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(71)申请人 百时美施贵宝公司
地址 美国新泽西州

(72)发明人 A·克利佩尔 L·C·梅纳德

(74)专利代理机构 北京市中咨律师事务所 11247
代理人 张莉 黄革生

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(54)发明名称

用于治疗和诊断癌症的TIM-3拮抗剂

(57)摘要

本文提供用于治疗罹患癌症的受试者的方法,所述方法包括向受试者单独或结合另一种免疫检查点抑制剂(例如,PD-1拮抗剂)一起施用TIM3激动剂(例如,抗TIM3抗体),其中受试者鉴定为具有高频率的TIM3阳性细胞(例如,在肿瘤浸润型炎性细胞上)或外周血可溶性TIM3。还提供在罹患癌症的受试者中评估包含TIM3拮抗剂的治疗的功效的方法,所述方法包括测量受试者的某些细胞群体中TIM3(和任选地PD-1)阳性细胞的频率和/或其外周血中的可溶性TIM3,其中TIM3(和任选地PD-1)阳性细胞高频率和/或受试者的可溶性TIM3外周血滴度指示对治疗的响应。

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1.一种确定患有癌症的受试者是否将响应于TIM-3拮抗剂治疗的体外方法,包括确定受试者中可溶性TIM-3的血清滴度,并且如果(i)该可溶性TIM-3血清滴度高于健康对照受试者中的血清滴度,或(ii)该可溶性TIM-3血清滴度是至少2100、2200、2300、2400或2500pg/ml(例如,如按实施例中描述的方法测定),则受试者可能响应于TIM-3拮抗剂治疗。

2.确定患有癌症的受试者是否将响应于TIM-3拮抗剂治疗的体外方法,包括确定呈TIM-3阳性的CD8+TIL的百分数,并且如果该百分数高于10%、20%、30%、40%、50%、60%或70%,则受试者可能响应于TIM-3拮抗剂治疗。

3.确定患有癌症的受试者是否将响应于TIM-3拮抗剂治疗的体外方法,包括确定呈TIM-3阳性的幼稚、中央记忆(CM)、效应记忆(EM)和效应TIL的百分数,并且如果呈TIM-3阳性的EM TIL和/或效应TIL的百分数高于呈TIM-3阳性的幼稚TIL和/或CM TIL的百分数,则受试者可能响应于TIM-3拮抗剂治疗。

4.确定患有癌症的受试者是否将响应于TIM-3拮抗剂治疗的体外方法,包括确定受试者的TIL中呈TIM-3阳性的树状细胞、巨噬细胞和自然杀伤(NK)细胞的百分数,并且如果该百分数高于对照受试者(例如,不响应于TIM-3拮抗剂治疗的相应癌症患者)中的百分数,则受试者可能响应于TIM-3拮抗剂治疗。

5.确定患有癌症的受试者是否将响应于PD-1/PD-L1轴拮抗剂和TIM-3拮抗剂的组合治疗的体外方法,包括确定受试者中PD-1阳性肿瘤浸润型淋巴细胞(TIL)的频率和TIM-3阳性TIL的频率,其中PD-1和TIM-3在受试者的至少5%的CD8+TIL上的共表达指示,受试者可能响应于PD-1/PD-L1轴拮抗剂和TIM3拮抗剂的组合治疗。

6.TIM-3拮抗剂用于治疗患有癌症的受试者,其中治疗包括:

(1)(a)确定受试者中可溶性TIM-3的血清滴度,并且(b)如果(i)该可溶性TIM-3的血清滴度高于健康对照受试者中的血清滴度,或(ii)该可溶性TIM-3的血清滴度是至少2100、2200、2300、2400或2500pg/ml(例如,如按实施例中描述的方法测定),则向受试者施用TIM-3拮抗剂;

(2)(a)确定受试者中呈TIM-3阳性的CD8+TIL的百分数,并且如果该百分数高于10%、20%、30%、40%、50%、60%或70%,则向受试者施用TIM-3拮抗剂;

(3)(a)确定呈TIM-3阳性的幼稚、中央记忆(CM)、效应记忆(EM)和效应TIL的百分数,和(b)如果呈TIM-3阳性的EM TIL和/或效应TIL的百分数高于呈TIM-3阳性的幼稚TIL和/或CM TIL的百分数,则向受试者施用TIM-3拮抗剂;或

(4)(a)确定受试者的TIL中呈TIM-3阳性的树状细胞、巨噬细胞和自然杀伤(NK)细胞的百分数,并且(b)如果该百分数高于对照受试者(例如,不响应于TIM-3拮抗剂治疗的相应癌症患者)中的百分数,则向受试者施用TIM-3拮抗剂。

7.包含PD-1/PD-L1轴拮抗剂和TIM-3拮抗剂的组合疗法用于治疗患有癌症的受试者,其中治疗包括(i)确定受试者中PD-1阳性肿瘤浸润型淋巴细胞(TIL)的频率和TIM-3阳性TIL的频率,并且(ii)如果至少5%的CD8+TIL共表达PD-1和TIM-3,则施用组合疗法。

8.根据权利要求1-5中任一项所述的体外方法、根据权利要求6所述TIM-3拮抗剂用途、或根据权利要求7所述组合疗法用途,其中TIM-3拮抗剂是抗TIM3抗体。

9.根据权利要求8所述的体外方法、所述TIM-3拮抗剂用途、或所述组合疗法用途,其中抗TIM3抗体包含:(i)包含CDR1、CDR2和CDR3的重链可变区,和(ii)包含CDR1、CDR2和CDR3的

轻链可变区,其中

(a)重链CDR1包含选自SEQ ID NOs:23-27的氨基酸序列;

(b)重链CDR2包含选自SEQ ID NOs:28-38的氨基酸序列;

(c)重链CDR3包含选自SEQ ID NOs:39-49的氨基酸序列;

(d)轻链CDR1包含选自SEQ ID NOs:50和51的氨基酸序列;

(e)轻链CDR2包含选自SEQ ID NOs:52和53的氨基酸序列;并且

(f)轻链CDR3包含选自SEQ ID NOs:54-57的氨基酸序列。

10.根据权利要求3所述的体外方法或根据权利要求6所述的TIM-3拮抗剂用途,其中TIL是CD4+TIL。

11.根据权利要求3所述的体外方法或根据权利要求6所述的TIM-3拮抗剂用途,其中TIL是CD8+TIL。

12.根据权利要求5所述的体外方法或根据权利要求7所述的组合疗法用途,其中PD-1/PD-L1轴拮抗剂包括抗PD-1抗体或抗PD-L1抗体。

13.根据权利要求12所述的体外方法或组合疗法用途,其中抗PD-1抗体包括纳武单抗(nivolumab)、派姆单抗(pembrolizumab)、MEDI0608、AMP-224、PDR001、BGB-A317或其任意组合。

14.根据权利要求12所述的体外方法或组合疗法用途,其中抗-PD-L1抗体包括BMS-936559、MPDL3280A、MEDI4736、MSB0010718C或其任意组合。

15.根据权利要求1-14中任一项所述的体外方法、所述的TIM-3拮抗剂用途、或所述的组合疗法用途,其中癌症包括结肠癌、肾癌或肺癌。

用于治疗和诊断癌症的TIM-3拮抗剂

[0001] 引用通过EFS网以电子方式提交的序列表

[0002] 以ASCII文本文件(名称:3338.093PC01_SequenceListing_ST25.txt;大小:717,820比特;及创建日期:2018年8月24日)随本申请一并提交的电子方式提交的序列表的内容通过引用的方式完整并入本文。

[0003] 发明背景

[0004] T细胞免疫球蛋白及含粘蛋白结构构-3(TIM3),也称作甲型肝炎病毒细胞受体2(HAVCR2),是作为免疫应答的关键调节物发挥作用的I型跨膜蛋白。最初在产生IFN-γ的活化T细胞(例如,1型$CD4^+$辅助T细胞和$CD8^+$细胞毒性T细胞)中鉴定TIM3,并且其显示与其配体之一(即,磷脂酰丝氨酸、半乳糖凝集素-9、HMGB1、CEACAM-1和ILT4)结合后,诱导T细胞死亡或耗竭。更新近的研究已经表明,TIM3表达在调节许多天然免疫细胞(例如,巨噬细胞、单核细胞、树状细胞、肥大细胞和自然杀伤细胞)的活性方面也重要。参见Han G等人,Front Immunol.4:449(2013)。

[0005] 如同许多抑制性受体(例如,PD-1和CTLA-4),TIM3表达已经相关于许多类型慢性病,包括癌症(例如,黑素瘤、肺癌、肝癌、卵巢癌等)。已经在来自晚期黑素瘤、非小细胞肺癌或滤泡性B细胞非霍奇金淋巴瘤患者的肿瘤浸润型淋巴细胞(TILs)和一些肿瘤中检测到高TIM3表达。并且已经将$TIM3^+$T细胞的存在描述为肺癌进展的有效指标,更高表达与不良预后相关。参见Anderson AC.Cancer Immunol Res.2:393-8(2014)。研究还已经显示TIM3和抑制性受体PD-1之间的密切关系。例如,许多肿瘤特异性T细胞表达PD-1和TIM3二者,并且已经显示与仅表达PD-1或TIM3的T细胞相比,这些T细胞更为机能不良。参见Fourcade J等人,J Exp Med.207:2175-2186(2010)。

[0006] 最近对几种免疫检查点途径抑制剂(例如,YERVOY和OPDIVO)的开发已经开始提供新的免疫治疗方案以治疗许多类型的疾病,包括癌症。尽管这类抑制剂已经产生有前景的结果,但庞大的患者群体不响应于这类治疗。参见Sharma P等人,Cell 168:707-723(2017)。因此,仍需要针对限定的子人群并最终针对个体患者定制治疗方案,旨在增强功效并最大限度减少不良作用。

[0007] 发明简述

[0008] 本文提供一种确定患有癌症的受试者是否将响应于TIM-3拮抗剂治疗的体外方法,所述方法包括确定受试者中可溶性TIM-3的血清滴度,并且如果(i)该可溶性TIM-3的血清滴度高于健康对照受试者中的血清滴度,或(ii)该可溶性TIM-3的血清滴度是至少2100、2200、2300、2400或2500pg/ml(例如,如按实施例中描述的方法测定),则受试者可能响应于TIM-3拮抗剂治疗。

[0009] 本文提供一种确定患有癌症的受试者是否将响应于TIM-3拮抗剂治疗的体外方法,所述方法包括确定呈TIM-3阳性的CD8+TIL的百分数,并且如果该百分数高于10%、20%、30%、40%、50%、60%或70%,则受试者可能响应于TIM-3拮抗剂治疗。

[0010] 本文提供一种确定患有癌症的受试者是否将响应于TIM-3拮抗剂治疗的体外方法,所述方法包括确定呈TIM-3阳性的幼稚、中央记忆(CM)、效应记忆(EM)和效应TIL的百分

数,并且如果呈TIM-3阳性的EM TIL和/或效应TIL的百分数高于呈TIM-3阳性的幼稚TIL和/或CM TIL的百分数,则受试者可能响应于TIM-3拮抗剂治疗。

[0011] 本文提供一种确定患有癌症的受试者是否将响应于TIM-3拮抗剂治疗的体外方法,所述方法包括确定受试者的TIL中呈TIM-3阳性的树状细胞、巨噬细胞和自然杀伤(NK)细胞的百分数,并且如果该百分数高于对照受试者(例如,不响应于TIM-3拮抗剂治疗的相应癌症患者)中的百分数,则受试者可能响应于TIM-3拮抗剂治疗。

[0012] 本文提供一种确定患有癌症的受试者是否将响应于PD-1/PD-L1轴拮抗剂和TIM-3拮抗剂的组合治疗的体外方法,所述方法包括确定受试者中PD-1阳性肿瘤浸润型淋巴细胞(TIL)的频率和TIM-3阳性TIL的频率,其中PD-1和TIM-3在受试者的至少5%的CD8+TIL上共表达表示,受试者可能响应于PD-1/PD-L1轴拮抗剂和TIM3拮抗剂的组合治疗。

[0013] 本文中还提供一种用于治疗患有癌症的受试者的TIM-3拮抗剂,其中治疗包括:(1)(a)确定受试者中可溶性TIM-3的血清滴度,和(b)如果(i)该可溶性TIM-3的血清滴度高于健康对照受试者中的血清滴度,或(ii)该可溶性TIM-3的血清滴度是至少2100、2200、2300、2400或2500pg/ml(例如,如按实施例中描述的方法测定),则向受试者施用TIM-3拮抗剂;(2)(a)确定受试者中呈TIM-3阳性的CD8+TIL的百分数,并且(b)如果该百分数高于10%、20%、30%、40%、50%、60%或70%,则向受试者施用TIM-3拮抗剂;(3)(a)确定呈TIM-3阳性的幼稚、中央记忆(CM)、效应记忆(EM)和效应TIL的百分数,和(b)如果呈TIM-3阳性的EM TIL和/或效应TIL的百分数高于呈TIM-3阳性的幼稚TIL和/或CM TIL的百分数,则向受试者施用TIM-3拮抗剂;或(4)(a)确定受试者的TIL中呈TIM-3阳性的树状细胞、巨噬细胞和自然杀伤(NK)细胞的百分数,和(b)如果该百分数高于对照受试者(例如,不响应于TIM-3拮抗剂治疗的相应癌症患者)中的百分数,则向受试者施用TIM-3拮抗剂。

[0014] 本公开进一步提供一种组合疗法,包含PD-1/PD-L1轴拮抗剂和TIM-3拮抗剂,用于治疗患有癌症的受试者,其中治疗包括(i)确定受试者中PD-1阳性肿瘤浸润型淋巴细胞(TIL)的频率和TIM-3阳性TIL的频率,并且(ii)如果至少5%的CD8+TIL共表达PD-1和TIM-3,则施用组合疗法。

[0015] 在一些实施方案中,用于治疗患有癌症的受试者(例如,单药疗法或组合疗法)的TIM-3拮抗剂是抗TIM3抗体。

[0016] 在一些实施方案中,抗TIM3抗体包含:(i)包含CDR1、CDR2和CDR3的重链可变区,和(ii)包含CDR1、CDR2和CDR3的轻链可变区,其中

[0017] (a)重链CDR1包含选自SEQ ID NOs:23-27的氨基酸序列;

[0018] (b)重链CDR2包含选自SEQ ID NOs:28-38的氨基酸序列;

[0019] (c)重链CDR3包含选自SEQ ID NOs:39-49的氨基酸序列;

[0020] (d)轻链CDR1包含选自SEQ ID NOs:50和51的氨基酸序列;

[0021] (e)轻链CDR2包含选自SEQ ID NOs:52和53的氨基酸序列;并且

[0022] (f)轻链CDR3包含选自SEQ ID NOs:54-57的氨基酸序列。

[0023] 在一些实施方案中,TIL是CD4+TIL。

[0024] 在一些实施方案中,TIL是CD8+TIL。

[0025] 在一些实施方案中,PD-1/PD-L1轴拮抗剂包括抗PD-1抗体或抗PD-L1抗体。

[0026] 在一些实施方案中,抗PD-1抗体包括纳武单抗(nivolumab)、派姆单抗

(pembrolizumab)、MEDI0608、AMP-224、PDR001、BGB-A317或其任意组合。

[0027] 在一些实施方案中，抗PD-L1抗体包括BMS-936559、MPDL3280A、MEDI4736、MSB0010718C或其任意组合。

[0028] 在一些实施方案中，癌症包括结肠癌、肾癌或肺癌。

[0029] 实施方案

[0030] 实施方案1.一种确定患有癌症的受试者是否将响应于TIM-3拮抗剂治疗的方法，包括确定受试者中可溶性TIM-3的血清滴度，并且如果该可溶性TIM-3的血清滴度高于对照受试者中的血清滴度，则受试者可能响应于TIM-3拮抗剂治疗。

[0031] 实施方案2.实施方案1的方法，其中如果受试者中可溶性TIM-3的血清滴度比对照受试者高至少10％，则受试者可能响应于TIM-3拮抗剂治疗。

[0032] 实施方案3.实施方案1或2的方法，其中如果受试者中可溶性TIM-3的血清滴度比对照受试者高至少20％、30％、40％、50％、60％、70％、80％、90％或100％(2倍)，则受试者可能响应于TIM-3拮抗剂治疗。

[0033] 实施方案4.实施方案1-3中任一者的方法，其中如果受试者具有至少2100、2200、2300、2400或2500pg/ml(例如，如按实施例中描述的方法测定)的可溶性TIM-3血清滴度，则受试者可能响应于TIM-3拮抗剂治疗。

[0034] 实施方案5.实施方案1-4中任一者的方法，其中如果受试者具有至少3000pg/ml(例如，如按实施例中描述的方法测定)的可溶性TIM-3血清滴度，则受试者可能响应于TIM-3拮抗剂治疗。

[0035] 实施方案6.实施方案1-5中任一者的方法，还包括，向具有比对照受试者更高的可溶性TIM-3血清滴度的受试者施用治疗有效量的TIM-3拮抗剂。

[0036] 实施方案7.一种治疗患有癌症的受试者的方法，包括向患有癌症且具有比对照受试者更高的可溶性TIM-3血清滴度的受试者施用治疗有效量的TIM-3拮抗剂。

[0037] 实施方案8.实施方案7的方法，其中受试者的可溶性TIM-3血清滴度比对照受试者高至少10％。

[0038] 实施方案9.实施方案7的方法，其中受试者具有高于对照受试者至少20％、30％、40％、50％、60％、70％、80％、90％或100％(2倍)的可溶性TIM-3血清滴度。

[0039] 实施方案10.实施方案7-9中任一者的方法，其中受试者具有至少2500pg/ml(例如，如按实施例中描述的方法测定)的可溶性TIM-3血清滴度。

[0040] 实施方案11.实施方案7-10中任一者的方法，其中受试者具有至少3000pg/ml(例如，如按实施例中描述的方法测定)的可溶性TIM-3血清滴度。

[0041] 实施方案12.实施方案7至11中任一者的方法，还包括在施用之前测量可溶性TIM-3的血清滴度。

[0042] 实施方案13.一种用TIM-3拮抗剂治疗患有癌症的受试者的方法，包括确定受试者中可溶性TIM-3的血清滴度，并且如果该可溶性TIM-3的血清滴度高于对照受试者的血清滴度，则向受试者施用治疗有效量的TIM-3拮抗剂。

[0043] 实施方案14.实施方案13的方法，其中如果受试者具有在受试者中高于对照受试者中至少10％的可溶性TIM-3血清滴度，则向受试者施用治疗有效量的TIM-3拮抗剂。

[0044] 实施方案15.实施方案13或14的方法，其中如果受试者具有高于对照受试者中至

少20％、30％、40％、50％、60％、70％、80％、90％或100％(2倍)的可溶性TIM-3血清滴度，则向受试者施用治疗有效量的TIM-3拮抗剂。

[0045] 实施方案16.实施方案13-15中任一者的方法，其中如果受试者具有至少2100、2200、2300、2400或2500pg/ml(例如，如按实施例中描述的方法测定)的可溶性TIM-3血清滴度，则向受试者施用治疗有效量的TIM-3拮抗剂。

[0046] 实施方案17.实施方案13-16中任一者的方法，其中如果受试者具有至少3000pg/ml(例如，如按实施例中描述的方法测定)的可溶性TIM-3血清滴度，则向受试者施用治疗有效量的TIM-3拮抗剂。

[0047] 实施方案18.实施方案1-17中任一者的方法，其中可溶性TIM-3是差异剪接的可溶性TIM-3和/或脱落型TIM-3(shed TIM-3)。

[0048] 实施方案19.实施方案1-18中任一者的方法，其中癌是实体瘤。

[0049] 实施方案20.实施方案1-19中任一者的方法，其中癌是结肠癌、肾癌或肺癌。

[0050] 实施方案21.实施方案1-20中任一者的方法，其中对照受试者中可溶性TIM-3的血清滴度是至少10、50或100位受试者中可溶性TIM-3的均数或平均滴度。

[0051] 实施方案22.实施方案1-21中任一者的方法，其中TIM-3拮抗剂是TIM-3抗体。

[0052] 实施方案23.实施方案22的方法，其中TIM-3抗体包含:包含CDR1、CDR2和CDR3的重链可变区和包含CDR1、CDR2和CDR3的轻链可变区，其中

[0053] (a)重链CDR1包含选自SEQ ID NOs:23-27的氨基酸序列；

[0054] (b)重链CDR2包含选自SEQ ID NOs:28-38的氨基酸序列；

[0055] (c)重链CDR3包含选自SEQ ID NOs:39-49的氨基酸序列；

[0056] (d)轻链CDR1包含选自SEQ ID NOs:50和51的氨基酸序列；

[0057] (e)轻链CDR2包含选自SEQ ID NOs:52和53的氨基酸序列；并且

[0058] (f)轻链CDR3包含选自SEQ ID NOs:54-57的氨基酸序列。

[0059] 实施方案24.一种确定患有癌症的受试者是否将响应于PD-1/PD-L1轴拮抗剂和TIM-3拮抗剂的组合治疗的体外方法，包括确定受试者的PD-1阳性肿瘤浸润型淋巴细胞(TIL)的频率和TIM-3阳性TIL的频率，其中PD-1和TIM-3在受试者的至少5％的CD8+TIL上共表达表示，受试者可能响应于PD-1/PD-L1轴拮抗剂和TIM3拮抗剂的组合治疗。

[0060] 实施方案25.实施方案24的方法，其中PD-1和TIM-3在受试者的至少10％、20％、30％或40％的CD8+TIL上共表达表示，受试者可能响应于PD-1/PD-L1轴拮抗剂和TIM3拮抗剂的组合治疗。

[0061] 实施方案26.实施方案24或25的方法，还包括向至少5％的CD8+TIL上共表达PD-1和TIM-3的受试者施用PD-1/PD-L1轴拮抗剂和TIM3拮抗剂的组合。

[0062] 实施方案27.一种用PD-1/PD-L1轴拮抗剂和TIM-3拮抗剂的组合治疗患有癌症的受试者的方法，包括向至少5％的CD8+TIL上具有PD-1和TIM-3共表达的受试者施用治疗有效量的PD-1/PD-L1轴拮抗剂和TIM-3拮抗剂的组合。

[0063] 实施方案28.实施方案27的方法，其中受试者在至少10％、20％、30％、40％的CD8+TIL上具有PD-1和TIM-3共表达。

[0064] 实施方案29.一种用PD-1/PD-L1轴拮抗剂和TIM-3拮抗剂的组合治疗患有癌症的受试者的方法，包括确定受试者的PD-1阳性肿瘤浸润型淋巴细胞(TIL)的频率和TIM-3阳性

TIL的频率，并且如果PD-1和TIM-3在受试者的至少5％的CD8+TIL上共表达，则向受试者施用PD-1/PD-L1轴拮抗剂和TIM-3拮抗剂的组合。

[0065] 实施方案30.实施方案29的方法，其中如果PD-1和TIM-3在受试者的至少10％、20％、30％、40％的CD8+TIL上共表达，则向受试者施用PD-1/PD-L1轴拮抗剂和TIM-3拮抗剂的组合。

[0066] 实施方案31.一种确定患有癌症的受试者是否将响应于TIM-3拮抗剂治疗的方法，包括确定呈TIM-3阳性的CD8+TIL的百分数，并且如果该百分数高于10％、20％、30％、40％、50％、60％或70％，则受试者可能响应于TIM-3拮抗剂治疗。

[0067] 实施方案32.一种用TIM-3拮抗剂治疗患有癌症的受试者的方法，包括向具有高于10％、20％、30％、40％、50％、60％或70％的CD8+TIL百分数的受试者施用治疗有效量的TIM-3拮抗剂。

[0068] 实施方案33.一种用TIM-3拮抗剂治疗患有癌症的受试者的方法，包括确定呈TIM-3阳性的CD8+TIL的百分数，并且如果该百分数高于10％、20％、30％、40％、50％、60％或70％，则向受试者施用治疗有效量的TIM-3拮抗剂。

[0069] 实施方案34.一种确定患有癌症的受试者是否将响应于TIM-3拮抗剂治疗的方法，包括确定呈TIM-3阳性的幼稚、CM、EM和Teff TIL的百分数，并且如果呈TIM-3阳性的TIL效应记忆(“EM”)T细胞和/或效应T(“Teff”)细胞的百分数高于呈TIM-3阳性的TIL幼稚T细胞和/或中央记忆T细胞(“CM T细胞”)的百分数，则受试者可能响应于TIM-3拮抗剂治疗。

[0070] 实施方案35.实施方案34的方法，其中TIL是CD4+TIL。

[0071] 实施方案36.实施方案34的方法，其中TIL是CD8+TIL。

[0072] 实施方案37.实施方案34的方法，其中在CD4+和CD8 T细胞中测量频率，并且如果在CD4+和CD8+TIL细胞二者中见到较高的百分数，则受试者可能响应于TIM-3拮抗剂治疗。

[0073] 实施方案38.一种用TIM-3拮抗剂治疗患有癌症的受试者的方法，包括向受试者施用治疗有效量的TIM-3拮抗剂，所述受试者具有的呈TIM-3阳性的TIL效应记忆(“EM”)T细胞和/或效应T(“Teff”)细胞的百分数高于呈TIM-3阳性的TIL幼稚T细胞和/或中央记忆T细胞(“CM T细胞”)的百分数。

[0074] 实施方案39.一种用TIM-3拮抗剂治疗患有癌症的受试者的方法，包括向受试者施用治疗有效量的TIM-3拮抗剂，所述受试者具有的呈TIM-3阳性的CD4+TIL效应记忆(“EM”)T细胞和/或CD4+效应T(“Teff”)细胞的百分数高于呈TIM-3阳性的CD4+TIL幼稚T细胞和/或CD4+中央记忆T细胞(“CM T细胞”)的百分数。

[0075] 实施方案40.一种用TIM-3拮抗剂治疗患有癌症的受试者的方法，包括向受试者施用治疗有效量的TIM-3拮抗剂，所述受试者具有的呈TIM-3阳性的CD8+TIL效应记忆(“EM”)T细胞和/或CD8+效应T(“Teff”)细胞的百分数高于呈TIM-3阳性的CD8+TIL幼稚T细胞和/或CD8+中央记忆T细胞(“CM T细胞”)的百分数。

[0076] 实施方案41.一种用TIM-3拮抗剂治疗患有癌症的受试者的方法，包括向受试者施用治疗有效量的TIM-3拮抗剂，所述受试者具有：(i)比呈TIM-3阳性的CD4+TIL幼稚T细胞和/或CD4+中央记忆T细胞(“CM T细胞”)百分数更高的呈TIM-3阳性的CD4+TIL效应记忆(“EM”)T细胞和/或CD4+效应T(“Teff”)细胞百分数；和(ii)比呈TIM-3阳性的CD8+TIL幼稚T细胞和/或CD8+中央记忆T细胞(“CM T细胞”)百分数更高的呈TIM-3阳性的CD8+TIL效应记

忆(“EM”)T细胞和/或CD8+效应T(“Teff”)细胞百分数。

[0077] 实施方案42.一种用TIM-3拮抗剂治疗患有癌症的受试者的方法,包括确定呈TIM-3阳性的幼稚、CM、EM和Teff TIL的百分数,并且如果呈TIM-3阳性的TIL效应记忆(“EM”)T细胞和/或效应T(“Teff”)细胞的百分数高于呈TIM-3阳性的TIL幼稚T细胞和/或中央记忆T细胞(“CM T细胞”)的百分数,则向受试者施用治疗有效量的TIM-3拮抗剂。

[0078] 实施方案43.实施方案42的方法,其中TIL是CD4+TIL。

[0079] 实施方案44.实施方案42的方法,其中TIL是CD8+TIL。

[0080] 实施方案45.实施方案42的方法,其中在CD4+和CD8 T细胞中测量频率,并且如果在CD4+和CD8+TIL细胞二者中见到较高的百分数,则向受试者施用治疗有效量的TIM-3拮抗剂。

[0081] 实施方案46.实施方案34-45中任一者的方法,其中TIM-3阳性细胞水平的差异是至少50%。

[0082] 实施方案47.实施方案34-46中任一者的方法,其中TIM-3阳性细胞水平的差异是至少100%。

[0083] 实施方案48.实施方案34-47中任一者的方法,其中幼稚T细胞呈CCR7+CD45RO-,Teff细胞呈CCR7-CD45RO-,CM T细胞呈CCR7+CD45RO+,并且EM T细胞呈CCR7-CD45RO+。

[0084] 实施方案49.确定患有癌症的受试者是否将响应于TIM-3拮抗剂治疗的体外方法,包括确定受试者的TIL中呈TIM-3阳性的树状细胞、巨噬细胞和自然杀伤(NK)细胞的百分数,并且如果该百分数高于对照受试者中的百分数,则受试者可能响应于TIM-3拮抗剂治疗。

[0085] 实施方案50.一种用TIM-3拮抗剂治疗患有癌症的受试者的方法,包括向受试者施用治疗有效量的TIM-3拮抗剂,所述受试者具有在受试者的TIL中以下百分数的呈TIM-3阳性的树状细胞、巨噬细胞和NK细胞,其中该百分数高于对照受试者中的百分数。

[0086] 实施方案51.一种用TIM-3拮抗剂治疗患有癌症的受试者的方法,包括在受试者中确定在受试者的TIL中呈TIM-3阳性的树状细胞、巨噬细胞和NK细胞的百分数,并且如果该百分数高于对照受试者中的百分数,则向受试者施用治疗有效量的TIM-3拮抗剂。

[0087] 实施方案52.实施方案24-51中任一者的方法,其中TIM-3拮抗剂是TIM-3抗体。

[0088] 实施方案53.实施方案52的方法,其中TIM-3抗体包含:包含CDR1、CDR2和CDR3的重链可变区和包含CDR1、CDR2和CDR3的轻链可变区,其中

[0089] (a)重链CDR1包含选自SEQ ID NOs:23-27的氨基酸序列;

[0090] (b)重链CDR2包含选自SEQ ID NOs:28-38的氨基酸序列;

[0091] (c)重链CDR3包含选自SEQ ID NOs:39-49的氨基酸序列;

[0092] (d)轻链CDR1包含选自SEQ ID NOs:50和51的氨基酸序列;

[0093] (e)轻链CDR2包含选自SEQ ID NOs:52和53的氨基酸序列;并且

[0094] (f)轻链CDR3包含选自SEQ ID NOs:54-57的氨基酸序列。

[0095] 实施方案54.实施方案52的方法,其中VH包含选自SEQ ID NOs:1-18的氨基酸序列并且VL包含选自SEQ ID NOs:19-22的氨基酸序列。

[0096] 实施方案55.实施方案24至30中任一者的方法,其中PD-1/PD-L1轴拮抗剂是抗PD-1抗体、抗PD-L1抗体或其任意组合。

[0097] 实施方案56.实施方案55的方法，其中抗PD-1抗体包括纳武单抗、派姆单抗、MEDI0608、AMP-224、PDR001、BGB-A317或其任意组合。

[0098] 实施方案57.实施方案55的方法，其中抗PD-L1抗体包括BMS-936559、MPDL3280A、MEDI4736、MSB0010718C或其任意组合。

[0099] 实施方案58.一种在患有癌症的受试者中评估包含TIM-3拮抗剂的治疗的功效的方法，包括向受试者施用治疗后，确定受试者中可溶性TIM-3的血清滴度，并且如果血清滴度与对照受试者的血清滴度相当，则该治疗可能是受试者中的有效性治疗。

[0100] 实施方案59.实施方案58的方法，其中与治疗之前的肿瘤大小相比，有效性治疗减少肿瘤大小至少约10％、约20％、约30％、约40％或约50％。

[0101] 实施方案60.实施方案58或59的方法，其中有效性治疗有效地增加受试者的总生存期至少约6个月、至少约7个月、至少约8个月、至少约9个月、至少约10个月、至少约11个月、至少约12个月、至少约13个月、至少约14个月、至少约15个月、至少约16个月、至少约17个月、至少约18个月、至少约19个月、至少约20个月、至少约21个月、至少约22个月、至少约23个月、至少约24个月、至少约25个月、至少约26个月、至少约27个月、至少约28个月、至少约29个月、至少约30个月、至少约3年、至少约3.5年、至少约4年、至少约4.5年、至少约5年或至少约10年。

[0102] 实施方案61.实施方案58至60中任一者的方法，其中有效性治疗增加受试者无进展生存期的持续时间至少约1个月、至少约2个月、至少约3个月、至少约4个月、至少约5个月、至少约6个月、至少约7个月、至少约8个月、至少约9个月、至少约10个月、至少约11个月、至少约1年、至少约15个月、至少约18个月、至少约2年、至少约3年、至少约4年或至少约5年。

[0103] 实施方案62.实施方案58至61中任一者的方法，其中TIM-3拮抗剂是TIM-3抗体。

[0104] 实施方案63.实实施方案62的方法，其中TIM-3抗体包含：包含CDR1、CDR2和CDR3的重链可变区和包含CDR1、CDR2和CDR3的轻链可变区，其中

[0105] (a)重链CDR1包含选自SEQ ID NOs:23-27的氨基酸序列；

[0106] (b)重链CDR2包含选自SEQ ID NOs:28-38的氨基酸序列；

[0107] (c)重链CDR3包含选自SEQ ID NOs:39-49的氨基酸序列；

[0108] (d)轻链CDR1包含选自SEQ ID NOs:50和51的氨基酸序列；

[0109] (e)轻链CDR2包含选自SEQ ID NOs:52和53的氨基酸序列；并且

[0110] (f)轻链CDR3包含选自SEQ ID NOs:54-57的氨基酸序列。

[0111] 实施方案64.实施方案23或53的方法，其中TIM-3抗体包含

[0112] (a1)分别包含SEQ ID NOs:23、28、39的重链可变区CDR1、CDR2和CDR3，和分别包含SEQ ID NOs:50、52、54的轻链可变区CDR1、CDR2和CDR3；

[0113] (a2)分别包含SEQ ID NOs:23、35、39的重链可变区CDR1、CDR2和CDR3，和分别包含SEQ ID NOs:50、52、54的轻链可变区CDR1、CDR2和CDR3；

[0114] (a3)分别包含SEQ ID NOs:23、36、39的重链可变区CDR1、CDR2和CDR3，和分别包含SEQ ID NOs:50、52、54的轻链可变区CDR1、CDR2和CDR3；

[0115] (a4)分别包含SEQ ID NOs:23、37、39的重链可变区CDR1、CDR2和CDR3，和分别包含SEQ ID NOs:50、52、54的轻链可变区CDR1、CDR2和CDR3；

[0116] (a5)分别包含SEQ ID NOs:23、28、46的重链可变区CDR1、CDR2和CDR3，和分别包含

SEQ ID NOs:50、52、54的轻链可变区CDR1、CDR2和CDR3；

[0117] (a6)分别包含SEQ ID NOs:23、28、47的重链可变区CDR1、CDR2和CDR3，和分别包含SEQ ID NOs:50、52、54的轻链可变区CDR1、CDR2和CDR3；

[0118] (a7)分别包含SEQ ID NOs:23、28、48的重链可变区CDR1、CDR2和CDR3，和分别包含SEQ ID NOs:50、52、54的轻链可变区CDR1、CDR2和CDR3；

[0119] (a8)分别包含SEQ ID NOs:23、28、49的重链可变区CDR1、CDR2和CDR3，和分别包含SEQ ID NOs:50、52、54的轻链可变区CDR1、CDR2和CDR3；

[0120] (a9)分别包含SEQ ID NOs:23、35、46的重链可变区CDR1、CDR2和CDR3，和分别包含SEQ ID NOs:50、52、54的轻链可变区CDR1、CDR2和CDR3；

[0121] (a10)分别包含SEQ ID NOs:23、35、48的重链可变区CDR1、CDR2和CDR3，和分别包含SEQ ID NOs:50、52、54的轻链可变区CDR1、CDR2和CDR3；

[0122] (b1)分别包含SEQ ID NOs:24、29、40的重链可变区CDR1、CDR2和CDR3，和分别包含SEQ ID NOs:50、52、55的轻链可变区CDR1、CDR2和CDR3；

[0123] (b2)分别包含SEQ ID NOs:24、38、40的重链可变区CDR1、CDR2和CDR3，和分别包含SEQ ID NOs:50、52、55的轻链可变区CDR1、CDR2和CDR3；

[0124] (c)分别包含SEQ ID NOs:25、30、41的重链可变区CDR1、CDR2和CDR3，和分别包含SEQ ID NOs:50、52、55的轻链可变区CDR1、CDR2和CDR3；

[0125] (d)分别包含SEQ ID NOs:26、31、42的重链可变区CDR1、CDR2和CDR3，和分别包含SEQ ID NOs:50、52、54的轻链可变区CDR1、CDR2和CDR3；

[0126] (e)分别包含SEQ ID NOs:27、32、43的重链可变区CDR1、CDR2和CDR3，和分别包含SEQ ID NOs:50、52、55的轻链可变区CDR1、CDR2和CDR3；

[0127] (f)分别包含SEQ ID NOs:27、32、43的重链可变区CDR1、CDR2和CDR3，和分别包含SEQ ID NOs:50、52、57的轻链可变区CDR1、CDR2和CDR3；

[0128] (g1)分别包含SEQ ID NOs:27、32、43的重链可变区CDR1、CDR2和CDR3，和分别包含SEQ ID NOs:51、53、56的轻链可变区CDR1、CDR2和CDR3；

[0129] (g2)分别包含SEQ ID NOs:27、32、43的重链可变区CDR1、CDR2和CDR3，和分别包含SEQ ID NOs:50、52、57的轻链可变区CDR1、CDR2和CDR3；

[0130] (g3)分别包含SEQ ID NOs:27、32、43的重链可变区CDR1、CDR2和CDR3，和分别包含SEQ ID NOs:50、52、55的轻链可变区CDR1、CDR2和CDR3；

[0131] (h)分别包含SEQ ID NOs:27、33、44的重链可变区CDR1、CDR2和CDR3和分别包含SEQ ID NOs:50、52、54的轻链可变区CDR1、CDR2和CDR3；或

[0132] (i)分别包含SEQ ID NOs:27、34、45的重链可变区CDR1、CDR2和CDR3，和分别包含SEQ ID NOs:50、52、55的轻链可变区CDR1、CDR2和CDR3；

[0133] 其中抗体与人TIM3特异性结合。

[0134] 实施方案65.实施方案23或53的方法，其中TIM-3抗体包含重链可变区(VH)和轻链可变区(VL)，其中VH和VL选自：

[0135] (a)分别包含SEQ ID NOs:1和19的VH和VL；

[0136] (b)分别包含SEQ ID NOs:2和20的VH和VL；

[0137] (c)分别包含SEQ ID NOs:3和20的VH和VL；

[0138] (d)分别包含SEQ ID NOs:4和19的VH和VL；

[0139] (e)分别包含SEQ ID NOs:5和20的VH和VL；

[0140] (f)分别包含SEQ ID NOs:5和21的VH和VL；

[0141] (g)分别包含SEQ ID NOs:5和22的VH和VL；

[0142] (h)分别包含SEQ ID NOs:6和19的VH和VL；

[0143] (i)分别包含SEQ ID NOs:7和20的VH和VL；

[0144] (j)分别包含SEQ ID NOs:17和22的VH和VL；

[0145] (k)分别包含SEQ ID NOs:16和20的VH和VL；

[0146] (l)分别包含SEQ ID NOs:8和19的VH和VL；

[0147] (m)分别包含SEQ ID NOs:9和19的VH和VL；

[0148] (n)分别包含SEQ ID NOs:10和19的VH和VL；

[0149] (o)分别包含SEQ ID NOs:11和19的VH和VL；

[0150] (p)分别包含SEQ ID NOs:12和19的VH和VL；

[0151] (q)分别包含SEQ ID NOs:13和19的VH和VL；

[0152] (r)分别包含SEQ ID NOs:14和19的VH和VL；

[0153] (s)分别包含SEQ ID NOs:15和19的VH和VL;和

[0154] (t)分别包含SEQ ID NOs:18和19的VH和VL。

[0155] 实施方案66.实施方案23或53的方法,其中TIM-3抗体包含：

[0156] (a1)分别包含SEQ ID NOs:136(或137)和190的重链序列和轻链序列；

[0157] (a2)分别包含SEQ ID NOs:68(或75)和190的重链序列和轻链序列；

[0158] (a3)分别包含SEQ ID NOs:82(或89))和190的重链序列和轻链序列；

[0159] (a4)分别包含SEQ ID NOs:138(或139)和190的重链序列和轻链序列；

[0160] (a5)分别包含SEQ ID NOs:96(或106)和190的重链序列和轻链序列；

[0161] (a6)分别包含SEQ ID NOs:116(或126)和190的重链序列和轻链序列；

[0162] (a7)分别包含SEQ ID NOs:140(或141)和190的重链序列和轻链序列；

[0163] (a8)分别包含SEQ ID NOs:97(或107)和190的重链序列和轻链序列；

[0164] (a9)分别包含SEQ ID NOs:117(或127)和190的重链序列和轻链序列；

[0165] (a10)分别包含SEQ ID NOs:142(或143)和190的重链序列和轻链序列；

[0166] (a11)分别包含SEQ ID NOs:98(或108)和190的重链序列和轻链序列；

[0167] (a12)分别包含SEQ ID NOs:118(或128)和190的重链序列和轻链序列；

[0168] (a13)分别包含SEQ ID NOs:144(或145)和190的重链序列和轻链序列；

[0169] (a14)分别包含SEQ ID NOs:99(或109)和190的重链序列和轻链序列；

[0170] (a15)分别包含SEQ ID NOs:119(或129)和190的重链序列和轻链序列；

[0171] (a16)分别包含SEQ ID NOs:146(或147)和190的重链序列和轻链序列；

[0172] (a17)分别包含SEQ ID NOs:100(或110)和190的重链序列和轻链序列；

[0173] (a18)分别包含SEQ ID NOs:120(或130)和190的重链序列和轻链序列；

[0174] (a19)分别包含SEQ ID NOs:148(或149)和190的重链序列和轻链序列；

[0175] (a20)分别包含SEQ ID NOs:101(或111)和190的重链序列和轻链序列；

[0176] (a21)分别包含SEQ ID NOs:121(或131)和190的重链序列和轻链序列；

[0177] (a22)分别包含SEQ ID NOs:150(或151)和190的重链序列和轻链序列;

[0178] (a23)分别包含SEQ ID NOs:102(或112)和190的重链序列和轻链序列;

[0179] (a24)分别包含SEQ ID NOs:122(或132)和190的重链序列和轻链序列;

[0180] (a25)分别包含SEQ ID NOs:152(或153)和190的重链序列和轻链序列;

[0181] (a26)分别包含SEQ ID NOs:103(或113)和190的重链序列和轻链序列;

[0182] (a27)分别包含SEQ ID NOs:123(或133)和190的重链序列和轻链序列;

[0183] (a28)分别包含SEQ ID NOs:154(或155)和190的重链序列和轻链序列;

[0184] (a29)分别包含SEQ ID NOs:184(或185)和190的重链序列和轻链序列;

[0185] (a30)分别包含SEQ ID NOs:186(或187)和190的重链序列和轻链序列;

[0186] (a31)分别包含SEQ ID NOs:188(或189)和190的重链序列和轻链序列;

[0187] (b1)分别包含SEQ ID NOs:156(或157)和191的重链序列和轻链序列;

[0188] (b2)分别包含SEQ ID NOs:69(或76)和191的重链序列和轻链序列;

[0189] (b3)分别包含SEQ ID NOs:83(或90)和191的重链序列和轻链序列;

[0190] (b4)分别包含SEQ ID NOs:158(或159)和191的重链序列和轻链序列;

[0191] (b5)分别包含SEQ ID NOs:104(或114)和191的重链序列和轻链序列;

[0192] (b6)分别包含SEQ ID NOs:124(或134)和191的重链序列和轻链序列;

[0193] (b7)分别包含SEQ ID NOs:160(或161)和191的重链序列和轻链序列;

[0194] (c1)分别包含SEQ ID NOs:162(或163)和191的重链序列和轻链序列;

[0195] (c2)分别包含SEQ ID NOs:70(或77)和191的重链序列和轻链序列;

[0196] (c3)分别包含SEQ ID NOs:84(或91)和191的重链序列和轻链序列;

[0197] (c4)分别包含SEQ ID NOs:164(或165)和191的重链序列和轻链序列;

[0198] (d1)分别包含SEQ ID NOs:166(或167)和190的重链序列和轻链序列;

[0199] (d2)分别包含SEQ ID NOs:71(或78)和190的重链序列和轻链序列;

[0200] (d3)分别包含SEQ ID NOs:85(或92)和190的重链序列和轻链序列;

[0201] (d4)分别包含SEQ ID NOs:168(或169)和190的重链序列和轻链序列;

[0202] (e1.1)分别包含SEQ ID NOs:170(或171)和192的重链序列和轻链序列;

[0203] (e1.2)分别包含SEQ ID NOs:170(或171)和193的重链序列和轻链序列;

[0204] (e1.3)分别包含SEQ ID NOs:170(或171)和191的重链序列和轻链序列;

[0205] (e2)分别包含SEQ ID NOs:72(或79)和193的重链序列和轻链序列;

[0206] (e3)分别包含SEQ ID NOs:86(或93)和193的重链序列和轻链序列;

[0207] (e4)分别包含SEQ ID NOs:172(或173)和193的重链序列和轻链序列;

[0208] (e5)分别包含SEQ ID NOs:105(或115)和193的重链序列和轻链序列;

[0209] (e6)分别包含SEQ ID NOs:125(或135)和193的重链序列和轻链序列;

[0210] (e7)分别包含SEQ ID NOs:174(或175)和193的重链序列和轻链序列;

[0211] (f1)分别包含SEQ ID NOs:176(或177)和190的重链序列和轻链序列;

[0212] (f2)分别包含SEQ ID NOs:73(或80)和190的重链序列和轻链序列;

[0213] (f3)分别包含SEQ ID NOs:87(或94)和190的重链序列和轻链序列;

[0214] (f4)分别包含SEQ ID NOs:178(或179)和190的重链序列和轻链序列;

[0215] (g1)分别包含SEQ ID NOs:180(或181)和191的重链序列和轻链序列;

[0216] (g2)分别包含SEQ ID NOs:74(或81)和191的重链序列和轻链序列；

[0217] (g3)分别包含SEQ ID NOs:88(或95)和191的重链序列和轻链序列;或

[0218] (g4)分别包含SEQ ID NOs:182(或183)和191的重链序列和轻链序列；

[0219] 其中抗体与人TIM3特异性结合。

[0220] 67.一种治疗患有癌症的受试者的方法,包括向患有癌症和具有比对照受试者中更高的可溶性TIM-3血清滴度的受试者施用治疗有效量的TIM-3拮抗剂,其中TIM-3拮抗剂是包含重链和轻链的抗体,其中(i)重链包含:分别包含SEQ ID NOs:23、35和46的重链CDR1、CDR2和CDR3,并且轻链包含:分别包含SEQ ID NOs:50、52和54的轻链CDR1、CDR2和CDR3;(ii)重链包含:包含SEQ ID NO:18的VH,并且轻链包含:包含SEQ ID NO:19的VL;或(iii)重链包含SEQ ID NO:186或187并且轻链包含SEQ ID NO:190。

[0221] 实施方案68.实施方案67的方法,其中受试者具有在受试者中高于对照受试者中至少10％的可溶性TIM-3血清滴度。

[0222] 实施方案69.实施方案67的方法,其中受试者具有高于对照受试者中至少20％、30％、40％、50％、60％、70％、80％、90％或100％(2倍)的可溶性TIM-3血清滴度。

[0223] 实施方案70.实施方案67-69中任一者的方法,其中受试者具有至少2100、2200、2300、2400或2500pg/ml(例如,如按实施例中描述的方法测定)的可溶性TIM-3血清滴度。

[0224] 实施方案71.实施方案67-70中任一者的方法,其中受试者具有至少3000pg/ml(例如,如按实施例中描述的方法测定)的可溶性TIM-3血清滴度。

[0225] 实施方案72.实施方案67至71中任一者的方法,还包括在施用之前测量可溶性TIM-3的血清滴度。

[0226] 实施方案73.一种用TIM-3拮抗剂治疗患有癌症的受试者的方法,包括确定受试者中可溶性TIM-3的血清滴度,并且如果该可溶性TIM-3的血清滴度高于对照受试者中的血清滴度,则向受试者施用治疗有效量的TIM-3拮抗剂,其中TIM-3拮抗剂是包含重链和轻链的抗体,其中(i)重链包含:分别包含SEQ ID NOs:23、35和46的重链CDR1、CDR2和CDR3,并且轻链包含:分别包含SEQ ID NOs:50、52和54的轻链CDR1、CDR2和CDR3;(ii)重链包含:包含SEQ ID NO:18的VH,并且轻链包含:包含SEQ ID NO:19的VL;或(iii)重链包含SEQ ID NO:186或187并且轻链包含SEQ ID NO:190。

[0227] 实施方案74.实施方案73的方法,其中如果受试者具有在受试者中高于对照受试者中至少10％的可溶性TIM-3血清滴度,则向受试者施用治疗有效量的TIM-3拮抗剂。

[0228] 实施方案75.实施方案73或74的方法,其中如果受试者具有高于对照受试者中至少20％、30％、40％、50％、60％、70％、80％、90％或100％(2倍)的可溶性TIM-3血清滴度,则向受试者施用治疗有效量的TIM-3拮抗剂。

[0229] 实施方案76.实施方案73-75中任一者的方法,其中如果受试者具有至少2500pg/ml(例如,如按实施例中描述的方法测定)的可溶性TIM-3血清滴度,则向受试者施用治疗有效量的TIM-3拮抗剂。

[0230] 实施方案77.实施方案73-76中任一者的方法,其中如果受试者具有至少3000pg/ml(例如,如按实施例中描述的方法测定)的可溶性TIM-3血清滴度,则向受试者施用治疗有效量的TIM-3拮抗剂。

[0231] 实施方案78.实施方案67-77中任一者的方法,其中可溶性TIM-3是差异剪接的可

溶性TIM-3和/或脱落型TIM-3。

[0232] 实施方案79.实施方案67-78中任一者的方法,其中癌是实体瘤。

[0233] 实施方案80.实施方案67-79中任一者的方法,其中癌是结肠癌、肾癌或肺癌。

[0234] 实施方案81.实施方案67-80中任一者的方法,其中对照受试者中可溶性TIM-3的血清滴度是至少10、50或100位受试者中可溶性TIM-3的中位或平均滴度。

[0235] 实施方案82.实施方案67-81中任一者的方法,其中TIM-3拮抗剂是TIM-3抗体。

[0236] 实施方案83.一种用PD-1/PD-L1轴拮抗剂和TIM-3拮抗剂的组合治疗患有癌症的受试者的方法,包括向至少5%的CD8+TIL上具有PD-1和TIM-3共表达的受试者施用治疗有效量的PD-1/PD-L1轴拮抗剂和TIM-3拮抗剂的组合,其中TIM-3拮抗剂是包含重链和轻链的抗体,其中(i)重链包含了分别包含SEQ ID NOs:23、35和46的重链CDR1、CDR2和CDR3,并且轻链包含了分别包含SEQ ID NOs:50、52和54的轻链CDR1、CDR2和CDR3;(ii)重链包含了包含SEQ ID NO:18的VH并且轻链包含了包含SEQ ID NO:19的VL;或(iii)重链包含SEQ ID NO:186或187并且轻链包含SEQ ID NO:190,并且其中PD-1拮抗剂是纳武单抗。

[0237] 实施方案84.实施方案83的方法,其中受试者在至少10%、20%、30%、40%的CD8+TIL上具有PD-1和TIM-3共表达。

[0238] 实施方案85.一种用PD-1/PD-L1轴拮抗剂和TIM-3拮抗剂的组合治疗患有癌症的受试者的方法,包括确定受试者的PD-1阳性肿瘤浸润型淋巴细胞(TIL)的频率和TIM-3阳性TIL的频率,并且如果PD-1和TIM-3在受试者的至少5%的CD8+TIL上共表达,则向受试者施用PD-1/PD-L1轴拮抗剂和TIM-3拮抗剂的组合,其中TIM-3拮抗剂是包含重链和轻链的抗体,其中(i)重链包含了分别包含SEQ ID NOs:23、35和46的重链CDR1、CDR2和CDR3,并且轻链包含了分别包含SEQ ID NOs:50、52和54的轻链CDR1、CDR2和CDR3;(ii)重链包含了包含SEQ ID NO:18的VH并且轻链包含了包含SEQ ID NO:19的VL;或(iii)重链包含SEQ ID NO:186或187并且轻链包含SEQ ID NO:190,并且其中PD-1拮抗剂是纳武单抗。

[0239] 实施方案86.实施方案85的方法,其中如果PD-1和TIM-3在受试者的至少10%、20%、30%、40%的CD8+TIL上共表达,则向受试者施用PD-1/PD-L1轴拮抗剂和TIM-3拮抗剂的组合。

[0240] 实施方案87.一种用TIM-3拮抗剂治疗患有癌症的受试者的方法,包括向具有高于10%、20%、30%、40%、50%、60%或70%的CD8+TIL百分数的受试者施用治疗有效量的TIM-3拮抗剂,其中TIM-3拮抗剂是包含重链和轻链的抗体,其中(i)重链包含了分别包含SEQ ID NOs:23、35和46的重链CDR1、CDR2和CDR3,并且轻链包含了分别包含SEQ ID NOs:50、52和54的轻链CDR1、CDR2和CDR3;(ii)重链包含了包含SEQ ID NO:18的VH并且轻链包含了包含SEQ ID NO:19的VL;或(iii)重链包含SEQ ID NO:186或187并且轻链包含SEQ ID NO:190。

[0241] 实施方案88.一种用TIM-3拮抗剂治疗患有癌症的受试者的方法,包括确定呈TIM-3阳性的CD8+TIL的百分数,并且如果该百分数高于10%、20%、30%、40%、50%、60%或70%,则向受试者施用治疗有效量的TIM-3拮抗剂,其中TIM-3拮抗剂是包含重链和轻链的抗体,其中(i)重链包含了分别包含SEQ ID NOs:23、35和46的重链CDR1、CDR2和CDR3,并且轻链包含了分别包含SEQ ID NOs:50、52和54的轻链CDR1、CDR2和CDR3;(ii)重链包含了包含SEQ ID NO:18的VH并且轻链包含了包含SEQ ID NO:19的VL;或(iii)重链包含SEQ ID

NO:186或187并且轻链包含SEQ ID NO:190。

[0242] 实施方案89.一种用TIM-3拮抗剂治疗患有癌症的受试者的方法,包括向在受试者的TIL中具有如下百分数的呈TIM-3阳性的树状细胞、巨噬细胞和NK细胞的受试者施用治疗有效量的TIM-3拮抗剂,其中该百分数高于对照受试者中的百分数,其中TIM-3拮抗剂是包含重链和轻链的抗体,其中(i)重链包含了分别包含SEQ ID NOs:23、35和46的重链CDR1、CDR2和CDR3,并且轻链包含了分别包含SEQ ID NOs:50、52和54的轻链CDR1、CDR2和CDR3;(ii)重链包含了包含SEQ ID NO:18的VH并且轻链包含了包含SEQ ID NO:19的VL;或(iii)重链包含SEQ ID NO:186或187并且轻链包含SEQ ID NO:190。

[0243] 实施方案90.一种用TIM-3拮抗剂治疗患有癌症的受试者的方法,包括在受试者中确定在受试者的TIL中呈TIM-3阳性的树状细胞、巨噬细胞和NK细胞的百分数,并且如果该百分数高于对照受试者中的百分数,则向受试者施用治疗有效量的TIM-3拮抗剂,其中TIM-3拮抗剂是包含重链和轻链的抗体,其中(i)重链包含了分别包含SEQ ID NOs:23、35和46的重链CDR1、CDR2和CDR3,并且轻链包含了分别包含SEQ ID NOs:50、52和54的轻链CDR1、CDR2和CDR3;(ii)重链包含了包含SEQ ID NO:18的VH并且轻链包含了包含SEQ ID NO:19的VL;或(iii)重链包含SEQ ID NO:186或187并且轻链包含SEQ ID NO:190。

[0244] 附图简述

[0245] 图1A和图1B显示来自健康人受试者(“正常”)和癌症(即,结肠癌、肾癌或肺癌)患者的外周血中TIM3+CD4+T细胞(图1A)和TIM3+CD8+T细胞(图1B)的频率。频率显示为总CD4+T细胞或CD8+T细胞的百分数。每圆圈代表个体患者并且每个组的均数由水平线显示。

[0246] 图2A至图2E显示,从不同癌症(即,结肠癌、肾癌或肺癌)患者分离的肿瘤浸润型淋巴细胞(TIL)中表达TIM3和/或PD-1的CD4+T细胞和CD8+T细胞的频率。图2A和图2B中分别显示TIM3+CD4+T细胞和TIM3+CD8+T细胞的频率。在图2A和图2B中,TIM3+细胞的频率分别显示为TIL中总CD4+和CD8+T细胞的百分数。图2C和图2D中分别显示TIL中还表达PD-1的TIM3+CD4+T细胞和TIM3+CD8+T细胞的频率。在图2C和图2D中,PD-1+细胞的频率分别显示为TIL中TIM3+CD4+T细胞和TIM3+CD8+T细胞的百分数。图2E比较在来自TIM3+CD8+T细胞频率低(<8%)(左栏)和TIM3+CD8+T细胞频率高(右栏)的全部癌症患者的TIL中CD8+T细胞上PD-1的表达情况。PD-1阳性表达的频率显示为TIM3+CD8+T细胞的百分数。所示的P值使用Mann Whitney检验计算。

[0247] 图3A至图3C显示来自不同癌症(肾癌、肺癌、结肠癌、肝癌、卵巢癌、胃癌、子宫癌或胃肠道癌)患者的TIL中表达TIM3的不同T细胞亚类的频率。图3A提供鉴定不同CD4+T细胞和CD8+T细胞亚类的设门策略:幼稚(CCR7+CD45RO-)、中央记忆(CCR7+CD45RO+)、效应记忆(CCR7-CD45RO+)和效应(CCR7-CD45RO-)T细胞。图3B显示来自不同癌症患者的TIL(n=27)中表达TIM3的不同CD4+(顶部小图)和CD8+(底部小图)T细胞亚类的频率。所示频率是上文描述的CD4+T细胞亚类或CD8+T细胞亚类中TIM3+细胞的百分数。图3C比较在TIL和匹配性血液之间不同CD4+T细胞亚类和CD8+T细胞亚类中的TIM3+细胞频率。

[0248] 图4A至图4B显示来自不同癌症(即,肾癌、结肠癌、子宫癌或肺癌)患者的TIL中表达TIM3和/或PD-1的CD8+T细胞的频率。图4A显示(i)仅表达PD-1(较浅灰色阴影)、(ii)仅表达TIM3(较深灰色阴影)和(ii)表达PD-1和TIM3二者(黑色)的CD8+T细胞的频率。x-轴代表个体癌症患者。图4B显示表达(i)仅PD-1(每幅小图中的左上象限)、(ii)仅TIM3(每幅小图

中的右下象限)和(ii)PD-1和TIM3二者(每幅小图中的右上象限)的CD8+(左小图)T细胞和CD4+(右小图)T细胞的频率的流式细胞分析。

[0249] 图5A和图5B显示,来自表达TIM3的不同癌症患者的TIL中不同髓样细胞(图5A)和NK细胞(图5B)的频率。在图5A中显示,来自10位癌症患者的TIL中(i)TIM3+CD15+粒细胞、(ii)TIM3+浆细胞样树状细胞(pDC)、(iii)TIM3+髓样树状细胞(mDC)和(iv)TIM3+单核细胞/巨噬细胞(CD14+CD64+)的频率。在图5B中显示,来自10位癌症患者的TIL中TIM3+CD16-CD56++和CD16+CD56+CD3-NK细胞的频率。

[0250] 图6A和图6B显示来自健康人受试者(“正常”)和癌症(即,结肠癌、肾癌和肺癌)患者的血清中可溶性TIM3蛋白的水平。图6A显示每位供体的数据。图6B显示相同数据作为箱图。使用来自不同患者(n=20)的血清,通过ELISA测量TIM3蛋白水平。数据点上方的“****”指示正常者和癌症患者之间的统计显著差异($p<0.0001$)。数据点上方的“***”指示正常者和癌症患者之间的统计显著差异($p<0.01$)。使用Mann Whitney检验计算p值。

[0251] 发明详述

[0252] 定义

[0253] 为了可以更易于理解本说明书,首先定义某些术语。其它定义在发明详述通篇范围内阐述。

[0254] 应当指出,术语“某个(a)”或“一个(an)”实体指一个或多个该实体;例如,“某个核苷酸序列”理解成代表一个或多个核苷酸序列。因此,术语“某个(a)”(或“一个(an)”)、“一个或多个”和“至少一个”可以在本文互换使用。

[0255] 另外,在本文使用时,“和/或”应理解为具体公开了两个指定特征或组分的每一者与或不与另一者组合的情况。因此,如本文在短语如“A和/或B”中使用的术语“和/或”,意在包括“A和B”、“A或B”、“A”(单独)和“B”(单独)。同样地,如本文在短语如“A、B、和/或C”中使用的术语“和/或”意在涵盖以下每个方面:A、B和C;A、B或C;A或C;A或B;B或C;A和C;A和B;B和C;A(单独);B(单独);和C(单独)。

[0256] 可以理解,本文中无论何处用语言“包括”描述发明方面,也提供了以术语“由……组成”和/或“基本上由……组成”描述的类似方面。

[0257] 除非另外定义,否则本文中所用的全部技术术语和科学术语具有与本公开所涉及领域的普通技术人员通常所理解的相同含义。例如,Concise Dictionary of Biomedicine and Molecular Biology,Juo,Pei-Show,第2版,2002,CRC Press;The Dictionary of Cell and Molecular Biology,第3版,1999,Academic Press;和Oxford Dictionary Of Biochemistry And Molecular Biology,修订版,2000,Oxford University Press,为技术人员提供了本公开中所用许多术语的一般词典。

[0258] 单位、前缀和符号按其国际单位制(SI)接受的形式表示。数值范围包括界定该范围的数值。除非另外说明,核苷酸序列从左至右以5’至3’方向书写。氨基酸从左至右以氨基至羧基的方向书写。本文提供的小标题不是对本公开的各个方面的限制,这些方面可以通过参考说明书整体来获得。因此,紧接下文定义的术语通过完整参考本说明书可以更完整限定。

[0259] 术语“约”在本文中用来指大约、大致、左右和在……范围内。术语“约”结合一个数字范围使用时,它通过扩展界限值高于和低于所述数值而修饰该范围。通常而言,术语“约”

可以修饰数值，通过例如10％向上或向下(更高或更低)的变化而高于和低于所述值。

[0260] 如本文所用的术语“T细胞免疫球蛋白和含粘蛋白结构域-3”、“TIM3”或“TIM-3”指作为T细胞免疫球蛋白和粘蛋白结构域(TIM)蛋白质家族成员的受体。TIM3的主要配体包括磷脂酰丝氨酸(TIM3-L)。TIM3也称作甲型肝炎病毒细胞受体2(HAVCR2)、T细胞免疫球蛋白粘蛋白受体3、TIM-3、TIMD3、TIMD-3、肾损伤分子-3、KIM-3和CD366。术语“TIM3”包括由细胞天然表达的任何TIM3变体或同种型。因此，本文所述的抗体可以与来自除人类之外物种的TIM3(例如，食蟹猴TIM3)交叉反应。备选地，抗体可以对人TIM3有特异性并且不显示与其他物种的任何交叉反应性。TIM3或其任何变体和同种型，可以分离自天然表达它们的细胞或组织或使用本领域熟知技术和/或本文所述的技术重组地生产。

[0261] 已经鉴定到人TIM3的两个同种型。同种型1(登录号NP_116171;SEQ ID NO:194)由301个氨基酸组成并且表示典型序列。同种型2(登录号AAH20843;SEQ ID NO:195)由142个氨基酸组成并且是可溶性的。它缺少氨基酸残基143-301，这些氨基酸残基编码TIM3的跨膜结构域、胞质结构域和部分胞外结构域。该氨基酸残基132-142还异于上文描述的典型序列。

[0262] 以下是已知两种人TIM3同种型的氨基酸序列：

[0263] (A)人TIM3同种型1(登录号NP_116171;SEQ ID NO:194;由具有登录号NM_032782.4;SEQ ID NO:196的核苷酸序列编码)：

[0264] MFSHLPFDCVLLLLLLLLTRSSEVEYRAEVGQNAYLPCFYTPAAPGNLVPVCWGKGACPVFECGNVVLRTDERDVNYWTSRYWLNGDFRKGDVSLTIENVTLADSGIYCCRIQIPGIMNDEKFNLKLVIKPAKVTPAPTRQRDFTAAFPRMLTTRGHGPAETQTLGSLPDINLTQISTLANELRDSRLANDLRDSGATIRIGIYIGAGICAGLALALIFGALIFKWYSHSKEKIQNLSLISLANLPPSGLANAVAEGIRSEENIYTIEENVYEVEEPNEYYCYVSSRQQPSQPLGCRFAMP

[0265] (B)人TIM3同种型2(登录号AAH20843;SEQ ID NO:195;由具有登录号BC020843.1;SEQ ID NO:197的核苷酸序列编码)：

[0266] MFSHLPFDCVLLLLLLLLTRSSEVEYRAEVGQNAYLPCFYTPAAPGNLVPVCWGKGACPVFECGNVVLRTDERDVNYWTSRYWLNGDFRKGDVSLTIENVTLADSGIYCCRIQIPGIMNDEKFNLKLVIKPGEWTFACHLYE

[0267] 同种型1和2的信号序列对应于氨基酸1-21(加下划线)。因此，成熟同种型1和2分别由氨基酸22至301或142组成。成熟的人TIM3的胞外结构域由SEQ ID NO:194的氨基酸22-202组成并具有氨基酸序列：

[0268] SEVEYRAEVGQNAYLPCFYTPAAPGNLVPVCWGKGACPVFECGNVVLRTDERDVNYWTSRYWLNGDFRKGDVSLTIENVTLADSGIYCCRIQIPGIMNDEKFNLKLVIKPAKVTPAPTRQRDFTAAFPRMLTTRGHGPAETQTLGSLPDINLTQISTLANELRDSRLANDLRDSGATIRIG

[0269] (SEQ ID NO:198)。

[0270] 食蟹猴TIM3蛋白由以下氨基酸序列组成(包含信号序列)：

[0271] MFSHLPFDCVLLLLLLLLTRSSEVEYIAEVGQNAYLPCSYTPAPPGNLVPVCWGKGACPVFDCSNVVLRTENRDVNDRTSGRYWLKGDFHKGDVSLTIENVTLADSGVYCCRIQIPGIMNDEKHNLKLVVIKPAKVTPAPTLQRDLTSAFPRMLTTGEHGPAETQTPGSLPDVNLTQIFTLTNELRDSGATIRTAIYIAAGISAGLALALIFGALIFKWYSHSKEKTQNLSLISLANIPPSGLANAVAEGIRSEENIYTIEEDVYEVEEPNEYYCYVSSGQQPSQPLGCRFAMP (SEQ ID NO:199)

[0272] 术语“TIM3拮抗剂”或“针对TIM3的拮抗剂”指与人TIM3蛋白或其配体或分别编码人TIM3或其配体的核酸结合并且阻遏或抑制人TIM3活性的全部拮抗剂。这类拮抗剂可以是肽、核酸或化合物。更具体地，拮抗剂可以是靶向人TIM3的反义寡核苷酸、siRNA、shRNA、miRNA、dsRNA、适配体、PNA(肽核酸)或包括前者的载体。在一些实施方案中，拮抗剂可以是与人TIM3特异性结合并阻遏或抑制人TIM3活性的抗体或其抗原结合部分。

[0273] 在某些实施方案中，术语“抗体”或“抗体”指包含由二硫键相互连接的至少两条重链(H)和两条轻链(L)的蛋白质。每条重链由重链可变区(本文中缩写为VH)和重链恒定区(本文中缩写为CH)组成。在某些抗体(例如，天然存在的IgG抗体)中，重链恒定区由铰链区和三个结构域CH1、CH2和CH3组成。在某些抗体(例如，天然存在的IgG抗体)中，每条轻链由轻链可变区(本文中缩写为VL)和轻链恒定区组成。轻链恒定结构域由一个结构域CL组成(本文中缩写为CL)。VH区和VL区可以进一步再划分为超变区，名为互补性决定区(CDR)，其间插有更保守的区域，名为构架区(FR)。每个VH和VL由三个CDR和四个FR组成，从氨基末端到羧基末端按以下顺序排列：FR1、CDR1、FR2、CDR2、FR3、CDR3、FR4。重链和轻链的可变区含有与抗原相互作用的结合结构域。抗体的恒定区可以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，效应细胞)和经典补体系统的第一组分(C1q))结合。重链可以具有或没有C末端赖氨酸。除非本文中另外具体说明，使用Kabat编号体系对可变区中的氨基酸编号，并且使用EU体系对恒定区中的氨基酸编号。

[0274] 在某些实施方案中，如本文所用的“IgG抗体”，例如，人IgG1、IgG2、IgG3和IgG4抗体，具有天然存在IgG抗体的结构，即，它与相同亚类的天然存在IgG抗体具有相同数目的重链和轻链和二硫键。例如，抗TIM3 IgG1、IgG2、IgG3或IgG4抗体由两条重链(HC)和两条轻链(LC)组成，其中两条重链和两条轻链通过二硫键连接，所述二硫键的数目和位置分别与天然存在的IgG1、IgG2、IgG3和IgG4抗体中的二硫键的数目和位置相同(除非所述抗体已经被突变以具有修饰的二硫键)。

[0275] 免疫球蛋白可以来自任何公知的同种型，包括但不限于IgA、分泌型IgA、IgG和IgM。IgG同种型在某些物种划分为亚类：人类中IgG1、IgG2、IgG3和IgG4；小鼠中IgG1、IgG2a、IgG2b和IgG3。在某些实施方案中，本文所述的抗TIM3抗体为IgG1亚型。免疫球蛋白，例如，IgG1，存在几种同种异型，彼此差异最多数个氨基酸。“抗体”包括例如，天然存在的和非天然存在的抗体；单克隆抗体和多克隆抗体；嵌合抗体和人源化抗体；人抗体和非人抗体；以及全合成性抗体。

[0276] 如本文所用，术语抗体的“抗原结合部分”(也称作“抗原结合片段”)指，抗体中保留与抗原(例如，人TIM3)特异性结合的能力的一个或多个片段。已经显示，抗体的抗原结合功能可以由全长抗体的片段执行。涵盖于术语抗体(例如，本文所述的抗TIM3抗体)的“抗原结合部分”中的结合片段的实例包括：(i)Fab片段(来自木瓜蛋白酶剪切的片段)或由VL、VH、LC和CH1结构域组成的相似单价片段；(ii)$F(ab')_2$片段(来自胃蛋白酶剪切的片段)或包含由二硫键在铰链区连接的两个Fab片段的类似双价片段；(iii)由VH和CH1结构域组成的Fd片段；(iv)由抗体单臂的VL和VH结构域组成的Fv片段；(v)由VH结构域组成的dAb片段(Ward等人，Nature 341:544-546(1989))；(vi)分离的互补性决定区(CDR)和(vii)可以任选地通过合成性接头连接的，两个或更多个分离的CDR的组合。另外，虽然Fv片段的两个结构域VL和VH可以由独立的基因编码，但是使用重组方法，可以将它们通过合成性接头连接，

所述接头能够使这两个结构域作为单条蛋白链产生，在所述单条蛋白链中，VL区和VH区配对以形成单价分子(称作单链Fv(“scFv”)；参见例如Bird等人，Science 242:423-426(1988)；和Huston等人，Proc.Natl.Acad.Sci.USA 85:5879-5883(1988))。术语抗体的“抗原结合部分”也意在涵盖这种单链抗体。可以使用本领域技术人员已知的常规技术，获得这些抗体片段，并且可以按照与完整抗体相同的方式筛选所述片段予以应用。可以通过重组DNA技术或通过酶切割或化学切割完整免疫球蛋白来产生抗原结合部分。

[0277] 如本文中所用，术语“单克隆抗体”指来自基本上同质的抗体群体中的抗体，即，该群体中所包含的各个抗体基本上相似并且结合相同的表位(例如，这些抗体显示单一结合特异性和亲和力)，除了产生该单克隆抗体期间可能出现的可能变体之外，此类变体通常以微小量存在。修饰语“单克隆的”指示该抗体的特征为从基本上同质的抗体群体获得，并且不得解释为要求通过任何特定方法产生该抗体。术语“人单克隆抗体”指来自一个基本上同质抗体群体的抗体，其显示单一结合特异性并且具有衍生自人种系免疫球蛋白序列的可变区和任选的恒定区。在一些实施方案中，人单克隆抗体由杂交瘤产生，所述杂交瘤包括与永生化细胞融合的、从非人转基因动物(例如，转基因小鼠)获得的B细胞，所述非人转基因动物具有包含人重链转基因和轻链转基因的基因组。

[0278] 如本文所用，术语“重组人抗体”包括，通过重组手段制备、表达、产生或分离的全部人抗体，如(a)从人免疫球蛋白基因的转基因或转染色体动物(例如，小鼠)或由其制备的杂交瘤分离的抗体，(b)从经转化以表达该抗体的宿主细胞(例如，从转染瘤)分离的抗体、(c)从重组人抗体组合文库分离的抗体，和(d)通过涉及将人免疫球蛋白基因序列剪接到其他DNA序列的任何其他手段，制备、表达、产生或分离的抗体。这类重组人抗体包含可变区和恒定区，所述可变区和恒定区利用种系基因编码的特定人种系免疫球蛋白序列，但是包含例如在抗体成熟期间发生的后续重排和突变。如本领域已知(参见，例如，Lonberg(2005)Nature Biotech.23(9):1117-1125)，可变区含有抗原结合结构域，由重排以形成外来抗原特异性抗体的各种基因的编码。除重排之外，还可以通过多个单氨基酸变化(称作体细胞突变或超变)，进一步修饰可变区，以增加抗体对外来抗原的亲和力。恒定区可以在进一步应答于抗原时变化(即，同种型交换)。因此，应答于抗原而经过重排和体细胞突变的编码免疫球蛋白多肽轻链和重链的核酸分子，可能与原始核酸分子不具有序列相同性，但仍将基本上相同或相似(即，具有至少80％同一性)。

[0279] “人”抗体(HuMAb)指，可变区中的构架区和CDR区均源自人种系免疫球蛋白序列的抗体。另外，如果抗体含有恒定区，则恒定区也源自人种系免疫球蛋白序列。本文所述的抗TIM3抗体可以包含并非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体内体细胞突变所引入的突变)。然而，如本文所用，术语“人抗体”不意在包括将源自另一个哺乳动物物种(如小鼠)种系的CDR序列移植到人构架序列上的抗体。术语“人”抗体和“全人”抗体以同义方式使用。

[0280] “人源化”抗体指这样的抗体，其中将非人抗体的CDR结构域外的一些、大部分或全部氨基酸替换为来自人免疫球蛋白的相应氨基酸。在抗体分子的人源化形式的一些实施方案中，已经将CDR结构域外的一些、大部分或全部氨基酸替换为来自人免疫球蛋白的相应氨基酸，而一个或多个CDR区内部的一些、大部分或全部氨基酸不变。可以允许氨基酸的小添加、缺失、插入、置换或修饰，只要它们不消除抗体与特定抗原结合的能力。“人源化”抗体保

留类似于原始抗体的抗原特异性。

[0281] “嵌合抗体”指其中可变区衍生自一个物种并且恒定区衍生自另一个物种的抗体，如其中可变区衍生自小鼠抗体并且恒定区衍生自人抗体的抗体。

[0282] 如本文所用，“同种型”指由重链恒定区基因编码的抗体类别(例如，IgG1、IgG2、IgG3、IgG4、IgM、IgA1、IgA2、IgD和IgE抗体)。

[0283] “同种异型”指特定同种型群组内部天然存在的变体，所述变体在一些氨基酸上不同(参见，例如，Jefferis等人(2009)mAbs 1:1)。本文所述的抗TIM3抗体可以是任何同种异型。如本文所用，称作“IgG1f”、”IgG1.1f”或“IgG1.3f”同种型的抗体分别是具有同种异型“f”的IgG1抗体、无效应子性(effectorless)IgG1.1抗体和无效应子性IgG1.3抗体，即，根据如Kabat中的EU索引，具有214R、356E和358M，例如，如SEQ ID NO:123中所示。

[0284] 短语“识别抗原的抗体”和“对抗原特异的抗体”在本文中与术语“与抗原特异性结合的抗体”可互换使用。

[0285] 如本文所用，“分离的抗体”意指一种基本上不含其他蛋白质和细胞物质的抗体。

[0286] “Fc受体”或“FcR”是与免疫球蛋白Fc区结合的受体。与IgG抗体结合的FcR包括FcγR家族的受体，包括这些受体的等位变体和可变剪接形式。FcγR家族由三种活化性受体(小鼠中FcγRI、FcγRIII和FcγRIV；人类中FcγRIA、FcγRIIA和FcγRIIIA)和一种抑制性受体(FcγRIIB)组成。本领域已知人FcγR的各种特性。大部分的先天效应细胞类型共表达一种或多种活化性FcγR和抑制性FcγRIIB，而在小鼠和人类中自然杀伤(NK)细胞选择性地表达一种活化性Fc受体(小鼠中FcγRIII和人类中FcγRIIIA)，但不表达抑制性FcγRIIB。人IgG1与大部分人Fc受体结合，并且就其结合的活化性Fc受体的类型而言，视为等同于鼠IgG2a。

[0287] “Fc区”(片段可结晶区域)或“Fc结构域”或“Fc”指抗体重链的C端区域，其介导免疫球蛋白结合于宿主组织或因子，包括结合于免疫系统的各种细胞(例如，效应细胞)上的Fc受体或结合于经典补体系统的第一组分(C1q)。因此，Fc区包含抗体的恒定区，但不包括第一恒定区免疫球蛋白结构域(例如，CH1或CL)。在IgG、IgA和IgD抗体同种型中，Fc区包含从抗体的两条重链的第二(CH2)和第三(CH3)恒定结构域衍生的两个相同蛋白质片段；IgM和IgE的Fc区在每条多肽链中包含三个重链恒定结构域(CH结构域2-4)。对于IgG，Fc区包含免疫球蛋白结构域CH2和CH3和在CH1和CH2结构域之间的铰链区。虽然免疫球蛋白重链Fc区的边界的定义可变动，但如本文定义，将人IgG重链Fc区定义为：对于IgG1从氨基酸残基D221延伸、对于IgG2从V222延伸、对于IgG3从L221延伸，对于IgG4从P224延伸，至重链羧基端，其中如Kabat中，根据EU索引进行编号。人IgG Fc区的CH2结构域从氨基酸237延伸至氨基酸340，并且CH3结构域位于Fc区中CH2结构域的C端侧上，即，它从IgG的氨基酸341延伸至氨基酸447或446(如果C末端赖氨酸残基不存在)或445(如果C末端甘氨酸和赖氨酸残基不存在)。如本文所用，Fc区可以是天然序列Fc，包括任何同种异型变体，或变体Fc(例如，非天然存在的Fc)。Fc还可以指分离的或在包含Fc的蛋白质多肽(如“包含Fc区的结合蛋白”，也称作“Fc融合蛋白”(例如，抗体或免疫黏附素))中的此区域。

[0288] “天然序列Fc区”或“天然序列Fc”包含与自然界中存在的Fc区的氨基酸序列相同的氨基酸序列。天然序列人Fc区包括天然序列人IgG1 Fc区；天然序列人IgG2 Fc区；天然序列人IgG3 Fc区；和天然序列人IgG4 Fc区，以及其天然存在的变体。天然序列Fc包括Fc的多

种同种异型(参见,例如,Jefferis等人(2009)mAbs 1:1)。

[0289] 如本文所用的术语“天然存在的”,当用于某对象时,指某对象可以存在于自然界这一事实。例如,存在于下述生物(包括病毒)中的多肽或多核苷酸序列是天然存在的,所述生物可以从自然来源分离并且尚未被有意地在实验室中人为修饰。

[0290] “多肽”指包含至少两个连续连接的氨基酸残基的链,链长度无上限。蛋白质中的一个或多个氨基酸残基可以含有修饰,如,但不限于,糖基化、磷酸化或二硫键形成。“蛋白质”可以包含一个或多个多肽。

[0291] “保守性氨基酸置换”指将氨基酸残基用具有相似侧链的氨基酸残基置换。已经在本领域中定义了具有相似侧链的氨基酸残基的家族。这些家族包括具有碱性侧链(例如,赖氨酸、精氨酸、组氨酸)、酸性侧链(例如,天冬氨酸、谷氨酸)、不带电荷极性侧链(例如,甘氨酸、天冬酰胺、谷氨酰胺、丝氨酸、苏氨酸、酪氨酸、半胱氨酸、色氨酸)、非极性侧链(例如,丙氨酸、缬氨酸、亮氨酸、异亮氨酸、脯氨酸、苯丙氨酸、甲硫氨酸)、β-分支的侧链(例如,苏氨酸、缬氨酸、异亮氨酸)和芳族侧链(例如,酪氨酸、苯丙氨酸、色氨酸、组氨酸)的氨基酸。在某些实施方案中,抗TIM3抗体中预测的非必需氨基酸残基可以替换为来自相同侧链家族的另一个氨基酸残基。本领域熟知鉴定不消除抗原结合作用的核苷酸及氨基酸保守性置换的方法(参见,例如Brummell等人,Biochem.32:1180-1187(1993);Kobayashi等人,Protein Eng.12(10):879-884(1999);和Burks等人,Proc.Natl.Acad.Sci.USA 94:412-417(1997))。

[0292] 对于多肽,术语“基本上同源”表示,在最佳对齐和比较时(具有适宜的氨基酸插入或缺失),两种多肽或其指定的序列在至少约80%的氨基酸、至少约90%至95%或至少约98%至99.5%的氨基酸中相同。

[0293] 考虑到需要为最佳比对这两个序列而导入的空位的数目和每个空位的长度,两个序列之间的同一性百分数是所述序列共有的相同位置的函数(即,%同源性=相同位置数#/位置总数#x 100)。可以使用如下文非限制性实例中所述的数学算法,完成序列的比较和两个序列之间同一性百分数的确定。

[0294] 如本文所用,术语“载体”意指能够运输已经与之连接的另一个核酸的核酸分子。一个类型的载体是“质粒”,其指可以向其中连接额外DNA区段的环状双链DNA环。另一类型的载体是病毒载体,其中额外的DNA区段可以连入病毒基因组中。某些载体能够在导入它们的宿主细胞中自主复制(例如,具有细菌复制起点的细菌载体和附加体型哺乳动物载体)。其他载体(例如非附加体型哺乳动物载体)可以在导入宿主细胞时整合到该宿主细胞的基因组中,并因而随宿主基因组一起复制。另外,某些载体能够指导与它们有效连接的基因表达。此类载体在本文中称作“重组表达载体”(或简单地称作,“表达载体”)。通常,重组DNA技术中使用的表达载体经常为质粒形式。在本说明书中,“质粒”和“载体”可以互换地使用,因为质粒是最常用形式的载体。然而,还包括起到同等功能的其他形式的表达载体,如病毒载体(例如,复制缺陷型逆转录病毒、腺病毒和腺相关病毒)。

[0295] “免疫应答”是如本领域那样理解,并且通常指脊椎动物对外来物或异常(例如,癌性)细胞的生物学应答,所述应答保护生物对抗这些物质和因其所致的疾病。“免疫应答”由一种或多种免疫系统细胞(例如,T淋巴细胞、B淋巴细胞、自然杀伤(NK)细胞、巨噬细胞、嗜酸性粒细胞、肥大细胞、树状细胞或嗜中性粒细胞)以及这些细胞中任意者或肝脏产生的可

溶性大分子(包括抗体、细胞因子和补体)的作用介导,所述作用导致选择性靶向、结合、损伤、摧毁和/或从脊椎动物的身体消除正在入侵的病原体、遭病原体感染的细胞或组织、癌性细胞或其他异常细胞、或在自身免疫性或病理炎症情况下人体正常细胞或组织。免疫应答包括例如,活化或抑制T细胞,例如,效应T细胞、Th细胞、CD4+细胞、CD8+T细胞或Treg细胞,或活化或抑制免疫系统的任何其他细胞,例如,NK细胞。

[0296] “免疫调整剂(immunomodulator)”或“免疫调节剂(immunoregulator)”指一种物质,例如,一种靶向可能参与调整、调节或修饰免疫应答的信号传导途径组分的物质。“调整”、“调节”或“修饰”免疫应答指,免疫系统细胞、或这类细胞(例如,效应T细胞,如Th1细胞)的活性方面的任何改变。这种调节作用包括刺激或抑制免疫系统,这可以表现为各种细胞类型的数目升高或降低、这些细胞的活性增加或减少、或可以在免疫系统内部发生的任何其他变化。已经鉴定抑制性和刺激性免疫调节剂,其中某些可以在肿瘤微环境中具有增强的功能。在一些实施方案中,免疫调节剂靶向T细胞表面上的分子。“免疫调节靶”或“免疫调节性靶”是通过物质、药剂、结构部分、化合物或分子结合而被靶向的、且其活性因所述结合而改变的分子,例如,细胞表面分子。免疫调节性靶包括例如,细胞表面上的受体(“免疫调节性受体”)和受体配体(“免疫调节性配体”)。

[0297] “免疫治疗”指,通过包括诱导、增强、阻抑或以其他方式改变免疫系统或免疫应答的方法,来治疗罹患疾病、或有感染疾病风险、或遭遇疾病复发的受试者。

[0298] “免疫刺激疗法”或“免疫刺激性疗法”指,导致受试者中免疫应答增加(诱导或增强)以例如治疗癌症的疗法。

[0299] “T效应细胞”(“Teff”)细胞指,具有溶胞活性的T细胞(例如,CD4+T细胞和CD8+T细胞)、以及分泌细胞因子并活化和指引其他免疫细胞的辅助T(Th)细胞,例如,Th1细胞,但不包括调节性T细胞(Treg细胞)。本文所述的某些抗TIM3抗体活化Teff细胞,例如,CD4+和CD8+Teff细胞和Th1细胞。

[0300] 增加的刺激免疫应答或免疫系统的能力,可以因T细胞共刺激受体的增强的激动剂活性和/或抑制性受体的增强的拮抗剂活性而产生。增加的刺激免疫应答或免疫系统的能力可以由测量免疫应答的测定法中EC_{50}或最大活性水平的倍数增长来反映,所述测定法可以为例如,测量在细胞因子或趋化因子释放、溶细胞活性(在靶细胞上直接确定或通过检测CD107a或颗粒酶间接确定)、以及增殖方面变化的测定法。刺激免疫应答或免疫系统活性的能力可以被增强至少10%、30%、50%、75%、2倍、3倍、5倍或更多倍。

[0301] 如本文所用,术语“连接”指两个或更多个分子的缔合。连接可以是共价或非共价的。连接还可以是遗传的(即,重组融合)。可以使用多种类型的本领域公知技术,如化学缀合和产生重组蛋白,来实现这类连接。

[0302] 如本文所用,“施用”指,使用本领域技术人员已知的多种方法和递送系统中的任何,向受试者物理引入包含治疗剂的组合物。对于本文所述的抗TIM3抗体,不同施用途径包括静脉内、腹膜内、肌内、皮下、脊柱或其他肠胃外施用途径,例如通过注射或输注。如本文所用,短语“肠胃外施用”意指,除了肠内和局部施用之外的施用模式,通常通过注射进行,并且包括而不限于静脉内、肌内、腹膜内、动脉内、鞘内、淋巴内、病灶内、囊内、眶内、心内、皮内、经气管、皮下、角质层下、关节内、被膜下、蛛网膜下、椎管内、硬膜外和胸骨内注射和输注,以及体内电穿孔。备选地,本发明所述的抗体可以通过非肠胃外途径,如局部、表皮或

粘膜施用途径，例如鼻内、口服、阴道、直肠、舌下或局部地施用。施用也可以例如，一次、多次和/或历经一个或多个长时段进行。

[0303] 如本文所用，术语“T细胞介导的应答”指由T细胞介导的应答，所述T细胞包括效应T细胞(例如，CD8+细胞)和辅助T细胞(例如，CD4+细胞)。T细胞介导的应答例如包括T细胞细胞毒性和增殖。

[0304] 如本文所用，术语“细胞毒T淋巴细胞(CTL)应答”指，由细胞毒T细胞诱导的免疫应答。CTL反应主要由CD8+T细胞介导。

[0305] 如本文所用，术语“抑制”或“阻断”(例如，指抑制/阻断TIM3配体(“TIM3-L”)与细胞上TIM3结合)可以互换使用并且涵盖部分和完全抑制/阻断。在一些实施方案中，抗TIM3抗体对TIM3-L与TIM3的结合造成至少约50％，例如，约60％、70％、80％、90％、95％、99％或100％的抑制，例如，如本文进一步描述那样测定。在一些实施方案中，抗TIM3抗体对TIM3-L与TIM3的结合造成的抑制不多于50％，例如，约40％、30％、20％、10％、5％或1％，例如，如本文进一步描述那样测定。

[0306] 如本文所用，短语“抑制肿瘤生长”包括任何可度量的肿瘤生长减少，例如，抑制肿瘤生长至少约10％、例如，至少约20％、至少约30％、至少约40％、至少约50％、至少约60％、至少约70％、至少约80％、至少约90％、至少约99％或100％。

