



(12)发明专利申请

(10)申请公布号 CN 111344394 A

(43)申请公布日 2020.06.26

(21)申请号 201880063656.4

(22)申请日 2018.09.17

(30)优先权数据

62/565,464 2017.09.29 US

(85)PCT国际申请进入国家阶段日

2020.03.30

(86)PCT国际申请的申请数据

PCT/US2018/051280 2018.09.17

(87)PCT国际申请的公布数据

W02019/067242 EN 2019.04.04

(71)申请人 美国卫生和人力服务部

地址 美国马里兰州

(72)发明人 德鲁·C·丹尼格尔

史蒂文·A·罗森伯格

帕里萨·马勒克扎德

(74)专利代理机构 北京英赛嘉华知识产权代理

有限责任公司 11204

代理人 王达佐 洪欣

(51)Int.Cl.

C12N 5/0783(2006.01)

C12N 5/0784(2006.01)

A61K 35/17(2006.01)

A61K 39/00(2006.01)

C07K 14/47(2006.01)

权利要求书2页 说明书61页

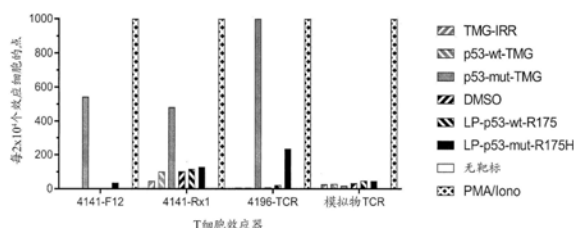
序列表336页 附图55页

(54)发明名称

分离对P53癌症-特异性突变具有抗原特异性的T细胞的方法

(57)摘要

本申请公开了分离对由癌症-特异性p53突变编码的突变的p53氨基酸序列具有抗原特异性的T细胞的方法,该方法包括:诱导患者的自体APC呈递突变的p53氨基酸序列;共培养患者的自体T细胞与呈递突变的p53氨基酸序列的自体APC;和选择自体T细胞。还公开了制备细胞群的相关方法、细胞群、药物组合物以及治疗或预防癌症的方法。



1. 分离对由癌症-特异性p53突变编码的突变的p53氨基酸序列具有抗原特异性的T细胞的方法,所述方法包括:

诱导患者的自体抗原呈递细胞 (APC) 呈递至少一种突变的p53氨基酸序列;

将所述患者的自体T细胞与呈递所述突变的p53氨基酸序列的所述自体APC共培养;和

选择以下自体T细胞,以提供对由所述癌症-特异性p53突变编码的突变的p53氨基酸序列具有抗原特异性的分离的T细胞:其 (a) 与呈递所述突变的p53氨基酸序列的自体APC共培养和 (b) 对在由所述患者表达的主要组织相容性复合物 (MHC) 分子的背景下呈递的所述突变的p53氨基酸序列具有抗原特异性。

2. 如权利要求1所述的方法,其中诱导所述患者的自体APC呈递所述突变的p53氨基酸序列包括用包含所述突变的p53氨基酸序列的肽或肽汇集物脉冲APC,所述汇集物中的每种肽包含不同的突变的p53氨基酸序列。

3. 如权利要求2所述的方法,其中所述肽或肽汇集物包括SEQ ID NO:2-13的一种或多种突变的p53肽。

3. 如权利要求1所述的方法,其中诱导所述患者的自体APC呈递所述突变的p53氨基酸序列包括将编码所述突变的p53氨基酸序列的核苷酸序列引入至所述APC中。

4. 如权利要求3所述的方法,其中引入所述自体APC中的所述核苷酸序列是串联微基因 (TMG) 构建体,每种微基因包含p53基因,每种p53基因包含编码突变的p53氨基酸序列的癌症-特异性p53突变,其中所述TMG构建体中的每种p53基因编码不同的突变的p53氨基酸序列。

5. 如权利要求4所述的方法,其中所述TMG构建体编码SEQ ID NO:2-13的一种或多种突变的p53肽。

6. 如权利要求4所述的方法,其中所述TMG构建体编码SEQ ID NO:14的氨基酸序列。

7. 如权利要求1-6中任一项所述的方法,其中选择对所述突变的p53氨基酸序列具有抗原特异性的自体T细胞包括选择性培养对所述突变的p53氨基酸序列具有抗原特异性的自体T细胞。

8. 如权利要求1-7中任一项所述的方法,其中选择对所述突变的p53氨基酸序列具有抗原特异性的自体T细胞包括选择表达程序性细胞死亡1 (PD-1)、淋巴细胞-激活基因3 (LAG-3)、T细胞免疫球蛋白和粘蛋白结构域3 (TIM-3)、4-1BB、OX40和CD107a中的任一种或多种的T细胞。

9. 如权利要求1-8中任一项所述的方法,其中选择对所述突变的p53氨基酸序列具有抗原特异性的自体T细胞包括选择以下T细胞: (i) 其在与呈递所述突变的p53氨基酸序列的APC共培养后,相比由阴性对照分泌的一种或多种细胞因子的量,分泌更大量的所述一种或多种细胞因子,或 (ii) 其中在与呈递所述突变的p53氨基酸序列的APC共培养后,相比分泌一种或多种细胞因子的阴性对照T细胞的数量,至少两倍数量的T细胞分泌所述一种或多种细胞因子。

10. 如权利要求9所述的方法,其中所述一种或多种细胞因子包括干扰素 (IFN) - γ 、白介素 (IL) -2、肿瘤坏死因子 α (TNF- α)、粒细胞/单核细胞集落刺激因子 (GM-CSF)、IL-4、IL-5、IL-9、IL-10、IL-17和IL-22。

11. 分离对由癌症-特异性p53突变编码的突变的p53氨基酸序列具有抗原特异性的T细

胞受体 (TCR) 或其抗原结合部分的方法,所述方法包括:

根据权利要求1-10中任一项所述的方法,分离对由癌症-特异性p53突变编码的突变的p53氨基酸序列具有抗原特异性的T细胞;和

从选定的自体T细胞分离编码所述TCR或其抗原结合部分的核苷酸序列,其中所述TCR或其抗原结合部分对由所述癌症-特异性p53突变编码的所述突变的p53氨基酸序列具有抗原特异性。

12. 制备表达对由癌症-特异性p53突变编码的突变的p53氨基酸序列具有抗原特异性的TCR或其抗原结合部分的细胞群的方法,所述方法包括:

根据权利要求11所述的方法分离TCR或其抗原结合部分,和

将编码分离的TCR或其抗原结合部分的核苷酸序列引入至外周血单核细胞 (PBMC) 中以获得表达所述TCR或其抗原结合部分的细胞。

13. 制备对由癌症-特异性p53突变编码的突变的p53氨基酸序列具有抗原特异性的T细胞群的方法,所述方法包括:

根据权利要求1-10中任一项所述的方法分离T细胞,和

扩大选定的自体T细胞的数量以获得对由所述癌症-特异性p53突变编码的所述突变的p53氨基酸序列具有抗原特异性的T细胞群。

14. 如权利要求13所述的方法,其中扩大其细胞的数量包括用饲养PBMC、白介素 (IL) -2 和OKT3抗体培养所述选定的细胞。

15. 分离的细胞群,其根据权利要求12-14中任一项所述的方法制备。

16. 药物组合物,其包含权利要求15所述的分离的细胞群和药学上可接受的载体。

17. 如权利要求15所述的分离的细胞群或如权利要求16所述的药物组合物,其用于治疗或预防患者中的癌症的用途。

18. 根据权利要求17所述用途的分离的细胞群或药物组合物,其中所述癌症是上皮癌。

19. 根据权利要求17所述用途的分离的细胞群或药物组合物,其中所述癌症是胆管癌、黑素瘤、结肠癌、直肠癌、卵巢癌、子宫内膜癌、非小细胞肺癌 (NSCLC)、成胶质细胞瘤、子宫颈癌、头颈癌、乳房癌、胰腺癌或膀胱癌。

20. 根据权利要求17-19中任一项所述用途的分离的细胞群或包含分离的细胞群的药物组合物,其中所述分离的细胞群对于所述患者是自体的。

21. 根据权利要求17-19中任一项所述用途的分离的细胞群或包含分离的细胞群的药物组合物,其中所述分离的细胞群对于所述患者是同种异体的。

分离对P53癌症-特异性突变具有抗原特异性的T细胞的方法

[0001] 相关申请的交叉引用

[0002] 本专利申请要求2017年9月29日提交的美国临时专利申请No.62/565,464的权益，其通过引用整体并入本文。

[0003] 关于联邦政府资助的研究和开发的声明

[0004] 本发明是由美国国立卫生研究院国家癌症研究所 (National Institutes of Health, National Cancer Institute) 在政府支持下完成的，项目号为ZIABC010984。政府拥有本发明的某些权利。

[0005] 通过引用并入以电子方式提交的材料

[0006] 通过引用整体并入本文的是与此同时提交并且标识如下的计算机可读核苷酸/氨基酸序列表：日期为2018年9月14日的一个名为“740175_ST25.txt”的687,616字节ASCII (文本) 文件。

[0007] 发明背景

[0008] 过继细胞疗法 (ACT) 在某些癌症患者中可以产生积极的临床响应。尽管如此，成功使用ACT广泛治疗癌症和其他疾病的障碍仍然存在。例如，特异性识别癌症抗原的T细胞可能难以从患者鉴定和/或分离。因此，需要获得癌症-反应性T细胞的改进方法。

[0009] 发明简述

[0010] 本发明的一个实施方案提供了分离T细胞的方法，所述T细胞对由癌症-特异性p53突变所编码的突变的p53氨基酸序列具有抗原特异性，所述方法包括：诱导患者的自体抗原呈递细胞 (APC) 呈递至少一种突变的p53氨基酸序列；共培养患者的自体T细胞与呈递突变的p53氨基酸序列的自体APC；以及选择 (a) 与呈递突变的p53氨基酸序列的自体APC共培养和 (b) 对在由患者表达的主要组织相容性复合物 (MHC) 分子的情况下呈递的经突变的p53氨基酸序列具有抗原特异性的自体T细胞，以提供对由癌症-特异性p53突变所编码的突变的p53氨基酸序列具有抗原特异性的经分离的T细胞。

[0011] 本发明的另一个实施方案提供了分离对由癌症-特异性p53突变所编码的突变的p53氨基酸序列具有抗原特异性的T细胞受体 (TCR) 或其抗原结合部分的方法，所述方法包括：根据本文所述的任一方法分离对由癌症-特异性p53突变所编码的突变的p53氨基酸序列具有抗原特异性的T细胞；和从选定的自体T细胞分离编码TCR或其抗原结合部分的核苷酸序列，其中TCR或其抗原结合部分对由癌症-特异性p53突变所编码的突变的p53氨基酸序列具有抗原特异性。

[0012] 本发明的又一个实施方案提供了制备表达TCR或其抗原结合部分的细胞群的方法，所述TCR或其抗原结合部分对由癌症-特异性p53突变所编码的突变的p53氨基酸序列具有抗原特异性，所述方法包括：根据本文所述的任一方法分离TCR或其抗原结合部分，以及将编码分离的TCR或其抗原结合部分的核苷酸序列引入至外周血单核细胞 (PBMC) 中以获得表达TCR或其抗原结合部分的细胞。

[0013] 本发明的另一个实施方案提供了制备对由癌症-特异性p53突变所编码的突变的p53氨基酸序列具有抗原特异性的T细胞群的方法，所述方法包括：根据本文所述的任一方法

法分离T细胞,和扩大选定的自体T细胞的数量以获得对由癌症-特异性p53突变所编码的突变的p53氨基酸序列具有抗原特异性的T细胞群。

[0014] 本发明的另外实施方案提供了相关的细胞群、药物组合物以及治疗或预防癌症的方法。

[0015] 若干附图视图的简述

[0016] 图1是显示在共培养效应细胞和靶细胞之后测量的每 2×10^4 个效应细胞的IFN- γ 阳性点的数量的图。效应细胞是来自患者4141的TIL片段F12,输液袋TIL (Rx1),来自患者4196的p53-R175H-特异性TCR-转导的细胞或模拟物转导的T细胞。靶细胞是HLA-A*02:01APC (对于患者4141是自体的),其(1)用由无关(IRR;左侧斜线灰条)、WT p53 (p53wt-TMG;右侧斜线灰条)或经突变的p53 (p53-mut-TMG;灰条)序列组成的TMG电穿孔或(2)用肽媒介物(DMSO;左侧斜线黑条)或由WT p53-R175序列(LP-p53-wt-R175;右侧斜线黑条)或经突变的p53-R175H(LP-p53-mut-R175H;黑条)序列组成的经纯化的(>95%,通过HPLC) 25个氨基酸的肽脉冲。仅T细胞(无靶标;空条)是阴性对照,并且佛波醇12-肉豆蔻酸酯13-乙酸酯(PMA)和离子霉素(Iono)是阳性对照(格条)。

