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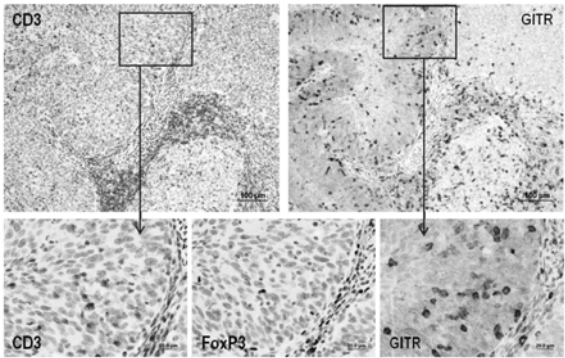
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(54) 发明名称
用于癌症诊断的抗GITR抗体

(57) 摘要
本文提供结合糖皮质激素诱导的肿瘤坏死因子受体 (GITR) 的诊断性抗体。此类抗体可用于检测生物样品 (例如肿瘤组织) 中GITR表达的方法, 以及鉴定可能对抗GITR免疫疗法有响应或预测癌症患者是否将对抗GITR免疫疗法有响应的癌症患者的方法。



1. 结合人糖皮质激素诱导的肿瘤坏死因子受体 (GITR) 的抗体或其抗原结合部分供制备用于确定组织样品中肿瘤浸润淋巴细胞 (TIL) 和/或肿瘤细胞上的GITR表达水平的试剂的用途,所述抗体或其抗原结合部分包含:由分别在SEQ ID NO:5-7中示出的氨基酸序列组成的重链可变区CDR1、CDR2和CDR3,和由分别在SEQ ID NO:8-10中示出的氨基酸序列组成的轻链可变区CDR1、CDR2和CDR3,其中所述确定包括

(a) 使来自患者的组织样品与所述抗体或其抗原结合部分接触,和

(b) 通过免疫组化检测所述抗体或其抗原结合部分与所述组织样品的TIL和/或肿瘤细胞上的GITR的结合。

2. 根据权利要求1所述的用途,其中所述确定还包括染色该组织样品以鉴定在步骤(b)中被鉴定为GITR阳性的TIL和/或肿瘤细胞。

3. 权利要求1或2的用途,其中所述组织样品是肿瘤样品。

4. 结合人糖皮质激素诱导的肿瘤坏死因子受体 (GITR) 的抗体或其抗原结合部分供制备用于检测生物样品中GITR的试剂的用途,所述抗体或其抗原结合部分包含:由分别在SEQ ID NO:5-7中示出的氨基酸序列组成的重链可变区CDR1、CDR2和CDR3,和由分别在SEQ ID NO:8-10中示出的氨基酸序列组成的轻链可变区CDR1、CDR2和CDR3,其中所述检测包括:使所述样品与所述抗体或其抗原结合部分接触,并通过免疫组化检测该抗体或其抗原结合部分与样品中GITR的结合。

5. 权利要求1-4中任一项所述的用途,其中所述样品是人组织样品。

6. 权利要求4的用途,其中所述生物样品是人肿瘤组织样品。

7. 结合人糖皮质激素诱导的肿瘤坏死因子受体 (GITR) 的抗体或其抗原结合部分供制备用于确定癌症患者的肿瘤是否为GITR阳性的试剂的用途,所述抗体或其抗原结合部分包含:由分别在SEQ ID NO:5-7中示出的氨基酸序列组成的重链可变区CDR1、CDR2和CDR3,和由分别在SEQ ID NO:8-10中示出的氨基酸序列组成的轻链可变区CDR1、CDR2和CDR3,所述确定包括:

(a) 使来自所述患者的肿瘤样品与所述抗体或其抗原结合部分接触,

(b) 通过免疫组化检测所述抗体或其抗原结合部分与所述样品中GITR的结合,和

(c) 确定所述样品中GITR蛋白质表达的水平。

8. 权利要求7的用途,其中所述肿瘤样品是福尔马林固定石蜡包埋的肿瘤样品、或冷冻的肿瘤组织。

9. 结合人糖皮质激素诱导的肿瘤坏死因子受体 (GITR) 的抗体或其抗原结合部分供制备用于鉴定可能对抗GITR免疫疗法有响应的癌症患者的试剂的用途,所述抗体或其抗原结合部分包含:由分别在SEQ ID NO:5-7中示出的氨基酸序列组成的重链可变区CDR1、CDR2和CDR3,和由分别在SEQ ID NO:8-10中示出的氨基酸序列组成的轻链可变区CDR1、CDR2和CDR3,其中所述鉴定包括:

(a) 使来自所述患者的肿瘤样品与所述抗体或其抗原结合部分接触,

(b) 通过免疫组化检测所述抗体或其抗原结合部分与所述肿瘤样品中GITR的结合,

(c) 确定所述样品中GITR蛋白质表达的水平,其中高于阈值水平的GITR蛋白质水平指示该肿瘤是GITR阳性肿瘤,并且该患者可能或预计对抗GITR免疫疗法有响应。

10. 权利要求9的用途,其中所述肿瘤样品是福尔马林固定石蜡包埋的肿瘤样品、或冷

冻的肿瘤组织。

11. 结合人糖皮质激素诱导的肿瘤坏死因子受体 (GITR) 的抗体或其抗原结合部分以及调变GITR信号传导的作用剂供制备用于治疗癌症患者的试剂的用途, 所述抗体或其抗原结合部分包含: 由分别在SEQ ID NO:5-7中示出的氨基酸序列组成的重链可变区CDR1、CDR2和CDR3, 和由分别在SEQ ID NO:8-10中示出的氨基酸序列组成的轻链可变区CDR1、CDR2和CDR3, 所述治疗包括:

(a) 如下所述确定癌症患者的肿瘤是否为GITR阳性: (i) 使来自患者的肿瘤样品与所述抗体或其抗原结合部分接触, (ii) 通过免疫组化检测所述抗体或其抗原结合部分与所述肿瘤样品中GITR的结合, 和 (iii) 确定所述样品中GITR蛋白质表达的水平, 其中高于阈值水平的GITR蛋白质水平指示该肿瘤是GITR阳性的, 并且

(b) 如果肿瘤被确定为GITR阳性, 则向患者施用调变GITR信号传导的作用剂。

12. 权利要求11的用途, 其中所述作用剂是激动性抗GITR抗体。

13. 结合人糖皮质激素诱导的肿瘤坏死因子受体 (GITR) 的抗体或其抗原结合部分供制备用于监测癌症患者中的GITR阳性肿瘤的试剂的用途, 所述抗体或其抗原结合部分包含: 由分别在SEQ ID NO:5-7中示出的氨基酸序列组成的重链可变区CDR1、CDR2和CDR3, 和由分别在SEQ ID NO:8-10中示出的氨基酸序列组成的轻链可变区CDR1、CDR2和CDR3, 其中所述监测包括:

(a) 通过免疫组化在第一时间点使用所述抗体或其抗原结合部分检测GITR阳性肿瘤中的GITR蛋白质表达,

(b) 确定第一时间点的GITR蛋白表达的水平,

(c) 通过免疫组化使用与步骤 (a) 中使用的相同的抗体或其抗原结合部分在第二时间点检测肿瘤中的GITR蛋白质表达,

(d) 确定来自第二时间点的肿瘤中GITR蛋白质表达的水平;

(e) 比较在第一和第二时间点确定的GITR蛋白质表达的水平, 其中第一时间点相对于第二时间点的水平较高指示肿瘤消退, 第一时间点相对于第二时间点的得分较低指示肿瘤进展, 在第一时间点相对于第二时间点的水平相对不变指示肿瘤稳定。

14. 结合人糖皮质激素诱导的肿瘤坏死因子受体 (GITR) 的抗体或其抗原结合部分供制备用于监测具有GITR阳性肿瘤的患者中的抗GITR免疫疗法的功效的试剂的用途, 所述抗体或其抗原结合部分包含: 由分别在SEQ ID NO:5-7中示出的氨基酸序列组成的重链可变区CDR1、CDR2和CDR3, 和由分别在SEQ ID NO:8-10中示出的氨基酸序列组成的轻链可变区CDR1、CDR2和CDR3, 所述监测包括:

(a) 通过免疫组化在启动抗GITR免疫疗法之前或之后的第一时间点使用所述抗体或其抗原结合部分检测GITR阳性肿瘤中的GITR蛋白质表达,

(b) 确定来自第一时间点的肿瘤中的GITR蛋白质表达水平,

(c) 通过免疫组化在启动抗GITR免疫疗法后的第二时间点使用与步骤 (a) 相同的抗体或其抗原结合部分检测所述GITR阳性肿瘤中的GITR蛋白质表达,

(d) 确定来自第二时间点的肿瘤中GITR蛋白质表达的水平;

(e) 比较在第一和第二时间点确定的GITR蛋白质表达水平, 其中第一时间点相对于第二时间点的水平较高指示抗GITR免疫疗法有效, 第一时间点相对于第二时间点的得分较低

指示抗GITR免疫疗法无效,第一时间点相对于第二时间点的得分未改变指示抗GITR免疫疗法在起稳定化作用。

15.权利要求14的用途,其中所述抗GITR免疫疗法包括向患者施用治疗有效量的抗GITR抗体或其抗原结合部分。

16.权利要求1-8中任一项的用途,其中所述抗体或其抗原结合部分包括由分别在SEQ ID NO:11和12中示出的氨基酸序列组成的重链和轻链可变区。

17.权利要求1-8中任一项的用途,其中所述抗体是IgG1,IgG2,IgG3或IgG4抗体。

18.权利要求1-8中任一项的用途,其中如Biacore所评估的,所述抗体或其抗原结合部分以10nM或更低的 K_D 结合可溶性人糖皮质激素诱导的肿瘤坏死因子受体(GITR)。

19.权利要求1-8中任一项的用途,其中所述抗体是人源化抗体、人抗体、或嵌合抗体。

20.权利要求1-8中任一项的用途,其中所述抗体是嵌合抗体。

21.权利要求20的用途,其中所述嵌合抗体具有人可变区序列和非人恒定区序列。

22.权利要求21的用途,其中所述非人恒定区包含小鼠Fc区。

23.权利要求22的用途,其中所述小鼠Fc区是小鼠IgG2a Fc区。

24.权利要求21的用途,其中所述嵌合抗体包含分别在SEQ ID NO:15和16中示出的重链和轻链序列。

25.权利要求1-8中任一项的用途,其中所述抗体或其抗原结合部分包含可检测模块。

26.权利要求25的用途,其中所述可检测模块是放射性标记、荧光标记、酶标记、生物素、发色团、或ECL标记。

27.权利要求9-15中任一项的用途,其中所述抗体或其抗原结合部分包括由分别在SEQ ID NO:11和12中示出的氨基酸序列组成的重链和轻链可变区。

28.权利要求9-15中任一项的用途,其中所述抗体是IgG1,IgG2,IgG3或IgG4抗体。

29.权利要求9-15中任一项的用途,其中如Biacore所评估的,所述抗体或其抗原结合部分以10nM或更低的 K_D 结合可溶性人糖皮质激素诱导的肿瘤坏死因子受体(GITR)。

30.权利要求9-15中任一项的用途,其中所述抗体是人源化抗体、人抗体、或嵌合抗体。

31.权利要求9-15中任一项的用途,其中所述抗体是嵌合抗体。

32.权利要求31的用途,其中所述嵌合抗体具有人可变区序列和非人恒定区序列。

33.权利要求32的用途,其中所述非人恒定区包含小鼠Fc区。

34.权利要求33的用途,其中所述小鼠Fc区是小鼠IgG2a Fc区。

35.权利要求32的用途,其中所述嵌合抗体包含分别在SEQ ID NO:15和16中示出的重链和轻链序列。

36.权利要求9-15中任一项的用途,其中所述抗体或其抗原结合部分包含可检测模块。

37.权利要求36的用途,其中所述可检测模块是放射性标记、荧光标记、酶标记、生物素、发色团、或ECL标记。

38.一种诊断试剂盒,其包含抗体或其抗原结合部分以及使用说明,所述抗体或其抗原结合部分结合人糖皮质激素诱导的肿瘤坏死因子受体(GITR)且包含:由分别在SEQ ID NO:5-7中示出的氨基酸序列组成的重链可变区CDR1、CDR2和CDR3,和由分别在SEQ ID NO:8-10所示的氨基酸序列组成的轻链可变区CDR1,CDR2和CDR3。

39.权利要求38的诊断试剂盒,其中所述抗体或其抗原结合部分包含由分别在SEQ ID

NO:11和12中示出的氨基酸序列组成的重链和轻链可变区。

40. 权利要求38或39的诊断试剂盒,其中所述抗体包含SEQ ID NO:13和14中示出的重链和轻链序列。

41. 权利要求40的诊断试剂盒,其中所述重链缺乏C末端氨基酸残基。

42. 权利要求38或39的诊断试剂盒,其中所述抗体包含SEQ ID NO:15和16中示出的重链和轻链序列。

43. 权利要求42的诊断试剂盒,其中所述重链缺乏C末端氨基酸残基。

44. 一种结合人糖皮质激素诱导的肿瘤坏死因子受体 (GITR) 的抗体,其包含分别如SEQ ID NO:15和16中示出的重链和轻链序列。

用于癌症诊断的抗GITR抗体

[0001] 相关申请的交叉引用

[0002] 本申请要求2015年6月3日提交的美国临时专利申请序列号62/170,579的优先权,将其内容通过引用明确并入本文。

[0003] 背景

[0004] 糖皮质激素诱导型TNF受体 (GITR) 是由活化的效应T (Teff) 细胞表达、且在B细胞、嗜酸性粒细胞、嗜碱性粒细胞、和巨噬细胞上以低水平表达的T细胞共刺激I型细胞表面跨膜糖蛋白 (Nocentini et al., Adv Exp Med Biol 2009;647:156-73)。GITR在调节性T细胞 (Treg) 上组成型表达。通过GITR的信号传导可增强T细胞的T细胞受体活化,并使得Teff细胞对Treg介导的抑制具有抗性 (Stephens et al., J Immunol 2004;173:5008-20)。确定肿瘤组织中的GITR阳性可以提供靶向最可能从抗GITR免疫治疗受益 (即,有响应) 的患者,以及监测GITR阳性肿瘤的状态和抗GITR免疫疗法的功效的机会。

[0005] 概要

[0006] 本文提供了诊断性抗GITR抗体和用于检测生物样品如肿瘤组织样品中的GITR蛋白表达的方法。这样的方法可用于例如鉴定可能对抗GITR免疫疗法有响应并监测GITR阳性肿瘤的状态和抗GITR免疫疗法的功效的癌症患者。

[0007] 因此,在一个方面,本文提供了用于检测生物样品,例如人组织样品 (例如,肿瘤组织样品) 中的人GITR的方法,包括使样品与抗体或其抗原结合片段接触,所述抗体或其抗原结合片段包含:包含分别在SEQ ID NO:5-7所示氨基酸序列的重链可变区CDR1、CDR2和CDR3,和包含分别在SEQ ID NO:8-10中示出的氨基酸序列的轻链可变区CDR1、CDR2和CDR3,其中抗体或其抗原结合片段特异性结合人GITR,并检测抗体与样品中GITR的结合。

[0008] 本文还提供了确定癌症患者的肿瘤是否为GITR阳性的方法,包括:

[0009] (a) 使来自患者的肿瘤样品与抗体或其抗原结合部分接触,所述抗体或其抗原结合部分包含:包含分别在SEQ ID NO:5-7中示出的氨基酸序列的重链可变区CDR1、CDR2和CDR3,和包含分别在SEQ ID NO:8-10中示出的氨基酸序列的轻链可变区CDR1、CDR2和CDR3,其中所述抗体或其抗原结合片段特异性结合人GITR,

[0010] (b) 检测所述抗体与所述样品中GITR的结合,

[0011] (c) 确定样品中GITR蛋白质表达水平,其中高于阈值水平的GITR蛋白质水平指示该肿瘤是GITR阳性的。

[0012] 本文还提供鉴定可能对抗GITR免疫疗法有响应的癌症患者的方法,包括:

[0013] (a) 使来自患者的肿瘤样品与抗体或其抗原结合部分接触,所述抗体或其抗原结合部分包含:分别包含SEQ ID NO:5-7中示出的氨基酸序列的重链可变区CDR1、CDR2和CDR3,和包含分别在SEQ ID NO:8-10所示的氨基酸序列的轻链可变区CDR1、CDR2和CDR3,其中所述抗体或其抗原结合片段特异性结合人GITR,

[0014] (b) 检测所述抗体与所述肿瘤样品中GITR的结合,

[0015] (c) 确定所述样品中GITR蛋白质表达的水平,其中高于阈值水平的GITR蛋白质水平指示该肿瘤是GITR阳性肿瘤,并且该患者可能或预计对抗GITR免疫疗法有响应。

[0016] 本文还提供了治疗癌症患者的方法,包括:

[0017] (a) 如下所述确定癌症患者的肿瘤是否为GITR阳性:(i) 使来自患者的肿瘤样品与抗体或其抗原结合部分接触,所述抗体或其抗原结合部分包含:包含分别在SEQ ID NO:5-7中示出的氨基酸序列的重链可变区CDR1、CDR2和CDR3,和包含分别在SEQ ID NO:8-10所示的氨基酸序列的轻链可变区CDR1、CDR2和CDR3,其中所述抗体或其抗原结合片段特异性结合人GITR;(ii) 检测所述抗体与所述肿瘤样品中GITR的结合,和(iii) 确定所述样品中GITR蛋白质表达的水平,其中GITR蛋白质的水平高于阈值水平指示肿瘤是GITR阳性的,而且

[0018] (b) 如果肿瘤被确定为GITR阳性,则向患者施用调变GITR信号传导的作用剂。在某些实施方案中,调变GITR信号传导的作用剂是激动性(即激动剂)抗GITR抗体。

[0019] 本文还提供监测癌症患者中的GITR阳性肿瘤的方法,包括:

[0020] (a) 在第一时间点使用抗体检测GITR阳性肿瘤中的GITR蛋白质表达,所述抗体包含:包含分别在SEQ ID NO:5-7中示出的氨基酸序列的重链可变区CDR1、CDR2和CDR3,和包含分别在SEQ ID NO:8-10中示出的氨基酸序列的轻链可变区CDR1、CDR2和CDR3,其中所述抗体或其抗原结合片段特异性结合人GITR,

[0021] (b) 确定第一时间点的GITR蛋白表达水平,

[0022] (c) 使用与步骤(a)中使用的相同的抗体在第二时间点检测肿瘤中的GITR蛋白质表达,

[0023] (d) 确定来自第二时间点的肿瘤中GITR蛋白质表达的水平;

[0024] (e) 比较在第一和第二时间点确定的GITR蛋白质表达水平,其中第一时间点相对于第二时间点的水平较高指示肿瘤消退,第一时间点相对于第二时间点的得分较低指示肿瘤进展,在第一时间点相对于第二时间点的水平相对不变指示肿瘤稳定。

[0025] 本文还提供监测具有GITR阳性肿瘤的患者中的抗GITR免疫疗法的功效的方法,包括:

[0026] (a) 在启动抗GITR免疫疗法之前或之后的第一时间点使用抗体检测GITR阳性肿瘤中的GITR蛋白质表达,所述抗体包含:包含分别在SEQ ID NO:5-7中示出的氨基酸序列的重链可变区CDR1、CDR2和CDR3,和包含分别在SEQ ID NO:8-10中示出的氨基酸序列的轻链可变区CDR1、CDR2和CDR3,其中所述抗体或其抗原结合片段特异性结合人GITR,

[0027] (b) 确定来自第一时间点的肿瘤中的GITR蛋白质表达水平,

[0028] (c) 在启动抗GITR免疫疗法后的第二时间点使用与步骤(a)相同的抗体检测所述GITR阳性肿瘤中的GITR蛋白质表达,

[0029] (d) 确定来自第二时间点的肿瘤中GITR蛋白质表达的水平;

[0030] (e) 比较在第一和第二时间点确定的GITR蛋白质表达水平,其中第一时间点相对于第二时间点的水平较高指示抗GITR免疫疗法有效,第一时间点相对于第二时间点的得分较低指示抗GITR免疫疗法无效,第一时间点相对于第二时间点的得分未改变指示抗GITR免疫疗法在起稳定化作用。在某些实施方案中,抗GITR免疫疗法包括向患者施用治疗有效量的抗GITR抗体或其抗原结合部分。

[0031] 在某些实施方案中,本文所述方法中使用的肿瘤样品是福尔马林固定石蜡包埋的肿瘤样品。在某些实施方案中,肿瘤样品是冷冻的肿瘤组织样品。在某些实施方案中,本文所述的方法通过免疫组化进行。在某些实施方案中,使用评分系统(例如H评分系统、Allred

评分系统、AQUA系统或自动化评分系统)确定GITR表达水平。

[0032] 在某些实施方案中,本文所述方法中使用的抗体包含这样的重链可变区和轻链可变区,它们包含分别在SEQ ID NO:11和12中示出的氨基酸序列。在某些实施方案中,本文所述方法中使用的抗体包含这样的重链和轻链,它们分别包含SEQ ID NO:13和14中示出的氨基酸序列。在某些实施方案中,重链缺少C端赖氨酸。在某些实施方案中,抗体是IgG1、IgG2、IgG3或IgG4抗体。在某些实施方案中,如Biacore所评估的,抗体以10nM或更小的 K_D 结合可溶性人GITR。

[0033] 在某些实施方案中,抗体是人源化抗体、人抗体或嵌合抗体。在某些实施方案中,抗体是嵌合抗体,其包含人可变区序列和非人恒定区序列,例如小鼠重链和轻链恒定区。在某些实施方案中,小鼠Fc区是小鼠IgG2a Fc区。在某些实施方案中,嵌合抗体包含分别在SEQ ID NO:15和16中示出的重链和轻链序列。在某些实施方案中,重链缺少C端赖氨酸。

[0034] 在某些实施方案中,本文所述方法中使用的抗体包含可检测模块,例如放射性标记、荧光标记、酶标记、生物素、发色团或ECL标记。

[0035] 本文还提供了包含抗体或其抗原结合部分、以及使用说明书的诊断试剂盒,所述抗体或其抗原结合部分包含:包含分别在SEQ ID NO:5-7中示出的氨基酸序列的重链可变区CDR1、CDR2和CDR3,和包含分别在SEQ ID NO:8-10所示的氨基酸序列的轻链可变区CDR1,CDR2和CDR3,其中所述抗体或其抗原结合片段特异性结合人GITR。在某些实施方案中,抗体或其抗原结合部分包含分别如SEQ ID NO:11和12所示的重链和轻链可变区序列。在某些实施方案中,抗体包含分别如SEQ ID NO:13和14所示的重链和轻链序列。在某些实施方案中,抗体包含分别如SEQ ID NO:15和16所示的重链和轻链序列。在某些实施方案中,重链缺少C端赖氨酸。

[0036] 附图简述

[0037] 图1显示了6G10人单克隆抗体的重链可变区的核苷酸序列(SEQ ID NO:17)和氨基酸序列(SEQ ID NO:11)。示出了CDR1(SEQ ID NO:5)、CDR2(SEQ ID NO:6)和CDR3(SEQ ID NO:7)区域,并指出了V、D和J种系衍生物。

[0038] 图2显示了6G10人单克隆抗体的 κ 轻链可变区的核苷酸序列(SEQ ID NO:18)和氨基酸序列(SEQ ID NO:12)。示出了CDR1(SEQ ID NO:8)、CDR2(SEQ ID NO:9)和CDR3(SEQ ID NO:10)区域,并指出了V和J种系衍生物。

[0039] 图3显示了6G10的重链可变区的氨基酸序列(SEQ ID NO:11)与人种系 V_H 3-33、3-10和JH6氨基酸序列的比对。

[0040] 图4显示了6G10的轻链可变区(VK1)的氨基酸序列(SEQ ID NO:12)与人种系 V_k L18和JK2氨基酸序列的比对。

[0041] 图5显示了嵌合6G10抗体重链的核苷酸序列(SEQ ID NO:21)和氨基酸序列(SEQ ID NO:15)。

[0042] 图6显示了嵌合6G10抗体的轻链的核苷酸序列(SEQ ID NO:22)和氨基酸序列(SEQ ID NO:16)。

[0043] 图7显示了使用嵌合6G10抗体通过免疫组织化学对来自子宫颈鳞状细胞癌样品的相邻福尔马林固定的石蜡包埋(FFPE)切片上的CD3、FoxP3和GITR的染色。

[0044] 定义

[0045] 为了更容易了解本说明,首先定义某些术语。其他定义在整个详细说明中进行阐释。

[0046] 如本文所用术语“糖皮质激素可诱导的TNF受体”或“GITR”是指一种结合GITR配体(GITR-L)的受体,其为TNF-受体超家族成员。GITR亦称作肿瘤坏死因子受体超家族成员18(TNFRSF18)、AITR及CD357。术语“GITR”包括由细胞天然表达的GITR的任何变体或同种型。因此,本文所述抗体可与来自除人外的物种的GITR(例如,食蟹猴GITR)交叉反应。或者,抗体可对人GITR具有特异性、且可不与其他物种展现任何交叉反应性。GITR或其任何变体及同种型可自天然表达它们的细胞或组织分离,或使用本领域熟知的技术及/或本文所述的技术以重组方式产生。

[0047] 已鉴别人GITR的三种同种型,三者都共有相同的细胞外结构域,但C-末端部分除外。变体1(登录号NP_004186;SEQ ID NO:1)由241个氨基酸组成,代表最长的转录物。与变体2相比,其含有一个导致移框的额外编码区段。与同种型2相比,所得的蛋白质(同种型1)含有一个不同的较短的C-末端。变体2(登录号NP_683699;SEQ ID NO:2)编码蛋白质的最长(同种型2),由255个氨基酸组成,且是可溶的。与变体2相比,变体3(登录号NP_683700;SEQ ID NO:3)含有一个导致移框的额外编码区段。与同种型2相比,所得的蛋白质(同种型3)含有一个不同的较短的C-末端,且由234个氨基酸组成。人GITR同种型1、2、3的氨基酸序列分别如SEQ ID NO:1、2、3所示,成熟GITR的胞外域的氨基酸序列如SEQ ID NO:4所示。

[0048] 如本文所用术语“抗体”包括全抗体及其任第一抗体原结合片段(即“抗原结合部分”)或单链。在一个实施方案中,“抗体”指包含由二硫键互连的至少两条重(H)链及两条轻(L)链的糖蛋白或其抗原结合部分。每一重链包括重链可变区(在本文中缩写为 V_H)及重链恒定区。在某些天然抗体中,重链恒定区包括三个结构域:CH1、CH2及CH3。在某些天然抗体中,每一轻链包括轻链可变区(在本文中缩写为 V_L)及轻链恒定区。轻链恒定区包括一个结构域(C_L)。可将 V_H 及 V_L 区进一步细分成超变区(称为互补决定区(CDR))及更保守的区(称为框架区(FR)),二者间杂排列。每一 V_H 及 V_L 由三个CDR及四个FR构成,其自氨基末端至羧基末端按下列顺序布置:FR1、CDR1、FR2、CDR2、FR3、CDR3、FR4。重链及轻链的可变区含有与抗原相互作用的结合结构域。抗体的恒定区可介导免疫球蛋白与宿主组织或因子(包括免疫系统的各种细胞(例如效应物细胞)及经典补系统的第一组分(C1q))的结合。

[0049] 抗体通常以高亲和力(由 $10^{-5}M$ 至 $10^{-11}M$ 或更小的解离常数(K_D)反映)特异性结合其关联抗原。通常将大于约 $10^{-4}M$ 的任何 K_D 视为指示非特异性结合。如本文所用的,“特异性结合”至抗原的抗体指以高亲和力(此意味着 K_D 为 $10^{-7}M$ 或更小、优选 $10^{-8}M$ 或更小、更优选 $5 \times 10^{-9}M$ 或更小、最优选介于 $10^{-8}M$ 与 $10^{-10}M$ 之间或更小)结合抗原及实质上相同抗原、但不以高亲和力结合无关抗原的抗体。

[0050] 免疫球蛋白可来自普遍已知的同型中的任一者,包括但不限于IgA、分泌型IgA、IgG及IgM。IgG同型在某些物种中分成亚类:在人类中为IgG1、IgG2、IgG3及IgG4,在小鼠中为IgG1、IgG2a、IgG2b及IgG3。在某些实施方案中,本文所述抗GITR抗体属IgG1或IgG2亚型。免疫球蛋白(例如IgG1)存在若干异型,这些异型在至少少数个氨基酸中彼此不同。“抗体”举例而言包括天然及非天然抗体;单克隆及多克隆抗体;嵌合及人源化抗体;人及非人抗体;全合成抗体;及单链抗体。

[0051] 如本文所用术语抗体的“抗原结合部分”指抗体的保持特异性结合抗原(例如,人

GITR)的能力的一个或多个片段。这些“片段”的长度为,例如,介于约8个与约1500个氨基酸之间,适宜地介于约8个与约745个氨基酸之间,适宜地约8个至约300个、例如约8个至约200个氨基酸、或约10个至约50个或100个氨基酸。已显示,抗体的抗原结合功能可由全长抗体的片段来执行。抗体(例如本文所述抗GITR抗体)的“抗原结合部分”这一术语内涵盖的结合片段的实例包括(i) Fab片段,即由 V_L 、 V_H 、CL及CH1结构域组成的单价片段;(ii) $F(ab')_2$ 片段,一种二价片段,包含两个在铰链区由二硫桥键连接的Fab片段;(iii) 由 V_H 及CH1结构域组成的Fd片段;(iv) 由抗体单臂的 V_L 及 V_H 结构域组成的Fv片段;(v) dAb片段(Ward等人,(1989) Nature 341:544-546),其由 V_H 结构域组成;及(vi) 分离的互补决定区(CDR)或(vii) 两个或更多个可视情况由合成接头接合的分离的CDR的组合。此外,尽管Fv片段的两个结构域(V_L 及 V_H)是由各别的基因编码的,但其可使用重组方法通过合成接头接合在一起,该合成接头使其能够成为单一蛋白链(称作单链Fv(scFv)),其中 V_L 及 V_H 区配对形成单价分子;例如,参见Bird等人,(1988) Science 242:423-426;及Huston等人(1988) Proc.Natl.Acad.Sci.USA 85:5879-5883)。此类单链抗体亦意欲涵盖于术语抗体的“抗原结合部分”内。这些抗体片段系使用本领域技术人员已知的常规技术获得,且以与完整抗体相同的方式筛选片段是否有效用。抗原结合部分可通过重组DNA技术、或通过酶或化学裂解完整免疫球蛋白来产生。

[0052] 如本文所用的,术语“单克隆抗体”指对抗体的特定表位或组合物展示单一结合特异性及亲和力的抗体,其中所有抗体皆对特定表位展示单一结合特异性及亲和力。因此,术语“人单克隆抗体”指展示单一结合特异性且具有源自人种系免疫球蛋白序列的可变区(及任选地恒定区)的抗体或抗体组合物。在一个实施方案中,人单克隆抗体由杂交瘤产生,该杂交瘤包括自转基因非人动物(例如转基因小鼠)获得的B细胞,其基因组包含与永生细胞融合的人重链转基因及人轻链转基因。

[0053] 如本文所用术语“重组人抗体”包括所有通过重组方式制备、表达、产生或分离的人抗体,例如(a) 自对人免疫球蛋白基因转基因或转染色体的动物(例如小鼠)或自其制备的杂交瘤分离的抗体;(b) 自经转化以表达抗体的宿主细胞、例如自转染瘤分离的抗体;(c) 自重组的组合人抗体文库分离的抗体;及(d) 通过任何其他涉及将人免疫球蛋白基因序列剪接至其他DNA序列的方式制备、表达、产生或分离的抗体。这些重组人抗体包含可变区及恒定区,其利用由种系基因编码的特定人种系免疫球蛋白序列,但包括在(例如)抗体成熟期间发生的后续重排及突变。如本领域已知的(例如参见Lonberg Nature Biotech 2005; 23:1117-25),可变区含有抗原结合结构域,抗原结合结构域由多种基因编码,这些基因为形成对外来抗原具有特异性的抗体而重排。除重排外,可变区可通过多个单一氨基酸变化(称作体细胞突变或超突变)进一步修饰,以增加抗体对外来抗原的亲和力。恒定区将进一步因应于抗原发生变化(即,同型切换)。因此,响应于抗原而经过重排且体细胞突变的编码轻链及重链免疫球蛋白多肽的核酸分子可不与初始核酸分子具有序列同一性,而是将实质上相同或类似(即,具有至少80%同一性)。

[0054] “人”抗体(HuMAb)指具有可变区的抗体,其中框架及CDR区二者皆源自人种系免疫球蛋白序列。此外,若抗体含有恒定区,则恒定区亦源自人种系免疫球蛋白序列。本文所述抗体可包括不由人种系免疫球蛋白序列编码的氨基酸残基(例如,通过体外随机诱变或位点特异性诱变或通过活体内体细胞突变引入的突变)。然而,如本文所用术语“人抗体”并不

意欲包括源自另一哺乳动物物种(例如小鼠)种系的CDR序列已移植至人框架序列上的抗体。术语“人”抗体及“完全人”抗体同义使用。

[0055] “人源化”抗体指非人抗体的CDR结构域外的一些、大部分或所有氨基酸经源自人免疫球蛋白的相应氨基酸置换的抗体。在抗体的人源化形式的一个实施方案中,CDR结构域外的一些、大部分或所有氨基酸经人免疫球蛋白的氨基酸置换,而一个或多个CDR区内的一些、大部分或所有氨基酸未改变。可允许存在氨基酸的小的添加、缺失、插入、取代或修饰,只要其不消除抗体结合给定抗原的能力即可。“人源化”抗体保留类似于初始抗体的抗原特异性的抗原特异性。

[0056] “嵌合抗体”指可变区源自一个物种(例如人可变区)且恒定区源自另一物种(例如小鼠恒定区)的抗体,例如可变区源自小鼠抗体且恒定区源自人抗体的抗体。多个物种的恒定区序列是本领域已知的,并且本领域技术人员可以容易地获得它们来产生嵌合抗体。示例性的嵌合抗GITR抗体包含人可变区序列和小鼠恒定链序列。例如,在一个实施方案中,嵌合抗GITR抗体包含分别在SEQ ID NO:15和16中示出的重链和轻链序列。在某些实施方案中,嵌合抗体的重链缺少C端赖氨酸。

[0057] 如本文所用的“分离的抗体”欲指实质上不含具有不同抗原特异性的其他抗体的抗体(例如,特异性结合GITR的分离的抗体实质上不含特异性结合除GITR以外的抗原的抗体)。然而,特异性结合GITR的表位的分离的抗体可与来自不同物种的其他GITR蛋白具有交叉反应性。

[0058] 如本文所用术语“特异性结合”(“specific binding”)、“选择性结合”(“selective binding”)、“选择性地结合”(“selectively binds”)及“特异性地结合”(“specifically binds”)指抗体结合预定抗原上的表位。通常,抗体(i)在通过(例如)在BIAcore 2000仪器中使用预定抗原(例如重组人GITR)作为分析物及抗体作为配体的表面等离子体共振(SPR)技术时,以约小于 10^{-7} M、例如约小于 10^{-8} M、 10^{-9} M或 10^{-10} M或甚至更低的平衡解离常数(K_D)结合。

[0059] 如本文所用术语“ $K_{\text{结合}}$ ”或“ K_a ”欲指特定抗体-抗原相互作用的缔合速率,而如本文所用术语“ $K_{\text{解离}}$ ”或“ K_d ”欲指特定抗体-抗原相互作用的解离速率。本文所用术语“ K_D ”欲指解离常数,其自 K_d 对 K_a 的比率(亦即 K_d/K_a)求得且以摩尔浓度(M)表示。可使用本领域充分确立的方法测定抗体的 K_D 值。测定抗体的 K_D 的一种优选方法是通过使用表面等离子体共振、优选使用生物检测器系统(例如Biacore®系统)。

[0060] “多肽”指包含至少两个连续连接的氨基酸残基的链,其中链的长度无上限。蛋白质中的一个或多个氨基酸残基可含有例如但不限于糖基化、磷酸化或二硫键形成等修饰。“蛋白质”可包含一种或多种多肽。

[0061] “免疫疗法”指通过包含诱导、增强、阻抑或以其他方式修饰免疫响应的方法治疗罹患疾病、或有感染疾病的风险、或疾病复发的受试者。在此语境中,“抗GITR免疫疗法”是指包括下述手段的方法来治疗患有或有风险患上疾病(例如癌症)的受试者:通过施用可调节GITR信号传导、并导致例如T细胞活化的诱导和/或增强(例如T细胞生成IL-2和/或IFN- γ 的增加,和/或T细胞的增殖的增加)、调节性T细胞的消耗等的作用剂(例如激动性抗GITR抗体),诱导,增强,抑制或以其他方式调节免疫响应。

[0062] 如本文所用的,术语“连接(的)”指两个或更多个分子的缔合。连接可为共价或非

共价连接。连接亦可为遗传性的(即,重组融合)。这些连接可使用多种本领域公认的技术(例如化学偶联及重组蛋白产生)来达成。

[0063] 如本文所用,“施用”指使用本领域技术人员已知的各种方法及递送系统向受试者导入包含治疗剂的组合物。本文所述抗体的优选施用途径包括静脉内、腹膜内、肌内、皮下、脊柱或其他非经肠施用途径(例如通过注射或输注)。如本文所用片语“非经肠施用”意指除经肠及局部施用以外的施用方式,通常通过注射,且包括(但不限于)静脉内、腹膜内、肌内、动脉内、鞘内、淋巴管内、病灶内、囊内、眶内、心内、皮内、经气管、皮下、表皮下、关节内、经囊下、蛛网膜下、脊柱内、硬膜外及胸骨内注射及输注、以及体内电穿孔。或者,本文所述抗体可经由非经肠途径施用,例如局部、表皮或粘膜施用途径,例如经鼻内、经口、经引道、经直肠、经舌下或经局部。施用亦可(例如)实施一次、多次及/或在一个或多个延长时段内实施。

[0064] 如本文所用的,“癌症”指特征在于体内异常细胞不受控生长的一大类疾病。失调的细胞分裂可导致形成恶性肿瘤或细胞,侵袭相邻组织且可经由淋巴系统或血流转移至身体的远端部分。

[0065] 如本文所用的,“肿瘤”指由于不受控的、进行性的过度细胞分裂导致的异常组织块。肿瘤可以是良性的或者恶性的。

[0066] 术语“患者”包括接受预防性或治疗性治疗的人及其他哺乳动物受试者。

[0067] 如本文所用术语“受试者”包括任何人或非人动物。举例而言,本文所述方法及组合物可用于治疗患有癌症的受试者。术语“非人动物”包括所有脊椎动物,例如哺乳动物及非哺乳动物,例如非人灵长类动物、绵羊、犬、牛、鸡、两栖动物、爬行类等。

[0068] 在以下子部分中进一步详细阐述本文所述各个方面。

[0069] 如本文所使用的,除非上下文另外清楚地指出,否则单数形式“一”和“该”包括复数指示物。除非另有说明,否则使用“或”或“和”意指“和/或”。此外,使用术语“包括”,及其其他形式,如“可包括”,“包括了”,不是限制性的。

[0070] 本文中使用的术语“约”,当指可测量值,例如量、持续时间等时,涵盖了距离指定值最多至 $\pm 10\%$ 的变化。除非另外指明,本文中使用的表示成分的量、性质如分子量、反应条件等,以及在本领域公认的评分系统中的分数等等的数字,均应理解为被“约”所修饰。

[0071] 术语“受试者(的)样品”是指从受试者分离的细胞(例如,肿瘤细胞,T细胞,B细胞或其他),组织(例如肿瘤),流体和/或其组合。

[0072] 本文中使用的术语“对照样品”或“参考样品”指任何临床上相关的对照或参考样品,包括,例如,来自健康受试者的样品或者从评估的受试者早先获得的样品。例如,对照样品或参考样品可以是在癌症发病之前、疾病的较早阶段、或施用治疗前采取的样品。

[0073] 如本文所用的,“阈值水平”或“截止水平”在表达水平的上下文中是指GITR蛋白质的一定表达水平,高于该水平,患者样品(患者肿瘤样品)被认为是“GITR阳性”;低于该水平,患者样品被认为是“GITR阴性”。阈值水平可以基于例如来自“正常”患者样品(例如,不具有GITR阳性肿瘤的患者群体)或来自被评估患者的匹配的正常组织的数据的一次或多次汇编。阈值可以置于本领域认可的评分系统(例如H评分系统)的框架中。例如,在一个实施方案中,如果患者的肿瘤的H分大于1,而患者的匹配的正常组织中的H分为1,则患者的肿瘤

将被视为GITR阳性。阈值检测水平可以是使用给定的检测方法时最低的检测水平。例如,阈值水平可以是这样的水平,在该水平下,使用免疫组化,例如使用本文中描述的免疫组化方法,无法检测到GITR。

[0074] 诊断性抗GITR抗体

[0075] 本申请提供诊断性抗GITR抗体,其可用于检测人组织(例如肿瘤组织)中的GITR蛋白表达。这种抗体可以用于,例如,鉴定/选择有可能受益于抗GITR免疫治疗(即对治疗有响应)的受试者,监测GITR阳性肿瘤的进展,和/或监测抗GITR免疫治疗的功效。

[0076] 相应地,在一些实施方案中,可用于诊断组织样品(例如人肿瘤组织样品)中GITR蛋白的表达的诊断性抗GITR抗体包括抗体6G10(一种全人抗GITR抗体)的重链及轻链可变区CDR序列、重链及可变区序列、或全长重链及轻链序列。表2中提供了6G10相关序列的总结。

[0077] 在一些实施方案中,抗GITR抗体具有如SEQ ID NO:5-7所示的重链可变区CDR1、CDR2和CDR3序列,和如SEQ ID NO:8-10所示的轻链可变区CDR1、CDR2和CDR3序列,并特异性结合人GITR。

[0078] 在一些实施方案中,抗GITR抗体具有如SEQ ID NO:11所示的重链可变区序列和如SEQ ID NO:12所示的轻链可变区序列。

[0079] 在一些实施方案中,抗GITR抗体具有分别如SEQ ID NO:13和14所示的重链和轻链序列。在某些实施方案中,重链缺少C端赖氨酸。

[0080] 在一些实施方案中,抗GITR抗体是IgG1,IgG2,IgG3或IgG4抗体或其变体。在其他实施方案中,抗体是IgA,IgD,IgE或IgM抗体。

[0081] 在一些实施方案中,抗GITR抗体是人抗体、人源化抗体或嵌合抗体。

[0082] 在一些实施方案中,如由Biacore测定的,抗GITR抗体以10nM或更低的 K_D 结合至可溶性GITR。

[0083] 在某些实施方案中,抗GITR抗体是嵌合抗体。在一个实施方案中,所述抗GITR抗体具有6G10抗体的重链和轻链可变区序列(分为为SEQ ID NO:11和12),以及非人类物种的恒定区,例如,小鼠IgG2a恒定区(SEQ ID NO:25)。这样的嵌合抗体可用于,例如,在检测人组织中的GITR蛋白质表达时减少免疫组织化学中的背景染色。因此,在一个实施方案中,诊断性抗GITR抗体是嵌合抗体,其包含如SEQ ID NO:15所示的重链序列和如SEQ ID NO:16所示的轻链序列。在某些实施方案中,嵌合抗体的重链缺少C端赖氨酸。

[0084] 在一些实施方案中,本文描述的诊断性抗GITR抗体包含可检测模块,以便于GITR表达(例如肿瘤样品中的GITR表达)的检测(例如通过如下所述的免疫组化的检测)。示例性的检测部分包括发光标记,荧光标记,放射性标记(例如, ^{99}Tc , ^{45}Ti , ^{112}In , ^{111}In , ^3H , ^{121}I , ^{125}I , ^{131}I , ^{14}C , ^{18}F , ^{36}Cl , ^{55}Co , ^{58}Co , ^{51}Cr , ^{67}Cu , ^{64}Cu , ^{66}Ga , ^{68}Ga , ^{76}Br , ^{89}Zr , ^{35}S , ^{32}P , ^{90}Y , ^{13}N , ^{15}O , ^{211}At , ^{186}Re , ^{188}Re , ^{75}Se),和酶标记(例如,辣根过氧化物酶,碱性磷酸酶,葡萄糖氧化酶,脲酶,乙酰胆碱转移酶,荧光素酶和 β -半乳糖苷酶),附加表位,发色团标记,磷光标记,光亲和分子,ECL标记,染料,生物素,半抗原等。这样的标记是公知的技术,并且可以使用本领域公知的方法来附接到抗GITR抗体。理想地,可检测标记的附接不显著干扰GITR抗体的结合。检测手段由选定的标记决定。在标记为颗粒,并可以积累到合适的水平的情况下,可以用肉眼来观察(achieve)标记或其反应产物的外观,或者可以使用分光光度计,光度计,荧光计等设备,

这些均根据标准操作进行。

[0085] 优选地,偶联标记的方法产生实质上(或几乎)非免疫原性的联接,例如肽-(即酰胺-)、硫化-(立体阻碍)、二硫化物-、胺-及醚联接。这些联接几乎是非免疫原性的,且在血清内显示合理的稳定性(例如,参见Senter et al.,Curr Opin Chem Biol 2009;13:235-44;WO 2009/059278;WO 95/17886)。

[0086] 可利用不同偶联策略,视部分及抗体的生物化学性质而定。在所述部分是50至500个天然或重组氨基酸的情况下,在描述蛋白偶联物之合成的化学法的教科书中有标准程序,本领域技术人员容易地遵循这些标准程序(参见例如,Hackenberger et al.,Angew Chem Int Ed Engl 2008;47:10030-74)。在一个实施方案中,使用抗体或部分内的马来酰亚胺基部分与半胱氨酸残基的反应。在使用抗体的Fab或Fab'-片段的情况下,这是非常适宜的一种偶联化学。或者,在一个实施方案中,偶联至抗体或部分的C-末端。蛋白质(例如Fab-片段)的C-末端修饰可如(例如)所述实施(Sunbul et al.,Org Biomol Chem 2009;7:3361-71)。

[0087] 一般而言,位点特异性反应及共价偶联是基于将天然氨基酸转变成具有与存在的其他官能基的反应性正交的反应性的氨基酸。举例而言,处于稀有序列背景中的特定半胱氨酸可经酶转化成醛(参见Frese et al.ChemBioChem 2009;10:425-7)。亦可通过利用某些酶与给定序列背景中的天然氨基酸特异性酶反应性来获得期望氨基酸修饰(例如,参见Taki et al.,Prot Eng Des Sel 2004;17:119-26;Gautier et al.Chem Biol 2008;15:128-36;Bordusa et al.,Bioorganic Chemistry (2004) 389-403)。

[0088] 亦可通过末端氨基酸与适当修饰试剂的选择性反应实现位点特异性反应及共价偶联。

[0089] N-末端半胱氨酸与苄腈的反应性(参见Ren et al.,Angew Chem Int Ed Engl 2009;48:9658-62)可用于实现位点特异性共价偶联。

[0090] 天然化学接合亦可依赖于C-末端半胱氨酸残基(Taylor et al.,Nucleic Acids and Molecular Biology 2009;22:65-96)。EP 1 074 563描述偶联方法,其是基于一段带负电荷氨基酸内的半胱氨酸与位于一段带正电氨基酸中的半胱氨酸的较快反应。

[0091] 所述部分亦可为合成肽或肽模拟物。在多肽为化学合成的情况下,合成期间可纳入具有正交化学反应性的氨基酸(参见例如,de Graaf et al.,Bioconjug Chem 2009;20:1281-95)。由于有许多正交官能基可用且可引入合成肽中,故该肽与接头的偶联是一种标准化学。

[0092] 在某些实施方案中,可检测标记间接缀合至抗体。例如,可以将抗体缀合至生物素,并且可以使用本领域公知的方法将标记缀合至亲和素。在另一个实施方案中,使用结合未标记抗体的标记抗体来检测未标记抗体。在某些实施方案中,用于检测的标记抗体是用上文所述的任一种标志物标记的。在一些实施方案中,标记和检测是像实施例中描述的那样,例如使用Leica Bond Polymer Refine Detection System(Leica, Buffalo Grove, IL, Catalog DS9800)来进行的。

[0093] 产生方法

[0094] 诊断性抗GITR抗体可以使用本领域公认的技术来产生。在某些实施方案中,抗体可以从产生抗体(例如6G10抗体)的杂交瘤纯化。例如,可以在2升转瓶中培养产生抗体的杂

交瘤以便于进行单克隆抗体纯化。可以将上清液过滤并浓缩,再过蛋白A-sepharose亲和色谱(Pharmacia,Piscataway,N.J.)。洗脱的IgG可通过凝胶电泳和高效液相色谱检验以确保纯度。可以将缓冲溶液交换为PBS,并可以使用1.43的消光系数通过OD280确定浓度。

[0095] 在某些实施方案中,本文中描述的抗体可以重组产生。例如,可以将编码本文所述的部分或全长轻链和重链的DNA插入到表达载体中,使得这些基因与转录和翻译控制序列操作连接。在此上下文中,术语“操作连接”旨在表示抗体基因被连接到载体中,使得在载体中的转录和翻译控制序列发挥其预期的调节抗体基因转录和翻译的功能。选择表达载体和表达控制序列以与所用的表达宿主细胞相容。可以将抗体轻链基因和重链抗体基因插入到不同的载体中,或者将两种基因插入同一表达载体中。通过标准方法将抗体基因插入表达载体中(例如连接抗体基因片段和载体上的互补限制位点,或者如果不存在限制位点,则平端连接)。通过下述方式,可以利用本文描述的抗体的轻链和重链可变区来创建任何抗体同型的全长抗体基因:将它们插入已经编码有期望同型的重链恒定区和轻链恒定区的表达载体,使得 V_H 区段与该载体内的 C_H 区段操作连接, V_L 区段与该载体内的 C_L 区段操作连接。

[0096] 除了抗体链基因之外,重组表达载体可携带控制抗体链基因在宿主细胞中的表达的调控序列。术语“调控序列”意欲包括控制抗体链基因转录或翻译的启动子、增强子和其它表达控制元件(例如聚腺苷化信号)。此类调控序列在例如Goeddel (Gene Expression Technology. Methods in Enzymology 185, Academic Press, San Diego, CA (1990))中有描述。本领域技术人员将理解,对表达载体的设计,包括对调控序列的选择,可能取决于要转化的宿主细胞的选择,想要的蛋白的表达水平等因素。优选的用于哺乳动物宿主细胞表达的调控序列包括指导哺乳动物细胞中高水平蛋白表达的病毒元件,例如,源于巨细胞病毒(CMV)、猿猴病毒40(SV40)、腺病毒(例如腺病毒主要晚期启动子(AdMLP))和多瘤病毒的启动子和/或增强子。备选地,可使用非病毒调控序列,例如,泛素启动子或 β -珠蛋白启动子。另外,由来自不同来源的序列构成的调控元件,例如SR α 启动子系统,其含有来自SV40早期启动子和人T细胞白血病病毒1型的长末端重复的序列(Takebe et al., MCB 1988;8:466-72)。

[0097] 除了抗体链基因和调控序列之外,本发明的重组表达载体可携带额外的序列,例如调控载体在宿主细胞中复制的序列(例如,复制起点)和选择标记基因。选择标记基因帮助人们选择引入了载体的宿主细胞(见,例如美国专利号4,399,216,4,634,665和5,179,017)。例如,典型地,选择标记基因赋予引入了载体的宿主细胞对药物,例如G418、潮霉素或甲氨喋呤的抗性。选择标记基因包括二氢叶酸还原酶(DHFR)基因(使用甲氨喋呤选择/扩增,用于dhfr-宿主细胞)和neo基因(用于G418选择)。

[0098] 为表达轻链和重链,通过标准技术将编码重链和轻链的表达载体转染进入宿主细胞。术语“转染”的多种形式意欲包括通常用于将外源DNA引入原核或真核宿主细胞的诸多技术,例如电穿孔、磷酸钙沉淀、DEAE-葡聚糖转染等等。虽然理论上说在原核或真核宿主细胞中都可以表达本发明的抗体,但在真核细胞中,最理想的是在哺乳动物宿主细胞中表达抗体是最优选的,因为此类真核细胞,特别是哺乳动物细胞,比原核细胞更有可能装配和分泌经正确折叠的并且具有免疫活性的抗体。已有报道称,抗体基因的原核生物表达对于生产高产率的活性抗体是无效的(Boss et al., Immunology Today 1985;6:12-13)。

[0099] 优选的用于表达本文所述的重组抗体的哺乳动物宿主细胞包括:中华仓鼠卵巢

(CHO) 细胞 (包括 dhfr-CHO 细胞, 在 Urlaub and Chasin, PNAS 1980; 77: 4216-220 中描述, 使用 DHFR 选择标记, 例如, 按照 Kaufman et al., Mol Biol 1982; 159: 601-21 所述), NSO 骨髓瘤细胞、COS 细胞和 SP2 细胞。特别地, 对于使用 NSO 骨髓瘤细胞而言, 另一优选的表达系统是 WO 87/04462、WO 89/01036 和 EP 338,841 中公开的 GS 基因表达系统。当编码抗体基因的重组表达载体被引入哺乳动物宿主细胞时, 通过将宿主细胞培养一段时间来产生抗体, 所述时间足以容许抗体在宿主细胞中表达, 或者更优选地, 容许抗体分泌到培养宿主细胞的培养基中。可使用标准的蛋白质纯化方法, 从培养基中回收抗体。

[0100] 本文所述的嵌合抗 GITR 抗体可以基于如上所述制备的人单克隆抗体的序列来制备。例如, 在一个实施方案中, 使用常规重组技术, 可以将编码 6G10 抗体的人重链和轻链可变区的 DNA 操作连接至非人恒定区 (例如, 鼠恒定区)。

[0101] 检测细胞上的人 GITR 的方法

[0102] 本文提供了检测生物样品 (例如人肿瘤组织样品) 中的 GITR 蛋白表达的方法, 所述检测是通过使样品与抗 GITR 抗体接触, 并检测 (例如通过免疫组化) 抗体与样品中 GITR 的结合来进行的, 所述抗 GITR 抗体例如本文所述的抗 GITR 抗体, 比如这样的抗 GITR 抗体: 其包含分别如 SEQ ID NO: 5-7 和 8-10 中示出的重链和轻链可变区 CDR 序列, 分别如 SEQ ID NO: 11 和 12 中示出的重链和轻链可变区序列, 或分别如 SEQ ID NO: 13 和 14 中示出的抗体 6G10 (一种全人抗 GITR 抗体) 的全长重链和轻链序列, 其中该抗体或其抗原结合片段特异性结合人 GITR。在某些实施方案中, 所述重链缺少 C 端赖氨酸。在一些实施方案中, 所述抗 GITR 抗体是包含抗体 6G10 的可变区, 但包含非人恒定区 (例如小鼠恒定区) 的嵌合抗体, 例如这样的嵌合 6G10 抗体: 其包含分别如 SEQ ID NO: 15 和 16 中示出的重链和轻链序列。在某些实施方案中, 嵌合抗体的重链缺少 C 端赖氨酸。

[0103] 在某些实施方案中, 示例性生物样品包括从癌症患者获得的血液样品、血清样品、细胞、手术切除的组织、和活检组织 (例如癌组织)。用于本文所述方法的生物样品可以是新鲜的, 冷冻的或固定的。生物样品, 例如肿瘤样品, 可以使用常规方法从患者获得, 所述常规方法例如但不限于活组织检查, 手术切除或抽吸。

[0104] 用于检测人组织 (例如肿瘤组织) 中的 GITR 表达的方法可以是定性的, 半定量的或定量的。用于检测生物样品中 GITR 蛋白水平的本领域公认的基于抗体的方法包括但不限于酶联免疫吸附测定 (ELISA), 放射免疫测定, 电化学发光 (ECL) 测定, 表面等离子共振, western 印迹, 免疫沉淀, 荧光活化细胞分选 (FACS), 免疫荧光, 免疫组化等。检测生物样品中 GITR 表达的方法可以包括对照样品 (阴性和阳性对照)。例如, 阴性对照样品可以是不含 GITR 蛋白的样品, 阳性对照样品是含有 GITR 蛋白的样品。将结果与阴性和阳性对照比较可以确认生物样品中 GITR 的有无。

[0105] 在一个实施方案中, 通过免疫组化评估肿瘤组织样品中的 GITR 表达。该技术允许检测特定细胞类型 (例如 Treg 细胞, 例如肿瘤内的 Treg 细胞) 和肿瘤细胞上的 GITR。

[0106] 一般的免疫组化方法在本领域中是公知的。进行免疫组化的具体条件、考虑和指导描述于例如 Immunohistochemical Staining Methods 6th Edition 2013, Taylor CR, Rudbeck L, eds., Dako North America, 可以在 www.dako.com 作为教育指导获得; “Immunohistochemical Staining Method guide”)。免疫组化染色可以在固定的组织切片或冷冻组织切片上进行。当使用固定的组织切片, 例如福尔马林固定石蜡包埋 (FFPE) 组织

切片时,该过程通常包括以下步骤:获得肿瘤组织样品(例如通过活组织检查),固定肿瘤样品;包埋(例如在石蜡中);切片和封固;抗原修复;与第一抗体(例如,本文所述的嵌合6G10抗体)温育,检测(例如在扩增抗原/抗体复合物信号之后)和由病理学家解读(例如使用本领域认可的评分系统)。

[0107] 合适的非限制性固定剂包括例如多聚甲醛、戊二醛、甲醛、乙酸、丙酮、四氧化锇、铬酸、氯化汞、苦味酸、醇(例如甲醇、乙醇)、Gendre氏液、Rossman氏液、B5固定剂、Bouin氏液、Carnoy氏固定剂、和甲氧基乙酰苯胺(methacarn)。在一个优选的实施方案中,将肿瘤样品固定在甲醛中(例如10%缓冲的福尔马林,其对应于缓冲溶液中4%的甲醛)。一旦固定,使用酒精或二甲苯将肿瘤样品连续脱水,包埋在石蜡中,并用切片机切割以产生肿瘤组织切片(例如,厚度约4-5 μ m),然后将其封固到显微镜载玻片上(例如,涂有粘合剂的玻璃载玻片)。

[0108] 示例性的包埋材料包括石蜡、火棉胶、OCTTM包埋剂、琼脂、塑料或丙烯酸树脂。在一个优选的实施方案中、包埋剂是石蜡。

[0109] 抗原修复可以使用本领域已知的任何方法进行。抗原修复处理可能涉及加热(例如,热诱导的表位修复(HIER)),如实施例3中所述的那样,或酶促降解(蛋白水解诱导的表位修复(PIER))。示例性的抗原修复方法包括微波加热、蛋白水解处理(例如用蛋白酶K)、压力锅加热和水浴加热。《免疫组化染色方法》(Immunohistochemical Staining)指南的第3章描述了抗原修复的详细通用方法。在某些实施方案中,通过HIER结合市售抗原修复缓冲液(如实施例3中所述)进行抗原修复。

[0110] 本文所述的方法使用抗GITR抗体来检测人GITR蛋白的表达水平。在某些实施方案中,诊断性抗GITR抗体包含分别在SEQ ID NO:5-7和8-10中示出的重链和轻链可变区CDR序列,分别在SEQ ID NO:11和12中示出的重链和轻链可变区序列,或者分别在SEQ ID NO:13和14中示出的抗体6G10(一种全人抗GITR抗体)的全长重链和轻链序列,其中所述抗体或其抗原结合片段特异性地结合人GITR,如上所述。在某些实施方案中,所述重链缺少C端赖氨酸。在一些实施方案中,抗GITR抗体是包含抗体6G10的可变区、但包含非人恒定区(例如小鼠恒定区)的嵌合抗体,例如包含分别在SEQ ID NO:15和16中示出的重链和轻链序列的嵌合6G10抗体。在某些实施方案中,嵌合抗体的重链缺少C端赖氨酸。此类抗体对于检测肿瘤组织切片中的GITR表达特别有用(参见例如实施例3)。

[0111] 可以使用直接或间接方法检测组织、例如肿瘤样品中的GITR蛋白质表达。例如,第一抗体可以包含可检测模块,例如如本文所述的辣根过氧化物酶(HRP)或荧光标记(例如FITC,TRITC)。在某些实施方案中,第一抗体本身不包含可检测模块,但通过第二抗体与其结合而被检测,用于间接免疫组化。因此,在某些实施方案中,第二抗体包含可检测标记,例如酶标记,显色标记或荧光标记。在某些实施方案中,第一抗体是包含人可变区序列和非人Fc区的嵌合抗体。第二抗体可用于识别第一抗体的非人Fc区,以减少背景染色。

[0112] 在一些实施方案中,可使用亲和素-生物素复合物方法(ABC方法)检测GITR蛋白质表达。在这些实施方案中,第二抗体是生物素化的,并且可以充当第一抗体和生物素-亲和素-过氧化物酶复合物之间的桥梁。用于免疫组化的其他合适的非限制性方法包括在免疫组化染色方法(Immunohistochemical Staining Method)指南的第6章中描述的那些方法,例如Chilosi et al.,*Biotech Histochem* 1994;69:235;Sabattini et al.,*J Clin*

Pathol 1998;51:506-11和Gross et al., JBC 1959;234:1622中描述的方法。

[0113] 用于制备和染色冷冻组织切片的一般方法是本领域公知的,并且描述于,例如:免疫组化染色方法指南;Immunohistochemistry and Methods (Buchwalow and Bocker, Springer-Verlag Berlin Heidelberg 2010)的第3章;Theory and Practice of Histological Techniques (Bancroft and Gamble, 6th Edition, Elsevier Ltd., 2008)的第21章。冷冻组织切片染色可以如实施例3所述进行。

[0114] GITR蛋白质可以如实施例中所述的那样检测。

[0115] 在一些实施方案中,可以进一步使用公知的技术中的方法对如本文描述的那样用抗GITR抗体染色的玻片进行复染,例如用苏木精和/或曙红进行复染。

[0116] 在解读步骤中,可以使用本领域公认的评分方法对通过免疫组化检测到的GITR蛋白质表达评分。评分方法的非限制性例子如下所述。

[0117] 例如,在一些实施方案中,GITR表达的评分使用H评分(组织化学评分)系统,由于其动态范围,且使用加权百分位数,该系统在本领域中有广泛的应用。H评分是一种基于下式的半定量评分系统:3×强烈染色(3+染色)细胞的百分比+2×中度染色(2+染色)细胞的百分比+1×弱染色(1+染色)细胞的百分比+0×无染色(0染色)细胞的百分比,给出的分数范围为0至300。参见例如,McCarty et al., Cancer Res 1986;46:4244-8;Bosman et al., J Clin Pathol 1992;45:120-4;Dieset et al., Analyt Quant Cytol Histol 1996;18:351-4。对照组织可以包括,例如,来自相同受试者的匹配的非肿瘤组织。因此,在一些实施方案中,使用本文的抗GITR抗体GITR染色阳性的细胞的数目,以及染色的强度,可以用于确定H评分。

[0118] 在其它实施方案中,使用Allred评分系统评估GITR表达(Allred et al., Mod Pathol 1998;11:155-68;Harvey et al., J Clin Oncol 1999;17:1474-91)。这个评分系统涉及将比例和强度分数相加来得到总分。因此,在一些实施方案中,基于GITR阳性肿瘤细胞的估计比例来获得比例分数(0:无;1:<1/100;2:1/100至1/10;3:1/10至1/3;4:1/3至2/3;5:>2/3),并且基于阳性肿瘤细胞中GITR表达的平均强度来获得强度得分(0:无;1:弱,2:中等,3:强)。因此,Allred分数范围是从0到8,3到8范围内的分数视为阳性(即,阳性检测)。因此,在一些实施方案中,GITR染色的Allred评分为3至8的肿瘤,例如,Allred得分为3,4,5,6,7,或8的肿瘤,被认为是GITR阳性肿瘤。

[0119] 在其他实施方案中,评分系统是自动化的,例如计算机化的,并通过图像分析进行定量。自动化方法在本领域中是众所周知的。例如,可以如例如Choudhury et al., J Histochem Cytochem 2010;58:95-107, Rizzardi et al., Diagnostic Pathology 2012;7:42-52中所述计算平均阈值测量(ATM)得分,该得分获得255个染色强度水平的平均值。另一种自动化评分系统是AQUA®(自动化定量分析),其使用例如组织微阵列(TMA)以连续的规模进行。AQUA®是标准的免疫组化与流式细胞术的杂糅,它提供1-255的客观数值分数,涉及抗原修复、第一抗体和第二抗体的使用、以及多重荧光检测。最佳截止点可以按照Camp et al. Clin Cancer Res 2004;10:7252-9所述测定。AQUA®评分系统在Camp et al., Nat Med 2002;8:1323-7;Camp et al., Cancer Res 2003;63:1445-8;Ghosh et al., Hum Pathol 2008;39:1835-43;Bose et al., BMC Cancer 2012;12:332;Mascaux et

al., Clin Cancer Res 2011;17:7796-807中有详细说明。其他合适的自动化免疫组化平台包括市售的平台,例如LeicaBOND RX染色平台。该平台基于下述量表上的染色强度检测肿瘤组织中的GITR表达:最小:每个20x物镜视野<1个细胞;轻微:每个20x物镜视野1~<10个细胞;中等:每个20x物镜视野10~<50个细胞,明显:每个20x物镜视野50~<200个细胞;强烈:每个20x物镜视野>200个细胞。

[0120] 因此,本文提供了用于确定癌症患者的肿瘤是否为GITR阳性和/或包含GITR阳性细胞的方法,包括使来自患者的肿瘤样品与抗体或其抗原结合部分接触,所述抗体或其抗原结合部分包含:包含分别在SEQ ID NO:5-7中示出的氨基酸序列的重链可变区CDR1, CDR2、CDR3,以及包含分别在SEQ ID NO:8-10中示出的氨基酸序列的轻链可变区CDR1, CDR2、CDR3;其中所述抗体或其抗原结合片段特异性结合人GITR。

[0121] 本文还提供了用于确定癌症患者的肿瘤是否为GITR阳性和/或包含GITR阳性细胞的方法,包括:

[0122] (a) 使来自患者的肿瘤样品与抗体或其抗原结合部分接触,所述抗体或其抗原结合部分包含:包含分别在SEQ ID NO:5-7中示出的氨基酸序列的重链可变区CDR1, CDR2、CDR3,以及包含分别在SEQ ID NO:8-10中示出的氨基酸序列的轻链可变区CDR1, CDR2、CDR3;其中所述抗体或其抗原结合片段特异性结合人GITR,和

[0123] (b) 检测所述样品中所述抗体与GITR的结合。

[0124] 本文还提供了用于确定癌症患者的肿瘤是否为GITR阳性和/或包含GITR阳性细胞的方法,其包括:

[0125] (a) 使来自患者的肿瘤样品与抗体或其抗原结合部分接触,所述抗体或其抗原结合部分包含:包含分别在SEQ ID NO:5-7中示出的氨基酸序列的重链可变区CDR1, CDR2、CDR3,以及包含分别在SEQ ID NO:8-10所示的氨基酸序列的轻链可变区CDR1, CDR2、CDR3;其中所述抗体或其抗原结合片段特异性结合人GITR,