[0307] 如本文所用，“癌症”指宽泛类别的多种疾病，其特征在于身体内异常细胞的失控生长。失调的细胞分裂可以导致形成恶性肿瘤或细胞，后者侵入临近组织并且可以通过淋巴系统或血流转移到身体远端部分。“癌症”或“癌组织”可以包括肿瘤。

[0308] 如本文所用的术语“肿瘤”指，因细胞过度生长或增殖产生的任何组织团块，良性的(非癌)或恶性的(癌性的)，包括癌前病灶。

[0309] “肿瘤浸润型炎性细胞”是，典型地参与受试者中炎症反应并浸润肿瘤组织的任何类型细胞。这类细胞包括肿瘤浸润型淋巴细胞(TIL)、巨噬细胞、单核细胞、嗜酸性粒细胞、组织细胞和树状细胞。

[0310] 如本文所用，“TIL”或“肿瘤浸润型淋巴细胞”指肿瘤浸润型淋巴细胞和其他非淋巴细胞性单核免疫细胞。

[0311] “响应于TIM3拮抗剂治疗”的癌症患者指，如肿瘤大小(例如，治疗后肿瘤尺寸更小或无肿瘤)、肿瘤生长速率(例如，治疗后生长更慢或停止生长)、肿瘤细胞数目(例如，治疗后肿瘤细胞数目减少)、免疫系统活性(例如，对外来抗原的活性更高和/或T细胞耗竭减少)或其任意组合所反映的，显示癌症改善的患者。

[0312] 如本文所用的术语“治疗”指，对受试者进行的任何类型干预或过程或向其施用活性剂，目的在于逆转、减轻、缓解、抑制、或减慢、或阻止症状、并发症、病状、或与疾病相关的生物化学指标的发展、进展、严重程度或复发，或增强总生存期。治疗可以涉及患有疾病的受试者或未患有疾病的受试者(例如，用于预防)。

[0313] “程序性死亡-1(PD-1)”指属于CD28家族的免疫抑制性受体。PD-1在体内主要地表达于事先活化的T细胞上，并且结合于二种配体PD-L1和PD-L2。如本文所用的术语“PD-1”包括人PD-1(hPD-1)、hPD-1的变体、同种型和物种同源物，及具有至少一个与hPD-1共同的表位的类似物。可以依据GenBank登录号U64863找到完整hPD-1序列。

[0314] “程序性死亡配体-1(PD-L1)”是PD-1的两种细胞表面糖蛋白配体之一(另一者是

PD-L2)，其与PD-1结合时下调T细胞活化和细胞因子分泌。如本文所用的术语“PD-L1”包括人PD-L1(hPD-L1)、hPD-L1的变体、同种型和物种同源物、及具有至少一个与hPD-L1共同的表位的类似物。可以依据GenBank登录号Q9NZQ7找到完整hPD-L1序列。

[0315] 如本文所用的术语“PD-1/PD-L1轴拮抗剂”是抑制PD-1和PD-L1之间相互作用的药剂。如本文所用，PD-1/PD-L1轴结合拮抗剂包括PD-1结合拮抗剂和PD-L1结合拮抗剂。

[0316] 术语“效应记忆TIL”和“效应记忆T细胞”指本公开中表征为CCR7-CD45RO+的T淋巴细胞。

[0317] 术语“中央记忆TIL”和”中央记忆T细胞”指本公开中表征为CCR7+CD45RO+的T淋巴细胞。

[0318] 术语“幼稚TIL”和“幼稚T细胞”指本公开中表征为CCR7+CD45RO-的T淋巴细胞。

[0319] 术语“效应TIL”和“效应T细胞”指本公开中表征为CCR7-CD45RO-的T淋巴细胞。

[0320] “血液恶性肿瘤”包括淋巴瘤、白血病、骨髓瘤、或淋巴样恶性瘤、以及脾和淋巴结的癌症。示例性淋巴瘤包括B细胞淋巴瘤(B细胞血液学癌症)和T细胞淋巴瘤。B细胞淋巴瘤包括霍奇金氏淋巴瘤和大部分非霍奇金淋巴瘤。B细胞淋巴瘤的非限制性实例包括弥漫性大B细胞淋巴瘤、滤泡淋巴瘤、粘膜相关的淋巴组织淋巴瘤、小细胞淋巴细胞性淋巴瘤(与慢性淋巴细胞白血病重叠)、套细胞淋巴瘤(MCL)、Burkitt淋巴瘤、纵隔大B细胞淋巴瘤、Waldenstrom巨球蛋白血症、淋巴结边缘区B细胞淋巴瘤、脾边缘区淋巴瘤、血管内大B细胞淋巴瘤、原发性渗出性淋巴瘤、淋巴瘤样肉芽肿。T细胞淋巴瘤的非限制性实例包括结外T细胞淋巴瘤、皮肤T细胞淋巴瘤、间变性大细胞淋巴瘤和血管免疫母细胞性T细胞淋巴瘤。血液学恶性肿瘤还包括白血病，如，但不限于，继发性白血病、慢性淋巴细胞白血病、急性髓细胞白血病、慢性髓性白血病和急性淋巴母细胞性白血病。血液学恶性肿瘤还包括骨髓瘤，如，但不限于，多发性骨髓瘤和冒烟型(smoldering)多发性骨髓瘤。术语“血液恶性肿瘤”也涵盖其他血液学癌症和/或B细胞相关或T细胞相关的癌症。

[0321] 术语“有效剂量”或“有效的剂量”定义为足以实现或至少部分实现所需效果的量。“治疗有效量”或“治疗有效剂量”的药物或治疗剂是下述任何量的药物，其中单独使用或与另一种治疗药组合使用时，所述量的药物促进疾病消退，所述消退可以由疾病症状的严重程度降低、无疾病症状期的频率和持续时间的增加、或因疾病侵袭所致的损伤或致残的防止来反映。药物的治疗有效量或剂量包括“预防有效量”或“预防有效剂量”，其是下述任何量的药物，其中单独施用或与另一种治疗药组合施用至有罹患疾病或遭遇疾病复发风险的受试者时，所述量的药物抑制该疾病的形成或复发。可以使用本领域技术人员已知的多种方法，如在临床试验期间在人类受试者中，在预示人体内功效的动物模型系统中、或通过体外测定法中分析药剂的活性，来评价治疗剂促进疾病消退或抑制疾病形成或复发的能力。

[0322] 例如，抗癌药可以是促进受试者中癌症消退的药物。在一些实施方案中，治疗有效量的药物促进癌症消退到消除癌症的程度。“促进癌症消退”意指，单独或与抗肿瘤药组合施用有效量的药物时，导致肿瘤生长或大小的减少、肿瘤坏死、至少一种疾病症状的严重程度下降、无疾病症状期的频率和持续时间的增加、防止因疾病侵袭所致的损伤或致残、或以其它方式改善患者中的疾病症状。此外，相对于治疗而言的术语“有效”和”有效性”包括药理学有效性和生理学安全性两者。药理学有效性指药物能够促进患者中癌症消退的能力。生理学安全性指，因施用药物带来的、在细胞、器官和/或生物体层面上的毒性或其他不良

生理效应的水平(不良作用)。

[0323] 以治疗肿瘤为例,相对于未治疗的受试者,药物的治疗有效量或剂量抑制细胞生长或肿瘤生长至少约20%、至少约40%、至少约60%或至少约80%。在一些实施方案中,药物的治疗有效量或剂量完全抑制细胞生长或肿瘤生长,即,抑制细胞生长或肿瘤生长达100%。可以使用下述测定法评价化合物抑制肿瘤生长的能力。备选地,可以通过检查化合物抑制细胞生长的能力,评价组合物的这种特性,可以通过本领域技术人员已知的测定法,体外测量这种抑制作用。在本文所述的其他实施方案中,可以观察到肿瘤消退并且其持续至少约20天、至少约40天或至少约60天时间。

[0324] 术语“患者”指人(或人类受试者)。

[0325] 如本文所用,术语“受试者”指人类受试者。受试者可以是患有癌症的受试者。

[0326] 如本文提到的术语“基于体重”的剂量或给药意指,基于患者体重,计算向患者施用的剂量。例如,当体重60kg的患者需要3mg/kg抗TIM3抗体时,可以计算并使用适宜量的抗TIM3抗体(即,180mg)供施用。

[0327] 就本公开的方法而言,术语“固定剂量”的应用意指,在单一组合物中两种或更多种不同抗体(例如,抗TIM3抗体和第二抗体、例如,PD-1或PD-L1抗体)按照彼此特定(固定)的比率存在于该组合物中。在一些实施方案中,固定剂量基于抗体重量(例如,mg)。在某些实施方案中,固定剂量基于抗体浓度(例如,mg/ml)。在一些实施方案中,两种抗体(例如,抗TIM3和抗PD1或抗PD-L1)的比率是至少约1:1、约1:2、约1:3、约1:4、约1:5、约1:6、约1:7、约1:8、约1:9、约1:10、约1:15、约1:20、约1:30、约1:40、约1:50、约1:60、约1:70、约1:80、约1:90、约1:100、约1:120、约1:140、约1:160、约1:180、约1:200、约200:1、约180:1、约160:1、约140:1、约120:1、约100:1、约90:1、约80:1、约70:1、约60:1、约50:1、约40:1、约30:1、约20:1、约15:1、约10:1、约9:1、约8:1、约7:1、约6:1、约5:1、约4:1、约3:1或约2:1mg第一抗体(例如,抗TIM3抗体):mg第二抗体。例如,2:1比率的抗TIM3抗体和PD-1抗体如纳武单抗可以意指,小瓶或注射剂可以含有约480mg抗TIM3抗体和240mg抗PD-1抗体、或约2mg/ml抗TIM3抗体和1mg/ml抗PD-1抗体。

[0328] 就本文所述的方法和剂量而言,术语“平剂量”(flat dose)的应用意指,不考虑患者体重或体表面积(BSA)情况下向患者施用的剂量。平剂量因此不按mg/kg剂量提供,而以药物(例如,抗-TIM3)的绝对量提供。例如,一个60kg的人和一个100kg的人将接受相同剂量的抗体(例如,480mg抗TIM3抗体)。

[0329] 如本文所用,术语“ug”和”uM”分别与“μg”和“μM”互换使用。

[0330] 以下子部分进一步详细本文所述的多个方面。

[0331] 本公开的方法

[0332] 本公开涉及鉴定如下受试者(例如,人类癌症患者)的方法,所述受试者适于用抗TIM3拮抗剂(例如,抗TIM3抗体)单独或结合其它免疫检查点抑制剂(例如,抗PD-1抗体)一起治疗。

[0333] 在一些实施方案中,本文公开的方法包括,测量或确定受试者的血清中可溶性TIM3的浓度(“血清TIM3浓度”)并且将该浓度与对照受试者(例如,健康患者)的血清TIM3浓度比较。如果受试者的血清TIM3浓度高于对照受试者,则受试者可能响应于抗TIM3拮抗剂治疗。在一些实施方案中,可能响应于抗TIM3拮抗剂治疗的受试者具有比对照受试者中观

察的浓度高至少10％的血清TIM3浓度。在其他实施方案中，受试者的血清TIM3浓度高于对照受试者至少20％、30％、40％、50％、60％、70％、80％、90％或100％(2倍)。在其他实施方案中，受试者的血清TIM3浓度是至少2500pg/mL或至少3000pg/mL。

[0334] 在一些实施方案中，本文所公开的方法包括，测量或确定受试者中呈TIM3阳性的肿瘤浸润型淋巴细胞(TIL)的百分数。在其他实施方案中，如果受试者中至少10％、20％、30％、40％、50％、60％或70％的TIL呈TIM3阳性，则受试者可能响应于TIM3拮抗剂治疗。在某些实施方案中，本文所公开的方法包括测量或确定受试者中呈TIM3阳性的$CD8^+$肿瘤浸润型淋巴细胞(TIL)的百分数。在一些实施方案中，如果受试者中至少10％、20％、30％、40％、50％、60％或70％的$CD8^+$TIL呈TIM3阳性，则受试者可能响应于TIM3拮抗剂治疗。在某些实施方案中，本文所公开的方法包括测量或确定受试者中呈TIM3阳性的$CD4^+$肿瘤浸润型淋巴细胞(TIL)的百分数。在一些实施方案中，如果受试者中至少10％、20％、30％、40％、50％、60％或70％的$CD4^+$TIL呈TIM3阳性，则受试者可能响应于TIM3拮抗剂治疗。在一些实施方案中，本文所公开的方法包括测量或确定受试者中呈TIM3阳性的$CD4^+$和$CD8^+$肿瘤浸润型淋巴细胞(TIL)的百分数。在其他实施方案中，如果受试者中至少10％、20％、30％、40％、50％、60％或70％的$CD4^+$和/或$CD8^+$TIL呈TIM3阳性，则受试者可能响应于TIM3拮抗剂治疗。

[0335] 在一些实施方案中，该方法包括测量或确定呈TIM3阳性的幼稚(CCR7+CD45RO-)、中央记忆(CM)(CCR7+CD45RO+)、效应记忆(EM)(CCR7-CDRO+)和效应(Teff)(CCR7-CD45RO-)TIL的百分数。如果TIM3阳性EM和/或Teff TIL的百分数高于TIM3阳性幼稚或CM TIL的百分数，则受试者可能响应于TIM3拮抗剂治疗。在一些实施方案中，TIL是CD4+TIL。在其他实施方案中，TIL是CD8+TIL。

[0336] 在一些实施方案中，本文所公开的方法允许鉴定适于TIM3拮抗剂和PD-1拮抗剂组合治疗的受试者(例如，人类癌症患者)。可以通过以下方式鉴定这类受试者：测量或确定受试者中呈PD-1阳性和TIM3阳性的肿瘤浸润型淋巴细胞(TIL)的百分数，其中如果至少5％的TIL呈PD-1和TIM3阳性，则受试者可能响应于包含TIM3拮抗剂和PD-1拮抗剂二者的治疗。在一些实施方案中，PD-1和TIM3二者在至少10％、20％、30％或40％的TIL上共表达表示，受试者可能响应于包含TIM-3拮抗剂和PD-1拮抗剂二者的治疗。在一些实施方案中，TIL是CD4+TIL。在其他实施方案中，TIL是CD8+TIL。在某些实施方案中，如果至少5％、10％、20％、30％或40％的CD4+和CD8+TIL呈PD-1和TIM3阳性，则受试者可能响应于包含TIM3拮抗剂和PD-1拮抗剂二者的治疗。

[0337] 本公开还提供治疗适于TIM3拮抗剂(例如，抗TIM3抗体)治疗的受试者(例如，人类癌症患者)的方法，所述方法包括向受试者施用治疗有效量的TIM3拮抗剂。可以通过上文描述的任一方法鉴定适合TIM3拮抗剂治疗的受试者。受试者可以适于TIM3拮抗剂单独治疗或结合其它免疫检查点抑制剂(例如，抗PD-1抗体)的治疗。

[0338] 在一些实施方案中，适于TIM3拮抗剂治疗的受试者在血清中的可溶性TIM3浓度(“血清TIM3浓度”)高于对照受试者(例如，健康患者)的血清中观察到的可溶性TIM3浓度。在一些实施方案中，受试者的血清TIM3浓度比对照受试者中观察的浓度高至少10％。在其他实施方案中，受试者的血清TIM3浓度高于对照受试者至少20％、30％、40％、50％、60％、70％、80％、90％或100％(2倍)。在某些实施方案中，受试者的血清TIM3浓度是至少2500pg/mL或至少3000pg/mL。在一些实施方案中，施用之前测量或确定受试者的血清TIM3浓度，并

且如果受试者的血清TIM3浓度高于对照受试者，则向受试者施用治疗有效量的TIM3拮抗剂。

[0339] 在一些实施方案中，适于TIM3拮抗剂治疗的受试者具有至少10％、20％、30％、40％、50％、60％或70％呈TIM3阳性的CD8+TIL。在一些实施方案中，施用之前确定TIM3阳性CD8+TIL的百分数并且如果该百分数高于总CD8+TIL的10％、20％、30％、40％、50％、60％或70％，则向受试者施用治疗有效量的TIM3拮抗剂。

[0340] 在一些实施方案中，可以通过测量或确定呈TIM3阳性的幼稚、中央记忆(CM)、效应记忆(EM)和效应(Teff)TIL的百分数，鉴定适于TIM3拮抗剂治疗的受试者。如果TIM3阳性EM和/或Teff TIL的百分数高于TIM3阳性幼稚或CM TIL的百分数，则向受试者施用治疗有效量的TIM3拮抗剂。在一些实施方案中，TIL是CD4+TIL。在其他实施方案中，TIL是CD8+TIL。在某些实施方案中，施用之前确定TIM3阳性幼稚、CM、EM、Teff TIL的百分数并且如果TIM3阳性EM和/或Teff TIL的百分数高于幼稚和/或CM TIL的百分数，则向受试者施用治疗有效量的TIM3拮抗剂。

[0341] 本文中还提供治疗适于用TIM3拮抗剂和PD-1拮抗剂组合治疗的受试者的方法，所述方法包括向这类受试者施用治疗有效量的PD-1拮抗剂和TIM3拮抗剂组合。在一个实施方案中，如果至少5％的受试者CD8+TIL呈PD1和TIM3表达二者阳性，则向受试者施用PD1拮抗剂和TIM3拮抗剂的组合。在一些实施方案中，受试者中表达PD-1和TIM3二者的CD8+TIL百分数是至少10％、20％、30％、40％、50％、60％或70％。在一个具体实施方案中，施用PD-1拮抗剂和TIM3拮抗剂的组合之前确定受试者中表达PD-1和TIM3二者的CD8+TIL的百分数。

[0342] 在一个实施方案中，如果至少5％的受试者CD4+TIL呈PD-1和TIM3表达二者阳性，则向受试者施用TIM3拮抗剂和PD-1拮抗剂的组合。在一些实施方案中，受试者中表达PD-1和TIM3二者的CD4+TIL百分数是至少10％、20％、30％、40％、50％、60％或70％。在某些具体实施方案中，施用PD-1拮抗剂和TIM3拮抗剂组合之前确定受试者中表达PD-1和TIM3二者的CD4+TIL的百分数。

[0343] 在一些实施方案中，如果至少5％的受试者CD8+和CD4+TIL呈PD-1和TIM3表达二者阳性，则向受试者施用TIM3拮抗剂和PD-1拮抗剂的组合。在一些实施方案中，受试者中表达PD-1和TIM3二者的CD8+和CD4+TIL百分数是至少10％、20％、30％、40％、50％、60％或70％。在某些具体实施方案中，施用PD-1拮抗剂和TIM3拮抗剂的组合之前确定受试者中表达PD-1和TIM3二者的CD4+和CD8+TIL的百分数。

[0344] 在一些实施方案中，TIM3拮抗剂与治疗有效量的PD-1拮抗剂(例如，抗PD-1抗体或抗PD-L1抗体)组合施用。在一些实施方案中，将PD-1拮抗剂(例如，抗PD-1抗体或抗PD-L1抗体)按范围从约80mg到约1280mg的平剂量或范围从约1mg/kg到约12mg/kg的基于体重的剂量施用。

[0345] 在一些实施方案中，与TIM3拮抗剂组合使用的PD-1拮抗剂(例如，抗PD-1抗体或抗PD-L1抗体)按约100mg、约200mg、约300mg、约400mg、约500mg、约600mg、约700mg、约800mg、约900mg、约1000mg、约1100mg或约1200mg的平剂量施用。

[0346] 在一些实施方案中，与TIM3拮抗剂组合使用的PD-1拮抗剂(例如，抗PD-1抗体或抗PD-L1抗体)按约1mg/kg、约2mg/kg、约3mg/kg、约4mg/kg、约5mg/kg、约6mg/kg、约7mg/kg、约8mg/kg、约9mg/kg、约10mg/kg、约11mg/kg或约12mg/kg基于体重的剂量施用。

[0347] 在一些实施方案中，用于TIM3拮抗剂(例如，抗TIM3抗体)组合疗法的PD-1拮抗剂(例如，抗PD-1抗体或抗PD-L1抗体)按约1周、约2周、约3周、约4周、约5周或约6周的给药间隔施用。在一些实施方案中，PD-1拮抗剂(例如，抗PD-1抗体或抗PD-L1抗体)的给药间隔是约2周。在一些实施方案中，PD-1拮抗剂(例如，抗PD-1抗体或抗PD-L1抗体)的给药间隔是约3周。在一些实施方案中，PD-1拮抗剂(例如，抗PD-1抗体或抗PD-L1抗体)的给药间隔是约4周。

[0348] 在一些实施方案中，每2周按约10mg/kg的基于体重的剂量施用PD-1拮抗剂。在一些实施方案中，每2周按约240mg的平剂量施用PD-1拮抗剂。在一些实施方案中，每4周按约480mg的平剂量施用PD-1拮抗剂。在一些实施方案中，每3周按约2mg/kg的基于体重的剂量施用PD-1拮抗剂。在一些实施方案中，每3周按约1200mg的平剂量施用PD-1拮抗剂。在一些实施方案中，每3周按约200mg的平剂量施用PD-1拮抗剂。

[0349] 本公开进一步提供在有需要的受试者(例如，人类癌症患者)中评估包含TIM3拮抗剂的治疗的功效的方法，所述方法包括确定或测量受试者中可溶性TIM3的血清滴度，其中受试者中可溶性TIM3的血清滴度指示受试者对治疗的反应(例如，疾病正常化，例如，免疫监视恢复)。在一个实施方案中，可溶性TIM3的正常血清滴度(例如，与对照受试者(例如，健康患者)中观察到的水平相当)提示该治疗在受试者中有效。在一个实施方案中，介于治疗前受试者中血清滴度和可溶性TIM3的正常血清滴度(例如，与对照受试者(例如，健康患者)中观察到的水平相当)之间的可溶性TIM3血清滴度，指示该治疗在受试者中有效。

[0350] 本公开提供在有需要的受试者(例如，人类癌症患者)中评估包含TIM3拮抗剂的治疗的功效的方法，所述方法包括确定或测量受试者中可溶性TIM3的血清滴度，其中受试者中可溶性TIM3的血清滴度指示受试者对治疗的反应。在一些实施方案中，向患有癌症的受试者施用第一剂TIIM3拮抗剂，并且在受试者的外周血中测量可溶性TIM3的水平，其中可溶性TIM3水平下降指示受试者响应于TIM3拮抗剂，并指示可以向受试者施用进一步剂量。在一些实施方案中，向患有癌症的受试者施用2剂或更多剂TIIM3拮抗剂，并且在受试者的外周血中测量可溶性TIM3的水平，其中可溶性TIM3水平下降指示受试者响应于TIM3拮抗剂，并指示可以向受试者施用进一步剂量。在一些实施方案中，向患有癌症的受试者施用1剂、2剂或更多剂TIM3拮抗剂，并且在不同时间测量受试者的外周血中可溶性TIM3的水平，其中基于受试者的外周血中可溶性TIM3降低的水平，调节向受试者施用的TIM3剂量。例如，如果在施用某给定剂量的TIM3拮抗剂后，可溶性TIM3的水平未显著地降低，则可以施用更高剂量。因此，通常，血液可溶性TIM3水平可以用作待用TIM3拮抗剂治疗的受试者的预测性或分层标志物。指示进一步TIM3拮抗剂治疗是合理的可溶性TIM3下降可以是至少5％、10％、20％、25％、30％、50％、75％、90％或100％的可溶性TIM3下降。在某些实施方案中，指示进一步TIM3拮抗剂治疗是合理的可溶性TIM3下降是至少5％、10％、20％、25％、30％、50％、75％、90％或100％的可溶性TIM3同种型下降。在某些实施方案中，指示进一步TIM3拮抗剂治疗是合理的可溶性TIM3下降是，从细胞表面脱落的TIM3的至少5％、10％、20％、25％、30％、50％、75％、90％或100％下降。在某些实施方案中，指示进一步TIM3拮抗剂治疗是合理的可溶性TIM3下降是，可溶性TIM3同种型和/或从细胞表面脱落的TIM3(以任何比率)的至少5％、10％、20％、25％、30％、50％、75％、90％或100％的下降。

[0351] 在一些实施方案中，有效性治疗可以治疗癌症(例如，减少或维持肿瘤大小)和/或

减少或减轻与癌症相关的症状。在某些实施方案中，与治疗之前的肿瘤大小相比，有效性治疗减少肿瘤大小至少约10％、约20％、约30％、约40％或约50％。

[0352] 在一些实施方案中，有效性治疗可以有效地增加受试者的存活持续时间，例如，受试者的总生存期。在某些实施方案中，有效性治疗增加受试者的总生存期至少约6个月、至少约7个月、至少约8个月、至少约9个月、至少约10个月、至少约11个月、至少约12个月、至少约13个月、至少约14个月、至少约15个月、至少约16个月、至少约17个月、至少约18个月、至少约19个月、至少约20个月、至少约21个月、至少约22个月、至少约23个月、至少约24个月、至少约25个月、至少约26个月、至少约27个月、至少约28个月、至少约29个月、至少约30个月、至少约3年、至少约3.5年、至少约4年、至少约4.5年、至少约5年或至少约10年。

[0353] 在一些实施方案中，有效性治疗增加受试者的无进展生存期的持续时间。在一些实施方案中，有效性治疗增加受试者的无进展生存期的持续时间至少约1个月、至少约2个月、至少约3个月、至少约4个月、至少约5个月、至少约6个月、至少约7个月、至少约8个月、至少约9个月、至少约10个月、至少约11个月、至少约1年、至少约15个月、至少约18个月、至少约2年、至少约3年、至少约4年或至少约5年。

[0354] 在其他实施方案中，例如，在TIL中，确定TIM3+髓样亚类或TIM3+NK细胞亚类的频率。例如，可以在患有癌症的受试者中确定pDC、mDC、或CD14+髓样细胞中或CD16-CD56+或CD16+CD56+NK细胞中TIM3+细胞的频率，其中这些类型细胞的一者或多者中TIM3+细胞的频率预示对TIM-3拮抗剂的响应。

[0355] 测量细胞群体当中TIM3表达和TIM3阳性细胞频率

[0356] 本公开提供鉴定如下受试者(例如，人类癌症患者)的方法，所述受试者适于用TIM3拮抗剂单独或组合其它免疫检查点抑制剂(例如，PD-1拮抗剂)治疗，所述方法包括测量或确定从受试者获得的组织样品中的TIM3表达。TIM3表达的测量或确定方法可以通过本文所述或本领域已知的任何方法来实施。

[0357] 在一些实施方案中，从受试者获得的组织样品包括但不限于，任何有临床意义的组织样品，如肿瘤活检样品、取芯活检组织样品、细针抽吸物、或体液(如血液、血浆、血清、淋巴液、腹水、囊液或尿)样品。在一些实施方案中，组织样品来自转移灶。在一些实施方案中，在多个时间点，例如，治疗前、治疗期间和/或治疗后，从受试者取得组织样品。在一些实施方案中，组织样品取自受试者中的不同位置，例如，来自原发肿瘤的样品和来自远端位置的转移灶的样品。

[0358] 在一些实施方案中，可以在不从受试者获得组织样品的情况下实现确定TIM3表达。在一些实施方案中，鉴定适合TIM3拮抗剂治疗的受试者包括(i)任选地提供从受试者获得的组织样品，其中组织样品包含肿瘤细胞和/或肿瘤浸润型炎性细胞(例如，TIL)；和(ii)考虑对照受试者(例如，健康患者)中表达的水平，测量或确定组织样品中表达TIM3的细胞的百分数。

[0359] 在包括确定或测量组织样品中TIM3表达的本文所述任何方法中，应当理解，包括从患者获得组织样品的步骤是任选的步骤。即，在某些实施方案中，该方法包括这个步骤，而在其他实施方案中不包括这个步骤。还应当理解在某些实施方案中，测量或确定TIM3表达的步骤通过分析TIM3表达的变换性方法(例如，流式细胞术)来执行。在其他实施方案中，不涉及变换性步骤，并且例如通过查看来自实验室的检验结果报告，确定TIM3表达。在某些

实施方案中，至多(并包括)确定或测量TIM3表达结果的这些方法的步骤，提供了中间结果，其中可以将所述中间结果提供给医师或其他医疗保健提供者，用于选择适于TIM3拮抗剂单独或结合其它免疫检查点抑制剂(例如，TIM3拮抗剂)治疗的候选者。在某些实施方案中，提供中间结果的步骤由医疗执业者或依据医疗执业者的指令行事的个体执行。在其他实施方案中，这些步骤由独立的实验室或由独立人员如实验室技师执行。

[0360] 在一些实施方案中，通过执行检测TIM3 RNA存在的测定法，评估表达TIM3的细胞的比例。在其他实施方案中，通过RT-PCR、原位杂交或RNA酶保护法，检测TIM3 RNA的存在。在一些实施方案中，通过基于RT-PCR的测定法检测TIM3 RNA的存在。在其他实施方案中，评分基于RT-PCR的测定包括，相对于(例如，对照受试者中观察到的)预定水平，测量或确定组织样品中TIM3 RNA表达的水平。

[0361] 在一些实施方案中，通过执行检测TIM3蛋白存在的测定法，评估表达TIM3的细胞的比例。在其他实施方案中，通过IHC(免疫组织化学)、酶联免疫吸附测定(ELISA)、体内成像或流式细胞术检测TIM3多肽的存在。在一些实施方案中，通过IHC分析TIM3表达。在其他实施方案中，例如使用IHC或体内成像，分析TIM3的细胞表面表达。

[0362] 在一些实施方案中，通过流式细胞术评估组织样品中表达TIM3的细胞的比例(或频率)。在一些实施方案中，通过流式细胞术分析的组织样品包含肿瘤浸润型免疫细胞(例如，TIL)。在一些实施方案中，通过流式细胞术分析的组织样品包含外周血细胞。在一些实施方案中，流式细胞术是多重分析。在一些实施方案中，评分流式细胞术测定包括，检测标志物表达，所述标志物包括TIM3、CD4、CD8、CCR7、CD45RO及其任意组合。在一些实施方案中，评分流式细胞术测定包括，评估供试组织样品中表达TIM3的CD4+T细胞和CD8+T细胞的比例。在一些实施方案中，评分流式细胞术测定包括，评估供试组织样品中表达TIM3且为(i)CCR7+CD45RO-(“幼稚T细胞”)、(ii)CCR7-CD45RO-(“Teff细胞”)、(iii)CCR7+CD45RO+(“CM细胞”)或(iv)CCR7-CD45RO+(“EM细胞”)的CD8+T细胞和CD4+T细胞的比例。

[0363] 在一些实施方案中，在受试者的外周血中测量可溶性TIM3。与可溶性TIM3结合的任何试剂(例如，与人TIM3的胞外结构域结合的任何试剂，如实施例中进一步描述)可以用来确定可溶性TIM3的水平。在一些实施方案中，测量可溶性TIM3同种型和自TIM3阳性细胞脱落的TIM3二者的水平。在一些实施方案中，测量这些形式的可溶性TIM3之一的水平。在一些实施方案中，单独测量这些形式的可溶性TIM3中每者的水平。

[0364] 测量细胞群体当中PD-1表达和PD1阳性细胞频率

[0365] 在某些实施方案中，鉴定适于包含TIM3拮抗剂和PD-1拮抗剂二者的治疗的受试者(例如，人类癌症患者)包括，测量或确定从受试者获得的组织样品中的PD-1表达。测量或确定PD-1表达的方法可以通过本文所述或本领域已知的任何方法实现。

[0366] 在一些实施方案中，从受试者获得的组织样品包括但不限于，包含CD4+T细胞和/或CD8+T细胞的任何有临床意义的组织样品，如肿瘤活检样品、取芯活检组织样品、细针抽吸物、或体液(如血液、血浆、血清、淋巴液、腹水、囊液或尿)样品。在一些实施方案中，组织样品来自转移灶。在某些实施方案中，在多个时间点，例如，治疗前、治疗期间和/或治疗后，从受试者取得组织样品。在其他实施方案中，组织样品取自受试者中的不同位置，例如，来自原发肿瘤的样品和来自远端位置的转移灶的样品。

[0367] 在一些实施方案中，可以在不从受试者获得组织样品的情况下实现确定PD-1表

达。在一些实施方案中，鉴定适合用TIM3拮抗剂和PD-1拮抗剂组合治疗的受试者包括(i)任选地提供从受试者获得的组织样品，其中组织样品包含CD4+和/或CD8+肿瘤浸润型淋巴细胞(TIL)；和(ii)考虑来自对照受试者(例如，健康人类受试者)的组织样品中观察到的频率，测量或确定组织样品中PD-1+CD4+和/或CD8+TIL的频率。

[0368] 在一些实施方案中，从受试者获得的组织样品包括但不限于，任何有临床意义的组织样品，如肿瘤活检样品、取芯活检组织样品、细针抽吸物、或体液(如血液、血浆、血清、淋巴液、腹水、囊液或尿)样品。在一些实施方案中，组织样品来自转移灶。在一些实施方案中，在多个时间点，例如，治疗前、治疗期间和/或治疗后，从受试者取得组织样品。在一些实施方案中，组织样品取自受试者中的不同位置，例如，来自原发肿瘤的样品和来自远端位置的转移灶的样品。

[0369] 在包括确定或测量组织样品中PD-1表达的本文所述任何方法中，应当理解，包括从患者获得组织样品的步骤是任选的步骤。即，在某些实施方案中，该方法包括这个步骤，而在其他实施方案中，不包括这个步骤。还应当理解在某些实施方案中，测量或确定PD-1表达的步骤通过分析PD-1表达的变换性方法(例如，流式细胞术)来执行。在某些其他实施方案中，不涉及变换性步骤，并且例如通过查看来自实验室的检验结果报告，确定PD-1表达。在某些实施方案中，至多(并包括)确定或测量PD-1表达结果的这些方法的步骤提供了中间结果，其中可以将所述中间结果提供给医师或其他医疗保健提供者，用于选择合适采用TIM3拮抗剂和PD-1拮抗剂组合治疗的候选者。在某些实施方案中，提供中间结果的步骤由医疗执业者或依据医疗执业者的指令行事的个人执行。在其他实施方案中，这些步骤由独立的实验室或由独立人员如实验室技师执行。

[0370] 在一些实施方案中，通过执行检测PD-1RNA存在的测定法，评估PD-1+CD4+和/或PD-1+CD8+TIL的频率。在其他实施方案中，通过RT-PCR、原位杂交或RNA酶保护法，检测PD-1RNA的存在。在一些实施方案中，通过基于RT-PCR的测定法检测PD-1RNA的存在。在其他实施方案中，评分基于RT-PCR的测定包括，相对于(例如，对照受试者中观察到的)预定频率，测量或确定组织样品中PD1+CD4+和/或PD-1+CD8+TIL的频率。

[0371] 在一些实施方案中，通过执行检测PD-1蛋白存在的测定法，评估PD-1+CD4+和/或PD-1+CD8+TIL的频率。在其他实施方案中，通过IHC(免疫组织化学)、酶联免疫吸附测定(ELISA)、体内成像或流式细胞术，检测PD-1蛋白的存在。在一些实施方案中，通过IHC分析PD-1表达。在其他实施方案中，例如使用IHC或体内成像，分析PD-1的细胞表面表达。

[0372] 在一些实施方案中，通过流式细胞术评估组织样品中表达PD-1的CD4+和/或CD8+细胞的比例(或频率)。在一些实施方案中，通过流式细胞术分析的组织样品包含肿瘤浸润型免疫细胞(例如，TIL)。在一些实施方案中，通过流式细胞术分析的组织样品包含外周血细胞。在一些实施方案中，流式细胞术是多重分析。在一些实施方案中，评分流式细胞术测定包括检测标志物表达，所述标志物包括PD-1、CD4、CD8、CCR7、CD45RO及其任意组合。在一些实施方案中，评分流式细胞术测定包括，评估组织样品中表达PD-1的CD4+T细胞和CD8+T细胞的比例。在一些实施方案中，评分流式细胞术测定包括，评估组织样品中表达PD-1且为(i)CCR7+CD45RO-(“幼稚T细胞”)、(ii)CCR7-CD45RO-(“Teff细胞”)、(iii)CCR7+CD45RO+(“CM细胞”)或(iv)CCR7-CD45RO+(“EM细胞”)的CD8+T细胞和CD4+T细胞的比例。

[0373] 本文提供用于确定(i)患有癌症的受试者是否可能响应于免疫治疗剂(如TIM3拮

抗剂)治疗、或(ii)患有癌症的受试者是否正响应于已经施用至受试者的免疫治疗剂(如TIM3拮抗剂)治疗的方法。这些方法包括确定一些细胞群体当中TIM3阳性细胞的频率。在某些实施方案中,一种方法包括确定癌症受试者的给定细胞群体中TIM3阳性细胞的频率,其中相对于对照受试者中的TIM3阳性细胞频率,该癌症受试者的给定细胞群体中更高的TIM3阳性细胞频率表示该受试者可能响应于免疫治疗剂(如TIM3拮抗剂)治疗。在某些实施方案中,一种方法包括确定已经接受过一次或多次免疫治疗剂(如TIM3拮抗剂)施用的癌症受试者的给定细胞群体中TIM3阳性细胞的频率,其中相对于施用免疫治疗剂之前或施用先前剂量的免疫治疗剂之前的癌症受试者中的TIM3阳性细胞频率,施用免疫治疗剂后该癌症受试者的给定细胞群体中更低的TIM3阳性细胞频率,表示该受试者可能响应于免疫治疗剂(如TIM3拮抗剂)治疗。上文方法可以包括(例如通过流式细胞术)测量以下细胞群体中TIM3阳性细胞的频率:肿瘤浸润型细胞,如肿瘤浸润型淋巴细胞和非淋巴细胞的肿瘤浸润型细胞。在某些实施方案中,这些方法包括测量以下细胞中TIM3阳性细胞的频率:CD8+TIL细胞;CD4+效应记忆TIL细胞(CD4+EM细胞;CD4+CCR7-CD45RO+TIL细胞);CD8+效应记忆TIL细胞(CD8+EM细胞;CD8+CCR7-CD45RO+TIL细胞);CD4+效应TIL细胞(CD4+Teff细胞;CD4+CCR7-CD45RO-T细胞);CD8+效应TIL细胞(CD8+Teff细胞;CD8+CCR7-CD45RO-T细胞);肿瘤浸润型髓样细胞,例如,pDC、mDC和CD14+髓样细胞;肿瘤浸润型NK细胞,例如,CD16-CD56++NK细胞和CD16+CD56+NK细胞。某些实施方案包括在这些细胞群体中的一个以上群体(例如,这些细胞群体中的2、3、4、5者或更多者或全体)中测量TIM3阳性细胞的频率,其中这些细胞群体的一者或多者中更高的TIM3阳性细胞频率指示受试者可能响应于免疫治疗剂(例如,TIM3拮抗剂),或其中在已经接受过某剂量免疫治疗剂(如TIM3拮抗剂)的受试者中,相对于已经接受该免疫治疗剂之前的频率,这些细胞群体的一者或多者中更低的TIM3阳性细胞频率指示受试者正响应于该免疫治疗剂治疗。

[0374] 本文中还提供用免疫治疗剂(如TIM3拮抗剂)治疗受试者的方法,所述方法包含向患有癌症的受试者施用治疗有效量的免疫治疗剂(如TIM3拮抗剂),其中,相对于对照受试者中的频率,在施用免疫治疗剂之前,受试者在一个或多个给定细胞群体中具有更高的TIM3阳性细胞频率,其中所述一个或多个给定群体细胞选自:CD8+TIL细胞;CD4+效应记忆TIL细胞(CD4+EM细胞;CD4+CCR7-CD45RO+TIL细胞);CD8+效应记忆TIL细胞(CD8+EM细胞;CD8+CCR7-CD45RO+TIL细胞);CD4+效应TIL细胞(CD4+Teff细胞;CD4+CCR7-CD45RO-T细胞);CD8+效应TIL细胞(CD8+Teff细胞;CD8+CCR7-CD45RO-T细胞);肿瘤浸润型髓样细胞,例如,pDC、mDC和CD14+髓样细胞;肿瘤浸润型NK细胞,例如,CD16-CD56++NK细胞和CD16+CD56+NK细胞。

[0375] 本文中还提供用免疫治疗剂(如TIM3拮抗剂)治疗受试者的方法,所述方法包含向患有癌症的受试者施用治疗有效量的免疫治疗剂(如TIM3拮抗剂),其中,相对于施用第一剂(或前数剂)免疫治疗剂(如TIM3拮抗剂)之前的频率,在施用第一剂(或前数剂)免疫治疗剂(如TIM3拮抗剂)后,受试者在一个或多个给定细胞群体中具有更低的TIM3阳性细胞频率,其中所述一个或多个给定细胞群体选自:CD8+TIL细胞;CD4+效应记忆TIL细胞(CD4+EM细胞;CD4+CCR7-CD45RO+TIL细胞);CD8+效应记忆TIL细胞(CD8+EM细胞;CD8+CCR7-CD45RO+TIL细胞);CD4+效应TIL细胞(CD4+Teff细胞;CD4+CCR7-CD45RO-T细胞);CD8+效应TIL细胞(CD8+Teff细胞;CD8+CCR7-CD45RO-T细胞);肿瘤浸润型髓样细胞,例如,pDC、mDC和CD14+髓

样细胞;肿瘤浸润型NK细胞,例如,CD16-CD56++NK细胞和CD16+CD56+NK细胞。

[0376] 本文还提供用免疫治疗剂(如TIM3拮抗剂)治疗受试者的方法,所述方法包括(例如,如本文(例如,先前段落)所述)首先确定受试者是否可能响应于免疫治疗剂(如TIM3拮抗剂)治疗,并且若响应,则施用治疗有效量的该免疫治疗剂,如TIM3拮抗剂。

[0377] TIM3拮抗剂

[0378] 在一个方面,本公开的特征在于使用TIM3拮抗剂治疗癌症的方法。如本文所用,TIM3拮抗剂包括但不限于抗TIM3抗体及其抗原结合部分,和可溶性TIM3多肽(例如,能够与TIM3配体结合的TIM3-Fc融合蛋白)。其他TIM3拮抗剂包括与TIM3的配体结合并且抑制这些配体与TIM3相互作用的药剂。

[0379] 抗TIM3抗体

[0380] 本公开的某些方面包括向有需要的受试者施用治疗有效量的抗TIM3抗体或其抗原结合部分。可以使用本领域熟知的方法生成适用于本公开中的抗TIM3抗体(或从中衍生的VH/VL结构域)。备选地,可以使用本领域认可的抗TIM3抗体。

[0381] 在一些实施方案中,抗TIM3抗体或其抗原结合部分显示出以下一个或多个功能特性:

[0382] (a)与可溶性和/或膜结合型人TIM3结合;

[0383] (b)与可溶性和/或膜结合型食蟹猴TIM3结合;

[0384] (c)诱导或刺激免疫应答;

[0385] (d)诱导或刺激T细胞活化,例如,Th1细胞活化(例如,如增强的细胞因子分泌和/或增殖反映的);

[0386] (e)诱导或刺激T细胞增殖(例如,CD4+、CD8+T细胞、Th1细胞、或TIL),例如,在共培养测定法中;

[0387] (f)诱导或刺激T细胞(例如,Th1细胞)或肿瘤浸润型淋巴细胞(TIL)(如来自人肾癌、肺癌、胰腺癌或乳腺癌肿瘤的TIL)产生IFN-γ;

[0388] (g)阻断或抑制人TIM3与PtdSer结合;

[0389] (h)与细胞上的TIM3结合时,不内化或下调细胞表面TIM3;

[0390] (i)与人TIM3胞外结构域(i)CPVFECG(SEQ ID NO:200);(ii)RIQIPGIMND(SEQ ID NO:202);(iii)CPVFECG和RIQIPGIMND(分别是SEQ ID NOs:200和202);或(iv)WTSRYWLNGDFR(SEQ ID NO:201)结合;

[0391] (j)与本文所述的结合TIM3的抗体(例如,13A3、3G4、17C3、17C8、9F6或TIM3.2至TIM3.18中任一者)竞争或交叉阻断与人TIM3的结合;

[0392] (k)结合于人TIM3,但不结合于具有如SEQ ID NO:194中编号的以下一个或多个氨基酸残基的氨基酸置换的人TIM3:L48、C58、P59、V60、F61、E62、C63、G64、W78、S80、R81、W83、L84、G86、D87、R89、D104、R111、Q113、G116、M118和D120;以及

[0393] (l)如通过HDX-MS所测定,结合于人TIM3区域^{49}VPVCWGKGACPVFE^{62}(SEQ ID NO:204)和^{111}RIQIPGIMNDEKFNLKL^{127}(SEQ ID NO:205);

[0394] (m)如通过X射线结晶学所测定,具有与至少5、10、15、20个或全部以下人TIM3氨基酸相互作用的重链可变区和/或轻链可变区:P50、V51、C52、P59、V60、F61、E62、C63、G64、N65、V66、V67、L68、R69、D71、E72、D74、R111、Q113、G116、I117、M118、D120和任选地T70和/或

I112;和/或

[0395] (n)与13A3或TIM3.18.IgG1.3竞争或交叉阻断与人TIM3的结合。

[0396] 在一些实施方案中,抗TIM3抗体以高亲和力,例如以10^{-7}M或更小、10^{-8}M或更小、10^{-9}M或更小、10^{-10}M或更小、10^{-11}M或更小、10^{-12}M或更小、10^{-12}M至10^{-7}M、10^{-11}M至10^{-7}M、10^{-10}M至10^{-7}M或10^{-9}M至10^{-7}M的K_D结合于人TIM3。在某些实施方案中,抗TIM3抗体,例如,如BIACORETM所测定,以10^{-7}M或更小、10^{-8}M或更小、10^{-9}M(1nM)或更小、10^{-10}M或更小、10^{-12}M至10^{-7}M、10^{-11}M至10^{-7}M、10^{-10}M至10^{-7}M、10^{-9}M至10^{-7}M、或10^{-8}M至10^{-7}M的K_D结合于可溶性人TIM3。在一些实施方案中,例如,如通过流式细胞术和Scatchard图所测定,抗TIM3抗体以10^{-7}M或更小、10^{-8}M或更小、10^{-9}M(1nM)或更小、$5x10^{-10}$ M或更小、10^{-10}M或更小、10^{-12}M至10^{-7}M、10^{-11}M至10^{-8}M、10^{-10}M至10^{-8}M、10^{-9}M至10^{-8}M、10^{-11}M至10^{-9}M或10^{-10}M至10^{-9}M的K_D结合于结合型(例如,细胞膜结合型)人TIM3,如活化的人CD4+和CD8+TIL上的TIM3。在一些实施方案中,抗TIM3抗体结合于(如活化的人CD4+和CD8+TIL上的)结合型(例如,细胞膜结合型)人TIM3,例如,如通过流式细胞术所测定,具有10ug/mL或更小、5ug/mL或更小、1ug/mL或更小、0.9ug/mL或更小、0.8ug/mL或更小、0.7ug/mL或更小、0.6ug/mL或更小、0.5ug/mL或更小、0.4ug/mL或更小、0.3ug/mL或更小、0.2ug/mL或更小、0.1ug/mL或更小、0.05ug/mL或更小、或0.01ug/mL或更小的EC_{50}。

[0397] 在一些实施方案中,适合于本公开的抗TIM3抗体结合于食蟹猴TIM3,例如以10^{-7}M或更小、10^{-8}M或更小、10^{-9}M或更小、10^{-10}M或更小、10^{-11}M或更小、10^{-12}M或更小、10^{-12}M至10^{-7}M、10^{-11}M至10^{-7}M、10^{-10}M至10^{-7}M或10^{-9}M至10^{-7}M的K_D。在某些实施方案中,抗TIM3抗体结合于可溶性食蟹猴TIM3,例如,如BIACORE™所测定,以10^{-7}M或更小、10^{-8}M或更小、10^{-9}M(1nM)或更小、10^{-10}M或更小、10^{-12}M至10^{-7}M、10^{-11}M至10^{-7}M、10^{-10}M至10^{-7}M、10^{-9}M至10^{-7}M、或10^{-8}M至10^{-7}M的K_D。在其他实施方案中,抗TIM3抗体可以结合于膜结合型食蟹猴TIM3,例如,如通过流式细胞术所测量,以100nM或更小、10nM或更小、100nM至0.01nM、100nM至0.1nM、100nM至1nM、或10nM至1nM的EC_{50}。在某些实施方案中,抗TIM3抗体结合于(如活化的人CD4+和CD8+TIL上的)结合型(例如,细胞膜结合型)食蟹猴TIM3,例如,如通过流式细胞术和Scatchard图所测定,以10^{-7}M或更小、10^{-8}M或更小、10^{-9}M(1nM)或更小、$5x10^{-10}$ M或更小、10^{-10}M或更小、10^{-12}M至10^{-7}M、10^{-11}M至10^{-8}M、10^{-10}M至10^{-8}M、10^{-9}M至10^{-8}M、10^{-11}M至10^{-9}M、或10^{-10}M至10^{-9}M的K_D。

[0398] 在一些实施方案中,抗TIM3抗体刺激或增强免疫应答,例如通过活化T细胞,例如在肿瘤中。例如,抗TIM3抗体可以激活或共刺激细胞,例如由增强的细胞因子(例如,IFN-γ)分泌和/或增强的增殖所反映的,这可因抑制TIM3介导的T细胞抑制性活性而引起。在某些实施方案中,TIM3抗体的T细胞活化或共刺激作用在CD3刺激作用存在下出现。在某些实施方案中,抗TIM3抗体增加IFN-γ分泌,达50%、100%(即,2倍)、3倍、4倍、5倍或更大倍数、任选地最高多达10倍、30倍、100倍,例如在原代人T细胞和/或表达人TIM3的T细胞(如肿瘤浸润型淋巴细胞(TIL))上测量的。

[0399] 在一些实施方案中,抗TIM3抗体抑制磷脂酰丝氨酸与表达人TIM3的细胞(例如,CHO细胞或活化T细胞)上的人TIM3结合,例如以10μg/ml或更小、1μg/ml或更小、0.01μg/ml至10μg/ml、0.1μg/ml至10μg/ml、或0.1μg/ml至1μg/ml的EC_{50}。

[0400] 在一些实施方案中,适于本公开的抗TIM3抗体与人TIM3的胞外部分中(例如,胞外区Ig样结构域(即,SEQ ID NO:194的氨基酸22至202)中)的表位(例如,构象表位)结合。在

某些实施方案中,抗TIM3抗体与位于人TIM3胞外结构域的氨基酸22至120(SEQ ID NO:194)或成熟人TIM3的氨基酸1-99(SEQ ID NO:198)内的表位结合。在一些实施方案中,抗TIM3抗体与由具有SEQ ID NO:194的人TIM3的氨基酸58-64组成的区域结合或与其内部的表位结合,所述区域对应于成熟人TIM3的氨基酸残基37-43(CPVFECG,SEQ ID NO:200)。在其他实施方案中,抗TIM3抗体与由具有SEQ ID NO:194的人TIM3的氨基酸111-120组成的区域结合或与其内部的表位结合,所述区域对应于成熟人TIM3的氨基酸残基90-99(RIQIPGIMND,SEQ ID NO:202)。在其他实施方案中,抗TIM3抗体与由具有SEQ ID NO:194的人TIM3的氨基酸58-64(CPVFECG,SEQ ID NO:200)组成的区域结合或与其内部的表位结合,并且与由具有SEQ ID NO:194的人TIM3的氨基酸111-120(RIQIPGIMND,SEQ ID NO:202)组成的区域结合或与其内部的表位结合。在一些实施方案中,抗TIM3抗体与由具有SEQ ID NO:194的人TIM3的氨基酸78-89组成的区域结合或与其内部的表位结合,所述区域对应于成熟人TIM3的氨基酸残基57-83(WTSRYWLNGDFR,SEQ ID NO:201)。

[0401] 在一些实施方案中,抗TIM3抗体与13A3结合于基本上相同的表位,即,包含SEQ ID NO:194的氨基酸残基C58、P59、F61、E62、C63、R111和D120中一者或多者的表位(或人TIM3的区域)。在一些实施方案中,抗TIM3抗体结合于包含SEQ ID NO:194的氨基酸残基C58、P59、F61、E62、C63、D104、R111、Q113和D120中一者或多者的表位(或人TIM3的区域)。在某些实施方案中,抗TIM3抗体不显著地结合于或仅以显著降低的结合亲和力结合于如下人TIM3蛋白,其中,所述人TIM3蛋白,例如,在非保守性氨基酸置换中,将SEQ ID NO:194的氨基酸残基C58、P59、F61、E62、C63、R111和D120中一者或多者改变成另一个氨基酸。在其他实施方案中,抗TIM3抗体不显著地结合于或仅以显著降低的结合亲和力结合于如下人TIM3蛋白,其中,所述人TIM3蛋白,例如,在非保守性氨基酸置换中,将SEQ ID NO:194的氨基酸残基C58、P59、F61、E62、C63、D104、R111、Q113和D120中一者或多者改变成另一个氨基酸。

[0402] 在一些实施方案中,抗TIM3抗体与3G4结合于基本上相同的表位,即,包含SEQ ID NO:194的氨基酸残基C58、P59、V60、F61、E62、C63、G116和M118中一者或多者的表位(或人TIM3的区域)。在一些实施方案中,抗TIM3抗体结合于包含SEQ ID NO:194的氨基酸残基C58、P59、V60、F61、E62、C63、D104、G116和M118中一者或多者的表位(或人TIM3的区域)。在某些实施方案中,抗TIM3抗体不显著地结合于或仅以显著降低的结合亲和力结合于如下人TIM3蛋白,其中,所述人TIM3蛋白,例如在非保守性氨基酸置换中,将SEQ ID NO:194的氨基酸残基C58、P59、V60、F61、E62、C63、G116和M118中一者或多者改变成另一氨基酸。在某些实施方案中,抗TIM3抗体不显著地结合于或仅以显著降低的结合亲和力结合于如下人TIM3蛋白,其中,所述人TIM3蛋白,例如在非保守性氨基酸置换中,将SEQ ID NO:194的氨基酸残基C58、P59、V60、F61、E62、C63、D104、G116和M118中一者或多者改变成另一氨基酸。

[0403] 在一些实施方案中,抗TIM3抗体与17C3结合于基本上相同的表位,即,包含SEQ ID NO:194的氨基酸残基C58、P59、V60、F61、E62、C63、G64和G116中一者或多者的表位(或人TIM3的区域)。在一些实施方案中,抗TIM3抗体结合于包含SEQ ID NO:194的氨基酸残基C58、P59、V60、F61、E62、C63、G64、D104和G116中一者或多者的表位(或人TIM3的区域)。在某些实施方案中,抗TIM3抗体不显著地结合于或仅以显著降低的结合亲和力结合于如下人TIM3蛋白,其中,所述人TIM3蛋白,例如在非保守性氨基酸置换中,将SEQ ID NO:194的氨基酸残基C58、P59、V60、F61、E62、C63、G64和G116中一者或多者改变成另一氨基酸。在某些实

施方案中，抗TIM3抗体不显著地结合于或仅以显著降低的结合亲和力结合于如下人TIM3蛋白，其中，所述人TIM3蛋白，例如在非保守性氨基酸置换中，将SEQ ID NO:194的氨基酸残基C58、P59、V60、F61、E62、C63、G64、D104和G116中一者或多者改变成另一氨基酸。

[0404] 在一些实施方案中，抗TIM3抗体与8B9结合于基本上相同的表位，即，包含SEQ ID NO:194的氨基酸残基L48、W78、S80、R81、W83、G86、D87和R89中一者或多者的表位(或人TIM3的区域)。在一些实施方案中，抗TIM3抗体结合于包含SEQ ID NO:194的氨基酸残基L48、W78、S80、R81、W83、L84、G86、D87和R89中一者或多者的表位(或人TIM3的区域)。在其他实施方案中，抗TIM3抗体结合于包含SEQ ID NO:194的氨基酸残基L48、W78、S80、R81、W83、G86、D87、R89和D104中一者或多者的表位(或人TIM3的区域)。在某些实施方案中，抗TIM3抗体不显著地结合于或仅以显著降低的结合亲和力结合于如下人TIM3蛋白，其中，所述人TIM3蛋白，例如在非保守性氨基酸置换中，将SEQ ID NO:194的氨基酸残基L48、W78、S80、R81、W83、G86、D87和R89中一者或多者改变成另一氨基酸。在其他实施方案中，抗TIM3抗体不显著地结合于或仅以显著降低的结合亲和力结合于如下人TIM3蛋白，其中，所述人TIM3蛋白，例如在非保守性氨基酸置换中，将SEQ ID NO:194的氨基酸残基L48、W78、S80、R81、W83、L84、G86、D87和R89中一者或多者改变成另一氨基酸。在一些实施方案中，抗TIM3抗体不显著地结合于或仅以显著降低的结合亲和力结合于如下人TIM3蛋白，其中，所述人TIM3蛋白，例如在非保守性氨基酸置换中，将SEQ ID NO:194的氨基酸残基L48、W78、S80、R81、W83、G86、D87、R89和D104中一者或多者改变成另一氨基酸。

[0405] 在其他实施方案中，适用于本公开的抗TIM3抗体与包含本文所述的CDR或可变区的抗TIM3抗体(例如，抗体13A3、3G4、17C3、17C8、9F6、8B9、8C4、和TIM3.2至TIM3.18中任一者)竞争(或抑制)与人TIM3的结合。在某些实施方案中，抗TIM3抗体抑制抗体13A3、3G4、17C3、17C8、9F6、8B9、8C4或TIM3.2至TIM3.18中任一者与人TIM3的结合作用，达至少50％、60％、70％、80％、90％或100％。在一些实施方案中，13A3、3G4、17C3、17C8、9F6、8B9、8C4或TIM3.2至TIM3.18中任一者抑制抗TIM3抗体与人TIM3的结合作用，达至少50％、60％、70％、80％、90％或100％。在其他实施方案中，抗TIM3抗体抑制13A3、3G4、17C3、17C8、9F6、8B9、8C4或TIM3.2至TIM3.18中任一者与人TIM3的结合作用，达至少50％、60％、70％、80％、90％或100％，并且13A3、3G4、17C3、17C8、9F6、8B9、8C4或TIM3.2至TIM3.18中任一者抑制抗TIM3抗体与人TIM3的结合作用，达至少50％、60％、70％、80％、90％或100％(例如，双向竞争)。

[0406] 在某些实施方案中，本文公开的抗TIM3抗体具有1、2、3、4、5、6、7、8、9、10、11、12、13、14、15个或全部以下特征：

[0407] (1)例如，以10nM或更小(例如，0.01nM至10nM)的K_D，与可溶性人TIM3结合，例如，如通过Biacore所测量；

[0408] (2)例如，以100nM或更小(例如，0.01nM至100nM)的K_D，与可溶性食蟹猴TIM3结合，例如，如通过Biacore所测量；

[0409] (3)例如，以1μg/mL或更小(例如，0.01μg/mL至1μg/mL)的EC_{50}，与膜结合型人TIM3结合，例如，如通过流式细胞术所测量；

[0410] (4)例如，以1nM或更小(例如，0.01nM至10nM)的K_D，与膜结合型人TIM3结合，例如，如通过Scatchard分析所测量；

[0411] (5)例如，以20μg/mL或更小(例如，0.01μg/mL至20μg/mL)的EC_{50}，与膜结合型食蟹

猴TIM3结合，例如，如通过流式细胞术所测量；

[0412] (6)例如，以1nM或更小(例如，0.01nM至10nM)的K_D，与膜结合型食蟹猴TIM3结合，例如，如通过Scatchard分析所测量；

[0413] (7)诱导或增强T细胞活化(例如，通过阻断或减少TIM3的抑制性效应)，如由(i)表达TIM3的T细胞(例如，Th1细胞或TIL)中IFN-γ产生增加和/或(ii)表达TIM3的T细胞(例如，Th1细胞或TIL)的增殖增强所反映的；

[0414] (8)在混合淋巴细胞反应(MLR)测定法中刺激T细胞增殖；

[0415] (9)抑制磷脂酰丝氨酸与TIM3结合；

[0416] (10)与细胞上的TIM3结合时，不内化或下调细胞表面TIM3；

[0417] (11)与人TIM3胞外结构域(SEQ ID NO:198)的以下区域之一结合：(a)CPVFECG(SEQ ID NO:200)；(b)RIQIPGIMND(SEQ ID NO:202)；(c)CPVFECG和RIQIPGIMND(分别是SEQ ID NOs:200和202)；和(d)WTSRYWLNGDFR(SEQ ID NO:201)；

[0418] (12)相对于与野生型人TIM3的结合作用，对其中氨基酸L48、C58、P59、V60、F61、E62、C63、G64、W78、S80、R81、W83、L84、G86、D87、R89、D104、R111、Q113、G116、M118和D120(按SEQ ID NO:194中编号)中一者或多者被另一氨基酸置换的人TIM3具有减少的结合作用；

[0419] (13)以任一方向或两个方向与包含13A3、3G4、17C3、17C8、9F6、8B9、8C4、或TIM3.7、TIM3.8、TIM3.10、TIM3.11、TIM3.12、TIM3.13、TIM3.14、TIM3.15、TIM3.16、TIM3.18中任一者的VH结构域和VL结构域的抗体竞争性结合人TIM3；

[0420] (14)如通过HDX-MS所测定，结合于人TIM3区域^{49}VPVCWGKGACPVFE^{62}(SEQ ID NO:204)和^{111}RIQIPGIMNDEKFNLKL^{127}(SEQ ID NO:205)；

[0421] (15)如通过X射线结晶学所测定，具有与至少5、10、15、20个或全部以下人TIM3氨基酸相互作用的重链可变区和/或轻链可变区：P50、V51、C52、P59、V60、F61、E62、C63、G64、N65、V66、V67、L68、R69、D71、E72、D74、R111、Q113、G116、I117、M118、D120和任选地T70和/或I112(根据SEQ ID NO:194编号)；和/或

[0422] (16)(a)相对于与野生型人TIM3的结合作用，对其中氨基酸C58、P59、F61、E62、C63、R111、D120和任选地D104和Q113(根据SEQ ID NO:194编号)中1、2、3、4、5、6、7、8或9个氨基酸被另一氨基酸置换的人TIM3具有减少的结合作用；(b)与^{49}VPVCWGKGACPVFE^{62}(SEQ ID NO:204)、^{111}RIQIPGIMNDEKFNLKL^{127}(SEQ ID NO:205)和^{119}NDEKFNLKL^{127}(SEQ ID NO:210)结合，如通过HDX-MS所测定；和/或(c)竞争13A3或TIM3.18.IgG1.3与人TIM3的结合，或交叉阻断该结合。

[0423] 因此，显示出如根据本领域已知和本文所述的方法所测定的这些功能特性(例如，生物化学活性、免疫化学活性、细胞活性、生理学活性或其他生物学活性等)中一者或多者的抗体，将理解为相对于抗体不存在时(例如，当具有不相关特异性的对照抗体存在时)观察到的所述特定活性，显示出所述特定活性的统计显著差异。在一些实施方案中，给定测定法中抗TIM3抗体诱导的所测量参数(例如，T细胞增殖、细胞因子产生)增加，实现了所测量参数至少10％、例如至少20％、30％、40％、50％、60％、70％、80％、90％、95％、100％(即，2倍)、3倍、5倍或10倍的统计显著增加，并且在某些实施方案中，相对于抗体不存在情况下实施的相同测定，本文所述的抗体可以导致所测量的参数增加，例如大于92％、94％、95％、97％、98％、99％、100％(即，2倍)、3倍、5倍或10倍。反过来，给定测定法中抗TIM3抗体诱导

的所测量参数(例如,肿瘤体积、TIM3-L与人TIM3的结合)减少,可以实现所测量参数的至少10%、例如至少20%、30%、40%、50%、60%、70%、80%或90%的统计显著减少,并且在某些实施方案中,相对于抗体不存在情况下实施的相同测定,本文所述的抗体可以导致测量的参数减少,例如大于92%、94%、95%、97%、98%或99%。

[0424] 评价抗体针对多个物种的TIM3的结合能力的标准测定法是本领域已知的,例如,包括ELISA、蛋白质印迹法和RIA。也可以通过本领域已知的标准测定法,如通过Biacore分析法,评估抗体的结合动力学(例如,结合亲和力)。

[0425] 在一些实施方案中,适于本公开的抗TIM3抗体不是天然抗体或不是天然存在的抗体。例如,在一些实施方案中,抗TIM3抗体具有与天然存在的抗体相异的翻译后修饰,如具有更多的、更少或不同类型的翻译后修饰。

[0426] 在一些实施方案中,抗TIM3抗体不具有激动剂活性,如在CHO-OKT3-CD32:T细胞共培养实验中在抗TIM3抗体的交联中所测定的,其中所述抗体不导致超过单独抗TIM3的增强活性。在某些实施方案中,抗TIM3抗体阻断TIM3与其配体相互作用,且不促进激动剂活性。

[0427] 在一些实施方案中,抗TIM3抗体增强来自LPS处理的单核细胞或树状细胞的IL-12产生。

[0428] 在一些实施方案中,抗TIM3抗体通过联合处理,恢复(revive)共表达PD-1和TIM3的肿瘤浸润型CD4+T细胞和CD8+T细胞,因此避免CD4+T细胞和CD8+T细胞耗尽。

[0429] 示例性抗TIM3抗体

[0430] 适于本公开的具体抗TIM3抗体是这样的抗体,例如,单克隆、重组、和/或人抗体,所述抗体具有如下抗体的CDR和/或可变区序列:抗体13A3、3G4、17C3、17C8、9F6、8B9、8C4或TIM3.2至TIM3.18中任一者、以及与其可变区或CDR序列具有至少80%同一性(例如,至少85%、至少90%、至少95%或至少99%同一性)的抗体。13A3、8B9、8C4、17C3、9F6、3G4和17C8的VH氨基酸序列分别在SEQ ID NOs:1-7中给出。13A3变体、8B9变体和9F6变体的VH氨基酸序列在SEQ ID NOs:8-18中给出。13A3、17C3和3G4的VL氨基酸序列在SEQ ID NO:19中给出。8B9、8C4和17C8的VL氨基酸序列在SEQ ID NO:20中给出。9F6或其变体的VL氨基酸序列在SEQ ID NOs:20、21或22中给出。13A3变体和8B9变体的VL氨基酸序列分别在SEQ ID NO:19和SEQ ID NO:20中给出。

[0431] 因此,在一些实施方案中,抗TIM3抗体包含重链可变区和轻链可变区,其中重链可变区包含选自SEQ ID NOs:1-18的氨基酸序列。在一些实施方案中,轻链可变区包含选自SEQ ID NOs:19-22的氨基酸序列。

[0432] 在一些实施方案中,抗TIM3抗体包含:

[0433] (a)分别包含SEQ ID NOs:1和19的重链可变区序列和轻链可变区序列;

[0434] (b)分别包含SEQ ID NOs:2和20的重链可变区序列和轻链可变区序列;

[0435] (c)分别包含SEQ ID NOs:3和20的重链可变区序列和轻链可变区序列;

[0436] (d)分别包含SEQ ID NOs:4和19的重链可变区序列和轻链可变区序列;

[0437] (e)分别包含SEQ ID NOs:5和20的重链可变区序列和轻链可变区序列;

[0438] (f)分别包含SEQ ID NOs:5和21的重链可变区序列和轻链可变区序列;

[0439] (g)分别包含SEQ ID NOs:5和22的重链可变区序列和轻链可变区序列;

[0440] (h)分别包含SEQ ID NOs:6和19的重链可变区序列和轻链可变区序列;

[0441] (i)分别包含SEQ ID NOs:7和20的重链可变区序列和轻链可变区序列;

[0442] (j)分别包含SEQ ID NOs:17和22的重链可变区序列和轻链可变区序列;

[0443] (k)分别包含SEQ ID NOs:16和20的重链可变区序列和轻链可变区序列;

[0444] (l)分别包含SEQ ID NOs:8和19的重链可变区序列和轻链可变区序列;

[0445] (m)分别包含SEQ ID NOs:9和19的重链可变区序列和轻链可变区序列;

[0446] (n)分别包含SEQ ID NOs:10和19的重链可变区序列和轻链可变区序列;

[0447] (o)分别包含SEQ ID NOs:11和19的重链可变区序列和轻链可变区序列;

[0448] (p)分别包含SEQ ID NOs:12和19的重链可变区序列和轻链可变区序列;

[0449] (q)分别包含SEQ ID NOs:13和19的重链可变区序列和轻链可变区序列;

[0450] (r)分别包含SEQ ID NOs:14和19的重链可变区序列和轻链可变区序列;

[0451] (s)分别包含SEQ ID NOs:15和19的重链可变区序列和轻链可变区序列;或

[0452] (t)分别包含SEQ ID NOs:18和19的重链可变区序列和轻链可变区序列。

[0453] 在一些实施方案中,抗TIM3抗体包含13A3、8B9、8C4、17C3、9F6、3G4和17C8或TIM3.2至TIM3.18中任一者的重链和轻链CDR1、CDR2和CDR3、或其组合。在SEQ ID NOs:23-26中分别阐述13A3、8B9、8C4和17C3的VH CDR1的氨基酸序列。在SEQ ID NO:27中阐述9F6、3G4和17C8的VH CDR1的氨基酸序列。突变的13A3抗体(即,TIM3.10-TIM3.18)的VH CDR1的氨基酸序列与未突变的13A3抗体的相应氨基酸序列(即,SEQ ID NO:23)相同。突变的8B9抗体(即,TIM3.8)的VH CDR1的氨基酸序列与未突变的8B9抗体的相应氨基酸序列(即,SEQ ID NO:24)相同。突变的9F6抗体(即,TIM3.7)的VH CDR1的氨基酸序列与未突变的9F6抗体的相应氨基酸序列(即,SEQ ID NO:27)相同。在SEQ ID NOs:28-34中分别阐述13A3、8B9、8C4、17C3、9F6、3G4和17C8的VH CDR2的氨基酸序列。SEQ ID NO:35中阐述突变的13A3抗体TIM3.10、TIM3.17和TIM3.18的VH CDR2的氨基酸序列。在SEQ ID NOs:36和37中分别阐述突变的13A3抗体TIM3.11和TIM3.12的VH CDR2的氨基酸序列。突变的13A3抗体TIM3.13和TIM3.16的VH CDR2的氨基酸序列是未突变的13A3抗体的相应氨基酸序列(即,SEQ ID NO:28)。SEQ ID NO:38中阐述突变的8B9抗体(即,TIM3.8)的VH CDR2的氨基酸序列。突变的9F6抗体(即,TIM3.7)的VH CDR2的氨基酸序列与未突变的9F6抗体的相应氨基酸序列(即,SEQ ID NO:32)相同。在SEQ ID NOs:39-45中分别阐述13A3、8B9、8C4、17C3、9F6、3G4和17C8的VH CDR3的氨基酸序列。

[0454] 突变的13A3抗体(即,TIM3.10至TIM3.12)的VH CDR3的氨基酸序列是未突变的13A3抗体的相应氨基酸序列(即,SEQ ID NO:39)。SEQ ID NO:46中阐述突变的13A3抗体TIM3.13和TIM3.18的VH CDR3的氨基酸序列。SEQ ID NO:48中阐述突变的13A3抗体TIM3.15和TIM3.17的VH CDR3的氨基酸序列。在SEQ ID NOs:47和49中分别阐述突变的13A3抗体TIM3.14和TIM3.16的VH CDR3的氨基酸序列。突变的8B9抗体(即,TIM3.8)的VH CDR3的氨基酸序列是未突变的8B9抗体的相应氨基酸序列(即,SEQ ID NO:40)。突变的9F6抗体(即,TIM3.7)的VH CDR3的氨基酸序列与未突变的9F6抗体的相应氨基酸序列(即,SEQ ID NO:43)相同。

[0455] 在SEQ ID NO:50中阐述13A3、8B9、8C4、17C3、3G4和17C8的VL CDR1的氨基酸序列。在SEQ ID NOs:50和51中阐述9F6的VL CDR1的氨基酸序列。在SEQ ID NO:52中阐述13A3、8B9、8C4、17C3、3G4和17C8的VL CDR2的氨基酸序列。在SEQ ID NOs:52和53中阐述9F6的VL

CDR2的氨基酸序列。在SEQ ID NO:54中阐述13A3、17C3和3G4的VL CDR3的氨基酸序列。在SEQ ID NO:55中阐述8B9、8C4和17C8的VL CDR3的氨基酸序列。在SEQ ID NOs:55-57中阐述9F6的VL CDR3的氨基酸序列。突变的抗体13A3、8B9和9F6的VL CDR的氨基酸序列是相应的未突变抗体的VL CDR的氨基酸序列。

[0456] 可以使用Kabat体系描述CDR区(Kabat,E.A.等人,(1991)Sequences of Proteins of Immunological Interest,第5版,美国卫生和公众服务部,NIH出版编号91-3242)。Kabat体系是最常见编号体系,用于称作EU索引或EU编号体系的方案,其基于首个测序的人IgG1(EU抗体;Edelman等人1969)的依次编号。基于本文公开的Kabat编号方案,抗体编号可以转化成本领域已知的其他体系,例如,Chothia、IMGT、Martin(增强的Chothia)或AHo编号方案。

[0457] 在一些实施方案中,抗TIM3抗体或其抗原结合部分包含:

[0458] (a)包含选自SEQ ID NOs:23-27的氨基酸序列的重链可变区CDR1;

[0459] (b)包含选自SEQ ID NOs:28-38的氨基酸序列的重链可变区CDR2;

[0460] (c)包含选自SEQ ID NOs:39-49的氨基酸序列的重链可变区CDR3;

[0461] (d)包含选自SEQ ID NOs:50和51的氨基酸序列的轻链可变区CDR1;

[0462] (e)包含选自SEQ ID NOs:52和53的氨基酸序列的轻链可变区CDR2;或

[0463] (f)包含选自SEQ ID NOs:54-57的氨基酸序列的轻链可变区CDR3;

[0464] 其中抗体与人TIM3特异性结合。

[0465] 在一些实施方案中,抗TIM3抗体包含重链可变区和轻链可变区,其中重链可变区CDR1、CDR2和CDR3区域包含:

[0466] (a)SEQ ID NOs:23、28和39;

[0467] (b)SEQ ID NOs:24、29和40;

[0468] (c)SEQ ID NOs:25、30和41;

[0469] (d)SEQ ID NOs:26、31和42;

[0470] (e)SEQ ID NOs:27、32和43;

[0471] (f)SEQ ID NOs:27、33和44;

[0472] (g)SEQ ID NOs:27、34和45;

[0473] (h)SEQ ID NOs:23、35和39;

[0474] (i)SEQ ID NOs:23、36和39;

[0475] (j)SEQ ID NOs:23、37和39;

[0476] (k)SEQ ID NOs:23、28和46;

[0477] (l)SEQ ID NOs:23、28和47;

[0478] (m)SEQ ID NOs:23、28和48;

[0479] (n)SEQ ID NOs:23、28和49;

[0480] (o)SEQ ID NOs:23、35和46;或

[0481] (p)SEQ ID NOs:23、35和48;

[0482] 其中抗体与人TIM3特异性结合。

[0483] 在一些实施方案中,抗人TIM3抗体包含重链可变区和轻链可变区,其中轻链可变区CDR1、CDR2和CDR3区域包含:

[0484] (a)SEQ ID NOs:50、52和54；

[0485] (b)SEQ ID NOs:50、52和55；

[0486] (c)SEQ ID NOs:51、53和56;或

[0487] (d)SEQ ID NOs:50、52和57；

[0488] 其中抗体与人TIM3特异性结合。

[0489] 在一些实施方案中,抗TIM3抗体包含重链可变区和轻链可变区,其中：

[0490] (a1)分别包含SEQ ID NOs:23、28和39的重链可变区CDR1、CDR2和CDR3,和分别包含SEQ ID NOs:50、52和54的轻链可变区CDR1、CDR2和CDR3；

[0491] (a2)分别包含SEQ ID NOs:23、35和39的重链可变区CDR1、CDR2和CDR3,和分别包含SEQ ID NOs:50、52和54的轻链可变区CDR1、CDR2和CDR3；

[0492] (a3)分别包含SEQ ID NOs:23、36和39的重链可变区CDR1、CDR2和CDR3,和分别包含SEQ ID NOs:50、52和54的轻链可变区CDR1、CDR2和CDR3；

[0493] (a4)分别包含SEQ ID NOs:23、37和39的重链可变区CDR1、CDR2和CDR3,和分别包含SEQ ID NOs:50、52和54的轻链可变区CDR1、CDR2和CDR3；

[0494] (a5)分别包含SEQ ID NOs:23、28和46的重链可变区CDR1、CDR2和CDR3,和分别包含SEQ ID NOs:50、52和54的轻链可变区CDR1、CDR2和CDR3；

[0495] (a6)分别包含SEQ ID NOs:23、28和47的重链可变区CDR1、CDR2和CDR3,和分别包含SEQ ID NOs:50、52和54的轻链可变区CDR1、CDR2和CDR3；

[0496] (a7)分别包含SEQ ID NOs:23、28和48的重链可变区CDR1、CDR2和CDR3,和分别包含SEQ ID NOs:50、52和54的轻链可变区CDR1、CDR2和CDR3；

[0497] (a8)分别包含SEQ ID NOs:23、28和49的重链可变区CDR1、CDR2和CDR3,和分别包含SEQ ID NOs:50、52和54的轻链可变区CDR1、CDR2和CDR3；

[0498] (a9)分别包含SEQ ID NOs:23、35和46的重链可变区CDR1、CDR2和CDR3,和分别包含SEQ ID NOs:50、52和54的轻链可变区CDR1、CDR2和CDR3；

[0499] (a10)分别包含SEQ ID NOs:23、35和48的重链可变区CDR1、CDR2和CDR3,和分别包含SEQ ID NOs:50、52和54的轻链可变区CDR1、CDR2和CDR3；

[0500] (b1)分别包含SEQ ID NOs:24、29和40的重链可变区CDR1、CDR2和CDR3,和分别包含SEQ ID NOs:50、52和55的轻链可变区CDR1、CDR2和CDR3；

[0501] (b2)分别包含SEQ ID NOs:24、38和40的重链可变区CDR1、CDR2和CDR3,和分别包含SEQ ID NOs:50、52和55的轻链可变区CDR1、CDR2和CDR3；

[0502] (c)分别包含SEQ ID NOs:25、30和41的重链可变区CDR1、CDR2和CDR3,和分别包含SEQ ID NOs:50、52和55的轻链可变区CDR1、CDR2和CDR3；

[0503] (d)分别包含SEQ ID NOs:26、31和42的重链可变区CDR1、CDR2和CDR3,和分别包含SEQ ID NOs:50、52和54的轻链可变区CDR1、CDR2和CDR3；

[0504] (e)分别包含SEQ ID NOs:27、32和43的重链可变区CDR1、CDR2和CDR3,和分别包含SEQ ID NOs:50、52和55的轻链可变区CDR1、CDR2和CDR3；

[0505] (f)分别包含SEQ ID NOs:27、32和43的重链可变区CDR1、CDR2和CDR3,和分别包含SEQ ID NOs:50、52和57的轻链可变区CDR1、CDR2和CDR3；

[0506] (g1)分别包含SEQ ID NOs:27、32和43的重链可变区CDR1、CDR2和CDR3,和分别包

含SEQ ID NOs:51、53和56的轻链可变区CDR1、CDR2和CDR3；

[0507] (g2)分别包含SEQ ID NOs:27、32和43的重链可变区CDR1、CDR2和CDR3，和分别包含SEQ ID NOs:50、52和57的轻链可变区CDR1、CDR2和CDR3；

[0508] (g3)分别包含SEQ ID NOs:27、32和43的重链可变区CDR1、CDR2和CDR3，和分别包含SEQ ID NOs:50、52和55的轻链可变区CDR1、CDR2和CDR3；

[0509] (h)分别包含SEQ ID NOs:27、33和44的重链可变区CDR1、CDR2和CDR3和分别地包含SEQ ID NOs:50、52和54的轻链可变区CDR1、CDR2和CDR3；或

[0510] (i)分别包含SEQ ID NOs:27、34和45的重链可变区CDR1、CDR2和CDR3，和分别包含SEQ ID NOs:50、52和55的轻链可变区CDR1、CDR2和CDR3；

[0511] 其中抗体与人TIM3特异性结合。

[0512] 在一些实施方案中，可用于本公开的抗TIM3抗体包含与13A3、3G4、17C3、17C8、9F6、8B9、8C4或TIM3.2至TIM3.18中任一者的相应CDR在1、2、3、4、5、1-2、1-3、1-4或1-5个氨基酸变化(即，氨基酸置换、添加或缺失)方面相异的VH CDR1、VH CDR2、VH CDR3、VL CDR1、VL CDR2和/或VL CDR3。在某些实施方案中，相对于13A3、3G4、17C3、17C8、9F6、8B9、8C4或TIM3.2至TIM3.18中任一者的相应序列，可用于本公开的抗TIM3抗体在1、2、3、4、5或6个CDR的每者中包含1-5个氨基酸变化。在某些实施方案中，相对于13A3、3G4、17C3、17C8、9F6、8B9、8C4或TIM3.2至TIM3.18中任一者的CDR，抗TIM3抗体包含在全部CDR中总计1-5个的氨基酸变化。

[0513] 在某些实施方案中，抗TIM3抗体包含由13A3的CDR组成的VH CDR和VL CDR，其中一个或多个CDR中的一个或多个氨基酸是本文公开的其他抗TIM3抗体之一者的那些氨基酸。

[0514] 例如，在某些实施方案中，抗TIM3抗体包含相对于SRSYYWG(SEQ ID NO:23)包含一个或多个氨基酸修饰的VH CDR1，并且可以例如包含以下简并序列：$X_1X_2X_3X_4YX_5X_6$(SEQ ID NO:211)，其中X_1是任何氨基酸，例如，S或无；X_2是任何氨基酸，例如，R或无；X3是任何氨基酸，例如，S、R或D；X_4是任何氨基酸，例如，Y或H；X_5是任何氨基酸，例如，W或M；并且X_6是任何氨基酸，例如，G、N、S或H。

[0515] 在某些实施方案中，抗TIM3抗体包含相对于SIYYSGFTYYNPSLKS(SEQ ID NO:28)包含一个或多个氨基酸修饰的VH CDR2，并且可以例如包含以下简并序列：$X_1IX_2X_3X_4GX_5X_6X_7X_8YX_9X_{10}X_{11}X_{12}X_{13}X_{14}$(SEQ ID NO:212)，其中$X_1$是任何氨基酸，例如，S、Y、I或F；$X_2$是任何氨基酸，例如，Y、H、N或S；$X_3$是任何氨基酸，例如，Y、P、G、T或S；$X_4$是任何氨基酸，例如，S、T、R或G；$X_5$是任何氨基酸，例如，F、S或D；$X_6$是任何氨基酸，例如，S、T或I；$X_7$是任何氨基酸，例如，I或无；$X_8$是任何氨基酸，例如，Y、N或I；$X_9$是任何氨基酸，例如，N、Q、S或A；$X_{10}$是任何氨基酸，例如，P、S、Q或D；$X_{11}$是任何氨基酸，例如，S或K；$X_{12}$是任何氨基酸，例如，L、F或V；$X_{13}$是任何氨基酸，例如，K或Q；并且$X_{14}$是任何氨基酸，例如，S或G。

[0516] 在某些实施方案中，抗TIM3抗体包含相对于GGPYGDYAHWFDP(SEQ ID NO:39)包含一个或多个氨基酸修饰的VH CDR3，并且可以例如包含以下简并序列::$X_1X_2X_3X_4X_5X_6X_7X_8X_9X_{10}YGX_{11}X_{12}X_{13}X_{14}X_{15}X_{16}X_{17}X_{18}$(SEQ ID NO:213)，其中$X_1$是任何氨基酸，例如，D、E或无；$X_2$是任何氨基酸，例如，F、G或无；$X_3$是任何氨基酸，例如，Y或无；$X_4$是任何氨基酸，例如，G、S或无；$X_5$是任何氨基酸，例如，G、T或S；$X_6$是任何氨基酸，例如，G或S；$X_7$是任何氨基酸，例如，N、W或无；$X_8$是任何氨基酸，例如，Y、S、E或无；$X_9$是任何氨基酸，例如，Y或无；$X_{10}$是任何氨基酸，例如，P或

Y;X_{11}是任何氨基酸,例如,D或无;X_{12}是任何氨基酸,例如,Y或无;X_{13}是任何氨基酸,例如,A或无;X_{14}是任何氨基酸,例如,H或无;X_{15}是任何氨基酸,例如,W或无;X_{16}是任何氨基酸,例如,F或M;X_{17}是任何氨基酸,例如,D或E;并且X_{18}是任何氨基酸,例如,P、I、V、Y或L。

[0517] 适于本公开的抗TIM3抗体的VH结构域或其一个或多个CDR可以连接于恒定结构域以形成重链,例如,全长重链。类似地,本文所述的VL结构域或其一个或多个CDR可以连接于恒定结构域以形成轻链,例如,全长轻链。全长重链(任选地缺少C末端赖氨酸(K)残基或C末端甘氨酸和赖氨酸(GK)残基)和全长轻链组合以形成全长抗体。

[0518] 抗TIM3抗体的VH结构域可以与人IgG(例如,IgG1、IgG2、IgG3或IgG4)的恒定结构域融合,所述恒定结构域是天然存在的或经修饰的,例如,如本文进一步描述。例如,VH结构域可以包含本文所述的任何VH结构域的氨基酸序列,所述氨基酸序列融合于人IgG(例如,IgG1)恒定区,如以下的野生型人IgG1恒定结构域氨基酸序列:

[0519] ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK(SEQ ID NO:58)

[0520] 或融合于SEQ ID NO:58的同种异型变体的氨基酸序列,并且具有以下氨基酸序列:

[0521] ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSG
LYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDK**R**VEPKSCDKTHTCPPCPAPELLGGPSV
FLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSR**E**E**M**TK
NQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQG
NVFSCSVMHEALHNHYTQKSLSLSPGK

(SEQ ID NO:59;同种异型特异性氨基酸残基加粗且加下划线)

[0522] 抗TIM3抗体的VH结构域可以包含本文所述的任何VH结构域的氨基酸序列,所述氨基酸序列融合于无效应子性恒定区,例如,以下的无效应子性人IgG1恒定结构域氨基酸序列:

[0523] ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSG
LYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDK**R**VEPKSCDKTHTCPPCPAPE<u>AE</u>G<u>A</u>PSV
FLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALP<u>SS</u>IEKTISKAKGQPREPQVYTLPPSR**E**E**M**TK
NQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQG
NVFSCSVMHEALHNHYTQKSLSLSPGK

(SEQ ID NO:60;“IgG1.1f”,包含加下划线的置换L234A、L235E、G237A、A330S和P331S);或

[0524] ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSG
LYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDK**R**VEPKSCDKTHTCPPCPAPE<u>AE</u>G<u>A</u>PSV
FLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALP<u>AP</u>IEKTISKAKGQPREPQVYTLPPSR**E**E**M**TK
NQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQG
NVFSCSVMHEALHNHYTQKSLSLSPGK

(SEQ ID NO:61;“IgG1.3f”,包含加下划线的置换L234A、L235E和G237A)

[0525] 例如,IgG1的同种异型变体包含K97R、D239E和/或L241M(以上加下划线和加粗)并根据SEQ ID NOs:59-61中进行编号。在全长重链区域(例如,8C4(SEQ ID NO:70))内部并且根据EU编号,这些氨基酸置换编号为K214R、D356E和L358M。在一些实施方案中,抗TIM3抗体的恒定区可以在如SEQ ID NO:59-61中编号的氨基酸L117、A118、G120、A213和P214(上文加下划线)或根据EU编号的L234、A235、G237、A330和P331处包含一个或多个突变或置换。在其他实施方案中,抗TIM3抗体的恒定区在SEQ ID NO:58的氨基酸L117A、A118E、G120A、A213S和P214S或根据EU编号的L234A、L235E、G237A、A330S和P331S处包含一个或多个突变或置换。抗TIM3抗体的恒定区还可以包含一个或多个突变或置换:SEQ ID NO:58的L117A、A118E和G120A、或根据EU编号的L234A、L235E和G237A。

[0526] 备选地,抗TIM3抗体的VH结构域可以包含本文所述的任何VH结构域的氨基酸序列,所述氨基酸序列融合于人IgG4恒定区,例如,以下的人IgG4氨基酸序列或其变体:

[0527] ASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTKTYTCNVDHKPSNTKVDKRVESKYGPPCPSCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSRLTVDKSRWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK(SEQ ID NO:63,包含S228P)。

[0528] 抗TIM3抗体的VL结构域可以与人κ或λ轻链的恒定结构域融合。例如,抗TIM3抗体的VL结构域可以包含本文所述的任何VL结构域的氨基酸序列,所述氨基酸序列融合于以下的人IgG1κ轻链氨基酸序列:

[0529] RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC(SEQ ID NO:64)

[0530] 在某些实施方案中,抗TIM3抗体的重链恒定区在C末端包含赖氨酸或另一个氨基酸,例如,它在重链中包含以下末尾氨基酸:LSPGK(SEQ ID NO:65)。在某些实施方案中,重链恒定区在C末端缺少一个或多个氨基酸,并且例如具有C末端序列LSPG(SEQ ID NO:66)或LSP(SEQ ID NO:67)。

[0531] 示例性抗TIM3抗体的重链和轻链的氨基酸序列分别对应于重链的SEQ ID NOs:68-189和轻链的SEQ ID NOs:190-193。

[0532] 在某些实施方案中,适于本公开的抗TIM3抗体包含:

[0533] (a1)分别包含SEQ ID NOs:136(或137)和190的重链序列和轻链序列;

[0534] (a2)分别包含SEQ ID NOs:68(或75)和190的重链序列和轻链序列;

