thr Thr Ala Leu His Leu Val Leu Gly Leu
195 200 205
Ser Ala Val Leu Gly Leu Leu Leu Leu Arg Trp Gln Phe Pro Ala His
210 215 220
Tyr Arg Arg Leu Arg His Ala Leu Trp Pro Ser Leu Pro Asp Leu His
225 230 235 240
Arg Val Leu Gly Gln Tyr Leu Arg Asp Thr Ala Ala Leu Ser Pro Pro
245 250 255
Lys Ala Thr Val Ser Asp Thr Cys Glu Glu Val Glu Pro Ser Leu Leu
260 265 270
Glu Ile Leu Pro Lys Ser Ser Glu Arg Thr Pro Leu Pro Leu Ala Arg
275 280 285
Asp Glu Val Glu Gly Phe Leu Gln Asp Thr Phe Pro Gln Gln Leu Glu
290 295 300
Glu Ser Glu Lys Gln Arg Leu Gly Gly Asp Val Gln Ser Pro Asn Cys
305 310 315 320
Pro Ser Glu Asp Val Val Ile Thr Pro Glu Ser Phe Gly Arg Asp Ser
325 330 335
Ser Leu Thr Cys Leu Ala Gly Asn Val Ser Ala Cys Asp Ala Pro Ile

340 345 350
Leu Ser Ser Ser Arg Ser Leu Asp Cys Arg Glu Ser Gly Lys Asn Gly
355 360 365
Pro His Val Tyr Gln Asp Leu Leu Leu Ser Leu Gly Thr Thr Asn Ser
370 375 380
Thr Leu Pro Pro Pro Phe Ser Leu Gln Ser Gly Ile Leu Thr Leu Asn
385 390 395 400
Pro Val Ala Gln Gly Gln Pro Ile Leu Thr Ser Leu Gly Ser Asn Gln
405 410 415
Glu Glu Ala Tyr Val Thr Met Ser Ser Phe Tyr Gln Asn Gln Ser Asp
420 425 430
Pro Lys Pro Glu Asn Pro Ala Cys Pro Trp Thr Val Leu Pro Ala Gly
435 440 445
Asp Leu Pro Thr His Asp Gly Tyr Leu Pro Ser Asn Ile Asp Asp Leu
450 455 460
Pro Ser His Glu Ala Pro Leu Ala Asp Ser Leu Glu Glu Leu Glu Pro
465 470 475 480
Gln

<210> 132
<211> 480
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
<221> source
[0075] <223> /注释 = “人工序列的描述：合成多肽”
<400> 132
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15
His Ala Ala Arg Pro Met Gly Arg Gly Leu Leu Arg Gly Leu Trp Pro
20 25 30
Leu His Ile Val Leu Trp Thr Arg Ile Ala Ser Thr Ile Pro Pro His
35 40 45
Val Gln Lys Ser Val Asn Asn Asp Met Ile Val Thr Asp Asn Asn Gly
50 55 60
Ala Val Lys Phe Pro Gln Leu Cys Lys Phe Cys Asp Val Arg Phe Ser
65 70 75 80
Thr Cys Asp Asn Gln Lys Ser Cys Met Ser Asn Cys Ser Ile Thr Ser
85 90 95
Ile Cys Glu Lys Pro Gln Glu Val Cys Val Ala Val Trp Arg Lys Asn
100 105 110
Asp Glu Asn Ile Thr Leu Glu Thr Val Cys His Asp Pro Lys Leu Pro
115 120 125
Tyr His Asp Phe Ile Leu Glu Asp Ala Ala Ser Pro Lys Cys Ile Met
130 135 140
Lys Glu Lys Lys Lys Pro Gly Glu Thr Phe Phe Met Cys Ser Cys Ser
145 150 155 160
Ser Asp Glu Cys Asn Asp Asn Ile Ile Phe Ser Glu Glu Tyr Asn Thr
165 170 175
Ser Asn Pro Asp Leu Leu Leu Val Ile Phe Gln Ser Asp Pro Thr Arg
180 185 190

Val Glu Thr Ala Thr Glu Thr Ala Leu His Leu Val Leu Gly Leu Ser
195 200 205
Ala Val Leu Gly Leu Leu Leu Leu Arg Trp Gln Phe Pro Ala His Tyr
210 215 220
Arg Arg Leu Arg His Ala Leu Trp Pro Ser Leu Pro Asp Leu His Arg
225 230 235 240
Val Leu Gly Gln Tyr Leu Arg Asp Thr Ala Ala Leu Ser Pro Pro Lys
245 250 255
Ala Thr Val Ser Asp Thr Cys Glu Glu Val Glu Pro Ser Leu Leu Glu
260 265 270
Ile Leu Pro Lys Ser Ser Glu Arg Thr Pro Leu Pro Leu Ala Arg Asp
275 280 285
Glu Val Glu Gly Phe Leu Gln Asp Thr Phe Pro Gln Gln Leu Glu Glu
290 295 300
Ser Glu Lys Gln Arg Leu Gly Gly Asp Val Gln Ser Pro Asn Cys Pro
305 310 315 320
Ser Glu Asp Val Val Ile Thr Pro Glu Ser Phe Gly Arg Asp Ser Ser
325 330 335
Leu Thr Cys Leu Ala Gly Asn Val Ser Ala Cys Asp Ala Pro Ile Leu
340 345 350
Ser Ser Ser Arg Ser Leu Asp Cys Arg Glu Ser Gly Lys Asn Gly Pro
355 360 365
His Val Tyr Gln Asp Leu Leu Leu Ser Leu Gly Thr Thr Asn Ser Thr
370 375 380
Leu Pro Pro Pro Phe Ser Leu Gln Ser Gly Ile Leu Thr Leu Asn Pro
[0076] 385 390 395 400
Val Ala Gln Gly Gln Pro Ile Leu Thr Ser Leu Gly Ser Asn Gln Glu
405 410 415
Glu Ala Tyr Val Thr Met Ser Ser Phe Tyr Gln Asn Gln Ser Asp Pro
420 425 430
Lys Pro Glu Asn Pro Ala Cys Pro Trp Thr Val Leu Pro Ala Gly Asp
435 440 445
Leu Pro Thr His Asp Gly Tyr Leu Pro Ser Asn Ile Asp Asp Leu Pro
450 455 460
Ser His Glu Ala Pro Leu Ala Asp Ser Leu Glu Glu Leu Glu Pro Gln
465 470 475 480
<210> 133
<211> 479
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 133
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15
His Ala Ala Arg Pro Met Gly Arg Gly Leu Leu Arg Gly Leu Trp Pro
20 25 30
Leu His Ile Val Leu Trp Thr Arg Ile Ala Ser Thr Ile Pro Pro His
35 40 45
Val Gln Lys Ser Val Asn Asn Asp Met Ile Val Thr Asp Asn Asn Gly

50 55 60

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

[0077] Thr Val Ser Asp Thr Cys Glu Glu Val Glu Pro Ser Leu Leu Glu Ile
260 265 270
Leu Pro Lys Ser Ser Glu Arg Thr Pro Leu Pro Leu Ala Arg Asp Glu
275 280 285
Val Glu Gly Phe Leu Gln Asp Thr Phe Pro Gln Gln Leu Glu Glu Ser
290 295 300
Glu Lys Gln Arg Leu Gly Gly Asp Val Gln Ser Pro Asn Cys Pro Ser
305 310 315 320
Glu Asp Val Val Ile Thr Pro Glu Ser Phe Gly Arg Asp Ser Ser Leu
325 330 335
Thr Cys Leu Ala Gly Asn Val Ser Ala Cys Asp Ala Pro Ile Leu Ser
340 345 350
Ser Ser Arg Ser Leu Asp Cys Arg Glu Ser Gly Lys Asn Gly Pro His
355 360 365
Val Tyr Gln Asp Leu Leu Leu Ser Leu Gly Thr Thr Asn Ser Thr Leu
370 375 380
Pro Pro Pro Phe Ser Leu Gln Ser Gly Ile Leu Thr Leu Asn Pro Val
385 390 395 400
Ala Gln Gly Gln Pro Ile Leu Thr Ser Leu Gly Ser Asn Gln Glu Glu
405 410 415
Ala Tyr Val Thr Met Ser Ser Phe Tyr Gln Asn Gln Ser Asp Pro Lys
420 425 430
Pro Glu Asn Pro Ala Cys Pro Trp Thr Val Leu Pro Ala Gly Asp Leu
435 440 445
Pro Thr His Asp Gly Tyr Leu Pro Ser Asn Ile Asp Asp Leu Pro Ser
450 455 460

His Glu Ala Pro Leu Ala Asp Ser Leu Glu Glu Leu Glu Pro Gln
465 470 475

<210> 134
<211> 478
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 134

Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15
His Ala Ala Arg Pro Met Gly Arg Gly Leu Leu Arg Gly Leu Trp Pro
20 25 30
Leu His Ile Val Leu Trp Thr Arg Ile Ala Ser Thr Ile Pro Pro His
35 40 45
Val Gln Lys Ser Val Asn Asn Asp Met Ile Val Thr Asp Asn Asn Gly
50 55 60
Ala Val Lys Phe Pro Gln Leu Cys Lys Phe Cys Asp Val Arg Phe Ser
65 70 75 80
Thr Cys Asp Asn Gln Lys Ser Cys Met Ser Asn Cys Ser Ile Thr Ser
85 90 95
Ile Cys Glu Lys Pro Gln Glu Val Cys Val Ala Val Trp Arg Lys Asn
100 105 110
Asp Glu Asn Ile Thr Leu Glu Thr Val Cys His Asp Pro Lys Leu Pro
[0078] 115 120 125
Tyr His Asp Phe Ile Leu Glu Asp Ala Ala Ser Pro Lys Cys Ile Met
130 135 140
Lys Glu Lys Lys Lys Pro Gly Glu Thr Phe Phe Met Cys Ser Cys Ser
145 150 155 160
Ser Asp Glu Cys Asn Asp Asn Ile Ile Phe Ser Glu Glu Tyr Asn Thr
165 170 175
Ser Asn Pro Asp Leu Leu Leu Val Ile Phe Gln Ser Asp Pro Thr Arg
180 185 190
Val Glu Thr Ala Thr Glu Thr His Leu Val Leu Gly Leu Ser Ala Val
195 200 205
Leu Gly Leu Leu Leu Leu Arg Trp Gln Phe Pro Ala His Tyr Arg Arg
210 215 220
Leu Arg His Ala Leu Trp Pro Ser Leu Pro Asp Leu His Arg Val Leu
225 230 235 240
Gly Gln Tyr Leu Arg Asp Thr Ala Ala Leu Ser Pro Pro Lys Ala Thr
245 250 255
Val Ser Asp Thr Cys Glu Glu Val Glu Pro Ser Leu Leu Glu Ile Leu
260 265 270
Pro Lys Ser Ser Glu Arg Thr Pro Leu Pro Leu Ala Arg Asp Glu Val
275 280 285
Glu Gly Phe Leu Gln Asp Thr Phe Pro Gln Gln Leu Glu Glu Ser Glu
290 295 300
Lys Gln Arg Leu Gly Gly Asp Val Gln Ser Pro Asn Cys Pro Ser Glu
305 310 315 320
Asp Val Val Ile Thr Pro Glu Ser Phe Gly Arg Asp Ser Ser Leu Thr

325 330 335
Cys Leu Ala Gly Asn Val Ser Ala Cys Asp Ala Pro Ile Leu Ser Ser
340 345 350
Ser Arg Ser Leu Asp Cys Arg Glu Ser Gly Lys Asn Gly Pro His Val
355 360 365
Tyr Gln Asp Leu Leu Leu Ser Leu Gly Thr Thr Asn Ser Thr Leu Pro
370 375 380
Pro Pro Phe Ser Leu Gln Ser Gly Ile Leu Thr Leu Asn Pro Val Ala
385 390 395 400
Gln Gly Gln Pro Ile Leu Thr Ser Leu Gly Ser Asn Gln Glu Glu Ala
405 410 415
Tyr Val Thr Met Ser Ser Phe Tyr Gln Asn Gln Ser Asp Pro Lys Pro
420 425 430
Glu Asn Pro Ala Cys Pro Trp Thr Val Leu Pro Ala Gly Asp Leu Pro
435 440 445
Thr His Asp Gly Tyr Leu Pro Ser Asn Ile Asp Asp Leu Pro Ser His
450 455 460
Glu Ala Pro Leu Ala Asp Ser Leu Glu Glu Leu Glu Pro Gln
465 470 475

<210> 135
<211> 477
<212> PRT
<213> 人工序列（Artificial Sequence）
<220>
<221> source
[0079] <223> /注释 = “人工序列的描述：合成多肽”
<400> 135
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15
His Ala Ala Arg Pro Met Gly Arg Gly Leu Leu Arg Gly Leu Trp Pro
20 25 30
Leu His Ile Val Leu Trp Thr Arg Ile Ala Ser Thr Ile Pro Pro His
35 40 45
Val Gln Lys Ser Val Asn Asn Asp Met Ile Val Thr Asp Asn Asn Gly
50 55 60
Ala Val Lys Phe Pro Gln Leu Cys Lys Phe Cys Asp Val Arg Phe Ser
65 70 75 80
Thr Cys Asp Asn Gln Lys Ser Cys Met Ser Asn Cys Ser Ile Thr Ser
85 90 95
Ile Cys Glu Lys Pro Gln Glu Val Cys Val Ala Val Trp Arg Lys Asn
100 105 110
Asp Glu Asn Ile Thr Leu Glu Thr Val Cys His Asp Pro Lys Leu Pro
115 120 125
Tyr His Asp Phe Ile Leu Glu Asp Ala Ala Ser Pro Lys Cys Ile Met
130 135 140
Lys Glu Lys Lys Lys Pro Gly Glu Thr Phe Phe Met Cys Ser Cys Ser
145 150 155 160
Ser Asp Glu Cys Asn Asp Asn Ile Ile Phe Ser Glu Glu Tyr Asn Thr
165 170 175
Ser Asn Pro Asp Leu Leu Leu Val Ile Phe Gln Ser Asp Pro Thr Arg
180 185 190

Val Glu Thr Ala Thr Glu Thr Leu Val Leu Gly Leu Ser Ala Val Leu
195 200 205
Gly Leu Leu Leu Leu Arg Trp Gln Phe Pro Ala His Tyr Arg Arg Leu
210 215 220
Arg His Ala Leu Trp Pro Ser Leu Pro Asp Leu His Arg Val Leu Gly
225 230 235 240
Gln Tyr Leu Arg Asp Thr Ala Ala Leu Ser Pro Pro Lys Ala Thr Val
245 250 255
Ser Asp Thr Cys Glu Glu Val Glu Pro Ser Leu Leu Glu Ile Leu Pro
260 265 270
Lys Ser Ser Glu Arg Thr Pro Leu Pro Leu Ala Arg Asp Glu Val Glu
275 280 285
Gly Phe Leu Gln Asp Thr Phe Pro Gln Gln Leu Glu Glu Ser Glu Lys
290 295 300
Gln Arg Leu Gly Gly Asp Val Gln Ser Pro Asn Cys Pro Ser Glu Asp
305 310 315 320
Val Val Ile Thr Pro Glu Ser Phe Gly Arg Asp Ser Ser Leu Thr Cys
325 330 335
Leu Ala Gly Asn Val Ser Ala Cys Asp Ala Pro Ile Leu Ser Ser Ser
340 345 350
Arg Ser Leu Asp Cys Arg Glu Ser Gly Lys Asn Gly Pro His Val Tyr
355 360 365
Gln Asp Leu Leu Leu Ser Leu Gly Thr Thr Asn Ser Thr Leu Pro Pro
370 375 380
Pro Phe Ser Leu Gln Ser Gly Ile Leu Thr Leu Asn Pro Val Ala Gln
[0080] 385 390 395 400
Gly Gln Pro Ile Leu Thr Ser Leu Gly Ser Asn Gln Glu Glu Ala Tyr
405 410 415
Val Thr Met Ser Ser Phe Tyr Gln Asn Gln Ser Asp Pro Lys Pro Glu
420 425 430
Asn Pro Ala Cys Pro Trp Thr Val Leu Pro Ala Gly Asp Leu Pro Thr
435 440 445
His Asp Gly Tyr Leu Pro Ser Asn Ile Asp Asp Leu Pro Ser His Glu
450 455 460
Ala Pro Leu Ala Asp Ser Leu Glu Glu Leu Glu Pro Gln
465 470 475

<210> 136
<211> 476
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 136
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15
His Ala Ala Arg Pro Met Gly Arg Gly Leu Leu Arg Gly Leu Trp Pro
20 25 30
Leu His Ile Val Leu Trp Thr Arg Ile Ala Ser Thr Ile Pro Pro His
35 40 45
Val Gln Lys Ser Val Asn Asn Asp Met Ile Val Thr Asp Asn Asn Gly

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

[0081] Asp Thr Cys Glu Glu Val Glu Pro Ser Leu Leu Glu Ile Leu Pro Lys
260 265 270
Ser Ser Glu Arg Thr Pro Leu Pro Leu Ala Arg Asp Glu Val Glu Gly
275 280 285
Phe Leu Gln Asp Thr Phe Pro Gln Gln Leu Glu Glu Ser Glu Lys Gln
290 295 300
Arg Leu Gly Gly Asp Val Gln Ser Pro Asn Cys Pro Ser Glu Asp Val
305 310 315 320
Val Ile Thr Pro Glu Ser Phe Gly Arg Asp Ser Ser Leu Thr Cys Leu
325 330 335
Ala Gly Asn Val Ser Ala Cys Asp Ala Pro Ile Leu Ser Ser Ser Arg
340 345 350
Ser Leu Asp Cys Arg Glu Ser Gly Lys Asn Gly Pro His Val Tyr Gln
355 360 365
Asp Leu Leu Leu Ser Leu Gly Thr Thr Asn Ser Thr Leu Pro Pro Pro
370 375 380
Phe Ser Leu Gln Ser Gly Ile Leu Thr Leu Asn Pro Val Ala Gln Gly
385 390 395 400
Gln Pro Ile Leu Thr Ser Leu Gly Ser Asn Gln Glu Glu Ala Tyr Val
405 410 415
Thr Met Ser Ser Phe Tyr Gln Asn Gln Ser Asp Pro Lys Pro Glu Asn
420 425 430
Pro Ala Cys Pro Trp Thr Val Leu Pro Ala Gly Asp Leu Pro Thr His
435 440 445
Asp Gly Tyr Leu Pro Ser Asn Ile Asp Asp Leu Pro Ser His Glu Ala
450 455 460

Pro Leu Ala Asp Ser Leu Glu Glu Leu Glu Pro Gln
465 470 475

<210> 137
<211> 475
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 137

Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15
His Ala Ala Arg Pro Met Gly Arg Gly Leu Leu Arg Gly Leu Trp Pro
20 25 30
Leu His Ile Val Leu Trp Thr Arg Ile Ala Ser Thr Ile Pro Pro His
35 40 45
Val Gln Lys Ser Val Asn Asn Asp Met Ile Val Thr Asp Asn Asn Gly
50 55 60
Ala Val Lys Phe Pro Gln Leu Cys Lys Phe Cys Asp Val Arg Phe Ser
65 70 75 80
Thr Cys Asp Asn Gln Lys Ser Cys Met Ser Asn Cys Ser Ile Thr Ser
85 90 95
Ile Cys Glu Lys Pro Gln Glu Val Cys Val Ala Val Trp Arg Lys Asn
100 105 110
Asp Glu Asn Ile Thr Leu Glu Thr Val Cys His Asp Pro Lys Leu Pro
[0082] 115 120 125
Tyr His Asp Phe Ile Leu Glu Asp Ala Ala Ser Pro Lys Cys Ile Met
130 135 140
Lys Glu Lys Lys Lys Pro Gly Glu Thr Phe Phe Met Cys Ser Cys Ser
145 150 155 160
Ser Asp Glu Cys Asn Asp Asn Ile Ile Phe Ser Glu Glu Tyr Asn Thr
165 170 175
Ser Asn Pro Asp Leu Leu Leu Val Ile Phe Gln Ser Asp Pro Thr Arg
180 185 190
Val Glu Thr Ala Thr Glu Thr Leu Gly Leu Ser Ala Val Leu Gly Leu
195 200 205
Leu Leu Leu Arg Trp Gln Phe Pro Ala His Tyr Arg Arg Leu Arg His
210 215 220
Ala Leu Trp Pro Ser Leu Pro Asp Leu His Arg Val Leu Gly Gln Tyr
225 230 235 240
Leu Arg Asp Thr Ala Ala Leu Ser Pro Pro Lys Ala Thr Val Ser Asp
245 250 255
Thr Cys Glu Glu Val Glu Pro Ser Leu Leu Glu Ile Leu Pro Lys Ser
260 265 270
Ser Glu Arg Thr Pro Leu Pro Leu Ala Arg Asp Glu Val Glu Gly Phe
275 280 285
Leu Gln Asp Thr Phe Pro Gln Gln Leu Glu Glu Ser Glu Lys Gln Arg
290 295 300
Leu Gly Gly Asp Val Gln Ser Pro Asn Cys Pro Ser Glu Asp Val Val
305 310 315 320
Ile Thr Pro Glu Ser Phe Gly Arg Asp Ser Ser Leu Thr Cys Leu Ala

325 330 335
Gly Asn Val Ser Ala Cys Asp Ala Pro Ile Leu Ser Ser Ser Arg Ser
340 345 350
Leu Asp Cys Arg Glu Ser Gly Lys Asn Gly Pro His Val Tyr Gln Asp
355 360 365
Leu Leu Leu Ser Leu Gly Thr Thr Asn Ser Thr Leu Pro Pro Pro Phe
370 375 380
Ser Leu Gln Ser Gly Ile Leu Thr Leu Asn Pro Val Ala Gln Gly Gln
385 390 395 400
Pro Ile Leu Thr Ser Leu Gly Ser Asn Gln Glu Glu Ala Tyr Val Thr
405 410 415
Met Ser Ser Phe Tyr Gln Asn Gln Ser Asp Pro Lys Pro Glu Asn Pro
420 425 430
Ala Cys Pro Trp Thr Val Leu Pro Ala Gly Asp Leu Pro Thr His Asp
435 440 445
Gly Tyr Leu Pro Ser Asn Ile Asp Asp Leu Pro Ser His Glu Ala Pro
450 455 460
Leu Ala Asp Ser Leu Glu Glu Leu Glu Pro Gln
465 470 475

<210> 138
<211> 474
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
<221> source
[0083] <223> /注释 = “人工序列的描述：合成多肽”
<400> 138
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15
His Ala Ala Arg Pro Met Gly Arg Gly Leu Leu Arg Gly Leu Trp Pro
20 25 30
Leu His Ile Val Leu Trp Thr Arg Ile Ala Ser Thr Ile Pro Pro His
35 40 45
Val Gln Lys Ser Val Asn Asn Asp Met Ile Val Thr Asp Asn Asn Gly
50 55 60
Ala Val Lys Phe Pro Gln Leu Cys Lys Phe Cys Asp Val Arg Phe Ser
65 70 75 80
Thr Cys Asp Asn Gln Lys Ser Cys Met Ser Asn Cys Ser Ile Thr Ser
85 90 95
Ile Cys Glu Lys Pro Gln Glu Val Cys Val Ala Val Trp Arg Lys Asn
100 105 110
Asp Glu Asn Ile Thr Leu Glu Thr Val Cys His Asp Pro Lys Leu Pro
115 120 125
Tyr His Asp Phe Ile Leu Glu Asp Ala Ala Ser Pro Lys Cys Ile Met
130 135 140
Lys Glu Lys Lys Lys Pro Gly Glu Thr Phe Phe Met Cys Ser Cys Ser
145 150 155 160
Ser Asp Glu Cys Asn Asp Asn Ile Ile Phe Ser Glu Glu Tyr Asn Thr
165 170 175
Ser Asn Pro Asp Leu Leu Leu Val Ile Phe Gln Ser Asp Pro Thr Arg
180 185 190

Val Glu Thr Ala Thr Glu Thr Gly Leu Ser Ala Val Leu Gly Leu Leu
195 200 205
Leu Leu Arg Trp Gln Phe Pro Ala His Tyr Arg Arg Leu Arg His Ala
210 215 220
Leu Trp Pro Ser Leu Pro Asp Leu His Arg Val Leu Gly Gln Tyr Leu
225 230 235 240
Arg Asp Thr Ala Ala Leu Ser Pro Pro Lys Ala Thr Val Ser Asp Thr
245 250 255
Cys Glu Glu Val Glu Pro Ser Leu Leu Glu Ile Leu Pro Lys Ser Ser
260 265 270
Glu Arg Thr Pro Leu Pro Leu Ala Arg Asp Glu Val Glu Gly Phe Leu
275 280 285
Gln Asp Thr Phe Pro Gln Gln Leu Glu Glu Ser Glu Lys Gln Arg Leu
290 295 300
Gly Gly Asp Val Gln Ser Pro Asn Cys Pro Ser Glu Asp Val Val Ile
305 310 315 320
Thr Pro Glu Ser Phe Gly Arg Asp Ser Ser Leu Thr Cys Leu Ala Gly
325 330 335
Asn Val Ser Ala Cys Asp Ala Pro Ile Leu Ser Ser Ser Arg Ser Leu
340 345 350
Asp Cys Arg Glu Ser Gly Lys Asn Gly Pro His Val Tyr Gln Asp Leu
355 360 365
Leu Leu Ser Leu Gly Thr Thr Asn Ser Thr Leu Pro Pro Pro Phe Ser
370 375 380
Leu Gln Ser Gly Ile Leu Thr Leu Asn Pro Val Ala Gln Gly Gln Pro
[0084] 385 390 395 400
Ile Leu Thr Ser Leu Gly Ser Asn Gln Glu Glu Ala Tyr Val Thr Met
405 410 415
Ser Ser Phe Tyr Gln Asn Gln Ser Asp Pro Lys Pro Glu Asn Pro Ala
420 425 430
Cys Pro Trp Thr Val Leu Pro Ala Gly Asp Leu Pro Thr His Asp Gly
435 440 445
Tyr Leu Pro Ser Asn Ile Asp Asp Leu Pro Ser His Glu Ala Pro Leu
450 455 460
Ala Asp Ser Leu Glu Glu Leu Glu Pro Gln
465 470

<210> 139
<211> 473
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 139
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15
His Ala Ala Arg Pro Met Gly Arg Gly Leu Leu Arg Gly Leu Trp Pro
20 25 30
Leu His Ile Val Leu Trp Thr Arg Ile Ala Ser Thr Ile Pro Pro His
35 40 45
Val Gln Lys Ser Val Asn Asn Asp Met Ile Val Thr Asp Asn Asn Gly

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

[0085] Glu Glu Val Glu Pro Ser Leu Leu Glu Ile Leu Pro Lys Ser Ser Glu
260 265 270
Arg Thr Pro Leu Pro Leu Ala Arg Asp Glu Val Glu Gly Phe Leu Gln
275 280 285
Asp Thr Phe Pro Gln Gln Leu Glu Glu Ser Glu Lys Gln Arg Leu Gly
290 295 300
Gly Asp Val Gln Ser Pro Asn Cys Pro Ser Glu Asp Val Val Ile Thr
305 310 315 320
Pro Glu Ser Phe Gly Arg Asp Ser Ser Leu Thr Cys Leu Ala Gly Asn
325 330 335
Val Ser Ala Cys Asp Ala Pro Ile Leu Ser Ser Ser Arg Ser Leu Asp
340 345 350
Cys Arg Glu Ser Gly Lys Asn Gly Pro His Val Tyr Gln Asp Leu Leu
355 360 365
Leu Ser Leu Gly Thr Thr Asn Ser Thr Leu Pro Pro Pro Phe Ser Leu
370 375 380
Gln Ser Gly Ile Leu Thr Leu Asn Pro Val Ala Gln Gly Gln Pro Ile
385 390 395 400
Leu Thr Ser Leu Gly Ser Asn Gln Glu Glu Ala Tyr Val Thr Met Ser
405 410 415
Ser Phe Tyr Gln Asn Gln Ser Asp Pro Lys Pro Glu Asn Pro Ala Cys
420 425 430
Pro Trp Thr Val Leu Pro Ala Gly Asp Leu Pro Thr His Asp Gly Tyr
435 440 445
Leu Pro Ser Asn Ile Asp Asp Leu Pro Ser His Glu Ala Pro Leu Ala
450 455 460

Asp Ser Leu Glu Glu Leu Glu Pro Gln
465 470

<210> 140
<211> 472
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 140

Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15
His Ala Ala Arg Pro Met Gly Arg Gly Leu Leu Arg Gly Leu Trp Pro
20 25 30
Leu His Ile Val Leu Trp Thr Arg Ile Ala Ser Thr Ile Pro Pro His
35 40 45
Val Gln Lys Ser Val Asn Asn Asp Met Ile Val Thr Asp Asn Asn Gly
50 55 60
Ala Val Lys Phe Pro Gln Leu Cys Lys Phe Cys Asp Val Arg Phe Ser
65 70 75 80
Thr Cys Asp Asn Gln Lys Ser Cys Met Ser Asn Cys Ser Ile Thr Ser
85 90 95
Ile Cys Glu Lys Pro Gln Glu Val Cys Val Ala Val Trp Arg Lys Asn
100 105 110
Asp Glu Asn Ile Thr Leu Glu Thr Val Cys His Asp Pro Lys Leu Pro
[0086] 115 120 125
Tyr His Asp Phe Ile Leu Glu Asp Ala Ala Ser Pro Lys Cys Ile Met
130 135 140
Lys Glu Lys Lys Lys Pro Gly Glu Thr Phe Phe Met Cys Ser Cys Ser
145 150 155 160
Ser Asp Glu Cys Asn Asp Asn Ile Ile Phe Ser Glu Glu Tyr Asn Thr
165 170 175
Ser Asn Pro Asp Leu Leu Leu Val Ile Phe Gln Ser Asp Pro Thr Arg
180 185 190
Val Glu Thr Ala Thr Glu Thr Ser Ala Val Leu Gly Leu Leu Leu Leu
195 200 205
Arg Trp Gln Phe Pro Ala His Tyr Arg Arg Leu Arg His Ala Leu Trp
210 215 220
Pro Ser Leu Pro Asp Leu His Arg Val Leu Gly Gln Tyr Leu Arg Asp
225 230 235 240
Thr Ala Ala Leu Ser Pro Pro Lys Ala Thr Val Ser Asp Thr Cys Glu
245 250 255
Glu Val Glu Pro Ser Leu Leu Glu Ile Leu Pro Lys Ser Ser Glu Arg
260 265 270
Thr Pro Leu Pro Leu Ala Arg Asp Glu Val Glu Gly Phe Leu Gln Asp
275 280 285
Thr Phe Pro Gln Gln Leu Glu Glu Ser Glu Lys Gln Arg Leu Gly Gly
290 295 300
Asp Val Gln Ser Pro Asn Cys Pro Ser Glu Asp Val Val Ile Thr Pro
305 310 315 320
Glu Ser Phe Gly Arg Asp Ser Ser Leu Thr Cys Leu Ala Gly Asn Val

325 330 335
Ser Ala Cys Asp Ala Pro Ile Leu Ser Ser Ser Arg Ser Leu Asp Cys
340 345 350
Arg Glu Ser Gly Lys Asn Gly Pro His Val Tyr Gln Asp Leu Leu Leu
355 360 365
Ser Leu Gly Thr Thr Asn Ser Thr Leu Pro Pro Pro Phe Ser Leu Gln
370 375 380
Ser Gly Ile Leu Thr Leu Asn Pro Val Ala Gln Gly Gln Pro Ile Leu
385 390 395 400
Thr Ser Leu Gly Ser Asn Gln Glu Glu Ala Tyr Val Thr Met Ser Ser
405 410 415
Phe Tyr Gln Asn Gln Ser Asp Pro Lys Pro Glu Asn Pro Ala Cys Pro
420 425 430
Trp Thr Val Leu Pro Ala Gly Asp Leu Pro Thr His Asp Gly Tyr Leu
435 440 445
Pro Ser Asn Ile Asp Asp Leu Pro Ser His Glu Ala Pro Leu Ala Asp
450 455 460
Ser Leu Glu Glu Leu Glu Pro Gln
465 470

<210> 141
<211> 471
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
<221> source
[0087] <223> /注释 = “人工序列的描述：合成多肽”
<400> 141
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15
His Ala Ala Arg Pro Met Gly Arg Gly Leu Leu Arg Gly Leu Trp Pro
20 25 30
Leu His Ile Val Leu Trp Thr Arg Ile Ala Ser Thr Ile Pro Pro His
35 40 45
Val Gln Lys Ser Val Asn Asn Asp Met Ile Val Thr Asp Asn Asn Gly
50 55 60
Ala Val Lys Phe Pro Gln Leu Cys Lys Phe Cys Asp Val Arg Phe Ser
65 70 75 80
Thr Cys Asp Asn Gln Lys Ser Cys Met Ser Asn Cys Ser Ile Thr Ser
85 90 95
Ile Cys Glu Lys Pro Gln Glu Val Cys Val Ala Val Trp Arg Lys Asn
100 105 110
Asp Glu Asn Ile Thr Leu Glu Thr Val Cys His Asp Pro Lys Leu Pro
115 120 125
Tyr His Asp Phe Ile Leu Glu Asp Ala Ala Ser Pro Lys Cys Ile Met
130 135 140
Lys Glu Lys Lys Lys Pro Gly Glu Thr Phe Phe Met Cys Ser Cys Ser
145 150 155 160
Ser Asp Glu Cys Asn Asp Asn Ile Ile Phe Ser Glu Glu Tyr Asn Thr
165 170 175
Ser Asn Pro Asp Leu Leu Leu Val Ile Phe Gln Ser Asp Pro Thr Arg
180 185 190

Val Glu Thr Ala Thr Glu Thr Ala Val Leu Gly Leu Leu Leu Leu Arg
195 200 205
Trp Gln Phe Pro Ala His Tyr Arg Arg Leu Arg His Ala Leu Trp Pro
210 215 220
Ser Leu Pro Asp Leu His Arg Val Leu Gly Gln Tyr Leu Arg Asp Thr
225 230 235 240
Ala Ala Leu Ser Pro Pro Lys Ala Thr Val Ser Asp Thr Cys Glu Glu
245 250 255
Val Glu Pro Ser Leu Leu Glu Ile Leu Pro Lys Ser Ser Glu Arg Thr
260 265 270
Pro Leu Pro Leu Ala Arg Asp Glu Val Glu Gly Phe Leu Gln Asp Thr
275 280 285
Phe Pro Gln Gln Leu Glu Glu Ser Glu Lys Gln Arg Leu Gly Gly Asp
290 295 300
Val Gln Ser Pro Asn Cys Pro Ser Glu Asp Val Val Ile Thr Pro Glu
305 310 315 320
Ser Phe Gly Arg Asp Ser Ser Leu Thr Cys Leu Ala Gly Asn Val Ser
325 330 335
Ala Cys Asp Ala Pro Ile Leu Ser Ser Ser Arg Ser Leu Asp Cys Arg
340 345 350
Glu Ser Gly Lys Asn Gly Pro His Val Tyr Gln Asp Leu Leu Leu Ser
355 360 365
Leu Gly Thr Thr Asn Ser Thr Leu Pro Pro Pro Phe Ser Leu Gln Ser
370 375 380
Gly Ile Leu Thr Leu Asn Pro Val Ala Gln Gly Gln Pro Ile Leu Thr
[0088] 385 390 395 400
Ser Leu Gly Ser Asn Gln Glu Glu Ala Tyr Val Thr Met Ser Ser Phe
405 410 415
Tyr Gln Asn Gln Ser Asp Pro Lys Pro Glu Asn Pro Ala Cys Pro Trp
420 425 430
Thr Val Leu Pro Ala Gly Asp Leu Pro Thr His Asp Gly Tyr Leu Pro
435 440 445
Ser Asn Ile Asp Asp Leu Pro Ser His Glu Ala Pro Leu Ala Asp Ser
450 455 460
Leu Glu Glu Leu Glu Pro Gln
465 470

<210> 142
<211> 470
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 142
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15
His Ala Ala Arg Pro Met Gly Arg Gly Leu Leu Arg Gly Leu Trp Pro
20 25 30
Leu His Ile Val Leu Trp Thr Arg Ile Ala Ser Thr Ile Pro Pro His
35 40 45
Val Gln Lys Ser Val Asn Asn Asp Met Ile Val Thr Asp Asn Asn Gly

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

[0089] Glu Pro Ser Leu Leu Glu Ile Leu Pro Lys Ser Ser Glu Arg Thr Pro
260 265 270
Leu Pro Leu Ala Arg Asp Glu Val Glu Gly Phe Leu Gln Asp Thr Phe
275 280 285
Pro Gln Gln Leu Glu Glu Ser Glu Lys Gln Arg Leu Gly Gly Asp Val
290 295 300
Gln Ser Pro Asn Cys Pro Ser Glu Asp Val Val Ile Thr Pro Glu Ser
305 310 315 320
Phe Gly Arg Asp Ser Ser Leu Thr Cys Leu Ala Gly Asn Val Ser Ala
325 330 335
Cys Asp Ala Pro Ile Leu Ser Ser Ser Arg Ser Leu Asp Cys Arg Glu
340 345 350
Ser Gly Lys Asn Gly Pro His Val Tyr Gln Asp Leu Leu Leu Ser Leu
355 360 365
Gly Thr Thr Asn Ser Thr Leu Pro Pro Pro Phe Ser Leu Gln Ser Gly
370 375 380
Ile Leu Thr Leu Asn Pro Val Ala Gln Gly Gln Pro Ile Leu Thr Ser
385 390 395 400
Leu Gly Ser Asn Gln Glu Glu Ala Tyr Val Thr Met Ser Ser Phe Tyr
405 410 415
Gln Asn Gln Ser Asp Pro Lys Pro Glu Asn Pro Ala Cys Pro Trp Thr
420 425 430
Val Leu Pro Ala Gly Asp Leu Pro Thr His Asp Gly Tyr Leu Pro Ser
435 440 445
Asn Ile Asp Asp Leu Pro Ser His Glu Ala Pro Leu Ala Asp Ser Leu
450 455 460

Glu Glu Leu Glu Pro Gln
465 470
<210> 143
<211> 469
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 143
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15
His Ala Ala Arg Pro Met Gly Arg Gly Leu Leu Arg Gly Leu Trp Pro
20 25 30
Leu His Ile Val Leu Trp Thr Arg Ile Ala Ser Thr Ile Pro Pro His
35 40 45
Val Gln Lys Ser Val Asn Asn Asp Met Ile Val Thr Asp Asn Asn Gly
50 55 60
Ala Val Lys Phe Pro Gln Leu Cys Lys Phe Cys Asp Val Arg Phe Ser
65 70 75 80
Thr Cys Asp Asn Gln Lys Ser Cys Met Ser Asn Cys Ser Ile Thr Ser
85 90 95
Ile Cys Glu Lys Pro Gln Glu Val Cys Val Ala Val Trp Arg Lys Asn
100 105 110
Asp Glu Asn Ile Thr Leu Glu Thr Val Cys His Asp Pro Lys Leu Pro
[0090] 115 120 125
Tyr His Asp Phe Ile Leu Glu Asp Ala Ala Ser Pro Lys Cys Ile Met
130 135 140
Lys Glu Lys Lys Lys Pro Gly Glu Thr Phe Phe Met Cys Ser Cys Ser
145 150 155 160
Ser Asp Glu Cys Asn Asp Asn Ile Ile Phe Ser Glu Glu Tyr Asn Thr
165 170 175
Ser Asn Pro Asp Leu Leu Leu Val Ile Phe Gln Ser Asp Pro Thr Arg
180 185 190
Val Glu Thr Ala Thr Glu Thr Leu Gly Leu Leu Leu Leu Arg Trp Gln
195 200 205
Phe Pro Ala His Tyr Arg Arg Leu Arg His Ala Leu Trp Pro Ser Leu
210 215 220
Pro Asp Leu His Arg Val Leu Gly Gln Tyr Leu Arg Asp Thr Ala Ala
225 230 235 240
Leu Ser Pro Pro Lys Ala Thr Val Ser Asp Thr Cys Glu Glu Val Glu
245 250 255
Pro Ser Leu Leu Glu Ile Leu Pro Lys Ser Ser Glu Arg Thr Pro Leu
260 265 270
Pro Leu Ala Arg Asp Glu Val Glu Gly Phe Leu Gln Asp Thr Phe Pro
275 280 285
Gln Gln Leu Glu Glu Ser Glu Lys Gln Arg Leu Gly Gly Asp Val Gln
290 295 300
Ser Pro Asn Cys Pro Ser Glu Asp Val Val Ile Thr Pro Glu Ser Phe
305 310 315 320
Gly Arg Asp Ser Ser Leu Thr Cys Leu Ala Gly Asn Val Ser Ala Cys

325 330 335
Asp Ala Pro Ile Leu Ser Ser Ser Arg Ser Leu Asp Cys Arg Glu Ser
340 345 350
Gly Lys Asn Gly Pro His Val Tyr Gln Asp Leu Leu Leu Ser Leu Gly
355 360 365
Thr Thr Asn Ser Thr Leu Pro Pro Pro Phe Ser Leu Gln Ser Gly Ile
370 375 380
Leu Thr Leu Asn Pro Val Ala Gln Gly Gln Pro Ile Leu Thr Ser Leu
385 390 395 400
Gly Ser Asn Gln Glu Glu Ala Tyr Val Thr Met Ser Ser Phe Tyr Gln
405 410 415
Asn Gln Ser Asp Pro Lys Pro Glu Asn Pro Ala Cys Pro Trp Thr Val
420 425 430
Leu Pro Ala Gly Asp Leu Pro Thr His Asp Gly Tyr Leu Pro Ser Asn
435 440 445
Ile Asp Asp Leu Pro Ser His Glu Ala Pro Leu Ala Asp Ser Leu Glu
450 455 460
Glu Leu Glu Pro Gln
465

<210> 144
<211> 488
<212> PRT
<213> 人工序列（Artificial Sequence）
<220>
<221> source
[0091] <223> /注释 = “人工序列的描述：合成多肽”
<400> 144
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15
His Ala Ala Arg Pro Met Gly Arg Gly Leu Leu Arg Gly Leu Trp Pro
20 25 30
Leu His Ile Val Leu Trp Thr Arg Ile Ala Ser Thr Ile Pro Pro His
35 40 45
Val Gln Lys Ser Val Asn Asn Asp Met Ile Val Thr Asp Asn Asn Gly
50 55 60
Ala Val Lys Phe Pro Gln Leu Cys Lys Phe Cys Asp Val Arg Phe Ser
65 70 75 80
Thr Cys Asp Asn Gln Lys Ser Cys Met Ser Asn Cys Ser Ile Thr Ser
85 90 95
Ile Cys Glu Lys Pro Gln Glu Val Cys Val Ala Val Trp Arg Lys Asn
100 105 110
Asp Glu Asn Ile Thr Leu Glu Thr Val Cys His Asp Pro Lys Leu Pro
115 120 125
Tyr His Asp Phe Ile Leu Glu Asp Ala Ala Ser Pro Lys Cys Ile Met
130 135 140
Lys Glu Lys Lys Lys Pro Gly Glu Thr Phe Phe Met Cys Ser Cys Ser
145 150 155 160
Ser Asp Glu Cys Asn Asp Asn Ile Ile Phe Ser Glu Glu Tyr Asn Thr
165 170 175
Ser Asn Pro Asp Leu Leu Leu Val Ile Phe Gln Ser Asp Pro Thr Arg
180 185 190

Val Glu Thr Ala Thr Glu Thr Ala Trp Leu Ile Ser Leu Val Thr Ala
195 200 205
Leu His Leu Val Leu Gly Leu Ser Ala Val Leu Gly Leu Leu Leu Leu
210 215 220
Arg Trp Gln Phe Pro Ala His Tyr Arg Arg Leu Arg His Ala Leu Trp
225 230 235 240
Pro Ser Leu Pro Asp Leu His Arg Val Leu Gly Gln Tyr Leu Arg Asp
245 250 255
Thr Ala Ala Leu Ser Pro Pro Lys Ala Thr Val Ser Asp Thr Cys Glu
260 265 270
Glu Val Glu Pro Ser Leu Leu Glu Ile Leu Pro Lys Ser Ser Glu Arg
275 280 285
Thr Pro Leu Pro Leu Ala Arg Asp Glu Val Glu Gly Phe Leu Gln Asp
290 295 300
Thr Phe Pro Gln Gln Leu Glu Glu Ser Glu Lys Gln Arg Leu Gly Gly
305 310 315 320
Asp Val Gln Ser Pro Asn Cys Pro Ser Glu Asp Val Val Ile Thr Pro
325 330 335
Glu Ser Phe Gly Arg Asp Ser Ser Leu Thr Cys Leu Ala Gly Asn Val
340 345 350
Ser Ala Cys Asp Ala Pro Ile Leu Ser Ser Ser Arg Ser Leu Asp Cys
355 360 365
Arg Glu Ser Gly Lys Asn Gly Pro His Val Tyr Gln Asp Leu Leu Leu
370 375 380
Ser Leu Gly Thr Thr Asn Ser Thr Leu Pro Pro Pro Phe Ser Leu Gln
[0092] 385 390 395 400
Ser Gly Ile Leu Thr Leu Asn Pro Val Ala Gln Gly Gln Pro Ile Leu
405 410 415
Thr Ser Leu Gly Ser Asn Gln Glu Glu Ala Tyr Val Thr Met Ser Ser
420 425 430
Phe Tyr Gln Asn Gln Ser Asp Pro Lys Pro Glu Asn Pro Ala Cys Pro
435 440 445
Trp Thr Val Leu Pro Ala Gly Asp Leu Pro Thr His Asp Gly Tyr Leu
450 455 460
Pro Ser Asn Ile Asp Asp Leu Pro Ser His Glu Ala Pro Leu Ala Asp
465 470 475 480
Ser Leu Glu Glu Leu Glu Pro Gln
485