[0126] (b) 检测所述样品中所述抗体与GITR的结合,

[0127] (c) 确定所述样品中GITR蛋白质表达水平,其中高于阈值水平(例如使用给定检测方法的检测水平)的GITR蛋白质水平指示该肿瘤是GITR阳性肿瘤。

[0128] 本文还提供了用于鉴定组织(例如肿瘤)样品中的GITR阳性细胞的方法,包括:

[0129] (a) 使来自患者的组织(例如肿瘤)样品与抗体或其抗原结合部分接触,所述抗体或其抗原结合部分包含:包含分别在SEQ ID NO:5-7中示出的氨基酸序列的重链可变区CDR1, CDR2、CDR3,以及包含分别在SEQ ID NO:8-10中示出的氨基酸序列的轻链可变区CDR1, CDR2、CDR3;其中所述抗体或其抗原结合片段特异性结合人GITR;和

[0130] (b) 检测抗体与组织(例如肿瘤)样品的特定或单个细胞上GITR的结合;并且任选地

[0131] (c) 染色组织(例如肿瘤)样品,例如用给定细胞类型的标志物(例如CD3, CD4, CD8, CD25或FoxP3标志物)和/或用苏木精和伊红染色,以鉴定在步骤(b)中鉴定为GITR阳性的细胞。

[0132] 步骤(c)允许将GITR阳性细胞鉴定为,例如,T细胞,如Treg细胞或肿瘤细胞。因此,本文提供了以下方法:

[0133] 用于在组织(例如肿瘤)样品中检测表达GITR的T细胞的存在和/或鉴定表达GITR

的T细胞的数目,和/或组织(例如肿瘤)样品的T细胞上的GITR的水平的方法,包括:

[0134] (a) 使组织(例如肿瘤)样品,例如来自受试者的组织(例如肿瘤)样品,与抗体或其抗原结合部分接触,所述抗体或其抗原结合部分包含:包含分别在SEQ ID NO:5-7中示出的氨基酸序列的重链可变区CDR1,CDR2、CDR3,以及包含分别在SEQ ID NO:8-10中示出的氨基酸序列的轻链可变区CDR1,CDR2、CDR3;其中所述抗体或其抗原结合片段特异性结合人GITR;和

[0135] (b) 检测所述抗体与所述组织(例如肿瘤)样品的T细胞上的GITR的结合;并且任选地

[0136] (c) 染色组织(例如肿瘤)样品,例如用给定细胞类型的标志物(例如CD3、CD4、CD8、CD25或FoxP3标志物)和/或用苏木精和伊红染色,以鉴定在步骤(b)中鉴定为GITR阳性的细胞。

[0137] 一种用于在组织(例如,肿瘤)样品中检测表达GITR的Treg细胞的存在和/或鉴定表达GITR的Treg细胞的数目,和/或组织(例如,肿瘤)样品的Treg细胞上GITR水平的方法,包括:

[0138] (a) 使组织(例如肿瘤)样品,例如来自受试者的组织(例如肿瘤)样品,与抗体或其抗原结合部分接触,所述抗体或其抗原结合部分包含:包含分别在SEQ ID NO:5-7中示出的氨基酸序列的重链可变区CDR1,CDR2、CDR3,以及包含分别在SEQ ID NO:8-10中示出的氨基酸序列的轻链可变区CDR1,CDR2、CDR3;其中所述抗体或其抗原结合片段特异性结合人GITR;和

[0139] (b) 检测所述抗体与所述组织(例如肿瘤)样品的Treg细胞上的GITR的结合;并且任选地

[0140] (c) 染色组织(例如肿瘤)样品,例如用Treg细胞的标志物(例如FoxP3标志物)和/或用苏木精和伊红染色,以鉴定在步骤(b)中鉴定为GITR阳性的Treg细胞。

[0141] 一种用于在组织(例如,肿瘤)样品中检测表达GITR的Teff细胞的存在和/或鉴定表达GITR的Teff细胞的数目,和/或组织(例如,肿瘤)样品的Teff细胞上GITR水平的方法,包括:

[0142] (a) 使组织(例如肿瘤)样品,例如来自受试者的组织(例如肿瘤)样品,与抗体或其抗原结合部分接触,所述抗体或其抗原结合部分包含:包含分别在SEQ ID NO:5-7所示的氨基酸序列的重链可变区CDR1,CDR2、CDR3,以及包含分别在SEQ ID NO:8-10中示出的氨基酸序列的轻链可变区CDR1,CDR2、CDR3;其中所述抗体或其抗原结合片段特异性结合人GITR;和

[0143] (b) 检测所述抗体与所述组织(例如肿瘤)样品的Teff细胞上的GITR的结合;并且任选地

[0144] (c) 染色组织(例如肿瘤)样品,例如用Teff细胞的标志物(例如FoxP3标志物)和/或用苏木精和伊红染色,以鉴定在步骤(b)中鉴定为GITR阳性的Teff细胞。

[0145] 一种用于在组织(例如,肿瘤)样品中检测表达GITR的Treg细胞和Teff细胞的存在和/或鉴定表达GITR的Treg细胞和Teff细胞的数目,和/或组织(例如,肿瘤)样品的Treg细胞和Teff细胞上GITR水平的方法,包括:

[0146] (a) 使组织(例如肿瘤)样品,例如来自受试者的组织(例如肿瘤)样品,与抗体或其

抗原结合部分接触,所述抗体或其抗原结合部分包含:包含分别在SEQ ID NO:5-7中示出的氨基酸序列的重链可变区CDR1,CDR2、CDR3,以及包含分别在SEQ ID NO:8-10中示出的氨基酸序列的轻链可变区CDR1,CDR2、CDR3;其中所述抗体或其抗原结合片段特异性结合人GITR;和

[0147] (b) 检测所述抗体与所述组织(例如肿瘤)样品的Treg细胞和Teff细胞上的GITR的结合;并且任选地

[0148] (c) 染色组织(例如肿瘤)样品,例如用Treg细胞和Teff细胞的标志物(例如CD3、CD4、CD8、CD25和/或FoxP3标志物)和/或用苏木精和伊红染色,以鉴定在步骤(b)中鉴定为GITR阳性的Treg细胞和Teff细胞。

[0149] 一种用于在肿瘤样品中检测表达GITR的肿瘤细胞的存在和/或鉴定表达GITR的肿瘤细胞的数目,和/或肿瘤样品的肿瘤细胞上GITR水平的方法,包括:

[0150] (a) 使肿瘤样品,例如来自受试者的肿瘤样品,与抗体或其抗原结合部分接触,所述抗体或其抗原结合部分包含:包含分别在SEQ ID NO:5-7所示的氨基酸序列的重链可变区CDR1,CDR2、CDR3,以及包含分别在SEQ ID NO:8-10中示出的氨基酸序列的轻链可变区CDR1,CDR2、CDR3;其中所述抗体或其抗原结合片段特异性结合人GITR;和

[0151] (b) 检测所述抗体与所述肿瘤样品的肿瘤细胞上的GITR的结合;并且任选地

[0152] (c) 染色肿瘤样品,例如用肿瘤细胞或其他细胞类型的标志物和/或用苏木精和伊红染色,以鉴定在步骤(b)中鉴定为GITR阳性的肿瘤细胞。

[0153] 一种用于在组织(例如,肿瘤)样品中检测表达GITR的肿瘤细胞与Treg细胞的存在和/或鉴定表达GITR的肿瘤细胞与Treg细胞的数目,和/或组织(例如,肿瘤)样品的肿瘤细胞与Treg细胞上的GITR的水平的方法,包括:

[0154] (a) 使组织(例如肿瘤)样品,例如来自受试者的组织(例如肿瘤)样品,与抗体或其抗原结合部分接触,所述抗体或其抗原结合部分包含:包含分别在SEQ ID NO:5-7中示出的氨基酸序列的重链可变区CDR1,CDR2、CDR3,以及包含分别在SEQ ID NO:8-10中示出的氨基酸序列的轻链可变区CDR1,CDR2、CDR3;其中所述抗体或其抗原结合片段特异性结合人GITR;和

[0155] (b) 检测所述抗体与所述组织(例如肿瘤)样品的肿瘤细胞与Treg细胞上的GITR的结合;并且任选地

[0156] (c) 染色组织(例如肿瘤)样品,例如用肿瘤细胞和Treg细胞的标志物(例如FoxP3标志物)和/或用苏木精和伊红染色,以鉴定在步骤(b)中鉴定为GITR阳性的肿瘤细胞和Treg细胞。

[0157] 一种用于在组织(例如,肿瘤)样品中检测表达GITR的肿瘤细胞、Treg细胞和Teff细胞的存在和/或鉴定表达GITR的肿瘤细胞、Treg细胞和Teff细胞的数目,和/或组织(例如,肿瘤)样品的肿瘤细胞、Treg细胞和Teff细胞上GITR水平的方法,包括:

[0158] (a) 使组织(例如肿瘤)样品,例如来自受试者的组织(例如肿瘤)样品,与抗体或其抗原结合部分接触,所述抗体或其抗原结合部分包含:包含分别在SEQ ID NO:5-7中示出的氨基酸序列的重链可变区CDR1,CDR2、CDR3,以及包含分别在SEQ ID NO:8-10中示出的氨基酸序列的轻链可变区CDR1,CDR2、CDR3;其中所述抗体或其抗原结合片段特异性结合人GITR;和

[0159] (b) 检测所述抗体与所述组织(例如肿瘤)样品的肿瘤细胞、Treg细胞和Teff细胞上的GITR的结合;并且任选地

[0160] (c) 染色组织(例如肿瘤)样品,例如用肿瘤细胞、Treg细胞和/或Teff细胞的标志物(例如CD3、CD4、CD8、CD25和/或FoxP3标志物)和/或用苏木精和伊红染色,以鉴定在步骤(b)中鉴定为GITR阳性的肿瘤细胞、Treg细胞和Teff细胞。

[0161] 示例性的肿瘤标志物包括、例如、ErbB受体、Melan A[MART1]、gp100、酪氨酸酶、TRP-1/gp 75、TRP-2、MAGE-1、MAGE-3、HPV E6和E7蛋白、粘蛋白[MUC-1]、前列腺特异性抗原[PSA]、癌胚抗原[CEA]、PIA肿瘤抗原、MAGE-2、MAGE-4、MAGE-6、MAGE-10、MAGE-12、BAGE-1、CAGE-1,2,8、CAGE-3至7、LAGE-1、NY-ESO-1/LAGE-2、NA-88、GnTV和TRP2-INT2。

[0162] T reg细胞表面标志物包括CD4、CD25和FOXP3。

[0163] 在某些实施方案中,使用检测方法的组合来增加将肿瘤指定为GITR阳性或GITR阴性的准确性。例如,在一个实施方案中,使用免疫组化和荧光原位杂交(FISH)的组合来将肿瘤分型为GITR阳性或阴性。这种方法已经被用来例如优化Her-2/neu测试。参见例如Ridolfi et al., Mod Pathol 2000;13:866-73。

[0164] 本文所述的任何基于抗体的检测方法可以组合使用,或者与基于RNA的检测方法,例如RNAscope和定量PCR结合使用。

[0165] 上述检测方法通常结合参照或对照样品进行。在一些实施方案中,对照样品是匹配的正常组织的切片(section)。在一些实施方案中,对照或参照样品源自未患有表达GITR的肿瘤或癌症的受试者(例如,健康受试者)。这样的样品可以提供生物样品中表达GITR的细胞的量的标准化参考。

[0166] 示例性的预后方法

[0167] 本文提供用于鉴定可能对抗GITR免疫疗法有响应的癌症患者、或预测癌症患者是否将对抗GITR免疫疗法有响应的方法,其包括:

[0168] (a) 使来自患者的肿瘤样品与抗GITR抗体或其抗原结合部分接触,

[0169] (b) 检测该抗体与该肿瘤样品中GITR的结合,

[0170] (c) 确定该样品中GITR蛋白质表达的水平,其中高于阈值水平的GITR蛋白质水平表明该肿瘤是GITR阳性肿瘤,并且该患者可能或预测对抗GITR免疫疗法有响应。在某些实施方案中,检测或监测特定免疫细胞(例如肿瘤浸润淋巴细胞(TIL),例如T细胞,如Treg细胞)上,例如肿瘤中的特定免疫细胞上的GITR表达水平,并且例如确定受试者对抗GITR疗法有响应的可能性。在某些实施方案中,检测或监测肿瘤细胞上GITR的表达水平,并且例如确定受试者对抗GITR疗法响应的可能性。

[0171] 在某些实施方案中,抗GITR抗体是这样的抗体,其包含:分别在SEQ ID NO:5-7和8-10中示出的重链和轻链可变区CDR序列;分别在SEQ ID NO:11和12中示出的重链和轻链可变区序列;或分别在SEQ ID NO:13和14中示出的抗体6G10(一种全人抗GITR抗体)的全长重链和轻链序列,其中所述抗体或其抗原结合片段特异性地结合人GITR。在某些实施方案中,所述重链缺少C端赖氨酸。在一些实施方案中,所述抗GITR抗体是嵌合抗体,其包含抗体6G10的可变区,但包含非人恒定区(例如小鼠恒定区),例如包含分别在SEQ ID NO:15和16中示出的重链和轻链序列的嵌合6G10抗体。在某些实施方案中,嵌合抗体的重链缺少C端赖氨酸。在某些实施方案中,通过免疫组化检测GITR表达,如上所述。在一个实施方案中,将免疫

组化与其他检测方法例如FISH组合。

[0172] 在某些实施方案中,将肿瘤样品制备成FFPE切片。在其他实施方案中,将肿瘤样品制备成冷冻组织切片。

[0173] 在一些实施方案中,如果肿瘤或其中的免疫细胞(例如肿瘤浸润淋巴细胞(TIL),例如Treg细胞)的样品与来自同一癌症患者的匹配的正常组织或免疫细胞(例如T reg细胞)相比具有更多的GITR阳性细胞,则认为该肿瘤是GITR阳性的,并且可能受益于抗GITR免疫疗法。

[0174] 在某些实施方案中,如果肿瘤样品中GITR阳性细胞(例如免疫细胞,例如肿瘤浸润淋巴细胞(TIL),如T reg细胞)和/或肿瘤细胞的数目超过阈值水平,则该患者可能受益于或者预计可受益于抗GITR免疫疗法。阈值水平可以用给定检测系统(例如免疫组化,如本文进一步描述的,例如见实施例)测得的最低的GITR的水平。在某些实施方案中,如果在使用前文所述的本领域公知的评分系统的条件下,肿瘤样品中GITR阳性细胞(例如免疫细胞,例如肿瘤浸润淋巴细胞(TIL),如T reg细胞)和/或肿瘤细胞的数目超过阈值数目或比例,则该患者可能受益于或者预测可受益于抗GITR免疫疗法。因此,在一些实施方案中,在使用前文所述的本领域公知的评分系统的条件下,GITR阳性细胞的数目或比例超过某个阈值数目或比例,并被定义为“GITR阳性”。

[0175] 在某些实施方案中,如果肿瘤样品的肿瘤的细胞(例如肿瘤细胞和/或免疫细胞(例如肿瘤浸润淋巴细胞(TIL),如T reg细胞)有至少1%,例如至少5%,至少10%,至少15%,至少20%,至少25%,至少30%,至少35%,至少40%,至少45%,至少50%,至少55%,至少60%,至少65%,至少70%,至少75%,至少80%,至少90%,或至少95%表达GITR蛋白,则该样品指定为“GITR阳性”,并表明癌症患者对抗GITR免疫疗法可能有响应或预测有响应。

[0176] 在一些实施方案中,计算肿瘤样品的H分数。因此,在某些实施方案中,H评分为至少5,如至少10,至少15,至少20,至少25,至少30,至少40,至少50,至少60,至少70,至少80,至少90,至少100,至少125,至少150,至少175,至少200,至少225,至少250,至少275或至少290的肿瘤样品被指定为“GITR阳性”,并且表明癌症患者可能或预测对抗GITR免疫疗法有响应。分数可基于肿瘤中的全部细胞或特定类型的细胞(例如免疫细胞,例如肿瘤浸润淋巴细胞(TIL),如Treg细胞和/或肿瘤细胞)来计算。

[0177] 在一些实施方案中,计算肿瘤样品的Allred分数。因此,在某些实施方案中,Allred评分为至少3,例如至少4,至少5,至少6,至少7或8的肿瘤样品被指定为“GITR阳性”并且指示癌症患者可能或预测对抗GITR免疫疗法有响应。分数可基于肿瘤中的全部细胞或特定类型的细胞(例如免疫细胞,例如肿瘤浸润淋巴细胞(TIL),如Treg细胞和/或肿瘤细胞)来计算。

[0178] 在一些实施方案中,计算AQUA分数。因此,在某些实施方案中,AQUA评分为至少5,例如至少10,至少15,至少20,至少25,至少30,至少40,至少50,至少70,至少80,至少90,至少100,至少125,至少150,至少175,至少200,至少225或至少250的肿瘤样品被指定为“GITR-阳性”并且表明癌症患者可能或预测对抗GITR免疫疗法有响应。评分可基于肿瘤中的全部细胞或特定类型的细胞(例如免疫细胞,例如肿瘤浸润淋巴细胞(TIL),如Treg细胞和/或肿瘤细胞)来计算。

[0179] 在某些实施方案中,使用上述评分系统之一与另一检测模态(例如FISH)的组合来增加确定肿瘤是GTR阳性还是GTR阴性的准确性。

[0180] 在某些实施方案中,患者具有选自下组的癌症:鳞状细胞癌、小细胞肺癌、非小细胞肺癌、鳞状非小细胞肺癌(NSCLC)、非鳞状NSCLC、神经胶质瘤、胃肠癌、肾癌(例如透明细胞癌)、卵巢癌、肝癌、结肠直肠癌、子宫内膜癌、肾癌(例如,肾细胞癌(RCC))、前列腺癌(例如激素难治性前列腺腺癌)、甲状腺癌、神经胚细胞瘤、胰腺癌、神经胶母细胞瘤(多形性神经胶母细胞瘤)、子宫颈癌、胃癌、膀胱癌、肝细胞瘤、乳癌、结肠癌及头颈癌(或癌瘤)、胃癌、生殖细胞肿瘤、儿科肉瘤、鼻窦天然杀伤、黑色素瘤(例如,转移性恶性黑色素瘤,例如皮肤或眼内恶性黑色素瘤)、骨癌、皮肤癌、子宫癌、肛区癌、睾丸癌、输卵管癌、子宫内膜癌、子宫颈癌、阴道癌、外阴癌、食道癌、小肠癌、内分泌系统癌、甲状旁腺癌、肾上腺癌、软组织肉瘤、尿道癌、阴茎癌、儿童期实体肿瘤、输尿管癌、肾盂癌、中枢神经系统的新生物(CNS)、原发性CNS淋巴瘤、肿瘤血管生成、脊轴肿瘤、脑癌、脑干胶质瘤、垂体腺瘤、卡波西氏肉瘤(Kaposi's sarcoma)、表皮样癌、鳞状细胞癌、T细胞淋巴瘤、环境诱导的癌症(包括那些由石棉诱导者)、病毒相关癌症或病毒起源的癌症(例如,人乳头瘤病毒(HPV)相关或起源的肿瘤)、及源自两种主要血细胞谱系(即骨髓细胞系(其产生粒细胞、红细胞、血栓细胞、巨噬细胞及肥大细胞)或淋巴细胞系(其产生B、T、NK及浆细胞))中的任一者的血液学恶性病,例如所有类型的白血病、淋巴瘤及骨髓瘤,例如急性、慢性、淋巴细胞性及/或骨髓性白血病,例如急性白血病(ALL)、急性骨髓性白血病(AML)、慢性淋巴细胞性白血病(CLL)及慢性骨髓性白血病(CML)、未分化的AML(M0)、骨髓母细胞性白血病(M1)、骨髓母细胞性白血病(M2;细胞成熟)、前髓球性白血病(M3或M3变体[M3V])、骨髓单核细胞性白血病(具有嗜酸性粒细胞增多症的M4或M4变体[M4E])、单核细胞性白血病(M5)、红白血病(M6)、巨核母细胞性白血病(M7)、分离的粒细胞性肉瘤及绿色瘤;淋巴瘤,例如霍奇金氏淋巴瘤(Hodgkin's lymphoma)(HL)、非霍奇金氏淋巴瘤(NHL)、B细胞血液学恶性病(例如B细胞淋巴瘤)、T细胞淋巴瘤、淋巴浆细胞样淋巴瘤、单核细胞样B细胞淋巴瘤、粘膜相关的淋巴组织(MALT)淋巴瘤、退行性(例如, Ki 1+)大细胞淋巴瘤、成人T细胞淋巴瘤/白血病、套细胞淋巴瘤、血管免疫母细胞T细胞淋巴瘤、血管中心淋巴瘤、肠T细胞淋巴瘤、原发性纵膈B细胞淋巴瘤、前体T-淋巴母细胞性淋巴瘤、T-淋巴母细胞性;及淋巴瘤/白血病(T-Lbly/T-ALL)、外周T细胞淋巴瘤、淋巴母细胞性淋巴瘤、移植后淋巴增殖病症、真实组织细胞性淋巴瘤、原发性中枢神经系统淋巴瘤、原发性积液淋巴瘤、B细胞淋巴瘤、淋巴母细胞性淋巴瘤(LBL)、淋巴谱系的造血性肿瘤、急性淋巴母细胞性白血病、弥漫性大B细胞淋巴瘤、伯基特氏淋巴瘤、滤泡性淋巴瘤、弥漫性组织细胞性淋巴瘤(DHL)、免疫母细胞大细胞淋巴瘤、前体B-淋巴母细胞性淋巴瘤、皮肤T细胞淋巴瘤(CTLC)(亦称作蕈样真菌病或塞扎里综合征(Sezary syndrome))及具有瓦尔登斯特伦氏巨球蛋白血症(Waldenstrom's macroglobulinemia)的淋巴浆细胞样淋巴瘤(LPL);骨髓瘤,例如IgG骨髓瘤、轻链骨髓瘤、非分泌骨髓瘤、浆细胞瘤(亦称作无瘤骨髓瘤)、孤立性浆细胞瘤及多发性骨髓瘤、慢性淋巴细胞性白血病(CLL)、毛细胞淋巴瘤;类骨髓谱系的造血性肿瘤、间质起源的肿瘤(包括纤维肉瘤及横纹肌肉瘤);精细胞瘤、畸胎瘤、中枢及周围神经肿瘤,包括星细胞瘤、神经鞘瘤;间质起源的肿瘤,包括纤维肉瘤、横纹肌肉瘤及骨肉瘤;及其他肿瘤,包括黑色素瘤、着色性干皮病、角质棘皮瘤、精细胞瘤、甲状腺滤泡性癌及畸胎瘤、淋巴谱系的造血性肿瘤,例如T细胞及B细胞肿瘤,包括但不限于T细胞病症,例如T

前淋巴细胞性白血病 (T-PLL), 包括小细胞及脑回状细胞类型; 优选T细胞类型的大的颗粒性淋巴细胞白血病 (LGL); a/d T-NHL肝脾淋巴瘤; 外周/胸腺后T细胞淋巴瘤 (多型及免疫母细胞亚型); 血管中心 (鼻) T细胞淋巴瘤; 头或颈癌、肾癌、直肠癌、甲状腺癌; 急性类骨髓性淋巴瘤以及这些癌症的任何组合。在某些实施方案中, 癌症是转移性癌症、难治性癌症、或复发性癌症。

[0181] 一旦癌症患者已被鉴定为可能从抗GITR免疫治疗获益 (即, 具有GITR阳性肿瘤), 就可以用治疗性抗GITR抗体治疗患者 (即, 抗GITR免疫疗法)。

[0182] 因此, 本文提供使用本文中提供的抗GITR抗体和方法治疗具有GITR阳性肿瘤 (如通过GITR蛋白表达水平确定的) 的癌症患者的方法, 包括向患者施用治疗有效量的抗GITR抗体或其抗原结合部分。

[0183] 在一些实施方案中, 用来确定GITR蛋白表达水平的抗GITR抗体是这样的抗体, 其包含: 分别在SEQ ID NO:5-7和8-10中示出的重链和轻链可变区CDR序列; 分别在SEQ ID NO:11和12中示出的重链和轻链可变区序列; 或者分别在SEQ ID NO:13和14中示出的抗体6G10 (一种全人抗GITR抗体) 的全长重链和轻链序列, 其中所述抗体或其抗原结合片段特异性结合人GITR。在某些实施方案中, 重链缺少C端赖氨酸。在一些实施方案中, 抗体是嵌合抗体, 包含抗体6G10的可变区, 但包含非人恒定区 (例如, 小鼠恒定区), 例如, 分别包含如SEQ ID NO:15和16中示出的重链和轻链序列的嵌合6G10抗体。在某些实施方案中, 嵌合抗体的重链缺少C端赖氨酸。在某些实施方案中, GITR表达是通过免疫组化检测的, 如上所述。

[0184] 在某些实施方案中, 对于使用本文所述的方法确定为具有GITR阳性肿瘤 (即, GITR阳性肿瘤细胞和/或免疫细胞, 例如肿瘤浸润淋巴细胞 (TIL), 如Treg细胞) 的癌症患者用任何调变GITR信号传导的作用剂 (例如激动性抗GITR抗体) 治疗, 并导致例如T细胞活化的诱导和/或增强 (例如T细胞IL-2和/或IFN- γ 产生的增加, 和/或T细胞增殖的增加), 调节性T细胞的消耗等。因此, 本文提供了治疗癌症患者的方法, 其包括:

[0185] (a) 使用本文所述的方法确定癌症患者的肿瘤 (肿瘤细胞和/或免疫细胞, 例如肿瘤浸润淋巴细胞 (TIL), 例如Treg细胞) 是否为GITR阳性, 例如使来自患者的肿瘤样品与抗体或其抗原结合部分接触, 所述抗体或其抗原结合部分包含: 分别包含SEQ ID NO:5-7中示出的氨基酸序列的重链可变区CDR1、CDR2、CDR3, 以及分别包含SEQ ID NO:8-10所示的氨基酸序列的轻链可变区CDR1、CDR2、CDR3, 其中所述抗体或其抗原结合片段特异性结合人GITR, 检测所述抗体与样品中GITR的结合, 以及测定样品中GITR蛋白质表达的水平, 其中, 高于肿瘤细胞和/或其中的免疫细胞 (例如肿瘤浸润淋巴细胞 (TIL), 如Treg细胞) 中的阈值水平的GITR蛋白质水平指示肿瘤为GITR阳性, 和

[0186] (b) 如果肿瘤被确定为GITR阳性, 则施用治疗有效量的调变GITR信号传导的作用剂, 例如增加IL-2、增加T细胞的IFN- γ 产生、和/或增加T细胞的增殖和/或调节性T细胞的消耗的作用剂。

[0187] 例如, 在一个实施方案中, 用治疗有效量的W015187835 (其内容通过引用并入本文) 中公开的激动性抗GITR抗体治疗患者, 例如具有下列抗体的重链及轻链可变区CDR、重链及轻链可变区、或重链及轻链的抗体: 28F3、19D3、18E10、3C3-1、3C3-2、2G6、9G7-1、9G7-2、14E3、19H8-1、19H8-2和/或6G10, 及其变体。表2中提供了PCT专利申请W015187835中公开的抗体的序列 (参见SEQ ID NO:5-14和27-228)。患者也可以用任何其他抗GITR抗体治疗、

例如TRX518 (Leap Therapeutics)、MK-4166 (Merck)、LKZ-145 (Novartis)、GWN-323 (Novartis Pharmaceuticals Corp.)、Medi 1873 (MedImmune)、INBRX-110 (Inhibrx)、GITR-Fc蛋白 (OncoMed), 以及W02006105021、W02009009116、W02011028683、US2014/0072565、US20140072566、US20140065152、W02015031667、W015184099、W02015184099或W02016054638中描述的抗体。

[0188] 监测GITR阳性肿瘤/癌症的示例性方法

[0189] 本文提供了用于监测癌症患者中表达GITR的肿瘤的方法。用于监测的方法可以以与用于确定癌症患者是否可能对上述抗GITR免疫疗法有响应的方法类似的方式进行。

[0190] 可以监测完整组织, 例如肿瘤或其特定细胞中GITR的存在。例如, 可以监测肿瘤细胞和/或肿瘤浸润淋巴细胞(TIL) (例如Treg细胞和Teff细胞) 上GITR的存在。

[0191] 监测GITR存在(或表达) 可以包括在两个或更多个时间点测定GITR存在。例如, 可以从受试者获得第一和第二组织样品(并且确定GITR的存在和/或水平), 其中, 例如, 第一和第二组织样品在彼此3-7天, 1周至3周, 或1个月至3个月以内获得。还可以每周或每月获得组织样本以确定GITR的存在和/或水平。

[0192] 因此, 在某些实施方案中, 用于监测癌症患者中表达GITR的肿瘤的方法包括:

[0193] (a) 在第一时间点使用抗GITR抗体或其抗原结合部分检测组织(例如肿瘤) 样品中的GITR蛋白质表达,

[0194] (b) 确定第一时间点的GITR蛋白表达水平,

[0195] (c) 在第二时间点使用与步骤(a) 中使用的相同的抗体检测组织(例如肿瘤, 其可以是与在第一时间点活检的肿瘤相同的肿瘤) 样品中的GITR蛋白质表达, 和

[0196] (d) 确定来自第二时间点的肿瘤中GITR蛋白质表达的水平。

[0197] 还提供了用于监测癌症患者中表达GITR的肿瘤的方法, 包括:

[0198] (a) 在第一时间点使用抗GITR抗体或其抗原结合部分检测组织(例如肿瘤) 样品中的Treg细胞中的GITR蛋白质表达,

[0199] (b) 确定第一时间点的GITR蛋白表达水平,

[0200] (c) 在第二时间点使用与步骤(a) 中使用的相同的抗体检测组织(例如肿瘤, 其可以是与在第一时间点活检的肿瘤相同的肿瘤) 样品中的Treg细胞中的GITR蛋白质表达,

[0201] (d) 确定来自第二时间点的肿瘤中的Treg细胞中的GITR蛋白质表达的水平。

[0202] 还提供了用于监测癌症患者中表达GITR的肿瘤的方法, 包括:

[0203] (a) 在第一时间点使用抗GITR抗体或其抗原结合部分检测组织(例如肿瘤) 样品中的Teff细胞中的GITR蛋白质表达,

[0204] (b) 确定第一时间点的GITR蛋白表达水平,

[0205] (c) 在第二时间点使用与步骤(a) 中使用的相同的抗体检测组织(例如肿瘤, 其可以是与在第一时间点活检的肿瘤相同的肿瘤) 样品中的Teff细胞中的GITR蛋白质表达,

[0206] (d) 确定来自第二时间点的肿瘤中的Teff细胞中的GITR蛋白质表达的水平。

[0207] 还提供了用于监测癌症患者中表达GITR的肿瘤的方法, 包括:

[0208] (a) 在第一时间点使用抗GITR抗体或其抗原结合部分检测肿瘤样品中的肿瘤细胞中的GITR蛋白质表达,

[0209] (b) 确定第一时间点的GITR蛋白表达水平,

[0210] (c) 在第二时间点使用与步骤(a)中使用的相同的抗体检测肿瘤样品(可以是与在第一时间点活检的肿瘤相同的肿瘤)中的肿瘤细胞中的GITR蛋白质表达,

[0211] (d) 确定来自第二时间点的肿瘤中的肿瘤细胞中的GITR蛋白质表达的水平。

[0212] 在某些方法中,确定Treg细胞和/或Teff细胞和/或肿瘤细胞中GITR的存在和/或水平。

[0213] 因此,在某些实施方案中,用于监测癌症患者中表达GITR的肿瘤的方法包括:

[0214] (a) 在第一时间点使用抗GITR抗体或其抗原结合部分检测GITR阳性肿瘤中的GITR蛋白质表达,

[0215] (b) 确定第一时间点的GITR蛋白表达水平,

[0216] (c) 在第二时间点使用步骤(a)中使用的相同抗体检测肿瘤中的GITR蛋白质表达,

[0217] (d) 确定来自第二时间点的肿瘤中GITR蛋白质表达的水平;和

[0218] (e) 比较在第一和第二时间点测定的GITR蛋白质表达水平。

[0219] GITR表达可以在肿瘤细胞和/或免疫细胞,例如肿瘤浸润淋巴细胞(TIL),例如肿瘤内的Treg细胞和/或Teff细胞中测定。第一时间点相对于第二时间点的水平更高可以指示肿瘤消退,第一时间点相对于第二时间点的得分较低可以指示肿瘤进展,并且在第一时间点的相对不变的水平相对于第二时间点的的时间点可以指示肿瘤稳定。

[0220] 在某些实施方案中,用于确定GITR蛋白表达水平的抗GITR抗体是这样的抗体,其包含:分别在SEQ ID NO:5-7和8-10中示出的重链和轻链可变区CDR序列;分别在SEQ ID NO:11和12中示出的重链和轻链可变区序列;或者分别在SEQ ID NO:13和14中示出的抗体6G10(一种全人抗GITR抗体)的全长重链和轻链序列,其中所述抗体或其抗原结合片段特异性结合人GITR。在某些实施方案中,重链缺少C端赖氨酸。在一些实施方案中,抗体是嵌合抗体,其包含抗体6G10的可变区,但包含非人恒定区(例如小鼠恒定区),例如包含分别在SEQ ID NO:15和16中示出的重链和轻链序列的嵌合6G10抗体。在某些实施方案中,嵌合抗体的重链缺少C端赖氨酸。在一个优选的实施方案中,如本文所述通过免疫组化进行GITR表达的检测。在一些实施方案中,如本文所述使用选自下组的评分系统来确定GITR蛋白质表达水平:H评分系统,Allred评分系统,AQUA®系统,或自动化评分系统。

[0221] 此类监测方法也可用于确定抗GITR免疫疗法是否可能有效。

[0222] 因此,本文提供了用于监测具有GITR阳性肿瘤的患者中的抗GITR免疫疗法的功效的方法,包括:

[0223] (a) 在启动抗GITR免疫疗法之后的第一时间点使用抗GITR抗体检测GITR阳性肿瘤中的GITR蛋白质表达,

[0224] (b) 确定来自第一时间点的肿瘤中的GITR蛋白表达水平,

[0225] (c) 在启动抗GITR免疫疗法之后的第二时间点使用步骤(a)中使用的相同抗体检测GITR阳性肿瘤中的GITR蛋白质表达,

[0226] (d) 确定来自第二时间点的肿瘤中GITR蛋白质表达的水平;和

[0227] (e) 比较在第一和第二时间点测定的GITR蛋白质表达水平,其中第一时间点相对于第二时间点的水平较高可指示抗GITR免疫疗法有效,第一时间点相对于第二时间点的分数较低指示抗GITR免疫疗法无效,并且第一时间点相对于第二时间点的分数未改变可指示抗GITR免疫疗法在起稳定化作用。GITR表达可以在肿瘤内的肿瘤细胞和/或免疫细胞(例如

肿瘤浸润淋巴细胞(TIL),如T reg细胞)中测定。

[0228] 在某些实施方案中,用于确定GITR蛋白表达水平的抗GITR抗体是这样的抗体,其包含:分别在SEQ ID NO:5-7和8-10中示出的重链和轻链可变区CDR序列;分别在SEQ ID NO:11和12中示出的重链和轻链可变区序列;或者分别在SEQ ID NO:13和14中示出的抗体6G10(一种全人抗GITR抗体)的全长重链和轻链序列,其中所述抗体或其抗原结合片段特异性结合人GITR。在某些实施方案中,重链缺少C端赖氨酸。在一些实施方案中,抗体是嵌合抗体,其包含抗体6G10的可变区,但包含非人恒定区(例如小鼠恒定区),例如包含分别在SEQ ID NO:15和16中示出的重链和轻链序列的嵌合6G10抗体。在某些实施方案中,嵌合抗体的重链缺少C端赖氨酸。在一个优选的实施方案中,如本文所述,通过免疫组织化学进行GITR表达的检测。在一些实施方案中,如本文所述,使用选自下组的评分系统来确定GITR蛋白质表达水平:H评分系统,Allred评分系统,AQUA®系统或自动化评分系统。

[0229] 在某些实施方案中,抗GITR免疫疗法包括向癌症患者施用治疗有效量的W015187835(其内容通过引用并入本文)中公开的抗GITR抗体,例如具有下述抗体的重链和轻链可变区CDR、重链和轻链可变区、或重链和轻链的抗体:28F3、19D3、18E10、3C3-1、3C3-2、2G6、9G7-1、9G7-2、14E3、19H8-1、19H8-2、和/或6G10,及其变体。表2中提供了PCT专利申请W015187835中公开的抗体序列(参见SEQ ID NO:5-14和27-228)。也可以用任何其它抗GITR抗体治疗患者,例如TRX518(Leap Therapeutics),MK-4166(Merck),LKZ-145(Novartis),GWN-323(Novartis Pharmaceuticals Corp.),Medi 1873(MedImmune),INBRX-110(Inhibrx),GITR-Fc蛋白(OncoMed)和W02006105021,W02009009116,W02011028683,US2014/0072565,US20140072566,US20140065152,W02015031667,W015184099,W02015184099或W02016054638中描述的抗体。

[0230] 在某些实施方案中,可以在初次诊断后(即,在确定肿瘤是GITR阳性后),例如初次诊断后1个月,初次诊断后2个月,初次诊断后3个月,初次诊断后4个月,初次诊断后5个月,初次诊断后6个月,初次诊断后1年等,重复地监测表达GITR的肿瘤的状态。在其他实施方案中,可以在启动抗GITR免疫治疗后,如启动治疗一个月后,启动治疗后两个月后,启动治疗后三个月后,启动治疗四个月后,启动治疗五个月后,启动治疗六个月后,启动治疗一年后等,重复地监测针对表达GITR的肿瘤的抗GITR免疫疗法的功效。

[0231] 诊断试剂盒

[0232] 本文提供了试剂盒,其包括本文所述的诊断性抗GITR抗体以及使用说明。相应地,在一些实施方案中,试剂盒包括这样的抗体,其包含:分别在SEQ ID NO:5-7和8-10中示出的重链和轻链可变区CDR序列,分别在SEQ ID NO:11和12中示出的重链和轻链可变区序列,其中所述抗体或其抗原结合片段特异性结合人GITR;或者分别在SEQ ID NO:13和14中示出的抗体6G10的全长重链和轻链序列。在某些实施方案中,重链缺少C端赖氨酸。在一些实施方案中,抗体是嵌合抗体,其包含抗体6G10的可变区,但包含非人恒定区(例如小鼠恒定区),例如包含分别在SEQ ID NO:15和16中示出的重链和轻链序列的嵌合6G10抗体。在某些实施方案中,嵌合抗体的重链缺少C端赖氨酸。在某些实施方案中,抗体包含可检测标记,例如抗体-标志物缀合物。这样的试剂盒可以包含至少一种另外的试剂。例如、在某些实施方案中、试剂盒包含缓冲液、稳定剂、底物、免疫检测试剂(例如用于免疫组织化学的第二抗体)和/或测定所需的辅因子。在某些实施方案中,抗体,任选地还有试剂,被适当地分成等

份。在某些实施方案中,试剂盒包含用于从癌症患者获得生物样品的手段。这样的手段可以包括,例如,可以用于从癌症患者获得流体或组织样品的试剂。

[0233] 通过以下实施例进一步说明本公开内容,这些实施例不应被解释为进一步的限制。将本申请通篇引用的所有附图和所有参考文献,Genbank序列,专利和公开的专利申请的内容明确地通过引用并入本文。具体而言,将W015187835的公开内容明确地通过引用并入本文。

实施例

[0234] 实施例1:6G10抗体的生成

[0235] 人抗GITR抗体6G10是在免疫HuMAb转基因小鼠(“HuMAb”是Medarex, Inc., Princeton, New Jersey的商标)及KM小鼠(KMMouse®品系含有SC20转染色体,如PCT公开W0 02/43478中所述)并筛选与GITR结合的抗体的融合物的过程中生成的(参见同时提交的PCT申请PCT/US15/33991)。cDNA测序鉴定了6G10抗体的一条重链和一条轻链。图1-4和表2列出了6G10抗体的可变区氨基酸序列和同种型。

[0236] 实施例2:6G10抗体的结合特性

[0237] 通过Biacore测定6G10抗体与可溶性GITR的结合。将6G10抗体捕获在人κ包被的芯片(~5KRU; Southernbiotech)上,让重组人GITR(rHGITR/Fc:R&D Systems)以500nM、250nM、125nM、62nM和31nM的浓度流过芯片。抗体/体积的捕获浓度为2-40μg/mL(5μL, 10μL/min)。抗原缔合时间在15μL/min下为5分钟,抗原解离时间为6分钟,用50mM HCl/50mM NaOH(各12μL, 100μL/分钟)进行再生。6G10显示与可溶性人GITR结合的 K_D 为 $1.87 \times 10^{-9}M$,其中 k_a 为 $3.83 \times 10^5 M^{-1} s^{-1}$, k_d 为 $7.15 \times 10^{-4} s^{-1}$ 。

[0238] 实施例3:用嵌合6G10抗体对癌组织进行免疫组化

[0239] 用两种免疫组化(IHC)技术检测组织切片中的GITR:一种IHC方法在福尔马林固定石蜡包埋(FFPE)组织切片上进行,另一种在冷冻组织切片上进行。

[0240] 在这些IHC方法中已经测试过几种抗GITR抗体,6G10一直是较好的。

[0241] 为了检测人组织中的GITR表达,制备了6G10抗体的一种荧光标记形式,命名为6G10-FITC。为了进一步开发用户和临床友好的方法,将6G10抗体改造成小鼠嵌合IgG2a形式,并优化以便使用Leica BondRX平台进行自动化免疫组化。嵌合6G10抗体的重链和轻链序列分别在图5和6中以及表2中示出。重链可以含有或不含有C端赖氨酸。

[0242] 简而言之,将载玻片按照常规组织学程序脱蜡和复水,然后手工实施HIER(热诱导的抗原修复):使用Decloaking Chamber(BioCare Medical), 110°C, pH6靶修复缓冲液(Dako), 历时10分钟。然后将载玻片加载到Leica BondRX自动免疫组化染色器上。将组织切片与0.5μg/ml的嵌合6G10抗体温育60分钟,然后用Leica Bond Polymer Refine Detection System(DS9800)按照制造商的说明进行检测。简言之,将组织切片与兔抗小鼠接头(Leica)温育30分钟,并与Novolink Max Polymer(Leica)温育30分钟。最后,将载玻片与DAB底物-发色团溶液反应6分钟。然后按照常规组织学程序将载玻片用Mayer苏木精复染,脱水,透明,并用Permount盖玻片封片。使用补充有0.5%Hu-γ-球蛋白(Sigma)的Dako蛋白质封闭剂来封闭非特异性结合,并且使用补充有0.5%人γ-球蛋白和0.5%BSA的PBS作为第一和第二抗体的稀释剂。

[0243] 为了剖析肿瘤浸润淋巴细胞 (TILs), 使用针对CD3 (T细胞标志物) 和FoxP3 (调节性T细胞标志物) 的市售单克隆抗体来染色相邻的切片。使用自制的改造小鼠嵌合人抗KLH IgG2a和市售的小鼠IgG1作为阴性对照抗体。使用稳定表达人GITR的HEK-293T细胞和增生的人扁桃体组织切片作为阳性对照。5种肿瘤类型的FFPE组织样品购自组织供应商, 每种肿瘤类型有13~26个病例。

[0244] 免疫染色后, 在光学显微镜下检查载玻片。对于GITR和TIL的评分, 使用Aperio® ScanScope和HALO™图像分析软件对整个载玻片进行自动定量分析。使用Aperio ScanScope或Olympus DP71数字显微镜相机拍摄代表性图像。

[0245] 表1总结了宫颈癌(CC)、黑色素瘤(Mel)、肝细胞癌(HCC)、结直肠癌(CRC)和头颈部鳞状细胞癌(HNSCC)中GITR阳性TIL的分布。通过在显微镜的20倍物镜下估计阳性细胞数来手动评分13至26例。最小: 每个20x的物镜视野<1个细胞; 轻微: 每个20x的物镜视野1~10个细胞; 中等: 每个20x的物镜视野10~50个细胞; 明显: 每个20x的物镜视野50~200个细胞; 强烈: 每个20x的物镜视野>200个细胞。整个肿瘤切片的1/3以上符合上述标准。

[0246] 表1

	染色强度	宫颈癌 (n=24)	黑色素瘤 (n=17)	肝细胞癌 (n=25)	结直肠癌 (n=26)	头颈部鳞状细胞癌 (n=13)
[0247]	最小	0%	6%	8%	12%	15%
	轻微	0%	24%	16%	15%	23%
	中等	58%	29%	36%	46%	38%
	明显	33%	29%	40%	27%	24%
	强烈	8%	12%	0%	0%	0%

[0248] 在增生的扁桃体中, 强的分散的阳性细胞, 以及分散的上皮浸润淋巴细胞, 分布于滤泡间区和生发中心。更多的阳性细胞倾向于分布在表皮下MNC的局灶性聚簇中。CD3+TIL存在于所检查的所有癌症样品中, 尽管其数量在各种癌症之间不同, 而且在同一组织内的分布是不均匀的。CD8+TIL存在于绝大多数组织中。在检查的多种癌症中, GITR阳性染色存在于一小部分TIL中。一般而言, GITR+细胞的丰度与TIL的丰度成正比。GITR阳性TIL在宫颈癌(CC), 黑色素瘤(Mel)和肝细胞癌(HCC)中丰富, 在结直肠癌(CRC)和头颈部鳞状细胞癌(HNSCC)中也可见一些染色, 其中宫颈鳞状细胞癌显示染色最为丰富。

[0249] 在NSCLC (非小细胞肺癌)、CC、HNSCC和HCC中的肿瘤细胞中也观察到GITR阳性染色(图7)。在NSCLC和CC中, 通过与GITR融合蛋白温育后染色被完全置换而证实了染色的特异性。

[0250] 还对冷冻组织样品进行了免疫组化。将5μm的冷冻切片机切片用丙酮固定10分钟, 并在室温下使用间接免疫过氧化物酶方法进行免疫染色。为了用CD3 (T细胞标记)、CD8 (细胞毒性T细胞标记) 和FoxP3 (调节性T细胞标记) 单克隆抗体进行染色, 将载玻片用10%NBF进一步固定2分钟。为了用6G10-FITC和HuIgG2-FITC染色, 将载玻片浸入10%NBF中1分钟。分别用EnVision+系统提供的过氧化物酶封闭剂和补充有0.5%人类γ球蛋白的Dako蛋白质封闭剂来封闭内源性过氧化物酶活性和非特异性结合。将第一抗体(5μg/mL的6G10-FITC、1:100的CD3、1:100的CD8或5、或10μg/mL的FoxP3) 或同种型对照抗体(5μg/mL的HuIgG2-FITC) 施加于切片, 并温育1小时。使用小鼠或兔IgG的EnVision+系统作为检测系统。

对于6G10-FITC及其同型对照HuIgG2-FITC,使用兔抗FITC抗体 (5 μ g/mL) 作为桥连抗体。最后,将载玻片与DAB底物-发色团溶液反应6分钟,然后用Mayer苏木精复染,脱水,透明,并用Permunt使用常规组织学程序封片。对于CD3、CD8和FoxP3单克隆抗体、使用Dako蛋白质阻断剂作为稀释剂,而对于6G10-FITC和HuIgG2-FITC,第一抗体和第二抗体均使用补充有0.5%人 γ 球蛋白和0.5%BSA的PBS作为稀释剂。来自3种肿瘤类型的冷冻组织样品购自组织供应商。

[0251] 在3种肿瘤类型中观察到不同量的GITR+TIL。FoxP3存在于一小部分TIL中。用抗GITR抗体也观察到一部分肿瘤细胞的染色,且染色的特异性通过与GITR融合蛋白温育后染色完全被置换而得到了证实。在冰冻切片上也观察到GITR肿瘤细胞中GITR mRNA的存在,这进一步证实了IHC结果。

[0252] 这些结果表明抗GITR抗体6G10可以有效地检测固定的和冷冻的组织样品中的人GITR蛋白。

[0253] 表2:序列汇总表

[0254]

SEQ ID	描述	序列
1	人GITR同型1	MAQHGMAGAFRALCGLALLCALS LGQRPTGGPGCGPGRLLLTGTG TDARCCRVHTTRCCRDYPGEECCSEWDCMCVQPEFHC GDCPCCTT CRHHPCPPGQGVQS QGKFSFGFQCIDCASGTFSGGHEGHCKPWT DCTQFGFLT VFPGNKTHNAVCPGSPPAEPLGWLTVVLLAVAAC VLLLTSAQLGLHIWQLRSQCMWPRETQLLLEVPPSTEDARSCQF PEEERGERSAEEKGR LGDLWV
2	人GITR同型2	MAQHGMAGAFRALCGLALLCALS LGQRPTGGPGCGPGRLLLTGTG TDARCCRVHTTRCCRDYPGEECCSEWDCMCVQPEFHC GDCPCCTT CRHHPCPPGQGVQS QGKFSFGFQCIDCASGTFSGGHEGHCKPWT DCCWRCRRRPKTPEAASSPRKSGASDRQRRRGWETCGCEPGRP PGPPTAASPSPGAPQAAGALRSALGRALLPWQKQWVQEGGSDQR PGPCSSAAAAGPCRRERETQSWPPSSLAGPDGVGS
3	人GITR同型3	MAQHGMAGAFRALCGLALLCALS LGQRPTGGPGCGPGRLLLTGTG TDARCCRVHTTRCCRDYPGEECCSEWDCMCVQPEFHC GDCPCCTT CRHHPCPPGQGVQS QGKFSFGFQCIDCASGTFSGGHEGHCKPWT DCTQFGFLT VFPGNKTHNAVCPGSPPAEPLGWLTVVLLAVAAC VLLLTSAQLGLHIWQLRKTQLLLEVPPSTEDARSCQFPEEERGER RSAEEKGR LGDLWV
4	成熟人GITR的胞外部分	QRPTGGPGCGPGRLLLTGTGTDARCCRVHTTRCCRDYPGEECCSE WDCMCVQPEFHC GDCPCCTTCRHHPCPPGQGVQS QGKFSFGFQCI DCASGTFSGGHEGHCKPWT DCTQFGFLT VFPGNKTHNAVCPGSP PPAEP
5	6G10 VH CDR1	TYGMH
6	6G10 VH CDR2	VTWYAGSNKFYADSVKG
7	6G10 VH CDR3	GGSMVRGLYYYYGMDV
8	6G10 VL CDR1	RASQGISSALA
9	6G10 VL CDR2	DASSLES
10	6G10 VL CDR3	QQFNSYPYT
11	6G10 VH	QVQLVESGGDVVQPGRSRLRLSCAASGFTFSTYGMHWVRQAPGKG LEWVAVTWYAGSNKFYADSVKGRFTISRDN SKNTLYLQMNSLRA EDTAVYYCARGGSMVRGLYYYYGMDVWGQGT TTVTVSS
12	6G10 VL	AIQLTQSPSSLSASVGD RVTITCRASQGISSALAWYQQKPGKAP KLLIYDASSLES GVP SRFSGSGSGTDFTLTIS SLQPEDFATYYC QQFNSYPYT FQGQTKLEIK
13	6G10全长重链	QVQLVESGGDVVQPGRSRLRLSCAASGFTFSTYGMHWVRQAPGKG LEWVAVTWYAGSNKFYADSVKGRFTISRDN SKNTLYLQMNSLRA EDTAVYYCARGGSMVRGLYYYYGMDVWGQGT TTVTVSSASTKGPSV FPLAPCSRSTSESTAALGCLVKDYFPEPVT VSWNSGALTSGVHT FPAVLQSSGLYSLSSVTVPSNFGTQT YTCNV DHKPSNTKVDK TVERKCCVECP PAPPVAGPSVFLFPPKPKDTLMISRTPEVTC VVVDVSHEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTFRVVS LTVVHQDWLNGKEYKCKVSNKGLPAPIEKTISKTKGQPREPQVY TLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKT TPPMLDS DGSFFLYSKLTVDKSRWQQGNV FSCSV MHEALHNHYT QKSLSLSPGK
14	6G10全长轻链	AIQLTQSPSSLSASVGD RVTITCRASQGISSALAWYQQKPGKAP KLLIYDASSLES GVP SRFSGSGSGTDFTLTIS SLQPEDFATYYC

[0255]

		QQFNSYPYTFGQGTKLEIKRTVAAPSVFIFPPSDEQLKSGTASV VCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDYSLSL STLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
15	嵌合6G10抗体—全长重链 恒定区加下划线	QVQLVESGGDVVQPGRSRLRLSCAASGFTFSTYGMHWVRQAPGKG LEWVAVTWYAGSNKFYADSVKGRFTISRDNKNTLYLQMNSLRA EDTAVYYCARGGSMVRGLYYYGMDVWGQGTITVYSSAKTTAPSV YPLAPVCGDITGSSVTLGCLVKGYFPEPVTLTWNSGSLSSGVHT FPAVLQSDLYTLSSSVTVTSSTWPSQSITCNVAHPASSTKVDKK IEPRGPTIKPCPPCKCPAPNLLGGPSVFIFPPKIKDVLMIISLSP IVTCVVVDVSEDDPDVQISWFEVNNVEVHTAQTQTHREDYNSTLR VVSALPIQHQQDWMGKEFKCKVNNKDLPAPIERTISKPKGSVRA PQVYVLPPEEEMTKKQVTLTCMVTDMPEDYIYVEWTNNGKTEL NYKNTPEVLDSDGSYFMYSKLRVEKKNWVERNSYSCSVVHEGLH NHHTTKSFSRTPGK
16	嵌合6G10抗体—全长轻链 恒定区加下划线	AIQLTQSPSSLSASVGRVITITCRASQGISSALAWYQQKPGKAP KLLIYDASSLESQVPSRFSGSGSGTDFTLTITSSLPEDFATYYC QQFNSYPYTFGQGTKLEIKRADAAPTVSIFPPSSEQLTSGGASV VCFLNNFYPKDINVWKIDGSEKQNGVLNSWTDQDSKDYSLSMS STLTTLTKDEYERHNSYTCEATHKSTSTSPIVKSFNRNEC
17	6G10 (VH)核苷酸序列	CAGGTGCAGCTGGTGGAGTCTGGGGGAGACG TGGTCCAGCCTGGGAGGTCCTGAGACTCTC CTGTGCAGCGTCTGGATTACCTTCAGTACC TATGGCATGCACTGGGTCCGCCAGGCTCCAG GCAAGGGGCTGGAGTGGGTGGCAGTTACATG GTATGCTGGAAGTAATAAATTTTATGCAGAC TCCGTGAAGGGCCGATTCACCATCTCCAGAG ACAATTCCAAGAACACGCTGTATCTGCAAT GAACAGCCTGAGAGCCGAGGACACGGCTGTG TATTACTGTGCGAGAGGAGGTAGTATGGTTC GGGGACTTTATTATTACGGTATGGACGTCTG GGGCCAAGGGACCACGGTCACCGTCTCCTCA
18	6G10 (VL)核苷酸序列	GCCATCCAGTTGACCCAGTCTCCATCCTCCC TGTCTGCATCTGTAGGAGACAGAGTCACCAT CACTTGCCGGGCAAGTCAGGGCATTAGCAGT GCTTTAGCCTGGTATCAGCAGAAACCAGGGA AAGCTCCTAAGCTCCTGATCTATGATGCCTC CAGTTTGGAAAGTGGGGTCCCATCAAGGTTT AGCGGCAGTGGATCTGGGACAGATTTCACTC TCACCATCAGCAGCCTGCAGCCTGAAGATTT TGCAACTTATTACTGTCAACAGTTTAATAGT TACCCGTACACTTTTGGCCAGGGGACCAAGC TGGAGATCAAA
19	6G10 (全长野生型重链) 核苷酸序列 编码恒定区的序列加下 划线	CAGGTGCAGCTGGTGGAGTCTGGGGGAGACGTGGTCCAGCCTGG GAGGTCCCTGAGACTCTCCTGTGCAGCGTCTGGATTACCTTCA GTACCTATGGCATGCACTGGGTCCGCCAGGCTCCAGGCAAGGGG CTGGAGTGGGTGGCAGTTACATGGTATGCTGGAAGTAATAAAT TTATGCAGACTCCGTGAAGGGCCGATTCACCATCTCCAGAGACA ATTCCAAGAACACGCTGTATCTGCAATGAACAGCCTGAGAGCC GAGGACACGGCTGTGTATTACTGTGCGAGAGGAGGTAGTATGGT

[0256]

		TCGGGGACTTTATTATTACGGTATGGACGTCTGGGGCCCAAGGGA CCACGGTCACCGTCTCCTCAGCCTCCACCAAGGGCCCATCGGTC TTCCCCCTGGCGCCCTGCTCCAGGAGCACCTCCGAGAGCACAGC GGCCCTGGGCTGCCTGGTCAAGGACTACTTCCCCGAACCGGTGA CGGTGTCGTGGAACCTCAGGCGCTCTGACCAGCGGCGTGACACCC TTCCACAGTGTCTACAGTCTCCTCAGGACTCTACTCCCTCAGCAG CGTGGTGACCGTGCCCTCCAGCAACTTCGGCACCCAGACCTACA CCTGCAACGTAGATCACAAGCCCAGCAACACCAAGGTGGACAAG ACAGTTGAGCGCAAATGTTGTGTGTCGAGTGCCACCGTGCCAGC ACCACCTGTGGCAGGACCGTCAGTCTTCTCTTCCCCCAAAAC CCAAGGACACCCCTCATGATCTCCCGGACCCCTGAGGTCACGTGC GTGGTGGTGGACGTGAGCCACGAAGACCCCGAGGTCCAGTTCAA CTGGTACGTGGACGGCGTGGAGGTGCATAATGCCAAGACAAGC CACGGGAGGAGCAGTTCAACAGCACGTTCCGTGTGGTCAGCGTC CTCACCGTTGTGCACCAGGACTGGCTGAACGGCAAGGAGTACAA GTGCAAGGTCTCCAACAAAGGCCCTCCAGCCCCCATCGAGAAAA CCATCTCCAAAACAAAGGGCAGCCCCGAGAACACAGGTGTAC ACCCTGCCCCCATCCCGGGAGGAGATGACCAAGAACCAGGTGAG CCTGACCTGCCTGGTCAAAGGCTTCTACCCAGCGACATCGCCG TGGAGTGGGAGAGCAATGGGCAGCCGGAGAACAACTACAAGACC ACACCTCCCATGCTGGACTCCGACGGCTCCTTCTCTCCTTACAG CAAGCTCACCGTGGACAAGAGCAGGTGGCAGCAGGGGAACGTCT TCTCATGCTCCGTGATGCATGAGGCTCTGCACAACCACTACACG CAGAAGAGCCTCTCCCTGTCTCCGGTAAA
20	6G10 (全长野生型轻链) 核苷酸序列 编码恒定区的序列加下 划线	GCCATCCAGTTGACCCAGTCTCCATCCTCCCTGTCTGCATCTGT AGGAGACAGAGTCACCATCACTTGCCGGGCAAGTCAGGGCATT GCAGTGCTTTAGCCTGGTATCAGCAGAAACAGGGAAAGCTCCT AAGCTCCTGATCTATGATGCCTCCAGTTTGGAAAGTGGGGTCCC ATCAAGGTTGAGCGGAGTGGATCTGGGACAGATTTCACTCTCA CCATCAGCAGCCTGCAGCCTGAAGATTTTGCAACTTATTACTGT CAACAGTTTAATAGTTACCCGTACACTTTTGGCCAGGGGACCAA GCTGGAGATCAAACGAACTGTGGCTGCACCATCTGTCTTCATCT TCCCGCCATCTGATGAGCAGTTGAAATCTGGAAGTGCCTCTGTT GTGTGCCTGCTGAATAACTTCTATCCAGAGAGGGCCAAAGTACA GTGGAAGGTGGATAACGCCCTCCAATCGGGTAACTCCAGGAGA GTGTCACAGAGCAGGACAGCAAGGACAGCACCTACAGCCCTCAGC AGCACCCCTGACGCTGAGCAAAGCAGACTACGAGAAACACAAAGT CTACGCCTGCGAAGTCACCCATCAGGGCCTGAGCTCGCCCGTCA CAAAGAGCTTCAACAGGGGAGAGTGT
21	嵌合6G10重链 编码恒定区的序列加下 划线	CAGGTGCAGCTGGTGGAGTCTGGGGGAGACGTGGTCCAGCCTGG GAGGTCCCTGAGACTCTCCTGTGCAGCGTCTGGATTACCTTCA GTACCTATGGCATGCACTGGGTCCGCCAGGCTCCAGGCAAGGGG CTGGAGTGGGTGGCAGTTACATGGTATGCTGGAAGTAATAAATT TTATGCAGACTCCGTGAAGGGCCGATTACCATCTCCAGAGACA ATTCCAAGAACACGCTGTATCTGCAAATGAACAGCCTGAGAGCC GAGGACACGGCTGTGTATTACTGTGCGAGAGGAGGTAGTATGGT TCGGGGACTTTATTATTACGGTATGGACGTCTGGGGCCAAAGGA CCACGGTCACCGTCTCCTCAGCCAAAACAACAGCCCCATCGGTC TATCCGCTAGCCCCCTGTGTGTGGAGATACAAGTGGCTCCTCGGT GACTCTAGGATGCCTGGTCAAGGGTTATTTCCCTGAGCCAGTGA CCTTGACCTGGAAGTCTGGATCCCTGTCCAGTGGTGTGCACACC TTCCAGCTGTCTGCAGTCTGACCTCTACACCCCTCAGCAGCTC AGTGAAGTAACTCGAGCACCTGGCCCAGCCAGTCCATCACCT GCAATGTGGCCAC CCGGCAAGCAGCACCAAGGTGGACAAGAAAATTGAGCCCAGAGG GCCCACAATCAAGCCCTGTCTCCATGCAAAATGCCCAGCACCTA ACCTCTTGGGTGGACCATCCGTCTTCATCTTCCCTCCAAAGATC AAGGATGTACTCATGATCTCCCTGAGCCCCATAGTCACATGTGT GGTGGTGGATGTGAGCGAGGATGACCCAGATGTCCAGATCAGCT GGTTTGTGAACAACGTGGAAGTACACACAGCTCAGACACAACC

[0257]

		CATAGAGAGGATTACAAACAGTACTCTCCGGGTGGTCAGTGCCCT CCCCATCCAGCACCAGGACTGGATGAGTGGCAAGGAGTTCAAAT GCAAGGTCAACAACAAAGACCTCCAGCGCCCATCGAGAGAACC ATCTCAAACCCAAAGGGTCAGTAAGAGCTCCACAGGTATATGT CTTGCCTCCACCAGAAGAAGAGATGACTAAGAAACAGGTCACCT TGACCTGCATGGTCACAGACTTCATGCCTGAAGACATTTACGTG GAGTGGACCAACAACGGGAAAACAGAGCTAAACTACAAGAACAC TGAACCAGTCTGGACTCTGATGGTTCTTACTTCATGTACAGCA AGCTGAGAGTGGA AAGAAGAACTGGGTGGAAAGAAATAGCTACTCCTGTTCACTGGT CCACGAGGGTCTGCACAATCACCACACGACTAAGAGCTTCTCCC GGACTCCGGGTAAATGA
22	嵌合6G10 轻链 编码恒定区的序列加下 划线	GCCATCCAGTTGACCCAGTCTCCATCCTCCCTGTCTGCATCTGT AGGAGACAGAGTCACCATCACTTGCCGGGCAAGTCAGGGCATT GCAGTGCCTTAGCCTGGTATCAGCAGAAACAGGGAAAGTCCT AAGCTCCTGATCTATGATGCCTCCAGTTTGGAAAGTGGGGTCCC ATCAAGGTTTCAGCGGAGTGGATCTGGGACAGATTTCACTCTCA CCATCAGCAGCCTGCAGCCTGAAGATTTTGCAACTTATTACTGT CAACAGTTTAATAGTTACCCGTACACTTTTGGCCAGGGGACCAA GCTGGAGATCAAACGGGCTGATGCTGCACCACTGTATCCATCT TCCCACCATCCAGTGAGCAATTGACATCTGGAGGTGCCTCAGTC GTGTGCTTCTTGAACAACTTCTACCCCAAAGACATCAATGTCAA GTGGAAGATTGATGGCAGTGAACGACAAAATGGCGTCCCTGAACA GTTGGACCGATCAGGACAGCAAAGACAGCACCTACAGCATGAGC AGCACCTCACGTTGACCAAGGACGAGTATGAACGACATAACAG CTATACCTGTGAGGCCACTCACAAGACATCAACTTCACCCATTG TCAAGAGCTTCAAC AGGAATGAGTGTAG
23	人IgG2重链恒定区	ASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSG ALTSGVHTFPAVLQSSGLYSLSSVTVPSNFGTQTYTCNVDPHK PSNTKVDKTVRKKCECPKPPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVSHEDPEVQFNWYVDGVEVHNAKTKPREEQFN STFRVVSFLTQVWDLNGKEYKCKVSNKGLPAPIEKTISKTKG QPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNG QPENNYKTTTPMLDSGSEFFLYSKLTVDKSRWQQGNVSCFVSMH EALHNHYTQKSLSLSPGK
24	人kappa轻链恒定区	RTVAAPSVEFIPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVD NALQSGNSQESVTEQDSKDYSLSSLTTLTKADYEKHKVYACE VTHQGLSSPVTKSFNRGEC
25	小鼠IgG2a重链恒定区	AKTTAPSVYPLAPVCGDTTGSSVTLGCLVKGYFPEPVTLTWNSG SLSSGVHTFPAVLQSDLYTLSSSVTVTSSTWPSQSITCNVAHPA SSTKVDKKIEPRGPTIKPCPPCKCPAPNLLGGPSVFIFFPKIKD VLMISLSPIVTCVVVDVSEDDPDVQISWFEVNNVEVHTAQTHR EDYNSTLRVVSALPIQHQQDWMGKEFKCKVNNKDLPAPIERTIS KPKGSVRAPQVYVLPPEEEMTKKQVTLTCMVTDMPEDIIYVEW TNNKTELNKNTPEVLDSDGSYFMYSKLRVEKKNWVERNSYSC SVVHEGLHNHHTTKSFSRTPGK
26	小鼠kappa轻链恒定区	RADAAPTVEIFPPSSEQLTSGGASVVCFLNNFYPKDINVKWKID GSERQNGVLNSWTDQDSKDYSLSSLTTLTKDEYERHNSYTCE ATHKTSSTPIVKSFNRECE
27	28F3 (VH)	QVQLVESGGGVVQPGSRSLRLSCAASGFTFSSYGMHWVRQAPGKLEWV AVIWEYSNKYYADSVKGRFTISRDNKNTLYLQMNSLRADTAVYYC ARGGSVRGDYYYGMDVWGQGT'TVTVSS
28	28F3 (VL)	AIQLTQSPSSLSASVGRVITITCRASQGISSALAWYQQKPGKAPKLLI YDASSLESQVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQFNSTPY TFGQGTKLEIK