[0535] (a3)分别包含SEQ ID NOs:82(或89))和190的重链序列和轻链序列;

[0536] (a4)分别包含SEQ ID NOs:138(或139)和190的重链序列和轻链序列;

[0537] (a5)分别包含SEQ ID NOs:96(或106)和190的重链序列和轻链序列；

[0538] (a6)分别包含SEQ ID NOs:116(或126)和190的重链序列和轻链序列；

[0539] (a7)分别包含SEQ ID NOs:140(或141)和190的重链序列和轻链序列；

[0540] (a8)分别包含SEQ ID NOs:97(或107)和190的重链序列和轻链序列；

[0541] (a9)分别包含SEQ ID NOs:117(或127)和190的重链序列和轻链序列；

[0542] (a10)分别包含SEQ ID NOs:142(或143)和190的重链序列和轻链序列；

[0543] (a11)分别包含SEQ ID NOs:98(或108)和190的重链序列和轻链序列；

[0544] (a12)分别包含SEQ ID NOs:118(或128)和190的重链序列和轻链序列；

[0545] (a13)分别包含SEQ ID NOs:144(或145)和190的重链序列和轻链序列；

[0546] (a14)分别包含SEQ ID NOs:99(或109)和190的重链序列和轻链序列；

[0547] (a15)分别包含SEQ ID NOs:119(或129)和190的重链序列和轻链序列；

[0548] (a16)分别包含SEQ ID NOs:146(或147)和190的重链序列和轻链序列；

[0549] (a17)分别包含SEQ ID NOs:100(或110)和190的重链序列和轻链序列；

[0550] (a18)分别包含SEQ ID NOs:120(或130)和190的重链序列和轻链序列；

[0551] (a19)分别包含SEQ ID NOs:148(或149)和190的重链序列和轻链序列；

[0552] (a20)分别包含SEQ ID NOs:101(或111)和190的重链序列和轻链序列；

[0553] (a21)分别包含SEQ ID NOs:121(或131)和190的重链序列和轻链序列；

[0554] (a22)分别包含SEQ ID NOs:150(或151)和190的重链序列和轻链序列；

[0555] (a23)分别包含SEQ ID NOs:102(或112)和190的重链序列和轻链序列；

[0556] (a24)分别包含SEQ ID NOs:122(或132)和190的重链序列和轻链序列；

[0557] (a25)分别包含SEQ ID NOs:152(或153)和190的重链序列和轻链序列；

[0558] (a26)分别包含SEQ ID NOs:103(或113)和190的重链序列和轻链序列；

[0559] (a27)分别包含SEQ ID NOs:123(或133)和190的重链序列和轻链序列；

[0560] (a28)分别包含SEQ ID NOs:154(或155)和190的重链序列和轻链序列；

[0561] (a29)分别包含SEQ ID NOs:184(或185)和190的重链序列和轻链序列；

[0562] (a30)分别包含SEQ ID NOs:186(或187)和190的重链序列和轻链序列；

[0563] (a31)分别包含SEQ ID NOs:188(或189)和190的重链序列和轻链序列；

[0564] (b1)分别包含SEQ ID NOs:156(或157)和191的重链序列和轻链序列；

[0565] (b2)分别包含SEQ ID NOs:69(或76)和191的重链序列和轻链序列；

[0566] (b3)分别包含SEQ ID NOs:83(或90)和191的重链序列和轻链序列；

[0567] (b4)分别包含SEQ ID NOs:158(或159)和191的重链序列和轻链序列；

[0568] (b5)分别包含SEQ ID NOs:104(或114)和191的重链序列和轻链序列；

[0569] (b6)分别包含SEQ ID NOs:124(或134)和191的重链序列和轻链序列；

[0570] (b7)分别包含SEQ ID NOs:160(或161)和191的重链序列和轻链序列；

[0571] (c1)分别包含SEQ ID NOs:162(或163)和191的重链序列和轻链序列；

[0572] (c2)分别包含SEQ ID NOs:70(或77)和191的重链序列和轻链序列；

[0573] (c3)分别包含SEQ ID NOs:84(或91)和191的重链序列和轻链序列；

[0574] (c4)分别包含SEQ ID NOs:164(或165)和191的重链序列和轻链序列；

[0575] (d1)分别包含SEQ ID NOs:166(或167)和190的重链序列和轻链序列；

[0576] (d2)分别包含SEQ ID NOs:71(或78)和190的重链序列和轻链序列；

[0577] (d3)分别包含SEQ ID NOs:85(或92)和190的重链序列和轻链序列；

[0578] (d4)分别包含SEQ ID NOs:168(或169)和190的重链序列和轻链序列；

[0579] (e1.1)分别包含SEQ ID NOs:170(或171)和192的重链序列和轻链序列；

[0580] (e1.2)分别包含SEQ ID NOs:170(或171)和193的重链序列和轻链序列；

[0581] (e1.3)分别包含SEQ ID NOs:170(或171)和191的重链序列和轻链序列；

[0582] (e2)分别包含SEQ ID NOs:72(或79)和193的重链序列和轻链序列；

[0583] (e3)分别包含SEQ ID NOs:86(或93)和193的重链序列和轻链序列；

[0584] (e4)分别包含SEQ ID NOs:172(或173)和193的重链序列和轻链序列；

[0585] (e5)分别包含SEQ ID NOs:105(或115)和193的重链序列和轻链序列；

[0586] (e6)分别包含SEQ ID NOs:125(或135)和193的重链序列和轻链序列；

[0587] (e7)分别包含SEQ ID NOs:174(或175)和193的重链序列和轻链序列；

[0588] (f1)分别包含SEQ ID NOs:176(或177)和190的重链序列和轻链序列；

[0589] (f2)分别包含SEQ ID NOs:73(或80)和190的重链序列和轻链序列；

[0590] (f3)分别包含SEQ ID NOs:87(或94)和190的重链序列和轻链序列；

[0591] (f4)分别包含SEQ ID NOs:178(或179)和190的重链序列和轻链序列；

[0592] (g1)分别包含SEQ ID NOs:180(或181)和191的重链序列和轻链序列；

[0593] (g2)分别包含SEQ ID NOs:74(或81)和191的重链序列和轻链序列；

[0594] (g3)分别包含SEQ ID NOs:88(或95)和191的重链序列和轻链序列;或

[0595] (g4)分别包含SEQ ID NOs:182(或183)和191的重链序列和轻链序列；

[0596] 其中抗体与人TIM3特异性结合。

[0597] 编码本文(例如,在前述段落中)公开的TIM3抗体的重链序列的核酸序列在SEQ ID NOs:214-241、247-291、294-297中提供。编码本文(例如,在前述段落中)公开的TIM3抗体的轻链序列的核酸序列在SEQ ID NOs:242-246和299中提供。

[0598] 在一些实施方案中,抗TIM3抗体包含本文(例如,在前述段落中)所述的重链序列和轻链序列的组合,其中抗体包含两条重链和两条轻链,并且可以还包含至少一个使两条重链连接在一起的二硫键。抗体还可以包含将每条轻链与每条重链连接的二硫键。

[0599] 在其他实施方案中,抗TIM3抗体是人抗体、人源化抗体或嵌合抗体。在一些实施方案中,抗TIM3抗体与构象表位结合。在其他实施方案中,抗TIM3抗体与成熟的人TIM3胞外结构域(SEQ ID NO:198)的以下区域内的氨基酸残基结合：

[0600] SEVEYRAEVGQNAYLPCFYTPAAPGNLVPVCWGKGACPVFECGNVVLRTDERDVNYWTSRYWLNGDFRKGDVSLTIENVTLADSGIYCCRIQIPGIMND(SEQ ID NO:203),其与成熟人TIM3胞外结构域(SEQ ID NO:198)的氨基酸残基1-99或具有SEQ ID NO:194的人TIM3的氨基酸22至120对应。

[0601] 在一些实施方案中,本文所述的抗TIM3抗体与成熟的人TIM3胞外结构域(SEQ ID NO:198)的以下区域内的氨基酸残基结合:CPVFECG(SEQ ID NO:200),其与成熟人TIM3胞外结构域(SEQ ID NO:198)的氨基酸残基37-43对应。

[0602] 在一些实施方案中,抗TIM3抗体与成熟的人TIM3胞外结构域(SEQ ID NO:198)的以下区域内的氨基酸残基结合:WTSRYWLNGDFR(SEQ ID NO:201),其与成熟人TIM3胞外结构域(SEQ ID NO:198)的氨基酸残基57-83对应。

[0603] 在一些实施方案中，抗TIM3抗体与成熟的人TIM3胞外结构域(SEQ ID NO:198)的以下区域内的氨基酸残基结合:RIQIPGIMND(SEQ ID NO:202)，其与成熟人TIM3胞外结构域(SEQ ID NO:198)的氨基酸残基90-99对应。

[0604] 在一些实施方案中，抗TIM3抗体具有与抗体13A3、3G4、17C3、17C8、9F6、8B9、8C4和TIM3.2至TIM3.18中一者或多者相同的野生型和突变型人TIM3结合样式。在一些实施方案中，抗TIM3抗体与成熟的人TIM3胞外结构域(SEQ ID NO:198)的以下区域内的氨基酸残基结合:CPVFECG(SEQ ID NO:200)、WTSRYWLNGDFRKGDVSLTIENVTLAD(SEQ ID NO:201)和/或RIQIPGIMND(SEQ ID NO:202)。

[0605] 在某些实施方案中，抗TIM3抗体结合于(1)^{49}VPVCWGKGACPVFE^{62}(SEQ ID NO:204)和^{111}RIQIPGIMNDEKFNLKL^{127}(SEQ ID NO:205)或(2)^{40}YTPAAPGNLVPVCWGKGACPVFE^{62}(SEQ ID NO:206)、^{66}VVLRTDERDVNY^{77}(SEQ ID NO:207)、^{78}WTSRYWLNGDFRKGDVSL^{95}(SEQ ID NO:208)、^{110}CRIQIPGIMNDEKFNLKL^{127}(SEQ ID NO:209)和^{119}NDEKFNLKL^{127}(SEQ ID NO:210)，如通过HDX-MS所测定。在某些实施方案中，抗TIM3抗体与hTIM3的氨基酸残基40-62和111-127的区域相互作用，但与其他区域(如氨基酸残基Y40的N端区域、位于氨基酸残基E62和R111之间的区域、和氨基酸残基L127的C端区域)无显著相互作用，如通过HDX-MS所测定。

[0606] 在一些实施方案中，相对于与野生型人TIM3的结合作用，抗TIM3抗体对其中氨基酸L48、C58、P59、V60、F61、E62、C63、G64、W78、S80、R81、W83、L84、G86、D87、R89、D104、R111、Q113、G116、M118和D120(如SEQ ID NO:194中编号)中一者或多者被另一氨基酸置换的人TIM3具有减少的结合作用，并且该抗体结合于(1)^{49}VPVCWGKGACPVFE^{62}(SEQ ID NO:204)和^{111}RIQIPGIMNDEKFNLKL^{127}(SEQ ID NO:205)或(2)^{40}YTPAAPGNLVPVCWGKGACPVFE^{62}(SEQ ID NO:206)、^{66}VVLRTDERDVNY^{77}(SEQ ID NO:207)、^{78}WTSRYWLNGDFRKGDVSL^{95}(SEQ ID NO:208)、^{110}CRIQIPGIMNDEKFNLKL^{127}(SEQ ID NO:209)和^{119}NDEKFNLKL^{127}(SEQ ID NO:210)，如通过HDX-MS所测定。

[0607] 在一些实施方案中，抗TIM3抗体具有与TIM3.18.IgG1.3或13A3相似的野生型和突变型人TIM3结合样式，即，该抗体：

[0608] (i)结合于(1)^{49}VPVCWGKGACPVFE^{62}(SEQ ID NO:204)、^{111}RIQIPGIMNDEKFNLKL^{127}(SEQ ID NO:205)和^{119}NDEKFNLKL^{127}(SEQ ID NO:210)，并且例如不显著结合于(a)具有位于氨基酸残基49的N端的序列的肽；(b)具有位于氨基酸残基62和111之间的序列的肽(例如，^{78}WTSRYWLNGDFRKGDVSL^{95}(SEQ ID NO:208))；和(c)具有位于氨基酸残基127的C端的序列的肽，如通过HDX-MS所测定；

[0609] (ii)例如，如使用酵母表面展示法所测定，不能结合于具有以下一个或多个氨基酸突变的人TIM3或具有显著降低的该人TIM3结合作用:C58、P59、F61、E62、C63、R111、D120和任选地D104和Q113(根据SEQ ID NO:194编号)；和/或

[0610] (iii)如通过X射线结晶学所测定，具有与至少5、10、15、20个或全部以下人TIM3氨基酸相互作用的重链可变区和/或轻链可变区:P50、V51、C52、P59、V60、F61、E62、C63、G64、N65、V66、V67、L68、R69、D71、E72、D74、R111、Q113、G116、I117、M118、D120和任选地T70和/或I112(根据SEQ ID NO:194编号)。

[0611] 在一些实施方案中，抗TIM3抗体包含重链和轻链，其中重链选自SEQ ID NOs:68-189并且轻链选自SEQ ID NOs:190-193。

[0612] 如本文中进一步讨论，本文所述的抗TIM3抗体的重链恒定区可以属于任何同种型，例如，IgG1、IgG2、IgG3和IgG4、或其组合和/或其修饰物。抗TIM3抗体可以具有效应子功能或可以具有减少的效应子功能或没有效应子功能。在某些实施方案中，抗TIM3抗体包含向抗体提供增强特性的修饰的重链恒定区。

[0613] 可以在本文所述方法中使用的其它TIM3拮抗剂包括MBG-453、TSR-022、TRL-6061、BGBA425、LY-3321367和任何其他TIM3抑制剂，例如，抗体、肽、小分子和双特异性分子，如双特异性抗体(例如，抗TIM3/抗PD-1双特异性分子)。例如以下文献中描述了TIM-3拮抗剂:WO 2011/155607、WO 2011/159877、WO 2013/006490、CN 2010/4592388、WO2015/109931、WO 2015/117002、WO 2016/068803、WO 2016/068802、WO 2016/071448、WO 2016/111947、WO 2016/144803、WO 2016/161270、WO 2017/019897、US 2017/0029485、WO 2017/031242、WO 2017/055399、WO 2017/055404、WO 2017/079112、WO 2017/079115、WO 2017/079116、PCT申请号PCT/US2017/041946、和/或CN 2010/6632675。

[0614] PD-1拮抗剂

[0615] 在一个方面，本公开特征在于组合PD-1拮抗剂使用TIM3拮抗剂的方法。如本文所用，PD-1拮抗剂包括但不限于PD-1结合剂、PD-L1结合剂、和PD-L2结合剂。PD-1结合剂包括与PD-1特异性结合的抗体。PD-L1和PD-L2结合剂包括与PD-L1和/或PD-L2特异性结合的抗体、以及与PD-L1和/或PD-L2结合的可溶性PD-1多肽。

[0616] 抗PD-1抗体

[0617] 本公开的某些方面包括向有需要的受试者施用治疗有效量的抗PD-1抗体或其抗原结合部分。已经在美国专利号8,008,449中公开了以高亲和力与PD-1特异性结合的人单克隆抗体(HuMabs)。已经例如在美国专利号6,808,710、7,488,802、8,168,757和8,354,509和PCT公开号WO 2012/145493中描述其他抗PD-1mAb。美国专利号8,008,449中公开的每种抗PD-1HuMAb已经展示显示出以下一个或多个特征：(a)以1x 10^{-7}M或更小的KD与人PD-1结合，如通过使用Biacore生物传感器系统的表面等离子体共振法所测定；(b)基本上与人CD28、CTLA-4或ICOS不结合；(c)在混合淋巴细胞反应(MLR)测定法中增加T细胞增殖；(d)在MLR测定法中增加干扰素-γ产生；(e)在MLR测定法中增加IL-2分泌；(f)与人PD-1和食蟹猴PD-1结合；(g)抑制PD-L1和/或PD-L2与PD-1结合；(h)刺激抗原特异性记忆应答；(i)刺激抗体应答；和(j)在体内抑制肿瘤细胞生长。可用于本发明中的抗PD-1Ab包括与人PD-1特异性结合并显示出至少一个、在一些实施方案中至少五个前述特征的mAb。在一些实施方案中，抗PD-1抗体是纳武单抗(OPDIVO®)。在一些实施方案中，抗PD-1抗体是派姆单抗(KEYTRUDA®)。

[0618] 在一些实施方案中，抗PD-1抗体是纳武单抗。纳武单抗(也称作“OPDIVO®”；以前命名为5C4、BMS-936558、MDX-1106或ONO-4538)是全人IgG4(S228P)PD-1免疫检查点抑制抗体，其选择性地阻止与PD-1配体(PD-L1和PD-L2)的相互作用，从而阻断抗肿瘤T细胞功能的下调(美国专利号8,008,449；Wang等人，2014Cancer Immunol Res.2(9):846-56)。

[0619] 在一些实施方案中，抗PD-1抗体是派姆单抗。派姆单抗(也称作“KEYTRUDA®”、lambrolizumab和MK-3475)是针对人细胞表面受体PD-1(程序性死亡-1或程序性细胞死亡-1)的人源化单克隆IgG4抗体。例如在美国专利号8,354,509和8,900,587中描述了派姆单

抗;还参见www.cancer.gov/drugdictionary?cdrid＝695789(最后访问时间:2014年12月14日)。派姆单抗已经由FDA批准用于治疗复发性或难治性黑素瘤。

[0620] 在其他实施方案中,抗PD-1抗体或其片段与MEDI0608交叉竞争。另外的实施方案中,抗PD-1抗体或其片段结合与MEDI0608相同的表位。在某些实施方案中,抗PD-1抗体具有与MEDI0608相同的CDR。在其他实施方案中,抗PD-1抗体是MEDI0608(前称AMP-514),其是单克隆抗体。例如美国专利号8,609,089B2中描述MEDI0608。

[0621] 在某些实施方案中,PD-1拮抗剂是AMP-224,后者为B7-DC Fc融合蛋白。美国公开号2013/0017199和worldwideweb.cancer.gov/publications/dictionaries/cancer-drug?cdrid＝700595(最后访问时间:2015年7月8日)中讨论了AMP-224。

[0622] 在某些实施方案中,抗PD-1抗体是BGB-A317,其是人源化单克隆抗体。美国公开号2015/0079109中描述了BGB-A317。

[0623] 可用于所公开方法中的抗PD-1抗体还包括分离的Ab,其与人PD-1特异性结合并且与纳武单抗交叉竞争结合于人PD-1(例如,参见美国专利号8,008,449和8,779,105;WO 2013/173223)。Ab交叉竞争结合于某抗原的能力表示,这些Ab与该抗原的相同表位区域结合并且空间上阻碍其他交叉竞争性Ab与这个特定表位区域结合。因为其与PD-1的相同表位区域结合,预期这些交叉竞争性Ab具有与纳武单抗非常类似的功能特性。可以基于这类交叉竞争性Ab在标准PD-1结合测定法(如Biacore分析、ELISA测定或流式细胞术)中与纳武单抗交叉竞争的能力,容易地鉴定这些Ab(例如,参见WO 2013/173223)。

[0624] 在某些实施方案中,与人PD-1抗体(纳武单抗)交叉竞争结合于人PD-1或与该抗体结合于相同表位区域的抗体,是单克隆抗体。为了施用至人类受试者,这些交叉竞争性抗体可以是嵌合抗体、人源化或人Ab。可以通过本领域熟知的方法制备并分离这类嵌合、人源化或人单克隆抗体。

[0625] 可用于所公开发明的方法中的抗PD-1Ab还包括以上抗体的抗原结合部分。已经充分显示,抗体的抗原结合功能可以由全长抗体的片段执行。涵盖于术语抗体的“抗原结合部分”范围内的结合片段的实例包括(i)Fab片段,一种由VL、VH、CL和CH1结构域组成的单价片段;(ii)F(ab')2片段,一种包含由二硫键在铰链区连接的两个Fab片段的双价片段;(iii)由VH和CH1结构域组成的Fd片段;和(iv)由抗体单臂的VL和VH结构域组成的Fv片段。

[0626] 适用于所公开方法或组合物中的抗PD-1抗体是这样的抗体,它们以高特异性和高亲和力与PD-1结合、阻断对PD-L1和或PD-L2的结合、并且抑制PD-1信号传导途径的免疫抑制作用。在本文所公开的任何组合物或方法中,抗PD-1“抗体”包括这样的抗原结合部分或片段,其与PD-1受体结合,并且在抑制配体结合及上调免疫系统方面显示与完整抗体相似的功能特性。在某些实施方案中,抗PD-1抗体或其抗原结合部分与纳武单抗交叉竞争结合人PD-1。在其他实施方案中,抗PD-1抗体或其抗原结合部分是嵌合、人源化或人单克隆抗体或其部分。在某些实施方案中,抗体是人源化抗体。在其他实施方案中,抗体是人抗体。可以使用IgG1、IgG2、IgG3或IgG4同种型Ab。

[0627] 在某些实施方案中,抗PD-1抗体或其抗原结合部分包含具有人IgG1或IgG4同种型的重链恒定区。在某些其他实施方案中,抗PD-1抗体或其抗原结合部分的IgG4重链恒定区的序列含有S228P突变,所述突变用正常情况在IgG1同种型抗体的相应位置处存在的脯氨酸残基替换铰链区中的丝氨酸残基。纳武单抗中存在的这个突变可以防止与内源IgG4抗体

的Fab臂交换，同时保留对与野生型IgG4抗体缔合的激活性Fc受体的低亲和力(Wang等人，2014Cancer Immunol Res.2(9):846-56)。在另外的其他实施方案中，抗体包含轻链恒定区，人κ或λ恒定区。在其他实施方案中，抗PD-1抗体或其抗原结合部分是mAb或其抗原结合部分。在本文所述的包括施用抗PD-1抗体的任何治疗方法的某些实施方案中，抗PD-1抗体是纳武单抗。在其他实施方案中，抗PD-1抗体是派姆单抗。在其他实施方案中，抗PD-1抗体选自美国专利号8,008,449中描述的人抗体17D8、2D3、4H1、4A11、7D3和5F4。在另外的实施方案中，抗PD-1抗体是MEDI0608(以前AMP-514)、AMP-224、PDR001或BGB-A317。

[0628] 抗PD-L1抗体

[0629] 在某些实施方案中，这些方法中所用的抗PD-1抗体可以替换为另一种PD-1或抗PD-L1拮抗剂。例如，因为抗PD-L1抗体可以阻碍PD-1和PD-L1之间的相互作用，因而向PD-1的信号传导途径施加相似的影响，故抗PD-L1抗体可以代替抗PD-1抗体用于本文所公开的方法中。因此，本公开的某些方面包括向有需要的受试者施用治疗有效量的抗PD-L1抗体或其抗原结合部分。在某些实施方案中，可用于该方法的抗PD-L1抗体是BMS-936559(前称12A4或MDX-1105)(例如，参见美国专利号7,943,743;WO 2013/173223)。在其他实施方案中，抗PD-L1抗体是MPDL3280A(也称作RG7446)(例如，参见Herbst等人，(2013)J Clin Oncol 31(suppl):3000.摘要;美国专利号8,217,149)、MEDI4736(也称作德瓦鲁单抗(durvalumab)(IMFINZI®);Khleif,2013,引自:Proceedings from the European Cancer Congress2013;2013年9月27日-10月1日;阿姆斯特丹，荷兰)。在某些实施方案中，与上文参考文献的PD-L1抗体交叉竞争结合于人PD-L1或与其结合于人PD-L1相同表位区域的抗体是mAb。在某些实施方案中，抗PD-L1抗体或其抗原结合部分与BMS-936559、MPDL3280A、MEDI4736、或MSB0010718C竞争结合于人PD-L1。为了施用至人类受试者，这些交叉竞争性抗体可以是嵌合抗体或可以是人源化或人抗体。可以通过本领域熟知的方法制备并分离这类嵌合、人源化或人mAb。参见美国专利号8,779,108或US 2014/0356353(2014年5月6日提交)、或MSB0010718C(也称作阿维鲁单抗(avelumab)(BAVENCIO®))；参见US 2014/0341917)。在某些实施方案中，抗PD-L1抗体或其抗原结合部分包含具有人IgG1或IgG4同种型的重链恒定区。在一些实施方案中，抗PD-L1抗体是BMS-936559。在一些实施方案中，抗PD-L1抗体是MPDL3280A(阿特朱单抗(TECENTRIQ®))。在一些实施方案中，抗PD-L1抗体是MEDI4736(德瓦鲁单抗(IMFINZI®))。在一些实施方案中，抗PD-L1抗体是MSB0010718C(阿维鲁单抗(BAVENCIO®))。

[0630] 药物组合物

[0631] 适于施用人类患者的药物组合物一般配制用于肠胃外施用，例如，配制在液态载体中，或适于复溶成液态溶液剂或混悬剂用于静脉内施用。

[0632] 通常，这类组合物一般包含可药用载体。如本文所用，术语“可药用”意指，由政府监管机构批准或者列于美国药典或其它普遍认可的药典中用于动物中，尤其用于人类中。术语“载体”指与化合物一起施用的稀释剂、辅助剂、赋形剂或溶媒。这类药用载体可以是无菌液体，如水和油，包括石油来源、动物来源、植物来源或合成来源的那些油，如花生油、大豆油、矿物油、芝麻油、甘油、聚乙二醇、蓖麻醇酸酯等。可以使用水或盐水溶液和水性右旋

糖和甘油溶液作为载体，特别地用于可注射溶液剂(例如，包含TIM3拮抗剂和/或PD-1拮抗剂)。可以配制用于肠胃外施用的液体组合物，以通过注射或连续输注施用。注射或输注施用途径包括静脉内、腹膜内、肌内、鞘内和皮下。在一些实施方案中，静脉内施用TIM3拮抗剂和PD-1拮抗剂(例如，在分立的制剂中或在一起(在相同制剂中或在分立的制剂中))。

[0633] 患者群体

[0634] 本文提供，在人类患者中，单独或结合另一免疫检查点抑制剂(例如，抗PD-1抗体)一起使用本文公开的免疫疗法，例如，TIM3拮抗剂(例如，抗TIM3抗体)，治疗癌症的临床方法。

[0635] 可以使用本发明方法治疗的癌症的实例包括，肝癌、肝细胞癌(HCC)、骨癌、胰腺癌、皮肤癌、口腔癌、头或颈癌、乳腺癌、肺癌、小细胞肺癌、NSCLC、皮肤或眼内恶性黑素瘤、肾癌、子宫癌、卵巢癌、结直肠癌、结肠癌、直肠癌、肛区癌、胃癌、睾丸癌、子宫癌、输卵管癌、子宫内膜癌、子宫颈癌、阴道癌、外阴癌、头颈鳞状细胞癌(SCCHN)、非霍奇金淋巴瘤、食道癌、小肠癌、内分泌系统癌、甲状腺癌、甲状旁腺癌、肾上腺癌、软组织肉瘤、尿道癌、阴茎癌、儿童实体瘤、淋巴细胞淋巴瘤、膀胱癌、肾或输尿管癌、肾盂癌、中枢神经系统肿瘤(CNS)、原发性CNS淋巴瘤、肿瘤血管生成、脊枢椎肿瘤、脑干胶质瘤、垂体腺瘤、Kaposi肉瘤、表皮样癌、鳞状细胞癌、环境所致癌(包括石棉诱导的那些癌)、血液学恶性病，例如包括多发性骨髓瘤、B细胞淋巴瘤、霍奇金淋巴瘤/原发性纵隔B细胞淋巴瘤、非霍奇金淋巴瘤、急性髓样淋巴瘤、慢性髓性白血病、慢性淋巴样白血病、滤泡淋巴瘤、弥漫性大B细胞淋巴瘤、Burkitt淋巴瘤、免疫母细胞大细胞淋巴瘤、前体B-淋巴母细胞淋巴瘤、套细胞淋巴瘤、急性淋巴母细胞性白血病、蕈样霉菌病、间变性大细胞淋巴瘤、T细胞淋巴瘤、和前体T-淋巴母细胞淋巴瘤，及所述癌症的任何组合。本发明还适用于治疗转移性癌症。

[0636] 在一些实施方案中，受试者罹患对免疫检查点抑制剂治疗具有顽固性的癌症。在一些实施方案中，受试者罹患对PD-1拮抗剂(例如，抗PD-1抗体或抗PD-L1抗体)治疗具有顽固性的癌症。在一些实施方案中，癌症是实体瘤。在其他实施方案中，癌症是结肠癌、肾癌或肺癌。

[0637] 可以在治疗之前、其期间或之后，针对一个或多个上述临床属性，检验或选择受试者。

[0638] 免疫治疗

[0639] 在一个方面，本文提供的免疫疗法涉及，单独或结合另一种免疫检查点抑制剂(例如，PD-1拮抗剂，例如，抗PD-1抗体)一起施用TIM3拮抗剂(例如，抗TIM3抗体)，以治疗患有癌症的受试者。在一个具体实施方案中，TIM3拮抗剂是本文所述的抗TIM3抗体。在某些实施方案中，PD-1拮抗剂是抗PD-1抗体纳武单抗。在一些实施方案中，调节给药方案以提供最佳的所需反应(例如，有效反应)。

[0640] 如本文所用，辅助或组合施用(共施用)包括，同时施用处于相同或不同剂型中的化合物，或分开施用化合物(例如，依次施用)。因此，例如，可以在单一制剂中同时施用TIM3拮抗剂和PD-1拮抗剂。备选地，可以配制TIM3拮抗剂和PD-1拮抗剂用于独立施用，并且将它们并行或依次施用(例如，将一种抗体在施用第二种抗体前约30分钟内施用)。

[0641] 例如，可以首先施用TIM3拮抗剂，接着(例如，紧接着)施用PD-1拮抗剂，或反之亦然。在一些实施方案中，施用TIM3拮抗剂之前，施用PD-1拮抗剂。在一些实施方案中，施用

TIM3拮抗剂之后，施用PD-1拮抗剂。在其他实施方案中，并行施用TIM3拮抗剂和PD-1拮抗剂。这种并行或依次施用优选地导致两种拮抗剂同时存在于所治疗的受试者中。

[0642] 以举例说明方式且不以限制方式提供以下实施例。本申请通篇范围内引用的全部参考文献均通过引用的方式明确并入本文。

实施例

[0643] 实施例1:分析来自癌症患者的CD4和CD8 T淋巴细胞上的TIM3表达水平

[0644] 为了开始评估利用TIM3表达鉴定适于TIM3拮抗剂治疗的受试者(例如，人类癌症患者)的适宜性，从肺癌、肾癌或结肠癌患者获得新鲜的肿瘤组织样品和匹配的外周血样品(ConversantBio,MT Group,Benaroya)并发运至实验室供分析。将肿瘤组织样品和血液样品分别在Hypothermosol FRS(Biolife Solutions)和ACD溶液A(BD Biosciences)中4℃过夜发运。在采集后的24小时以内处理并分析样品。

[0645] 用于免疫表型分型的组织加工

[0646] 将肿瘤组织称重并使用Miltenyi解离试剂盒(Miltenyi，目录号130-095-929)解离。外周血细胞用红细胞(RBC)裂解缓冲液(BioLegend，目录号420301)处理。随后，将细胞悬液(来自肿瘤组织或外周血)在HBSS(无Ca，无Mg)中洗涤两次，用NIR Viability染料(Molecular Probes by Life Technologies，目录号L34976)染色，用Dulbecco磷酸盐缓冲盐水(dPBS)中的人AB血清封闭，并添加至含有混合抗体(参见表1，下文)的孔，以便冰上黑暗温育45分钟。随后，用dPBS/BSA/叠氮化钠洗涤细胞两次，固定，并且使用FoxP3缓冲液试剂盒(BioLegend，目录号421403)透化。对于全部抗体，配制荧光减一(Fluorescence Minus One，FMO)对照并且将其用来确定阳性细胞群体。在Fortess流式细胞仪(BD Biosciences)上获取样品并且使用FlowJo软件(TreeStar)分析数据。

[0647] 用于流式细胞分析的抗体染色

[0648] 如表1(下文)中所示，设计一个15色方案来检查多个标志物的表达情况；重点在于CD8+T细胞和CD4+T细胞上的TIM3表达。

[0649] 表1:用于T细胞亚类免疫荧光染色的抗体

[0650]

标志物	克隆	荧光团	供应商	目录号
存活力	--	近 IR	ThermoFisher Scientific	L10119
CD45	HI30	AF700	BD Biosciences	560566
CD3	SK7	BUV 395	BD Biosciences	564001
CD4	OKT4	BV 785	BioLegend	317442
FoxP3	206D	AF647	BioLegend	320114
CD8a	SK1	BV605	BD Biosciences	564116

[0651] 表1:用于T细胞亚类免疫荧光染色的抗体

[0652]

标志物	克隆	荧光团	供应商	目录号
CD25	4E3	PE-e610	eBioscience	61-0257-42
PD-1	EH12.1	PerCP-Cy5.5	Biolegend	329914
Tim-3	FAB2365G	AlexaFluor488	R&D	

[0653] 如表2(下文)和图1A和图1B中所示,健康受试者和癌症患者的全血中极少数CD4+T细胞和CD8+T细胞表达TIM3。相比全血,TIL中TIM3+CD4+的频率略高,肿瘤类型之间无重大差异(参见图2A和图2B)。相比CD4+T细胞,较大百分数的CD8+T细胞呈TIM3+,取决于肿瘤类型,平均频率范围从9.9%至21%。RCC和(较小程度地)CRC通常显示比肺癌患者更高的TIM3+CD8 T细胞频率。参见表3(下文)和图2A和图2B。

[0654] 表2:来自健康供体和癌症患者的外周血样品中TIM3+CD4+和TIM3+CD8+T细胞的平均频率±SD

[0655]

	健康 (N=20)	肺 (N=15)	RCC (N=19)	CRC (N=16)
TIM3+ CD4+ T 细胞%	1.1 ±0.4	1.3 ±0.6	1.4 ±0.8	1.2 ±0.6
TIM3+ CD8+ T 细胞%	1.3 ±0.4	1.9 ±1.3	1.8 ±1.2	23 ±14

[0656] 缩写:N:样品数;SD:标准差;RCC:肾细胞癌;CRC;结直肠癌

[0657] 除TIM3表达之外,还在上文描述的TIL中评估了PD-1表达。如表3(下文)和图2C和图2D中所示,取决于患者,TIM3+细胞的PD-1共表达大幅度变动,其中,与TIM3+CD8+T细胞频率较低的患者相比,TIM3+CD8+T细胞频率较高(即,至少8%,其代表全部三个癌类型之间的中位TIM3+CD8+T细胞%)的患者显示更高的PD-1共表达(参见图2E,依据Mann Whitney,$p<0.0001$)。

[0658] 表3:来自癌症患者的TIL中TIM3+和PD-1+TIM3+CD4+和CD8+T细胞的平均频率±SD

[0659]

	肺 (N=18)	RCC (N=23)	CRC (N=17)
TIM3+ CD4+ T 细胞%	6.7 ±4.5	6.2 ±6.6	7.4 ±7.1
TIM3+ CD8+ T 细胞%	9.9 ±11	21 ±23	15 ±15
(TIM3+ CD4+ T 细胞中的) PD-1+%	58 ±11	47 ±20	53 ±25
(TIM3+ CD8+ T 细胞中的) PD-1+%	58 ±17	63 ±32	72 ±16

[0660]

[0661] 缩写:SD:标准差;TIL:肿瘤浸润型淋巴细胞;RCC:肾细胞癌;CRC:结直肠癌;N:样品数

[0662] 实施例2:分析不同T细胞亚群中的TIM3表达

[0663] 为了评估不同T细胞亚群上的TIM3表达,从以下多种癌症类型的患者获得新鲜的肿瘤组织样品和匹配的外周血样品(MT Group,CINJ):肾细胞癌(n=16)、结直肠癌(n=2)、肝癌(n=2)、子宫癌(n=3)、肺癌(n=1)、卵巢癌(n=1)、胃癌(n=1)和胃肠道癌(n=1)。将

样品分别在Hypothermosol FRS(Biolife Solutions)中和肝素(BD Biosciences)上4℃过夜发运到实验室以供分析。全部样品均在采集24小时以内处理并染色。

[0664] 用于免疫表型分型的组织加工

[0665] 将肿瘤组织称重并使用胶原酶I、II、IV和DNA酶I的温和混合物解离,随后进行Ficoll分离。使用沉降缓冲液(Miltenyi Biotech),使外周白细胞与红细胞分离。将细胞悬液(来自肿瘤组织或外周血)在无钙和镁的磷酸盐缓冲盐水(PBS)中洗涤两次,用近红外(NIR)存活力染料(Molecular Probes by Life Technologies,目录号L34976)染色。用'FACS缓冲液'(含有0.5%胎牛血清和0.1%叠氮化钠的PBS)中的人γ球蛋白(Jackson Immunoresearch)或小鼠IgG血清(Sigma Aldrich)封闭Fc受体,随后将样品用多种抗体混合物(参见表1、2、3、4)在4℃于黑暗下染色45分钟。随后将细胞用FACS缓冲液洗涤两次,并用FACS裂解溶液(BD Biosciences,目录号349202)固定。对于抗体子集,配制荧光减一(FMO)对照并且将其用来确定阳性细胞群体。在Fortess流式细胞仪(BD Biosciences)上获取样品并且使用FlowJo软件(TreeStar)分析数据。

[0666] 用于流式细胞分析的抗体染色

[0667] 为了评估不同T细胞亚群上的TIM3表达,用表4(下文)中提供的抗体混合物对来自上文的已处理细胞染色。图3A中显示设门策略的代表性实例:CCR7+CD45RO-("幼稚")、CCR7+CD45RO+("中央记忆")、CCR7-CD45RO+("效应记忆")和CCR7-CD45RO-("效应")。表5(下文)中提供TIL中这些亚群的中位频率。

[0668] 表4:用于T细胞亚群中TIM3表达分析的抗体组

[0669]

标志物	克隆	荧光团	供应商	目录号
存活力	--	近 IR	Invitrogen	L34976
CD45	HI30	BV480	BDBiosciences	566115
CD3	UCHT1	BUV496	BDBiosciences	564809
CD4	SK3	AF700	Biolegend	344622
CD8	RPA-T8	BUV395	BDBiosciences	563795
CD45RO	HI100	BV421	Biolegend	304224
CD197	G043H7	BV711	Biolegend	353228
PD-1	MIH4	APC	BDBiosciences	558694
TIM3	7D3	BB515	BDBiosciences	565568

[0670] 如图3B中所示,TIM3+细胞的频率根据T细胞亚群和个体患者而变动,存在朝向更高百分数的效应记忆和效应CD4+T细胞和CD8+T细胞表达TIM3的总体趋势。一些患者中更高百分数的效应T细胞和效应记忆T细胞表达TIM3的事实,指示通过TIM3抑制作用再活化T细胞应答的可能性。此外,数据表明,在患有癌症的受试者的TIL中更大频率的TIM-3+效应T细胞和/或TIM3+效应记忆T细胞指示受试者将响应于采用TIM-3拮抗剂(如抗TIM-3抗体)的癌症疗法。

[0671] 在全血中,因为TIM3+T细胞频率很低,在TIL中和相应全血中的TIM3+T细胞频率之间看起来不存在显著相关性(参见图3C)。

[0672] 表5:CD4 T细胞亚群和CD8 T细胞亚群的中位频率

[0673]

TIL 中的中位频率	幼稚	中央记忆	效应记忆	效应
CD4+%	2.9	32	60	1.5
CD8+%	2.1	5.2	68	19

[0674] 除上文之外,还在以上癌症患者的TIL中评估了PD-1共表达。如实施例1中观察到,大多数分析的样品中大部分TIM3+CD8+TIL也呈PD-1阳性(参见图4A和图4B)。极少数CD8+TIL为TIM3+PD-1-,并且约半数样品中,大部分PD1+CD8+TIL也呈TIM3表达阳性。这个结果,连同来自实施例1的结果,支持使用PD-1拮抗剂(例如,抗PD-1抗体,例如,纳武单抗)与TIM3拮抗剂的组合治疗癌症,例如,在呈TIM-3+PD-1+的受试者中使用。

[0675] 实施例3:分析不同免疫细胞亚群中的TIM3表达

[0676] 因为T细胞不是表达TIM3的唯一免疫细胞,所以还对分离自实施例2所述样品的一个子集中的髓样细胞和NK细胞,评估了TIM3表达。表6和表7(下文)中提供用来鉴定这些免疫细胞亚群的抗体混合物。

[0677] 表6:用于髓样细胞亚群中TIM3表达分析的抗体组

[0678]

标志物	克隆	荧光团	供应商	目录号
存活力	-	近 IR	Invitrogen	L34976
CD3	SK7	BV605	BD biosciences	563219
CD19	HIB19	BV605	BD biosciences	562653
CD56	5.1H11	BV605	BD biosciences	562780
CD45	2D1	PerCP-Cy5.5	Biolegend	340953
HLA-DR	G46-6	BV510	BD biosciences	563083
CD14	M5E2	AF700	BD biosciences	557923
CD15	W6D3	BUV395	BD biosciences	740318
CD11c	B-ly6	BV650	BD biosciences	563404
CD64	10.1	BV785	BD biosciences	740980
CD303	201A	PE-Cy7	Biolegend	354214
TIM3	7D3	BV421	BD biosciences	565562

[0679] 表7:用于NK细胞中TIM3表达分析的抗体组

[0680]

标志物	克隆	荧光团	供应商	目录号
存活力	-	APC-Cy7	Invitrogen L34976	L34976
CD45	2D1	PerCP-Cy5.5	Biolegend	340953
CD19	SJ25C1	BV605	BD biosciences	562653
CD27	L128	BV510	BD biosciences	563092
CD3	SK7	BV786	Biolegend	344842
CD16	3G8	AF700	BD biosciences	560713
CD56	NCAM16.2	BV650	BD biosciences	564057
CD57	NK-1	APC	BD biosciences	560845
TIM3	7D3	BV421	BD biosciences	565562

[0681] 如图5A中所示,很少的CD15+粒细胞表达TIM3。相反,表达TIM3的浆细胞样树状细胞(pDC)、髓样树状细胞(mDC)和CD14+CD64+单核细胞/巨噬细胞的频率跨患者变动,频率高达80%或更大。TIM3+CD16-CD56+和CD16+CD56+NK细胞亚群的频率也跨患者变动,范围从15%至95%(图5B)。

[0682] 实施例4:分析血清中的可溶性TIM3表达

[0683] 为了比较健康受试者和癌症患者的血清中的可溶性TIM3表达,在冰上解冻来自20位正常健康志愿者、20位结肠癌患者、20位肾癌患者和20位肺癌患者的冷冻的血清样品,并且按1:4稀释度用市售ELISA试剂盒(Quantikine ELISA,目录号DTIM30,R&D Systems)检验可溶性Tim-3。

[0684] 如图6A和图6B中所示,癌症患者中的可溶性TIM3表达(包括TIM3可溶性同种型和从细胞膜脱落的TIM3)显著高于健康供体中观察到的表达(结肠癌和肺癌vs.正常,$p<0.0001$;肾癌vs.正常,$p<0.01$,Mann Whitney检验)。此结果显示,相比正常对照,癌症患者的血清中可溶性TIM3水平升高。因此,可溶性TIM-3可以用作分层标志物。其它的分析将确定可溶性TIM3表达和相应TIL亚群上TIM3表达水平之间的相关性。

[0685] 表8.

[0686]

SEQ ID	抗体	描述	序列
1	13A3	VH	QLQLQESGPGLVKPSETLSLTCTVSGGSISSRSYYWGWIRQPPGKGLEWIGSIYYSG FTYYNPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCATGGPYGDYAHWFDP WGQGTLVTVSS
2	8B9	VH	QVQLQESGPGLVKPSETLSLTCTVSGGSISRHYWNWIRQPPGKGLEWIGYIHYSGS TNYNSSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCARDTGYYGMDIWGQGT TVTVSS
3	8C4	VH	QVQLQESGPGLVKPSETLSLTCTVSGGSISRYYWSWIRQPPGKGLEWIGYIHYTGS TNYNPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCATDTGYYGMDVWGQG TTVTVSS
4	17C3	VH	QVQLVQSGAEVKKPGASVKVSCKASGYTFTSYYMHWVRQAPGQGLEWMGIINP RGDSIIYAQKFQGRVTMTRDTSTSTVYMELSSLRSEDTAVYYCARDFYGSGNYYY GMDVWGQGTTVTVSS
5	9F6	VH	QVQLVESGGGLVKPGGSLRLSCAASGFTFSDYYMSWIRQAPGKGLEWVSFISGGG STIYYADSVKGRFTISRDNAKNSLFLQMNSLRVEDTAVYYCARDGYSSGWYYYG MDVWGQGTAVTVSS
6	3G4	VH	QVQLVESGGGLVKPGGSLRLSCAASGFTFSDYYMSWIRQAPGKGLEWVSFISTSGS IIYYADSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCAREGYSSSWSYYYGM DVWGQGTTVTVSS
7	17C8	VH	QVQLVESGGGLVKPGGSLRLSCAASGFTFSDYYMSWIRQAPGKGLEWVSFISSSGS IIYYADSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARDGYSSGWEYYGM DVWGQGTTVTVSS
8	13A3 (N60Q)	VH	QLQLQESGPGLVKPSETLSLTCTVSGGSISSRSYYWGWIRQPPGKGLEWIGSIYYSG FTYYQPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCATGGPYGDYAHWFDP WGQGTLVTVSS
9	13A3 (N60S)	VH	QLQLQESGPGLVKPSETLSLTCTVSGGSISSRSYYWGWIRQPPGKGLEWIGSIYYSG FTYYSPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCATGGPYGDYAHWFDP WGQGTLVTVSS

[0687]

SEQ ID	抗体	描述	序列
10	13A3 (N60A)	VH	QLQLQESGPGLVKPSETLSLTCTVSGGSISSRSYYWGWIRQPPGKGLEWIGSIYYSG FTYY**A**PSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCATGGPYGDYAHWFDP WGQGTLVTVSS
11	13A3 (D101E)	VH	QLQLQESGPGLVKPSETLSLTCTVSGGSISSRSYYWGWIRQPPGKGLEWIGSIYYSG FTYYNPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCATGGPYGDYAHWF**E**P WGQGTLVTVSS
12	13A3 (P102V)	VH	QLQLQESGPGLVKPSETLSLTCTVSGGSISSRSYYWGWIRQPPGKGLEWIGSIYYSG FTYYNPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCATGGPYGDYAHWFD**V** WGQGTLVTVSS
13	13A3 (P102Y)	VH	QLQLQESGPGLVKPSETLSLTCTVSGGSISSRSYYWGWIRQPPGKGLEWIGSIYYSG FTYYNPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCATGGPYGDYAHWFD**Y** WGQGTLVTVSS
14	13A3 (P102L)	VH	QLQLQESGPGLVKPSETLSLTCTVSGGSISSRSYYWGWIRQPPGKGLEWIGSIYYSG FTYYNPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCATGGPYGDYAHWFD**L** WGQGTLVTVSS
15	13A3 (N60Q, P102Y)	VH	QLQLQESGPGLVKPSETLSLTCTVSGGSISSRSYYWGWIRQPPGKGLEWIGSIYYSG FTYY**Q**PSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCATGGPYGDYAHWFD**Y** WGQGTLVTVSS
16	8B9 (S61P)	VH	QVQLQESGPGLVKPSETLSLTCTVSGGSISRHYWNWIRQPPGKGLEWIGYIHYSGS TNYN**P**SLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCARDTGYYGMDIWGQGT TVTVSS
17	9F6 (A108T)	VH	QVQLVESGGGLVKPGGSLRLSCAASGFTFSDYYMSWIRQAPGKGLEWVSFISGGG STIYYADSVKGRFTISRDNAKNSLFLQMNSLRVEDTAVYYCARDGYSSGWYYYG MDVWGQGT**T**VTVSS
18	13A3 (N60Q, D101E)	VH	QLQLQESGPGLVKPSETLSLTCTVSGGSISSRSYYWGWIRQPPGKGLEWIGSIYYSG FTYY**Q**PSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCATGGPYGDYAHWF**E**P WGQGTLVTVSS
19	13A3, 17C3, 3G4	VL	EIVLTQSPGTLSLSPGERATLSCRASQSVSSSYLAWYQQ KPGQAPRLLIYGASSRATGIPDRFSGSGSGTDFTLTISRLEPEDFAVYYCQQYGSSPI TF GQGTRLEIK
20	8B9, 8C4, 17C8 , 9F6 (VK3)	VL	EIVLTQSPGTLSLSPGERATLSCRASQSVSSSYLAWYQQKPGQAPRLLIYGASSRAT GIPDRFSGSGSGTDFTLTISRLEPEDFAVYYCQQYGSS**P**LTFGGGTKVEIK
21	9F6 (VK1)	VL	AIQLTQSPSSLSASVGDRVTITCRASQGISSALAWYQQKPGKAPKLLIYDASSLESG VPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQFNSYPRTFGQGTKVEIK
22	9F6 (VK2)	VL	EIVLTQSPGTLSLSPGERATLSCRASQSVSSSYLAWYQQKPGQAPRLLIYGASSRAT GIPDRFSGSGSGTDFTLTISRLEPEDFAVYYCQQYGSSLTFGGGTKVEIK
23	13A3，包括以下 13A3 变体：N60Q；N60S；N60A；D101E；P102V；P102Y；P102L；N60Q 和 P102Y；N60Q 和 D101E	CDR1 (VH)	SRSYYWG
24	8B9，包括 8B9 (S61P) 变体	CDR1 (VH)	RHYWN
25	8C4	CDR1 (VH)	RYYWS
26	17C3	CDR1 (VH)	SYYMH
27	9F6，包括 9F6	CDR1 (VH)	DYYMS

[0688]

SEQ ID	抗体	描述	序列
	(A108T)变体；3G4；17C8		
28	13A3，包括以下 13A3 变体：D101E、P102V、P102Y 和 P102L	CDR2 (VH)	SIYYSGFTYYNPSLKS
29	8B9	CDR2 (VH)	YIHYSGSTNYNSSLKS
30	8C4	CDR2 (VH)	YIHYTGSTNYNPSLKS
31	17C3	CDR2 (VH)	IINPRGDSIIYAQKFQG
32	9F6，包括 9F6 (A108T)变体	CDR2 (VH)	FISGGGSTIYYADSVKG
33	3G4	CDR2 (VH)	FISTSGSIIYYADSVKG
34	17C8	CDR2 (VH)	FISSSGSIIYYADSVKG
35	13A3 (N60Q)；13A3 (N60Q, P102Y)；13A3 (N60Q, D101E)	CDR2 (VH)	SIYYSGFTYYQPSLKS
36	13A3 (N60S)	CDR2 (VH)	SIYYSGFTYYSPSLKS
37	13A3 (N60A)	CDR2 (VH)	SIYYSGFTYYAPSLKS
38	8B9 (S61P)	CDR2 (VH)	YIHYSGSTNYNPSLKS
39	13A3，包括以下 13A3 变体：N60Q、N60S、N60A	CDR3 (VH)	GGPYGDYAHWFDP
40	8B9，包括 8B9 (S61P) 变体	CDR3 (VH)	DTGYYGMDI
41	8C4	CDR3 (VH)	DTGYYGMDV
42	17C3	CDR3 (VH)	DFYGSGNYYYGMDV
43	9F6，包括 9F6 (A108T)变体	CDR3 (VH)	DGYSSGWYYYGMDV
44	3G4	CDR3 (VH)	EGYSSSWSYYYGMDV
45	17C8	CDR3 (VH)	DGYSSGWEYYGMDV
46	13A3 (D101E)；13A3 (N60Q, D101E)	CDR3 (VH)	GGPYGDYAHWFEP
47	13A3 (P102V)	CDR3 (VH)	GGPYGDYAHWFDV

[0689]

SEQ ID	抗体	描述	序列
48	13A3 (P102Y); 13A3 (N60Q, P102Y)	CDR3 (VH)	GGPYGDYAHWFDY
49	13A3 (P102L)	CDR3 (VH)	GGPYGDYAHWFDL
50	13A3, 8B9, 8C4, 17C3, 9F6 (VK2, VK3), 3G4, 17C8	CDR1 (VL)	RASQSVSSSYLA
51	9F6 (VK1)	CDR1 (VL)	RASQGISSALA
52	13A3, 8B9, 8C4, 17C3, 9F6 (VK2, VK3), 3G4, 17C8	CDR2 (VL)	GASSRAT
53	9F6 (VK1)	CDR2 (VL)	DASSLES
54	13A3, 17C3, 3G4	CDR3 (VL)	QQYGSSPIT
55	8B9, 8C4, 9F6 (VK3), 17C8	CDR3 (VL)	QQYGSSPLT
56	9F6 (VK1)	CDR3 (VL)	QQFNSYPRT
57	9F6 (VK2)	CDR3 (VL)	QQYGSSLT
58		WT 人 IgG1 恒定结构域 (与 IgG1za 相同)	ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAV LQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPC PAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEV HNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKA KGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTP PVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK
59		人 IgG1(同种异型变体)	ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAV LQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEPKSCDKTHTCPPCP APELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVH NAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAK GQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPP VLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK
60		IgG1.1 恒定结构域(用于抗 TIM3 抗体中)	ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAV LQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEPKSCDKTHTCPPCP APEAEGAPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVH NAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPSSIEKTISKAK GQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPP VLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK
61		IgG1.3 恒定结构域(用于抗 TIM3 抗体中)	ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAV LQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEPKSCDKTHTCPPCP APEAEGAPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVH NAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAK GQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPP VLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK
63		人 IgG4 恒定结构域	RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQES VTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
64		人 IgG1 κ 轻链	LSPGK
65		LSPGK (重链的 C 末端)	LSPG
66		LSPG (重链的 C 末端)	LSP

[0690]

SEQ ID	抗体	描述	序列
67		LSP (重链的C末端)	RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQES VTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
68	13A3	IgG1.1f HC	QLQLQESGPGLVKPSETLSLTCTVSGGSISSRSYYWGWIRQPPGKGLEWIGSIYYSG FTYYNPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCATGGPYGDYAHWFDP WGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSG ALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEP KSCDKTHTCPPCPAPEAEGAPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEV KFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNK ALPSSIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWES NGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYT QKSLSLSPGK*
69	8B9	IgG1.1f HC	QVQLQESGPGLVKPSETLSLTCTVSGGSISRHYWNWIRQPPGKGLEWIGYIHYSGS TNYNSSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCARDTGYYGMDIWGQGT TVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGV HTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEPKSCDKT HTCPPCPAPEAEGAPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYV DGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPSSIE KTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPEN NYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLS PGK*
70	8C4	IgG1.1f HC	QVQLQESGPGLVKPSETLSLTCTVSGGSISRYYWSWIRQPPGKGLEWIGYIHYTGS TNYNPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCATDTGYYGMDVWGQG TTVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSG VHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEPKSCDK THTCPPCPAPEAEGAPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWY VDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPSSI EKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPE NNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSL SPGK*
71	17C3	IgG1.1f HC	QVQLVQSGAEVKKPGASVKVSCKASGYTFTSYYMHWVRQAPGQGLEWMGIINP RGDSIIYAQKFQGRVTMTRDTSTSTVYMELSSLRSEDTAVYYCARDFYGSGNYYY GMDVWGQGTTVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVS WNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDK RVEPKSCDKTHTCPPCPAPEAEGAPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHED PEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKV SNKALPSSIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVE WESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHN HYTQKSLSLSPGK*
72	9F6	IgG1.1f HC	QVQLVESGGGLVKPGGSLRLSCAASGFTFSDYYMSWIRQAPGKGLEWVSFISGGG STIYYADSVKGRFTISRDNAKNSLFLQMNSLRVEDTAVYYCARDGYSSGWYYYG MDVWGQGTAVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSW NSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKR VEPKSCDKTHTCPPCPAPEAEGAPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDP EVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVS NKALPSSIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEW ESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNH YTQKSLSLSPGK*
73	3G4	IgG1.1f HC	QVQLVESGGGLVKPGGSLRLSCAASGFTFSDYYMSWIRQAPGKGLEWVSFISTSGS IIYYADSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCAREGYSSSWSYYYGM DVWGQGTTVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWN SGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRV EPKSCDKTHTCPPCPAPEAEGAPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPE VKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSN KALPSSIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHY TQKSLSLSPGK*
74	17C8	IgG1.1f HC	QVQLVESGGGLVKPGGSLRLSCAASGFTFSDYYMSWIRQAPGKGLEWVSFISSSGS IIYYADSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARDGYSSGWEYYGM DVWGQGTTVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWN SGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRV EPKSCDKTHTCPPCPAPEAEGAPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPE VKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSN KALPSSIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWE

[0691]

SEQ ID	抗体	描述	序列
			SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHY TQKSLSLSPGK*
75	13A3	IgG1.1f HC (无 C 末端 K)	QLQLQESGPGLVKPSETLSLTCTVSGGSISSRSYYWGWIRQPPGKGLEWIGSIYYSG FTYYNPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCATGGPYGDYAHWFDP WGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSG ALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEP KSCDKTHTCPPCPAPEAEGAPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEV KFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNK ALPSSIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWES NGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYT QKSLSLSPG*
76	8B9	IgG1.1f HC (无 C 末端 K)	QVQLQESGPGLVKPSETLSLTCTVSGGSISRHYWNWIRQPPGKGLEWIGYIHYSGS TNYNSSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCARDTGYYGMDIWGQGT TVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGV HTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEPKSCDKT HTCPPCPAPEAEGAPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYV DGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPSSIE KTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPEN NYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLS PG*
77	8C4	IgG1.1f HC (无 C 末端 K)	QVQLQESGPGLVKPSETLSLTCTVSGGSISRYYWSWIRQPPGKGLEWIGYIHYTGS TNYNPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCATDTGYYGMDVWGQG TTVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSG VHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEPKSCDK THTCPPCPAPEAEGAPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWY VDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPSSI EKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPE NNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSL SPG*
78	17C3	IgG1.1f HC (无 C 末端 K)	QVQLVQSGAEVKKPGASVKVSCKASGYTFTSYYMHWVRQAPGQGLEWMGIINP RGDSIIYAQKFQGRVTMTRDTSTSTVYMELSSLRSEDTAVYYCARDFYGSGNYYY GMDVWGQGTTVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVS WNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDK RVEPKSCDKTHTCPPCPAPEAEGAPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHED PEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKV SNKALPSSIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVE WESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHN HYTQKSLSLSPG*
79	9F6	IgG1.1f HC (无 C 末端 K)	QVQLVESGGGLVKPGGSLRLSCAASGFTFSDYYMSWIRQAPGKGLEWVSFISGGG STIYYADSVKGRFTISRDNAKNSLFLQMNSLRVEDTAVYYCARDGYSSGWYYYG MDVWGQGTAVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSW NSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKR VEPKSCDKTHTCPPCPAPEAEGAPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDP EVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVS NKALPSSIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEW ESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNH YTQKSLSLSPG*
80	3G4	IgG1.1f HC (无 C 末端 K)	QVQLVESGGGLVKPGGSLRLSCAASGFTFSDYYMSWIRQAPGKGLEWVSFISTSGS IIYYADSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCAREGYSSSWSYYYGM DVWGQGTTVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWN SGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRV EPKSCDKTHTCPPCPAPEAEGAPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPE VKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSN KALPSSIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHY TQKSLSLSPG*
81	17C8	IgG1.1f HC (无 C 末端 K)	QVQLVESGGGLVKPGGSLRLSCAASGFTFSDYYMSWIRQAPGKGLEWVSFISSSGS IIYYADSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARDGYSSGWEYYGM DVWGQGTTVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWN SGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRV EPKSCDKTHTCPPCPAPEAEGAPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPE VKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSN KALPSSIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWE

[0692]

SEQ ID	抗体	描述	序列
			SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHY TQKSLSLSPG*
82	13A3	IgG1.3f HC	QLQLQESGPGLVKPSETLSLTCTVSGGSISSRSYYWGWIRQPPGKGLEWIGSIYYSG FTYYNPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCATGGPYGDYAHWFDP WGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSG ALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEP KSCDKTHTCPPCPAPEAEGAPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEV KFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNK ALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWES NGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYT QKSLSLSPGK*
83	8B9	IgG1.3f HC	QVQLQESGPGLVKPSETLSLTCTVSGGSISRHYWNWIRQPPGKGLEWIGYIHYSGS TNYNSSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCARDTGYYGMDIWGQGT TVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGV HTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEPKSCDKT HTCPPCPAPEAEGAPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYV DGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIE KTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPEN NYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLS PGK*
84	8C4	IgG1.3f HC	QVQLQESGPGLVKPSETLSLTCTVSGGSISRYYWSWIRQPPGKGLEWIGYIHYTGS TNYNPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCATDTGYYGMDVWGQG TTVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSG VHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEPKSCDK THTCPPCPAPEAEGAPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWY VDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPI EKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPE NNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSL SPGK*
85	17C3	IgG1.3f HC	QVQLVQSGAEVKKPGASVKVSCKASGYTFTSYYMHWVRQAPGQGLEWMGIINP RGDSIIYAQKFQGRVTMTRDTSTSTVYMELSSLRSEDTAVYYCARDFYGSGNYYY GMDVWGQGTTVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVS WNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDK RVEPKSCDKTHTCPPCPAPEAEGAPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHED PEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKV SNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVE WESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHN HYTQKSLSLSPGK*
86	9F6	IgG1.3f HC	QVQLVESGGGLVKPGGSLRLSCAASGFTFSDYYMSWIRQAPGKGLEWVSFISGGG STIYYADSVKGRFTISRDNAKNSLFLQMNSLRVEDTAVYYCARDGYSSGWYYYG MDVWGQGTAVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSW NSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKR VEPKSCDKTHTCPPCPAPEAEGAPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDP EVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVS NKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVE WESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHN HYTQKSLSLSPGK*
87	3G4	IgG1.3f HC	QVQLVESGGGLVKPGGSLRLSCAASGFTFSDYYMSWIRQAPGKGLEWVSFISTSGS IIYYADSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCAREGYSSSWSYYYGM DVWGQGTTVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWN SGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRV EPKSCDKTHTCPPCPAPEAEGAPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPE VKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSN KALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEW ESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNH YTQKSLSLSPGK*
88	17C8	IgG1.3f HC	QVQLVESGGGLVKPGGSLRLSCAASGFTFSDYYMSWIRQAPGKGLEWVSFISSSGS IIYYADSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARDGYSSGWEYYGM DVWGQGTTVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWN SGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRV EPKSCDKTHTCPPCPAPEAEGAPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPE VKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSN KALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEW

[0693]

SEQ ID	抗体	描述	序列
			ESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNH YTQKSLSLSPGK*
89	13A3	IgG1.3f HC (无 C 末端 K)	QLQLQESGPGLVKPSETLSLTCTVSGGSISSRSYYWGWIRQPPGKGLEWIGSIYYSG FTYYNPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCATGGPYGDYAHWFDP WGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSG ALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEP KSCDKTHTCPPCPAPEAEGAPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEV KFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNK ALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWES NGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYT QKSLSLSPG*
90	8B9	IgG1.3f HC (无 C 末端 K)	QVQLQESGPGLVKPSETLSLTCTVSGGSISRHYWNWIRQPPGKGLEWIGYIHYSGS TNYNSSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCARDTGYYGMDIWGQGT TVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGV HTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEPKSCDKT HTCPPCPAPEAEGAPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYV DGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIE KTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPEN NYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLS PG*
91	8C4	IgG1.3f HC (无 C 末端 K)	QVQLQESGPGLVKPSETLSLTCTVSGGSISRYYWSWIRQPPGKGLEWIGYIHYTGS TNYNPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCATDTGYYGMDVWGQG TTVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSG VHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEPKSCDK THTCPPCPAPEAEGAPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWY VDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPI EKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPE NNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSL SPG*
92	17C3	IgG1.3f HC (无 C 末端 K)	QVQLVQSGAEVKKPGASVKVSCKASGYTFTSYYMHWVRQAPGQGLEWMGIINP RGDSIIYAQKFQGRVTMTRDTSTSTVYMELSSLRSEDTAVYYCARDFYGSGNYYY GMDVWGQGTTVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVS WNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDK RVEPKSCDKTHTCPPCPAPEAEGAPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHED PEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKV SNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVE WESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHN HYTQKSLSLSPG*
93	9F6	IgG1.3f HC (无 C 末端 K)	QVQLVESGGGLVKPGGSLRLSCAASGFTFSDYYMSWIRQAPGKGLEWVSFISGGG STIYYADSVKGRFTISRDNAKNSLFLQMNSLRVEDTAVYYCARDGYSSGWYYYG MDVWGQGTAVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSW NSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKR VEPKSCDKTHTCPPCPAPEAEGAPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDP EVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVS NKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVE WESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHN HYTQKSLSLSPG*
94	3G4	IgG1.3f HC (无 C 末端 K)	QVQLVESGGGLVKPGGSLRLSCAASGFTFSDYYMSWIRQAPGKGLEWVSFISTSGS IIYYADSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCAREGYSSSWSYYYGM DVWGQGTTVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWN SGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRV EPKSCDKTHTCPPCPAPEAEGAPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPE VKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSN KALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEW ESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNH YTQKSLSLSPG*
95	17C8	IgG1.3f HC (无 C 末端 K)	QVQLVESGGGLVKPGGSLRLSCAASGFTFSDYYMSWIRQAPGKGLEWVSFISSSGS IIYYADSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARDGYSSGWEYYGM DVWGQGTTVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWN SGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRV EPKSCDKTHTCPPCPAPEAEGAPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPE VKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSN KALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEW

[0694]

SEQ ID	抗体	描述	序列
			ESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNH YTQKSLSLSPG*
96	13A3 (N60Q)	IgG1.1f HC	QLQLQESGPGLVKPSETLSLTCTVSGGSISSRSYYWGWIRQPPGKGLEWIGSIYYSG FTYY**Q**PSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCATGGPYGDYAHWFDP WGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSG ALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEP KSCDKTHTCPPCPAPEAEGAPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEV KFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNK ALPSSIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWES NGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYT QKSLSLSPGK*
97	13A3 (N60S)	IgG1.1f HC	QLQLQESGPGLVKPSETLSLTCTVSGGSISSRSYYWGWIRQPPGKGLEWIGSIYYSG FTYY**S**PSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCATGGPYGDYAHWFDP WGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSG ALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEP KSCDKTHTCPPCPAPEAEGAPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEV KFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNK ALPSSIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWES NGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYT QKSLSLSPGK*
98	13A3 (N60A)	IgG1.1f HC	QLQLQESGPGLVKPSETLSLTCTVSGGSISSRSYYWGWIRQPPGKGLEWIGSIYYSG FTYY**A**PSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCATGGPYGDYAHWFDP WGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSG ALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEP KSCDKTHTCPPCPAPEAEGAPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEV KFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNK ALPSSIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWES NGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYT QKSLSLSPGK*
99	13A3 (D101E)	IgG1.1f HC	QLQLQESGPGLVKPSETLSLTCTVSGGSISSRSYYWGWIRQPPGKGLEWIGSIYYSG FTYYNPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCATGGPYGDYAHW**F**EP WGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSG ALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEP KSCDKTHTCPPCPAPEAEGAPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEV KFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNK ALPSSIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWES NGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYT QKSLSLSPGK*
100	13A3 (P102V)	IgG1.1f HC	QLQLQESGPGLVKPSETLSLTCTVSGGSISSRSYYWGWIRQPPGKGLEWIGSIYYSG FTYYNPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCATGGPYGDYAHWFD**V** WGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSG ALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEP KSCDKTHTCPPCPAPEAEGAPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEV KFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNK ALPSSIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWES NGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYT QKSLSLSPGK*
101	13A3 (P102Y)	IgG1.1f HC	QLQLQESGPGLVKPSETLSLTCTVSGGSISSRSYYWGWIRQPPGKGLEWIGSIYYSG FTYYNPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCATGGPYGDYAHWFD**Y** WGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSG ALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEP KSCDKTHTCPPCPAPEAEGAPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEV KFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNK ALPSSIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWES NGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYT QKSLSLSPGK*
102	13A3 (P102L)	IgG1.1f HC	QLQLQESGPGLVKPSETLSLTCTVSGGSISSRSYYWGWIRQPPGKGLEWIGSIYYSG FTYYNPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCATGGPYGDYAHWFD**L** WGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSG ALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEP KSCDKTHTCPPCPAPEAEGAPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEV KFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNK ALPSSIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWES

[0695]

SEQ ID	抗体	描述	序列
			NGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYT QKSLSLSPGK*
103	13A3 (N60Q, P102Y)	IgG1.1f HC	QLQLQESGPGLVKPSETLSLTCTVSGGSISSRSYYWGWIRQPPGKGLEWIGSIYYSG FTYY**Q**PSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCATGGPYGDYAHWFD**Y** WGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSG ALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEP KSCDKTHTCPPCPAPEAEGAPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEV KFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNK ALPSSIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWES NGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYT QKSLSLSPGK*
104	8B9 (S61P)	IgG1.1f HC	QVQLQESGPGLVKPSETLSLTCTVSGGSISRHYWNWIRQPPGKGLEWIGYIHYSGS TNYNPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCARDTGYYGMDIWGQGT TVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGV HTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEPKSCDKT HTCPPCPAPEAEGAPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYV DGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPSSIE KTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPEN NYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLS PGK*
105	9F6 (A108T)	IgG1.1f HC	QVQLVESGGGLVKPGGSLRLSCAASGFTFSDYYMSWIRQAPGKGLEWVSFISGGG STIYYADSVKGRFTISRDNAKNSLFLQMNSLRVEDTAVYYCARDGYSSGWYYYG MDVWGQGTTVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSW NSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKR VEPKSCDKTHTCPPCPAPEAEGAPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDP EVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVS NKALPSSIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEW ESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNH YTQKSLSLSPGK*
106	13A3 (N60Q)	IgG1.1f HC (无 C 末端 K)	QLQLQESGPGLVKPSETLSLTCTVSGGSISSRSYYWGWIRQPPGKGLEWIGSIYYSG FTYYQPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCATGGPYGDYAHWFDP WGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSG ALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEP KSCDKTHTCPPCPAPEAEGAPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEV KFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNK ALPSSIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWES NGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYT QKSLSLSPG*
107	13A3 (N60S)	IgG1.1f HC (无 C 末端 K)	QLQLQESGPGLVKPSETLSLTCTVSGGSISSRSYYWGWIRQPPGKGLEWIGSIYYSG FTYYSPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCATGGPYGDYAHWFDP WGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSG ALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEP KSCDKTHTCPPCPAPEAEGAPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEV KFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNK ALPSSIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWES NGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYT QKSLSLSPG*
108	13A3 (N60A)	IgG1.1f HC (无 C 末端 K)	QLQLQESGPGLVKPSETLSLTCTVSGGSISSRSYYWGWIRQPPGKGLEWIGSIYYSG FTYYAPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCATGGPYGDYAHWFDP WGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSG ALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEP KSCDKTHTCPPCPAPEAEGAPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEV KFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNK ALPSSIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWES NGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYT QKSLSLSPG*
109	13A3 (D101E)	IgG1.1f HC (无 C 末端 K)	QLQLQESGPGLVKPSETLSLTCTVSGGSISSRSYYWGWIRQPPGKGLEWIGSIYYSG FTYYNPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCATGGPYGDYAHWFEP WGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSG ALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEP KSCDKTHTCPPCPAPEAEGAPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEV KFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNK ALPSSIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWES

[0696]

SEQ ID	抗体	描述	序列
			NGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYT QKSLSLSPG*
110	13A3 (P102V)	IgG1.1f HC (无 C 末端 K)	QLQLQESGPGLVKPSETLSLTCTVSGGSISSRSYYWGWIRQPPGKGLEWIGSIYYSG FTYYNPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCATGGPYGDYAHWFDV WGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSG ALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEP KSCDKTHTCPPCPAPEAEGAPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEV KFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNK ALPSSIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWES NGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYT QKSLSLSPG*
111	13A3 (P102Y)	IgG1.1f HC (无 C 末端 K)	QLQLQESGPGLVKPSETLSLTCTVSGGSISSRSYYWGWIRQPPGKGLEWIGSIYYSG FTYYNPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCATGGPYGDYAHWFDY WGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSG ALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEP KSCDKTHTCPPCPAPEAEGAPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEV KFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNK ALPSSIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWES NGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYT QKSLSLSPG*
112	13A3 (P102L)	IgG1.1f HC (无 C 末端 K)	QLQLQESGPGLVKPSETLSLTCTVSGGSISSRSYYWGWIRQPPGKGLEWIGSIYYSG FTYYNPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCATGGPYGDYAHWFDL WGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSG ALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEP KSCDKTHTCPPCPAPEAEGAPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEV KFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNK ALPSSIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWES NGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYT QKSLSLSPG*
113	13A3 (N60Q, P102Y)	IgG1.1f HC (无 C 末端 K)	QLQLQESGPGLVKPSETLSLTCTVSGGSISSRSYYWGWIRQPPGKGLEWIGSIYYSG FTYYQPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCATGGPYGDYAHWFDY WGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSG ALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEP KSCDKTHTCPPCPAPEAEGAPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEV KFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNK ALPSSIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWES NGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYT QKSLSLSPG*
114	8B9 (S61P)	IgG1.1f HC (无 C 末端 K)	QVQLQESGPGLVKPSETLSLTCTVSGGSISRHYWNWIRQPPGKGLEWIGYIHYSGS TNYNPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCARDTGYYGMDIWGQGT TVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGV HTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEPKSCDKT HTCPPCPAPEAEGAPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYV DGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPSSIE KTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPEN NYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLS PG*
115	9F6 (A108T)	IgG1.1f HC (无 C 末端 K)	QVQLVESGGGLVKPGGSLRLSCAASGFTFSDYYMSWIRQAPGKGLEWVSFISGGG STIYYADSVKGRFTISRDNAKNSLFLQMNSLRVEDTAVYYCARDGYSSGWYYYG MDVWGQGTTVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSW NSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKR VEPKSCDKTHTCPPCPAPEAEGAPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDP EVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVS NKALPSSIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEW ESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNH YTQKSLSLSPG*
116	13A3 (N60Q)	IgG1.3f HC	QLQLQESGPGLVKPSETLSLTCTVSGGSISSRSYYWGWIRQPPGKGLEWIGSIYYSG FTYYQPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCATGGPYGDYAHWFDP WGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSG ALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEP KSCDKTHTCPPCPAPEAEGAPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEV KFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNK ALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWES

[0697]

SEQ ID	抗体	描述	序列
			NGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYT QKSLSLSPGK*
117	13A3 (N60S)	IgG1.3f HC	QLQLQESGPGLVKPSETLSLTCTVSGGSISSRSYYWGWIRQPPGKGLEWIGSIYYSG FTYYSPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCATGGPYGDYAHWFDP WGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSG ALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEP KSCDKTHTCPPCPAPEAEGAPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEV KFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNK ALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWES NGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYT QKSLSLSPGK*
118	13A3 (N60A)	IgG1.3f HC	QLQLQESGPGLVKPSETLSLTCTVSGGSISSRSYYWGWIRQPPGKGLEWIGSIYYSG FTYYAPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCATGGPYGDYAHWFDP WGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSG ALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEP KSCDKTHTCPPCPAPEAEGAPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEV KFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNK ALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWES NGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYT QKSLSLSPGK*
119	13A3 (D101E)	IgG1.3f HC	QLQLQESGPGLVKPSETLSLTCTVSGGSISSRSYYWGWIRQPPGKGLEWIGSIYYSG FTYYNPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCATGGPYGDYAHWFEP WGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSG ALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEP KSCDKTHTCPPCPAPEAEGAPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEV KFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNK ALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWES NGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYT QKSLSLSPGK*
120	13A3 (P102V)	IgG1.3f HC	QLQLQESGPGLVKPSETLSLTCTVSGGSISSRSYYWGWIRQPPGKGLEWIGSIYYSG FTYYNPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCATGGPYGDYAHWFDV WGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSG ALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEP KSCDKTHTCPPCPAPEAEGAPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEV KFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNK ALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWES NGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYT QKSLSLSPGK*
121	13A3 (P102Y)	IgG1.3f HC	QLQLQESGPGLVKPSETLSLTCTVSGGSISSRSYYWGWIRQPPGKGLEWIGSIYYSG FTYYNPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCATGGPYGDYAHWFDY WGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSG ALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEP KSCDKTHTCPPCPAPEAEGAPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEV KFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNK ALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWES NGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYT QKSLSLSPGK*
122	13A3 (P102L)	IgG1.3f HC	QLQLQESGPGLVKPSETLSLTCTVSGGSISSRSYYWGWIRQPPGKGLEWIGSIYYSG FTYYNPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCATGGPYGDYAHWFDL WGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSG ALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEP KSCDKTHTCPPCPAPEAEGAPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEV KFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNK ALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWES NGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYT QKSLSLSPGK*
123	13A3 (N60Q, P102Y)	IgG1.3f HC	QLQLQESGPGLVKPSETLSLTCTVSGGSISSRSYYWGWIRQPPGKGLEWIGSIYYSG FTYYQPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCATGGPYGDYAHWFDY WGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSG ALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEP KSCDKTHTCPPCPAPEAEGAPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEV KFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNK ALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWES

[0698]

SEQ ID	抗体	描述	序列
			NGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYT QKSLSLSPGK*
124	8B9 (S61P)	IgG1.3f HC	QVQLQESGPGLVKPSETLSLTCTVSGGSISRHYWNWIRQPPGKGLEWIGYIHYSGS TNYNPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCARDTGYYGMDIWGQGT TVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGV HTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEPKSCDKT HTCPPCPAPEAEGAPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYV DGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIE KTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPEN NYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLS PGK*
125	9F6 (A108T)	IgG1.3f HC	QVQLVESGGGLVKPGGSLRLSCAASGFTFSDYYMSWIRQAPGKGLEWVSFISGGG STIYYADSVKGRFTISRDNAKNSLFLQMNSLRVEDTAVYYCARDGYSSGWYYYG MDVWGQGTTVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSW NSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKR VEPKSCDKTHTCPPCPAPEAEGAPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDP EVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVS NKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVE WESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHN HYTQKSLSLSPGK*
126	13A3 (N60Q)	IgG1.3f HC (无 C 末端 K)	QLQLQESGPGLVKPSETLSLTCTVSGGSISSRSYYWGWIRQPPGKGLEWIGSIYYSG FTYYQPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCATGGPYGDYAHWFDP WGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSG ALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEP KSCDKTHTCPPCPAPEAEGAPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEV KFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNK ALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWES NGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYT QKSLSLSPG*
127	13A3 (N60S)	IgG1.3f HC (无 C 末端 K)	QLQLQESGPGLVKPSETLSLTCTVSGGSISSRSYYWGWIRQPPGKGLEWIGSIYYSG FTYYSPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCATGGPYGDYAHWFDP WGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSG ALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEP KSCDKTHTCPPCPAPEAEGAPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEV KFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNK ALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWES NGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYT QKSLSLSPG*
128	13A3 (N60A)	IgG1.3f HC (无 C 末端 K)	QLQLQESGPGLVKPSETLSLTCTVSGGSISSRSYYWGWIRQPPGKGLEWIGSIYYSG FTYYAPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCATGGPYGDYAHWFDP WGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSG ALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEP KSCDKTHTCPPCPAPEAEGAPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEV KFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNK ALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWES NGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYT QKSLSLSPG*
129	13A3 (D101E)	IgG1.3f HC (无 C 末端 K)	QLQLQESGPGLVKPSETLSLTCTVSGGSISSRSYYWGWIRQPPGKGLEWIGSIYYSG FTYYNPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCATGGPYGDYAHWFEP WGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSG ALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEP KSCDKTHTCPPCPAPEAEGAPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEV KFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNK ALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWES NGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYT QKSLSLSPG*
130	13A3 (P102V)	IgG1.3f HC (无 C 末端 K)	QLQLQESGPGLVKPSETLSLTCTVSGGSISSRSYYWGWIRQPPGKGLEWIGSIYYSG FTYYNPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCATGGPYGDYAHWFDV WGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSG ALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEP KSCDKTHTCPPCPAPEAEGAPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEV KFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNK ALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWES

[0699]

SEQ ID	抗体	描述	序列
			NGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYT QKSLSLSPG*
131	13A3 (P102Y)	IgG1.3f HC (无 C 末端 K)	QLQLQESGPGLVKPSETLSLTCTVSGGSISSRSYYWGWIRQPPGKGLEWIGSIYYSG FTYYNPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCATGGPYGDYAHWFDY WGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSG ALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEP KSCDKTHTCPPCPAPEAEGAPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEV KFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNK ALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWES NGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYT QKSLSLSPG*
132	13A3 (P102L)	IgG1.3f HC (无 C 末端 K)	QLQLQESGPGLVKPSETLSLTCTVSGGSISSRSYYWGWIRQPPGKGLEWIGSIYYSG FTYYNPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCATGGPYGDYAHWFDL WGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSG ALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEP KSCDKTHTCPPCPAPEAEGAPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEV KFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNK ALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWES NGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYT QKSLSLSPG*
133	13A3 (N60Q, P102Y)	IgG1.3f HC (无 C 末端 K)	QLQLQESGPGLVKPSETLSLTCTVSGGSISSRSYYWGWIRQPPGKGLEWIGSIYYSG FTYYQPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCATGGPYGDYAHWFDY WGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSG ALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEP KSCDKTHTCPPCPAPEAEGAPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEV KFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNK ALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWES NGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYT QKSLSLSPG*
134	8B9 (S61P)	IgG1.3f HC (无 C 末端 K)	QVQLQESGPGLVKPSETLSLTCTVSGGSISRHYWNWIRQPPGKGLEWIGYIHYSGS TNYNPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCARDTGYYGMDIWGQGT TVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGV HTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEPKSCDKT HTCPPCPAPEAEGAPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYV DGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIE KTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPEN NYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLS PG*
135	9F6 (A108T)	IgG1.3f HC (无 C 末端 K)	QVQLVESGGGLVKPGGSLRLSCAASGFTFSDYYMSWIRQAPGKGLEWVSFISGGG STIYYADSVKGRFTISRDNAKNSLFLQMNSLRVEDTAVYYCARDGYSSGWYYYG MDVWGQGTTVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSW NSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKR VEPKSCDKTHTCPPCPAPEAEGAPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDP EVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVS NKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVE WESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHN HYTQKSLSLSPG*
136	13A3	hIgG4 HC	QLQLQESGPGLVKPSETLSLTCTVSGGSISSRSYYWGWIRQPPGKGLEWIGSIYYSG FTYYNPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCATGGPYGDYAHWFDP WGQGTLVTVSSASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGA LTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTKTYTCNVDHKPSNTKVDKRVESK YGPPCPSCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQFNW YVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSS IEKTISKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQP ENNYKTTPPVLDSDGSFFLYSRLTVDKSRWQEGNVFSCSVMHEALHNHYTQKSLS LSLGK*
137	13A3	hIgG4 HC (无 C 末端 K)	QLQLQESGPGLVKPSETLSLTCTVSGGSISSRSYYWGWIRQPPGKGLEWIGSIYYSG FTYYNPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCATGGPYGDYAHWFDP WGQGTLVTVSSASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGA LTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTKTYTCNVDHKPSNTKVDKRVESK YGPPCPSCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQFNW YVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSS IEKTISKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQP

[0700]

SEQ ID	抗体	描述	序列
			ENNYKTTPPVLDSDGSFFLYSRLTVDKSRWQEGNVFSCSVMHEALHNHYTQKSLS LSLG*
138	TIM3.5 – 13A3	IgG4P HC	QLQLQESGPGLVKPSETLSLTCTVSGGSISSRSYYWGWIRQPPGKGLEWIGSIYYSG FTYYNPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCATGGPYGDYAHWFDP WGQGTLVTVSSASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGA LTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTKTYTCNVDHKPSNTKVDKRVESK YGPPCPPCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQFNW YVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSS IEKTISKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQP ENNYKTTPPVLDSDGSFFLYSRLTVDKSRWQEGNVFSCSVMHEALHNHYTQKSLS LSLGK*
139	TIM3.5 – 13A3	IgG4P HC (无 C 末端 K)	QLQLQESGPGLVKPSETLSLTCTVSGGSISSRSYYWGWIRQPPGKGLEWIGSIYYSG FTYYNPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCATGGPYGDYAHWFDP WGQGTLVTVSSASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGA LTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTKTYTCNVDHKPSNTKVDKRVESK YGPPCPPCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQFNW YVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSS IEKTISKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQP ENNYKTTPPVLDSDGSFFLYSRLTVDKSRWQEGNVFSCSVMHEALHNHYTQKSLS LSLG*
140	TIM3.10 – 13A3 (N60Q)	IgG4P HC	QLQLQESGPGLVKPSETLSLTCTVSGGSISSRSYYWGWIRQPPGKGLEWIGSIYYSG FTYYQPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCATGGPYGDYAHWFDP WGQGTLVTVSSASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGA LTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTKTYTCNVDHKPSNTKVDKRVESK YGPPCPPCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQFNW YVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSS IEKTISKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQP ENNYKTTPPVLDSDGSFFLYSRLTVDKSRWQEGNVFSCSVMHEALHNHYTQKSLS LSLGK*
141	TIM3.10 – 13A3 (N60Q)	IgG4P HC (无 C 末端 K)	QLQLQESGPGLVKPSETLSLTCTVSGGSISSRSYYWGWIRQPPGKGLEWIGSIYYSG FTYYQPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCATGGPYGDYAHWFDP WGQGTLVTVSSASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGA LTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTKTYTCNVDHKPSNTKVDKRVESK YGPPCPPCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQFNW YVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSS IEKTISKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQP ENNYKTTPPVLDSDGSFFLYSRLTVDKSRWQEGNVFSCSVMHEALHNHYTQKSLS LSLG*
142	TIM3.11 – 13A3 (N60S)	IgG4P HC	QLQLQESGPGLVKPSETLSLTCTVSGGSISSRSYYWGWIRQPPGKGLEWIGSIYYSG FTYYSPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCATGGPYGDYAHWFDP WGQGTLVTVSSASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGA LTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTKTYTCNVDHKPSNTKVDKRVESK YGPPCPPCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQFNW YVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSS IEKTISKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQP ENNYKTTPPVLDSDGSFFLYSRLTVDKSRWQEGNVFSCSVMHEALHNHYTQKSLS LSLGK*
143	TIM3.11 – 13A3 (N60S)	IgG4P HC (无 C 末端 K)	QLQLQESGPGLVKPSETLSLTCTVSGGSISSRSYYWGWIRQPPGKGLEWIGSIYYSG FTYYSPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCATGGPYGDYAHWFDP WGQGTLVTVSSASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGA LTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTKTYTCNVDHKPSNTKVDKRVESK YGPPCPPCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQFNW YVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSS IEKTISKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQP ENNYKTTPPVLDSDGSFFLYSRLTVDKSRWQEGNVFSCSVMHEALHNHYTQKSLS LSLG*
144	TIM3.12 – 13A3 (N60A)	IgG4P HC	QLQLQESGPGLVKPSETLSLTCTVSGGSISSRSYYWGWIRQPPGKGLEWIGSIYYSG FTYYAPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCATGGPYGDYAHWFDP WGQGTLVTVSSASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGA LTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTKTYTCNVDHKPSNTKVDKRVESK YGPPCPPCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQFNW YVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSS IEKTISKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQP

[0701]

SEQ ID	抗体	描述	序列
			ENNYKTTPPVLDSDGSFFLYSRLTVDKSRWQEGNVFSCSVMHEALHNHYTQKSLS LSLGK*
145	TIM3.12 – 13A3 (N60A)	IgG4P HC (无 C 末端 K)	QLQLQESGPGLVKPSETLSLTCTVSGGSISSRSYYWGWIRQPPGKGLEWIGSIYYSG FTYYAPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCATGGPYGDYAHWFDP WGQGTLVTVSSASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGA LTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTKTYTCNVDHKPSNTKVDKRVESK YGPPCPPCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQFNW YVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSS IEKTISKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQP ENNYKTTPPVLDSDGSFFLYSRLTVDKSRWQEGNVFSCSVMHEALHNHYTQKSLS LSLG*
146	TIM3.13 – 13A3 (D101E)	IgG4P HC	QLQLQESGPGLVKPSETLSLTCTVSGGSISSRSYYWGWIRQPPGKGLEWIGSIYYSG FTYYNPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCATGGPYGDYAHWFEP WGQGTLVTVSSASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGA LTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTKTYTCNVDHKPSNTKVDKRVESK YGPPCPPCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQFNW YVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSS IEKTISKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQP ENNYKTTPPVLDSDGSFFLYSRLTVDKSRWQEGNVFSCSVMHEALHNHYTQKSLS LSLGK*
147	TIM3.13 – 13A3 (D101E)	IgG4P HC (无 C 末端 K)	QLQLQESGPGLVKPSETLSLTCTVSGGSISSRSYYWGWIRQPPGKGLEWIGSIYYSG FTYYNPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCATGGPYGDYAHWFEP WGQGTLVTVSSASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGA LTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTKTYTCNVDHKPSNTKVDKRVESK YGPPCPPCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQFNW YVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSS IEKTISKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQP ENNYKTTPPVLDSDGSFFLYSRLTVDKSRWQEGNVFSCSVMHEALHNHYTQKSLS LSLG*
148	TIM 3.14 – 13A3 (P102V)	IgG4P HC	QLQLQESGPGLVKPSETLSLTCTVSGGSISSRSYYWGWIRQPPGKGLEWIGSIYYSG FTYYNPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCATGGPYGDYAHWFDV WGQGTLVTVSSASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGA LTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTKTYTCNVDHKPSNTKVDKRVESK YGPPCPPCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQFNW YVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSS IEKTISKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQP ENNYKTTPPVLDSDGSFFLYSRLTVDKSRWQEGNVFSCSVMHEALHNHYTQKSLS LSLGK*
149	TIM 3.14 – 13A3 (P102V)	IgG4P HC (无 C 末端 K)	QLQLQESGPGLVKPSETLSLTCTVSGGSISSRSYYWGWIRQPPGKGLEWIGSIYYSG FTYYNPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCATGGPYGDYAHWFDV WGQGTLVTVSSASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGA LTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTKTYTCNVDHKPSNTKVDKRVESK YGPPCPPCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQFNW YVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSS IEKTISKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQP ENNYKTTPPVLDSDGSFFLYSRLTVDKSRWQEGNVFSCSVMHEALHNHYTQKSLS LSLG*
150	TIM3.15 – 13A3 (P102Y)	IgG4P HC	QLQLQESGPGLVKPSETLSLTCTVSGGSISSRSYYWGWIRQPPGKGLEWIGSIYYSG FTYYNPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCATGGPYGDYAHWFDY WGQGTLVTVSSASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGA LTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTKTYTCNVDHKPSNTKVDKRVESK YGPPCPPCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQFNW YVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSS IEKTISKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQP ENNYKTTPPVLDSDGSFFLYSRLTVDKSRWQEGNVFSCSVMHEALHNHYTQKSLS LSLGK*
151	TIM3.15 – 13A3 (P102Y)	IgG4P HC (无 C 末端 K)	QLQLQESGPGLVKPSETLSLTCTVSGGSISSRSYYWGWIRQPPGKGLEWIGSIYYSG FTYYNPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCATGGPYGDYAHWFDY WGQGTLVTVSSASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGA LTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTKTYTCNVDHKPSNTKVDKRVESK YGPPCPPCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQFNW YVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSS IEKTISKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQP

[0702]

SEQ ID	抗体	描述	序列
			ENNYKTTPPVLDSDGSFFLYSRLTVDKSRWQEGNVFSCSVMHEALHNHYTQKSLS LSLG*
152	TIM3.16 – 13A3 (P102L)	IgG4P HC	QLQLQESGPGLVKPSETLSLTCTVSGGSISSRSYYWGWIRQPPGKGLEWIGSIYYSG FTYYNPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCATGGPYGDYAHWFDL WGQGTLVTVSSASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGA LTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTKTYTCNVDHKPSNTKVDKRVESK YGPPCPPCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQFNW YVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSS IEKTISKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQP ENNYKTTPPVLDSDGSFFLYSRLTVDKSRWQEGNVFSCSVMHEALHNHYTQKSLS LSLGK*
153	TIM3.16 – 13A3 (P102L)	IgG4P HC (无 C 末端 K)	QLQLQESGPGLVKPSETLSLTCTVSGGSISSRSYYWGWIRQPPGKGLEWIGSIYYSG FTYYNPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCATGGPYGDYAHWFDL WGQGTLVTVSSASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGA LTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTKTYTCNVDHKPSNTKVDKRVESK YGPPCPPCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQFNW YVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSS IEKTISKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQP ENNYKTTPPVLDSDGSFFLYSRLTVDKSRWQEGNVFSCSVMHEALHNHYTQKSLS LSLG*
154	TIM3.17 – 13A3 (N60Q, P102Y)	IgG4P HC	QLQLQESGPGLVKPSETLSLTCTVSGGSISSRSYYWGWIRQPPGKGLEWIGSIYYSG FTYYQPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCATGGPYGDYAHWFDY WGQGTLVTVSSASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGA LTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTKTYTCNVDHKPSNTKVDKRVESK YGPPCPPCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQFNW YVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSS IEKTISKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQP ENNYKTTPPVLDSDGSFFLYSRLTVDKSRWQEGNVFSCSVMHEALHNHYTQKSLS LSLGK*
155	TIM3.17 – 13A3 (N60Q, P102Y)	IgG4P HC (无 C 末端 K)	QLQLQESGPGLVKPSETLSLTCTVSGGSISSRSYYWGWIRQPPGKGLEWIGSIYYSG FTYYQPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCATGGPYGDYAHWFDY WGQGTLVTVSSASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGA LTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTKTYTCNVDHKPSNTKVDKRVESK YGPPCPPCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQFNW YVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSS IEKTISKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQP ENNYKTTPPVLDSDGSFFLYSRLTVDKSRWQEGNVFSCSVMHEALHNHYTQKSLS LSLG*
156	8B9	IgG1za HC	QVQLQESGPGLVKPSETLSLTCTVSGGSISRHYWNWIRQPPGKGLEWIGYIHYSGS TNYNSSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCARDTGYYGMDIWGQGT TVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGV HTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKT HTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYV DGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIE KTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPEN NYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLS PGK*
157	8B9	IgG1za HC (无 C 末端 K)	QVQLQESGPGLVKPSETLSLTCTVSGGSISRHYWNWIRQPPGKGLEWIGYIHYSGS TNYNSSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCARDTGYYGMDIWGQGT TVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGV HTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKT HTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYV DGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIE KTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPEN NYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLS PG*
158	8B9	IgG4P HC	QVQLQESGPGLVKPSETLSLTCTVSGGSISRHYWNWIRQPPGKGLEWIGYIHYSGS TNYNSSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCARDTGYYGMDIWGQGT TVTVSSASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGV HTFPAVLQSSGLYSLSSVVTVPSSSLGTKTYTCNVDHKPSNTKVDKRVESKYGPPC PPCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQFNWYVDGV EVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTIS KAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYK

[0703]

SEQ ID	抗体	描述	序列
			TTPPVLDSDGSFFLYSRLTVDKSRWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK*
159	8B9	IgG4P HC (无 C 末端 K)	QVQLQESGPGLVKPSETLSLTCTVSGGSISRHYWNWIRQPPGKGLEWIGYIHYSGS TNYNSSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCARDTGYYGMDIWGQGT TVTVSSASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGV HTFPAVLQSSGLYSLSSVVTVPSSSLGTKTYTCNVDHKPSNTKVDKRVESKYGPPC PPCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQFNWYVDGV EVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTIS KAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYK TTPPVLDSDGSFFLYSRLTVDKSRWQEGNVFSCSVMHEALHNHYTQKSLSLSLG*
160	TIM3.8 – 8B9 (S61P)	IgG4P HC	QVQLQESGPGLVKPSETLSLTCTVSGGSISRHYWNWIRQPPGKGLEWIGYIHYSGS TNYNPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCARDTGYYGMDIWGQGT TVTVSSASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGV HTFPAVLQSSGLYSLSSVVTVPSSSLGTKTYTCNVDHKPSNTKVDKRVESKYGPPC PPCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQFNWYVDGV EVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTIS KAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYK TTPPVLDSDGSFFLYSRLTVDKSRWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK*
161	TIM3.8 – 8B9 (S61P)	IgG4P HC (无 C 末端 K)	QVQLQESGPGLVKPSETLSLTCTVSGGSISRHYWNWIRQPPGKGLEWIGYIHYSGS TNYNPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCARDTGYYGMDIWGQGT TVTVSSASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGV HTFPAVLQSSGLYSLSSVVTVPSSSLGTKTYTCNVDHKPSNTKVDKRVESKYGPPC PPCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQFNWYVDGV EVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTIS KAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYK TTPPVLDSDGSFFLYSRLTVDKSRWQEGNVFSCSVMHEALHNHYTQKSLSLSLG*
162	8C4	IgG1za HC	QVQLQESGPGLVKPSETLSLTCTVSGGSISRYYWSWIRQPPGKGLEWIGYIHYTGS TNYNPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCATDTGYYGMDVWGQG TTVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSG VHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDK THTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWY VDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPI EKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPE NNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSL SPGK*
163	8C4	IgG1za HC (无 C 末端 K)	QVQLQESGPGLVKPSETLSLTCTVSGGSISRYYWSWIRQPPGKGLEWIGYIHYTGS TNYNPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCATDTGYYGMDVWGQG TTVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSG VHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDK THTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWY VDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPI EKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPE NNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSL SPG*
164	TIM3.6 – 8C4	IgG4P HC	QVQLQESGPGLVKPSETLSLTCTVSGGSISRYYWSWIRQPPGKGLEWIGYIHYTGS TNYNPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCATDTGYYGMDVWGQG TTVTVSSTKTYTCNVDHKPSNTKVDKRVESKYGPPCPPCPAPEFLGGPSVFLFPPKP KDTLMISRTPEVTCVVVDVSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYR VVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPREPQVYTLPPSQEE MTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSRLTV DKSRWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK*
165	TIM3.6 – 8C4	IgG4P HC (无 C 末端 K)	QVQLQESGPGLVKPSETLSLTCTVSGGSISRYYWSWIRQPPGKGLEWIGYIHYTGS TNYNPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCATDTGYYGMDVWGQG TTVTVSSTKTYTCNVDHKPSNTKVDKRVESKYGPPCPPCPAPEFLGGPSVFLFPPKP KDTLMISRTPEVTCVVVDVSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYR VVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPREPQVYTLPPSQEE MTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSRLTV DKSRWQEGNVFSCSVMHEALHNHYTQKSLSLSLG*
166	17C3	IgG1za HC	QVQLVQSGAEVKKPGASVKVSCKASGYTFTSYYMHWVRQAPGQGLEWMGIINP RGDSIIYAQKFQGRVTMTRDTSTSTVYMELSSLRSEDTAVYYCARDFYGSGNYYY GMDVWGQGTTVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVS WNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDK

[0704]

SEQ ID	抗体	描述	序列
			KVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHED PEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKV SNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVE WESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHN HYTQKSLSLSPGK*
167	17C3	IgG1za HC (无 C 末端 K)	QVQLVQSGAEVKKPGASVKVSCKASGYTFTSYYMHWVRQAPGQGLEWMGIINP RGDSIIYAQKFQGRVTMTRDTSTSTVYMELSSLRSEDTAVYYCARDFYGSGNYYY GMDVWGQGTTVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVS WNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDK KVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHED PEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKV SNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVE WESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHN HYTQKSLSLSPG*
168	TIM3.2 – 17C3	IgG4P HC	QVQLVQSGAEVKKPGASVKVSCKASGYTFTSYYMHWVRQAPGQGLEWMGIINP RGDSIIYAQKFQGRVTMTRDTSTSTVYMELSSLRSEDTAVYYCARDFYGSGNYYY GMDVWGQGTTVTVSSASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVS WNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTKTYTCNVDHKPSNTKVD KRVESKYGPPCPPCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSQEDPE VQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSN KGLPSSIEKTISKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWE SNGQPENNYKTTPPVLDSDGSFFLYSRLTVDKSRWQEGNVFSCSVMHEALHNHYT QKSLSLSLGK*
169	TIM3.2 – 17C3	IgG4P HC (无 C 末端 K)	QVQLVQSGAEVKKPGASVKVSCKASGYTFTSYYMHWVRQAPGQGLEWMGIINP RGDSIIYAQKFQGRVTMTRDTSTSTVYMELSSLRSEDTAVYYCARDFYGSGNYYY GMDVWGQGTTVTVSSASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVS WNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTKTYTCNVDHKPSNTKVD KRVESKYGPPCPPCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSQEDPE VQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSN KGLPSSIEKTISKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWE SNGQPENNYKTTPPVLDSDGSFFLYSRLTVDKSRWQEGNVFSCSVMHEALHNHYT QKSLSLSLG*
170	9F6	IgG1za HC	QVQLVESGGGLVKPGGSLRLSCAASGFTFSDYYMSWIRQAPGKGLEWVSFISGGG STIYYADSVKGRFTISRDNAKNSLFLQMNSLRVEDTAVYYCARDGYSSGWYYYG MDVWGQGTAVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSW NSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKK VEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDP EVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVS NKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEW ESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNH YTQKSLSLSPGK*
171	9F6	IgG1za HC (无 C 末端 K)	QVQLVESGGGLVKPGGSLRLSCAASGFTFSDYYMSWIRQAPGKGLEWVSFISGGG STIYYADSVKGRFTISRDNAKNSLFLQMNSLRVEDTAVYYCARDGYSSGWYYYG MDVWGQGTAVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSW NSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKK VEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDP EVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVS NKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEW ESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNH YTQKSLSLSPG*
172	9F6	IgG4P HC	QVQLVESGGGLVKPGGSLRLSCAASGFTFSDYYMSWIRQAPGKGLEWVSFISGGG STIYYADSVKGRFTISRDNAKNSLFLQMNSLRVEDTAVYYCARDGYSSGWYYYG MDVWGQGTAVTVSSASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSW NSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTKTYTCNVDHKPSNTKVDKR VESKYGPPCPPCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQ FNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKG LPSSIEKTISKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESN GQPENNYKTTPPVLDSDGSFFLYSRLTVDKSRWQEGNVFSCSVMHEALHNHYTQ KSLSLSLGK*
173	9F6	IgG4P HC (无 C 末端 K)	QVQLVESGGGLVKPGGSLRLSCAASGFTFSDYYMSWIRQAPGKGLEWVSFISGGG STIYYADSVKGRFTISRDNAKNSLFLQMNSLRVEDTAVYYCARDGYSSGWYYYG MDVWGQGTAVTVSSASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSW NSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTKTYTCNVDHKPSNTKVDKR

[0705]

SEQ ID	抗体	描述	序列
			VESKYGPPCPPCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQ FNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKG LPSSIEKTISKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESN GQPENNYKTTPPVLDSDGSFFLYSRLTVDKSRWQEGNVFSCSVMHEALHNHYTQ KSLSLSLG*
174	TIM3.7 – 9F6 (A108T)	IgG4P HC	QVQLVESGGGLVKPGGSLRLSCAASGFTFSDYYMSWIRQAPGKGLEWVSFISGGG STIYYADSVKGRFTISRDNAKNSLFLQMNSLRVEDTAVYYCARDGYSSGWYYYG MDVWGQGTTVTVSSASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSW NSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTKTYTCNVDHKPSNTKVDKR VESKYGPPCPPCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQ FNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKG LPSSIEKTISKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESN GQPENNYKTTPPVLDSDGSFFLYSRLTVDKSRWQEGNVFSCSVMHEALHNHYTQ KSLSLSLGK*
175	TIM3.7 – 9F6 (A108T)	IgG4P HC (无 C 末端 K)	QVQLVESGGGLVKPGGSLRLSCAASGFTFSDYYMSWIRQAPGKGLEWVSFISGGG STIYYADSVKGRFTISRDNAKNSLFLQMNSLRVEDTAVYYCARDGYSSGWYYYG MDVWGQGTTVTVSSASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSW NSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTKTYTCNVDHKPSNTKVDKR VESKYGPPCPPCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQ FNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKG LPSSIEKTISKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESN GQPENNYKTTPPVLDSDGSFFLYSRLTVDKSRWQEGNVFSCSVMHEALHNHYTQ KSLSLSLG*
176	3G4	IgG1za HC	QVQLVESGGGLVKPGGSLRLSCAASGFTFSDYYMSWIRQAPGKGLEWVSFISTSGS IIYYADSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCAREGYSSSWSYYYGM DVWGQGTTVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWN SGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKV EPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPE VKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSN KALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHY TQKSLSLSPGK*
177	3G4	IgG1za HC (无 C 末端 K)	QVQLVESGGGLVKPGGSLRLSCAASGFTFSDYYMSWIRQAPGKGLEWVSFISTSGS IIYYADSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCAREGYSSSWSYYYGM DVWGQGTTVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWN SGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKV EPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPE VKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSN KALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHY TQKSLSLSPG*
178	TIM3.4 – 3G4	IgG4P HC	QVQLVESGGGLVKPGGSLRLSCAASGFTFSDYYMSWIRQAPGKGLEWVSFISTSGS IIYYADSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCAREGYSSSWSYYYGM DVWGQGTTVTVSSASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNS GALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTKTYTCNVDHKPSNTKVDKRVE SKYGPPCPPCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQFN WYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLP SSIEKTISKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNG QPENNYKTTPPVLDSDGSFFLYSRLTVDKSRWQEGNVFSCSVMHEALHNHYTQKS LSLSLGK*
179	TIM3.4 – 3G4	IgG4P HC (无 C 末端 K)	QVQLVESGGGLVKPGGSLRLSCAASGFTFSDYYMSWIRQAPGKGLEWVSFISTSGS IIYYADSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCAREGYSSSWSYYYGM DVWGQGTTVTVSSASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNS GALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTKTYTCNVDHKPSNTKVDKRVE SKYGPPCPPCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQFN WYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLP SSIEKTISKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNG QPENNYKTTPPVLDSDGSFFLYSRLTVDKSRWQEGNVFSCSVMHEALHNHYTQKS LSLSLG*
180	17C8	IgG4 HC	QVQLVESGGGLVKPGGSLRLSCAASGFTFSDYYMSWIRQAPGKGLEWVSFISSSGS IIYYADSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARDGYSSGWEYYGM DVWGQGTTVTVSSASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNS GALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTKTYTCNVDHKPSNTKVDKRVE

[0706]

SEQ ID	抗体	描述	序列
			SKYGPPCPSCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQFN WYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLP SSIEKTISKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNG QPENNYKTTPPVLDSDGSFFLYSRLTVDKSRWQEGNVFSCSVMHEALHNHYTQKS LSLSLGK*
181	17C8	IgG4 HC (无 C 末端 K)	QVQLVESGGGLVKPGGSLRLSCAASGFTFSDYYMSWIRQAPGKGLEWVSFISSSGS IIYYADSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARDGYSSGWEYYGM DVWGQGTTVTVSSASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNS GALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTKTYTCNVDHKPSNTKVDKRVE SKYGPPCPSCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQFN WYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLP SSIEKTISKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNG QPENNYKTTPPVLDSDGSFFLYSRLTVDKSRWQEGNVFSCSVMHEALHNHYTQKS LSLSLG*
182	TIM3.9 – 17C8	IgG4P HC	QVQLVESGGGLVKPGGSLRLSCAASGFTFSDYYMSWIRQAPGKGLEWVSFISSSGS IIYYADSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARDGYSSGWEYYGM DVWGQGTTVTVSSASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNS GALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTKTYTCNVDHKPSNTKVDKRVE SKYGPPCPPCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQFN WYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLP SSIEKTISKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNG QPENNYKTTPPVLDSDGSFFLYSRLTVDKSRWQEGNVFSCSVMHEALHNHYTQKS LSLSLGK*
183	TIM3.9 – 17C8	IgG4P HC (无 C 末端 K)	QVQLVESGGGLVKPGGSLRLSCAASGFTFSDYYMSWIRQAPGKGLEWVSFISSSGS IIYYADSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARDGYSSGWEYYGM DVWGQGTTVTVSSASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNS GALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTKTYTCNVDHKPSNTKVDKRVE SKYGPPCPPCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQFN WYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLP SSIEKTISKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNG QPENNYKTTPPVLDSDGSFFLYSRLTVDKSRWQEGNVFSCSVMHEALHNHYTQKS LSLSLG*
184	13A3 (N60Q, D101E)	IgG1.1f HC	QLQLQESGPGLVKPSETLSLTCTVSGGSISSRSYYWGWIRQPPGKGLEWIGSIYYSG FTYY**Q**PSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCATGGPYGDYAHWF**EP** WGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSG ALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEP KSCDKTHTCPPCPAPEAEGAPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEV KFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNK ALPSSIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWES NGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYT QKSLSLSPGK*
185	13A3 (N60Q, D101E)	IgG1.1f HC (无 C 末端 K)	QLQLQESGPGLVKPSETLSLTCTVSGGSISSRSYYWGWIRQPPGKGLEWIGSIYYSG FTYYQPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCATGGPYGDYAHWFEP WGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSG ALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEP KSCDKTHTCPPCPAPEAEGAPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEV KFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNK ALPSSIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWES NGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYT QKSLSLSPG*
186	13A3 (N60Q, D101E)	IgG1.3f HC	QLQLQESGPGLVKPSETLSLTCTVSGGSISSRSYYWGWIRQPPGKGLEWIGSIYYSG FTYYQPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCATGGPYGDYAHWFEP WGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSG ALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEP KSCDKTHTCPPCPAPEAEGAPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEV KFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNK ALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWES NGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYT QKSLSLSPGK*
187	13A3 (N60Q, D101E)	IgG1.3f HC (无 C 末端 K)	QLQLQESGPGLVKPSETLSLTCTVSGGSISSRSYYWGWIRQPPGKGLEWIGSIYYSG FTYYQPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCATGGPYGDYAHWFEP WGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSG ALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEP

[0707]

SEQ ID	抗体	描述	序列
			KSCDKTHTCPPCPAPEAEGAPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEV KFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNK ALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWES NGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYT QKSLSLSPG*
188	TIM3.18 – 13A3 (N60Q, D101E)	IgG4P HC	QLQLQESGPGLVKPSETLSLTCTVSGGSISSRSYYWGWIRQPPGKGLEWIGSIYYSG FTYYQPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCATGGPYGDYAHWFEP WGQGTLVTVSSASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGA LTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTKTYTCNVDHKPSNTKVDKRVESK YGPPCPPCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQFNW YVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSS IEKTISKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQP ENNYKTTPPVLDSDGSFFLYSRLTVDKSRWQEGNVFSCSVMHEALHNHYTQKSLS LSLGK*
189	TIM3.18 – 13A3 (N60Q, D101E)	IgG4P HC (无 C 末端 K)	QLQLQESGPGLVKPSETLSLTCTVSGGSISSRSYYWGWIRQPPGKGLEWIGSIYYSG FTYYQPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCATGGPYGDYAHWFEP WGQGTLVTVSSASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGA LTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTKTYTCNVDHKPSNTKVDKRVESK YGPPCPPCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQFNW YVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSS IEKTISKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQP ENNYKTTPPVLDSDGSFFLYSRLTVDKSRWQEGNVFSCSVMHEALHNHYTQKSLS LSLG*
190	13A3, 17C3, 3G4	LC	EIVLTQSPGTLSLSPGERATLSCRASQSVSSSYLAWYQQKPGQAPRLLIYGASSRAT GIPDRFSGSGSGTDFTLTISRLEPEDFAVYYCQQYGSSPITFGQGTRLEIKRTVAAPS VFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSK DSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC*
191	8B9, 8C4, 17C8, 9F6 (VK3)	LC	EIVLTQSPGTLSLSPGERATLSCRASQSVSSSYLAWYQQKPGQAPRLLIYGASSRAT GIPDRFSGSGSGTDFTLTISRLEPEDFAVYYCQQYGSSPLTFGGGTKVEIKRTVAAP SVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDS KDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC*
192	9F6 (VK1)	LC	AIQLTQSPSSLSASVGDRVTITCRASQGISSALAWYQQKPGKAPKLLIYDASSLESG VPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQFNSYPRTFGQGTKVEIKRTVAAPS VFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSK DSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC*
193	9F6 (VK2)	LC	EIVLTQSPGTLSLSPGERATLSCRASQSVSSSYLAWYQQKPGQAPRLLIYGASSRAT GIPDRFSGSGSGTDFTLTISRLEPEDFAVYYCQQYGSSLTFGGGTKVEIKRTVAAPS VFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSK DSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC*
194		TIM3 同种型 1 (aa)	MFSHLPFDCVLLLLLLLLTRSSEVEYRAEVGQNAYLPCFYTPAAPGNLVPVCWGK GACPVFECGNVVLRTDERDVNYWTSRYWLNGDFRKGDVSLTIENVTLADSGIYC CRIQIPGIMNDEKFNLKLVIKPAKVTPAPTRQRDFTAAFPRMLTTRGHGPAETQTL GSLPDINLTQISTLANELRDSRLANDLRDSGATIRIGIYIGAGICAGLALALIFGALIF KWYSHSKEKIQNLSLISLANLPPSGLANAVAEGIRSEENIYTIEENVYEVEEPNEYY CYVSSRQQPSQPLGCRFAM
195		TIM3 同种型 2 (aa)	MFSHLPFDCVLLLLLLLLTRSSEVEYRAEVGQNAYLPCFYTPAAPGNLVPVCWGK GACPVFECGNVVLRTDERDVNYWTSRYWLNGDFRKGDVSLTIENVTLADSGIYC CRIQIPGIMNDEKFNLKLVIKPGEWTFACHLYE
196		TIM3 同种型 1 (nt)	AGAACACTTACAGGATGTGTGTAGTGTGGCATGACAGAGAACTTTGGTTTCCT TTAATGTGACTGTAGAC CTGGCAGTGTTACTATAAGAATCACTGGCAATCAGACACCCGGGTGTGCTGAG CTAGCACTCAGTGGGGG CGGCTACTGCTCATGTGATTGTGGAGTAGACAGTTGGAAGAAGTACCCAGTCC ATTTGGAGAGTTAAAAC TGTGCCTAACAGAGGTGTCCTCTGACTTTTCTTCTGCAAGCTCCATGTTTTCAC ATCTTCCCTTTGACTG TGTCCTGCTGCTGCTGCTGCTACTACTTACAAGGTCCTCAGAAGTGGAATACAG AGCGGAGGTCGGTCAG AATGCCTATCTGCCCTGCTTCTACACCCCAGCCGCCCCAGGGAACCTCGTGCCC GTCTGCTGGGGCAAAG GAGCCTGTCCTGTGTTTGAATGTGGCAACGTGGTGCTCAGGACTGATGAAAGG GATGTGAATTATTGGAC

[0708]

SEQ ID	抗体	描述	序列
			ATCCAGATACTGGCTAAATGGGGATTTCCGCAAAGGAGATGTGTCCCTGACCA TAGAGAATGTGACTCTA GCAGACAGTGGGATCTACTGCTGCCGGATCCAAATCCCAGGCATAATGAATGA TGAAAAATTTAACCTGA AGTTGGTCATCAAACCAGCCAAGGTCACCCCTGCACCGACTCGGCAGAGAGAC TTCACTGCAGCCTTTCC AAGGATGCTTACCACCAGGGGACATGGCCCAGCAGAGACACAGACACTGGGG AGCCTCCCTGATATAAAT CTAACACAAATATCCACATTGGCCAATGAGTTACGGGACTCTAGATTGGCCAA TGACTTACGGGACTCTG GAGCAACCATCAGAATAGGCATCTACATCGGAGCAGGGATCTGTGCTGGGCTG GCTCTGGCTCTTATCTT CGGCGCTTTAATTTTCAAATGGTATTCTCATAGCAAAGAGAAGATACAGAATT TAAGCCTCATCTCTTTG GCCAACCTCCCTCCCTCAGGATTGGCAAATGCAGTAGCAGAGGGAATTCGCTC AGAAGAAAACATCTATA CCATTGAAGAGAACGTATATGAAGTGGAGGAGCCCAATGAGTATTATTGCTAT GTCAGCAGCAGGCAGCA ACCCTCACAACCTTTGGGTTGTCGCTTTGCAATGCCATAGATCCAACCACCTTA TTTTTGAGCTTGGTGT TTTGTCTTTTTCAGAAACTATGAGCTGTGTCACCTGACTGGTTTTGGAGGTTCT GTCCACTGCTATGGAG CAGAGTTTTCCCATTTTCAGAAGATAATGACTCACATGGGAATTGAACTGGGA CCTGCACTGAACTTAAA CAGGCATGTCATTGCCTCTGTATTTAAGCCAACAGAGTTACCCAACCCAGAGA CTGTTAATCATGGATGT TAGAGCTCAAACGGGCTTTTATATACACTAGGAATTCTTGACGTGGGGTCTCTG GAGCTCCAGGAAATTC GGGCACATCATATGTCCATGAAACTTCAGATAAACTAGGGAAAACTGGGTGCT GAGGTGAAAGCATAACT TTTTTGGCACAGAAAGTCTAAAGGGGCCACTGATTTTCAAAGAGATCTGTGAT CCCTTTTTGTTTTTTGT TTTTGAGATGGAGTCTTGCTCTGTTGCCCAGGCTGGAGTGCAATGGCACAATCT CGGCTCACTGCAAGCT CCGCCTCCTGGGTTCAAGCGATTCTCCTGCCTCAGCCTCCTGAGTGGCTGGGAT TACAGGCATGCACCAC CATGCCCAGCTAATTTGTTGTATTTTTAGTAGAGACAGGGTTTCACCATGTTGG CCAGTGTGGTCTCAAA CTCCTGACCTCATGATTTGCCTGCCTCGGCCTCCCAAAGCACTGGGATTACAGG CGTGAGCCACCACATC CAGCCAGTGATCCTTAAAAGATTAAGAGATGACTGGACCAGGTCTACCTTGAT CTTGAAGATTCCCTTGG AATGTTGAGATTTAGGCTTATTTGAGCACTGCCTGCCCAACTGTCAGTGCCAGT GCATAGCCCTTCTTTT GTCTCCCTTATGAAGACTGCCCTGCAGGGCTGAGATGTGGCAGGAGCTCCCAG GGAAAAACGAAGTGCAT TTGATTGGTGTGTATTGGCCAAGTTTTGCTTGTTGTGTGCTTGAAAGAAAATAT CTCTGACCAACTTCTG TATTCGTGGACCAAACTGAAGCTATATTTTTCACAGAAGAAGAAGCAGTGACG GGGACACAAATTCTGTT GCCTGGTGGAAAGAAGGCAAAGGCCTTCAGCAATCTATATTACCAGCGCTGGA TCCTTTGACAGAGAGTG GTCCCTAAACTTAAATTTCAAGACGGTATAGGCTTGATCTGTCTTGCTTATTGT TGCCCCCTGCGCCTAG CACAATTCTGACACACAATTGGAACTTACTAAAAATTTTTTTTTACTGTTAAAA AAAAAAAAAAAAAA
197		TIM3 同种型 2 (nt)	ACTGCTCATGTGATTGTGGAGTAGACAGTTGGAAGAAGTACCCAGTCCATTTG GAGAGTTAAAACTGTGC CTAACAGAGGTGTCCTCTGACTTTTCTTCTGCAAGCTCCATGTTTTCACATCTTC CCTTTGACTGTGTCC TGCTGCTGCTGCTGCTACTACTTACAAGGTCCTCAGAAGTGGAATACAGAGCG GAGGTCGGTCAGAATGC CTATCTGCCCTGCTTCTACACCCCAGCCGCCCCAGGGAACCTCGTGCCCGTCTG CTGGGGCAAAGGAGCC TGTCCTGTGTTTGAATGTGGCAACGTGGTGCTCAGGACTGATGAAAGGGATGT

[0709]

SEQ ID	抗体	描述	序列
			GAATTATTGGACATCCA GATACTGGCTAAATGGGGATTTCCGCAAAGGAGATGTGTCCCTGACCATAGAG AATGTGACTCTAGCAGA CAGTGGGATCTACTGCTGCCGGATCCAAATCCCAGGCATAATGAATGATGAAA AATTTAACCTGAAGTTG GTCATCAAACCAGGTGAGTGGACATTTGCATGCCATCTTTATGAATAAGATTTA TCTGTGGATCATATTA AAGGTACTGATTGTTCTCATCTCTGACTTCCCTAATTATAGCCCTGGAGGAGGG CCACTAAGACCTAAAG TTTAACAGGCCCCATTGGTGATGCTCAGTGATATTTAACACCTTCTCTCTGTTTT AAAACTCATGGGTGT GCCTGGGCGTGGTGGCTCGCGCCTCTGGTCCCAGCACTTTGGGAGGCTGAGGC CGGTGGATCATGAGGTC AGGAATTCGAGACCAGCCTGGCCAACATGGTAAAACCTTGTCTCCACTAAAAA TACAAAAAATTAGCCAG GCATGGTTACGGGAGCCTGTAATTCTAGCTACTTGGGGGGCTGAAGCAGGAGA ATCACTTGAACCTGGAA GTCGGAGGTTGCGGTAAGCCAAGATCTCGCCATTGTACTCCAGCCTGGCTGAC AAGAGTGAAACTCTGTC CCAAAAAAAAAAAAAAAAAAAAAAAAAAAAA
198		TIM3 的胞外结构域	SEVEYRAEVGQNAYLPCFYTPAAPGNLVPVCWGKGACPVFECGNVVLRTDERDV NYWTSRYWLNGDFRKGDVSLTIENVTLADSGIYCCRIQIPGIMNDEKFNLKLVIKP AKVTPAPTRQRDFTAAFPRMLTTRGHGPAETQTLGSLPDINLTQISTLANELRDSRL ANDLRDSGATIRIG
199		食蟹猴 TIM3 蛋白	MFSHLPFDCVLLLLLLLLTRSSEVEYIAEVGQNAYLPCSYTPAPPGNLVPVCWGKG ACPVFDCSNVVLRTENRDVNDRTSGRYWLKGDFHKGDVSLTIENVTLADSGVYC CRIQIPGIMNDEKHNLKLVVIKPAKVTPAPTLQRDLTSAFPRMLTTGEHGPAETQTP GSLPDVNLTQIFTLTNELRDSGATIRTAIYIAAGISAGLALALIFGALIFKWYSHSKE KTQNLSLISLANIPPSGLANAVAEGIRSEENIYTIEEDVYEVEEPNEYYCYVSSGQQP SQPLGCRFAMP
200		成熟 TIM3 ECD 的残基 37-43	CPVFECG
201		成熟 TIM3 ECD 的残基 57-83	WTSRYWLNGDFR
202		成熟 TIM3 ECD 的残基 90-99	RIQIPGIMND
203		成熟 TIM3 ECD 的残基 1-99	SEVEYRAEVGQNAYLPCFYTPAAPGNLVPVCWGKGACPVFECGNVVLRTDERDV NYWTSRYWLNGDFRKGDVSLTIENVTLADSGIYCCRIQIPGIMND
204		成熟人类 TIM3 ECD 的残基 49-62	VPVCWGKGACPVFE
205		成熟人类 TIM3 ECD 的残基 111-127	RIQIPGIMNDEKFNLKL
206		成熟人类 TIM3 ECD 的残基 40-62	YTPAAPGNLVPVCWGKGACPVFE
207		成熟人类 TIM3 ECD 的残基 66-77	VVLRTDERDVNY
208		成熟人类 TIM3 ECD 的残基 78-95	WTSRYWLNGDFRKGDVSL
209		成熟人类	CRIQIPGIMNDEKFNLKL

[0710]

SEQ ID	抗体	描述	序列
		TIM3 ECD 的残基 110-127	
210		成熟人类 TIM3 ECD 的残基 119-127	NDEKFNLKL
211	13A3	简并 VH CDR1	X1X2X3X4YX5X6(数字是亚型)
212	13A3	简并 VH CDR2	X1IX2X3X4GX5X6X7X8YX9X10X11X12X13X14 (数字是亚型)
213	13A3	简并 VH CDR3	X1X2X3X4X5X6X7X8X9X10YGX11X12X13X14X15X16X17X18 (数字是亚型)
214	13A3	IgG1.1f HC	CAGCTGCAGCTGCAGGAGTCGGGCCCAGGACTGGTGAAGCCTTCGGAGACCCT GTCCCTCACCTGCACTGTCTCTGGTGGCTCCATCAGCAGTAGAAGTTACTACTG GGGCTGGATCCGCCAGCCCCCAGGGAAGGGGCTGGAGTGGATTGGGAGTATCT ATTATAGTGGGTTCACCTACTACAACCCGTCCCTCAAGAGTCGAGTCACCATAT CCGTTGACACGTCCAAGAACCAGTTCTCCCTGAAGCTGAGCTCTGTGACCGCC GCAGACACGGCTGTGTATTATTGTGCGACAGGGGGGCCCTACGGTGACTACGC CCACTGGTTCGACCCCTGGGGCCAGGGAACCCTGGTCACCGTCTCCTCAGCTA GCACCAAGGGCCCATCGGTCTTCCCCCTGGCACCCTCCTCCAAGAGCACCTCTG GGGGCACAGCGGCCCTGGGCTGCCTGGTCAAGGACTACTTCCCCGAACCGGTG ACGGTGTCGTGGAACTCAGGCGCCCTGACCAGCGGCGTGCACACCTTCCCGGC TGTCCTACAGTCCTCAGGACTCTACTCCCTCAGCAGCGTGGTGACCGTGCCCTC CAGCAGCTTGGGCACCCAGACCTACATCTGCAACGTGAATCACAAGCCCAGCA ACACCAAGGTGGACAAGAGAGTTGAGCCCAAATCTTGTGACAAAACTCACAC ATGCCCACCGTGCCCAGCACCTGAAGCCGAAGGGGCCCCGTCAGTCTTCCTCT TCCCCCCAAAACCCAAGGACACCCTCATGATCTCCCGGACCCCTGAGGTCACA TGCGTGGTGGTGGACGTGAGCCACGAAGACCCTGAGGTCAAGTTCAACTGGTA CGTGGACGGCGTGGAGGTGCATAATGCCAAGACAAAGCCGCGGGAGGAGCAG TACAACAGCACGTACCGTGTGGTCAGCGTCCTCACCGTCCTGCACCAGGACTG GCTGAATGGCAAGGAGTACAAGTGCAAGGTCTCCAACAAAGCCCTCCCAAGC AGCATCGAGAAAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAACCACAGG TGTACACCCTGCCCCCATCCCGGGAGGAGATGACCAAGAACCAGGTCAGCCTG ACCTGCCTGGTCAAAGGCTTCTATCCCAGCGACATCGCCGTGGAGTGGGAGAG CAATGGGCAGCCGGAGAACAACTACAAGACCACGCCTCCCGTGCTGGACTCCG ACGGCTCCTTCTTCCTCTATAGCAAGCTCACCGTGGACAAGAGCAGGTGGCAG CAGGGGAACGTCTTCTCATGCTCCGTGATGCATGAGGCTCTGCACAACCACTA CACGCAGAAGAGCCTCTCCCTGTCCCCGGGTAAATGA
215	8B9	IgG1.1f HC	CAGGTGCAGCTGCAGGAGTCGGGCCCAGGACTGGTGAAGCCTTCGGAGACCCT GTCCCTCACCTGCACTGTCTCTGGTGGCTCCATCAGTCGTCACTACTGGAACTG GATCCGGCAGCCCCCAGGGAAGGGACTGGAGTGGATTGGGTATATCCATTACA GTGGAAGCACCAACTACAATTCCTCCCTCAAGAGTCGAGTCACCATATCAGTA GACACGTCCAAGAACCAGTTCTCCCTGAAGCTGAGCTCTGTGACCGCTGCGGA CACGGCCGTGTATTACTGTGCGAGAGATACTGGGTACTACGGTATGGACATCT GGGGCCAAGGGACCACGGTCACCGTCTCCTCAGCTAGCACCAAGGGCCCATCG GTCTTCCCCCTGGCACCCTCCTCCAAGAGCACCTCTGGGGGCACAGCGGCCCT GGGCTGCCTGGTCAAGGACTACTTCCCCGAACCGGTGACGGTGTCGTGGAACT CAGGCGCCCTGACCAGCGGCGTGCACACCTTCCCGGCTGTCCTACAGTCCTCA GGACTCTACTCCCTCAGCAGCGTGGTGACCGTGCCCTCCAGCAGCTTGGGCAC CCAGACCTACATCTGCAACGTGAATCACAAGCCCAGCAACACCAAGGTGGACA AGAGAGTTGAGCCCAAATCTTGTGACAAAACTCACACATGCCCACCGTGCCCA GCACCTGAAGCCGAAGGGGCCCCGTCAGTCTTCCTCTTCCCCCCAAAACCCAA GGACACCCTCATGATCTCCCGGACCCCTGAGGTCACATGCGTGGTGGTGGACG TGAGCCACGAAGACCCTGAGGTCAAGTTCAACTGGTACGTGGACGGCGTGGAG GTGCATAATGCCAAGACAAAGCCGCGGGAGGAGCAGTACAACAGCACGTACC GTGTGGTCAGCGTCCTCACCGTCCTGCACCAGGACTGGCTGAATGGCAAGGAG TACAAGTGCAAGGTCTCCAACAAAGCCCTCCCAAGCAGCATCGAGAAAACCAT CTCCAAAGCCAAAGGGCAGCCCCGAGAACCACAGGTGTACACCCTGCCCCCAT CCCGGGAGGAGATGACCAAGAACCAGGTCAGCCTGACCTGCCTGGTCAAAGG CTTCTATCCCAGCGACATCGCCGTGGAGTGGGAGAGCAATGGGCAGCCGGAGA ACAACTACAAGACCACGCCTCCCGTGCTGGACTCCGACGGCTCCTTCTTCCTCT ATAGCAAGCTCACCGTGGACAAGAGCAGGTGGCAGCAGGGGAACGTCTTCTC ATGCTCCGTGATGCATGAGGCTCTGCACAACCACTACACGCAGAAGAGCCTCT

[0711]

SEQ ID	抗体	描述	序列
			CCCTGTCCCCGGGTAAATGA
216	8C4	IgG1.1f HC	CAGGTGCAGCTGCAGGAGTCGGGCCCAGGACTGGTGAAGCCTTCGGAGACCCT GTCCCTCACCTGCACTGTCTCTGGTGGCTCCATCAGTCGTTACTACTGGAGCTG GATCCGGCAGCCCCCAGGGAAGGGACTGGAGTGGATTGGGTATATCCATTACA CTGGGAGCACCAACTACAACCCCTCCCTCAAGAGTCGAGTCACCATATCAGTA GACACGTCCAAGAACCAGTTCTCCCTGAAGCTGAGCTCTGTGACCGCAGCGGA CACGGCCGTGTATTACTGTGCGACAGATACGGGCTACTACGGTATGGACGTCT GGGGCCAAGGGACCACGGTCACCGTCTCCTCAGCTAGCACCAAGGGCCCATCG GTCTTCCCCCTGGCACCCTCCTCCAAGAGCACCTCTGGGGGCACAGCGGCCCT GGGCTGCCTGGTCAAGGACTACTTCCCCGAACCGGTGACGGTGTCGTGGAACT CAGGCGCCCTGACCAGCGGCGTGCACACCTTCCCGGCTGTCCTACAGTCCTCA GGACTCTACTCCCTCAGCAGCGTGGTGACCGTGCCCTCCAGCAGCTTGGGCAC CCAGACCTACATCTGCAACGTGAATCACAAGCCCAGCAACACCAAGGTGGACA AGAGAGTTGAGCCCAAATCTTGTGACAAAACTCACACATGCCCACCGTGCCCA GCACCTGAAGCCGAAGGGGCCCCGTCAGTCTTCCTCTTCCCCCCAAAACCCAA GGACACCCTCATGATCTCCCGGACCCCTGAGGTCACATGCGTGGTGGTGGACG TGAGCCACGAAGACCCTGAGGTCAAGTTCAACTGGTACGTGGACGGCGTGGAG GTGCATAATGCCAAGACAAAGCCGCGGGAGGAGCAGTACAACAGCACGTACC GTGTGGTCAGCGTCCTCACCGTCCTGCACCAGGACTGGCTGAATGGCAAGGAG TACAAGTGCAAGGTCTCCAACAAAGCCCTCCCAAGCAGCATCGAGAAAACCAT CTCCAAAGCCAAAGGGCAGCCCCGAGAACCACAGGTGTACACCCTGCCCCCAT CCCGGGAGGAGATGACCAAGAACCAGGTCAGCCTGACCTGCCTGGTCAAAGG CTTCTATCCCAGCGACATCGCCGTGGAGTGGGAGAGCAATGGGCAGCCGGAGA ACAACTACAAGACCACGCCTCCCGTGCTGGACTCCGACGGCTCCTTCTTCCTCT ATAGCAAGCTCACCGTGGACAAGAGCAGGTGGCAGCAGGGGAACGTCTTCTC ATGCTCCGTGATGCATGAGGCTCTGCACAACCACTACACGCAGAAGAGCCTCT CCCTGTCCCCGGGTAAATGA
217	17C3	IgG1.1f HC	CAGGTGCAGTTGGTGCAGTCTGGGGCTGAGGTGAAGAAGCCTGGGGCCTCAGT GAAGGTCTCCTGCAAGGCATCTGGATACACTTTCACCAGCTACTATATGCACTG GGTGCGACAGGCCCCTGGACAAGGGCTTGAGTGGATGGGAATAATCAACCCTA GGGGTGATAGCATAATCTACGCACAGAAGTTCCAGGGCAGAGTCACCATGACC AGGGACACGTCCACGAGCACAGTCTACATGGAGCTGAGCAGCCTGAGATCTGA GGACACGGCCGTGTATTACTGTGCGAGAGATTTCTATGGTTCGGGAAACTACT ACTACGGTATGGACGTCTGGGGCCAAGGGACCACGGTCACCGTCTCCTCAGCT AGCACCAAGGGCCCATCGGTCTTCCCCCTGGCACCCTCCTCCAAGAGCACCTCT GGGGGCACAGCGGCCCTGGGCTGCCTGGTCAAGGACTACTTCCCCGAACCGGT GACGGTGTCGTGGAACTCAGGCGCCCTGACCAGCGGCGTGCACACCTTCCCGG CTGTCCTACAGTCCTCAGGACTCTACTCCCTCAGCAGCGTGGTGACCGTGCCCT CCAGCAGCTTGGGCACCCAGACCTACATCTGCAACGTGAATCACAAGCCCAGC AACACCAAGGTGGACAAGAGAGTTGAGCCCAAATCTTGTGACAAAACTCACA CATGCCCACCGTGCCCAGCACCTGAAGCCGAAGGGGCCCCGTCAGTCTTCCTC TTCCCCCCAAAACCCAAGGACACCCTCATGATCTCCCGGACCCCTGAGGTCAC ATGCGTGGTGGTGGACGTGAGCCACGAAGACCCTGAGGTCAAGTTCAACTGGT ACGTGGACGGCGTGGAGGTGCATAATGCCAAGACAAAGCCGCGGGAGGAGCA GTACAACAGCACGTACCGTGTGGTCAGCGTCCTCACCGTCCTGCACCAGGACT GGCTGAATGGCAAGGAGTACAAGTGCAAGGTCTCCAACAAAGCCCTCCCAAG CAGCATCGAGAAAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAACCACAG GTGTACACCCTGCCCCCATCCCGGGAGGAGATGACCAAGAACCAGGTCAGCCT GACCTGCCTGGTCAAAGGCTTCTATCCCAGCGACATCGCCGTGGAGTGGGAGA GCAATGGGCAGCCGGAGAACAACTACAAGACCACGCCTCCCGTGCTGGACTCC GACGGCTCCTTCTTCCTCTATAGCAAGCTCACCGTGGACAAGAGCAGGTGGCA GCAGGGGAACGTCTTCTCATGCTCCGTGATGCATGAGGCTCTGCACAACCACT ACACGCAGAAGAGCCTCTCCCTGTCCCCGGGTAAATGA
218	9F6	IgG1.1f HC	CAGGTGCAGCTGGTGGAGTCTGGGGGAGGCTTGGTCAAGCCTGGAGGGTCCCT GAGACTCTCCTGTGCAGCCTCTGGATTCACCTTCAGTGACTACTACATGAGCTG GATCCGCCAGGCTCCAGGGAAGGGGCTGGAGTGGGTTTCATTCATTAGTGGTG GTGGTAGTACCATATACTACGCAGACTCTGTGAAGGGCCGATTCACCATCTCC AGGGACAACGCCAAGAACTCGCTGTTTCTGCAAATGAACAGCCTGAGAGTCGA GGACACGGCTGTGTATTACTGTGCGAGAGATGGCTATAGCAGTGGCTGGTACT ACTACGGTATGGACGTCTGGGGCCAAGGGACCGCGGTCACCGTCTCCTCAGCT AGCACCAAGGGCCCATCGGTCTTCCCCCTGGCACCCTCCTCCAAGAGCACCTCT GGGGGCACAGCGGCCCTGGGCTGCCTGGTCAAGGACTACTTCCCCGAACCGGT GACGGTGTCGTGGAACTCAGGCGCCCTGACCAGCGGCGTGCACACCTTCCCGG CTGTCCTACAGTCCTCAGGACTCTACTCCCTCAGCAGCGTGGTGACCGTGCCCT

[0712]

SEQ ID	抗体	描述	序列
			CCAGCAGCTTGGGCACCCAGACCTACATCTGCAACGTGAATCACAAGCCCAGC AACACCAAGGTGGACAAGAGAGTTGAGCCCAAATCTTGTGACAAAACTCACA CATGCCCACCGTGCCCAGCACCTGAAGCCGAAGGGGCCCCGTCAGTCTTCCTC TTCCCCCCAAAACCCAAGGACACCCTCATGATCTCCCGGACCCCTGAGGTCAC ATGCGTGGTGGTGGACGTGAGCCACGAAGACCCTGAGGTCAAGTTCAACTGGT ACGTGGACGGCGTGGAGGTGCATAATGCCAAGACAAAGCCGCGGGAGGAGCA GTACAACAGCACGTACCGTGTGGTCAGCGTCCTCACCGTCCTGCACCAGGACT GGCTGAATGGCAAGGAGTACAAGTGCAAGGTCTCCAACAAAGCCCTCCCAAG CAGCATCGAGAAAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAACCACAG GTGTACACCCTGCCCCCATCCCGGGAGGAGATGACCAAGAACCAGGTCAGCCT GACCTGCCTGGTCAAAGGCTTCTATCCCAGCGACATCGCCGTGGAGTGGGAGA GCAATGGGCAGCCGGAGAACAACTACAAGACCACGCCTCCCGTGCTGGACTCC GACGGCTCCTTCTTCCTCTATAGCAAGCTCACCGTGGACAAGAGCAGGTGGCA GCAGGGGAACGTCTTCTCATGCTCCGTGATGCATGAGGCTCTGCACAACCACT ACACGCAGAAGAGCCTCTCCCTGTCCCCGGGTAAATGA
219	3G4	IgG1.1f HC	CAGGTGCAGCTGGTGGAGTCTGGGGGAGGCTTGGTCAAGCCTGGAGGGTCCCT GAGACTCTCCTGTGCAGCCTCTGGATTCACCTTCAGTGACTACTACATGAGCTG GATCCGCCAGGCTCCAGGGAAGGGGCTGGAGTGGGTTTCATTCATTAGTACTA GTGGTAGTATCATATACTACGCAGACTCTGTGAAGGGCCGATTCACCATCTCC AGGGACAACGCCAAGAACTCACTGTATCTGCAAATGAACAGCCTGAGAGCCG AGGACACGGCTGTGTATTACTGTGCGAGAGAAGGGTATAGCAGCAGCTGGTCC TACTACTACGGTATGGACGTCTGGGGCCAAGGGACCACGGTCACCGTCTCCTC AGCTAGCACCAAGGGCCCATCGGTCTTCCCCCTGGCACCCTCCTCCAAGAGCA CCTCTGGGGGCACAGCGGCCCTGGGCTGCCTGGTCAAGGACTACTTCCCCGAA CCGGTGACGGTGTCGTGGAACTCAGGCGCCCTGACCAGCGGCGTGCACACCTT CCCGGCTGTCCTACAGTCCTCAGGACTCTACTCCCTCAGCAGCGTGGTGACCGT GCCCTCCAGCAGCTTGGGCACCCAGACCTACATCTGCAACGTGAATCACAAGC CCAGCAACACCAAGGTGGACAAGAGAGTTGAGCCCAAATCTTGTGACAAAAC TCACACATGCCCACCGTGCCCAGCACCTGAAGCCGAAGGGGCCCCGTCAGTCT TCCTCTTCCCCCCAAAACCCAAGGACACCCTCATGATCTCCCGGACCCCTGAGG TCACATGCGTGGTGGTGGACGTGAGCCACGAAGACCCTGAGGTCAAGTTCAAC TGGTACGTGGACGGCGTGGAGGTGCATAATGCCAAGACAAAGCCGCGGGAGG AGCAGTACAACAGCACGTACCGTGTGGTCAGCGTCCTCACCGTCCTGCACCAG GACTGGCTGAATGGCAAGGAGTACAAGTGCAAGGTCTCCAACAAAGCCCTCCC AAGCAGCATCGAGAAAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAACCA CAGGTGTACACCCTGCCCCCATCCCGGGAGGAGATGACCAAGAACCAGGTCAG CCTGACCTGCCTGGTCAAAGGCTTCTATCCCAGCGACATCGCCGTGGAGTGGG AGAGCAATGGGCAGCCGGAGAACAACTACAAGACCACGCCTCCCGTGCTGGA CTCCGACGGCTCCTTCTTCCTCTATAGCAAGCTCACCGTGGACAAGAGCAGGT GGCAGCAGGGGAACGTCTTCTCATGCTCCGTGATGCATGAGGCTCTGCACAAC CACTACACGCAGAAGAGCCTCTCCCTGTCCCCGGGTAAATGA
220	17C8	IgG1.1f HC	CAGGTGCAGCTGGTGGAGTCTGGGGGAGGCTTGGTCAAGCCTGGAGGGTCCCT GAGACTCTCCTGTGCAGCCTCTGGATTCACCTTCAGTGACTACTACATGAGCTG GATCCGCCAGGCTCCAGGGAAGGGGCTGGAGTGGGTTTCATTCATTAGTAGTA GTGGTAGTATCATATACTACGCAGACTCTGTGAAGGGCCGATTCACCATCTCC AGGGACAACGCCAAGAACTCACTGTATCTGCAAATGAACAGCCTGAGAGCCG AGGACACGGCTGTGTATTACTGTGCGAGAGATGGGTATAGCAGTGGCTGGGAG TACTACGGTATGGACGTCTGGGGCCAAGGGACCACGGTCACCGTCTCCTCAGC TAGCACCAAGGGCCCATCGGTCTTCCCCCTGGCACCCTCCTCCAAGAGCACCTC TGGGGGCACAGCGGCCCTGGGCTGCCTGGTCAAGGACTACTTCCCCGAACCGG TGACGGTGTCGTGGAACTCAGGCGCCCTGACCAGCGGCGTGCACACCTTCCCG GCTGTCCTACAGTCCTCAGGACTCTACTCCCTCAGCAGCGTGGTGACCGTGCCC TCCAGCAGCTTGGGCACCCAGACCTACATCTGCAACGTGAATCACAAGCCCAG CAACACCAAGGTGGACAAGAGAGTTGAGCCCAAATCTTGTGACAAAACTCAC ACATGCCCACCGTGCCCAGCACCTGAAGCCGAAGGGGCCCCGTCAGTCTTCCT CTTCCCCCCAAAACCCAAGGACACCCTCATGATCTCCCGGACCCCTGAGGTCA CATGCGTGGTGGTGGACGTGAGCCACGAAGACCCTGAGGTCAAGTTCAACTGG TACGTGGACGGCGTGGAGGTGCATAATGCCAAGACAAAGCCGCGGGAGGAGC AGTACAACAGCACGTACCGTGTGGTCAGCGTCCTCACCGTCCTGCACCAGGAC TGGCTGAATGGCAAGGAGTACAAGTGCAAGGTCTCCAACAAAGCCCTCCCAAG CAGCATCGAGAAAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAACCACAG GTGTACACCCTGCCCCCATCCCGGGAGGAGATGACCAAGAACCAGGTCAGCCT GACCTGCCTGGTCAAAGGCTTCTATCCCAGCGACATCGCCGTGGAGTGGGAGA GCAATGGGCAGCCGGAGAACAACTACAAGACCACGCCTCCCGTGCTGGACTCC GACGGCTCCTTCTTCCTCTATAGCAAGCTCACCGTGGACAAGAGCAGGTGGCA

[0713]

SEQ ID	抗体	描述	序列
			GCAGGGGAACGTCTTCTCATGCTCCGTGATGCATGAGGCTCTGCACAACCACT ACACGCAGAAGAGCCTCTCCCTGTCCCCGGGTAAATGA
221	13A3	IgG1.1f HC (无 C 末端 K)	CAGCTGCAGCTGCAGGAGTCGGGCCCAGGACTGGTGAAGCCTTCGGAGACCCT GTCCCTCACCTGCACTGTCTCTGGTGGCTCCATCAGCAGTAGAAGTTACTACTG GGGCTGGATCCGCCAGCCCCCAGGGAAGGGGCTGGAGTGGATTGGGAGTATCT ATTATAGTGGGTTCACCTACTACAACCCGTCCCTCAAGAGTCGAGTCACCATAT CCGTTGACACGTCCAAGAACCAGTTCTCCCTGAAGCTGAGCTCTGTGACCGCC GCAGACACGGCTGTGTATTATTGTGCGACAGGGGGGCCCTACGGTGACTACGC CCACTGGTTCGACCCCTGGGGCCAGGGAACCCTGGTCACCGTCTCCTCAGCTA GCACCAAGGGCCCATCGGTCTTCCCCCTGGCACCCTCCTCCAAGAGCACCTCTG GGGGCACAGCGGCCCTGGGCTGCCTGGTCAAGGACTACTTCCCCGAACCGGTG ACGGTGTCGTGGAACTCAGGCGCCCTGACCAGCGGCGTGCACACCTTCCCGGC TGTCCTACAGTCCTCAGGACTCTACTCCCTCAGCAGCGTGGTGACCGTGCCCTC CAGCAGCTTGGGCACCCAGACCTACATCTGCAACGTGAATCACAAGCCCAGCA ACACCAAGGTGGACAAGAGAGTTGAGCCCAAATCTTGTGACAAAACTCACAC ATGCCCACCGTGCCCAGCACCTGAAGCCGAAGGGGCCCCGTCAGTCTTCCTCT TCCCCCCAAAACCCAAGGACACCCTCATGATCTCCCGGACCCCTGAGGTCACA TGCGTGGTGGTGGACGTGAGCCACGAAGACCCTGAGGTCAAGTTCAACTGGTA CGTGGACGGCGTGGAGGTGCATAATGCCAAGACAAAGCCGCGGGAGGAGCAG TACAACAGCACGTACCGTGTGGTCAGCGTCCTCACCGTCCTGCACCAGGACTG GCTGAATGGCAAGGAGTACAAGTGCAAGGTCTCCAACAAAGCCCTCCCAAGC AGCATCGAGAAAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAACCACAGG TGTACACCCTGCCCCCATCCCGGGAGGAGATGACCAAGAACCAGGTCAGCCTG ACCTGCCTGGTCAAAGGCTTCTATCCCAGCGACATCGCCGTGGAGTGGGAGAG CAATGGGCAGCCGGAGAACAACTACAAGACCACGCCTCCCGTGCTGGACTCCG ACGGCTCCTTCTTCCTCTATAGCAAGCTCACCGTGGACAAGAGCAGGTGGCAG CAGGGGAACGTCTTCTCATGCTCCGTGATGCATGAGGCTCTGCACAACCACTA CACGCAGAAGAGCCTCTCCCTGTCCCCGGGTTGA
222	8B9	IgG1.1f HC (无 C 末端 K)	CAGGTGCAGCTGCAGGAGTCGGGCCCAGGACTGGTGAAGCCTTCGGAGACCCT GTCCCTCACCTGCACTGTCTCTGGTGGCTCCATCAGTCGTCACTACTGGAACTG GATCCGGCAGCCCCCAGGGAAGGGACTGGAGTGGATTGGGTATATCCATTACA GTGGAAGCACCAACTACAATTCCTCCCTCAAGAGTCGAGTCACCATATCAGTA GACACGTCCAAGAACCAGTTCTCCCTGAAGCTGAGCTCTGTGACCGCTGCGGA CACGGCCGTGTATTACTGTGCGAGAGATACTGGGTACTACGGTATGGACATCT GGGGCCAAGGGACCACGGTCACCGTCTCCTCAGCTAGCACCAAGGGCCCATCG GTCTTCCCCCTGGCACCCTCCTCCAAGAGCACCTCTGGGGGCACAGCGGCCCT GGGCTGCCTGGTCAAGGACTACTTCCCCGAACCGGTGACGGTGTCGTGGAACT CAGGCGCCCTGACCAGCGGCGTGCACACCTTCCCGGCTGTCCTACAGTCCTCA GGACTCTACTCCCTCAGCAGCGTGGTGACCGTGCCCTCCAGCAGCTTGGGCAC CCAGACCTACATCTGCAACGTGAATCACAAGCCCAGCAACACCAAGGTGGACA AGAGAGTTGAGCCCAAATCTTGTGACAAAACTCACACATGCCCACCGTGCCCA GCACCTGAAGCCGAAGGGGCCCCGTCAGTCTTCCTCTTCCCCCCAAAACCCAA GGACACCCTCATGATCTCCCGGACCCCTGAGGTCACATGCGTGGTGGTGGACG TGAGCCACGAAGACCCTGAGGTCAAGTTCAACTGGTACGTGGACGGCGTGGAG GTGCATAATGCCAAGACAAAGCCGCGGGAGGAGCAGTACAACAGCACGTACC GTGTGGTCAGCGTCCTCACCGTCCTGCACCAGGACTGGCTGAATGGCAAGGAG TACAAGTGCAAGGTCTCCAACAAAGCCCTCCCAAGCAGCATCGAGAAAACCAT CTCCAAAGCCAAAGGGCAGCCCCGAGAACCACAGGTGTACACCCTGCCCCCAT CCCGGGAGGAGATGACCAAGAACCAGGTCAGCCTGACCTGCCTGGTCAAAGG CTTCTATCCCAGCGACATCGCCGTGGAGTGGGAGAGCAATGGGCAGCCGGAGA ACAACTACAAGACCACGCCTCCCGTGCTGGACTCCGACGGCTCCTTCTTCCTCT ATAGCAAGCTCACCGTGGACAAGAGCAGGTGGCAGCAGGGGAACGTCTTCTC ATGCTCCGTGATGCATGAGGCTCTGCACAACCACTACACGCAGAAGAGCCTCT CCCTGTCCCCGGGTTGA
223	8C4	IgG1.1f HC (无 C 末端 K)	CAGGTGCAGCTGCAGGAGTCGGGCCCAGGACTGGTGAAGCCTTCGGAGACCCT GTCCCTCACCTGCACTGTCTCTGGTGGCTCCATCAGTCGTTACTACTGGAGCTG GATCCGGCAGCCCCCAGGGAAGGGACTGGAGTGGATTGGGTATATCCATTACA CTGGGAGCACCAACTACAACCCCTCCCTCAAGAGTCGAGTCACCATATCAGTA GACACGTCCAAGAACCAGTTCTCCCTGAAGCTGAGCTCTGTGACCGCAGCGGA CACGGCCGTGTATTACTGTGCGACAGATACGGGCTACTACGGTATGGACGTCT GGGGCCAAGGGACCACGGTCACCGTCTCCTCAGCTAGCACCAAGGGCCCATCG GTCTTCCCCCTGGCACCCTCCTCCAAGAGCACCTCTGGGGGCACAGCGGCCCT GGGCTGCCTGGTCAAGGACTACTTCCCCGAACCGGTGACGGTGTCGTGGAACT CAGGCGCCCTGACCAGCGGCGTGCACACCTTCCCGGCTGTCCTACAGTCCTCA

[0714]

SEQ ID	抗体	描述	序列
			GGACTCTACTCCCTCAGCAGCGTGGTGACCGTGCCCTCCAGCAGCTTGGGCAC CCAGACCTACATCTGCAACGTGAATCACAAGCCCAGCAACACCAAGGTGGACA AGAGAGTTGAGCCCAAATCTTGTGACAAAACTCACACATGCCCACCGTGCCCA GCACCTGAAGCCGAAGGGGCCCCGTCAGTCTTCCTCTTCCCCCCAAAACCCAA GGACACCCTCATGATCTCCCGGACCCCTGAGGTCACATGCGTGGTGGTGGACG TGAGCCACGAAGACCCTGAGGTCAAGTTCAACTGGTACGTGGACGGCGTGGAG GTGCATAATGCCAAGACAAAGCCGCGGGAGGAGCAGTACAACAGCACGTACC GTGTGGTCAGCGTCCTCACCGTCCTGCACCAGGACTGGCTGAATGGCAAGGAG TACAAGTGCAAGGTCTCCAACAAAGCCCTCCCAAGCAGCATCGAGAAAACCAT CTCCAAAGCCAAAGGGCAGCCCCGAGAACCACAGGTGTACACCCTGCCCCCAT CCCGGGAGGAGATGACCAAGAACCAGGTCAGCCTGACCTGCCTGGTCAAAGG CTTCTATCCCAGCGACATCGCCGTGGAGTGGGAGAGCAATGGGCAGCCGGAGA ACAACTACAAGACCACGCCTCCCGTGCTGGACTCCGACGGCTCCTTCTTCCTCT ATAGCAAGCTCACCGTGGACAAGAGCAGGTGGCAGCAGGGGAACGTCTTCTC ATGCTCCGTGATGCATGAGGCTCTGCACAACCACTACACGCAGAAGAGCCTCT CCCTGTCCCCGGGTTGA
224	17C3	IgG1.1f HC (无 C 末端 K)	CAGGTGCAGTTGGTGCAGTCTGGGGCTGAGGTGAAGAAGCCTGGGGCCTCAGT GAAGGTCTCCTGCAAGGCATCTGGATACACTTTCACCAGCTACTATATGCACTG GGTGCGACAGGCCCCTGGACAAGGGCTTGAGTGGATGGGAATAATCAACCCTA GGGGTGATAGCATAATCTACGCACAGAAGTTCCAGGGCAGAGTCACCATGACC AGGGACACGTCCACGAGCACAGTCTACATGGAGCTGAGCAGCCTGAGATCTGA GGACACGGCCGTGTATTACTGTGCGAGAGATTTCTATGGTTCGGGAAACTACT ACTACGGTATGGACGTCTGGGGCCAAGGGACCACGGTCACCGTCTCCTCAGCT AGCACCAAGGGCCCATCGGTCTTCCCCCTGGCACCCTCCTCCAAGAGCACCTCT GGGGGCACAGCGGCCCTGGGCTGCCTGGTCAAGGACTACTTCCCCGAACCGGT GACGGTGTCGTGGAACTCAGGCGCCCTGACCAGCGGCGTGCACACCTTCCCGG CTGTCCTACAGTCCTCAGGACTCTACTCCCTCAGCAGCGTGGTGACCGTGCCCT CCAGCAGCTTGGGCACCCAGACCTACATCTGCAACGTGAATCACAAGCCCAGC AACACCAAGGTGGACAAGAGAGTTGAGCCCAAATCTTGTGACAAAACTCACA CATGCCCACCGTGCCCAGCACCTGAAGCCGAAGGGGCCCCGTCAGTCTTCCTC TTCCCCCCAAAACCCAAGGACACCCTCATGATCTCCCGGACCCCTGAGGTCAC ATGCGTGGTGGTGGACGTGAGCCACGAAGACCCTGAGGTCAAGTTCAACTGGT ACGTGGACGGCGTGGAGGTGCATAATGCCAAGACAAAGCCGCGGGAGGAGCA GTACAACAGCACGTACCGTGTGGTCAGCGTCCTCACCGTCCTGCACCAGGACT GGCTGAATGGCAAGGAGTACAAGTGCAAGGTCTCCAACAAAGCCCTCCCAAG CAGCATCGAGAAAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAACCACAG GTGTACACCCTGCCCCCATCCCGGGAGGAGATGACCAAGAACCAGGTCAGCCT GACCTGCCTGGTCAAAGGCTTCTATCCCAGCGACATCGCCGTGGAGTGGGAGA GCAATGGGCAGCCGGAGAACAACTACAAGACCACGCCTCCCGTGCTGGACTCC GACGGCTCCTTCTTCCTCTATAGCAAGCTCACCGTGGACAAGAGCAGGTGGCA GCAGGGGAACGTCTTCTCATGCTCCGTGATGCATGAGGCTCTGCACAACCACT ACACGCAGAAGAGCCTCTCCCTGTCCCCGGGTTGA
225	9F6	IgG1.1f HC (无 C 末端 K)	CAGGTGCAGCTGGTGGAGTCTGGGGGAGGCTTGGTCAAGCCTGGAGGGTCCCT GAGACTCTCCTGTGCAGCCTCTGGATTCACCTTCAGTGACTACTACATGAGCTG GATCCGCCAGGCTCCAGGGAAGGGGCTGGAGTGGGTTTCATTCATTAGTGGTG GTGGTAGTACCATATACTACGCAGACTCTGTGAAGGGCCGATTCACCATCTCC AGGGACAACGCCAAGAACTCGCTGTTTCTGCAAATGAACAGCCTGAGAGTCGA GGACACGGCTGTGTATTACTGTGCGAGAGATGGCTATAGCAGTGGCTGGTACT ACTACGGTATGGACGTCTGGGGCCAAGGGACCGCGGTCACCGTCTCCTCAGCT AGCACCAAGGGCCCATCGGTCTTCCCCCTGGCACCCTCCTCCAAGAGCACCTCT GGGGGCACAGCGGCCCTGGGCTGCCTGGTCAAGGACTACTTCCCCGAACCGGT GACGGTGTCGTGGAACTCAGGCGCCCTGACCAGCGGCGTGCACACCTTCCCGG CTGTCCTACAGTCCTCAGGACTCTACTCCCTCAGCAGCGTGGTGACCGTGCCCT CCAGCAGCTTGGGCACCCAGACCTACATCTGCAACGTGAATCACAAGCCCAGC AACACCAAGGTGGACAAGAGAGTTGAGCCCAAATCTTGTGACAAAACTCACA CATGCCCACCGTGCCCAGCACCTGAAGCCGAAGGGGCCCCGTCAGTCTTCCTC TTCCCCCCAAAACCCAAGGACACCCTCATGATCTCCCGGACCCCTGAGGTCAC ATGCGTGGTGGTGGACGTGAGCCACGAAGACCCTGAGGTCAAGTTCAACTGGT ACGTGGACGGCGTGGAGGTGCATAATGCCAAGACAAAGCCGCGGGAGGAGCA GTACAACAGCACGTACCGTGTGGTCAGCGTCCTCACCGTCCTGCACCAGGACT GGCTGAATGGCAAGGAGTACAAGTGCAAGGTCTCCAACAAAGCCCTCCCAAG CAGCATCGAGAAAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAACCACAG GTGTACACCCTGCCCCCATCCCGGGAGGAGATGACCAAGAACCAGGTCAGCCT GACCTGCCTGGTCAAAGGCTTCTATCCCAGCGACATCGCCGTGGAGTGGGAGA GCAATGGGCAGCCGGAGAACAACTACAAGACCACGCCTCCCGTGCTGGACTCC

[0715]

SEQ ID	抗体	描述	序列
			GACGGCTCCTTCTTCCTCTATAGCAAGCTCACCGTGGACAAGAGCAGGTGGCA GCAGGGGAACGTCTTCTCATGCTCCGTGATGCATGAGGCTCTGCACAACCACT ACACGCAGAAGAGCCTCTCCCTGTCCCCGGGTTGA
226	3G4	IgG1.1f HC (无 C 末端 K)	CAGGTGCAGCTGGTGGAGTCTGGGGGAGGCTTGGTCAAGCCTGGAGGGTCCCT GAGACTCTCCTGTGCAGCCTCTGGATTCACCTTCAGTGACTACTACATGAGCTG GATCCGCCAGGCTCCAGGGAAGGGGCTGGAGTGGGTTTCATTCATTAGTACTA GTGGTAGTATCATATACTACGCAGACTCTGTGAAGGGCCGATTCACCATCTCC AGGGACAACGCCAAGAACTCACTGTATCTGCAAATGAACAGCCTGAGAGCCG AGGACACGGCTGTGTATTACTGTGCGAGAGAAGGGTATAGCAGCAGCTGGTCC TACTACTACGGTATGGACGTCTGGGGCCAAGGGACCACGGTCACCGTCTCCTC AGCTAGCACCAAGGGCCCATCGGTCTTCCCCCTGGCACCCTCCTCCAAGAGCA CCTCTGGGGGCACAGCGGCCCTGGGCTGCCTGGTCAAGGACTACTTCCCCGAA CCGGTGACGGTGTCGTGGAACTCAGGCGCCCTGACCAGCGGCGTGCACACCTT CCCGGCTGTCCTACAGTCCTCAGGACTCTACTCCCTCAGCAGCGTGGTGACCGT GCCCTCCAGCAGCTTGGGCACCCAGACCTACATCTGCAACGTGAATCACAAGC CCAGCAACACCAAGGTGGACAAGAGAGTTGAGCCCAAATCTTGTGACAAAAC TCACACATGCCCACCGTGCCCAGCACCTGAAGCCGAAGGGGCCCCGTCAGTCT TCCTCTTCCCCCCAAAACCCAAGGACACCCTCATGATCTCCCGGACCCCTGAGG TCACATGCGTGGTGGTGGACGTGAGCCACGAAGACCCTGAGGTCAAGTTCAAC TGGTACGTGGACGGCGTGGAGGTGCATAATGCCAAGACAAAGCCGCGGGAGG AGCAGTACAACAGCACGTACCGTGTGGTCAGCGTCCTCACCGTCCTGCACCAG GACTGGCTGAATGGCAAGGAGTACAAGTGCAAGGTCTCCAACAAAGCCCTCCC AAGCAGCATCGAGAAAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAACCA CAGGTGTACACCCTGCCCCCATCCCGGGAGGAGATGACCAAGAACCAGGTCAG CCTGACCTGCCTGGTCAAAGGCTTCTATCCCAGCGACATCGCCGTGGAGTGGG AGAGCAATGGGCAGCCGGAGAACAACTACAAGACCACGCCTCCCGTGCTGGA CTCCGACGGCTCCTTCTTCCTCTATAGCAAGCTCACCGTGGACAAGAGCAGGT GGCAGCAGGGGAACGTCTTCTCATGCTCCGTGATGCATGAGGCTCTGCACAAC CACTACACGCAGAAGAGCCTCTCCCTGTCCCCGGGTTGA
227	17C8	IgG1.1f HC (无 C 末端 K)	CAGGTGCAGCTGGTGGAGTCTGGGGGAGGCTTGGTCAAGCCTGGAGGGTCCCT GAGACTCTCCTGTGCAGCCTCTGGATTCACCTTCAGTGACTACTACATGAGCTG GATCCGCCAGGCTCCAGGGAAGGGGCTGGAGTGGGTTTCATTCATTAGTAGTA GTGGTAGTATCATATACTACGCAGACTCTGTGAAGGGCCGATTCACCATCTCC AGGGACAACGCCAAGAACTCACTGTATCTGCAAATGAACAGCCTGAGAGCCG AGGACACGGCTGTGTATTACTGTGCGAGAGATGGGTATAGCAGTGGCTGGGAG TACTACGGTATGGACGTCTGGGGCCAAGGGACCACGGTCACCGTCTCCTCAGC TAGCACCAAGGGCCCATCGGTCTTCCCCCTGGCACCCTCCTCCAAGAGCACCTC TGGGGGCACAGCGGCCCTGGGCTGCCTGGTCAAGGACTACTTCCCCGAACCGG TGACGGTGTCGTGGAACTCAGGCGCCCTGACCAGCGGCGTGCACACCTTCCCG GCTGTCCTACAGTCCTCAGGACTCTACTCCCTCAGCAGCGTGGTGACCGTGCCC TCCAGCAGCTTGGGCACCCAGACCTACATCTGCAACGTGAATCACAAGCCCAG CAACACCAAGGTGGACAAGAGAGTTGAGCCCAAATCTTGTGACAAAACTCAC ACATGCCCACCGTGCCCAGCACCTGAAGCCGAAGGGGCCCCGTCAGTCTTCCT CTTCCCCCCAAAACCCAAGGACACCCTCATGATCTCCCGGACCCCTGAGGTCA CATGCGTGGTGGTGGACGTGAGCCACGAAGACCCTGAGGTCAAGTTCAACTGG TACGTGGACGGCGTGGAGGTGCATAATGCCAAGACAAAGCCGCGGGAGGAGC AGTACAACAGCACGTACCGTGTGGTCAGCGTCCTCACCGTCCTGCACCAGGAC TGGCTGAATGGCAAGGAGTACAAGTGCAAGGTCTCCAACAAAGCCCTCCCAAG CAGCATCGAGAAAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAACCACAG GTGTACACCCTGCCCCCATCCCGGGAGGAGATGACCAAGAACCAGGTCAGCCT GACCTGCCTGGTCAAAGGCTTCTATCCCAGCGACATCGCCGTGGAGTGGGAGA GCAATGGGCAGCCGGAGAACAACTACAAGACCACGCCTCCCGTGCTGGACTCC GACGGCTCCTTCTTCCTCTATAGCAAGCTCACCGTGGACAAGAGCAGGTGGCA GCAGGGGAACGTCTTCTCATGCTCCGTGATGCATGAGGCTCTGCACAACCACT ACACGCAGAAGAGCCTCTCCCTGTCCCCGGGTTGA
228	13A3	IgG1.3f HC	CAGCTGCAGCTGCAGGAGTCGGGCCCAGGACTGGTGAAGCCTTCGGAGACCCT GTCCCTCACCTGCACTGTCTCTGGTGGCTCCATCAGCAGTAGAAGTTACTACTG GGGCTGGATCCGCCAGCCCCCAGGGAAGGGGCTGGAGTGGATTGGGAGTATCT ATTATAGTGGGTTCACCTACTACAACCCGTCCCTCAAGAGTCGAGTCACCATAT CCGTTGACACGTCCAAGAACCAGTTCTCCCTGAAGCTGAGCTCTGTGACCGCC GCAGACACGGCTGTGTATTATTGTGCGACAGGGGGGCCCTACGGTGACTACGC CCACTGGTTCGACCCCTGGGGCCAGGGAACCCTGGTCACCGTCTCCTCAGCTA GCACCAAGGGCCCATCGGTCTTCCCCCTGGCACCCTCCTCCAAGAGCACCTCTG GGGGCACAGCGGCCCTGGGCTGCCTGGTCAAGGACTACTTCCCCGAACCGGTG

[0716]

SEQ ID	抗体	描述	序列
			ACGGTGTCGTGGAACTCAGGCGCCCTGACCAGCGGCGTGCACACCTTCCCGGC TGTCCTACAGTCCTCAGGACTCTACTCCCTCAGCAGCGTGGTGACCGTGCCCTC CAGCAGCTTGGGCACCCAGACCTACATCTGCAACGTGAATCACAAGCCCAGCA ACACCAAGGTGGACAAGAGAGTTGAGCCCAAATCTTGTGACAAAACTCACAC ATGCCCACCGTGCCCAGCACCTGAAGCCGAAGGGGCCCCGTCAGTCTTCCTCT TCCCCCCAAAACCCAAGGACACCCTCATGATCTCCCGGACCCCTGAGGTCACA TGCGTGGTGGTGGACGTGAGCCACGAAGACCCTGAGGTCAAGTTCAACTGGTA CGTGGACGGCGTGGAGGTGCATAATGCCAAGACAAAGCCGCGGGAGGAGCAG TACAACAGCACGTACCGTGTGGTCAGCGTCCTCACCGTCCTGCACCAGGACTG GCTGAATGGCAAGGAGTACAAGTGCAAGGTCTCCAACAAAGCCCTCCCAGCCC CCATCGAGAAAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAACCACAGGT GTACACCCTGCCCCCATCCCGGGAGGAGATGACCAAGAACCAGGTCAGCCTGA CCTGCCTGGTCAAAGGCTTCTATCCCAGCGACATCGCCGTGGAGTGGGAGAGC AATGGGCAGCCGGAGAACAACTACAAGACCACGCCTCCCGTGCTGGACTCCGA CGGCTCCTTCTTCCTCTATAGCAAGCTCACCGTGGACAAGAGCAGGTGGCAGC AGGGGAACGTCTTCTCATGCTCCGTGATGCATGAGGCTCTGCACAACCACTAC ACGCAGAAGAGCCTCTCCCTGTCCCCGGGTAAATGA
229	8B9	IgG1.3f HC	AGGTGCAGCTGCAGGAGTCGGGCCCAGGACTGGTGAAGCCTTCGGAGACCCTG TCCCTCACCTGCACTGTCTCTGGTGGCTCCATCAGTCGTCACTACTGGAACTGG ATCCGGCAGCCCCCAGGGAAGGGACTGGAGTGGATTGGGTATATCCATTACAG TGGAAGCACCAACTACAATTCCTCCCTCAAGAGTCGAGTCACCATATCAGTAG ACACGTCCAAGAACCAGTTCTCCCTGAAGCTGAGCTCTGTGACCGCTGCGGAC ACGGCCGTGTATTACTGTGCGAGAGATACTGGGTACTACGGTATGGACATCTG GGGCCAAGGGACCACGGTCACCGTCTCCTCAGCTAGCACCAAGGGCCCATCGG TCTTCCCCCTGGCACCCTCCTCCAAGAGCACCTCTGGGGGCACAGCGGCCCTG GGCTGCCTGGTCAAGGACTACTTCCCCGAACCGGTGACGGTGTCGTGGAACTC AGGCGCCCTGACCAGCGGCGTGCACACCTTCCCGGCTGTCCTACAGTCCTCAG GACTCTACTCCCTCAGCAGCGTGGTGACCGTGCCCTCCAGCAGCTTGGGCACC CAGACCTACATCTGCAACGTGAATCACAAGCCCAGCAACACCAAGGTGGACA AGAGAGTTGAGCCCAAATCTTGTGACAAAACTCACACATGCCCACCGTGCCCA GCACCTGAAGCCGAAGGGGCCCCGTCAGTCTTCCTCTTCCCCCCAAAACCCAA GGACACCCTCATGATCTCCCGGACCCCTGAGGTCACATGCGTGGTGGTGGACG TGAGCCACGAAGACCCTGAGGTCAAGTTCAACTGGTACGTGGACGGCGTGGAG GTGCATAATGCCAAGACAAAGCCGCGGGAGGAGCAGTACAACAGCACGTACC GTGTGGTCAGCGTCCTCACCGTCCTGCACCAGGACTGGCTGAATGGCAAGGAG TACAAGTGCAAGGTCTCCAACAAAGCCCTCCCAGCCCCCATCGAGAAAACCAT CTCCAAAGCCAAAGGGCAGCCCCGAGAACCACAGGTGTACACCCTGCCCCCAT CCCGGGAGGAGATGACCAAGAACCAGGTCAGCCTGACCTGCCTGGTCAAAGG CTTCTATCCCAGCGACATCGCCGTGGAGTGGGAGAGCAATGGGCAGCCGGAGA ACAACTACAAGACCACGCCTCCCGTGCTGGACTCCGACGGCTCCTTCTTCCTCT ATAGCAAGCTCACCGTGGACAAGAGCAGGTGGCAGCAGGGGAACGTCTTCTC ATGCTCCGTGATGCATGAGGCTCTGCACAACCACTACACGCAGAAGAGCCTCT CCCTGTCCCCGGGTAAATGA
230	8C4	IgG1.3f HC	CAGGTGCAGCTGCAGGAGTCGGGCCCAGGACTGGTGAAGCCTTCGGAGACCCT GTCCCTCACCTGCACTGTCTCTGGTGGCTCCATCAGTCGTTACTACTGGAGCTG GATCCGGCAGCCCCCAGGGAAGGGACTGGAGTGGATTGGGTATATCCATTACA CTGGGAGCACCAACTACAACCCCTCCCTCAAGAGTCGAGTCACCATATCAGTA GACACGTCCAAGAACCAGTTCTCCCTGAAGCTGAGCTCTGTGACCGCAGCGGA CACGGCCGTGTATTACTGTGCGACAGATACGGGCTACTACGGTATGGACGTCT GGGGCCAAGGGACCACGGTCACCGTCTCCTCAGCTAGCACCAAGGGCCCATCG GTCTTCCCCCTGGCACCCTCCTCCAAGAGCACCTCTGGGGGCACAGCGGCCCT GGGCTGCCTGGTCAAGGACTACTTCCCCGAACCGGTGACGGTGTCGTGGAACT CAGGCGCCCTGACCAGCGGCGTGCACACCTTCCCGGCTGTCCTACAGTCCTCA GGACTCTACTCCCTCAGCAGCGTGGTGACCGTGCCCTCCAGCAGCTTGGGCAC CCAGACCTACATCTGCAACGTGAATCACAAGCCCAGCAACACCAAGGTGGACA AGAGAGTTGAGCCCAAATCTTGTGACAAAACTCACACATGCCCACCGTGCCCA GCACCTGAAGCCGAAGGGGCCCCGTCAGTCTTCCTCTTCCCCCCAAAACCCAA GGACACCCTCATGATCTCCCGGACCCCTGAGGTCACATGCGTGGTGGTGGACG TGAGCCACGAAGACCCTGAGGTCAAGTTCAACTGGTACGTGGACGGCGTGGAG GTGCATAATGCCAAGACAAAGCCGCGGGAGGAGCAGTACAACAGCACGTACC GTGTGGTCAGCGTCCTCACCGTCCTGCACCAGGACTGGCTGAATGGCAAGGAG TACAAGTGCAAGGTCTCCAACAAAGCCCTCCCAGCCCCCATCGAGAAAACCAT CTCCAAAGCCAAAGGGCAGCCCCGAGAACCACAGGTGTACACCCTGCCCCCAT CCCGGGAGGAGATGACCAAGAACCAGGTCAGCCTGACCTGCCTGGTCAAAGG CTTCTATCCCAGCGACATCGCCGTGGAGTGGGAGAGCAATGGGCAGCCGGAGA

[0717]

SEQ ID	抗体	描述	序列
			ACAACTACAAGACCACGCCTCCCGTGCTGGACTCCGACGGCTCCTTCTTCCTCT ATAGCAAGCTCACCGTGGACAAGAGCAGGTGGCAGCAGGGGAACGTCTTCTC ATGCTCCGTGATGCATGAGGCTCTGCACAACCACTACACGCAGAAGAGCCTCT CCCTGTCCCCGGGTAAATGA
231	17C3	IgG1.3f HC	CAGGTGCAGTTGGTGCAGTCTGGGGCTGAGGTGAAGAAGCCTGGGGCCTCAGT GAAGGTCTCCTGCAAGGCATCTGGATACACTTTCACCAGCTACTATATGCACTG GGTGCGACAGGCCCCTGGACAAGGGCTTGAGTGGATGGGAATAATCAACCCTA GGGGTGATAGCATAATCTACGCACAGAAGTTCCAGGGCAGAGTCACCATGACC AGGGACACGTCCACGAGCACAGTCTACATGGAGCTGAGCAGCCTGAGATCTGA GGACACGGCCGTGTATTACTGTGCGAGAGATTTCTATGGTTCGGGAAACTACT ACTACGGTATGGACGTCTGGGGCCAAGGGACCACGGTCACCGTCTCCTCAGCT AGCACCAAGGGCCCATCGGTCTTCCCCCTGGCACCCTCCTCCAAGAGCACCTCT GGGGGCACAGCGGCCCTGGGCTGCCTGGTCAAGGACTACTTCCCCGAACCGGT GACGGTGTCGTGGAACTCAGGCGCCCTGACCAGCGGCGTGCACACCTTCCCGG CTGTCCTACAGTCCTCAGGACTCTACTCCCTCAGCAGCGTGGTGACCGTGCCCT CCAGCAGCTTGGGCACCCAGACCTACATCTGCAACGTGAATCACAAGCCCAGC AACACCAAGGTGGACAAGAGAGTTGAGCCCAAATCTTGTGACAAAACTCACA CATGCCCACCGTGCCCAGCACCTGAAGCCGAAGGGGCCCCGTCAGTCTTCCTC TTCCCCCCAAAACCCAAGGACACCCTCATGATCTCCCGGACCCCTGAGGTCAC ATGCGTGGTGGTGGACGTGAGCCACGAAGACCCTGAGGTCAAGTTCAACTGGT ACGTGGACGGCGTGGAGGTGCATAATGCCAAGACAAAGCCGCGGGAGGAGCA GTACAACAGCACGTACCGTGTGGTCAGCGTCCTCACCGTCCTGCACCAGGACT GGCTGAATGGCAAGGAGTACAAGTGCAAGGTCTCCAACAAAGCCCTCCCAGCC CCCATCGAGAAAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAACCACAGG TGTACACCCTGCCCCCATCCCGGGAGGAGATGACCAAGAACCAGGTCAGCCTG ACCTGCCTGGTCAAAGGCTTCTATCCCAGCGACATCGCCGTGGAGTGGGAGAG CAATGGGCAGCCGGAGAACAACTACAAGACCACGCCTCCCGTGCTGGACTCCG ACGGCTCCTTCTTCCTCTATAGCAAGCTCACCGTGGACAAGAGCAGGTGGCAG CAGGGGAACGTCTTCTCATGCTCCGTGATGCATGAGGCTCTGCACAACCACTA CACGCAGAAGAGCCTCTCCCTGTCCCCGGGTAAATGA
232	9F6	IgG1.3f HC	CAGGTGCAGCTGGTGGAGTCTGGGGGAGGCTTGGTCAAGCCTGGAGGGTCCCT GAGACTCTCCTGTGCAGCCTCTGGATTCACCTTCAGTGACTACTACATGAGCTG GATCCGCCAGGCTCCAGGGAAGGGGCTGGAGTGGGTTTCATTCATTAGTGGTG GTGGTAGTACCATATACTACGCAGACTCTGTGAAGGGCCGATTCACCATCTCC AGGGACAACGCCAAGAACTCGCTGTTTCTGCAAATGAACAGCCTGAGAGTCGA GGACACGGCTGTGTATTACTGTGCGAGAGATGGCTATAGCAGTGGCTGGTACT ACTACGGTATGGACGTCTGGGGCCAAGGGACCGCGGTCACCGTCTCCTCAGCT AGCACCAAGGGCCCATCGGTCTTCCCCCTGGCACCCTCCTCCAAGAGCACCTCT GGGGGCACAGCGGCCCTGGGCTGCCTGGTCAAGGACTACTTCCCCGAACCGGT GACGGTGTCGTGGAACTCAGGCGCCCTGACCAGCGGCGTGCACACCTTCCCGG CTGTCCTACAGTCCTCAGGACTCTACTCCCTCAGCAGCGTGGTGACCGTGCCCT CCAGCAGCTTGGGCACCCAGACCTACATCTGCAACGTGAATCACAAGCCCAGC AACACCAAGGTGGACAAGAGAGTTGAGCCCAAATCTTGTGACAAAACTCACA CATGCCCACCGTGCCCAGCACCTGAAGCCGAAGGGGCCCCGTCAGTCTTCCTC TTCCCCCCAAAACCCAAGGACACCCTCATGATCTCCCGGACCCCTGAGGTCAC ATGCGTGGTGGTGGACGTGAGCCACGAAGACCCTGAGGTCAAGTTCAACTGGT ACGTGGACGGCGTGGAGGTGCATAATGCCAAGACAAAGCCGCGGGAGGAGCA GTACAACAGCACGTACCGTGTGGTCAGCGTCCTCACCGTCCTGCACCAGGACT GGCTGAATGGCAAGGAGTACAAGTGCAAGGTCTCCAACAAAGCCCTCCCAGCC CCCATCGAGAAAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAACCACAGG TGTACACCCTGCCCCCATCCCGGGAGGAGATGACCAAGAACCAGGTCAGCCTG ACCTGCCTGGTCAAAGGCTTCTATCCCAGCGACATCGCCGTGGAGTGGGAGAG CAATGGGCAGCCGGAGAACAACTACAAGACCACGCCTCCCGTGCTGGACTCCG ACGGCTCCTTCTTCCTCTATAGCAAGCTCACCGTGGACAAGAGCAGGTGGCAG CAGGGGAACGTCTTCTCATGCTCCGTGATGCATGAGGCTCTGCACAACCACTA CACGCAGAAGAGCCTCTCCCTGTCCCCGGGTAAATGA
233	3G4	IgG1.3f HC	CAGGTGCAGCTGGTGGAGTCTGGGGGAGGCTTGGTCAAGCCTGGAGGGTCCCT GAGACTCTCCTGTGCAGCCTCTGGATTCACCTTCAGTGACTACTACATGAGCTG GATCCGCCAGGCTCCAGGGAAGGGGCTGGAGTGGGTTTCATTCATTAGTACTA GTGGTAGTATCATATACTACGCAGACTCTGTGAAGGGCCGATTCACCATCTCC AGGGACAACGCCAAGAACTCACTGTATCTGCAAATGAACAGCCTGAGAGCCG AGGACACGGCTGTGTATTACTGTGCGAGAGAAGGGTATAGCAGCAGCTGGTCC TACTACTACGGTATGGACGTCTGGGGCCAAGGGACCACGGTCACCGTCTCCTC AGCTAGCACCAAGGGCCCATCGGTCTTCCCCCTGGCACCCTCCTCCAAGAGCA

