



(12) 发明专利

(10) 授权公告号 CN 114127107 B

(45) 授权公告日 2024. 11. 01

(21) 申请号 202080034654.X

(22) 申请日 2020.03.31

(65) 同一申请的已公布的文献号
申请公布号 CN 114127107 A

(43) 申请公布日 2022.03.01

(30) 优先权数据
62/827,381 2019.04.01 US

(85) PCT国际申请进入国家阶段日
2021.11.09

(86) PCT国际申请的申请数据
PCT/US2020/025979 2020.03.31

(87) PCT国际申请的公布数据
W02020/205875 EN 2020.10.08

(73) 专利权人 IMMETAS治疗股份有限公司
地址 美国新泽西州

(72) 发明人 J·王 G·J·雷尼

(74) 专利代理机构 北京戈程知识产权代理有限公司 11314
专利代理师 程伟 程云

(51) Int.Cl.
C07K 16/24 (2006.01)
C07K 16/28 (2006.01)

(56) 对比文件
CN 106432506 A, 2017.02.22
CN 105189557 A, 2015.12.23
CN 109152835 A, 2019.01.04

审查员 吴志琳

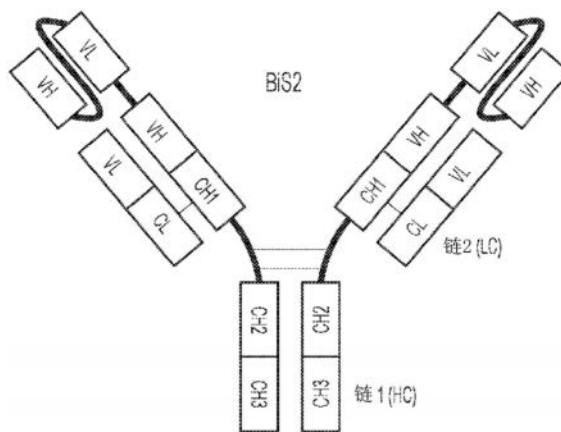
权利要求书2页 说明书22页
序列表224页 附图40页

(54) 发明名称

靶向肿瘤微环境和免疫检查点蛋白的双特异性结合分子

(57) 摘要

提供结合IP-1β或IL-1R及检查点蛋白的双特异性结合蛋白,以及制备所述蛋白的方法。检查点蛋白可以是PD-1或PD-L1。结合蛋白可以具有包含人类Fab或scFv结构域的免疫球蛋白样结构。提供了新颖的双特异性抗体形式。提供了制备结合蛋白的方法以及包含所述蛋白的药物组合物。结合蛋白及药物组合物可用于治疗或预防疾病,例如癌症。



1. 一种双特异性抗体, 包含第一结合结构域及第二结合结构域, 其中所述第一结合结构域特异性结合且抑制PD-1的活化, 并且其中所述第二结合结构域特异性结合且抑制IL-1 β 的活性;

其中所述双特异性抗体包含:

a) 重链, 从N端至C端所述重链包含scFv和第二VH结构域, 所述scFv包含第一VH结构域和第一VL结构域;

其中所述scFv形成所述第一结合结构域,

其中所述第一VH结构域包含: SEQ ID NO:7的CDR1, SEQ ID NO:8的CDR2, 和SEQ ID NO:9的CDR3;

其中所述第一VL结构域包含: SEQ ID NO:10的CDR1, SEQ ID NO:11的CDR2, 和SEQ ID NO:12的CDR3;

以及

其中所述第二VH结构域包含: SEQ ID NO:49的CDR1, SEQ ID NO:50的CDR2, 和SEQ ID NO:51的CDR3, 其中所述重链还包含CH1结构域、CH2结构域及CH3结构域;

以及

b) 轻链, 其包含第二VL结构域, 所述第二VL结构域包含SEQ ID NO:52的CDR1, SEQ ID NO:53的CDR2, 和SEQ ID NO:54的CDR3, 其中所述轻链还包含CL结构域;

其中所述第二VH结构域和所述第二VL结构域形成所述第二结合结构域。

2. 如权利要求1所述的双特异性抗体, 其中所述结合结构域是人免疫球蛋白结合结构域。

3. 根据权利要求1所述的双特异性抗体, 其中所述CH1结构域经由抗体铰链区连接到所述CH2结构域, 并且进一步包含铰链区之间的至少一个二硫键, 以及CH1和CL结构域之间的至少一个二硫键。

4. 根据权利要求1所述的双特异性抗体, 其中所述重链包含SEQ ID NO:106的氨基酸序列。

5. 根据权利要求1所述的双特异性抗体, 其中所述轻链包含SEQ ID NO:74的氨基酸序列。

6. 根据权利要求5所述的双特异性抗体, 其中所述重链包含SEQ ID NO:106的氨基酸序列, 所述轻链包含SEQ ID NO:74的氨基酸序列。

7. 一种如权利要求1所述的双特异性抗体的制备方法, 包括下列步骤: a) 用包含编码所述第一结合结构域和所述第二结合结构域的核酸分子的载体转化宿主细胞; b) 在允许所述双特异性抗体合成的条件下培养所述宿主细胞; 以及c) 从培养物中回收所述双特异性抗体。

8. 一种宿主细胞, 其包含载体, 所述载体包含编码权利要求1所限定的第一结合结构域和第二结合结构域的核酸分子。

9. 一种药物组合物, 其包含权利要求1所述的双特异性抗体及药学上可接受的赋形剂。

10. 权利要求1所述的双特异性抗体在制备药物中的用途, 所述药物用于治疗有需求的受试者中的癌症, 其中所述癌症选自: 肺癌、前列腺的小细胞癌、食道癌、胰腺癌、肝癌、结直肠癌、乳癌、卵巢癌、多发性骨髓瘤和微卫星不稳定性癌症。

11. 根据权利要求10所述的用途,其中所述肺癌为小细胞肺癌。
12. 根据权利要求11所述的用途,其中所述小细胞肺癌是复合型小细胞肺癌。
13. 根据权利要求10所述的用途,其中所述肺癌是非小细胞肺癌。
14. 根据权利要求13所述的用途,其中所述非小细胞肺癌选自:鳞状细胞肺癌、大细胞肺癌、肺腺癌、肺多形性癌、肺类癌、唾液腺癌。
15. 权利要求1所述的双特异性抗体在制备药物中的用途,所述药物用于预防或降低处于风险中的受试者的癌症风险,其中所述癌症是肺癌。

靶向肿瘤微环境和免疫检查点蛋白的双特异性结合分子

技术领域

[0001] 提供了可用于治疗癌症和其他疾病的双特异性结合分子。

背景技术

[0002] 免疫检查点蛋白可作为免疫系统调节剂,并且是自我耐受机制的关键组成部分。抑制性免疫检查点蛋白包括:程序性细胞死亡蛋白1(PD-1);程序性细胞死亡配体1(PD-L1);腺苷A2A受体(A2AR);B7-H3(CD276);B7-H4(VTCN1),B和T淋巴细胞弱化子(Attenuator)(BTLA);细胞毒性T淋巴细胞相关蛋白4(CTLA-4,CD152);吲哚胺2,3-二氧酶(Indoleamine 2,3-dioxygenase,IDO);杀伤细胞免疫球蛋白样受体(Killer-cell Immunoglobulin-like Receptor,KIR);淋巴细胞激活基因3(LAG3);烟碱酰胺腺嘌呤二核苷酸磷酸NADPH氧化酶同功型2(Nicotinamide adenine dinucleotide phosphate NADPH oxidase isoform 2,NOX2);T细胞免疫球蛋白结构域和黏蛋白结构域3(T-cell Immunoglobulin domain and Mucin domain 3,TIM-3);T细胞活化的V结构域Ig抑制剂(V-domain Ig suppressor of T cell activation,VISTA);唾液酸结合免疫球蛋白型凝集素7(Sialic acid-binding immunoglobulin-type lectin 7,SIGLEC7,CD328);和唾液酸结合免疫球蛋白型凝集素9(SIGLEC9,CD329)。

[0003] 程序性细胞死亡蛋白1(PD-1)是在T细胞上表达的受体蛋白,可作为免疫检查点。作为免疫耐受机制的一部分,PD-1的表达在活化的T细胞上被上调。PD-1的配体是程序性细胞死亡配体1(PD-L1),PD-L1与PD-1的结合会传递抑制信号,从而减少淋巴结中抗原特异性T细胞的活化和增殖,并且减少调节性T细胞的细胞凋亡。肿瘤细胞通常过度表达PD-L1作为避免免疫监视(immune surveillance)的机制。通过结合配体或受体,抑制PD-1和PD-L1之间结合的单克隆抗体已显示出在多种癌症的患者亚群中作为单一疗法或与其他药物联用是有效的,然而在许多其他癌症中是无效或难以治疗的(refractory)。帕博利珠单抗(Pembrolizumab)是一种人源化抗体(humanized antibody),于2014年首次获得FDA批准,用于治疗肿瘤细胞表达升高的PD-L1的多种癌症。罗伯特(Robert)等人的文献(N Engl J Med.372:2521-2532(2015))纳武单抗(Nivolumab)是一种全人化的抗体,于2014年首次获得FDA批准,亦用于治疗多种癌症。

[0004] 肿瘤相关巨噬细胞(Tumor-associated macrophage,TAM)是一类大量存在于肿瘤微环境(tumor microenvironment,TME)中的免疫细胞,并与癌症相关的炎症相关。已经显示PD-1在TAM细胞上的表达减少了巨噬细胞对肿瘤细胞的吞噬作用,并赋予了肿瘤细胞“免疫性”。请参照高登(Gordon)等人的文献(Nature545:495(2017))。

[0005] 白介素-1 β (Interleukin-1 β ,IL-1 β)是一种促炎症细胞因子,与慢性和急性炎症相关,并且在多种炎症相关疾病中扮演重要角色。亦显示出升高的IL-1 β 程度可将TAM细胞和骨髓来源抑制细胞(myeloid-derived suppressor cell,MDSC)募集至TME,并促进乳腺癌的肿瘤生长和转移。请参照郭(Guo)等人的文献(Sci.Rep.6,36107;doi:10.1038/srep36107(2016))。在其他研究中,肺损伤(lung lesion)已显示为充满(populated with)

TAM,其促肿瘤活性(pro-tumor activity)通过NLRP3炎症小体(inflammasome)的活化和IL-1 β 的释放而被上调。请参照Terlizzi等人的文献(Oncotarget 7:58181(2016))。最后,IL-1 β 已显示出可促进TAM细胞的促肿瘤表现型,并且细胞因子的水平与肾细胞癌的肿瘤大小和分期相关(Chittezhath等人,Immunity 41:815(2014))。

[0006] 在缺乏IL-1 β 的小鼠中,较少的动物发展为肿瘤,并且肿瘤的发展较慢。请参照Apte等人的文献(European Journal of Cancer,42:751(2006))。另外,显示出肺癌风险基因型IL-1 β -31TT导致IL-1 β 表达增加,从而提供炎症性刺激上升的微环境,并增加了肺癌风险。请参照Bhat等人的文献(Meta Gene 2:123(2014))。已显示IL-1受体拮抗剂通过抑制血管生成因子(如VEGF和IL-8)可抑制转移和肿瘤增殖。请参照Konishi等人的文献(Oncology 68:138(2005));Lewis等人的文献(J.Transl.Med.4:48(2006))。卡那奴单抗(Canakinumab)是一种抑制IL-1 β 活性的单克隆抗体,已被证明可以降低意外肺癌(incident lung cancer)和肺癌死亡率。请参照Ridker等人的文献(Lancet,390:P1833-1842,(2017))。

[0007] 工程化的双特异性单克隆抗体是包含免疫球蛋白结构域的非天然存在的蛋白质,可以同时结合两种不同类型的抗原。双特异性抗体可以多种形式制备,并且已经用于例如癌症免疫疗法和药物递送。请参照下列文献,例如,Fan等人的文献(J.Hemat.Oncol.8:130(2015));Brinkmann和Kontermann的文献(mAbs 9:182(2017));以及Spiess等人的文献(Molecular Immunology,67:95-106(2015))。

发明内容

[0008] 本案提供了一种结合蛋白,其可以包含第一结合结构域(first binding domain)和第二结合结构域(second binding domain),其中第一结合结构域特异性结合并抑制免疫检查点蛋白的活化,且其中第二结合结构域特异性结合并抑制IL- β 或IL-1R的活性。免疫检查点蛋白可以是例如PD-1或PD-L1。第一结合结构域与第二结合结构域可包含免疫球蛋白结合结构域,例如人免疫球蛋白结合结构域。这些结合蛋白可以进一步包含特异性结合并抑制免疫检查点蛋白(例如是PD-1或PD-L1)活化的第三结合结构域,以及特异性结合并抑制IL- β 或IL-1R的活性的第四结合结构域。第一结合结构域和第三结合结构域可以包含相同的互补决定区(CDR),第二结合结构域和第四结合结构域可以包含相同的CDR区。

[0009] 在一实施方案中,这些蛋白质的第一结合结构域可包含:a) SEQ ID NO:1的重链CDR1;(b) SEQ ID NO:2的重链CDR2;(c) SEQ ID NO:3的重链CDR3;(d) SEQ ID NO:4的轻链CDR1;(e) SEQ ID NO:5的轻链CDR2;和(f) SEQ ID NO:6的轻链CDR3。在这种结合蛋白中,第一结合结构域可包含SEQ ID NO:37的重链可变区和SEQ ID NO:38的轻链可变区。

[0010] 在另一实施方案中,第一结合结构域可包含:a) SEQ ID NO:7的重链CDR1;(b) SEQ ID NO:8的重链CDR2;(c) SEQ ID NO:9的重链CDR3;(d) SEQ ID NO:10的轻链CDR1;(e) SEQ ID NO:11的轻链CDR2;和(f) SEQ ID NO:12的轻链CDR3。在这种结合蛋白中,第一结合结构域可包含SEQ ID NO:39的重链可变区和SEQ ID NO:40的轻链可变区。

[0011] 在又一实施方案中,第一结合结构域可包含:a) SEQ ID NO:13的重链CDR1;(b) SEQ ID NO:15的重链CDR2;(c) SEQ ID NO:15的重链CDR3;(d) SEQ ID NO:16的轻链CDR1;(e) SEQ ID NO:17的轻链CDR2;以及(f) SEQ ID NO:18的轻链CDR3。在这种结合蛋白中,第一结合结

构域可包含SEQ ID NO:41的重链可变区和SEQ ID NO:42的轻链可变区。

[0012] 在又一实施方案中,第一结合结构域可包含(a)SEQ ID NO:19的重链CDR1;(b)SEQ ID NO:20的重链CDR2;(c)SEQ ID NO:21的重链CDR3;(d)SEQ ID NO:22的轻链CDR1;(e)SEQ ID NO:23的轻链CDR2;和(f)SEQ ID NO:24的轻链CDR3。在这种结合蛋白中,第一结合结构域可包含SEQ ID NO:43的重链可变区和SEQ ID NO:44的轻链可变区。

[0013] 在另一实施方案中,第一结合结构域可包含(a)SEQ ID NO:25的重链CDR1;(b)SEQ ID NO:26的重链CDR2;(c)SEQ ID NO:27的重链CDR3;(d)SEQ ID NO:28的轻链CDR1;(e)SEQ ID NO:29的轻链CDR2;和(f)SEQ ID NO:30的轻链CDR3。在这种结合蛋白中,第一结合结构域可包含SEQ ID NO:45的重链可变区和SEQ ID NO:46的轻链可变区。

[0014] 在又一实施方案中,第一结合结构域可包含(a)SEQ ID NO:31的重链CDR1;(b)SEQ ID NO:32的重链CDR2;(c)SEQ ID NO:33的重链CDR3;(d)SEQ ID NO:34的轻链CDR1;(e)SEQ ID NO:35的轻链CDR2;和(f)SEQ ID NO:36的轻链CDR3。在这种结合蛋白中,第一结合结构域可包含SEQ ID NO:47的重链可变区和SEQ ID NO:48的轻链可变区。

[0015] 在任何的这些结合蛋白中,第二结合结构域可包含(a)SEQ ID NO:49的重链CDR1;(b)SEQ ID NO:50的重链CDR2;(c)SEQ ID NO:51的重链CDR3;(d)SEQ ID NO:52的轻链CDR1;(e)SEQ ID NO:53的轻链CDR2;和(f)SEQ ID NO:54的轻链CDR3。在这种结合蛋白中,第一结合结构域可包含SEQ ID NO:55的重链可变区和SEQ ID NO:56的轻链可变区。

[0016] 本案进一步提供了结合蛋白,其中第一结合结构域是特异性结合并抑制PD-1或PD-L1活化的抗体结合结构域,并且第二结合结构域包含来自白介素-1-受体1型(IL-1R1)或白介素-1-受体2型(IL-1R2)的白介素-1 β -结合结构域,任选地与IL-1R辅助蛋白的配体结合结构域偶联。例如,这样的结合蛋白可以包含第一蛋白链以及第二蛋白链,第一蛋白链包含(a)IL-1R1的白介素-1 β -结合结构域,(b)结合并抑制PD-1或PD-L1的免疫球蛋白的VH结构域及(c)免疫球蛋白Fc结构域,其中(a)连接于(b),(b)连接于(c);第二蛋白链包含结合PD-1或PD-L1的免疫球蛋白的VL结构域。在另一实例中,结合蛋白可包含第一蛋白链及第二蛋白链,第一蛋白链包含(a)结合并抑制PD-1或PD-L1的免疫球蛋白的VH结构域(b)IL-1R1的白介素-1 β -结合结构域(c)免疫球蛋白Fc结构域,其中(a)连接于(b),(b)连接于(c);第二蛋白链包含结合并抑制PD-1或PD-L1的免疫球蛋白的VL结构域。在又一实例中,结合蛋白可包含两条相同的蛋白链,其中每条蛋白链包含(a)IL-1R1的白介素-1 β -结合结构域(b)免疫球蛋白Fc结构域(c)结合并抑制PD-1或PD-L1的活化的scFV结构域,其中(a)连接于(b),(b)连接于(c)。在又一实例中,结合蛋白可包含:第一蛋白链以及第二蛋白链,第一蛋白链包含(a)IL-1R1的白介素-1 β -结合结构域(b)结合并抑制PD-1或PD-L1的免疫球蛋白的VL和CL结构域(c)免疫球蛋白Fc结构域,其中(a)连接于(b),(b)连接于(c);第二蛋白链包含结合并抑制PD-1或PD-L1的免疫球蛋白的VH和CH1结构域。在另一实例中,结合蛋白可包含:第一蛋白链及第二蛋白链,第一蛋白链包含(a)结合并抑制PD-1或PD-L1的免疫球蛋白的VL和CL结构域(b)IL-1R1的白介素-1 β -结合结构域(c)免疫球蛋白Fc结构域,其中(a)连接于(b),(b)连接于(c);第二蛋白链包含结合并抑制PD-1或PD-L1的免疫球蛋白的VH和CH1结构域。

[0017] 提供了编码上述蛋白链的核酸分子以及载体,包括含有这些核酸分子的表达载体。

[0018] 还提供了用于如上所述制备结合蛋白的方法,其中所述方法包括以下步骤:a)用含有编码第一结合结构域和第二结合结构域的核酸分子的载体转化宿主细胞;b)在允许结合蛋白合成的条件下培养宿主细胞;和c)从培养物中回收结合蛋白。宿主细胞可以包含含有编码第一结合结构域和第二结合结构域的核酸分子的载体。

[0019] 还提供了包含如上所述的结合蛋白以及药学上可接受的赋形剂的药物组合物。

[0020] 还提供了包含第一蛋白链、第二蛋白链和第三蛋白链的双特异性结合蛋白(“FAT”结合蛋白),其中第一蛋白链包含重链及第一Fab结构域(Fab1),重链具有VH结构域、CH1结构域、CH2结构域和CH3结构域的重链,第一Fab结构域位于CH2结构域、CH3结构域的溶剂暴露环或在CH2结构域与CH3结构域的界面上;其中第二链包含第二Fab结构域,其中第三链包含第三Fab结构域。在这些结合蛋白中,第二链Fab结构域与第一蛋白链的VH结构域和CH1结构域结合,形成第一结合结构域,第三链Fab结构域与在第一蛋白中溶剂暴露环上第一Fab结构域结合,以形成第二结合结构域。在这些结合蛋白中,溶剂暴露环可以包含来自CH2结构域的氨基酸序列,例如ISRTP(SEQ ID NO:57)。溶剂暴露环可包含来自CH3结构域的氨基酸序列,例如SNG。溶剂暴露环可以包含来自CH2结构域和CH3结构域的界面的氨基酸序列,例如AKGQP(SEQ ID NO:58)。CH1结构域可以经由抗体铰链区连接至CH2结构域。CH2结构域和CH3结构域可以包含Fc区,例如来自IgG1、IgG2、IgG3、IgG4、IgA、IgM、IgE和IgD的Fc区。第一蛋白链可进一步包含第一肽接头和/或第二肽接头,第一肽接头位于第一Fab结构域的第一末端与CH2结构域、CH3结构域或CH2和CH3结构域的界面之间,第二肽接头位于第一Fab结构域的第二末端与CH2结构域、CH3结构域或CH2和CH3结构域的界面之间。第一肽接头与第二肽接头可以是,例如,(G4S)₂(SEQ ID NO:59)、(G4S)₃(SEQ ID NO:60)和(G4S)₄(SEQ ID NO:61)。在第一实施方案中,第一蛋白链可包含从N末端到C末端的下列多肽结构域:VH1-CH1-铰链-CH2(N-末端)-Fab1-CH2(C-末端)-CH3,或在第二实施方案中,第一蛋白链可包含从N末端到C末端的下列多肽结构域:VH1-CH1-铰链-CH2-CH3(N-末端)-Fab1-CH3(C-末端)。在第三实施方案中,第一蛋白链可包含从N末端到C末端的下列多肽结构域:VH1-CH1-CH2-Fab1-CH3。第一结合结构域可以特异性结合PD-1或PD-L1,第二结合结构域可以特异性结合IL-1 β 或IL-1R,或者第一结合结构域可以特异性结合IL-1 β 或IL-1R,并且第二结合结构域可以与PD-1或PD-L1特异性结合。

[0021] 在FAT结合蛋白的一些实施方案中,第一结合结构域的CDR区可以选自:SEQ ID NO:1-6的CDR结构域、SEQ ID NO:7-12的CDR结构域、SEQ ID NO:13-18的CDR结构域、SEQ ID NO:19-24的CDR结构域、SEQ ID NO:25-30的CDR结构域以及SEQ ID NO:31-36的CDR结构域,第二结合结构域的CDR区可以是SEQ ID NO:49-54的CDR结构域。

[0022] 在FAT结合蛋白的其他实施方案中,第一结合结构域的CDR区可以是SEQ ID NO:49-54的CDR结构域,并且第二结合结构域的CDR区可以选自:SEQ ID NO:1-6的CDR结构域、SEQ ID NO:7-12的CDR结构域、SEQ ID NO:13-18的CDR结构域、SEQ ID NO:19-24的CDR结构域、SEQ ID NO:25-30的CDR结构域以及SEQ ID NO:31-36的CDR结构域。

[0023] 本案提供了编码上述FAT结合蛋白链的核酸分子,以及载体(vector),包括含有这些核酸分子的表达载体。

[0024] 本案还提供了包含一种或多种FAT结合蛋白和药学上可接受的载体(carrier)的药物组合物。

[0025] 本案提供了制备FAT结合蛋白的方法,所述方法包括以下步骤:a)用可以包含编码第一蛋白链、第二蛋白链和第三蛋白链的核酸分子的载体转化宿主细胞;b)在允许结合蛋白合成的条件下培养宿主细胞;以及c)从培养物中回收FAT结合蛋白。载体可包含编码FAT蛋白的第一蛋白链、第二蛋白链和第三蛋白链的核酸分子。

[0026] 本案提供了治疗受试者的癌症的方法,其包括向有此需要的受试者施用如上所述的结合蛋白或药物组合物。这些方法任选地包括向受试者施用除结合蛋白之外的抗肿瘤剂。

[0027] 在这些治疗癌症的方法中,受试者可能先前已经接受过癌症免疫疗法的治疗或已发现对所述疗法具有抗性。所述受试者可能先前已经接受过癌症免疫疗法的治疗,或者被发现对癌症免疫疗法是难治的。癌症免疫疗法可以是例如用至少一种免疫检查点抑制剂治疗。

[0028] 治疗癌症的方法还可以包括对受试者施用额外的抗肿瘤疗法,例如化学疗法、免疫疗法、生物制剂或小分子疗法、疫苗接种和/或细胞疗法。

[0029] 本案还提供了预防或降低处于风险中的受试者的癌症风险的方法,包括向受试者施用有效量的如上所述的结合蛋白或药物组合物。所述受试者先前可能已经被诊断出患有癌症并且已经缓解,或者先前已经接受过癌症治疗。受试者由于环境暴露、使用或接触烟草、基因突变或癌症家族史而被认为处于患癌症的风险。

[0030] 在这些癌症治疗的方法中,癌症可以是肺癌,例如小细胞肺癌,复合型小细胞肺癌和/或非小细胞肺癌。非小细胞肺癌可以是例如鳞状细胞肺癌、大细胞肺癌、肺腺癌、肺多形性癌、肺类癌,唾液腺癌或未明确分类(NOS,未特指)的癌症。所述癌症可以是复合型小细胞肺癌、肺外小细胞癌、局限在淋巴结中的肺外小细胞癌或前列腺小细胞癌,或者可以是微卫星不稳定性癌症。

[0031] 根据以下详细描述,本公开的其他目的、特征和优点将变得显而易见。然而,应当理解,根据详细描述,由于本公开的精神和范围内的各种改变和修饰对于本领域技术人员而言将是显而易见的,因此仅通过说明的方式给出了详细描述和具体实例。

附图说明

[0032] 图1显示BiS2双特异性抗体的链结构。

[0033] 图2A显示BiS3双特异性抗体的链结构。

[0034] 图2B显示包含(a)源自IL-1R1和IL-1R辅助蛋白的IL-1 β 结合结构域以及(b)抗体结合结构域的结合分子的链结构。

[0035] 图3A显示FIT-Ig双特异性抗体的链结构。

[0036] 图3B至图3E显示包含(a)源自IL-1R1和IL-1R辅助蛋白的IL-1 β 结合结构域以及(b)抗体结合结构域的4个结合分子的链结构。

[0037] 图4显示FAT-Ig双特异性抗体的链结构。

[0038] 图5显示结合IL-1 β 和PD-1的双特异性抗体的氨基酸序列。

[0039] 图6A至图6C显示结合IL-1 β 、IL-1R、PD-1或PD-L1的已知抗体和结合分子的表格。

[0040] 图7显示双特异性抗体在多剂量夹心测定(multiple-dose sandwich assay)中同时与细胞膜结合的PD-1和可溶性IL-1 β 的结合,如通过流式细胞术所检测的。证明了ITA系

列双特异性抗体的可变结合亲和力,并且所有结合亲和力均实质上高于对照人IgG (control human IgG)。

[0041] 图8显示了双特异性抗体在多剂量夹心测定中同时与细胞膜结合的PD-1和可溶性IL-1 β 结合,如通过流式细胞术所检测的。证明了ITC、ITD和ITE系列双特异性抗体的可变结合亲和力,并且所有结合亲和力均实质上高于对照人IgG。

[0042] 图9A至图9C显示在多剂量夹心测定中双特异性抗体与细胞膜结合的PD-1的结合,如通过流式细胞术所检测的。证明了ITB和ITF系列双特异性抗体的可变结合亲和力,并且所有结合亲和力均实质上高于对照人IgG。

[0043] 图10显示双特异性抗体在多剂量夹心测定中同时与细胞膜结合的PD-1和可溶性IL-1 β 结合,如通过流式细胞术所检测的。证明了ITB和ITF系列双特异性抗体的可变结合亲和力。所有结合亲和力均实质上高于对照人IgG。

[0044] 图11显示双特异性抗体在PD-1/PD-L1报告分子分析中阻断PD-1活性。证明了ITA系列双特异性抗体具有可变的阻断活性。所有的阻断活性均实质上高于对照人IgG。

[0045] 图12A及图12B显示双特异性抗体在IL-1 β 功能测定中阻断IL-1 β 活性。证明了ITA系列双特异性抗体具有可变的阻断活性。所有的阻断活性均实质上高于对照人IgG。

具体实施方式

[0046] 本案提供了双特异性结合蛋白,其包含特异性结合免疫检查点蛋白的至少一第一结合结构域和结合IL-1 β 的至少一第二结合蛋白。免疫检查点蛋白可以是例如PD-1、PD-L1、A2AR、B7-H3 (CD276)、B7-H4 (VTCN1)、BTLA、CTLA-4 (CD152)、IDO、KIR、LAG3、NOX2、TIM-3、VISTA、SIGLEC7、(CD328)或SIGLEC9 (CD329)。有利地,检查点蛋白是PD-1或PD-L1。

[0047] 结合蛋白同时结合检查点蛋白PD-1或PD-L1以及IL-1 β 或IL-1R,从而抑制CD8 T细胞上的PD-1与靶标细胞(例如肿瘤细胞)上的PD-L1之间的结合以及IL-1 β 活性。以这种方式同时抑制IL-1 β 活性和PD-1/PD-L1结合提供了改进的癌症治疗方法。第一结合结构域和第二结合结构域有利地是人类抗体可变结构域。亦提供了新颖的双特异性结合蛋白形式,其允许两种抗原特异性结合,包括但不限于检查点蛋白和细胞因子(cytokine)(例如IL-1 β)。亦提供了使用双特异性结合蛋白来治疗疾病(例如癌症)的方法。

[0048] 结合结构域(binding domain)

[0049] 在本文所述的结合蛋白中使用的结合结构域可以是特异性结合靶标蛋白的任何形式。例如,为了结合IL-1 β ,可以使用白介素I型或II型受体的配体结合结构域,选择性地与来自IL-1受体辅助蛋白(如同利隆西普(Rilonacept))的序列融合。然而,有利地,结合结构域衍生自人免疫球蛋白分子的可变结构域。具体地,结合结构域可以源自结合检查点蛋白的抗体和结合IL-1 β 或IL-1R的抗体。制备结合预选抗原的全人抗体的方法是本领域已知的。例如,人类抗体可以选自在丝状噬菌体(filamentous phage)上展示的大型抗体文库,并且通过已知的方法鉴定所选抗体的重链和轻链可变区。请参照,例如,Winter等人的文献(Annual Review of Immunology 12:433-455(1994))。然后将编码这些可变区的核酸用于构建编码本文所述的双特异性结合蛋白的基因。或者,可以使用来自已知抗体的抗体可变结构域。特别地,抗IL-1 β 、PD-1和PD-L1的人类抗体被批准用于治疗人类的多种疾病状态中,并且来自这些抗体的可变区可用于构建本文所述的双特异性结合蛋白。合适的抗体的

实施例显示在下列表1和6中。

[0050] 或者,可以使用本领域熟知的互补决定区移植(CDR grafting)方法,将来自具有已知特异于IL-1 β 、IL-1R、PD-1或PD-L1的抗体的CDR区插入已知的人类框架区(human framework region)。请参照,例如,威廉斯与马修斯(Williams和Matthews)的文献(《抗体工程》(Antibody Engineering)中(Kontermann和Dübel编辑),pp 319-339(Springer, 2010),“Humanising Antibodies by CDR Grafting”)。这些CDR区可以衍生自图1所示的CDR区或表6中描述的抗体的CDR区。本领域技术人员将认识到,除了本文所述的特异性结合IL-1 β 、IL-1R、PD-1或PDL-1的抗体之外的其他抗体,那些抗体的CDR区可用于构建本文所述的结合蛋白。

[0051] 关于IL-1 β ,卡那奴单抗(canakinumab)是结合IL-1 β 的FDA批准的人类抗体,并且重链和轻链可变区的氨基酸序列是众所周知的。请参照Rondeau等人的文献(MAbs 7:1151 (2015))。卡那奴单抗的整个重链和轻链可变区可用于构建本文所述的双特异性蛋白;或者,可以使用本领域众所周知的CDR移植方法将卡那奴单抗的CDR区插入替代的人类可变框架序列中。请参见,例如,Winter和Harris的文献(Trends in Pharmacological Sciences 14:139-143(1993))。另一种IL-1 β 结合抗体是文献W01995/01997中所述的人源化SK48-E26抗体。

[0052] 关于IL-1R,anakinra是FDA批准的人类白介素-1受体拮抗剂(IL-1Ra)的重组、非糖基化形式。与天然的人类IL-1Ra相比,anakinra包含额外的N末端甲硫氨酸残基。Anakinra竞争性地抑制IL-1 α 和IL-1 β 与1型IL-1受体的结合。IL-1R1结合结构域可用于构建双特异性蛋白,以阻断IL-1 β 与IL-1受体的结合。可以用作合适的结合结构域的anakinra的IL-1R1结合部分的序列为

MRPSGRKSSKMQAfriwDvNqkTFyLRnnQLVagYlQgPnvnLEEKIDVvPIEPHALFLGIH

[0053] GGKMCLSCVKSGDETRLQLEAVNITDLSENrkQDKRFAFIRSDSGPTTSFESAACPGWFLCTAMEADQP
VSLTNMPDEGVMVTKFYFQEDE (SEQ ID NO:72)

[0054] 关于PD-1,帕博利珠单抗(pembrolizumab)是一种人源化抗体,于2014年首次获得FDA批准,用于治疗肿瘤细胞表达升高的PD-1的多种癌症。纳武单抗(Nivolumab)是一种全人抗体,于2014年首次获得FDA批准,也可用于治疗多种癌症。Cemiplimab是一种人类抗体,于2018年首次批准用于治疗转移性皮肤鳞状细胞癌。帕博利珠单抗、纳武单抗和Cemiplimab的重链和轻链可变结构域的氨基酸序列是已知的,CDR区的序列也是已知的。

[0055] 关于PD-L1,durvalumab是一种人类抗体,于2017年首次获批用于治疗转移性尿路上皮癌。Atezolizumab于2016年首次获得批准,用于治疗肺癌。durvalumab和atezolizumab的重链和轻链可变结构域的氨基酸序列以及CDR区的序列都是已知的。

[0056] 帕博利珠单抗(Pembrolizumab)、纳武单抗(Nivolumab)、cemeplimab,atezolizumab,avelumab,durvalumab和卡那奴单抗的可变结构域和CDR区的序列显示在下列表1中。其他已知抗IL-1 β 、PD-1和PD-L1抗体的清单如图6A至图6C所示。

[0057] 表1

[0058]

抗体	结构域	序列	SEQ ID NO
Pembrolizumab	VH CDR1	NYYMY	1
	VH CDR2	GINPSNGGTNFNEKFKN	2
	VH CDR3	RDYRFDMGFDY	3
	VL CDR1	RASKGVSTSGYSYLH	4
	VL CDR2	LASYL	5
	VL CDR3	QHSRDLPLT	6
	VH	QVQLVQSGVEVKKPGASVKVSKASGYTFTNYM YWVRQAPGQGLEWMGGINPSNGGTNFNEKFKN RVTLTDSSTTTAYMELKSLQFDDTAVYYCARRDY RFDMGFDYWGGTTVTVSS	37
	VL	EIVLTQSPATLSLSPGERATLSCRASKGVSTSGYSYL HWYQQKPGQAPRLLIYLAYLESGVPARFSGSGSG TDFLTISLLEPEDFAVYYCQHSRDLPLTFGGGKVE IK	38
Nivolumab	VH CDR1	NSGMH	7
	VH CDR2	VIWYDGSKRYYADSVKG	8
	VH CDR3	NDDY	9
	VL CDR1	RASQSVSSYLA	10
	VL CDR2	DASNRAT	11
	VL CDR3	QQSSNWPRT	12
	VH	QVQLVESGGGVVQPGRSLRLDCKASGITFSNSGM HWVRQAPGKGLEWVAVIWIWYDGSKRYYADSVKGR FTISRDNKNTLFLQMNSLRAEDTAVYYCATNDDY WGQGTLVTVSS	39

[0059]

	VL	s	40
Cemiplimab	VH CDR1	GFTFSNFG	13
	VH CDR2	ISGGGRDT	14
	VH CDR3	VKWGNIYFDY	15
	VL CDR1	LSINTF	16
	VL CDR2	AAS	17
	VL CDR3	QQSNTPF	18
	VH	EVQLLESGGVLVQPGGSLRLSCAASGFTFSNFGMT WVRQAPGKGLEWVSGISGGGRDITYFADSVKGRF TISRDN SKNTLYLQMNSLKGEDTAVYYCVKWGNIY FDYWGQGLTVTVSS	41
	VL	DIQMTQSPSSLSASVGD SITITCRASLSINTFLNWF QQKPGKAPNLLIYAASSLHGGVPSRFSGSGSGTDF TLTIRTLQPEDFATYYCQQSNTPF TFGPGTVVDFR	42
SK48-E26	VH CDR1	SYDMS	62
	VH CDR2	YISSGGGGTYYPDTVKG	63
	VH CDR3	GGVRRGYFDV	64
	VL CDR1	RASGNIHNYLT	65
	VL CDR2	NAKTLAD	66
	VL CDR3	QHFWSIPYT	67
	VH	EVQLVESGGGVVQPGRSLRLSCSSSGFIFSSYDMS WVRQAPGKGLEWVAYISSGGGGTYYPDTVKGRFT ISRDN SKNTLFLQMDSL RPEDTGVYFCARGGVRRG YFDVWGQGPVTVSS	68
	VL	DIQMTQSPSSLSASVGD RVTITCRASGNIHNYLTW YQQTPGKAPKLLIYNAKTLADGVPSRFSGSGSGTD YFTISSLQPEDATYYCQHFWSIPYTFGQGTKLQIT	69
Atezolizumab	VH CDR1	GFTFSDSWIH	19
	VH CDR2	AWISPYGGST	20
	VH CDR3	RHWPGGFYD	21
	VL CDR1	RASQDVSTAVA	22
	VL CDR2	SASFLYS	23
	VL CDR3	QQYLYHPAT	24
	VH	EVQLVESGGGLVQPGGSLRLSCAASGFTFSDSWIH WVRQAPGKGLEWVAWISPYGGSTYYADSVKGRF TISADTSKNTAYLQMNSLRAEDTAVYYCARRHWP GGFDYWGQGLTVTVSS	43
	VL	DIQMTQSPSSLSASVGD RVTITCRASQDVSTAVA WYQQKPGKAPKLLIYSASFLYSGVPSRFSGSGSGT DFTLTISSLQPEDFATYYCQQYLYHPATFGQGTKVE IK	44
Avelumab	VH CDR1	SYIM	25
	VH CDR2	SIYPSGGITFYADTVKG	26
	VH CDR3	IKLGTVTTVDY	27
	VL CDR1	TGTSSDVGGYNYVS	28
	VL CDR2	DVSNRPS	29
	VL CDR3	SSYTSSTRV	30

[0060]

	VH	EVQLLESGGGLVQPGGSLRLSCAASGFTFSSYIMM WVRQAPGKGLEWVSSIYPSGGITFYADTVKGRFTI SRDNSKNTLYLQMNSLRAEDTAVYYCARIKLGTVT TVDYWGQGLTVTVSS	45
	VL	QSALTQPASVSGSPGQSITISCTGTSSDVGGYNYVS WYQQHPGKAPKLMYDVSNRPSGVSNRFGSKSG NTASLTISGLQAEDEADYYCSSYSSSTRVFGTGK VTVL	46
Durvalumab	VH CDR1	RYWMS	31
	VH CDR2	NIKQDGSEKYYVDSVKG	32
	VH CDR3	EGGWFGELAFDY	33
	VL CDR1	RASQRVSSSYLA	34
	VL CDR2	DASSRAT	35
	VL CDR3	QQYGSLPWT	36
	VH	EVQLVESGGGLVQPGGSLRLSCAASGFTFSRYWM SWVRQAPGKGLEWVANIKQDGSEKYYVDSVKGR FTISRDNKNSLYLQMNSLRAEDTAVYYCAREGG WFGELAFDYWGQGLTVTVSS	47
	VL	EIVLTQSPGTLSPGERATLSCRASQRVSSSYLAW YQQKPGQAPRLIYDASSRATGIPDRFSGSGSGTDF TLTISRLEPEDFAVYYCQQYGSLPWTFGQGTKVEIK	48
Canakinumab	VH CDR1	VYGMN	49
	VH CDR2	IIWYDGDNQYADSVKG	50
	VH CDR3	DLRTGP	51
	VL CDR1	RASQSIGSSLH	52
	VL CDR2	ASQSFS	53
	VL CDR3	HQSSSLP	54
	VH	QVQLVESGGGVVQPGRSLRLSCAASGFTFSVYGM NWVRQAPGKGLEWVAIIWYDGDNQYADSVKG RFTISRDNKNTLYLQMNSLRAEDTAVYYCARDLR TGPFDYWGQGLTVTVSS	55
	VL	EIVLTQSPDFQSVTPKEKVTITCRASQSIGSSLHWY QQKPDQSPKLLIKYASQSFSGVPSRFSGSGSGTDF LTINSLEAEDAAAYYCHQSSSLPFTFGPGTKVDIK	56

[0061] IL-1受体类型具有如下序列的结合结构域：

KCKEREKIIIVSSANEIDVRPCPLNPNEHKGTITWYKDDSKTPVSTEQASRIHQHKEKLWFVPAK
VEDSGHYCVVRNSSYCLRIKISAKFVENEPNLCYNAQAIFKQKLPVAGDGGLVCPYMEFFKNENNELPKL
[0062] QWYKDCKPLLDNIHFSGVKDRILIVMNVAEKHRGNYTCHASYTYLGKQYPITRVIEFITLEENKPTRPVIVS
PANETMEVDLGSQILICNVTGQLSDIAYWKWNGSVIDEDDPVLGEDYYSVENPANKRRSTLITVLNISEI
ESRFYKHPFTCFAKNTHGIDAAIYQLIYPVTN (SEQID NO:70)

[0063] Riloncept是一种免疫球蛋白融合蛋白,其中的结合结构域包含与I型IL-1受体融合的IL-1受体辅助蛋白(IL-1RAP)。Riloncept的IL-1结合部分的序列(可以用作合适的结合结构域)为：

SERCDDWGLDTMRQIQVFEDEPARIKCPLFEHFLKFNYSTAHSAGLTLIWYWTRQDRDLLEEPIN
 FRLPENRISKEKDVLFWRPTLLNDTGNYTCMLRNTTYCSKVAFFLEVVQKDCSFNSPMKLPVHKLYIEYGI
 QRITCPNVDGYFPSSVKPTITWYMGYKIQNFNNVIPEGMNLFLIALISNNGNYTCVVVYPENGRTFHLT
 RTLTVKVVGSPKNAVPPVIHSPNDHVVVEKEPGEELLIPCTVYFSFLMDSRNEVWWTIDGKKPDDITDVT
 [0064] INESISHSRTEDETRTQILSIKKVTSSEDLKRSYVCHARSAGEVAKAAVKQKVPAPRYTVEKCKEREKIILV
 SSANEIDVRPCPLNPNHKGITWYKDDSKTPVSTEQASRIHQHKEKLWFVPAKVEDSGHYCVVRNSSY
 CLRIKISAKFVENEPNLCYNAQAIFKQKLPVAGDGLVCPYMEFFKNENNELPKLQWYKDKPLLLDNIHF
 SGVKDRLIVMNVAEKHRGNYTCHASYTYLGKQYPITRVIEFITLEENKPTRPVIVSPANETMEVDLGSQIQL
 ICNVTGQLSDIAYWKWNGSVIDEDDPVLGEDYYSVENPANKRRSTLITVLNISEIESRFYKHPFTCFANKTH
 GIDAAYIQLIYPVTN (SEQ ID NO:71)

[0065] 双特异性结合蛋白结构

[0066] 一旦选择了合适的结合结构域,就将它们并入包含至少一特异性结合IL-1 β 或IL-1R的结合结构域和至少一特异性结合检查点蛋白的结构域的形式。有利地,结合蛋白的形式是二价或多价双特异性抗体的形式,其包含免疫球蛋白可变和恒定链结构域,其被安排为包含两个不同的结合结构域,这与自然存在的二价但单特异性人类抗体的同二聚体结构(homodimeric structure)不同。

[0067] 制备双特异性抗体的方法是本领域已知的,并且描述于下列文献中,例如Brinkmann和Kontermann的文献(mAbs 9:182 (2017))和Spiess等人的文献(Molecular Immunology,67:95-106 (2015))。本文所述的双特异性结合蛋白可以是本领域已知的任何稳定的形式,适合于对受试者施用,并且包含结合IL-1 β 或IL-1R的至少一结合结构域和结合检查点蛋白的至少一结合结构域。

[0068] 本领域已知的合适的双特异性结合蛋白形式的例子包括:

[0069] 无Fc (Fc-less) 的双特异性抗体形式包括:通过接头连接的两个scFv分子(Kontermann,Acta Pharmacol Sin 26:1-9 (2005));双特异性单结构域抗体融合蛋白(Weidle等人,Cancer Genomics Proteomics 10:155-68 (2013;));双体(Diabody) (Atwell等人,Mol Immunol 33:1301-12 (1996));Fab融合蛋白(Schoonjans等人,J Immunol;165:7050-7 (2000)以及微型抗体(miniantibody) (Pluckthun与Pack,Immunotechnology 3:83-105 (1997)及Muller等人,FEBS Lett 432:45-49 (1998));

[0070] 具有来自两种不同抗体的重链和轻链的不对称IgG (Suresh等人,Methods Enzymol;121:210-28 (1986));以及

[0071] 具有不对称Fc区的双特异性IgG,例如使用“钮入孔(knobs into holes)”方法形成不对称的Fc区(Ridgway等人,Protein Eng;9:617-21 (1996);Shatz等人,MAbs;5:872-81 (2013));Sampei等人,PLoS One;8:e57479 (2013);Spiess等人,Biotechnol;31:753-8 (2013);Juntilla等人,Cancer Res.74:5561-71 (2014);和Sun等人,J Clin Invest.125):4077-4090 (2015))。

[0072] 技术人员将认识到,除了上述特定形式之外,大量的双特异性抗体形式可用于构建结合IL-1 β 或IL-1R与检查点蛋白的双特异性抗体。有利地,双特异性抗体是基于2+2scFv的结构或基于2+2Fab的结构,如下文更详细地描述。

[0073] 基于2+2scFv的结构

[0074] 第一个基于2+2scFv的结构是图1中所示的结构,在此称为BiS2。如图1所示,BiS2形式包含两条蛋白链:

[0075] (1) 重链,包含(从N末端到C末端)单链Fv;单链Fv包含第一VH结构域和第一VL结构域(排列为VH-VL或VL-VH,即这些结构域可以是任何顺序);第二VH结构域;CH1、CH2和CH3结构域,其中scFv结合第一靶标(分别是IL-1 β 、IL-1R或检查点蛋白);以及

[0076] (2) 包含(从N末端到C末端)第二VL结构域和CL结构域的轻链。

[0077] BiS2蛋白经由CH3结构域和CH2结构域的非共价同二聚体结合,以及重链上的CH1结构域和CL结构域与轻链上的第二VH结构域与VL结构域之间的异二聚体结合而组装。CH1和CL结构域与VH和VL结构域之间的结合形成了一个Fab结构域,所述结构域结合了第二靶标(分别是检查点蛋白或IL-1 β /IL-1R)。有利地,以与自然存在的IgG分子中相同的方式,双硫键也在铰链区(hinge region)之间以及CH1和CL结构域之间形成。

[0078] 第二个基于2+2sc Fv的结构是图2A中所示的结构,在此称为BiS3。如图2A所示,BiS3形式亦包含两条蛋白链:

[0079] (1) 重链,其包含(从N末端到C末端):第一VH结构域;CH1、CH2和CH3结构域;以及单链Fv,单链Fv包含第二VH结构域和第二VL结构域(其中VH和VL结构域可以是任意顺序),其中scFv结合第一靶标(分别是IL-1 β 或检查点蛋白);

[0080] (2) 包含(从N末端到C末端)第二VL结构域和CL结构域的轻链。

[0081] BiS3蛋白亦经由CH3和CH2结构域的同二聚体结合以及重链上的CH1和CL结构域与轻链上的第二VH和VL结构域之间的异二聚体结合而组装。CH1和CL结构域与VH和VL结构域之间的结合形成了Fab结构域,所述结构域结合了第二靶标(分别是检查点蛋白或IL-1 β /IL-1R)。有利地,以与自然存在的IgG分子中相同的方式,双硫键也在CH2结构域之间以及在CH1和CL结构域之间形成。

[0082] 替代的结合蛋白结构是图2B中所示的同二聚体结构,其中重链VH和CH1结构域被衍生自白介素-1受体的细胞外配体结合结构域的结合结构域所取代。所述结合结构域包含来自1型或2型IL-1R的全部或部分细胞外结合结构域,选择性地缀合至来自白介素-1辅助蛋白(IL-1RAcP)的细胞外蛋白结合结构域。IL-1RAcP是功能性IL-1受体的受体亚基,与IL-1RI形成受体异二聚体。在图2B所示的结构中,结合蛋白经由CH3和CH2结构域的非共价同二聚体结合而组装。有利地,以与自然存在的IgG分子中相同的方式,双硫键也在CH2结构域之间和铰链结构域之间形成。

[0083] 基于2+2Fab的结构

[0084] 第一个基于2+2Fab的结构是图3A中所示的结构,在本文中称为FIT-Ig(请参照Gong等人的文献:MABS,2017,9:1118-1128(2017))。如图3A所示,FIT-Ig形式包含三个蛋白链:

[0085] (1) 重链,其包含(从N末端到C末端):第一VL结构域;第一CL结构域,第一VH结构域,第一CH1结构域以及CH2和CH3结构域;

[0086] (2) 轻链,其包含(从N末端至C末端):第二VL结构域和第二CL结构域;以及

[0087] (3) Fd链,其包含(从N末端到C末端):第二VH结构域和第二CH1结构域。

[0088] 在重链中,第一CL结构域可以经由肽接头(例如具有序列(GGGGS)_x(其中x为1-5)的柔性亲水接头)与第一VH结构域连接。然而,有利地,不存在接头。

[0089] FIT-Ig蛋白经由以下方式组装:CH3和CH2结构域的非共价同二聚体结合;重链上的第一VH和CH1结构域与轻链上的第二VL和CL结构域之间的异二聚体结合;Fd链上第一VL

和CL结构域与第二VH和CH1结构域之间的异源二聚体结合。两个相同的Fab结合结构域通过重链与轻链的结合形成,两个独特(distinct)但相同的Fab结构域通过重链与Fd链之间的结合形成,如图3中所示。有利地,以与自然存在的IgG分子中相同的方式,双硫键亦在CH2结构域之间以及铰链结构域之间形成。

[0090] 另一种2+2结合蛋白显示在图3B至图3E中,其中抗体Fab结合结构域之一被衍生自白介素-1受体的细胞外配体结合结构域的结合结构域所取代。所述结合结构域包含来自1型或2型IL-1R的全部或部分细胞外结合结构域,任选地缀合至来自白介素-1辅助蛋白(IL-1RAcP)的细胞外蛋白结合结构域。IL-1RAcP是功能性IL-1受体的受体亚基,与IL-1RI形成受体异二聚体。在图3B至图3E所示的结构中,结合蛋白经由CH3和CH2结构域的非共价同二聚体结合而组装;一条链上的VH和CH1结构域与第二蛋白链上的VL和CL结构域之间的异源二聚体结合。有利地,双硫键也以与自然存在的IgG分子中相同的方式在CH1和CL结构域之间,CH2结构域之间以及铰链结构域之间形成。

[0091] 第二个基于2+2Fab的结构是图4所示的新颖结构,在本文中称为FAT-Ig。如图4所示,FAT-Ig格式包含三个蛋白链:

[0092] (1) 重链,其包含(从N末端到C末端):第一VH结构域;第一CH1结构域,以及CH2结构域和CH3结构域;加上第一VL结构域和第一CL结构域,其中第一VL结构域和第一CL结构域位于CH2结构域、CH3结构域中的溶剂暴露环(solvent exposed loop)处,或位于CH2和CH3结构域的界面处。有利地,第一CL结构域和第一CL结构域位于CH3结构域中的溶剂暴露环处。

[0093] (2) 轻链,其包含(从N末端至C末端):第二VL结构域和第二CL结构域;和

[0094] (3) Fd链包含(从N末端到C末端):第二VH结构域和第二CH1结构域。

[0095] 在重链中,位于溶剂暴露环上的第一VL和CL经由柔性肽接头连接到CH2结构域、CH3结构域,或CH2和CH3结构域的界面。接头可具有4至25个氨基酸,并且有利地包含(GGGGS)_x单元,其中x=1至5。如下面更详细描述,也可以使用其他接头。

[0096] FAT-Ig蛋白的组装如图4所示,经由下列方式:CH3和CH2结构域的非共价同二聚体结合;重链CH1和VH结构域与轻链CL和VL结构域的异二聚体结合;以及重链CL和VL结构域与Fd链CH1和VH结构域的异二聚体结合。如图4所示,通过重链与轻链的结合形成两个相同的Fab结合结构域,经由重链与Fd链的结合形成两个独特但相同的Fab结构域。有利地,以与自然存在的IgG分子相同的连接方式,双硫键亦在铰链结构域之间以及CH1和CL结构域之间形成。本领域中普通技术人员将认识到,新颖FAT-Ig抗体形式可用于结合任何两种所需抗原,并且不限于IL-1 β /IL-1R和检查点蛋白。

[0097] 在上述四种特异性结合蛋白的每一种中,特异性结合IL-1 β /IL-1R和检查点蛋白的结合结构域不对称地位于结合蛋白内,亦即,相较于当第一结合结构域结合检查点蛋白并且第二结合结构域结合IL-1 β /IL-1R时的结构而言,当第一结合结构域结合IL-1 β /IL-1R而第二结合结构域结合检查点蛋白时结合蛋白的结构是有所不同。因此,对于任何给定的结合结构域对(pair),四种特异性结合蛋白中的每一种可以两种替代形式存在。

[0098] 多肽接头

[0099] 可以使用接头将本文所述的双特异性结合蛋白的结构域连接成连续的蛋白链。接头可用于例如连接scFv的可变重链及轻链,或将CL/VL结构域连接成FAT-Ig格式的重链恒定结构域。

[0100] 合适的接头是本领域已知的,并且当存在时,有利地包含至少四个氨基酸,尽管也可以使用更长或更短的接头。所述接头有利地是柔性的、亲水的并且本身具有很少或没有二级结构。接头可能约为1、2、3、4、5、6、7、8、9、10、11、12、13、14、15、16、17、18、19、20、25、30、35、40、45或大约50个残基的长度。如本文所述,当多个接头用于互连双特异性蛋白的部分时,接头可以相同,或具有不同的长度和/或氨基酸序列。

[0101] 接头促进所需双特异性结合蛋白结构的形成。接头可包含(Gly-Ser)_x单元,其中x=1-5。如有必要,还可将谷氨酸(Glutamic acid)或赖氨酸(Lysine)残基置于接头序列中以增加溶解度。接头的长度可以变化以促进蛋白质折叠、靶标结合和/或表达。例如,使用本领域已知的方法,可以使用(Gly-Ser)_x单位的不同倍数来改善或优化蛋白质折叠、靶标结合和/或表达。

[0102] 双特异性结合蛋白的制备

[0103] 制备双特异性结合蛋白的方法例如是无Fc的双特异性抗体、具有来自两种不同抗体的重链和轻链的不对称IgG及具有不对称Fc区的双特异性IgG,在本领域中是已知的,并在上文提供的参考文献中进行了描述。

[0104] 可以使用重组宿主细胞中的合适表达构建体(construct)产生上述特定的2+2双特异性抗体。编码重、轻和Fd链的核酸可以使用例如商业基因合成供货商(例如Thermo Fisher(Carlsbad,CA))合成制备。有利地,宿主细胞是真核细胞,并且有利地用编码N末端信号序列的序列合成每个链的基因,所述N末端信号序列使得翻译的蛋白质从宿主细胞分泌。将每条链的基因插入合适的表达载体,例如pTT5载体(Durocher等人,Nucleic Acids Res.30:E9(2002)),然后将得到的表达构建体转染(transfect)到合适宿主的培养物中,以瞬时表达。使用例如阳离子脂质将表达载体有效转染到宿主细胞中的方法是本领域已知的(请参见Felgner等人的文献,Proc.Nat'l Acad.Sci USA 84:7413(1987))。将表达载体递送到细胞中的其他方法也是本领域已知的。通过将表达构建体整合至合适的宿主细胞的基因组中来制备能够稳定表达所需蛋白质的宿主细胞的方法也是已知的,使用包含哺乳动物复制起点(作为宿主细胞核中的染色体外组件)的附加型载体(episomal vector)的稳定表达的方法也是已知的。

[0105] 宿主细胞有利地是真核细胞,例如单细胞真核生物(例如酵母或其他真菌)、植物细胞(例如烟草或西红柿植物细胞)、动物细胞(例如人类细胞、猴子细胞、仓鼠细胞、大鼠细胞、小鼠细胞或昆虫细胞)或杂交瘤(hybridoma)。宿主细胞的范例包括猴肾细胞的COS-7系(ATCC CRL 1651)(请参照Gluzman等人的文献,1981,Cell 23:175)、L细胞、C127细胞,3T3细胞(ATCC CCL 163),在无血清介质中生长的中国仓鼠卵巢(CHO)细胞或其衍生物,例如Veggie CHO和相关细胞系(请参照Rasmussen等人的文献,1998,Cytotechnology 28:31)或DHFR缺乏的CHO株DX-B11(请参照Urlaub等人的文献,1980,Proc.Natl.Acad.Sci.USA 77:4216-20)、希拉细胞(HeLa cell)、BHK(ATCC CRL 10)细胞系、源自非洲绿猴肾CV1细胞系(ATCC CCL 70)的CV1/EBNA细胞系(请参照McMahan等人的文献,1991,EMBO J.10:2821)、人类胚胎肾细胞(例如293、293EBNA或MSR 293)、人类表皮A431细胞、人类Colo205细胞、其他转化的灵长类动物细胞系(transformed primate cell line)、正常二倍体细胞、源自原代组织体外培养的细胞株、原代外植体(primary explant)、HL-60、U937、HaK或Jurkat细胞。有利地,宿主细胞是CHO细胞,例如CHO-3E7。