<210> 145
<211> 489
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 145
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15
His Ala Ala Arg Pro Met Gly Arg Gly Leu Leu Arg Gly Leu Trp Pro
20 25 30
Leu His Ile Val Leu Trp Thr Arg Ile Ala Ser Thr Ile Pro Pro His

35 40 45

Val Gln Lys Ser Val Asn Asn Asp Met Ile Val Thr Asp Asn Asn Gly
50 55 60

Ala Val Lys Phe Pro Gln Leu Cys Lys Phe Cys Asp Val Arg Phe Ser
65 70 75 80

Thr Cys Asp Asn Gln Lys Ser Cys Met Ser Asn Cys Ser Ile Thr Ser
85 90 95

Ile Cys Glu Lys Pro Gln Glu Val Cys Val Ala Val Trp Arg Lys Asn
100 105 110

Asp Glu Asn Ile Thr Leu Glu Thr Val Cys His Asp Pro Lys Leu Pro
115 120 125

Tyr His Asp Phe Ile Leu Glu Asp Ala Ala Ser Pro Lys Cys Ile Met
130 135 140

Lys Glu Lys Lys Lys Pro Gly Glu Thr Phe Phe Met Cys Ser Cys Ser
145 150 155 160

Ser Asp Glu Cys Asn Asp Asn Ile Ile Phe Ser Glu Glu Tyr Asn Thr
165 170 175

Ser Asn Pro Asp Leu Leu Leu Val Ile Phe Gln Ser Asp Pro Thr Arg
180 185 190

Val Glu Thr Ala Thr Glu Thr Ala Trp Val Leu Ile Ser Leu Val Thr
195 200 205

Ala Leu His Leu Val Leu Gly Leu Ser Ala Val Leu Gly Leu Leu Leu
210 215 220

Leu Arg Trp Gln Phe Pro Ala His Tyr Arg Arg Leu Arg His Ala Leu
225 230 235 240

[0093] Trp Pro Ser Leu Pro Asp Leu His Arg Val Leu Gly Gln Tyr Leu Arg
245 250 255

Asp Thr Ala Ala Leu Ser Pro Pro Lys Ala Thr Val Ser Asp Thr Cys
260 265 270

Glu Glu Val Glu Pro Ser Leu Leu Glu Ile Leu Pro Lys Ser Ser Glu
275 280 285

Arg Thr Pro Leu Pro Leu Ala Arg Asp Glu Val Glu Gly Phe Leu Gln
290 295 300

Asp Thr Phe Pro Gln Gln Leu Glu Glu Ser Glu Lys Gln Arg Leu Gly
305 310 315 320

Gly Asp Val Gln Ser Pro Asn Cys Pro Ser Glu Asp Val Val Ile Thr
325 330 335

Pro Glu Ser Phe Gly Arg Asp Ser Ser Leu Thr Cys Leu Ala Gly Asn
340 345 350

Val Ser Ala Cys Asp Ala Pro Ile Leu Ser Ser Ser Arg Ser Leu Asp
355 360 365

Cys Arg Glu Ser Gly Lys Asn Gly Pro His Val Tyr Gln Asp Leu Leu
370 375 380

Leu Ser Leu Gly Thr Thr Asn Ser Thr Leu Pro Pro Pro Phe Ser Leu
385 390 395 400

Gln Ser Gly Ile Leu Thr Leu Asn Pro Val Ala Gln Gly Gln Pro Ile
405 410 415

Leu Thr Ser Leu Gly Ser Asn Gln Glu Glu Ala Tyr Val Thr Met Ser
420 425 430

Ser Phe Tyr Gln Asn Gln Ser Asp Pro Lys Pro Glu Asn Pro Ala Cys
435 440 445

Pro Trp Thr Val Leu Pro Ala Gly Asp Leu Pro Thr His Asp Gly Tyr
450 455 460
Leu Pro Ser Asn Ile Asp Asp Leu Pro Ser His Glu Ala Pro Leu Ala
465 470 475 480
Asp Ser Leu Glu Glu Leu Glu Pro Gln
485

<210> 146
<211> 490
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 146

[0094]

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

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

[0095] <210> 147
<211> 491
<212> PRT
<213> 人工序列（Artificial Sequence）
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 147
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15
His Ala Ala Arg Pro Met Gly Arg Gly Leu Leu Arg Gly Leu Trp Pro
20 25 30
Leu His Ile Val Leu Trp Thr Arg Ile Ala Ser Thr Ile Pro Pro His
35 40 45
Val Gln Lys Ser Val Asn Asn Asp Met Ile Val Thr Asp Asn Asn Gly
50 55 60
Ala Val Lys Phe Pro Gln Leu Cys Lys Phe Cys Asp Val Arg Phe Ser
65 70 75 80
Thr Cys Asp Asn Gln Lys Ser Cys Met Ser Asn Cys Ser Ile Thr Ser
85 90 95
Ile Cys Glu Lys Pro Gln Glu Val Cys Val Ala Val Trp Arg Lys Asn
100 105 110
Asp Glu Asn Ile Thr Leu Glu Thr Val Cys His Asp Pro Lys Leu Pro
115 120 125
Tyr His Asp Phe Ile Leu Glu Asp Ala Ala Ser Pro Lys Cys Ile Met
130 135 140

Lys Glu Lys Lys Lys Pro Gly Glu Thr Phe Phe Met Cys Ser Cys Ser
145 150 155 160
Ser Asp Glu Cys Asn Asp Asn Ile Ile Phe Ser Glu Glu Tyr Asn Thr
165 170 175
Ser Asn Pro Asp Leu Leu Leu Val Ile Phe Gln Ser Asp Pro Thr Arg
180 185 190
Val Glu Thr Ala Thr Glu Thr Ala Trp Ile Leu Val Leu Ile Ser Leu
195 200 205
Val Thr Ala Leu His Leu Val Leu Gly Leu Ser Ala Val Leu Gly Leu
210 215 220
Leu Leu Leu Arg Trp Gln Phe Pro Ala His Tyr Arg Arg Leu Arg His
225 230 235 240
Ala Leu Trp Pro Ser Leu Pro Asp Leu His Arg Val Leu Gly Gln Tyr
245 250 255
Leu Arg Asp Thr Ala Ala Leu Ser Pro Pro Lys Ala Thr Val Ser Asp
260 265 270
Thr Cys Glu Glu Val Glu Pro Ser Leu Leu Glu Ile Leu Pro Lys Ser
275 280 285
Ser Glu Arg Thr Pro Leu Pro Leu Ala Arg Asp Glu Val Glu Gly Phe
290 295 300
Leu Gln Asp Thr Phe Pro Gln Gln Leu Glu Glu Ser Glu Lys Gln Arg
305 310 315 320
Leu Gly Gly Asp Val Gln Ser Pro Asn Cys Pro Ser Glu Asp Val Val
325 330 335
Ile Thr Pro Glu Ser Phe Gly Arg Asp Ser Ser Leu Thr Cys Leu Ala
[0096] 340 345 350
Gly Asn Val Ser Ala Cys Asp Ala Pro Ile Leu Ser Ser Ser Arg Ser
355 360 365
Leu Asp Cys Arg Glu Ser Gly Lys Asn Gly Pro His Val Tyr Gln Asp
370 375 380
Leu Leu Leu Ser Leu Gly Thr Thr Asn Ser Thr Leu Pro Pro Pro Phe
385 390 395 400
Ser Leu Gln Ser Gly Ile Leu Thr Leu Asn Pro Val Ala Gln Gly Gln
405 410 415
Pro Ile Leu Thr Ser Leu Gly Ser Asn Gln Glu Glu Ala Tyr Val Thr
420 425 430
Met Ser Ser Phe Tyr Gln Asn Gln Ser Asp Pro Lys Pro Glu Asn Pro
435 440 445
Ala Cys Pro Trp Thr Val Leu Pro Ala Gly Asp Leu Pro Thr His Asp
450 455 460
Gly Tyr Leu Pro Ser Asn Ile Asp Asp Leu Pro Ser His Glu Ala Pro
465 470 475 480
Leu Ala Asp Ser Leu Glu Glu Leu Glu Pro Gln
485 490

<210> 148
<211> 492
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”

<400> 148

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

[0097]

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

Phe Ser Leu Gln Ser Gly Ile Leu Thr Leu Asn Pro Val Ala Gln Gly
405 410 415
Gln Pro Ile Leu Thr Ser Leu Gly Ser Asn Gln Glu Glu Ala Tyr Val
420 425 430
Thr Met Ser Ser Phe Tyr Gln Asn Gln Ser Asp Pro Lys Pro Glu Asn
435 440 445
Pro Ala Cys Pro Trp Thr Val Leu Pro Ala Gly Asp Leu Pro Thr His
450 455 460
Asp Gly Tyr Leu Pro Ser Asn Ile Asp Asp Leu Pro Ser His Glu Ala
465 470 475 480
Pro Leu Ala Asp Ser Leu Glu Glu Leu Glu Pro Gln
485 490

<210> 149
<211> 493
<212> PRT
<213> 人工序列（Artificial Sequence）
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 149
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15
His Ala Ala Arg Pro Met Gly Arg Gly Leu Leu Arg Gly Leu Trp Pro
20 25 30
Leu His Ile Val Leu Trp Thr Arg Ile Ala Ser Thr Ile Pro Pro His
[0098] 35 40 45
Val Gln Lys Ser Val Asn Asn Asp Met Ile Val Thr Asp Asn Asn Gly
50 55 60
Ala Val Lys Phe Pro Gln Leu Cys Lys Phe Cys Asp Val Arg Phe Ser
65 70 75 80
Thr Cys Asp Asn Gln Lys Ser Cys Met Ser Asn Cys Ser Ile Thr Ser
85 90 95
Ile Cys Glu Lys Pro Gln Glu Val Cys Val Ala Val Trp Arg Lys Asn
100 105 110
Asp Glu Asn Ile Thr Leu Glu Thr Val Cys His Asp Pro Lys Leu Pro
115 120 125
Tyr His Asp Phe Ile Leu Glu Asp Ala Ala Ser Pro Lys Cys Ile Met
130 135 140
Lys Glu Lys Lys Lys Pro Gly Glu Thr Phe Phe Met Cys Ser Cys Ser
145 150 155 160
Ser Asp Glu Cys Asn Asp Asn Ile Ile Phe Ser Glu Glu Tyr Asn Thr
165 170 175
Ser Asn Pro Asp Leu Leu Leu Val Ile Phe Gln Ser Asp Pro Thr Arg
180 185 190
Val Glu Thr Ala Thr Glu Thr Ala Trp Leu Leu Ile Leu Val Leu Ile
195 200 205
Ser Leu Val Thr Ala Leu His Leu Val Leu Gly Leu Ser Ala Val Leu
210 215 220
Gly Leu Leu Leu Leu Arg Trp Gln Phe Pro Ala His Tyr Arg Arg Leu
225 230 235 240
Arg His Ala Leu Trp Pro Ser Leu Pro Asp Leu His Arg Val Leu Gly

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

[0099]

Asn Pro Ala Cys Pro Trp Thr Val Leu Pro Ala Gly Asp Leu Pro Thr
450 455 460
His Asp Gly Tyr Leu Pro Ser Asn Ile Asp Asp Leu Pro Ser His Glu
465 470 475 480
Ala Pro Leu Ala Asp Ser Leu Glu Glu Leu Glu Pro Gln
485 490

<210> 150
<211> 494
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 150
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15
His Ala Ala Arg Pro Met Gly Arg Gly Leu Leu Arg Gly Leu Trp Pro
20 25 30
Leu His Ile Val Leu Trp Thr Arg Ile Ala Ser Thr Ile Pro Pro His
35 40 45
Val Gln Lys Ser Val Asn Asn Asp Met Ile Val Thr Asp Asn Asn Gly
50 55 60
Ala Val Lys Phe Pro Gln Leu Cys Lys Phe Cys Asp Val Arg Phe Ser
65 70 75 80
Thr Cys Asp Asn Gln Lys Ser Cys Met Ser Asn Cys Ser Ile Thr Ser
85 90 95

Ile Cys Glu Lys Pro Gln Glu Val Cys Val Ala Val Trp Arg Lys Asn
100 105 110
Asp Glu Asn Ile Thr Leu Glu Thr Val Cys His Asp Pro Lys Leu Pro
115 120 125
Tyr His Asp Phe Ile Leu Glu Asp Ala Ala Ser Pro Lys Cys Ile Met
130 135 140
Lys Glu Lys Lys Lys Pro Gly Glu Thr Phe Phe Met Cys Ser Cys Ser
145 150 155 160
Ser Asp Glu Cys Asn Asp Asn Ile Ile Phe Ser Glu Glu Tyr Asn Thr
165 170 175
Ser Asn Pro Asp Leu Leu Leu Val Ile Phe Gln Ser Asp Pro Thr Arg
180 185 190
Val Glu Thr Ala Thr Glu Thr Ala Trp Val Leu Leu Ile Leu Val Leu
195 200 205
Ile Ser Leu Val Thr Ala Leu His Leu Val Leu Gly Leu Ser Ala Val
210 215 220
Leu Gly Leu Leu Leu Leu Arg Trp Gln Phe Pro Ala His Tyr Arg Arg
225 230 235 240
Leu Arg His Ala Leu Trp Pro Ser Leu Pro Asp Leu His Arg Val Leu
245 250 255
Gly Gln Tyr Leu Arg Asp Thr Ala Ala Leu Ser Pro Pro Lys Ala Thr
260 265 270
Val Ser Asp Thr Cys Glu Glu Val Glu Pro Ser Leu Leu Glu Ile Leu
275 280 285
Pro Lys Ser Ser Glu Arg Thr Pro Leu Pro Leu Ala Arg Asp Glu Val
[0100] 290 295 300
Glu Gly Phe Leu Gln Asp Thr Phe Pro Gln Gln Leu Glu Glu Ser Glu
305 310 315 320
Lys Gln Arg Leu Gly Gly Asp Val Gln Ser Pro Asn Cys Pro Ser Glu
325 330 335
Asp Val Val Ile Thr Pro Glu Ser Phe Gly Arg Asp Ser Ser Leu Thr
340 345 350
Cys Leu Ala Gly Asn Val Ser Ala Cys Asp Ala Pro Ile Leu Ser Ser
355 360 365
Ser Arg Ser Leu Asp Cys Arg Glu Ser Gly Lys Asn Gly Pro His Val
370 375 380
Tyr Gln Asp Leu Leu Leu Ser Leu Gly Thr Thr Asn Ser Thr Leu Pro
385 390 395 400
Pro Pro Phe Ser Leu Gln Ser Gly Ile Leu Thr Leu Asn Pro Val Ala
405 410 415
Gln Gly Gln Pro Ile Leu Thr Ser Leu Gly Ser Asn Gln Glu Glu Ala
420 425 430
Tyr Val Thr Met Ser Ser Phe Tyr Gln Asn Gln Ser Asp Pro Lys Pro
435 440 445
Glu Asn Pro Ala Cys Pro Trp Thr Val Leu Pro Ala Gly Asp Leu Pro
450 455 460
Thr His Asp Gly Tyr Leu Pro Ser Asn Ile Asp Asp Leu Pro Ser His
465 470 475 480
Glu Ala Pro Leu Ala Asp Ser Leu Glu Glu Leu Glu Pro Gln
485 490

<210> 151

<211> 495
<212> PRT
<213> 人工序列（Artificial Sequence）
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 151

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

[0101]

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

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

<210> 152
<211> 13
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
<221> source
<223> /注释 = “人工序列的描述：合成肽”

[0102] <400> 152
Lys Pro Ile Pro Asn Pro Leu Leu Gly Leu Asp Ser Thr
1 5 10

<210> 153
<211> 246
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 153
Glu Ile Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Glu
1 5 10 15
Ser Leu Arg Ile Ser Cys Lys Gly Ser Gly Phe Asn Ile Glu Asp Tyr
20 25 30
Tyr Ile His Trp Val Arg Gln Met Pro Gly Lys Gly Leu Glu Trp Met
35 40 45
Gly Arg Ile Asp Pro Glu Asn Asp Glu Thr Lys Tyr Gly Pro Ile Phe
50 55 60
Gln Gly His Val Thr Ile Ser Ala Asp Thr Ser Ile Asn Thr Val Tyr
65 70 75 80
Leu Gln Trp Ser Ser Leu Lys Ala Ser Asp Thr Ala Met Tyr Tyr Cys
85 90 95
Ala Phe Arg Gly Gly Val Tyr Trp Gly Gln Gly Thr Thr 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 Gly Gly Gly Gly Ser Asp Val Val Met Thr Gln Ser Pro Asp Ser
130 135 140
Leu Ala Val Ser Leu Gly Glu Arg Ala Thr Ile Asn Cys Lys Ser Ser
145 150 155 160
Gln Ser Leu Leu Asp Ser Asp Gly Lys Thr Tyr Leu Asn Trp Leu Gln
165 170 175
Gln Lys Pro Gly Gln Pro Pro Lys Arg Leu Ile Ser Leu Val Ser Lys
180 185 190
Leu Asp Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr
195 200 205
Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Ala Glu Asp Val Ala Val
210 215 220
Tyr Tyr Cys Trp Gln Gly Thr His Phe Pro Gly Thr Phe Gly Gly Gly
225 230 235 240
Thr Lys Val Glu Ile Lys
245

<210> 154
<211> 69
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 154

[0103]
Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala
1 5 10 15
Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly
20 25 30
Gly Ala Val His Thr Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr Ile
35 40 45
Trp Ala Pro Leu Ala Gly Thr Cys Gly Val Leu Leu Leu Ser Leu Val
50 55 60
Ile Thr Leu Tyr Cys
65

<210> 155
<211> 42
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 155
Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met
1 5 10 15
Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe
20 25 30
Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu
35 40

<210> 156
<211> 112

<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 156

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

<210> 157
<211> 233
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
[0104] <221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 157

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

180 185 190
Tyr Tyr Val Asp Tyr Arg Leu Glu Arg Ile Lys Glu Ala Asn Asn Glu
195 200 205
Thr Tyr Val Glu Gln His Glu Val Ala Val Ala Arg Tyr Cys Asp Leu
210 215 220
Pro Ser Lys Leu Gly His Lys Leu Asn
225 230
<210> 158
<211> 22
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
<221> source
<223> /注释 = “人工序列的描述：合成肽”
<400> 158
Gly Ser Gly Ala Thr Asn Phe Ser Leu Leu Lys Gln Ala Gly Asp Val
1 5 10 15
Glu Glu Asn Pro Gly Pro
20
<210> 159
<211> 143
<212> PRT
<213> 智人 (Homo sapiens)
<400> 159
Ile Pro Pro His Val Gln Lys Ser Val Asn Asn Asp Met Ile Val Thr
[0105] 1 5 10 15
Asp Asn Asn Gly Ala Val Lys Phe Pro Gln Leu Cys Lys Phe Cys Asp
20 25 30
Val Arg Phe Ser Thr Cys Asp Asn Gln Lys Ser Cys Met Ser Asn Cys
35 40 45
Ser Ile Thr Ser Ile Cys Glu Lys Pro Gln Glu Val Cys Val Ala Val
50 55 60
Trp Arg Lys Asn Asp Glu Asn Ile Thr Leu Glu Thr Val Cys His Asp
65 70 75 80
Pro Lys Leu Pro Tyr His Asp Phe Ile Leu Glu Asp Ala Ala Ser Pro
85 90 95
Lys Cys Ile Met Lys Glu Lys Lys Lys Pro Gly Glu Thr Phe Phe Met
100 105 110
Cys Ser Cys Ser Ser Asp Glu Cys Asn Asp Asn Ile Ile Phe Ser Glu
115 120 125
Glu Tyr Asn Thr Ser Asn Pro Asp Leu Leu Leu Val Ile Phe Gln
130 135 140
<210> 160
<211> 105
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 160
Ser Asp Pro Thr Arg Val Glu Thr Ala Thr Glu Thr Ala Trp Ile Ser

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

<210> 161
<211> 197
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 161
Ala Arg Asp Glu Val Glu Gly Phe Leu Gln Asp Thr Phe Pro Gln Gln
1 5 10 15
Leu Glu Glu Ser Glu Lys Gln Arg Leu Gly Gly Asp Val Gln Ser Pro
20 25 30

[0106]
Asn Cys Pro Ser Glu Asp Val Val Ile Thr Pro Glu Ser Phe Gly Arg
35 40 45
Asp Ser Ser Leu Thr Cys Leu Ala Gly Asn Val Ser Ala Cys Asp Ala
50 55 60
Pro Ile Leu Ser Ser Ser Arg Ser Leu Asp Cys Arg Glu Ser Gly Lys
65 70 75 80
Asn Gly Pro His Val Tyr Gln Asp Leu Leu Leu Ser Leu Gly Thr Thr
85 90 95
Asn Ser Thr Leu Pro Pro Pro Phe Ser Leu Gln Ser Gly Ile Leu Thr
100 105 110
Leu Asn Pro Val Ala Gln Gly Gln Pro Ile Leu Thr Ser Leu Gly Ser
115 120 125
Asn Gln Glu Glu Ala Tyr Val Thr Met Ser Ser Phe Tyr Gln Asn Gln
130 135 140
Ser Arg Ser Asp Pro Lys Pro Glu Asn Pro Ala Cys Pro Trp Thr Val
145 150 155 160
Leu Pro Ala Gly Asp Leu Pro Thr His Asp Gly Tyr Leu Pro Ser Asn
165 170 175
Ile Asp Asp Leu Pro Ser His Glu Ala Pro Leu Ala Asp Ser Leu Glu
180 185 190
Glu Leu Glu Pro Gln
195

<210> 162
<211> 491
<212> PRT
<213> 人工序列 (Artificial Sequence)

<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 162

Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15
His Ala Ala Arg Pro Met Gly Arg Gly Leu Leu Arg Gly Leu Trp Pro
20 25 30
Leu His Ile Val Leu Trp Thr Arg Ile Ala Ser Thr Ile Pro Pro His
35 40 45
Val Gln Lys Ser Val Asn Asn Asp Met Ile Val Thr Asp Asn Asn Gly
50 55 60
Ala Val Lys Phe Pro Gln Leu Cys Lys Phe Cys Asp Val Arg Phe Ser
65 70 75 80
Thr Cys Asp Asn Gln Lys Ser Cys Met Ser Asn Cys Ser Ile Thr Ser
85 90 95
Ile Cys Glu Lys Pro Gln Glu Val Cys Val Ala Val Trp Arg Lys Asn
100 105 110
Asp Glu Asn Ile Thr Leu Glu Thr Val Cys His Asp Pro Lys Leu Pro
115 120 125
Tyr His Asp Phe Ile Leu Glu Asp Ala Ala Ser Pro Lys Cys Ile Met
130 135 140
Lys Glu Lys Lys Lys Pro Gly Glu Thr Phe Phe Met Cys Ser Cys Ser
145 150 155 160
Ser Asp Glu Cys Asn Asp Asn Ile Ile Phe Ser Glu Glu Tyr Asn Thr
165 170 175
[0107]
Ser Asn Pro Asp Leu Leu Leu Val Ile Phe Gln Ser Asp Pro Thr Arg
180 185 190
Val Glu Thr Ala Thr Glu Thr Ala Trp Ile Ser Leu Val Thr Ala Leu
195 200 205
His Leu Val Leu Gly Leu Ser Ala Val Leu Gly Leu Leu Leu Leu Arg
210 215 220
Trp Gln Phe Pro Ala His Tyr Arg Arg Leu Arg His Ala Leu Trp Pro
225 230 235 240
Ser Leu Pro Asp Leu His Arg Val Leu Gly Gln Tyr Leu Arg Asp Thr
245 250 255
Ala Ala Leu Ser Pro Pro Lys Ala Thr Val Ser Asp Thr Cys Glu Glu
260 265 270
Val Glu Pro Ser Leu Leu Glu Ile Leu Pro Lys Ser Ser Glu Arg Thr
275 280 285
Pro Leu Pro Leu Leu Glu Ala Arg Asp Glu Val Glu Gly Phe Leu Gln
290 295 300
Asp Thr Phe Pro Gln Gln Leu Glu Glu Ser Glu Lys Gln Arg Leu Gly
305 310 315 320
Gly Asp Val Gln Ser Pro Asn Cys Pro Ser Glu Asp Val Val Ile Thr
325 330 335
Pro Glu Ser Phe Gly Arg Asp Ser Ser Leu Thr Cys Leu Ala Gly Asn
340 345 350
Val Ser Ala Cys Asp Ala Pro Ile Leu Ser Ser Ser Arg Ser Leu Asp
355 360 365
Cys Arg Glu Ser Gly Lys Asn Gly Pro His Val Tyr Gln Asp Leu Leu

370 375 380
Leu Ser Leu Gly Thr Thr Asn Ser Thr Leu Pro Pro Pro Phe Ser Leu
385 390 395 400
Gln Ser Gly Ile Leu Thr Leu Asn Pro Val Ala Gln Gly Gln Pro Ile
405 410 415
Leu Thr Ser Leu Gly Ser Asn Gln Glu Glu Ala Tyr Val Thr Met Ser
420 425 430
Ser Phe Tyr Gln Asn Gln Ser Arg Ser Asp Pro Lys Pro Glu Asn Pro
435 440 445
Ala Cys Pro Trp Thr Val Leu Pro Ala Gly Asp Leu Pro Thr His Asp
450 455 460
Gly Tyr Leu Pro Ser Asn Ile Asp Asp Leu Pro Ser His Glu Ala Pro
465 470 475 480
Leu Ala Asp Ser Leu Glu Glu Leu Glu Pro Gln
485 490

<210> 163
<211> 491
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 163
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15
[0108] His Ala Ala Arg Pro Met Gly Arg Gly Leu Leu Arg Gly Leu Trp Pro
20 25 30
Leu His Ile Val Leu Trp Thr Arg Ile Ala Ser Thr Ile Pro Pro His
35 40 45
Val Gln Lys Ser Val Asn Asn Asp Met Ile Val Thr Asp Asn Asn Gly
50 55 60
Ala Val Lys Phe Pro Gln Leu Cys Lys Phe Cys Asp Val Arg Phe Ser
65 70 75 80
Thr Cys Asp Asn Gln Lys Ser Cys Met Ser Asn Cys Ser Ile Thr Ser
85 90 95
Ile Cys Glu Lys Pro Gln Glu Val Cys Val Ala Val Trp Arg Lys Asn
100 105 110
Asp Glu Asn Ile Thr Leu Glu Thr Val Cys His Asp Pro Lys Leu Pro
115 120 125
Tyr His Asp Phe Ile Leu Glu Asp Ala Ala Ser Pro Lys Cys Ile Met
130 135 140
Lys Glu Lys Lys Lys Pro Gly Glu Thr Phe Phe Met Cys Ser Cys Ser
145 150 155 160
Ser Asp Glu Cys Asn Asp Asn Ile Ile Phe Ser Glu Glu Tyr Asn Thr
165 170 175
Ser Asn Pro Asp Leu Leu Leu Val Ile Phe Gln Ser Asp Pro Thr Arg
180 185 190
Val Glu Thr Ala Thr Glu Thr Ala Trp Ile Ser Leu Val Thr Ala Leu
195 200 205
His Leu Val Leu Gly Leu Asn Ala Val Leu Gly Leu Leu Leu Leu Arg
210 215 220

Lys Gln Phe Pro Ala His Tyr Arg Arg Leu Arg His Ala Leu Trp Pro
225 230 235 240
Ser Leu Pro Asp Leu His Arg Val Leu Gly Gln Tyr Leu Arg Asp Thr
245 250 255
Ala Ala Leu Ser Pro Pro Lys Ala Thr Val Ser Asp Thr Cys Glu Glu
260 265 270
Val Glu Pro Ser Leu Leu Glu Ile Leu Pro Lys Ser Ser Glu Arg Thr
275 280 285
Pro Leu Pro Leu Leu Glu Ala Arg Asp Glu Val Glu Gly Phe Leu Gln
290 295 300
Asp Thr Phe Pro Gln Gln Leu Glu Glu Ser Glu Lys Gln Arg Leu Gly
305 310 315 320
Gly Asp Val Gln Ser Pro Asn Cys Pro Ser Glu Asp Val Val Ile Thr
325 330 335
Pro Glu Ser Phe Gly Arg Asp Ser Ser Leu Thr Cys Leu Ala Gly Asn
340 345 350
Val Ser Ala Cys Asp Ala Pro Ile Leu Ser Ser Ser Arg Ser Leu Asp
355 360 365
Cys Arg Glu Ser Gly Lys Asn Gly Pro His Val Tyr Gln Asp Leu Leu
370 375 380
Leu Ser Leu Gly Thr Thr Asn Ser Thr Leu Pro Pro Pro Phe Ser Leu
385 390 395 400
Gln Ser Gly Ile Leu Thr Leu Asn Pro Val Ala Gln Gly Gln Pro Ile
405 410 415
Leu Thr Ser Leu Gly Ser Asn Gln Glu Glu Ala Tyr Val Thr Met Ser
[0109] 420 425 430
Ser Phe Tyr Gln Asn Gln Ser Arg Ser Asp Pro Lys Pro Glu Asn Pro
435 440 445
Ala Cys Pro Trp Thr Val Leu Pro Ala Gly Asp Leu Pro Thr His Asp
450 455 460
Gly Tyr Leu Pro Ser Asn Ile Asp Asp Leu Pro Ser His Glu Ala Pro
465 470 475 480
Leu Ala Asp Ser Leu Glu Glu Leu Glu Pro Gln
485 490

<210> 164
<211> 369
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 164
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15
His Ala Ala Arg Pro Met Gly Arg Gly Leu Leu Arg Gly Leu Trp Pro
20 25 30
Leu His Ile Val Leu Trp Thr Arg Ile Ala Ser Thr Ile Pro Pro His
35 40 45
Val Gln Lys Ser Val Asn Asn Asp Met Ile Val Thr Asp Asn Asn Gly
50 55 60
Ala Val Lys Phe Pro Gln Leu Cys Lys Phe Cys Asp Val Arg Phe Ser

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

[0110] Val Glu Pro Ser Leu Leu Glu Ile Leu Pro Lys Ser Ser Glu Arg Thr
275 280 285
Pro Leu Pro Leu Leu Glu Asp Glu Gly Val Ala Gly Ala Pro Thr Gly
290 295 300
Ser Ser Pro Gln Pro Leu Gln Pro Leu Ser Gly Glu Asp Asp Ala Tyr
305 310 315 320
Cys Thr Phe Pro Ser Arg Asp Asp Leu Leu Leu Phe Ser Pro Ser Gly
325 330 335
Gln Gly Glu Phe Arg Ala Leu Asn Ala Arg Leu Pro Leu Asn Thr Asp
340 345 350
Ala Tyr Leu Ser Leu Gln Glu Leu Gln Gly Gln Asp Pro Thr His Leu
355 360 365
Val

<210> 165
<211> 491
<212> PRT
<213> 人工序列（Artificial Sequence）
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 165
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15
His Ala Ala Arg Pro Met Gly Arg Gly Leu Leu Arg Gly Leu Trp Pro
20 25 30

Leu His Ile Val Leu Trp Thr Arg Ile Ala Ser Thr Ile Pro Pro His
35 40 45
Val Gln Lys Ser Val Asn Asn Asp Met Ile Val Thr Asp Asn Asn Gly
50 55 60
Ala Val Lys Phe Pro Gln Leu Cys Lys Phe Cys Asp Val Arg Phe Ser
65 70 75 80
Thr Cys Asp Asn Gln Lys Ser Cys Met Ser Asn Cys Ser Ile Thr Ser
85 90 95
Ile Cys Glu Lys Pro Gln Glu Val Cys Val Ala Val Trp Arg Lys Asn
100 105 110
Asp Glu Asn Ile Thr Leu Glu Thr Val Cys His Asp Pro Lys Leu Pro
115 120 125
Tyr His Asp Phe Ile Leu Glu Asp Ala Ala Ser Pro Lys Cys Ile Met
130 135 140
Lys Glu Lys Lys Lys Pro Gly Glu Thr Phe Phe Met Cys Ser Cys Ser
145 150 155 160
Ser Asp Glu Cys Asn Asp Asn Ile Ile Phe Ser Glu Glu Tyr Asn Thr
165 170 175
Ser Asn Pro Asp Leu Leu Leu Val Ile Phe Gln Ser Asp Pro Thr Arg
180 185 190
Val Glu Thr Ala Thr Glu Thr Ala Trp Ile Ser Leu Val Thr Ala Leu
195 200 205
His Leu Val Leu Gly Leu Asn Ala Val Leu Gly Leu Leu Leu Leu Arg
210 215 220
Lys Gln Phe Pro Ala His Tyr Arg Arg Leu Arg His Ala Leu Trp Pro
[0111] 225 230 235 240
Ser Leu Pro Asp Leu His Arg Val Leu Gly Gln Tyr Leu Arg Asp Thr
245 250 255
Ala Ala Leu Ser Pro Pro Arg Ala Thr Val Ser Asp Thr Cys Glu Glu
260 265 270
Val Glu Pro Ser Leu Leu Glu Ile Leu Pro Arg Ser Ser Glu Arg Thr
275 280 285
Pro Leu Pro Leu Leu Glu Ala Arg Asp Glu Val Glu Gly Phe Leu Gln
290 295 300
Asp Thr Phe Pro Gln Gln Leu Glu Glu Ser Glu Lys Gln Arg Leu Gly
305 310 315 320
Gly Asp Val Gln Ser Pro Asn Cys Pro Ser Glu Asp Val Val Ile Thr
325 330 335
Pro Glu Ser Phe Gly Arg Asp Ser Ser Leu Thr Cys Leu Ala Gly Asn
340 345 350
Val Ser Ala Cys Asp Ala Pro Ile Leu Ser Ser Ser Arg Ser Leu Asp
355 360 365
Cys Arg Glu Ser Gly Lys Asn Gly Pro His Val Tyr Gln Asp Leu Leu
370 375 380
Leu Ser Leu Gly Thr Thr Asn Ser Thr Leu Pro Pro Pro Phe Ser Leu
385 390 395 400
Gln Ser Gly Ile Leu Thr Leu Asn Pro Val Ala Gln Gly Gln Pro Ile
405 410 415
Leu Thr Ser Leu Gly Ser Asn Gln Glu Glu Ala Tyr Val Thr Met Ser
420 425 430
Ser Phe Tyr Gln Asn Gln Ser Arg Ser Asp Pro Lys Pro Glu Asn Pro

435 440 445
Ala Cys Pro Trp Thr Val Leu Pro Ala Gly Asp Leu Pro Thr His Asp
450 455 460
Gly Tyr Leu Pro Ser Asn Ile Asp Asp Leu Pro Ser His Glu Ala Pro
465 470 475 480
Leu Ala Asp Ser Leu Glu Glu Leu Glu Pro Gln
485 490

<210> 166
<211> 369
<212> PRT
<213> 人工序列（Artificial Sequence）
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 166
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15
His Ala Ala Arg Pro Met Gly Arg Gly Leu Leu Arg Gly Leu Trp Pro
20 25 30
Leu His Ile Val Leu Trp Thr Arg Ile Ala Ser Thr Ile Pro Pro His
35 40 45
Val Gln Lys Ser Val Asn Asn Asp Met Ile Val Thr Asp Asn Asn Gly
50 55 60
Ala Val Lys Phe Pro Gln Leu Cys Lys Phe Cys Asp Val Arg Phe Ser
65 70 75 80
[0112] Thr Cys Asp Asn Gln Lys Ser Cys Met Ser Asn Cys Ser Ile Thr Ser
85 90 95
Ile Cys Glu Lys Pro Gln Glu Val Cys Val Ala Val Trp Arg Lys Asn
100 105 110
Asp Glu Asn Ile Thr Leu Glu Thr Val Cys His Asp Pro Lys Leu Pro
115 120 125
Tyr His Asp Phe Ile Leu Glu Asp Ala Ala Ser Pro Lys Cys Ile Met
130 135 140
Lys Glu Lys Lys Lys Pro Gly Glu Thr Phe Phe Met Cys Ser Cys Ser
145 150 155 160
Ser Asp Glu Cys Asn Asp Asn Ile Ile Phe Ser Glu Glu Tyr Asn Thr
165 170 175
Ser Asn Pro Asp Leu Leu Leu Val Ile Phe Gln Ser Asp Pro Thr Arg
180 185 190
Val Glu Thr Ala Thr Glu Thr Ala Trp Ile Ser Leu Val Thr Ala Leu
195 200 205
His Leu Val Leu Gly Leu Asn Ala Val Leu Gly Leu Leu Leu Leu Arg
210 215 220
Lys Gln Phe Pro Ala His Tyr Arg Arg Leu Arg His Ala Leu Trp Pro
225 230 235 240
Ser Leu Pro Asp Leu His Arg Val Leu Gly Gln Tyr Leu Arg Asp Thr
245 250 255
Ala Ala Leu Ser Pro Pro Arg Ala Thr Val Ser Asp Thr Cys Glu Glu
260 265 270
Val Glu Pro Ser Leu Leu Glu Ile Leu Pro Arg Ser Ser Glu Arg Thr
275 280 285

Pro Leu Pro Leu Leu Glu Asp Glu Gly Val Ala Gly Ala Pro Thr Gly
290 295 300
Ser Ser Pro Gln Pro Leu Gln Pro Leu Ser Gly Glu Asp Asp Ala Tyr
305 310 315 320
Cys Thr Phe Pro Ser Arg Asp Asp Leu Leu Leu Phe Ser Pro Ser Gly
325 330 335
Gln Gly Glu Phe Arg Ala Leu Asn Ala Arg Leu Pro Leu Asn Thr Asp
340 345 350
Ala Tyr Leu Ser Leu Gln Glu Leu Gln Gly Gln Asp Pro Thr His Leu
355 360 365
Val

<210> 167
<211> 348
<212> PRT
<213> 人工序列（Artificial Sequence）
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 167
Met Gly Arg Gly Leu Leu Arg Gly Leu Trp Pro Leu His Ile Val Leu
1 5 10 15
Trp Thr Arg Ile Ala Ser Thr Ile Pro Pro His Val Gln Lys Ser Val
20 25 30
Asn Asn Asp Met Ile Val Thr Asp Asn Asn Gly Ala Val Lys Phe Pro
[0113] 35 40 45
Gln Leu Cys Lys Phe Cys Asp Val Arg Phe Ser Thr Cys Asp Asn Gln
50 55 60
Lys Ser Cys Met Ser Asn Cys Ser Ile Thr Ser Ile Cys Glu Lys Pro
65 70 75 80
Gln Glu Val Cys Val Ala Val Trp Arg Lys Asn Asp Glu Asn Ile Thr
85 90 95
Leu Glu Thr Val Cys His Asp Pro Lys Leu Pro Tyr His Asp Phe Ile
100 105 110
Leu Glu Asp Ala Ala Ser Pro Lys Cys Ile Met Lys Glu Lys Lys Lys
115 120 125
Pro Gly Glu Thr Phe Phe Met Cys Ser Cys Ser Ser Asp Glu Cys Asn
130 135 140
Asp Asn Ile Ile Phe Ser Glu Glu Tyr Asn Thr Ser Asn Pro Asp Leu
145 150 155 160
Leu Leu Val Ile Phe Gln Ser Asp Pro Thr Arg Val Glu Thr Ala Thr
165 170 175
Glu Thr Ala Trp Ile Ser Leu Val Thr Ala Leu His Leu Val Leu Gly
180 185 190
Leu Asn Ala Val Leu Gly Leu Leu Leu Leu Arg Lys Gln Phe Pro Ala
195 200 205
His Tyr Arg Arg Leu Arg His Ala Leu Trp Pro Ser Leu Pro Asp Leu
210 215 220
His Arg Val Leu Gly Gln Tyr Leu Arg Asp Thr Ala Ala Leu Ser Pro
225 230 235 240
Pro Lys Ala Thr Val Ser Asp Thr Cys Glu Glu Val Glu Pro Ser Leu

245 250 255
Leu Glu Ile Leu Pro Lys Ser Ser Glu Arg Thr Pro Leu Pro Leu Leu
260 265 270
Glu Asp Glu Gly Val Ala Gly Ala Pro Thr Gly Ser Ser Pro Gln Pro
275 280 285
Leu Gln Pro Leu Ser Gly Glu Asp Asp Ala Tyr Cys Thr Phe Pro Ser
290 295 300
Arg Asp Asp Leu Leu Leu Phe Ser Pro Ser Gly Gln Gly Glu Phe Arg
305 310 315 320
Ala Leu Asn Ala Arg Leu Pro Leu Asn Thr Asp Ala Tyr Leu Ser Leu
325 330 335
Gln Glu Leu Gln Gly Gln Asp Pro Thr His Leu Val
340 345

<210> 168
<211> 348
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 168
Met Gly Arg Gly Leu Leu Arg Gly Leu Trp Pro Leu His Ile Val Leu
1 5 10 15
Trp Thr Arg Ile Ala Ser Thr Ile Pro Pro His Val Gln Lys Ser Val
20 25 30

[0114] Asn Asn Asp Met Ile Val Thr Asp Asn Asn Gly Ala Val Lys Phe Pro
35 40 45
Gln Leu Cys Lys Phe Cys Asp Val Arg Phe Ser Thr Cys Asp Asn Gln
50 55 60
Lys Ser Cys Met Ser Asn Cys Ser Ile Thr Ser Ile Cys Glu Lys Pro
65 70 75 80
Gln Glu Val Cys Val Ala Val Trp Arg Lys Asn Asp Glu Asn Ile Thr
85 90 95
Leu Glu Thr Val Cys His Asp Pro Lys Leu Pro Tyr His Asp Phe Ile
100 105 110
Leu Glu Asp Ala Ala Ser Pro Lys Cys Ile Met Lys Glu Lys Lys Lys
115 120 125
Pro Gly Glu Thr Phe Phe Met Cys Ser Cys Ser Ser Asp Glu Cys Asn
130 135 140
Asp Asn Ile Ile Phe Ser Glu Glu Tyr Asn Thr Ser Asn Pro Asp Leu
145 150 155 160
Leu Leu Val Ile Phe Gln Ser Asp Pro Thr Arg Val Glu Thr Ala Thr
165 170 175
Glu Thr Ala Trp Ile Ser Leu Val Thr Ala Leu His Leu Val Leu Gly
180 185 190
Leu Asn Ala Val Leu Gly Leu Leu Leu Leu Arg Lys Gln Phe Pro Ala
195 200 205
His Tyr Arg Arg Leu Arg His Ala Leu Trp Pro Ser Leu Pro Asp Leu
210 215 220
His Arg Val Leu Gly Gln Tyr Leu Arg Asp Thr Ala Ala Leu Ser Pro
225 230 235 240

Pro Arg Ala Thr Val Ser Asp Thr Cys Glu Glu Val Glu Pro Ser Leu
245 250 255
Leu Glu Ile Leu Pro Arg Ser Ser Glu Arg Thr Pro Leu Pro Leu Leu
260 265 270
Glu Asp Glu Gly Val Ala Gly Ala Pro Thr Gly Ser Ser Pro Gln Pro
275 280 285
Leu Gln Pro Leu Ser Gly Glu Asp Asp Ala Tyr Cys Thr Phe Pro Ser
290 295 300
Arg Asp Asp Leu Leu Leu Phe Ser Pro Ser Gly Gln Gly Glu Phe Arg
305 310 315 320
Ala Leu Asn Ala Arg Leu Pro Leu Asn Thr Asp Ala Tyr Leu Ser Leu
325 330 335
Gln Glu Leu Gln Gly Gln Asp Pro Thr His Leu Val
340 345

<210> 169
<211> 438
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 169

[0115]