[0718]

SEQ ID	抗体	描述	序列
			CCTCTGGGGGCACAGCGGCCCTGGGCTGCCTGGTCAAGGACTACTTCCCCGAA CCGGTGACGGTGTCGTGGAACTCAGGCGCCCTGACCAGCGGCGTGCACACCTT CCCGGCTGTCCTACAGTCCTCAGGACTCTACTCCCTCAGCAGCGTGGTGACCGT GCCCTCCAGCAGCTTGGGCACCCAGACCTACATCTGCAACGTGAATCACAAGC CCAGCAACACCAAGGTGGACAAGAGAGTTGAGCCCAAATCTTGTGACAAAAC TCACACATGCCCACCGTGCCCAGCACCTGAAGCCGAAGGGGCCCCGTCAGTCT TCCTCTTCCCCCCAAAACCCAAGGACACCCTCATGATCTCCCGGACCCCTGAGG TCACATGCGTGGTGGTGGACGTGAGCCACGAAGACCCTGAGGTCAAGTTCAAC TGGTACGTGGACGGCGTGGAGGTGCATAATGCCAAGACAAAGCCGCGGGAGG AGCAGTACAACAGCACGTACCGTGTGGTCAGCGTCCTCACCGTCCTGCACCAG GACTGGCTGAATGGCAAGGAGTACAAGTGCAAGGTCTCCAACAAAGCCCTCCC AGCCCCCATCGAGAAAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAACCA CAGGTGTACACCCTGCCCCCATCCCGGGAGGAGATGACCAAGAACCAGGTCAG CCTGACCTGCCTGGTCAAAGGCTTCTATCCCAGCGACATCGCCGTGGAGTGGG AGAGCAATGGGCAGCCGGAGAACAACTACAAGACCACGCCTCCCGTGCTGGA CTCCGACGGCTCCTTCTTCCTCTATAGCAAGCTCACCGTGGACAAGAGCAGGT GGCAGCAGGGGAACGTCTTCTCATGCTCCGTGATGCATGAGGCTCTGCACAAC CACTACACGCAGAAGAGCCTCTCCCTGTCCCCGGGTAAATGA
234	17C8	IgG1.3f HC	CAGGTGCAGCTGGTGGAGTCTGGGGGAGGCTTGGTCAAGCCTGGAGGGTCCCT GAGACTCTCCTGTGCAGCCTCTGGATTCACCTTCAGTGACTACTACATGAGCTG GATCCGCCAGGCTCCAGGGAAGGGGCTGGAGTGGGTTTCATTCATTAGTAGTA GTGGTAGTATCATATACTACGCAGACTCTGTGAAGGGCCGATTCACCATCTCC AGGGACAACGCCAAGAACTCACTGTATCTGCAAATGAACAGCCTGAGAGCCG AGGACACGGCTGTGTATTACTGTGCGAGAGATGGGTATAGCAGTGGCTGGGAG TACTACGGTATGGACGTCTGGGGCCAAGGGACCACGGTCACCGTCTCCTCAGC TAGCACCAAGGGCCCATCGGTCTTCCCCCTGGCACCCTCCTCCAAGAGCACCTC TGGGGGCACAGCGGCCCTGGGCTGCCTGGTCAAGGACTACTTCCCCGAACCGG TGACGGTGTCGTGGAACTCAGGCGCCCTGACCAGCGGCGTGCACACCTTCCCG GCTGTCCTACAGTCCTCAGGACTCTACTCCCTCAGCAGCGTGGTGACCGTGCCC TCCAGCAGCTTGGGCACCCAGACCTACATCTGCAACGTGAATCACAAGCCCAG CAACACCAAGGTGGACAAGAGAGTTGAGCCCAAATCTTGTGACAAAACTCAC ACATGCCCACCGTGCCCAGCACCTGAAGCCGAAGGGGCCCCGTCAGTCTTCCT CTTCCCCCCAAAACCCAAGGACACCCTCATGATCTCCCGGACCCCTGAGGTCA CATGCGTGGTGGTGGACGTGAGCCACGAAGACCCTGAGGTCAAGTTCAACTGG TACGTGGACGGCGTGGAGGTGCATAATGCCAAGACAAAGCCGCGGGAGGAGC AGTACAACAGCACGTACCGTGTGGTCAGCGTCCTCACCGTCCTGCACCAGGAC TGGCTGAATGGCAAGGAGTACAAGTGCAAGGTCTCCAACAAAGCCCTCCCAGC CCCCATCGAGAAAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAACCACAG GTGTACACCCTGCCCCCATCCCGGGAGGAGATGACCAAGAACCAGGTCAGCCT GACCTGCCTGGTCAAAGGCTTCTATCCCAGCGACATCGCCGTGGAGTGGGAGA GCAATGGGCAGCCGGAGAACAACTACAAGACCACGCCTCCCGTGCTGGACTCC GACGGCTCCTTCTTCCTCTATAGCAAGCTCACCGTGGACAAGAGCAGGTGGCA GCAGGGGAACGTCTTCTCATGCTCCGTGATGCATGAGGCTCTGCACAACCACT ACACGCAGAAGAGCCTCTCCCTGTCCCCGGGTAAATGA
235	13A3	IgG1.3f HC (无 C 末端 K)	CAGCTGCAGCTGCAGGAGTCGGGCCCAGGACTGGTGAAGCCTTCGGAGACCCT GTCCCTCACCTGCACTGTCTCTGGTGGCTCCATCAGCAGTAGAAGTTACTACTG GGGCTGGATCCGCCAGCCCCCAGGGAAGGGGCTGGAGTGGATTGGGAGTATCT ATTATAGTGGGTTCACCTACTACAACCCGTCCCTCAAGAGTCGAGTCACCATAT CCGTTGACACGTCCAAGAACCAGTTCTCCCTGAAGCTGAGCTCTGTGACCGCC GCAGACACGGCTGTGTATTATTGTGCGACAGGGGGGCCCTACGGTGACTACGC CCACTGGTTCGACCCCTGGGGCCAGGGAACCCTGGTCACCGTCTCCTCAGCTA GCACCAAGGGCCCATCGGTCTTCCCCCTGGCACCCTCCTCCAAGAGCACCTCTG GGGGCACAGCGGCCCTGGGCTGCCTGGTCAAGGACTACTTCCCCGAACCGGTG ACGGTGTCGTGGAACTCAGGCGCCCTGACCAGCGGCGTGCACACCTTCCCGGC TGTCCTACAGTCCTCAGGACTCTACTCCCTCAGCAGCGTGGTGACCGTGCCCTC CAGCAGCTTGGGCACCCAGACCTACATCTGCAACGTGAATCACAAGCCCAGCA ACACCAAGGTGGACAAGAGAGTTGAGCCCAAATCTTGTGACAAAACTCACAC ATGCCCACCGTGCCCAGCACCTGAAGCCGAAGGGGCCCCGTCAGTCTTCCTCT TCCCCCCAAAACCCAAGGACACCCTCATGATCTCCCGGACCCCTGAGGTCACA TGCGTGGTGGTGGACGTGAGCCACGAAGACCCTGAGGTCAAGTTCAACTGGTA CGTGGACGGCGTGGAGGTGCATAATGCCAAGACAAAGCCGCGGGAGGAGCAG TACAACAGCACGTACCGTGTGGTCAGCGTCCTCACCGTCCTGCACCAGGACTG GCTGAATGGCAAGGAGTACAAGTGCAAGGTCTCCAACAAAGCCCTCCCAGCCC CCATCGAGAAAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAACCACAGGT GTACACCCTGCCCCCATCCCGGGAGGAGATGACCAAGAACCAGGTCAGCCTGA

[0719]

SEQ ID	抗体	描述	序列
			CCTGCCTGGTCAAAGGCTTCTATCCCAGCGACATCGCCGTGGAGTGGGAGAGC AATGGGCAGCCGGAGAACAACTACAAGACCACGCCTCCCGTGCTGGACTCCGA CGGCTCCTTCTTCCTCTATAGCAAGCTCACCGTGGACAAGAGCAGGTGGCAGC AGGGGAACGTCTTCTCATGCTCCGTGATGCATGAGGCTCTGCACAACCACTAC ACGCAGAAGAGCCTCTCCCTGTCCCCGGGTTGA
236	8B9	IgG1.3f HC (无 C 末端 K)	AGGTGCAGCTGCAGGAGTCGGGCCCAGGACTGGTGAAGCCTTCGGAGACCCTG TCCCTCACCTGCACTGTCTCTGGTGGCTCCATCAGTCGTCACTACTGGAACTGG ATCCGGCAGCCCCCAGGGAAGGGACTGGAGTGGATTGGGTATATCCATTACAG TGGAAGCACCAACTACAATTCCTCCCTCAAGAGTCGAGTCACCATATCAGTAG ACACGTCCAAGAACCAGTTCTCCCTGAAGCTGAGCTCTGTGACCGCTGCGGAC ACGGCCGTGTATTACTGTGCGAGAGATACTGGGTACTACGGTATGGACATCTG GGGCCAAGGGACCACGGTCACCGTCTCCTCAGCTAGCACCAAGGGCCCATCGG TCTTCCCCCTGGCACCCTCCTCCAAGAGCACCTCTGGGGGCACAGCGGCCCTG GGCTGCCTGGTCAAGGACTACTTCCCCGAACCGGTGACGGTGTCGTGGAACTC AGGCGCCCTGACCAGCGGCGTGCACACCTTCCCGGCTGTCCTACAGTCCTCAG GACTCTACTCCCTCAGCAGCGTGGTGACCGTGCCCTCCAGCAGCTTGGGCACC CAGACCTACATCTGCAACGTGAATCACAAGCCCAGCAACACCAAGGTGGACA AGAGAGTTGAGCCCAAATCTTGTGACAAAACTCACACATGCCCACCGTGCCCA GCACCTGAAGCCGAAGGGGCCCCGTCAGTCTTCCTCTTCCCCCCAAAACCCAA GGACACCCTCATGATCTCCCGGACCCCTGAGGTCACATGCGTGGTGGTGGACG TGAGCCACGAAGACCCTGAGGTCAAGTTCAACTGGTACGTGGACGGCGTGGAG GTGCATAATGCCAAGACAAAGCCGCGGGAGGAGCAGTACAACAGCACGTACC GTGTGGTCAGCGTCCTCACCGTCCTGCACCAGGACTGGCTGAATGGCAAGGAG TACAAGTGCAAGGTCTCCAACAAAGCCCTCCCAGCCCCCATCGAGAAAACCAT CTCCAAAGCCAAAGGGCAGCCCCGAGAACCACAGGTGTACACCCTGCCCCCAT CCCGGGAGGAGATGACCAAGAACCAGGTCAGCCTGACCTGCCTGGTCAAAGG CTTCTATCCCAGCGACATCGCCGTGGAGTGGGAGAGCAATGGGCAGCCGGAGA ACAACTACAAGACCACGCCTCCCGTGCTGGACTCCGACGGCTCCTTCTTCCTCT ATAGCAAGCTCACCGTGGACAAGAGCAGGTGGCAGCAGGGGAACGTCTTCTC ATGCTCCGTGATGCATGAGGCTCTGCACAACCACTACACGCAGAAGAGCCTCT CCCTGTCCCCGGGTTGA
237	8C4	IgG1.3f HC (无 C 末端 K)	CAGGTGCAGCTGCAGGAGTCGGGCCCAGGACTGGTGAAGCCTTCGGAGACCCT GTCCCTCACCTGCACTGTCTCTGGTGGCTCCATCAGTCGTTACTACTGGAGCTG GATCCGGCAGCCCCCAGGGAAGGGACTGGAGTGGATTGGGTATATCCATTACA CTGGGAGCACCAACTACAACCCCTCCCTCAAGAGTCGAGTCACCATATCAGTA GACACGTCCAAGAACCAGTTCTCCCTGAAGCTGAGCTCTGTGACCGCAGCGGA CACGGCCGTGTATTACTGTGCGACAGATACGGGCTACTACGGTATGGACGTCT GGGGCCAAGGGACCACGGTCACCGTCTCCTCAGCTAGCACCAAGGGCCCATCG GTCTTCCCCCTGGCACCCTCCTCCAAGAGCACCTCTGGGGGCACAGCGGCCCT GGGCTGCCTGGTCAAGGACTACTTCCCCGAACCGGTGACGGTGTCGTGGAACT CAGGCGCCCTGACCAGCGGCGTGCACACCTTCCCGGCTGTCCTACAGTCCTCA GGACTCTACTCCCTCAGCAGCGTGGTGACCGTGCCCTCCAGCAGCTTGGGCAC CCAGACCTACATCTGCAACGTGAATCACAAGCCCAGCAACACCAAGGTGGACA AGAGAGTTGAGCCCAAATCTTGTGACAAAACTCACACATGCCCACCGTGCCCA GCACCTGAAGCCGAAGGGGCCCCGTCAGTCTTCCTCTTCCCCCCAAAACCCAA GGACACCCTCATGATCTCCCGGACCCCTGAGGTCACATGCGTGGTGGTGGACG TGAGCCACGAAGACCCTGAGGTCAAGTTCAACTGGTACGTGGACGGCGTGGAG GTGCATAATGCCAAGACAAAGCCGCGGGAGGAGCAGTACAACAGCACGTACC GTGTGGTCAGCGTCCTCACCGTCCTGCACCAGGACTGGCTGAATGGCAAGGAG TACAAGTGCAAGGTCTCCAACAAAGCCCTCCCAGCCCCCATCGAGAAAACCAT CTCCAAAGCCAAAGGGCAGCCCCGAGAACCACAGGTGTACACCCTGCCCCCAT CCCGGGAGGAGATGACCAAGAACCAGGTCAGCCTGACCTGCCTGGTCAAAGG CTTCTATCCCAGCGACATCGCCGTGGAGTGGGAGAGCAATGGGCAGCCGGAGA ACAACTACAAGACCACGCCTCCCGTGCTGGACTCCGACGGCTCCTTCTTCCTCT ATAGCAAGCTCACCGTGGACAAGAGCAGGTGGCAGCAGGGGAACGTCTTCTC ATGCTCCGTGATGCATGAGGCTCTGCACAACCACTACACGCAGAAGAGCCTCT CCCTGTCCCCGGGTTGA
238	17C3	IgG1.3f HC (无 C 末端 K)	CAGGTGCAGTTGGTGCAGTCTGGGGCTGAGGTGAAGAAGCCTGGGGCCTCAGT GAAGGTCTCCTGCAAGGCATCTGGATACACTTTCACCAGCTACTATATGCACTG GGTGCGACAGGCCCCTGGACAAGGGCTTGAGTGGATGGGAATAATCAACCCTA GGGGTGATAGCATAATCTACGCACAGAAGTTCCAGGGCAGAGTCACCATGACC AGGGACACGTCCACGAGCACAGTCTACATGGAGCTGAGCAGCCTGAGATCTGA GGACACGGCCGTGTATTACTGTGCGAGAGATTTCTATGGTTCGGGAAACTACT ACTACGGTATGGACGTCTGGGGCCAAGGGACCACGGTCACCGTCTCCTCAGCT

[0720]

SEQ ID	抗体	描述	序列
			AGCACCAAGGGCCCATCGGTCTTCCCCCTGGCACCCTCCTCCAAGAGCACCTCT GGGGGCACAGCGGCCCTGGGCTGCCTGGTCAAGGACTACTTCCCCGAACCGGT GACGGTGTCGTGGAACTCAGGCGCCCTGACCAGCGGCGTGCACACCTTCCCGG CTGTCCTACAGTCCTCAGGACTCTACTCCCTCAGCAGCGTGGTGACCGTGCCCT CCAGCAGCTTGGGCACCCAGACCTACATCTGCAACGTGAATCACAAGCCCAGC AACACCAAGGTGGACAAGAGAGTTGAGCCCAAATCTTGTGACAAAACTCACA CATGCCCACCGTGCCCAGCACCTGAAGCCGAAGGGGCCCCGTCAGTCTTCCTC TTCCCCCCAAAACCCAAGGACACCCTCATGATCTCCCGGACCCCTGAGGTCAC ATGCGTGGTGGTGGACGTGAGCCACGAAGACCCTGAGGTCAAGTTCAACTGGT ACGTGGACGGCGTGGAGGTGCATAATGCCAAGACAAAGCCGCGGGAGGAGCA GTACAACAGCACGTACCGTGTGGTCAGCGTCCTCACCGTCCTGCACCAGGACT GGCTGAATGGCAAGGAGTACAAGTGCAAGGTCTCCAACAAAGCCCTCCCAGCC CCCATCGAGAAAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAACCACAGG TGTACACCCTGCCCCCATCCCGGGAGGAGATGACCAAGAACCAGGTCAGCCTG ACCTGCCTGGTCAAAGGCTTCTATCCCAGCGACATCGCCGTGGAGTGGGAGAG CAATGGGCAGCCGGAGAACAACTACAAGACCACGCCTCCCGTGCTGGACTCCG ACGGCTCCTTCTTCCTCTATAGCAAGCTCACCGTGGACAAGAGCAGGTGGCAG CAGGGGAACGTCTTCTCATGCTCCGTGATGCATGAGGCTCTGCACAACCACTA CACGCAGAAGAGCCTCTCCCTGTCCCCGGGTTGA
239	9F6	IgG1.3f HC (无 C 末端 K)	CAGGTGCAGCTGGTGGAGTCTGGGGGAGGCTTGGTCAAGCCTGGAGGGTCCCT GAGACTCTCCTGTGCAGCCTCTGGATTCACCTTCAGTGACTACTACATGAGCTG GATCCGCCAGGCTCCAGGGAAGGGGCTGGAGTGGGTTTCATTCATTAGTGGTG GTGGTAGTACCATATACTACGCAGACTCTGTGAAGGGCCGATTCACCATCTCC AGGGACAACGCCAAGAACTCGCTGTTTCTGCAAATGAACAGCCTGAGAGTCGA GGACACGGCTGTGTATTACTGTGCGAGAGATGGCTATAGCAGTGGCTGGTACT ACTACGGTATGGACGTCTGGGGCCAAGGGACCGCGGTCACCGTCTCCTCAGCT AGCACCAAGGGCCCATCGGTCTTCCCCCTGGCACCCTCCTCCAAGAGCACCTCT GGGGGCACAGCGGCCCTGGGCTGCCTGGTCAAGGACTACTTCCCCGAACCGGT GACGGTGTCGTGGAACTCAGGCGCCCTGACCAGCGGCGTGCACACCTTCCCGG CTGTCCTACAGTCCTCAGGACTCTACTCCCTCAGCAGCGTGGTGACCGTGCCCT CCAGCAGCTTGGGCACCCAGACCTACATCTGCAACGTGAATCACAAGCCCAGC AACACCAAGGTGGACAAGAGAGTTGAGCCCAAATCTTGTGACAAAACTCACA CATGCCCACCGTGCCCAGCACCTGAAGCCGAAGGGGCCCCGTCAGTCTTCCTC TTCCCCCCAAAACCCAAGGACACCCTCATGATCTCCCGGACCCCTGAGGTCAC ATGCGTGGTGGTGGACGTGAGCCACGAAGACCCTGAGGTCAAGTTCAACTGGT ACGTGGACGGCGTGGAGGTGCATAATGCCAAGACAAAGCCGCGGGAGGAGCA GTACAACAGCACGTACCGTGTGGTCAGCGTCCTCACCGTCCTGCACCAGGACT GGCTGAATGGCAAGGAGTACAAGTGCAAGGTCTCCAACAAAGCCCTCCCAGCC CCCATCGAGAAAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAACCACAGG TGTACACCCTGCCCCCATCCCGGGAGGAGATGACCAAGAACCAGGTCAGCCTG ACCTGCCTGGTCAAAGGCTTCTATCCCAGCGACATCGCCGTGGAGTGGGAGAG CAATGGGCAGCCGGAGAACAACTACAAGACCACGCCTCCCGTGCTGGACTCCG ACGGCTCCTTCTTCCTCTATAGCAAGCTCACCGTGGACAAGAGCAGGTGGCAG CAGGGGAACGTCTTCTCATGCTCCGTGATGCATGAGGCTCTGCACAACCACTA CACGCAGAAGAGCCTCTCCCTGTCCCCGGGTTGA
240	3G4	IgG1.3f HC (无 C 末端 K)	CAGGTGCAGCTGGTGGAGTCTGGGGGAGGCTTGGTCAAGCCTGGAGGGTCCCT GAGACTCTCCTGTGCAGCCTCTGGATTCACCTTCAGTGACTACTACATGAGCTG GATCCGCCAGGCTCCAGGGAAGGGGCTGGAGTGGGTTTCATTCATTAGTACTA GTGGTAGTATCATATACTACGCAGACTCTGTGAAGGGCCGATTCACCATCTCC AGGGACAACGCCAAGAACTCACTGTATCTGCAAATGAACAGCCTGAGAGCCG AGGACACGGCTGTGTATTACTGTGCGAGAGAAGGGTATAGCAGCAGCTGGTCC TACTACTACGGTATGGACGTCTGGGGCCAAGGGACCACGGTCACCGTCTCCTC AGCTAGCACCAAGGGCCCATCGGTCTTCCCCCTGGCACCCTCCTCCAAGAGCA CCTCTGGGGGCACAGCGGCCCTGGGCTGCCTGGTCAAGGACTACTTCCCCGAA CCGGTGACGGTGTCGTGGAACTCAGGCGCCCTGACCAGCGGCGTGCACACCTT CCCGGCTGTCCTACAGTCCTCAGGACTCTACTCCCTCAGCAGCGTGGTGACCGT GCCCTCCAGCAGCTTGGGCACCCAGACCTACATCTGCAACGTGAATCACAAGC CCAGCAACACCAAGGTGGACAAGAGAGTTGAGCCCAAATCTTGTGACAAAAC TCACACATGCCCACCGTGCCCAGCACCTGAAGCCGAAGGGGCCCCGTCAGTCT TCCTCTTCCCCCCAAAACCCAAGGACACCCTCATGATCTCCCGGACCCCTGAGG TCACATGCGTGGTGGTGGACGTGAGCCACGAAGACCCTGAGGTCAAGTTCAAC TGGTACGTGGACGGCGTGGAGGTGCATAATGCCAAGACAAAGCCGCGGGAGG AGCAGTACAACAGCACGTACCGTGTGGTCAGCGTCCTCACCGTCCTGCACCAG GACTGGCTGAATGGCAAGGAGTACAAGTGCAAGGTCTCCAACAAAGCCCTCCC AGCCCCCATCGAGAAAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAACCA

[0721]

SEQ ID	抗体	描述	序列
			CAGGTGTACACCCTGCCCCCATCCCGGGAGGAGATGACCAAGAACCAGGTCAG CCTGACCTGCCTGGTCAAAGGCTTCTATCCCAGCGACATCGCCGTGGAGTGGG AGAGCAATGGGCAGCCGGAGAACAACTACAAGACCACGCCTCCCGTGCTGGA CTCCGACGGCTCCTTCTTCCTCTATAGCAAGCTCACCGTGGACAAGAGCAGGT GGCAGCAGGGGAACGTCTTCTCATGCTCCGTGATGCATGAGGCTCTGCACAAC CACTACACGCAGAAGAGCCTCTCCCTGTCCCCGGGTTGA
241	17C8	IgG1.3f HC (无 C 末端 K)	CAGGTGCAGCTGGTGGAGTCTGGGGGAGGCTTGGTCAAGCCTGGAGGGTCCCT GAGACTCTCCTGTGCAGCCTCTGGATTCACCTTCAGTGACTACTACATGAGCTG GATCCGCCAGGCTCCAGGGAAGGGGCTGGAGTGGGTTTCATTCATTAGTAGTA GTGGTAGTATCATATACTACGCAGACTCTGTGAAGGGCCGATTCACCATCTCC AGGGACAACGCCAAGAACTCACTGTATCTGCAAATGAACAGCCTGAGAGCCG AGGACACGGCTGTGTATTACTGTGCGAGAGATGGGTATAGCAGTGGCTGGGAG TACTACGGTATGGACGTCTGGGGCCAAGGGACCACGGTCACCGTCTCCTCAGC TAGCACCAAGGGCCCATCGGTCTTCCCCCTGGCACCCTCCTCCAAGAGCACCTC TGGGGGCACAGCGGCCCTGGGCTGCCTGGTCAAGGACTACTTCCCCGAACCGG TGACGGTGTCGTGGAACTCAGGCGCCCTGACCAGCGGCGTGCACACCTTCCCG GCTGTCCTACAGTCCTCAGGACTCTACTCCCTCAGCAGCGTGGTGACCGTGCCC TCCAGCAGCTTGGGCACCCAGACCTACATCTGCAACGTGAATCACAAGCCCAG CAACACCAAGGTGGACAAGAGAGTTGAGCCCAAATCTTGTGACAAAACTCAC ACATGCCCACCGTGCCCAGCACCTGAAGCCGAAGGGGCCCCGTCAGTCTTCCT CTTCCCCCCAAAACCCAAGGACACCCTCATGATCTCCCGGACCCCTGAGGTCA CATGCGTGGTGGTGGACGTGAGCCACGAAGACCCTGAGGTCAAGTTCAACTGG TACGTGGACGGCGTGGAGGTGCATAATGCCAAGACAAAGCCGCGGGAGGAGC AGTACAACAGCACGTACCGTGTGGTCAGCGTCCTCACCGTCCTGCACCAGGAC TGGCTGAATGGCAAGGAGTACAAGTGCAAGGTCTCCAACAAAGCCCTCCCAGC CCCCATCGAGAAAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAACCACAG GTGTACACCCTGCCCCCATCCCGGGAGGAGATGACCAAGAACCAGGTCAGCCT GACCTGCCTGGTCAAAGGCTTCTATCCCAGCGACATCGCCGTGGAGTGGGAGA GCAATGGGCAGCCGGAGAACAACTACAAGACCACGCCTCCCGTGCTGGACTCC GACGGCTCCTTCTTCCTCTATAGCAAGCTCACCGTGGACAAGAGCAGGTGGCA GCAGGGGAACGTCTTCTCATGCTCCGTGATGCATGAGGCTCTGCACAACCACT ACACGCAGAAGAGCCTCTCCCTGTCCCCGGGTTGA
242	13A3, 17C3, 3G4	LC	GAAATTGTGTTGACGCAGTCTCCAGGCACCCTGTCTTTGTCTCCAGGGGAAAG AGCCACCCTCTCCTGCAGGGCCAGTCAGAGTGTTAGCAGCAGCTACTTAGCCT GGTACCAGCAGAAACCTGGCCAGGCTCCCAGGCTCCTCATCTATGGTGCATCC AGCAGGGCCACTGGCATCCCAGACAGGTTCAGTGGCAGTGGGTCTGGGACAG ACTTCACTCTCACCATCAGCAGACTGGAGCCTGAAGATTTTGCAGTGTATTACT GTCAGCAGTATGGTAGCTCACCGATCACCTTCGGCCAAGGGACACGACTGGAG ATTAAACGTACGGTGGCTGCACCATCTGTCTTCATCTTCCCGCCATCTGATGAG CAGTTGAAATCTGGAACTGCCTCTGTTGTGTGCCTGCTGAATAACTTCTATCCC AGAGAGGCCAAAGTACAGTGGAAGGTGGATAACGCCCTCCAATCGGGTAACT CCCAGGAGAGTGTCACAGAGCAGGACAGCAAGGACAGCACCTACAGCCTCAG CAGCACCCTGACGCTGAGCAAAGCAGACTACGAGAAACACAAAGTCTACGCC TGCGAAGTCACCCATCAGGGCCTGAGCTCGCCCGTCACAAAGAGCTTCAACAG GGGAGAGTGTTAG
243	8B9, 8C4, 17C8	LC	GAAATTGTGTTGACGCAGTCTCCAGGCACCCTGTCTTTGTCTCCAGGGGAAAG AGCCACCCTCTCCTGCAGGGCCAGTCAGAGTGTTAGCAGCAGCTACTTAGCCT GGTACCAGCAGAAACCTGGCCAGGCTCCCAGGCTCCTCATCTATGGTGCATCC AGCAGGGCCACTGGCATCCCAGACAGGTTCAGTGGCAGTGGGTCTGGGACAG ACTTCACTCTCACCATCAGCAGACTGGAGCCTGAAGATTTTGCAGTGTATTACT GTCAGCAGTATGGTAGCTCACCTCTCACTTTCGGCGGAGGGACCAAGGTGGAG ATCAAACGTACGGTGGCTGCACCATCTGTCTTCATCTTCCCGCCATCTGATGAG CAGTTGAAATCTGGAACTGCCTCTGTTGTGTGCCTGCTGAATAACTTCTATCCC AGAGAGGCCAAAGTACAGTGGAAGGTGGATAACGCCCTCCAATCGGGTAACT CCCAGGAGAGTGTCACAGAGCAGGACAGCAAGGACAGCACCTACAGCCTCAG CAGCACCCTGACGCTGAGCAAAGCAGACTACGAGAAACACAAAGTCTACGCC TGCGAAGTCACCCATCAGGGCCTGAGCTCGCCCGTCACAAAGAGCTTCAACAG GGGAGAGTGTTAG
244	9F6 (VK3)	LC	GAAATTGTGTTGACGCAGTCTCCAGGCACCCTGTCTTTGTCTCCAGGGGAAAG AGCCACCCTCTCCTGCAGGGCCAGTCAGAGTGTTAGCAGCAGCTACTTAGCCT GGTACCAGCAGAAACCTGGCCAGGCTCCCAGGCTCCTCATCTATGGTGCATCC AGCAGGGCCACTGGCATCCCAGACAGGTTCAGTGGCAGTGGGTCTGGGACAG ACTTCACTCTCACCATCAGCAGACTGGAGCCTGAAGATTTTGCAGTGTATTACT GTCAGCAGTATGGTAGCTCACCGCTCACTTTCGGCGGAGGGACCAAGGTGGAG

[0722]

SEQ ID	抗体	描述	序列
			ATCAAACGTACGGTGGCTGCACCATCTGTCTTCATCTTCCCGCCATCTGATGAG CAGTTGAAATCTGGAACTGCCTCTGTTGTGTGCCTGCTGAATAACTTCTATCCC AGAGAGGCCAAAGTACAGTGGAAGGTGGATAACGCCCTCCAATCGGGTAACT CCCAGGAGAGTGTCACAGAGCAGGACAGCAAGGACAGCACCTACAGCCTCAG CAGCACCCTGACGCTGAGCAAAGCAGACTACGAGAAACACAAAGTCTACGCC TGCGAAGTCACCCATCAGGGCCTGAGCTCGCCCGTCACAAAGAGCTTCAACAG GGGAGAGTGTTAG
245	9F6 (VK1)	LC	GCCATCCAGTTGACCCAGTCTCCATCCTCCCTGTCTGCATCTGTAGGAGACAGA GTCACCATCACTTGCCGGGCAAGTCAGGGCATTAGCAGTGCTTTAGCCTGGTA TCAGCAGAAACCAGGGAAAGCTCCTAAGCTCCTGATCTATGATGCCTCCAGTT TGGAAAGTGGGGTCCCATCAAGGTTCAGCGGCAGTGGATCTGGGACAGATTTC ACTCTCACCATCAGCAGCCTGCAGCCTGAAGATTTTGCAACTTATTACTGTCAA CAGTTTAATAGTTACCCTCGGACGTTCGGCCAAGGGACCAAGGTGGAAATCAA ACGTACGGTGGCTGCACCATCTGTCTTCATCTTCCCGCCATCTGATGAGCAGTT GAAATCTGGAACTGCCTCTGTTGTGTGCCTGCTGAATAACTTCTATCCCAGAGA GGCCAAAGTACAGTGGAAGGTGGATAACGCCCTCCAATCGGGTAACTCCCAGG AGAGTGTCACAGAGCAGGACAGCAAGGACAGCACCTACAGCCTCAGCAGCAC CCTGACGCTGAGCAAAGCAGACTACGAGAAACACAAAGTCTACGCCTGCGAA GTCACCCATCAGGGCCTGAGCTCGCCCGTCACAAAGAGCTTCAACAGGGGAGA GTGTTAG
246	9F6 (VK2)	LC	GAAATTGTGTTGACGCAGTCTCCAGGCACCCTGTCTTTGTCTCCAGGGGAAAG AGCCACCCTCTCCTGCAGGGCCAGTCAGAGTGTTAGCAGCAGCTACTTAGCCT GGTACCAGCAGAAACCTGGCCAGGCTCCCAGGCTCCTCATCTATGGTGCATCC AGCAGGGCCACTGGCATCCCAGACAGGTTCAGTGGCAGTGGGTCTGGGACAG ACTTCACTCTCACCATCAGCAGACTGGAGCCTGAAGATTTTGCAGTGTATTACT GTCAGCAGTATGGTAGCTCACTCACTTTCGGCGGAGGGACCAAGGTGGAGATC AAACGTACGGTGGCTGCACCATCTGTCTTCATCTTCCCGCCATCTGATGAGCAG TTGAAATCTGGAACTGCCTCTGTTGTGTGCCTGCTGAATAACTTCTATCCCAGA GAGGCCAAAGTACAGTGGAAGGTGGATAACGCCCTCCAATCGGGTAACTCCCA GGAGAGTGTCACAGAGCAGGACAGCAAGGACAGCACCTACAGCCTCAGCAGC ACCCTGACGCTGAGCAAAGCAGACTACGAGAAACACAAAGTCTACGCCTGCG AAGTCACCCATCAGGGCCTGAGCTCGCCCGTCACAAAGAGCTTCAACAGGGGA GAGTGTTAG
247	13A3 (N60Q)	IgG1.1f HC	CAGCTGCAGCTGCAGGAGTCGGGCCCAGGACTGGTGAAGCCTTCGGAGACCCT GTCCCTCACCTGCACTGTCTCTGGTGGCTCCATCAGCAGTAGAAGTTACTACTG GGGCTGGATCCGCCAGCCCCCAGGGAAGGGGCTGGAGTGGATTGGGAGTATCT ATTATAGTGGGTTCACCTACTAC**CAACCG**TCCCTCAAGAGTCGAGTCACCATA TCCGTTGACACGTCCAAGAACCAGTTCTCCCTGAAGCTGAGCTCTGTGACCGCC GCAGACACGGCTGTGTATTATTGTGCGACAGGGGGGCCCTACGGTGACTACGC CCACTGGTTCGACCCCTGGGGCCAGGGAACCCTGGTCACCGTCTCCTCAGCTA GCACCAAGGGCCCATCGGTCTTCCCCCTGGCACCCTCCTCCAAGAGCACCTCTG GGGGCACAGCGGCCCTGGGCTGCCTGGTCAAGGACTACTTCCCCGAACCGGTG ACGGTGTCGTGGAACTCAGGCGCCCTGACCAGCGGCGTGCACACCTTCCCGGC TGTCCTACAGTCCTCAGGACTCTACTCCCTCAGCAGCGTGGTGACCGTGCCCTC CAGCAGCTTGGGCACCCAGACCTACATCTGCAACGTGAATCACAAGCCCAGCA ACACCAAGGTGGACAAGAGAGTTGAGCCCAAATCTTGTGACAAAACTCACAC ATGCCCACCGTGCCCAGCACCTGAAGCCGAAGGGGCCCCGTCAGTCTTCCTCT TCCCCCCAAAACCCAAGGACACCCTCATGATCTCCCGGACCCCTGAGGTCACA TGCGTGGTGGTGGACGTGAGCCACGAAGACCCTGAGGTCAAGTTCAACTGGTA CGTGGACGGCGTGGAGGTGCATAATGCCAAGACAAAGCCGCGGGAGGAGCAG TACAACAGCACGTACCGTGTGGTCAGCGTCCTCACCGTCCTGCACCAGGACTG GCTGAATGGCAAGGAGTACAAGTGCAAGGTCTCCAACAAAGCCCTCCCAAGC AGCATCGAGAAAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAACCACAGG TGTACACCCTGCCCCCATCCCGGGAGGAGATGACCAAGAACCAGGTCAGCCTG ACCTGCCTGGTCAAAGGCTTCTATCCCAGCGACATCGCCGTGGAGTGGGAGAG CAATGGGCAGCCGGAGAACAACTACAAGACCACGCCTCCCGTGCTGGACTCCG ACGGCTCCTTCTTCCTCTATAGCAAGCTCACCGTGGACAAGAGCAGGTGGCAG CAGGGGAACGTCTTCTCATGCTCCGTGATGCATGAGGCTCTGCACAACCACTA CACGCAGAAGAGCCTCTCCCTGTCCCCGGGTAAATGA
248	13A3 (N60S)	IgG1.1f HC	CAGCTGCAGCTGCAGGAGTCGGGCCCAGGACTGGTGAAGCCTTCGGAGACCCT GTCCCTCACCTGCACTGTCTCTGGTGGCTCCATCAGCAGTAGAAGTTACTACTG GGGCTGGATCCGCCAGCCCCCAGGGAAGGGGCTGGAGTGGATTGGGAGTATCT ATTATAGTGGGTTCACCTACTACTCACCGTCCCTCAAGAGTCGAGTCACCATAT CCGTTGACACGTCCAAGAACCAGTTCTCCCTGAAGCTGAGCTCTGTGACCGCC

[0723]

SEQ ID	抗体	描述	序列
			GCAGACACGGCTGTGTATTATTGTGCGACAGGGGGGCCCTACGGTGACTACGC CCACTGGTTCGACCCCTGGGGCCAGGGAACCCTGGTCACCGTCTCCTCAGCTA GCACCAAGGGCCCATCGGTCTTCCCCCTGGCACCCTCCTCCAAGAGCACCTCTG GGGGCACAGCGGCCCTGGGCTGCCTGGTCAAGGACTACTTCCCCGAACCGGTG ACGGTGTCGTGGAACTCAGGCGCCCTGACCAGCGGCGTGCACACCTTCCCGGC TGTCCTACAGTCCTCAGGACTCTACTCCCTCAGCAGCGTGGTGACCGTGCCCTC CAGCAGCTTGGGCACCCAGACCTACATCTGCAACGTGAATCACAAGCCCAGCA ACACCAAGGTGGACAAGAGAGTTGAGCCCAAATCTTGTGACAAAACTCACAC ATGCCCACCGTGCCCAGCACCTGAAGCCGAAGGGGCCCCGTCAGTCTTCCTCT TCCCCCCAAAACCCAAGGACACCCTCATGATCTCCCGGACCCCTGAGGTCACA TGCGTGGTGGTGGACGTGAGCCACGAAGACCCTGAGGTCAAGTTCAACTGGTA CGTGGACGGCGTGGAGGTGCATAATGCCAAGACAAAGCCGCGGGAGGAGCAG TACAACAGCACGTACCGTGTGGTCAGCGTCCTCACCGTCCTGCACCAGGACTG GCTGAATGGCAAGGAGTACAAGTGCAAGGTCTCCAACAAAGCCCTCCCAAGC AGCATCGAGAAAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAACCACAGG TGTACACCCTGCCCCCATCCCGGGAGGAGATGACCAAGAACCAGGTCAGCCTG ACCTGCCTGGTCAAAGGCTTCTATCCCAGCGACATCGCCGTGGAGTGGGAGAG CAATGGGCAGCCGGAGAACAACTACAAGACCACGCCTCCCGTGCTGGACTCCG ACGGCTCCTTCTTCCTCTATAGCAAGCTCACCGTGGACAAGAGCAGGTGGCAG CAGGGGAACGTCTTCTCATGCTCCGTGATGCATGAGGCTCTGCACAACCACTA CACGCAGAAGAGCCTCTCCCTGTCCCCGGGTAAATGA
249	13A3 (N60A)	IgG1.1f HC	CAGCTGCAGCTGCAGGAGTCGGGCCCAGGACTGGTGAAGCCTTCGGAGACCCT GTCCCTCACCTGCACTGTCTCTGGTGGCTCCATCAGCAGTAGAAGTTACTACTG GGGCTGGATCCGCCAGCCCCCAGGGAAGGGGCTGGAGTGGATTGGGAGTATCT ATTATAGTGGGTTCACCTACTACGCACCGTCCCTCAAGAGTCGAGTCACCATAT CCGTTGACACGTCCAAGAACCAGTTCTCCCTGAAGCTGAGCTCTGTGACCGCC GCAGACACGGCTGTGTATTATTGTGCGACAGGGGGGCCCTACGGTGACTACGC CCACTGGTTCGACCCCTGGGGCCAGGGAACCCTGGTCACCGTCTCCTCAGCTA GCACCAAGGGCCCATCGGTCTTCCCCCTGGCACCCTCCTCCAAGAGCACCTCTG GGGGCACAGCGGCCCTGGGCTGCCTGGTCAAGGACTACTTCCCCGAACCGGTG ACGGTGTCGTGGAACTCAGGCGCCCTGACCAGCGGCGTGCACACCTTCCCGGC TGTCCTACAGTCCTCAGGACTCTACTCCCTCAGCAGCGTGGTGACCGTGCCCTC CAGCAGCTTGGGCACCCAGACCTACATCTGCAACGTGAATCACAAGCCCAGCA ACACCAAGGTGGACAAGAGAGTTGAGCCCAAATCTTGTGACAAAACTCACAC ATGCCCACCGTGCCCAGCACCTGAAGCCGAAGGGGCCCCGTCAGTCTTCCTCT TCCCCCCAAAACCCAAGGACACCCTCATGATCTCCCGGACCCCTGAGGTCACA TGCGTGGTGGTGGACGTGAGCCACGAAGACCCTGAGGTCAAGTTCAACTGGTA CGTGGACGGCGTGGAGGTGCATAATGCCAAGACAAAGCCGCGGGAGGAGCAG TACAACAGCACGTACCGTGTGGTCAGCGTCCTCACCGTCCTGCACCAGGACTG GCTGAATGGCAAGGAGTACAAGTGCAAGGTCTCCAACAAAGCCCTCCCAAGC AGCATCGAGAAAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAACCACAGG TGTACACCCTGCCCCCATCCCGGGAGGAGATGACCAAGAACCAGGTCAGCCTG ACCTGCCTGGTCAAAGGCTTCTATCCCAGCGACATCGCCGTGGAGTGGGAGAG CAATGGGCAGCCGGAGAACAACTACAAGACCACGCCTCCCGTGCTGGACTCCG ACGGCTCCTTCTTCCTCTATAGCAAGCTCACCGTGGACAAGAGCAGGTGGCAG CAGGGGAACGTCTTCTCATGCTCCGTGATGCATGAGGCTCTGCACAACCACTA CACGCAGAAGAGCCTCTCCCTGTCCCCGGGTAAATGA
250	13A3 (D101E)	IgG1.1f HC	CAGCTGCAGCTGCAGGAGTCGGGCCCAGGACTGGTGAAGCCTTCGGAGACCCT GTCCCTCACCTGCACTGTCTCTGGTGGCTCCATCAGCAGTAGAAGTTACTACTG GGGCTGGATCCGCCAGCCCCCAGGGAAGGGGCTGGAGTGGATTGGGAGTATCT ATTATAGTGGGTTCACCTACTACAACCCGTCCCTCAAGAGTCGAGTCACCATAT CCGTTGACACGTCCAAGAACCAGTTCTCCCTGAAGCTGAGCTCTGTGACCGCC GCAGACACGGCTGTGTATTATTGTGCGACAGGGGGGCCCTACGGTGACTACGC CCACTGGTTCGAACCCTGGGGCCAGGGAACCCTGGTCACCGTCTCCTCAGCTA GCACCAAGGGCCCATCGGTCTTCCCCCTGGCACCCTCCTCCAAGAGCACCTCTG GGGGCACAGCGGCCCTGGGCTGCCTGGTCAAGGACTACTTCCCCGAACCGGTG ACGGTGTCGTGGAACTCAGGCGCCCTGACCAGCGGCGTGCACACCTTCCCGGC TGTCCTACAGTCCTCAGGACTCTACTCCCTCAGCAGCGTGGTGACCGTGCCCTC CAGCAGCTTGGGCACCCAGACCTACATCTGCAACGTGAATCACAAGCCCAGCA ACACCAAGGTGGACAAGAGAGTTGAGCCCAAATCTTGTGACAAAACTCACAC ATGCCCACCGTGCCCAGCACCTGAAGCCGAAGGGGCCCCGTCAGTCTTCCTCT TCCCCCCAAAACCCAAGGACACCCTCATGATCTCCCGGACCCCTGAGGTCACA TGCGTGGTGGTGGACGTGAGCCACGAAGACCCTGAGGTCAAGTTCAACTGGTA CGTGGACGGCGTGGAGGTGCATAATGCCAAGACAAAGCCGCGGGAGGAGCAG TACAACAGCACGTACCGTGTGGTCAGCGTCCTCACCGTCCTGCACCAGGACTG

[0724]

SEQ ID	抗体	描述	序列
			GCTGAATGGCAAGGAGTACAAGTGCAAGGTCTCCAACAAAGCCCTCCCAAGC AGCATCGAGAAAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAACCACAGG TGTACACCCTGCCCCCATCCCGGGAGGAGATGACCAAGAACCAGGTCAGCCTG ACCTGCCTGGTCAAAGGCTTCTATCCCAGCGACATCGCCGTGGAGTGGGAGAG CAATGGGCAGCCGGAGAACAACTACAAGACCACGCCTCCCGTGCTGGACTCCG ACGGCTCCTTCTTCCTCTATAGCAAGCTCACCGTGGACAAGAGCAGGTGGCAG CAGGGGAACGTCTTCTCATGCTCCGTGATGCATGAGGCTCTGCACAACCACTA CACGCAGAAGAGCCTCTCCCTGTCCCCGGGTAAATGA
251	13A3 (P102V)	IgG1.1f HC	CAGCTGCAGCTGCAGGAGTCGGGCCCAGGACTGGTGAAGCCTTCGGAGACCCT GTCCCTCACCTGCACTGTCTCTGGTGGCTCCATCAGCAGTAGAAGTTACTACTG GGGCTGGATCCGCCAGCCCCCAGGGAAGGGGCTGGAGTGGATTGGGAGTATCT ATTATAGTGGGTTCACCTACTACAACCCGTCCCTCAAGAGTCGAGTCACCATAT CCGTTGACACGTCCAAGAACCAGTTCTCCCTGAAGCTGAGCTCTGTGACCGCC GCAGACACGGCTGTGTATTATTGTGCGACAGGGGGGCCCTACGGTGACTACGC CCACTGGTTCGACGTATGGGGCCAGGGAACCCTGGTCACCGTCTCCTCAGCTA GCACCAAGGGCCCATCGGTCTTCCCCCTGGCACCCTCCTCCAAGAGCACCTCTG GGGGCACAGCGGCCCTGGGCTGCCTGGTCAAGGACTACTTCCCCGAACCGGTG ACGGTGTCGTGGAACTCAGGCGCCCTGACCAGCGGCGTGCACACCTTCCCGGC TGTCCTACAGTCCTCAGGACTCTACTCCCTCAGCAGCGTGGTGACCGTGCCCTC CAGCAGCTTGGGCACCCAGACCTACATCTGCAACGTGAATCACAAGCCCAGCA ACACCAAGGTGGACAAGAGAGTTGAGCCCAAATCTTGTGACAAAACTCACAC ATGCCCACCGTGCCCAGCACCTGAAGCCGAAGGGGCCCCGTCAGTCTTCCTCT TCCCCCCAAAACCCAAGGACACCCTCATGATCTCCCGGACCCCTGAGGTCACA TGCGTGGTGGTGGACGTGAGCCACGAAGACCCTGAGGTCAAGTTCAACTGGTA CGTGGACGGCGTGGAGGTGCATAATGCCAAGACAAAGCCGCGGGAGGAGCAG TACAACAGCACGTACCGTGTGGTCAGCGTCCTCACCGTCCTGCACCAGGACTG GCTGAATGGCAAGGAGTACAAGTGCAAGGTCTCCAACAAAGCCCTCCCAAGC AGCATCGAGAAAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAACCACAGG TGTACACCCTGCCCCCATCCCGGGAGGAGATGACCAAGAACCAGGTCAGCCTG ACCTGCCTGGTCAAAGGCTTCTATCCCAGCGACATCGCCGTGGAGTGGGAGAG CAATGGGCAGCCGGAGAACAACTACAAGACCACGCCTCCCGTGCTGGACTCCG ACGGCTCCTTCTTCCTCTATAGCAAGCTCACCGTGGACAAGAGCAGGTGGCAG CAGGGGAACGTCTTCTCATGCTCCGTGATGCATGAGGCTCTGCACAACCACTA CACGCAGAAGAGCCTCTCCCTGTCCCCGGGTAAATGA
252	13A3 (P102Y)	IgG1.1f HC	CAGCTGCAGCTGCAGGAGTCGGGCCCAGGACTGGTGAAGCCTTCGGAGACCCT GTCCCTCACCTGCACTGTCTCTGGTGGCTCCATCAGCAGTAGAAGTTACTACTG GGGCTGGATCCGCCAGCCCCCAGGGAAGGGGCTGGAGTGGATTGGGAGTATCT ATTATAGTGGGTTCACCTACTACAACCCGTCCCTCAAGAGTCGAGTCACCATAT CCGTTGACACGTCCAAGAACCAGTTCTCCCTGAAGCTGAGCTCTGTGACCGCC GCAGACACGGCTGTGTATTATTGTGCGACAGGGGGGCCCTACGGTGACTACGC CCACTGGTTCGACTACTGGGGCCAGGGAACCCTGGTCACCGTCTCCTCAGCTA GCACCAAGGGCCCATCGGTCTTCCCCCTGGCACCCTCCTCCAAGAGCACCTCTG GGGGCACAGCGGCCCTGGGCTGCCTGGTCAAGGACTACTTCCCCGAACCGGTG ACGGTGTCGTGGAACTCAGGCGCCCTGACCAGCGGCGTGCACACCTTCCCGGC TGTCCTACAGTCCTCAGGACTCTACTCCCTCAGCAGCGTGGTGACCGTGCCCTC CAGCAGCTTGGGCACCCAGACCTACATCTGCAACGTGAATCACAAGCCCAGCA ACACCAAGGTGGACAAGAGAGTTGAGCCCAAATCTTGTGACAAAACTCACAC ATGCCCACCGTGCCCAGCACCTGAAGCCGAAGGGGCCCCGTCAGTCTTCCTCT TCCCCCCAAAACCCAAGGACACCCTCATGATCTCCCGGACCCCTGAGGTCACA TGCGTGGTGGTGGACGTGAGCCACGAAGACCCTGAGGTCAAGTTCAACTGGTA CGTGGACGGCGTGGAGGTGCATAATGCCAAGACAAAGCCGCGGGAGGAGCAG TACAACAGCACGTACCGTGTGGTCAGCGTCCTCACCGTCCTGCACCAGGACTG GCTGAATGGCAAGGAGTACAAGTGCAAGGTCTCCAACAAAGCCCTCCCAAGC AGCATCGAGAAAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAACCACAGG TGTACACCCTGCCCCCATCCCGGGAGGAGATGACCAAGAACCAGGTCAGCCTG ACCTGCCTGGTCAAAGGCTTCTATCCCAGCGACATCGCCGTGGAGTGGGAGAG CAATGGGCAGCCGGAGAACAACTACAAGACCACGCCTCCCGTGCTGGACTCCG ACGGCTCCTTCTTCCTCTATAGCAAGCTCACCGTGGACAAGAGCAGGTGGCAG CAGGGGAACGTCTTCTCATGCTCCGTGATGCATGAGGCTCTGCACAACCACTA CACGCAGAAGAGCCTCTCCCTGTCCCCGGGTAAATGA
253	13A3 (P102L)	IgG1.1f HC	CAGCTGCAGCTGCAGGAGTCGGGCCCAGGACTGGTGAAGCCTTCGGAGACCCT GTCCCTCACCTGCACTGTCTCTGGTGGCTCCATCAGCAGTAGAAGTTACTACTG GGGCTGGATCCGCCAGCCCCCAGGGAAGGGGCTGGAGTGGATTGGGAGTATCT ATTATAGTGGGTTCACCTACTACAACCCGTCCCTCAAGAGTCGAGTCACCATAT

[0725]

SEQ ID	抗体	描述	序列
			CCGTTGACACGTCCAAGAACCAGTTCTCCCTGAAGCTGAGCTCTGTGACCGCC GCAGACACGGCTGTGTATTATTGTGCGACAGGGGGGCCCTACGGTGACTACGC CCACTGGTTCGACCTATGGGGCCAGGGAACCCTGGTCACCGTCTCCTCAGCTA GCACCAAGGGCCCATCGGTCTTCCCCCTGGCACCCTCCTCCAAGAGCACCTCTG GGGGCACAGCGGCCCTGGGCTGCCTGGTCAAGGACTACTTCCCCGAACCGGTG ACGGTGTCGTGGAACTCAGGCGCCCTGACCAGCGGCGTGCACACCTTCCCGGC TGTCCTACAGTCCTCAGGACTCTACTCCCTCAGCAGCGTGGTGACCGTGCCCTC CAGCAGCTTGGGCACCCAGACCTACATCTGCAACGTGAATCACAAGCCCAGCA ACACCAAGGTGGACAAGAGAGTTGAGCCCAAATCTTGTGACAAAACTCACAC ATGCCCACCGTGCCCAGCACCTGAAGCCGAAGGGGCCCCGTCAGTCTTCCTCT TCCCCCCAAAACCCAAGGACACCCTCATGATCTCCCGGACCCCTGAGGTCACA TGCGTGGTGGTGGACGTGAGCCACGAAGACCCTGAGGTCAAGTTCAACTGGTA CGTGGACGGCGTGGAGGTGCATAATGCCAAGACAAAGCCGCGGGAGGAGCAG TACAACAGCACGTACCGTGTGGTCAGCGTCCTCACCGTCCTGCACCAGGACTG GCTGAATGGCAAGGAGTACAAGTGCAAGGTCTCCAACAAAGCCCTCCCAAGC AGCATCGAGAAAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAACCACAGG TGTACACCCTGCCCCCATCCCGGGAGGAGATGACCAAGAACCAGGTCAGCCTG ACCTGCCTGGTCAAAGGCTTCTATCCCAGCGACATCGCCGTGGAGTGGGAGAG CAATGGGCAGCCGGAGAACAACTACAAGACCACGCCTCCCGTGCTGGACTCCG ACGGCTCCTTCTTCCTCTATAGCAAGCTCACCGTGGACAAGAGCAGGTGGCAG CAGGGGAACGTCTTCTCATGCTCCGTGATGCATGAGGCTCTGCACAACCACTA CACGCAGAAGAGCCTCTCCCTGTCCCCGGGTAAATGA
254	13A3 (N60Q, P102Y)	IgG1.1f HC	CAGCTGCAGCTGCAGGAGTCGGGCCCAGGACTGGTGAAGCCTTCGGAGACCCT GTCCCTCACCTGCACTGTCTCTGGTGGCTCCATCAGCAGTAGAAGTTACTACTG GGGCTGGATCCGCCAGCCCCCAGGGAAGGGGCTGGAGTGGATTGGGAGTATCT ATTATAGTGGGTTCACCTACTACCAACCGTCCCTCAAGAGTCGAGTCACCATAT CCGTTGACACGTCCAAGAACCAGTTCTCCCTGAAGCTGAGCTCTGTGACCGCC GCAGACACGGCTGTGTATTATTGTGCGACAGGGGGGCCCTACGGTGACTACGC CCACTGGTTCGACTACTGGGGCCAGGGAACCCTGGTCACCGTCTCCTCAGCTA GCACCAAGGGCCCATCGGTCTTCCCCCTGGCACCCTCCTCCAAGAGCACCTCTG GGGGCACAGCGGCCCTGGGCTGCCTGGTCAAGGACTACTTCCCCGAACCGGTG ACGGTGTCGTGGAACTCAGGCGCCCTGACCAGCGGCGTGCACACCTTCCCGGC TGTCCTACAGTCCTCAGGACTCTACTCCCTCAGCAGCGTGGTGACCGTGCCCTC CAGCAGCTTGGGCACCCAGACCTACATCTGCAACGTGAATCACAAGCCCAGCA ACACCAAGGTGGACAAGAGAGTTGAGCCCAAATCTTGTGACAAAACTCACAC ATGCCCACCGTGCCCAGCACCTGAAGCCGAAGGGGCCCCGTCAGTCTTCCTCT TCCCCCCAAAACCCAAGGACACCCTCATGATCTCCCGGACCCCTGAGGTCACA TGCGTGGTGGTGGACGTGAGCCACGAAGACCCTGAGGTCAAGTTCAACTGGTA CGTGGACGGCGTGGAGGTGCATAATGCCAAGACAAAGCCGCGGGAGGAGCAG TACAACAGCACGTACCGTGTGGTCAGCGTCCTCACCGTCCTGCACCAGGACTG GCTGAATGGCAAGGAGTACAAGTGCAAGGTCTCCAACAAAGCCCTCCCAAGC AGCATCGAGAAAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAACCACAGG TGTACACCCTGCCCCCATCCCGGGAGGAGATGACCAAGAACCAGGTCAGCCTG ACCTGCCTGGTCAAAGGCTTCTATCCCAGCGACATCGCCGTGGAGTGGGAGAG CAATGGGCAGCCGGAGAACAACTACAAGACCACGCCTCCCGTGCTGGACTCCG ACGGCTCCTTCTTCCTCTATAGCAAGCTCACCGTGGACAAGAGCAGGTGGCAG CAGGGGAACGTCTTCTCATGCTCCGTGATGCATGAGGCTCTGCACAACCACTA CACGCAGAAGAGCCTCTCCCTGTCCCCGGGTAAATGA
255	8B9 (S61P)	IgG1.1f HC	CAGGTGCAGCTGCAGGAGTCGGGCCCAGGACTGGTGAAGCCTTCGGAGACCCT GTCCCTCACCTGCACTGTCTCTGGTGGCTCCATCAGTCGTCACTACTGGAACTG GATCCGGCAGCCCCCAGGGAAGGGACTGGAGTGGATTGGGTATATCCATTACA GTGGAAGCACCAACTACAATCCCTCCCTCAAGAGTCGAGTCACCATATCAGTA GACACGTCCAAGAACCAGTTCTCCCTGAAGCTGAGCTCTGTGACCGCTGCGGA CACGGCCGTGTATTACTGTGCGAGAGATACTGGGTACTACGGTATGGACATCT GGGGCCAAGGGACCACGGTCACCGTCTCCTCAGCTAGCACCAAGGGCCCATCG GTCTTCCCCCTGGCACCCTCCTCCAAGAGCACCTCTGGGGGCACAGCGGCCCT GGGCTGCCTGGTCAAGGACTACTTCCCCGAACCGGTGACGGTGTCGTGGAACT CAGGCGCCCTGACCAGCGGCGTGCACACCTTCCCGGCTGTCCTACAGTCCTCA GGACTCTACTCCCTCAGCAGCGTGGTGACCGTGCCCTCCAGCAGCTTGGGCAC CCAGACCTACATCTGCAACGTGAATCACAAGCCCAGCAACACCAAGGTGGACA AGAGAGTTGAGCCCAAATCTTGTGACAAAACTCACACATGCCCACCGTGCCCA GCACCTGAAGCCGAAGGGGCCCCGTCAGTCTTCCTCTTCCCCCCAAAACCCAA GGACACCCTCATGATCTCCCGGACCCCTGAGGTCACATGCGTGGTGGTGGACG TGAGCCACGAAGACCCTGAGGTCAAGTTCAACTGGTACGTGGACGGCGTGGAG GTGCATAATGCCAAGACAAAGCCGCGGGAGGAGCAGTACAACAGCACGTACC

[0726]

SEQ ID	抗体	描述	序列
			GTGTGGTCAGCGTCCTCACCGTCCTGCACCAGGACTGGCTGAATGGCAAGGAG TACAAGTGCAAGGTCTCCAACAAAGCCCTCCCAAGCAGCATCGAGAAAACCAT CTCCAAAGCCAAAGGGCAGCCCCGAGAACCACAGGTGTACACCCTGCCCCCAT CCCGGGAGGAGATGACCAAGAACCAGGTCAGCCTGACCTGCCTGGTCAAAGG CTTCTATCCCAGCGACATCGCCGTGGAGTGGGAGAGCAATGGGCAGCCGGAGA ACAACTACAAGACCACGCCTCCCGTGCTGGACTCCGACGGCTCCTTCTTCCTCT ATAGCAAGCTCACCGTGGACAAGAGCAGGTGGCAGCAGGGGAACGTCTTCTC ATGCTCCGTGATGCATGAGGCTCTGCACAACCACTACACGCAGAAGAGCCTCT CCCTGTCCCCGGGTAAATGA
256	9F6 (A108T)	IgG1.1f HC	CAGGTGCAGCTGGTGGAGTCTGGGGGAGGCTTGGTCAAGCCTGGAGGGTCCCT GAGACTCTCCTGTGCAGCCTCTGGATTCACCTTCAGTGACTACTACATGAGCTG GATCCGCCAGGCTCCAGGGAAGGGGCTGGAGTGGGTTTCATTCATTAGTGGTG GTGGTAGTACCATATACTACGCAGACTCTGTGAAGGGCCGATTCACCATCTCC AGGGACAACGCCAAGAACTCGCTGTTTCTGCAAATGAACAGCCTGAGAGTCGA GGACACGGCTGTGTATTACTGTGCGAGAGATGGCTATAGCAGTGGCTGGTACT ACTACGGTATGGACGTCTGGGGCCAAGGGACCACGGTCACCGTCTCCTCAGCT AGCACCAAGGGCCCATCGGTCTTCCCCCTGGCACCCTCCTCCAAGAGCACCTCT GGGGGCACAGCGGCCCTGGGCTGCCTGGTCAAGGACTACTTCCCCGAACCGGT GACGGTGTCGTGGAACTCAGGCGCCCTGACCAGCGGCGTGCACACCTTCCCGG CTGTCCTACAGTCCTCAGGACTCTACTCCCTCAGCAGCGTGGTGACCGTGCCCT CCAGCAGCTTGGGCACCCAGACCTACATCTGCAACGTGAATCACAAGCCCAGC AACACCAAGGTGGACAAGAGAGTTGAGCCCAAATCTTGTGACAAAACTCACA CATGCCCACCGTGCCCAGCACCTGAAGCCGAAGGGGCCCCGTCAGTCTTCCTC TTCCCCCCAAAACCCAAGGACACCCTCATGATCTCCCGGACCCCTGAGGTCAC ATGCGTGGTGGTGGACGTGAGCCACGAAGACCCTGAGGTCAAGTTCAACTGGT ACGTGGACGGCGTGGAGGTGCATAATGCCAAGACAAAGCCGCGGGAGGAGCA GTACAACAGCACGTACCGTGTGGTCAGCGTCCTCACCGTCCTGCACCAGGACT GGCTGAATGGCAAGGAGTACAAGTGCAAGGTCTCCAACAAAGCCCTCCCAAG CAGCATCGAGAAAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAACCACAG GTGTACACCCTGCCCCCATCCCGGGAGGAGATGACCAAGAACCAGGTCAGCCT GACCTGCCTGGTCAAAGGCTTCTATCCCAGCGACATCGCCGTGGAGTGGGAGA GCAATGGGCAGCCGGAGAACAACTACAAGACCACGCCTCCCGTGCTGGACTCC GACGGCTCCTTCTTCCTCTATAGCAAGCTCACCGTGGACAAGAGCAGGTGGCA GCAGGGGAACGTCTTCTCATGCTCCGTGATGCATGAGGCTCTGCACAACCACT ACACGCAGAAGAGCCTCTCCCTGTCCCCGGGTAAATGA
257	13A3 (N60Q)	IgG1.1f HC (无 C 末端 K)	CAGCTGCAGCTGCAGGAGTCGGGCCCAGGACTGGTGAAGCCTTCGGAGACCCT GTCCCTCACCTGCACTGTCTCTGGTGGCTCCATCAGCAGTAGAAGTTACTACTG GGGCTGGATCCGCCAGCCCCCAGGGAAGGGGCTGGAGTGGATTGGGAGTATCT ATTATAGTGGGTTCACCTACTACCAACCGTCCCTCAAGAGTCGAGTCACCATAT CCGTTGACACGTCCAAGAACCAGTTCTCCCTGAAGCTGAGCTCTGTGACCGCC GCAGACACGGCTGTGTATTATTGTGCGACAGGGGGGCCCTACGGTGACTACGC CCACTGGTTCGACCCCTGGGGCCAGGGAACCCTGGTCACCGTCTCCTCAGCTA GCACCAAGGGCCCATCGGTCTTCCCCCTGGCACCCTCCTCCAAGAGCACCTCTG GGGGCACAGCGGCCCTGGGCTGCCTGGTCAAGGACTACTTCCCCGAACCGGTG ACGGTGTCGTGGAACTCAGGCGCCCTGACCAGCGGCGTGCACACCTTCCCGGC TGTCCTACAGTCCTCAGGACTCTACTCCCTCAGCAGCGTGGTGACCGTGCCCTC CAGCAGCTTGGGCACCCAGACCTACATCTGCAACGTGAATCACAAGCCCAGCA ACACCAAGGTGGACAAGAGAGTTGAGCCCAAATCTTGTGACAAAACTCACAC ATGCCCACCGTGCCCAGCACCTGAAGCCGAAGGGGCCCCGTCAGTCTTCCTCT TCCCCCCAAAACCCAAGGACACCCTCATGATCTCCCGGACCCCTGAGGTCACA TGCGTGGTGGTGGACGTGAGCCACGAAGACCCTGAGGTCAAGTTCAACTGGTA CGTGGACGGCGTGGAGGTGCATAATGCCAAGACAAAGCCGCGGGAGGAGCAG TACAACAGCACGTACCGTGTGGTCAGCGTCCTCACCGTCCTGCACCAGGACTG GCTGAATGGCAAGGAGTACAAGTGCAAGGTCTCCAACAAAGCCCTCCCAAGC AGCATCGAGAAAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAACCACAGG TGTACACCCTGCCCCCATCCCGGGAGGAGATGACCAAGAACCAGGTCAGCCTG ACCTGCCTGGTCAAAGGCTTCTATCCCAGCGACATCGCCGTGGAGTGGGAGAG CAATGGGCAGCCGGAGAACAACTACAAGACCACGCCTCCCGTGCTGGACTCCG ACGGCTCCTTCTTCCTCTATAGCAAGCTCACCGTGGACAAGAGCAGGTGGCAG CAGGGGAACGTCTTCTCATGCTCCGTGATGCATGAGGCTCTGCACAACCACTA CACGCAGAAGAGCCTCTCCCTGTCCCCGGGTTGA
258	13A3 (N60S)	IgG1.1f HC (无 C 末端 K)	CAGCTGCAGCTGCAGGAGTCGGGCCCAGGACTGGTGAAGCCTTCGGAGACCCT GTCCCTCACCTGCACTGTCTCTGGTGGCTCCATCAGCAGTAGAAGTTACTACTG GGGCTGGATCCGCCAGCCCCCAGGGAAGGGGCTGGAGTGGATTGGGAGTATCT

[0727]

SEQ ID	抗体	描述	序列
			ATTATAGTGGGTTCACCTACTACTCACCGTCCCTCAAGAGTCGAGTCACCATAT CCGTTGACACGTCCAAGAACCAGTTCTCCCTGAAGCTGAGCTCTGTGACCGCC GCAGACACGGCTGTGTATTATTGTGCGACAGGGGGGCCCTACGGTGACTACGC CCACTGGTTCGACCCCTGGGGCCAGGGAACCCTGGTCACCGTCTCCTCAGCTA GCACCAAGGGCCCATCGGTCTTCCCCCTGGCACCCTCCTCCAAGAGCACCTCTG GGGGCACAGCGGCCCTGGGCTGCCTGGTCAAGGACTACTTCCCCGAACCGGTG ACGGTGTCGTGGAACTCAGGCGCCCTGACCAGCGGCGTGCACACCTTCCCGGC TGTCCTACAGTCCTCAGGACTCTACTCCCTCAGCAGCGTGGTGACCGTGCCCTC CAGCAGCTTGGGCACCCAGACCTACATCTGCAACGTGAATCACAAGCCCAGCA ACACCAAGGTGGACAAGAGAGTTGAGCCCAAATCTTGTGACAAAACTCACAC ATGCCCACCGTGCCCAGCACCTGAAGCCGAAGGGGCCCCGTCAGTCTTCCTCT TCCCCCCAAAACCCAAGGACACCCTCATGATCTCCCGGACCCCTGAGGTCACA TGCGTGGTGGTGGACGTGAGCCACGAAGACCCTGAGGTCAAGTTCAACTGGTA CGTGGACGGCGTGGAGGTGCATAATGCCAAGACAAAGCCGCGGGAGGAGCAG TACAACAGCACGTACCGTGTGGTCAGCGTCCTCACCGTCCTGCACCAGGACTG GCTGAATGGCAAGGAGTACAAGTGCAAGGTCTCCAACAAAGCCCTCCCAAGC AGCATCGAGAAAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAACCACAGG TGTACACCCTGCCCCCATCCCGGGAGGAGATGACCAAGAACCAGGTCAGCCTG ACCTGCCTGGTCAAAGGCTTCTATCCCAGCGACATCGCCGTGGAGTGGGAGAG CAATGGGCAGCCGGAGAACAACTACAAGACCACGCCTCCCGTGCTGGACTCCG ACGGCTCCTTCTTCCTCTATAGCAAGCTCACCGTGGACAAGAGCAGGTGGCAG CAGGGGAACGTCTTCTCATGCTCCGTGATGCATGAGGCTCTGCACAACCACTA CACGCAGAAGAGCCTCTCCCTGTCCCCGGGTTGA
259	13A3 (N60A)	IgG1.1f HC (无 C 末端 K)	CAGCTGCAGCTGCAGGAGTCGGGCCCAGGACTGGTGAAGCCTTCGGAGACCCT GTCCCTCACCTGCACTGTCTCTGGTGGCTCCATCAGCAGTAGAAGTTACTACTG GGGCTGGATCCGCCAGCCCCCAGGGAAGGGGCTGGAGTGGATTGGGAGTATCT ATTATAGTGGGTTCACCTACTACGCACCGTCCCTCAAGAGTCGAGTCACCATAT CCGTTGACACGTCCAAGAACCAGTTCTCCCTGAAGCTGAGCTCTGTGACCGCC GCAGACACGGCTGTGTATTATTGTGCGACAGGGGGGCCCTACGGTGACTACGC CCACTGGTTCGACCCCTGGGGCCAGGGAACCCTGGTCACCGTCTCCTCAGCTA GCACCAAGGGCCCATCGGTCTTCCCCCTGGCACCCTCCTCCAAGAGCACCTCTG GGGGCACAGCGGCCCTGGGCTGCCTGGTCAAGGACTACTTCCCCGAACCGGTG ACGGTGTCGTGGAACTCAGGCGCCCTGACCAGCGGCGTGCACACCTTCCCGGC TGTCCTACAGTCCTCAGGACTCTACTCCCTCAGCAGCGTGGTGACCGTGCCCTC CAGCAGCTTGGGCACCCAGACCTACATCTGCAACGTGAATCACAAGCCCAGCA ACACCAAGGTGGACAAGAGAGTTGAGCCCAAATCTTGTGACAAAACTCACAC ATGCCCACCGTGCCCAGCACCTGAAGCCGAAGGGGCCCCGTCAGTCTTCCTCT TCCCCCCAAAACCCAAGGACACCCTCATGATCTCCCGGACCCCTGAGGTCACA TGCGTGGTGGTGGACGTGAGCCACGAAGACCCTGAGGTCAAGTTCAACTGGTA CGTGGACGGCGTGGAGGTGCATAATGCCAAGACAAAGCCGCGGGAGGAGCAG TACAACAGCACGTACCGTGTGGTCAGCGTCCTCACCGTCCTGCACCAGGACTG GCTGAATGGCAAGGAGTACAAGTGCAAGGTCTCCAACAAAGCCCTCCCAAGC AGCATCGAGAAAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAACCACAGG TGTACACCCTGCCCCCATCCCGGGAGGAGATGACCAAGAACCAGGTCAGCCTG ACCTGCCTGGTCAAAGGCTTCTATCCCAGCGACATCGCCGTGGAGTGGGAGAG CAATGGGCAGCCGGAGAACAACTACAAGACCACGCCTCCCGTGCTGGACTCCG ACGGCTCCTTCTTCCTCTATAGCAAGCTCACCGTGGACAAGAGCAGGTGGCAG CAGGGGAACGTCTTCTCATGCTCCGTGATGCATGAGGCTCTGCACAACCACTA CACGCAGAAGAGCCTCTCCCTGTCCCCGGGTTGA
260	13A3 (D101E)	IgG1.1f HC (无 C 末端 K)	CAGCTGCAGCTGCAGGAGTCGGGCCCAGGACTGGTGAAGCCTTCGGAGACCCT GTCCCTCACCTGCACTGTCTCTGGTGGCTCCATCAGCAGTAGAAGTTACTACTG GGGCTGGATCCGCCAGCCCCCAGGGAAGGGGCTGGAGTGGATTGGGAGTATCT ATTATAGTGGGTTCACCTACTACAACCCGTCCCTCAAGAGTCGAGTCACCATAT CCGTTGACACGTCCAAGAACCAGTTCTCCCTGAAGCTGAGCTCTGTGACCGCC GCAGACACGGCTGTGTATTATTGTGCGACAGGGGGGCCCTACGGTGACTACGC CCACTGGTTCGAACCCTGGGGCCAGGGAACCCTGGTCACCGTCTCCTCAGCTA GCACCAAGGGCCCATCGGTCTTCCCCCTGGCACCCTCCTCCAAGAGCACCTCTG GGGGCACAGCGGCCCTGGGCTGCCTGGTCAAGGACTACTTCCCCGAACCGGTG ACGGTGTCGTGGAACTCAGGCGCCCTGACCAGCGGCGTGCACACCTTCCCGGC TGTCCTACAGTCCTCAGGACTCTACTCCCTCAGCAGCGTGGTGACCGTGCCCTC CAGCAGCTTGGGCACCCAGACCTACATCTGCAACGTGAATCACAAGCCCAGCA ACACCAAGGTGGACAAGAGAGTTGAGCCCAAATCTTGTGACAAAACTCACAC ATGCCCACCGTGCCCAGCACCTGAAGCCGAAGGGGCCCCGTCAGTCTTCCTCT TCCCCCCAAAACCCAAGGACACCCTCATGATCTCCCGGACCCCTGAGGTCACA TGCGTGGTGGTGGACGTGAGCCACGAAGACCCTGAGGTCAAGTTCAACTGGTA

[0728]

SEQ ID	抗体	描述	序列
			CGTGGACGGCGTGGAGGTGCATAATGCCAAGACAAAGCCGCGGGAGGAGCAG TACAACAGCACGTACCGTGTGGTCAGCGTCCTCACCGTCCTGCACCAGGACTG GCTGAATGGCAAGGAGTACAAGTGCAAGGTCTCCAACAAAGCCCTCCCAAGC AGCATCGAGAAAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAACCACAGG TGTACACCCTGCCCCCATCCCGGGAGGAGATGACCAAGAACCAGGTCAGCCTG ACCTGCCTGGTCAAAGGCTTCTATCCCAGCGACATCGCCGTGGAGTGGGAGAG CAATGGGCAGCCGGAGAACAACTACAAGACCACGCCTCCCGTGCTGGACTCCG ACGGCTCCTTCTTCCTCTATAGCAAGCTCACCGTGGACAAGAGCAGGTGGCAG CAGGGGAACGTCTTCTCATGCTCCGTGATGCATGAGGCTCTGCACAACCACTA CACGCAGAAGAGCCTCTCCCTGTCCCCGGGTTGA
261	13A3 (P102V)	IgG1.1f HC (无 C 末端 K)	CAGCTGCAGCTGCAGGAGTCGGGCCCAGGACTGGTGAAGCCTTCGGAGACCCT GTCCCTCACCTGCACTGTCTCTGGTGGCTCCATCAGCAGTAGAAGTTACTACTG GGGCTGGATCCGCCAGCCCCCAGGGAAGGGGCTGGAGTGGATTGGGAGTATCT ATTATAGTGGGTTCACCTACTACAACCCGTCCCTCAAGAGTCGAGTCACCATAT CCGTTGACACGTCCAAGAACCAGTTCTCCCTGAAGCTGAGCTCTGTGACCGCC GCAGACACGGCTGTGTATTATTGTGCGACAGGGGGGCCCTACGGTGACTACGC CCACTGGTTCGACGTATGGGGCCAGGGAACCCTGGTCACCGTCTCCTCAGCTA GCACCAAGGGCCCATCGGTCTTCCCCCTGGCACCCTCCTCCAAGAGCACCTCTG GGGGCACAGCGGCCCTGGGCTGCCTGGTCAAGGACTACTTCCCCGAACCGGTG ACGGTGTCGTGGAACTCAGGCGCCCTGACCAGCGGCGTGCACACCTTCCCGGC TGTCCTACAGTCCTCAGGACTCTACTCCCTCAGCAGCGTGGTGACCGTGCCCTC CAGCAGCTTGGGCACCCAGACCTACATCTGCAACGTGAATCACAAGCCCAGCA ACACCAAGGTGGACAAGAGAGTTGAGCCCAAATCTTGTGACAAAACTCACAC ATGCCCACCGTGCCCAGCACCTGAAGCCGAAGGGGCCCCGTCAGTCTTCCTCT TCCCCCCAAAACCCAAGGACACCCTCATGATCTCCCGGACCCCTGAGGTCACA TGCGTGGTGGTGGACGTGAGCCACGAAGACCCTGAGGTCAAGTTCAACTGGTA CGTGGACGGCGTGGAGGTGCATAATGCCAAGACAAAGCCGCGGGAGGAGCAG TACAACAGCACGTACCGTGTGGTCAGCGTCCTCACCGTCCTGCACCAGGACTG GCTGAATGGCAAGGAGTACAAGTGCAAGGTCTCCAACAAAGCCCTCCCAAGC AGCATCGAGAAAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAACCACAGG TGTACACCCTGCCCCCATCCCGGGAGGAGATGACCAAGAACCAGGTCAGCCTG ACCTGCCTGGTCAAAGGCTTCTATCCCAGCGACATCGCCGTGGAGTGGGAGAG CAATGGGCAGCCGGAGAACAACTACAAGACCACGCCTCCCGTGCTGGACTCCG ACGGCTCCTTCTTCCTCTATAGCAAGCTCACCGTGGACAAGAGCAGGTGGCAG CAGGGGAACGTCTTCTCATGCTCCGTGATGCATGAGGCTCTGCACAACCACTA CACGCAGAAGAGCCTCTCCCTGTCCCCGGGTTGA
262	13A3 (P102Y)	IgG1.1f HC (无 C 末端 K)	CAGCTGCAGCTGCAGGAGTCGGGCCCAGGACTGGTGAAGCCTTCGGAGACCCT GTCCCTCACCTGCACTGTCTCTGGTGGCTCCATCAGCAGTAGAAGTTACTACTG GGGCTGGATCCGCCAGCCCCCAGGGAAGGGGCTGGAGTGGATTGGGAGTATCT ATTATAGTGGGTTCACCTACTACAACCCGTCCCTCAAGAGTCGAGTCACCATAT CCGTTGACACGTCCAAGAACCAGTTCTCCCTGAAGCTGAGCTCTGTGACCGCC GCAGACACGGCTGTGTATTATTGTGCGACAGGGGGGCCCTACGGTGACTACGC CCACTGGTTCGACTACTGGGGCCAGGGAACCCTGGTCACCGTCTCCTCAGCTA GCACCAAGGGCCCATCGGTCTTCCCCCTGGCACCCTCCTCCAAGAGCACCTCTG GGGGCACAGCGGCCCTGGGCTGCCTGGTCAAGGACTACTTCCCCGAACCGGTG ACGGTGTCGTGGAACTCAGGCGCCCTGACCAGCGGCGTGCACACCTTCCCGGC TGTCCTACAGTCCTCAGGACTCTACTCCCTCAGCAGCGTGGTGACCGTGCCCTC CAGCAGCTTGGGCACCCAGACCTACATCTGCAACGTGAATCACAAGCCCAGCA ACACCAAGGTGGACAAGAGAGTTGAGCCCAAATCTTGTGACAAAACTCACAC ATGCCCACCGTGCCCAGCACCTGAAGCCGAAGGGGCCCCGTCAGTCTTCCTCT TCCCCCCAAAACCCAAGGACACCCTCATGATCTCCCGGACCCCTGAGGTCACA TGCGTGGTGGTGGACGTGAGCCACGAAGACCCTGAGGTCAAGTTCAACTGGTA CGTGGACGGCGTGGAGGTGCATAATGCCAAGACAAAGCCGCGGGAGGAGCAG TACAACAGCACGTACCGTGTGGTCAGCGTCCTCACCGTCCTGCACCAGGACTG GCTGAATGGCAAGGAGTACAAGTGCAAGGTCTCCAACAAAGCCCTCCCAAGC AGCATCGAGAAAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAACCACAGG TGTACACCCTGCCCCCATCCCGGGAGGAGATGACCAAGAACCAGGTCAGCCTG ACCTGCCTGGTCAAAGGCTTCTATCCCAGCGACATCGCCGTGGAGTGGGAGAG CAATGGGCAGCCGGAGAACAACTACAAGACCACGCCTCCCGTGCTGGACTCCG ACGGCTCCTTCTTCCTCTATAGCAAGCTCACCGTGGACAAGAGCAGGTGGCAG CAGGGGAACGTCTTCTCATGCTCCGTGATGCATGAGGCTCTGCACAACCACTA CACGCAGAAGAGCCTCTCCCTGTCCCCGGGTTGA
263	13A3 (P102L)	IgG1.1f HC (无 C 末端 K)	CAGCTGCAGCTGCAGGAGTCGGGCCCAGGACTGGTGAAGCCTTCGGAGACCCT GTCCCTCACCTGCACTGTCTCTGGTGGCTCCATCAGCAGTAGAAGTTACTACTG

[0729]

SEQ ID	抗体	描述	序列
			GGGCTGGATCCGCCAGCCCCCAGGGAAGGGGCTGGAGTGGATTGGGAGTATCT ATTATAGTGGGTTCACCTACTACAACCCGTCCCTCAAGAGTCGAGTCACCATAT CCGTTGACACGTCCAAGAACCAGTTCTCCCTGAAGCTGAGCTCTGTGACCGCC GCAGACACGGCTGTGTATTATTGTGCGACAGGGGGGCCCTACGGTGACTACGC CCACTGGTTCGACCTATGGGGCCAGGGAACCCTGGTCACCGTCTCCTCAGCTA GCACCAAGGGCCCATCGGTCTTCCCCCTGGCACCCTCCTCCAAGAGCACCTCTG GGGGCACAGCGGCCCTGGGCTGCCTGGTCAAGGACTACTTCCCCGAACCGGTG ACGGTGTCGTGGAACTCAGGCGCCCTGACCAGCGGCGTGCACACCTTCCCGGC TGTCCTACAGTCCTCAGGACTCTACTCCCTCAGCAGCGTGGTGACCGTGCCCTC CAGCAGCTTGGGCACCCAGACCTACATCTGCAACGTGAATCACAAGCCCAGCA ACACCAAGGTGGACAAGAGAGTTGAGCCCAAATCTTGTGACAAAACTCACAC ATGCCCACCGTGCCCAGCACCTGAAGCCGAAGGGGCCCCGTCAGTCTTCCTCT TCCCCCCAAAACCCAAGGACACCCTCATGATCTCCCGGACCCCTGAGGTCACA TGCGTGGTGGTGGACGTGAGCCACGAAGACCCTGAGGTCAAGTTCAACTGGTA CGTGGACGGCGTGGAGGTGCATAATGCCAAGACAAAGCCGCGGGAGGAGCAG TACAACAGCACGTACCGTGTGGTCAGCGTCCTCACCGTCCTGCACCAGGACTG GCTGAATGGCAAGGAGTACAAGTGCAAGGTCTCCAACAAAGCCCTCCCAAGC AGCATCGAGAAAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAACCACAGG TGTACACCCTGCCCCCATCCCGGGAGGAGATGACCAAGAACCAGGTCAGCCTG ACCTGCCTGGTCAAAGGCTTCTATCCCAGCGACATCGCCGTGGAGTGGGAGAG CAATGGGCAGCCGGAGAACAACTACAAGACCACGCCTCCCGTGCTGGACTCCG ACGGCTCCTTCTTCCTCTATAGCAAGCTCACCGTGGACAAGAGCAGGTGGCAG CAGGGGAACGTCTTCTCATGCTCCGTGATGCATGAGGCTCTGCACAACCACTA CACGCAGAAGAGCCTCTCCCTGTCCCCGGGTTGA
264	13A3 (N60Q, P102Y)	IgG1.1f HC (无 C 末端 K)	CAGCTGCAGCTGCAGGAGTCGGGCCCAGGACTGGTGAAGCCTTCGGAGACCCT GTCCCTCACCTGCACTGTCTCTGGTGGCTCCATCAGCAGTAGAAGTTACTACTG GGGCTGGATCCGCCAGCCCCCAGGGAAGGGGCTGGAGTGGATTGGGAGTATCT ATTATAGTGGGTTCACCTACTACCAACCGTCCCTCAAGAGTCGAGTCACCATAT CCGTTGACACGTCCAAGAACCAGTTCTCCCTGAAGCTGAGCTCTGTGACCGCC GCAGACACGGCTGTGTATTATTGTGCGACAGGGGGGCCCTACGGTGACTACGC CCACTGGTTCGACTACTGGGGCCAGGGAACCCTGGTCACCGTCTCCTCAGCTA GCACCAAGGGCCCATCGGTCTTCCCCCTGGCACCCTCCTCCAAGAGCACCTCTG GGGGCACAGCGGCCCTGGGCTGCCTGGTCAAGGACTACTTCCCCGAACCGGTG ACGGTGTCGTGGAACTCAGGCGCCCTGACCAGCGGCGTGCACACCTTCCCGGC TGTCCTACAGTCCTCAGGACTCTACTCCCTCAGCAGCGTGGTGACCGTGCCCTC CAGCAGCTTGGGCACCCAGACCTACATCTGCAACGTGAATCACAAGCCCAGCA ACACCAAGGTGGACAAGAGAGTTGAGCCCAAATCTTGTGACAAAACTCACAC ATGCCCACCGTGCCCAGCACCTGAAGCCGAAGGGGCCCCGTCAGTCTTCCTCT TCCCCCCAAAACCCAAGGACACCCTCATGATCTCCCGGACCCCTGAGGTCACA TGCGTGGTGGTGGACGTGAGCCACGAAGACCCTGAGGTCAAGTTCAACTGGTA CGTGGACGGCGTGGAGGTGCATAATGCCAAGACAAAGCCGCGGGAGGAGCAG TACAACAGCACGTACCGTGTGGTCAGCGTCCTCACCGTCCTGCACCAGGACTG GCTGAATGGCAAGGAGTACAAGTGCAAGGTCTCCAACAAAGCCCTCCCAAGC AGCATCGAGAAAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAACCACAGG TGTACACCCTGCCCCCATCCCGGGAGGAGATGACCAAGAACCAGGTCAGCCTG ACCTGCCTGGTCAAAGGCTTCTATCCCAGCGACATCGCCGTGGAGTGGGAGAG CAATGGGCAGCCGGAGAACAACTACAAGACCACGCCTCCCGTGCTGGACTCCG ACGGCTCCTTCTTCCTCTATAGCAAGCTCACCGTGGACAAGAGCAGGTGGCAG CAGGGGAACGTCTTCTCATGCTCCGTGATGCATGAGGCTCTGCACAACCACTA CACGCAGAAGAGCCTCTCCCTGTCCCCGGGTTGA
265	8B9 (S61P)	IgG1.1f HC (无 C 末端 K)	CAGGTGCAGCTGCAGGAGTCGGGCCCAGGACTGGTGAAGCCTTCGGAGACCCT GTCCCTCACCTGCACTGTCTCTGGTGGCTCCATCAGTCGTCACTACTGGAACTG GATCCGGCAGCCCCCAGGGAAGGGACTGGAGTGGATTGGGTATATCCATTACA GTGGAAGCACCAACTACAATCCCTCCCTCAAGAGTCGAGTCACCATATCAGTA GACACGTCCAAGAACCAGTTCTCCCTGAAGCTGAGCTCTGTGACCGCTGCGGA CACGGCCGTGTATTACTGTGCGAGAGATACTGGGTACTACGGTATGGACATCT GGGGCCAAGGGACCACGGTCACCGTCTCCTCAGCTAGCACCAAGGGCCCATCG GTCTTCCCCCTGGCACCCTCCTCCAAGAGCACCTCTGGGGGGCACAGCGGCCCT GGGCTGCCTGGTCAAGGACTACTTCCCCGAACCGGTGACGGTGTCGTGGAACT CAGGCGCCCTGACCAGCGGCGTGCACACCTTCCCGGCTGTCCTACAGTCCTCA GGACTCTACTCCCTCAGCAGCGTGGTGACCGTGCCCTCCAGCAGCTTGGGCAC CCAGACCTACATCTGCAACGTGAATCACAAGCCCAGCAACACCAAGGTGGACA AGAGAGTTGAGCCCAAATCTTGTGACAAAACTCACACATGCCCACCGTGCCCA GCACCTGAAGCCGAAGGGGCCCCGTCAGTCTTCCTCTTCCCCCCAAAACCCAA GGACACCCTCATGATCTCCCGGACCCCTGAGGTCACATGCGTGGTGGTGGACG