[0106] 典型地, 宿主细胞是可以编码多肽的核酸转化或转染的培养细胞, 然后可以在宿主细胞中表达所述多肽。“重组宿主细胞”的用语可用于表示已经用待表达的核酸转化或转染的宿主细胞。宿主细胞也可以是包含核酸但不以所需水平表达的细胞, 除非将调控序列引入宿主细胞中, 从而使其与核酸可操作地连接。如本文所使用的“宿主细胞”的术语不仅是指特定的个体细胞 (subject cell), 而且是指这种细胞的后代或潜在后代。因为某些修饰可能由于例如突变或环境影响而在后代中发生, 所以这种后代实际上可能不会与亲本细胞相同, 但仍包括在本文所用术语的范围内。用于真核宿主细胞生长的合适的细胞培养基在本领域中是已知的, 并且可以从例如 Thermo Fisher (Grand Island, NY) 商购获得。

[0107] 在合适的条件下培养宿主细胞, 以使蛋白链在宿主细胞的内质网中组装, 然后将双特异性结合蛋白分泌到细胞培养上清液中。通过改变用于转染宿主细胞的表达载体的相对比例, 可以改善结合蛋白正确结构的组装 (例如, 与导致非活性蛋白形成的链的非特异性配对相反)。载体比例的这种变化也可以用来抵消, 例如, 与不同链相比, 链之一的生产效率较低。本领域技术人员将认识到, 优化载体比例的方法在本领域中是已知的。

[0108] 以合适的时间长度在合适的表达介质中培养宿主细胞之后, 收集含有双特异性结合蛋白的条件介质, 并使用本领域已知的方法纯化双特异性结合蛋白。例如, 可以使用可包括离子交换色谱法、尺寸排阻色谱法和亲和性色谱法 (例如是蛋白 A 亲和色谱) 的方法来纯化结合蛋白。蛋白质纯化的方法例如是描述于 Burgess 和 Deutscher (Eds) 的文献 (“Guide to Protein Purification, Volume 436 (Methods in Enzymology) 2nd Edition (2009)”)。可以使用本领域已知的方法 (例如 RT-HPLC、SDS-PAGE 及其他方法) 来确认蛋白质的纯度。

[0109] 多链结合蛋白的正确组装可以通过例如非变性凝胶电泳来显示, 以显示结合蛋白具有预期的分子量。SDS-PAGE 可用于显示存在每个预期的蛋白链并具有预期的分子量。使用合适的抗人 IgG 抗体的 western 印记可以进一步显示所测蛋白是免疫球蛋白链。

[0110] 药物组合物和施用方法

[0111] 制备双特异性结合分子并将其施用至有需要的受试者的方法是本领域技术人员已知的或容易确定的。结合分子的施用途径可以是例如口服、非口服、通过吸入或局部施用。本文所用的术语非口服包括例如静脉内、动脉内、腹膜内、肌内、皮下、直肠或阴道施用。然而, 在与本文的教导兼容的其他方法中, 可以将结合分子直接递送至不良细胞群体的位点, 从而增加患病组织对治疗剂的暴露。

[0112] 可以以药物有效量施用结合分子以治疗疾病, 例如某些类型的癌症。药物组合物可以包含药学上可接受的载体, 包括例如水、离子交换剂、蛋白质、缓冲物质和盐。防腐剂和其他添加剂也可以存在。载体可以是溶剂或分散介质。下列文献描述了适用于本文揭露的治疗方法的制剂 (Remington's Pharmaceutical Sciences (Mack Publishing Co.) 第 16 版 (1980))。

[0113] 在任何情况下, 可以通过将结合分子本身或与有效量的其他活性剂在适当的溶剂中组合, 然后过滤灭菌来制备无菌注射溶液。制剂也可以以药盒 (kit) 的形式包装和出售。这种制品可以具有标签或包装插页, 表明相关的组合物可用于治疗患有或易患疾病或病症的受试者。

[0114] 非口服制剂可以是单次推注剂量 (single bolus dose)、输注 (infusion) 或负荷推注剂量 (loading bolus dose), 然后是维持剂量 (maintenance dose)。这些组合物可以

以特定的固定或可变间隔施用,例如每周或每月一次,或在“根据需要”的基础上施用。

[0115] 所述组合物可以以单剂量、多剂量或在输注的确定时间段内施用。剂量方案也可以调整以提供最佳的期望反应(例如,治疗或预防反应)。

[0116] 所述组合物可用于治疗细胞介导的疾病,例如某些类型的癌症,包括例如骨癌、胰腺癌、头颈癌、皮肤或眼内黑素瘤、子宫癌、中枢神经系统癌(CNS)、卵巢癌、直肠癌、肛门区域癌、胃癌、结肠癌、乳腺癌、黑素瘤、结肠直肠癌、睾丸癌、霍奇金病、食道癌、小肠癌、内分泌系统癌、软组织肉瘤、尿道癌、阴茎癌、前列腺癌、慢性或急性白血病、儿童实体瘤、淋巴瘤性淋巴瘤、膀胱癌、肾脏或输尿管癌、肾上腺皮质癌、艾滋病相关癌症、儿童小脑星形细胞瘤、儿童脑星形细胞瘤、基底细胞癌、肝外胆管癌、骨肉瘤/恶性纤维组织细胞瘤骨癌、脑肿瘤、支气管腺瘤/类癌、类癌肿瘤、胃肠道类癌肿瘤、小脑星形细胞瘤、脑星形细胞瘤/恶性神经胶质瘤、子宫颈癌、儿童期癌症、慢性骨髓单核细胞白血病(CMML)、慢性淋巴细胞性白血病,慢性骨髓性白血病、慢性骨髓增生性疾病、室管膜瘤、尤文氏肿瘤、颅外生殖细胞肿瘤(extracranial germ cell tumor)、性腺外生殖细胞肿瘤、肝外胆管癌、胆囊癌、胃肠道类癌肿瘤、生殖细胞肿瘤、妊娠滋养细胞肿瘤、神经胶质瘤、毛细胞白血病、肝细胞癌、下咽癌、下丘脑和视神经胶质瘤、胰岛细胞癌、卡波济氏肉瘤、喉癌、白血病、嘴唇和口腔癌、非小细胞肺癌(包括鳞状细胞肺癌、大细胞肺癌、肺腺癌、肺多形性癌、肺类癌、唾液腺癌)、小细胞肺癌(包括复合型小细胞癌)、未明确分类的(NOS)肺癌、肺外小细胞癌(包括位于淋巴结内的肺外小细胞癌和前列腺小细胞癌)、淋巴瘤、华氏巨球蛋白血症(Waldenstrom's Macroglobulinemia)、髓母细胞瘤、间皮瘤、口腔原发不明鳞状细胞癌的颈部转移(metastatic squamous neck cancer with occult primary)、多发性内分泌肿瘤综合征、多发性骨髓瘤/浆细胞瘤、蕈状肉芽肿(mycosis fungoide)、骨髓增生不良综合征(myelodysplastic syndrome)、骨髓增生异常/骨髓增生性疾病、鼻腔和副鼻窦癌(nasal cavity and paranasal sinus cancer)、鼻咽癌、神经母细胞瘤、口腔癌、口咽癌、卵巢上皮癌、卵巢生殖细胞肿瘤、卵巢癌低恶性肿瘤、胰岛细胞胰腺癌、副甲状腺癌(parathyroid cancer)、嗜铬细胞瘤(pheochromocytoma)、松果体母细胞瘤(pineoblastoma)、脑下垂体瘤、胸膜肺母细胞瘤(pleuropulmonary blastoma)、输尿管移行细胞癌(ureter transitional cell cancer)、视网膜母细胞瘤、横纹肌肉瘤、唾液腺癌、塞札里综合征(Sezary Syndrome)、皮肤癌、非黑素瘤皮肤癌、默克尔细胞皮肤癌(Merkel Cell Skin Carcinoma)、鳞状细胞癌、睾丸癌、胸腺瘤、妊娠性滋养层细胞肿瘤(gestational trophoblastic tumor)、威尔姆氏肿瘤(Wilms' Tumor)和微卫星不稳定性癌症(cancers with microsatellite instability)。

[0117] 关于食道癌,所述癌症可以是例如食道鳞状细胞癌(esophageal squamous-cell carcinomas,ESCC)或食道腺癌(esophageal adenocarcinomas,EAC)。关于胰腺癌,所述癌症可以是例如外分泌癌、胰腺腺癌、胰腺导管癌、胰腺腺泡细胞癌、囊腺癌、胰脏母细胞瘤、腺鳞癌、未分化癌、胰腺黏液性囊性肿瘤、神经内分泌癌、或胰脏神经内分泌肿瘤(pancreatic neuroendocrine tumors,PanNETs)。关于肝癌,所述癌症可以是例如肝细胞癌(hepatocellular carcinoma,HCC)、肝母细胞瘤、胆管癌、胆管细胞囊腺癌、血管肉瘤或平滑肌肉瘤。关于结直肠癌,所述癌症可以是腺癌、类癌肿瘤、胃肠道间质瘤(gastrointestinal stromal tumor,GIST)、淋巴瘤、肉瘤、腺鳞癌(adenosquamous

carcinoma, Ad-SCC) 或鳞癌 (squamous carcinoma, SCC)。关于乳癌, 所述癌症可以是原位癌、原位导管癌 (ductal carcinoma in situ, DCIS)、浸润性、浸润性导管癌 (invasive ductal carcinoma, IDC)、浸润性小叶癌 (invasive lobular carcinoma, ILC)、三阴性乳腺癌 (triple-negative breast cancer)、炎症性乳癌、血管肉瘤或乳房柏哲德氏症 (Paget disease of the breast)。关于卵巢癌, 所述癌症可以是上皮肿瘤、良性上皮性卵巢肿瘤、交界性上皮性卵巢肿瘤、恶性上皮性卵巢肿瘤、生殖细胞肿瘤、畸胎瘤、无性细胞瘤 (dysgerminoma)、内胚窦肿瘤和绒毛膜癌、原发性腹膜癌、输卵管癌或卵巢间质瘤。关于多发性骨髓瘤和癌前疾病, 所述癌症可能是轻链骨髓瘤、非分泌性骨髓瘤、孤立性浆细胞瘤、髓外浆细胞瘤、意义不明单克隆球蛋白病 (monoclonal gammopathy of undetermined significance, MGUS)、冒烟型多发性骨髓瘤 (smoldering multiple myeloma, SMM)、免疫球蛋白 D (IgD) 骨髓瘤或免疫球蛋白 E (IgE) 骨髓瘤。

[0118] 用于治疗这些疾病的组合物的治疗有效剂量取决于许多不同因素, 包括施用方式、靶标位点、患者的生理状态、患者是人还是动物、所施用的其他药物以及治疗是预防性的还是治疗性的。通常, 患者是人类, 但是也可以治疗非人类哺乳动物, 包括转基因的哺乳动物。可以使用本领域技术人员已知的常规方法来滴定 (titrate) 治疗剂量以优化安全性和功效。

[0119] 至少一种结合分子的施用量可以通过本领域普通技术人员容易地确定, 而无需进行过多的实验。影响施用方式和至少一种结合分子的各自量的因素包括但不限于疾病的严重程度、病史、以及其年龄、身高、体重、健康状况及正在接受治疗的个人的身体状况。类似地, 要施用的结合分子的量将取决于施用方式以及受试者将接受单剂或者多剂的试剂。

[0120] 结合分子还可以用于制备用于治疗一种癌症 (包括例如以上所列的癌症) 的药物。

[0121] 在接受包含结合分子的药物之前, 用本文所述的组合物治疗的受试者可以是未经治疗的或可以用一种或多种其他疗法 (例如, 至少一种其他抗癌疗法) 进行预处理。受试者不必是对先前疗法或一些疗法的预处理的反应者。因此, 接受包含结合分子的药物的受试者, 可能已经反应、反应较差、最初有反应但是随后却没有反应、或者可能对先前疗法的预处理、或预处理包括多种疗法的一种或多种先前疗法没有反应。因此, 本公开提供了治疗对其他疗法反应差或无反应的患者的方法, 包括施用本文所述的结合分子。还提供了克服或预防对癌症疗法的抗性或预防或延迟复发的方法, 其包括施用本文公开的结合分子或本文所述的组合物。

[0122] 即使患者先前已经用抗癌药物治疗过, 本领域技术人员也可以确定所述人是否对所述药物无反应或具有抗性 (refractory)。例如, 对抗癌药物的无反应可能反应出罹患癌症的痛苦增加 (例如, 癌症/肿瘤的生长增加和/或肿瘤的大小增加, 形成转移或转移增加、或转移的数量或大小的增加)。无反应也可能是肿瘤的发展或转移, 例如在切除 (resection) 肿瘤之后, 缩短疾病进展时间或增加一或多个肿瘤的大小和/或转移, 例如在新辅助治疗中。基于这些参数或本领域已知的其他参数, 可以确定对抗癌药物的治疗没有反应的患者组, 然后可以用本文所述的结合分子治疗所述患者组。

[0123] 结合分子和包含结合分子的组合物还可用于治疗例如对另一种疗法的反应较差或无反应的患者。如本文所用, 术语“无反应者”可以指不太可能对使用抗癌药物的治疗反应的个体/患者/受试者。如本文所用, “反应可能性较小”是指在用抗癌药物治疗的患者中

发生病理完全反应的可能性降低。在一些方面,患者最初可以是良好的反应者,并且在用这种抗癌药物治疗期间可以产生对治疗的抗性,导致对治疗的反应较差或无反应。

[0124] 如本文所用术语“良好反应者”是指其肿瘤在使用抗癌药治疗期间或之后(例如基于连续性的影像研究)未表现出生长、转移、转移的数量或大小的增加等的个体;是指在一段时间内(例如,初诊后约1年)未经历肿瘤生长、转移、转移的数量或大小增加等的个体,和/或经历一定寿命的个体(例如,最初诊断后大约2年或更长时间)。

[0125] 如本文所用术语“不良反应者”是指在标准疗法(例如使用抗癌药物)期间或之后不久肿瘤生长或转移,或经历可归因于肿瘤的不良临床作用的个体。术语“不良反应者”还包括在使用抗癌药物治疗期间从“良好反应者”转变为“不良反应者”的个体。

[0126] 如果受试者被评估为“无反应者”、“反应较差”或“反应可能性较小”(例如,基于癌细胞中某些生物标记物的存在),受试者可以用本文所公开的结合分子治疗。

[0127] 还提供了用于本文所述结合分子与至少一种其他疗法的共同施用的方法。结合分子和至少一种其他疗法可以在单一组合中一起共同施用,或者可以在分开的组合中同时或重迭时间一起共同施用。在一些方面,结合分子可以用作辅助疗法。

[0128] 结合分子还可以用于制备用于治疗患有癌症的受试者的药物,其中在已经用至少一种其他疗法治疗受试者之前施用结合分子。

[0129] 通过向受试者施用有效量的结合蛋白或含有所述结合蛋白的组合物,结合分子还可用于预防或降低受试者癌症风险的方法中。癌症可以是肺癌,并且患者可以从先前诊断和/或先前治疗的癌症中缓解。由于环境暴露、使用或接触烟草、基因突变或癌症家族史,可以认为患者有患癌症的风险。

[0130] 实施例

[0131] 在下列实施例中,结合结构域是基于人类抗体(已获得监管机构批准可用于人类)的重链和轻链可变区。“O”、“E”和“K”表示结合IL-1 β 的结构域,而“M”和“B”表示结合PD-1的结合结构域。结合蛋白链的氨基酸序列如图5所示。

[0132] 实施例1:双特异性抗体的表达

[0133] 1. 质粒制备

[0134] 合成编码结合蛋白的靶标DNA序列,并将其亚克隆到pTT5载体中(Durocher等人, *Nucleic Acids Res.* 30:E9 (2002)),用于在CHO-3E7细胞中表达。编码序列的氨基酸序列如图5所示。

[0135] 2. 细胞培养和瞬间转染

[0136] CHO-3E7细胞在无血清FreeStyle™ CHO表达介质(Life Technologies, Carlsbad, CA, USA)中生长。将细胞在回转式振荡机(VWR Scientific, Chester, PA)上在37°C和5%CO₂的条件下保持在锥形瓶(Corning Inc., Acton, MA)中。转染前一天,将细胞接种在康宁锥形瓶中。转染当天,将DNA和转染试剂混合,然后添加到细胞培养物中,在此期间,将编码靶标抗体的重组质粒瞬间转染到CHO-3E7细胞中。在第6天收集的细胞培养上清液是用于纯化。表2列出了每种抗体的重链、轻链和Fd链组合以及所筛选的每种质粒比例。

[0137] 表2. 每个抗体的重链(HC)、轻链(LC)和Fd链(Fd)组合以及质粒比例的摘要

[0138]

抗体名称	抗体形式	重链名称	轻链名称	Fd	比例 1	比例 2	比例 3	比例 4
					HC : LC: Fd	HC : LC: Fd	HC : LC: Fd	HC : LC: Fd
ITA101	BiS2-OB	BscFv-OH C	OLC	/	1: 1: 0	3: 1: 0	1: 3: 0	/
ITA102	BiS2-OM	MscFv-OH C	OLC	/	1: 1: 0	3: 1: 0	1: 3: 0	/
ITA103	BiS2-PC	OscFv-BH C	BLC	/	1: 1: 0	3: 1: 0	1: 3: 0	/
ITA104	BiS2-MO	OscFv-MH C	MLC	/	1: 1: 0	3: 1: 0	1: 3: 0	/
ITA201	BiS3-OB	OHC-BscF v	OLC	/	1: 1: 0	3: 1: 0	1: 3: 0	/

[0139]

ITA202	BiS3-OM	OHC-Msc Fv	OLC	/	1: 1: 0	3: 1: 0	1: 3: 0	/
ITA203	BiS3-BO	BHC-OscFv	BLC	/	1: 1: 0	3: 1: 0	1: 3: 0	/
ITA204	BiS3-MO	MHC-Osc Fv	MLC	/	1: 1: 0	3: 1: 0	1: 3: 0	/
ITA301	FiT-OB	BLC-OHC	OLC	BFd	1: 1: 1	1: 3: 3	1: 1: 3	1: 3: 1
ITA302	FiT-OM	MLC-OHC	OLC	MFd	1: 1: 1	1: 3: 3	1: 1: 3	1: 3: 1
ITA303	FiT-BO	OLC-BHC	BLC	OFd	1: 1: 1	1: 3: 3	1: 1: 3	1: 3: 1
ITA304	FiT-MO	OLC-MHC	MLC	OFd	1: 1: 1	1: 3: 3	1: 1: 3	1: 3: 1
ITA401	FAT-OB	OHC-BLC	OLC	BFd	1: 1: 1	1: 3: 3	1: 1: 3	1: 3: 1
ITA402	FAT-OM	OHC-MLC	OLC	MFd	1: 1: 1	1: 3: 3	1: 1: 3	1: 3: 1
ITA403	FAT-BO	BHC-OLC	BLC	OFd	1: 1: 1	1: 3: 3	1: 1: 3	1: 3: 1
ITA404	FAT-MO	MHC-OLC	MLC	OFd	1: 1: 1	1: 3: 3	1: 1: 3	1: 3: 1
ITB101	FP2-BK	K BHC	BLC	/	1: 1			
ITB102	FP2-MK	K MHC	MLC	/	1: 1			
ITB103	FFP1(FI T)- KM	MFd-K-G4 P	MLC	/	1: 1			
ITB104	FFP1(FI T)-KB	BFd-K-G4 P	BLC	/	1: 1			
ITB105	FFP3-K M	K-G4P-Ms cFv	/	/	N/A			
ITB106	FP1-(cross mab)BK	K-BLC-Fc	/	BFd	1: 1			
ITB107	FP1-(cross mab) MK	K-MLC-Fc	/	MFd	1: 1			
ITB108	FFP2-K M	MLC-KG4 P	/	MFd	1: 1			
ITB109	FFP2-KB	BLC-K-G4 P	/	BFd	1: 1			
ITC401	FAT-O/B 1+5	OHC-BLC 1+5	OLC	BFd	1: 1: 1	1: 3: 3	1: 1: 3	1: 3: 1
ITC402	FAT-O/B 3+3	OHC-BLC 3+3	OLC	BFd	1: 1: 1	1: 3: 3	1: 1: 3	1: 3: 1
ITC403	FAT-O/B 4+2	OHC-BLC 4+2	OLC	BFd	1: 1: 1	1: 3: 3	1: 1: 3	1: 3: 1
ITC404	FAT-O/B 5+1	OHC-BLC 5+1	OLC	BFd	1: 1: 1	1: 3: 3	1: 1: 3	1: 3: 1
ITC405	FAT-O/B 4+4	OHC-BLC 4+4	OLC	BFd	1: 1: 1	1: 3: 3	1: 1: 3	1: 3: 1
ITC406	FAT-O/B 2+2	OHC-BLC 2+2	OLC	BFd	1: 1: 1	1: 3: 3	1: 1: 3	1: 3: 1
ITD401	FAT-O/B 5+5	FAT-O/B 5+5	OLC	BFd	1: 1: 1	1: 3: 3	1: 1: 3	1: 3: 1
ITD402	FAT-O/B 4+5	FAT-O/B 4+5	OLC	BFd	1: 1: 1	1: 3: 3	1: 1: 3	1: 3: 1
ITD403	FAT-O/B 5+4	FAT-O/B 5+4	OLC	BFd	1: 1: 1	1: 3: 3	1: 1: 3	1: 3: 1
ITE101	BiS2-O/ MVH/VL DSB	M scFv-OHC VH/VL DSB	OLC	/	1: 1: 0	3: 1: 0	1: 3: 0	/

[0140]

ITE102	BiS2-O/ MVL/VH DSB	M scFv-OHC VL/VH DSB	OLC	/	1: 1: 0	3: 1: 0	1: 3: 0	/
ITE201	BiS3-M/ OVH/VL DSB	MHC-O scFv_ VH/VL DSB	MLC	/	1: 1: 0	3: 1: 0	1: 3: 0	
ITE202	BiS3-M/ OVL/VH DSB	MHC-O scFv_ VL/VH DSB	MLC	/	1: 1: 0	3: 1: 0	1: 3: 0	
ITE301	FIT-B/O- L3	OLC-B HC-L3	BLC	O Fd	1: 1: 1	1: 3: 3	1: 1: 3	1: 3: 1
ITE302	FIT-B/O- L7	OLC-B HC-L7	BLC	O Fd	1: 1: 1	1: 3: 3	1: 1: 3	1: 3: 1
ITF101	BiS2-E/ MVL/VH DSB	BiS2-E /M VL/VH DSB	E13 LC	/	1: 1: 0,	1: 3: 0	3: 1: 0	
ITF102	BiS2-M/ E VL/VH DSB	BiS2-M/E VL/VH DSB	MLC	/	1: 1: 0,	1: 3: 0	3: 1: 0	
ITF103	BiS2-M/ E VH/VL DSB	BiS2-M/E VH/VL DSB	MLC	/	1: 1: 0,	1: 3: 0	3: 1: 0	
ITF201	BiS3-M/ E VL/VH DSB	BiS3-M/E VL/VH DSB	MLC	/	1: 1: 0,	1: 3: 0	3: 1: 0	
ITF202	BiS3-M/ E VH/VL DSB	BiS3-M/E VH/VL DSB	MLC	/	1: 1: 0,	1: 3: 0	3: 1: 0	
ITF301	FIT-B/E L3	FIT-B/E-L 3	BLC	E Fd	1: 1: 1	1: 1: 1,	1: 1: 1,	1: 1: 1,
ITF302	FIT-B/E L7	FIT-B/ E-L7	BLC	E Fd	1: 1: 1	1: 1: 1,	1: 1: 1,	1: 1: 1,
ITF401	FAT-E/B	FAT-E/B	E13LC	B Fd	1: 1: 1	1: 1: 1,	1: 1: 1,	1: 1: 1,
ITF402	FAT-B/E	FAT-B/E	BLC	E Fd	1: 1: 1	1: 1: 1,	1: 1: 1,	1: 1: 1,
ITF403	FAT-M/E	FAT-M/E	MLC	E Fd	1: 1: 1	1: 1: 1,	1: 1: 1,	1: 1: 1,

[0141] 3. 纯化及结果

[0142] 离心细胞培养上清液,然后过滤。将过滤的上清液以1.0ml/min的速度加载到1ml Monofinity A树脂预填充柱上(GenScript,Cat.No.L00433-11)。洗涤步骤后,洗脱抗体,然后将缓冲液更换为pH 7.2的PBS。通过标准技术进一步纯化抗体。例如,一些样品通过尺寸排阻色谱法(SEC)使用Superdex 200Increase 10/300GL柱,或通过陶瓷羟磷灰石色谱法(ceramic hydroxyapatite chromatography)使用CHT™陶瓷羟磷灰石柱(Bio-Rad)进一步纯化。对于其他蛋白质,蛋白A亲和性色谱用于初步纯化,然后根据需要进行SEC。

[0143] 在还原和非还原条件下,通过SDS-PAGE和Western印记分析(使用山羊抗人类IgG-HRP(GenScript,Cat.No.A00166))对每种表达的蛋白质进行了分析,结果表示蛋白质和组成链具有所需的分子量。使用尺寸排阻HPLC评估蛋白质的纯度。

[0144] 实施例2

[0145] 使用流式细胞术分析实施例1中所述16种不同双特异性抗体中的9种与细胞表面上的PD-1的结合。使用的细胞系是CHO-K1细胞(阴性对照)并表达CHO-K1/PD-1。使用的抗体是无关的人类的IgG(阴性对照)和市售的抗PD-1(阳性对照)。使用的二抗是山羊抗人类的

IgG(H+L) iFluor 647 (1 μ g/ml) (数据未显示)。为了证明双特异性分子与PD1和IL-1 β 同时结合,进行了夹心式FACS分析。结合曲线显示在图7中。表达PD1的CHO细胞被指定浓度的双特异性抗体结合。洗去未结合的抗体,并用生物素化的IL-1 β (2 μ g/ml),然后用SA-iFluor 647 (1 μ g/ml) 进行检测。荧光强度既表示BiSAb固定在PD1+细胞上,又表示其同时结合IL-1 β 的能力。抗IL-1 β VH/VL结合结构域与两对不同的抗PD-1VH/VL结合结构域的各种组合被格式化为BiS2、BiS3、FIT-IG或FAT-IG分子。相较于包含由SEQ ID Nos:6-12的序列定义的CDR区的抗PD-1VH/VL结合区的5个结合分子而言,在所测试的构建体 (construct) 中,包含由SEQ ID No:1-6的序列定义的CDR区的抗PD-1VH/VL结合区的4个结合分子均达成更高的平均荧光强度。

[0146] 图8至图12显示了另外的结合蛋白的另外的结合数据。图8显示了在多剂量夹心测定中双特异性抗体同时与细胞膜结合的PD-1及可溶性IL-1 β 结合的结合曲线,例如通过流式细胞术检测。显示了ITC、ITD与ITE系列双特异性抗体的可变的结合亲和力。所有的结合亲和力均实质上高于对照人IgG。

[0147] 图9显示了在多剂量夹心测定中与细胞膜结合的PD-1结合的结合曲线,例如是通过流式细胞术检测。显示了ITB和ITF系列双特异性抗体的可变结合亲和力。所有结合亲和力均实质上高于对照人IgG。

[0148] 图10显示了通过流式细胞术检测到的在多剂量夹心测定中同时与细胞膜结合的PD-1和可溶性IL-1 β 结合的结合曲线。显示了ITB和ITF系列双特异性抗体的可变结合亲和力。所有结合亲和力均实质上高于对照人IgG。

[0149] 图11显示双特异性抗体在PD-1/PD-L1报告分子分析中阻断PD-1活性。显示了针对ITA系列双特异性抗体的可变阻断活性。所有的阻断活性均实质上高于对照人IgG。

[0150] 图12显示双特异性抗体在IL-1 β 功能测定中阻断IL-1 β 活性。ITA系列双特异性抗体证明了可变的阻断活性。所有的阻断活性均实质上高于对照人IgG。

序列表

- <110> IMMETAS治疗股份有限公司
 <120> 靶向肿瘤微环境和免疫检查点蛋白的双特异性结合分子
 <130> 1563.0001I
 <140> PCT/US2020/025979
 <141> 2020-03-31
 <150> 62/827,381
 <151> 2019-04-01
 <160> 133
 <170> PatentIn version 3.5
 <210> 1
 <211> 5
 <212> PRT
 <213> 人工序列
 <220>
 <223> 人工序列的描述: 合成肽
 <400> 1
 Asn Tyr Tyr Met Tyr
 [0001] 1 5
 <210> 2
 <211> 17
 <212> PRT
 <213> 人工序列
 <220>
 <223> 人工序列的描述: 合成肽
 <400> 2
 Gly Ile Asn Pro Ser Asn Gly Gly Thr Asn Phe Asn Glu Lys Phe Lys
 1 5 10 15
 Asn
 <210> 3
 <211> 11
 <212> PRT
 <213> 人工序列
 <220>
 <223> 人工序列的描述: 合成肽
 <400> 3
 Arg Asp Tyr Arg Phe Asp Met Gly Phe Asp Tyr

1 5 10

<210> 4
 <211> 15
 <212> PRT
 <213> 人工序列

<220>
 <223> 人工序列的描述：合成肽

<400> 4
 Arg Ala Ser Lys Gly Val Ser Thr Ser Gly Tyr Ser Tyr Leu His
 1 5 10 15

<210> 5
 <211> 5
 <212> PRT
 <213> 人工序列

<220>
 <223> 人工序列的描述：合成肽

<400> 5
 Leu Ala Ser Tyr Leu
 1 5

[0002]

<210> 6
 <211> 9
 <212> PRT
 <213> 人工序列

<220>
 <223> 人工序列的描述：合成肽

<400> 6
 Gln His Ser Arg Asp Leu Pro Leu Thr
 1 5

<210> 7
 <211> 5
 <212> PRT
 <213> 人工序列

<220>
 <223> 人工序列的描述：合成肽

<400> 7
 Asn Ser Gly Met His
 1 5

<210> 8
 <211> 17
 <212> PRT
 <213> 人工序列

<220>
 <223> 人工序列的描述：合成肽

<400> 8
 Val Ile Trp Tyr Asp Gly Ser Lys Arg Tyr Tyr Ala Asp Ser Val Lys
 1 5 10 15

Gly

<210> 9
 <211> 4
 <212> PRT
 <213> 人工序列

<220>
 <223> 人工序列的描述：合成肽

[0003] <400> 9
 Asn Asp Asp Tyr
 1

<210> 10
 <211> 11
 <212> PRT
 <213> 人工序列

<220>
 <223> 人工序列的描述：合成肽

<400> 10
 Arg Ala Ser Gln Ser Val Ser Ser Tyr Leu Ala
 1 5 10

<210> 11
 <211> 7
 <212> PRT
 <213> 人工序列

<220>
 <223> 人工序列的描述：合成肽

<400> 11

Asp Ala Ser Asn Arg Ala Thr
1 5

<210> 12
<211> 9
<212> PRT
<213> 人工序列

<220>
<223> 人工序列的描述：合成肽

<400> 12
Gln Gln Ser Ser Asn Trp Pro Arg Thr
1 5

<210> 13
<211> 8
<212> PRT
<213> 人工序列

<220>
<223> 人工序列的描述：合成肽

[0004] <400> 13
Gly Phe Thr Phe Ser Asn Phe Gly
1 5

<210> 14
<211> 8
<212> PRT
<213> 人工序列

<220>
<223> 人工序列的描述：合成肽

<400> 14
Ile Ser Gly Gly Gly Arg Asp Thr
1 5

<210> 15
<211> 10
<212> PRT
<213> 人工序列

<220>
<223> 人工序列的描述：合成肽

<400> 15
Val Lys Trp Gly Asn Ile Tyr Phe Asp Tyr

1	5	10
<210> 16 <211> 6 <212> PRT <213> 人工序列		
<220> <223> 人工序列的描述：合成肽		
<400> 16 Leu Ser Ile Asn Thr Phe 1 5		
<210> 17 <211> 3 <212> PRT <213> 人工序列		
<220> <223> 人工序列的描述：合成肽		
[0005] <400> 17 Ala Ala Ser 1		
<210> 18 <211> 9 <212> PRT <213> 人工序列		
<220> <223> 人工序列的描述：合成肽		
<400> 18 Gln Gln Ser Ser Asn Thr Pro Phe Thr 1 5		
<210> 19 <211> 10 <212> PRT <213> 人工序列		
<220> <223> 人工序列的描述：合成肽		
<400> 19 Gly Phe Thr Phe Ser Asp Ser Trp Ile His 1 5 10		

<210> 20
 <211> 10
 <212> PRT
 <213> 人工序列

<220>
 <223> 人工序列的描述：合成肽

<400> 20
 Ala Trp Ile Ser Pro Tyr Gly Gly Ser Thr
 1 5 10

<210> 21
 <211> 9
 <212> PRT
 <213> 人工序列

<220>
 <223> 人工序列的描述：合成肽

<400> 21
 Arg His Trp Pro Gly Gly Phe Asp Tyr
 1 5

[0006]

<210> 22
 <211> 11
 <212> PRT
 <213> 人工序列

<220>
 <223> 人工序列的描述：合成肽

<400> 22
 Arg Ala Ser Gln Asp Val Ser Thr Ala Val Ala
 1 5 10

<210> 23
 <211> 7
 <212> PRT
 <213> 人工序列

<220>
 <223> 人工序列的描述：合成肽

<400> 23
 Ser Ala Ser Phe Leu Tyr Ser
 1 5

<210> 24
<211> 9
<212> PRT
<213> 人工序列

<220>
<223> 人工序列的描述：合成肽

<400> 24
Gln Gln Tyr Leu Tyr His Pro Ala Thr
1 5

<210> 25
<211> 4
<212> PRT
<213> 人工序列

<220>
<223> 人工序列的描述：合成肽

<400> 25
Ser Tyr Ile Met
1

[0007]

<210> 26
<211> 17
<212> PRT
<213> 人工序列

<220>
<223> 人工序列的描述：合成肽

<400> 26
Ser Ile Tyr Pro Ser Gly Gly Ile Thr Phe Tyr Ala Asp Thr Val Lys
1 5 10 15

Gly

<210> 27
<211> 11
<212> PRT
<213> 人工序列

<220>
<223> 人工序列的描述：合成肽

<400> 27

Ile Lys Leu Gly Thr Val Thr Thr Val Asp Tyr
1 5 10

<210> 28
<211> 14
<212> PRT
<213> 人工序列

<220>
<223> 人工序列的描述：合成肽

<400> 28
Thr Gly Thr Ser Ser Asp Val Gly Gly Tyr Asn Tyr Val Ser
1 5 10

<210> 29
<211> 7
<212> PRT
<213> 人工序列

<220>
<223> 人工序列的描述：合成肽

[0008] <400> 29
Asp Val Ser Asn Arg Pro Ser
1 5

<210> 30
<211> 10
<212> PRT
<213> 人工序列

<220>
<223> 人工序列的描述：合成肽

<400> 30
Ser Ser Tyr Thr Ser Ser Ser Thr Arg Val
1 5 10

<210> 31
<211> 5
<212> PRT
<213> 人工序列

<220>
<223> 人工序列的描述：合成肽

<400> 31
Arg Tyr Trp Met Ser

1 5

<210> 32
 <211> 17
 <212> PRT
 <213> 人工序列

<220>
 <223> 人工序列的描述：合成肽

<400> 32
 Asn Ile Lys Gln Asp Gly Ser Glu Lys Tyr Tyr Val Asp Ser Val Lys
 1 5 10 15

Gly

<210> 33
 <211> 12
 <212> PRT
 <213> 人工序列

[0009] <220>
 <223> 人工序列的描述：合成肽

<400> 33
 Glu Gly Gly Trp Phe Gly Glu Leu Ala Phe Asp Tyr
 1 5 10

<210> 34
 <211> 12
 <212> PRT
 <213> 人工序列

<220>
 <223> 人工序列的描述：合成肽

<400> 34
 Arg Ala Ser Gln Arg Val Ser Ser Ser Tyr Leu Ala
 1 5 10

<210> 35
 <211> 7
 <212> PRT
 <213> 人工序列

<220>
 <223> 人工序列的描述：合成肽

<400> 35
Asp Ala Ser Ser Arg Ala Thr
1 5

<210> 36
<211> 9
<212> PRT
<213> 人工序列

<220>
<223> 人工序列的描述: 合成肽

<400> 36
Gln Gln Tyr Gly Ser Leu Pro Trp Thr
1 5

<210> 37
<211> 120
<212> PRT
<213> 人工序列

<220>
<223> 人工序列的描述: 合成多肽

[0010]

<400> 37
Gln Val Gln Leu Val Gln Ser Gly Val 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 Asn Tyr
20 25 30

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

Gly Gly Ile Asn Pro Ser Asn Gly Gly Thr Asn Phe Asn Glu Lys Phe
50 55 60

Lys Asn Arg Val Thr Leu Thr Thr Asp Ser Ser Thr Thr Thr Ala Tyr
65 70 75 80

Met Glu Leu Lys Ser Leu Gln Phe Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Arg Asp Tyr Arg Phe Asp Met Gly Phe Asp Tyr Trp Gly Gln
100 105 110

Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 38
<211> 111
<212> PRT
<213> 人工序列

<220>
<223> 人工序列的描述：合成多肽

<400> 38
Glu Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
1 5 10 15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Lys Gly Val Ser Thr Ser
20 25 30

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

Arg Leu Leu Ile Tyr Leu Ala Ser Tyr Leu Glu Ser Gly Val Pro Ala
50 55 60

[0011]

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

Ser Leu Glu Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln His Ser Arg
85 90 95

Asp Leu Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
100 105 110

<210> 39
<211> 113
<212> PRT
<213> 人工序列

<220>
<223> 人工序列的描述：合成多肽

<400> 39
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg
1 5 10 15

Ser Leu Arg Leu Asp Cys Lys Ala Ser Gly Ile Thr Phe Ser Asn Ser
20 25 30

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

Ala Val Ile Trp Tyr Asp Gly Ser Lys Arg Tyr Tyr Ala Asp Ser Val
 50 55 60

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

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

Ala Thr Asn Asp Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser
 100 105 110

Ser

<210> 40

<211> 1

<212> PRT

<213> 人工序列

[0012]

<220>

<223> 人工序列的描述：合成肽

<400> 40

Ser

1

<210> 41

<211> 117

<212> PRT

<213> 人工序列

<220>

<223> 人工序列的描述：合成多肽

<400> 41

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

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asn Phe
 20 25 30

Gly Met Thr Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val

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

<210> 42
 <211> 107
 <212> PRT
 <213> 人工序列

[0013]

<220>
 <223> 人工序列的描述：合成多肽

<400>	42																
Asp	Ile	Gln	Met	Thr	Gln	Ser	Pro	Ser	Ser	Leu	Ser	Ala	Ser	Val	Gly		
1				5					10					15			
Asp	Ser	Ile	Thr	Ile	Thr	Cys	Arg	Ala	Ser	Leu	Ser	Ile	Asn	Thr	Phe		
			20					25					30				
Leu	Asn	Trp	Tyr	Gln	Gln	Lys	Pro	Gly	Lys	Ala	Pro	Asn	Leu	Leu	Ile		
		35					40					45					
Tyr	Ala	Ala	Ser	Ser	Leu	His	Gly	Gly	Val	Pro	Ser	Arg	Phe	Ser	Gly		
	50					55					60						
Ser	Gly	Ser	Gly	Thr	Asp	Phe	Thr	Leu	Thr	Ile	Arg	Thr	Leu	Gln	Pro		
65					70					75				80			
Glu	Asp	Phe	Ala	Thr	Tyr	Tyr	Cys	Gln	Gln	Ser	Ser	Asn	Thr	Pro	Phe		
				85					90					95			
Thr	Phe	Gly	Pro	Gly	Thr	Val	Val	Asp	Phe	Arg							

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

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

Tyr Ser Ala Ser Phe Leu Tyr 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 Tyr Leu Tyr His Pro Ala
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
100 105

<210> 45

<211> 120

<212> PRT

[0015] <213> 人工序列

<220>

<223> 人工序列的描述：合成多肽

<400> 45

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

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20 25 30

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

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

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

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

Ala Arg Ile Lys Leu Gly Thr Val Thr Thr Val Asp Tyr Trp Gly Gln
 100 105 110

Gly Thr Leu Val Thr Val Ser Ser
 115 120

<210> 46
 <211> 110
 <212> PRT
 <213> 人工序列

<220>
 <223> 人工序列的描述：合成多肽

<400> 46
 Gln Ser Ala Leu Thr Gln Pro Ala Ser Val Ser Gly Ser Pro Gly Gln
 1 5 10 15

Ser Ile Thr Ile Ser Cys Thr Gly Thr Ser Ser Asp Val Gly Gly Tyr
 20 25 30

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

[0016]

Met Ile Tyr Asp Val Ser Asn Arg Pro Ser Gly Val Ser Asn Arg Phe
 50 55 60

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

Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Ser Ser Tyr Thr Ser Ser
 85 90 95

Ser Thr Arg Val Phe Gly Thr Gly Thr Lys Val Thr Val Leu
 100 105 110

<210> 47
 <211> 121
 <212> PRT
 <213> 人工序列

<220>
 <223> 人工序列的描述：合成多肽

<400> 47
 Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
 1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Arg Tyr
 20 25 30

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

Ala Asn Ile Lys Gln Asp Gly Ser Glu Lys Tyr Tyr Val 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 Gly Trp Phe Gly Glu Leu Ala Phe Asp Tyr Trp Gly
 100 105 110

Gln Gly Thr Leu Val Thr Val Ser Ser
 115 120

[0017]

<210> 48
 <211> 108
 <212> PRT
 <213> 人工序列

<220>
 <223> 人工序列的描述：合成多肽

<400> 48
 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 Arg 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 Asp 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 Leu Pro
85 90 95

Trp Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
100 105

<210> 49
<211> 5
<212> PRT
<213> 人工序列

<220>
<223> 人工序列的描述：合成肽

<400> 49
Val Tyr Gly Met Asn
1 5

<210> 50
<211> 17
<212> PRT
<213> 人工序列

[0018] <220>
<223> 人工序列的描述：合成肽

<400> 50
Ile Ile Trp Tyr Asp Gly Asp Asn Gln Tyr Tyr Ala Asp Ser Val Lys
1 5 10 15

Gly

<210> 51
<211> 6
<212> PRT
<213> 人工序列

<220>
<223> 人工序列的描述：合成肽

<400> 51
Asp Leu Arg Thr Gly Pro
1 5

<210> 52
<211> 11
<212> PRT

<213> 人工序列

<220>

<223> 人工序列的描述：合成肽

<400> 52

Arg Ala Ser Gln Ser Ile Gly Ser Ser Leu His
1 5 10

<210> 53

<211> 6

<212> PRT

<213> 人工序列

<220>

<223> 人工序列的描述：合成肽

<400> 53

Ala Ser Gln Ser Phe Ser
1 5

<210> 54

<211> 7

<212> PRT

[0019] <213> 人工序列

<220>

<223> 人工序列的描述：合成肽

<400> 54

His Gln Ser Ser Ser Leu Pro
1 5

<210> 55

<211> 118

<212> PRT

<213> 人工序列

<220>

<223> 人工序列的描述：合成多肽

<400> 55

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

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Val Tyr
20 25 30

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

	35		40		45														
	Ala	Ile	Ile	Trp	Tyr	Asp	Gly	Asp	Asn	Gln	Tyr	Tyr	Ala	Asp	Ser	Val			
	50						55					60							
	Lys	Gly	Arg	Phe	Thr	Ile	Ser	Arg	Asp	Asn	Ser	Lys	Asn	Thr	Leu	Tyr			
	65					70					75					80			
	Leu	Gln	Met	Asn	Gly	Leu	Arg	Ala	Glu	Asp	Thr	Ala	Val	Tyr	Tyr	Cys			
					85					90					95				
	Ala	Arg	Asp	Leu	Arg	Thr	Gly	Pro	Phe	Asp	Tyr	Trp	Gly	Gln	Gly	Thr			
				100					105					110					
	Leu	Val	Thr	Val	Ser	Ser													
				115															
	<210>	56																	
	<211>	107																	
	<212>	PRT																	
	<213>	人工序列																	
[0020]	<220>																		
	<223>	人工序列的描述：合成多肽																	
	<400>	56																	
	Glu	Ile	Val	Leu	Thr	Gln	Ser	Pro	Asp	Phe	Gln	Ser	Val	Thr	Pro	Lys			
	1				5					10					15				
	Glu	Lys	Val	Thr	Ile	Thr	Cys	Arg	Ala	Ser	Gln	Ser	Ile	Gly	Ser	Ser			
				20					25					30					
	Leu	His	Trp	Tyr	Gln	Gln	Lys	Pro	Asp	Gln	Ser	Pro	Lys	Leu	Leu	Ile			
			35					40					45						
	Lys	Tyr	Ala	Ser	Gln	Ser	Phe	Ser	Gly	Val	Pro	Ser	Arg	Phe	Ser	Gly			
	50						55					60							
	Ser	Gly	Ser	Gly	Thr	Asp	Phe	Thr	Leu	Thr	Ile	Asn	Ser	Leu	Glu	Ala			
	65					70					75				80				
	Glu	Asp	Ala	Ala	Ala	Tyr	Tyr	Cys	His	Gln	Ser	Ser	Ser	Leu	Pro	Phe			
				85						90				95					
	Thr	Phe	Gly	Pro	Gly	Thr	Lys	Val	Asp	Ile	Lys								

100

105

<210> 57
 <211> 5
 <212> PRT
 <213> 人工序列

<220>
 <223> 人工序列的描述：合成肽

<400> 57
 Ile Ser Arg Thr Pro
 1 5

<210> 58
 <211> 5
 <212> PRT
 <213> 人工序列

<220>
 <223> 人工序列的描述：合成肽

[0021] <400> 58
 Ala Lys Gly Gln Pro
 1 5

<210> 59
 <211> 10
 <212> PRT
 <213> 人工序列

<220>
 <223> 人工序列的描述：合成肽

<400> 59
 Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
 1 5 10

<210> 60
 <211> 15
 <212> PRT
 <213> 人工序列

<220>
 <223> 人工序列的描述：合成肽

<400> 60
 Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
 1 5 10 15

<210> 61
 <211> 20
 <212> PRT
 <213> 人工序列

<220>
 <223> 人工序列的描述：合成肽

<400> 61
 Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
 1 5 10 15

Gly Gly Gly Ser
 20

<210> 62
 <211> 5
 <212> PRT
 <213> 人工序列

<220>
 <223> 人工序列的描述：合成肽

[0022]

<400> 62
 Ser Tyr Asp Met Ser
 1 5

<210> 63
 <211> 17
 <212> PRT
 <213> 人工序列

<220>
 <223> 人工序列的描述：合成肽

<400> 63
 Tyr Ile Ser Ser Gly Gly Gly Gly Thr Tyr Tyr Pro Asp Thr Val Lys
 1 5 10 15

Gly

<210> 64
 <211> 10
 <212> PRT
 <213> 人工序列

<220>

<223> 人工序列的描述：合成肽

<400> 64

Gly Gly Val Arg Arg Gly Tyr Phe Asp Val
1 5 10

<210> 65

<211> 11

<212> PRT

<213> 人工序列

<220>

<223> 人工序列的描述：合成肽

<400> 65

Arg Ala Ser Gly Asn Ile His Asn Tyr Leu Thr
1 5 10

<210> 66

<211> 7

<212> PRT

<213> 人工序列

[0023]

<220>

<223> 人工序列的描述：合成肽

<400> 66

Asn Ala Lys Thr Leu Ala Asp
1 5

<210> 67

<211> 9

<212> PRT

<213> 人工序列

<220>

<223> 人工序列的描述：合成肽

<400> 67

Gln His Phe Trp Ser Ile Pro Tyr Thr
1 5

<210> 68

<211> 119

<212> PRT

<213> 人工序列

<220>

<223> 人工序列的描述：合成多肽

<400> 68

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

Ser Leu Arg Leu Ser Cys Ser Ser Ser Gly Phe Ile Phe Ser Ser Tyr
20 25 30

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

Ala Tyr Ile Ser Ser Gly Gly Gly Gly Thr Tyr Tyr Pro Asp Thr Val
50 55 60

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

Leu Gln Met Asp Ser Leu Arg Pro Glu Asp Thr Gly Val Tyr Phe Cys
85 90 95

[0024] Ala Arg Gly Gly Val Arg Arg Gly Tyr Phe Asp Val Trp Gly Gln Gly
100 105 110

Thr Pro Val Thr Val Ser Ser
115

<210> 69

<211> 107

<212> PRT

<213> 人工序列

<220>

<223> 人工序列的描述：合成多肽

<400> 69

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

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gly Asn Ile His Asn Tyr
20 25 30

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

Tyr Asn Ala Lys Thr Leu Ala Asp Gly Val Pro Ser Arg Phe Ser Gly

	50		55		60														
	Ser	Gly	Ser	Gly	Thr	Asp	Tyr	Thr	Phe	Thr	Ile	Ser	Ser	Leu	Gln	Pro			
	65					70					75					80			
	Glu	Asp	Ile	Ala	Thr	Tyr	Tyr	Cys	Gln	His	Phe	Trp	Ser	Ile	Pro	Tyr			
					85					90					95				
	Thr	Phe	Gly	Gln	Gly	Thr	Lys	Leu	Gln	Ile	Thr								
				100					105										
	<210>	70																	
	<211>	312																	
	<212>	PRT																	
	<213>	人工序列																	
	<220>																		
	<223>	人工序列的描述：合成多肽																	
	<400>	70																	
	Lys	Cys	Lys	Glu	Arg	Glu	Glu	Lys	Ile	Ile	Leu	Val	Ser	Ser	Ala	Asn			
	1				5					10					15				
[0025]	Glu	Ile	Asp	Val	Arg	Pro	Cys	Pro	Leu	Asn	Pro	Asn	Glu	His	Lys	Gly			
				20					25					30					
	Thr	Ile	Thr	Trp	Tyr	Lys	Asp	Asp	Ser	Lys	Thr	Pro	Val	Ser	Thr	Glu			
				35				40					45						
	Gln	Ala	Ser	Arg	Ile	His	Gln	His	Lys	Glu	Lys	Leu	Trp	Phe	Val	Pro			
		50					55					60							
	Ala	Lys	Val	Glu	Asp	Ser	Gly	His	Tyr	Tyr	Cys	Val	Val	Arg	Asn	Ser			
	65					70					75				80				
	Ser	Tyr	Cys	Leu	Arg	Ile	Lys	Ile	Ser	Ala	Lys	Phe	Val	Glu	Asn	Glu			
					85					90					95				
	Pro	Asn	Leu	Cys	Tyr	Asn	Ala	Gln	Ala	Ile	Phe	Lys	Gln	Lys	Leu	Pro			
				100					105						110				
	Val	Ala	Gly	Asp	Gly	Gly	Leu	Val	Cys	Pro	Tyr	Met	Glu	Phe	Phe	Lys			
				115				120					125						
	Asn	Glu	Asn	Asn	Glu	Leu	Pro	Lys	Leu	Gln	Trp	Tyr	Lys	Asp	Cys	Lys			

	1	5	10	15
	Val	Phe Glu Asp 20	Glu Pro Ala Arg 25	Ile Lys Cys Pro Leu Phe Glu His 30
	Phe	Leu Lys Phe 35	Asn Tyr Ser Thr 40	Ala His Ser Ala Gly Leu Thr Leu 45
	Ile	Trp Tyr Trp 50	Thr Arg Gln Asp 55	Arg Asp Leu Glu Glu Pro Ile Asn 60
	Phe	Arg Leu Pro 65	Glu Asn Arg Ile 70	Ser Lys Glu Lys Asp Val Leu Trp 75 80
	Phe	Arg Pro Thr 85	Leu Leu Asn Asp 90	Thr Gly Asn Tyr Thr Cys Met Leu 95
	Arg	Asn Thr Thr 100	Tyr Cys Ser Lys 105	Val Ala Phe Pro Leu Glu Val Val 110
[0027]	Gln	Lys Asp Ser 115	Cys Phe Asn Ser 120	Pro Met Lys Leu Pro Val His Lys 125
	Leu	Tyr Ile Glu 130	Tyr Gly Ile Gln 135	Arg Ile Thr Cys Pro Asn Val Asp 140
	Gly	Tyr Phe Pro 145	Ser Ser Val Lys 150	Pro Thr Ile Thr Trp Tyr Met Gly 155 160
	Cys	Tyr Lys Ile 165	Gln Asn Phe Asn 170	Asn Val Ile Pro Glu Gly Met Asn 175
	Leu	Ser Phe Leu 180	Ile Ala Leu Ile 185	Ser Asn Asn Gly Asn Tyr Thr Cys 190
	Val	Val Thr Tyr 195	Pro Glu Asn Gly 200	Arg Thr Phe His Leu Thr Arg Thr 205
	Leu	Thr Val Lys 210	Val Val Gly Ser 215	Pro Lys Asn Ala Val Pro Pro Val 220
	Ile	His Ser Pro 225	Asn Asp His Val 230	Val Val Tyr Glu Lys Glu Pro Gly Glu 235 240

Glu Leu Leu Ile Pro Cys Thr Val Tyr Phe Ser Phe Leu Met Asp Ser
 245 250 255

Arg Asn Glu Val Trp Trp Thr Ile Asp Gly Lys Lys Pro Asp Asp Ile
 260 265 270

Thr Ile Asp Val Thr Ile Asn Glu Ser Ile Ser His Ser Arg Thr Glu
 275 280 285

Asp Glu Thr Arg Thr Gln Ile Leu Ser Ile Lys Lys Val Thr Ser Glu
 290 295 300

Asp Leu Lys Arg Ser Tyr Val Cys His Ala Arg Ser Ala Lys Gly Glu
 305 310 315 320

Val Ala Lys Ala Ala Lys Val Lys Gln Lys Val Pro Ala Pro Arg Tyr
 325 330 335

Thr Val Glu Lys Cys Lys Glu Arg Glu Glu Lys Ile Ile Leu Val Ser
 340 345 350

[0028]

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

His Lys Gly Thr Ile Thr Trp Tyr Lys Asp Asp Ser Lys Thr Pro Val
 370 375 380

Ser Thr Glu Gln Ala Ser Arg Ile His Gln His Lys Glu Lys Leu Trp
 385 390 395 400

Phe Val Pro Ala Lys Val Glu Asp Ser Gly His Tyr Tyr Cys Val Val
 405 410 415

Arg Asn Ser Ser Tyr Cys Leu Arg Ile Lys Ile Ser Ala Lys Phe Val
 420 425 430

Glu Asn Glu Pro Asn Leu Cys Tyr Asn Ala Gln Ala Ile Phe Lys Gln
 435 440 445

Lys Leu Pro Val Ala Gly Asp Gly Gly Leu Val Cys Pro Tyr Met Glu
 450 455 460

Phe Phe Lys Asn Glu Asn Asn Glu Leu Pro Lys Leu Gln Trp Tyr Lys
465 470 475 480

Asp Cys Lys Pro Leu Leu Leu Asp Asn Ile His Phe Ser Gly Val Lys
485 490 495

Asp Arg Leu Ile Val Met Asn Val Ala Glu Lys His Arg Gly Asn Tyr
500 505 510

Thr Cys His Ala Ser Tyr Thr Tyr Leu Gly Lys Gln Tyr Pro Ile Thr
515 520 525

Arg Val Ile Glu Phe Ile Thr Leu Glu Glu Asn Lys Pro Thr Arg Pro
530 535 540

Val Ile Val Ser Pro Ala Asn Glu Thr Met Glu Val Asp Leu Gly Ser
545 550 555 560

Gln Ile Gln Leu Ile Cys Asn Val Thr Gly Gln Leu Ser Asp Ile Ala
565 570 575

[0029]

Tyr Trp Lys Trp Asn Gly Ser Val Ile Asp Glu Asp Asp Pro Val Leu
580 585 590

Gly Glu Asp Tyr Tyr Ser Val Glu Asn Pro Ala Asn Lys Arg Arg Ser
595 600 605

Thr Leu Ile Thr Val Leu Asn Ile Ser Glu Ile Glu Ser Arg Phe Tyr
610 615 620

Lys His Pro Phe Thr Cys Phe Ala Lys Asn Thr His Gly Ile Asp Ala
625 630 635 640

Ala Tyr Ile Gln Leu Ile Tyr Pro Val Thr Asn
645 650

<210> 72

<211> 153

<212> PRT

<213> 人工序列

<220>

<223> 人工序列的描述：合成多肽

<400> 72
 Met Arg Pro Ser Gly Arg Lys Ser Ser Lys Met Gln Ala Phe Arg Ile
 1 5 10 15

Trp Asp Val Asn Gln Lys Thr Phe Tyr Leu Arg Asn Asn Gln Leu Val
 20 25 30

Ala Gly Tyr Leu Gln Gly Pro Asn Val Asn Leu Glu Glu Lys Ile Asp
 35 40 45

Val Val Pro Ile Glu Pro His Ala Leu Phe Leu Gly Ile His Gly Gly
 50 55 60

Lys Met Cys Leu Ser Cys Val Lys Ser Gly Asp Glu Thr Arg Leu Gln
 65 70 75 80

Leu Glu Ala Val Asn Ile Thr Asp Leu Ser Glu Asn Arg Lys Gln Asp
 85 90 95

Lys Arg Phe Ala Phe Ile Arg Ser Asp Ser Gly Pro Thr Thr Ser Phe
 100 105 110

[0030]