[0017] 图2是显示在来自患者4130的TIL片段(F14、F20或F24)与自体APC共培养之后检测的4-1BB+细胞的百分比(CD4+百分比)的图,所述自体APC(1)用由无关(IRR;空条)、WT p53 (p53-WT;水平黑条)或突变的p53 (p53-MUT;灰条)序列组成的TMG电穿孔或(2)用肽媒介物(DMSO;左侧斜线黑条)或由WT p53-R273序列(LP-p53-R273-WT;左侧斜线灰条)或突变的p53-R273H(LP-p53-R273H-MUT;黑条)序列组成的经纯化的(>95%,通过HPLC) 25个氨基酸的肽脉冲。

[0018] 图3是显示在共培养来自患者4259的TIL片段(F1-6、F9、F13-23, n=18)与自体APC之后测量的每 2×10^4 个效应细胞的IFN- γ 阳性点的数量的图,所述自体APC用由无关(IRR;空条)、WT p53 (p53-WT;灰条)或经突变的p53 (p53-MUT;黑条)序列组成的TMG电穿孔。

[0019] 图4是显示在共培养来自患者4259的TIL片段(F1-F6、F9、F13-F23, n=18)与自体APC之后检测的4-1BB+细胞的百分比(CD4+百分比)的图,所述自体APC用由无关(IRR;空条)、WT p53 (p53-WT;灰条)或突变的p53 (p53-MUT;黑条)序列组成的TMG电穿孔。

[0020] 图5是显示在共培养来自患者4259的TIL片段(F1-F6、F9、F13-F23, n=18)与自体APC之后检测的4-1BB+细胞的百分比(CD8+百分比)的图,所述自体APC用由无关(IRR;空条)、WT p53 (p53-WT;灰条)或突变的p53 (p53-MUT;黑条)序列组成的TMG电穿孔。

[0021] 图6是显示在共培养来自患者4259的TIL片段(F1-F6、F9、F13-23, n=18)与自体APC之后测量的每 2×10^4 个效应细胞的IFN- γ 阳性点的数量的图,所述自体APC用肽媒介物(DMSO;空条)或由WT p53-Y220序列(LP-p53-Y220-WT;灰条)或突变的p53-Y220C(LP-p53-Y220C-MUT;黑条)序列组成的经纯化的(>95%,通过HPLC) 25个氨基酸的肽脉冲。

[0022] 图7是显示在共培养来自患者4259的TIL片段(F1-F6、F9、F13-F23, n=18)与自体APC之后检测的4-1BB+细胞的百分比(CD4+百分比)的图,所述自体APC用肽媒介物(DMSO;空条)或由WT p53-Y220序列(LP-p53-Y220-WT;灰条)或突变的p53-Y220C(LP-p53-Y220C-MUT;黑条)序列组成的经纯化的(>95%,通过HPLC) 25个氨基酸的肽脉冲。

[0023] 图8是显示在共培养来自患者4259的TIL片段(F1-F6、F9、F13-F23, n=18)与自体APC之后检测的4-1BB+细胞的百分比(CD8+百分比)的图,所述自体APC用肽媒介物(DMSO;空

条)或由WT p53-Y220序列(LP-p53-Y220-WT;灰条)或突变的p53-Y220C(LP-p53-Y220C-MUT;黑条)序列组成的经纯化的(>95%,通过HPLC)25个氨基酸的肽脉冲。

[0024] 图9是显示在共培养来自患者4127的TIL与同种异体的(DRB3*01:01:01或DRB3*02:02:01)APC之后测量的每 2×10^4 个效应细胞的IFN- γ 阳性点的数量的图,所述同种异体的(DRB3*01:01:01或DRB3*02:02:01)APC(1)用由无关(IRR;左侧斜线空条)WT p53(p53-WT;左侧斜线灰条)或突变的p53(p53-MUT;灰条)序列组成的TMG电穿孔或(2)用肽媒介物(DMSO;右侧斜线空条)或由WT p53-G245序列(LP-p53-wt-G245;右侧斜线灰条)或突变的p53-G245S(LP-p53-mut-G245S;黑条)序列组成的经纯化的(>95%,通过HPLC)25个氨基酸的肽脉冲。

[0025] 图10是显示在共培养表达4127-TCR1的T细胞与同种异体的(DRB3*01:01:01或DRB3*02:02:01)APC之后测量的每 2×10^4 个效应细胞的IFN- γ 阳性点的数量的图,所述同种异体的(DRB3*01:01:01或DRB3*02:02:01)APC(1)用由无关(IRR;左侧斜线空条)、WT p53(p53-WT;左侧斜线灰条)或经突变的p53(p53-MUT;灰条)序列组成的TMG电穿孔或(2)用肽媒介物(DMSO;右侧斜线空条)或由WT p53-G245序列(LP-p53-wt-G245;右侧斜线灰条)或经突变的p53-G245S(LP-p53-mut-G245S;黑条)序列组成的经纯化的(>95%,通过HPLC)25个氨基酸的肽脉冲。

[0026] 图11是显示在共培养来自患者4273的TIL片段(F1-F24, n=24)与自体APC之后测量的每 2×10^4 个效应细胞的IFN- γ -阳性点的数量的图,所述自体APC用由无关(IRR;空条)WT p53(p53-WT;灰条)或经突变的p53(p53-MUT;黑条)序列组成的TMG(TMG)电穿孔。

[0027] 图12是显示在共培养患者4273TIL片段F1-F24(n=24)与自体APC之后检测的4-1BB+(CD4+百分比)细胞的百分比的图,所述自体APC用由无关(IRR;空条)WT p53(p53-WT;灰条)或经突变的p53(p53-MUT;黑条)序列组成的TMG电穿孔。

[0028] 图13是显示在共培养来自患者4273的TIL片段(F1-F24, n=24)与自体APC之后测量的每 2×10^4 个效应细胞的IFN- γ -阳性点的数量的图,所述自体APC用肽媒介物(DMSO;空条)或由WT p53-R248序列(LP-p53-R248-WT;灰条)或经突变的p53-R248W(LP-p53-R248W-MUT;黑条)序列组成的经纯化的(>95%,通过HPLC)25个氨基酸的肽脉冲。

[0029] 图14是显示在共培养来自患者4273的TIL片段(F1-F24, n=24)与自体APC之后检测的4-1BB+(CD4+百分比)细胞的百分比的图,所述自体APC用肽媒介物(DMSO;空条)或由WT p53-R248序列(LP-p53-R248-WT;灰条)或经突变的p53-R248W(LP-p53-R248W-MUT;黑条)序列组成的经纯化的(>95%,通过HPLC)25个氨基酸的肽脉冲。

[0030] 图15是显示在共培养来自患者4149的自体PBL(用4149-TCRa2b1或4149-TCRa2b2转座)与自体APC之后测量的每 2×10^4 个效应细胞的IFN- γ -阳性点的数量的图,所述自体APC(1)用由无关(IRR;右侧斜线黑条)、WT p53(p53-wt-TMG;左侧斜线黑条)或经突变的p53(p53-mut-TMG;灰条)序列组成的TMG电穿孔或(2)用肽媒介物(DMSO;空条)或由WT p53-Y220序列(LP-p53-Y220-WT;水平斜线黑条)或经突变的p53-Y220C(LP-p53-Y220C-MUT;黑条)序列组成的经纯化的(>95%,通过HPLC)25个氨基酸的肽脉冲。佛波醇12-肉豆蔻酸酯13-乙酸酯(PMA)和离子霉素(Iono)是阳性对照(灰条)。

[0031] 图16是显示在共培养来自患者4149的用TCR(4149-TCRa2b1或4149-TCRa2b2)转座的自体PBL与自体APC之后检测的4-1BB+(CD4+百分比)细胞的百分比的图,所述自体APC(1)

用由无关 (IRR; 右侧斜线黑条)、WT p53 (p53-wt-TMG; 左侧斜线黑条) 或经突变的p53 (p53-mut-TMG; 灰条) 序列组成的TMG电穿孔或 (2) 用肽媒介物 (DMSO; 空条) 或由WT p53-Y220序列 (LP-p53-Y220-WT; 水平斜线黑条) 或经突变的p53-Y220C (LP-p53-Y220C-MUT; 黑条) 序列组成的经纯化的 (>95%, 通过HPLC) 25-个氨基酸的肽脉冲。PMA和Iono是阳性对照 (灰条)。

[0032] 图17是显示在共培养来自患者4149的TIL与用表10的一种肽脉冲的自体DC之后检测的4-1BB+细胞的百分比 (CD4+T细胞百分比) 的图。

[0033] 图18是显示在共培养4149-TCRa2b2转座的T细胞与同单独HLA等位基因+/-TMG共转染的Cos7细胞之后的IFN- γ 分泌 (pg/mL) 的图。将未用TMG转染的细胞用p53Y220C 15-mer肽脉冲。经脉冲的靶细胞由阴影条表示。用TMG转染的靶细胞由无阴影条表示。

[0034] 图19是显示在共培养来自患者4213的TIL片段 (F2和F24) 与自体APC之后检测的4-1BB+细胞的百分比 (CD8+百分比) 的图, 所述自体APC用肽媒介物 (DMSO; 空条) 或由经突变的p53-R248Q (LP-p53-R248Q-MUT; 黑条) 序列组成的经纯化的 (>95%, 通过HPLC) 25-个氨基酸的肽脉冲。

[0035] 图20是显示在共培养来自患者4213的CD4+T细胞与自体APC之后测量的每 2×10^4 个效应细胞的IFN- γ -阳性点的数量的图, 所述自体APC用肽媒介物 (DMSO; 空条) 或由突变的p53-R248Q (LP-p53-R248Q-MUT; 黑条) 序列组成的经纯化的 (>95%, 通过HPLC) 25-个氨基酸的肽脉冲。IFN- γ 的分泌由空条显示。4-1BB的表达由实心条显示。

[0036] 图21是显示在共培养来自患者4268的TIL片段 (F1-F24, n=24) 与自体APC之后测量的每 2×10^4 个效应细胞的IFN- γ -阳性点的数量的图, 所述自体APC用由无关 (IRR; 空条)、WT p53 (p53-WT; 灰条) 或经突变的p53 (p53-MUT; 黑条) 序列组成的TMG电穿孔。

[0037] 图22是显示在共培养来自患者4268的TIL片段 (F1-F24, n=24) 与自体APC之后测量的每 2×10^4 个效应细胞的IFN- γ -阳性点的数量的图, 所述自体APC用肽媒介物 (DMSO; 空条) 或由WT p53-R248序列 (LP-p53-R248-WT; 灰条) 或经突变的p53-R248Q (LP-p53-R248Q-MUT; 黑条) 序列组成的经纯化的 (>95%, 通过HPLC) 25-个氨基酸的肽脉冲。

[0038] 图23是显示在共培养来自患者4268的TIL片段 (F1-F24, n=24) 与自体APC之后检测的4-1BB+细胞的百分比 (CD4+百分比) 的图, 所述自体APC用肽媒介物 (DMSO; 空条) 或由WT p53-R248序列 (LP-p53-R248-WT; 灰条) 或经突变的p53-R248Q (LP-p53-R248Q-MUT; 黑条) 序列组成的经纯化的 (>95%, 通过HPLC) 25-个氨基酸的肽脉冲。

[0039] 图24是显示在共培养来自患者4268的TIL片段 (F1-F24, n=24) 与自体APC之后检测的4-1BB+细胞的百分比 (CD8+百分比) 的图, 所述自体APC用肽媒介物 (DMSO; 空条) 或由WT p53-R248序列 (LP-p53-R248-WT; 灰条) 或经突变的p53-R248Q (LP-p53-R248Q-MUT; 黑条) 序列组成的经纯化的 (>95%, 通过HPLC) 25-个氨基酸的肽脉冲。