[0730]

SEQ ID	抗体	描述	序列
			TGAGCCACGAAGACCCTGAGGTCAAGTTCAACTGGTACGTGGACGGCGTGGAG GTGCATAATGCCAAGACAAAGCCGCGGGAGGAGCAGTACAACAGCACGTACC GTGTGGTCAGCGTCCTCACCGTCCTGCACCAGGACTGGCTGAATGGCAAGGAG TACAAGTGCAAGGTCTCCAACAAAGCCCTCCCAAGCAGCATCGAGAAAACCAT CTCCAAAGCCAAAGGGCAGCCCCGAGAACCACAGGTGTACACCCTGCCCCCAT CCCGGGAGGAGATGACCAAGAACCAGGTCAGCCTGACCTGCCTGGTCAAAGG CTTCTATCCCAGCGACATCGCCGTGGAGTGGGAGAGCAATGGGCAGCCGGAGA ACAACTACAAGACCACGCCTCCCGTGCTGGACTCCGACGGCTCCTTCTTCCTCT ATAGCAAGCTCACCGTGGACAAGAGCAGGTGGCAGCAGGGGAACGTCTTCTC ATGCTCCGTGATGCATGAGGCTCTGCACAACCACTACACGCAGAAGAGCCTCT CCCTGTCCCCGGGTTGA
266	9F6 (A108T)	IgG1.1f HC (无 C 末端 K)	CAGGTGCAGCTGGTGGAGTCTGGGGGAGGCTTGGTCAAGCCTGGAGGGTCCCT GAGACTCTCCTGTGCAGCCTCTGGATTCACCTTCAGTGACTACTACATGAGCTG GATCCGCCAGGCTCCAGGGAAGGGGCTGGAGTGGGTTTCATTCATTAGTGGTG GTGGTAGTACCATATACTACGCAGACTCTGTGAAGGGCCGATTCACCATCTCC AGGGACAACGCCAAGAACTCGCTGTTTCTGCAAATGAACAGCCTGAGAGTCGA GGACACGGCTGTGTATTACTGTGCGAGAGATGGCTATAGCAGTGGCTGGTACT ACTACGGTATGGACGTCTGGGGCCAAGGGACCACGGTCACCGTCTCCTCAGCT AGCACCAAGGGCCCATCGGTCTTCCCCCTGGCACCCTCCTCCAAGAGCACCTCT GGGGGCACAGCGGCCCTGGGCTGCCTGGTCAAGGACTACTTCCCCGAACCGGT GACGGTGTCGTGGAACTCAGGCGCCCTGACCAGCGGCGTGCACACCTTCCCGG CTGTCCTACAGTCCTCAGGACTCTACTCCCTCAGCAGCGTGGTGACCGTGCCCT CCAGCAGCTTGGGCACCCAGACCTACATCTGCAACGTGAATCACAAGCCCAGC AACACCAAGGTGGACAAGAGAGTTGAGCCCAAATCTTGTGACAAAACTCACA CATGCCCACCGTGCCCAGCACCTGAAGCCGAAGGGGCCCCGTCAGTCTTCCTC TTCCCCCCAAAACCCAAGGACACCCTCATGATCTCCCGGACCCCTGAGGTCAC ATGCGTGGTGGTGGACGTGAGCCACGAAGACCCTGAGGTCAAGTTCAACTGGT ACGTGGACGGCGTGGAGGTGCATAATGCCAAGACAAAGCCGCGGGAGGAGCA GTACAACAGCACGTACCGTGTGGTCAGCGTCCTCACCGTCCTGCACCAGGACT GGCTGAATGGCAAGGAGTACAAGTGCAAGGTCTCCAACAAAGCCCTCCCAAG CAGCATCGAGAAAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAACCACAG GTGTACACCCTGCCCCCATCCCGGGAGGAGATGACCAAGAACCAGGTCAGCCT GACCTGCCTGGTCAAAGGCTTCTATCCCAGCGACATCGCCGTGGAGTGGGAGA GCAATGGGCAGCCGGAGAACAACTACAAGACCACGCCTCCCGTGCTGGACTCC GACGGCTCCTTCTTCCTCTATAGCAAGCTCACCGTGGACAAGAGCAGGTGGCA GCAGGGGAACGTCTTCTCATGCTCCGTGATGCATGAGGCTCTGCACAACCACT ACACGCAGAAGAGCCTCTCCCTGTCCCCGGGTTGA
267	13A3 (N60Q)	IgG1.3f HC	CAGCTGCAGCTGCAGGAGTCGGGCCCAGGACTGGTGAAGCCTTCGGAGACCCT GTCCCTCACCTGCACTGTCTCTGGTGGCTCCATCAGCAGTAGAAGTTACTACTG GGGCTGGATCCGCCAGCCCCCAGGGAAGGGGCTGGAGTGGATTGGGAGTATCT ATTATAGTGGGTTCACCTACTACCAACCGTCCCTCAAGAGTCGAGTCACCATAT CCGTTGACACGTCCAAGAACCAGTTCTCCCTGAAGCTGAGCTCTGTGACCGCC GCAGACACGGCTGTGTATTATTGTGCGACAGGGGGGCCCTACGGTGACTACGC CCACTGGTTCGACCCCTGGGGCCAGGGAACCCTGGTCACCGTCTCCTCAGCTA GCACCAAGGGCCCATCGGTCTTCCCCCTGGCACCCTCCTCCAAGAGCACCTCTG GGGGCACAGCGGCCCTGGGCTGCCTGGTCAAGGACTACTTCCCCGAACCGGTG ACGGTGTCGTGGAACTCAGGCGCCCTGACCAGCGGCGTGCACACCTTCCCGGC TGTCCTACAGTCCTCAGGACTCTACTCCCTCAGCAGCGTGGTGACCGTGCCCTC CAGCAGCTTGGGCACCCAGACCTACATCTGCAACGTGAATCACAAGCCCAGCA ACACCAAGGTGGACAAGAGAGTTGAGCCCAAATCTTGTGACAAAACTCACAC ATGCCCACCGTGCCCAGCACCTGAAGCCGAAGGGGCCCCGTCAGTCTTCCTCT TCCCCCCAAAACCCAAGGACACCCTCATGATCTCCCGGACCCCTGAGGTCACA TGCGTGGTGGTGGACGTGAGCCACGAAGACCCTGAGGTCAAGTTCAACTGGTA CGTGGACGGCGTGGAGGTGCATAATGCCAAGACAAAGCCGCGGGAGGAGCAG TACAACAGCACGTACCGTGTGGTCAGCGTCCTCACCGTCCTGCACCAGGACTG GCTGAATGGCAAGGAGTACAAGTGCAAGGTCTCCAACAAAGCCCTCCCAGCCC CCATCGAGAAAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAACCACAGGT GTACACCCTGCCCCCATCCCGGGAGGAGATGACCAAGAACCAGGTCAGCCTGA CCTGCCTGGTCAAAGGCTTCTATCCCAGCGACATCGCCGTGGAGTGGGAGAGC AATGGGCAGCCGGAGAACAACTACAAGACCACGCCTCCCGTGCTGGACTCCGA CGGCTCCTTCTTCCTCTATAGCAAGCTCACCGTGGACAAGAGCAGGTGGCAGC AGGGGAACGTCTTCTCATGCTCCGTGATGCATGAGGCTCTGCACAACCACTAC ACGCAGAAGAGCCTCTCCCTGTCCCCGGGTAAATGA
268	13A3	IgG1.3f HC	CAGCTGCAGCTGCAGGAGTCGGGCCCAGGACTGGTGAAGCCTTCGGAGACCCT

[0731]

SEQ ID	抗体	描述	序列
	(N60S)		GTCCCTCACCTGCACTGTCTCTGGTGGCTCCATCAGCAGTAGAAGTTACTACTG GGGCTGGATCCGCCAGCCCCCAGGGAAGGGGCTGGAGTGGATTGGGAGTATCT ATTATAGTGGGTTCACCTACTACTCACCGTCCCTCAAGAGTCGAGTCACCATAT CCGTTGACACGTCCAAGAACCAGTTCTCCCTGAAGCTGAGCTCTGTGACCGCC GCAGACACGGCTGTGTATTATTGTGCGACAGGGGGGCCCTACGGTGACTACGC CCACTGGTTCGACCCCTGGGGCCAGGGAACCCTGGTCACCGTCTCCTCAGCTA GCACCAAGGGCCCATCGGTCTTCCCCCTGGCACCCTCCTCCAAGAGCACCTCTG GGGGCACAGCGGCCCTGGGCTGCCTGGTCAAGGACTACTTCCCCGAACCGGTG ACGGTGTCGTGGAACTCAGGCGCCCTGACCAGCGGCGTGCACACCTTCCCGGC TGTCCTACAGTCCTCAGGACTCTACTCCCTCAGCAGCGTGGTGACCGTGCCCTC CAGCAGCTTGGGCACCCAGACCTACATCTGCAACGTGAATCACAAGCCCAGCA ACACCAAGGTGGACAAGAGAGTTGAGCCCAAATCTTGTGACAAAACTCACAC ATGCCCACCGTGCCCAGCACCTGAAGCCGAAGGGGCCCCGTCAGTCTTCCTCT TCCCCCCAAAACCCAAGGACACCCTCATGATCTCCCGGACCCCTGAGGTCACA TGCGTGGTGGTGGACGTGAGCCACGAAGACCCTGAGGTCAAGTTCAACTGGTA CGTGGACGGCGTGGAGGTGCATAATGCCAAGACAAAGCCGCGGGAGGAGCAG TACAACAGCACGTACCGTGTGGTCAGCGTCCTCACCGTCCTGCACCAGGACTG GCTGAATGGCAAGGAGTACAAGTGCAAGGTCTCCAACAAAGCCCTCCCAGCCC CCATCGAGAAAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAACCACAGGT GTACACCCTGCCCCCATCCCGGGAGGAGATGACCAAGAACCAGGTCAGCCTGA CCTGCCTGGTCAAAGGCTTCTATCCCAGCGACATCGCCGTGGAGTGGGAGAGC AATGGGCAGCCGGAGAACAACTACAAGACCACGCCTCCCGTGCTGGACTCCGA CGGCTCCTTCTTCCTCTATAGCAAGCTCACCGTGGACAAGAGCAGGTGGCAGC AGGGGAACGTCTTCTCATGCTCCGTGATGCATGAGGCTCTGCACAACCACTAC ACGCAGAAGAGCCTCTCCCTGTCCCCGGGTAAATGA
269	13A3 (N60A)	IgG1.3f HC	CAGCTGCAGCTGCAGGAGTCGGGCCCAGGACTGGTGAAGCCTTCGGAGACCCT GTCCCTCACCTGCACTGTCTCTGGTGGCTCCATCAGCAGTAGAAGTTACTACTG GGGCTGGATCCGCCAGCCCCCAGGGAAGGGGCTGGAGTGGATTGGGAGTATCT ATTATAGTGGGTTCACCTACTACGCACCGTCCCTCAAGAGTCGAGTCACCATAT CCGTTGACACGTCCAAGAACCAGTTCTCCCTGAAGCTGAGCTCTGTGACCGCC GCAGACACGGCTGTGTATTATTGTGCGACAGGGGGGCCCTACGGTGACTACGC CCACTGGTTCGACCCCTGGGGCCAGGGAACCCTGGTCACCGTCTCCTCAGCTA GCACCAAGGGCCCATCGGTCTTCCCCCTGGCACCCTCCTCCAAGAGCACCTCTG GGGGCACAGCGGCCCTGGGCTGCCTGGTCAAGGACTACTTCCCCGAACCGGTG ACGGTGTCGTGGAACTCAGGCGCCCTGACCAGCGGCGTGCACACCTTCCCGGC TGTCCTACAGTCCTCAGGACTCTACTCCCTCAGCAGCGTGGTGACCGTGCCCTC CAGCAGCTTGGGCACCCAGACCTACATCTGCAACGTGAATCACAAGCCCAGCA ACACCAAGGTGGACAAGAGAGTTGAGCCCAAATCTTGTGACAAAACTCACAC ATGCCCACCGTGCCCAGCACCTGAAGCCGAAGGGGCCCCGTCAGTCTTCCTCT TCCCCCCAAAACCCAAGGACACCCTCATGATCTCCCGGACCCCTGAGGTCACA TGCGTGGTGGTGGACGTGAGCCACGAAGACCCTGAGGTCAAGTTCAACTGGTA CGTGGACGGCGTGGAGGTGCATAATGCCAAGACAAAGCCGCGGGAGGAGCAG TACAACAGCACGTACCGTGTGGTCAGCGTCCTCACCGTCCTGCACCAGGACTG GCTGAATGGCAAGGAGTACAAGTGCAAGGTCTCCAACAAAGCCCTCCCAGCCC CCATCGAGAAAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAACCACAGGT GTACACCCTGCCCCCATCCCGGGAGGAGATGACCAAGAACCAGGTCAGCCTGA CCTGCCTGGTCAAAGGCTTCTATCCCAGCGACATCGCCGTGGAGTGGGAGAGC AATGGGCAGCCGGAGAACAACTACAAGACCACGCCTCCCGTGCTGGACTCCGA CGGCTCCTTCTTCCTCTATAGCAAGCTCACCGTGGACAAGAGCAGGTGGCAGC AGGGGAACGTCTTCTCATGCTCCGTGATGCATGAGGCTCTGCACAACCACTAC ACGCAGAAGAGCCTCTCCCTGTCCCCGGGTAAATGA
270	13A3 (D101E)	IgG1.3f HC	CAGCTGCAGCTGCAGGAGTCGGGCCCAGGACTGGTGAAGCCTTCGGAGACCCT GTCCCTCACCTGCACTGTCTCTGGTGGCTCCATCAGCAGTAGAAGTTACTACTG GGGCTGGATCCGCCAGCCCCCAGGGAAGGGGCTGGAGTGGATTGGGAGTATCT ATTATAGTGGGTTCACCTACTACAACCCGTCCCTCAAGAGTCGAGTCACCATAT CCGTTGACACGTCCAAGAACCAGTTCTCCCTGAAGCTGAGCTCTGTGACCGCC GCAGACACGGCTGTGTATTATTGTGCGACAGGGGGGCCCTACGGTGACTACGC CCACTGGTTCGAACCCTGGGGCCAGGGAACCCTGGTCACCGTCTCCTCAGCTA GCACCAAGGGCCCATCGGTCTTCCCCCTGGCACCCTCCTCCAAGAGCACCTCTG GGGGCACAGCGGCCCTGGGCTGCCTGGTCAAGGACTACTTCCCCGAACCGGTG ACGGTGTCGTGGAACTCAGGCGCCCTGACCAGCGGCGTGCACACCTTCCCGGC TGTCCTACAGTCCTCAGGACTCTACTCCCTCAGCAGCGTGGTGACCGTGCCCTC CAGCAGCTTGGGCACCCAGACCTACATCTGCAACGTGAATCACAAGCCCAGCA ACACCAAGGTGGACAAGAGAGTTGAGCCCAAATCTTGTGACAAAACTCACAC ATGCCCACCGTGCCCAGCACCTGAAGCCGAAGGGGCCCCGTCAGTCTTCCTCT

[0732]

SEQ ID	抗体	描述	序列
			TCCCCCCAAAACCCAAGGACACCCTCATGATCTCCCGGACCCCTGAGGTCACA TGCGTGGTGGTGGACGTGAGCCACGAAGACCCTGAGGTCAAGTTCAACTGGTA CGTGGACGGCGTGGAGGTGCATAATGCCAAGACAAAGCCGCGGGAGGAGCAG TACAACAGCACGTACCGTGTGGTCAGCGTCCTCACCGTCCTGCACCAGGACTG GCTGAATGGCAAGGAGTACAAGTGCAAGGTCTCCAACAAAGCCCTCCCAGCCC CCATCGAGAAAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAACCACAGGT GTACACCCTGCCCCCATCCCGGGAGGAGATGACCAAGAACCAGGTCAGCCTGA CCTGCCTGGTCAAAGGCTTCTATCCCAGCGACATCGCCGTGGAGTGGGAGAGC AATGGGCAGCCGGAGAACAACTACAAGACCACGCCTCCCGTGCTGGACTCCGA CGGCTCCTTCTTCCTCTATAGCAAGCTCACCGTGGACAAGAGCAGGTGGCAGC AGGGGAACGTCTTCTCATGCTCCGTGATGCATGAGGCTCTGCACAACCACTAC ACGCAGAAGAGCCTCTCCCTGTCCCCGGGTAAATGA
271	13A3 (P102V)	IgG1.3f HC	CAGCTGCAGCTGCAGGAGTCGGGCCCAGGACTGGTGAAGCCTTCGGAGACCCT GTCCCTCACCTGCACTGTCTCTGGTGGCTCCATCAGCAGTAGAAGTTACTACTG GGGCTGGATCCGCCAGCCCCCAGGGAAGGGGCTGGAGTGGATTGGGAGTATCT ATTATAGTGGGTTCACCTACTACAACCCGTCCCTCAAGAGTCGAGTCACCATAT CCGTTGACACGTCCAAGAACCAGTTCTCCCTGAAGCTGAGCTCTGTGACCGCC GCAGACACGGCTGTGTATTATTGTGCGACAGGGGGGCCCTACGGTGACTACGC CCACTGGTTCGACGTATGGGGCCAGGGAACCCTGGTCACCGTCTCCTCAGCTA GCACCAAGGGCCCATCGGTCTTCCCCCTGGCACCCTCCTCCAAGAGCACCTCTG GGGGCACAGCGGCCCTGGGCTGCCTGGTCAAGGACTACTTCCCCGAACCGGTG ACGGTGTCGTGGAACTCAGGCGCCCTGACCAGCGGCGTGCACACCTTCCCGGC TGTCCTACAGTCCTCAGGACTCTACTCCCTCAGCAGCGTGGTGACCGTGCCCTC CAGCAGCTTGGGCACCCAGACCTACATCTGCAACGTGAATCACAAGCCCAGCA ACACCAAGGTGGACAAGAGAGTTGAGCCCAAATCTTGTGACAAAACTCACAC ATGCCCACCGTGCCCAGCACCTGAAGCCGAAGGGGCCCCGTCAGTCTTCCTCT TCCCCCCAAAACCCAAGGACACCCTCATGATCTCCCGGACCCCTGAGGTCACA TGCGTGGTGGTGGACGTGAGCCACGAAGACCCTGAGGTCAAGTTCAACTGGTA CGTGGACGGCGTGGAGGTGCATAATGCCAAGACAAAGCCGCGGGAGGAGCAG TACAACAGCACGTACCGTGTGGTCAGCGTCCTCACCGTCCTGCACCAGGACTG GCTGAATGGCAAGGAGTACAAGTGCAAGGTCTCCAACAAAGCCCTCCCAGCCC CCATCGAGAAAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAACCACAGGT GTACACCCTGCCCCCATCCCGGGAGGAGATGACCAAGAACCAGGTCAGCCTGA CCTGCCTGGTCAAAGGCTTCTATCCCAGCGACATCGCCGTGGAGTGGGAGAGC AATGGGCAGCCGGAGAACAACTACAAGACCACGCCTCCCGTGCTGGACTCCGA CGGCTCCTTCTTCCTCTATAGCAAGCTCACCGTGGACAAGAGCAGGTGGCAGC AGGGGAACGTCTTCTCATGCTCCGTGATGCATGAGGCTCTGCACAACCACTAC ACGCAGAAGAGCCTCTCCCTGTCCCCGGGTAAATGA
272	13A3 (P102Y)	IgG1.3f HC	CAGCTGCAGCTGCAGGAGTCGGGCCCAGGACTGGTGAAGCCTTCGGAGACCCT GTCCCTCACCTGCACTGTCTCTGGTGGCTCCATCAGCAGTAGAAGTTACTACTG GGGCTGGATCCGCCAGCCCCCAGGGAAGGGGCTGGAGTGGATTGGGAGTATCT ATTATAGTGGGTTCACCTACTACAACCCGTCCCTCAAGAGTCGAGTCACCATAT CCGTTGACACGTCCAAGAACCAGTTCTCCCTGAAGCTGAGCTCTGTGACCGCC GCAGACACGGCTGTGTATTATTGTGCGACAGGGGGGCCCTACGGTGACTACGC CCACTGGTTCGACTACTGGGGCCAGGGAACCCTGGTCACCGTCTCCTCAGCTA GCACCAAGGGCCCATCGGTCTTCCCCCTGGCACCCTCCTCCAAGAGCACCTCTG GGGGCACAGCGGCCCTGGGCTGCCTGGTCAAGGACTACTTCCCCGAACCGGTG ACGGTGTCGTGGAACTCAGGCGCCCTGACCAGCGGCGTGCACACCTTCCCGGC TGTCCTACAGTCCTCAGGACTCTACTCCCTCAGCAGCGTGGTGACCGTGCCCTC CAGCAGCTTGGGCACCCAGACCTACATCTGCAACGTGAATCACAAGCCCAGCA ACACCAAGGTGGACAAGAGAGTTGAGCCCAAATCTTGTGACAAAACTCACAC ATGCCCACCGTGCCCAGCACCTGAAGCCGAAGGGGCCCCGTCAGTCTTCCTCT TCCCCCCAAAACCCAAGGACACCCTCATGATCTCCCGGACCCCTGAGGTCACA TGCGTGGTGGTGGACGTGAGCCACGAAGACCCTGAGGTCAAGTTCAACTGGTA CGTGGACGGCGTGGAGGTGCATAATGCCAAGACAAAGCCGCGGGAGGAGCAG TACAACAGCACGTACCGTGTGGTCAGCGTCCTCACCGTCCTGCACCAGGACTG GCTGAATGGCAAGGAGTACAAGTGCAAGGTCTCCAACAAAGCCCTCCCAGCCC CCATCGAGAAAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAACCACAGGT GTACACCCTGCCCCCATCCCGGGAGGAGATGACCAAGAACCAGGTCAGCCTGA CCTGCCTGGTCAAAGGCTTCTATCCCAGCGACATCGCCGTGGAGTGGGAGAGC AATGGGCAGCCGGAGAACAACTACAAGACCACGCCTCCCGTGCTGGACTCCGA CGGCTCCTTCTTCCTCTATAGCAAGCTCACCGTGGACAAGAGCAGGTGGCAGC AGGGGAACGTCTTCTCATGCTCCGTGATGCATGAGGCTCTGCACAACCACTAC ACGCAGAAGAGCCTCTCCCTGTCCCCGGGTAAATGA

[0733]

SEQ ID	抗体	描述	序列
273	13A3 (P102L)	IgG1.3f HC	CAGCTGCAGCTGCAGGAGTCGGGCCCAGGACTGGTGAAGCCTTCGGAGACCCT GTCCCTCACCTGCACTGTCTCTGGTGGCTCCATCAGCAGTAGAAGTTACTACTG GGGCTGGATCCGCCAGCCCCCAGGGAAGGGGCTGGAGTGGATTGGGAGTATCT ATTATAGTGGGTTCACCTACTACAACCCGTCCCTCAAGAGTCGAGTCACCATAT CCGTTGACACGTCCAAGAACCAGTTCTCCCTGAAGCTGAGCTCTGTGACCGCC GCAGACACGGCTGTGTATTATTGTGCGACAGGGGGGCCCTACGGTGACTACGC CCACTGGTTCGACCTATGGGGCCAGGGAACCCTGGTCACCGTCTCCTCAGCTA GCACCAAGGGCCCATCGGTCTTCCCCCTGGCACCCTCCTCCAAGAGCACCTCTG GGGGCACAGCGGCCCTGGGCTGCCTGGTCAAGGACTACTTCCCCGAACCGGTG ACGGTGTCGTGGAACTCAGGCGCCCTGACCAGCGGCGTGCACACCTTCCCGGC TGTCCTACAGTCCTCAGGACTCTACTCCCTCAGCAGCGTGGTGACCGTGCCCTC CAGCAGCTTGGGCACCCAGACCTACATCTGCAACGTGAATCACAAGCCCAGCA ACACCAAGGTGGACAAGAGAGTTGAGCCCAAATCTTGTGACAAAACTCACAC ATGCCCACCGTGCCCAGCACCTGAAGCCGAAGGGGCCCCGTCAGTCTTCCTCT TCCCCCCAAAACCCAAGGACACCCTCATGATCTCCCGGACCCCTGAGGTCACA TGCGTGGTGGTGGACGTGAGCCACGAAGACCCTGAGGTCAAGTTCAACTGGTA CGTGGACGGCGTGGAGGTGCATAATGCCAAGACAAAGCCGCGGGAGGAGCAG TACAACAGCACGTACCGTGTGGTCAGCGTCCTCACCGTCCTGCACCAGGACTG GCTGAATGGCAAGGAGTACAAGTGCAAGGTCTCCAACAAAGCCCTCCCAGCCC CCATCGAGAAAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAACCACAGGT GTACACCCTGCCCCCATCCCGGGAGGAGATGACCAAGAACCAGGTCAGCCTGA CCTGCCTGGTCAAAGGCTTCTATCCCAGCGACATCGCCGTGGAGTGGGAGAGC AATGGGCAGCCGGAGAACAACTACAAGACCACGCCTCCCGTGCTGGACTCCGA CGGCTCCTTCTTCCTCTATAGCAAGCTCACCGTGGACAAGAGCAGGTGGCAGC AGGGGAACGTCTTCTCATGCTCCGTGATGCATGAGGCTCTGCACAACCACTAC ACGCAGAAGAGCCTCTCCCTGTCCCCGGGTAAATGA
274	13A3 (N60Q, P102Y)	IgG1.3f HC	CAGCTGCAGCTGCAGGAGTCGGGCCCAGGACTGGTGAAGCCTTCGGAGACCCT GTCCCTCACCTGCACTGTCTCTGGTGGCTCCATCAGCAGTAGAAGTTACTACTG GGGCTGGATCCGCCAGCCCCCAGGGAAGGGGCTGGAGTGGATTGGGAGTATCT ATTATAGTGGGTTCACCTACTACCAACCGTCCCTCAAGAGTCGAGTCACCATAT CCGTTGACACGTCCAAGAACCAGTTCTCCCTGAAGCTGAGCTCTGTGACCGCC GCAGACACGGCTGTGTATTATTGTGCGACAGGGGGGCCCTACGGTGACTACGC CCACTGGTTCGACTACTGGGGCCAGGGAACCCTGGTCACCGTCTCCTCAGCTA GCACCAAGGGCCCATCGGTCTTCCCCCTGGCACCCTCCTCCAAGAGCACCTCTG GGGGCACAGCGGCCCTGGGCTGCCTGGTCAAGGACTACTTCCCCGAACCGGTG ACGGTGTCGTGGAACTCAGGCGCCCTGACCAGCGGCGTGCACACCTTCCCGGC TGTCCTACAGTCCTCAGGACTCTACTCCCTCAGCAGCGTGGTGACCGTGCCCTC CAGCAGCTTGGGCACCCAGACCTACATCTGCAACGTGAATCACAAGCCCAGCA ACACCAAGGTGGACAAGAGAGTTGAGCCCAAATCTTGTGACAAAACTCACAC ATGCCCACCGTGCCCAGCACCTGAAGCCGAAGGGGCCCCGTCAGTCTTCCTCT TCCCCCCAAAACCCAAGGACACCCTCATGATCTCCCGGACCCCTGAGGTCACA TGCGTGGTGGTGGACGTGAGCCACGAAGACCCTGAGGTCAAGTTCAACTGGTA CGTGGACGGCGTGGAGGTGCATAATGCCAAGACAAAGCCGCGGGAGGAGCAG TACAACAGCACGTACCGTGTGGTCAGCGTCCTCACCGTCCTGCACCAGGACTG GCTGAATGGCAAGGAGTACAAGTGCAAGGTCTCCAACAAAGCCCTCCCAGCCC CCATCGAGAAAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAACCACAGGT GTACACCCTGCCCCCATCCCGGGAGGAGATGACCAAGAACCAGGTCAGCCTGA CCTGCCTGGTCAAAGGCTTCTATCCCAGCGACATCGCCGTGGAGTGGGAGAGC AATGGGCAGCCGGAGAACAACTACAAGACCACGCCTCCCGTGCTGGACTCCGA CGGCTCCTTCTTCCTCTATAGCAAGCTCACCGTGGACAAGAGCAGGTGGCAGC AGGGGAACGTCTTCTCATGCTCCGTGATGCATGAGGCTCTGCACAACCACTAC ACGCAGAAGAGCCTCTCCCTGTCCCCGGGTAAATGA
275	8B9 (S61P)	IgG1.3f HC	CAGGTGCAGCTGCAGGAGTCGGGCCCAGGACTGGTGAAGCCTTCGGAGACCCT GTCCCTCACCTGCACTGTCTCTGGTGGCTCCATCAGTCGTCACTACTGGAACTG GATCCGGCAGCCCCCAGGGAAGGGACTGGAGTGGATTGGGTATATCCATTACA GTGGAAGCACCAACTACAATCCCTCCCTCAAGAGTCGAGTCACCATATCAGTA GACACGTCCAAGAACCAGTTCTCCCTGAAGCTGAGCTCTGTGACCGCTGCGGA CACGGCCGTGTATTACTGTGCGAGAGATACTGGGTACTACGGTATGGACATCT GGGGCCAAGGGACCACGGTCACCGTCTCCTCAGCTAGCACCAAGGGCCCATCG GTCTTCCCCCTGGCACCCTCCTCCAAGAGCACCTCTGGGGGCACAGCGGCCCT GGGCTGCCTGGTCAAGGACTACTTCCCCGAACCGGTGACGGTGTCGTGGAACT CAGGCGCCCTGACCAGCGGCGTGCACACCTTCCCGGCTGTCCTACAGTCCTCA GGACTCTACTCCCTCAGCAGCGTGGTGACCGTGCCCTCCAGCAGCTTGGGCAC CCAGACCTACATCTGCAACGTGAATCACAAGCCCAGCAACACCAAGGTGGACA AGAGAGTTGAGCCCAAATCTTGTGACAAAACTCACACATGCCCACCGTGCCCA

[0734]

SEQ ID	抗体	描述	序列
			GCACCTGAAGCCGAAGGGGCCCCGTCAGTCTTCCTCTTCCCCCCAAAACCCAA GGACACCCTCATGATCTCCCGGACCCCTGAGGTCACATGCGTGGTGGTGGACG TGAGCCACGAAGACCCTGAGGTCAAGTTCAACTGGTACGTGGACGGCGTGGAG GTGCATAATGCCAAGACAAAGCCGCGGGAGGAGCAGTACAACAGCACGTACC GTGTGGTCAGCGTCCTCACCGTCCTGCACCAGGACTGGCTGAATGGCAAGGAG TACAAGTGCAAGGTCTCCAACAAAGCCCTCCCAGCCCCCATCGAGAAAACCAT CTCCAAAGCCAAAGGGCAGCCCCGAGAACCACAGGTGTACACCCTGCCCCCAT CCCGGGAGGAGATGACCAAGAACCAGGTCAGCCTGACCTGCCTGGTCAAAGG CTTCTATCCCAGCGACATCGCCGTGGAGTGGGAGAGCAATGGGCAGCCGGAGA ACAACTACAAGACCACGCCTCCCGTGCTGGACTCCGACGGCTCCTTCTTCCTCT ATAGCAAGCTCACCGTGGACAAGAGCAGGTGGCAGCAGGGGAACGTCTTCTC ATGCTCCGTGATGCATGAGGCTCTGCACAACCACTACACGCAGAAGAGCCTCT CCCTGTCCCCGGGTAAATGA
	276	9F6 (A108T)	IgG1.3f HC	CAGGTGCAGCTGGTGGAGTCTGGGGGAGGCTTGGTCAAGCCTGGAGGGTCCCT GAGACTCTCCTGTGCAGCCTCTGGATTCACCTTCAGTGACTACTACATGAGCTG GATCCGCCAGGCTCCAGGGAAGGGGCTGGAGTGGGTTTCATTCATTAGTGGTG GTGGTAGTACCATATACTACGCAGACTCTGTGAAGGGCCGATTCACCATCTCC AGGGACAACGCCAAGAACTCGCTGTTTCTGCAAATGAACAGCCTGAGAGTCGA GGACACGGCTGTGTATTACTGTGCGAGAGATGGCTATAGCAGTGGCTGGTACT ACTACGGTATGGACGTCTGGGGCCAAGGGACCACGGTCACCGTCTCCTCAGCT AGCACCAAGGGCCCATCGGTCTTCCCCCTGGCACCCTCCTCCAAGAGCACCTCT GGGGGCACAGCGGCCCTGGGCTGCCTGGTCAAGGACTACTTCCCCGAACCGGT GACGGTGTCGTGGAACTCAGGCGCCCTGACCAGCGGCGTGCACACCTTCCCGG CTGTCCTACAGTCCTCAGGACTCTACTCCCTCAGCAGCGTGGTGACCGTGCCCT CCAGCAGCTTGGGCACCCAGACCTACATCTGCAACGTGAATCACAAGCCCAGC AACACCAAGGTGGACAAGAGAGTTGAGCCCAAATCTTGTGACAAAACTCACA CATGCCCACCGTGCCCAGCACCTGAAGCCGAAGGGGCCCCGTCAGTCTTCCTC TTCCCCCCAAAACCCAAGGACACCCTCATGATCTCCCGGACCCCTGAGGTCAC ATGCGTGGTGGTGGACGTGAGCCACGAAGACCCTGAGGTCAAGTTCAACTGGT ACGTGGACGGCGTGGAGGTGCATAATGCCAAGACAAAGCCGCGGGAGGAGCA GTACAACAGCACGTACCGTGTGGTCAGCGTCCTCACCGTCCTGCACCAGGACT GGCTGAATGGCAAGGAGTACAAGTGCAAGGTCTCCAACAAAGCCCTCCCAGCC CCCATCGAGAAAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAACCACAGG TGTACACCCTGCCCCCATCCCGGGAGGAGATGACCAAGAACCAGGTCAGCCTG ACCTGCCTGGTCAAAGGCTTCTATCCCAGCGACATCGCCGTGGAGTGGGAGAG CAATGGGCAGCCGGAGAACAACTACAAGACCACGCCTCCCGTGCTGGACTCCG ACGGCTCCTTCTTCCTCTATAGCAAGCTCACCGTGGACAAGAGCAGGTGGCAG CAGGGGAACGTCTTCTCATGCTCCGTGATGCATGAGGCTCTGCACAACCACTA CACGCAGAAGAGCCTCTCCCTGTCCCCGGGTAAATGA
	277	13A3 (N60Q)	IgG1.3f HC (无 C 末端 K)	CAGCTGCAGCTGCAGGAGTCGGGCCCAGGACTGGTGAAGCCTTCGGAGACCCT GTCCCTCACCTGCACTGTCTCTGGTGGCTCCATCAGCAGTAGAAGTTACTACTG GGGCTGGATCCGCCAGCCCCCAGGGAAGGGGCTGGAGTGGATTGGGAGTATCT ATTATAGTGGGTTCACCTACTACCAACCGTCCCTCAAGAGTCGAGTCACCATAT CCGTTGACACGTCCAAGAACCAGTTCTCCCTGAAGCTGAGCTCTGTGACCGCC GCAGACACGGCTGTGTATTATTGTGCGACAGGGGGGCCCTACGGTGACTACGC CCACTGGTTCGACCCCTGGGGCCAGGGAACCCTGGTCACCGTCTCCTCAGCTA GCACCAAGGGCCCATCGGTCTTCCCCCTGGCACCCTCCTCCAAGAGCACCTCTG GGGGCACAGCGGCCCTGGGCTGCCTGGTCAAGGACTACTTCCCCGAACCGGTG ACGGTGTCGTGGAACTCAGGCGCCCTGACCAGCGGCGTGCACACCTTCCCGGC TGTCCTACAGTCCTCAGGACTCTACTCCCTCAGCAGCGTGGTGACCGTGCCCTC CAGCAGCTTGGGCACCCAGACCTACATCTGCAACGTGAATCACAAGCCCAGCA ACACCAAGGTGGACAAGAGAGTTGAGCCCAAATCTTGTGACAAAACTCACAC ATGCCCACCGTGCCCAGCACCTGAAGCCGAAGGGGCCCCGTCAGTCTTCCTCT TCCCCCCAAAACCCAAGGACACCCTCATGATCTCCCGGACCCCTGAGGTCACA TGCGTGGTGGTGGACGTGAGCCACGAAGACCCTGAGGTCAAGTTCAACTGGTA CGTGGACGGCGTGGAGGTGCATAATGCCAAGACAAAGCCGCGGGAGGAGCAG TACAACAGCACGTACCGTGTGGTCAGCGTCCTCACCGTCCTGCACCAGGACTG GCTGAATGGCAAGGAGTACAAGTGCAAGGTCTCCAACAAAGCCCTCCCAGCCC CCATCGAGAAAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAACCACAGGT GTACACCCTGCCCCCATCCCGGGAGGAGATGACCAAGAACCAGGTCAGCCTGA CCTGCCTGGTCAAAGGCTTCTATCCCAGCGACATCGCCGTGGAGTGGGAGAGC AATGGGCAGCCGGAGAACAACTACAAGACCACGCCTCCCGTGCTGGACTCCGA CGGCTCCTTCTTCCTCTATAGCAAGCTCACCGTGGACAAGAGCAGGTGGCAGC AGGGGAACGTCTTCTCATGCTCCGTGATGCATGAGGCTCTGCACAACCACTAC ACGCAGAAGAGCCTCTCCCTGTCCCCGGGTTGA

[0735]

SEQ ID	抗体	描述	序列
278	13A3 (N60S)	IgG1.3f HC (无 C 末端 K)	CAGCTGCAGCTGCAGGAGTCGGGCCCAGGACTGGTGAAGCCTTCGGAGACCCT GTCCCTCACCTGCACTGTCTCTGGTGGCTCCATCAGCAGTAGAAGTTACTACTG GGGCTGGATCCGCCAGCCCCCAGGGAAGGGGCTGGAGTGGATTGGGAGTATCT ATTATAGTGGGTTCACCTACTACTCACCGTCCCTCAAGAGTCGAGTCACCATAT CCGTTGACACGTCCAAGAACCAGTTCTCCCTGAAGCTGAGCTCTGTGACCGCC GCAGACACGGCTGTGTATTATTGTGCGACAGGGGGGCCCTACGGTGACTACGC CCACTGGTTCGACCCCTGGGGCCAGGGAACCCTGGTCACCGTCTCCTCAGCTA GCACCAAGGGCCCATCGGTCTTCCCCCTGGCACCCTCCTCCAAGAGCACCTCTG GGGGCACAGCGGCCCTGGGCTGCCTGGTCAAGGACTACTTCCCCGAACCGGTG ACGGTGTCGTGGAACTCAGGCGCCCTGACCAGCGGCGTGCACACCTTCCCGGC TGTCCTACAGTCCTCAGGACTCTACTCCCTCAGCAGCGTGGTGACCGTGCCCTC CAGCAGCTTGGGCACCCAGACCTACATCTGCAACGTGAATCACAAGCCCAGCA ACACCAAGGTGGACAAGAGAGTTGAGCCCAAATCTTGTGACAAAACTCACAC ATGCCCACCGTGCCCAGCACCTGAAGCCGAAGGGGCCCCGTCAGTCTTCCTCT TCCCCCCAAAACCCAAGGACACCCTCATGATCTCCCGGACCCCTGAGGTCACA TGCGTGGTGGTGGACGTGAGCCACGAAGACCCTGAGGTCAAGTTCAACTGGTA CGTGGACGGCGTGGAGGTGCATAATGCCAAGACAAAGCCGCGGGAGGAGCAG TACAACAGCACGTACCGTGTGGTCAGCGTCCTCACCGTCCTGCACCAGGACTG GCTGAATGGCAAGGAGTACAAGTGCAAGGTCTCCAACAAAGCCCTCCCAGCCC CCATCGAGAAAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAACCACAGGT GTACACCCTGCCCCCATCCCGGGAGGAGATGACCAAGAACCAGGTCAGCCTGA CCTGCCTGGTCAAAGGCTTCTATCCCAGCGACATCGCCGTGGAGTGGGAGAGC AATGGGCAGCCGGAGAACAACTACAAGACCACGCCTCCCGTGCTGGACTCCGA CGGCTCCTTCTTCCTCTATAGCAAGCTCACCGTGGACAAGAGCAGGTGGCAGC AGGGGAACGTCTTCTCATGCTCCGTGATGCATGAGGCTCTGCACAACCACTAC ACGCAGAAGAGCCTCTCCCTGTCCCCGGGTTGA
279	13A3 (N60A)	IgG1.3f HC (无 C 末端 K)	CAGCTGCAGCTGCAGGAGTCGGGCCCAGGACTGGTGAAGCCTTCGGAGACCCT GTCCCTCACCTGCACTGTCTCTGGTGGCTCCATCAGCAGTAGAAGTTACTACTG GGGCTGGATCCGCCAGCCCCCAGGGAAGGGGCTGGAGTGGATTGGGAGTATCT ATTATAGTGGGTTCACCTACTACGCACCGTCCCTCAAGAGTCGAGTCACCATAT CCGTTGACACGTCCAAGAACCAGTTCTCCCTGAAGCTGAGCTCTGTGACCGCC GCAGACACGGCTGTGTATTATTGTGCGACAGGGGGGCCCTACGGTGACTACGC CCACTGGTTCGACCCCTGGGGCCAGGGAACCCTGGTCACCGTCTCCTCAGCTA GCACCAAGGGCCCATCGGTCTTCCCCCTGGCACCCTCCTCCAAGAGCACCTCTG GGGGCACAGCGGCCCTGGGCTGCCTGGTCAAGGACTACTTCCCCGAACCGGTG ACGGTGTCGTGGAACTCAGGCGCCCTGACCAGCGGCGTGCACACCTTCCCGGC TGTCCTACAGTCCTCAGGACTCTACTCCCTCAGCAGCGTGGTGACCGTGCCCTC CAGCAGCTTGGGCACCCAGACCTACATCTGCAACGTGAATCACAAGCCCAGCA ACACCAAGGTGGACAAGAGAGTTGAGCCCAAATCTTGTGACAAAACTCACAC ATGCCCACCGTGCCCAGCACCTGAAGCCGAAGGGGCCCCGTCAGTCTTCCTCT TCCCCCCAAAACCCAAGGACACCCTCATGATCTCCCGGACCCCTGAGGTCACA TGCGTGGTGGTGGACGTGAGCCACGAAGACCCTGAGGTCAAGTTCAACTGGTA CGTGGACGGCGTGGAGGTGCATAATGCCAAGACAAAGCCGCGGGAGGAGCAG TACAACAGCACGTACCGTGTGGTCAGCGTCCTCACCGTCCTGCACCAGGACTG GCTGAATGGCAAGGAGTACAAGTGCAAGGTCTCCAACAAAGCCCTCCCAGCCC CCATCGAGAAAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAACCACAGGT GTACACCCTGCCCCCATCCCGGGAGGAGATGACCAAGAACCAGGTCAGCCTGA CCTGCCTGGTCAAAGGCTTCTATCCCAGCGACATCGCCGTGGAGTGGGAGAGC AATGGGCAGCCGGAGAACAACTACAAGACCACGCCTCCCGTGCTGGACTCCGA CGGCTCCTTCTTCCTCTATAGCAAGCTCACCGTGGACAAGAGCAGGTGGCAGC AGGGGAACGTCTTCTCATGCTCCGTGATGCATGAGGCTCTGCACAACCACTAC ACGCAGAAGAGCCTCTCCCTGTCCCCGGGTTGA
280	13A3 (D101E)	IgG1.3f HC (无 C 末端 K)	CAGCTGCAGCTGCAGGAGTCGGGCCCAGGACTGGTGAAGCCTTCGGAGACCCT GTCCCTCACCTGCACTGTCTCTGGTGGCTCCATCAGCAGTAGAAGTTACTACTG GGGCTGGATCCGCCAGCCCCCAGGGAAGGGGCTGGAGTGGATTGGGAGTATCT ATTATAGTGGGTTCACCTACTACAACCCGTCCCTCAAGAGTCGAGTCACCATAT CCGTTGACACGTCCAAGAACCAGTTCTCCCTGAAGCTGAGCTCTGTGACCGCC GCAGACACGGCTGTGTATTATTGTGCGACAGGGGGGCCCTACGGTGACTACGC CCACTGGTTCGAACCCTGGGGCCAGGGAACCCTGGTCACCGTCTCCTCAGCTA GCACCAAGGGCCCATCGGTCTTCCCCCTGGCACCCTCCTCCAAGAGCACCTCTG GGGGCACAGCGGCCCTGGGCTGCCTGGTCAAGGACTACTTCCCCGAACCGGTG ACGGTGTCGTGGAACTCAGGCGCCCTGACCAGCGGCGTGCACACCTTCCCGGC TGTCCTACAGTCCTCAGGACTCTACTCCCTCAGCAGCGTGGTGACCGTGCCCTC CAGCAGCTTGGGCACCCAGACCTACATCTGCAACGTGAATCACAAGCCCAGCA ACACCAAGGTGGACAAGAGAGTTGAGCCCAAATCTTGTGACAAAACTCACAC

[0736]

SEQ ID	抗体	描述	序列
			ATGCCCACCGTGCCCAGCACCTGAAGCCGAAGGGGCCCCGTCAGTCTTCCTCT TCCCCCCAAAACCCAAGGACACCCTCATGATCTCCCGGACCCCTGAGGTCACA TGCGTGGTGGTGGACGTGAGCCACGAAGACCCTGAGGTCAAGTTCAACTGGTA CGTGGACGGCGTGGAGGTGCATAATGCCAAGACAAAGCCGCGGGAGGAGCAG TACAACAGCACGTACCGTGTGGTCAGCGTCCTCACCGTCCTGCACCAGGACTG GCTGAATGGCAAGGAGTACAAGTGCAAGGTCTCCAACAAAGCCCTCCCAGCCC CCATCGAGAAAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAACCACAGGT GTACACCCTGCCCCCATCCCGGGAGGAGATGACCAAGAACCAGGTCAGCCTGA CCTGCCTGGTCAAAGGCTTCTATCCCAGCGACATCGCCGTGGAGTGGGAGAGC AATGGGCAGCCGGAGAACAACTACAAGACCACGCCTCCCGTGCTGGACTCCGA CGGCTCCTTCTTCCTCTATAGCAAGCTCACCGTGGACAAGAGCAGGTGGCAGC AGGGGAACGTCTTCTCATGCTCCGTGATGCATGAGGCTCTGCACAACCACTAC ACGCAGAAGAGCCTCTCCCTGTCCCCGGGTTGA
281	13A3 (P102V)	IgG1.3f HC (无 C 末端 K)	CAGCTGCAGCTGCAGGAGTCGGGCCCAGGACTGGTGAAGCCTTCGGAGACCCT GTCCCTCACCTGCACTGTCTCTGGTGGCTCCATCAGCAGTAGAAGTTACTACTG GGGCTGGATCCGCCAGCCCCCAGGGAAGGGGCTGGAGTGGATTGGGAGTATCT ATTATAGTGGGTTCACCTACTACAACCCGTCCCTCAAGAGTCGAGTCACCATAT CCGTTGACACGTCCAAGAACCAGTTCTCCCTGAAGCTGAGCTCTGTGACCGCC GCAGACACGGCTGTGTATTATTGTGCGACAGGGGGGCCCTACGGTGACTACGC CCACTGGTTCGACGTATGGGGCCAGGGAACCCTGGTCACCGTCTCCTCAGCTA GCACCAAGGGCCCATCGGTCTTCCCCCTGGCACCCTCCTCCAAGAGCACCTCTG GGGGCACAGCGGCCCTGGGCTGCCTGGTCAAGGACTACTTCCCCGAACCGGTG ACGGTGTCGTGGAACTCAGGCGCCCTGACCAGCGGCGTGCACACCTTCCCGGC TGTCCTACAGTCCTCAGGACTCTACTCCCTCAGCAGCGTGGTGACCGTGCCCTC CAGCAGCTTGGGCACCCAGACCTACATCTGCAACGTGAATCACAAGCCCAGCA ACACCAAGGTGGACAAGAGAGTTGAGCCCAAATCTTGTGACAAAACTCACAC ATGCCCACCGTGCCCAGCACCTGAAGCCGAAGGGGCCCCGTCAGTCTTCCTCT TCCCCCCAAAACCCAAGGACACCCTCATGATCTCCCGGACCCCTGAGGTCACA TGCGTGGTGGTGGACGTGAGCCACGAAGACCCTGAGGTCAAGTTCAACTGGTA CGTGGACGGCGTGGAGGTGCATAATGCCAAGACAAAGCCGCGGGAGGAGCAG TACAACAGCACGTACCGTGTGGTCAGCGTCCTCACCGTCCTGCACCAGGACTG GCTGAATGGCAAGGAGTACAAGTGCAAGGTCTCCAACAAAGCCCTCCCAGCCC CCATCGAGAAAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAACCACAGGT GTACACCCTGCCCCCATCCCGGGAGGAGATGACCAAGAACCAGGTCAGCCTGA CCTGCCTGGTCAAAGGCTTCTATCCCAGCGACATCGCCGTGGAGTGGGAGAGC AATGGGCAGCCGGAGAACAACTACAAGACCACGCCTCCCGTGCTGGACTCCGA CGGCTCCTTCTTCCTCTATAGCAAGCTCACCGTGGACAAGAGCAGGTGGCAGC AGGGGAACGTCTTCTCATGCTCCGTGATGCATGAGGCTCTGCACAACCACTAC ACGCAGAAGAGCCTCTCCCTGTCCCCGGGTTGA
282	13A3 (P102Y)	IgG1.3f HC (无 C 末端 K)	CAGCTGCAGCTGCAGGAGTCGGGCCCAGGACTGGTGAAGCCTTCGGAGACCCT GTCCCTCACCTGCACTGTCTCTGGTGGCTCCATCAGCAGTAGAAGTTACTACTG GGGCTGGATCCGCCAGCCCCCAGGGAAGGGGCTGGAGTGGATTGGGAGTATCT ATTATAGTGGGTTCACCTACTACAACCCGTCCCTCAAGAGTCGAGTCACCATAT CCGTTGACACGTCCAAGAACCAGTTCTCCCTGAAGCTGAGCTCTGTGACCGCC GCAGACACGGCTGTGTATTATTGTGCGACAGGGGGGCCCTACGGTGACTACGC CCACTGGTTCGACTACTGGGGCCAGGGAACCCTGGTCACCGTCTCCTCAGCTA GCACCAAGGGCCCATCGGTCTTCCCCCTGGCACCCTCCTCCAAGAGCACCTCTG GGGGCACAGCGGCCCTGGGCTGCCTGGTCAAGGACTACTTCCCCGAACCGGTG ACGGTGTCGTGGAACTCAGGCGCCCTGACCAGCGGCGTGCACACCTTCCCGGC TGTCCTACAGTCCTCAGGACTCTACTCCCTCAGCAGCGTGGTGACCGTGCCCTC CAGCAGCTTGGGCACCCAGACCTACATCTGCAACGTGAATCACAAGCCCAGCA ACACCAAGGTGGACAAGAGAGTTGAGCCCAAATCTTGTGACAAAACTCACAC ATGCCCACCGTGCCCAGCACCTGAAGCCGAAGGGGCCCCGTCAGTCTTCCTCT TCCCCCCAAAACCCAAGGACACCCTCATGATCTCCCGGACCCCTGAGGTCACA TGCGTGGTGGTGGACGTGAGCCACGAAGACCCTGAGGTCAAGTTCAACTGGTA CGTGGACGGCGTGGAGGTGCATAATGCCAAGACAAAGCCGCGGGAGGAGCAG TACAACAGCACGTACCGTGTGGTCAGCGTCCTCACCGTCCTGCACCAGGACTG GCTGAATGGCAAGGAGTACAAGTGCAAGGTCTCCAACAAAGCCCTCCCAGCCC CCATCGAGAAAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAACCACAGGT GTACACCCTGCCCCCATCCCGGGAGGAGATGACCAAGAACCAGGTCAGCCTGA CCTGCCTGGTCAAAGGCTTCTATCCCAGCGACATCGCCGTGGAGTGGGAGAGC AATGGGCAGCCGGAGAACAACTACAAGACCACGCCTCCCGTGCTGGACTCCGA CGGCTCCTTCTTCCTCTATAGCAAGCTCACCGTGGACAAGAGCAGGTGGCAGC AGGGGAACGTCTTCTCATGCTCCGTGATGCATGAGGCTCTGCACAACCACTAC ACGCAGAAGAGCCTCTCCCTGTCCCCGGGTTGA

[0737]

SEQ ID	抗体	描述	序列
283	13A3 (P102L)	IgG1.3f HC (无 C 末端 K)	CAGCTGCAGCTGCAGGAGTCGGGCCCAGGACTGGTGAAGCCTTCGGAGACCCT GTCCCTCACCTGCACTGTCTCTGGTGGCTCCATCAGCAGTAGAAGTTACTACTG GGGCTGGATCCGCCAGCCCCCAGGGAAGGGGCTGGAGTGGATTGGGAGTATCT ATTATAGTGGGTTCACCTACTACAACCCGTCCCTCAAGAGTCGAGTCACCATAT CCGTTGACACGTCCAAGAACCAGTTCTCCCTGAAGCTGAGCTCTGTGACCGCC GCAGACACGGCTGTGTATTATTGTGCGACAGGGGGGCCCTACGGTGACTACGC CCACTGGTTCGACCTATGGGGCCAGGGAACCCTGGTCACCGTCTCCTCAGCTA GCACCAAGGGCCCATCGGTCTTCCCCCTGGCACCCTCCTCCAAGAGCACCTCTG GGGGCACAGCGGCCCTGGGCTGCCTGGTCAAGGACTACTTCCCCGAACCGGTG ACGGTGTCGTGGAACTCAGGCGCCCTGACCAGCGGCGTGCACACCTTCCCGGC TGTCCTACAGTCCTCAGGACTCTACTCCCTCAGCAGCGTGGTGACCGTGCCCTC CAGCAGCTTGGGCACCCAGACCTACATCTGCAACGTGAATCACAAGCCCAGCA ACACCAAGGTGGACAAGAGAGTTGAGCCCAAATCTTGTGACAAAACTCACAC ATGCCCACCGTGCCCAGCACCTGAAGCCGAAGGGGCCCCGTCAGTCTTCCTCT TCCCCCCAAAACCCAAGGACACCCTCATGATCTCCCGGACCCCTGAGGTCACA TGCGTGGTGGTGGACGTGAGCCACGAAGACCCTGAGGTCAAGTTCAACTGGTA CGTGGACGGCGTGGAGGTGCATAATGCCAAGACAAAGCCGCGGGAGGAGCAG TACAACAGCACGTACCGTGTGGTCAGCGTCCTCACCGTCCTGCACCAGGACTG GCTGAATGGCAAGGAGTACAAGTGCAAGGTCTCCAACAAAGCCCTCCCAGCCC CCATCGAGAAAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAACCACAGGT GTACACCCTGCCCCCATCCCGGGAGGAGATGACCAAGAACCAGGTCAGCCTGA CCTGCCTGGTCAAAGGCTTCTATCCCAGCGACATCGCCGTGGAGTGGGAGAGC AATGGGCAGCCGGAGAACAACTACAAGACCACGCCTCCCGTGCTGGACTCCGA CGGCTCCTTCTTCCTCTATAGCAAGCTCACCGTGGACAAGAGCAGGTGGCAGC AGGGGAACGTCTTCTCATGCTCCGTGATGCATGAGGCTCTGCACAACCACTAC ACGCAGAAGAGCCTCTCCCTGTCCCCGGGTTGA
284	13A3 (N60Q, P102Y)	IgG1.3f HC (无 C 末端 K)	CAGCTGCAGCTGCAGGAGTCGGGCCCAGGACTGGTGAAGCCTTCGGAGACCCT GTCCCTCACCTGCACTGTCTCTGGTGGCTCCATCAGCAGTAGAAGTTACTACTG GGGCTGGATCCGCCAGCCCCCAGGGAAGGGGCTGGAGTGGATTGGGAGTATCT ATTATAGTGGGTTCACCTACTACCAACCGTCCCTCAAGAGTCGAGTCACCATAT CCGTTGACACGTCCAAGAACCAGTTCTCCCTGAAGCTGAGCTCTGTGACCGCC GCAGACACGGCTGTGTATTATTGTGCGACAGGGGGGCCCTACGGTGACTACGC CCACTGGTTCGACTACTGGGGCCAGGGAACCCTGGTCACCGTCTCCTCAGCTA GCACCAAGGGCCCATCGGTCTTCCCCCTGGCACCCTCCTCCAAGAGCACCTCTG GGGGCACAGCGGCCCTGGGCTGCCTGGTCAAGGACTACTTCCCCGAACCGGTG ACGGTGTCGTGGAACTCAGGCGCCCTGACCAGCGGCGTGCACACCTTCCCGGC TGTCCTACAGTCCTCAGGACTCTACTCCCTCAGCAGCGTGGTGACCGTGCCCTC CAGCAGCTTGGGCACCCAGACCTACATCTGCAACGTGAATCACAAGCCCAGCA ACACCAAGGTGGACAAGAGAGTTGAGCCCAAATCTTGTGACAAAACTCACAC ATGCCCACCGTGCCCAGCACCTGAAGCCGAAGGGGCCCCGTCAGTCTTCCTCT TCCCCCCAAAACCCAAGGACACCCTCATGATCTCCCGGACCCCTGAGGTCACA TGCGTGGTGGTGGACGTGAGCCACGAAGACCCTGAGGTCAAGTTCAACTGGTA CGTGGACGGCGTGGAGGTGCATAATGCCAAGACAAAGCCGCGGGAGGAGCAG TACAACAGCACGTACCGTGTGGTCAGCGTCCTCACCGTCCTGCACCAGGACTG GCTGAATGGCAAGGAGTACAAGTGCAAGGTCTCCAACAAAGCCCTCCCAGCCC CCATCGAGAAAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAACCACAGGT GTACACCCTGCCCCCATCCCGGGAGGAGATGACCAAGAACCAGGTCAGCCTGA CCTGCCTGGTCAAAGGCTTCTATCCCAGCGACATCGCCGTGGAGTGGGAGAGC AATGGGCAGCCGGAGAACAACTACAAGACCACGCCTCCCGTGCTGGACTCCGA CGGCTCCTTCTTCCTCTATAGCAAGCTCACCGTGGACAAGAGCAGGTGGCAGC AGGGGAACGTCTTCTCATGCTCCGTGATGCATGAGGCTCTGCACAACCACTAC ACGCAGAAGAGCCTCTCCCTGTCCCCGGGTTGA
285	8B9 (S61P)	IgG1.3f HC (无 C 末端 K)	CAGGTGCAGCTGCAGGAGTCGGGCCCAGGACTGGTGAAGCCTTCGGAGACCCT GTCCCTCACCTGCACTGTCTCTGGTGGCTCCATCAGTCGTCACTACTGGAACTG GATCCGGCAGCCCCCAGGGAAGGGACTGGAGTGGATTGGGTATATCCATTACA GTGGAAGCACCAACTACAATCCCTCCCTCAAGAGTCGAGTCACCATATCAGTA GACACGTCCAAGAACCAGTTCTCCCTGAAGCTGAGCTCTGTGACCGCTGCGGA CACGGCCGTGTATTACTGTGCGAGAGATACTGGGTACTACGGTATGGACATCT GGGGCCAAGGGACCACGGTCACCGTCTCCTCAGCTAGCACCAAGGGCCCATCG GTCTTCCCCCTGGCACCCTCCTCCAAGAGCACCTCTGGGGGCACAGCGGCCCT GGGCTGCCTGGTCAAGGACTACTTCCCCGAACCGGTGACGGTGTCGTGGAACT CAGGCGCCCTGACCAGCGGCGTGCACACCTTCCCGGCTGTCCTACAGTCCTCA GGACTCTACTCCCTCAGCAGCGTGGTGACCGTGCCCTCCAGCAGCTTGGGCAC CCAGACCTACATCTGCAACGTGAATCACAAGCCCAGCAACACCAAGGTGGACA AGAGAGTTGAGCCCAAATCTTGTGACAAAACTCACACATGCCCACCGTGCCCA

[0738]

SEQ ID	抗体	描述	序列
			GCACCTGAAGCCGAAGGGGCCCCGTCAGTCTTCCTCTTCCCCCCAAAACCCAA GGACACCCTCATGATCTCCCGGACCCCTGAGGTCACATGCGTGGTGGTGGACG TGAGCCACGAAGACCCTGAGGTCAAGTTCAACTGGTACGTGGACGGCGTGGAG GTGCATAATGCCAAGACAAAGCCGCGGGAGGAGCAGTACAACAGCACGTACC GTGTGGTCAGCGTCCTCACCGTCCTGCACCAGGACTGGCTGAATGGCAAGGAG TACAAGTGCAAGGTCTCCAACAAAGCCCTCCCAGCCCCCATCGAGAAAACCAT CTCCAAAGCCAAAGGGCAGCCCCGAGAACCACAGGTGTACACCCTGCCCCCAT CCCGGGAGGAGATGACCAAGAACCAGGTCAGCCTGACCTGCCTGGTCAAAGG CTTCTATCCCAGCGACATCGCCGTGGAGTGGGAGAGCAATGGGCAGCCGGAGA ACAACTACAAGACCACGCCTCCCGTGCTGGACTCCGACGGCTCCTTCTTCCTCT ATAGCAAGCTCACCGTGGACAAGAGCAGGTGGCAGCAGGGGAACGTCTTCTC ATGCTCCGTGATGCATGAGGCTCTGCACAACCACTACACGCAGAAGAGCCTCT CCCTGTCCCCGGGTTGA
286	9F6 (A108T)	IgG1.3f HC (无 C 末端 K)	CAGGTGCAGCTGGTGGAGTCTGGGGGAGGCTTGGTCAAGCCTGGAGGGTCCCT GAGACTCTCCTGTGCAGCCTCTGGATTCACCTTCAGTGACTACTACATGAGCTG GATCCGCCAGGCTCCAGGGAAGGGGCTGGAGTGGGTTTCATTCATTAGTGGTG GTGGTAGTACCATATACTACGCAGACTCTGTGAAGGGCCGATTCACCATCTCC AGGGACAACGCCAAGAACTCGCTGTTTCTGCAAATGAACAGCCTGAGAGTCGA GGACACGGCTGTGTATTACTGTGCGAGAGATGGCTATAGCAGTGGCTGGTACT ACTACGGTATGGACGTCTGGGGCCAAGGGACCACGGTCACCGTCTCCTCAGCT AGCACCAAGGGCCCATCGGTCTTCCCCCTGGCACCCTCCTCCAAGAGCACCTCT GGGGGCACAGCGGCCCTGGGCTGCCTGGTCAAGGACTACTTCCCCGAACCGGT GACGGTGTCGTGGAACTCAGGCGCCCTGACCAGCGGCGTGCACACCTTCCCGG CTGTCCTACAGTCCTCAGGACTCTACTCCCTCAGCAGCGTGGTGACCGTGCCCT CCAGCAGCTTGGGCACCCAGACCTACATCTGCAACGTGAATCACAAGCCCAGC AACACCAAGGTGGACAAGAGAGTTGAGCCCAAATCTTGTGACAAAACTCACA CATGCCCACCGTGCCCAGCACCTGAAGCCGAAGGGGCCCCGTCAGTCTTCCTC TTCCCCCCAAAACCCAAGGACACCCTCATGATCTCCCGGACCCCTGAGGTCAC ATGCGTGGTGGTGGACGTGAGCCACGAAGACCCTGAGGTCAAGTTCAACTGGT ACGTGGACGGCGTGGAGGTGCATAATGCCAAGACAAAGCCGCGGGAGGAGCA GTACAACAGCACGTACCGTGTGGTCAGCGTCCTCACCGTCCTGCACCAGGACT GGCTGAATGGCAAGGAGTACAAGTGCAAGGTCTCCAACAAAGCCCTCCCAGCC CCCATCGAGAAAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAACCACAGG TGTACACCCTGCCCCCATCCCGGGAGGAGATGACCAAGAACCAGGTCAGCCTG ACCTGCCTGGTCAAAGGCTTCTATCCCAGCGACATCGCCGTGGAGTGGGAGAG CAATGGGCAGCCGGAGAACAACTACAAGACCACGCCTCCCGTGCTGGACTCCG ACGGCTCCTTCTTCCTCTATAGCAAGCTCACCGTGGACAAGAGCAGGTGGCAG CAGGGGAACGTCTTCTCATGCTCCGTGATGCATGAGGCTCTGCACAACCACTA CACGCAGAAGAGCCTCTCCCTGTCCCCGGGTTGA
287	13A3 (N60Q, D101E)	IgG1.1f HC	CAGCTGCAGCTGCAGGAGTCGGGCCCAGGACTGGTGAAGCCTTCGGAGACCCT GTCCCTCACCTGCACTGTCTCTGGTGGCTCCATCAGCAGTAGAAGTTACTACTG GGGCTGGATCCGCCAGCCCCCAGGGAAGGGGCTGGAGTGGATTGGGAGTATCT ATTATAGTGGGTTCACCTACTACCAACCGTCCCTCAAGAGTCGAGTCACCATAT CCGTTGACACGTCCAAGAACCAGTTCTCCCTGAAGCTGAGCTCTGTGACCGCC GCAGACACGGCTGTGTATTATTGTGCGACAGGGGGGCCCTACGGTGACTACGC CCACTGGTTCGAACCCTGGGGCCAGGGAACCCTGGTCACCGTCTCCTCAGCTA GCACCAAGGGCCCATCGGTCTTCCCCCTGGCACCCTCCTCCAAGAGCACCTCTG GGGGCACAGCGGCCCTGGGCTGCCTGGTCAAGGACTACTTCCCCGAACCGGTG ACGGTGTCGTGGAACTCAGGCGCCCTGACCAGCGGCGTGCACACCTTCCCGGC TGTCCTACAGTCCTCAGGACTCTACTCCCTCAGCAGCGTGGTGACCGTGCCCTC CAGCAGCTTGGGCACCCAGACCTACATCTGCAACGTGAATCACAAGCCCAGCA ACACCAAGGTGGACAAGAGAGTTGAGCCCAAATCTTGTGACAAAACTCACAC ATGCCCACCGTGCCCAGCACCTGAAGCCGAAGGGGCCCCGTCAGTCTTCCTCT TCCCCCCAAAACCCAAGGACACCCTCATGATCTCCCGGACCCCTGAGGTCACA TGCGTGGTGGTGGACGTGAGCCACGAAGACCCTGAGGTCAAGTTCAACTGGTA CGTGGACGGCGTGGAGGTGCATAATGCCAAGACAAAGCCGCGGGAGGAGCAG TACAACAGCACGTACCGTGTGGTCAGCGTCCTCACCGTCCTGCACCAGGACTG GCTGAATGGCAAGGAGTACAAGTGCAAGGTCTCCAACAAAGCCCTCCCAAGC AGCATCGAGAAAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAACCACAGG TGTACACCCTGCCCCCATCCCGGGAGGAGATGACCAAGAACCAGGTCAGCCTG ACCTGCCTGGTCAAAGGCTTCTATCCCAGCGACATCGCCGTGGAGTGGGAGAG CAATGGGCAGCCGGAGAACAACTACAAGACCACGCCTCCCGTGCTGGACTCCG ACGGCTCCTTCTTCCTCTATAGCAAGCTCACCGTGGACAAGAGCAGGTGGCAG CAGGGGAACGTCTTCTCATGCTCCGTGATGCATGAGGCTCTGCACAACCACTA CACGCAGAAGAGCCTCTCCCTGTCCCCGGGTAAATGA

[0739]

SEQ ID	抗体	描述	序列
288	13A3 (N60Q, D101E)	IgG1.1f HC (无 C 末端 K)	CAGCTGCAGCTGCAGGAGTCGGGCCCAGGACTGGTGAAGCCTTCGGAGACCCT GTCCCTCACCTGCACTGTCTCTGGTGGCTCCATCAGCAGTAGAAGTTACTACTG GGGCTGGATCCGCCAGCCCCCAGGGAAGGGGCTGGAGTGGATTGGGAGTATCT ATTATAGTGGGTTCACCTACTACCAACCGTCCCTCAAGAGTCGAGTCACCATAT CCGTTGACACGTCCAAGAACCAGTTCTCCCTGAAGCTGAGCTCTGTGACCGCC GCAGACACGGCTGTGTATTATTGTGCGACAGGGGGGCCCTACGGTGACTACGC CCACTGGTTCGAACCCTGGGGCCAGGGAACCCTGGTCACCGTCTCCTCAGCTA GCACCAAGGGCCCATCGGTCTTCCCCCTGGCACCCTCCTCCAAGAGCACCTCTG GGGGCACAGCGGCCCTGGGCTGCCTGGTCAAGGACTACTTCCCCGAACCGGTG ACGGTGTCGTGGAACTCAGGCGCCCTGACCAGCGGCGTGCACACCTTCCCGGC TGTCCTACAGTCCTCAGGACTCTACTCCCTCAGCAGCGTGGTGACCGTGCCCTC CAGCAGCTTGGGCACCCAGACCTACATCTGCAACGTGAATCACAAGCCCAGCA ACACCAAGGTGGACAAGAGAGTTGAGCCCAAATCTTGTGACAAAACTCACAC ATGCCCACCGTGCCCAGCACCTGAAGCCGAAGGGGCCCCGTCAGTCTTCCTCT TCCCCCCAAAACCCAAGGACACCCTCATGATCTCCCGGACCCCTGAGGTCACA TGCGTGGTGGTGGACGTGAGCCACGAAGACCCTGAGGTCAAGTTCAACTGGTA CGTGGACGGCGTGGAGGTGCATAATGCCAAGACAAAGCCGCGGGAGGAGCAG TACAACAGCACGTACCGTGTGGTCAGCGTCCTCACCGTCCTGCACCAGGACTG GCTGAATGGCAAGGAGTACAAGTGCAAGGTCTCCAACAAAGCCCTCCCAAGC AGCATCGAGAAAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAACCACAGG TGTACACCCTGCCCCCATCCCGGGAGGAGATGACCAAGAACCAGGTCAGCCTG ACCTGCCTGGTCAAAGGCTTCTATCCCAGCGACATCGCCGTGGAGTGGGAGAG CAATGGGCAGCCGGAGAACAACTACAAGACCACGCCTCCCGTGCTGGACTCCG ACGGCTCCTTCTTCCTCTATAGCAAGCTCACCGTGGACAAGAGCAGGTGGCAG CAGGGGAACGTCTTCTCATGCTCCGTGATGCATGAGGCTCTGCACAACCACTA CACGCAGAAGAGCCTCTCCCTGTCCCCGGGTTGA
289	13A3 (N60Q, D101E)	IgG1.3f HC	CAGCTGCAGCTGCAGGAGTCGGGCCCAGGACTGGTGAAGCCTTCGGAGACCCT GTCCCTCACCTGCACTGTCTCTGGTGGCTCCATCAGCAGTAGAAGTTACTACTG GGGCTGGATCCGCCAGCCCCCAGGGAAGGGGCTGGAGTGGATTGGGAGTATCT ATTATAGTGGGTTCACCTACTACCAACCGTCCCTCAAGAGTCGAGTCACCATAT CCGTTGACACGTCCAAGAACCAGTTCTCCCTGAAGCTGAGCTCTGTGACCGCC GCAGACACGGCTGTGTATTATTGTGCGACAGGGGGGCCCTACGGTGACTACGC CCACTGGTTCGAACCCTGGGGCCAGGGAACCCTGGTCACCGTCTCCTCAGCTA GCACCAAGGGCCCATCGGTCTTCCCCCTGGCACCCTCCTCCAAGAGCACCTCTG GGGGCACAGCGGCCCTGGGCTGCCTGGTCAAGGACTACTTCCCCGAACCGGTG ACGGTGTCGTGGAACTCAGGCGCCCTGACCAGCGGCGTGCACACCTTCCCGGC TGTCCTACAGTCCTCAGGACTCTACTCCCTCAGCAGCGTGGTGACCGTGCCCTC CAGCAGCTTGGGCACCCAGACCTACATCTGCAACGTGAATCACAAGCCCAGCA ACACCAAGGTGGACAAGAGAGTTGAGCCCAAATCTTGTGACAAAACTCACAC ATGCCCACCGTGCCCAGCACCTGAAGCCGAAGGGGCCCCGTCAGTCTTCCTCT TCCCCCCAAAACCCAAGGACACCCTCATGATCTCCCGGACCCCTGAGGTCACA TGCGTGGTGGTGGACGTGAGCCACGAAGACCCTGAGGTCAAGTTCAACTGGTA CGTGGACGGCGTGGAGGTGCATAATGCCAAGACAAAGCCGCGGGAGGAGCAG TACAACAGCACGTACCGTGTGGTCAGCGTCCTCACCGTCCTGCACCAGGACTG GCTGAATGGCAAGGAGTACAAGTGCAAGGTCTCCAACAAAGCCCTCCCAGCCC CCATCGAGAAAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAACCACAGGT GTACACCCTGCCCCCATCCCGGGAGGAGATGACCAAGAACCAGGTCAGCCTGA CCTGCCTGGTCAAAGGCTTCTATCCCAGCGACATCGCCGTGGAGTGGGAGAGC AATGGGCAGCCGGAGAACAACTACAAGACCACGCCTCCCGTGCTGGACTCCGA CGGCTCCTTCTTCCTCTATAGCAAGCTCACCGTGGACAAGAGCAGGTGGCAGC AGGGGAACGTCTTCTCATGCTCCGTGATGCATGAGGCTCTGCACAACCACTAC ACGCAGAAGAGCCTCTCCCTGTCCCCGGGTAAATGA
290	13A3 (N60Q, D101E)	IgG1.3f HC (无 C 末端 K)	CAGCTGCAGCTGCAGGAGTCGGGCCCAGGACTGGTGAAGCCTTCGGAGACCCT GTCCCTCACCTGCACTGTCTCTGGTGGCTCCATCAGCAGTAGAAGTTACTACTG GGGCTGGATCCGCCAGCCCCCAGGGAAGGGGCTGGAGTGGATTGGGAGTATCT ATTATAGTGGGTTCACCTACTACCAACCGTCCCTCAAGAGTCGAGTCACCATAT CCGTTGACACGTCCAAGAACCAGTTCTCCCTGAAGCTGAGCTCTGTGACCGCC GCAGACACGGCTGTGTATTATTGTGCGACAGGGGGGCCCTACGGTGACTACGC CCACTGGTTCGAACCCTGGGGCCAGGGAACCCTGGTCACCGTCTCCTCAGCTA GCACCAAGGGCCCATCGGTCTTCCCCCTGGCACCCTCCTCCAAGAGCACCTCTG GGGGCACAGCGGCCCTGGGCTGCCTGGTCAAGGACTACTTCCCCGAACCGGTG ACGGTGTCGTGGAACTCAGGCGCCCTGACCAGCGGCGTGCACACCTTCCCGGC TGTCCTACAGTCCTCAGGACTCTACTCCCTCAGCAGCGTGGTGACCGTGCCCTC CAGCAGCTTGGGCACCCAGACCTACATCTGCAACGTGAATCACAAGCCCAGCA ACACCAAGGTGGACAAGAGAGTTGAGCCCAAATCTTGTGACAAAACTCACAC

[0740]

SEQ ID	抗体	描述	序列
			ATGCCCACCGTGCCCAGCACCTGAAGCCGAAGGGGCCCCGTCAGTCTTCCTCT TCCCCCCAAAACCCAAGGACACCCTCATGATCTCCCGGACCCCTGAGGTCACA TGCGTGGTGGTGGACGTGAGCCACGAAGACCCTGAGGTCAAGTTCAACTGGTA CGTGGACGGCGTGGAGGTGCATAATGCCAAGACAAAGCCGCGGGAGGAGCAG TACAACAGCACGTACCGTGTGGTCAGCGTCCTCACCGTCCTGCACCAGGACTG GCTGAATGGCAAGGAGTACAAGTGCAAGGTCTCCAACAAAGCCCTCCCAGCCC CCATCGAGAAAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAACCACAGGT GTACACCCTGCCCCCATCCCGGGAGGAGATGACCAAGAACCAGGTCAGCCTGA CCTGCCTGGTCAAAGGCTTCTATCCCAGCGACATCGCCGTGGAGTGGGAGAGC AATGGGCAGCCGGAGAACAACTACAAGACCACGCCTCCCGTGCTGGACTCCGA CGGCTCCTTCTTCCTCTATAGCAAGCTCACCGTGGACAAGAGCAGGTGGCAGC AGGGGAACGTCTTCTCATGCTCCGTGATGCATGAGGCTCTGCACAACCACTAC ACGCAGAAGAGCCTCTCCCTGTCCCCGGGTTGA
291	13A3 (N60Q, D101E) (TIM3.18)	IgG1.3f (T168C) (无 C 末端 K)	CAGCTGCAGCTGCAGGAGTCGGGCCCAGGACTGGTGAAGCCTTCGGAGACCCT GTCCCTCACCTGCACTGTCTCTGGTGGCTCCATCAGCAGTAGAAGTTACTACTG GGGCTGGATTCGCCAGCCCCCAGGGAAGGGGCTGGAGTGGATTGGGAGTATCT ATTATAGTGGGTTCACCTACTACCAACCGTCCCTCAAGAGTCGAGTCACCATAT CCGTTGACACGTCCAAGAACCAGTTCTCCCTGAAGCTGAGCTCTGTGACCGCC GCAGACACGGCTGTGTATTATTGTGCGACAGGGGGGCCCTACGGTGACTACGC CCACTGGTTCGAACCCTGGGGCCAGGGAACCCTGGTCACCGTCTCCTCAGCTA GCACCAAGGGCCCATCGGTCTTCCCCCTGGCACCCTCCTCCAAGAGCACCTCTG GGGGCACAGCGGCCCTGGGCTGCCTGGTCAAGGACTACTTCCCCGAACCGGTG ACGGTGTCGTGGAACTCAGGCGCCCTGACCAGCGGCGTGCACACCTTCCCGGC TGTCCTACAGTCCTCAGGACTCTACTCCCTCAGCAGCGTGGTGACCGTGCCCTC CAGCAGCTTGGGCACCCAGACCTACATCTGCAACGTGAATCACAAGCCCAGCA ACACCAAGGTGGACAAGAGAGTTGAGCCCAAATCTTGTGACAAAACTCACAC ATGCCCACCGTGCCCAGCACCTGAAGCCGAAGGGGCCCCGTCAGTCTTCCTCT TCCCCCCAAAACCCAAGGACACCCTCATGATCTCCCGGACCCCTGAGGTCACA TGCGTGGTGGTGGACGTGAGCCACGAAGACCCTGAGGTCAAGTTCAACTGGTA CGTGGACGGCGTGGAGGTGCATAATGCCAAGACAAAGCCGCGGGAGGAGCAG TACAACAGCACGTACCGTGTGGTCAGCGTCCTCACCGTCCTGCACCAGGACTG GCTGAATGGCAAGGAGTACAAGTGCAAGGTCTCCAACAAAGCCCTCCCAGCCC CCATCGAGAAAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAACCACAGGT GTACACCCTGCCCCCATCCCGGGAGGAGATGACCAAGAACCAGGTCAGCCTGA CCTGCCTGGTCAAAGGCTTCTATCCCAGCGACATCGCCGTGGAGTGGGAGAGC AATGGGCAGCCGGAGAACAACTACAAGACCACGCCTCCCGTGCTGGACTCCGA CGGCTCCTTCTTCCTCTATAGCAAGCTCACCGTGGACAAGAGCAGGTGGCAGC AGGGGAACGTCTTCTCATGCTCCGTGATGCATGAGGCTCTGCACAACCACTAC ACGCAGAAGAGCCTCTCCCTGTCCCCGGGTTGA
292	13A3 (N60Q, D101E) (TIM3.18)	带信号肽(下划线)的 IgG1.3f HC	MRAWIFFLLCLAGRALAQLQLQESGPGLVKPSETLSLTCTVSGGSISSRSYYWGWI RQPPGKGLEWIGSIYYSGFTYYQPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVY YCATGGPYGDYAHWFEPWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGC LVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYIC NVNHKPSNTKVDKRVEPKSCDKTHTCPPCPAPEAEGAPSVFLFPPKPKDTLMISRT PEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSL TCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQG NVFSCSVMHEALHNHYTQKSLSLSPGK*
293	13A3 (N60Q, D101E) (TIM3.18)	带信号肽(下划线)的 IgG1.3f HC (无 C 末端 K)	MRAWIFFLLCLAGRALAQLQLQESGPGLVKPSETLSLTCTVSGGSISSRSYYWGWI RQPPGKGLEWIGSIYYSGFTYYQPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVY YCATGGPYGDYAHWFEPWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGC LVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYIC NVNHKPSNTKVDKRVEPKSCDKTHTCPPCPAPEAEGAPSVFLFPPKPKDTLMISRT PEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSL TCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQG NVFSCSVMHEALHNHYTQKSLSLSPG*
294	13A3 (N60Q, D101E) (TIM3.18)	带信号肽(下划线)的 IgG1.3f HC	ATGAGGGCTTGGATCTTCTTTCTGCTCTGCCTGGCCGGGAGAGCGCTCGCACAG CTGCAGCTGCAGGAGTCGGGCCCAGGACTGGTGAAGCCTTCGGAGACCCTGTC CCTCACCTGCACTGTCTCTGGTGGCTCCATCAGCAGTAGAAGTTACTACTGGGG CTGGATCCGCCAGCCCCCAGGGAAGGGGCTGGAGTGGATTGGGAGTATCTATT ATAGTGGGTTCACCTACTACCAACCGTCCCTCAAGAGTCGAGTCACCATATCC GTTGACACGTCCAAGAACCAGTTCTCCCTGAAGCTGAGCTCTGTGACCGCCGC AGACACGGCTGTGTATTATTGTGCGACAGGGGGGCCCTACGGTGACTACGCCC

[0741]

SEQ ID	抗体	描述	序列
			ACTGGTTCGAACCCTGGGGCCAGGGAACCCTGGTCACCGTCTCCTCAGCTAGC ACCAAGGGCCCATCGGTCTTCCCCCTGGCACCCTCCTCCAAGAGCACCTCTGG GGGCACAGCGGCCCTGGGCTGCCTGGTCAAGGACTACTTCCCCGAACCGGTGA CGGTGTCGTGGAACTCAGGCGCCCTGACCAGCGGCGTGCACACCTTCCCGGCT GTCCTACAGTCCTCAGGACTCTACTCCCTCAGCAGCGTGGTGACCGTGCCCTCC AGCAGCTTGGGCACCCAGACCTACATCTGCAACGTGAATCACAAGCCCAGCAA CACCAAGGTGGACAAGAGAGTTGAGCCCAAATCTTGTGACAAAACTCACACAT GCCCACCGTGCCCAGCACCTGAAGCCGAAGGGGCCCCGTCAGTCTTCCTCTTC CCCCCAAAACCCAAGGACACCCTCATGATCTCCCGGACCCCTGAGGTCACATG CGTGGTGGTGGACGTGAGCCACGAAGACCCTGAGGTCAAGTTCAACTGGTACG TGGACGGCGTGGAGGTGCATAATGCCAAGACAAAGCCGCGGGAGGAGCAGTA CAACAGCACGTACCGTGTGGTCAGCGTCCTCACCGTCCTGCACCAGGACTGGC TGAATGGCAAGGAGTACAAGTGCAAGGTCTCCAACAAAGCCCTCCCAGCCCCC ATCGAGAAAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAACCACAGGTGT ACACCCTGCCCCCATCCCGGGAGGAGATGACCAAGAACCAGGTCAGCCTGACC TGCCTGGTCAAAGGCTTCTATCCCAGCGACATCGCCGTGGAGTGGGAGAGCAA TGGGCAGCCGGAGAACAACTACAAGACCACGCCTCCCGTGCTGGACTCCGACG GCTCCTTCTTCCTCTATAGCAAGCTCACCGTGGACAAGAGCAGGTGGCAGCAG GGGAACGTCTTCTCATGCTCCGTGATGCATGAGGCTCTGCACAACCACTACAC GCAGAAGAGCCTCTCCCTGTCCCCGGGTAAATGA
295	13A3 (N60Q, D101E) (TIM3.18)	带信号肽(下划线)的 IgG1.3f HC (无 C 末端 K)	ATGAGGGCTTGGATCTTCTTTCTGCTCTGCCTGGCCGGGAGAGCGCTCGCACAG CTGCAGCTGCAGGAGTCGGGCCCAGGACTGGTGAAGCCTTCGGAGACCCTGTC CCTCACCTGCACTGTCTCTGGTGGCTCCATCAGCAGTAGAAGTTACTACTGGGG CTGGATCCGCCAGCCCCCAGGGAAGGGGCTGGAGTGGATTGGGAGTATCTATT ATAGTGGGTTCACCTACTACCAACCGTCCCTCAAGAGTCGAGTCACCATATCC GTTGACACGTCCAAGAACCAGTTCTCCCTGAAGCTGAGCTCTGTGACCGCCGC AGACACGGCTGTGTATTATTGTGCGACAGGGGGGCCCTACGGTGACTACGCCC ACTGGTTCGAACCCTGGGGCCAGGGAACCCTGGTCACCGTCTCCTCAGCTAGC ACCAAGGGCCCATCGGTCTTCCCCCTGGCACCCTCCTCCAAGAGCACCTCTGG GGGCACAGCGGCCCTGGGCTGCCTGGTCAAGGACTACTTCCCCGAACCGGTGA CGGTGTCGTGGAACTCAGGCGCCCTGACCAGCGGCGTGCACACCTTCCCGGCT GTCCTACAGTCCTCAGGACTCTACTCCCTCAGCAGCGTGGTGACCGTGCCCTCC AGCAGCTTGGGCACCCAGACCTACATCTGCAACGTGAATCACAAGCCCAGCAA CACCAAGGTGGACAAGAGAGTTGAGCCCAAATCTTGTGACAAAACTCACACAT GCCCACCGTGCCCAGCACCTGAAGCCGAAGGGGCCCCGTCAGTCTTCCTCTTC CCCCCAAAACCCAAGGACACCCTCATGATCTCCCGGACCCCTGAGGTCACATG CGTGGTGGTGGACGTGAGCCACGAAGACCCTGAGGTCAAGTTCAACTGGTACG TGGACGGCGTGGAGGTGCATAATGCCAAGACAAAGCCGCGGGAGGAGCAGTA CAACAGCACGTACCGTGTGGTCAGCGTCCTCACCGTCCTGCACCAGGACTGGC TGAATGGCAAGGAGTACAAGTGCAAGGTCTCCAACAAAGCCCTCCCAGCCCCC ATCGAGAAAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAACCACAGGTGT ACACCCTGCCCCCATCCCGGGAGGAGATGACCAAGAACCAGGTCAGCCTGACC TGCCTGGTCAAAGGCTTCTATCCCAGCGACATCGCCGTGGAGTGGGAGAGCAA TGGGCAGCCGGAGAACAACTACAAGACCACGCCTCCCGTGCTGGACTCCGACG GCTCCTTCTTCCTCTATAGCAAGCTCACCGTGGACAAGAGCAGGTGGCAGCAG GGGAACGTCTTCTCATGCTCCGTGATGCATGAGGCTCTGCACAACCACTACAC GCAGAAGAGCCTCTCCCTGTCCCCGGGTTGA
296	13A3 (N60Q, D101E) (TIM3.18)	有信号序列(下划线)的 IgG1.3f HC (T168C)	ATGAGGGCTTGGATCTTCTTTCTGCTCTGCCTGGCCGGGAGAGCGCTCGCACAG CTGCAGCTGCAGGAGTCGGGCCCAGGACTGGTGAAGCCTTCGGAGACCCTGTC CCTCACCTGCACTGTCTCTGGTGGCTCCATCAGCAGTAGAAGTTACTACTGGGG CTGGATTCGCCAGCCCCCAGGGAAGGGGCTGGAGTGGATTGGGAGTATCTATT ATAGTGGGTTCACCTACTACCAACCGTCCCTCAAGAGTCGAGTCACCATATCC GTTGACACGTCCAAGAACCAGTTCTCCCTGAAGCTGAGCTCTGTGACCGCCGC AGACACGGCTGTGTATTATTGTGCGACAGGGGGGCCCTACGGTGACTACGCCC ACTGGTTCGAACCCTGGGGCCAGGGAACCCTGGTCACCGTCTCCTCAGCTAGC ACCAAGGGCCCATCGGTCTTCCCCCTGGCACCCTCCTCCAAGAGCACCTCTGG GGGCACAGCGGCCCTGGGCTGCCTGGTCAAGGACTACTTCCCCGAACCGGTGA CGGTGTCGTGGAACTCAGGCGCCCTGACCAGCGGCGTGCACACCTTCCCGGCT GTCCTACAGTCCTCAGGACTCTACTCCCTCAGCAGCGTGGTGACCGTGCCCTCC AGCAGCTTGGGCACCCAGACCTACATCTGCAACGTGAATCACAAGCCCAGCAA CACCAAGGTGGACAAGAGAGTTGAGCCCAAATCTTGTGACAAAACTCACACAT GCCCACCGTGCCCAGCACCTGAAGCCGAAGGGGCCCCGTCAGTCTTCCTCTTC CCCCCAAAACCCAAGGACACCCTCATGATCTCCCGGACCCCTGAGGTCACATG CGTGGTGGTGGACGTGAGCCACGAAGACCCTGAGGTCAAGTTCAACTGGTACG TGGACGGCGTGGAGGTGCATAATGCCAAGACAAAGCCGCGGGAGGAGCAGTA

