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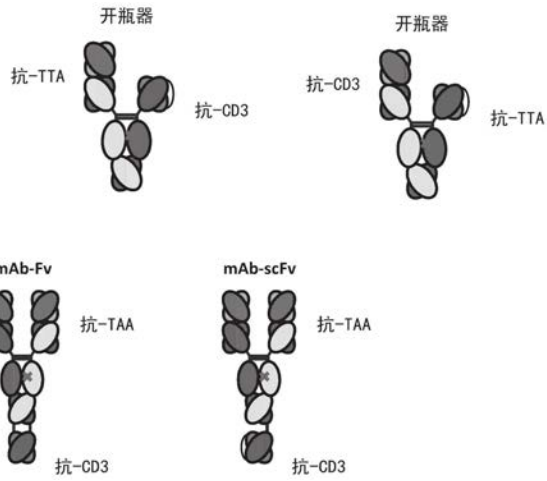
(54)发明名称

# 结合CD3和肿瘤抗原的异二聚体抗体

(57)摘要

本发明涉及结合CD3和肿瘤抗原的异二聚体抗体。所述异二聚体抗体可包含:a)第一单体,其包含:i)第一重链,其包含:1)第一可变重链结构域,2)包含第一Fc结构域的第一恒定重链和3)包含scFv可变轻链结构域,scFv接头和scFv可变重链结构域的scFv,其中所述scFv用结构域接头共价接合至所述Fc结构域的C-端;b)包含第二重链的第二单体,所述第二重链包含第二可变重链结构域和第二恒定重链,所述第二恒定重链包含第二Fc结构域;和c)包含可变轻链结构域和恒定轻链结构域的共同轻链;并且其中所述第一可变重链结构域和所述可变轻链结构域结合第一靶肿瘤抗原(TTA),所述第二可变重链结构域和所述可变轻链结构域结合所述第一TTA,所述scFv结合人CD3。

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1.一种异二聚体抗体,其包含:

a)第一单体,其包含:

i)第一重链,其包含:

1)第一可变重链结构域;

2)包含第一Fc结构域的第一恒定重链;

3)包含scFv可变轻链结构域,scFv接头和scFv可变重链结构域的scFv;其中所述scFv用结构域接头共价接合至所述Fc结构域的C-端;

b)包含第二重链的第二单体,所述第二重链包含第二可变重链结构域和第二恒定重链,所述第二恒定重链包含第二Fc结构域;和

c)包含可变轻链结构域和恒定轻链结构域的共同轻链;

其中所述第一和第二Fc结构域具有选自以下的组合氨基酸取代:S364K/E357Q:L368D/K370S、L368D/K370S:S364K、L368E/K370S:S364K、T411T/E360E/Q362E:D401K、L368D/K370S:S364K/E357L和K370S:S364K/E357Q,并且其中所述第一可变重链结构域和所述可变轻链结构域结合第一靶肿瘤抗原(TTA),所述第二可变重链结构域和所述可变轻链结构域结合所述第一TTA,所述scFv结合人CD3(SEQ ID NO:XX)。

2.如权利要求1所述的异二聚体抗体,其中所述scFv的多肽序列选自:SEQ ID NO:XX(scFv 13551)、SEQ ID NO:XX(scFv 15426)、SEQ ID NO:XX(scFv 13423)和SEQ ID NO:XX(scFv 14702)。

3.如权利要求1或2所述的异二聚体抗体,其中所述第一可变重链结构域和所述可变轻链结构域结合选自以下的TTA:CD19、CD20和CD123。

4.一种异二聚体抗体,其包含:

a)第一单体,其包含:

i)第一重链,其包含:

1)第一可变重链结构域;

2)包含第一Fc结构域的第一恒定重链结构域;和

3)第一可变轻链结构域,其中所述第一可变轻链结构域用结构域接头共价接合至所述第一Fc结构域的C-端;

b)第二单体,其包含:

i)第二可变重链结构域;

ii)包含第二Fc结构域的第二恒定重链结构域;和

iii)第三可变重链结构域,其中所述第二可变重链结构域用结构域接头共价接合至所述第二Fc结构域的C-端;

c)包含可变轻链结构域和恒定轻链结构域的共同轻链;

其中所述第一和第二Fc结构域具有选自以下的组合氨基酸取代:S364K/E357Q:L368D/K370S、L368D/K370S:S364K、L368E/K370S:S364K、T411T/E360E/Q362E:D401K、L368D/K370S:S364K/E357L和K370S:S364K/E357Q,其中所述第一可变重链结构域和所述可变轻链结构域结合第一TTA,所述第二可变重链结构域和所述可变轻链结构域结合所述TTA,所述第二可变轻链结构域和所述第三可变重链结构域结合CD3。

5.如权利要求4所述的异二聚体抗体,其中所述scFv的多肽序列选自:SEQ ID NO:XX

(scFv 13551)、SEQ ID NO:XX(scFv 15426)、SEQ ID NO:XX(scFv 13423)和SEQ ID NO:XX(scFv 14702)。

6.如权利要求4或5所述的异二聚体抗体,其中所述第一可变重链结构域和所述可变轻链结构域结合选自以下的TTA:CD19、CD20和CD123。

7.一种异二聚体抗体,其包含:

a)第一单体,其包含:

i)第一重链,其包含:

1)第一可变重链结构域;

2)包含第一CH1结构域和第一Fc结构域的第一恒定重链;

3)包含scFv可变轻链结构域、scFv接头和scFv可变重链结构域的scFv;其中所述scFv用结构域接头共价接合至所述CH1结构域的C-端和所述第一Fc结构域的N-端之间;

b)包含第二重链的第二单体,所述第二重链包含第二可变重链结构域和第二恒定重链,所述第二恒定重链包含第二Fc结构域;和

c)包含可变轻链结构域和恒定轻链结构域的共同轻链;

其中所述第一和第二Fc结构域具有选自以下的组合氨基酸取代:S364K/E357Q:L368D/K370S、L368D/K370S:S364K、L368E/K370S:S364K、T411T/E360E/Q362E:D401K、L368D/K370S:S364K/E357L和K370S:S364K/E357Q,其中所述第一可变重链结构域和所述可变轻链结构域结合第一TTA,所述第二可变重链结构域和所述可变轻链结构域结合所述TTA,并且所述scFv结合人CD3。

8.如权利要求7所述的异二聚体抗体,其中所述scFv的多肽序列选自:SEQ ID NO:XX(scFv 13551)、SEQ ID NO:XX(scFv 15426)、SEQ ID NO:XX(scFv 13423)和SEQ ID NO:XX(scFv 14702)。

9.如权利要求7或8所述的异二聚体抗体,其中所述第一可变重链结构域和所述可变轻链结构域结合选自以下的TTA:CD19、CD20和CD123。

10.一种异二聚体抗体,其包含:

a)第一单体,其包含:

i)第一重链,其包含:

1)第一可变重链结构域;

2)包含第一Fc结构域的第一恒定重链结构域;和

3)第一可变轻链结构域,其中所述第二可变轻链结构域用结构域接头共价接合至所述第一恒定重链结构域的CH1结构域的C-端和所述第一Fc结构域的N-端之间;

b)第二单体,其包含

i)第二可变重链结构域;

ii)包含第二Fc结构域的第二恒定重链结构域;和

iii)第三可变重链结构域,其中所述第二可变重链结构域用结构域接头共价接合至所述第二Fc结构域的C-端;

c)包含可变轻链结构域和恒定轻链结构域的共同轻链;

其中所述第一和第二Fc结构域具有选自以下的组合氨基酸取代:S364K/E357Q:L368D/K370S、L368D/K370S:S364K、L368E/K370S:S364K、T411T/E360E/Q362E:D401K、L368D/

K370S:S364K/E357L和K370S:S364K/E357Q,其中所述第一可变重链结构域和所述可变轻链结构域结合第一TTA,所述第二可变重链结构域和所述可变轻链结构域结合所述TTA,并且所述第二可变轻链结构域和所述第三可变重链结构域结合人CD3。

11.如权利要求10所述的异二聚体抗体,其中所述scFv的多肽序列选自:SEQ ID NO:XX(scFv 13551)、SEQ ID NO:XX(scFv 15426)、SEQ ID NO:XX(scFv 13423)和SEQ ID NO:XX(scFv 14702)。

12.如权利要求10或11所述的异二聚体抗体,其中所述第一可变重链结构域和所述可变轻链结构域结合选自以下的TTA:CD19、CD20和CD123。

13.一种异二聚体抗体,其包含:

a)第一单体,其包含:

i)第一重链,其包含:

1)第一可变重链结构域;

2)包含第一CH1结构域和第一Fc结构域的第一恒定重链;

3)包含scFv可变轻链结构域、scFv接头和scFv可变重链结构域的scFv;其中所述scFv用结构域接头共价接合至所述CH1结构域的C-端和所述第一Fc结构域的N-端之间;

b)包含第二Fc结构域的第二单体;和

c)包含可变轻链结构域和恒定轻链结构域的轻链;

其中所述第一和第二Fc结构域具有选自以下的组合氨基酸取代:S364K/E357Q:L368D/K370S、L368D/K370S:S364K、L368E/K370S:S364K、T411T/E360E/Q362E:D401K、L368D/K370S:S364K/E357L和K370S:S364K/E357Q,其中所述第一可变重链结构域和所述可变轻链结构域结合第一抗原,所述scFv结合第二抗原。

14.如权利要求13所述的异二聚体抗体,其中所述scFv的多肽序列选自:SEQ ID NO:XX(scFv 13551)、SEQ ID NO:XX(scFv 15426)、SEQ ID NO:XX(scFv 13423)和SEQ ID NO:XX(scFv 14702)。

15.如权利要求13或14所述的异二聚体抗体,其中所述第一可变重链结构域和所述可变轻链结构域结合选自以下的TTA:CD19、CD20和CD123。

16.一种抗-CD3抗体结合结构域,其包含:

a)包含序列为GSSTGAVTTSNYAN(SEQ ID NO:XX)的vlCDR1、序列为GTNKRAP(SEQ ID NO:XX)的vlCDR2、和序列为ALWYSNHWV(SEQ ID NO:XX)的vlCDR3的可变轻链结构域;和

b)包含序列为TYAMN(SEQ ID NO:XX)的vhCDR1、序列为RIRSKANNYATYYADSVKG(SEQ ID NO:XX)的vhCDR2、和序列为HGNFGDSYVSWFAY(SEQ ID NO:XX)的vhCDR3的可变重链结构域。

17.如权利要求16所述的抗-CD3抗体结合结构域,其中所述结合结构域是scFv。

18.如权利要求16或17所述的抗-CD3抗体结合结构域,其中所述可变轻链结构域具有序列L1.47(SEQ ID NO:XX)并且所述可变重链结构域具有序列H1.32(SEQ ID NO:XX)。

19.如权利要求18所述的抗-CD3抗体结合结构域,其中所述scFv具有序列H1.32_L1.47(SEQ ID NO:XX)。

20.一种编码如权利要求19所述scFv的核酸组合物。

21.一种表达载体,所述表达载体包含如权利要求20所述的核酸组合物。

22.一种包含权利要求21所述表达载体的宿主细胞。

23.一种抗-CD3抗体结合结构域,其包含:

a)包含序列为GSSTGAVTTSNYAN(SEQ ID NO:XX)的vlCDR1、序列为GTNKRAP(SEQ ID NO:XX)的vlCDR2、和序列为ALWYSNHWV(SEQ ID NO:XX)的vlCDR3的可变轻链结构域;和

b)包含序列为TYAMN(SEQ ID NO:XX)的vhCDR1、序列为RIRSKYNNYATYYADSVKG(SEQ ID NO:XX)的vhCDR2、和序列为HGNFGDEYVSWFAY(SEQ ID NO:XX)的vhCDR3的可变重链结构域。

24.如权利要求23所述的抗-CD3抗体结合结构域,其中所述结合结构域是scFv。

25.如权利要求23或24所述的抗-CD3抗体结合结构域,其中所述可变轻链结构域具有序列L1.47(SEQ ID NO:XX)并且所述可变重链结构域具有序列H1.89(SEQ ID NO:XX)。

26.如权利要求23所述的抗-CD3抗体结合结构域,其中所述scFv具有序列H1.89_L1.47(SEQ ID NO:XX)。

27.一种编码如权利要求26所述scFv的核酸组合物。

28.一种表达载体,所述表达载体包含如权利要求27所述的核酸组合物。

29.一种包含权利要求28所述表达载体的宿主细胞。

30.一种抗-CD3抗体结合结构域,其包含:

a)包含序列为GSSTGAVTTSNYAN(SEQ ID NO:XX)的vlCDR1、序列为GTNKRAP(SEQ ID NO:XX)的vlCDR2、和序列为ALWYSNHWV(SEQ ID NO:XX)的vlCDR3的可变轻链结构域;和

b)包含序列为TYAMN(SEQ ID NO:XX)的vhCDR1、序列为RIRSKYNNYATYYADSVKG(SEQ ID NO:XX)的vhCDR2、和序列为HGNFGDPYVSWFAY(SEQ ID NO:XX)的vhCDR3的可变重链结构域。

31.如权利要求30所述的抗-CD3抗体结合结构域,其中所述结合结构域是scFv。

32.如权利要求30或31所述的抗-CD3抗体结合结构域,其中所述可变轻链结构域具有序列L1.47(SEQ ID NO:XX)并且所述可变重链结构域具有序列H1.90(SEQ ID NO:XX)。

33.如权利要求30所述的抗-CD3抗体结合结构域,其中所述scFv具有序列H1.90_L1.47(SEQ ID NO:XX)。

34.一种编码如权利要求33所述scFv的核酸组合物。

35.一种表达载体,所述表达载体包含如权利要求34所述的核酸组合物。

36.一种包含权利要求35所述表达载体的宿主细胞。

37.一种抗-CD3抗体结合结构域,其包含:

a)包含序列为GSSTGAVTTSNYAN(SEQ ID NO:XX)的vlCDR1、序列为GTNKRAP(SEQ ID NO:XX)的vlCDR2、和序列为ALWYSNHWV(SEQ ID NO:XX)的vlCDR3的可变轻链结构域;和

b)包含序列为TYAMN(SEQ ID NO:XX)的vhCDR1、序列为RIRSKYNNYATYYADSVKG(SEQ ID NO:XX)的vhCDR2、和序列为HGNFGDSYVSWFDY(SEQ ID NO:XX)的vhCDR3的可变重链结构域。

38.如权利要求37所述的抗-CD3抗体结合结构域,其中所述结合结构域是scFv。

39.如权利要求37或38所述的抗-CD3抗体结合结构域,其中所述可变轻链结构域具有序列L1.47(SEQ ID NO:XX)并且所述可变重链结构域具有序列H1.33(SEQ ID NO:XX)。

40.如权利要求38所述的抗-CD3抗体结合结构域,其中所述scFv具有序列H1.33_L1.47(SEQ ID NO:XX)。

41.一种编码如权利要求38所述scFv的核酸组合物。

42.一种表达载体,所述表达载体包含如权利要求41所述的核酸组合物。

43.一种包含权利要求42所述表达载体的宿主细胞。

44.一种抗-CD3抗体结合结构域,其包含:

a)包含序列为GSSTGAVTTSNYAN(SEQ ID NO:XX)的vlCDR1、序列为GTNKRAP(SEQ ID NO:XX)的vlCDR2、和序列为ALWYSNHWV(SEQ ID NO:XX)的vlCDR3的可变轻链结构域;和

b)包含序列为TYAMS(SEQ ID NO:XX)的vhCDR1、序列为RIRSKYNNYATYYADSVKG(SEQ ID NO:XX)的vhCDR2、和序列为HGNFGDSYVSWFAY(SEQ ID NO:XX)的vhCDR3的可变重链结构域。

45.如权利要求44所述的抗-CD3抗体结合结构域,其中所述结合结构域是scFv。

46.如权利要求44或45所述的抗-CD3抗体结合结构域,其中所述可变轻链结构域具有序列L1.47(SEQ ID NO:XX)并且所述可变重链结构域具有序列H1.31(SEQ ID NO:XX)。

47.如权利要求46所述的抗-CD3抗体结合结构域,其中所述scFv具有序列H1.31_L1.47(SEQ ID NO:XX)。

48.一种编码如权利要求47所述scFv的核酸组合物。

49.一种表达载体,所述表达载体包含如权利要求48所述的核酸组合物。

50.一种包含权利要求49所述表达载体的宿主细胞。

51.一种异二聚体抗体,其包含:

a)第一单体,其包含:

i)第一Fc结构域;

ii)包含scFv可变轻链结构域,scFv接头和scFv可变重链结构域的抗-CD3 scFv;其中所述scFv用结构域接头共价接合至所述Fc结构域的N-端;

b)第二单体,包含重链,其包含:

i)重链可变结构域;和

ii)包含第二Fc结构域的第二重链恒定结构域;和

c)包含可变轻链结构域和可变轻链恒定结构域的轻链;

其中所述抗-CD3 scFv选自:抗-CD3 H1.32_L1.47(SEQ ID NO:XX)、抗-CD3 H1.89_L1.47(SEQ ID NO:XX)、抗-CD3 H1.90_L1.47(SEQ ID NO:XX)和抗-CD3 H1.33_L1.47(SEQ ID NO:XX),并且所述重链可变结构域和所述轻链可变结构域结合TTA。

52.如权利要求51所述的异二聚体抗体,其中所述TTA选自:CD19、CD20和CD123。

53.一种抗-CD20抗体结合结构域,其包含:

a)包含序列为RASWSVSYIH(SEQ ID NO:XX)的vlCDR1、序列为ATSNLAS(SEQ ID NO:XX)的vlCDR2、和序列为QQWTHNPPT(SEQ ID NO:XX)的vlCDR3的可变轻链结构域;和

b)包含序列为SYNMH(SEQ ID NO:XX)的vhCDR1、序列为AIYPGNGATSYSQKFQG(SEQ ID NO:XX)的vhCDR2、和序列为SYYMGGDWYFDV(SEQ ID NO:XX)的vhCDR3的可变重链结构域。

54.如权利要求53所述的抗-CD20抗体结合结构域,其中所述可变轻链结构域具有序列C2B8 L1.113(SEQ ID NO:XX)并且所述可变重链结构域具有序列C2B8 H1.202(SEQ ID NO:XX)。

55.一种编码如权利要求53所述结合结构域的核酸组合物。

56.一种表达载体,所述表达载体包含如权利要求55所述的核酸组合物。

57.一种包含权利要求56所述表达载体的宿主细胞。

58.一种抗-CD20抗体结合结构域,其包含:

a)包含序列为RASSSVSYIH(SEQ ID NO:XX)的vlCDR1、序列为ATSNLAS(SEQ ID NO:XX)

的vlCDR2、和序列为QQWTSNPPT(SEQ ID NO:XX)的vlCDR3的可变轻链结构域;和

b)包含序列为SYNMH(SEQ ID NO:XX)的vhCDR1、序列为AIYPGNGDTSYNQKFQG(SEQ ID NO:XX)的vhCDR2、和序列为STYYGGDWYFNV(SEQ ID NO:XX)的vhCDR3的可变重链结构域。

59.如权利要求58所述的抗-CD20抗体结合结构域,其中所述可变轻链结构域具有序列C2B8 L1(SEQ ID NO:XX)并且所述可变重链结构域具有序列C2B8 H1(SEQ ID NO:XX)。

60.一种编码如权利要求58所述结合结构域的核酸组合物。

61.一种表达载体,所述表达载体包含如权利要求60所述的核酸组合物。

62.一种包含权利要求61所述表达载体的宿主细胞。

63.一种异二聚体抗体,其包含:

a)第一单体,其包含:

i)第一Fc结构域;

ii)包含scFv可变轻链结构域,scFv接头和scFv可变重链结构域的抗-CD3 scFv;其中所述scFv用结构域接头共价接合至所述Fc结构域的N-端;

b)第二单体,包含重链,其包含:

i)重链可变结构域;和

ii)包含第二Fc结构域的第二重链恒定结构域;和

c)包含可变轻链结构域和可变轻链恒定结构域的轻链;其中所述可变轻链结构域包含具有序列RASSSVSYIH(SEQ ID NO:XX)的v1CDR1,具有序列ATSNLAS(SEQ ID NO:XX)的v1CDR2,和具有序列QQWTSNPPT(SEQ ID NO:XX)的vlCDR3,并且所述可变重链结构域包含具有序列SYNMH(SEQ ID NO:XX)的vhCDR1,具有序列AIYPGNGDTSYNQKFQG(SEQ ID NO:XX)的vhCDR2和具有序列STYYGGDWYFNV(SEQ ID NO:XX)的vhCDR3。

64.一种异二聚体抗体,其包含:

a)第一单体,其包含:

i)第一Fc结构域;

ii)包含scFv可变轻链结构域,scFv接头和scFv可变重链结构域的抗-CD3 scFv;其中所述scFv用结构域接头共价接合至所述Fc结构域的N-端;

b)第二单体,包含重链,其包含:

i)重链可变结构域;和

ii)包含第二Fc结构域的第二重链恒定结构域;和

c)包含可变轻链结构域和可变轻链恒定结构域的轻链;

其中所述可变轻链结构域包含具有序列RASSSVSYIH(SEQ ID NO:XX)的v1CDR1,具有序列ATSNLAS(SEQ ID NO:XX)的v1CDR2,和具有序列QQWTSNPPT(SEQ ID NO:XX)的vlCDR3,并且所述可变重链结构域包含具有序列SYNMH(SEQ ID NO:XX)的vhCDR1,具有序列AIYPGNGDTSYNQKFQG(SEQ ID NO:XX)的vhCDR2和具有序列STYYGGDWYFNV(SEQ ID NO:XX)的vhCDR3。

65.一种异二聚体抗体,其包含:

a)第一单体,其包含:

i)第一Fc结构域;

ii)包含scFv可变轻链结构域,scFv接头和scFv可变重链结构域的抗-CD3 scFv;其中

所述scFv用结构域接头共价接合至所述Fc结构域的N-端;

b)第二单体,包含重链,其包含:

i)重链可变结构域;和

ii)包含第二Fc结构域的重链恒定结构域;和

c)包含可变轻链结构域和可变轻链恒定结构域的轻链;其中所述可变轻链结构域包含具有序列KSSQSLLNTGNQKNYLT(SEQ ID NO:XX)的v1CDR1,具有序列WASTRES(SEQ ID NO:XX)的v1CDR2,和具有序列QNDYSYPYT(SEQ ID NO:XX)的v1CDR3,并且所述可变重链结构域包含具有序列DYYMK(SEQ ID NO:XX)的vhCDR1,具有序列DIIPSNGATFYNQKFKG(SEQ ID NO:XX)的vhCDR2和具有序列SHLLRASWFAY(SEQ ID NO:XX)的vhCDR3。

66.一种异二聚体抗体,其选自:XENP15049,XENP15051;XENP15050,XENP13676,XENP14696,XENP15629,XENP15053,XENP15630,XENP15631,XENP15632,XENP15633,XENP15634,XENP15635,XENP15636,XENP15638,XENP15639,XENP13677,XENP14388,XENP14389,XENP14390,XENP14391,XENP14392,XENP14393,XENP16366,XENP16367,XENP16368,XENP16369,XENP16370,XENP16371,XENP16372,XENP16373,XENP16375,XENP16376和XENP16377。

67.一种核酸组合物,其包含编码选自以下的异二聚体抗体的三种核酸:XENP15049,XENP15051;XENP15050,XENP13676,XENP14696,XENP15629,XENP15053,XENP15630,XENP15631,XENP15632,XENP15633,XENP15634,XENP15635,XENP15636,XENP15638,XENP15639,XENP13677,XENP14388,XENP14389,XENP14390,XENP14391,XENP14392,XENP14393,XENP16366,XENP16367,XENP16368,XENP16369,XENP16370,XENP16371,XENP16372,XENP16373,XENP16375,XENP16376和XENP16377。

68.一种表达载体组合物,其包含三种表达载体,所述表达载体各自含有核酸使得所述三种表达载体编码选自以下的异二聚体抗体:XENP15049,XENP15051;XENP15050,XENP13676,XENP14696,XENP15629,XENP15053,XENP15630,XENP15631,XENP15632,XENP15633,XENP15634,XENP15635,XENP15636,XENP15638,XENP15639,XENP13677,XENP14388,XENP14389,XENP14390,XENP14391,XENP14392,XENP14393,XENP16366,XENP16367,XENP16368,XENP16369,XENP16370,XENP16371,XENP16372,XENP16373,XENP16375,XENP16376和XENP16377。

69.一种宿主细胞,包含如权利要求67所述的核酸组合物。

70.一种宿主细胞,包含权利要求68所述的表达载体组合物。

71.一种制备如权利要求66所述异二聚体抗体的方法,包括在所述抗体被表达的条件下培养如权利要求69或70所述的宿主细胞,并且回收所述抗体。

72.一种治疗癌症的方法,包括向有此需要的患者给予如权利要求66所述的异二聚体抗体。

# 结合CD3和肿瘤抗原的异二聚体抗体

[0001] 相关申请的交叉引用

[0002] 本申请根据35U.S.C.§19(e)要求2014年11月26日提交的美国临时专利申请号62/085,117、2014年11月26日提交的美国临时专利申请号62/084,908、2014年11月26日提交的美国临时专利申请号62/085,027、2014年11月26 日提交的美国临时专利申请号62/085,106、2015年5月8日提交的美国临时专利申请号62/159,111、2015年11月4日提交的美国临时专利申请号62/251,005 和2015年11月4日提交的美国临时专利申请号62/250,971的优先权,其全部内容通过引用全文纳入本文,尤其是参考其中的附图、说明和权利要求。

[0003] 发明背景

[0004] 基于抗体的治疗已经成功用于治疗多种疾病,包括癌症和自身免疫/炎性病症。但仍然需要对这类药物的改进,尤其是增强其临床功效。正在探索的一条路是将其他和新抗原结合位点改造成基于抗体的药物,使得单个免疫球蛋白分子共结合两个不同的抗原。这种结合两个不同抗原的非天然或变换抗体形式通常被称为双特异性抗体。由于抗体可变区(Fv)的显著多样性理论上能产生上识别任何分子的Fv,双特异性抗体生成的一般方法是向抗体中引入新的可变区。

[0005] 已经探索的多种变换抗体形式用于双特异性靶向(Chames和Baty,2009, mAbs 1[6]:1-9;Holliger和Hudson,2005,Nature Biotechnology 23[9]:1126-1136;Kontermann,mAbs 4(2):182(2012),其全部通过引用纳入本文)。最初,通过将各自产生单个单克隆抗体的两个细胞系融合来制备双特异性抗体(Milstein等, 1983,Nature 305:537-540)。尽管得到的杂种杂交瘤或四倍体确实产生双特异性抗体,但它们仅是少数群体,并且需要大量纯化以分离所需抗体。其改造解决方案是使用抗体片段制备双特异性抗体。因为这样的片段缺乏全长抗体的复杂四级结构,所以可以在单个遗传构建体中连接可变轻链和重链。已经产生了许多不同形式的抗体片段,包括双抗体、单链双抗体、串联scFv和$Fab_2$双特异性抗体(Chames和Baty,2009,mAbs 1[6]:1-9;Holliger和Hudson,2005,Nature Biotechnology 23[9]:1126-1136;通过引用明确地并入本文)。虽然这些形式可以在细菌中以高水平表达,并且由于其小尺寸可能具有有利的渗透益处,但它们在体内迅速清除,并且可能存在与其生产和稳定性有关的制造困难。这些缺点的主要原因是抗体片段通常缺乏具有相关功能的抗体恒定区,包括较大尺寸、高稳定性以及与血清中保持长半衰期的各种Fc受体和配体结合(即,新生儿Fc受体FcRn)或用作纯化的结合位点(即蛋白A和蛋白G)。

[0006] 已开始尝试通过将双重结合改造为全长抗体-样形式来解决基于片段的双特异性抗体的缺点(Wu等,2007,Nature Biotechnology 25[11]:1290-1297; USSN12/477,711;Michaelson等,2009,mAbs 1[2]:128-141; PCT/US2008/074693;Zuo等,2000,Protein Engineering 13[5]:361-367; USSN09/865,198;Shen等,2006,J Biol Chem 281[16]:10706-10714;Lu等, 2005,J Biol Chem 280[20]:19665-19672;PCT/US2005/025472;明确地通过引用并入本文)。这些形式克服了抗体片段双特异性抗体的一些障碍,主要是因为它们含有Fc区。这些形式的一个明显缺点在于,因为它们在同二聚体恒定链顶部构建新的抗

原结合位点,所以与新抗原的结合总是二价的。

[0007] 对于作为治疗性双特异性抗体形式中共同靶标而受瞩目的许多抗原而言,希望结合是单价的而不是二价的。对于许多免疫受体而言,通过一价结合相互作用的交联来实现细胞活化。交联机制通常由抗体/抗原免疫复合物介导,或通过效应细胞与靶细胞结合。例如,低亲和性Fcγ受体(FcγR)如FcγRIIa、FcγRIIb 和FcγRIIIa与抗体Fc区单价结合。单价结合不会激活表达这些FcγR的细胞;然而,在免疫复合或细胞与细胞接触之后,受体被交联并聚集在细胞表面上,导致活化。对于负责介导细胞杀伤的受体,例如天然杀伤(NK)细胞上的 FcγRIIIa,当效应细胞以高亲合形式结合靶细胞时,发生受体交联和细胞活化(Bowles和Weiner,2005,J Immunol Methods 304:88-99,通过引用纳入本文)。类似地,在B细胞上,抑制性受体FcγRIIb仅在其与细胞表面B细胞受体(BCR) 结合到免疫复合物中时才下调B细胞活化,一种由可溶性IgG与BCR识别的相同抗原的免疫复合介导的机制(Heyman 2003,Immunol Lett 88[2]:157-161;Smith和Clatworthy,2010,Nature Reviews Immunology 10:328-343;明确地通过引用并入)。作为另一个实施例,T细胞的CD3激活仅在其相关联的T细胞受体(TCR)在高亲合细胞-细胞突触中与抗原呈递细胞上加载了抗原的MHC结合时发生(Kuhns等,2006,Immunity 24:133-139)。实际上,使用抗CD3抗体的CD3的非特异性二价交联引起细胞因子风暴和毒性(Perruche等,2009,J Immunol 183[2]:953-61;Chatenoud和Bluestone,2007,Nature Reviews Immunology 7:622-632;明确地通过引用并入)。因此,对于实际临床应用,用于重定向杀伤靶细胞的CD3共结合的优选模式是单价结合,仅在与共结合靶标结合时才导致活化。

[0008] CD38也称为环ADP核糖水解酶,是II型跨膜糖蛋白,具有长C末端胞外结构域和短N末端胞质结构域。在造血细胞中,多种功能效应被归结于CD38 介导的信号传导,包括淋巴细胞增殖、细胞因子释放、调节B细胞和骨髓细胞发育和存活、以及诱导树突状细胞成熟。CD38在许多造血恶性肿瘤和源自各种造血恶性肿瘤的细胞系中上调,包括非霍奇金淋巴瘤(NHL),伯基特淋巴瘤 (BL),多发性骨髓瘤(MM),B慢性淋巴细胞白血病(B-CLL),B和T急性淋巴细胞白血病(ALL),T细胞淋巴瘤(TCL),急性骨髓性白血病(AML),毛细胞白血病(HCL),霍奇金淋巴瘤(HL)和慢性骨髓性白血病(CML)。另一方面,造血系统的大多数原始多能干细胞是CD38-的。尽管抗癌药物有最新的发现和进展,但涉及CD38表达性肿瘤的许多癌症仍然预后不良。因此,需要更好的治疗此类癌症的方法。

[0009] B细胞抗原CD19(CD19,也称为B细胞表面抗原B4,Leu-12)是人泛-B 细胞表面标志物,从前-B细胞发育早期至终末分化为浆细胞都有表达。CD19 促进成熟B细胞的增殖和存活。它与细胞表面上的CD21复合。它还与CD81 和Leu-13结合并增强B细胞受体(BCR)信号传导。与BCR一起,CD19调节对于B细胞的克隆扩增和体液免疫至关重要的内在及抗原受体诱导的信号传导阈值。与CD21合作,它将适应性和先天免疫系统关联起来。激活后,CD19 的胞质尾磷酸化,引起Src家族激酶结合和PI-3激酶的募集。它是一种受瞩目的淋巴源癌症免疫治疗靶标,因为它在绝大多数的NHL细胞上以及一些白血病中也有表达。

[0010] 已有许多靶向CD19的抗体或抗体偶联物接受癌症治疗的临床前研究或临床试验评估。这些抗CD19抗体或抗体偶联物包括但不限于MT-103(单链双特异性CD19/CD3抗体;Hoffman等,2005 Int J Cancer 115:98-104;Schlereth 等,2006 Cancer Immunol Immunother 55:503-514)、CD19/CD16双抗体 (Schlenzka等,2004 Anti-cancer Drugs

15:915-919;Kipriyanov等,2002 J Immunol 169:137-144)、BU12-皂草毒蛋白(Flavell等,1995 Br J Cancer 72: 1373-1379)、和抗-CD19-伊达比星(Rowland等,1993 Cancer Immunol Immunother 55:503-514);全部明确地通过引用纳入本文。

[0011] CD123也称为白细胞介素-3受体α(IL-3Rα),在树突状细胞、单核细胞、嗜酸性粒细胞和嗜碱性粒细胞上表达。大多数髓系细胞(CD13+,CD14+, CD33+,CD15低)和一些CD19+细胞、定向造血干细胞/祖细胞也组成型地表达CD123。它不存在于CD3+细胞。

[0012] 因此,尽管由抗体片段产生的双特异性抗体遭遇有生物物理和药代动力学上的障碍,用全长抗体样形式构建的缺点则在于它们在主要靶抗原不存在的情况下会多价结合副靶标抗原,导致非特异性活化并可能导致毒性作用。本发明通过引入针对CD3和CD38的新型双特异性抗体来解决这个问题。

## 发明内容

[0013] 因此,本发明提供异二聚体抗体,其包含:a)第一单体,其包含:i)第一重链,其包含:1)第一可变重链结构域;2)包含第一Fc结构域的第一恒定重链; 3)包含scFv可变轻链结构域、scFv接头和scFv可变重链结构域的scFv;其中所述scFv用结构域接头共价连接到所述Fc结构域的C末端;b)包含第二重链的第二单体,所述第二重链包含第二可变重链结构域和第二恒定重链,所述第二恒定重链包含第二Fc结构域;和c)包含可变轻链结构域和恒定轻链结构域的共同轻链。

[0014] 另一方面,本发明提供如下异二聚体抗体,其包含:a)第一单体,其包含: i)第一重链,其包含:1)第一可变重链结构域;2)包含第一Fc结构域的第一恒定重链结构域;和3)第一可变轻链结构域,其中所述第一可变轻链结构域用结构域接头共价连接到所述第一Fc结构域的C-末端;b)第二单体,其包含:i) 第二可变重链结构域;ii)包含第二Fc结构域的第二恒定重链结构域;和iii)第三可变重链结构域,其中所述第二可变重链结构域用结构域接头共价连接到所述第二Fc结构域的C-末端;c)包含可变轻链结构域和恒定轻链结构域的共同轻链。

[0015] 在另一方面,本发明提供如下异二聚体抗体,其包含:a)第一单体,其包含:i)第一重链,其包含:1)第一可变重链结构域;2)包含第一CH1结构域和第一Fc结构域的第一恒定重链;3)包含scFv可变轻链结构域、scFv接头和scFv 可变重链结构域的scFv;其中所述scFv用结构域接头共价连接在所述CH1结构域的C-末端和所述第一Fc结构域的N-末端之间;b)包含第二重链的第二单体,所述第二重链包含第二可变重链结构域和第二恒定重链,所述第二恒定重链包含第二Fc结构域;和c)包含可变轻链结构域和恒定轻链结构域的共同轻链。

[0016] 另一方面,本发明提供如下异二聚体抗体,其包含:a)第一单体,其包含: i)第一重链,其包含:1)第一可变重链结构域;2)包含第一Fc结构域的第一恒定重链结构域;和3)第一可变轻链结构域,其中所述第二可变轻链结构域用结构域接头共价连接到所述第一恒定重链结构域的CH1结构域的C-末端和所述第一Fc结构域的N-末端之间;b)第二单体,其包含:i)第二可变重链结构域; ii)包含第二Fc结构域的第二恒定重链结构域;和iii)第三可变重链结构域,其中所述第二可变重链结构域用结构域接头共价连接到所述第二Fc结构域的C- 末端;c)包含可变轻链结构域和恒定轻链结构域的共同轻链。

[0017] 在另一方面，本发明提供如下异二聚体抗体，其包含：a)第一单体，其包含：i)第一重链，其包含：1)第一可变重链结构域；2)包含第一CH1结构域和第一Fc结构域的第一恒定重链；3)包含scFv可变轻链结构域、scFv接头和scFv 可变重链结构域的scFv；其中所述scFv用结构域接头共价连接在所述CH1结构域的C-末端和所述第一Fc结构域的N-末端之间；b)包含第二Fc结构域的第二单体；和c)包含可变轻链结构域和恒定轻链结构域的轻链。

[0018] 在一些方面，第一和第二Fc结构域具有组合氨基酸取代，选自：S364K/ E357Q：L368D/K370S；L368D/K370S：S364K；L368E/K370S：S364K；T411T /E360E/Q362E：D401K；L368D/K370S：S364K/E357L和K370S：S364K/ E357Q。此外，可变重链结构域和可变轻链结构域结合第一靶肿瘤抗原(TTA)， scFv结合第二TTA或人CD3。某些实施方式中，TTA选自CD19、CD20和 CD123。

[0019] 在另一方面，本发明提供抗-CD3抗原结合结构域，其CDR和/或可变结构域和/或scFv的序列如H1.32_L1.47，H1.89_L1.47，H1.90_L1.47，H1.33_L.1.47 和H1.31_L1.47的图中所示。本发明还提供核酸组合物、表达载体组合物和宿主细胞。

[0020] 在另一方面，本发明还提供如下异二聚体抗体，其包含a)第一单体，其包含：i)第一Fc结构域；ii)包含scFv可变轻链结构域、scFv接头和scFv可变重链结构域的抗-CD3 scFv；其中所述scFv用结构域接头共价连接到所述Fc结构域的N-末端；b)包含重链的第二单体，其包含：i)重链可变结构域；和ii)包含第二Fc结构域的重链恒定结构域；和c)包含可变轻链结构域和可变轻链恒定结构域的轻链；其中抗-CD3 scFv选自抗CD3 H1.32_L1.47，抗CD3 H1.89_L1.47，抗CD3 H1.90_L1.47和抗CD3 H1.33_L1.47(SEQ ID NO:XX)。重链可变结构域和轻链可变结构域结合TTA(包括但不限于CD19，CD20，CD38 和CD123)。

[0021] 另一方面，本发明提供抗-CD20抗体结合结构域，其包含：a)包含具有序列RASWSVSYIH(SEQ ID NO:XX)的v1CDR1，具有序列ATSNLAS(SEQ ID NO:XX)的v1CDR2，和具有序列QQWTHNPPT(SEQ ID NO:XX)的v1CDR3 的可变轻链结构域；和b)包含具有序列SYNMH(SEQ ID NO:XX)的vhCDR1，具有序列AIYPGNGATSYSQKFQG(SEQ ID NO:XX)的vhCDR2和具有序列 SYYMGGDWYFDV(SEQ ID NO:XX)的vhCDR3的可变重链结构域。某些实施方式中，抗-CD20抗体结合结构域具有C2B8 H1.202_L1.113序列。

[0022] 另一方面，本发明提供抗-CD20抗体结合结构域，其包含：a)包含具有序列RASSSVSYIH(SEQ ID NO:XX)的v1CDR1，具有序列ATSNLAS(SEQ ID NO:XX)的v1CDR2，和具有序列QQWTSNPPT(SEQ ID NO:XX)的v1CDR3 的可变轻链结构域；和b)包含具有序列SYNMH(SEQ ID NO:XX)的vhCDR1，具有序列AIYPGNGDTSYNQKFQG(SEQ ID NO:XX)的vhCDR2和具有序列 STYYGGDWYFNV(SEQ ID NO:XX)的vhCDR3的可变重链结构域。

[0023] 某些实施方式中，抗-CD20抗体结合结构域具有C2B8_H1L1序列。

[0024] 在另一方面，本发明提供如下异二聚体抗体，其包含a)第一单体，其包含： i)第一Fc结构域；ii)包含scFv可变轻链结构域、scFv接头和scFv可变重链结构域的抗-CD3 scFv；其中所述scFv用结构域接头共价连接到所述Fc结构域的 N-末端；b)包含重链的第二单体，其包含：i)重链可变结构域；和ii)包含第二 Fc结构域的重链恒定结构域；和c)包含可变轻链结构域和可变轻链恒定结构域的轻链；其中所述可变重链和轻链形成C2B8 H1.202_L1.113或C2B8_H1L1结合结构域。

[0025] 在另一方面，本发明提供如下异二聚体抗体，其包含a)第一单体，其包含： i)第一

Fc结构域;ii)包含scFv可变轻链结构域、scFv接头和scFv可变重链结构域的抗-CD3 scFv;其中所述scFv用结构域接头共价连接到所述Fc结构域的 N-末端;b)包含重链的第二单体,其包含:i)重链可变结构域;和ii)包含第二 Fc结构域的重链恒定结构域;和c)包含可变轻链结构域和可变轻链恒定结构域的轻链。在该实施方式中,可变结构域结合CD123并且可以具有 7G3_H1.109_L1.47的序列。

[0026] 另外,本发明提供选自以下的异二聚体抗体:XENP15049,XENP15051, XENP15050, XENP13676,XENP14696,XENP15629,XENP15053,XENP15630, XENP15631,XENP15632, XENP15633,XENP15634,XENP15635,XENP15636, XENP15638,XENP15639,XENP13677, XENP14388,XENP14389,XENP14390, XENP14391,XENP14392,XENP14393,XENP16366, XENP16367,XENP16368, XENP16369,XENP16370,XENP16371,XENP16372,XENP16373, XENP16375, XENP16376和XENP16377。本发明提供制备这些蛋白质并用它们治疗患者的方法,此外还提供了核酸、表达载体和宿主细胞。

## 附图说明

[0027] 图1A和1B、1C显示本发明的多种形式。显示了两种样式的“开瓶器”形式,一种的抗CD3抗原结合结构域含scFv而抗TTA抗原结合结构域含Fab,另一种则与此相反。mAb-Fv,mAb-scFv,中心-scFv和中心-Fv形式全部展示于图中。另外,还显示了单体之一仅含Fc结构域的“单臂”形式,既有单臂中心scFv也有单臂中心Fv。还显示了双scFv形式。

[0028] 图2显示“高CD3”抗-CD3-H1.30_L1.47构建体的各序列,包括可变重链结构域和可变轻链结构域(CDR标有下划线),各单列v1CDR和vhCDR,以及具有带电荷接头(双下划线)的scFv构建体。该带电荷接头可根据需要用不带电荷接头或不同的其他带电荷接头替代,附图中所有序列皆是如此。

[0029] 图3显示“高-中#1”抗-CD3_H1.32_L1.47构建体的各序列,包括可变重链结构域和可变轻链结构域(CDR标有下划线),各单列v1CDR和vhCDR,以及具有带电荷接头(双下划线)的scFv构建体。该带电荷接头可根据需要用不带电荷接头或不同的其他带电荷接头替代,附图中所有序列皆是如此。

[0030] 图4显示“高-中#2”抗-CD3_H1.89_L1.47构建体的各序列,包括可变重链结构域和可变轻链结构域(CDR标有下划线),各单列v1CDR和vhCDR,以及具有带电荷接头(双下划线)的scFv构建体。该带电荷接头可根据需要用不带电荷接头或不同的其他带电荷接头替代,附图中所有序列皆是如此。

[0031] 图5显示“高-中#3”抗-CD3_H1.90_L1.47构建体的各序列,包括可变重链结构域和可变轻链结构域(CDR标有下划线),各单列v1CDR和vhCDR,以及具有带电荷接头(双下划线)的scFv构建体。该带电荷接头可根据需要用不带电荷接头或不同的其他带电荷接头替代,附图中所有序列皆是如此。

[0032] 图6显示“中”抗-CD3_H1.90_L1.47构建体的各序列,包括可变重链结构域和可变轻链结构域(CDR标有下划线),各单列v1CDR和vhCDR,以及具有带电荷接头(双下划线)的scFv构建体。该带电荷接头可根据需要用不带电荷接头或不同的其他带电荷接头替代,附图中所有序列皆是如此。

[0033] 图7显示“低”抗-CD3_H1.31_L1.47构建体的各序列,包括可变重链结构域和可变

轻链结构域(CDR标有下划线),各单列v1CDR和vhCDR,以及具有带电荷接头(双下划线)的scFv构建体。该带电荷接头可根据需要用不带电荷接头或不同的其他带电荷接头替代,附图中所有序列皆是如此。

[0034] 图8显示高CD38:OKT10_H1.77_L1.24构建体的各序列,包括可变重链结构域和可变轻链结构域(CDR标有下划线),各单列v1CDR和vhCDR,以及具有带电荷接头(双下划线)的scFv构建体。

[0035] 图9显示中CD38:OKT10_H1L1.24构建体的各序列,包括可变重链结构域和可变轻链结构域(CDR标有下划线),各单列v1CDR和vhCDR,以及具有带电荷接头(双下划线)的scFv构建体。

[0036] 图10显示低CD38:OKT10_H1L1构建体的各序列,包括可变重链结构域和可变轻链结构域(CDR标有下划线),各单列v1CDR和vhCDR,以及具有带电荷接头(双下划线)的scFv构建体。

[0037] 图11显示XENP15331的序列。

[0038] 图12显示XENP13243的序列。

[0039] 图13显示XENP14702的序列。

[0040] 图14显示XENP15426的序列。

[0041] 图15显示XENP14701的序列。

[0042] 图16显示XENP14703的序列。

[0043] 图17显示XENP13243的序列。

[0044] 图18显示XENP18967的序列。

[0045] 图19显示XENP18971的序列。

[0046] 图20显示XENP18969的序列。

[0047] 图21显示XENP18970的序列。

[0048] 图22显示XENP18972的序列。

[0049] 图23显示XENP18973的序列。

[0050] 图24显示XENP15055的序列。

[0051] 图25显示XENP13544的序列。

[0052] 图26显示XENP13694的序列。

[0053] 图27显示人CD3ε的序列。

[0054] 图28显示全长人CD38蛋白(SEQ ID NO:130)及其胞外结构域(ECD;SEQ ID NO:131)。

[0055] 图29A-29E显示有用的配对异源二聚化变体组合(包括偏向变体和pI变体)。

[0056] 图30显示一系列等排变体抗体恒定区及相应取代。pI_(-)表示低pI变体,而pI_(+)表示高pI变体。这些可以任选地、独立地与本发明的其它异二聚化变体(以及如本文所述的其它变体类型)组合。

[0057] 图31显示有用的消除FcγR结合的消除变体(有时亦称“敲除”或“KO”变体)。

[0058] 图32显示本发明两个特别有用的实施方式。

[0059] 图33显示多种带电荷的scFv接头,用于提高或降低采用单scFv或多scFv 作为组分的异二聚体抗体的pI。有一种单电荷现有技术scFv接头,称为“Whitlow”,见Whitlow等,

Protein Engineering 6(8):989-995(1993)。需要指出的是,该接头被用于减少scFv聚集和增强蛋白水解稳定性。

[0060] 图34显示一系列改造的异二聚体-偏向Fc变体,及其异二聚体得率(据 HPLC-CIEX测定)和热稳定性(据DSC测定)。热稳定性未测定则用“n.d.”表示。

[0061] 图35:蛋白A亲和纯化后双特异性抗体的表达产率。

[0062] 图36:阳离子交换纯化色谱图。

[0063] 图37:重定向T细胞细胞毒性测定,24小时孵育,10k RPMI8226细胞, 400k T细胞。试验品为抗-CD38×抗-CD3双特异性抗体。采用LDH检测。

[0064] 图38:重定向T细胞细胞毒性测定,24小时孵育,10k RPMI8226细胞, 500k人PBMC。试验品为抗-CD38×抗-CD3双特异性抗体。采用LDH检测。

[0065] 图39显示XENP14419的序列。

[0066] 图40显示XENP14420的序列。

[0067] 图41显示XENP14421的序列。

[0068] 图42显示XENP14422的序列。

[0069] 图43显示XENP14423的序列。

[0070] 图44:重定向T细胞细胞毒性测定,96小时孵育,40k RPMI8226细胞, 400k人PBMC。试验品为抗-CD38×抗-CD3 Fab-scFv-Fc。用流式细胞术进行检测,具体为检测CD38+细胞的消失。

[0071] 图45:对图1所示重定向T细胞细胞毒性试验的进一步分析。第一行显示流式细胞术测得的CD4+和CD8+T细胞上激活标志物CD69的平均荧光强度(MFI)。第二行显示Ki-67+的CD4+和CD8+T细胞的百分比,作为细胞增殖的指标。第三行显示流式细胞术测得的CD4+和CD8+T细胞上粒酶B抑制剂 PI-9的胞内平均荧光强度(MFI)。

[0072] 图46:小鼠试验的设计,用以检测抗-CD38×抗-CD3 Fab-scFv-Fc双特异性抗体的抗肿瘤活性。

[0073] 图47:IVIS®测量的肿瘤大小与时间和治疗的关系。

[0074] 图48:IVIS®生物发光图像(第10天)。

[0075] 图49:单剂次指定试验品后猕猴中$CD38^{+}$细胞的清除。

[0076] 图50:据CD69平均荧光强度(MFI)测定的猕猴中T细胞活化,颜色标注如图49所示。

[0077] 图51单剂次指定试验品后的IL-6血清水平。

[0078] 图52显示XENP15427的序列。

[0079] 图53显示XENP15428的序列。

[0080] 图54显示XENP15429的序列。

[0081] 图55显示XENP15430的序列。

[0082] 图56显示XENP15431的序列。

[0083] 图57显示XENP15432的序列。

[0084] 图58显示XENP15433的序列。

[0085] 图59显示XENP15434的序列。

[0086] 图60显示XENP15435的序列。

[0087] 图61显示XENP15436的序列。

[0088] 图62显示XENP15437的序列。

[0089] 图63显示XENP15438的序列。

[0090] 图64显示Biacore试验中的结合亲和性。

[0091] 图65显示采用不同的轻链、Fab-Fc和scFv-Fc比例，稳定集合形成期间的异二聚体纯度。

[0092] 图66：huPBMC小鼠模型中抗-CD38×抗-CD3双特异性抗体的人IgM和 IgG2清除。

[0093] 图67显示稳定性优化的人源化抗-CD3变体scFv。显示相比H1_L1.4 scFv 序列的取代。氨基酸编号是Kabat编号。

[0094] 图68：稳定性优化的人源化抗-CD3变体scFv的氨基酸序列。CDR标有下划线。对于每个重链/轻链组合，列出四个序列：(i)具有C-末端6×His标签的scFv，(ii)仅scFv，(iii)仅VH，(iv)仅VL。

[0095] 图69：重定向T细胞细胞毒性测定，24小时孵育，10k RPMI8226细胞， 500k PBMC。试验品为抗-CD38(OKT10_H1L1，OKT10_H1.77_L1.24)×抗-CD3 Fab-scFv-Fc。采用LDH检测。

[0096] 图70：huPBL-SCID Ig-清除实验。PBMC移植后8天给予试验品，剂量为0.03、0.3或3mg/kg。给药途径是腹膜内。在PBMC移植后14天采取血样，加工得血清，测定人IgM和IgG2。

[0097] 图71显示XENP15049的序列。

[0098] 图72显示XENP15051的序列。

[0099] 图73显示XENP15050的序列。

[0100] 图74显示XENP13676的序列。

[0101] 图75显示XENP14696的序列。

[0102] 图76显示XENP15629的序列。

[0103] 图77显示XENP15053的序列。

[0104] 图78显示XENP15630的序列。

[0105] 图79显示XENP15631的序列。

[0106] 图80显示XENP15632的序列。

[0107] 图81显示XENP15633的序列。

[0108] 图82显示XENP15634的序列。

[0109] 图83显示XENP15635的序列。

[0110] 图84显示XENP15636的序列。

[0111] 图85显示XENP15638的序列。

[0112] 图86显示XENP15639的序列。

[0113] 图87显示XENP13677的序列。

[0114] 图88显示XENP14388的序列。

[0115] 图89显示XENP14389的序列。

[0116] 图90显示XENP14390的序列。

[0117] 图91显示XENP14391的序列。

[0118] 图92显示XENP14392的序列。

[0119] 图93显示XENP14393的序列。

[0120] 图94显示XENP16366的序列。

[0121] 图95显示XENP16367的序列。

[0122] 图96显示XENP16368的序列。

[0123] 图97显示XENP16369的序列。

[0124] 图98显示XENP16370的序列。

[0125] 图99显示XENP16371的序列。

[0126] 图100显示XENP16372的序列。

[0127] 图101显示XENP16373的序列。

[0128] 图102显示XENP16374的序列。

[0129] 图103显示XENP16375的序列。

[0130] 图104显示XENP16376的序列。

[0131] 图105显示XENP16377的序列。

[0132] 图106显示CD20和CD123抗原的序列。

[0133] 图107:CD3亲和性的表面等离振子共振测定。试验品为抗 -CD20(C2B8_H1.202_L1.113)×抗-CD3 Fab-scFv-Fc。人CD3δε-Fc(义翘神州生物技术公司(Sino Biological))共价结合于芯片表面。试验品以3.125、12.5、50 和200nM通过。

[0134] 图108:CD3亲和性的表面等离振子共振测定。试验品为抗 -CD20(C2B8_H1.202_L1.113)×抗-CD3 Fab-scFv-Fc。猕猴CD3δε-Fc(义翘神州生物技术公司)共价结合于芯片表面。试验品以3.125、12.5、50和200nM通过。

[0135] 图109:CD3亲和性的表面等离振子共振测定。试验品为抗 -CD20(C2B8_H1.202_L1.113)×抗-CD3 Fab-scFv-Fc。人CD3δε-Fc(义翘神州生物技术公司(Sino Biological))共价结合于芯片表面。试验品以31.25、125、500 和2000nM通过。

[0136] 图110:CD3亲和性的表面等离振子共振测定。试验品为抗 -CD20(C2B8_H1.202_L1.113)×抗-CD3 Fab-scFv-Fc。猕猴CD3δε-Fc(义翘神州生物技术公司)共价结合于芯片表面。试验品以31.25、125、500和2000nM通过。

[0137] 图111:CD3亲和性的表面等离振子共振测定。试验品为抗 -CD20(C2B8_H1.202_L1.113)×抗-CD3 Fab-scFv-Fc。猕猴CD3δε-Fc(义翘神州生物技术公司)共价结合于芯片表面。试验品以31.25、125、500和2000nM通过。

[0138] 图112:重定向T细胞细胞毒性测定,24小时孵育,10k拉莫斯细胞,250k PBMC。试验品为抗-CD20(C2B8_H1.202_L1.113)×抗-CD3 Fab-scFv-Fc。采用 LDH检测。

[0139] 图113:重定向T细胞细胞毒性测定,24小时孵育,20k Jeko细胞,200k PBMC(CD19-清除)。试验品为抗-CD20(C2B8_H1.202_L1.113)×抗-CD3 Fab-scFv-Fc。采用流式细胞术检测,具体检测$CD19^{+}$细胞的消失。

[0140] 图114:图113中所述实验的24小时后IL-6产出。

[0141] 图115:重定向T细胞细胞毒性测定,5小时孵育,20k Jeko细胞,500k PBMC(CD19-清除)。试验品为抗-CD20(C2B8_H1L1)×抗-CD3 Fab-scFv-Fc。采用流式细胞术检测,具体检测$CD19^{+}$细胞的消失。

[0142] 图116:重定向T细胞细胞毒性测定,24小时孵育,20k Jeko细胞,500k PBMC(CD19-清除)。试验品为抗-CD20(C2B8_H1.202_L1.113)×抗-CD3 Fab-scFv-Fc。采用流式细胞术

检测,具体检测$CD19^+$细胞的消失。

[0143] 图117:图113中所述的实验24小时后的IL-6产生。

[0144] 图118:重定向T细胞细胞毒性测定,24小时孵育,10k RPMI8226细胞, 500k PBMC。试验品为抗-CD38(OKT10_H1L1,OKT10_H1.77_L1.24)×抗-CD3 Fab-scFv-Fc。采用LDH检测。

[0145] 图119:huPBL-SCID Ig-清除实验。PBMC移植后1和8天给予5mg/kg 的试验品。给药途径是腹膜内。在PBMC移植后14天采取血样,加工得血清,检测人IgM和IgG2。

[0146] 图120:huPBL-SCID Ig-清除实验。PBMC植入后8天给予0.03、0.3或3 mg/kg的试验品。给药途径是腹膜内。在PBMC移植后14天采取血样,加工得血清,检测人IgM和IgG2。

[0147] 图121显示高CD20 C2B8_H1.202_L1.113的序列。

[0148] 图122显示低CD20 C2B8_H1L1的序列。

[0149] 图123显示CD123 7G3_H1.109_L1.57的序列。

[0150] 图124中的矩阵为本发明可能的组合形式。“A”表示参比CD3序列CDR 可与右手侧的TTA上的CDR组合。即,来自可变重链CD3 H1.30序列的vhCDR 和来自CD3 L1.57序列的可变轻链的vlCDR可与来自CD38 OKT10 H1.77序列的vhCDR和来自OKT10L1.24序列的vlCDR组合。“B”表示来自CD3构建体的CDR可与TTA的可变重链结构域和可变轻链结构域组合。即,来自可变重链CD3 H1.30序列的vhCDR和来自CD3 L1.57序列的可变轻链的vlCDR可与可变重链结构域CD38 OKT10 H1.77序列和OKT10L1.24序列组合。“C”相反,即CD3序列的可变重链结构域和可变轻链结构域与TTA的CDR联用。“D”:每一个的可变重链和可变轻链的组合。“E”:CD3的scFv与TTA 的CDR联用,“F”:CD3的scFv与TTA抗原结合结构域的可变重链结构域和可变轻链结构域联用。

[0151] 发明详述

[0152] I.定义

[0153] 为了使本申请得到更完整的理解,下面给出若干定义。这些定义包括其语语法同义和等同形式。

[0154] 本文中的“消除”表示降低或去除活性。因此,例如,“消除Fcγ R结合”表示,与不含特定变体的Fc区相比,Fc区氨基酸变体的结合低于初始结合的 50%,优选活性丧失70-80-90-95-98%或以上,总体上,活性低于biacore实验中可检测结合水平。消除Fcγ R结合特别有用的那些见图16。

[0155] 本文所用的“ADCC”或“抗体依赖性细胞介导的细胞毒性”表示如下所述细胞介导的反应:表达Fcγ R的非特异性细胞毒性细胞识别靶细胞上结合的抗体,随后引起靶细胞裂解。ADCC和与Fcγ RIIIa结合相关;增加Fcγ RIIIa结合导致ADCC活性增强。

[0156] 本文所用的“ADCP”或抗体依赖性细胞介导的吞噬作用表示如下所述细胞介导的反应:表达Fcγ R的非特异性细胞毒性细胞识别靶细胞上结合的抗体,随后引起对靶细胞的吞噬作用。

[0157] 本文所用的“修饰”表示多肽序列中的氨基酸取代、插入和/或缺失,或蛋白质上化学连接的结构单元的改变。例如,修饰可以是蛋白质上相连的糖或 PEG结构改变。本文的“氨基酸修饰”表示多肽序列中的氨基酸取代、插入和 /或缺失。为了清楚起见,除非另外说明,氨基酸修饰总是对DNA编码的氨基酸进行,例如,具有DNA和RNA密码子的那20个氨基酸。

[0158] 本文中的“氨基酸取代”或“取代”表示用不同的氨基酸置换在亲本多肽序列中的特定位置的氨基酸。具体地，某些实施方式中，取代指非天然存在于某位置的氨基酸，非天然存在于该生物或非天然存在于任何生物中。例如，取代E272Y是指这样的变体多肽，在此为Fc变体，其中在272位处的谷氨酸被酪氨酸替代。为了清楚起见，经改造改变了核酸编码序列而没有改变初始氨基酸(例如，将CGG(编码精氨酸)改成CGA(仍然编码精氨酸)以提高宿主表达水平)的蛋白质不属于“氨基酸取代”；即，尽管生成了编码相同蛋白质的新基因，如果蛋白质特定位置仍为原初同样的氨基酸，则不是氨基酸取代。

[0159] 本文所用的“氨基酸插入”或“插入”表示在亲本多肽序列中的特定位置处加入氨基酸序列。例如，-233E或233E是指在233位之后234位之前插入谷氨酸。另外，-233ADE或A233ADE是指在233位之后234位之前插入 AlaAspGlu。

[0160] 本文所用的“氨基酸缺失”或“缺失”表示在亲本多肽序列中的特定位置去除氨基酸序列。例如，E233-或E233#或E233()是指233位谷氨酸缺失。另外，EDA233-或EDA233#是指在233位处序列GluAspAla缺失。

[0161] 本文所用的“变体蛋白质”或“蛋白质变体”或“变体”表示与亲本蛋白质相差至少一个氨基酸修饰的蛋白质。蛋白质变体可以指蛋白质本身、包含蛋白质的组合物、或编码蛋白质的氨基酸序列。优选地，与亲本蛋白质相比，蛋白质变体具有至少一个氨基酸修饰，例如，与亲本相比约1个至约70个氨基酸修饰，优选约1个至约5个氨基酸修饰。如下所述，某些实施方式中，亲本多肽，例如Fc亲本多肽，是人野生型序列，如来自IgG1、IgG2、IgG3或IgG4的Fc区，但是，具有变体的人序列也可作为“亲本多肽”，例如，图19中的 IgG1/2杂合体。本文中的蛋白质变体序列优选与亲本蛋白质序列至少约80％相同，优选至少约90％相同，更优选至少约95-98-99％相同。变体蛋白质可指代变体蛋白质本身、包含蛋白质变体的组合物、或编码变体蛋白质的DNA序列。因此，本文所用的“抗体变体”或“变体抗体”表示与亲本抗体相差至少1个氨基酸修饰的抗体，本文所用的“IgG变体”或“变体IgG”表示与亲本IgG(同样，许多情况中是人IgG序列)相差至少1个氨基酸修饰的抗体，并且，本文所用的“免疫球蛋白变体”或“变体免疫球蛋白”表示与亲本免疫球蛋白序列相差至少1个氨基酸修饰的免疫球蛋白序列。本文所用的“Fc变体”或“变体 Fc”表示包含Fc结构域内氨基酸修饰的蛋白质。本发明的Fc变体按照所含氨基酸修饰来描述。因此，例如，N434S或434S是相比亲本Fc多肽在434位处有取代丝氨酸的Fc变体，其中编码是按照EU索引。类似地，M428L/N434S 描述的是相比亲本Fc多肽具有M428L和N434S取代的Fc变体。可能不标明野生(WT)氨基酸，例如以428L/434S描述的变体。需要说明的是，取代描述的顺序是任意的，也就是说，例如，428L/434S和M428L/N434S是相同Fc变体，以此类推。本发明中与抗体相关的所有位置，除非另有说明，均按照EU 索引对氨基酸位置进行编号。EU索引或Kabat或EU编码方案中的EU索引是指EU抗体编码体系(Edelman等，1969，Proc Natl Acad Sci USA 63:78-85，通过引用全文纳入本文)。修饰可以是添加、缺失或取代。取代可包括天然氨基酸，有时还包括合成氨基酸。示例包括美国专利号6,586,207；WO 98/48032；WO 03/073238；US2004-0214988A1；WO 05/35727A2；WO 05/74524A2；J.W.Chin 等，(2002)，Journal of the American Chemical Society 124:9026-9027；J.W.Chin 和P.G.Schultz，(2002)，ChemBioChem 11:1135-1137；J.W.Chin等，(2002)， PICAS United States of America 99:11020-11024；和L.Wang和P.G.Schultz， (2002)，Chem.1-10，全部通过引用纳入本文。

[0162] 本文所用的“蛋白质”表示共价接合的至少两个氨基酸，其包括蛋白质、多肽、寡肽和肽。肽基可包含天然氨基酸和肽键或合成的拟肽结构，即“类似物”，如类肽(参见Simon等，PNAS USA 89(20):9367(1992)，通过引用全文纳入)。氨基酸可以是天然的或是合成的(例如不是由DNA编码的氨基酸)；正如本领域技术人员所能理解的。例如，高苯丙氨酸、瓜氨酸、鸟氨酸和正亮氨酸在本发明中视为合成氨基酸，并且，D-和L-(R或S)构象的氨基酸均可采用。本发明的变体可包括采用合成氨基酸的修饰，合成氨基酸掺入可采用例如 Schultz及其同事开发的技术，包括但与限于以下所述的方法：Cropp和Shultz, 2004,Trends Genet.20(12):625-30，Anderson等，2004,Proc Natl Acad Sci USA 101(2):7566-71，Zhang等，2003,303(5656):371-3，和Chin等，2003,Science 301(5635):964-7，全部通过引用全文纳入本文。另外，多肽可包括一条或多条侧链、一个或多个末端的合成衍生化、糖基化、PEG化、环状排列、环化、连接其他分子的接头、与蛋白质或蛋白质结构域的融合、以及添加肽标签或标记物。

[0163] 本文所用的“残基”表示蛋白质中的位置及该位置上的氨基酸。例如，天冬酰胺297(也称为Asn297或N297)指人抗体IgG1中297位处的残基。

[0164] 本文所用的“Fab”或“Fab区”表示包含VH、CH1、VL和CL免疫球蛋白结构域的多肽。Fab可以指分离出来的该区域或包含于全长抗体、抗体片段或Fab融合蛋白中的该区域。本文所用的“Fv”或“Fv片段”或“Fv区”表示包含单个抗体的VL和VH结构域的多肽。本领域技术人员可以看出，这些一般由两条链组成。

[0165] 本文所用的“IgG亚类修饰”或“同种型修饰”表示将某IgG同种型内某氨基酸转变成另一并列IgG同种型中相应氨基酸的氨基酸修饰。例如，因为 IgG1在EU第296位是酪氨酸而IgG2是苯丙氨酸，则IgG2中的F296Y取代被认为是IgG亚类修饰。

[0166] 本文所用的“非天然修饰”表示非同种型氨基酸修饰。例如，由于所有IgG 第434位处都不是丝氨酸，则IgG1、IgG2、IgG3、或IgG4(或其杂合体)中的取代434S被认为是非天然修饰。

[0167] 本文所用的“氨基酸”和“具体的氨基酸”表示由DNA和RNA编码的 20种天然氨基酸之一。

[0168] 本文所用的“效应物功能”表示由抗体Fc区与Fc受体或配体的相互作用产生的生物化学事件。效应物功能包括但不限于ADCC、ADCP和CDC。

[0169] 本文所用的“IgG Fc配体”表示来自各种生物体的这样的分子，优选多肽，其结合IgG抗体的Fc区以形成Fc/Fc配体复合物。Fc配体包括但不限于FcγRI、 FcγRII、FcγRIII、FcRn、C1q、C3、甘露聚糖结合凝集素、甘露糖受体、葡萄球菌蛋白A、链球菌蛋白G、和病毒FcγR。Fc配体还包括Fc受体同源物(FcRH)，这是一个与FcγR同源的Fc受体家族(Davis等，2002,Immunological Reviews 190:123-136，通过引用全文纳入)。Fc配体包括尚未发现的结合Fc的分子。特定的IgG Fc配体是FcRn和Fcγ受体。本文所用的“Fc配体”表示来自各种生物体的这样的分子，优选多肽，其结合抗体的Fc区以形成Fc/Fc配体复合物。

[0170] 本文所用的“Fcγ受体”、“FcγR”或“FcqammaR”表示这样一个蛋白质家族的成员，该家族蛋白结合IgG抗体Fc区并由FcγR基因编码。在人类中，该家族包括但不限于FcγRI(CD64)，包括亚型FcγRIa、FcγRIb、和FcγRIc； FcγRII(CD32)，包括亚型FcγRIIa(包括同种异型H131和R131)、FcγRIIb(包括 FcγRIIb-1和FcγRIIb-2)、和FcγRIIc；和Fcγ

RIII(CD16),包括亚型FcγRIIIa(包括同种异型V158和F158)和FcγRIIIb(包括同种异型FcγRIIb-NA1和 FcγRIIb-NA2)(Jefferis等,2002,Immunol Lett 82:57-65,全文通过引用纳入)、还包括尚未发现的人FcγR或FcγR亚型或同种异型。FcγR可来自任何生物体,包括但不限于人、小鼠、大鼠、兔和猴。小鼠FcγR包括但不限于FcγRI(CD64)、FcγRII(CD32)、FcγRIII(CD16)、和FcγRIII-2(CD16-2),还包括尚未发现的小鼠 FcγR或FcγR亚型或同种异型。

[0171] 本文所用术语"FcRn"或"新生儿Fc受体"表示结合IgG抗体Fc区并至少部分由FcRn基因编码的蛋白质。FcRn可来自任何生物体,包括但不限于人、小鼠、大鼠、兔和猴。如本领域所知,功能性FcRn蛋白质包括通常称为重链和轻链的两条多肽。轻链是β-2-微球蛋白,重链由FcRn基因编码。除非本文另外说明,FcRn或FcRn蛋白质是指FcRn重链和β-2-微球蛋白的复合物。各种FcRn变体用于增强与FcRn受体的结合,有时用于延长血清半衰期,见图83及其说明。

[0172] 本文所用的"亲本多肽"指初始多肽,后经修饰而成变体。亲本多肽可以是天然多肽,或天然多肽的变体或改造版本。亲本多肽可以指多肽本身\包含亲本多肽的组合物\或编码亲本多肽的氨基酸序列。因此,本文所用的"亲本免疫球蛋白"是指未修饰的免疫球蛋白多肽,其经修饰而成变体,本文所用的"亲本抗体"是指未修饰的抗体,经修饰而成变体抗体。需要说明的是,"亲本抗体"包括已知的市售、重组产生的抗体,如后文所述。

[0173] 本文所用的"Fc"或"Fc区"或"Fc结构域"表示包含抗体恒定区除第一恒定区免疫球蛋白结构域之外部分的多肽,有时还排除部分铰链区。因此, Fc指IgA、IgD和IgG的后两个恒定区免疫球蛋白结构域,IgE和IgM的后三个恒定区免疫球蛋白结构域,以及这些结构域N末端的柔性绞链区。对于IgA 和IgM而言,Fc可包含J链。对于IgG而言,Fc区包括免疫球蛋白结构域Cγ2 和Cγ3(Cγ2和Cγ3)以及Cγ1(Cγ1)和Cγ2(Cγ2)之间的铰链区下部。虽然Fc区的边界可变,但人IgG重链Fc区通常被定义为包含残基C226或P230至羧基端的区域,其中编号是根据Kabat的EU索引。某些实施方式中,如后文所述,对Fc区进行氨基酸修饰,例如,由此改变与一个或多个FcγR受体或FcRn受体的结合。

[0174] 本文的"重链恒定区"表示抗体的CH1-铰链-CH2-CH3部分。

[0175] 本文的"Fc融合蛋白"或"免疫粘附素"是指这样一种蛋白质,其包含 Fc区,一般连接(任选地通过接头连接,如本文所述)至另外的蛋白质,如针对靶蛋白的结合部分,如本文所述。在一些情况中,异二聚体抗体的单体之一包含抗体重链(或者包括scFV或者还包括轻链)并且另一个单体是Fc融合体,包含可变Fc结构域和配体。某些实施方式中,这些"半抗体-半融合蛋白"被称为"融合体(Fuisionbody)"。

[0176] 本文所用的"位置"是指蛋白质序列中的位置。位置可依次顺序编号,或者按照既有格式,例如用于抗体编号的EU索引。

[0177] 本文所用的"靶抗原"是指被给定抗体的可变区特异性结合的分子。靶抗原可以是蛋白质、糖、脂质或其他化合物。下文描述了多种合适的靶抗原。

[0178] 就本发明异二聚体抗体的单体而言,"链型"是指,与"相互匹配"的 DNA双链相似,在各单体中引入异二聚体变体从而保留"相互匹配"以形成异二聚体的能力。例如,如果某些pI变体被改造成单体A(例如,使pI更高),则同样可采用"电荷对"的立构变体不干扰pI变体,例如,使pI更高的电荷变体被放在同一"链"或"单体"上以保留两种官能团。类似的,对

于下文配对组合方式出现的“偏向(skew)”变体，本领域技术人员在决定将配对中某组纳入哪一链或哪一单体时会考虑pI，从而同时利用偏向变体的pI使pI分离最大化。

[0179] 本文所用的“靶细胞”是指表达靶抗原的细胞。

[0180] 本文所用的“可变区”是免疫球蛋白的如下所述的区域：其包含一个或多个基本由V.κ、V.λ和/或分别构成κ、λ和重链免疫球蛋白遗传基因座的VH基因编码的Ig结构域。

[0181] 本文的“野生型或WT”表示在自然中发现的氨基酸序列或核苷酸序列，包括等位基因变异。WT蛋白质具有还未经特意修饰的氨基酸序列或核苷酸序列。

[0182] 本发明的抗体一般是分离的或重组的。当用于描述本文公开的各种多肽时，“分离的”表示多肽已经从其表达的细胞或细胞培养物中分离和/或回收并鉴定。通常，分离的多肽其制备经历至少一个纯化步骤。“分离抗体”指基本不含抗原特异性不同的其他抗体。“重组”表示抗体是用重组核酸技术在外源宿主细胞中生成的。

[0183] “特异性结合”或“特异性结合至”或“特异性针对”特定抗原或表位表示结合可测知地区别于非特异性相互作用。例如，特异性结合可通过测定某分子的结合并与对照分子的结合进行比较来测定，对照分子一般是结构上相似但没有结合活性的分子。例如，可通过与靶标相似的对照分子的竞争来确定特异性结合。

[0184] 针对特定抗原或表位的特异性结合可表现为抗体对抗原或表位的$K_D$至少约$10^{-4}$M、至少约$10^{-5}$M、至少约$10^{-6}$M、至少约$10^{-7}$M、至少约$10^{-8}$M、至少约$10^{-9}$M、或者至少约$10^{-10}$M、至少约$10^{-11}$M、至少约$10^{-12}$M或更高，其中$K_D$是指特定抗体-抗原相互作用的解离率。一般而言，特异性结合某抗原的抗体的$K_D$比该抗原或表位相关对照分子高20、50、100、500、1000、5,000、10000或更多倍。

[0185] 同时，针对特定抗原或表位的特异性结合还可表现为，例如，抗体对某抗原或表位的$K_A$或$K_a$比对照高至少20、50、100、500、1000、5000、10000或更多倍，其中$K_A$或$K_a$是指特定抗体-抗原相互作用的结合率。

[0186] II.概述

[0187] 已设计了CD3和肿瘤抗原靶标共结合的双特异性抗体用于重定向T细胞以攻击并裂解靶向的肿瘤细胞。例如BiTE和DART型，它们单价结合CD3 和肿瘤抗原。虽然CD3-靶向策略已显示出相当的前景，这类疗法的常见副作用是与之关联的细胞因子产生，通常导致有害的细胞因子释放综合征。因为双特异性抗体的抗-CD3结合结构域结合所有的T细胞，募集了细胞因子高产的 CD4 T细胞亚组。并且，CD4 T细胞亚组包括调节性T细胞，其募集和扩增会导致免疫抑制并对长期肿瘤抑制有负面影响。另外，这些形式的双特异性抗体不含Fc结构域，在患者中血清半衰期非常短。

[0188] 虽然CD3-靶向策略显示出相当的前景，这类疗法的常见副作用是与之关联的细胞因子产生，通常导致有害的细胞因子释放综合征。因为双特异性抗体的抗-CD3结合结构域结合所有的T细胞，募集了细胞因子高产的CD4 T细胞亚组。并且，CD4 T细胞亚组包括调节性T细胞，其募集和扩增会导致免疫抑制并对长期肿瘤抑制有负面影响。一种降低细胞因子产生并可能降低CD4 T 细胞活化的可行方式是通过降低抗-CD3结构域对CD3的亲和性。

[0189] 因此，某些实施方式中，本发明提供的抗体构建体具有抗-CD3抗原结合结构域，其为对CD3的“强”或“高亲和性”结合者(例如，H1.30_L1.47的重链和轻链可变结构域(任选地包括适当的带电荷的接头))，还结合CD38。另一些实施方式中，本发明提供的抗体构建体具

有抗-CD3抗原结合结构域，其为对CD3的“轻度”或“低亲和性”结合者。另一些实施方式中，抗体构建体具有抗-CD3抗原结合结构域，其对CD3的亲和性为中等或“中度”，还结合CD38。

[0190] 应理解本发明的“高、中、低”抗-CD3序列可用于各种形式的异二聚化。虽然本文中大多采用“开瓶器”型异二聚体，这些可变重链序列和可变轻链序列，以及scFv序列(和包含可变重链序列和可变轻链序列的Fab序列)可以用于其他形式，如WO公开号2014/145806的图2中那些，该申请的附图、所示形式和附图说明通过引用纳入本文。

[0191] 因此，本发明提供可结合两种不同抗原的异二聚体抗体，例如，该抗体是“双特异性的”，即它们结合两种不同的靶抗原，一般是下文所述的肿瘤抗原 (TTA)。这些异二聚体抗体可以单价(例如，只有一个抗原结合结构域，如可变重链结构域和可变轻链结构域对)或二价(有两个抗原结合结构域，各自独立结合抗原)结合这些靶抗原。本发明的异二聚体抗体基于采用不同的单体，这些单体含有相比同二聚体“偏向”形成异二聚体的氨基酸取代(如后文所述)联合“pI变体”，“pI变体”使得异二聚体易于与同二聚体纯化分离(亦如下文所述)。对于本发明的异二聚体双特异性抗体，本发明主要依赖于采用改造的Fc 结构域或变体Fc结构域，它们能在生产细胞中自组装成异二聚体蛋白质，本发明同时还基于生成并纯化这种异二聚体蛋白质的方法。