Glu Ser Ala Ala Cys Pro Gly Trp Phe Leu Cys Thr Ala Met Glu Ala
 115 120 125

Asp Gln Pro Val Ser Leu Thr Asn Met Pro Asp Glu Gly Val Met Val
 130 135 140

Thr Lys Phe Tyr Phe Gln Glu Asp Glu
 145 150

<210> 73

<211> 725

<212> PRT

<213> 人工序列

<220>

<223> 人工序列的描述：合成多肽

<400> 73

Met Gly Trp Ser Cys Ile Ile Leu Phe Leu Val Ala Thr Ala Thr Gly
 1 5 10 15

Val His Ser Gln Val Gln Leu Val Gln Ser Gly Val Glu Val Lys Lys
 20 25 30

Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe
 35 40 45

Thr Asn Tyr Tyr Met Tyr Trp Val Arg Gln Ala Pro Gly Gln Gly Leu
 50 55 60

Glu Trp Met Gly Gly Ile Asn Pro Ser Asn Gly Gly Thr Asn Phe Asn
 65 70 75 80

Glu Lys Phe Lys Asn Arg Val Thr Leu Thr Thr Asp Ser Ser Thr Thr
 85 90 95

Thr Ala Tyr Met Glu Leu Lys Ser Leu Gln Phe Asp Asp Thr Ala Val
 100 105 110

Tyr Tyr Cys Ala Arg Arg Asp Tyr Arg Phe Asp Met Gly Phe Asp Tyr
 115 120 125

Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser
 130 135 140

[0031]

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu
 145 150 155 160

Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu
 165 170 175

Arg Ala Thr Leu Ser Cys Arg Ala Ser Lys Gly Val Ser Thr Ser Gly
 180 185 190

Tyr Ser Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg
 195 200 205

Leu Leu Ile Tyr Leu Ala Ser Tyr Leu Glu Ser Gly Val Pro Ala Arg
 210 215 220

Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser
 225 230 235 240

Leu Glu Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln His Ser Arg Asp
 245 250 255

Leu Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Gly Gly
 260 265 270

Gly Gly Ser Gly Gly Gly Gly Ser Gln Val Gln Leu Val Glu Ser Gly
 275 280 285

Gly Gly Val Val Gln Pro Gly Arg Ser Leu Arg Leu Ser Cys Ala Ala
 290 295 300

Ser Gly Phe Thr Phe Ser Val Tyr Gly Met Asn Trp Val Arg Gln Ala
 305 310 315 320

Pro Gly Lys Gly Leu Glu Trp Val Ala Ile Ile Trp Tyr Asp Gly Asp
 325 330 335

Asn Gln Tyr Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg
 340 345 350

Asp Asn Ser Lys Asn Thr Leu Tyr Leu Gln Met Asn Gly Leu Arg Ala
 355 360 365

[0032] Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Asp Leu Arg Thr Gly Pro
 370 375 380

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

Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr
 405 410 415

Ser Glu Ser Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro
 420 425 430

Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val
 435 440 445

His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser
 450 455 460

Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Lys Thr Tyr Thr
 465 470 475 480

Cys Asn Val Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val

	485	490	495
	Glu Ser Lys Tyr Gly Pro Pro Cys Pro Pro Cys Pro Ala Pro Glu Phe 500 505 510		
	Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr 515 520 525		
	Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val 530 535 540		
	Ser Gln Glu Asp Pro Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val 545 550 555 560		
	Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser 565 570 575		
	Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu 580 585 590		
[0033]	Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ser 595 600 605		
	Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro 610 615 620		
	Gln Val Tyr Thr Leu Pro Pro Ser Gln Glu Glu Met Thr Lys Asn Gln 625 630 635 640		
	Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala 645 650 655		
	Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr 660 665 670		
	Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Arg Leu 675 680 685		
	Thr Val Asp Lys Ser Arg Trp Gln Glu Gly Asn Val Phe Ser Cys Ser 690 695 700		
	Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser 705 710 715 720		

Leu Ser Leu Gly Lys
725

<210> 74

<211> 233

<212> PRT

<213> 人工序列

<220>

<223> 人工序列的描述: 合成多肽

<400> 74

Met Gly Trp Ser Cys Ile Ile Leu Phe Leu Val Ala Thr Ala Thr Gly
1 5 10 15

Val His Ser Glu Ile Val Leu Thr Gln Ser Pro Asp Phe Gln Ser Val
20 25 30

Thr Pro Lys Glu Lys Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile
35 40 45

Gly Ser Ser Leu His Trp Tyr Gln Gln Lys Pro Asp Gln Ser Pro Lys
50 55 60

[0034]

Leu Leu Ile Lys Tyr Ala Ser Gln Ser Phe Ser Gly Val Pro Ser Arg
65 70 75 80

Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Asn Ser
85 90 95

Leu Glu Ala Glu Asp Ala Ala Ala Tyr Tyr Cys His Gln Ser Ser Ser
100 105 110

Leu Pro Phe Thr Phe Gly Pro Gly Thr Lys Val Asp Ile Lys Arg Thr
115 120 125

Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu
130 135 140

Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro
145 150 155 160

Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly
165 170 175

Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr
180 185 190

Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His
195 200 205

Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val
210 215 220

Thr Lys Ser Phe Asn Arg Gly Glu Cys
225 230

<210> 75

<211> 714

<212> PRT

<213> 人工序列

<220>

<223> 人工序列的描述：合成多肽

<400> 75

Met Gly Trp Ser Cys Ile Ile Leu Phe Leu Val Ala Thr Ala Thr Gly
1 5 10 15

[0035]

Val His Ser Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln
20 25 30

Pro Gly Arg Ser Leu Arg Leu Asp Cys Lys Ala Ser Gly Ile Thr Phe
35 40 45

Ser Asn Ser Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu
50 55 60

Glu Trp Val Ala Val Ile Trp Tyr Asp Gly Ser Lys Arg Tyr Tyr Ala
65 70 75 80

Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn
85 90 95

Thr Leu Phe Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val
100 105 110

Tyr Tyr Cys Ala Thr Asn Asp Asp Tyr Trp Gly Gln Gly Thr Leu Val
115 120 125

Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
130 135 140

Gly Gly Ser Gly Gly Gly Gly Ser Glu Ile Val Leu Thr Gln Ser Pro
145 150 155 160

Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg
165 170 175

Ala Ser Gln Ser Val Ser Ser Tyr Leu Ala Trp Tyr Gln Gln Lys Pro
180 185 190

Gly Gln Ala Pro Arg Leu Leu Ile Tyr Asp Ala Ser Asn Arg Ala Thr
195 200 205

Gly Ile Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr
210 215 220

Leu Thr Ile Ser Ser Leu Glu Pro Glu Asp Phe Ala Val Tyr Tyr Cys
225 230 235 240

[0036]

Gln Gln Ser Ser Asn Trp Pro Arg Thr Phe Gly Gln Gly Thr Lys Val
245 250 255

Glu Ile Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Val Gln
260 265 270

Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg Ser Leu Arg
275 280 285

Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Val Tyr Gly Met Asn
290 295 300

Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala Ile Ile
305 310 315 320

Trp Tyr Asp Gly Asp Asn Gln Tyr Tyr Ala Asp Ser Val Lys Gly Arg
325 330 335

Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr Leu Gln Met
340 345 350

Asn Gly Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Asp
355 360 365

Leu Arg Thr Gly Pro Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr
370 375 380

Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro
385 390 395 400

Cys Ser Arg Ser Thr Ser Glu Ser Thr Ala Ala Leu Gly Cys Leu Val
405 410 415

Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala
420 425 430

Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly
435 440 445

Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly
450 455 460

[0037]

Thr Lys Thr Tyr Thr Cys Asn Val Asp His Lys Pro Ser Asn Thr Lys
465 470 475 480

Val Asp Lys Arg Val Glu Ser Lys Tyr Gly Pro Pro Cys Pro Pro Cys
485 490 495

Pro Ala Pro Glu Phe Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro
500 505 510

Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys
515 520 525

Val Val Val Asp Val Ser Gln Glu Asp Pro Glu Val Gln Phe Asn Trp
530 535 540

Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu
545 550 555 560

Glu Gln Phe Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu
565 570 575

His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn
580 585 590

Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly
595 600 605

Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Gln Glu Glu
610 615 620

Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr
625 630 635 640

Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn
645 650 655

Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe
660 665 670

Leu Tyr Ser Arg Leu Thr Val Asp Lys Ser Arg Trp Gln Glu Gly Asn
675 680 685

[0038]

Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr
690 695 700

Gln Lys Ser Leu Ser Leu Ser Leu Gly Lys
705 710

<210> 76

<211> 721

<212> PRT

<213> 人工序列

<220>

<223> 人工序列的描述: 合成多肽

<400> 76

Met Gly Trp Ser Cys Ile Ile Leu Phe Leu Val Ala Thr Ala Thr Gly
1 5 10 15

Val His Ser Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln
20 25 30

Pro Gly Arg Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe
35 40 45

Ser Val Tyr Gly Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu
 50 55 60

Glu Trp Val Ala Ile Ile Trp Tyr Asp Gly Asp Asn Gln Tyr Tyr Ala
 65 70 75 80

Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn
 85 90 95

Thr Leu Tyr Leu Gln Met Asn Gly Leu Arg Ala Glu Asp Thr Ala Val
 100 105 110

Tyr Tyr Cys Ala Arg Asp Leu Arg Thr Gly Pro Phe Asp Tyr Trp Gly
 115 120 125

Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly
 130 135 140

Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Ile Val
 145 150 155 160

[0039] Leu Thr Gln Ser Pro Asp Phe Gln Ser Val Thr Pro Lys Glu Lys Val
 165 170 175

Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Gly Ser Ser Leu His Trp
 180 185 190

Tyr Gln Gln Lys Pro Asp Gln Ser Pro Lys Leu Leu Ile Lys Tyr Ala
 195 200 205

Ser Gln Ser Phe Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser
 210 215 220

Gly Thr Asp Phe Thr Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala
 225 230 235 240

Ala Ala Tyr Tyr Cys His Gln Ser Ser Ser Leu Pro Phe Thr Phe Gly
 245 250 255

Pro Gly Thr Lys Val Asp Ile Lys Gly Gly Gly Gly Ser Gly Gly Gly
 260 265 270

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

	275		280		285											
	Gly 290	Ala	Ser	Val	Lys	Val	Ser	Cys	Lys	Ala	Ser	Gly 300	Tyr	Thr	Phe	Thr
	Asn 305	Tyr	Tyr	Met	Tyr	Trp	Val	Arg	Gln	Ala	Pro 315	Gly	Gln	Gly	Leu	Glu 320
	Trp	Met	Gly	Gly	Ile 325	Asn	Pro	Ser	Asn	Gly 330	Gly	Thr	Asn	Phe	Asn	Glu 335
	Lys	Phe	Lys	Asn 340	Arg	Val	Thr	Leu	Thr	Thr	Asp	Ser	Ser	Thr	Thr	Thr
	Ala	Tyr	Met 355	Glu	Leu	Lys	Ser	Leu	Gln	Phe	Asp	Asp	Thr 365	Ala	Val	Tyr
	Tyr 370	Cys	Ala	Arg	Arg	Asp	Tyr 375	Arg	Phe	Asp	Met	Gly 380	Phe	Asp	Tyr	Trp
[0040]	Gly 385	Gln	Gly	Thr	Thr	Val 390	Thr	Val	Ser	Ser	Ala 395	Ser	Thr	Lys	Gly	Pro 400
	Ser	Val	Phe	Pro	Leu 405	Ala	Pro	Cys	Ser	Arg 410	Ser	Thr	Ser	Glu	Ser	Thr 415
	Ala	Ala	Leu	Gly 420	Cys	Leu	Val	Lys	Asp 425	Tyr	Phe	Pro	Glu	Pro 430	Val	Thr
	Val	Ser	Trp 435	Asn	Ser	Gly	Ala	Leu 440	Thr	Ser	Gly	Val	His 445	Thr	Phe	Pro
	Ala 450	Val	Leu	Gln	Ser	Ser	Gly 455	Leu	Tyr	Ser	Leu	Ser	Ser	Val	Val	Thr
	Val 465	Pro	Ser	Ser	Ser	Leu 470	Gly	Thr	Lys	Thr	Tyr 475	Thr	Cys	Asn	Val	Asp 480
	His	Lys	Pro	Ser	Asn 485	Thr	Lys	Val	Asp	Lys 490	Arg	Val	Glu	Ser	Lys	Tyr 495
	Gly	Pro	Pro	Cys 500	Pro	Pro	Cys	Pro	Ala 505	Pro	Glu	Phe	Leu	Gly 510	Gly	Pro

Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser
515 520 525

Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser Gln Glu Asp
530 535 540

Pro Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn
545 550 555 560

Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr Tyr Arg Val
565 570 575

Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu
580 585 590

Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys
595 600 605

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

[0041]

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

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

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

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

Ser Arg Trp Gln Glu Gly Asn Val Phe Ser Cys Ser Val Met His Glu
690 695 700

Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Leu Gly
705 710 715 720

Lys

<210> 77
 <211> 237
 <212> PRT
 <213> 人工序列

<220>
 <223> 人工序列的描述: 合成多肽

<400> 77
 Met Gly Trp Ser Cys Ile Ile Leu Phe Leu Val Ala Thr Ala Thr Gly
 1 5 10 15

Val His Ser Glu Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu
 20 25 30

Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Lys Gly Val
 35 40 45

Ser Thr Ser Gly Tyr Ser Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly
 50 55 60

Gln Ala Pro Arg Leu Leu Ile Tyr Leu Ala Ser Tyr Leu Glu Ser Gly
 65 70 75 80

[0042]

Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu
 85 90 95

Thr Ile Ser Ser Leu Glu Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln
 100 105 110

His Ser Arg Asp Leu Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu
 115 120 125

Ile Lys Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser
 130 135 140

Asp Glu Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn
 145 150 155 160

Asn Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala
 165 170 175

Leu Gln Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys
 180 185 190

Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp
 195 200 205

Tyr Glu Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu
 210 215 220

Ser Ser Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
 225 230 235

<210> 78

<211> 714

<212> PRT

<213> 人工序列

<220>

<223> 人工序列的描述：合成多肽

<400> 78

Met Gly Trp Ser Cys Ile Ile Leu Phe Leu Val Ala Thr Ala Thr Gly
 1 5 10 15

Val His Ser Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln
 20 25 30

[0043]

Pro Gly Arg Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe
 35 40 45

Ser Val Tyr Gly Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu
 50 55 60

Glu Trp Val Ala Ile Ile Trp Tyr Asp Gly Asp Asn Gln Tyr Tyr Ala
 65 70 75 80

Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn
 85 90 95

Thr Leu Tyr Leu Gln Met Asn Gly Leu Arg Ala Glu Asp Thr Ala Val
 100 105 110

Tyr Tyr Cys Ala Arg Asp Leu Arg Thr Gly Pro Phe Asp Tyr Trp Gly
 115 120 125

Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly
 130 135 140

Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Ile Val
145 150 155 160

Leu Thr Gln Ser Pro Asp Phe Gln Ser Val Thr Pro Lys Glu Lys Val
165 170 175

Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Gly Ser Ser Leu His Trp
180 185 190

Tyr Gln Gln Lys Pro Asp Gln Ser Pro Lys Leu Leu Ile Lys Tyr Ala
195 200 205

Ser Gln Ser Phe Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser
210 215 220

Gly Thr Asp Phe Thr Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala
225 230 235 240

Ala Ala Tyr Tyr Cys His Gln Ser Ser Ser Leu Pro Phe Thr Phe Gly
245 250 255

[0044]

Pro Gly Thr Lys Val Asp Ile Lys Gly Gly Gly Gly Ser Gly Gly Gly
260 265 270

Gly Ser Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro
275 280 285

Gly Arg Ser Leu Arg Leu Asp Cys Lys Ala Ser Gly Ile Thr Phe Ser
290 295 300

Asn Ser Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu
305 310 315 320

Trp Val Ala Val Ile Trp Tyr Asp Gly Ser Lys Arg Tyr Tyr Ala Asp
325 330 335

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr
340 345 350

Leu Phe Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr
355 360 365

Tyr Cys Ala Thr Asn Asp Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr
 370 375 380

Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro
 385 390 395 400

Cys Ser Arg Ser Thr Ser Glu Ser Thr Ala Ala Leu Gly Cys Leu Val
 405 410 415

Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala
 420 425 430

Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly
 435 440 445

Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly
 450 455 460

Thr Lys Thr Tyr Thr Cys Asn Val Asp His Lys Pro Ser Asn Thr Lys
 465 470 475 480

[0045] Val Asp Lys Arg Val Glu Ser Lys Tyr Gly Pro Pro Cys Pro Pro Cys
 485 490 495

Pro Ala Pro Glu Phe Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro
 500 505 510

Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys
 515 520 525

Val Val Val Asp Val Ser Gln Glu Asp Pro Glu Val Gln Phe Asn Trp
 530 535 540

Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu
 545 550 555 560

Glu Gln Phe Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu
 565 570 575

His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn
 580 585 590

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

	595		600		605														
	Gln	Pro	Arg	Glu	Pro	Gln	Val	Tyr	Thr	Leu	Pro	Pro	Ser	Gln	Glu	Glu			
	610						615					620							
	Met	Thr	Lys	Asn	Gln	Val	Ser	Leu	Thr	Cys	Leu	Val	Lys	Gly	Phe	Tyr			
	625					630					635					640			
	Pro	Ser	Asp	Ile	Ala	Val	Glu	Trp	Glu	Ser	Asn	Gly	Gln	Pro	Glu	Asn			
					645					650					655				
	Asn	Tyr	Lys	Thr	Thr	Pro	Pro	Val	Leu	Asp	Ser	Asp	Gly	Ser	Phe	Phe			
				660					665					670					
	Leu	Tyr	Ser	Arg	Leu	Thr	Val	Asp	Lys	Ser	Arg	Trp	Gln	Glu	Gly	Asn			
			675					680					685						
	Val	Phe	Ser	Cys	Ser	Val	Met	His	Glu	Ala	Leu	His	Asn	His	Tyr	Thr			
	690						695					700							
[0046]	Gln	Lys	Ser	Leu	Ser	Leu	Ser	Leu	Gly	Lys									
	705					710													
	<210>	79																	
	<211>	233																	
	<212>	PRT																	
	<213>	人工序列																	
	<220>																		
	<223>	人工序列的描述：	合成多肽																
	<400>	79																	
	Met	Gly	Trp	Ser	Cys	Ile	Ile	Leu	Phe	Leu	Val	Ala	Thr	Ala	Thr	Gly			
	1				5					10					15				
	Val	His	Ser	Glu	Ile	Val	Leu	Thr	Gln	Ser	Pro	Ala	Thr	Leu	Ser	Leu			
				20					25					30					
	Ser	Pro	Gly	Glu	Arg	Ala	Thr	Leu	Ser	Cys	Arg	Ala	Ser	Gln	Ser	Val			
			35					40					45						
	Ser	Ser	Tyr	Leu	Ala	Trp	Tyr	Gln	Gln	Lys	Pro	Gly	Gln	Ala	Pro	Arg			
	50						55					60							
	Leu	Leu	Ile	Tyr	Asp	Ala	Ser	Asn	Arg	Ala	Thr	Gly	Ile	Pro	Ala	Arg			

65	70	75	80
Phe Ser Gly Ser	Gly Ser Gly Thr Asp	Phe Thr Leu Thr Ile	Ser Ser
	85	90	95
Leu Glu Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Ser Ser Asn			
	100	105	110
Trp Pro Arg Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg Thr			
	115	120	125
Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu			
	130	135	140
Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro			
	145	150	155
Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly			
	165	170	175
Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr			
	180	185	190
Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His			
	195	200	205
Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val			
	210	215	220
Thr Lys Ser Phe Asn Arg Gly Glu Cys			
	225	230	
<210> 80			
<211> 725			
<212> PRT			
<213> 人工序列			
<220>			
<223> 人工序列的描述：合成多肽			
<400> 80			
Met Gly Trp Ser Cys Ile Ile Leu Phe Leu Val Ala Thr Ala Thr Gly			
1	5	10	15
Val His Ser Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln			

	20	25	30
	Pro Gly Arg Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe 35	40	45
	Ser Val Tyr Gly Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu 50	55	60
	Glu Trp Val Ala Ile Ile Trp Tyr Asp Gly Asp Asn Gln Tyr Tyr Ala 65	70	75
	Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn 85	90	95
	Thr Leu Tyr Leu Gln Met Asn Gly Leu Arg Ala Glu Asp Thr Ala Val 100	105	110
	Tyr Tyr Cys Ala Arg Asp Leu Arg Thr Gly Pro Phe Asp Tyr Trp Gly 115	120	125
[0048]	Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser 130	135	140
	Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser Thr Ala 145	150	155
	Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val 165	170	175
	Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala 180	185	190
	Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val 195	200	205
	Pro Ser Ser Ser Leu Gly Thr Lys Thr Tyr Thr Cys Asn Val Asp His 210	215	220
	Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Ser Lys Tyr Gly 225	230	235
	Pro Pro Cys Pro Pro Cys Pro Ala Pro Glu Phe Leu Gly Gly Pro Ser 245	250	255

Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg
260 265 270

Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser Gln Glu Asp Pro
275 280 285

Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala
290 295 300

Lys Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr Tyr Arg Val Val
305 310 315 320

Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr
325 330 335

Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr
340 345 350

Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu
355 360 365

[0049]

Pro Pro Ser Gln Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys
370 375 380

Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser
385 390 395 400

Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp
405 410 415

Ser Asp Gly Ser Phe Phe Leu Tyr Ser Arg Leu Thr Val Asp Lys Ser
420 425 430

Arg Trp Gln Glu Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala
435 440 445

Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Leu Gly Lys
450 455 460

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Val Gln Leu Val Gln
465 470 475 480

Ser Gly Val Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys
485 490 495

Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr Tyr Met Tyr Trp Val Arg
500 505 510

Gln Ala Pro Gly Gln Gly Leu Glu Trp Met Gly Gly Ile Asn Pro Ser
515 520 525

Asn Gly Gly Thr Asn Phe Asn Glu Lys Phe Lys Asn Arg Val Thr Leu
530 535 540

Thr Thr Asp Ser Ser Thr Thr Thr Ala Tyr Met Glu Leu Lys Ser Leu
545 550 555 560

Gln Phe Asp Asp Thr Ala Val Tyr Tyr Cys Ala Arg Arg Asp Tyr Arg
565 570 575

Phe Asp Met Gly Phe Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val
580 585 590

[0050]

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

Ser Gly Gly Gly Gly Ser Glu Ile Val Leu Thr Gln Ser Pro Ala Thr
610 615 620

Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser
625 630 635 640

Lys Gly Val Ser Thr Ser Gly Tyr Ser Tyr Leu His Trp Tyr Gln Gln
645 650 655

Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr Leu Ala Ser Tyr Leu
660 665 670

Glu Ser Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp
675 680 685

Phe Thr Leu Thr Ile Ser Ser Leu Glu Pro Glu Asp Phe Ala Val Tyr
690 695 700

Tyr Cys Gln His Ser Arg Asp Leu Pro Leu Thr Phe Gly Gly Gly Thr
705 710 715 720

Lys Val Glu Ile Lys
725

<210> 81

<211> 714

<212> PRT

<213> 人工序列

<220>

<223> 人工序列的描述：合成多肽

<400> 81

Met Gly Trp Ser Cys Ile Ile Leu Phe Leu Val Ala Thr Ala Thr Gly
1 5 10 15

Val His Ser Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln
20 25 30

Pro Gly Arg Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe
35 40 45

[0051]

Ser Val Tyr Gly Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu
50 55 60

Glu Trp Val Ala Ile Ile Trp Tyr Asp Gly Asp Asn Gln Tyr Tyr Ala
65 70 75 80

Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn
85 90 95

Thr Leu Tyr Leu Gln Met Asn Gly Leu Arg Ala Glu Asp Thr Ala Val
100 105 110

Tyr Tyr Cys Ala Arg Asp Leu Arg Thr Gly Pro Phe Asp Tyr Trp Gly
115 120 125

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

Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser Thr Ala
145 150 155 160

Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val
165 170 175

Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala
180 185 190

Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val
195 200 205

Pro Ser Ser Ser Leu Gly Thr Lys Thr Tyr Thr Cys Asn Val Asp His
210 215 220

Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Ser Lys Tyr Gly
225 230 235 240

Pro Pro Cys Pro Pro Cys Pro Ala Pro Glu Phe Leu Gly Gly Pro Ser
245 250 255

Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg
260 265 270

[0052] Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser Gln Glu Asp Pro
275 280 285

Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala
290 295 300

Lys Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr Tyr Arg Val Val
305 310 315 320

Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr
325 330 335

Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr
340 345 350

Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu
355 360 365

Pro Pro Ser Gln Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys
370 375 380

Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser

	385		390			395			400							
	Asn	Gly	Gln	Pro	Glu	Asn	Asn	Tyr	Lys	Thr	Thr	Pro	Pro	Val	Leu	Asp
					405					410					415	
	Ser	Asp	Gly	Ser	Phe	Phe	Leu	Tyr	Ser	Arg	Leu	Thr	Val	Asp	Lys	Ser
				420					425					430		
	Arg	Trp	Gln	Glu	Gly	Asn	Val	Phe	Ser	Cys	Ser	Val	Met	His	Glu	Ala
			435					440					445			
	Leu	His	Asn	His	Tyr	Thr	Gln	Lys	Ser	Leu	Ser	Leu	Ser	Leu	Gly	Lys
		450					455					460				
	Gly	Gly	Gly	Gly	Ser	Gly	Gly	Gly	Gly	Ser	Gln	Val	Gln	Leu	Val	Glu
	465					470					475					480
	Ser	Gly	Gly	Gly	Val	Val	Gln	Pro	Gly	Arg	Ser	Leu	Arg	Leu	Asp	Cys
					485					490					495	
[0053]	Lys	Ala	Ser	Gly	Ile	Thr	Phe	Ser	Asn	Ser	Gly	Met	His	Trp	Val	Arg
				500					505					510		
	Gln	Ala	Pro	Gly	Lys	Gly	Leu	Glu	Trp	Val	Ala	Val	Ile	Trp	Tyr	Asp
			515					520					525			
	Gly	Ser	Lys	Arg	Tyr	Tyr	Ala	Asp	Ser	Val	Lys	Gly	Arg	Phe	Thr	Ile
		530					535					540				
	Ser	Arg	Asp	Asn	Ser	Lys	Asn	Thr	Leu	Phe	Leu	Gln	Met	Asn	Ser	Leu
	545					550					555					560
	Arg	Ala	Glu	Asp	Thr	Ala	Val	Tyr	Tyr	Cys	Ala	Thr	Asn	Asp	Asp	Tyr
					565					570					575	
	Trp	Gly	Gln	Gly	Thr	Leu	Val	Thr	Val	Ser	Ser	Gly	Gly	Gly	Gly	Ser
				580					585						590	
	Gly	Gly	Gly	Gly	Ser	Gly	Gly	Gly	Gly	Ser	Gly	Gly	Gly	Gly	Ser	Glu
			595					600					605			
	Ile	Val	Leu	Thr	Gln	Ser	Pro	Ala	Thr	Leu	Ser	Leu	Ser	Pro	Gly	Glu
		610					615					620				

Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Tyr Leu
625 630 635 640

Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr
645 650 655

Asp Ala Ser Asn Arg Ala Thr Gly Ile Pro Ala Arg Phe Ser Gly Ser
660 665 670

Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Glu Pro Glu
675 680 685

Asp Phe Ala Val Tyr Tyr Cys Gln Gln Ser Ser Asn Trp Pro Arg Thr
690 695 700

Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
705 710

<210> 82

<211> 721

<212> PRT

[0054] <213> 人工序列

<220>

<223> 人工序列的描述：合成多肽

<400> 82

Met Gly Trp Ser Cys Ile Ile Leu Phe Leu Val Ala Thr Ala Thr Gly
1 5 10 15

Val His Ser Gln Val Gln Leu Val Gln Ser Gly Val Glu Val Lys Lys
20 25 30

Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe
35 40 45

Thr Asn Tyr Tyr Met Tyr Trp Val Arg Gln Ala Pro Gly Gln Gly Leu
50 55 60

Glu Trp Met Gly Gly Ile Asn Pro Ser Asn Gly Gly Thr Asn Phe Asn
65 70 75 80

Glu Lys Phe Lys Asn Arg Val Thr Leu Thr Thr Asp Ser Ser Thr Thr
85 90 95

Thr Ala Tyr Met Glu Leu Lys Ser Leu Gln Phe Asp Asp Thr Ala Val
100 105 110

Tyr Tyr Cys Ala Arg Arg Asp Tyr Arg Phe Asp Met Gly Phe Asp Tyr
115 120 125

Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly
130 135 140

Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser
145 150 155 160

Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val
165 170 175

Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe
180 185 190

Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val
195 200 205

[0055]

Thr Val Pro Ser Ser Ser Leu Gly Thr Lys Thr Tyr Thr Cys Asn Val
210 215 220

Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Ser Lys
225 230 235 240

Tyr Gly Pro Pro Cys Pro Pro Cys Pro Ala Pro Glu Phe Leu Gly Gly
245 250 255

Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile
260 265 270

Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser Gln Glu
275 280 285

Asp Pro Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val His
290 295 300

Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr Tyr Arg
305 310 315 320

Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys
325 330 335

Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu
340 345 350

Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr
355 360 365

Thr Leu Pro Pro Ser Gln Glu Glu Met Thr Lys Asn Gln Val Ser Leu
370 375 380

Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp
385 390 395 400

Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val
405 410 415

Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Arg Leu Thr Val Asp
420 425 430

[0056]

Lys Ser Arg Trp Gln Glu Gly Asn Val Phe Ser Cys Ser Val Met His
435 440 445

Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Leu
450 455 460

Gly Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Val Gln Leu
465 470 475 480

Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg Ser Leu Arg Leu
485 490 495

Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Val Tyr Gly Met Asn Trp
500 505 510

Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala Ile Ile Trp
515 520 525

Tyr Asp Gly Asp Asn Gln Tyr Tyr Ala Asp Ser Val Lys Gly Arg Phe
530 535 540

Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr Leu Gln Met Asn
545 550 555 560

Gly Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Asp Leu
565 570 575

Arg Thr Gly Pro Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val
580 585 590

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

Ser Gly Gly Gly Gly Ser Glu Ile Val Leu Thr Gln Ser Pro Asp Phe
610 615 620

Gln Ser Val Thr Pro Lys Glu Lys Val Thr Ile Thr Cys Arg Ala Ser
625 630 635 640

Gln Ser Ile Gly Ser Ser Leu His Trp Tyr Gln Gln Lys Pro Asp Gln
645 650 655

[0057] Ser Pro Lys Leu Leu Ile Lys Tyr Ala Ser Gln Ser Phe Ser Gly Val
660 665 670

Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
675 680 685

Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Ala Tyr Tyr Cys His Gln
690 695 700

Ser Ser Ser Leu Pro Phe Thr Phe Gly Pro Gly Thr Lys Val Asp Ile
705 710 715 720

Lys

<210> 83

<211> 714

<212> PRT

<213> 人工序列

<220>

<223> 人工序列的描述：合成多肽

<400> 83

Met Gly Trp Ser Cys Ile Ile Leu Phe Leu Val Ala Thr Ala Thr Gly
 1 5 10 15

Val His Ser Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln
 20 25 30

Pro Gly Arg Ser Leu Arg Leu Asp Cys Lys Ala Ser Gly Ile Thr Phe
 35 40 45

Ser Asn Ser Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu
 50 55 60

Glu Trp Val Ala Val Ile Trp Tyr Asp Gly Ser Lys Arg Tyr Tyr Ala
 65 70 75 80

Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn
 85 90 95

Thr Leu Phe Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val
 100 105 110

[0058] Tyr Tyr Cys Ala Thr Asn Asp Asp Tyr Trp Gly Gln Gly Thr Leu Val
 115 120 125

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

Pro Cys Ser Arg Ser Thr Ser Glu Ser Thr Ala Ala Leu Gly Cys Leu
 145 150 155 160

Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly
 165 170 175

Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser
 180 185 190

Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu
 195 200 205

Gly Thr Lys Thr Tyr Thr Cys Asn Val Asp His Lys Pro Ser Asn Thr
 210 215 220

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

Gly Gly Gly Gly Ser Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val
 465 470 475 480
 Val Gln Pro Gly Arg Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe
 485 490 495
 Thr Phe Ser Val Tyr Gly Met Asn Trp Val Arg Gln Ala Pro Gly Lys
 500 505 510
 Gly Leu Glu Trp Val Ala Ile Ile Trp Tyr Asp Gly Asp Asn Gln Tyr
 515 520 525
 Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser
 530 535 540
 Lys Asn Thr Leu Tyr Leu Gln Met Asn Gly Leu Arg Ala Glu Asp Thr
 545 550 555 560
 Ala Val Tyr Tyr Cys Ala Arg Asp Leu Arg Thr Gly Pro Phe Asp Tyr
 565 570 575
 [0060]
 Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser
 580 585 590
 Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu
 595 600 605
 Ile Val Leu Thr Gln Ser Pro Asp Phe Gln Ser Val Thr Pro Lys Glu
 610 615 620
 Lys Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Gly Ser Ser Leu
 625 630 635 640
 His Trp Tyr Gln Gln Lys Pro Asp Gln Ser Pro Lys Leu Leu Ile Lys
 645 650 655
 Tyr Ala Ser Gln Ser Phe Ser Gly Val Pro Ser Arg Phe Ser Gly Ser
 660 665 670
 Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Asn Ser Leu Glu Ala Glu
 675 680 685

Asp Ala Ala Ala Tyr Tyr Cys His Gln Ser Ser Ser Leu Pro Phe Thr
690 695 700

Phe Gly Pro Gly Thr Lys Val Asp Ile Lys
705 710

<210> 84

<211> 682

<212> PRT

<213> 人工序列

<220>

<223> 人工序列的描述: 合成多肽

<400> 84

Met Gly Trp Ser Cys Ile Ile Leu Phe Leu Val Ala Thr Ala Thr Gly
1 5 10 15

Val His Ser Glu Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu
20 25 30

Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Lys Gly Val
35 40 45

[0061]

Ser Thr Ser Gly Tyr Ser Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly
50 55 60

Gln Ala Pro Arg Leu Leu Ile Tyr Leu Ala Ser Tyr Leu Glu Ser Gly
65 70 75 80

Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu
85 90 95

Thr Ile Ser Ser Leu Glu Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln
100 105 110

His Ser Arg Asp Leu Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu
115 120 125

Ile Lys Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser
130 135 140

Asp Glu Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn
145 150 155 160

Asn Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala
 165 170 175

Leu Gln Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys
 180 185 190

Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp
 195 200 205

Tyr Glu Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu
 210 215 220

Ser Ser Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys Gln Val Gln
 225 230 235 240

Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg Ser Leu Arg
 245 250 255

Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Val Tyr Gly Met Asn
 260 265 270

[0062]

Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala Ile Ile
 275 280 285

Trp Tyr Asp Gly Asp Asn Gln Tyr Tyr Ala Asp Ser Val Lys Gly Arg
 290 295 300

Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr Leu Gln Met
 305 310 315 320

Asn Gly Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Asp
 325 330 335

Leu Arg Thr Gly Pro Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr
 340 345 350

Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro
 355 360 365

Cys Ser Arg Ser Thr Ser Glu Ser Thr Ala Ala Leu Gly Cys Leu Val
 370 375 380

Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala
 385 390 395 400

Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly
 405 410 415

Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly
 420 425 430

Thr Lys Thr Tyr Thr Cys Asn Val Asp His Lys Pro Ser Asn Thr Lys
 435 440 445

Val Asp Lys Arg Val Glu Ser Lys Tyr Gly Pro Pro Cys Pro Pro Cys
 450 455 460

Pro Ala Pro Glu Phe Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro
 465 470 475 480

Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys
 485 490 495

[0063] Val Val Val Asp Val Ser Gln Glu Asp Pro Glu Val Gln Phe Asn Trp
 500 505 510

Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu
 515 520 525

Glu Gln Phe Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu
 530 535 540

His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn
 545 550 555 560

Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly
 565 570 575

Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Gln Glu Glu
 580 585 590

Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr
 595 600 605

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

	610		615		620												
	Asn	Tyr	Lys	Thr	Thr	Pro	Pro	Val	Leu	Asp	Ser	Asp	Gly	Ser	Phe	Phe	
	625					630					635					640	
	Leu	Tyr	Ser	Arg	Leu	Thr	Val	Asp	Lys	Ser	Arg	Trp	Gln	Glu	Gly	Asn	
					645					650					655		
	Val	Phe	Ser	Cys	Ser	Val	Met	His	Glu	Ala	Leu	His	Asn	His	Tyr	Thr	
				660					665					670			
	Gln	Lys	Ser	Leu	Ser	Leu	Ser	Leu	Gly	Lys							
			675						680								
	<210>	85															
	<211>	242															
	<212>	PRT															
	<213>	人工序列															
	<220>																
	<223>	人工序列的描述：合成多肽															
	<400>	85															
[0064]	Met	Gly	Trp	Ser	Cys	Ile	Ile	Leu	Phe	Leu	Val	Ala	Thr	Ala	Thr	Gly	
	1				5					10					15		
	Val	His	Ser	Gln	Val	Gln	Leu	Val	Gln	Ser	Gly	Val	Glu	Val	Lys	Lys	
				20					25					30			
	Pro	Gly	Ala	Ser	Val	Lys	Val	Ser	Cys	Lys	Ala	Ser	Gly	Tyr	Thr	Phe	
			35					40					45				
	Thr	Asn	Tyr	Tyr	Met	Tyr	Trp	Val	Arg	Gln	Ala	Pro	Gly	Gln	Gly	Leu	
	50						55					60					
	Glu	Trp	Met	Gly	Gly	Ile	Asn	Pro	Ser	Asn	Gly	Gly	Thr	Asn	Phe	Asn	
	65					70					75					80	
	Glu	Lys	Phe	Lys	Asn	Arg	Val	Thr	Leu	Thr	Thr	Asp	Ser	Ser	Thr	Thr	
					85					90					95		
	Thr	Ala	Tyr	Met	Glu	Leu	Lys	Ser	Leu	Gln	Phe	Asp	Asp	Thr	Ala	Val	
				100					105					110			
	Tyr	Tyr	Cys	Ala	Arg	Arg	Asp	Tyr	Arg	Phe	Asp	Met	Gly	Phe	Asp	Tyr	

	115		120		125														
	Trp	Gly	Gln	Gly	Thr	Thr	Val	Thr	Val	Ser	Ser	Ala	Ser	Thr	Lys	Gly			
	130						135					140							
	Pro	Ser	Val	Phe	Pro	Leu	Ala	Pro	Ser	Ser	Lys	Ser	Thr	Ser	Gly	Gly			
	145					150					155					160			
	Thr	Ala	Ala	Leu	Gly	Cys	Leu	Val	Lys	Asp	Tyr	Phe	Pro	Glu	Pro	Val			
					165					170					175				
	Thr	Val	Ser	Trp	Asn	Ser	Gly	Ala	Leu	Thr	Ser	Gly	Val	His	Thr	Phe			
				180						185				190					
	Pro	Ala	Val	Leu	Gln	Ser	Ser	Gly	Leu	Tyr	Ser	Leu	Ser	Ser	Val	Val			
			195					200					205						
	Thr	Val	Pro	Ser	Ser	Ser	Leu	Gly	Thr	Gln	Thr	Tyr	Ile	Cys	Asn	Val			
			210				215					220							
[0065]	Asn	His	Lys	Pro	Ser	Asn	Thr	Lys	Val	Asp	Lys	Arg	Val	Glu	Pro	Lys			
	225					230					235					240			
	Ser	Cys																	
	<210>	86																	
	<211>	678																	
	<212>	PRT																	
	<213>	人工序列																	
	<220>																		
	<223>	人工序列的描述：合成多肽																	
	<400>	86																	
	Met	Gly	Trp	Ser	Cys	Ile	Ile	Leu	Phe	Leu	Val	Ala	Thr	Ala	Thr	Gly			
	1				5					10					15				
	Val	His	Ser	Glu	Ile	Val	Leu	Thr	Gln	Ser	Pro	Ala	Thr	Leu	Ser	Leu			
				20					25					30					
	Ser	Pro	Gly	Glu	Arg	Ala	Thr	Leu	Ser	Cys	Arg	Ala	Ser	Gln	Ser	Val			
			35					40					45						
	Ser	Ser	Tyr	Leu	Ala	Trp	Tyr	Gln	Gln	Lys	Pro	Gly	Gln	Ala	Pro	Arg			

	50					55						60					
	Leu 65	Leu	Ile	Tyr	Asp	Ala 70	Ser	Asn	Arg	Ala	Thr 75	Gly	Ile	Pro	Ala	Arg 80	
	Phe	Ser	Gly	Ser	Gly 85	Ser	Gly	Thr	Asp	Phe 90	Thr	Leu	Thr	Ile	Ser	Ser 95	
	Leu	Glu	Pro	Glu 100	Asp	Phe	Ala	Val	Tyr 105	Tyr	Cys	Gln	Gln	Ser	Ser	Asn 110	
	Trp	Pro	Arg 115	Thr	Phe	Gly	Gln	Gly 120	Thr	Lys	Val	Glu	Ile 125	Lys	Arg	Thr	
	Val 130	Ala	Ala	Pro	Ser	Val	Phe 135	Ile	Phe	Pro	Pro	Ser 140	Asp	Glu	Gln	Leu	
	Lys 145	Ser	Gly	Thr	Ala	Ser 150	Val	Val	Cys	Leu	Leu 155	Asn	Asn	Phe	Tyr	Pro 160	
[0066]	Arg	Glu	Ala	Lys	Val 165	Gln	Trp	Lys	Val	Asp 170	Asn	Ala	Leu	Gln	Ser	Gly 175	
	Asn	Ser	Gln	Glu 180	Ser	Val	Thr	Glu	Gln 185	Asp	Ser	Lys	Asp	Ser	Thr	Tyr 190	
	Ser	Leu	Ser 195	Ser	Thr	Leu	Thr	Leu 200	Ser	Lys	Ala	Asp	Tyr 205	Glu	Lys	His	
	Lys 210	Val	Tyr	Ala	Cys	Glu	Val 215	Thr	His	Gln	Gly	Leu 220	Ser	Ser	Pro	Val	
	Thr 225	Lys	Ser	Phe	Asn 230	Arg	Gly	Glu	Cys	Gln	Val 235	Gln	Leu	Val	Glu	Ser 240	
	Gly	Gly	Gly	Val	Val 245	Gln	Pro	Gly	Arg	Ser 250	Leu	Arg	Leu	Ser	Cys	Ala 255	
	Ala	Ser	Gly	Phe 260	Thr	Phe	Ser	Val	Tyr 265	Gly	Met	Asn	Trp	Val	Arg	Gln 270	
	Ala	Pro	Gly 275	Lys	Gly	Leu	Glu	Trp 280	Val	Ala	Ile	Ile	Trp 285	Tyr	Asp	Gly	

Asp Asn Gln Tyr Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser
290 295 300

Arg Asp Asn Ser Lys Asn Thr Leu Tyr Leu Gln Met Asn Gly Leu Arg
305 310 315 320

Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Asp Leu Arg Thr Gly
325 330 335

Pro Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala
340 345 350

Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser
355 360 365

Thr Ser Glu Ser Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe
370 375 380

Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly
385 390 395 400

[0067]

Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu
405 410 415

Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Lys Thr Tyr
420 425 430

Thr Cys Asn Val Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg
435 440 445

Val Glu Ser Lys Tyr Gly Pro Pro Cys Pro Pro Cys Pro Ala Pro Glu
450 455 460

Phe Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
465 470 475 480

Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp
485 490 495

Val Ser Gln Glu Asp Pro Glu Val Gln Phe Asn Trp Tyr Val Asp Gly
500 505 510

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe Asn
515 520 525

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

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro
545 550 555 560

Ser Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
565 570 575

Pro Gln Val Tyr Thr Leu Pro Pro Ser Gln Glu Glu Met Thr Lys Asn
580 585 590

Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
595 600 605

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
610 615 620

[0068]

Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Arg
625 630 635 640

Leu Thr Val Asp Lys Ser Arg Trp Gln Glu Gly Asn Val Phe Ser Cys
645 650 655

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
660 665 670

Ser Leu Ser Leu Gly Lys
675

<210> 87

<211> 235

<212> PRT

<213> 人工序列

<220>

<223> 人工序列的描述：合成多肽

<400> 87

Met Gly Trp Ser Cys Ile Ile Leu Phe Leu Val Ala Thr Ala Thr Gly
1 5 10 15

Val His Ser Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln
 20 25 30

Pro Gly Arg Ser Leu Arg Leu Asp Cys Lys Ala Ser Gly Ile Thr Phe
 35 40 45

Ser Asn Ser Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu
 50 55 60

Glu Trp Val Ala Val Ile Trp Tyr Asp Gly Ser Lys Arg Tyr Tyr Ala
 65 70 75 80

Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn
 85 90 95

Thr Leu Phe Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val
 100 105 110

Tyr Tyr Cys Ala Thr Asn Asp Asp Tyr Trp Gly Gln Gly Thr Leu Val
 115 120 125

[0069]

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

Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu
 145 150 155 160

Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly
 165 170 175

Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser
 180 185 190

Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu
 195 200 205

Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr
 210 215 220

Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys
 225 230 235

<210> 88
 <211> 680
 <212> PRT
 <213> 人工序列

<220>
 <223> 人工序列的描述: 合成多肽

<400> 88
 Met Gly Trp Ser Cys Ile Ile Leu Phe Leu Val Ala Thr Ala Thr Gly
 1 5 10 15

Val His Ser Glu Ile Val Leu Thr Gln Ser Pro Asp Phe Gln Ser Val
 20 25 30

Thr Pro Lys Glu Lys Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile
 35 40 45

Gly Ser Ser Leu His Trp Tyr Gln Gln Lys Pro Asp Gln Ser Pro Lys
 50 55 60

Leu Leu Ile Lys Tyr Ala Ser Gln Ser Phe Ser Gly Val Pro Ser Arg
 65 70 75 80

[0070]

Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Asn Ser
 85 90 95

Leu Glu Ala Glu Asp Ala Ala Ala Tyr Tyr Cys His Gln Ser Ser Ser
 100 105 110

Leu Pro Phe Thr Phe Gly Pro Gly Thr Lys Val Asp Ile Lys Arg Thr
 115 120 125

Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu
 130 135 140

Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro
 145 150 155 160

Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly
 165 170 175

Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr
 180 185 190

Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His
 195 200 205

Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val
 210 215 220

Thr Lys Ser Phe Asn Arg Gly Glu Cys Gln Val Gln Leu Val Gln Ser
 225 230 235 240

Gly Val Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys
 245 250 255

Ala Ser Gly Tyr Thr Phe Thr Asn Tyr Tyr Met Tyr Trp Val Arg Gln
 260 265 270

Ala Pro Gly Gln Gly Leu Glu Trp Met Gly Gly Ile Asn Pro Ser Asn
 275 280 285

Gly Gly Thr Asn Phe Asn Glu Lys Phe Lys Asn Arg Val Thr Leu Thr
 290 295 300

[0071] Thr Asp Ser Ser Thr Thr Thr Ala Tyr Met Glu Leu Lys Ser Leu Gln
 305 310 315 320

Phe Asp Asp Thr Ala Val Tyr Tyr Cys Ala Arg Arg Asp Tyr Arg Phe
 325 330 335

Asp Met Gly Phe Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser
 340 345 350

Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Cys Ser
 355 360 365

Arg Ser Thr Ser Glu Ser Thr Ala Ala Leu Gly Cys Leu Val Lys Asp
 370 375 380

Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr
 385 390 395 400

Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr
 405 410 415

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

	420		425		430															
	Thr	Tyr	Thr	Cys	Asn	Val	Asp	His	Lys	Pro	Ser	Asn	Thr	Lys	Val	Asp				
			435					440					445							
	Lys	Arg	Val	Glu	Ser	Lys	Tyr	Gly	Pro	Pro	Cys	Pro	Pro	Cys	Pro	Ala				
		450					455					460								
	Pro	Glu	Phe	Leu	Gly	Gly	Pro	Ser	Val	Phe	Leu	Phe	Pro	Pro	Lys	Pro				
	465					470					475									480
	Lys	Asp	Thr	Leu	Met	Ile	Ser	Arg	Thr	Pro	Glu	Val	Thr	Cys	Val	Val				
					485					490					495					
	Val	Asp	Val	Ser	Gln	Glu	Asp	Pro	Glu	Val	Gln	Phe	Asn	Trp	Tyr	Val				
				500					505					510						
	Asp	Gly	Val	Glu	Val	His	Asn	Ala	Lys	Thr	Lys	Pro	Arg	Glu	Glu	Gln				
			515					520					525							
[0072]	Phe	Asn	Ser	Thr	Tyr	Arg	Val	Val	Ser	Val	Leu	Thr	Val	Leu	His	Gln				
		530					535					540								
	Asp	Trp	Leu	Asn	Gly	Lys	Glu	Tyr	Lys	Cys	Lys	Val	Ser	Asn	Lys	Gly				
	545					550					555									560
	Leu	Pro	Ser	Ser	Ile	Glu	Lys	Thr	Ile	Ser	Lys	Ala	Lys	Gly	Gln	Pro				
					565					570					575					
	Arg	Glu	Pro	Gln	Val	Tyr	Thr	Leu	Pro	Pro	Ser	Gln	Glu	Glu	Met	Thr				
				580					585					590						
	Lys	Asn	Gln	Val	Ser	Leu	Thr	Cys	Leu	Val	Lys	Gly	Phe	Tyr	Pro	Ser				
			595					600					605							
	Asp	Ile	Ala	Val	Glu	Trp	Glu	Ser	Asn	Gly	Gln	Pro	Glu	Asn	Asn	Tyr				
		610					615					620								
	Lys	Thr	Thr	Pro	Pro	Val	Leu	Asp	Ser	Asp	Gly	Ser	Phe	Phe	Leu	Tyr				
	625					630					635					640				
	Ser	Arg	Leu	Thr	Val	Asp	Lys	Ser	Arg	Trp	Gln	Glu	Gly	Asn	Val	Phe				
					645					650					655					

Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys
660 665 670

Ser Leu Ser Leu Ser Leu Gly Lys
675 680

<210> 89

<211> 240

<212> PRT

<213> 人工序列

<220>

<223> 人工序列的描述: 合成多肽

<400> 89

Met Gly Trp Ser Cys Ile Ile Leu Phe Leu Val Ala Thr Ala Thr Gly
1 5 10 15

Val His Ser Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln
20 25 30

Pro Gly Arg Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe
35 40 45

[0073]

Ser Val Tyr Gly Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu
50 55 60

Glu Trp Val Ala Ile Ile Trp Tyr Asp Gly Asp Asn Gln Tyr Tyr Ala
65 70 75 80

Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn
85 90 95

Thr Leu Tyr Leu Gln Met Asn Gly Leu Arg Ala Glu Asp Thr Ala Val
100 105 110

Tyr Tyr Cys Ala Arg Asp Leu Arg Thr Gly Pro Phe Asp Tyr Trp Gly
115 120 125

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

Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala
145 150 155 160

Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val
165 170 175

Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala
180 185 190

Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val
195 200 205

Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His
210 215 220

Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys
225 230 235 240

<210> 90

<211> 673

<212> PRT

<213> 人工序列

<220>

<223> 人工序列的描述: 合成多肽

[0074]

<400> 90

Met Gly Trp Ser Cys Ile Ile Leu Phe Leu Val Ala Thr Ala Thr Gly
1 5 10 15

Val His Ser Glu Ile Val Leu Thr Gln Ser Pro Asp Phe Gln Ser Val
20 25 30

Thr Pro Lys Glu Lys Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile
35 40 45

Gly Ser Ser Leu His Trp Tyr Gln Gln Lys Pro Asp Gln Ser Pro Lys
50 55 60

Leu Leu Ile Lys Tyr Ala Ser Gln Ser Phe Ser Gly Val Pro Ser Arg
65 70 75 80

Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Asn Ser
85 90 95

Leu Glu Ala Glu Asp Ala Ala Ala Tyr Tyr Cys His Gln Ser Ser Ser
100 105 110

Leu Pro Phe Thr Phe Gly Pro Gly Thr Lys Val Asp Ile Lys Arg Thr
115 120 125

Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu
130 135 140

Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro
145 150 155 160

Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly
165 170 175

Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr
180 185 190

Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His
195 200 205

Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val
210 215 220

[0075]

Thr Lys Ser Phe Asn Arg Gly Glu Cys Gln Val Gln Leu Val Glu Ser
225 230 235 240

Gly Gly Gly Val Val Gln Pro Gly Arg Ser Leu Arg Leu Asp Cys Lys
245 250 255

Ala Ser Gly Ile Thr Phe Ser Asn Ser Gly Met His Trp Val Arg Gln
260 265 270

Ala Pro Gly Lys Gly Leu Glu Trp Val Ala Val Ile Trp Tyr Asp Gly
275 280 285

Ser Lys Arg Tyr Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser
290 295 300

Arg Asp Asn Ser Lys Asn Thr Leu Phe Leu Gln Met Asn Ser Leu Arg
305 310 315 320

Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Thr Asn Asp Asp Tyr Trp
325 330 335

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

Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser Thr
355 360 365

Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr
370 375 380

Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro
385 390 395 400

Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr
405 410 415

Val Pro Ser Ser Ser Leu Gly Thr Lys Thr Tyr Thr Cys Asn Val Asp
420 425 430

His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Ser Lys Tyr
435 440 445

[0076]

Gly Pro Pro Cys Pro Pro Cys Pro Ala Pro Glu Phe Leu Gly Gly Pro
450 455 460

Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser
465 470 475 480

Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser Gln Glu Asp
485 490 495

Pro Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn
500 505 510

Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr Tyr Arg Val
515 520 525

Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu
530 535 540

Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys
545 550 555 560

Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr
565 570 575

Leu Pro Pro Ser Gln Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr
580 585 590

Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu
595 600 605

Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu
610 615 620

Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Arg Leu Thr Val Asp Lys
625 630 635 640

Ser Arg Trp Gln Glu Gly Asn Val Phe Ser Cys Ser Val Met His Glu
645 650 655

Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Leu Gly
660 665 670

[0077]

Lys

<210> 91

<211> 711

<212> PRT

<213> 人工序列

<220>

<223> 人工序列的描述：合成多肽

<400> 91

Met Gly Trp Ser Cys Ile Ile Leu Phe Leu Val Ala Thr Ala Thr Gly
1 5 10 15

Val His Ser Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln
20 25 30

Pro Gly Arg Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe
35 40 45

Ser Val Tyr Gly Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu
50 55 60

Glu Trp Val Ala Ile Ile Trp Tyr Asp Gly Asp Asn Gln Tyr Tyr Ala
 65 70 75 80

Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn
 85 90 95

Thr Leu Tyr Leu Gln Met Asn Gly Leu Arg Ala Glu Asp Thr Ala Val
 100 105 110

Tyr Tyr Cys Ala Arg Asp Leu Arg Thr Gly Pro Phe Asp Tyr Trp Gly
 115 120 125

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

Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser Thr Ala
 145 150 155 160

Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val
 165 170 175

[0078] Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala
 180 185 190

Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val
 195 200 205

Pro Ser Ser Ser Leu Gly Thr Lys Thr Tyr Thr Cys Asn Val Asp His
 210 215 220

Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Ser Lys Tyr Gly
 225 230 235 240

Pro Pro Cys Pro Pro Cys Pro Ala Pro Glu Phe Leu Gly Gly Pro Ser
 245 250 255

Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg
 260 265 270

Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser Gln Glu Asp Pro
 275 280 285

Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala

	290		295				300												
	Lys	Thr	Lys	Pro	Arg	Glu	Glu	Gln	Phe	Asn	Ser	Thr	Tyr	Arg	Val	Val			
	305					310					315								320
	Ser	Val	Leu	Thr	Val	Leu	His	Gln	Asp	Trp	Leu	Asn	Gly	Lys	Glu	Tyr			
					325					330					335				
	Lys	Cys	Lys	Val	Ser	Asn	Lys	Gly	Leu	Pro	Ser	Ser	Ile	Glu	Lys	Thr			
				340					345					350					
	Ile	Ser	Lys	Ala	Lys	Gly	Gln	Pro	Arg	Glu	Pro	Gln	Val	Tyr	Thr	Leu			
			355					360					365						
	Pro	Pro	Ser	Gln	Glu	Glu	Met	Thr	Lys	Asn	Gln	Val	Ser	Leu	Thr	Cys			
							375					380							
	Leu	Val	Lys	Gly	Phe	Tyr	Pro	Ser	Asp	Ile	Ala	Val	Glu	Trp	Glu	Ser			
	385					390					395								400
[0079]	Asn	Gly	Gly	Gly	Gly	Ser	Gly	Gly	Gly	Gly	Ser	Glu	Ile	Val	Leu	Thr			
					405					410					415				
	Gln	Ser	Pro	Ala	Thr	Leu	Ser	Leu	Ser	Pro	Gly	Glu	Arg	Ala	Thr	Leu			
				420					425					430					
	Ser	Cys	Arg	Ala	Ser	Lys	Gly	Val	Ser	Thr	Ser	Gly	Tyr	Ser	Tyr	Leu			
			435					440					445						
	His	Trp	Tyr	Gln	Gln	Lys	Pro	Gly	Gln	Ala	Pro	Arg	Leu	Leu	Ile	Tyr			
	450					455						460							
	Leu	Ala	Ser	Tyr	Leu	Glu	Ser	Gly	Val	Pro	Ala	Arg	Phe	Ser	Gly	Ser			
	465					470					475								480
	Gly	Ser	Gly	Thr	Asp	Phe	Thr	Leu	Thr	Ile	Ser	Ser	Leu	Glu	Pro	Glu			
					485					490					495				
	Asp	Phe	Ala	Val	Tyr	Tyr	Cys	Gln	His	Ser	Arg	Asp	Leu	Pro	Leu	Thr			
				500					505					510					
	Phe	Gly	Gly	Gly	Thr	Lys	Val	Glu	Ile	Lys	Arg	Thr	Val	Ala	Ala	Pro			
			515					520					525						

Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr
530 535 540

Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys
545 550 555 560

Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu
565 570 575

Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser
580 585 590

Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala
595 600 605

Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe
610 615 620

Asn Arg Gly Glu Cys Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
625 630 635 640

[0080]

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Pro Glu Asn Asn Tyr Lys
645 650 655

Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser
660 665 670

Arg Leu Thr Val Asp Lys Ser Arg Trp Gln Glu Gly Asn Val Phe Ser
675 680 685

Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser
690 695 700

Leu Ser Leu Ser Leu Gly Lys
705 710

<210> 92

<211> 242

<212> PRT

<213> 人工序列

<220>

<223> 人工序列的描述：合成多肽

<400> 92
 Met Gly Trp Ser Cys Ile Ile Leu Phe Leu Val Ala Thr Ala Thr Gly
 1 5 10 15