[0742]

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297	13A3 (N60Q, D101E) (TIM3.18)	有信号序列(下划线)的IgG1.3f HC (T168C)(无C末端K)	ATGAGGGCTTGGATCTTCTTTCTGCTCTGCCTGGCCGGGAGAGCGCTCGCACAG CTGCAGCTGCAGGAGTCGGGCCCAGGACTGGTGAAGCCTTCGGAGACCCTGTC CCTCACCTGCACTGTCTCTGGTGGCTCCATCAGCAGTAGAAGTTACTACTGGGG CTGGATTCGCCAGCCCCCAGGGAAGGGGCTGGAGTGGATTGGGAGTATCTATT ATAGTGGGTTCACCTACTACCAACCGTCCCTCAAGAGTCGAGTCACCATATCC GTTGACACGTCCAAGAACCAGTTCTCCCTGAAGCTGAGCTCTGTGACCGCCGC AGACACGGCTGTGTATTATTGTGCGACAGGGGGGCCCTACGGTGACTACGCCC ACTGGTTCGAACCCTGGGGCCAGGGAACCCTGGTCACCGTCTCCTCAGCTAGC ACCAAGGGCCCATCGGTCTTCCCCCTGGCACCCTCCTCCAAGAGCACCTCTGG GGGCACAGCGGCCCTGGGCTGCCTGGTCAAGGACTACTTCCCCGAACCGGTGA CGGTGTCGTGGAACTCAGGCGCCCTGACCAGCGGCGTGCACACCTTCCCGGCT GTCCTACAGTCCTCAGGACTCTACTCCCTCAGCAGCGTGGTGACCGTGCCCTCC AGCAGCTTGGGCACCCAGACCTACATCTGCAACGTGAATCACAAGCCCAGCAA CACCAAGGTGGACAAGAGAGTTGAGCCCAAATCTTGTGACAAAACTCACACAT GCCCACCGTGCCCAGCACCTGAAGCCGAAGGGGCCCCGTCAGTCTTCCTCTTC CCCCCAAAACCCAAGGACACCCTCATGATCTCCCGGACCCCTGAGGTCACATG CGTGGTGGTGGACGTGAGCCACGAAGACCCTGAGGTCAAGTTCAACTGGTACG TGGACGGCGTGGAGGTGCATAATGCCAAGACAAAGCCGCGGGAGGAGCAGTA CAACAGCACGTACCGTGTGGTCAGCGTCCTCACCGTCCTGCACCAGGACTGGC TGAATGGCAAGGAGTACAAGTGCAAGGTCTCCAACAAAGCCCTCCCAGCCCCC ATCGAGAAAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAACCACAGGTGT ACACCCTGCCCCCATCCCGGGAGGAGATGACCAAGAACCAGGTCAGCCTGACC TGCCTGGTCAAAGGCTTCTATCCCAGCGACATCGCCGTGGAGTGGGAGAGCAA TGGGCAGCCGGAGAACAACTACAAGACCACGCCTCCCGTGCTGGACTCCGACG GCTCCTTCTTCCTCTATAGCAAGCTCACCGTGGACAAGAGCAGGTGGCAGCAG GGGAACGTCTTCTCATGCTCCGTGATGCATGAGGCTCTGCACAACCACTACAC GCAGAAGAGCCTCTCCCTGTCCCCGGGTTGA
298	13A3 (N60Q, D101E) (TIM3.18)	有信号序列(下划线)的LC	MRAWIFFLLCLAGRALAEIVLTQSPGTLSLSPGERATLSCRASQSVSSSYLAWYQQ KPGQAPRLLIYGASSRATGIPDRFSGSGSGTDFTLTISRLEPEDFAVYYCQQYGSSPI TFGQGTRLEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDN ALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKS FNRGEC*
299	13A3 (N60Q, D101E) (TIM3.18)	有信号序列(下划线)的LC	ATGAGGGCTTGGATCTTCTTTCTGCTCTGCCTGGCCGGGCGCGCCTTGGCCGAA ATTGTGTTGACGCAGTCTCCAGGCACCCTGTCTTTGTCTCCAGGGGAAAGAGCC ACCCTCTCCTGCAGGGCCAGTCAGAGTGTTAGCAGCAGCTACTTAGCCTGGTA CCAGCAGAAACCTGGCCAGGCTCCCAGGCTCCTCATCTATGGTGCATCCAGCA GGGCCACTGGCATCCCAGACAGGTTCAGTGGCAGTGGGTCTGGGACAGACTTC ACTCTCACCATCAGCAGACTGGAGCCTGAAGATTTTGCAGTGTATTACTGTCAG CAGTATGGTAGCTCACCGATCACCTTCGGCCAAGGGACACGACTGGAGATTAA ACGTACGGTGGCTGCACCATCTGTCTTCATCTTCCCGCCATCTGATGAGCAGTT GAAATCTGGAACTGCCTCTGTTGTGTGCCTGCTGAATAACTTCTATCCCAGAGA GGCCAAAGTACAGTGGAAGGTGGATAACGCCCTCCAATCGGGTAACTCCCAGG AGAGTGTCACAGAGCAGGACAGCAAGGACAGCACCTACAGCCTCAGCAGCAC CCTGACGCTGAGCAAAGCAGACTACGAGAAACACAAAGTCTACGCCTGCGAA GTCACCCATCAGGGCCTGAGCTCGCCCGTCACAAAGAGCTTCAACAGGGGAGA GTGTTAG

[0743] 本PCT申请要求2017年8月28日提交的美国临时申请号62/551,137的优先权,所述文献通过引用方式完整并入本文。

序列表

<110> 百时美施贵宝公司(BRISTOL-MYERS SQUIBB COMPANY)
<120> 用于治疗和诊断癌症的 TIM-3 拮抗剂
<130> 3338.093PC01/ELE/C-K/DKC
<150> 62/551,137
<151> 2017-08-28
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35 40 45
Trp Ile Gly Ser Ile Tyr Tyr Ser Gly Phe Thr Tyr Tyr Asn Pro Ser
50 55 60
Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
65 70 75 80
Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
85 90 95
Cys Ala Thr Gly Gly Pro Tyr Gly Asp Tyr Ala His Trp Phe Asp Pro
100 105 110
Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

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35 40 45
Gly Tyr Ile His Tyr Ser Gly Ser Thr Asn Tyr Asn Ser Ser Leu Lys

50 55 60
Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe Ser Leu
65 70 75 80
Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala
85 90 95
Arg Asp Thr Gly Tyr Tyr Gly Met Asp Ile Trp Gly Gln Gly Thr Thr
100 105 110
Val Thr Val Ser Ser
115

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20 25 30
Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile
35 40 45

[0002] Gly Tyr Ile His Tyr Thr Gly Ser Thr Asn Tyr Asn Pro Ser Leu Lys
50 55 60
Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe Ser Leu
65 70 75 80
Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala
85 90 95
Thr Asp Thr Gly Tyr Tyr Gly Met Asp Val Trp Gly Gln Gly Thr Thr
100 105 110
Val Thr Val Ser Ser
115

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

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

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Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp Tyr
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Tyr Met Ser Trp Ile Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
[0003] 35 40 45
Ser Phe Ile Ser Gly Gly Gly Ser Thr Ile Tyr Tyr Ala Asp Ser Val
50 55 60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Phe
65 70 75 80
Leu Gln Met Asn Ser Leu Arg Val Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95
Ala Arg Asp Gly Tyr Ser Ser Gly Trp Tyr Tyr Tyr Gly Met Asp Val
100 105 110
Trp Gly Gln Gly Thr Ala Val Thr Val Ser Ser
115 120

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Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
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Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp Tyr
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Tyr Met Ser Trp Ile Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val

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

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

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

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Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Arg
20 25 30

[0005]

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

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

Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
85 90 95
Cys Ala Thr Gly Gly Pro Tyr Gly Asp Tyr Ala His Trp Phe Asp Pro
100 105 110
Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

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[0006]
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Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Arg
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Ser Tyr Tyr Trp Gly Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu
35 40 45
Trp Ile Gly Ser Ile Tyr Tyr Ser Gly Phe Thr Tyr Tyr Asn Pro Ser
50 55 60
Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
65 70 75 80
Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
85 90 95

Cys Ala Thr Gly Gly Pro Tyr Gly Asp Tyr Ala His Trp Phe Glu Pro
100 105 110
Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

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

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[0007] <400> 13

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

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

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35 40 45
Gly Tyr Ile His Tyr Ser Gly Ser Thr Asn Tyr Asn Pro Ser Leu Lys
50 55 60
Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe Ser Leu
65 70 75 80
Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala
85 90 95
Arg Asp Thr Gly Tyr Tyr Gly Met Asp Ile Trp Gly Gln Gly Thr Thr
100 105 110
Val Thr Val Ser Ser
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<210> 17
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Tyr Met Ser Trp Ile Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45
Ser Phe Ile Ser Gly Gly Gly Ser Thr Ile Tyr Tyr Ala Asp Ser Val
50 55 60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Phe
65 70 75 80
Leu Gln Met Asn Ser Leu Arg Val Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95
Ala Arg Asp Gly Tyr Ser Ser Gly Trp Tyr Tyr Tyr Gly Met Asp Val
100 105 110
Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
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Ser Tyr Tyr Trp Gly Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu
35 40 45
Trp Ile Gly Ser Ile Tyr Tyr Ser Gly Phe Thr Tyr Tyr Gln Pro Ser
50 55 60
Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
65 70 75 80
Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
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Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
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20 25 30
Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu
35 40 45
Ile Tyr Gly Ala Ser Ser Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser
50 55 60
Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu
65 70 75 80
Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr Gly Ser Ser Pro
85 90 95
Ile Thr Phe Gly Gln Gly Thr Arg Leu Glu Ile Lys
100 105
<210> 20
<211> 108
<212> PRT
<213> 人工序列
<220>

<223> VL
<400> 20
Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly
1 5 10 15
Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Ser
20 25 30
Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu
35 40 45
Ile Tyr Gly Ala Ser Ser Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser
50 55 60
Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu
65 70 75 80
Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr Gly Ser Ser Pro
85 90 95
Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
100 105
<210> 21
<211> 107
<212> PRT
<213> 人工序列
<220>
<223> VL

[0011]

<400> 21
Ala Ile Gln Leu Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Ser Ser Ala
20 25 30
Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45
Tyr Asp Ala Ser Ser Leu Glu Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60
Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80
Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Phe Asn Ser Tyr Pro Arg
85 90 95
Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
100 105
<210> 22
<211> 107
<212> PRT
<213> 人工序列
<220>
<223> VL
<400> 22
Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly

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

Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr Gly Ser Ser Leu
85 90 95
Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
100 105

<210> 23
<211> 7
<212> PRT
<213> 人工序列
<220>
<223> CDR1 (VH)
<400> 23
Ser Arg Ser Tyr Tyr Trp Gly
1 5

[0012]

<210> 24
<211> 5
<212> PRT
<213> 人工序列
<220>
<223> CDR1 (VH)
<400> 24
Arg His Tyr Trp Asn
1 5

<210> 25
<211> 5
<212> PRT
<213> 人工序列
<220>
<223> CDR1 (VH)
<400> 25
Arg Tyr Tyr Trp Ser
1 5

<210> 26
<211> 5
<212> PRT
<213> 人工序列

<220>
<223> CDR1 (VH)
<400> 26
Ser Tyr Tyr Met His
1 5
<210> 27
<211> 5
<212> PRT
<213> 人工序列
<220>
<223> CDR1 (VH)
<400> 27
Asp Tyr Tyr Met Ser
1 5
<210> 28
<211> 16
<212> PRT
<213> 人工序列
<220>
<223> CDR2 (VH)
<400> 28
Ser Ile Tyr Tyr Ser Gly Phe Thr Tyr Tyr Asn Pro Ser Leu Lys Ser
[0013] 1 5 10 15
<210> 29
<211> 16
<212> PRT
<213> 人工序列
<220>
<223> CDR2 (VH)
<400> 29
Tyr Ile His Tyr Ser Gly Ser Thr Asn Tyr Asn Ser Ser Leu Lys Ser
1 5 10 15
<210> 30
<211> 16
<212> PRT
<213> 人工序列
<220>
<223> CDR2 (VH)
<400> 30
Tyr Ile His Tyr Thr Gly Ser Thr Asn Tyr Asn Pro Ser Leu Lys Ser
1 5 10 15
<210> 31
<211> 17
<212> PRT
<213> 人工序列

<220>
<223> CDR2 (VH)
<400> 31
Ile Ile Asn Pro Arg Gly Asp Ser Ile Ile Tyr Ala Gln Lys Phe Gln
1 5 10 15
Gly

<210> 32
<211> 17
<212> PRT
<213> 人工序列
<220>
<223> CDR2 (VH)
<400> 32
Phe Ile Ser Gly Gly Gly Ser Thr Ile Tyr Tyr Ala Asp Ser Val Lys
1 5 10 15
Gly

<210> 33
<211> 17
<212> PRT
<213> 人工序列
[0014] <220>
<223> CDR2 (VH)
<400> 33
Phe Ile Ser Thr Ser Gly Ser Ile Ile Tyr Tyr Ala Asp Ser Val Lys
1 5 10 15
Gly

<210> 34
<211> 17
<212> PRT
<213> 人工序列
<220>
<223> CDR2 (VH)
<400> 34
Phe Ile Ser Ser Ser Gly Ser Ile Ile Tyr Tyr Ala Asp Ser Val Lys
1 5 10 15
Gly

<210> 35
<211> 16
<212> PRT
<213> 人工序列
<220>

<223> CDR2 (VH)
<400> 35
Ser Ile Tyr Tyr Ser Gly Phe Thr Tyr Tyr Gln Pro Ser Leu Lys Ser
1 5 10 15
<210> 36
<211> 16
<212> PRT
<213> 人工序列
<220>
<223> CDR2 (VH)
<400> 36
Ser Ile Tyr Tyr Ser Gly Phe Thr Tyr Tyr Ser Pro Ser Leu Lys Ser
1 5 10 15
<210> 37
<211> 16
<212> PRT
<213> 人工序列
<220>
<223> CDR2 (VH)
<400> 37
Ser Ile Tyr Tyr Ser Gly Phe Thr Tyr Tyr Ala Pro Ser Leu Lys Ser
1 5 10 15

[0015]

<210> 38
<211> 16
<212> PRT
<213> 人工序列
<220>
<223> CDR2 (VH)
<400> 38
Tyr Ile His Tyr Ser Gly Ser Thr Asn Tyr Asn Pro Ser Leu Lys Ser
1 5 10 15
<210> 39
<211> 13
<212> PRT
<213> 人工序列
<220>
<223> CDR3 (VH)
<400> 39
Gly Gly Pro Tyr Gly Asp Tyr Ala His Trp Phe Asp Pro
1 5 10
<210> 40
<211> 9
<212> PRT
<213> 人工序列
<220>

<223> CDR3 (VH)
<400> 40
Asp Thr Gly Tyr Tyr Gly Met Asp Ile
1 5
<210> 41
<211> 9
<212> PRT
<213> 人工序列
<220>
<223> CDR3 (VH)
<400> 41
Asp Thr Gly Tyr Tyr Gly Met Asp Val
1 5
<210> 42
<211> 14
<212> PRT
<213> 人工序列
<220>
<223> CDR3 (VH)
<400> 42
Asp Phe Tyr Gly Ser Gly Asn Tyr Tyr Tyr Gly Met Asp Val
1 5 10

[0016]
<210> 43
<211> 14
<212> PRT
<213> 人工序列
<220>
<223> CDR3 (VH)
<400> 43
Asp Gly Tyr Ser Ser Gly Trp Tyr Tyr Tyr Gly Met Asp Val
1 5 10
<210> 44
<211> 15
<212> PRT
<213> 人工序列
<220>
<223> CDR3 (VH)
<400> 44
Glu Gly Tyr Ser Ser Ser Trp Ser Tyr Tyr Tyr Gly Met Asp Val
1 5 10 15
<210> 45
<211> 14
<212> PRT
<213> 人工序列
<220>

<223> CDR3 (VH)
<400> 45
Asp Gly Tyr Ser Ser Gly Trp Glu Tyr Tyr Gly Met Asp Val
1 5 10
<210> 46
<211> 13
<212> PRT
<213> 人工序列
<220>
<223> CDR3 (VH)
<400> 46
Gly Gly Pro Tyr Gly Asp Tyr Ala His Trp Phe Glu Pro
1 5 10
<210> 47
<211> 13
<212> PRT
<213> 人工序列
<220>
<223> CDR3 (VH)
<400> 47
Gly Gly Pro Tyr Gly Asp Tyr Ala His Trp Phe Asp Val
1 5 10

[0017]
<210> 48
<211> 13
<212> PRT
<213> 人工序列
<220>
<223> CDR3 (VH)
<400> 48
Gly Gly Pro Tyr Gly Asp Tyr Ala His Trp Phe Asp Tyr
1 5 10
<210> 49
<211> 13
<212> PRT
<213> 人工序列
<220>
<223> CDR3 (VH)
<400> 49
Gly Gly Pro Tyr Gly Asp Tyr Ala His Trp Phe Asp Leu
1 5 10
<210> 50
<211> 12
<212> PRT
<213> 人工序列
<220>

<223> CDR1 (VL)
<400> 50
Arg Ala Ser Gln Ser Val Ser Ser Ser Tyr Leu Ala
1 5 10
<210> 51
<211> 11
<212> PRT
<213> 人工序列
<220>
<223> CDR1 (VL)
<400> 51
Arg Ala Ser Gln Gly Ile Ser Ser Ala Leu Ala
1 5 10
<210> 52
<211> 7
<212> PRT
<213> 人工序列
<220>
<223> CDR2 (VL)
<400> 52
Gly Ala Ser Ser Arg Ala Thr
1 5

[0018]

<210> 53
<211> 7
<212> PRT
<213> 人工序列
<220>
<223> CDR2 (VL)
<400> 53
Asp Ala Ser Ser Leu Glu Ser
1 5
<210> 54
<211> 9
<212> PRT
<213> 人工序列
<220>
<223> CDR3 (VL)
<400> 54
Gln Gln Tyr Gly Ser Ser Pro Ile Thr
1 5
<210> 55
<211> 9
<212> PRT
<213> 人工序列
<220>

<223> CDR3 (VL)
<400> 55
Gln Gln Tyr Gly Ser Ser Pro Leu Thr
1 5
<210> 56
<211> 9
<212> PRT
<213> 人工序列
<220>
<223> CDR3 (VL)
<400> 56
Gln Gln Phe Asn Ser Tyr Pro Arg Thr
1 5
<210> 57
<211> 8
<212> PRT
<213> 人工序列
<220>
<223> CDR3 (VL)
<400> 57
Gln Gln Tyr Gly Ser Ser Leu Thr
1 5

[0019] <210> 58
<211> 330
<212> PRT
<213> 智人(Homo sapiens)
<400> 58
Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys
1 5 10 15
Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr
20 25 30
Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser
35 40 45
Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser
50 55 60
Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr
65 70 75 80
Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys
85 90 95
Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys
100 105 110
Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro
115 120 125
Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys
130 135 140

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

[0020] Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
325 330

<210> 59
<211> 330
<212> PRT
<213> 人工序列
<220>
<223> 人 IgG1 (同种异型变体)
<400> 59

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

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

[0021]

Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn
290 295 300
Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr
305 310 315 320
Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
325 330

<210> 60
<211> 330
<212> PRT
<213> 智人(Homo sapiens)
<400> 60

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

[0022]

```
Arg Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys
            100                 105                 110
Pro Ala Pro Glu Ala Glu Gly Ala Pro Ser Val Phe Leu Phe Pro Pro
        115                 120                 125
Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys
    130                 135                 140
Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp
145                 150                 155                 160
Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu
                165                 170                 175
Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu
            180                 185                 190
His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn
        195                 200                 205
Lys Ala Leu Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly
    210                 215                 220
Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu
225                 230                 235                 240
Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr
                245                 250                 255
Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn
            260                 265                 270
Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe
        275                 280                 285
Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn
    290                 295                 300
Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr
305                 310                 315                 320
Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
                325                 330
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<210> 61
<211> 330
<212> PRT
<213> 人工序列
<220>
<223> IgG1.3 恒定结构域（用于抗 TIM3 抗体中）
<400> 61

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

[0023] Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr
245 250 255
Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn
260 265 270
Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe
275 280 285
Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn
290 295 300
Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr
305 310 315 320
Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
325 330

<210> 62
<400> 62
000
<210> 63
<211> 327
<212> PRT
<213> 智人(Homo sapiens)
<400> 63
Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg
1 5 10 15
Ser Thr Ser Glu Ser Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr

20 25 30

Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser
35 40 45

Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser
50 55 60

Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Lys Thr
65 70 75 80

Tyr Thr Cys Asn Val Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys
85 90 95

Arg Val Glu Ser Lys Tyr Gly Pro Pro Cys Pro Ser Cys Pro Ala Pro
100 105 110

Glu Phe Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys
115 120 125

Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val
130 135 140

Asp Val Ser Gln Glu Asp Pro Glu Val Gln Phe Asn Trp Tyr Val Asp
145 150 155 160

Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe
165 170 175

Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp
180 185 190

[0024] Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu
195 200 205

Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg
210 215 220

Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Gln Glu Glu Met Thr Lys
225 230 235 240

Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp
245 250 255

Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys
260 265 270

Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser
275 280 285

Arg Leu Thr Val Asp Lys Ser Arg Trp Gln Glu Gly Asn Val Phe Ser
290 295 300

Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser
305 310 315 320

Leu Ser Leu Ser Leu Gly Lys
325

<210> 64
<211> 107
<212> PRT
<213> 人工序列
<220>

<223> 人 IgG1 κ 轻链
<400> 64
Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu
1 5 10 15
Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe
20 25 30
Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln
35 40 45
Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser
50 55 60
Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu
65 70 75 80
Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser
85 90 95
Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
100 105
<210> 65
<211> 5
<212> PRT
<213> 人工序列
<220>
<223> LSPGK (重链 C 末端)

[0025] <400> 65
Leu Ser Pro Gly Lys
1 5
<210> 66
<211> 4
<212> PRT
<213> 人工序列
<220>
<223> LSPG (重链 C 末端)
<400> 66
Leu Ser Pro Gly
1
<210> 67
<211> 3
<212> PRT
<213> 人工序列
<220>
<223> LSP (重链 C 末端)
<400> 67
Leu Ser Pro
1
<210> 68
<211> 453

<212> PRT
<213> 人工序列
<220>
<223> IgG1.1f HC
<400> 68

Gln Leu Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu
1 5 10 15
Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Arg
20 25 30
Ser Tyr Tyr Trp Gly Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu
35 40 45
Trp Ile Gly Ser Ile Tyr Tyr Ser Gly Phe Thr Tyr Tyr Asn Pro Ser
50 55 60
Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
65 70 75 80
Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
85 90 95
Cys Ala Thr Gly Gly Pro Tyr Gly Asp Tyr Ala His Trp Phe Asp Pro
100 105 110
Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly
115 120 125
Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly
[0026] 130 135 140
Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val
145 150 155 160
Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe
165 170 175
Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val
180 185 190
Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val
195 200 205
Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys
210 215 220
Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Ala
225 230 235 240
Glu Gly Ala Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
245 250 255
Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val
260 265 270
Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
275 280 285
Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
290 295 300
Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
305 310 315 320

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

<210> 69
<211> 447
<212> PRT
<213> 人工序列

[0027] <220>
<223> IgG1.1f HC
<400> 69

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

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

Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp Lys Thr His
210 215 220
Thr Cys Pro Pro Cys Pro Ala Pro Glu Ala Glu Gly Ala Pro Ser Val
225 230 235 240
Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr
245 250 255
Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu
260 265 270
Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys
275 280 285
Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser
290 295 300
Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys
305 310 315 320
Cys Lys Val Ser Asn Lys Ala Leu Pro Ser Ser Ile Glu Lys Thr Ile
[0028] 325 330 335
Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro
340 345 350
Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu
355 360 365
Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn
370 375 380
Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser
385 390 395 400
Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg
405 410 415
Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu
420 425 430
His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
435 440 445

<210> 70
<211> 447
<212> PRT
<213> 人工序列
<220>
<223> IgG1.1f HC
<400> 70
Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu

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

Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala
                85                  90                  95
Thr Asp Thr Gly Tyr Tyr Gly Met Asp Val Trp Gly Gln Gly Thr Thr
            100                 105                 110
Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu
        115                 120                 125
Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys
    130                 135                 140
Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser
145                 150                 155                 160
Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser
                165                 170                 175
Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser
            180                 185                 190
Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn
        195                 200                 205
Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp Lys Thr His
    210                 215                 220
Thr Cys Pro Pro Cys Pro Ala Pro Glu Ala Glu Gly Ala Pro Ser Val
225                 230                 235                 240
Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr
                245                 250                 255
Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu
            260                 265                 270
Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys
        275                 280                 285
Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser
    290                 295                 300
Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys
305                 310                 315                 320
Cys Lys Val Ser Asn Lys Ala Leu Pro Ser Ser Ile Glu Lys Thr Ile
                325                 330                 335
Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro
            340                 345                 350
Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu
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[0029]

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

<210> 71
<211> 453
<212> PRT
<213> 人工序列
<220>
<223> IgG1.1f HC
<400> 71
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30

[0030] Tyr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45
Gly Ile Ile Asn Pro Arg Gly Asp Ser Ile Ile Tyr Ala Gln Lys Phe
50 55 60
Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Thr Ser Thr Val Tyr
65 70 75 80
Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95
Ala Arg Asp Phe Tyr Gly Ser Gly Asn Tyr Tyr Tyr Gly Met Asp Val
100 105 110
Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly
115 120 125
Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly
130 135 140
Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val
145 150 155 160
Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe
165 170 175
Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val
180 185 190
Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val
195 200 205
Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys

210 215 220
Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Ala
225 230 235 240
Glu Gly Ala Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
245 250 255
Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val
260 265 270
Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
275 280 285
Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
290 295 300
Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
305 310 315 320
Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ser
325 330 335
Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
340 345 350
Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln
355 360 365
Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala
370 375 380
Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
[0031] 385 390 395 400
Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
405 410 415
Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
420 425 430
Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
435 440 445
Leu Ser Pro Gly Lys
450

<210> 72
<211> 453
<212> PRT
<213> 人工序列
<220>
<223> IgG1.1f HC
<400> 72
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1 5 10 15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp Tyr
20 25 30
Tyr Met Ser Trp Ile Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45
Ser Phe Ile Ser Gly Gly Gly Ser Thr Ile Tyr Tyr Ala Asp Ser Val

50 55 60

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

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

Ala Arg Asp Gly Tyr Ser Ser Gly Trp Tyr Tyr Tyr Gly Met Asp Val
100 105 110

Trp Gly Gln Gly Thr Ala Val Thr Val Ser Ser Ala Ser Thr Lys Gly
115 120 125

Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly
130 135 140

Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val
145 150 155 160

Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe
165 170 175

Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val
180 185 190

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

Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys
210 215 220

Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Ala
[0032] 225 230 235 240

Glu Gly Ala Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
245 250 255

Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val
260 265 270

Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
275 280 285

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
290 295 300

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
305 310 315 320

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ser
325 330 335

Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
340 345 350

Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln
355 360 365

Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala
370 375 380

Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
385 390 395 400

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
405 410 415

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
420 425 430
Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
435 440 445
Leu Ser Pro Gly Lys
450

<210> 73
<211> 454
<212> PRT
<213> 人工序列
<220>
<223> IgG1.1f HC
<400> 73

Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1 5 10 15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp Tyr
20 25 30
Tyr Met Ser Trp Ile Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45
Ser Phe Ile Ser Thr Ser Gly Ser Ile Ile Tyr Tyr Ala Asp Ser Val
50 55 60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
[0033] 65 70 75 80
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95
Ala Arg Glu Gly Tyr Ser Ser Ser Trp Ser Tyr Tyr Tyr Gly Met Asp
100 105 110
Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys
115 120 125
Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly
130 135 140
Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro
145 150 155 160
Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr
165 170 175
Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val
180 185 190
Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn
195 200 205
Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro
210 215 220

Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu
225 230 235 240
Ala Glu Gly Ala Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp

245 250 255
Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp
260 265 270
Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
275 280 285
Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn
290 295 300
Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
305 310 315 320
Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro
325 330 335
Ser Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
340 345 350
Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn
355 360 365
Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
370 375 380
Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
385 390 395 400
Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys
405 410 415
Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
[0034] 420 425 430
Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
435 440 445
Ser Leu Ser Pro Gly Lys
450

<210> 74
<211> 453
<212> PRT
<213> 人工序列
<220>
<223> IgG1.1f HC
<400> 74
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1 5 10 15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp Tyr
20 25 30
Tyr Met Ser Trp Ile Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45
Ser Phe Ile Ser Ser Ser Gly Ser Ile Ile Tyr Tyr Ala Asp Ser Val
50 55 60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65 70 75 80
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys

85 90 95
Ala Arg Asp Gly Tyr Ser Ser Gly Trp Glu Tyr Tyr Gly Met Asp Val
100 105 110
Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly
115 120 125
Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly
130 135 140
Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val
145 150 155 160
Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe
165 170 175
Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val
180 185 190
Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val
195 200 205
Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys
210 215 220
Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Ala
225 230 235 240
Glu Gly Ala Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
245 250 255
Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val
[0035] 260 265 270
Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
275 280 285
Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
290 295 300
Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
305 310 315 320
Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ser
325 330 335
Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
340 345 350
Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln
355 360 365
Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala
370 375 380
Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
385 390 395 400
Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
405 410 415
Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
420 425 430
Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
435 440 445

Leu Ser Pro Gly Lys
450

<210> 75
<211> 452
<212> PRT
<213> 人工序列
<220>
<223> IgG1.1f HC (无C末端K)
<400> 75

Gln Leu Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu
1 5 10 15
Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Arg
20 25 30
Ser Tyr Tyr Trp Gly Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu
35 40 45
Trp Ile Gly Ser Ile Tyr Tyr Ser Gly Phe Thr Tyr Tyr Asn Pro Ser
50 55 60
Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
65 70 75 80
Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
85 90 95
Cys Ala Thr Gly Gly Pro Tyr Gly Asp Tyr Ala His Trp Phe Asp Pro
[0036] 100 105 110
Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly
115 120 125
Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly
130 135 140
Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val
145 150 155 160
Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe
165 170 175
Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val
180 185 190
Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val
195 200 205
Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys
210 215 220
Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Ala
225 230 235 240
Glu Gly Ala Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
245 250 255
Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val
260 265 270
Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
275 280 285

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

[0037] <210> 76
<211> 446
<212> PRT
<213> 人工序列
<220>
<223> IgG1.1f HC (无C末端K)
<400> 76
Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu
1 5 10 15
Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Arg His
20 25 30
Tyr Trp Asn Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile
35 40 45
Gly Tyr Ile His Tyr Ser Gly Ser Thr Asn Tyr Asn Ser Ser Leu Lys
50 55 60
Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe Ser Leu
65 70 75 80
Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala
85 90 95
Arg Asp Thr Gly Tyr Tyr Gly Met Asp Ile Trp Gly Gln Gly Thr Thr
100 105 110
Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu
115 120 125

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

[0038]
Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys
305 310 315 320
Cys Lys Val Ser Asn Lys Ala Leu Pro Ser Ser Ile Glu Lys Thr Ile
325 330 335
Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro
340 345 350
Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu
355 360 365
Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn
370 375 380
Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser
385 390 395 400
Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg
405 410 415
Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu
420 425 430
His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
435 440 445

<210> 77
<211> 446
<212> PRT
<213> 人工序列
<220>

<223> IgG1.1f HC (无C末端K)

<400> 77

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Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu
1               5                  10                  15
Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Arg Tyr
            20                  25                  30
Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile
        35                  40                  45
Gly Tyr Ile His Tyr Thr Gly Ser Thr Asn Tyr Asn Pro Ser Leu Lys
    50                  55                  60
Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe Ser Leu
65                  70                  75                  80
Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala
                85                  90                  95
Thr Asp Thr Gly Tyr Tyr Gly Met Asp Val Trp Gly Gln Gly Thr Thr
            100                 105                 110
Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu
        115                 120                 125
Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys
    130                 135                 140
Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser
145                 150                 155                 160
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[0039]

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

<210> 78
<211> 452
<212> PRT
<213> 人工序列
<220>
<223> IgG1.1f HC (无C末端K)
<400> 78

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

[0040]
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30
Tyr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45
Gly Ile Ile Asn Pro Arg Gly Asp Ser Ile Ile Tyr Ala Gln Lys Phe
50 55 60
Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Thr Ser Thr Val Tyr
65 70 75 80
Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95
Ala Arg Asp Phe Tyr Gly Ser Gly Asn Tyr Tyr Tyr Gly Met Asp Val
100 105 110
Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly
115 120 125
Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly
130 135 140
Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val
145 150 155 160
Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe
165 170 175
Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val
180 185 190
Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val

195 200 205

Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys
210 215 220

Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Ala
225 230 235 240

Glu Gly Ala Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
245 250 255

Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val
260 265 270

Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
275 280 285

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
290 295 300

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
305 310 315 320

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ser
325 330 335

Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
340 345 350

Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln
355 360 365

Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala
[0041] 370 375 380

Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
385 390 395 400

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
405 410 415

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
420 425 430

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
435 440 445

Leu Ser Pro Gly
450

<210> 79
<211> 452
<212> PRT
<213> 人工序列
<220>
<223> IgG1.1f HC (无C末端K)
<400> 79

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

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

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

[0042]

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

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

<210> 80
<211> 453
<212> PRT
<213> 人工序列
<220>
<223> IgG1.1f HC (无C末端K)
<400> 80

Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1 5 10 15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp Tyr
20 25 30
Tyr Met Ser Trp Ile Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45
[0043] Ser Phe Ile Ser Thr Ser Gly Ser Ile Ile Tyr Tyr Ala Asp Ser Val
50 55 60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65 70 75 80
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95
Ala Arg Glu Gly Tyr Ser Ser Ser Trp Ser Tyr Tyr Tyr Gly Met Asp
100 105 110
Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys
115 120 125

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

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

[0044] Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys
405 410 415
Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
420 425 430
Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
435 440 445
Ser Leu Ser Pro Gly
450

<210> 81
<211> 452
<212> PRT
<213> 人工序列
<220>
<223> IgG1.1f HC (无C末端K)
<400> 81
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1 5 10 15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp Tyr
20 25 30
Tyr Met Ser Trp Ile Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45
Ser Phe Ile Ser Ser Ser Gly Ser Ile Ile Tyr Tyr Ala Asp Ser Val
50 55 60

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

[0045]

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

420 425 430

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
435 440 445

Leu Ser Pro Gly
450

<210> 82
<211> 453
<212> PRT
<213> 人工序列
<220>
<223> IgG1.3f HC
<400> 82

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

[0046] Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
85 90 95
Cys Ala Thr Gly Gly Pro Tyr Gly Asp Tyr Ala His Trp Phe Asp Pro
100 105 110
Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly
115 120 125

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

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

[0047] Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
435 440 445
Leu Ser Pro Gly Lys
450

<210> 83
<211> 447
<212> PRT
<213> 人工序列
<220>
<223> IgG1.3f HC
<400> 83

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

Arg Asp Thr Gly Tyr Tyr Gly Met Asp Ile Trp Gly Gln Gly Thr Thr
100 105 110
Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu
115 120 125
Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys
130 135 140

Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser
145 150 155 160
Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser
165 170 175
Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser
180 185 190
Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn
195 200 205
Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp Lys Thr His
210 215 220
Thr Cys Pro Pro Cys Pro Ala Pro Glu Ala Glu Gly Ala Pro Ser Val
225 230 235 240
Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr
245 250 255
Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu
[0048] 260 265 270
Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys
275 280 285
Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser
290 295 300
Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys
305 310 315 320
Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile
325 330 335
Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro
340 345 350
Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu
355 360 365
Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn
370 375 380
Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser
385 390 395 400
Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg
405 410 415
Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu
420 425 430
His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
435 440 445

<210> 84
<211> 447
<212> PRT
<213> 人工序列
<220>
<223> IgG1.3f HC
<400> 84

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu
1 5 10 15
Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Arg Tyr
20 25 30
Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile
35 40 45
Gly Tyr Ile His Tyr Thr Gly Ser Thr Asn Tyr Asn Pro Ser Leu Lys
50 55 60
Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe Ser Leu
65 70 75 80
Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala
85 90 95
Thr Asp Thr Gly Tyr Tyr Gly Met Asp Val Trp Gly Gln Gly Thr Thr
100 105 110
Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu
[0049] 115 120 125
Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys
130 135 140
Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser
145 150 155 160
Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser
165 170 175
Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser
180 185 190
Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn
195 200 205
Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp Lys Thr His
210 215 220
Thr Cys Pro Pro Cys Pro Ala Pro Glu Ala Glu Gly Ala Pro Ser Val
225 230 235 240
Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr
245 250 255
Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu
260 265 270
Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys
275 280 285
Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser
290 295 300

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

<210> 85
<211> 453
<212> PRT
<213> 人工序列

[0050] <220>
<223> IgG1.3f HC
<400> 85

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

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

[0051] Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
340 345 350
Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln
355 360 365
Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala
370 375 380
Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
385 390 395 400
Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
405 410 415
Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
420 425 430
Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
435 440 445
Leu Ser Pro Gly Lys
450

<210> 86
<211> 453
<212> PRT
<213> 人工序列
<220>
<223> IgG1.3f HC
<400> 86

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

Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val
145                 150                 155                 160
Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe
                165                 170                 175
Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val
            180                 185                 190
Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val
        195                 200                 205
Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys
    210                 215                 220
Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Ala
225                 230                 235                 240
Glu Gly Ala Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
                245                 250                 255
Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val
            260                 265                 270
Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
        275                 280                 285
Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
    290                 295                 300
Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
305                 310                 315                 320
Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
                325                 330                 335
Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
            340                 345                 350
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[0052]

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

<210> 87
<211> 454
<212> PRT
<213> 人工序列
<220>
<223> IgG1.3f HC
<400> 87

[0053]

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

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

180 185 190
Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn
195 200 205
Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro
210 215 220
Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu
225 230 235 240
Ala Glu Gly Ala Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
245 250 255
Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp
260 265 270
Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
275 280 285
Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn
290 295 300
Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
305 310 315 320
Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro
325 330 335
Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
340 345 350
Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn
[0054] 355 360 365
Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
370 375 380
Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
385 390 395 400
Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys
405 410 415
Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
420 425 430
Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
435 440 445
Ser Leu Ser Pro Gly Lys
450

<210> 88
<211> 453
<212> PRT
<213> 人工序列
<220>
<223> IgG1.3f HC
<400> 88
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1 5 10 15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp Tyr

20 25 30

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

Ser Phe Ile Ser Ser Ser Gly Ser Ile Ile Tyr Tyr Ala Asp Ser Val
50 55 60

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

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

Ala Arg Asp Gly Tyr Ser Ser Gly Trp Glu Tyr Tyr Gly Met Asp Val
100 105 110

Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly
115 120 125

Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly
130 135 140

Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val
145 150 155 160

Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe
165 170 175

Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val
180 185 190

Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val
[0055] 195 200 205

Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys
210 215 220

Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Ala
225 230 235 240

Glu Gly Ala Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
245 250 255

Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val
260 265 270

Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
275 280 285

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
290 295 300

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
305 310 315 320

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
325 330 335

Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
340 345 350

Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln
355 360 365

Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala
370 375 380

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

<210> 89
<211> 452
<212> PRT
<213> 人工序列
<220>
<223> IgG1.3f HC (无C末端K)
<400> 89
Gln Leu Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu
1 5 10 15
Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Arg
20 25 30
Ser Tyr Tyr Trp Gly Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu
[0056] 35 40 45
Trp Ile Gly Ser Ile Tyr Tyr Ser Gly Phe Thr Tyr Tyr Asn Pro Ser
50 55 60
Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
65 70 75 80
Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
85 90 95
Cys Ala Thr Gly Gly Pro Tyr Gly Asp Tyr Ala His Trp Phe Asp Pro
100 105 110
Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly
115 120 125

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

210 215 220
Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Ala
225 230 235 240
Glu Gly Ala Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
245 250 255
Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val
260 265 270
Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
275 280 285
Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
290 295 300
Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
305 310 315 320
Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
325 330 335
Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
340 345 350
Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln
355 360 365
Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala
370 375 380
Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
[0057] 385 390 395 400
Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
405 410 415
Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
420 425 430
Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
435 440 445
Leu Ser Pro Gly
450

<210> 90
<211> 446
<212> PRT
<213> 人工序列
<220>
<223> IgG1.3f HC (无C末端K)
<400> 90
Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu
1 5 10 15
Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Arg His
20 25 30
Tyr Trp Asn Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile
35 40 45
Gly Tyr Ile His Tyr Ser Gly Ser Thr Asn Tyr Asn Ser Ser Leu Lys

50 55 60

Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe Ser Leu
65 70 75 80
Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala
85 90 95
Arg Asp Thr Gly Tyr Tyr Gly Met Asp Ile Trp Gly Gln Gly Thr Thr
100 105 110
Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu
115 120 125
Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys
130 135 140
Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser
145 150 155 160
Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser
165 170 175
Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser
180 185 190
Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn
195 200 205
Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp Lys Thr His
210 215 220
Thr Cys Pro Pro Cys Pro Ala Pro Glu Ala Glu Gly Ala Pro Ser Val
[0058] 225 230 235 240
Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr
245 250 255
Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu
260 265 270
Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys
275 280 285
Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser
290 295 300
Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys
305 310 315 320
Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile
325 330 335
Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro
340 345 350
Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu
355 360 365
Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn
370 375 380
Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser
385 390 395 400
Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg
405 410 415

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

<210> 91
<211> 446
<212> PRT
<213> 人工序列
<220>
<223> IgG1.3f HC (无C末端K)
<400> 91

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu
1 5 10 15
Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Arg Tyr
20 25 30
Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile
35 40 45
Gly Tyr Ile His Tyr Thr Gly Ser Thr Asn Tyr Asn Pro Ser Leu Lys
50 55 60
Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe Ser Leu
65 70 75 80
Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala
[0059] 85 90 95
Thr Asp Thr Gly Tyr Tyr Gly Met Asp Val Trp Gly Gln Gly Thr Thr
100 105 110
Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu
115 120 125
Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys
130 135 140
Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser
145 150 155 160
Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser
165 170 175
Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser
180 185 190
Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn
195 200 205
Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp Lys Thr His
210 215 220

Thr Cys Pro Pro Cys Pro Ala Pro Glu Ala Glu Gly Ala Pro Ser Val
225 230 235 240
Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr
245 250 255
Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu

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

[0060]

<210> 92
<211> 452
<212> PRT
<213> 人工序列
<220>
<223> IgG1.3f HC (无C末端K)
<400> 92
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30
Tyr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45
Gly Ile Ile Asn Pro Arg Gly Asp Ser Ile Ile Tyr Ala Gln Lys Phe
50 55 60
Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Thr Ser Thr Val Tyr
65 70 75 80
Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95
Ala Arg Asp Phe Tyr Gly Ser Gly Asn Tyr Tyr Tyr Gly Met Asp Val
100 105 110
Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly

115 120 125

Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly
130 135 140

Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val
145 150 155 160

Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe
165 170 175

Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val
180 185 190

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

Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys
210 215 220

Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Ala
225 230 235 240

Glu Gly Ala Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
245 250 255

Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val
260 265 270

Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
275 280 285

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
[0061] 290 295 300

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
305 310 315 320

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
325 330 335

Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
340 345 350

Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln
355 360 365

Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala
370 375 380

Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
385 390 395 400

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
405 410 415

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
420 425 430

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
435 440 445

Leu Ser Pro Gly
450

<210> 93

<211> 452

<212> PRT
<213> 人工序列
<220>
<223> IgG1.3f HC (无C末端K)
<400> 93

Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1 5 10 15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp Tyr
20 25 30
Tyr Met Ser Trp Ile Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45
Ser Phe Ile Ser Gly Gly Gly Ser Thr Ile Tyr Tyr Ala Asp Ser Val
50 55 60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Phe
65 70 75 80
Leu Gln Met Asn Ser Leu Arg Val Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95
Ala Arg Asp Gly Tyr Ser Ser Gly Trp Tyr Tyr Tyr Gly Met Asp Val
100 105 110
Trp Gly Gln Gly Thr Ala Val Thr Val Ser Ser Ala Ser Thr Lys Gly
115 120 125
Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly
[0062] 130 135 140
Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val
145 150 155 160
Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe
165 170 175
Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val
180 185 190
Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val
195 200 205
Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys
210 215 220
Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Ala
225 230 235 240
Glu Gly Ala Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
245 250 255
Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val
260 265 270
Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
275 280 285
Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
290 295 300
Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
305 310 315 320

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

[0063]

<210> 94
<211> 453
<212> PRT
<213> 人工序列
<220>
<223> IgG1.3f HC (无C末端K)
<400> 94
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1 5 10 15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp Tyr
20 25 30
Tyr Met Ser Trp Ile Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45
Ser Phe Ile Ser Thr Ser Gly Ser Ile Ile Tyr Tyr Ala Asp Ser Val
50 55 60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65 70 75 80
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95
Ala Arg Glu Gly Tyr Ser Ser Ser Trp Ser Tyr Tyr Tyr Gly Met Asp
100 105 110
Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys
115 120 125
Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly
130 135 140
Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro

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

[0064]

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

<210> 95
<211> 452
<212> PRT
<213> 人工序列
<220>
<223> IgG1.3f HC (无C末端K)

<400> 95

Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1 5 10 15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp Tyr
20 25 30
Tyr Met Ser Trp Ile Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45
Ser Phe Ile Ser Ser Ser Gly Ser Ile Ile Tyr Tyr Ala Asp Ser Val
50 55 60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65 70 75 80
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95
Ala Arg Asp Gly Tyr Ser Ser Gly Trp Glu Tyr Tyr Gly Met Asp Val
100 105 110
Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly
115 120 125
Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly
130 135 140
Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val
145 150 155 160
Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe
[0065] 165 170 175
Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val
180 185 190
Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val
195 200 205
Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys
210 215 220
Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Ala
225 230 235 240
Glu Gly Ala Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
245 250 255
Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val
260 265 270
Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
275 280 285

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
290 295 300
Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
305 310 315 320
Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
325 330 335
Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro

340 345 350

Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln
355 360 365

Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala
370 375 380

Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
385 390 395 400

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
405 410 415

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
420 425 430

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
435 440 445

Leu Ser Pro Gly
450

<210> 96
<211> 453
<212> PRT
<213> 人工序列
<220>
<223> IgG1.1f HC
<400> 96

[0066] Gln Leu Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu
1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Arg
20 25 30

Ser Tyr Tyr Trp Gly Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu
35 40 45

Trp Ile Gly Ser Ile Tyr Tyr Ser Gly Phe Thr Tyr Tyr Gln Pro Ser
50 55 60

Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
65 70 75 80

Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
85 90 95

Cys Ala Thr Gly Gly Pro Tyr Gly Asp Tyr Ala His Trp Phe Asp Pro
100 105 110

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly
115 120 125

Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly
130 135 140

Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val
145 150 155 160

Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe
165 170 175

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

[0067] Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln
355 360 365
Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala
370 375 380
Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
385 390 395 400
Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
405 410 415
Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
420 425 430
Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
435 440 445
Leu Ser Pro Gly Lys
450

<210> 97
<211> 453
<212> PRT
<213> 人工序列
<220>
<223> IgG1.1f HC
<400> 97
Gln Leu Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu
1 5 10 15

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

[0068] Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val
195 200 205
Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys
210 215 220
Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Ala
225 230 235 240
Glu Gly Ala Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
245 250 255
Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val
260 265 270
Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
275 280 285
Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
290 295 300
Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
305 310 315 320
Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ser
325 330 335
Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
340 345 350
Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln
355 360 365
Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala

370 375 380

Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
385 390 395 400

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
405 410 415

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
420 425 430

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
435 440 445

Leu Ser Pro Gly Lys
450

<210> 98
<211> 453
<212> PRT
<213> 人工序列
<220>
<223> IgG1.1f HC
<400> 98

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

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Arg
20 25 30

[0069] Ser Tyr Tyr Trp Gly Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu
35 40 45

Trp Ile Gly Ser Ile Tyr Tyr Ser Gly Phe Thr Tyr Tyr Ala Pro Ser
50 55 60

Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
65 70 75 80

Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
85 90 95

Cys Ala Thr Gly Gly Pro Tyr Gly Asp Tyr Ala His Trp Phe Asp Pro
100 105 110

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly
115 120 125

Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly
130 135 140

Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val
145 150 155 160

Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe
165 170 175

Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val
180 185 190

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

Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys

210 215 220
Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Ala
225 230 235 240
Glu Gly Ala Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
245 250 255
Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val
260 265 270
Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
275 280 285
Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
290 295 300
Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
305 310 315 320
Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ser
325 330 335
Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
340 345 350
Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln
355 360 365
Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala
370 375 380
Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
[0070] 385 390 395 400
Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
405 410 415
Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
420 425 430
Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
435 440 445
Leu Ser Pro Gly Lys
450

<210> 99
<211> 453
<212> PRT
<213> 人工序列
<220>
<223> IgG1.1f HC
<400> 99
Gln Leu Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu
1 5 10 15
Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Arg
20 25 30
Ser Tyr Tyr Trp Gly Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu
35 40 45
Trp Ile Gly Ser Ile Tyr Tyr Ser Gly Phe Thr Tyr Tyr Asn Pro Ser

50 55 60

Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
65 70 75 80
Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
85 90 95
Cys Ala Thr Gly Gly Pro Tyr Gly Asp Tyr Ala His Trp Phe Glu Pro
100 105 110
Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly
115 120 125
Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly
130 135 140
Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val
145 150 155 160
Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe
165 170 175
Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val
180 185 190
Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val
195 200 205
Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys
210 215 220
Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Ala
[0071] 225 230 235 240
Glu Gly Ala Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
245 250 255
Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val
260 265 270
Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
275 280 285
Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
290 295 300
Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
305 310 315 320
Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ser
325 330 335
Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
340 345 350

Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln
355 360 365
Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala
370 375 380
Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
385 390 395 400
Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu

405 410 415
Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
420 425 430
Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
435 440 445
Leu Ser Pro Gly Lys
450

<210> 100
<211> 453
<212> PRT
<213> 人工序列
<220>
<223> IgG1.1f HC
<400> 100

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

[0072]
Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
65 70 75 80
Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
85 90 95
Cys Ala Thr Gly Gly Pro Tyr Gly Asp Tyr Ala His Trp Phe Asp Val
100 105 110
Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly
115 120 125
Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly
130 135 140
Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val
145 150 155 160
Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe
165 170 175
Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val
180 185 190
Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val
195 200 205
Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys
210 215 220
Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Ala
225 230 235 240
Glu Gly Ala Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr

245 250 255
Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val
260 265 270
Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
275 280 285
Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
290 295 300
Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
305 310 315 320
Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ser
325 330 335
Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
340 345 350
Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln
355 360 365
Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala
370 375 380
Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
385 390 395 400
Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
405 410 415
Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
[0073] 420 425 430
Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
435 440 445
Leu Ser Pro Gly Lys
450

<210> 101
<211> 453
<212> PRT
<213> 人工序列
<220>
<223> IgG1.1f HC
<400> 101

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

85 90 95
Cys Ala Thr Gly Gly Pro Tyr Gly Asp Tyr Ala His Trp Phe Asp Tyr
100 105 110

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly
115 120 125
Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly
130 135 140
Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val
145 150 155 160
Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe
165 170 175
Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val
180 185 190
Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val
195 200 205
Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys
210 215 220
Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Ala
225 230 235 240
Glu Gly Ala Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
245 250 255
[0074] Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val
260 265 270
Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
275 280 285
Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
290 295 300
Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
305 310 315 320
Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ser
325 330 335
Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
340 345 350
Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln
355 360 365
Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala
370 375 380
Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
385 390 395 400
Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
405 410 415
Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
420 425 430
Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser

435 440 445

Leu Ser Pro Gly Lys
450

<210> 102
<211> 453
<212> PRT
<213> 人工序列
<220>
<223> IgG1.1f HC
<400> 102

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

[0075]

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

275 280 285

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
290 295 300

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
305 310 315 320

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ser
325 330 335

Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
340 345 350

Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln
355 360 365

Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala
370 375 380

Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
385 390 395 400

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
405 410 415

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
420 425 430

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
435 440 445

Leu Ser Pro Gly Lys
450

[0076]

<210> 103
<211> 453
<212> PRT
<213> 人工序列
<220>
<223> IgG1.1f HC
<400> 103

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

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Arg
20 25 30

Ser Tyr Tyr Trp Gly Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu
35 40 45

Trp Ile Gly Ser Ile Tyr Tyr Ser Gly Phe Thr Tyr Tyr Gln Pro Ser
50 55 60

Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
65 70 75 80

Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
85 90 95

Cys Ala Thr Gly Gly Pro Tyr Gly Asp Tyr Ala His Trp Phe Asp Tyr
100 105 110

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

115 120 125

Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly
130 135 140

Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val
145 150 155 160

Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe
165 170 175

Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val
180 185 190

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

Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys
210 215 220

Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Ala
225 230 235 240

Glu Gly Ala Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
245 250 255

Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val
260 265 270

Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
275 280 285

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
[0077] 290 295 300

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
305 310 315 320

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ser
325 330 335

Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
340 345 350

Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln
355 360 365

Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala
370 375 380

Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
385 390 395 400

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
405 410 415

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
420 425 430

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
435 440 445

Leu Ser Pro Gly Lys
450

<210> 104

<211> 447
<212> PRT
<213> 人工序列
<220>
<223> IgG1.1f HC
<400> 104

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

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

<210> 105
<211> 453
<212> PRT
<213> 人工序列
<220>
[0079] <223> IgG1.1f HC
<400> 105

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

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

[0080] Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
340 345 350
Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln
355 360 365
Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala
370 375 380
Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
385 390 395 400
Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
405 410 415
Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
420 425 430
Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
435 440 445
Leu Ser Pro Gly Lys
450

<210> 106
<211> 452
<212> PRT
<213> 人工序列
<220>
<223> IgG1.1f HC (无C末端K)
<400> 106

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Gln Leu Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu
1               5                  10                  15
Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Arg
            20                  25                  30
Ser Tyr Tyr Trp Gly Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu
        35                  40                  45
Trp Ile Gly Ser Ile Tyr Tyr Ser Gly Phe Thr Tyr Tyr Gln Pro Ser
    50                  55                  60
Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
65                  70                  75                  80
Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
                85                  90                  95
Cys Ala Thr Gly Gly Pro Tyr Gly Asp Tyr Ala His Trp Phe Asp Pro
            100                 105                 110
Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly
        115                 120                 125
Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly
    130                 135                 140
Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val
145                 150                 155                 160
Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe
                165                 170                 175
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[0081]

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

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

<210> 107
<211> 452
<212> PRT
<213> 人工序列
<220>
<223> IgG1.1f HC (无C末端K)
<400> 107

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

[0082] Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Arg
20 25 30
Ser Tyr Tyr Trp Gly Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu
35 40 45
Trp Ile Gly Ser Ile Tyr Tyr Ser Gly Phe Thr Tyr Tyr Ser Pro Ser
50 55 60
Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
65 70 75 80
Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
85 90 95
Cys Ala Thr Gly Gly Pro Tyr Gly Asp Tyr Ala His Trp Phe Asp Pro
100 105 110
Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly
115 120 125
Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly
130 135 140
Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val
145 150 155 160
Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe
165 170 175
Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val
180 185 190
Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val

195 200 205

Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys
210 215 220

Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Ala
225 230 235 240

Glu Gly Ala Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
245 250 255

Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val
260 265 270

Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
275 280 285

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
290 295 300

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
305 310 315 320

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ser
325 330 335

Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
340 345 350

Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln
355 360 365

Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala
[0083] 370 375 380

Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
385 390 395 400

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
405 410 415

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
420 425 430

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
435 440 445

Leu Ser Pro Gly
450

<210> 108
<211> 452
<212> PRT
<213> 人工序列
<220>
<223> IgG1.1f HC (无C末端K)
<400> 108

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

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Arg
20 25 30

Ser Tyr Tyr Trp Gly Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu

```
          35                  40                  45
Trp Ile Gly Ser Ile Tyr Tyr Ser Gly Phe Thr Tyr Tyr Ala Pro Ser
      50                  55                  60
Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
65                  70                  75                  80
Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
                  85                  90                  95
Cys Ala Thr Gly Gly Pro Tyr Gly Asp Tyr Ala His Trp Phe Asp Pro
             100                 105                 110
Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly
         115                 120                 125
Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly
     130                 135                 140
Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val
145                 150                 155                 160
Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe
                 165                 170                 175
Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val
             180                 185                 190
Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val
         195                 200                 205
Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys
     210                 215                 220
Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Ala
225                 230                 235                 240
Glu Gly Ala Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
                 245                 250                 255
Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val
             260                 265                 270
Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
         275                 280                 285
Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
     290                 295                 300
Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
305                 310                 315                 320
Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ser
                 325                 330                 335
Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
             340                 345                 350
Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln
         355                 360                 365
Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala
     370                 375                 380
Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
385                 390                 395                 400
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[0084]

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
405 410 415
Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
420 425 430
Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
435 440 445
Leu Ser Pro Gly
450

<210> 109
<211> 452
<212> PRT
<213> 人工序列
<220>
<223> IgG1.1f HC (无C末端K)
<400> 109

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

[0085]

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

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

[0086] Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
420 425 430
Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
435 440 445

Leu Ser Pro Gly
450

<210> 110
<211> 452
<212> PRT
<213> 人工序列
<220>
<223> IgG1.1f HC (无C末端K)
<400> 110
Gln Leu Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu
1 5 10 15
Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Arg
20 25 30
Ser Tyr Tyr Trp Gly Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu
35 40 45
Trp Ile Gly Ser Ile Tyr Tyr Ser Gly Phe Thr Tyr Tyr Asn Pro Ser
50 55 60
Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe

65 70 75 80
Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
85 90 95
Cys Ala Thr Gly Gly Pro Tyr Gly Asp Tyr Ala His Trp Phe Asp Val
100 105 110
Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly
115 120 125
Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly
130 135 140
Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val
145 150 155 160
Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe
165 170 175
Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val
180 185 190
Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val
195 200 205
Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys
210 215 220
Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Ala
225 230 235 240
Glu Gly Ala Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
[0087] 245 250 255
Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val
260 265 270
Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
275 280 285
Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
290 295 300
Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
305 310 315 320
Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ser
325 330 335
Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
340 345 350
Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln
355 360 365
Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala
370 375 380
Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
385 390 395 400
Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
405 410 415
Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
420 425 430

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
435 440 445
Leu Ser Pro Gly
450

<210> 111
<211> 452
<212> PRT
<213> 人工序列
<220>
<223> IgG1.1f HC (无C末端K)
<400> 111

Gln Leu Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu
1 5 10 15
Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Arg
20 25 30
Ser Tyr Tyr Trp Gly Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu
35 40 45
Trp Ile Gly Ser Ile Tyr Tyr Ser Gly Phe Thr Tyr Tyr Asn Pro Ser
50 55 60
Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
65 70 75 80
Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
[0088] 85 90 95
Cys Ala Thr Gly Gly Pro Tyr Gly Asp Tyr Ala His Trp Phe Asp Tyr
100 105 110
Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly
115 120 125
Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly
130 135 140
Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val
145 150 155 160
Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe
165 170 175
Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val
180 185 190
Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val
195 200 205
Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys
210 215 220
Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Ala
225 230 235 240
Glu Gly Ala Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
245 250 255
Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val
260 265 270

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

[0089] Leu Ser Pro Gly
450

<210> 112
<211> 452
<212> PRT
<213> 人工序列
<220>
<223> IgG1.1f HC (无C末端K)
<400> 112

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

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly
115 120 125
Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly
130 135 140
Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val
145 150 155 160

Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe
165 170 175
Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val
180 185 190
Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val
195 200 205
Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys
210 215 220
Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Ala
225 230 235 240
Glu Gly Ala Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
245 250 255
Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val
260 265 270
Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
[0090] 275 280 285
Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
290 295 300
Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
305 310 315 320
Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ser
325 330 335
Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
340 345 350
Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln
355 360 365
Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala
370 375 380
Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
385 390 395 400
Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
405 410 415
Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
420 425 430
Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
435 440 445
Leu Ser Pro Gly
450

<210> 113
<211> 452
<212> PRT
<213> 人工序列
<220>
<223> IgG1.1f HC (无C末端K)
<400> 113

Gln Leu Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu
1 5 10 15
Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Arg
20 25 30
Ser Tyr Tyr Trp Gly Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu
35 40 45
Trp Ile Gly Ser Ile Tyr Tyr Ser Gly Phe Thr Tyr Tyr Gln Pro Ser
50 55 60
Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
65 70 75 80
Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
85 90 95
Cys Ala Thr Gly Gly Pro Tyr Gly Asp Tyr Ala His Trp Phe Asp Tyr
100 105 110
Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly
[0091] 115 120 125
Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly
130 135 140

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

290 295 300

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

<210> 114

[0092] <211> 446

<212> PRT

<213> 人工序列

<220>

<223> IgG1.1f HC (无C末端K)

<400> 114

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

130 135 140
Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser
145 150 155 160
Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser
165 170 175
Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser
180 185 190
Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn
195 200 205
Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp Lys Thr His
210 215 220
Thr Cys Pro Pro Cys Pro Ala Pro Glu Ala Glu Gly Ala Pro Ser Val
225 230 235 240
Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr
245 250 255
Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu
260 265 270
Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys
275 280 285
Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser
290 295 300
Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys
[0093] 305 310 315 320
Cys Lys Val Ser Asn Lys Ala Leu Pro Ser Ser Ile Glu Lys Thr Ile
325 330 335
Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro
340 345 350
Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu
355 360 365
Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn
370 375 380
Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser
385 390 395 400
Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg
405 410 415
Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu
420 425 430
His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
435 440 445

<210> 115
<211> 452
<212> PRT
<213> 人工序列
<220>
<223> IgG1.1f HC (无C末端K)

<400> 115

Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1 5 10 15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp Tyr
20 25 30
Tyr Met Ser Trp Ile Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45
Ser Phe Ile Ser Gly Gly Gly Ser Thr Ile Tyr Tyr Ala Asp Ser Val
50 55 60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Phe
65 70 75 80
Leu Gln Met Asn Ser Leu Arg Val Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95
Ala Arg Asp Gly Tyr Ser Ser Gly Trp Tyr Tyr Tyr Gly Met Asp Val
100 105 110
Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly
115 120 125
Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly
130 135 140
Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val
145 150 155 160
Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe
[0094] 165 170 175
Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val
180 185 190
Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val
195 200 205
Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys
210 215 220
Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Ala
225 230 235 240
Glu Gly Ala Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
245 250 255
Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val
260 265 270
Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
275 280 285
Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
290 295 300
Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
305 310 315 320
Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ser
325 330 335
Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
340 345 350

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

<210> 116
<211> 453
<212> PRT
<213> 人工序列
<220>
<223> IgG1.3f HC
<400> 116

[0095]
Gln Leu Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu
1 5 10 15
Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Arg
20 25 30
Ser Tyr Tyr Trp Gly Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu
35 40 45
Trp Ile Gly Ser Ile Tyr Tyr Ser Gly Phe Thr Tyr Tyr Gln Pro Ser
50 55 60
Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
65 70 75 80
Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
85 90 95
Cys Ala Thr Gly Gly Pro Tyr Gly Asp Tyr Ala His Trp Phe Asp Pro
100 105 110
Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly
115 120 125
Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly
130 135 140
Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val
145 150 155 160
Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe
165 170 175
Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val
180 185 190

Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val
195 200 205
Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys
210 215 220
Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Ala
225 230 235 240
Glu Gly Ala Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
245 250 255

Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val
260 265 270
Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
275 280 285
Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
290 295 300
Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
305 310 315 320
Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
325 330 335
Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
340 345 350
Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln
[0096] 355 360 365
Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala
370 375 380
Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
385 390 395 400
Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
405 410 415
Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
420 425 430
Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
435 440 445
Leu Ser Pro Gly Lys
450

<210> 117
<211> 453
<212> PRT
<213> 人工序列
<220>
<223> IgG1.3f HC
<400> 117
Gln Leu Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu
1 5 10 15
Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Arg

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

[0097]

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

<210> 118
<211> 453
<212> PRT
<213> 人工序列
<220>
<223> IgG1.3f HC
<400> 118
Gln Leu Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu
1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Arg
20 25 30
[0098] Ser Tyr Tyr Trp Gly Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu
35 40 45
Trp Ile Gly Ser Ile Tyr Tyr Ser Gly Phe Thr Tyr Tyr Ala Pro Ser
50 55 60
Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
65 70 75 80
Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
85 90 95
Cys Ala Thr Gly Gly Pro Tyr Gly Asp Tyr Ala His Trp Phe Asp Pro
100 105 110
Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly
115 120 125
Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly
130 135 140
Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val
145 150 155 160
Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe
165 170 175
Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val
180 185 190
Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val
195 200 205
Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys

210 215 220
Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Ala
225 230 235 240
Glu Gly Ala Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
245 250 255
Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val
260 265 270
Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
275 280 285
Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
290 295 300
Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
305 310 315 320
Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
325 330 335
Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
340 345 350
Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln
355 360 365
Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala
370 375 380
Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
[0099] 385 390 395 400
Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
405 410 415
Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
420 425 430
Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
435 440 445
Leu Ser Pro Gly Lys
450

<210> 119
<211> 453
<212> PRT
<213> 人工序列
<220>
<223> IgG1.3f HC
<400> 119
Gln Leu Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu
1 5 10 15
Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Arg
20 25 30
Ser Tyr Tyr Trp Gly Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu
35 40 45
Trp Ile Gly Ser Ile Tyr Tyr Ser Gly Phe Thr Tyr Tyr Asn Pro Ser

50 55 60

Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
65 70 75 80

Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
85 90 95

Cys Ala Thr Gly Gly Pro Tyr Gly Asp Tyr Ala His Trp Phe Glu Pro
100 105 110

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly
115 120 125

Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly
130 135 140

Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val
145 150 155 160

Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe
165 170 175

Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val
180 185 190

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

Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys
210 215 220

Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Ala

[0100] 225 230 235 240

Glu Gly Ala Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
245 250 255

Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val
260 265 270

Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
275 280 285

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
290 295 300

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
305 310 315 320

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
325 330 335

Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
340 345 350

Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln
355 360 365

Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala
370 375 380

Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
385 390 395 400

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
405 410 415

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
420 425 430
Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
435 440 445
Leu Ser Pro Gly Lys
450

<210> 120
<211> 453
<212> PRT
<213> 人工序列
<220>
<223> IgG1.3f HC
<400> 120

Gln Leu Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu
1 5 10 15
Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Arg
20 25 30
Ser Tyr Tyr Trp Gly Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu
35 40 45
Trp Ile Gly Ser Ile Tyr Tyr Ser Gly Phe Thr Tyr Tyr Asn Pro Ser
50 55 60
Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
[0101] 65 70 75 80
Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
85 90 95
Cys Ala Thr Gly Gly Pro Tyr Gly Asp Tyr Ala His Trp Phe Asp Val
100 105 110
Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly
115 120 125
Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly
130 135 140
Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val
145 150 155 160
Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe
165 170 175
Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val
180 185 190
Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val
195 200 205
Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys
210 215 220
Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Ala
225 230 235 240
Glu Gly Ala Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
245 250 255

Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val
260 265 270
Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
275 280 285

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
290 295 300
Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
305 310 315 320
Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
325 330 335
Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
340 345 350
Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln
355 360 365
Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala
370 375 380
Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
385 390 395 400
Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
405 410 415
Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
[0102] 420 425 430
Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
435 440 445
Leu Ser Pro Gly Lys
450

<210> 121
<211> 453
<212> PRT
<213> 人工序列
<220>
<223> IgG1.3f HC
<400> 121

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

85 90 95
Cys Ala Thr Gly Gly Pro Tyr Gly Asp Tyr Ala His Trp Phe Asp Tyr
100 105 110
Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly
115 120 125
Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly
130 135 140
Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val
145 150 155 160
Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe
165 170 175
Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val
180 185 190
Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val
195 200 205
Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys
210 215 220
Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Ala
225 230 235 240
Glu Gly Ala Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
245 250 255
Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val
[0103] 260 265 270
Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
275 280 285
Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
290 295 300
Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
305 310 315 320
Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
325 330 335
Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
340 345 350
Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln
355 360 365
Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala
370 375 380
Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
385 390 395 400
Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
405 410 415
Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
420 425 430
Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
435 440 445

Leu Ser Pro Gly Lys
450

<210> 122
<211> 453
<212> PRT
<213> 人工序列
<220>
<223> IgG1.3f HC
<400> 122

Gln Leu Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu
1 5 10 15
Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Arg
20 25 30
Ser Tyr Tyr Trp Gly Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu
35 40 45

Trp Ile Gly Ser Ile Tyr Tyr Ser Gly Phe Thr Tyr Tyr Asn Pro Ser
50 55 60
Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
65 70 75 80
Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
85 90 95
[0104] Cys Ala Thr Gly Gly Pro Tyr Gly Asp Tyr Ala His Trp Phe Asp Leu
100 105 110
Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly
115 120 125
Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly
130 135 140
Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val
145 150 155 160
Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe
165 170 175
Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val
180 185 190
Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val
195 200 205
Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys
210 215 220
Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Ala
225 230 235 240
Glu Gly Ala Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
245 250 255
Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val
260 265 270
Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val

275 280 285

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
290 295 300

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
305 310 315 320

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
325 330 335

Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
340 345 350

Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln
355 360 365

Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala
370 375 380

Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
385 390 395 400

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
405 410 415

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
420 425 430

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
435 440 445

Leu Ser Pro Gly Lys
450

[0105]

<210> 123
<211> 453
<212> PRT
<213> 人工序列
<220>
<223> IgG1.3f HC
<400> 123

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

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Arg
20 25 30

Ser Tyr Tyr Trp Gly Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu
35 40 45

Trp Ile Gly Ser Ile Tyr Tyr Ser Gly Phe Thr Tyr Tyr Gln Pro Ser
50 55 60

Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
65 70 75 80

Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
85 90 95

Cys Ala Thr Gly Gly Pro Tyr Gly Asp Tyr Ala His Trp Phe Asp Tyr
100 105 110

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

115 120 125

Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly
130 135 140

Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val
145 150 155 160

Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe
165 170 175

Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val
180 185 190

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

Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys
210 215 220

Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Ala
225 230 235 240

Glu Gly Ala Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
245 250 255

Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val
260 265 270

Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
275 280 285

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
[0106] 290 295 300

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
305 310 315 320

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
325 330 335

Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
340 345 350

Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln
355 360 365

Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala
370 375 380

Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
385 390 395 400

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
405 410 415

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
420 425 430

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
435 440 445

Leu Ser Pro Gly Lys
450

<210> 124

<211> 447

<212> PRT
<213> 人工序列
<220>
<223> IgG1.3f HC
<400> 124

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

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

<210> 125
<211> 453
<212> PRT
<213> 人工序列
<220>
<223> IgG1.3f HC

[0108]

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

165 170 175
Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val
180 185 190
Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val
195 200 205
Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys
210 215 220
Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Ala
225 230 235 240
Glu Gly Ala Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
245 250 255
Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val
260 265 270
Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
275 280 285
Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
290 295 300
Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
305 310 315 320
Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
325 330 335
Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
[0109] 340 345 350
Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln
355 360 365
Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala
370 375 380
Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
385 390 395 400
Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
405 410 415
Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
420 425 430
Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
435 440 445
Leu Ser Pro Gly Lys
450

<210> 126
<211> 452
<212> PRT
<213> 人工序列
<220>
<223> IgG1.3f HC (无C末端K)
<400> 126
Gln Leu Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu

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1               5                   10                  15
Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Arg
            20                  25                  30
Ser Tyr Tyr Trp Gly Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu
        35                  40                  45
Trp Ile Gly Ser Ile Tyr Tyr Ser Gly Phe Thr Tyr Tyr Gln Pro Ser
    50                  55                  60
Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
65                  70                  75                  80
Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
                85                  90                  95
Cys Ala Thr Gly Gly Pro Tyr Gly Asp Tyr Ala His Trp Phe Asp Pro
            100                 105                 110
Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly
        115                 120                 125
Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly
    130                 135                 140
Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val
145                 150                 155                 160
Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe
                165                 170                 175
Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val
            180                 185                 190
Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val
        195                 200                 205
Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys
    210                 215                 220
Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Ala
225                 230                 235                 240
Glu Gly Ala Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
                245                 250                 255
Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val
            260                 265                 270
Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
        275                 280                 285
Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
    290                 295                 300
Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
305                 310                 315                 320
Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
                325                 330                 335
Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
            340                 345                 350
Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln
        355                 360                 365
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[0110]

Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala
370 375 380
Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
385 390 395 400
Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
405 410 415

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
420 425 430
Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
435 440 445
Leu Ser Pro Gly
450

<210> 127
<211> 452
<212> PRT
<213> 人工序列
<220>
<223> IgG1.3f HC (无C末端K)
<400> 127

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

[0111] Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Arg
20 25 30
Ser Tyr Tyr Trp Gly Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu
35 40 45
Trp Ile Gly Ser Ile Tyr Tyr Ser Gly Phe Thr Tyr Tyr Ser Pro Ser
50 55 60
Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
65 70 75 80
Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
85 90 95
Cys Ala Thr Gly Gly Pro Tyr Gly Asp Tyr Ala His Trp Phe Asp Pro
100 105 110
Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly
115 120 125
Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly
130 135 140
Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val
145 150 155 160
Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe
165 170 175
Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val
180 185 190
Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val

195 200 205

Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys
210 215 220

Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Ala
225 230 235 240

Glu Gly Ala Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
245 250 255

Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val
260 265 270

Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
275 280 285

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
290 295 300

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
305 310 315 320

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
325 330 335

Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
340 345 350

Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln
355 360 365

Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala
[0112] 370 375 380

Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
385 390 395 400

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
405 410 415

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
420 425 430

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
435 440 445

Leu Ser Pro Gly
450

<210> 128
<211> 452
<212> PRT
<213> 人工序列
<220>
<223> IgG1.3f HC (无C末端K)
<400> 128

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

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Arg
20 25 30

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

[0113]

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

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

<210> 129
<211> 452
<212> PRT
<213> 人工序列
<220>
<223> IgG1.3f HC (无C末端K)
<400> 129

Gln Leu Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu
1 5 10 15
Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Arg
20 25 30
Ser Tyr Tyr Trp Gly Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu
35 40 45

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

225 230 235 240
Glu Gly Ala Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
245 250 255
Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val
260 265 270
Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
275 280 285
Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
290 295 300
Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
305 310 315 320
Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
325 330 335
Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
340 345 350
Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln
355 360 365
Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala
370 375 380
Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
385 390 395 400
Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
[0115] 405 410 415
Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
420 425 430
Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
435 440 445
Leu Ser Pro Gly
450

<210> 130
<211> 452
<212> PRT
<213> 人工序列
<220>
<223> IgG1.3f HC (无C末端K)
<400> 130
Gln Leu Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu
1 5 10 15
Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Arg
20 25 30
Ser Tyr Tyr Trp Gly Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu
35 40 45
Trp Ile Gly Ser Ile Tyr Tyr Ser Gly Phe Thr Tyr Tyr Asn Pro Ser
50 55 60
Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe

65 70 75 80
Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
85 90 95
Cys Ala Thr Gly Gly Pro Tyr Gly Asp Tyr Ala His Trp Phe Asp Val
100 105 110

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

[0116]
Glu Gly Ala Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
245 250 255
Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val
260 265 270
Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
275 280 285
Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
290 295 300
Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
305 310 315 320
Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
325 330 335
Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
340 345 350
Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln
355 360 365
Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala
370 375 380
Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
385 390 395 400
Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
405 410 415
Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser

420 425 430
Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
435 440 445
Leu Ser Pro Gly
450

<210> 131
<211> 452
<212> PRT
<213> 人工序列
<220>
<223> IgG1.3f HC (无C末端K)
<400> 131

Gln Leu Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu
1 5 10 15
Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Arg
20 25 30
Ser Tyr Tyr Trp Gly Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu
35 40 45
Trp Ile Gly Ser Ile Tyr Tyr Ser Gly Phe Thr Tyr Tyr Asn Pro Ser
50 55 60
Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
65 70 75 80
[0117] Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
85 90 95

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

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

[0118] Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
435 440 445
Leu Ser Pro Gly
450

<210> 132
<211> 452
<212> PRT
<213> 人工序列
<220>
<223> IgG1.3f HC (无C末端K)
<400> 132

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

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

[0119] Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
275 280 285
Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
290 295 300
Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
305 310 315 320
Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
325 330 335
Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
340 345 350
Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln
355 360 365
Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala
370 375 380
Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
385 390 395 400
Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
405 410 415
Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
420 425 430
Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
435 440 445
Leu Ser Pro Gly

450

<210> 133
<211> 452
<212> PRT
<213> 人工序列
<220>
<223> IgG1.3f HC (无C末端K)
<400> 133

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

[0120]

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

290 295 300

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

<210> 134

[0121] <211> 446

<212> PRT

<213> 人工序列

<220>

<223> IgG1.3f HC (无C末端K)

<400> 134

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

130 135 140

Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser
145 150 155 160
Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser
165 170 175
Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser
180 185 190
Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn
195 200 205
Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp Lys Thr His
210 215 220
Thr Cys Pro Pro Cys Pro Ala Pro Glu Ala Glu Gly Ala Pro Ser Val
225 230 235 240
Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr
245 250 255
Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu
260 265 270
Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys
275 280 285
Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser
290 295 300
Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys
[0122] 305 310 315 320

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

<210> 135
<211> 452
<212> PRT
<213> 人工序列
<220>

<223> IgG1.3f HC (无C末端K)

<400> 135

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Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1               5                  10                  15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp Tyr
            20                  25                  30
Tyr Met Ser Trp Ile Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45
Ser Phe Ile Ser Gly Gly Gly Ser Thr Ile Tyr Tyr Ala Asp Ser Val
    50                  55                  60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Phe
65                  70                  75                  80
Leu Gln Met Asn Ser Leu Arg Val Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95
Ala Arg Asp Gly Tyr Ser Ser Gly Trp Tyr Tyr Tyr Gly Met Asp Val
            100                 105                 110
Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly
        115                 120                 125
Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly
    130                 135                 140
Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val
145                 150                 155                 160
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[0123]

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

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

<210> 136
<211> 450
<212> PRT
<213> 人工序列
<220>
<223> hIgG4 HC

[0124] <400> 136

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

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

[0125]

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

Gly Lys
450

<210> 137
<211> 449
<212> PRT
<213> 人工序列
<220>
<223> hIgG4 HC (无C末端K)
<400> 137
Gln Leu Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu

1 5 10 15
Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Arg
20 25 30
Ser Tyr Tyr Trp Gly Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu
35 40 45
Trp Ile Gly Ser Ile Tyr Tyr Ser Gly Phe Thr Tyr Tyr Asn Pro Ser
50 55 60
Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
65 70 75 80
Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
85 90 95
Cys Ala Thr Gly Gly Pro Tyr Gly Asp Tyr Ala His Trp Phe Asp Pro
100 105 110
Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly
115 120 125
Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser
130 135 140
Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val
145 150 155 160
Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe
165 170 175
Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val
[0126] 180 185 190
Thr Val Pro Ser Ser Ser Leu Gly Thr Lys Thr Tyr Thr Cys Asn Val
195 200 205
Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Ser Lys
210 215 220
Tyr Gly Pro Pro Cys Pro Ser Cys Pro Ala Pro Glu Phe Leu Gly Gly
225 230 235 240
Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile
245 250 255
Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser Gln Glu
260 265 270
Asp Pro Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val His
275 280 285
Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr Tyr Arg
290 295 300
Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys
305 310 315 320
Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu
325 330 335
Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr
340 345 350
Thr Leu Pro Pro Ser Gln Glu Glu Met Thr Lys Asn Gln Val Ser Leu
355 360 365

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

<210> 138
<211> 450
<212> PRT
<213> 人工序列
<220>
<223> IgG4P HC
<400> 138
Gln Leu Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu
1 5 10 15
Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Arg
[0127] 20 25 30
Ser Tyr Tyr Trp Gly Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu
35 40 45
Trp Ile Gly Ser Ile Tyr Tyr Ser Gly Phe Thr Tyr Tyr Asn Pro Ser
50 55 60
Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
65 70 75 80
Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
85 90 95
Cys Ala Thr Gly Gly Pro Tyr Gly Asp Tyr Ala His Trp Phe Asp Pro
100 105 110
Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly
115 120 125
Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser
130 135 140
Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val
145 150 155 160
Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe
165 170 175
Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val
180 185 190
Thr Val Pro Ser Ser Ser Leu Gly Thr Lys Thr Tyr Thr Cys Asn Val
195 200 205

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

[0128] Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val
385 390 395 400
Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Arg Leu Thr Val Asp
405 410 415
Lys Ser Arg Trp Gln Glu Gly Asn Val Phe Ser Cys Ser Val Met His
420 425 430
Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Leu
435 440 445
Gly Lys
450

<210> 139
<211> 449
<212> PRT
<213> 人工序列
<220>
<223> IgG4P HC (无C末端K)
<400> 139
Gln Leu Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu
1 5 10 15
Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Arg
20 25 30
Ser Tyr Tyr Trp Gly Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu
35 40 45

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

[0129]

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

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

<210> 140
<211> 450
<212> PRT
<213> 人工序列
<220>
<223> IgG4P HC
<400> 140
Gln Leu Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu
1 5 10 15
Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Arg
20 25 30
Ser Tyr Tyr Trp Gly Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu
35 40 45
Trp Ile Gly Ser Ile Tyr Tyr Ser Gly Phe Thr Tyr Tyr Gln Pro Ser
50 55 60
[0130] Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
65 70 75 80
Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
85 90 95
Cys Ala Thr Gly Gly Pro Tyr Gly Asp Tyr Ala His Trp Phe Asp Pro
100 105 110
Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly
115 120 125
Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser
130 135 140
Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val
145 150 155 160
Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe
165 170 175
Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val
180 185 190
Thr Val Pro Ser Ser Ser Leu Gly Thr Lys Thr Tyr Thr Cys Asn Val
195 200 205
Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Ser Lys
210 215 220
Tyr Gly Pro Pro Cys Pro Pro Cys Pro Ala Pro Glu Phe Leu Gly Gly
225 230 235 240
Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile

245 250 255
Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser Gln Glu
260 265 270
Asp Pro Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val His
275 280 285
Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr Tyr Arg
290 295 300
Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys
305 310 315 320
Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu
325 330 335
Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr
340 345 350
Thr Leu Pro Pro Ser Gln Glu Glu Met Thr Lys Asn Gln Val Ser Leu
355 360 365

Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp
370 375 380
Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val
385 390 395 400
Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Arg Leu Thr Val Asp
405 410 415
[0131] Lys Ser Arg Trp Gln Glu Gly Asn Val Phe Ser Cys Ser Val Met His
420 425 430
Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Leu
435 440 445
Gly Lys
450

<210> 141
<211> 449
<212> PRT
<213> 人工序列
<220>
<223> IgG4P HC (无C末端K)
<400> 141
Gln Leu Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu
1 5 10 15
Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Arg
20 25 30
Ser Tyr Tyr Trp Gly Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu
35 40 45
Trp Ile Gly Ser Ile Tyr Tyr Ser Gly Phe Thr Tyr Tyr Gln Pro Ser
50 55 60
Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
65 70 75 80

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

[0132] Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser Gln Glu
260 265 270
Asp Pro Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val His
275 280 285
Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr Tyr Arg
290 295 300
Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys
305 310 315 320
Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu
325 330 335
Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr
340 345 350
Thr Leu Pro Pro Ser Gln Glu Glu Met Thr Lys Asn Gln Val Ser Leu
355 360 365
Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp
370 375 380
Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val
385 390 395 400
Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Arg Leu Thr Val Asp
405 410 415
Lys Ser Arg Trp Gln Glu Gly Asn Val Phe Ser Cys Ser Val Met His
420 425 430
Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Leu

435 440 445

Gly

<210> 142
<211> 450
<212> PRT
<213> 人工序列
<220>
<223> IgG4P HC
<400> 142

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

[0133]

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

275 280 285

Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr Tyr Arg
290 295 300

Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys
305 310 315 320

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

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

Thr Leu Pro Pro Ser Gln Glu Glu Met Thr Lys Asn Gln Val Ser Leu
355 360 365

Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp
370 375 380

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

Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Arg Leu Thr Val Asp
405 410 415

Lys Ser Arg Trp Gln Glu Gly Asn Val Phe Ser Cys Ser Val Met His
420 425 430

Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Leu
435 440 445

Gly Lys
450

[0134]

<210> 143
<211> 449
<212> PRT
<213> 人工序列
<220>
<223> IgG4P HC (无C末端K)
<400> 143

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

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Arg
20 25 30

Ser Tyr Tyr Trp Gly Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu
35 40 45

Trp Ile Gly Ser Ile Tyr Tyr Ser Gly Phe Thr Tyr Tyr Ser Pro Ser
50 55 60

Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
65 70 75 80

Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
85 90 95

Cys Ala Thr Gly Gly Pro Tyr Gly Asp Tyr Ala His Trp Phe Asp Pro
100 105 110

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

115 120 125

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

Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val
145 150 155 160

Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe
165 170 175

Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val
180 185 190

Thr Val Pro Ser Ser Ser Leu Gly Thr Lys Thr Tyr Thr Cys Asn Val
195 200 205

Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Ser Lys
210 215 220

Tyr Gly Pro Pro Cys Pro Pro Cys Pro Ala Pro Glu Phe Leu Gly Gly
225 230 235 240

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

Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser Gln Glu
260 265 270

Asp Pro Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val His
275 280 285

Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr Tyr Arg
[0135] 290 295 300

Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys
305 310 315 320

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

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

Thr Leu Pro Pro Ser Gln Glu Glu Met Thr Lys Asn Gln Val Ser Leu
355 360 365

Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp
370 375 380

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

Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Arg Leu Thr Val Asp
405 410 415

Lys Ser Arg Trp Gln Glu Gly Asn Val Phe Ser Cys Ser Val Met His
420 425 430

Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Leu
435 440 445

Gly

<210> 144
<211> 450

<212> PRT
<213> 人工序列
<220>
<223> IgG4P HC
<400> 144

Gln Leu Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu
1 5 10 15
Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Arg
20 25 30
Ser Tyr Tyr Trp Gly Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu
35 40 45
Trp Ile Gly Ser Ile Tyr Tyr Ser Gly Phe Thr Tyr Tyr Ala Pro Ser
50 55 60
Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
65 70 75 80
Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
85 90 95
Cys Ala Thr Gly Gly Pro Tyr Gly Asp Tyr Ala His Trp Phe Asp Pro
100 105 110
Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly
115 120 125
Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser
[0136] 130 135 140
Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val
145 150 155 160
Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe
165 170 175
Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val
180 185 190
Thr Val Pro Ser Ser Ser Leu Gly Thr Lys Thr Tyr Thr Cys Asn Val
195 200 205
Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Ser Lys
210 215 220
Tyr Gly Pro Pro Cys Pro Pro Cys Pro Ala Pro Glu Phe Leu Gly Gly
225 230 235 240
Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile
245 250 255
Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser Gln Glu
260 265 270
Asp Pro Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val His
275 280 285
Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr Tyr Arg
290 295 300
Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys
305 310 315 320

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

<210> 145
<211> 449
<212> PRT
<213> 人工序列

[0137] <220>
<223> IgG4P HC (无C末端K)
<400> 145

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

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

[0138] Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr
340 345 350
Thr Leu Pro Pro Ser Gln Glu Glu Met Thr Lys Asn Gln Val Ser Leu
355 360 365
Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp
370 375 380
Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val
385 390 395 400
Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Arg Leu Thr Val Asp
405 410 415
Lys Ser Arg Trp Gln Glu Gly Asn Val Phe Ser Cys Ser Val Met His
420 425 430
Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Leu
435 440 445
Gly

<210> 146
<211> 450
<212> PRT
<213> 人工序列
<220>
<223> IgG4P HC
<400> 146

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

[0139]

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

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

<210> 147
<211> 449
<212> PRT
<213> 人工序列
<220>
<223> IgG4P HC (无C末端K)
<400> 147

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

[0140] Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Arg
20 25 30
Ser Tyr Tyr Trp Gly Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu
35 40 45
Trp Ile Gly Ser Ile Tyr Tyr Ser Gly Phe Thr Tyr Tyr Asn Pro Ser
50 55 60
Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
65 70 75 80
Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
85 90 95
Cys Ala Thr Gly Gly Pro Tyr Gly Asp Tyr Ala His Trp Phe Glu Pro
100 105 110
Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly
115 120 125
Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser
130 135 140
Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val
145 150 155 160
Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe
165 170 175
Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val
180 185 190
Thr Val Pro Ser Ser Ser Leu Gly Thr Lys Thr Tyr Thr Cys Asn Val

195 200 205

Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Ser Lys
210 215 220

Tyr Gly Pro Pro Cys Pro Pro Cys Pro Ala Pro Glu Phe Leu Gly Gly
225 230 235 240

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

Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser Gln Glu
260 265 270

Asp Pro Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val His
275 280 285

Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr Tyr Arg
290 295 300

Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys
305 310 315 320

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

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

Thr Leu Pro Pro Ser Gln Glu Glu Met Thr Lys Asn Gln Val Ser Leu
355 360 365

Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp
[0141] 370 375 380

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

Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Arg Leu Thr Val Asp
405 410 415