[0040] 图25是显示在共培养来自患者4266的TIL片段 (F1-F24, n=24) 与自体APC之后测量的每 2×10^4 个效应细胞的IFN- γ -阳性点的数量的图, 所述自体APC用由无关 (IRR; 空条)、WT p53 (p53-WT; 灰条) 或经突变的p53 (p53-MUT; 黑条) 序列组成的TMG电穿孔。

[0041] 图26是显示在共培养来自患者4266的TIL片段 (F1-F24, n=24) 与自体APC之后检测的4-1BB+细胞的百分比 (CD8+百分比) 的图, 所述自体APC用由无关 (IRR; 空条)、WT p53 (p53-WT; 灰条) 或经突变的p53 (p53-MUT; 黑条) 序列组成的TMG电穿孔。

[0042] 图27是显示在共培养来自患者4266的TIL片段 (F1-F24, n=24) 与自体APC之后测

量的每 2×10^4 个效应细胞的IFN- γ -阳性点的数量的图,所述自体APC用肽媒介物(DMSO;空条)或由WT p53-R248序列(LP-p53-R248-WT;灰条)或经突变的p53-R248W(LP-p53-R248W-MUT;黑条)序列组成的经纯化的(>95%,通过HPLC) 25-个氨基酸的肽脉冲。

[0043] 图28是显示在共培养来自患者4266的TIL片段(F1-F24, n=24)与自体APC之后检测的4-1BB+细胞的百分比(CD8+百分比)的图,所述自体APC用肽媒介物(DMSO;空条)或由WT p53-R248序列(LP-p53-R248-WT;灰条)或经突变的p53-R248W(LP-p53-R248W-MUT;黑条)序列组成的经纯化的(>95%,通过HPLC) 25-个氨基酸的肽脉冲。

[0044] 图29是显示在共培养来自患者4266的TIL与Cos7细胞之后检测的4-1BB+细胞的百分比(CD8+百分比)的图,所述Cos7细胞用来自患者4266的单独HLA等位基因共转染以及用无肽(空条)、DMSO(肽媒介物;灰条)、WT p53-R248肽(灰斜线条)或经突变的p53-R248W肽(黑条)脉冲。数据是平均值 $\pm$ SEM(n=3)。

[0045] 图30是显示在共培养表达模拟物(无TCR)、4266-TCR1、4266-TCR2、4266-TCR3或4266-TCR4的T细胞与自体APC之后检测的4-1BB+细胞的百分比(CD8+百分比)的图,所述自体APC用肽媒介物(DMSO;灰条)或由WT p53-R248序列(斜线灰条)或经突变的p53-R248W(黑条)序列组成的经纯化的(>95%,通过HPLC) 25个氨基酸的肽脉冲。单独的培养基(空条)及PMA和离子霉素(格条)分别是阴性对照和阳性对照。

[0046] 图31是显示在共培养表达模拟物(无TCR)或p53-R248W-特异性TCR(4266-TCR2、4266-TCR3或4266-TCR4)的T细胞与从由患者4266切除的异种移植的肿瘤碎片建立然后通过免疫受损小鼠(TC#4266)连续传代的肿瘤细胞(TC)系之后检测的4-1BB+细胞的百分比(CD8+百分比)的图。将TC#4266细胞不与任何物质孵育(黑条)、或将TC#4266细胞与W6/32泛-HLA I类特异性阻断抗体(右侧灰斜线条)、IVA12泛-HLA II类特异性阻断抗体(灰条)或突变的p53-R248W肽(左侧灰斜线条)孵育。单独的培养基(无TC;空条)及PMA和离子霉素(灰格条)分别是阴性对照和阳性对照。

[0047] 图32显示了九种p53剪接变体的氨基酸序列的比对。SP|P04637|P53_HUMAN(SEQ ID NO:1);SP|P04637-2|P53_HUMAN(SEQ ID NO:535);SP|P04637-3|P53_HUMAN(SEQ ID NO:536);SP|P04637-4|P53_HUMAN(SEQ ID NO:537);SP|P04637-5|P53_HUMAN(SEQ ID NO:538);SP|P04637-6|P53_HUMAN(SEQ ID NO:539);SP|P04637-7|P53_HUMAN(SEQ ID NO:540);SP|P04637-8|P53_HUMAN(SEQ ID NO:541);和SP|P04637-9|P53_HUMAN(SEQ ID NO:542)。

[0048] 图33是显示在共培养来自患者4273的TIL与自体APC之后检测的4-1BB+细胞的百分比(CD8+百分比)的图,所述自体APC用编码无关突变(灰条)、WT p53序列(灰斜线条)或突变的p53序列(包括p53-R248W(黑条))的TMG转染。单独的培养基(空条)及PMA和离子霉素(格条)分别是阴性对照和阳性对照。

[0049] 图34是显示在共培养来自患者4273的TIL与自体APC之后检测的4-1BB+细胞的百分比(CD4+百分比)的图,所述自体APC用对应于来自p53-R248W新表位的WT(空环)或突变的(实心方块)的25个氨基酸的肽脉冲。DMSO是肽媒介物。

[0050] 图35是显示在共培养来自患者4273的TIL与自体APC之后检测的4-1BB+细胞的百分比(CD4+百分比)的图,所述自体APC用来自p53-R248W新表位的重叠14个氨基酸的15个氨基酸的肽(氨基酸取代呈粗体)脉冲。DMSO是肽媒介物,单独的培养基(仅T细胞)及PMA和离

子霉素是对照。25个氨基酸的肽(wt p53-R248和经突变的p53-R248W)是15个氨基酸的肽的另外对照。肽是:YMCNSSCMGGMNWRP (SEQ ID NO:592); MCNSSCMGGMNWRPI (SEQ ID NO:593); CNSSCMGGMNWRPIL (SEQ ID NO:594); NSSCMGGMNWRPILT (SEQ ID NO:595); SSCMGGMNWRPILTI (SEQ ID NO:596); SCMGGMNWRPILTII (SEQ ID NO:597); CMGGMNWRPILTIIT (SEQ ID NO:598); MGGMNWRPILTIITL (SEQ ID NO:599); GGMNWRPILTIITLE (SEQ ID NO:600); GMNWRPILTIITLED (SEQ ID NO:601); 和MNWRPILTIITLEDs (SEQ ID NO:602)。

[0051] 图36是显示来自患者4273的TIL与Cos7细胞共培养之后分泌的IFN- γ (pg/mL)的浓度的图,所述Cos7细胞用来自患者4273的HLA等位基因以及分别在有或无p53-R248W新抗原的情况下的WT(空条)或突变的(黑条)TP53 TMG共转染。

[0052] 图37是显示在表达模拟物(无TCR)或4273-TCR1a2的T细胞与自体APC的共培养之后测量的每 2×10^4 个效应细胞的IFN- γ 点的数量的图,所述自体APC用肽媒介物(DMSO;灰条)或由WT p53-R248序列(斜线灰条)或经突变的p53-R248W(黑条)序列组成的经纯化的(>95%,通过HPLC)25个氨基酸的肽脉冲。单独的培养基(空条)及PMA和离子霉素(格条)分别是阴性对照和阳性对照。

[0053] 图38是显示在共培养来自患者4252的TIL片段F1、F3、F7或F19与自体APC(不成熟的DC)之后检测的4-1BB+细胞的百分比(CD4+百分比)的图,所述自体APC(不成熟的DC)(1)用由无关(IRR;左侧斜线灰条)、WT p53(p53wt-TMG;右侧斜线灰条)或经突变的p53(p53-mut-TMG;灰条)序列组成的TMG电穿孔,或(2)用肽媒介物(DMSO;左侧斜线黑条)或由WT p53-R175序列(LP-p53-wt-R175;右侧斜线黑条)或经突变的p53-R175H(LP-p53-mut-R175H;黑条)序列组成的经纯化的(>95%,通过HPLC)25个氨基酸的肽脉冲。仅T细胞(无靶标;空条)是阴性对照并且PMA和Iono是阳性对照(格条)。数据是平均值 $\pm$ SEM(n=3)。学生t检验按系在指定组之间进行。 $*p<0.05$, $**p<0.01$, $***p<0.001$ 。

[0054] 图39是显示在共培养来自患者4270的TIL片段F13或F16与自体APC(不成熟的DC)之后测量的每 2×10^4 个细胞的IFN- γ 点的数量的图,所述自体APC(不成熟的DC)(1)用由无关(IRR;左侧斜线灰条)、WT p53(p53wt-TMG;右侧斜线灰条)或突变的p53(p53-mut-TMG;灰条)序列组成的TMG电穿孔,或(2)用肽媒介物(DMSO;左侧斜线黑条)或由WT p53-R282序列(LP-p53-wt-R282;右侧斜线黑条)或突变的p53-R282W(LP-p53-mut-R282W;黑条)序列组成的经纯化的(>95%,通过HPLC)25个氨基酸的肽脉冲。仅T细胞(无靶标;空条)是阴性对照并且PMA和Iono是阳性对照(格条)。数据是平均值 $\pm$ SEM(n=3)。

[0055] 图40是显示在共培养来自患者4285的TIL片段(F1-F24,n=18)与自体APC之后测量的每 2×10^4 个细胞的IFN- γ 点的数量的图,所述自体APC用由无关(IRR;空条)、WT p53(p53-WT;灰条)或突变的p53(p53-MUT;黑条)序列组成的TMG电穿孔。

[0056] 图41是显示在共培养来自患者4285的TIL片段(F1-F24,n=18)与自体APC之后测量的每 2×10^4 个细胞的IFN- γ 点的数量的图,所述自体APC用肽媒介物(DMSO;空条)或由WT p53-R175序列(LP-p53-R175-WT;灰条)或经突变的p53-R175H(LP-p53-R175H-MUT;黑条)序

列组成的经纯化的(>95%,通过HPLC)25个氨基酸的肽脉冲。

[0057] 图42是显示在共培养来自患者4285的TIL片段(F1-F24,n=18)与自体APC之后检测的4-1BB+细胞的百分比(CD4+百分比)的图,所述自体APC用由无关(IRR;空条)WT p53(p53-WT;灰条)或经突变的p53(p53-MUT;黑条)序列组成的TMG电穿孔。

[0058] 图43是显示在共培养来自患者4285的TIL片段(F1-F24,n=18)与自体APC之后检测的4-1BB+细胞的百分比(CD4+百分比)的图,所述自体APC用肽媒介物(DMSO;空条)或由WT p53-R175序列(LP-p53-R175-WT;灰条)或经突变的p53-R175H(LP-p53-R175H-MUT;黑条)序列组成的经纯化的(>95%,通过HPLC)25个氨基酸的肽脉冲。

[0059] 图44是显示在经测序的141种上皮肿瘤的位于指定p53密码子处的每种错义p53突变的总突变频率(%)的图。

[0060] 图45是显示在共培养来自患者4141的TIL(片段培养物12)与自体APC之后测量的4-1BB阳性细胞的百分比(CD8+百分比)(右侧y-轴;黑条)和IFN- γ (每 2×10^4 个细胞的点)(左侧y-轴;斜线条)的图,所述自体APC用编码无关突变(TM-G-IRR)、WT p53序列(TP53-wt-TMG)或包含R175H的经突变的p53序列(TP53-mut-TMG)的TMG转染。单独的培养基及PMA和离子霉素分别是阴性对照和阳性对照。

[0061] 图46是显示在共培养来自患者4141的TIL(片段培养物12)与Cos7细胞之后测量的每 2×10^4 个效应细胞的IFN- γ -阳性点的数量的图,所述Cos7细胞用指定的HLA等位基因以及无额外基因(仅HLA;空条)、WT TP53 TMG(灰斜线条)或突变的(黑条)TP53 TMG(含p53-R175H序列)共转染。

[0062] 图47是显示在共培养表达模拟物(无TCR)或4141-TCR1a2的T细胞与T2肿瘤细胞(表达HLA-A*02:01)之后测量的IFN- γ (pg/mL)的浓度的图。将T2细胞用肽媒介物(DMSO;灰条)或由WT p53-R175肽(斜线灰条)或经突变的p53-R175H肽(黑条)组成的经纯化的(>95%,通过HPLC)肽脉冲。单独的培养基(空条)及PMA和离子霉素(格条)分别是阴性对照和阳性对照。数据是平均值 $\pm$ SEM(n=3)。