[0192] III.抗体

[0193] 本发明涉及生成结合两种不同抗原，例如CD3和靶肿瘤抗原如CD20、 CD38和CD123，并且总体而言为治疗性抗体的双特异性抗体。文中“抗体”是广义的。可用于本发明的抗体可采用本文所述的多种形式，包括传统抗体以及抗体衍生物、片段和模拟物，如本文所述。

[0194] 常规抗体结构单元一般包括四聚体。各四聚体一般由相同的两对多肽链构成，各对有一条“轻链”(分子量一般为约25kDa)和一条“重链”(分子量一般为约50-70kDa)。人轻链分类为κ和λ轻链。本发明涉及IgG类，其具有几个亚类，包括但不限于IgG1、IgG2、IgG3、和IgG4。因此，本文所用的“同种型”表示由恒定区的化学和抗原特征决定的免疫球蛋白各亚类。应理解，治疗性抗体还可包含同种型和/或亚类的杂合体。如美国公开号2009/0163699中所述，其通过引用纳入，本发明包括对IgG1/G2杂合体的pI改造。

[0195] 各链的氨基末端部分包括约100-110或更多个氨基酸的可变区，其主要负责抗原识别，一般在本领域和本文中被称为“Fv结构域”或“Fv区”。在可变区中，重链和轻链各自V结构域中的3个环共同形成抗原结合位点。各环称为互补决定区(下文中称为“CDR”)，其中氨基酸序列的变化最显著。“可变”是指可变区某些区段的序列在抗体间存在广泛差异。可变区内的变化并不是均匀分布的。事实上，V区由称为框架区(FR)的相对稳定的15-30个氨基酸的延伸部分和分布在框架区之间称为“高变区”的各自长9-15个氨基酸或更长的高度可变短区域组成。

[0196] 每一VH和VL由三个高变区(“互补决定区”，“CDR”)和四个FR组成，从氨基端到羧基端按照以下顺序排列：FR1-CDR1-FR2-CDR2-FR3-CDR3-FR4。

[0197] 高变区一般包含轻链可变区的约氨基酸残基24-34(LCDR1；“L”表示轻链)、50-56(LCDR2)和89-97(LCDR3)以及重链可变区的约氨基酸残基 31-35B(HCDR1；“H”表示重链)、50-65(HCDR2)和95-102(HCDR3)；Kabat等，《免疫学感兴趣蛋白质的序列》(SEQUENCES OF PROTEINS OF IMMUNOLOGICAL INTEREST)，第5版，马里兰州贝塞斯达的国立卫生研究院公

共健康服务部(Public Health Service,National Institutes of Health,Bethesda,Md.)(1991)和/或形成高变环(例如,轻链可变区中的残基26-32(LCDR1)、50-52(LCDR2)和91-96(LCDR3)以及重链可变区中的残基26-32(HCDR1)、53-55(HCDR2)和96-101(HCDR3)的那些残基;Chothia和Lesk(1987)J.Mol. Biol.196:901-917。下面描述本发明的具体CDR。

[0198] 本说明书中,提及可变结构域中的残基时,一般采用Kabat编号系统(大致上,轻链可变区残基1-107,重链可变区残基1-113),并且,Fc区采用EU 编号系统(例如,Kabat等,同上(1991))。

[0199] 本发明提供了大量不同的CDR组合。在这种情况中,"全CDR组"包括 3个可变轻链CDR和3个可变重链CDR,例如,vlCDR1、vlCDR2、vlCDR3、 vhCDR1、vhCDR2和vhCDR3。这可以分别是更大的可变轻链结构域和可变重链结构域的局部。另外,如本文更详细的论述,可变重链结构域和可变轻链结构域可分处于分开的多肽链中,当采用重链和轻链时(例如,当采用Fab时),或在同一多肽链上,例如scFv序列。

[0200] CDR参与形成抗原结合位点,或更具体地说是表位结合位点。"表位"是指与抗体分子可变区中特定抗原结合位点("抗体决定簇")相互作用的决定簇。表位由氨基酸或糖侧链等分子集合而成,且通常具有特定的结构特征以及特定电荷特征。一个抗原可具有一个以上表位。

[0201] 表位可包含直接参与结合的氨基酸残基(也称为表位的免疫决定组分)和不参与结合的其他氨基酸残基,如被特异性抗原结合肽有效封闭的氨基酸残基;换而言之,这些氨基酸残基包括在特异性抗原结合肽的足迹(footprint)内。

[0202] 表位可以是构象表位或线性表位。构象表位由线性多肽链不同区段的氨基酸空间并列形成。线性表位由多肽链中的相邻氨基酸残基形成。构象表位和非构象表位的区别在于:变性溶剂存在下,与构象表位的结合会丢失,而非构象表位的则不会。

[0203] 表位通常包含呈独特空间构象的至少3个、或更常见的是至少5个或8-10 个氨基酸。可以通过简单的免疫实验显示一种抗体阻断另一种抗体与靶抗原结合的能力来认证识别相同表位的抗体,例如,"聚类试验(binning)"。

[0204] 各链的羧基末端部分定义为主要负责效应物功能的恒定区。Kabat等汇总了众多重链和轻链可变区的一级序列。根据序列的保守程度,各一级序列被分类为CDR和框架区,并且制成列表(参见《免疫学感兴趣蛋白质的序列》(SEQUENCES OF PROTEINS OF IMMUNOLOGICAL INTEREST),第5版, NIH出版号91-3242,E.A.Kabat等,通过引用全文纳入)。

[0205] 在免疫球蛋白的IgG亚类中,重链中存在多个免疫球蛋白结构域。本文中"免疫球蛋白(Ig)结构域"表示免疫球蛋白中具有独特三级结构的区域。本发明感兴趣的是重链结构域,包括恒定重链(CH)结构域和铰链结构域。就IgG抗体而言,IgG同种型各有3个CH区。因此,IgG的"CH"结构域如下:按照 kabat的EU索引,"CH1"指118-220位。按照kabat的EU索引,"CH2"指237-340 位,并且按照kabat的EU索引,"CH3"指341-447位。如本文所述,pI变体可存在于一个或多个CH区以及铰链区中,如后文所述。

[0206] 需要说明的是,此处的序列自CH1,118位开始;不包括可变区,除非另有说明。例如,SEQ ID NO:2的第一氨基酸,虽然在序列表中指为"1"位,根据EU编号,对应的是CH1区的118位。

[0207] 另一类重链Ig结构域是铰链区。本文中的“铰链”或“铰链区”或“抗体铰链区”或“免疫球蛋白铰链区”表示包含抗体第一和第二恒定结构域之间氨基酸的挠性多肽。结构上,IgG CH1结构域终止于EU第220位,IgG CH2 结构域始于EU第237位残基。因此,对于IgG而言,抗体铰链在此定义为包括221(IgG1中的D221)至236(IgG1中的G236)位,其中编号是根据Kabat的 EU索引。某些实施方式中,例如,就Fc区而言,包括铰链下部,“铰链下部”一般是指226或230位。如本文所述,也可在铰链区中制造pI变体。

[0208] 轻链一般包括两个结构域,轻链可变结构域(含有轻链CDR并与重链可变结构域一起形成Fv区)和轻链恒定区(通常称为CL或Cκ)。

[0209] 另一其他取代属意的区域是Fc区。

[0210] 因此,本发明提供了不同的抗体结构域。如本文所述和本领域所知,本发明异二聚体抗体的重链和轻链内包含不同结构域,还可以是重叠的。这些结构域包括但不限于,Fc结构域、CH1结构域、CH2结构域、CH3结构域、铰链结构域、重链恒定结构域(CH1-铰链-Fc结构域或CH1-铰链-CH2-CH3)、可变重链结构域、可变轻链结构域、轻链恒定结构域、FAb结构域和scFv结构域。

[0211] 因此,“Fc结构域”包括-CH2-CH3结构域和可选的铰链结构域。重链包括可变重链结构域和恒定结构域,这包括CH1-可选的铰链-Fc结构域,Fc结构域包含CH2-CH3。轻链包括轻链可变结构域和轻链恒定结构域。

[0212] 本发明的一些实施方式包括至少一个scFv结构域,这不是天然的,一般包括通过scFv接头连接在一起的可变重链结构域和可变轻链结构域。如本文所示,可采用多种合适的scFv接头,包括通过重组技术产生的常规肽键。

[0213] 接头肽可主要包括以下氨基酸残基:Gly、Ser、Ala、或Thr。接头肽应具有足够的长度以确保两个分子彼此都以正确的构象连接在一起从而保留各自活性。实施方式之一中,接头长约1-50个氨基酸,优选长约1-30个氨基酸。实施方式之一中,可使用长度为1-20个氨基酸的接头,某些实施方式中使用约5至约10个氨基酸的。可用的接头包括甘氨酸-丝氨酸聚合物,包括例如 (GS)n、(GSGGS)n、(GGGGS)n、和(GGGS)n,其中n是至少为1的整数(一般是3-4),甘氨酸-丙氨酸聚合物,丙氨酸-丝氨酸聚合物,以及其他柔性接头。或者,多种非蛋白性聚合物可用作接头,包括但不限于聚乙二醇(PEG)、聚丙二醇、聚氧化烯、或聚乙二醇和聚丙二醇的共聚物。

[0214] 其他接头序列可包括CL/CH1结构域内各种长度的序列,但不包括 CL/CH1结构域全部残基;例如,CL/CH1结构域的前5-12个氨基酸残基。接头可衍生自免疫球蛋白轻链,例如Cκ或Cλ。接头可衍生自各同种型的免疫球蛋白重链,例如,Cγ1、Cγ2、Cγ3、Cγ4、Cα1、Cα2、Cδ、Cε、和Cμ。接头序列也可来自于其它蛋白质,如Ig-样蛋白质(如TCR、FcR、KIR),来源于绞链区的序列,以及来自其它蛋白质的其它天然序列。

[0215] 某些实施方式中,接头是用于将任意两个本文所述的结构域连接在一起的“结构域接头”。虽然可使用各种合适的接头,许多实施方式采用甘氨酸-丝氨酸聚合物,包括例如(GS)n、(GSGGS)n、(GGGGS)n、和(GGGS)n,其中n 是至少为1的整数(一般是3至4至5),以及具有足够长度和柔性、能将两个结构域重组连接并保留各自生物学功能的各种肽序列。某些情形中,同时注意到“链型”的情况下,如后文所述,可使用带电荷的结构域接头,如scFv接头的一些实施方式中所用。

[0216] 某些实施方式中，scFv接头是带电荷的scFv接头，图33显示了多个这样的接头。因此，本发明还提供了带电荷的scFv接头，用以促进第一和第二单体之间pI的分离。即，通过纳入带电荷的scFv接头，不论正电或负电(或两者，如果是在不同单体上使用scFv的构架)，包含带电荷接头的单体能够改变pI而无需在Fc结构域中制造其他改变。这些带电荷的接头可被取代成各种含scFv 的标准接头。同样，本领域技术人员可以看出，根据所需的pI，将带电荷的scFv 接头用在正确的“链”或单体上。例如，如本文所述，为了制备三F形式的异二聚体抗体，计算各所需抗原结合结构域的Fv区的原始pI，并且选择其中之一来制备scFv，并根据pI选择正电或负电接头。

[0217] 带电荷的结构域接头还可用于增强本发明单体的pI分离，因此，图33中的那些可用于本文中用到接头的各种实施方式。

[0218] 某些实施方式中，抗体是全长抗体。本文中“全长抗体”表示构成抗体天然生物形式的结构，包括可变区和恒定区，包括本文所述的一个或多个修饰，尤其是在Fc结构域中，以形成异二聚化或将异二聚体与同二聚体纯化分离。全长抗体一般包括Fab和Fc结构域，并且还可含有额外的抗原结合结构域，如scFv，如图所示。

[0219] 实施方式之一中，抗体是抗体片段，只要该片段含有可经改造(例如pI改造)以产生异二聚体的至少一个恒定结构域。可使用的其他抗体片段包括含有一个或多个经pI改造的本发明的CH1、CH2、CH3、铰链和CL结构域的片段。例如，Fc融合体是Fc区(CH2和CH3，可以带有铰链区)与另一个蛋白质融合而成的融合体。本领域已知多个Fc融合体，可通过添加本发明的异二聚化变体对其进行改善。在此，用本文各种异二聚化变体组合，抗体融合体可制成包含CH1；CH1，CH2和CH3；CH2；CH3；CH2和CH3；CH1和CH3，其中任一或全部可制备成还可选性地带有铰链区。

[0220] 具体地说，图1所示的形式是抗体，通常称为“异二聚体抗体”，表示该蛋白质具有至少两个关联的Fc序列，它们自组装成异二聚体Fc结构域。

[0221] 嵌合抗体和人源化抗体

[0222] 某些实施方式中，抗体可以是来自不同物种的混合物，例如，嵌合抗体和 /或人源化抗体。通常，“嵌合抗体”和“人源化抗体”是指组合了超过一个物种的区域的抗体。例如，“嵌合抗体”通常包含小鼠(有时是大鼠)的可变区和人的恒定区。“人源化抗体”一般是指可变结构域的框架区被换成人抗体中序列的非人抗体。一般而言，在人源化抗体中，整个抗体，除了CDR以外，由人源多核苷酸编码，且除CDR以外与该抗体相同。其中部分或全部由非人生物核酸编码的CDR移植到人抗体可变区的β片层构架中以形成抗体，该抗体的特异性由移植过来的CDR决定。这类抗体的产生可见例如WO 92/11018, Jones,1986,Nature 321:522-525,Verhoeyen等,1988,Science 239:1534-1536,其全部通过引用纳入本文。经常需要把选定受体的框架区残基“回复突变”成相应的供体残基，从而恢复初始移植构建体中丢失的亲合力(US 5530101、US 5585089、US 5693761、US 5693762、US 6180370、US 5859205、US 5821337、US 6054297、US 6407213，全部通过引用全文纳入本文)。人源化抗体还可或选性地包含免疫球蛋白恒定区的至少一部分，一般是人免疫球蛋白因此通常包含人Fc区。人源化还可采用带有经遗传改造的免疫系统的小鼠来生成。Roque 等，2004，Biotechnol.Prog.20:639-654，其全文通过引用纳入本文。本领域有多种熟知的非人抗体人源化和改形技术与方法(参见，Tsurushita和Vasquez, 2004，抗体的人源化，B细胞分子

生物学(Humanization of Monoclonal Antibodies, Molecular Biology of B Cells),533-545,Elsevier Science(USA)以及本文所引用的参考文献,其全部通过引用全文纳入本文)。人源化方法包括但不限于:Jones 等,1986,Nature 321:522-525;Riechmann等,1988;Nature 332:323-329; Verhoeyen等,1988,Science,239:1534-1536;Queen等,1989,Proc Natl Acad Sci, USA 86:10029-33;He等,1998,J.Immunol.160:1029-1035;Carter等,1992,Proc Natl Acad Sci USA 89:4285-9,Presta等,1997,Cancer Res.57(20):4593-9; Gorman等,1991,Proc.Natl.Acad.Sci.USA 88:4181-4185;O'Connor等,1998,Protein Eng 11:321-8中所述的方法,其全部通过引用全文纳入本文。人源化或其他减少非人抗体可变区免疫原性的方法可包括表面重塑法,如Roguska等, 1994,Proc.Natl.Acad.Sci.USA 91:969-973所述,其通过引用全文纳入本文。实施方式之一中,亲本抗体是已经亲合力熟化的,如本领域所知的那样。可采用基于结构的方法来进行人源化和亲合力熟化,例如USSN 11/004,590中所述。可采用基于选择的方法来将抗体可变区人源化和/或亲合力熟化,包括但不限于:Wu等,1999,J.Mol.Biol.294:151-162;Baca等,1997,J.Biol.Chem. 272(16):10678-10684;Rosok等,1996,J.Biol.Chem.271(37):22611-22618; Rader等,1998,Proc.Natl.Acad.Sci.USA 95:8910-8915;Krauss等,2003,Protein Engineering 16(10):753-759中所述的方法,其全部通过引用全文纳入本文。其他人源化方法可包括仅移植部分CDR,包括但不限于USSN 09/810,510; Tan等,2002,J.Immunol.169:1119-1125;De Pascalis等,2002,J.Immunol. 169:3076-3084中所述的方法,其全部通过引用全文纳入本文。

[0223] IV.异二聚体抗体

[0224] 因此,某些实施方式中,本发明提供异二聚体抗体,其依赖于采用两个不同重链变体Fc序列,它们会自组装成异二聚体Fc结构域和异二聚体抗体。

[0225] 本发明涉及提供异二聚体抗体的新构建体,所述异二聚体抗体允许结合超过一种抗原或配体,例如,允许双特异性结合。异二聚体抗体构建体是基于抗体两个重链Fc结构域的自组装性质,例如,两个"单体"自组装成"二聚体"。如下文所述,通过改变各单体的氨基酸序列来制备异二聚体抗体。因此,本发明涉及异二聚体抗体的创制,这依赖于由各链上不同的恒定区内氨基酸变体促进异二聚体形成和/或简化异二聚体与同二聚体的纯化分离,这些异二聚体抗体能够以多种方式共结合多个或多种抗原。

[0226] 因此,本发明提供了双特异性抗体。抗体技术领域当前的一个问题是需要同时结合两个不同抗原的"双特异性"抗体,由此令不同抗原靠近并产生新功能和新疗法。一般而言,这些抗体通过将包含各重链和轻链的基因引入宿主细胞来制备。这一般形成所需的异二聚体(A-B),还有两种同二聚体(A-A和B-B(不包括轻链异二聚体问题))。然而,形成双特异性抗体的主要障碍在于难以将异二聚体抗体与同二聚体抗体纯化分离,和/或难以相对于同二聚体偏向性地更多形成异二聚体。

[0227] 有多种可用于生成本发明异二聚体的机制。另外,本领域技术人员可以看出,这些机制可相互组合以确保高度异二聚化。因此,产生异二聚体的氨基酸变体被称为"异二聚化变体"。如下文所述,异二聚化变体可包括立构变体(例如,下文所述的"球与孔"或"偏向"变体和下文所述的"电荷对"变体)以及"pI变体",这能将同二聚体与异二聚体纯化分离。如WO2014/145806中所述,该申请通过引用全文纳入,并具体如下文"异二聚化变体"所述,可

用于异二聚化的机制包括“球与孔”(“KIH”;本文中有时称为“偏向”变体(参见WO2014/145806中所述)、WO2014/145806中所述的“静电操控”或“电荷对”、WO2014/145806中所述的pI变体、以及WO2014/145806和下文中所示的其他Fc变体。

[0228] 在本发明中,有几种基本机制可使异二聚体抗体的纯化变得容易:一种依赖于采用pI变体,使各单体具有不同的pI,由此允许等电纯化A-A、A-B和 B-B二聚体蛋白质。或者,部分构架形式如“三F”形式,允许基于大小的分离。如后文所述,还可以相对于同二聚体“偏向”地更多形成异二聚体。因此,立构异二聚化变体和pI或电荷对变体的组合在本发明中特别有用。

[0229] 一般而言,本发明中特别有用的实施方式依赖于包括偏向变体和pI变体在内的组合变体,偏向变体促进高于同二聚化的优势性异二聚化,pI变体加大两种单体之间的pI差异。

[0230] 另外,如后文所述,根据异二聚体抗体的形式,pI变体既可包含在单体的恒定和/或Fc结构域内,也可包含在带电荷的接头中,即可采用结构域接头也可采用scFv接头。即,采用scFv的构架如三F形式可包括带电荷的(正电或负电)scFv接头,这通过pI优化了纯化。本领域技术人员可以看出,某些三F形式只要有带电荷的scFv接头就可用,无需其他pI调整,尽管本发明确实提供存在于单体之一或两者之上的pI变体,和/或带电荷的结构域接头。另外,其他官能团的氨基酸改造也可能造成pI变化,如Fc、FcRn和KO变体。

[0231] 在利用pI作为分离机制来纯化异二聚体蛋白质的本发明中,可在单体多肽之一或两者中引入氨基酸变体;即,可将单体之一(简称“单体A”)的pI改造成不同于单体B,或改变单体A和B两者,其中单体A的pI升高而单体B 的pI降低。如后文所述,单体之一或两者的pI改变可如下进行:去除或添加带电荷残基(例如,中性氨基酸取代成带正电或带负电的氨基酸残基,例如,甘氨酸替换为谷氨酸),将正电残基改为负电残基或反之(例如天冬氨酸改成赖氨酸),或将带电荷残基改为中性残基(例如,电荷丢失;赖氨酸改为丝氨酸)。附图显示了多种此类变体。

[0232] 因此,本发明的这一实施方式令人能在至少单体之一中产生足够的pI变化从而将异二聚体与同二聚体分离。本领域技术人员可以看出,并如后文所述,这可以如下进行:使用“野生型”重链恒定区和已被升高或降低其pI的变体区(wt A-+B或wt A--B),或升高一个区域而降低另一个区域(A+-B-或A-B+)。

[0233] 因此,总体而言,本发明的部分实施方式内容之一是抗体恒定区中的氨基酸变体,针对的是改变二聚体蛋白质单体至少其一(如果不是两者)的等电点(pI) 以形成“pI抗体”,通过向单体之一或两者中引入氨基酸取代(“pI变体”或“pI取代”)来进行。如本文所示,如果两个单体的pI差仅0.1个pH单位,就能够将异二聚体与两个同二聚体分离,0.2、0.3、0.4和0.5pH单位或更大的pI 差在本发明中都可采用。

[0234] 本领域技术人员可以看出,欲实现良好分离而引入各单体或两单体上的 pI变体数量部分取决于组分的初始pI,以三F形式为例,即目标scFv和Fab 的初始pI。即,为了确定对哪个单体进行改造或改造“方向”(例如,是更多正电还是更多负电),计算两种靶抗原的Fc序列并且由此进行决定。如本领域所知,不同的Fv具有不同的初始pI,本发明利用了这一点。一般而言,如本文所述,对pI进行改造以使各单体的总pI差异至少约0.1log,优选0.2-0.5。

[0235] 此外，本领域技术人员可以看出，并如本文所示，部分实施方式中，可基于大小将异二聚体与同二聚体分离。例如图1所示，有几种形式允许基于大小分离异二聚体和同二聚体。

[0236] 在使用pI变体来实现异二聚化的情形中，通过使用重链的恒定区，提供了设计和纯化双特异性蛋白质(包括抗体)的更模块化的方法。因此，某些实施方式中，异二聚化变体(包括偏向和纯化异二聚化变体)不在可变区中，这样，每个抗体都必须改造。另外，某些实施方式中，通过其他IgG同种型引入pI 变体来改变pI而不引入显著的免疫原性，由此降低pI变体导致免疫原性的可能性。因此，有待解决的另一个问题是阐明高人序列含量恒定结构域的低pI，例如，最小化或避免在任何特定位置的非人残基。

[0237] 这种pI改造可能的附带好处还在于血清半衰期延长和FcRn结合增强。即，如USSN 13/194,904所述(通过引用全文纳入本文)，降低抗体恒定结构域(包括在抗体和Fc融合体中的那些)的pI可产生更长的体内血清存留。此类延长血清半衰期的pI变体也有利于纯化目的的pI改变。

[0238] 另外，需要说明的是，异二聚化变体的pI变体对双特异性抗体的分析和质量控制过程有额外的好处，即存在同二聚体时显著的消除、最小化或区分能力。类似地，可靠地测试异二聚体抗体产生的再现性的能力是重要的。

[0239] 异二聚化变体

[0240] 本发明提供异二聚体蛋白质，包括多种形式的异二聚体抗体，其采用异二聚体变体以允许异二聚体形成和/或与同二聚体纯化分离。

[0241] 存在有多种合适的配对异二聚化偏向变体组合。这些变体以“配对”的“组合”方式出现。即，配对中的一组纳入第一单体而另一组纳入第二单体。需要说明的是，这些组合不一定象“球与孔”变体那样，其中一个单体上的残基与另一个单体上的残基一一对应；即，这些配对的组合在两个单体之间形成一个界面，促进异二聚体的形成而阻碍同二聚体形成，从而生物条件下自发形成的异二聚体的百分比超过90％，而不是原以为的50％(25％同二聚体A/A:50％异二聚体A/B:25％同二聚体B/B)。

[0242] 立构变体

[0243] 某些实施方式中，可通过添加立构变体来促进异二聚体形成。即，通过改变各重链中的氨基酸，不同的重链更可能结合成异二聚体结构而不是与相同的 Fc氨基酸序列形成同二聚体。图29中包括合适的立构变体。

[0244] 在此还可采用本领域中一般称为“球与孔(knobs and holes)”的一种机制，指产生立构影响有利于异二聚体形成而不利于同二聚体形成的氨基酸改造；这有时被称为“球与孔”，如USSN 61/596,846,Ridgway等,Protein Engineering 9(7):617(1996);Atwell等,J.Mol.Biol.1997 270:26;美国专利号8,216,805中所述，以上全部通过引用全文纳入本文。附图指示了多种依赖于“球与孔”的“单体A-单体B”配对。另外，如Merchant等,Nature Biotech.16:677(1998) 中所述，这些“球与孔”突变可与二硫键组合以偏向性地形成异二聚化。

[0245] 用于生成异二聚体的另一种机制有时被称为“静电操控”，如Gunasekaran 等，J.Biol.Chem.285(25):19637(2010)所述，其通过引用全文纳入本文。这有时在本文中被称为“电荷对”。在该实施方式中，使用静电来偏向于形成异二聚化。本领域技术人员可以看

出,这些也可能对pI有影响,继而对纯化有影响,因此,某些情形下也可被认为是pI变体。然而,由于制造这些是为驱动二聚化而非用作纯化工具,将它们归类为“立构变体”。这些变体包括但不限于:D221E/P228E/L368E配对D221R/P228R/K409R(例如,这些是“单体对应组合”)和C220E/P228E/368E配对C220R/E224R/P228R/K409R。

[0246] 单体A变体和单体B变体可以任选地、独立地与任意数量的其他变体联用,如pI变体或US 2012/0149876中图37所示的其他立构变体,这些附图和附图说明以及SEQ ID NO通过引用纳入本文。

[0247] 某些实施方式中,本文所述立构变体可任选地、独立地与各种pI变体(或其他变体如Fc变体、FcRn变体等)纳入一个或两个单体,并可独立地、任选地包括或不包括于本发明的蛋白质中。

[0248] 图29显示合适的偏向变体,图34显示某些实施方式中特别有用的一些配对。多个实施方式中特别有用配对组合包括但不限于:S364K/E357Q: L368D/K370S;L368D/K370S:S364K;L368E/K370S:S364K; T411T/E360E/Q362E:D401K;L368D/K370S:S364K/E357L和K370S: S364K/E357Q。命名上,“S364K/E357Q:L368D/K370S”配对表示单体之一具有双变体组合S364K/E357Q而另一个具有双变体组合L368D/K370S。

[0249] 异二聚体的pI(等电点)变体

[0250] 一般而言,本领域技术人员可以看出,存在两类pI变体:升高蛋白质pI 的(碱性改变)和降低蛋白质pI的(酸性改变)。如本文所述,这些变体可以任意组合:一个单体可以是野生型,或者pI与野生型无明显差异的变体,另一个可以更具碱性或更具酸性。或者,每个单体都改变,一个变得更具碱性而另一个变得更具酸性。

[0251] pI变体的优选组合见图30。如本文所述和附图所示,这些变化是就IgG1 而言的,但所有同种型和同种型杂交体都可照此改变。重链恒定结构域来自 IgG2至4时,还可使用R133E和R133Q。

[0252] 抗体异二聚体轻链变体

[0253] 如果是基于抗体的异二聚体,例如,至少单体之一除重链结构域之外还包含轻链,也可在轻链中制造pI变体。用于降低轻链pI的氨基酸取代包括但不限于:K126E、K126Q、K145E、K145Q、N152D、S156E、K169E、S202E、 K207E,以及在轻链的c-端添加肽DEDE。基于恒定λ轻链的此类改变包括在 R108Q、Q124E、K126Q、N138D、K145T和Q199E处的一个或多个取代。另外,也可提高轻链的pI。

[0254] 同种型变体

[0255] 另外,本发明的许多实施方式是基于将一种IgG同种型特定位置的pI氨基酸“引入”另一同种型,由此降低或消除在变体中引入不希望有的免疫原性的可能性。就此可见美国公开号2014/0370013的图21,以上通过引用纳入本文。即,出于包括高效应物功能等多种原因,IgG1是治疗性抗体的常用同种型。然而,IgG1重链恒定区的pI高于IgG2的重链恒定区(8.10对比7.31)。通过将特定位置的IgG2残基引入IgG1主链,所得单体的pI降低(或升高),并且还表现出更长的血清半衰期。例如,IgG1在137位处有甘氨酸(pI 5.97),而IgG2 为谷氨酸(pI 3.22);引入谷氨酸将影响所得蛋白质的pI。如下文所述,一般需要多个氨基酸取代来显著影响变体抗体的pI。然而,需要说明的是,如下文所述,IgG2分子中的改变也能延长血清半衰期。

[0256] 在另一些实施方式中，进行非同种型氨基酸变化，用以降低所得蛋白质的总体电荷状态(例如，将高pI氨基酸换成低pI氨基酸)或是针对稳定性的结构调整等，如后文所述。

[0257] 另外，通过对重链恒定区和轻链恒定区的pI改造，可在异二聚体的各单体中看到显著改变。如本文所述，使两种单体的pI相差至少0.5可允许通过离子交换色谱或等电聚焦或对等电点敏感的其他方法实现分离。

[0258] 计算pI

[0259] 各单体的pI可能取决于变体的重链恒定结构域pI和包括变体重链恒定结构域和融合伴侣在内整个单体的pI。因此，某些实施方式中，使用美国公开号 2014/0370013的图19中的图表，基于变体重链恒定结构域来计算pI的改变。如本文所述，改造哪个单体一般决定于Fv和框架区的固有pI决定。或者，可对各单体的pI进行比对。

[0260] 还提供更好FcRn体内结合的pI变体

[0261] 在pI变体降低单体pI的情形中，它们还会额外地改善体内血清留存。

[0262] 虽然仍在验证中，Fc区被认为具有较长的体内半衰期，因为核内体中pH 6下与FcRn的结合隔离了Fc(Ghetie和Ward,1997Immunol Today.18(12): 592-598，通过引用全文纳入本文)。核内体隔室然后将Fc再循环至细胞表面。一旦隔室向胞外空间打开，较高pH(～7.4)诱导Fc释放回血液中。在小鼠中，Dall'Acqua等显示在pH 6和pH 7.4FcRn结合增强的Fc突变体实际上其血清浓度降低并具有与野生型Fc相同的半衰期(Dall'Acqua等，2002,J.Immunol. 169:5171-5180，通过引用全文纳入本文)。在pH 7.4下Fc对FcRn亲和性提高被认为抑制了Fc释放回血液中。因此，理想的是，增强Fc体内半衰期的Fc 突变增强低pH下的FcRn结合，同时仍然允许在高pH下释放Fc。氨基酸组氨酸在6.0-7.4的pH范围内其电荷状态会变化。因此，不出意外地在Fc/FcRn 复合物的重要位置发现有His残基。

[0263] 最近已经提出具有低等电点可变区的抗体也可具有更长的血清半衰期 (Igawa等,2010 PEDS.23(5):385-392，通过引用全文纳入本文)。然而，对其机制尚知之甚少。此外，抗体的可变区各不相同。具有低pI和长半衰期的恒定区能提供更模块化的方法来改善抗体的药代动力学性质，如本文所述。

[0264] 针对其他功能的其他Fc变体

[0265] 除了pI氨基酸变体以外，可出于多种原因制造多种其他有用的Fc氨基酸修饰，这些原因包括但不限于，改变与一个或多个FcγR受体的结合，改变与 FcRn受体的结合等。

[0266] 因此，本发明的蛋白质可包括氨基酸修饰，包括本文的异二聚化变体，这包括pI变体和立构变体。各种组合变体可独立地、任选地包括或不包括于各种特定异二聚体蛋白质中。

[0267] FcγR变体

[0268] 因此，可制造多种可用的Fc取代来改变与FcγR受体中一种或多种的结合。有用的包括增强结合和降低结合的取代。例如，已知与FcγRIIIa结合加强通常会增强ADCC(抗体依赖性细胞介导的细胞毒作用;细胞介导的反应，其中表达FcγR的非特异性细胞毒性细胞识别靶细胞上结合的抗体然后引起靶细胞裂解)。类似地，某些情形中，与FcγRIIb(抑制性受体)结合降低是有益的。本发明中有用的氨基酸取代包括USSN 11/124,620(尤其是图41)、11/174,287、 11/396,495、11/538,406中所列的那些，以上全部通过引用全文纳入本文，尤其其中的变体。有用的具体变体包括但不限于:236A、239D、239E、332E、 332D、239D/

332E、267D、267E、328F、267E/328F、236A/332E、239D/332E/330Y、 239D、332E/330L、243A、243L、264A、264V和299T。

[0269] 另外，还有其他Fc取代用于增强与FcRn受体的结合并延长血清半衰期，如USSN 12/341,769中具体所示，通过引用将其全文纳入本文，包括但不限于： 434S、434A、428L、308F、259I、428L/434S、259I/308F、436I/428L、436I 或V/434S、436V/428L和259I/308F/428L。

[0270] 消除变体

[0271] 类似地，另一类功能性变体是“Fcγ R消除变体”或“Fc敲除(FcKO或KO)”变体。在这些实施方式中，对某些治疗性应用而言，需要降低或去除Fc结构域与Fcγ受体(例如Fcγ R1、Fcγ RIIa、Fcγ RIIb、Fcγ RIIIa等)之一、多种或全部的正常结合，以避免其他作用机制。即，例如，在许多实施方式中，尤其是单价结合CD3的双特异性抗体的使用中，通常需要消除Fcγ RIIIa结合以消除或显著降低ADCC活性，其中Fc结构域之一含有一个或多个Fcγ受体消除变体。这些消除变体见图31，每一个都可以独立地、任选地被包括或不包括，优选采用选自以下的消除变体:G236R/L328R、E233P/L234V/L235A/G236del/S239K、 E233P/L234V/L235A/G236del/S267K、 E233P/L234V/L235A/G236del/S239K/A327G、 E233P/L234V/L235A/G236del/S267K/A327G和E233P/L234V/L235A/G236del。需要说明的是，本文引用的消除变体消除Fcγ R结合但一般不消除FcRn结合。

[0272] 异二聚体和Fc变体的组合

[0273] 本领域技术人员可以看出，提到的所有异二聚化变体(包括偏向变体和/或 pI变体)可任选地、独立地以任意方式组合，只要它们保留其“链型”或“单体分配”。另外，所有这些变体可结合到任意异二聚化形式中。

[0274] 就pI变体而言，虽然附图中显示了若干特别有用的实施方式，但是，按照改变两个单体之间的pI差以促进纯化这一基本原理，可以形成其他实施方式。

[0275] 另外，异二聚化变体、偏向和pI中任一个独立地、任选地与Fc消除变体、Fc变体、FcRn变体相互组合，如本文的通用说明。

[0276] 本发明的有用抗体形式

[0277] 本领域技术人员可以看出，并如后文所述，本发明的异二聚体融合蛋白可采用多种构型，总体如图1所示。一些图显示“单末端”构型，其中，分子的一个“臂”上有一种特异性而另一个“臂”上则为不同的特异性。另一些图显示“双末端”构型，其中，分子的“顶部”有至少一种特异性而分子的“底部”有一种或多种其他特异性。因此，本发明涉及共结合不同的第一和第二抗原的新型免疫球蛋白组合物。

[0278] 本领域技术人员可以看出，本发明的异二聚体形式除双特异性外可具有不同的价态。即，本发明的异二聚体抗体可以是二价双特异性的，其中一个靶肿瘤抗原(例如，CD3)被一个结合结构域结合而另一个靶肿瘤抗原(例如，CD20、 CD19、CD38、CD123等)被第二结合结构域结合。异二聚体抗体也可以是三价双特异性的，其中第一抗原被两个结合结构域结合而第二抗原被第二结合结构域结合。如本文所述，当CD3是靶抗原之一时，优选CD3仅被单价结合，旨在降低潜在副作用。

[0279] 本发明将抗-CD3抗原结合结构域与抗-靶肿瘤抗原(TTA)抗原结合结构域联合。本领域技术人员可以看出，可采用各附图(具体见图2-7和图68)中所示的抗-CD3 CDR、抗-CD3

可变轻链结构域和可变重链结构域、Fab和scFv。类似地，可采用各种抗-TTA抗原结合结构域，例如，抗-CD38、抗-CD20、抗-CD19 和抗-CD123抗原结合结构域，可采用各附图中所示的CDR、可变轻链结构域和可变重链结构域、Fab和scFv，任选地、独立地任意组合。

[0280] 开瓶器型

[0281] 本发明中特别有用的异二聚体构架之一是图1A、A和B中所示的“三F”或“开瓶器”构架形式。在该实施方式中，抗体的一条重链含有单链Fv(本文所述“scFv”)而另一条重链是包含可变重链和可变轻链的“常规”Fab形式。这种结构有时在本文中被称为“三F”型(scFv-FAb-Fc)或“开瓶器”型，由于看上去与开瓶器相当相似(见图1)。两条链通过恒定区(例如，Fc结构域、CH1 结构域和/或铰链区)中采用氨基酸变体合在一起，所述变体促进异二聚体抗体的形成，如后文所述。

[0282] “三F”型有诸多优点。如本领域所知，依赖于两种scFv构建体的抗体类似物通常有稳定性和聚集问题，在本发明中这可以通过添加“常规”的重轻链配对来缓解。另外，与依赖于两条重链和两条轻链的形式相反，不存在重链和轻链错配的问题(例如，重链1与轻链2配对，等等)。

[0283] 本文实施方式中许多是基于开瓶器形式，其第一单体包含scFv，该scFv 包含可变重链结构域和可变轻链结构域，用scFv接头(许多情形下带电荷，但非所有情形)共价接合，其中的scFv通常通过结构域接头(带电或不带电，如本文所述)共价接合至第一Fc结构域的N-端。开瓶器形式的第二单体是重链，该组合物还包括轻链。

[0284] 一般而言，在许多优选的实施方式中，scFv是结合CD3的结构域，重链和轻链的Fab结合TTA。另外，本发明的Fc结构域一般包含偏向变体(例如，如图29和图34所示的组合氨基酸取代，特别有用的偏向变体选自：S364K/E357Q:L368D/K370S;L368D/K370S:S364K;L368E/K370S:S364K; T411T/E360E/Q362E:D401K;L368D/K370S:S364K/E357L和K370S:S364K/E357Q)，可选的消除变体(包括图31中所示的那些)，可选的带电scFv 接头(包括图33中所示的那些)，重链包含pI变体(包括图30中所示的那些)。

[0285] 本发明提供其中抗-CD3 scFv序列如图2至图7和图68中所示的开瓶器形式。

[0286] 本发明提供具有CD38抗原结合结构域的开瓶器形式，其中抗-CD38序列如图中所示，包括图8-10。

[0287] 本发明提供具有CD20抗原结合结构域的开瓶器形式，其中抗-CD20序列如图所示。

[0288] 本发明提供具有CD19抗原结合结构域的开瓶器形式，其中抗-CD19序列如图所示。

[0289] 本发明提供具有CD123抗原结合结构域的开瓶器形式，其中抗-CD123序列如图所示。

[0290] mAb-Fv型

[0291] 本发明中特别有用的异二聚体构架之一是图1所示的mAb-Fv形式。在该实施方式中，该形式将“额外”的可变重链结构域接合于单体之一的C-端，“额外”可变轻链结构域接合于另一个单体的C-端，由此形成第三抗原结合结构域，其中两个单体的Fab部分结合TTA而“额外”scFv结构域结合CD3。

[0292] 在该实施方式中，第一单体包括第一重链，第一重链包含第一可变重链结构域和含第一Fc结构域的第一恒定重链结构域，第一可变轻链结构域通过结构域接头共价接合于第一Fc结构域的C-端。第二单体包括第二可变重链结构域和含第二Fc结构域的第二恒定重

链结构域，还包括用结构域接头共价接合至第二Fc结构域的C-端的第三可变重链结构域。两个C-端接合的可变结构域组成结合CD3的scFv。该实施方式还采用包含可变轻链结构域和恒定轻链结构域的共同轻链，与重链缔合形成结合TTA的两个相同Fab。如同本发明许多实施方式，这些构建体根据需要包含偏向变体、pI变体、消除变体、其他Fc 变体等，如本文所述。

[0293] 本发明提供其中抗-CD3 scFv序列如图2至图7和图68中所示的mAb-Fv 型。

[0294] 本发明提供其中抗-CD38序列如图8-10中所示的mAb-Fv形式。

[0295] 本发明提供具有CD20抗原结合结构域的mAb-Fv形式，其中抗-CD20序列如图所示。

[0296] 本发明提供具有CD19抗原结合结构域的mAb-Fv形式，其中抗-CD19序列如图所示。

[0297] 本发明提供具有CD123抗原结合结构域的mAb-Fv形式，其中抗-CD123 序列如图所示。

[0298] 本发明提供包含图31所示消除变体的mAb-Fv形式。

[0299] 本发明提供包含图29和34所示偏向变体的mAb-Fv形式。

[0300] mAb-scFv

[0301] 本发明中特别有用的异二聚体构架之一是图1所示的mAb-Fv形式。在该实施方式中，此类形式是基于单体之一的C-端接合scFv，由此形成第三抗原结合结构域，其中两个单体的Fab部分结合TTA而“额外”scFv结构域结合 CD3。因此，第一单体包含第一重链(包含可变重链结构域和恒定结构域)，C- 端共价接合的scFv包含scFv可变轻链结构域，scFv接头和scFv可变重链结构域。该实施方式还采用包含可变轻链结构域和恒定轻链结构域的共同轻链，与重链缔合形成结合TTA的两个相同Fab。如同本发明许多实施方式，这些构建体根据需要包含偏向变体、pI变体、消除变体、其他Fc变体等，如本文所述。

[0302] 本发明提供其中抗-CD3 scFv序列如图2至图7和图68中所示的mAb-Fv 形式。

[0303] 本发明提供其中抗-CD38序列如图8-10中所示的mAb-Fv形式。

[0304] 本发明提供具有CD20抗原结合结构域的mAb-Fv形式，其中抗-CD20序列如图所示。

[0305] 本发明提供具有CD19抗原结合结构域的mAb-Fv形式，其中抗-CD19序列如图所示。

[0306] 本发明提供具有CD123抗原结合结构域的mAb-Fv形式，其中抗-CD123 序列如图所示。

[0307] 本发明提供包含图31所示的消除变体的mAb-Fv形式。

[0308] 本发明提供包含图29和34所示的偏向变体的mAb-Fv形式。

[0309] 中心scFv

[0310] 本发明中特别有用的异二聚体构架之一是图1所示的中心-scFv形式。该形式采用插入scFv结构域形成第三抗原结合结构域，其中两个单体的Fab部分结合TTA而“额外”scFv结构域结合CD3。在单体之一的Fc结构域和CH1-Fv 区之间插入scFv结构域，由此提供第三抗原结合结构域。

[0311] 在该实施方式中，单体之一包括第一重链，第一重链包含第一可变重链结构域、CH1结构域和Fc结构域，还包括包含scFv可变轻链结构域、scFv接头和scFv可变重链结构域的scFv。该scFv用结构域接头共价接合在重链恒定结构域的CH1结构域的C-端和第一Fc结构域的N-端之间。该实施方式还采用包含可变轻链结构域和恒定轻链结构域的共同轻链，与重链缔合形成结合TTA 的两个相同Fab。如同本发明许多实施方式，这些构建体根据需要

包含偏向变体、pI变体、消除变体、其他Fc变体等，如本文所述。

[0312] 本发明提供其中抗-CD3 scFv序列如图2至图7和图68中所示的中心-scFv 形式。

[0313] 本发明提供其中抗-CD38序列如图8-10中所示的中心-scFv形式。

[0314] 本发明提供具有CD20抗原结合结构域的中心-scFv形式，其中抗-CD20 序列如图所示。

[0315] 本发明提供具有CD19抗原结合结构域的中心-scFv形式，其中抗-CD19 序列如图所示。

[0316] 本发明提供具有CD123抗原结合结构域的中心-scFv形式，其中抗-CD123 序列示于v中。

[0317] 本发明提供包含图31所示消除变体的中心-scFv形式。

[0318] 本发明提供包含图29和34所示偏向变体的中心-scFv形式。

[0319] 中心-Fv型

[0320] 本发明中特别有用的异二聚体构架之一是图1所示的中心-Fv形式。该形式采用插入的scFv结构域，由此形成第三抗原结合结构域，其中两个单体的 Fab部分结合TTA而“额外”scFv结构域结合CD3。scFv结构域插入在单体的CH1-Fv区和Fc结构域之间，由此提供第三抗原结合结构域，其中各单体各含scFv的组分之一(例如，单体之一包含可变重链结构域而另一个包含可变轻链结构域)。

[0321] 在该实施方式中，单体之一包括包含第一可变重链结构域、CH1结构域和Fc结构域和附加可变轻链结构域的第一重链。该附加轻链结构域用结构域接头共价接合在重链恒定结构域CH1结构域的C-端和第一Fc结构域的N-端之间。另一个单体包括包含第一可变重链结构域、CH1结构域和Fc结构域和附加可变重链结构域的第一重链。该附加轻链结构域用结构域接头共价接合在重链恒定结构域CH1结构域的C-端和第一Fc结构域的N-端之间。

[0322] 该实施方式还采用包含可变轻链结构域和恒定轻链结构域的共同轻链，与重链缔合形成结合TTA的两个相同Fab。如同本发明许多实施方式，这些构建体根据需要包含偏向变体、pI变体、消除变体、其他Fc变体等，如本文所述。

[0323] 本发明提供其中抗-CD3 scFv序列如图2至图7和图68中所示的中心-Fv 形式。

[0324] 本发明提供其中抗-CD38序列如图8-10中所示的中心-Fv形式。

[0325] 本发明提供具有CD20抗原结合结构域的中心-Fv形式，其中抗-CD20序列如图所示。

[0326] 本发明提供具有CD19抗原结合结构域的中心-Fv形式，其中抗-CD19序列如图所示。

[0327] 本发明提供具有CD123抗原结合结构域的中心-Fv形式，其中抗-CD123 序列如图所示。

[0328] 本发明提供包含图31所示消除变体的中心-Fv形式。

[0329] 本发明提供包含图29和34所示偏向变体的中心-Fv形式。

[0330] 单臂中心-scFv

[0331] 本发明中特别有用的异二聚体构架之一是图1所示的单臂中心-scFv形式。在该实施方式中，单体之一仅包含Fc结构域，而另一个单体采用插入scFv结构域形成第二抗原结合结构域。在该形式中，Fab部分结合TTA而scFv结合 CD3，或反之。scFv结构域插入在单体

之一的CH1-Fv区和Fc结构域之间。

[0332] 在该实施方式中,单体之一包括包含第一可变重链结构域、CH1结构域和Fc结构域的第一重链,还带有包含scFv可变轻链结构域、scFv接头和scFv 可变重链结构域的scFv。该scFv用结构域接头共价接合在重链恒定结构域CH1 结构域的C-端和第一Fc结构域的N-端之间。第二单体包括Fc结构域。该实施方式还采用包含可变轻链结构域和恒定轻链结构域的轻链,与重链缔合形成 Fab。如同本发明许多实施方式,这些构建体根据需要包含偏向变体、pI变体、消除变体、其他Fc变体等,如本文所述。

[0333] 本发明提供其中抗-CD3 scFv序列如图2至图7和图68中所示的单臂中心 -scFv形式。

[0334] 本发明提供其中抗-CD38序列如图8-10中所示的单臂中心-scFv形式。

[0335] 本发明提供具有CD20抗原结合结构域的单臂中心-scFv形式,其中抗 -CD20序列如图所示。

[0336] 本发明提供具有CD19抗原结合结构域的单臂中心-scFv形式,其中抗 -CD19序列如图所示。

[0337] 本发明提供具有CD123抗原结合结构域的单臂中心-scFv形式,其中抗 -CD123序列如图所示。

[0338] 本发明提供包含图31所示的消除变体的单臂中心-scFv形式。

[0339] 本发明提供包含图29和34所示的偏向变体的单臂中心-scFv形式。

[0340] 双scFv型

[0341] 本发明还提供如本领域所知亦如图1所示的双scFv形式。

[0342] 本发明提供其中抗-CD3 scFv序列如图2至图7和图68中所示的双scFv 形式。

[0343] 本发明提供其中抗-CD38序列如图8-10中所示的双scFv形式。

[0344] 本发明提供具有CD20抗原结合结构域的双scFv形式,其中抗-CD20序列如图所示。

[0345] 本发明提供具有CD19抗原结合结构域的双scFv形式,其中抗-CD19序列如图所示。

[0346] 本发明提供具有CD123抗原结合结构域的双scFv形式,其中抗-CD123 序列如图所示。

[0347] 本发明提供包含图31所示的消除变体的双scFv形式。

[0348] 本发明提供包含图29和34所示的偏向变体的双scFv形式。

[0349] 靶抗原

[0350] 本发明的双特异性抗体具有两个不同的抗原结合结构域:一个结合 CD3(通常为单价结合),另一个结合靶肿瘤抗原(本文中有时称为“TTA”)。合适的靶肿瘤抗原包括,但不限于:CD20、CD38、CD123;ROR1、ROR2、BCMA; PSMA;SSTR2;SSTR5、CD19、FLT3、CD33、PSCA、ADAM 17、CEA、 Her2、EGFR、EGFR-vIII、CD30、FOLR1、GD-2、CA-IX、Trop-2、CD70、 CD38、间皮素、EphA2、CD22、CD79b、GPNMB、CD56、CD138、CD52、 CD74、CD30、CD123、RON、ERBB2、和EGFR。

[0351] “三F”型特别适合靶向两个(或更多个)不同抗原。(如本文所述,根据抗体形式,这种靶向作用可以是单价结合和二价结合的任意组合)。因此,本文中免疫球蛋白优选共结合两个靶抗原。各单体的特异性可选自本文中的列表。采用抗-CD3结合结构域的其他有用双特异性抗体形式见图1。

[0352] 本文的异二聚体抗体特别合适的应用是单价结合各靶抗原有益或至关重要的合

共靶对(co-target pairs)。这类抗原可以是,例如,免疫复合后活化的免疫受体。许多免疫受体的细胞活化仅通过交联发生,通常由抗体/抗原免疫复合物实现,或通过效应细胞靶与细胞的结合。对于某些免疫受体,例如T细胞上的CD3信号转导受体,在共结合靶标结合后才活化是至关重要的,因为临床环境中的非特异性交联会引发细胞因子风暴和毒性。治疗上,通过使用本文的免疫球蛋白单价而不是多价结合这类抗原,这种活化仅在主靶标抗原的微环境中仅应交联而发生。以不同价态靶向两种不同抗原的能力是本发明创新且有用的地方。治疗上最好或必需以单价共结合的靶抗原的示例包括但不限于免疫活化受体,如CD3、FcγR、toll-样受体(TLR)如TLR4和TLR9、细胞因子、趋化因子、细胞因子受体和趋化因子受体。在许多实施方式中,抗原结合位点之一结合CD3,某些实施方式中,这是含scFv的单体。

[0353] 理论上,本文的免疫球蛋白可靶向任何抗原,这包括但不限于属于以下靶抗原列表的蛋白质、亚基、结构域、基序、和/或表位,包括可溶性因子如细胞因子和膜结合因子,包括跨膜受体:17-IA、4-1BB、4Dc、6-酮-PGF1a、8-异 -PGF2a、8-氧代-dG、A1腺苷受体、A33、ACE、ACE-2、激活素、激活素A、激活素AB、激活素B、激活素C、激活素RIA、激活素RIA ALK-2、激活素 RIB ALK-4、激活素RIIA、激活素RIIB、ADAM、ADAM10、ADAM12、 ADAM15、ADAM17/TACE、ADAM8、ADAM9、ADAMTS、ADAMTS4、 ADAMTS5、地址素(addressins)、aFGF、ALCAM、ALK、ALK-1、ALK-7、α-1- 抗胰蛋白酶、α-V/β-1拮抗剂、ANG、Ang、APAF-1、APE、APJ、APP、APRIL、AR、ARC、ART、青蒿琥酯、抗-Id、ASPARTIC、心房利钠因子、av/b3整联蛋白、Axl、b2M、B7-1、B7-2、B7-H、B-淋巴细胞刺激物(BlyS)、BACE、 BACE-1、Bad、BAFF、BAFF-R、Bag-1、BAK、Bax、BCA-1、BCAM、Bcl、 BCMA、BDNF、b-ECGF、bFGF、BID、Bik、BIM、BLC、BL-CAM、BLK、 BMP、BMP-2BMP-2a、BMP-3成骨素、BMP-4BMP-2b、BMP-5、BMP-6Vgr-1、 BMP-7(OP-1)、BMP-8(BMP-8a、OP-2)、BMPR、BMPR-IA(ALK-3)、BMPR-IB (ALK-6)、BRK-2、RPK-1、BMPR-II(BRK-3)、BMP、b-NGF、BOK、铃蟾肽、骨源性神经营养因子、BPDE、BPDE-DNA、BTC、补体因子3(C3)、C3a、C4、 C5、C5a、C10、CA125、CAD-8、降钙素、cAMP、癌胚抗原(CEA)、癌相关抗原、组织蛋白酶A、组织蛋白酶B、组织蛋白酶C/DPPI、组织蛋白酶D、组织蛋白酶E、组织蛋白酶H、组织蛋白酶L、组织蛋白酶O、组织蛋白酶S、组织蛋白酶V、组织蛋白酶X/Z/P、CBL、CCI、CCK2、CCL、CCL1、CCL11、CCL12、CCL13、CCL14、CCL15、CCL16、CCL17、CCL18、CCL19、CCL2、 CCL20、CCL21、CCL22、CCL23、CCL24、CCL25、CCL26、CCL27、CCL28、 CCL3、CCL4、CCL5、CCL6、CCL7、CCL8、CCL9/10、CCR、CCR1、CCR10、 CCR10、CCR2、CCR3、CCR4、CCR5、CCR6、CCR7、CCR8、CCR9、CD1、 CD2、CD3、CD3E、CD4、CD5、CD6、CD7、CD8、CD10、CD11a、CD11b、CD11c、CD13、CD14、CD15、CD16、CD18、CD19、CD20、CD21、CD22、 CD23、CD25、CD27L、CD28、CD29、CD30、CD30L、CD32、CD33(p67蛋白)、CD34、CD38、CD40、CD40L、CD44、CD45、CD46、CD49a、CD52、 CD54、CD55、CD56、CD61、CD64、CD66e、CD74、CD80(B7-1)、CD89、 CD95、CD123、CD137、CD138、CD140a、CD146、CD147、CD148、CD152、 CD164、CEACAM5、CFTR、cGMP、CINC、肉毒梭菌毒素、产气荚膜梭菌毒素、CKb8-1、CLC、CMV、CMV UL、CNTF、CNTN-1、COX、C-Ret、CRG-2、 CT-1、CTACK、CTGF、CTLA-4、CX3CL1、CX3CR1、CXCL、CXCL1、CXCL2、 CXCL3、CXCL4、CXCL5、CXCL6、CXCL7、CXCL8、CXCL9、CXCL10、 CXCL11、CXCL12、CXCL13、CXCL14、CXCL15、CXCL16、CXCR、CXCR1、 CXCR2、CXCR3、CXCR4、CXCR5、CXCR6、细胞角蛋白肿瘤相关抗原、 DAN、DCC、DcR3、DC-SIGN、衰减加速因子、des(1-3)-IGF-I(脑IGF-1)、 Dhh、地高辛、DNAM-1、DNA酶、Dpp、DPPIV/CD26、Dtk、ECAD、EDA、 EDA-A1、EDA-A2、EDAR、EGF、EGFR(ErbB-1)、EMA、EMMPRIN、ENA、内皮素受体、脑啡肽酶、eNOS、Eot、嗜酸性粒细

胞趋化因子1、EpCAM、肝配蛋白B2/EphB4、EPO、ERCC、E-选择蛋白、ET-1、因子IIa、因子VII、因子VIIIc、因子IX、成纤维细胞活化蛋白(FAP)、Fas、FcR1、FEN-1、铁蛋白、FGF、FGF-19、FGF-2、FGF3、FGF-8、FGFR、FGFR-3、纤维蛋白、FL、FLIP、Flt-3、Flt-4、促卵泡激素、分形趋化因子、FZD1、FZD2、FZD3、FZD4、FZD5、FZD6、FZD7、FZD8、FZD9、FZD10、G250、Gas 6、GCP-2、GCSF、GD2、GD3、GDF、GDF-1、GDF-3(Vgr-2)、GDF-5(BMP-14、CDMP-1)、GDF-6 (BMP-13、CDMP-2)、GDF-7(BMP-12、CDMP-3)、GDF-8(肌肉抑制素)、GDF-9、GDF-15(MIC-1)、GDNF、GDNF、GFAP、GFRa-1、GFR-α1、GFR-α2、GFR-α3、GITR、胰高血糖素、Glut 4、糖蛋白IIb/IIIa(GP IIb/IIIa)、GM-CSF、gp130、gp72、GRO、生长激素释放因子、半抗原(NP-cap或NIP-cap)、HB-EGF、HCC、HCMV gB包膜糖蛋白,HCMV)gH包膜糖蛋白、HCMV UL、造血生长因子 (HGF)、Hep B gp120、肝素酶、Her2、Her2/neu(ErbB-2)、Her3(ErbB-3)、Her4(ErbB-4)、单纯疱疹病毒(HSV)gB糖蛋白、HSV gD糖蛋白、HGFA、高分子量黑素瘤相关抗原(HMW-MAA)、HIV gp120、HIV IIIB gp 120V3环、HLA、HLA-DR、HM1.24、HMFG PEM、HRG、Hrk、人心肌肌球蛋白、人巨细胞病毒(HCMV)、人生长激素(HGH)、HVEM、I-309、IAP、ICAM、ICAM-1、ICAM-3、ICE、ICOS、IFNg、Ig、IgA受体、IgE、IGF、IGF结合蛋白、IGF-1R、IGFBP、IGF-I、IGF-II、IL、IL-1、IL-1R、IL-2、IL-2R、IL-4、IL-4R、IL-5、IL-5R、IL-6、IL-6R、IL-8、IL-9、IL-10、IL-12、IL-13、IL-15、IL-18、IL-18R、IL-23、干扰素(INF)-α、INF-β、INF-γ、抑制素、iNOS、胰岛素A-链、胰岛素B-链、胰岛素-样生长因子1、整联蛋白α2、整联蛋白α3、整联蛋白α4、整联蛋白α4/β1、整联蛋白α4/β7、整联蛋白α5(αV)、整联蛋白α5/β1、整联蛋白α5/β3、整联蛋白α6、整联蛋白β1、整联蛋白β2、干扰素γ、IP-10、I-TAC、JE、激肽释放酶2、激肽释放酶5、激肽释放酶6、激肽释放酶11、激肽释放酶12、激肽释放酶14、激肽释放酶15、激肽释放酶L1、激肽释放酶L2、激肽释放酶L3、激肽释放酶L4、KC、KDR、角质形成细胞生长因子(KGF)、层粘连蛋白5、LAMP、LAP、LAP(TGF-1)、潜伏性TGF-1、潜伏性TGF-βb1、LBP、LDGF、LECT2、Lefty、Lewis-Y抗原、Lewis-Y相关抗原、LFA-1、LFA-3、Lfo、LIF、LIGHT、脂蛋白、LIX、LKN、Lptn、L-选择素、LT-a、LT-b、LTB4、LTBP-1、肺表面活性剂、促黄体激素、淋巴毒素B受体、Mac-1、MAdCAM、MAG、MAP2、MARC、MCAM、MCAM、MCK-2、MCP、M-CSF、MDC、Mer、METALLOPROTEASES、MGDF受体、MGMT、MHC(HLA-DR)、MIF、MIG、MIP、MIP-1-α、MK、MMAC1、MMP、MMP-1、MMP-10、MMP-11、MMP-12、MMP-13、MMP-14、MMP-15、MMP-2、MMP-24、MMP-3、MMP-7、MMP-8、MMP-9、MPIF、Mpo、MSK、MSP、粘蛋白(Muc1)、MUC18、Muellerian-抑钠素物质、Mug、MuSK、NAIP、NAP、NCAD、N-钙粘蛋白、NCA 90、NCAM、NCAM、脑啡肽酶、神经营养蛋白-3,-4,或-6、神经秩蛋白(Neurturin)、神经生长因子(NGF)、NGFR、NGF-β、nNOS、NO、NOS、Npn、NRG-3、NT、NTN、OB、OGG1、OPG、OPN、OSM、OX40L、OX40R、p150、p95、PADPr、甲状旁腺激素、PARC、PARP、PBR、PBSF、PCAD、P-钙粘蛋白、PCNA、PDGF、PDGF、PDK-1、PECAM、PEM、PF4、PGE、PGF、PGI2、PGJ2、PIN、PLA2、胎盘碱性磷酸酶(PLAP)、PlGF、PLP、PP14、胰岛素原、松弛素原、蛋白C、PS、PSA、PSCA、前列腺特异性膜抗原(PSMA)、PTEN、PTHrp、Ptk、PTN、R51、RANK、RANKL、RANTES、RANTES、松弛素A-链、松弛素 B-链、肾素、呼吸道合胞体病毒(RSV)F、RSV Fgp、Ret、类风湿因子、RLIP76、RPA2、RSK、S100、SCF/KL、SDF-1、SERINE、血清白蛋白、sFRP-3、Shh、SIGIRR、SK-1、SLAM、SLPI、SMAC、SMDF、SMOH、SOD、SPARC、Stat、STEAP、STEAP-II、TACE、TACI、TAG-72(肿瘤相关糖蛋白-72)、TARC、TCA-3、T-细胞受体(例如,T-细胞受体α/β)、TdT、TECK、TEM1、TEM5、TEM7、TEM8、TERT、睾丸PLAP-样碱性磷酸酶、TfR、TGF、TGF-α、TGF-β、TGF-β泛特异性、TGF-βRI(ALK-5)、TGF-βRII、

TGF-βRIIb、TGF-βRIII、TGF-β1、 TGF-β2、TGF-β3、TGF-β4、TGF-β5、凝血酶、胸腺Ck-1、甲状腺刺激激素、 Tie、TIMP、TIQ、组织因子、TMEFF2、Tmpo、TMPRSS2、TNF、TNF-α、 TNF-αβ、TNF-β2、TNFc、TNF-RI、TNF-RII、TNFRSF10A(TRAIL R1 Apo-2、 DR4)、TNFRSF10B(TRAIL R2 DR5、KILLER、TRICK-2A、TRICK-B)、 TNFRSF10C(TRAIL R3 DcR1、LIT、TRID)、TNFRSF10D(TRAIL R4 DcR2、 TRUNDD)、TNFRSF11A(RANK ODF R、TRANCE R)、TNFRSF11B(OPG OCIF、TR1)、TNFRSF12(TWEAK R FN14)、TNFRSF13B(TACI)、TNFRSF13C (BAFF R)、TNFRSF14(HVEM ATAR、HveA、LIGHT R、TR2)、TNFRSF16 (NGFR p75NTR)、TNFRSF17(BCMA)、TNFRSF18(GITR AITR)、TNFRSF19 (TROY TAJ、TRADE)、TNFRSF19L(RELT)、TNFRSF1A(TNF RI CD120a、 p55-60)、TNFRSF1B(TNF RII CD120b、p75-80)、TNFRSF26(TNFRH3)、 TNFRSF3(LTbR TNF RIII、TNFCR)、TNFRSF4(OX40 ACT35、TXGP1 R)、 TNFRSF5(CD40 p50)、TNFRSF6(Fas Apo-1、APT1、CD95)、TNFRSF6B(DcR3 M68、TR6)、TNFRSF7(CD27)、TNFRSF8(CD30)、TNFRSF9(4-1BB CD137、ILA)、TNFRSF21(DR6)、TNFRSF22(DcTRAIL R2 TNFRH2)、TNFRST23 (DcTRAIL R1 TNFRH1)、TNFRSF25(DR3 Apo-3、LARD、TR-3、TRAMP、 WSL-1)、TNFSF10(TRAIL Apo-2配体、TL2)、TNFSF11(TRANCE/RANK配体ODF、OPG配体)、TNFSF12(TWEAK Apo-3配体、DR3配体)、TNFSF13(APRIL TALL2)、TNFSF13B(BAFF BLYS、TALL1、THANK、TNFSF20)、 TNFSF14(LIGHT HVEM配体、LTg)、TNFSF15(TL1A/VEGI)、TNFSF18(GITR 配体AITR配体、TL6)、TNFSF1A(TNF-a肌连蛋白、DIF、TNFSF2)、TNFSF1B (TNF-b LTa、TNFSF1)、TNFSF3(LTb TNFC、p33)、TNFSF4(OX40配体gp34、 TXGP1)、TNFSF5(CD40配体CD154、gp39、HIGM1、IMD3、TRAP)、TNFSF6 (Fas配体Apo-1配体、APT1配体)、TNFSF7(CD27配体CD70)、TNFSF8(CD30 配体CD153)、TNFSF9(4-1BB配体CD137配体)、TP-1、t-PA、Tpo、TRAIL、 TRAIL R、TRAIL-R1、TRAIL-R2、TRANCE、转移受体、TRF、Trk、TROP-2、 TSG、TSLP、肿瘤相关抗原CA 125、表达Lewis Y相关糖的肿瘤相关抗原、TWEAK、TXB2、Ung、uPAR、uPAR-1、尿激酶、VCAM、VCAM-1、VECAD、 VE-钙粘蛋白、VE-钙粘蛋白-2、VEFGR-1(flt-1)、VEGF、VEGFR、VEGFR-3 (flt-4)、VEGI、VIM、病毒抗原、VLA、VLA-1、VLA-4、VNR整联蛋白、血管性血友病因子、WIF-1、WNT1、WNT2、WNT2B/13、WNT3、WNT3A、 WNT4、WNT5A、WNT5B、WNT6、WNT7A、WNT7B、WNT8A、WNT8B、 WNT9A、WNT9A、WNT9B、WNT10A、WNT10B、WNT11、WNT16、XCL1、 XCL2、XCR1、XCR1、XEDAR、XIAP、XPD、以及激素和生长因子的受体。

[0354] 可被本发明免疫球蛋白特异性靶向的示例性抗原包括但不限于:CD20、 CD19、Her2、EGFR、EpCAM、CD3、FcγRIIIa(CD16)、FcγRIIa(CD32a)、 FcγRIIb(CD32b)、FcγRI(CD64)、Toll-样受体(TLR)如TLR4和TLR9,细胞因子如IL-2、IL-5、IL-13、IL-12、IL-23、和TNFα,细胞因子受体如IL-2R、趋化因子、趋化因子受体、生长因子如VEGF和HGF等。为了形成本发明的双特异性抗体,可制造针对这些抗原任意组合的抗体;即这些抗原中的每一个可任选地、独立地被本发明双特异性抗体包括或不包括。

[0355] 双特异性抗体特别优选的组合是针对CD3的抗原结合结构域和选自结合 CD19、CD20、CD38和CD123的结构域的抗原结合结构域,其序列如图所示。

[0356] 本发明的核酸

[0357] 本发明还提供编码本发明双特异性抗体的核酸组合物。本领域技术人员可以看出,核酸组合物将取决于异二聚体蛋白质的形式和构架。因此,例如,当抗体形式需要三个氨基酸序列,如三F形式(例如,第一氨基酸单体包含Fc结构域和scFv,第二氨基酸单体包含重链和轻链),可将三个核酸序列纳入一个或多个表达载体进行表达。类似地,有些形式(例

如图1中的双scFv形式)仅需要两个核酸;同样,它们可被放入一个或两个表达载体中。

[0358] 如本领域所知,编码本发明组分的核酸可如本领域所知地、根据用于生产本发明异二聚体抗体的宿主细胞纳入表达载体中。核酸一般可操作地与任意数量的调节元件(启动子,复制起点,选择性标记物,核糖体结合位点,诱导物等)相连。表达载体可以是染色体外载体或是整合载体。

[0359] 然后,本发明的核酸和/或表达载体可如本领域所熟知地转化到任意数量不同类型的宿主细胞中,包括哺乳动物、细菌、酵母、昆虫和/或真菌细胞,许多实施方式中特别有用的是哺乳动物细胞(例如CHO细胞)。

[0360] 某些实施方式中,编码各单体的各个核酸和可选的编码轻链的核酸(这取决于抗体的形式)包含在单个表达载体中,通常处于不同或相同启动子控制下。本发明中特别有用的实施方式中,这两个或三个核酸分别包含在不同表达载体上。如本文所述亦如62/025,931(通过引用纳入本文)所述,可采用不同的载体比率来驱动异二聚体形成。即,出人意料地,虽然蛋白质包含1:1:2比率的第一单体:第二单体:轻链(本文许多实施方式中的异二聚体抗体包含三个多肽),但这些并非最佳效果的比率。

[0361] 本发明的异二聚体抗体通过培养包含表达载体的宿主细胞来制备,如本领域所熟知的那样。抗体生成后,进行常规抗体纯化步骤,包括离子交换色谱。如本文所述,使两种单体的pI相差至少0.5可允许通过离子交换色谱或等电聚焦或对等电点敏感的其他方法进行分离。即,包含改变各单体等电点(pI)的pI 取代使得各单体具有不同的pI并使异二聚体也具有不同pI,由此促进“三F”异二聚体的等电纯化(例如,阴离子交换柱,阳离子交换柱)。这些取代还有助于测定和监测纯化(例如,IEF凝胶、cIEF、和分析型IEX柱)后的各种污染性双scFv-Fc和mAb同二聚体。

[0362] 治疗

[0363] 制得的本发明组合物有多种应用。CD20、CD38和CD123在许多造血恶性肿瘤和各种造血恶性肿瘤的细胞系中失调,因此,本发明异二聚体抗体可用于治疗癌症,这些癌症包括但不限于所有B细胞淋巴瘤和白血病,这包括但不限于,非霍奇金淋巴瘤(NHL),伯基特淋巴瘤(BL),多发性骨髓瘤(MM),B型慢性淋巴细胞性白血病(B-CLL),B型和T型急性淋巴细胞白血病(ALL),T细胞淋巴瘤(TCL),急性骨髓性白血病(AML),毛细胞白血病(HCL),霍奇金淋巴瘤(HL),慢性淋巴细胞白血病(CLL),非霍奇金淋巴瘤和慢性骨髓性白血病 (CML)。

[0364] 因此,本发明的异二聚体组合物可用于治疗这些癌症。

[0365] 用于体内给药的抗体组合物

[0366] 按照本发明使用的抗体制剂通过如下方式制备保存:将具有所需纯度的抗体与可选的药学上可接受的运载体、赋形剂或稳定剂(Remington’s Pharmaceutical Sciences(《雷明顿药物科学》)第16版,Osol,A.编,[1980])混合,制成冻干制剂或水性溶液的形式。可接受的载体、赋形剂或稳定剂在所用剂量和浓度下对接受者无毒,这包括:缓冲剂如磷酸盐、柠檬酸盐和其它有机酸缓冲剂;抗氧化剂,包括抗坏血酸和甲硫氨酸;防腐剂(如十八烷基二甲基苄基氯化铵;氯化六烃季铵;苯扎氯铵、苄索氯铵;苯酚、丁基或苄基醇;对羟基苯甲酸烷酯,如对羟基苯甲酸甲酯或丙酯;邻苯二酚;间苯二酚;环己醇; 3-戊醇;和间甲酚);低分子量(小于约10个残基)的多肽;蛋白质,如血清白蛋白、明胶或免疫球蛋白;亲水性聚合物,如聚乙烯吡咯烷酮;氨基酸,如甘氨酸、谷胺酰胺、天冬酰胺、组氨酸、精氨酸或赖氨

酸;单糖、二糖和其它糖,包括葡萄糖、甘露糖或糊精;螯合剂,如EDTA;糖,如蔗糖、甘露醇、海藻糖或山梨糖醇;形成盐的抗衡离子,如钠;金属络合物(如Zn-蛋白质络合物);和/或非离子型表面活性剂,如吐温(TWEEN™)、普罗流尼克(PLURONICSTM) 或聚乙二醇(PEG)。

[0367] 根据治疗的具体适应症所需,本文制剂还可含有一种以上活性化合物,优选哪些活性互补、不会相互干扰的化合物。例如,可能需要提供具有其他特异性的抗体。或者,或在此之外,组合物可包含细胞毒剂、细胞因子、生长抑制剂和/或小分子拮抗剂。这些分子适合以目标效果有效量存在于组合中。

[0368] 活性成分还可包入微胶囊中,例如通过凝聚技术或界面聚合,例如羟甲基纤维素或明胶-微胶囊和聚-(甲基丙烯酸甲酯)各自的微胶囊,或包入胶体药物递送系统(例如脂质体、白蛋白微球、微乳剂、纳米颗粒和纳米胶囊)或包入乳浊液(macroemulsion)。这些技术可参见《雷明顿药物科学》第16版,Osol, A.编(1980)。

[0369] 用于体内给药的制剂应该是无菌的或近乎无菌的。这可通过无菌滤膜过滤容易地实现。

[0370] 可制备缓释制剂。缓释制剂的合适例子包括抗体含于固体疏水性聚合物的半渗透基质中,其中基质为成型制品的形式,例如膜或微胶囊。缓释基质的例子包括:聚酯、水凝胶(例如,聚(2-羟乙基-甲基丙烯酸酯)或聚(乙烯醇)),聚丙交酯(美国专利号3,773,919),L-谷氨酸和γ-乙基-L-谷氨酸的共聚物,不可降解的乙烯-乙酸乙烯酯,可降解的乳酸-乙醇酸共聚物如LUPRON DEPOTTM(由乳酸-乙醇酸共聚物和乙酸亮丙瑞林组成的可注射微球)和聚-D-(-)-3-羟基丁酸。诸如乙烯-乙酸乙烯酯和乳酸-乙醇酸等聚合物释放分子的时间能够超过100天,某些水凝胶释放蛋白质的时间则较短。

[0371] 包入胶囊的抗体能在体内长期留存,它们会因接触37℃潮湿环境而变性或聚集,导致生物学活性降低、免疫原型也可能改变。可设计合理方案实现稳定化,这取决于相关的机制。例如,如果发现聚集的机制是分子间通过巯基- 二硫键互变形成S-S键,则稳定化可通过修饰巯基残基、用酸性溶液冻干、控制水分含量、采用合适的添加剂和开发特定聚合物基质组成来实现。

[0372] 给药模式

[0373] 根据已知方法将本发明的抗体和化疗剂给予受治者,例如通过推注或通过一段时间内连续输注等静脉内给药,通过肌内、腹膜内、脊髓内、皮下、关节内、滑膜内、鞘内、口服、局部、或吸入途径。优先静脉内或皮下抗体给药。

[0374] 治疗模式

[0375] 在本发明的方法中,治疗提供就某疾病或病症而言的积极治疗效果。“积极治疗效果”是指疾病或病症的改善和/或与疾病或病症相关症状的改善。例如,积极治疗效果将指一种或多种以下改善:(1)肿瘤细胞数量减少;(2)肿瘤细胞死亡增加;(3)肿瘤细胞生存抑制;(5)肿瘤生长抑制(即减缓到一定程度,最好是停止);(6)患者生存率升高;和(7)与疾病或病症相关的一种或多种症状的一定程度缓解。

[0376] 各种特定疾病或病症中的积极治疗效果可以通过该疾病或病症的专门标准化效果标准来评价。肿瘤疗效可根据肿瘤形态变化(即,总肿瘤负荷,肿瘤大小等)来评估,可以采用诸如磁共振成像(MRI)扫描、X射线照相成像、计算机断层扫描(CT)扫描、骨骼扫描成像、内窥镜检查、和肿瘤活检取样,包括骨髓抽吸(BMA)等筛查技术和循环肿瘤细胞计数。

[0377] 除了这些积极治疗效果之外，接受治疗的对象还会有疾病相关症状的改善。

[0378] 疾病的改善可以被表征为完全缓解。“完全缓解”指无临床可检疾病，之前异常的放射成像检查、(就骨髓瘤而言)骨髓和脑脊液(CSF)或异常单克隆蛋白质正常。

[0379] 在根据本发明的方法处理后，这种效果可持续至少4至8周，有时6至8 周。或者，疾病改善可分类为部分缓解。“部分缓解”是指所有可测肿瘤负荷 (即对象中的恶性细胞数目、或测得的肿瘤块体积或异常单克隆蛋白质的量)降低至少约50％，没有新的病灶，持续4至8周或6至8周。

[0380] 本发明的治疗包括所用药物的“治疗有效量”。“治疗有效量”指按照一定剂量和必要时程能够实现所需治疗效果的量。

[0381] 治疗有效量会根据个体的疾病状态、年龄、性别和体重等因素以及药物在个体中引起所需效果的能力而不同。治疗有效量也是抗体或抗体部分的治疗有益效果胜过毒性或有害效果的量。

[0382] 肿瘤治疗的“治疗有效量”还可以根据其稳定疾病进展的能力来衡量。在动物模型系统中评价化合物抑制癌症的能力，该动物模型可预测在人肿瘤中的功效。

[0383] 或者，组合物的这种性质可通过检测化合物抑制细胞生长或诱导凋亡的能力来评价，如可采用本领域技术人员已知的体外试验。治疗有效量的治疗性化合物可减小肿瘤尺寸，或者缓解对象的症状。本领域一般技术人员能够基于如对象体格、对象症状严重性和特定组合物或所选给药途径等因素来确定治疗有效量。

[0384] 给药方案经调节能提供最优的所需效果(例如治疗效果)。例如，可以是一次推注、按时间分次给药或根据治疗情况的紧急性成比例地降低或增加给药。肠胃外组合物可以配制成单位剂型以便于给药和剂量均匀。本文中单位剂型指作为单个剂量用于待治疗对象的物理上离散的单位，每个单位包含预定量的活性化合物与所需药物运载体，该预定量经测算能够产生所需治疗效果。

[0385] 本发明中单位剂型的规格取决于或直接依赖于(a)活性化合物的独特特性和待实现的具体治疗效果，以及(b)本领域对于这种活性化合物应对个体敏感性的固有限制。

[0386] 本发明双特异性抗体的有效剂量和给药方案取决于待治疗的疾病或病症，可由本领域技术人员来确定。

[0387] 本发明中所用双特异性抗体治疗有效量的示例性而非限制性范围是约0.1-100mg/kg，如约0.1-50mg/kg，例如约0.1-20mg/kg，如约0.1-10mg/kg，例如约0.5、约0.3、约1或约3mg/kg。另一实施方式中，抗体的给药剂量是 1mg/kg或更高，例如1至20mg/kg，例如5至20mg/kg，例如8mg/kg。

[0388] 本领域普通医疗专业人员能够容易地确定和给出所需药物组合物有效量的处方。例如，对于药物组合物中的某药物，医师或兽医可以从低于期望治效所需的水平开始，然后逐渐增加剂量直到达到期望的效果。

[0389] 实施方式之一中，双特异性抗体以10至500mg/kg(例如200至400mg/kg) 的周剂量输注给予。可以重复这样的给药，例如，1至8次，如3至5次。给药可以是2至24小时(例如2至12小时)的持续输注。

[0390] 实施方式之一中，如果需要降低副作用(包括毒性)，则长时间例如超过24 小时缓慢连续输注给予双特异性抗体。

[0391] 实施方式之一中，双特异性抗体以250mg至2000mg(例如300mg，500mg， 700mg，1000mg，1500mg或2000mg)的周剂量给药，多达8次，如4到6次。给药可以是2至24小时(例如2至12小时)的连续输注。这种方案可以根据需要重复一次或多次，例如在6个月或12个月后重复。本发明化合物的剂量可通测量给药后血液中化合物的量来确定或调整，所述测量可以是例如采取生物样品和采用靶向双特异性抗体抗原结合区的抗独特型抗体。

[0392] 另一实施方式中，双特异性抗体每周一次，2至12周，例如3至10周，例如4至8周。

[0393] 实施方式之一中，双特异性抗体的给药为维持治疗，例如每周一次，持续 6个月或更长时间。

[0394] 实施方式之一中，双特异性抗体的给药方案包括一次双特异性抗体输注，然后输注与放射性同位素偶联的双特异性抗体。可以重复该方案，例如在7至 9天后。

[0395] 作为非限制性举例，根据本发明的治疗可以是按照约0.1-100mg/kg的日剂量提供抗体，例如，每天0.5、0.9、1.0、1.1、1.5、2、3、4、5、6、7、8、 9、10、11、12、13、14、15、16、17、18、19、20、21、22、23、24、25、 26、27、28、29、30、40、45、50、60、70、80、90或100mg/kg，在治疗开始后的第1、2、3、4、5、6、7、8、9、10、11、12、13、14、15、16、17、 18、19、20、21、22、23、24、25、26、27、28、29、30、31、32、33、34、 35、36、37、38、39、或40天中的至少一天，或者第1、2、3、4、5、6、7、 8、9、10、11、12、13、14、15、16、17、18、19或20周中的至少一周，或其任意组合，使用单剂次或间隔24、12、8、6、4或2小时的分剂次，或其任意组合。

[0396] 某些实施方式中，双特异性抗体分子与一种或多种其他治疗剂例如化疗剂组合使用。DNA损伤化疗剂的非限制性举例包括拓扑异构酶I抑制剂(例如伊立替康，拓扑替康，喜树碱及其类似物或代谢物，以及多柔比星)；拓扑异构酶II抑制剂(如依托泊苷，替尼泊苷和柔红霉素)；烷化剂(例如美法仑，苯丁酸氮芥，白消安，噻替派，异环磷酰胺，卡莫司汀，洛莫司汀，乌司他丁，链脲佐菌素，去甲基吡嗪，甲氨蝶呤，丝裂霉素C和环磷酰胺)；DNA嵌入剂(例如顺铂，奥沙利铂和卡铂)；DNA嵌入剂和自由基发生剂如博来霉素；和核苷模拟物(例如5-氟尿嘧啶，卡培他滨，吉西他滨，氟达拉滨，阿糖胞苷，巯嘌呤，硫鸟嘌呤，喷司他丁和羟基脲)。

[0397] 破坏细胞复制的化疗剂包括：紫杉醇，多西他赛，相关类似物；长春新碱，长春花碱，相关类似物；沙利度胺，来那度胺，相关类似物(例如CC-5013和 CC-4047)；蛋白酪氨酸激酶抑制剂(例如甲磺酸伊马替尼和吉非替尼)；蛋白酶体抑制剂(例如硼替佐米)；NF-κB抑制剂，包括IκB激酶抑制剂；结合癌症中过表达的蛋白质并由此下调细胞复制的抗体(例如曲妥单抗，利妥昔单抗，西妥昔单抗和贝伐单抗)；和已知在癌症中上调、过表达或活化的蛋白质或酶的其它抑制剂，这些蛋白质或酶的抑制下调细胞复制。

[0398] 某些实施方式中，本发明的抗体可以在Velcade®(硼替佐米)治疗之前、同时或之后使用。

[0399] 所有引用的参考文献其全部内容均明确通过引用纳入本文。

[0400] 以上虽然出于说明目的描述了本发明若干具体实施方式，但本领域技术人员可以看出，可以对细节作出许多改变，这些都属于权利要求所述本发明范围之内。

## 实施例

[0401] 下面通过实施例来说明本发明。这些实施例无意于将本发明限制于任何特定应用

或原理。本发明中所述的所有恒定区位置其编号都是根据Kabat的EU 索引(Kabat等,1991,《免疫学感兴趣的蛋白质的序列》(Sequences of Proteins of Immunological Interest),第5版,公共卫生署,国立卫生研究院,贝塞斯达,通过引用全文纳入本文)。抗体领域的技术人员知道,这一惯例对免疫球蛋白序列的特定区进行非顺序性编号,从而为免疫球蛋白家族中保守位置给出了标准化参照。因此,由EU索引定义的任何给定免疫球蛋白的位置不必然对应于其顺序性序列。

[0402] 美国公开2015/0307629,2014/0288275和WO2014/145806记载了通用技术和特定技术,这些文献全部通过引用纳入本文,并且其中的技术。

[0403] 实施例

[0404] 实施例1:变换形式

[0405] 双特异性抗体的产生

[0406] 抗-CD38×抗-CD3双特异性抗体的示意图见图1。各种变换形式的抗 -CD38×抗-CD3双特异性抗体的氨基酸序列列于图39至图43中。双特异性抗体表达所需三条链的编码DNA通过基因合成产生(华盛顿州博塞尔的蓝鹭生物技术公司(Blue Heron Biotechnology)),使用标准分子生物学技术亚克隆到表达载体pTT5中。使用定点诱变(QuikChange,Stratagene,德克萨斯州锡达溪)或其他基因合成和亚克隆引入取代。将DNA转染到HEK293E细胞中进行表达,使用蛋白A亲和层析(GE医疗公司)和阳离子交换层析从上清液中纯化所得蛋白质。蛋白A亲和纯化的得率如图35所示。阳离子交换层析纯化采用HiTrap SP HP柱(GE医疗公司),50mM MES,pH 6.0洗涤/平衡缓冲液和50mM MES 洗脱缓冲液,pH 6.0+1M NaCl线性梯度(见图36的色谱图)。

[0407] 重定向T细胞细胞毒性

[0408] 体外鉴定抗-CD38×抗-CD3双特异性抗体对$CD38^+$RPMI8266骨髓瘤细胞系的重定向T细胞细胞毒性(RTCC)。将10k RPMI8266细胞与500k人PBMC 一起孵育24小时。由LDH荧光测定RTCC(见图37)。

[0409] 实施例2

[0410] 重定向T细胞细胞毒性

[0411] 体外鉴定抗CD38×抗CD3 Fab-scFv-Fc双特异性抗体对CD38+ RPMI8266骨髓瘤细胞系的重定向T细胞毒性(RTCC)。将40k RPMI8266细胞与400k人PBMC一起孵育96小时。通过流式细胞术测量RTCC,如图44所示。还通过流式细胞术鉴定CD4+和CD8+T细胞的CD69、Ki-67和PI-9表达,如图45所示。

[0412] 抗-肿瘤活性的小鼠模型

[0413] 在第-23日,每组五只共四组NODscidγ (NSG)小鼠每只尾静脉注射植入5 ×$10^6$个RPMI8226TrS肿瘤细胞(多发性骨髓瘤,表达荧光素酶)。在第0天,小鼠腹膜内植入10×$10^6$个人PBMC。在第0天的PBMC植入后,每周(第0、7天)通过腹膜内注射给予试验品,剂量水平如图4所示。图46概括了实验设计。通过使用体内成像系统(IVIS®)测量每只小鼠的总通量来监测肿瘤生长。XmAb13551和XmAb15426都显示出显著的抗肿瘤作用(见图47和图48)。

[0414] 猕猴实验

[0415] 给予猕猴单剂量的抗-CD38×抗-CD3双特异性抗体。实验还包括抗-RSV ×抗-CD3双特异性抗体对照。剂量水平为:20μg/kg XmAb13551(n=2),0.5 mg/kg XmAb15426(n=

3)，3mg/kg XmAb14702(n＝3)或3mg/kg XmAb13245(抗-RSV×抗-CD3对照，n＝3)(3次独立实验)。抗-CD38×抗-CD3 双特异性抗体迅速清除外周血中的CD38+细胞(见图49)。据CD69表达测定，抗-CD38×抗-CD3双特异性抗体导致T细胞活化(见图50)。还测量了血清IL-6 水平(见图51)。发现与XmAb13551相比，XmAb15426的CD38+细胞清除持续时间延长，T细胞活化和IL-6生成水平较低。

[0416] 以0.5mg/kg和3mg/kg的单剂量测试XmAb15426和XmAb14702。两种抗体在这样的高剂量都耐受良好，与此一致的是受治猴的血清IL6水平为中等。此外，与以2、5或20μg/kg给药的原高亲和性XmAb13551相比，0.5mg/kg 中等CD3亲和性的XmAb15426清除CD38+细胞更有效。与此前的最高剂量 XmAb13551相比，XmAb15426的清除作用持续更久(XmAb15426为7天， XmAb13551为2天)。值得注意的是，尽管XmAb15426的靶细胞清除效力更大，但T细胞活化(CD69，CD25和PD1诱导)低得多，即便是在以比20μg/kg XmAb13551组高25倍剂量给药的XmAb15426处理的猴子中。CD3亲和性非常低的XmAb14702对CD38+细胞和T细胞活化几乎没有效果。

[0417] 这些结果表明，通过减弱CD3亲和性来调节T细胞活化是改善T细胞结合性双特异性抗体治疗窗口的可行方法。这种策略改善耐受性并允许以高剂量克服靶标(如CD38)的抗原沉默清除现象(antigen sink clearance)，由此能够扩展适合于靶向T细胞免疫治疗的抗原组。我们已经证明，通过降低对CD3的亲和性，XmAb15426有效清除CD38+细胞，同时最大程度降低了其高亲和性对应物XmAb13551在相当剂量可见的CRS效应。

序列表

<110> 森科股份有限公司(XENCOR, INC.)