 Val His Ser Gln Val Gln Leu Val Gln Ser Gly Val Glu Val Lys Lys
 20 25 30

 Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe
 35 40 45

 Thr Asn Tyr Tyr Met Tyr Trp Val Arg Gln Ala Pro Gly Gln Gly Leu
 50 55 60

 Glu Trp Met Gly Gly Ile Asn Pro Ser Asn Gly Gly Thr Asn Phe Asn
 65 70 75 80

 Glu Lys Phe Lys Asn Arg Val Thr Leu Thr Thr Asp Ser Ser Thr Thr
 85 90 95

 Thr Ala Tyr Met Glu Leu Lys Ser Leu Gln Phe Asp Asp Thr Ala Val
 100 105 110
 [0081]
 Tyr Tyr Cys Ala Arg Arg Asp Tyr Arg Phe Asp Met Gly Phe Asp Tyr
 115 120 125

 Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly
 130 135 140

 Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly
 145 150 155 160

 Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val
 165 170 175

 Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe
 180 185 190

 Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val
 195 200 205

 Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val
 210 215 220

Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys
225 230 235 240

Ser Cys

<210> 93

<211> 708

<212> PRT

<213> 人工序列

<220>

<223> 人工序列的描述：合成多肽

<400> 93

Met Gly Trp Ser Cys Ile Ile Leu Phe Leu Val Ala Thr Ala Thr Gly
1 5 10 15

Val His Ser Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln
20 25 30

Pro Gly Arg Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe
35 40 45

[0082]

Ser Val Tyr Gly Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu
50 55 60

Glu Trp Val Ala Ile Ile Trp Tyr Asp Gly Asp Asn Gln Tyr Tyr Ala
65 70 75 80

Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn
85 90 95

Thr Leu Tyr Leu Gln Met Asn Gly Leu Arg Ala Glu Asp Thr Ala Val
100 105 110

Tyr Tyr Cys Ala Arg Asp Leu Arg Thr Gly Pro Phe Asp Tyr Trp Gly
115 120 125

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

Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser Thr Ala
145 150 155 160

Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val
 165 170 175

Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala
 180 185 190

Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val
 195 200 205

Pro Ser Ser Ser Leu Gly Thr Lys Thr Tyr Thr Cys Asn Val Asp His
 210 215 220

Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Ser Lys Tyr Gly
 225 230 235 240

Pro Pro Cys Pro Pro Cys Pro Ala Pro Glu Phe Leu Gly Gly Pro Ser
 245 250 255

Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg
 260 265 270

[0083]

Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser Gln Glu Asp Pro
 275 280 285

Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala
 290 295 300

Lys Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr Tyr Arg Val Val
 305 310 315 320

Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr
 325 330 335

Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr
 340 345 350

Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu
 355 360 365

Pro Pro Ser Gln Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys
 370 375 380

Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser
 385 390 395 400

Asn Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Ile Val Leu Thr
 405 410 415

Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu
 420 425 430

Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Tyr Leu Ala Trp Tyr Gln
 435 440 445

Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr Asp Ala Ser Asn
 450 455 460

Arg Ala Thr Gly Ile Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr
 465 470 475 480

Asp Phe Thr Leu Thr Ile Ser Ser Leu Glu Pro Glu Asp Phe Ala Val
 485 490 495

[0084] Tyr Tyr Cys Gln Gln Ser Ser Asn Trp Pro Arg Thr Phe Gly Gln Gly
 500 505 510

Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala Pro Ser Val Phe Ile
 515 520 525

Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr Ala Ser Val Val
 530 535 540

Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys
 545 550 555 560

Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser Val Thr Glu
 565 570 575

Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu
 580 585 590

Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala Cys Glu Val Thr
 595 600 605

His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe Asn Arg Gly Glu

	610		615			620										
	Cys	Gly	Gly	Gly	Gly	Ser	Gly	Gly	Gly	Gly	Ser	Gly	Gly	Gly	Gly	Ser
	625					630					635					640
	Gly	Gly	Gly	Gly	Ser	Gly	Gln	Pro	Glu	Asn	Asn	Tyr	Lys	Thr	Thr	Pro
					645					650						655
	Pro	Val	Leu	Asp	Ser	Asp	Gly	Ser	Phe	Phe	Leu	Tyr	Ser	Arg	Leu	Thr
				660					665					670		
	Val	Asp	Lys	Ser	Arg	Trp	Gln	Glu	Gly	Asn	Val	Phe	Ser	Cys	Ser	Val
			675					680					685			
	Met	His	Glu	Ala	Leu	His	Asn	His	Tyr	Thr	Gln	Lys	Ser	Leu	Ser	Leu
		690					695					700				
	Ser	Leu	Gly	Lys												
	705															
[0085]	<210>	94														
	<211>	710														
	<212>	PRT														
	<213>	人工序列														
	<220>															
	<223>	人工序列的描述:	合成多肽													
	<400>	94														
	Met	Gly	Trp	Ser	Cys	Ile	Ile	Leu	Phe	Leu	Val	Ala	Thr	Ala	Thr	Gly
	1				5					10					15	
	Val	His	Ser	Gln	Val	Gln	Leu	Val	Gln	Ser	Gly	Val	Glu	Val	Lys	Lys
				20					25					30		
	Pro	Gly	Ala	Ser	Val	Lys	Val	Ser	Cys	Lys	Ala	Ser	Gly	Tyr	Thr	Phe
			35					40					45			
	Thr	Asn	Tyr	Tyr	Met	Tyr	Trp	Val	Arg	Gln	Ala	Pro	Gly	Gln	Gly	Leu
		50					55					60				
	Glu	Trp	Met	Gly	Gly	Ile	Asn	Pro	Ser	Asn	Gly	Gly	Thr	Asn	Phe	Asn
	65					70					75					80
	Glu	Lys	Phe	Lys	Asn	Arg	Val	Thr	Leu	Thr	Thr	Asp	Ser	Ser	Thr	Thr

	85	90	95
	Thr Ala Tyr Met 100	Glu Leu Lys Ser Leu 105	Gln Phe Asp Asp Thr Ala Val 110
	Tyr Tyr Cys Ala Arg Arg Asp 115	Tyr Arg Phe Asp Met Gly 120	Phe Asp Tyr 125
	Trp Gly Gln Gly Thr Thr Val 130	Thr Val Ser Ser Ala Ser 135	Thr Lys Gly 140
	Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser 145	150	155
	Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val 165	170	175
	Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe 180	185	190
[0086]	Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val 195	200	205
	Thr Val Pro Ser Ser Ser Leu Gly Thr Lys Thr Tyr Thr Cys Asn Val 210	215	220
	Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Ser Lys 225	230	235
	Tyr Gly Pro Pro Cys Pro Pro Cys Pro Ala Pro Glu Phe Leu Gly Gly 245	250	255
	Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile 260	265	270
	Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser Gln Glu 275	280	285
	Asp Pro Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val His 290	295	300
	Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr Tyr Arg 305	310	315
			320

Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys
 325 330 335
 Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu
 340 345 350
 Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr
 355 360 365
 Thr Leu Pro Pro Ser Gln Glu Glu Met Thr Lys Asn Gln Val Ser Leu
 370 375 380
 Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp
 385 390 395 400
 Glu Ser Asn Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Ile Val
 405 410 415
 Leu Thr Gln Ser Pro Asp Phe Gln Ser Val Thr Pro Lys Glu Lys Val
 420 425 430
 [0087]
 Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Gly Ser Ser Leu His Trp
 435 440 445
 Tyr Gln Gln Lys Pro Asp Gln Ser Pro Lys Leu Leu Ile Lys Tyr Ala
 450 455 460
 Ser Gln Ser Phe Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser
 465 470 475 480
 Gly Thr Asp Phe Thr Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala
 485 490 495
 Ala Ala Tyr Tyr Cys His Gln Ser Ser Ser Leu Pro Phe Thr Phe Gly
 500 505 510
 Pro Gly Thr Lys Val Asp Ile Lys Arg Thr Val Ala Ala Pro Ser Val
 515 520 525
 Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr Ala Ser
 530 535 540

Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val Gln
545 550 555 560

Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser Val
565 570 575

Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu
580 585 590

Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala Cys Glu
595 600 605

Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe Asn Arg
610 615 620

Gly Glu Cys Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly
625 630 635 640

Gly Ser Gly Gly Gly Gly Ser Gly Gln Pro Glu Asn Asn Tyr Lys Thr
645 650 655

[0088]

Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Arg
660 665 670

Leu Thr Val Asp Lys Ser Arg Trp Gln Glu Gly Asn Val Phe Ser Cys
675 680 685

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
690 695 700

Ser Leu Ser Leu Gly Lys
705 710

<210> 95

<211> 703

<212> PRT

<213> 人工序列

<220>

<223> 人工序列的描述：合成多肽

<400> 95

Met Gly Trp Ser Cys Ile Ile Leu Phe Leu Val Ala Thr Ala Thr Gly
1 5 10 15

Val His Ser Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln
 20 25 30

Pro Gly Arg Ser Leu Arg Leu Asp Cys Lys Ala Ser Gly Ile Thr Phe
 35 40 45

Ser Asn Ser Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu
 50 55 60

Glu Trp Val Ala Val Ile Trp Tyr Asp Gly Ser Lys Arg Tyr Tyr Ala
 65 70 75 80

Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn
 85 90 95

Thr Leu Phe Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val
 100 105 110

Tyr Tyr Cys Ala Thr Asn Asp Asp Tyr Trp Gly Gln Gly Thr Leu Val
 115 120 125

[0089]

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

Pro Cys Ser Arg Ser Thr Ser Glu Ser Thr Ala Ala Leu Gly Cys Leu
 145 150 155 160

Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly
 165 170 175

Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser
 180 185 190

Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu
 195 200 205

Gly Thr Lys Thr Tyr Thr Cys Asn Val Asp His Lys Pro Ser Asn Thr
 210 215 220

Lys Val Asp Lys Arg Val Glu Ser Lys Tyr Gly Pro Pro Cys Pro Pro
 225 230 235 240

Cys Pro Ala Pro Glu Phe Leu Gly Gly Pro Ser Val Phe Leu Phe Pro
 245 250 255

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

Cys Val Val Val Asp Val Ser Gln Glu Asp Pro Glu Val Gln Phe Asn
 275 280 285

Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg
 290 295 300

Glu Glu Gln Phe Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val
 305 310 315 320

Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser
 325 330 335

Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys
 340 345 350

[0090] Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Gln Glu
 355 360 365

Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe
 370 375 380

Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gly Gly Gly
 385 390 395 400

Ser Gly Gly Gly Gly Ser Glu Ile Val Leu Thr Gln Ser Pro Asp Phe
 405 410 415

Gln Ser Val Thr Pro Lys Glu Lys Val Thr Ile Thr Cys Arg Ala Ser
 420 425 430

Gln Ser Ile Gly Ser Ser Leu His Trp Tyr Gln Gln Lys Pro Asp Gln
 435 440 445

Ser Pro Lys Leu Leu Ile Lys Tyr Ala Ser Gln Ser Phe Ser Gly Val
 450 455 460

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

465	470	475	480
Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Ala Tyr Tyr Cys His Gln 485 490 495			
Ser Ser Ser Leu Pro Phe Thr Phe Gly Pro Gly Thr Lys Val Asp Ile 500 505 510			
Lys Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp 515 520 525			
Glu Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn 530 535 540			
Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu 545 550 555 560			
Gln Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp 565 570 575			
[0091] Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr 580 585 590			
Glu Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser 595 600 605			
Ser Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys Gly Gly Gly Gly 610 615 620			
Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser 625 630 635 640			
Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser 645 650 655			
Asp Gly Ser Phe Phe Leu Tyr Ser Arg Leu Thr Val Asp Lys Ser Arg 660 665 670			
Trp Gln Glu Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu 675 680 685			
His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Leu Gly Lys 690 695 700			

<210> 96
 <211> 1127
 <212> PRT
 <213> 人工序列

<220>
 <223> 人工序列的描述: 合成多肽

<400> 96
 Met Gly Trp Ser Cys Ile Ile Leu Phe Leu Val Ala Thr Ala Thr Gly
 1 5 10 15

Val His Ser Ser Glu Arg Cys Asp Asp Trp Gly Leu Asp Thr Met Arg
 20 25 30

Gln Ile Gln Val Phe Glu Asp Glu Pro Ala Arg Ile Lys Cys Pro Leu
 35 40 45

Phe Glu His Phe Leu Lys Phe Asn Tyr Ser Thr Ala His Ser Ala Gly
 50 55 60

Leu Thr Leu Ile Trp Tyr Trp Thr Arg Gln Asp Arg Asp Leu Glu Glu
 65 70 75 80

[0092]

Pro Ile Asn Phe Arg Leu Pro Glu Asn Arg Ile Ser Lys Glu Lys Asp
 85 90 95

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

Cys Met Leu Arg Asn Thr Thr Tyr Cys Ser Lys Val Ala Phe Pro Leu
 115 120 125

Glu Val Val Gln Lys Asp Ser Cys Phe Asn Ser Pro Met Lys Leu Pro
 130 135 140

Val His Lys Leu Tyr Ile Glu Tyr Gly Ile Gln Arg Ile Thr Cys Pro
 145 150 155 160

Asn Val Asp Gly Tyr Phe Pro Ser Ser Val Lys Pro Thr Ile Thr Trp
 165 170 175

Tyr Met Gly Cys Tyr Lys Ile Gln Asn Phe Asn Asn Val Ile Pro Glu
 180 185 190

Gly Met Asn Leu Ser Phe Leu Ile Ala Leu Ile Ser Asn Asn Gly Asn
195 200 205

Tyr Thr Cys Val Val Thr Tyr Pro Glu Asn Gly Arg Thr Phe His Leu
210 215 220

Thr Arg Thr Leu Thr Val Lys Val Val Gly Ser Pro Lys Asn Ala Val
225 230 235 240

Pro Pro Val Ile His Ser Pro Asn Asp His Val Val Tyr Glu Lys Glu
245 250 255

Pro Gly Glu Glu Leu Leu Ile Pro Cys Thr Val Tyr Phe Ser Phe Leu
260 265 270

Met Asp Ser Arg Asn Glu Val Trp Trp Thr Ile Asp Gly Lys Lys Pro
275 280 285

Asp Asp Ile Thr Ile Asp Val Thr Ile Asn Glu Ser Ile Ser His Ser
290 295 300

[0093]

Arg Thr Glu Asp Glu Thr Arg Thr Gln Ile Leu Ser Ile Lys Lys Val
305 310 315 320

Thr Ser Glu Asp Leu Lys Arg Ser Tyr Val Cys His Ala Arg Ser Ala
325 330 335

Lys Gly Glu Val Ala Lys Ala Ala Lys Val Lys Gln Lys Val Pro Ala
340 345 350

Pro Arg Tyr Thr Val Glu Lys Cys Lys Glu Arg Glu Glu Lys Ile Ile
355 360 365

Leu Val Ser Ser Ala Asn Glu Ile Asp Val Arg Pro Cys Pro Leu Asn
370 375 380

Pro Asn Glu His Lys Gly Thr Ile Thr Trp Tyr Lys Asp Asp Ser Lys
385 390 395 400

Thr Pro Val Ser Thr Glu Gln Ala Ser Arg Ile His Gln His Lys Glu
405 410 415

Lys Leu Trp Phe Val Pro Ala Lys Val Glu Asp Ser Gly His Tyr Tyr
420 425 430

Cys Val Val Arg Asn Ser Ser Tyr Cys Leu Arg Ile Lys Ile Ser Ala
435 440 445

Lys Phe Val Glu Asn Glu Pro Asn Leu Cys Tyr Asn Ala Gln Ala Ile
450 455 460

Phe Lys Gln Lys Leu Pro Val Ala Gly Asp Gly Gly Leu Val Cys Pro
465 470 475 480

Tyr Met Glu Phe Phe Lys Asn Glu Asn Asn Glu Leu Pro Lys Leu Gln
485 490 495

Trp Tyr Lys Asp Cys Lys Pro Leu Leu Leu Asp Asn Ile His Phe Ser
500 505 510

Gly Val Lys Asp Arg Leu Ile Val Met Asn Val Ala Glu Lys His Arg
515 520 525

[0094]

Gly Asn Tyr Thr Cys His Ala Ser Tyr Thr Tyr Leu Gly Lys Gln Tyr
530 535 540

Pro Ile Thr Arg Val Ile Glu Phe Ile Thr Leu Glu Glu Asn Lys Pro
545 550 555 560

Thr Arg Pro Val Ile Val Ser Pro Ala Asn Glu Thr Met Glu Val Asp
565 570 575

Leu Gly Ser Gln Ile Gln Leu Ile Cys Asn Val Thr Gly Gln Leu Ser
580 585 590

Asp Ile Ala Tyr Trp Lys Trp Asn Gly Ser Val Ile Asp Glu Asp Asp
595 600 605

Pro Val Leu Gly Glu Asp Tyr Tyr Ser Val Glu Asn Pro Ala Asn Lys
610 615 620

Arg Arg Ser Thr Leu Ile Thr Val Leu Asn Ile Ser Glu Ile Glu Ser
625 630 635 640

Arg Phe Tyr Lys His Pro Phe Thr Cys Phe Ala Lys Asn Thr His Gly
 645 650 655

Ile Asp Ala Ala Tyr Ile Gln Leu Ile Tyr Pro Val Thr Asn Gly Gly
 660 665 670

Gly Gly Ser Gly Gly Gly Gly Ser Gln Val Gln Leu Val Gln Ser Gly
 675 680 685

Val Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala
 690 695 700

Ser Gly Tyr Thr Phe Thr Asn Tyr Tyr Met Tyr Trp Val Arg Gln Ala
 705 710 715 720

Pro Gly Gln Gly Leu Glu Trp Met Gly Gly Ile Asn Pro Ser Asn Gly
 725 730 735

Gly Thr Asn Phe Asn Glu Lys Phe Lys Asn Arg Val Thr Leu Thr Thr
 740 745 750

[0095] Asp Ser Ser Thr Thr Thr Ala Tyr Met Glu Leu Lys Ser Leu Gln Phe
 755 760 765

Asp Asp Thr Ala Val Tyr Tyr Cys Ala Arg Arg Asp Tyr Arg Phe Asp
 770 775 780

Met Gly Phe Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
 785 790 795 800

Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg
 805 810 815

Ser Thr Ser Glu Ser Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr
 820 825 830

Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser
 835 840 845

Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser
 850 855 860

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

	865		870		875		880									
	Tyr	Thr	Cys	Asn	Val	Asp	Lys	Pro	Ser	Asn	Thr	Lys	Val	Asp	Lys	
				885					890					895		
	Arg	Val	Glu	Ser	Lys	Tyr	Gly	Pro	Pro	Cys	Pro	Pro	Cys	Pro	Ala	Pro
				900					905					910		
	Glu	Phe	Leu	Gly	Gly	Pro	Ser	Val	Phe	Leu	Phe	Pro	Pro	Lys	Pro	Lys
			915					920					925			
	Asp	Thr	Leu	Met	Ile	Ser	Arg	Thr	Pro	Glu	Val	Thr	Cys	Val	Val	Val
		930					935					940				
	Asp	Val	Ser	Gln	Glu	Asp	Pro	Glu	Val	Gln	Phe	Asn	Trp	Tyr	Val	Asp
	945					950					955					960
	Gly	Val	Glu	Val	His	Asn	Ala	Lys	Thr	Lys	Pro	Arg	Glu	Glu	Gln	Phe
				965						970					975	
[0096]	Asn	Ser	Thr	Tyr	Arg	Val	Val	Ser	Val	Leu	Thr	Val	Leu	His	Gln	Asp
				980					985					990		
	Trp	Leu	Asn	Gly	Lys	Glu	Tyr	Lys	Cys	Lys	Val	Ser	Asn	Lys	Gly	Leu
			995					1000					1005			
	Pro	Ser	Ser	Ile	Glu	Lys	Thr	Ile	Ser	Lys	Ala	Lys	Gly	Gln	Pro	
	1010						1015					1020				
	Arg	Glu	Pro	Gln	Val	Tyr	Thr	Leu	Pro	Pro	Ser	Gln	Glu	Glu	Met	
	1025						1030					1035				
	Thr	Lys	Asn	Gln	Val	Ser	Leu	Thr	Cys	Leu	Val	Lys	Gly	Phe	Tyr	
	1040						1045					1050				
	Pro	Ser	Asp	Ile	Ala	Val	Glu	Trp	Glu	Ser	Asn	Gly	Gln	Pro	Glu	
	1055						1060					1065				
	Asn	Asn	Tyr	Lys	Thr	Thr	Pro	Pro	Val	Leu	Asp	Ser	Asp	Gly	Ser	
	1070						1075					1080				
	Phe	Phe	Leu	Tyr	Ser	Arg	Leu	Thr	Val	Asp	Lys	Ser	Arg	Trp	Gln	
	1085						1090					1095				

Glu Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His
1100 1105 1110

Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Leu Gly Lys
1115 1120 1125

<210> 97

<211> 1120

<212> PRT

<213> 人工序列

<220>

<223> 人工序列的描述：合成多肽

<400> 97

Met Gly Trp Ser Cys Ile Ile Leu Phe Leu Val Ala Thr Ala Thr Gly
1 5 10 15

Val His Ser Ser Glu Arg Cys Asp Asp Trp Gly Leu Asp Thr Met Arg
20 25 30

Gln Ile Gln Val Phe Glu Asp Glu Pro Ala Arg Ile Lys Cys Pro Leu
35 40 45

[0097]

Phe Glu His Phe Leu Lys Phe Asn Tyr Ser Thr Ala His Ser Ala Gly
50 55 60

Leu Thr Leu Ile Trp Tyr Trp Thr Arg Gln Asp Arg Asp Leu Glu Glu
65 70 75 80

Pro Ile Asn Phe Arg Leu Pro Glu Asn Arg Ile Ser Lys Glu Lys Asp
85 90 95

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

Cys Met Leu Arg Asn Thr Thr Tyr Cys Ser Lys Val Ala Phe Pro Leu
115 120 125

Glu Val Val Gln Lys Asp Ser Cys Phe Asn Ser Pro Met Lys Leu Pro
130 135 140

Val His Lys Leu Tyr Ile Glu Tyr Gly Ile Gln Arg Ile Thr Cys Pro
145 150 155 160

Asn Val Asp Gly Tyr Phe Pro Ser Ser Val Lys Pro Thr Ile Thr Trp
165 170 175

Tyr Met Gly Cys Tyr Lys Ile Gln Asn Phe Asn Asn Val Ile Pro Glu
180 185 190

Gly Met Asn Leu Ser Phe Leu Ile Ala Leu Ile Ser Asn Asn Gly Asn
195 200 205

Tyr Thr Cys Val Val Thr Tyr Pro Glu Asn Gly Arg Thr Phe His Leu
210 215 220

Thr Arg Thr Leu Thr Val Lys Val Val Gly Ser Pro Lys Asn Ala Val
225 230 235 240

Pro Pro Val Ile His Ser Pro Asn Asp His Val Val Tyr Glu Lys Glu
245 250 255

Pro Gly Glu Glu Leu Leu Ile Pro Cys Thr Val Tyr Phe Ser Phe Leu
260 265 270

[0098]

Met Asp Ser Arg Asn Glu Val Trp Trp Thr Ile Asp Gly Lys Lys Pro
275 280 285

Asp Asp Ile Thr Ile Asp Val Thr Ile Asn Glu Ser Ile Ser His Ser
290 295 300

Arg Thr Glu Asp Glu Thr Arg Thr Gln Ile Leu Ser Ile Lys Lys Val
305 310 315 320

Thr Ser Glu Asp Leu Lys Arg Ser Tyr Val Cys His Ala Arg Ser Ala
325 330 335

Lys Gly Glu Val Ala Lys Ala Ala Lys Val Lys Gln Lys Val Pro Ala
340 345 350

Pro Arg Tyr Thr Val Glu Lys Cys Lys Glu Arg Glu Glu Lys Ile Ile
355 360 365

Leu Val Ser Ser Ala Asn Glu Ile Asp Val Arg Pro Cys Pro Leu Asn
370 375 380

Pro Asn Glu His Lys Gly Thr Ile Thr Trp Tyr Lys Asp Asp Ser Lys
 385 390 395 400
 Thr Pro Val Ser Thr Glu Gln Ala Ser Arg Ile His Gln His Lys Glu
 405 410 415
 Lys Leu Trp Phe Val Pro Ala Lys Val Glu Asp Ser Gly His Tyr Tyr
 420 425 430
 Cys Val Val Arg Asn Ser Ser Tyr Cys Leu Arg Ile Lys Ile Ser Ala
 435 440 445
 Lys Phe Val Glu Asn Glu Pro Asn Leu Cys Tyr Asn Ala Gln Ala Ile
 450 455 460
 Phe Lys Gln Lys Leu Pro Val Ala Gly Asp Gly Gly Leu Val Cys Pro
 465 470 475 480
 Tyr Met Glu Phe Phe Lys Asn Glu Asn Asn Glu Leu Pro Lys Leu Gln
 485 490 495
 [0099]
 Trp Tyr Lys Asp Cys Lys Pro Leu Leu Leu Asp Asn Ile His Phe Ser
 500 505 510
 Gly Val Lys Asp Arg Leu Ile Val Met Asn Val Ala Glu Lys His Arg
 515 520 525
 Gly Asn Tyr Thr Cys His Ala Ser Tyr Thr Tyr Leu Gly Lys Gln Tyr
 530 535 540
 Pro Ile Thr Arg Val Ile Glu Phe Ile Thr Leu Glu Glu Asn Lys Pro
 545 550 555 560
 Thr Arg Pro Val Ile Val Ser Pro Ala Asn Glu Thr Met Glu Val Asp
 565 570 575
 Leu Gly Ser Gln Ile Gln Leu Ile Cys Asn Val Thr Gly Gln Leu Ser
 580 585 590
 Asp Ile Ala Tyr Trp Lys Trp Asn Gly Ser Val Ile Asp Glu Asp Asp
 595 600 605

Pro Val Leu Gly Glu Asp Tyr Tyr Ser Val Glu Asn Pro Ala Asn Lys
 610 615 620

Arg Arg Ser Thr Leu Ile Thr Val Leu Asn Ile Ser Glu Ile Glu Ser
 625 630 635 640

Arg Phe Tyr Lys His Pro Phe Thr Cys Phe Ala Lys Asn Thr His Gly
 645 650 655

Ile Asp Ala Ala Tyr Ile Gln Leu Ile Tyr Pro Val Thr Asn Gly Gly
 660 665 670

Gly Gly Ser Gly Gly Gly Gly Ser Gln Val Gln Leu Val Glu Ser Gly
 675 680 685

Gly Gly Val Val Gln Pro Gly Arg Ser Leu Arg Leu Asp Cys Lys Ala
 690 695 700

Ser Gly Ile Thr Phe Ser Asn Ser Gly Met His Trp Val Arg Gln Ala
 705 710 715 720

[0100] Pro Gly Lys Gly Leu Glu Trp Val Ala Val Ile Trp Tyr Asp Gly Ser
 725 730 735

Lys Arg Tyr Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg
 740 745 750

Asp Asn Ser Lys Asn Thr Leu Phe Leu Gln Met Asn Ser Leu Arg Ala
 755 760 765

Glu Asp Thr Ala Val Tyr Tyr Cys Ala Thr Asn Asp Asp Tyr Trp Gly
 770 775 780

Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser
 785 790 795 800

Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser Thr Ala
 805 810 815

Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val
 820 825 830

Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala

	835	840	845
	Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val 850	855	860
	Pro Ser Ser Ser Leu Gly Thr Lys Thr Tyr Thr Cys Asn Val Asp His 865	870	875 880
	Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Ser Lys Tyr Gly 885	890	895
	Pro Pro Cys Pro Pro Cys Pro Ala Pro Glu Phe Leu Gly Gly Pro Ser 900	905	910
	Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg 915	920	925
	Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser Gln Glu Asp Pro 930	935	940
[0101]	Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala 945	950	955 960
	Lys Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr Tyr Arg Val Val 965	970	975
	Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr 980	985	990
	Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr 995	1000	1005
	Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr 1010	1015	1020
	Leu Pro Pro Ser Gln Glu Glu Met Thr Lys Asn Gln Val Ser Leu 1025	1030	1035
	Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu 1040	1045	1050
	Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro 1055	1060	1065

Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Arg Leu
1070 1075 1080

Thr Val Asp Lys Ser Arg Trp Gln Glu Gly Asn Val Phe Ser Cys
1085 1090 1095

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser
1100 1105 1110

Leu Ser Leu Ser Leu Gly Lys
1115 1120

<210> 98

<211> 1123

<212> PRT

<213> 人工序列

<220>

<223> 人工序列的描述：合成多肽

<400> 98

Met Gly Trp Ser Cys Ile Ile Leu Phe Leu Val Ala Thr Ala Thr Gly
1 5 10 15

[0102]

Val His Ser Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln
20 25 30

Pro Gly Arg Ser Leu Arg Leu Asp Cys Lys Ala Ser Gly Ile Thr Phe
35 40 45

Ser Asn Ser Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu
50 55 60

Glu Trp Val Ala Val Ile Trp Tyr Asp Gly Ser Lys Arg Tyr Tyr Ala
65 70 75 80

Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn
85 90 95

Thr Leu Phe Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val
100 105 110

Tyr Tyr Cys Ala Thr Asn Asp Asp Tyr Trp Gly Gln Gly Thr Leu Val
115 120 125

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

Pro Cys Ser Arg Ser Thr Ser Glu Ser Thr Ala Ala Leu Gly Cys Leu
145 150 155 160

Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly
165 170 175

Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser
180 185 190

Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu
195 200 205

Gly Thr Lys Thr Tyr Thr Cys Asn Val Asp His Lys Pro Ser Asn Thr
210 215 220

Lys Val Asp Lys Arg Val Glu Ser Lys Tyr Gly Gly Gly Gly Ser Gly
225 230 235 240

[0103]

Gly Gly Gly Ser Glu Arg Cys Asp Asp Trp Gly Leu Asp Thr Met Arg
245 250 255

Gln Ile Gln Val Phe Glu Asp Glu Pro Ala Arg Ile Lys Cys Pro Leu
260 265 270

Phe Glu His Phe Leu Lys Phe Asn Tyr Ser Thr Ala His Ser Ala Gly
275 280 285

Leu Thr Leu Ile Trp Tyr Trp Thr Arg Gln Asp Arg Asp Leu Glu Glu
290 295 300

Pro Ile Asn Phe Arg Leu Pro Glu Asn Arg Ile Ser Lys Glu Lys Asp
305 310 315 320

Val Leu Trp Phe Arg Pro Thr Leu Leu Asn Asp Thr Gly Asn Tyr Thr
325 330 335

Cys Met Leu Arg Asn Thr Thr Tyr Cys Ser Lys Val Ala Phe Pro Leu
340 345 350

Glu Val Val Gln Lys Asp Ser Cys Phe Asn Ser Pro Met Lys Leu Pro
 355 360 365

Val His Lys Leu Tyr Ile Glu Tyr Gly Ile Gln Arg Ile Thr Cys Pro
 370 375 380

Asn Val Asp Gly Tyr Phe Pro Ser Ser Val Lys Pro Thr Ile Thr Trp
 385 390 395 400

Tyr Met Gly Cys Tyr Lys Ile Gln Asn Phe Asn Asn Val Ile Pro Glu
 405 410 415

Gly Met Asn Leu Ser Phe Leu Ile Ala Leu Ile Ser Asn Asn Gly Asn
 420 425 430

Tyr Thr Cys Val Val Thr Tyr Pro Glu Asn Gly Arg Thr Phe His Leu
 435 440 445

Thr Arg Thr Leu Thr Val Lys Val Val Gly Ser Pro Lys Asn Ala Val
 450 455 460

[0104]

Pro Pro Val Ile His Ser Pro Asn Asp His Val Val Tyr Glu Lys Glu
 465 470 475 480

Pro Gly Glu Glu Leu Leu Ile Pro Cys Thr Val Tyr Phe Ser Phe Leu
 485 490 495

Met Asp Ser Arg Asn Glu Val Trp Trp Thr Ile Asp Gly Lys Lys Pro
 500 505 510

Asp Asp Ile Thr Ile Asp Val Thr Ile Asn Glu Ser Ile Ser His Ser
 515 520 525

Arg Thr Glu Asp Glu Thr Arg Thr Gln Ile Leu Ser Ile Lys Lys Val
 530 535 540

Thr Ser Glu Asp Leu Lys Arg Ser Tyr Val Cys His Ala Arg Ser Ala
 545 550 555 560

Lys Gly Glu Val Ala Lys Ala Ala Lys Val Lys Gln Lys Val Pro Ala
 565 570 575

Pro Arg Tyr Thr Val Glu Lys Cys Lys Glu Arg Glu Glu Lys Ile Ile
 580 585 590

Leu Val Ser Ser Ala Asn Glu Ile Asp Val Arg Pro Cys Pro Leu Asn
 595 600 605

Pro Asn Glu His Lys Gly Thr Ile Thr Trp Tyr Lys Asp Asp Ser Lys
 610 615 620

Thr Pro Val Ser Thr Glu Gln Ala Ser Arg Ile His Gln His Lys Glu
 625 630 635 640

Lys Leu Trp Phe Val Pro Ala Lys Val Glu Asp Ser Gly His Tyr Tyr
 645 650 655

Cys Val Val Arg Asn Ser Ser Tyr Cys Leu Arg Ile Lys Ile Ser Ala
 660 665 670

Lys Phe Val Glu Asn Glu Pro Asn Leu Cys Tyr Asn Ala Gln Ala Ile
 675 680 685

[0105] Phe Lys Gln Lys Leu Pro Val Ala Gly Asp Gly Gly Leu Val Cys Pro
 690 695 700

Tyr Met Glu Phe Phe Lys Asn Glu Asn Asn Glu Leu Pro Lys Leu Gln
 705 710 715 720

Trp Tyr Lys Asp Cys Lys Pro Leu Leu Leu Asp Asn Ile His Phe Ser
 725 730 735

Gly Val Lys Asp Arg Leu Ile Val Met Asn Val Ala Glu Lys His Arg
 740 745 750

Gly Asn Tyr Thr Cys His Ala Ser Tyr Thr Tyr Leu Gly Lys Gln Tyr
 755 760 765

Pro Ile Thr Arg Val Ile Glu Phe Ile Thr Leu Glu Glu Asn Lys Pro
 770 775 780

Thr Arg Pro Val Ile Val Ser Pro Ala Asn Glu Thr Met Glu Val Asp
 785 790 795 800

Leu Gly Ser Gln Ile Gln Leu Ile Cys Asn Val Thr Gly Gln Leu Ser

	805	810	815
	Asp Ile Ala Tyr Trp Lys Trp Asn Gly Ser Val Ile Asp Glu Asp Asp 820 825 830		
	Pro Val Leu Gly Glu Asp Tyr Tyr Ser Val Glu Asn Pro Ala Asn Lys 835 840 845		
	Arg Arg Ser Thr Leu Ile Thr Val Leu Asn Ile Ser Glu Ile Glu Ser 850 855 860		
	Arg Phe Tyr Lys His Pro Phe Thr Cys Phe Ala Lys Asn Thr His Gly 865 870 875 880		
	Ile Asp Ala Ala Tyr Ile Gln Leu Ile Tyr Pro Val Thr Asn Ser Gly 885 890 895		
	Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Phe Leu Gly 900 905 910		
[0106]	Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met 915 920 925		
	Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser Gln 930 935 940		
	Glu Asp Pro Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val 945 950 955 960		
	His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr Tyr 965 970 975		
	Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly 980 985 990		
	Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ser Ser Ile 995 1000 1005		
	Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln 1010 1015 1020		
	Val Tyr Thr Leu Pro Pro Ser Gln Glu Glu Met Thr Lys Asn Gln 1025 1030 1035		

Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
1040 1045 1050

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys
1055 1060 1065

Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr
1070 1075 1080

Ser Arg Leu Thr Val Asp Lys Ser Arg Trp Gln Glu Gly Asn Val
1085 1090 1095

Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr
1100 1105 1110

Gln Lys Ser Leu Ser Leu Ser Leu Gly Lys
1115 1120

<210> 99

<211> 1130

<212> PRT

[0107] <213> 人工序列

<220>

<223> 人工序列的描述：合成多肽

<400> 99

Met Gly Trp Ser Cys Ile Ile Leu Phe Leu Val Ala Thr Ala Thr Gly
1 5 10 15

Val His Ser Gln Val Gln Leu Val Gln Ser Gly Val Glu Val Lys Lys
20 25 30

Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe
35 40 45

Thr Asn Tyr Tyr Met Tyr Trp Val Arg Gln Ala Pro Gly Gln Gly Leu
50 55 60

Glu Trp Met Gly Gly Ile Asn Pro Ser Asn Gly Gly Thr Asn Phe Asn
65 70 75 80

Glu Lys Phe Lys Asn Arg Val Thr Leu Thr Thr Asp Ser Ser Thr Thr
85 90 95

Thr Ala Tyr Met Glu Leu Lys Ser Leu Gln Phe Asp Asp Thr Ala Val
100 105 110

Tyr Tyr Cys Ala Arg Arg Asp Tyr Arg Phe Asp Met Gly Phe Asp Tyr
115 120 125

Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly
130 135 140

Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser
145 150 155 160

Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val
165 170 175

Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe
180 185 190

Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val
195 200 205

[0108]

Thr Val Pro Ser Ser Ser Leu Gly Thr Lys Thr Tyr Thr Cys Asn Val
210 215 220

Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Ser Lys
225 230 235 240

Tyr Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Arg Cys Asp Asp
245 250 255

Trp Gly Leu Asp Thr Met Arg Gln Ile Gln Val Phe Glu Asp Glu Pro
260 265 270

Ala Arg Ile Lys Cys Pro Leu Phe Glu His Phe Leu Lys Phe Asn Tyr
275 280 285

Ser Thr Ala His Ser Ala Gly Leu Thr Leu Ile Trp Tyr Trp Thr Arg
290 295 300

Gln Asp Arg Asp Leu Glu Glu Pro Ile Asn Phe Arg Leu Pro Glu Asn
305 310 315 320

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

Asn Asp Thr Gly Asn Tyr Thr Cys Met Leu Arg Asn Thr Thr Tyr Cys
340 345 350

Ser Lys Val Ala Phe Pro Leu Glu Val Val Gln Lys Asp Ser Cys Phe
355 360 365

Asn Ser Pro Met Lys Leu Pro Val His Lys Leu Tyr Ile Glu Tyr Gly
370 375 380

Ile Gln Arg Ile Thr Cys Pro Asn Val Asp Gly Tyr Phe Pro Ser Ser
385 390 395 400

Val Lys Pro Thr Ile Thr Trp Tyr Met Gly Cys Tyr Lys Ile Gln Asn
405 410 415

Phe Asn Asn Val Ile Pro Glu Gly Met Asn Leu Ser Phe Leu Ile Ala
420 425 430

[0109]

Leu Ile Ser Asn Asn Gly Asn Tyr Thr Cys Val Val Thr Tyr Pro Glu
435 440 445

Asn Gly Arg Thr Phe His Leu Thr Arg Thr Leu Thr Val Lys Val Val
450 455 460

Gly Ser Pro Lys Asn Ala Val Pro Pro Val Ile His Ser Pro Asn Asp
465 470 475 480

His Val Val Tyr Glu Lys Glu Pro Gly Glu Glu Leu Leu Ile Pro Cys
485 490 495

Thr Val Tyr Phe Ser Phe Leu Met Asp Ser Arg Asn Glu Val Trp Trp
500 505 510

Thr Ile Asp Gly Lys Lys Pro Asp Asp Ile Thr Ile Asp Val Thr Ile
515 520 525

Asn Glu Ser Ile Ser His Ser Arg Thr Glu Asp Glu Thr Arg Thr Gln
530 535 540

Ile Leu Ser Ile Lys Lys Val Thr Ser Glu Asp Leu Lys Arg Ser Tyr
 545 550 555 560
 Val Cys His Ala Arg Ser Ala Lys Gly Glu Val Ala Lys Ala Ala Lys
 565 570 575
 Val Lys Gln Lys Val Pro Ala Pro Arg Tyr Thr Val Glu Lys Cys Lys
 580 585 590
 Glu Arg Glu Glu Lys Ile Ile Leu Val Ser Ser Ala Asn Glu Ile Asp
 595 600 605
 Val Arg Pro Cys Pro Leu Asn Pro Asn Glu His Lys Gly Thr Ile Thr
 610 615 620
 Trp Tyr Lys Asp Asp Ser Lys Thr Pro Val Ser Thr Glu Gln Ala Ser
 625 630 635 640
 Arg Ile His Gln His Lys Glu Lys Leu Trp Phe Val Pro Ala Lys Val
 645 650 655
 [0110] Glu Asp Ser Gly His Tyr Tyr Cys Val Val Arg Asn Ser Ser Tyr Cys
 660 665 670
 Leu Arg Ile Lys Ile Ser Ala Lys Phe Val Glu Asn Glu Pro Asn Leu
 675 680 685
 Cys Tyr Asn Ala Gln Ala Ile Phe Lys Gln Lys Leu Pro Val Ala Gly
 690 695 700
 Asp Gly Gly Leu Val Cys Pro Tyr Met Glu Phe Phe Lys Asn Glu Asn
 705 710 715 720
 Asn Glu Leu Pro Lys Leu Gln Trp Tyr Lys Asp Cys Lys Pro Leu Leu
 725 730 735
 Leu Asp Asn Ile His Phe Ser Gly Val Lys Asp Arg Leu Ile Val Met
 740 745 750
 Asn Val Ala Glu Lys His Arg Gly Asn Tyr Thr Cys His Ala Ser Tyr
 755 760 765
 Thr Tyr Leu Gly Lys Gln Tyr Pro Ile Thr Arg Val Ile Glu Phe Ile

Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys
1010 1015 1020

Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Gln
1025 1030 1035

Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys
1040 1045 1050

Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly
1055 1060 1065

Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser
1070 1075 1080

Asp Gly Ser Phe Phe Leu Tyr Ser Arg Leu Thr Val Asp Lys Ser
1085 1090 1095

Arg Trp Gln Glu Gly Asn Val Phe Ser Cys Ser Val Met His Glu
1100 1105 1110

[0112]

Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Leu
1115 1120 1125

Gly Lys
1130

<210> 100

<211> 1149

<212> PRT

<213> 人工序列

<220>

<223> 人工序列的描述: 合成多肽

<400> 100

Met Gly Trp Ser Cys Ile Ile Leu Phe Leu Val Ala Thr Ala Thr Gly
1 5 10 15

Val His Ser Ser Glu Arg Cys Asp Asp Trp Gly Leu Asp Thr Met Arg
20 25 30

Gln Ile Gln Val Phe Glu Asp Glu Pro Ala Arg Ile Lys Cys Pro Leu
35 40 45

Phe Glu His Phe Leu Lys Phe Asn Tyr Ser Thr Ala His Ser Ala Gly
 50 55 60

Leu Thr Leu Ile Trp Tyr Trp Thr Arg Gln Asp Arg Asp Leu Glu Glu
 65 70 75 80

Pro Ile Asn Phe Arg Leu Pro Glu Asn Arg Ile Ser Lys Glu Lys Asp
 85 90 95

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

Cys Met Leu Arg Asn Thr Thr Tyr Cys Ser Lys Val Ala Phe Pro Leu
 115 120 125

Glu Val Val Gln Lys Asp Ser Cys Phe Asn Ser Pro Met Lys Leu Pro
 130 135 140

Val His Lys Leu Tyr Ile Glu Tyr Gly Ile Gln Arg Ile Thr Cys Pro
 145 150 155 160

[0113]

Asn Val Asp Gly Tyr Phe Pro Ser Ser Val Lys Pro Thr Ile Thr Trp
 165 170 175

Tyr Met Gly Cys Tyr Lys Ile Gln Asn Phe Asn Asn Val Ile Pro Glu
 180 185 190

Gly Met Asn Leu Ser Phe Leu Ile Ala Leu Ile Ser Asn Asn Gly Asn
 195 200 205

Tyr Thr Cys Val Val Thr Tyr Pro Glu Asn Gly Arg Thr Phe His Leu
 210 215 220

Thr Arg Thr Leu Thr Val Lys Val Val Gly Ser Pro Lys Asn Ala Val
 225 230 235 240

Pro Pro Val Ile His Ser Pro Asn Asp His Val Val Tyr Glu Lys Glu
 245 250 255

Pro Gly Glu Glu Leu Leu Ile Pro Cys Thr Val Tyr Phe Ser Phe Leu
 260 265 270

Met Asp Ser Arg Asn Glu Val Trp Trp Thr Ile Asp Gly Lys Lys Pro
 275 280 285

Asp Asp Ile Thr Ile Asp Val Thr Ile Asn Glu Ser Ile Ser His Ser
 290 295 300

Arg Thr Glu Asp Glu Thr Arg Thr Gln Ile Leu Ser Ile Lys Lys Val
 305 310 315 320

Thr Ser Glu Asp Leu Lys Arg Ser Tyr Val Cys His Ala Arg Ser Ala
 325 330 335

Lys Gly Glu Val Ala Lys Ala Ala Lys Val Lys Gln Lys Val Pro Ala
 340 345 350

Pro Arg Tyr Thr Val Glu Lys Cys Lys Glu Arg Glu Glu Lys Ile Ile
 355 360 365

Leu Val Ser Ser Ala Asn Glu Ile Asp Val Arg Pro Cys Pro Leu Asn
 370 375 380

[0114]

Pro Asn Glu His Lys Gly Thr Ile Thr Trp Tyr Lys Asp Asp Ser Lys
 385 390 395 400

Thr Pro Val Ser Thr Glu Gln Ala Ser Arg Ile His Gln His Lys Glu
 405 410 415

Lys Leu Trp Phe Val Pro Ala Lys Val Glu Asp Ser Gly His Tyr Tyr
 420 425 430

Cys Val Val Arg Asn Ser Ser Tyr Cys Leu Arg Ile Lys Ile Ser Ala
 435 440 445

Lys Phe Val Glu Asn Glu Pro Asn Leu Cys Tyr Asn Ala Gln Ala Ile
 450 455 460

Phe Lys Gln Lys Leu Pro Val Ala Gly Asp Gly Gly Leu Val Cys Pro
 465 470 475 480

Tyr Met Glu Phe Phe Lys Asn Glu Asn Asn Glu Leu Pro Lys Leu Gln
 485 490 495

Trp Tyr Lys Asp Cys Lys Pro Leu Leu Leu Asp Asn Ile His Phe Ser
 500 505 510

Gly Val Lys Asp Arg Leu Ile Val Met Asn Val Ala Glu Lys His Arg
 515 520 525

Gly Asn Tyr Thr Cys His Ala Ser Tyr Thr Tyr Leu Gly Lys Gln Tyr
 530 535 540

Pro Ile Thr Arg Val Ile Glu Phe Ile Thr Leu Glu Glu Asn Lys Pro
 545 550 555 560

Thr Arg Pro Val Ile Val Ser Pro Ala Asn Glu Thr Met Glu Val Asp
 565 570 575

Leu Gly Ser Gln Ile Gln Leu Ile Cys Asn Val Thr Gly Gln Leu Ser
 580 585 590

Asp Ile Ala Tyr Trp Lys Trp Asn Gly Ser Val Ile Asp Glu Asp Asp
 595 600 605

[0115] Pro Val Leu Gly Glu Asp Tyr Tyr Ser Val Glu Asn Pro Ala Asn Lys
 610 615 620

Arg Arg Ser Thr Leu Ile Thr Val Leu Asn Ile Ser Glu Ile Glu Ser
 625 630 635 640

Arg Phe Tyr Lys His Pro Phe Thr Cys Phe Ala Lys Asn Thr His Gly
 645 650 655

Ile Asp Ala Ala Tyr Ile Gln Leu Ile Tyr Pro Val Thr Asn Ser Gly
 660 665 670

Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Phe Leu Gly
 675 680 685

Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
 690 695 700

Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser Gln
 705 710 715 720

Glu Asp Pro Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val

	725		730		735
	His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr Tyr	740	745		750
	Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly	755	760		765
	Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ser Ser Ile	770	775		780
	Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val	785	790	795	800
	Tyr Thr Leu Pro Pro Ser Gln Glu Glu Met Thr Lys Asn Gln Val Ser	805		810	815
	Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu	820		825	830
[0116]	Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro	835	840		845
	Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Arg Leu Thr Val	850	855		860
	Asp Lys Ser Arg Trp Gln Glu Gly Asn Val Phe Ser Cys Ser Val Met	865	870	875	880
	His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser	885		890	895
	Leu Gly Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Val Gln	900		905	910
	Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg Ser Leu Arg	915		920	925
	Leu Asp Cys Lys Ala Ser Gly Ile Thr Phe Ser Asn Ser Gly Met His	930		935	940
	Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala Val Ile	945		950	955
					960

Trp Tyr Asp Gly Ser Lys Arg Tyr Tyr Ala Asp Ser Val Lys Gly Arg
 965 970 975

Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Phe Leu Gln Met
 980 985 990

Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Thr Asn
 995 1000 1005

Asp Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly
 1010 1015 1020

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
 1025 1030 1035

Gly Gly Gly Ser Glu Ile Val Leu Thr Gln Ser Pro Ala Thr Leu
 1040 1045 1050

Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser
 1055 1060 1065

[0117]

Gln Ser Val Ser Ser Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly
 1070 1075 1080

Gln Ala Pro Arg Leu Leu Ile Tyr Asp Ala Ser Asn Arg Ala Thr
 1085 1090 1095

Gly Ile Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe
 1100 1105 1110

Thr Leu Thr Ile Ser Ser Leu Glu Pro Glu Asp Phe Ala Val Tyr
 1115 1120 1125

Tyr Cys Gln Gln Ser Ser Asn Trp Pro Arg Thr Phe Gly Gln Gly
 1130 1135 1140

Thr Lys Val Glu Ile Lys
 1145

<210> 101
 <211> 1123
 <212> PRT

<213> 人工序列

<220>

<223> 人工序列的描述：合成多肽

<400> 101

Met Gly Trp Ser Cys Ile Ile Leu Phe Leu Val Ala Thr Ala Thr Gly
1 5 10 15

Val His Ser Ser Glu Arg Cys Asp Asp Trp Gly Leu Asp Thr Met Arg
20 25 30

Gln Ile Gln Val Phe Glu Asp Glu Pro Ala Arg Ile Lys Cys Pro Leu
35 40 45

Phe Glu His Phe Leu Lys Phe Asn Tyr Ser Thr Ala His Ser Ala Gly
50 55 60

Leu Thr Leu Ile Trp Tyr Trp Thr Arg Gln Asp Arg Asp Leu Glu Glu
65 70 75 80

Pro Ile Asn Phe Arg Leu Pro Glu Asn Arg Ile Ser Lys Glu Lys Asp
85 90 95

[0118]

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

Cys Met Leu Arg Asn Thr Thr Tyr Cys Ser Lys Val Ala Phe Pro Leu
115 120 125

Glu Val Val Gln Lys Asp Ser Cys Phe Asn Ser Pro Met Lys Leu Pro
130 135 140

Val His Lys Leu Tyr Ile Glu Tyr Gly Ile Gln Arg Ile Thr Cys Pro
145 150 155 160

Asn Val Asp Gly Tyr Phe Pro Ser Ser Val Lys Pro Thr Ile Thr Trp
165 170 175

Tyr Met Gly Cys Tyr Lys Ile Gln Asn Phe Asn Asn Val Ile Pro Glu
180 185 190

Gly Met Asn Leu Ser Phe Leu Ile Ala Leu Ile Ser Asn Asn Gly Asn
195 200 205

Tyr Thr Cys Val Val Thr Tyr Pro Glu Asn Gly Arg Thr Phe His Leu
210 215 220

Thr Arg Thr Leu Thr Val Lys Val Val Gly Ser Pro Lys Asn Ala Val
225 230 235 240

Pro Pro Val Ile His Ser Pro Asn Asp His Val Val Tyr Glu Lys Glu
245 250 255

Pro Gly Glu Glu Leu Leu Ile Pro Cys Thr Val Tyr Phe Ser Phe Leu
260 265 270

Met Asp Ser Arg Asn Glu Val Trp Trp Thr Ile Asp Gly Lys Lys Pro
275 280 285

Asp Asp Ile Thr Ile Asp Val Thr Ile Asn Glu Ser Ile Ser His Ser
290 295 300

Arg Thr Glu Asp Glu Thr Arg Thr Gln Ile Leu Ser Ile Lys Lys Val
305 310 315 320

[0119]

Thr Ser Glu Asp Leu Lys Arg Ser Tyr Val Cys His Ala Arg Ser Ala
325 330 335

Lys Gly Glu Val Ala Lys Ala Ala Lys Val Lys Gln Lys Val Pro Ala
340 345 350

Pro Arg Tyr Thr Val Glu Lys Cys Lys Glu Arg Glu Glu Lys Ile Ile
355 360 365

Leu Val Ser Ser Ala Asn Glu Ile Asp Val Arg Pro Cys Pro Leu Asn
370 375 380

Pro Asn Glu His Lys Gly Thr Ile Thr Trp Tyr Lys Asp Asp Ser Lys
385 390 395 400

Thr Pro Val Ser Thr Glu Gln Ala Ser Arg Ile His Gln His Lys Glu
405 410 415

Lys Leu Trp Phe Val Pro Ala Lys Val Glu Asp Ser Gly His Tyr Tyr
420 425 430

Cys Val Val Arg Asn Ser Ser Tyr Cys Leu Arg Ile Lys Ile Ser Ala
 435 440 445

Lys Phe Val Glu Asn Glu Pro Asn Leu Cys Tyr Asn Ala Gln Ala Ile
 450 455 460

Phe Lys Gln Lys Leu Pro Val Ala Gly Asp Gly Gly Leu Val Cys Pro
 465 470 475 480

Tyr Met Glu Phe Phe Lys Asn Glu Asn Asn Glu Leu Pro Lys Leu Gln
 485 490 495

Trp Tyr Lys Asp Cys Lys Pro Leu Leu Leu Asp Asn Ile His Phe Ser
 500 505 510

Gly Val Lys Asp Arg Leu Ile Val Met Asn Val Ala Glu Lys His Arg
 515 520 525

Gly Asn Tyr Thr Cys His Ala Ser Tyr Thr Tyr Leu Gly Lys Gln Tyr
 530 535 540

[0120] Pro Ile Thr Arg Val Ile Glu Phe Ile Thr Leu Glu Glu Asn Lys Pro
 545 550 555 560

Thr Arg Pro Val Ile Val Ser Pro Ala Asn Glu Thr Met Glu Val Asp
 565 570 575

Leu Gly Ser Gln Ile Gln Leu Ile Cys Asn Val Thr Gly Gln Leu Ser
 580 585 590

Asp Ile Ala Tyr Trp Lys Trp Asn Gly Ser Val Ile Asp Glu Asp Asp
 595 600 605

Pro Val Leu Gly Glu Asp Tyr Tyr Ser Val Glu Asn Pro Ala Asn Lys
 610 615 620

Arg Arg Ser Thr Leu Ile Thr Val Leu Asn Ile Ser Glu Ile Glu Ser
 625 630 635 640

Arg Phe Tyr Lys His Pro Phe Thr Cys Phe Ala Lys Asn Thr His Gly
 645 650 655

Ile Asp Ala Ala Tyr Ile Gln Leu Ile Tyr Pro Val Thr Asn Gly Gly

	660		665		670													
	Gly	Gly	Ser	Gly	Gly	Gly	Gly	Ser	Glu	Ile	Val	Leu	Thr	Gln	Ser	Pro		
			675					680					685					
	Ala	Thr	Leu	Ser	Leu	Ser	Pro	Gly	Glu	Arg	Ala	Thr	Leu	Ser	Cys	Arg		
		690					695					700						
	Ala	Ser	Lys	Gly	Val	Ser	Thr	Ser	Gly	Tyr	Ser	Tyr	Leu	His	Trp	Tyr		
	705					710					715					720		
	Gln	Gln	Lys	Pro	Gly	Gln	Ala	Pro	Arg	Leu	Leu	Ile	Tyr	Leu	Ala	Ser		
					725					730					735			
	Tyr	Leu	Glu	Ser	Gly	Val	Pro	Ala	Arg	Phe	Ser	Gly	Ser	Gly	Ser	Gly		
				740					745					750				
	Thr	Asp	Phe	Thr	Leu	Thr	Ile	Ser	Ser	Leu	Glu	Pro	Glu	Asp	Phe	Ala		
			755					760					765					
[0121]	Val	Tyr	Tyr	Cys	Gln	His	Ser	Arg	Asp	Leu	Pro	Leu	Thr	Phe	Gly	Gly		
	770						775					780						
	Gly	Thr	Lys	Val	Glu	Ile	Lys	Arg	Thr	Val	Ala	Ala	Pro	Ser	Val	Phe		
	785					790					795					800		
	Ile	Phe	Pro	Pro	Ser	Asp	Glu	Gln	Leu	Lys	Ser	Gly	Thr	Ala	Ser	Val		
					805					810					815			
	Val	Cys	Leu	Leu	Asn	Asn	Phe	Tyr	Pro	Arg	Glu	Ala	Lys	Val	Gln	Trp		
				820					825					830				
	Lys	Val	Asp	Asn	Ala	Leu	Gln	Ser	Gly	Asn	Ser	Gln	Glu	Ser	Val	Thr		
			835					840					845					
	Glu	Gln	Asp	Ser	Lys	Asp	Ser	Thr	Tyr	Ser	Leu	Ser	Ser	Thr	Leu	Thr		
	850						855					860						
	Leu	Ser	Lys	Ala	Asp	Tyr	Glu	Lys	His	Lys	Val	Tyr	Ala	Cys	Glu	Val		
	865					870					875				880			
	Thr	His	Gln	Gly	Leu	Ser	Ser	Pro	Val	Thr	Lys	Ser	Phe	Asn	Arg	Gly		
					885					890					895			

Glu Cys Gly Pro Pro Cys Pro Pro Cys Pro Ala Pro Glu Phe Leu Gly
 900 905 910

Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
 915 920 925

Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser Gln
 930 935 940

Glu Asp Pro Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val
 945 950 955 960

His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr Tyr
 965 970 975

Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly
 980 985 990

Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ser Ser Ile
 995 1000 1005

[0122]

Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln
 1010 1015 1020

Val Tyr Thr Leu Pro Pro Ser Gln Glu Glu Met Thr Lys Asn Gln
 1025 1030 1035

Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
 1040 1045 1050

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys
 1055 1060 1065

Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr
 1070 1075 1080

Ser Arg Leu Thr Val Asp Lys Ser Arg Trp Gln Glu Gly Asn Val
 1085 1090 1095

Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr
 1100 1105 1110

Gln Lys Ser Leu Ser Leu Ser Leu Gly Lys
1115 1120

<210> 102
<211> 1119
<212> PRT
<213> 人工序列

<220>
<223> 人工序列的描述: 合成多肽

<400> 102
Met Gly Trp Ser Cys Ile Ile Leu Phe Leu Val Ala Thr Ala Thr Gly
1 5 10 15