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

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

[0116] Ser Phe Tyr Gln Asn Gln
435

<210> 170
<211> 438
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 170
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15
His Ala Ala Arg Pro Met Gly Arg Gly Leu Leu Arg Gly Leu Trp Pro
20 25 30
Leu His Ile Val Leu Trp Thr Arg Ile Ala Ser Thr Ile Pro Pro His
35 40 45
Val Gln Lys Ser Val Asn Asn Asp Met Ile Val Thr Asp Asn Asn Gly
50 55 60
Ala Val Lys Phe Pro Gln Leu Cys Lys Phe Cys Asp Val Arg Phe Ser
65 70 75 80
Thr Cys Asp Asn Gln Lys Ser Cys Met Ser Asn Cys Ser Ile Thr Ser
85 90 95
Ile Cys Glu Lys Pro Gln Glu Val Cys Val Ala Val Trp Arg Lys Asn
100 105 110
Asp Glu Asn Ile Thr Leu Glu Thr Val Cys His Asp Pro Lys Leu Pro
115 120 125

Tyr His Asp Phe Ile Leu Glu Asp Ala Ala Ser Pro Lys Cys Ile Met
130 135 140
Lys Glu Lys Lys Lys Pro Gly Glu Thr Phe Phe Met Cys Ser Cys Ser
145 150 155 160
Ser Asp Glu Cys Asn Asp Asn Ile Ile Phe Ser Glu Glu Tyr Asn Thr
165 170 175
Ser Asn Pro Asp Leu Leu Leu Val Ile Phe Gln Ser Asp Pro Thr Arg
180 185 190
Val Glu Thr Ala Thr Glu Thr Ala Trp Ile Ser Leu Val Thr Ala Leu
195 200 205
His Leu Val Leu Gly Leu Asn Ala Val Leu Gly Leu Leu Leu Leu Arg
210 215 220
Lys Gln Phe Pro Ala His Tyr Arg Arg Leu Arg His Ala Leu Trp Pro
225 230 235 240
Ser Leu Pro Asp Leu His Arg Val Leu Gly Gln Tyr Leu Arg Asp Thr
245 250 255
Ala Ala Leu Ser Pro Pro Arg Ala Thr Val Ser Asp Thr Cys Glu Glu
260 265 270
Val Glu Pro Ser Leu Leu Glu Ile Leu Pro Arg Ser Ser Glu Arg Thr
275 280 285
Pro Leu Pro Leu Leu Glu Ala Arg Asp Glu Val Glu Gly Phe Leu Gln
290 295 300
Asp Thr Phe Pro Gln Gln Leu Glu Glu Ser Glu Lys Gln Arg Leu Gly
305 310 315 320
Gly Asp Val Gln Ser Pro Asn Cys Pro Ser Glu Asp Val Val Ile Thr
[0117] 325 330 335
Pro Glu Ser Phe Gly Arg Asp Ser Ser Leu Thr Cys Leu Ala Gly Asn
340 345 350
Val Ser Ala Cys Asp Ala Pro Ile Leu Ser Ser Ser Arg Ser Leu Asp
355 360 365
Cys Arg Glu Ser Gly Lys Asn Gly Pro His Val Tyr Gln Asp Leu Leu
370 375 380
Leu Ser Leu Gly Thr Thr Asn Ser Thr Leu Pro Pro Pro Phe Ser Leu
385 390 395 400
Gln Ser Gly Ile Leu Thr Leu Asn Pro Val Ala Gln Gly Gln Pro Ile
405 410 415
Leu Thr Ser Leu Gly Ser Asn Gln Glu Glu Ala Tyr Val Thr Met Ser
420 425 430
Ser Phe Tyr Gln Asn Gln
435

<210> 171
<211> 410
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 171
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15
His Ala Ala Arg Pro Met Gly Arg Gly Leu Leu Arg Gly Leu Trp Pro

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

[0118]
Lys Gln Phe Pro Ala His Tyr Arg Arg Leu Arg His Ala Leu Trp Pro
225 230 235 240
Ser Leu Pro Asp Leu His Arg Val Leu Gly Gln Tyr Leu Arg Asp Thr
245 250 255
Ala Ala Leu Ser Pro Pro Lys Ala Thr Val Ser Asp Thr Cys Glu Glu
260 265 270
Val Glu Pro Ser Leu Leu Glu Ile Leu Pro Lys Ser Ser Glu Arg Thr
275 280 285
Pro Leu Pro Leu Leu Glu Gln Gln Asp Lys Val Pro Glu Pro Ala Ser
290 295 300
Leu Ser Ser Asn His Ser Leu Thr Ser Cys Phe Thr Asn Gln Gly Tyr
305 310 315 320
Phe Phe Phe His Leu Pro Asp Ala Leu Glu Ile Glu Ala Cys Gln Asp
325 330 335
Glu Gly Val Ala Gly Ala Pro Thr Gly Ser Ser Pro Gln Pro Leu Gln
340 345 350
Pro Leu Ser Gly Glu Asp Asp Ala Tyr Cys Thr Phe Pro Ser Arg Asp
355 360 365
Asp Leu Leu Leu Phe Ser Pro Ser Gly Gln Gly Glu Phe Arg Ala Leu
370 375 380
Asn Ala Arg Leu Pro Leu Asn Thr Asp Ala Tyr Leu Ser Leu Gln Glu
385 390 395 400
Leu Gln Gly Gln Asp Pro Thr His Leu Val
405 410

<210> 172
<211> 490

<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 172

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Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1               5                  10                  15
His Ala Ala Arg Pro Met Gly Arg Gly Leu Leu Arg Gly Leu Trp Pro
            20                  25                  30
Leu His Ile Val Leu Trp Thr Arg Ile Ala Ser Thr Ile Pro Pro His
        35                  40                  45
Val Gln Lys Ser Val Asn Asn Asp Met Ile Val Thr Asp Asn Asn Gly
    50                  55                  60
Ala Val Lys Phe Pro Gln Leu Cys Lys Phe Cys Asp Val Arg Phe Ser
65                  70                  75                  80
Thr Cys Asp Asn Gln Lys Ser Cys Met Ser Asn Cys Ser Ile Thr Ser
                85                  90                  95
Ile Cys Glu Lys Pro Gln Glu Val Cys Val Ala Val Trp Arg Lys Asn
            100                 105                 110
Asp Glu Asn Ile Thr Leu Glu Thr Val Cys His Asp Pro Lys Leu Pro
        115                 120                 125
Tyr His Asp Phe Ile Leu Glu Asp Ala Ala Ser Pro Lys Cys Ile Met
    130                 135                 140
Lys Glu Lys Lys Lys Pro Gly Glu Thr Phe Phe Met Cys Ser Cys Ser
145                 150                 155                 160
Ser Asp Glu Cys Asn Asp Asn Ile Ile Phe Ser Glu Glu Tyr Asn Thr
                165                 170                 175
Ser Asn Pro Asp Leu Leu Leu Val Ile Phe Gln Ser Asp Pro Thr Arg
            180                 185                 190
Val Glu Thr Ala Thr Glu Thr Trp Ile Ser Leu Val Thr Ala Leu His
        195                 200                 205
Leu Val Leu Gly Leu Ser Ala Val Leu Gly Leu Leu Leu Leu Arg Trp
    210                 215                 220
Gln Phe Pro Ala His Tyr Arg Arg Leu Arg His Ala Leu Trp Pro Ser
225                 230                 235                 240
Leu Pro Asp Leu His Arg Val Leu Gly Gln Tyr Leu Arg Asp Thr Ala
                245                 250                 255
Ala Leu Ser Pro Pro Lys Ala Thr Val Ser Asp Thr Cys Glu Glu Val
            260                 265                 270
Glu Pro Ser Leu Leu Glu Ile Leu Pro Lys Ser Ser Glu Arg Thr Pro
        275                 280                 285
Leu Pro Leu Leu Glu Ala Arg Asp Glu Val Glu Gly Phe Leu Gln Asp
    290                 295                 300
Thr Phe Pro Gln Gln Leu Glu Glu Ser Glu Lys Gln Arg Leu Gly Gly
305                 310                 315                 320
Asp Val Gln Ser Pro Asn Cys Pro Ser Glu Asp Val Val Ile Thr Pro
                325                 330                 335
Glu Ser Phe Gly Arg Asp Ser Ser Leu Thr Cys Leu Ala Gly Asn Val
            340                 345                 350
Ser Ala Cys Asp Ala Pro Ile Leu Ser Ser Ser Arg Ser Leu Asp Cys
```

[0119]

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

<210> 173
<211> 489
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 173

[0120] Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15
His Ala Ala Arg Pro Met Gly Arg Gly Leu Leu Arg Gly Leu Trp Pro
20 25 30
Leu His Ile Val Leu Trp Thr Arg Ile Ala Ser Thr Ile Pro Pro His
35 40 45
Val Gln Lys Ser Val Asn Asn Asp Met Ile Val Thr Asp Asn Asn Gly
50 55 60
Ala Val Lys Phe Pro Gln Leu Cys Lys Phe Cys Asp Val Arg Phe Ser
65 70 75 80
Thr Cys Asp Asn Gln Lys Ser Cys Met Ser Asn Cys Ser Ile Thr Ser
85 90 95
Ile Cys Glu Lys Pro Gln Glu Val Cys Val Ala Val Trp Arg Lys Asn
100 105 110
Asp Glu Asn Ile Thr Leu Glu Thr Val Cys His Asp Pro Lys Leu Pro
115 120 125
Tyr His Asp Phe Ile Leu Glu Asp Ala Ala Ser Pro Lys Cys Ile Met
130 135 140
Lys Glu Lys Lys Lys Pro Gly Glu Thr Phe Phe Met Cys Ser Cys Ser
145 150 155 160
Ser Asp Glu Cys Asn Asp Asn Ile Ile Phe Ser Glu Glu Tyr Asn Thr
165 170 175
Ser Asn Pro Asp Leu Leu Leu Val Ile Phe Gln Ser Asp Pro Thr Arg
180 185 190
Val Glu Thr Ala Thr Glu Thr Ile Ser Leu Val Thr Ala Leu His Leu
195 200 205

Val Leu Gly Leu Ser Ala Val Leu Gly Leu Leu Leu Leu Arg Trp Gln
210 215 220
Phe Pro Ala His Tyr Arg Arg Leu Arg His Ala Leu Trp Pro Ser Leu
225 230 235 240
Pro Asp Leu His Arg Val Leu Gly Gln Tyr Leu Arg Asp Thr Ala Ala
245 250 255
Leu Ser Pro Pro Lys Ala Thr Val Ser Asp Thr Cys Glu Glu Val Glu
260 265 270
Pro Ser Leu Leu Glu Ile Leu Pro Lys Ser Ser Glu Arg Thr Pro Leu
275 280 285
Pro Leu Leu Glu Ala Arg Asp Glu Val Glu Gly Phe Leu Gln Asp Thr
290 295 300
Phe Pro Gln Gln Leu Glu Glu Ser Glu Lys Gln Arg Leu Gly Gly Asp
305 310 315 320
Val Gln Ser Pro Asn Cys Pro Ser Glu Asp Val Val Ile Thr Pro Glu
325 330 335
Ser Phe Gly Arg Asp Ser Ser Leu Thr Cys Leu Ala Gly Asn Val Ser
340 345 350
Ala Cys Asp Ala Pro Ile Leu Ser Ser Ser Arg Ser Leu Asp Cys Arg
355 360 365
Glu Ser Gly Lys Asn Gly Pro His Val Tyr Gln Asp Leu Leu Leu Ser
370 375 380
Leu Gly Thr Thr Asn Ser Thr Leu Pro Pro Pro Phe Ser Leu Gln Ser
385 390 395 400
Gly Ile Leu Thr Leu Asn Pro Val Ala Gln Gly Gln Pro Ile Leu Thr
[0121] 405 410 415
Ser Leu Gly Ser Asn Gln Glu Glu Ala Tyr Val Thr Met Ser Ser Phe
420 425 430
Tyr Gln Asn Gln Ser Arg Ser Asp Pro Lys Pro Glu Asn Pro Ala Cys
435 440 445
Pro Trp Thr Val Leu Pro Ala Gly Asp Leu Pro Thr His Asp Gly Tyr
450 455 460
Leu Pro Ser Asn Ile Asp Asp Leu Pro Ser His Glu Ala Pro Leu Ala
465 470 475 480
Asp Ser Leu Glu Glu Leu Glu Pro Gln
485

<210> 174
<211> 490
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 174
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15
His Ala Ala Arg Pro Met Gly Arg Gly Leu Leu Arg Gly Leu Trp Pro
20 25 30
Leu His Ile Val Leu Trp Thr Arg Ile Ala Ser Thr Ile Pro Pro His
35 40 45
Val Gln Lys Ser Val Asn Asn Asp Met Ile Val Thr Asp Asn Asn Gly

50 55 60

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

[0122] Ala Leu Ser Pro Pro Lys Ala Thr Val Ser Asp Thr Cys Glu Glu Val
260 265 270
Glu Pro Ser Leu Leu Glu Ile Leu Pro Lys Ser Ser Glu Arg Thr Pro
275 280 285
Leu Pro Leu Leu Glu Ala Arg Asp Glu Val Glu Gly Phe Leu Gln Asp
290 295 300
Thr Phe Pro Gln Gln Leu Glu Glu Ser Glu Lys Gln Arg Leu Gly Gly
305 310 315 320
Asp Val Gln Ser Pro Asn Cys Pro Ser Glu Asp Val Val Ile Thr Pro
325 330 335
Glu Ser Phe Gly Arg Asp Ser Ser Leu Thr Cys Leu Ala Gly Asn Val
340 345 350
Ser Ala Cys Asp Ala Pro Ile Leu Ser Ser Ser Arg Ser Leu Asp Cys
355 360 365
Arg Glu Ser Gly Lys Asn Gly Pro His Val Tyr Gln Asp Leu Leu Leu
370 375 380
Ser Leu Gly Thr Thr Asn Ser Thr Leu Pro Pro Pro Phe Ser Leu Gln
385 390 395 400
Ser Gly Ile Leu Thr Leu Asn Pro Val Ala Gln Gly Gln Pro Ile Leu
405 410 415
Thr Ser Leu Gly Ser Asn Gln Glu Glu Ala Tyr Val Thr Met Ser Ser
420 425 430
Phe Tyr Gln Asn Gln Ser Arg Ser Asp Pro Lys Pro Glu Asn Pro Ala
435 440 445
Cys Pro Trp Thr Val Leu Pro Ala Gly Asp Leu Pro Thr His Asp Gly
450 455 460

Tyr Leu Pro Ser Asn Ile Asp Asp Leu Pro Ser His Glu Ala Pro Leu
465 470 475 480
Ala Asp Ser Leu Glu Glu Leu Glu Pro Gln
485 490

<210> 175
<211> 488
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 175
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15
His Ala Ala Arg Pro Met Gly Arg Gly Leu Leu Arg Gly Leu Trp Pro
20 25 30
Leu His Ile Val Leu Trp Thr Arg Ile Ala Ser Thr Ile Pro Pro His
35 40 45
Val Gln Lys Ser Val Asn Asn Asp Met Ile Val Thr Asp Asn Asn Gly
50 55 60
Ala Val Lys Phe Pro Gln Leu Cys Lys Phe Cys Asp Val Arg Phe Ser
65 70 75 80
Thr Cys Asp Asn Gln Lys Ser Cys Met Ser Asn Cys Ser Ile Thr Ser
85 90 95
Ile Cys Glu Lys Pro Gln Glu Val Cys Val Ala Val Trp Arg Lys Asn
[0123] 100 105 110
Asp Glu Asn Ile Thr Leu Glu Thr Val Cys His Asp Pro Lys Leu Pro
115 120 125
Tyr His Asp Phe Ile Leu Glu Asp Ala Ala Ser Pro Lys Cys Ile Met
130 135 140
Lys Glu Lys Lys Lys Pro Gly Glu Thr Phe Phe Met Cys Ser Cys Ser
145 150 155 160
Ser Asp Glu Cys Asn Asp Asn Ile Ile Phe Ser Glu Glu Tyr Asn Thr
165 170 175
Ser Asn Pro Asp Leu Leu Leu Val Ile Phe Gln Ser Asp Pro Thr Arg
180 185 190
Val Glu Thr Ala Thr Glu Thr Ser Leu Val Thr Ala Leu His Leu Val
195 200 205
Leu Gly Leu Ser Ala Val Leu Gly Leu Leu Leu Leu Arg Trp Gln Phe
210 215 220
Pro Ala His Tyr Arg Arg Leu Arg His Ala Leu Trp Pro Ser Leu Pro
225 230 235 240
Asp Leu His Arg Val Leu Gly Gln Tyr Leu Arg Asp Thr Ala Ala Leu
245 250 255
Ser Pro Pro Lys Ala Thr Val Ser Asp Thr Cys Glu Glu Val Glu Pro
260 265 270
Ser Leu Leu Glu Ile Leu Pro Lys Ser Ser Glu Arg Thr Pro Leu Pro
275 280 285
Leu Leu Glu Ala Arg Asp Glu Val Glu Gly Phe Leu Gln Asp Thr Phe
290 295 300
Pro Gln Gln Leu Glu Glu Ser Glu Lys Gln Arg Leu Gly Gly Asp Val

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

<210> 176
<211> 487
[0124] <212> PRT
<213> 人工序列（Artificial Sequence）
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 176
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15
His Ala Ala Arg Pro Met Gly Arg Gly Leu Leu Arg Gly Leu Trp Pro
20 25 30
Leu His Ile Val Leu Trp Thr Arg Ile Ala Ser Thr Ile Pro Pro His
35 40 45
Val Gln Lys Ser Val Asn Asn Asp Met Ile Val Thr Asp Asn Asn Gly
50 55 60
Ala Val Lys Phe Pro Gln Leu Cys Lys Phe Cys Asp Val Arg Phe Ser
65 70 75 80
Thr Cys Asp Asn Gln Lys Ser Cys Met Ser Asn Cys Ser Ile Thr Ser
85 90 95
Ile Cys Glu Lys Pro Gln Glu Val Cys Val Ala Val Trp Arg Lys Asn
100 105 110
Asp Glu Asn Ile Thr Leu Glu Thr Val Cys His Asp Pro Lys Leu Pro
115 120 125
Tyr His Asp Phe Ile Leu Glu Asp Ala Ala Ser Pro Lys Cys Ile Met
130 135 140
Lys Glu Lys Lys Lys Pro Gly Glu Thr Phe Phe Met Cys Ser Cys Ser
145 150 155 160

Ser Asp Glu Cys Asn Asp Asn Ile Ile Phe Ser Glu Glu Tyr Asn Thr
165 170 175
Ser Asn Pro Asp Leu Leu Leu Val Ile Phe Gln Ser Asp Pro Thr Arg
180 185 190
Val Glu Thr Ala Thr Glu Thr Leu Val Thr Ala Leu His Leu Val Leu
195 200 205
Gly Leu Ser Ala Val Leu Gly Leu Leu Leu Leu Arg Trp Gln Phe Pro
210 215 220
Ala His Tyr Arg Arg Leu Arg His Ala Leu Trp Pro Ser Leu Pro Asp
225 230 235 240
Leu His Arg Val Leu Gly Gln Tyr Leu Arg Asp Thr Ala Ala Leu Ser
245 250 255
Pro Pro Lys Ala Thr Val Ser Asp Thr Cys Glu Glu Val Glu Pro Ser
260 265 270
Leu Leu Glu Ile Leu Pro Lys Ser Ser Glu Arg Thr Pro Leu Pro Leu
275 280 285
Leu Glu Ala Arg Asp Glu Val Glu Gly Phe Leu Gln Asp Thr Phe Pro
290 295 300
Gln Gln Leu Glu Glu Ser Glu Lys Gln Arg Leu Gly Gly Asp Val Gln
305 310 315 320
Ser Pro Asn Cys Pro Ser Glu Asp Val Val Ile Thr Pro Glu Ser Phe
325 330 335
Gly Arg Asp Ser Ser Leu Thr Cys Leu Ala Gly Asn Val Ser Ala Cys
340 345 350
Asp Ala Pro Ile Leu Ser Ser Ser Arg Ser Leu Asp Cys Arg Glu Ser
[0125] 355 360 365
Gly Lys Asn Gly Pro His Val Tyr Gln Asp Leu Leu Leu Ser Leu Gly
370 375 380
Thr Thr Asn Ser Thr Leu Pro Pro Pro Phe Ser Leu Gln Ser Gly Ile
385 390 395 400
Leu Thr Leu Asn Pro Val Ala Gln Gly Gln Pro Ile Leu Thr Ser Leu
405 410 415
Gly Ser Asn Gln Glu Glu Ala Tyr Val Thr Met Ser Ser Phe Tyr Gln
420 425 430
Asn Gln Ser Arg Ser Asp Pro Lys Pro Glu Asn Pro Ala Cys Pro Trp
435 440 445
Thr Val Leu Pro Ala Gly Asp Leu Pro Thr His Asp Gly Tyr Leu Pro
450 455 460
Ser Asn Ile Asp Asp Leu Pro Ser His Glu Ala Pro Leu Ala Asp Ser
465 470 475 480
Leu Glu Glu Leu Glu Pro Gln
485

<210> 177
<211> 488
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 177
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu

```
1               5                  10                  15
His Ala Ala Arg Pro Met Gly Arg Gly Leu Leu Arg Gly Leu Trp Pro
            20                  25                  30
Leu His Ile Val Leu Trp Thr Arg Ile Ala Ser Thr Ile Pro Pro His
        35                  40                  45
Val Gln Lys Ser Val Asn Asn Asp Met Ile Val Thr Asp Asn Asn Gly
    50                  55                  60
Ala Val Lys Phe Pro Gln Leu Cys Lys Phe Cys Asp Val Arg Phe Ser
65                  70                  75                  80
Thr Cys Asp Asn Gln Lys Ser Cys Met Ser Asn Cys Ser Ile Thr Ser
                85                  90                  95
Ile Cys Glu Lys Pro Gln Glu Val Cys Val Ala Val Trp Arg Lys Asn
            100                 105                 110
Asp Glu Asn Ile Thr Leu Glu Thr Val Cys His Asp Pro Lys Leu Pro
        115                 120                 125
Tyr His Asp Phe Ile Leu Glu Asp Ala Ala Ser Pro Lys Cys Ile Met
    130                 135                 140
Lys Glu Lys Lys Lys Pro Gly Glu Thr Phe Phe Met Cys Ser Cys Ser
145                 150                 155                 160
Ser Asp Glu Cys Asn Asp Asn Ile Ile Phe Ser Glu Glu Tyr Asn Thr
                165                 170                 175
Ser Asn Pro Asp Leu Leu Leu Val Ile Phe Gln Ser Asp Pro Thr Arg
            180                 185                 190
Val Glu Thr Ala Thr Glu Thr Ile Leu Val Thr Ala Leu His Leu Val
        195                 200                 205
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[0126]

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

Leu Gly Ser Asn Gln Glu Glu Ala Tyr Val Thr Met Ser Ser Phe Tyr
420 425 430
Gln Asn Gln Ser Arg Ser Asp Pro Lys Pro Glu Asn Pro Ala Cys Pro
435 440 445
Trp Thr Val Leu Pro Ala Gly Asp Leu Pro Thr His Asp Gly Tyr Leu
450 455 460
Pro Ser Asn Ile Asp Asp Leu Pro Ser His Glu Ala Pro Leu Ala Asp
465 470 475 480
Ser Leu Glu Glu Leu Glu Pro Gln
485

<210> 178
<211> 486
<212> PRT
<213> 人工序列（Artificial Sequence）
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 178

Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15
His Ala Ala Arg Pro Met Gly Arg Gly Leu Leu Arg Gly Leu Trp Pro
20 25 30
Leu His Ile Val Leu Trp Thr Arg Ile Ala Ser Thr Ile Pro Pro His
35 40 45
Val Gln Lys Ser Val Asn Asn Asp Met Ile Val Thr Asp Asn Asn Gly
[0127] 50 55 60
Ala Val Lys Phe Pro Gln Leu Cys Lys Phe Cys Asp Val Arg Phe Ser
65 70 75 80
Thr Cys Asp Asn Gln Lys Ser Cys Met Ser Asn Cys Ser Ile Thr Ser
85 90 95
Ile Cys Glu Lys Pro Gln Glu Val Cys Val Ala Val Trp Arg Lys Asn
100 105 110
Asp Glu Asn Ile Thr Leu Glu Thr Val Cys His Asp Pro Lys Leu Pro
115 120 125
Tyr His Asp Phe Ile Leu Glu Asp Ala Ala Ser Pro Lys Cys Ile Met
130 135 140
Lys Glu Lys Lys Lys Pro Gly Glu Thr Phe Phe Met Cys Ser Cys Ser
145 150 155 160
Ser Asp Glu Cys Asn Asp Asn Ile Ile Phe Ser Glu Glu Tyr Asn Thr
165 170 175
Ser Asn Pro Asp Leu Leu Leu Val Ile Phe Gln Ser Asp Pro Thr Arg
180 185 190
Val Glu Thr Ala Thr Glu Thr Val Thr Ala Leu His Leu Val Leu Gly
195 200 205
Leu Ser Ala Val Leu Gly Leu Leu Leu Leu Arg Trp Gln Phe Pro Ala
210 215 220
His Tyr Arg Arg Leu Arg His Ala Leu Trp Pro Ser Leu Pro Asp Leu
225 230 235 240
His Arg Val Leu Gly Gln Tyr Leu Arg Asp Thr Ala Ala Leu Ser Pro
245 250 255
Pro Lys Ala Thr Val Ser Asp Thr Cys Glu Glu Val Glu Pro Ser Leu

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

[0128] Asn Ile Asp Asp Leu Pro Ser His Glu Ala Pro Leu Ala Asp Ser Leu
465 470 475 480
Glu Glu Leu Glu Pro Gln
485

<210> 179
<211> 485
<212> PRT
<213> 人工序列（Artificial Sequence）
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 179
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15
His Ala Ala Arg Pro Met Gly Arg Gly Leu Leu Arg Gly Leu Trp Pro
20 25 30
Leu His Ile Val Leu Trp Thr Arg Ile Ala Ser Thr Ile Pro Pro His
35 40 45
Val Gln Lys Ser Val Asn Asn Asp Met Ile Val Thr Asp Asn Asn Gly
50 55 60
Ala Val Lys Phe Pro Gln Leu Cys Lys Phe Cys Asp Val Arg Phe Ser
65 70 75 80
Thr Cys Asp Asn Gln Lys Ser Cys Met Ser Asn Cys Ser Ile Thr Ser
85 90 95
Ile Cys Glu Lys Pro Gln Glu Val Cys Val Ala Val Trp Arg Lys Asn
100 105 110

Asp Glu Asn Ile Thr Leu Glu Thr Val Cys His Asp Pro Lys Leu Pro
115 120 125
Tyr His Asp Phe Ile Leu Glu Asp Ala Ala Ser Pro Lys Cys Ile Met
130 135 140
Lys Glu Lys Lys Lys Pro Gly Glu Thr Phe Phe Met Cys Ser Cys Ser
145 150 155 160
Ser Asp Glu Cys Asn Asp Asn Ile Ile Phe Ser Glu Glu Tyr Asn Thr
165 170 175
Ser Asn Pro Asp Leu Leu Leu Val Ile Phe Gln Ser Asp Pro Thr Arg
180 185 190
Val Glu Thr Ala Thr Glu Thr Thr Ala Leu His Leu Val Leu Gly Leu
195 200 205
Ser Ala Val Leu Gly Leu Leu Leu Leu Arg Trp Gln Phe Pro Ala His
210 215 220
Tyr Arg Arg Leu Arg His Ala Leu Trp Pro Ser Leu Pro Asp Leu His
225 230 235 240
Arg Val Leu Gly Gln Tyr Leu Arg Asp Thr Ala Ala Leu Ser Pro Pro
245 250 255
Lys Ala Thr Val Ser Asp Thr Cys Glu Glu Val Glu Pro Ser Leu Leu
260 265 270
Glu Ile Leu Pro Lys Ser Ser Glu Arg Thr Pro Leu Pro Leu Leu Glu
275 280 285
Ala Arg Asp Glu Val Glu Gly Phe Leu Gln Asp Thr Phe Pro Gln Gln
290 295 300
Leu Glu Glu Ser Glu Lys Gln Arg Leu Gly Gly Asp Val Gln Ser Pro
[0129] 305 310 315 320
Asn Cys Pro Ser Glu Asp Val Val Ile Thr Pro Glu Ser Phe Gly Arg
325 330 335
Asp Ser Ser Leu Thr Cys Leu Ala Gly Asn Val Ser Ala Cys Asp Ala
340 345 350
Pro Ile Leu Ser Ser Ser Arg Ser Leu Asp Cys Arg Glu Ser Gly Lys
355 360 365
Asn Gly Pro His Val Tyr Gln Asp Leu Leu Leu Ser Leu Gly Thr Thr
370 375 380
Asn Ser Thr Leu Pro Pro Pro Phe Ser Leu Gln Ser Gly Ile Leu Thr
385 390 395 400
Leu Asn Pro Val Ala Gln Gly Gln Pro Ile Leu Thr Ser Leu Gly Ser
405 410 415
Asn Gln Glu Glu Ala Tyr Val Thr Met Ser Ser Phe Tyr Gln Asn Gln
420 425 430
Ser Arg Ser Asp Pro Lys Pro Glu Asn Pro Ala Cys Pro Trp Thr Val
435 440 445
Leu Pro Ala Gly Asp Leu Pro Thr His Asp Gly Tyr Leu Pro Ser Asn
450 455 460
Ile Asp Asp Leu Pro Ser His Glu Ala Pro Leu Ala Asp Ser Leu Glu
465 470 475 480
Glu Leu Glu Pro Gln
485

<210> 180
<211> 484
<212> PRT

<213> 人工序列 (Artificial Sequence)
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 180

Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15
His Ala Ala Arg Pro Met Gly Arg Gly Leu Leu Arg Gly Leu Trp Pro
20 25 30
Leu His Ile Val Leu Trp Thr Arg Ile Ala Ser Thr Ile Pro Pro His
35 40 45
Val Gln Lys Ser Val Asn Asn Asp Met Ile Val Thr Asp Asn Asn Gly
50 55 60
Ala Val Lys Phe Pro Gln Leu Cys Lys Phe Cys Asp Val Arg Phe Ser
65 70 75 80
Thr Cys Asp Asn Gln Lys Ser Cys Met Ser Asn Cys Ser Ile Thr Ser
85 90 95
Ile Cys Glu Lys Pro Gln Glu Val Cys Val Ala Val Trp Arg Lys Asn
100 105 110
Asp Glu Asn Ile Thr Leu Glu Thr Val Cys His Asp Pro Lys Leu Pro
115 120 125
Tyr His Asp Phe Ile Leu Glu Asp Ala Ala Ser Pro Lys Cys Ile Met
130 135 140
Lys Glu Lys Lys Lys Pro Gly Glu Thr Phe Phe Met Cys Ser Cys Ser
145 150 155 160
[0130] Ser Asp Glu Cys Asn Asp Asn Ile Ile Phe Ser Glu Glu Tyr Asn Thr
165 170 175
Ser Asn Pro Asp Leu Leu Leu Val Ile Phe Gln Ser Asp Pro Thr Arg
180 185 190
Val Glu Thr Ala Thr Glu Thr Ala Leu His Leu Val Leu Gly Leu Ser
195 200 205
Ala Val Leu Gly Leu Leu Leu Leu Arg Trp Gln Phe Pro Ala His Tyr
210 215 220
Arg Arg Leu Arg His Ala Leu Trp Pro Ser Leu Pro Asp Leu His Arg
225 230 235 240
Val Leu Gly Gln Tyr Leu Arg Asp Thr Ala Ala Leu Ser Pro Pro Lys
245 250 255
Ala Thr Val Ser Asp Thr Cys Glu Glu Val Glu Pro Ser Leu Leu Glu
260 265 270
Ile Leu Pro Lys Ser Ser Glu Arg Thr Pro Leu Pro Leu Leu Glu Ala
275 280 285
Arg Asp Glu Val Glu Gly Phe Leu Gln Asp Thr Phe Pro Gln Gln Leu
290 295 300
Glu Glu Ser Glu Lys Gln Arg Leu Gly Gly Asp Val Gln Ser Pro Asn
305 310 315 320
Cys Pro Ser Glu Asp Val Val Ile Thr Pro Glu Ser Phe Gly Arg Asp
325 330 335
Ser Ser Leu Thr Cys Leu Ala Gly Asn Val Ser Ala Cys Asp Ala Pro
340 345 350
Ile Leu Ser Ser Ser Arg Ser Leu Asp Cys Arg Glu Ser Gly Lys Asn
355 360 365

Gly Pro His Val Tyr Gln Asp Leu Leu Leu Ser Leu Gly Thr Thr Asn
370 375 380
Ser Thr Leu Pro Pro Pro Phe Ser Leu Gln Ser Gly Ile Leu Thr Leu
385 390 395 400
Asn Pro Val Ala Gln Gly Gln Pro Ile Leu Thr Ser Leu Gly Ser Asn
405 410 415
Gln Glu Glu Ala Tyr Val Thr Met Ser Ser Phe Tyr Gln Asn Gln Ser
420 425 430
Arg Ser Asp Pro Lys Pro Glu Asn Pro Ala Cys Pro Trp Thr Val Leu
435 440 445
Pro Ala Gly Asp Leu Pro Thr His Asp Gly Tyr Leu Pro Ser Asn Ile
450 455 460
Asp Asp Leu Pro Ser His Glu Ala Pro Leu Ala Asp Ser Leu Glu Glu
465 470 475 480
Leu Glu Pro Gln

<210> 181
<211> 483
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 181

[0131]
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15
His Ala Ala Arg Pro Met Gly Arg Gly Leu Leu Arg Gly Leu Trp Pro
20 25 30
Leu His Ile Val Leu Trp Thr Arg Ile Ala Ser Thr Ile Pro Pro His
35 40 45
Val Gln Lys Ser Val Asn Asn Asp Met Ile Val Thr Asp Asn Asn Gly
50 55 60
Ala Val Lys Phe Pro Gln Leu Cys Lys Phe Cys Asp Val Arg Phe Ser
65 70 75 80
Thr Cys Asp Asn Gln Lys Ser Cys Met Ser Asn Cys Ser Ile Thr Ser
85 90 95
Ile Cys Glu Lys Pro Gln Glu Val Cys Val Ala Val Trp Arg Lys Asn
100 105 110
Asp Glu Asn Ile Thr Leu Glu Thr Val Cys His Asp Pro Lys Leu Pro
115 120 125
Tyr His Asp Phe Ile Leu Glu Asp Ala Ala Ser Pro Lys Cys Ile Met
130 135 140
Lys Glu Lys Lys Lys Pro Gly Glu Thr Phe Phe Met Cys Ser Cys Ser
145 150 155 160
Ser Asp Glu Cys Asn Asp Asn Ile Ile Phe Ser Glu Glu Tyr Asn Thr
165 170 175
Ser Asn Pro Asp Leu Leu Leu Val Ile Phe Gln Ser Asp Pro Thr Arg
180 185 190
Val Glu Thr Ala Thr Glu Thr Leu His Leu Val Leu Gly Leu Ser Ala
195 200 205
Val Leu Gly Leu Leu Leu Leu Leu Arg Trp Gln Phe Pro Ala His Tyr Arg

210 215 220
Arg Leu Arg His Ala Leu Trp Pro Ser Leu Pro Asp Leu His Arg Val
225 230 235 240
Leu Gly Gln Tyr Leu Arg Asp Thr Ala Ala Leu Ser Pro Pro Lys Ala
245 250 255
Thr Val Ser Asp Thr Cys Glu Glu Val Glu Pro Ser Leu Leu Glu Ile
260 265 270
Leu Pro Lys Ser Ser Glu Arg Thr Pro Leu Pro Leu Leu Glu Ala Arg
275 280 285
Asp Glu Val Glu Gly Phe Leu Gln Asp Thr Phe Pro Gln Gln Leu Glu
290 295 300
Glu Ser Glu Lys Gln Arg Leu Gly Gly Asp Val Gln Ser Pro Asn Cys
305 310 315 320
Pro Ser Glu Asp Val Val Ile Thr Pro Glu Ser Phe Gly Arg Asp Ser
325 330 335
Ser Leu Thr Cys Leu Ala Gly Asn Val Ser Ala Cys Asp Ala Pro Ile
340 345 350
Leu Ser Ser Ser Arg Ser Leu Asp Cys Arg Glu Ser Gly Lys Asn Gly
355 360 365
Pro His Val Tyr Gln Asp Leu Leu Leu Ser Leu Gly Thr Thr Asn Ser
370 375 380
Thr Leu Pro Pro Pro Phe Ser Leu Gln Ser Gly Ile Leu Thr Leu Asn
385 390 395 400
Pro Val Ala Gln Gly Gln Pro Ile Leu Thr Ser Leu Gly Ser Asn Gln
405 410 415
[0132] Glu Glu Ala Tyr Val Thr Met Ser Ser Phe Tyr Gln Asn Gln Ser Arg
420 425 430
Ser Asp Pro Lys Pro Glu Asn Pro Ala Cys Pro Trp Thr Val Leu Pro
435 440 445
Ala Gly Asp Leu Pro Thr His Asp Gly Tyr Leu Pro Ser Asn Ile Asp
450 455 460
Asp Leu Pro Ser His Glu Ala Pro Leu Ala Asp Ser Leu Glu Glu Leu
465 470 475 480
Glu Pro Gln

<210> 182
<211> 482
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 182
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15
His Ala Ala Arg Pro Met Gly Arg Gly Leu Leu Arg Gly Leu Trp Pro
20 25 30
Leu His Ile Val Leu Trp Thr Arg Ile Ala Ser Thr Ile Pro Pro His
35 40 45
Val Gln Lys Ser Val Asn Asn Asp Met Ile Val Thr Asp Asn Asn Gly
50 55 60

Ala Val Lys Phe Pro Gln Leu Cys Lys Phe Cys Asp Val Arg Phe Ser
65 70 75 80
Thr Cys Asp Asn Gln Lys Ser Cys Met Ser Asn Cys Ser Ile Thr Ser
85 90 95
Ile Cys Glu Lys Pro Gln Glu Val Cys Val Ala Val Trp Arg Lys Asn
100 105 110
Asp Glu Asn Ile Thr Leu Glu Thr Val Cys His Asp Pro Lys Leu Pro
115 120 125
Tyr His Asp Phe Ile Leu Glu Asp Ala Ala Ser Pro Lys Cys Ile Met
130 135 140
Lys Glu Lys Lys Lys Pro Gly Glu Thr Phe Phe Met Cys Ser Cys Ser
145 150 155 160
Ser Asp Glu Cys Asn Asp Asn Ile Ile Phe Ser Glu Glu Tyr Asn Thr
165 170 175
Ser Asn Pro Asp Leu Leu Leu Val Ile Phe Gln Ser Asp Pro Thr Arg
180 185 190
Val Glu Thr Ala Thr Glu Thr His Leu Val Leu Gly Leu Ser Ala Val
195 200 205
Leu Gly Leu Leu Leu Leu Arg Trp Gln Phe Pro Ala His Tyr Arg Arg
210 215 220
Leu Arg His Ala Leu Trp Pro Ser Leu Pro Asp Leu His Arg Val Leu
225 230 235 240
Gly Gln Tyr Leu Arg Asp Thr Ala Ala Leu Ser Pro Pro Lys Ala Thr
245 250 255
Val Ser Asp Thr Cys Glu Glu Val Glu Pro Ser Leu Leu Glu Ile Leu
[0133] 260 265 270
Pro Lys Ser Ser Glu Arg Thr Pro Leu Pro Leu Leu Glu Ala Arg Asp
275 280 285
Glu Val Glu Gly Phe Leu Gln Asp Thr Phe Pro Gln Gln Leu Glu Glu
290 295 300
Ser Glu Lys Gln Arg Leu Gly Gly Asp Val Gln Ser Pro Asn Cys Pro
305 310 315 320
Ser Glu Asp Val Val Ile Thr Pro Glu Ser Phe Gly Arg Asp Ser Ser
325 330 335
Leu Thr Cys Leu Ala Gly Asn Val Ser Ala Cys Asp Ala Pro Ile Leu
340 345 350
Ser Ser Ser Arg Ser Leu Asp Cys Arg Glu Ser Gly Lys Asn Gly Pro
355 360 365
His Val Tyr Gln Asp Leu Leu Leu Ser Leu Gly Thr Thr Asn Ser Thr
370 375 380
Leu Pro Pro Pro Phe Ser Leu Gln Ser Gly Ile Leu Thr Leu Asn Pro
385 390 395 400
Val Ala Gln Gly Gln Pro Ile Leu Thr Ser Leu Gly Ser Asn Gln Glu
405 410 415
Glu Ala Tyr Val Thr Met Ser Ser Phe Tyr Gln Asn Gln Ser Arg Ser
420 425 430
Asp Pro Lys Pro Glu Asn Pro Ala Cys Pro Trp Thr Val Leu Pro Ala
435 440 445
Gly Asp Leu Pro Thr His Asp Gly Tyr Leu Pro Ser Asn Ile Asp Asp
450 455 460
Leu Pro Ser His Glu Ala Pro Leu Ala Asp Ser Leu Glu Glu Leu Glu

465 470 475 480
Pro Gln

<210> 183
<211> 481
<212> PRT
<213> 人工序列（Artificial Sequence）
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 183
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15
His Ala Ala Arg Pro Met Gly Arg Gly Leu Leu Arg Gly Leu Trp Pro
20 25 30
Leu His Ile Val Leu Trp Thr Arg Ile Ala Ser Thr Ile Pro Pro His
35 40 45
Val Gln Lys Ser Val Asn Asn Asp Met Ile Val Thr Asp Asn Asn Gly
50 55 60
Ala Val Lys Phe Pro Gln Leu Cys Lys Phe Cys Asp Val Arg Phe Ser
65 70 75 80
Thr Cys Asp Asn Gln Lys Ser Cys Met Ser Asn Cys Ser Ile Thr Ser
85 90 95
Ile Cys Glu Lys Pro Gln Glu Val Cys Val Ala Val Trp Arg Lys Asn
100 105 110
[0134] Asp Glu Asn Ile Thr Leu Glu Thr Val Cys His Asp Pro Lys Leu Pro
115 120 125
Tyr His Asp Phe Ile Leu Glu Asp Ala Ala Ser Pro Lys Cys Ile Met
130 135 140
Lys Glu Lys Lys Lys Pro Gly Glu Thr Phe Phe Met Cys Ser Cys Ser
145 150 155 160
Ser Asp Glu Cys Asn Asp Asn Ile Ile Phe Ser Glu Glu Tyr Asn Thr
165 170 175
Ser Asn Pro Asp Leu Leu Leu Val Ile Phe Gln Ser Asp Pro Thr Arg
180 185 190
Val Glu Thr Ala Thr Glu Thr Leu Val Leu Gly Leu Ser Ala Val Leu
195 200 205
Gly Leu Leu Leu Leu Arg Trp Gln Phe Pro Ala His Tyr Arg Arg Leu
210 215 220
Arg His Ala Leu Trp Pro Ser Leu Pro Asp Leu His Arg Val Leu Gly
225 230 235 240
Gln Tyr Leu Arg Asp Thr Ala Ala Leu Ser Pro Pro Lys Ala Thr Val
245 250 255
Ser Asp Thr Cys Glu Glu Val Glu Pro Ser Leu Leu Glu Ile Leu Pro
260 265 270
Lys Ser Ser Glu Arg Thr Pro Leu Pro Leu Leu Glu Ala Arg Asp Glu
275 280 285
Val Glu Gly Phe Leu Gln Asp Thr Phe Pro Gln Gln Leu Glu Glu Ser
290 295 300
Glu Lys Gln Arg Leu Gly Gly Asp Val Gln Ser Pro Asn Cys Pro Ser
305 310 315 320

Glu Asp Val Val Ile Thr Pro Glu Ser Phe Gly Arg Asp Ser Ser Leu
325 330 335
Thr Cys Leu Ala Gly Asn Val Ser Ala Cys Asp Ala Pro Ile Leu Ser
340 345 350
Ser Ser Arg Ser Leu Asp Cys Arg Glu Ser Gly Lys Asn Gly Pro His
355 360 365
Val Tyr Gln Asp Leu Leu Leu Ser Leu Gly Thr Thr Asn Ser Thr Leu
370 375 380
Pro Pro Pro Phe Ser Leu Gln Ser Gly Ile Leu Thr Leu Asn Pro Val
385 390 395 400
Ala Gln Gly Gln Pro Ile Leu Thr Ser Leu Gly Ser Asn Gln Glu Glu
405 410 415
Ala Tyr Val Thr Met Ser Ser Phe Tyr Gln Asn Gln Ser Arg Ser Asp
420 425 430
Pro Lys Pro Glu Asn Pro Ala Cys Pro Trp Thr Val Leu Pro Ala Gly
435 440 445
Asp Leu Pro Thr His Asp Gly Tyr Leu Pro Ser Asn Ile Asp Asp Leu
450 455 460
Pro Ser His Glu Ala Pro Leu Ala Asp Ser Leu Glu Glu Leu Glu Pro
465 470 475 480
Gln