<120> 结合CD3和肿瘤抗原的异二聚体抗体

<130> 067461-5180-WO

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<141> 2015-11-25

<150> 62/251,005

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

Tyr Cys Val Arg His Gly Asn Phe Gly Asp Ser Tyr Val Ser Trp Phe

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Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser

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Val Lys Gly

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Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg Gly
35 40 45

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

Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly Ala
65 70 75 80

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

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

85 90 95

Tyr Cys Val Arg His Gly Asn Phe Gly Asp Glu Tyr Val Ser Trp Phe

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Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser

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Val Lys Gly

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

Asn His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
245 250

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

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

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

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

85 90 95

Tyr Cys Val Arg His Gly Asn Phe Gly Asp Ser Tyr Val Ser Trp Phe

100 105 110

Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser

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Val Lys Gly

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

Asn His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
245 250

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<400> 46

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

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<400> 47

Thr Tyr Ala Met Ser
1 5

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Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp Ser
1 5 10 15
Val Lys Gly
<210> 49
<211> 14
<212> PRT
<213> 人工序列
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<400> 49
His Gly Asn Phe Gly Asp Ser Tyr Val Ser Trp Phe Ala Tyr
1 5 10
<210> 50
<211> 109
<212> PRT
<213> 人工序列
<220>
<221> 来源
<223> /注="人工序列说明:合成多肽"
<400> 50
Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly Gly
1 5 10 15
Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr Ser
20 25 30
Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg Gly
35 40 45
Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg Phe
50 55 60
Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly Ala
65 70 75 80
Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser Asn
85 90 95
His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
100 105
<210> 51
<211> 14
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<221> 来源
<223> /注=“人工序列说明:合成肽”
<400> 51
Gly Ser Ser Thr Gly Ala Val Thr Thr Ser Asn Tyr Ala Asn
1 5 10
<210> 52
<211> 7
<212> PRT
<213> 人工序列
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<223> /注=“人工序列说明:合成肽”
<400> 52
Gly Thr Asn Lys Arg Ala Pro
1 5
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<211> 9
<212> PRT
<213> 人工序列
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<221> 来源
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<400> 53
Ala Leu Trp Tyr Ser Asn His Trp Val
1 5
<210> 54
<211> 254
<212> PRT
<213> 人工序列
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<221> 来源
<223> /注=“人工序列说明:合成多肽”
<400> 54
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Thr Tyr
20 25 30
Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45
Gly Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
50 55 60
Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr

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

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<211> 116
<212> PRT
<213> 人工序列
<220>
<221> 来源
<223> /注="人工序列说明:合成多肽"
<400> 55
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Tyr Ser
20 25 30
Trp Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45
Ser Glu Ile Asn Pro Gln Ser Ser Thr Ile Asn Tyr Ala Thr Ser Val
50 55 60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys

85 90 95
Ala Arg Tyr Gly Asn Trp Phe Pro Tyr Trp Gly Gln Gly Thr Leu Val
100 105 110
Thr Val Ser Ser
115
<210> 56
<211> 5
<212> PRT
<213> 人工序列
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<221> 来源
<223> /注=“人工序列说明:合成肽”
<400> 56
Tyr Ser Trp Met Asn
1 5
<210> 57
<211> 17
<212> PRT
<213> 人工序列
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<221> 来源
<223> /注=“人工序列说明:合成肽”
<400> 57
Glu Ile Asn Pro Gln Ser Ser Thr Ile Asn Tyr Ala Thr Ser Val Lys
1 5 10 15
Gly
<210> 58
<211> 7
<212> PRT
<213> 人工序列
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<221> 来源
<223> /注=“人工序列说明:合成肽”
<400> 58
Tyr Gly Asn Trp Phe Pro Tyr
1 5
<210> 59
<211> 107
<212> PRT
<213> 人工序列
<220>
<221> 来源

<223> /注="人工序列说明:合成多肽"
<400> 59
Asp Ile Val Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asn Val Asp Thr Trp
20 25 30
Val Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ser Pro Lys Ala Leu Ile
35 40 45
Tyr Ser Ala Ser Tyr Arg Tyr Ser Gly Val Pro Asp Arg Phe Thr Gly
50 55 60
Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80
Glu Asp Phe Ala Thr Tyr Phe Cys Gln Gln Tyr Asp Ser Tyr Pro Leu
85 90 95
Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
100 105
<210> 60
<211> 11
<212> PRT
<213> 人工序列
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<221> 来源
<223> /注="人工序列说明:合成肽"
<400> 60
Arg Ala Ser Gln Asn Val Asp Thr Trp Val Ala
1 5 10
<210> 61
<211> 7
<212> PRT
<213> 人工序列
<220>
<221> 来源
<223> /注="人工序列说明:合成肽"
<400> 61
Ser Ala Ser Tyr Arg Tyr Ser
1 5
<210> 62
<211> 9
<212> PRT
<213> 人工序列
<220>
<221> 来源

<223> /注="人工序列说明:合成肽"
<400> 62
Gln Gln Tyr Asp Ser Tyr Pro Leu Thr
1 5
<210> 63
<211> 243
<212> PRT
<213> 人工序列
<220>
<221> 来源
<223> /注="人工序列说明:合成多肽"
<400> 63
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Tyr Ser
20 25 30
Trp Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45
Ser Glu Ile Asn Pro Gln Ser Ser Thr Ile Asn Tyr Ala Thr Ser Val
50 55 60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95
Ala Arg Tyr Gly Asn Trp Phe Pro Tyr Trp Gly Gln Gly Thr Leu Val
100 105 110
Thr Val Ser Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys
115 120 125
Pro Gly Ser Gly Lys Pro Gly Ser Asp Ile Val Met Thr Gln Ser Pro
130 135 140
Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg
145 150 155 160
Ala Ser Gln Asn Val Asp Thr Trp Val Ala Trp Tyr Gln Gln Lys Pro
165 170 175
Gly Gln Ser Pro Lys Ala Leu Ile Tyr Ser Ala Ser Tyr Arg Tyr Ser
180 185 190
Gly Val Pro Asp Arg Phe Thr Gly Ser Gly Ser Gly Thr Asp Phe Thr
195 200 205
Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Phe Cys
210 215 220
Gln Gln Tyr Asp Ser Tyr Pro Leu Thr Phe Gly Gly Gly Thr Lys Leu
225 230 235 240

Glu Ile Lys
<210> 64
<211> 116
<212> PRT
<213> 人工序列
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<221> 来源
<223> /注="人工序列说明:合成多肽"
<400> 64
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Asp Phe Ser Arg Ser
20 25 30
Trp Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45
Ser Glu Ile Asn Pro Asp Ser Ser Thr Ile Asn Tyr Ala Thr Ser Val
50 55 60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95
Ala Arg Tyr Gly Asn Trp Phe Pro Tyr Trp Gly Gln Gly Thr Leu Val
100 105 110
Thr Val Ser Ser
115
<210> 65
<211> 5
<212> PRT
<213> 人工序列
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<223> /注="人工序列说明:合成肽"
<400> 65
Arg Ser Trp Met Asn
1 5
<210> 66
<211> 17
<212> PRT
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<400> 66
Glu Ile Asn Pro Asp Ser Ser Thr Ile Asn Tyr Ala Thr Ser Val Lys
1 5 10 15
Gly
<210> 67
<211> 7
<212> PRT
<213> 人工序列
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<223> /注="人工序列说明:合成肽"
<400> 67
Tyr Gly Asn Trp Phe Pro Tyr
1 5
<210> 68
<211> 107
<212> PRT
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<221> 来源
<223> /注="人工序列说明:合成多肽"
<400> 68
Asp Ile Val Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asn Val Asp Thr Trp
20 25 30
Val Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ser Pro Lys Ala Leu Ile
35 40 45
Tyr Ser Ala Ser Tyr Arg Tyr Ser Gly Val Pro Asp Arg Phe Thr Gly
50 55 60
Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80
Glu Asp Phe Ala Thr Tyr Phe Cys Gln Gln Tyr Asp Ser Tyr Pro Leu
85 90 95
Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
100 105
<210> 69
<211> 11
<212> PRT
<213> 人工序列
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<221> 来源

<223> /注="人工序列说明:合成肽"
<400> 69
Arg Ala Ser Gln Asn Val Asp Thr Trp Val Ala
1 5 10
<210> 70
<211> 7
<212> PRT
<213> 人工序列
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<221> 来源
<223> /注="人工序列说明:合成肽"
<400> 70
Ser Ala Ser Tyr Arg Tyr Ser
1 5
<210> 71
<211> 9
<212> PRT
<213> 人工序列
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<221> 来源
<223> /注="人工序列说明:合成肽"
<400> 71
Gln Gln Tyr Asp Ser Tyr Pro Leu Thr
1 5
<210> 72
<211> 243
<212> PRT
<213> 人工序列
<220>
<221> 来源
<223> /注="人工序列说明:合成多肽"
<400> 72
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Asp Phe Ser Arg Ser
20 25 30
Trp Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45
Ser Glu Ile Asn Pro Asp Ser Ser Thr Ile Asn Tyr Ala Thr Ser Val
50 55 60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

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

<210> 73
<211> 116
<212> PRT
<213> 人工序列
<220>
<221> 来源
<223> /注=“人工序列说明:合成多肽”
<400> 73

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

100 105 110

Thr Val Ser Ser

115

<210> 74

<211> 5

<212> PRT

<213> 人工序列

<220>

<221> 来源

<223> /注=“人工序列说明:合成肽”

<400> 74

Arg Ser Trp Met Asn

1 5

<210> 75

<211> 17

<212> PRT

<213> 人工序列

<220>

<221> 来源

<223> /注=“人工序列说明:合成肽”

<400> 75

Glu Ile Asn Pro Asp Ser Ser Thr Ile Asn Tyr Ala Thr Ser Val Lys

1 5 10 15

Gly

<210> 76

<211> 7

<212> PRT

<213> 人工序列

<220>

<221> 来源

<223> /注=“人工序列说明:合成肽”

<400> 76

Tyr Gly Asn Trp Phe Pro Tyr

1 5

<210> 77

<211> 116

<212> PRT

<213> 人工序列

<220>

<221> 来源

<223> /注=“人工序列说明:合成多肽”

<400> 77

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

<210> 78
<211> 11
<212> PRT
<213> 人工序列
<220>
<221> 来源
<223> /注=“人工序列说明:合成肽”
<400> 78
Arg Ala Ser Gln Asn Val Asp Thr Asn Val Ala
1 5 10

<210> 79
<211> 7
<212> PRT
<213> 人工序列
<220>
<221> 来源
<223> /注=“人工序列说明:合成肽”
<400> 79
Ser Ala Ser Tyr Arg Tyr Ser
1 5

<210> 80
<211> 9
<212> PRT
<213> 人工序列
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<221> 来源

<223> /注="人工序列说明:合成肽"
<400> 80
Gln Gln Tyr Asp Ser Tyr Pro Leu Thr
1 5
<210> 81
<211> 252
<212> PRT
<213> 人工序列
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<221> 来源
<223> /注="人工序列说明:合成多肽"
<400> 81
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Asp Phe Ser Arg Ser
20 25 30
Trp Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45
Ser Glu Ile Asn Pro Asp Ser Ser Thr Ile Asn Tyr Ala Thr Ser Val
50 55 60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95
Ala Arg Tyr Gly Asn Trp Phe Pro Tyr Trp Gly Gln Gly Thr Leu Val
100 105 110
Thr Val Ser Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys
115 120 125
Pro Gly Ser Gly Lys Pro Gly Ser Glu Val Gln Leu Val Glu Ser Gly
130 135 140
Gly Gly Leu Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala
145 150 155 160
Ser Gly Phe Asp Phe Ser Arg Ser Trp Met Asn Trp Val Arg Gln Ala
165 170 175
Pro Gly Lys Gly Leu Glu Trp Val Ser Glu Ile Asn Pro Asp Ser Ser
180 185 190
Thr Ile Asn Tyr Ala Thr Ser Val Lys Gly Arg Phe Thr Ile Ser Arg
195 200 205
Asp Asn Ser Lys Asn Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala
210 215 220
Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Tyr Gly Asn Trp Phe Pro
225 230 235 240

Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
245 250

<210> 82
<211> 445
<212> PRT
<213> 人工序列
<220>
<221> 来源
<223> /注="人工序列说明:合成多肽"
<400> 82

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

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

<210> 83
<211> 485
<212> PRT
<213> 人工序列
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<221> 来源
<223> /注=“人工序列说明:合成多肽”
<400> 83
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Thr Tyr
20 25 30
Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45
Gly Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
50 55 60
Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
65 70 75 80

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

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

<210> 84
<211> 214
<212> PRT
<213> 人工序列
<220>
<221> 来源
<223> /注="人工序列说明:合成多肽"
<400> 84
Asp Ile Val Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asn Val Asp Thr Trp
20 25 30
Val Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ser Pro Lys Ala Leu Ile
35 40 45
Tyr Ser Ala Ser Tyr Arg Tyr Ser Gly Val Pro Asp Arg Phe Thr Gly
50 55 60
Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80
Glu Asp Phe Ala Thr Tyr Phe Cys Gln Gln Tyr Asp Ser Tyr Pro Leu
85 90 95
Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Arg Thr Val Ala Ala
100 105 110
Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly
115 120 125
Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala
130 135 140
Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln
145 150 155 160
Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser
165 170 175
Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr
180 185 190

Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser
195 200 205
Phe Asn Arg Gly Glu Cys
210
<210> 85
<211> 445
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<400> 85
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Asp Phe Ser Arg Ser
20 25 30
Trp Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45
Ser Glu Ile Asn Pro Asp Ser Ser Thr Ile Asn Tyr Ala Thr Ser Val
50 55 60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95
Ala Arg Tyr Gly Asn Trp Phe Pro Tyr Trp Gly Gln Gly Thr Leu Val
100 105 110
Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala
115 120 125
Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu
130 135 140
Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly
145 150 155 160
Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser
165 170 175
Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu
180 185 190
Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asp Thr
195 200 205
Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr
210 215 220
Cys Pro Pro Cys Pro Ala Pro Pro Val Ala Gly Pro Ser Val Phe Leu
225 230 235 240

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

<210> 86
<211> 485
<212> PRT
<213> 人工序列
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<223> /注=“人工序列说明:合成多肽”
<400> 86

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

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

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

<210> 87
<211> 214
<212> PRT
<213> 人工序列
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<223> /注="人工序列说明:合成多肽"
<400> 87
Asp Ile Val Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asn Val Asp Thr Asn
20 25 30
Val Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ser Pro Lys Ala Leu Ile
35 40 45
Tyr Ser Ala Ser Tyr Arg Tyr Ser Gly Val Pro Asp Arg Phe Thr Gly
50 55 60
Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80
Glu Asp Phe Ala Thr Tyr Phe Cys Gln Gln Tyr Asp Ser Tyr Pro Leu
85 90 95
Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Arg Thr Val Ala Ala
100 105 110
Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly
115 120 125
Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala
130 135 140
Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln
145 150 155 160
Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser
165 170 175

Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr
180 185 190
Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser
195 200 205
Phe Asn Arg Gly Glu Cys
210

<210> 88
<211> 445
<212> PRT
<213> 人工序列
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<223> /注="人工序列说明:合成多肽"
<400> 88
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Tyr Ser
20 25 30
Trp Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45
Ser Glu Ile Asn Pro Gln Ser Ser Thr Ile Asn Tyr Ala Thr Ser Val
50 55 60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95
Ala Arg Tyr Gly Asn Trp Phe Pro Tyr Trp Gly Gln Gly Thr Leu Val
100 105 110
Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala
115 120 125
Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu
130 135 140
Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly
145 150 155 160
Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser
165 170 175
Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu
180 185 190
Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asp Thr
195 200 205
Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr
210 215 220

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

<210> 89
<211> 485
<212> PRT
<213> 人工序列
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<221> 来源
<223> /注=“人工序列说明:合成多肽”
<400> 89

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
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Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Thr Tyr
20 25 30
Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

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

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

<210> 90
<211> 214
<212> PRT
<213> 人工序列
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<221> 来源
<223> /注="人工序列说明:合成多肽"
<400> 90
Asp Ile Val Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asn Val Asp Thr Trp
20 25 30
Val Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ser Pro Lys Ala Leu Ile
35 40 45
Tyr Ser Ala Ser Tyr Arg Tyr Ser Gly Val Pro Asp Arg Phe Thr Gly
50 55 60
Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80
Glu Asp Phe Ala Thr Tyr Phe Cys Gln Gln Tyr Asp Ser Tyr Pro Leu
85 90 95
Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Arg Thr Val Ala Ala
100 105 110
Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly
115 120 125
Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala
130 135 140
Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln
145 150 155 160

Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser
165 170 175
Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr
180 185 190
Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser
195 200 205
Phe Asn Arg Gly Glu Cys
210

<210> 91
<211> 445
<212> PRT
<213> 人工序列
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<223> /注="人工序列说明:合成多肽"
<400> 91

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

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

<210> 92
<211> 485
<212> PRT
<213> 人工序列
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<223> /注=“人工序列说明:合成多肽”
<400> 92
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Thr Tyr
20 25 30

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

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

<210> 93
<211> 214
<212> PRT
<213> 人工序列
<220>
<221> 来源
<223> /注="人工序列说明:合成多肽"
<400> 93
Asp Ile Val Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asn Val Asp Thr Trp
20 25 30
Val Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ser Pro Lys Ala Leu Ile
35 40 45
Tyr Ser Ala Ser Tyr Arg Tyr Ser Gly Val Pro Asp Arg Phe Thr Gly
50 55 60
Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80
Glu Asp Phe Ala Thr Tyr Phe Cys Gln Gln Tyr Asp Ser Tyr Pro Leu
85 90 95
Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Arg Thr Val Ala Ala
100 105 110
Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly
115 120 125
Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala
130 135 140

Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln
145 150 155 160
Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser
165 170 175
Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr
180 185 190
Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser
195 200 205
Phe Asn Arg Gly Glu Cys
210

<210> 94
<211> 445
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<213> 人工序列
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<223> /注="人工序列说明:合成多肽"
<400> 94
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Asp Phe Ser Arg Ser
20 25 30
Trp Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45
Ser Glu Ile Asn Pro Asp Ser Ser Thr Ile Asn Tyr Ala Thr Ser Val
50 55 60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95
Ala Arg Tyr Gly Asn Trp Phe Pro Tyr Trp Gly Gln Gly Thr Leu Val
100 105 110
Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala
115 120 125
Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu
130 135 140
Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly
145 150 155 160
Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser
165 170 175
Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu
180 185 190

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

<210> 95
<211> 485
<212> PRT
<213> 人工序列
<220>
<221> 来源
<223> /注=“人工序列说明:合成多肽”
<400> 95

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

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

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

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

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

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<212> PRT
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Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Asp Phe Ser Arg Ser
20 25 30
Trp Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45
Ser Glu Ile Asn Pro Asp Ser Ser Thr Ile Asn Tyr Ala Thr Ser Val
50 55 60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95
Ala Arg Tyr Gly Asn Trp Phe Pro Tyr Trp Gly Gln Gly Thr Leu Val
100 105 110
Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala
115 120 125
Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu
130 135 140
Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly
145 150 155 160
Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser
165 170 175

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

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<212> PRT
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Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Thr Tyr
20 25 30
Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45
Gly Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
50 55 60
Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
65 70 75 80
Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr
85 90 95
Tyr Cys Val Arg His Gly Asn Phe Gly Asp Ser Tyr Val Ser Trp Phe
100 105 110
Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Lys Pro
115 120 125
Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly
130 135 140
Ser Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly
145 150 155 160
Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr
165 170 175
Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg
180 185 190
Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg
195 200 205
Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly
210 215 220
Ala Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser
225 230 235 240
Asn His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Glu Pro
245 250 255
Lys Ser Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Pro
260 265 270
Val Ala Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
275 280 285
Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val
290 295 300
Lys His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
305 310 315 320
Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
325 330 335

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

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

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

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

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

<210> 101
<211> 485
<212> PRT
<213> 人工序列
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<223> /注="人工序列说明:合成多肽"

<400> 101

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

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

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<213> 人工序列
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<223> /注="人工序列说明:合成多肽"
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Asp Ile Val Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asn Val Asp Thr Asn
20 25 30
Val Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ser Pro Lys Ala Leu Ile
35 40 45
Tyr Ser Ala Ser Tyr Arg Tyr Ser Gly Val Pro Asp Arg Phe Thr Gly
50 55 60
Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80
Glu Asp Phe Ala Thr Tyr Phe Cys Gln Gln Tyr Asp Ser Tyr Pro Leu
85 90 95

Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Arg Thr Val Ala Ala
100 105 110
Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly
115 120 125
Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala
130 135 140
Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln
145 150 155 160
Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser
165 170 175
Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr
180 185 190
Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser
195 200 205
Phe Asn Arg Gly Glu Cys
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<210> 103
<211> 445
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<223> /注=“人工序列说明:合成多肽”
<400> 103
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
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Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Tyr Ser
20 25 30
Trp Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45
Ser Glu Ile Asn Pro Gln Ser Ser Thr Ile Asn Tyr Ala Thr Ser Val
50 55 60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95
Ala Arg Tyr Gly Asn Trp Phe Pro Tyr Trp Gly Gln Gly Thr Leu Val
100 105 110
Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala
115 120 125
Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu
130 135 140

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

<210> 104
<211> 485
<212> PRT
<213> 人工序列

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<221> 来源

<223> /注=“人工序列说明:合成多肽”

<400> 104

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

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

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<212> PRT
<213> 人工序列
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<221> 来源
<223> /注=“人工序列说明:合成多肽”
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Asp Ile Val Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
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Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asn Val Asp Thr Trp
20 25 30
Val Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ser Pro Lys Ala Leu Ile
35 40 45
Tyr Ser Ala Ser Tyr Arg Tyr Ser Gly Val Pro Asp Arg Phe Thr Gly
50 55 60
Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

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

<210> 106
<211> 445
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<213> 人工序列
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<221> 来源
<223> /注=“人工序列说明:合成多肽”
<400> 106
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
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Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Asp Phe Ser Arg Ser
20 25 30
Trp Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45
Ser Glu Ile Asn Pro Asp Ser Ser Thr Ile Asn Tyr Ala Thr Ser Val
50 55 60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95
Ala Arg Tyr Gly Asn Trp Phe Pro Tyr Trp Gly Gln Gly Thr Leu Val
100 105 110
Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala
115 120 125

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

<210> 107

<211> 485

<212> PRT
<213> 人工序列
<220>
<221> 来源
<223> /注="人工序列说明:合成多肽"
<400> 107

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

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

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<213> 人工序列
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<223> /注="人工序列说明:合成多肽"
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1 5 10 15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asn Val Asp Thr Asn
20 25 30
Val Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ser Pro Lys Ala Leu Ile
35 40 45
Tyr Ser Ala Ser Tyr Arg Tyr Ser Gly Val Pro Asp Arg Phe Thr Gly
50 55 60

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

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<211> 445
<212> PRT
<213> 人工序列
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<223> /注="人工序列说明:合成多肽"
<400> 109
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Asp Phe Ser Arg Ser
20 25 30
Trp Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45
Ser Glu Ile Asn Pro Asp Ser Ser Thr Ile Asn Tyr Ala Thr Ser Val
50 55 60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95
Ala Arg Tyr Gly Asn Trp Phe Pro Tyr Trp Gly Gln Gly Thr Leu Val
100 105 110

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

<210> 110
<211> 485
<212> PRT
<213> 人工序列
<220>
<221> 来源
<223> /注="人工序列说明:合成多肽"
<400> 110

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

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

<210> 111
<211> 214
<212> PRT
<213> 人工序列
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<223> /注="人工序列说明:合成多肽"
<400> 111
Asp Ile Val Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asn Val Asp Thr Trp
20 25 30
Val Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ser Pro Lys Ala Leu Ile
35 40 45

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

<210> 112
<211> 445
<212> PRT
<213> 人工序列
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<223> /注="人工序列说明:合成多肽"
<400> 112
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Asp Phe Ser Arg Ser
20 25 30
Trp Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45
Ser Glu Ile Asn Pro Asp Ser Ser Thr Ile Asn Tyr Ala Thr Ser Val
50 55 60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

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

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
435 440 445

<210> 113
<211> 485
<212> PRT
<213> 人工序列
<220>
<221> 来源
<223> /注="人工序列说明:合成多肽"
<400> 113

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

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

<210> 114
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<212> PRT
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<223> /注=“人工序列说明:合成多肽”
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Asp Ile Val Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
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Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asn Val Asp Thr Trp
20 25 30

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

<210> 115
<211> 445
<212> PRT
<213> 人工序列
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<221> 来源
<223> /注=“人工序列说明:合成多肽”
<400> 115

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

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

Gln Gly Asp Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
420 425 430
His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
435 440 445

<210> 116
<211> 485
<212> PRT
<213> 人工序列
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<221> 来源
<223> /注="人工序列说明:合成多肽"
<400> 116

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

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

<210> 117
<211> 214
<212> PRT
<213> 人工序列
<220>
<221> 来源
<223> /注=“人工序列说明:合成多肽”
<400> 117

Asp Ile Val Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

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

<210> 118
<211> 445
<212> PRT
<213> 人工序列
<220>
<221> 来源
<223> /注="人工序列说明:合成多肽"
<400> 118
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Asp Phe Ser Arg Ser
20 25 30
Trp Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45
Ser Glu Ile Asn Pro Asp Ser Ser Thr Ile Asn Tyr Ala Thr Ser Val
50 55 60

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

Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Glu
405 410 415
Gln Gly Asp Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
420 425 430
His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
435 440 445

<210> 119
<211> 485
<212> PRT
<213> 人工序列
<220>
<221> 来源
<223> /注="人工序列说明:合成多肽"
<400> 119

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

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

<210> 120
<211> 214
<212> PRT
<213> 人工序列
<220>
<221> 来源
<223> /注=“人工序列说明:合成多肽”
<400> 120

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

<210> 121
<211> 445
<212> PRT
<213> 人工序列
<220>
<221> 来源
<223> /注=“人工序列说明:合成多肽”
<400> 121

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Asp Phe Ser Arg Ser
20 25 30
Trp Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

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

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

<210> 122
<211> 485
<212> PRT
<213> 人工序列
<220>
<221> 来源
<223> /注="人工序列说明:合成多肽"
<400> 122
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Thr Tyr
20 25 30
Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45
Gly Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
50 55 60
Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
65 70 75 80
Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr
85 90 95
Tyr Cys Val Arg His Gly Asn Phe Gly Asp Ser Tyr Val Ser Trp Phe
100 105 110
Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Lys Pro
115 120 125
Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly
130 135 140
Ser Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly
145 150 155 160
Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr
165 170 175
Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg
180 185 190
Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg
195 200 205

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

<210> 123
<211> 214
<212> PRT
<213> 人工序列
<220>
<221> 来源

<223> /注="人工序列说明:合成多肽"

<400> 123

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

<210> 124

<211> 445

<212> PRT

<213> 人工序列

<220>

<221> 来源

<223> /注="人工序列说明:合成多肽"

<400> 124

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Asp Phe Ser Arg Ser
20 25 30

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

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

<210> 125
<211> 485
<212> PRT
<213> 人工序列
<220>
<221> 来源
<223> /注="人工序列说明:合成多肽"
<400> 125
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Thr Tyr
20 25 30
Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Cys Leu Glu Trp Val
35 40 45
Gly Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
50 55 60
Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
65 70 75 80
Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr
85 90 95
Tyr Cys Val Arg His Gly Asn Phe Gly Asp Ser Tyr Val Ser Trp Phe
100 105 110
Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Lys Pro
115 120 125
Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly
130 135 140
Ser Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly
145 150 155 160
Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr
165 170 175
Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg
180 185 190

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

<210> 126
<211> 214
<212> PRT
<213> 人工序列

<220>
<221> 来源
<223> /注=“人工序列说明:合成多肽”
<400> 126

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

<210> 127
<211> 445
<212> PRT
<213> 人工序列
<220>
<221> 来源
<223> /注=“人工序列说明:合成多肽”
<400> 127

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

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

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

<210> 128
<211> 485
<212> PRT
<213> 人工序列
<220>
<221> 来源
<223> /注="人工序列说明:合成多肽"
<400> 128

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

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

<210> 129
<211> 214

<212> PRT
<213> 人工序列
<220>
<221> 来源
<223> /注=“人工序列说明:合成多肽”
<400> 129

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

<210> 130
<211> 207
<212> PRT
<213> 智人(Homo sapiens)
<400> 130

Met Gln Ser Gly Thr His Trp Arg Val Leu Gly Leu Cys Leu Leu Ser
1 5 10 15
Val Gly Val Trp Gly Gln Asp Gly Asn Glu Glu Met Gly Gly Ile Thr

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

<210> 131
<211> 300
<212> PRT
<213> 智人(Homo sapiens)
<400> 131
Met Ala Asn Cys Glu Phe Ser Pro Val Ser Gly Asp Lys Pro Cys Cys
1 5 10 15
Arg Leu Ser Arg Arg Ala Gln Leu Cys Leu Gly Val Ser Ile Leu Val
20 25 30
Leu Ile Leu Val Val Val Leu Ala Val Val Val Pro Arg Trp Arg Gln
35 40 45
Gln Trp Ser Gly Pro Gly Thr Thr Lys Arg Phe Pro Glu Thr Val Leu
50 55 60
Ala Arg Cys Val Lys Tyr Thr Glu Ile His Pro Glu Met Arg His Val
65 70 75 80
Asp Cys Gln Ser Val Trp Asp Ala Phe Lys Gly Ala Phe Ile Ser Lys
85 90 95
His Pro Cys Asn Ile Thr Glu Glu Asp Tyr Gln Pro Leu Met Lys Leu
100 105 110

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

<210> 132
<211> 258
<212> PRT
<213> 智人(Homo sapiens)
<400> 132

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

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

<210> 133
<211> 15
<212> PRT
<213> 人工序列
<220>
<221> 来源
<223> /注=“人工序列说明:合成肽”
<400> 133
Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
1 5 10 15

<210> 134
<211> 18
<212> PRT
<213> 人工序列
<220>
<221> 来源
<223> /注=“人工序列说明:合成肽”
<400> 134
Gly Ser Thr Ser Gly Ser Gly Lys Pro Gly Ser Gly Glu Gly Ser Thr
1 5 10 15
Lys Gly

<210> 135

<211> 14
<212> PRT
<213> 人工序列
<220>
<221> 来源
<223> /注="人工序列说明:合成肽"
<400> 135
Ile Arg Pro Arg Ala Ile Gly Gly Ser Lys Pro Arg Val Ala
1 5 10
<210> 136
<211> 15
<212> PRT
<213> 人工序列
<220>
<221> 来源
<223> /注="人工序列说明:合成肽"
<400> 136
Gly Lys Gly Gly Ser Gly Lys Gly Gly Ser Gly Lys Gly Gly Ser
1 5 10 15
<210> 137
<211> 15
<212> PRT
<213> 人工序列
<220>
<221> 来源
<223> /注="人工序列说明:合成肽"
<400> 137
Gly Gly Lys Gly Ser Gly Gly Lys Gly Ser Gly Gly Lys Gly Ser
1 5 10 15
<210> 138
<211> 15
<212> PRT
<213> 人工序列
<220>
<221> 来源
<223> /注="人工序列说明:合成肽"
<400> 138
Gly Gly Gly Lys Ser Gly Gly Gly Lys Ser Gly Gly Gly Lys Ser
1 5 10 15
<210> 139
<211> 15
<212> PRT

<213> 人工序列
<220>
<221> 来源
<223> /注="人工序列说明:合成肽"
<400> 139
Gly Lys Gly Lys Ser Gly Lys Gly Lys Ser Gly Lys Gly Lys Ser
1 5 10 15
<210> 140
<211> 15
<212> PRT
<213> 人工序列
<220>
<221> 来源
<223> /注="人工序列说明:合成肽"
<400> 140
Gly Gly Gly Lys Ser Gly Gly Lys Gly Ser Gly Lys Gly Gly Ser
1 5 10 15
<210> 141
<211> 15
<212> PRT
<213> 人工序列
<220>
<221> 来源
<223> /注="人工序列说明:合成肽"
<400> 141
Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser
1 5 10 15
<210> 142
<211> 20
<212> PRT
<213> 人工序列
<220>
<221> 来源
<223> /注="人工序列说明:合成肽"
<400> 142
Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly
1 5 10 15
Lys Pro Gly Ser
20
<210> 143
<211> 20
<212> PRT

<213> 人工序列
<220>
<221> 来源
<223> /注="人工序列说明:合成肽"
<400> 143
Gly Lys Gly Lys Ser Gly Lys Gly Lys Ser Gly Lys Gly Lys Ser Gly
1 5 10 15
Lys Gly Lys Ser
20
<210> 144
<211> 20
<212> PRT
<213> 人工序列
<220>
<221> 来源
<223> /注="人工序列说明:合成肽"
<400> 144
Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
1 5 10 15
Gly Gly Gly Ser
20
<210> 145
<211> 14
<212> PRT
<213> 人工序列
<220>
<221> 来源
<223> /注="人工序列说明:合成肽"
<400> 145
Ser Thr Ala Gly Asp Thr His Leu Gly Gly Glu Asp Phe Asp
1 5 10
<210> 146
<211> 15
<212> PRT
<213> 人工序列
<220>
<221> 来源
<223> /注="人工序列说明:合成肽"
<400> 146
Gly Glu Gly Gly Ser Gly Glu Gly Gly Ser Gly Glu Gly Gly Ser
1 5 10 15
<210> 147

<211> 15
<212> PRT
<213> 人工序列
<220>
<221> 来源
<223> /注="人工序列说明:合成肽"
<400> 147
Gly Gly Glu Gly Ser Gly Gly Glu Gly Ser Gly Gly Glu Gly Ser
1 5 10 15
<210> 148
<211> 15
<212> PRT
<213> 人工序列
<220>
<221> 来源
<223> /注="人工序列说明:合成肽"
<400> 148
Gly Gly Gly Glu Ser Gly Gly Gly Glu Ser Gly Gly Gly Glu Ser
1 5 10 15
<210> 149
<211> 15
<212> PRT
<213> 人工序列
<220>
<221> 来源
<223> /注="人工序列说明:合成肽"
<400> 149
Gly Glu Gly Glu Ser Gly Glu Gly Glu Ser Gly Glu Gly Glu Ser
1 5 10 15
<210> 150
<211> 15
<212> PRT
<213> 人工序列
<220>
<221> 来源
<223> /注="人工序列说明:合成肽"
<400> 150
Gly Gly Gly Glu Ser Gly Gly Glu Gly Ser Gly Glu Gly Gly Ser
1 5 10 15
<210> 151
<211> 20
<212> PRT

<213> 人工序列
<220>
<221> 来源
<223> /注="人工序列说明:合成肽"
<400> 151
Gly Glu Gly Glu Ser Gly Glu Gly Glu Ser Gly Glu Gly Glu Ser Gly
1 5 10 15
Glu Gly Glu Ser
20
<210> 152
<211> 15
<212> PRT
<213> 人工序列
<220>
<221> 来源
<223> /注="人工序列说明:合成肽"
<400> 152
Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
1 5 10 15
<210> 153
<211> 20
<212> PRT
<213> 人工序列
<220>
<221> 来源
<223> /注="人工序列说明:合成肽"
<400> 153
Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
1 5 10 15
Gly Gly Gly Ser
20
<210> 154
<211> 18
<212> PRT
<213> 人工序列
<220>
<221> 来源
<223> /注="人工序列说明:合成肽"
<400> 154
Gly Ser Thr Ser Gly Ser Gly Lys Pro Gly Ser Gly Glu Gly Ser Thr
1 5 10 15
Lys Gly

<210> 155
<211> 19
<212> PRT
<213> 人工序列
<220>
<221> 来源
<223> /注="人工序列说明:合成肽"
<400> 155
Pro Arg Gly Ala Ser Lys Ser Gly Ser Ala Ser Gln Thr Gly Ser Ala
1 5 10 15
Pro Gly Ser
<210> 156
<211> 19
<212> PRT
<213> 人工序列
<220>
<221> 来源
<223> /注="人工序列说明:合成肽"
<400> 156
Gly Thr Ala Ala Ala Gly Ala Gly Ala Ala Gly Gly Ala Ala Ala Gly
1 5 10 15
Ala Ala Gly
<210> 157
<211> 19
<212> PRT
<213> 人工序列
<220>
<221> 来源
<223> /注="人工序列说明:合成肽"
<400> 157
Gly Thr Ser Gly Ser Ser Gly Ser Gly Ser Gly Gly Ser Gly Ser Gly
1 5 10 15
Gly Gly Gly
<210> 158
<211> 20
<212> PRT
<213> 人工序列
<220>
<221> 来源
<223> /注="人工序列说明:合成肽"
<400> 158
Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly

1 5 10 15
Lys Pro Gly Ser
20
<210> 159
<211> 445
<212> PRT
<213> 人工序列
<220>
<221> 来源
<223> /注=“人工序列说明:合成多肽”
<400> 159
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Asp Phe Ser Arg Ser
20 25 30
Trp Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45
Ser Glu Ile Asn Pro Asp Ser Ser Thr Ile Asn Tyr Ala Thr Ser Val
50 55 60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95
Ala Arg Tyr Gly Asn Trp Phe Pro Tyr Trp Gly Gln Gly Thr Leu Val
100 105 110
Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala
115 120 125
Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu
130 135 140
Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly
145 150 155 160
Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser
165 170 175
Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu
180 185 190
Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asp Thr
195 200 205
Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr
210 215 220
Cys Pro Pro Cys Pro Ala Pro Pro Val Ala Gly Pro Ser Val Phe Leu
225 230 235 240
Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu

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

<210> 160
<211> 714
<212> PRT
<213> 人工序列
<220>
<221> 来源
<223> /注=“人工序列说明:合成多肽”
<400> 160
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Asp Phe Ser Arg Ser
20 25 30
Trp Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45
Ser Glu Ile Asn Pro Asp Ser Ser Thr Ile Asn Tyr Ala Thr Ser Val
50 55 60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr

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

405 410 415

Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn

420 425 430

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys Gly Gly Gly

435 440 445

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

450 455 460

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

465 470 475 480

Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Thr Tyr Ala Met Asn Trp

485 490 495

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

500 505 510

Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp Ser Val Lys Gly

515 520 525

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

530 535 540

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

545 550 555 560

His Gly Asn Phe Gly Asp Ser Tyr Val Ser Trp Phe Ala Tyr Trp Gly

565 570 575

Gln Gly Thr Leu Val Thr Val Ser Ser Gly Lys Pro Gly Ser Gly Lys

580 585 590

Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gln Ala Val

595 600 605

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

610 615 620

Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr Ser Asn Tyr Ala

625 630 635 640

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

645 650 655

Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg Phe Ser Gly Ser

660 665 670

Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly Ala Gln Pro Glu

675 680 685

Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser Asn His Trp Val

690 695 700

Phe Gly Gly Gly Thr Lys Leu Thr Val Leu

705 710

<210> 161

<211> 214

<212> PRT

<213> 人工序列
<220>
<221> 来源
<223> /注="人工序列说明:合成多肽"
<400> 161

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

<210> 162
<211> 585
<212> PRT
<213> 人工序列
<220>
<221> 来源
<223> /注="人工序列说明:合成多肽"
<400> 162

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

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

340 345 350

Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Asp Val Ser

355 360 365

Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asp Gly Gln

370 375 380

Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly

385 390 395 400

Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Glu

405 410 415

Gln Gly Asp Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn

420 425 430

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys Gly Gly Gly

435 440 445

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

450 455 460

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

465 470 475 480

Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Thr Tyr Ala Met Asn Trp

485 490 495

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

500 505 510

Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp Ser Val Lys Gly

515 520 525

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

530 535 540

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

545 550 555 560

His Gly Asn Phe Gly Asp Ser Tyr Val Ser Trp Phe Ala Tyr Trp Gly

565 570 575

Gln Gly Thr Leu Val Thr Val Ser Ser

580 585

<210> 163

<211> 569

<212> PRT

<213> 人工序列

<220>

<221> 来源

<223> /注=“人工序列说明:合成多肽”

<400> 163

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

1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Asp Phe Ser Arg Ser

20 25 30

Trp Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Glu Ile Asn Pro Asp Ser Ser Thr Ile Asn Tyr Ala Thr Ser Val
50 55 60

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

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Tyr Gly Asn Trp Phe Pro Tyr Trp Gly Gln Gly Thr Leu Val
100 105 110

Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala
115 120 125

Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu
130 135 140

Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly
145 150 155 160

Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser
165 170 175

Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu
180 185 190

Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr
195 200 205

Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr
210 215 220

Cys Pro Pro Cys Pro Ala Pro Pro Val Ala Gly Pro Ser Val Phe Leu
225 230 235 240

Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu
245 250 255

Val Thr Cys Val Val Val Asp Val Lys His Glu Asp Pro Glu Val Lys
260 265 270

Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys
275 280 285

Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu
290 295 300

Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys
305 310 315 320

Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys
325 330 335

Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser
340 345 350

Arg Glu Gln Met Thr Lys Asn Gln Val Lys Leu Thr Cys Leu Val Lys

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

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

50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Phe Cys Gln Gln Tyr Asp Ser Tyr Pro Leu
85 90 95

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

Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly
115 120 125

Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala
130 135 140

Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln
145 150 155 160

Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser
165 170 175

Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr
180 185 190

Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser
195 200 205

Phe Asn Arg Gly Glu Cys
210

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<400> 165

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Asp Phe Ser Arg Ser
20 25 30

Trp Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Glu Ile Asn Pro Asp Ser Ser Thr Ile Asn Tyr Ala Thr Ser Val
50 55 60

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

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

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

100 105 110

Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala
115 120 125

Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu
130 135 140

Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly
145 150 155 160

Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser
165 170 175

Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu
180 185 190

Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asp Thr
195 200 205

Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr
210 215 220

Cys Pro Pro Cys Pro Ala Pro Pro Val Ala Gly Pro Ser Val Phe Leu
225 230 235 240

Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu
245 250 255

Val Thr Cys Val Val Val Asp Val Lys His Glu Asp Pro Glu Val Lys
260 265 270

Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys
275 280 285

Pro Arg Glu Glu Glu Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu
290 295 300

Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys
305 310 315 320

Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys
325 330 335

Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser
340 345 350

Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Asp Val Ser
355 360 365

Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asp Gly Gln
370 375 380

Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly
385 390 395 400

Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Glu
405 410 415

Gln Gly Asp Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
420 425 430

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys

435 440 445

<210> 166
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<223> /注=“人工序列说明:合成多肽”
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Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Asp Phe Ser Arg Ser
20 25 30
Trp Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45
Ser Glu Ile Asn Pro Asp Ser Ser Thr Ile Asn Tyr Ala Thr Ser Val
50 55 60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95
Ala Arg Tyr Gly Asn Trp Phe Pro Tyr Trp Gly Gln Gly Thr Leu Val
100 105 110
Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala
115 120 125
Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu
130 135 140
Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly
145 150 155 160
Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser
165 170 175
Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu
180 185 190
Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr
195 200 205
Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Gly Gly Gly Gly Ser
210 215 220
Gly Gly Gly Gly Ser Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu
225 230 235 240
Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe
245 250 255
Thr Phe Ser Thr Tyr Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys

260 265 270

Gly Leu Glu Trp Val Gly Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala

275 280 285

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

290 295 300

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

305 310 315 320

Asp Thr Ala Val Tyr Tyr Cys Val Arg His Gly Asn Phe Gly Asp Ser

325 330 335

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

340 345 350

Ser Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly

355 360 365

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

370 375 380

Thr Val Ser Pro Gly Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr

385 390 395 400

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

405 410 415

Gly Lys Ser Pro Arg Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro

420 425 430

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

435 440 445

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

450 455 460

Ala Leu Trp Tyr Ser Asn His Trp Val Phe Gly Gly Gly Thr Lys Leu

465 470 475 480

Thr Val Leu Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Lys Thr His

485 490 495

Thr Cys Pro Pro Cys Pro Ala Pro Pro Val Ala Gly Pro Ser Val Phe

500 505 510

Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro

515 520 525

Glu Val Thr Cys Val Val Val Asp Val Lys His Glu Asp Pro Glu Val

530 535 540

Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr

545 550 555 560

Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val

565 570 575

Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys

580 585 590

Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser

595 600 605

Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro
610 615 620

Ser Arg Glu Gln Met Thr Lys Asn Gln Val Lys Leu Thr Cys Leu Val
625 630 635 640

Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly
645 650 655

Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp
660 665 670

Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp
675 680 685

Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His
690 695 700

Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
705 710 715

<210> 167
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<223> /注=“人工序列说明:合成多肽”
<400> 167

Asp Ile Val Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asn Val Asp Thr Asn
20 25 30

Val Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ser Pro Lys Ala Leu Ile
35 40 45

Tyr Ser Ala Ser Tyr Arg Tyr Ser Gly Val Pro Asp Arg Phe Thr Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Phe Cys Gln Gln Tyr Asp Ser Tyr Pro Leu
85 90 95

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

Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly
115 120 125

Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala
130 135 140

Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln

145 150 155 160
Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser
165 170 175
Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr
180 185 190
Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser
195 200 205
Phe Asn Arg Gly Glu Cys
210

<210> 168
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<223> /注="人工序列说明:合成多肽"
<400> 168
Glu Pro Lys Ser Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala
1 5 10 15
Pro Pro Val Ala Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys
20 25 30
Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val
35 40 45
Asp Val Lys His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp
50 55 60
Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Glu Tyr
65 70 75 80
Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp
85 90 95
Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu
100 105 110
Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg
115 120 125
Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys
130 135 140
Asn Gln Val Ser Leu Thr Cys Asp Val Ser Gly Phe Tyr Pro Ser Asp
145 150 155 160
Ile Ala Val Glu Trp Glu Ser Asp Gly Gln Pro Glu Asn Asn Tyr Lys
165 170 175
Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser
180 185 190
Lys Leu Thr Val Asp Lys Ser Arg Trp Glu Gln Gly Asp Val Phe Ser

195 200 205
Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser
210 215 220
Leu Ser Leu Ser Pro Gly Lys
225 230
<210> 169
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<223> /注="人工序列说明:合成多肽"
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Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Asp Phe Ser Arg Ser
20 25 30
Trp Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45
Ser Glu Ile Asn Pro Asp Ser Ser Thr Ile Asn Tyr Ala Thr Ser Val
50 55 60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95
Ala Arg Tyr Gly Asn Trp Phe Pro Tyr Trp Gly Gln Gly Thr Leu Val
100 105 110
Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala
115 120 125
Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu
130 135 140
Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly
145 150 155 160
Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser
165 170 175
Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu
180 185 190
Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr
195 200 205
Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Gly Gly Gly Gly Ser
210 215 220
Gly Gly Gly Gly Ser Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu

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

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

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<223> /注=“人工序列说明:合成多肽”
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Asp Ile Val Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asn Val Asp Thr Asn
20 25 30
Val Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ser Pro Lys Ala Leu Ile
35 40 45
Tyr Ser Ala Ser Tyr Arg Tyr Ser Gly Val Pro Asp Arg Phe Thr Gly
50 55 60
Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80
Glu Asp Phe Ala Thr Tyr Phe Cys Gln Gln Tyr Asp Ser Tyr Pro Leu
85 90 95
Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Arg Thr Val Ala Ala
100 105 110
Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly

115 120 125

Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala
130 135 140

Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln
145 150 155 160

Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser
165 170 175

Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr
180 185 190

Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser
195 200 205

Phe Asn Arg Gly Glu Cys
210

<210> 171

<211> 589

<212> PRT

<213> 人工序列

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<221> 来源

<223> /注="人工序列说明:合成多肽"

<400> 171

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Asp Phe Ser Arg Ser
20 25 30

Trp Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Glu Ile Asn Pro Asp Ser Ser Thr Ile Asn Tyr Ala Thr Ser Val
50 55 60

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

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Tyr Gly Asn Trp Phe Pro Tyr Trp Gly Gln Gly Thr Leu Val
100 105 110

Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala
115 120 125

Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu
130 135 140

Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly
145 150 155 160

Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser

165 170 175

Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu

180 185 190

Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asp Thr

195 200 205

Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Gly Gly Gly Gly Ser

210 215 220

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

225 230 235 240

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

245 250 255

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

260 265 270

Gly Leu Glu Trp Val Gly Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala

275 280 285

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

290 295 300

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

305 310 315 320

Asp Thr Ala Val Tyr Tyr Cys Val Arg His Gly Asn Phe Gly Asp Ser

325 330 335

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

340 345 350

Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Lys Thr His Thr

355 360 365

Cys Pro Pro Cys Pro Ala Pro Pro Val Ala Gly Pro Ser Val Phe Leu

370 375 380

Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu

385 390 395 400

Val Thr Cys Val Val Val Asp Val Lys His Glu Asp Pro Glu Val Lys

405 410 415

Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys

420 425 430

Pro Arg Glu Glu Glu Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu

435 440 445

Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys

450 455 460

Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys

465 470 475 480

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

485 490 495

Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Asp Val Ser

500 505 510

Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asp Gly Gln
515 520 525

Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly
530 535 540

Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Glu
545 550 555 560

Gln Gly Asp Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
565 570 575

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
580 585

<210> 172

<211> 573

<212> PRT

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<221> 来源

<223> /注="人工序列说明:合成多肽"

<400> 172

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Asp Phe Ser Arg Ser
20 25 30

Trp Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Glu Ile Asn Pro Asp Ser Ser Thr Ile Asn Tyr Ala Thr Ser Val
50 55 60

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

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Tyr Gly Asn Trp Phe Pro Tyr Trp Gly Gln Gly Thr Leu Val
100 105 110

Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala
115 120 125

Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu
130 135 140

Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly
145 150 155 160

Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser
165 170 175

Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu

180 185 190

Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr

195 200 205

Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Gly Gly Gly Gly Ser

210 215 220

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

225 230 235 240

Val Ser Pro Gly Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly

245 250 255

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

260 265 270

Lys Ser Pro Arg Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly

275 280 285

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

290 295 300

Thr Ile Ser Gly Ala Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala

305 310 315 320

Leu Trp Tyr Ser Asn His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr

325 330 335

Val Leu Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Lys Thr His Thr

340 345 350

Cys Pro Pro Cys Pro Ala Pro Pro Val Ala Gly Pro Ser Val Phe Leu

355 360 365

Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu

370 375 380

Val Thr Cys Val Val Val Asp Val Lys His Glu Asp Pro Glu Val Lys

385 390 395 400

Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys

405 410 415

Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu

420 425 430

Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys

435 440 445

Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys

450 455 460

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

465 470 475 480

Arg Glu Gln Met Thr Lys Asn Gln Val Lys Leu Thr Cys Leu Val Lys

485 490 495

Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln

500 505 510

Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly

515 520 525

Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln
530 535 540

Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
545 550 555 560

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
565 570

<210> 173
<211> 214
<212> PRT
<213> 人工序列
<220>
<221> 来源
<223> /注="人工序列说明:合成多肽"
<400> 173

Asp Ile Val Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asn Val Asp Thr Asn
20 25 30

Val Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ser Pro Lys Ala Leu Ile
35 40 45

Tyr Ser Ala Ser Tyr Arg Tyr Ser Gly Val Pro Asp Arg Phe Thr Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Phe Cys Gln Gln Tyr Asp Ser Tyr Pro Leu
85 90 95

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

Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly
115 120 125

Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala
130 135 140

Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln
145 150 155 160

Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser
165 170 175

Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr
180 185 190

Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser
195 200 205

Phe Asn Arg Gly Glu Cys

210

<210> 174
<211> 231
<212> PRT
<213> 人工序列
<220>
<221> 来源
<223> /注=“人工序列说明:合成多肽”
<400> 174

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

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

290 295 300

Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys
305 310 315 320

Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys
325 330 335

Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser
340 345 350

Arg Glu Gln Met Thr Lys Asn Gln Val Lys Leu Thr Cys Leu Val Lys
355 360 365

Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln
370 375 380

Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly
385 390 395 400

Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln
405 410 415

Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
420 425 430

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys Gly Gly Gly
435 440 445

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Val Gln Leu
450 455 460

Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Leu Arg Leu
465 470 475 480

Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Thr Tyr Ala Met Ser Trp
485 490 495

Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Gly Arg Ile Arg
500 505 510

Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp Ser Val Lys Gly
515 520 525

Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr Leu Tyr Leu Gln
530 535 540

Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Val Arg
545 550 555 560

His Gly Asn Phe Gly Asp Ser Tyr Val Ser Trp Phe Ala Tyr Trp Gly
565 570 575

Gln Gly Thr Leu Val Thr Val Ser Ser Gly Lys Pro Gly Ser Gly Lys
580 585 590

Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gln Ala Val
595 600 605

Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly Gly Thr Val Thr
610 615 620

Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr Ser Asn Tyr Ala

625 630 635 640
Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg Gly Leu Ile Gly
645 650 655
Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg Phe Ser Gly Ser
660 665 670
Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly Ala Gln Pro Glu
675 680 685
Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser Asn His Trp Val
690 695 700
Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
705 710

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<212> PRT
<213> 人工序列
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<400> 176
Asp Ile Val Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asn Val Asp Thr Asn
20 25 30
Val Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ser Pro Lys Ala Leu Ile
35 40 45
Tyr Ser Ala Ser Tyr Arg Tyr Ser Gly Val Pro Asp Arg Phe Thr Gly
50 55 60
Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80
Glu Asp Phe Ala Thr Tyr Phe Cys Gln Gln Tyr Asp Ser Tyr Pro Leu
85 90 95
Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Arg Thr Val Ala Ala
100 105 110
Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly
115 120 125
Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala
130 135 140
Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln
145 150 155 160
Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser
165 170 175
Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr

180 185 190
Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser
195 200 205
Phe Asn Arg Gly Glu Cys
210
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<400> 177
Glu Pro Lys Ser Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala
1 5 10 15
Pro Pro Val Ala Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys
20 25 30
Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val
35 40 45
Asp Val Lys His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp
50 55 60
Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Glu Tyr
65 70 75 80
Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp
85 90 95
Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu
100 105 110
Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg
115 120 125
Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys
130 135 140
Asn Gln Val Ser Leu Thr Cys Asp Val Ser Gly Phe Tyr Pro Ser Asp
145 150 155 160
Ile Ala Val Glu Trp Glu Ser Asp Gly Gln Pro Glu Asn Asn Tyr Lys
165 170 175
Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser
180 185 190
Lys Leu Thr Val Asp Lys Ser Arg Trp Glu Gln Gly Asp Val Phe Ser
195 200 205
Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser
210 215 220
Leu Ser Leu Ser Pro Gly Lys

225 230

<210> 178

<211> 714

<212> PRT

<213> 人工序列

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<221> 来源

<223> /注=“人工序列说明:合成多肽”

<400> 178

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

260 265 270

Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys

275 280 285

Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu

290 295 300

Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys

305 310 315 320

Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys

325 330 335

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

340 345 350

Arg Glu Gln Met Thr Lys Asn Gln Val Lys Leu Thr Cys Leu Val Lys

355 360 365

Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln

370 375 380

Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly

385 390 395 400

Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln

405 410 415

Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn

420 425 430

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys Gly Gly Gly

435 440 445

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

450 455 460

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

465 470 475 480

Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Thr Tyr Ala Met Asn Trp

485 490 495

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

500 505 510

Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp Ser Val Lys Gly

515 520 525

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

530 535 540

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

545 550 555 560

His Gly Asn Phe Gly Asp Ser Tyr Val Ser Trp Phe Asp Tyr Trp Gly

565 570 575

Gln Gly Thr Leu Val Thr Val Ser Ser Gly Lys Pro Gly Ser Gly Lys

580 585 590

Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gln Ala Val

595 600 605

Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly Gly Thr Val Thr
610 615 620

Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr Ser Asn Tyr Ala
625 630 635 640

Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg Gly Leu Ile Gly
645 650 655

Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg Phe Ser Gly Ser
660 665 670

Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly Ala Gln Pro Glu
675 680 685

Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser Asn His Trp Val
690 695 700

Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
705 710

<210> 179
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<212> PRT
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<221> 来源
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<400> 179

Asp Ile Val Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asn Val Asp Thr Asn
20 25 30

Val Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ser Pro Lys Ala Leu Ile
35 40 45

Tyr Ser Ala Ser Tyr Arg Tyr Ser Gly Val Pro Asp Arg Phe Thr Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Phe Cys Gln Gln Tyr Asp Ser Tyr Pro Leu
85 90 95

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

Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly
115 120 125

Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala
130 135 140

Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln

145 150 155 160
Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser
165 170 175
Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr
180 185 190
Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser
195 200 205
Phe Asn Arg Gly Glu Cys
210

<210> 180
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<400> 180
Glu Pro Lys Ser Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala
1 5 10 15
Pro Pro Val Ala Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys
20 25 30
Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val
35 40 45
Asp Val Lys His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp
50 55 60
Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Glu Tyr
65 70 75 80
Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp
85 90 95
Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu
100 105 110
Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg
115 120 125
Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys
130 135 140
Asn Gln Val Ser Leu Thr Cys Asp Val Ser Gly Phe Tyr Pro Ser Asp
145 150 155 160
Ile Ala Val Glu Trp Glu Ser Asp Gly Gln Pro Glu Asn Asn Tyr Lys
165 170 175
Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser
180 185 190
Lys Leu Thr Val Asp Lys Ser Arg Trp Glu Gln Gly Asp Val Phe Ser

195 200 205
Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser
210 215 220
Leu Ser Leu Ser Pro Gly Lys
225 230
<210> 181
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<212> PRT
<213> 人工序列
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<221> 来源
<223> /注="人工序列说明:合成多肽"
<400> 181
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Asp Phe Ser Arg Ser
20 25 30
Trp Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45
Ser Glu Ile Asn Pro Asp Ser Ser Thr Ile Asn Tyr Ala Thr Ser Val
50 55 60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95
Ala Arg Tyr Gly Asn Trp Phe Pro Tyr Trp Gly Gln Gly Thr Leu Val
100 105 110
Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala
115 120 125
Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu
130 135 140
Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly
145 150 155 160
Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser
165 170 175
Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu
180 185 190
Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr
195 200 205
Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr
210 215 220
Cys Pro Pro Cys Pro Ala Pro Pro Val Ala Gly Pro Ser Val Phe Leu

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

565 570 575
Gln Gly Thr Leu Val Thr Val Ser Ser Gly Lys Pro Gly Ser Gly Lys
580 585 590
Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gln Ala Val
595 600 605
Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly Gly Thr Val Thr
610 615 620
Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr Ser Asn Tyr Ala
625 630 635 640
Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg Gly Leu Ile Gly
645 650 655
Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg Phe Ser Gly Ser
660 665 670
Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly Ala Gln Pro Glu
675 680 685
Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser Asn His Trp Val
690 695 700
Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
705 710

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

115 120 125

Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala
130 135 140

Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln
145 150 155 160

Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser
165 170 175

Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr
180 185 190

Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser
195 200 205

Phe Asn Arg Gly Glu Cys
210

<210> 183

<211> 231

<212> PRT

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<221> 来源

<223> /注=“人工序列说明:合成多肽”

<400> 183

Glu Pro Lys Ser Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala
1 5 10 15

Pro Pro Val Ala Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys
20 25 30

Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val
35 40 45

Asp Val Lys His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp
50 55 60

Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Glu Tyr
65 70 75 80

Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp
85 90 95

Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu
100 105 110

Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg
115 120 125

Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys
130 135 140

Asn Gln Val Ser Leu Thr Cys Asp Val Ser Gly Phe Tyr Pro Ser Asp
145 150 155 160

Ile Ala Val Glu Trp Glu Ser Asp Gly Gln Pro Glu Asn Asn Tyr Lys

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

<210> 184
<211> 718
<212> PRT
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<220>
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<223> /注="人工序列说明:合成多肽"
<400> 184
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Asp Phe Ser Arg Ser
20 25 30
Trp Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45
Ser Glu Ile Asn Pro Asp Ser Ser Thr Ile Asn Tyr Ala Thr Ser Val
50 55 60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95
Ala Arg Tyr Gly Asn Trp Phe Pro Tyr Trp Gly Gln Gly Thr Leu Val
100 105 110
Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala
115 120 125
Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu
130 135 140
Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly
145 150 155 160
Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser
165 170 175
Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu
180 185 190
Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr

195 200 205

Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Gly Gly Gly Gly Ser
210 215 220

Gly Gly Gly Gly Ser Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu
225 230 235 240

Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe
245 250 255

Thr Phe Ser Thr Tyr Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys
260 265 270

Gly Leu Glu Trp Val Gly Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala
275 280 285

Thr Tyr Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp
290 295 300

Asp Ser Lys Asn Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu
305 310 315 320

Asp Thr Ala Val Tyr Tyr Cys Val Arg His Gly Asn Phe Gly Asp Ser
325 330 335

Tyr Val Ser Trp Phe Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val
340 345 350

Ser Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly
355 360 365

Ser Gly Lys Pro Gly Ser Gln Ala Val Val Thr Gln Glu Pro Ser Leu
370 375 380

Thr Val Ser Pro Gly Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr
385 390 395 400

Gly Ala Val Thr Thr Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro
405 410 415

Gly Lys Ser Pro Arg Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro
420 425 430

Gly Val Pro Ala Arg Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala
435 440 445

Leu Thr Ile Ser Gly Ala Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys
450 455 460

Ala Leu Trp Tyr Ser Asn His Trp Val Phe Gly Gly Gly Thr Lys Leu
465 470 475 480

Thr Val Leu Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Lys Thr His
485 490 495

Thr Cys Pro Pro Cys Pro Ala Pro Pro Val Ala Gly Pro Ser Val Phe
500 505 510

Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro
515 520 525

Glu Val Thr Cys Val Val Val Asp Val Lys His Glu Asp Pro Glu Val

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

<210> 185
<211> 214
<212> PRT
<213> 人工序列
<220>
<221> 来源
<223> /注="人工序列说明:合成多肽"
<400> 185
Asp Ile Val Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asn Val Asp Thr Asn
20 25 30
Val Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ser Pro Lys Ala Leu Ile
35 40 45
Tyr Ser Ala Ser Tyr Arg Tyr Ser Gly Val Pro Asp Arg Phe Thr Gly
50 55 60
Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80
Glu Asp Phe Ala Thr Tyr Phe Cys Gln Gln Tyr Asp Ser Tyr Pro Leu

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

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

130 135 140

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

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

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

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

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

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

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

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

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

130 135 140

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

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

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<223> /注=“人工序列说明:合成多肽”
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Asp Ile Val Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asn Val Asp Thr Asn

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

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

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

405 410 415
Gln Gly Asp Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
420 425 430
His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
435 440 445

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

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

565 570 575
Gln Gly Thr Leu Val Thr Val Ser Ser Gly Lys Pro Gly Ser Gly Lys
580 585 590
Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gln Ala Val
595 600 605
Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly Gly Thr Val Thr
610 615 620
Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr Ser Asn Tyr Ala
625 630 635 640
Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg Gly Leu Ile Gly
645 650 655
Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg Phe Ser Gly Ser
660 665 670
Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly Ala Gln Pro Glu
675 680 685
Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser Asn His Trp Val
690 695 700
Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
705 710

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<223> /注="人工序列说明:合成多肽"
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Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asn Val Asp Thr Asn
20 25 30
Val Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ser Pro Lys Ala Leu Ile
35 40 45
Tyr Ser Ala Ser Tyr Arg Tyr Ser Gly Val Pro Asp Arg Phe Thr Gly
50 55 60
Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80
Glu Asp Phe Ala Thr Tyr Phe Cys Gln Gln Tyr Asp Ser Tyr Pro Leu
85 90 95
Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Arg Thr Val Ala Ala
100 105 110
Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly

115 120 125

Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala
130 135 140

Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln
145 150 155 160

Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser
165 170 175

Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr
180 185 190

Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser
195 200 205

Phe Asn Arg Gly Glu Cys
210

<210> 195

<211> 445

<212> PRT

<213> 人工序列

<220>

<221> 来源

<223> /注=“人工序列说明:合成多肽”

<400> 195

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Asp Phe Ser Arg Ser
20 25 30

Trp Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Glu Ile Asn Pro Asp Ser Ser Thr Ile Asn Tyr Ala Thr Ser Val
50 55 60

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

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Tyr Gly Asn Trp Phe Pro Tyr Trp Gly Gln Gly Thr Leu Val
100 105 110

Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala
115 120 125

Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu
130 135 140

Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly
145 150 155 160

Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser

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

<210> 196
<211> 714
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<213> 人工序列
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<221> 来源
<223> /注=“人工序列说明:合成多肽”

<400> 196

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

325 330 335
Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser
340 345 350
Arg Glu Gln Met Thr Lys Asn Gln Val Lys Leu Thr Cys Leu Val Lys
355 360 365
Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln
370 375 380
Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly
385 390 395 400
Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln
405 410 415
Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
420 425 430
His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys Gly Gly Gly
435 440 445
Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Val Gln Leu
450 455 460
Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Leu Arg Leu
465 470 475 480
Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Thr Tyr Ala Met Asn Trp
485 490 495
Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Gly Arg Ile Arg
500 505 510
Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp Ser Val Lys Gly
515 520 525
Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr Leu Tyr Leu Gln
530 535 540
Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Val Arg
545 550 555 560
His Gly Asn Phe Gly Asp Ser Tyr Val Ser Trp Phe Asp Tyr Trp Gly
565 570 575
Gln Gly Thr Leu Val Thr Val Ser Ser Gly Lys Pro Gly Ser Gly Lys
580 585 590
Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gln Ala Val
595 600 605
Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly Gly Thr Val Thr
610 615 620
Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr Ser Asn Tyr Ala
625 630 635 640
Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg Gly Leu Ile Gly
645 650 655
Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg Phe Ser Gly Ser

660 665 670
Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly Ala Gln Pro Glu
675 680 685
Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser Asn His Trp Val
690 695 700
Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
705 710

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<211> 214
<212> PRT
<213> 人工序列
<220>
<221> 来源
<223> /注="人工序列说明:合成多肽"
<400> 197
Asp Ile Val Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asn Val Asp Thr Asn
20 25 30
Val Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ser Pro Lys Ala Leu Ile
35 40 45
Tyr Ser Ala Ser Tyr Arg Tyr Ser Gly Val Pro Asp Arg Phe Thr Gly
50 55 60
Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80
Glu Asp Phe Ala Thr Tyr Phe Cys Gln Gln Tyr Asp Ser Tyr Pro Leu
85 90 95
Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Arg Thr Val Ala Ala
100 105 110
Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly
115 120 125
Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala
130 135 140
Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln
145 150 155 160
Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser
165 170 175
Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr
180 185 190
Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser
195 200 205
Phe Asn Arg Gly Glu Cys

210

<210> 198

<211> 445

<212> PRT

<213> 人工序列

<220>

<221> 来源

<223> /注=“人工序列说明:合成多肽”

<400> 198

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

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

<210> 199
<211> 714
<212> PRT
<213> 人工序列
<220>
<221> 来源
<223> /注=“人工序列说明:合成多肽”
<400> 199
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Asp Phe Ser Arg Ser
20 25 30
Trp Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45
Ser Glu Ile Asn Pro Asp Ser Ser Thr Ile Asn Tyr Ala Thr Ser Val
50 55 60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys

85 90 95

Ala Arg Tyr Gly Asn Trp Phe Pro Tyr Trp Gly Gln Gly Thr Leu Val
100 105 110

Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala
115 120 125

Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu
130 135 140

Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly
145 150 155 160

Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser
165 170 175

Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu
180 185 190

Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr
195 200 205

Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr
210 215 220

Cys Pro Pro Cys Pro Ala Pro Pro Val Ala Gly Pro Ser Val Phe Leu
225 230 235 240

Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu
245 250 255

Val Thr Cys Val Val Val Asp Val Lys His Glu Asp Pro Glu Val Lys
260 265 270

Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys
275 280 285

Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu
290 295 300

Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys
305 310 315 320

Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys
325 330 335

Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser
340 345 350

Arg Glu Gln Met Thr Lys Asn Gln Val Lys Leu Thr Cys Leu Val Lys
355 360 365

Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln
370 375 380

Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly
385 390 395 400

Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln
405 410 415

Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn

420 425 430

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys Gly Gly Gly

435 440 445

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

450 455 460

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

465 470 475 480

Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Thr Tyr Ala Met Asn Trp

485 490 495

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

500 505 510

Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp Ser Val Lys Gly

515 520 525

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

530 535 540

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

545 550 555 560

His Gly Asn Phe Gly Asp Ser Tyr Val Ser Trp Phe Ala Tyr Trp Gly

565 570 575

Gln Gly Thr Leu Val Thr Val Ser Ser Gly Lys Pro Gly Ser Gly Lys

580 585 590

Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gln Ala Val

595 600 605

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

610 615 620

Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr Ser Asn Tyr Ala

625 630 635 640

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

645 650 655

Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg Phe Ser Gly Ser

660 665 670

Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly Ala Gln Pro Glu

675 680 685

Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser Asn His Trp Val

690 695 700

Phe Gly Gly Gly Thr Lys Leu Thr Val Leu

705 710

<210> 200

<211> 214

<212> PRT

<213> 人工序列

<220>

<221> 来源
<223> /注=“人工序列说明:合成多肽”
<400> 200

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

<210> 201
<211> 445
<212> PRT
<213> 人工序列
<220>
<221> 来源
<223> /注=“人工序列说明:合成多肽”
<400> 201

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Asp Phe Ser Arg Ser

20 25 30

Trp Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Glu Ile Asn Pro Asp Ser Ser Thr Ile Asn Tyr Ala Thr Ser Val
50 55 60

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

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Tyr Gly Asn Trp Phe Pro Tyr Trp Gly Gln Gly Thr Leu Val
100 105 110

Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala
115 120 125

Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu
130 135 140

Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly
145 150 155 160

Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser
165 170 175

Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu
180 185 190

Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asp Thr
195 200 205

Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr
210 215 220

Cys Pro Pro Cys Pro Ala Pro Pro Val Ala Gly Pro Ser Val Phe Leu
225 230 235 240

Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu
245 250 255

Val Thr Cys Val Val Val Asp Val Lys His Glu Asp Pro Glu Val Lys
260 265 270

Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys
275 280 285

Pro Arg Glu Glu Glu Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu
290 295 300

Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys
305 310 315 320

Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys
325 330 335

Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser
340 345 350

Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Asp Val Ser

355 360 365

Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asp Gly Gln
370 375 380

Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly
385 390 395 400

Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Glu
405 410 415

Gln Gly Asp Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
420 425 430

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
435 440 445

<210> 202
<211> 718
<212> PRT
<213> 人工序列
<220>
<221> 来源
<223> /注="人工序列说明:合成多肽"
<400> 202

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Asp Phe Ser Arg Ser
20 25 30

Trp Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Glu Ile Asn Pro Asp Ser Ser Thr Ile Asn Tyr Ala Thr Ser Val
50 55 60

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

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Tyr Gly Asn Trp Phe Pro Tyr Trp Gly Gln Gly Thr Leu Val
100 105 110

Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala
115 120 125

Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu
130 135 140

Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly
145 150 155 160

Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser
165 170 175

Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu

180 185 190

Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr

195 200 205

Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Gly Gly Gly Gly Ser

210 215 220

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

225 230 235 240

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

245 250 255

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

260 265 270

Gly Leu Glu Trp Val Gly Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala

275 280 285

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

290 295 300

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

305 310 315 320

Asp Thr Ala Val Tyr Tyr Cys Val Arg His Gly Asn Phe Gly Asp Ser

325 330 335

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

340 345 350

Ser Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly

355 360 365

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

370 375 380

Thr Val Ser Pro Gly Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr

385 390 395 400

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

405 410 415

Gly Lys Ser Pro Arg Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro

420 425 430

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

435 440 445

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

450 455 460

Ala Leu Trp Tyr Ser Asn His Trp Val Phe Gly Gly Gly Thr Lys Leu

465 470 475 480

Thr Val Leu Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Lys Thr His

485 490 495

Thr Cys Pro Pro Cys Pro Ala Pro Pro Val Ala Gly Pro Ser Val Phe

500 505 510

Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro

515 520 525

Glu Val Thr Cys Val Val Val Asp Val Lys His Glu Asp Pro Glu Val
530 535 540

Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr
545 550 555 560

Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val
565 570 575

Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys
580 585 590

Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser
595 600 605

Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro
610 615 620

Ser Arg Glu Gln Met Thr Lys Asn Gln Val Lys Leu Thr Cys Leu Val
625 630 635 640

Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly
645 650 655

Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp
660 665 670

Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp
675 680 685

Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His
690 695 700

Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
705 710 715

<210> 203
<211> 214
<212> PRT
<213> 人工序列
<220>
<221> 来源
<223> /注=“人工序列说明:合成多肽”
<400> 203

Asp Ile Val Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asn Val Asp Thr Asn
20 25 30

Val Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ser Pro Lys Ala Leu Ile
35 40 45

Tyr Ser Ala Ser Tyr Arg Tyr Ser Gly Val Pro Asp Arg Phe Thr Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro

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

<210> 204
<211> 445
<212> PRT
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<220>
<221> 来源
<223> /注=“人工序列说明:合成多肽”
<400> 204
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Asp Phe Ser Arg Ser
20 25 30
Trp Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45
Ser Glu Ile Asn Pro Asp Ser Ser Thr Ile Asn Tyr Ala Thr Ser Val
50 55 60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95
Ala Arg Tyr Gly Asn Trp Phe Pro Tyr Trp Gly Gln Gly Thr Leu Val
100 105 110
Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala

115 120 125

Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu
130 135 140

Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly
145 150 155 160

Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser
165 170 175

Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu
180 185 190

Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asp Thr
195 200 205

Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr
210 215 220

Cys Pro Pro Cys Pro Ala Pro Pro Val Ala Gly Pro Ser Val Phe Leu
225 230 235 240

Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu
245 250 255

Val Thr Cys Val Val Val Asp Val Lys His Glu Asp Pro Glu Val Lys
260 265 270

Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys
275 280 285

Pro Arg Glu Glu Glu Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu
290 295 300

Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys
305 310 315 320

Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys
325 330 335

Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser
340 345 350

Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Asp Val Ser
355 360 365

Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asp Gly Gln
370 375 380

Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly
385 390 395 400

Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Glu
405 410 415

Gln Gly Asp Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
420 425 430

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
435 440 445

<210> 205

<211> 718
<212> PRT
<213> 人工序列
<220>
<221> 来源
<223> /注="人工序列说明:合成多肽"
<400> 205

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

275 280 285

Thr Tyr Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp
290 295 300

Asp Ser Lys Asn Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu
305 310 315 320

Asp Thr Ala Val Tyr Tyr Cys Val Arg His Gly Asn Phe Gly Asp Ser
325 330 335

Tyr Val Ser Trp Phe Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val
340 345 350

Ser Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly
355 360 365

Ser Gly Lys Pro Gly Ser Gln Ala Val Val Thr Gln Glu Pro Ser Leu
370 375 380

Thr Val Ser Pro Gly Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr
385 390 395 400

Gly Ala Val Thr Thr Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro
405 410 415

Gly Lys Ser Pro Arg Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro
420 425 430

Gly Val Pro Ala Arg Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala
435 440 445

Leu Thr Ile Ser Gly Ala Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys
450 455 460

Ala Leu Trp Tyr Ser Asn His Trp Val Phe Gly Gly Gly Thr Lys Leu
465 470 475 480

Thr Val Leu Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Lys Thr His
485 490 495

Thr Cys Pro Pro Cys Pro Ala Pro Pro Val Ala Gly Pro Ser Val Phe
500 505 510

Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro
515 520 525

Glu Val Thr Cys Val Val Val Asp Val Lys His Glu Asp Pro Glu Val
530 535 540

Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr
545 550 555 560

Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val
565 570 575

Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys
580 585 590

Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser
595 600 605

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

610 615 620
Ser Arg Glu Gln Met Thr Lys Asn Gln Val Lys Leu Thr Cys Leu Val
625 630 635 640
Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly
645 650 655
Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp
660 665 670
Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp
675 680 685
Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His
690 695 700
Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
705 710 715

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

165 170 175
Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr
180 185 190
Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser
195 200 205
Phe Asn Arg Gly Glu Cys
210

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<400> 207
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1 5 10 15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Asp Phe Ser Arg Ser
20 25 30
Trp Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45
Ser Glu Ile Asn Pro Asp Ser Ser Thr Ile Asn Tyr Ala Thr Ser Val
50 55 60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95
Ala Arg Tyr Gly Asn Trp Phe Pro Tyr Trp Gly Gln Gly Thr Leu Val
100 105 110
Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala
115 120 125
Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu
130 135 140
Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly
145 150 155 160
Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser
165 170 175
Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu
180 185 190
Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asp Thr
195 200 205
Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr

210 215 220

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

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

35 40 45

Ser Glu Ile Asn Pro Asp Ser Ser Thr Ile Asn Tyr Ala Thr Ser Val
50 55 60

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

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Tyr Gly Asn Trp Phe Pro Tyr Trp Gly Gln Gly Thr Leu Val
100 105 110

Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala
115 120 125

Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu
130 135 140

Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly
145 150 155 160

Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser
165 170 175

Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu
180 185 190

Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr
195 200 205

Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Gly Gly Gly Gly Ser
210 215 220

Gly Gly Gly Gly Ser Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu
225 230 235 240

Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe
245 250 255

Thr Phe Ser Thr Tyr Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys
260 265 270

Gly Leu Glu Trp Val Gly Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala
275 280 285

Thr Tyr Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp
290 295 300

Asp Ser Lys Asn Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu
305 310 315 320

Asp Thr Ala Val Tyr Tyr Cys Val Arg His Gly Asn Phe Gly Asp Ser
325 330 335

Tyr Val Ser Trp Phe Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val
340 345 350

Ser Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly
355 360 365

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

370 375 380
Thr Val Ser Pro Gly Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr
385 390 395 400
Gly Ala Val Thr Thr Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro
405 410 415
Gly Lys Ser Pro Arg Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro
420 425 430
Gly Val Pro Ala Arg Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala
435 440 445
Leu Thr Ile Ser Gly Ala Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys
450 455 460
Ala Leu Trp Tyr Ser Asn His Trp Val Phe Gly Gly Gly Thr Lys Leu
465 470 475 480
Thr Val Leu Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Lys Thr His
485 490 495
Thr Cys Pro Pro Cys Pro Ala Pro Pro Val Ala Gly Pro Ser Val Phe
500 505 510
Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro
515 520 525
Glu Val Thr Cys Val Val Val Asp Val Lys His Glu Asp Pro Glu Val
530 535 540
Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr
545 550 555 560
Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val
565 570 575
Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys
580 585 590
Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser
595 600 605
Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro
610 615 620
Ser Arg Glu Gln Met Thr Lys Asn Gln Val Lys Leu Thr Cys Leu Val
625 630 635 640
Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly
645 650 655
Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp
660 665 670
Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp
675 680 685
Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His
690 695 700
Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys

705 710 715

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<223> /注="人工序列说明:合成多肽"
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Asp Ile Val Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asn Val Asp Thr Asn
20 25 30
Val Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ser Pro Lys Ala Leu Ile
35 40 45
Tyr Ser Ala Ser Tyr Arg Tyr Ser Gly Val Pro Asp Arg Phe Thr Gly
50 55 60
Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80
Glu Asp Phe Ala Thr Tyr Phe Cys Gln Gln Tyr Asp Ser Tyr Pro Leu
85 90 95
Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Arg Thr Val Ala Ala
100 105 110
Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly
115 120 125
Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala
130 135 140
Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln
145 150 155 160
Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser
165 170 175
Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr
180 185 190
Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser
195 200 205
Phe Asn Arg Gly Glu Cys
210

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Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                  10                  15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Thr Tyr
            20                  25                  30
Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45
Gly Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
    50                  55                  60
Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
65                  70                  75                  80
Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr
                85                  90                  95
Tyr Cys Val Arg His Gly Asn Phe Gly Asp Ser Tyr Val Ser Trp Phe
            100                 105                 110
Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Lys Pro
        115                 120                 125
Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly
    130                 135                 140
Ser Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly
145                 150                 155                 160
Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr
                165                 170                 175
Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg
            180                 185                 190
Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg
        195                 200                 205
Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly
    210                 215                 220
Ala Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser
225                 230                 235                 240
Asn His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly Ser
                245                 250                 255
His His His His His His
            260
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<210> 211
<211> 254
<212> PRT
<213> 人工序列
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<221> 来源
<223> /注=“人工序列说明:合成多肽”
<400> 211

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Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                  10                  15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Thr Tyr
            20                  25                  30
Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45
Gly Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
    50                  55                  60
Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
65                  70                  75                  80
Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr
                85                  90                  95
Tyr Cys Val Arg His Gly Asn Phe Gly Asp Ser Tyr Val Ser Trp Phe
            100                 105                 110
Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Lys Pro
        115                 120                 125
Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly
    130                 135                 140
Ser Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly
145                 150                 155                 160
Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr
                165                 170                 175
Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg
            180                 185                 190
Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg
        195                 200                 205
Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly
    210                 215                 220
Ala Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser
225                 230                 235                 240
Asn His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
                245                 250
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<400> 212

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

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<400> 213

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

<210> 214
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Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                  10                  15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Thr Tyr
            20                  25                  30
Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45
Gly Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
    50                  55                  60
Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
65                  70                  75                  80
Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr
                85                  90                  95
Tyr Cys Val Arg His Gly Asn Phe Gly Asp Ser Tyr Val Ser Trp Phe
            100                 105                 110
Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Lys Pro
        115                 120                 125
Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly
    130                 135                 140
Ser Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly
145                 150                 155                 160
Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr
                165                 170                 175
Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg
            180                 185                 190
Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg
        195                 200                 205
Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly
    210                 215                 220
Ala Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser
225                 230                 235                 240
Asn His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly Ser
                245                 250                 255
His His His His His His
            260
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<210> 215
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<223> /注="人工序列说明:合成多肽"
<400> 215

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

<210> 216
<211> 125
<212> PRT
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<221> 来源
<223> /注=“人工序列说明:合成多肽”
<400> 216

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

<210> 217
<211> 109
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<221> 来源
<223> /注=“人工序列说明:合成多肽”
<400> 217

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

<210> 218

<211> 262
<212> PRT
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<400> 218

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

<210> 219

<211> 254
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<221> 来源
<223> /注="人工序列说明:合成多肽"
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Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Thr Tyr
20 25 30
Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45
Gly Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
50 55 60
Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
65 70 75 80
Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr
85 90 95
Tyr Cys Val Arg His Gly Asn Phe Gly Asp Ser Tyr Val Ser Trp Phe
100 105 110
Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Lys Pro
115 120 125
Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly
130 135 140
Ser Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly
145 150 155 160
Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr
165 170 175
Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg
180 185 190
Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg
195 200 205
Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly
210 215 220
Ala Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser
225 230 235 240
Asn His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
245 250

<210> 220
<211> 125
<212> PRT

<213> 人工序列
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<221> 来源
<223> /注="人工序列说明:合成多肽"
<400> 220

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

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<400> 221

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

100 105

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

260

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<400> 223

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

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

<210> 225
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<400> 225

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

85 90 95

His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
100 105

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<400> 226

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

245 250 255

His His His His His His
260

<210> 227
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<400> 227

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

245 250

<210> 228
<211> 125
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<400> 228

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

<210> 229
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<400> 229

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

65 70 75 80
Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser Asn
85 90 95
His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
100 105

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<223> /注="人工序列说明:合成多肽"
<400> 230
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Thr Tyr
20 25 30
Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45
Gly Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
50 55 60
Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
65 70 75 80
Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr
85 90 95
Tyr Cys Val Arg His Gly Asn Phe Gly Pro Ser Tyr Val Ser Trp Phe
100 105 110
Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Lys Pro
115 120 125
Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly
130 135 140
Ser Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly
145 150 155 160
Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr
165 170 175
Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg
180 185 190
Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg
195 200 205
Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly
210 215 220
Ala Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser

225 230 235 240
Asn His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly Ser
245 250 255
His His His His His His
260

<210> 231
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<213> 人工序列
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<223> /注="人工序列说明:合成多肽"
<400> 231
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Thr Tyr
20 25 30
Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45
Gly Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
50 55 60
Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
65 70 75 80
Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr
85 90 95
Tyr Cys Val Arg His Gly Asn Phe Gly Pro Ser Tyr Val Ser Trp Phe
100 105 110
Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Lys Pro
115 120 125
Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly
130 135 140
Ser Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly
145 150 155 160
Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr
165 170 175
Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg
180 185 190
Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg
195 200 205
Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly
210 215 220
Ala Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser

225 230 235 240
Asn His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
245 250

<210> 232
<211> 125
<212> PRT
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<220>
<221> 来源
<223> /注="人工序列说明:合成多肽"
<400> 232
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Thr Tyr
20 25 30
Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45
Gly Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
50 55 60
Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
65 70 75 80
Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr
85 90 95
Tyr Cys Val Arg His Gly Asn Phe Gly Pro Ser Tyr Val Ser Trp Phe
100 105 110
Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120 125

<210> 233
<211> 109
<212> PRT
<213> 人工序列
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<221> 来源
<223> /注="人工序列说明:合成多肽"
<400> 233
Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly Gly
1 5 10 15
Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr Ser
20 25 30
Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg Gly
35 40 45
Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg Phe

50 55 60

Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly Ala
65 70 75 80

Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser Asn
85 90 95

His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
100 105

<210> 234

<211> 262

<212> PRT

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<220>

<221> 来源

<223> /注="人工序列说明:合成多肽"

<400> 234

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Thr Tyr
20 25 30

Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

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

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
65 70 75 80

Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Val Arg His Gly Asn Phe Gly Asp Glu Tyr Val Ser Trp Phe
100 105 110

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Lys Pro
115 120 125

Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly
130 135 140

Ser Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly
145 150 155 160

Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr
165 170 175

Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg
180 185 190

Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg
195 200 205

Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly

210 215 220

Ala Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser
225 230 235 240

Asn His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly Ser
245 250 255

His His His His His His
260

<210> 235

<211> 254

<212> PRT

<213> 人工序列

<220>

<221> 来源

<223> /注=“人工序列说明:合成多肽”

<400> 235

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Thr Tyr
20 25 30

Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

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

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
65 70 75 80

Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Val Arg His Gly Asn Phe Gly Asp Glu Tyr Val Ser Trp Phe
100 105 110

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Lys Pro
115 120 125

Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly
130 135 140

Ser Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly
145 150 155 160

Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr
165 170 175

Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg
180 185 190

Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg
195 200 205

Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly

210 215 220

Ala Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser
225 230 235 240

Asn His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
245 250

<210> 236
<211> 125
<212> PRT
<213> 人工序列
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<221> 来源
<223> /注="人工序列说明:合成多肽"
<400> 236

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Thr Tyr
20 25 30

Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

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

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
65 70 75 80

Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Val Arg His Gly Asn Phe Gly Asp Glu Tyr Val Ser Trp Phe
100 105 110

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120 125

<210> 237
<211> 109
<212> PRT
<213> 人工序列
<220>
<221> 来源
<223> /注="人工序列说明:合成多肽"
<400> 237

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

Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr Ser
20 25 30

Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg Gly

35 40 45

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

Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly Ala
65 70 75 80

Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser Asn
85 90 95

His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
100 105

<210> 238

<211> 262

<212> PRT

<213> 人工序列

<220>

<221> 来源

<223> /注="人工序列说明:合成多肽"

<400> 238

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Thr Tyr
20 25 30

Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

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

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
65 70 75 80

Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Val Arg His Gly Asn Phe Gly Asp Pro Tyr Val Ser Trp Phe
100 105 110

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Lys Pro
115 120 125

Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly
130 135 140

Ser Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly
145 150 155 160

Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr
165 170 175

Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg
180 185 190

Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg

195 200 205

Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly
210 215 220

Ala Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser
225 230 235 240

Asn His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly Ser
245 250 255

His His His His His His
260

<210> 239
<211> 254
<212> PRT
<213> 人工序列
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<221> 来源
<223> /注=“人工序列说明:合成多肽”
<400> 239

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Thr Tyr
20 25 30

Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

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

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
65 70 75 80

Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Val Arg His Gly Asn Phe Gly Asp Pro Tyr Val Ser Trp Phe
100 105 110

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Lys Pro
115 120 125

Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly
130 135 140

Ser Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly
145 150 155 160

Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr
165 170 175

Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg
180 185 190

Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg

195 200 205

Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly
210 215 220

Ala Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser
225 230 235 240

Asn His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
245 250

<210> 240
<211> 125
<212> PRT
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<221> 来源
<223> /注="人工序列说明:合成多肽"
<400> 240

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Thr Tyr
20 25 30

Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

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

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
65 70 75 80

Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Val Arg His Gly Asn Phe Gly Asp Pro Tyr Val Ser Trp Phe
100 105 110

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120 125

<210> 241
<211> 109
<212> PRT
<213> 人工序列
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<221> 来源
<223> /注="人工序列说明:合成多肽"
<400> 241

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

Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr Ser

20 25 30

Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg Gly
35 40 45

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

Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly Ala
65 70 75 80

Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser Asn
85 90 95

His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
100 105

<210> 242
<211> 262
<212> PRT
<213> 人工序列
<220>
<221> 来源
<223> /注="人工序列说明:合成多肽"
<400> 242

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Thr Tyr
20 25 30

Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

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

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
65 70 75 80

Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Val Arg His Gly Asn Phe Gly Asp Ser Tyr Val Ser Trp Phe
100 105 110

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Lys Pro
115 120 125

Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly
130 135 140

Ser Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly
145 150 155 160

Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr
165 170 175

Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg

180 185 190

Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg
195 200 205

Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly
210 215 220

Ala Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser
225 230 235 240

Asn His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly Ser
245 250 255

His His His His His His
260

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Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Thr Tyr
20 25 30

Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

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

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
65 70 75 80

Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Val Arg His Gly Asn Phe Gly Asp Ser Tyr Val Ser Trp Phe
100 105 110

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Lys Pro
115 120 125

Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly
130 135 140

Ser Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly
145 150 155 160

Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr
165 170 175

Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg

180 185 190

Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg
195 200 205

Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly
210 215 220

Ala Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser
225 230 235 240

Asn His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
245 250

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Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Thr Tyr
20 25 30

Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

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

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
65 70 75 80

Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Val Arg His Gly Asn Phe Gly Asp Ser Tyr Val Ser Trp Phe
100 105 110

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120 125

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

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

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

165 170 175

Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg
180 185 190

Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg
195 200 205

Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly
210 215 220

Ala Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser
225 230 235 240

Asn His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly Ser
245 250 255

His His His His His His
260

<210> 247

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<400> 247

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Thr Tyr
20 25 30

Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

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

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
65 70 75 80

Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Val Arg His Gly Asn Phe Gly Asp Ser Tyr Val Ser Trp Phe
100 105 110

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Lys Pro
115 120 125

Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly
130 135 140

Ser Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly
145 150 155 160

Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr

165 170 175
Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg
180 185 190
Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg
195 200 205
Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly
210 215 220
Ala Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser
225 230 235 240
Asn His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
245 250

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

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<400> 249

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

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

145 150 155 160
Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr
165 170 175
Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg
180 185 190
Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg
195 200 205
Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly
210 215 220
Ala Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser
225 230 235 240
Asn His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly Ser
245 250 255
His His His His His His
260

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

145 150 155 160
Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr
165 170 175
Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg
180 185 190
Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg
195 200 205
Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly
210 215 220
Ala Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser
225 230 235 240
Asn His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
245 250

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

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

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

130 135 140

Ser Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly
145 150 155 160
Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr
165 170 175
Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg
180 185 190
Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg
195 200 205
Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly
210 215 220
Ala Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser
225 230 235 240
Asn His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly Ser
245 250 255
His His His His His His
260

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

130 135 140

Ser Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly
145 150 155 160
Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr
165 170 175
Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg
180 185 190
Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg
195 200 205
Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly
210 215 220
Ala Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser
225 230 235 240
Asn His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
245 250

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

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

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

115 120 125

Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly
130 135 140

Ser Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly
145 150 155 160

Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr
165 170 175

Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg
180 185 190

Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg
195 200 205

Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly
210 215 220

Ala Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser
225 230 235 240

Asn His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly Ser
245 250 255

His His His His His His
260

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Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Thr Tyr
20 25 30

Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

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

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
65 70 75 80

Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Val Arg His Gly Asn Phe Gly Asp Asn Tyr Val Ser Trp Phe
100 105 110

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

115 120 125

Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly
130 135 140

Ser Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly
145 150 155 160

Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr
165 170 175

Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg
180 185 190

Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg
195 200 205

Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly
210 215 220

Ala Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser
225 230 235 240

Asn His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
245 250

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Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Thr Tyr
20 25 30

Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

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

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
65 70 75 80

Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Val Arg His Gly Asn Phe Gly Asp Asn Tyr Val Ser Trp Phe
100 105 110

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120 125

<210> 261

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Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly Gly
1               5                  10                  15
Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr Ser
            20                  25                  30
Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg Gly
        35                  40                  45
Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg Phe
    50                  55                  60
Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly Ala
65                  70                  75                  80
Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser Asn
                85                  90                  95
His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
            100                 105
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<400> 262

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

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

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

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

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

115 120 125

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

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

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

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

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

100 105 110

Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120 125

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

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

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

<210> 271
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Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Thr Tyr
20 25 30
Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45
Gly Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Ala Tyr Ala Asp
50 55 60
Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr

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

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

85 90 95
Tyr Cys Val Arg His Gly Asn Phe Gly Asp Ser Tyr Val Ser Trp Phe
100 105 110
Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120 125
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Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly Gly
1 5 10 15
Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr Ser
20 25 30
Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg Gly
35 40 45
Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg Phe
50 55 60
Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly Ala
65 70 75 80
Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser Asn
85 90 95
His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
100 105
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<400> 274
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Thr Tyr
20 25 30
Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45
Gly Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp

50 55 60

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

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

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

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

35 40 45

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

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
65 70 75 80

Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Val Arg His Gly Asn Phe Gly Gln Ser Tyr Val Ser Trp Phe
100 105 110

Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Lys Pro
115 120 125

Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly
130 135 140

Ser Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly
145 150 155 160

Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr
165 170 175

Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg
180 185 190

Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg
195 200 205

Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly
210 215 220

Ala Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser
225 230 235 240

Asn His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly Ser
245 250 255

His His His His His His
260

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Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Thr Tyr
20 25 30

Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val

35 40 45

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

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
65 70 75 80

Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Val Arg His Gly Asn Phe Gly Gln Ser Tyr Val Ser Trp Phe
100 105 110

Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Lys Pro
115 120 125

Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly
130 135 140

Ser Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly
145 150 155 160

Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr
165 170 175

Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg
180 185 190

Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg
195 200 205

Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly
210 215 220

Ala Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser
225 230 235 240

Asn His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
245 250

<210> 280
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<221> 来源
<223> /注=“人工序列说明:合成多肽”
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Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Thr Tyr
20 25 30

Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Gly Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp

50 55 60
Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
65 70 75 80
Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr
85 90 95
Tyr Cys Val Arg His Gly Asn Phe Gly Gln Ser Tyr Val Ser Trp Phe
100 105 110
Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120 125

<210> 281
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<223> /注="人工序列说明:合成多肽"
<400> 281
Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly Gly
1 5 10 15
Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr Ser
20 25 30
Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg Gly
35 40 45
Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg Phe
50 55 60
Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly Ala
65 70 75 80
Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser Asn
85 90 95
His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
100 105

<210> 282
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<223> /注="人工序列说明:合成多肽"
<400> 282
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Thr Tyr

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

<210> 283
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Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Thr Tyr

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

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

35 40 45

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

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
65 70 75 80

Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Val Arg His Gly Asn Phe Gly Asp Glu Tyr Val Ser Trp Phe
100 105 110

Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120 125

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

Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr Ser
20 25 30

Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg Gly
35 40 45

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

Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly Ala
65 70 75 80

Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser Asn
85 90 95

His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
100 105

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

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

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

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

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<400> 288
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Thr Tyr

20 25 30

Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

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

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
65 70 75 80

Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Val Arg His Gly Asn Phe Gly Asp Asn Tyr Val Ser Trp Phe
100 105 110

Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120 125

<210> 289
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<212> PRT
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<223> /注=“人工序列说明:合成多肽”
<400> 289

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

Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr Ser
20 25 30

Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg Gly
35 40 45

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

Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly Ala
65 70 75 80

Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser Asn
85 90 95

His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
100 105

<210> 290
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<212> PRT
<213> 人工序列
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<400> 290

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

<210> 291

<211> 254

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<400> 291

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

<210> 292
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<212> PRT
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<400> 292

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

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

<210> 293
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<223> /注=“人工序列说明:合成多肽”
<400> 293
Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly Gly
1 5 10 15
Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr Ser
20 25 30
Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg Gly
35 40 45
Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg Phe
50 55 60
Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly Ala
65 70 75 80
Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser Asn
85 90 95
His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
100 105

<210> 294
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<221> 来源
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Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                  10                  15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Thr Tyr
            20                  25                  30
Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45
Gly Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
    50                  55                  60
Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
65                  70                  75                  80
Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr
                85                  90                  95
Tyr Cys Val Arg His Gly Asn Phe Gly Asp Gln Tyr Val Ser Trp Phe
            100                 105                 110
Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Lys Pro
        115                 120                 125
Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly
    130                 135                 140
Ser Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly
145                 150                 155                 160
Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr
                165                 170                 175
Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg
            180                 185                 190
Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg
        195                 200                 205
Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly
    210                 215                 220
Ala Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser
225                 230                 235                 240
Asn His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly Ser
                245                 250                 255
His His His His His His
            260
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<210> 295
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<221> 来源
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Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                  10                  15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Thr Tyr
            20                  25                  30
Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45
Gly Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
    50                  55                  60
Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
65                  70                  75                  80
Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr
                85                  90                  95
Tyr Cys Val Arg His Gly Asn Phe Gly Asp Gln Tyr Val Ser Trp Phe
            100                 105                 110
Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Lys Pro
        115                 120                 125
Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly
    130                 135                 140
Ser Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly
145                 150                 155                 160
Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr
                165                 170                 175
Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg
            180                 185                 190
Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg
        195                 200                 205
Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly
    210                 215                 220
Ala Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser
225                 230                 235                 240
Asn His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
                245                 250
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<210> 296
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<212> PRT
<213> 人工序列
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<221> 来源
<223> /注=“人工序列说明:合成多肽”

<400> 296

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

<210> 297
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<223> /注=“人工序列说明:合成多肽”

<400> 297

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

<210> 298
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<212> PRT

<213> 人工序列
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<223> /注="人工序列说明:合成多肽"
<400> 298

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Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                  10                  15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Thr Tyr
            20                  25                  30
Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45
Gly Arg Ile Arg Ser Lys Ala Asn Asn Tyr Ala Thr Ala Tyr Ala Asp
    50                  55                  60
Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
65                  70                  75                  80
Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr
                85                  90                  95
Tyr Cys Val Arg His Gly Asn Phe Gly Asp Ser Tyr Val Ser Trp Phe
            100                 105                 110
Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Lys Pro
        115                 120                 125
Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly
    130                 135                 140
Ser Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly
145                 150                 155                 160
Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr
                165                 170                 175
Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg
            180                 185                 190
Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg
        195                 200                 205
Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly
    210                 215                 220
Ala Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser
225                 230                 235                 240
Asn His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly Ser
                245                 250                 255
His His His His His His
            260
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<210> 299
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<212> PRT

<213> 人工序列
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<221> 来源
<223> /注="人工序列说明:合成多肽"
<400> 299

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

<210> 300
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<221> 来源
<223> /注=“人工序列说明:合成多肽”
<400> 300

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

<210> 301
<211> 109
<212> PRT
<213> 人工序列
<220>
<221> 来源
<223> /注=“人工序列说明:合成多肽”
<400> 301

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

<210> 302

<211> 262
<212> PRT
<213> 人工序列
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<223> /注="人工序列说明:合成多肽"
<400> 302

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Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                  10                  15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Thr Tyr
            20                  25                  30
Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45
Gly Arg Ile Arg Ser Lys Ala Asn Asn Tyr Ala Thr Ala Tyr Ala Asp
    50                  55                  60
Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
65                  70                  75                  80
Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr
                85                  90                  95
Tyr Cys Val Arg His Gly Asn Phe Gly Ala Ser Tyr Val Ser Trp Phe
            100                 105                 110
Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Lys Pro
        115                 120                 125
Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly
    130                 135                 140
Ser Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly
145                 150                 155                 160
Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr
                165                 170                 175
Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg
            180                 185                 190
Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg
        195                 200                 205
Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly
    210                 215                 220
Ala Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser
225                 230                 235                 240
Asn His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly Ser
                245                 250                 255
His His His His His His
            260
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<210> 303

<211> 254
<212> PRT
<213> 人工序列
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<221> 来源
<223> /注="人工序列说明:合成多肽"
<400> 303

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Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                  10                  15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Thr Tyr
            20                  25                  30
Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45
Gly Arg Ile Arg Ser Lys Ala Asn Asn Tyr Ala Thr Ala Tyr Ala Asp
    50                  55                  60
Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
65                  70                  75                  80
Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr
                85                  90                  95
Tyr Cys Val Arg His Gly Asn Phe Gly Ala Ser Tyr Val Ser Trp Phe
            100                 105                 110
Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Lys Pro
        115                 120                 125
Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly
    130                 135                 140
Ser Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly
145                 150                 155                 160
Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr
                165                 170                 175
Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg
            180                 185                 190
Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg
        195                 200                 205
Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly
    210                 215                 220
Ala Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser
225                 230                 235                 240
Asn His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
                245                 250
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<210> 304
<211> 125
<212> PRT

<213> 人工序列
<220>
<221> 来源
<223> /注="人工序列说明:合成多肽"
<400> 304

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

<210> 305
<211> 109
<212> PRT
<213> 人工序列
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<221> 来源
<223> /注="人工序列说明:合成多肽"
<400> 305

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

100 105

<210> 306
<211> 262
<212> PRT
<213> 人工序列
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<223> /注=“人工序列说明:合成多肽”
<400> 306

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

260

<210> 307
<211> 254
<212> PRT
<213> 人工序列
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<221> 来源
<223> /注="人工序列说明:合成多肽"
<400> 307

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

<210> 308

<211> 125
<212> PRT
<213> 人工序列
<220>
<221> 来源
<223> /注="人工序列说明:合成多肽"
<400> 308

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

<210> 309
<211> 109
<212> PRT
<213> 人工序列
<220>
<221> 来源
<223> /注="人工序列说明:合成多肽"
<400> 309

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

85 90 95

His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
100 105

<210> 310
<211> 262
<212> PRT
<213> 人工序列
<220>
<221> 来源
<223> /注="人工序列说明:合成多肽"
<400> 310

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

245 250 255

His His His His His His
260

<210> 311
<211> 254
<212> PRT
<213> 人工序列
<220>
<221> 来源
<223> /注=“人工序列说明:合成多肽”
<400> 311

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

245 250

<210> 312
<211> 125
<212> PRT
<213> 人工序列
<220>
<221> 来源
<223> /注=“人工序列说明:合成多肽”
<400> 312

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

<210> 313
<211> 109
<212> PRT
<213> 人工序列
<220>
<221> 来源
<223> /注=“人工序列说明:合成多肽”
<400> 313

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

65 70 75 80
Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser Asn
85 90 95
His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
100 105

<210> 314
<211> 450
<212> PRT
<213> 人工序列
<220>
<221> 来源
<223> /注="人工序列说明:合成多肽"
<400> 314
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1 5 10 15
Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30
Val Met His Trp Val Arg Gln Ala Pro Gly Gly Gly Leu Glu Trp Ile
35 40 45
Gly Tyr Ile Asn Pro Tyr Asn Asp Gly Thr Lys Tyr Asn Glu Lys Phe
50 55 60
Lys Gly Arg Val Thr Ile Ser Ser Asp Lys Ser Lys Ser Thr Ala Tyr
65 70 75 80
Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95
Ala Arg Gly Thr Tyr Tyr Tyr Gly Thr Arg Val Phe Asp Tyr Trp Gly
100 105 110
Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser
115 120 125
Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala
130 135 140
Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val
145 150 155 160
Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala
165 170 175
Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val
180 185 190
Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His
195 200 205
Lys Pro Ser Asp Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys
210 215 220
Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Pro Val Ala Gly

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

<210> 315
<211> 485
<212> PRT
<213> 人工序列
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<221> 来源
<223> /注=“人工序列说明:合成多肽”
<400> 315
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Thr Tyr
20 25 30
Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val

35 40 45

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

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
65 70 75 80

Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Val Arg His Gly Asn Phe Gly Asp Ser Tyr Val Ser Trp Phe
100 105 110

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Lys Pro
115 120 125

Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly
130 135 140

Ser Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly
145 150 155 160

Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr
165 170 175

Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg
180 185 190

Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg
195 200 205

Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly
210 215 220

Ala Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser
225 230 235 240

Asn His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Glu Pro
245 250 255

Lys Ser Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Pro
260 265 270

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

Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val
290 295 300

Lys His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
305 310 315 320

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
325 330 335

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
340 345 350

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
355 360 365

Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro

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

<210> 316
<211> 219
<212> PRT
<213> 人工序列
<220>
<221> 来源
<223> /注=“人工序列说明:合成多肽”
<400> 316
Asp Ile Val Met Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
1 5 10 15
Glu Arg Ala Thr Ile Ser Cys Arg Ser Ser Lys Ser Leu Gln Asn Val
20 25 30
Asn Gly Asn Thr Tyr Leu Tyr Trp Phe Gln Gln Lys Pro Gly Gln Ser
35 40 45
Pro Lys Leu Leu Ile Tyr Arg Ala Ser Asn Leu Asn Ser Gly Val Pro
50 55 60
Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile
65 70 75 80
Ser Ser Leu Glu Pro Glu Asp Phe Ala Val Tyr Tyr Cys Met Gln His
85 90 95
Leu Glu Tyr Pro Ile Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
100 105 110
Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu
115 120 125
Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe
130 135 140
Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln

145 150 155 160
Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser
165 170 175
Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu
180 185 190
Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser
195 200 205
Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
210 215

<210> 317
<211> 450
<212> PRT
<213> 人工序列
<220>
<221> 来源
<223> /注=“人工序列说明:合成多肽”
<400> 317
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1 5 10 15
Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30
Val Met His Trp Val Arg Gln Ala Pro Gly Gly Gly Leu Glu Trp Ile
35 40 45
Gly Tyr Ile Asn Pro Tyr Asn Asp Gly Thr Lys Tyr Asn Glu Lys Phe
50 55 60
Lys Gly Arg Val Thr Ile Ser Ser Asp Lys Ser Lys Ser Thr Ala Tyr
65 70 75 80
Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95
Ala Arg Gly Thr Tyr Tyr Tyr Gly Thr Arg Val Phe Asp Tyr Trp Gly
100 105 110
Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser
115 120 125
Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala
130 135 140
Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val
145 150 155 160
Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala
165 170 175
Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val
180 185 190
Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His

195 200 205

Lys Pro Ser Asp Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys
210 215 220

Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Pro Val Ala Gly
225 230 235 240

Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile
245 250 255

Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Lys His Glu
260 265 270

Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His
275 280 285

Asn Ala Lys Thr Lys Pro Arg Glu Glu Glu Tyr Asn Ser Thr Tyr Arg
290 295 300

Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys
305 310 315 320

Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu
325 330 335

Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr
340 345 350

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

Thr Cys Asp Val Ser Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp
370 375 380

Glu Ser Asp Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val
385 390 395 400

Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp
405 410 415

Lys Ser Arg Trp Glu Gln Gly Asp Val Phe Ser Cys Ser Val Met His
420 425 430

Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
435 440 445

Gly Lys
450

<210> 318
<211> 485
<212> PRT
<213> 人工序列
<220>
<221> 来源
<223> /注=“人工序列说明:合成多肽”
<400> 318
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly

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

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

<210> 319
<211> 219
<212> PRT
<213> 人工序列
<220>
<221> 来源
<223> /注=“人工序列说明:合成多肽”
<400> 319
Asp Ile Val Met Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
1 5 10 15
Glu Arg Ala Thr Ile Ser Cys Arg Ser Ser Lys Ser Leu Gln Asn Val
20 25 30
Asn Gly Asn Thr Tyr Leu Tyr Trp Phe Gln Gln Lys Pro Gly Gln Ser
35 40 45
Pro Lys Leu Leu Ile Tyr Arg Ala Ser Asn Leu Asn Ser Gly Val Pro
50 55 60
Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile
65 70 75 80
Ser Ser Leu Glu Pro Glu Asp Phe Ala Val Tyr Tyr Cys Met Gln His
85 90 95
Leu Glu Tyr Pro Ile Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
100 105 110
Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu

115 120 125

Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe
130 135 140

Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln
145 150 155 160

Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser
165 170 175

Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu
180 185 190

Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser
195 200 205

Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
210 215

<210> 320

<211> 450

<212> PRT

<213> 人工序列

<220>

<221> 来源

<223> /注=“人工序列说明:合成多肽”

<400> 320

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1 5 10 15

Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30

Val Met His Trp Val Arg Gln Ala Pro Gly Gly Gly Leu Glu Trp Ile
35 40 45

Gly Tyr Ile Asn Pro Tyr Asn Asp Gly Thr Lys Tyr Asn Glu Lys Phe
50 55 60

Lys Gly Arg Val Thr Ile Ser Ser Asp Lys Ser Lys Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Thr Tyr Tyr Tyr Gly Thr Arg Val Phe Asp Tyr Trp Gly
100 105 110

Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser
115 120 125

Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala
130 135 140

Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val
145 150 155 160

Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala

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

<210> 321
<211> 485
<212> PRT
<213> 人工序列
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<221> 来源

<223> /注=“人工序列说明:合成多肽”

<400> 321

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

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

<210> 322
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<213> 人工序列
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<223> /注="人工序列说明:合成多肽"
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Asp Ile Val Met Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
1 5 10 15
Glu Arg Ala Thr Ile Ser Cys Arg Ser Ser Lys Ser Leu Gln Asn Val
20 25 30
Asn Gly Asn Thr Tyr Leu Tyr Trp Phe Gln Gln Lys Pro Gly Gln Ser
35 40 45
Pro Lys Leu Leu Ile Tyr Arg Ala Ser Asn Leu Asn Ser Gly Val Pro
50 55 60
Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile
65 70 75 80
Ser Ser Leu Glu Pro Glu Asp Phe Ala Val Tyr Tyr Cys Met Gln His

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

<210> 323
<211> 450
<212> PRT
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<221> 来源
<223> /注="人工序列说明:合成多肽"
<400> 323
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30
Asn Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45
Gly Ala Ile Tyr Pro Gly Asn Gly Asp Thr Ser Tyr Asn Gln Lys Phe
50 55 60
Gln Gly Arg Val Thr Ile Thr Ala Asp Lys Ser Ile Ser Thr Ala Tyr
65 70 75 80
Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95
Ala Arg Ser Thr Tyr Tyr Gly Gly Asp Trp Tyr Phe Asn Val Trp Gly
100 105 110
Ala Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser
115 120 125
Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala

130 135 140

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

<210> 324

<211> 485
<212> PRT
<213> 人工序列
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<221> 来源
<223> /注="人工序列说明:合成多肽"
<400> 324

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

275 280 285

Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val
290 295 300

Lys His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
305 310 315 320

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
325 330 335

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
340 345 350

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
355 360 365

Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
370 375 380

Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Gln Met Thr Lys Asn Gln
385 390 395 400

Val Lys Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala
405 410 415

Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
420 425 430

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
435 440 445

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
450 455 460

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
465 470 475 480

Leu Ser Pro Gly Lys
485

<210> 325
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<213> 人工序列
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<221> 来源
<223> /注="人工序列说明:合成多肽"
<400> 325

Gln Ile Val Leu Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Ser Ser Val Ser Tyr Ile
20 25 30

His Trp Phe Gln Gln Lys Pro Gly Lys Ser Pro Lys Pro Leu Ile Tyr
35 40 45

Ala Thr Ser Asn Leu Ala Ser Gly Val Pro Val Arg Phe Ser Gly Ser

50 55 60

Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu
65 70 75 80

Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Trp Thr Ser Asn Pro Pro Thr
85 90 95

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala Pro
100 105 110

Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr
115 120 125

Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys
130 135 140

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

Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser
165 170 175

Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala
180 185 190

Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe
195 200 205

Asn Arg Gly Glu Cys
210

<210> 326
<211> 450
<212> PRT
<213> 人工序列
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<221> 来源
<223> /注="人工序列说明:合成多肽"
<400> 326

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30

Asn Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Ala Ile Tyr Pro Gly Asn Gly Asp Thr Ser Tyr Asn Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Ile Thr Ala Asp Lys Ser Ile Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Ser Thr Tyr Tyr Gly Gly Asp Trp Tyr Phe Asn Val Trp Gly

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

435 440 445

Gly Lys
450

<210> 327
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<212> PRT
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<223> /注="人工序列说明:合成多肽"
<400> 327

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

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

<210> 328
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<212> PRT
<213> 人工序列
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<221> 来源
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<400> 328
Gln Ile Val Leu Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Ser Ser Val Ser Tyr Ile

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

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<400> 329
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30
Asn Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45
Gly Ala Ile Tyr Pro Gly Asn Gly Asp Thr Ser Tyr Asn Gln Lys Phe
50 55 60
Gln Gly Arg Val Thr Ile Thr Ala Asp Lys Ser Ile Ser Thr Ala Tyr

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

405 410 415
Lys Ser Arg Trp Glu Gln Gly Asp Val Phe Ser Cys Ser Val Met His
420 425 430
Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
435 440 445
Gly Lys
450
<210> 330
<211> 485
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<223> /注="人工序列说明:合成多肽"
<400> 330
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Thr Tyr
20 25 30
Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45
Gly Arg Ile Arg Ser Lys Ala Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
50 55 60
Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
65 70 75 80
Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr
85 90 95
Tyr Cys Val Arg His Gly Asn Phe Gly Asp Ser Tyr Val Ser Trp Phe
100 105 110
Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Lys Pro
115 120 125
Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly
130 135 140
Ser Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly
145 150 155 160
Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr
165 170 175
Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg
180 185 190
Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg
195 200 205
Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly

210 215 220

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

<210> 331
<211> 213
<212> PRT
<213> 人工序列
<220>
<221> 来源
<223> /注=“人工序列说明:合成多肽”

<400> 331

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

<210> 332

<211> 450

<212> PRT

<213> 人工序列

<220>

<221> 来源

<223> /注=“人工序列说明:合成多肽”

<400> 332

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

35 40 45

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

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

<210> 333
<211> 485
<212> PRT
<213> 人工序列
<220>
<221> 来源
<223> /注="人工序列说明:合成多肽"
<400> 333
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Thr Tyr
20 25 30
Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45
Gly Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
50 55 60
Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
65 70 75 80
Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr
85 90 95
Tyr Cys Val Arg His Gly Asn Phe Gly Asp Ser Tyr Val Ser Trp Phe
100 105 110
Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Lys Pro
115 120 125
Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly
130 135 140
Ser Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly
145 150 155 160
Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr
165 170 175
Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg

180 185 190

Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg
195 200 205

Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly
210 215 220

Ala Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser
225 230 235 240

Asn His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Glu Pro
245 250 255

Lys Ser Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Pro
260 265 270

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

Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val
290 295 300

Lys His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
305 310 315 320

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
325 330 335

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
340 345 350

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
355 360 365

Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
370 375 380

Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Gln Met Thr Lys Asn Gln
385 390 395 400

Val Lys Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala
405 410 415

Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
420 425 430

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
435 440 445

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
450 455 460

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
465 470 475 480

Leu Ser Pro Gly Lys
485

<210> 334
<211> 213
<212> PRT

<213> 人工序列
<220>
<221> 来源
<223> /注="人工序列说明:合成多肽"
<400> 334

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

<210> 335
<211> 450
<212> PRT
<213> 人工序列
<220>
<221> 来源
<223> /注="人工序列说明:合成多肽"
<400> 335

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

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

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

<210> 336
<211> 485
<212> PRT
<213> 人工序列
<220>
<221> 来源
<223> /注="人工序列说明:合成多肽"
<400> 336
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Thr Tyr
20 25 30
Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45
Gly Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
50 55 60
Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
65 70 75 80
Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr
85 90 95
Tyr Cys Val Arg His Gly Asn Phe Gly Pro Ser Tyr Val Ser Trp Phe
100 105 110
Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Lys Pro
115 120 125
Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly
130 135 140
Ser Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly

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

485

<210> 337
<211> 213
<212> PRT
<213> 人工序列
<220>
<221> 来源
<223> /注=“人工序列说明:合成多肽”
<400> 337

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

<210> 338
<211> 450
<212> PRT
<213> 人工序列
<220>

<221> 来源

<223> /注=“人工序列说明:合成多肽”

<400> 338

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

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

<210> 339
<211> 485
<212> PRT
<213> 人工序列
<220>
<221> 来源
<223> /注=“人工序列说明:合成多肽”
<400> 339
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Thr Tyr
20 25 30
Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45
Gly Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
50 55 60
Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
65 70 75 80
Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr
85 90 95
Tyr Cys Val Arg His Gly Asn Phe Gly Asp Glu Tyr Val Ser Trp Phe
100 105 110
Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Lys Pro

115 120 125

Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly

130 135 140

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

145 150 155 160

Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr

165 170 175

Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg

180 185 190

Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg

195 200 205

Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly

210 215 220

Ala Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser

225 230 235 240

Asn His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Glu Pro

245 250 255

Lys Ser Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Pro

260 265 270

Val Ala Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr

275 280 285

Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val

290 295 300

Lys His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val

305 310 315 320

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser

325 330 335

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu

340 345 350

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala

355 360 365

Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro

370 375 380

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

385 390 395 400

Val Lys Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala

405 410 415

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

420 425 430

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu

435 440 445

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser

450 455 460

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
465 470 475 480

Leu Ser Pro Gly Lys
485

<210> 340
<211> 213
<212> PRT
<213> 人工序列
<220>
<221> 来源
<223> /注="人工序列说明:合成多肽"
<400> 340

Gln Ile Val Leu Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Ser Ser Val Ser Tyr Ile
20 25 30

His Trp Phe Gln Gln Lys Pro Gly Lys Ser Pro Lys Pro Leu Ile Tyr
35 40 45

Ala Thr Ser Asn Leu Ala Ser Gly Val Pro Val Arg Phe Ser Gly Ser
50 55 60

Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu
65 70 75 80

Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Trp Thr Ser Asn Pro Pro Thr
85 90 95

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala Pro
100 105 110

Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr
115 120 125

Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys
130 135 140

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

Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser
165 170 175

Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala
180 185 190

Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe
195 200 205

Asn Arg Gly Glu Cys
210

<210> 341

<211> 450
<212> PRT
<213> 人工序列
<220>
<221> 来源
<223> /注="人工序列说明:合成多肽"
<400> 341

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

275 280 285

Asn Ala Lys Thr Lys Pro Arg Glu Glu Glu Tyr Asn Ser Thr Tyr Arg
290 295 300

Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys
305 310 315 320

Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu
325 330 335

Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr
340 345 350

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

Thr Cys Asp Val Ser Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp
370 375 380

Glu Ser Asp Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val
385 390 395 400

Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp
405 410 415

Lys Ser Arg Trp Glu Gln Gly Asp Val Phe Ser Cys Ser Val Met His
420 425 430

Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
435 440 445

Gly Lys
450

<210> 342
<211> 485
<212> PRT
<213> 人工序列
<220>
<221> 来源
<223> /注="人工序列说明:合成多肽"
<400> 342

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Thr Tyr
20 25 30

Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

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

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
65 70 75 80

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

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

420 425 430

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
435 440 445

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
450 455 460

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
465 470 475 480

Leu Ser Pro Gly Lys
485

<210> 343
<211> 213
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<213> 人工序列
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<400> 343

Gln Ile Val Leu Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Ser Ser Val Ser Tyr Ile
20 25 30

His Trp Phe Gln Gln Lys Pro Gly Lys Ser Pro Lys Pro Leu Ile Tyr
35 40 45

Ala Thr Ser Asn Leu Ala Ser Gly Val Pro Val Arg Phe Ser Gly Ser
50 55 60

Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu
65 70 75 80

Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Trp Thr Ser Asn Pro Pro Thr
85 90 95

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala Pro
100 105 110

Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr
115 120 125

Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys
130 135 140

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

Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser
165 170 175

Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala
180 185 190

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

195 200 205

Asn Arg Gly Glu Cys
210

<210> 344
<211> 450
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<213> 人工序列
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<400> 344

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

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

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<211> 485
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<400> 345
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Thr Tyr
20 25 30
Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45
Gly Arg Ile Arg Ser Lys Ala Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp

50 55 60

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

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

<210> 346
<211> 213
<212> PRT
<213> 人工序列
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<223> /注=“人工序列说明:合成多肽”
<400> 346
Gln Ile Val Leu Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Ser Ser Val Ser Tyr Ile
20 25 30
His Trp Phe Gln Gln Lys Pro Gly Lys Ser Pro Lys Pro Leu Ile Tyr
35 40 45
Ala Thr Ser Asn Leu Ala Ser Gly Val Pro Val Arg Phe Ser Gly Ser
50 55 60
Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu
65 70 75 80
Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Trp Thr Ser Asn Pro Pro Thr
85 90 95
Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala Pro
100 105 110
Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr
115 120 125
Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys
130 135 140
Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu
145 150 155 160
Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser

165 170 175
Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala
180 185 190
Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe
195 200 205
Asn Arg Gly Glu Cys
210

<210> 347
<211> 450
<212> PRT
<213> 人工序列
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<221> 来源
<223> /注="人工序列说明:合成多肽"
<400> 347
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30
Asn Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45
Gly Ala Ile Tyr Pro Gly Asn Gly Asp Thr Ser Tyr Asn Gln Lys Phe
50 55 60
Gln Gly Arg Val Thr Ile Thr Ala Asp Lys Ser Ile Ser Thr Ala Tyr
65 70 75 80
Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95
Ala Arg Ser Thr Tyr Tyr Gly Gly Asp Trp Tyr Phe Asn Val Trp Gly
100 105 110
Ala Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser
115 120 125
Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala
130 135 140
Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val
145 150 155 160
Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala
165 170 175
Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val
180 185 190
Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His
195 200 205
Lys Pro Ser Asp Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys

210 215 220

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

<210> 348
<211> 485
<212> PRT
<213> 人工序列
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<221> 来源
<223> /注=“人工序列说明:合成多肽”
<400> 348
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Thr Tyr

20 25 30

Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

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

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
65 70 75 80

Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Val Arg His Gly Asn Phe Gly Asp Ser Tyr Val Ser Trp Phe
100 105 110

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Lys Pro
115 120 125

Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly
130 135 140

Ser Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly
145 150 155 160

Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr
165 170 175

Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg
180 185 190

Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg
195 200 205

Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly
210 215 220

Ala Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser
225 230 235 240

Asn His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Glu Pro
245 250 255

Lys Ser Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Pro
260 265 270

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

Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val
290 295 300

Lys His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
305 310 315 320

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
325 330 335

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
340 345 350

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala

355 360 365

Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
370 375 380

Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Gln Met Thr Lys Asn Gln
385 390 395 400

Val Lys Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala
405 410 415

Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
420 425 430

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
435 440 445

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
450 455 460

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
465 470 475 480

Leu Ser Pro Gly Lys
485

<210> 349
<211> 213
<212> PRT
<213> 人工序列
<220>
<221> 来源
<223> /注="人工序列说明:合成多肽"
<400> 349

Gln Ile Val Leu Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Ser Ser Val Ser Tyr Ile
20 25 30

His Trp Phe Gln Gln Lys Pro Gly Lys Ser Pro Lys Pro Leu Ile Tyr
35 40 45

Ala Thr Ser Asn Leu Ala Ser Gly Val Pro Val Arg Phe Ser Gly Ser
50 55 60

Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu
65 70 75 80

Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Trp Thr Ser Asn Pro Pro Thr
85 90 95

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala Pro
100 105 110

Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr
115 120 125

Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys

130 135 140

Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu
145 150 155 160
Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser
165 170 175
Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala
180 185 190
Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe
195 200 205
Asn Arg Gly Glu Cys
210

<210> 350
<211> 450
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<400> 350

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

180 185 190

Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His

195 200 205

Lys Pro Ser Asp Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys

210 215 220

Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Pro Val Ala Gly

225 230 235 240

Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile

245 250 255

Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Lys His Glu

260 265 270

Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His

275 280 285

Asn Ala Lys Thr Lys Pro Arg Glu Glu Glu Tyr Asn Ser Thr Tyr Arg

290 295 300

Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys

305 310 315 320

Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu

325 330 335

Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr

340 345 350

Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu

355 360 365

Thr Cys Asp Val Ser Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp

370 375 380

Glu Ser Asp Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val

385 390 395 400

Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp

405 410 415

Lys Ser Arg Trp Glu Gln Gly Asp Val Phe Ser Cys Ser Val Met His

420 425 430

Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro

435 440 445

Gly Lys

450

<210> 351

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<221> 来源

<223> /注=“人工序列说明:合成多肽”

<400> 351

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

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

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<212> PRT
<213> 人工序列
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<221> 来源
<223> /注="人工序列说明:合成多肽"
<400> 352
Gln Ile Val Leu Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Ser Ser Val Ser Tyr Ile
20 25 30
His Trp Phe Gln Gln Lys Pro Gly Lys Ser Pro Lys Pro Leu Ile Tyr
35 40 45
Ala Thr Ser Asn Leu Ala Ser Gly Val Pro Val Arg Phe Ser Gly Ser
50 55 60
Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu
65 70 75 80
Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Trp Thr Ser Asn Pro Pro Thr
85 90 95
Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala Pro

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

<210> 353
<211> 450
<212> PRT
<213> 人工序列
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<221> 来源
<223> /注="人工序列说明:合成多肽"
<400> 353
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30
Asn Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45
Gly Ala Ile Tyr Pro Gly Asn Gly Asp Thr Ser Tyr Asn Gln Lys Phe
50 55 60
Gln Gly Arg Val Thr Ile Thr Ala Asp Lys Ser Ile Ser Thr Ala Tyr
65 70 75 80
Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95
Ala Arg Ser Thr Tyr Tyr Gly Gly Asp Trp Tyr Phe Asn Val Trp Gly
100 105 110
Ala Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser
115 120 125
Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala
130 135 140
Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val

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

<210> 354
<211> 485
<212> PRT

<213> 人工序列

<220>

<221> 来源

<223> /注="人工序列说明:合成多肽"

<400> 354

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

290 295 300

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

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

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

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<400> 356
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30
Asn Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45
Gly Ala Ile Tyr Pro Gly Asn Gly Asp Thr Ser Tyr Asn Gln Lys Phe
50 55 60
Gln Gly Arg Val Thr Ile Thr Ala Asp Lys Ser Ile Ser Thr Ala Tyr
65 70 75 80
Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95
Ala Arg Ser Thr Tyr Tyr Gly Gly Asp Trp Tyr Phe Asn Val Trp Gly
100 105 110
Ala Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser

115 120 125

Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala
130 135 140

Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val
145 150 155 160

Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala
165 170 175

Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val
180 185 190

Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His
195 200 205

Lys Pro Ser Asp Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys
210 215 220

Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Pro Val Ala Gly
225 230 235 240

Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile
245 250 255

Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Lys His Glu
260 265 270

Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His
275 280 285

Asn Ala Lys Thr Lys Pro Arg Glu Glu Glu Tyr Asn Ser Thr Tyr Arg
290 295 300

Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys
305 310 315 320

Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu
325 330 335

Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr
340 345 350

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

Thr Cys Asp Val Ser Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp
370 375 380

Glu Ser Asp Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val
385 390 395 400

Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp
405 410 415

Lys Ser Arg Trp Glu Gln Gly Asp Val Phe Ser Cys Ser Val Met His
420 425 430

Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
435 440 445

Gly Lys

450

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

260 265 270

Val Ala Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr

275 280 285

Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val

290 295 300

Lys His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val

305 310 315 320

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser

325 330 335

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu

340 345 350

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala

355 360 365

Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro

370 375 380

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

385 390 395 400

Val Lys Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala

405 410 415

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

420 425 430

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu

435 440 445

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser

450 455 460

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser

465 470 475 480

Leu Ser Pro Gly Lys

485

<210> 358

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

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Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Ser Ser Val Ser Tyr Ile

20 25 30

His Trp Phe Gln Gln Lys Pro Gly Lys Ser Pro Lys Pro Leu Ile Tyr

35 40 45

Ala Thr Ser Asn Leu Ala Ser Gly Val Pro Val Arg Phe Ser Gly Ser
50 55 60

Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu
65 70 75 80

Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Trp Thr Ser Asn Pro Pro Thr
85 90 95

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala Pro
100 105 110

Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr
115 120 125

Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys
130 135 140

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

Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser
165 170 175

Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala
180 185 190

Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe
195 200 205

Asn Arg Gly Glu Cys
210

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Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30

Asn Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Ala Ile Tyr Pro Gly Asn Gly Asp Thr Ser Tyr Asn Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Ile Thr Ala Asp Lys Ser Ile Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys

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

420 425 430
Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
435 440 445
Gly Lys
450
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20 25 30
Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45
Gly Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
50 55 60
Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
65 70 75 80
Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr
85 90 95
Tyr Cys Val Arg His Gly Asn Phe Gly Asp Gln Tyr Val Ser Trp Phe
100 105 110
Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Lys Pro
115 120 125
Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly
130 135 140
Ser Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly
145 150 155 160
Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr
165 170 175
Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg
180 185 190
Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg
195 200 205
Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly
210 215 220
Ala Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser

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

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

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

50 55 60

Gln Gly Arg Val Thr Ile Thr Ala Asp Thr Ser Ala Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Ser Tyr Tyr Met Gly Gly Asp Trp Tyr Phe Asp Val Trp Gly
100 105 110

Ala Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser
115 120 125

Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala
130 135 140

Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val
145 150 155 160

Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala
165 170 175

Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val
180 185 190

Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His
195 200 205

Lys Pro Ser Asp Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys
210 215 220

Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Pro Val Ala Gly
225 230 235 240

Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile
245 250 255

Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Lys His Glu
260 265 270

Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His
275 280 285

Asn Ala Lys Thr Lys Pro Arg Glu Glu Glu Tyr Asn Ser Thr Tyr Arg
290 295 300

Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys
305 310 315 320

Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu
325 330 335

Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr
340 345 350

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

Thr Cys Asp Val Ser Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp
370 375 380

Glu Ser Asp Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val

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

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<211> 485
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Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Thr Tyr
20 25 30
Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45
Gly Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
50 55 60
Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
65 70 75 80
Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr
85 90 95
Tyr Cys Val Arg His Gly Asn Phe Gly Asp Ser Tyr Val Ser Trp Phe
100 105 110
Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Lys Pro
115 120 125
Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly
130 135 140
Ser Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly
145 150 155 160
Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr
165 170 175
Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg
180 185 190
Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg

195 200 205

Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly
210 215 220

Ala Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser
225 230 235 240

Asn His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Glu Pro
245 250 255

Lys Ser Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Pro
260 265 270

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

Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val
290 295 300

Lys His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
305 310 315 320

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
325 330 335

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
340 345 350

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
355 360 365

Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
370 375 380

Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Gln Met Thr Lys Asn Gln
385 390 395 400

Val Lys Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala
405 410 415

Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
420 425 430

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
435 440 445

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
450 455 460

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
465 470 475 480

Leu Ser Pro Gly Lys
485

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<400> 364

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1               5                  10                  15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Trp Ser Val Ser Tyr Ile
            20                  25                  30
His Trp Phe Gln Gln Lys Pro Gly Lys Ser Pro Lys Pro Leu Ile Tyr
        35                  40                  45
Ala Thr Ser Asn Leu Ala Ser Gly Val Pro Val Arg Phe Ser Gly Ser
    50                  55                  60
Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu
65                  70                  75                  80
Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Trp Thr His Asn Pro Pro Thr
                85                  90                  95
Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala Pro
            100                 105                 110
Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr
        115                 120                 125
Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys
    130                 135                 140
Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu
145                 150                 155                 160
Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser
                165                 170                 175
Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala
            180                 185                 190
Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe
        195                 200                 205
Asn Arg Gly Glu Cys
    210
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<210> 365
<211> 450
<212> PRT
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<400> 365

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Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1               5                  10                  15
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
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20 25 30

Asn Met His Trp Val Arg Gln Ala Pro Gly Gln Arg Leu Glu Trp Met
35 40 45

Gly Ala Ile Tyr Pro Gly Asn Gly Ala Thr Ser Tyr Ser Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Ile Thr Ala Asp Thr Ser Ala Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Ser Tyr Tyr Met Gly Gly Asp Trp Tyr Phe Asp Val Trp Gly
100 105 110

Ala Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser
115 120 125

Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala
130 135 140

Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val
145 150 155 160

Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala
165 170 175

Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val
180 185 190

Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His
195 200 205

Lys Pro Ser Asp Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys
210 215 220

Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Pro Val Ala Gly
225 230 235 240

Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile
245 250 255

Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Lys His Glu
260 265 270

Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His
275 280 285

Asn Ala Lys Thr Lys Pro Arg Glu Glu Glu Tyr Asn Ser Thr Tyr Arg
290 295 300

Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys
305 310 315 320

Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu
325 330 335

Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr
340 345 350

Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu

355 360 365
Thr Cys Asp Val Ser Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp
370 375 380
Glu Ser Asp Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val
385 390 395 400
Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp
405 410 415
Lys Ser Arg Trp Glu Gln Gly Asp Val Phe Ser Cys Ser Val Met His
420 425 430
Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
435 440 445
Gly Lys
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Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Thr Tyr
20 25 30
Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45
Gly Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
50 55 60
Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
65 70 75 80
Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr
85 90 95
Tyr Cys Val Arg His Gly Asn Phe Gly Asp Ser Tyr Val Ser Trp Phe
100 105 110
Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Lys Pro
115 120 125
Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly
130 135 140
Ser Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly
145 150 155 160
Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr

165 170 175

Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg

180 185 190

Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg

195 200 205

Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly

210 215 220

Ala Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser

225 230 235 240

Asn His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Glu Pro

245 250 255

Lys Ser Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Pro

260 265 270

Val Ala Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr

275 280 285

Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val

290 295 300

Lys His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val

305 310 315 320

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser

325 330 335

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu

340 345 350

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala

355 360 365

Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro

370 375 380

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

385 390 395 400

Val Lys Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala

405 410 415

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

420 425 430

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu

435 440 445

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser

450 455 460

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser

465 470 475 480

Leu Ser Pro Gly Lys

485

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

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

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

130 135 140

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

465 470 475 480
Leu Ser Pro Gly Lys
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Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Trp Ser Val Ser Tyr Ile
20 25 30
His Trp Phe Gln Gln Lys Pro Gly Lys Ser Pro Lys Pro Leu Ile Tyr
35 40 45
Ala Thr Ser Asn Leu Ala Ser Gly Val Pro Val Arg Phe Ser Gly Ser
50 55 60
Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu
65 70 75 80
Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Trp Thr His Asn Pro Pro Thr
85 90 95
Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala Pro
100 105 110
Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr
115 120 125
Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys
130 135 140
Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu
145 150 155 160
Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser
165 170 175
Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala
180 185 190
Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe
195 200 205
Asn Arg Gly Glu Cys
210

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Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
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Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
            20                  25                  30
Asn Met His Trp Val Arg Gln Ala Pro Gly Gln Arg Leu Glu Trp Met
        35                  40                  45
Gly Ala Ile Tyr Pro Gly Asn Gly Ala Thr Ser Tyr Ser Gln Lys Phe
    50                  55                  60
Gln Gly Arg Val Thr Ile Thr Ala Asp Thr Ser Ala Ser Thr Ala Tyr
65                  70                  75                  80
Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95
Ala Arg Ser Tyr Tyr Met Gly Gly Asp Trp Tyr Phe Asp Val Trp Gly
            100                 105                 110
Ala Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser
        115                 120                 125
Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala
    130                 135                 140
Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val
145                 150                 155                 160
Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala
                165                 170                 175
Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val
            180                 185                 190
Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His
        195                 200                 205
Lys Pro Ser Asp Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys
    210                 215                 220
Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Pro Val Ala Gly
225                 230                 235                 240
Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile
                245                 250                 255
Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Lys His Glu
            260                 265                 270
Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His
        275                 280                 285
Asn Ala Lys Thr Lys Pro Arg Glu Glu Glu Tyr Asn Ser Thr Tyr Arg
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290 295 300
Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys
305 310 315 320
Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu
325 330 335
Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr
340 345 350
Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu
355 360 365
Thr Cys Asp Val Ser Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp
370 375 380
Glu Ser Asp Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val
385 390 395 400
Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp
405 410 415
Lys Ser Arg Trp Glu Gln Gly Asp Val Phe Ser Cys Ser Val Met His
420 425 430
Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
435 440 445
Gly Lys
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Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Thr Tyr
20 25 30
Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45
Gly Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
50 55 60
Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
65 70 75 80
Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr
85 90 95
Tyr Cys Val Arg His Gly Asn Phe Gly Asp Ser Tyr Val Ser Trp Phe

100 105 110

Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Lys Pro

115 120 125

Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly

130 135 140

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

145 150 155 160

Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr

165 170 175

Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg

180 185 190

Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg

195 200 205

Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly

210 215 220

Ala Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser

225 230 235 240

Asn His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Glu Pro

245 250 255

Lys Ser Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Pro

260 265 270

Val Ala Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr

275 280 285

Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val

290 295 300

Lys His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val

305 310 315 320

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser

325 330 335

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu

340 345 350

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala

355 360 365

Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro

370 375 380

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

385 390 395 400

Val Lys Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala

405 410 415

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

420 425 430

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu

435 440 445

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
450 455 460

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
465 470 475 480

Leu Ser Pro Gly Lys
485

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Gln Ile Val Leu Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
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Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Trp Ser Val Ser Tyr Ile
20 25 30

His Trp Phe Gln Gln Lys Pro Gly Lys Ser Pro Lys Pro Leu Ile Tyr
35 40 45

Ala Thr Ser Asn Leu Ala Ser Gly Val Pro Val Arg Phe Ser Gly Ser
50 55 60

Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu
65 70 75 80

Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Trp Thr His Asn Pro Pro Thr
85 90 95

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala Pro
100 105 110

Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr
115 120 125

Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys
130 135 140

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

Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser
165 170 175

Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala
180 185 190

Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe
195 200 205

Asn Arg Gly Glu Cys

210

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

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

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

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

405 410 415

Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
420 425 430

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
435 440 445

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
450 455 460

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
465 470 475 480

Leu Ser Pro Gly Lys
485

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Gln Ile Val Leu Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Trp Ser Val Ser Tyr Ile
20 25 30

His Trp Phe Gln Gln Lys Pro Gly Lys Ser Pro Lys Pro Leu Ile Tyr
35 40 45

Ala Thr Ser Asn Leu Ala Ser Gly Val Pro Val Arg Phe Ser Gly Ser
50 55 60

Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu
65 70 75 80

Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Trp Thr His Asn Pro Pro Thr
85 90 95

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala Pro
100 105 110

Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr
115 120 125

Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys
130 135 140

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

Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser
165 170 175

Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala

180 185 190
Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe
195 200 205
Asn Arg Gly Glu Cys
210
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<400> 377
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30
Asn Met His Trp Val Arg Gln Ala Pro Gly Gln Arg Leu Glu Trp Met
35 40 45
Gly Ala Ile Tyr Pro Gly Asn Gly Ala Thr Ser Tyr Ser Gln Lys Phe
50 55 60
Gln Gly Arg Val Thr Ile Thr Ala Asp Thr Ser Ala Ser Thr Ala Tyr
65 70 75 80
Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95
Ala Arg Ser Tyr Tyr Met Gly Gly Asp Trp Tyr Phe Asp Val Trp Gly
100 105 110
Ala Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser
115 120 125
Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala
130 135 140
Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val
145 150 155 160
Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala
165 170 175
Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val
180 185 190
Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His
195 200 205
Lys Pro Ser Asp Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys
210 215 220
Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Pro Val Ala Gly

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

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

35 40 45

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

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
65 70 75 80

Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Val Arg His Gly Asn Phe Gly Asp Glu Tyr Val Ser Trp Phe
100 105 110

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Lys Pro
115 120 125

Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly
130 135 140

Ser Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly
145 150 155 160

Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr
165 170 175

Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg
180 185 190

Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg
195 200 205

Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly
210 215 220

Ala Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser
225 230 235 240

Asn His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Glu Pro
245 250 255

Lys Ser Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Pro
260 265 270

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

Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val
290 295 300

Lys His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
305 310 315 320

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
325 330 335

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
340 345 350

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
355 360 365

Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro

370 375 380
Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Gln Met Thr Lys Asn Gln
385 390 395 400
Val Lys Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala
405 410 415
Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
420 425 430
Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
435 440 445
Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
450 455 460
Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
465 470 475 480
Leu Ser Pro Gly Lys
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Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Trp Ser Val Ser Tyr Ile
20 25 30
His Trp Phe Gln Gln Lys Pro Gly Lys Ser Pro Lys Pro Leu Ile Tyr
35 40 45
Ala Thr Ser Asn Leu Ala Ser Gly Val Pro Val Arg Phe Ser Gly Ser
50 55 60
Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu
65 70 75 80
Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Trp Thr His Asn Pro Pro Thr
85 90 95
Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala Pro
100 105 110
Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr
115 120 125
Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys
130 135 140
Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu

145 150 155 160
Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser
165 170 175
Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala
180 185 190
Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe
195 200 205
Asn Arg Gly Glu Cys
210

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

195 200 205

Lys Pro Ser Asp Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys
210 215 220

Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Pro Val Ala Gly
225 230 235 240

Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile
245 250 255

Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Lys His Glu
260 265 270

Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His
275 280 285

Asn Ala Lys Thr Lys Pro Arg Glu Glu Glu Tyr Asn Ser Thr Tyr Arg
290 295 300

Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys
305 310 315 320

Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu
325 330 335

Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr
340 345 350

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

Thr Cys Asp Val Ser Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp
370 375 380

Glu Ser Asp Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val
385 390 395 400

Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp
405 410 415

Lys Ser Arg Trp Glu Gln Gly Asp Val Phe Ser Cys Ser Val Met His
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Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
435 440 445

Gly Lys
450

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

340 345 350
Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
355 360 365
Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
370 375 380
Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Gln Met Thr Lys Asn Gln
385 390 395 400
Val Lys Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala
405 410 415
Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
420 425 430
Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
435 440 445
Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
450 455 460
Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
465 470 475 480
Leu Ser Pro Gly Lys
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Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Trp Ser Val Ser Tyr Ile
20 25 30
His Trp Phe Gln Gln Lys Pro Gly Lys Ser Pro Lys Pro Leu Ile Tyr
35 40 45
Ala Thr Ser Asn Leu Ala Ser Gly Val Pro Val Arg Phe Ser Gly Ser
50 55 60
Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu
65 70 75 80
Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Trp Thr His Asn Pro Pro Thr
85 90 95
Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala Pro
100 105 110
Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr

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

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

165 170 175
Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val
180 185 190
Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His
195 200 205
Lys Pro Ser Asp Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys
210 215 220
Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Pro Val Ala Gly
225 230 235 240
Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile
245 250 255
Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Lys His Glu
260 265 270
Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His
275 280 285
Asn Ala Lys Thr Lys Pro Arg Glu Glu Glu Tyr Asn Ser Thr Tyr Arg
290 295 300
Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys
305 310 315 320
Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu
325 330 335
Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr
340 345 350
Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu
355 360 365
Thr Cys Asp Val Ser Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp
370 375 380
Glu Ser Asp Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val
385 390 395 400
Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp
405 410 415
Lys Ser Arg Trp Glu Gln Gly Asp Val Phe Ser Cys Ser Val Met His
420 425 430
Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
435 440 445
Gly Lys
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20 25 30
Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45
Gly Arg Ile Arg Ser Lys Ala Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
50 55 60
Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
65 70 75 80
Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr
85 90 95
Tyr Cys Val Arg His Gly Asn Phe Gly Asp Ser Tyr Val Ser Trp Phe
100 105 110
Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Lys Pro
115 120 125
Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly
130 135 140
Ser Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly
145 150 155 160
Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr
165 170 175
Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg
180 185 190
Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg
195 200 205
Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly
210 215 220
Ala Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser
225 230 235 240
Asn His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Glu Pro
245 250 255
Lys Ser Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Pro
260 265 270
Val Ala Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
275 280 285
Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val
290 295 300
Lys His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val

305 310 315 320
Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
325 330 335
Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
340 345 350
Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
355 360 365
Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
370 375 380
Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Gln Met Thr Lys Asn Gln
385 390 395 400
Val Lys Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala
405 410 415
Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
420 425 430
Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
435 440 445
Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
450 455 460
Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
465 470 475 480
Leu Ser Pro Gly Lys
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Gln Ile Val Leu Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
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20 25 30
His Trp Phe Gln Gln Lys Pro Gly Lys Ser Pro Lys Pro Leu Ile Tyr
35 40 45
Ala Thr Ser Asn Leu Ala Ser Gly Val Pro Val Arg Phe Ser Gly Ser
50 55 60
Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu
65 70 75 80
Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Trp Thr His Asn Pro Pro Thr

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

130 135 140

Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val
145 150 155 160

Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala
165 170 175

Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val
180 185 190

Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His
195 200 205

Lys Pro Ser Asp Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys
210 215 220

Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Pro Val Ala Gly
225 230 235 240

Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile
245 250 255

Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Lys His Glu
260 265 270

Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His
275 280 285

Asn Ala Lys Thr Lys Pro Arg Glu Glu Glu Tyr Asn Ser Thr Tyr Arg
290 295 300

Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys
305 310 315 320

Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu
325 330 335

Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr
340 345 350

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

Thr Cys Asp Val Ser Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp
370 375 380

Glu Ser Asp Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val
385 390 395 400

Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp
405 410 415

Lys Ser Arg Trp Glu Gln Gly Asp Val Phe Ser Cys Ser Val Met His
420 425 430

Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
435 440 445

Gly Lys
450

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

Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val
290 295 300

Lys His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
305 310 315 320

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
325 330 335

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
340 345 350

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
355 360 365

Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
370 375 380

Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Gln Met Thr Lys Asn Gln
385 390 395 400

Val Lys Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala
405 410 415

Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
420 425 430

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
435 440 445

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
450 455 460

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
465 470 475 480

Leu Ser Pro Gly Lys
485

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<223> /注=“人工序列说明:合成多肽”
<400> 388

Gln Ile Val Leu Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Trp Ser Val Ser Tyr Ile
20 25 30

His Trp Phe Gln Gln Lys Pro Gly Lys Ser Pro Lys Pro Leu Ile Tyr
35 40 45

Ala Thr Ser Asn Leu Ala Ser Gly Val Pro Val Arg Phe Ser Gly Ser

50 55 60

Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu
65 70 75 80

Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Trp Thr His Asn Pro Pro Thr
85 90 95

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala Pro
100 105 110

Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr
115 120 125

Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys
130 135 140

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

Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser
165 170 175

Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala
180 185 190

Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe
195 200 205

Asn Arg Gly Glu Cys
210

<210> 389
<211> 450
<212> PRT
<213> 人工序列
<220>
<221> 来源
<223> /注=“人工序列说明:合成多肽”
<400> 389