Val His Ser Ser Glu Arg Cys Asp Asp Trp Gly Leu Asp Thr Met Arg
20 25 30

Gln Ile Gln Val Phe Glu Asp Glu Pro Ala Arg Ile Lys Cys Pro Leu
35 40 45

Phe Glu His Phe Leu Lys Phe Asn Tyr Ser Thr Ala His Ser Ala Gly
50 55 60

[0123]

Leu Thr Leu Ile Trp Tyr Trp Thr Arg Gln Asp Arg Asp Leu Glu Glu
65 70 75 80

Pro Ile Asn Phe Arg Leu Pro Glu Asn Arg Ile Ser Lys Glu Lys Asp
85 90 95

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

Cys Met Leu Arg Asn Thr Thr Tyr Cys Ser Lys Val Ala Phe Pro Leu
115 120 125

Glu Val Val Gln Lys Asp Ser Cys Phe Asn Ser Pro Met Lys Leu Pro
130 135 140

Val His Lys Leu Tyr Ile Glu Tyr Gly Ile Gln Arg Ile Thr Cys Pro
145 150 155 160

Asn Val Asp Gly Tyr Phe Pro Ser Ser Val Lys Pro Thr Ile Thr Trp
165 170 175

Tyr Met Gly Cys Tyr Lys Ile Gln Asn Phe Asn Asn Val Ile Pro Glu
180 185 190

Gly Met Asn Leu Ser Phe Leu Ile Ala Leu Ile Ser Asn Asn Gly Asn
195 200 205

Tyr Thr Cys Val Val Thr Tyr Pro Glu Asn Gly Arg Thr Phe His Leu
210 215 220

Thr Arg Thr Leu Thr Val Lys Val Val Gly Ser Pro Lys Asn Ala Val
225 230 235 240

Pro Pro Val Ile His Ser Pro Asn Asp His Val Val Tyr Glu Lys Glu
245 250 255

Pro Gly Glu Glu Leu Leu Ile Pro Cys Thr Val Tyr Phe Ser Phe Leu
260 265 270

Met Asp Ser Arg Asn Glu Val Trp Trp Thr Ile Asp Gly Lys Lys Pro
275 280 285

[0124]

Asp Asp Ile Thr Ile Asp Val Thr Ile Asn Glu Ser Ile Ser His Ser
290 295 300

Arg Thr Glu Asp Glu Thr Arg Thr Gln Ile Leu Ser Ile Lys Lys Val
305 310 315 320

Thr Ser Glu Asp Leu Lys Arg Ser Tyr Val Cys His Ala Arg Ser Ala
325 330 335

Lys Gly Glu Val Ala Lys Ala Ala Lys Val Lys Gln Lys Val Pro Ala
340 345 350

Pro Arg Tyr Thr Val Glu Lys Cys Lys Glu Arg Glu Glu Lys Ile Ile
355 360 365

Leu Val Ser Ser Ala Asn Glu Ile Asp Val Arg Pro Cys Pro Leu Asn
370 375 380

Pro Asn Glu His Lys Gly Thr Ile Thr Trp Tyr Lys Asp Asp Ser Lys
385 390 395 400

Thr Pro Val Ser Thr Glu Gln Ala Ser Arg Ile His Gln His Lys Glu
 405 410 415

Lys Leu Trp Phe Val Pro Ala Lys Val Glu Asp Ser Gly His Tyr Tyr
 420 425 430

Cys Val Val Arg Asn Ser Ser Tyr Cys Leu Arg Ile Lys Ile Ser Ala
 435 440 445

Lys Phe Val Glu Asn Glu Pro Asn Leu Cys Tyr Asn Ala Gln Ala Ile
 450 455 460

Phe Lys Gln Lys Leu Pro Val Ala Gly Asp Gly Gly Leu Val Cys Pro
 465 470 475 480

Tyr Met Glu Phe Phe Lys Asn Glu Asn Asn Glu Leu Pro Lys Leu Gln
 485 490 495

Trp Tyr Lys Asp Cys Lys Pro Leu Leu Leu Asp Asn Ile His Phe Ser
 500 505 510

[0125] Gly Val Lys Asp Arg Leu Ile Val Met Asn Val Ala Glu Lys His Arg
 515 520 525

Gly Asn Tyr Thr Cys His Ala Ser Tyr Thr Tyr Leu Gly Lys Gln Tyr
 530 535 540

Pro Ile Thr Arg Val Ile Glu Phe Ile Thr Leu Glu Glu Asn Lys Pro
 545 550 555 560

Thr Arg Pro Val Ile Val Ser Pro Ala Asn Glu Thr Met Glu Val Asp
 565 570 575

Leu Gly Ser Gln Ile Gln Leu Ile Cys Asn Val Thr Gly Gln Leu Ser
 580 585 590

Asp Ile Ala Tyr Trp Lys Trp Asn Gly Ser Val Ile Asp Glu Asp Asp
 595 600 605

Pro Val Leu Gly Glu Asp Tyr Tyr Ser Val Glu Asn Pro Ala Asn Lys
 610 615 620

Arg Arg Ser Thr Leu Ile Thr Val Leu Asn Ile Ser Glu Ile Glu Ser

	625		630		635		640									
	Arg	Phe	Tyr	Lys	His	Pro	Phe	Thr	Cys	Phe	Ala	Lys	Asn	Thr	His	Gly
					645					650					655	
	Ile	Asp	Ala	Ala	Tyr	Ile	Gln	Leu	Ile	Tyr	Pro	Val	Thr	Asn	Gly	Gly
				660					665					670		
	Gly	Gly	Ser	Gly	Gly	Gly	Gly	Ser	Glu	Ile	Val	Leu	Thr	Gln	Ser	Pro
			675					680					685			
	Ala	Thr	Leu	Ser	Leu	Ser	Pro	Gly	Glu	Arg	Ala	Thr	Leu	Ser	Cys	Arg
		690					695					700				
	Ala	Ser	Gln	Ser	Val	Ser	Ser	Tyr	Leu	Ala	Trp	Tyr	Gln	Gln	Lys	Pro
	705					710					715					720
	Gly	Gln	Ala	Pro	Arg	Leu	Leu	Ile	Tyr	Asp	Ala	Ser	Asn	Arg	Ala	Thr
					725					730					735	
[0126]	Gly	Ile	Pro	Ala	Arg	Phe	Ser	Gly	Ser	Gly	Ser	Gly	Thr	Asp	Phe	Thr
				740					745					750		
	Leu	Thr	Ile	Ser	Ser	Leu	Glu	Pro	Glu	Asp	Phe	Ala	Val	Tyr	Tyr	Cys
			755					760					765			
	Gln	Gln	Ser	Ser	Asn	Trp	Pro	Arg	Thr	Phe	Gly	Gln	Gly	Thr	Lys	Val
		770					775					780				
	Glu	Ile	Lys	Arg	Thr	Val	Ala	Ala	Pro	Ser	Val	Phe	Ile	Phe	Pro	Pro
	785					790					795					800
	Ser	Asp	Glu	Gln	Leu	Lys	Ser	Gly	Thr	Ala	Ser	Val	Val	Cys	Leu	Leu
					805					810					815	
	Asn	Asn	Phe	Tyr	Pro	Arg	Glu	Ala	Lys	Val	Gln	Trp	Lys	Val	Asp	Asn
				820					825					830		
	Ala	Leu	Gln	Ser	Gly	Asn	Ser	Gln	Glu	Ser	Val	Thr	Glu	Gln	Asp	Ser
			835					840					845			
	Lys	Asp	Ser	Thr	Tyr	Ser	Leu	Ser	Ser	Thr	Leu	Thr	Leu	Ser	Lys	Ala
		850					855					860				

Asp Tyr Glu Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly
865 870 875 880

Leu Ser Ser Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys Gly Pro
885 890 895

Pro Cys Pro Pro Cys Pro Ala Pro Glu Phe Leu Gly Gly Pro Ser Val
900 905 910

Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr
915 920 925

Pro Glu Val Thr Cys Val Val Val Asp Val Ser Gln Glu Asp Pro Glu
930 935 940

Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys
945 950 955 960

Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr Tyr Arg Val Val Ser
965 970 975

[0127]

Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys
980 985 990

Cys Lys Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr Ile
995 1000 1005

Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu
1010 1015 1020

Pro Pro Ser Gln Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr
1025 1030 1035

Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp
1040 1045 1050

Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro
1055 1060 1065

Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Arg Leu Thr
1070 1075 1080

Val Asp Lys Ser Arg Trp Gln Glu Gly Asn Val Phe Ser Cys Ser
1085 1090 1095

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
1100 1105 1110

Ser Leu Ser Leu Gly Lys
1115

<210> 103

<211> 1122

<212> PRT

<213> 人工序列

<220>

<223> 人工序列的描述：合成多肽

<400> 103

Met Gly Trp Ser Cys Ile Ile Leu Phe Leu Val Ala Thr Ala Thr Gly
1 5 10 15

Val His Ser Glu Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu
20 25 30

[0128]

Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val
35 40 45

Ser Ser Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg
50 55 60

Leu Leu Ile Tyr Asp Ala Ser Asn Arg Ala Thr Gly Ile Pro Ala Arg
65 70 75 80

Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser
85 90 95

Leu Glu Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Ser Ser Asn
100 105 110

Trp Pro Arg Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg Thr
115 120 125

Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu
130 135 140

Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro
145 150 155 160

Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly
165 170 175

Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr
180 185 190

Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His
195 200 205

Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val
210 215 220

Thr Lys Ser Phe Asn Arg Gly Glu Cys Gly Gly Gly Ser Gly Gly
225 230 235 240

Gly Gly Ser Glu Arg Cys Asp Asp Trp Gly Leu Asp Thr Met Arg Gln
245 250 255

[0129]

Ile Gln Val Phe Glu Asp Glu Pro Ala Arg Ile Lys Cys Pro Leu Phe
260 265 270

Glu His Phe Leu Lys Phe Asn Tyr Ser Thr Ala His Ser Ala Gly Leu
275 280 285

Thr Leu Ile Trp Tyr Trp Thr Arg Gln Asp Arg Asp Leu Glu Glu Pro
290 295 300

Ile Asn Phe Arg Leu Pro Glu Asn Arg Ile Ser Lys Glu Lys Asp Val
305 310 315 320

Leu Trp Phe Arg Pro Thr Leu Leu Asn Asp Thr Gly Asn Tyr Thr Cys
325 330 335

Met Leu Arg Asn Thr Thr Tyr Cys Ser Lys Val Ala Phe Pro Leu Glu
340 345 350

Val Val Gln Lys Asp Ser Cys Phe Asn Ser Pro Met Lys Leu Pro Val
355 360 365

His Lys Leu Tyr Ile Glu Tyr Gly Ile Gln Arg Ile Thr Cys Pro Asn
 370 375 380

Val Asp Gly Tyr Phe Pro Ser Ser Val Lys Pro Thr Ile Thr Trp Tyr
 385 390 395 400

Met Gly Cys Tyr Lys Ile Gln Asn Phe Asn Asn Val Ile Pro Glu Gly
 405 410 415

Met Asn Leu Ser Phe Leu Ile Ala Leu Ile Ser Asn Asn Gly Asn Tyr
 420 425 430

Thr Cys Val Val Thr Tyr Pro Glu Asn Gly Arg Thr Phe His Leu Thr
 435 440 445

Arg Thr Leu Thr Val Lys Val Val Gly Ser Pro Lys Asn Ala Val Pro
 450 455 460

Pro Val Ile His Ser Pro Asn Asp His Val Val Tyr Glu Lys Glu Pro
 465 470 475 480

[0130] Gly Glu Glu Leu Leu Ile Pro Cys Thr Val Tyr Phe Ser Phe Leu Met
 485 490 495

Asp Ser Arg Asn Glu Val Trp Trp Thr Ile Asp Gly Lys Lys Pro Asp
 500 505 510

Asp Ile Thr Ile Asp Val Thr Ile Asn Glu Ser Ile Ser His Ser Arg
 515 520 525

Thr Glu Asp Glu Thr Arg Thr Gln Ile Leu Ser Ile Lys Lys Val Thr
 530 535 540

Ser Glu Asp Leu Lys Arg Ser Tyr Val Cys His Ala Arg Ser Ala Lys
 545 550 555 560

Gly Glu Val Ala Lys Ala Ala Lys Val Lys Gln Lys Val Pro Ala Pro
 565 570 575

Arg Tyr Thr Val Glu Lys Cys Lys Glu Arg Glu Glu Lys Ile Ile Leu
 580 585 590

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

	595		600		605													
	Asn 610	Glu	His	Lys	Gly	Thr	Ile 615	Thr	Trp	Tyr	Lys	Asp 620	Asp	Ser	Lys	Thr		
	Pro 625	Val	Ser	Thr	Glu	Gln 630	Ala	Ser	Arg	Ile	His 635	Gln	His	Lys	Glu	Lys 640		
	Leu	Trp	Phe	Val	Pro 645	Ala	Lys	Val	Glu	Asp 650	Ser	Gly	His	Tyr	Tyr	Cys 655		
	Val	Val	Arg	Asn 660	Ser	Ser	Tyr	Cys	Leu 665	Arg	Ile	Lys	Ile	Ser	Ala	Lys 670		
	Phe	Val	Glu 675	Asn	Glu	Pro	Asn 680	Leu	Cys	Tyr	Asn	Ala	Gln 685	Ala	Ile	Phe		
	Lys 690	Gln	Lys	Leu	Pro	Val	Ala 695	Gly	Asp	Gly	Gly	Leu 700	Val	Cys	Pro	Tyr		
[0131]	Met 705	Glu	Phe	Phe	Lys	Asn 710	Glu	Asn	Asn	Glu	Leu 715	Pro	Lys	Leu	Gln	Trp 720		
	Tyr	Lys	Asp	Cys	Lys 725	Pro	Leu	Leu	Leu	Asp 730	Asn	Ile	His	Phe	Ser	Gly 735		
	Val	Lys	Asp	Arg 740	Leu	Ile	Val	Met	Asn 745	Val	Ala	Glu	Lys	His 750	Arg	Gly		
	Asn	Tyr	Thr 755	Cys	His	Ala	Ser	Tyr 760	Thr	Tyr	Leu	Gly	Lys 765	Gln	Tyr	Pro		
	Ile 770	Thr	Arg	Val	Ile	Glu	Phe 775	Ile	Thr	Leu	Glu	Glu	Asn	Lys	Pro	Thr		
	Arg 785	Pro	Val	Ile	Val	Ser 790	Pro	Ala	Asn	Glu	Thr 795	Met	Glu	Val	Asp	Leu 800		
	Gly	Ser	Gln	Ile	Gln 805	Leu	Ile	Cys	Asn	Val 810	Thr	Gly	Gln	Leu	Ser	Asp 815		
	Ile	Ala	Tyr	Trp 820	Lys	Trp	Asn	Gly	Ser 825	Val	Ile	Asp	Glu	Asp	Asp	Pro 830		

Val Leu Gly Glu Asp Tyr Tyr Ser Val Glu Asn Pro Ala Asn Lys Arg
835 840 845

Arg Ser Thr Leu Ile Thr Val Leu Asn Ile Ser Glu Ile Glu Ser Arg
850 855 860

Phe Tyr Lys His Pro Phe Thr Cys Phe Ala Lys Asn Thr His Gly Ile
865 870 875 880

Asp Ala Ala Tyr Ile Gln Leu Ile Tyr Pro Val Thr Asn Ser Gly Asp
885 890 895

Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Phe Leu Gly Gly
900 905 910

Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile
915 920 925

Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser Gln Glu
930 935 940

[0132]

Asp Pro Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val His
945 950 955 960

Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr Tyr Arg
965 970 975

Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys
980 985 990

Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu
995 1000 1005

Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val
1010 1015 1020

Tyr Thr Leu Pro Pro Ser Gln Glu Glu Met Thr Lys Asn Gln Val
1025 1030 1035

Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala
1040 1045 1050

Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
1055 1060 1065

Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser
1070 1075 1080

Arg Leu Thr Val Asp Lys Ser Arg Trp Gln Glu Gly Asn Val Phe
1085 1090 1095

Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln
1100 1105 1110

Lys Ser Leu Ser Leu Ser Leu Gly Lys
1115 1120

<210> 104

<211> 1126

<212> PRT

<213> 人工序列

<220>

<223> 人工序列的描述：合成多肽

[0133]

<400> 104

Met Gly Trp Ser Cys Ile Ile Leu Phe Leu Val Ala Thr Ala Thr Gly
1 5 10 15

Val His Ser Glu Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu
20 25 30

Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Lys Gly Val
35 40 45

Ser Thr Ser Gly Tyr Ser Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly
50 55 60

Gln Ala Pro Arg Leu Leu Ile Tyr Leu Ala Ser Tyr Leu Glu Ser Gly
65 70 75 80

Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu
85 90 95

Thr Ile Ser Ser Leu Glu Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln
100 105 110

His Ser Arg Asp Leu Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu
115 120 125

Ile Lys Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser
130 135 140

Asp Glu Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn
145 150 155 160

Asn Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala
165 170 175

Leu Gln Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys
180 185 190

Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp
195 200 205

Tyr Glu Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu
210 215 220

[0134]

Ser Ser Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys Gly Gly Gly
225 230 235 240

Gly Ser Gly Gly Gly Gly Ser Glu Arg Cys Asp Asp Trp Gly Leu Asp
245 250 255

Thr Met Arg Gln Ile Gln Val Phe Glu Asp Glu Pro Ala Arg Ile Lys
260 265 270

Cys Pro Leu Phe Glu His Phe Leu Lys Phe Asn Tyr Ser Thr Ala His
275 280 285

Ser Ala Gly Leu Thr Leu Ile Trp Tyr Trp Thr Arg Gln Asp Arg Asp
290 295 300

Leu Glu Glu Pro Ile Asn Phe Arg Leu Pro Glu Asn Arg Ile Ser Lys
305 310 315 320

Glu Lys Asp Val Leu Trp Phe Arg Pro Thr Leu Leu Asn Asp Thr Gly
325 330 335

Asn Tyr Thr Cys Met Leu Arg Asn Thr Thr Tyr Cys Ser Lys Val Ala
 340 345 350

Phe Pro Leu Glu Val Val Gln Lys Asp Ser Cys Phe Asn Ser Pro Met
 355 360 365

Lys Leu Pro Val His Lys Leu Tyr Ile Glu Tyr Gly Ile Gln Arg Ile
 370 375 380

Thr Cys Pro Asn Val Asp Gly Tyr Phe Pro Ser Ser Val Lys Pro Thr
 385 390 395 400

Ile Thr Trp Tyr Met Gly Cys Tyr Lys Ile Gln Asn Phe Asn Asn Val
 405 410 415

Ile Pro Glu Gly Met Asn Leu Ser Phe Leu Ile Ala Leu Ile Ser Asn
 420 425 430

Asn Gly Asn Tyr Thr Cys Val Val Thr Tyr Pro Glu Asn Gly Arg Thr
 435 440 445

[0135] Phe His Leu Thr Arg Thr Leu Thr Val Lys Val Val Gly Ser Pro Lys
 450 455 460

Asn Ala Val Pro Pro Val Ile His Ser Pro Asn Asp His Val Val Tyr
 465 470 475 480

Glu Lys Glu Pro Gly Glu Glu Leu Leu Ile Pro Cys Thr Val Tyr Phe
 485 490 495

Ser Phe Leu Met Asp Ser Arg Asn Glu Val Trp Trp Thr Ile Asp Gly
 500 505 510

Lys Lys Pro Asp Asp Ile Thr Ile Asp Val Thr Ile Asn Glu Ser Ile
 515 520 525

Ser His Ser Arg Thr Glu Asp Glu Thr Arg Thr Gln Ile Leu Ser Ile
 530 535 540

Lys Lys Val Thr Ser Glu Asp Leu Lys Arg Ser Tyr Val Cys His Ala
 545 550 555 560

Arg Ser Ala Lys Gly Glu Val Ala Lys Ala Ala Lys Val Lys Gln Lys

	565		570		575														
	Val	Pro	Ala	Pro	Arg	Tyr	Thr	Val	Glu	Lys	Cys	Lys	Glu	Arg	Glu	Glu			
				580					585					590					
	Lys	Ile	Ile	Leu	Val	Ser	Ser	Ala	Asn	Glu	Ile	Asp	Val	Arg	Pro	Cys			
			595					600					605						
	Pro	Leu	Asn	Pro	Asn	Glu	His	Lys	Gly	Thr	Ile	Thr	Trp	Tyr	Lys	Asp			
		610					615						620						
	Asp	Ser	Lys	Thr	Pro	Val	Ser	Thr	Glu	Gln	Ala	Ser	Arg	Ile	His	Gln			
	625					630					635					640			
	His	Lys	Glu	Lys	Leu	Trp	Phe	Val	Pro	Ala	Lys	Val	Glu	Asp	Ser	Gly			
					645					650						655			
	His	Tyr	Tyr	Cys	Val	Val	Arg	Asn	Ser	Ser	Tyr	Cys	Leu	Arg	Ile	Lys			
				660					665					670					
[0136]	Ile	Ser	Ala	Lys	Phe	Val	Glu	Asn	Glu	Pro	Asn	Leu	Cys	Tyr	Asn	Ala			
			675					680					685						
	Gln	Ala	Ile	Phe	Lys	Gln	Lys	Leu	Pro	Val	Ala	Gly	Asp	Gly	Gly	Leu			
		690					695					700							
	Val	Cys	Pro	Tyr	Met	Glu	Phe	Phe	Lys	Asn	Glu	Asn	Asn	Glu	Leu	Pro			
	705					710					715					720			
	Lys	Leu	Gln	Trp	Tyr	Lys	Asp	Cys	Lys	Pro	Leu	Leu	Leu	Asp	Asn	Ile			
					725					730					735				
	His	Phe	Ser	Gly	Val	Lys	Asp	Arg	Leu	Ile	Val	Met	Asn	Val	Ala	Glu			
				740					745					750					
	Lys	His	Arg	Gly	Asn	Tyr	Thr	Cys	His	Ala	Ser	Tyr	Thr	Tyr	Leu	Gly			
			755					760					765						
	Lys	Gln	Tyr	Pro	Ile	Thr	Arg	Val	Ile	Glu	Phe	Ile	Thr	Leu	Glu	Glu			
		770					775					780							
	Asn	Lys	Pro	Thr	Arg	Pro	Val	Ile	Val	Ser	Pro	Ala	Asn	Glu	Thr	Met			
	785					790					795					800			

Glu Val Asp Leu Gly Ser Gln Ile Gln Leu Ile Cys Asn Val Thr Gly
805 810 815

Gln Leu Ser Asp Ile Ala Tyr Trp Lys Trp Asn Gly Ser Val Ile Asp
820 825 830

Glu Asp Asp Pro Val Leu Gly Glu Asp Tyr Tyr Ser Val Glu Asn Pro
835 840 845

Ala Asn Lys Arg Arg Ser Thr Leu Ile Thr Val Leu Asn Ile Ser Glu
850 855 860

Ile Glu Ser Arg Phe Tyr Lys His Pro Phe Thr Cys Phe Ala Lys Asn
865 870 875 880

Thr His Gly Ile Asp Ala Ala Tyr Ile Gln Leu Ile Tyr Pro Val Thr
885 890 895

Asn Ser Gly Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu
900 905 910

[0137]

Phe Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
915 920 925

Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp
930 935 940

Val Ser Gln Glu Asp Pro Glu Val Gln Phe Asn Trp Tyr Val Asp Gly
945 950 955 960

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe Asn
965 970 975

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
980 985 990

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro
995 1000 1005

Ser Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg
1010 1015 1020

Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Gln Glu Glu Met Thr
1025 1030 1035

Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro
1040 1045 1050

Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn
1055 1060 1065

Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe
1070 1075 1080

Phe Leu Tyr Ser Arg Leu Thr Val Asp Lys Ser Arg Trp Gln Glu
1085 1090 1095

Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
1100 1105 1110

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Leu Gly Lys
1115 1120 1125

[0138]

<210> 105

<211> 714

<212> PRT

<213> 人工序列

<220>

<223> 人工序列的描述：合成多肽

<400> 105

Met Gly Trp Ser Cys Ile Ile Leu Phe Leu Val Ala Thr Ala Thr Gly
1 5 10 15

Val His Ser Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln
20 25 30

Pro Gly Arg Ser Leu Arg Leu Asp Cys Lys Ala Ser Gly Ile Thr Phe
35 40 45

Ser Asn Ser Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Cys Leu
50 55 60

Glu Trp Val Ala Val Ile Trp Tyr Asp Gly Ser Lys Arg Tyr Tyr Ala
65 70 75 80

Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn
85 90 95

Thr Leu Phe Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val
100 105 110

Tyr Tyr Cys Ala Thr Asn Asp Asp Tyr Trp Gly Gln Gly Thr Leu Val
115 120 125

Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
130 135 140

Gly Gly Ser Gly Gly Gly Gly Ser Glu Ile Val Leu Thr Gln Ser Pro
145 150 155 160

Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg
165 170 175

Ala Ser Gln Ser Val Ser Ser Tyr Leu Ala Trp Tyr Gln Gln Lys Pro
180 185 190

[0139]

Gly Gln Ala Pro Arg Leu Leu Ile Tyr Asp Ala Ser Asn Arg Ala Thr
195 200 205

Gly Ile Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr
210 215 220

Leu Thr Ile Ser Ser Leu Glu Pro Glu Asp Phe Ala Val Tyr Tyr Cys
225 230 235 240

Gln Gln Ser Ser Asn Trp Pro Arg Thr Phe Gly Cys Gly Thr Lys Val
245 250 255

Glu Ile Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Val Gln
260 265 270

Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg Ser Leu Arg
275 280 285

Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Val Tyr Gly Met Asn
290 295 300

Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala Ile Ile
 305 310 315 320

Trp Tyr Asp Gly Asp Asn Gln Tyr Tyr Ala Asp Ser Val Lys Gly Arg
 325 330 335

Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr Leu Gln Met
 340 345 350

Asn Gly Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Asp
 355 360 365

Leu Arg Thr Gly Pro Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr
 370 375 380

Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro
 385 390 395 400

Cys Ser Arg Ser Thr Ser Glu Ser Thr Ala Ala Leu Gly Cys Leu Val
 405 410 415

[0140] Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala
 420 425 430

Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly
 435 440 445

Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly
 450 455 460

Thr Lys Thr Tyr Thr Cys Asn Val Asp His Lys Pro Ser Asn Thr Lys
 465 470 475 480

Val Asp Lys Arg Val Glu Ser Lys Tyr Gly Pro Pro Cys Pro Pro Cys
 485 490 495

Pro Ala Pro Glu Phe Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro
 500 505 510

Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys
 515 520 525

Val Val Val Asp Val Ser Gln Glu Asp Pro Glu Val Gln Phe Asn Trp

	530		535		540															
	Tyr	Val	Asp	Gly	Val	Glu	Val	His	Asn	Ala	Lys	Thr	Lys	Pro	Arg	Glu				
	545					550					555					560				
	Glu	Gln	Phe	Asn	Ser	Thr	Tyr	Arg	Val	Val	Ser	Val	Leu	Thr	Val	Leu				
					565					570					575					
	His	Gln	Asp	Trp	Leu	Asn	Gly	Lys	Glu	Tyr	Lys	Cys	Lys	Val	Ser	Asn				
				580					585					590						
	Lys	Gly	Leu	Pro	Ser	Ser	Ile	Glu	Lys	Thr	Ile	Ser	Lys	Ala	Lys	Gly				
			595					600					605							
	Gln	Pro	Arg	Glu	Pro	Gln	Val	Tyr	Thr	Leu	Pro	Pro	Ser	Gln	Glu	Glu				
		610					615					620								
	Met	Thr	Lys	Asn	Gln	Val	Ser	Leu	Thr	Cys	Leu	Val	Lys	Gly	Phe	Tyr				
	625					630					635					640				
[0141]	Pro	Ser	Asp	Ile	Ala	Val	Glu	Trp	Glu	Ser	Asn	Gly	Gln	Pro	Glu	Asn				
					645					650					655					
	Asn	Tyr	Lys	Thr	Thr	Pro	Pro	Val	Leu	Asp	Ser	Asp	Gly	Ser	Phe	Phe				
				660					665					670						
	Leu	Tyr	Ser	Arg	Leu	Thr	Val	Asp	Lys	Ser	Arg	Trp	Gln	Glu	Gly	Asn				
			675					680					685							
	Val	Phe	Ser	Cys	Ser	Val	Met	His	Glu	Ala	Leu	His	Asn	His	Tyr	Thr				
		690					695					700								
	Gln	Lys	Ser	Leu	Ser	Leu	Ser	Leu	Gly	Lys										
	705					710														
	<210>	106																		
	<211>	714																		
	<212>	PRT																		
	<213>	人工序列																		
	<220>																			
	<223>	人工序列的描述: 合成多肽																		
	<400>	106																		
	Met	Gly	Trp	Ser	Cys	Ile	Ile	Leu	Phe	Leu	Val	Ala	Thr	Ala	Thr	Gly				

	1	5	10	15
	Val His Ser	Glu Ile Val	Leu Thr Gln Ser	Pro Ala Thr Leu Ser Leu
		20	25	30
	Ser Pro Gly	Glu Arg Ala Thr	Leu Ser Cys Arg	Ala Ser Gln Ser Val
		35	40	45
	Ser Ser Tyr	Leu Ala Trp Tyr	Gln Gln Lys Pro	Gly Gln Ala Pro Arg
		50	55	60
	Leu Leu Ile	Tyr Asp Ala Ser	Asn Arg Ala Thr	Gly Ile Pro Ala Arg
		65	70	75
	Phe Ser Gly	Ser Gly Ser Gly	Thr Asp Phe Thr	Leu Thr Ile Ser Ser
		85	90	95
	Leu Glu Pro	Glu Asp Phe Ala	Val Tyr Tyr Cys	Gln Gln Ser Ser Asn
		100	105	110
[0142]	Trp Pro Arg	Thr Phe Gly Cys	Gly Thr Lys Val	Glu Ile Lys Gly Gly
		115	120	125
	Gly Gly Ser	Gly Gly Gly Gly	Ser Gly Gly Gly	Gly Ser Gly Gly Gly
		130	135	140
	Gly Ser Gln	Val Gln Leu Val	Glu Ser Gly Gly	Gly Val Val Gln Pro
		145	150	155
	Gly Arg Ser	Leu Arg Leu Asp	Cys Lys Ala Ser	Gly Ile Thr Phe Ser
		165	170	175
	Asn Ser Gly	Met His Trp Val	Arg Gln Ala Pro	Gly Lys Cys Leu Glu
		180	185	190
	Trp Val Ala	Val Ile Trp Tyr	Asp Gly Ser Lys	Arg Tyr Tyr Ala Asp
		195	200	205
	Ser Val Lys	Gly Arg Phe Thr	Ile Ser Arg Asp	Asn Ser Lys Asn Thr
		210	215	220
	Leu Phe Leu	Gln Met Asn Ser	Leu Arg Ala Glu	Asp Thr Ala Val Tyr
		225	230	235
				240

Tyr Cys Ala Thr Asn Asp Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr
245 250 255

Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Val Gln
260 265 270

Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg Ser Leu Arg
275 280 285

Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Val Tyr Gly Met Asn
290 295 300

Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala Ile Ile
305 310 315 320

Trp Tyr Asp Gly Asp Asn Gln Tyr Tyr Ala Asp Ser Val Lys Gly Arg
325 330 335

Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr Leu Gln Met
340 345 350

[0143]

Asn Gly Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Asp
355 360 365

Leu Arg Thr Gly Pro Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr
370 375 380

Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro
385 390 395 400

Cys Ser Arg Ser Thr Ser Glu Ser Thr Ala Ala Leu Gly Cys Leu Val
405 410 415

Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala
420 425 430

Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly
435 440 445

Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly
450 455 460

Thr Lys Thr Tyr Thr Cys Asn Val Asp His Lys Pro Ser Asn Thr Lys
 465 470 475 480

Val Asp Lys Arg Val Glu Ser Lys Tyr Gly Pro Pro Cys Pro Pro Cys
 485 490 495

Pro Ala Pro Glu Phe Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro
 500 505 510

Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys
 515 520 525

Val Val Val Asp Val Ser Gln Glu Asp Pro Glu Val Gln Phe Asn Trp
 530 535 540

Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu
 545 550 555 560

Glu Gln Phe Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu
 565 570 575

[0144]

His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn
 580 585 590

Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly
 595 600 605

Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Gln Glu Glu
 610 615 620

Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr
 625 630 635 640

Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn
 645 650 655

Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe
 660 665 670

Leu Tyr Ser Arg Leu Thr Val Asp Lys Ser Arg Trp Gln Glu Gly Asn
 675 680 685

Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr
690 695 700

Gln Lys Ser Leu Ser Leu Ser Leu Gly Lys
705 710

<210> 107

<211> 714

<212> PRT

<213> 人工序列

<220>

<223> 人工序列的描述: 合成多肽

<400> 107

Met Gly Trp Ser Cys Ile Ile Leu Phe Leu Val Ala Thr Ala Thr Gly
1 5 10 15

Val His Ser Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln
20 25 30

Pro Gly Arg Ser Leu Arg Leu Asp Cys Lys Ala Ser Gly Ile Thr Phe
35 40 45

[0145]

Ser Asn Ser Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu
50 55 60

Glu Trp Val Ala Val Ile Trp Tyr Asp Gly Ser Lys Arg Tyr Tyr Ala
65 70 75 80

Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn
85 90 95

Thr Leu Phe Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val
100 105 110

Tyr Tyr Cys Ala Thr Asn Asp Asp Tyr Trp Gly Gln Gly Thr Leu Val
115 120 125

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

Pro Cys Ser Arg Ser Thr Ser Glu Ser Thr Ala Ala Leu Gly Cys Leu
145 150 155 160

Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly
 165 170 175

Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser
 180 185 190

Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu
 195 200 205

Gly Thr Lys Thr Tyr Thr Cys Asn Val Asp His Lys Pro Ser Asn Thr
 210 215 220

Lys Val Asp Lys Arg Val Glu Ser Lys Tyr Gly Pro Pro Cys Pro Pro
 225 230 235 240

Cys Pro Ala Pro Glu Phe Leu Gly Gly Pro Ser Val Phe Leu Phe Pro
 245 250 255

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

[0146] Cys Val Val Val Asp Val Ser Gln Glu Asp Pro Glu Val Gln Phe Asn
 275 280 285

Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg
 290 295 300

Glu Glu Gln Phe Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val
 305 310 315 320

Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser
 325 330 335

Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys
 340 345 350

Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Gln Glu
 355 360 365

Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe
 370 375 380

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

	385		390			395		400								
	Asn	Asn	Tyr	Lys	Thr	Thr	Pro	Pro	Val	Leu	Asp	Ser	Asp	Gly	Ser	Phe
					405					410					415	
	Phe	Leu	Tyr	Ser	Arg	Leu	Thr	Val	Asp	Lys	Ser	Arg	Trp	Gln	Glu	Gly
				420					425					430		
	Asn	Val	Phe	Ser	Cys	Ser	Val	Met	His	Glu	Ala	Leu	His	Asn	His	Tyr
			435					440					445			
	Thr	Gln	Lys	Ser	Leu	Ser	Leu	Ser	Leu	Gly	Lys	Gly	Gly	Gly	Gly	Ser
		450					455					460				
	Gly	Gly	Gly	Gly	Ser	Gln	Val	Gln	Leu	Val	Glu	Ser	Gly	Gly	Gly	Val
	465					470					475					480
	Val	Gln	Pro	Gly	Arg	Ser	Leu	Arg	Leu	Ser	Cys	Ala	Ala	Ser	Gly	Phe
					485					490					495	
[0147]	Thr	Phe	Ser	Val	Tyr	Gly	Met	Asn	Trp	Val	Arg	Gln	Ala	Pro	Gly	Lys
				500					505					510		
	Cys	Leu	Glu	Trp	Val	Ala	Ile	Ile	Trp	Tyr	Asp	Gly	Asp	Asn	Gln	Tyr
			515					520					525			
	Tyr	Ala	Asp	Ser	Val	Lys	Gly	Arg	Phe	Thr	Ile	Ser	Arg	Asp	Asn	Ser
		530					535						540			
	Lys	Asn	Thr	Leu	Tyr	Leu	Gln	Met	Asn	Gly	Leu	Arg	Ala	Glu	Asp	Thr
	545					550					555					560
	Ala	Val	Tyr	Tyr	Cys	Ala	Arg	Asp	Leu	Arg	Thr	Gly	Pro	Phe	Asp	Tyr
					565					570					575	
	Trp	Gly	Gln	Gly	Thr	Leu	Val	Thr	Val	Ser	Ser	Gly	Gly	Gly	Gly	Ser
				580					585					590		
	Gly	Gly	Gly	Gly	Ser	Gly	Gly	Gly	Gly	Ser	Gly	Gly	Gly	Gly	Ser	Glu
			595					600					605			
	Ile	Val	Leu	Thr	Gln	Ser	Pro	Asp	Phe	Gln	Ser	Val	Thr	Pro	Lys	Glu
		610					615					620				

Lys Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Gly Ser Ser Leu
625 630 635 640

His Trp Tyr Gln Gln Lys Pro Asp Gln Ser Pro Lys Leu Leu Ile Lys
645 650 655

Tyr Ala Ser Gln Ser Phe Ser Gly Val Pro Ser Arg Phe Ser Gly Ser
660 665 670

Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Asn Ser Leu Glu Ala Glu
675 680 685

Asp Ala Ala Ala Tyr Tyr Cys His Gln Ser Ser Ser Leu Pro Phe Thr
690 695 700

Phe Gly Cys Gly Thr Lys Val Asp Ile Lys
705 710

<210> 108

<211> 714

<212> PRT

[0148] <213> 人工序列

<220>

<223> 人工序列的描述：合成多肽

<400> 108

Met Gly Trp Ser Cys Ile Ile Leu Phe Leu Val Ala Thr Ala Thr Gly
1 5 10 15

Val His Ser Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln
20 25 30

Pro Gly Arg Ser Leu Arg Leu Asp Cys Lys Ala Ser Gly Ile Thr Phe
35 40 45

Ser Asn Ser Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu
50 55 60

Glu Trp Val Ala Val Ile Trp Tyr Asp Gly Ser Lys Arg Tyr Tyr Ala
65 70 75 80

Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn
85 90 95

Thr Leu Phe Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val
 100 105 110

Tyr Tyr Cys Ala Thr Asn Asp Asp Tyr Trp Gly Gln Gly Thr Leu Val
 115 120 125

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

Pro Cys Ser Arg Ser Thr Ser Glu Ser Thr Ala Ala Leu Gly Cys Leu
 145 150 155 160

Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly
 165 170 175

Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser
 180 185 190

Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu
 195 200 205

[0149]

Gly Thr Lys Thr Tyr Thr Cys Asn Val Asp His Lys Pro Ser Asn Thr
 210 215 220

Lys Val Asp Lys Arg Val Glu Ser Lys Tyr Gly Pro Pro Cys Pro Pro
 225 230 235 240

Cys Pro Ala Pro Glu Phe Leu Gly Gly Pro Ser Val Phe Leu Phe Pro
 245 250 255

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

Cys Val Val Val Asp Val Ser Gln Glu Asp Pro Glu Val Gln Phe Asn
 275 280 285

Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg
 290 295 300

Glu Glu Gln Phe Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val
 305 310 315 320

Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser
325 330 335

Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys
340 345 350

Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Gln Glu
355 360 365

Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe
370 375 380

Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu
385 390 395 400

Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe
405 410 415

Phe Leu Tyr Ser Arg Leu Thr Val Asp Lys Ser Arg Trp Gln Glu Gly
420 425 430

[0150]

Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr
435 440 445

Thr Gln Lys Ser Leu Ser Leu Ser Leu Gly Lys Gly Gly Gly Ser
450 455 460

Gly Gly Gly Gly Ser Glu Ile Val Leu Thr Gln Ser Pro Asp Phe Gln
465 470 475 480

Ser Val Thr Pro Lys Glu Lys Val Thr Ile Thr Cys Arg Ala Ser Gln
485 490 495

Ser Ile Gly Ser Ser Leu His Trp Tyr Gln Gln Lys Pro Asp Gln Ser
500 505 510

Pro Lys Leu Leu Ile Lys Tyr Ala Ser Gln Ser Phe Ser Gly Val Pro
515 520 525

Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile
530 535 540

Asn Ser Leu Glu Ala Glu Asp Ala Ala Ala Tyr Tyr Cys His Gln Ser
545 550 555 560

Ser Ser Leu Pro Phe Thr Phe Gly Cys Gly Thr Lys Val Asp Ile Lys
565 570 575

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
580 585 590

Gly Gly Gly Ser Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val
595 600 605

Gln Pro Gly Arg Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr
610 615 620

Phe Ser Val Tyr Gly Met Asn Trp Val Arg Gln Ala Pro Gly Lys Cys
625 630 635 640

Leu Glu Trp Val Ala Ile Ile Trp Tyr Asp Gly Asp Asn Gln Tyr Tyr
645 650 655

[0151]

Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys
660 665 670

Asn Thr Leu Tyr Leu Gln Met Asn Gly Leu Arg Ala Glu Asp Thr Ala
675 680 685

Val Tyr Tyr Cys Ala Arg Asp Leu Arg Thr Gly Pro Phe Asp Tyr Trp
690 695 700

Gly Gln Gly Thr Leu Val Thr Val Ser Ser
705 710

<210> 109

<211> 683

<212> PRT

<213> 人工序列

<220>

<223> 人工序列的描述：合成多肽

<400> 109

Met Gly Trp Ser Cys Ile Ile Leu Phe Leu Val Ala Thr Ala Thr Gly
1 5 10 15

Val His Ser Glu Ile Val Leu Thr Gln Ser Pro Asp Phe Gln Ser Val
 20 25 30

Thr Pro Lys Glu Lys Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile
 35 40 45

Gly Ser Ser Leu His Trp Tyr Gln Gln Lys Pro Asp Gln Ser Pro Lys
 50 55 60

Leu Leu Ile Lys Tyr Ala Ser Gln Ser Phe Ser Gly Val Pro Ser Arg
 65 70 75 80

Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Asn Ser
 85 90 95

Leu Glu Ala Glu Asp Ala Ala Ala Tyr Tyr Cys His Gln Ser Ser Ser
 100 105 110

Leu Pro Phe Thr Phe Gly Pro Gly Thr Lys Val Asp Ile Lys Arg Thr
 115 120 125

[0152] Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu
 130 135 140

Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro
 145 150 155 160

Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly
 165 170 175

Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr
 180 185 190

Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His
 195 200 205

Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val
 210 215 220

Thr Lys Ser Phe Asn Arg Gly Glu Cys Gly Ser Gly Gln Val Gln Leu
 225 230 235 240

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

	245	250	255																
	Ser	Cys	Lys	Ala	Ser	Gly	Tyr	Thr	Phe	Thr	Asn	Tyr	Tyr	Met	Tyr	Trp			
				260					265					270					
	Val	Arg	Gln	Ala	Pro	Gly	Gln	Gly	Leu	Glu	Trp	Met	Gly	Gly	Ile	Asn			
			275					280					285						
	Pro	Ser	Asn	Gly	Gly	Thr	Asn	Phe	Asn	Glu	Lys	Phe	Lys	Asn	Arg	Val			
		290					295					300							
	Thr	Leu	Thr	Thr	Asp	Ser	Ser	Thr	Thr	Thr	Ala	Tyr	Met	Glu	Leu	Lys			
	305					310					315					320			
	Ser	Leu	Gln	Phe	Asp	Asp	Thr	Ala	Val	Tyr	Tyr	Cys	Ala	Arg	Arg	Asp			
				325						330					335				
	Tyr	Arg	Phe	Asp	Met	Gly	Phe	Asp	Tyr	Trp	Gly	Gln	Gly	Thr	Thr	Val			
			340						345					350					
[0153]	Thr	Val	Ser	Ser	Ala	Ser	Thr	Lys	Gly	Pro	Ser	Val	Phe	Pro	Leu	Ala			
			355					360					365						
	Pro	Cys	Ser	Arg	Ser	Thr	Ser	Glu	Ser	Thr	Ala	Ala	Leu	Gly	Cys	Leu			
		370					375					380							
	Val	Lys	Asp	Tyr	Phe	Pro	Glu	Pro	Val	Thr	Val	Ser	Trp	Asn	Ser	Gly			
	385					390					395					400			
	Ala	Leu	Thr	Ser	Gly	Val	His	Thr	Phe	Pro	Ala	Val	Leu	Gln	Ser	Ser			
				405						410					415				
	Gly	Leu	Tyr	Ser	Leu	Ser	Ser	Val	Val	Thr	Val	Pro	Ser	Ser	Ser	Leu			
				420					425					430					
	Gly	Thr	Lys	Thr	Tyr	Thr	Cys	Asn	Val	Asp	His	Lys	Pro	Ser	Asn	Thr			
			435					440					445						
	Lys	Val	Asp	Lys	Arg	Val	Glu	Ser	Lys	Tyr	Gly	Pro	Pro	Cys	Pro	Pro			
		450					455					460							
	Cys	Pro	Ala	Pro	Glu	Phe	Leu	Gly	Gly	Pro	Ser	Val	Phe	Leu	Phe	Pro			
	465					470					475				480				

Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr
485 490 495

Cys Val Val Val Asp Val Ser Gln Glu Asp Pro Glu Val Gln Phe Asn
500 505 510

Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg
515 520 525

Glu Glu Gln Phe Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val
530 535 540

Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser
545 550 555 560

Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys
565 570 575

Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Gln Glu
580 585 590

[0154]

Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe
595 600 605

Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu
610 615 620

Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe
625 630 635 640

Phe Leu Tyr Ser Arg Leu Thr Val Asp Lys Ser Arg Trp Gln Glu Gly
645 650 655

Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr
660 665 670

Thr Gln Lys Ser Leu Ser Leu Ser Leu Gly Lys
675 680

<210> 110

<211> 687

<212> PRT

<213> 人工序列

<220>

<223> 人工序列的描述：合成多肽

<400> 110

Met Gly Trp Ser Cys Ile Ile Leu Phe Leu Val Ala Thr Ala Thr Gly
1 5 10 15

Val His Ser Glu Ile Val Leu Thr Gln Ser Pro Asp Phe Gln Ser Val
20 25 30

Thr Pro Lys Glu Lys Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile
35 40 45

Gly Ser Ser Leu His Trp Tyr Gln Gln Lys Pro Asp Gln Ser Pro Lys
50 55 60

Leu Leu Ile Lys Tyr Ala Ser Gln Ser Phe Ser Gly Val Pro Ser Arg
65 70 75 80

Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Asn Ser
85 90 95

[0155]

Leu Glu Ala Glu Asp Ala Ala Ala Tyr Tyr Cys His Gln Ser Ser Ser
100 105 110

Leu Pro Phe Thr Phe Gly Pro Gly Thr Lys Val Asp Ile Lys Arg Thr
115 120 125

Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu
130 135 140

Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro
145 150 155 160

Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly
165 170 175

Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr
180 185 190

Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His
195 200 205

Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val
210 215 220

Thr Lys Ser Phe Asn Arg Gly Glu Cys Gly Gly Gly Ser Gly Ser
225 230 235 240

Gln Val Gln Leu Val Gln Ser Gly Val Glu Val Lys Lys Pro Gly Ala
245 250 255

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
260 265 270

Tyr Met Tyr Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
275 280 285

Gly Gly Ile Asn Pro Ser Asn Gly Gly Thr Asn Phe Asn Glu Lys Phe
290 295 300

Lys Asn Arg Val Thr Leu Thr Thr Asp Ser Ser Thr Thr Thr Ala Tyr
305 310 315 320

[0156]

Met Glu Leu Lys Ser Leu Gln Phe Asp Asp Thr Ala Val Tyr Tyr Cys
325 330 335

Ala Arg Arg Asp Tyr Arg Phe Asp Met Gly Phe Asp Tyr Trp Gly Gln
340 345 350

Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val
355 360 365

Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser Thr Ala Ala
370 375 380

Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser
385 390 400

Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val
405 410 415

Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro
420 425 430

Ser Ser Ser Leu Gly Thr Lys Thr Tyr Thr Cys Asn Val Asp His Lys
 435 440 445

Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Ser Lys Tyr Gly Pro
 450 455 460

Pro Cys Pro Pro Cys Pro Ala Pro Glu Phe Leu Gly Gly Pro Ser Val
 465 470 475 480

Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr
 485 490 495

Pro Glu Val Thr Cys Val Val Val Asp Val Ser Gln Glu Asp Pro Glu
 500 505 510

Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys
 515 520 525

Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr Tyr Arg Val Val Ser
 530 535 540

[0157] Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys
 545 550 555 560

Cys Lys Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr Ile
 565 570 575

Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro
 580 585 590

Pro Ser Gln Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu
 595 600 605

Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn
 610 615 620

Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser
 625 630 635 640

Asp Gly Ser Phe Phe Leu Tyr Ser Arg Leu Thr Val Asp Lys Ser Arg
 645 650 655

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

	660		665			670												
	His	Asn	His	Tyr	Thr	Gln	Lys	Ser	Leu	Ser	Leu	Ser	Leu	Gly	Lys			
			675					680					685					
	<210>	111																
	<211>	715																
	<212>	PRT																
	<213>	人工序列																
	<220>																	
	<223>	人工序列的描述: 合成多肽																
	<400>	111																
	Met	Gly	Trp	Ser	Cys	Ile	Ile	Leu	Phe	Leu	Val	Ala	Thr	Ala	Thr	Gly		
	1				5					10					15			
	Val	His	Ser	Glu	Ile	Val	Leu	Thr	Gln	Ser	Pro	Ala	Thr	Leu	Ser	Leu		
				20					25					30				
	Ser	Pro	Gly	Glu	Arg	Ala	Thr	Leu	Ser	Cys	Arg	Ala	Ser	Gln	Ser	Val		
			35					40					45					
[0158]	Ser	Ser	Tyr	Leu	Ala	Trp	Tyr	Gln	Gln	Lys	Pro	Gly	Gln	Ala	Pro	Arg		
		50					55					60						
	Leu	Leu	Ile	Tyr	Asp	Ala	Ser	Asn	Arg	Ala	Thr	Gly	Ile	Pro	Ala	Arg		
	65				70						75					80		
	Phe	Ser	Gly	Ser	Gly	Ser	Gly	Thr	Asp	Phe	Thr	Leu	Thr	Ile	Ser	Ser		
					85					90					95			
	Leu	Glu	Pro	Glu	Asp	Phe	Ala	Val	Tyr	Tyr	Cys	Gln	Gln	Ser	Ser	Asn		
				100					105						110			
	Trp	Pro	Arg	Thr	Phe	Gly	Cys	Gly	Thr	Lys	Val	Glu	Ile	Lys	Gly	Gly		
			115					120						125				
	Gly	Gly	Ser	Gly	Gly	Gly	Gly	Ser	Gly	Gly	Gly	Gly	Ser	Gly	Gly	Gly		
		130					135						140					
	Gly	Ser	Gln	Val	Gln	Leu	Val	Glu	Ser	Gly	Gly	Gly	Val	Val	Gln	Pro		
	145					150					155					160		
	Gly	Arg	Ser	Leu	Arg	Leu	Asp	Cys	Lys	Ala	Ser	Gly	Ile	Thr	Phe	Ser		

	165		170		175														
	Asn	Ser	Gly	Met	His	Trp	Val	Arg	Gln	Ala	Pro	Gly	Lys	Cys	Leu	Glu			
				180					185					190					
	Trp	Val	Ala	Val	Ile	Trp	Tyr	Asp	Gly	Ser	Lys	Arg	Tyr	Tyr	Ala	Asp			
			195					200					205						
	Ser	Val	Lys	Gly	Arg	Phe	Thr	Ile	Ser	Arg	Asp	Asn	Ser	Lys	Asn	Thr			
		210					215					220							
	Leu	Phe	Leu	Gln	Met	Asn	Ser	Leu	Arg	Ala	Glu	Asp	Thr	Ala	Val	Tyr			
	225					230					235					240			
	Tyr	Cys	Ala	Thr	Asn	Asp	Asp	Tyr	Trp	Gly	Gln	Gly	Thr	Leu	Val	Thr			
					245					250					255				
	Val	Ser	Ser	Gly	Gly	Gly	Gly	Ser	Gly	Gly	Gly	Gly	Ser	Glu	Val	Gln			
				260					265					270					
[0159]	Leu	Val	Glu	Ser	Gly	Gly	Gly	Val	Val	Gln	Pro	Gly	Arg	Ser	Leu	Arg			
			275					280					285						
	Leu	Ser	Cys	Ser	Ser	Ser	Gly	Phe	Ile	Phe	Ser	Ser	Tyr	Asp	Met	Ser			
		290					295					300							
	Trp	Val	Arg	Gln	Ala	Pro	Gly	Lys	Gly	Leu	Glu	Trp	Val	Ala	Tyr	Ile			
	305					310					315					320			
	Ser	Ser	Gly	Gly	Gly	Gly	Thr	Tyr	Tyr	Pro	Asp	Thr	Val	Lys	Gly	Arg			
					325					330					335				
	Phe	Thr	Ile	Ser	Arg	Asp	Asn	Ser	Lys	Asn	Thr	Leu	Phe	Leu	Gln	Met			
				340					345					350					
	Asp	Ser	Leu	Arg	Pro	Glu	Asp	Thr	Gly	Val	Tyr	Phe	Cys	Ala	Arg	Gly			
			355					360					365						
	Gly	Val	Thr	Lys	Gly	Tyr	Phe	Asp	Val	Trp	Gly	Gln	Gly	Thr	Pro	Val			
		370					375					380							
	Thr	Val	Ser	Ser	Ala	Ser	Thr	Lys	Gly	Pro	Ser	Val	Phe	Pro	Leu	Ala			
	385					390					395					400			

Pro Cys Ser Arg Ser Thr Ser Glu Ser Thr Ala Ala Leu Gly Cys Leu
 405 410 415

Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly
 420 425 430

Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser
 435 440 445

Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu
 450 455 460

Gly Thr Lys Thr Tyr Thr Cys Asn Val Asp His Lys Pro Ser Asn Thr
 465 470 475 480

Lys Val Asp Lys Arg Val Glu Ser Lys Tyr Gly Pro Pro Cys Pro Pro
 485 490 495

Cys Pro Ala Pro Glu Phe Leu Gly Gly Pro Ser Val Phe Leu Phe Pro
 500 505 510

[0160]

Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr
 515 520 525

Cys Val Val Val Asp Val Ser Gln Glu Asp Pro Glu Val Gln Phe Asn
 530 535 540

Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg
 545 550 555 560

Glu Glu Gln Phe Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val
 565 570 575

Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser
 580 585 590

Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys
 595 600 605

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

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

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

Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe
660 665 670

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

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

Thr Gln Lys Ser Leu Ser Leu Ser Leu Gly Lys
705 710 715

<210> 112

<211> 233

<212> PRT

[0161] <213> 人工序列

<220>

<223> 人工序列的描述：合成多肽

<400> 112

Met Gly Trp Ser Cys Ile Ile Leu Phe Leu Val Ala Thr Ala Thr Gly
1 5 10 15

Val His Ser Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala
20 25 30

Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gly Asn Ile
35 40 45

His Asn Tyr Leu Thr Trp Tyr Gln Gln Thr Pro Gly Lys Ala Pro Lys
50 55 60

Leu Leu Ile Tyr Asn Ala Lys Thr Leu Ala Asp Gly Val Pro Ser Arg
65 70 75 80

Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Thr Phe Thr Ile Ser Ser
85 90 95

Leu Gln Pro Glu Asp Ile Ala Thr Tyr Tyr Cys Gln His Phe Trp Ser
 100 105 110

Ile Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys Arg Thr
 115 120 125

Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu
 130 135 140

Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro
 145 150 155 160

Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly
 165 170 175

Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr
 180 185 190

Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His
 195 200 205

[0162]

Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val
 210 215 220

Thr Lys Ser Phe Asn Arg Gly Glu Cys
 225 230

<210> 113

<211> 715

<212> PRT

<213> 人工序列

<220>

<223> 人工序列的描述: 合成多肽

<400> 113

Met Gly Trp Ser Cys Ile Ile Leu Phe Leu Val Ala Thr Ala Thr Gly
 1 5 10 15

Val His Ser Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala
 20 25 30

Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gly Asn Ile
 35 40 45

His Asn Tyr Leu Thr Trp Tyr Gln Gln Thr Pro Gly Lys Ala Pro Lys
 50 55 60

Leu Leu Ile Tyr Asn Ala Lys Thr Leu Ala Asp Gly Val Pro Ser Arg
 65 70 75 80

Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Thr Phe Thr Ile Ser Ser
 85 90 95

Leu Gln Pro Glu Asp Ile Ala Thr Tyr Tyr Cys Gln His Phe Trp Ser
 100 105 110

Ile Pro Tyr Thr Phe Gly Cys Gly Thr Lys Leu Glu Ile Lys Gly Gly
 115 120 125

Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly
 130 135 140

Gly Ser Glu Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro
 145 150 155 160

[0163]

Gly Arg Ser Leu Arg Leu Ser Cys Ser Ser Ser Gly Phe Ile Phe Ser
 165 170 175

Ser Tyr Asp Met Ser Trp Val Arg Gln Ala Pro Gly Lys Cys Leu Glu
 180 185 190

Trp Val Ala Tyr Ile Ser Ser Gly Gly Gly Gly Thr Tyr Tyr Pro Asp
 195 200 205

Thr Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr
 210 215 220

Leu Phe Leu Gln Met Asp Ser Leu Arg Pro Glu Asp Thr Gly Val Tyr
 225 230 235 240

Phe Cys Ala Arg Gly Gly Val Thr Lys Gly Tyr Phe Asp Val Trp Gly
 245 250 255

Gln Gly Thr Pro Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly
 260 265 270

Gly Gly Ser Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln
 275 280 285

Pro Gly Arg Ser Leu Arg Leu Asp Cys Lys Ala Ser Gly Ile Thr Phe
 290 295 300

Ser Asn Ser Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu
 305 310 315 320