<210> 184
<211> 480
<212> PRT
[0135] <213> 人工序列 (Artificial Sequence)
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 184
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15
His Ala Ala Arg Pro Met Gly Arg Gly Leu Leu Arg Gly Leu Trp Pro
20 25 30
Leu His Ile Val Leu Trp Thr Arg Ile Ala Ser Thr Ile Pro Pro His
35 40 45
Val Gln Lys Ser Val Asn Asn Asp Met Ile Val Thr Asp Asn Asn Gly
50 55 60
Ala Val Lys Phe Pro Gln Leu Cys Lys Phe Cys Asp Val Arg Phe Ser
65 70 75 80
Thr Cys Asp Asn Gln Lys Ser Cys Met Ser Asn Cys Ser Ile Thr Ser
85 90 95
Ile Cys Glu Lys Pro Gln Glu Val Cys Val Ala Val Trp Arg Lys Asn
100 105 110
Asp Glu Asn Ile Thr Leu Glu Thr Val Cys His Asp Pro Lys Leu Pro
115 120 125
Tyr His Asp Phe Ile Leu Glu Asp Ala Ala Ser Pro Lys Cys Ile Met
130 135 140
Lys Glu Lys Lys Lys Pro Gly Glu Thr Phe Phe Met Cys Ser Cys Ser
145 150 155 160
Ser Asp Glu Cys Asn Asp Asn Ile Ile Phe Ser Glu Glu Tyr Asn Thr

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

[0136] Tyr Gln Asp Leu Leu Leu Ser Leu Gly Thr Thr Asn Ser Thr Leu Pro
370 375 380
Pro Pro Phe Ser Leu Gln Ser Gly Ile Leu Thr Leu Asn Pro Val Ala
385 390 395 400
Gln Gly Gln Pro Ile Leu Thr Ser Leu Gly Ser Asn Gln Glu Glu Ala
405 410 415
Tyr Val Thr Met Ser Ser Phe Tyr Gln Asn Gln Ser Arg Ser Asp Pro
420 425 430
Lys Pro Glu Asn Pro Ala Cys Pro Trp Thr Val Leu Pro Ala Gly Asp
435 440 445
Leu Pro Thr His Asp Gly Tyr Leu Pro Ser Asn Ile Asp Asp Leu Pro
450 455 460
Ser His Glu Ala Pro Leu Ala Asp Ser Leu Glu Glu Leu Glu Pro Gln
465 470 475 480
<210> 185
<211> 479
<212> PRT
<213> 人工序列（Artificial Sequence）
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 185
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15
His Ala Ala Arg Pro Met Gly Arg Gly Leu Leu Arg Gly Leu Trp Pro
20 25 30

Leu His Ile Val Leu Trp Thr Arg Ile Ala Ser Thr Ile Pro Pro His
35 40 45
Val Gln Lys Ser Val Asn Asn Asp Met Ile Val Thr Asp Asn Asn Gly
50 55 60
Ala Val Lys Phe Pro Gln Leu Cys Lys Phe Cys Asp Val Arg Phe Ser
65 70 75 80
Thr Cys Asp Asn Gln Lys Ser Cys Met Ser Asn Cys Ser Ile Thr Ser
85 90 95
Ile Cys Glu Lys Pro Gln Glu Val Cys Val Ala Val Trp Arg Lys Asn
100 105 110
Asp Glu Asn Ile Thr Leu Glu Thr Val Cys His Asp Pro Lys Leu Pro
115 120 125
Tyr His Asp Phe Ile Leu Glu Asp Ala Ala Ser Pro Lys Cys Ile Met
130 135 140
Lys Glu Lys Lys Lys Pro Gly Glu Thr Phe Phe Met Cys Ser Cys Ser
145 150 155 160
Ser Asp Glu Cys Asn Asp Asn Ile Ile Phe Ser Glu Glu Tyr Asn Thr
165 170 175
Ser Asn Pro Asp Leu Leu Leu Val Ile Phe Gln Ser Asp Pro Thr Arg
180 185 190
Val Glu Thr Ala Thr Glu Thr Leu Gly Leu Ser Ala Val Leu Gly Leu
195 200 205
Leu Leu Leu Arg Trp Gln Phe Pro Ala His Tyr Arg Arg Leu Arg His
210 215 220
Ala Leu Trp Pro Ser Leu Pro Asp Leu His Arg Val Leu Gly Gln Tyr
[0137] 225 230 235 240
Leu Arg Asp Thr Ala Ala Leu Ser Pro Pro Lys Ala Thr Val Ser Asp
245 250 255
Thr Cys Glu Glu Val Glu Pro Ser Leu Leu Glu Ile Leu Pro Lys Ser
260 265 270
Ser Glu Arg Thr Pro Leu Pro Leu Leu Glu Ala Arg Asp Glu Val Glu
275 280 285
Gly Phe Leu Gln Asp Thr Phe Pro Gln Gln Leu Glu Glu Ser Glu Lys
290 295 300
Gln Arg Leu Gly Gly Asp Val Gln Ser Pro Asn Cys Pro Ser Glu Asp
305 310 315 320
Val Val Ile Thr Pro Glu Ser Phe Gly Arg Asp Ser Ser Leu Thr Cys
325 330 335
Leu Ala Gly Asn Val Ser Ala Cys Asp Ala Pro Ile Leu Ser Ser Ser
340 345 350
Arg Ser Leu Asp Cys Arg Glu Ser Gly Lys Asn Gly Pro His Val Tyr
355 360 365
Gln Asp Leu Leu Leu Ser Leu Gly Thr Thr Asn Ser Thr Leu Pro Pro
370 375 380
Pro Phe Ser Leu Gln Ser Gly Ile Leu Thr Leu Asn Pro Val Ala Gln
385 390 395 400
Gly Gln Pro Ile Leu Thr Ser Leu Gly Ser Asn Gln Glu Glu Ala Tyr
405 410 415
Val Thr Met Ser Ser Phe Tyr Gln Asn Gln Ser Arg Ser Asp Pro Lys
420 425 430
Pro Glu Asn Pro Ala Cys Pro Trp Thr Val Leu Pro Ala Gly Asp Leu

435 440 445
Pro Thr His Asp Gly Tyr Leu Pro Ser Asn Ile Asp Asp Leu Pro Ser
450 455 460
His Glu Ala Pro Leu Ala Asp Ser Leu Glu Glu Leu Glu Pro Gln
465 470 475
<210> 186
<211> 478
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 186
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15
His Ala Ala Arg Pro Met Gly Arg Gly Leu Leu Arg Gly Leu Trp Pro
20 25 30
Leu His Ile Val Leu Trp Thr Arg Ile Ala Ser Thr Ile Pro Pro His
35 40 45
Val Gln Lys Ser Val Asn Asn Asp Met Ile Val Thr Asp Asn Asn Gly
50 55 60
Ala Val Lys Phe Pro Gln Leu Cys Lys Phe Cys Asp Val Arg Phe Ser
65 70 75 80
Thr Cys Asp Asn Gln Lys Ser Cys Met Ser Asn Cys Ser Ile Thr Ser
85 90 95
[0138] Ile Cys Glu Lys Pro Gln Glu Val Cys Val Ala Val Trp Arg Lys Asn
100 105 110
Asp Glu Asn Ile Thr Leu Glu Thr Val Cys His Asp Pro Lys Leu Pro
115 120 125
Tyr His Asp Phe Ile Leu Glu Asp Ala Ala Ser Pro Lys Cys Ile Met
130 135 140
Lys Glu Lys Lys Lys Pro Gly Glu Thr Phe Phe Met Cys Ser Cys Ser
145 150 155 160
Ser Asp Glu Cys Asn Asp Asn Ile Ile Phe Ser Glu Glu Tyr Asn Thr
165 170 175
Ser Asn Pro Asp Leu Leu Leu Val Ile Phe Gln Ser Asp Pro Thr Arg
180 185 190
Val Glu Thr Ala Thr Glu Thr Gly Leu Ser Ala Val Leu Gly Leu Leu
195 200 205
Leu Leu Arg Trp Gln Phe Pro Ala His Tyr Arg Arg Leu Arg His Ala
210 215 220
Leu Trp Pro Ser Leu Pro Asp Leu His Arg Val Leu Gly Gln Tyr Leu
225 230 235 240
Arg Asp Thr Ala Ala Leu Ser Pro Pro Lys Ala Thr Val Ser Asp Thr
245 250 255
Cys Glu Glu Val Glu Pro Ser Leu Leu Glu Ile Leu Pro Lys Ser Ser
260 265 270
Glu Arg Thr Pro Leu Pro Leu Leu Glu Ala Arg Asp Glu Val Glu Gly
275 280 285
Phe Leu Gln Asp Thr Phe Pro Gln Gln Leu Glu Glu Ser Glu Lys Gln
290 295 300

Arg Leu Gly Gly Asp Val Gln Ser Pro Asn Cys Pro Ser Glu Asp Val
305 310 315 320
Val Ile Thr Pro Glu Ser Phe Gly Arg Asp Ser Ser Leu Thr Cys Leu
325 330 335
Ala Gly Asn Val Ser Ala Cys Asp Ala Pro Ile Leu Ser Ser Ser Arg
340 345 350
Ser Leu Asp Cys Arg Glu Ser Gly Lys Asn Gly Pro His Val Tyr Gln
355 360 365
Asp Leu Leu Leu Ser Leu Gly Thr Thr Asn Ser Thr Leu Pro Pro Pro
370 375 380
Phe Ser Leu Gln Ser Gly Ile Leu Thr Leu Asn Pro Val Ala Gln Gly
385 390 395 400
Gln Pro Ile Leu Thr Ser Leu Gly Ser Asn Gln Glu Glu Ala Tyr Val
405 410 415
Thr Met Ser Ser Phe Tyr Gln Asn Gln Ser Arg Ser Asp Pro Lys Pro
420 425 430
Glu Asn Pro Ala Cys Pro Trp Thr Val Leu Pro Ala Gly Asp Leu Pro
435 440 445
Thr His Asp Gly Tyr Leu Pro Ser Asn Ile Asp Asp Leu Pro Ser His
450 455 460
Glu Ala Pro Leu Ala Asp Ser Leu Glu Glu Leu Glu Pro Gln
465 470 475

<210> 187
<211> 477
<212> PRT

[0139] <213> 人工序列 (Artificial Sequence)

<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 187

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

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

[0140] Leu Leu Leu Ser Leu Gly Thr Thr Asn Ser Thr Leu Pro Pro Pro Phe
370 375 380
Ser Leu Gln Ser Gly Ile Leu Thr Leu Asn Pro Val Ala Gln Gly Gln
385 390 395 400
Pro Ile Leu Thr Ser Leu Gly Ser Asn Gln Glu Glu Ala Tyr Val Thr
405 410 415
Met Ser Ser Phe Tyr Gln Asn Gln Ser Arg Ser Asp Pro Lys Pro Glu
420 425 430
Asn Pro Ala Cys Pro Trp Thr Val Leu Pro Ala Gly Asp Leu Pro Thr
435 440 445
His Asp Gly Tyr Leu Pro Ser Asn Ile Asp Asp Leu Pro Ser His Glu
450 455 460
Ala Pro Leu Ala Asp Ser Leu Glu Glu Leu Glu Pro Gln
465 470 475

<210> 188
<211> 476
<212> PRT
<213> 人工序列（Artificial Sequence）
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 188
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15
His Ala Ala Arg Pro Met Gly Arg Gly Leu Leu Arg Gly Leu Trp Pro
20 25 30

```
Leu His Ile Val Leu Trp Thr Arg Ile Ala Ser Thr Ile Pro Pro His
        35                  40                  45
Val Gln Lys Ser Val Asn Asn Asp Met Ile Val Thr Asp Asn Asn Gly
    50                  55                  60
Ala Val Lys Phe Pro Gln Leu Cys Lys Phe Cys Asp Val Arg Phe Ser
65                  70                  75                  80
Thr Cys Asp Asn Gln Lys Ser Cys Met Ser Asn Cys Ser Ile Thr Ser
                85                  90                  95
Ile Cys Glu Lys Pro Gln Glu Val Cys Val Ala Val Trp Arg Lys Asn
            100                 105                 110
Asp Glu Asn Ile Thr Leu Glu Thr Val Cys His Asp Pro Lys Leu Pro
        115                 120                 125
Tyr His Asp Phe Ile Leu Glu Asp Ala Ala Ser Pro Lys Cys Ile Met
    130                 135                 140
Lys Glu Lys Lys Lys Pro Gly Glu Thr Phe Phe Met Cys Ser Cys Ser
145                 150                 155                 160
Ser Asp Glu Cys Asn Asp Asn Ile Ile Phe Ser Glu Glu Tyr Asn Thr
                165                 170                 175
Ser Asn Pro Asp Leu Leu Leu Val Ile Phe Gln Ser Asp Pro Thr Arg
            180                 185                 190
Val Glu Thr Ala Thr Glu Thr Ser Ala Val Leu Gly Leu Leu Leu Leu
        195                 200                 205
Arg Trp Gln Phe Pro Ala His Tyr Arg Arg Leu Arg His Ala Leu Trp
    210                 215                 220
Pro Ser Leu Pro Asp Leu His Arg Val Leu Gly Gln Tyr Leu Arg Asp
225                 230                 235                 240
Thr Ala Ala Leu Ser Pro Pro Lys Ala Thr Val Ser Asp Thr Cys Glu
                245                 250                 255
Glu Val Glu Pro Ser Leu Leu Glu Ile Leu Pro Lys Ser Ser Glu Arg
            260                 265                 270
Thr Pro Leu Pro Leu Leu Glu Ala Arg Asp Glu Val Glu Gly Phe Leu
        275                 280                 285
Gln Asp Thr Phe Pro Gln Gln Leu Glu Glu Ser Glu Lys Gln Arg Leu
    290                 295                 300
Gly Gly Asp Val Gln Ser Pro Asn Cys Pro Ser Glu Asp Val Val Ile
305                 310                 315                 320
Thr Pro Glu Ser Phe Gly Arg Asp Ser Ser Leu Thr Cys Leu Ala Gly
                325                 330                 335
Asn Val Ser Ala Cys Asp Ala Pro Ile Leu Ser Ser Ser Arg Ser Leu
            340                 345                 350
Asp Cys Arg Glu Ser Gly Lys Asn Gly Pro His Val Tyr Gln Asp Leu
        355                 360                 365
Leu Leu Ser Leu Gly Thr Thr Asn Ser Thr Leu Pro Pro Pro Phe Ser
    370                 375                 380
Leu Gln Ser Gly Ile Leu Thr Leu Asn Pro Val Ala Gln Gly Gln Pro
385                 390                 395                 400
Ile Leu Thr Ser Leu Gly Ser Asn Gln Glu Glu Ala Tyr Val Thr Met
                405                 410                 415
Ser Ser Phe Tyr Gln Asn Gln Ser Arg Ser Asp Pro Lys Pro Glu Asn
            420                 425                 430
Pro Ala Cys Pro Trp Thr Val Leu Pro Ala Gly Asp Leu Pro Thr His
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[0141]

435 440 445
Asp Gly Tyr Leu Pro Ser Asn Ile Asp Asp Leu Pro Ser His Glu Ala
450 455 460
Pro Leu Ala Asp Ser Leu Glu Glu Leu Glu Pro Gln
465 470 475
<210> 189
<211> 475
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 189
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15
His Ala Ala Arg Pro Met Gly Arg Gly Leu Leu Arg Gly Leu Trp Pro
20 25 30
Leu His Ile Val Leu Trp Thr Arg Ile Ala Ser Thr Ile Pro Pro His
35 40 45
Val Gln Lys Ser Val Asn Asn Asp Met Ile Val Thr Asp Asn Asn Gly
50 55 60
Ala Val Lys Phe Pro Gln Leu Cys Lys Phe Cys Asp Val Arg Phe Ser
65 70 75 80
Thr Cys Asp Asn Gln Lys Ser Cys Met Ser Asn Cys Ser Ile Thr Ser
85 90 95
[0142] Ile Cys Glu Lys Pro Gln Glu Val Cys Val Ala Val Trp Arg Lys Asn
100 105 110
Asp Glu Asn Ile Thr Leu Glu Thr Val Cys His Asp Pro Lys Leu Pro
115 120 125
Tyr His Asp Phe Ile Leu Glu Asp Ala Ala Ser Pro Lys Cys Ile Met
130 135 140
Lys Glu Lys Lys Lys Pro Gly Glu Thr Phe Phe Met Cys Ser Cys Ser
145 150 155 160
Ser Asp Glu Cys Asn Asp Asn Ile Ile Phe Ser Glu Glu Tyr Asn Thr
165 170 175
Ser Asn Pro Asp Leu Leu Leu Val Ile Phe Gln Ser Asp Pro Thr Arg
180 185 190
Val Glu Thr Ala Thr Glu Thr Ala Val Leu Gly Leu Leu Leu Leu Arg
195 200 205
Trp Gln Phe Pro Ala His Tyr Arg Arg Leu Arg His Ala Leu Trp Pro
210 215 220
Ser Leu Pro Asp Leu His Arg Val Leu Gly Gln Tyr Leu Arg Asp Thr
225 230 235 240
Ala Ala Leu Ser Pro Pro Lys Ala Thr Val Ser Asp Thr Cys Glu Glu
245 250 255
Val Glu Pro Ser Leu Leu Glu Ile Leu Pro Lys Ser Ser Glu Arg Thr
260 265 270
Pro Leu Pro Leu Leu Glu Ala Arg Asp Glu Val Glu Gly Phe Leu Gln
275 280 285
Asp Thr Phe Pro Gln Gln Leu Glu Glu Ser Glu Lys Gln Arg Leu Gly
290 295 300

Gly Asp Val Gln Ser Pro Asn Cys Pro Ser Glu Asp Val Val Ile Thr
305 310 315 320
Pro Glu Ser Phe Gly Arg Asp Ser Ser Leu Thr Cys Leu Ala Gly Asn
325 330 335
Val Ser Ala Cys Asp Ala Pro Ile Leu Ser Ser Ser Arg Ser Leu Asp
340 345 350
Cys Arg Glu Ser Gly Lys Asn Gly Pro His Val Tyr Gln Asp Leu Leu
355 360 365
Leu Ser Leu Gly Thr Thr Asn Ser Thr Leu Pro Pro Pro Phe Ser Leu
370 375 380
Gln Ser Gly Ile Leu Thr Leu Asn Pro Val Ala Gln Gly Gln Pro Ile
385 390 395 400
Leu Thr Ser Leu Gly Ser Asn Gln Glu Glu Ala Tyr Val Thr Met Ser
405 410 415
Ser Phe Tyr Gln Asn Gln Ser Arg Ser Asp Pro Lys Pro Glu Asn Pro
420 425 430
Ala Cys Pro Trp Thr Val Leu Pro Ala Gly Asp Leu Pro Thr His Asp
435 440 445
Gly Tyr Leu Pro Ser Asn Ile Asp Asp Leu Pro Ser His Glu Ala Pro
450 455 460
Leu Ala Asp Ser Leu Glu Glu Leu Glu Pro Gln
465 470 475

<210> 190
<211> 474
<212> PRT

[0143] <213> 人工序列 (Artificial Sequence)
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 190

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

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

[0144] Ser Leu Gly Thr Thr Asn Ser Thr Leu Pro Pro Pro Phe Ser Leu Gln
370 375 380
Ser Gly Ile Leu Thr Leu Asn Pro Val Ala Gln Gly Gln Pro Ile Leu
385 390 395 400
Thr Ser Leu Gly Ser Asn Gln Glu Glu Ala Tyr Val Thr Met Ser Ser
405 410 415
Phe Tyr Gln Asn Gln Ser Arg Ser Asp Pro Lys Pro Glu Asn Pro Ala
420 425 430
Cys Pro Trp Thr Val Leu Pro Ala Gly Asp Leu Pro Thr His Asp Gly
435 440 445
Tyr Leu Pro Ser Asn Ile Asp Asp Leu Pro Ser His Glu Ala Pro Leu
450 455 460
Ala Asp Ser Leu Glu Glu Leu Glu Pro Gln
465 470

<210> 191
<211> 473
<212> PRT
<213> 人工序列（Artificial Sequence）
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 191
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15
His Ala Ala Arg Pro Met Gly Arg Gly Leu Leu Arg Gly Leu Trp Pro
20 25 30

Leu His Ile Val Leu Trp Thr Arg Ile Ala Ser Thr Ile Pro Pro His
35 40 45
Val Gln Lys Ser Val Asn Asn Asp Met Ile Val Thr Asp Asn Asn Gly
50 55 60
Ala Val Lys Phe Pro Gln Leu Cys Lys Phe Cys Asp Val Arg Phe Ser
65 70 75 80
Thr Cys Asp Asn Gln Lys Ser Cys Met Ser Asn Cys Ser Ile Thr Ser
85 90 95
Ile Cys Glu Lys Pro Gln Glu Val Cys Val Ala Val Trp Arg Lys Asn
100 105 110
Asp Glu Asn Ile Thr Leu Glu Thr Val Cys His Asp Pro Lys Leu Pro
115 120 125
Tyr His Asp Phe Ile Leu Glu Asp Ala Ala Ser Pro Lys Cys Ile Met
130 135 140
Lys Glu Lys Lys Lys Pro Gly Glu Thr Phe Phe Met Cys Ser Cys Ser
145 150 155 160
Ser Asp Glu Cys Asn Asp Asn Ile Ile Phe Ser Glu Glu Tyr Asn Thr
165 170 175
Ser Asn Pro Asp Leu Leu Leu Val Ile Phe Gln Ser Asp Pro Thr Arg
180 185 190
Val Glu Thr Ala Thr Glu Thr Leu Gly Leu Leu Leu Leu Arg Trp Gln
195 200 205
Phe Pro Ala His Tyr Arg Arg Leu Arg His Ala Leu Trp Pro Ser Leu
210 215 220
Pro Asp Leu His Arg Val Leu Gly Gln Tyr Leu Arg Asp Thr Ala Ala
[0145] 225 230 235 240
Leu Ser Pro Pro Lys Ala Thr Val Ser Asp Thr Cys Glu Glu Val Glu
245 250 255
Pro Ser Leu Leu Glu Ile Leu Pro Lys Ser Ser Glu Arg Thr Pro Leu
260 265 270
Pro Leu Leu Glu Ala Arg Asp Glu Val Glu Gly Phe Leu Gln Asp Thr
275 280 285
Phe Pro Gln Gln Leu Glu Glu Ser Glu Lys Gln Arg Leu Gly Gly Asp
290 295 300
Val Gln Ser Pro Asn Cys Pro Ser Glu Asp Val Val Ile Thr Pro Glu
305 310 315 320
Ser Phe Gly Arg Asp Ser Ser Leu Thr Cys Leu Ala Gly Asn Val Ser
325 330 335
Ala Cys Asp Ala Pro Ile Leu Ser Ser Ser Arg Ser Leu Asp Cys Arg
340 345 350
Glu Ser Gly Lys Asn Gly Pro His Val Tyr Gln Asp Leu Leu Leu Ser
355 360 365
Leu Gly Thr Thr Asn Ser Thr Leu Pro Pro Pro Phe Ser Leu Gln Ser
370 375 380
Gly Ile Leu Thr Leu Asn Pro Val Ala Gln Gly Gln Pro Ile Leu Thr
385 390 395 400
Ser Leu Gly Ser Asn Gln Glu Glu Ala Tyr Val Thr Met Ser Ser Phe
405 410 415
Tyr Gln Asn Gln Ser Arg Ser Asp Pro Lys Pro Glu Asn Pro Ala Cys
420 425 430
Pro Trp Thr Val Leu Pro Ala Gly Asp Leu Pro Thr His Asp Gly Tyr

435 440 445
Leu Pro Ser Asn Ile Asp Asp Leu Pro Ser His Glu Ala Pro Leu Ala
450 455 460
Asp Ser Leu Glu Glu Leu Glu Pro Gln
465 470
<210> 192
<211> 492
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 192
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15
His Ala Ala Arg Pro Met Gly Arg Gly Leu Leu Arg Gly Leu Trp Pro
20 25 30
Leu His Ile Val Leu Trp Thr Arg Ile Ala Ser Thr Ile Pro Pro His
35 40 45
Val Gln Lys Ser Val Asn Asn Asp Met Ile Val Thr Asp Asn Asn Gly
50 55 60
Ala Val Lys Phe Pro Gln Leu Cys Lys Phe Cys Asp Val Arg Phe Ser
65 70 75 80
Thr Cys Asp Asn Gln Lys Ser Cys Met Ser Asn Cys Ser Ile Thr Ser
85 90 95
[0146] Ile Cys Glu Lys Pro Gln Glu Val Cys Val Ala Val Trp Arg Lys Asn
100 105 110
Asp Glu Asn Ile Thr Leu Glu Thr Val Cys His Asp Pro Lys Leu Pro
115 120 125
Tyr His Asp Phe Ile Leu Glu Asp Ala Ala Ser Pro Lys Cys Ile Met
130 135 140
Lys Glu Lys Lys Lys Pro Gly Glu Thr Phe Phe Met Cys Ser Cys Ser
145 150 155 160
Ser Asp Glu Cys Asn Asp Asn Ile Ile Phe Ser Glu Glu Tyr Asn Thr
165 170 175
Ser Asn Pro Asp Leu Leu Leu Val Ile Phe Gln Ser Asp Pro Thr Arg
180 185 190
Val Glu Thr Ala Thr Glu Thr Ala Trp Leu Ile Ser Leu Val Thr Ala
195 200 205
Leu His Leu Val Leu Gly Leu Ser Ala Val Leu Gly Leu Leu Leu Leu
210 215 220
Arg Trp Gln Phe Pro Ala His Tyr Arg Arg Leu Arg His Ala Leu Trp
225 230 235 240
Pro Ser Leu Pro Asp Leu His Arg Val Leu Gly Gln Tyr Leu Arg Asp
245 250 255
Thr Ala Ala Leu Ser Pro Pro Lys Ala Thr Val Ser Asp Thr Cys Glu
260 265 270
Glu Val Glu Pro Ser Leu Leu Glu Ile Leu Pro Lys Ser Ser Glu Arg
275 280 285
Thr Pro Leu Pro Leu Leu Glu Ala Arg Asp Glu Val Glu Gly Phe Leu
290 295 300

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

<210> 193

[0147] <211> 493
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 193
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15
His Ala Ala Arg Pro Met Gly Arg Gly Leu Leu Arg Gly Leu Trp Pro
20 25 30
Leu His Ile Val Leu Trp Thr Arg Ile Ala Ser Thr Ile Pro Pro His
35 40 45
Val Gln Lys Ser Val Asn Asn Asp Met Ile Val Thr Asp Asn Asn Gly
50 55 60
Ala Val Lys Phe Pro Gln Leu Cys Lys Phe Cys Asp Val Arg Phe Ser
65 70 75 80
Thr Cys Asp Asn Gln Lys Ser Cys Met Ser Asn Cys Ser Ile Thr Ser
85 90 95
Ile Cys Glu Lys Pro Gln Glu Val Cys Val Ala Val Trp Arg Lys Asn
100 105 110
Asp Glu Asn Ile Thr Leu Glu Thr Val Cys His Asp Pro Lys Leu Pro
115 120 125
Tyr His Asp Phe Ile Leu Glu Asp Ala Ala Ser Pro Lys Cys Ile Met
130 135 140
Lys Glu Lys Lys Lys Pro Gly Glu Thr Phe Phe Met Cys Ser Cys Ser

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

[0148]
Gly Asn Val Ser Ala Cys Asp Ala Pro Ile Leu Ser Ser Ser Arg Ser
355 360 365
Leu Asp Cys Arg Glu Ser Gly Lys Asn Gly Pro His Val Tyr Gln Asp
370 375 380
Leu Leu Leu Ser Leu Gly Thr Thr Asn Ser Thr Leu Pro Pro Pro Phe
385 390 395 400
Ser Leu Gln Ser Gly Ile Leu Thr Leu Asn Pro Val Ala Gln Gly Gln
405 410 415
Pro Ile Leu Thr Ser Leu Gly Ser Asn Gln Glu Glu Ala Tyr Val Thr
420 425 430
Met Ser Ser Phe Tyr Gln Asn Gln Ser Arg Ser Asp Pro Lys Pro Glu
435 440 445
Asn Pro Ala Cys Pro Trp Thr Val Leu Pro Ala Gly Asp Leu Pro Thr
450 455 460
His Asp Gly Tyr Leu Pro Ser Asn Ile Asp Asp Leu Pro Ser His Glu
465 470 475 480
Ala Pro Leu Ala Asp Ser Leu Glu Glu Leu Glu Pro Gln
485 490

<210> 194
<211> 494
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 194

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Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1               5                  10                  15
His Ala Ala Arg Pro Met Gly Arg Gly Leu Leu Arg Gly Leu Trp Pro
            20                  25                  30
Leu His Ile Val Leu Trp Thr Arg Ile Ala Ser Thr Ile Pro Pro His
        35                  40                  45
Val Gln Lys Ser Val Asn Asn Asp Met Ile Val Thr Asp Asn Asn Gly
    50                  55                  60
Ala Val Lys Phe Pro Gln Leu Cys Lys Phe Cys Asp Val Arg Phe Ser
65                  70                  75                  80
Thr Cys Asp Asn Gln Lys Ser Cys Met Ser Asn Cys Ser Ile Thr Ser
                85                  90                  95
Ile Cys Glu Lys Pro Gln Glu Val Cys Val Ala Val Trp Arg Lys Asn
            100                 105                 110
Asp Glu Asn Ile Thr Leu Glu Thr Val Cys His Asp Pro Lys Leu Pro
        115                 120                 125
Tyr His Asp Phe Ile Leu Glu Asp Ala Ala Ser Pro Lys Cys Ile Met
    130                 135                 140
Lys Glu Lys Lys Lys Pro Gly Glu Thr Phe Phe Met Cys Ser Cys Ser
145                 150                 155                 160
Ser Asp Glu Cys Asn Asp Asn Ile Ile Phe Ser Glu Glu Tyr Asn Thr
                165                 170                 175
Ser Asn Pro Asp Leu Leu Leu Val Ile Phe Gln Ser Asp Pro Thr Arg
            180                 185                 190
Val Glu Thr Ala Thr Glu Thr Ala Trp Leu Val Leu Ile Ser Leu Val
        195                 200                 205
Thr Ala Leu His Leu Val Leu Gly Leu Ser Ala Val Leu Gly Leu Leu
    210                 215                 220
Leu Leu Arg Trp Gln Phe Pro Ala His Tyr Arg Arg Leu Arg His Ala
225                 230                 235                 240
Leu Trp Pro Ser Leu Pro Asp Leu His Arg Val Leu Gly Gln Tyr Leu
                245                 250                 255
Arg Asp Thr Ala Ala Leu Ser Pro Pro Lys Ala Thr Val Ser Asp Thr
            260                 265                 270
Cys Glu Glu Val Glu Pro Ser Leu Leu Glu Ile Leu Pro Lys Ser Ser
        275                 280                 285
Glu Arg Thr Pro Leu Pro Leu Leu Glu Ala Arg Asp Glu Val Glu Gly
    290                 295                 300
Phe Leu Gln Asp Thr Phe Pro Gln Gln Leu Glu Glu Ser Glu Lys Gln
305                 310                 315                 320
Arg Leu Gly Gly Asp Val Gln Ser Pro Asn Cys Pro Ser Glu Asp Val
                325                 330                 335
Val Ile Thr Pro Glu Ser Phe Gly Arg Asp Ser Ser Leu Thr Cys Leu
            340                 345                 350
Ala Gly Asn Val Ser Ala Cys Asp Ala Pro Ile Leu Ser Ser Ser Arg
        355                 360                 365
Ser Leu Asp Cys Arg Glu Ser Gly Lys Asn Gly Pro His Val Tyr Gln
    370                 375                 380
Asp Leu Leu Leu Ser Leu Gly Thr Thr Asn Ser Thr Leu Pro Pro Pro
385                 390                 395                 400
Phe Ser Leu Gln Ser Gly Ile Leu Thr Leu Asn Pro Val Ala Gln Gly
```

[0149]

405 410 415
Gln Pro Ile Leu Thr Ser Leu Gly Ser Asn Gln Glu Glu Ala Tyr Val
420 425 430
Thr Met Ser Ser Phe Tyr Gln Asn Gln Ser Arg Ser Asp Pro Lys Pro
435 440 445
Glu Asn Pro Ala Cys Pro Trp Thr Val Leu Pro Ala Gly Asp Leu Pro
450 455 460
Thr His Asp Gly Tyr Leu Pro Ser Asn Ile Asp Asp Leu Pro Ser His
465 470 475 480
Glu Ala Pro Leu Ala Asp Ser Leu Glu Glu Leu Glu Pro Gln
485 490

<210> 195
<211> 495
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 195
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15
His Ala Ala Arg Pro Met Gly Arg Gly Leu Leu Arg Gly Leu Trp Pro
20 25 30
Leu His Ile Val Leu Trp Thr Arg Ile Ala Ser Thr Ile Pro Pro His
35 40 45
[0150] Val Gln Lys Ser Val Asn Asn Asp Met Ile Val Thr Asp Asn Asn Gly
50 55 60
Ala Val Lys Phe Pro Gln Leu Cys Lys Phe Cys Asp Val Arg Phe Ser
65 70 75 80
Thr Cys Asp Asn Gln Lys Ser Cys Met Ser Asn Cys Ser Ile Thr Ser
85 90 95
Ile Cys Glu Lys Pro Gln Glu Val Cys Val Ala Val Trp Arg Lys Asn
100 105 110
Asp Glu Asn Ile Thr Leu Glu Thr Val Cys His Asp Pro Lys Leu Pro
115 120 125
Tyr His Asp Phe Ile Leu Glu Asp Ala Ala Ser Pro Lys Cys Ile Met
130 135 140
Lys Glu Lys Lys Lys Pro Gly Glu Thr Phe Phe Met Cys Ser Cys Ser
145 150 155 160
Ser Asp Glu Cys Asn Asp Asn Ile Ile Phe Ser Glu Glu Tyr Asn Thr
165 170 175
Ser Asn Pro Asp Leu Leu Leu Val Ile Phe Gln Ser Asp Pro Thr Arg
180 185 190
Val Glu Thr Ala Thr Glu Thr Ala Trp Ile Leu Val Leu Ile Ser Leu
195 200 205
Val Thr Ala Leu His Leu Val Leu Gly Leu Ser Ala Val Leu Gly Leu
210 215 220
Leu Leu Leu Arg Trp Gln Phe Pro Ala His Tyr Arg Arg Leu Arg His
225 230 235 240
Ala Leu Trp Pro Ser Leu Pro Asp Leu His Arg Val Leu Gly Gln Tyr
245 250 255

Leu Arg Asp Thr Ala Ala Leu Ser Pro Pro Lys Ala Thr Val Ser Asp
260 265 270
Thr Cys Glu Glu Val Glu Pro Ser Leu Leu Glu Ile Leu Pro Lys Ser
275 280 285
Ser Glu Arg Thr Pro Leu Pro Leu Leu Glu Ala Arg Asp Glu Val Glu
290 295 300
Gly Phe Leu Gln Asp Thr Phe Pro Gln Gln Leu Glu Glu Ser Glu Lys
305 310 315 320
Gln Arg Leu Gly Gly Asp Val Gln Ser Pro Asn Cys Pro Ser Glu Asp
325 330 335
Val Val Ile Thr Pro Glu Ser Phe Gly Arg Asp Ser Ser Leu Thr Cys
340 345 350
Leu Ala Gly Asn Val Ser Ala Cys Asp Ala Pro Ile Leu Ser Ser Ser
355 360 365
Arg Ser Leu Asp Cys Arg Glu Ser Gly Lys Asn Gly Pro His Val Tyr
370 375 380
Gln Asp Leu Leu Leu Ser Leu Gly Thr Thr Asn Ser Thr Leu Pro Pro
385 390 395 400
Pro Phe Ser Leu Gln Ser Gly Ile Leu Thr Leu Asn Pro Val Ala Gln
405 410 415
Gly Gln Pro Ile Leu Thr Ser Leu Gly Ser Asn Gln Glu Glu Ala Tyr
420 425 430
Val Thr Met Ser Ser Phe Tyr Gln Asn Gln Ser Arg Ser Asp Pro Lys
435 440 445
Pro Glu Asn Pro Ala Cys Pro Trp Thr Val Leu Pro Ala Gly Asp Leu
[0151] 450 455 460
Pro Thr His Asp Gly Tyr Leu Pro Ser Asn Ile Asp Asp Leu Pro Ser
465 470 475 480
His Glu Ala Pro Leu Ala Asp Ser Leu Glu Glu Leu Glu Pro Gln
485 490 495

<210> 196
<211> 496
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 196
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15
His Ala Ala Arg Pro Met Gly Arg Gly Leu Leu Arg Gly Leu Trp Pro
20 25 30
Leu His Ile Val Leu Trp Thr Arg Ile Ala Ser Thr Ile Pro Pro His
35 40 45
Val Gln Lys Ser Val Asn Asn Asp Met Ile Val Thr Asp Asn Asn Gly
50 55 60
Ala Val Lys Phe Pro Gln Leu Cys Lys Phe Cys Asp Val Arg Phe Ser
65 70 75 80
Thr Cys Asp Asn Gln Lys Ser Cys Met Ser Asn Cys Ser Ile Thr Ser
85 90 95
Ile Cys Glu Lys Pro Gln Glu Val Cys Val Ala Val Trp Arg Lys Asn

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

[0152] Glu Gly Phe Leu Gln Asp Thr Phe Pro Gln Gln Leu Glu Glu Ser Glu
305 310 315 320
Lys Gln Arg Leu Gly Gly Asp Val Gln Ser Pro Asn Cys Pro Ser Glu
325 330 335
Asp Val Val Ile Thr Pro Glu Ser Phe Gly Arg Asp Ser Ser Leu Thr
340 345 350
Cys Leu Ala Gly Asn Val Ser Ala Cys Asp Ala Pro Ile Leu Ser Ser
355 360 365
Ser Arg Ser Leu Asp Cys Arg Glu Ser Gly Lys Asn Gly Pro His Val
370 375 380
Tyr Gln Asp Leu Leu Leu Ser Leu Gly Thr Thr Asn Ser Thr Leu Pro
385 390 395 400
Pro Pro Phe Ser Leu Gln Ser Gly Ile Leu Thr Leu Asn Pro Val Ala
405 410 415
Gln Gly Gln Pro Ile Leu Thr Ser Leu Gly Ser Asn Gln Glu Glu Ala
420 425 430
Tyr Val Thr Met Ser Ser Phe Tyr Gln Asn Gln Ser Arg Ser Asp Pro
435 440 445
Lys Pro Glu Asn Pro Ala Cys Pro Trp Thr Val Leu Pro Ala Gly Asp
450 455 460
Leu Pro Thr His Asp Gly Tyr Leu Pro Ser Asn Ile Asp Asp Leu Pro
465 470 475 480
Ser His Glu Ala Pro Leu Ala Asp Ser Leu Glu Glu Leu Glu Pro Gln
485 490 495

<210> 197
<211> 497

<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 197

Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15
His Ala Ala Arg Pro Met Gly Arg Gly Leu Leu Arg Gly Leu Trp Pro
20 25 30
Leu His Ile Val Leu Trp Thr Arg Ile Ala Ser Thr Ile Pro Pro His
35 40 45
Val Gln Lys Ser Val Asn Asn Asp Met Ile Val Thr Asp Asn Asn Gly
50 55 60
Ala Val Lys Phe Pro Gln Leu Cys Lys Phe Cys Asp Val Arg Phe Ser
65 70 75 80
Thr Cys Asp Asn Gln Lys Ser Cys Met Ser Asn Cys Ser Ile Thr Ser
85 90 95
Ile Cys Glu Lys Pro Gln Glu Val Cys Val Ala Val Trp Arg Lys Asn
100 105 110
Asp Glu Asn Ile Thr Leu Glu Thr Val Cys His Asp Pro Lys Leu Pro
115 120 125
Tyr His Asp Phe Ile Leu Glu Asp Ala Ala Ser Pro Lys Cys Ile Met
130 135 140
Lys Glu Lys Lys Lys Pro Gly Glu Thr Phe Phe Met Cys Ser Cys Ser
[0153] 145 150 155 160
Ser Asp Glu Cys Asn Asp Asn Ile Ile Phe Ser Glu Glu Tyr Asn Thr
165 170 175
Ser Asn Pro Asp Leu Leu Leu Val Ile Phe Gln Ser Asp Pro Thr Arg
180 185 190
Val Glu Thr Ala Thr Glu Thr Ala Trp Leu Leu Ile Leu Val Leu Ile
195 200 205
Ser Leu Val Thr Ala Leu His Leu Val Leu Gly Leu Ser Ala Val Leu
210 215 220
Gly Leu Leu Leu Leu Arg Trp Gln Phe Pro Ala His Tyr Arg Arg Leu
225 230 235 240
Arg His Ala Leu Trp Pro Ser Leu Pro Asp Leu His Arg Val Leu Gly
245 250 255
Gln Tyr Leu Arg Asp Thr Ala Ala Leu Ser Pro Pro Lys Ala Thr Val
260 265 270
Ser Asp Thr Cys Glu Glu Val Glu Pro Ser Leu Leu Glu Ile Leu Pro
275 280 285
Lys Ser Ser Glu Arg Thr Pro Leu Pro Leu Leu Glu Ala Arg Asp Glu
290 295 300
Val Glu Gly Phe Leu Gln Asp Thr Phe Pro Gln Gln Leu Glu Glu Ser
305 310 315 320
Glu Lys Gln Arg Leu Gly Gly Asp Val Gln Ser Pro Asn Cys Pro Ser
325 330 335
Glu Asp Val Val Ile Thr Pro Glu Ser Phe Gly Arg Asp Ser Ser Leu
340 345 350
Thr Cys Leu Ala Gly Asn Val Ser Ala Cys Asp Ala Pro Ile Leu Ser

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        355                 360                 365
Ser Ser Arg Ser Leu Asp Cys Arg Glu Ser Gly Lys Asn Gly Pro His
    370                 375                 380
Val Tyr Gln Asp Leu Leu Leu Ser Leu Gly Thr Thr Asn Ser Thr Leu
385                 390                 395                 400
Pro Pro Pro Phe Ser Leu Gln Ser Gly Ile Leu Thr Leu Asn Pro Val
                405                 410                 415
Ala Gln Gly Gln Pro Ile Leu Thr Ser Leu Gly Ser Asn Gln Glu Glu
            420                 425                 430
Ala Tyr Val Thr Met Ser Ser Phe Tyr Gln Asn Gln Ser Arg Ser Asp
        435                 440                 445
Pro Lys Pro Glu Asn Pro Ala Cys Pro Trp Thr Val Leu Pro Ala Gly
    450                 455                 460
Asp Leu Pro Thr His Asp Gly Tyr Leu Pro Ser Asn Ile Asp Asp Leu
465                 470                 475                 480
Pro Ser His Glu Ala Pro Leu Ala Asp Ser Leu Glu Glu Leu Glu Pro
                485                 490                 495
Gln
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<210> 198
<211> 498
<212> PRT
<213> 人工序列（Artificial Sequence）
<220>
<221> source
[0154] <223> /注释 = “人工序列的描述：合成多肽”
<400> 198

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

Val Glu Thr Ala Thr Glu Thr Ala Trp Val Leu Leu Ile Leu Val Leu
195 200 205
Ile Ser Leu Val Thr Ala Leu His Leu Val Leu Gly Leu Ser Ala Val
210 215 220
Leu Gly Leu Leu Leu Leu Arg Trp Gln Phe Pro Ala His Tyr Arg Arg
225 230 235 240
Leu Arg His Ala Leu Trp Pro Ser Leu Pro Asp Leu His Arg Val Leu
245 250 255
Gly Gln Tyr Leu Arg Asp Thr Ala Ala Leu Ser Pro Pro Lys Ala Thr
260 265 270
Val Ser Asp Thr Cys Glu Glu Val Glu Pro Ser Leu Leu Glu Ile Leu
275 280 285
Pro Lys Ser Ser Glu Arg Thr Pro Leu Pro Leu Leu Glu Ala Arg Asp
290 295 300
Glu Val Glu Gly Phe Leu Gln Asp Thr Phe Pro Gln Gln Leu Glu Glu
305 310 315 320
Ser Glu Lys Gln Arg Leu Gly Gly Asp Val Gln Ser Pro Asn Cys Pro
325 330 335
Ser Glu Asp Val Val Ile Thr Pro Glu Ser Phe Gly Arg Asp Ser Ser
340 345 350
Leu Thr Cys Leu Ala Gly Asn Val Ser Ala Cys Asp Ala Pro Ile Leu
355 360 365
Ser Ser Ser Arg Ser Leu Asp Cys Arg Glu Ser Gly Lys Asn Gly Pro
370 375 380
His Val Tyr Gln Asp Leu Leu Leu Ser Leu Gly Thr Thr Asn Ser Thr
[0155] 385 390 395 400
Leu Pro Pro Pro Phe Ser Leu Gln Ser Gly Ile Leu Thr Leu Asn Pro
405 410 415
Val Ala Gln Gly Gln Pro Ile Leu Thr Ser Leu Gly Ser Asn Gln Glu
420 425 430
Glu Ala Tyr Val Thr Met Ser Ser Phe Tyr Gln Asn Gln Ser Arg Ser
435 440 445
Asp Pro Lys Pro Glu Asn Pro Ala Cys Pro Trp Thr Val Leu Pro Ala
450 455 460
Gly Asp Leu Pro Thr His Asp Gly Tyr Leu Pro Ser Asn Ile Asp Asp
465 470 475 480
Leu Pro Ser His Glu Ala Pro Leu Ala Asp Ser Leu Glu Glu Leu Glu
485 490 495
Pro Gln