[0063] 图48是显示在共培养表达4141-TCR1a2的T细胞与Saos2细胞(p53-NUL和HLA-A*02:01+)之后对于一种指定标志物的表达呈阳性的细胞的百分比的图,所述细胞未经操纵(无阴影条),或被使得过表达全长p53-R175H蛋白(阴影条)。数据是平均值 $\pm$ SEM(n=3)。对两个细胞系之间的每种细胞因子进行了学生双尾t检验,以进行统计分析(**p<0.001)。

[0064] 图49是显示在共培养TIL(来自患者4259的片段培养物6)与自体APC之后检测的CD4+4-1BB阳性细胞的百分比的图,所述自体APC(1)用由无关(TM-G-IRR)、WT p53(TM-G-p53-WT)或经突变的p53(TM-G-p53-MUT)序列组成的TMG电穿孔,或(2)用肽媒介物(DMSO)或由WT p53-Y220序列(LP-p53-Y220-WT)或经突变的p53-Y220C(LP-p53-Y220C-MUT)序列组成的经纯化的(>95%,通过HPLC)25个氨基酸的肽脉冲。

[0065] 图50是显示共培养来自患者4259的TIL片段培养物(no.6)与自体APC之后检测的CD4+4-1BB阳性细胞的百分比的图,所述自体APC用降低浓度的25个氨基酸的肽(对应于WT p53序列(空心环)或突变的p53-Y220C(实心方块))在37℃下脉冲2小时。

[0066] 图51是显示在共培养来自患者4259的TIL与用DMSO、WT p53-Y220肽或经突变的p53-Y220C肽脉冲的自体APC之后检测的CD4+4-1BB阳性细胞的百分比的图。

[0067] 图52是显示在共培养来自患者4259的TIL片段培养物no.6与Cos7细胞之后检测的

4-1BB阳性细胞的百分比(CD4+百分比)的图,所述Cos7细胞用来自患者4259的指定的HLA等位基因共转染并用DMSO(空条)或p53-Y220C肽(实心条)脉冲。

[0068] 图53是显示在共培养TC#4259靶细胞(内源性表达p53-Y220C和HLA-DRB1*04:01:01)与表达模拟物(无TCR;空条)或p53-Y220C-特异性TCR(4259-F6-TCR;黑条)的效应T细胞(10^5)之后检测的4-1BB+细胞的百分比的图。将TC#4259细胞不与任何物质孵育、或将TC#4259细胞与W6/32泛-HLA I类特异性阻断抗体、IVA12泛-HLA II类特异性阻断抗体或经突变的p53-Y220C肽孵育。单独的培养基(无TC)及PMA和离子霉素分别是阴性对照和阳性对照。数据是平均值 $\pm$ SEM(n=3)。在如指定进行统计分析的组之间进行学生双尾t检验(**p<0.01和***p<0.001)。

[0069] 图54是显示在共培养TIL片段培养物4285-F6、4285-F9和4285-F10与Cos7细胞之后检测的4-1BB+细胞的百分比(CD4+百分比)的图,所述Cos7细胞用指定HLA等位基因转染并用DMSO(肽媒介物;灰和黑斜线条)或突变的p53-R175H肽(灰、格子和黑条)脉冲。

[0070] 图55是显示在共培养用4285-TCR1转座的T细胞与自体APC之后检测的4-1BB+细胞的百分比(CD4+百分比)的图,所述自体APC用降低浓度的25-个或15-个氨基酸的肽(对应于WT(空心环和方块)或经突变的(实心环和方块)p53-R175H序列)脉冲。

[0071] 发明详述

[0072] 肿瘤蛋白P53(也称为“TP53”或“p53”)通过例如调节细胞分裂而作为肿瘤遏制物。p53蛋白位于细胞核中,在那里其直接结合至DNA。当DNA受损时,p53蛋白参与确定DNA是否会被修复或受损的细胞是否会发生凋亡。如果DNA可以被修复,则p53激活其他基因以恢复损伤。如果DNA无法被修复,则p53蛋白阻止细胞分裂并向其发出进行凋亡的信号。通过阻止具有突变或受损DNA的细胞分裂,p53有助于预防肿瘤发展。野生型(WT)全长p53包含SEQ ID NO:1的氨基酸序列。

[0073] p53蛋白中的突变可降低或消除p53蛋白的肿瘤遏制功能。可替代地或另外地,p53突变可以是通过以显性负性方式干扰野生型p53的功能获得性突变。经突变的p53蛋白可以在多种人类癌症中的任一种中表达,诸如例如,胆管癌、黑素瘤、结肠癌、直肠癌、卵巢癌、子宫内膜癌、非小细胞肺癌(NSCLC)、成胶质细胞瘤、子宫颈癌、头颈癌、乳房癌、胰腺癌或膀胱癌。

[0074] 本发明的一个实施方案提供了分离对由癌症-特异性p53突变编码的p53突变的氨基酸序列具有抗原特异性的T细胞的方法。p53的突变在本文中通过参考全长氨基酸酸序列WT p53(SEQ ID NO:1)来定义。因此,p53的突变在本文中通过参考在特定位置存在的氨基酸残基,然后是位置编号,然后是在所讨论的特定突变中取代此残基的氨基酸来描述。例如,当位置如由SEQ ID NO:1所定义时,术语“R175”是指存在于SEQ ID NO:1的位置175处的精氨酸,“R175H”表示存在于SEQ ID NO:1的位置175处的精氨酸被组氨酸替代,而“G245S”表示存在于SEQ ID NO:1的位置245处的甘氨酸已经被丝氨酸替代。P53具有九种已知的剪接变体。本文所述的p53突变在所有九种p53剪接变体中是保守的。图32中显示了9种p53剪接变体的比对。因此,通过本发明的方法分离的T细胞可对由九种p53剪接变体中任一种编码的本文所述的任何经突变的p53氨基酸序列具有抗原特异性。当位置如SEQ ID NO:1所定义时,则p53的特定剪接变体的氨基酸序列的实际位置是相对于SEQ ID NO:1的相应位置来定义的,并且如由SEQ ID NO:1定义的位置可与特定剪接变体中的实际位置不同。因此,例

如,突变是指对应于SEQ ID NO:1的393个氨基酸的序列的指定位置的p53的特定剪接变体的氨基酸序列中的氨基酸残基的替代,要理解剪接变体中的实际位置可有所不同。

[0075] 本发明的实施方案可以提供许多优势中的任一个或多个。经突变的p53由癌细胞表达并且不在正常的非癌性细胞中表达。不受特定理论或机制的束缚,认为通过本发明方法分离的T细胞有利地靶向癌细胞的破坏,同时最小化或消除了正常的非癌性细胞的破坏,从而例如通过最小化或消除来减少毒性。此外,通过本发明方法分离的T细胞可以有利地成功治疗或预防对其他类型的治疗(诸如例如化疗、手术或辐照)无响应的突变的p53阳性癌症。另外,通过本发明的方法分离的T细胞可以提供对突变的p53的高度亲合的识别,其可以提供识别未经操纵的肿瘤细胞(如,未用干扰素(IFN)- γ 处理、用编码经突变的p53和适用的HLA分子中的一种或两种的载体转染、用带有p53突变的p53肽脉冲或其组合的肿瘤细胞)的能力。在所有肿瘤中,大约有一半的肿瘤具有在p53中的突变,其中大约一半是错义突变并且约30%的错义突变发生在以下“热点”残基处:R175H、Y220C、G245D、G245S、R248L、R248Q、R248W、R249S、R273C、R273L、R273H和R282W。此外,p53中的相同“热点”突变(如,R175H、Y220C、G245D、G245S、R248L、R248Q、R248W、R249S、R273H、R273C、R273L或R282W)在无关人群的肿瘤中频繁发生(累计约占p53错义突变的30%)。因此,通过本发明方法分离的T细胞可增加可能适合用免疫疗法治疗的患者数量。

[0076] 与分离癌症突变-反应性T细胞的传统方法相比,本发明的方法可以更快、更专注且更有特异性。此类传统方法包括在将患者自体T细胞与呈递包含由一种或多种经鉴定的基因编码的癌症-特异性突变的肽的患者自体抗原呈递细胞共培养之前,鉴定由患者表达的含有癌症-特异性突变(如新抗原)的一种或多种基因,如在例如US 2017/0218042和US 2017/0224800中所述(下文称“传统筛选方法”)。利用本发明的方法,可以在筛选患者之前生产、储存和验证包含p53突变的肽和串联微基因(TMG),使得一旦在患者的肿瘤中鉴定出p53突变,就可不依赖于患者肿瘤中其他突变的知识,对患者的T细胞进行测试。这可以减少执行该方法所需的时间,这在评价终末期患者时特别有利。例如,本发明方法的持续时间可以比传统的筛选方法短如约3至约6周。在不存在其他竞争性突变的情况下,本发明的方法还可提供p53突变响应的高度专注的研究。不受特定理论或机制的束缚,认为患者突变-来源的TMG中的肽汇集物或竞争性肽汇集物(突变存在于除p53以外的蛋白中)可干扰突变的p53肽,并可能掩盖T细胞响应。因为本发明的方法只关注一种基因p53中的突变,所以与传统的筛选方法相比,本发明的方法可以提供提高的速度和效率来尝试鉴定p53突变-特异性T细胞和TCR,其涉及解析肽汇集物或TMG中的新抗原以确定哪种新抗原产生了T细胞响应。本发明的方法可以有利地产生可用于自体或同种异体疗法的T细胞和/或TCR。通过关注p53突变,可能会鉴定低频响应,其可在传统筛选方法的高通量中被稀释,并且可允许鉴定否则会因筛选数十至数百种新抗原的复杂性而丢失的T细胞和TCR。本发明的方法可以不依赖于患者是否患有相应的突变或甚至肿瘤的知识而用于测试患者中的T细胞响应。本发明的方法可用于筛选具有确定的HLA单倍型和预测的p53突变结合的患者,但不限于筛选该类型的群组。

[0077] 癌症-特异性p53突变可以是编码经突变的p53氨基酸序列(也称为“非沉默突变”)并且在癌细胞中表达但在正常非癌性细胞中不表达的p53基因中的任何突变。癌症-特异性p53突变的非限制性实例包括错义、无义、插入、缺失、重复、移码和重复扩增突变。在一个优

选的实施方案中,p53突变是错义突变。

[0078] 在本发明的一个实施方案中,经突变的p53氨基酸序列包括在SEQ ID NO:1的位置175、220、245、248、249、273或282处具有突变的人p53氨基酸序列。p53突变可以是任何错义突变。因此,SEQ ID NO:1的位置175、220、245、248、249、273或282处的突变可以是SEQ ID NO:1的位置175、220、245、248、249、273或282处存在的天然(WT)氨基酸残基的取代,其中在所讨论的特定位置处存在除天然(WT)氨基酸残基以外的任何氨基酸残基。在本发明的一个实施方案中,经突变的p53氨基酸序列包括具有以下人p53突变中的一种的人p53氨基酸序列:R175H、Y220C、G245D、G245S、R248L、R248Q、R248W、R249S、R273H、R273C、R273L或R282W。例如,突变的p53氨基酸序列可包括选自SEQ ID NO:2-13组成的组的突变的p53氨基酸序列。

[0079] 该方法可以包括诱导患者的自体抗原呈递细胞(APC)呈递至少一种经突变的p53氨基酸序列。APC可包括在其细胞表面上呈递与主要组织相容性复合物(MHC)分子缔合的蛋白质的肽片段的任何细胞。APC可包括例如巨噬细胞、DC、朗格汉斯细胞、B-淋巴细胞和T-细胞中的任一种或多种。优选地,APC是DC。通过使用来自患者的自体APC,本发明的方法可以有利地鉴定对由癌症-特异性p53突变编码的经突变的p53氨基酸序列具有抗原特异性的T细胞,所述经突变的p53氨基酸序列在由患者表达的MHC分子的情况下呈递。MHC分子可以是患者表达的任何MHC分子,包括但不限于MHC I类、MHC II类、HLA-A、HLA-B、HLA-C、HLA-DM、HLA-DO、HLA-DP、HLA-DQ和HLA-DR分子。本发明的方法可以有利地鉴定在由患者表达的任何MHC分子的情况下呈递的经突变的p53氨基酸序列,而不使用例如表位预测算法来鉴定MHC分子或经突变的p53氨基酸序列,其仅可用于选定的少量MHC I类等位基因并且可受限于有限可用的选择p53突变-反应性T细胞的试剂(如,不完整组的MHC四聚体)。因此,在本发明的一个实施方案中,本发明的方法有利地诱导APC在由患者表达的任何MHC分子的情况下呈递经突变的p53氨基酸序列,并且不限于任何特定的MHC分子。优选地,自体APC是抗原-阴性的自体APC。