Glu Trp Val Ala Val Ile Trp Tyr Asp Gly Ser Lys Arg Tyr Tyr Ala
 325 330 335

Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn
 340 345 350

Thr Leu Phe Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val
 355 360 365

Tyr Tyr Cys Ala Thr Asn Asp Asp Tyr Trp Gly Gln Gly Thr Leu Val
 370 375 380

[0164] Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala
 385 390 395 400

Pro Cys Ser Arg Ser Thr Ser Glu Ser Thr Ala Ala Leu Gly Cys Leu
 405 410 415

Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly
 420 425 430

Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser
 435 440 445

Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu
 450 455 460

Gly Thr Lys Thr Tyr Thr Cys Asn Val Asp His Lys Pro Ser Asn Thr
 465 470 475 480

Lys Val Asp Lys Arg Val Glu Ser Lys Tyr Gly Pro Pro Cys Pro Pro
 485 490 495

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

	500		505		510
	Pro Lys	Pro Lys Asp Thr Leu Met Ile Ser Arg Thr	Pro Glu Val Thr		
	515		520		525
	Cys Val Val Val Asp Val Ser Gln Glu Asp Pro Glu Val Gln Phe Asn				
	530		535		540
	Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg				
	545		550		555
	Glu Glu Gln Phe Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val				
			565		570
	Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser				
			580		585
	Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys				
			595		600
[0165]	Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Gln Glu				
			610		615
	Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe				
	625		630		635
	Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu				
			645		650
	Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe				
			660		665
	Phe Leu Tyr Ser Arg Leu Thr Val Asp Lys Ser Arg Trp Gln Glu Gly				
			675		680
	Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr				
			690		700
	Thr Gln Lys Ser Leu Ser Leu Ser Leu Gly Lys				
	705		710		715
	<210> 114				
	<211> 715				

<212> PRT

<213> 人工序列

<220>

<223> 人工序列的描述：合成多肽

<400> 114

Met Gly Trp Ser Cys Ile Ile Leu Phe Leu Val Ala Thr Ala Thr Gly
1 5 10 15

Val His Ser Glu Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln
20 25 30

Pro Gly Arg Ser Leu Arg Leu Ser Cys Ser Ser Ser Gly Phe Ile Phe
35 40 45

Ser Ser Tyr Asp Met Ser Trp Val Arg Gln Ala Pro Gly Lys Cys Leu
50 55 60

Glu Trp Val Ala Tyr Ile Ser Ser Gly Gly Gly Gly Thr Tyr Tyr Pro
65 70 75 80

[0166]

Asp Thr Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn
85 90 95

Thr Leu Phe Leu Gln Met Asp Ser Leu Arg Pro Glu Asp Thr Gly Val
100 105 110

Tyr Phe Cys Ala Arg Gly Gly Val Thr Lys Gly Tyr Phe Asp Val Trp
115 120 125

Gly Gln Gly Thr Pro Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly
130 135 140

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile
145 150 155 160

Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg
165 170 175

Val Thr Ile Thr Cys Arg Ala Ser Gly Asn Ile His Asn Tyr Leu Thr
180 185 190

Trp Tyr Gln Gln Thr Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Asn
195 200 205

Ala Lys Thr Leu Ala Asp Gly Val Pro Ser Arg Phe Ser Gly Ser Gly
210 215 220

Ser Gly Thr Asp Tyr Thr Phe Thr Ile Ser Ser Leu Gln Pro Glu Asp
225 230 235 240

Ile Ala Thr Tyr Tyr Cys Gln His Phe Trp Ser Ile Pro Tyr Thr Phe
245 250 255

Gly Cys Gly Thr Lys Leu Glu Ile Lys Gly Gly Gly Ser Gly Gly
260 265 270

Gly Gly Ser Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln
275 280 285

Pro Gly Arg Ser Leu Arg Leu Asp Cys Lys Ala Ser Gly Ile Thr Phe
290 295 300

Ser Asn Ser Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu
305 310 315 320

[0167]

Glu Trp Val Ala Val Ile Trp Tyr Asp Gly Ser Lys Arg Tyr Tyr Ala
325 330 335

Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn
340 345 350

Thr Leu Phe Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val
355 360 365

Tyr Tyr Cys Ala Thr Asn Asp Asp Tyr Trp Gly Gln Gly Thr Leu Val
370 375 380

Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala
385 390 395 400

Pro Cys Ser Arg Ser Thr Ser Glu Ser Thr Ala Ala Leu Gly Cys Leu
405 410 415

Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly
420 425 430

Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser
435 440 445

Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu
450 455 460

Gly Thr Lys Thr Tyr Thr Cys Asn Val Asp His Lys Pro Ser Asn Thr
465 470 475 480

Lys Val Asp Lys Arg Val Glu Ser Lys Tyr Gly Pro Pro Cys Pro Pro
485 490 495

Cys Pro Ala Pro Glu Phe Leu Gly Gly Pro Ser Val Phe Leu Phe Pro
500 505 510

Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr
515 520 525

Cys Val Val Val Asp Val Ser Gln Glu Asp Pro Glu Val Gln Phe Asn
530 535 540

[0168]

Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg
545 550 555 560

Glu Glu Gln Phe Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val
565 570 575

Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser
580 585 590

Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys
595 600 605

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

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

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

Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe
660 665 670

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

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

Thr Gln Lys Ser Leu Ser Leu Ser Leu Gly Lys
705 710 715

<210> 115

<211> 715

<212> PRT

<213> 人工序列

<220>

<223> 人工序列的描述：合成多肽

<400> 115

Met Gly Trp Ser Cys Ile Ile Leu Phe Leu Val Ala Thr Ala Thr Gly
1 5 10 15

[0169]

Val His Ser Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln
20 25 30

Pro Gly Arg Ser Leu Arg Leu Asp Cys Lys Ala Ser Gly Ile Thr Phe
35 40 45

Ser Asn Ser Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu
50 55 60

Glu Trp Val Ala Val Ile Trp Tyr Asp Gly Ser Lys Arg Tyr Tyr Ala
65 70 75 80

Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn
85 90 95

Thr Leu Phe Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val
100 105 110

Tyr Tyr Cys Ala Thr Asn Asp Asp Tyr Trp Gly Gln Gly Thr Leu Val
115 120 125

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

Pro Cys Ser Arg Ser Thr Ser Glu Ser Thr Ala Ala Leu Gly Cys Leu
 145 150 155 160

Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly
 165 170 175

Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser
 180 185 190

Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu
 195 200 205

Gly Thr Lys Thr Tyr Thr Cys Asn Val Asp His Lys Pro Ser Asn Thr
 210 215 220

Lys Val Asp Lys Arg Val Glu Ser Lys Tyr Gly Pro Pro Cys Pro Pro
 225 230 235 240

[0170] Cys Pro Ala Pro Glu Phe Leu Gly Gly Pro Ser Val Phe Leu Phe Pro
 245 250 255

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

Cys Val Val Val Asp Val Ser Gln Glu Asp Pro Glu Val Gln Phe Asn
 275 280 285

Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg
 290 295 300

Glu Glu Gln Phe Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val
 305 310 315 320

Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser
 325 330 335

Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys
 340 345 350

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

	355							360									365
	Glu	Met	Thr	Lys	Asn	Gln	Val	Ser	Leu	Thr	Cys	Leu	Val	Lys	Gly	Phe	
	370						375					380					
	Tyr	Pro	Ser	Asp	Ile	Ala	Val	Glu	Trp	Glu	Ser	Asn	Gly	Gln	Pro	Glu	
	385					390					395					400	
	Asn	Asn	Tyr	Lys	Thr	Thr	Pro	Pro	Val	Leu	Asp	Ser	Asp	Gly	Ser	Phe	
					405					410					415		
	Phe	Leu	Tyr	Ser	Arg	Leu	Thr	Val	Asp	Lys	Ser	Arg	Trp	Gln	Glu	Gly	
				420					425					430			
	Asn	Val	Phe	Ser	Cys	Ser	Val	Met	His	Glu	Ala	Leu	His	Asn	His	Tyr	
			435					440					445				
	Thr	Gln	Lys	Ser	Leu	Ser	Leu	Ser	Leu	Gly	Lys	Gly	Gly	Gly	Gly	Ser	
			450				455						460				
[0171]	Gly	Gly	Gly	Gly	Ser	Asp	Ile	Gln	Met	Thr	Gln	Ser	Pro	Ser	Ser	Leu	
	465					470					475					480	
	Ser	Ala	Ser	Val	Gly	Asp	Arg	Val	Thr	Ile	Thr	Cys	Arg	Ala	Ser	Gly	
					485					490					495		
	Asn	Ile	His	Asn	Tyr	Leu	Thr	Trp	Tyr	Gln	Gln	Thr	Pro	Gly	Lys	Ala	
				500					505					510			
	Pro	Lys	Leu	Leu	Ile	Tyr	Asn	Ala	Lys	Thr	Leu	Ala	Asp	Gly	Val	Pro	
			515					520					525				
	Ser	Arg	Phe	Ser	Gly	Ser	Gly	Ser	Gly	Thr	Asp	Tyr	Thr	Phe	Thr	Ile	
		530					535					540					
	Ser	Ser	Leu	Gln	Pro	Glu	Asp	Ile	Ala	Thr	Tyr	Tyr	Cys	Gln	His	Phe	
	545					550					555					560	
	Trp	Ser	Ile	Pro	Tyr	Thr	Phe	Gly	Cys	Gly	Thr	Lys	Leu	Glu	Ile	Lys	
					565					570					575		
	Gly	Gly	Gly	Gly	Ser	Gly	Gly	Gly	Gly	Ser	Gly	Gly	Gly	Gly	Ser	Gly	
				580					585					590			

Gly Gly Gly Ser Glu Val Gln Leu Val Glu Ser Gly Gly Gly Val Val
595 600 605

Gln Pro Gly Arg Ser Leu Arg Leu Ser Cys Ser Ser Ser Gly Phe Ile
610 615 620

Phe Ser Ser Tyr Asp Met Ser Trp Val Arg Gln Ala Pro Gly Lys Cys
625 630 635 640

Leu Glu Trp Val Ala Tyr Ile Ser Ser Gly Gly Gly Gly Thr Tyr Tyr
645 650 655

Pro Asp Thr Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys
660 665 670

Asn Thr Leu Phe Leu Gln Met Asp Ser Leu Arg Pro Glu Asp Thr Gly
675 680 685

Val Tyr Phe Cys Ala Arg Gly Gly Val Thr Lys Gly Tyr Phe Asp Val
690 695 700

[0172]

Trp Gly Gln Gly Thr Pro Val Thr Val Ser Ser
705 710 715

<210> 116

<211> 715

<212> PRT

<213> 人工序列

<220>

<223> 人工序列的描述：合成多肽

<400> 116

Met Gly Trp Ser Cys Ile Ile Leu Phe Leu Val Ala Thr Ala Thr Gly
1 5 10 15

Val His Ser Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln
20 25 30

Pro Gly Arg Ser Leu Arg Leu Asp Cys Lys Ala Ser Gly Ile Thr Phe
35 40 45

Ser Asn Ser Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu
50 55 60

Glu Trp Val Ala Val Ile Trp Tyr Asp Gly Ser Lys Arg Tyr Tyr Ala
 65 70 75 80

Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn
 85 90 95

Thr Leu Phe Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val
 100 105 110

Tyr Tyr Cys Ala Thr Asn Asp Asp Tyr Trp Gly Gln Gly Thr Leu Val
 115 120 125

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

Pro Cys Ser Arg Ser Thr Ser Glu Ser Thr Ala Ala Leu Gly Cys Leu
 145 150 155 160

Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly
 165 170 175

[0173]

Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser
 180 185 190

Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu
 195 200 205

Gly Thr Lys Thr Tyr Thr Cys Asn Val Asp His Lys Pro Ser Asn Thr
 210 215 220

Lys Val Asp Lys Arg Val Glu Ser Lys Tyr Gly Pro Pro Cys Pro Pro
 225 230 235 240

Cys Pro Ala Pro Glu Phe Leu Gly Gly Pro Ser Val Phe Leu Phe Pro
 245 250 255

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

Cys Val Val Val Asp Val Ser Gln Glu Asp Pro Glu Val Gln Phe Asn
 275 280 285

Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg
290 295 300

Glu Glu Gln Phe Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val
305 310 315 320

Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser
325 330 335

Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys
340 345 350

Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Gln Glu
355 360 365

Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe
370 375 380

Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu
385 390 395 400

[0174]

Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe
405 410 415

Phe Leu Tyr Ser Arg Leu Thr Val Asp Lys Ser Arg Trp Gln Glu Gly
420 425 430

Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr
435 440 445

Thr Gln Lys Ser Leu Ser Leu Ser Leu Gly Lys Gly Gly Gly Gly Ser
450 455 460

Gly Gly Gly Gly Ser Glu Val Gln Leu Val Glu Ser Gly Gly Gly Val
465 470 475 480

Val Gln Pro Gly Arg Ser Leu Arg Leu Ser Cys Ser Ser Ser Gly Phe
485 490 495

Ile Phe Ser Ser Tyr Asp Met Ser Trp Val Arg Gln Ala Pro Gly Lys
500 505 510

Cys Leu Glu Trp Val Ala Tyr Ile Ser Ser Gly Gly Gly Gly Thr Tyr
515 520 525

Tyr Pro Asp Thr Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser
530 535 540

Lys Asn Thr Leu Phe Leu Gln Met Asp Ser Leu Arg Pro Glu Asp Thr
545 550 555 560

Gly Val Tyr Phe Cys Ala Arg Gly Gly Val Thr Lys Gly Tyr Phe Asp
565 570 575

Val Trp Gly Gln Gly Thr Pro Val Thr Val Ser Ser Gly Gly Gly Gly
580 585 590

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

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
610 615 620

[0175]

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gly Asn Ile His Asn Tyr
625 630 635 640

Leu Thr Trp Tyr Gln Gln Thr Pro Gly Lys Ala Pro Lys Leu Leu Ile
645 650 655

Tyr Asn Ala Lys Thr Leu Ala Asp Gly Val Pro Ser Arg Phe Ser Gly
660 665 670

Ser Gly Ser Gly Thr Asp Tyr Thr Phe Thr Ile Ser Ser Leu Gln Pro
675 680 685

Glu Asp Ile Ala Thr Tyr Tyr Cys Gln His Phe Trp Ser Ile Pro Tyr
690 695 700

Thr Phe Gly Cys Gly Thr Lys Leu Glu Ile Lys
705 710 715

<210> 117

<211> 683

<212> PRT

<213> 人工序列

<220>

<223> 人工序列的描述：合成多肽

<400> 117

Met Gly Trp Ser Cys Ile Ile Leu Phe Leu Val Ala Thr Ala Thr Gly
1 5 10 15

Val His Ser Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala
20 25 30

Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gly Asn Ile
35 40 45

His Asn Tyr Leu Thr Trp Tyr Gln Gln Thr Pro Gly Lys Ala Pro Lys
50 55 60

Leu Leu Ile Tyr Asn Ala Lys Thr Leu Ala Asp Gly Val Pro Ser Arg
65 70 75 80

Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Thr Phe Thr Ile Ser Ser
85 90 95

[0176] Leu Gln Pro Glu Asp Ile Ala Thr Tyr Tyr Cys Gln His Phe Trp Ser
100 105 110

Ile Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys Arg Thr
115 120 125

Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu
130 135 140

Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro
145 150 155 160

Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly
165 170 175

Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr
180 185 190

Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His
195 200 205

Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val

	210	215	220	
	Thr Lys Ser Phe Asn Arg Gly Glu Cys Gly Ser Gly Gln Val Gln Leu 225	230	235	240
	Val Gln Ser Gly Val Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val 245	250	255	
	Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr Tyr Met Tyr Trp 260	265	270	
	Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met Gly Gly Ile Asn 275	280	285	
	Pro Ser Asn Gly Gly Thr Asn Phe Asn Glu Lys Phe Lys Asn Arg Val 290	295	300	
	Thr Leu Thr Thr Asp Ser Ser Thr Thr Thr Ala Tyr Met Glu Leu Lys 305	310	315	320
[0177]	Ser Leu Gln Phe Asp Asp Thr Ala Val Tyr Tyr Cys Ala Arg Arg Asp 325	330	335	
	Tyr Arg Phe Asp Met Gly Phe Asp Tyr Trp Gly Gln Gly Thr Thr Val 340	345	350	
	Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala 355	360	365	
	Pro Cys Ser Arg Ser Thr Ser Glu Ser Thr Ala Ala Leu Gly Cys Leu 370	375	380	
	Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly 385	390	395	400
	Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser 405	410	415	
	Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu 420	425	430	
	Gly Thr Lys Thr Tyr Thr Cys Asn Val Asp His Lys Pro Ser Asn Thr 435	440	445	

Lys Val Asp Lys Arg Val Glu Ser Lys Tyr Gly Pro Pro Cys Pro Pro
 450 455 460

Cys Pro Ala Pro Glu Phe Leu Gly Gly Pro Ser Val Phe Leu Phe Pro
 465 470 475 480

Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr
 485 490 495

Cys Val Val Val Asp Val Ser Gln Glu Asp Pro Glu Val Gln Phe Asn
 500 505 510

Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg
 515 520 525

Glu Glu Gln Phe Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val
 530 535 540

Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser
 545 550 555 560

[0178]

Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys
 565 570 575

Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Gln Glu
 580 585 590

Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe
 595 600 605

Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu
 610 615 620

Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe
 625 630 635 640

Phe Leu Tyr Ser Arg Leu Thr Val Asp Lys Ser Arg Trp Gln Glu Gly
 645 650 655

Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr
 660 665 670

Thr Gln Lys Ser Leu Ser Leu Ser Leu Gly Lys
675 680

<210> 118
<211> 241
<212> PRT
<213> 人工序列

<220>
<223> 人工序列的描述: 合成多肽

<400> 118
Met Gly Trp Ser Cys Ile Ile Leu Phe Leu Val Ala Thr Ala Thr Gly
1 5 10 15

Val His Ser Glu Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln
20 25 30

Pro Gly Arg Ser Leu Arg Leu Ser Cys Ser Ser Ser Gly Phe Ile Phe
35 40 45

Ser Ser Tyr Asp Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu
50 55 60

[0179]

Glu Trp Val Ala Tyr Ile Ser Ser Gly Gly Gly Gly Thr Tyr Tyr Pro
65 70 75 80

Asp Thr Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn
85 90 95

Thr Leu Phe Leu Gln Met Asp Ser Leu Arg Pro Glu Asp Thr Gly Val
100 105 110

Tyr Phe Cys Ala Arg Gly Gly Val Thr Lys Gly Tyr Phe Asp Val Trp
115 120 125

Gly Gln Gly Thr Pro Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro
130 135 140

Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr
145 150 155 160

Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr
165 170 175

Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro
180 185 190

Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr
195 200 205

Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn
210 215 220

His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser
225 230 235 240

Cys

<210> 119

<211> 687

<212> PRT

<213> 人工序列

<220>

<223> 人工序列的描述：合成多肽

[0180]

<400> 119

Met Gly Trp Ser Cys Ile Ile Leu Phe Leu Val Ala Thr Ala Thr Gly
1 5 10 15

Val His Ser Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala
20 25 30

Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gly Asn Ile
35 40 45

His Asn Tyr Leu Thr Trp Tyr Gln Gln Thr Pro Gly Lys Ala Pro Lys
50 55 60

Leu Leu Ile Tyr Asn Ala Lys Thr Leu Ala Asp Gly Val Pro Ser Arg
65 70 75 80

Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Thr Phe Thr Ile Ser Ser
85 90 95

Leu Gln Pro Glu Asp Ile Ala Thr Tyr Tyr Cys Gln His Phe Trp Ser
100 105 110

Ile Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys Arg Thr
 115 120 125

Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu
 130 135 140

Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro
 145 150 155 160

Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly
 165 170 175

Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr
 180 185 190

Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His
 195 200 205

Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val
 210 215 220

[0181]

Thr Lys Ser Phe Asn Arg Gly Glu Cys Gly Gly Gly Ser Gly Ser
 225 230 235 240

Gln Val Gln Leu Val Gln Ser Gly Val Glu Val Lys Lys Pro Gly Ala
 245 250 255

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
 260 265 270

Tyr Met Tyr Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
 275 280 285

Gly Gly Ile Asn Pro Ser Asn Gly Gly Thr Asn Phe Asn Glu Lys Phe
 290 295 300

Lys Asn Arg Val Thr Leu Thr Thr Asp Ser Ser Thr Thr Thr Ala Tyr
 305 310 315 320

Met Glu Leu Lys Ser Leu Gln Phe Asp Asp Thr Ala Val Tyr Tyr Cys
 325 330 335

Ala Arg Arg Asp Tyr Arg Phe Asp Met Gly Phe Asp Tyr Trp Gly Gln
 340 345 350

Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val
 355 360 365

Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser Thr Ala Ala
 370 375 380

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

Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val
 405 410 415

Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro
 420 425 430

Ser Ser Ser Leu Gly Thr Lys Thr Tyr Thr Cys Asn Val Asp His Lys
 435 440 445

[0182] Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Ser Lys Tyr Gly Pro
 450 455 460

Pro Cys Pro Pro Cys Pro Ala Pro Glu Phe Leu Gly Gly Pro Ser Val
 465 470 475 480

Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr
 485 490 495

Pro Glu Val Thr Cys Val Val Val Asp Val Ser Gln Glu Asp Pro Glu
 500 505 510

Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys
 515 520 525

Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr Tyr Arg Val Val Ser
 530 535 540

Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys
 545 550 555 560

Cys Lys Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr Ile

	565	570	575																	
	Ser	Lys	Ala	Lys	Gly	Gln	Pro	Arg	Glu	Pro	Gln	Val	Tyr	Thr	Leu	Pro				
				580					585					590						
	Pro	Ser	Gln	Glu	Glu	Met	Thr	Lys	Asn	Gln	Val	Ser	Leu	Thr	Cys	Leu				
			595					600					605							
	Val	Lys	Gly	Phe	Tyr	Pro	Ser	Asp	Ile	Ala	Val	Glu	Trp	Glu	Ser	Asn				
		610					615					620								
	Gly	Gln	Pro	Glu	Asn	Asn	Tyr	Lys	Thr	Thr	Pro	Pro	Val	Leu	Asp	Ser				
		625				630					635					640				
	Asp	Gly	Ser	Phe	Phe	Leu	Tyr	Ser	Arg	Leu	Thr	Val	Asp	Lys	Ser	Arg				
				645						650					655					
	Trp	Gln	Glu	Gly	Asn	Val	Phe	Ser	Cys	Ser	Val	Met	His	Glu	Ala	Leu				
				660					665					670						
[0183]	His	Asn	His	Tyr	Thr	Gln	Lys	Ser	Leu	Ser	Leu	Ser	Leu	Gly	Lys					
			675					680					685							
	<210>	120																		
	<211>	733																		
	<212>	PRT																		
	<213>	人工序列																		
	<220>																			
	<223>	人工序列的描述：合成多肽																		
	<400>	120																		
	Met	Gly	Trp	Ser	Cys	Ile	Ile	Leu	Phe	Leu	Val	Ala	Thr	Ala	Thr	Gly				
	1				5					10					15					
	Val	His	Ser	Glu	Val	Gln	Leu	Val	Glu	Ser	Gly	Gly	Gly	Val	Val	Gln				
				20					25					30						
	Pro	Gly	Arg	Ser	Leu	Arg	Leu	Ser	Cys	Ser	Ser	Ser	Gly	Phe	Ile	Phe				
			35					40					45							
	Ser	Ser	Tyr	Asp	Met	Ser	Trp	Val	Arg	Gln	Ala	Pro	Gly	Lys	Gly	Leu				
		50					55					60								
	Glu	Trp	Val	Ala	Tyr	Ile	Ser	Ser	Gly	Gly	Gly	Gly	Thr	Tyr	Tyr	Pro				

	65		70		75		80									
	Asp	Thr	Val	Lys	Gly	Arg	Phe	Thr	Ile	Ser	Arg	Asp	Asn	Ser	Lys	Asn
					85					90					95	
	Thr	Leu	Phe	Leu	Gln	Met	Asp	Ser	Leu	Arg	Pro	Glu	Asp	Thr	Gly	Val
				100					105					110		
	Tyr	Phe	Cys	Ala	Arg	Gly	Gly	Val	Thr	Lys	Gly	Tyr	Phe	Asp	Val	Trp
			115					120					125			
	Gly	Gln	Gly	Thr	Pro	Val	Thr	Val	Ser	Ser	Ala	Ser	Thr	Lys	Gly	Pro
		130					135					140				
	Ser	Val	Phe	Pro	Leu	Ala	Pro	Cys	Ser	Arg	Ser	Thr	Ser	Glu	Ser	Thr
	145					150					155					160
	Ala	Ala	Leu	Gly	Cys	Leu	Val	Lys	Asp	Tyr	Phe	Pro	Glu	Pro	Val	Thr
					165					170					175	
[0184]	Val	Ser	Trp	Asn	Ser	Gly	Ala	Leu	Thr	Ser	Gly	Val	His	Thr	Phe	Pro
				180					185					190		
	Ala	Val	Leu	Gln	Ser	Ser	Gly	Leu	Tyr	Ser	Leu	Ser	Ser	Val	Val	Thr
			195					200					205			
	Val	Pro	Ser	Ser	Ser	Leu	Gly	Thr	Lys	Thr	Tyr	Thr	Cys	Asn	Val	Asp
		210					215						220			
	His	Lys	Pro	Ser	Asn	Thr	Lys	Val	Asp	Lys	Arg	Val	Glu	Ser	Lys	Tyr
	225					230					235					240
	Gly	Pro	Pro	Cys	Pro	Pro	Cys	Pro	Ala	Pro	Glu	Phe	Leu	Gly	Gly	Pro
					245					250					255	
	Ser	Val	Phe	Leu	Phe	Pro	Pro	Lys	Pro	Lys	Asp	Thr	Leu	Met	Ile	Ser
				260					265					270		
	Arg	Thr	Pro	Glu	Val	Thr	Cys	Val	Val	Val	Asp	Val	Ser	Gln	Glu	Asp
			275					280					285			
	Pro	Glu	Val	Gln	Phe	Asn	Trp	Tyr	Val	Asp	Gly	Val	Glu	Val	His	Asn
		290					295					300				

Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr Tyr Arg Val
305 310 315 320

Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu
325 330 335

Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys
340 345 350

Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr
355 360 365

Leu Pro Pro Ser Gln Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr
370 375 380

Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu
385 390 395 400

Ser Asn Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly
405 410 415

[0185]

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Ile Val Leu Thr
420 425 430

Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu
435 440 445

Ser Cys Arg Ala Ser Lys Gly Val Ser Thr Ser Gly Tyr Ser Tyr Leu
450 455 460

His Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr
465 470 475 480

Leu Ala Ser Tyr Leu Glu Ser Gly Val Pro Ala Arg Phe Ser Gly Ser
485 490 495

Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Glu Pro Glu
500 505 510

Asp Phe Ala Val Tyr Tyr Cys Gln His Ser Arg Asp Leu Pro Leu Thr
515 520 525

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala Pro
530 535 540

Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr
545 550 555 560

Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys
565 570 575

Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu
580 585 590

Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser
595 600 605

Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala
610 615 620

Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe
625 630 635 640

[0186]

Asn Arg Gly Glu Cys Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
645 650 655

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gln
660 665 670

Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly
675 680 685

Ser Phe Phe Leu Tyr Ser Arg Leu Thr Val Asp Lys Ser Arg Trp Gln
690 695 700

Glu Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
705 710 715 720

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Leu Gly Lys
725 730

<210> 121

<211> 730

<212> PRT

<213> 人工序列

<220>

<223> 人工序列的描述: 合成多肽

<400> 121

Met Gly Trp Ser Cys Ile Ile Leu Phe Leu Val Ala Thr Ala Thr Gly
 1 5 10 15

Val His Ser Gln Val Gln Leu Val Gln Ser Gly Val Glu Val Lys Lys
 20 25 30

Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe
 35 40 45

Thr Asn Tyr Tyr Met Tyr Trp Val Arg Gln Ala Pro Gly Gln Gly Leu
 50 55 60

Glu Trp Met Gly Gly Ile Asn Pro Ser Asn Gly Gly Thr Asn Phe Asn
 65 70 75 80

Glu Lys Phe Lys Asn Arg Val Thr Leu Thr Thr Asp Ser Ser Thr Thr
 85 90 95

[0187]

Thr Ala Tyr Met Glu Leu Lys Ser Leu Gln Phe Asp Asp Thr Ala Val
 100 105 110

Tyr Tyr Cys Ala Arg Arg Asp Tyr Arg Phe Asp Met Gly Phe Asp Tyr
 115 120 125

Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly
 130 135 140

Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser
 145 150 155 160

Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val
 165 170 175

Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe
 180 185 190

Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val
 195 200 205

Thr Val Pro Ser Ser Ser Leu Gly Thr Lys Thr Tyr Thr Cys Asn Val
 210 215 220

Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Ser Lys
 225 230 235 240

Tyr Gly Pro Pro Cys Pro Pro Cys Pro Ala Pro Glu Phe Leu Gly Gly
 245 250 255

Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile
 260 265 270

Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser Gln Glu
 275 280 285

Asp Pro Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val His
 290 295 300

Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr Tyr Arg
 305 310 315 320

[0188] Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys
 325 330 335

Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu
 340 345 350

Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr
 355 360 365

Thr Leu Pro Pro Ser Gln Glu Glu Met Thr Lys Asn Gln Val Ser Leu
 370 375 380

Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp
 385 390 395 400

Glu Ser Asn Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly
 405 410 415

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Ser Asp Ile Gln Met
 420 425 430

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

	435		440		445															
	Ile	Thr	Cys	Arg	Ala	Ser	Gly	Asn	Ile	His	Asn	Tyr	Leu	Thr	Trp	Tyr				
	450						455					460								
	Gln	Gln	Thr	Pro	Gly	Lys	Ala	Pro	Lys	Leu	Leu	Ile	Tyr	Asn	Ala	Lys				
	465					470					475					480				
	Thr	Leu	Ala	Asp	Gly	Val	Pro	Ser	Arg	Phe	Ser	Gly	Ser	Gly	Ser	Gly				
					485					490					495					
	Thr	Asp	Tyr	Thr	Phe	Thr	Ile	Ser	Ser	Leu	Gln	Pro	Glu	Asp	Ile	Ala				
				500					505					510						
	Thr	Tyr	Tyr	Cys	Gln	His	Phe	Trp	Ser	Ile	Pro	Tyr	Thr	Phe	Gly	Gln				
			515					520					525							
	Gly	Thr	Lys	Leu	Glu	Ile	Lys	Arg	Thr	Val	Ala	Ala	Pro	Ser	Val	Phe				
		530					535					540								
[0189]	Ile	Phe	Pro	Pro	Ser	Asp	Glu	Gln	Leu	Lys	Ser	Gly	Thr	Ala	Ser	Val				
	545					550					555					560				
	Val	Cys	Leu	Leu	Asn	Asn	Phe	Tyr	Pro	Arg	Glu	Ala	Lys	Val	Gln	Trp				
					565					570					575					
	Lys	Val	Asp	Asn	Ala	Leu	Gln	Ser	Gly	Asn	Ser	Gln	Glu	Ser	Val	Thr				
				580					585					590						
	Glu	Gln	Asp	Ser	Lys	Asp	Ser	Thr	Tyr	Ser	Leu	Ser	Ser	Thr	Leu	Thr				
			595					600					605							
	Leu	Ser	Lys	Ala	Asp	Tyr	Glu	Lys	His	Lys	Val	Tyr	Ala	Cys	Glu	Val				
		610					615					620								
	Thr	His	Gln	Gly	Leu	Ser	Ser	Pro	Val	Thr	Lys	Ser	Phe	Asn	Arg	Gly				
	625					630					635					640				
	Glu	Cys	Gly	Gly	Gly	Gly	Ser	Gly	Gly	Gly	Gly	Ser	Gly	Gly	Gly	Gly				
				645						650					655					
	Ser	Gly	Gly	Gly	Gly	Ser	Gly	Gly	Gly	Gly	Ser	Gly	Gln	Pro	Glu	Asn				
				660					665				670							

Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe
675 680 685

Leu Tyr Ser Arg Leu Thr Val Asp Lys Ser Arg Trp Gln Glu Gly Asn
690 695 700

Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr
705 710 715 720

Gln Lys Ser Leu Ser Leu Ser Leu Gly Lys
725 730

<210> 122

<211> 723

<212> PRT

<213> 人工序列

<220>

<223> 人工序列的描述：合成多肽

<400> 122

Met Gly Trp Ser Cys Ile Ile Leu Phe Leu Val Ala Thr Ala Thr Gly
1 5 10 15

[0190]

Val His Ser Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln
20 25 30

Pro Gly Arg Ser Leu Arg Leu Asp Cys Lys Ala Ser Gly Ile Thr Phe
35 40 45

Ser Asn Ser Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu
50 55 60

Glu Trp Val Ala Val Ile Trp Tyr Asp Gly Ser Lys Arg Tyr Tyr Ala
65 70 75 80

Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn
85 90 95

Thr Leu Phe Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val
100 105 110

Tyr Tyr Cys Ala Thr Asn Asp Asp Tyr Trp Gly Gln Gly Thr Leu Val
115 120 125

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

Pro Cys Ser Arg Ser Thr Ser Glu Ser Thr Ala Ala Leu Gly Cys Leu
145 150 155 160

Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly
165 170 175

Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser
180 185 190

Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu
195 200 205

Gly Thr Lys Thr Tyr Thr Cys Asn Val Asp His Lys Pro Ser Asn Thr
210 215 220

Lys Val Asp Lys Arg Val Glu Ser Lys Tyr Gly Pro Pro Cys Pro Pro
225 230 235 240

[0191]

Cys Pro Ala Pro Glu Phe Leu Gly Gly Pro Ser Val Phe Leu Phe Pro
245 250 255

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

Cys Val Val Val Asp Val Ser Gln Glu Asp Pro Glu Val Gln Phe Asn
275 280 285

Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg
290 295 300

Glu Glu Gln Phe Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val
305 310 315 320

Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser
325 330 335

Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys
340 345 350

Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Gln Glu
355 360 365

Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe
370 375 380

Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gly Gly Gly
385 390 395 400

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
405 410 415

Gly Gly Gly Gly Ser Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu
420 425 430

Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gly
435 440 445

Asn Ile His Asn Tyr Leu Thr Trp Tyr Gln Gln Thr Pro Gly Lys Ala
450 455 460

[0192]

Pro Lys Leu Leu Ile Tyr Asn Ala Lys Thr Leu Ala Asp Gly Val Pro
465 470 475 480

Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Thr Phe Thr Ile
485 490 495

Ser Ser Leu Gln Pro Glu Asp Ile Ala Thr Tyr Tyr Cys Gln His Phe
500 505 510

Trp Ser Ile Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
515 520 525

Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu
530 535 540

Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe
545 550 555 560

Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln
565 570 575

Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser
 580 585 590

Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu
 595 600 605

Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser
 610 615 620

Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys Gly Gly Gly Gly Ser
 625 630 635 640

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
 645 650 655

Gly Gly Gly Ser Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro
 660 665 670

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

[0193] Asp Lys Ser Arg Trp Gln Glu Gly Asn Val Phe Ser Cys Ser Val Met
 690 695 700

His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser
 705 710 715 720

Leu Gly Lys

<210> 123
 <211> 25
 <212> PRT
 <213> 人工序列

<220>
 <223> 人工序列的描述：合成肽

<220>
 <221> MISC_FEATURE
 <222> (1)..(25)
 <223> 本序列可包含1-5“Gly Gly Gly Gly Ser”重复单元

<400> 123
 Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly

	85	90	95
	Thr Leu Tyr Leu Gln Met Asn Gly Leu Arg Ala Glu Asp Thr Ala Val 100	105	110
	Tyr Tyr Cys Ala Arg Asp Leu Arg Thr Gly Pro Phe Asp Tyr Trp Gly 115	120	125
	Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser 130	135	140
	Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser Thr Ala 145	150	155
	Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val 165	170	175
	Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala 180	185	190
[0195]	Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val 195	200	205
	Pro Ser Ser Ser Leu Gly Thr Lys Thr Tyr Thr Cys Asn Val Asp His 210	215	220
	Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Ser Lys Tyr Gly 225	230	235
	Pro Pro Cys Pro Pro Cys Pro Ala Pro Glu Phe Leu Gly Gly Pro Ser 245	250	255
	Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg 260	265	270
	Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser Gln Glu Asp Pro 275	280	285
	Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala 290	295	300
	Lys Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr Tyr Arg Val Val 305	310	315
			320

Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr
325 330 335

Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr
340 345 350

Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu
355 360 365

Pro Pro Ser Gln Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys
370 375 380

Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser
385 390 395 400

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

Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser
420 425 430

[0196]

Lys Gly Val Ser Thr Ser Gly Tyr Ser Tyr Leu His Trp Tyr Gln Gln
435 440 445

Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr Leu Ala Ser Tyr Leu
450 455 460

Glu Ser Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp
465 470 475 480

Phe Thr Leu Thr Ile Ser Ser Leu Glu Pro Glu Asp Phe Ala Val Tyr
485 490 495

Tyr Cys Gln His Ser Arg Asp Leu Pro Leu Thr Phe Gly Gly Gly Thr
500 505 510

Lys Val Glu Ile Lys Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe
515 520 525

Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys
530 535 540

Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val
545 550 555 560

Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln
565 570 575

Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser
580 585 590

Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala Cys Glu Val Thr His
595 600 605

Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
610 615 620

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
625 630 635 640

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Pro Glu Asn Asn Tyr Lys
645 650 655

[0197]

Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser
660 665 670

Arg Leu Thr Val Asp Lys Ser Arg Trp Gln Glu Gly Asn Val Phe Ser
675 680 685

Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser
690 695 700

Leu Ser Leu Ser Leu Gly Lys
705 710

<210> 126

<211> 711

<212> PRT

<213> 人工序列

<220>

<223> 人工序列的描述：合成多肽

<400> 126

Met Gly Trp Ser Cys Ile Ile Leu Phe Leu Val Ala Thr Ala Thr Gly
1 5 10 15

Val His Ser Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln
20 25 30

Pro Gly Arg Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe
35 40 45

Ser Val Tyr Gly Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu
50 55 60

Glu Trp Val Ala Ile Ile Trp Tyr Asp Gly Asp Asn Gln Tyr Tyr Ala
65 70 75 80

Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn
85 90 95

Thr Leu Tyr Leu Gln Met Asn Gly Leu Arg Ala Glu Asp Thr Ala Val
100 105 110

Tyr Tyr Cys Ala Arg Asp Leu Arg Thr Gly Pro Phe Asp Tyr Trp Gly
115 120 125

[0198]

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

Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser Thr Ala
145 150 155 160

Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val
165 170 175

Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala
180 185 190

Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val
195 200 205

Pro Ser Ser Ser Leu Gly Thr Lys Thr Tyr Thr Cys Asn Val Asp His
210 215 220

Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Ser Lys Tyr Gly
225 230 235 240

Pro Pro Cys Pro Pro Cys Pro Ala Pro Glu Phe Leu Gly Gly Pro Ser
 245 250 255

Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg
 260 265 270

Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser Gln Glu Asp Pro
 275 280 285

Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala
 290 295 300

Lys Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr Tyr Arg Val Val
 305 310 315 320

Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr
 325 330 335

Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr
 340 345 350

[0199] Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu
 355 360 365

Pro Pro Ser Gln Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys
 370 375 380

Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser
 385 390 395 400

Asn Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
 405 410 415

Glu Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
 420 425 430

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Lys Gly Val Ser Thr Ser
 435 440 445

Gly Tyr Ser Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro
 450 455 460

Arg Leu Leu Ile Tyr Leu Ala Ser Tyr Leu Glu Ser Gly Val Pro Ala

	465				470						475					480
	Arg	Phe	Ser	Gly	Ser	Gly	Ser	Gly	Thr	Asp	Phe	Thr	Leu	Thr	Ile	Ser
					485					490						495
	Ser	Leu	Glu	Pro	Glu	Asp	Phe	Ala	Val	Tyr	Tyr	Cys	Gln	His	Ser	Arg
				500					505					510		
	Asp	Leu	Pro	Leu	Thr	Phe	Gly	Gly	Gly	Thr	Lys	Val	Glu	Ile	Lys	Arg
			515						520				525			
	Thr	Val	Ala	Ala	Pro	Ser	Val	Phe	Ile	Phe	Pro	Pro	Ser	Asp	Glu	Gln
		530					535					540				
	Leu	Lys	Ser	Gly	Thr	Ala	Ser	Val	Val	Cys	Leu	Leu	Asn	Asn	Phe	Tyr
	545					550					555					560
	Pro	Arg	Glu	Ala	Lys	Val	Gln	Trp	Lys	Val	Asp	Asn	Ala	Leu	Gln	Ser
					565					570						575
[0200]	Gly	Asn	Ser	Gln	Glu	Ser	Val	Thr	Glu	Gln	Asp	Ser	Lys	Asp	Ser	Thr
				580					585					590		
	Tyr	Ser	Leu	Ser	Ser	Thr	Leu	Thr	Leu	Ser	Lys	Ala	Asp	Tyr	Glu	Lys
			595					600					605			
	His	Lys	Val	Tyr	Ala	Cys	Glu	Val	Thr	His	Gln	Gly	Leu	Ser	Ser	Pro
		610					615					620				
	Val	Thr	Lys	Ser	Phe	Asn	Arg	Gly	Glu	Cys	Gly	Gly	Gly	Gly	Ser	Gly
	625					630					635					640
	Gly	Gly	Gly	Ser	Gly	Gly	Gly	Gly	Ser	Gln	Pro	Glu	Asn	Asn	Tyr	Lys
					645					650						655
	Thr	Thr	Pro	Pro	Val	Leu	Asp	Ser	Asp	Gly	Ser	Phe	Phe	Leu	Tyr	Ser
				660					665						670	
	Arg	Leu	Thr	Val	Asp	Lys	Ser	Arg	Trp	Gln	Glu	Gly	Asn	Val	Phe	Ser
			675					680					685			
	Cys	Ser	Val	Met	His	Glu	Ala	Leu	His	Asn	His	Tyr	Thr	Gln	Lys	Ser
		690					695					700				

Leu Ser Leu Ser Leu Gly Lys
705 710

<210> 127
<211> 711
<212> PRT
<213> 人工序列

<220>
<223> 人工序列的描述: 合成多肽

<400> 127
Met Gly Trp Ser Cys Ile Ile Leu Phe Leu Val Ala Thr Ala Thr Gly
1 5 10 15

Val His Ser Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln
20 25 30

Pro Gly Arg Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe
35 40 45

Ser Val Tyr Gly Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu
50 55 60

[0201]

Glu Trp Val Ala Ile Ile Trp Tyr Asp Gly Asp Asn Gln Tyr Tyr Ala
65 70 75 80

Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn
85 90 95

Thr Leu Tyr Leu Gln Met Asn Gly Leu Arg Ala Glu Asp Thr Ala Val
100 105 110

Tyr Tyr Cys Ala Arg Asp Leu Arg Thr Gly Pro Phe Asp Tyr Trp Gly
115 120 125

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

Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser Thr Ala
145 150 155 160

Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val
165 170 175

Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala
180 185 190

Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val
195 200 205

Pro Ser Ser Ser Leu Gly Thr Lys Thr Tyr Thr Cys Asn Val Asp His
210 215 220

Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Ser Lys Tyr Gly
225 230 235 240

Pro Pro Cys Pro Pro Cys Pro Ala Pro Glu Phe Leu Gly Gly Pro Ser
245 250 255

Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg
260 265 270

Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser Gln Glu Asp Pro
275 280 285

[0202]

Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala
290 295 300

Lys Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr Tyr Arg Val Val
305 310 315 320

Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr
325 330 335

Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr
340 345 350

Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu
355 360 365

Pro Pro Ser Gln Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys
370 375 380

Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser
385 390 395 400

Asn Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
405 410 415

Gly Gly Gly Gly Ser Glu Ile Val Leu Thr Gln Ser Pro Ala Thr Leu
420 425 430

Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Lys
435 440 445

Gly Val Ser Thr Ser Gly Tyr Ser Tyr Leu His Trp Tyr Gln Gln Lys
450 455 460

Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr Leu Ala Ser Tyr Leu Glu
465 470 475 480

Ser Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe
485 490 495

Thr Leu Thr Ile Ser Ser Leu Glu Pro Glu Asp Phe Ala Val Tyr Tyr
500 505 510

[0203]

Cys Gln His Ser Arg Asp Leu Pro Leu Thr Phe Gly Gly Gly Thr Lys
515 520 525

Val Glu Ile Lys Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro
530 535 540

Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu
545 550 555 560

Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp
565 570 575

Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp
580 585 590

Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys
595 600 605

Ala Asp Tyr Glu Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln
610 615 620

Gly Leu Ser Ser Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys Gly
625 630 635 640

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Pro Glu Asn Asn Tyr Lys
645 650 655

Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser
660 665 670

Arg Leu Thr Val Asp Lys Ser Arg Trp Gln Glu Gly Asn Val Phe Ser
675 680 685

Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser
690 695 700

Leu Ser Leu Ser Leu Gly Lys
705 710

<210> 128

<211> 711

<212> PRT

[0204] <213> 人工序列

<220>

<223> 人工序列的描述：合成多肽

<400> 128

Met Gly Trp Ser Cys Ile Ile Leu Phe Leu Val Ala Thr Ala Thr Gly
1 5 10 15

Val His Ser Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln
20 25 30

Pro Gly Arg Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe
35 40 45

Ser Val Tyr Gly Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu
50 55 60

Glu Trp Val Ala Ile Ile Trp Tyr Asp Gly Asp Asn Gln Tyr Tyr Ala
65 70 75 80

Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn
85 90 95

Thr Leu Tyr Leu Gln Met Asn Gly Leu Arg Ala Glu Asp Thr Ala Val
 100 105 110

Tyr Tyr Cys Ala Arg Asp Leu Arg Thr Gly Pro Phe Asp Tyr Trp Gly
 115 120 125

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

Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser Thr Ala
 145 150 155 160

Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val
 165 170 175

Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala
 180 185 190

Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val
 195 200 205

[0205] Pro Ser Ser Ser Leu Gly Thr Lys Thr Tyr Thr Cys Asn Val Asp His
 210 215 220

Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Ser Lys Tyr Gly
 225 230 235 240

Pro Pro Cys Pro Pro Cys Pro Ala Pro Glu Phe Leu Gly Gly Pro Ser
 245 250 255

Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg
 260 265 270

Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser Gln Glu Asp Pro
 275 280 285

Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala
 290 295 300

Lys Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr Tyr Arg Val Val
 305 310 315 320

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

	325		330		335
	Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr	340	345		350
	Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu	355	360		365
	Pro Pro Ser Gln Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys	370	375		380
	Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser	385	390	395	400
	Asn Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser	405		410	415
	Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Ile Val Leu Thr Gln	420	425		430
[0206]	Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser	435	440		445
	Cys Arg Ala Ser Lys Gly Val Ser Thr Ser Gly Tyr Ser Tyr Leu His	450	455		460
	Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr Leu	465	470	475	480
	Ala Ser Tyr Leu Glu Ser Gly Val Pro Ala Arg Phe Ser Gly Ser Gly	485		490	495
	Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Glu Pro Glu Asp	500	505		510
	Phe Ala Val Tyr Tyr Cys Gln His Ser Arg Asp Leu Pro Leu Thr Phe	515	520		525
	Gly Gly Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala Pro Ser	530	535		540
	Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr Ala	545	550	555	560

Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val
565 570 575

Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser
580 585 590

Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr
595 600 605

Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala Cys
610 615 620

Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe Asn
625 630 635 640

Arg Gly Glu Cys Gly Gly Gly Gly Ser Gln Pro Glu Asn Asn Tyr Lys
645 650 655

Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser
660 665 670

[0207]

Arg Leu Thr Val Asp Lys Ser Arg Trp Gln Glu Gly Asn Val Phe Ser
675 680 685

Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser
690 695 700

Leu Ser Leu Ser Leu Gly Lys
705 710

<210> 129

<211> 721

<212> PRT

<213> 人工序列

<220>

<223> 人工序列的描述：合成多肽

<400> 129

Met Gly Trp Ser Cys Ile Ile Leu Phe Leu Val Ala Thr Ala Thr Gly
1 5 10 15

Val His Ser Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln
20 25 30

Pro Gly Arg Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe
 35 40 45

Ser Val Tyr Gly Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu
 50 55 60

Glu Trp Val Ala Ile Ile Trp Tyr Asp Gly Asp Asn Gln Tyr Tyr Ala
 65 70 75 80

Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn
 85 90 95

Thr Leu Tyr Leu Gln Met Asn Gly Leu Arg Ala Glu Asp Thr Ala Val
 100 105 110

Tyr Tyr Cys Ala Arg Asp Leu Arg Thr Gly Pro Phe Asp Tyr Trp Gly
 115 120 125

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

[0208]

Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser Thr Ala
 145 150 155 160

Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val
 165 170 175

Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala
 180 185 190

Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val
 195 200 205

Pro Ser Ser Ser Leu Gly Thr Lys Thr Tyr Thr Cys Asn Val Asp His
 210 215 220

Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Ser Lys Tyr Gly
 225 230 235 240

Pro Pro Cys Pro Pro Cys Pro Ala Pro Glu Phe Leu Gly Gly Pro Ser
 245 250 255

Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg
260 265 270

Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser Gln Glu Asp Pro
275 280 285

Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala
290 295 300

Lys Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr Tyr Arg Val Val
305 310 315 320

Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr
325 330 335

Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr
340 345 350

Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu
355 360 365

[0209]

Pro Pro Ser Gln Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys
370 375 380

Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser
385 390 395 400

Asn Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
405 410 415

Gly Gly Gly Gly Ser Glu Ile Val Leu Thr Gln Ser Pro Ala Thr Leu
420 425 430

Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Lys
435 440 445

Gly Val Ser Thr Ser Gly Tyr Ser Tyr Leu His Trp Tyr Gln Gln Lys
450 455 460

Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr Leu Ala Ser Tyr Leu Glu
465 470 475 480

Ser Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe
 485 490 495

Thr Leu Thr Ile Ser Ser Leu Glu Pro Glu Asp Phe Ala Val Tyr Tyr
 500 505 510

Cys Gln His Ser Arg Asp Leu Pro Leu Thr Phe Gly Gly Gly Thr Lys
 515 520 525

Val Glu Ile Lys Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro
 530 535 540

Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu
 545 550 555 560

Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp
 565 570 575

Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp
 580 585 590

[0210] Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys
 595 600 605

Ala Asp Tyr Glu Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln
 610 615 620

Gly Leu Ser Ser Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys Gly
 625 630 635 640

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
 645 650 655

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

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

Ser Arg Trp Gln Glu Gly Asn Val Phe Ser Cys Ser Val Met His Glu
 690 695 700

Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Leu Gly

	705	710	715	720												
	Lys															
	<210> 130															
	<211> 701															
	<212> PRT															
	<213> 人工序列															
	<220>															
	<223> 人工序列的描述: 合成多肽															
	<400> 130															
	Met	Gly	Trp	Ser	Cys	Ile	Ile	Leu	Phe	Leu	Val	Ala	Thr	Ala	Thr	Gly
	1				5					10					15	
	Val	His	Ser	Gln	Val	Gln	Leu	Val	Glu	Ser	Gly	Gly	Gly	Val	Val	Gln
				20					25					30		
	Pro	Gly	Arg	Ser	Leu	Arg	Leu	Ser	Cys	Ala	Ala	Ser	Gly	Phe	Thr	Phe
			35					40					45			
[0211]	Ser	Val	Tyr	Gly	Met	Asn	Trp	Val	Arg	Gln	Ala	Pro	Gly	Lys	Gly	Leu
		50					55					60				
	Glu	Trp	Val	Ala	Ile	Ile	Trp	Tyr	Asp	Gly	Asp	Asn	Gln	Tyr	Tyr	Ala
	65					70					75					80
	Asp	Ser	Val	Lys	Gly	Arg	Phe	Thr	Ile	Ser	Arg	Asp	Asn	Ser	Lys	Asn
				85						90					95	
	Thr	Leu	Tyr	Leu	Gln	Met	Asn	Gly	Leu	Arg	Ala	Glu	Asp	Thr	Ala	Val
				100					105						110	
	Tyr	Tyr	Cys	Ala	Arg	Asp	Leu	Arg	Thr	Gly	Pro	Phe	Asp	Tyr	Trp	Gly
			115					120					125			
	Gln	Gly	Thr	Leu	Val	Thr	Val	Ser	Ser	Ala	Ser	Thr	Lys	Gly	Pro	Ser
		130					135						140			
	Val	Phe	Pro	Leu	Ala	Pro	Cys	Ser	Arg	Ser	Thr	Ser	Glu	Ser	Thr	Ala
	145					150					155					160
	Ala	Leu	Gly	Cys	Leu	Val	Lys	Asp	Tyr	Phe	Pro	Glu	Pro	Val	Thr	Val

	165	170	175
	Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala 180 185 190		
	Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val 195 200 205		
	Pro Ser Ser Ser Leu Gly Thr Lys Thr Tyr Thr Cys Asn Val Asp His 210 215 220		
	Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Ser Lys Tyr Gly 225 230 235 240		
	Pro Pro Cys Pro Pro Cys Pro Ala Pro Glu Phe Leu Gly Gly Pro Ser 245 250 255		
	Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg 260 265 270		
[0212]	Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser Gln Glu Asp Pro 275 280 285		
	Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala 290 295 300		
	Lys Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr Tyr Arg Val Val 305 310 315 320		
	Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr 325 330 335		
	Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr 340 345 350		
	Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu 355 360 365		
	Pro Pro Ser Gln Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys 370 375 380		
	Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser 385 390 395 400		

Asn Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Ile Val Leu Thr
405 410 415

Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu
420 425 430

Ser Cys Arg Ala Ser Lys Gly Val Ser Thr Ser Gly Tyr Ser Tyr Leu
435 440 445

His Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr
450 455 460

Leu Ala Ser Tyr Leu Glu Ser Gly Val Pro Ala Arg Phe Ser Gly Ser
465 470 475 480

Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Glu Pro Glu
485 490 495

Asp Phe Ala Val Tyr Tyr Cys Gln His Ser Arg Asp Leu Pro Leu Thr
500 505 510

[0213]

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala Pro
515 520 525

Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr
530 535 540

Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys
545 550 555 560

Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu
565 570 575

Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser
580 585 590

Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala
595 600 605

Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe
610 615 620

Asn Arg Gly Glu Cys Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln
625 630 635 640

Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly
645 650 655

Ser Phe Phe Leu Tyr Ser Arg Leu Thr Val Asp Lys Ser Arg Trp Gln
660 665 670

Glu Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
675 680 685

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Leu Gly Lys
690 695 700

<210> 131

<211> 731

<212> PRT

<213> 人工序列

<220>

<223> 人工序列的描述：合成多肽

[0214]

<400> 131

Met Gly Trp Ser Cys Ile Ile Leu Phe Leu Val Ala Thr Ala Thr Gly
1 5 10 15

Val His Ser Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln
20 25 30

Pro Gly Arg Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe
35 40 45

Ser Val Tyr Gly Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu
50 55 60

Glu Trp Val Ala Ile Ile Trp Tyr Asp Gly Asp Asn Gln Tyr Tyr Ala
65 70 75 80

Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn
85 90 95

Thr Leu Tyr Leu Gln Met Asn Gly Leu Arg Ala Glu Asp Thr Ala Val
100 105 110

Tyr Tyr Cys Ala Arg Asp Leu Arg Thr Gly Pro Phe Asp Tyr Trp Gly
 115 120 125

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

Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser Thr Ala
 145 150 155 160

Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val
 165 170 175

Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala
 180 185 190

Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val
 195 200 205

Pro Ser Ser Ser Leu Gly Thr Lys Thr Tyr Thr Cys Asn Val Asp His
 210 215 220

[0215]

Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Ser Lys Tyr Gly
 225 230 235 240

Pro Pro Cys Pro Pro Cys Pro Ala Pro Glu Phe Leu Gly Gly Pro Ser
 245 250 255

Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg
 260 265 270

Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser Gln Glu Asp Pro
 275 280 285

Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala
 290 295 300

Lys Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr Tyr Arg Val Val
 305 310 315 320

Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr
 325 330 335

Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr
 340 345 350

Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu
 355 360 365

Pro Pro Ser Gln Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys
 370 375 380

Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser
 385 390 395 400

Asn Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
 405 410 415

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Ile Val Leu Thr Gln
 420 425 430

Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser
 435 440 445

[0216] Cys Arg Ala Ser Lys Gly Val Ser Thr Ser Gly Tyr Ser Tyr Leu His
 450 455 460

Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr Leu
 465 470 475 480

Ala Ser Tyr Leu Glu Ser Gly Val Pro Ala Arg Phe Ser Gly Ser Gly
 485 490 495

Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Glu Pro Glu Asp
 500 505 510

Phe Ala Val Tyr Tyr Cys Gln His Ser Arg Asp Leu Pro Leu Thr Phe
 515 520 525

Gly Gly Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala Pro Ser
 530 535 540

Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr Ala
 545 550 555 560

Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val

	565	570	575
	Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser 580	585	590
	Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr 595	600	605
	Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala Cys 610	615	620
	Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe Asn 625	630	635
	Arg Gly Glu Cys Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly 645	650	655
	Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Ser Gln Pro Glu 660	665	670
[0217]	Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe 675	680	685
	Phe Leu Tyr Ser Arg Leu Thr Val Asp Lys Ser Arg Trp Gln Glu Gly 690	695	700
	Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr 705	710	715
	Thr Gln Lys Ser Leu Ser Leu Ser Leu Gly Lys 725	730	
	<210> 132		
	<211> 726		
	<212> PRT		
	<213> 人工序列		
	<220>		
	<223> 人工序列的描述：合成多肽		
	<400> 132		
	Met Gly Trp Ser Cys Ile Ile Leu Phe Leu Val Ala Thr Ala Thr Gly 1	5	10
	Val His Ser Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln		

	20	25	30
	Pro Gly Arg Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe 35	40	45
	Ser Val Tyr Gly Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu 50	55	60
	Glu Trp Val Ala Ile Ile Trp Tyr Asp Gly Asp Asn Gln Tyr Tyr Ala 65	70	75
	Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn 85	90	95
	Thr Leu Tyr Leu Gln Met Asn Gly Leu Arg Ala Glu Asp Thr Ala Val 100	105	110
	Tyr Tyr Cys Ala Arg Asp Leu Arg Thr Gly Pro Phe Asp Tyr Trp Gly 115	120	125
[0218]	Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser 130	135	140
	Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser Thr Ala 145	150	155
	Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val 165	170	175
	Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala 180	185	190
	Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val 195	200	205
	Pro Ser Ser Ser Leu Gly Thr Lys Thr Tyr Thr Cys Asn Val Asp His 210	215	220
	Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Ser Lys Tyr Gly 225	230	235
	Pro Pro Cys Pro Pro Cys Pro Ala Pro Glu Phe Leu Gly Gly Pro Ser 245	250	255

Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg
260 265 270

Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser Gln Glu Asp Pro
275 280 285

Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala
290 295 300

Lys Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr Tyr Arg Val Val
305 310 315 320

Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr
325 330 335

Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr
340 345 350

Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu
355 360 365

[0219]

Pro Pro Ser Gln Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys
370 375 380

Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser
385 390 395 400

Asn Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
405 410 415

Gly Gly Gly Gly Ser Glu Ile Val Leu Thr Gln Ser Pro Ala Thr Leu
420 425 430

Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Lys
435 440 445

Gly Val Ser Thr Ser Gly Tyr Ser Tyr Leu His Trp Tyr Gln Gln Lys
450 455 460

Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr Leu Ala Ser Tyr Leu Glu
465 470 475 480

Ser Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe
485 490 495

Thr Leu Thr Ile Ser Ser Leu Glu Pro Glu Asp Phe Ala Val Tyr Tyr
500 505 510

Cys Gln His Ser Arg Asp Leu Pro Leu Thr Phe Gly Gly Gly Thr Lys
515 520 525

Val Glu Ile Lys Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro
530 535 540

Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu
545 550 555 560

Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp
565 570 575

Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp
580 585 590

[0220]

Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys
595 600 605

Ala Asp Tyr Glu Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln
610 615 620

Gly Leu Ser Ser Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys Gly
625 630 635 640

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
645 650 655

Gly Gly Ser Gly Gly Gly Gly Ser Gln Pro Glu Asn Asn Tyr Lys Thr
660 665 670

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

Leu Thr Val Asp Lys Ser Arg Trp Gln Glu Gly Asn Val Phe Ser Cys
690 695 700

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
705 710 715 720

Ser Leu Ser Leu Gly Lys
725

<210> 133

<211> 726

<212> PRT

<213> 人工序列

<220>

<223> 人工序列的描述: 合成多肽

<400> 133

Met Gly Trp Ser Cys Ile Ile Leu Phe Leu Val Ala Thr Ala Thr Gly
1 5 10 15

Val His Ser Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln
20 25 30

Pro Gly Arg Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe
35 40 45

[0221]

Ser Val Tyr Gly Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu
50 55 60

Glu Trp Val Ala Ile Ile Trp Tyr Asp Gly Asp Asn Gln Tyr Tyr Ala
65 70 75 80

Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn
85 90 95

Thr Leu Tyr Leu Gln Met Asn Gly Leu Arg Ala Glu Asp Thr Ala Val
100 105 110

Tyr Tyr Cys Ala Arg Asp Leu Arg Thr Gly Pro Phe Asp Tyr Trp Gly
115 120 125

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

Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser Thr Ala
145 150 155 160

Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val
165 170 175

Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala
180 185 190

Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val
195 200 205

Pro Ser Ser Ser Leu Gly Thr Lys Thr Tyr Thr Cys Asn Val Asp His
210 215 220

Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Ser Lys Tyr Gly
225 230 235 240

Pro Pro Cys Pro Pro Cys Pro Ala Pro Glu Phe Leu Gly Gly Pro Ser
245 250 255

Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg
260 265 270

[0222] Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser Gln Glu Asp Pro
275 280 285

Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala
290 295 300

Lys Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr Tyr Arg Val Val
305 310 315 320

Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr
325 330 335

Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr
340 345 350

Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu
355 360 365

Pro Pro Ser Gln Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys
370 375 380

Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser

	385		390				395							400		
	Asn	Gly	Gly	Gly	Gly	Ser	Gly	Gly	Gly	Gly	Ser	Gly	Gly	Gly	Ser	
					405					410				415		
	Gly	Gly	Gly	Gly	Ser	Gly	Gly	Gly	Gly	Ser	Glu	Ile	Val	Leu	Thr	Gln
				420					425					430		
	Ser	Pro	Ala	Thr	Leu	Ser	Leu	Ser	Pro	Gly	Glu	Arg	Ala	Thr	Leu	Ser
			435					440					445			
	Cys	Arg	Ala	Ser	Lys	Gly	Val	Ser	Thr	Ser	Gly	Tyr	Ser	Tyr	Leu	His
		450					455					460				
	Trp	Tyr	Gln	Gln	Lys	Pro	Gly	Gln	Ala	Pro	Arg	Leu	Leu	Ile	Tyr	Leu
	465					470					475					480
	Ala	Ser	Tyr	Leu	Glu	Ser	Gly	Val	Pro	Ala	Arg	Phe	Ser	Gly	Ser	Gly
					485					490						495
[0223]	Ser	Gly	Thr	Asp	Phe	Thr	Leu	Thr	Ile	Ser	Ser	Leu	Glu	Pro	Glu	Asp
				500					505					510		
	Phe	Ala	Val	Tyr	Tyr	Cys	Gln	His	Ser	Arg	Asp	Leu	Pro	Leu	Thr	Phe
			515					520					525			
	Gly	Gly	Gly	Thr	Lys	Val	Glu	Ile	Lys	Arg	Thr	Val	Ala	Ala	Pro	Ser
		530					535					540				
	Val	Phe	Ile	Phe	Pro	Pro	Ser	Asp	Glu	Gln	Leu	Lys	Ser	Gly	Thr	Ala
	545					550					555					560
	Ser	Val	Val	Cys	Leu	Leu	Asn	Asn	Phe	Tyr	Pro	Arg	Glu	Ala	Lys	Val
					565					570					575	
	Gln	Trp	Lys	Val	Asp	Asn	Ala	Leu	Gln	Ser	Gly	Asn	Ser	Gln	Glu	Ser
				580					585					590		
	Val	Thr	Glu	Gln	Asp	Ser	Lys	Asp	Ser	Thr	Tyr	Ser	Leu	Ser	Ser	Thr
			595					600					605			
	Leu	Thr	Leu	Ser	Lys	Ala	Asp	Tyr	Glu	Lys	His	Lys	Val	Tyr	Ala	Cys
		610					615					620				

Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe Asn
 625 630 635 640

Arg Gly Glu Cys Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
 645 650 655

Gly Gly Ser Gly Gly Gly Gly Ser Gln Pro Glu Asn Asn Tyr Lys Thr
 660 665 670

[0224] Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Arg
 675 680 685

Leu Thr Val Asp Lys Ser Arg Trp Gln Glu Gly Asn Val Phe Ser Cys
 690 695 700

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
 705 710 715 720

Ser Leu Ser Leu Gly Lys
 725

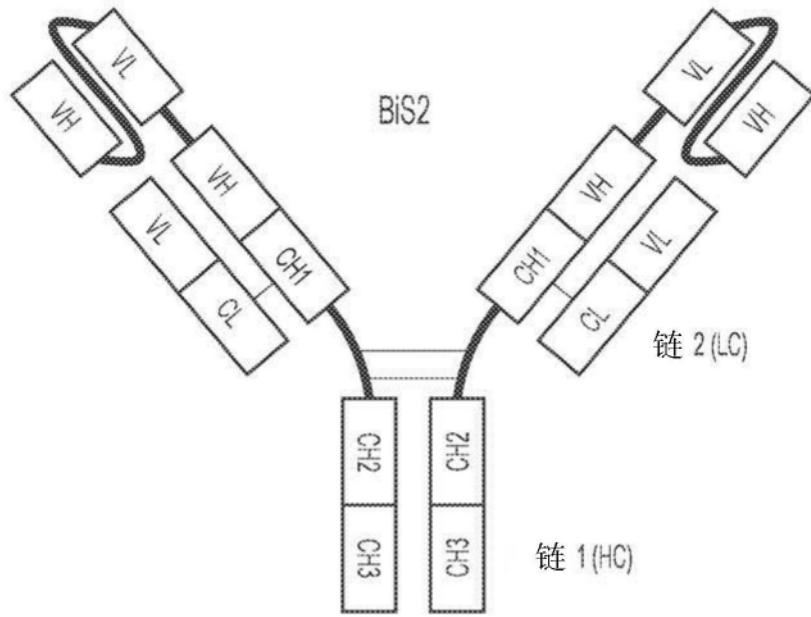


图1

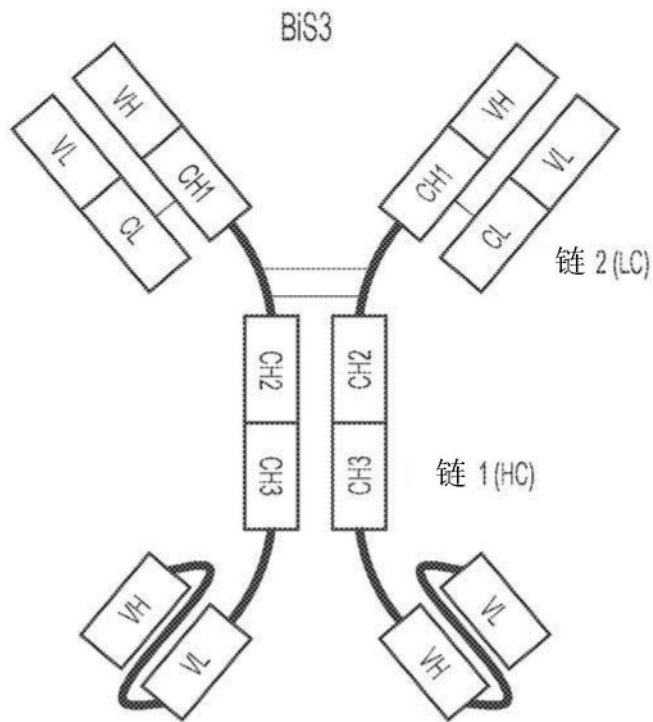


图2A

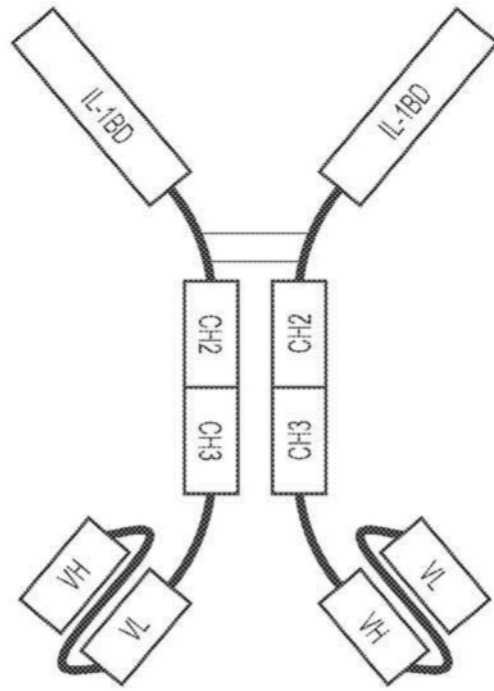


图2B

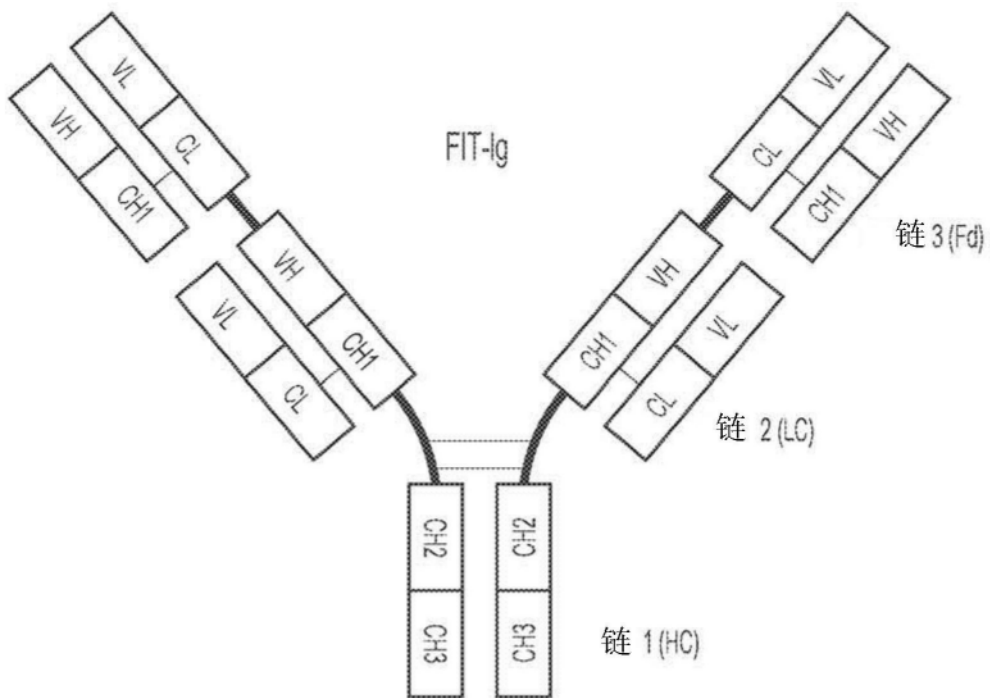


图3A

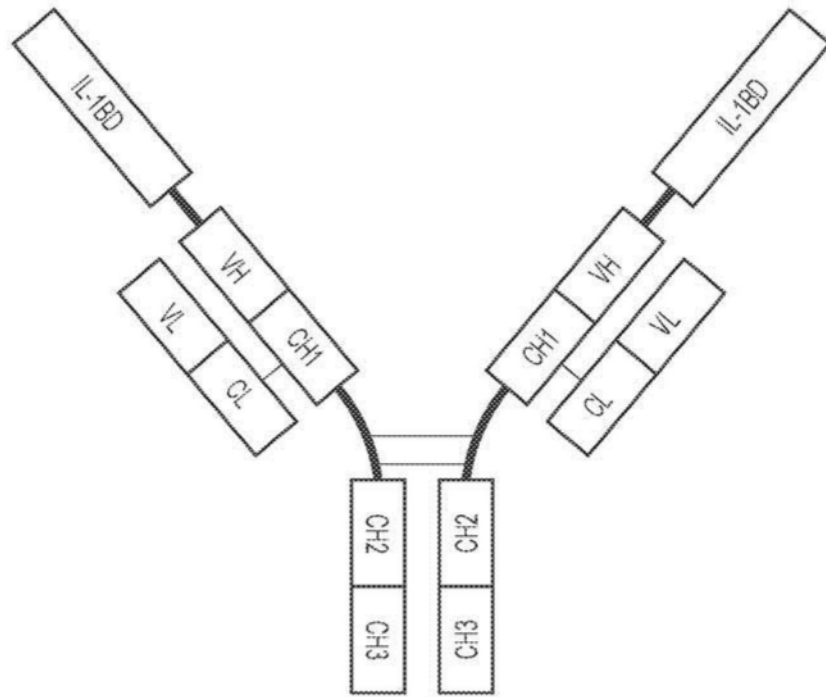


图3B

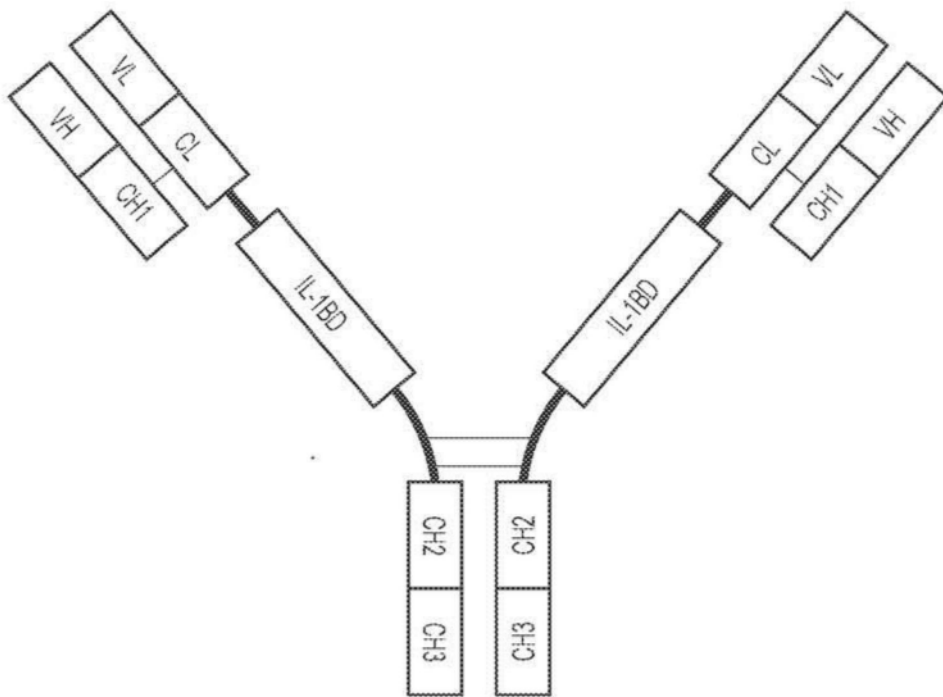


图3C

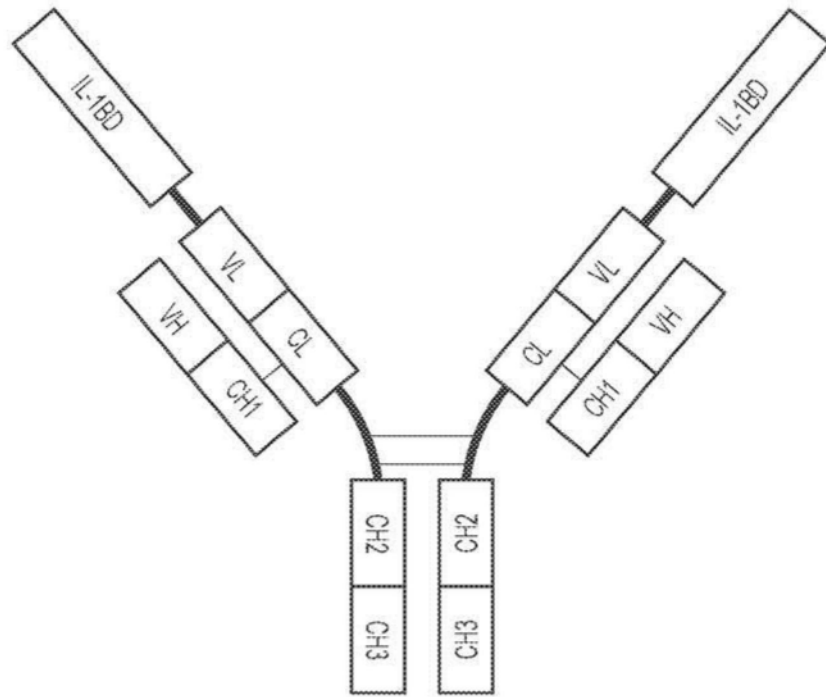


图3D

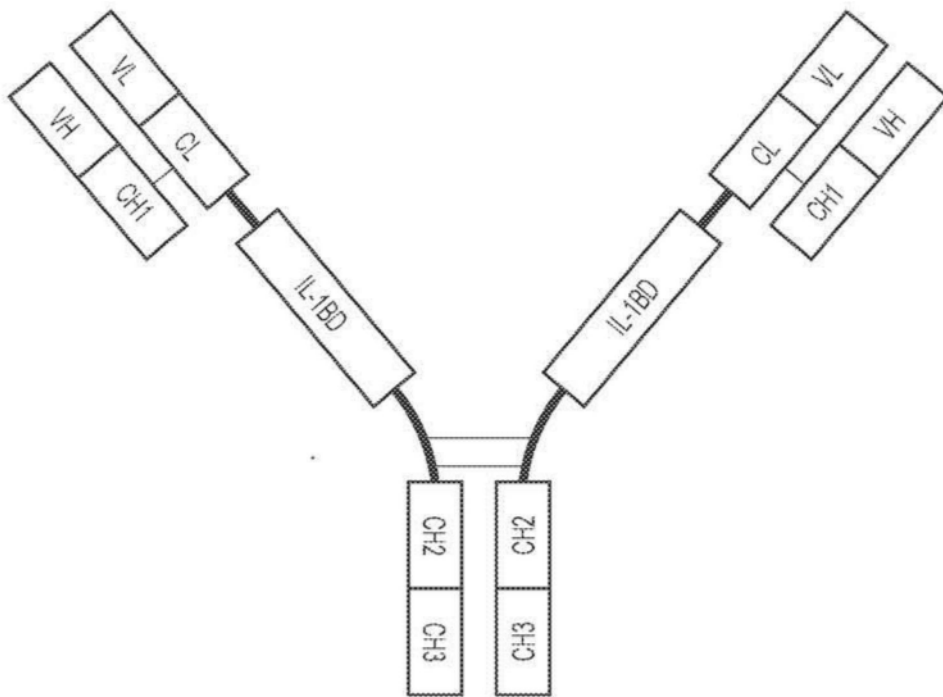


图3E

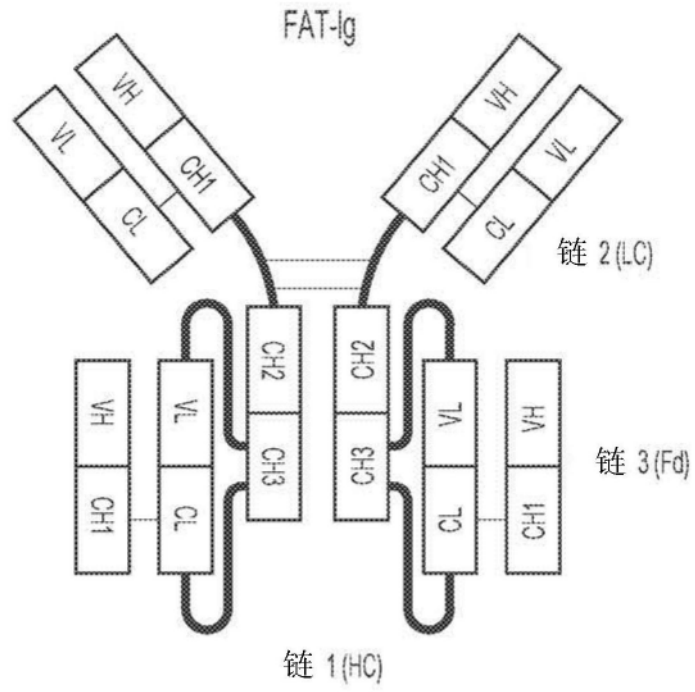


图4

结合蛋白的氨基酸序列:

ITA101

链 1

MGWSCILFLVATATGVHSQVQLVQSGVEVKKPGASVKVSCKASGYTFTNYYMYW
VRQAPGQGLEWMGGINPSNGGTNFNEKFKNRVTLTDSSTTTAYMELKSLQFDDTA
VYYCARRDYRFDMGFDYWGQGTTVTVSSGGGGSGGGGSGGGGSGGGGSEIVLTQS
PATLSLSPGERATLSCRASKGVSTSGYSYLHWYQQKPGQAPRLLIYLASYLESVPA
RFSGSGSGTDFTLTISSLEPEDFAVYYCQHSRDLPLTFGGGKVEIKGGGGSGGGGSQ
VQLVESGGGVVQPGRSLRLSCAASGFTFSVYGMNWVRQAPGKGLEWVAIIWYDGD
NQYYADSVKGRFTISRDNKNTLYLQMNGLRAEDTAVYYCARDLRTGPFQDYWGQG
TLVTVSSASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGVH
TFPAVLQSSGLYSLSSVTVPSSSLGKTYTCNVDPKPSNTKVDKRVESKYGPPCPPC
PAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVDVSDPEVQFNWYVDGVEVHN
AKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQP
REPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSD
DGSFFLYSRLTVDKSRWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK

链 2

MGWSCILFLVATATGVHSEIVLTQSPDFQSVTPKEKVTITCRASQSIGSSLHWYQQK
PDQSPKLLIKYASQSFSGVPSRFSGSGSGTDFLTINSLEAEDAAAYYCHQSSSLPFTF
GPGTKVDIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQ
SGNSQESVTEQDSKSTYLSSTLTLSKADYEEKHKVYACEVTHQGLSSPVTKSFNRG
EC

ITA102

链 1

MGWSCILFLVATATGVHSQVQLVESGGGVVQPGRSLRLDCKASGITFSNSGMHW
RQAPGKGLEWVAIIWYDGSKRYADSVKGRFTISRDNKNTLFLQMNSLRAEDTA
VYYCATNDYWGQGTTLVTVSSGGGGSGGGGSGGGGSGGGGSEIVLTQSPATLSLSP
GERATLSCRASQSVSSYLAWYQQKPGQAPRLLIYDASNRAATGIPARFSGSGTDFTL
TISSLEPEDFAVYYCQSSNWPRTFGQGTKEIKGGGGSGGGGSQVQLVESGGGVV
QPGRSLRLSCAASGFTFSVYGMNWVRQAPGKGLEWVAIIWYDGDNQYYADSVKGR
FTISRDNKNTLYLQMNGLRAEDTAVYYCARDLRTGPFQDYWGQGTTLVTVSSASTKG
PSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLY
SLSSVTVPSSSLGKTYTCNVDPKPSNTKVDKRVESKYGPPCPPCPAPEFLGGPSV
FLFPPKPKDTLMISRTPEVTCVVDVSDPEVQFNWYVDGVEVHNAKTKPREEQFN
STYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPREPQVYTLPPS
QEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGSFFLYSRLT
VDKSRWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK

图5

链2和ITA101的链2相同

ITA103

链 1

MGWSCIIIFLVATATGVHSQVQLVESGGGVVQPGRSLRLSCAASGFTFSVYGMNWW
RQAPGKGLEWVAIIWYDGDNQYYADSVKGRFTISRDNKNTLYLQMNGLRAEDTA
VYYCARDLRTGPFDYWGQGTLLTVSSGGGGSGGGGSGGGGSGGGGSEIVLTQSPDF
QSVTPKEKVTITCRASQSIGSSLHWYQQKPDQSPKLLIKYASQSFSGVPSRFSGSGSGT
DFTLTINSLEAEDAAAYYCHQSSSLPFTFGPGTKVDIKGGGGSGGGGSGVQLVQSGV
EVKKPGASVKVSKASGYFTNYYMYWVRQAPGQGLEWMGGINPSNGGTFNFEK
KNRVTLTDSSTTTAYMELKSLQFDDTAVYYCARRDYRFDMGFDYWGQGTITVTS
SASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVL
QSSGLYSLSSVTVPSSSLGKTYTCNVDHKPSNTKVDKRVESKYGPPCPPCPAPEFL
GGPSVFLFPPKPKDTLMISRTPEVTCVVDVSDQEDPEVQFNWYVDGVEVHNAKTKP
REEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPREPQV
YTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFF
LYSRLTVDKSRWQEGNVFSCSVMHEALHNHYTQKSLSLGLGK

链 2

MGWSCIIIFLVATATGVHSEIVLTQSPATLSLSPGERATLSCRASKGVSTSGYSYLHW
YQQKPGQAPRLLIYLAAYLESQVAPRFSGSGSGTDFLTITSSLEPEDFAVYYCQHSRD
LPLTFGGGKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKV
DNALQSGNSQESVTEQDSKDYSLSSLTLSKADYEEKHKVYACEVTHQGLSSPVTK
SFNRGEC

ITA104

链 1

MGWSCIIIFLVATATGVHSQVQLVESGGGVVQPGRSLRLSCAASGFTFSVYGMNWW
RQAPGKGLEWVAIIWYDGDNQYYADSVKGRFTISRDNKNTLYLQMNGLRAEDTA
VYYCARDLRTGPFDYWGQGTLLTVSSGGGGSGGGGSGGGGSGGGGSEIVLTQSPDF
QSVTPKEKVTITCRASQSIGSSLHWYQQKPDQSPKLLIKYASQSFSGVPSRFSGSGSGT
DFTLTINSLEAEDAAAYYCHQSSSLPFTFGPGTKVDIKGGGGSGGGGSGVQLVESGG
GVVQPGRSLRLDCKASGITFSNSGMHWVRQAPGKGLEWVAIIWYDGSKRYYADSV
KGRFTISRDNKNTLFLQMNSLRAEDTAVYYCATNDDYWGQGTLLTVSSASTKGPS
VFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSL
SSVTVPSSSLGKTYTCNVDHKPSNTKVDKRVESKYGPPCPPCPAPEFLGGPSVFLF
PPKPKDTLMISRTPEVTCVVDVSDQEDPEVQFNWYVDGVEVHNAKTKPREEQFNST
YRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPREPQVYTLPPSQE
EMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSRLTV
DKSRWQEGNVFSCSVMHEALHNHYTQKSLSLGLGK

图5续

链 2

MGWSCIIIFLVATATGVHSEIVLTQSPATLSLSPGERATLSCRASQSVSSYLAWYQQK
 PGQAPRLLIYDASNRATGIPARFSGSGSGTDFTLTISSELPEDFAVYYCQQSSNWPRTF
 GQGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQ
 SGNSQESVTEQDSKDYSLSTLTLKADYEEKHKVYACEVTHQGLSSPVTKSFNRG
 EC

ITA201

链 1

MGWSCIIIFLVATATGVHSQVQLVESGGGVVQPGRSLRLSCAASGFTFSVYGMNWW
 RQAPGKGLEWVAIIWYDGDNQYYADSVKGRFTISRDNKNTLYLQMNGLRAEDTA
 VYYCARDLRTGPFDYWGQGLVTVSSASTKGPSVFPLAPCSRSTSESTAALGCLVKD
 YFPEPVTVSWNSGALTSQVHTFPAVLQSSGLYSLSSVTVPSSSLGKTYTCNVDPK
 PSNTKVDKRVESKYGPPCPPCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDV
 SQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKC
 KVSNGKLPSSIEKTISKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAV
 EWESNGQPENNYKTTTPVLDSDGSFFLYSRLTVDKSRWQEGNVFSCSVMHEALHNH
 YTQKSLSLGKGGGGSGGGGSQVQLVQSGVEVKKPGASVKVSCKASGYTFTNYY
 MYWVRQAPGQGLEWMGGINPSNGGTNFNEKFKNRVTLTDSSTTTAYMELKSLQF
 DDTAVYYCARRDYRFDMGFYWGQGTITVTVSSGGGGSGGGGSQVQLVQSGVEVKKPGASVKVSCKASGYTFTNYY
 VLTQSPATLSLSPGERATLSCRASKGVSTSGYSYLHWYQQKPGQAPRLLIYLASYLES
 GVPARFSGSGSGTDFTLTISSELPEDFAVYYCQHSRDLPLTFGGGKVEIK

链2和ITA101的链2相同

ITA202

链 1

MGWSCIIIFLVATATGVHSQVQLVESGGGVVQPGRSLRLSCAASGFTFSVYGMNWW
 RQAPGKGLEWVAIIWYDGDNQYYADSVKGRFTISRDNKNTLYLQMNGLRAEDTA
 VYYCARDLRTGPFDYWGQGLVTVSSASTKGPSVFPLAPCSRSTSESTAALGCLVKD
 YFPEPVTVSWNSGALTSQVHTFPAVLQSSGLYSLSSVTVPSSSLGKTYTCNVDPK
 PSNTKVDKRVESKYGPPCPPCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDV
 SQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKC
 KVSNGKLPSSIEKTISKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAV
 EWESNGQPENNYKTTTPVLDSDGSFFLYSRLTVDKSRWQEGNVFSCSVMHEALHNH
 YTQKSLSLGKGGGGSGGGGSQVQLVESGGGVVQPGRSLRLDCKASGITFSNSGM
 HWVRQAPGKGLEWVAIIWYDGSKRYADSVKGRFTISRDNKNTLFLQMNSLRAE
 DTAVYYCATNDDYWGQGLVTVSSGGGGSGGGGSQVQLVQSGVEVKKPGASVKVSCKASGYTFTNYY
 VLTQSPATLSLSPGERATLSCRASQSVSSYLAWYQQKPGQAPRLLIYDASNRATGIPARFSGSGSGT
 DFTLTISSELPEDFAVYYCQQSSNWPRTFGQGKVEIK

图5续

链2和ITA101的链2相同

ITA203

链 1

MGWSCILFLVATATGVHSQVQLVQSGVEVKKPGASVKVSCKASGYTFTNYYMYW
 VRQAPGQGLEWMGGINPSNGGTNFNEKFKNRVTLTTDSSTTTAYMELKSLQFDDTA
 VYYCARRDYRFDMGFDYWGQGTTVTVSSASTKGPSVFPLAPCSRSTSESTAALGCL
 VKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGKTYTCNV
 DHKPSNTKVDKRVESKYGPPCPPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVV
 VDVSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKE
 YKCKVSNKGLPSSIEKTISKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSD
 IAVEWESNGQPENNYKTTTPVLDSDGSFFLYSRLTVDKSRWQEGNVFSCSVMHEAL
 HNHYTQKSLSLGKGGGGSGGGGSQVQLVESGGGVVQPGRSLRLSCAASGFTFSV
 YGMNWVRQAPGKGLEWVAIIWYDGDNQYYADSVKGRFTISRDNKNTLYLQMNG
 LRAEDTAVYYCARDLRTGPFDYWGQGLTVTVSSGGGGSGGGGSQVQLVESGGGVV
 VLTQSPDFQSVTPKEKVTITCRASQSIGSSLHWYQQKPDQSPKLLIKYASQSFSGVPSR
 FSGSGSGTDFTLTINSLEAEDAAAYYCHQSSSLPFTFGPGTKVDIK

链2和ITA103的链2相同

ITA204

链 1

MGWSCILFLVATATGVHSQVQLVESGGGVVQPGRSLRLDCKASGITFSNSGMHWV
 RQAPGKGLEWVAIIWYDGSKRYYADSVKGRFTISRDNKNTLFLQMNSLRAEDTA
 VYYCATNDDYWGQGLTVTVSSASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEP
 VTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGKTYTCNVVVDHPSNTK
 VDKRVESKYGPPCPPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSQEDP
 EVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSN
 KGLPSSIEKTISKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWES
 NGQPENNYKTTTPVLDSDGSFFLYSRLTVDKSRWQEGNVFSCSVMHEALHNHNTQK
 SLSLGKGGGGSGGGGSQVQLVESGGGVVQPGRSLRLSCAASGFTFSVYGMNWVR
 QAPGKGLEWVAIIWYDGDNQYYADSVKGRFTISRDNKNTLYLQMNGLRAEDTAV
 YYCARDLRTGPFDYWGQGLTVTVSSGGGGSGGGGSQVQLVESGGGVV
 VLTQSPDFQSVTPKEKVTITCRASQSIGSSLHWYQQKPDQSPKLLIKYASQSFSGVPSR
 FSGSGSGTDFTLTINSLEAEDAAAYYCHQSSSLPFTFGPGTKVDIK

图5续

链2和ITA104的链2相同

ITA301

链 1

MGWSCILFLVATATGVHSEIVLTQSPATLSLSPGERATLSCRASKGVSTSGYSYLHW
YQQKPGQAPRLLIYLASYLESQVGFARFSGSGSDFTLTISSELEPEDFAVYYCQHSRD
LPLTFGGGKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKV
DNALQSGNSQESVTEQDSKSTYSLSSSTLTLSKADYEKHKVYACEVTHQGLSSPVTK
SFNRGECQVQLVESGGGVVQPGRSLRLSCAASGFTFSVYGMNWVRQAPGKGLEWV
AIIWYDGDNQYYADSVKGRFTISRDNKNTLYLQMNGLRRAEDTAVYYCARDLRTGP
FDYWGQGTLLTVSSASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNS
GALTSQVHTFPAVLQSSGLYSLSVTVPSSSLGKTYTCNVDPHKPSNTKVDKRVES
KYGPPCPPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSDPEVQFNWY
VDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEK
TISKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNY
KTTTPVLDSDGSFFLYSRLTVDKSRWQEGNVFSCSVMEALHNHYTQKSLSLGLGK

链2和ITA101的链2相同

链 3:

MGWSCILFLVATATGVHSQVQLVQSGVEVKKPGASVKVSKASGYFTFTNYMYW
VRQAPGQGLEWMGGINPSNGGTNFNEKFKNRVTLTDSSTTTAYMELKSLQFDDTA
VYYCARRDYRFDMGFYWGQGTITVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCL
VKDYFPEPVTVSWNSGALTSQVHTFPAVLQSSGLYSLSVTVPSSSLGKTYICNVN
HKPSNTKVDKRVKPKSC

ITA302

链 1

MGWSCILFLVATATGVHSEIVLTQSPATLSLSPGERATLSCRASQSVSSYLAWYQQK
PGQAPRLLIYDASNRATGIPARFSGSGSDFTLTISSELEPEDFAVYYCQSSNWPRTF
GQGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQ
SGNSQESVTEQDSKSTYSLSSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRG
ECQVQLVESGGGVVQPGRSLRLSCAASGFTFSVYGMNWVRQAPGKGLEWVAIIWY
DGDNQYYADSVKGRFTISRDNKNTLYLQMNGLRRAEDTAVYYCARDLRTGPFYD
WGQGTLLTVSSASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTS
GVHTFPAVLQSSGLYSLSVTVPSSSLGKTYTCNVDPHKPSNTKVDKRVESKYGPP
CPPCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSDPEVQFNWYVDG
VEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKA
KGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTP
VLDSDGSFFLYSRLTVDKSRWQEGNVFSCSVMEALHNHYTQKSLSLGLGK

图5续

链2和ITA101的链2相同

链 3:

MGWSCIIIFLVATATGVHSQVQLVESGGGVVQPGRSLRLDCKASGITFSNSGMHWV
RQAPGKGLEWVAVIWDGSKRYYADSVKGRFTISRDNKNTLFLQMNSLRAEDTA
VYYCATNDDYWGQGTLLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEP
VTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPSNTK
VDKRVEPKSC

ITA303

链 1

MGWSCIIIFLVATATGVHSEIVLTQSPDFQSVTPKEKVTITCRASQSIGSSLHWYQQK
PDQSPKLLIKYASQSFSGVPSRFSGSGSGTDFLTINSLEAEDAAAYYCHQSSSLPFTF
GPGTKVDIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQ
SGNSQESVTEQDSKDYSLSTLTLSKADYEEKHKVYACEVTHQGLSPVTKSFNRG
ECVQLVQSGVEVKKPGASVKVSCKASGYFTFTNYMYWVRQAPGQGLEWMGGIN
PSNGGTNFNEKFKNRVTLTDSSTTTAYMELKSLQFDDTAVYYCARRDYRFDMGFD
YWGQGTITVTVSSASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGA
LTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYTCNVDPKPSNTKVDKRVESKY
GPPCPPCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSDPEVQFNWYVD
GVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTI
KAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKT
TPPVLDSDGSFFLYSRLTVDKSRWQEGNVFSCSVMHEALHNHYTQKSLSLGLGK

链2和ITA103的链2相同

链 3:

MGWSCIIIFLVATATGVHSQVQLVESGGGVVQPGRSLRLSCAASGFTFSVYGMNWV
RQAPGKGLEWVAIIWYDGDNQYYADSVKGRFTISRDNKNTLYLQMNGLRAEDTA
VYYCARDLRTGPFDYWGQGTLLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVK
DYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHK
PSNTKVDKRVKPKSC

ITA304

链 1

MGWSCIIIFLVATATGVHSEIVLTQSPDFQSVTPKEKVTITCRASQSIGSSLHWYQQK
PDQSPKLLIKYASQSFSGVPSRFSGSGSGTDFLTINSLEAEDAAAYYCHQSSSLPFTF
GPGTKVDIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQ
SGNSQESVTEQDSKDYSLSTLTLSKADYEEKHKVYACEVTHQGLSPVTKSFNRG
ECVQLVESGGGVVQPGRSLRLDCKASGITFSNSGMHWVVRQAPGKGLEWVAVIWDG

图5续

DGSKRYYADSVKGRFTISRDN SKNTLFLQMNSLRAEDTAVYYCATNDDYWGQGL
 VTVSSASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTS
 GVTHTFPAVLQSSGLYSLSSVVTVPSSSLGKTYTCNV DHKPSNTKVDKRVESKY
 GPPCPPCPAPEFLGGPSVFLFPPKPKDTLMISRTP E VTCVVDVVSQEDPEVQFNWY
 VDGV E V H N A K T K P R E E Q F N S T Y R V V S V L T V L H Q D W L N G K E Y K C K V S N K G L P S S I E K T I S K A K G Q P R E
 P Q V Y T L P P S Q E E M T K N Q V S L T C L V K G F Y P S D I A V E W E S N G Q P E N N Y K T T P P V L D S D G
 S F F L Y S R L T V D K S R W Q E G N V F S C S V M H E A L H N H Y T Q K S L S L S L G K

链2和ITA104的链2相同

链3和ITA303的链3相同

ITA401: X=2, Y=4; ITC401: X=1, Y=5; ITC402: X=3, Y=3; ITC403: X=4, Y=2;
 ITC404: X=5, Y=1; ITC405: X=4, Y=4; ITC406: X=2, Y=2; ITD401: X=5, Y=5;
 ITD402: X=4, Y=5; ITD403: X=5, Y=4

链 1:

MGWSCILFLVATATGVHSQVQLVESGGGVVQPGRSLRLSCAASGFTFSVYGMNWV
 RQAPGKGLEWVAIIWYDGDNQYYADSVKGRFTISRDN SKNTLYLQMNGLRAEDTA
 VYYCARDLRTGPFDYWGQGLVTVSSASTKGPSVFPLAPCSRSTSESTAALGCLVKD
 YFPEPVTVSWNSGALTS GVTHTFPAVLQSSGLYSLSSVVTVPSSSLGKTYTCNV D H K
 PSNTKVDKRVESKYGPPCPPCPAPEFLGGPSVFLFPPKPKDTLMISRTP E VTCVVDV
 SQEDPEVQFNWYVDGV E V H N A K T K P R E E Q F N S T Y R V V S V L T V L H Q D W L N G K E Y K C
 K V S N K G L P S S I E K T I S K A K G Q P R E P Q V Y T L P P S Q E E M T K N Q V S L T C L V K G F Y P S D I A V
 E W E S N (G G G G S)_x E I V L T Q S P A T L S L S P G E R A T L S C R A S K G V S T S G Y S Y L H W Y Q Q K P G
 Q A P R L L I Y L A S Y L E S G V P A R F S G S G S G T D F T L T I S S L E P E D F A V Y Y C Q H S R D L P L T F G G
 G T K V E I K R T V A A P S V F I F P P S D E Q L K S G T A S V V C L L N N F Y P R E A K V Q W K V D N A L Q S G
 N S Q E S V T E Q D S K D S T Y S L S S T L T L S K A D Y E K H K V Y A C E V T H Q G L S S P V T K S F N R G E C (G G G G S)_y
 Q P E N N Y K T T P P V L D S D G S F F L Y S R L T V D K S R W Q E G N V F S C S V M H E A L H N H
 Y T Q K S L S L S L G K

链2和ITA101的链2相同

链 3:

MGWSCILFLVATATGVHSQVQLVQSGVEVKKPGASVKVCKASGYFTFTNYYMYW
 VRQAPGQGLEWMGGINPSNGGTNFNEKFKNRVTLTTDSSTTTAYMELKSLQFDDTA
 VYYCARRDYRFDMGFYWGQGTITVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCL
 VKDYFPEPVTVSWNSGALTS GVTHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVN
 HKPSNTKVDKRV E P K S C

图5续

ITA402

链 1

MGWSCILFLVATATGVHSQVQLVESGGGVVQPGRSLRLSCAASGFTFSVYGMNWV
 RQAPGKGLEWVAHWYDGDNQYYADSVKGRFTISRDN SKNTLYLQMNGLRAEDTA
 VYYCARDLRTGPFDYWGQGLVTVSSASTKGPSVFPLAPCSRSTSESTAALGCLVKD
 YFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGKTYTCNV DHK
 PSNTKVDKRVESKYGPPCPPCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVDV
 SQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKC
 KVS NKGLPSSIEKTISKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAV
 EWESNGGGGSGGGGSEIVLTQSPATLSLSPGERATLSCRASQSVSSYLAWYQQKPGQ
 APRLLIYDASNRATGIPARFSGSGSGTDFTLTISSELPEDFAVYYCQQSSNWPRTFGQG
 TKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGN
 SQESVTEQDSKDYSLSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGECG
 GGGSGGGGSGGGGSGGGGSGQPENNYKTPPVLDSDGSFFLYSRLTVDKSRWQEGN
 VFSCSVMHEALHNHYTQKSLSLGLGK

链2和ITA101的链2相同

链3和ITA302的链3相同

TA403

链 1

MGWSCILFLVATATGVHSQVQLVQSGVEVKKPGASVKVCKASGYTFTNYYMYW
 VRQAPGQGLEWMGGINPSNGGTNFKNEKFKNRVTLTDSSTTTAYMELKSLQFDDTA
 VYYCARRDYRFDMGFDYWGQGTTVTVSSASTKGPSVFPLAPCSRSTSESTAALGCL
 VKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGKTYTCNV
 DHKPSNTKVDKRVESKYGPPCPPCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCV
 VDVSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKE
 YKCKVSNKGLPSSIEKTISKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSD
 IAVEWESNGGGGSGGGGSEIVLTQSPDFQSVTPKEKVTITCRASQSIGSSLHWYQQKP
 DQSPKLLIKYASQSFSGVPSRFSGSGSGTDFTLTINSLEAEDAAAYYCHQSSSLPFTFG
 PGTKVDIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQS
 GNSQESVTEQDSKDYSLSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGE
 CGGGGSGGGGSGGGGSGGGGSGQPENNYKTPPVLDSDGSFFLYSRLTVDKSRWQE
 GNVFSCSVMHEALHNHYTQKSLSLGLGK

链2和ITA103的链2相同

链3和ITA303的链3相同

图5续

ITA404

链 1

MGWSCILFLVATATGVHSQVQLVESGGGVVQPGRSLRLDCKASGITFSNSGMHWV
 RQAPGKGLEWVAVIWIYDGSKRYYADSVKGRFTISRDNKNTLFLQMNSLRAEDTA
 VYYCATNDDYWGQGLVTVSSASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEP
 VTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGKTYTCNVDHKPSNTK
 VDKRVESKYGPPCPPCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSDQEDP
 EVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSN
 KGLPSSIEKTISKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWES
 NGGGGSGGGGSEIVLTQSPDFQSVTPKEKVTITCRASQSIGSSLHWYQQKPKDQSPKLL
 IKYASQSFSGVPSRFSGSGSGTDFLTINSLEAEDAAAYYCHQSSSLPFTFGPGTKVDI
 KRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESV
 TEQDSKDYSTLSSTLTLKADYEEKHKVYACEVTHQGLSSPVTKSFNRGECGGGGSG
 GGGSGGGGSGGGGSGQPENNYKTTTPVLDSDGSFFLYSRLTVDKSRWQEGNVFSCS
 VMHEALHNHYTQKSLSLGLK

链2和ITA104的链2相同

链3和ITA303的链3相同

ITB101

链 1

MGWSCILFLVATATGVHSSERCDDWGLDTMRQIQVFEDEPARIKCPLFEHFLKFNY
 STAHSAGLTLIYWTRQDRDLEEPINFRLPENRISKEKDVLWFRPTLLNDTGNYTCM
 LRNTTYCSKVAFPLEVVQKDFNSPMKLPVHKLYIEYGIQRITCPNVDGYFPSSVKP
 TITWYMGYKIQNFNNVIPEGMNLFLIALISNNGNYTCVVTYPENGRTRFHLTRTLTV
 KVVGSPKNAVPPVIHSPNDHVVEKEPGEELLIPCTVYFSFLMDSRNEVWWTIDGKK
 PDDITIDVTINESISHSRTEDETRTQILSIKKVTSEDLKRSYVCHARSAKGEVAKAAKV
 KQKVPAPRYTVEKCKEREKIIILVSSANEIDVRPCPLNPNEHKGTITWYKDDSKTPVS
 TEQASRIHQHKEKLWFVPAKVEDSGHYCVVRNSSYCLRIKISAKFVENEPNLCYNA
 QAIFKQKLPVAGDGLVCPYMEFFKNENNELPKLQWYKDCKPLLLDNIHFSGVKDR
 LIVMNVAEKHRGNYTCHASYTYLGKQYPITRVIEFITLEENKPTRPVIVSPANETMEV
 DLGSQIQLICNVTGQLSDIAYWKWNGSVIDEDDPVLGEDYYSVENPANKRRSTLITV
 LNISEIESRFYKHPFTCFANKTHGIDAAYIQLIYPVTNNGGGGSGGGGSQVQLVQSGVE
 VKKPGASVKVSKASGYTFTNYMYWVRQAPGQGLEWMGGINPSNGGTNFNEKF
 KNRVTLTDSSTTTAYMELKSLQFDDTAVYYCARRDYRFDMGFDYWGQGTITVTVS
 SASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVL
 QSSGLYSLSSVVTVPSSSLGKTYTCNVDHKPSNTKVDKRVESKYGPPCPPCPAPEFL
 GGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSDQEDPEVQFNWYVDGVEVHNAKTKP
 REEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPREPQV

图5续

YTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSGDSFF
LYSRLTVDKSRWQEGNVFSCSVMHEALHNHYTQKSLSLSLKG

链2和ITA103的链2相同

ITB102

链 1

MGWSCIIIFLVATATGVHSSERCDDWGLDTMRQIQVFEDEPARIKCPLFEHFLKFNY
STAHSAGLTLIWYWTRQDRDLEEPINFRLPENRISKEKDVLWFRPTLLNDTGNYTCM
LRNTTYCSKVAFFLEVQKDSFCNSPMKLPVHKLIEYGIQRITCPNVDGYFPSSVKP
TITWYMGYKIQNFNNVIPEGMNLFLIALISNNGNYTCVVYPENGRTFHLTRTLTV
KVVGSPKNAVPPVIHSPNDHVVEKEPGEELLIPCTVYFSFLMDSRNEVWWTIDGKK
PDDITIDVTINESISHSRTEDETRTQILSIKKVTSEDLKRSYVCHARSAKGEVAKAAKV
KQKVPAPRYTVEKCKEREKIIIVSSANEIDVRPCPLNPNEHKGTITWYKDDSKTPVS
TEQASRIHQHKEKLWFVPAKVEDSGHYCVVRNSSYCLRIKISAKFVENEPNLCYNA
QAIFKQKLPVAGDGGLVCPYMEFFKNENNELPKLQWYKDCKPLLLDNIHFSGVKDR
LIVMNAEKHRGNYTCHASYTYLGKQYPITRVIEFITLEENKPTRPVIVSPANETMEV
DLGSQIQLICNVTGQLSDIAYWKWNGSVIDEDDPVLGEDYYSVENPANKRRSTLITV
LNISEIESRFYKHPFTCFAKNTHGIDAAYIQLIYPVTNNGGGSGGGGSQVQLVESGGG
VVQPGRSLRLDCKASGITFSNSGMHWVRQAPGKGLEWVAVIWDGSKRYYADSVK
GRFTISRDNKNTLFLQMNSLRAEDTAVYYCATNDDYWGQGLTVTVSSASTKGPSV
FPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSKVHTFPAVLQSSGLYSLS
SVVTVPSSSLGKTYTCNVDHKPSNTKVDKRVESKYGPPCPPCPAPEFLGGPSVFLFP
PKPKDTLMISRTPEVTCVVDVDSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPREPQVYTLPPSQEE
MTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSGDSFFLYSRLTVDK
SRWQEGNVFSCSVMHEALHNHYTQKSLSLSLKG

链2和ITA104的链2相同

ITB103

链 1

MGWSCIIIFLVATATGVHSQVQLVESGGGVVQPGRSLRLDCKASGITFSNSGMHWV
RQAPGKGLEWVAVIWDGSKRYYADSVKGRFTISRDNKNTLFLQMNSLRAEDTA
VYYCATNDDYWGQGLTVTVSSASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEP
VTVSWNSGALTSKVHTFPAVLQSSGLYSLSVTVPSSSLGKTYTCNVDHKPSNTK
VDKRVESKYGGGGSGGGGSERCDDWGLDTMRQIQVFEDEPARIKCPLFEHFLKFNY
STAHSAGLTLIWYWTRQDRDLEEPINFRLPENRISKEKDVLWFRPTLLNDTGNYTCM
LRNTTYCSKVAFFLEVQKDSFCNSPMKLPVHKLIEYGIQRITCPNVDGYFPSSVKP
TITWYMGYKIQNFNNVIPEGMNLFLIALISNNGNYTCVVYPENGRTFHLTRTLTV
KVVGSPKNAVPPVIHSPNDHVVEKEPGEELLIPCTVYFSFLMDSRNEVWWTIDGKK

图5续

PDDITIDVTINESISHSRTEDETRTQILSIKKVTSEDLKRSYVCHARSAKGEVAKAAKV
 KQKVPAPRYTVEKCKEREEKIILVSSANEIDVRPCPLNPNEHKGTITWYKDDSKTPVS
 TEQASRIHQHKEKLWFVPAKVEDSGHYCVVRNSSYCLRIKISAKFVENEPNLCYNA
 QAIFKQKLPVAGDGGLVCPYMEFFKNENNELPKLQWYKDCKPLLLDNIHFSGVKDR
 LIVMNVAEKHRGNYTCHASYTYLGKQYPITRVIEFITLEENKPTRPVIVSPANETMEV
 DLGSQIQLICNVTGQLSDIAYWKWNGSVIDEDDPVLGEDYYSVENPANKRRSTLITV
 LNISEIESRFYKHPFTCFKANTHGIDAAYIQLIYPVTNSGDKTHTCPPCPAPEFLGGPSV
 FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQFNWYVDGVEVHNAKTKPREEQF
 NSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPREPQVYTLPP
 SQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSRL
 TVDKSRWQEGNVFSCSVMHEALHNHYTQKSLSLGLGK

链2和ITA104的链2相同

ITB104

链 1

MGWSCILFLVATATGVHSQVQLVQSGVEVKKPGASVKVSKASGYTFTNYYMYW
 VRQAPGQGLEWMGGINPSNGGTNFNEKFKNRVTLTTDSSTTTAYMELKSLQFDDTA
 VYYCARRDYRFDMGFYWGQGTITVTVSSASTKGPSVFPLAPCSRSTSESTAALGCL
 VKDYFPEPVTVSWNSGALTSQVHTFPAVLQSSGLYSLSSVTVPSSSLGKTKYTCNV
 DHKPSNTKVDKRVESKYGGGGSGGGGSERCDDWGLDTRMQIQVFEDEPARIKCPLF
 EHFLKFNSTAHSAAGLTLIYWTRQDRDLEEPINFRLPENRISKEKDVLWFRPTLLND
 TGNVTCMLRNTTYCSKVAFPLEVVQKDFNSPMKLPVHKLYIEYGIQRITCPNVDG
 YFPSSVKPTITWYMGCYKIQNFNNVIPEGMNLISFLIALISNNGNYTCVVTPENGRTF
 HLTRTLTVKVVGSPKNAVPPVIHSPNDHVVEKEPGEELLIPCTVYFSFLMDSRNEV
 WWTIDGKKPDDITIDVTINESISHSRTEDETRTQILSIKKVTSEDLKRSYVCHARSAK
 EVAKAAKVQKQKVPAPRYTVEKCKEREEKIILVSSANEIDVRPCPLNPNEHKGTITWY
 KDDSKTPVSTEQASRIHQHKEKLWFVPAKVEDSGHYCVVRNSSYCLRIKISAKFVE
 NEPNLCYNAQAIFKQKLPVAGDGGLVCPYMEFFKNENNELPKLQWYKDCKPLLLD
 NIHFSGVKDRLIVMNVAEKHRGNYTCHASYTYLGKQYPITRVIEFITLEENKPTRPVI
 VSPANETMEVDLGSQIQLICNVTGQLSDIAYWKWNGSVIDEDDPVLGEDYYSVENP
 ANKRRSTLITV LNISEIESRFYKHPFTCFKANTHGIDAAYIQLIYPVTNSGDKTHTCPPC
 PAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQFNWYVDGVEVHN
 AKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQ
 REPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLD
 S DGSFFLYSRLTVDKSRWQEGNVFSCSVMHEALHNHYTQKSLSLGLGK

链2和ITA103的链2相同

图5续

ITB105

MGWSCILFLVATATGVHSSERCDDWGLDTMRQIQVFEDEPARIKCPLFEHFLKFNY
 STAHSAGLTLIYWTRQDRDLEEPINFRLPENRISKEKDVLWFRPTLLNDTGNYTCM
 LRNTTYCSKVAFPLEVQKDSFCFNSPMKLPVHKLYIEYGIQRITCPNVDGYFPSSVKP
 TITWYMGYKIQNFNNVIPEGMNLFLIALISNNGNYTCVVITYPENGRTFHLTRTLTV
 KVVGSPKNAVPPVIHSPNDHVVEKEPGEELLIPCTVYFSFLMDSRNEVWWTIDGKK
 PDDITIDVTINESISHSRTEDETRTQILSIKKVTSEDLKRSYVCHARSAKGEVAKAAKV
 KQKVPAPRYTVEKCKEREKIIILVSSANEIDVRPCPLNPNEHKGTITWYKDDSKTPVS
 TEQASRIHQHKEKLWFVPAKVEDSGHYCVVRNSSYCLRIKISAKFVENEPNLCYNA
 QAIFKQKLPVAGDGGLVCPYMEFFKNENNELPKLQWYKDCKPLLLDNIHFSGVKDR
 LIVMNVAEKHRGNYTCHASYTYLGKQYPITRVIEFITLEENKPTRPVIVSPANETMEV
 DLGSQIQLICNVTGQLSDIAYWKWNGSVIDEDDPVLGEDYYSVENPANKRRSTLITV
 LNISEIESRFYKHPFTCFACKNTHGIDAAYIQLIYPVTNSGDKTHTCPPCPAPEFLGGPSV
 FLFPKPKDITLMISRTPEVTCVVVDVSQEDPEVQFNWYVDGVEVHNAKTKPREEQF
 NSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPREPQVYTLPP
 SQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSRL
 TVDKSRWQEGNVFSCSVMHEALHNHYTQKSLSLGLKGGGGSGGGGSQVQLVESG
 GGVVQPGRSLRLDCKASGITFSNSGMHWVRQAPGKGLEWVAWIWYDGSKRYYADS
 VKGRFTISRDNSKNTLFLQMNSLRAEDTAVYYCATNDDYWGQGLTVTVSSGGGGGS
 GGGGSGGGGSGGGGSEIVLTQSPATLSLSPGERATLSCRASQSVSSYLAWYQQKPGQ
 APRLLIYDASNRATGIPARFSGSGSGTDFTLTISSLEPEDFAVYYCQQSSNWPRTFGQG
 TKVEIK