<210> 199
<211> 499
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 199
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15
His Ala Ala Arg Pro Met Gly Arg Gly Leu Leu Arg Gly Leu Trp Pro

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                20                  25                  30
Leu His Ile Val Leu Trp Thr Arg Ile Ala Ser Thr Ile Pro Pro His
        35                  40                  45
Val Gln Lys Ser Val Asn Asn Asp Met Ile Val Thr Asp Asn Asn Gly
    50                  55                  60
Ala Val Lys Phe Pro Gln Leu Cys Lys Phe Cys Asp Val Arg Phe Ser
65                  70                  75                  80
Thr Cys Asp Asn Gln Lys Ser Cys Met Ser Asn Cys Ser Ile Thr Ser
                85                  90                  95
Ile Cys Glu Lys Pro Gln Glu Val Cys Val Ala Val Trp Arg Lys Asn
            100                 105                 110
Asp Glu Asn Ile Thr Leu Glu Thr Val Cys His Asp Pro Lys Leu Pro
        115                 120                 125
Tyr His Asp Phe Ile Leu Glu Asp Ala Ala Ser Pro Lys Cys Ile Met
    130                 135                 140
Lys Glu Lys Lys Lys Pro Gly Glu Thr Phe Phe Met Cys Ser Cys Ser
145                 150                 155                 160
Ser Asp Glu Cys Asn Asp Asn Ile Ile Phe Ser Glu Glu Tyr Asn Thr
                165                 170                 175
Ser Asn Pro Asp Leu Leu Leu Val Ile Phe Gln Ser Asp Pro Thr Arg
            180                 185                 190
Val Glu Thr Ala Thr Glu Thr Ala Trp Leu Val Leu Leu Ile Leu Val
        195                 200                 205
Leu Ile Ser Leu Val Thr Ala Leu His Leu Val Leu Gly Leu Ser Ala
    210                 215                 220
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[0156]

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

Glu Glu Ala Tyr Val Thr Met Ser Ser Phe Tyr Gln Asn Gln Ser Arg
435 440 445
Ser Asp Pro Lys Pro Glu Asn Pro Ala Cys Pro Trp Thr Val Leu Pro
450 455 460
Ala Gly Asp Leu Pro Thr His Asp Gly Tyr Leu Pro Ser Asn Ile Asp
465 470 475 480
Asp Leu Pro Ser His Glu Ala Pro Leu Ala Asp Ser Leu Glu Glu Leu
485 490 495
Glu Pro Gln

<210> 200
<211> 481
<212> PRT
<213> 人工序列（Artificial Sequence）
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 200
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15
His Ala Ala Arg Pro Met Gly Arg Gly Leu Leu Arg Gly Leu Trp Pro
20 25 30
Leu His Ile Val Leu Trp Thr Arg Ile Ala Ser Thr Ile Pro Pro His
35 40 45
Val Gln Lys Ser Val Asn Asn Asp Met Ile Val Thr Asp Asn Asn Gly
[0157] 50 55 60
Ala Val Lys Phe Pro Gln Leu Cys Lys Phe Cys Asp Val Arg Phe Ser
65 70 75 80
Thr Cys Asp Asn Gln Lys Ser Cys Met Ser Asn Cys Ser Ile Thr Ser
85 90 95
Ile Cys Glu Lys Pro Gln Glu Val Cys Val Ala Val Trp Arg Lys Asn
100 105 110
Asp Glu Asn Ile Thr Leu Glu Thr Val Cys His Asp Pro Lys Leu Pro
115 120 125
Tyr His Asp Phe Ile Leu Glu Asp Ala Ala Ser Pro Lys Cys Ile Met
130 135 140
Lys Glu Lys Lys Lys Pro Gly Glu Thr Phe Phe Met Cys Ser Cys Ser
145 150 155 160
Ser Asp Glu Cys Asn Asp Asn Ile Ile Phe Ser Glu Glu Tyr Asn Thr
165 170 175
Ser Asn Pro Asp Leu Leu Leu Val Ile Phe Gln Ser Asp Pro Thr Arg
180 185 190
Val Glu Thr Ala Thr Glu His Leu Val Leu Gly Leu Ser Ala Val Leu
195 200 205
Gly Leu Leu Leu Leu Arg Trp Gln Phe Pro Ala His Tyr Arg Arg Leu
210 215 220
Arg His Ala Leu Trp Pro Ser Leu Pro Asp Leu His Arg Val Leu Gly
225 230 235 240
Gln Tyr Leu Arg Asp Thr Ala Ala Leu Ser Pro Pro Lys Ala Thr Val
245 250 255
Ser Asp Thr Cys Glu Glu Val Glu Pro Ser Leu Leu Glu Ile Leu Pro

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

[0158] Pro Ser His Glu Ala Pro Leu Ala Asp Ser Leu Glu Glu Leu Glu Pro
465 470 475 480
Gln

<210> 201
<211> 480
<212> PRT
<213> 人工序列（Artificial Sequence）
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 201
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15
His Ala Ala Arg Pro Met Gly Arg Gly Leu Leu Arg Gly Leu Trp Pro
20 25 30
Leu His Ile Val Leu Trp Thr Arg Ile Ala Ser Thr Ile Pro Pro His
35 40 45
Val Gln Lys Ser Val Asn Asn Asp Met Ile Val Thr Asp Asn Asn Gly
50 55 60
Ala Val Lys Phe Pro Gln Leu Cys Lys Phe Cys Asp Val Arg Phe Ser
65 70 75 80
Thr Cys Asp Asn Gln Lys Ser Cys Met Ser Asn Cys Ser Ile Thr Ser
85 90 95
Ile Cys Glu Lys Pro Gln Glu Val Cys Val Ala Val Trp Arg Lys Asn
100 105 110

Asp Glu Asn Ile Thr Leu Glu Thr Val Cys His Asp Pro Lys Leu Pro
115 120 125
Tyr His Asp Phe Ile Leu Glu Asp Ala Ala Ser Pro Lys Cys Ile Met
130 135 140
Lys Glu Lys Lys Lys Pro Gly Glu Thr Phe Phe Met Cys Ser Cys Ser
145 150 155 160
Ser Asp Glu Cys Asn Asp Asn Ile Ile Phe Ser Glu Glu Tyr Asn Thr
165 170 175
Ser Asn Pro Asp Leu Leu Leu Val Ile Phe Gln Ser Asp Pro Thr Arg
180 185 190
Val Glu Thr Ala Thr His Leu Val Leu Gly Leu Ser Ala Val Leu Gly
195 200 205
Leu Leu Leu Leu Arg Trp Gln Phe Pro Ala His Tyr Arg Arg Leu Arg
210 215 220
His Ala Leu Trp Pro Ser Leu Pro Asp Leu His Arg Val Leu Gly Gln
225 230 235 240
Tyr Leu Arg Asp Thr Ala Ala Leu Ser Pro Pro Lys Ala Thr Val Ser
245 250 255
Asp Thr Cys Glu Glu Val Glu Pro Ser Leu Leu Glu Ile Leu Pro Lys
260 265 270
Ser Ser Glu Arg Thr Pro Leu Pro Leu Leu Glu Ala Arg Asp Glu Val
275 280 285
Glu Gly Phe Leu Gln Asp Thr Phe Pro Gln Gln Leu Glu Glu Ser Glu
290 295 300
Lys Gln Arg Leu Gly Gly Asp Val Gln Ser Pro Asn Cys Pro Ser Glu
[0159] 305 310 315 320
Asp Val Val Ile Thr Pro Glu Ser Phe Gly Arg Asp Ser Ser Leu Thr
325 330 335
Cys Leu Ala Gly Asn Val Ser Ala Cys Asp Ala Pro Ile Leu Ser Ser
340 345 350
Ser Arg Ser Leu Asp Cys Arg Glu Ser Gly Lys Asn Gly Pro His Val
355 360 365
Tyr Gln Asp Leu Leu Leu Ser Leu Gly Thr Thr Asn Ser Thr Leu Pro
370 375 380
Pro Pro Phe Ser Leu Gln Ser Gly Ile Leu Thr Leu Asn Pro Val Ala
385 390 395 400
Gln Gly Gln Pro Ile Leu Thr Ser Leu Gly Ser Asn Gln Glu Glu Ala
405 410 415
Tyr Val Thr Met Ser Ser Phe Tyr Gln Asn Gln Ser Arg Ser Asp Pro
420 425 430
Lys Pro Glu Asn Pro Ala Cys Pro Trp Thr Val Leu Pro Ala Gly Asp
435 440 445
Leu Pro Thr His Asp Gly Tyr Leu Pro Ser Asn Ile Asp Asp Leu Pro
450 455 460
Ser His Glu Ala Pro Leu Ala Asp Ser Leu Glu Glu Leu Glu Pro Gln
465 470 475 480

<210> 202
<211> 479
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>

<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 202

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

[0160] Ser Asn Pro Asp Leu Leu Leu Val Ile Phe Gln Ser Asp Pro Thr Arg
180 185 190
Val Glu Thr Ala His Leu Val Leu Gly Leu Ser Ala Val Leu Gly Leu
195 200 205
Leu Leu Leu Arg Trp Gln Phe Pro Ala His Tyr Arg Arg Leu Arg His
210 215 220
Ala Leu Trp Pro Ser Leu Pro Asp Leu His Arg Val Leu Gly Gln Tyr
225 230 235 240
Leu Arg Asp Thr Ala Ala Leu Ser Pro Pro Lys Ala Thr Val Ser Asp
245 250 255
Thr Cys Glu Glu Val Glu Pro Ser Leu Leu Glu Ile Leu Pro Lys Ser
260 265 270
Ser Glu Arg Thr Pro Leu Pro Leu Leu Glu Ala Arg Asp Glu Val Glu
275 280 285
Gly Phe Leu Gln Asp Thr Phe Pro Gln Gln Leu Glu Glu Ser Glu Lys
290 295 300
Gln Arg Leu Gly Gly Asp Val Gln Ser Pro Asn Cys Pro Ser Glu Asp
305 310 315 320
Val Val Ile Thr Pro Glu Ser Phe Gly Arg Asp Ser Ser Leu Thr Cys
325 330 335
Leu Ala Gly Asn Val Ser Ala Cys Asp Ala Pro Ile Leu Ser Ser Ser
340 345 350
Arg Ser Leu Asp Cys Arg Glu Ser Gly Lys Asn Gly Pro His Val Tyr
355 360 365
Gln Asp Leu Leu Leu Ser Leu Gly Thr Thr Asn Ser Thr Leu Pro Pro
370 375 380

Pro Phe Ser Leu Gln Ser Gly Ile Leu Thr Leu Asn Pro Val Ala Gln
385 390 395 400
Gly Gln Pro Ile Leu Thr Ser Leu Gly Ser Asn Gln Glu Glu Ala Tyr
405 410 415
Val Thr Met Ser Ser Phe Tyr Gln Asn Gln Ser Arg Ser Asp Pro Lys
420 425 430
Pro Glu Asn Pro Ala Cys Pro Trp Thr Val Leu Pro Ala Gly Asp Leu
435 440 445
Pro Thr His Asp Gly Tyr Leu Pro Ser Asn Ile Asp Asp Leu Pro Ser
450 455 460
His Glu Ala Pro Leu Ala Asp Ser Leu Glu Glu Leu Glu Pro Gln
465 470 475

<210> 203
<211> 478
<212> PRT
<213> 人工序列（Artificial Sequence）
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 203

[0161]

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

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

[0162] Thr His Asp Gly Tyr Leu Pro Ser Asn Ile Asp Asp Leu Pro Ser His
450 455 460
Glu Ala Pro Leu Ala Asp Ser Leu Glu Glu Leu Glu Pro Gln
465 470 475

<210> 204
<211> 477
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 204
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15
His Ala Ala Arg Pro Met Gly Arg Gly Leu Leu Arg Gly Leu Trp Pro
20 25 30
Leu His Ile Val Leu Trp Thr Arg Ile Ala Ser Thr Ile Pro Pro His
35 40 45
Val Gln Lys Ser Val Asn Asn Asp Met Ile Val Thr Asp Asn Asn Gly
50 55 60
Ala Val Lys Phe Pro Gln Leu Cys Lys Phe Cys Asp Val Arg Phe Ser
65 70 75 80
Thr Cys Asp Asn Gln Lys Ser Cys Met Ser Asn Cys Ser Ile Thr Ser
85 90 95
Ile Cys Glu Lys Pro Gln Glu Val Cys Val Ala Val Trp Arg Lys Asn
100 105 110

Asp Glu Asn Ile Thr Leu Glu Thr Val Cys His Asp Pro Lys Leu Pro
115 120 125
Tyr His Asp Phe Ile Leu Glu Asp Ala Ala Ser Pro Lys Cys Ile Met
130 135 140
Lys Glu Lys Lys Lys Pro Gly Glu Thr Phe Phe Met Cys Ser Cys Ser
145 150 155 160
Ser Asp Glu Cys Asn Asp Asn Ile Ile Phe Ser Glu Glu Tyr Asn Thr
165 170 175
Ser Asn Pro Asp Leu Leu Leu Val Ile Phe Gln Ser Asp Pro Thr Arg
180 185 190
Val Glu His Leu Val Leu Gly Leu Ser Ala Val Leu Gly Leu Leu Leu
195 200 205
Leu Arg Trp Gln Phe Pro Ala His Tyr Arg Arg Leu Arg His Ala Leu
210 215 220
Trp Pro Ser Leu Pro Asp Leu His Arg Val Leu Gly Gln Tyr Leu Arg
225 230 235 240
Asp Thr Ala Ala Leu Ser Pro Pro Lys Ala Thr Val Ser Asp Thr Cys
245 250 255
Glu Glu Val Glu Pro Ser Leu Leu Glu Ile Leu Pro Lys Ser Ser Glu
260 265 270
Arg Thr Pro Leu Pro Leu Leu Glu Ala Arg Asp Glu Val Glu Gly Phe
275 280 285
Leu Gln Asp Thr Phe Pro Gln Gln Leu Glu Glu Ser Glu Lys Gln Arg
290 295 300
Leu Gly Gly Asp Val Gln Ser Pro Asn Cys Pro Ser Glu Asp Val Val
[0163] 305 310 315 320
Ile Thr Pro Glu Ser Phe Gly Arg Asp Ser Ser Leu Thr Cys Leu Ala
325 330 335
Gly Asn Val Ser Ala Cys Asp Ala Pro Ile Leu Ser Ser Ser Arg Ser
340 345 350
Leu Asp Cys Arg Glu Ser Gly Lys Asn Gly Pro His Val Tyr Gln Asp
355 360 365
Leu Leu Leu Ser Leu Gly Thr Thr Asn Ser Thr Leu Pro Pro Pro Phe
370 375 380
Ser Leu Gln Ser Gly Ile Leu Thr Leu Asn Pro Val Ala Gln Gly Gln
385 390 395 400
Pro Ile Leu Thr Ser Leu Gly Ser Asn Gln Glu Glu Ala Tyr Val Thr
405 410 415
Met Ser Ser Phe Tyr Gln Asn Gln Ser Arg Ser Asp Pro Lys Pro Glu
420 425 430
Asn Pro Ala Cys Pro Trp Thr Val Leu Pro Ala Gly Asp Leu Pro Thr
435 440 445
His Asp Gly Tyr Leu Pro Ser Asn Ile Asp Asp Leu Pro Ser His Glu
450 455 460
Ala Pro Leu Ala Asp Ser Leu Glu Glu Leu Glu Pro Gln
465 470 475

<210> 205
<211> 476
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>

<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 205

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

[0164]

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

Leu Gln Ser Gly Ile Leu Thr Leu Asn Pro Val Ala Gln Gly Gln Pro
385 390 395 400
Ile Leu Thr Ser Leu Gly Ser Asn Gln Glu Glu Ala Tyr Val Thr Met
405 410 415
Ser Ser Phe Tyr Gln Asn Gln Ser Arg Ser Asp Pro Lys Pro Glu Asn
420 425 430
Pro Ala Cys Pro Trp Thr Val Leu Pro Ala Gly Asp Leu Pro Thr His
435 440 445
Asp Gly Tyr Leu Pro Ser Asn Ile Asp Asp Leu Pro Ser His Glu Ala
450 455 460
Pro Leu Ala Asp Ser Leu Glu Glu Leu Glu Pro Gln
465 470 475

<210> 206
<211> 475
<212> PRT
<213> 人工序列（Artificial Sequence）
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 206

Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15
His Ala Ala Arg Pro Met Gly Arg Gly Leu Leu Arg Gly Leu Trp Pro
20 25 30
Leu His Ile Val Leu Trp Thr Arg Ile Ala Ser Thr Ile Pro Pro His
[0165] 35 40 45
Val Gln Lys Ser Val Asn Asn Asp Met Ile Val Thr Asp Asn Asn Gly
50 55 60
Ala Val Lys Phe Pro Gln Leu Cys Lys Phe Cys Asp Val Arg Phe Ser
65 70 75 80
Thr Cys Asp Asn Gln Lys Ser Cys Met Ser Asn Cys Ser Ile Thr Ser
85 90 95
Ile Cys Glu Lys Pro Gln Glu Val Cys Val Ala Val Trp Arg Lys Asn
100 105 110
Asp Glu Asn Ile Thr Leu Glu Thr Val Cys His Asp Pro Lys Leu Pro
115 120 125
Tyr His Asp Phe Ile Leu Glu Asp Ala Ala Ser Pro Lys Cys Ile Met
130 135 140
Lys Glu Lys Lys Lys Pro Gly Glu Thr Phe Phe Met Cys Ser Cys Ser
145 150 155 160
Ser Asp Glu Cys Asn Asp Asn Ile Ile Phe Ser Glu Glu Tyr Asn Thr
165 170 175
Ser Asn Pro Asp Leu Leu Leu Val Ile Phe Gln Ser Asp Pro Thr Arg
180 185 190
His Leu Val Leu Gly Leu Ser Ala Val Leu Gly Leu Leu Leu Leu Arg
195 200 205
Trp Gln Phe Pro Ala His Tyr Arg Arg Leu Arg His Ala Leu Trp Pro
210 215 220
Ser Leu Pro Asp Leu His Arg Val Leu Gly Gln Tyr Leu Arg Asp Thr
225 230 235 240
Ala Ala Leu Ser Pro Pro Lys Ala Thr Val Ser Asp Thr Cys Glu Glu

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

[0166] Gly Tyr Leu Pro Ser Asn Ile Asp Asp Leu Pro Ser His Glu Ala Pro
450 455 460
Leu Ala Asp Ser Leu Glu Glu Leu Glu Pro Gln
465 470 475

<210> 207
<211> 474
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 207
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15
His Ala Ala Arg Pro Met Gly Arg Gly Leu Leu Arg Gly Leu Trp Pro
20 25 30
Leu His Ile Val Leu Trp Thr Arg Ile Ala Ser Thr Ile Pro Pro His
35 40 45
Val Gln Lys Ser Val Asn Asn Asp Met Ile Val Thr Asp Asn Asn Gly
50 55 60
Ala Val Lys Phe Pro Gln Leu Cys Lys Phe Cys Asp Val Arg Phe Ser
65 70 75 80
Thr Cys Asp Asn Gln Lys Ser Cys Met Ser Asn Cys Ser Ile Thr Ser
85 90 95
Ile Cys Glu Lys Pro Gln Glu Val Cys Val Ala Val Trp Arg Lys Asn
100 105 110

Asp Glu Asn Ile Thr Leu Glu Thr Val Cys His Asp Pro Lys Leu Pro
115 120 125
Tyr His Asp Phe Ile Leu Glu Asp Ala Ala Ser Pro Lys Cys Ile Met
130 135 140
Lys Glu Lys Lys Lys Pro Gly Glu Thr Phe Phe Met Cys Ser Cys Ser
145 150 155 160
Ser Asp Glu Cys Asn Asp Asn Ile Ile Phe Ser Glu Glu Tyr Asn Thr
165 170 175
Ser Asn Pro Asp Leu Leu Leu Val Ile Phe Gln Ser Asp Pro Thr His
180 185 190
Leu Val Leu Gly Leu Ser Ala Val Leu Gly Leu Leu Leu Leu Arg Trp
195 200 205
Gln Phe Pro Ala His Tyr Arg Arg Leu Arg His Ala Leu Trp Pro Ser
210 215 220
Leu Pro Asp Leu His Arg Val Leu Gly Gln Tyr Leu Arg Asp Thr Ala
225 230 235 240
Ala Leu Ser Pro Pro Lys Ala Thr Val Ser Asp Thr Cys Glu Glu Val
245 250 255
Glu Pro Ser Leu Leu Glu Ile Leu Pro Lys Ser Ser Glu Arg Thr Pro
260 265 270
Leu Pro Leu Leu Glu Ala Arg Asp Glu Val Glu Gly Phe Leu Gln Asp
275 280 285
Thr Phe Pro Gln Gln Leu Glu Glu Ser Glu Lys Gln Arg Leu Gly Gly
290 295 300
Asp Val Gln Ser Pro Asn Cys Pro Ser Glu Asp Val Val Ile Thr Pro
[0167] 305 310 315 320
Glu Ser Phe Gly Arg Asp Ser Ser Leu Thr Cys Leu Ala Gly Asn Val
325 330 335
Ser Ala Cys Asp Ala Pro Ile Leu Ser Ser Ser Arg Ser Leu Asp Cys
340 345 350
Arg Glu Ser Gly Lys Asn Gly Pro His Val Tyr Gln Asp Leu Leu Leu
355 360 365
Ser Leu Gly Thr Thr Asn Ser Thr Leu Pro Pro Pro Phe Ser Leu Gln
370 375 380
Ser Gly Ile Leu Thr Leu Asn Pro Val Ala Gln Gly Gln Pro Ile Leu
385 390 395 400
Thr Ser Leu Gly Ser Asn Gln Glu Glu Ala Tyr Val Thr Met Ser Ser
405 410 415
Phe Tyr Gln Asn Gln Ser Arg Ser Asp Pro Lys Pro Glu Asn Pro Ala
420 425 430
Cys Pro Trp Thr Val Leu Pro Ala Gly Asp Leu Pro Thr His Asp Gly
435 440 445
Tyr Leu Pro Ser Asn Ile Asp Asp Leu Pro Ser His Glu Ala Pro Leu
450 455 460
Ala Asp Ser Leu Glu Glu Leu Glu Pro Gln
465 470
<210> 208
<211> 473
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>

<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 208

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

[0168]

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

Gly Ile Leu Thr Leu Asn Pro Val Ala Gln Gly Gln Pro Ile Leu Thr
385 390 395 400
Ser Leu Gly Ser Asn Gln Glu Glu Ala Tyr Val Thr Met Ser Ser Phe
405 410 415
Tyr Gln Asn Gln Ser Arg Ser Asp Pro Lys Pro Glu Asn Pro Ala Cys
420 425 430
Pro Trp Thr Val Leu Pro Ala Gly Asp Leu Pro Thr His Asp Gly Tyr
435 440 445
Leu Pro Ser Asn Ile Asp Asp Leu Pro Ser His Glu Ala Pro Leu Ala
450 455 460
Asp Ser Leu Glu Glu Leu Glu Pro Gln
465 470

<210> 209
<211> 472
<212> PRT
<213> 人工序列（Artificial Sequence）
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 209

[0169]

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

245 250 255
Ser Leu Leu Glu Ile Leu Pro Lys Ser Ser Glu Arg Thr Pro Leu Pro
260 265 270
Leu Leu Glu Ala Arg Asp Glu Val Glu Gly Phe Leu Gln Asp Thr Phe
275 280 285
Pro Gln Gln Leu Glu Glu Ser Glu Lys Gln Arg Leu Gly Gly Asp Val
290 295 300
Gln Ser Pro Asn Cys Pro Ser Glu Asp Val Val Ile Thr Pro Glu Ser
305 310 315 320
Phe Gly Arg Asp Ser Ser Leu Thr Cys Leu Ala Gly Asn Val Ser Ala
325 330 335
Cys Asp Ala Pro Ile Leu Ser Ser Ser Arg Ser Leu Asp Cys Arg Glu
340 345 350
Ser Gly Lys Asn Gly Pro His Val Tyr Gln Asp Leu Leu Leu Ser Leu
355 360 365
Gly Thr Thr Asn Ser Thr Leu Pro Pro Pro Phe Ser Leu Gln Ser Gly
370 375 380
Ile Leu Thr Leu Asn Pro Val Ala Gln Gly Gln Pro Ile Leu Thr Ser
385 390 395 400
Leu Gly Ser Asn Gln Glu Glu Ala Tyr Val Thr Met Ser Ser Phe Tyr
405 410 415
Gln Asn Gln Ser Arg Ser Asp Pro Lys Pro Glu Asn Pro Ala Cys Pro
420 425 430
Trp Thr Val Leu Pro Ala Gly Asp Leu Pro Thr His Asp Gly Tyr Leu
435 440 445
[0170] Pro Ser Asn Ile Asp Asp Leu Pro Ser His Glu Ala Pro Leu Ala Asp
450 455 460
Ser Leu Glu Glu Leu Glu Pro Gln
465 470
<210> 210
<211> 471
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 210
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15
His Ala Ala Arg Pro Met Gly Arg Gly Leu Leu Arg Gly Leu Trp Pro
20 25 30
Leu His Ile Val Leu Trp Thr Arg Ile Ala Ser Thr Ile Pro Pro His
35 40 45
Val Gln Lys Ser Val Asn Asn Asp Met Ile Val Thr Asp Asn Asn Gly
50 55 60
Ala Val Lys Phe Pro Gln Leu Cys Lys Phe Cys Asp Val Arg Phe Ser
65 70 75 80
Thr Cys Asp Asn Gln Lys Ser Cys Met Ser Asn Cys Ser Ile Thr Ser
85 90 95
Ile Cys Glu Lys Pro Gln Glu Val Cys Val Ala Val Trp Arg Lys Asn
100 105 110

Asp Glu Asn Ile Thr Leu Glu Thr Val Cys His Asp Pro Lys Leu Pro
115 120 125
Tyr His Asp Phe Ile Leu Glu Asp Ala Ala Ser Pro Lys Cys Ile Met
130 135 140
Lys Glu Lys Lys Lys Pro Gly Glu Thr Phe Phe Met Cys Ser Cys Ser
145 150 155 160
Ser Asp Glu Cys Asn Asp Asn Ile Ile Phe Ser Glu Glu Tyr Asn Thr
165 170 175
Ser Asn Pro Asp Leu Leu Leu Val Ile Phe Gln Ser His Leu Val Leu
180 185 190
Gly Leu Ser Ala Val Leu Gly Leu Leu Leu Leu Arg Trp Gln Phe Pro
195 200 205
Ala His Tyr Arg Arg Leu Arg His Ala Leu Trp Pro Ser Leu Pro Asp
210 215 220
Leu His Arg Val Leu Gly Gln Tyr Leu Arg Asp Thr Ala Ala Leu Ser
225 230 235 240
Pro Pro Lys Ala Thr Val Ser Asp Thr Cys Glu Glu Val Glu Pro Ser
245 250 255
Leu Leu Glu Ile Leu Pro Lys Ser Ser Glu Arg Thr Pro Leu Pro Leu
260 265 270
Leu Glu Ala Arg Asp Glu Val Glu Gly Phe Leu Gln Asp Thr Phe Pro
275 280 285
Gln Gln Leu Glu Glu Ser Glu Lys Gln Arg Leu Gly Gly Asp Val Gln
290 295 300
Ser Pro Asn Cys Pro Ser Glu Asp Val Val Ile Thr Pro Glu Ser Phe
[0171] 305 310 315 320
Gly Arg Asp Ser Ser Leu Thr Cys Leu Ala Gly Asn Val Ser Ala Cys
325 330 335
Asp Ala Pro Ile Leu Ser Ser Ser Arg Ser Leu Asp Cys Arg Glu Ser
340 345 350
Gly Lys Asn Gly Pro His Val Tyr Gln Asp Leu Leu Leu Ser Leu Gly
355 360 365
Thr Thr Asn Ser Thr Leu Pro Pro Pro Phe Ser Leu Gln Ser Gly Ile
370 375 380
Leu Thr Leu Asn Pro Val Ala Gln Gly Gln Pro Ile Leu Thr Ser Leu
385 390 395 400
Gly Ser Asn Gln Glu Glu Ala Tyr Val Thr Met Ser Ser Phe Tyr Gln
405 410 415
Asn Gln Ser Arg Ser Asp Pro Lys Pro Glu Asn Pro Ala Cys Pro Trp
420 425 430
Thr Val Leu Pro Ala Gly Asp Leu Pro Thr His Asp Gly Tyr Leu Pro
435 440 445
Ser Asn Ile Asp Asp Leu Pro Ser His Glu Ala Pro Leu Ala Asp Ser
450 455 460
Leu Glu Glu Leu Glu Pro Gln
465 470

<210> 211
<211> 470
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>

<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 211

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

[0172]

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

Thr Leu Asn Pro Val Ala Gln Gly Gln Pro Ile Leu Thr Ser Leu Gly
385 390 395 400
Ser Asn Gln Glu Glu Ala Tyr Val Thr Met Ser Ser Phe Tyr Gln Asn
405 410 415
Gln Ser Arg Ser Asp Pro Lys Pro Glu Asn Pro Ala Cys Pro Trp Thr
420 425 430
Val Leu Pro Ala Gly Asp Leu Pro Thr His Asp Gly Tyr Leu Pro Ser
435 440 445
Asn Ile Asp Asp Leu Pro Ser His Glu Ala Pro Leu Ala Asp Ser Leu
450 455 460
Glu Glu Leu Glu Pro Gln
465 470

<210> 212
<211> 434
<212> PRT
<213> 人工序列（Artificial Sequence）
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 212

Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15
His Ala Ala Arg Pro Gln Leu Cys Lys Phe Cys Asp Val Arg Phe Ser
20 25 30
Thr Cys Asp Asn Gln Lys Ser Cys Met Ser Asn Cys Ser Ile Thr Ser
[0173] 35 40 45
Ile Cys Glu Lys Pro Gln Glu Val Cys Val Ala Val Trp Arg Lys Asn
50 55 60
Asp Glu Asn Ile Thr Leu Glu Thr Val Cys His Asp Pro Lys Leu Pro
65 70 75 80
Tyr His Asp Phe Ile Leu Glu Asp Ala Ala Ser Pro Lys Cys Ile Met
85 90 95
Lys Glu Lys Lys Lys Pro Gly Glu Thr Phe Phe Met Cys Ser Cys Ser
100 105 110
Ser Asp Glu Cys Asn Asp Asn Ile Ile Phe Ser Glu Glu Tyr Asn Thr
115 120 125
Ser Asn Pro Asp Leu Leu Leu Val Ile Phe Gln Ser Asp Pro Thr Arg
130 135 140
Val Glu Thr Ala Thr Glu Thr His Leu Val Leu Gly Leu Ser Ala Val
145 150 155 160
Leu Gly Leu Leu Leu Leu Arg Trp Gln Phe Pro Ala His Tyr Arg Arg
165 170 175
Leu Arg His Ala Leu Trp Pro Ser Leu Pro Asp Leu His Arg Val Leu
180 185 190
Gly Gln Tyr Leu Arg Asp Thr Ala Ala Leu Ser Pro Pro Lys Ala Thr
195 200 205
Val Ser Asp Thr Cys Glu Glu Val Glu Pro Ser Leu Leu Glu Ile Leu
210 215 220
Pro Lys Ser Ser Glu Arg Thr Pro Leu Pro Leu Leu Glu Ala Arg Asp
225 230 235 240
Glu Val Glu Gly Phe Leu Gln Asp Thr Phe Pro Gln Gln Leu Glu Glu

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

[0174] <210> 213
<211> 447
<212> PRT
<213> 人工序列（Artificial Sequence）
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 213
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15
His Ala Ala Arg Pro Gln Leu Cys Lys Phe Cys Asp Val Arg Phe Ser
20 25 30
Thr Cys Asp Asn Gln Lys Ser Cys Met Ser Asn Cys Ser Ile Thr Ser
35 40 45
Ile Cys Glu Lys Pro Gln Glu Val Cys Val Ala Val Trp Arg Lys Asn
50 55 60
Asp Glu Asn Ile Thr Leu Glu Thr Val Cys His Asp Pro Lys Leu Pro
65 70 75 80
Tyr His Asp Phe Ile Leu Glu Asp Ala Ala Ser Pro Lys Cys Ile Met
85 90 95
Lys Glu Lys Lys Lys Pro Gly Glu Thr Phe Phe Met Cys Ser Cys Ser
100 105 110
Ser Asp Glu Cys Asn Asp Asn Ile Ile Phe Ser Glu Glu Tyr Asn Thr
115 120 125
Ser Asn Pro Asp Leu Leu Leu Val Ile Phe Gln Ser Asp Pro Thr Arg
130 135 140

Val Glu Thr Ala Thr Glu Thr Ala Trp Ile Leu Val Leu Ile Ser Leu
145 150 155 160
Val Thr Ala Leu His Leu Val Leu Gly Leu Ser Ala Val Leu Gly Leu
165 170 175
Leu Leu Leu Arg Trp Gln Phe Pro Ala His Tyr Arg Arg Leu Arg His
180 185 190
Ala Leu Trp Pro Ser Leu Pro Asp Leu His Arg Val Leu Gly Gln Tyr
195 200 205
Leu Arg Asp Thr Ala Ala Leu Ser Pro Pro Lys Ala Thr Val Ser Asp
210 215 220
Thr Cys Glu Glu Val Glu Pro Ser Leu Leu Glu Ile Leu Pro Lys Ser
225 230 235 240
Ser Glu Arg Thr Pro Leu Pro Leu Leu Glu Ala Arg Asp Glu Val Glu
245 250 255
Gly Phe Leu Gln Asp Thr Phe Pro Gln Gln Leu Glu Glu Ser Glu Lys
260 265 270
Gln Arg Leu Gly Gly Asp Val Gln Ser Pro Asn Cys Pro Ser Glu Asp
275 280 285
Val Val Ile Thr Pro Glu Ser Phe Gly Arg Asp Ser Ser Leu Thr Cys
290 295 300
Leu Ala Gly Asn Val Ser Ala Cys Asp Ala Pro Ile Leu Ser Ser Ser
305 310 315 320
Arg Ser Leu Asp Cys Arg Glu Ser Gly Lys Asn Gly Pro His Val Tyr
325 330 335
Gln Asp Leu Leu Leu Ser Leu Gly Thr Thr Asn Ser Thr Leu Pro Pro
[0175] 340 345 350
Pro Phe Ser Leu Gln Ser Gly Ile Leu Thr Leu Asn Pro Val Ala Gln
355 360 365
Gly Gln Pro Ile Leu Thr Ser Leu Gly Ser Asn Gln Glu Glu Ala Tyr
370 375 380
Val Thr Met Ser Ser Phe Tyr Gln Asn Gln Ser Arg Ser Asp Pro Lys
385 390 395 400
Pro Glu Asn Pro Ala Cys Pro Trp Thr Val Leu Pro Ala Gly Asp Leu
405 410 415
Pro Thr His Asp Gly Tyr Leu Pro Ser Asn Ile Asp Asp Leu Pro Ser
420 425 430
His Glu Ala Pro Leu Ala Asp Ser Leu Glu Glu Leu Glu Pro Gln
435 440 445
<210> 214
<211> 430
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 214
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15
His Ala Ala Arg Pro Gln Leu Cys Lys Phe Cys Asp Val Arg Phe Ser
20 25 30
Thr Cys Asp Asn Gln Lys Ser Cys Met Ser Asn Cys Ser Ile Thr Ser

35 40 45
Ile Cys Glu Lys Pro Gln Glu Val Cys Val Ala Val Trp Arg Lys Asn
50 55 60
Asp Glu Asn Ile Thr Leu Glu Thr Val Cys His Asp Pro Lys Leu Pro
65 70 75 80
Tyr His Asp Phe Ile Leu Glu Asp Ala Ala Ser Pro Lys Cys Ile Met
85 90 95
Lys Glu Lys Lys Lys Pro Gly Glu Thr Phe Phe Met Cys Ser Cys Ser
100 105 110
Ser Asp Glu Cys Asn Asp Asn Ile Ile Phe Ser Glu Glu Tyr Asn Thr
115 120 125
Ser Asn Pro Asp Leu Leu Leu Val Ile Phe Gln Ser Asp Pro Thr Arg
130 135 140
Val Glu Thr His Leu Val Leu Gly Leu Ser Ala Val Leu Gly Leu Leu
145 150 155 160
Leu Leu Arg Trp Gln Phe Pro Ala His Tyr Arg Arg Leu Arg His Ala
165 170 175
Leu Trp Pro Ser Leu Pro Asp Leu His Arg Val Leu Gly Gln Tyr Leu
180 185 190
Arg Asp Thr Ala Ala Leu Ser Pro Pro Lys Ala Thr Val Ser Asp Thr
195 200 205
Cys Glu Glu Val Glu Pro Ser Leu Leu Glu Ile Leu Pro Lys Ser Ser
210 215 220
Glu Arg Thr Pro Leu Pro Leu Leu Glu Ala Arg Asp Glu Val Glu Gly
225 230 235 240
[0176] Phe Leu Gln Asp Thr Phe Pro Gln Gln Leu Glu Glu Ser Glu Lys Gln
245 250 255
Arg Leu Gly Gly Asp Val Gln Ser Pro Asn Cys Pro Ser Glu Asp Val
260 265 270
Val Ile Thr Pro Glu Ser Phe Gly Arg Asp Ser Ser Leu Thr Cys Leu
275 280 285
Ala Gly Asn Val Ser Ala Cys Asp Ala Pro Ile Leu Ser Ser Ser Arg
290 295 300
Ser Leu Asp Cys Arg Glu Ser Gly Lys Asn Gly Pro His Val Tyr Gln
305 310 315 320
Asp Leu Leu Leu Ser Leu Gly Thr Thr Asn Ser Thr Leu Pro Pro Pro
325 330 335
Phe Ser Leu Gln Ser Gly Ile Leu Thr Leu Asn Pro Val Ala Gln Gly
340 345 350
Gln Pro Ile Leu Thr Ser Leu Gly Ser Asn Gln Glu Glu Ala Tyr Val
355 360 365
Thr Met Ser Ser Phe Tyr Gln Asn Gln Ser Arg Ser Asp Pro Lys Pro
370 375 380
Glu Asn Pro Ala Cys Pro Trp Thr Val Leu Pro Ala Gly Asp Leu Pro
385 390 395 400
Thr His Asp Gly Tyr Leu Pro Ser Asn Ile Asp Asp Leu Pro Ser His
405 410 415
Glu Ala Pro Leu Ala Asp Ser Leu Glu Glu Leu Glu Pro Gln
420 425 430
<210> 215
<211> 425

<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 215

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Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1               5                  10                  15
His Ala Ala Arg Pro Gln Leu Cys Lys Phe Cys Asp Val Arg Phe Ser
            20                  25                  30
Thr Cys Asp Asn Gln Lys Ser Cys Met Ser Asn Cys Ser Ile Thr Ser
        35                  40                  45
Ile Cys Glu Lys Pro Gln Glu Val Cys Val Ala Val Trp Arg Lys Asn
    50                  55                  60
Asp Glu Asn Ile Thr Leu Glu Thr Val Cys His Asp Pro Lys Leu Pro
65                  70                  75                  80
Tyr His Asp Phe Ile Leu Glu Asp Ala Ala Ser Pro Lys Cys Ile Met
                85                  90                  95
Lys Glu Lys Lys Lys Pro Gly Glu Thr Phe Phe Met Cys Ser Cys Ser
            100                 105                 110
Ser Asp Glu Cys Asn Asp Asn Ile Ile Phe Ser Glu Glu Tyr Asn Thr
        115                 120                 125
Ser Asn Pro Asp Leu Leu Leu Val Ile Phe Gln Ser Asp Pro His Leu
    130                 135                 140
Val Leu Gly Leu Ser Ala Val Leu Gly Leu Leu Leu Leu Arg Trp Gln
145                 150                 155                 160
Phe Pro Ala His Tyr Arg Arg Leu Arg His Ala Leu Trp Pro Ser Leu
                165                 170                 175
Pro Asp Leu His Arg Val Leu Gly Gln Tyr Leu Arg Asp Thr Ala Ala
            180                 185                 190
Leu Ser Pro Pro Lys Ala Thr Val Ser Asp Thr Cys Glu Glu Val Glu
        195                 200                 205
Pro Ser Leu Leu Glu Ile Leu Pro Lys Ser Ser Glu Arg Thr Pro Leu
    210                 215                 220
Pro Leu Leu Glu Ala Arg Asp Glu Val Glu Gly Phe Leu Gln Asp Thr
225                 230                 235                 240
Phe Pro Gln Gln Leu Glu Glu Ser Glu Lys Gln Arg Leu Gly Gly Asp
                245                 250                 255
Val Gln Ser Pro Asn Cys Pro Ser Glu Asp Val Val Ile Thr Pro Glu
            260                 265                 270
Ser Phe Gly Arg Asp Ser Ser Leu Thr Cys Leu Ala Gly Asn Val Ser
        275                 280                 285
Ala Cys Asp Ala Pro Ile Leu Ser Ser Ser Arg Ser Leu Asp Cys Arg
    290                 295                 300
Glu Ser Gly Lys Asn Gly Pro His Val Tyr Gln Asp Leu Leu Leu Ser
305                 310                 315                 320
Leu Gly Thr Thr Asn Ser Thr Leu Pro Pro Pro Phe Ser Leu Gln Ser
                325                 330                 335
Gly Ile Leu Thr Leu Asn Pro Val Ala Gln Gly Gln Pro Ile Leu Thr
            340                 345                 350
Ser Leu Gly Ser Asn Gln Glu Glu Ala Tyr Val Thr Met Ser Ser Phe
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[0177]

355 360 365
Tyr Gln Asn Gln Ser Arg Ser Asp Pro Lys Pro Glu Asn Pro Ala Cys
370 375 380
Pro Trp Thr Val Leu Pro Ala Gly Asp Leu Pro Thr His Asp Gly Tyr
385 390 395 400
Leu Pro Ser Asn Ile Asp Asp Leu Pro Ser His Glu Ala Pro Leu Ala
405 410 415
Asp Ser Leu Glu Glu Leu Glu Pro Gln
420 425

<210> 216
<211> 424
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 216
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15
His Ala Ala Arg Pro Gln Leu Cys Lys Phe Cys Asp Val Arg Phe Ser
20 25 30
Thr Cys Asp Asn Gln Lys Ser Cys Met Ser Asn Cys Ser Ile Thr Ser
35 40 45
Ile Cys Glu Lys Pro Gln Glu Val Cys Val Ala Val Trp Arg Lys Asn
50 55 60

[0178]
Asp Glu Asn Ile Thr Leu Glu Thr Val Cys His Asp Pro Lys Leu Pro
65 70 75 80
Tyr His Asp Phe Ile Leu Glu Asp Ala Ala Ser Pro Lys Cys Ile Met
85 90 95
Lys Glu Lys Lys Lys Pro Gly Glu Thr Phe Phe Met Cys Ser Cys Ser
100 105 110
Ser Asp Glu Cys Asn Asp Asn Ile Ile Phe Ser Glu Glu Tyr Asn Thr
115 120 125
Ser Asn Pro Asp Leu Leu Leu Val Ile Phe Gln Ser Asp His Leu Val
130 135 140
Leu Gly Leu Ser Ala Val Leu Gly Leu Leu Leu Leu Arg Trp Gln Phe
145 150 155 160
Pro Ala His Tyr Arg Arg Leu Arg His Ala Leu Trp Pro Ser Leu Pro
165 170 175
Asp Leu His Arg Val Leu Gly Gln Tyr Leu Arg Asp Thr Ala Ala Leu
180 185 190
Ser Pro Pro Lys Ala Thr Val Ser Asp Thr Cys Glu Glu Val Glu Pro
195 200 205
Ser Leu Leu Glu Ile Leu Pro Lys Ser Ser Glu Arg Thr Pro Leu Pro
210 215 220
Leu Leu Glu Ala Arg Asp Glu Val Glu Gly Phe Leu Gln Asp Thr Phe
225 230 235 240
Pro Gln Gln Leu Glu Glu Ser Glu Lys Gln Arg Leu Gly Gly Asp Val
245 250 255
Gln Ser Pro Asn Cys Pro Ser Glu Asp Val Val Ile Thr Pro Glu Ser
260 265 270