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30

Asn Met His Trp Val Arg Gln Ala Pro Gly Gln Arg Leu Glu Trp Met
35 40 45

Gly Ala Ile Tyr Pro Gly Asn Gly Ala Thr Ser Tyr Ser Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Ile Thr Ala Asp Thr Ser Ala Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Ser Tyr Tyr Met Gly Gly Asp Trp Tyr Phe Asp Val Trp Gly

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

435 440 445

Gly Lys
450

<210> 390
<211> 485
<212> PRT
<213> 人工序列
<220>
<221> 来源
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<400> 390

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

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

<210> 391
<211> 213
<212> PRT
<213> 人工序列
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<221> 来源
<223> /注="人工序列说明:合成多肽"
<400> 391
Gln Ile Val Leu Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Trp Ser Val Ser Tyr Ile

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

<210> 392
<211> 450
<212> PRT
<213> 人工序列
<220>
<221> 来源
<223> /注=“人工序列说明:合成多肽”
<400> 392
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30
Asn Met His Trp Val Arg Gln Ala Pro Gly Gln Arg Leu Glu Trp Met
35 40 45
Gly Ala Ile Tyr Pro Gly Asn Gly Ala Thr Ser Tyr Ser Gln Lys Phe
50 55 60
Gln Gly Arg Val Thr Ile Thr Ala Asp Thr Ser Ala Ser Thr Ala Tyr

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

405 410 415
Lys Ser Arg Trp Glu Gln Gly Asp Val Phe Ser Cys Ser Val Met His
420 425 430
Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
435 440 445
Gly Lys
450
<210> 393
<211> 485
<212> PRT
<213> 人工序列
<220>
<221> 来源
<223> /注=“人工序列说明:合成多肽”
<400> 393
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Thr Tyr
20 25 30
Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45
Gly Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
50 55 60
Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
65 70 75 80
Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr
85 90 95
Tyr Cys Val Arg His Gly Asn Phe Gly Gln Ser Tyr Val Ser Trp Phe
100 105 110
Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Lys Pro
115 120 125
Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly
130 135 140
Ser Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly
145 150 155 160
Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr
165 170 175
Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg
180 185 190
Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg
195 200 205
Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly

210 215 220

Ala Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser
225 230 235 240

Asn His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Glu Pro
245 250 255

Lys Ser Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Pro
260 265 270

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

Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val
290 295 300

Lys His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
305 310 315 320

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
325 330 335

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
340 345 350

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
355 360 365

Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
370 375 380

Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Gln Met Thr Lys Asn Gln
385 390 395 400

Val Lys Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala
405 410 415

Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
420 425 430

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
435 440 445

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
450 455 460

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
465 470 475 480

Leu Ser Pro Gly Lys
485

<210> 394

<211> 213

<212> PRT

<213> 人工序列

<220>

<221> 来源

<223> /注=“人工序列说明:合成多肽”

<400> 394

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

<210> 395

<211> 450

<212> PRT

<213> 人工序列

<220>

<221> 来源

<223> /注=“人工序列说明:合成多肽”

<400> 395

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

35 40 45

Gly Ala Ile Tyr Pro Gly Asn Gly Ala Thr Ser Tyr Ser Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Ile Thr Ala Asp Thr Ser Ala Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Ser Tyr Tyr Met Gly Gly Asp Trp Tyr Phe Asp Val Trp Gly
100 105 110

Ala Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser
115 120 125

Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala
130 135 140

Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val
145 150 155 160

Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala
165 170 175

Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val
180 185 190

Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His
195 200 205

Lys Pro Ser Asp Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys
210 215 220

Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Pro Val Ala Gly
225 230 235 240

Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile
245 250 255

Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Lys His Glu
260 265 270

Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His
275 280 285

Asn Ala Lys Thr Lys Pro Arg Glu Glu Glu Tyr Asn Ser Thr Tyr Arg
290 295 300

Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys
305 310 315 320

Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu
325 330 335

Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr
340 345 350

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

Thr Cys Asp Val Ser Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp

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

<210> 396
<211> 485
<212> PRT
<213> 人工序列
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<223> /注="人工序列说明:合成多肽"
<400> 396
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Thr Tyr
20 25 30
Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45
Gly Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
50 55 60
Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
65 70 75 80
Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr
85 90 95
Tyr Cys Val Arg His Gly Asn Phe Gly Asp Glu Tyr Val Ser Trp Phe
100 105 110
Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Lys Pro
115 120 125
Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly
130 135 140
Ser Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly
145 150 155 160
Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr
165 170 175
Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg

180 185 190

Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg
195 200 205

Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly
210 215 220

Ala Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser
225 230 235 240

Asn His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Glu Pro
245 250 255

Lys Ser Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Pro
260 265 270

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

Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val
290 295 300

Lys His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
305 310 315 320

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
325 330 335

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
340 345 350

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
355 360 365

Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
370 375 380

Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Gln Met Thr Lys Asn Gln
385 390 395 400

Val Lys Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala
405 410 415

Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
420 425 430

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
435 440 445

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
450 455 460

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
465 470 475 480

Leu Ser Pro Gly Lys
485

<210> 397
<211> 213
<212> PRT

<213> 人工序列
<220>
<221> 来源
<223> /注="人工序列说明:合成多肽"
<400> 397

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

<210> 398
<211> 450
<212> PRT
<213> 人工序列
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<221> 来源
<223> /注="人工序列说明:合成多肽"
<400> 398

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

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

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

<210> 399
<211> 485
<212> PRT
<213> 人工序列
<220>
<221> 来源
<223> /注="人工序列说明:合成多肽"
<400> 399
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Thr Tyr
20 25 30
Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45
Gly Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
50 55 60
Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
65 70 75 80
Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr
85 90 95
Tyr Cys Val Arg His Gly Asn Phe Gly Asp Asn Tyr Val Ser Trp Phe
100 105 110
Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Lys Pro
115 120 125
Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly
130 135 140
Ser Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly

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

485

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<213> 人工序列
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<223> /注="人工序列说明:合成多肽"
<400> 400

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

<210> 401
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<221> 来源

<223> /注=“人工序列说明:合成多肽”

<400> 401

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

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

<210> 402
<211> 485
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<400> 402
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Thr Tyr
20 25 30
Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45
Gly Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
50 55 60
Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
65 70 75 80
Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr
85 90 95
Tyr Cys Val Arg His Gly Asn Phe Gly Asp Pro Tyr Val Ser Trp Phe
100 105 110
Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Lys Pro

115 120 125

Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly

130 135 140

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

145 150 155 160

Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr

165 170 175

Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg

180 185 190

Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg

195 200 205

Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly

210 215 220

Ala Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser

225 230 235 240

Asn His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Glu Pro

245 250 255

Lys Ser Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Pro

260 265 270

Val Ala Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr

275 280 285

Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val

290 295 300

Lys His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val

305 310 315 320

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser

325 330 335

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu

340 345 350

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala

355 360 365

Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro

370 375 380

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

385 390 395 400

Val Lys Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala

405 410 415

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

420 425 430

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu

435 440 445

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser

450 455 460

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
465 470 475 480

Leu Ser Pro Gly Lys
485

<210> 403
<211> 213
<212> PRT
<213> 人工序列
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<221> 来源
<223> /注="人工序列说明:合成多肽"
<400> 403

Gln Ile Val Leu Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Trp Ser Val Ser Tyr Ile
20 25 30

His Trp Phe Gln Gln Lys Pro Gly Lys Ser Pro Lys Pro Leu Ile Tyr
35 40 45

Ala Thr Ser Asn Leu Ala Ser Gly Val Pro Val Arg Phe Ser Gly Ser
50 55 60

Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu
65 70 75 80

Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Trp Thr His Asn Pro Pro Thr
85 90 95

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala Pro
100 105 110

Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr
115 120 125

Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys
130 135 140

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

Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser
165 170 175

Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala
180 185 190

Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe
195 200 205

Asn Arg Gly Glu Cys
210

<210> 404

<211> 450
<212> PRT
<213> 人工序列
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<221> 来源
<223> /注="人工序列说明:合成多肽"
<400> 404

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

275 280 285

Asn Ala Lys Thr Lys Pro Arg Glu Glu Glu Tyr Asn Ser Thr Tyr Arg
290 295 300

Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys
305 310 315 320

Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu
325 330 335

Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr
340 345 350

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

Thr Cys Asp Val Ser Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp
370 375 380

Glu Ser Asp Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val
385 390 395 400

Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp
405 410 415

Lys Ser Arg Trp Glu Gln Gly Asp Val Phe Ser Cys Ser Val Met His
420 425 430

Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
435 440 445

Gly Lys
450

<210> 405
<211> 485
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<213> 人工序列
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<221> 来源
<223> /注=“人工序列说明:合成多肽”
<400> 405

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Thr Tyr
20 25 30

Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

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

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
65 70 75 80

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

85 90 95

Tyr Cys Val Arg His Gly Asn Phe Gly Asp Gln Tyr Val Ser Trp Phe
100 105 110

Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Lys Pro
115 120 125

Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly
130 135 140

Ser Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly
145 150 155 160

Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr
165 170 175

Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg
180 185 190

Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg
195 200 205

Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly
210 215 220

Ala Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser
225 230 235 240

Asn His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Glu Pro
245 250 255

Lys Ser Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Pro
260 265 270

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

Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val
290 295 300

Lys His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
305 310 315 320

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
325 330 335

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
340 345 350

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
355 360 365

Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
370 375 380

Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Gln Met Thr Lys Asn Gln
385 390 395 400

Val Lys Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala
405 410 415

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

420 425 430

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
435 440 445

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
450 455 460

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
465 470 475 480

Leu Ser Pro Gly Lys
485

<210> 406
<211> 213
<212> PRT
<213> 人工序列
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<221> 来源
<223> /注="人工序列说明:合成多肽"
<400> 406

Gln Ile Val Leu Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Trp Ser Val Ser Tyr Ile
20 25 30

His Trp Phe Gln Gln Lys Pro Gly Lys Ser Pro Lys Pro Leu Ile Tyr
35 40 45

Ala Thr Ser Asn Leu Ala Ser Gly Val Pro Val Arg Phe Ser Gly Ser
50 55 60

Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu
65 70 75 80

Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Trp Thr His Asn Pro Pro Thr
85 90 95

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala Pro
100 105 110

Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr
115 120 125

Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys
130 135 140

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

Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser
165 170 175

Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala
180 185 190

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

195 200 205

Asn Arg Gly Glu Cys
210

<210> 407
<211> 450
<212> PRT
<213> 人工序列
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<221> 来源
<223> /注=“人工序列说明:合成多肽”
<400> 407

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

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

<210> 408
<211> 485
<212> PRT
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<223> /注=“人工序列说明:合成多肽”
<400> 408
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Thr Tyr
20 25 30
Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45
Gly Arg Ile Arg Ser Lys Ala Asn Asn Tyr Ala Thr Ala Tyr Ala Asp

50 55 60

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

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

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<223> /注=“人工序列说明:合成多肽”
<400> 409
Gln Ile Val Leu Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Trp Ser Val Ser Tyr Ile
20 25 30
His Trp Phe Gln Gln Lys Pro Gly Lys Ser Pro Lys Pro Leu Ile Tyr
35 40 45
Ala Thr Ser Asn Leu Ala Ser Gly Val Pro Val Arg Phe Ser Gly Ser
50 55 60
Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu
65 70 75 80
Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Trp Thr His Asn Pro Pro Thr
85 90 95
Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala Pro
100 105 110
Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr
115 120 125
Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys
130 135 140
Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu
145 150 155 160
Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser

165 170 175
Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala
180 185 190
Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe
195 200 205
Asn Arg Gly Glu Cys
210

<210> 410
<211> 450
<212> PRT
<213> 人工序列
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<221> 来源
<223> /注="人工序列说明:合成多肽"
<400> 410
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30
Asn Met His Trp Val Arg Gln Ala Pro Gly Gln Arg Leu Glu Trp Met
35 40 45
Gly Ala Ile Tyr Pro Gly Asn Gly Ala Thr Ser Tyr Ser Gln Lys Phe
50 55 60
Gln Gly Arg Val Thr Ile Thr Ala Asp Thr Ser Ala Ser Thr Ala Tyr
65 70 75 80
Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95
Ala Arg Ser Tyr Tyr Met Gly Gly Asp Trp Tyr Phe Asp Val Trp Gly
100 105 110
Ala Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser
115 120 125
Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala
130 135 140
Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val
145 150 155 160
Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala
165 170 175
Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val
180 185 190
Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His
195 200 205
Lys Pro Ser Asp Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys

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

<210> 411
<211> 485
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<213> 人工序列
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<221> 来源
<223> /注="人工序列说明:合成多肽"
<400> 411
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Thr Tyr

20 25 30

Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

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

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
65 70 75 80

Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Val Arg His Gly Asn Phe Gly Ala Ser Tyr Val Ser Trp Phe
100 105 110

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Lys Pro
115 120 125

Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly
130 135 140

Ser Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly
145 150 155 160

Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr
165 170 175

Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg
180 185 190

Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg
195 200 205

Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly
210 215 220

Ala Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser
225 230 235 240

Asn His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Glu Pro
245 250 255

Lys Ser Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Pro
260 265 270

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

Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val
290 295 300

Lys His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
305 310 315 320

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
325 330 335

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
340 345 350

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala

355 360 365

Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
370 375 380

Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Gln Met Thr Lys Asn Gln
385 390 395 400

Val Lys Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala
405 410 415

Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
420 425 430

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
435 440 445

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
450 455 460

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
465 470 475 480

Leu Ser Pro Gly Lys
485

<210> 412
<211> 213
<212> PRT
<213> 人工序列
<220>
<221> 来源
<223> /注="人工序列说明:合成多肽"
<400> 412

Gln Ile Val Leu Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Trp Ser Val Ser Tyr Ile
20 25 30

His Trp Phe Gln Gln Lys Pro Gly Lys Ser Pro Lys Pro Leu Ile Tyr
35 40 45

Ala Thr Ser Asn Leu Ala Ser Gly Val Pro Val Arg Phe Ser Gly Ser
50 55 60

Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu
65 70 75 80

Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Trp Thr His Asn Pro Pro Thr
85 90 95

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala Pro
100 105 110

Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr
115 120 125

Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys

130 135 140

Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu
145 150 155 160
Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser
165 170 175
Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala
180 185 190
Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe
195 200 205
Asn Arg Gly Glu Cys
210

<210> 413
<211> 450
<212> PRT
<213> 人工序列
<220>
<221> 来源
<223> /注="人工序列说明:合成多肽"
<400> 413
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30
Asn Met His Trp Val Arg Gln Ala Pro Gly Gln Arg Leu Glu Trp Met
35 40 45
Gly Ala Ile Tyr Pro Gly Asn Gly Ala Thr Ser Tyr Ser Gln Lys Phe
50 55 60
Gln Gly Arg Val Thr Ile Thr Ala Asp Thr Ser Ala Ser Thr Ala Tyr
65 70 75 80
Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95
Ala Arg Ser Tyr Tyr Met Gly Gly Asp Trp Tyr Phe Asp Val Trp Gly
100 105 110
Ala Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser
115 120 125
Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala
130 135 140
Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val
145 150 155 160
Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala
165 170 175
Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val

180 185 190

Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His

195 200 205

Lys Pro Ser Asp Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys

210 215 220

Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Pro Val Ala Gly

225 230 235 240

Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile

245 250 255

Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Lys His Glu

260 265 270

Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His

275 280 285

Asn Ala Lys Thr Lys Pro Arg Glu Glu Glu Tyr Asn Ser Thr Tyr Arg

290 295 300

Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys

305 310 315 320

Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu

325 330 335

Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr

340 345 350

Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu

355 360 365

Thr Cys Asp Val Ser Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp

370 375 380

Glu Ser Asp Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val

385 390 395 400

Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp

405 410 415

Lys Ser Arg Trp Glu Gln Gly Asp Val Phe Ser Cys Ser Val Met His

420 425 430

Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro

435 440 445

Gly Lys

450

<210> 414

<211> 485

<212> PRT

<213> 人工序列

<220>

<221> 来源

<223> /注=“人工序列说明:合成多肽”

<400> 414

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

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

<210> 415
<211> 213
<212> PRT
<213> 人工序列
<220>
<221> 来源
<223> /注="人工序列说明:合成多肽"
<400> 415
Gln Ile Val Leu Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Trp Ser Val Ser Tyr Ile
20 25 30
His Trp Phe Gln Gln Lys Pro Gly Lys Ser Pro Lys Pro Leu Ile Tyr
35 40 45
Ala Thr Ser Asn Leu Ala Ser Gly Val Pro Val Arg Phe Ser Gly Ser
50 55 60
Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu
65 70 75 80
Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Trp Thr His Asn Pro Pro Thr
85 90 95
Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala Pro

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

<210> 416
<211> 450
<212> PRT
<213> 人工序列
<220>
<221> 来源
<223> /注="人工序列说明:合成多肽"
<400> 416
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30
Asn Met His Trp Val Arg Gln Ala Pro Gly Gln Arg Leu Glu Trp Met
35 40 45
Gly Ala Ile Tyr Pro Gly Asn Gly Ala Thr Ser Tyr Ser Gln Lys Phe
50 55 60
Gln Gly Arg Val Thr Ile Thr Ala Asp Thr Ser Ala Ser Thr Ala Tyr
65 70 75 80
Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95
Ala Arg Ser Tyr Tyr Met Gly Gly Asp Trp Tyr Phe Asp Val Trp Gly
100 105 110
Ala Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser
115 120 125
Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala
130 135 140
Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val

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

<210> 417
<211> 485
<212> PRT

<213> 人工序列

<220>

<221> 来源

<223> /注="人工序列说明:合成多肽"

<400> 417

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

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

<210> 418
<211> 213
<212> PRT
<213> 人工序列
<220>
<221> 来源
<223> /注=“人工序列说明:合成多肽”
<400> 418
Gln Ile Val Leu Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Trp Ser Val Ser Tyr Ile
20 25 30
His Trp Phe Gln Gln Lys Pro Gly Lys Ser Pro Lys Pro Leu Ile Tyr
35 40 45
Ala Thr Ser Asn Leu Ala Ser Gly Val Pro Val Arg Phe Ser Gly Ser
50 55 60
Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu

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

<210> 419
<211> 297
<212> PRT
<213> 智人(Homo sapiens)
<400> 419
Met Thr Thr Pro Arg Asn Ser Val Asn Gly Thr Phe Pro Ala Glu Pro
1 5 10 15
Met Lys Gly Pro Ile Ala Met Gln Ser Gly Pro Lys Pro Leu Phe Arg
20 25 30
Arg Met Ser Ser Leu Val Gly Pro Thr Gln Ser Phe Phe Met Arg Glu
35 40 45
Ser Lys Thr Leu Gly Ala Val Gln Ile Met Asn Gly Leu Phe His Ile
50 55 60
Ala Leu Gly Gly Leu Leu Met Ile Pro Ala Gly Ile Tyr Ala Pro Ile
65 70 75 80
Cys Val Thr Val Trp Tyr Pro Leu Trp Gly Gly Ile Met Tyr Ile Ile
85 90 95
Ser Gly Ser Leu Leu Ala Ala Thr Glu Lys Asn Ser Arg Lys Cys Leu
100 105 110
Val Lys Gly Lys Met Ile Met Asn Ser Leu Ser Leu Phe Ala Ala Ile
115 120 125
Ser Gly Met Ile Leu Ser Ile Met Asp Ile Leu Asn Ile Lys Ile Ser
130 135 140

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

<210> 420
<211> 378
<212> PRT
<213> 智人(Homo sapiens)
<400> 420

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

130 135 140

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

<210> 421
<211> 116
<212> PRT
<213> 人工序列
<220>
<221> 来源
<223> /注="人工序列说明:合成多肽"
<400> 421
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Trp Val

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

<210> 422
<211> 5
<212> PRT
<213> 人工序列
<220>
<221> 来源
<223> /注=“人工序列说明:合成肽”
<400> 422
Ser Tyr Asn Met His
1 5

<210> 423
<211> 17
<212> PRT
<213> 人工序列
<220>
<221> 来源
<223> /注=“人工序列说明:合成肽”
<400> 423
Ala Ile Tyr Pro Gly Asn Gly Ala Thr Ser Tyr Ser Gln Lys Phe Gln
1 5 10 15
Gly

<210> 424
<211> 12
<212> PRT
<213> 人工序列
<220>
<221> 来源
<223> /注=“人工序列说明:合成肽”
<400> 424

Ser Tyr Tyr Met Gly Gly Asp Trp Tyr Phe Asp Val
1 5 10

<210> 425
<211> 106
<212> PRT
<213> 人工序列
<220>
<221> 来源
<223> /注=“人工序列说明:合成多肽”
<400> 425

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

<210> 426
<211> 10
<212> PRT
<213> 人工序列
<220>
<221> 来源
<223> /注=“人工序列说明:合成肽”
<400> 426

Arg Ala Ser Trp Ser Val Ser Tyr Ile His
1 5 10

<210> 427
<211> 7
<212> PRT
<213> 人工序列
<220>
<221> 来源
<223> /注=“人工序列说明:合成肽”
<400> 427

Ala Thr Ser Asn Leu Ala Ser
1 5

<210> 428
<211> 9
<212> PRT
<213> 人工序列
<220>
<221> 来源
<223> /注="人工序列说明:合成肽"
<400> 428
Gln Gln Trp Thr His Asn Pro Pro Thr
1 5

<210> 429
<211> 242
<212> PRT
<213> 人工序列
<220>
<221> 来源
<223> /注="人工序列说明:合成多肽"
<400> 429
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Trp Val
20 25 30
Arg Gln Ala Pro Gly Gln Arg Leu Glu Trp Met Gly Ala Ile Tyr Pro
35 40 45
Gly Asn Gly Ala Thr Ser Tyr Ser Gln Lys Phe Gln Gly Arg Val Thr
50 55 60
Ile Thr Ala Asp Thr Ser Ala Ser Thr Ala Tyr Met Glu Leu Ser Ser
65 70 75 80
Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Ser Tyr Tyr
85 90 95
Met Gly Gly Asp Trp Tyr Phe Asp Val Trp Gly Ala Gly Thr Leu Val
100 105 110
Thr Val Ser Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys
115 120 125
Pro Gly Ser Gly Lys Pro Gly Ser Gln Ile Val Leu Thr Gln Ser Pro
130 135 140
Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg
145 150 155 160
Ala Ser Trp Ser Val Ser Tyr Ile His Trp Phe Gln Gln Lys Pro Gly
165 170 175

Lys Ser Pro Lys Pro Leu Ile Tyr Ala Thr Ser Asn Leu Ala Ser Gly
180 185 190
Val Pro Val Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Thr Leu
195 200 205
Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln
210 215 220
Gln Trp Thr His Asn Pro Pro Thr Phe Gly Gly Gly Thr Lys Val Glu
225 230 235 240
Ile Lys

<210> 430
<211> 121
<212> PRT
<213> 人工序列
<220>
<221> 来源
<223> /注=“人工序列说明:合成多肽”
<400> 430
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30
Asn Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45
Gly Ala Ile Tyr Pro Gly Asn Gly Asp Thr Ser Tyr Asn Gln Lys Phe
50 55 60
Gln Gly Arg Val Thr Ile Thr Ala Asp Lys Ser Ile Ser Thr Ala Tyr
65 70 75 80
Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95
Ala Arg Ser Thr Tyr Tyr Gly Gly Asp Trp Tyr Phe Asn Val Trp Gly
100 105 110
Ala Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 431
<211> 5
<212> PRT
<213> 人工序列
<220>
<221> 来源
<223> /注=“人工序列说明:合成肽”
<400> 431
Ser Tyr Asn Met His

1 5

<210> 432
<211> 17
<212> PRT
<213> 人工序列
<220>
<221> 来源
<223> /注="人工序列说明:合成肽"
<400> 432

Ala Ile Tyr Pro Gly Asn Gly Asp Thr Ser Tyr Asn Gln Lys Phe Gln
1 5 10 15
Gly

<210> 433
<211> 12
<212> PRT
<213> 人工序列
<220>
<221> 来源
<223> /注="人工序列说明:合成肽"
<400> 433

Ser Thr Tyr Tyr Gly Gly Asp Trp Tyr Phe Asn Val
1 5 10

<210> 434
<211> 106
<212> PRT
<213> 人工序列
<220>
<221> 来源
<223> /注="人工序列说明:合成多肽"
<400> 434

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

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
100 105

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<211> 10
<212> PRT
<213> 人工序列
<220>
<221> 来源
<223> /注=“人工序列说明:合成肽”
<400> 435
Arg Ala Ser Ser Ser Val Ser Tyr Ile His
1 5 10

<210> 436
<211> 7
<212> PRT
<213> 人工序列
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<221> 来源
<223> /注=“人工序列说明:合成肽”
<400> 436
Ala Thr Ser Asn Leu Ala Ser
1 5

<210> 437
<211> 9
<212> PRT
<213> 人工序列
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<221> 来源
<223> /注=“人工序列说明:合成肽”
<400> 437
Gln Gln Trp Thr Ser Asn Pro Pro Thr
1 5

<210> 438
<211> 247
<212> PRT
<213> 人工序列
<220>
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<400> 438
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

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

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<211> 120
<212> PRT
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<400> 439
Gln Val Gln Leu Gln Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asp Tyr
20 25 30

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

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<400> 440
Asp Tyr Tyr Met Lys
1 5

<210> 441
<211> 17
<212> PRT
<213> 人工序列
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<221> 来源
<223> /注="人工序列说明:合成肽"
<400> 441
Asp Ile Ile Pro Ser Asn Gly Ala Thr Phe Tyr Asn Gln Lys Phe Lys
1 5 10 15
Gly

<210> 442
<211> 11
<212> PRT
<213> 人工序列
<220>
<221> 来源
<223> /注="人工序列说明:合成肽"
<400> 442
Ser His Leu Leu Arg Ala Ser Trp Phe Ala Tyr

1 5 10

<210> 443
<211> 113
<212> PRT
<213> 人工序列
<220>
<221> 来源
<223> /注=“人工序列说明:合成多肽”
<400> 443

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

<210> 444
<211> 17
<212> PRT
<213> 人工序列
<220>
<221> 来源
<223> /注=“人工序列说明:合成肽”
<400> 444

Lys Ser Ser Gln Ser Leu Leu Asn Thr Gly Asn Gln Lys Asn Tyr Leu
1 5 10 15
Thr

<210> 445
<211> 7
<212> PRT
<213> 人工序列
<220>
<221> 来源
<223> /注=“人工序列说明:合成肽”

<400> 445
Trp Ala Ser Thr Arg Glu Ser
1 5
<210> 446
<211> 9
<212> PRT
<213> 人工序列
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<221> 来源
<223> /注=“人工序列说明:合成肽”
<400> 446
Gln Asn Asp Tyr Ser Tyr Pro Tyr Thr
1 5
<210> 447
<211> 253
<212> PRT
<213> 人工序列
<220>
<221> 来源
<223> /注=“人工序列说明:合成多肽”
<400> 447
Gln Val Gln Leu Gln Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asp Tyr
20 25 30
Tyr Met Lys Trp Val Lys Gln Ser His Gly Lys Ser Leu Glu Trp Met
35 40 45
Gly Asp Ile Ile Pro Ser Asn Gly Ala Thr Phe Tyr Asn Gln Lys Phe
50 55 60
Lys Gly Lys Ala Thr Leu Thr Val Asp Arg Ser Thr Ser Thr Ala Tyr
65 70 75 80
Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95
Ala Arg Ser His Leu Leu Arg Ala Ser Trp Phe Ala Tyr Trp Gly Gln
100 105 110
Gly Thr Leu Val Thr Val Ser Ser Gly Lys Pro Gly Ser Gly Lys Pro
115 120 125
Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Asp Phe Val Met
130 135 140
Thr Gln Ser Pro Asp Ser Leu Ala Val Ser Leu Gly Glu Arg Ala Thr
145 150 155 160
Ile Asn Cys Lys Ser Ser Gln Ser Leu Leu Asn Thr Gly Asn Gln Lys

165 170 175
Asn Tyr Leu Thr Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro Lys Leu
180 185 190
Leu Ile Tyr Trp Ala Ser Thr Arg Glu Ser Gly Val Pro Asp Arg Phe
195 200 205
Thr Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu
210 215 220
Gln Ala Glu Asp Val Ala Val Tyr Tyr Cys Gln Asn Asp Tyr Ser Tyr
225 230 235 240
Pro Tyr Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
245 250

<210> 448
<211> 6
<212> PRT
<213> 人工序列
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<221> 来源
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His His His His His His
1 5
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<211> 5
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<221> 来源
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<400> 449
Gly Ser Gly Gly Ser
1 5
<210> 450
<211> 5
<212> PRT
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<220>
<221> 来源
<223> /注=“人工序列说明:合成肽”
<400> 450
Gly Gly Gly Gly Ser
1 5
<210> 451

<211> 4
<212> PRT
<213> 人工序列
<220>
<221> 来源
<223> /注="人工序列说明:合成肽"
<400> 451
Gly Gly Gly Ser
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<210> 452
<211> 4
<212> PRT
<213> 人工序列
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<221> 来源
<223> /注="人工序列说明:合成肽"
<400> 452
Asp Glu Asp Glu
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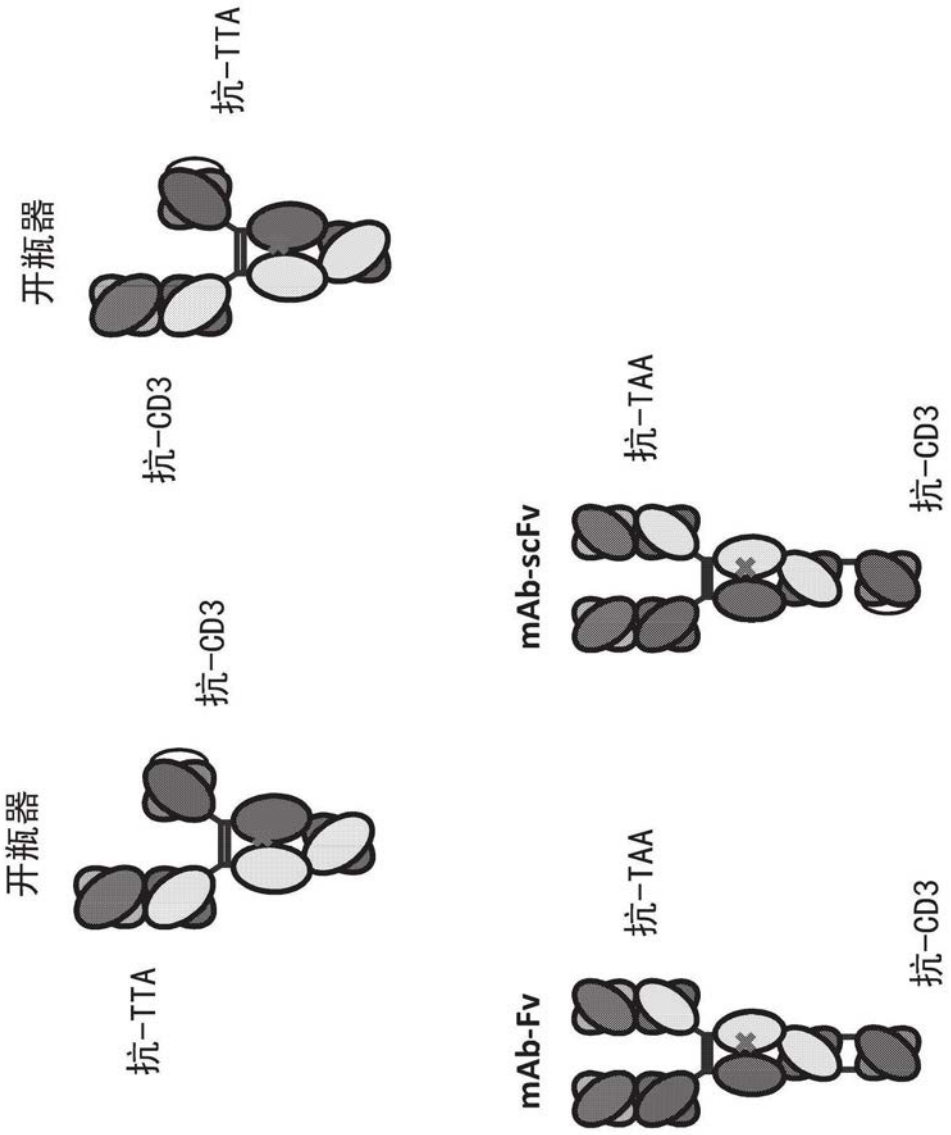
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抗-CD3
开瓶器
抗-CD3
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mAb-scFv
抗-TAA
抗-CD3

图1A

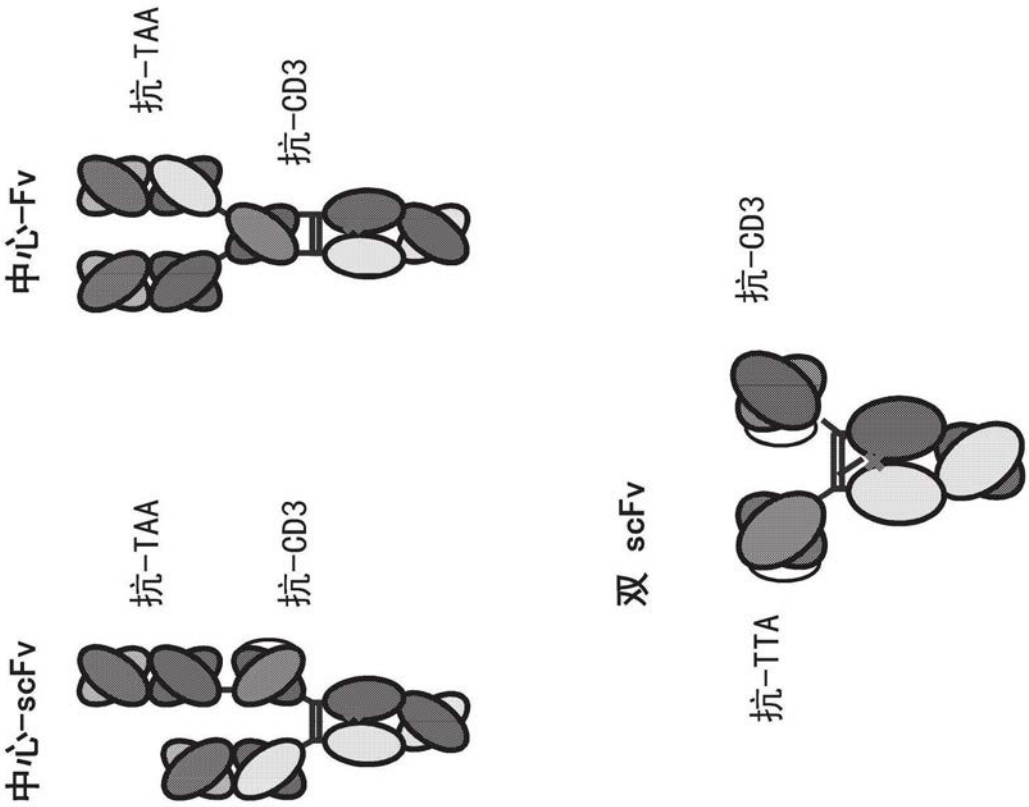



图1B

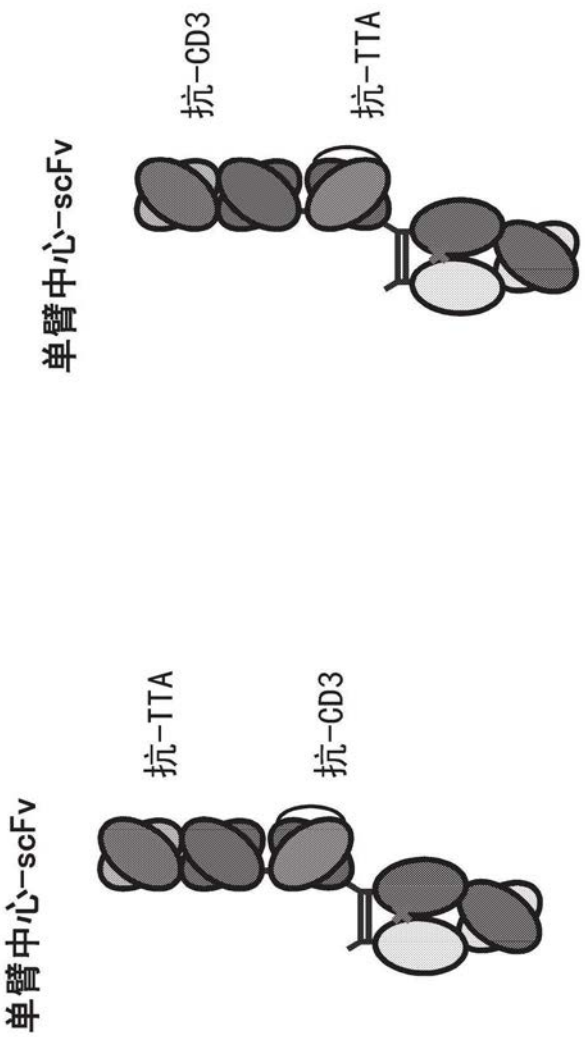



图1C

高 CD3: 抗-CD3_H1.30_L1.47

| 是什么 | 序列 | SEQ ID NO: |
|---|---|---|
| 可变重链(vh)结构域 | EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDSKNTLYLQMNSLRAEDTAVYYCVRHGNFGDSYVSWFAYWGQGTLVTVSS | 1 |
| vhCDR1 | TYAMN | 2 |
| vhCDR2 | RIRSKYNNYATYYADSVKG | 3 |
| vhCDR3 | HGNFGDSYVSWFAY | 4 |
| 可变轻链(vl)结构域 | QAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDEADYYCALWYSNHWVFGGGTKLTVL | 5 |
| vlCDR1 | GSSTGAVTTSNYAN | 6 |
| vlCDR2 | GTNKRAP | 7 |
| vlCDR3 | ALWYSNHWV | 8 |
| scFv(含带电荷的接头) | EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDSKNTLYLQMNSLRAEDTAVYYCVRHGNFGDSYVSWFAYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDEADYYCALWYSNHWVFGGGTKLTVL | 9 |

图2

高-中 #1 CD3:抗-CD3_H1.32_L1.47

| 是什么 | 序列 | SEQ ID NO: |
|---|---|---|
| 可变重链(vh)结构域 | EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKANNYATYYADSVKGRFTISRDDSKNTLYLQMNSLRAEDTAVYYCVRHGNFGDSYVSWFAYWGQGTLVTVSS | 10 |
| vhCDR1 | TYAMN | 11 |
| vhCDR2 | RIRSKANNYATYYADSVKG | 12 |
| vhCDR3 | HGNFGDSYVSWFAY | 13 |
| 可变轻链(vl)结构域 | QAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDEADYYCALWYSNHWVFGGGTKLTVL | 14 |
| vlCDR1 | GSSTGAVTTSNYAN | 15 |
| vlCDR2 | GTNKRAP | 16 |
| vlCDR3 | ALWYSNHWV | 17 |
| scFv (含带电荷的接头) | EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKANNYATYYADSVKGRFTISRDDSKNTLYLQMNSLRAEDTAVYYCVRHGNFGDSYVSWFAYWGQGTLVTVSSGKPGSGKPGSGKPGSQAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDEADYYCALWYSNHWVFGGGTKLTVL | 18 |

图3

高-中 #2 CD3: 抗-CD3_H1.89_L1.47

| 是什么 | 序列 | SEQ ID NO: |
|---|---|---|
| 可变重链(vh)结构域 | EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDSKNTLYLQMNSLRAEDTAVYYCVRHGNFGDEYVSWFAYWGQGTLVTVSS | 19 |
| vhCDR1 | TYAMN | 20 |
| vhCDR2 | RIRSKYNNYATYYADSVKG | 21 |
| vhCDR3 | HGNFGDEYVSWFAY | 22 |
| 可变轻链(vl)结构域 | QAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDEADYYCALWYSNHWVFGGGTKLTVL | 23 |
| vlCDR1 | GSSTGAVTTSNYAN | 24 |
| vlCDR2 | GTNKRAP | 25 |
| vlCDR3 | ALWYSNHWV | 26 |
| scFv (含带电荷的接头) | EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDSKNTLYLQMNSLRAEDTAVYYCVRHGNFGDEYVSWFAYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDEADYYCALWYSNHWVFGGGTKLTVL | 27 |

图4

高-中 #3 CD3: 抗-CD3_H1.90_L1.47

| 是什么 | 序列 | SEQ ID NO: |
|---|---|---|
| 可变重链(vh)结构域 | EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDSKNTLYLQMNSLRAEDTAVYYCVRHGNFGDPYVSWFAYWGQGTLVTVSS | 28 |
| vhCDR1 | TYAMN | 29 |
| vhCDR2 | RIRSKYNNYATYYADSVKG | 30 |
| vhCDR3 | HGNFGDPYVSWFAY | 31 |
| 可变轻链(vl)结构域 | QAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDEADYYCALWYSNHWVFGGGTKLTVL | 32 |
| vlCDR1 | GSSTGAVTTSNYAN | 33 |
| vlCDR2 | GTNKRAP | 34 |
| vlCDR3 | ALWYSNHWV | 35 |
| scFv (含带电荷的接头) | EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDSKNTLYLQMNSLRAEDTAVYYCVRHGNFGDPYVSWFAYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDEADYYCALWYSNHWVFGGGTKLTVL | 36 |

图5

中 ermediate CD3: 抗-CD3_H1.33_L1.47

| 是什么 | 序列 | SEQ ID NO: |
|---|---|---|
| 可变重链(vh)结构域 | EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDSKNTLY LQMNSLRAEDTAVYYCVRHGNFGDSYVSWFDYWGQGTLVTVSS | 37 |
| vhCDR1 | TYAMN | 38 |
| vhCDR2 | RIRSKYNNYATYYADSVKG | 39 |
| vhCDR3 | HGNFGDSYVSWFDY | 40 |
| 可变轻链(vl)结构域 | QAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPE DEADYYCALWYSNHWVFGGGTKLTVL | 41 |
| vlCDR1 | GSSTGAVTTSNYAN | 42 |
| vlCDR2 | GTNKRAP | 43 |
| vlCDR3 | ALWYSNHWV | 44 |
| scFv (含带电荷的接头) | EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDSKNTLY LQMNSLRAEDTAVYYCVRHGNFGDSYVSWFDYWGQGTLVTVSSGKPGSGKPGSGKPGSQAVVTQEPSLTVSPGGT VTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDEADYYCALWYSNHW VFGGGTKLTVL | 45 |

图6

低 CD3: 抗-CD3_H1.31_L1.47

| 是什么 | 序列 | SEQ ID NO: |
|---|---|---|
| 可变重链(vh)结构域 | EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMSWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDSKNTLYLQMNSLRAEDTAVYYCVRHGNFGDSYVSWFAYWGQGTLVTVSS | 46 |
| vhCDR1 | TYAMS | 47 |
| vhCDR2 | RIRSKYNNYATYYADSVKG | 48 |
| vhCDR3 | HGNFGDSYVSWFAY | 49 |
| 可变轻链(vl)结构域 | QAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDEADYYCALWYSNHWVFGGGTKLTVL | 50 |
| vlCDR1 | GSSTGAVTTSNYAN | 51 |
| vlCDR2 | GTNKRAP | 52 |
| vlCDR3 | ALWYSNHWV | 53 |
| scFv (含带电荷的接头) | EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMSWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDSKNTLYLQMNSLRAEDTAVYYCVRHGNFGDSYVSWFAYWGQGTLVTVSSGKPGSGKPGSGKPGSQAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDEADYYCALWYSNHWVFGGGTKLTVL | 54 |

图7

高 CD38: OKT10_H1.77_L1.24

| 是什么 | 序列 | SEQ ID NO: |
|---|---|---|
| 可变重链(vh)结构域 | EVQLVESGGGLVQPGGSLRLSCAASGFTFSYSWMNWVRQAPGKGLEWVSEINPQSSTINYATSVKGRFTISRDNSKNTLYLQ MNSLRAEDTAVYYCARYGNWFPYWGQGTLVTVSS | 55 |
| vhCDR1 | YSWMN | 56 |
| vhCDR2 | EINPQSSTINYATSVKG | 57 |
| vhCDR3 | YGNWFPY | 58 |
| 可变轻链(vl)结构域 | DIVMTQSPSSLSASVGDRVTITCRASQNVDTWVAWYQQKPGQSPKALIYSASRYSGVPDRFTGSGSGTDFTLTISSLQPEDFA TYFCQQYDSYPLTFGGGTKLEIK | 59 |
| vlCDR1 | RASQNVDTWVA | 60 |
| vlCDR2 | SASYRYS | 61 |
| vlCDR3 | QQYDSYPLT | 62 |
| scFv(含带电荷的接头) | EVQLVESGGGLVQPGGSLRLSCAASGFTFSYSWMNWVRQAPGKGLEWVSEINPQSSTINYATSVKGRFTISRDNSKNTLYLQ MNSLRAEDTAVYYCARYGNWFPYWGQGTLVTVSSGKPGSGKPGSGKPGSDIVMTQSPSSLSASVGDRVTITCRASQ NVDTWVAWYQQKPGQSPKALIYSASRYSGVPDRFTGSGSGTDFTLTISSLQPEDFATYFCQQYDSYPLTFGGGTKLEIK | 63 |

图8

中 CD38: OKT10_H1L1.24

| 是什么 | 序列 | SEQ ID NO: |
|---|---|---|
| 可变重链(vh)结构域 | EVQLVESGGGLVQPGGSLRLSCAASGFDFSRSWMNWVRQAPGKGLEWVSEINPDSSTINYATSVKGRFTISRDNSKNTLYLQ MNSLRAEDTAVYYCARYGNWFPYWGQGTLVTVSS | 64 |
| vhCDR1 | RSWMN | 65 |
| vhCDR2 | EINPDSSTINYATSVKG | 66 |
| vhCDR3 | YGNWFPY | 67 |
| 可变轻链(vl)结构域 | DIVMTQSPSSLSASVGDRVTITCRASQNVDTWVAWYQQKPGQSPKALIYSASRYSGVPDRFTGSGSGTDFTLTISSLQPEDFA TYFCQQYDSYPLTFGGGTKLEIK | 68 |
| vlCDR1 | RASQNVDTWVA | 69 |
| vlCDR2 | SASYRYS | 70 |
| vlCDR3 | QQYDSYPLT | 71 |
| scFv(含带电荷的接头) | EVQLVESGGGLVQPGGSLRLSCAASGFDFSRSWMNWVRQAPGKGLEWVSEINPDSSTINYATSVKGRFTISRDNSKNTLYLQ MNSLRAEDTAVYYCARYGNWFPYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSDIVMTQSPSSLSASVGDRVTITCRASQ NVDTWVAWYQQKPGQSPKALIYSASRYSGVPDRFTGSGSGTDFTLTISSLQPEDFATYFCQQYDSYPLTFGGGTKLEIK | 72 |

图9

低 CD38: OKT10_H1L1

| 是什么 | 序列 | SEQ ID NO: |
|---|---|---|
| 可变重链(vh)结构域 | EVQLVESGGGLVQPGGSLRLSCAASGFDFSRSWMNWVRQAPGKGLEWVSEINPDSSTINYATSVKGRFTISRDNSKNTLYLQ MNSLRAEDTAVYYCARYGNWFPYWGQGTLVTVSS | 73 |
| vhCDR1 | RSWMN | 74 |
| vhCDR2 | EINPDSSTINYATSVKG | 75 |
| vhCDR3 | YGNWFPY | 76 |
| 可变轻链(vl)结构域 | EVQLVESGGGLVQPGGSLRLSCAASGFDFSRSWMNWVRQAPGKGLEWVSEINPDSSTINYATSVKGRFTISRDNSKNTLYLQ MNSLRAEDTAVYYCARYGNWFPYWGQGTLVTVSS | 77 |
| vlCDR1 | RASQNVDTNVA | 78 |
| vlCDR2 | SASYRYS | 79 |
| vlCDR3 | QQYDSYPLT | 80 |
| scFv (含带电荷的接头) | EVQLVESGGGLVQPGGSLRLSCAASGFDFSRSWMNWVRQAPGKGLEWVSEINPDSSTINYATSVKGRFTISRDNSKNTLYLQ MNSLRAEDTAVYYCARYGNWFPYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSEVQLVESGGGLVQPGGSLRLSCAASGF DFSRSWMNWVRQAPGKGLEWVSEINPDSSTINYATSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARYGNWFPYWG QGTLVTVSS | 81 |

图10

XENP15331

XENP13551 HC-Fab SEQ ID NO:82

EVQLVESGGGLVQPGGSLRLSCAASGFTFSYSWMNWVRQAPGKGLEWVSEINPQSSTINYATSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARYGNWFPYWG
QGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSDTKVDKKVEPKSC
DKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALP
APIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQ
KSLSLSPGK

XENP13551 HC-scFv SEQ ID NO:83

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDSKNTLYLQMNSLRAEDTAVYYCVRHGNFGDS
YVSWFAYWGQGTLVTVSSGKPGSGKPGSGKPGSQAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLL
GGKAALTISGAQPEDEADYYCALWYSNHWVFGGGTKLTVLEPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEV
HNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKT
TPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

XENP13551 LC SEQ ID NO:84

DIVMTQSPSSLSASVGDRVTITCRASQNVDTWVAWYQQKPGQSPKALIYSASYRYSGVPDRFTGSGSGTDFTLTISSLQPEDFATYFCQQYDSYPLTFGGGTKLEIKRTVA
APSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

图11

XENP13243 HC-Fab SEQ ID NO:85

EVQLVESGGGLVQPGGSLRLSCAASGFDFSRSWMNWVRQAPGKGLEWVSEINPDSSTINYATSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARYGNWFPYW
GQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSDTKVDKKVEPKS
CDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKAL
PAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYT
QKSLSLSPGK

XENP13243 HC-scFv SEQ ID NO:86

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDSKNTLYLQMNSLRAEDTAVYYCVRHGNFGDS
YVSWFAYWGQGTLVTVSSGKPGSGKPGSGKPGSQAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLL
GGKAALTISGAQPEDEADYYCALWYSNHWVFGGGTKLTVLEPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEV
HNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKT
TPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

XENP13243 LC SEQ ID NO:87

DIVMTQSPSSLSASVGDRVTITCRASQNVDTNVAWYQQKPGQSPKALIYSASYRYSGVPDRFTGSGSGTDFTLTISSLQPEDFATYFCQQYDSYPLTFGGGTKLEIKRTVA
APSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

图12

XENP14702 抗-CD38 x 抗-CD3 Fab-scFv-Fc 重链 1 (抗-CD38 Fab-Fc (OKT10_H1.77)) SEQ ID NO:88

EVQLVESGGGLVQPGGSLRLSCAASGFTFSYSWMNWVRQAPGKGLEWVSEINPQSSTINYATSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARYGNWFPYWG
QGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSDTKVDKKVEPKSC
DKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALP
APIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQ
KSLSLSPGK

XENP14702 抗-CD38 x 抗-CD3 Fab-scFv-Fc 重链 2 (抗-CD3 scFv-Fc (αCD3_H1.31_L1.47)) SEQ ID NO:89

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMSWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDSKNTLYLQMNSLRAEDTAVYYCVRHGNFGDSY
VSWFAYWGQGTLVTVSSGKPGSGKPGSGKPGSQAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLG
GKAALTISGAQPEDEADYYCALWYSNHWVFGGGTKLTVLEPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVH
NAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTT
PPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

XENP14702 抗-CD38 x 抗-CD3 Fab-scFv-Fc 轻链 (抗-CD38 (OKT10_L1.24)) SEQ ID NO:90

DIVMTQSPSSLSASVGDRVTITCRASQNVDTWVAWYQQKPGQSPKALIYSASYRYSGVPDRFTGSGSGTDFTLTISSLQPEDFATYFCQQYDSYPLTFGGGTKLEIKRTVA
APSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

图13

XENP15426 抗-CD38 (OKT10_H1.77_L1.24, CD38 高) x 抗-CD3 (H1.33_L1.47, CD3 中) Fab-scFv-Fc

HC 1 (Fab-Fc) (SEQ ID NO:91)

EVQLVESGGGLVQPGGSLRLSCAASGFTFSYSWMNWVRQAPGKGLEWVSEINPQSSTINYATSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARYGNWFPYW
GQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSDTKVDKKVEPK
SCDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKA
LPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHY
TQKSLSLSPGK

HC 2 (scFv-Fc) (SEQ ID NO:92)

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDSKNTLYLQMNSLRAEDTAVYYCVRHGNFGD
SYVSWFDYWGQGTLVTVSSGKPGSGKPGSGKPGSQAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGS
LLGGKAALTISGAQPEDEADYYCALWYSNHWVFGGGTKLTVLEPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGV
EVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENN
YKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

LC (SEQ ID NO:93)

DIVMTQSPSSLSASVGDRVTITCRASQNVDTWVAWYQQKPGQSPKALIYSASYRYSGVPDRFTGSGSGTDFTLTISSLQPEDFATYFCQQYDSYPLTFGGGTKLEIKRTV
AAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

图14

XENP14701 抗-CD38 x 抗-CD3 Fab-scFv-Fc 重链 1 (抗-CD38 Fab-Fc (OKT10 H1)) (SEQ ID NO:94)

EVQLVESGGGLVQPGGSLRLSCAASGFDFSRSWMNWVRQAPGKGLEWVSEINPDSSTINYATSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARYGNWFPYW
GQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSDTKVDKKVEPKS
CDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKAL
PAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYT
QKSLSLSPGK

XENP14701 抗-CD38 x 抗-CD3 Fab-scFv-Fc 重链 2 (抗-CD3 scFv-Fc (αCD3 H1.31 L1.47)) (SEQ ID NO:95)

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMSWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDSKNTLYLQMNSLRAEDTAVYYCVRHGNFGDSY
VSWFAYWGQGTLVTVSSGKPGSGKPGSGKPGSQAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLG
GKAALTISGAQPEDEADYYCALWYSNHWVFGGGTKLTVLEPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVH
NAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTT
PPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

XENP14701 抗-CD38 x 抗-CD3 Fab-scFv-Fc 轻链 (抗-CD38 (OKT10 L1)) (SEQ ID NO:96)

DIVMTQSPSSLSASVGDRVTITCRASQNVDTNVAWYQQKPGQSPKALIYSASYRYSGVPDRFTGSGSGTDFTLTISSLQPEDFATYFCQQYDSYPLTFGGGTKLEIKRTVA
APSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

图15

XENP14703 抗-CD38 x 抗-CD3 Fab-scFv-Fc 重链 1 (抗-CD38 Fab-Fc (OKT10 H1)) (SEQ ID NO:97)

EVQLVESGGGLVQPGGSLRLSCAASGFDFSRSWMNWVRQAPGKGLEWVSEINPDSSTINYATSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARYGNWFPYW
GQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSDTKVDKKVEPKS
CDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKAL
PAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYT
QKSLSLSPGK

XENP14703 抗-CD38 x 抗-CD3 Fab-scFv-Fc 重链 2 (抗-CD3 scFv-Fc (αCD3 H1.31 L1.47)) (SEQ ID NO:98)

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMSWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDSKNTLYLQMNSLRAEDTAVYYCVRHGNFGDSY
VSWFAYWGQGTLVTVSSGKPGSGKPGSGKPGSQAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLG
GKAALTISGAQPEDEADYYCALWYSNHWVFGGGTKLTVLEPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVH
NAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTT
PPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

XENP14703 抗-CD38 x 抗-CD3 Fab-scFv-Fc 轻链 (抗-CD38 (OKT10 L1.53)) (SEQ ID NO:99)

DIVMTQSPSSLSASVGDRVTITCRASQNVDTNVAWYQQKPGQSPKALIYSASYRKSGVPDRFTGSGSGTDFTLTISSLQPEDFATYFCQQYDSYPLTFGGGTKLEIKRTVA
APSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

图16

**XENP13243 抗-CD38 (OKT10_H1L1) x 抗-CD3 (H1.30_L1.47) Fab-scFv-Fc**

HC 1 (Fab-Fc) (SEQ ID NO:100)

EVQLVESGGGLVQPGGSLRLSCAASGFDFSRSWMNWVRQAPGKGLEWVSEINPDSSTINYATSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARYGNWFPYW
GQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSDTKVDKKVEPK
SCDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKAL
PAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYT
QKSLSLSPGK

HC 2 (scFv-Fc) (SEQ ID NO:101)

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDSKNTLYLQMNSLRAEDTAVYYCVRHGNFGDS
YVSWFAYWGQGTLVTVSSGKPGSGKPGSGKPGSQAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLL
GGKAALTISGAQPEDEADYYCALWYSNHWVFGGGTKLTVL/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

LC (SEQ ID NO:102)

DIVMTQSPSSLSASVGDRVTITCRASQNVDTNVAWYQQKPGQSPKALIYSASYRYSGVPDRFTGSGSGTDFTLTISSLQPEDFATYFCQQYDSYPLTFGGGT/KLEIKRTV
AAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

图17

**XENP18967 抗-CD38 (OKT10_H1.77_L1.24) x 抗-CD3 (SP34_H1.32_L1.47) mAb-scFv**

HC 1 (SEQ ID NO:103)

EVQLVESGGGLVQPGGSLRLSCAASGFTFSYSWMNWVRQAPGKGLEWVSEINPQSSTINYATSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARYGNWFPYWG
QGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSDTKVDKKVEPKS
CDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKAL
PAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYT
QKSLSLSPGK

HC 2 (SEQ ID NO:104)

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKANNYATYYADSVKGRFTISRDDSKNTLYLQMNSLRAEDTAVYYCVRHGNFGDS
YVSWFAYWGQGTLVTVSS/GKPGSGKPGSGKPGS/QAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGS
LLGGKAALTISGAQPEDEADYYCALWYSNHWVFGGGTKLTVL/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGV
EVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNY
KTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

LC (SEQ ID NO:105)

DIVMTQSPSSLSASVGDRVTITCRASQNVDTWVAWYQQKPGQSPKALIYSASYRYSGVPDRFTGSGSGTDFTLTISSLQPEDFATYFCQQYDSYPLTFGGGTKLEIK/RTV
AAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

图18

**XENP18971 抗-CD38 (OKT10_H1L1) x 抗-CD3 (SP34_H1.32_L1.47) mAb-scFv**

HC 1 (SEQ ID NO:106)

EVQLVESGGGLVQPGGSLRLSCAASGFDFSRSWMNWVRQAPGKGLEWVSEINPDSSTINYATSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARYGNWFPYW
GQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSDTKVDKKVEPK
SCDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKAL
PAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYT
QKSLSLSPGK

HC 2 (SEQ ID NO:107)

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKANNYATYYADSVKGRFTISRDDSKNTLYLQMNSLRAEDTAVYYCVRHGNFGDS
YVSWFAYWGQGTLVTVSS/GKPGSGKPGSGKPGS/QAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGS
LLGGKAALTISGAQPEDEADYYCALWYSNHWVFGGGTKLTVL/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGV
EVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNY
KTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

LC (SEQ ID NO:108)

DIVMTQSPSSLSASVGDRVTITCRASQNVDTNVAWYQQKPGQSPKALIYSASYRYSGVPDRFTGSGSGTDFTLTISSLQPEDFATYFCQQYDSYPLTFGGGTKLEIK/RTV
AAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

图19

**XENP18969 抗-CD38 (OKT10_H1L1.24) x 抗-CD3 (SP34_H1.33_L1.47) mAb-scFv**

HC 1 (SEQ ID NO:109)

EVQLVESGGGLVQPGGSLRLSCAASGFDFSRSWMNWVRQAPGKGLEWVSEINPDSSTINYATSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARYGNWFPYW
GQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSDTKVDKKVEPK
SCDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKAL
PAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYT
QKSLSLSPGK

HC 2 (SEQ ID NO:110)

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDSKNTLYLQMNSLRAEDTAVYYCVRHGNFGDS
YVSWFDYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/QAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGS
LLGGKAALTISGAQPEDEADYYCALWYSNHWVFGGGTKLTVL/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGV
EVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNY
KTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

LC (SEQ ID NO:111)

DIVMTQSPSSLSASVGDRVTITCRASQNVDTWVAWYQQKPGQSPKALIYSASYRYSGVPDRFTGSGSGTDFTLTISSLQPEDFATYFCQQYDSYPLTFGGGTKLEIK/RTV
AAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

图20

**XENP18970 抗-CD38 (OKT10_H1L1.24) x 抗-CD3 (SP34_H1.31_L1.47) mAb-scFv**

HC 1 (SEQ ID NO:112)

EVQLVESGGGLVQPGGSLRLSCAASGFDFSRSWMNWVRQAPGKGLEWVSEINPDSSTINYATSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARYGNWFPYW
GQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSDTKVDKKVEPK
SCDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKAL
PAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYT
QKSLSLSPGK

HC 2 (SEQ ID NO:113)

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMSWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDSKNTLYLQMNSLRAEDTAVYYCVRHGNFGDSY
VSWFAYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/QAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLL
GGKAALTISGAQPEDEADYYCALWYSNHWVFGGGTKLTVL/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

LC (SEQ ID NO:114)

DIVMTQSPSSLSASVGDRVTITCRASQNVDTWVAWYQQKPGQSPKALIYSASYRYSGVPDRFTGSGSGTDFTLTISSLQPEDFATYFCQQYDSYPLTFGGGTKLEIK/RTV
AAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

图21

**XENP18972 抗-CD38 (OKT10_H1L1) x 抗-CD3 (SP34_H1.33_L1.47) mAb-scFv**

HC 1 (SEQ ID NO:115)

EVQLVESGGGLVQPGGSLRLSCAASGFDFSRSWMNWVRQAPGKGLEWVSEINPDSSTINYATSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARYGNWFPYW
GQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSDTKVDKKVEPK
SCDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKAL
PAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYT
QKSLSLSPGK

HC 2 (SEQ ID NO:116)

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDSKNTLYLQMNSLRAEDTAVYYCVRHGNFGDS
YVSWFDYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/QAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGS
LLGGKAALTISGAQPEDEADYYCALWYSNHWVFGGGTKLTVL/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGV
EVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNY
KTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

LC (SEQ ID NO:117)

DIVMTQSPSSLSASVGDRVTITCRASQNVDTNVAWYQQKPGQSPKALIYSASYRYSGVPDRFTGSGSGTDFTLTISSLQPEDFATYFCQQYDSYPLTFGGGTKLEIK/RTV
AAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

图22

**XENP18973 抗-CD38 (OKT10_H1L1) x 抗-CD3 (SP34_H1.31_L1.47) mAb-scFv**

HC 1 (SEQ ID NO:118)

EVQLVESGGGLVQPGGSLRLSCAASGFDFSRSWMNWVRQAPGKGLEWVSEINPDSSTINYATSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARYGNWFPYW
GQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSDTKVDKKVEPK
SCDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKAL
PAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYT
QKSLSLSPGK

HC 2 (SEQ ID NO:119)

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMSWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDSKNTLYLQMNSLRAEDTAVYYCVRHGNFGDSY
VSWFAYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/QAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLL
GGKAALTISGAQPEDEADYYCALWYSNHWVFGGGTKLTVL/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

LC (SEQ ID NO:120)

DIVMTQSPSSLSASVGDRVTITCRASQNVDTNVAWYQQKPGQSPKALIYSASYRYSGVPDRFTGSGSGTDFTLTISSLQPEDFATYFCQQYDSYPLTFGGGTKLEIK/RTV
AAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

图23

XENP15055 抗-CD38 (OKT10_H1L1, CD38 低) x 抗-CD3 (H1.33_L1.47, CD3 中) Fab-scFv-Fc

HC 1 (Fab-Fc) (SEQ ID NO:121)

EVQLVESGGGLVQPGGSLRLSCAASGFDFSRSWMNWVRQAPGKGLEWVSEINPDSSTINYATSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARYGNWFPYW
GQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSDTKVDKKVEPK
SCDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKA
LPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHY
TQKSLSLSPGK

HC 2 (scFv-Fc) (SEQ ID NO:122)

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDSKNTLYLQMNSLRAEDTAVYYCVRHGNFGD
SYVSWFDYWGQGTLVTVSSGKPGSGKPGSGKPGSQAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGS
LLGGKAALTISGAQPEDEADYYCALWYSNHWVFGGGTKLTVLEPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGV
EVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENN
YKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

LC (SEQ ID NO:123)

DIVMTQSPSSLSASVGDRVTITCRASQNVDTNVAWYQQKPGQSPKALIYSASYRYSGVPDRFTGSGSGTDFTLTISSLQPEDFATYFCQQYDSYPLTFGGGTKLEIKRTV
AAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

图24

XENP13544 抗-CD38 (OKT10_H1L1, CD38 低) x 抗-CD3 (H1.79_L1.48) Fab-scFv-Fc

HC 1 (Fab-Fc) (SEQ ID NO:124)

EVQLVESGGGLVQPGGSLRLSCAASGFDFSRSWMNWVRQAPGKGLEWVSEINPDSSTINYATSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARYGNWFPYW
GQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSDTKVDKKVEPK
SCDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKA
LPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHY
TQKSLSLSPGK

HC 2 (scFv-Fc) (SEQ ID NO:125)

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKCLEWVGRIRSKYNNYATYYADSVKGRFTISRDDSKNTLYLQMNSLRAEDTAVYYCVRHGNFGDS
YVSWFAYWGQGTLVTVSSGKPGSGKPGSGKPGSQAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSL
LGGKAALTISGAQPEDEADYYCALWYSNHWVFGCGTKLTVLEPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNY
KTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

LC (SEQ ID NO:126)

DIVMTQSPSSLSASVGDRVTITCRASQNVDTNVAWYQQKPGQSPKALIYSASYRYSGVPDRFTGSGSGTDFTLTISSLQPEDFATYFCQQYDSYPLTFGGGTKLEIKRTV
AAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

图25

XENP13694 抗-CD38 (OKT10_H1.77_L1.24, CD38 高) x 抗-CD3 (H1.79_L1.48) Fab-scFv-Fc

HC 1 (Fab-Fc) (SEQ ID NO:127)

EVQLVESGGGLVQPGGSLRLSCAASGFTFSYSWMNWVRQAPGKGLEWVSEINPQSSTINYATSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARYGNWFPYW
GQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSDTKVDKKVEPK
SCDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKA
LPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHY
TQKSLSLSPGK

HC 2 (scFv-Fc) (SEQ ID NO:128)

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKCLEWVGRIRSKYNNYATYYADSVKGRFTISRDDSKNTLYLQMNSLRAEDTAVYYCVRHGNFGDS
YVSWFAYWGQGTLVTVSSGKPGSGKPGSGKPGSQAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSL
LGGKAALTISGAQPEDEADYYCALWYSNHWVFGCGTKLTVLEPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNY
KTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

LC (SEQ ID NO:129)

DIVMTQSPSSLSASVGDRVTITCRASQNVDTWVAWYQQKPGQSPKALIYSASYRYSGVPDRFTGSGSGTDFTLTISSLQPEDFATYFCQQYDSYPLTFGGGTKLEIKRTV
AAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

图26

>sp|P07766|CD3E_人 T-细胞表面糖蛋白 CD3 ε 链

(SEQ ID NO:130)

MQSGTHWRVLGLCLLSVGVWGQDGNEEMGGITQTPYKVSISGTTVILTCPQYPGSEILWQ

HNDKNIGGDEDDKNIGSDEDHLSLKEFSELEQSGYYVCYPRGSKPEDANFYLYLRARVCE

NCMEMDVMSVATIVIVDICITGGLLLLVYYWSKNRKAKAKPVTRGAGAGGRQRGQNKERP

PPVPNPDYEPIRKGQRDLYSGLNQRRI

图27

人 CD38 序列, "/" 表示与胞外结构域(ECD)的连接

(SEQ ID NO:131)

MANCEFSPVSGDKPCCRLSRRAQLCLGVSILVLILVVVLAVV/VPRWRQQWSGPGTTKRFP

ETVLARCVKYTEIHPEMRHVDCQSVWDAFKGAFISKHPCNITEEDYQPLMKLGTQTVPCN

KILLWSRIKDLAHQFTQVQRDMFTLEDTLLGYLADDLTWCGEFNTSKINYQSCPDWRKDC

SNNPVSVFWKTVSRRFAEAACDVVHVMLNGSRSKIFDKNSTFGSVEVHNLQPEKVQTLEA

WVIHGGREDSRDLCQDPTIKELESIISKRNIQFSCKNIYRPDKFLQCVKNPEDSSCTSEI

ECD 结构域 (SEQ ID NO:132)

VPRWRQQWSGPGTTKRFPETVLARCVKYTEIHPEMRHVDCQSVWDAFKGAFISKHPCNITEEDYQPLMKLGTQTVPC
NKILLWSRIKDLAHQFTQVQRDMFTLEDTLLGYLADDLTWCGEFNTSKINYQSCPDWRKDC

SNNPVSVFWKTVSRRFAEAACDVVHVMLNGSRSKIFDKNSTFGSVEVHNLQPEKVQTLEA

WVIHGGREDSRDLCQDPTIKELESIISKRNIQFSCKNIYRPDKFLQCVKNPEDSSCTSEI

图28

| 单体 1 | 单体 2 |
|---|---|
| F405A | T394F |
| S364D | Y349K |
| S364E | L368K |
| S364E | Y349K |
| S364F | K370G |
| S364H | Y349K |
| S364H | Y349T |
| S364Y | K370G |
| T411K | K370E |
| V397S/F405A | T394F |
| K370R/T411K | K370E/T411E |
| L351E/S364D | Y349K/L351K |
| L351E/S364E | Y349K/L351K |
| L351E/T366D | L351K/T366K |
| P395T/V397S/F405A | T394F |
| S364D/K370G | S364Y/K370R |
| S364D/T394F | Y349K/F405A |
| S364E/F405A | Y349K/T394F |
| S364E/F405S | Y349K/T394Y |
| S364E/T411E | Y349K/D401K |
| S364H/D401K | Y349T/T411E |
| S364H/F405A | Y349T/T394F |
| S364H/T394F | Y349T/F405A |
| Y349C/S364E | Y349K/S354C |
| L351E/S364D/F405A | Y349K/L351K/T394F |
| L351K/S364H/D401K | Y349T/L351E/T411E |
| S364E/T411E/F405A | Y349K/T394F/D401K |
| S364H/D401K/F405A | Y349T/T394F/T411E |
| S364H/F405A/T411E | Y349T/T394F/D401K |

图29A

| 单体 1 | 单体 2 |
|---|---|
| K370E/T411D | T411K |
| L368E/K409E | L368K |
| Y349T/T394F/S354C | S364H/F405A/Y349C |
| T411E | D401K |
| T411E | D401R/T411R |
| Q347E/K360E | Q347R |
| L368E | S364K |
| L368E/K370S | S364K |
| L368E/K370T | S364K |
| L368E/D401R | S364K |
| L368E/D401N | S364K |
| L368E | E357S/S364K |
| L368E | S364K/K409E |
| L368E | S364K/K409V |
| L368D | S364K |
| L368D/K370S | S364K |
| L368D/K370S | S364K/E357L |
| L368D/K370S | S364K/E357Q |
| T411E/K360E/Q362E | D401K |
| K370S | S364K |
| L368E/K370S | S364K/E357Q |
| K370S | S364K/E357Q |
| T411E/K360D | D401K |
| T411E/K360E | D401K |
| T411E/Q362E | D401K |
| T411E/N390D | D401K |
| T411E | D401K/Q347K |
| T411E | D401K/Q347R |
| T411E/K360D/Q362E | D401K |

图29B

| 单体 1 | 单体 2 |
|---|---|
| T411E/K360E/N390D | D401K |
| T411E/Q362E/N390D | D401K |
| T411E/Q347R | D401K/K360D |
| T411E/Q347R | D401K/K360E |
| T411E/K360 | D401K/Q347K |
| T411E/K360D | D401K/Q347R |
| T411E/K360E | D401K/Q347K |
| T411E/K360E | D401K/Q347R |
| T411E/S364K | D401K/K370S |
| T411E/K370S | D401K/S364K |
| Q347E | E357Q |
| Q347E | E357Q/Q362K |
| K360D/Q362E | Q347R |
| K360D/Q362E | D401K |
| K360D/Q362E | Q347R/D401K |
| K360E/Q362E | Q347R |
| K360E/Q362E | D401K |
| K360E/Q362E | Q347R/D401K |
| Q362E/N390D | D401K |
| Q347E/K360D | D401N |
| K360D | Q347R/N390K |
| K360D | N390K/D401N |
| K360E | Y349H |
| K370S/Q347E | S364K |
| K370S/E357L | S364K |
| K370S/E357Q | S364K |
| K370S/Q347E/E357L | S364K |
| K370S/Q347E/E357Q | S364K |

图29C

| 单体 1 | 单体 2 |
|---|---|
| L368D/K370S/Q347E | S364K |
| L368D/K370S/E357L | S364K |
| L368D/K370S/E357Q | S364K |
| L368D/K370S/Q347E/E357L | S364K |
| L368D/K370S/Q347E/E357Q | S364K |
| L368E/K370S/Q347E | S364K |
| L368E/K370S/E357L | S364K |
| L368E/K370S/E357Q | S364K |
| L368E/K370S/Q347E/E357L | S364K |
| L368E/K370S/Q347E/E357Q | S364K |
| L368D/K370T/Q347E | S364K |
| L368D/K370T/E357L | S364K |
| L368D/K370T/E357Q | S364K |
| L368D/K370T/Q347E/E357L | S364K |
| L368D/K370T/Q347E/E357Q | S364K |
| L368E/K370T/Q347E | S364K |
| L368E/K370T/E357L | S364K |
| L368E/K370T/E357Q | S364K |
| L368E/K370T/Q347E/E357L | S364K |
| L368E/K370T/Q347E/E357Q | S364K |
| T411E/Q362E | D401K/T411K |
| T411E/N390D | D401K/T411K |
| T411E/Q362E | D401R/T411R |
| T411E/N390D | D401R/T411R |
| Y407T | T366Y |
| F405A | T394W |
| T366Y/F405A | T394W/Y407T |
| Y407A | T366W |
| T366S/L368A/Y407V | T366W |
| T366S/L368A/Y407V/Y349C | T366W/S354C |

图29D

| 单体 1 | 单体 2 |
|---|---|
| K392D/K409D | E356K/D399K |
| K370D/K392D/K409D | E356K/E357K/D399K |
| I199T/N203D/K247Q/R355Q/N384S/K392N/V397M/Q419E/K447_ | Q196K/I199T/P217R/P228R/N276K |
| I199T/N203D/K247Q/R355Q/N384S/K392N/V397M/Q419E/K447_ | Q196K/I199T/N276K |
| N384S/K392N/V397M/Q419E | N276K |
| D221E/P228E/L368E | D221R/P228R/K409R |
| C220E/P228E/L368E | C220R/E224R/P228R/K409R |
| F405L | K409R |
| T366I/K392M/T394W | F405A/Y407V |
| T366V/K409F | L351Y/Y407A |
| T366A/K392E/K409F/T411E | D399R/S400R/Y407A |
| L351K | L351E |
| I199T/N203D/K247Q/R355Q/Q419E/K447_ | Q196K/I199T/P217R/P228R/N276K |
| I199T/N203D/K247Q/R355Q/Q419E/K447_ | Q196K/I199T/N276K |
| I199T N203D K274Q R355Q N384S K392N V397M Q419E DEL447 | |
| N208D Q295E N384D Q418E N421D | |
| N208D Q295E Q418E N421D | |
| Q196K I199T P217R P228R N276K | |
| Q196K I199T N276K | |
| E269Q E272Q E283Q E357Q | |
| E269Q E272Q E283Q | |
| E269Q E272Q | |
| E269Q E283Q | |
| E272Q E283Q | |
| E269Q | |

图29E

**pI 变体**

| 变体恒定区 | 取代 |
|---|---|
| pI_ISO(-) | I199T N203D K274Q R355Q N384S K392N V397M Q419E DEL447 |
| pI_(-)_等排_A | N208D Q295E N384D Q418E N421D |
| pI_(-)_等排_B | N208D Q295E Q418E N421D |
| pI_ISO(+RR) | Q196K I199T P217R P228R N276K |
| pI_ISO(+) | Q196K I199T N276K |
| pI_(+)_等排_A | E269Q E272Q E283Q E357Q |
| pI_(+)_等排_B | E269Q E272Q E283Q |
| pI_(+)_等排_E269Q/E272Q | E269Q E272Q |
| pI_(+)_等排_E269Q/E283Q | E269Q E283Q |
| pI_(+)_等排_E272Q/E283Q | E272Q E283Q |
| pI_(+)_等排_E269Q | E269Q |

图30

消除变体

| 变体 | 变体，续 |
|---|---|
| G236R | P329K |
| S239G | A330L |
| S239K | A330S/P331S |
| S239Q | I332K |
| S239R | I332R |
| V266D | V266D/A327Q |
| S267K | V266D/P329K |
| S267R | S267R/A327Q |
| H268K | S267R/P329K |
| E269R | G236R/L328R |
| 299R | E233P/L234V/L235A/G236del/S239K |
| 299K | E233P/L234V/L235A/G236del/S267K |
| K322A | E233P/L234V/L235A/G236del/S239K/A327G |
| A327G | E233P/L234V/L235A/G236del/S267K/A327G |
| A327L | E233P/L234V/L235A/G236del |
| A327N | S239K/S267K |
| A327Q | 267K/P329K |
| L328E | |
| L328R | |
| P329A | |
| P329H | |

图31

| | |
|---|---|
| scFv 单体(+) | Fab 单体(-) |
| 异二聚体 pI 变体 S364K/E357Q | 异二聚体化 pI 变体 L368D/K370S |
| 可选 scFv 带电荷接头包括但不限于 $(GKPGS)_4$ (SEQ ID NOS 142 & 158) | 等排 pI 取代 N208D/Q295E/N384D/Q418E/N421D |
| FcKO E233P/L234V/L235A/G236del/S267K | FcKO E233P/L234V/L235A/G236del/S267K |
| 针对 FcRn 的± 428L/434S | 针对 FcRn 的± 428L/434S |
| scFv of 抗-CD3 | 抗-CD38 Fv 序列 |

| | |
|---|---|
| scFv 单体 | Fab 单体 |
| 异二聚体 pI 变体 S364K/E357Q | 异二聚体化 pI 变体 L368D/K370S |
| ± 428L/434S $(GKPGS)_4$ (SEQ ID NOS 142 & 158) | pI 取代 I199T N203D K274Q R355Q Q419E K447del |
| FcKO E233P/L234V/L235A/G236del/S267K | FcKO E233P/L234V/L235A/G236del/S267K |
| 针对 FcRn 的± 428L/434S (可选) | 针对 FcRn 的± 428L/434S (可选) |
| 抗-CD3 的 scFv | 抗-CD38 的 scFv |