[0258]

29	28F3 (全长野生型重链) 恒定区加下划线	<u>QVQLVESGGGVVQPGRSLRLSCAASGFTFSSYGMHWVRQAPGKGLEWV</u> <u>AVIWEYEGSNKYYADSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYC</u> <u>ARGGSMVRGDYYYGMDVWGQGTITVTVSSASTKGFSVFPLAPCSRSTSE</u> <u>STAALGCLVKDYFPEPVTWSWNSGALTSGVHTFPAVLQSSGLYSLSSV</u> <u>VTVPSSNFGTQTYTCNV DHKPSNTKVDKTV ERKCCVCEPFCPPAPPVAG</u> <u>PSVFLFPPKPKDTLMI SRTPEVTCVVVDVSHEDPEVQFNWYVDGVEVH</u> <u>NAKTKPREEQFNSTFRVVS VLT VVHQDWLNGKEYKCKVSNKGLPAPIE</u> <u>KTISKTKGQPREPQVYITLPPSREEMTKNQVSLTCLVKGFYPSDIAVEW</u> <u>ESNGQPENNYKTTTPMLDSDGSFFLYSKLTVDKSRWQQGNV FSCSVMH</u> <u>EALHNHYTQKSLSLSPGK</u>
30	28F3 (全长野生型轻链) 恒定区加下划线	<u>AIQLTQSPSSLSASVGDRTITCRASQGISSALAWYQQKPGKAPKLLI</u> <u>YDASSLESQVPSRFRSGSGSGTDFTLTITSLQPEDFATYYCQQFN SYPY</u> <u>TFGQGTKLEIKRTVAAPS VFI FPPSDEQLKSGTASVCLLN FYPREA</u> <u>KVQWKVDNALQSGNSQESVTEQDSKDS TYSLSSTLTLSKADYEKHKVY</u> <u>ACEVTHQGLSSPVTKSFNRGEC</u>
31	28F3.IgG1 (VH + IgG1)	<u>QVQLVESGGGVVQPGRSLRLSCAASGFTFSSYGMHWVRQAPGKGLEWV</u> <u>AVIWEYEGSNKYYADSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYC</u> <u>ARGGSMVRGDYYYGMDVWGQGTITVTVSSASTKGFSVFPLAPSSKSTSG</u> <u>GTAALGCLVKDYFPEPVTWSWNSGALTSGVHTFPAVLQSSGLYSLSSV</u> <u>VTVPSSSLGTQTYICNVNHKPSNTKVDKRV EPKSCDKTHTCPPCPAPE</u> <u>LLGGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVSHEDPEVKFNWYVDG</u> <u>VEVHNAKTKPREEQYNSTYRVVSVLT VLVHQDWLNGKEYKCKVSNKALP</u> <u>APIEKTISKAKGQPREPQVYITLPPSREEMTKNQVSLTCLVKGFYPSDI</u> <u>AVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNV FSC</u> <u>SVMHEALHNHYTQKSLSLSPG</u>
32	28F3.IgG1.1 (VH + IgG1.1)	<u>QVQLVESGGGVVQPGRSLRLSCAASGFTFSSYGMHWVRQAPGKGLEWV</u> <u>AVIWEYEGSNKYYADSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYC</u> <u>ARGGSMVRGDYYYGMDVWGQGTITVTVSSASTKGFSVFPLAPSSKSTSG</u> <u>GTAALGCLVKDYFPEPVTWSWNSGALTSGVHTFPAVLQSSGLYSLSSV</u> <u>VTVPSSSLGTQTYICNVNHKPSNTKVDKRV EPKSCDKTHTCPPCPAPE</u> <u>AEGAPSVFLFPPKPKDTLMI SRTPEVTCVVVDVSHEDPEVKFNWYVDG</u> <u>VEVHNAKTKPREEQYNSTYRVVSVLT VLVHQDWLNGKEYKCKVSNKALP</u> <u>SSIEKTISKAKGQPREPQVYITLPPSREEMTKNQVSLTCLVKGFYPSDI</u> <u>AVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNV FSC</u> <u>SVMHEALHNHYTQKSLSLSPG</u>
33	28F3.IgG1 (VL + CL)	<u>AIQLTQSPSSLSASVGDRTITCRASQGISSALAWYQQKPGKAPKLLI</u> <u>YDASSLESQVPSRFRSGSGSGTDFTLTITSLQPEDFATYYCQQFN SYPY</u> <u>TFGQGTKLEIKRTVAAPS VFI FPPSDEQLKSGTASVCLLN FYPREA</u> <u>KVQWKVDNALQSGNSQESVTEQDSKDS TYSLSSTLTLSKADYEKHKVY</u> <u>ACEVTHQGLSSPVTKSFNRGEC</u>
34	28F3 VH CDR1	SYGMH
35	28F3 VH CDR2	VIWEYEGSNKYYADSVKG
36	28F3 VH CDR3	GGSMVRGDYYYGMDV
37	28F3 VL CDR1	RASQGISSALA
38	28F3 VL CDR2	DASSLES
39	28F3 VL CDR3	QQFN SYPYT
40	28F3 (VH + G2(C219S)) 或 28F3-IgG2-C219S	<u>QVQLVESGGGVVQPGRSLRLSCAASGFTFSSYGMHWVRQAPGKGLEWV</u> <u>AVIWEYEGSNKYYADSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYC</u> <u>ARGGSMVRGDYYYGMDVWGQGTITVTVSSASTKGFSVFPLAPCSRSTSE</u> <u>STAALGCLVKDYFPEPVTWSWNSGALTSGVHTFPAVLQSSGLYSLSSV</u> <u>VTVPSSNFGTQTYTCNV DHKPSNTKVDKTV ERKSCVCEPFCPPAPPVAG</u> <u>PSVFLFPPKPKDTLMI SRTPEVTCVVVDVSHEDPEVQFNWYVDGVEVH</u> <u>NAKTKPREEQFNSTFRVVS VLT VVHQDWLNGKEYKCKVSNKGLPAPIE</u> <u>KTISKTKGQPREPQVYITLPPSREEMTKNQVSLTCLVKGFYPSDIAVEW</u>

[0259]

		ESNGQPENNYKTTTPMLDSGSEFLYSLKLTVDKSRWQQGNVFSCSVMH EALHNHYTQKSLSLSPG
41	28F3 (VH + G2.g1)或 28F3-IgG2-IgG1	<u>QVQLVESGGGVVQPGRSRLRLSCAASGFTFSSYGMHWVRQAPGKGLEWV</u> <u>AVIWEYEGSNKYYADSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYC</u> <u>ARGGSMVRGDYYYGMDVWGQGTITVTVSSASTKGPSVFPLAPCSRSTSE</u> <u>STAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSV</u> <u>VTVPSSNFGTQTYTCNV DHKPSNTKVDKTV ERKCCVCP PCPAP ELLG</u> <u>GPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEV</u> <u>HNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPI</u> <u>EKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVE</u> <u>WESNGQPENNYKTTTPVLDSGSEFLYSLKLTVDKSRWQQGNVFSCSVMH</u> <u>HEALHNHYTQKSLSLSPG</u>
42	28F3 (VH + G2.g1.1)或 28F3-IgG2-IgG1.1	<u>QVQLVESGGGVVQPGRSRLRLSCAASGFTFSSYGMHWVRQAPGKGLEWV</u> <u>AVIWEYEGSNKYYADSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYC</u> <u>ARGGSMVRGDYYYGMDVWGQGTITVTVSSASTKGPSVFPLAPCSRSTSE</u> <u>STAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSV</u> <u>VTVPSSNFGTQTYTCNV DHKPSNTKVDKTV ERKCCVCP PCPAP PVAG</u> <u>PSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVH</u> <u>NAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPSSIE</u> <u>KTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEW</u> <u>ESNGQPENNYKTTTPVLDSGSEFLYSLKLTVDKSRWQQGNVFSCSVMH</u> <u>EALHNHYTQKSLSLSPG</u>
43	28F3 (VH + G2(C219S).g1)或 28F3-IgG2-C219S-IgG1	<u>QVQLVESGGGVVQPGRSRLRLSCAASGFTFSSYGMHWVRQAPGKGLEWV</u> <u>AVIWEYEGSNKYYADSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYC</u> <u>ARGGSMVRGDYYYGMDVWGQGTITVTVSSASTKGPSVFPLAPCSRSTSE</u> <u>STAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSV</u> <u>VTVPSSNFGTQTYTCNV DHKPSNTKVDKTV ERKSCVCP PCPAP ELLG</u> <u>GPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEV</u> <u>HNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPI</u> <u>EKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVE</u> <u>WESNGQPENNYKTTTPVLDSGSEFLYSLKLTVDKSRWQQGNVFSCSVMH</u> <u>HEALHNHYTQKSLSLSPG</u>
44	28F3 (VH + G2(C219S).g1.1)或 28F3-IgG2-C219S-IgG1.1	<u>QVQLVESGGGVVQPGRSRLRLSCAASGFTFSSYGMHWVRQAPGKGLEWV</u> <u>AVIWEYEGSNKYYADSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYC</u> <u>ARGGSMVRGDYYYGMDVWGQGTITVTVSSASTKGPSVFPLAPCSRSTSE</u> <u>STAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSV</u> <u>VTVPSSNFGTQTYTCNV DHKPSNTKVDKTV ERKSCVCP PCPAP PVAG</u> <u>PSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVH</u> <u>NAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPSSIE</u> <u>KTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEW</u> <u>ESNGQPENNYKTTTPVLDSGSEFLYSLKLTVDKSRWQQGNVFSCSVMH</u> <u>EALHNHYTQKSLSLSPG</u>
45	28F3 (VH) (SEQ ID NO: 13)带信号肽 信号肽加下划线	<u>MR</u> AWIFFLLCLAGRALAQVQLVESGGGVVQPGRSRLRLSCAASGFTFSS YGMHWVRQAPGKGLEWVAVIWEYEGSNKYYADSVKGRFTISRDN SKNTL YLQMNSLRAEDTAVYYCARGGSMVRGDYYYGMDVWGQGTITVTVSS
46	28F3 (VL) (SEQ ID NO: 14)带信号肽 信号肽加下划线	<u>MR</u> AWIFFLLCLAGRALAAIQLTQSPSSLSASVGDRTITCRASQGISS ALAWYQQKPGKAPKLLIYDASSLESVPSPRFGSGSGTDFTLTITSSIQ PEDFATYYCQQFNSTYPTFGQGTKLEIK
47	28F3.IgG1 (VH + IgG1) 带信号肽 信号肽和恒定区加下划	<u>MR</u> AWIFFLLCLAGRALAQVQLVESGGGVVQPGRSRLRLSCAASGFTFSS YGMHWVRQAPGKGLEWVAVIWEYEGSNKYYADSVKGRFTISRDN SKNTL YLQMNSLRAEDTAVYYCARGGSMVRGDYYYGMDVWGQGTITVTVSSAST KGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVH TFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRV PKSCDKTHTCPPCPAPPELLGGPSVFLFPPKPKDTLMISRTPEVTCVV VDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQD WLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK

[0260]

	线	<u>NQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGSFFLYS</u> <u>KLTVDKSRWQQGNVFSCSVMEALHNHYTQKSLSLSPG</u>
48	28F3.IgG1.1 (VH + IgG1.1)带信号肽 信号肽和恒定区加下划线	<u>MRWIFFLLCLAGRALAQVQLVESGGGVVQPGRSRLRLSCAASGFTFSS</u> <u>YGMHWVRQAPGKGLEWVAIVWYEGSNKYADSVKGRFTISRDNKNTLYLQMN</u> <u>SLRAEDTAVYYCARGGSMVRGDDYYGMDVWGQGTITVTVSSAST</u> <u>KGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVH</u> <u>TFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPSNTKVDKRV</u> <u>PKSCDKHTHTCPPCPAPEAEAGAPSVFLFPPKPKDTLMISRTPEVTCVV</u> <u>DVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVTLVH</u> <u>QDWLNQKEYKCKVSNKALPSSIEKTIKAKGQPREPQVYTLPPSREEMTK</u> <u>NQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGSFFLYS</u> <u>KLTVDKSRWQQGNVFSCSVMEALHNHYTQKSLSLSPG</u>
49	28F3.IgG1 (VL+CL)带信号肽 信号肽和恒定区加下划线	<u>MRWIFFLLCLAGRALAAIQLTQSPSSLSASVGDRTITCRASQGISS</u> <u>ALAWYQQKPKAPKLLIYDASSLESGVPSRFSGSGSGTDFTLTISS</u> <u>LQPEDFATYYCQQFNSTYPTFGQGTKLEIKRTVAAPSVFIFPPSDEQLK</u> <u>SGTASVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDS</u> <u>STYLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC</u>
50	19D3 (VH)	<u>QVQLVESGGGVVQPGRSRLRLSCAASGFTFSSYGFHWVRQAPGKGLEWV</u> <u>AVIWYAGSNKFYADSVKGRFTISRDNKNTLYLQMN</u> <u>SLRAEDTAVYYCARGGQLDY</u> <u>YYYYYVMDVWGQGTITVTVSS</u>
51	19D3 (VL)	<u>DIQMTQSPSSLSASVGDRTITCRASQGISSWLAWYQQKPEKAPKSLI</u> <u>YAASSLQSGVP</u> <u>SRFSGSGSGTDFTLTISSLPEDFATYYCQQYNSYPYTFGQGTKLEIK</u>
52	19D3 (全长野生型重链) 恒定区加下划线	<u>QVQLVESGGGVVQPGRSRLRLSCAASGFTFSSYGFHWVRQAPGKGLEWV</u> <u>AVIWYAGSNKFYADSVKGRFTISRDNKNTLYLQMN</u> <u>SLRAEDTAVYYCARGGQLDY</u> <u>YYYYYVMDVWGQGTITVTVSSASTKGPSVFPLAPCSRSTES</u> <u>TAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSV</u> <u>TVPSNFGTQTYTCNVN</u> <u>DKPSNTKVDKTV</u> <u>VERKCCVECP</u> <u>PCPAPPVAGF</u> <u>SVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHN</u> <u>AKTKPREEQFNSTFRVVS</u> <u>VLTVVHQDWLNQKEYKCKVSNKGLPAPIEK</u> <u>TISKTKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWE</u> <u>SNGQPENNYKTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVME</u> <u>ALHNHYTQKSLSLSPGK</u>
53	19D3 (全长野生型轻链) 恒定区加下划线	<u>DIQMTQSPSSLSASVGDRTITCRASQGISSWLAWYQQKPEKAPKSLI</u> <u>YAASSLQSGVPSRFSGSGSGTDFTLTISSLPEDFATYYCQQYNSYPY</u> <u>TFGQGTKLEIKRTVAAPSVFIFPPSDEQLKSGTASVCLLNNFYPREA</u> <u>KVQWKVDNALQSGNSQESVTEQDSKDS</u> <u>STYLSSTLTLSKADYEKHKVY</u> <u>ACEVTHQGLSSPVTKSFNRGEC</u>
54	19D3.IgG1 (VH + IgG1)	<u>QVQLVESGGGVVQPGRSRLRLSCAASGFTFSSYGFHWVRQAPGKGLEWV</u> <u>AVIWYAGSNKFYADSVKGRFTISRDNKNTLYLQMN</u> <u>SLRAEDTAVYYCARGGQLDY</u> <u>YYYYYVMDVWGQGTITVTVSSASTKGPSVFPLAPSSKSTSGG</u> <u>TAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSV</u> <u>TVPSSSLGTQTYICNVNHKPSNTKVDKRV</u> <u>EPKSCDKHTHTCPPCPAPEL</u> <u>LGGPSVFPLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDG</u> <u>VEVHN</u> <u>AKTKPREEQYNSTYRVVSVTLVH</u> <u>QDWLNQKEYKCKVSNKALPA</u> <u>PIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIA</u> <u>VEWESNGQPENNYKTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCS</u> <u>VMHEALHNHYTQKSLSLSPG</u>
55	19D3.IgG1.1 (VH + IgG1.1)	<u>QVQLVESGGGVVQPGRSRLRLSCAASGFTFSSYGFHWVRQAPGKGLEWV</u> <u>AVIWYAGSNKFYADSVKGRFTISRDNKNTLYLQMN</u> <u>SLRAEDTAVYYCARGGQLDY</u> <u>YYYYYVMDVWGQGTITVTVSSASTKGPSVFPLAPSSKSTSGG</u> <u>TAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSV</u> <u>TVPSSSLGTQTYICNVNHKPSNTKVDKRV</u> <u>EPKSCDKHTHTCPPCPAPEA</u> <u>EGAPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDG</u> <u>VEVHN</u> <u>AKTKPREEQYNSTYRVVSVTLVH</u> <u>QDWLNQKEYKCKVSNKALPS</u> <u>SIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIA</u>

[0261]

		VEWESNGQPENNYKTTTPVLDSGSGFFLYSKLTVDKSRWQQGNVFSCS VMHEALHNHYTQKSLSLSPG
56	19D3.IgG1 (VL + CL)	DIQMTQSPSSLSASVGDRVTITCRASQGISWLAWYQQKPEKAPKSLI YAASSLQSGVPSRFRSGSGTDFTLTISSLQPEDFATYYCQQYNSYPY TFGGGTKLEIKRTVAAPSVFIFPPSDEQLKSGTASVCLLNNFYPREA KVQWKVDNALQSGNSQESVTEQDSKDSYSLSTLTLSKADYEKHKVY ACEVTHQGLSSPVTKSFNRGEC
57	19D3 VH CDR1	SYGFH
58	19D3 VH CDR2	VIWYAGSNKFYADSVKG
59	19D3 VH CDR3	GGQLDYIIIIYVMDV
60	19D3 VL CDR1	RASQGISWLA
61	19D3 VL CDR2	AASSLQS
62	19D3 VL CDR3	QQYNSYPYT
63	19D3 (VH + G2(C219S)) 或 19D3-IgG2-C219S	<u>QVQLVESGGGVVQPGRSLRLSCAASGFTFSSYGFHWVRQAPGKGLEWV</u> <u>AVIWIYAGSNKFYADSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYC</u> <u>ARGGQLDYIIIIYVMDVWGQGTITVTVSSASTKGPSVFPLAPCSRSTSES</u> <u>TAALGCLVKDYFPEPVTISWNSGALTSGVHTFPAVLQSSGLYSLSSV</u> <u>TVPSNFGTQTYTCNV DHKPSNTKVDKTV ERKSCVECPPCPAPPVAGP</u> <u>SVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHN</u> <u>AKTKPREEQFNSTFRVSVLTIVVHQDWLNGKEYKCKVSNKGLPAPIEK</u> <u>TISKTKGQPREPQVYITLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWE</u> <u>SNGQPENNYKTTTPMLDSGSGFFLYSKLTVDKSRWQQGNVFSCSVMHE</u> <u>ALHNHYTQKSLSLSPG</u>
64	19D3 (VH + G2.g1)或 19D3-IgG2-IgG1	<u>QVQLVESGGGVVQPGRSLRLSCAASGFTFSSYGFHWVRQAPGKGLEWV</u> <u>AVIWIYAGSNKFYADSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYC</u> <u>ARGGQLDYIIIIYVMDVWGQGTITVTVSSASTKGPSVFPLAPCSRSTSES</u> <u>TAALGCLVKDYFPEPVTISWNSGALTSGVHTFPAVLQSSGLYSLSSV</u> <u>TVPSNFGTQTYTCNV DHKPSNTKVDKTV ERKCCVECPPCPAPELLGG</u> <u>PSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVH</u> <u>NAKTKPREEQYNSTYRVVSVLTIVLHQDWLNGKEYKCKVSNKALPAPIE</u> <u>KTISKAKGQPREPQVYITLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWE</u> <u>ESNGQPENNYKTTTPVLDSGSGFFLYSKLTVDKSRWQQGNVFSCSVMHE</u> <u>EALHNHYTQKSLSLSPG</u>
65	19D3 (VH + G2.g1.1)或 19D3-IgG2-IgG1.1	<u>QVQLVESGGGVVQPGRSLRLSCAASGFTFSSYGFHWVRQAPGKGLEWV</u> <u>AVIWIYAGSNKFYADSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYC</u> <u>ARGGQLDYIIIIYVMDVWGQGTITVTVSSASTKGPSVFPLAPCSRSTSES</u> <u>TAALGCLVKDYFPEPVTISWNSGALTSGVHTFPAVLQSSGLYSLSSV</u> <u>TVPSNFGTQTYTCNV DHKPSNTKVDKTV ERKCCVECPPCPAPPVAGP</u> <u>SVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHN</u> <u>AKTKPREEQYNSTYRVVSVLTIVLHQDWLNGKEYKCKVSNKALPSSIEK</u> <u>TISKAKGQPREPQVYITLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWE</u> <u>SNGQPENNYKTTTPVLDSGSGFFLYSKLTVDKSRWQQGNVFSCSVMHE</u> <u>ALHNHYTQKSLSLSPG</u>
66	19D3 (VH + G2(C219S).g1)或 19D3-IgG2-C219S-IgG1	<u>QVQLVESGGGVVQPGRSLRLSCAASGFTFSSYGFHWVRQAPGKGLEWV</u> <u>AVIWIYAGSNKFYADSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYC</u> <u>ARGGQLDYIIIIYVMDVWGQGTITVTVSSASTKGPSVFPLAPCSRSTSES</u> <u>TAALGCLVKDYFPEPVTISWNSGALTSGVHTFPAVLQSSGLYSLSSV</u> <u>TVPSNFGTQTYTCNV DHKPSNTKVDKTV ERKSCVECPPCPAPELLGG</u> <u>PSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVH</u> <u>NAKTKPREEQYNSTYRVVSVLTIVLHQDWLNGKEYKCKVSNKALPAPIE</u> <u>KTISKAKGQPREPQVYITLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWE</u> <u>ESNGQPENNYKTTTPVLDSGSGFFLYSKLTVDKSRWQQGNVFSCSVMHE</u> <u>EALHNHYTQKSLSLSPG</u>

[0262]

67	19D3 (VH + G2(C219S).g1.1)或 19D3-IgG2-C219S-IgG1.1	<u>QVQLVESGGGVVQPGRSLRLSCAASGFTFSSYGFWVRQAPGKGLEWV</u> <u>AVIWIYAGSNKFYADSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYC</u> <u>ARGGQLDYIYYVMDVWGQGTITVTVSSASTKGPSVFPLAPCSRSTSE</u> <u>TAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSV</u> <u>TVPSNFGTQTYTCNV DHKPSNTKVDKTV ERKSCVECPPCPAPPVAGP</u> <u>SVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHN</u> <u>AKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPSSIEK</u> <u>TISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWE</u> <u>SNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHE</u> <u>ALHNHYTQKSLSLSPG</u>
68	19D3 (VH + G2(C219S)) 或 19D3-IgG2-C219S	<u>QVQLVESGGGVVQPGRSLRLSCAASGFTFSSYGFWVRQAPGKGLEWV</u> <u>AVIWIYAGSNKFYADSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYC</u> <u>ARGGQLDYIYYVMDVWGQGTITVTVSSASTKGPSVFPLAPCSRSTSE</u> <u>TAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSV</u> <u>TVPSNFGTQTYTCNV DHKPSNTKVDKTV ERKSCVECPPCPAPPVAGP</u> <u>SVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHN</u> <u>AKTKPREEQFNSTFRVSVLTVVHQDWLNGKEYKCKVSNKGLPAPIEK</u> <u>TISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWE</u> <u>SNGQPENNYKTTTPMLDS DGSFFLYSKLTVDKSRWQQGNVFSCSVMHE</u> <u>ALHNHYTQKSLSLSPG</u>
69	19D3 (VH + G2.g1)或 19D3-IgG2-IgG1	<u>QVQLVESGGGVVQPGRSLRLSCAASGFTFSSYGFWVRQAPGKGLEWV</u> <u>AVIWIYAGSNKFYADSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYC</u> <u>ARGGQLDYIYYVMDVWGQGTITVTVSSASTKGPSVFPLAPCSRSTSE</u> <u>TAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSV</u> <u>TVPSNFGTQTYTCNV DHKPSNTKVDKTV ERKCCVECPPCPAPELLGG</u> <u>PSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHN</u> <u>NAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIE</u> <u>KTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEW</u> <u>ESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMH</u> <u>EALHNHYTQKSLSLSPG</u>
70	19D3 (VH + G2.g1.1)或 19D3-IgG2-IgG1.1	<u>QVQLVESGGGVVQPGRSLRLSCAASGFTFSSYGFWVRQAPGKGLEWV</u> <u>AVIWIYAGSNKFYADSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYC</u> <u>ARGGQLDYIYYVMDVWGQGTITVTVSSASTKGPSVFPLAPCSRSTSE</u> <u>TAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSV</u> <u>TVPSNFGTQTYTCNV DHKPSNTKVDKTV ERKCCVECPPCPAPPVAGP</u> <u>SVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHN</u> <u>AKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPSSIEK</u> <u>TISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWE</u> <u>SNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHE</u> <u>ALHNHYTQKSLSLSPG</u>
71	19D3 (VH + G2(C219S).g1)或 19D3-IgG2-C219S-IgG1	<u>QVQLVESGGGVVQPGRSLRLSCAASGFTFSSYGFWVRQAPGKGLEWV</u> <u>AVIWIYAGSNKFYADSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYC</u> <u>ARGGQLDYIYYVMDVWGQGTITVTVSSASTKGPSVFPLAPCSRSTSE</u> <u>TAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSV</u> <u>TVPSNFGTQTYTCNV DHKPSNTKVDKTV ERKSCVECPPCPAPELLGG</u> <u>PSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHN</u> <u>NAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIE</u> <u>KTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEW</u> <u>ESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMH</u> <u>EALHNHYTQKSLSLSPG</u>
72	19D3 (VH + G2(C219S).g1.1)或 19D3-IgG2-C219S-IgG1.1	<u>QVQLVESGGGVVQPGRSLRLSCAASGFTFSSYGFWVRQAPGKGLEWV</u> <u>AVIWIYAGSNKFYADSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYC</u> <u>ARGGQLDYIYYVMDVWGQGTITVTVSSASTKGPSVFPLAPCSRSTSE</u> <u>TAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSV</u> <u>TVPSNFGTQTYTCNV DHKPSNTKVDKTV ERKSCVECPPCPAPPVAGP</u> <u>SVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHN</u> <u>AKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPSSIEK</u> <u>TISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWE</u> <u>SNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHE</u> <u>ALHNHYTQKSLSLSPG</u>

[0263]

73	18E10 (VH)	QVQLVESGGGVVQPGRSLRLSCAASGFTFSSYGMHWVRQAPGKGLEWV AVIWYAGSNKYYADSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYC ARGGRIAVAFYYSDMVWGQGT TTVVSS
74	18E10 (VL)	DIQMTQSPSSLSASVGDRVTITCRASQGISSWLAWYQQKPEKAPKSLI YAASSLQSGVPSRFRSGSGSGTDFTLTISSLQPEDFATYYCQQYNSYPY TFGQGTKLEIK
75	18E10 (全长野生型重链) 恒定区加下划线	QVQLVESGGGVVQPGRSLRLSCAASGFTFSSYGMHWVRQAPGKGLEWV AVIWYAGSNKYYADSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYC ARGGRIAVAFYYSDMVWGQGT TTVVSSASTKGPSVFPLAPCSRSTES <u>TAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSV</u> <u>TVPSSTNGFTQYTCNV D HKPSNTKVDKTV ERKCCVECPCPAPFPVAGP</u> <u>SVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHN</u> <u>AKTKPREEQFNSTFRVSVLT VVHQDWLNGKEYKCKVSNKGLPAPIEK</u> <u>TISKTKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWE</u> <u>SNQGPENNYKTTTPMLDS DGSFFLYSKLTVDKSRWQQGNV FSCSV MHE</u> <u>ALHNHYTQKSLSLSPGK</u>
76	18E10 (全长野生型轻链) 恒定区加下划线	DIQMTQSPSSLSASVGDRVTITCRASQGISSWLAWYQQKPEKAPKSLI YAASSLQSGVPSRFRSGSGSGTDFTLTISSLQPEDFATYYCQQYNSYPY TFGQGTKLEIKRTVAAPS VFI FPPSDEQLKSGTASVVC LLN NFYPREA <u>KVQWKVDNALQSGNSQESVTEQDSKDS TYSLSSTLTLSKADYEKHKVY</u> <u>ACEVTHQGLSSPVTKSFNRGEC</u>
77	18E10.IgG1 (VH + IgG1)	QVQLVESGGGVVQPGRSLRLSCAASGFTFSSYGMHWVRQAPGKGLEWV AVIWYAGSNKYYADSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYC ARGGRIAVAFYYSDMVWGQGT TTVVSSASTKGPSVFPLAPSSKSTSGG TAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSV TVPSSTNGFTQYICNVNHKPSNTKVDKRV EPKSCDKTHTCPCPAPEL LGGPSVFLF PPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVE VHNAKTKPREEQYNSTYRVVSVLT VLVHQDWLNGKEYKCKV SNKALPAPIEK TISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKG FYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQ GNVFSCSV MHEALHNHYTQKSLSLSPG
78	18E10.IgG1.1 (VH + IgG1.1)	QVQLVESGGGVVQPGRSLRLSCAASGFTFSSYGMHWVRQAPGKGLEWV AVIWYAGSNKYYADSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYC ARGGRIAVAFYYSDMVWGQGT TTVVSSASTKGPSVFPLAPSSKSTSGG TAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSV TVPSSTNGFTQYICNVNHKPSNTKVDKRV EPKSCDKTHTCPCPAPEA <u>EGAPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVE</u> <u>EVHNAKTKPREEQYNSTYRVVSVLT VLVHQDWLNGKEYKCKVSNKALPS</u> <u>SIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIA</u> <u>VEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNV FSCS</u> <u>VMHEALHNHYTQKSLSLSPG</u>
79	18E10.IgG1 (VL + CL)	DIQMTQSPSSLSASVGDRVTITCRASQGISSWLAWYQQKPEKAPKSLI YAASSLQSGVPSRFRSGSGSGTDFTLTISSLQPEDFATYYCQQYNSYPY TFGQGTKLEIKRTVAAPS VFI FPPSDEQLKSGTASVVC LLN NFYPREA KVQWKVDNALQSGNSQESVTEQDSKDS TYSLSSTLTLSKADYEKHKVY ACEVTHQGLSSPVTKSFNRGEC
80	18E10 VH CDR1	SYGMH
81	18E10 VH CDR2	VIWYAGSNKYYADSVKG
82	18E10 VH CDR3	GGRIAVAFYYSDMV
83	18E10 VL CDR1	RASQGISSWLA
84	18E10 VL CDR2	AASSLQS
85	18E10 VL CDR3	QQYNSYPYT

[0264]

86	18E10 (VH + G2(C219S)) 或 18E10-IgG2-C219S	QVQLVESGGGVVQPGRSLRLSCAASGFTFSSYGMHWVRQAPGKGLEWV AVIYWAGSNKYADSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYC ARGGRIAVAFYYSDMVWGQGTITVTVSSASTKGPSVFPLAPCSRSTSES TAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSV TVPSSNFGTQTYTCNV D HKPSNTKVDKTV ERKSCVECP PCPAPPVAGP SVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHN AKTKPREEQFNSTFRVVS VLT VVHQDWLNGKEYKCKVSNKGLPAPIEK TISKAKGQPREPQVYITLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWE SNGQPENNYKTTTPMLDS DGSFFLYSKLTVDKSRWQQGNV FSCSV MHE ALHNHYTQKSLSLSPG
87	18E10 (VH + G2.g1)或 18E10-IgG2-IgG1	QVQLVESGGGVVQPGRSLRLSCAASGFTFSSYGMHWVRQAPGKGLEWV AVIYWAGSNKYADSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYC ARGGRIAVAFYYSDMVWGQGTITVTVSSASTKGPSVFPLAPCSRSTSES TAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSV TVPSSNFGTQTYTCNV D HKPSNTKVDKTV ERKCCVECP PCPAPPELLGG PSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVH NAKTKPREEQYNSTYRVVSVLT V LHQDWLNGKEYKCKVSNKALPAPIE KTISKAKGQPREPQVYITLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWE ESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNV FSCSV MHE EALHNHYTQKSLSLSPG
88	18E10 (VH + G2.g1.1)或 18E10-IgG2-IgG1.1	QVQLVESGGGVVQPGRSLRLSCAASGFTFSSYGMHWVRQAPGKGLEWV AVIYWAGSNKYADSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYC ARGGRIAVAFYYSDMVWGQGTITVTVSSASTKGPSVFPLAPCSRSTSES TAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSV TVPSSNFGTQTYTCNV D HKPSNTKVDKTV ERKCCVECP PCPAPPVAGP SVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHN AKTKPREEQYNSTYRVVSVLT V LHQDWLNGKEYKCKVSNKALPSSIEK TISKAKGQPREPQVYITLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWE SNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNV FSCSV MHE ALHNHYTQKSLSLSPG
89	18E10 (VH + G2(C219S).g1)或 18E10-IgG2-C219S-IgG1	QVQLVESGGGVVQPGRSLRLSCAASGFTFSSYGMHWVRQAPGKGLEWV AVIYWAGSNKYADSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYC ARGGRIAVAFYYSDMVWGQGTITVTVSSASTKGPSVFPLAPCSRSTSES TAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSV TVPSSNFGTQTYTCNV D HKPSNTKVDKTV ERKSCVECP PCPAPPELLGG PSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVH NAKTKPREEQYNSTYRVVSVLT V LHQDWLNGKEYKCKVSNKALPAPIE KTISKAKGQPREPQVYITLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWE ESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNV FSCSV MHE EALHNHYTQKSLSLSPG
90	18E10 (VH + G2(C219S).g1.1)或 18E10-IgG2-C219S-IgG1. 1	QVQLVESGGGVVQPGRSLRLSCAASGFTFSSYGMHWVRQAPGKGLEWV AVIYWAGSNKYADSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYC ARGGRIAVAFYYSDMVWGQGTITVTVSSASTKGPSVFPLAPCSRSTSES TAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSV TVPSSNFGTQTYTCNV D HKPSNTKVDKTV ERKSCVECP PCPAPPVAGP SVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHN AKTKPREEQYNSTYRVVSVLT V LHQDWLNGKEYKCKVSNKALPSSIEK TISKAKGQPREPQVYITLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWE SNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNV FSCSV MHE ALHNHYTQKSLSLSPG
91	3C3 (VH)	QVQLQQWAGALLKPSSETLSLTCAVYGGSFSGYYWTWIRQPPGKGLEWI GKINHS GNTNYPNPSLKS RVTISVDTSKNQFSLKLSSTVAADTAVYYCA RLGAFDAFDI W GQGTMTVTVSS
92	3C3 (VL1)	DIQMTQSPSSLSASVGDRVTITCRASQGISSWLAWYQQKPEKAPKSLI YAASSLQSGVPSRFSGSGSGTDFTLT ISSLPEDFATYYCQQYNSYPY TFGGTKLEIK
93	3C3 (VL2)	EIVLTQSPATLSLSPGERATLSCRASQGVSSYLAWYQQKPGQAPRLLI YDASNRATGIPARFSGSGPGTDFTLT ISSLEPEDFAVYYCQQRSNWHT FGQGTKEIK

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94	3C3 (全长野生型重链) 恒定区加下划线	<u>QVQLQQWGAGLLKPSETLSLTCAVYGGSFSGYYWTWIRQPPGKGLEWI</u> <u>GKINHSGNTNYPNPSLKSRTVISVDTSKNQFSLKLSVTAADTAVYYCA</u> <u>RLGAFDAFDIWGGQTMVTVSSASTKGPSVFPLAPSSKSTSGGTAALGC</u> <u>LVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPPSS</u> <u>LGTQTYICNVNHKPSNTKVDKRVKSCDKTHTCPPCPAPELLGGPSV</u> <u>FLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAK</u> <u>TKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTI</u> <u>SKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESN</u> <u>GQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFSVMHEAL</u> <u>HNHYTQKSLSLSPGK</u>
95	3C3 L1 (全长野生型轻链 1) 恒定区加下划线	<u>DIQMTQSPSSLSASVGDRVTITCRASQGISWLAHYQQKPEKAPKSLI</u> <u>YAASSLQSGVPSRFRSGSGSGTDFTLTITSSLPEDFATYYCQQYNSYPY</u> <u>TFGQGTKLEIKRTVAAPSVFIFPPSDEQLKSGTASVCLLNNFYPREA</u> <u>KVQWKVDNALQSGNSQESVTEQDSKDYSLSTLTLSKADYEKHKVY</u> <u>ACEVTHQGLSSPVTKSFNRGEC</u>
96	3C3 L2 (全长野生型轻链 2) 恒定区加下划线	<u>EIVLTQSPATLSLSPGERATLSCRASQGVSSYLAHYQQKPGQAPRLLI</u> <u>YDASNRATGIPARFSGSGPGTDFTLTITSSLPEDFATYYCQQRSNWHT</u> <u>FGQGTKLEIKRTVAAPSVFIFPPSDEQLKSGTASVCLLNNFYPREA</u> <u>VQWKVDNALQSGNSQESVTEQDSKDYSLSTLTLSKADYEKHKVYA</u> <u>CEVTHQGLSSPVTKSFNRGEC</u>
97	3C3.IgG1 (VH + IgG1)	<u>QVQLQQWGAGLLKPSETLSLTCAVYGGSFSGYYWTWIRQPPGKGLEWI</u> <u>GKINHSGNTNYPNPSLKSRTVISVDTSKNQFSLKLSVTAADTAVYYCA</u> <u>RLGAFDAFDIWGGQTMVTVSSASTKGPSVFPLAPSSKSTSGGTAALGC</u> <u>LVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPPSS</u> <u>LGTQTYICNVNHKPSNTKVDKRVKSCDKTHTCPPCPAPELLGGPSV</u> <u>FLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVE</u> <u>VHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKV</u> <u>SNKALPAPIEKTI</u> <u>SKAKGQPREPQVYTLPPSR</u> <u>REEMTKNQVSLTCLVKG</u> <u>FYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQ</u> <u>GNVFCFSVMHEALHNHYTQKSLSLSPG</u>
98	3C3.IgG1.1 (VH + IgG1.1)	<u>QVQLQQWGAGLLKPSETLSLTCAVYGGSFSGYYWTWIRQPPGKGLEWI</u> <u>GKINHSGNTNYPNPSLKSRTVISVDTSKNQFSLKLSVTAADTAVYYCA</u> <u>RLGAFDAFDIWGGQTMVTVSSASTKGPSVFPLAPSSKSTSGGTAALGC</u> <u>LVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPPSS</u> <u>LGTQTYICNVNHKPSNTKVDKRVKSCDKTHTCPPCPAPEAEGAPSV</u> <u>FLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAK</u> <u>TKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPSSIEKTI</u> <u>SKAKGQPREPQVYTLPPSR</u> <u>REEMTKNQVSLTCLVKGFYPSDIAVEWESN</u> <u>GQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFSVMHEAL</u> <u>HNHYTQKSLSLSPG</u>
99	3C3.IgG1 (VL1 + CL)	<u>DIQMTQSPSSLSASVGDRVTITCRASQGISWLAHYQQKPEKAPKSLI</u> <u>YAASSLQSGVPSRFRSGSGSGTDFTLTITSSLPEDFATYYCQQYNSYPY</u> <u>TFGQGTKLEIKRTVAAPSVFIFPPSDEQLKSGTASVCLLNNFYPREA</u> <u>KVQWKVDNALQSGNSQESVTEQDSKDYSLSTLTLSKADYEKHKVY</u> <u>ACEVTHQGLSSPVTKSFNRGEC</u>
100	3C3IgG1.2 (VL2 + CL)	<u>EIVLTQSPATLSLSPGERATLSCRASQGVSSYLAHYQQKPGQAPRLLI</u> <u>YDASNRATGIPARFSGSGPGTDFTLTITSSLPEDFATYYCQQRSNWHT</u> <u>FGQGTKLEIKRTVAAPSVFIFPPSDEQLKSGTASVCLLNNFYPREA</u> <u>VQWKVDNALQSGNSQESVTEQDSKDYSLSTLTLSKADYEKHKVYA</u> <u>CEVTHQGLSSPVTKSFNRGEC</u>
101	3C3 VH CDR1	GYWT
102	3C3 VH CDR2	KINHSGNTNYPNPSLKS
103	3C3 VH CDR3	LGAFDAFDI

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104	3C3 VL1 CDR1	RASQGISSWLA
105	3C3 VL1 CDR2	AASSLQS
106	3C3 VL1 CDR3	QQYNSYPYT
107	3C3 VL2 CDR1	RASQGVSSYLA
108	3C3 VL2 CDR2	DASNRAT
109	3C3 VL2 CDR3	QQRSNWHT
110	3C3 (VH + G2)或 3C3-IgG2	QVQLQQWGAGLLKPSETLSLTCAVYGGSFSGYYWTWIRQPPGKGLEWI GKINHSNGNTNYPNPSLKSRTISVDTSKNQFSLKLSSVTAADTAVYYCA RLGAFDAFDIWGGQTMVTVSSASTKGPSVFPLAPCSRSTSESTAALGC LVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPPSSN FGTQYTYTCNVDHKPSNTKVDKTVKCCVECPPCPAPPVAGPSVFLFP PKPKDTLMISRTPEVTCVVVDVSHEDPEVQFNWYVDGVEVHNAKTKPR EEQFNSTFRVVSIVLVHQQDWLNGKEYKCKVSNKGLPAPIEKTISKTK GQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPE NNYKTTTPMLDSDGSFFLYSKLTVDKSRWQQGNVFCSCVMHEALHNY TQKSLSLSPG
111	3C3 (VH + G2(C219S))或 3C3-IgG2-C219S	QVQLQQWGAGLLKPSETLSLTCAVYGGSFSGYYWTWIRQPPGKGLEWI GKINHSNGNTNYPNPSLKSRTISVDTSKNQFSLKLSSVTAADTAVYYCA RLGAFDAFDIWGGQTMVTVSSASTKGPSVFPLAPCSRSTSESTAALGC LVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPPSSN FGTQYTYTCNVDHKPSNTKVDKTVKCCVECPPCPAPPVAGPSVFLFP PKPKDTLMISRTPEVTCVVVDVSHEDPEVQFNWYVDGVEVHNAKTKPR EEQFNSTFRVVSIVLVHQQDWLNGKEYKCKVSNKGLPAPIEKTISKTK GQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPE NNYKTTTPMLDSDGSFFLYSKLTVDKSRWQQGNVFCSCVMHEALHNY TQKSLSLSPG
112	3C3 (VH + G2.g1)或 3C3-IgG2-IgG1	QVQLQQWGAGLLKPSETLSLTCAVYGGSFSGYYWTWIRQPPGKGLEWI GKINHSNGNTNYPNPSLKSRTISVDTSKNQFSLKLSSVTAADTAVYYCA RLGAFDAFDIWGGQTMVTVSSASTKGPSVFPLAPCSRSTSESTAALGC LVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPPSSN FGTQYTYTCNVDHKPSNTKVDKTVKCCVECPPCPAPELLGGPSVFLFP PKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPR REEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAK KGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPE ENNYKTTTPVLDSGDSFFLYSKLTVDKSRWQQGNVFCSCVMHEALHNY YTQKSLSLSPG
113	3C3 (VH + G2.g1.1)或 3C3-IgG2-IgG1.1	QVQLQQWGAGLLKPSETLSLTCAVYGGSFSGYYWTWIRQPPGKGLEWI GKINHSNGNTNYPNPSLKSRTISVDTSKNQFSLKLSSVTAADTAVYYCA RLGAFDAFDIWGGQTMVTVSSASTKGPSVFPLAPCSRSTSESTAALGC LVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPPSSN FGTQYTYTCNVDHKPSNTKVDKTVKCCVECPPCPAPPVAGPSVFLFP PKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPR EEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPSSIEKTISKAK GQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPE NNYKTTTPVLDSGDSFFLYSKLTVDKSRWQQGNVFCSCVMHEALHNY TQKSLSLSPG
114	3C3 (VH + G2(C219S).g1)或 3C3-IgG2-C219S-IgG1	QVQLQQWGAGLLKPSETLSLTCAVYGGSFSGYYWTWIRQPPGKGLEWI GKINHSNGNTNYPNPSLKSRTISVDTSKNQFSLKLSSVTAADTAVYYCA RLGAFDAFDIWGGQTMVTVSSASTKGPSVFPLAPCSRSTSESTAALGC LVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPPSSN FGTQYTYTCNVDHKPSNTKVDKTVKCCVECPPCPAPELLGGPSVFLFP PKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPR REEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAK KGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPE

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		ENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNH YTQKSLSLSPG
115	3C3 (VH + G2(C219S).g1.1)或 3C3-IgG2-C219S-IgG1.1	QVQLQQWAGLLKPKSETLSLTCAVYGGSFSGYYWTWIRQPPGKGLEWI GKINHSNGNTNYPNLSKSRVTISVDTSKNQFSLKLSVTAADTAVYYCA RLGAFDAFDIWGGTMVTVSSASTKGPSVFPLAPCSRSTSESTAALGC LVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSN FGTQTYTCNVDHKPSNTKVDKTVKSKVECPPCPAPPVAGPSVFLFP PKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPR EEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPSSIEKTIKAK GQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPE NNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNH YTQKSLSLSPG
116	2G6 (VH)	QVQLVESGGGVVQPGGSLRLSCAASGFIISDYGMHWVRQAPGKGLEWV TVIWDGSGNKFYVDSVKGRFTISRDNKNTLYLQMNSLRVEDTAVYYC ARGGRLATGHFYVMDVWGQGTITVTVSS
117	2G6 (VL)	DIQMTQSPSSLSASVGDRVTITCRASQGISWLAWYQQKPEKAPKSLI YAASSLQSGVPSRFRSGSGSDTFTLTISLQPEDFATYYCQQYNSYPY TFGGGTKLEIK
118	2G6 (全长野生型重链) 恒定区加下划线	QVQLVESGGGVVQPGGSLRLSCAASGFIISDYGMHWVRQAPGKGLEWV TVIWDGSGNKFYVDSVKGRFTISRDNKNTLYLQMNSLRVEDTAVYYC ARGGRLATGHFYVMDVWGQGTITVTVSSASTKGPSVFPLAPCSRSTSE STAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSV TVTPSSNFGTQTYTCNVDHKPSNTKVDKTVKSKVECPPCPAPPVAG PSVFLFPKPKDTLMISRTPEVTCVVVDVSHEDPEVFQFNWYVDGVEVH NAKTKPREEQFNSTFRVSVLTVVHQDWLNGKEYKCKVSNKGLPAPIE KTISKTKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEW ESNGQPENNYKTTPMLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMH EALHNHNTQKSLSLSPGK
119	2G6 (全长野生型轻链) 恒定区加下划线	DIQMTQSPSSLSASVGDRVTITCRASQGISWLAWYQQKPEKAPKSLI YAASSLQSGVPSRFRSGSGSDTFTLTISLQPEDFATYYCQQYNSYPY TFGGGTKLEIKRTVAAPSVFIFPPSDEQLKSGTASVVCCLNNFYPREA KVQWKVDNALQSGNSQESVTEQDSKSTYLSSTLTLSKADYEKHKVY ACEVTHQGLSSPVTKSFNRGEC
120	2G6.IgG1 (VH + IgG1)	QVQLVESGGGVVQPGGSLRLSCAASGFIISDYGMHWVRQAPGKGLEWV TVIWDGSGNKFYVDSVKGRFTISRDNKNTLYLQMNSLRVEDTAVYYC ARGGRLATGHFYVMDVWGQGTITVTVSSASTKGPSVFPLAPSSKSTSG GTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSV TVTPSSSLGTQTYICNVNHKPSNTKVDKRVKPKSCDKTHTCPPCPAPE LLGGPSVFLF PPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVE VHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKV SNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKG FYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQ GNVFSCSVMHEALHNHNTQKSLSLSPG
121	2G6.IgG1.1 (VH + IgG1.1)	QVQLVESGGGVVQPGGSLRLSCAASGFIISDYGMHWVRQAPGKGLEWV TVIWDGSGNKFYVDSVKGRFTISRDNKNTLYLQMNSLRVEDTAVYYC ARGGRLATGHFYVMDVWGQGTITVTVSSASTKGPSVFPLAPSSKSTSG GTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSV TVTPSSSLGTQTYICNVNHKPSNTKVDKRVKPKSCDKTHTCPPCPAPE AEGAPSVFLFPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDG VEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALP SSIEKTIKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDI AVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSC SVMHEALHNHNTQKSLSLSPG
122	2G6.IgG1 (VL + CL)	DIQMTQSPSSLSASVGDRVTITCRASQGISWLAWYQQKPEKAPKSLI YAASSLQSGVPSRFRSGSGSDTFTLTISLQPEDFATYYCQQYNSYPY TFGGGTKLEIKRTVAAPSVFIFPPSDEQLKSGTASVVCCLNNFYPREA KVQWKVDNALQSGNSQESVTEQDSKSTYLSSTLTLSKADYEKHKVY ACEVTHQGLSSPVTKSFNRGEC

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123	2G6 VH CDR1	DYGMH
124	2G6 VH CDR2	VIWYDGSNKFYVDSVKG
125	2G6 VH CDR3	GGRLATGHFYVMDV
126	2G6 VL CDR1	RASQGISSWLA
127	2G6 VL CDR2	AASSLQS
128	2G6 VL CDR3	QQYNSYPYT
129	2G6 (VH + G2)或 2G6-IgG2	<u>QVQLVESGGGVVQPGGSLRLSCAASG</u> <u>FILSDYGMHWVRQAPGKGLEWV</u> <u>TVIWDGSNKFYVDSVKGRFTISRDN</u> <u>SKNTLYLQMNSLRVEDTAVYYC</u> <u>ARGGRLATGHFYVMDVWGQGT</u> <u>TVTVSSASTKGPSVFPLAPCSRSTSE</u> <u>STAALGCLVKDYFPEPVT</u> <u>SWNSGALTSGVHTFPAVLQSSGLYSLSSV</u> <u>VTVPSSNFGTQTYTCNV</u> <u>DHKPSNTKVDKTV</u> <u>ERKCCVECP</u> <u>PCPAPPVAG</u> <u>PSVFLFPPKPKDTLMISRTPEV</u> <u>TCVVVDVSHEDPEVQFNWYVDGVEVH</u> <u>NAKTKPREEQFNSTFRV</u> <u>SVLTVVHQD</u> <u>WLN</u> <u>KEYKCKV</u> <u>SNKGLP</u> <u>APIE</u> <u>KTISKAKGQPREPQVY</u> <u>TLPPSREEMTKNQVSLTCLVKGF</u> <u>YPSDIAVEW</u> <u>ESNGQPENNYKTT</u> <u>PPMLDS</u> <u>DGSFFLYSKLTVDKSRWQQGNV</u> <u>FSCVMH</u> <u>EALHNHYTQKSLSLSPG</u>
130	2G6 (VH + G2(C219S))或 2G6-IgG2-C219S	<u>QVQLVESGGGVVQPGGSLRLSCAASG</u> <u>FILSDYGMHWVRQAPGKGLEWV</u> <u>TVIWDGSNKFYVDSVKGRFTISRDN</u> <u>SKNTLYLQMNSLRVEDTAVYYC</u> <u>ARGGRLATGHFYVMDVWGQGT</u> <u>TVTVSSASTKGPSVFPLAPCSRSTSE</u> <u>STAALGCLVKDYFPEPVT</u> <u>SWNSGALTSGVHTFPAVLQSSGLYSLSSV</u> <u>VTVPSSNFGTQTYTCNV</u> <u>DHKPSNTKVDKTV</u> <u>ERKCCVECP</u> <u>PCPAPPVAG</u> <u>PSVFLFPPKPKDTLMISRTPEV</u> <u>TCVVVDVSHEDPEVQFNWYVDGVEVH</u> <u>NAKTKPREEQFNSTFRV</u> <u>SVLTVVHQD</u> <u>WLN</u> <u>KEYKCKV</u> <u>SNKGLP</u> <u>APIE</u> <u>KTISKAKGQPREPQVY</u> <u>TLPPSREEMTKNQVSLTCLVKGF</u> <u>YPSDIAVEW</u> <u>ESNGQPENNYKTT</u> <u>PPMLDS</u> <u>DGSFFLYSKLTVDKSRWQQGNV</u> <u>FSCVMH</u> <u>EALHNHYTQKSLSLSPG</u>
131	2G6 (VH + G2.g1)或 2G6-IgG2-IgG1	<u>QVQLVESGGGVVQPGGSLRLSCAASG</u> <u>FILSDYGMHWVRQAPGKGLEWV</u> <u>TVIWDGSNKFYVDSVKGRFTISRDN</u> <u>SKNTLYLQMNSLRVEDTAVYYC</u> <u>ARGGRLATGHFYVMDVWGQGT</u> <u>TVTVSSASTKGPSVFPLAPCSRSTSE</u> <u>STAALGCLVKDYFPEPVT</u> <u>SWNSGALTSGVHTFPAVLQSSGLYSLSSV</u> <u>VTVPSSNFGTQTYTCNV</u> <u>DHKPSNTKVDKTV</u> <u>ERKCCVECP</u> <u>PCPAPELLG</u> <u>GPSVFLFPPKPKDTLMISRTPEV</u> <u>TCVVVDVSHEDPEVKFNWYVDGVEV</u> <u>HNAKTKPREEQYNSTYRV</u> <u>SVLTVLHQD</u> <u>WLN</u> <u>KEYKCKV</u> <u>SNKALP</u> <u>API</u> <u>EKTISKAKGQPREPQVY</u> <u>TLPPSREEMTKNQVSLTCLVKGF</u> <u>YPSDIAVE</u> <u>WESNGQPENNYKTT</u> <u>PPVLD</u> <u>SDGSFFLYSKLTVDKSRWQQGNV</u> <u>FSCVM</u> <u>HEALHNHYTQKSLSLSPG</u>
132	2G6 (VH + G2.g1.1)或 2G6-IgG2-IgG1.1	<u>QVQLVESGGGVVQPGGSLRLSCAASG</u> <u>FILSDYGMHWVRQAPGKGLEWV</u> <u>TVIWDGSNKFYVDSVKGRFTISRDN</u> <u>SKNTLYLQMNSLRVEDTAVYYC</u> <u>ARGGRLATGHFYVMDVWGQGT</u> <u>TVTVSSASTKGPSVFPLAPCSRSTSE</u> <u>STAALGCLVKDYFPEPVT</u> <u>SWNSGALTSGVHTFPAVLQSSGLYSLSSV</u> <u>VTVPSSNFGTQTYTCNV</u> <u>DHKPSNTKVDKTV</u> <u>ERKCCVECP</u> <u>PCPAPPVAG</u> <u>PSVFLFPPKPKDTLMISRTPEV</u> <u>TCVVVDVSHEDPEVKFNWYVDGVEVH</u> <u>NAKTKPREEQYNSTYRV</u> <u>SVLTVLHQD</u> <u>WLN</u> <u>KEYKCKV</u> <u>SNKALP</u> <u>SSIE</u> <u>KTISKAKGQPREPQVY</u> <u>TLPPSREEMTKNQVSLTCLVKGF</u> <u>YPSDIAVEW</u> <u>ESNGQPENNYKTT</u> <u>PPVLD</u> <u>SDGSFFLYSKLTVDKSRWQQGNV</u> <u>FSCVMH</u> <u>EALHNHYTQKSLSLSPG</u>
133	2G6 (VH + G2(C219S).g1)或 2G6-IgG2-C219S-IgG1	<u>QVQLVESGGGVVQPGGSLRLSCAASG</u> <u>FILSDYGMHWVRQAPGKGLEWV</u> <u>TVIWDGSNKFYVDSVKGRFTISRDN</u> <u>SKNTLYLQMNSLRVEDTAVYYC</u> <u>ARGGRLATGHFYVMDVWGQGT</u> <u>TVTVSSASTKGPSVFPLAPCSRSTSE</u> <u>STAALGCLVKDYFPEPVT</u> <u>SWNSGALTSGVHTFPAVLQSSGLYSLSSV</u> <u>VTVPSSNFGTQTYTCNV</u> <u>DHKPSNTKVDKTV</u> <u>ERKCCVECP</u> <u>PCPAPELLG</u> <u>GPSVFLFPPKPKDTLMISRTPEV</u> <u>TCVVVDVSHEDPEVKFNWYVDGVEV</u> <u>HNAKTKPREEQYNSTYRV</u> <u>SVLTVLHQD</u> <u>WLN</u> <u>KEYKCKV</u> <u>SNKALP</u> <u>API</u> <u>EKTISKAKGQPREPQVY</u> <u>TLPPSREEMTKNQVSLTCLVKGF</u> <u>YPSDIAVE</u>

[0269]

		WESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVM HEALHNHYTQKSLSLSPG
134	2G6 (VH + G2(C219S).g1.1)或 2G6-IgG2-C219S-IgG1.1	QVQLVESGGGVVQPGRSLRLSCTASGFTFSSYGMQWVRQAPGKGLEWV TVIWDGSGNKFYVDSVKGRTTISRDNSTNTLYLQMNSLRAEDTAVYYC ARGGRLATGHFYVMDVWGQGTITVTVSSASTKGPSVFPLAPCSRSTSE STAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSV VTVPSSNFGTQTYTCNVDPKPSNTKVDKTKVERKSCVECPCCPAPPVAG PSVFLFPPKPKDTLMI SRTEPVTCTVVDVSHEDPEVKFNWYVDGVEVH NAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPSSIE KTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEW ESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMH EALHNHYTQKSLSLSPG
135	8A6 (VH)	QVQLVESGGGVVQPGRSLRLSCTASGFTFSSYGMQWVRQAPGKGLEWV AVIWEYEGSNKYYADSVKGRFTISRDNSTNTLYLQMNSLRAEDTAVYYC ARGGLMVRGLFYYGMDVWGQGTITVTVSS
136	8A6 (VL)	AIQLTQSPSSLSASVGDRTITCRASQGISSALAWYQQKPGKAPKFLI YDASSLESQVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQFNISYPY TFGGGTKLEIK
137	8A6 (全长野生型重链) 恒定区加下划线	QVQLVESGGGVVQPGRSLRLSCTASGFTFSSYGMQWVRQAPGKGLEWV AVIWEYEGSNKYYADSVKGRFTISRDNSTNTLYLQMNSLRAEDTAVYYC ARGGLMVRGLFYYGMDVWGQGTITVTVSSASTKGPSVFPLAPCSRSTSE STAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSV VTVPSSNFGTQTYTCNVDPKPSNTKVDKTKVERKSCVECPCCPAPPVAG PSVFLFPPKPKDTLMI SRTEPVTCTVVDVSHEDPEVKFNWYVDGVEVH NAKTKPREEQYNSTYRVVSVLTVVHQDWLNGKEYKCKVSNKGLPAPIE KTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEW ESNGQPENNYKTTTPMLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMH EALHNHYTQKSLSLSPGK
138	8A6 (全长野生型轻链) 恒定区加下划线	AIQLTQSPSSLSASVGDRTITCRASQGISSALAWYQQKPGKAPKFLI YDASSLESQVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQFNISYPY TFGGGTKLEIKRTVAAPSVFIFPPSDEQLKSGTASVCLLNNFYPREA KVQWKVDNALQSGNSQESVTEQDSKDSYSTLSSTLTLSKADYEKHKVY ACEVTHQGLSSPVTKSFNRGEC
139	8A6.IgG1 (VH + IgG1)	QVQLVESGGGVVQPGRSLRLSCTASGFTFSSYGMQWVRQAPGKGLEWV AVIWEYEGSNKYYADSVKGRFTISRDNSTNTLYLQMNSLRAEDTAVYYC ARGGLMVRGLFYYGMDVWGQGTITVTVSSASTKGPSVFPLAPSSKSTSG GTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSV VTVPSSSLGTQTYICNVNPKPSNTKVDKRVKPKSCDKHTCTCPCPAPE LLGPGSVFLFPPKPKDTLMI SRTEPVTCTVVDVSHEDPEVKFNWYVDG VEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALP APIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDI AVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFSC SVMHEALHNHYTQKSLSLSPG
140	8A6.IgG1.1 (VH + IgG1.1)	QVQLVESGGGVVQPGRSLRLSCTASGFTFSSYGMQWVRQAPGKGLEWV AVIWEYEGSNKYYADSVKGRFTISRDNSTNTLYLQMNSLRAEDTAVYYC ARGGLMVRGLFYYGMDVWGQGTITVTVSSASTKGPSVFPLAPSSKSTSG GTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSV VTVPSSSLGTQTYICNVNPKPSNTKVDKRVKPKSCDKHTCTCPCPAPE AEGAPSVFLFPPKPKDTLMI SRTEPVTCTVVDVSHEDPEVKFNWYVDG VEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALP SSIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDI AVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFSC SVMHEALHNHYTQKSLSLSPG
141	8A6.IgG1 (VL + CL)	AIQLTQSPSSLSASVGDRTITCRASQGISSALAWYQQKPGKAPKFLI YDASSLESQVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQFNISYPY TFGGGTKLEIKRTVAAPSVFIFPPSDEQLKSGTASVCLLNNFYPREA KVQWKVDNALQSGNSQESVTEQDSKDSYSTLSSTLTLSKADYEKHKVY ACEVTHQGLSSPVTKSFNRGEC

[0270]

142	8A6 VH CDR1	SYGMQ
143	8A6 VH CDR2	VIWYEGSNKYADSVKG
144	8A6 VH CDR3	GGLMVRGLFYGYMDV
145	8A6 VL CDR1	RASQGISSALA
146	8A6 VL CDR2	DASSLES
147	8A6 VL CDR3	QQFNSTPYT
148	8A6 (VH + G2(C219S))或 8A6-IgG2-C219S	QVQLVESGGGVVQPGRSLRLSCTASGFTFSSYGMQWVRQAPGKGLEWV AVIWEYEGSNKYADSVKGRFTISRENSKNTLYLQMNSLRAEDTAVYYC ARGGLMVRGLFYGYMDVWGQGTITVTVSSASTKGPSVFPLAPCSRSTSE STAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSV VTPSSNFGTQTYTCNVDHKPSNTKVDKTKVERKSCVECPFCPPAVVAG PSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVQFNWYVDGVEVH NAKTKPREEQFNSTFRVSVLTIVHQQDWLNGKEYCKVSNKGLPAPIE KTISKAKGQPREPQVYITLPPSREEMTKNQVSLTCLVKGFYPSDIAVEW ESNGQPENNYKTTTPMLDSGDSFFLYSKLTVDKSRWQQGNVFCFSVMH EALHNHYTQKSLSLSPG
149	8A6 (VH + G2.g1)或 8A6 -IgG2-IgG1	QVQLVESGGGVVQPGRSLRLSCTASGFTFSSYGMQWVRQAPGKGLEWV AVIWEYEGSNKYADSVKGRFTISRENSKNTLYLQMNSLRAEDTAVYYC ARGGLMVRGLFYGYMDVWGQGTITVTVSSASTKGPSVFPLAPCSRSTSE STAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSV VTPSSNFGTQTYTCNVDHKPSNTKVDKTKVERKSCVECPFCPAPELLG GPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVH HNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYCKVSNKALPAPI EKTISKAKGQPREPQVYITLPPSREEMTKNQVSLTCLVKGFYPSDIAVE WESNGQPENNYKTTTPVLDSGDSFFLYSKLTVDKSRWQQGNVFCFSVMH EALHNHYTQKSLSLSPG
150	8A6 (VH + G2.g1.1)或 8A6 -IgG2-IgG1.1	QVQLVESGGGVVQPGRSLRLSCTASGFTFSSYGMQWVRQAPGKGLEWV AVIWEYEGSNKYADSVKGRFTISRENSKNTLYLQMNSLRAEDTAVYYC ARGGLMVRGLFYGYMDVWGQGTITVTVSSASTKGPSVFPLAPCSRSTSE STAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSV VTPSSNFGTQTYTCNVDHKPSNTKVDKTKVERKSCVECPFCPPAVVAG PSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVH NAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYCKVSNKALPSSIE KTISKAKGQPREPQVYITLPPSREEMTKNQVSLTCLVKGFYPSDIAVEW ESNGQPENNYKTTTPVLDSGDSFFLYSKLTVDKSRWQQGNVFCFSVMH EALHNHYTQKSLSLSPG
151	8A6 (VH + G2(C219S).g1)或 8A6-IgG2-C219S-IgG1	QVQLVESGGGVVQPGRSLRLSCTASGFTFSSYGMQWVRQAPGKGLEWV AVIWEYEGSNKYADSVKGRFTISRENSKNTLYLQMNSLRAEDTAVYYC ARGGLMVRGLFYGYMDVWGQGTITVTVSSASTKGPSVFPLAPCSRSTSE STAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSV VTPSSNFGTQTYTCNVDHKPSNTKVDKTKVERKSCVECPFCPAPELLG GPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVH HNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYCKVSNKALPAPI EKTISKAKGQPREPQVYITLPPSREEMTKNQVSLTCLVKGFYPSDIAVE WESNGQPENNYKTTTPVLDSGDSFFLYSKLTVDKSRWQQGNVFCFSVMH EALHNHYTQKSLSLSPG
152	8A6 (VH + G2(C219S).g1.1)或 8A6-IgG2-C219S-IgG1.1	QVQLVESGGGVVQPGRSLRLSCTASGFTFSSYGMQWVRQAPGKGLEWV AVIWEYEGSNKYADSVKGRFTISRENSKNTLYLQMNSLRAEDTAVYYC ARGGLMVRGLFYGYMDVWGQGTITVTVSSASTKGPSVFPLAPCSRSTSE STAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSV VTPSSNFGTQTYTCNVDHKPSNTKVDKTKVERKSCVECPFCPPAVVAG PSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVH NAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYCKVSNKALPSSIE KTISKAKGQPREPQVYITLPPSREEMTKNQVSLTCLVKGFYPSDIAVEW

[0271]

		ESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFSQSVMH EALHNHYTQKSLSLSPG
153	9G7 (VH)	EVQLVESGGGLVLPKGGSLRLSCAASGFTFSTVWMSWVRQAPGKGLEWV GRIKSKTDGGTTDYAAPVKGRFTISRDDSKNTLYLQMNSLHTEDTAVY YCTTGQLIPYSYYGMDVWGQGTSTVTVSS
154	9G7 (VL1)	EIVLTQSPGTLSLSPGERATLSCRASQSVSSSYLAWYQQKPGQAPRLL IYGASSRATGIPDRFSGSGSGTDFTLTISRLEPEDFAVYYCQQYGSSP WTFGQGTKVEIK
155	9G7 (VL2)	EIVLTQSPGTLSLSPGERATLSCRASQSVTSSSYLAWYQQKPGQAPRLL IYGASSRATGIPERFSGSGSGTDFTLTISRLEPEDFAVYYCQQYGSSP ITFGQGTREIK
156	9G7 (全长野生型重链) 恒定区加下划线	EVQLVESGGGLVLPKGGSLRLSCAASGFTFSTVWMSWVRQAPGKGLEWV GRIKSKTDGGTTDYAAPVKGRFTISRDDSKNTLYLQMNSLHTEDTAVY YCTTGQLIPYSYYGMDVWGQGTSTVTVSSASTKGPSVFPLAPCSRSTS <u>ESTAALGCLVKDYFPEPTVSWNSGALTSGVHTFPAVLQSSGLYSLSS</u> <u>VVTVFSSSLGTQTYICNVNHPKPSNTKVDKRVESKYGPCCPSCPAPPEFL</u> <u>GGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSDPEVQFNWYVDGVE</u> <u>VHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSS</u> <u>IEKTIKAKAGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAV</u> <u>EWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQEGNVFSCSV</u> <u>MHEALHNHYTQKSLSLSLGK</u>
157	9G7 L2 (全长野生型轻链 2) 恒定区加下划线	EIVLTQSPGTLSLSPGERATLSCRASQSVTSSSYLAWYQQKPGQAPRLL IYGASSRATGIPERFSGSGSGTDFTLTISRLEPEDFAVYYCQQYGSSP ITFGQGTREIKRTVAAPSVFIFPPSDEQLKSGTASVCLLNNFYPRE <u>AKVQWKVDNALQSGNSQESVTEQDSKDSSTYSLSSTLTLSKADYEKHKV</u> <u>YACEVTHQGLSSPVTKSFNRGEC</u>
158	9G7.IgG1 (VH + IgG1)	EVQLVESGGGLVLPKGGSLRLSCAASGFTFSTVWMSWVRQAPGKGLEWV GRIKSKTDGGTTDYAAPVKGRFTISRDDSKNTLYLQMNSLHTEDTAVY YCTTGQLIPYSYYGMDVWGQGTSTVTVSSASTKGPSVFPLAPSSKSTS GGTAALGCLVKDYFPEPTVSWNSGALTSGVHTFPAVLQSSGLYSLSS VVTVFSSSLGTQTYICNVNHPKPSNTKVDKRVESKSCDKTHTCPPCPAP ELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVD GVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKAL PAPIEKTIKAKAGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSD IAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFS CSVMHEALHNHYTQKSLSLSPG
159	9G7.IgG1.1 (VH + IgG1.1)	EVQLVESGGGLVLPKGGSLRLSCAASGFTFSTVWMSWVRQAPGKGLEWV GRIKSKTDGGTTDYAAPVKGRFTISRDDSKNTLYLQMNSLHTEDTAVY YCTTGQLIPYSYYGMDVWGQGTSTVTVSSASTKGPSVFPLAPSSKSTS GGTAALGCLVKDYFPEPTVSWNSGALTSGVHTFPAVLQSSGLYSLSS VVTVFSSSLGTQTYICNVNHPKPSNTKVDKRVESKSCDKTHTCPPCPAP EAEGAPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVD GVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKAL PSSIIEKTIKAKAGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSD IAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFS CSVMHEALHNHYTQKSLSLSPG
160	9G7.IgG1 (VL1 + CL)	EIVLTQSPGTLSLSPGERATLSCRASQSVSSSYLAWYQQKPGQAPRLL IYGASSRATGIPDRFSGSGSGTDFTLTISRLEPEDFAVYYCQQYGSSP WTFGQGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVCLLNNFYPRE AKVQWKVDNALQSGNSQESVTEQDSKDSSTYSLSSTLTLSKADYEKHKV YACEVTHQGLSSPVTKSFNRGEC
161	9G7.IgG1.2 (VL2 + CL)	EIVLTQSPGTLSLSPGERATLSCRASQSVTSSSYLAWYQQKPGQAPRLL IYGASSRATGIPERFSGSGSGTDFTLTISRLEPEDFAVYYCQQYGSSP ITFGQGTREIKRTVAAPSVFIFPPSDEQLKSGTASVCLLNNFYPRE AKVQWKVDNALQSGNSQESVTEQDSKDSSTYSLSSTLTLSKADYEKHKV YACEVTHQGLSSPVTKSFNRGEC

[0272]

162	9G7 VH CDR1	TVWMS
163	9G7 VH CDR2	RIKSKTDGGTTDYAAPVKG
164	9G7 VH CDR3	GQLIPYSYYYGMDV
165	9G7 VL1 CDR1	RASQSVSSSYLA
166	9G7 VL1 CDR2	GASSRAT
167	9G7 VL1 CDR3	QQYGSSPWT
168	9G7 VL2 CDR1	RASQSVTSSSYLA
169	9G7 VL2 CDR2	GASSRAT
170	9G7 VL2 CDR3	QQYGSSPIT
171	9G7 (VH + G2)或 9G7-IgG2	EVQLVESGGGLVLPKPGGSLRLSCAASGFTFSTVWMSWVRQAPGKGLEWV GRIKSKTDGGTTDYAAPVKGRFTISRDDSKNTLYLQMNSLHTEDTAVY YCTTGQLIPYSYYYGMDVWGQGTSTVTVSSASTKGPSVFPLAPCSRSTS ESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSS VVTVPSSNFGTQTYTCNVDHKPSNTKVDKTVKCCVECPPCPAPPVA GPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVQFNWYVDGVEV HNAKTKPREEQFNSTFRVVSIVLTVVHQDWLNGKEYCKVSNKGLPAPI EKTISKTKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVE WESNGQPENNYKTTTPMLDSGGSFFLYSKLTVDKSRWQQGNVFCFSVM HEALHNHYTQKSLSLSPG
172	9G7 (VH + G2(C219S))或 9G7-IgG2-C219S	EVQLVESGGGLVLPKPGGSLRLSCAASGFTFSTVWMSWVRQAPGKGLEWV GRIKSKTDGGTTDYAAPVKGRFTISRDDSKNTLYLQMNSLHTEDTAVY YCTTGQLIPYSYYYGMDVWGQGTSTVTVSSASTKGPSVFPLAPCSRSTS ESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSS VVTVPSSNFGTQTYTCNVDHKPSNTKVDKTVKCCVECPPCPAPPVA GPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVQFNWYVDGVEV HNAKTKPREEQFNSTFRVVSIVLTVVHQDWLNGKEYCKVSNKGLPAPI EKTISKTKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVE WESNGQPENNYKTTTPMLDSGGSFFLYSKLTVDKSRWQQGNVFCFSVM HEALHNHYTQKSLSLSPG
173	9G7 (VH + G2.g1)或 9G7-IgG2-IgG1	EVQLVESGGGLVLPKPGGSLRLSCAASGFTFSTVWMSWVRQAPGKGLEWV GRIKSKTDGGTTDYAAPVKGRFTISRDDSKNTLYLQMNSLHTEDTAVY YCTTGQLIPYSYYYGMDVWGQGTSTVTVSSASTKGPSVFPLAPCSRSTS ESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSS VVTVPSSNFGTQTYTCNVDHKPSNTKVDKTVKCCVECPPCPAPELL GGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVE VHNAKTKPREEQYNSTYRVVSIVLTVLHQDWLNGKEYCKVSNKALPAP TEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAV EWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFSVM MHEALHNHYTQKSLSLSPG
174	9G7 (VH + G2.g1.1)或 9G7-IgG2-IgG1.1	EVQLVESGGGLVLPKPGGSLRLSCAASGFTFSTVWMSWVRQAPGKGLEWV GRIKSKTDGGTTDYAAPVKGRFTISRDDSKNTLYLQMNSLHTEDTAVY YCTTGQLIPYSYYYGMDVWGQGTSTVTVSSASTKGPSVFPLAPCSRSTS ESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSS VVTVPSSNFGTQTYTCNVDHKPSNTKVDKTVKCCVECPPCPAPPVA GPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEV HNAKTKPREEQYNSTYRVVSIVLTVLHQDWLNGKEYCKVSNKALPSSI EKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVE WESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFSVM HEALHNHYTQKSLSLSPG
175	9G7 (VH +	EVQLVESGGGLVLPKPGGSLRLSCAASGFTFSTVWMSWVRQAPGKGLEWV GRIKSKTDGGTTDYAAPVKGRFTISRDDSKNTLYLQMNSLHTEDTAVY

[0273]

	G2(C219S).g1)或 9G7-IgG2-C219S-IgG1	<u>YCTTGQLIPYSYYYGMDVWGQGTSVTVSSASTKGPSVFPLAPCSRSTS</u> <u>ESTAALGCLVKDYFPEPTVSWNSGALTSGVHTFPAVLQSSGLYSLSS</u> <u>VVTVPSNFGTQTYTCNVDPKPSNTKVDKVERKSCVECPCCPAPELL</u> <u>GGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVE</u> <u>VHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAP</u> <u>IEKTIISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAV</u> <u>EWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSCSV</u> <u>MHEALHNHYTQKSLSLSPG</u>
176	9G7 (VH + G2(C219S).g1.1)或 9G7-IgG2-C219S-IgG1.1	<u>EVQLVESGGGLVLPKGGSLRLSCAASGFTFSTVWMSWVRQAPGKGLEWV</u> <u>GRIKSKTDGGTTDYAAPVKGRFTISRDDSKNTLYLQMNSLHTEDTAVY</u> <u>YCTTGQLIPYSYYYGMDVWGQGTSVTVSSASTKGPSVFPLAPCSRSTS</u> <u>ESTAALGCLVKDYFPEPTVSWNSGALTSGVHTFPAVLQSSGLYSLSS</u> <u>VVTVPSNFGTQTYTCNVDPKPSNTKVDKVERKSCVECPCCPAFPPVA</u> <u>GPVFGFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEV</u> <u>HNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPSSI</u> <u>EKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVE</u> <u>WESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSCVM</u> <u>HEALHNHYTQKSLSLSPG</u>
177	9G7 L1 (全长野生型轻链 1) 恒定区加下划线	<u>EIVLTQSPGTLSLSPGERATLSCRASQSVSSSYLAWYQQKPGQAPRLI</u> <u>IYGASSRATGIPDRFSGSGSGTDFTLTISRLEPEDFAVYYCQQYGSSP</u> <u>WTFGQGTKEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPRE</u> <u>AKVQWKVDNALQSGNSQESVTEQDSKDSYSTLSSTLTLSKADYEKHKV</u> <u>YACEVTHQGLSPVTKSFNRGEC</u>
178	14E3 (VH)	<u>QVQLQQWAGALLKPSSETLSLTCAVYGGSFSGYYWSWIRQPPGKGLEWI</u> <u>GEINHSNGNTYYPNLSKSRVTISVDTSKNQSLSLSSVTAADTAVYYCA</u> <u>RFGSNDADFIDWGQGTMTVSS</u>
179	14E3 (VL)	<u>DIQMTQSPSSLSASVGDRTITCRASQGISWLAHWYQQKPEKAPKSLI</u> <u>YAASSLQSGVPSRFRSGSGSGTDFTLTISLQPEDFATYYCQYNSYPP</u> <u>TFGQGTKEIK</u>
180	14E3 (全长野生型重链) 恒定区加下划线	<u>QVQLQQWAGALLKPSSETLSLTCAVYGGSFSGYYWSWIRQPPGKGLEWI</u> <u>GEINHSNGNTYYPNLSKSRVTISVDTSKNQSLSLSSVTAADTAVYYCA</u> <u>RFGSNDADFIDWGQGTMTVSSASTKGPSVFPLAPSSKSTSGGTAALGC</u> <u>LVKDYFPEPTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSS</u> <u>LGTQTYICNVNHKPSNTKVDKRVPEPKSCDKHTCPCPAPELLGGPSV</u> <u>FLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAK</u> <u>TKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKT</u> <u>ISKAKGQPREPQVYTLPPSDELTKNQVSLTCLVKGFYPSDIAVEWESN</u> <u>GQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSCVMHEAL</u> <u>HNHYTQKSLSLSPGK</u>
181	14E3 (全长野生型轻链) 恒定区加下划线	<u>DIQMTQSPSSLSASVGDRTITCRASQGISWLAHWYQQKPEKAPKSLI</u> <u>YAASSLQSGVPSRFRSGSGSGTDFTLTISLQPEDFATYYCQYNSYPP</u> <u>TFGQGTKEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA</u> <u>KVQWKVDNALQSGNSQESVTEQDSKDSYSTLSSTLTLSKADYEKHKVY</u> <u>ACEVTHQGLSPVTKSFNRGEC</u>
182	14E3.IgG1 (VH + IgG1)	<u>QVQLQQWAGALLKPSSETLSLTCAVYGGSFSGYYWSWIRQPPGKGLEWI</u> <u>GEINHSNGNTYYPNLSKSRVTISVDTSKNQSLSLSSVTAADTAVYYCA</u> <u>RFGSNDADFIDWGQGTMTVSSASTKGPSVFPLAPSSKSTSGGTAALGC</u> <u>LVKDYFPEPTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSS</u> <u>LGTQTYICNVNHKPSNTKVDKRVPEPKSCDKHTCPCPAPELLGGPSV</u> <u>FLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVE</u> <u>VHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKV</u> <u>SNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKG</u> <u>FYPDSIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQ</u> <u>GNVFCSCVMHEALHNHYTQKSLSLSPG</u>
183	14E3.IgG1.1 (VH + IgG1.1)	<u>QVQLQQWAGALLKPSSETLSLTCAVYGGSFSGYYWSWIRQPPGKGLEWI</u> <u>GEINHSNGNTYYPNLSKSRVTISVDTSKNQSLSLSSVTAADTAVYYCA</u> <u>RFGSNDADFIDWGQGTMTVSSASTKGPSVFPLAPSSKSTSGGTAALGC</u> <u>LVKDYFPEPTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSS</u>

[0274]

		LGTQTYICNVNHNKPSNTKVDKRVKPKSCDKTHTCPPCPAPEAEGAPSV FLFPKPKDITLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAK TKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPSSIEKTI SKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESN GQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEAL HNHYTQKSLSLSPG
184	14E3.IgG1 (VL + CL)	DIQMTQSPSSLSASVGDRVTITCRASQGISSWLAWYQQKPEKAPKSLI YAASSLQSGVPSRFSGSGSGTDFTLTITSSLPEDFATYYCQQYNSYPP TFGGQGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVCLLNNFYPREA KVQWKVDNALQSGNSQESVTEQDSKDSYSTLSSTLTLSKADYEKHKVY ACEVTHQGLSSPVTKSFNRGEC
185	14E3 VH CDR1	GYYS
186	14E3 VH CDR2	EINHSNGNTYYNPSLKS
187	14E3 VH CDR3	FGSNDAFDI
188	14E3 VL CDR1	RASQGISSWLA
189	14E3 VL CDR2	AASSLQS
190	14E3 VL CDR3	QQYNSYPPT
191	14E3 (VH + G2)或 14E3-IgG2	QVQLQQWGAGLLKPSETLSLTCAVYGGSFSGYYWSWIRQPPGKGLEWI GEINHSNGNTYYNPSLKSRTISVDTSKNQLSLKSSVTAADTAVYYCA RFGSNDAFDIWGQGMVTVSSASTKGPSVFPLAPCSRSTSESTAALGC LVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVTPSSN FGTQTYTCNVDHKPSNTKVDKTVKCCVECPPCPAPPVAGPSVFLFP PKPKDITLMISRTPEVTCVVVDVSHEDPEVQFNWYVDGVEVHNAKTKPR EEQFNSTFRVSVSLTVVHQDWLNGKEYKCKVSNKGLPAPIEKTISKTK QQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPE NNYKTTTPMLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHY TQKSLSLSPG
192	14E3 (VH + G2(C219S)) 或 14E3-IgG2-C219S	QVQLQQWGAGLLKPSETLSLTCAVYGGSFSGYYWSWIRQPPGKGLEWI GEINHSNGNTYYNPSLKSRTISVDTSKNQLSLKSSVTAADTAVYYCA RFGSNDAFDIWGQGMVTVSSASTKGPSVFPLAPCSRSTSESTAALGC LVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVTPSSN FGTQTYTCNVDHKPSNTKVDKTVKCCVECPPCPAPPVAGPSVFLFP PKPKDITLMISRTPEVTCVVVDVSHEDPEVQFNWYVDGVEVHNAKTKPR EEQFNSTFRVSVSLTVVHQDWLNGKEYKCKVSNKGLPAPIEKTISKTK QQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPE NNYKTTTPMLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHY TQKSLSLSPG
193	14E3 (VH + G2.g1)或 14E3-IgG2-IgG1	QVQLQQWGAGLLKPSETLSLTCAVYGGSFSGYYWSWIRQPPGKGLEWI GEINHSNGNTYYNPSLKSRTISVDTSKNQLSLKSSVTAADTAVYYCA RFGSNDAFDIWGQGMVTVSSASTKGPSVFPLAPCSRSTSESTAALGC LVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVTPSSN FGTQTYTCNVDHKPSNTKVDKTVKCCVECPPCPAPELLGGPSVFLF PPKPKDITLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKP REEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKA KGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPE ENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNH YTQKSLSLSPG
194	14E3 (VH + G2.g1.1)或 14E3-IgG2-IgG1.1	QVQLQQWGAGLLKPSETLSLTCAVYGGSFSGYYWSWIRQPPGKGLEWI GEINHSNGNTYYNPSLKSRTISVDTSKNQLSLKSSVTAADTAVYYCA RFGSNDAFDIWGQGMVTVSSASTKGPSVFPLAPCSRSTSESTAALGC LVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVTPSSN FGTQTYTCNVDHKPSNTKVDKTVKCCVECPPCPAPPVAGPSVFLFP PKPKDITLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPR EEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPSSIEKTISKAK

[0275]

		<u>QQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPE</u> <u>NNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHY</u> <u>TQKSLSLSPG</u>
195	14E3 (VH + G2(C219S).g1)或 14E3-IgG2-C219S-IgG1	<u>QVQLQQWAGLLKPKSETLSLTCAVYGGSFSGYYWSWIRQPPGKGLEWI</u> <u>GEINHSNGNTYYNPSLKSRTVISVDTSKNQLSLKSSVTAADTAVYYCA</u> <u>RFGSNDADFIDWGQGMVTVSSASTKGPSVFPLAPCSRSTSESTAALGC</u> <u>LVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVTPSSN</u> <u>FGTQTYTCNVDHKPSNTKVDKTVKSKVECPPEPPAPPELLGGPSVFLF</u> <u>PPKPKDTLMISRTPEVTCVVDVSHEDPEVKFNWYVDGVEVHNAKTKP</u> <u>REEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKA</u> <u>KGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPE</u> <u>NNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNH</u> <u>YTQKSLSLSPG</u>
196	14E3 (VH + G2(C219S).g1.1)或 14E3-IgG2-C219S-IgG1.1	<u>QVQLQQWAGLLKPKSETLSLTCAVYGGSFSGYYWSWIRQPPGKGLEWI</u> <u>GEINHSNGNTYYNPSLKSRTVISVDTSKNQLSLKSSVTAADTAVYYCA</u> <u>RFGSNDADFIDWGQGMVTVSSASTKGPSVFPLAPCSRSTSESTAALGC</u> <u>LVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVTPSSN</u> <u>FGTQTYTCNVDHKPSNTKVDKTVKSKVECPPEPPAPPVAGPSVFLFP</u> <u>PKPKDTLMISRTPEVTCVVDVSHEDPEVKFNWYVDGVEVHNAKTKPR</u> <u>EEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPSSIEKTIKAK</u> <u>GQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPE</u> <u>NNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHY</u> <u>TQKSLSLSPG</u>
197	19H8 (VH)	<u>QVQLVESGGGVVQPGSRSLRLSCAASGFTFSNYGMHWVRQAPGKGLEWM</u> <u>AVIYGGSNKFYADSVKGRFTISRDNKSNLSLQMNSLRAEDTAVYYC</u> <u>ARGGAMVRGVYYYGMDVWGQGTITVTVSS</u>
198	19H8 (VL1)	<u>AIQLTQSPSSLSASVGDRTITCRASQGISSALAWYQQKPKGAPKFLI</u> <u>YDASLESQVPSRFRSGSGSGTDFTLTITSSLPEDFATYYCQQFNSYPQ</u> <u>TFGGGTKEIK</u>
199	19H8 (VL2)	<u>EIVLTQSPATLSLSPGERATLSCRASQSVSSYLAWYQQKPGQAPRLLI</u> <u>YDASNRATGIPARFSGSGSGTDFTLTITSSLEPEDFAVYYCQQRSNWPL</u> <u>TFGGGTKEIK</u>
200	19H8 (全长野生型重链) 恒定区加下划线	<u>QVQLVESGGGVVQPGSRSLRLSCAASGFTFSNYGMHWVRQAPGKGLEWM</u> <u>AVIYGGSNKFYADSVKGRFTISRDNKSNLSLQMNSLRAEDTAVYYC</u> <u>ARGGAMVRGVYYYGMDVWGQGTITVTVSSASTKGPSVFPLAPCSRSTSE</u> <u>STAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSV</u> <u>VTVPSSNFGTQTYTCNVDHKPSNTKVDKTVKSKVECPPEPPAPPVAG</u> <u>PSVFLFPPKPKDTLMISRTPEVTCVVDVSHEDPEVKFNWYVDGVEVH</u> <u>NAKTKPREEQFNSTFRVSVLTVVHQDWLNGKEYKCKVSNKGLPAPIE</u> <u>KTIKTKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEW</u> <u>ESNGQPENNYKTTTPMLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMH</u> <u>EALHNHYTQKSLSLSPGK</u>
201	19H8 L1 (全长野生型轻 链 1) 恒定区加下划线	<u>AIQLTQSPSSLSASVGDRTITCRASQGISSALAWYQQKPKGAPKFLI</u> <u>YDASLESQVPSRFRSGSGSGTDFTLTITSSLPEDFATYYCQQFNSYPQ</u> <u>TFGGGTKEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNFPYPREA</u> <u>KVQWKVDNALQSGNSQESVTEQDSKDSYSTLSSTLTLSKADYEKHKVY</u> <u>ACEVTHQGLSSPVTKSFNRGEC</u>
202	19H8 L2 (全长野生型轻 链 2)	<u>EIVLTQSPATLSLSPGERATLSCRASQSVSSYLAWYQQKPGQAPRLLI</u> <u>YDASNRATGIPARFSGSGSGTDFTLTITSSLEPEDFAVYYCQQRSNWPL</u> <u>TFGGGTKEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNFPYPREA</u> <u>KVQWKVDNALQSGNSQESVTEQDSKDSYSTLSSTLTLSKADYEKHKVY</u> <u>ACEVTHQGLSSPVTKSFNRGEC</u>
203	19H8.IgG1 (VH + IgG1)	<u>QVQLVESGGGVVQPGSRSLRLSCAASGFTFSNYGMHWVRQAPGKGLEWM</u> <u>AVIYGGSNKFYADSVKGRFTISRDNKSNLSLQMNSLRAEDTAVYYC</u> <u>ARGGAMVRGVYYYGMDVWGQGTITVTVSSASTKGPSVFPLAPSSKSTSG</u> <u>GTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSV</u> <u>VTVPSSSLGTQTYICNVNHKPSNTKVDKRVKPKSCDKTHTCPPCPAPE</u>

[0276]

		LLGGPSVFLF PPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVE VHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKV SNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKG FYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQ GNVFSCSVMEALHNHYTQKSLSLSPG
204	19H8.IgG1.1 (VH + IgG1.1)	QVQLVESGGGVVQPGRSLRLSCAASGFTFSNYGMHWVRQAPGKGLEWM AVIWYGGSNKFYADSVKGRFTISRDNKNSLSLQMNSLRAEDTAVYYC ARGGAMVRGVYYYGMDVWGQGTITVSSASTKGPSVFPLAPSSKSTSG GTAALGCLVKDYFPEPVTWSWNSGALTSGVHTFPAVLQSSGLYSLSSV VTVPSSSLGTQTYICNVNHKPSNTKVDKRVKSCDKTHTCPPCPAPE AEGAPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDG VEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALP SSIEKTIKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDI AVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFSC SVMEALHNHYTQKSLSLSPG
205	19H8.IgG1 (VL1 + CL)	AIQLTQSPSSLSASVGDRTITCRASQGISSALAWYQQKPGKAPKFLI YDASSLESQVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQFNSYPQ TFGGQTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVCLLNNFYPREA KVQWKVDNALQSGNSQESVTEQDSKDSSTLSLTLSKADYEKHKVY ACEVTHQGLSSPVTKSFNRGEC
206	19H8.IgG1.2 (VL2 + CL)	EIVLTQSPATLSLSPGERATLSCRASQSVSSYLAWYQQKPGQAPRLLI YDASNRATGIPARFSGSGSGTDFTLTISLEPEDFAVYYCQQRSNWPL TFGGGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVCLLNNFYPREA KVQWKVDNALQSGNSQESVTEQDSKDSSTLSLTLSKADYEKHKVY ACEVTHQGLSSPVTKSFNRGEC
207	19H8 VH CDR1	NYGMH
208	19H8 VH CDR2	VIWYGGSNKFYADSVKG
209	19H8 VH CDR3	GGAMVRGVYYYGMDV
210	19H8 VL1 CDR1	RASQGISSALA
211	19H8 VL1 CDR2	DASSLES
212	19H8 VL1 CDR3	QQFNSYPQT
213	19H8 VL2 CDR1	RASQSVSSYLA
214	19H8 VL2 CDR2	DASNRAT
215	19H8 VL2 CDR3	QQRSNWPLT
216	19H8 (VH + G2(C219S)) 或 19H8-IgG2-C219S	QVQLVESGGGVVQPGRSLRLSCAASGFTFSNYGMHWVRQAPGKGLEWM AVIWYGGSNKFYADSVKGRFTISRDNKNSLSLQMNSLRAEDTAVYYC ARGGAMVRGVYYYGMDVWGQGTITVSSASTKGPSVFPLAPCSRSTSE STAALGCLVKDYFPEPVTWSWNSGALTSGVHTFPAVLQSSGLYSLSSV VTVPSSNFGTQTYTCNVNKHPSNTKVDKTVKRCVCECPFCPPAVAG PSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVH NAKTKPREEQFNSTFRVSVLTVVHQDWLNGKEYKCKVSNKGLPAPIE KTISKTKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEW ESNGQPENNYKTTTPMLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMH EALHNHYTQKSLSLSPG
217	19H8 (VH + G2.g1)或 19H8-IgG2-IgG1	QVQLVESGGGVVQPGRSLRLSCAASGFTFSNYGMHWVRQAPGKGLEWM AVIWYGGSNKFYADSVKGRFTISRDNKNSLSLQMNSLRAEDTAVYYC ARGGAMVRGVYYYGMDVWGQGTITVSSASTKGPSVFPLAPCSRSTSE STAALGCLVKDYFPEPVTWSWNSGALTSGVHTFPAVLQSSGLYSLSSV VTVPSSNFGTQTYTCNVNKHPSNTKVDKTVKRCVCECPFCPAPELLG

[0277]

		<u>GPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEV</u> <u>HNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPI</u> <u>EKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVE</u> <u>WESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFC</u> <u>HEALHNHYTQKSLSLSPG</u>
218	19H8 (VH + G2.g1.1)或 19H8-IgG2-IgG1.1	<u>QVQLVESGGGVVQPGRSLRLSCAASGFTFSNYGMHWVRQAPGKGLEWM</u> <u>AVIWYGGSNKFYADSVKGRFTISRDNKSNLSLQMNSLRAEDTAVYYC</u> <u>ARGGAMVRGVYYYGMDVWGQGTITVTVSSASTKGFSVFPLAPCSRSTSE</u> <u>STAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSV</u> <u>VTVPSSNFGTQTYTCNVDHKPSNTKVDKTVKRCCKVECPPCPAPPVAG</u> <u>PSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVH</u> <u>NAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPSSIE</u> <u>KTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEW</u> <u>ESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFC</u> <u>HEALHNHYTQKSLSLSPG</u>
219	19H8 (VH + G2(C219S).g1)或 19H8-IgG2-C219S-IgG1	<u>QVQLVESGGGVVQPGRSLRLSCAASGFTFSNYGMHWVRQAPGKGLEWM</u> <u>AVIWYGGSNKFYADSVKGRFTISRDNKSNLSLQMNSLRAEDTAVYYC</u> <u>ARGGAMVRGVYYYGMDVWGQGTITVTVSSASTKGFSVFPLAPCSRSTSE</u> <u>STAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSV</u> <u>VTVPSSNFGTQTYTCNVDHKPSNTKVDKTVKRCCKVECPPCPAPELLG</u> <u>GPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEV</u> <u>HNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPI</u> <u>EKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVE</u> <u>WESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFC</u> <u>HEALHNHYTQKSLSLSPG</u>
220	19H8 (VH + G2(C219S).g1.1)或 19H8-IgG2-C219S-IgG1.1	<u>QVQLVESGGGVVQPGRSLRLSCAASGFTFSNYGMHWVRQAPGKGLEWM</u> <u>AVIWYGGSNKFYADSVKGRFTISRDNKSNLSLQMNSLRAEDTAVYYC</u> <u>ARGGAMVRGVYYYGMDVWGQGTITVTVSSASTKGFSVFPLAPCSRSTSE</u> <u>STAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSV</u> <u>VTVPSSNFGTQTYTCNVDHKPSNTKVDKTVKRCCKVECPPCPAPPVAG</u> <u>PSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVH</u> <u>NAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPSSIE</u> <u>KTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEW</u> <u>ESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFC</u> <u>HEALHNHYTQKSLSLSPG</u>
221	6G10.IgG1 (VH + IgG1)	<u>QVQLVESGGDVVQPGRSLRLSCAASGFTFSTYGMHWVRQAPGKGLEWV</u> <u>AVTWYAGSNKFYADSVKGRFTISRDNKNTLYLQMNSLRAEDTAVYYC</u> <u>ARGGSMVRGLYYYGMDVWGQGTITVTVSSASTKGFSVFPLAPSSKSTSG</u> <u>GTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSV</u> <u>VTVPSSSLGTQTYICNVNHKPSNTKVDKRVKPKSCDKTHTCTPCPAPE</u> <u>LLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDG</u> <u>VEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALP</u> <u>APIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDI</u> <u>AVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFC</u> <u>SVMHEALHNHYTQKSLSLSPG</u>
222	6G10.IgG1.1 (VH + IgG1.1)	<u>QVQLVESGGDVVQPGRSLRLSCAASGFTFSTYGMHWVRQAPGKGLEWV</u> <u>AVTWYAGSNKFYADSVKGRFTISRDNKNTLYLQMNSLRAEDTAVYYC</u> <u>ARGGSMVRGLYYYGMDVWGQGTITVTVSSASTKGFSVFPLAPSSKSTSG</u> <u>GTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSV</u> <u>VTVPSSSLGTQTYICNVNHKPSNTKVDKRVKPKSCDKTHTCTPCPAPE</u> <u>AEGAPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDG</u> <u>VEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALP</u> <u>SSIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDI</u> <u>AVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFC</u> <u>SVMHEALHNHYTQKSLSLSPG</u>
223	6G10.IgG1 (VL + CL)	<u>AIQLTQSPSSLSASVGDRTITCRASQGISSALAWYQQKPGKAPKLLI</u> <u>YDASSLESQVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQFN</u> <u>SYPTFGQGTKEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA</u> <u>KVQWKVDNALQSGNSQESVTEQDSKDSYSTLSSTLTLSKADYEKHKVY</u> <u>ACEVTHQGLSSPVTKSFNRGEC</u>

[0278]

224	6G10 (VH + G2(C219S)) 或 6G10-IgG2-C219S	QVQLVESGGDVVQPGRSRLRLSCAASGFTFSTYGMHWVRQAPGKGLEWV AVTWYAGSNKIFYADSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYC ARGGSMVRGLYYYGMDVWGQGTTVTVSSASTKGPSVFPLAPCSRSTSE STAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSV VTVPSSNFGTQTYTCNV DHKPSNTKVDKTV ERKSCVCEPPCPAPPVAG PSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVH NAKTKPREEQFNSTFRVVS VLT VVHQDWLNGKEYKCKVSNKGLPAPIE KTISKTKGQPREPQVYITLPPSREEMTKNQVSLTCLVKGFYPSDIAVEW ESNGQPENNYKTTTPMLDS DGSFFLYSKLTVDKSRWQQGNV FSCSVMH EALHNHYTQKSLSLSPG
225	6G10 (VH + G2.g1)或 6G10-IgG2-IgG1	QVQLVESGGDVVQPGRSRLRLSCAASGFTFSTYGMHWVRQAPGKGLEWV AVTWYAGSNKIFYADSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYC ARGGSMVRGLYYYGMDVWGQGTTVTVSSASTKGPSVFPLAPCSRSTSE STAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSV VTVPSSNFGTQTYTCNV DHKPSNTKVDKTV ERKCCVCEPPCPAPELLG GPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEV HNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPI EKTISKAKGQPREPQVYITLPPSREEMTKNQVSLTCLVKGFYPSDIAVEW WESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNV FSCSVM HEALHNHYTQKSLSLSPG
226	6G10 (VH + G2.g1.1)或 6G10-IgG2-IgG1.1	QVQLVESGGDVVQPGRSRLRLSCAASGFTFSTYGMHWVRQAPGKGLEWV AVTWYAGSNKIFYADSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYC ARGGSMVRGLYYYGMDVWGQGTTVTVSSASTKGPSVFPLAPCSRSTSE STAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSV VTVPSSNFGTQTYTCNV DHKPSNTKVDKTV ERKCCVCEPPCPAPPVAG PSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVH NAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPSSIE KTISKAKGQPREPQVYITLPPSREEMTKNQVSLTCLVKGFYPSDIAVEW ESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNV FSCSVMH EALHNHYTQKSLSLSPG
227	6G10 (VH + G2(C219S).g1)或 6G10-IgG2-C219S-IgG1	QVQLVESGGDVVQPGRSRLRLSCAASGFTFSTYGMHWVRQAPGKGLEWV AVTWYAGSNKIFYADSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYC ARGGSMVRGLYYYGMDVWGQGTTVTVSSASTKGPSVFPLAPCSRSTSE STAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSV VTVPSSNFGTQTYTCNV DHKPSNTKVDKTV ERKSCVCEPPCPAPELLG GPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEV HNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPI EKTISKAKGQPREPQVYITLPPSREEMTKNQVSLTCLVKGFYPSDIAVEW WESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNV FSCSVM HEALHNHYTQKSLSLSPG
228	6G10 (VH + G2(C219S).g1.1)或 6G10-IgG2-C219S-IgG1.1	QVQLVESGGDVVQPGRSRLRLSCAASGFTFSTYGMHWVRQAPGKGLEWV AVTWYAGSNKIFYADSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYC ARGGSMVRGLYYYGMDVWGQGTTVTVSSASTKGPSVFPLAPCSRSTSE STAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSV VTVPSSNFGTQTYTCNV DHKPSNTKVDKTV ERKSCVCEPPCPAPPVAG PSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVH NAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPSSIE KTISKAKGQPREPQVYITLPPSREEMTKNQVSLTCLVKGFYPSDIAVEW ESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNV FSCSVMH EALHNHYTQKSLSLSPG

[0279] 表2提供了成熟可变区以及轻链和重链的序列,以及,在有标示时,带有信号肽的序列。

[0280] 等同方式

[0281] 本领域技术人员会认识到,或者能够通过不超过常规实验的实验确定,本申请所公开的具体实施方案的诸多等同方式。下面的权利要求意图涵盖这些等同方式。

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[0230]	Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
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[0232]	Ala Arg Gly Gly Ser Met Val Arg Gly Leu Tyr Tyr Tyr Gly Met Asp
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[0247]	Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
[0248]	35 40 45
[0249]	Tyr Asp Ala Ser Ser Leu Glu Ser Gly Val Pro Ser Arg Phe Ser Gly
[0250]	50 55 60
[0251]	Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro

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[0253]	Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Phe Asn Ser Tyr Pro Tyr			
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[0255]	Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys			
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[0268]	Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val			
[0269]		35	40	45
[0270]	Ala Val Thr Trp Tyr Ala Gly Ser Asn Lys Phe Tyr Ala Asp Ser Val			
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[0272]	Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr			
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[0274]	Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys			
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[0276]	Ala Arg Gly Gly Ser Met Val Arg Gly Leu Tyr Tyr Tyr Gly Met Asp			
[0277]		100	105	110
[0278]	Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys			
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[0288]	Val Thr Val Pro Ser Ser Asn Phe Gly Thr Gln Thr Tyr Thr Cys Asn			
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[0290]	Val Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys Thr Val Glu Arg			
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[0292]	Lys Cys Cys Val Glu Cys Pro Pro Cys Pro Ala Pro Pro Val Ala Gly			
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[0296]	Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu		
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[0298]	Asp Pro Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val His		
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[0302]	Val Val Ser Val Leu Thr Val Val His Gln Asp Trp Leu Asn Gly Lys		
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[0304]	Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ala Pro Ile Glu		
[0305]		325	330 335
[0306]	Lys Thr Ile Ser Lys Thr Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr		
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[0308]	Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu		
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[0310]	Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp		
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[0316]	Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His		
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[0318]	Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro		
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[0333]	Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile		
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[0337]	Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro		
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[0347]	Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln		
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[0349]	Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser		
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[0353]	Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser		
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[0366]	Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Thr Tyr		
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[0368]	Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val		
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[0370]	Ala Val Thr Trp Tyr Ala Gly Ser Asn Lys Phe Tyr Ala Asp Ser Val		
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[0372]	Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr		
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[0374]	Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys		
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[0376]	Ala Arg Gly Gly Ser Met Val Arg Gly Leu Tyr Tyr Tyr Gly Met Asp		
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[0385]					165					170					175	
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[0389]			195					200					205			
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[0407]				340						345					350	
[0408]	Pro	Gln	Val	Tyr	Val	Leu	Pro	Pro	Pro	Glu	Glu	Glu	Met	Thr	Lys	Lys
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[0413]	385					390					395				400	
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[0415]					405					410					415	
[0416]	Leu	Arg	Val	Glu	Lys	Lys	Asn	Trp	Val	Glu	Arg	Asn	Ser	Tyr	Ser	Cys
[0417]				420						425				430		
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[0419]			435						440					445		

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 [0435] Tyr Asp Ala Ser Ser Leu Glu Ser Gly Val Pro Ser Arg Phe Ser Gly
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 [0437] Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
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[0472] <211> 321

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[0475] <220>

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[0480] gggaaagctc ctaagctcct gatctatgat gcctccagtt tggaaagtgg ggtcccatca 180

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[0482] gaagattttg caacttatta ctgtcaacag tttaatagtt acccgtagc ttttggccag 300

[0483] gggaccaagc tggagatcaa a 321

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[0485] <211> 1350

[0486] <212> DNA

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[0488] <220>

[0489] <223> 合成的: 6G10 (全长野生型重链) 核苷酸序列

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[0494] gcagactccg tgaaggcccg attcaccatc tccagagaca attccaagaa cacgctgtat 240

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[0607]	Val	Ser	His	Glu	Asp	Pro	Glu	Val	Gln	Phe	Asn	Trp	Tyr	Val	Asp	Gly	
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[0609]	Val	Glu	Val	His	Asn	Ala	Lys	Thr	Lys	Pro	Arg	Glu	Glu	Gln	Phe	Asn	
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[0615]	Ala	Pro	Ile	Glu	Lys	Thr	Ile	Ser	Lys	Thr	Lys	Gly	Gln	Pro	Arg	Glu	
[0616]		210					215					220					
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[0618]	225					230				235						240	
[0619]	Gln	Val	Ser	Leu	Thr	Cys	Leu	Val	Lys	Gly	Phe	Tyr	Pro	Ser	Asp	Ile	
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[0622]				260					265					270			
[0623]	Thr	Pro	Pro	Met	Leu	Asp	Ser	Asp	Gly	Ser	Phe	Phe	Leu	Tyr	Ser	Lys	
[0624]			275					280					285				
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[0643]	20 25 30
[0644]	Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln
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[0646]	Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser
[0647]	50 55 60
[0648]	Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu
[0649]	65 70 75 80
[0650]	Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser
[0651]	85 90 95
[0652]	Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
[0653]	100 105
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[0665]	Asp Thr Thr Gly Ser Ser Val Thr Leu Gly Cys Leu Val Lys Gly Tyr
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[0667]	Phe Pro Glu Pro Val Thr Leu Thr Trp Asn Ser Gly Ser Leu Ser Ser
[0668]	35 40 45
[0669]	Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Asp Leu Tyr Thr Leu
[0670]	50 55 60
[0671]	Ser Ser Ser Val Thr Val Thr Ser Ser Thr Trp Pro Ser Gln Ser Ile

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[0673]	Thr Cys Asn Val Ala His Pro Ala Ser Ser Thr Lys Val Asp Lys Lys			
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[0675]	Ile Glu Pro Arg Gly Pro Thr Ile Lys Pro Cys Pro Pro Cys Lys Cys			
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[0677]	Pro Ala Pro Asn Leu Leu Gly Gly Pro Ser Val Phe Ile Phe Pro Pro			
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[0679]	Lys Ile Lys Asp Val Leu Met Ile Ser Leu Ser Pro Ile Val Thr Cys			
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[0681]	Val Val Val Asp Val Ser Glu Asp Asp Pro Asp Val Gln Ile Ser Trp			
[0682]	145	150	155	160
[0683]	Phe Val Asn Asn Val Glu Val His Thr Ala Gln Thr Gln Thr His Arg			
[0684]		165	170	175
[0685]	Glu Asp Tyr Asn Ser Thr Leu Arg Val Val Ser Ala Leu Pro Ile Gln			
[0686]		180	185	190
[0687]	His Gln Asp Trp Met Ser Gly Lys Glu Phe Lys Cys Lys Val Asn Asn			
[0688]		195	200	205
[0689]	Lys Asp Leu Pro Ala Pro Ile Glu Arg Thr Ile Ser Lys Pro Lys Gly			
[0690]		210	215	220
[0691]	Ser Val Arg Ala Pro Gln Val Tyr Val Leu Pro Pro Pro Glu Glu Glu			
[0692]	225	230	235	240
[0693]	Met Thr Lys Lys Gln Val Thr Leu Thr Cys Met Val Thr Asp Phe Met			
[0694]		245	250	255
[0695]	Pro Glu Asp Ile Tyr Val Glu Trp Thr Asn Asn Gly Lys Thr Glu Leu			
[0696]		260	265	270
[0697]	Asn Tyr Lys Asn Thr Glu Pro Val Leu Asp Ser Asp Gly Ser Tyr Phe			
[0698]		275	280	285
[0699]	Met Tyr Ser Lys Leu Arg Val Glu Lys Lys Asn Trp Val Glu Arg Asn			
[0700]		290	295	300
[0701]	Ser Tyr Ser Cys Ser Val Val His Glu Gly Leu His Asn His His Thr			
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[0703]	Thr Lys Ser Phe Ser Arg Thr Pro Gly Lys			
[0704]		325	330	
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[0716]	Gln Leu Thr Ser Gly Gly Ala Ser Val Val Cys Phe Leu Asn Asn Phe
[0717]	20 25 30
[0718]	Tyr Pro Lys Asp Ile Asn Val Lys Trp Lys Ile Asp Gly Ser Glu Arg
[0719]	35 40 45
[0720]	Gln Asn Gly Val Leu Asn Ser Trp Thr Asp Gln Asp Ser Lys Asp Ser
[0721]	50 55 60
[0722]	Thr Tyr Ser Met Ser Ser Thr Leu Thr Leu Thr Lys Asp Glu Tyr Glu
[0723]	65 70 75 80
[0724]	Arg His Asn Ser Tyr Thr Cys Glu Ala Thr His Lys Thr Ser Thr Ser
[0725]	85 90 95
[0726]	Pro Ile Val Lys Ser Phe Asn Arg Asn Glu Cys
[0727]	100 105
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[0730]	<212> PRT
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[0733]	<223> 合成的: 28F3 (VH)
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[0735]	Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg
[0736]	1 5 10 15
[0737]	Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
[0738]	20 25 30
[0739]	Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
[0740]	35 40 45
[0741]	Ala Val Ile Trp Tyr Glu Gly Ser Asn Lys Tyr Tyr Ala Asp Ser Val
[0742]	50 55 60
[0743]	Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
[0744]	65 70 75 80
[0745]	Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
[0746]	85 90 95
[0747]	Ala Arg Gly Gly Ser Met Val Arg Gly Asp Tyr Tyr Tyr Gly Met Asp
[0748]	100 105 110
[0749]	Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
[0750]	115 120
[0751]	<210> 28
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[0753]	<212> PRT
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 [0761] 20 25 30
 [0762] Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
 [0763] 35 40 45
 [0764] Tyr Asp Ala Ser Ser Leu Glu Ser Gly Val Pro Ser Arg Phe Ser Gly
 [0765] 50 55 60
 [0766] Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
 [0767] 65 70 75 80
 [0768] Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Phe Asn Ser Tyr Pro Tyr
 [0769] 85 90 95
 [0770] Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
 [0771] 100 105
 [0772] <210> 29
 [0773] <211> 450
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 [0781] Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
 [0782] 20 25 30
 [0783] Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
 [0784] 35 40 45
 [0785] Ala Val Ile Trp Tyr Glu Gly Ser Asn Lys Tyr Tyr Ala Asp Ser Val
 [0786] 50 55 60
 [0787] Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
 [0788] 65 70 75 80
 [0789] Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
 [0790] 85 90 95
 [0791] Ala Arg Gly Gly Ser Met Val Arg Gly Asp Tyr Tyr Tyr Gly Met Asp
 [0792] 100 105 110
 [0793] Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys
 [0794] 115 120 125
 [0795] Gly Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu
 [0796] 130 135 140
 [0797] Ser Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro

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[0799]	Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr			
[0800]		165	170	175
[0801]	Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val			
[0802]		180	185	190
[0803]	Val Thr Val Pro Ser Ser Asn Phe Gly Thr Gln Thr Tyr Thr Cys Asn			
[0804]		195	200	205
[0805]	Val Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys Thr Val Glu Arg			
[0806]		210	215	220
[0807]	Lys Cys Cys Val Glu Cys Pro Pro Cys Pro Ala Pro Pro Val Ala Gly			
[0808]	225	230	235	240
[0809]	Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile			
[0810]		245	250	255
[0811]	Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu			
[0812]		260	265	270
[0813]	Asp Pro Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val His			
[0814]		275	280	285
[0815]	Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr Phe Arg			
[0816]		290	295	300
[0817]	Val Val Ser Val Leu Thr Val Val His Gln Asp Trp Leu Asn Gly Lys			
[0818]	305	310	315	320
[0819]	Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ala Pro Ile Glu			
[0820]		325	330	335
[0821]	Lys Thr Ile Ser Lys Thr Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr			
[0822]		340	345	350
[0823]	Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu			
[0824]		355	360	365
[0825]	Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp			
[0826]		370	375	380
[0827]	Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Met			
[0828]	385	390	395	400
[0829]	Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp			
[0830]		405	410	415
[0831]	Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His			
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[0833]	Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro			
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[0848]	Leu	Ala	Trp	Tyr	Gln	Gln	Lys	Pro	Gly	Lys	Ala	Pro	Lys	Leu	Leu	Ile				
[0849]			35					40						45						
[0850]	Tyr	Asp	Ala	Ser	Ser	Leu	Glu	Ser	Gly	Val	Pro	Ser	Arg	Phe	Ser	Gly				
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[0852]	Ser	Gly	Ser	Gly	Thr	Asp	Phe	Thr	Leu	Thr	Ile	Ser	Ser	Leu	Gln	Pro				
[0853]	65					70					75					80				
[0854]	Glu	Asp	Phe	Ala	Thr	Tyr	Tyr	Cys	Gln	Gln	Phe	Asn	Ser	Tyr	Pro	Tyr				
[0855]					85					90						95				
[0856]	Thr	Phe	Gly	Gln	Gly	Thr	Lys	Leu	Glu	Ile	Lys	Arg	Thr	Val	Ala	Ala				
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[0858]	Pro	Ser	Val	Phe	Ile	Phe	Pro	Pro	Ser	Asp	Glu	Gln	Leu	Lys	Ser	Gly				
[0859]			115					120								125				
[0860]	Thr	Ala	Ser	Val	Val	Cys	Leu	Leu	Asn	Asn	Phe	Tyr	Pro	Arg	Glu	Ala				
[0861]		130						135								140				
[0862]	Lys	Val	Gln	Trp	Lys	Val	Asp	Asn	Ala	Leu	Gln	Ser	Gly	Asn	Ser	Gln				
[0863]	145					150					155					160				
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[0865]					165					170						175				
[0866]	Ser	Thr	Leu	Thr	Leu	Ser	Lys	Ala	Asp	Tyr	Glu	Lys	His	Lys	Val	Tyr				
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[0868]	Ala	Cys	Glu	Val	Thr	His	Gln	Gly	Leu	Ser	Ser	Pro	Val	Thr	Lys	Ser				
[0869]			195						200							205				
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[0887]	Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr		
[0888]	65	70	75
[0889]	Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys		
[0890]	85	90	95
[0891]	Ala Arg Gly Gly Ser Met Val Arg Gly Asp Tyr Tyr Tyr Gly Met Asp		
[0892]	100	105	110
[0893]	Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys		
[0894]	115	120	125
[0895]	Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly		
[0896]	130	135	140
[0897]	Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro		
[0898]	145	150	155
[0899]	Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr		
[0900]	165	170	175
[0901]	Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val		
[0902]	180	185	190
[0903]	Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn		
[0904]	195	200	205
[0905]	Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro		
[0906]	210	215	220
[0907]	Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu		
[0908]	225	230	235
[0909]	Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp		
[0910]	245	250	255
[0911]	Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp		
[0912]	260	265	270
[0913]	Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly		
[0914]	275	280	285
[0915]	Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn		
[0916]	290	295	300
[0917]	Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp		
[0918]	305	310	315
[0919]	Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro		
[0920]	325	330	335
[0921]	Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu		
[0922]	340	345	350
[0923]	Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn		

[0924]	355	360	365
[0925]	Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile		
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[0927]	Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr		
[0928]	385	390	395
[0929]	Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys		
[0930]	405	410	415
[0931]	Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys		
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[0952]	Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr		
[0953]	65	70	75
[0954]	Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys		
[0955]	85	90	95
[0956]	Ala Arg Gly Gly Ser Met Val Arg Gly Asp Tyr Tyr Tyr Gly Met Asp		
[0957]	100	105	110
[0958]	Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys		
[0959]	115	120	125
[0960]	Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly		
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[0962]	Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro		
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[0964]	Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr		
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[0966]	Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val
[0967]	180 185 190
[0968]	Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn
[0969]	195 200 205
[0970]	Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro
[0971]	210 215 220
[0972]	Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu
[0973]	225 230 235 240
[0974]	Ala Glu Gly Ala Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
[0975]	245 250 255
[0976]	Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp
[0977]	260 265 270
[0978]	Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
[0979]	275 280 285
[0980]	Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn
[0981]	290 295 300
[0982]	Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
[0983]	305 310 315 320
[0984]	Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro
[0985]	325 330 335
[0986]	Ser Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
[0987]	340 345 350
[0988]	Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn
[0989]	355 360 365
[0990]	Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
[0991]	370 375 380
[0992]	Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
[0993]	385 390 395 400
[0994]	Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys
[0995]	405 410 415
[0996]	Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
[0997]	420 425 430
[0998]	Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
[0999]	435 440 445
[1000]	Ser Leu Ser Pro Gly
[1001]	450
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[1011]	Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Ser Ser Ala
[1012]	20 25 30
[1013]	Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
[1014]	35 40 45
[1015]	Tyr Asp Ala Ser Ser Leu Glu Ser Gly Val Pro Ser Arg Phe Ser Gly
[1016]	50 55 60
[1017]	Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
[1018]	65 70 75 80
[1019]	Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Phe Asn Ser Tyr Pro Tyr
[1020]	85 90 95
[1021]	Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys Arg Thr Val Ala Ala
[1022]	100 105 110
[1023]	Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly
[1024]	115 120 125
[1025]	Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala
[1026]	130 135 140
[1027]	Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln
[1028]	145 150 155 160
[1029]	Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser
[1030]	165 170 175
[1031]	Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr
[1032]	180 185 190
[1033]	Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser
[1034]	195 200 205
[1035]	Phe Asn Arg Gly Glu Cys
[1036]	210
[1037]	<210> 34
[1038]	<211> 5
[1039]	<212> PRT
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[1042]	<223> 合成的: 28F3 VH CDR1
[1043]	<400> 34
[1044]	Ser Tyr Gly Met His
[1045]	1 5
[1046]	<210> 35
[1047]	<211> 17
[1048]	<212> PRT
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 [1052] <400> 35
 [1053] Val Ile Trp Tyr Glu Gly Ser Asn Lys Tyr Tyr Ala Asp Ser Val Lys
 [1054] 1 5 10 15
 [1055] Gly
 [1056] <210> 36
 [1057] <211> 15
 [1058] <212> PRT
 [1059] <213> 人工序列
 [1060] <220>
 [1061] <223> 合成的: 28F3 VH CDR3
 [1062] <400> 36
 [1063] Gly Gly Ser Met Val Arg Gly Asp Tyr Tyr Tyr Gly Met Asp Val
 [1064] 1 5 10 15
 [1065] <210> 37
 [1066] <211> 11
 [1067] <212> PRT
 [1068] <213> 人工序列
 [1069] <220>
 [1070] <223> 合成的: 28F3 VL CDR1
 [1071] <400> 37
 [1072] Arg Ala Ser Gln Gly Ile Ser Ser Ala Leu Ala
 [1073] 1 5 10
 [1074] <210> 38
 [1075] <211> 7
 [1076] <212> PRT
 [1077] <213> 人工序列
 [1078] <220>
 [1079] <223> 合成的: 28F3 VL CDR2
 [1080] <400> 38
 [1081] Asp Ala Ser Ser Leu Glu Ser
 [1082] 1 5
 [1083] <210> 39
 [1084] <211> 9
 [1085] <212> PRT
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 [1087] <220>
 [1088] <223> 合成的: 28F3 VL CDR3
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 [1090] Gln Gln Phe Asn Ser Tyr Pro Tyr Thr
 [1091] 1 5

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[1094]	<212>	PRT
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[1098]	<400>	40
[1099]	Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg	
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[1101]	Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr	
[1102]	20	30
[1103]	Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val	
[1104]	35	45
[1105]	Ala Val Ile Trp Tyr Glu Gly Ser Asn Lys Tyr Tyr Ala Asp Ser Val	
[1106]	50	60
[1107]	Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr	
[1108]	65	80
[1109]	Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys	
[1110]	85	95
[1111]	Ala Arg Gly Gly Ser Met Val Arg Gly Asp Tyr Tyr Tyr Gly Met Asp	
[1112]	100	110
[1113]	Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys	
[1114]	115	125
[1115]	Gly Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu	
[1116]	130	140
[1117]	Ser Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro	
[1118]	145	160
[1119]	Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr	
[1120]	165	175
[1121]	Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val	
[1122]	180	190
[1123]	Val Thr Val Pro Ser Ser Asn Phe Gly Thr Gln Thr Tyr Thr Cys Asn	
[1124]	195	205
[1125]	Val Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys Thr Val Glu Arg	
[1126]	210	220
[1127]	Lys Ser Cys Val Glu Cys Pro Pro Cys Pro Ala Pro Pro Val Ala Gly	
[1128]	225	240
[1129]	Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile	
[1130]	245	255
[1131]	Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu	
[1132]	260	270
[1133]	Asp Pro Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val His	

[1134]	275	280	285
[1135]	Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr Phe Arg		
[1136]	290	295	300
[1137]	Val Val Ser Val Leu Thr Val Val His Gln Asp Trp Leu Asn Gly Lys		
[1138]	305	310	315
[1139]	Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ala Pro Ile Glu		
[1140]	325	330	335
[1141]	Lys Thr Ile Ser Lys Thr Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr		
[1142]	340	345	350
[1143]	Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu		
[1144]	355	360	365
[1145]	Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp		
[1146]	370	375	380
[1147]	Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Met		
[1148]	385	390	395
[1149]	Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp		
[1150]	405	410	415
[1151]	Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His		
[1152]	420	425	430
[1153]	Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro		
[1154]	435	440	445
[1155]	Gly		
[1156]	<210> 41		
[1157]	<211> 450		
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[1162]	<400> 41		
[1163]	Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg		
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[1165]	Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr		
[1166]	20	25	30
[1167]	Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val		
[1168]	35	40	45
[1169]	Ala Val Ile Trp Tyr Glu Gly Ser Asn Lys Tyr Tyr Ala Asp Ser Val		
[1170]	50	55	60
[1171]	Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr		
[1172]	65	70	75
[1173]	Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys		
[1174]	85	90	95
[1175]	Ala Arg Gly Gly Ser Met Val Arg Gly Asp Tyr Tyr Tyr Gly Met Asp		

[1176]	100	105	110
[1177]	Val Trp Gly Gln Gly Thr Thr	Val Thr Val Ser Ser Ala Ser Thr Lys	
[1178]	115	120	125
[1179]	Gly Pro Ser Val Phe Pro Leu	Ala Pro Cys Ser Arg Ser Thr Ser Glu	
[1180]	130	135	140
[1181]	Ser Thr Ala Ala Leu Gly Cys Leu	Val Lys Asp Tyr Phe Pro Glu Pro	
[1182]	145	150	155 160
[1183]	Val Thr Val Ser Trp Asn Ser Gly	Ala Leu Thr Ser Gly Val His Thr	
[1184]	165	170	175
[1185]	Phe Pro Ala Val Leu Gln Ser Ser	Gly Leu Tyr Ser Leu Ser Ser Val	
[1186]	180	185	190
[1187]	Val Thr Val Pro Ser Ser Asn Phe	Gly Thr Gln Thr Tyr Thr Cys Asn	
[1188]	195	200	205
[1189]	Val Asp His Lys Pro Ser Asn Thr	Lys Val Asp Lys Thr Val Glu Arg	
[1190]	210	215	220
[1191]	Lys Cys Cys Val Glu Cys Pro Pro	Cys Pro Ala Pro Glu Leu Leu Gly	
[1192]	225	230	235 240
[1193]	Gly Pro Ser Val Phe Leu Phe Pro	Pro Lys Pro Lys Asp Thr Leu Met	
[1194]	245	250	255
[1195]	Ile Ser Arg Thr Pro Glu Val Thr	Cys Val Val Val Asp Val Ser His	
[1196]	260	265	270
[1197]	Glu Asp Pro Glu Val Lys Phe Asn	Trp Tyr Val Asp Gly Val Glu Val	
[1198]	275	280	285
[1199]	His Asn Ala Lys Thr Lys Pro Arg	Glu Glu Gln Tyr Asn Ser Thr Tyr	
[1200]	290	295	300
[1201]	Arg Val Val Ser Val Leu Thr Val	Leu His Gln Asp Trp Leu Asn Gly	
[1202]	305	310	315 320
[1203]	Lys Glu Tyr Lys Cys Lys Val Ser	Asn Lys Ala Leu Pro Ala Pro Ile	
[1204]	325	330	335
[1205]	Glu Lys Thr Ile Ser Lys Ala Lys	Gly Gln Pro Arg Glu Pro Gln Val	
[1206]	340	345	350
[1207]	Tyr Thr Leu Pro Pro Ser Arg Glu	Glu Met Thr Lys Asn Gln Val Ser	
[1208]	355	360	365
[1209]	Leu Thr Cys Leu Val Lys Gly Phe	Tyr Pro Ser Asp Ile Ala Val Glu	
[1210]	370	375	380
[1211]	Trp Glu Ser Asn Gly Gln Pro Glu	Asn Asn Tyr Lys Thr Thr Pro Pro	
[1212]	385	390	395 400
[1213]	Val Leu Asp Ser Asp Gly Ser Phe	Phe Leu Tyr Ser Lys Leu Thr Val	
[1214]	405	410	415
[1215]	Asp Lys Ser Arg Trp Gln Gln Gly	Asn Val Phe Ser Cys Ser Val Met	
[1216]	420	425	430
[1217]	His Glu Ala Leu His Asn His Tyr	Thr Gln Lys Ser Leu Ser Leu Ser	

[1218]	435	440	445
[1219]	Pro Gly		
[1220]	450		
[1221]	<210> 42		
[1222]	<211> 449		
[1223]	<212> PRT		
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[1228]	Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg		
[1229]	1 5 10 15		
[1230]	Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr		
[1231]	20 25 30		
[1232]	Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val		
[1233]	35 40 45		
[1234]	Ala Val Ile Trp Tyr Glu Gly Ser Asn Lys Tyr Tyr Ala Asp Ser Val		
[1235]	50 55 60		
[1236]	Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr		
[1237]	65 70 75 80		
[1238]	Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys		
[1239]	85 90 95		
[1240]	Ala Arg Gly Gly Ser Met Val Arg Gly Asp Tyr Tyr Tyr Gly Met Asp		
[1241]	100 105 110		
[1242]	Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys		
[1243]	115 120 125		
[1244]	Gly Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu		
[1245]	130 135 140		
[1246]	Ser Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro		
[1247]	145 150 155 160		
[1248]	Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr		
[1249]	165 170 175		
[1250]	Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val		
[1251]	180 185 190		
[1252]	Val Thr Val Pro Ser Ser Asn Phe Gly Thr Gln Thr Tyr Thr Cys Asn		
[1253]	195 200 205		
[1254]	Val Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys Thr Val Glu Arg		
[1255]	210 215 220		
[1256]	Lys Cys Cys Val Glu Cys Pro Pro Cys Pro Ala Pro Pro Val Ala Gly		
[1257]	225 230 235 240		
[1258]	Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile		
[1259]	245 250 255		

[1260]	Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu		
[1261]	260	265	270
[1262]	Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His		
[1263]	275	280	285
[1264]	Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg		
[1265]	290	295	300
[1266]	Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys		
[1267]	305	310	315
[1268]	Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ser Ser Ile Glu		
[1269]	325	330	335
[1270]	Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr		
[1271]	340	345	350
[1272]	Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu		
[1273]	355	360	365
[1274]	Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp		
[1275]	370	375	380
[1276]	Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val		
[1277]	385	390	395
[1278]	Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp		
[1279]	405	410	415
[1280]	Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His		
[1281]	420	425	430
[1282]	Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro		
[1283]	435	440	445
[1284]	Gly		
[1285]	<210> 43		
[1286]	<211> 450		
[1287]	<212> PRT		
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[1292]	Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg		
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[1294]	Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr		
[1295]	20	25	30
[1296]	Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val		
[1297]	35	40	45
[1298]	Ala Val Ile Trp Tyr Glu Gly Ser Asn Lys Tyr Tyr Ala Asp Ser Val		
[1299]	50	55	60
[1300]	Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr		
[1301]	65	70	75

[1302]	Leu	Gln	Met	Asn	Ser	Leu	Arg	Ala	Glu	Asp	Thr	Ala	Val	Tyr	Tyr	Cys
[1303]				85					90					95		
[1304]	Ala	Arg	Gly	Gly	Ser	Met	Val	Arg	Gly	Asp	Tyr	Tyr	Tyr	Gly	Met	Asp
[1305]				100					105					110		
[1306]	Val	Trp	Gly	Gln	Gly	Thr	Thr	Val	Thr	Val	Ser	Ser	Ala	Ser	Thr	Lys
[1307]				115					120					125		
[1308]	Gly	Pro	Ser	Val	Phe	Pro	Leu	Ala	Pro	Cys	Ser	Arg	Ser	Thr	Ser	Glu
[1309]				130					135					140		
[1310]	Ser	Thr	Ala	Ala	Leu	Gly	Cys	Leu	Val	Lys	Asp	Tyr	Phe	Pro	Glu	Pro
[1311]				145					150					155		
[1312]	Val	Thr	Val	Ser	Trp	Asn	Ser	Gly	Ala	Leu	Thr	Ser	Gly	Val	His	Thr
[1313]									165					170		
[1314]	Phe	Pro	Ala	Val	Leu	Gln	Ser	Ser	Gly	Leu	Tyr	Ser	Leu	Ser	Ser	Val
[1315]				180					185					190		
[1316]	Val	Thr	Val	Pro	Ser	Ser	Asn	Phe	Gly	Thr	Gln	Thr	Tyr	Thr	Cys	Asn
[1317]				195					200					205		
[1318]	Val	Asp	His	Lys	Pro	Ser	Asn	Thr	Lys	Val	Asp	Lys	Thr	Val	Glu	Arg
[1319]				210					215					220		
[1320]	Lys	Ser	Cys	Val	Glu	Cys	Pro	Pro	Cys	Pro	Ala	Pro	Glu	Leu	Leu	Gly
[1321]				225					230					235		
[1322]	Gly	Pro	Ser	Val	Phe	Leu	Phe	Pro	Pro	Lys	Pro	Lys	Asp	Thr	Leu	Met
[1323]									245					250		
[1324]	Ile	Ser	Arg	Thr	Pro	Glu	Val	Thr	Cys	Val	Val	Val	Asp	Val	Ser	His
[1325]				260					265					270		
[1326]	Glu	Asp	Pro	Glu	Val	Lys	Phe	Asn	Trp	Tyr	Val	Asp	Gly	Val	Glu	Val
[1327]				275					280					285		
[1328]	His	Asn	Ala	Lys	Thr	Lys	Pro	Arg	Glu	Glu	Gln	Tyr	Asn	Ser	Thr	Tyr
[1329]				290					295					300		
[1330]	Arg	Val	Val	Ser	Val	Leu	Thr	Val	Leu	His	Gln	Asp	Trp	Leu	Asn	Gly
[1331]				305					310					315		
[1332]	Lys	Glu	Tyr	Lys	Cys	Lys	Val	Ser	Asn	Lys	Ala	Leu	Pro	Ala	Pro	Ile
[1333]									325					330		
[1334]	Glu	Lys	Thr	Ile	Ser	Lys	Ala	Lys	Gly	Gln	Pro	Arg	Glu	Pro	Gln	Val
[1335]				340					345					350		
[1336]	Tyr	Thr	Leu	Pro	Pro	Ser	Arg	Glu	Glu	Met	Thr	Lys	Asn	Gln	Val	Ser
[1337]				355					360					365		
[1338]	Leu	Thr	Cys	Leu	Val	Lys	Gly	Phe	Tyr	Pro	Ser	Asp	Ile	Ala	Val	Glu
[1339]				370					375					380		
[1340]	Trp	Glu	Ser	Asn	Gly	Gln	Pro	Glu	Asn	Asn	Tyr	Lys	Thr	Thr	Pro	Pro
[1341]				385					390					395		
[1342]	Val	Leu	Asp	Ser	Asp	Gly	Ser	Phe	Phe	Leu	Tyr	Ser	Lys	Leu	Thr	Val
[1343]									405					410		

[1344]	Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met
[1345]	420 425 430
[1346]	His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser
[1347]	435 440 445
[1348]	Pro Gly
[1349]	450
[1350]	<210> 44
[1351]	<211> 449
[1352]	<212> PRT
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[1357]	Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg
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[1359]	Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
[1360]	20 25 30
[1361]	Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
[1362]	35 40 45
[1363]	Ala Val Ile Trp Tyr Glu Gly Ser Asn Lys Tyr Tyr Ala Asp Ser Val
[1364]	50 55 60
[1365]	Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
[1366]	65 70 75 80
[1367]	Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
[1368]	85 90 95
[1369]	Ala Arg Gly Gly Ser Met Val Arg Gly Asp Tyr Tyr Tyr Gly Met Asp
[1370]	100 105 110
[1371]	Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys
[1372]	115 120 125
[1373]	Gly Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu
[1374]	130 135 140
[1375]	Ser Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro
[1376]	145 150 155 160
[1377]	Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr
[1378]	165 170 175
[1379]	Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val
[1380]	180 185 190
[1381]	Val Thr Val Pro Ser Ser Asn Phe Gly Thr Gln Thr Tyr Thr Cys Asn
[1382]	195 200 205
[1383]	Val Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys Thr Val Glu Arg
[1384]	210 215 220
[1385]	Lys Ser Cys Val Glu Cys Pro Pro Cys Pro Ala Pro Pro Val Ala Gly