Lys Ser Arg Trp Gln Glu Gly Asn Val Phe Ser Cys Ser Val Met His
420 425 430

Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Leu
435 440 445

Gly

<210> 148
<211> 450
<212> PRT
<213> 人工序列
<220>
<223> IgG4P HC
<400> 148

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

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Arg
20 25 30

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

[0142]

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

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

<210> 149
<211> 449
<212> PRT
<213> 人工序列
<220>
<223> IgG4P HC (无C末端K)
<400> 149

Gln Leu Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu
1 5 10 15
Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Arg
20 25 30
Ser Tyr Tyr Trp Gly Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu
35 40 45

[0143]
Trp Ile Gly Ser Ile Tyr Tyr Ser Gly Phe Thr Tyr Tyr Asn Pro Ser
50 55 60
Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
65 70 75 80
Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
85 90 95
Cys Ala Thr Gly Gly Pro Tyr Gly Asp Tyr Ala His Trp Phe Asp Val
100 105 110
Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly
115 120 125
Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser
130 135 140
Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val
145 150 155 160
Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe
165 170 175
Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val
180 185 190
Thr Val Pro Ser Ser Ser Leu Gly Thr Lys Thr Tyr Thr Cys Asn Val
195 200 205
Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Ser Lys
210 215 220
Tyr Gly Pro Pro Cys Pro Pro Cys Pro Ala Pro Glu Phe Leu Gly Gly

225 230 235 240
Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile
245 250 255
Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser Gln Glu
260 265 270
Asp Pro Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val His
275 280 285
Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr Tyr Arg
290 295 300
Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys
305 310 315 320
Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu
325 330 335
Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr
340 345 350
Thr Leu Pro Pro Ser Gln Glu Glu Met Thr Lys Asn Gln Val Ser Leu
355 360 365
Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp
370 375 380
Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val
385 390 395 400
Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Arg Leu Thr Val Asp
[0144] 405 410 415
Lys Ser Arg Trp Gln Glu Gly Asn Val Phe Ser Cys Ser Val Met His
420 425 430
Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Leu
435 440 445
Gly

<210> 150
<211> 450
<212> PRT
<213> 人工序列
<220>
<223> IgG4P HC
<400> 150
Gln Leu Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu
1 5 10 15
Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Arg
20 25 30
Ser Tyr Tyr Trp Gly Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu
35 40 45
Trp Ile Gly Ser Ile Tyr Tyr Ser Gly Phe Thr Tyr Tyr Asn Pro Ser
50 55 60
Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe

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

Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Leu
435 440 445
Gly Lys
450

<210> 151
<211> 449
<212> PRT
<213> 人工序列
<220>
<223> IgG4P HC (无C末端K)
<400> 151

Gln Leu Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu
1 5 10 15
Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Arg
20 25 30
Ser Tyr Tyr Trp Gly Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu
35 40 45
Trp Ile Gly Ser Ile Tyr Tyr Ser Gly Phe Thr Tyr Tyr Asn Pro Ser
50 55 60
Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
65 70 75 80
Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
[0146] 85 90 95
Cys Ala Thr Gly Gly Pro Tyr Gly Asp Tyr Ala His Trp Phe Asp Tyr
100 105 110
Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly
115 120 125
Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser
130 135 140
Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val
145 150 155 160
Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe
165 170 175
Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val
180 185 190
Thr Val Pro Ser Ser Ser Leu Gly Thr Lys Thr Tyr Thr Cys Asn Val
195 200 205
Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Ser Lys
210 215 220
Tyr Gly Pro Pro Cys Pro Pro Cys Pro Ala Pro Glu Phe Leu Gly Gly
225 230 235 240
Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile
245 250 255
Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser Gln Glu
260 265 270

Asp Pro Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val His
275 280 285
Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr Tyr Arg
290 295 300
Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys
305 310 315 320

Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu
325 330 335
Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr
340 345 350
Thr Leu Pro Pro Ser Gln Glu Glu Met Thr Lys Asn Gln Val Ser Leu
355 360 365
Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp
370 375 380
Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val
385 390 395 400
Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Arg Leu Thr Val Asp
405 410 415
Lys Ser Arg Trp Gln Glu Gly Asn Val Phe Ser Cys Ser Val Met His
420 425 430
Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Leu
[0147] 435 440 445
Gly

<210> 152
<211> 450
<212> PRT
<213> 人工序列
<220>
<223> IgG4P HC
<400> 152
Gln Leu Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu
1 5 10 15
Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Arg
20 25 30
Ser Tyr Tyr Trp Gly Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu
35 40 45
Trp Ile Gly Ser Ile Tyr Tyr Ser Gly Phe Thr Tyr Tyr Asn Pro Ser
50 55 60
Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
65 70 75 80
Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
85 90 95
Cys Ala Thr Gly Gly Pro Tyr Gly Asp Tyr Ala His Trp Phe Asp Leu

100 105 110
Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly
115 120 125
Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser
130 135 140
Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val
145 150 155 160
Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe
165 170 175
Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val
180 185 190
Thr Val Pro Ser Ser Ser Leu Gly Thr Lys Thr Tyr Thr Cys Asn Val
195 200 205
Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Ser Lys
210 215 220
Tyr Gly Pro Pro Cys Pro Pro Cys Pro Ala Pro Glu Phe Leu Gly Gly
225 230 235 240
Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile
245 250 255
Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser Gln Glu
260 265 270
Asp Pro Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val His
[0148] 275 280 285
Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr Tyr Arg
290 295 300
Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys
305 310 315 320
Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu
325 330 335
Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr
340 345 350
Thr Leu Pro Pro Ser Gln Glu Glu Met Thr Lys Asn Gln Val Ser Leu
355 360 365
Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp
370 375 380
Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val
385 390 395 400

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

450

<210> 153
<211> 449
<212> PRT
<213> 人工序列
<220>
<223> IgG4P HC (无C末端K)
<400> 153

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

[0149]

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

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

[0150]
<210> 154
<211> 450
<212> PRT
<213> 人工序列
<220>
<223> IgG4P HC
<400> 154
Gln Leu Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu
1 5 10 15
Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Arg
20 25 30
Ser Tyr Tyr Trp Gly Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu
35 40 45
Trp Ile Gly Ser Ile Tyr Tyr Ser Gly Phe Thr Tyr Tyr Gln Pro Ser
50 55 60
Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
65 70 75 80
Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
85 90 95
Cys Ala Thr Gly Gly Pro Tyr Gly Asp Tyr Ala His Trp Phe Asp Tyr
100 105 110
Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly
115 120 125
Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser

130 135 140

Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val
145 150 155 160
Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe
165 170 175
Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val
180 185 190
Thr Val Pro Ser Ser Ser Leu Gly Thr Lys Thr Tyr Thr Cys Asn Val
195 200 205
Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Ser Lys
210 215 220
Tyr Gly Pro Pro Cys Pro Pro Cys Pro Ala Pro Glu Phe Leu Gly Gly
225 230 235 240
Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile
245 250 255
Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser Gln Glu
260 265 270
Asp Pro Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val His
275 280 285
Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr Tyr Arg
290 295 300
Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys
[0151] 305 310 315 320
Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu
325 330 335
Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr
340 345 350
Thr Leu Pro Pro Ser Gln Glu Glu Met Thr Lys Asn Gln Val Ser Leu
355 360 365
Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp
370 375 380
Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val
385 390 395 400
Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Arg Leu Thr Val Asp
405 410 415
Lys Ser Arg Trp Gln Glu Gly Asn Val Phe Ser Cys Ser Val Met His
420 425 430
Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Leu
435 440 445
Gly Lys
450

<210> 155
<211> 449
<212> PRT
<213> 人工序列

<220>
<223> IgG4P HC (无C末端K)
<400> 155

Gln Leu Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu
1 5 10 15
Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Arg
20 25 30
Ser Tyr Tyr Trp Gly Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu
35 40 45
Trp Ile Gly Ser Ile Tyr Tyr Ser Gly Phe Thr Tyr Tyr Gln Pro Ser
50 55 60
Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
65 70 75 80
Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
85 90 95
Cys Ala Thr Gly Gly Pro Tyr Gly Asp Tyr Ala His Trp Phe Asp Tyr
100 105 110
Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly
115 120 125
Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser
130 135 140
Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val
[0152] 145 150 155 160
Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe
165 170 175
Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val
180 185 190
Thr Val Pro Ser Ser Ser Leu Gly Thr Lys Thr Tyr Thr Cys Asn Val
195 200 205
Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Ser Lys
210 215 220
Tyr Gly Pro Pro Cys Pro Pro Cys Pro Ala Pro Glu Phe Leu Gly Gly
225 230 235 240
Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile
245 250 255
Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser Gln Glu
260 265 270
Asp Pro Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val His
275 280 285
Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr Tyr Arg
290 295 300
Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys
305 310 315 320
Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu
325 330 335

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

<210> 156
<211> 447
<212> PRT
<213> 人工序列
<220>
<223> IgG1za HC

[0153] <400> 156

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

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

[0154]

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

<210> 157
<211> 446
<212> PRT
<213> 人工序列
<220>
<223> IgG1za HC (无C末端K)
<400> 157

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu
1 5 10 15
Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Arg His
20 25 30

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Tyr Trp Asn Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile
        35                  40                  45
Gly Tyr Ile His Tyr Ser Gly Ser Thr Asn Tyr Asn Ser Ser Leu Lys
    50                  55                  60
Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe Ser Leu
65                  70                  75                  80
Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala
                85                  90                  95
Arg Asp Thr Gly Tyr Tyr Gly Met Asp Ile Trp Gly Gln Gly Thr Thr
            100                 105                 110
Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu
        115                 120                 125
Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys
    130                 135                 140
Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser
145                 150                 155                 160
Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser
                165                 170                 175
Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser
            180                 185                 190
Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn
        195                 200                 205
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[0155]

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

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

<210> 158
<211> 444
<212> PRT
<213> 人工序列
<220>
<223> IgG4P HC
<400> 158

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

[0156]

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

245 250 255
Thr Cys Val Val Val Asp Val Ser Gln Glu Asp Pro Glu Val Gln Phe
260 265 270
Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro
275 280 285
Arg Glu Glu Gln Phe Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr
290 295 300
Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val
305 310 315 320
Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys Ala
325 330 335
Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Gln
340 345 350
Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly
355 360 365
Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro
370 375 380
Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser
385 390 395 400
Phe Phe Leu Tyr Ser Arg Leu Thr Val Asp Lys Ser Arg Trp Gln Glu
405 410 415
Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His
[0157] 420 425 430
Tyr Thr Gln Lys Ser Leu Ser Leu Ser Leu Gly Lys
435 440

<210> 159
<211> 443
<212> PRT
<213> 人工序列
<220>
<223> IgG4P HC (无C末端K)
<400> 159
Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu
1 5 10 15
Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Arg His
20 25 30
Tyr Trp Asn Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile
35 40 45
Gly Tyr Ile His Tyr Ser Gly Ser Thr Asn Tyr Asn Ser Ser Leu Lys
50 55 60
Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe Ser Leu
65 70 75 80
Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala
85 90 95
Arg Asp Thr Gly Tyr Tyr Gly Met Asp Ile Trp Gly Gln Gly Thr Thr

100 105 110

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

Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser Thr Ala Ala Leu Gly Cys
130 135 140

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

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

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

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

Thr Lys Val Asp Lys Arg Val Glu Ser Lys Tyr Gly Pro Pro Cys Pro
210 215 220

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

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

Thr Cys Val Val Val Asp Val Ser Gln Glu Asp Pro Glu Val Gln Phe
260 265 270

Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro
[0158] 275 280 285

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

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

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

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

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

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

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

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

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

Tyr Thr Gln Lys Ser Leu Ser Leu Ser Leu Gly
435 440

<210> 160

<211> 444

<212> PRT
<213> 人工序列
<220>
<223> IgG4P HC
<400> 160

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

Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala
                85                  90                  95
Arg Asp Thr Gly Tyr Tyr Gly Met Asp Ile Trp Gly Gln Gly Thr Thr
            100                 105                 110
Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu
        115                 120                 125
Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser Thr Ala Ala Leu Gly Cys
    130                 135                 140
Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser
145                 150                 155                 160
Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser
                165                 170                 175
Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser
            180                 185                 190
Leu Gly Thr Lys Thr Tyr Thr Cys Asn Val Asp His Lys Pro Ser Asn
        195                 200                 205
Thr Lys Val Asp Lys Arg Val Glu Ser Lys Tyr Gly Pro Pro Cys Pro
    210                 215                 220
Pro Cys Pro Ala Pro Glu Phe Leu Gly Gly Pro Ser Val Phe Leu Phe
225                 230                 235                 240
Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val
                245                 250                 255
Thr Cys Val Val Val Asp Val Ser Gln Glu Asp Pro Glu Val Gln Phe
            260                 265                 270
Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro
        275                 280                 285
Arg Glu Glu Gln Phe Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr
    290                 295                 300
Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val
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[0159]

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

<210> 161
<211> 443
<212> PRT
<213> 人工序列
<220>

[0160] <223> IgG4P HC (无C末端K)
<400> 161

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

165 170 175
Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser
180 185 190
Leu Gly Thr Lys Thr Tyr Thr Cys Asn Val Asp His Lys Pro Ser Asn
195 200 205
Thr Lys Val Asp Lys Arg Val Glu Ser Lys Tyr Gly Pro Pro Cys Pro
210 215 220
Pro Cys Pro Ala Pro Glu Phe Leu Gly Gly Pro Ser Val Phe Leu Phe
225 230 235 240
Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val
245 250 255
Thr Cys Val Val Val Asp Val Ser Gln Glu Asp Pro Glu Val Gln Phe
260 265 270
Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro
275 280 285
Arg Glu Glu Gln Phe Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr
290 295 300
Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val
305 310 315 320
Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys Ala
325 330 335
Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Gln
[0161] 340 345 350
Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly
355 360 365
Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro
370 375 380
Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser
385 390 395 400
Phe Phe Leu Tyr Ser Arg Leu Thr Val Asp Lys Ser Arg Trp Gln Glu
405 410 415
Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His
420 425 430
Tyr Thr Gln Lys Ser Leu Ser Leu Ser Leu Gly
435 440

<210> 162
<211> 447
<212> PRT
<213> 人工序列
<220>
<223> IgG1za HC
<400> 162
Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu
1 5 10 15
Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Arg Tyr

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

[0162]

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

<210> 163
<211> 446
<212> PRT
<213> 人工序列
<220>
<223> IgG1za HC (无C末端K)
<400> 163

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

[0163]

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

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

[0164] Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu
420 425 430
His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
435 440 445

<210> 164
<211> 367
<212> PRT
<213> 人工序列
<220>
<223> IgG4P HC
<400> 164

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

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

[0165] Pro Ser Gln Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu
275 280 285
Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn
290 295 300
Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser
305 310 315 320
Asp Gly Ser Phe Phe Leu Tyr Ser Arg Leu Thr Val Asp Lys Ser Arg
325 330 335
Trp Gln Glu Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu
340 345 350

His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Leu Gly Lys
355 360 365

<210> 165
<211> 366
<212> PRT
<213> 人工序列
<220>
<223> IgG4P HC (无C末端K)
<400> 165
Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu
1 5 10 15
Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Arg Tyr

20 25 30

Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile
35 40 45

Gly Tyr Ile His Tyr Thr Gly Ser Thr Asn Tyr Asn Pro Ser Leu Lys
50 55 60

Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe Ser Leu
65 70 75 80

Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala
85 90 95

Thr Asp Thr Gly Tyr Tyr Gly Met Asp Val Trp Gly Gln Gly Thr Thr
100 105 110

Val Thr Val Ser Ser Thr Lys Thr Tyr Thr Cys Asn Val Asp His Lys
115 120 125

Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Ser Lys Tyr Gly Pro
130 135 140

Pro Cys Pro Pro Cys Pro Ala Pro Glu Phe Leu Gly Gly Pro Ser Val
145 150 155 160

Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr
165 170 175

Pro Glu Val Thr Cys Val Val Val Asp Val Ser Gln Glu Asp Pro Glu
180 185 190

Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys
[0166] 195 200 205

Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr Tyr Arg Val Val Ser
210 215 220

Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys
225 230 235 240

Cys Lys Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr Ile
245 250 255

Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro
260 265 270

Pro Ser Gln Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu
275 280 285

Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn
290 295 300

Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser
305 310 315 320

Asp Gly Ser Phe Phe Leu Tyr Ser Arg Leu Thr Val Asp Lys Ser Arg
325 330 335

Trp Gln Glu Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu
340 345 350

His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Leu Gly
355 360 365

<210> 166

<211> 453

<212> PRT
<213> 人工序列
<220>
<223> IgG1za HC
<400> 166

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Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1               5                  10                  15
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
            20                  25                  30
Tyr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
        35                  40                  45
Gly Ile Ile Asn Pro Arg Gly Asp Ser Ile Ile Tyr Ala Gln Lys Phe
    50                  55                  60
Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Thr Ser Thr Val Tyr
65                  70                  75                  80
Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95
Ala Arg Asp Phe Tyr Gly Ser Gly Asn Tyr Tyr Tyr Gly Met Asp Val
            100                 105                 110
Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly
        115                 120                 125
Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly
    130                 135                 140
Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val
145                 150                 155                 160
Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe
                165                 170                 175
Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val
            180                 185                 190
Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val
        195                 200                 205
Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys
    210                 215                 220
Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu
225                 230                 235                 240
Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
                245                 250                 255
Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val
            260                 265                 270
Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
        275                 280                 285
Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
    290                 295                 300
Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
305                 310                 315                 320
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[0167]

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

<210> 167
<211> 452
<212> PRT
<213> 人工序列

[0168] <220>
<223> IgG1za HC (无C末端K)
<400> 167

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

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

[0169] Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
340 345 350
Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln
355 360 365
Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala
370 375 380
Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
385 390 395 400
Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
405 410 415
Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
420 425 430
Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
435 440 445
Leu Ser Pro Gly
450

<210> 168
<211> 450
<212> PRT
<213> 人工序列
<220>
<223> IgG4P HC
<400> 168

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

[0170] Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val
180 185 190
Thr Val Pro Ser Ser Ser Leu Gly Thr Lys Thr Tyr Thr Cys Asn Val
195 200 205
Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Ser Lys
210 215 220
Tyr Gly Pro Pro Cys Pro Pro Cys Pro Ala Pro Glu Phe Leu Gly Gly
225 230 235 240
Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile
245 250 255
Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser Gln Glu
260 265 270
Asp Pro Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val His
275 280 285
Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr Tyr Arg
290 295 300
Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys
305 310 315 320
Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu
325 330 335
Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr
340 345 350
Thr Leu Pro Pro Ser Gln Glu Glu Met Thr Lys Asn Gln Val Ser Leu

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

<210> 169
<211> 449
<212> PRT
<213> 人工序列
<220>
<223> IgG4P HC (无C末端K)
<400> 169
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15
[0171] Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30
Tyr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45
Gly Ile Ile Asn Pro Arg Gly Asp Ser Ile Ile Tyr Ala Gln Lys Phe
50 55 60
Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Thr Ser Thr Val Tyr
65 70 75 80
Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95
Ala Arg Asp Phe Tyr Gly Ser Gly Asn Tyr Tyr Tyr Gly Met Asp Val
100 105 110
Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly
115 120 125
Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser
130 135 140
Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val
145 150 155 160
Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe
165 170 175
Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val
180 185 190
Thr Val Pro Ser Ser Ser Leu Gly Thr Lys Thr Tyr Thr Cys Asn Val

195 200 205

Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Ser Lys
210 215 220

Tyr Gly Pro Pro Cys Pro Pro Cys Pro Ala Pro Glu Phe Leu Gly Gly
225 230 235 240

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

Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser Gln Glu
260 265 270

Asp Pro Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val His
275 280 285

Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr Tyr Arg
290 295 300

Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys
305 310 315 320

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

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

Thr Leu Pro Pro Ser Gln Glu Glu Met Thr Lys Asn Gln Val Ser Leu
355 360 365

Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp
[0172] 370 375 380

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

Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Arg Leu Thr Val Asp
405 410 415

Lys Ser Arg Trp Gln Glu Gly Asn Val Phe Ser Cys Ser Val Met His
420 425 430

Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Leu
435 440 445

Gly

<210> 170
<211> 453
<212> PRT
<213> 人工序列
<220>
<223> IgG1za HC
<400> 170

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

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

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

35 40 45

Ser Phe Ile Ser Gly Gly Gly Ser Thr Ile Tyr Tyr Ala Asp Ser Val
50 55 60

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

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

Ala Arg Asp Gly Tyr Ser Ser Gly Trp Tyr Tyr Tyr Gly Met Asp Val
100 105 110

Trp Gly Gln Gly Thr Ala Val Thr Val Ser Ser Ala Ser Thr Lys Gly
115 120 125

Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly
130 135 140

Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val
145 150 155 160

Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe
165 170 175

Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val
180 185 190

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

Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys
[0173] 210 215 220

Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu
225 230 235 240

Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
245 250 255

Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val
260 265 270

Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
275 280 285

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
290 295 300

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
305 310 315 320

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
325 330 335

Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
340 345 350

Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln
355 360 365

Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala
370 375 380

Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
385 390 395 400

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
405 410 415
Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
420 425 430
Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
435 440 445
Leu Ser Pro Gly Lys
450

<210> 171
<211> 452
<212> PRT
<213> 人工序列
<220>
<223> IgG1za HC (无C末端K)
<400> 171

Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1 5 10 15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp Tyr
20 25 30
Tyr Met Ser Trp Ile Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45
Ser Phe Ile Ser Gly Gly Gly Ser Thr Ile Tyr Tyr Ala Asp Ser Val
[0174] 50 55 60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Phe
65 70 75 80
Leu Gln Met Asn Ser Leu Arg Val Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95
Ala Arg Asp Gly Tyr Ser Ser Gly Trp Tyr Tyr Tyr Gly Met Asp Val
100 105 110
Trp Gly Gln Gly Thr Ala Val Thr Val Ser Ser Ala Ser Thr Lys Gly
115 120 125
Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly
130 135 140
Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val
145 150 155 160
Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe
165 170 175
Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val
180 185 190
Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val
195 200 205
Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys
210 215 220
Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu
225 230 235 240

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

[0175] Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
420 425 430
Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
435 440 445
Leu Ser Pro Gly
450

<210> 172
<211> 450
<212> PRT
<213> 人工序列
<220>
<223> IgG4P HC
<400> 172

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

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

[0176] Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser Gln Glu
260 265 270
Asp Pro Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val His
275 280 285

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

Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Leu
435 440 445
Gly Lys
450

<210> 173
<211> 449
<212> PRT
<213> 人工序列
<220>
<223> IgG4P HC (无C末端K)
<400> 173

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

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

[0178] Gly

<210> 174
<211> 450
<212> PRT
<213> 人工序列
<220>
<223> IgG4P HC
<400> 174
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1 5 10 15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp Tyr
20 25 30
Tyr Met Ser Trp Ile Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45
Ser Phe Ile Ser Gly Gly Gly Ser Thr Ile Tyr Tyr Ala Asp Ser Val
50 55 60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Phe
65 70 75 80
Leu Gln Met Asn Ser Leu Arg Val Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95
Ala Arg Asp Gly Tyr Ser Ser Gly Trp Tyr Tyr Tyr Gly Met Asp Val
100 105 110

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

[0179] Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr Tyr Arg
290 295 300
Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys
305 310 315 320
Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu
325 330 335
Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr
340 345 350
Thr Leu Pro Pro Ser Gln Glu Glu Met Thr Lys Asn Gln Val Ser Leu
355 360 365
Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp
370 375 380
Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val
385 390 395 400
Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Arg Leu Thr Val Asp
405 410 415
Lys Ser Arg Trp Gln Glu Gly Asn Val Phe Ser Cys Ser Val Met His
420 425 430
Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Leu
435 440 445
Gly Lys
450

<210> 175

<211> 449
<212> PRT
<213> 人工序列
<220>
<223> IgG4P HC (无C末端K)
<400> 175

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

[0180]

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

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

<210> 176
<211> 454
<212> PRT
[0181] <213> 人工序列
<220>
<223> IgG1za HC
<400> 176
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1 5 10 15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp Tyr
20 25 30
Tyr Met Ser Trp Ile Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45
Ser Phe Ile Ser Thr Ser Gly Ser Ile Ile Tyr Tyr Ala Asp Ser Val
50 55 60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65 70 75 80
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95
Ala Arg Glu Gly Tyr Ser Ser Ser Trp Ser Tyr Tyr Tyr Gly Met Asp
100 105 110
Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys
115 120 125
Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly
130 135 140
Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro

145 150 155 160
Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr
165 170 175
Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val
180 185 190
Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn
195 200 205
Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro
210 215 220
Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu
225 230 235 240
Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
245 250 255
Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp
260 265 270
Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
275 280 285
Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn
290 295 300
Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
305 310 315 320
Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro
[0182] 325 330 335
Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
340 345 350
Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn
355 360 365
Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
370 375 380
Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
385 390 395 400
Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys
405 410 415
Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
420 425 430
Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
435 440 445
Ser Leu Ser Pro Gly Lys
450

<210> 177
<211> 453
<212> PRT
<213> 人工序列
<220>
<223> IgG1za HC (无C末端K)

<400> 177

Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1 5 10 15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp Tyr
20 25 30
Tyr Met Ser Trp Ile Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45
Ser Phe Ile Ser Thr Ser Gly Ser Ile Ile Tyr Tyr Ala Asp Ser Val
50 55 60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65 70 75 80
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95
Ala Arg Glu Gly Tyr Ser Ser Ser Trp Ser Tyr Tyr Tyr Gly Met Asp
100 105 110
Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys
115 120 125
Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly
130 135 140
Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro
145 150 155 160
Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr
[0183] 165 170 175
Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val
180 185 190
Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn
195 200 205
Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro
210 215 220
Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu
225 230 235 240
Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
245 250 255
Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp
260 265 270
Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
275 280 285
Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn
290 295 300
Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
305 310 315 320
Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro
325 330 335
Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
340 345 350

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

<210> 178
<211> 451
<212> PRT
<213> 人工序列
<220>
<223> IgG4P HC
<400> 178

[0184]
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1 5 10 15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp Tyr
20 25 30
Tyr Met Ser Trp Ile Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45
Ser Phe Ile Ser Thr Ser Gly Ser Ile Ile Tyr Tyr Ala Asp Ser Val
50 55 60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65 70 75 80
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95
Ala Arg Glu Gly Tyr Ser Ser Ser Trp Ser Tyr Tyr Tyr Gly Met Asp
100 105 110
Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys
115 120 125
Gly Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu
130 135 140
Ser Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro
145 150 155 160
Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr
165 170 175
Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val
180 185 190

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

[0185]

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

<210> 179
<211> 450
<212> PRT
<213> 人工序列
<220>
<223> IgG4P HC (无C末端K)
<400> 179
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1 5 10 15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp Tyr
20 25 30

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

[0186]

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

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

<210> 180
<211> 450
<212> PRT
<213> 人工序列
<220>
<223> IgG4 HC
<400> 180

Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1 5 10 15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp Tyr
20 25 30
Tyr Met Ser Trp Ile Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45
[0187] Ser Phe Ile Ser Ser Ser Gly Ser Ile Ile Tyr Tyr Ala Asp Ser Val
50 55 60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65 70 75 80
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95
Ala Arg Asp Gly Tyr Ser Ser Gly Trp Glu Tyr Tyr Gly Met Asp Val
100 105 110
Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly
115 120 125
Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser
130 135 140
Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val
145 150 155 160
Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe
165 170 175
Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val
180 185 190
Thr Val Pro Ser Ser Ser Leu Gly Thr Lys Thr Tyr Thr Cys Asn Val
195 200 205
Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Ser Lys
210 215 220
Tyr Gly Pro Pro Cys Pro Ser Cys Pro Ala Pro Glu Phe Leu Gly Gly

225 230 235 240
Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile
245 250 255
Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser Gln Glu
260 265 270
Asp Pro Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val His
275 280 285
Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr Tyr Arg
290 295 300
Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys
305 310 315 320
Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu
325 330 335
Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr
340 345 350
Thr Leu Pro Pro Ser Gln Glu Glu Met Thr Lys Asn Gln Val Ser Leu
355 360 365
Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp
370 375 380
Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val
385 390 395 400
Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Arg Leu Thr Val Asp
[0188] 405 410 415
Lys Ser Arg Trp Gln Glu Gly Asn Val Phe Ser Cys Ser Val Met His
420 425 430
Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Leu
435 440 445
Gly Lys
450

<210> 181
<211> 449
<212> PRT
<213> 人工序列
<220>
<223> IgG4 HC (无 C 末端 K)
<400> 181
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1 5 10 15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp Tyr
20 25 30
Tyr Met Ser Trp Ile Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45
Ser Phe Ile Ser Ser Ser Gly Ser Ile Ile Tyr Tyr Ala Asp Ser Val
50 55 60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr

65 70 75 80
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95
Ala Arg Asp Gly Tyr Ser Ser Gly Trp Glu Tyr Tyr Gly Met Asp Val
100 105 110
Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly
115 120 125
Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser
130 135 140
Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val
145 150 155 160
Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe
165 170 175
Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val
180 185 190
Thr Val Pro Ser Ser Ser Leu Gly Thr Lys Thr Tyr Thr Cys Asn Val
195 200 205
Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Ser Lys
210 215 220
Tyr Gly Pro Pro Cys Pro Ser Cys Pro Ala Pro Glu Phe Leu Gly Gly
225 230 235 240
Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile
[0189] 245 250 255
Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser Gln Glu
260 265 270
Asp Pro Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val His
275 280 285
Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr Tyr Arg
290 295 300
Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys
305 310 315 320
Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu
325 330 335
Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr
340 345 350
Thr Leu Pro Pro Ser Gln Glu Glu Met Thr Lys Asn Gln Val Ser Leu
355 360 365
Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp
370 375 380
Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val
385 390 395 400
Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Arg Leu Thr Val Asp
405 410 415
Lys Ser Arg Trp Gln Glu Gly Asn Val Phe Ser Cys Ser Val Met His
420 425 430

Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Leu
435 440 445
Gly

<210> 182
<211> 450
<212> PRT
<213> 人工序列
<220>
<223> IgG4P HC
<400> 182
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1 5 10 15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp Tyr
20 25 30
Tyr Met Ser Trp Ile Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45
Ser Phe Ile Ser Ser Ser Gly Ser Ile Ile Tyr Tyr Ala Asp Ser Val
50 55 60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65 70 75 80
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
[0190] 85 90 95
Ala Arg Asp Gly Tyr Ser Ser Gly Trp Glu Tyr Tyr Gly Met Asp Val
100 105 110
Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly
115 120 125
Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser
130 135 140
Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val
145 150 155 160
Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe
165 170 175
Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val
180 185 190
Thr Val Pro Ser Ser Ser Leu Gly Thr Lys Thr Tyr Thr Cys Asn Val
195 200 205
Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Ser Lys
210 215 220
Tyr Gly Pro Pro Cys Pro Pro Cys Pro Ala Pro Glu Phe Leu Gly Gly
225 230 235 240
Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile
245 250 255
Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser Gln Glu
260 265 270

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

[0191] Gly Lys
450

<210> 183
<211> 449
<212> PRT
<213> 人工序列
<220>
<223> IgG4P HC (无C末端K)
<400> 183

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

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

[0192]

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                100                 105                 110
Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly
        115                 120                 125
Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser
    130                 135                 140
Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val
145                 150                 155                 160
Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe
                165                 170                 175
Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val
            180                 185                 190
Thr Val Pro Ser Ser Ser Leu Gly Thr Lys Thr Tyr Thr Cys Asn Val
        195                 200                 205
Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Ser Lys
    210                 215                 220
Tyr Gly Pro Pro Cys Pro Pro Cys Pro Ala Pro Glu Phe Leu Gly Gly
225                 230                 235                 240
Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile
                245                 250                 255
Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser Gln Glu
            260                 265                 270
Asp Pro Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val His
        275                 280                 285
Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr Tyr Arg
    290                 295                 300
Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys
305                 310                 315                 320
Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu
                325                 330                 335
Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr
            340                 345                 350
Thr Leu Pro Pro Ser Gln Glu Glu Met Thr Lys Asn Gln Val Ser Leu
        355                 360                 365
Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp
    370                 375                 380
Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val
385                 390                 395                 400
Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Arg Leu Thr Val Asp
                405                 410                 415
Lys Ser Arg Trp Gln Glu Gly Asn Val Phe Ser Cys Ser Val Met His
            420                 425                 430
Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Leu
        435                 440                 445
Gly
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<210> 184
<211> 453
<212> PRT
<213> 人工序列
<220>
<223> IgG1.1f HC
<400> 184

Gln Leu Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu
1 5 10 15
Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Arg
20 25 30
Ser Tyr Tyr Trp Gly Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu
35 40 45
Trp Ile Gly Ser Ile Tyr Tyr Ser Gly Phe Thr Tyr Tyr Gln Pro Ser
50 55 60
Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
65 70 75 80
Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
85 90 95
Cys Ala Thr Gly Gly Pro Tyr Gly Asp Tyr Ala His Trp Phe Glu Pro
100 105 110
Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly
[0193] 115 120 125
Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly
130 135 140
Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val
145 150 155 160
Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe
165 170 175
Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val
180 185 190
Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val
195 200 205
Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys
210 215 220
Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Ala
225 230 235 240
Glu Gly Ala Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
245 250 255
Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val
260 265 270
Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
275 280 285
Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
290 295 300

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

<210> 185
<211> 452
[0194] <212> PRT
<213> 人工序列
<220>
<223> IgG1.1f HC (无C末端K)
<400> 185
Gln Leu Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu
1 5 10 15
Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Arg
20 25 30
Ser Tyr Tyr Trp Gly Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu
35 40 45
Trp Ile Gly Ser Ile Tyr Tyr Ser Gly Phe Thr Tyr Tyr Gln Pro Ser
50 55 60
Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
65 70 75 80
Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
85 90 95
Cys Ala Thr Gly Gly Pro Tyr Gly Asp Tyr Ala His Trp Phe Glu Pro
100 105 110
Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly
115 120 125
Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly
130 135 140

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

[0195]

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ser
325 330 335
Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
340 345 350
Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln
355 360 365
Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala
370 375 380

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

<210> 186
<211> 453
<212> PRT
<213> 人工序列

<220>
<223> IgG1.3f HC
<400> 186

Gln Leu Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu
1 5 10 15
Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Arg
20 25 30
Ser Tyr Tyr Trp Gly Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu
35 40 45
Trp Ile Gly Ser Ile Tyr Tyr Ser Gly Phe Thr Tyr Tyr Gln Pro Ser
50 55 60
Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
65 70 75 80
Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
85 90 95
Cys Ala Thr Gly Gly Pro Tyr Gly Asp Tyr Ala His Trp Phe Glu Pro
100 105 110
Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly
115 120 125
Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly
130 135 140
Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val
[0196] 145 150 155 160
Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe
165 170 175
Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val
180 185 190
Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val
195 200 205
Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys
210 215 220
Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Ala
225 230 235 240
Glu Gly Ala Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
245 250 255
Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val
260 265 270
Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
275 280 285
Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
290 295 300
Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
305 310 315 320
Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
325 330 335

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

<210> 187
<211> 452
<212> PRT
<213> 人工序列
<220>
<223> IgG1.3f HC (无C末端K)

[0197] <400> 187

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

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

[0198] Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln
355 360 365
Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala
370 375 380
Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
385 390 395 400
Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
405 410 415
Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
420 425 430
Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
435 440 445
Leu Ser Pro Gly
450

<210> 188
<211> 450
<212> PRT
<213> 人工序列
<220>
<223> IgG4P HC
<400> 188

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

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

[0199]

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

370 375 380

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

<210> 189
<211> 449
<212> PRT
<213> 人工序列
<220>
<223> IgG4P HC (无C末端K)
<400> 189

Gln Leu Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu
1 5 10 15
Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Arg
20 25 30
[0200] Ser Tyr Tyr Trp Gly Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu
35 40 45
Trp Ile Gly Ser Ile Tyr Tyr Ser Gly Phe Thr Tyr Tyr Gln Pro Ser
50 55 60
Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
65 70 75 80
Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
85 90 95
Cys Ala Thr Gly Gly Pro Tyr Gly Asp Tyr Ala His Trp Phe Glu Pro
100 105 110
Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly
115 120 125
Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser
130 135 140
Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val
145 150 155 160
Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe
165 170 175
Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val
180 185 190
Thr Val Pro Ser Ser Ser Leu Gly Thr Lys Thr Tyr Thr Cys Asn Val
195 200 205
Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Ser Lys

210 215 220
Tyr Gly Pro Pro Cys Pro Pro Cys Pro Ala Pro Glu Phe Leu Gly Gly
225 230 235 240
Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile
245 250 255
Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser Gln Glu
260 265 270
Asp Pro Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val His
275 280 285
Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr Tyr Arg
290 295 300
Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys
305 310 315 320
Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu
325 330 335
Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr
340 345 350
Thr Leu Pro Pro Ser Gln Glu Glu Met Thr Lys Asn Gln Val Ser Leu
355 360 365
Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp
370 375 380
Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val
[0201] 385 390 395 400
Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Arg Leu Thr Val Asp
405 410 415
Lys Ser Arg Trp Gln Glu Gly Asn Val Phe Ser Cys Ser Val Met His
420 425 430
Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Leu
435 440 445
Gly

<210> 190
<211> 215
<212> PRT
<213> 人工序列
<220>
<223> LC
<400> 190
Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly
1 5 10 15
Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Ser
20 25 30
Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu
35 40 45
Ile Tyr Gly Ala Ser Ser Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser

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

<210> 191
[0202] <211> 215
<212> PRT
<213> 人工序列
<220>
<223> LC
<400> 191
Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly
1 5 10 15
Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Ser
20 25 30
Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu
35 40 45
Ile Tyr Gly Ala Ser Ser Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser
50 55 60
Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu
65 70 75 80
Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr Gly Ser Ser Pro
85 90 95
Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala
100 105 110
Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser
115 120 125
Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu

130 135 140

Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser
145 150 155 160
Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu
165 170 175
Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val
180 185 190
Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys
195 200 205
Ser Phe Asn Arg Gly Glu Cys
210 215

<210> 192
<211> 214
<212> PRT
<213> 人工序列
<220>
<223> LC
<400> 192

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

[0203] Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45
Tyr Asp Ala Ser Ser Leu Glu Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60
Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80
Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Phe Asn Ser Tyr Pro Arg
85 90 95
Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala
100 105 110
Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly
115 120 125
Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala
130 135 140
Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln
145 150 155 160
Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser
165 170 175
Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr
180 185 190
Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser
195 200 205
Phe Asn Arg Gly Glu Cys

210

<210> 193
<211> 214
<212> PRT
<213> 人工序列
<220>
<223> LC
<400> 193

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

[0204] Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly
115 120 125
Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala
130 135 140
Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln
145 150 155 160
Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser
165 170 175
Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr
180 185 190
Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser
195 200 205
Phe Asn Arg Gly Glu Cys
210

<210> 194
<211> 300
<212> PRT
<213> 智人(Homo sapiens)
<400> 194

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

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

[0205] Ile Cys Ala Gly Leu Ala Leu Ala Leu Ile Phe Gly Ala Leu Ile Phe
210 215 220
Lys Trp Tyr Ser His Ser Lys Glu Lys Ile Gln Asn Leu Ser Leu Ile
225 230 235 240
Ser Leu Ala Asn Leu Pro Pro Ser Gly Leu Ala Asn Ala Val Ala Glu
245 250 255
Gly Ile Arg Ser Glu Glu Asn Ile Tyr Thr Ile Glu Glu Asn Val Tyr
260 265 270
Glu Val Glu Glu Pro Asn Glu Tyr Tyr Cys Tyr Val Ser Ser Arg Gln
275 280 285
Gln Pro Ser Gln Pro Leu Gly Cys Arg Phe Ala Met
290 295 300

<210> 195
<211> 142
<212> PRT
<213> 智人(Homo sapiens)
<400> 195

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

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

<210> 196
<211> 2448
<212> DNA
<213> 智人(Homo sapiens)
<400> 196

agaacactta caggatgtgt gtagtgtggc atgacagaga actttggttt cctttaatgt 60
gactgtagac ctggcagtgt tactataaga atcactggca atcagacacc cgggtgtgct 120
gagctagcac tcagtggggg cggctactgc tcatgtgatt gtggagtaga cagttggaag 180
aagtacccag tccatttgga gagttaaaac tgtgcctaac agaggtgtcc tctgactttt 240
cttctgcaag ctccatgttt tcacatcttc cctttgactg tgtcctgctg ctgctgctgc 300
[0206] tactacttac aaggtcctca gaagtggaat acagagcgga ggtcggtcag aatgcctatc 360
tgccctgctt ctacacccca gccgccccag ggaacctcgt gcccgtctgc tggggcaaag 420
gagcctgtcc tgtgtttgaa tgtggcaacg tggtgctcag gactgatgaa agggatgtga 480
attattggac atccagatac tggctaaatg gggatttccg caaaggagat gtgtccctga 540
ccatagagaa tgtgactcta gcagacagtg ggatctactg ctgccggatc caaatcccag 600
gcataatgaa tgatgaaaaa tttaacctga agttggtcat caaaccagcc aaggtcaccc 660
ctgcaccgac tcggcagaga gacttcactg cagcctttcc aaggatgctt accaccaggg 720
gacatggccc agcagagaca cagacactgg ggagcctccc tgatataaat ctaacacaaa 780
tatccacatt ggccaatgag ttacgggact ctagattggc caatgactta cgggactctg 840
gagcaaccat cagaataggc atctacatcg gagcagggat ctgtgctggg ctggctctgg 900
ctcttatctt cggcgcttta attttcaaat ggtattctca tagcaaagag aagatacaga 960
atttaagcct catctctttg gccaacctcc ctccctcagg attggcaaat gcagtagcag 1020
agggaattcg ctcagaagaa aacatctata ccattgaaga gaacgtatat gaagtggagg 1080
agcccaatga gtattattgc tatgtcagca gcaggcagca accctcacaa cctttgggtt 1140
gtcgctttgc aatgccatag atccaaccac cttatttttg agcttggtgt tttgtctttt 1200
tcagaaacta tgagctgtgt cacctgactg gttttggagg ttctgtccac tgctatggag 1260
cagagttttc ccattttcag aagataatga ctcacatggg aattgaactg ggacctgcac 1320
tgaacttaaa caggcatgtc attgcctctg tatttaagcc aacagagtta cccaacccag 1380
agactgttaa tcatggatgt tagagctcaa acgggctttt atatacacta ggaattcttg 1440
acgtggggtc tctggagctc caggaaattc gggcacatca tatgtccatg aaacttcaga 1500
taaactaggg aaaactgggt gctgaggtga aagcataact tttttggcac agaaagtcta 1560
aaggggccac tgattttcaa agagatctgt gatccctttt tgtttttttgt ttttgagatg 1620
gagtcttgct ctgttgccca ggctggagtg caatggcaca atctcggctc actgcaagct 1680

ccgcctcctg ggttcaagcg attctcctgc ctcagcctcc tgagtggctg ggattacagg 1740
catgcaccac catgcccagc taatttgttg tatttttagt agagacaggg tttcaccatg 1800
ttggccagtg tggtctcaaa ctcctgacct catgatttgc ctgcctcggc ctcccaaagc 1860
actgggatta caggcgtgag ccaccacatc cagccagtga tccttaaaag attaagagat 1920
gactggacca ggtctacctt gatcttgaag attcccttgg aatgttgaga tttaggctta 1980
tttgagcact gcctgcccaa ctgtcagtgc cagtgcatag cccttctttt gtctccctta 2040
tgaagactgc cctgcagggc tgagatgtgg caggagctcc cagggaaaaa cgaagtgcat 2100
ttgattggtg tgtattggcc aagttttgct tgttgtgtgc ttgaaagaaa atatctctga 2160
ccaacttctg tattcgtgga ccaaactgaa gctatatttt tcacagaaga agaagcagtg 2220
acggggacac aaattctgtt gcctggtgga aagaaggcaa aggccttcag caatctatat 2280
taccagcgct ggatcctttg acagagagtg gtccctaaac ttaaatttca agacggtata 2340
ggcttgatct gtcttgctta ttgttgcccc ctgcgcctag cacaattctg acacacaatt 2400
ggaacttact aaaaattttt ttttactgtt aaaaaaaaaa aaaaaaaa 2448

<210> 197
<211> 1012
<212> DNA
<213> 智人(Homo sapiens)
<400> 197

actgctcatg tgattgtgga gtagacagtt ggaagaagta cccagtccat ttggagagtt 60
aaaactgtgc ctaacagagg tgtcctctga cttttcttct gcaagctcca tgttttcaca 120
tcttcccttt gactgtgtcc tgctgctgct gctgctacta cttacaaggt cctcagaagt 180
ggaatacaga gcggaggtcg gtcagaatgc ctatctgccc tgcttctaca ccccagccgc 240
[0207] cccagggaac ctcgtgcccg tctgctgggg caaaggagcc tgtcctgtgt ttgaatgtgg 300
caacgtggtg ctcaggactg atgaaaggga tgtgaattat tggacatcca gatactggct 360
aaatggggat ttccgcaaag gagatgtgtc cctgaccata gagaatgtga ctctagcaga 420
cagtgggatc tactgctgcc ggatccaaat cccaggcata atgaatgatg aaaaatttaa 480
cctgaagttg gtcatcaaac caggtgagtg gacatttgca tgccatcttt atgaataaga 540
tttatctgtg gatcatatta aaggtactga ttgttctcat ctctgacttc cctaattata 600
gccctggagg agggccacta agacctaaag tttaacaggc cccattggtg atgctcagtg 660
atatttaaca ccttctctct gttttaaaac tcatgggtgt gcctgggcgt ggtggctcgc 720
gcctctggtc ccagcacttt gggaggctga ggccggtgga tcatgaggtc aggaattcga 780
gaccagcctg gccaacatgg taaaaccttg tctccactaa aaatacaaaa aattagccag 840
gcatggttac gggagcctgt aattctagct acttgggggg ctgaagcagg agaatcactt 900
gaacctggaa gtcggaggtt gcggtaagcc aagatctcgc cattgtactc cagcctggct 960
gacaagagtg aaactctgtc ccaaaaaaaa aaaaaaaaaa aaaaaaaaaa aa 1012

<210> 198
<211> 181
<212> PRT
<213> 智人(Homo sapiens)
<400> 198

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

35 40 45

Thr Asp Glu Arg Asp Val Asn Tyr Trp Thr Ser Arg Tyr Trp Leu Asn
50 55 60

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

Leu Ala Asp Ser Gly Ile Tyr Cys Cys Arg Ile Gln Ile Pro Gly Ile
85 90 95

Met Asn Asp Glu Lys Phe Asn Leu Lys Leu Val Ile Lys Pro Ala Lys
100 105 110

Val Thr Pro Ala Pro Thr Arg Gln Arg Asp Phe Thr Ala Ala Phe Pro
115 120 125

Arg Met Leu Thr Thr Arg Gly His Gly Pro Ala Glu Thr Gln Thr Leu
130 135 140

Gly Ser Leu Pro Asp Ile Asn Leu Thr Gln Ile Ser Thr Leu Ala Asn
145 150 155 160

Glu Leu Arg Asp Ser Arg Leu Ala Asn Asp Leu Arg Asp Ser Gly Ala
165 170 175

Thr Ile Arg Ile Gly
180

<210> 199
<211> 294
<212> PRT

[0208] <213> Macaca fascicularis
<400> 199

Met Phe Ser His Leu Pro Phe Asp Cys Val Leu Leu Leu Leu Leu Leu
1 5 10 15

Leu Leu Thr Arg Ser Ser Glu Val Glu Tyr Ile Ala Glu Val Gly Gln
20 25 30

Asn Ala Tyr Leu Pro Cys Ser Tyr Thr Pro Ala Pro Pro Gly Asn Leu
35 40 45

Val Pro Val Cys Trp Gly Lys Gly Ala Cys Pro Val Phe Asp Cys Ser
50 55 60

Asn Val Val Leu Arg Thr Glu Asn Arg Asp Val Asn Asp Arg Thr Ser
65 70 75 80

Gly Arg Tyr Trp Leu Lys Gly Asp Phe His Lys Gly Asp Val Ser Leu
85 90 95

Thr Ile Glu Asn Val Thr Leu Ala Asp Ser Gly Val Tyr Cys Cys Arg
100 105 110

Ile Gln Ile Pro Gly Ile Met Asn Asp Glu Lys His Asn Leu Lys Leu
115 120 125

Val Val Ile Lys Pro Ala Lys Val Thr Pro Ala Pro Thr Leu Gln Arg
130 135 140

Asp Leu Thr Ser Ala Phe Pro Arg Met Leu Thr Thr Gly Glu His Gly
145 150 155 160

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

165 170 175
Gln Ile Phe Thr Leu Thr Asn Glu Leu Arg Asp Ser Gly Ala Thr Ile
180 185 190
Arg Thr Ala Ile Tyr Ile Ala Ala Gly Ile Ser Ala Gly Leu Ala Leu
195 200 205
Ala Leu Ile Phe Gly Ala Leu Ile Phe Lys Trp Tyr Ser His Ser Lys
210 215 220
Glu Lys Thr Gln Asn Leu Ser Leu Ile Ser Leu Ala Asn Ile Pro Pro
225 230 235 240
Ser Gly Leu Ala Asn Ala Val Ala Glu Gly Ile Arg Ser Glu Glu Asn
245 250 255
Ile Tyr Thr Ile Glu Glu Asp Val Tyr Glu Val Glu Glu Pro Asn Glu
260 265 270
Tyr Tyr Cys Tyr Val Ser Ser Gly Gln Gln Pro Ser Gln Pro Leu Gly
275 280 285
Cys Arg Phe Ala Met Pro
290

<210> 200
<211> 7
<212> PRT
<213> 智人(Homo sapiens)
<400> 200

[0209] Cys Pro Val Phe Glu Cys Gly
1 5

<210> 201
<211> 12
<212> PRT
<213> 智人(Homo sapiens)
<400> 201
Trp Thr Ser Arg Tyr Trp Leu Asn Gly Asp Phe Arg
1 5 10

<210> 202
<211> 10
<212> PRT
<213> 智人(Homo sapiens)
<400> 202
Arg Ile Gln Ile Pro Gly Ile Met Asn Asp
1 5 10

<210> 203
<211> 99
<212> PRT
<213> 智人(Homo sapiens)
<400> 203
Ser Glu Val Glu Tyr Arg Ala Glu Val Gly Gln Asn Ala Tyr Leu Pro
1 5 10 15

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

<210> 204
<211> 14
<212> PRT
<213> 智人(Homo sapiens)
<400> 204
Val Pro Val Cys Trp Gly Lys Gly Ala Cys Pro Val Phe Glu
1 5 10
<210> 205
<211> 17
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[0210] <213> 智人(Homo sapiens)
<400> 205
Arg Ile Gln Ile Pro Gly Ile Met Asn Asp Glu Lys Phe Asn Leu Lys
1 5 10 15
Leu

<210> 206
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<213> 智人(Homo sapiens)
<400> 206
Tyr Thr Pro Ala Ala Pro Gly Asn Leu Val Pro Val Cys Trp Gly Lys
1 5 10 15
Gly Ala Cys Pro Val Phe Glu
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<213> 智人(Homo sapiens)
<400> 207
Val Val Leu Arg Thr Asp Glu Arg Asp Val Asn Tyr
1 5 10
<210> 208

<211> 18
<212> PRT
<213> 智人(Homo sapiens)
<400> 208
Trp Thr Ser Arg Tyr Trp Leu Asn Gly Asp Phe Arg Lys Gly Asp Val
1 5 10 15
Ser Leu

<210> 209
<211> 18
<212> PRT
<213> 智人(Homo sapiens)
<400> 209
Cys Arg Ile Gln Ile Pro Gly Ile Met Asn Asp Glu Lys Phe Asn Leu
1 5 10 15
Lys Leu

<210> 210
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<400> 210
[0211] Asn Asp Glu Lys Phe Asn Leu Lys Leu
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<213> 人工序列
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<223> Xaa 可以是任何天然存在的氨基酸
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<213> 人工序列

<220>
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Xaa

[0212]

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<213> 人工序列
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<221> misc_feature
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1 5 10 15
Xaa Xaa Xaa Xaa
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<210> 214
<211> 1362

<212> DNA
<213> 人工序列
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<223> IgG1.1f HC
<400> 214

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cagcccccag ggaaggggct ggagtggatt gggagtatct attatagtgg gttcacctac 180
tacaacccgt ccctcaagag tcgagtcacc atatccgttg acacgtccaa gaaccagttc 240
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<210> 215
<211> 1344
<212> DNA
<213> 人工序列
<220>
<223> IgG1.1f HC
<400> 215

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ccagggaagg gactggagtg gattgggtat atccattaca gtggaagcac caactacaat 180
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<210> 216
<211> 1344
<212> DNA
<213> 人工序列
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<223> IgG1.1f HC
<400> 216

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ctctccctgt ccccgggtaa atga 1344

<210> 217
<211> 1362

<212> DNA
<213> 人工序列
<220>
<223> IgG1.1f HC
<400> 217

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<210> 218
<211> 1362
<212> DNA
<213> 人工序列
<220>
<223> IgG1.1f HC
<400> 218

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<210> 219
<211> 1365
<212> DNA
<213> 人工序列
<220>
<223> IgG1.1f HC
<400> 219

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<210> 220
<211> 1362

<212> DNA
<213> 人工序列
<220>
<223> IgG1.1f HC
<400> 220

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<210> 221
<211> 1359
<212> DNA
<213> 人工序列
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<223> IgG1.1f HC (无C末端K)
<400> 221

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<210> 222
<211> 1341
<212> DNA
<213> 人工序列
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<223> IgG1.1f HC (无C末端K)
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<400> 223

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<400> 265

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<210> 272
<211> 1362
<212> DNA
<213> 人工序列
<220>
<223> IgG1.3f HC

[0250] <400> 272

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<210> 273
<211> 1362
<212> DNA
<213> 人工序列
<220>
<223> IgG1.3f HC
<400> 273

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<210> 274
<211> 1362
<212> DNA
<213> 人工序列
<220>
<223> IgG1.3f HC
<400> 274

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<210> 275
<211> 1344
<212> DNA
<213> 人工序列
<220>
<223> IgG1.3f HC

[0252] <400> 275

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ctctccctgt ccccgggtaa atga 1344

<210> 276
<211> 1362
<212> DNA
<213> 人工序列
<220>
<223> IgG1.3f HC
<400> 276

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<210> 277
<211> 1359
<212> DNA
<213> 人工序列
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<223> IgG1.3f HC (无C末端K)
<400> 277

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<211> 1359
<212> DNA
<213> 人工序列
<220>
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[0254] <400> 278

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<210> 279
<211> 1359
<212> DNA
<213> 人工序列
<220>
<223> IgG1.3f HC (无C末端K)
<400> 279

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<211> 1359
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<223> IgG1.3f HC (无C末端K)
<400> 280

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<211> 1359
<212> DNA
<213> 人工序列
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[0256] <223> IgG1.3f HC (无C末端K)

<400> 281

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<211> 1359
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<213> 人工序列
<220>
<223> IgG1.3f HC (无C末端K)
<400> 282

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<211> 1359
<212> DNA
<213> 人工序列
<220>
<223> IgG1.3f HC (无C末端K)
<400> 283

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<210> 284
<211> 1359
<212> DNA
<213> 人工序列
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[0258] <223> IgG1.3f HC (无C末端K)

<400> 284

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<210> 285
<211> 1341
<212> DNA
<213> 人工序列
<220>
<223> IgG1.3f HC (无C末端K)
<400> 285

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ccagggaagg gactggagtg gattgggtat atccattaca gtggaagcac caactacaat 180
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<211> 1359
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<213> 人工序列
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<223> IgG1.3f HC (无C末端K)
<400> 286

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<211> 1362
<212> DNA
<213> 人工序列
<220>

[0260] <223> IgG1.1f HC
<400> 287

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<400> 288
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<400> 289
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<211> 1359
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[0262] <223> IgG1.3f HC (无C末端K)
<400> 290

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<400> 292

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Ala	Gln	Leu	Gln	Leu	Gln	Glu	Ser	Gly	Pro	Gly	Leu	Val	Lys	Pro	Ser
			20					25					30		
Glu	Thr	Leu	Ser	Leu	Thr	Cys	Thr	Val	Ser	Gly	Gly	Ser	Ile	Ser	Ser
		35					40					45			

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

[0264] Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro
225 230 235 240
Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu
245 250 255
Ala Glu Gly Ala Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
260 265 270
Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp
275 280 285
Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
290 295 300
Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn
305 310 315 320
Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
325 330 335
Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro
340 345 350
Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
355 360 365
Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn
370 375 380
Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
385 390 395 400
Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr

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

<210> 293
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<212> PRT
<213> 人工序列
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Glu Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser
35 40 45
[0265] Arg Ser Tyr Tyr Trp Gly Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu
50 55 60
Glu Trp Ile Gly Ser Ile Tyr Tyr Ser Gly Phe Thr Tyr Tyr Gln Pro
65 70 75 80
Ser Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln
85 90 95
Phe Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr
100 105 110
Tyr Cys Ala Thr Gly Gly Pro Tyr Gly Asp Tyr Ala His Trp Phe Glu
115 120 125
Pro Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys
130 135 140
Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly
145 150 155 160
Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro
165 170 175
Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr
180 185 190
Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val
195 200 205
Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn
210 215 220
Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro

225 230 235 240
Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu
245 250 255
Ala Glu Gly Ala Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
260 265 270
Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp
275 280 285
Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
290 295 300
Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn
305 310 315 320
Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
325 330 335
Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro
340 345 350
Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
355 360 365
Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn
370 375 380
Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
385 390 395 400
Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
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420 425 430
Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
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Ser Leu Ser Pro Gly
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<223> IgG1.3f HC 带有信号肽
<400> 294

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gggaaggggc tggagtggat tgggagtatc tattatagtg ggttcaccta ctaccaaccg 240
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<210> 295
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<212> DNA
<213> 人工序列
[0267] <220>
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<210> 296
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<212> DNA
<213> 人工序列
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<212> DNA
<213> 人工序列

<220>
<223> IgG1.3f HC (T168C) (无C末端K) 带有信号序列
<400> 297

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ggtgactacg cccactggtt cgaaccctgg ggccagggaa ccctggtcac cgtctcctca 420
gctagcacca agggcccatc ggtcttcccc ctggcaccct cctccaagag cacctctggg 480
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ggactctact ccctcagcag cgtggtgacc gtgccctcca gcagcttggg cacccagacc 660
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[0269] <210> 298
<211> 232
<212> PRT
<213> 人工序列
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<223> LC 带有信号序列
<400> 298

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

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

<210> 299
<211> 699
[0270] <212> DNA
<213> 人工序列
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<223> LC 带有信号序列
<400> 299

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agtggcagtg ggtctgggac agacttcact ctcaccatca gcagactgga gcctgaagat 300
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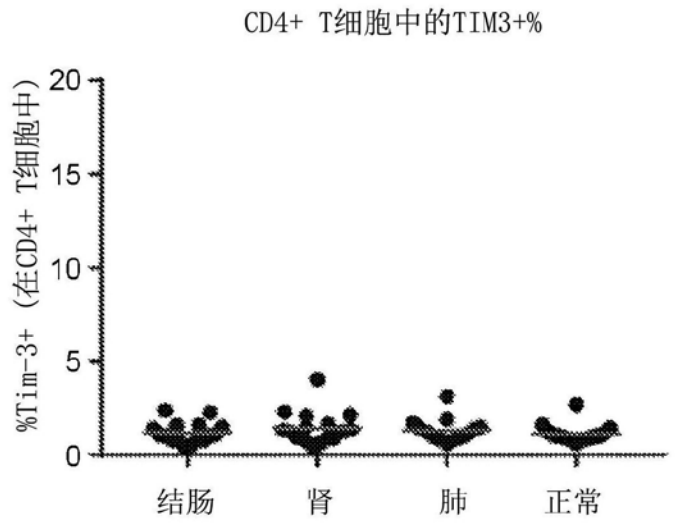

CD4+ T细胞中的TIM3+%
%Tim-3+ (在CD4+ T细胞中)
20
15
10
5
0
结肠
肾
肺
正常

图1A

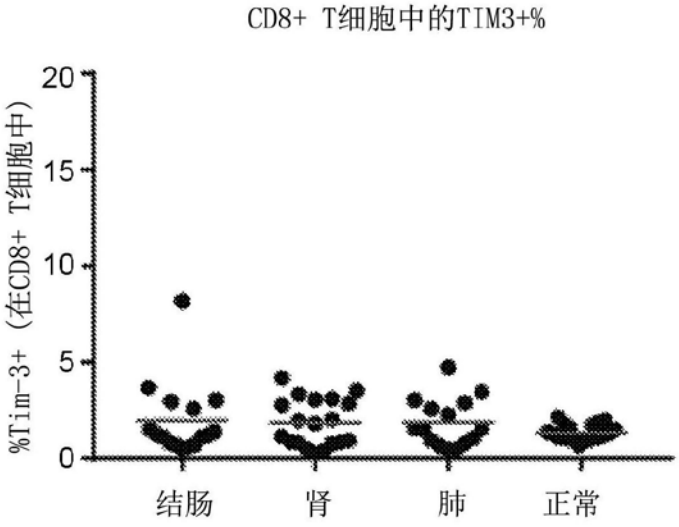

CD8+ T细胞中的TIM3+%
%Tim-3+ (在CD8+ T细胞中)
20
15
10
5
0
结肠
肾
肺
正常

图1B

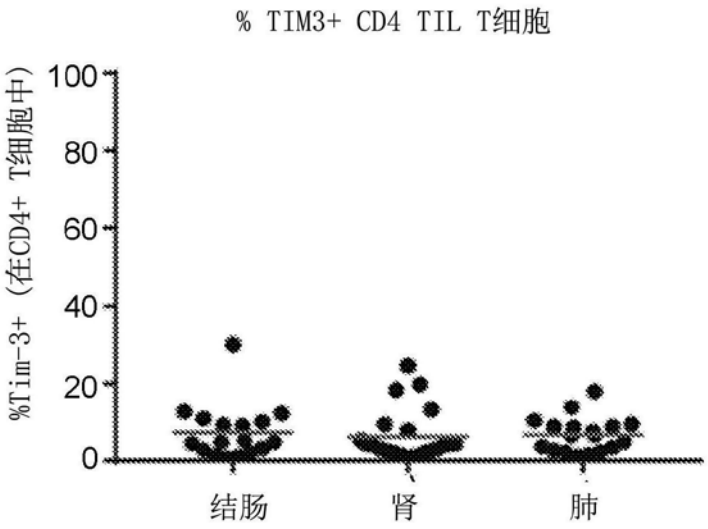

% TIM3+ CD4 TIL T细胞
%Tim-3+ (在CD4+ T细胞中)
100
80
60
40
20
0
结肠
肾
肺

图2A

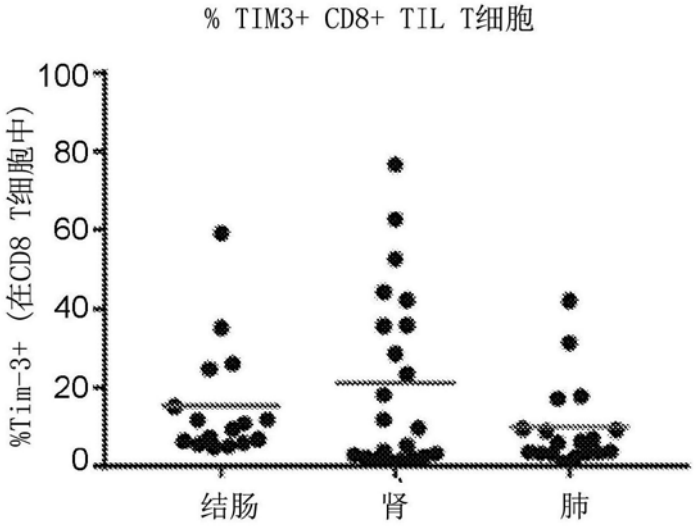

% TIM3+ CD8+ TIL T细胞
%Tim-3+ (在CD8 T细胞中)
100
80
60
40
20
0
结肠
肾
肺

图2B

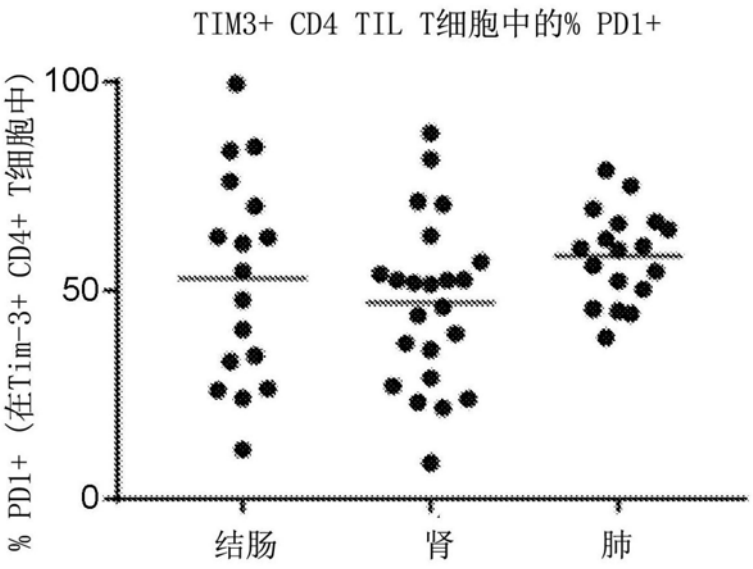

TIM3+ CD4 TIL T细胞中的% PD1+
% PD1+ (在Tim-3+ CD4+ T细胞中)
100
50
0
结肠
肾
肺

图2C

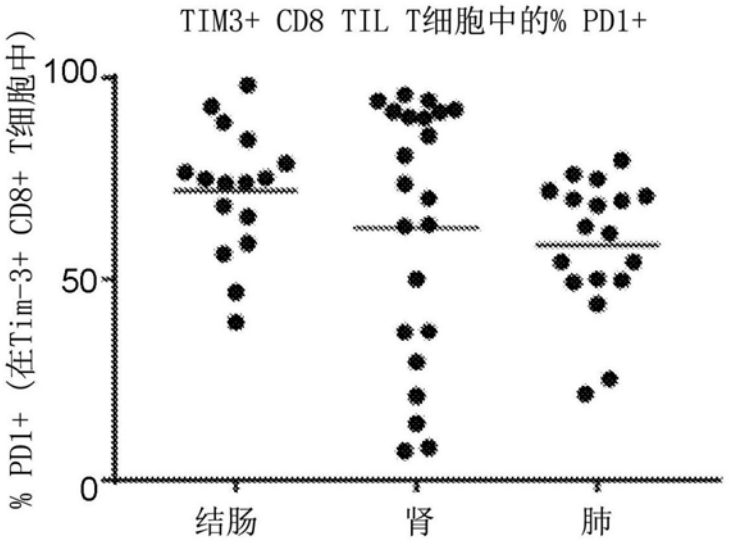

TIM3+ CD8 TIL T细胞中的% PD1+
% PD1+ (在Tim-3+ CD8+ T细胞中)
100
50
0
结肠
肾
肺

图2D

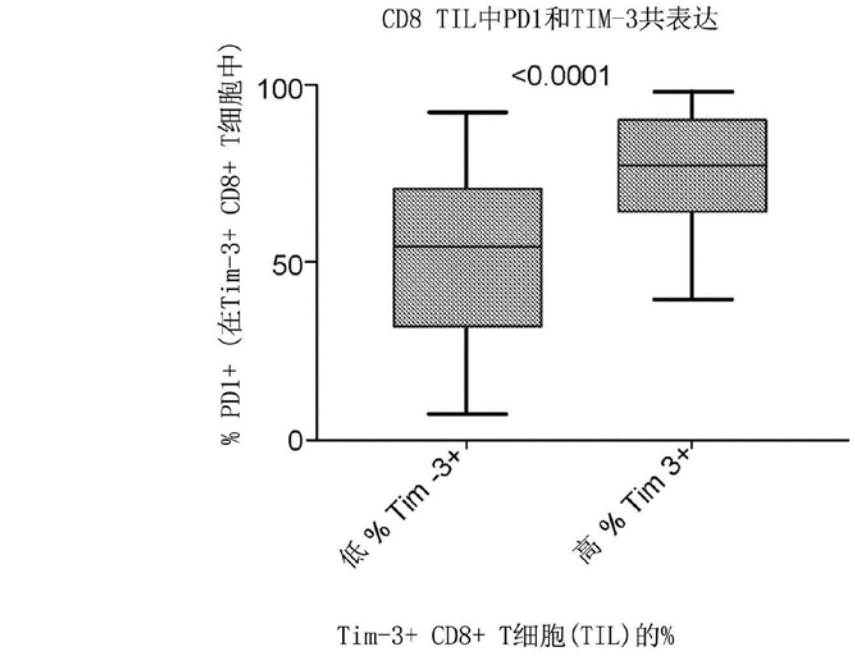

CD8 TIL中PD1和TIM-3共表达
<0.0001
% PD1+ (在Tim-3+ CD8+ T细胞中)
100
50
0
低 % Tim -3+
高 % Tim 3+
Tim-3+ CD8+ T细胞(TIL)的%

图2E

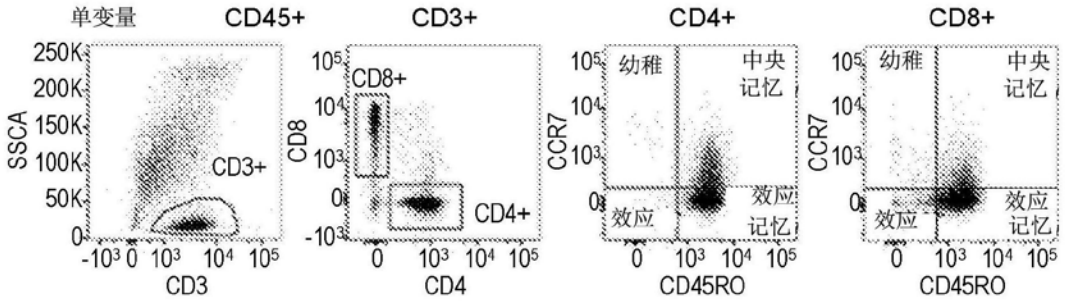

单变量
CD45+
CD3+
CD4+
CD8+
SSCA
CD3
CD8
CD4
CCR7
CD45RO
CD3+
CD8+
CD4+
幼稚
中央记忆
效应
效应记忆

图3A

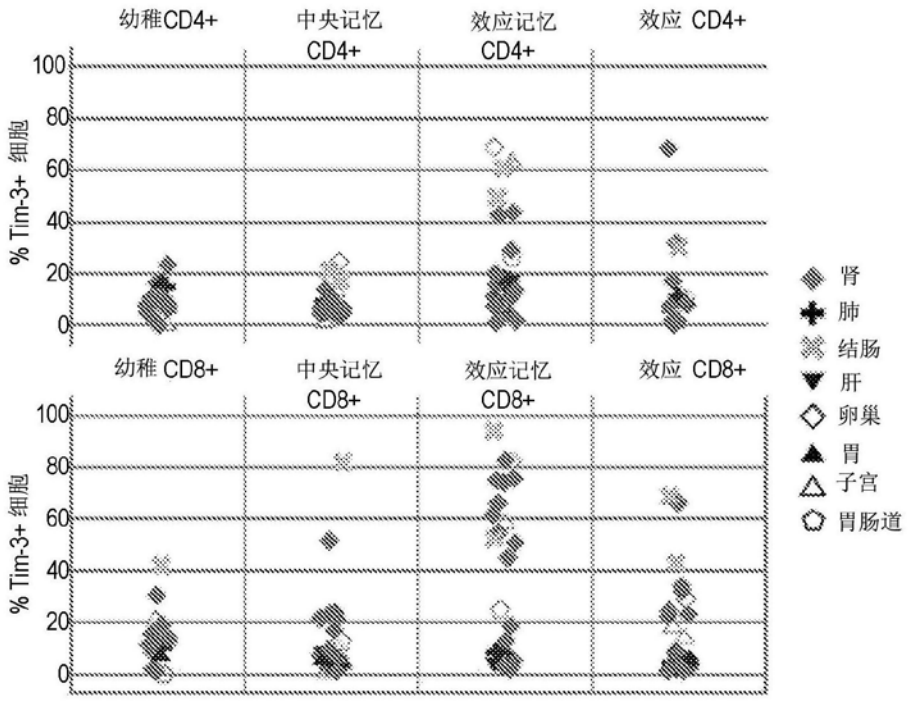

幼稚CD4+
中央记忆 CD4+
效应记忆 CD4+
效应 CD4+
% Tim-3+ 细胞
幼稚 CD8+
中央记忆 CD8+
效应记忆 CD8+
效应 CD8+
肾
肺
结肠
肝
卵巢
胃
子宫
胃肠道

图3B

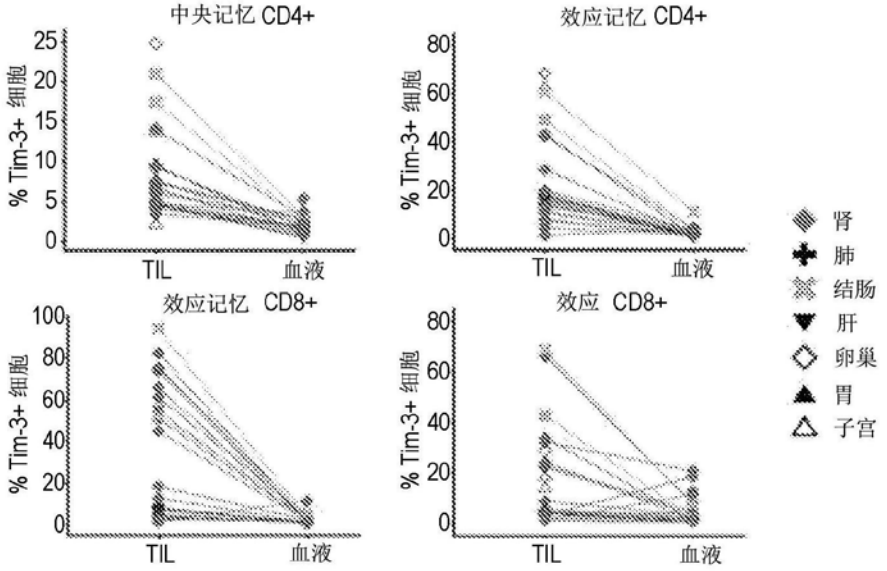

中央记忆 CD4+
效应记忆 CD4+
效应记忆 CD8+
效应 CD8+
% Tim-3+ 细胞
TIL
血液
肾
肺
结肠
肝
卵巢
胃
子宫

图3C

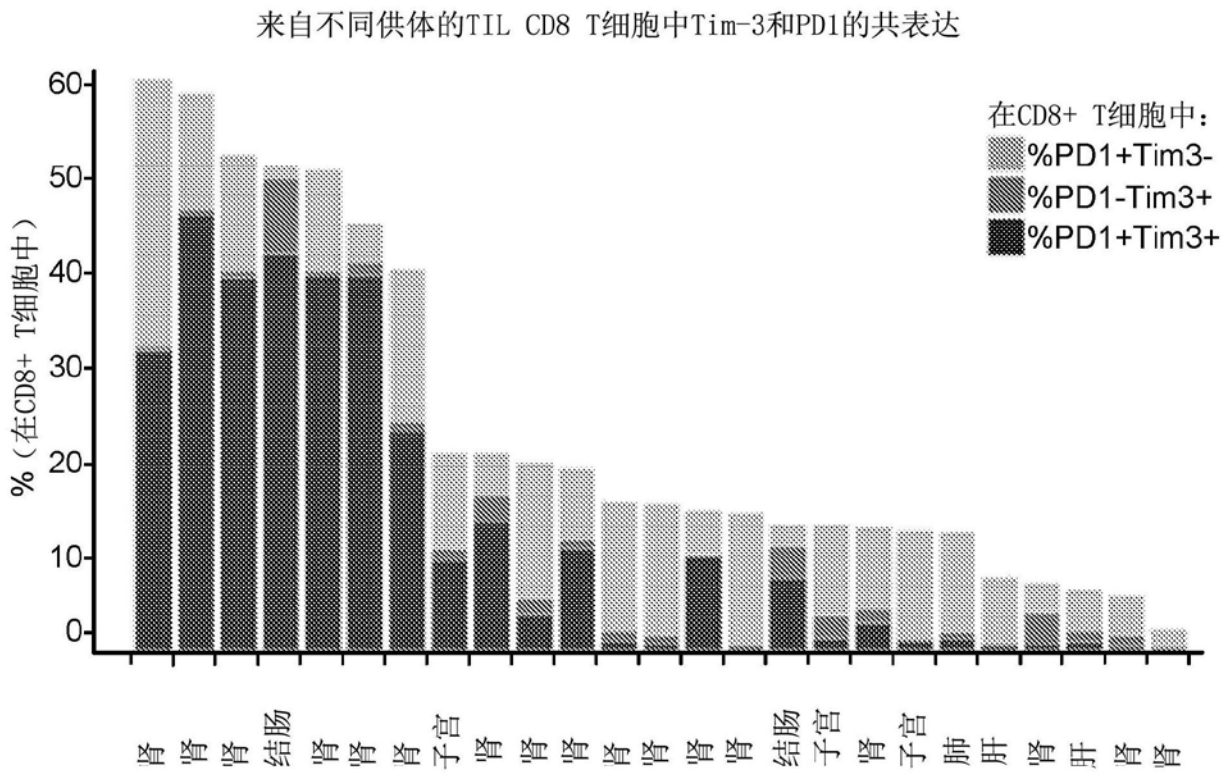

来自不同供体的TIL CD8 T细胞中Tim-3和PD1的共表达
%（在CD8+ T细胞中）
60
50
40
30
20
10
0
在CD8+ T细胞中：
%PD1+Tim3-
%PD1-Tim3+
%PD1+Tim3+
肾 肾 肾 结肠 肾 肾 肾 子宫 肾 肾 肾 肾 肾 肾 肾 结肠 子宫 肾 子宫 肺 肝 肾 肝 肾 肾

图4A

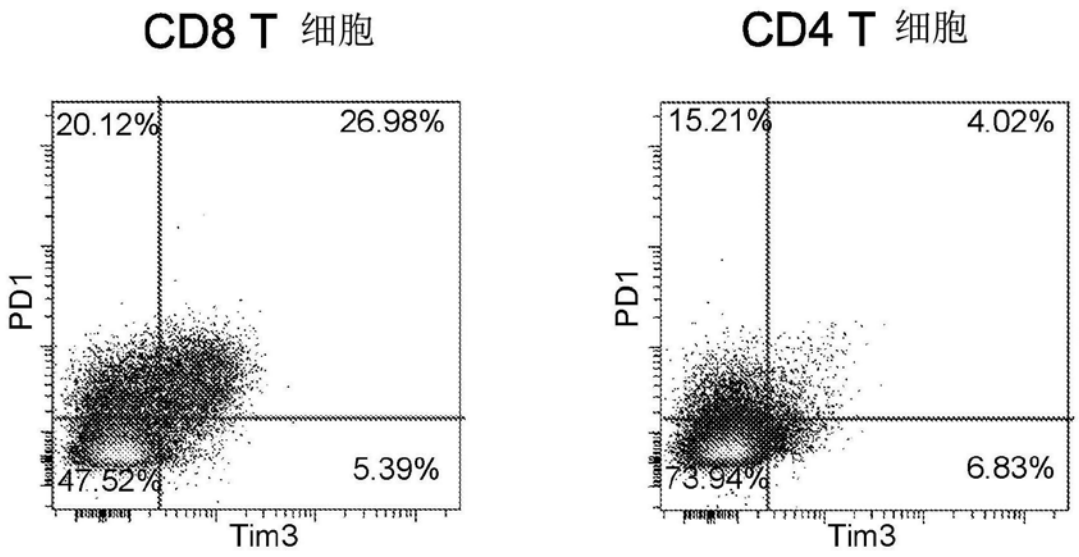

CD8 T 细胞
20.12%
26.98%
47.52%
5.39%
PD1
Tim3
CD4 T 细胞
15.21%
4.02%
73.94%
6.83%
PD1
Tim3

图4B

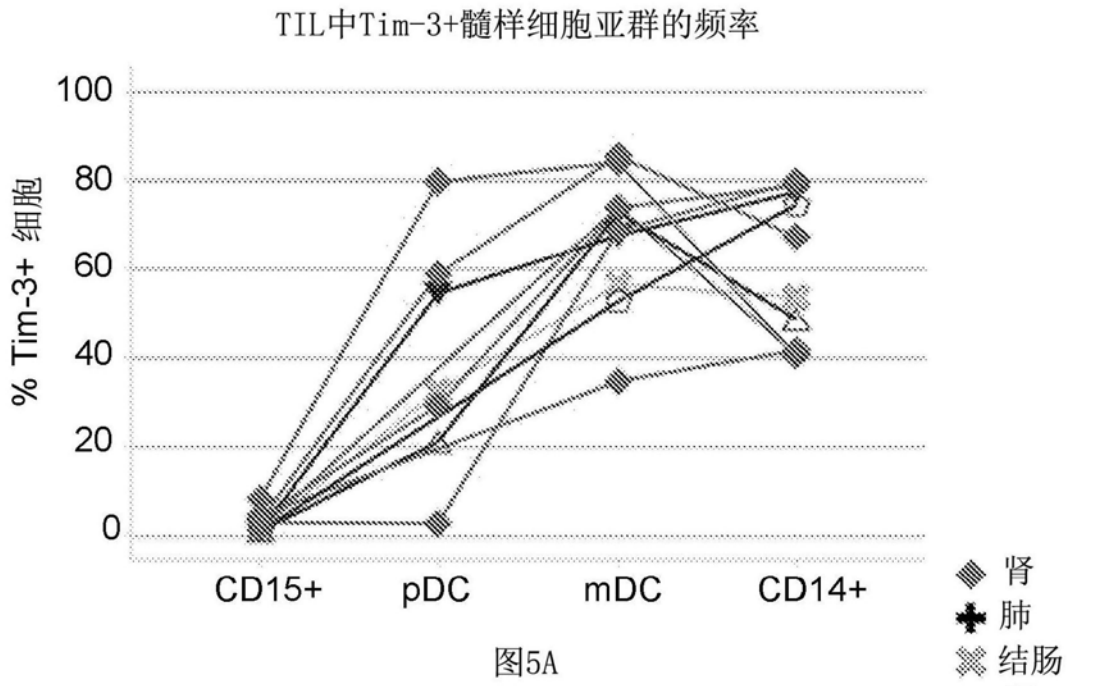

TIL中Tim-3+髓样细胞亚群的频率
% Tim-3+ 细胞
100
80
60
40
20
0
CD15+
pDC
mDC
CD14+
肾
肺
结肠
肝
卵巢
胃
子宫
胃肠道

图5A

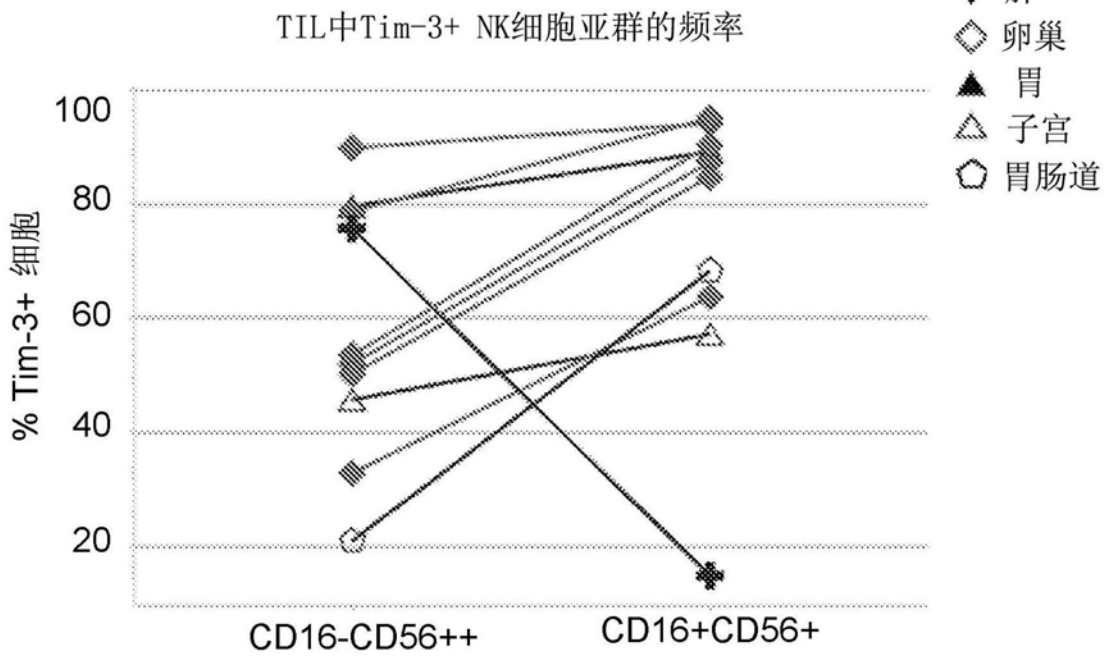

TIL中Tim-3+ NK细胞亚群的频率
% Tim-3+ 细胞
100
80
60
40
20
CD16-CD56++
CD16+CD56+

图5B

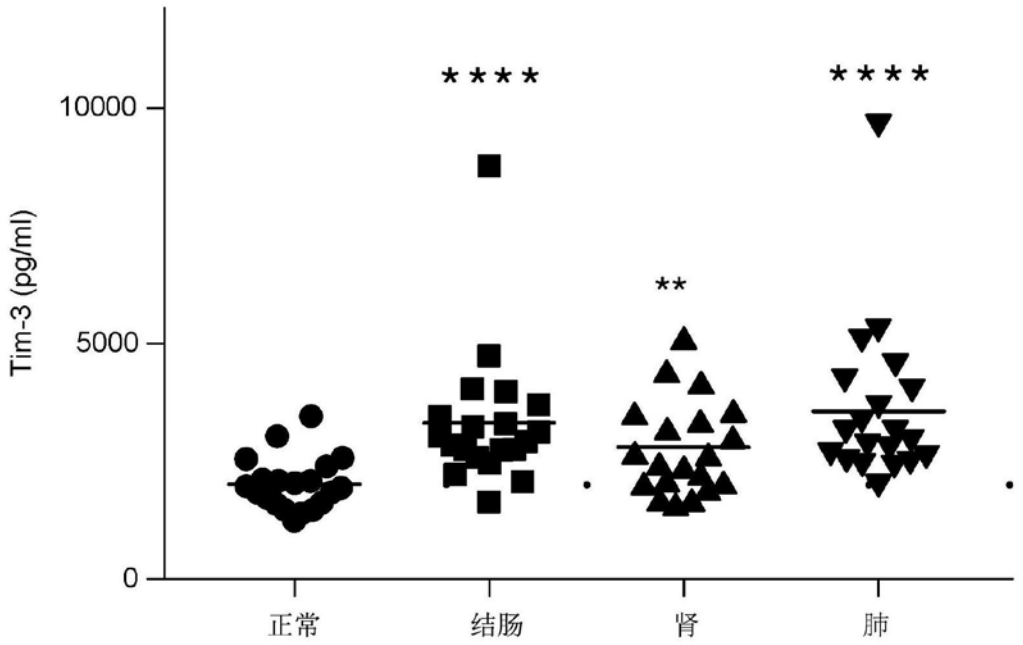
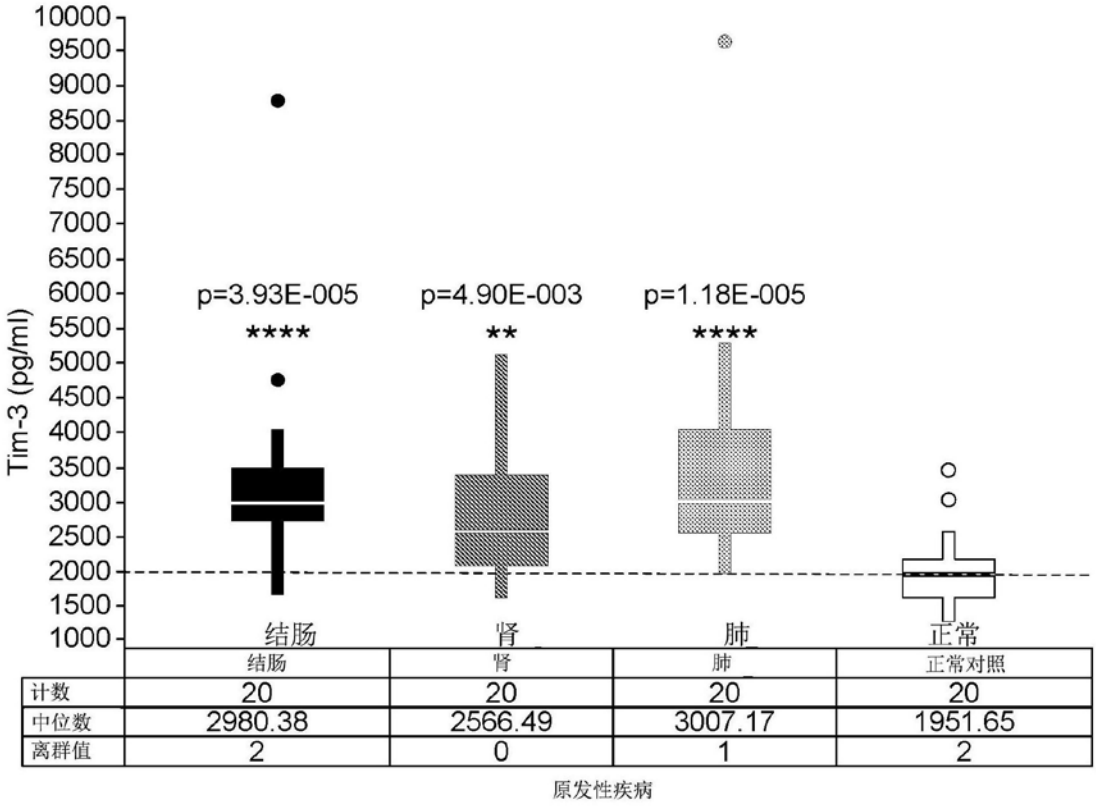


图6A



	结肠	肾	肺	正常对照
计数	20	20	20	20
中位数	2980.38	2566.49	3007.17	1951.65
离群值	2	0	1	2

图6B