图32

**带正电 scFv 接头**

| 名称 | 序列 | 长度 | 电荷 | SEQ ID NO: |
|---|---|---|---|---|
| Gly-Ser 15 | GGGGSGGGGSGGGGS | 15 | 0 | 133 |
| Whitlow 接头 | GSTSGSGKPGSGEGSTKG | 18 | +1 | 134 |
| 6paxA_1 (+A) | IRPRAIGGSKPRVA | 14 | +4 | 135 |
| +B | GKGGSGKGGSGKGGS | 15 | +3 | 136 |
| +C | GGKGSGGKGSGGKGS | 15 | +3 | 137 |
| +D | GGGKSGGGKSGGGKS | 15 | +3 | 138 |
| +E | GKGKSGKGKSGKGKS | 15 | +6 | 139 |
| +F | GGGKSGGKGSGKGGS | 15 | +3 | 140 |
| +G | GKPGSGKPGSGKPGS | 15 | +3 | 141 |
| +H | GKPGSGKPGSGKPGSGKPGS | 20 | +4 | 142 |
| +I | GKGKSGKGKSGKGKSGKGKS | 20 | +8 | 143 |

**带负电 scFv 接头**

| 名称 | 序列 | 长度 | 电荷 | SEQ ID NO: |
|---|---|---|---|---|
| Gly-Ser 15 | GGGGSGGGGSGGGGSGGGGS | 20 | 0 | 144 |
| 3hsc_2 (-A) | STAGDTHLGGEDFD | 14 | -4 | 145 |
| -B | GEGGSGEGGSGEGGS | 15 | -3 | 146 |
| -C | GGEGSGGEGSGGEGS | 15 | -3 | 147 |
| -D | GGGESGGGESGGGES | 15 | -3 | 148 |
| -E | GEGESGEGESGEGES | 15 | -6 | 149 |
| -F | GGGESGGEGSGEGGS | 15 | -3 | 150 |
| -G | GEGESGEGESGEGESGEGES | 20 | -8 | 151 |

图33A

**scFv 接头**

| | |
|---|---|
| GGGGSGGGGSGGGGS | (SEQ ID NO:152) |
| GGGGSGGGGSGGGGSGGGGS | (SEQ ID NO:153) |
| GSTSGSGKPGSGEGSTKG | (SEQ ID NO:154) |
| PRGASKSGSASQTGSAPGS | (SEQ ID NO:155) |
| GTAAAGAGAAGGAAAGAAG | (SEQ ID NO:156) |
| GTSGSSGSGSGGSGSGGGG | (SEQ ID NO:157) |
| GKPGSGKPGSGKPGSGKPGS | (SEQ ID NO:158) |

图33B

| XENP | 异二聚体-偏向变体, 链 1 | 异二聚体-偏向变体, 链 2 | 异二聚体得率 (%) | CH3 Tm (°C) |
|---|---|---|---|---|
| 12757 | 无 | 无 | 52.7 | 83.1 |
| 12758 | L368D/K370S | S364K | 94.4 | 76.6 |
| 12759 | L368D/K370S | S364K/E357L | 90.2 | 77.2 |
| 12760 | L368D/K370S | S364K/E357Q | 95.2 | 77.5 |
| 12761 | T411E/K360E/Q362E | D401K | 85.6 | 80.6 |
| 12496 | L368E/K370S | S364K | 91.5 | n.d. |
| 12511 | K370S | S364K | 59.9 | n.d. |
| 12840 | L368E/K370S | S364K/E357Q | 59.5 | n.d. |
| 12841 | K370S | S364K/E357Q | 90.4 | n.d. |
| 12894 | L368E/K370S | S364K | 41.0 | n.d. |
| 12895 | K370S | S364K | 49.3 | n.d. |
| 12896 | L368E/K370S | S364K/E357Q | 73.9 | n.d. |
| 12901 | K370S | S364K/E357Q | 87.9 | n.d. |

图34

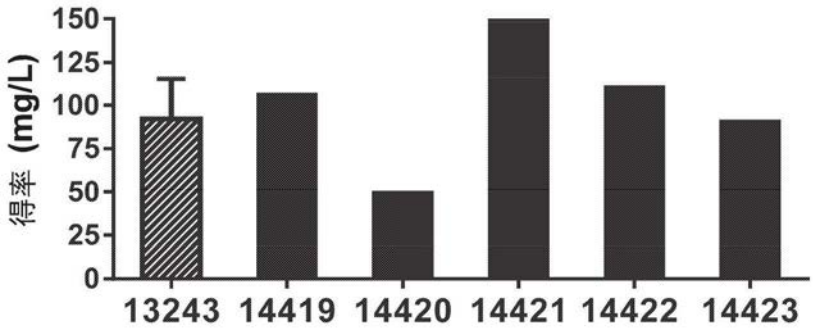

得率 (mg/L)
150
125
100
75
50
25
0
13243
14419
14420
14421
14422
14423

图35

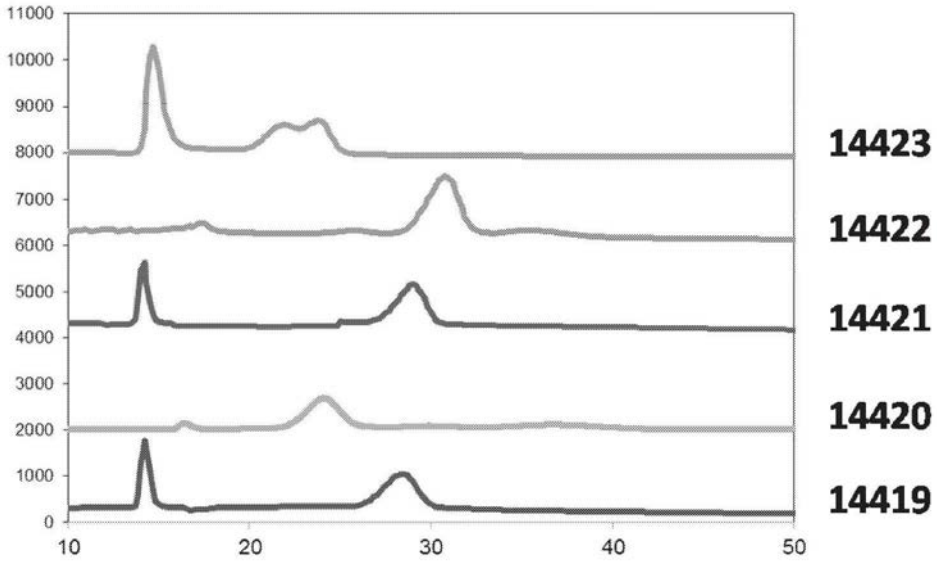

11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
10
20
30
40
50
14423
14422
14421
14420
14419

图36

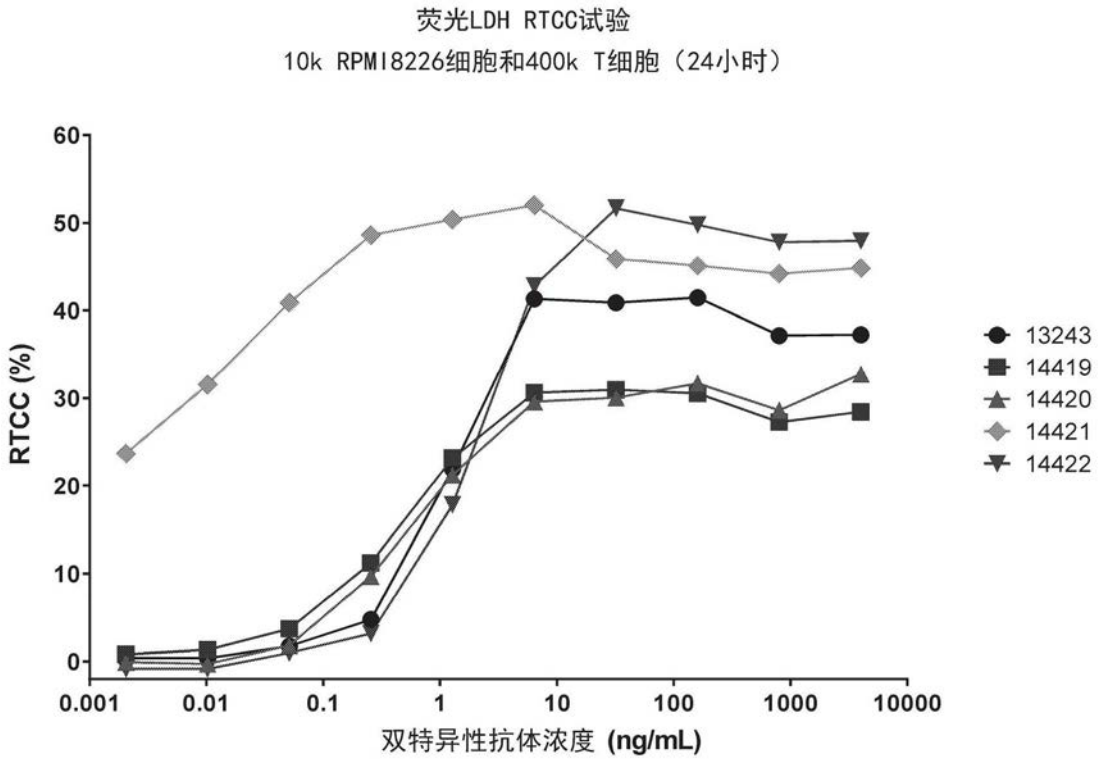
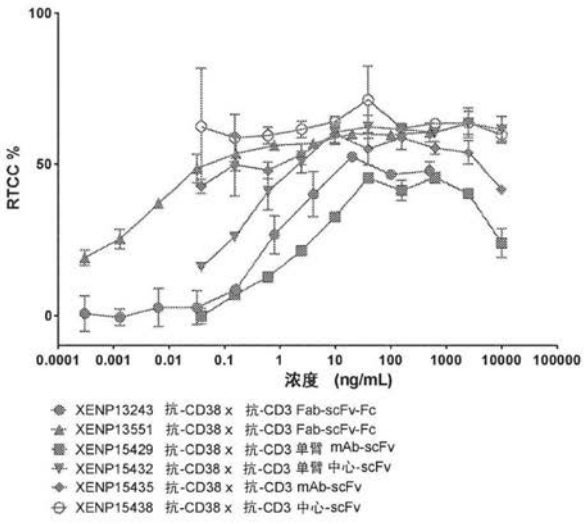
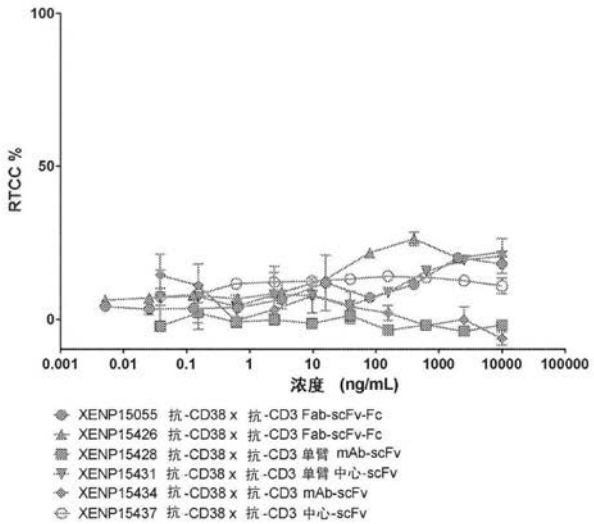

荧光LDH RTCC试验
10k RPMI8226细胞和400k T细胞（24小时）
RTCC (%)
60
50
40
30
20
10
0
0.001
0.01
0.1
1
10
100
1000
10000
双特异性抗体浓度 (ng/mL)
13243
14419
14420
14421
14422

图37


RTCC %
100
50
0
0.0001 0.001 0.01 0.1 1 10 100 1000 10000 100000
浓度 (ng/mL)
XENP13243 抗-CD38 x 抗-CD3 Fab-scFv-Fc
XENP13551 抗-CD38 x 抗-CD3 Fab-scFv-Fc
XENP15429 抗-CD38 x 抗-CD3 单臂 mAb-scFv
XENP15432 抗-CD38 x 抗-CD3 单臂 中心-scFv
XENP15435 抗-CD38 x 抗-CD3 mAb-scFv
XENP15438 抗-CD38 x 抗-CD3 中心-scFv


RTCC %
100
50
0
0.001 0.01 0.1 1 10 100 1000 10000 100000
浓度 (ng/mL)
XENP15055 抗-CD38 x 抗-CD3 Fab-scFv-Fc
XENP15426 抗-CD38 x 抗-CD3 Fab-scFv-Fc
XENP15428 抗-CD38 x 抗-CD3 单臂 mAb-scFv
XENP15431 抗-CD38 x 抗-CD3 单臂 中心-scFv
XENP15434 抗-CD38 x 抗-CD3 mAb-scFv
XENP15437 抗-CD38 x 抗-CD3 中心-scFv

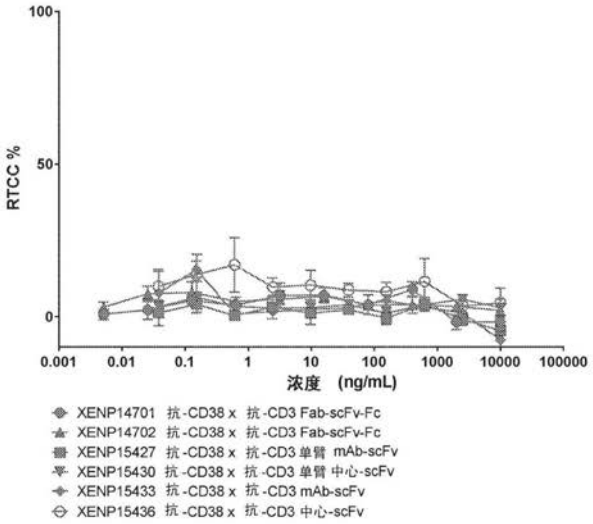

RTCC %
100
50
0
0.001 0.01 0.1 1 10 100 1000 10000 100000
浓度 (ng/mL)
XENP14701 抗-CD38 x 抗-CD3 Fab-scFv-Fc
XENP14702 抗-CD38 x 抗-CD3 Fab-scFv-Fc
XENP15427 抗-CD38 x 抗-CD3 单臂 mAb-scFv
XENP15430 抗-CD38 x 抗-CD3 单臂 中心-scFv
XENP15433 抗-CD38 x 抗-CD3 mAb-scFv
XENP15436 抗-CD38 x 抗-CD3 中心-scFv

图38

**XENP14419 抗-CD38 (OKT10_H1L1) x 抗-CD3 (H1.30_L1.47) mAb-scFv**

HC 1 (SEQ ID NO:159)

EVQLVESGGGLVQPGGSLRLSCAASGFDFSRSWMNWVRQAPGKGLEWVSEINPDSSTINYATSVKGRFTISRDNSKNT
LYLQMNSLRAEDTAVYYCARYGNWFPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVS
WNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSDTKVDKKVEPKSCDKTHTCPPCPAPPVAG
PSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTP
PVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSLSLSPGK

HC 2 (SEQ ID NO:160)

EVQLVESGGGLVQPGGSLRLSCAASGFDFSRSWMNWVRQAPGKGLEWVSEINPDSSTINYATSVKGRFTISRDNSKNT
LYLQMNSLRAEDTAVYYCARYGNWFPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVS
WNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPPVAG
PSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTT
PPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGKGGGGSGGGGSGGGGS/EVQLVESG
GGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDSKNTLYLQM
NSLRAEDTAVYYCVRHGNFGDSYVSWFAYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQEPSLTVSPGGT
VTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDEADYYCALWYS
NHWVFGGGTKLTVL

LC (SEQ ID NO:161)

DIVMTQSPSSLSASVGDRVTITCRASQNVDTNVAWYQQKPGQSPKALIYSASYRYSGVPDRFTGSGSGTDFTLTISSLQP
EDFATYFCQQYDSYPLTFGGGT/KLEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNS
QESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

图39

**XENP14420 抗-CD38 (OKT10_H1L1) x 抗-CD3 (H1.30_L1.47) mAb-Fv**

HC 1 (SEQ ID NO:162)

EVQLVESGGGLVQPGGSLRLSCAASGFDFSRSWMNWVRQAPGKGLEWVSEINPDSSTINYATSVKGRFTISRDNSKNT
LYLQMNSLRAEDTAVYYCARYGNWFPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVS
WNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSDTKVDKKVEPKSCDKTHTCPPCPAPPVAG
PSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTP
PVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSLSLSPGKGGGGSGGGGSGGGGS/EVQLVESGG
GLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDSKNTLYLQMN
SLRAEDTAVYYCVRHGNFGDSYVSWFAYWGQGTLVTVSS

HC 2 (SEQ ID NO:163)

EVQLVESGGGLVQPGGSLRLSCAASGFDFSRSWMNWVRQAPGKGLEWVSEINPDSSTINYATSVKGRFTISRDNSKNT
LYLQMNSLRAEDTAVYYCARYGNWFPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVS
WNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPPVAG
PSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTT
PPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGKGGGGSGGGGSGGGGS/QAVVTQE
PSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDEA
DYYCALWYSNHWVFGGGTKLTVL

LC (SEQ ID NO:164)

DIVMTQSPSSLSASVGDRVTITCRASQNVDTNVAWYQQKPGQSPKALIYSASYRYSGVPDRFTGSGSGTDFTLTISSLQP
EDFATYFCQQYDSYPLTFGGGT/KLEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNS
QESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

图40

**XENP14421 抗-CD38 (OKT10_H1L1) x 抗-CD3 (H1.30_L1.47)中心-scFv**

HC 1 (SEQ ID NO:165)

EVQLVESGGGLVQPGGSLRLSCAASGFDFSRSWMNWVRQAPGKGLEWVSEINPDSSTINYATSVKGRFTISRDNSKNT
LYLQMNSLRAEDTAVYYCARYGNWFPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVS
WNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSDTKVDKKVEPKSCDKTHTCPPCPAPPVAG
PSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTP
PVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSLSLSPGK

HC 2 (SEQ ID NO:166)

EVQLVESGGGLVQPGGSLRLSCAASGFDFSRSWMNWVRQAPGKGLEWVSEINPDSSTINYATSVKGRFTISRDNSKNT
LYLQMNSLRAEDTAVYYCARYGNWFPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVS
WNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCGGGGSGGGGS/EVQLV
ESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDSKNTLYL
QMNSLRAEDTAVYYCVRHGNFGDSYVSWFAYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQEPSLTVSP
GGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDEADYYCAL
WYSNHWVFGGGTKLTVL/GGGGSGGGGSKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDP
EVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVY
TLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSV
MHEALHNHYTQKSLSLSPGK

LC (SEQ ID NO:167)

DIVMTQSPSSLSASVGDRVTITCRASQNVDTNVAWYQQKPGQSPKALIYSASYRYSGVPDRFTGSGSGTDFTLTISSLQP
EDFATYFCQQYDSYPLTFGGGT/KLEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNS
QESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

图41

**XENP14422 抗-CD38 (OKT10_H1L1) x 抗-CD3 (H1.30_L1.47)单臂中心-scFv**

HC 1 (SEQ ID NO:168)

EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEE
YNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPS
DIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSLSLSPGK

HC 2 (SEQ ID NO:169)

EVQLVESGGGLVQPGGSLRLSCAASGFDFSRSWMNWVRQAPGKGLEWVSEINPDSSTINYATSVKGRFTISRDNSKNT
LYLQMNSLRAEDTAVYYCARYGNWFPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVS
WNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCGGGGSGGGGS/EVQLV
ESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDSKNTLYL
QMNSLRAEDTAVYYCVRHGNFGDSYVSWFAYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQEPSLTVSP
GGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDEADYYCAL
WYSNHWVFGGGTKLTVL/GGGGSGGGGSKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDP
EVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVY
TLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSV
MHEALHNHYTQKSLSLSPGK

LC (SEQ ID NO:170)

DIVMTQSPSSLSASVGDRVTITCRASQNVDTNVAWYQQKPGQSPKALIYSASYRYSGVPDRFTGSGSGTDFTLTISSLQP
EDFATYFCQQYDSYPLTFGGGT/KLEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNS
QESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

图42

**XENP14423 抗-CD38 (OKT10_H1L1) x 抗-CD3 (H1.30_L1.47)中心-Fv**

HC 1 (SEQ ID NO:171)

EVQLVESGGGLVQPGGSLRLSCAASGFDFSRSWMNWVRQAPGKGLEWVSEINPDSSTINYATSVKGRFTISRDNSKNT
LYLQMNSLRAEDTAVYYCARYGNWFPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVS
WNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSDTKVDKKVEPKSCGGGGSGGGGS/EVQLV
ESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDSKNTLYL
QMNSLRAEDTAVYYCVRHGNFGDSYVSWFAYWGQGTLVTVSS/GGGGSGGGGSKTHTCPPCPAPPVAGPSVFLFPP
KPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCK
VSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTPPVLDSD
GSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSLSLSPGK

HC 2 (SEQ ID NO:172)

EVQLVESGGGLVQPGGSLRLSCAASGFDFSRSWMNWVRQAPGKGLEWVSEINPDSSTINYATSVKGRFTISRDNSKNT
LYLQMNSLRAEDTAVYYCARYGNWFPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVS
WNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCGGGGSGGGGS/QAVV
TQEPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPE
DEADYYCALWYSNHWVFGGGTKLTVL/GGGGSGGGGSKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVV
VDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKG
QPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQ
GNVFSCSVMHEALHNHYTQKSLSLSPGK

LC (SEQ ID NO:173)

DIVMTQSPSSLSASVGDRVTITCRASQNVDTNVAWYQQKPGQSPKALIYSASYRYSGVPDRFTGSGSGTDFTLTISSLQP
EDFATYFCQQYDSYPLTFGGGT/KLEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNS
QESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

图43

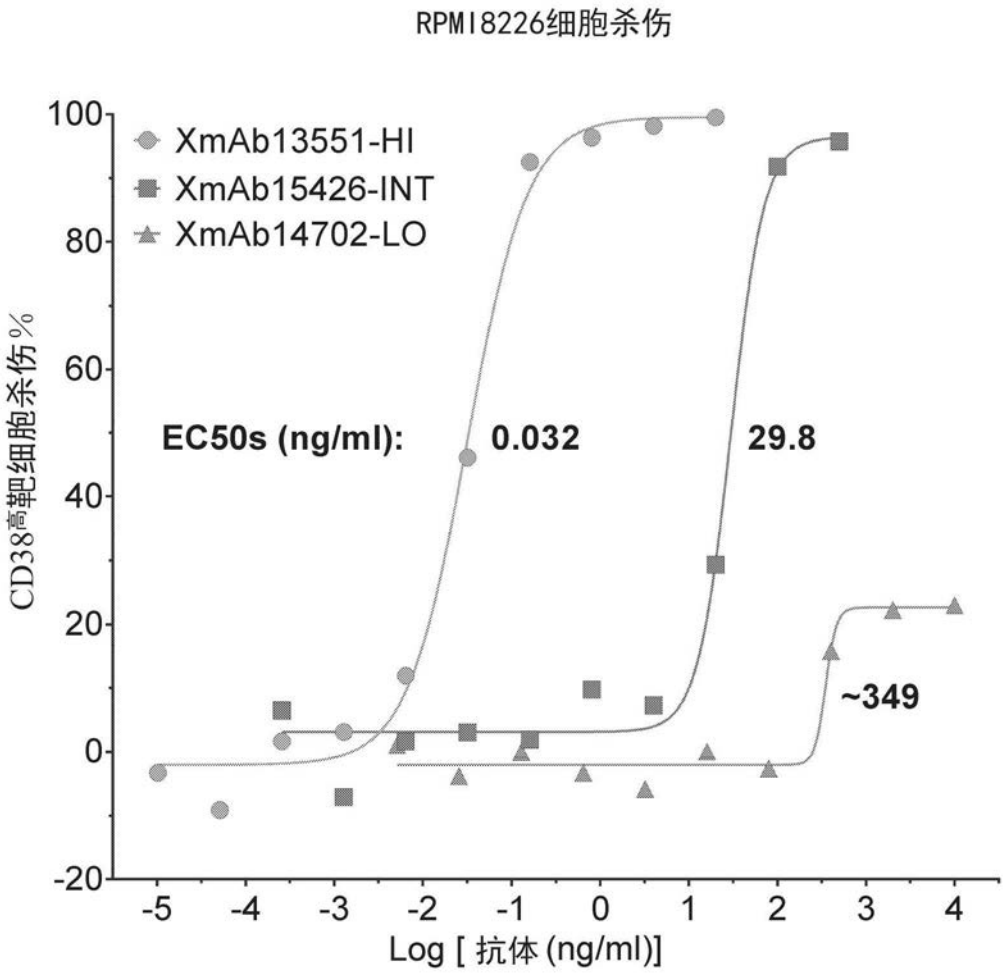

RPMI8226细胞杀伤
XmAb13551-HI
XmAb15426-INT
XmAb14702-LO
EC50s (ng/ml):
0.032
29.8
~349
CD38高靶细胞杀伤%
Log [ 抗体 (ng/ml)]
100
80
60
40
20
0
-20
-5
-4
-3
-2
-1
0
1
2
3
4

图44

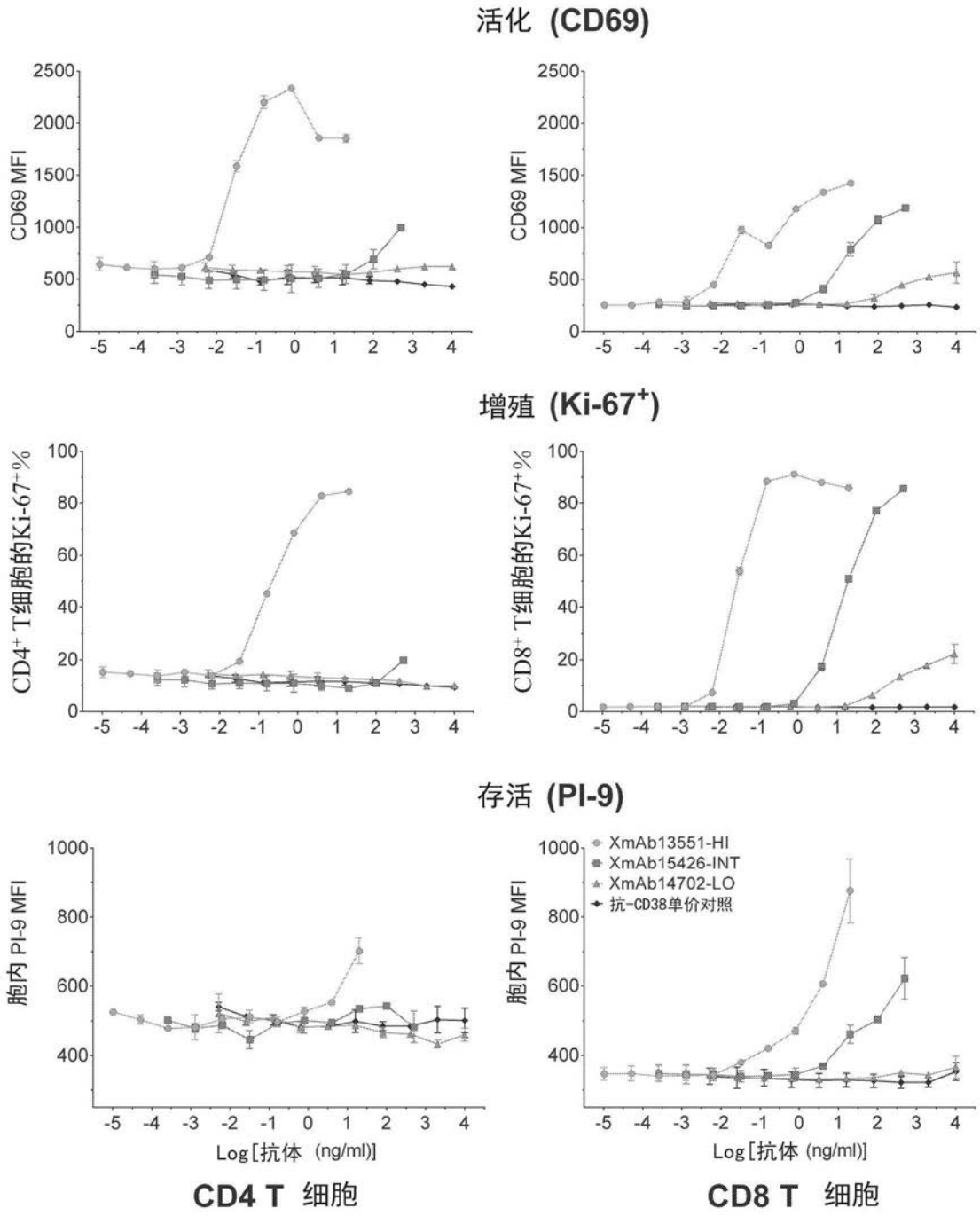

活化 (CD69)
CD69 MFI
增殖 (Ki-67+)
CD4+ T细胞的Ki-67+%
CD8+ T细胞的Ki-67+%
存活 (PI-9)
胞内 PI-9 MFI
XmAb13551-HI
XmAb15426-INT
XmAb14702-LO
抗-CD38单价对照
Log[抗体 (ng/ml)]
CD4 T 细胞
CD8 T 细胞

图45

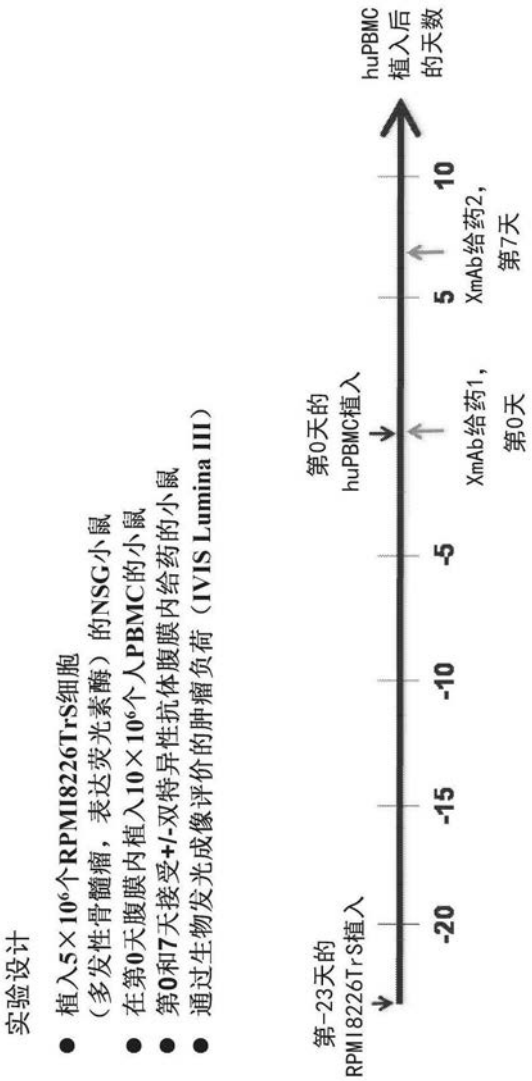

实验设计
● 植入5×10⁶个RPMI8226TrS细胞
（多发性骨髓瘤，表达荧光素酶）的NSG小鼠
● 在第0天腹膜内植入10×10⁶个人PBMC的小鼠
● 第0和7天接受+/-双特异性抗体腹膜内给药的小鼠
● 通过生物发光成像评价的肿瘤负荷（IVIS Lumina III）
第-23天的
RPMI8226TrS植入
-20
-15
-10
-5
第0天的
huPBMC植入
XmAb给药1，
第0天
5
10
XmAb给药2，
第7天
huPBMC
植入后
的天数

图46

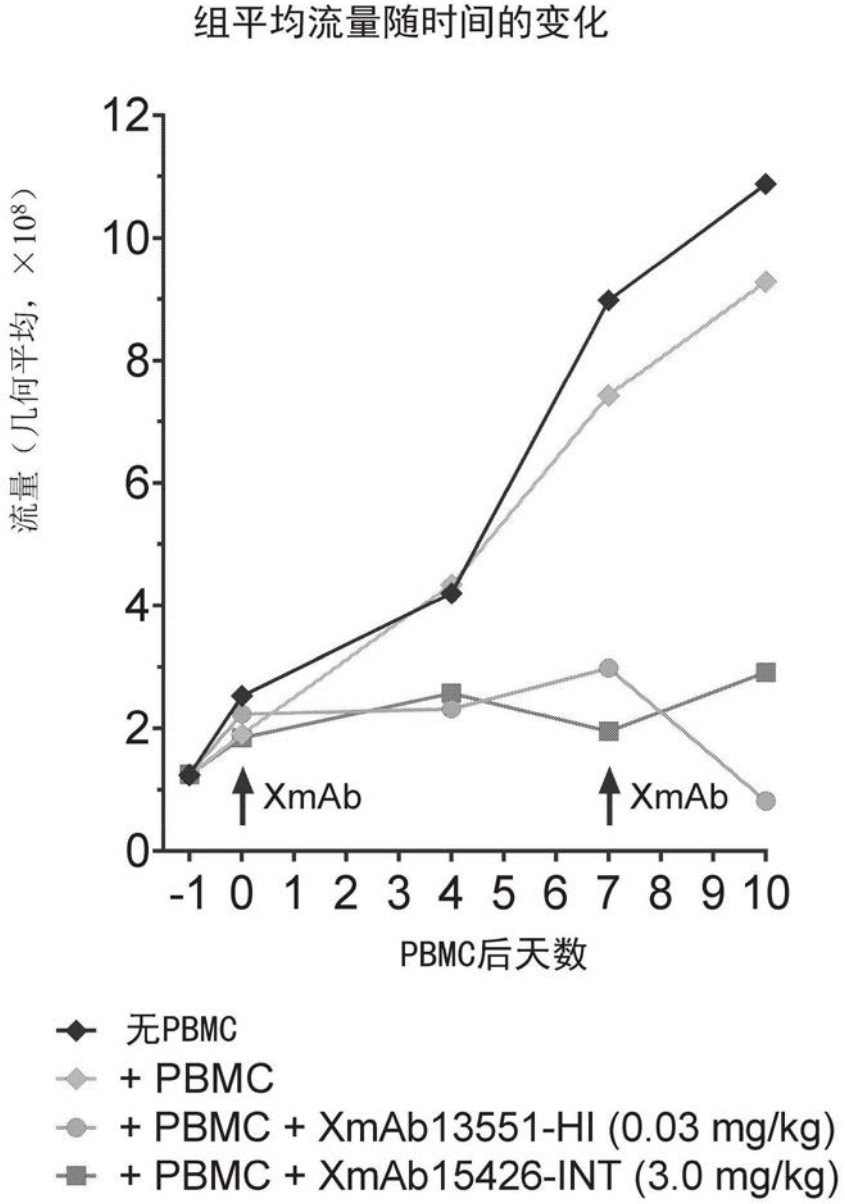

组平均流量随时间的变化
流量（几何平均，×10⁸）
12
10
8
6
4
2
0
XmAb
XmAb
-1 0 1 2 3 4 5 6 7 8 9 10
PBMC后天数
无PBMC
+ PBMC
+ PBMC + XmAb13551-HI (0.03 mg/kg)
+ PBMC + XmAb15426-INT (3.0 mg/kg)

图47

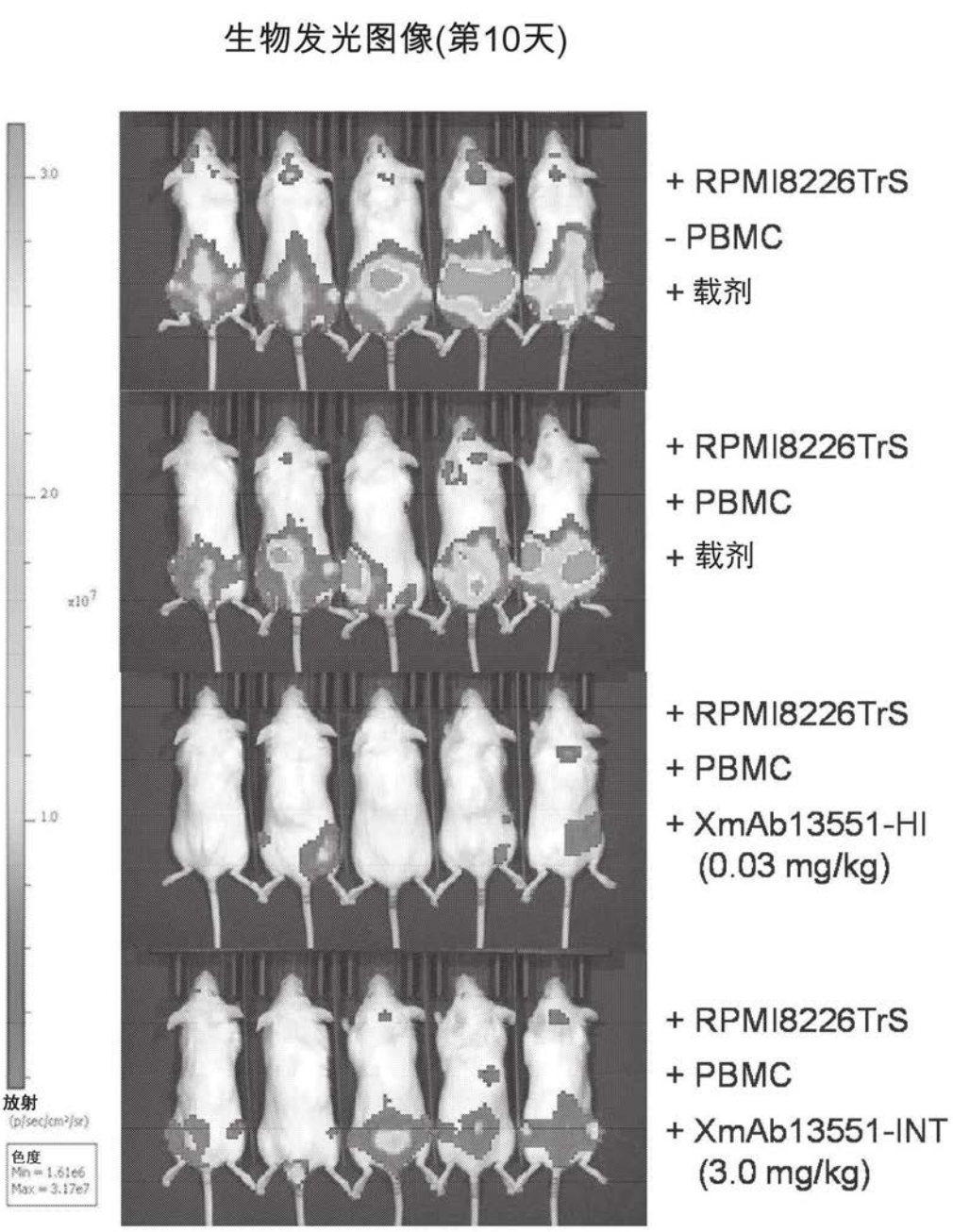

生物发光图像(第10天)
3.0
2.0
x10^7
1.0
放射
(p/sec/cm²/sr)
色度
Min = 1.61e6
Max = 3.17e7
+ RPMI8226TrS
- PBMC
+ 载剂
+ RPMI8226TrS
+ PBMC
+ 载剂
+ RPMI8226TrS
+ PBMC
+ XmAb13551-HI
(0.03 mg/kg)
+ RPMI8226TrS
+ PBMC
+ XmAb13551-INT
(3.0 mg/kg)

图48

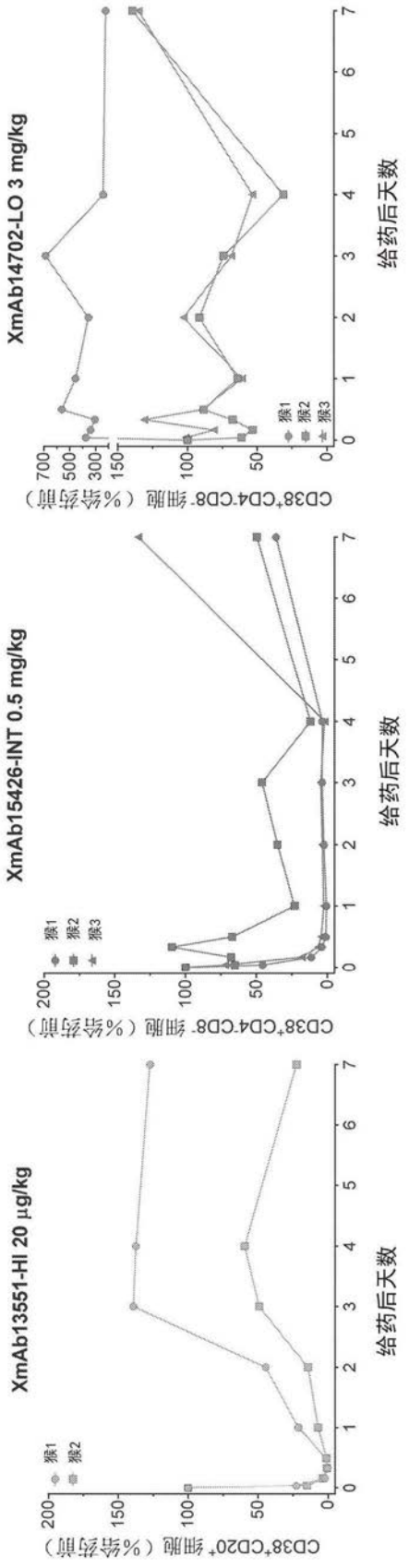

XmAb13551-HI 20 μg/kg
XmAb15426-INT 0.5 mg/kg
XmAb14702-LO 3 mg/kg
CD38+CD20+ 细胞（%给药前）
CD38+CD4-CD8- 细胞（%给药前）
给药后天数
猴1
猴2
猴3

图49

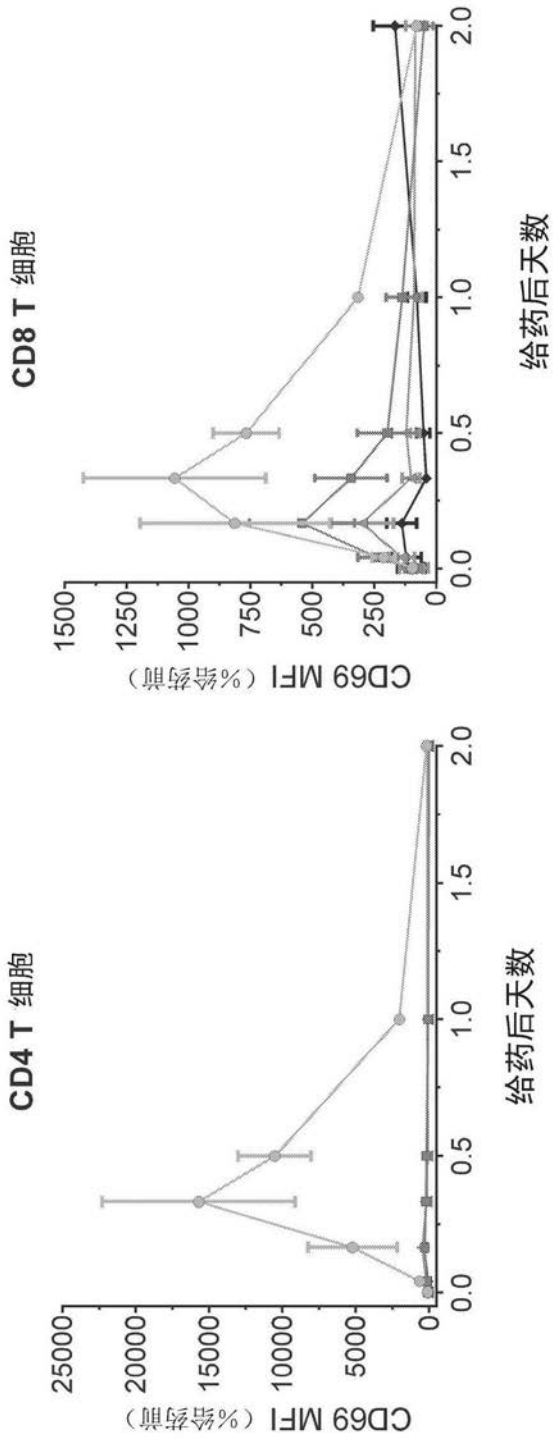

CD8 T 细胞
CD69 MFI（%给药前）
1500
1250
1000
750
500
250
0
0.0
0.5
1.0
1.5
2.0
给药后天数
CD4 T 细胞
CD69 MFI（%给药前）
25000
20000
15000
10000
5000
0
0.0
0.5
1.0
1.5
2.0
给药后天数

图50

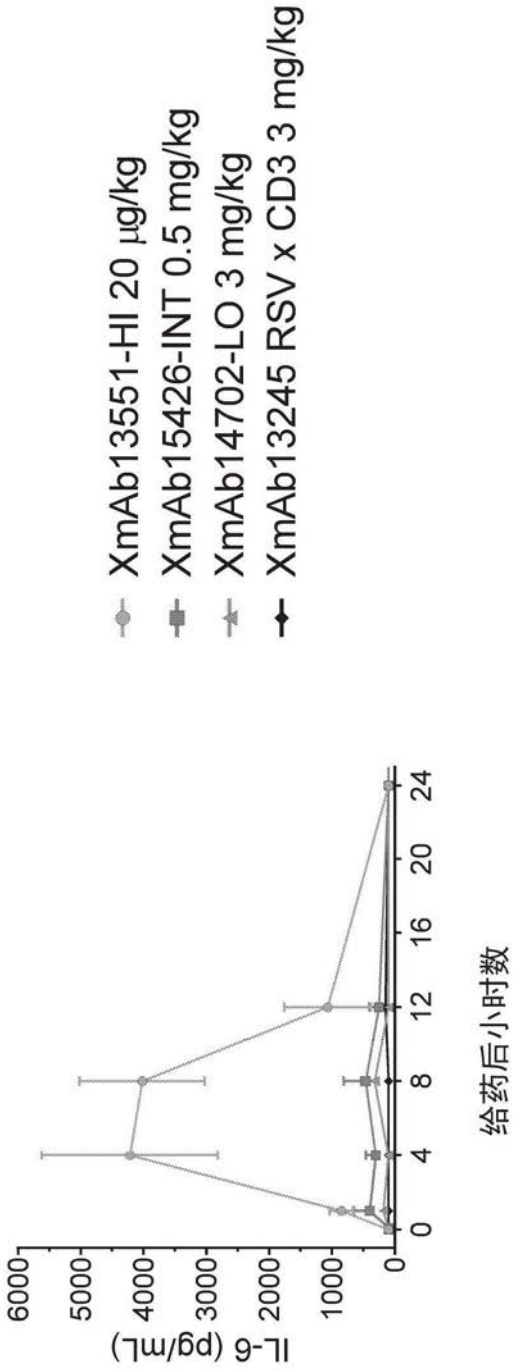

XmAb13551-HI 20 μg/kg
XmAb15426-INT 0.5 mg/kg
XmAb14702-LO 3 mg/kg
XmAb13245 RSV x CD3 3 mg/kg
IL-6 (pg/mL)
6000
5000
4000
3000
2000
1000
0
0
4
8
12
16
20
24
给药后小时数

图51

**XENP15427 抗-CD38 (OKT10_H1L1) x 抗-CD3 (H1.31_L1.47)单臂 mAb-scFv**

HC 1 (SEQ ID NO:174)

EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEE
YNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPS
DIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSLSLSPGK

HC 2 (SEQ ID NO:175)

EVQLVESGGGLVQPGGSLRLSCAASGFDFSRSWMNWVRQAPGKGLEWVSEINPDSSTINYATSVKGRFTISRDNSKNT
LYLQMNSLRAEDTAVYYCARYGNWFPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVS
WNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPPVAG
PSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTT
PPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGKGGGGSGGGGSGGGGSEVQLVESG
GGLVQPGGSLRLSCAASGFTFSTYAMSWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDSKNTLYLQM
NSLRAEDTAVYYCVRHGNFGDSYVSWFAYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQEPSLTVSPGGT
VTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDEADYYCALWYS
NHWVFGGGTKLTVL

LC (SEQ ID NO:176)

DIVMTQSPSSLSASVGDRVTITCRASQNVDTNVAWYQQKPGQSPKALIYSASYRYSGVPDRFTGSGSGTDFTLTISSLQP
EDFATYFCQQYDSYPLTFGGGTKLEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNS
QESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

图52

**XENP15428 抗-CD38 (OKT10_H1L1) x 抗-CD3 (H1.33_L1.47)单臂 mAb-scFv**

HC 1 (SEQ ID NO:177)

EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEE
YNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPS
DIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSLSLSPGK

HC 2 (SEQ ID NO:178)

EVQLVESGGGLVQPGGSLRLSCAASGFDFSRSWMNWVRQAPGKGLEWVSEINPDSSTINYATSVKGRFTISRDNSKNT
LYLQMNSLRAEDTAVYYCARYGNWFPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVS
WNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPPVAG
PSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTT
PPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGKGGGGSGGGGSGGGGSEVQLVESG
GGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDSKNTLYLQM
NSLRAEDTAVYYCVRHGNFGDSYVSWFDYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQEPSLTVSPGGT
VTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDEADYYCALWYS
NHWVFGGGTKLTVL

LC (SEQ ID NO:179)

DIVMTQSPSSLSASVGDRVTITCRASQNVDTNVAWYQQKPGQSPKALIYSASYRYSGVPDRFTGSGSGTDFTLTISSLQP
EDFATYFCQQYDSYPLTFGGGTKLEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNS
QESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

图53

**XENP15429 抗-CD38 (OKT10_H1L1) x 抗-CD3 (H1.30_L1.47)单臂 mAb-scFv**

HC 1 (SEQ ID NO:180)

EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEE
YNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPS
DIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSLSLSPGK

HC 2 (SEQ ID NO:181)

EVQLVESGGGLVQPGGSLRLSCAASGFDFSRSWMNWVRQAPGKGLEWVSEINPDSSTINYATSVKGRFTISRDNSKNT
LYLQMNSLRAEDTAVYYCARYGNWFPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVS
WNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPPVAG
PSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTT
PPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGKGGGGSGGGGSGGGGSEVQLVESG
GGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDSKNTLYLQM
NSLRAEDTAVYYCVRHGNFGDSYVSWFAYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQEPSLTVSPGGT
VTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDEADYYCALWYS
NHWVFGGGTKLTVL

LC (SEQ ID NO:182)

DIVMTQSPSSLSASVGDRVTITCRASQNVDTNVAWYQQKPGQSPKALIYSASYRYSGVPDRFTGSGSGTDFTLTISSLQP
EDFATYFCQQYDSYPLTFGGGTKLEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNS
QESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

图54

**XENP15430 抗-CD38 (OKT10_H1L1) x 抗-CD3 (H1.31_L1.47)单臂中心-scFv**

HC 1 (SEQ ID NO:183)

EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEE
YNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPS
DIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSLSLSPGK

HC 2 (SEQ ID NO:184)

EVQLVESGGGLVQPGGSLRLSCAASGFDFSRSWMNWVRQAPGKGLEWVSEINPDSSTINYATSVKGRFTISRDNSKNT
LYLQMNSLRAEDTAVYYCARYGNWFPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVS
WNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCGGGGSGGGGSEVQLVE
SGGGLVQPGGSLRLSCAASGFTFSTYAMSWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDSKNTLYLQ
MNSLRAEDTAVYYCVRHGNFGDSYVSWFAYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQEPSLTVSPG
GTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDEADYYCALW
YSNHWVFGGGTKLTVLGGGGSGGGGSKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVK
FNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLP
PSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMH
EALHNHYTQKSLSLSPGK

LC (SEQ ID NO:185)

DIVMTQSPSSLSASVGDRVTITCRASQNVDTNVAWYQQKPGQSPKALIYSASYRYSGVPDRFTGSGSGTDFTLTISSLQP
EDFATYFCQQYDSYPLTFGGGTKLEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNS
QESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

图55

**XENP15431 抗-CD38 (OKT10_H1L1) x 抗-CD3 (H1.33_L1.47)单臂中心-scFv**

HC 1 (SEQ ID NO:186)

EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEE
YNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPS
DIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSLSLSPGK

HC 2 (SEQ ID NO:187)

EVQLVESGGGLVQPGGSLRLSCAASGFDFSRSWMNWVRQAPGKGLEWVSEINPDSSTINYATSVKGRFTISRDNSKNT
LYLQMNSLRAEDTAVYYCARYGNWFPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVS
WNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCGGGGSGGGGSEVQLVE
SGGGLVQPGGSLRLSCAASGFTFSTYAMSWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDSKNTLYLQ
MNSLRAEDTAVYYCVRHGNFGDSYVSWFAYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQEPSLTVSPG
GTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDEADYYCALW
YSNHWVFGGGTKLTVLGGGGSGGGGSKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVK
FNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLP
PSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMH
EALHNHYTQKSLSLSPGK

LC (SEQ ID NO:188)

DIVMTQSPSSLSASVGDRVTITCRASQNVDTNVAWYQQKPGQSPKALIYSASYRYSGVPDRFTGSGSGTDFTLTISSLQP
EDFATYFCQQYDSYPLTFGGGTKLEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNS
QESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

图56

**XENP15432 抗-CD38 (OKT10_H1L1) x 抗-CD3 (H1.30_L1.47)单臂中心-scFv**

HC 1 (SEQ ID NO:189)

EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEE
YNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPS
DIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSLSLSPGK

HC 2 (SEQ ID NO:190)

EVQLVESGGGLVQPGGSLRLSCAASGFDFSRSWMNWVRQAPGKGLEWVSEINPDSSTINYATSVKGRFTISRDNSKNT
LYLQMNSLRAEDTAVYYCARYGNWFPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVS
WNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCGGGGSGGGGSEVQLVE
SGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDSKNTLYLQ
MNSLRAEDTAVYYCVRHGNFGDSYVSWFAYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQEPSLTVSPG
GTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDEADYYCALW
YSNHWVFGGGTKLTVLGGGGSGGGGSKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVK
FNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLP
PSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMH
EALHNHYTQKSLSLSPGK

LC (SEQ ID NO:191)

DIVMTQSPSSLSASVGDRVTITCRASQNVDTNVAWYQQKPGQSPKALIYSASYRYSGVPDRFTGSGSGTDFTLTISSLQP
EDFATYFCQQYDSYPLTFGGGTKLEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNS
QESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

图57

**XENP15433 抗-CD38 (OKT10_H1L1) x 抗-CD3 (H1.31_L1.47) mAb-scFv**

HC 1 (SEQ ID NO:192)

EVQLVESGGGLVQPGGSLRLSCAASGFDFSRSWMNWVRQAPGKGLEWVSEINPDSSTINYATSVKGRFTISRDNSKNT
LYLQMNSLRAEDTAVYYCARYGNWFPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVS
WNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSDTKVDKKVEPKSCDKTHTCPPCPAPPVAG
PSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTP
PVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSLSLSPGK

HC 2 (SEQ ID NO:193)

EVQLVESGGGLVQPGGSLRLSCAASGFDFSRSWMNWVRQAPGKGLEWVSEINPDSSTINYATSVKGRFTISRDNSKNT
LYLQMNSLRAEDTAVYYCARYGNWFPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVS
WNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPPVAG
PSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTT
PPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGKGGGGSGGGGSGGGGSEVQLVESG
GGLVQPGGSLRLSCAASGFTFSTYAMSWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDSKNTLYLQM
NSLRAEDTAVYYCVRHGNFGDSYVSWFAYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQEPSLTVSPGGT
VTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDEADYYCALWYS
NHWVFGGGTKLTVL

LC (SEQ ID NO:194)

DIVMTQSPSSLSASVGDRVTITCRASQNVDTNVAWYQQKPGQSPKALIYSASYRYSGVPDRFTGSGSGTDFTLTISSLQP
EDFATYFCQQYDSYPLTFGGGTKLEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNS
QESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

图58

**XENP15434 抗-CD38 (OKT10_H1L1) x 抗-CD3 (H1.33_L1.47) mAb-scFv**

HC 1 (SEQ ID NO:195)

EVQLVESGGGLVQPGGSLRLSCAASGFDFSRSWMNWVRQAPGKGLEWVSEINPDSSTINYATSVKGRFTISRDNSKNT
LYLQMNSLRAEDTAVYYCARYGNWFPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVS
WNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSDTKVDKKVEPKSCDKTHTCPPCPAPPVAG
PSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTP
PVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSLSLSPGK

HC 2 (SEQ ID NO:196)

EVQLVESGGGLVQPGGSLRLSCAASGFDFSRSWMNWVRQAPGKGLEWVSEINPDSSTINYATSVKGRFTISRDNSKNT
LYLQMNSLRAEDTAVYYCARYGNWFPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVS
WNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPPVAG
PSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTT
PPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGKGGGGSGGGGSGGGGSEVQLVESG
GGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDSKNTLYLQM
NSLRAEDTAVYYCVRHGNFGDSYVSWFDYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQEPSLTVSPGGT
VTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDEADYYCALWYS
NHWVFGGGTKLTVL

LC (SEQ ID NO:197)

DIVMTQSPSSLSASVGDRVTITCRASQNVDTNVAWYQQKPGQSPKALIYSASYRYSGVPDRFTGSGSGTDFTLTISSLQP
EDFATYFCQQYDSYPLTFGGGTKLEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNS
QESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

图59

**XENP15435 抗-CD38 (OKT10_H1L1) x 抗-CD3 (H1.30_L1.47) mAb-scFv**

HC 1 (SEQ ID NO:198)

EVQLVESGGGLVQPGGSLRLSCAASGFDFSRSWMNWVRQAPGKGLEWVSEINPDSSTINYATSVKGRFTISRDNSKNT
LYLQMNSLRAEDTAVYYCARYGNWFPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVS
WNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSDTKVDKKVEPKSCDKTHTCPPCPAPPVAG
PSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTP
PVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSLSLSPGK

HC 2 (SEQ ID NO:199)

EVQLVESGGGLVQPGGSLRLSCAASGFDFSRSWMNWVRQAPGKGLEWVSEINPDSSTINYATSVKGRFTISRDNSKNT
LYLQMNSLRAEDTAVYYCARYGNWFPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVS
WNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPPVAG
PSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTT
PPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGKGGGGSGGGGSGGGGSEVQLVESG
GGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDSKNTLYLQM
NSLRAEDTAVYYCVRHGNFGDSYVSWFAYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQEPSLTVSPGGT
VTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDEADYYCALWYS
NHWVFGGGTKLTVL

LC (SEQ ID NO:200)

DIVMTQSPSSLSASVGDRVTITCRASQNVDTNVAWYQQKPGQSPKALIYSASYRYSGVPDRFTGSGSGTDFTLTISSLQP
EDFATYFCQQYDSYPLTFGGGTKLEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNS
QESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

图60

**XENP15436 抗-CD38 (OKT10_H1L1) x 抗-CD3 (H1.31_L1.47)中心-scFv**

HC 1 (SEQ ID NO:201)

EVQLVESGGGLVQPGGSLRLSCAASGFDFSRSWMNWVRQAPGKGLEWVSEINPDSSTINYATSVKGRFTISRDNSKNT
LYLQMNSLRAEDTAVYYCARYGNWFPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVS
WNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSDTKVDKKVEPKSCDKTHTCPPCPAPPVAG
PSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTP
PVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSLSLSPGK

HC 2 (SEQ ID NO:202)

EVQLVESGGGLVQPGGSLRLSCAASGFDFSRSWMNWVRQAPGKGLEWVSEINPDSSTINYATSVKGRFTISRDNSKNT
LYLQMNSLRAEDTAVYYCARYGNWFPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVS
WNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCGGGGSGGGGSEVQLVE
SGGGLVQPGGSLRLSCAASGFTFSTYAMSWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDSKNTLYLQ
MNSLRAEDTAVYYCVRHGNFGDSYVSWFAYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQEPSLTVSPG
GTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDEADYYCALW
YSNHWVFGGGTKLTVLGGGGSGGGGSKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVK
FNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLP
PSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMH
EALHNHYTQKSLSLSPGK

LC (SEQ ID NO:203)

DIVMTQSPSSLSASVGDRVTITCRASQNVDTNVAWYQQKPGQSPKALIYSASYRYSGVPDRFTGSGSGTDFTLTISSLQP
EDFATYFCQQYDSYPLTFGGGTKLEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNS
QESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

图61

**XENP15437 抗-CD38 (OKT10_H1L1) x 抗-CD3 (H1.33_L1.47)中心-scFv**

HC 1 (SEQ ID NO:204)

EVQLVESGGGLVQPGGSLRLSCAASGFDFSRSWMNWVRQAPGKGLEWVSEINPDSSTINYATSVKGRFTISRDNSKNT
LYLQMNSLRAEDTAVYYCARYGNWFPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVS
WNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSDTKVDKKVEPKSCDKTHTCPPCPAPPVAG
PSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTP
PVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSLSLSPGK

HC 2 (SEQ ID NO:205)

EVQLVESGGGLVQPGGSLRLSCAASGFDFSRSWMNWVRQAPGKGLEWVSEINPDSSTINYATSVKGRFTISRDNSKNT
LYLQMNSLRAEDTAVYYCARYGNWFPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVS
WNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCGGGGSGGGGSEVQLVE
SGGGLVQPGGSLRLSCAASGFTFSTYAMSWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDSKNTLYLQ
MNSLRAEDTAVYYCVRHGNFGDSYVSWFAYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQEPSLTVSPG
GTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDEADYYCALW
YSNHWVFGGGTKLTVLGGGGSGGGGSKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVK
FNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLP
PSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMH
EALHNHYTQKSLSLSPGK

LC (SEQ ID NO:206)

DIVMTQSPSSLSASVGDRVTITCRASQNVDTNVAWYQQKPGQSPKALIYSASYRYSGVPDRFTGSGSGTDFTLTISSLQP
EDFATYFCQQYDSYPLTFGGGTKLEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNS
QESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

图62

**XENP15438 抗-CD38 (OKT10_H1L1) x 抗-CD3 (H1.30_L1.47)中心-scFv**

HC 1 (SEQ ID NO:207)

EVQLVESGGGLVQPGGSLRLSCAASGFDFSRSWMNWVRQAPGKGLEWVSEINPDSSTINYATSVKGRFTISRDNSKNT
LYLQMNSLRAEDTAVYYCARYGNWFPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVS
WNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSDTKVDKKVEPKSCDKTHTCPPCPAPPVAG
PSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTP
PVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSLSLSPGK

HC 2 (SEQ ID NO:208)

EVQLVESGGGLVQPGGSLRLSCAASGFDFSRSWMNWVRQAPGKGLEWVSEINPDSSTINYATSVKGRFTISRDNSKNT
LYLQMNSLRAEDTAVYYCARYGNWFPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVS
WNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCGGGGSGGGGSEVQLVE
SGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDSKNTLYLQ
MNSLRAEDTAVYYCVRHGNFGDSYVSWFAYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQEPSLTVSPG
GTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDEADYYCALW
YSNHWVFGGGTKLTVLGGGGSGGGGSKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVK
FNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLP
PSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMH
EALHNHYTQKSLSLSPGK

LC (SEQ ID NO:209)

DIVMTQSPSSLSASVGDRVTITCRASQNVDTNVAWYQQKPGQSPKALIYSASYRYSGVPDRFTGSGSGTDFTLTISSLQP
EDFATYFCQQYDSYPLTFGGGTKLEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNS
QESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

图63

| XENP | CD38 亲和性 | αCD3 scFv-Fc | $K_D$ (nM)* | 相比 H1.30_L1.47 的 CD3 结合下降倍数 |
|---|---|---|---|---|
| 13243 | 低 | H1.30_L1.47 | 4.91 | 1 |
| 14701 | 低 | H1.31_L1.47 | 1640 | 330 |
| 14702 | 高 | H1.31_L1.47 | 1640 | 330 |
| 14703 | 非常低 | H1.31_L1.47 | 1640 | 330 |

图64

| | DNA 量 (%) | | | | |
|---|---|---|---|---|---|
| 集合 | 轻链 | HC1 (Fab-Fc) | HC2 (scFv-Fc) | XENP13243 异二聚体 (%) | XENP13551 异二聚体 (%) |
| A | 47.4 | 31.6 | 21.1 | 65.6 | 57.6 |
| B | 42.9 | 28.6 | 28.6 | 61.2 | 83.5 |
| C | 37.5 | 25.0 | 37.5 | 96.2 | 90.5 |
| D | 33.3 | 22.2 | 44.4 | 92.8 | 84.4 |
| E | 54.5 | 27.3 | 18.2 | -- | 65.7 |
| F | 50.0 | 25.0 | 25.0 | 93.0 | 91.1 |
| G | 44.4 | 22.2 | 33.3 | 85.7 | 89.6 |
| H | 40.0 | 20.0 | 40.0 | 95.0 | 100.0 |

图65

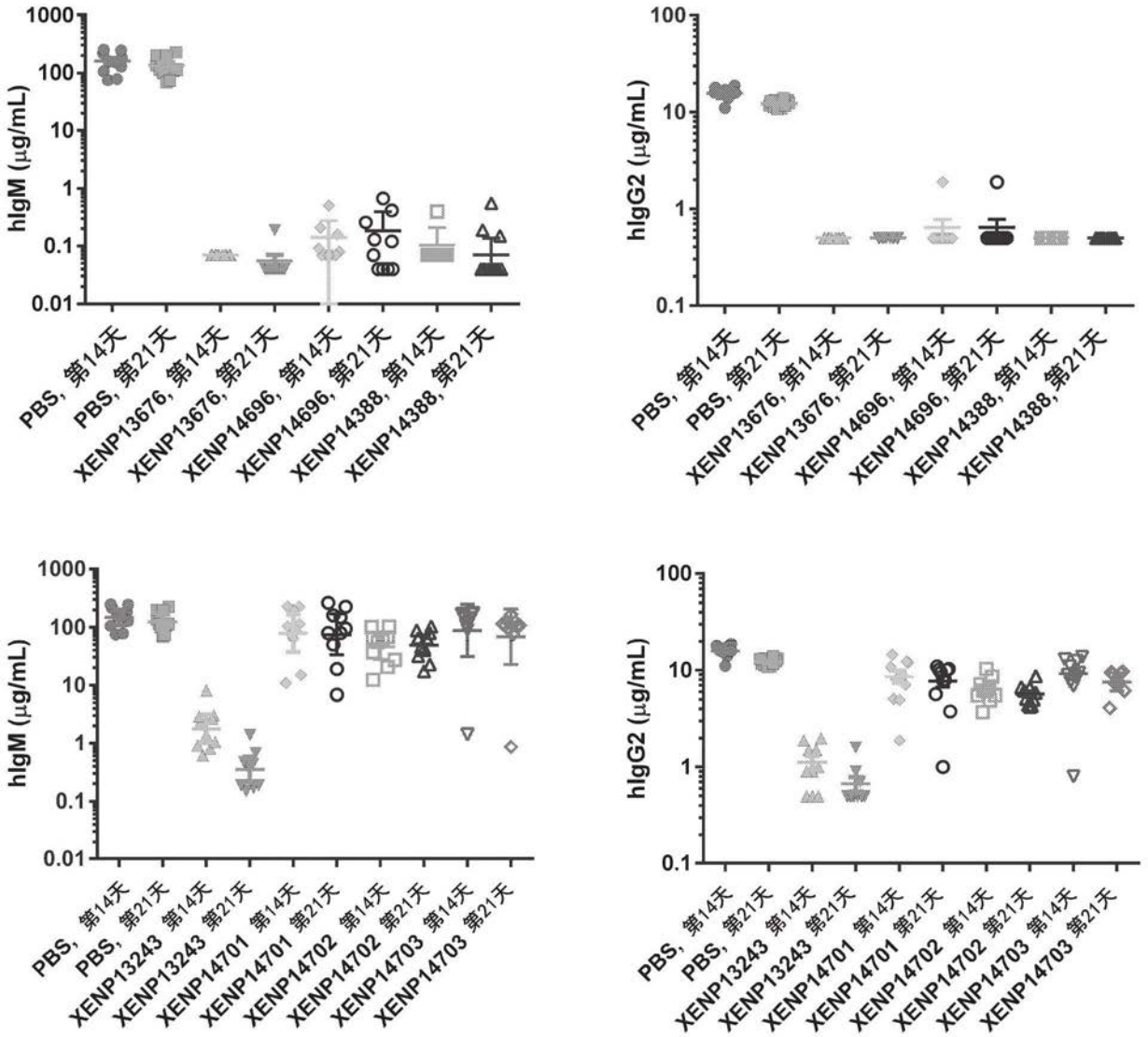

hIgM (μg/mL)
1000
100
10
1
0.1
0.01
PBS, 第14天
PBS, 第21天
XENP13676, 第14天
XENP13676, 第21天
XENP14696, 第14天
XENP14696, 第21天
XENP14388, 第14天
XENP14388, 第21天
hIgG2 (μg/mL)
100
10
1
0.1
PBS, 第14天
PBS, 第21天
XENP13676, 第14天
XENP13676, 第21天
XENP14696, 第14天
XENP14696, 第21天
XENP14388, 第14天
XENP14388, 第21天
hIgM (μg/mL)
1000
100
10
1
0.1
0.01
PBS, 第14天
PBS, 第21天
XENP13243 第14天
XENP13243 第21天
XENP14701 第14天
XENP14701 第21天
XENP14702 第14天
XENP14702 第21天
XENP14703 第14天
XENP14703 第21天
hIgG2 (μg/mL)
100
10
1
0.1
PBS, 第14天
PBS, 第21天
XENP13243 第14天
XENP13243 第21天
XENP14701 第14天
XENP14701 第21天
XENP14702 第14天
XENP14702 第21天
XENP14703 第14天
XENP14703 第21天

图66

| VH ID | VL ID | VH 取代 | VL 取代 |
|---|---|---|---|
| H1 | L1.4 | | |
| H1.30 | L1.47 | N30S/N100D | Q42K/A43S/L75I/E85D/L95H |
| H1.33 | L1.47 | N30S/N100D/A101D | Q42K/A43S/L75I/E85D/L95H |
| H1.31 | L1.47 | N30S/N35S/N100D | Q42K/A43S/L75I/E85D/L95H |
| H1.32 | L1.47 | N30S/Y52CA/N100D | Q42K/A43S/L75I/E85D/L95H |
| H1.88 | L1.47 | N30S/N100P | Q42K/A43S/L75I/E85D/L95H |
| H1.89 | L1.47 | N30S/N100D/S100AE | Q42K/A43S/L75I/E85D/L95H |
| H1.90 | L1.47 | N30S/N100D/S100AP | Q42K/A43S/L75I/E85D/L95H |
| H1.91 | L1.47 | N30S/Y52CA/N100D | Q42K/A43S/L75I/E85D/L95H |
| H1.92 | L1.47 | N30S/Y58A/N100D | Q42K/A43S/L75I/E85D/L95H |
| H1.93 | L1.47 | N30S/N100E | Q42K/A43S/L75I/E85D/L95H |
| H1.94 | L1.47 | N30S/N100Q | Q42K/A43S/L75I/E85D/L95H |
| H1.96 | L1.47 | N30S/N100D/S100AN | Q42K/A43S/L75I/E85D/L95H |
| H1.97 | L1.47 | N30S/N100D/S100AQ | Q42K/A43S/L75I/E85D/L95H |
| H1.98 | L1.47 | N30S/Y52CA/N100D/A101D | Q42K/A43S/L75I/E85D/L95H |
| H1.99 | L1.47 | N30S/Y58A/N100D/A101D | Q42K/A43S/L75I/E85D/L95H |
| H1.100 | L1.47 | N30S/N100A/A101D | Q42K/A43S/L75I/E85D/L95H |
| H1.101 | L1.47 | N30S/N100Q/A101D | Q42K/A43S/L75I/E85D/L95H |
| H1.102 | L1.47 | N30S/N100D/S100AE/A101D | Q42K/A43S/L75I/E85D/L95H |
| H1.103 | L1.47 | N30S/N100D/S100AN/A101D | Q42K/A43S/L75I/E85D/L95H |
| H1.104 | L1.47 | N30S/N100D/S100AP/A101D | Q42K/A43S/L75I/E85D/L95H |
| H1.105 | L1.47 | N30S/N100D/S100AQ/A101D | Q42K/A43S/L75I/E85D/L95H |

图67A

| VH ID | VL ID | VH 取代 | VL 取代 |
|---|---|---|---|
| H1.106 | L1.47 | N30S/Y52CA/Y58A/N100D | Q42K/A43S/L75I/E85D/L95H |
| H1.107 | L1.47 | N30S/Y52CA/Y58A/N100A | Q42K/A43S/L75I/E85D/L95H |
| H1.108 | L1.47 | N30S/Y52CA/Y58A/N100Q | Q42K/A43S/L75I/E85D/L95H |
| H1.109 | L1.47 | N30S/Y52CA/Y58A/N100D/A101D | Q42K/A43S/L75I/E85D/L95H |

图67B

H1_L1.4

**SEQ ID NO:210**

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDS
KNTLYLQMNSLRAEDTAVYYCVRHGNFGDSYVSWFAYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQE
PSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDE
ADYYCALWYSNHWVFGGGTKLTVLGSHHHHHH

**SEQ ID NO:211**

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDS
KNTLYLQMNSLRAEDTAVYYCVRHGNFGDSYVSWFAYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQE
PSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDE
ADYYCALWYSNHWVFGGGTKLTVL

**SEQ ID NO:212**

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDS
KNTLYLQMNSLRAEDTAVYYCVRHGNFGDSYVSWFAYWGQGTLVTVSS

**SEQ ID NO:213**

QAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTIS
GAQPEDEADYYCALWYSNHWVFGGGTKLTVL

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**SEQ ID NO:214**

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDS
KNTLYLQMNSLRAEDTAVYYCVRHGNFGDSYVSWFAYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQE
PSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDE
ADYYCALWYSNHWVFGGGTKLTVLGSHHHHHH

**SEQ ID NO:215**

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDS
KNTLYLQMNSLRAEDTAVYYCVRHGNFGDSYVSWFAYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQE
PSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDE
ADYYCALWYSNHWVFGGGTKLTVL

**SEQ ID NO:216**

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDS
KNTLYLQMNSLRAEDTAVYYCVRHGNFGDSYVSWFAYWGQGTLVTVSS

**SEQ ID NO:217**

QAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTIS
GAQPEDEADYYCALWYSNHWVFGGGTKLTVL

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**SEQ ID NO:218**

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDS
KNTLYLQMNSLRAEDTAVYYCVRHGNFGDSYVSWFDYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQE
PSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDE
ADYYCALWYSNHWVFGGGTKLTVLGSHHHHHH

**SEQ ID NO:219**

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDS
KNTLYLQMNSLRAEDTAVYYCVRHGNFGDSYVSWFDYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQE
PSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDE
ADYYCALWYSNHWVFGGGTKLTVL

**SEQ ID NO:220**

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDS
KNTLYLQMNSLRAEDTAVYYCVRHGNFGDSYVSWFDYWGQGTLVTVSS

**SEQ ID NO:221**

QAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTIS
GAQPEDEADYYCALWYSNHWVFGGGTKLTVL

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**SEQ ID NO:222**

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMSWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDS
KNTLYLQMNSLRAEDTAVYYCVRHGNFGDSYVSWFAYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQE
PSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDE
ADYYCALWYSNHWVFGGGTKLTVLGSHHHHHH

**SEQ ID NO:223**

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMSWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDS
KNTLYLQMNSLRAEDTAVYYCVRHGNFGDSYVSWFAYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQE
PSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDE
ADYYCALWYSNHWVFGGGTKLTVL

**SEQ ID NO:224**

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMSWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDS
KNTLYLQMNSLRAEDTAVYYCVRHGNFGDSYVSWFAYWGQGTLVTVSS

**SEQ ID NO:225**

QAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTIS
GAQPEDEADYYCALWYSNHWVFGGGTKLTVL

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**SEQ ID NO:226**

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKANNYATYYADSVKGRFTISRDDS
KNTLYLQMNSLRAEDTAVYYCVRHGNFGDSYVSWFAYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQE
PSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDE
ADYYCALWYSNHWVFGGGTKLTVLGSHHHHHH

**SEQ ID NO:227**

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKANNYATYYADSVKGRFTISRDDS
KNTLYLQMNSLRAEDTAVYYCVRHGNFGDSYVSWFAYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQE
PSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDE
ADYYCALWYSNHWVFGGGTKLTVL

**SEQ ID NO:228**

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKANNYATYYADSVKGRFTISRDDS
KNTLYLQMNSLRAEDTAVYYCVRHGNFGDSYVSWFAYWGQGTLVTVSS

**SEQ ID NO:229**

QAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTIS
GAQPEDEADYYCALWYSNHWVFGGGTKLTVL

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**SEQ ID NO:230**

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDS
KNTLYLQMNSLRAEDTAVYYCVRHGNFGPSYVSWFAYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQE
PSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDE
ADYYCALWYSNHWVFGGGTKLTVLGSHHHHHH

**SEQ ID NO:231**

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDS
KNTLYLQMNSLRAEDTAVYYCVRHGNFGPSYVSWFAYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQE
PSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDE
ADYYCALWYSNHWVFGGGTKLTVL

**SEQ ID NO:232**

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDS
KNTLYLQMNSLRAEDTAVYYCVRHGNFGPSYVSWFAYWGQGTLVTVSS

**SEQ ID NO:233**

QAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTIS
GAQPEDEADYYCALWYSNHWVFGGGTKLTVL

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**SEQ ID NO:234**

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDS
KNTLYLQMNSLRAEDTAVYYCVRHGNFGDEYVSWFAYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQE
PSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDE
ADYYCALWYSNHWVFGGGTKLTVLGSHHHHHH