[1386]	225	230	235	240
[1387]	Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile			
[1388]		245	250	255
[1389]	Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu			
[1390]		260	265	270
[1391]	Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His			
[1392]		275	280	285
[1393]	Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg			
[1394]		290	295	300
[1395]	Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys			
[1396]		305	310	315
[1397]	Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ser Ser Ile Glu			
[1398]		325	330	335
[1399]	Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr			
[1400]		340	345	350
[1401]	Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu			
[1402]		355	360	365
[1403]	Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp			
[1404]		370	375	380
[1405]	Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val			
[1406]		385	390	395
[1407]	Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp			
[1408]		405	410	415
[1409]	Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His			
[1410]		420	425	430
[1411]	Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro			
[1412]		435	440	445
[1413]	Gly			
[1414]	<210> 45			
[1415]	<211> 141			
[1416]	<212> PRT			
[1417]	<213> 人工序列			
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[1419]	<223> 合成的: 28F3 (VH) (SEQ ID NO: 13) with signal peptide			
[1420]	<400> 45			
[1421]	Met Arg Ala Trp Ile Phe Phe Leu Leu Cys Leu Ala Gly Arg Ala Leu			
[1422]	1	5	10	15
[1423]	Ala Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly			
[1424]		20	25	30
[1425]	Arg Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser			
[1426]		35	40	45
[1427]	Tyr Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp			

[1428]	50	55	60
[1429]	Val Ala Val Ile Trp Tyr Glu Gly Ser Asn Lys Tyr Tyr Ala Asp Ser		
[1430]	65	70	75
[1431]	Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu		
[1432]	85	90	95
[1433]	Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr		
[1434]	100	105	110
[1435]	Cys Ala Arg Gly Gly Ser Met Val Arg Gly Asp Tyr Tyr Tyr Gly Met		
[1436]	115	120	125
[1437]	Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser		
[1438]	130	135	140
[1439]	<210> 46		
[1440]	<211> 124		
[1441]	<212> PRT		
[1442]	<213> 人工序列		
[1443]	<220>		
[1444]	<223> 合成的: 28F3 (VL) (SEQ ID NO: 14) with signal peptide		
[1445]	<400> 46		
[1446]	Met Arg Ala Trp Ile Phe Phe Leu Leu Cys Leu Ala Gly Arg Ala Leu		
[1447]	1	5	10
[1448]	Ala Ala Ile Gln Leu Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val		
[1449]	20	25	30
[1450]	Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Ser Ser		
[1451]	35	40	45
[1452]	Ala Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu		
[1453]	50	55	60
[1454]	Ile Tyr Asp Ala Ser Ser Leu Glu Ser Gly Val Pro Ser Arg Phe Ser		
[1455]	65	70	75
[1456]	Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln		
[1457]	85	90	95
[1458]	Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Phe Asn Ser Tyr Pro		
[1459]	100	105	110
[1460]	Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys		
[1461]	115	120	
[1462]	<210> 47		
[1463]	<211> 470		
[1464]	<212> PRT		
[1465]	<213> 人工序列		
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[1467]	<223> 合成的: 28F3.IgG1 (VH + IgG1) with signal peptide		
[1468]	<400> 47		
[1469]	Met Arg Ala Trp Ile Phe Phe Leu Leu Cys Leu Ala Gly Arg Ala Leu		

[1470]	1	5	10	15
[1471]	Ala Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly			
[1472]	20	25	30	
[1473]	Arg Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser			
[1474]	35	40	45	
[1475]	Tyr Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp			
[1476]	50	55	60	
[1477]	Val Ala Val Ile Trp Tyr Glu Gly Ser Asn Lys Tyr Tyr Ala Asp Ser			
[1478]	65	70	75	80
[1479]	Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu			
[1480]	85	90	95	
[1481]	Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr			
[1482]	100	105	110	
[1483]	Cys Ala Arg Gly Gly Ser Met Val Arg Gly Asp Tyr Tyr Tyr Gly Met			
[1484]	115	120	125	
[1485]	Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr			
[1486]	130	135	140	
[1487]	Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser			
[1488]	145	150	155	160
[1489]	Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu			
[1490]	165	170	175	
[1491]	Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His			
[1492]	180	185	190	
[1493]	Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser			
[1494]	195	200	205	
[1495]	Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys			
[1496]	210	215	220	
[1497]	Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu			
[1498]	225	230	235	240
[1499]	Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro			
[1500]	245	250	255	
[1501]	Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys			
[1502]	260	265	270	
[1503]	Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val			
[1504]	275	280	285	
[1505]	Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp			
[1506]	290	295	300	
[1507]	Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr			
[1508]	305	310	315	320
[1509]	Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp			
[1510]	325	330	335	
[1511]	Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu			

[1512]	340	345	350
[1513]	Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg		
[1514]	355	360	365
[1515]	Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys		
[1516]	370	375	380
[1517]	Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp		
[1518]	385	390	395
[1519]	Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys		
[1520]	405	410	415
[1521]	Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser		
[1522]	420	425	430
[1523]	Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser		
[1524]	435	440	445
[1525]	Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser		
[1526]	450	455	460
[1527]	Leu Ser Leu Ser Pro Gly		
[1528]	465	470	
[1529]	<210> 48		
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[1531]	<212> PRT		
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[1534]	<223> 合成的: 28F3.IgG1.1 (VH + IgG1.1) with signal peptide		
[1535]	<400> 48		
[1536]	Met Arg Ala Trp Ile Phe Phe Leu Leu Cys Leu Ala Gly Arg Ala Leu		
[1537]	1	5	10
[1538]	Ala Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly		
[1539]	20	25	30
[1540]	Arg Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser		
[1541]	35	40	45
[1542]	Tyr Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp		
[1543]	50	55	60
[1544]	Val Ala Val Ile Trp Tyr Glu Gly Ser Asn Lys Tyr Tyr Ala Asp Ser		
[1545]	65	70	75
[1546]	Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu		
[1547]	85	90	95
[1548]	Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr		
[1549]	100	105	110
[1550]	Cys Ala Arg Gly Gly Ser Met Val Arg Gly Asp Tyr Tyr Tyr Gly Met		
[1551]	115	120	125
[1552]	Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr		
[1553]	130	135	140

[1554]	Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser
[1555]	145 150 155 160
[1556]	Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu
[1557]	165 170 175
[1558]	Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His
[1559]	180 185 190
[1560]	Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser
[1561]	195 200 205
[1562]	Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys
[1563]	210 215 220
[1564]	Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu
[1565]	225 230 235 240
[1566]	Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro
[1567]	245 250 255
[1568]	Glu Ala Glu Gly Ala Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys
[1569]	260 265 270
[1570]	Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val
[1571]	275 280 285
[1572]	Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp
[1573]	290 295 300
[1574]	Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr
[1575]	305 310 315 320
[1576]	Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp
[1577]	325 330 335
[1578]	Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu
[1579]	340 345 350
[1580]	Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg
[1581]	355 360 365
[1582]	Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys
[1583]	370 375 380
[1584]	Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp
[1585]	385 390 395 400
[1586]	Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys
[1587]	405 410 415
[1588]	Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser
[1589]	420 425 430
[1590]	Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser
[1591]	435 440 445
[1592]	Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser
[1593]	450 455 460
[1594]	Leu Ser Leu Ser Pro Gly
[1595]	465 470

[1596]	<210>	49
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[1601]	<223>	合成的: 28F3.IgG1 (VL+CL) with signal peptide
[1602]	<400>	49
[1603]	Met Arg Ala Trp Ile Phe Phe Leu Leu Cys Leu Ala Gly Arg Ala Leu	
[1604]	1 5 10 15	
[1605]	Ala Ala Ile Gln Leu Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val	
[1606]	20 25 30	
[1607]	Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Ser Ser	
[1608]	35 40 45	
[1609]	Ala Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu	
[1610]	50 55 60	
[1611]	Ile Tyr Asp Ala Ser Ser Leu Glu Ser Gly Val Pro Ser Arg Phe Ser	
[1612]	65 70 75 80	
[1613]	Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln	
[1614]	85 90 95	
[1615]	Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Phe Asn Ser Tyr Pro	
[1616]	100 105 110	
[1617]	Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys Arg Thr Val Ala	
[1618]	115 120 125	
[1619]	Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser	
[1620]	130 135 140	
[1621]	Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu	
[1622]	145 150 155 160	
[1623]	Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser	
[1624]	165 170 175	
[1625]	Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu	
[1626]	180 185 190	
[1627]	Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val	
[1628]	195 200 205	
[1629]	Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys	
[1630]	210 215 220	
[1631]	Ser Phe Asn Arg Gly Glu Cys	
[1632]	225 230	
[1633]	<210>	50
[1634]	<211>	123
[1635]	<212>	PRT
[1636]	<213>	人工序列
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[1638]	<223> 合成的: 19D3 (VH)
[1639]	<400> 50
[1640]	Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg
[1641]	1 5 10 15
[1642]	Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
[1643]	20 25 30
[1644]	Gly Phe His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
[1645]	35 40 45
[1646]	Ala Val Ile Trp Tyr Ala Gly Ser Asn Lys Phe Tyr Ala Asp Ser Val
[1647]	50 55 60
[1648]	Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
[1649]	65 70 75 80
[1650]	Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
[1651]	85 90 95
[1652]	Ala Arg Gly Gly Gln Leu Asp Tyr Tyr Tyr Tyr Tyr Val Met Asp Val
[1653]	100 105 110
[1654]	Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
[1655]	115 120
[1656]	<210> 51
[1657]	<211> 107
[1658]	<212> PRT
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[1661]	<223> 合成的: 19D3 (VL)
[1662]	<400> 51
[1663]	Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
[1664]	1 5 10 15
[1665]	Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Ser Ser Trp
[1666]	20 25 30
[1667]	Leu Ala Trp Tyr Gln Gln Lys Pro Glu Lys Ala Pro Lys Ser Leu Ile
[1668]	35 40 45
[1669]	Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
[1670]	50 55 60
[1671]	Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
[1672]	65 70 75 80
[1673]	Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Asn Ser Tyr Pro Tyr
[1674]	85 90 95
[1675]	Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
[1676]	100 105
[1677]	<210> 52
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[1679]	<212> PRT

[1680]	<213> 人工序列																		
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[1683]	<400> 52																		
[1684]	Gln	Val	Gln	Leu	Val	Glu	Ser	Gly	Gly	Gly	Val	Val	Gln	Pro	Gly	Arg			
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[1686]	Ser	Leu	Arg	Leu	Ser	Cys	Ala	Ala	Ser	Gly	Phe	Thr	Phe	Ser	Ser	Tyr			
[1687]					20					25					30				
[1688]	Gly	Phe	His	Trp	Val	Arg	Gln	Ala	Pro	Gly	Lys	Gly	Leu	Glu	Trp	Val			
[1689]					35					40					45				
[1690]	Ala	Val	Ile	Trp	Tyr	Ala	Gly	Ser	Asn	Lys	Phe	Tyr	Ala	Asp	Ser	Val			
[1691]					50					55					60				
[1692]	Lys	Gly	Arg	Phe	Thr	Ile	Ser	Arg	Asp	Asn	Ser	Lys	Asn	Thr	Leu	Tyr			
[1693]	65					70						75				80			
[1694]	Leu	Gln	Met	Asn	Ser	Leu	Arg	Ala	Glu	Asp	Thr	Ala	Val	Tyr	Tyr	Cys			
[1695]					85					90					95				
[1696]	Ala	Arg	Gly	Gly	Gln	Leu	Asp	Tyr	Tyr	Tyr	Tyr	Tyr	Val	Met	Asp	Val			
[1697]					100					105					110				
[1698]	Trp	Gly	Gln	Gly	Thr	Thr	Val	Thr	Val	Ser	Ser	Ala	Ser	Thr	Lys	Gly			
[1699]					115					120					125				
[1700]	Pro	Ser	Val	Phe	Pro	Leu	Ala	Pro	Cys	Ser	Arg	Ser	Thr	Ser	Glu	Ser			
[1701]					130					135					140				
[1702]	Thr	Ala	Ala	Leu	Gly	Cys	Leu	Val	Lys	Asp	Tyr	Phe	Pro	Glu	Pro	Val			
[1703]	145					150						155				160			
[1704]	Thr	Val	Ser	Trp	Asn	Ser	Gly	Ala	Leu	Thr	Ser	Gly	Val	His	Thr	Phe			
[1705]					165							170				175			
[1706]	Pro	Ala	Val	Leu	Gln	Ser	Ser	Gly	Leu	Tyr	Ser	Leu	Ser	Ser	Val	Val			
[1707]					180					185					190				
[1708]	Thr	Val	Pro	Ser	Ser	Asn	Phe	Gly	Thr	Gln	Thr	Tyr	Thr	Cys	Asn	Val			
[1709]					195					200					205				
[1710]	Asp	His	Lys	Pro	Ser	Asn	Thr	Lys	Val	Asp	Lys	Thr	Val	Glu	Arg	Lys			
[1711]					210					215					220				
[1712]	Cys	Cys	Val	Glu	Cys	Pro	Pro	Cys	Pro	Ala	Pro	Pro	Val	Ala	Gly	Pro			
[1713]	225					230						235				240			
[1714]	Ser	Val	Phe	Leu	Phe	Pro	Pro	Lys	Pro	Lys	Asp	Thr	Leu	Met	Ile	Ser			
[1715]					245							250				255			
[1716]	Arg	Thr	Pro	Glu	Val	Thr	Cys	Val	Val	Val	Asp	Val	Ser	His	Glu	Asp			
[1717]					260							265				270			
[1718]	Pro	Glu	Val	Gln	Phe	Asn	Trp	Tyr	Val	Asp	Gly	Val	Glu	Val	His	Asn			
[1719]					275							280				285			
[1720]	Ala	Lys	Thr	Lys	Pro	Arg	Glu	Glu	Gln	Phe	Asn	Ser	Thr	Phe	Arg	Val			
[1721]					290							295				300			

[1722]	Val Ser Val Leu Thr Val Val His Gln Asp Trp Leu Asn Gly Lys Glu		
[1723]	305	310	315 320
[1724]	Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ala Pro Ile Glu Lys		
[1725]	325	330	335
[1726]	Thr Ile Ser Lys Thr Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr		
[1727]	340	345	350
[1728]	Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr		
[1729]	355	360	365
[1730]	Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu		
[1731]	370	375	380
[1732]	Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Met Leu		
[1733]	385	390	395 400
[1734]	Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys		
[1735]	405	410	415
[1736]	Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu		
[1737]	420	425	430
[1738]	Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly		
[1739]	435	440	445
[1740]	Lys		
[1741]	<210> 53		
[1742]	<211> 214		
[1743]	<212> PRT		
[1744]	<213> 人工序列		
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[1746]	<223> 合成的: 19D3 (全长野生型轻链)		
[1747]	<400> 53		
[1748]	Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly		
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[1750]	Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Ser Ser Trp		
[1751]	20	25	30
[1752]	Leu Ala Trp Tyr Gln Gln Lys Pro Glu Lys Ala Pro Lys Ser Leu Ile		
[1753]	35	40	45
[1754]	Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly		
[1755]	50	55	60
[1756]	Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro		
[1757]	65	70	75 80
[1758]	Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Asn Ser Tyr Pro Tyr		
[1759]	85	90	95
[1760]	Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys Arg Thr Val Ala Ala		
[1761]	100	105	110
[1762]	Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly		
[1763]	115	120	125

[1764]	Thr	Ala	Ser	Val	Val	Cys	Leu	Leu	Asn	Asn	Phe	Tyr	Pro	Arg	Glu	Ala
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[1766]	Lys	Val	Gln	Trp	Lys	Val	Asp	Asn	Ala	Leu	Gln	Ser	Gly	Asn	Ser	Gln
[1767]	145					150					155				160	
[1768]	Glu	Ser	Val	Thr	Glu	Gln	Asp	Ser	Lys	Asp	Ser	Thr	Tyr	Ser	Leu	Ser
[1769]					165					170				175		
[1770]	Ser	Thr	Leu	Thr	Leu	Ser	Lys	Ala	Asp	Tyr	Glu	Lys	His	Lys	Val	Tyr
[1771]				180					185					190		
[1772]	Ala	Cys	Glu	Val	Thr	His	Gln	Gly	Leu	Ser	Ser	Pro	Val	Thr	Lys	Ser
[1773]		195					200					205				
[1774]	Phe	Asn	Arg	Gly	Glu	Cys										
[1775]	210															
[1776]	<210>	54														
[1777]	<211>	452														
[1778]	<212>	PRT														
[1779]	<213>	人工序列														
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[1781]	<223>	合成的: 19D3.IgG1 (VH + IgG1)														
[1782]	<400>	54														
[1783]	Gln	Val	Gln	Leu	Val	Glu	Ser	Gly	Gly	Gly	Val	Val	Gln	Pro	Gly	Arg
[1784]	1			5					10					15		
[1785]	Ser	Leu	Arg	Leu	Ser	Cys	Ala	Ala	Ser	Gly	Phe	Thr	Phe	Ser	Ser	Tyr
[1786]			20					25					30			
[1787]	Gly	Phe	His	Trp	Val	Arg	Gln	Ala	Pro	Gly	Lys	Gly	Leu	Glu	Trp	Val
[1788]		35					40						45			
[1789]	Ala	Val	Ile	Trp	Tyr	Ala	Gly	Ser	Asn	Lys	Phe	Tyr	Ala	Asp	Ser	Val
[1790]	50					55					60					
[1791]	Lys	Gly	Arg	Phe	Thr	Ile	Ser	Arg	Asp	Asn	Ser	Lys	Asn	Thr	Leu	Tyr
[1792]	65				70				75				80			
[1793]	Leu	Gln	Met	Asn	Ser	Leu	Arg	Ala	Glu	Asp	Thr	Ala	Val	Tyr	Tyr	Cys
[1794]			85					90					95			
[1795]	Ala	Arg	Gly	Gly	Gln	Leu	Asp	Tyr	Tyr	Tyr	Tyr	Tyr	Val	Met	Asp	Val
[1796]		100						105					110			
[1797]	Trp	Gly	Gln	Gly	Thr	Thr	Val	Thr	Val	Ser	Ser	Ala	Ser	Thr	Lys	Gly
[1798]		115						120					125			
[1799]	Pro	Ser	Val	Phe	Pro	Leu	Ala	Pro	Ser	Ser	Lys	Ser	Thr	Ser	Gly	Gly
[1800]	130					135					140					
[1801]	Thr	Ala	Ala	Leu	Gly	Cys	Leu	Val	Lys	Asp	Tyr	Phe	Pro	Glu	Pro	Val
[1802]	145					150					155				160	
[1803]	Thr	Val	Ser	Trp	Asn	Ser	Gly	Ala	Leu	Thr	Ser	Gly	Val	His	Thr	Phe
[1804]				165						170				175		
[1805]	Pro	Ala	Val	Leu	Gln	Ser	Ser	Gly	Leu	Tyr	Ser	Leu	Ser	Ser	Val	Val

[1806]	180	185	190
[1807]	Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val		
[1808]	195	200	205
[1809]	Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys		
[1810]	210	215	220
[1811]	Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu		
[1812]	225	230	235 240
[1813]	Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr		
[1814]	245	250	255
[1815]	Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val		
[1816]	260	265	270
[1817]	Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val		
[1818]	275	280	285
[1819]	Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser		
[1820]	290	295	300
[1821]	Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu		
[1822]	305	310	315 320
[1823]	Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala		
[1824]	325	330	335
[1825]	Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro		
[1826]	340	345	350
[1827]	Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln		
[1828]	355	360	365
[1829]	Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala		
[1830]	370	375	380
[1831]	Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr		
[1832]	385	390	395 400
[1833]	Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu		
[1834]	405	410	415
[1835]	Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser		
[1836]	420	425	430
[1837]	Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser		
[1838]	435	440	445
[1839]	Leu Ser Pro Gly		
[1840]	450		
[1841]	<210> 55		
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[1843]	<212> PRT		
[1844]	<213> 人工序列		
[1845]	<220>		
[1846]	<223> 合成的: 19D3.IgG1.1 (VH + IgG1.1)		
[1847]	<400> 55		

[1848]	Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg
[1849]	1 5 10 15
[1850]	Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
[1851]	20 25 30
[1852]	Gly Phe His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
[1853]	35 40 45
[1854]	Ala Val Ile Trp Tyr Ala Gly Ser Asn Lys Phe Tyr Ala Asp Ser Val
[1855]	50 55 60
[1856]	Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
[1857]	65 70 75 80
[1858]	Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
[1859]	85 90 95
[1860]	Ala Arg Gly Gly Gln Leu Asp Tyr Tyr Tyr Tyr Tyr Val Met Asp Val
[1861]	100 105 110
[1862]	Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly
[1863]	115 120 125
[1864]	Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly
[1865]	130 135 140
[1866]	Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val
[1867]	145 150 155 160
[1868]	Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe
[1869]	165 170 175
[1870]	Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val
[1871]	180 185 190
[1872]	Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val
[1873]	195 200 205
[1874]	Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys
[1875]	210 215 220
[1876]	Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Ala
[1877]	225 230 235 240
[1878]	Glu Gly Ala Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
[1879]	245 250 255
[1880]	Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val
[1881]	260 265 270
[1882]	Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
[1883]	275 280 285
[1884]	Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
[1885]	290 295 300
[1886]	Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
[1887]	305 310 315 320
[1888]	Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ser
[1889]	325 330 335

[1890]	Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
[1891]	340 345 350
[1892]	Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln
[1893]	355 360 365
[1894]	Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala
[1895]	370 375 380
[1896]	Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
[1897]	385 390 395 400
[1898]	Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
[1899]	405 410 415
[1900]	Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
[1901]	420 425 430
[1902]	Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
[1903]	435 440 445
[1904]	Leu Ser Pro Gly
[1905]	450
[1906]	<210> 56
[1907]	<211> 214
[1908]	<212> PRT
[1909]	<213> 人工序列
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[1911]	<223> 合成的: 19D3.IgG1 (VL + CL)
[1912]	<400> 56
[1913]	Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
[1914]	1 5 10 15
[1915]	Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Ser Ser Trp
[1916]	20 25 30
[1917]	Leu Ala Trp Tyr Gln Gln Lys Pro Glu Lys Ala Pro Lys Ser Leu Ile
[1918]	35 40 45
[1919]	Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
[1920]	50 55 60
[1921]	Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
[1922]	65 70 75 80
[1923]	Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Asn Ser Tyr Pro Tyr
[1924]	85 90 95
[1925]	Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys Arg Thr Val Ala Ala
[1926]	100 105 110
[1927]	Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly
[1928]	115 120 125
[1929]	Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala
[1930]	130 135 140
[1931]	Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln

[1932]	145	150	155	160
[1933]	Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser			
[1934]		165	170	175
[1935]	Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr			
[1936]		180	185	190
[1937]	Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser			
[1938]		195	200	205
[1939]	Phe Asn Arg Gly Glu Cys			
[1940]	210			
[1941]	<210> 57			
[1942]	<211> 5			
[1943]	<212> PRT			
[1944]	<213> 人工序列			
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[1946]	<223> 合成的: 19D3 VH CDR1			
[1947]	<400> 57			
[1948]	Ser Tyr Gly Phe His			
[1949]	1	5		
[1950]	<210> 58			
[1951]	<211> 17			
[1952]	<212> PRT			
[1953]	<213> 人工序列			
[1954]	<220>			
[1955]	<223> 合成的: 19D3 VH CDR2			
[1956]	<400> 58			
[1957]	Val Ile Trp Tyr Ala Gly Ser Asn Lys Phe Tyr Ala Asp Ser Val Lys			
[1958]	1	5	10	15
[1959]	Gly			
[1960]	<210> 59			
[1961]	<211> 14			
[1962]	<212> PRT			
[1963]	<213> 人工序列			
[1964]	<220>			
[1965]	<223> 合成的: 19D3 VH CDR3			
[1966]	<400> 59			
[1967]	Gly Gly Gln Leu Asp Tyr Tyr Tyr Tyr Tyr Val Met Asp Val			
[1968]	1	5	10	
[1969]	<210> 60			
[1970]	<211> 11			
[1971]	<212> PRT			
[1972]	<213> 人工序列			
[1973]	<220>			

[1974]	<223> 合成的: 19D3 VL CDR1
[1975]	<400> 60
[1976]	Arg Ala Ser Gln Gly Ile Ser Ser Trp Leu Ala
[1977]	1 5 10
[1978]	<210> 61
[1979]	<211> 7
[1980]	<212> PRT
[1981]	<213> 人工序列
[1982]	<220>
[1983]	<223> 合成的: 19D3 VL CDR2
[1984]	<400> 61
[1985]	Ala Ala Ser Ser Leu Gln Ser
[1986]	1 5
[1987]	<210> 62
[1988]	<211> 9
[1989]	<212> PRT
[1990]	<213> 人工序列
[1991]	<220>
[1992]	<223> 合成的: 19D3 VL CDR3
[1993]	<400> 62
[1994]	Gln Gln Tyr Asn Ser Tyr Pro Tyr Thr
[1995]	1 5
[1996]	<210> 63
[1997]	<211> 448
[1998]	<212> PRT
[1999]	<213> 人工序列
[2000]	<220>
[2001]	<223> 合成的: 19D3 (VH + G2 (C219S)) 或19D3-IgG2-C219S
[2002]	<400> 63
[2003]	Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg
[2004]	1 5 10 15
[2005]	Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
[2006]	20 25 30
[2007]	Gly Phe His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
[2008]	35 40 45
[2009]	Ala Val Ile Trp Tyr Ala Gly Ser Asn Lys Phe Tyr Ala Asp Ser Val
[2010]	50 55 60
[2011]	Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
[2012]	65 70 75 80
[2013]	Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
[2014]	85 90 95
[2015]	Ala Arg Gly Gly Gln Leu Asp Tyr Tyr Tyr Tyr Tyr Val Met Asp Val

[2016]	100					105					110					
[2017]	Trp	Gly	Gln	Gly	Thr	Thr	Val	Thr	Val	Ser	Ser	Ala	Ser	Thr	Lys	Gly
[2018]	115					120					125					
[2019]	Pro	Ser	Val	Phe	Pro	Leu	Ala	Pro	Cys	Ser	Arg	Ser	Thr	Ser	Glu	Ser
[2020]	130					135					140					
[2021]	Thr	Ala	Ala	Leu	Gly	Cys	Leu	Val	Lys	Asp	Tyr	Phe	Pro	Glu	Pro	Val
[2022]	145		150					155					160			
[2023]	Thr	Val	Ser	Trp	Asn	Ser	Gly	Ala	Leu	Thr	Ser	Gly	Val	His	Thr	Phe
[2024]	165					170					175					
[2025]	Pro	Ala	Val	Leu	Gln	Ser	Ser	Gly	Leu	Tyr	Ser	Leu	Ser	Ser	Val	Val
[2026]	180					185					190					
[2027]	Thr	Val	Pro	Ser	Ser	Asn	Phe	Gly	Thr	Gln	Thr	Tyr	Thr	Cys	Asn	Val
[2028]	195					200					205					
[2029]	Asp	His	Lys	Pro	Ser	Asn	Thr	Lys	Val	Asp	Lys	Thr	Val	Glu	Arg	Lys
[2030]	210					215					220					
[2031]	Ser	Cys	Val	Glu	Cys	Pro	Pro	Cys	Pro	Ala	Pro	Pro	Val	Ala	Gly	Pro
[2032]	225		230					235					240			
[2033]	Ser	Val	Phe	Leu	Phe	Pro	Pro	Lys	Pro	Lys	Asp	Thr	Leu	Met	Ile	Ser
[2034]	245					250					255					
[2035]	Arg	Thr	Pro	Glu	Val	Thr	Cys	Val	Val	Val	Asp	Val	Ser	His	Glu	Asp
[2036]	260					265					270					
[2037]	Pro	Glu	Val	Gln	Phe	Asn	Trp	Tyr	Val	Asp	Gly	Val	Glu	Val	His	Asn
[2038]	275					280					285					
[2039]	Ala	Lys	Thr	Lys	Pro	Arg	Glu	Glu	Gln	Phe	Asn	Ser	Thr	Phe	Arg	Val
[2040]	290					295					300					
[2041]	Val	Ser	Val	Leu	Thr	Val	Val	His	Gln	Asp	Trp	Leu	Asn	Gly	Lys	Glu
[2042]	305		310					315					320			
[2043]	Tyr	Lys	Cys	Lys	Val	Ser	Asn	Lys	Gly	Leu	Pro	Ala	Pro	Ile	Glu	Lys
[2044]	325					330					335					
[2045]	Thr	Ile	Ser	Lys	Thr	Lys	Gly	Gln	Pro	Arg	Glu	Pro	Gln	Val	Tyr	Thr
[2046]	340					345					350					
[2047]	Leu	Pro	Pro	Ser	Arg	Glu	Glu	Met	Thr	Lys	Asn	Gln	Val	Ser	Leu	Thr
[2048]	355					360					365					
[2049]	Cys	Leu	Val	Lys	Gly	Phe	Tyr	Pro	Ser	Asp	Ile	Ala	Val	Glu	Trp	Glu
[2050]	370					375					380					
[2051]	Ser	Asn	Gly	Gln	Pro	Glu	Asn	Asn	Tyr	Lys	Thr	Thr	Pro	Pro	Met	Leu
[2052]	385		390					395					400			
[2053]	Asp	Ser	Asp	Gly	Ser	Phe	Phe	Leu	Tyr	Ser	Lys	Leu	Thr	Val	Asp	Lys
[2054]	405					410					415					
[2055]	Ser	Arg	Trp	Gln	Gln	Gly	Asn	Val	Phe	Ser	Cys	Ser	Val	Met	His	Glu
[2056]	420					425					430					
[2057]	Ala	Leu	His	Asn	His	Tyr	Thr	Gln	Lys	Ser	Leu	Ser	Leu	Ser	Pro	Glu

[2058]	435	440	445
[2059]	<210> 64		
[2060]	<211> 449		
[2061]	<212> PRT		
[2062]	<213> 人工序列		
[2063]	<220>		
[2064]	<223> 合成的: 19D3 (VH + G2.g1) 或19D3-IgG2-IgG1		
[2065]	<400> 64		
[2066]	Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg		
[2067]	1 5 10 15		
[2068]	Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr		
[2069]	20 25 30		
[2070]	Gly Phe His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val		
[2071]	35 40 45		
[2072]	Ala Val Ile Trp Tyr Ala Gly Ser Asn Lys Phe Tyr Ala Asp Ser Val		
[2073]	50 55 60		
[2074]	Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr		
[2075]	65 70 75 80		
[2076]	Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys		
[2077]	85 90 95		
[2078]	Ala Arg Gly Gly Gln Leu Asp Tyr Tyr Tyr Tyr Tyr Val Met Asp Val		
[2079]	100 105 110		
[2080]	Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly		
[2081]	115 120 125		
[2082]	Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser		
[2083]	130 135 140		
[2084]	Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val		
[2085]	145 150 155 160		
[2086]	Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe		
[2087]	165 170 175		
[2088]	Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val		
[2089]	180 185 190		
[2090]	Thr Val Pro Ser Ser Asn Phe Gly Thr Gln Thr Tyr Thr Cys Asn Val		
[2091]	195 200 205		
[2092]	Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys Thr Val Glu Arg Lys		
[2093]	210 215 220		
[2094]	Cys Cys Val Glu Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly		
[2095]	225 230 235 240		
[2096]	Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile		
[2097]	245 250 255		
[2098]	Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu		
[2099]	260 265 270		

[2100]	Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His		
[2101]	275	280	285
[2102]	Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg		
[2103]	290	295	300
[2104]	Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys		
[2105]	305	310	315 320
[2106]	Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu		
[2107]	325	330	335
[2108]	Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr		
[2109]	340	345	350
[2110]	Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu		
[2111]	355	360	365
[2112]	Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp		
[2113]	370	375	380
[2114]	Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val		
[2115]	385	390	395 400
[2116]	Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp		
[2117]	405	410	415
[2118]	Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His		
[2119]	420	425	430
[2120]	Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro		
[2121]	435	440	445
[2122]	Gly		
[2123]	<210> 65		
[2124]	<211> 448		
[2125]	<212> PRT		
[2126]	<213> 人工序列		
[2127]	<220>		
[2128]	<223> 合成的: 19D3 (VH + G2.g1.1)或19D3-IgG2-IgG1.1		
[2129]	<400> 65		
[2130]	Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg		
[2131]	1 5 10 15		
[2132]	Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr		
[2133]	20 25 30		
[2134]	Gly Phe His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val		
[2135]	35 40 45		
[2136]	Ala Val Ile Trp Tyr Ala Gly Ser Asn Lys Phe Tyr Ala Asp Ser Val		
[2137]	50 55 60		
[2138]	Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr		
[2139]	65 70 75 80		
[2140]	Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys		
[2141]	85 90 95		

[2142]	Ala	Arg	Gly	Gly	Gln	Leu	Asp	Tyr	Tyr	Tyr	Tyr	Tyr	Val	Met	Asp	Val
[2143]				100					105					110		
[2144]	Trp	Gly	Gln	Gly	Thr	Thr	Val	Thr	Val	Ser	Ser	Ala	Ser	Thr	Lys	Gly
[2145]				115					120					125		
[2146]	Pro	Ser	Val	Phe	Pro	Leu	Ala	Pro	Cys	Ser	Arg	Ser	Thr	Ser	Glu	Ser
[2147]				130					135					140		
[2148]	Thr	Ala	Ala	Leu	Gly	Cys	Leu	Val	Lys	Asp	Tyr	Phe	Pro	Glu	Pro	Val
[2149]				145					150					155		160
[2150]	Thr	Val	Ser	Trp	Asn	Ser	Gly	Ala	Leu	Thr	Ser	Gly	Val	His	Thr	Phe
[2151]					165					170					175	
[2152]	Pro	Ala	Val	Leu	Gln	Ser	Ser	Gly	Leu	Tyr	Ser	Leu	Ser	Ser	Val	Val
[2153]					180					185					190	
[2154]	Thr	Val	Pro	Ser	Ser	Asn	Phe	Gly	Thr	Gln	Thr	Tyr	Thr	Cys	Asn	Val
[2155]					195					200					205	
[2156]	Asp	His	Lys	Pro	Ser	Asn	Thr	Lys	Val	Asp	Lys	Thr	Val	Glu	Arg	Lys
[2157]					210					215				220		
[2158]	Cys	Cys	Val	Glu	Cys	Pro	Pro	Cys	Pro	Ala	Pro	Pro	Val	Ala	Gly	Pro
[2159]					225					230				235		240
[2160]	Ser	Val	Phe	Leu	Phe	Pro	Pro	Lys	Pro	Lys	Asp	Thr	Leu	Met	Ile	Ser
[2161]						245					250				255	
[2162]	Arg	Thr	Pro	Glu	Val	Thr	Cys	Val	Val	Val	Asp	Val	Ser	His	Glu	Asp
[2163]					260						265				270	
[2164]	Pro	Glu	Val	Lys	Phe	Asn	Trp	Tyr	Val	Asp	Gly	Val	Glu	Val	His	Asn
[2165]					275						280				285	
[2166]	Ala	Lys	Thr	Lys	Pro	Arg	Glu	Glu	Gln	Tyr	Asn	Ser	Thr	Tyr	Arg	Val
[2167]					290						295				300	
[2168]	Val	Ser	Val	Leu	Thr	Val	Leu	His	Gln	Asp	Trp	Leu	Asn	Gly	Lys	Glu
[2169]					305					310				315		320
[2170]	Tyr	Lys	Cys	Lys	Val	Ser	Asn	Lys	Ala	Leu	Pro	Ser	Ser	Ile	Glu	Lys
[2171]						325					330				335	
[2172]	Thr	Ile	Ser	Lys	Ala	Lys	Gly	Gln	Pro	Arg	Glu	Pro	Gln	Val	Tyr	Thr
[2173]					340						345				350	
[2174]	Leu	Pro	Pro	Ser	Arg	Glu	Glu	Met	Thr	Lys	Asn	Gln	Val	Ser	Leu	Thr
[2175]					355						360				365	
[2176]	Cys	Leu	Val	Lys	Gly	Phe	Tyr	Pro	Ser	Asp	Ile	Ala	Val	Glu	Trp	Glu
[2177]					370						375				380	
[2178]	Ser	Asn	Gly	Gln	Pro	Glu	Asn	Asn	Tyr	Lys	Thr	Thr	Pro	Pro	Val	Leu
[2179]					385						390				395	400
[2180]	Asp	Ser	Asp	Gly	Ser	Phe	Phe	Leu	Tyr	Ser	Lys	Leu	Thr	Val	Asp	Lys
[2181]						405					410				415	
[2182]	Ser	Arg	Trp	Gln	Gln	Gly	Asn	Val	Phe	Ser	Cys	Ser	Val	Met	His	Glu
[2183]						420					425				430	

[2184]	Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
[2185]	435 440 445
[2186]	<210> 66
[2187]	<211> 449
[2188]	<212> PRT
[2189]	<213> 人工序列
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[2197]	Gly Phe His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
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[2199]	Ala Val Ile Trp Tyr Ala Gly Ser Asn Lys Phe Tyr Ala Asp Ser Val
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[2201]	Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
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[2203]	Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
[2204]	85 90 95
[2205]	Ala Arg Gly Gly Gln Leu Asp Tyr Tyr Tyr Tyr Tyr Val Met Asp Val
[2206]	100 105 110
[2207]	Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly
[2208]	115 120 125
[2209]	Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser
[2210]	130 135 140
[2211]	Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val
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[2213]	Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe
[2214]	165 170 175
[2215]	Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val
[2216]	180 185 190
[2217]	Thr Val Pro Ser Ser Asn Phe Gly Thr Gln Thr Tyr Thr Cys Asn Val
[2218]	195 200 205
[2219]	Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys Thr Val Glu Arg Lys
[2220]	210 215 220
[2221]	Ser Cys Val Glu Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly
[2222]	225 230 235 240
[2223]	Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile
[2224]	245 250 255
[2225]	Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu

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[2227]	Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His		
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[2229]	Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg		
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[2231]	Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys		
[2232]	305	310	315
[2233]	Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu		
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[2235]	Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr		
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[2237]	Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu		
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[2239]	Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp		
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[2243]	Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp		
[2244]	405	410	415
[2245]	Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His		
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[2247]	Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro		
[2248]	435	440	445
[2249]	Gly		
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[2263]	Ala Val Ile Trp Tyr Ala Gly Ser Asn Lys Phe Tyr Ala Asp Ser Val		
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[2265]	Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr		
[2266]	65	70	75
[2267]	Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys		

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[2269]	Ala Arg Gly Gly Gln Leu Asp Tyr Tyr Tyr Tyr Tyr Val Met Asp Val					
[2270]		100		105		110
[2271]	Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly					
[2272]		115		120		125
[2273]	Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser					
[2274]		130		135		140
[2275]	Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val					
[2276]	145		150		155	160
[2277]	Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe					
[2278]		165		170		175
[2279]	Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val					
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[2281]	Thr Val Pro Ser Ser Asn Phe Gly Thr Gln Thr Tyr Thr Cys Asn Val					
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[2283]	Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys Thr Val Glu Arg Lys					
[2284]		210		215		220
[2285]	Ser Cys Val Glu Cys Pro Pro Cys Pro Ala Pro Pro Val Ala Gly Pro					
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[2287]	Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser					
[2288]		245		250		255
[2289]	Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp					
[2290]		260		265		270
[2291]	Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn					
[2292]		275		280		285
[2293]	Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val					
[2294]		290		295		300
[2295]	Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu					
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[2297]	Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ser Ser Ile Glu Lys					
[2298]		325		330		335
[2299]	Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr					
[2300]		340		345		350
[2301]	Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr					
[2302]		355		360		365
[2303]	Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu					
[2304]		370		375		380
[2305]	Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu					
[2306]	385		390		395	400
[2307]	Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys					
[2308]		405		410		415
[2309]	Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu					

[2310]	420	425	430
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[2322]	Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr		
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[2324]	Gly Phe His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val		
[2325]	35	40	45
[2326]	Ala Val Ile Trp Tyr Ala Gly Ser Asn Lys Phe Tyr Ala Asp Ser Val		
[2327]	50	55	60
[2328]	Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr		
[2329]	65	70	75
[2330]	Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys		
[2331]	85	90	95
[2332]	Ala Arg Gly Gly Gln Leu Asp Tyr Tyr Tyr Tyr Tyr Val Met Asp Val		
[2333]	100	105	110
[2334]	Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly		
[2335]	115	120	125
[2336]	Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser		
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[2338]	Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val		
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[2340]	Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe		
[2341]	165	170	175
[2342]	Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val		
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[2344]	Thr Val Pro Ser Ser Asn Phe Gly Thr Gln Thr Tyr Thr Cys Asn Val		
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[2346]	Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys Thr Val Glu Arg Lys		
[2347]	210	215	220
[2348]	Ser Cys Val Glu Cys Pro Pro Cys Pro Ala Pro Pro Val Ala Gly Pro		
[2349]	225	230	235
[2350]	Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser		
[2351]	245	250	255

[2352]	Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp
[2353]	260 265 270
[2354]	Pro Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn
[2355]	275 280 285
[2356]	Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr Phe Arg Val
[2357]	290 295 300
[2358]	Val Ser Val Leu Thr Val Val His Gln Asp Trp Leu Asn Gly Lys Glu
[2359]	305 310 315 320
[2360]	Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ala Pro Ile Glu Lys
[2361]	325 330 335
[2362]	Thr Ile Ser Lys Thr Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr
[2363]	340 345 350
[2364]	Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr
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[2366]	Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu
[2367]	370 375 380
[2368]	Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Met Leu
[2369]	385 390 395 400
[2370]	Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys
[2371]	405 410 415
[2372]	Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu
[2373]	420 425 430
[2374]	Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
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[2376]	<210> 69
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[2386]	20 25 30
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[2388]	35 40 45
[2389]	Ala Val Ile Trp Tyr Ala Gly Ser Asn Lys Phe Tyr Ala Asp Ser Val
[2390]	50 55 60
[2391]	Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
[2392]	65 70 75 80
[2393]	Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys

[2394]		85		90		95
[2395]	Ala Arg Gly Gly Gln Leu Asp Tyr Tyr Tyr Tyr Tyr Val Met Asp Val					
[2396]		100		105		110
[2397]	Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly					
[2398]		115		120		125
[2399]	Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser					
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[2401]	Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val					
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[2403]	Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe					
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[2405]	Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val					
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[2407]	Thr Val Pro Ser Ser Asn Phe Gly Thr Gln Thr Tyr Thr Cys Asn Val					
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[2409]	Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys Thr Val Glu Arg Lys					
[2410]		210		215		220
[2411]	Cys Cys Val Glu Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly					
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[2413]	Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile					
[2414]		245		250		255
[2415]	Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu					
[2416]		260		265		270
[2417]	Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His					
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[2419]	Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg					
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[2421]	Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys					
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[2423]	Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu					
[2424]		325		330		335
[2425]	Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr					
[2426]		340		345		350
[2427]	Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu					
[2428]		355		360		365
[2429]	Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp					
[2430]		370		375		380
[2431]	Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val					
[2432]		385		390		395
[2433]	Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp					
[2434]		405		410		415
[2435]	Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His					

[2436]	420	425	430
[2437]	Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro		
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[2439]	Gly		
[2440]	<210> 70		
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[2449]	Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr		
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[2451]	Gly Phe His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val		
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[2453]	Ala Val Ile Trp Tyr Ala Gly Ser Asn Lys Phe Tyr Ala Asp Ser Val		
[2454]	50	55	60
[2455]	Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr		
[2456]	65	70	75
[2457]	Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys		
[2458]	85	90	95
[2459]	Ala Arg Gly Gly Gln Leu Asp Tyr Tyr Tyr Tyr Tyr Val Met Asp Val		
[2460]	100	105	110
[2461]	Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly		
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[2463]	Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser		
[2464]	130	135	140
[2465]	Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val		
[2466]	145	150	155
[2467]	Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe		
[2468]	165	170	175
[2469]	Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val		
[2470]	180	185	190
[2471]	Thr Val Pro Ser Ser Asn Phe Gly Thr Gln Thr Tyr Thr Cys Asn Val		
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[2473]	Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys Thr Val Glu Arg Lys		
[2474]	210	215	220
[2475]	Cys Cys Val Glu Cys Pro Pro Cys Pro Ala Pro Pro Val Ala Gly Pro		
[2476]	225	230	235
[2477]	Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser		

[2478]		245		250		255
[2479]	Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp					
[2480]		260		265		270
[2481]	Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn					
[2482]		275		280		285
[2483]	Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val					
[2484]		290		295		300
[2485]	Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu					
[2486]	305		310		315	320
[2487]	Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ser Ser Ile Glu Lys					
[2488]		325		330		335
[2489]	Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr					
[2490]		340		345		350
[2491]	Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr					
[2492]		355		360		365
[2493]	Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu					
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[2495]	Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu					
[2496]	385		390		395	400
[2497]	Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys					
[2498]		405		410		415
[2499]	Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu					
[2500]		420		425		430
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[2512]	Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr					
[2513]		20		25		30
[2514]	Gly Phe His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val					
[2515]		35		40		45
[2516]	Ala Val Ile Trp Tyr Ala Gly Ser Asn Lys Phe Tyr Ala Asp Ser Val					
[2517]	50		55		60	
[2518]	Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr					
[2519]	65		70		75	80

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[2523]					100					105					110	
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[2525]					115					120					125	
[2526]	Pro	Ser	Val	Phe	Pro	Leu	Ala	Pro	Cys	Ser	Arg	Ser	Thr	Ser	Glu	Ser
[2527]					130					135					140	
[2528]	Thr	Ala	Ala	Leu	Gly	Cys	Leu	Val	Lys	Asp	Tyr	Phe	Pro	Glu	Pro	Val
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[2530]	Thr	Val	Ser	Trp	Asn	Ser	Gly	Ala	Leu	Thr	Ser	Gly	Val	His	Thr	Phe
[2531]					165						170					175
[2532]	Pro	Ala	Val	Leu	Gln	Ser	Ser	Gly	Leu	Tyr	Ser	Leu	Ser	Ser	Val	Val
[2533]					180						185					190
[2534]	Thr	Val	Pro	Ser	Ser	Asn	Phe	Gly	Thr	Gln	Thr	Tyr	Thr	Cys	Asn	Val
[2535]					195						200					205
[2536]	Asp	His	Lys	Pro	Ser	Asn	Thr	Lys	Val	Asp	Lys	Thr	Val	Glu	Arg	Lys
[2537]					210						215					220
[2538]	Ser	Cys	Val	Glu	Cys	Pro	Pro	Cys	Pro	Ala	Pro	Glu	Leu	Leu	Gly	Gly
[2539]	225					230					235					240
[2540]	Pro	Ser	Val	Phe	Leu	Phe	Pro	Pro	Lys	Pro	Lys	Asp	Thr	Leu	Met	Ile
[2541]					245						250					255
[2542]	Ser	Arg	Thr	Pro	Glu	Val	Thr	Cys	Val	Val	Val	Asp	Val	Ser	His	Glu
[2543]					260						265					270
[2544]	Asp	Pro	Glu	Val	Lys	Phe	Asn	Trp	Tyr	Val	Asp	Gly	Val	Glu	Val	His
[2545]					275						280					285
[2546]	Asn	Ala	Lys	Thr	Lys	Pro	Arg	Glu	Glu	Gln	Tyr	Asn	Ser	Thr	Tyr	Arg
[2547]					290						295					300
[2548]	Val	Val	Ser	Val	Leu	Thr	Val	Leu	His	Gln	Asp	Trp	Leu	Asn	Gly	Lys
[2549]	305					310					315					320
[2550]	Glu	Tyr	Lys	Cys	Lys	Val	Ser	Asn	Lys	Ala	Leu	Pro	Ala	Pro	Ile	Glu
[2551]					325						330					335
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[2553]					340						345					350
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[2555]					355						360					365
[2556]	Thr	Cys	Leu	Val	Lys	Gly	Phe	Tyr	Pro	Ser	Asp	Ile	Ala	Val	Glu	Trp
[2557]					370						375					380
[2558]	Glu	Ser	Asn	Gly	Gln	Pro	Glu	Asn	Asn	Tyr	Lys	Thr	Thr	Pro	Pro	Val
[2559]	385					390					395					400
[2560]	Leu	Asp	Ser	Asp	Gly	Ser	Phe	Phe	Leu	Tyr	Ser	Lys	Leu	Thr	Val	Asp
[2561]					405						410					415

[2562]	Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His
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[2564]	Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
[2565]	435 440 445
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[2567]	<210> 72
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[2578]	Gly Phe His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
[2579]	35 40 45
[2580]	Ala Val Ile Trp Tyr Ala Gly Ser Asn Lys Phe Tyr Ala Asp Ser Val
[2581]	50 55 60
[2582]	Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
[2583]	65 70 75 80
[2584]	Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
[2585]	85 90 95
[2586]	Ala Arg Gly Gly Gln Leu Asp Tyr Tyr Tyr Tyr Tyr Val Met Asp Val
[2587]	100 105 110
[2588]	Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly
[2589]	115 120 125
[2590]	Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser
[2591]	130 135 140
[2592]	Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val
[2593]	145 150 155 160
[2594]	Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe
[2595]	165 170 175
[2596]	Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val
[2597]	180 185 190
[2598]	Thr Val Pro Ser Ser Asn Phe Gly Thr Gln Thr Tyr Thr Cys Asn Val
[2599]	195 200 205
[2600]	Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys Thr Val Glu Arg Lys
[2601]	210 215 220
[2602]	Ser Cys Val Glu Cys Pro Pro Cys Pro Ala Pro Pro Val Ala Gly Pro
[2603]	225 230 235 240

[2604]	Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser		
[2605]		245	250 255
[2606]	Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp		
[2607]		260	265 270
[2608]	Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn		
[2609]		275	280 285
[2610]	Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val		
[2611]		290	295 300
[2612]	Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu		
[2613]		305	310 315 320
[2614]	Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ser Ser Ile Glu Lys		
[2615]		325	330 335
[2616]	Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr		
[2617]		340	345 350
[2618]	Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr		
[2619]		355	360 365
[2620]	Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu		
[2621]		370	375 380
[2622]	Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu		
[2623]		385	390 395 400
[2624]	Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys		
[2625]		405	410 415
[2626]	Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu		
[2627]		420	425 430
[2628]	Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly		
[2629]		435	440 445
[2630]	<210> 73		
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[2639]	Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr		
[2640]		20	25 30
[2641]	Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val		
[2642]		35	40 45
[2643]	Ala Val Ile Trp Tyr Ala Gly Ser Asn Lys Tyr Tyr Ala Asp Ser Val		
[2644]		50	55 60
[2645]	Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr		

[2646]	65	70	75	80
[2647]	Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys			
[2648]		85	90	95
[2649]	Ala Arg Gly Gly Arg Ile Ala Val Ala Phe Tyr Tyr Ser Met Asp Val			
[2650]		100	105	110
[2651]	Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser			
[2652]		115	120	
[2653]	<210> 74			
[2654]	<211> 107			
[2655]	<212> PRT			
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[2658]	<223> 合成的: 18E10 (VL)			
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[2660]	Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly			
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[2662]	Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Ser Ser Trp			
[2663]		20	25	30
[2664]	Leu Ala Trp Tyr Gln Gln Lys Pro Glu Lys Ala Pro Lys Ser Leu Ile			
[2665]		35	40	45
[2666]	Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly			
[2667]		50	55	60
[2668]	Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro			
[2669]	65	70	75	80
[2670]	Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Asn Ser Tyr Pro Tyr			
[2671]		85	90	95
[2672]	Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys			
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[2681]	Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg			
[2682]	1	5	10	15
[2683]	Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr			
[2684]		20	25	30
[2685]	Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val			
[2686]		35	40	45
[2687]	Ala Val Ile Trp Tyr Ala Gly Ser Asn Lys Tyr Tyr Ala Asp Ser Val			

[2688]	50	55	60
[2689]	Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr		
[2690]	65	70	75
[2691]	Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys		
[2692]	85	90	95
[2693]	Ala Arg Gly Gly Arg Ile Ala Val Ala Phe Tyr Tyr Ser Met Asp Val		
[2694]	100	105	110
[2695]	Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly		
[2696]	115	120	125
[2697]	Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser		
[2698]	130	135	140
[2699]	Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val		
[2700]	145	150	155
[2701]	Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe		
[2702]	165	170	175
[2703]	Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val		
[2704]	180	185	190
[2705]	Thr Val Pro Ser Ser Asn Phe Gly Thr Gln Thr Tyr Thr Cys Asn Val		
[2706]	195	200	205
[2707]	Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys Thr Val Glu Arg Lys		
[2708]	210	215	220
[2709]	Cys Cys Val Glu Cys Pro Pro Cys Pro Ala Pro Pro Val Ala Gly Pro		
[2710]	225	230	235
[2711]	Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser		
[2712]	245	250	255
[2713]	Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp		
[2714]	260	265	270
[2715]	Pro Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn		
[2716]	275	280	285
[2717]	Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr Phe Arg Val		
[2718]	290	295	300
[2719]	Val Ser Val Leu Thr Val Val His Gln Asp Trp Leu Asn Gly Lys Glu		
[2720]	305	310	315
[2721]	Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ala Pro Ile Glu Lys		
[2722]	325	330	335
[2723]	Thr Ile Ser Lys Thr Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr		
[2724]	340	345	350
[2725]	Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr		
[2726]	355	360	365
[2727]	Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu		
[2728]	370	375	380
[2729]	Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Met Leu		

[2730]	385	390	395	400
[2731]	Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys			
[2732]		405	410	415
[2733]	Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu			
[2734]		420	425	430
[2735]	Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly			
[2736]		435	440	445
[2737]	Lys			
[2738]	<210> 76			
[2739]	<211> 214			
[2740]	<212> PRT			
[2741]	<213> 人工序列			
[2742]	<220>			
[2743]	<223> 合成的: 18E10 (全长野生型轻链)			
[2744]	<400> 76			
[2745]	Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly			
[2746]	1	5	10	15
[2747]	Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Ser Ser Trp			
[2748]		20	25	30
[2749]	Leu Ala Trp Tyr Gln Gln Lys Pro Glu Lys Ala Pro Lys Ser Leu Ile			
[2750]		35	40	45
[2751]	Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly			
[2752]	50	55	60	
[2753]	Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro			
[2754]	65	70	75	80
[2755]	Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Asn Ser Tyr Pro Tyr			
[2756]		85	90	95
[2757]	Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys Arg Thr Val Ala Ala			
[2758]		100	105	110
[2759]	Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly			
[2760]		115	120	125
[2761]	Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala			
[2762]	130	135	140	
[2763]	Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln			
[2764]	145	150	155	160
[2765]	Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser			
[2766]		165	170	175
[2767]	Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr			
[2768]		180	185	190
[2769]	Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser			
[2770]		195	200	205
[2771]	Phe Asn Arg Gly Glu Cys			

[2772]	210																
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[2775]	<212> PRT																
[2776]	<213> 人工序列																
[2777]	<220>																
[2778]	<223> 合成的: 18E10.IgG1 (VH + IgG1)																
[2779]	<400> 77																
[2780]	Gln	Val	Gln	Leu	Val	Glu	Ser	Gly	Gly	Gly	Val	Val	Gln	Pro	Gly	Arg	
[2781]	1				5					10					15		
[2782]	Ser	Leu	Arg	Leu	Ser	Cys	Ala	Ala	Ser	Gly	Phe	Thr	Phe	Ser	Ser	Tyr	
[2783]				20					25					30			
[2784]	Gly	Met	His	Trp	Val	Arg	Gln	Ala	Pro	Gly	Lys	Gly	Leu	Glu	Trp	Val	
[2785]			35					40					45				
[2786]	Ala	Val	Ile	Trp	Tyr	Ala	Gly	Ser	Asn	Lys	Tyr	Tyr	Ala	Asp	Ser	Val	
[2787]		50					55				60						
[2788]	Lys	Gly	Arg	Phe	Thr	Ile	Ser	Arg	Asp	Asn	Ser	Lys	Asn	Thr	Leu	Tyr	
[2789]	65					70				75					80		
[2790]	Leu	Gln	Met	Asn	Ser	Leu	Arg	Ala	Glu	Asp	Thr	Ala	Val	Tyr	Tyr	Cys	
[2791]				85					90					95			
[2792]	Ala	Arg	Gly	Gly	Arg	Ile	Ala	Val	Ala	Phe	Tyr	Tyr	Ser	Met	Asp	Val	
[2793]				100					105					110			
[2794]	Trp	Gly	Gln	Gly	Thr	Thr	Val	Thr	Val	Ser	Ser	Ala	Ser	Thr	Lys	Gly	
[2795]			115					120					125				
[2796]	Pro	Ser	Val	Phe	Pro	Leu	Ala	Pro	Ser	Ser	Lys	Ser	Thr	Ser	Gly	Gly	
[2797]		130					135				140						
[2798]	Thr	Ala	Ala	Leu	Gly	Cys	Leu	Val	Lys	Asp	Tyr	Phe	Pro	Glu	Pro	Val	
[2799]	145					150				155				160			
[2800]	Thr	Val	Ser	Trp	Asn	Ser	Gly	Ala	Leu	Thr	Ser	Gly	Val	His	Thr	Phe	
[2801]				165					170					175			
[2802]	Pro	Ala	Val	Leu	Gln	Ser	Ser	Gly	Leu	Tyr	Ser	Leu	Ser	Ser	Val	Val	
[2803]				180					185					190			
[2804]	Thr	Val	Pro	Ser	Ser	Ser	Leu	Gly	Thr	Gln	Thr	Tyr	Ile	Cys	Asn	Val	
[2805]		195					200				205						
[2806]	Asn	His	Lys	Pro	Ser	Asn	Thr	Lys	Val	Asp	Lys	Arg	Val	Glu	Pro	Lys	
[2807]		210					215				220						
[2808]	Ser	Cys	Asp	Lys	Thr	His	Thr	Cys	Pro	Pro	Cys	Pro	Ala	Pro	Glu	Leu	
[2809]	225					230				235				240			
[2810]	Leu	Gly	Gly	Pro	Ser	Val	Phe	Leu	Phe	Pro	Pro	Lys	Pro	Lys	Asp	Thr	
[2811]				245					250					255			
[2812]	Leu	Met	Ile	Ser	Arg	Thr	Pro	Glu	Val	Thr	Cys	Val	Val	Val	Asp	Val	
[2813]				260					265					270			

[2814]	Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val		
[2815]	275	280	285
[2816]	Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser		
[2817]	290	295	300
[2818]	Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu		
[2819]	305	310	315 320
[2820]	Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala		
[2821]	325	330	335
[2822]	Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro		
[2823]	340	345	350
[2824]	Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln		
[2825]	355	360	365
[2826]	Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala		
[2827]	370	375	380
[2828]	Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr		
[2829]	385	390	395 400
[2830]	Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu		
[2831]	405	410	415
[2832]	Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser		
[2833]	420	425	430
[2834]	Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser		
[2835]	435	440	445
[2836]	Leu Ser Pro Gly		
[2837]	450		
[2838]	<210> 78		
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[2840]	<212> PRT		
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[2845]	Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg		
[2846]	1 5 10 15		
[2847]	Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr		
[2848]	20 25 30		
[2849]	Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val		
[2850]	35 40 45		
[2851]	Ala Val Ile Trp Tyr Ala Gly Ser Asn Lys Tyr Tyr Ala Asp Ser Val		
[2852]	50 55 60		
[2853]	Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr		
[2854]	65 70 75 80		
[2855]	Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys		

[2856]		85		90		95
[2857]	Ala Arg Gly Gly Arg Ile Ala Val	Ala Phe Tyr Tyr Ser Met Asp Val				
[2858]		100		105		110
[2859]	Trp Gly Gln Gly Thr Thr Val Thr Val	Ser Ser Ala Ser Thr Lys Gly				
[2860]		115		120		125
[2861]	Pro Ser Val Phe Pro Leu Ala Pro Ser Ser	Lys Ser Thr Ser Gly Gly				
[2862]		130		135		140
[2863]	Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe	Pro Glu Pro Val				
[2864]	145		150		155	160
[2865]	Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe					
[2866]		165		170		175
[2867]	Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val					
[2868]		180		185		190
[2869]	Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val					
[2870]		195		200		205
[2871]	Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys					
[2872]		210		215		220
[2873]	Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Ala					
[2874]	225		230		235	240
[2875]	Glu Gly Ala Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr					
[2876]		245		250		255
[2877]	Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val					
[2878]		260		265		270
[2879]	Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val					
[2880]		275		280		285
[2881]	Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser					
[2882]		290		295		300
[2883]	Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu					
[2884]	305		310		315	320
[2885]	Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ser					
[2886]		325		330		335
[2887]	Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro					
[2888]		340		345		350
[2889]	Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln					
[2890]		355		360		365
[2891]	Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala					
[2892]		370		375		380
[2893]	Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr					
[2894]	385		390		395	400
[2895]	Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu					
[2896]		405		410		415
[2897]	Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser					

[2898]	420	425	430
[2899]	Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser		
[2900]	435	440	445
[2901]	Leu Ser Pro Gly		
[2902]	450		
[2903]	<210> 79		
[2904]	<211> 214		
[2905]	<212> PRT		
[2906]	<213> 人工序列		
[2907]	<220>		
[2908]	<223> 合成的: 18E10.IgG1 (VL + CL)		
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[2910]	Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly		
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[2912]	Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Ser Ser Trp		
[2913]	20 25 30		
[2914]	Leu Ala Trp Tyr Gln Gln Lys Pro Glu Lys Ala Pro Lys Ser Leu Ile		
[2915]	35 40 45		
[2916]	Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly		
[2917]	50 55 60		
[2918]	Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro		
[2919]	65 70 75 80		
[2920]	Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Asn Ser Tyr Pro Tyr		
[2921]	85 90 95		
[2922]	Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys Arg Thr Val Ala Ala		
[2923]	100 105 110		
[2924]	Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly		
[2925]	115 120 125		
[2926]	Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala		
[2927]	130 135 140		
[2928]	Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln		
[2929]	145 150 155 160		
[2930]	Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser		
[2931]	165 170 175		
[2932]	Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr		
[2933]	180 185 190		
[2934]	Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser		
[2935]	195 200 205		
[2936]	Phe Asn Arg Gly Glu Cys		
[2937]	210		
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[2939]	<211> 5		

[2940] <212> PRT
[2941] <213> 人工序列
[2942] <220>
[2943] <223> 合成的: 18E10 VH CDR1
[2944] <400> 80
[2945] Ser Tyr Gly Met His
[2946] 1 5
[2947] <210> 81
[2948] <211> 17
[2949] <212> PRT
[2950] <213> 人工序列
[2951] <220>
[2952] <223> 合成的: 18E10 VH CDR2
[2953] <400> 81
[2954] Val Ile Trp Tyr Ala Gly Ser Asn Lys Tyr Tyr Ala Asp Ser Val Lys
[2955] 1 5 10 15
[2956] Gly
[2957] <210> 82
[2958] <211> 14
[2959] <212> PRT
[2960] <213> 人工序列
[2961] <220>
[2962] <223> 合成的: 18E10 VH CDR3
[2963] <400> 82
[2964] Gly Gly Arg Ile Ala Val Ala Phe Tyr Tyr Ser Met Asp Val
[2965] 1 5 10
[2966] <210> 83
[2967] <211> 11
[2968] <212> PRT
[2969] <213> 人工序列
[2970] <220>
[2971] <223> 合成的: 18E10 VL CDR1
[2972] <400> 83
[2973] Arg Ala Ser Gln Gly Ile Ser Ser Trp Leu Ala
[2974] 1 5 10
[2975] <210> 84
[2976] <211> 7
[2977] <212> PRT
[2978] <213> 人工序列
[2979] <220>
[2980] <223> 合成的: 18E10 VL CDR2
[2981] <400> 84

[2982]	Ala Ala Ser Ser Leu Gln Ser
[2983]	1 5
[2984]	<210> 85
[2985]	<211> 9
[2986]	<212> PRT
[2987]	<213> 人工序列
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[2989]	<223> 合成的: 18E10 VL CDR3
[2990]	<400> 85
[2991]	Gln Gln Tyr Asn Ser Tyr Pro Tyr Thr
[2992]	1 5
[2993]	<210> 86
[2994]	<211> 448
[2995]	<212> PRT
[2996]	<213> 人工序列
[2997]	<220>
[2998]	<223> 合成的: 18E10 (VH + G2 (C219S)) 或18E10-IgG2-C219S
[2999]	<400> 86
[3000]	Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg
[3001]	1 5 10 15
[3002]	Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
[3003]	20 25 30
[3004]	Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
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[3006]	Ala Val Ile Trp Tyr Ala Gly Ser Asn Lys Tyr Tyr Ala Asp Ser Val
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[3008]	Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
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[3012]	Ala Arg Gly Gly Arg Ile Ala Val Ala Phe Tyr Tyr Ser Met Asp Val
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[3015]	115 120 125
[3016]	Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser
[3017]	130 135 140
[3018]	Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val
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[3020]	Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe
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[3022]	Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val
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[3024]	Thr Val Pro Ser Ser Asn Phe Gly Thr Gln Thr Tyr Thr Cys Asn Val		
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[3028]	Ser Cys Val Glu Cys Pro Pro Cys Pro Ala Pro Pro Val Ala Gly Pro		
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[3030]	Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser		
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[3032]	Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp		
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[3034]	Pro Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn		
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[3036]	Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr Phe Arg Val		
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[3038]	Val Ser Val Leu Thr Val Val His Gln Asp Trp Leu Asn Gly Lys Glu		
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[3040]	Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ala Pro Ile Glu Lys		
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[3042]	Thr Ile Ser Lys Thr Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr		
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[3044]	Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr		
[3045]	355	360	365
[3046]	Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu		
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[3048]	Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Met Leu		
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[3050]	Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys		
[3051]	405	410	415
[3052]	Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu		
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[3054]	Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly		
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[3090]	210					215					220						
[3091]	Cys	Cys	Val	Glu	Cys	Pro	Pro	Cys	Pro	Ala	Pro	Glu	Leu	Leu	Gly	Gly	
[3092]	225					230					235					240	
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[3104]	325					330					335						
[3105]	Lys	Thr	Ile	Ser	Lys	Ala	Lys	Gly	Gln	Pro	Arg	Glu	Pro	Gln	Val	Tyr	
[3106]	340					345					350						
[3107]	Thr	Leu	Pro	Pro	Ser	Arg	Glu	Glu	Met	Thr	Lys	Asn	Gln	Val	Ser	Leu	

[3108]	355	360	365
[3109]	Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp		
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[3111]	Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val		
[3112]	385	390	395 400
[3113]	Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp		
[3114]	405	410	415
[3115]	Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His		
[3116]	420	425	430
[3117]	Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro		
[3118]	435	440	445
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[3135]	Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr		
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[3143]	Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser		
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[3145]	Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val		
[3146]	145 150 155 160		
[3147]	Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe		
[3148]	165 170 175		
[3149]	Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val		