[0080] 可以使用本领域已知的任何适合的方法来进行诱导患者的自体APC呈递至少一种突变的p53氨基酸序列。在本发明的一个实施方案中,诱导患者的自体APC呈递至少一种经突变的p53氨基酸序列包括用包含不超过一种突变的p53氨基酸序列的肽或者肽汇集物脉冲自体APC,肽汇集物中的每种肽均包含不同的突变的p53氨基酸序列。在这方面,可以以一定方式将自体APC与包含经突变的p53氨基酸序列的肽或肽汇集物一起培养,以使APC内化一种或多种肽并在细胞膜上展示结合至MHC分子的一种或多种突变的p53氨基酸序列。脉冲APC的方法在本领域中是已知的,并且在如Solheim(Ed.),Antigen Processing and Presentation Protocols(Methods in Molecular Biology),Human Press,(2010)中进行了描述。用于脉冲APC的一种或多种肽可包含由癌症-特异性p53突变编码的一种或多种经突变的p53氨基酸。一种或多种肽还可在一个或多个经突变的氨基酸的每个羧基侧和氨基侧上包含来自p53基因编码的内源p53蛋白的任何适合数量的连续氨基酸。侧接突变的每一侧的来自内源性p53蛋白的连续氨基酸的数量不受限制,并且可以是例如约4、约5、约6、约7、约8、约9、约10、约11、约12、约13、约14、约15、约16、约17、约18、约19、约20,或由前述值的任两个限定的范围。优选地,一种或多种肽在经突变的氨基酸的每一侧上包含来自内源p53蛋白的约12个连续氨基酸。在一个实施方案中,肽或肽汇集物包含SEQ ID NO:2-13的经

突变的p53肽中的一种或多种(表1)。

[0081] 在本发明的一个实施方案中,诱导患者的自体APC呈递经突变的p53氨基酸序列包括将编码经突变的p53氨基酸序列的核苷酸序列引入至APC中。将核苷酸序列引入APC中,使得APC表达并在细胞膜上展示结合至MHC分子的经突变的p53氨基酸序列。编码经突变的p53氨基酸的核苷酸序列可以是RNA或DNA。可以以本领域已知的多种不同方式中的任一种将核苷酸序列引入APC中,如在例如Solheim等人,同上中所述。可用于将核苷酸序列引入APC中的技术的非限制性实例包括转化、转导、转染和电穿孔。在一个实施方案中,该方法可以包括制备超过一种核苷酸序列,每种编码不同的经突变的p53氨基酸序列,以及将每种核苷酸序列引入不同的自体APC群中。在这方面,可以获得自体APC的多个群体,每个群体表达并展示不同的经突变的p53氨基酸序列。

[0082] 在一个实施方案中,该方法可以包括引入编码多于一种经突变的p53氨基酸序列的核苷酸序列。在这方面,在本发明的一个实施方案中,引入自体APC中的核苷酸序列是串联微基因(TM)构建体,每种微基因包含p53基因,每种p53基因包括编码不同的经突变的p53氨基酸序列的癌症-特异性p53突变。每种微基因可编码一种p53突变,所述p53突变在p53突变的每一侧上侧接有来自内源性p53蛋白的任何适合数量的连续氨基酸,如本文关于本发明其他方面所述。构建体中的微基因的数量不受限制,并且可以包括例如约5、约10、约11、约12、约13、约14、约15、约20、约25或更多,或由前述值的任两个限定的范围。在本发明的一个实施方案中,TM构建体编码SEQ ID NO:2-13的一种或多种经突变的p53肽。例如,TM构建体可以编码SEQ ID NO:14的氨基酸序列。APC表达由TM构建体编码的经突变的p53氨基酸序列,并在细胞膜上展示与MHC分子结合的经突变的p53氨基酸序列。在一个实施方案中,该方法可以包括制备超过一种TM构建体,每种构建体编码不同组的经突变的p53氨基酸序列,并且将每个TM构建体引入不同的自体APC群体中。在这一点上,可以获得多个自体APC群体,每个群体表达并展示由不同TM构建体编码的经突变的p53氨基酸序列。

[0083] 该方法可以包括培养患者的自体T细胞与呈递经突变的p53氨基酸序列的自体APC。T细胞可从患者中的许多来源获得,包括但不限于肿瘤、血液、骨髓、淋巴结、胸腺或其他组织或流体。T细胞可以包括任何类型的T细胞,并且可以处于任何发育阶段,包括但不限于CD4⁺/CD8⁺双阳性T细胞,CD4⁺辅助T细胞如Th1和Th2细胞,CD8⁺T细胞(如细胞毒性T细胞),肿瘤浸润细胞(如肿瘤浸润淋巴细胞(TIL)),外周血T细胞,记忆T细胞,初始T细胞等。T细胞可为CD8⁺T细胞、CD4⁺T细胞,或CD4⁺和CD8⁺T细胞两者。该方法可包括共培养自体T细胞和自体APC,使得T细胞以一种方式遇到由APC呈递的经突变的p53氨基酸序列以使自体T细胞特异性结合至并免疫识别由APC呈递的经突变的p53氨基酸序列。在本发明的一个实施方案中,将自体T细胞与自体APC直接接触共培养。

[0084] 该方法可以包括选择如下自体T细胞:其(a)与呈递经突变的p53氨基酸序列的自体APC共培养,和(b)对在由患者表达的MHC分子的情况下呈递的经突变的p53氨基酸序列具有抗原特异性。如本文所用的短语“抗原特异性”意指自体T细胞可以特异性结合并免疫识别由癌症-特异性p53突变编码的经突变的p53氨基酸序列。选择可以包括鉴定对突变的p53氨基酸序列具有抗原特异性的T细胞,并将它们与对经突变的p53氨基酸序列不具有抗原特异性的T细胞分离。可以以任何适合的方式选择对经突变的p53氨基酸序列具有抗原特异性的自体T细胞。在本发明的一个实施方案中,该方法包括如通过与T细胞生长因子(诸如

白介素 (IL)-2 或 IL-15) 共培养或如本文关于本发明的其他方面所述在选择自体 T 细胞之前来扩大自体 T 细胞的数量。在本发明的一个实施方案中,该方法不包括在选择自体 T 细胞之前用诸如 IL-2 或 IL-15 的 T 细胞生长因子来扩大自体 T 细胞的数量。

[0085] 例如,当自体 T 细胞与呈递突变的 p53 氨基酸序列的 APC 共培养后,对突变的 p53 氨基酸序列具有抗原特异性的 T 细胞可以表达多种 T 细胞激活标记中的任一种或多种,其可用于鉴定对突变的 p53 氨基酸序列具有抗原特异性的那些 T 细胞。此类 T 细胞激活标记可包括但不限于程序性细胞死亡 1 (PD-1)、淋巴细胞-激活基因 3 (LAG-3)、T 细胞免疫球蛋白和粘蛋白结构域 3 (TIM-3)、4-1BB、OX40 和 CD107a。因此,在本发明的一个实施方案中,选择对突变的 p53 氨基酸序列具有抗原特异性的自体 T 细胞包括选择表达以下中的任一种或多种的 T 细胞: PD-1、LAG-3、TIM-3、4-1BB、OX40 和 CD107a。可以使用本领域已知的多种技术中的任一种,诸如例如荧光激活的细胞分选 (FACS) 或磁激活的细胞分选,基于标记的表达来对表达一种或多种 T 细胞激活标志物的细胞进行分选,如在如 Turcotte 等人, Clin. Cancer Res., 20 (2): 331-43 (2013) 和 Gros 等人, J. Clin. Invest., 124 (5): 2246-59 (2014) 中所述。

[0086] 在本发明的另一个实施方案中,选择对突变的 p53 氨基酸序列具有抗原特异性的自体 T 细胞包括选择如下 T 细胞: (i) 与由阴性对照分泌的一种或多种细胞因子分泌的量相比,在与呈递经突变的 p53 氨基酸序列的 APC 共培养之后分泌更大量的一种或多种细胞因子,或 (ii) 其中与分泌一种或多种细胞因子的阴性对照 T 细胞的数量相比,至少两倍数量的 T 细胞在与呈递经突变的 p53 氨基酸序列的 APC 共培养后分泌一种或多种细胞因子。一种或多种细胞因子可以包含任何细胞因子,其由 T 细胞分泌是 T 细胞激活的特征 (如,由 T 细胞表达的 T 细胞受体 (TCR) 特异性结合至并免疫识别经突变的 p53 氨基酸序列)。其分泌是 T 细胞激活的特征的细胞因子的非限制性实例包括 IFN- γ 、IL-2 和肿瘤坏死因子 α (TNF- α)、粒细胞/单核细胞菌落刺激因子 (GM-CSF)、IL-4、IL-5、IL-9、IL-10、IL-17 和 IL-22。

[0087] 例如,如果与由阴性对照分泌的 IFN- γ 的量相比, T 细胞在与 (a) 用一定浓度的包含突变的 p53 氨基酸序列的肽 (如约 0.05 ng/mL 至约 10 μ g/mL, 如 0.05 ng/mL、0.1 ng/mL、0.5 ng/mL、1 ng/mL、5 ng/mL、100 ng/mL、1 μ g/mL、5 μ g/mL 或 10 μ g/mL) 脉冲的抗原-阴性 APC 或 (b) 已引入编码经突变的 p53 氨基酸序列的核苷酸序列于其中的 APC 共培养之后分泌至少两倍 IFN- γ , 则可认为自体 T 细胞对经突变的 p53 氨基酸序列具有“抗原特异性”。阴性对照可以是例如与以下共培养的自体 T 细胞 (如,源自外周血单核细胞 (PBMC)): (a) 用相同浓度的无关肽 (如,野生型氨基酸序列,或具有与经突变的 p53 氨基酸序列不同的序列的一些其他肽) 脉冲的抗原-阴性 APC, 或 (b) 已将编码无关肽序列的核苷酸序列引入其中的 APC。如果与阴性对照 (例如上述的阴性对照) 相比, T 细胞在与用更高浓度的包含经突变的 p53 氨基酸序列的肽脉冲的抗原-阴性 APC 共培养之后分泌更大量的 IFN- γ , 则自体 T 细胞还可对经突变的 p53 氨基酸序列具有“抗原特异性”。IFN- γ 分泌可以通过本领域已知的方法,诸如例如酶联免疫吸附测定 (ELISA) 来测量。

[0088] 可替代地或另外地,如果与分泌 IFN- γ 的阴性对照 T 细胞的数量相比,至少两倍数量的 T 细胞在与 (a) 用一定浓度的包含经突变的 p53 氨基酸序列的肽脉冲的抗原-阴性 APC 或 (b) 已引入编码经突变的 p53 氨基酸序列的核苷酸序列于其中的 APC 共培养之后分泌 IFN- γ , 则可认为自体 T 细胞对经突变的 p53 氨基酸序列具有“抗原特异性”。肽和阴性对照的浓度可以如本文关于本发明的其他方面所述。分泌 IFN- γ 的细胞的数量可以通过本领域已知

的方法诸如例如ELISPOT来测量。

[0089] 可替代地或另外地,如果与通过ELISPOT检测的与相同靶细胞共培养的阴性对照T细胞的点的数量相比,通过ELISPOT检测到在与以下共培养之后的T细胞的至少两倍数量的点:(a)用低浓度的经突变的p53肽脉冲的抗原-阴性、可适用的HLA分子阳性靶细胞或(b)已引入编码经突变的p53的核苷酸序列于其中以使得靶细胞表达经突变的p53的抗原-阴性、可适用的HLA分子阳性靶细胞,则可认为自体T细胞对经突变的p53具有“抗原特异性”。肽和阴性对照的浓度可以如本文关于本发明的其他方面所述。