**SEQ ID NO:235**

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDS
KNTLYLQMNSLRAEDTAVYYCVRHGNFGDEYVSWFAYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQE
PSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDE
ADYYCALWYSNHWVFGGGTKLTVL

**SEQ ID NO:236**

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDS
KNTLYLQMNSLRAEDTAVYYCVRHGNFGDEYVSWFAYWGQGTLVTVSS

**SEQ ID NO:237**

QAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTIS
GAQPEDEADYYCALWYSNHWVFGGGTKLTVL

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**SEQ ID NO:238**

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDS
KNTLYLQMNSLRAEDTAVYYCVRHGNFGDPYVSWFAYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQE
PSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDE
ADYYCALWYSNHWVFGGGTKLTVLGSHHHHHH

**SEQ ID NO:239**

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDS
KNTLYLQMNSLRAEDTAVYYCVRHGNFGDPYVSWFAYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQE
PSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDE
ADYYCALWYSNHWVFGGGTKLTVL

**SEQ ID NO:240**

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDS
KNTLYLQMNSLRAEDTAVYYCVRHGNFGDPYVSWFAYWGQGTLVTVSS

**SEQ ID NO:241**

QAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTIS
GAQPEDEADYYCALWYSNHWVFGGGTKLTVL

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**SEQ ID NO:242**

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKANNYATYYADSVKGRFTISRDDS
KNTLYLQMNSLRAEDTAVYYCVRHGNFGDSYVSWFAYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQE
PSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDE
ADYYCALWYSNHWVFGGGTKLTVLGSHHHHHH

**SEQ ID NO:243**

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKANNYATYYADSVKGRFTISRDDS
KNTLYLQMNSLRAEDTAVYYCVRHGNFGDSYVSWFAYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQE
PSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDE
ADYYCALWYSNHWVFGGGTKLTVL

**SEQ ID NO:244**

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKANNYATYYADSVKGRFTISRDDS
KNTLYLQMNSLRAEDTAVYYCVRHGNFGDSYVSWFAYWGQGTLVTVSS

**SEQ ID NO:245**

QAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTIS
GAQPEDEADYYCALWYSNHWVFGGGTKLTVL

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**SEQ ID NO:246**

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATAYADSVKGRFTISRDDS
KNTLYLQMNSLRAEDTAVYYCVRHGNFGDSYVSWFAYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQE
PSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDE
ADYYCALWYSNHWVFGGGTKLTVLGSHHHHHH

**SEQ ID NO:247**

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATAYADSVKGRFTISRDDS
KNTLYLQMNSLRAEDTAVYYCVRHGNFGDSYVSWFAYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQE
PSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDE
ADYYCALWYSNHWVFGGGTKLTVL

**SEQ ID NO:248**

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATAYADSVKGRFTISRDDS
KNTLYLQMNSLRAEDTAVYYCVRHGNFGDSYVSWFAYWGQGTLVTVSS

**SEQ ID NO:249**

QAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTIS
GAQPEDEADYYCALWYSNHWVFGGGTKLTVL

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**SEQ ID NO:250**

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDS
KNTLYLQMNSLRAEDTAVYYCVRHGNFGESYVSWFAYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQE
PSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDE
ADYYCALWYSNHWVFGGGTKLTVLGSHHHHHH

**SEQ ID NO:251**

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDS
KNTLYLQMNSLRAEDTAVYYCVRHGNFGESYVSWFAYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQE
PSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDE
ADYYCALWYSNHWVFGGGTKLTVL

**SEQ ID NO:252**

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDS
KNTLYLQMNSLRAEDTAVYYCVRHGNFGESYVSWFAYWGQGTLVTVSS

**SEQ ID NO:253**

QAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTIS
GAQPEDEADYYCALWYSNHWVFGGGTKLTVL

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**SEQ ID NO:254**

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDS
KNTLYLQMNSLRAEDTAVYYCVRHGNFGQSYVSWFAYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQE
PSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDE
ADYYCALWYSNHWVFGGGTKLTVLGSHHHHHH

**SEQ ID NO:255**

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDS
KNTLYLQMNSLRAEDTAVYYCVRHGNFGQSYVSWFAYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQE
PSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDE
ADYYCALWYSNHWVFGGGTKLTVL

**SEQ ID NO:256**

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDS
KNTLYLQMNSLRAEDTAVYYCVRHGNFGQSYVSWFAYWGQGTLVTVSS

**SEQ ID NO:** 257

QAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTIS
GAQPEDEADYYCALWYSNHWVFGGGTKLTVL

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**SEQ ID NO:** 258

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDS
KNTLYLQMNSLRAEDTAVYYCVRHGNFGDNYVSWFAYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQE
PSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDE
ADYYCALWYSNHWVFGGGTKLTVLGSHHHHHH

**SEQ ID NO:** 259

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDS
KNTLYLQMNSLRAEDTAVYYCVRHGNFGDNYVSWFAYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQE
PSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDE
ADYYCALWYSNHWVFGGGTKLTVL

**SEQ ID NO:** 260

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDS
KNTLYLQMNSLRAEDTAVYYCVRHGNFGDNYVSWFAYWGQGTLVTVSS

**SEQ ID NO:** 261

QAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTIS
GAQPEDEADYYCALWYSNHWVFGGGTKLTVL

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**SEQ ID NO:** 262

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDS
KNTLYLQMNSLRAEDTAVYYCVRHGNFGDQYVSWFAYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQE
PSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDE
ADYYCALWYSNHWVFGGGTKLTVLGSHHHHHH

**SEQ ID NO:** 263

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDS
KNTLYLQMNSLRAEDTAVYYCVRHGNFGDQYVSWFAYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQE
PSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDE
ADYYCALWYSNHWVFGGGTKLTVL

**SEQ ID NO:** 264

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDS
KNTLYLQMNSLRAEDTAVYYCVRHGNFGDQYVSWFAYWGQGTLVTVSS

**SEQ ID NO:** 265

QAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTIS
GAQPEDEADYYCALWYSNHWVFGGGTKLTVL

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**SEQ ID NO:** 266

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKANNYATYYADSVKGRFTISRDDS
KNTLYLQMNSLRAEDTAVYYCVRHGNFGDSYVSWFDYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQE
PSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDE
ADYYCALWYSNHWVFGGGTKLTVLGSHHHHHH

**SEQ ID NO:** 267

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKANNYATYYADSVKGRFTISRDDS
KNTLYLQMNSLRAEDTAVYYCVRHGNFGDSYVSWFDYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQE
PSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDE
ADYYCALWYSNHWVFGGGTKLTVL

**SEQ ID NO:** 268

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKANNYATYYADSVKGRFTISRDDS
KNTLYLQMNSLRAEDTAVYYCVRHGNFGDSYVSWFDYWGQGTLVTVSS

**SEQ ID NO:** 269

QAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTIS
GAQPEDEADYYCALWYSNHWVFGGGTKLTVL

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**SEQ ID NO:** 270

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATAYADSVKGRFTISRDDS
KNTLYLQMNSLRAEDTAVYYCVRHGNFGDSYVSWFDYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQE
PSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDE
ADYYCALWYSNHWVFGGGTKLTVLGSHHHHHH

**SEQ ID NO:** 271

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATAYADSVKGRFTISRDDS
KNTLYLQMNSLRAEDTAVYYCVRHGNFGDSYVSWFDYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQE
PSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDE
ADYYCALWYSNHWVFGGGTKLTVL

**SEQ ID NO:** 272

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATAYADSVKGRFTISRDDS
KNTLYLQMNSLRAEDTAVYYCVRHGNFGDSYVSWFDYWGQGTLVTVSS

**SEQ ID NO:** 273

QAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTIS
GAQPEDEADYYCALWYSNHWVFGGGTKLTVL

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**SEQ ID NO:** 274

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDS
KNTLYLQMNSLRAEDTAVYYCVRHGNFGASYVSWFDYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQE
PSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDE
ADYYCALWYSNHWVFGGGTKLTVLGSHHHHHH

**SEQ ID NO:** 275

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDS
KNTLYLQMNSLRAEDTAVYYCVRHGNFGASYVSWFDYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQE
PSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDE
ADYYCALWYSNHWVFGGGTKLTVL

**SEQ ID NO:** 276

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDS
KNTLYLQMNSLRAEDTAVYYCVRHGNFGASYVSWFDYWGQGTLVTVSS

**SEQ ID NO:** 277

QAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTIS
GAQPEDEADYYCALWYSNHWVFGGGTKLTVL

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H1.101_L1.47

**SEQ ID NO:** 278

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDS
KNTLYLQMNSLRAEDTAVYYCVRHGNFGQSYVSWFDYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQE
PSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDE
ADYYCALWYSNHWVFGGGTKLTVLGSHHHHHH

**SEQ ID NO:** 279

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDS
KNTLYLQMNSLRAEDTAVYYCVRHGNFGQSYVSWFDYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQE
PSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDE
ADYYCALWYSNHWVFGGGTKLTVL

**SEQ ID NO:** 280

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDS
KNTLYLQMNSLRAEDTAVYYCVRHGNFGQSYVSWFDYWGQGTLVTVSS

**SEQ ID NO:** 281

QAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTIS
GAQPEDEADYYCALWYSNHWVFGGGTKLTVL

图68R

H1.102_L1.47

**SEQ ID NO:** 282

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDS
KNTLYLQMNSLRAEDTAVYYCVRHGNFGDEYVSWFDYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQE
PSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDE
ADYYCALWYSNHWVFGGGTKLTVLGSHHHHHH

**SEQ ID NO:** 283

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDS
KNTLYLQMNSLRAEDTAVYYCVRHGNFGDEYVSWFDYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQE
PSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDE
ADYYCALWYSNHWVFGGGTKLTVL

**SEQ ID NO:** 284

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDS
KNTLYLQMNSLRAEDTAVYYCVRHGNFGDEYVSWFDYWGQGTLVTVSS

**SEQ ID NO:** 285

QAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTIS
GAQPEDEADYYCALWYSNHWVFGGGTKLTVL

图68S

H1.103_L1.47

**SEQ ID NO:** 286

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDS
KNTLYLQMNSLRAEDTAVYYCVRHGNFGDNYVSWFDYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQE
PSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDE
ADYYCALWYSNHWVFGGGTKLTVLGSHHHHHH

**SEQ ID NO:** 287

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDS
KNTLYLQMNSLRAEDTAVYYCVRHGNFGDNYVSWFDYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQE
PSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDE
ADYYCALWYSNHWVFGGGTKLTVL

**SEQ ID NO:** 288

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDS
KNTLYLQMNSLRAEDTAVYYCVRHGNFGDNYVSWFDYWGQGTLVTVSS

**SEQ ID NO:** 289

QAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTIS
GAQPEDEADYYCALWYSNHWVFGGGTKLTVL

图68T

H1.104_L1.47

**SEQ ID NO:** 290

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDS
KNTLYLQMNSLRAEDTAVYYCVRHGNFGDPYVSWFDYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQE
PSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDE
ADYYCALWYSNHWVFGGGTKLTVLGSHHHHHH

**SEQ ID NO:** 291

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDS
KNTLYLQMNSLRAEDTAVYYCVRHGNFGDPYVSWFDYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQE
PSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDE
ADYYCALWYSNHWVFGGGTKLTVL

**SEQ ID NO:** 292

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDS
KNTLYLQMNSLRAEDTAVYYCVRHGNFGDPYVSWFDYWGQGTLVTVSS

**SEQ ID NO:** 293

QAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTIS
GAQPEDEADYYCALWYSNHWVFGGGTKLTVL

图68U

H1.105_L1.47

**SEQ ID NO:** 294

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDS
KNTLYLQMNSLRAEDTAVYYCVRHGNFGDQYVSWFDYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQE
PSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDE
ADYYCALWYSNHWVFGGGTKLTVLGSHHHHHH

**SEQ ID NO:** 295

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDS
KNTLYLQMNSLRAEDTAVYYCVRHGNFGDQYVSWFDYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQE
PSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDE
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**SEQ ID NO:** 296

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDS
KNTLYLQMNSLRAEDTAVYYCVRHGNFGDQYVSWFDYWGQGTLVTVSS

**SEQ ID NO:** 297

QAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTIS
GAQPEDEADYYCALWYSNHWVFGGGTKLTVL

图68V

H1.106_L1.47

**SEQ ID NO:** 298

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKANNYATAYADSVKGRFTISRDD
SKNTLYLQMNSLRAEDTAVYYCVRHGNFGDSYVSWFAYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQ
EPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPED
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**SEQ ID NO:** 299

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKANNYATAYADSVKGRFTISRDD
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EPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPED
EADYYCALWYSNHWVFGGGTKLTVL

**SEQ ID NO:** 300

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKANNYATAYADSVKGRFTISRDD
SKNTLYLQMNSLRAEDTAVYYCVRHGNFGDSYVSWFAYWGQGTLVTVSS

**SEQ ID NO:** 301

QAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTIS
GAQPEDEADYYCALWYSNHWVFGGGTKLTVL

图68W

H1.107_L1.47

**SEQ ID NO:** 302

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKANNYATAYADSVKGRFTISRDD
SKNTLYLQMNSLRAEDTAVYYCVRHGNFGASYVSWFAYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQ
EPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPED
EADYYCALWYSNHWVFGGGTKLTVLGSHHHHHH

**SEQ ID NO:** 303

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKANNYATAYADSVKGRFTISRDD
SKNTLYLQMNSLRAEDTAVYYCVRHGNFGASYVSWFAYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQ
EPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPED
EADYYCALWYSNHWVFGGGTKLTVL

**SEQ ID NO:** 304

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKANNYATAYADSVKGRFTISRDD
SKNTLYLQMNSLRAEDTAVYYCVRHGNFGASYVSWFAYWGQGTLVTVSS

**SEQ ID NO:** 305

QAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTIS
GAQPEDEADYYCALWYSNHWVFGGGTKLTVL

图68X

H1.108_L1.47

**SEQ ID NO:** 306

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKANNYATAYADSVKGRFTISRDD
SKNTLYLQMNSLRAEDTAVYYCVRHGNFGQSYVSWFAYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQ
EPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPED
EADYYCALWYSNHWVFGGGTKLTVLGSHHHHHH

**SEQ ID NO:** 307

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKANNYATAYADSVKGRFTISRDD
SKNTLYLQMNSLRAEDTAVYYCVRHGNFGQSYVSWFAYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQ
EPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPED
EADYYCALWYSNHWVFGGGTKLTVL

**SEQ ID NO:** 308

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKANNYATAYADSVKGRFTISRDD
SKNTLYLQMNSLRAEDTAVYYCVRHGNFGQSYVSWFAYWGQGTLVTVSS

**SEQ ID NO:** 309

QAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTIS
GAQPEDEADYYCALWYSNHWVFGGGTKLTVL

图68Y

H1.109_L1.47

**SEQ ID NO:** 310

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKANNYATAYADSVKGRFTISRDD
SKNTLYLQMNSLRAEDTAVYYCVRHGNFGDSYVSWFDYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQ
EPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPED
EADYYCALWYSNHWVFGGGTKLTVLGSHHHHHH

**SEQ ID NO:** 311

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKANNYATAYADSVKGRFTISRDD
SKNTLYLQMNSLRAEDTAVYYCVRHGNFGDSYVSWFDYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQ
EPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPED
EADYYCALWYSNHWVFGGGTKLTVL

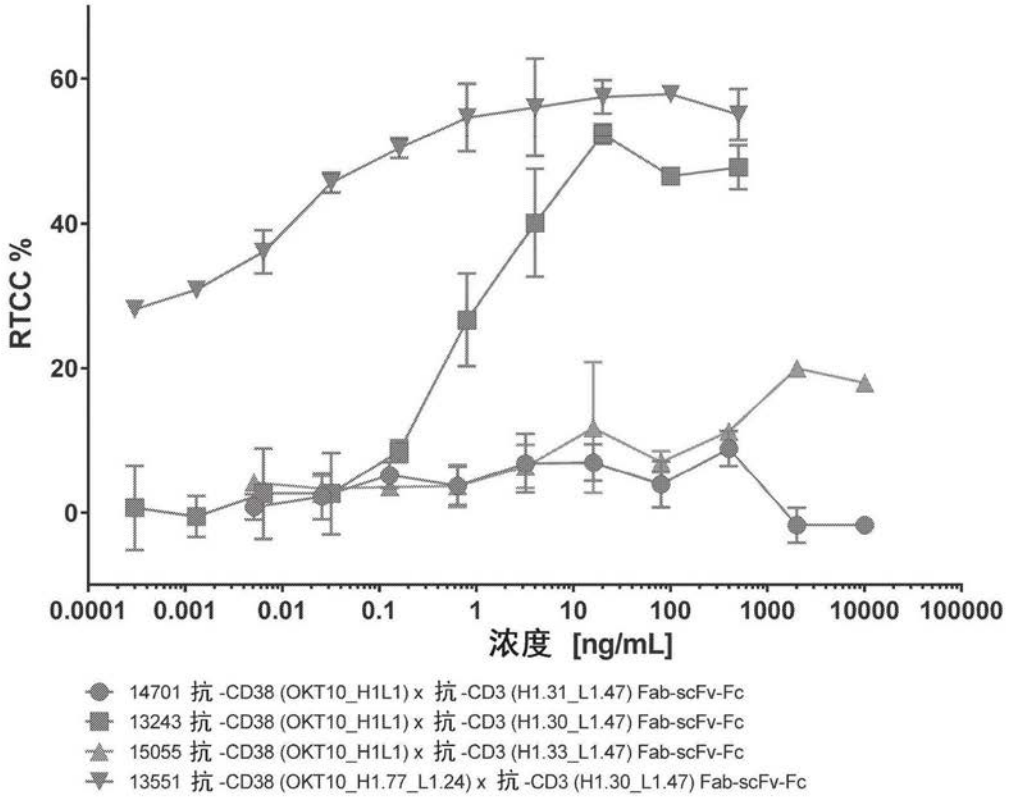
**SEQ ID NO:** 312

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKANNYATAYADSVKGRFTISRDD
SKNTLYLQMNSLRAEDTAVYYCVRHGNFGDSYVSWFDYWGQGTLVTVSS

**SEQ ID NO:** 313

QAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTIS
GAQPEDEADYYCALWYSNHWVFGGGTKLTVL

图68Z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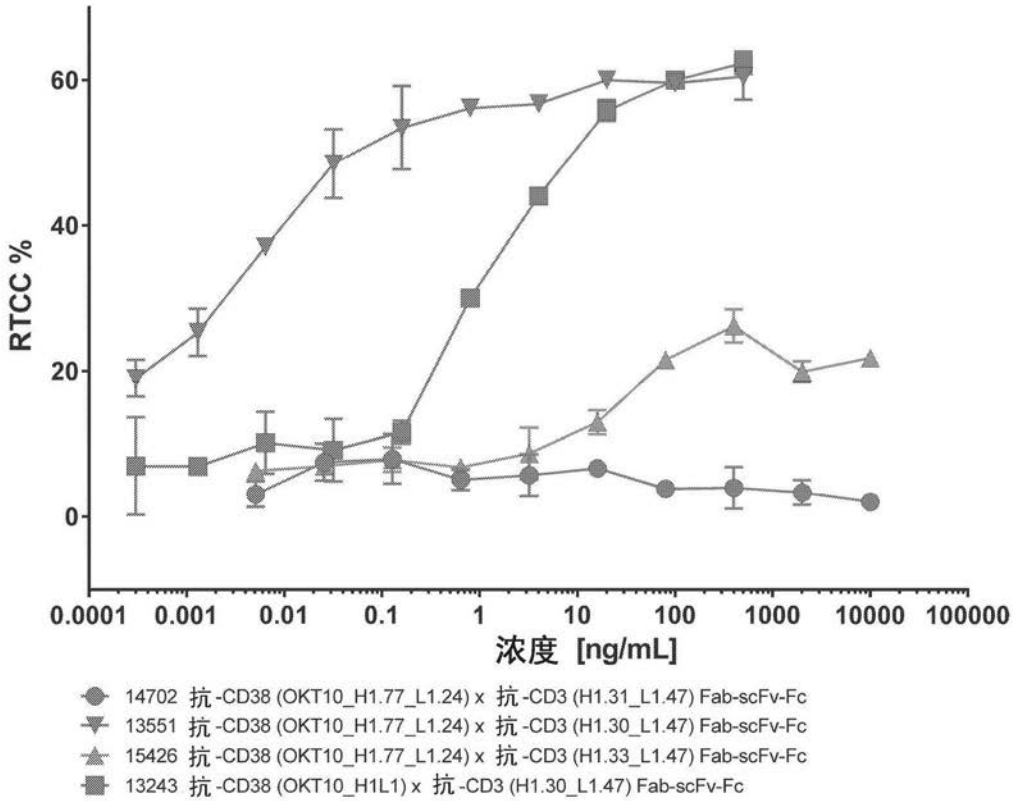
60
40
20
0
0.0001
0.001
0.01
0.1
1
10
100
1000
10000
100000
浓度 [ng/mL]
14701 抗 -CD38 (OKT10_H1L1) x 抗 -CD3 (H1.31_L1.47) Fab-scFv-Fc
13243 抗 -CD38 (OKT10_H1L1) x 抗 -CD3 (H1.30_L1.47) Fab-scFv-Fc
15055 抗 -CD38 (OKT10_H1L1) x 抗 -CD3 (H1.33_L1.47) Fab-scFv-Fc
13551 抗 -CD38 (OKT10_H1.77_L1.24) x 抗 -CD3 (H1.30_L1.47) Fab-scFv-Fc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20
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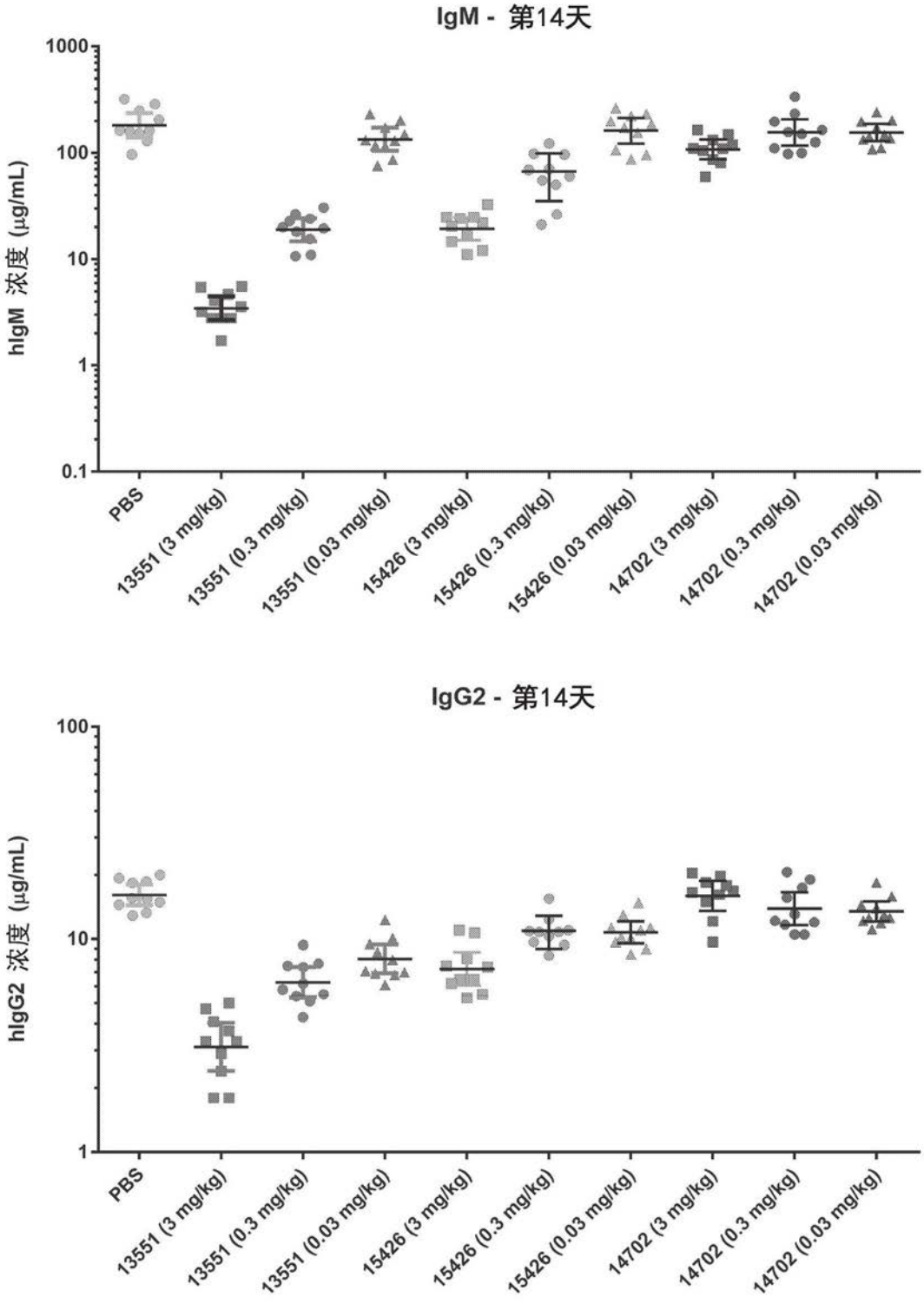
0.0001
0.001
0.01
0.1
1
10
100
1000
10000
100000
浓度 [ng/mL]
14702 抗 -CD38 (OKT10_H1.77_L1.24) x 抗 -CD3 (H1.31_L1.47) Fab-scFv-Fc
13551 抗 -CD38 (OKT10_H1.77_L1.24) x 抗 -CD3 (H1.30_L1.47) Fab-scFv-Fc
15426 抗 -CD38 (OKT10_H1.77_L1.24) x 抗 -CD3 (H1.33_L1.47) Fab-scFv-Fc
13243 抗 -CD38 (OKT10_H1L1) x 抗 -CD3 (H1.30_L1.47) Fab-scFv-Fc

图69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hIgM 浓度 (μg/mL)
1000
100
10
1
0.1
PBS
13551 (3 mg/kg)
13551 (0.3 mg/kg)
13551 (0.03 mg/kg)
15426 (3 mg/kg)
15426 (0.3 mg/kg)
15426 (0.03 mg/kg)
14702 (3 mg/kg)
14702 (0.3 mg/kg)
14702 (0.03 mg/kg)
IgG2 - 第14天
hIgG2 浓度 (μg/mL)
100
10
1
PBS
13551 (3 mg/kg)
13551 (0.3 mg/kg)
13551 (0.03 mg/kg)
15426 (3 mg/kg)
15426 (0.3 mg/kg)
15426 (0.03 mg/kg)
14702 (3 mg/kg)
14702 (0.3 mg/kg)
14702 (0.03 mg/kg)

图70

XENP15049 抗-CD19 (4G7_H1.227_L1.199) x 抗-CD3 (H1.30_L1.47) Fab-scFv-Fc

HC 1 (Fab-Fc) (SEQ ID NO: 314)

EVQLVESGGGLVKPGGSLKLSCAASGYTFTSYVMHWVRQAPGGGLEWIGYINPYNDGTKYNEKFKGRVTISSDKSKST
AYMELSSLRSEDTAVYYCARGTYYYGTRVFDYWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPV
TVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSDTKVDKKVEPKSCDKTHTCPPCPAPPV
AGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDW
LNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSLSLSPGK

HC 2 (scFv-Fc) (SEQ ID NO: 315)

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDSK
NTLYLQMNSLRAEDTAVYYCVRHGNFGDSYVSWFAYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQEPS
LTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDEAD
YYCALWYSNHWVFGGGTKLTVLEPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEV
KFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTL
PPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVM
HEALHNHYTQKSLSLSPGK

LC (SEQ ID NO: 316)

DIVMTQSPATLSLSPGERATISCRSSKSLQNVNGNTYLYWFQQKPGQSPKLLIYRASNLNSGVPDRFSGSGSGTEFTLTIS
SLEPEDFAVYYCMQHLEYPITFGGGTKLEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQS
GNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

图71

XENP15051 抗-CD19 (4G7_H1.227_L1.199) x 抗-CD3 (H1.31_L1.47) Fab-scFv-Fc

HC 1 (Fab-Fc) (SEQ ID NO: 317)

EVQLVESGGGLVKPGGSLKLSCAASGYTFTSYVMHWVRQAPGGGLEWIGYINPYNDGTKYNEKFKGRVTISSDKSKST
AYMELSSLRSEDTAVYYCARGTYYYGTRVFDYWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPV
TVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSDTKVDKKVEPKSCDKTHTCPPCPAPPV
AGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDW
LNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSLSLSPGK

HC 2 (scFv-Fc) (SEQ ID NO: 318)

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMSWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDSK
NTLYLQMNSLRAEDTAVYYCVRHGNFGDSYVSWFAYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQEPS
LTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDEAD
YYCALWYSNHWVFGGGTKLTVLEPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEV
KFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTL
PPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVM
HEALHNHYTQKSLSLSPGK

LC (SEQ ID NO: 319)

DIVMTQSPATLSLSPGERATISCRSSKSLQNVNGNTYLYWFQQKPGQSPKLLIYRASNLNSGVPDRFSGSGSGTEFTLTIS
SLEPEDFAVYYCMQHLEYPITFGGGTKLEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQS
GNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

图72

XENP15050 抗-CD19 (4G7_H1.227_L1.199) x 抗-CD3 (H1.33_L1.47) Fab-scFv-Fc

HC 1 (Fab-Fc) (SEQ ID NO: 320)

EVQLVESGGGLVKPGGSLKLSCAASGYTFTSYVMHWVRQAPGGGLEWIGYINPYNDGTKYNEKFKGRVTISSDKSKST
AYMELSSLRSEDTAVYYCARGTYYYGTRVFDYWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPV
TVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSDTKVDKKVEPKSCDKTHTCPPCPAPPV
AGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDW
LNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSLSLSPGK

HC 2 (scFv-Fc) (SEQ ID NO: 321)

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDSK
NTLYLQMNSLRAEDTAVYYCVRHGNFGDSYVSWFDYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQEPS
LTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDEAD
YYCALWYSNHWVFGGGTKLTVLEPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEV
KFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTL
PPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVM
HEALHNHYTQKSLSLSPGK

LC (SEQ ID NO: 322)

DIVMTQSPATLSLSPGERATISCRSSKSLQNVNGNTYLYWFQQKPGQSPKLLIYRASNLNSGVPDRFSGSGSGTEFTLTIS
SLEPEDFAVYYCMQHLEYPITFGGGTKLEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQS
GNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

图73

XENP13676 抗-CD20 (C2B8_H1L1) x 抗-CD3 (H1.30_L1.47) Fab-scFv-Fc

HC 1 (Fab-Fc) (SEQ ID NO: 323)

QVQLVQSGAEVKKPGASVKVSCKASGYTFTSYNMHWVRQAPGQGLEWMGAIYPGNGDTSYNQKFQGRVTITADKSI
STAYMELSSLRSEDTAVYYCARSTYYGGDWYFNVWGAGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFP
EPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSDTKVDKKVEPKSCDKTHTCPPCPA
PPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQ
DWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPEN
NYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSLSLSPGK

HC 2 (scFv-Fc) (SEQ ID NO: 324)

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDSK
NTLYLQMNSLRAEDTAVYYCVRHGNFGDSYVSWFAYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQEPS
LTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDEAD
YYCALWYSNHWVFGGGTKLTVLEPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEV
KFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTL
PPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVM
HEALHNHYTQKSLSLSPGK

LC (SEQ ID NO: 325)

QIVLTQSPSSLSASVGDRVTITCRASSSVSYIHWFQQKPGKSPKPLIYATSNLASGVPVRFSGSGSGTDYTLTISSLQPEDF
ATYYCQQWTSNPPTFGGGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQE
SVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

图74

XENP14696 抗-CD20 (C2B8_H1L1) x 抗-CD3 (H1.31_L1.47) Fab-scFv-Fc

HC 1 (Fab-Fc) (SEQ ID NO: 326)

QVQLVQSGAEVKKPGASVKVSCKASGYTFTSYNMHWVRQAPGQGLEWMGAIYPGNGDTSYNQKFQGRVTITADKSI
STAYMELSSLRSEDTAVYYCARSTYYGGDWYFNVWGAGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFP
EPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSDTKVDKKVEPKSCDKTHTCPPCPA
PPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQ
DWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPEN
NYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSLSLSPGK

HC 2 (scFv-Fc) (SEQ ID NO: 327)

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMSWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDSK
NTLYLQMNSLRAEDTAVYYCVRHGNFGDSYVSWFAYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQEPS
LTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDEAD
YYCALWYSNHWVFGGGTKLTVLEPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEV
KFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTL
PPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVM
HEALHNHYTQKSLSLSPGK

LC (SEQ ID NO: 328)

QIVLTQSPSSLSASVGDRVTITCRASSSVSYIHWFQQKPGKSPKPLIYATSNLASGVPVRFSGSGSGTDYTLTISSLQPEDF
ATYYCQQWTSNPPTFGGGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQE
SVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

图75

XENP15629 抗-CD20 (C2B8_H1L1) x 抗-CD3 (H1.32_L1.47) Fab-scFv-Fc

HC 1 (Fab-Fc) (SEQ ID NO: 329)

QVQLVQSGAEVKKPGASVKVSCKASGYTFTSYNMHWVRQAPGQGLEWMGAIYPGNGDTSYNQKFQGRVTITADKSI
STAYMELSSLRSEDTAVYYCARSTYYGGDWYFNVWGAGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFP
EPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSDTKVDKKVEPKSCDKTHTCPPCPA
PPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQ
DWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPEN
NYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSLSLSPGK

HC 2 (scFv-Fc) (SEQ ID NO: 330)

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKANNYATYYADSVKGRFTISRDDS
KNTLYLQMNSLRAEDTAVYYCVRHGNFGDSYVSWFAYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQEP
SLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDEA
DYYCALWYSNHWVFGGGTKLTVLEPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPE
VKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYT
LPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSV
MHEALHNHYTQKSLSLSPGK

LC (SEQ ID NO: 331)

QIVLTQSPSSLSASVGDRVTITCRASSSVSYIHWFQQKPGKSPKPLIYATSNLASGVPVRFSGSGSGTDYTLTISSLQPEDF
ATYYCQQWTSNPPTFGGGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQE
SVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

图76

XENP15053 抗-CD20 (C2B8_H1L1) x 抗-CD3 (H1.33_L1.47) Fab-scFv-Fc

HC 1 (Fab-Fc) (SEQ ID NO: 332)

QVQLVQSGAEVKKPGASVKVSCKASGYTFTSYNMHWVRQAPGQGLEWMGAIYPGNGDTSYNQKFQGRVTITADKSI
STAYMELSSLRSEDTAVYYCARSTYYGGDWYFNVWGAGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFP
EPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSDTKVDKKVEPKSCDKTHTCPPCPA
PPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQ
DWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPEN
NYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSLSLSPGK

HC 2 (scFv-Fc) (SEQ ID NO: 333)

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDSK
NTLYLQMNSLRAEDTAVYYCVRHGNFGDSYVSWFDYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQEPS
LTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDEAD
YYCALWYSNHWVFGGGTKLTVLEPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEV
KFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTL
PPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVM
HEALHNHYTQKSLSLSPGK

LC (SEQ ID NO: 334)

QIVLTQSPSSLSASVGDRVTITCRASSSVSYIHWFQQKPGKSPKPLIYATSNLASGVPVRFSGSGSGTDYTLTISSLQPEDF
ATYYCQQWTSNPPTFGGGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQE
SVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

图77

XENP15630 抗-CD20 (C2B8_H1L1) x 抗-CD3 (H1.88_L1.47) Fab-scFv-Fc

HC 1 (Fab-Fc) (SEQ ID NO: 335)

QVQLVQSGAEVKKPGASVKVSCKASGYTFTSYNMHWVRQAPGQGLEWMGAIYPGNGDTSYNQKFQGRVTITADKSI
STAYMELSSLRSEDTAVYYCARSTYYGGDWYFNVWGAGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFP
EPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSDTKVDKKVEPKSCDKTHTCPPCPA
PPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQ
DWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPEN
NYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSLSLSPGK

HC 2 (scFv-Fc) (SEQ ID NO: 336)

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDSK
NTLYLQMNSLRAEDTAVYYCVRHGNFGPSYVSWFAYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQEPS
LTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDEAD
YYCALWYSNHWVFGGGTKLTVLEPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEV
KFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTL
PPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVM
HEALHNHYTQKSLSLSPGK

LC (SEQ ID NO: 337)

QIVLTQSPSSLSASVGDRVTITCRASSSVSYIHWFQQKPGKSPKPLIYATSNLASGVPVRFSGSGSGTDYTLTISSLQPEDF
ATYYCQQWTSNPPTFGGGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQE
SVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

图78

XENP15631 抗-CD20 (C2B8_H1L1) x 抗-CD3 (H1.89_L1.47) Fab-scFv-Fc

HC 1 (Fab-Fc) (SEQ ID NO: 338)

QVQLVQSGAEVKKPGASVKVSCKASGYTFTSYNMHWVRQAPGQGLEWMGAIYPGNGDTSYNQKFQGRVTITADKSI
STAYMELSSLRSEDTAVYYCARSTYYGGDWYFNVWGAGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFP
EPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSDTKVDKKVEPKSCDKTHTCPPCPA
PPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQ
DWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPEN
NYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSLSLSPGK

HC 2 (scFv-Fc) (SEQ ID NO: 339)

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDSK
NTLYLQMNSLRAEDTAVYYCVRHGNFGDEYVSWFAYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQEPS
LTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDEAD
YYCALWYSNHWVFGGGTKLTVLEPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEV
KFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTL
PPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVM
HEALHNHYTQKSLSLSPGK

LC (SEQ ID NO: 340)

QIVLTQSPSSLSASVGDRVTITCRASSSVSYIHWFQQKPGKSPKPLIYATSNLASGVPVRFSGSGSGTDYTLTISSLQPEDF
ATYYCQQWTSNPPTFGGGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQE
SVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

图79

XENP15632 抗-CD20 (C2B8_H1L1) x 抗-CD3 (H1.90_L1.47) Fab-scFv-Fc

HC 1 (Fab-Fc) (SEQ ID NO: 341)

QVQLVQSGAEVKKPGASVKVSCKASGYTFTSYNMHWVRQAPGQGLEWMGAIYPGNGDTSYNQKFQGRVTITADKSI
STAYMELSSLRSEDTAVYYCARSTYYGGDWYFNVWGAGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFP
EPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSDTKVDKKVEPKSCDKTHTCPPCPA
PPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQ
DWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPEN
NYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSLSLSPGK

HC 2 (scFv-Fc) (SEQ ID NO: 342)

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDSK
NTLYLQMNSLRAEDTAVYYCVRHGNFGDPYVSWFAYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQEPS
LTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDEAD
YYCALWYSNHWVFGGGTKLTVLEPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEV
KFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTL
PPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVM
HEALHNHYTQKSLSLSPGK

LC (SEQ ID NO: 343)

QIVLTQSPSSLSASVGDRVTITCRASSSVSYIHWFQQKPGKSPKPLIYATSNLASGVPVRFSGSGSGTDYTLTISSLQPEDF
ATYYCQQWTSNPPTFGGGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQE
SVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

图80

XENP15633 抗-CD20 (C2B8_H1L1) x 抗-CD3 (H1.91_L1.47) Fab-scFv-Fc

HC 1 (Fab-Fc) (SEQ ID NO: 344)

QVQLVQSGAEVKKPGASVKVSCKASGYTFTSYNMHWVRQAPGQGLEWMGAIYPGNGDTSYNQKFQGRVTITADKSI
STAYMELSSLRSEDTAVYYCARSTYYGGDWYFNVWGAGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFP
EPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSDTKVDKKVEPKSCDKTHTCPPCPA
PPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQ
DWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPEN
NYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSLSLSPGK

HC 2 (scFv-Fc) (SEQ ID NO: 345)

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKANNYATYYADSVKGRFTISRDDS
KNTLYLQMNSLRAEDTAVYYCVRHGNFGDSYVSWFAYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSGKPGSQAVVTQEP
SLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDEA
DYYCALWYSNHWVFGGGTKLTVLEPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPE
VKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYT
LPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSV
MHEALHNHYTQKSLSLSPGK

LC (SEQ ID NO: 346)

QIVLTQSPSSLSASVGDRVTITCRASSSVSYIHWFQQKPGKSPKPLIYATSNLASGVPVRFSGSGSGTDYTLTISSLQPEDF
ATYYCQQWTSNPPTFGGGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQE
SVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

图81

XENP15634 抗-CD20 (C2B8_H1L1) x 抗-CD3 (H1.92_L1.47) Fab-scFv-Fc

HC 1 (Fab-Fc) (SEQ ID NO: 347)

QVQLVQSGAEVKKPGASVKVSCKASGYTFTSYNMHWVRQAPGQGLEWMGAIYPGNGDTSYNQKFQGRVTITADKSI
STAYMELSSLRSEDTAVYYCARSTYYGGDWYFNVWGAGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFP
EPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSDTKVDKKVEPKSCDKTHTCPPCPA
PPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQ
DWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPEN
NYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSLSLSPGK

HC 2 (scFv-Fc) (SEQ ID NO: 348)

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATAYADSVKGRFTISRDDS
KNTLYLQMNSLRAEDTAVYYCVRHGNFGDSYVSWFAYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQEP
SLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDEA
DYYCALWYSNHWVFGGGTKLTVLEPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPE
VKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYT
LPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSV
MHEALHNHYTQKSLSLSPGK

LC (SEQ ID NO: 349)

QIVLTQSPSSLSASVGDRVTITCRASSSVSYIHWFQQKPGKSPKPLIYATSNLASGVPVRFSGSGSGTDYTLTISSLQPEDF
ATYYCQQWTSNPPTFGGGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQE
SVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

图82

XENP15635 抗-CD20 (C2B8_H1L1) x 抗-CD3 (H1.93_L1.47) Fab-scFv-Fc

HC 1 (Fab-Fc) (SEQ ID NO: 350)

QVQLVQSGAEVKKPGASVKVSCKASGYTFTSYNMHWVRQAPGQGLEWMGAIYPGNGDTSYNQKFQGRVTITADKSI
STAYMELSSLRSEDTAVYYCARSTYYGGDWYFNVWGAGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFP
EPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSDTKVDKKVEPKSCDKTHTCPPCPA
PPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQ
DWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPEN
NYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSLSLSPGK

HC 2 (scFv-Fc) (SEQ ID NO: 351)

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDSK
NTLYLQMNSLRAEDTAVYYCVRHGNFGESYVSWFAYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQEPS
LTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDEAD
YYCALWYSNHWVFGGGTKLTVLEPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEV
KFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTL
PPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVM
HEALHNHYTQKSLSLSPGK

LC (SEQ ID NO: 352)

QIVLTQSPSSLSASVGDRVTITCRASSSVSYIHWFQQKPGKSPKPLIYATSNLASGVPVRFSGSGSGTDYTLTISSLQPEDF
ATYYCQQWTSNPPTFGGGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQE
SVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

图83

XENP15636 抗-CD20 (C2B8_H1L1) x 抗-CD3 (H1.94_L1.47) Fab-scFv-Fc

HC 1 (Fab-Fc) (SEQ ID NO: 353)

QVQLVQSGAEVKKPGASVKVSCKASGYTFTSYNMHWVRQAPGQGLEWMGAIYPGNGDTSYNQKFQGRVTITADKSI
STAYMELSSLRSEDTAVYYCARSTYYGGDWYFNVWGAGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFP
EPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSDTKVDKKVEPKSCDKTHTCPPCPA
PPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQ
DWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPEN
NYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSLSLSPGK

HC 2 (scFv-Fc) (SEQ ID NO: 354)

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDSK
NTLYLQMNSLRAEDTAVYYCVRHGNFGQSYVSWFAYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQEPS
LTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDEAD
YYCALWYSNHWVFGGGTKLTVLEPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEV
KFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTL
PPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVM
HEALHNHYTQKSLSLSPGK

LC (SEQ ID NO: 355)

QIVLTQSPSSLSASVGDRVTITCRASSSVSYIHWFQQKPGKSPKPLIYATSNLASGVPVRFSGSGSGTDYTLTISSLQPEDF
ATYYCQQWTSNPPTFGGGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQE
SVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

图84

XENP15638 抗-CD20 (C2B8_H1L1) x 抗-CD3 (H1.95_L1.47) Fab-scFv-Fc

HC 1 (Fab-Fc) (SEQ ID NO: 356)

QVQLVQSGAEVKKPGASVKVSCKASGYTFTSYNMHWVRQAPGQGLEWMGAIYPGNGDTSYNQKFQGRVTITADKSI
STAYMELSSLRSEDTAVYYCARSTYYGGDWYFNVWGAGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFP
EPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSDTKVDKKVEPKSCDKTHTCPPCPA
PPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQ
DWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPEN
NYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSLSLSPGK

HC 2 (scFv-Fc) (SEQ ID NO: 357)

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDSK
NTLYLQMNSLRAEDTAVYYCVRHGNFGDEYVSWFAYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQEPS
LTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDEAD
YYCALWYSNHWVFGGGTKLTVLEPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEV
KFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTL
PPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVM
HEALHNHYTQKSLSLSPGK

LC (SEQ ID NO: 358)

QIVLTQSPSSLSASVGDRVTITCRASSSVSYIHWFQQKPGKSPKPLIYATSNLASGVPVRFSGSGSGTDYTLTISSLQPEDF
ATYYCQQWTSNPPTFGGGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQE
SVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

图85

XENP15639 抗-CD20 (C2B8_H1L1) x 抗-CD3 (H1.96_L1.47) Fab-scFv-Fc

HC 1 (Fab-Fc) (SEQ ID NO: 359)

QVQLVQSGAEVKKPGASVKVSCKASGYTFTSYNMHWVRQAPGQGLEWMGAIYPGNGDTSYNQKFQGRVTITADKSI
STAYMELSSLRSEDTAVYYCARSTYYGGDWYFNVWGAGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFP
EPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSDTKVDKKVEPKSCDKTHTCPPCPA
PPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQ
DWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPEN
NYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSLSLSPGK

HC 2 (scFv-Fc) (SEQ ID NO: 360)

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDSK
NTLYLQMNSLRAEDTAVYYCVRHGNFGDQYVSWFAYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQEPS
LTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDEAD
YYCALWYSNHWVFGGGTKLTVLEPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEV
KFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTL
PPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVM
HEALHNHYTQKSLSLSPGK

LC (SEQ ID NO: 361)

QIVLTQSPSSLSASVGDRVTITCRASSSVSYIHWFQQKPGKSPKPLIYATSNLASGVPVRFSGSGSGTDYTLTISSLQPEDF
ATYYCQQWTSNPPTFGGGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQE
SVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

图86

XENP13677 抗-CD20 (C2B8_H1.202_L1.113) x 抗-CD3 (H1.30_L1.47) Fab-scFv-Fc

HC 1 (Fab-Fc) (SEQ ID NO: 362)

QVQLVQSGAEVKKPGASVKVSCKASGYTFTSYNMHWVRQAPGQRLEWMGAIYPGNGATSYSQKFQGRVTITADTSA
STAYMELSSLRSEDTAVYYCARSYYMGGDWYFDVWGAGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFP
EPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSDTKVDKKVEPKSCDKTHTCPPCPA
PPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQ
DWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPEN
NYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSLSLSPGK

HC 2 (scFv-Fc) (SEQ ID NO: 363)

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDSK
NTLYLQMNSLRAEDTAVYYCVRHGNFGDSYVSWFAYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQEPS
LTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDEAD
YYCALWYSNHWVFGGGTKLTVLEPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEV
KFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTL
PPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVM
HEALHNHYTQKSLSLSPGK

LC (SEQ ID NO: 364)

QIVLTQSPSSLSASVGDRVTITCRASWSVSYIHWFQQKPGKSPKPLIYATSNLASGVPVRFSGSGSGTDYTLTISSLQPEDF
ATYYCQQWTHNPPTFGGGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQE
SVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

图87

XENP14388 抗-CD20 (C2B8_H1.202_L1.113) x 抗-CD3 (H1.31_L1.47) Fab-scFv-Fc

HC 1 (Fab-Fc) (SEQ ID NO: 365)

QVQLVQSGAEVKKPGASVKVSCKASGYTFTSYNMHWVRQAPGQRLEWMGAIYPGNGATSYSQKFQGRVTITADTSA
STAYMELSSLRSEDTAVYYCARSYYMGGDWYFDVWGAGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFP
EPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSDTKVDKKVEPKSCDKTHTCPPCPA
PPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQ
DWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPEN
NYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSLSLSPGK

HC 2 (scFv-Fc) (SEQ ID NO: 366)

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMSWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDSK
NTLYLQMNSLRAEDTAVYYCVRHGNFGDSYVSWFAYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQEPS
LTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDEAD
YYCALWYSNHWVFGGGTKLTVLEPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEV
KFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTL
PPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVM
HEALHNHYTQKSLSLSPGK

LC (SEQ ID NO: 367)

QIVLTQSPSSLSASVGDRVTITCRASWSVSYIHWFQQKPGKSPKPLIYATSNLASGVPVRFSGSGSGTDYTLTISSLQPEDF
ATYYCQQWTHNPPTFGGGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQE
SVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

图88

XENP14389 抗-CD20 (C2B8_H1.202_L1.113) x 抗-CD3 (H1.32_L1.47) Fab-scFv-Fc

HC 1 (Fab-Fc) (SEQ ID NO: 368)

QVQLVQSGAEVKKPGASVKVSCKASGYTFTSYNMHWVRQAPGQRLEWMGAIYPGNGATSYSQKFQGRVTITADTSA
STAYMELSSLRSEDTAVYYCARSYYMGGDWYFDVWGAGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFP
EPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSDTKVDKKVEPKSCDKTHTCPPCPA
PPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQ
DWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPEN
NYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSLSLSPGK

HC 2 (scFv-Fc) (SEQ ID NO: 369)

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKANNYATYYADSVKGRFTISRDDS
KNTLYLQMNSLRAEDTAVYYCVRHGNFGDSYVSWFAYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQEP
SLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDEA
DYYCALWYSNHWVFGGGTKLTVLEPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPE
VKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYT
LPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSV
MHEALHNHYTQKSLSLSPGK

LC (SEQ ID NO: 370)

QIVLTQSPSSLSASVGDRVTITCRASWSVSYIHWFQQKPGKSPKPLIYATSNLASGVPVRFSGSGSGTDYTLTISSLQPEDF
ATYYCQQWTHNPPTFGGGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQE
SVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

图89

XENP14390 抗-CD20 (C2B8_H1.202_L1.113) x 抗-CD3 (H1.33_L1.47) Fab-scFv-Fc

HC 1 (Fab-Fc) (SEQ ID NO: 371)

QVQLVQSGAEVKKPGASVKVSCKASGYTFTSYNMHWVRQAPGQRLEWMGAIYPGNGATSYSQKFQGRVTITADTSA
STAYMELSSLRSEDTAVYYCARSYYMGGDWYFDVWGAGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFP
EPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSDTKVDKKVEPKSCDKTHTCPPCPA
PPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQ
DWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPEN
NYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSLSLSPGK

HC 2 (scFv-Fc) (SEQ ID NO: 372)

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDSK
NTLYLQMNSLRAEDTAVYYCVRHGNFGDSYVSWFDYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQEPS
LTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDEAD
YYCALWYSNHWVFGGGTKLTVLEPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEV
KFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTL
PPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVM
HEALHNHYTQKSLSLSPGK

LC (SEQ ID NO: 373)

QIVLTQSPSSLSASVGDRVTITCRASWSVSYIHWFQQKPGKSPKPLIYATSNLASGVPVRFSGSGSGTDYTLTISSLQPEDF
ATYYCQQWTHNPPTFGGGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQE
SVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

图90

XENP14391 抗-CD20 (C2B8_H1.202_L1.113) x 抗-CD3 (H1.88_L1.47) Fab-scFv-Fc

HC 1 (Fab-Fc) (SEQ ID NO: 374)

QVQLVQSGAEVKKPGASVKVSCKASGYTFTSYNMHWVRQAPGQRLEWMGAIYPGNGATSYSQKFQGRVTITADTSA
STAYMELSSLRSEDTAVYYCARSYYMGGDWYFDVWGAGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFP
EPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSDTKVDKKVEPKSCDKTHTCPPCPA
PPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQ
DWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPEN
NYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSLSLSPGK

HC 2 (scFv-Fc) (SEQ ID NO: 375)

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDSK
NTLYLQMNSLRAEDTAVYYCVRHGNFGPSYVSWFAYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQEPS
LTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDEAD
YYCALWYSNHWVFGGGTKLTVLEPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEV
KFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTL
PPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVM
HEALHNHYTQKSLSLSPGK

LC (SEQ ID NO: 376)

QIVLTQSPSSLSASVGDRVTITCRASWSVSYIHWFQQKPGKSPKPLIYATSNLASGVPVRFSGSGSGTDYTLTISSLQPEDF
ATYYCQQWTHNPPTFGGGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQE
SVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

图91

XENP14392 抗-CD20 (C2B8_H1.202_L1.113) x 抗-CD3 (H1.89_L1.47) Fab-scFv-Fc

HC 1 (Fab-Fc) (SEQ ID NO: 377)

QVQLVQSGAEVKKPGASVKVSCKASGYTFTSYNMHWVRQAPGQRLEWMGAIYPGNGATSYSQKFQGRVTITADTSA
STAYMELSSLRSEDTAVYYCARSYYMGGDWYFDVWGAGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFP
EPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSDTKVDKKVEPKSCDKTHTCPPCPA
PPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQ
DWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPEN
NYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSLSLSPGK

HC 2 (scFv-Fc) (SEQ ID NO: 378)

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDSK
NTLYLQMNSLRAEDTAVYYCVRHGNFGDEYVSWFAYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQEPS
LTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDEAD
YYCALWYSNHWVFGGGTKLTVLEPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEV
KFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTL
PPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVM
HEALHNHYTQKSLSLSPGK

LC (SEQ ID NO: 379)

QIVLTQSPSSLSASVGDRVTITCRASWSVSYIHWFQQKPGKSPKPLIYATSNLASGVPVRFSGSGSGTDYTLTISSLQPEDF
ATYYCQQWTHNPPTFGGGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQE
SVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

图92

XENP14393 抗-CD20 (C2B8_H1.202_L1.113) x 抗-CD3 (H1.90_L1.47) Fab-scFv-Fc

HC 1 (Fab-Fc) (SEQ ID NO: 380)

QVQLVQSGAEVKKPGASVKVSCKASGYTFTSYNMHWVRQAPGQRLEWMGAIYPGNGATSYSQKFQGRVTITADTSA
STAYMELSSLRSEDTAVYYCARSYYMGGDWYFDVWGAGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFP
EPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSDTKVDKKVEPKSCDKTHTCPPCPA
PPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQ
DWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPEN
NYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSLSLSPGK

HC 2 (scFv-Fc) (SEQ ID NO: 381)

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDSK
NTLYLQMNSLRAEDTAVYYCVRHGNFGDPYVSWFAYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQEPS
LTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDEAD
YYCALWYSNHWVFGGGTKLTVLEPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEV
KFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTL
PPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVM
HEALHNHYTQKSLSLSPGK

LC (SEQ ID NO: 382)

QIVLTQSPSSLSASVGDRVTITCRASWSVSYIHWFQQKPGKSPKPLIYATSNLASGVPVRFSGSGSGTDYTLTISSLQPEDF
ATYYCQQWTHNPPTFGGGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQE
SVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

图93

XENP16366 抗-CD20 (C2B8_H1.202_L1.113) x 抗-CD3 (H1.98_L1.47) Fab-scFv-Fc

HC 1 (Fab-Fc) (SEQ ID NO: 383)

QVQLVQSGAEVKKPGASVKVSCKASGYTFTSYNMHWVRQAPGQRLEWMGAIYPGNGATSYSQKFQGRVTITADTSA
STAYMELSSLRSEDTAVYYCARSYYMGGDWYFDVWGAGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFP
EPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSDTKVDKKVEPKSCDKTHTCPPCPA
PPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQ
DWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPEN
NYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSLSLSPGK

HC 2 (scFv-Fc) (SEQ ID NO: 384)

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKANNYATYYADSVKGRFTISRDDS
KNTLYLQMNSLRAEDTAVYYCVRHGNFGDSYVSWFDYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSGKPGSQAVVTQEP
SLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDEA
DYYCALWYSNHWVFGGGTKLTVLEPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPE
VKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYT
LPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSV
MHEALHNHYTQKSLSLSPGK

LC (SEQ ID NO: 385)

QIVLTQSPSSLSASVGDRVTITCRASWSVSYIHWFQQKPGKSPKPLIYATSNLASGVPVRFSGSGSGTDYTLTISSLQPEDF
ATYYCQQWTHNPPTFGGGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQE
SVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

图94

XENP16367 抗-CD20 (C2B8_H1.202_L1.113) x 抗-CD3 (H1.99_L1.47) Fab-scFv-Fc

HC 1 (Fab-Fc) (SEQ ID NO: 386)

QVQLVQSGAEVKKPGASVKVSCKASGYTFTSYNMHWVRQAPGQRLEWMGAIYPGNGATSYSQKFQGRVTITADTSA
STAYMELSSLRSEDTAVYYCARSYYMGGDWYFDVWGAGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFP
EPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSDTKVDKKVEPKSCDKTHTCPPCPA
PPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQ
DWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPEN
NYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSLSLSPGK

HC 2 (scFv-Fc) (SEQ ID NO: 387)

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATAYADSVKGRFTISRDDS
KNTLYLQMNSLRAEDTAVYYCVRHGNFGDSYVSWFDYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQEP
SLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDEA
DYYCALWYSNHWVFGGGTKLTVLEPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPE
VKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYT
LPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSV
MHEALHNHYTQKSLSLSPGK

LC (SEQ ID NO: 388)

QIVLTQSPSSLSASVGDRVTITCRASWSVSYIHWFQQKPGKSPKPLIYATSNLASGVPVRFSGSGSGTDYTLTISSLQPEDF
ATYYCQQWTHNPPTFGGGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQE
SVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

图95

XENP16368 抗-CD20 (C2B8_H1.202_L1.113) x 抗-CD3 (H1.100_L1.47) Fab-scFv-Fc

HC 1 (Fab-Fc) (SEQ ID NO: 389)

QVQLVQSGAEVKKPGASVKVSCKASGYTFTSYNMHWVRQAPGQRLEWMGAIYPGNGATSYSQKFQGRVTITADTSA
STAYMELSSLRSEDTAVYYCARSYYMGGDWYFDVWGAGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFP
EPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSDTKVDKKVEPKSCDKTHTCPPCPA
PPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQ
DWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPEN
NYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSLSLSPGK

HC 2 (scFv-Fc) (SEQ ID NO: 390)

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDSK
NTLYLQMNSLRAEDTAVYYCVRHGNFGASYVSWFDYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQEPS
LTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDEAD
YYCALWYSNHWVFGGGTKLTVLEPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEV
KFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTL
PPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVM
HEALHNHYTQKSLSLSPGK

LC (SEQ ID NO: 391)

QIVLTQSPSSLSASVGDRVTITCRASWSVSYIHWFQQKPGKSPKPLIYATSNLASGVPVRFSGSGSGTDYTLTISSLQPEDF
ATYYCQQWTHNPPTFGGGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQE
SVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

图96

XENP16369 抗-CD20 (C2B8_H1.202_L1.113) x 抗-CD3 (H1.101_L1.47) Fab-scFv-Fc

HC 1 (Fab-Fc) (SEQ ID NO: 392)

QVQLVQSGAEVKKPGASVKVSCKASGYTFTSYNMHWVRQAPGQRLEWMGAIYPGNGATSYSQKFQGRVTITADTSA
STAYMELSSLRSEDTAVYYCARSYYMGGDWYFDVWGAGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFP
EPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSDTKVDKKVEPKSCDKTHTCPPCPA
PPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQ
DWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPEN
NYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSLSLSPGK

HC 2 (scFv-Fc) (SEQ ID NO: 393)

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDSK
NTLYLQMNSLRAEDTAVYYCVRHGNFGQSYVSWFDYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQEPS
LTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDEAD
YYCALWYSNHWVFGGGTKLTVLEPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEV
KFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTL
PPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVM
HEALHNHYTQKSLSLSPGK

LC (SEQ ID NO: 394)

QIVLTQSPSSLSASVGDRVTITCRASWSVSYIHWFQQKPGKSPKPLIYATSNLASGVPVRFSGSGSGTDYTLTISSLQPEDF
ATYYCQQWTHNPPTFGGGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQE
SVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

图97

XENP16370 抗-CD20 (C2B8_H1.202_L1.113) x 抗-CD3 (H1.102_L1.47) Fab-scFv-Fc

HC 1 (Fab-Fc) (SEQ ID NO: 395)

QVQLVQSGAEVKKPGASVKVSCKASGYTFTSYNMHWVRQAPGQRLEWMGAIYPGNGATSYSQKFQGRVTITADTSA
STAYMELSSLRSEDTAVYYCARSYYMGGDWYFDVWGAGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFP
EPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSDTKVDKKVEPKSCDKTHTCPPCPA
PPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQ
DWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPEN
NYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSLSLSPGK

HC 2 (scFv-Fc) (SEQ ID NO: 396)

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDSK
NTLYLQMNSLRAEDTAVYYCVRHGNFGDEYVSWFDYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQEPS
LTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDEAD
YYCALWYSNHWVFGGGTKLTVLEPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEV
KFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTL
PPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVM
HEALHNHYTQKSLSLSPGK

LC (SEQ ID NO: 397)

QIVLTQSPSSLSASVGDRVTITCRASWSVSYIHWFQQKPGKSPKPLIYATSNLASGVPVRFSGSGSGTDYTLTISSLQPEDF
ATYYCQQWTHNPPTFGGGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQE
SVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

图98

XENP16371 抗-CD20 (C2B8_H1.202_L1.113) x 抗-CD3 (H1.103_L1.47) Fab-scFv-Fc

HC 1 (Fab-Fc) (SEQ ID NO: 398)

QVQLVQSGAEVKKPGASVKVSCKASGYTFTSYNMHWVRQAPGQRLEWMGAIYPGNGATSYSQKFQGRVTITADTSA
STAYMELSSLRSEDTAVYYCARSYYMGGDWYFDVWGAGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFP
EPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSDTKVDKKVEPKSCDKTHTCPPCPA
PPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQ
DWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPEN
NYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSLSLSPGK

HC 2 (scFv-Fc) (SEQ ID NO: 399)

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDSK
NTLYLQMNSLRAEDTAVYYCVRHGNFGDNYVSWFDYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQEPS
LTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDEAD
YYCALWYSNHWVFGGGTKLTVLEPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEV
KFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTL
PPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVM
HEALHNHYTQKSLSLSPGK

LC (SEQ ID NO: 400)

QIVLTQSPSSLSASVGDRVTITCRASWSVSYIHWFQQKPGKSPKPLIYATSNLASGVPVRFSGSGSGTDYTLTISSLQPEDF
ATYYCQQWTHNPPTFGGGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQE
SVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

图99

XENP16372 抗-CD20 (C2B8_H1.202_L1.113) x 抗-CD3 (H1.104_L1.47) Fab-scFv-Fc

HC 1 (Fab-Fc) (SEQ ID NO: 401)

QVQLVQSGAEVKKPGASVKVSCKASGYTFTSYNMHWVRQAPGQRLEWMGAIYPGNGATSYSQKFQGRVTITADTSA
STAYMELSSLRSEDTAVYYCARSYYMGGDWYFDVWGAGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFP
EPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSDTKVDKKVEPKSCDKTHTCPPCPA
PPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQ
DWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPEN
NYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSLSLSPGK

HC 2 (scFv-Fc) (SEQ ID NO: 402)

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDSK
NTLYLQMNSLRAEDTAVYYCVRHGNFGDPYVSWFDYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQEPS
LTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDEAD
YYCALWYSNHWVFGGGTKLTVLEPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEV
KFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTL
PPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVM
HEALHNHYTQKSLSLSPGK

LC (SEQ ID NO: 403)

QIVLTQSPSSLSASVGDRVTITCRASWSVSYIHWFQQKPGKSPKPLIYATSNLASGVPVRFSGSGSGTDYTLTISSLQPEDF
ATYYCQQWTHNPPTFGGGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQE
SVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

图100

XENP16373 抗-CD20 (C2B8_H1.202_L1.113) x 抗-CD3 (H1.105_L1.47) Fab-scFv-Fc

HC 1 (Fab-Fc) (SEQ ID NO: 404)

QVQLVQSGAEVKKPGASVKVSCKASGYTFTSYNMHWVRQAPGQRLEWMGAIYPGNGATSYSQKFQGRVTITADTSA
STAYMELSSLRSEDTAVYYCARSYYMGGDWYFDVWGAGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFP
EPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSDTKVDKKVEPKSCDKTHTCPPCPA
PPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQ
DWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPEN
NYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSLSLSPGK

HC 2 (scFv-Fc) (SEQ ID NO: 405)

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDSK
NTLYLQMNSLRAEDTAVYYCVRHGNFGDQYVSWFDYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQEP
SLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDEA
DYYCALWYSNHWVFGGGTKLTVLEPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPE
VKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYT
LPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSV
MHEALHNHYTQKSLSLSPGK

LC (SEQ ID NO: 406)

QIVLTQSPSSLSASVGDRVTITCRASWSVSYIHWFQQKPGKSPKPLIYATSNLASGVPVRFSGSGSGTDYTLTISSLQPEDF
ATYYCQQWTHNPPTFGGGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQE
SVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

图101

XENP16374 抗-CD20 (C2B8_H1.202_L1.113) x 抗-CD3 (H1.106_L1.47) Fab-scFv-Fc

HC 1 (Fab-Fc) (SEQ ID NO: 407)

QVQLVQSGAEVKKPGASVKVSCKASGYTFTSYNMHWVRQAPGQRLEWMGAIYPGNGATSYSQKFQGRVTITADTSA
STAYMELSSLRSEDTAVYYCARSYYMGGDWYFDVWGAGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFP
EPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSDTKVDKKVEPKSCDKTHTCPPCPA
PPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQ
DWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPEN
NYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSLSLSPGK

HC 2 (scFv-Fc) (SEQ ID NO: 408)

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKANNYATAYADSVKGRFTISRDDS
KNTLYLQMNSLRAEDTAVYYCVRHGNFGDSYVSWFAYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQEP
SLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDEA
DYYCALWYSNHWVFGGGTKLTVLEPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPE
VKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYT
LPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSV
MHEALHNHYTQKSLSLSPGK

LC (SEQ ID NO: 409)

QIVLTQSPSSLSASVGDRVTITCRASWSVSYIHWFQQKPGKSPKPLIYATSNLASGVPVRFSGSGSGTDYTLTISSLQPEDF
ATYYCQQWTHNPPTFGGGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQE
SVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

图102

XENP16375 抗-CD20 (C2B8_H1.202_L1.113) x 抗-CD3 (H1.107_L1.47) Fab-scFv-Fc

HC 1 (Fab-Fc) (SEQ ID NO: 410)

QVQLVQSGAEVKKPGASVKVSCKASGYTFTSYNMHWVRQAPGQRLEWMGAIYPGNGATSYSQKFQGRVTITADTSA
STAYMELSSLRSEDTAVYYCARSYYMGGDWYFDVWGAGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFP
EPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSDTKVDKKVEPKSCDKTHTCPPCPA
PPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQ
DWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPEN
NYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSLSLSPGK

HC 2 (scFv-Fc) (SEQ ID NO: 411)

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKANNYATAYADSVKGRFTISRDDS
KNTLYLQMNSLRAEDTAVYYCVRHGNFGASYVSWFAYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQEP
SLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDEA
DYYCALWYSNHWVFGGGTKLTVLEPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPE
VKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYT
LPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSV
MHEALHNHYTQKSLSLSPGK

LC (SEQ ID NO: 412)

QIVLTQSPSSLSASVGDRVTITCRASWSVSYIHWFQQKPGKSPKPLIYATSNLASGVPVRFSGSGSGTDYTLTISSLQPEDF
ATYYCQQWTHNPPTFGGGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQE
SVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

图103

XENP16376 抗-CD20 (C2B8_H1.202_L1.113) x 抗-CD3 (H1.108_L1.47) Fab-scFv-Fc

HC 1 (Fab-Fc) (SEQ ID NO: 413)

QVQLVQSGAEVKKPGASVKVSCKASGYTFTSYNMHWVRQAPGQRLEWMGAIYPGNGATSYSQKFQGRVTITADTSA
STAYMELSSLRSEDTAVYYCARSYYMGGDWYFDVWGAGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFP
EPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSDTKVDKKVEPKSCDKTHTCPPCPA
PPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQ
DWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPEN
NYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSLSLSPGK

HC 2 (scFv-Fc) (SEQ ID NO: 414)

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKANNYATAYADSVKGRFTISRDDS
KNTLYLQMNSLRAEDTAVYYCVRHGNFGQSYVSWFAYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSGKPGSQAVVTQEP
SLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDEA
DYYCALWYSNHWVFGGGTKLTVLEPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPE
VKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYT
LPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSV
MHEALHNHYTQKSLSLSPGK

LC (SEQ ID NO: 415)

QIVLTQSPSSLSASVGDRVTITCRASWSVSYIHWFQQKPGKSPKPLIYATSNLASGVPVRFSGSGSGTDYTLTISSLQPEDF
ATYYCQQWTHNPPTFGGGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQE
SVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

图104

抗-CD20 (C2B8_H1.202_L1.113) x 抗-CD3 (H1.109_L1.47) Fab-scFv-Fc

HC 1 (Fab-Fc) (SEQ ID NO: 416)

QVQLVQSGAEVKKPGASVKVSCKASGYTFTSYNMHWVRQAPGQRLEWMGAIYPGNGATSYSQKFQGRVTITADTSA
STAYMELSSLRSEDTAVYYCARSYYMGGDWYFDVWGAGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFP
EPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSDTKVDKKVEPKSCDKTHTCPPCPA
PPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQ
DWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPEN
NYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSLSLSPGK

HC 2 (scFv-Fc) (SEQ ID NO: 417)

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKANNYATAYADSVKGRFTISRDDS
KNTLYLQMNSLRAEDTAVYYCVRHGNFGDSYVSWFDYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSGKPGSQAVVTQEP
SLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDEA
DYYCALWYSNHWVFGGGTKLTVLEPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPE
VKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYT
LPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSV
MHEALHNHYTQKSLSLSPGK

LC (SEQ ID NO: 418)

QIVLTQSPSSLSASVGDRVTITCRASWSVSYIHWFQQKPGKSPKPLIYATSNLASGVPVRFSGSGSGTDYTLTISSLQPEDF
ATYYCQQWTHNPPTFGGGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQE
SVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

图105

>sp|P11836|CD20_人 B-淋巴细胞抗原 CD20

SEQ ID NO: 419

MTTPRNSVNGTFPAEPMKGPIAMQSGPKPLFRRMSSLVGPTQSFFMRESKTLGAVQIMNG

LFHIALGGLLMIPAGIYAPICVTVWYPLWGGIMYIISGSLLAATEKNSRKCLVKGKMIMN

SLSLFAAISGMILSIMDILNIKISHFLKMESLNFIRAHTPYINIYNCEPANPSEKNSPST

QYCYSIQSLFLGILSVMLIFAFFQELVIAGIVENEWKRTCSRPKSNIVLLSAEEKKEQTI

EIKEEVVGLTETSSQPKNEEDIEIIPIQEEEEEETETNFPEPPQDQESSPIENDSSP

>sp|P26951|IL3RA_人 中白介素-3 受体 $\alpha$ 亚基(CD123)

SEQ ID NO: 420

MVLLWLTLLLIALPCLLQTKEDPNPPITNLRMKAKAQQLTWDLNRNVTDIECVKDADYSM

PAVNNSYCQFGAISLCEVTNYTVRVANPPFSTWILFPENSGKPWAGAENLTCWIHDVDFL

SCSWAVGPGAPADVQYDLYLNVANRRQQYECLHYKTDAQGTRIGCRFDDISRLSSGSQSS

HILVRGRSAAFGIPCTDKFVVFSQIEILTPPNMTAKCNKTHSFMHWKMRSHFNRKFRYEL

QIQKRMQPVITEQVRDRTSFQLLNPGTYTVQIRARERVYEFLSAWSTPQRFECDQEEGAN

TRAWRTSLLIALGTLLALVCVFVICRRYLVMQRLFPRIPHMKDPIGDSFQNDKLVVWEAG

KAGLEECLVTEVQVVQKT

图106

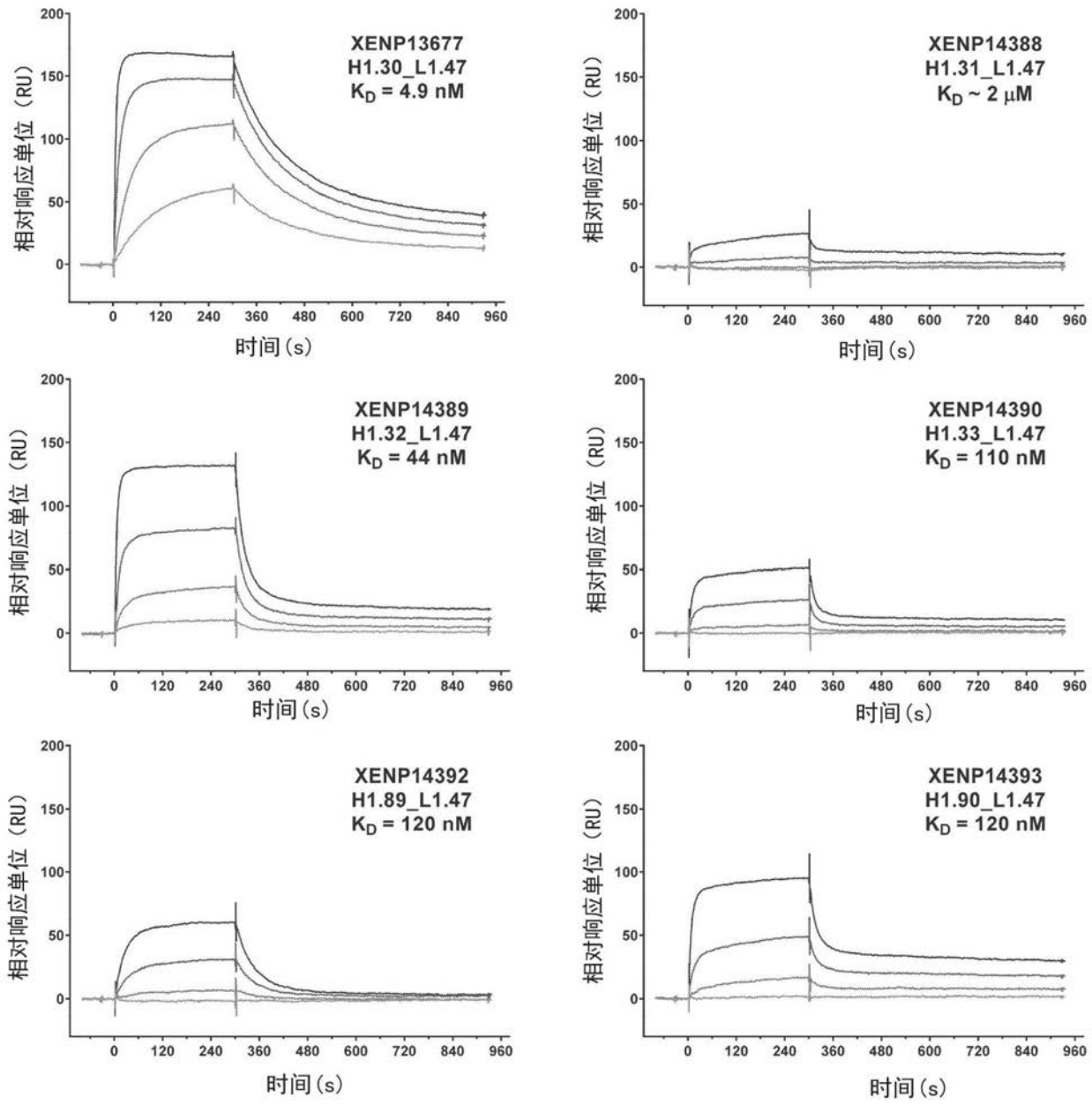

XENP13677
H1.30_L1.47
$K_D$ = 4.9 nM
XENP14388
H1.31_L1.47
$K_D$ ~ 2 μM
XENP14389
H1.32_L1.47
$K_D$ = 44 nM
XENP14390
H1.33_L1.47
$K_D$ = 110 nM
XENP14392
H1.89_L1.47
$K_D$ = 120 nM
XENP14393
H1.90_L1.47
$K_D$ = 120 nM
相对响应单位（RU）
时间(s)
0
50
100
150
200
0
120
240
360
480
600
720
840
960