ITB106

链 1

MGWSCILFLVATATGVHSSERCDDWGLDTMRQIQVFEDEPARIKCPLFEHFLKFNY
 STAHSAGLTLIYWTRQDRDLEEPINFRLPENRISKEKDVLWFRPTLLNDTGNYTCM
 LRNTTYCSKVAFPLEVQKDSFCFNSPMKLPVHKLYIEYGIQRITCPNVDGYFPSSVKP
 TITWYMGYKIQNFNNVIPEGMNLFLIALISNNGNYTCVVITYPENGRTFHLTRTLTV
 KVVGSPKNAVPPVIHSPNDHVVEKEPGEELLIPCTVYFSFLMDSRNEVWWTIDGKK
 PDDITIDVTINESISHSRTEDETRTQILSIKKVTSEDLKRSYVCHARSAKGEVAKAAKV
 KQKVPAPRYTVEKCKEREKIIILVSSANEIDVRPCPLNPNEHKGTITWYKDDSKTPVS
 TEQASRIHQHKEKLWFVPAKVEDSGHYCVVRNSSYCLRIKISAKFVENEPNLCYNA
 QAIFKQKLPVAGDGGLVCPYMEFFKNENNELPKLQWYKDCKPLLLDNIHFSGVKDR
 LIVMNVAEKHRGNYTCHASYTYLGKQYPITRVIEFITLEENKPTRPVIVSPANETMEV
 DLGSQIQLICNVTGQLSDIAYWKWNGSVIDEDDPVLGEDYYSVENPANKRRSTLITV
 LNISEIESRFYKHPFTCFACKNTHGIDAAYIQLIYPVTNNGGGGSGGGGSEIVLTQSPATLS
 LSPGERATLSCRASKGVSTSGYSYLHWYQQKPGQAPRLLIYLASYLESVGPVRFSGS
 GSGTDFTLTISSLEPEDFAVYYCQHSRDLPLTFGGGKVEIKRTVAAPSVFIFPPSDEQ
 LKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDYSLSTLT

图5续

LSKADYKHKVYACEVTHQGLSSPVTKSFNRGECGPPCPPAPEFLGGPSVFLFPPK
PKDTLMISRTPEVTCVVVDVSDQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRV
VSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPREPQVYITLPPSQEEMT
KNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGSFFLYSRLTVDKSR
WQEGNVFSCSVMHEALHNHYTQKSLSLGLGK

链2和ITA301的链2相同

ITB107

链 1

MGWSCIIIFLVATATGVHSSERCDDWGLDTMRQIQVFEDEPARIKCPLFEHFLKFNY
STAHSAGLTLIWYWTRQDRDLEEPINFRLPENRISKEKDVLWFRPTLLNDTGNYTCM
LRNTTYCSKVAFPLEVVQKDSFCFNSPMKLPVHKLIEYGIQRITCPNVGDGYFPSSVKP
TITWYMGCYKIQNFNNVIPEGMNLFLIALISNNGNYTCVVVYPENGRTFHLTRTLTV
KVVGSPKNAVPPVIHSPNDHVVEKEPGEELLIPCTVYFSFLMDSRNEVWWTIDGKK
PDDITIDVTINESISHSRTEDETRTQILSIKKVTSEDLKRSYVCHARSAKGEVAKAAKV
KQKVPAPRYTVEKCKEREKILVSSANEIDVRPCPLNPNEHKGTITWYKDDSKTPVS
TEQASRIHQHKEKLWFPVAKVEDSGHYCVVRNSSYCLRIKISAKFVENEPNLCYNA
QAIFKQKLPVAGDGGLVCPYMEFFKNENNELPKLQWYKDCKPLLLDNIHFGVKDR
LIVMNVAEKHRGNYTCHASYTYLGKQYPITRVIEFITLEENKPTRPVIVSPANETMEV
DLGSQIQLICNVTGQLSDIAYWKWNGSVIDEDDPVLGEDYYSVENPANKRRSTLITV
LNISEIESRFYKHPFTCFAKNTHGIDAAYIQLIYPVTNGGGGSGGGGSEIVLTQSPATLS
LSPGERATLSCRASQSVSSYLAWYQQKPGQAPRLLIYDASNRATGIPARFSGSGSGTD
FTLTISSLEPEDFAVYYCQSSNWPRTFGQGTKVEIKRTVAAPSVFIFPPSDEQLKSGT
ASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYLSSTLTLKAD
YEKHKVYACEVTHQGLSSPVTKSFNRGECGPPCPPAPEFLGGPSVFLFPPKPKDTL
MISRTPEVTCVVVDVSDQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLT
VLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPREPQVYITLPPSQEEMTKNQVS
LTCLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGSFFLYSRLTVDKSRWQEGN
VFSCSVMHEALHNHYTQKSLSLGLGK

链2和ITA302的链2相同

ITB108

链 1

MGWSCIIIFLVATATGVHSEIVLTQSPATLSLSPGERATLSCRASQSVSSYLAWYQQK
PGQAPRLLIYDASNRATGIPARFSGSGSGTDFTLTISSLEPEDFAVYYCQSSNWPRTF
GQGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQ
SGNSQESVTEQDSKDSTYLSSTLTLKADYKHKVYACEVTHQGLSSPVTKSFNRG
ECGGGSGGGGSERCDDWGLDTMRQIQVFEDEPARIKCPLFEHFLKFNYSTAHSAGL
TLIWYWTRQDRDLEEPINFRLPENRISKEKDVLWFRPTLLNDTGNYTCMLRNTTYCS

图5续

KVAFPLEVVQKDSFCFNSPMKLPVHKLYIEYGIQRITCPNVDGYFPSSVKPTITWYMG
 CYKIQNFNNVIPEGMNLISFLIALISNNGNYTCVVVTPENGRTFHLTRTLTVKVVGSPK
 NAVPPVIHSPNDHVVEKEPGEELLIPCTVYFSFLMDSRNEVWWTIDGKKPDDITIDV
 TINESISHSRTEDETRTQILSIKKVTSEDLKRSYVCHARSAKGEVAKAAKVQKVPAP
 RYTVEKCKEREEKIILVSSANEIDVRPCPLNPNEHKGTTITWYKDDSKTPVSTEQASRIH
 QHKEKLWFVPAKVEDSGHYCVVRNSSYCLRIKISAKFVENEPNLCYNAQAIFKQKL
 PVAGDGGLVCPYMEFFKNENNELPKLQWYKDCKPLLLDNIHFSGVKDRLIVMNVAE
 KHRGNYTCHASYTYLGKQYPITRVIEFITLEENKPTRPVIVSPANETMEVDLGSQIQLI
 CNVTGQLSDIAYWKWNGSVIDEDDPVLGEDYYSVENPANKRRSTLITVLNISEIESRF
 YKHPFTCFKNTHGIDAAYIQLIYPVTNSGDKTHTCPPCPAPEFLGGPSVFLFPPKPKD
 TLMISRTPEVTCVVVDVSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSV
 LTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPREPQVYTLPPSQEEMTKNQ
 VSLTCLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGSFFLYSRLTVDKSRWQE
 GNVFSCSVMHEALHNHYTQKSLSLGLGK

链2和ITA302的链2相同

ITB109

链 1

MGWSCILFLVATATGVHSEIVLTQSPATLSLSPGERATLSCRASKGVSTSGYSYLHW
 YQKPGQAPRLLIYLAASYLESGVPARFSGSGGTDFLTISLLEPEDFAVYYCQHSRD
 LPLTFGGGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKV
 DNALQSGNSQESVTEQDSKSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTK
 SFNRGECGGGGSGGGGSERCDDWGLDTMRQIQVFEDEPARIKCPLFEHFLKFNSTA
 HSAGLTLIYWTRQDRDLEEPINFRLPENRISKEKDVLWFRPTLLNDTGNYTCMLRN
 TTYCSKVAFPLEVVQKDSFCFNSPMKLPVHKLYIEYGIQRITCPNVDGYFPSSVKPTIT
 WYMGCYKIQNFNNVIPEGMNLISFLIALISNNGNYTCVVVTPENGRTFHLTRTLTVK
 VGSPKNAVPPVIHSPNDHVVEKEPGEELLIPCTVYFSFLMDSRNEVWWTIDGKKPD
 DITIDVTINESISHSRTEDETRTQILSIKKVTSEDLKRSYVCHARSAKGEVAKAAKVQ
 KVPAPRYTVEKCKEREEKIILVSSANEIDVRPCPLNPNEHKGTTITWYKDDSKTPVSTE
 QASRIHQHKEKLWFVPAKVEDSGHYCVVRNSSYCLRIKISAKFVENEPNLCYNAQ
 AIFKQKLVPVAGDGGLVCPYMEFFKNENNELPKLQWYKDCKPLLLDNIHFSGVKDRLI
 VMNVAEKHRGNYTCHASYTYLGKQYPITRVIEFITLEENKPTRPVIVSPANETMEVD
 LGSQIQLICNVTGQLSDIAYWKWNGSVIDEDDPVLGEDYYSVENPANKRRSTLITVL
 NISEIESRFYKHPFTCFKNTHGIDAAYIQLIYPVTNSGDKTHTCPPCPAPEFLGGPSV
 FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQFNWYVDGVEVHNAKTKPREEQFN
 STYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPREPQVYTLPPS
 QEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGSFFLYSRLT
 VDKSRWQEGNVFSCSVMHEALHNHYTQKSLSLGLGK

链2和ITA301的链2相同

图5续

ITE101

链 1

MGWSCIIIFLVATATGVHSQVQLVESGGGVVQPGRSLRLDCKASGITFSNSGMHWV
 RQAPGKCLEWVAVIWDGSKRYYADSVKGRFTISRDNKNTLFLQMNSLRAEDTA
 VYYCATNDDYWGQGLVTVSSGGGGSGGGGSGGGGSGGGGSEIVLTQSPATLSLSP
 GERATLSCRASQSVSSYLAWYQQKPGQAPRLLIYDASNRATGIPARFSGSGSGTDFTL
 TISSLEPEDFAVYYCQQSSNWPRTFGCGTKVEIKGGGGSGGGGSGVQLVESGGGVV
 QPGRSLRLSCAASGFTFSVYGMNWVRQAPGKGLEWVAIIWYDGDNQYYADSVKGR
 FTISRDNKNTLYLQMNSLRAEDTAVYYCARDLRTGPFDYWGQGLVTVSSASTKG
 PSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLY
 SLSSVTVPSSSLGKTYTCNVDPKPSNTKVDKRVESKYGPPCPPCPAPEFLGGPSVF
 LFPPKPKDTLMISRTPEVTCVVVDVSDPEVQFNWYVDGVEVHNAKTKPREEQFN
 STYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPREPQVYTLPPS
 QEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGSFFLYSRLT
 VDKSRWQEGNVFSCSVMHEALHNHYTQKSLSLGLK

链2和ITA101的链2相同

ITE102

MGWSCIIIFLVATATGVHSEIVLTQSPATLSLSPGERATLSCRASQSVSSYLAWYQQK
 PGQAPRLLIYDASNRATGIPARFSGSGSGTDFTLTISSLEPEDFAVYYCQQSSNWPRTF
 GCGTKVEIKGGGGSGGGGSGGGGSGGGGSGVQLVESGGGVVQPGRSLRLDCKASGI
 TFSNSGMHWVRQAPGKCLEWVAVIWDGSKRYYADSVKGRFTISRDNKNTLFLQ
 MNSLRAEDTAVYYCATNDDYWGQGLVTVSSGGGGSGGGGSGVQLVESGGGVVQ
 PGRSLRLSCAASGFTFSVYGMNWVRQAPGKGLEWVAIIWYDGDNQYYADSVKGRF
 TISRDNKNTLYLQMNSLRAEDTAVYYCARDLRTGPFDYWGQGLVTVSSASTKGP
 SVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYS
 LSSVTVPSSSLGKTYTCNVDPKPSNTKVDKRVESKYGPPCPPCPAPEFLGGPSVFL
 FPPKPKDTLMISRTPEVTCVVVDVSDPEVQFNWYVDGVEVHNAKTKPREEQFNS
 TYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPREPQVYTLPPSQ
 EEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGSFFLYSRLTV
 DKSRWQEGNVFSCSVMHEALHNHYTQKSLSLGLK

链2和ITA101的链2相同

ITE201

链 1

MGWSCIIIFLVATATGVHSQVQLVESGGGVVQPGRSLRLDCKASGITFSNSGMHWV
 RQAPGKGLEWVAVIWDGSKRYYADSVKGRFTISRDNKNTLFLQMNSLRAEDTA
 VYYCATNDDYWGQGLVTVSSASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEP

图5续

VTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGKTYTCNVDPKPSNTK
 VDKRVESKYGPPCPPCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSDQEDP
 EVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSN
 KGLPSSIEKTISKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWES
 NGQPENNYKTTPPVLDSDGSFFLYSRLTVDKSRWQEGNVFSCSVMHEALHNHYTQK
 SLSLSLGKGGGGSGGGGSQVQLVESGGGVVQPGRSLRLSCAASGFTFSVYGMNWVR
 QAPGKCLEWVAIIWYDGDNQYYADSVKGRFTISRDN SKNTLYLQMNGLRAEDTAV
 YYCARDLRTGPFDYWGQGLTVTVSSGGGGSGGGGSQVQLVESGGGVVQPGRSLRLS
 CAASGFTFSVYGMNWVRQAPGKCLEWVAIIWYDGDNQYYADSVKGRFTISRDN SKNTLYLQ
 MNGLRAEDTAVYYCARDLRTGPFDYWGQGLTVTVSSGGGGSGGGGSQVQLVESGGGVV
 QPGRSLRLSCAASGFTFSVYGMNWVRQAPGKCLEWVAIIWYDGDNQYYADSVKGRFTISR
 DN SKNTLYLQMNGLRAEDTAVYYCARDLRTGPFDYWGQGLTVTVSSGGGGSGGGGSQVQL
 VESGGGVVQPGRSLRLSCAASGFTFSVYGMNWVRQAPGKCLEWVAIIWYDGDNQYYADSVK
 GRFTISRDN SKNTLYLQMNGLRAEDTAVYYCARDLRTGPFDYWGQGLTVTVSSGGGGSGGGG
 SQVQLVESGGGVVQPGRSLRLSCAASGFTFSVYGMNWVRQAPGKCLEWVAIIWYDGDNQYYADSVK
 GRFTISRDN SKNTLYLQMNGLRAEDTAVYYCARDLRTGPFDYWGQGLTVTVSSGGGGSGGGG

链2和ITA104的链2相同

ITE202

链 1

MGWSCIIIFLVATATGVHSQVQLVESGGGVVQPGRSLRLDCKASGITFSNSGMHWV
 RQAPGKGLEWVAIIWYDGSKRYADSVKGRFTISRDN SKNTLYLQMNGLRAEDTAV
 YYCATNDDYWGQGLTVTVSSASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEP
 VTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGKTYTCNVDPKPSNTK
 VDKRVESKYGPPCPPCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSDQEDP
 EVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSN
 KGLPSSIEKTISKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWES
 NGQPENNYKTTPPVLDSDGSFFLYSRLTVDKSRWQEGNVFSCSVMHEALHNHYTQK
 SLSLSLGKGGGGSGGGGSEIVLTQSPDFQS VTPKEKVTITCRASQSIGSSLHWYQQK
 PDQSPKLLIKYASQSFSGVPSRFSGSGSGTDFTLTINSLEAEDA AYYCHQSSSLPFTFG
 CGTKVDIKGGGGSGGGGSQVQLVESGGGVVQPGRSLRLSCAASGFTFSVYGMNWVR
 QAPGKCLEWVAIIWYDGDNQYYADSVKGRFTISRDN SKNTLYLQMNGLRAEDTAV
 YYCARDLRTGPFDYWGQGLTVTVSSGGGGSGGGGSQVQLVESGGGVVQPGRSLRLS
 CAASGFTFSVYGMNWVRQAPGKCLEWVAIIWYDGDNQYYADSVKGRFTISRDN SKNTLYLQ
 MNGLRAEDTAVYYCARDLRTGPFDYWGQGLTVTVSSGGGGSGGGGSQVQLVESGGGVV
 QPGRSLRLSCAASGFTFSVYGMNWVRQAPGKCLEWVAIIWYDGDNQYYADSVKGRFTISR
 DN SKNTLYLQMNGLRAEDTAVYYCARDLRTGPFDYWGQGLTVTVSSGGGGSGGGGSQVQL
 VESGGGVVQPGRSLRLSCAASGFTFSVYGMNWVRQAPGKCLEWVAIIWYDGDNQYYADSVK
 GRFTISRDN SKNTLYLQMNGLRAEDTAVYYCARDLRTGPFDYWGQGLTVTVSSGGGGSGGGG

链2和ITA104的链2相同

ITE301

链 1

MGWSCIIIFLVATATGVHSEIVLTQSPDFQS VTPKEKVTITCRASQSIGSSLHWYQQK
 PDQSPKLLIKYASQSFSGVPSRFSGSGSGTDFTLTINSLEAEDA AYYCHQSSSLPFTF
 GPGTKVDIKRTVAAPS FIFPPSDEQLKSGTASVVC LLNFPYAPREKVKVQWVDNALQ
 SGNSQESVTEQDSKDYSLSSLTLSKADYEEKHKVYACEVTHQGLSSPVTKSFNRG
 ECGSGQVQLVQSGVEVKKPGASVKVSCKASGYTFTNYYMYWVRQAPGQGLEWMG
 GINPSNGGTNFNEKFKNRVTLTDSSTTTAYMELKSLQFDDTAVYYCARRDYRFDM
 GFDYWGQGTITVTVSSASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWN
 SGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGKTYTCNVDPKPSNTKVDKRVE

图5续

SKYGPPCPPCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSDQEDPEVQFNW
 YVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIE
 KTISKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENN
 YKTTTPVLDSGDGSFFLYSRLTVDKSRWQEGNVFSCSVMHEALHNHYTQKSLSLGLG
 K

链2和链3与ITA301的链2和链3相同

ITE302

链 1

MGWSCIIIFLVATATGVHSEIVLTQSPDFQSVTPKEKVTITCRASQSIGSSLHWYQQK
 PDQSPKLLIKYASQSFSGVPSRFSGSGSGTDFLTINSLEAEDAAAYYCHQSSSLPFTF
 GPGTKVDIKRTVAAPS VFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQ
 SGNQESVTEQDSKDYSLSTLTLKADYKHKVYACEVTHQGLSSPVTKSFNRG
 ECGGGGSGSQVQLVQSGVEVKKPGASVKVSKASGYTFTNYMYWVRQAPGQGL
 EWMGGINPSNGGTNFNEKFKNRVTLTDSSTTTAYMELKSLQFDDTAVYYCARRDY
 RFDMGFDYWGQGTITVTVSSASTKGPSVFPLAPCSSTSESTAALGCLVKDYFPEPVT
 VSWNSGALTSKVHTFPAVLQSSGLYSLSSVTVPSSSLGKTYTCNVDPHKPSNTKVD
 KRVESKYGPPCPPCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSDQEDPEV
 QFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGL
 LPSSIEKTISKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNG
 QPENNYKTTTPVLDSGDGSFFLYSRLTVDKSRWQEGNVFSCSVMHEALHNHYTQKSL
 SLSLGLK

链2和链3与ITA301的链2和链3相同

ITF101

链 1

MGWSCIIIFLVATATGVHSEIVLTQSPATLSLSPGERATLSCRASQSVSSYLAWYQQK
 PGQAPRLLIYDASNRAATGIPARFSGSGSGTDFLTISSELEPEDFAVYYCQQSSNWPRTF
 GCGTKVEIKGGGGSGGGGSGGGGSGGGGSQVQLVESGGGVVQPGRSLRLDCKASGI
 TFSNSGMHWVRQAPGKCLEWVAVIWDGSKRYYADSVKGRFTISRDNKNTLFLQ
 MNSLRAEDTAVYYCATNDDYWGQGLTVTVSSGGGGSGGGGSEVQLVESGGGVVQ
 PGRSLRLSCSSSGFIFSSYDMSWVRQAPGKLEWVAYISSGGGGTYYPDTVKGRFTIS
 RDNKNTLFLQMDSLRLPEDTGVYFCARGGVTKGYFDVWGQGTPTVTVSSASTKGPSV
 FPLAPCSSTSESTAALGCLVKDYFPEPVTVSWNSGALTSKVHTFPAVLQSSGLYSLS
 SVVTVPSSSLGKTYTCNVDPHKPSNTKVDKRVESKYGPPCPPCPAPEFLGGPSVFLF
 PKPKDTLMISRTPEVTCVVVDVSDQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTY
 RVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPREPQVYTLPPSQE
 MTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSGDGSFFLYSRLTVDK
 SRWQEGNVFSCSVMHEALHNHYTQKSLSLGLK

图5续

链 2

MGWSCIIIFLVATATGVHSDIQMTQSPSSLSASVGDRVTITCRASGNIHNYLTWYQQ
TPGKAPKLLIYNAKTLADGVPSRFSGSGSGTDYFTFTISSLQPEDIATYYCQHFWSIPYT
FGQGTKLEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNMFYPREAKVQWKVDNAL
QSGNSQESVTEQDSKSTYSLSTLTLSKADYEEKHKVYACEVTHQGLSSPVTKSFNR
GEC

ITF102

链 1

MGWSCIIIFLVATATGVHSDIQMTQSPSSLSASVGDRVTITCRASGNIHNYLTWYQQ
TPGKAPKLLIYNAKTLADGVPSRFSGSGSGTDYFTFTISSLQPEDIATYYCQHFWSIPYT
FGCGTKLEIKGGGGSGGGGSGGGGSEVQLVESGGGVVQPGRSLRLSCSSSGF
IFSSYDMSWVRQAPGKCLEWVAYISSGGGGTYYPDTVKGRTISRDNKNTLFLQM
DSLRPEDTGVYFCARGGVTKGYFDVWGQGPVTVSSGGGGSGGGGSQVQLVESGG
GVVQPGRSLRLDCKASGITFSNSGMHWVRQAPGKGLEWVAVIWDGSKRYYADSV
KGRFTISRDNKNTLFLQMNSLRAEDTAVYYCATNDDYWGQGLTVTVSSASTKGPS
VFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSL
SSVVTVPSSSLGKTYTCNVDPKPSNTKVDKRVESKYGPPCPPCPAPEFLGGPSVFLF
PPKPKDTLMISRTPEVTCVVVDVSDPEVQFNWYVDGVEVHNAKTKPREEQFNST
YRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPREPQVYTLPPSQE
EMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSRLTVD
KSRWQEGNVFSCSVMEALHNHYTQKSLSLGLGK

链2和ITA104的链2相同

ITF103

链 1

MGWSCIIIFLVATATGVHSEVQLVESGGGVVQPGRSLRLSCSSSGFIFSSYDMSWVR
QAPGKCLEWVAYISSGGGGTYYPDTVKGRTISRDNKNTLFLQMDSLPEDTGVYF
CARGGVTKGYFDVWGQGPVTVSSGGGGSGGGGSGGGGSDIQMTQSPSSL
SASVGDRVTITCRASGNIHNYLTWYQQTPGKAPKLLIYNAKTLADGVPSRFSGSGSG
TDYFTFTISSLQPEDIATYYCQHFWSIPYTFGCGTKLEIKGGGGSGGGGSQVQLVESGG
GVVQPGRSLRLDCKASGITFSNSGMHWVRQAPGKGLEWVAVIWDGSKRYYADSV
KGRFTISRDNKNTLFLQMNSLRAEDTAVYYCATNDDYWGQGLTVTVSSASTKGPS
VFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSL
SSVVTVPSSSLGKTYTCNVDPKPSNTKVDKRVESKYGPPCPPCPAPEFLGGPSVFLF
PPKPKDTLMISRTPEVTCVVVDVSDPEVQFNWYVDGVEVHNAKTKPREEQFNST
YRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPREPQVYTLPPSQE
EMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSRLTVD
KSRWQEGNVFSCSVMEALHNHYTQKSLSLGLGK

图5续

链2和ITA104的链2相同

ITF201

链 1

MGWSCILFLVATATGVHSQVQLVESGGGVVQPGRSLRLDCKASGITFSNSGMHWV
 RQAPGKGLEWVAVIWIYDGSKRYYADSVKGRFTISRDN SKNTLFLQMNSLRAEDTA
 VYYCATNDDYWGQGLVTVSSASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEP
 VTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGKTYTCNV D HKPSNTK
 VDKRVESKYGPPCPPCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSDQEDP
 EVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSN
 KGLPSSIEKTISKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWES
 NGQPENNYKTTTPVLDSDGSFFLYSRLTVDKSRWQEGNVFSCSVMHEALHNHYTQK
 SLSLSLGKGGGGSGGGGSDIQMTQSPSSLSASVGDRVTITCRASGNIHNYLTWYQQT
 PGKAPKLLIYNAKTLADGVPSRFSGSGSGTDYFTFTISLQPED IATYYCQHFWSIPYTF
 GCGTKLEIKGGGGSGGGGSGGGGSGGGGSEVQLVESGGGVVQPGRSLRLSCSSSGFI
 FSSYDMSWVRQAPGKC LEWVAYISSGGGGTYYPDTV KGRFTISRDN SKNTLFLQMD
 SLRPEDTGVYFCARGGVTKGYFDVWGQGTPVTVSS

链2和ITA104相同

ITF202

链 1

MGWSCILFLVATATGVHSQVQLVESGGGVVQPGRSLRLDCKASGITFSNSGMHWV
 RQAPGKGLEWVAVIWIYDGSKRYYADSVKGRFTISRDN SKNTLFLQMNSLRAEDTA
 VYYCATNDDYWGQGLVTVSSASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEP
 VTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGKTYTCNV D HKPSNTK
 VDKRVESKYGPPCPPCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSDQEDP
 EVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSN
 KGLPSSIEKTISKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWES
 NGQPENNYKTTTPVLDSDGSFFLYSRLTVDKSRWQEGNVFSCSVMHEALHNHYTQK
 SLSLSLGKGGGGSGGGGSEVQLVESGGGVVQPGRSLRLSCSSSGFIFSSYDMSWVRQ
 APGKC LEWVAYISSGGGGTYYPDTV KGRFTISRDN SKNTLFLQMDSLRPEDTGVYFC
 ARGGVTKGYFDVWGQGTPVTVSSGGGGSGGGGSGGGGSGGGGSDIQMTQSPSSLS
 ASVGDRVTITCRASGNIHNYLTWYQQTPGKAPKLLIYNAKTLADGVPSRFSGSGSGT
 DYTFTISLQPED IATYYCQHFWSIPYTFGCGTKLEIK

链2和ITA104相同

图5续

ITF301

链 1

MGWSCILFLVATATGVHSDIQMTQSPSSLSASVGDRVTITCRASGNIHNYLTWYQQ
 TPGKAPKLLIYNAKTLADGVPSRFSGSGSGTDYFTFTISSLQPEDIATYYCQHFWSIPYT
 FGQGTKLEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNAL
 QSGNSQESVTEQDSKDYSLSSITLSKADYEEKHKVYACEVTHQGLSSPVTKSFNR
 GECGSGQVQLVQSGVEVKKPGASVKVCKASGYTFTNYYMYWVRQAPGQGLEWM
 GGINPSNGGTNFNEKFKNRVTLTDSSTTTAYMELKSLQFDDTAVYYCARRDYRFD
 MGFDYWGQGTITVTVSSASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSW
 NSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGKTYTCNVDPKPSNTKVDKRV
 ESKYGPPCPPCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVDVDSQEDPEVQFN
 WYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSS
 IEKTISKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPEN
 NYKTTTPVLDSDGSFFLYSRLTVDKSRWQEGNVFSCSVMHEALHNHYTQKSLSLGL
 GK

链2和ITA103的链2相同

链 3

MGWSCILFLVATATGVHSEVQLVESGGGVVQPGRSLRLSCSSSGFIFSSYDMSWVR
 QAPGKGLEWVAYISSGGGGTYYPDTVKGRFTISRDNKNTLFLQMDSLRPEDTGVYF
 CARGGVTKGYFDVWGQGTPTVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
 FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPS
 NTKVDKRVEPKSC

ITF302

链 1

MGWSCILFLVATATGVHSDIQMTQSPSSLSASVGDRVTITCRASGNIHNYLTWYQQ
 TPGKAPKLLIYNAKTLADGVPSRFSGSGSGTDYFTFTISSLQPEDIATYYCQHFWSIPYT
 FGQGTKLEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNAL
 QSGNSQESVTEQDSKDYSLSSITLSKADYEEKHKVYACEVTHQGLSSPVTKSFNR
 GECGGGSGSQVQLVQSGVEVKKPGASVKVCKASGYTFTNYYMYWVRQAPGQ
 LEWMGINPSNGGTNFNEKFKNRVTLTDSSTTTAYMELKSLQFDDTAVYYCARRD
 YRFDMGFDYWGQGTITVTVSSASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPV
 TVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGKTYTCNVDPKPSNTKV
 DKRVESKYGPPCPPCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVDVDSQEDPE
 VQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNK
 GLPSSIEKTISKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESN
 GQPENNYKTTTPVLDSDGSFFLYSRLTVDKSRWQEGNVFSCSVMHEALHNHYTQKS
 LSLSLGK

图5续

链2和链3与ITF301的链2和链3相同

ITF401

链 1

MGWSCILFLVATATGVHSEVQLVESGGGVVQPGRSLRLSCSSSGFIFSSYDMSWVR
QAPGKGLEWVAYISSGGGGTYYPDTVKGRFTISRDNKNTLFLQMDSLRLPEDTGVIYF
CARGGVTKGYFDVWGQGPVTVSSASTKGPSVFPLAPCSRSTSESTAALGCLVKDYF
PEPVTVSWNSGALTSQVHTFPAVLQSSGLYSLSSVTVPSSSLGKTYTCNVVHKPS
NTKVDKRVESKYGPPCPPAPEFLGGPSVFLFPPKPKDTLMISRTPPEVTCVVVDVSDQ
EDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCK
VSNKGLPSSIEKTISKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVE
WESNGGGGSGGGGSGGGGSGGGGSGGGGSEIVLTQSPATLSLSPGERATLSCRASKG
VSTSGYSYLHWYQQKPGQAPRLLIYLASYLESGVPARFSGSGSGTDFTLTISSELEPEDF
AVYYCQHSRDLPLTFGGGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYP
REAKVQWKVDNALQSGNSQESVTEQDSKSTYLSSTLTLSKADYEKHKVYACEVT
HQGLSSPVTKSFNRGECGGGGSGGGGSGGGGSGGGGSGGGGSGGGGSGQPENNYKTPPVL
DSDGSFFLYSRLTVDKSRWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK

链2和ITF101的链2相同

链3和ITA301的链3相同

ITF402

链 1

MGWSCILFLVATATGVHSQVQLVQSGVEVKKPGASVKVSKASGYTFTNYYMYW
VRQAPGQGLEWMGGINPSNGGTNFKNEKFKNRVTLTDSSTTTAYMELKSLQFDDTA
VYYCARRDYRFDMGFDYWGQGTTVTVSSASTKGPSVFPLAPCSRSTSESTAALGCL
VKDYFPEPVTVSWNSGALTSQVHTFPAVLQSSGLYSLSSVTVPSSSLGKTYTCNV
DHKPSNTKVDKRVESKYGPPCPPAPEFLGGPSVFLFPPKPKDTLMISRTPPEVTCVV
VDVSDQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKE
YKCKVSNKGLPSSIEKTISKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSD
IAVEWESNGGGGSGGGGSGGGGSGGGGSGGGGSDIQMTQSPSSLSASVGDRTITCR
ASGNIHNYLTWYQQTPGKAPKLLIYNAKTLADGVPSRFSGSGSGTDYFTISSLQPED
IATYYCQHFWSIPYTFGQGTKLEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYP
REAKVQWKVDNALQSGNSQESVTEQDSKSTYLSSTLTLSKADYEKHKVYACEVT
HQGLSSPVTKSFNRGECGGGGSGGGGSGGGGSGGGGSGGGGSGGGGSGQPENNYKTPPVL
DSDGSFFLYSRLTVDKSRWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK

链2和链3与ITF302的链2和链3相同

图5续

ITF403

链 1

MGWSCILFLVATATGVHSQVQLVESGGGVVQPGRSLRLDCKASGITFSNSGMHWV
RQAPGKGLEWVAVIWDGSKRYYADSVKGRFTISRDNKNTLFLQMNSLRAEDTA
VYYCATNDDYWGQGLVTVSSASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEP
VTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGKTYTCNVDPKPSNTK
VDKRVESKYGPPCPPCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSDQEDP
EVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSN
KGLPSSIEKTISKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWES
NGGGGSGGGGSGGGGSGGGGSGGGGSDIQMTQSPSSLSASVGDRTITCRASGNIHN
YLTWYQQTPGKAPKLLIYNAKTLADGVPSRFSGSGSGTDYFTFISLQPEDATYYCQ
HFWSIPYTFGQGTKLEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQ
WKVDNALQSGNSQESVTEQDSKDSSTLSKADYEEKHKVYACEVTHQGLSS
PVTKSFNRGECGGGGSGGGGSGGGGSGGGGSGGGGSGQPENNYKTTTPVLDSDGSF
FLYSRLTVDKSRWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK

链2和ITA104的链2相同

链3和ITF402的链3相同

图5续

结合蛋白	摘要
ABT-981 (Abbvie)	ABT-981是一种抗IL-1 α / β 双可变结构域免疫球蛋白 (DVD-Ig), 正在开发用于治疗骨关节炎 (OA)
Anakinra (Biovitrum)	Anakinra是重组的非糖化人类白介素1受体拮抗剂
Avelumab (Merck KGaA)	Avelumab (MSB-0010718C) 是针对PD-L1 (程序性细胞死亡配体) 的单克隆抗体 (MAb), 开发用于实体肿瘤的治疗
BCD-100, (Biocad)	BCD-100是抗PD1单克隆抗体, 用于治疗黑素瘤、非小细胞肺癌和肾细胞癌
Bermekimab (XBiotech)	Bermekimab (MABp1) 是一种特异于人类白介素-1 α 的人类IgG1单克隆抗体, 用于治疗周围血管疾病、第2型糖尿病、坏疽性脓皮症 (pyoderma gangrenosum)、化脓性汗腺炎 (hidradentis suppurtiva), 结直肠结直肠癌, 非小细胞肺癌 (NSCLC)、胰脏癌、牛皮癣、痤疮、异位性皮肤炎 (atopic dermatitis) 和恶病质。
BGB-A333 (BeiGene)	BGB-A333是针对程序性细胞死亡1-配体1 (PD-L1) 的人源化IgG1变异单克隆抗体, 正在开发用于癌症的治疗
Camrelizumab (江苏恒瑞医药股份有限公司)	Camrelizumab (SHR-1210) 是人源化的抗PD1 IgG4单克隆抗体, 正在开发用于癌症的治疗
Canakinumab (Novartis)	Canakinumab (ACZ-885) 是一种抗白介素1 β 的人类单克隆抗体, 开发用于治疗冷吡啉相关周期性综合征 (cryopyrin-associated periodic syndrome, CAPS) (家族性冷荨麻疹综合征 (familial cold urticaria syndrome, FCAS)、穆-韦二氏综合征 (Muckle-Wells syndrome, MWS) 和新生儿发作的多重系统炎症疾病 (Neonatal-Onset Multisystem Inflammatory disease, NOMID) (慢性不育性神经系统皮肤关节综合征 (chronic infertile neurological cutaneous articular Syndrome, CINCA))

图6A

Cemiplimab (Regeneron)	Cemiplimab (REGN-2810) 是针对PD-1的完全人源化单克隆抗体, 开发用于癌症的治疗
CS-1001 (CStone Pharmaceuticals)	CS-1001 (WBP3155) 是一种完全人源化的重组抗PD-L1 IgG单克隆抗体, 开发用于癌症的治疗
Durvalumab (MedImmune)	Durvalumab (MEDI-4736) 是抗PDL1单克隆抗体, 开发用于癌症的治疗
envafolimab (Alphamab)	Envafolimab (KN-035) 是靶向PDL1的纳米抗体, 开发用于癌症的治疗
Gevokizumab (Xoma)	Gevokizumab (XOMA-052) 是可与白介素1 β (IL-1 β) 结合的一种抗炎人源化IgG2单克隆抗体, 用于坏疽性脓皮症的治疗
JNJ-63723283 (Johnson & Johnson)	JNJ-3283 (JNJ-63723283) 是抗PD-1单克隆抗体, 开发用于癌症的治疗
M-7824 (Merck KGaA)	M-7824 (MSB0011359C) 是靶向PD-L1单克隆抗体和TGF β 的双功能融合蛋白, 用于治疗癌症
MEDI-0680 (MedImmune)	MEDI-0680 (AMP-514) 是抗PD-1单克隆抗体, 开发用于癌症和传染病的治疗
MGA-012 (MacroGenics)	MGA-012是人源化抗PD-1单克隆抗体, 开发用于实体肿瘤的治疗
Nivolumab (BMS)	Nivolumab (MDX-1106; ONO-4538) 是抗PD-1的全人IgG4 单克隆抗体, 用于癌症和慢性病毒感染的治疗
Rilonacept (Regeneron)	Rilonacept (RGN-303; Arcalyst) 是一种人类细胞因子陷阱蛋白 (Cytokine Trap protein), 可阻断白介素-1a和白介素-1b的活性, 可用于治疗冷吡啉相关周期性综合征 (CAPS), 一系列罕见的炎症性疾病 (包括穆-韦二氏综合征 (MWS)、

图6B

	家族性寒冷性炎症性综合征 (FCAS) 及某些其他状况)
Sintilimab (Innovent Biologics)	Sintilimab是一种全人抗PD-1单克隆抗体， 开发用于癌症的治疗
SOBI-006 (Affibody)	SOBI-006是一种白介素-1 (IL-1) 抑制剂， 开发用于治疗炎症性和自体免疫性疾病
Spartalizumab (Novartis)	Spartalizumab (PDR-001) 是PD-1人源化 IgG4抗体，开发用于癌症的治疗

图6C

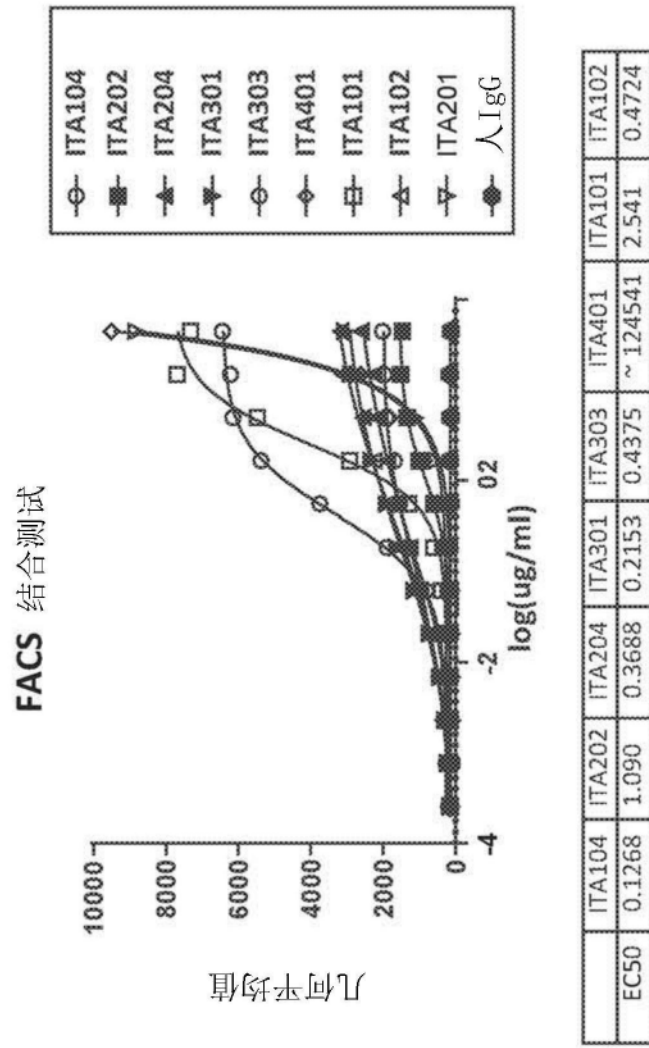


图7

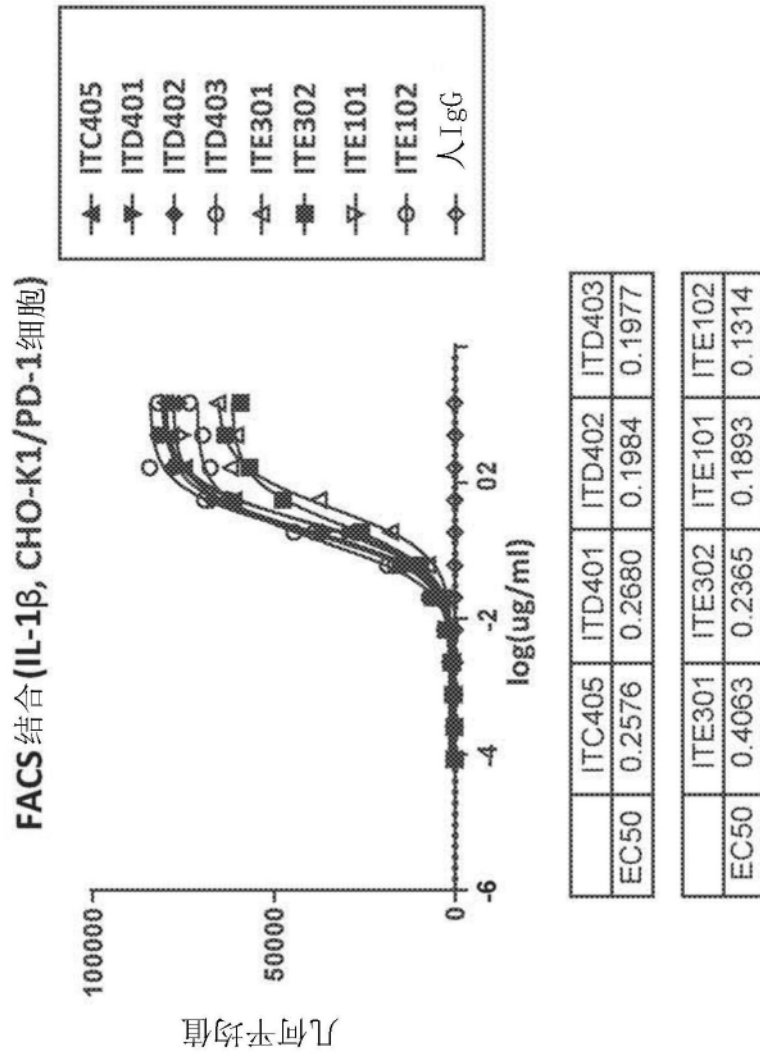
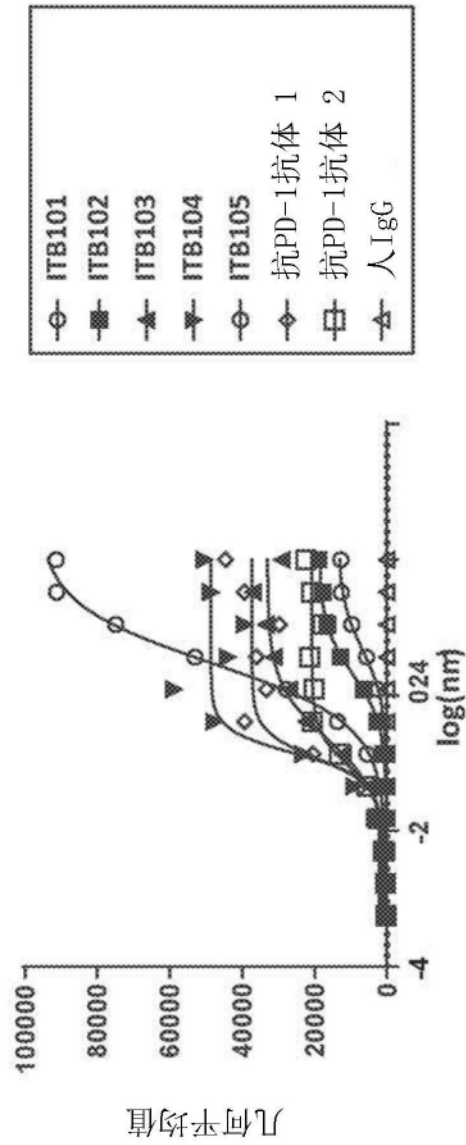


图8

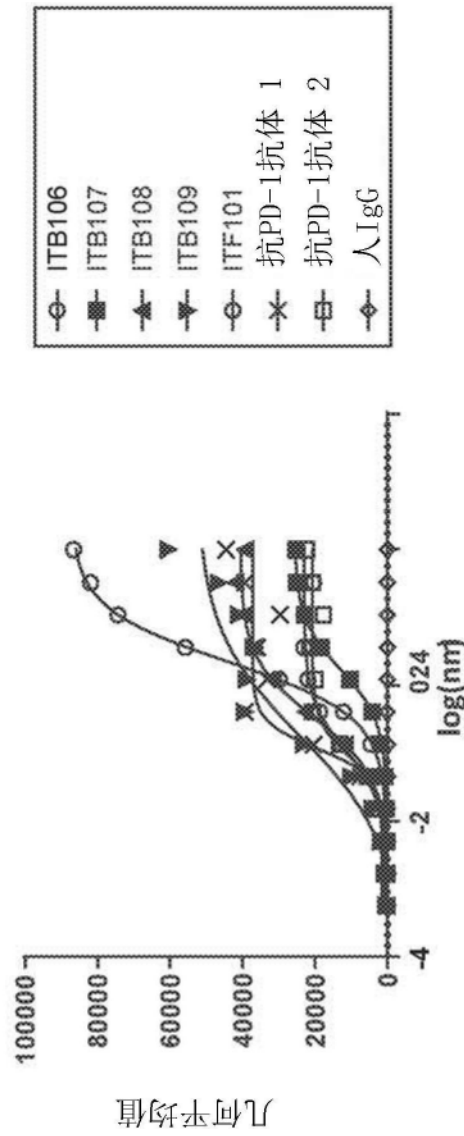
FACS 结合 (CHO-K1/PD-1 细胞)



ITB101	ITB102	ITB103	ITB104	ITB105	抗PD-1抗体 1	抗PD-1抗体 2	人IgG
3.024	2.068	0.2304	0.1394	4.739	0.1188	0.09180	26.15

图9A

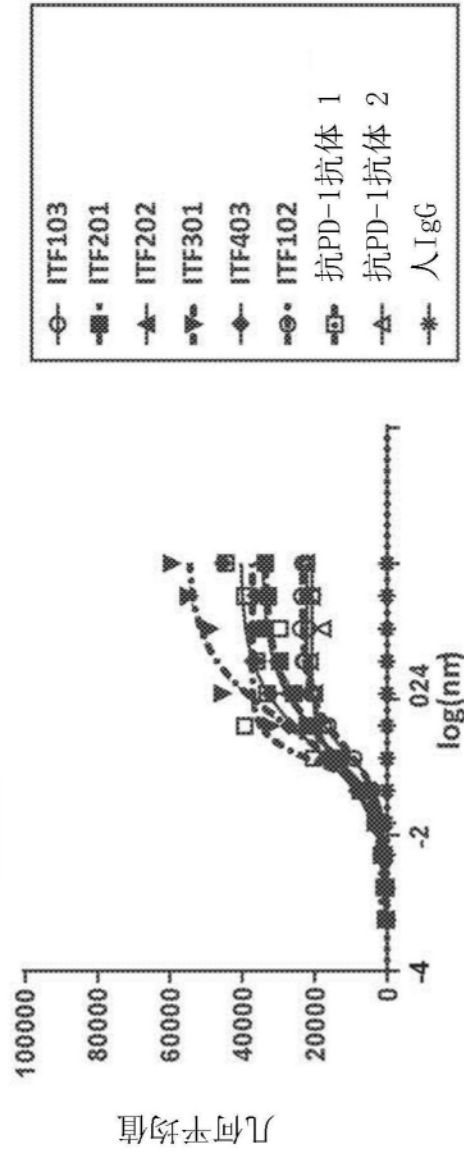
FACS 结合(CHO-K1/PD-1细胞)



ITB106	ITB107	ITB108	ITB109	ITF101	抗PD-1抗体 1	抗PD-1抗体 2	人IgG
EC50	2.244	1.752	0.3413	0.1852	0.1149	0.1188	0.09180
							26.15

图9B

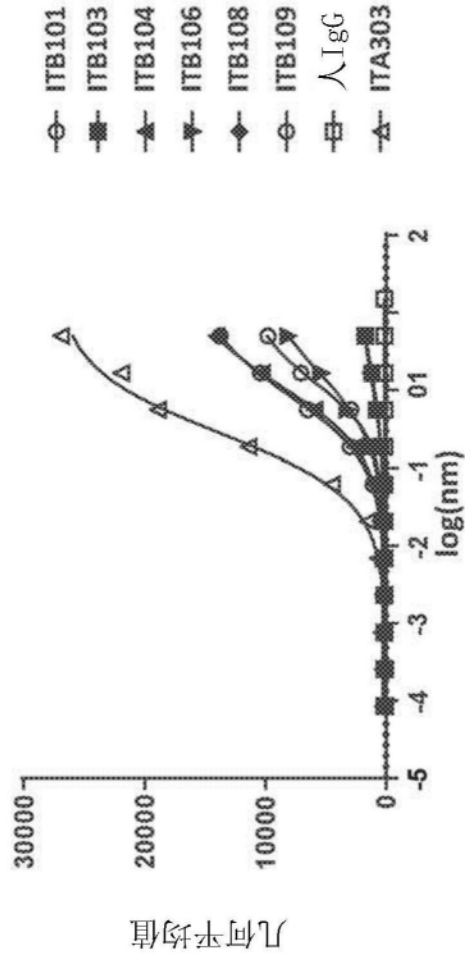
FACS 结合 (CHO-K1/PD-1细胞)



ITF103	ITF201	ITF202	ITF301	ITF403	ITF102	抗PD-1抗体 1	抗PD-1抗体 2	人IgG
EC50	0.1716	0.2061	0.2088	0.2014	0.2090	0.1188	0.09180	26.15

图9C

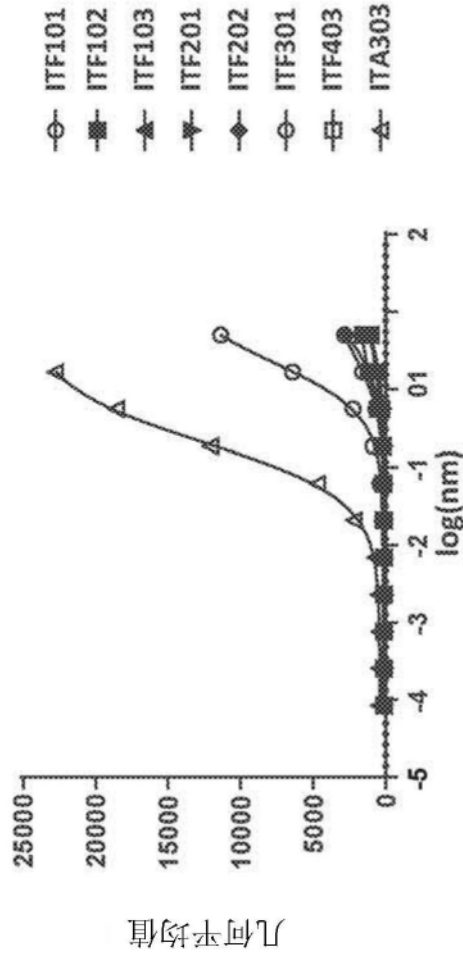
FACS 结合 (IL-1 β , CHO-K1/PD-1 细胞)



ITB101	ITB103	ITB104	ITB106	ITB108	ITB109	人IgG	ITA303
1.260	2.893	1.092	1.715	1.472	0.8741	~ 3.022e+019	0.2762

图10A

FACS 结合 (IL-1 β , CHO-K1/PD-1 细胞)



ITF101	ITF102	ITF103	ITF201	ITF202	ITF301	ITF403	ITA303
2.620	1.122	2.344	~ 1.1565	6.566	2.174	~ 55712	0.2049

几何平均值

图10B

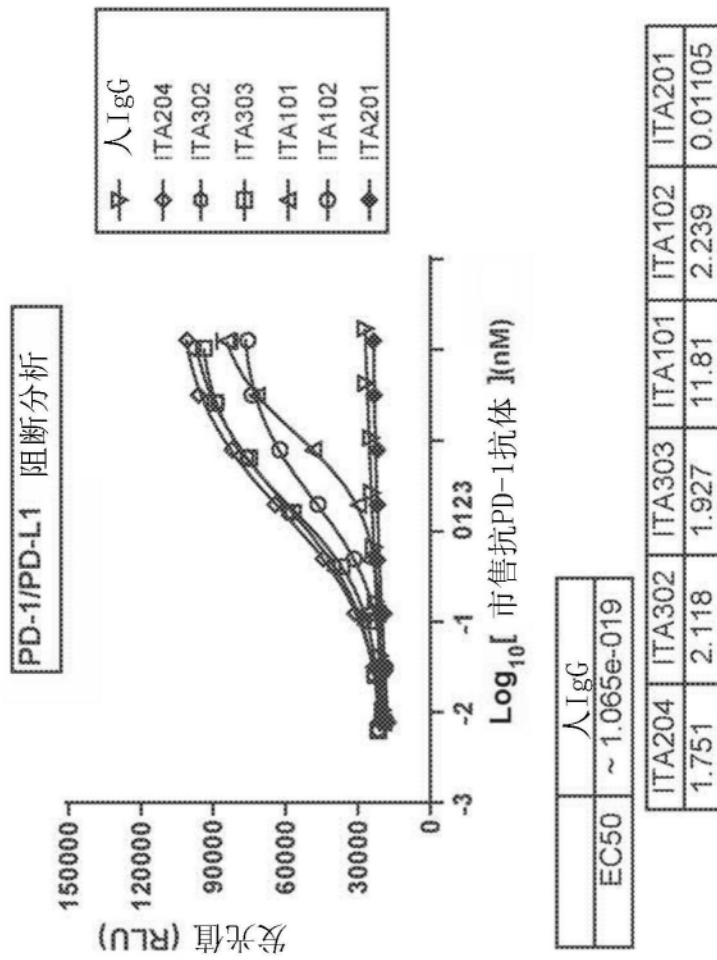


图11

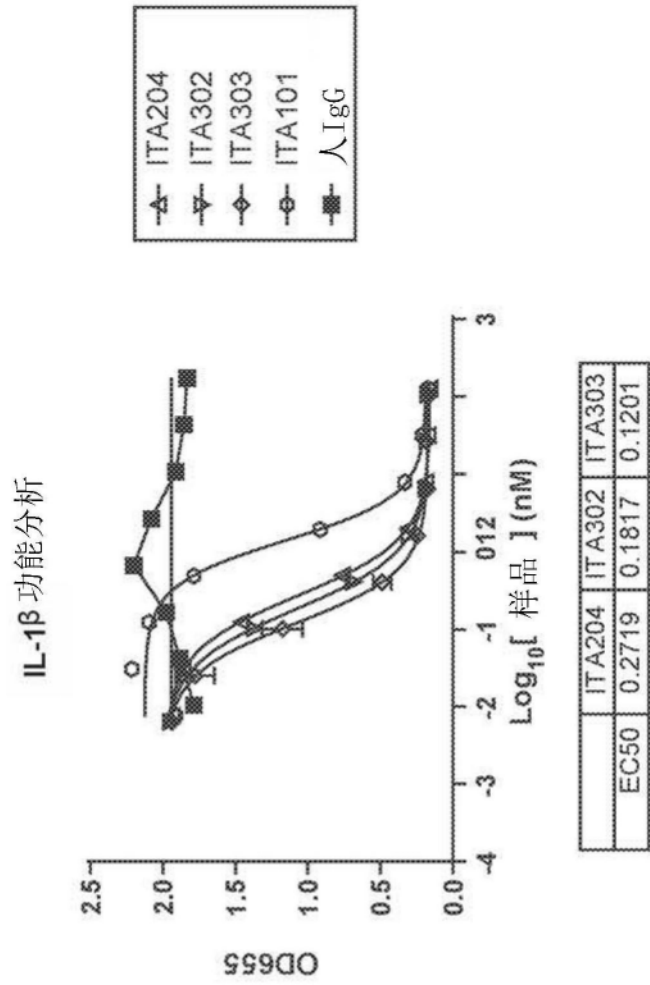


图12A

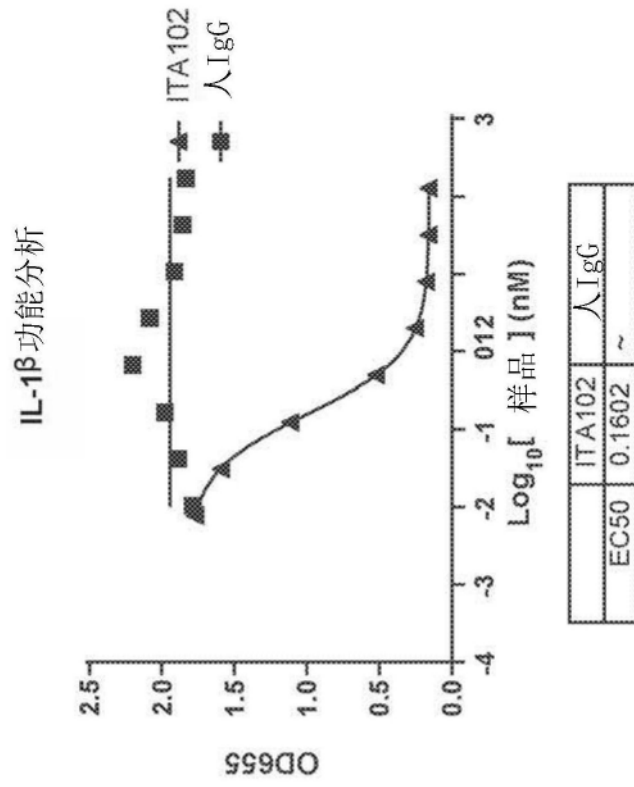


图12B