[0090] 可替代地或另外地,如果通过ELISPOT检测到在与以下共培养之后表达TCR的T细胞的大于约50个点:(a)用低浓度的经突变的p53肽脉冲的抗原-阴性、可适用的HLA分子阳性靶细胞或(b)已引入编码经突变的p53的核苷酸序列于其中以使得靶细胞表达经突变的p53的抗原-阴性、可适用的HLA分子阳性靶细胞,则可认为自体T细胞对经突变的p53具有“抗原特异性”。肽的浓度可以如本文关于本发明的其他方面所述。

[0091] 尽管对经突变的p53氨基酸序列具有抗原特异性的T细胞既可(1)表达本文所述的任一种或多种T细胞激活标志物,也可(2)分泌更大量的如本文所述的一种或多种细胞因子,但在本发明的一个实施方案中,对经突变的p53氨基酸序列具有抗原特异性的T细胞可以表达任一种或多种T细胞激活标志物,而不会分泌更大量的一种或多种细胞因子,或者可以分泌更大量的一种或多种细胞因子而不表达任一种或多种T细胞激活标志物。

[0092] 在本发明的另一个实施方案中,选择对突变的p53氨基酸序列具有抗原特异性的自体T细胞包括选择性地生长对突变的p53氨基酸序列具有抗原特异性的自体T细胞。在这方面,该方法可以包括以此类方式共培养自体T细胞与自体APC,以有利于对突变的p53氨基酸序列具有抗原特异性的T细胞的生长超过对突变的p53氨基酸序列不具有抗原特异性的T细胞。因此,提供了与对突变的p53氨基酸序列不具有抗原特异性的T细胞相比,具有更高比例的对突变的p53氨基酸序列具有抗原特异性的T细胞的T细胞群。

[0093] 在本发明的一个实施方案中,该方法还包括从患者获得肿瘤的多个碎片,分别将来自多个碎片的每一个的自体T细胞与呈递突变的p53氨基酸序列的自体APC共同培养(如本文中关于本发明的其他方面所述),和分别评估来自多个碎片中的每一个的T细胞对突变的p53氨基酸序列的抗原特异性(如本文中关于本发明的其他方面所述)。

[0094] 在其中T细胞与表达多种经突变的p53氨基酸序列(如,由TMG构建体编码的多种突变的p53氨基酸序列或脉冲至自体APC上的肽汇集物中多种经突变的p53氨基酸序列)的自体APC共培养的本发明的一个实施方案中,选择自体T细胞还可包括分别评估自体T细胞对多种突变的p53氨基酸序列中的每一种的抗原特异性。例如,如本文关于本发明的其他方面所述,本发明的方法还可以包括分别诱导患者的自体APC呈递由构建体编码(或包含在汇集物中)的每种经突变的p53氨基酸序列(例如,通过提供分别的APC群,每个呈递由构建体编码(或包含在汇集物中)的不同的经突变的p53氨基酸序列)。如本文关于本发明的其他方面所述,所述方法还可包括将患者的自体T细胞与呈递每种突变的p53氨基酸序列的不同自体APC群分别共培养。如本文关于本发明的其他方面所述,所述方法还可以包括分别选择以下的自体T细胞:(a)与呈递突变的p53氨基酸序列的自体APC共培养,和(b)对在由患者表达的MHC分子的情况下呈递的经突变的p53氨基酸序列具有抗原特异性。在这方面,所述方法可以包括确定哪些由编码多种突变的p53氨基酸序列(或包含在汇集物中)的TMG构建体编码

的突变的p53氨基酸序列被自体T细胞在免疫学上识别(如,通过消除的过程)。

[0095] 在本发明的一个实施方案中,方法还包括扩大选定的自体T细胞的数量以获得对由癌症-特异性p53突变编码的经突变的p53氨基酸序列具有抗原特异性的T细胞群。选定细胞的数量可通过本领域已知的多种方法中的任一种实现,如例如在美国专利8,034,334;美国专利8,383,099;美国专利申请公开No.2012/0244133;Dudley等人,J.Immunother.,26:332-42(2003);和Riddell等人,J.Immunol.Methods,128:189-201(1990)中所述。在一个实施方案中,T细胞的数量通过培养T细胞与OKT3抗体、IL-2和饲养PBMC(如,经辐照的同种异体PBMC)来进行。在这方面,本发明的方法可以有利地产生大量的对经突变的p53氨基酸序列具有抗原特异性的T细胞。

[0096] 通过本发明方法分离的T细胞可用于制备用于过继细胞疗法的细胞。在这方面,本发明的一个实施方案提供了制备对由癌症-特异性p53突变编码的经突变的p53氨基酸序列具有抗原特异性的T细胞群的方法,该方法包括分离如在本文中关于本发明的其他方面所述的T细胞,并且扩大选定自体T细胞的数量以获得对由癌症-特异性突变编码的经突变的p53氨基酸序列具有抗原特异性的T细胞群。如本文关于本发明的其他方面所述,可以进行选定细胞的数量扩大。

[0097] 本发明的另一个实施方案提供了分离对由癌症-特异性p53突变编码的经突变的p53氨基酸序列具有抗原特异性的T细胞受体(TCR)或其抗原结合部分的方法。如本文关于本发明的其他方面所述,该方法可以包括分离对由癌症-特异性p53突变编码的经突变的p53氨基酸序列具有抗原特异性的T细胞。

[0098] 本发明的方法还可以包括从选定T细胞中分离编码TCR或其抗原结合部分的核苷酸序列,其中TCR或其抗原结合部分对由癌症-特异性p53突变编码的经突变的p53氨基酸序列具有抗原特异性。在本发明的一个实施方案中,在分离编码TCR或其抗原结合部分的核苷酸序列之前,可以扩大对经突变的p53氨基酸序列具有抗原选择性的选定T细胞的数量。如本文关于本发明的其他方面所述,可以进行选定细胞数量的扩大。在本发明的另一个实施方案中,在分离编码TCR或其抗原结合部分的核苷酸序列之前,没有扩大对经突变的p53氨基酸序列具有抗原特异性的选定T细胞的数量。例如,可以从单个细胞分离TCR或其抗原结合部分。

[0099] 如本文所用,TCR的“抗原结合部分”是指作为TCR一部分的包含TCR连续氨基酸的任何部分,前提是抗原结合部分特异性结合至经突变的p53氨基酸序列,如本文关于本发明的其他方面所述。术语“抗原结合部分”是指TCR的任何部分或片段,所述部分或片段作为TCR一部分的保留了TCR(母体TCR)的生物学活性。抗原结合部分涵盖了例如,TCR中保留与经突变的p53氨基酸序列特异性结合,或与母体TCR相比以相似的程度、相同的程度或以更高的程度检测、治疗或预防癌症的能力的那些部分。关于母体TCR,功能部分可包含例如约10%、约25%、约30%、约50%、约68%、约80%、约90%、约95%或更多的母体TCR。

[0100] 抗原结合部分可包含TCR的 α 链和 β 链中任一条或两条的抗原结合部分,诸如包含TCR的 α 链和/或 β 链的可变区的互补决定区(CDR)1、CDR2和CDR3中的一个或多个的部分。在本发明的一个实施方案中,抗原结合部分可包含以下的氨基酸序列: α 链的CDR1(CDR1 α)、 α 链的CDR2(CDR2 α)、 α 链的CDR3(CDR3 α)、 β 链的CDR1(CDR1 β)、 β 链的CDR2(CDR2 β)、 β 链的CDR3(CDR3 β)或其任何组合。优选地,抗原结合部分包含TCR的CDR1 α 、CDR2 α 和CDR3 α 的氨基酸序

列;CDR1 β 、CDR2 β 和CDR3 β 的氨基酸序列;或所有CDR1 α 、CDR2 α 、CDR3 α 、CDR1 β 、CDR2 β 和CDR3 β 的氨基酸序列。

[0101] 在本发明的一个实施方案中,抗原结合部分可以包括,例如,TCR的可变区,其包括上述CDR区的组合。在这方面,抗原结合部分可以包含TCR的 α 链的可变区(V α)的氨基酸序列, β 链的可变区的氨基酸序列(V β)或V α 和V β 两者的氨基酸序列。

[0102] 在本发明的一个实施方案中,抗原结合部分可包含可变区和恒定区的组合。在这方面,抗原结合部分可包含TCR的全长 α 或 β 链,或 α 和 β 链两者。

[0103] 从选定T细胞中分离编码TCR或其抗原结合部分的核苷酸序列可以本领域已知的任何适合的方式进行。例如,该方法可以包括使用已建立的分子克隆技术和试剂诸如例如使用TCR- α 和- β 链恒定引物的cDNA末端5'快速扩增(RACE)聚合酶链式反应(PCR),从选定T细胞中分离RNA,并对TCR或其抗原结合部分进行测序。可替代地或另外地,可用于分离TCR核酸序列的技术和系统可包括例如单细胞逆转录聚合酶链式反应(RT-PCR)、生物信息重建、有限稀释克隆、Fluidigm系统(Fluidigm Corporation, South San Francisco, CA),通过频率配对对TCR α 和TCR β 链进行深度测序,来自Adaptive Biotechnologies (Seattle, WA)的鉴定TCR α 和 β 链对的PAIRSEQ方法,以及其组合。

[0104] 在本发明的一个实施方案中,所述方法可以包括使用例如如Green等人(Eds.), Molecular Cloning: A Laboratory Manual, Cold Spring Harbor Laboratory Press; 第4版(2012)所述的确定的分子克隆技术将编码TCR或其抗原结合部分的核苷酸序列克隆至重组表达载体中。为了本文的目的,术语“重组表达载体”意指经遗传修饰的寡核苷酸或多核苷酸构建体,当该构建体包含编码mRNA、蛋白、多肽或肽的核苷酸序列并且载体在足以使mRNA、蛋白、多肽或肽在细胞内表达的条件下与细胞接触时,其允许宿主细胞表达mRNA、蛋白、多肽或肽。载体可以不是作为整体天然存在的。然而,载体的部分可以是天然存在的。重组表达载体可以包含任何类型的核苷酸,包括但不限于DNA(如互补DNA(cDNA)) 和RNA,其可以是单链或双链的、合成的或部分地从天然来源获得的并且可以含有天然、非天然或改变的核苷酸。重组表达载体可以包含天然存在的、非天然存在的核苷酸间键联,或两种类型的键联。优选地,非天然存在或改变的核苷酸或核苷酸间键联不阻碍载体的转录或复制。

[0105] 重组表达载体可以是任何适合的重组表达载体,并且可以用于转化或转染任何适合的宿主细胞。适合的载体包括经设计用于繁殖和扩增或用于表达或两者的那些,诸如质粒和病毒。载体可以选自:转座子/转座酶、pUC系列(Fermentas Life Sciences)、pBluescript系列(Stratagene, La Jolla, CA)、pET系列(Novagen, Madison, WI)、pGEX系列(Pharmacia Biotech, Uppsala, Sweden)和pEX系列(Clontech, Palo Alto, CA)。也可以使用噬菌体载体,诸如 λ GT10、 λ GT11、 λ ZapII (Stratagene)、 λ EMBL4和 λ NM1149。植物表达载体的实例包括pBI01、pBI101.2、pBI101.3、pBI121和pBIN19(Clontech)。动物表达载体的实例包括pEUK-C1、pMAM和pMAMneo(Clontech)。优选地,重组表达载体是病毒载体,如逆转录病毒载体。

[0106] 通过本发明的方法分离的TCR或其抗原结合部分可用于制备用于过继细胞疗法的细胞。在这方面,本发明的一个实施方案提供了制备表达对由癌症-特异性p53突变编码的经突变的p53氨基酸序列具有抗原特异性的TCR或其抗原结合部分的细胞群的方法,该方法包括分离TCR或其抗原结合部分(如本文关于本发明的其他方面所述)并将编码分离的TCR

或其抗原结合部分的核苷酸序列引入宿主细胞中,以获得表达TCR或其抗原结合部分的细胞。

[0107] 可以以本领域已知的多种不同方式中的任一种,如例如Green等人(同上)所述,进行将编码经分离的TCR或其抗原结合部分的核苷酸序列(如重组表达载体)引入宿主细胞中。可用于将核苷酸序列引入宿主细胞中的技术的非限制性实例包括转化、转导、转染、转座和电穿孔。