图107

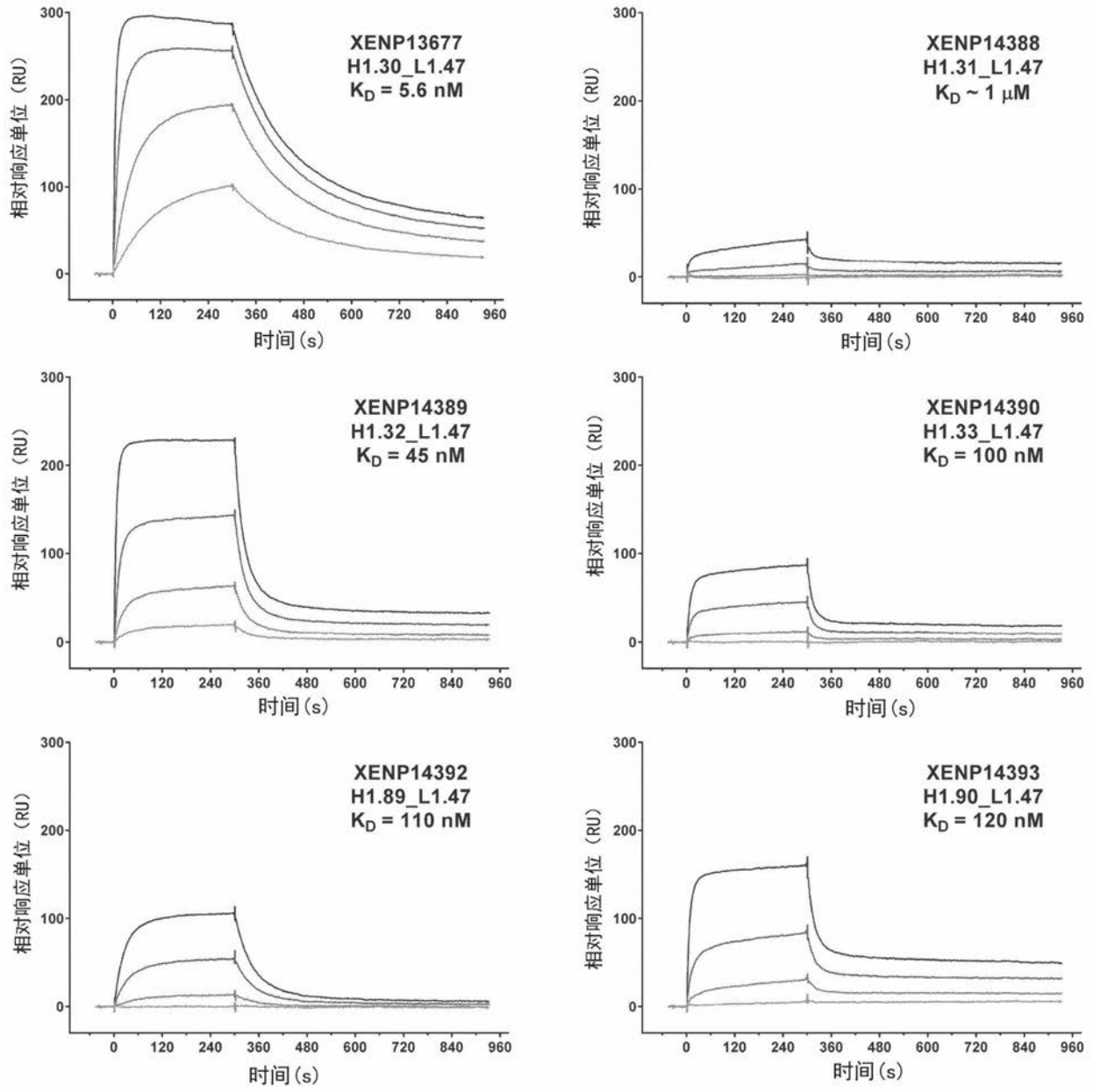

XENP13677
H1.30_L1.47
K_D = 5.6 nM
XENP14388
H1.31_L1.47
K_D ~ 1 μM
XENP14389
H1.32_L1.47
K_D = 45 nM
XENP14390
H1.33_L1.47
K_D = 100 nM
XENP14392
H1.89_L1.47
K_D = 110 nM
XENP14393
H1.90_L1.47
K_D = 120 nM
相对响应单位（RU）
时间(s)
0
100
200
300
0
120
240
360
480
600
720
840
960

图108

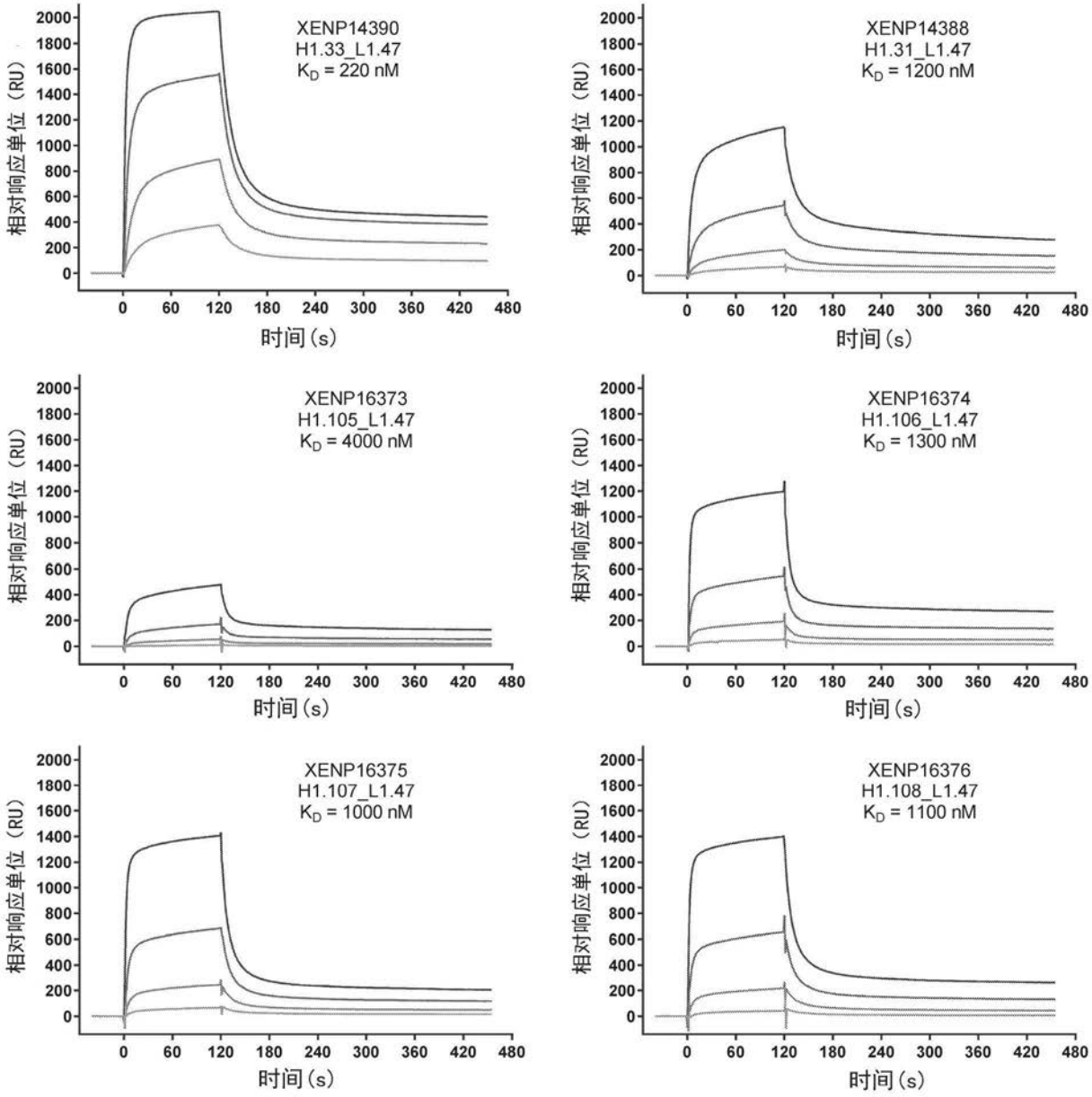

XENP14390
H1.33_L1.47
$K_D$ = 220 nM
XENP14388
H1.31_L1.47
$K_D$ = 1200 nM
XENP16373
H1.105_L1.47
$K_D$ = 4000 nM
XENP16374
H1.106_L1.47
$K_D$ = 1300 nM
XENP16375
H1.107_L1.47
$K_D$ = 1000 nM
XENP16376
H1.108_L1.47
$K_D$ = 1100 nM
相对响应单位（RU）
时间(s)

图109

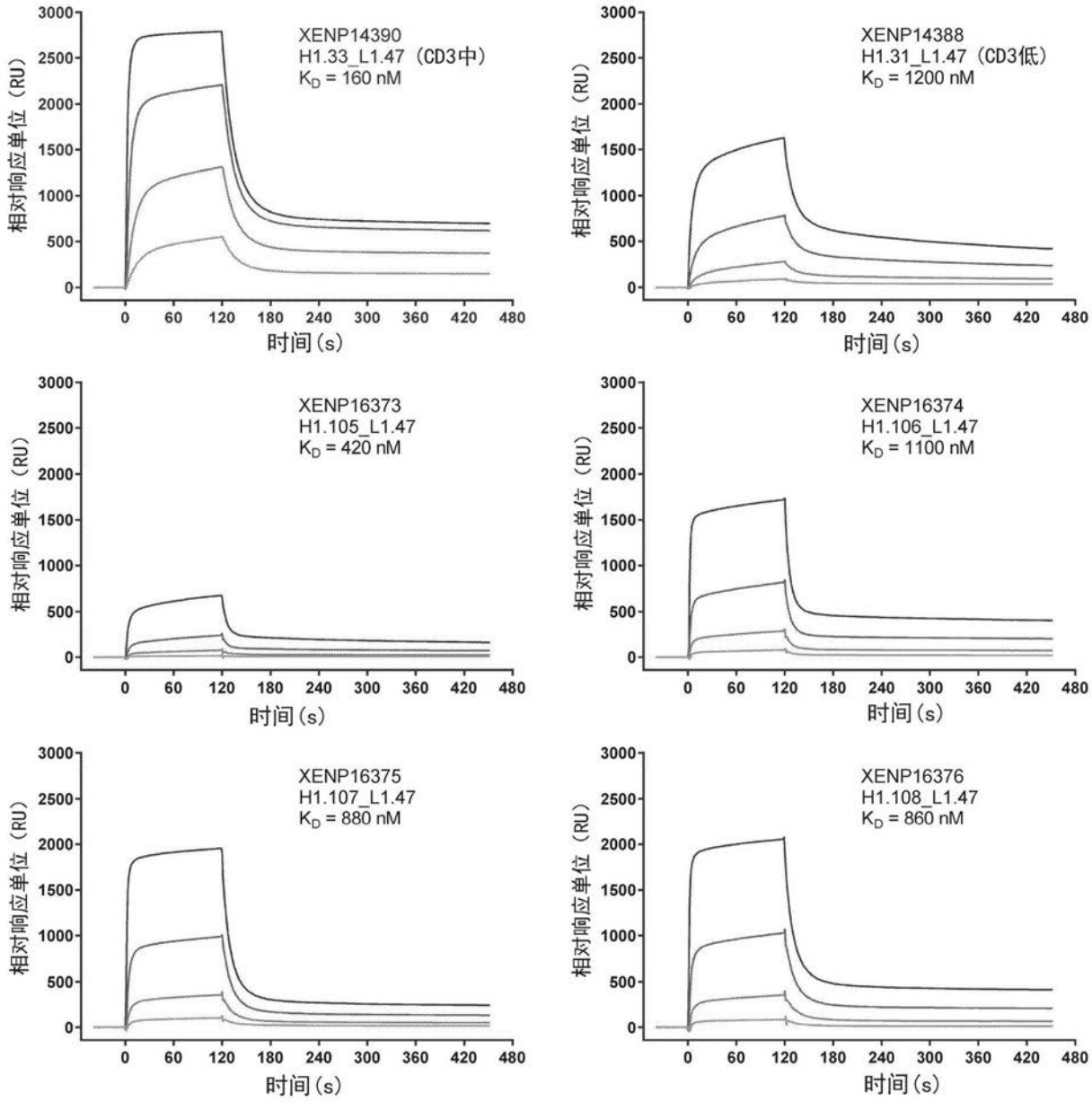

XENP14390
H1.33_L1.47（CD3中）
$K_D$ = 160 nM
XENP14388
H1.31_L1.47（CD3低）
$K_D$ = 1200 nM
XENP16373
H1.105_L1.47
$K_D$ = 420 nM
XENP16374
H1.106_L1.47
$K_D$ = 1100 nM
XENP16375
H1.107_L1.47
$K_D$ = 880 nM
XENP16376
H1.108_L1.47
$K_D$ = 860 nM
相对响应单位（RU）
时间(s)
0
500
1000
1500
2000
2500
3000
0
60
120
180
240
300
360
420
480

图110

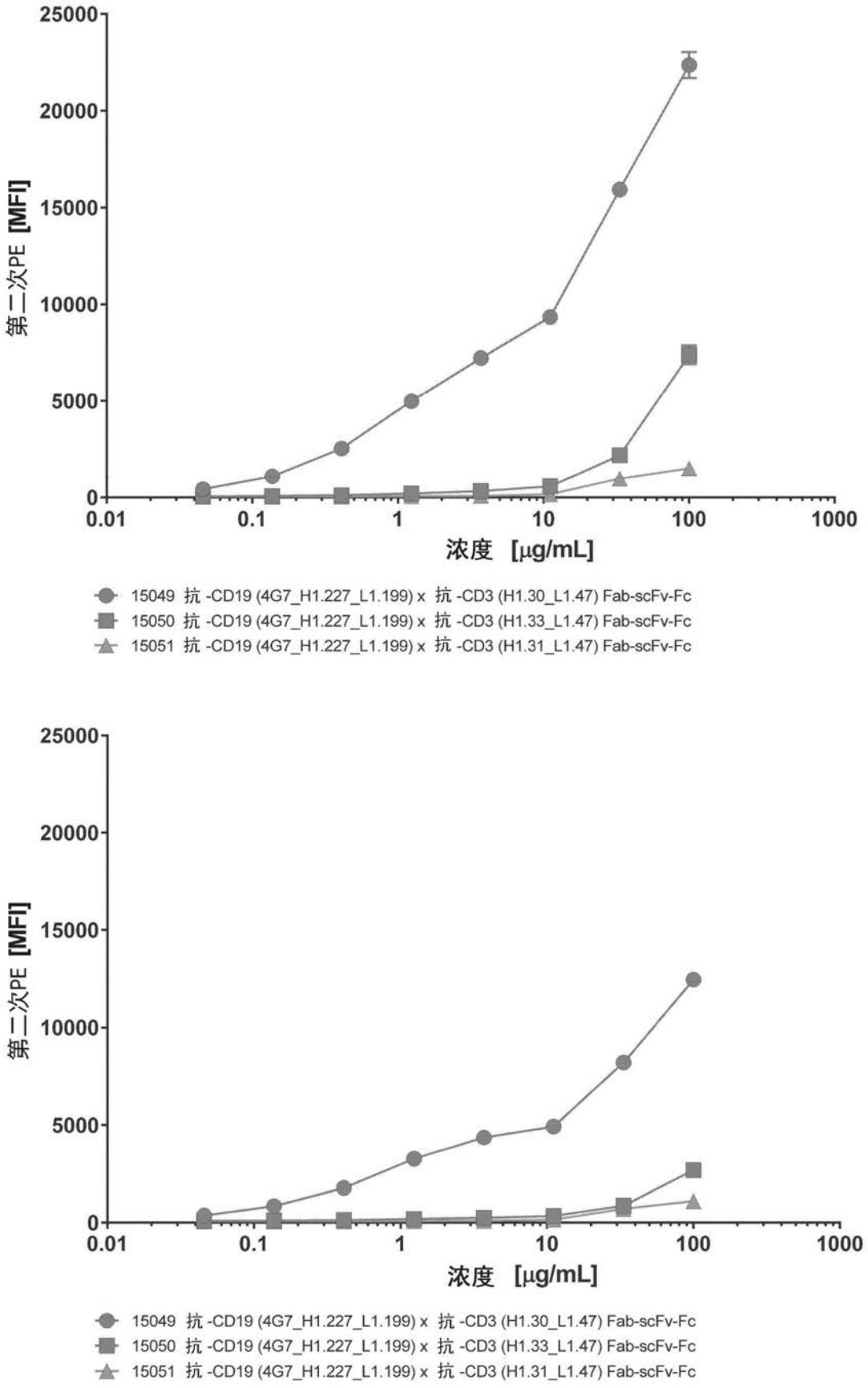
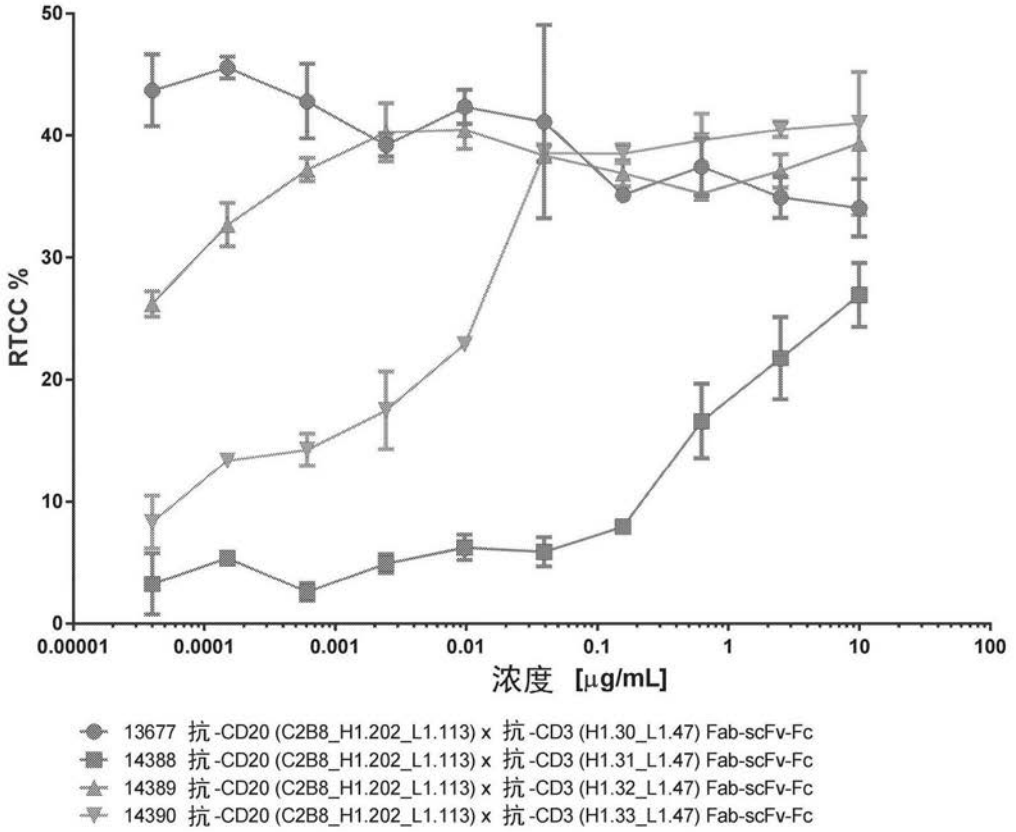

25000
20000
15000
10000
5000
0
第二次PE [MFI]
0.01
0.1
1
10
100
1000
浓度 [μg/mL]
15049 抗 -CD19 (4G7_H1.227_L1.199) x 抗 -CD3 (H1.30_L1.47) Fab-scFv-Fc
15050 抗 -CD19 (4G7_H1.227_L1.199) x 抗 -CD3 (H1.33_L1.47) Fab-scFv-Fc
15051 抗 -CD19 (4G7_H1.227_L1.199) x 抗 -CD3 (H1.31_L1.47) Fab-scFv-Fc

图111


RTCC %
浓度 [μg/mL]
13677 抗-CD20 (C2B8_H1.202_L1.113) x 抗-CD3 (H1.30_L1.47) Fab-scFv-Fc
14388 抗-CD20 (C2B8_H1.202_L1.113) x 抗-CD3 (H1.31_L1.47) Fab-scFv-Fc
14389 抗-CD20 (C2B8_H1.202_L1.113) x 抗-CD3 (H1.32_L1.47) Fab-scFv-Fc
14390 抗-CD20 (C2B8_H1.202_L1.113) x 抗-CD3 (H1.33_L1.47) Fab-scFv-Fc

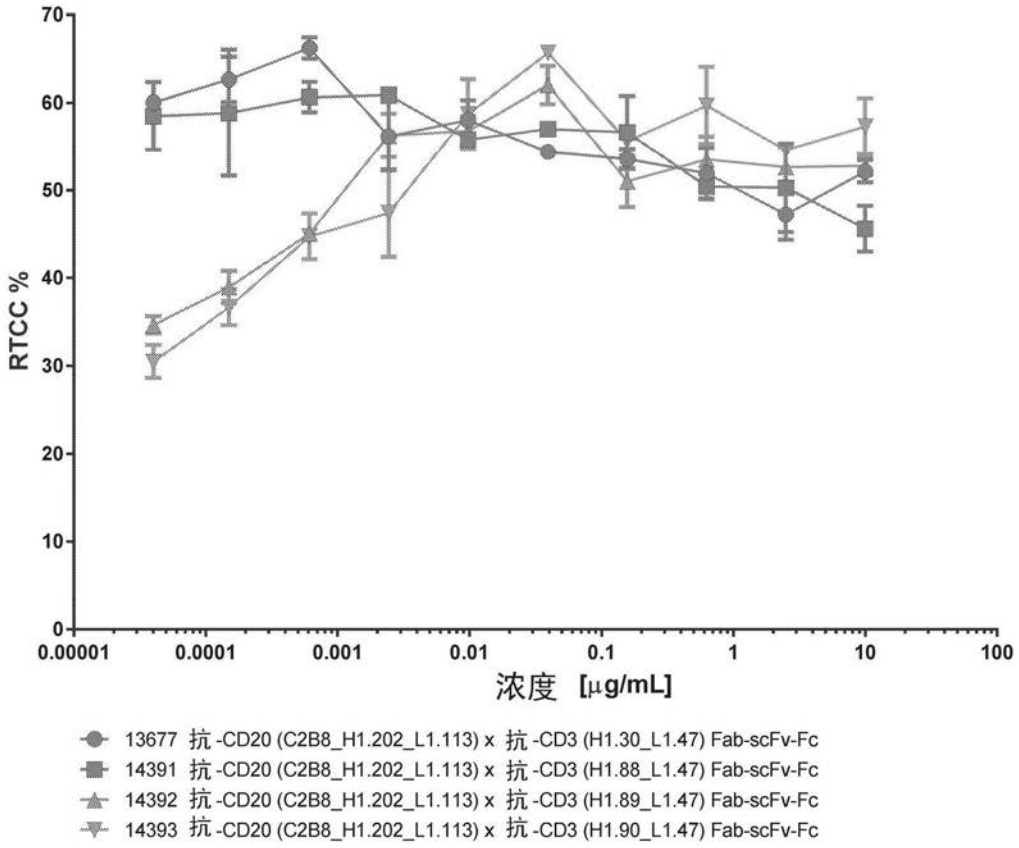

RTCC %
浓度 [μg/mL]
13677 抗-CD20 (C2B8_H1.202_L1.113) x 抗-CD3 (H1.30_L1.47) Fab-scFv-Fc
14391 抗-CD20 (C2B8_H1.202_L1.113) x 抗-CD3 (H1.88_L1.47) Fab-scFv-Fc
14392 抗-CD20 (C2B8_H1.202_L1.113) x 抗-CD3 (H1.89_L1.47) Fab-scFv-Fc
14393 抗-CD20 (C2B8_H1.202_L1.113) x 抗-CD3 (H1.90_L1.47) Fab-scFv-Fc

图112

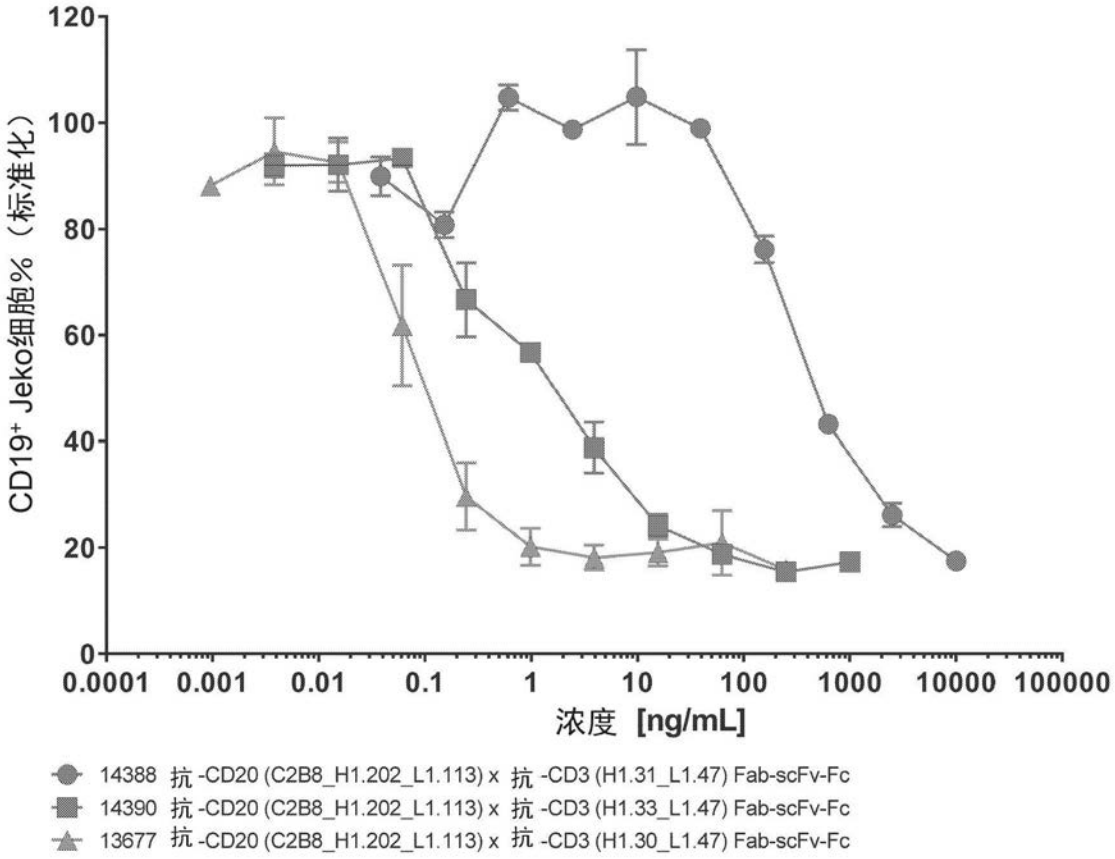

120
100
80
60
40
20
0
CD19+ Jeko细胞%（标准化）
0.0001
0.001
0.01
0.1
1
10
100
1000
10000
100000
浓度 [ng/mL]
14388 抗-CD20 (C2B8_H1.202_L1.113) x 抗-CD3 (H1.31_L1.47) Fab-scFv-Fc
14390 抗-CD20 (C2B8_H1.202_L1.113) x 抗-CD3 (H1.33_L1.47) Fab-scFv-Fc
13677 抗-CD20 (C2B8_H1.202_L1.113) x 抗-CD3 (H1.30_L1.47) Fab-scFv-Fc

图113

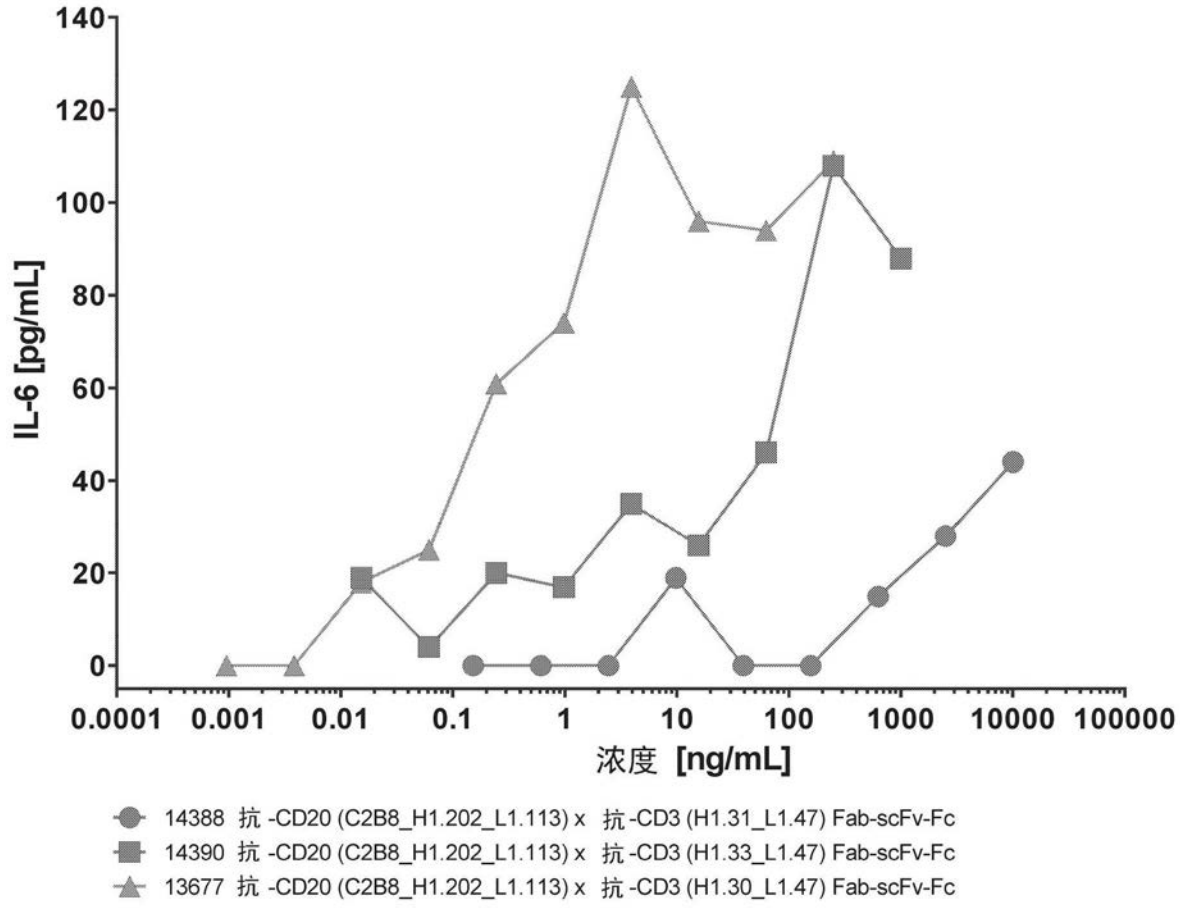

140
120
100
80
60
40
20
0
IL-6 [pg/mL]
0.0001
0.001
0.01
0.1
1
10
100
1000
10000
100000
浓度 [ng/mL]
14388 抗 -CD20 (C2B8_H1.202_L1.113) x 抗 -CD3 (H1.31_L1.47) Fab-scFv-Fc
14390 抗 -CD20 (C2B8_H1.202_L1.113) x 抗 -CD3 (H1.33_L1.47) Fab-scFv-Fc
13677 抗 -CD20 (C2B8_H1.202_L1.113) x 抗 -CD3 (H1.30_L1.47) Fab-scFv-Fc

图114

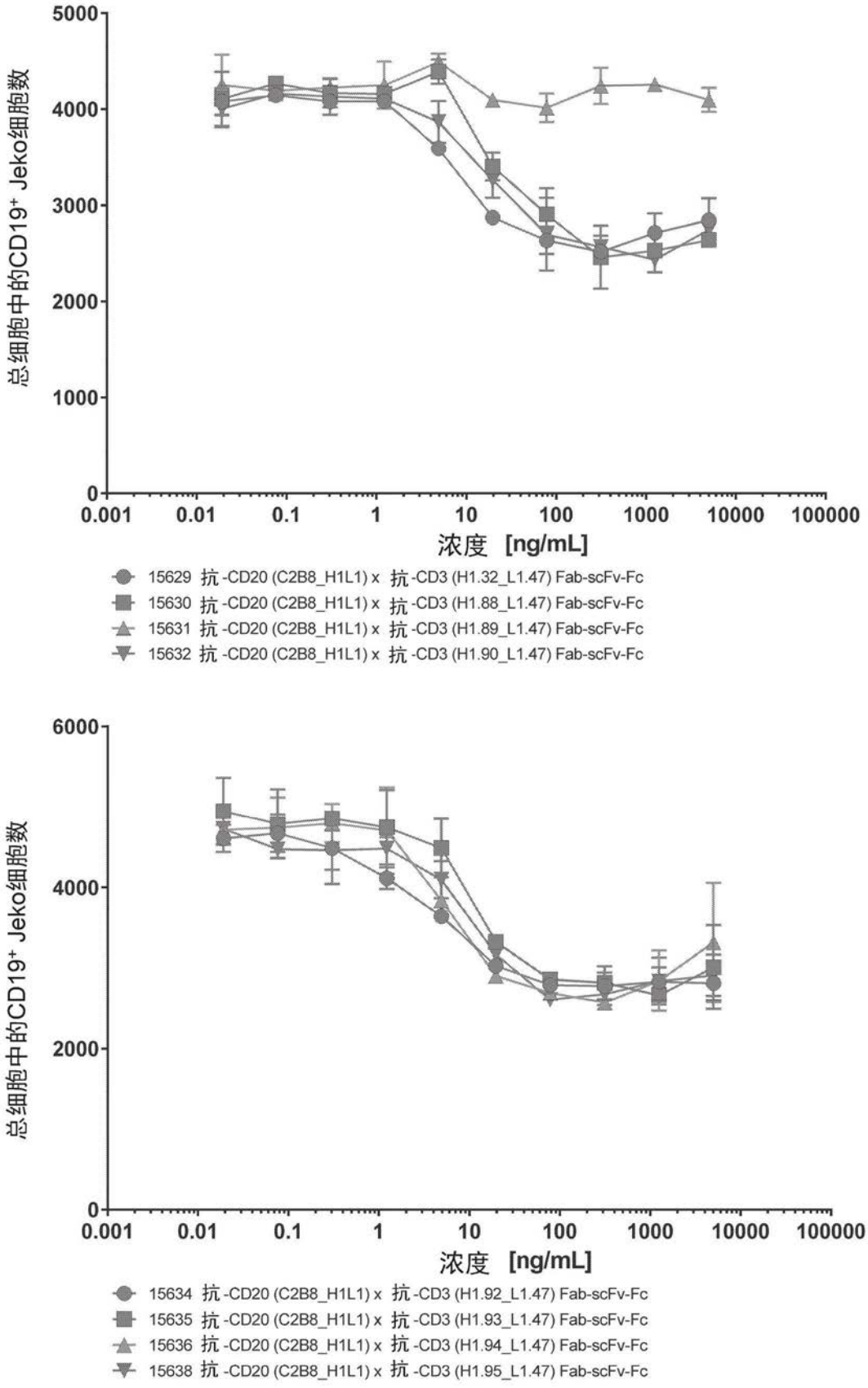

总细胞中的CD19+ Jeko细胞数
5000
4000
3000
2000
1000
0
0.001
0.01
0.1
1
10
100
1000
10000
100000
浓度 [ng/mL]
15629 抗-CD20 (C2B8_H1L1) x 抗-CD3 (H1.32_L1.47) Fab-scFv-Fc
15630 抗-CD20 (C2B8_H1L1) x 抗-CD3 (H1.88_L1.47) Fab-scFv-Fc
15631 抗-CD20 (C2B8_H1L1) x 抗-CD3 (H1.89_L1.47) Fab-scFv-Fc
15632 抗-CD20 (C2B8_H1L1) x 抗-CD3 (H1.90_L1.47) Fab-scFv-Fc
总细胞中的CD19+ Jeko细胞数
6000
4000
2000
0
0.001
0.01
0.1
1
10
100
1000
10000
100000
浓度 [ng/mL]
15634 抗-CD20 (C2B8_H1L1) x 抗-CD3 (H1.92_L1.47) Fab-scFv-Fc
15635 抗-CD20 (C2B8_H1L1) x 抗-CD3 (H1.93_L1.47) Fab-scFv-Fc
15636 抗-CD20 (C2B8_H1L1) x 抗-CD3 (H1.94_L1.47) Fab-scFv-Fc
15638 抗-CD20 (C2B8_H1L1) x 抗-CD3 (H1.95_L1.47) Fab-scFv-Fc

图115A

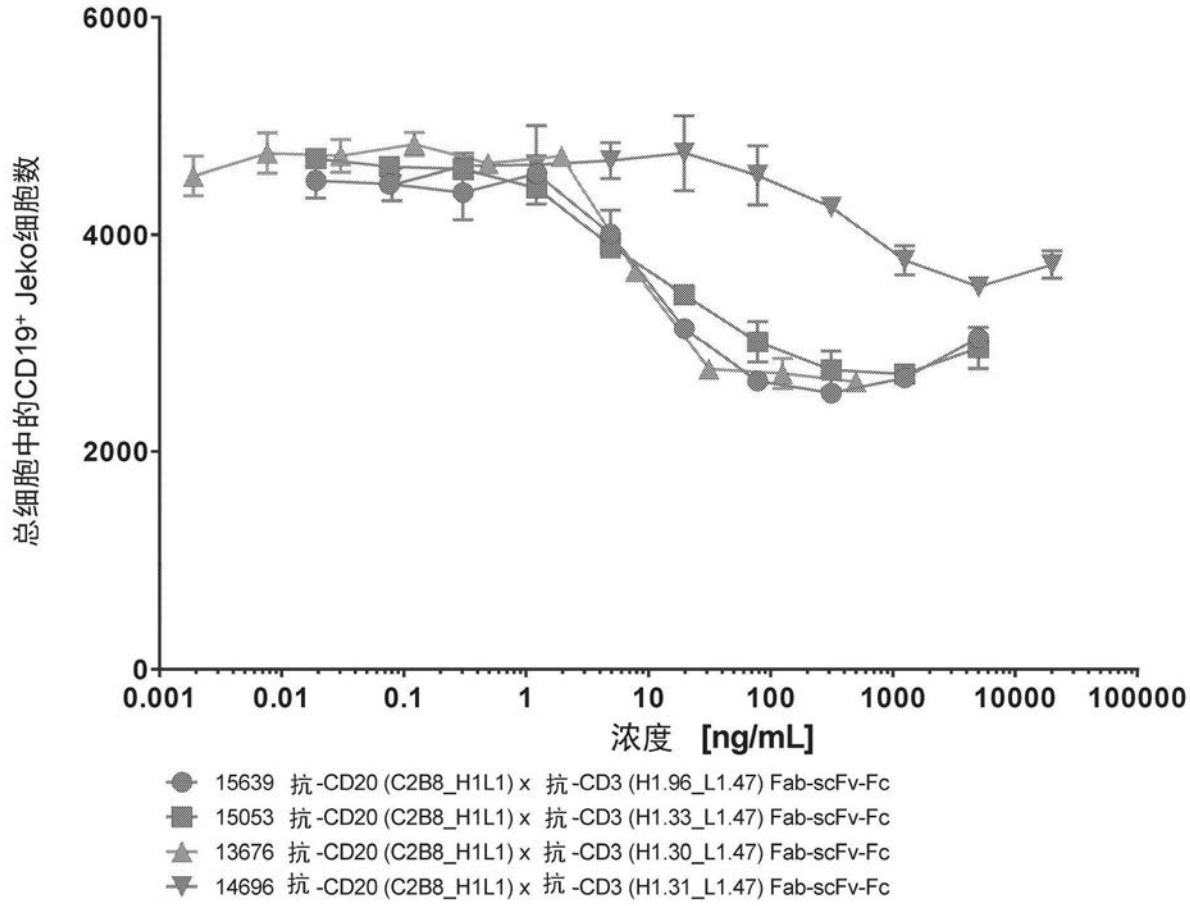
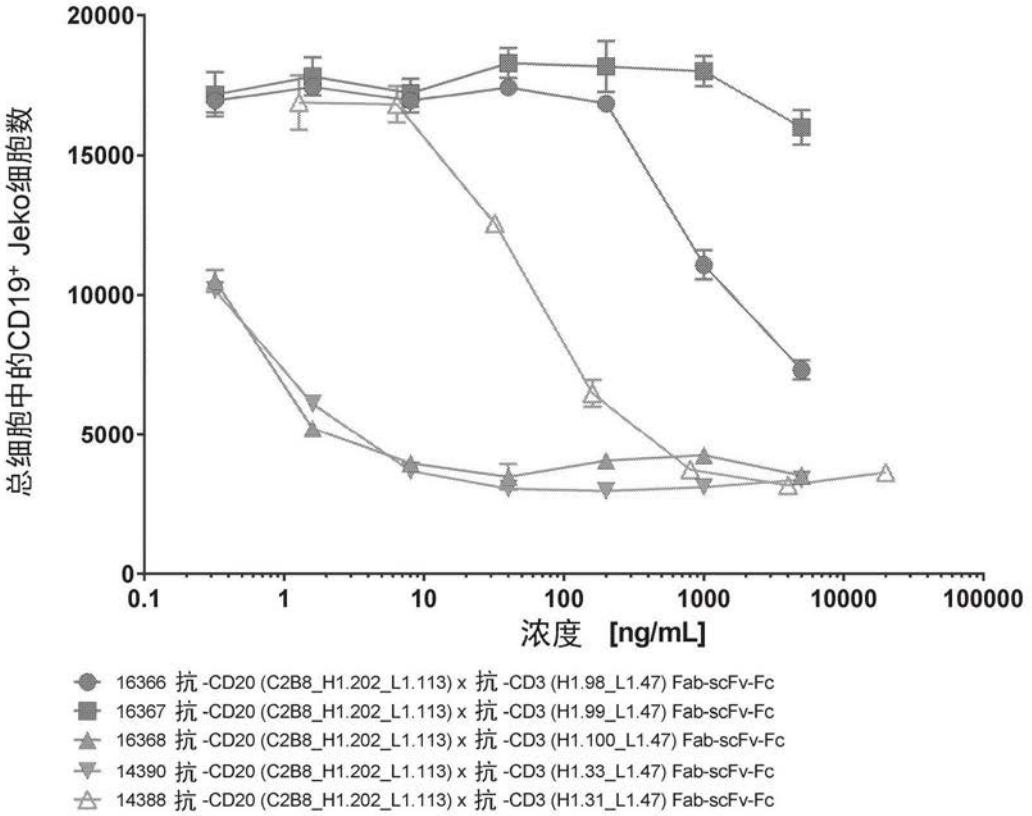

6000
4000
2000
0
总细胞中的CD19+ Jeko细胞数
0.001
0.01
0.1
1
10
100
1000
10000
100000
浓度 [ng/mL]
15639 抗-CD20 (C2B8_H1L1) x 抗-CD3 (H1.96_L1.47) Fab-scFv-Fc
15053 抗-CD20 (C2B8_H1L1) x 抗-CD3 (H1.33_L1.47) Fab-scFv-Fc
13676 抗-CD20 (C2B8_H1L1) x 抗-CD3 (H1.30_L1.47) Fab-scFv-Fc
14696 抗-CD20 (C2B8_H1L1) x 抗-CD3 (H1.31_L1.47) Fab-scFv-Fc

图115B


20000
15000
10000
5000
0
总细胞中的CD19+ Jeko细胞数
0.1
1
10
100
1000
10000
100000
浓度 [ng/mL]
16366 抗-CD20 (C2B8_H1.202_L1.113) x 抗-CD3 (H1.98_L1.47) Fab-scFv-Fc
16367 抗-CD20 (C2B8_H1.202_L1.113) x 抗-CD3 (H1.99_L1.47) Fab-scFv-Fc
16368 抗-CD20 (C2B8_H1.202_L1.113) x 抗-CD3 (H1.100_L1.47) Fab-scFv-Fc
14390 抗-CD20 (C2B8_H1.202_L1.113) x 抗-CD3 (H1.33_L1.47) Fab-scFv-Fc
14388 抗-CD20 (C2B8_H1.202_L1.113) x 抗-CD3 (H1.31_L1.47) Fab-scFv-Fc

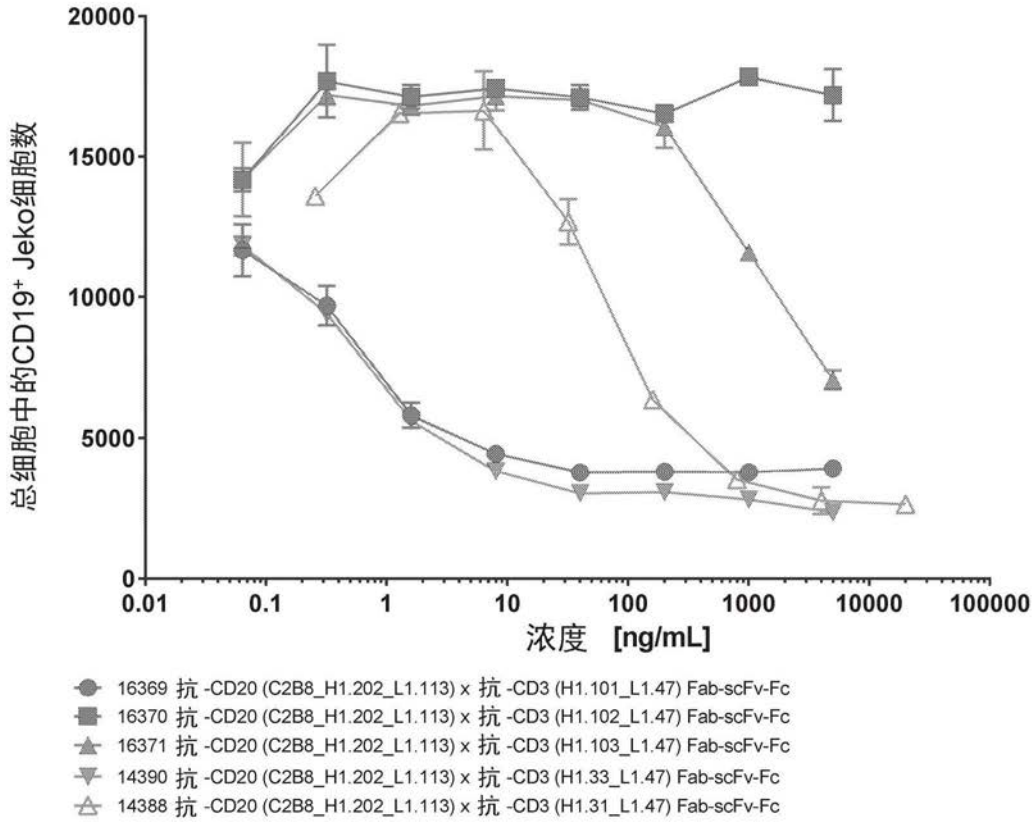

20000
15000
10000
5000
0
总细胞中的CD19+ Jeko细胞数
0.01
0.1
1
10
100
1000
10000
100000
浓度 [ng/mL]
16369 抗-CD20 (C2B8_H1.202_L1.113) x 抗-CD3 (H1.101_L1.47) Fab-scFv-Fc
16370 抗-CD20 (C2B8_H1.202_L1.113) x 抗-CD3 (H1.102_L1.47) Fab-scFv-Fc
16371 抗-CD20 (C2B8_H1.202_L1.113) x 抗-CD3 (H1.103_L1.47) Fab-scFv-Fc
14390 抗-CD20 (C2B8_H1.202_L1.113) x 抗-CD3 (H1.33_L1.47) Fab-scFv-Fc
14388 抗-CD20 (C2B8_H1.202_L1.113) x 抗-CD3 (H1.31_L1.47) Fab-scFv-Fc

图116A

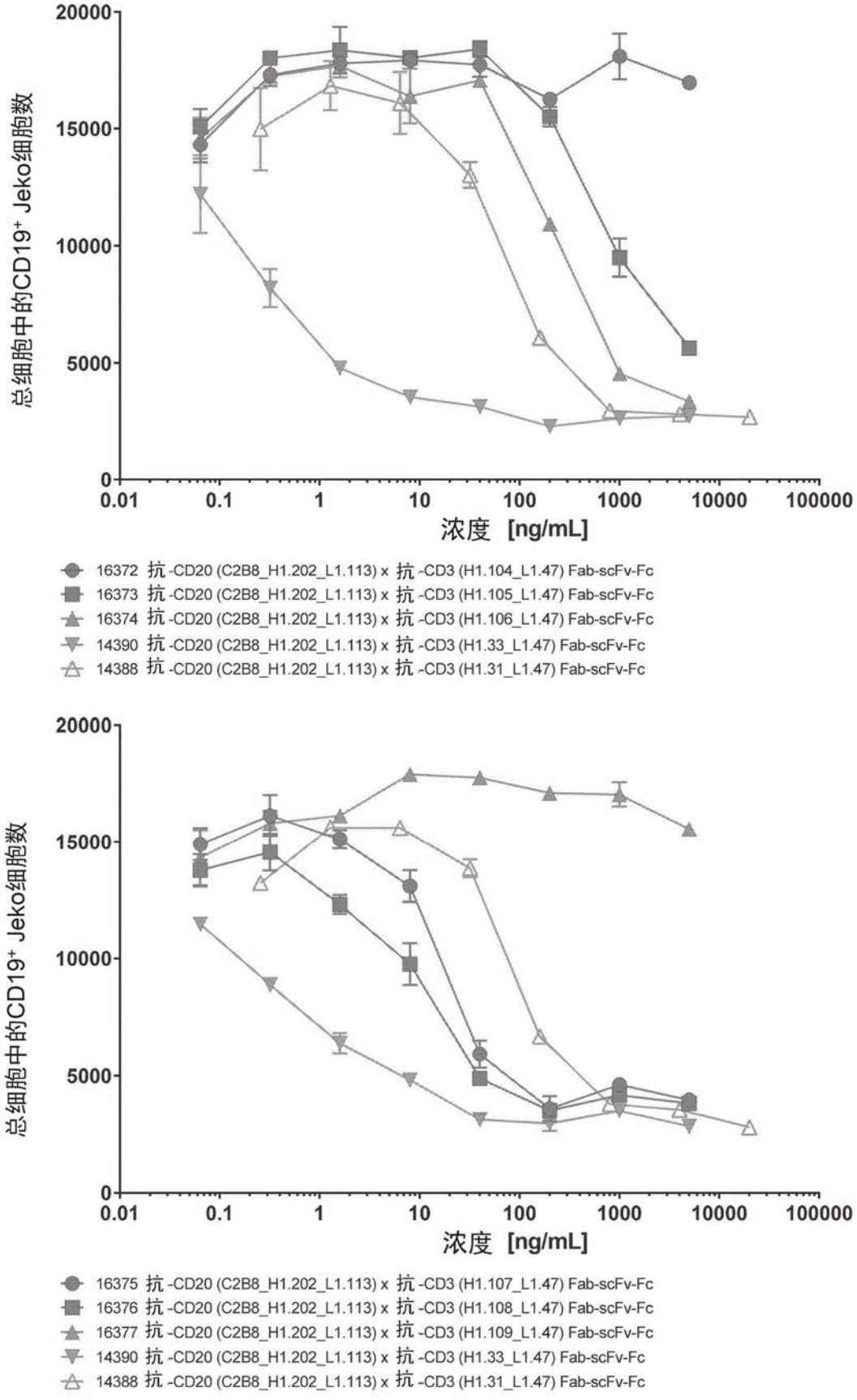

20000
15000
10000
5000
0
总细胞中的CD19+ Jeko细胞数
0.01
0.1
1
10
100
1000
10000
100000
浓度 [ng/mL]
16372 抗-CD20 (C2B8_H1.202_L1.113) x 抗-CD3 (H1.104_L1.47) Fab-scFv-Fc
16373 抗-CD20 (C2B8_H1.202_L1.113) x 抗-CD3 (H1.105_L1.47) Fab-scFv-Fc
16374 抗-CD20 (C2B8_H1.202_L1.113) x 抗-CD3 (H1.106_L1.47) Fab-scFv-Fc
14390 抗-CD20 (C2B8_H1.202_L1.113) x 抗-CD3 (H1.33_L1.47) Fab-scFv-Fc
14388 抗-CD20 (C2B8_H1.202_L1.113) x 抗-CD3 (H1.31_L1.47) Fab-scFv-Fc
20000
15000
10000
5000
0
总细胞中的CD19+ Jeko细胞数
0.01
0.1
1
10
100
1000
10000
100000
浓度 [ng/mL]
16375 抗-CD20 (C2B8_H1.202_L1.113) x 抗-CD3 (H1.107_L1.47) Fab-scFv-Fc
16376 抗-CD20 (C2B8_H1.202_L1.113) x 抗-CD3 (H1.108_L1.47) Fab-scFv-Fc
16377 抗-CD20 (C2B8_H1.202_L1.113) x 抗-CD3 (H1.109_L1.47) Fab-scFv-Fc
14390 抗-CD20 (C2B8_H1.202_L1.113) x 抗-CD3 (H1.33_L1.47) Fab-scFv-Fc
14388 抗-CD20 (C2B8_H1.202_L1.113) x 抗-CD3 (H1.31_L1.47) Fab-scFv-Fc

图116B

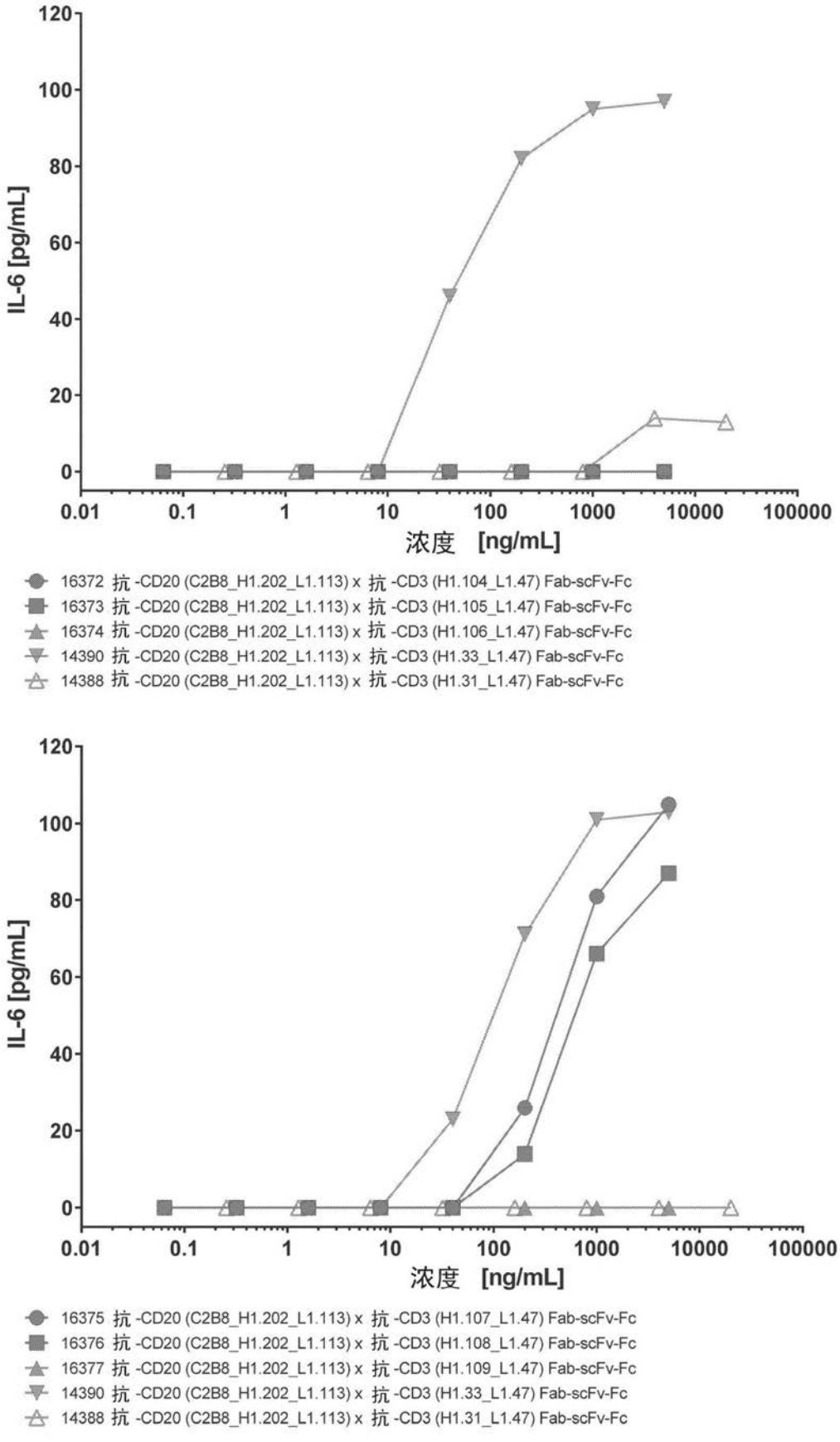

120
100
80
60
40
20
0
IL-6 [pg/mL]
0.01
0.1
1
10
100
1000
10000
100000
浓度 [ng/mL]
16372 抗 -CD20 (C2B8_H1.202_L1.113) x 抗 -CD3 (H1.104_L1.47) Fab-scFv-Fc
16373 抗 -CD20 (C2B8_H1.202_L1.113) x 抗 -CD3 (H1.105_L1.47) Fab-scFv-Fc
16374 抗 -CD20 (C2B8_H1.202_L1.113) x 抗 -CD3 (H1.106_L1.47) Fab-scFv-Fc
14390 抗 -CD20 (C2B8_H1.202_L1.113) x 抗 -CD3 (H1.33_L1.47) Fab-scFv-Fc
14388 抗 -CD20 (C2B8_H1.202_L1.113) x 抗 -CD3 (H1.31_L1.47) Fab-scFv-Fc
120
100
80
60
40
20
0
IL-6 [pg/mL]
0.01
0.1
1
10
100
1000
10000
100000
浓度 [ng/mL]
16375 抗 -CD20 (C2B8_H1.202_L1.113) x 抗 -CD3 (H1.107_L1.47) Fab-scFv-Fc
16376 抗 -CD20 (C2B8_H1.202_L1.113) x 抗 -CD3 (H1.108_L1.47) Fab-scFv-Fc
16377 抗 -CD20 (C2B8_H1.202_L1.113) x 抗 -CD3 (H1.109_L1.47) Fab-scFv-Fc
14390 抗 -CD20 (C2B8_H1.202_L1.113) x 抗 -CD3 (H1.33_L1.47) Fab-scFv-Fc
14388 抗 -CD20 (C2B8_H1.202_L1.113) x 抗 -CD3 (H1.31_L1.47) Fab-scFv-Fc

图117

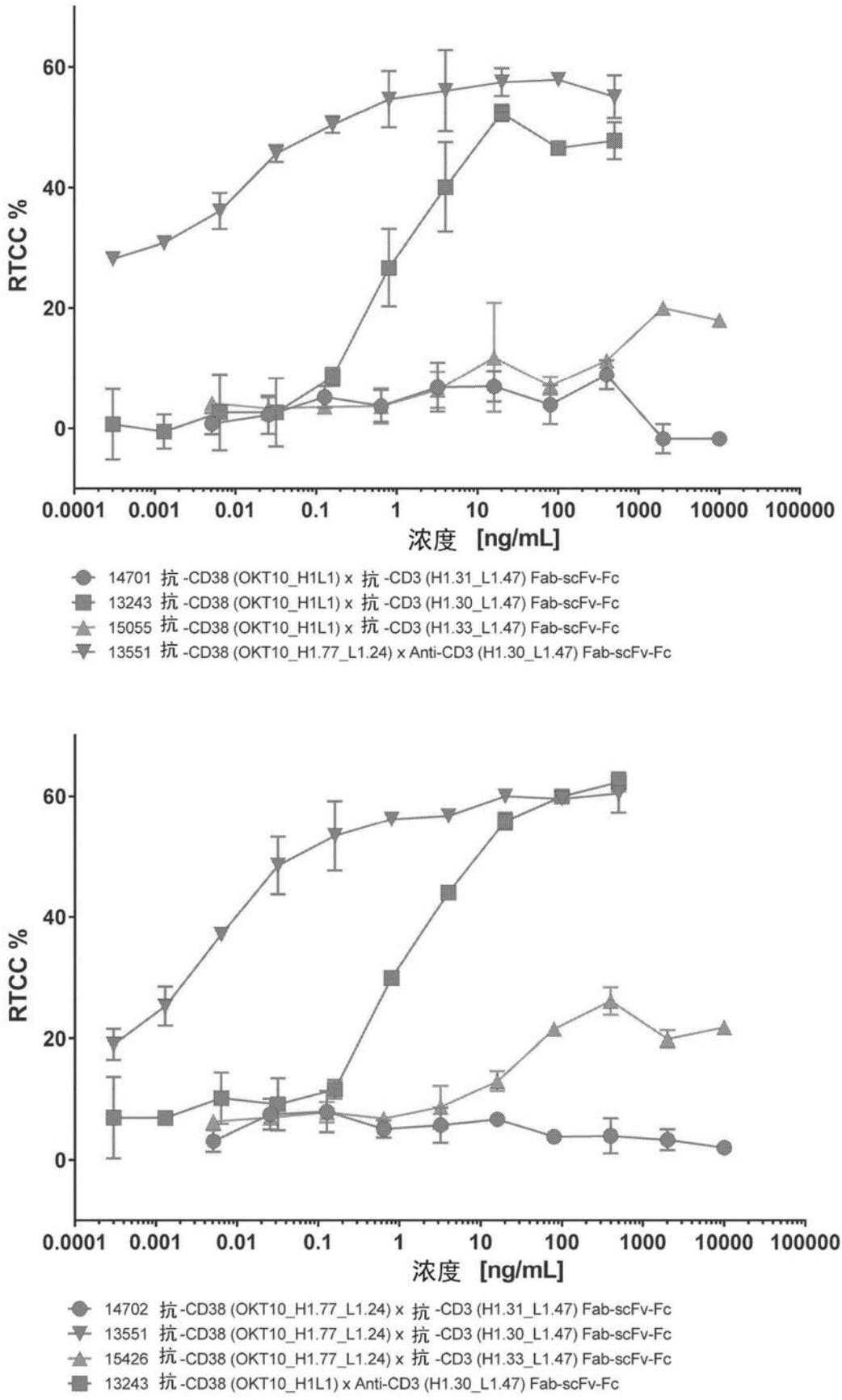

RTCC %
60
40
20
0
0.0001
0.001
0.01
0.1
1
10
100
1000
10000
100000
浓度 [ng/mL]
14701 抗-CD38 (OKT10_H1L1) x 抗-CD3 (H1.31_L1.47) Fab-scFv-Fc
13243 抗-CD38 (OKT10_H1L1) x 抗-CD3 (H1.30_L1.47) Fab-scFv-Fc
15055 抗-CD38 (OKT10_H1L1) x 抗-CD3 (H1.33_L1.47) Fab-scFv-Fc
13551 抗-CD38 (OKT10_H1.77_L1.24) x Anti-CD3 (H1.30_L1.47) Fab-scFv-Fc
RTCC %
60
40
20
0
0.0001
0.001
0.01
0.1
1
10
100
1000
10000
100000
浓度 [ng/mL]
14702 抗-CD38 (OKT10_H1.77_L1.24) x 抗-CD3 (H1.31_L1.47) Fab-scFv-Fc
13551 抗-CD38 (OKT10_H1.77_L1.24) x 抗-CD3 (H1.30_L1.47) Fab-scFv-Fc
15426 抗-CD38 (OKT10_H1.77_L1.24) x 抗-CD3 (H1.33_L1.47) Fab-scFv-Fc
13243 抗-CD38 (OKT10_H1L1) x Anti-CD3 (H1.30_L1.47) Fab-scFv-Fc

图118

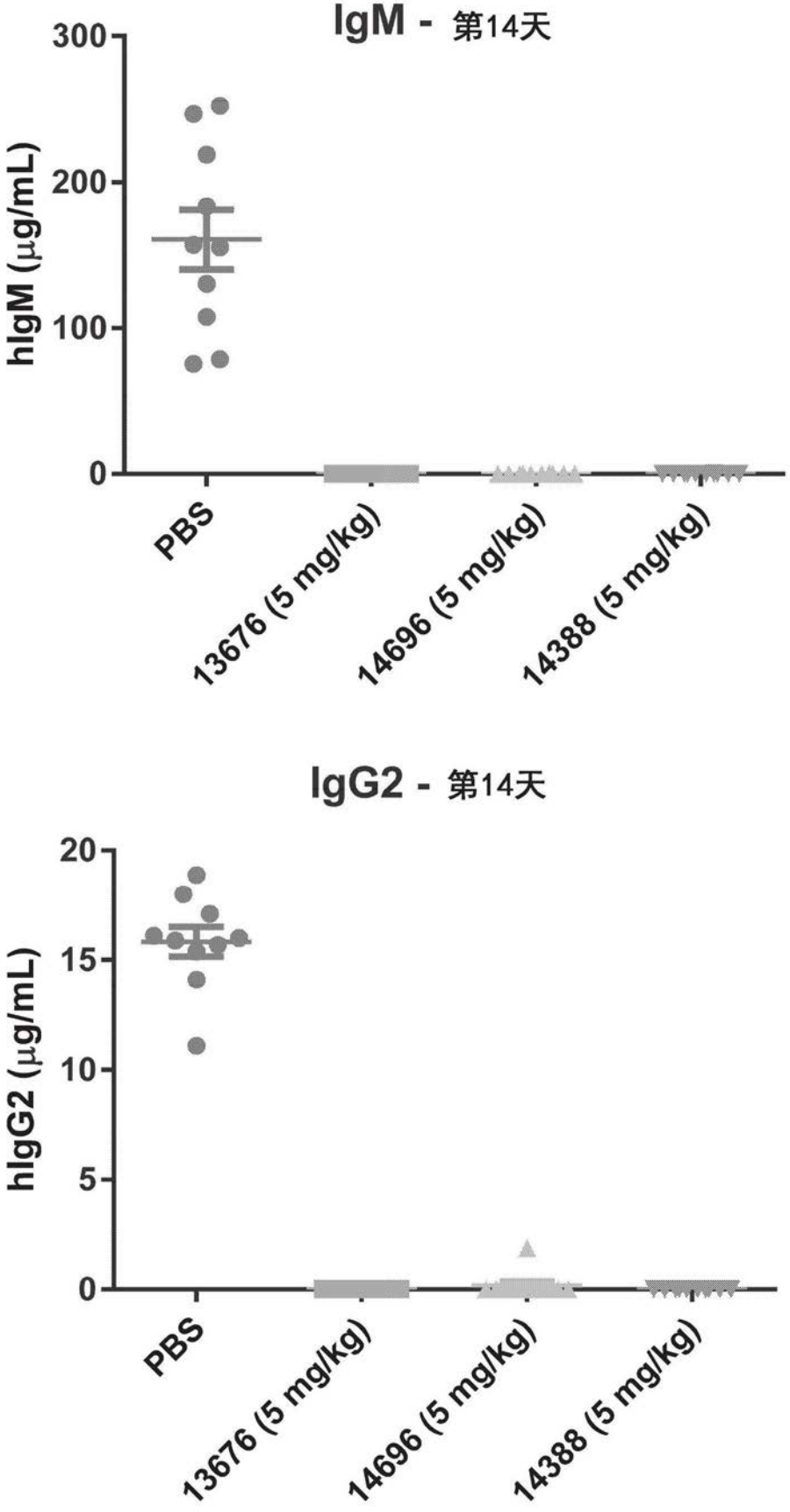

IgM - 第14天
hIgM (μg/mL)
300
200
100
0
PBS
13676 (5 mg/kg)
14696 (5 mg/kg)
14388 (5 mg/kg)
IgG2 - 第14天
hIgG2 (μg/mL)
20
15
10
5
0
PBS
13676 (5 mg/kg)
14696 (5 mg/kg)
14388 (5 mg/kg)

图119

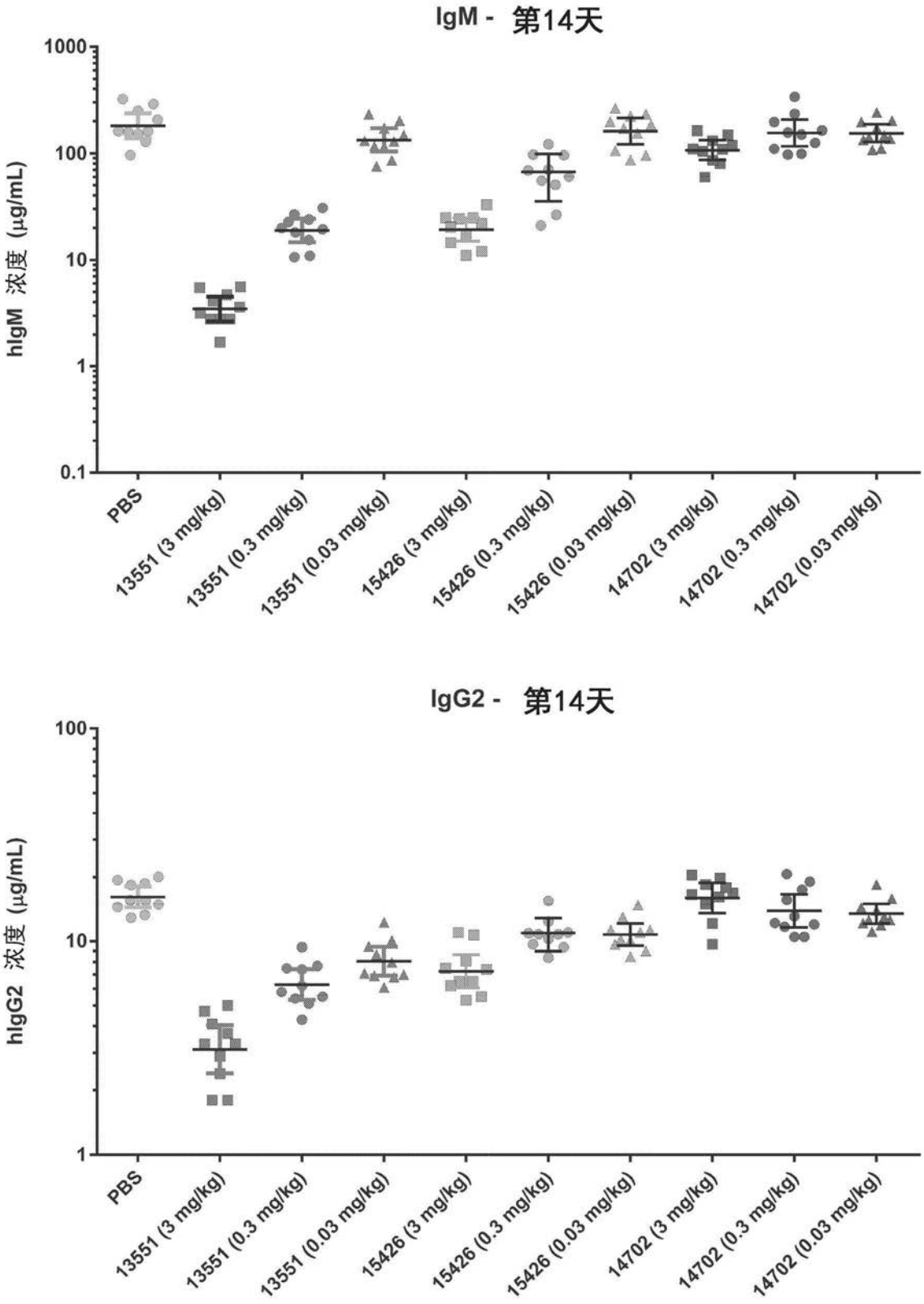

IgM - 第14天
hIgM 浓度 (μg/mL)
1000
100
10
1
0.1
IgG2 - 第14天
hIgG2 浓度 (μg/mL)
100
10
1
PBS
13551 (3 mg/kg)
13551 (0.3 mg/kg)
13551 (0.03 mg/kg)
15426 (3 mg/kg)
15426 (0.3 mg/kg)
15426 (0.03 mg/kg)
14702 (3 mg/kg)
14702 (0.3 mg/kg)
14702 (0.03 mg/kg)

图120

高 CD20 C2B8_H1.202_L1.113

| 是什么 | 序列 | SEQ ID NO: |
|---|---|---|
| 可变重链(vh)结构域 | QVQLVQSGAEVKKPGASVKVSCKASGYTFTWVRQAPGQRLEWMGAIYPGNGATSYSQKFQGRVTITADTSASTAYMELSSL RSEDTAVYYCARSYYMGGDWYFDVWGAGTLVTVSS | 421 |
| vhCDR1 | SYNMH | 422 |
| vhCDR2 | AIYPGNGATSYSQKFQG | 423 |
| vhCDR3 | SYYMGGDWYFDV | 424 |
| 可变轻链(vl)结构域 | QIVLTQSPSSLSASVGDRVTITCRASWSVSYIHWFQQKPGKSPKPLIYATSNLASGVPVRFSGSGSGTDYTLTISSLQPEDFATYY CQQWTHNPPTFGGGTKVEIK | 425 |
| vlCDR1 | RASWSVSYIH | 426 |
| vlCDR2 | ATSNLAS | 427 |
| vlCDR3 | QQWTHNPPT | 428 |
| scFv(含带电荷的接头) | QVQLVQSGAEVKKPGASVKVSCKASGYTFTWVRQAPGQRLEWMGAIYPGNGATSYSQKFQGRVTITADTSASTAYMELSSL RSEDTAVYYCARSYYMGGDWYFDVWGAGTLVTVSSGKPGSGKPGSGKPGSGKPGSQIVLTQSPSSLSASVGDRVTITCRASW SVSYIHWFQQKPGKSPKPLIYATSNLASGVPVRFSGSGSGTDYTLTISSLQPEDFATYYCQQWTHNPPTFGGGTKVEIK | 429 |

图121

低 CD20 C2B8_H1L1

| 是什么 | 序列 | SEQ ID NO: |
|---|---|---|
| 可变重链(vh)结构域 | QVQLVQSGAEVKKPGASVKVSCKASGYTFTSYNMHWVRQAPGQGLEWMGAIYPGNGDTSYNQKFQGRVTITADKSISTAY MELSSLRSEDTAVYYCARSTYYGGDWYFNVWGAGTLVTVSS | 430 |
| vhCDR1 | SYNMH | 431 |
| vhCDR2 | AIYPGNGDTSYNQKFQG | 432 |
| vhCDR3 | STYYGGDWYFNV | 433 |
| 可变轻链(vl)结构域 | QIVLTQSPSSLSASVGDRVTITCRASSSVSYIHWFQQKPGKSPKPLIYATSNLASGVPVRFSGSGSGTDYTLTISSLQPEDFATYYC QQWTSNPPTFGGGTKVEIK | 434 |
| vlCDR1 | RASSSVSYIH | 435 |
| vlCDR2 | ATSNLAS | 436 |
| vlCDR3 | QQWTSNPPT | 437 |
| scFv(含带电荷的接头) | QVQLVQSGAEVKKPGASVKVSCKASGYTFTSYNMHWVRQAPGQGLEWMGAIYPGNGDTSYNQKFQGRVTITADKSISTAY MELSSLRSEDTAVYYCARSTYYGGDWYFNVWGAGTLVTVSSGKPGSGKPGSGKPGSQIVLTQSPSSLSASVGDRVTIT CRASSSVSYIHWFQQKPGKSPKPLIYATSNLASGVPVRFSGSGSGTDYTLTISSLQPEDFATYYCQQWTSNPPTFGGGTKVEIK | 438 |

图122

CD123 7G3_H1.109_L1.57

| 是什么 | 序列 | SEQ ID NO: |
|---|---|---|
| 可变重链(vh)结构域 | QVQLQQSGAEVKKPGASVKVSCKASGYTFTDYYMKWVKQSHGKSLEWMGDIIPSNGATFYNQKFKGKATLTVDRSTSTAY MELSSLRSEDTAVYYCARSHLLRASWFAYWGQGTLVTVSS | 439 |
| vhCDR1 | DYYMK | 440 |
| vhCDR2 | DIIPSNGATFYNQKFKG | 441 |
| vhCDR3 | SHLLRASWFAY | 442 |
| 可变轻链(vl)结构域 | DFVMTQSPDSLAVSLGERATINCKSSQSLLNTGNQKNYLTWYQQKPGQPPKLLIYWASTRESGVPDRFTGSGSGTDFTLTISSL QAEDVAVYYCQNDYSYPYTFGGGTKLEIK | 443 |
| vlCDR1 | KSSQSLLNTGNQKNYLT | 444 |
| vlCDR2 | WASTRES | 445 |
| vlCDR3 | QNDYSYPYT | 446 |
| scFv(含带电荷的接头) | QVQLQQSGAEVKKPGASVKVSCKASGYTFTDYYMKWVKQSHGKSLEWMGDIIPSNGATFYNQKFKGKATLTVDRSTSTAY MELSSLRSEDTAVYYCARSHLLRASWFAYWGQGTLVTVSSGKPGSGKPGSGKPGSDFVMTQSPDSLAVSLGERATIN CKSSQSLLNTGNQKNYLTWYQQKPGQPPKLLIYWASTRESGVPDRFTGSGSGTDFTLTISSLQAEDVAVYYCQNDYSYPYTFG GGTKLEIK | 447 |

图123

| | | 高 CD3 | 高-中 #1 CD3 | 高-中 #2 CD3 | 高-中 #3 CD3 | 中 CD3 | 低 CD3 |
|---|---|---|---|---|---|---|---|
| | | 抗-CD3 H1.30_L1.47 | 抗-CD3 H1.32_L1.47 | 抗-CD3 H1.89_L1.47 | 抗-CD3 H1.90_L1.47 | 抗-CD3 H1.33_L1.47 | 抗-CD3 H1.31_L1.47 |
| 高 CD38 | OKT10 H1.77_L1.24 | A, B, C, D, E. F | A, B, C, D, E. F | A, B, C, D, E. F | A, B, C, D, E. F | A, B, C, D, E. F | A, B, C, D, E. F |
| 中 CD38 | OKT10 H1L1.24 | A, B, C, D, E. F | A, B, C, D, E. F | A, B, C, D, E. F | A, B, C, D, E. F | A, B, C, D, E. F | A, B, C, D, E. F |
| 低 CD38 | OKT10 H1L1 | A, B, C, D, E. F | A, B, C, D, E. F | A, B, C, D, E. F | A, B, C, D, E. F | A, B, C, D, E. F | A, B, C, D, E. F |
| 高 CD20 | C2B8_H1.202_L1.113 | A, B, C, D, E. F | A, B, C, D, E. F | A, B, C, D, E. F | A, B, C, D, E. F | A, B, C, D, E. F | A, B, C, D, E. F |
| 低 CD20 | C2B8_H1L1 | A, B, C, D, E. F | A, B, C, D, E. F | A, B, C, D, E. F | A, B, C, D, E. F | A, B, C, D, E. F | A, B, C, D, E. F |
| CD123 | 7G3_H1.109_L1.57 | A, B, C, D, E. F | A, B, C, D, E. F | A, B, C, D, E. F | A, B, C, D, E. F | A, B, C, D, E. F | A, B, C, D, E. F |

图124