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

<210> 217
<211> 105
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>

[0179]

<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 217
Ser Asp Pro Thr Arg Val Glu Thr Ala Thr Glu Thr Ala Trp Ile Ser
1 5 10 15
Leu Val Thr Ala Leu Leu Leu Val Leu Gly Leu Asn Ala Val Leu Gly
20 25 30
Leu Leu Leu Leu Arg Lys Gln Phe Pro Ala His Tyr Arg Arg Leu Arg
35 40 45
His Ala Leu Trp Pro Ser Leu Pro Asp Leu His Arg Val Leu Gly Gln
50 55 60
Tyr Leu Arg Asp Thr Ala Ala Leu Ser Pro Pro Arg Ala Thr Val Ser
65 70 75 80
Asp Thr Cys Glu Glu Val Glu Pro Ser Leu Leu Glu Ile Leu Pro Arg
85 90 95
Ser Ser Glu Arg Thr Pro Leu Pro Leu
100 105

<210> 218
<211> 105
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 218
Ser Asp Pro Thr Arg Val Glu Thr Ala Thr Glu Thr Ala Trp Ile Ser

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

<210> 219
<211> 98
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 219
Ser Asp Pro Thr Arg Val Glu Thr Ala Thr Glu Thr Ala Leu His Leu
1 5 10 15
Val Leu Gly Leu Asn Ala Val Leu Gly Leu Leu Leu Leu Arg Lys Gln
20 25 30
[0180] Phe Pro Ala His Tyr Arg Arg Leu Arg His Ala Leu Trp Pro Ser Leu
35 40 45
Pro Asp Leu His Arg Val Leu Gly Gln Tyr Leu Arg Asp Thr Ala Ala
50 55 60
Leu Ser Pro Pro Lys Ala Thr Val Ser Asp Thr Cys Glu Glu Val Glu
65 70 75 80
Pro Ser Leu Leu Glu Ile Leu Pro Lys Ser Ser Glu Arg Thr Pro Leu
85 90 95
Pro Leu

<210> 220
<211> 98
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 220
Ser Asp Pro Thr Arg Val Glu Thr Ala Thr Glu Thr Ala Leu His Leu
1 5 10 15
Val Leu Gly Leu Asn Ala Val Leu Gly Leu Leu Leu Leu Arg Lys Gln
20 25 30
Phe Pro Ala His Tyr Arg Arg Leu Arg His Ala Leu Trp Pro Ser Leu
35 40 45
Pro Asp Leu His Arg Val Leu Gly Gln Tyr Leu Arg Asp Thr Ala Ala
50 55 60

Leu Ser Pro Pro Arg Ala Thr Val Ser Asp Thr Cys Glu Glu Val Glu
65 70 75 80
Pro Ser Leu Leu Glu Ile Leu Pro Arg Ser Ser Glu Arg Thr Pro Leu
85 90 95
Pro Leu

<210> 221
<211> 97
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 221
Ser Asp Pro Thr Arg Val Glu Thr Ala Thr Glu Thr Leu His Leu Val
1 5 10 15
Leu Gly Leu Asn Ala Val Leu Gly Leu Leu Leu Leu Arg Lys Gln Phe
20 25 30
Pro Ala His Tyr Arg Arg Leu Arg His Ala Leu Trp Pro Ser Leu Pro
35 40 45
Asp Leu His Arg Val Leu Gly Gln Tyr Leu Arg Asp Thr Ala Ala Leu
50 55 60
Ser Pro Pro Lys Ala Thr Val Ser Asp Thr Cys Glu Glu Val Glu Pro
65 70 75 80
Ser Leu Leu Glu Ile Leu Pro Lys Ser Ser Glu Arg Thr Pro Leu Pro
[0181] 85 90 95
Leu

<210> 222
<211> 97
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 222
Ser Asp Pro Thr Arg Val Glu Thr Ala Thr Glu Thr Leu His Leu Val
1 5 10 15
Leu Gly Leu Asn Ala Val Leu Gly Leu Leu Leu Leu Arg Lys Gln Phe
20 25 30
Pro Ala His Tyr Arg Arg Leu Arg His Ala Leu Trp Pro Ser Leu Pro
35 40 45
Asp Leu His Arg Val Leu Gly Gln Tyr Leu Arg Asp Thr Ala Ala Leu
50 55 60
Ser Pro Pro Arg Ala Thr Val Ser Asp Thr Cys Glu Glu Val Glu Pro
65 70 75 80
Ser Leu Leu Glu Ile Leu Pro Arg Ser Ser Glu Arg Thr Pro Leu Pro
85 90 95
Leu

<210> 223

<211> 96
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 223
Ser Asp Pro Thr Arg Val Glu Thr Ala Thr Glu Thr His Leu Val Leu
1 5 10 15
Gly Leu Asn Ala Val Leu Gly Leu Leu Leu Leu Arg Lys Gln Phe Pro
20 25 30
Ala His Tyr Arg Arg Leu Arg His Ala Leu Trp Pro Ser Leu Pro Asp
35 40 45
Leu His Arg Val Leu Gly Gln Tyr Leu Arg Asp Thr Ala Ala Leu Ser
50 55 60
Pro Pro Lys Ala Thr Val Ser Asp Thr Cys Glu Glu Val Glu Pro Ser
65 70 75 80
Leu Leu Glu Ile Leu Pro Lys Ser Ser Glu Arg Thr Pro Leu Pro Leu
85 90 95
<210> 224
<211> 96
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
<221> source
[0182] <223> /注释 = “人工序列的描述：合成多肽”
<400> 224
Ser Asp Pro Thr Arg Val Glu Thr Ala Thr Glu Thr His Leu Val Leu
1 5 10 15
Gly Leu Asn Ala Val Leu Gly Leu Leu Leu Leu Arg Lys Gln Phe Pro
20 25 30
Ala His Tyr Arg Arg Leu Arg His Ala Leu Trp Pro Ser Leu Pro Asp
35 40 45
Leu His Arg Val Leu Gly Gln Tyr Leu Arg Asp Thr Ala Ala Leu Ser
50 55 60
Pro Pro Arg Ala Thr Val Ser Asp Thr Cys Glu Glu Val Glu Pro Ser
65 70 75 80
Leu Leu Glu Ile Leu Pro Arg Ser Ser Glu Arg Thr Pro Leu Pro Leu
85 90 95
<210> 225
<211> 109
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 225
Ser Asp Pro Thr Arg Val Glu Thr Ala Thr Glu Thr Ala Trp Ile Leu
1 5 10 15
Val Leu Ile Ser Leu Val Thr Ala Leu His Leu Val Leu Gly Leu Asn
20 25 30

Ala Val Leu Gly Leu Leu Leu Leu Arg Lys Gln Phe Pro Ala His Tyr
35 40 45
Arg Arg Leu Arg His Ala Leu Trp Pro Ser Leu Pro Asp Leu His Arg
50 55 60
Val Leu Gly Gln Tyr Leu Arg Asp Thr Ala Ala Leu Ser Pro Pro Lys
65 70 75 80
Ala Thr Val Ser Asp Thr Cys Glu Glu Val Glu Pro Ser Leu Leu Glu
85 90 95
Ile Leu Pro Lys Ser Ser Glu Arg Thr Pro Leu Pro Leu
100 105

<210> 226
<211> 109
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 226
Ser Asp Pro Thr Arg Val Glu Thr Ala Thr Glu Thr Ala Trp Ile Leu
1 5 10 15
Val Leu Ile Ser Leu Val Thr Ala Leu His Leu Val Leu Gly Leu Asn
20 25 30
Ala Val Leu Gly Leu Leu Leu Leu Arg Lys Gln Phe Pro Ala His Tyr
35 40 45
Arg Arg Leu Arg His Ala Leu Trp Pro Ser Leu Pro Asp Leu His Arg
[0183] 50 55 60
Val Leu Gly Gln Tyr Leu Arg Asp Thr Ala Ala Leu Ser Pro Pro Arg
65 70 75 80
Ala Thr Val Ser Asp Thr Cys Glu Glu Val Glu Pro Ser Leu Leu Glu
85 90 95
Ile Leu Pro Arg Ser Ser Glu Arg Thr Pro Leu Pro Leu
100 105

<210> 227
<211> 95
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 227
Ser Asp Pro Thr Arg Val Glu Thr Ala Thr Glu His Leu Val Leu Gly
1 5 10 15
Leu Asn Ala Val Leu Gly Leu Leu Leu Leu Arg Lys Gln Phe Pro Ala
20 25 30
His Tyr Arg Arg Leu Arg His Ala Leu Trp Pro Ser Leu Pro Asp Leu
35 40 45
His Arg Val Leu Gly Gln Tyr Leu Arg Asp Thr Ala Ala Leu Ser Pro
50 55 60
Pro Lys Ala Thr Val Ser Asp Thr Cys Glu Glu Val Glu Pro Ser Leu
65 70 75 80
Leu Glu Ile Leu Pro Lys Ser Ser Glu Arg Thr Pro Leu Pro Leu

85 90 95

<210> 228
<211> 95
<212> PRT
<213> 人工序列（Artificial Sequence）
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 228
Ser Asp Pro Thr Arg Val Glu Thr Ala Thr Glu His Leu Val Leu Gly
1 5 10 15
Leu Asn Ala Val Leu Gly Leu Leu Leu Leu Arg Lys Gln Phe Pro Ala
20 25 30
His Tyr Arg Arg Leu Arg His Ala Leu Trp Pro Ser Leu Pro Asp Leu
35 40 45
His Arg Val Leu Gly Gln Tyr Leu Arg Asp Thr Ala Ala Leu Ser Pro
50 55 60
Pro Arg Ala Thr Val Ser Asp Thr Cys Glu Glu Val Glu Pro Ser Leu
65 70 75 80
Leu Glu Ile Leu Pro Arg Ser Ser Glu Arg Thr Pro Leu Pro Leu
85 90 95

<210> 229
<211> 92
<212> PRT
<213> 人工序列（Artificial Sequence）
[0184] <220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 229
Ser Asp Pro Thr Arg Val Glu Thr His Leu Val Leu Gly Leu Asn Ala
1 5 10 15
Val Leu Gly Leu Leu Leu Leu Arg Lys Gln Phe Pro Ala His Tyr Arg
20 25 30
Arg Leu Arg His Ala Leu Trp Pro Ser Leu Pro Asp Leu His Arg Val
35 40 45
Leu Gly Gln Tyr Leu Arg Asp Thr Ala Ala Leu Ser Pro Pro Lys Ala
50 55 60
Thr Val Ser Asp Thr Cys Glu Glu Val Glu Pro Ser Leu Leu Glu Ile
65 70 75 80
Leu Pro Lys Ser Ser Glu Arg Thr Pro Leu Pro Leu
85 90

<210> 230
<211> 92
<212> PRT
<213> 人工序列（Artificial Sequence）
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 230
Ser Asp Pro Thr Arg Val Glu Thr His Leu Val Leu Gly Leu Asn Ala
1 5 10 15

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

<210> 231
<211> 87
<212> PRT
<213> 人工序列（Artificial Sequence）
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 231
Ser Asp Pro His Leu Val Leu Gly Leu Asn Ala Val Leu Gly Leu Leu
1 5 10 15
Leu Leu Arg Lys Gln Phe Pro Ala His Tyr Arg Arg Leu Arg His Ala
20 25 30
Leu Trp Pro Ser Leu Pro Asp Leu His Arg Val Leu Gly Gln Tyr Leu
35 40 45
Arg Asp Thr Ala Ala Leu Ser Pro Pro Lys Ala Thr Val Ser Asp Thr
[0185] 50 55 60
Cys Glu Glu Val Glu Pro Ser Leu Leu Glu Ile Leu Pro Lys Ser Ser
65 70 75 80
Glu Arg Thr Pro Leu Pro Leu
85

<210> 232
<211> 87
<212> PRT
<213> 人工序列（Artificial Sequence）
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 232
Ser Asp Pro His Leu Val Leu Gly Leu Asn Ala Val Leu Gly Leu Leu
1 5 10 15
Leu Leu Arg Lys Gln Phe Pro Ala His Tyr Arg Arg Leu Arg His Ala
20 25 30
Leu Trp Pro Ser Leu Pro Asp Leu His Arg Val Leu Gly Gln Tyr Leu
35 40 45
Arg Asp Thr Ala Ala Leu Ser Pro Pro Arg Ala Thr Val Ser Asp Thr
50 55 60
Cys Glu Glu Val Glu Pro Ser Leu Leu Glu Ile Leu Pro Arg Ser Ser
65 70 75 80
Glu Arg Thr Pro Leu Pro Leu
85

<210> 233

<211> 86
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 233
Ser Asp His Leu Val Leu Gly Leu Asn Ala Val Leu Gly Leu Leu Leu
1 5 10 15
Leu Arg Lys Gln Phe Pro Ala His Tyr Arg Arg Leu Arg His Ala Leu
20 25 30
Trp Pro Ser Leu Pro Asp Leu His Arg Val Leu Gly Gln Tyr Leu Arg
35 40 45
Asp Thr Ala Ala Leu Ser Pro Pro Lys Ala Thr Val Ser Asp Thr Cys
50 55 60
Glu Glu Val Glu Pro Ser Leu Leu Glu Ile Leu Pro Lys Ser Ser Glu
65 70 75 80
Arg Thr Pro Leu Pro Leu
85

<210> 234
<211> 86
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
<221> source
[0186] <223> /注释 = “人工序列的描述：合成多肽”
<400> 234
Ser Asp His Leu Val Leu Gly Leu Asn Ala Val Leu Gly Leu Leu Leu
1 5 10 15
Leu Arg Lys Gln Phe Pro Ala His Tyr Arg Arg Leu Arg His Ala Leu
20 25 30
Trp Pro Ser Leu Pro Asp Leu His Arg Val Leu Gly Gln Tyr Leu Arg
35 40 45
Asp Thr Ala Ala Leu Ser Pro Pro Arg Ala Thr Val Ser Asp Thr Cys
50 55 60
Glu Glu Val Glu Pro Ser Leu Leu Glu Ile Leu Pro Arg Ser Ser Glu
65 70 75 80
Arg Thr Pro Leu Pro Leu
85

<210> 235
<211> 55
<212> PRT
<213> 智人 (Homo sapiens)
<400> 235
Ser Asp Pro Thr Arg Val Glu Thr Ala Thr Glu Thr Ala Trp Ile Ser
1 5 10 15
Leu Val Thr Ala Leu His Leu Val Leu Gly Leu Ser Ala Val Leu Gly
20 25 30
Leu Leu Leu Leu Arg Trp Gln Phe Pro Ala His Tyr Arg Arg Leu Arg
35 40 45
His Ala Leu Trp Pro Ser Leu

50 55

<210> 236
<211> 54
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 236
Ser Asp Pro Thr Arg Val Glu Thr Ala Thr Glu Thr Trp Ile Ser Leu
1 5 10 15
Val Thr Ala Leu His Leu Val Leu Gly Leu Ser Ala Val Leu Gly Leu
20 25 30
Leu Leu Leu Arg Trp Gln Phe Pro Ala His Tyr Arg Arg Leu Arg His
35 40 45
Ala Leu Trp Pro Ser Leu
50
<210> 237
<211> 53
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 237
[0187] Ser Asp Pro Thr Arg Val Glu Thr Ala Thr Glu Thr Ile Ser Leu Val
1 5 10 15
Thr Ala Leu His Leu Val Leu Gly Leu Ser Ala Val Leu Gly Leu Leu
20 25 30
Leu Leu Arg Trp Gln Phe Pro Ala His Tyr Arg Arg Leu Arg His Ala
35 40 45
Leu Trp Pro Ser Leu
50
<210> 238
<211> 54
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 238
Ser Asp Pro Thr Arg Val Glu Thr Ala Thr Glu Thr Leu Ile Ser Leu
1 5 10 15
Val Thr Ala Leu His Leu Val Leu Gly Leu Ser Ala Val Leu Gly Leu
20 25 30
Leu Leu Leu Arg Trp Gln Phe Pro Ala His Tyr Arg Arg Leu Arg His
35 40 45
Ala Leu Trp Pro Ser Leu
50
<210> 239
<211> 52

<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 239
Ser Asp Pro Thr Arg Val Glu Thr Ala Thr Glu Thr Ser Leu Val Thr
1 5 10 15
Ala Leu His Leu Val Leu Gly Leu Ser Ala Val Leu Gly Leu Leu Leu
20 25 30
Leu Arg Trp Gln Phe Pro Ala His Tyr Arg Arg Leu Arg His Ala Leu
35 40 45
Trp Pro Ser Leu
50
<210> 240
<211> 51
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 240
Ser Asp Pro Thr Arg Val Glu Thr Ala Thr Glu Thr Leu Val Thr Ala
1 5 10 15
Leu His Leu Val Leu Gly Leu Ser Ala Val Leu Gly Leu Leu Leu Leu
[0188] 20 25 30
Arg Trp Gln Phe Pro Ala His Tyr Arg Arg Leu Arg His Ala Leu Trp
35 40 45
Pro Ser Leu
50
<210> 241
<211> 52
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 241
Ser Asp Pro Thr Arg Val Glu Thr Ala Thr Glu Thr Ile Leu Val Thr
1 5 10 15
Ala Leu His Leu Val Leu Gly Leu Ser Ala Val Leu Gly Leu Leu Leu
20 25 30
Leu Arg Trp Gln Phe Pro Ala His Tyr Arg Arg Leu Arg His Ala Leu
35 40 45
Trp Pro Ser Leu
50
<210> 242
<211> 50
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>

<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 242
Ser Asp Pro Thr Arg Val Glu Thr Ala Thr Glu Thr Val Thr Ala Leu
1 5 10 15
His Leu Val Leu Gly Leu Ser Ala Val Leu Gly Leu Leu Leu Leu Arg
20 25 30
Trp Gln Phe Pro Ala His Tyr Arg Arg Leu Arg His Ala Leu Trp Pro
35 40 45
Ser Leu
50
<210> 243
<211> 49
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 243
Ser Asp Pro Thr Arg Val Glu Thr Ala Thr Glu Thr Thr Ala Leu His
1 5 10 15
Leu Val Leu Gly Leu Ser Ala Val Leu Gly Leu Leu Leu Leu Arg Trp
20 25 30
Gln Phe Pro Ala His Tyr Arg Arg Leu Arg His Ala Leu Trp Pro Ser
35 40 45

[0189] Leu

<210> 244
<211> 48
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 244
Ser Asp Pro Thr Arg Val Glu Thr Ala Thr Glu Thr Ala Leu His Leu
1 5 10 15
Val Leu Gly Leu Ser Ala Val Leu Gly Leu Leu Leu Leu Arg Trp Gln
20 25 30
Phe Pro Ala His Tyr Arg Arg Leu Arg His Ala Leu Trp Pro Ser Leu
35 40 45
<210> 245
<211> 47
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 245
Ser Asp Pro Thr Arg Val Glu Thr Ala Thr Glu Thr Leu His Leu Val
1 5 10 15

Leu Gly Leu Ser Ala Val Leu Gly Leu Leu Leu Leu Arg Trp Gln Phe
20 25 30
Pro Ala His Tyr Arg Arg Leu Arg His Ala Leu Trp Pro Ser Leu
35 40 45
<210> 246
<211> 46
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 246
Ser Asp Pro Thr Arg Val Glu Thr Ala Thr Glu Thr His Leu Val Leu
1 5 10 15
Gly Leu Ser Ala Val Leu Gly Leu Leu Leu Leu Arg Trp Gln Phe Pro
20 25 30
Ala His Tyr Arg Arg Leu Arg His Ala Leu Trp Pro Ser Leu
35 40 45
<210> 247
<211> 56
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”

[0190]

<400> 247
Ser Asp Pro Thr Arg Val Glu Thr Ala Thr Glu Thr Ala Trp Leu Ile
1 5 10 15
Ser Leu Val Thr Ala Leu His Leu Val Leu Gly Leu Ser Ala Val Leu
20 25 30
Gly Leu Leu Leu Leu Arg Trp Gln Phe Pro Ala His Tyr Arg Arg Leu
35 40 45
Arg His Ala Leu Trp Pro Ser Leu
50 55
<210> 248
<211> 57
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 248
Ser Asp Pro Thr Arg Val Glu Thr Ala Thr Glu Thr Ala Trp Val Leu
1 5 10 15
Ile Ser Leu Val Thr Ala Leu His Leu Val Leu Gly Leu Ser Ala Val
20 25 30
Leu Gly Leu Leu Leu Leu Arg Trp Gln Phe Pro Ala His Tyr Arg Arg
35 40 45
Leu Arg His Ala Leu Trp Pro Ser Leu
50 55
<210> 249

<211> 58
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 249
Ser Asp Pro Thr Arg Val Glu Thr Ala Thr Glu Thr Ala Trp Leu Val
1 5 10 15
Leu Ile Ser Leu Val Thr Ala Leu His Leu Val Leu Gly Leu Ser Ala
20 25 30
Val Leu Gly Leu Leu Leu Leu Arg Trp Gln Phe Pro Ala His Tyr Arg
35 40 45
Arg Leu Arg His Ala Leu Trp Pro Ser Leu
50 55
<210> 250
<211> 59
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 250
Ser Asp Pro Thr Arg Val Glu Thr Ala Thr Glu Thr Ala Trp Ile Leu
1 5 10 15
[0191] Val Leu Ile Ser Leu Val Thr Ala Leu His Leu Val Leu Gly Leu Ser
20 25 30
Ala Val Leu Gly Leu Leu Leu Leu Arg Trp Gln Phe Pro Ala His Tyr
35 40 45
Arg Arg Leu Arg His Ala Leu Trp Pro Ser Leu
50 55
<210> 251
<211> 60
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 251
Ser Asp Pro Thr Arg Val Glu Thr Ala Thr Glu Thr Ala Trp Leu Ile
1 5 10 15
Leu Val Leu Ile Ser Leu Val Thr Ala Leu His Leu Val Leu Gly Leu
20 25 30
Ser Ala Val Leu Gly Leu Leu Leu Leu Arg Trp Gln Phe Pro Ala His
35 40 45
Tyr Arg Arg Leu Arg His Ala Leu Trp Pro Ser Leu
50 55 60
<210> 252
<211> 61
<212> PRT
<213> 人工序列 (Artificial Sequence)

<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 252
Ser Asp Pro Thr Arg Val Glu Thr Ala Thr Glu Thr Ala Trp Leu Leu
1 5 10 15
Ile Leu Val Leu Ile Ser Leu Val Thr Ala Leu His Leu Val Leu Gly
20 25 30
Leu Ser Ala Val Leu Gly Leu Leu Leu Leu Arg Trp Gln Phe Pro Ala
35 40 45
His Tyr Arg Arg Leu Arg His Ala Leu Trp Pro Ser Leu
50 55 60
<210> 253
<211> 62
<212> PRT
<213> 人工序列（Artificial Sequence）
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 253
Ser Asp Pro Thr Arg Val Glu Thr Ala Thr Glu Thr Ala Trp Val Leu
1 5 10 15
Leu Ile Leu Val Leu Ile Ser Leu Val Thr Ala Leu His Leu Val Leu
20 25 30
Gly Leu Ser Ala Val Leu Gly Leu Leu Leu Leu Arg Trp Gln Phe Pro
[0192] 35 40 45
Ala His Tyr Arg Arg Leu Arg His Ala Leu Trp Pro Ser Leu
50 55 60
<210> 254
<211> 63
<212> PRT
<213> 人工序列（Artificial Sequence）
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 254
Ser Asp Pro Thr Arg Val Glu Thr Ala Thr Glu Thr Ala Trp Leu Val
1 5 10 15
Leu Leu Ile Leu Val Leu Ile Ser Leu Val Thr Ala Leu His Leu Val
20 25 30
Leu Gly Leu Ser Ala Val Leu Gly Leu Leu Leu Leu Arg Trp Gln Phe
35 40 45
Pro Ala His Tyr Arg Arg Leu Arg His Ala Leu Trp Pro Ser Leu
50 55 60
<210> 255
<211> 45
<212> PRT
<213> 人工序列（Artificial Sequence）
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”

<400> 255
Ser Asp Pro Thr Arg Val Glu Thr Ala Thr Glu Thr Leu Val Leu Gly
1 5 10 15
Leu Ser Ala Val Leu Gly Leu Leu Leu Leu Arg Trp Gln Phe Pro Ala
20 25 30
His Tyr Arg Arg Leu Arg His Ala Leu Trp Pro Ser Leu
35 40 45
<210> 256
<211> 44
<212> PRT
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<220>
<221> source
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<400> 256
Ser Asp Pro Thr Arg Val Glu Thr Ala Thr Glu Thr Val Leu Gly Leu
1 5 10 15
Ser Ala Val Leu Gly Leu Leu Leu Leu Arg Trp Gln Phe Pro Ala His
20 25 30
Tyr Arg Arg Leu Arg His Ala Leu Trp Pro Ser Leu
35 40
<210> 257
<211> 43
<212> PRT
<213> 人工序列 (Artificial Sequence)
[0193] <220>
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<400> 257
Ser Asp Pro Thr Arg Val Glu Thr Ala Thr Glu Thr Leu Gly Leu Ser
1 5 10 15
Ala Val Leu Gly Leu Leu Leu Leu Arg Trp Gln Phe Pro Ala His Tyr
20 25 30
Arg Arg Leu Arg His Ala Leu Trp Pro Ser Leu
35 40
<210> 258
<211> 42
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<220>
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<400> 258
Ser Asp Pro Thr Arg Val Glu Thr Ala Thr Glu Thr Gly Leu Ser Ala
1 5 10 15
Val Leu Gly Leu Leu Leu Leu Arg Trp Gln Phe Pro Ala His Tyr Arg
20 25 30
Arg Leu Arg His Ala Leu Trp Pro Ser Leu
35 40
<210> 259
<211> 41

<212> PRT
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<220>
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<400> 259
Ser Asp Pro Thr Arg Val Glu Thr Ala Thr Glu Thr Leu Ser Ala Val
1 5 10 15
Leu Gly Leu Leu Leu Leu Arg Trp Gln Phe Pro Ala His Tyr Arg Arg
20 25 30
Leu Arg His Ala Leu Trp Pro Ser Leu
35 40
<210> 260
<211> 45
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
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Ser Asp Pro Thr Arg Val Glu Thr Ala Thr Glu His Leu Val Leu Gly
1 5 10 15
Leu Ser Ala Val Leu Gly Leu Leu Leu Leu Arg Trp Gln Phe Pro Ala
20 25 30
His Tyr Arg Arg Leu Arg His Ala Leu Trp Pro Ser Leu
[0194] 35 40 45
<210> 261
<211> 44
<212> PRT
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<400> 261
Ser Asp Pro Thr Arg Val Glu Thr Ala Thr His Leu Val Leu Gly Leu
1 5 10 15
Ser Ala Val Leu Gly Leu Leu Leu Leu Arg Trp Gln Phe Pro Ala His
20 25 30
Tyr Arg Arg Leu Arg His Ala Leu Trp Pro Ser Leu
35 40
<210> 262
<211> 43
<212> PRT
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<221> source
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<400> 262
Ser Asp Pro Thr Arg Val Glu Thr Ala His Leu Val Leu Gly Leu Ser
1 5 10 15
Ala Val Leu Gly Leu Leu Leu Leu Arg Trp Gln Phe Pro Ala His Tyr

20 25 30
Arg Arg Leu Arg His Ala Leu Trp Pro Ser Leu
35 40
<210> 263
<211> 42
<212> PRT
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<220>
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<400> 263
Ser Asp Pro Thr Arg Val Glu Thr His Leu Val Leu Gly Leu Ser Ala
1 5 10 15
Val Leu Gly Leu Leu Leu Leu Arg Trp Gln Phe Pro Ala His Tyr Arg
20 25 30
Arg Leu Arg His Ala Leu Trp Pro Ser Leu
35 40
<210> 264
<211> 41
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<400> 264
[0195] Ser Asp Pro Thr Arg Val Glu His Leu Val Leu Gly Leu Ser Ala Val
1 5 10 15
Leu Gly Leu Leu Leu Leu Arg Trp Gln Phe Pro Ala His Tyr Arg Arg
20 25 30
Leu Arg His Ala Leu Trp Pro Ser Leu
35 40
<210> 265
<211> 40
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<213> 人工序列 (Artificial Sequence)
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 265
Ser Asp Pro Thr Arg Val His Leu Val Leu Gly Leu Ser Ala Val Leu
1 5 10 15
Gly Leu Leu Leu Leu Arg Trp Gln Phe Pro Ala His Tyr Arg Arg Leu
20 25 30
Arg His Ala Leu Trp Pro Ser Leu
35 40
<210> 266
<211> 39
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
<221> source

<223> /注释 = “人工序列的描述：合成多肽”
<400> 266
Ser Asp Pro Thr Arg His Leu Val Leu Gly Leu Ser Ala Val Leu Gly
1 5 10 15
Leu Leu Leu Leu Arg Trp Gln Phe Pro Ala His Tyr Arg Arg Leu Arg
20 25 30
His Ala Leu Trp Pro Ser Leu
35
<210> 267
<211> 38
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 267
Ser Asp Pro Thr His Leu Val Leu Gly Leu Ser Ala Val Leu Gly Leu
1 5 10 15
Leu Leu Leu Arg Trp Gln Phe Pro Ala His Tyr Arg Arg Leu Arg His
20 25 30
Ala Leu Trp Pro Ser Leu
35
<210> 268
<211> 37
<212> PRT
[0196] <213> 人工序列 (Artificial Sequence)
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Ser Asp Pro His Leu Val Leu Gly Leu Ser Ala Val Leu Gly Leu Leu
1 5 10 15
Leu Leu Arg Trp Gln Phe Pro Ala His Tyr Arg Arg Leu Arg His Ala
20 25 30
Leu Trp Pro Ser Leu
35
<210> 269
<211> 36
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 269
Ser Asp His Leu Val Leu Gly Leu Ser Ala Val Leu Gly Leu Leu Leu
1 5 10 15
Leu Arg Trp Gln Phe Pro Ala His Tyr Arg Arg Leu Arg His Ala Leu
20 25 30
Trp Pro Ser Leu
35
<210> 270

<211> 35
<212> PRT
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<220>
<221> source
<223> /注释 = “人工序列的描述：合成多肽”
<400> 270
Ser His Leu Val Leu Gly Leu Ser Ala Val Leu Gly Leu Leu Leu Leu
1 5 10 15
Arg Trp Gln Phe Pro Ala His Tyr Arg Arg Leu Arg His Ala Leu Trp
20 25 30
Pro Ser Leu
35
<210> 271
<211> 34
<212> PRT
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<221> source
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<400> 271
His Leu Val Leu Gly Leu Ser Ala Val Leu Gly Leu Leu Leu Leu Arg
1 5 10 15
Trp Gln Phe Pro Ala His Tyr Arg Arg Leu Arg His Ala Leu Trp Pro
20 25 30

[0197] Ser Leu

<210> 272
<211> 244
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
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<223> /注释 = “人工序列的描述：合成多肽”
<400> 272
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15
His Ala Ala Arg Pro Ser Asp Pro Thr Arg Val Glu Thr Ala Thr Glu
20 25 30
Thr Ala Trp Ile Ser Leu Val Thr Ala Leu Leu Leu Val Leu Gly Leu
35 40 45
Asn Ala Val Leu Gly Leu Leu Leu Leu Arg Lys Gln Phe Pro Ala His
50 55 60
Tyr Arg Arg Leu Arg His Ala Leu Trp Pro Ser Leu Pro Asp Leu His
65 70 75 80
Arg Val Leu Gly Gln Tyr Leu Arg Asp Thr Ala Ala Leu Ser Pro Pro
85 90 95
Arg Ala Thr Val Ser Asp Thr Cys Glu Glu Val Glu Pro Ser Leu Leu
100 105 110
Glu Ile Leu Pro Arg Ser Ser Glu Arg Thr Pro Leu Pro Leu Leu Glu
115 120 125

Gln Gln Asp Lys Val Pro Glu Pro Ala Ser Leu Ser Ser Asn His Ser
130 135 140
Leu Thr Ser Cys Phe Thr Asn Gln Gly Tyr Phe Phe Phe His Leu Pro
145 150 155 160
Asp Ala Leu Glu Ile Glu Ala Cys Gln Asp Glu Gly Val Ala Gly Ala
165 170 175
Pro Thr Gly Ser Ser Pro Gln Pro Leu Gln Pro Leu Ser Gly Glu Asp
180 185 190
Asp Ala Tyr Cys Thr Phe Pro Ser Arg Asp Asp Leu Leu Leu Phe Ser
195 200 205
Pro Ser Gly Gln Gly Glu Phe Arg Ala Leu Asn Ala Arg Leu Pro Leu
210 215 220
Asn Thr Asp Ala Tyr Leu Ser Leu Gln Glu Leu Gln Gly Gln Asp Pro
225 230 235 240
Thr His Leu Val

<210> 273
<211> 203
<212> PRT
<213> 人工序列 (Artificial Sequence)
<220>
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<223> /注释 = “人工序列的描述：合成多肽”
<400> 273
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
[0198] 1 5 10 15
His Ala Ala Arg Pro Ser Asp Pro Thr Arg Val Glu Thr Ala Thr Glu
20 25 30
Thr Ala Trp Ile Ser Leu Val Thr Ala Leu His Leu Val Leu Gly Leu
35 40 45
Asn Ala Val Leu Gly Leu Leu Leu Leu Arg Lys Gln Phe Pro Ala His
50 55 60
Tyr Arg Arg Leu Arg His Ala Leu Trp Pro Ser Leu Pro Asp Leu His
65 70 75 80
Arg Val Leu Gly Gln Tyr Leu Arg Asp Thr Ala Ala Leu Ser Pro Pro
85 90 95
Arg Ala Thr Val Ser Asp Thr Cys Glu Glu Val Glu Pro Ser Leu Leu
100 105 110
Glu Ile Leu Pro Arg Ser Ser Glu Arg Thr Pro Leu Pro Leu Leu Glu
115 120 125
Asp Glu Gly Val Ala Gly Ala Pro Thr Gly Ser Ser Pro Gln Pro Leu
130 135 140
Gln Pro Leu Ser Gly Glu Asp Asp Ala Tyr Cys Thr Phe Pro Ser Arg
145 150 155 160
Asp Asp Leu Leu Leu Phe Ser Pro Ser Gly Gln Gly Glu Phe Arg Ala
165 170 175
Leu Asn Ala Arg Leu Pro Leu Asn Thr Asp Ala Tyr Leu Ser Leu Gln
180 185 190
Glu Leu Gln Gly Gln Asp Pro Thr His Leu Val
195 200
<210> 274

<211> 394
<212> PRT
<213> 人工序列（Artificial Sequence）
<220>
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<223> /注释 = “人工序列的描述：合成多肽”
<400> 274

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

[0199]

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

Asp Leu Leu Leu Phe Ser Pro Ser Gly Gln Gly Glu Phe Arg Ala Leu
355 360 365
Asn Ala Arg Leu Pro Leu Asn Thr Asp Ala Tyr Leu Ser Leu Gln Glu
370 375 380
Leu Gln Gly Gln Asp Pro Thr His Leu Val
385 390
<210> 275
<211> 353
<212> PRT
<213> 人工序列（Artificial Sequence）
<220>
<221> source
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<400> 275
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15
His Ala Ala Arg Pro Pro Gly Trp Phe Leu Asp Ser Pro Asp Arg Pro
20 25 30
Trp Asn Pro Pro Thr Phe Ser Pro Ala Leu Leu Val Val Thr Glu Gly
35 40 45
Asp Asn Ala Thr Phe Thr Cys Ser Phe Ser Asn Thr Ser Glu Ser Phe
50 55 60
His Val Ile Trp His Arg Glu Ser Pro Ser Gly Gln Thr Asp Thr Leu
65 70 75 80
Ala Ala Phe Pro Glu Asp Arg Ser Gln Pro Gly Gln Asp Cys Arg Phe
[0200] 85 90 95
Arg Val Thr Gln Leu Pro Asn Gly Arg Asp Phe His Met Ser Val Val
100 105 110
Arg Ala Arg Arg Asn Asp Ser Gly Thr Tyr Val Cys Gly Val Ile Ser
115 120 125
Leu Ala Pro Lys Ile Gln Ile Lys Glu Ser Leu Arg Ala Glu Leu Arg
130 135 140
Val Thr Glu Arg Arg Ala Glu Val Pro Thr Ala His Pro Ser Pro Ser
145 150 155 160
Pro Arg Pro Ala Gly Gln Phe Gln Thr Leu Val Ser Asp Pro Thr Arg
165 170 175
Val Glu Thr Ala Thr Glu Thr Ala Trp Ile Ser Leu Val Thr Ala Leu
180 185 190
His Leu Val Leu Gly Leu Asn Ala Val Leu Gly Leu Leu Leu Leu Arg
195 200 205
Lys Gln Phe Pro Ala His Tyr Arg Arg Leu Arg His Ala Leu Trp Pro
210 215 220
Ser Leu Pro Asp Leu His Arg Val Leu Gly Gln Tyr Leu Arg Asp Thr
225 230 235 240
Ala Ala Leu Ser Pro Pro Arg Ala Thr Val Ser Asp Thr Cys Glu Glu
245 250 255
Val Glu Pro Ser Leu Leu Glu Ile Leu Pro Arg Ser Ser Glu Arg Thr
260 265 270
Pro Leu Pro Leu Leu Glu Asp Glu Gly Val Ala Gly Ala Pro Thr Gly
275 280 285
Ser Ser Pro Gln Pro Leu Gln Pro Leu Ser Gly Glu Asp Asp Ala Tyr

[0201]

290 295 300

Cys Thr Phe Pro Ser Arg Asp Asp Leu Leu Leu Phe Ser Pro Ser Gly
305 310 315 320
Gln Gly Glu Phe Arg Ala Leu Asn Ala Arg Leu Pro Leu Asn Thr Asp
325 330 335
Ala Tyr Leu Ser Leu Gln Glu Leu Gln Gly Gln Asp Pro Thr His Leu
340 345 350
Val

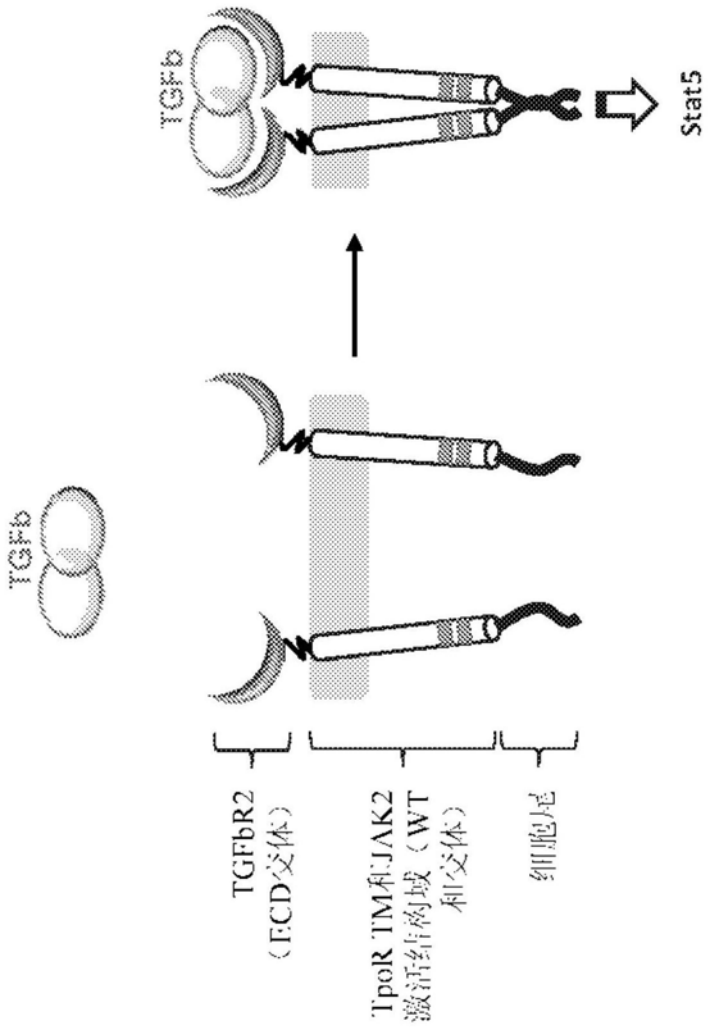


图1

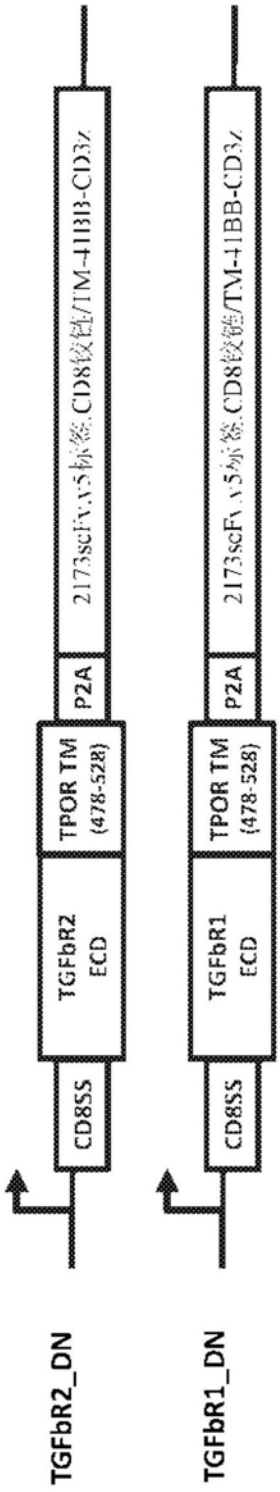

CD8SS
TGFbR2 ECD
TPOR TM (478-528)
P2A
2173scFv-v5标签-CD8铰链/TM-41BB-CD3z
TGFbR2_DN
CD8SS
TGFbR1 ECD
TPOR TM (478-528)
P2A
2173scFv-v5标签-CD8铰链/TM-41BB-CD3z
TGFbR1_DN