[0108] 引入编码TCR或其抗原结合部分的核苷酸序列的宿主细胞可以是可含有重组表达载体的任何类型的细胞。宿主细胞可以是真核细胞,如植物、动物、真菌或藻类,或者可以是原核细胞,如细菌或原生动物。宿主细胞可以是培养的细胞或原代细胞,即直接从生物体如人类中分离。宿主细胞可以是贴壁细胞或悬浮细胞,即在悬浮液中生长的细胞。适合的宿主细胞是本领域已知的,并且包括例如DH5 α 大肠埃希氏菌细胞、中国仓鼠卵巢细胞、猴VERO细胞、COS细胞、HEK293细胞等。为了扩增或复制重组表达载体,宿主细胞优选是原核细胞,如DH5 α 细胞。为了产生TCR或其抗原结合部分,宿主细胞优选是哺乳动物细胞。最优选地,宿主细胞是人细胞。尽管宿主细胞可以属于任何细胞类型、可以源自任何类型的组织并且可以属于任何发育阶段,但是宿主细胞优选是PBL或PBMC。更优选地,宿主细胞是T细胞。

[0109] 在本发明的一个实施方案中,PBMC包括T细胞。T细胞可以是任何类型的T细胞。不受特定理论或机制的束缚,认为与分化程度更高的“较老”T细胞相比,分化程度更低的“较年轻”T细胞可能与更高的体内持久性、增殖和抗肿瘤活性的任一种或多种有关。因此,本发明的方法可以有利地鉴定和分离对经突变的p53氨基酸序列具有抗原特异性的TCR或其抗原结合部分,并将TCR或其抗原结合部分引入与“较老”T细胞(如,患者肿瘤中的效应细胞)相比可提供更高的体内持久性、增殖和抗肿瘤活性中的任一种或多种的“较年轻”T细胞中。

[0110] 在本发明的一个实施方案中,本发明的方法鉴定并分离对由频发(也称为“热点”)癌症-特异性p53突变编码的经突变的p53氨基酸序列具有抗原特异性的TCR或抗原结合部分。在这方面,该方法可以包括将编码经分离的TCR或其抗原结合部分的核苷酸序列引入对于患者是同种异体的宿主细胞中。例如,所述方法可以包括将编码经分离的TCR或其抗原结合部分的核苷酸序列引入来自另一名患者的宿主细胞中,所述另一名患者的肿瘤在相同的MHC分子的背景下表达相同的p53突变。

[0111] 在本发明的一个实施方案中,所述方法还包括扩大表达TCR或其抗原结合部分的宿主细胞的数量。例如,如本文关于本发明的其他方面所述,可以扩大宿主细胞的数量。在这方面,本发明的方法可以有利地产生大量的对经突变的p53氨基酸序列具有抗原特异性的T细胞。

[0112] 本发明的另一个实施方案提供了根据本文关于本发明其他方面所述的任何方法制备的经分离的细胞群。细胞群体可以是异质群体,其除了至少一种其他细胞之外还包括对由癌症-特异性p53突变编码的经突变的p53氨基酸序列具有抗原特异性的T细胞,所述其他细胞如对由癌症-特异性p53突变编码的经突变的p53氨基酸序列不具有抗原特异性的PBMC,或除了T细胞以外的细胞,如B细胞、巨噬细胞、嗜中性粒细胞、红细胞、肝细胞、内皮细胞。肌肉细胞、脑细胞等。可选地,细胞群可以是基本上同质的群,其中该群主要包括(如,基本上由以下组成)对由癌症-特异性p53突变编码的经突变的p53氨基酸序列具有抗原特异性的T细胞。所述群也可以是细胞的克隆群,其中群体的所有细胞都是单个T细胞的克隆,使

得群体中的所有细胞都对由癌症-特异性p53突变编码的经突变的p53氨基酸序列具有抗原特异性。如本文所述,在本发明的一个实施方案中,细胞群是包含对由癌症-特异性p53突变编码的经突变的p53氨基酸序列具有抗原特异性的T细胞的克隆群。在本发明的一个实施方案中,细胞群体的约1%至约100%,例如约1%、约5%、约10%、约15%、约20%、约25%、约30%、约35%、约40%、约45%、约50%、约55%、约60%、约65%、约70%、约75%、约80%、约85%、约90%、约95%、约96%、约97%、约98%、约99%或约100%,或由前述值的任两个限定的范围的包含对经突变的p53氨基酸序列具有抗原特异性的T细胞。不受特定理论或机制的束缚,认为包含高比例的对经突变的p53氨基酸序列具有抗原特异性的T细胞的细胞群可以有利地具有较低比例的无关细胞,所述无关细胞可阻碍T细胞的功能,如T细胞靶向癌细胞的破坏和/或治疗或预防癌症的能力。

[0113] 可以将本发明的细胞群配制成组合物,诸如药物组合物。在这方面,本发明提供了包含本发明的任何细胞群和药物上可接受的载体的药物组合物。本发明的药物组合物可以包含与另一种或多种药理学活性剂或药物(诸如化学治疗剂,如天冬酰胺酶、白消安、卡铂、顺铂、道诺霉素、多柔比星、氟尿嘧啶、吉西他滨、羟基脲、甲氨蝶呤、紫杉醇、利妥昔单抗、长春碱,长春新碱等)组合的本发明的细胞群。

[0114] 优选地,载体是药学上可接受的载体。关于药物组合物,载体可以是所考虑的本发明特定细胞群常规使用的那些中任一种。此类药学上可接受的载体是本领域技术人员众所周知的,并且容易被公众使用。优选地,药学上可接受的载体是在使用条件下不具有有害的副作用或毒性的载体。

[0115] 载体的选择将部分地由本发明的特定细胞群以及用于施用本发明的细胞群的特定方法决定。因此,有多种本发明的药物组合物的适合制剂。适合制剂可以包括用于肠胃外、皮下、静脉内、肌肉内、动脉内、肿瘤内、鞘内或腹膜内施用那些中任一种。可以使用多于一种的途径来施用本发明的细胞群,并且在某些情况下,特定的途径可以提供比另一种途径更直接和更有效的响应。

[0116] 优选地,本发明的细胞群通过注射如静脉内施用。当要施用本发明的细胞群时,用于注射用细胞的药物上可接受的载体可以包括任何等渗载体,诸如例如生理盐水(约0.90%w/v的NaCl水溶液,约300mOsm/L NaCl水溶液,或约9.0g NaCl/L水)、NORMOSOL R电解质溶液(Abbott, Chicago, IL)、PLASMA-LYTE A(Baxter, Deerfield, IL)、约5%葡萄糖水溶液或林格氏乳酸盐。在一个实施方案中,药学上可接受的载体补充有人血清白蛋白。

[0117] 预期本发明的细胞群和药物组合物可以用于治疗或预防癌症的方法中。不受特定理论或机制的束缚,本发明的T细胞被认为特异性结合至由癌症-特异性p53突变编码的经突变的p53氨基酸序列,使得细胞表达的TCR能够介导针对表达经突变的p53氨基酸序列的靶细胞的免疫反应。在这方面,本发明的一个实施方案提供了治疗或预防哺乳动物中的癌症的方法,其包括以有效治疗或预防哺乳动物中的癌症的量向哺乳动物施用本文所述的任何药物组合物或细胞群。

[0118] 如本文所用的,术语“治疗”和“预防”以及由此衍生的词不一定意味着100%或完全的治疗或预防。而是,存在不同程度的治疗或预防,本领域普通技术人员认为这具有潜在的益处或治疗效果。在这方面,本发明的方法可以在哺乳动物中提供任何量的任何水平的癌症治疗或预防。此外,通过本发明的方法提供的治疗或预防可以包括治疗或预防所治疗

或预防的癌症的一种或多种病状或症状。例如,治疗或预防可以包括促进肿瘤的消退。此外,出于本文的目的,“预防”可以涵盖延迟癌症或其症状或病状的发作。

[0119] 为了本发明的目的,所施用的本发明细胞群或药物组合物的量或剂量(如,当施用本发明的细胞群时的细胞数)应足以在合理的时间范围内在哺乳动物中实现如治疗或预防应答。例如,本发明的细胞群或药物组合物的剂量应足以与由癌症-特异性p53突变编码的经突变的p53氨基酸序列结合,或在从施用时起约2小时或更久(如12至24或更多小时)时间段内检测、治疗或预防癌症。在某些实施方案中,时间段可以甚至更长。剂量将由所施用的特定本发明细胞群或药物组合物的功效以及哺乳动物(如人)的状况以及待治疗的哺乳动物(如人)的体重来确定。

[0120] 用于确定施用剂量的许多测定法是本领域已知的。为了本发明的目的,测定可用于确定要向哺乳动物施用的起始剂量,所述测定包括比较在各自给予不同剂量的T细胞的一组哺乳动物中,在施用给定剂量的此类T细胞至哺乳动物之后,裂解靶细胞或由T细胞分泌IFN- γ 的程度。施用一定剂量后,裂解靶细胞或分泌IFN- γ 的程度可以通过本领域已知的方法来测定。

[0121] 本发明的细胞群或药物组合物的剂量也将由可能伴随施用特定的本发明的细胞群或药物组合物的任何不良副作用的存在、性质和程度来确定。通常,主治医师将考虑各种因素,诸如年龄、体重、总体健康状况、饮食、性别、待施用的本发明的细胞群或药物组合物、施用途径和治疗的疾患的严重程度,决定治疗每个个体患者的本发明的细胞群或药物组合物的剂量。

[0122] 在其中待施用本发明的细胞群的一个实施方案中,每次输注施用的细胞数可以变化,例如在100万个至1000亿个细胞的范围内;然而,低于或高于该示例性范围的量在本发明的范围内。例如,本发明的宿主细胞的每日剂量可以是约100万个至约1500亿个细胞(如约500万个细胞、约2500万个细胞、约5亿个细胞、约10亿个细胞、约50亿个细胞、约200亿个细胞、约300亿个细胞、约400亿个细胞、约600亿个细胞、约800亿个细胞、约1000亿个细胞、约1200亿个细胞、约1300亿个细胞、约1500亿个细胞,或由前述值的任两个限定的范围),优选约1000万个细胞至约1300亿个细胞(如约2000万个细胞、约3000万个细胞、约4000万个细胞、约6000万个细胞、约7000万个细胞、约8000万个细胞、约9000万个细胞、约100亿个细胞、约250亿个细胞、约500亿个细胞、约750亿个细胞、约900亿个细胞、约1000亿个细胞、约1100亿个细胞、约1200亿个细胞、约1300亿个细胞,或由前述值的任两个限定的范围),更优选约1亿个细胞至约1300亿个细胞(如约1.2亿个细胞、约2.5亿个细胞、约3.5亿个细胞、约4.50亿个细胞、约6.50亿个细胞、约8亿个细胞、约9亿个细胞、约30亿个细胞、约300亿个细胞、约450亿个细胞、约500亿个细胞、约750亿个细胞、约900亿个细胞、约1000亿个细胞、约1100亿个细胞、约1200亿个细胞、约1300亿个细胞,或由前述值的任两个限定的范围)。

[0123] 为了本发明方法的目的,其中施用细胞群,所述细胞可以是哺乳动物同种异体的或自体的细胞。优选地,细胞对于哺乳动物是自体的。

[0124] 本发明的另一个实施方案提供了用于治疗或预防哺乳动物中的癌症的本文所述的经分离的细胞群或药物组合物中的任一种。

[0125] 就本发明的方法而言,癌症可以是任何癌症,包括以下中的任一种:急性淋巴细胞癌,急性髓细胞性白血病,肺泡横纹肌肉瘤,骨癌,脑癌,癌,乳腺癌,肛门癌、肛管癌或肛门