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[3153]	Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys Thr Val Glu Arg Lys		
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[3155]	Cys Cys Val Glu Cys Pro Pro Cys Pro Ala Pro Pro Val Ala Gly Pro		
[3156]	225	230	235 240
[3157]	Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser		
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[3159]	Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp		
[3160]	260	265	270
[3161]	Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn		
[3162]	275	280	285
[3163]	Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val		
[3164]	290	295	300
[3165]	Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu		
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[3167]	Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ser Ser Ile Glu Lys		
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[3169]	Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr		
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[3171]	Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr		
[3172]	355	360	365
[3173]	Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu		
[3174]	370	375	380
[3175]	Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu		
[3176]	385	390	395 400
[3177]	Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys		
[3178]	405	410	415
[3179]	Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu		
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[3195]			35					40					45			
[3196]	Ala	Val	Ile	Trp	Tyr	Ala	Gly	Ser	Asn	Lys	Tyr	Tyr	Ala	Asp	Ser	Val
[3197]		50					55					60				
[3198]	Lys	Gly	Arg	Phe	Thr	Ile	Ser	Arg	Asp	Asn	Ser	Lys	Asn	Thr	Leu	Tyr
[3199]	65					70				75					80	
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[3205]			115					120					125			
[3206]	Pro	Ser	Val	Phe	Pro	Leu	Ala	Pro	Cys	Ser	Arg	Ser	Thr	Ser	Glu	Ser
[3207]		130					135					140				
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[3209]	145					150				155				160		
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[3211]				165					170					175		
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[3213]			180					185					190			
[3214]	Thr	Val	Pro	Ser	Ser	Asn	Phe	Gly	Thr	Gln	Thr	Tyr	Thr	Cys	Asn	Val
[3215]		195					200					205				
[3216]	Asp	His	Lys	Pro	Ser	Asn	Thr	Lys	Val	Asp	Lys	Thr	Val	Glu	Arg	Lys
[3217]		210					215				220					
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[3219]	225					230				235				240		
[3220]	Pro	Ser	Val	Phe	Leu	Phe	Pro	Pro	Lys	Pro	Lys	Asp	Thr	Leu	Met	Ile
[3221]			245						250					255		
[3222]	Ser	Arg	Thr	Pro	Glu	Val	Thr	Cys	Val	Val	Val	Asp	Val	Ser	His	Glu
[3223]			260						265					270		
[3224]	Asp	Pro	Glu	Val	Lys	Phe	Asn	Trp	Tyr	Val	Asp	Gly	Val	Glu	Val	His
[3225]		275					280					285				
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[3228]	Val	Val	Ser	Val	Leu	Thr	Val	Leu	His	Gln	Asp	Trp	Leu	Asn	Gly	Lys
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[3232]	Lys	Thr	Ile	Ser	Lys	Ala	Lys	Gly	Gln	Pro	Arg	Glu	Pro	Gln	Val	Tyr
[3233]			340						345					350		

[3234]	Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu
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[3236]	Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp
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[3238]	Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val
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[3241]	405 410 415
[3242]	Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His
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[3260]	Ala Val Ile Trp Tyr Ala Gly Ser Asn Lys Tyr Tyr Ala Asp Ser Val
[3261]	50 55 60
[3262]	Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
[3263]	65 70 75 80
[3264]	Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
[3265]	85 90 95
[3266]	Ala Arg Gly Gly Arg Ile Ala Val Ala Phe Tyr Tyr Ser Met Asp Val
[3267]	100 105 110
[3268]	Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly
[3269]	115 120 125
[3270]	Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser
[3271]	130 135 140
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[3274]	Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe
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[3287]				260					265						270	
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[3299]				355				360					365			
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[3303]				385				390				395			400	
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[3325]	Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe Ser Leu			
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[3327]	Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala			
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[3329]	Arg Leu Gly Ala Phe Asp Ala Phe Asp Ile Trp Gly Gln Gly Thr Met			
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[3331]	Val Thr Val Ser Ser			
[3332]	115			
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[3344]	Leu Ala Trp Tyr Gln Gln Lys Pro Glu Lys Ala Pro Lys Ser Leu Ile			
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[3348]	Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro			
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[3350]	Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Asn Ser Tyr Pro Tyr			
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[3352]	Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys			
[3353]	100	105		
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[3359]	<223> 合成的: 3C3 (VL2)			

[3360]	<400> 93
[3361]	Glu Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
[3362]	1 5 10 15
[3363]	Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Gly Val Ser Ser Tyr
[3364]	20 25 30
[3365]	Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile
[3366]	35 40 45
[3367]	Tyr Asp Ala Ser Asn Arg Ala Thr Gly Ile Pro Ala Arg Phe Ser Gly
[3368]	50 55 60
[3369]	Ser Gly Pro Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Glu Pro
[3370]	65 70 75 80
[3371]	Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Arg Ser Asn Trp His Thr
[3372]	85 90 95
[3373]	Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
[3374]	100 105
[3375]	<210> 94
[3376]	<211> 447
[3377]	<212> PRT
[3378]	<213> 人工序列
[3379]	<220>
[3380]	<223> 合成的: 3C3 (全长野生型重链)
[3381]	<400> 94
[3382]	Gln Val Gln Leu Gln Gln Trp Gly Ala Gly Leu Leu Lys Pro Ser Glu
[3383]	1 5 10 15
[3384]	Thr Leu Ser Leu Thr Cys Ala Val Tyr Gly Gly Ser Phe Ser Gly Tyr
[3385]	20 25 30
[3386]	Tyr Trp Thr Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile
[3387]	35 40 45
[3388]	Gly Lys Ile Asn His Ser Gly Asn Thr Asn Tyr Asn Pro Ser Leu Lys
[3389]	50 55 60
[3390]	Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe Ser Leu
[3391]	65 70 75 80
[3392]	Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala
[3393]	85 90 95
[3394]	Arg Leu Gly Ala Phe Asp Ala Phe Asp Ile Trp Gly Gln Gly Thr Met
[3395]	100 105 110
[3396]	Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu
[3397]	115 120 125
[3398]	Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys
[3399]	130 135 140
[3400]	Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser
[3401]	145 150 155 160

[3402]	Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser		
[3403]		165	170
[3404]	Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser		175
[3405]		180	185
[3406]	Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn		190
[3407]		195	200
[3408]	Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp Lys Thr His		205
[3409]		210	215
[3410]	Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val		220
[3411]		225	230
[3412]	Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr		235
[3413]		245	250
[3414]	Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu		255
[3415]		260	265
[3416]	Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys		270
[3417]		275	280
[3418]	Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser		285
[3419]		290	295
[3420]	Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys		300
[3421]		305	310
[3422]	Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile		315
[3423]		325	330
[3424]	Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro		335
[3425]		340	345
[3426]	Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr Cys Leu		350
[3427]		355	360
[3428]	Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn		365
[3429]		370	375
[3430]	Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser		380
[3431]		385	390
[3432]	Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg		395
[3433]		405	410
[3434]	Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu		415
[3435]		420	425
[3436]	His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys		430
[3437]		435	440
[3438]	<210> 95		445
[3439]	<211> 214		
[3440]	<212> PRT		
[3441]	<213> 人工序列		
[3442]	<220>		
[3443]	<223> 合成的: 3C3 L1 (全长野生型轻链 1)		

[3444]	<400> 95
[3445]	Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
[3446]	1 5 10 15
[3447]	Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Ser Ser Trp
[3448]	20 25 30
[3449]	Leu Ala Trp Tyr Gln Gln Lys Pro Glu Lys Ala Pro Lys Ser Leu Ile
[3450]	35 40 45
[3451]	Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
[3452]	50 55 60
[3453]	Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
[3454]	65 70 75 80
[3455]	Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Asn Ser Tyr Pro Tyr
[3456]	85 90 95
[3457]	Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys Arg Thr Val Ala Ala
[3458]	100 105 110
[3459]	Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly
[3460]	115 120 125
[3461]	Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala
[3462]	130 135 140
[3463]	Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln
[3464]	145 150 155 160
[3465]	Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser
[3466]	165 170 175
[3467]	Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr
[3468]	180 185 190
[3469]	Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser
[3470]	195 200 205
[3471]	Phe Asn Arg Gly Glu Cys
[3472]	210
[3473]	<210> 96
[3474]	<211> 213
[3475]	<212> PRT
[3476]	<213> 人工序列
[3477]	<220>
[3478]	<223> 合成的: 3C3 L2 (全长野生型轻链 2)
[3479]	<400> 96
[3480]	Glu Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
[3481]	1 5 10 15
[3482]	Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Gly Val Ser Ser Tyr
[3483]	20 25 30
[3484]	Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile
[3485]	35 40 45

[3486]	Tyr Asp Ala Ser Asn Arg Ala Thr Gly Ile Pro Ala Arg Phe Ser Gly
[3487]	50 55 60
[3488]	Ser Gly Pro Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Glu Pro
[3489]	65 70 75 80
[3490]	Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Arg Ser Asn Trp His Thr
[3491]	85 90 95
[3492]	Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys Arg Thr Val Ala Ala Pro
[3493]	100 105 110
[3494]	Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr
[3495]	115 120 125
[3496]	Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys
[3497]	130 135 140
[3498]	Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu
[3499]	145 150 155 160
[3500]	Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser
[3501]	165 170 175
[3502]	Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala
[3503]	180 185 190
[3504]	Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe
[3505]	195 200 205
[3506]	Asn Arg Gly Glu Cys
[3507]	210
[3508]	<210> 97
[3509]	<211> 446
[3510]	<212> PRT
[3511]	<213> 人工序列
[3512]	<220>
[3513]	<223> 合成的: 3C3.IgG1 (VH + IgG1)
[3514]	<400> 97
[3515]	Gln Val Gln Leu Gln Gln Trp Gly Ala Gly Leu Leu Lys Pro Ser Glu
[3516]	1 5 10 15
[3517]	Thr Leu Ser Leu Thr Cys Ala Val Tyr Gly Gly Ser Phe Ser Gly Tyr
[3518]	20 25 30
[3519]	Tyr Trp Thr Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile
[3520]	35 40 45
[3521]	Gly Lys Ile Asn His Ser Gly Asn Thr Asn Tyr Asn Pro Ser Leu Lys
[3522]	50 55 60
[3523]	Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe Ser Leu
[3524]	65 70 75 80
[3525]	Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala
[3526]	85 90 95
[3527]	Arg Leu Gly Ala Phe Asp Ala Phe Asp Ile Trp Gly Gln Gly Thr Met

[3528]	100	105	110
[3529]	Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu		
[3530]	115	120	125
[3531]	Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys		
[3532]	130	135	140
[3533]	Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser		
[3534]	145	150	155
[3535]	Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser		
[3536]	165	170	175
[3537]	Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser		
[3538]	180	185	190
[3539]	Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn		
[3540]	195	200	205
[3541]	Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp Lys Thr His		
[3542]	210	215	220
[3543]	Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val		
[3544]	225	230	235
[3545]	Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr		
[3546]	245	250	255
[3547]	Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu		
[3548]	260	265	270
[3549]	Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys		
[3550]	275	280	285
[3551]	Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser		
[3552]	290	295	300
[3553]	Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys		
[3554]	305	310	315
[3555]	Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile		
[3556]	325	330	335
[3557]	Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro		
[3558]	340	345	350
[3559]	Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu		
[3560]	355	360	365
[3561]	Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn		
[3562]	370	375	380
[3563]	Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser		
[3564]	385	390	395
[3565]	Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg		
[3566]	405	410	415
[3567]	Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu		
[3568]	420	425	430
[3569]	His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly		

[3570]	435	440	445
[3571]	<210> 98		
[3572]	<211> 446		
[3573]	<212> PRT		
[3574]	<213> 人工序列		
[3575]	<220>		
[3576]	<223> 合成的: 3C3.IgG1.1 (VH + IgG1.1)		
[3577]	<400> 98		
[3578]	Gln Val Gln Leu Gln Gln Trp Gly Ala Gly Leu Leu Lys Pro Ser Glu		
[3579]	1 5 10 15		
[3580]	Thr Leu Ser Leu Thr Cys Ala Val Tyr Gly Gly Ser Phe Ser Gly Tyr		
[3581]	20 25 30		
[3582]	Tyr Trp Thr Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile		
[3583]	35 40 45		
[3584]	Gly Lys Ile Asn His Ser Gly Asn Thr Asn Tyr Asn Pro Ser Leu Lys		
[3585]	50 55 60		
[3586]	Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe Ser Leu		
[3587]	65 70 75 80		
[3588]	Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala		
[3589]	85 90 95		
[3590]	Arg Leu Gly Ala Phe Asp Ala Phe Asp Ile Trp Gly Gln Gly Thr Met		
[3591]	100 105 110		
[3592]	Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu		
[3593]	115 120 125		
[3594]	Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys		
[3595]	130 135 140		
[3596]	Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser		
[3597]	145 150 155 160		
[3598]	Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser		
[3599]	165 170 175		
[3600]	Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser		
[3601]	180 185 190		
[3602]	Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn		
[3603]	195 200 205		
[3604]	Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp Lys Thr His		
[3605]	210 215 220		
[3606]	Thr Cys Pro Pro Cys Pro Ala Pro Glu Ala Glu Gly Ala Pro Ser Val		
[3607]	225 230 235 240		
[3608]	Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr		
[3609]	245 250 255		
[3610]	Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu		
[3611]	260 265 270		

[3612]	Val	Lys	Phe	Asn	Trp	Tyr	Val	Asp	Gly	Val	Glu	Val	His	Asn	Ala	Lys
[3613]			275					280					285			
[3614]	Thr	Lys	Pro	Arg	Glu	Glu	Gln	Tyr	Asn	Ser	Thr	Tyr	Arg	Val	Val	Ser
[3615]			290					295					300			
[3616]	Val	Leu	Thr	Val	Leu	His	Gln	Asp	Trp	Leu	Asn	Gly	Lys	Glu	Tyr	Lys
[3617]	305					310					315					320
[3618]	Cys	Lys	Val	Ser	Asn	Lys	Ala	Leu	Pro	Ser	Ser	Ile	Glu	Lys	Thr	Ile
[3619]					325					330					335	
[3620]	Ser	Lys	Ala	Lys	Gly	Gln	Pro	Arg	Glu	Pro	Gln	Val	Tyr	Thr	Leu	Pro
[3621]					340					345					350	
[3622]	Pro	Ser	Arg	Glu	Glu	Met	Thr	Lys	Asn	Gln	Val	Ser	Leu	Thr	Cys	Leu
[3623]					355					360					365	
[3624]	Val	Lys	Gly	Phe	Tyr	Pro	Ser	Asp	Ile	Ala	Val	Glu	Trp	Glu	Ser	Asn
[3625]					370					375					380	
[3626]	Gly	Gln	Pro	Glu	Asn	Asn	Tyr	Lys	Thr	Thr	Pro	Pro	Val	Leu	Asp	Ser
[3627]	385					390					395					400
[3628]	Asp	Gly	Ser	Phe	Phe	Leu	Tyr	Ser	Lys	Leu	Thr	Val	Asp	Lys	Ser	Arg
[3629]					405					410					415	
[3630]	Trp	Gln	Gln	Gly	Asn	Val	Phe	Ser	Cys	Ser	Val	Met	His	Glu	Ala	Leu
[3631]					420					425					430	
[3632]	His	Asn	His	Tyr	Thr	Gln	Lys	Ser	Leu	Ser	Leu	Ser	Pro	Gly		
[3633]					435					440					445	
[3634]	<210> 99															
[3635]	<211> 214															
[3636]	<212> PRT															
[3637]	<213> 人工序列															
[3638]	<220>															
[3639]	<223> 合成的: 3C3.IgG1 (VL1 + CL)															
[3640]	<400> 99															
[3641]	Asp	Ile	Gln	Met	Thr	Gln	Ser	Pro	Ser	Ser	Leu	Ser	Ala	Ser	Val	Gly
[3642]	1				5					10					15	
[3643]	Asp	Arg	Val	Thr	Ile	Thr	Cys	Arg	Ala	Ser	Gln	Gly	Ile	Ser	Ser	Trp
[3644]					20					25					30	
[3645]	Leu	Ala	Trp	Tyr	Gln	Gln	Lys	Pro	Glu	Lys	Ala	Pro	Lys	Ser	Leu	Ile
[3646]					35					40					45	
[3647]	Tyr	Ala	Ala	Ser	Ser	Leu	Gln	Ser	Gly	Val	Pro	Ser	Arg	Phe	Ser	Gly
[3648]					50					55					60	
[3649]	Ser	Gly	Ser	Gly	Thr	Asp	Phe	Thr	Leu	Thr	Ile	Ser	Ser	Leu	Gln	Pro
[3650]	65					70					75				80	
[3651]	Glu	Asp	Phe	Ala	Thr	Tyr	Tyr	Cys	Gln	Gln	Tyr	Asn	Ser	Tyr	Pro	Tyr
[3652]					85					90					95	
[3653]	Thr	Phe	Gly	Gln	Gly	Thr	Lys	Leu	Glu	Ile	Lys	Arg	Thr	Val	Ala	Ala

[3654]	100	105	110
[3655]	Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly		
[3656]	115	120	125
[3657]	Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala		
[3658]	130	135	140
[3659]	Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln		
[3660]	145	150	155
[3661]	Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser		
[3662]	165	170	175
[3663]	Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr		
[3664]	180	185	190
[3665]	Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser		
[3666]	195	200	205
[3667]	Phe Asn Arg Gly Glu Cys		
[3668]	210		
[3669]	<210> 100		
[3670]	<211> 213		
[3671]	<212> PRT		
[3672]	<213> 人工序列		
[3673]	<220>		
[3674]	<223> 合成的: 3C3IgG1.2 (VL2 + CL)		
[3675]	<400> 100		
[3676]	Glu Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly		
[3677]	1	5	10
[3678]	Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Gly Val Ser Ser Tyr		
[3679]	20	25	30
[3680]	Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile		
[3681]	35	40	45
[3682]	Tyr Asp Ala Ser Asn Arg Ala Thr Gly Ile Pro Ala Arg Phe Ser Gly		
[3683]	50	55	60
[3684]	Ser Gly Pro Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Glu Pro		
[3685]	65	70	75
[3686]	Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Arg Ser Asn Trp His Thr		
[3687]	85	90	95
[3688]	Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys Arg Thr Val Ala Ala Pro		
[3689]	100	105	110
[3690]	Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr		
[3691]	115	120	125
[3692]	Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys		
[3693]	130	135	140
[3694]	Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu		
[3695]	145	150	155

[3696]	Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser
[3697]	165 170 175
[3698]	Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala
[3699]	180 185 190
[3700]	Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe
[3701]	195 200 205
[3702]	Asn Arg Gly Glu Cys
[3703]	210
[3704]	<210> 101
[3705]	<211> 5
[3706]	<212> PRT
[3707]	<213> 人工序列
[3708]	<220>
[3709]	<223> 合成的: 3C3 VH CDR1
[3710]	<400> 101
[3711]	Gly Tyr Tyr Trp Thr
[3712]	1 5
[3713]	<210> 102
[3714]	<211> 16
[3715]	<212> PRT
[3716]	<213> 人工序列
[3717]	<220>
[3718]	<223> 合成的: 3C3 VH CDR2
[3719]	<400> 102
[3720]	Lys Ile Asn His Ser Gly Asn Thr Asn Tyr Asn Pro Ser Leu Lys Ser
[3721]	1 5 10 15
[3722]	<210> 103
[3723]	<211> 9
[3724]	<212> PRT
[3725]	<213> 人工序列
[3726]	<220>
[3727]	<223> 合成的: 3C3 VH CDR3
[3728]	<400> 103
[3729]	Leu Gly Ala Phe Asp Ala Phe Asp Ile
[3730]	1 5
[3731]	<210> 104
[3732]	<211> 11
[3733]	<212> PRT
[3734]	<213> 人工序列
[3735]	<220>
[3736]	<223> 合成的: 3C3 VL1 CDR1
[3737]	<400> 104

[3738] Arg Ala Ser Gln Gly Ile Ser Ser Trp Leu Ala
[3739] 1 5 10
[3740] <210> 105
[3741] <211> 7
[3742] <212> PRT
[3743] <213> 人工序列
[3744] <220>
[3745] <223> 合成的: 3C3 VL1 CDR2
[3746] <400> 105
[3747] Ala Ala Ser Ser Leu Gln Ser
[3748] 1 5
[3749] <210> 106
[3750] <211> 9
[3751] <212> PRT
[3752] <213> 人工序列
[3753] <220>
[3754] <223> 合成的: 3C3 VL1 CDR3
[3755] <400> 106
[3756] Gln Gln Tyr Asn Ser Tyr Pro Tyr Thr
[3757] 1 5
[3758] <210> 107
[3759] <211> 11
[3760] <212> PRT
[3761] <213> 人工序列
[3762] <220>
[3763] <223> 合成的: 3C3 VL2 CDR1
[3764] <400> 107
[3765] Arg Ala Ser Gln Gly Val Ser Ser Tyr Leu Ala
[3766] 1 5 10
[3767] <210> 108
[3768] <211> 7
[3769] <212> PRT
[3770] <213> 人工序列
[3771] <220>
[3772] <223> 合成的: 3C3 VL2 CDR2
[3773] <400> 108
[3774] Asp Ala Ser Asn Arg Ala Thr
[3775] 1 5
[3776] <210> 109
[3777] <211> 8
[3778] <212> PRT
[3779] <213> 人工序列

[3780]	<220>
[3781]	<223> 合成的: 3C3 VL2 CDR3
[3782]	<400> 109
[3783]	Gln Gln Arg Ser Asn Trp His Thr
[3784]	1 5
[3785]	<210> 110
[3786]	<211> 442
[3787]	<212> PRT
[3788]	<213> 人工序列
[3789]	<220>
[3790]	<223> 合成的: 3C3 (VH + G2)或3C3-IgG2
[3791]	<400> 110
[3792]	Gln Val Gln Leu Gln Gln Trp Gly Ala Gly Leu Leu Lys Pro Ser Glu
[3793]	1 5 10 15
[3794]	Thr Leu Ser Leu Thr Cys Ala Val Tyr Gly Gly Ser Phe Ser Gly Tyr
[3795]	20 25 30
[3796]	Tyr Trp Thr Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile
[3797]	35 40 45
[3798]	Gly Lys Ile Asn His Ser Gly Asn Thr Asn Tyr Asn Pro Ser Leu Lys
[3799]	50 55 60
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[3804]	Arg Leu Gly Ala Phe Asp Ala Phe Asp Ile Trp Gly Gln Gly Thr Met
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[3806]	Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu
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[3808]	Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser Thr Ala Ala Leu Gly Cys
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[3812]	Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser
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[3814]	Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Asn
[3815]	180 185 190
[3816]	Phe Gly Thr Gln Thr Tyr Thr Cys Asn Val Asp His Lys Pro Ser Asn
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[3818]	Thr Lys Val Asp Lys Thr Val Glu Arg Lys Cys Cys Val Glu Cys Pro
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[3820]	Pro Cys Pro Ala Pro Pro Val Ala Gly Pro Ser Val Phe Leu Phe Pro
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[3822]	Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr		
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[3824]	Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Gln Phe Asn		
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[3826]	Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg		
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[3828]	Glu Glu Gln Phe Asn Ser Thr Phe Arg Val Val Ser Val Leu Thr Val		
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[3830]	Val His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser		
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[3832]	Asn Lys Gly Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Thr Lys		
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[3836]	Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe		
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[3838]	Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu		
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[3861]	Gly Lys Ile Asn His Ser Gly Asn Thr Asn Tyr Asn Pro Ser Leu Lys		
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[3863]	Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe Ser Leu		

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[3869]	Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu			
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[3875]	Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser			
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[3877]	Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Asn			
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[3879]	Phe Gly Thr Gln Thr Tyr Thr Cys Asn Val Asp His Lys Pro Ser Asn			
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[3881]	Thr Lys Val Asp Lys Thr Val Glu Arg Lys Ser Cys Val Glu Cys Pro			
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[3883]	Pro Cys Pro Ala Pro Pro Val Ala Gly Pro Ser Val Phe Leu Phe Pro			
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[3885]	Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr			
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[3887]	Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Gln Phe Asn			
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[3889]	Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg			
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[3893]	Val His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser			
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[3899]	Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe			
[3900]		355	360	365
[3901]	Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu			
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[3903]	Asn Asn Tyr Lys Thr Thr Pro Pro Met Leu Asp Ser Asp Gly Ser Phe			
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[3905]	Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly			

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[3907]	Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr					
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[3909]	Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly					
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[3922]	Tyr Trp Thr Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile					
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[3928]	Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala					
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[3930]	Arg Leu Gly Ala Phe Asp Ala Phe Asp Ile Trp Gly Gln Gly Thr Met					
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[3938]	Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser					
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[3940]	Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Asn					
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[3942]	Phe Gly Thr Gln Thr Tyr Thr Cys Asn Val Asp His Lys Pro Ser Asn					
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[3944]	Thr Lys Val Asp Lys Thr Val Glu Arg Lys Cys Cys Val Glu Cys Pro					
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[3946]	Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe					
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[3952]	Asn	Trp	Tyr	Val	Asp	Gly	Val	Glu	Val	His	Asn	Ala	Lys	Thr	Lys	Pro
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[3956]	Val	Leu	His	Gln	Asp	Trp	Leu	Asn	Gly	Lys	Glu	Tyr	Lys	Cys	Lys	Val
[3957]	305										310				315	
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[3959]											325				330	
[3960]	Lys	Gly	Gln	Pro	Arg	Glu	Pro	Gln	Val	Tyr	Thr	Leu	Pro	Pro	Ser	Arg
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[3963]											355				360	
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[3967]	385										390				395	
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[3969]											405				410	
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[3997]	Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser Thr Ala Ala Leu Gly Cys			
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[3999]	Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser			
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[4001]	Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser			
[4002]		165	170	175
[4003]	Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Asn			
[4004]		180	185	190
[4005]	Phe Gly Thr Gln Thr Tyr Thr Cys Asn Val Asp His Lys Pro Ser Asn			
[4006]		195	200	205
[4007]	Thr Lys Val Asp Lys Thr Val Glu Arg Lys Cys Cys Val Glu Cys Pro			
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[4009]	Pro Cys Pro Ala Pro Pro Val Ala Gly Pro Ser Val Phe Leu Phe Pro			
[4010]	225	230	235	240
[4011]	Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr			
[4012]		245	250	255
[4013]	Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn			
[4014]		260	265	270
[4015]	Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg			
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[4017]	Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val			
[4018]		290	295	300
[4019]	Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser			
[4020]	305	310	315	320
[4021]	Asn Lys Ala Leu Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys			
[4022]		325	330	335
[4023]	Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu			
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[4025]	Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe			
[4026]		355	360	365
[4027]	Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu			
[4028]		370	375	380
[4029]	Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe			
[4030]	385	390	395	400
[4031]	Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly			

[4032]		405		410		415
[4033]	Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr					
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[4035]	Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly					
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[4068]	Phe Gly Thr Gln Thr Tyr Thr Cys Asn Val Asp His Lys Pro Ser Asn					
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[4070]	Thr Lys Val Asp Lys Thr Val Glu Arg Lys Ser Cys Val Glu Cys Pro					
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[4072]	Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe					
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[4082]	Val	Leu	His	Gln	Asp	Trp	Leu	Asn	Gly	Lys	Glu	Tyr	Lys	Cys	Lys	Val
[4083]	305										310				315	320
[4084]	Ser	Asn	Lys	Ala	Leu	Pro	Ala	Pro	Ile	Glu	Lys	Thr	Ile	Ser	Lys	Ala
[4085]						325					330				335	
[4086]	Lys	Gly	Gln	Pro	Arg	Glu	Pro	Gln	Val	Tyr	Thr	Leu	Pro	Pro	Ser	Arg
[4087]						340					345				350	
[4088]	Glu	Glu	Met	Thr	Lys	Asn	Gln	Val	Ser	Leu	Thr	Cys	Leu	Val	Lys	Gly
[4089]						355					360				365	
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[4131]	Phe Gly Thr Gln Thr Tyr Thr Cys Asn Val Asp His Lys Pro Ser Asn			
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[4155]	Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe			
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[4169]	<400> 116		
[4170]	Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Gly		
[4171]	1 5 10 15		
[4172]	Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Ile Leu Ser Asp Tyr		
[4173]	20 25 30		
[4174]	Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val		
[4175]	35 40 45		
[4176]	Thr Val Ile Trp Tyr Asp Gly Ser Asn Lys Phe Tyr Val Asp Ser Val		
[4177]	50 55 60		
[4178]	Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr		
[4179]	65 70 75 80		
[4180]	Leu Gln Met Asn Ser Leu Arg Val Glu Asp Thr Ala Val Tyr Tyr Cys		
[4181]	85 90 95		
[4182]	Ala Arg Gly Gly Arg Leu Ala Thr Gly His Phe Tyr Tyr Val Met Asp		
[4183]	100 105 110		
[4184]	Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser		
[4185]	115 120		
[4186]	<210> 117		
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[4188]	<212> PRT		
[4189]	<213> 人工序列		
[4190]	<220>		
[4191]	<223> 合成的: 2G6 (VL)		
[4192]	<400> 117		
[4193]	Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly		
[4194]	1 5 10 15		
[4195]	Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Ser Ser Trp		
[4196]	20 25 30		
[4197]	Leu Ala Trp Tyr Gln Gln Lys Pro Glu Lys Ala Pro Lys Ser Leu Ile		
[4198]	35 40 45		
[4199]	Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly		

[4200]	50	55	60
[4201]	Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro		
[4202]	65	70	75
[4203]	Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Asn Ser Tyr Pro Tyr		
[4204]	85	90	95
[4205]	Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys		
[4206]	100	105	
[4207]	<210> 118		
[4208]	<211> 450		
[4209]	<212> PRT		
[4210]	<213> 人工序列		
[4211]	<220>		
[4212]	<223> 合成的: 2G6 (全长野生型重链)		
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[4214]	Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Gly		
[4215]	1	5	10
[4216]	Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Ile Leu Ser Asp Tyr		
[4217]	20	25	30
[4218]	Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val		
[4219]	35	40	45
[4220]	Thr Val Ile Trp Tyr Asp Gly Ser Asn Lys Phe Tyr Val Asp Ser Val		
[4221]	50	55	60
[4222]	Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr		
[4223]	65	70	75
[4224]	Leu Gln Met Asn Ser Leu Arg Val Glu Asp Thr Ala Val Tyr Tyr Cys		
[4225]	85	90	95
[4226]	Ala Arg Gly Gly Arg Leu Ala Thr Gly His Phe Tyr Tyr Val Met Asp		
[4227]	100	105	110
[4228]	Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys		
[4229]	115	120	125
[4230]	Gly Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu		
[4231]	130	135	140
[4232]	Ser Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro		
[4233]	145	150	155
[4234]	Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr		
[4235]	165	170	175
[4236]	Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val		
[4237]	180	185	190
[4238]	Val Thr Val Pro Ser Ser Asn Phe Gly Thr Gln Thr Tyr Thr Cys Asn		
[4239]	195	200	205
[4240]	Val Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys Thr Val Glu Arg		
[4241]	210	215	220

[4242]	Lys Cys Cys Val Glu Cys Pro Pro Cys Pro Ala Pro Pro Val Ala Gly		
[4243]	225	230	235 240
[4244]	Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile		
[4245]		245	250 255
[4246]	Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu		
[4247]		260	265 270
[4248]	Asp Pro Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val His		
[4249]		275	280 285
[4250]	Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr Phe Arg		
[4251]		290	295 300
[4252]	Val Val Ser Val Leu Thr Val Val His Gln Asp Trp Leu Asn Gly Lys		
[4253]	305	310	315 320
[4254]	Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ala Pro Ile Glu		
[4255]		325	330 335
[4256]	Lys Thr Ile Ser Lys Thr Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr		
[4257]		340	345 350
[4258]	Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu		
[4259]		355	360 365
[4260]	Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp		
[4261]		370	375 380
[4262]	Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Met		
[4263]	385	390	395 400
[4264]	Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp		
[4265]		405	410 415
[4266]	Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His		
[4267]		420	425 430
[4268]	Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro		
[4269]		435	440 445
[4270]	Gly Lys		
[4271]		450	
[4272]	<210>	119	
[4273]	<211>	214	
[4274]	<212>	PRT	
[4275]	<213>	人工序列	
[4276]	<220>		
[4277]	<223>	合成的: 2G6 (全长野生型轻链)	
[4278]	<400>	119	
[4279]	Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly		
[4280]	1	5	10 15
[4281]	Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Ser Ser Trp		
[4282]		20	25 30
[4283]	Leu Ala Trp Tyr Gln Gln Lys Pro Glu Lys Ala Pro Lys Ser Leu Ile		

[4284]	35	40	45
[4285]	Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly		
[4286]	50	55	60
[4287]	Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro		
[4288]	65	70	75
[4289]	Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Asn Ser Tyr Pro Tyr		
[4290]	85	90	95
[4291]	Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys Arg Thr Val Ala Ala		
[4292]	100	105	110
[4293]	Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly		
[4294]	115	120	125
[4295]	Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala		
[4296]	130	135	140
[4297]	Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln		
[4298]	145	150	155
[4299]	Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser		
[4300]	165	170	175
[4301]	Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr		
[4302]	180	185	190
[4303]	Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser		
[4304]	195	200	205
[4305]	Phe Asn Arg Gly Glu Cys		
[4306]	210		
[4307]	<210> 120		
[4308]	<211> 453		
[4309]	<212> PRT		
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[4311]	<220>		
[4312]	<223> 合成的: 2G6.IgG1 (VH + IgG1)		
[4313]	<400> 120		
[4314]	Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Gly		
[4315]	1	5	10
[4316]	Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Ile Leu Ser Asp Tyr		
[4317]	20	25	30
[4318]	Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val		
[4319]	35	40	45
[4320]	Thr Val Ile Trp Tyr Asp Gly Ser Asn Lys Phe Tyr Val Asp Ser Val		
[4321]	50	55	60
[4322]	Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr		
[4323]	65	70	75
[4324]	Leu Gln Met Asn Ser Leu Arg Val Glu Asp Thr Ala Val Tyr Tyr Cys		
[4325]	85	90	95

[4326]	Ala Arg Gly Gly Arg Leu Ala Thr Gly His Phe Tyr Tyr Val Met Asp
[4327]	100 105 110
[4328]	Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys
[4329]	115 120 125
[4330]	Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly
[4331]	130 135 140
[4332]	Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro
[4333]	145 150 155 160
[4334]	Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr
[4335]	165 170 175
[4336]	Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val
[4337]	180 185 190
[4338]	Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn
[4339]	195 200 205
[4340]	Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro
[4341]	210 215 220
[4342]	Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu
[4343]	225 230 235 240
[4344]	Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
[4345]	245 250 255
[4346]	Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp
[4347]	260 265 270
[4348]	Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
[4349]	275 280 285
[4350]	Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn
[4351]	290 295 300
[4352]	Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
[4353]	305 310 315 320
[4354]	Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro
[4355]	325 330 335
[4356]	Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
[4357]	340 345 350
[4358]	Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn
[4359]	355 360 365
[4360]	Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
[4361]	370 375 380
[4362]	Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
[4363]	385 390 395 400
[4364]	Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys
[4365]	405 410 415
[4366]	Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
[4367]	420 425 430

[4368]	Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
[4369]	435 440 445
[4370]	Ser Leu Ser Pro Gly
[4371]	450
[4372]	<210> 121
[4373]	<211> 453
[4374]	<212> PRT
[4375]	<213> 人工序列
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[4377]	<223> 合成的: 2G6.IgG1.1 (VH + IgG1.1)
[4378]	<400> 121
[4379]	Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Gly
[4380]	1 5 10 15
[4381]	Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Ile Leu Ser Asp Tyr
[4382]	20 25 30
[4383]	Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
[4384]	35 40 45
[4385]	Thr Val Ile Trp Tyr Asp Gly Ser Asn Lys Phe Tyr Val Asp Ser Val
[4386]	50 55 60
[4387]	Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
[4388]	65 70 75 80
[4389]	Leu Gln Met Asn Ser Leu Arg Val Glu Asp Thr Ala Val Tyr Tyr Cys
[4390]	85 90 95
[4391]	Ala Arg Gly Gly Arg Leu Ala Thr Gly His Phe Tyr Tyr Val Met Asp
[4392]	100 105 110
[4393]	Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys
[4394]	115 120 125
[4395]	Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly
[4396]	130 135 140
[4397]	Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro
[4398]	145 150 155 160
[4399]	Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr
[4400]	165 170 175
[4401]	Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val
[4402]	180 185 190
[4403]	Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn
[4404]	195 200 205
[4405]	Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro
[4406]	210 215 220
[4407]	Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu
[4408]	225 230 235 240
[4409]	Ala Glu Gly Ala Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp

[4410]	245	250	255
[4411]	Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp		
[4412]	260	265	270
[4413]	Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly		
[4414]	275	280	285
[4415]	Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn		
[4416]	290	295	300
[4417]	Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp		
[4418]	305	310	315
[4419]	Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro		
[4420]	325	330	335
[4421]	Ser Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu		
[4422]	340	345	350
[4423]	Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn		
[4424]	355	360	365
[4425]	Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile		
[4426]	370	375	380
[4427]	Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr		
[4428]	385	390	395
[4429]	Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys		
[4430]	405	410	415
[4431]	Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys		
[4432]	420	425	430
[4433]	Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu		
[4434]	435	440	445
[4435]	Ser Leu Ser Pro Gly		
[4436]	450		
[4437]	<210> 122		
[4438]	<211> 214		
[4439]	<212> PRT		
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[4442]	<223> 合成的: 2G6.IgG1 (VL + CL)		
[4443]	<400> 122		
[4444]	Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly		
[4445]	1	5	10
[4446]	Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Ser Ser Trp		
[4447]	20	25	30
[4448]	Leu Ala Trp Tyr Gln Gln Lys Pro Glu Lys Ala Pro Lys Ser Leu Ile		
[4449]	35	40	45
[4450]	Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly		
[4451]	50	55	60

[4452]	Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro		
[4453]	65	70	75 80
[4454]	Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Asn Ser Tyr Pro Tyr		
[4455]	85	90	95
[4456]	Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys Arg Thr Val Ala Ala		
[4457]	100	105	110
[4458]	Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly		
[4459]	115	120	125
[4460]	Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala		
[4461]	130	135	140
[4462]	Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln		
[4463]	145	150	155 160
[4464]	Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser		
[4465]	165	170	175
[4466]	Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr		
[4467]	180	185	190
[4468]	Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser		
[4469]	195	200	205
[4470]	Phe Asn Arg Gly Glu Cys		
[4471]	210		
[4472]	<210> 123		
[4473]	<211> 5		
[4474]	<212> PRT		
[4475]	<213> 人工序列		
[4476]	<220>		
[4477]	<223> 合成的: 2G6 VH CDR1		
[4478]	<400> 123		
[4479]	Asp Tyr Gly Met His		
[4480]	1	5	
[4481]	<210> 124		
[4482]	<211> 17		
[4483]	<212> PRT		
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[4485]	<220>		
[4486]	<223> 合成的: 2G6 VH CDR2		
[4487]	<400> 124		
[4488]	Val Ile Trp Tyr Asp Gly Ser Asn Lys Phe Tyr Val Asp Ser Val Lys		
[4489]	1	5	10 15
[4490]	Gly		
[4491]	<210> 125		
[4492]	<211> 15		
[4493]	<212> PRT		

[4494] <213> 人工序列
 [4495] <220>
 [4496] <223> 合成的: 2G6 VH CDR3
 [4497] <400> 125
 [4498] Gly Gly Arg Leu Ala Thr Gly His Phe Tyr Tyr Val Met Asp Val
 [4499] 1 5 10 15
 [4500] <210> 126
 [4501] <211> 11
 [4502] <212> PRT
 [4503] <213> 人工序列
 [4504] <220>
 [4505] <223> 合成的: 2G6 VL CDR1
 [4506] <400> 126
 [4507] Arg Ala Ser Gln Gly Ile Ser Ser Trp Leu Ala
 [4508] 1 5 10
 [4509] <210> 127
 [4510] <211> 7
 [4511] <212> PRT
 [4512] <213> 人工序列
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 [4514] <223> 合成的: 2G6 VL CDR2
 [4515] <400> 127
 [4516] Ala Ala Ser Ser Leu Gln Ser
 [4517] 1 5
 [4518] <210> 128
 [4519] <211> 9
 [4520] <212> PRT
 [4521] <213> 人工序列
 [4522] <220>
 [4523] <223> 合成的: 2G6 VL CDR3
 [4524] <400> 128
 [4525] Gln Gln Tyr Asn Ser Tyr Pro Tyr Thr
 [4526] 1 5
 [4527] <210> 129
 [4528] <211> 449
 [4529] <212> PRT
 [4530] <213> 人工序列
 [4531] <220>
 [4532] <223> 合成的: 2G6 (VH + G2) 或2G6-IgG2
 [4533] <400> 129
 [4534] Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Gly
 [4535] 1 5 10 15

[4536]	Ser	Leu	Arg	Leu	Ser	Cys	Ala	Ala	Ser	Gly	Phe	Ile	Leu	Ser	Asp	Tyr
[4537]				20					25					30		
[4538]	Gly	Met	His	Trp	Val	Arg	Gln	Ala	Pro	Gly	Lys	Gly	Leu	Glu	Trp	Val
[4539]				35				40					45			
[4540]	Thr	Val	Ile	Trp	Tyr	Asp	Gly	Ser	Asn	Lys	Phe	Tyr	Val	Asp	Ser	Val
[4541]		50					55					60				
[4542]	Lys	Gly	Arg	Phe	Thr	Ile	Ser	Arg	Asp	Asn	Ser	Lys	Asn	Thr	Leu	Tyr
[4543]	65					70					75				80	
[4544]	Leu	Gln	Met	Asn	Ser	Leu	Arg	Val	Glu	Asp	Thr	Ala	Val	Tyr	Tyr	Cys
[4545]				85					90					95		
[4546]	Ala	Arg	Gly	Gly	Arg	Leu	Ala	Thr	Gly	His	Phe	Tyr	Tyr	Val	Met	Asp
[4547]				100					105					110		
[4548]	Val	Trp	Gly	Gln	Gly	Thr	Thr	Val	Thr	Val	Ser	Ser	Ala	Ser	Thr	Lys
[4549]				115				120						125		
[4550]	Gly	Pro	Ser	Val	Phe	Pro	Leu	Ala	Pro	Cys	Ser	Arg	Ser	Thr	Ser	Glu
[4551]		130					135					140				
[4552]	Ser	Thr	Ala	Ala	Leu	Gly	Cys	Leu	Val	Lys	Asp	Tyr	Phe	Pro	Glu	Pro
[4553]	145					150					155				160	
[4554]	Val	Thr	Val	Ser	Trp	Asn	Ser	Gly	Ala	Leu	Thr	Ser	Gly	Val	His	Thr
[4555]					165					170					175	
[4556]	Phe	Pro	Ala	Val	Leu	Gln	Ser	Ser	Gly	Leu	Tyr	Ser	Leu	Ser	Ser	Val
[4557]				180					185					190		
[4558]	Val	Thr	Val	Pro	Ser	Ser	Asn	Phe	Gly	Thr	Gln	Thr	Tyr	Thr	Cys	Asn
[4559]				195				200					205			
[4560]	Val	Asp	His	Lys	Pro	Ser	Asn	Thr	Lys	Val	Asp	Lys	Thr	Val	Glu	Arg
[4561]		210					215					220				
[4562]	Lys	Cys	Cys	Val	Glu	Cys	Pro	Pro	Cys	Pro	Ala	Pro	Pro	Val	Ala	Gly
[4563]	225					230					235				240	
[4564]	Pro	Ser	Val	Phe	Leu	Phe	Pro	Pro	Lys	Pro	Lys	Asp	Thr	Leu	Met	Ile
[4565]				245					250						255	
[4566]	Ser	Arg	Thr	Pro	Glu	Val	Thr	Cys	Val	Val	Val	Asp	Val	Ser	His	Glu
[4567]				260					265					270		
[4568]	Asp	Pro	Glu	Val	Gln	Phe	Asn	Trp	Tyr	Val	Asp	Gly	Val	Glu	Val	His
[4569]				275				280					285			
[4570]	Asn	Ala	Lys	Thr	Lys	Pro	Arg	Glu	Glu	Gln	Phe	Asn	Ser	Thr	Phe	Arg
[4571]		290					295						300			
[4572]	Val	Val	Ser	Val	Leu	Thr	Val	Val	His	Gln	Asp	Trp	Leu	Asn	Gly	Lys
[4573]	305					310					315				320	
[4574]	Glu	Tyr	Lys	Cys	Lys	Val	Ser	Asn	Lys	Gly	Leu	Pro	Ala	Pro	Ile	Glu
[4575]				325						330					335	
[4576]	Lys	Thr	Ile	Ser	Lys	Thr	Lys	Gly	Gln	Pro	Arg	Glu	Pro	Gln	Val	Tyr
[4577]				340					345					350		

[4578]	Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu
[4579]	355 360 365
[4580]	Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp
[4581]	370 375 380
[4582]	Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Met
[4583]	385 390 395 400
[4584]	Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp
[4585]	405 410 415
[4586]	Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His
[4587]	420 425 430
[4588]	Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
[4589]	435 440 445
[4590]	Gly
[4591]	<210> 130
[4592]	<211> 449
[4593]	<212> PRT
[4594]	<213> 人工序列
[4595]	<220>
[4596]	<223> 合成的: 2G6 (VH + G2 (C219S)) or 2G6-IgG2-C219S
[4597]	<400> 130
[4598]	Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Gly
[4599]	1 5 10 15
[4600]	Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Ile Leu Ser Asp Tyr
[4601]	20 25 30
[4602]	Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
[4603]	35 40 45
[4604]	Thr Val Ile Trp Tyr Asp Gly Ser Asn Lys Phe Tyr Val Asp Ser Val
[4605]	50 55 60
[4606]	Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
[4607]	65 70 75 80
[4608]	Leu Gln Met Asn Ser Leu Arg Val Glu Asp Thr Ala Val Tyr Tyr Cys
[4609]	85 90 95
[4610]	Ala Arg Gly Gly Arg Leu Ala Thr Gly His Phe Tyr Tyr Val Met Asp
[4611]	100 105 110
[4612]	Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys
[4613]	115 120 125
[4614]	Gly Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu
[4615]	130 135 140
[4616]	Ser Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro
[4617]	145 150 155 160
[4618]	Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr
[4619]	165 170 175

[4620]	Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val
[4621]	180 185 190
[4622]	Val Thr Val Pro Ser Ser Asn Phe Gly Thr Gln Thr Tyr Thr Cys Asn
[4623]	195 200 205
[4624]	Val Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys Thr Val Glu Arg
[4625]	210 215 220
[4626]	Lys Ser Cys Val Glu Cys Pro Pro Cys Pro Ala Pro Pro Val Ala Gly
[4627]	225 230 235 240
[4628]	Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile
[4629]	245 250 255
[4630]	Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu
[4631]	260 265 270
[4632]	Asp Pro Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val His
[4633]	275 280 285
[4634]	Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr Phe Arg
[4635]	290 295 300
[4636]	Val Val Ser Val Leu Thr Val Val His Gln Asp Trp Leu Asn Gly Lys
[4637]	305 310 315 320
[4638]	Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ala Pro Ile Glu
[4639]	325 330 335
[4640]	Lys Thr Ile Ser Lys Thr Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr
[4641]	340 345 350
[4642]	Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu
[4643]	355 360 365
[4644]	Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp
[4645]	370 375 380
[4646]	Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Met
[4647]	385 390 395 400
[4648]	Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp
[4649]	405 410 415
[4650]	Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His
[4651]	420 425 430
[4652]	Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
[4653]	435 440 445
[4654]	Gly
[4655]	<210> 131
[4656]	<211> 450
[4657]	<212> PRT
[4658]	<213> 人工序列
[4659]	<220>
[4660]	<223> 合成的: 2G6 (VH + G2.g1) or2G6-IgG2-IgG1
[4661]	<400> 131

[4662]	Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Gly
[4663]	1 5 10 15
[4664]	Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Ile Leu Ser Asp Tyr
[4665]	20 25 30
[4666]	Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
[4667]	35 40 45
[4668]	Thr Val Ile Trp Tyr Asp Gly Ser Asn Lys Phe Tyr Val Asp Ser Val
[4669]	50 55 60
[4670]	Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
[4671]	65 70 75 80
[4672]	Leu Gln Met Asn Ser Leu Arg Val Glu Asp Thr Ala Val Tyr Tyr Cys
[4673]	85 90 95
[4674]	Ala Arg Gly Gly Arg Leu Ala Thr Gly His Phe Tyr Tyr Val Met Asp
[4675]	100 105 110
[4676]	Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys
[4677]	115 120 125
[4678]	Gly Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu
[4679]	130 135 140
[4680]	Ser Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro
[4681]	145 150 155 160
[4682]	Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr
[4683]	165 170 175
[4684]	Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val
[4685]	180 185 190
[4686]	Val Thr Val Pro Ser Ser Asn Phe Gly Thr Gln Thr Tyr Thr Cys Asn
[4687]	195 200 205
[4688]	Val Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys Thr Val Glu Arg
[4689]	210 215 220
[4690]	Lys Cys Cys Val Glu Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly
[4691]	225 230 235 240
[4692]	Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
[4693]	245 250 255
[4694]	Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His
[4695]	260 265 270
[4696]	Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val
[4697]	275 280 285
[4698]	His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr
[4699]	290 295 300
[4700]	Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly
[4701]	305 310 315 320
[4702]	Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile
[4703]	325 330 335

[4704]	Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val
[4705]	340 345 350
[4706]	Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser
[4707]	355 360 365
[4708]	Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu
[4709]	370 375 380
[4710]	Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro
[4711]	385 390 395 400
[4712]	Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val
[4713]	405 410 415
[4714]	Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met
[4715]	420 425 430
[4716]	His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser
[4717]	435 440 445
[4718]	Pro Gly
[4719]	450
[4720]	<210> 132
[4721]	<211> 449
[4722]	<212> PRT
[4723]	<213> 人工序列
[4724]	<220>
[4725]	<223> 合成的: 2G6 (VH + G2.g1.1) or2G6-IgG2-IgG1.1
[4726]	<400> 132
[4727]	Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Gly
[4728]	1 5 10 15
[4729]	Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Ile Leu Ser Asp Tyr
[4730]	20 25 30
[4731]	Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
[4732]	35 40 45
[4733]	Thr Val Ile Trp Tyr Asp Gly Ser Asn Lys Phe Tyr Val Asp Ser Val
[4734]	50 55 60
[4735]	Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
[4736]	65 70 75 80
[4737]	Leu Gln Met Asn Ser Leu Arg Val Glu Asp Thr Ala Val Tyr Tyr Cys
[4738]	85 90 95
[4739]	Ala Arg Gly Gly Arg Leu Ala Thr Gly His Phe Tyr Tyr Val Met Asp
[4740]	100 105 110
[4741]	Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys
[4742]	115 120 125
[4743]	Gly Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu
[4744]	130 135 140
[4745]	Ser Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro

[4746]	145	150	155	160
[4747]	Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr			
[4748]		165	170	175
[4749]	Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val			
[4750]		180	185	190
[4751]	Val Thr Val Pro Ser Ser Asn Phe Gly Thr Gln Thr Tyr Thr Cys Asn			
[4752]		195	200	205
[4753]	Val Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys Thr Val Glu Arg			
[4754]		210	215	220
[4755]	Lys Cys Cys Val Glu Cys Pro Pro Cys Pro Ala Pro Pro Val Ala Gly			
[4756]	225	230	235	240
[4757]	Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile			
[4758]		245	250	255
[4759]	Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu			
[4760]		260	265	270
[4761]	Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His			
[4762]		275	280	285
[4763]	Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg			
[4764]		290	295	300
[4765]	Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys			
[4766]	305	310	315	320
[4767]	Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ser Ser Ile Glu			
[4768]		325	330	335
[4769]	Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr			
[4770]		340	345	350
[4771]	Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu			
[4772]		355	360	365
[4773]	Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp			
[4774]		370	375	380
[4775]	Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val			
[4776]	385	390	395	400
[4777]	Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp			
[4778]		405	410	415
[4779]	Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His			
[4780]		420	425	430
[4781]	Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro			
[4782]		435	440	445
[4783]	Gly			
[4784]	<210> 133			
[4785]	<211> 450			
[4786]	<212> PRT			
[4787]	<213> 人工序列			

[4788]	<220>
[4789]	<223> 合成的: 2G6 (VH + G2 (C219S) .g1) 或2G6-IgG2-C219S-IgG1
[4790]	<400> 133
[4791]	Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Gly
[4792]	1 5 10 15
[4793]	Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Ile Leu Ser Asp Tyr
[4794]	20 25 30
[4795]	Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
[4796]	35 40 45
[4797]	Thr Val Ile Trp Tyr Asp Gly Ser Asn Lys Phe Tyr Val Asp Ser Val
[4798]	50 55 60
[4799]	Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
[4800]	65 70 75 80
[4801]	Leu Gln Met Asn Ser Leu Arg Val Glu Asp Thr Ala Val Tyr Tyr Cys
[4802]	85 90 95
[4803]	Ala Arg Gly Gly Arg Leu Ala Thr Gly His Phe Tyr Tyr Val Met Asp
[4804]	100 105 110
[4805]	Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys
[4806]	115 120 125
[4807]	Gly Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu
[4808]	130 135 140
[4809]	Ser Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro
[4810]	145 150 155 160
[4811]	Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr
[4812]	165 170 175
[4813]	Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val
[4814]	180 185 190
[4815]	Val Thr Val Pro Ser Ser Asn Phe Gly Thr Gln Thr Tyr Thr Cys Asn
[4816]	195 200 205
[4817]	Val Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys Thr Val Glu Arg
[4818]	210 215 220
[4819]	Lys Ser Cys Val Glu Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly
[4820]	225 230 235 240
[4821]	Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
[4822]	245 250 255
[4823]	Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His
[4824]	260 265 270
[4825]	Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val
[4826]	275 280 285
[4827]	His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr
[4828]	290 295 300
[4829]	Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly

[4830]	305	310	315	320
[4831]	Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile			
[4832]		325	330	335
[4833]	Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val			
[4834]		340	345	350
[4835]	Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser			
[4836]		355	360	365
[4837]	Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu			
[4838]		370	375	380
[4839]	Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro			
[4840]	385	390	395	400
[4841]	Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val			
[4842]		405	410	415
[4843]	Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met			
[4844]		420	425	430
[4845]	His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser			
[4846]		435	440	445
[4847]	Pro Gly			
[4848]	450			
[4849]	<210> 134			
[4850]	<211> 449			
[4851]	<212> PRT			
[4852]	<213> 人工序列			
[4853]	<220>			
[4854]	<223> 合成的: 2G6 (VH + G2 (C219S) .g1.1) or2G6-IgG2-C219S-IgG1.1			
[4855]	<400> 134			
[4856]	Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Gly			
[4857]	1	5	10	15
[4858]	Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Ile Leu Ser Asp Tyr			
[4859]		20	25	30
[4860]	Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val			
[4861]		35	40	45
[4862]	Thr Val Ile Trp Tyr Asp Gly Ser Asn Lys Phe Tyr Val Asp Ser Val			
[4863]		50	55	60
[4864]	Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr			
[4865]	65	70	75	80
[4866]	Leu Gln Met Asn Ser Leu Arg Val Glu Asp Thr Ala Val Tyr Tyr Cys			
[4867]		85	90	95
[4868]	Ala Arg Gly Gly Arg Leu Ala Thr Gly His Phe Tyr Tyr Val Met Asp			
[4869]		100	105	110
[4870]	Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys			
[4871]		115	120	125

[4872]	Gly Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu		
[4873]	130	135	140
[4874]	Ser Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro		
[4875]	145	150	155 160
[4876]	Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr		
[4877]	165	170	175
[4878]	Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val		
[4879]	180	185	190
[4880]	Val Thr Val Pro Ser Ser Asn Phe Gly Thr Gln Thr Tyr Thr Cys Asn		
[4881]	195	200	205
[4882]	Val Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys Thr Val Glu Arg		
[4883]	210	215	220
[4884]	Lys Ser Cys Val Glu Cys Pro Pro Cys Pro Ala Pro Pro Val Ala Gly		
[4885]	225	230	235 240
[4886]	Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile		
[4887]	245	250	255
[4888]	Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu		
[4889]	260	265	270
[4890]	Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His		
[4891]	275	280	285
[4892]	Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg		
[4893]	290	295	300
[4894]	Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys		
[4895]	305	310	315 320
[4896]	Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ser Ser Ile Glu		
[4897]	325	330	335
[4898]	Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr		
[4899]	340	345	350
[4900]	Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu		
[4901]	355	360	365
[4902]	Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp		
[4903]	370	375	380
[4904]	Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val		
[4905]	385	390	395 400
[4906]	Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp		
[4907]	405	410	415
[4908]	Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His		
[4909]	420	425	430
[4910]	Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro		
[4911]	435	440	445
[4912]	Gly		
[4913]	<210> 135		

[4914]	<211> 124
[4915]	<212> PRT
[4916]	<213> 人工序列
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[4918]	<223> 合成的: 8A6 (VH)
[4919]	<400> 135
[4920]	Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg
[4921]	1 5 10 15
[4922]	Ser Leu Arg Leu Ser Cys Thr Ala Ser Gly Phe Thr Phe Ser Ser Tyr
[4923]	20 25 30
[4924]	Gly Met Gln Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
[4925]	35 40 45
[4926]	Ala Val Ile Trp Tyr Glu Gly Ser Asn Lys Tyr Tyr Ala Asp Ser Val
[4927]	50 55 60
[4928]	Lys Gly Arg Phe Thr Ile Ser Arg Glu Asn Ser Lys Asn Thr Leu Tyr
[4929]	65 70 75 80
[4930]	Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
[4931]	85 90 95
[4932]	Ala Arg Gly Gly Leu Met Val Arg Gly Leu Phe Tyr Tyr Gly Met Asp
[4933]	100 105 110
[4934]	Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
[4935]	115 120
[4936]	<210> 136
[4937]	<211> 107
[4938]	<212> PRT
[4939]	<213> 人工序列
[4940]	<220>
[4941]	<223> 合成的: 8A6 (VL)
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[4943]	Ala Ile Gln Leu Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
[4944]	1 5 10 15
[4945]	Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Ser Ser Ala
[4946]	20 25 30
[4947]	Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Phe Leu Ile
[4948]	35 40 45
[4949]	Tyr Asp Ala Ser Ser Leu Glu Ser Gly Val Pro Ser Arg Phe Ser Gly
[4950]	50 55 60
[4951]	Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
[4952]	65 70 75 80
[4953]	Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Phe Asn Ser Tyr Pro Tyr
[4954]	85 90 95
[4955]	Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys

[4956]	100	105
[4957]	<210> 137	
[4958]	<211> 450	
[4959]	<212> PRT	
[4960]	<213> 人工序列	
[4961]	<220>	
[4962]	<223> 合成的：8A6（全长野生型重链）	
[4963]	<400> 137	
[4964]	Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg	
[4965]	1 5 10 15	
[4966]	Ser Leu Arg Leu Ser Cys Thr Ala Ser Gly Phe Thr Phe Ser Ser Tyr	
[4967]	20 25 30	
[4968]	Gly Met Gln Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val	
[4969]	35 40 45	
[4970]	Ala Val Ile Trp Tyr Glu Gly Ser Asn Lys Tyr Tyr Ala Asp Ser Val	
[4971]	50 55 60	
[4972]	Lys Gly Arg Phe Thr Ile Ser Arg Glu Asn Ser Lys Asn Thr Leu Tyr	
[4973]	65 70 75 80	
[4974]	Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys	
[4975]	85 90 95	
[4976]	Ala Arg Gly Gly Leu Met Val Arg Gly Leu Phe Tyr Tyr Gly Met Asp	
[4977]	100 105 110	
[4978]	Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys	
[4979]	115 120 125	
[4980]	Gly Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu	
[4981]	130 135 140	
[4982]	Ser Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro	
[4983]	145 150 155 160	
[4984]	Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr	
[4985]	165 170 175	
[4986]	Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val	
[4987]	180 185 190	
[4988]	Val Thr Val Pro Ser Ser Asn Phe Gly Thr Gln Thr Tyr Thr Cys Asn	
[4989]	195 200 205	
[4990]	Val Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys Thr Val Glu Arg	
[4991]	210 215 220	
[4992]	Lys Cys Cys Val Glu Cys Pro Pro Cys Pro Ala Pro Pro Val Ala Gly	
[4993]	225 230 235 240	
[4994]	Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile	
[4995]	245 250 255	
[4996]	Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu	
[4997]	260 265 270	

[4998]	Asp	Pro	Glu	Val	Gln	Phe	Asn	Trp	Tyr	Val	Asp	Gly	Val	Glu	Val	His
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[5000]	Asn	Ala	Lys	Thr	Lys	Pro	Arg	Glu	Glu	Gln	Phe	Asn	Ser	Thr	Phe	Arg
[5001]			290					295					300			
[5002]	Val	Val	Ser	Val	Leu	Thr	Val	Val	His	Gln	Asp	Trp	Leu	Asn	Gly	Lys
[5003]	305						310					315				320
[5004]	Glu	Tyr	Lys	Cys	Lys	Val	Ser	Asn	Lys	Gly	Leu	Pro	Ala	Pro	Ile	Glu
[5005]					325					330					335	
[5006]	Lys	Thr	Ile	Ser	Lys	Thr	Lys	Gly	Gln	Pro	Arg	Glu	Pro	Gln	Val	Tyr
[5007]					340					345					350	
[5008]	Thr	Leu	Pro	Pro	Ser	Arg	Glu	Glu	Met	Thr	Lys	Asn	Gln	Val	Ser	Leu
[5009]					355					360					365	
[5010]	Thr	Cys	Leu	Val	Lys	Gly	Phe	Tyr	Pro	Ser	Asp	Ile	Ala	Val	Glu	Trp
[5011]					370					375					380	
[5012]	Glu	Ser	Asn	Gly	Gln	Pro	Glu	Asn	Asn	Tyr	Lys	Thr	Thr	Pro	Pro	Met
[5013]	385						390					395				400
[5014]	Leu	Asp	Ser	Asp	Gly	Ser	Phe	Phe	Leu	Tyr	Ser	Lys	Leu	Thr	Val	Asp
[5015]					405					410					415	
[5016]	Lys	Ser	Arg	Trp	Gln	Gln	Gly	Asn	Val	Phe	Ser	Cys	Ser	Val	Met	His
[5017]					420					425					430	
[5018]	Glu	Ala	Leu	His	Asn	His	Tyr	Thr	Gln	Lys	Ser	Leu	Ser	Leu	Ser	Pro
[5019]					435					440					445	
[5020]	Gly	Lys														
[5021]					450											
[5022]	<210>	138														
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[5025]	<213>	人工序列														
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[5028]	<400>	138														
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[5031]	Asp	Arg	Val	Thr	Ile	Thr	Cys	Arg	Ala	Ser	Gln	Gly	Ile	Ser	Ser	Ala
[5032]					20						25				30	
[5033]	Leu	Ala	Trp	Tyr	Gln	Gln	Lys	Pro	Gly	Lys	Ala	Pro	Lys	Phe	Leu	Ile
[5034]					35						40				45	
[5035]	Tyr	Asp	Ala	Ser	Ser	Leu	Glu	Ser	Gly	Val	Pro	Ser	Arg	Phe	Ser	Gly
[5036]					50						55				60	
[5037]	Ser	Gly	Ser	Gly	Thr	Asp	Phe	Thr	Leu	Thr	Ile	Ser	Ser	Leu	Gln	Pro
[5038]	65						70					75				80
[5039]	Glu	Asp	Phe	Ala	Thr	Tyr	Tyr	Cys	Gln	Gln	Phe	Asn	Ser	Tyr	Pro	Tyr

[5040]		85		90		95
[5041]	Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys Arg Thr Val Ala Ala					
[5042]		100		105		110
[5043]	Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly					
[5044]		115		120		125
[5045]	Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala					
[5046]		130		135		140
[5047]	Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln					
[5048]		145		150		155
[5049]	Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser					
[5050]		165		170		175
[5051]	Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr					
[5052]		180		185		190
[5053]	Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser					
[5054]		195		200		205
[5055]	Phe Asn Arg Gly Glu Cys					
[5056]		210				
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[5059]	<212> PRT					
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[5066]	Ser Leu Arg Leu Ser Cys Thr Ala Ser Gly Phe Thr Phe Ser Ser Tyr					
[5067]		20		25		30
[5068]	Gly Met Gln Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val					
[5069]		35		40		45
[5070]	Ala Val Ile Trp Tyr Glu Gly Ser Asn Lys Tyr Tyr Ala Asp Ser Val					
[5071]		50		55		60
[5072]	Lys Gly Arg Phe Thr Ile Ser Arg Glu Asn Ser Lys Asn Thr Leu Tyr					
[5073]		65		70		75
[5074]	Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys					
[5075]		85		90		95
[5076]	Ala Arg Gly Gly Leu Met Val Arg Gly Leu Phe Tyr Tyr Gly Met Asp					
[5077]		100		105		110
[5078]	Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys					
[5079]		115		120		125
[5080]	Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly					
[5081]		130		135		140

[5082]	Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro		
[5083]	145	150	155 160
[5084]	Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr		
[5085]	165	170	175
[5086]	Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val		
[5087]	180	185	190
[5088]	Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn		
[5089]	195	200	205
[5090]	Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro		
[5091]	210	215	220
[5092]	Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu		
[5093]	225	230	235 240
[5094]	Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp		
[5095]	245	250	255
[5096]	Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp		
[5097]	260	265	270
[5098]	Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly		
[5099]	275	280	285
[5100]	Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn		
[5101]	290	295	300
[5102]	Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp		
[5103]	305	310	315 320
[5104]	Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro		
[5105]	325	330	335
[5106]	Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu		
[5107]	340	345	350
[5108]	Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn		
[5109]	355	360	365
[5110]	Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile		
[5111]	370	375	380
[5112]	Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr		
[5113]	385	390	395 400
[5114]	Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys		
[5115]	405	410	415
[5116]	Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys		
[5117]	420	425	430
[5118]	Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu		
[5119]	435	440	445
[5120]	Ser Leu Ser Pro Gly		
[5121]	450		
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[5124]	<212>	PRT
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[5131]	Ser Leu Arg Leu Ser Cys Thr Ala Ser Gly Phe Thr Phe Ser Ser Tyr	
[5132]	20 25 30	
[5133]	Gly Met Gln Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val	
[5134]	35 40 45	
[5135]	Ala Val Ile Trp Tyr Glu Gly Ser Asn Lys Tyr Tyr Ala Asp Ser Val	
[5136]	50 55 60	
[5137]	Lys Gly Arg Phe Thr Ile Ser Arg Glu Asn Ser Lys Asn Thr Leu Tyr	
[5138]	65 70 75 80	
[5139]	Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys	
[5140]	85 90 95	
[5141]	Ala Arg Gly Gly Leu Met Val Arg Gly Leu Phe Tyr Tyr Gly Met Asp	
[5142]	100 105 110	
[5143]	Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys	
[5144]	115 120 125	
[5145]	Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly	
[5146]	130 135 140	
[5147]	Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro	
[5148]	145 150 155 160	
[5149]	Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr	
[5150]	165 170 175	
[5151]	Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val	
[5152]	180 185 190	
[5153]	Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn	
[5154]	195 200 205	
[5155]	Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro	
[5156]	210 215 220	
[5157]	Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu	
[5158]	225 230 235 240	
[5159]	Ala Glu Gly Ala Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp	
[5160]	245 250 255	
[5161]	Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp	
[5162]	260 265 270	
[5163]	Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly	
[5164]	275 280 285	
[5165]	Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn	

[5166]	290	295	300
[5167]	Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp		
[5168]	305	310	315 320
[5169]	Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro		
[5170]		325 330	335
[5171]	Ser Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu		
[5172]		340 345	350
[5173]	Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn		
[5174]		355 360	365
[5175]	Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile		
[5176]		370 375	380
[5177]	Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr		
[5178]		385 390	395 400
[5179]	Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys		
[5180]		405 410	415
[5181]	Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys		
[5182]		420 425	430
[5183]	Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu		
[5184]		435 440	445
[5185]	Ser Leu Ser Pro Gly		
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[5195]	1 5 10 15		
[5196]	Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Ser Ser Ala		
[5197]	20 25 30		
[5198]	Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Phe Leu Ile		
[5199]	35 40 45		
[5200]	Tyr Asp Ala Ser Ser Leu Glu Ser Gly Val Pro Ser Arg Phe Ser Gly		
[5201]	50 55 60		
[5202]	Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro		
[5203]	65 70 75 80		
[5204]	Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Phe Asn Ser Tyr Pro Tyr		
[5205]	85 90 95		
[5206]	Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys Arg Thr Val Ala Ala		
[5207]	100 105 110		