图2A

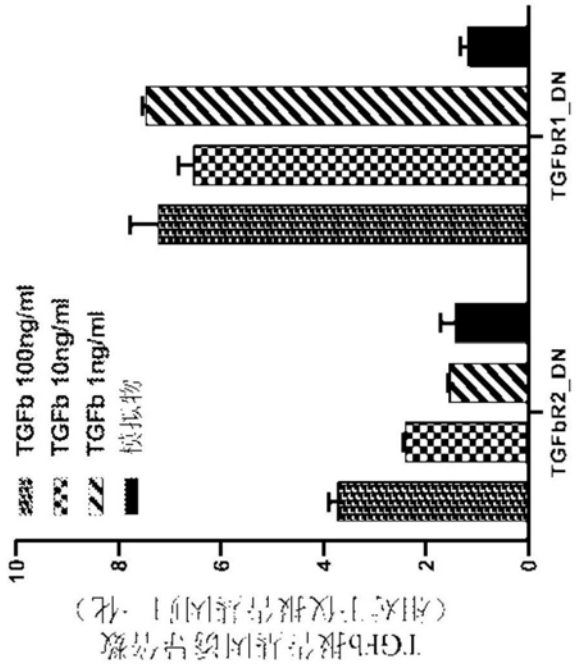

TGFb 100ng/ml
TGFb 10ng/ml
TGFb 1ng/ml
载体物
TGFbR1_DN
TGFbR2_DN
0
2
4
6
8
10

图2B

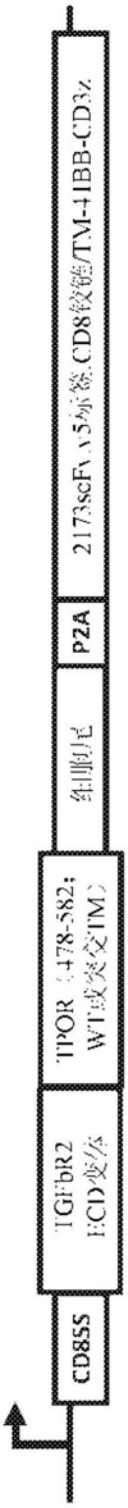

CD8SS
TGFbR2
ECD变体
TPOR
WT或突变TM
细胞内
P2A
2173scFv
CD8铰链/TM-4IBB-CD3z

图3

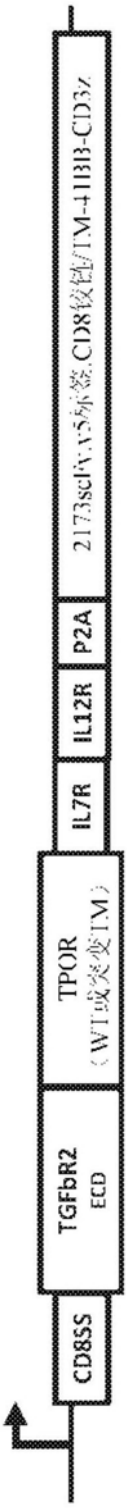


图4A

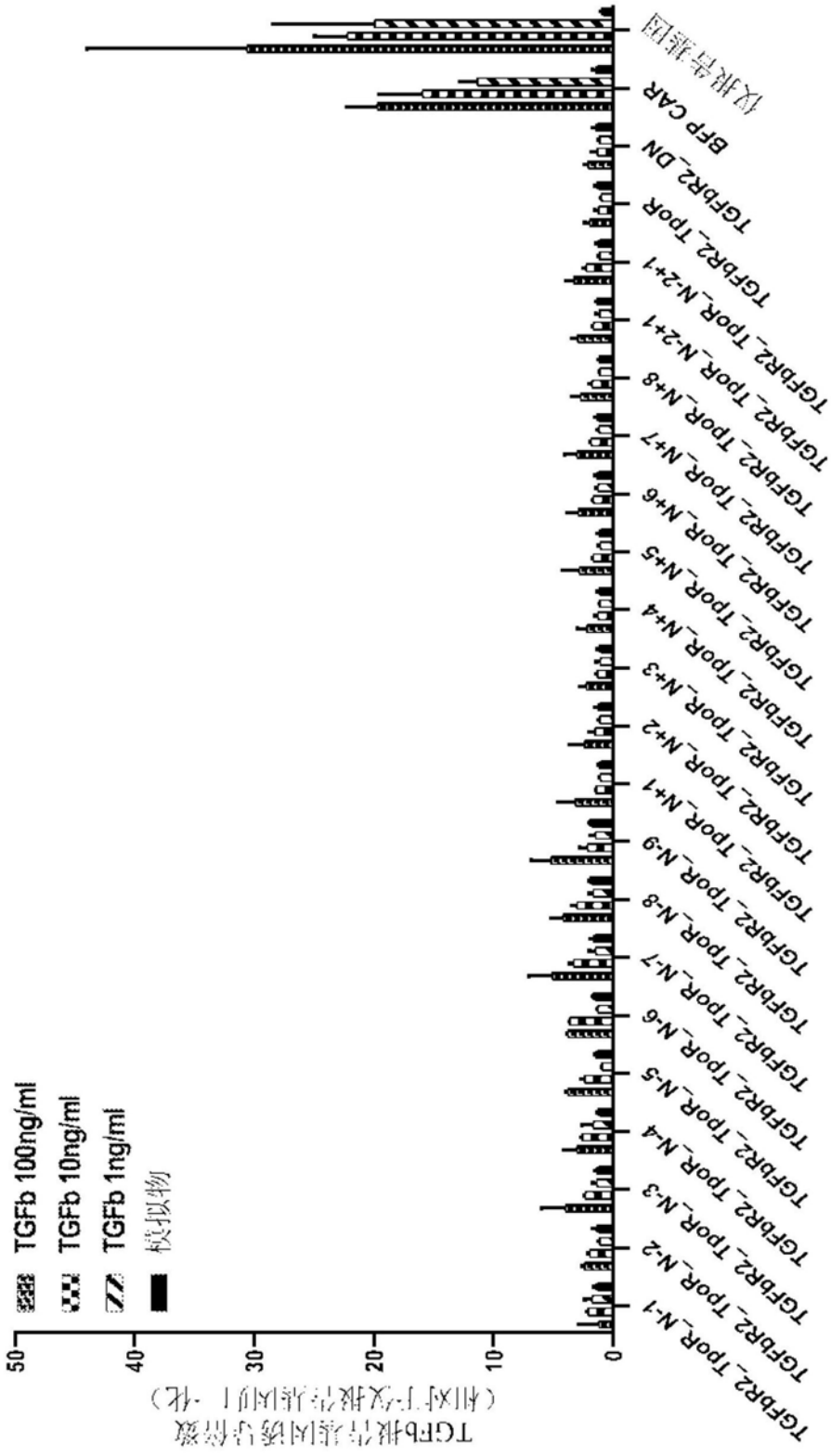

TGFb 100ng/ml
TGFb 10ng/ml
TGFb 1ng/ml
模拟物
TGFb抵抗逆转诱导倍数
（相对于仅抵抗逆转dl -化）
0
10
20
30
40
50
TGFbR2_TPoR_N-1
TGFbR2_TPoR_N-2
TGFbR2_TPoR_N-3
TGFbR2_TPoR_N-4
TGFbR2_TPoR_N-5
TGFbR2_TPoR_N-6
TGFbR2_TPoR_N-7
TGFbR2_TPoR_N-8
TGFbR2_TPoR_N-9
TGFbR2_TPoR_N+1
TGFbR2_TPoR_N+2
TGFbR2_TPoR_N+3
TGFbR2_TPoR_N+4
TGFbR2_TPoR_N+5
TGFbR2_TPoR_N+6
TGFbR2_TPoR_N+7
TGFbR2_TPoR_N+8
TGFbR2_TPoR_N-2+1
TGFbR2_TPoR_N-2+1
TGFbR2_TPoR
TGFbR2_DN
BFP CAR
仅抵抗逆转

图4B

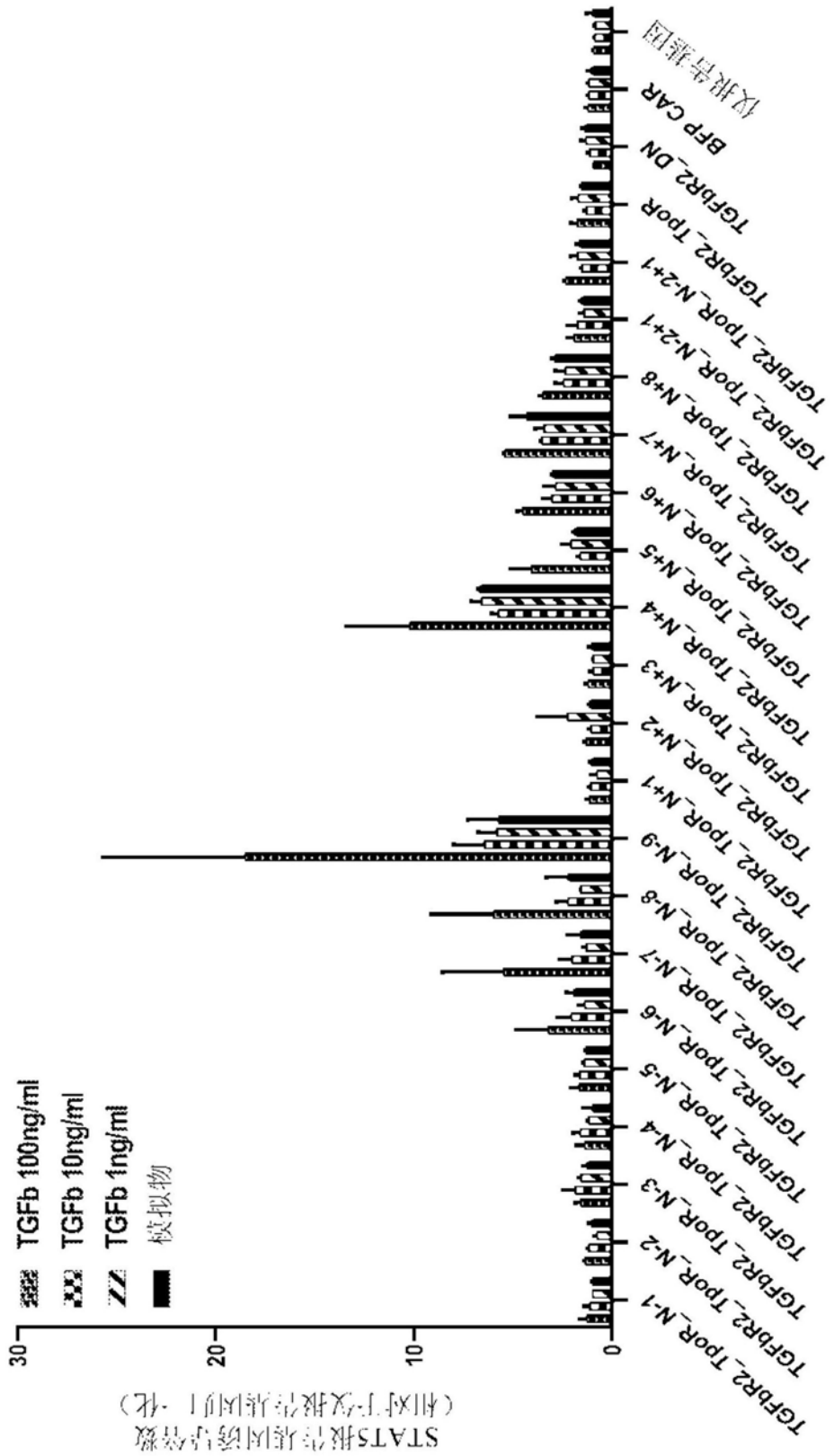

STAT5报告基因检测诱导倍数
（相对于仅报告基因的上一化）
30
20
10
0
TGFb 100ng/ml
TGFb 10ng/ml
TGFb 1ng/ml
模拟物
TGFbR2_TporR_N-1
TGFbR2_TporR_N-2
TGFbR2_TporR_N-3
TGFbR2_TporR_N-4
TGFbR2_TporR_N-5
TGFbR2_TporR_N-6
TGFbR2_TporR_N-7
TGFbR2_TporR_N-8
TGFbR2_TporR_N-9
TGFbR2_TporR_N+1
TGFbR2_TporR_N+2
TGFbR2_TporR_N+3
TGFbR2_TporR_N+4
TGFbR2_TporR_N+5
TGFbR2_TporR_N+6
TGFbR2_TporR_N+7
TGFbR2_TporR_N+8
TGFbR2_TporR_N-2+1
TGFbR2_TporR_N-2+1
TGFbR2_TporR
TGFbR2_DN
BFP CAR
仅报告基因

图4C

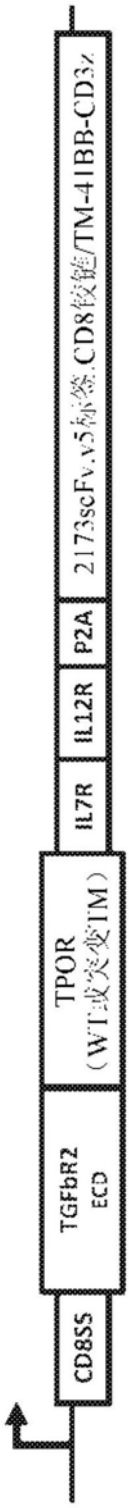

CD8SS
TGFbR2
ECD
TPOR
(WT或突变TM)
IL7R
IL12R
P2A
2173scFv.v5标签.CD8铰链/TM-41BB-CD3z

图5A

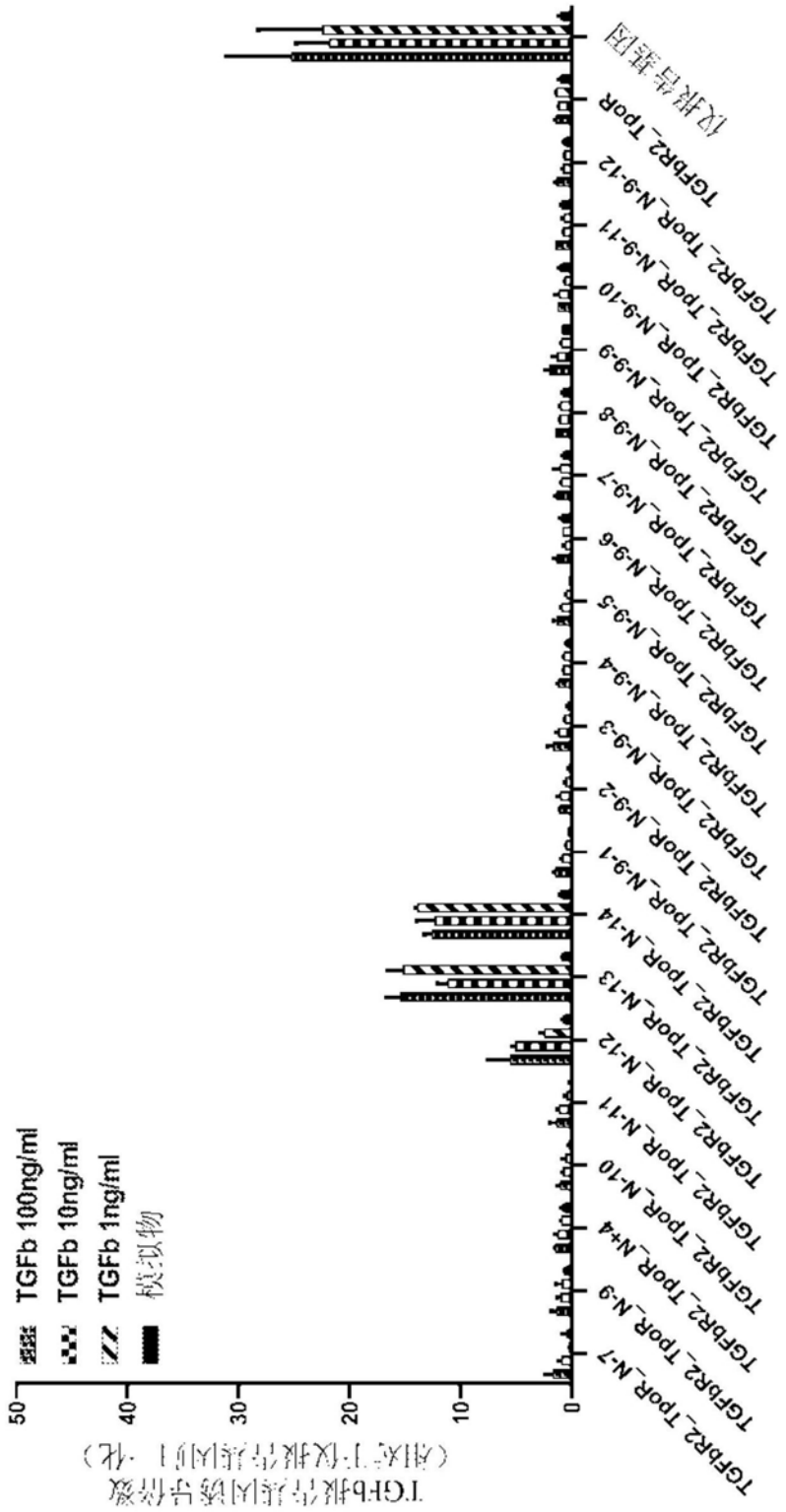

TGFb 100ng/ml
TGFb 10ng/ml
TGFb 1ng/ml
模拟物
TGF-β报告基因诱导倍数
（相对于仅报告基因对照）
0
10
20
30
40
50
仅报告基因
TGFbR2_TporA
TGFbR2_TporA_N-9-12
TGFbR2_TporA_N-9-11
TGFbR2_TporA_N-9-10
TGFbR2_TporA_N-9-9
TGFbR2_TporA_N-9-8
TGFbR2_TporA_N-9-7
TGFbR2_TporA_N-9-6
TGFbR2_TporA_N-9-5
TGFbR2_TporA_N-9-4
TGFbR2_TporA_N-9-3
TGFbR2_TporA_N-9-2
TGFbR2_TporA_N-9-1
TGFbR2_TporA_N-14
TGFbR2_TporA_N-13
TGFbR2_TporA_N-12
TGFbR2_TporA_N-11
TGFbR2_TporA_N-10
TGFbR2_TporA_N+4
TGFbR2_TporA_N-9
TGFbR2_TporA_N-7

图5B

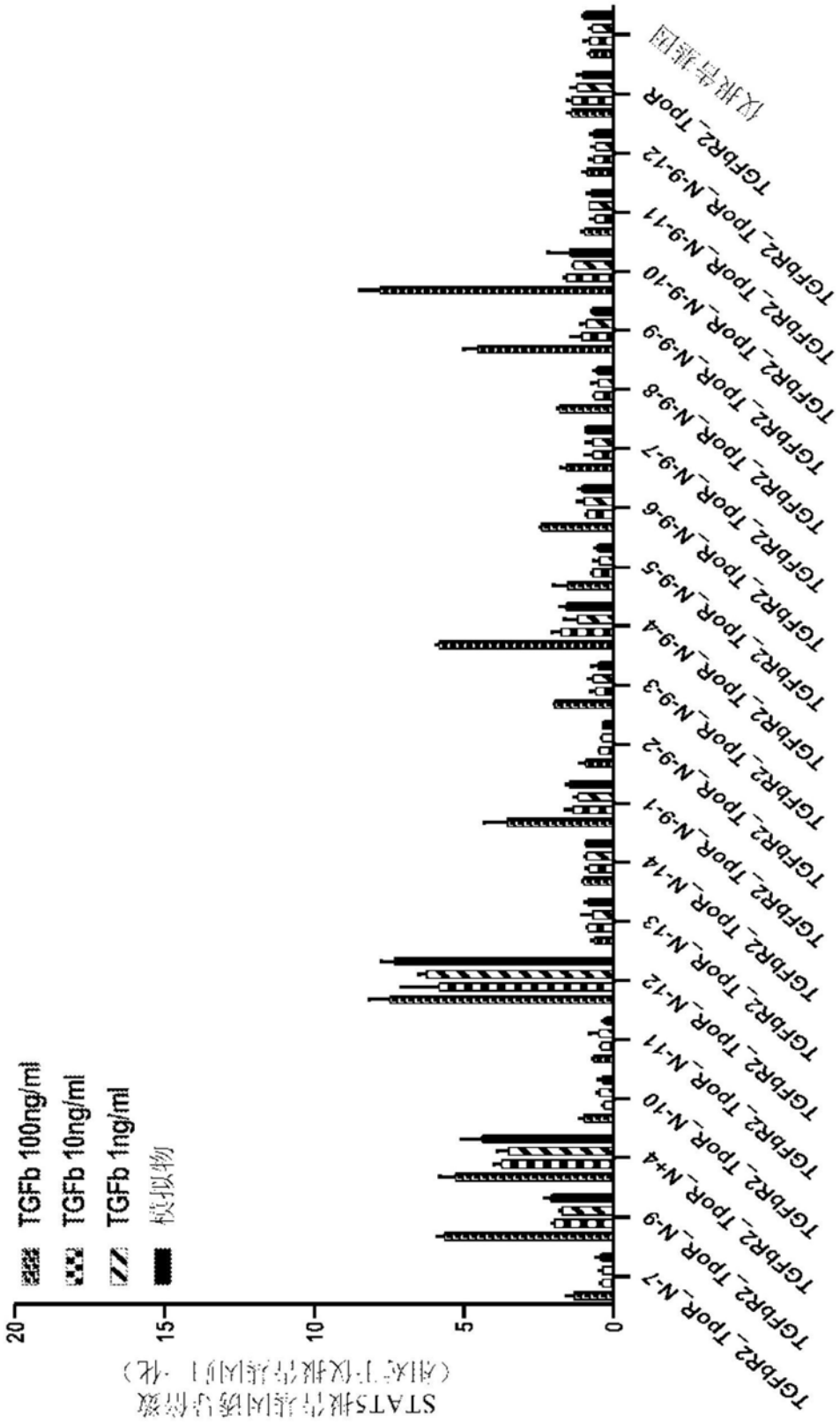

TGFbR2_TPoR_N-7
TGFbR2_TPoR_N-9
TGFbR2_TPoR_N+4
TGFbR2_TPoR_N-10
TGFbR2_TPoR_N-11
TGFbR2_TPoR_N-12
TGFbR2_TPoR_N-13
TGFbR2_TPoR_N-14
TGFbR2_TPoR_N-9-1
TGFbR2_TPoR_N-9-2
TGFbR2_TPoR_N-9-3
TGFbR2_TPoR_N-9-4
TGFbR2_TPoR_N-9-5
TGFbR2_TPoR_N-9-6
TGFbR2_TPoR_N-9-7
TGFbR2_TPoR_N-9-8
TGFbR2_TPoR_N-9-9
TGFbR2_TPoR_N-9-10
TGFbR2_TPoR_N-9-11
TGFbR2_TPoR_N-9-12
TGFbR2_TPoR
仅抗体对照
0
5
10
15
20
STAT5批次间诱导倍数
（相对于仅抗体对照归一化）
模拟物
TGFb 1ng/ml
TGFb 10ng/ml
TGFb 100ng/ml

图5C

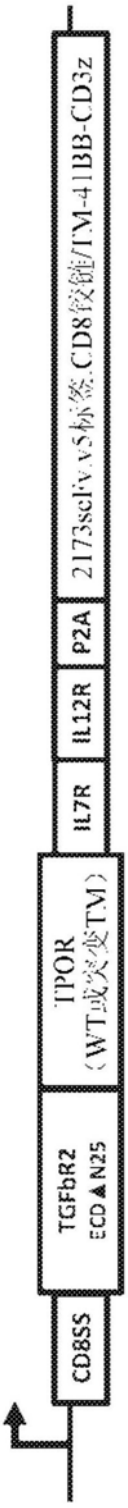

CD8SS
TGFbR2
ECD▲N25
TPOR
（WT或突变TM）
IL7R
IL12R
P2A
2173scFv-v5标签-CD8铰链/TM-41BB-CD3z

图6A

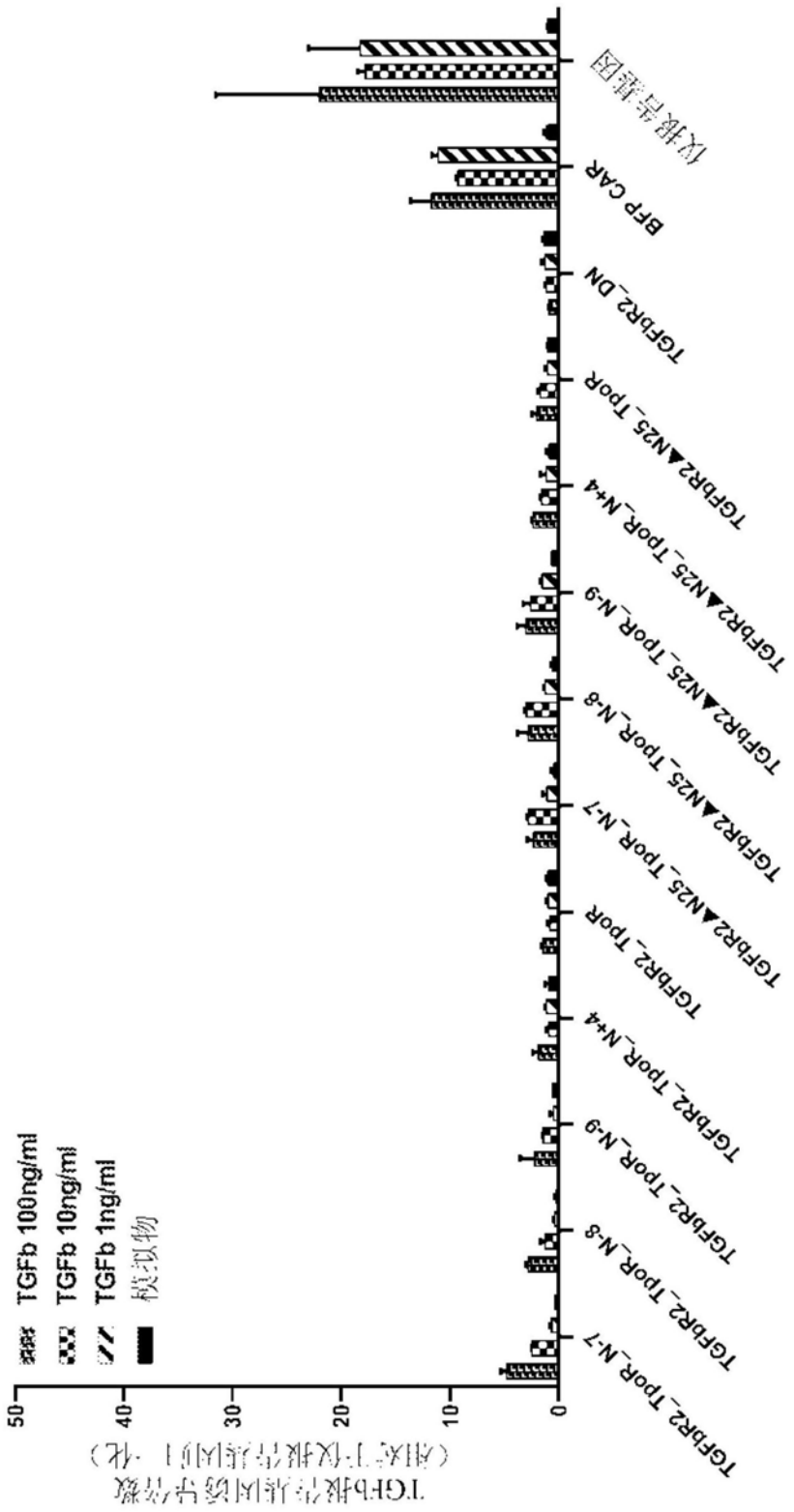

TGFb 100ng/ml
TGFb 10ng/ml
TGFb 1ng/ml
模拟物
0
10
20
30
40
50
TGFbR2_TporR_N-7
TGFbR2_TporR_N-8
TGFbR2_TporR_N-9
TGFbR2_TporR_N+4
TGFbR2_TporR
TGFbR2▲N25_TporR_N-7
TGFbR2▲N25_TporR_N-8
TGFbR2▲N25_TporR_N-9
TGFbR2▲N25_TporR_N+4
TGFbR2▲N25_TporR
TGFbR2_DN
BFP CAR
仅报告基因

图6B

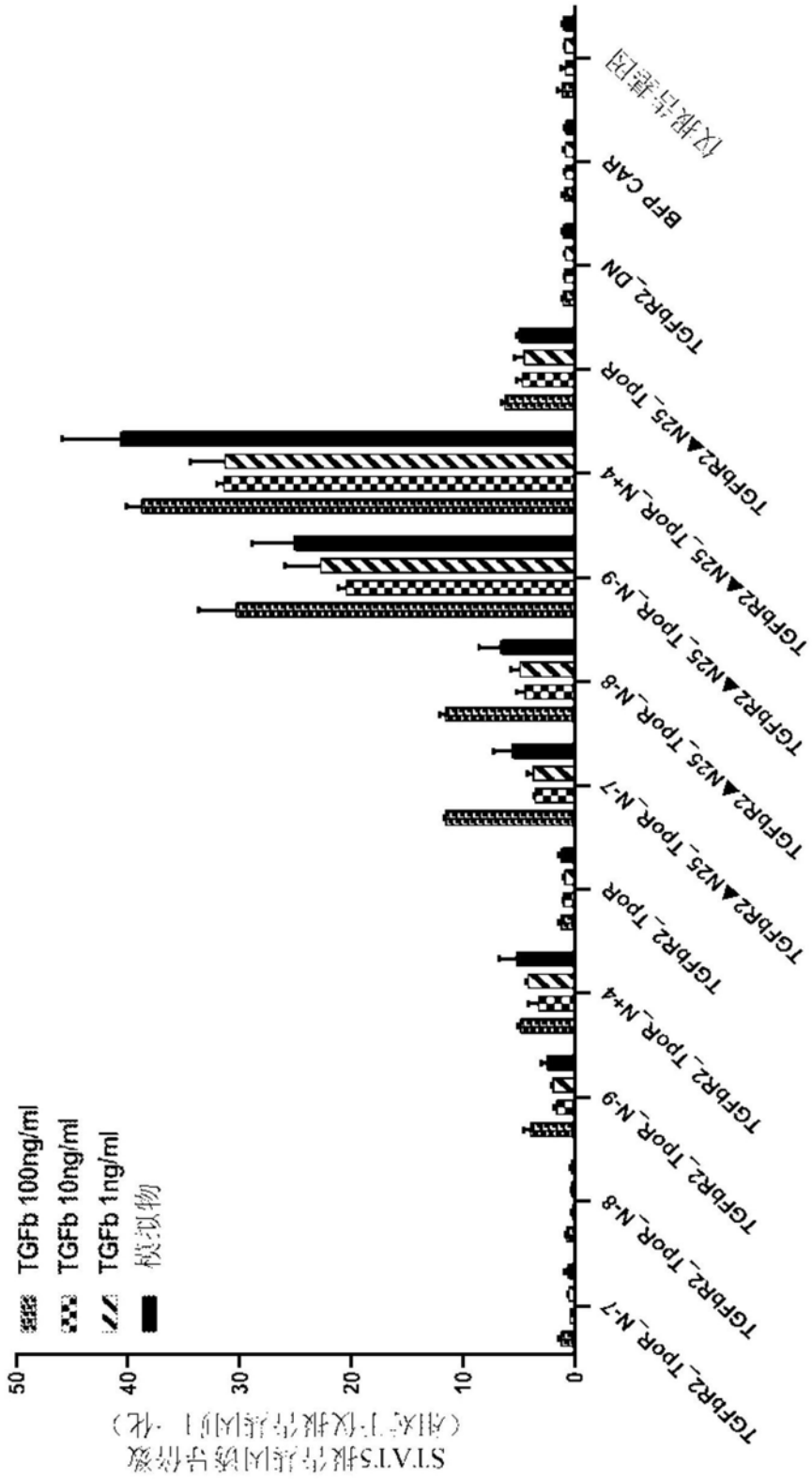

STAT5报告基因诱导倍数
（相对于仅报告基因对照）
0
10
20
30
40
50
模拟物
TGFb 1ng/ml
TGFb 10ng/ml
TGFb 100ng/ml
仅报告基因
BFP CAR
TGFbR2_DN
TGFbR2▲N25_TporR
TGFbR2▲N25_TporR_N+4
TGFbR2▲N25_TporR_N-9
TGFbR2▲N25_TporR_N-8
TGFbR2▲N25_TporR_N-7
TGFbR2_TporR
TGFbR2_TporR_N+4
TGFbR2_TporR_N-9
TGFbR2_TporR_N-8
TGFbR2_TporR_N-7

图6C

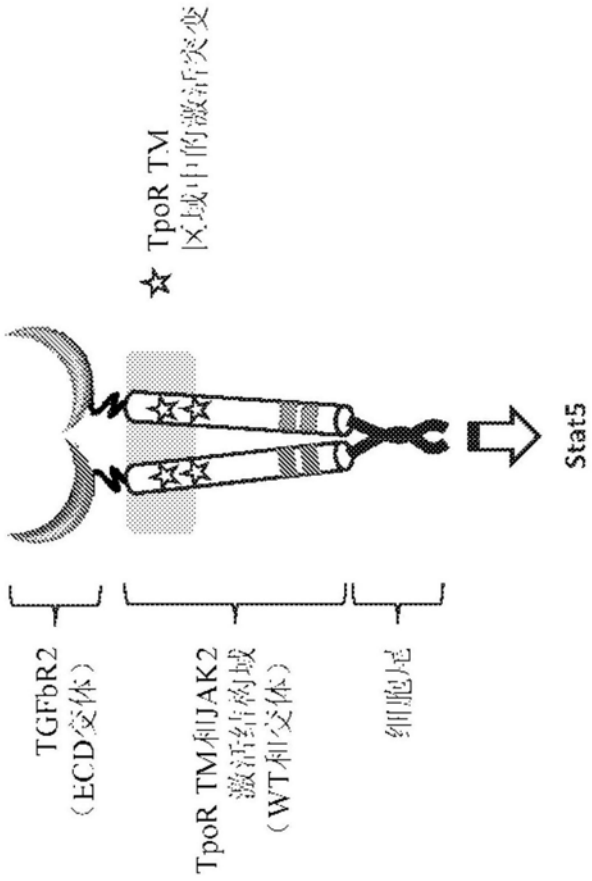

TpoR TM
区域中的激活突变
Stat5
TGFbR2
（ECD受体）
TpoR TM和JAK2
激活结构域
（WT和受体）
细胞尾

图7

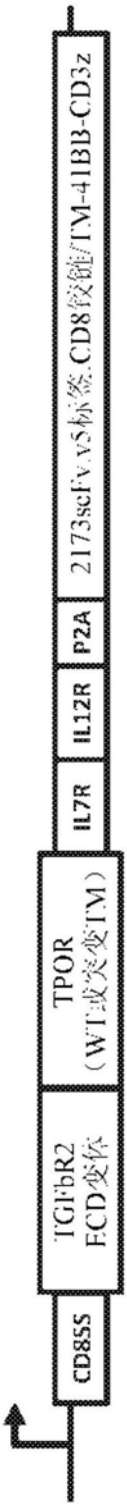

CD8SS
TGFbR2
ECD变体
TPOR
(WT或突变TM)
IL7R
IL12R
P2A
2173scFv-v5标签-CD8铰链TM-41BB-CD3z

图8A

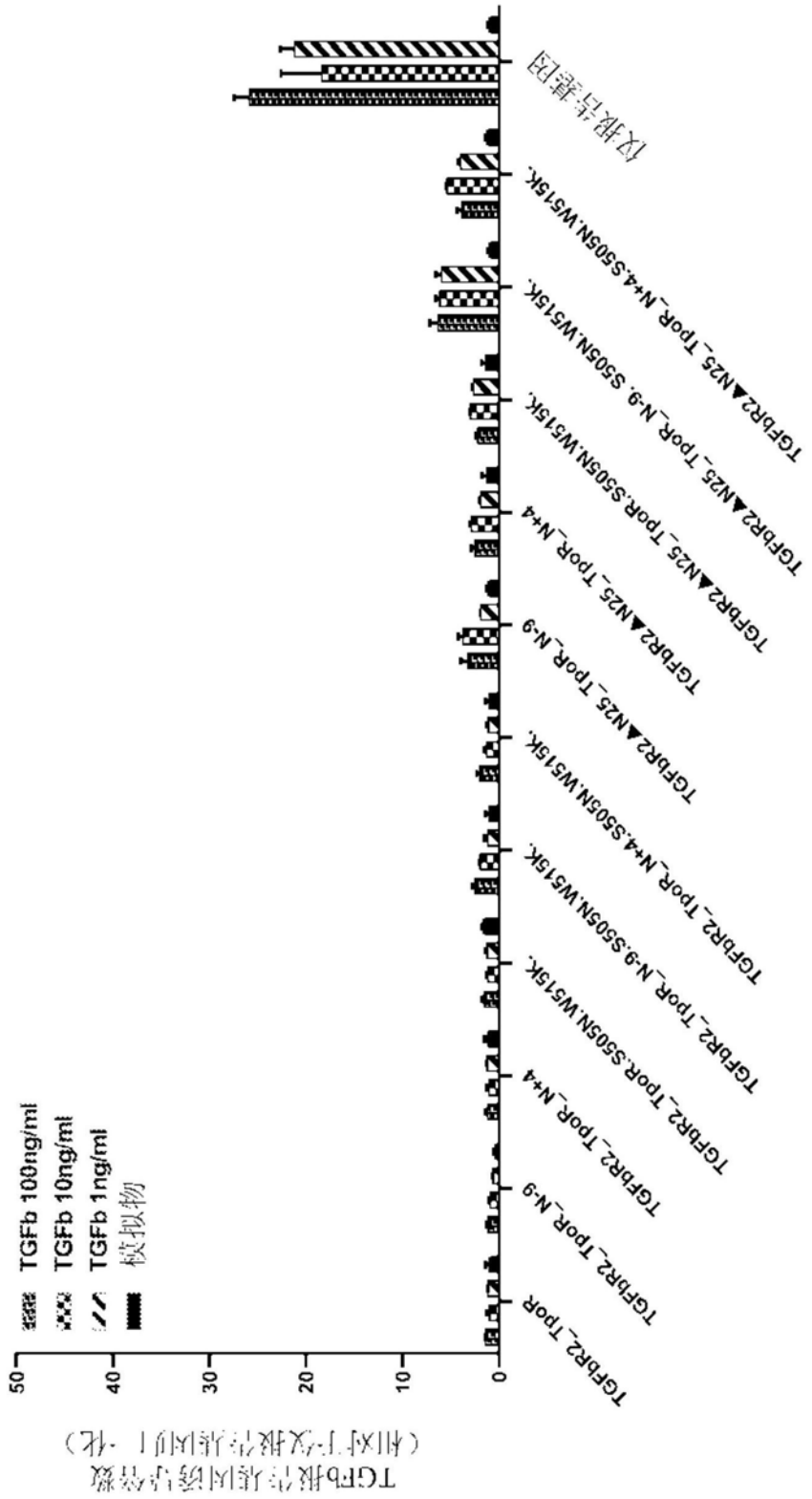

TGFb 100ng/ml
TGFb 10ng/ml
TGFb 1ng/ml
模拟物
0
10
20
30
40
50
TGFbR2_Tpor
TGFbR2_Tpor_N-9
TGFbR2_Tpor_N+4
TGFbR2_Tpor_S505N.W515K
TGFbR2_Tpor_N-9_S505N.W515K
TGFbR2_Tpor_N+4_S505N.W515K
TGFbR2▲N25_Tpor_N-9
TGFbR2▲N25_Tpor_N+4
TGFbR2▲N25_Tpor_S505N.W515K
TGFbR2▲N25_Tpor_N-9_S505N.W515K
TGFbR2▲N25_Tpor_N+4_S505N.W515K
仅报告基因
TGFb报告基因诱导倍数
（相对于仅报告基因而言）

图8B

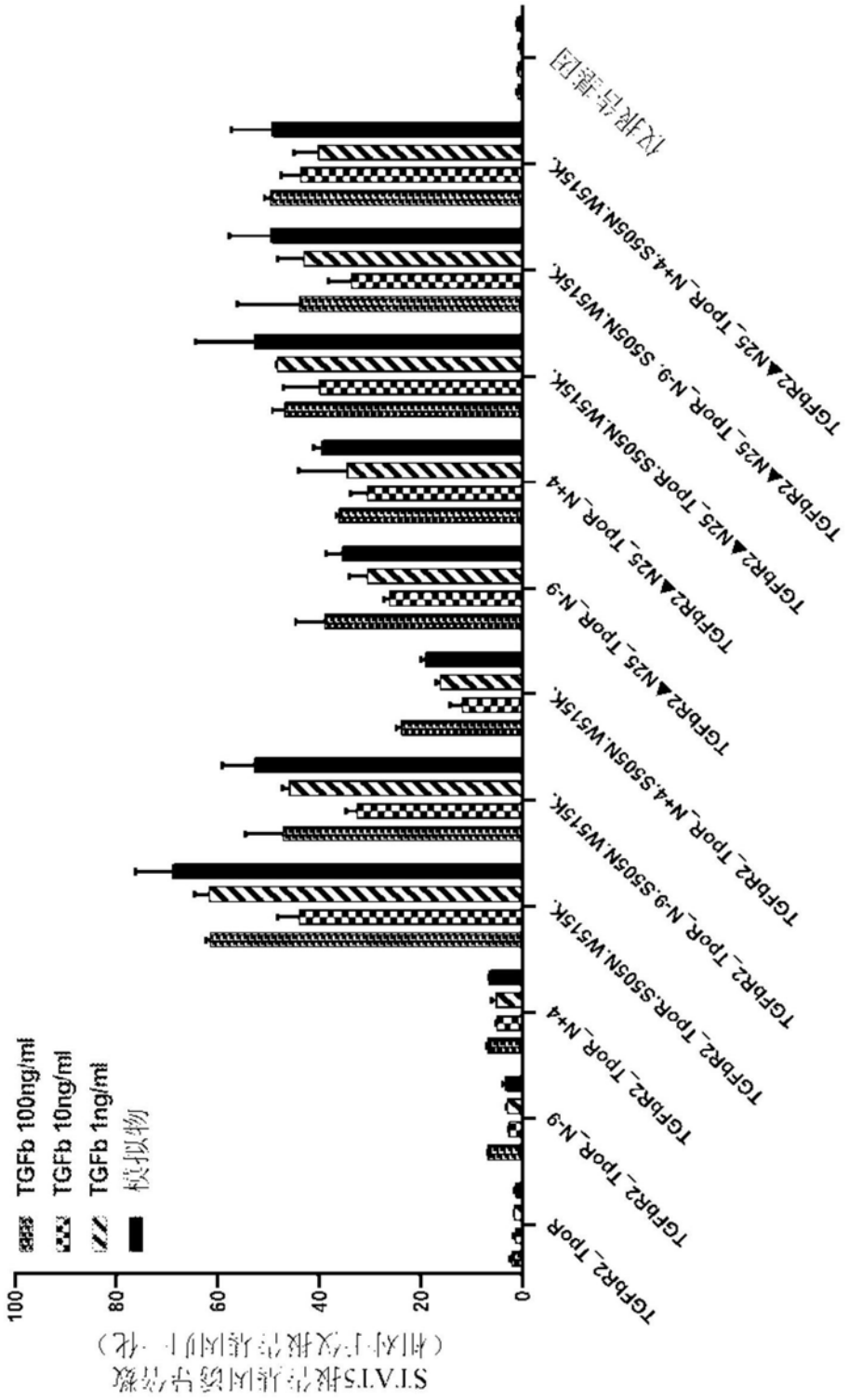

STAT5报告基因活性相对上一个对照（相对于仅报告基因）
0
20
40
60
80
100
模拟物
TGFb 1ng/ml
TGFb 10ng/ml
TGFb 100ng/ml
TGFbR2_TporR
TGFbR2_TporR_N-9
TGFbR2_TporR_N+4
TGFbR2_TporR_S505N.W515K
TGFbR2_TporR_N-9.S505N.W515K
TGFbR2_TporR_N+4.S505N.W515K
TGFbR2▲N25_TporR_N-9
TGFbR2▲N25_TporR_N+4
TGFbR2▲N25_TporR_S505N.W515K
TGFbR2▲N25_TporR_N-9.S505N.W515K
TGFbR2▲N25_TporR_N+4.S505N.W515K

图8C

下划线：野生型TpoR TM区
粗体：总指插入

(4138 - 4302 bp)

模板: SDPTRVETATETAWTSLVTALHLVCGLSAVCGTLLRWQFPAHYRRLRHATWPSL SEQ ID NO. 235
N-1: SDPTRVETATET-WTSLVTALHLVCGLSAVCGTLLRWQFPAITYRRIRHATWPSI SEQ ID NO. 236
N-2: SDPTRVETATELT--ISLVTALHLVCGLSAVCGTLLRWQFPAHYRRLRHATWPSL SEQ ID NO. 237
N-21: SDPTRVETATET-**L**ISLVTALHLVCGLSAVCGTLLRWQFPAHYRRLRHATWPSL SEQ ID NO. 238
N-3: SDPTRVETATELT--SLVTALHLVCGLSAVCGTLLRWQFPAHYRRLRHATWPSL SEQ ID NO. 239
N-4: SDPTRVETATELT---LVTALHLVCGLSAVCGTLLRWQFPAHYRRLRHATWPSL SEQ ID NO. 240
N-41: SDPTRVETATET---ILVTALHLVCGLSAVCGTLLRWQFPAHYRRLRHATWPSL SEQ ID NO. 241
N-5: SDPTRVETATET----VTALHLVCGLSAVCGTLLRWQFPAITYRRIRHATWPSI SEQ ID NO. 242
N-6: SDPTRVETATET-------TALHLVCGLSAVCGTLLRWQFPAITYRRIRHATWPSI SEQ ID NO. 243
N-7: SDPTRVETATET----------ALHLVCGLSAVCGTLLRWQFPAITYRRIRHATWPSI SEQ ID NO. 244
N-8: SDPTRVETATET----------LHLVCGLSAVCGTLLRWQFPAITYRRIRHATWPSI SEQ ID NO. 245
N-9: SDPTRVETATET----------HLVCGLSAVCGTLLRWQFPAITYRRIRHATWPSI SEQ ID NO. 246

图9A

(4138 4302 bp)
模板: SDPTRVETATETAW---------TSTVTALETVGSTSAVLGTTTRWQTPAHYRRLREATWPSL SEQ ID NO. 235
N-1: SDPTRVETATETAW---------LITSTVTALETVGLTSAVLGTTTRWQTPAHYRRLREATWPSL SEQ ID NO. 247
N-2: SDPTRVETATETAW---------VLITSTVTALETVGLTSAVLGTTTRWQTPAHYRRLREATWPSL SEQ ID NO. 248
N-3: SDPTRVETATETAW----LVLITSTVTALETVGLTSAVLGTTTRWQTPAHYRRLREATWPSL SEQ ID NO. 249
N-4: SDPTRVETATETAW---IILVLTSTVTALETVGLTSAVLGTTTRWQTPAIYRRLREATWPSL SEQ ID NO. 250
N-5: SDPTRVETATETAW---LIILVLTSTVTALETVGLTSAVLGTTTRWQTPAIYRRLREATWPSL SEQ ID NO. 251
N-6: SDPTRVETATETAW--LLIILVLTSTVTALETVGLTSAVLGTTTRWQTPAIYRRLREATWPSL SEQ ID NO. 252
N-7: SDPTRVETATETAW-VLLIILVLTSTVTALETVGLTSAVLGTTTRWQTPAIYRRLREATWPSL SEQ ID NO. 253
N-8: SDPTRVETATETAWLVLLIILVLTSTVTALETVGLTSAVLGTTTRWQTPAHYRRLREATWPSL SEQ ID NO. 254

图9B

(414 42/8 bp)
模板:
SDPTRVETATETAWISLVTALHLVLGLSAVGLLLLRWQFPAEVRRLRHAWPSL SEQ ID NO. 235
N-8-10: SDPTRVETATET----------VLGLSAVGLLLLRWQFPAEVRRLRHAWPSL SEQ ID NO. 255
N-8-11: SDPTRVETATET----------VLGLSAVGLLLLRWQFPAEVRRLRHAWPSL SEQ ID NO. 256
N-8-12: SDPTRVETATET----------LGLSAVGLLLLRWQFPAEVRRLRHAWPSL SEQ ID NO. 257
N-8-13: SDPTRVETATET----------GLSAVGLLLLRWQFPAEVRRLRHAWPSL SEQ ID NO. 258
N-8-14: SDPTRVETATET----------LSAVGLLLLRWQFPAEVRRLRHAWPSL SEQ ID NO. 259
N-9-1: SDPTRVETATE----------HLVLGLSAVGLLLLRWQFPAEVRRLRHAWPSL SEQ ID NO. 260
N-9-2: SDPTRVETAT----------HLVLGLSAVGLLLLRWQFPAEVRRLRHAWPSL SEQ ID NO. 261
N-9-3: SDPTRVETA----------HLVLGLSAVGLLLLRWQFPAEVRRLRHAWPSL SEQ ID NO. 262
N-9-4: SDPTRVET----------HLVLGLSAVGLLLLRWQFPAEVRRLRHAWPSL SEQ ID NO. 263
N-9-5: SDPTRVE----------HLVLGLSAVGLLLLRWQFPAEVRRLRHAWPSL SEQ ID NO. 264
N-9-6: SDPTRV----------HLVLGLSAVGLLLLRWQFPAEVRRLRHAWPSL SEQ ID NO. 265
N-9-7: SDPTR----------HLVLGLSAVGLLLLRWQFPAEVRRLRHAWPSL SEQ ID NO. 266
N-9-8: SDPT----------HLVLGLSAVGLLLLRWQFPAEVRRLRHAWPSL SEQ ID NO. 267
N-9-9: SDP----------HLVLGLSAVGLLLLRWQFPAEVRRLRHAWPSL SEQ ID NO. 268
N-9-10: SD----------HLVLGLSAVGLLLLRWQFPAEVRRLRHAWPSL SEQ ID NO. 269
N-9-11: S----------HLVLGLSAVGLLLLRWQFPAEVRRLRHAWPSL SEQ ID NO. 270
N-9-12: ----------HLVLGLSAVGLLLLRWQFPAEVRRLRHAWPSL SEQ ID NO. 271

图10A

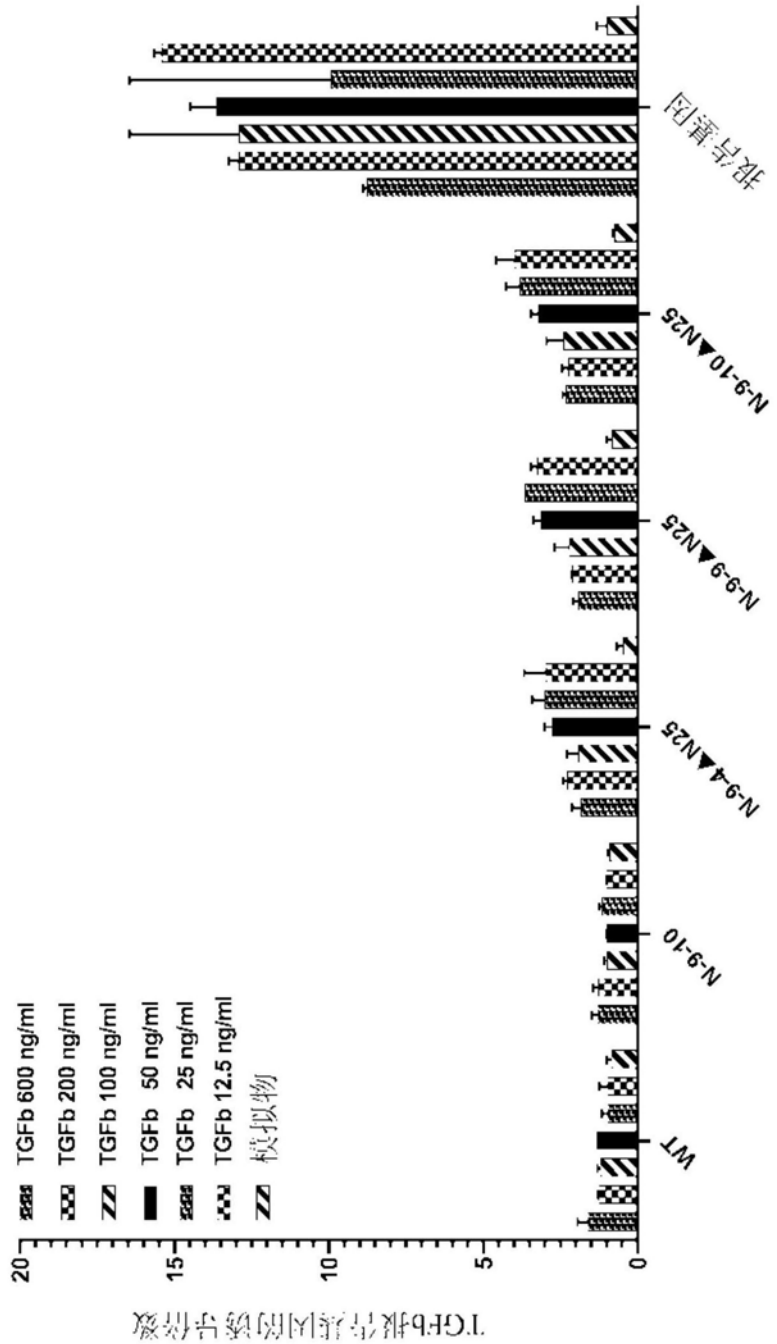

TGFb 600 ng/ml
TGFb 200 ng/ml
TGFb 100 ng/ml
TGFb 50 ng/ml
TGFb 25 ng/ml
TGFb 12.5 ng/ml
模拟物
WT
N-9-10
N-9-4▲N25
N-9-9▲N25
N-9-10▲N25
报告基因
TGFb抵抗诱导的倍数
0
5
10
15
20

图10B

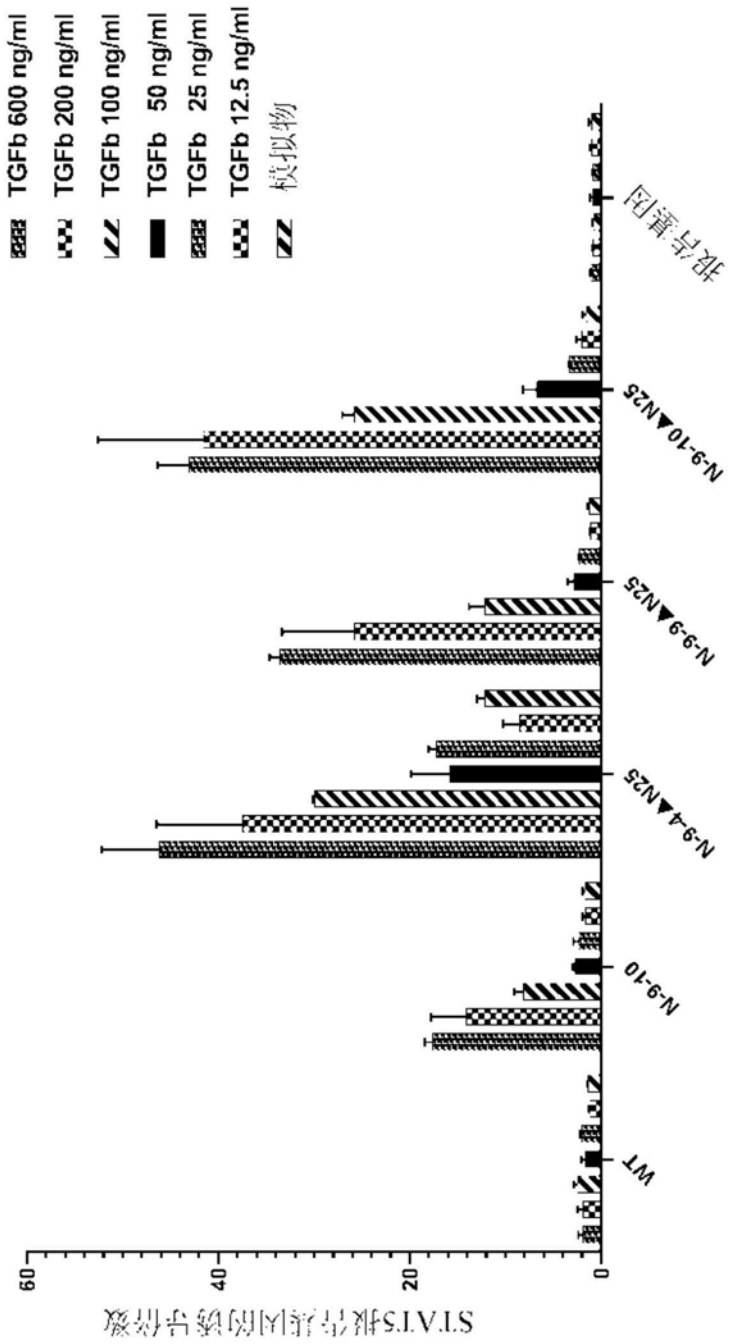

TGFb 600 ng/ml
TGFb 200 ng/ml
TGFb 100 ng/ml
TGFb 50 ng/ml
TGFb 25 ng/ml
TGFb 12.5 ng/ml
模拟物
报告基因
N-9-10▲N25
N-9-9▲N25
N-9-4▲N25
N-9-10
WT
0
20
40
60
STAT5报告基因的诱导倍数

图10C

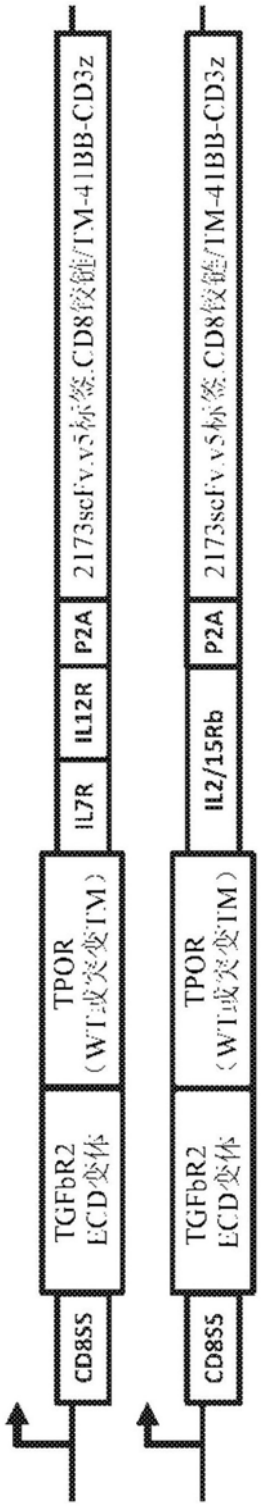

CD8SS
TGFbR2 ECD变体
TPOR （WT或突变TM）
IL7R
IL12R
P2A
2173scFv.v5标签.CD8铰链/TM-41BB-CD3z
CD8SS
TGFbR2 ECD变体
TPOR （WT或突变TM）
IL2/15Rb
P2A
2173scFv.v5标签.CD8铰链/TM-41BB-CD3z

图11A

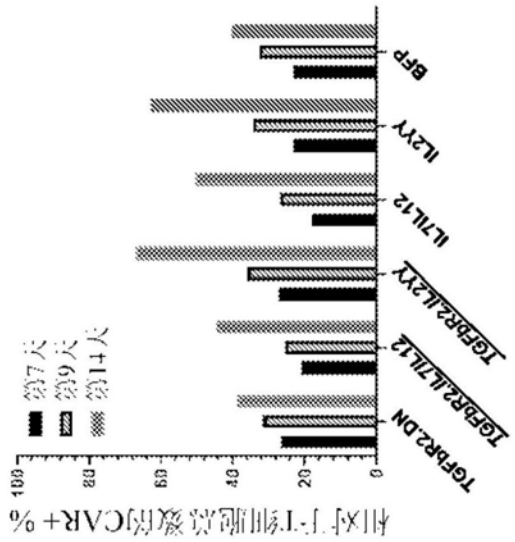

相对于T细胞总数的CAR+ %
100
80
60
40
20
0
第7天
第9天
第14天
TGFBR2.DN
TGFBR2.IL7IL12
TGFBR2.IL2YY
IL7IL12
IL2YY
BFP

图11B

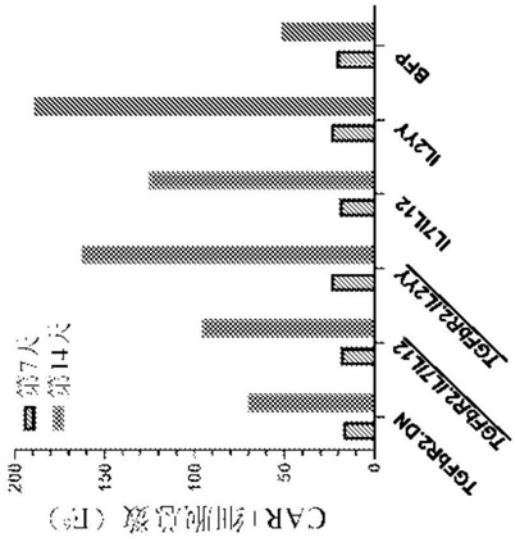

CAR+细胞总数（F°）
200
150
100
50
0
第7天
第14天
TGFBR2.DN
TGFBR2.IL7IL12
TGFBR2.IL2YY
IL7IL12
IL2YY
BFP

图11C

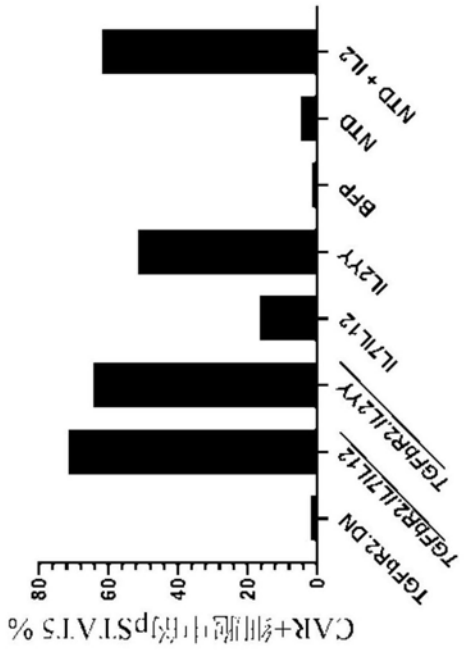

CAR+细胞中的pSTAT5 %
0
20
40
60
80
TGFbR2.DN
TGFbR2.IL7IL12
TGFbR2.IL2YY
IL7IL12
IL2YY
BFP
NTD
NTD + IL2

图11D

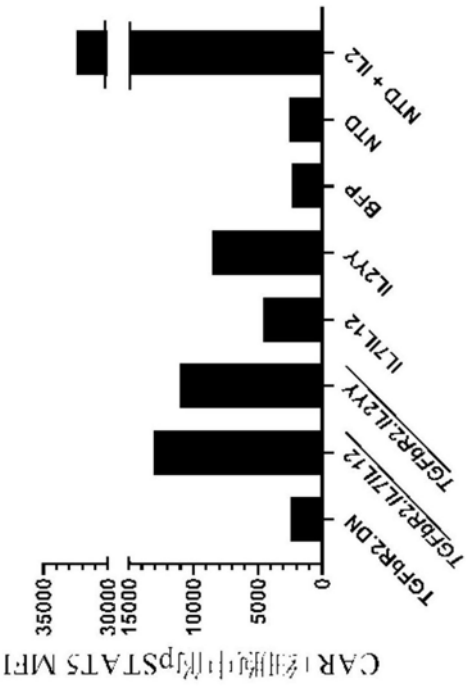

CAR+细胞中的pSTAT5 MFI
0
5000
10000
15000
30000
35000
TGFbR2.DN
TGFbR2.IL7IL12
TGFbR2.IL2YY
IL7IL12
IL2YY
BFP
NTD
NTD + IL2

图11E

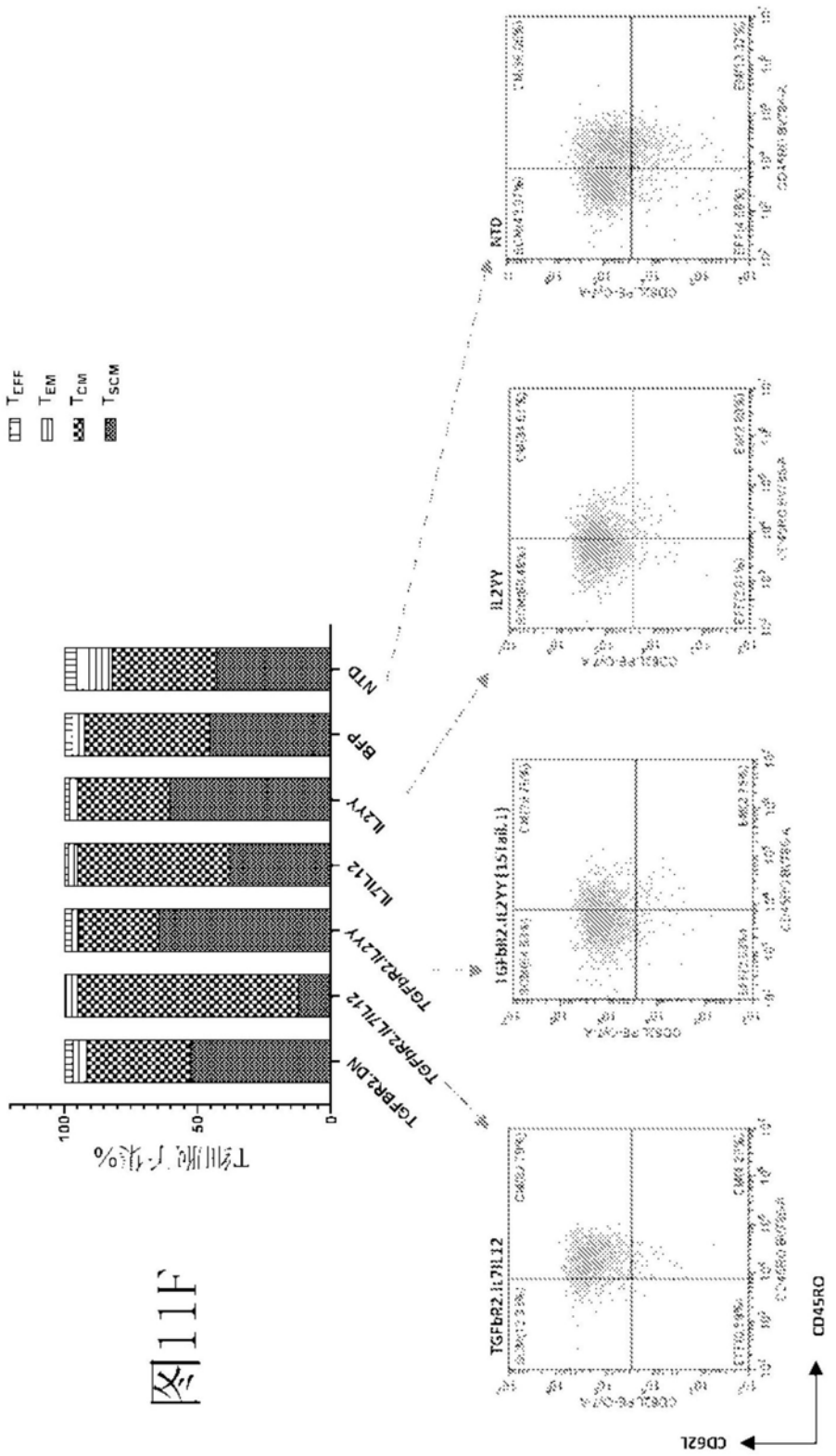

TEFF
TEM
TCM
TSCM
NTD
BFP
IL2YY
IL7IL12
TGFBR2IL2YY
TGFBR2IL7IL12
TGFBR2.DN
100
50
0
CD62L
CD45RO
KTD
IL2YY
TGFBR2.IL7IL12

图11F

图11G

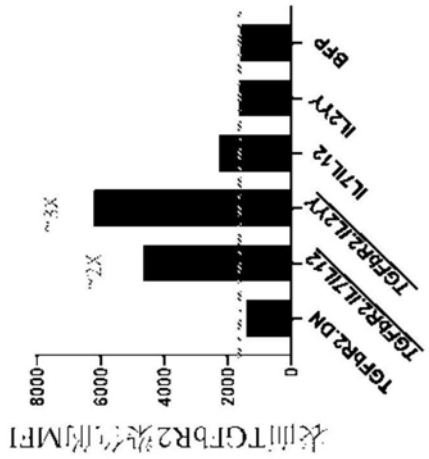

表面TGFbR2表达的MFI
8000
6000
4000
2000
0
TGFbR2.DN
TGFbR2.IL7IL12
TGFbR2.IL2YY
IL7IL12
IL2YY
BFP
NTD
~2X
~3X

图11H

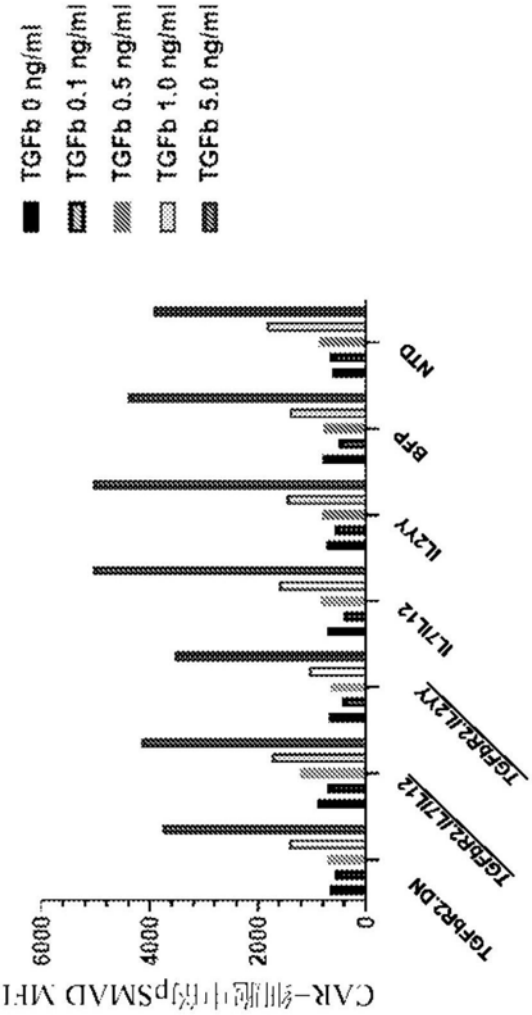

TGFb 0 ng/ml
TGFb 0.1 ng/ml
TGFb 0.5 ng/ml
TGFb 1.0 ng/ml
TGFb 5.0 ng/ml
CAR-细胞中的pSMAD MFI
6000
4000
2000
0
TGFbR2.DN
TGFbR2.IL7IL12
TGFbR2.IL2YY
IL7IL12
IL2YY
BFP
NTD

图11I

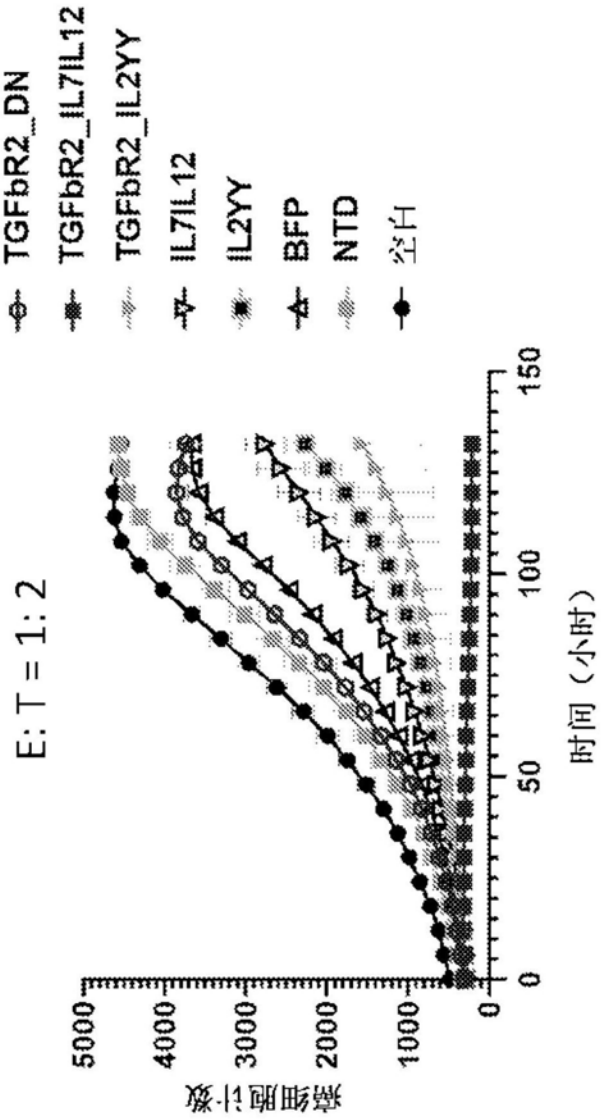

TGFbR2_DN
TGFbR2_IL7IL12
TGFbR2_IL2YY
IL7IL12
IL2YY
BFP
NTD
空白
E: T = 1: 2
癌细胞计数
5000
4000
3000
2000
1000
0
0
50
100
150
时间（小时）

图12A

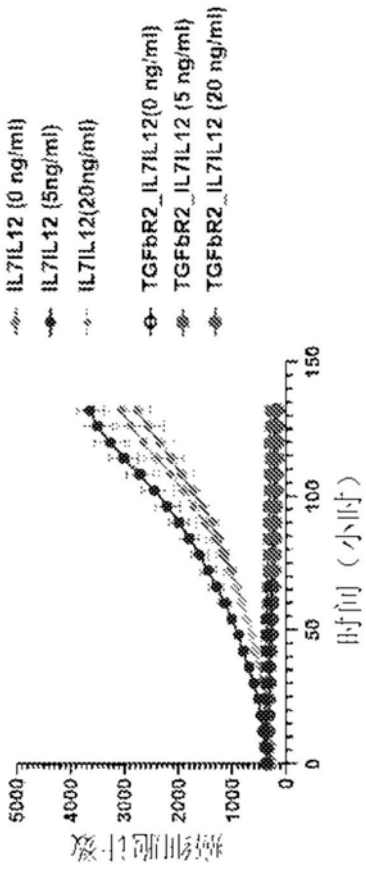

IL7IL12 (0 ng/ml)
IL7IL12 (5ng/ml)
IL7IL12(20ng/ml)
TGFbR2_IL7IL12(0 ng/ml)
TGFbR2_IL7IL12 (5 ng/ml)
TGFbR2_IL7IL12 (20 ng/ml)
5000
4000
3000
2000
1000
0
0
50
100
150

图12B

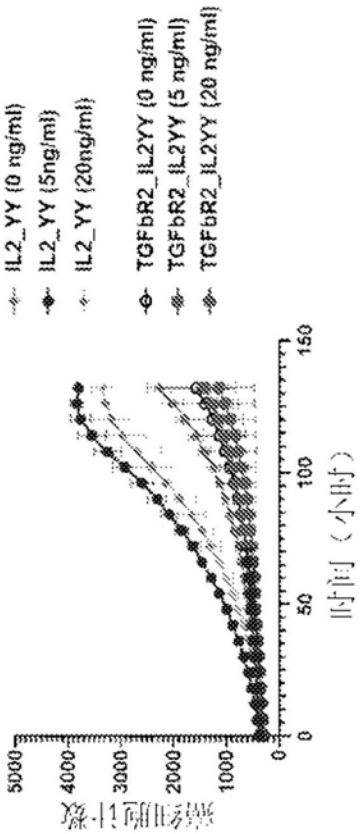

IL2_YY (0 ng/ml)
IL2_YY (5ng/ml)
IL2_YY (20ng/ml)
TGFbR2_IL2YY (0 ng/ml)
TGFbR2_IL2YY (5 ng/ml)
TGFbR2_IL2YY (20 ng/ml)
5000
4000
3000
2000
1000
0
0
50
100
150

图12C

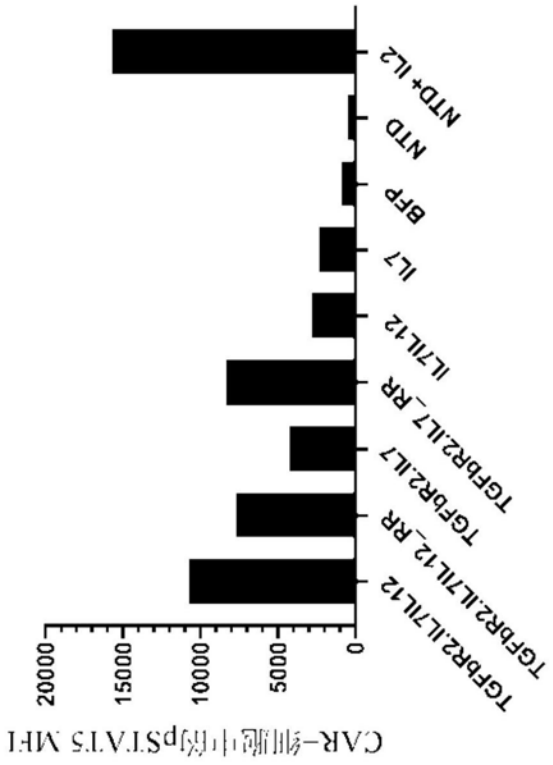

CAR-细胞中的pSTAT5 MFI
20000
15000
10000
5000
0
TGFbR2.IL7.IL12
TGFbR2.IL7.IL12_RR
TGFbR2.IL7
TGFbR2.IL7_RR
IL7.IL12
IL7
BFP
NTD
NTD+ IL2

图13A

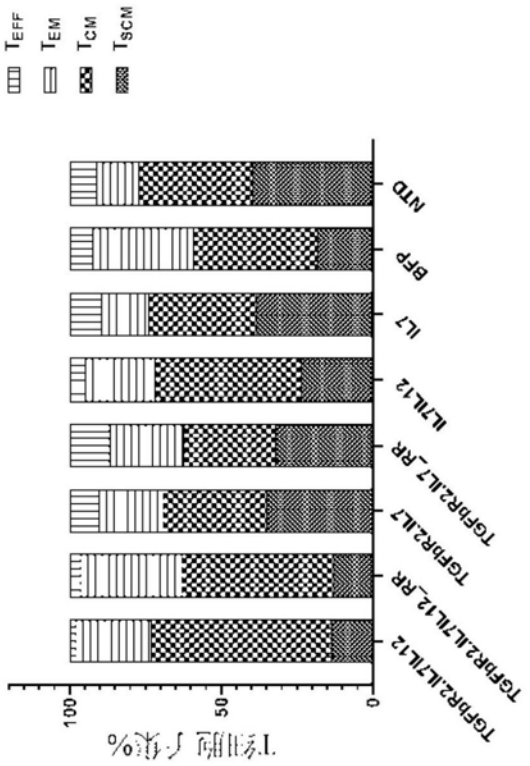

TEFF
TEM
TCM
TSCM
T细胞 产生%
100
50
0
TGFbR2.IL7.IL12
TGFbR2.IL7.IL12_RR
TGFbR2.IL7
TGFbR2.IL7_RR
IL7.IL12
IL7
BFP
NTD

图13B

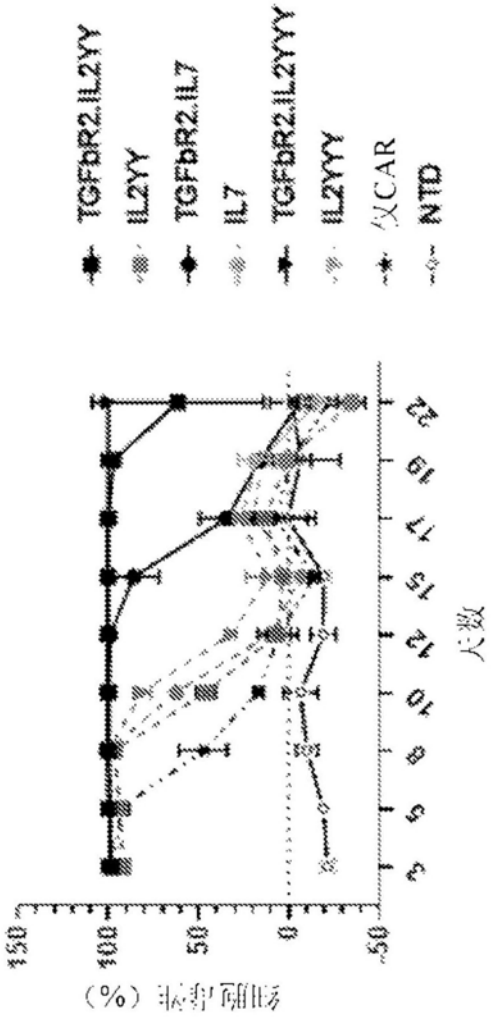

TGFbR2.IL2YY
IL2YY
TGFbR2.IL7
IL7
TGFbR2.IL2YYY
IL2YYY
/XCAR
NTD
150
100
50
0
-50
3
5
8
10
12
15
17
19
22
天数

图14A

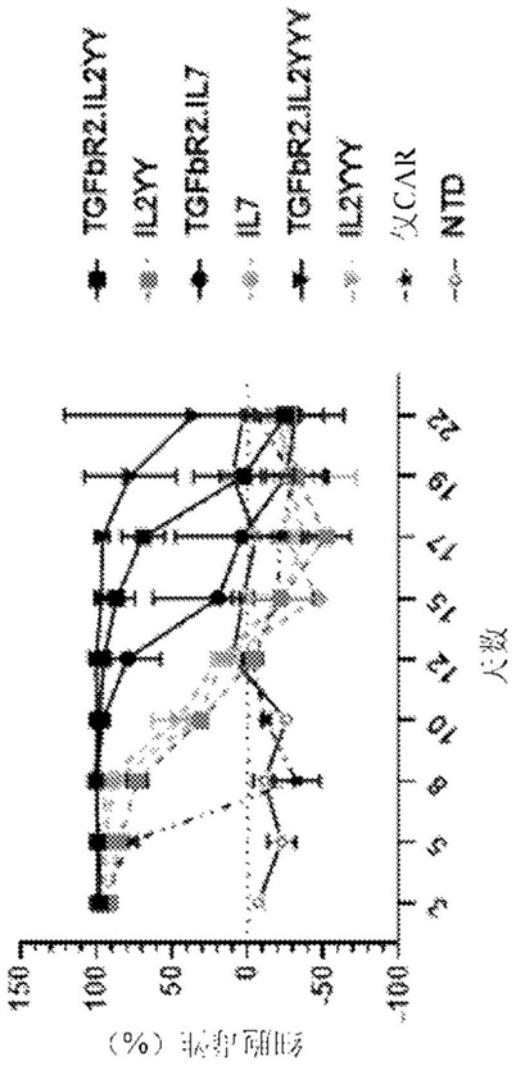

TGFbR2.IL2YY
IL2YY
TGFbR2.IL7
IL7
TGFbR2.IL2YYY
IL2YYY
仅CAR
NTD
150
100
50
0
-50
-100
2
5
8
10
12
15
17
19
22
天数
细胞杀伤（%）

图14B

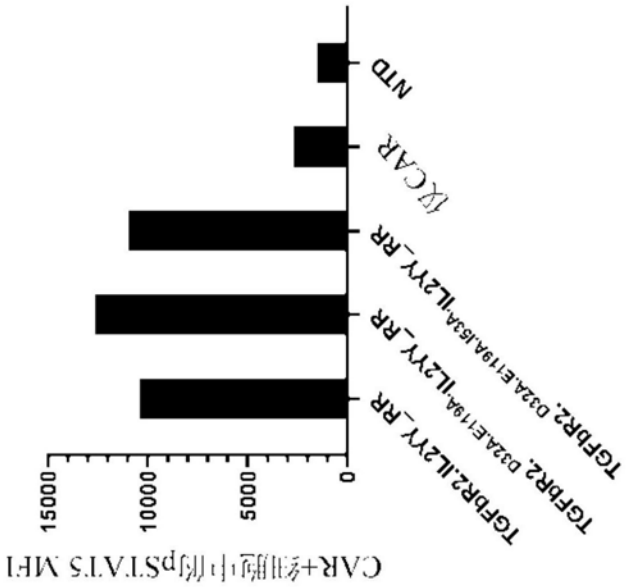

CAR+细胞中的pSTAT5 MFI
15000
10000
5000
0
NTD
1XCAR
TGFBR2.D32A.E119A.I53A.IL2YY_RR
TGFBR2.D32A.E119A.IL2YY_RR
TGFBR2.IL2YY_RR

图15A

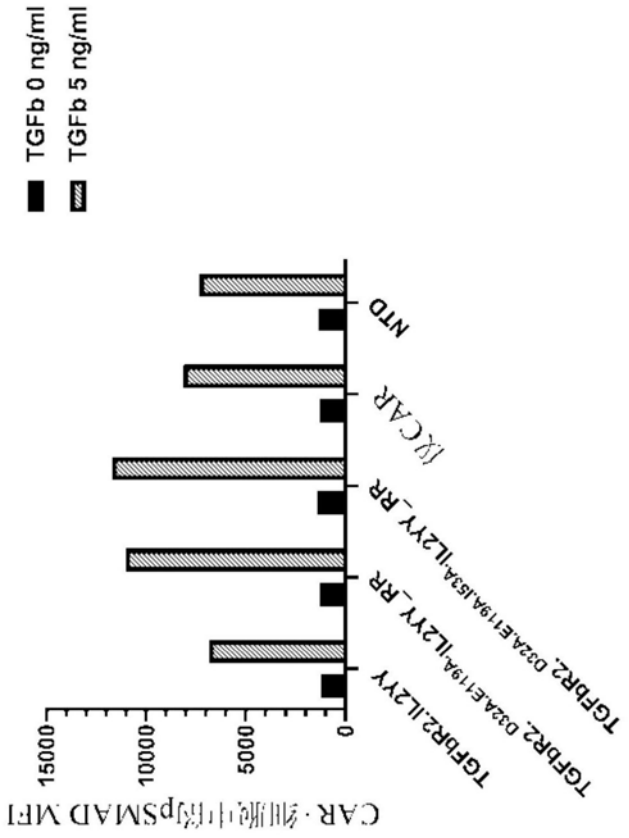

TGFb 0 ng/ml
TGFb 5 ng/ml
CAR+细胞中的pSMAD MFI
15000
10000
5000
0
NTD
1XCAR
TGFBR2.D32A.E119A.I53A.IL2YY_RR
TGFBR2.D32A.E119A.IL2YY_RR
TGFBR2.IL2YY

图15B

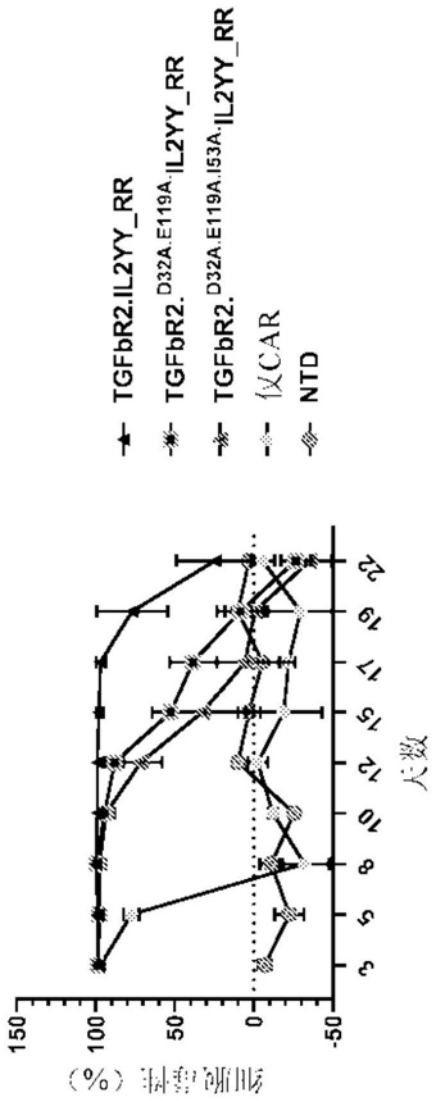

TGFbR2.IL2YY_RR
TGFbR2.D32A.E119A.IL2YY_RR
TGFbR2.D32A.E119A.I53A.IL2YY_RR
仅CAR
NTD
细胞毒性（%）
150
100
50
0
-50
3
5
8
10
12
15
17
19
22
天数

图15C

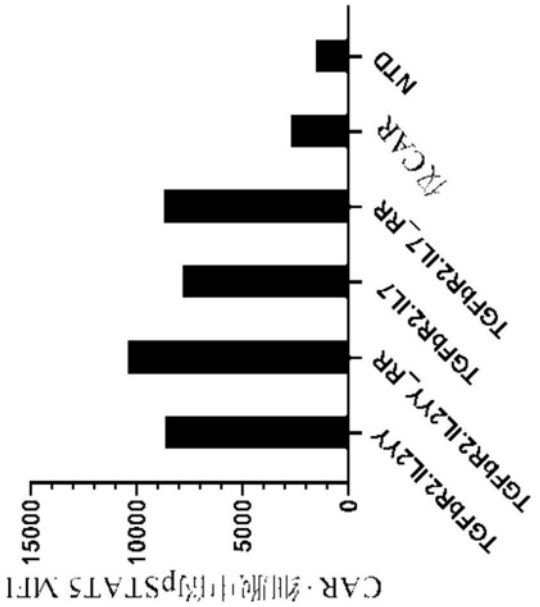

CAR-细胞中的pSTAT5 MFI
15000
10000
5000
0
TGFBR2.IL2YY
TGFBR2.IL2YY_RR
TGFBR2.IL7
TGFBR2.IL7_RR
仅CAR
NTD

图16A

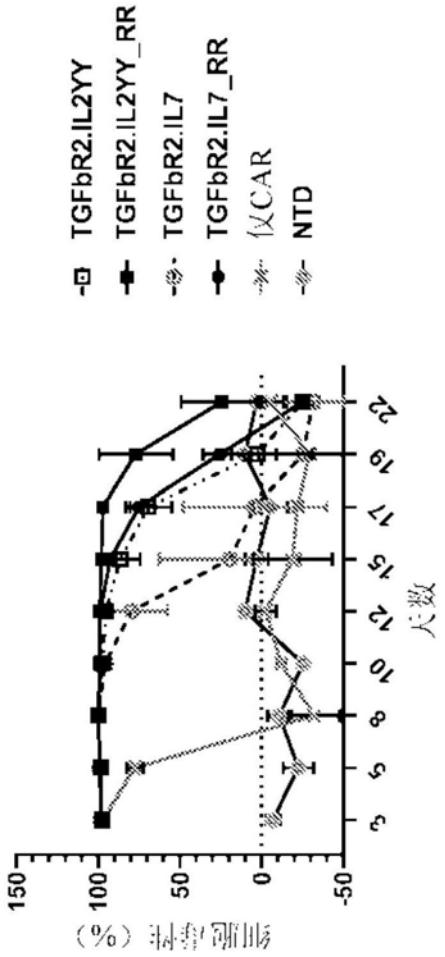

TGFbR2.IL2YY
TGFbR2.IL2YY_RR
TGFbR2.IL7
TGFbR2.IL7_RR
仅CAR
NTD
细胞活性（%）
150
100
50
0
-50
3
5
8
10
12
15
17
19
22
天数

图16B