[5208]	Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly
[5209]	115 120 125
[5210]	Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala
[5211]	130 135 140
[5212]	Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln
[5213]	145 150 155 160
[5214]	Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser
[5215]	165 170 175
[5216]	Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr
[5217]	180 185 190
[5218]	Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser
[5219]	195 200 205
[5220]	Phe Asn Arg Gly Glu Cys
[5221]	210
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[5224]	<212> PRT
[5225]	<213> 人工序列
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[5227]	<223> 合成的: 8A6 VH CDR1
[5228]	<400> 142
[5229]	Ser Tyr Gly Met Gln
[5230]	1 5
[5231]	<210> 143
[5232]	<211> 17
[5233]	<212> PRT
[5234]	<213> 人工序列
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[5236]	<223> 合成的: 8A6 VH CDR2
[5237]	<400> 143
[5238]	Val Ile Trp Tyr Glu Gly Ser Asn Lys Tyr Tyr Ala Asp Ser Val Lys
[5239]	1 5 10 15
[5240]	Gly
[5241]	<210> 144
[5242]	<211> 15
[5243]	<212> PRT
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[5247]	<400> 144
[5248]	Gly Gly Leu Met Val Arg Gly Leu Phe Tyr Tyr Gly Met Asp Val
[5249]	1 5 10 15

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[5252]	<212>	PRT		
[5253]	<213>	人工序列		
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[5257]		Arg Ala Ser Gln Gly Ile Ser Ser Ala Leu Ala		
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[5259]	<210>	146		
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[5261]	<212>	PRT		
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[5267]		1 5		
[5268]	<210>	147		
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[5274]	<400>	147		
[5275]		Gln Gln Phe Asn Ser Tyr Pro Tyr Thr		
[5276]		1 5		
[5277]	<210>	148		
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[5279]	<212>	PRT		
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[5283]	<400>	148		
[5284]		Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg		
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[5286]		Ser Leu Arg Leu Ser Cys Thr Ala Ser Gly Phe Thr Phe Ser Ser Tyr		
[5287]		20 25 30		
[5288]		Gly Met Gln Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val		
[5289]		35 40 45		
[5290]		Ala Val Ile Trp Tyr Glu Gly Ser Asn Lys Tyr Tyr Ala Asp Ser Val		
[5291]		50 55 60		

[5292]	Lys Gly Arg Phe Thr Ile Ser Arg Glu Asn Ser Lys Asn Thr Leu Tyr
[5293]	65 70 75 80
[5294]	Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
[5295]	85 90 95
[5296]	Ala Arg Gly Gly Leu Met Val Arg Gly Leu Phe Tyr Tyr Gly Met Asp
[5297]	100 105 110
[5298]	Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys
[5299]	115 120 125
[5300]	Gly Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu
[5301]	130 135 140
[5302]	Ser Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro
[5303]	145 150 155 160
[5304]	Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr
[5305]	165 170 175
[5306]	Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val
[5307]	180 185 190
[5308]	Val Thr Val Pro Ser Ser Asn Phe Gly Thr Gln Thr Tyr Thr Cys Asn
[5309]	195 200 205
[5310]	Val Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys Thr Val Glu Arg
[5311]	210 215 220
[5312]	Lys Ser Cys Val Glu Cys Pro Pro Cys Pro Ala Pro Pro Val Ala Gly
[5313]	225 230 235 240
[5314]	Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile
[5315]	245 250 255
[5316]	Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu
[5317]	260 265 270
[5318]	Asp Pro Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val His
[5319]	275 280 285
[5320]	Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr Phe Arg
[5321]	290 295 300
[5322]	Val Val Ser Val Leu Thr Val Val His Gln Asp Trp Leu Asn Gly Lys
[5323]	305 310 315 320
[5324]	Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ala Pro Ile Glu
[5325]	325 330 335
[5326]	Lys Thr Ile Ser Lys Thr Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr
[5327]	340 345 350
[5328]	Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu
[5329]	355 360 365
[5330]	Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp
[5331]	370 375 380
[5332]	Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Met
[5333]	385 390 395 400

[5334]	Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp
[5335]	405 410 415
[5336]	Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His
[5337]	420 425 430
[5338]	Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
[5339]	435 440 445
[5340]	Gly
[5341]	<210> 149
[5342]	<211> 450
[5343]	<212> PRT
[5344]	<213> 人工序列
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[5346]	<223> 合成的: 8A6 (VH + G2.g1)或8A6 -IgG2-IgG1
[5347]	<400> 149
[5348]	Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg
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[5350]	Ser Leu Arg Leu Ser Cys Thr Ala Ser Gly Phe Thr Phe Ser Ser Tyr
[5351]	20 25 30
[5352]	Gly Met Gln Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
[5353]	35 40 45
[5354]	Ala Val Ile Trp Tyr Glu Gly Ser Asn Lys Tyr Tyr Ala Asp Ser Val
[5355]	50 55 60
[5356]	Lys Gly Arg Phe Thr Ile Ser Arg Glu Asn Ser Lys Asn Thr Leu Tyr
[5357]	65 70 75 80
[5358]	Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
[5359]	85 90 95
[5360]	Ala Arg Gly Gly Leu Met Val Arg Gly Leu Phe Tyr Tyr Gly Met Asp
[5361]	100 105 110
[5362]	Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys
[5363]	115 120 125
[5364]	Gly Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu
[5365]	130 135 140
[5366]	Ser Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro
[5367]	145 150 155 160
[5368]	Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr
[5369]	165 170 175
[5370]	Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val
[5371]	180 185 190
[5372]	Val Thr Val Pro Ser Ser Asn Phe Gly Thr Gln Thr Tyr Thr Cys Asn
[5373]	195 200 205
[5374]	Val Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys Thr Val Glu Arg
[5375]	210 215 220

[5376]	Lys Cys Cys Val Glu Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly		
[5377]	225	230	235 240
[5378]	Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met		
[5379]		245	250 255
[5380]	Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His		
[5381]		260	265 270
[5382]	Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val		
[5383]		275	280 285
[5384]	His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr		
[5385]	290	295	300
[5386]	Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly		
[5387]	305	310	315 320
[5388]	Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile		
[5389]		325	330 335
[5390]	Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val		
[5391]		340	345 350
[5392]	Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser		
[5393]		355	360 365
[5394]	Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu		
[5395]		370	375 380
[5396]	Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro		
[5397]	385	390	395 400
[5398]	Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val		
[5399]		405	410 415
[5400]	Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met		
[5401]		420	425 430
[5402]	His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser		
[5403]		435	440 445
[5404]	Pro Gly		
[5405]	450		
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[5408]	<212> PRT		
[5409]	<213> 人工序列		
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[5411]	<223> 合成的: 8A6 (VH + G2.g1.1)或8A6 -IgG2-IgG1.1		
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[5413]	Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg		
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[5415]	Ser Leu Arg Leu Ser Cys Thr Ala Ser Gly Phe Thr Phe Ser Ser Tyr		
[5416]		20	25 30
[5417]	Gly Met Gln Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val		

[5418]	35	40	45
[5419]	Ala Val Ile Trp Tyr Glu Gly Ser Asn Lys Tyr Tyr Ala Asp Ser Val		
[5420]	50	55	60
[5421]	Lys Gly Arg Phe Thr Ile Ser Arg Glu Asn Ser Lys Asn Thr Leu Tyr		
[5422]	65	70	75
[5423]	Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys		
[5424]	85	90	95
[5425]	Ala Arg Gly Gly Leu Met Val Arg Gly Leu Phe Tyr Tyr Gly Met Asp		
[5426]	100	105	110
[5427]	Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys		
[5428]	115	120	125
[5429]	Gly Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu		
[5430]	130	135	140
[5431]	Ser Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro		
[5432]	145	150	155
[5433]	Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr		
[5434]	165	170	175
[5435]	Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val		
[5436]	180	185	190
[5437]	Val Thr Val Pro Ser Ser Asn Phe Gly Thr Gln Thr Tyr Thr Cys Asn		
[5438]	195	200	205
[5439]	Val Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys Thr Val Glu Arg		
[5440]	210	215	220
[5441]	Lys Cys Cys Val Glu Cys Pro Pro Cys Pro Ala Pro Pro Val Ala Gly		
[5442]	225	230	235
[5443]	Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile		
[5444]	245	250	255
[5445]	Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu		
[5446]	260	265	270
[5447]	Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His		
[5448]	275	280	285
[5449]	Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg		
[5450]	290	295	300
[5451]	Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys		
[5452]	305	310	315
[5453]	Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ser Ser Ile Glu		
[5454]	325	330	335
[5455]	Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr		
[5456]	340	345	350
[5457]	Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu		
[5458]	355	360	365
[5459]	Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp		

[5460]	370	375	380
[5461]	Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val		
[5462]	385	390	395 400
[5463]	Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp		
[5464]	405	410	415
[5465]	Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His		
[5466]	420	425	430
[5467]	Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro		
[5468]	435	440	445
[5469]	Gly		
[5470]	<210> 151		
[5471]	<211> 450		
[5472]	<212> PRT		
[5473]	<213> 人工序列		
[5474]	<220>		
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[5476]	<400> 151		
[5477]	Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg		
[5478]	1 5 10 15		
[5479]	Ser Leu Arg Leu Ser Cys Thr Ala Ser Gly Phe Thr Phe Ser Ser Tyr		
[5480]	20 25 30		
[5481]	Gly Met Gln Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val		
[5482]	35 40 45		
[5483]	Ala Val Ile Trp Tyr Glu Gly Ser Asn Lys Tyr Tyr Ala Asp Ser Val		
[5484]	50 55 60		
[5485]	Lys Gly Arg Phe Thr Ile Ser Arg Glu Asn Ser Lys Asn Thr Leu Tyr		
[5486]	65 70 75 80		
[5487]	Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys		
[5488]	85 90 95		
[5489]	Ala Arg Gly Gly Leu Met Val Arg Gly Leu Phe Tyr Tyr Gly Met Asp		
[5490]	100 105 110		
[5491]	Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys		
[5492]	115 120 125		
[5493]	Gly Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu		
[5494]	130 135 140		
[5495]	Ser Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro		
[5496]	145 150 155 160		
[5497]	Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr		
[5498]	165 170 175		
[5499]	Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val		
[5500]	180 185 190		
[5501]	Val Thr Val Pro Ser Ser Asn Phe Gly Thr Gln Thr Tyr Thr Cys Asn		

[5502]	195	200	205
[5503]	Val Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys Thr Val Glu Arg		
[5504]	210	215	220
[5505]	Lys Ser Cys Val Glu Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly		
[5506]	225	230	235
[5507]	Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met		
[5508]	245	250	255
[5509]	Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His		
[5510]	260	265	270
[5511]	Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val		
[5512]	275	280	285
[5513]	His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr		
[5514]	290	295	300
[5515]	Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly		
[5516]	305	310	315
[5517]	Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile		
[5518]	325	330	335
[5519]	Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val		
[5520]	340	345	350
[5521]	Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser		
[5522]	355	360	365
[5523]	Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu		
[5524]	370	375	380
[5525]	Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro		
[5526]	385	390	395
[5527]	Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val		
[5528]	405	410	415
[5529]	Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met		
[5530]	420	425	430
[5531]	His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser		
[5532]	435	440	445
[5533]	Pro Gly		
[5534]	450		
[5535]	<210> 152		
[5536]	<211> 449		
[5537]	<212> PRT		
[5538]	<213> 人工序列		
[5539]	<220>		
[5540]	<223> 合成的: 8A6 (VH + G2 (C219S) .g1.1) 或8A6-IgG2-C219S-IgG1.1		
[5541]	<400> 152		
[5542]	Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg		
[5543]	1	5	10

[5544]	Ser Leu Arg Leu Ser Cys Thr Ala Ser Gly Phe Thr Phe Ser Ser Tyr
[5545]	20 25 30
[5546]	Gly Met Gln Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
[5547]	35 40 45
[5548]	Ala Val Ile Trp Tyr Glu Gly Ser Asn Lys Tyr Tyr Ala Asp Ser Val
[5549]	50 55 60
[5550]	Lys Gly Arg Phe Thr Ile Ser Arg Glu Asn Ser Lys Asn Thr Leu Tyr
[5551]	65 70 75 80
[5552]	Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
[5553]	85 90 95
[5554]	Ala Arg Gly Gly Leu Met Val Arg Gly Leu Phe Tyr Tyr Gly Met Asp
[5555]	100 105 110
[5556]	Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys
[5557]	115 120 125
[5558]	Gly Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu
[5559]	130 135 140
[5560]	Ser Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro
[5561]	145 150 155 160
[5562]	Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr
[5563]	165 170 175
[5564]	Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val
[5565]	180 185 190
[5566]	Val Thr Val Pro Ser Ser Asn Phe Gly Thr Gln Thr Tyr Thr Cys Asn
[5567]	195 200 205
[5568]	Val Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys Thr Val Glu Arg
[5569]	210 215 220
[5570]	Lys Ser Cys Val Glu Cys Pro Pro Cys Pro Ala Pro Pro Val Ala Gly
[5571]	225 230 235 240
[5572]	Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile
[5573]	245 250 255
[5574]	Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu
[5575]	260 265 270
[5576]	Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His
[5577]	275 280 285
[5578]	Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg
[5579]	290 295 300
[5580]	Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys
[5581]	305 310 315 320
[5582]	Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ser Ser Ile Glu
[5583]	325 330 335
[5584]	Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr
[5585]	340 345 350

[5586]	Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu
[5587]	355 360 365
[5588]	Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp
[5589]	370 375 380
[5590]	Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val
[5591]	385 390 395 400
[5592]	Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp
[5593]	405 410 415
[5594]	Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His
[5595]	420 425 430
[5596]	Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
[5597]	435 440 445
[5598]	Gly
[5599]	<210> 153
[5600]	<211> 125
[5601]	<212> PRT
[5602]	<213> 人工序列
[5603]	<220>
[5604]	<223> 合成的: 9G7 (VH)
[5605]	<400> 153
[5606]	Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
[5607]	1 5 10 15
[5608]	Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Thr Val
[5609]	20 25 30
[5610]	Trp Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
[5611]	35 40 45
[5612]	Gly Arg Ile Lys Ser Lys Thr Asp Gly Gly Thr Thr Asp Tyr Ala Ala
[5613]	50 55 60
[5614]	Pro Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
[5615]	65 70 75 80
[5616]	Leu Tyr Leu Gln Met Asn Ser Leu His Thr Glu Asp Thr Ala Val Tyr
[5617]	85 90 95
[5618]	Tyr Cys Thr Thr Gly Gln Leu Ile Pro Tyr Ser Tyr Tyr Tyr Gly Met
[5619]	100 105 110
[5620]	Asp Val Trp Gly Gln Gly Thr Ser Val Thr Val Ser Ser
[5621]	115 120 125
[5622]	<210> 154
[5623]	<211> 108
[5624]	<212> PRT
[5625]	<213> 人工序列
[5626]	<220>
[5627]	<223> 合成的: 9G7 (VL1)

[5628]	<400> 154
[5629]	Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly
[5630]	1 5 10 15
[5631]	Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Ser
[5632]	20 25 30
[5633]	Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu
[5634]	35 40 45
[5635]	Ile Tyr Gly Ala Ser Ser Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser
[5636]	50 55 60
[5637]	Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu
[5638]	65 70 75 80
[5639]	Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr Gly Ser Ser Pro
[5640]	85 90 95
[5641]	Trp Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
[5642]	100 105
[5643]	<210> 155
[5644]	<211> 108
[5645]	<212> PRT
[5646]	<213> 人工序列
[5647]	<220>
[5648]	<223> 合成的: 9G7 (VL2)
[5649]	<400> 155
[5650]	Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly
[5651]	1 5 10 15
[5652]	Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Thr Ser Ser
[5653]	20 25 30
[5654]	Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu
[5655]	35 40 45
[5656]	Ile Tyr Gly Ala Ser Ser Arg Ala Thr Gly Ile Pro Glu Arg Phe Ser
[5657]	50 55 60
[5658]	Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu
[5659]	65 70 75 80
[5660]	Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr Gly Ser Ser Pro
[5661]	85 90 95
[5662]	Ile Thr Phe Gly Gln Gly Thr Arg Leu Glu Ile Lys
[5663]	100 105
[5664]	<210> 156
[5665]	<211> 452
[5666]	<212> PRT
[5667]	<213> 人工序列
[5668]	<220>
[5669]	<223> 合成的: 9G7 (全长野生型重链)

[5670]	<400> 156
[5671]	Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
[5672]	1 5 10 15
[5673]	Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Thr Val
[5674]	20 25 30
[5675]	Trp Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
[5676]	35 40 45
[5677]	Gly Arg Ile Lys Ser Lys Thr Asp Gly Gly Thr Thr Asp Tyr Ala Ala
[5678]	50 55 60
[5679]	Pro Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
[5680]	65 70 75 80
[5681]	Leu Tyr Leu Gln Met Asn Ser Leu His Thr Glu Asp Thr Ala Val Tyr
[5682]	85 90 95
[5683]	Tyr Cys Thr Thr Gly Gln Leu Ile Pro Tyr Ser Tyr Tyr Tyr Gly Met
[5684]	100 105 110
[5685]	Asp Val Trp Gly Gln Gly Thr Ser Val Thr Val Ser Ser Ala Ser Thr
[5686]	115 120 125
[5687]	Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser
[5688]	130 135 140
[5689]	Glu Ser Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu
[5690]	145 150 155 160
[5691]	Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His
[5692]	165 170 175
[5693]	Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser
[5694]	180 185 190
[5695]	Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Lys Thr Tyr Thr Cys
[5696]	195 200 205
[5697]	Asn Val Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu
[5698]	210 215 220
[5699]	Ser Lys Tyr Gly Pro Pro Cys Pro Ser Cys Pro Ala Pro Glu Phe Leu
[5700]	225 230 235 240
[5701]	Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu
[5702]	245 250 255
[5703]	Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser
[5704]	260 265 270
[5705]	Gln Glu Asp Pro Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu
[5706]	275 280 285
[5707]	Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr
[5708]	290 295 300
[5709]	Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn
[5710]	305 310 315 320
[5711]	Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ser Ser

[5712]		325		330		335
[5713]	Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln					
[5714]		340		345		350
[5715]	Val Tyr Thr Leu Pro Pro Ser Gln Glu Glu Met Thr Lys Asn Gln Val					
[5716]		355		360		365
[5717]	Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val					
[5718]		370		375		380
[5719]	Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro					
[5720]		385		390		395
[5721]	Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Arg Leu Thr					
[5722]		405		410		415
[5723]	Val Asp Lys Ser Arg Trp Gln Glu Gly Asn Val Phe Ser Cys Ser Val					
[5724]		420		425		430
[5725]	Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu					
[5726]		435		440		445
[5727]	Ser Leu Gly Lys					
[5728]		450				
[5729]	<210> 157					
[5730]	<211> 215					
[5731]	<212> PRT					
[5732]	<213> 人工序列					
[5733]	<220>					
[5734]	<223> 合成的: 9G7 L2 (全长野生型轻链 2)					
[5735]	<400> 157					
[5736]	Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly					
[5737]	1	5		10		15
[5738]	Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Thr Ser Ser					
[5739]		20		25		30
[5740]	Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu					
[5741]		35		40		45
[5742]	Ile Tyr Gly Ala Ser Ser Arg Ala Thr Gly Ile Pro Glu Arg Phe Ser					
[5743]		50		55		60
[5744]	Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu					
[5745]		65		70		75
[5746]	Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr Gly Ser Ser Pro					
[5747]		85		90		95
[5748]	Ile Thr Phe Gly Gln Gly Thr Arg Leu Glu Ile Lys Arg Thr Val Ala					
[5749]		100		105		110
[5750]	Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser					
[5751]		115		120		125
[5752]	Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu					
[5753]		130		135		140

[5754]	Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser
[5755]	145 150 155 160
[5756]	Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu
[5757]	165 170 175
[5758]	Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val
[5759]	180 185 190
[5760]	Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys
[5761]	195 200 205
[5762]	Ser Phe Asn Arg Gly Glu Cys
[5763]	210 215
[5764]	<210> 158
[5765]	<211> 454
[5766]	<212> PRT
[5767]	<213> 人工序列
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[5769]	<223> 合成的: 9G7.IgG1 (VH + IgG1)
[5770]	<400> 158
[5771]	Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
[5772]	1 5 10 15
[5773]	Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Thr Val
[5774]	20 25 30
[5775]	Trp Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
[5776]	35 40 45
[5777]	Gly Arg Ile Lys Ser Lys Thr Asp Gly Gly Thr Thr Asp Tyr Ala Ala
[5778]	50 55 60
[5779]	Pro Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
[5780]	65 70 75 80
[5781]	Leu Tyr Leu Gln Met Asn Ser Leu His Thr Glu Asp Thr Ala Val Tyr
[5782]	85 90 95
[5783]	Tyr Cys Thr Thr Gly Gln Leu Ile Pro Tyr Ser Tyr Tyr Tyr Gly Met
[5784]	100 105 110
[5785]	Asp Val Trp Gly Gln Gly Thr Ser Val Thr Val Ser Ser Ala Ser Thr
[5786]	115 120 125
[5787]	Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser
[5788]	130 135 140
[5789]	Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu
[5790]	145 150 155 160
[5791]	Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His
[5792]	165 170 175
[5793]	Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser
[5794]	180 185 190
[5795]	Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys

[5796]	195	200	205
[5797]	Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu		
[5798]	210	215	220
[5799]	Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro		
[5800]	225	230	235
[5801]	Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys		
[5802]	245	250	255
[5803]	Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val		
[5804]	260	265	270
[5805]	Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp		
[5806]	275	280	285
[5807]	Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr		
[5808]	290	295	300
[5809]	Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp		
[5810]	305	310	315
[5811]	Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu		
[5812]	325	330	335
[5813]	Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg		
[5814]	340	345	350
[5815]	Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys		
[5816]	355	360	365
[5817]	Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp		
[5818]	370	375	380
[5819]	Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys		
[5820]	385	390	395
[5821]	Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser		
[5822]	405	410	415
[5823]	Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser		
[5824]	420	425	430
[5825]	Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser		
[5826]	435	440	445
[5827]	Leu Ser Leu Ser Pro Gly		
[5828]	450		
[5829]	<210> 159		
[5830]	<211> 454		
[5831]	<212> PRT		
[5832]	<213> 人工序列		
[5833]	<220>		
[5834]	<223> 合成的: 9G7.IgG1.1 (VH + IgG1.1)		
[5835]	<400> 159		
[5836]	Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly		
[5837]	1	5	10

[5838]	Ser	Leu	Arg	Leu	Ser	Cys	Ala	Ala	Ser	Gly	Phe	Thr	Phe	Ser	Thr	Val
[5839]				20					25					30		
[5840]	Trp	Met	Ser	Trp	Val	Arg	Gln	Ala	Pro	Gly	Lys	Gly	Leu	Glu	Trp	Val
[5841]				35				40					45			
[5842]	Gly	Arg	Ile	Lys	Ser	Lys	Thr	Asp	Gly	Gly	Thr	Thr	Asp	Tyr	Ala	Ala
[5843]		50					55					60				
[5844]	Pro	Val	Lys	Gly	Arg	Phe	Thr	Ile	Ser	Arg	Asp	Asp	Ser	Lys	Asn	Thr
[5845]	65					70				75					80	
[5846]	Leu	Tyr	Leu	Gln	Met	Asn	Ser	Leu	His	Thr	Glu	Asp	Thr	Ala	Val	Tyr
[5847]				85						90					95	
[5848]	Tyr	Cys	Thr	Thr	Gly	Gln	Leu	Ile	Pro	Tyr	Ser	Tyr	Tyr	Tyr	Gly	Met
[5849]				100					105						110	
[5850]	Asp	Val	Trp	Gly	Gln	Gly	Thr	Ser	Val	Thr	Val	Ser	Ser	Ala	Ser	Thr
[5851]				115					120						125	
[5852]	Lys	Gly	Pro	Ser	Val	Phe	Pro	Leu	Ala	Pro	Ser	Ser	Lys	Ser	Thr	Ser
[5853]		130					135					140				
[5854]	Gly	Gly	Thr	Ala	Ala	Leu	Gly	Cys	Leu	Val	Lys	Asp	Tyr	Phe	Pro	Glu
[5855]	145					150					155				160	
[5856]	Pro	Val	Thr	Val	Ser	Trp	Asn	Ser	Gly	Ala	Leu	Thr	Ser	Gly	Val	His
[5857]				165						170					175	
[5858]	Thr	Phe	Pro	Ala	Val	Leu	Gln	Ser	Ser	Gly	Leu	Tyr	Ser	Leu	Ser	Ser
[5859]				180					185						190	
[5860]	Val	Val	Thr	Val	Pro	Ser	Ser	Ser	Leu	Gly	Thr	Gln	Thr	Tyr	Ile	Cys
[5861]				195					200						205	
[5862]	Asn	Val	Asn	His	Lys	Pro	Ser	Asn	Thr	Lys	Val	Asp	Lys	Arg	Val	Glu
[5863]		210					215					220				
[5864]	Pro	Lys	Ser	Cys	Asp	Lys	Thr	His	Thr	Cys	Pro	Pro	Cys	Pro	Ala	Pro
[5865]	225					230					235				240	
[5866]	Glu	Ala	Glu	Gly	Ala	Pro	Ser	Val	Phe	Leu	Phe	Pro	Pro	Lys	Pro	Lys
[5867]				245						250					255	
[5868]	Asp	Thr	Leu	Met	Ile	Ser	Arg	Thr	Pro	Glu	Val	Thr	Cys	Val	Val	Val
[5869]				260						265					270	
[5870]	Asp	Val	Ser	His	Glu	Asp	Pro	Glu	Val	Lys	Phe	Asn	Trp	Tyr	Val	Asp
[5871]				275					280						285	
[5872]	Gly	Val	Glu	Val	His	Asn	Ala	Lys	Thr	Lys	Pro	Arg	Glu	Glu	Gln	Tyr
[5873]		290					295					300				
[5874]	Asn	Ser	Thr	Tyr	Arg	Val	Val	Ser	Val	Leu	Thr	Val	Leu	His	Gln	Asp
[5875]	305					310					315				320	
[5876]	Trp	Leu	Asn	Gly	Lys	Glu	Tyr	Lys	Cys	Lys	Val	Ser	Asn	Lys	Ala	Leu
[5877]				325						330					335	
[5878]	Pro	Ser	Ser	Ile	Glu	Lys	Thr	Ile	Ser	Lys	Ala	Lys	Gly	Gln	Pro	Arg
[5879]				340						345					350	

[5880]	Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys
[5881]	355 360 365
[5882]	Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp
[5883]	370 375 380
[5884]	Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys
[5885]	385 390 395 400
[5886]	Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser
[5887]	405 410 415
[5888]	Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser
[5889]	420 425 430
[5890]	Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser
[5891]	435 440 445
[5892]	Leu Ser Leu Ser Pro Gly
[5893]	450
[5894]	<210> 160
[5895]	<211> 215
[5896]	<212> PRT
[5897]	<213> 人工序列
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[5903]	Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Ser
[5904]	20 25 30
[5905]	Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu
[5906]	35 40 45
[5907]	Ile Tyr Gly Ala Ser Ser Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser
[5908]	50 55 60
[5909]	Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu
[5910]	65 70 75 80
[5911]	Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr Gly Ser Ser Pro
[5912]	85 90 95
[5913]	Trp Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala
[5914]	100 105 110
[5915]	Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser
[5916]	115 120 125
[5917]	Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu
[5918]	130 135 140
[5919]	Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser
[5920]	145 150 155 160
[5921]	Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu

[5922]	165	170	175
[5923]	Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val		
[5924]	180	185	190
[5925]	Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys		
[5926]	195	200	205
[5927]	Ser Phe Asn Arg Gly Glu Cys		
[5928]	210	215	
[5929]	<210> 161		
[5930]	<211> 215		
[5931]	<212> PRT		
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[5934]	<223> 合成的: 9G7.IgG1.2 (VL2 + CL)		
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[5937]	1	5	10
[5938]	Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Thr Ser Ser		
[5939]	20	25	30
[5940]	Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu		
[5941]	35	40	45
[5942]	Ile Tyr Gly Ala Ser Ser Arg Ala Thr Gly Ile Pro Glu Arg Phe Ser		
[5943]	50	55	60
[5944]	Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu		
[5945]	65	70	75
[5946]	Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr Gly Ser Ser Pro		
[5947]	85	90	95
[5948]	Ile Thr Phe Gly Gln Gly Thr Arg Leu Glu Ile Lys Arg Thr Val Ala		
[5949]	100	105	110
[5950]	Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser		
[5951]	115	120	125
[5952]	Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu		
[5953]	130	135	140
[5954]	Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser		
[5955]	145	150	155
[5956]	Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu		
[5957]	165	170	175
[5958]	Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val		
[5959]	180	185	190
[5960]	Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys		
[5961]	195	200	205
[5962]	Ser Phe Asn Arg Gly Glu Cys		
[5963]	210	215	

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[5971] Thr Val Trp Met Ser
[5972] 1 5
[5973] <210> 163
[5974] <211> 19
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[5976] <213> 人工序列
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[5979] <400> 163
[5980] Arg Ile Lys Ser Lys Thr Asp Gly Gly Thr Thr Asp Tyr Ala Ala Pro
[5981] 1 5 10 15
[5982] Val Lys Gly
[5983] <210> 164
[5984] <211> 14
[5985] <212> PRT
[5986] <213> 人工序列
[5987] <220>
[5988] <223> 合成的: 9G7 VH CDR3
[5989] <400> 164
[5990] Gly Gln Leu Ile Pro Tyr Ser Tyr Tyr Tyr Gly Met Asp Val
[5991] 1 5 10
[5992] <210> 165
[5993] <211> 12
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[5999] Arg Ala Ser Gln Ser Val Ser Ser Ser Tyr Leu Ala
[6000] 1 5 10
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[6002] <211> 7
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[6006] <223> 合成的: 9G7 VL1 CDR2
[6007] <400> 166
[6008] Gly Ala Ser Ser Arg Ala Thr
[6009] 1 5
[6010] <210> 167
[6011] <211> 9
[6012] <212> PRT
[6013] <213> 人工序列
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[6015] <223> 合成的: 9G7 VL1 CDR3
[6016] <400> 167
[6017] Gln Gln Tyr Gly Ser Ser Pro Trp Thr
[6018] 1 5
[6019] <210> 168
[6020] <211> 12
[6021] <212> PRT
[6022] <213> 人工序列
[6023] <220>
[6024] <223> 合成的: 9G7 VL2 CDR1
[6025] <400> 168
[6026] Arg Ala Ser Gln Ser Val Thr Ser Ser Tyr Leu Ala
[6027] 1 5 10
[6028] <210> 169
[6029] <211> 7
[6030] <212> PRT
[6031] <213> 人工序列
[6032] <220>
[6033] <223> 合成的: 9G7 VL2 CDR2
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[6035] Gly Ala Ser Ser Arg Ala Thr
[6036] 1 5
[6037] <210> 170
[6038] <211> 9
[6039] <212> PRT
[6040] <213> 人工序列
[6041] <220>
[6042] <223> 合成的: 9G7 VL2 CDR3
[6043] <400> 170
[6044] Gln Gln Tyr Gly Ser Ser Pro Ile Thr
[6045] 1 5
[6046] <210> 171
[6047] <211> 450

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[6049]	<213> 人工序列															
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[6051]	<223> 合成的: 9G7 (VH + G2) 或9G7-IgG2															
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[6054]	1				5					10					15	
[6055]	Ser	Leu	Arg	Leu	Ser	Cys	Ala	Ala	Ser	Gly	Phe	Thr	Phe	Ser	Thr	Val
[6056]				20					25					30		
[6057]	Trp	Met	Ser	Trp	Val	Arg	Gln	Ala	Pro	Gly	Lys	Gly	Leu	Glu	Trp	Val
[6058]			35					40					45			
[6059]	Gly	Arg	Ile	Lys	Ser	Lys	Thr	Asp	Gly	Gly	Thr	Thr	Asp	Tyr	Ala	Ala
[6060]		50					55						60			
[6061]	Pro	Val	Lys	Gly	Arg	Phe	Thr	Ile	Ser	Arg	Asp	Asp	Ser	Lys	Asn	Thr
[6062]	65					70					75				80	
[6063]	Leu	Tyr	Leu	Gln	Met	Asn	Ser	Leu	His	Thr	Glu	Asp	Thr	Ala	Val	Tyr
[6064]					85					90					95	
[6065]	Tyr	Cys	Thr	Thr	Gly	Gln	Leu	Ile	Pro	Tyr	Ser	Tyr	Tyr	Tyr	Gly	Met
[6066]				100						105					110	
[6067]	Asp	Val	Trp	Gly	Gln	Gly	Thr	Ser	Val	Thr	Val	Ser	Ser	Ala	Ser	Thr
[6068]			115						120					125		
[6069]	Lys	Gly	Pro	Ser	Val	Phe	Pro	Leu	Ala	Pro	Cys	Ser	Arg	Ser	Thr	Ser
[6070]		130						135					140			
[6071]	Glu	Ser	Thr	Ala	Ala	Leu	Gly	Cys	Leu	Val	Lys	Asp	Tyr	Phe	Pro	Glu
[6072]	145					150					155				160	
[6073]	Pro	Val	Thr	Val	Ser	Trp	Asn	Ser	Gly	Ala	Leu	Thr	Ser	Gly	Val	His
[6074]				165						170					175	
[6075]	Thr	Phe	Pro	Ala	Val	Leu	Gln	Ser	Ser	Gly	Leu	Tyr	Ser	Leu	Ser	Ser
[6076]				180						185					190	
[6077]	Val	Val	Thr	Val	Pro	Ser	Ser	Asn	Phe	Gly	Thr	Gln	Thr	Tyr	Thr	Cys
[6078]			195					200						205		
[6079]	Asn	Val	Asp	His	Lys	Pro	Ser	Asn	Thr	Lys	Val	Asp	Lys	Thr	Val	Glu
[6080]		210						215					220			
[6081]	Arg	Lys	Cys	Cys	Val	Glu	Cys	Pro	Pro	Cys	Pro	Ala	Pro	Pro	Val	Ala
[6082]	225					230					235				240	
[6083]	Gly	Pro	Ser	Val	Phe	Leu	Phe	Pro	Pro	Lys	Pro	Lys	Asp	Thr	Leu	Met
[6084]				245						250					255	
[6085]	Ile	Ser	Arg	Thr	Pro	Glu	Val	Thr	Cys	Val	Val	Val	Asp	Val	Ser	His
[6086]				260						265				270		
[6087]	Glu	Asp	Pro	Glu	Val	Gln	Phe	Asn	Trp	Tyr	Val	Asp	Gly	Val	Glu	Val
[6088]			275					280					285			
[6089]	His	Asn	Ala	Lys	Thr	Lys	Pro	Arg	Glu	Glu	Gln	Phe	Asn	Ser	Thr	Phe

[6090]	290	295	300
[6091]	Arg Val Val Ser Val Leu Thr Val Val His Gln Asp Trp Leu Asn Gly		
[6092]	305	310	315
[6093]	Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ala Pro Ile		
[6094]		325	330
[6095]	Glu Lys Thr Ile Ser Lys Thr Lys Gly Gln Pro Arg Glu Pro Gln Val		
[6096]		340	345
[6097]	Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser		
[6098]		355	360
[6099]	Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu		
[6100]	370	375	380
[6101]	Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro		
[6102]	385	390	395
[6103]	Met Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val		
[6104]		405	410
[6105]	Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met		
[6106]		420	425
[6107]	His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser		
[6108]		435	440
[6109]	Pro Gly		
[6110]	450		
[6111]	<210> 172		
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[6118]	Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly		
[6119]	1	5	10
[6120]	Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Thr Val		
[6121]		20	25
[6122]	Trp Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val		
[6123]		35	40
[6124]	Gly Arg Ile Lys Ser Lys Thr Asp Gly Gly Thr Thr Asp Tyr Ala Ala		
[6125]		50	55
[6126]	Pro Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr		
[6127]	65	70	75
[6128]	Leu Tyr Leu Gln Met Asn Ser Leu His Thr Glu Asp Thr Ala Val Tyr		
[6129]		85	90
[6130]	Tyr Cys Thr Thr Gly Gln Leu Ile Pro Tyr Ser Tyr Tyr Tyr Gly Met		
[6131]		100	105

[6132]	Asp Val Trp Gly Gln Gly Thr Ser Val Thr Val Ser Ser Ala Ser Thr		
[6133]	115	120	125
[6134]	Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser		
[6135]	130	135	140
[6136]	Glu Ser Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu		
[6137]	145	150	155
[6138]	Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His		
[6139]	165	170	175
[6140]	Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser		
[6141]	180	185	190
[6142]	Val Val Thr Val Pro Ser Ser Asn Phe Gly Thr Gln Thr Tyr Thr Cys		
[6143]	195	200	205
[6144]	Asn Val Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys Thr Val Glu		
[6145]	210	215	220
[6146]	Arg Lys Ser Cys Val Glu Cys Pro Pro Cys Pro Ala Pro Pro Val Ala		
[6147]	225	230	235
[6148]	Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met		
[6149]	245	250	255
[6150]	Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His		
[6151]	260	265	270
[6152]	Glu Asp Pro Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val		
[6153]	275	280	285
[6154]	His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr Phe		
[6155]	290	295	300
[6156]	Arg Val Val Ser Val Leu Thr Val Val His Gln Asp Trp Leu Asn Gly		
[6157]	305	310	315
[6158]	Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ala Pro Ile		
[6159]	325	330	335
[6160]	Glu Lys Thr Ile Ser Lys Thr Lys Gly Gln Pro Arg Glu Pro Gln Val		
[6161]	340	345	350
[6162]	Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser		
[6163]	355	360	365
[6164]	Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu		
[6165]	370	375	380
[6166]	Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro		
[6167]	385	390	395
[6168]	Met Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val		
[6169]	405	410	415
[6170]	Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met		
[6171]	420	425	430
[6172]	His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser		
[6173]	435	440	445

[6174]	Pro Gly
[6175]	450
[6176]	<210> 173
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[6183]	Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
[6184]	1 5 10 15
[6185]	Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Thr Val
[6186]	20 25 30
[6187]	Trp Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
[6188]	35 40 45
[6189]	Gly Arg Ile Lys Ser Lys Thr Asp Gly Gly Thr Thr Asp Tyr Ala Ala
[6190]	50 55 60
[6191]	Pro Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
[6192]	65 70 75 80
[6193]	Leu Tyr Leu Gln Met Asn Ser Leu His Thr Glu Asp Thr Ala Val Tyr
[6194]	85 90 95
[6195]	Tyr Cys Thr Thr Gly Gln Leu Ile Pro Tyr Ser Tyr Tyr Tyr Gly Met
[6196]	100 105 110
[6197]	Asp Val Trp Gly Gln Gly Thr Ser Val Thr Val Ser Ser Ala Ser Thr
[6198]	115 120 125
[6199]	Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser
[6200]	130 135 140
[6201]	Glu Ser Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu
[6202]	145 150 155 160
[6203]	Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His
[6204]	165 170 175
[6205]	Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser
[6206]	180 185 190
[6207]	Val Val Thr Val Pro Ser Ser Asn Phe Gly Thr Gln Thr Tyr Thr Cys
[6208]	195 200 205
[6209]	Asn Val Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys Thr Val Glu
[6210]	210 215 220
[6211]	Arg Lys Cys Cys Val Glu Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu
[6212]	225 230 235 240
[6213]	Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu
[6214]	245 250 255
[6215]	Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser

[6216]	260	265	270
[6217]	His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu		
[6218]	275	280	285
[6219]	Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr		
[6220]	290	295	300
[6221]	Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn		
[6222]	305	310	315
[6223]	Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro		
[6224]	325	330	335
[6225]	Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln		
[6226]	340	345	350
[6227]	Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val		
[6228]	355	360	365
[6229]	Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val		
[6230]	370	375	380
[6231]	Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro		
[6232]	385	390	395
[6233]	Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr		
[6234]	405	410	415
[6235]	Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val		
[6236]	420	425	430
[6237]	Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu		
[6238]	435	440	445
[6239]	Ser Pro Gly		
[6240]	450		
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[6248]	Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly		
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[6250]	Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Thr Val		
[6251]	20	25	30
[6252]	Trp Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val		
[6253]	35	40	45
[6254]	Gly Arg Ile Lys Ser Lys Thr Asp Gly Gly Thr Thr Asp Tyr Ala Ala		
[6255]	50	55	60
[6256]	Pro Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr		
[6257]	65	70	75
			80

[6258]	Leu Tyr Leu Gln Met Asn Ser Leu His Thr Glu Asp Thr Ala Val Tyr		
[6259]		85	90 95
[6260]	Tyr Cys Thr Thr Gly Gln Leu Ile Pro Tyr Ser Tyr Tyr Tyr Gly Met		
[6261]		100	105 110
[6262]	Asp Val Trp Gly Gln Gly Thr Ser Val Thr Val Ser Ser Ala Ser Thr		
[6263]		115	120 125
[6264]	Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser		
[6265]		130	135 140
[6266]	Glu Ser Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu		
[6267]		145	150 155 160
[6268]	Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His		
[6269]		165	170 175
[6270]	Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser		
[6271]		180	185 190
[6272]	Val Val Thr Val Pro Ser Ser Asn Phe Gly Thr Gln Thr Tyr Thr Cys		
[6273]		195	200 205
[6274]	Asn Val Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys Thr Val Glu		
[6275]		210	215 220
[6276]	Arg Lys Cys Cys Val Glu Cys Pro Pro Cys Pro Ala Pro Pro Val Ala		
[6277]		225	230 235 240
[6278]	Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met		
[6279]		245	250 255
[6280]	Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His		
[6281]		260	265 270
[6282]	Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val		
[6283]		275	280 285
[6284]	His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr		
[6285]		290	295 300
[6286]	Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly		
[6287]		305	310 315 320
[6288]	Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ser Ser Ile		
[6289]		325	330 335
[6290]	Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val		
[6291]		340	345 350
[6292]	Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser		
[6293]		355	360 365
[6294]	Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu		
[6295]		370	375 380
[6296]	Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro		
[6297]		385	390 395 400
[6298]	Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val		
[6299]		405	410 415

[6300]	Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met
[6301]	420 425 430
[6302]	His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser
[6303]	435 440 445
[6304]	Pro Gly
[6305]	450
[6306]	<210> 175
[6307]	<211> 451
[6308]	<212> PRT
[6309]	<213> 人工序列
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[6311]	<223> 合成的: 9G7 (VH + G2 (C219S) .g1) 或9G7-IgG2-C219S-IgG1
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[6315]	Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Thr Val
[6316]	20 25 30
[6317]	Trp Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
[6318]	35 40 45
[6319]	Gly Arg Ile Lys Ser Lys Thr Asp Gly Gly Thr Thr Asp Tyr Ala Ala
[6320]	50 55 60
[6321]	Pro Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
[6322]	65 70 75 80
[6323]	Leu Tyr Leu Gln Met Asn Ser Leu His Thr Glu Asp Thr Ala Val Tyr
[6324]	85 90 95
[6325]	Tyr Cys Thr Thr Gly Gln Leu Ile Pro Tyr Ser Tyr Tyr Tyr Gly Met
[6326]	100 105 110
[6327]	Asp Val Trp Gly Gln Gly Thr Ser Val Thr Val Ser Ser Ala Ser Thr
[6328]	115 120 125
[6329]	Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser
[6330]	130 135 140
[6331]	Glu Ser Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu
[6332]	145 150 155 160
[6333]	Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His
[6334]	165 170 175
[6335]	Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser
[6336]	180 185 190
[6337]	Val Val Thr Val Pro Ser Ser Asn Phe Gly Thr Gln Thr Tyr Thr Cys
[6338]	195 200 205
[6339]	Asn Val Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys Thr Val Glu
[6340]	210 215 220
[6341]	Arg Lys Ser Cys Val Glu Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu

[6342]	225	230	235	240
[6343]	Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu			
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[6345]	Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser			
[6346]		260	265	270
[6347]	His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu			
[6348]		275	280	285
[6349]	Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr			
[6350]		290	295	300
[6351]	Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn			
[6352]	305	310	315	320
[6353]	Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro			
[6354]		325	330	335
[6355]	Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln			
[6356]		340	345	350
[6357]	Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val			
[6358]		355	360	365
[6359]	Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val			
[6360]		370	375	380
[6361]	Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro			
[6362]	385	390	395	400
[6363]	Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr			
[6364]		405	410	415
[6365]	Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val			
[6366]		420	425	430
[6367]	Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu			
[6368]		435	440	445
[6369]	Ser Pro Gly			
[6370]	450			
[6371]	<210> 176			
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[6380]	Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Thr Val			
[6381]		20	25	30
[6382]	Trp Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val			
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[6384]	Gly	Arg	Ile	Lys	Ser	Lys	Thr	Asp	Gly	Gly	Thr	Thr	Asp	Tyr	Ala	Ala
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[6386]	Pro	Val	Lys	Gly	Arg	Phe	Thr	Ile	Ser	Arg	Asp	Asp	Ser	Lys	Asn	Thr
[6387]	65						70				75				80	
[6388]	Leu	Tyr	Leu	Gln	Met	Asn	Ser	Leu	His	Thr	Glu	Asp	Thr	Ala	Val	Tyr
[6389]					85					90					95	
[6390]	Tyr	Cys	Thr	Thr	Gly	Gln	Leu	Ile	Pro	Tyr	Ser	Tyr	Tyr	Tyr	Gly	Met
[6391]					100				105						110	
[6392]	Asp	Val	Trp	Gly	Gln	Gly	Thr	Ser	Val	Thr	Val	Ser	Ser	Ala	Ser	Thr
[6393]					115				120					125		
[6394]	Lys	Gly	Pro	Ser	Val	Phe	Pro	Leu	Ala	Pro	Cys	Ser	Arg	Ser	Thr	Ser
[6395]	130							135					140			
[6396]	Glu	Ser	Thr	Ala	Ala	Leu	Gly	Cys	Leu	Val	Lys	Asp	Tyr	Phe	Pro	Glu
[6397]	145						150					155				160
[6398]	Pro	Val	Thr	Val	Ser	Trp	Asn	Ser	Gly	Ala	Leu	Thr	Ser	Gly	Val	His
[6399]					165				170						175	
[6400]	Thr	Phe	Pro	Ala	Val	Leu	Gln	Ser	Ser	Gly	Leu	Tyr	Ser	Leu	Ser	Ser
[6401]					180				185						190	
[6402]	Val	Val	Thr	Val	Pro	Ser	Ser	Asn	Phe	Gly	Thr	Gln	Thr	Tyr	Thr	Cys
[6403]					195				200					205		
[6404]	Asn	Val	Asp	His	Lys	Pro	Ser	Asn	Thr	Lys	Val	Asp	Lys	Thr	Val	Glu
[6405]	210							215					220			
[6406]	Arg	Lys	Ser	Cys	Val	Glu	Cys	Pro	Pro	Cys	Pro	Ala	Pro	Pro	Val	Ala
[6407]	225						230					235				240
[6408]	Gly	Pro	Ser	Val	Phe	Leu	Phe	Pro	Pro	Lys	Pro	Lys	Asp	Thr	Leu	Met
[6409]					245					250					255	
[6410]	Ile	Ser	Arg	Thr	Pro	Glu	Val	Thr	Cys	Val	Val	Val	Asp	Val	Ser	His
[6411]					260					265					270	
[6412]	Glu	Asp	Pro	Glu	Val	Lys	Phe	Asn	Trp	Tyr	Val	Asp	Gly	Val	Glu	Val
[6413]					275					280				285		
[6414]	His	Asn	Ala	Lys	Thr	Lys	Pro	Arg	Glu	Glu	Gln	Tyr	Asn	Ser	Thr	Tyr
[6415]	290							295						300		
[6416]	Arg	Val	Val	Ser	Val	Leu	Thr	Val	Leu	His	Gln	Asp	Trp	Leu	Asn	Gly
[6417]	305						310					315				320
[6418]	Lys	Glu	Tyr	Lys	Cys	Lys	Val	Ser	Asn	Lys	Ala	Leu	Pro	Ser	Ser	Ile
[6419]					325					330					335	
[6420]	Glu	Lys	Thr	Ile	Ser	Lys	Ala	Lys	Gly	Gln	Pro	Arg	Glu	Pro	Gln	Val
[6421]					340					345					350	
[6422]	Tyr	Thr	Leu	Pro	Pro	Ser	Arg	Glu	Glu	Met	Thr	Lys	Asn	Gln	Val	Ser
[6423]					355					360					365	
[6424]	Leu	Thr	Cys	Leu	Val	Lys	Gly	Phe	Tyr	Pro	Ser	Asp	Ile	Ala	Val	Glu
[6425]	370							375						380		

[6426]	Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro
[6427]	385 390 395 400
[6428]	Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val
[6429]	405 410 415
[6430]	Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met
[6431]	420 425 430
[6432]	His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser
[6433]	435 440 445
[6434]	Pro Gly
[6435]	450
[6436]	<210> 177
[6437]	<211> 215
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[6439]	<213> 人工序列
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[6441]	<223> 合成的: 9G7 L1 (全长野生型轻链 1)
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[6443]	Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly
[6444]	1 5 10 15
[6445]	Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Ser
[6446]	20 25 30
[6447]	Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu
[6448]	35 40 45
[6449]	Ile Tyr Gly Ala Ser Ser Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser
[6450]	50 55 60
[6451]	Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu
[6452]	65 70 75 80
[6453]	Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr Gly Ser Ser Pro
[6454]	85 90 95
[6455]	Trp Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala
[6456]	100 105 110
[6457]	Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser
[6458]	115 120 125
[6459]	Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu
[6460]	130 135 140
[6461]	Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser
[6462]	145 150 155 160
[6463]	Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu
[6464]	165 170 175
[6465]	Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val
[6466]	180 185 190
[6467]	Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys

[6468]	195	200	205
[6469]	Ser Phe Asn Arg Gly Glu Cys		
[6470]	210	215	
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[6473]	<212> PRT		
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[6476]	<223> 合成的: 14E3 (VH)		
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[6478]	Gln Val Gln Leu Gln Gln Trp Gly Ala Gly Leu Leu Lys Pro Ser Glu		
[6479]	1	5	10 15
[6480]	Thr Leu Ser Leu Thr Cys Ala Val Tyr Gly Gly Ser Phe Ser Gly Tyr		
[6481]	20	25	30
[6482]	Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile		
[6483]	35	40	45
[6484]	Gly Glu Ile Asn His Ser Gly Asn Thr Tyr Tyr Asn Pro Ser Leu Lys		
[6485]	50	55	60
[6486]	Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Leu Ser Leu		
[6487]	65	70	75 80
[6488]	Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala		
[6489]	85	90	95
[6490]	Arg Phe Gly Ser Asn Asp Ala Phe Asp Ile Trp Gly Gln Gly Thr Met		
[6491]	100	105	110
[6492]	Val Thr Val Ser Ser		
[6493]	115		
[6494]	<210> 179		
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[6496]	<212> PRT		
[6497]	<213> 人工序列		
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[6499]	<223> 合成的: 14E3 (VL)		
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[6503]	Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Ser Ser Trp		
[6504]	20	25	30
[6505]	Leu Ala Trp Tyr Gln Gln Lys Pro Glu Lys Ala Pro Lys Ser Leu Ile		
[6506]	35	40	45
[6507]	Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly		
[6508]	50	55	60
[6509]	Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro		

[6510]	65	70	75	80
[6511]	Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Asn Ser Tyr Pro Pro			
[6512]		85	90	95
[6513]	Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys			
[6514]		100	105	
[6515]	<210> 180			
[6516]	<211> 447			
[6517]	<212> PRT			
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[6520]	<223> 合成的: 14E3 (全长野生型重链)			
[6521]	<400> 180			
[6522]	Gln Val Gln Leu Gln Gln Trp Gly Ala Gly Leu Leu Lys Pro Ser Glu			
[6523]	1	5	10	15
[6524]	Thr Leu Ser Leu Thr Cys Ala Val Tyr Gly Gly Ser Phe Ser Gly Tyr			
[6525]		20	25	30
[6526]	Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile			
[6527]		35	40	45
[6528]	Gly Glu Ile Asn His Ser Gly Asn Thr Tyr Tyr Asn Pro Ser Leu Lys			
[6529]		50	55	60
[6530]	Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Leu Ser Leu			
[6531]	65	70	75	80
[6532]	Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala			
[6533]		85	90	95
[6534]	Arg Phe Gly Ser Asn Asp Ala Phe Asp Ile Trp Gly Gln Gly Thr Met			
[6535]		100	105	110
[6536]	Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu			
[6537]		115	120	125
[6538]	Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys			
[6539]		130	135	140
[6540]	Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser			
[6541]		145	150	155
[6542]	Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser			
[6543]		165	170	175
[6544]	Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser			
[6545]		180	185	190
[6546]	Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn			
[6547]		195	200	205
[6548]	Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp Lys Thr His			
[6549]		210	215	220
[6550]	Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val			
[6551]		225	230	235
				240

[6552]	Phe	Leu	Phe	Pro	Pro	Lys	Pro	Lys	Asp	Thr	Leu	Met	Ile	Ser	Arg	Thr
[6553]						245				250					255	
[6554]	Pro	Glu	Val	Thr	Cys	Val	Val	Val	Asp	Val	Ser	His	Glu	Asp	Pro	Glu
[6555]						260				265					270	
[6556]	Val	Lys	Phe	Asn	Trp	Tyr	Val	Asp	Gly	Val	Glu	Val	His	Asn	Ala	Lys
[6557]						275				280					285	
[6558]	Thr	Lys	Pro	Arg	Glu	Glu	Gln	Tyr	Asn	Ser	Thr	Tyr	Arg	Val	Val	Ser
[6559]						290				295					300	
[6560]	Val	Leu	Thr	Val	Leu	His	Gln	Asp	Trp	Leu	Asn	Gly	Lys	Glu	Tyr	Lys
[6561]	305						310					315				320
[6562]	Cys	Lys	Val	Ser	Asn	Lys	Ala	Leu	Pro	Ala	Pro	Ile	Glu	Lys	Thr	Ile
[6563]							325					330				335
[6564]	Ser	Lys	Ala	Lys	Gly	Gln	Pro	Arg	Glu	Pro	Gln	Val	Tyr	Thr	Leu	Pro
[6565]							340					345				350
[6566]	Pro	Ser	Arg	Asp	Glu	Leu	Thr	Lys	Asn	Gln	Val	Ser	Leu	Thr	Cys	Leu
[6567]							355					360				365
[6568]	Val	Lys	Gly	Phe	Tyr	Pro	Ser	Asp	Ile	Ala	Val	Glu	Trp	Glu	Ser	Asn
[6569]							370					375				380
[6570]	Gly	Gln	Pro	Glu	Asn	Asn	Tyr	Lys	Thr	Thr	Pro	Pro	Val	Leu	Asp	Ser
[6571]	385							390				395				400
[6572]	Asp	Gly	Ser	Phe	Phe	Leu	Tyr	Ser	Lys	Leu	Thr	Val	Asp	Lys	Ser	Arg
[6573]								405				410				415
[6574]	Trp	Gln	Gln	Gly	Asn	Val	Phe	Ser	Cys	Ser	Val	Met	His	Glu	Ala	Leu
[6575]							420					425				430
[6576]	His	Asn	His	Tyr	Thr	Gln	Lys	Ser	Leu	Ser	Leu	Ser	Pro	Gly	Lys	
[6577]							435					440				445
[6578]	<210> 181															
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[6581]	<213> 人工序列															
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[6585]	Asp	Ile	Gln	Met	Thr	Gln	Ser	Pro	Ser	Ser	Leu	Ser	Ala	Ser	Val	Gly
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[6587]	Asp	Arg	Val	Thr	Ile	Thr	Cys	Arg	Ala	Ser	Gln	Gly	Ile	Ser	Ser	Trp
[6588]						20					25				30	
[6589]	Leu	Ala	Trp	Tyr	Gln	Gln	Lys	Pro	Glu	Lys	Ala	Pro	Lys	Ser	Leu	Ile
[6590]						35					40				45	
[6591]	Tyr	Ala	Ala	Ser	Ser	Leu	Gln	Ser	Gly	Val	Pro	Ser	Arg	Phe	Ser	Gly
[6592]						50					55				60	
[6593]	Ser	Gly	Ser	Gly	Thr	Asp	Phe	Thr	Leu	Thr	Ile	Ser	Ser	Leu	Gln	Pro

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[6595]	Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Asn Ser Tyr Pro Pro			
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[6597]	Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala			
[6598]		100	105	110
[6599]	Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly			
[6600]		115	120	125
[6601]	Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala			
[6602]		130	135	140
[6603]	Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln			
[6604]	145	150	155	160
[6605]	Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser			
[6606]		165	170	175
[6607]	Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr			
[6608]		180	185	190
[6609]	Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser			
[6610]		195	200	205
[6611]	Phe Asn Arg Gly Glu Cys			
[6612]	210			
[6613]	<210> 182			
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[6615]	<212> PRT			
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[6618]	<223> 合成的: 14E3.IgG1 (VH + IgG1)			
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[6622]	Thr Leu Ser Leu Thr Cys Ala Val Tyr Gly Gly Ser Phe Ser Gly Tyr			
[6623]		20	25	30
[6624]	Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile			
[6625]		35	40	45
[6626]	Gly Glu Ile Asn His Ser Gly Asn Thr Tyr Tyr Asn Pro Ser Leu Lys			
[6627]		50	55	60
[6628]	Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Leu Ser Leu			
[6629]	65	70	75	80
[6630]	Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala			
[6631]		85	90	95
[6632]	Arg Phe Gly Ser Asn Asp Ala Phe Asp Ile Trp Gly Gln Gly Thr Met			
[6633]		100	105	110
[6634]	Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu			
[6635]		115	120	125

[6636]	Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys
[6637]	130 135 140
[6638]	Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser
[6639]	145 150 155 160
[6640]	Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser
[6641]	165 170 175
[6642]	Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser
[6643]	180 185 190
[6644]	Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn
[6645]	195 200 205
[6646]	Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp Lys Thr His
[6647]	210 215 220
[6648]	Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val
[6649]	225 230 235 240
[6650]	Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr
[6651]	245 250 255
[6652]	Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu
[6653]	260 265 270
[6654]	Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys
[6655]	275 280 285
[6656]	Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser
[6657]	290 295 300
[6658]	Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys
[6659]	305 310 315 320
[6660]	Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile
[6661]	325 330 335
[6662]	Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro
[6663]	340 345 350
[6664]	Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu
[6665]	355 360 365
[6666]	Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn
[6667]	370 375 380
[6668]	Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser
[6669]	385 390 395 400
[6670]	Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg
[6671]	405 410 415
[6672]	Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu
[6673]	420 425 430
[6674]	His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
[6675]	435 440 445
[6676]	<210> 183
[6677]	<211> 446

[6678]	<212>	PRT
[6679]	<213>	人工序列
[6680]	<220>	
[6681]	<223>	合成的: 14E3.IgG1.1 (VH + IgG1.1)
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[6684]	1	5 10 15
[6685]	Thr Leu Ser Leu Thr Cys Ala Val Tyr Gly Gly Ser Phe Ser Gly Tyr	
[6686]	20	25 30
[6687]	Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile	
[6688]	35	40 45
[6689]	Gly Glu Ile Asn His Ser Gly Asn Thr Tyr Tyr Asn Pro Ser Leu Lys	
[6690]	50	55 60
[6691]	Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Leu Ser Leu	
[6692]	65	70 75 80
[6693]	Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala	
[6694]	85	90 95
[6695]	Arg Phe Gly Ser Asn Asp Ala Phe Asp Ile Trp Gly Gln Gly Thr Met	
[6696]	100	105 110
[6697]	Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu	
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[6703]	Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser	
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[6705]	Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser	
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[6707]	Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn	
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[6709]	Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp Lys Thr His	
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[6711]	Thr Cys Pro Pro Cys Pro Ala Pro Glu Ala Glu Gly Ala Pro Ser Val	
[6712]	225	230 235 240
[6713]	Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr	
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[6715]	Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu	
[6716]	260	265 270
[6717]	Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys	
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[6719]	Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser	

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[6723]	Cys Lys Val Ser Asn Lys Ala Leu Pro Ser Ser Ile Glu Lys Thr Ile		
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[6725]	Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro		
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[6727]	Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu		
[6728]		355	360
[6729]	Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn		
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[6731]	Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser		
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[6733]	Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg		
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[6735]	Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu		
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[6737]	His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly		
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[6750]	Leu Ala Trp Tyr Gln Gln Lys Pro Glu Lys Ala Pro Lys Ser Leu Ile		
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[6752]	Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly		
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[6754]	Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro		
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[6756]	Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Asn Ser Tyr Pro Pro		
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[6758]	Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala		
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[6760]	Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly		
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 [6766] Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser
 [6767] 165 170 175
 [6768] Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr
 [6769] 180 185 190
 [6770] Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser
 [6771] 195 200 205
 [6772] Phe Asn Arg Gly Glu Cys
 [6773] 210
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 [6782] 1 5
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 [6800] 1 5
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[6838]		20 25 30
[6839]		Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile
[6840]		35 40 45
[6841]		Gly Glu Ile Asn His Ser Gly Asn Thr Tyr Tyr Asn Pro Ser Leu Lys
[6842]		50 55 60
[6843]		Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Leu Ser Leu
[6844]		65 70 75 80
[6845]		Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala

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[6847]	Arg Phe Gly Ser Asn Asp Ala Phe Asp Ile Trp Gly Gln Gly Thr Met					
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[6849]	Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu					
[6850]		115		120		125
[6851]	Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser Thr Ala Ala Leu Gly Cys					
[6852]		130		135		140
[6853]	Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser					
[6854]	145		150		155	160
[6855]	Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser					
[6856]		165		170		175
[6857]	Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Asn					
[6858]		180		185		190
[6859]	Phe Gly Thr Gln Thr Tyr Thr Cys Asn Val Asp His Lys Pro Ser Asn					
[6860]		195		200		205
[6861]	Thr Lys Val Asp Lys Thr Val Glu Arg Lys Cys Cys Val Glu Cys Pro					
[6862]		210		215		220
[6863]	Pro Cys Pro Ala Pro Pro Val Ala Gly Pro Ser Val Phe Leu Phe Pro					
[6864]	225		230		235	240
[6865]	Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr					
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[6867]	Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Gln Phe Asn					
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[6869]	Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg					
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[6871]	Glu Glu Gln Phe Asn Ser Thr Phe Arg Val Val Ser Val Leu Thr Val					
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[6873]	Val His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser					
[6874]	305		310		315	320
[6875]	Asn Lys Gly Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Thr Lys					
[6876]		325		330		335
[6877]	Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu					
[6878]		340		345		350
[6879]	Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe					
[6880]		355		360		365
[6881]	Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu					
[6882]		370		375		380
[6883]	Asn Asn Tyr Lys Thr Thr Pro Pro Met Leu Asp Ser Asp Gly Ser Phe					
[6884]	385		390		395	400
[6885]	Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly					
[6886]		405		410		415
[6887]	Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr					

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[6900]	Thr Leu Ser Leu Thr Cys Ala Val Tyr Gly Gly Ser Phe Ser Gly Tyr		
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[6902]	Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile		
[6903]	35 40 45		
[6904]	Gly Glu Ile Asn His Ser Gly Asn Thr Tyr Tyr Asn Pro Ser Leu Lys		
[6905]	50 55 60		
[6906]	Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Leu Ser Leu		
[6907]	65 70 75 80		
[6908]	Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala		
[6909]	85 90 95		
[6910]	Arg Phe Gly Ser Asn Asp Ala Phe Asp Ile Trp Gly Gln Gly Thr Met		
[6911]	100 105 110		
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[6918]	Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser		
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[6920]	Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Asn		
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[6924]	Thr Lys Val Asp Lys Thr Val Glu Arg Lys Ser Cys Val Glu Cys Pro		
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[6926]	Pro Cys Pro Ala Pro Pro Val Ala Gly Pro Ser Val Phe Leu Phe Pro		
[6927]	225 230 235 240		
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[6930]	Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Gln Phe Asn
[6931]	260 265 270
[6932]	Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg
[6933]	275 280 285
[6934]	Glu Glu Gln Phe Asn Ser Thr Phe Arg Val Val Ser Val Leu Thr Val
[6935]	290 295 300
[6936]	Val His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser
[6937]	305 310 315 320
[6938]	Asn Lys Gly Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Thr Lys
[6939]	325 330 335
[6940]	Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu
[6941]	340 345 350
[6942]	Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe
[6943]	355 360 365
[6944]	Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu
[6945]	370 375 380
[6946]	Asn Asn Tyr Lys Thr Thr Pro Pro Met Leu Asp Ser Asp Gly Ser Phe
[6947]	385 390 395 400
[6948]	Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly
[6949]	405 410 415
[6950]	Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr
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[6952]	Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
[6953]	435 440
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[6963]	Thr Leu Ser Leu Thr Cys Ala Val Tyr Gly Gly Ser Phe Ser Gly Tyr
[6964]	20 25 30
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[6966]	35 40 45
[6967]	Gly Glu Ile Asn His Ser Gly Asn Thr Tyr Tyr Asn Pro Ser Leu Lys
[6968]	50 55 60
[6969]	Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Leu Ser Leu
[6970]	65 70 75 80
[6971]	Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala

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[6983]	Ser	Gly	Leu	Tyr	Ser	Leu	Ser	Ser	Val	Val	Thr	Val	Pro	Ser	Ser	Asn		
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[6991]	Pro	Pro	Lys	Pro	Lys	Asp	Thr	Leu	Met	Ile	Ser	Arg	Thr	Pro	Glu	Val		
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[6995]	Asn	Trp	Tyr	Val	Asp	Gly	Val	Glu	Val	His	Asn	Ala	Lys	Thr	Lys	Pro		
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[7011]	Phe	Phe	Leu	Tyr	Ser	Lys	Leu	Thr	Val	Asp	Lys	Ser	Arg	Trp	Gln	Gln		
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[7054]	Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr		
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[7057]	260 265 270
[7058]	Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg
[7059]	275 280 285
[7060]	Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val
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[7062]	Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser
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[7064]	Asn Lys Ala Leu Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys
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[7070]	Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu
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[7072]	Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe
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[7075]	405 410 415
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[7078]	Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
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[7089]	Thr Leu Ser Leu Thr Cys Ala Val Tyr Gly Gly Ser Phe Ser Gly Tyr
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[7093]	Gly Glu Ile Asn His Ser Gly Asn Thr Tyr Tyr Asn Pro Ser Leu Lys
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[7096]	65 70 75 80
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[7111]	Phe	Gly	Thr	Gln	Thr	Tyr	Thr	Cys	Asn	Val	Asp	His	Lys	Pro	Ser	Asn		
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[7114]	210							215							220			
[7115]	Pro	Cys	Pro	Ala	Pro	Glu	Leu	Leu	Gly	Gly	Pro	Ser	Val	Phe	Leu	Phe		
[7116]	225							230							235			240
[7117]	Pro	Pro	Lys	Pro	Lys	Asp	Thr	Leu	Met	Ile	Ser	Arg	Thr	Pro	Glu	Val		
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[7119]	Thr	Cys	Val	Val	Val	Asp	Val	Ser	His	Glu	Asp	Pro	Glu	Val	Lys	Phe		
[7120]	260							265							270			
[7121]	Asn	Trp	Tyr	Val	Asp	Gly	Val	Glu	Val	His	Asn	Ala	Lys	Thr	Lys	Pro		
[7122]	275							280							285			
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[7124]	290							295							300			
[7125]	Val	Leu	His	Gln	Asp	Trp	Leu	Asn	Gly	Lys	Glu	Tyr	Lys	Cys	Lys	Val		
[7126]	305							310							315			320
[7127]	Ser	Asn	Lys	Ala	Leu	Pro	Ala	Pro	Ile	Glu	Lys	Thr	Ile	Ser	Lys	Ala		
[7128]	325							330							335			
[7129]	Lys	Gly	Gln	Pro	Arg	Glu	Pro	Gln	Val	Tyr	Thr	Leu	Pro	Pro	Ser	Arg		
[7130]	340							345							350			
[7131]	Glu	Glu	Met	Thr	Lys	Asn	Gln	Val	Ser	Leu	Thr	Cys	Leu	Val	Lys	Gly		
[7132]	355							360							365			
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[7135]	Glu	Asn	Asn	Tyr	Lys	Thr	Thr	Pro	Pro	Val	Leu	Asp	Ser	Asp	Gly	Ser		
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[7137]	Phe	Phe	Leu	Tyr	Ser	Lys	Leu	Thr	Val	Asp	Lys	Ser	Arg	Trp	Gln	Gln		
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[7152]	Thr Leu Ser Leu Thr Cys Ala Val Tyr Gly Gly Ser Phe Ser Gly Tyr		
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[7154]	Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile		
[7155]	35 40 45		
[7156]	Gly Glu Ile Asn His Ser Gly Asn Thr Tyr Tyr Asn Pro Ser Leu Lys		
[7157]	50 55 60		
[7158]	Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Leu Ser Leu		
[7159]	65 70 75 80		
[7160]	Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala		
[7161]	85 90 95		
[7162]	Arg Phe Gly Ser Asn Asp Ala Phe Asp Ile Trp Gly Gln Gly Thr Met		
[7163]	100 105 110		
[7164]	Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu		
[7165]	115 120 125		
[7166]	Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser Thr Ala Ala Leu Gly Cys		
[7167]	130 135 140		
[7168]	Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser		
[7169]	145 150 155 160		
[7170]	Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser		
[7171]	165 170 175		
[7172]	Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Asn		
[7173]	180 185 190		
[7174]	Phe Gly Thr Gln Thr Tyr Thr Cys Asn Val Asp His Lys Pro Ser Asn		
[7175]	195 200 205		
[7176]	Thr Lys Val Asp Lys Thr Val Glu Arg Lys Ser Cys Val Glu Cys Pro		
[7177]	210 215 220		
[7178]	Pro Cys Pro Ala Pro Pro Val Ala Gly Pro Ser Val Phe Leu Phe Pro		
[7179]	225 230 235 240		
[7180]	Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr		
[7181]	245 250 255		

[7182]	Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn
[7183]	260 265 270
[7184]	Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg
[7185]	275 280 285
[7186]	Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val
[7187]	290 295 300
[7188]	Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser
[7189]	305 310 315 320
[7190]	Asn Lys Ala Leu Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys
[7191]	325 330 335
[7192]	Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu
[7193]	340 345 350
[7194]	Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe
[7195]	355 360 365
[7196]	Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu
[7197]	370 375 380
[7198]	Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe
[7199]	385 390 395 400
[7200]	Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly
[7201]	405 410 415
[7202]	Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr
[7203]	420 425 430
[7204]	Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
[7205]	435 440
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[7212]	<400> 197
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[7214]	1 5 10 15
[7215]	Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asn Tyr
[7216]	20 25 30
[7217]	Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Met
[7218]	35 40 45
[7219]	Ala Val Ile Trp Tyr Gly Gly Ser Asn Lys Phe Tyr Ala Asp Ser Val
[7220]	50 55 60
[7221]	Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Ser Leu Ser
[7222]	65 70 75 80
[7223]	Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys

[7224]		85		90		95
[7225]	Ala Arg Gly Gly Ala Met Val Arg Gly Val Tyr Tyr Tyr Gly Met Asp					
[7226]		100		105		110
[7227]	Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser					
[7228]		115		120		
[7229]	<210> 198					
[7230]	<211> 107					
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[7234]	<223> 合成的: 19H8 (VL1)					
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[7236]	Ala Ile Gln Leu Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly					
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[7238]	Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Ser Ser Ala					
[7239]		20		25		30
[7240]	Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Phe Leu Ile					
[7241]		35		40		45
[7242]	Tyr Asp Ala Ser Ser Leu Glu Ser Gly Val Pro Ser Arg Phe Ser Gly					
[7243]		50		55		60
[7244]	Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro					
[7245]	65		70		75	80
[7246]	Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Phe Asn Ser Tyr Pro Gln					
[7247]		85		90		95
[7248]	Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys					
[7249]		100		105		
[7250]	<210> 199					
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[7252]	<212> PRT					
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[7257]	Glu Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly					
[7258]	1	5		10		15
[7259]	Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Tyr					
[7260]		20		25		30
[7261]	Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile					
[7262]		35		40		45
[7263]	Tyr Asp Ala Ser Asn Arg Ala Thr Gly Ile Pro Ala Arg Phe Ser Gly					
[7264]		50		55		60
[7265]	Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Glu Pro					

[7266]	65	70	75	80
[7267]	Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Arg Ser Asn Trp Pro Leu			
[7268]		85	90	95
[7269]	Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys			
[7270]		100	105	
[7271]	<210> 200			
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[7278]	Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg			
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[7280]	Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asn Tyr			
[7281]		20	25	30
[7282]	Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Met			
[7283]		35	40	45
[7284]	Ala Val Ile Trp Tyr Gly Gly Ser Asn Lys Phe Tyr Ala Asp Ser Val			
[7285]		50	55	60
[7286]	Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Ser Leu Ser			
[7287]	65	70	75	80
[7288]	Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys			
[7289]		85	90	95
[7290]	Ala Arg Gly Gly Ala Met Val Arg Gly Val Tyr Tyr Tyr Gly Met Asp			
[7291]		100	105	110
[7292]	Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys			
[7293]		115	120	125
[7294]	Gly Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu			
[7295]		130	135	140
[7296]	Ser Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro			
[7297]	145	150	155	160
[7298]	Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr			
[7299]		165	170	175
[7300]	Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val			
[7301]		180	185	190
[7302]	Val Thr Val Pro Ser Ser Asn Phe Gly Thr Gln Thr Tyr Thr Cys Asn			
[7303]		195	200	205
[7304]	Val Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys Thr Val Glu Arg			
[7305]		210	215	220
[7306]	Lys Cys Cys Val Glu Cys Pro Pro Cys Pro Ala Pro Pro Val Ala Gly			
[7307]	225	230	235	240

[7308]	Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile		
[7309]		245	250 255
[7310]	Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu		
[7311]		260	265 270
[7312]	Asp Pro Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val His		
[7313]		275	280 285
[7314]	Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr Phe Arg		
[7315]		290	295 300
[7316]	Val Val Ser Val Leu Thr Val Val His Gln Asp Trp Leu Asn Gly Lys		
[7317]	305	310	315 320
[7318]	Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ala Pro Ile Glu		
[7319]		325	330 335
[7320]	Lys Thr Ile Ser Lys Thr Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr		
[7321]		340	345 350
[7322]	Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu		
[7323]		355	360 365
[7324]	Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp		
[7325]		370	375 380
[7326]	Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Met		
[7327]	385	390	395 400
[7328]	Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp		
[7329]		405	410 415
[7330]	Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His		
[7331]		420	425 430
[7332]	Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro		
[7333]		435	440 445
[7334]	Gly Lys		
[7335]	450		
[7336]	<210> 201		
[7337]	<211> 214		
[7338]	<212> PRT		
[7339]	<213> 人工序列		
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[7341]	<223> 合成的: 19H8 L1 (全长野生型轻链 1)		
[7342]	<400> 201		
[7343]	Ala Ile Gln Leu Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly		
[7344]	1	5	10 15
[7345]	Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Ser Ser Ala		
[7346]		20	25 30
[7347]	Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Phe Leu Ile		
[7348]		35	40 45
[7349]	Tyr Asp Ala Ser Ser Leu Glu Ser Gly Val Pro Ser Arg Phe Ser Gly		

[7350]	50	55	60
[7351]	Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro		
[7352]	65	70	75
[7353]	Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Phe Asn Ser Tyr Pro Gln		
[7354]	85	90	95
[7355]	Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala		
[7356]	100	105	110
[7357]	Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly		
[7358]	115	120	125
[7359]	Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala		
[7360]	130	135	140
[7361]	Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln		
[7362]	145	150	155
[7363]	Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser		
[7364]	165	170	175
[7365]	Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr		
[7366]	180	185	190
[7367]	Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser		
[7368]	195	200	205
[7369]	Phe Asn Arg Gly Glu Cys		
[7370]	210		
[7371]	<210> 202		
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[7373]	<212> PRT		
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[7376]	<223> 合成的: 19H8 L2 (全长野生型轻链 2)		
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[7379]	1	5	10
[7380]	Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Tyr		
[7381]	20	25	30
[7382]	Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile		
[7383]	35	40	45
[7384]	Tyr Asp Ala Ser Asn Arg Ala Thr Gly Ile Pro Ala Arg Phe Ser Gly		
[7385]	50	55	60
[7386]	Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Glu Pro		
[7387]	65	70	75
[7388]	Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Arg Ser Asn Trp Pro Leu		
[7389]	85	90	95
[7390]	Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala		
[7391]	100	105	110

[7392]	Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly
[7393]	115 120 125
[7394]	Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala
[7395]	130 135 140
[7396]	Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln
[7397]	145 150 155 160
[7398]	Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser
[7399]	165 170 175
[7400]	Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr
[7401]	180 185 190
[7402]	Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser
[7403]	195 200 205
[7404]	Phe Asn Arg Gly Glu Cys
[7405]	210
[7406]	<210> 203
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[7408]	<212> PRT
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[7415]	Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asn Tyr
[7416]	20 25 30
[7417]	Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Met
[7418]	35 40 45
[7419]	Ala Val Ile Trp Tyr Gly Gly Ser Asn Lys Phe Tyr Ala Asp Ser Val
[7420]	50 55 60
[7421]	Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Ser Leu Ser
[7422]	65 70 75 80
[7423]	Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
[7424]	85 90 95
[7425]	Ala Arg Gly Gly Ala Met Val Arg Gly Val Tyr Tyr Tyr Gly Met Asp
[7426]	100 105 110
[7427]	Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys
[7428]	115 120 125
[7429]	Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly
[7430]	130 135 140
[7431]	Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro
[7432]	145 150 155 160
[7433]	Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr

[7434]	165							170							175				
[7435]	Phe	Pro	Ala	Val	Leu	Gln	Ser	Ser	Gly	Leu	Tyr	Ser	Leu	Ser	Ser	Val			
[7436]	180							185							190				
[7437]	Val	Thr	Val	Pro	Ser	Ser	Ser	Leu	Gly	Thr	Gln	Thr	Tyr	Ile	Cys	Asn			
[7438]	195							200							205				
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[7440]	210							215							220				
[7441]	Lys	Ser	Cys	Asp	Lys	Thr	His	Thr	Cys	Pro	Pro	Cys	Pro	Ala	Pro	Glu			
[7442]	225							230							235			240	
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[7445]	Thr	Leu	Met	Ile	Ser	Arg	Thr	Pro	Glu	Val	Thr	Cys	Val	Val	Val	Asp			
[7446]	260							265							270				
[7447]	Val	Ser	His	Glu	Asp	Pro	Glu	Val	Lys	Phe	Asn	Trp	Tyr	Val	Asp	Gly			
[7448]	275							280							285				
[7449]	Val	Glu	Val	His	Asn	Ala	Lys	Thr	Lys	Pro	Arg	Glu	Glu	Gln	Tyr	Asn			
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[7455]	Ala	Pro	Ile	Glu	Lys	Thr	Ile	Ser	Lys	Ala	Lys	Gly	Gln	Pro	Arg	Glu			
[7456]	340							345							350				
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[7458]	355							360							365				
[7459]	Gln	Val	Ser	Leu	Thr	Cys	Leu	Val	Lys	Gly	Phe	Tyr	Pro	Ser	Asp	Ile			
[7460]	370							375							380				
[7461]	Ala	Val	Glu	Trp	Glu	Ser	Asn	Gly	Gln	Pro	Glu	Asn	Asn	Tyr	Lys	Thr			
[7462]	385							390							395			400	
[7463]	Thr	Pro	Pro	Val	Leu	Asp	Ser	Asp	Gly	Ser	Phe	Phe	Leu	Tyr	Ser	Lys			
[7464]	405							410							415				
[7465]	Leu	Thr	Val	Asp	Lys	Ser	Arg	Trp	Gln	Gln	Gly	Asn	Val	Phe	Ser	Cys			
[7466]	420							425							430				
[7467]	Ser	Val	Met	His	Glu	Ala	Leu	His	Asn	His	Tyr	Thr	Gln	Lys	Ser	Leu			
[7468]	435							440							445				
[7469]	Ser	Leu	Ser	Pro	Gly														
[7470]	450																		
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[7472]	<211> 453																		
[7473]	<212> PRT																		
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[7480]	Ser	Leu	Arg	Leu	Ser	Cys	Ala	Ala	Ser	Gly	Phe	Thr	Phe	Ser	Asn	Tyr				
[7481]					20					25					30					
[7482]	Gly	Met	His	Trp	Val	Arg	Gln	Ala	Pro	Gly	Lys	Gly	Leu	Glu	Trp	Met				
[7483]					35					40					45					
[7484]	Ala	Val	Ile	Trp	Tyr	Gly	Gly	Ser	Asn	Lys	Phe	Tyr	Ala	Asp	Ser	Val				
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[7486]	Lys	Gly	Arg	Phe	Thr	Ile	Ser	Arg	Asp	Asn	Ser	Lys	Asn	Ser	Leu	Ser				
[7487]	65					70					75					80				
[7488]	Leu	Gln	Met	Asn	Ser	Leu	Arg	Ala	Glu	Asp	Thr	Ala	Val	Tyr	Tyr	Cys				
[7489]					85					90					95					
[7490]	Ala	Arg	Gly	Gly	Ala	Met	Val	Arg	Gly	Val	Tyr	Tyr	Tyr	Gly	Met	Asp				
[7491]					100					105					110					
[7492]	Val	Trp	Gly	Gln	Gly	Thr	Thr	Val	Thr	Val	Ser	Ser	Ala	Ser	Thr	Lys				
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[7494]	Gly	Pro	Ser	Val	Phe	Pro	Leu	Ala	Pro	Ser	Ser	Lys	Ser	Thr	Ser	Gly				
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[7496]	Gly	Thr	Ala	Ala	Leu	Gly	Cys	Leu	Val	Lys	Asp	Tyr	Phe	Pro	Glu	Pro				
[7497]	145					150					155					160				
[7498]	Val	Thr	Val	Ser	Trp	Asn	Ser	Gly	Ala	Leu	Thr	Ser	Gly	Val	His	Thr				
[7499]					165					170					175					
[7500]	Phe	Pro	Ala	Val	Leu	Gln	Ser	Ser	Gly	Leu	Tyr	Ser	Leu	Ser	Ser	Val				
[7501]					180					185					190					
[7502]	Val	Thr	Val	Pro	Ser	Ser	Ser	Leu	Gly	Thr	Gln	Thr	Tyr	Ile	Cys	Asn				
[7503]					195					200					205					
[7504]	Val	Asn	His	Lys	Pro	Ser	Asn	Thr	Lys	Val	Asp	Lys	Arg	Val	Glu	Pro				
[7505]		210							215					220						
[7506]	Lys	Ser	Cys	Asp	Lys	Thr	His	Thr	Cys	Pro	Pro	Cys	Pro	Ala	Pro	Glu				
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[7508]	Ala	Glu	Gly	Ala	Pro	Ser	Val	Phe	Leu	Phe	Pro	Pro	Lys	Pro	Lys	Asp				
[7509]					245					250					255					
[7510]	Thr	Leu	Met	Ile	Ser	Arg	Thr	Pro	Glu	Val	Thr	Cys	Val	Val	Val	Asp				
[7511]					260					265					270					
[7512]	Val	Ser	His	Glu	Asp	Pro	Glu	Val	Lys	Phe	Asn	Trp	Tyr	Val	Asp	Gly				
[7513]					275					280					285					
[7514]	Val	Glu	Val	His	Asn	Ala	Lys	Thr	Lys	Pro	Arg	Glu	Glu	Gln	Tyr	Asn				
[7515]		290							295					300						
[7516]	Ser	Thr	Tyr	Arg	Val	Val	Ser	Val	Leu	Thr	Val	Leu	His	Gln	Asp	Trp				
[7517]	305					310					315					320				

[7518]	Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro		
[7519]		325	330 335
[7520]	Ser Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu		
[7521]		340	345 350
[7522]	Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn		
[7523]		355	360 365
[7524]	Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile		
[7525]		370	375 380
[7526]	Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr		
[7527]		385	390 395 400
[7528]	Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys		
[7529]		405	410 415
[7530]	Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys		
[7531]		420	425 430
[7532]	Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu		
[7533]		435	440 445
[7534]	Ser Leu Ser Pro Gly		
[7535]		450	
[7536]	<210>	205	
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[7545]	Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Ser Ser Ala		
[7546]		20	25 30
[7547]	Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Phe Leu Ile		
[7548]		35	40 45
[7549]	Tyr Asp Ala Ser Ser Leu Glu Ser Gly Val Pro Ser Arg Phe Ser Gly		
[7550]		50	55 60
[7551]	Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro		
[7552]	65	70	75 80
[7553]	Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Phe Asn Ser Tyr Pro Gln		
[7554]		85	90 95
[7555]	Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala		
[7556]		100	105 110
[7557]	Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly		
[7558]		115	120 125
[7559]	Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala		

[7560]	130	135	140
[7561]	Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln		
[7562]	145	150	155
[7563]	Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser		
[7564]	165	170	175
[7565]	Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr		
[7566]	180	185	190
[7567]	Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser		
[7568]	195	200	205
[7569]	Phe Asn Arg Gly Glu Cys		
[7570]	210		
[7571]	<210> 206		
[7572]	<211> 214		
[7573]	<212> PRT		
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[7580]	Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Tyr		
[7581]	20	25	30
[7582]	Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile		
[7583]	35	40	45
[7584]	Tyr Asp Ala Ser Asn Arg Ala Thr Gly Ile Pro Ala Arg Phe Ser Gly		
[7585]	50	55	60
[7586]	Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Glu Pro		
[7587]	65	70	75
[7588]	Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Arg Ser Asn Trp Pro Leu		
[7589]	85	90	95
[7590]	Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala		
[7591]	100	105	110
[7592]	Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly		
[7593]	115	120	125
[7594]	Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala		
[7595]	130	135	140
[7596]	Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln		
[7597]	145	150	155
[7598]	Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser		
[7599]	165	170	175
[7600]	Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr		
[7601]	180	185	190

[7602]	Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser
[7603]	195 200 205
[7604]	Phe Asn Arg Gly Glu Cys
[7605]	210
[7606]	<210> 207
[7607]	<211> 5
[7608]	<212> PRT
[7609]	<213> 人工序列
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[7611]	<223> 合成的: 19H8 VH CDR1
[7612]	<400> 207
[7613]	Asn Tyr Gly Met His
[7614]	1 5
[7615]	<210> 208
[7616]	<211> 17
[7617]	<212> PRT
[7618]	<213> 人工序列
[7619]	<220>
[7620]	<223> 合成的: 19H8 VH CDR2
[7621]	<400> 208
[7622]	Val Ile Trp Tyr Gly Gly Ser Asn Lys Phe Tyr Ala Asp Ser Val Lys
[7623]	1 5 10 15
[7624]	Gly
[7625]	<210> 209
[7626]	<211> 15
[7627]	<212> PRT
[7628]	<213> 人工序列
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[7630]	<223> 合成的: 19H8 VH CDR3
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[7632]	Gly Gly Ala Met Val Arg Gly Val Tyr Tyr Tyr Gly Met Asp Val
[7633]	1 5 10 15
[7634]	<210> 210
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[7639]	<223> 合成的: 19H8 VL1 CDR1
[7640]	<400> 210
[7641]	Arg Ala Ser Gln Gly Ile Ser Ser Ala Leu Ala
[7642]	1 5 10
[7643]	<210> 211

[7644] <211> 7
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[7647] <220>
[7648] <223> 合成的: 19H8 VL1 CDR2
[7649] <400> 211
[7650] Asp Ala Ser Ser Leu Glu Ser
[7651] 1 5
[7652] <210> 212
[7653] <211> 9
[7654] <212> PRT
[7655] <213> 人工序列
[7656] <220>
[7657] <223> 合成的: 19H8 VL1 CDR3
[7658] <400> 212
[7659] Gln Gln Phe Asn Ser Tyr Pro Gln Thr
[7660] 1 5
[7661] <210> 213
[7662] <211> 11
[7663] <212> PRT
[7664] <213> 人工序列
[7665] <220>
[7666] <223> 合成的: 19H8 VL2 CDR1
[7667] <400> 213
[7668] Arg Ala Ser Gln Ser Val Ser Ser Tyr Leu Ala
[7669] 1 5 10
[7670] <210> 214
[7671] <211> 7
[7672] <212> PRT
[7673] <213> 人工序列
[7674] <220>
[7675] <223> 合成的: 19H8 VL2 CDR2
[7676] <400> 214
[7677] Asp Ala Ser Asn Arg Ala Thr
[7678] 1 5
[7679] <210> 215
[7680] <211> 9
[7681] <212> PRT
[7682] <213> 人工序列
[7683] <220>
[7684] <223> 合成的: 19H8 VL2 CDR3
[7685] <400> 215

[7686]	Gln Gln Arg Ser Asn Trp Pro Leu Thr
[7687]	1 5
[7688]	<210> 216
[7689]	<211> 449
[7690]	<212> PRT
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[7693]	<223> 合成的: 19H8 (VH + G2 (C219S)) 或19H8-IgG2-C219S
[7694]	<400> 216
[7695]	Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg
[7696]	1 5 10 15
[7697]	Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asn Tyr
[7698]	20 25 30
[7699]	Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Met
[7700]	35 40 45
[7701]	Ala Val Ile Trp Tyr Gly Gly Ser Asn Lys Phe Tyr Ala Asp Ser Val
[7702]	50 55 60
[7703]	Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Ser Leu Ser
[7704]	65 70 75 80
[7705]	Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
[7706]	85 90 95
[7707]	Ala Arg Gly Gly Ala Met Val Arg Gly Val Tyr Tyr Tyr Gly Met Asp
[7708]	100 105 110
[7709]	Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys
[7710]	115 120 125
[7711]	Gly Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu
[7712]	130 135 140
[7713]	Ser Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro
[7714]	145 150 155 160
[7715]	Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr
[7716]	165 170 175
[7717]	Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val
[7718]	180 185 190
[7719]	Val Thr Val Pro Ser Ser Asn Phe Gly Thr Gln Thr Tyr Thr Cys Asn
[7720]	195 200 205
[7721]	Val Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys Thr Val Glu Arg
[7722]	210 215 220
[7723]	Lys Ser Cys Val Glu Cys Pro Pro Cys Pro Ala Pro Pro Val Ala Gly
[7724]	225 230 235 240
[7725]	Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile
[7726]	245 250 255
[7727]	Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu

[7728]	260	265	270
[7729]	Asp Pro Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val His		
[7730]	275	280	285
[7731]	Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr Phe Arg		
[7732]	290	295	300
[7733]	Val Val Ser Val Leu Thr Val Val His Gln Asp Trp Leu Asn Gly Lys		
[7734]	305	310	315
[7735]	Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ala Pro Ile Glu		
[7736]	325	330	335
[7737]	Lys Thr Ile Ser Lys Thr Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr		
[7738]	340	345	350
[7739]	Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu		
[7740]	355	360	365
[7741]	Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp		
[7742]	370	375	380
[7743]	Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Met		
[7744]	385	390	395
[7745]	Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp		
[7746]	405	410	415
[7747]	Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His		
[7748]	420	425	430
[7749]	Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro		
[7750]	435	440	445
[7751]	Gly		
[7752]	<210> 217		
[7753]	<211> 450		
[7754]	<212> PRT		
[7755]	<213> 人工序列		
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[7757]	<223> 合成的: 19H8 (VH + G2.g1)或19H8-IgG2-IgG1		
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[7759]	Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg		
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[7761]	Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asn Tyr		
[7762]	20	25	30
[7763]	Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Met		
[7764]	35	40	45
[7765]	Ala Val Ile Trp Tyr Gly Gly Ser Asn Lys Phe Tyr Ala Asp Ser Val		
[7766]	50	55	60
[7767]	Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Ser Leu Ser		
[7768]	65	70	75
[7769]	Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys		

[7770]		85		90		95
[7771]	Ala Arg Gly Gly Ala Met Val Arg Gly Val Tyr Tyr Tyr Gly Met Asp					
[7772]		100		105		110
[7773]	Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys					
[7774]		115		120		125
[7775]	Gly Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu					
[7776]		130		135		140
[7777]	Ser Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro					
[7778]	145		150		155	160
[7779]	Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr					
[7780]		165		170		175
[7781]	Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val					
[7782]		180		185		190
[7783]	Val Thr Val Pro Ser Ser Asn Phe Gly Thr Gln Thr Tyr Thr Cys Asn					
[7784]		195		200		205
[7785]	Val Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys Thr Val Glu Arg					
[7786]		210		215		220
[7787]	Lys Cys Cys Val Glu Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly					
[7788]	225		230		235	240
[7789]	Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met					
[7790]		245		250		255
[7791]	Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His					
[7792]		260		265		270
[7793]	Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val					
[7794]		275		280		285
[7795]	His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr					
[7796]		290		295		300
[7797]	Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly					
[7798]	305		310		315	320
[7799]	Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile					
[7800]		325		330		335
[7801]	Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val					
[7802]		340		345		350
[7803]	Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser					
[7804]		355		360		365
[7805]	Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu					
[7806]		370		375		380
[7807]	Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro					
[7808]	385		390		395	400
[7809]	Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val					
[7810]		405		410		415
[7811]	Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met					

[7812]	420	425	430
[7813]	His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser		
[7814]	435	440	445
[7815]	Pro Gly		
[7816]	450		
[7817]	<210> 218		
[7818]	<211> 449		
[7819]	<212> PRT		
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[7826]	Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asn Tyr		
[7827]	20 25 30		
[7828]	Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Met		
[7829]	35 40 45		
[7830]	Ala Val Ile Trp Tyr Gly Gly Ser Asn Lys Phe Tyr Ala Asp Ser Val		
[7831]	50 55 60		
[7832]	Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Ser Leu Ser		
[7833]	65 70 75 80		
[7834]	Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys		
[7835]	85 90 95		
[7836]	Ala Arg Gly Gly Ala Met Val Arg Gly Val Tyr Tyr Tyr Gly Met Asp		
[7837]	100 105 110		
[7838]	Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys		
[7839]	115 120 125		
[7840]	Gly Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu		
[7841]	130 135 140		
[7842]	Ser Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro		
[7843]	145 150 155 160		
[7844]	Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr		
[7845]	165 170 175		
[7846]	Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val		
[7847]	180 185 190		
[7848]	Val Thr Val Pro Ser Ser Asn Phe Gly Thr Gln Thr Tyr Thr Cys Asn		
[7849]	195 200 205		
[7850]	Val Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys Thr Val Glu Arg		
[7851]	210 215 220		
[7852]	Lys Cys Cys Val Glu Cys Pro Pro Cys Pro Ala Pro Pro Val Ala Gly		
[7853]	225 230 235 240		

[7854]	Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile		
[7855]		245	250 255
[7856]	Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu		
[7857]		260	265 270
[7858]	Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His		
[7859]		275	280 285
[7860]	Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg		
[7861]		290	295 300
[7862]	Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys		
[7863]		305	310 315 320
[7864]	Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ser Ser Ile Glu		
[7865]		325	330 335
[7866]	Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr		
[7867]		340	345 350
[7868]	Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu		
[7869]		355	360 365
[7870]	Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp		
[7871]		370	375 380
[7872]	Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val		
[7873]		385	390 395 400
[7874]	Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp		
[7875]		405	410 415
[7876]	Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His		
[7877]		420	425 430
[7878]	Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro		
[7879]		435	440 445
[7880]	Gly		
[7881]	<210> 219		
[7882]	<211> 450		
[7883]	<212> PRT		
[7884]	<213> 人工序列		
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[7888]	Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg		
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[7890]	Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asn Tyr		
[7891]		20	25 30
[7892]	Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Met		
[7893]		35	40 45
[7894]	Ala Val Ile Trp Tyr Gly Gly Ser Asn Lys Phe Tyr Ala Asp Ser Val		
[7895]		50	55 60

[7896]	Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Ser Leu Ser
[7897]	65 70 75 80
[7898]	Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
[7899]	85 90 95
[7900]	Ala Arg Gly Gly Ala Met Val Arg Gly Val Tyr Tyr Tyr Gly Met Asp
[7901]	100 105 110
[7902]	Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys
[7903]	115 120 125
[7904]	Gly Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu
[7905]	130 135 140
[7906]	Ser Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro
[7907]	145 150 155 160
[7908]	Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr
[7909]	165 170 175
[7910]	Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val
[7911]	180 185 190
[7912]	Val Thr Val Pro Ser Ser Asn Phe Gly Thr Gln Thr Tyr Thr Cys Asn
[7913]	195 200 205
[7914]	Val Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys Thr Val Glu Arg
[7915]	210 215 220
[7916]	Lys Ser Cys Val Glu Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly
[7917]	225 230 235 240
[7918]	Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
[7919]	245 250 255
[7920]	Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His
[7921]	260 265 270
[7922]	Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val
[7923]	275 280 285
[7924]	His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr
[7925]	290 295 300
[7926]	Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly
[7927]	305 310 315 320
[7928]	Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile
[7929]	325 330 335
[7930]	Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val
[7931]	340 345 350
[7932]	Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser
[7933]	355 360 365
[7934]	Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu
[7935]	370 375 380
[7936]	Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro
[7937]	385 390 395 400

[7938]	Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val
[7939]	405 410 415
[7940]	Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met
[7941]	420 425 430
[7942]	His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser
[7943]	435 440 445
[7944]	Pro Gly
[7945]	450
[7946]	<210> 220
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[7953]	Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg
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[7955]	Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asn Tyr
[7956]	20 25 30
[7957]	Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Met
[7958]	35 40 45
[7959]	Ala Val Ile Trp Tyr Gly Gly Ser Asn Lys Phe Tyr Ala Asp Ser Val
[7960]	50 55 60
[7961]	Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Ser Leu Ser
[7962]	65 70 75 80
[7963]	Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
[7964]	85 90 95
[7965]	Ala Arg Gly Gly Ala Met Val Arg Gly Val Tyr Tyr Tyr Gly Met Asp
[7966]	100 105 110
[7967]	Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys
[7968]	115 120 125
[7969]	Gly Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu
[7970]	130 135 140
[7971]	Ser Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro
[7972]	145 150 155 160
[7973]	Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr
[7974]	165 170 175
[7975]	Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val
[7976]	180 185 190
[7977]	Val Thr Val Pro Ser Ser Asn Phe Gly Thr Gln Thr Tyr Thr Cys Asn
[7978]	195 200 205
[7979]	Val Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys Thr Val Glu Arg

[7980]	210	215	220
[7981]	Lys Ser Cys Val Glu Cys Pro Pro Cys Pro Ala Pro Pro Val Ala Gly		
[7982]	225	230	235 240
[7983]	Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile		
[7984]	245	250	255
[7985]	Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu		
[7986]	260	265	270
[7987]	Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His		
[7988]	275	280	285
[7989]	Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg		
[7990]	290	295	300
[7991]	Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys		
[7992]	305	310	315 320
[7993]	Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ser Ser Ile Glu		
[7994]	325	330	335
[7995]	Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr		
[7996]	340	345	350
[7997]	Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu		
[7998]	355	360	365
[7999]	Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp		
[8000]	370	375	380
[8001]	Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val		
[8002]	385	390	395 400
[8003]	Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp		
[8004]	405	410	415
[8005]	Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His		
[8006]	420	425	430
[8007]	Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro		
[8008]	435	440	445
[8009]	Gly		
[8010]	<210> 221		
[8011]	<211> 453		
[8012]	<212> PRT		
[8013]	<213> 人工序列		
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[8015]	<223> 合成的: 6G10.IgG1 (VH + IgG1)		
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[8019]	Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Thr Tyr		
[8020]	20	25	30
[8021]	Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val		

[8022]	35	40	45
[8023]	Ala Val Thr Trp Tyr Ala Gly Ser Asn Lys Phe Tyr Ala Asp Ser Val		
[8024]	50	55	60
[8025]	Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr		
[8026]	65	70	75
[8027]	Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys		
[8028]	85	90	95
[8029]	Ala Arg Gly Gly Ser Met Val Arg Gly Leu Tyr Tyr Tyr Gly Met Asp		
[8030]	100	105	110
[8031]	Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys		
[8032]	115	120	125
[8033]	Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly		
[8034]	130	135	140
[8035]	Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro		
[8036]	145	150	155
[8037]	Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr		
[8038]	165	170	175
[8039]	Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val		
[8040]	180	185	190
[8041]	Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn		
[8042]	195	200	205
[8043]	Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro		
[8044]	210	215	220
[8045]	Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu		
[8046]	225	230	235
[8047]	Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp		
[8048]	245	250	255
[8049]	Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp		
[8050]	260	265	270
[8051]	Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly		
[8052]	275	280	285
[8053]	Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn		
[8054]	290	295	300
[8055]	Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp		
[8056]	305	310	315
[8057]	Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro		
[8058]	325	330	335
[8059]	Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu		
[8060]	340	345	350
[8061]	Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn		
[8062]	355	360	365
[8063]	Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile		

[8064]	370	375	380
[8065]	Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr		
[8066]	385	390	395 400
[8067]	Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys		
[8068]	405	410	415
[8069]	Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys		
[8070]	420	425	430
[8071]	Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu		
[8072]	435	440	445
[8073]	Ser Leu Ser Pro Gly		
[8074]	450		
[8075]	<210> 222		
[8076]	<211> 453		
[8077]	<212> PRT		
[8078]	<213> 人工序列		
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[8082]	Gln Val Gln Leu Val Glu Ser Gly Gly Asp Val Val Gln Pro Gly Arg		
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[8084]	Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Thr Tyr		
[8085]	20 25 30		
[8086]	Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val		
[8087]	35 40 45		
[8088]	Ala Val Thr Trp Tyr Ala Gly Ser Asn Lys Phe Tyr Ala Asp Ser Val		
[8089]	50 55 60		
[8090]	Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr		
[8091]	65 70 75 80		
[8092]	Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys		
[8093]	85 90 95		
[8094]	Ala Arg Gly Gly Ser Met Val Arg Gly Leu Tyr Tyr Tyr Gly Met Asp		
[8095]	100 105 110		
[8096]	Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys		
[8097]	115 120 125		
[8098]	Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly		
[8099]	130 135 140		
[8100]	Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro		
[8101]	145 150 155 160		
[8102]	Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr		
[8103]	165 170 175		
[8104]	Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val		
[8105]	180 185 190		

[8106]	Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn
[8107]	195 200 205
[8108]	Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro
[8109]	210 215 220
[8110]	Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu
[8111]	225 230 235 240
[8112]	Ala Glu Gly Ala Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
[8113]	245 250 255
[8114]	Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp
[8115]	260 265 270
[8116]	Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
[8117]	275 280 285
[8118]	Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn
[8119]	290 295 300
[8120]	Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
[8121]	305 310 315 320
[8122]	Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro
[8123]	325 330 335
[8124]	Ser Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
[8125]	340 345 350
[8126]	Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn
[8127]	355 360 365
[8128]	Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
[8129]	370 375 380
[8130]	Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
[8131]	385 390 395 400
[8132]	Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys
[8133]	405 410 415
[8134]	Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
[8135]	420 425 430
[8136]	Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
[8137]	435 440 445
[8138]	Ser Leu Ser Pro Gly
[8139]	450
[8140]	<210> 223
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[8142]	<212> PRT
[8143]	<213> 人工序列
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[8145]	<223> 合成的: 6G10.IgG1 (VL + CL)
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[8147]	Ala Ile Gln Leu Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly

[8148]	1	5	10	15
[8149]	Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Ser Ser Ala			
[8150]	20	25	30	
[8151]	Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile			
[8152]	35	40	45	
[8153]	Tyr Asp Ala Ser Ser Leu Glu Ser Gly Val Pro Ser Arg Phe Ser Gly			
[8154]	50	55	60	
[8155]	Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro			
[8156]	65	70	75	80
[8157]	Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Phe Asn Ser Tyr Pro Tyr			
[8158]	85	90	95	
[8159]	Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys Arg Thr Val Ala Ala			
[8160]	100	105	110	
[8161]	Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly			
[8162]	115	120	125	
[8163]	Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala			
[8164]	130	135	140	
[8165]	Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln			
[8166]	145	150	155	160
[8167]	Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser			
[8168]	165	170	175	
[8169]	Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr			
[8170]	180	185	190	
[8171]	Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser			
[8172]	195	200	205	
[8173]	Phe Asn Arg Gly Glu Cys			
[8174]	210			
[8175]	<210> 224			
[8176]	<211> 449			
[8177]	<212> PRT			
[8178]	<213> 人工序列			
[8179]	<220>			
[8180]	<223> 合成的: 6G10 (VH + G2 (C219S)) 或6G10-IgG2-C219S			
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[8182]	Gln Val Gln Leu Val Glu Ser Gly Gly Asp Val Val Gln Pro Gly Arg			
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[8184]	Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Thr Tyr			
[8185]	20	25	30	
[8186]	Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val			
[8187]	35	40	45	
[8188]	Ala Val Thr Trp Tyr Ala Gly Ser Asn Lys Phe Tyr Ala Asp Ser Val			
[8189]	50	55	60	

[8190]	Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
[8191]	65 70 75 80
[8192]	Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
[8193]	85 90 95
[8194]	Ala Arg Gly Gly Ser Met Val Arg Gly Leu Tyr Tyr Tyr Gly Met Asp
[8195]	100 105 110
[8196]	Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys
[8197]	115 120 125
[8198]	Gly Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu
[8199]	130 135 140
[8200]	Ser Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro
[8201]	145 150 155 160
[8202]	Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr
[8203]	165 170 175
[8204]	Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val
[8205]	180 185 190
[8206]	Val Thr Val Pro Ser Ser Asn Phe Gly Thr Gln Thr Tyr Thr Cys Asn
[8207]	195 200 205
[8208]	Val Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys Thr Val Glu Arg
[8209]	210 215 220
[8210]	Lys Ser Cys Val Glu Cys Pro Pro Cys Pro Ala Pro Pro Val Ala Gly
[8211]	225 230 235 240
[8212]	Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile
[8213]	245 250 255
[8214]	Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu
[8215]	260 265 270
[8216]	Asp Pro Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val His
[8217]	275 280 285
[8218]	Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr Phe Arg
[8219]	290 295 300
[8220]	Val Val Ser Val Leu Thr Val Val His Gln Asp Trp Leu Asn Gly Lys
[8221]	305 310 315 320
[8222]	Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ala Pro Ile Glu
[8223]	325 330 335
[8224]	Lys Thr Ile Ser Lys Thr Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr
[8225]	340 345 350
[8226]	Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu
[8227]	355 360 365
[8228]	Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp
[8229]	370 375 380
[8230]	Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Met
[8231]	385 390 395 400

[8232]	Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp
[8233]	405 410 415
[8234]	Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His
[8235]	420 425 430
[8236]	Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
[8237]	435 440 445
[8238]	Gly
[8239]	<210> 225
[8240]	<211> 450
[8241]	<212> PRT
[8242]	<213> 人工序列
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[8244]	<223> 合成的: 6G10 (VH + G2.g1)或6G10-IgG2-IgG1
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[8246]	Gln Val Gln Leu Val Glu Ser Gly Gly Asp Val Val Gln Pro Gly Arg
[8247]	1 5 10 15
[8248]	Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Thr Tyr
[8249]	20 25 30
[8250]	Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
[8251]	35 40 45
[8252]	Ala Val Thr Trp Tyr Ala Gly Ser Asn Lys Phe Tyr Ala Asp Ser Val
[8253]	50 55 60
[8254]	Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
[8255]	65 70 75 80
[8256]	Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
[8257]	85 90 95
[8258]	Ala Arg Gly Gly Ser Met Val Arg Gly Leu Tyr Tyr Tyr Gly Met Asp
[8259]	100 105 110
[8260]	Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys
[8261]	115 120 125
[8262]	Gly Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu
[8263]	130 135 140
[8264]	Ser Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro
[8265]	145 150 155 160
[8266]	Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr
[8267]	165 170 175
[8268]	Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val
[8269]	180 185 190
[8270]	Val Thr Val Pro Ser Ser Asn Phe Gly Thr Gln Thr Tyr Thr Cys Asn
[8271]	195 200 205
[8272]	Val Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys Thr Val Glu Arg
[8273]	210 215 220

[8274]	Lys Cys Cys Val Glu Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly		
[8275]	225	230	235 240
[8276]	Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met		
[8277]		245	250 255
[8278]	Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His		
[8279]		260	265 270
[8280]	Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val		
[8281]		275	280 285
[8282]	His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr		
[8283]		290	295 300
[8284]	Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly		
[8285]		305	310 315 320
[8286]	Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile		
[8287]		325	330 335
[8288]	Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val		
[8289]		340	345 350
[8290]	Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser		
[8291]		355	360 365
[8292]	Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu		
[8293]		370	375 380
[8294]	Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro		
[8295]		385	390 395 400
[8296]	Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val		
[8297]		405	410 415
[8298]	Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met		
[8299]		420	425 430
[8300]	His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser		
[8301]		435	440 445
[8302]	Pro Gly		
[8303]		450	
[8304]	<210>	226	
[8305]	<211>	449	
[8306]	<212>	PRT	
[8307]	<213>	人工序列	
[8308]	<220>		
[8309]	<223>	合成的: 6G10 (VH + G2.g1.1)或6G10-IgG2-IgG1.1	
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[8311]	Gln Val Gln Leu Val Glu Ser Gly Gly Asp Val Val Gln Pro Gly Arg		
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[8313]	Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Thr Tyr		
[8314]		20	25 30
[8315]	Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val		

[8316]	35	40	45
[8317]	Ala Val Thr Trp Tyr Ala Gly Ser Asn Lys Phe Tyr Ala Asp Ser Val		
[8318]	50	55	60
[8319]	Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr		
[8320]	65	70	75
[8321]	Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys		
[8322]	85	90	95
[8323]	Ala Arg Gly Gly Ser Met Val Arg Gly Leu Tyr Tyr Tyr Gly Met Asp		
[8324]	100	105	110
[8325]	Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys		
[8326]	115	120	125
[8327]	Gly Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu		
[8328]	130	135	140
[8329]	Ser Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro		
[8330]	145	150	155
[8331]	Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr		
[8332]	165	170	175
[8333]	Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val		
[8334]	180	185	190
[8335]	Val Thr Val Pro Ser Ser Asn Phe Gly Thr Gln Thr Tyr Thr Cys Asn		
[8336]	195	200	205
[8337]	Val Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys Thr Val Glu Arg		
[8338]	210	215	220
[8339]	Lys Cys Cys Val Glu Cys Pro Pro Cys Pro Ala Pro Pro Val Ala Gly		
[8340]	225	230	235
[8341]	Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile		
[8342]	245	250	255
[8343]	Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu		
[8344]	260	265	270
[8345]	Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His		
[8346]	275	280	285
[8347]	Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg		
[8348]	290	295	300
[8349]	Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys		
[8350]	305	310	315
[8351]	Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ser Ser Ile Glu		
[8352]	325	330	335
[8353]	Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr		
[8354]	340	345	350
[8355]	Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu		
[8356]	355	360	365
[8357]	Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp		

[8358]	370	375	380
[8359]	Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val		
[8360]	385	390	395 400
[8361]	Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp		
[8362]	405	410	415
[8363]	Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His		
[8364]	420	425	430
[8365]	Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro		
[8366]	435	440	445
[8367]	Gly		
[8368]	<210> 227		
[8369]	<211> 450		
[8370]	<212> PRT		
[8371]	<213> 人工序列		
[8372]	<220>		
[8373]	<223> 合成的: 6G10 (VH + G2 (C219S) .g1) 或6G10-IgG2-C219S-IgG1		
[8374]	<400> 227		
[8375]	Gln Val Gln Leu Val Glu Ser Gly Gly Asp Val Val Gln Pro Gly Arg		
[8376]	1 5 10 15		
[8377]	Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Thr Tyr		
[8378]	20 25 30		
[8379]	Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val		
[8380]	35 40 45		
[8381]	Ala Val Thr Trp Tyr Ala Gly Ser Asn Lys Phe Tyr Ala Asp Ser Val		
[8382]	50 55 60		
[8383]	Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr		
[8384]	65 70 75 80		
[8385]	Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys		
[8386]	85 90 95		
[8387]	Ala Arg Gly Gly Ser Met Val Arg Gly Leu Tyr Tyr Tyr Gly Met Asp		
[8388]	100 105 110		
[8389]	Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys		
[8390]	115 120 125		
[8391]	Gly Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu		
[8392]	130 135 140		
[8393]	Ser Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro		
[8394]	145 150 155 160		
[8395]	Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr		
[8396]	165 170 175		
[8397]	Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val		
[8398]	180 185 190		
[8399]	Val Thr Val Pro Ser Ser Asn Phe Gly Thr Gln Thr Tyr Thr Cys Asn		

[8400]	195	200	205
[8401]	Val Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys Thr Val Glu Arg		
[8402]	210	215	220
[8403]	Lys Ser Cys Val Glu Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly		
[8404]	225	230	235
[8405]	Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met		
[8406]	245	250	255
[8407]	Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His		
[8408]	260	265	270
[8409]	Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val		
[8410]	275	280	285
[8411]	His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr		
[8412]	290	295	300
[8413]	Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly		
[8414]	305	310	315
[8415]	Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile		
[8416]	325	330	335
[8417]	Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val		
[8418]	340	345	350
[8419]	Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser		
[8420]	355	360	365
[8421]	Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu		
[8422]	370	375	380
[8423]	Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro		
[8424]	385	390	395
[8425]	Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val		
[8426]	405	410	415
[8427]	Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met		
[8428]	420	425	430
[8429]	His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser		
[8430]	435	440	445
[8431]	Pro Gly		
[8432]	450		
[8433]	<210> 228		
[8434]	<211> 449		
[8435]	<212> PRT		
[8436]	<213> 人工序列		
[8437]	<220>		
[8438]	<223> 合成的: 6G10 (VH + G2 (C219S) .g1.1) 或6G10-IgG2-C219S-IgG1.1		
[8439]	<400> 228		
[8440]	Gln Val Gln Leu Val Glu Ser Gly Gly Asp Val Val Gln Pro Gly Arg		
[8441]	1	5	10

[8442]	Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Thr Tyr
[8443]	20 25 30
[8444]	Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
[8445]	35 40 45
[8446]	Ala Val Thr Trp Tyr Ala Gly Ser Asn Lys Phe Tyr Ala Asp Ser Val
[8447]	50 55 60
[8448]	Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
[8449]	65 70 75 80
[8450]	Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
[8451]	85 90 95
[8452]	Ala Arg Gly Gly Ser Met Val Arg Gly Leu Tyr Tyr Tyr Gly Met Asp
[8453]	100 105 110
[8454]	Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys
[8455]	115 120 125
[8456]	Gly Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu
[8457]	130 135 140
[8458]	Ser Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro
[8459]	145 150 155 160
[8460]	Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr
[8461]	165 170 175
[8462]	Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val
[8463]	180 185 190
[8464]	Val Thr Val Pro Ser Ser Asn Phe Gly Thr Gln Thr Tyr Thr Cys Asn
[8465]	195 200 205
[8466]	Val Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys Thr Val Glu Arg
[8467]	210 215 220
[8468]	Lys Ser Cys Val Glu Cys Pro Pro Cys Pro Ala Pro Pro Val Ala Gly
[8469]	225 230 235 240
[8470]	Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile
[8471]	245 250 255
[8472]	Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu
[8473]	260 265 270
[8474]	Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His
[8475]	275 280 285
[8476]	Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg
[8477]	290 295 300
[8478]	Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys
[8479]	305 310 315 320
[8480]	Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ser Ser Ile Glu
[8481]	325 330 335
[8482]	Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr
[8483]	340 345 350

[8484]	Thr	Leu	Pro	Pro	Ser	Arg	Glu	Glu	Met	Thr	Lys	Asn	Gln	Val	Ser	Leu
[8485]			355					360					365			
[8486]	Thr	Cys	Leu	Val	Lys	Gly	Phe	Tyr	Pro	Ser	Asp	Ile	Ala	Val	Glu	Trp
[8487]			370				375						380			
[8488]	Glu	Ser	Asn	Gly	Gln	Pro	Glu	Asn	Asn	Tyr	Lys	Thr	Thr	Pro	Pro	Val
[8489]		385				390					395					400
[8490]	Leu	Asp	Ser	Asp	Gly	Ser	Phe	Phe	Leu	Tyr	Ser	Lys	Leu	Thr	Val	Asp
[8491]					405					410						415
[8492]	Lys	Ser	Arg	Trp	Gln	Gln	Gly	Asn	Val	Phe	Ser	Cys	Ser	Val	Met	His
[8493]					420					425					430	
[8494]	Glu	Ala	Leu	His	Asn	His	Tyr	Thr	Gln	Lys	Ser	Leu	Ser	Leu	Ser	Pro
[8495]				435					440						445	
[8496]	Gly															

抗 GITR 6G10 VH (hIgG2)

V 区段: 3-33

D 区段: 3-10

J 区段: JH6b

1	Q	V	Q	L	V	E	S	G	G	D	V	V	Q	P	G	R	S
	CAG	GTG	CAG	CTG	GTG	GAG	TCT	GGG	GGA	GAC	GTG	GTC	CAG	CCT	GGG	AGG	TCC
52	L	R	L	S	C	A	A	S	G	F	T	F	S	CDR1			
	CTG	AGA	CTC	TCC	TGT	GCA	GCG	TCT	GGA	TTC	ACC	TTC	AGT	ACC	TAT	GGC	ATG
103	H	W	V	R	Q	A	P	G	K	G	L	E	W	V	A	CDR2	
	CAC	TGG	GTC	CGC	CAG	GCT	CCA	GGC	AAG	GGG	CTG	GAG	TGG	GTG	GCA	GTT	ACA
154	W	Y	A	G	S	N	K	F	Y	A	D	S	V	K	G	R	F
	TGG	TAT	GCT	GGA	AGT	AAT	AAA	TTT	TAT	GCA	GAC	TCC	GTG	AAG	GGC	CGA	TTC
205	T	I	S	R	D	N	S	K	N	T	L	Y	L	Q	M	N	S
	ACC	ATC	TCC	AGA	GAC	AAT	TCC	AAG	AAC	ACG	CTG	TAT	CTG	CAA	ATG	AAC	AGC
256	L	R	A	E	D	T	A	V	Y	Y	C	A	R	CDR3			
	CTG	AGA	GCC	GAG	GAC	ACG	GCT	GTG	TAT	TAC	TGT	GCG	AGA	GGA	GGT	AGT	ATG
307	V	R	G	L	Y	Y	Y	G	M	D	V	W	G	Q	G	T	T
	GTT	CGG	GGA	CTT	TAT	TAT	TAC	GGT	ATG	GAC	GTC	TGG	GGC	CAA	GGG	ACC	ACG
358	V	T	V	S	S												
	GTC	ACC	GTC	TCC	TCA												

图1

J 区段: JK2

图2

抗 GITR 6G10 VH (hIgG2)

3-33 输入	Q	V	Q	L	V	E	S	G	G	G	V	V	Q	P	G	R	S	L	R	L	S	C	A		
	-	-	-	-	-	-	-	-	-	D	-	-	-	-	-	-	-	-	-	-	-	-	-		
3-33 输入	A	S	G	F	T	F	S	S	Y	G	M	H	W	V	R	Q	A	P	G	K	G	L	E		
	-	-	-	-	-	-	-	T	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-		
3-33 输入	W	V	A	V	I	W	Y	D	G	S	N	K	Y	Y	A	D	S	V	K	G	R	F	T		
	-	-	-	-	T	-	-	A	-	-	-	-	F	-	-	-	-	-	-	-	-	-	-		
3-33 输入	I	S	R	D	N	S	K	N	T	L	Y	L	Q	M	N	S	L	R	A	E	D	T	A		
	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-		
3-33 3-10 JH6 输入	V	Y	Y	C	A	R					M	V	R	G			Y	Y	Y	G	M	D	V	W	G
	-	-	-	-	-	-	G	G	S	-	-	-	-	L	-	-	-	-	-	-	-	-	-	-	-
JH6 输入	Q	G	T	T	V	T	V	S	S																
	-	-	-	-	-	-	-	-	-																

图3

抗 GITR 6G10 VK1 (hKappa)

L18 输入	A	I	Q	L	T	Q	S	P	S	S	L	S	A	S	V	G	D	R	V	T	I	T	C
	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
L18 输入	R	A	S	Q	G	I	S	S	A	L	A	W	Y	Q	Q	K	P	G	K	A	P	K	L
	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
L18 输入	L	I	Y	D	A	S	S	L	E	S	G	V	P	S	R	F	S	G	S	G	S	G	T
	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
L18 输入	D	F	T	L	T	I	S	S	L	Q	P	E	D	F	A	T	Y	Y	C	Q	Q	F	N
	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
L18 JK2 输入	N	Y																					
	S	-	P	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

图4

```

      G1TR 6G10 VH
      ~~~~~
    Q  V  Q  L  V  E  S  G  G  D  V  V  Q  P  G
1   CAG GTG CAG CTG GTG GAG TCT GGG GGA GAC GTG GTC CAG CCT GGG
      G1TR 6G10 VH
      ~~~~~
    R  S  L  R  L  S  C  A  A  S  G  F  T  F  S
46  AGG TCC CTG AGA CTC TCC TGT GCA GCG TCT GGA TTC ACC TTC AGT
      G1TR 6G10 VH
      ~~~~~
    T  Y  G  M  H  W  V  R  Q  A  P  G  K  G  L
91  ACC TAT GGC ATG CAC TGG GTC CGC CAG GCT CCA GGC AAG GGG CTG
      G1TR 6G10 VH
      ~~~~~
    E  W  V  A  V  T  W  Y  A  G  S  N  K  F  Y
136 GAG TGG GTG GCA GTT ACA TGG TAT GCT GGA AGT AAT AAA TTT TAT
      G1TR 6G10 VH
      ~~~~~
    A  D  S  V  K  G  R  F  T  I  S  R  D  N  S
181 GCA GAC TCC GTG AAG GGC CGA TTC ACC ATC TCC AGA GAC AAT TCC
      G1TR 6G10 VH
      ~~~~~
    K  N  T  L  Y  L  Q  M  N  S  L  R  A  E  D
226 AAG AAC ACG CTG TAT CTG CAA ATG AAC AGC CTG AGA GCC GAG GAC
      G1TR 6G10 VH
      ~~~~~
    T  A  V  Y  Y  C  A  R  G  G  S  M  V  R  G
271 ACG GCT GTG TAT TAC TGT GCG AGA GGA GGT AGT ATG GTT CGG GGA
      G1TR 6G10 VH
      ~~~~~
    L  Y  Y  Y  G  M  D  V  W  G  Q  G  T  T  V
316 CTT TAT TAT TAC GGT ATG GAC GTC TGG GGC CAA GGG ACC ACG GTC
      mIgG2a恒定区
      ~~~~~
      G1TR 6G10 VH
      ~~~~~
    T  V  S  S  A  K  T  T  A  P  S  V  Y  P  L
361 ACC GTC TCC TCA GCC AAA ACA ACA GCC CCA TCG GTC TAT CCG CTA
      mIgG2a恒定区
      ~~~~~
    A  P  V  C  G  D  T  T  G  S  S  V  T  L  G
406 GCC CCT GTG TGT GGA GAT ACA ACT GGC TCC TCG GTG ACT CTA GGA
      mIgG2a恒定区
      ~~~~~
    C  L  V  K  G  Y  F  P  E  P  V  T  L  T  W
451 TGC CTG GTC AAG GGT TAT TTC CCT GAG CCA GTG ACC TTG ACC TGG
      mIgG2a恒定区
      ~~~~~
    N  S  G  S  L  S  S  G  V  H  T  F  P  A  V
496 AAC TCT GGA TCC CTG TCC AGT GGT GTG CAC ACC TTC CCA GCT GTC
      mIgG2a恒定区
      ~~~~~
    L  Q  S  D  L  Y  T  L  S  S  S  V  T  V  T
541 CTG CAG TCT GAC CTC TAC ACC CTC AGC AGC TCA GTG ACT GTA ACC
      mIgG2a恒定区
      ~~~~~
    S  S  T  W  P  S  Q  S  I  T  C  N  V  A  H
586 TCG AGC ACC TGG CCC AGC CAG TCC ATC ACC TGC AAT GTG GCC CAC
      mIgG2a恒定区
      ~~~~~
    P  A  S  S  T  K  V  D  K  K  I  E  P  R  G
631 CCG GCA AGC AGC ACC AAG GTG GAC AAG AAA ATT GAG CCC AGA GGG

```

图5

```

                                mIgG2a恒定区
~~~~~
      P   T   I   K   P   C   P   P   C   K   C   P   A   P   N
676 CCC ACA ATC AAG CCC TGT CCT CCA TGC AAA TGC CCA GCA CCT AAC
                                mIgG2a恒定区
~~~~~
      L   L   G   G   P   S   V   F   I   F   P   P   K   I   K
721 CTC TTG GGT GGA CCA TCC GTC TTC ATC TTC CCT CCA AAG ATC AAG
                                mIgG2a恒定区
~~~~~
      D   V   L   M   I   S   L   S   P   I   V   T   C   V   V
766 GAT GTA CTC ATG ATC TCC CTG AGC CCC ATA GTC ACA TGT GTG GTG
                                mIgG2a恒定区
~~~~~
      V   D   V   S   E   D   D   P   D   V   Q   I   S   W   F
811 GTG GAT GTG AGC GAG GAT GAC CCA GAT GTC CAG ATC AGC TGG TTT
                                mIgG2a恒定区
~~~~~
      V   N   N   V   E   V   H   T   A   Q   T   Q   T   H   R
856 GTG AAC AAC GTG GAA GTA CAC ACA GCT CAG ACA CAA ACC CAT AGA
                                mIgG2a恒定区
~~~~~
      E   D   Y   N   S   T   L   R   V   V   S   A   L   P   I
901 GAG GAT TAC AAC AGT ACT CTC CGG GTG GTC AGT GCC CTC CCC ATC
                                mIgG2a恒定区
~~~~~
      Q   H   Q   D   W   M   S   G   K   E   F   K   C   K   V
946 CAG CAC CAG GAC TGG ATG AGT GGC AAG GAG TTC AAA TGC AAG GTC
                                mIgG2a恒定区
~~~~~
      N   N   K   D   L   P   A   P   I   E   R   T   I   S   K
991 AAC AAC AAA GAC CTC CCA GCG CCC ATC GAG AGA ACC ATC TCA AAA
                                mIgG2a恒定区
~~~~~
      P   K   G   S   V   R   A   P   Q   V   Y   V   L   P   P
1036 CCC AAA GGG TCA GTA AGA GCT CCA CAG GTA TAT GTC TTG CCT CCA
                                mIgG2a恒定区
~~~~~
      P   E   E   E   M   T   K   K   Q   V   T   L   T   C   M
1081 CCA GAA GAA GAG ATG ACT AAG AAA CAG GTC ACT CTG ACC TGC ATG
                                mIgG2a恒定区
~~~~~
      V   T   D   F   M   P   E   D   I   Y   V   E   W   T   N
1126 GTC ACA GAC TTC ATG CCT GAA GAC ATT TAC GTG GAG TGG ACC AAC
                                mIgG2a恒定区
~~~~~
      N   G   K   T   E   L   N   Y   K   N   T   E   P   V   L
1171 AAC GGG AAA ACA GAG CTA AAC TAC AAG AAC ACT GAA CCA GTC CTG
                                mIgG2a恒定区
~~~~~
      D   S   D   G   S   Y   F   M   Y   S   K   L   R   V   E
1216 GAC TCT GAT GGT TCT TAC TTC ATG TAC AGC AAG CTG AGA GTG GAA
                                mIgG2a恒定区
~~~~~
      K   K   N   W   V   E   R   N   S   Y   S   C   S   V   V
1261 AAG AAG AAC TGG GTG GAA AGA AAT AGC TAC TCC TGT TCA GTG GTC

```

图5(续)

```

                                mIgG2a恒定区
                                ~~~~~
                                H   E   G   L   H   N   H   H   T   T   K   S   F   S   R
1306 CAC GAG GGT CTG CAC AAT CAC CAC ACG ACT AAG AGC TTC TCC CGG
                                mIgG2a恒定区
                                ~~~~~
                                T   P   G   K   *
1351 ACT CCG GGT AAA TGA

```

图5(续)

GITR 6G10 VK

```

~~~~~
  A  I  Q  L  T  Q  S  P  S  S  L  S  A  S  V
1  GCC ATC CAG TTG ACC CAG TCT CCA TCC TCC CTG TCT GCA TCT GTA
    GITR 6G10 VK
~~~~~
  G  D  R  V  T  I  T  C  R  A  S  Q  G  I  S
46 GGA GAC AGA GTC ACC ATC ACT TGC CGG GCA AGT CAG GGC ATT AGC
    GITR 6G10 VK
~~~~~
  S  A  L  A  W  Y  Q  Q  K  P  G  K  A  P  K
91 AGT GCT TTA GCC TGG TAT CAG CAG AAA CCA GGG AAA GCT CCT AAG
    GITR 6G10 VK
~~~~~
  L  L  I  Y  D  A  S  S  L  E  S  G  V  P  S
136 CTC CTG ATC TAT GAT GCC TCC AGT TTG GAA AGT GGG GTC CCA TCA
    GITR 6G10 VK
~~~~~
  R  F  S  G  S  G  S  G  T  D  F  T  L  T  I
181 AGG TTC AGC GGC AGT GGA TCT GGG ACA GAT TTC ACT CTC ACC ATC
    GITR 6G10 VK
~~~~~
  S  S  L  Q  P  E  D  F  A  T  Y  Y  C  Q  Q
226 AGC AGC CTG CAG CCT GAA GAT TTT GCA ACT TAT TAC TGT CAA CAG
    GITR 6G10 VK
~~~~~
  F  N  S  Y  P  Y  T  F  G  Q  G  T  K  L  E
271 TTT AAT AGT TAC CCG TAC ACT TTT GGC CAG GGG ACC AAG CTG GAG
    鼠kappa C
~~~~~

```

GITR 6G10 VK

```

~~~~~
  I  K  R  A  D  A  A  P  T  V  S  I  F  P  P
316 ATC AAA CGG GCT GAT GCT GCA CCA ACT GTA TCC ATC TTC CCA CCA
    ~~~~~
                                DMTm89
    ~~~~~
                                DMTm88

```

鼠kappa C

```

~~~~~
  S  S  E  Q  L  T  S  G  G  A  S  V  V  C  F
361 TCC AGT GAG CAA TTG ACA TCT GGA GGT GCC TCA GTC GTG TGC TTC
    ~~~~~
    .....
    ~~~~~
    ...

```

鼠kappa C

```

~~~~~
  L  N  N  F  Y  P  K  D  I  N  V  K  W  K  I
406 TTG AAC AAC TTC TAC CCC AAA GAC ATC AAT GTC AAG TGG AAG ATT
    鼠kappa C
~~~~~
  D  G  S  E  R  Q  N  G  V  L  N  S  W  T  D
451 GAT GGC AGT GAA CGA CAA AAT GGC GTC CTG AAC AGT TGG ACC GAT
    鼠kappa C
~~~~~
  Q  D  S  K  D  S  T  Y  S  M  S  S  T  L  T
496 CAG GAC AGC AAA GAC AGC ACC TAC AGC ATG AGC AGC ACC CTC ACG
    鼠kappa C
~~~~~

```

图6

```

      L   T   K   D   E   Y   E   R   H   N   S   Y   T   C   E
541  TTG ACC AAG GAC GAG TAT GAA CGA CAT AAC AGC TAT ACC TGT GAG
      鼠kappa C
      ~~~~~~
      A   T   H   K   T   S   T   S   P   I   V   K   S   F   N
586  GCC ACT CAC AAG ACA TCA ACT TCA CCC ATT GTC AAG AGC TTC AAC
      鼠kappa C
      ~~~~~~
      R   N   E   C   *
631  AGG AAT GAG TGT TAG

```

图6(续)

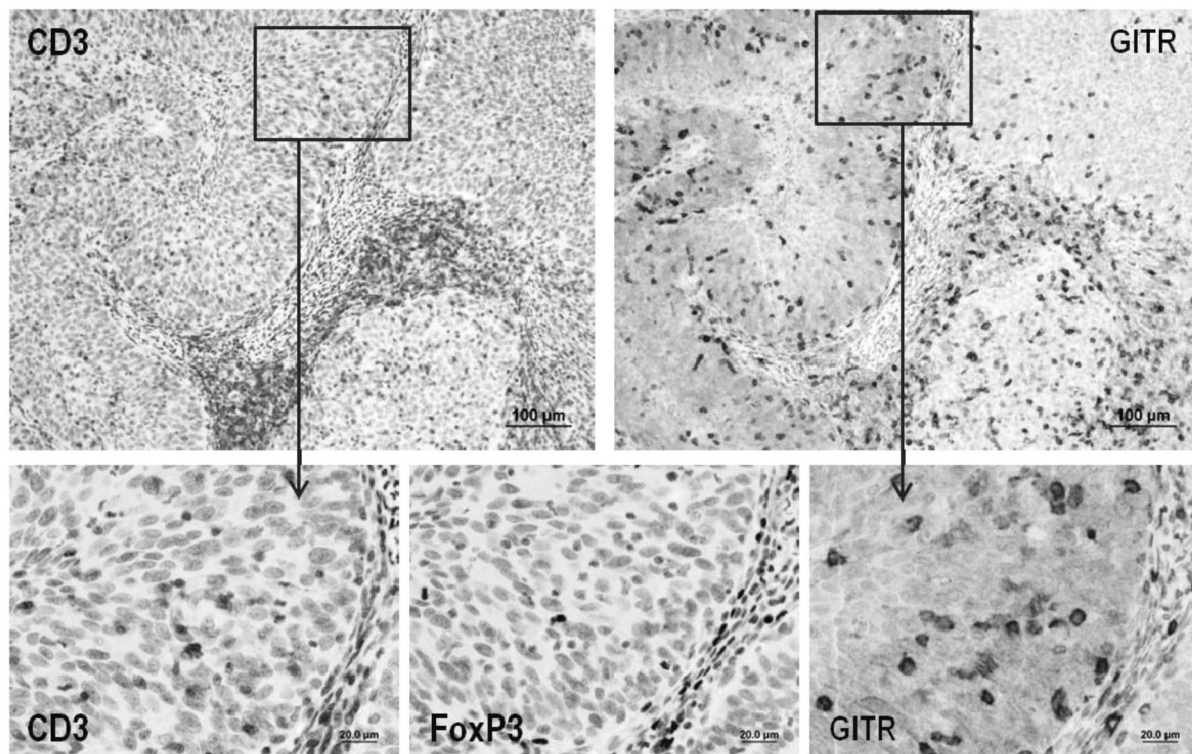


图7