直肠癌,眼癌,肝内胆管癌,关节癌,颈癌、胆囊癌或胸膜癌,鼻癌、鼻腔癌或中耳癌,口腔癌,阴道癌,外阴癌,慢性淋巴细胞性白血病,慢性髓样癌,结肠癌,结直肠癌,子宫内膜癌,食道癌,子宫颈癌,胃肠道类癌瘤,神经胶质瘤,霍奇金淋巴瘤,下咽癌,肾癌,喉癌,肝癌,肺癌,恶性间皮瘤,黑素瘤,多发性骨髓瘤,鼻咽癌,非霍奇金淋巴瘤,口咽癌,卵巢癌,阴茎癌,胰腺癌,腹膜癌、网膜癌和肠系膜癌,舌咽癌,前列腺癌,直肠癌,肾癌,皮肤癌,小肠癌,软组织癌,胃癌,睾丸癌,甲状腺癌,子宫癌,输尿管癌和尿道膀胱癌。在一个优选的实施方案中,癌症是表达突变的p53的癌症。癌症可以在SEQ ID NO:1的位置175、220、245、248、249、273或282中的一个或多个处表达具有突变的p53。癌症可表达具有以下人p53突变中的一种或多种的p53:R175H、Y220C、G245D、G245S、R248L、R248Q、R248W、R249S、R273H、R273C、R273L或R282W。优选地,癌症是上皮癌或胆管癌、黑素瘤、结肠癌、直肠癌、卵巢癌、子宫内膜癌、非小细胞肺癌(NSCLC)、成胶质细胞瘤、子宫颈癌、头颈癌、乳房癌、胰腺癌或膀胱癌。

[0126] 本发明方法中提及的哺乳动物可以是任何哺乳动物。如本文所用,术语“哺乳动物”是指任何哺乳动物,包括但不限于啮齿目的哺乳动物,诸如小鼠和仓鼠,以及兔形目的哺乳动物,诸如兔。优选地,哺乳动物来自食肉目,包括猫科动物(猫)和犬科动物(狗)。优选地,哺乳动物来自偶蹄目,包括牛科动物(牛)和猪科动物(猪),或属于奇蹄目,包括马科动物(马)。优选地,哺乳动物属于灵长目、阔鼻小目或Simoid(猴),或属于类人猿亚目(人类和猿类)。更优选的哺乳动物是人类。

[0127] 以下实施例进一步说明了本发明,但是当然不应理解为以任何方式限制其范围。

实施例

[0128] 在以下实施例中描述的实验中使用表1-3中列出的氨基酸序列。

[0129] 表1

SEQ ID NO:	名称	序列
2	LP-p53-R175H-MUT	YKQSQHMTEVVVR <u>H</u> CPHHERCSDSDG
3	LP-p53-R273H-MUT	SGNLLGRNSFEV <u>H</u> VCACPGRDRRTE
4	LP-p53-R248L-MUT	YMCNSSCMGGMN <u>L</u> RPILTIITLEDSS
5	LP-p53-R282W-MUT	FEVRVCACPGRD <u>W</u> RTEEEENLRKKGE
6	LP-p53-R273C-MUT	SGNLLGRNSFEV <u>C</u> VCACPGRDRRTE
[0130] 7	LP-p53-G245S-MUT	HNYMCNSSCMG <u>S</u> MNRRPILTIITL
8	LP-p53-R248Q-MUT	YMCNSSCMGGMN <u>Q</u> RPILTIITLEDSS
9	LP-p53-G245D-MUT	HNYMCNSSCMG <u>D</u> MNRRPILTIITL
10	LP-p53-R273L-MUT	SGNLLGRNSFEV <u>L</u> VCACPGRDRRTE
11	LP-p53-R248W-MUT	YMCNSSCMGGMN <u>W</u> RPILTIITLEDSS
12	LP-p53-Y220C-MUT	DRNTFRHSVVVP <u>C</u> EPPEVGSDCTTI
13	LP-p53-R249S-MUT	MCNSSCMGGMNR <u>S</u> PILTIITLEDSS

[0131] 表2列出了表1的肽的野生型形式。

[0132] 表2

[0133]

SEQ ID NO:	名称	序列
15	LP-p53-R175-WT	YKQSQHMTEVVRR <u>R</u> CPHHERCSDSDG
16	LP-p53-R273-WT	SGNLLGRNSFEV <u>R</u> VCACPGRDRRTE
17	LP-p53-R248-WT	YMCNSSCMGGMN <u>R</u> RPILTIITLEDSS
18	LP-p53-R282-WT	FEVRVCACPGRD <u>R</u> RTEENLRKKGE
19	LP-p53-G245-WT	HNYMCNSSCMGG <u>M</u> NRRPILTIITL
20	LP-p53-Y220-WT	DRNTFRHSVVVP <u>Y</u> EPPEVGSDCTTI
21	LP-p53-R249-WT	MCNSSCMGGMN <u>R</u> RPILTIITLEDSS

[0134] 表3

[0135]

SEQ ID NO:	名称	序列
14	TMG-p53-MUT	YKQSQHMTEVVRR <u>H</u> CPHHERCSDSDGSGNLLGRNS FEV <u>H</u> VCACPGRDRRTEYMCNSSCMGGMN <u>L</u> RPILTI ITLEDSEFEVRVCACPGRD <u>W</u> RTEENLRKKGESGNL LGRNSFEV <u>C</u> VCACPGRDRRTEHNYMCNSSCMG <u>S</u> MNRPRILTIITLYMCNSSCMGGMN <u>Q</u> RPILTIITLEDSS HNYMCNSSCMG <u>D</u> MNRPRILTIITLSGNLLGRNSFE V <u>L</u> VCACPGRDRRTEYMCNSSCMGGMN <u>W</u> RPILTIIT LEDSDRNTFRHSVVVP <u>C</u> EPPEVGSDCTTIMCNSSC MGGMN <u>R</u> RPILTIITLEDSS
22	TMG-p53-WT	YKQSQHMTEVVRR <u>R</u> CPHHERCSDSDGSGNLLGRNS FEV <u>R</u> VCACPGRDRRTEYMCNSSCMGGMN <u>R</u> RPILTI ITLEDSEFEVRVCACPGRD <u>R</u> RTEENLRKKGESGNLL GRNSFEV <u>R</u> VCACPGRDRRTEHNYMCNSSCMG <u>G</u> MNRPRILTIITLYMCNSSCMGGMN <u>R</u> RPILTIITLEDSS
		HNYMCNSSCMG <u>G</u> MNRPRILTIITLSGNLLGRNSFE V <u>R</u> VCACPGRDRRTEYMCNSSCMGGMN <u>R</u> RPILTIIT LEDSDRNTFRHSVVVP <u>Y</u> EPPEVGSDCTTIMCNSSC MGGMN <u>R</u> RPILTIITLEDSS

[0136] 实施例1

[0137] 该实施例证实了通过在自体T细胞内共培养经诱导以表达突变的p53的自体APC来鉴定患者4141中的抗-突变的p53 T细胞(“p53热点突变通用筛选”)。该实施例还证实了来自患者4141的TCR的分离和特异的反应性。

[0138] 如图1和45-48针对患者4141所述进行实验。来自患者4141的TIL片段F12和输液袋TIL (Rx1) 及来自患者4196的p53-R175H-特异性TCR或模拟物转导的T细胞用作效应器。T细胞效应器与HLA-A*02:01APCs (对于患者4141是自体) 的共培养物(1) 用由无关、WT p53或突变的p53序列组成的TMG电穿孔, 或者(2) 用肽媒介物(DMSO) 或由WT p53-R175序列或突变的p53-R175H序列组成的经纯化的(>95%, 通过HPLC) 25个氨基酸的肽脉冲。仅T细胞(无靶标) 是阴性对照, 并且PMA和Iono是阳性对照(格条)。在37℃下进行共培养过夜。使用ELISPOT测定评价IFN- γ 的分泌。结果示于图1中。

[0139] 将自体APC用编码无关突变、WT p53序列或包含R175H的突变的p53序列的TMG转染。单独的培养基以及PMA和离子霉素分别为阴性对照和阳性对照。第二天, 将来自患者4141的TIL (片段培养物12) 与TMG-转染的APC在37℃下共培养过夜。通过ELISPOT评价IFN- γ 的分泌。对于淋巴细胞→活细胞(PI阴性) →CD3+ (T细胞) →CD4-CD8+设门后, 通过流式细胞术评价4-1BB的表达。结果示于图45中。

[0140] 将Cos7细胞(每孔 2.5×10^4 个) 涂铺在平底96孔板的孔上。第二天, 将细胞用来自患者4141的单独HLA等位基因以及无额外基因、WT TP53TMG或含有p53-R175H序列的突变的TP53 TMG共转染。第二天, 将来自患者4141的对p53-R175H具有特异性的TIL (片段培养物12) 与转染的Cos7细胞共培养, 并在37℃下孵育过夜。通过ELISPOT评价IFN- γ 的分泌。结果示于图46中。

[0141] 将表达模拟物(无TCR) 或4141-TCR1a2的T细胞与T2肿瘤细胞(表达HLA-A*02:01) 共培养。将T2细胞在37℃下用肽媒介物(DMSO) 或由WT p53-R175肽HMTEVVRRC (SEQ ID NO: 532) 或经突变的p53-R175H肽HMTEVVRHC (SEQ ID NO: 530) 组成的纯化的(>95%, 通过HPLC) 肽脉冲。单独的培养基及PMA和离子霉素分别为阴性对照和阳性对照。在37℃下进行共培养过夜。IFN- γ 的分泌通过ELISA评价。结果示于图47中。

[0142] 将表达4141-TCR1a2的T细胞与Saos2细胞(p53-NUL和HLA-A*02:01+) 在37℃下共培养过夜, 这些细胞未经处理, 或使得过表达全长p53-R175H蛋白。将分泌的抑制剂(莫能菌素和布雷菲德菌素A) 添加至共培养物, 以捕获T细胞内的细胞因子。共培养6小时后, 将细胞固定并透化, 然后针对IL-2、CD107a、IFN- γ 和肿瘤坏死因子- α (TNF α) 染色。流式细胞术用于基于淋巴细胞门分析共培养物。结果示于图48中。

[0143] 从患者4141分离的TCR 4141-TCR1a2的序列示于以下。从氨基末端开始, 第一加下划线的区是CDR1 α (SEQ ID NO: 467), 第二加下划线的区是CDR2 α (SEQ ID NO: 468), 第三加下划线的区是CDR3 α (SEQ ID NO: 469), 第四加下划线的区是CDR1 β (SEQ ID NO: 470), 第五加下划线的区是CDR2 β (SEQ ID NO: 471), 并且第六加下划线的区是CDR3 β (SEQ ID NO: 472)。粗体区是连接子(SEQ ID NO: 26)。从氨基末端开始, 第一斜体区是 α 链恒定区(SEQ ID NO: 23) 并且第二斜体区是 β 链恒定区(SEQ ID NO: 25)。 α 链可变区(SEQ ID NO: 473) 包含从氨基末端开始并且就在 α 链恒定区开始前结束的序列。 β 链可变区(SEQ ID NO: 474) 包含在连接子之后立即开始并且就在 β 链恒定区开始之前结束的序列。全长 α 链(SEQ ID NO: 475) 包含从氨基末端开始并且就在连接子开始之前结束的序列。全长 β 链(SEQ ID NO: 476) 包含在连接子之后立即开始并且以羧基末端结束的序列。

[0144] 如下所述鉴定癌症反应性T细胞。如下所述分离TCR。

[0145] TCR名称: 4141-TCR1a2

[0146] P53突变的识别:R175H

[0147] 筛选方法:p53“热点”突变通用筛选

[0148] 共培养以鉴定TCR:共培养4141输液袋TIL与p53mutTMG,和分选CD8+41BB+T细胞

[0149] 鉴定TCR的方法:单细胞RT-PCR,然后TA TOPO克隆试剂盒(Thermo Fisher Scientific,Waltham,MA)用于 α 链

[0150] TCR取向: α - β

[0151] 表达载体:SB转座子

[0152] MASIRAVFIFLWLQLDLVNGENVEQHPSTLSVQEGDSAVIKCTYSDSASNYFPWYKQELGKGPQLIID
IRSNVGEKKDQRIAVTLNKTAKHFSLHITETQPEDSAVYFCAASKSAIMVVLQTSSSLELALCLLSSQVNIQNPEP
AVYQLKDPQRSQDSTLCLFTDFDSQINVPKTMESGTFITDKCVLDMKAMDSKSNGAIAWSNQTSFTCQDIFKETNAT
YPSSDVPCDATLTEKSFETDMNLFQNLVIVLRILLKLVAGFNLLMTLRLWSSRAKRSGSGATNFSLLKQAGDVE
ENPGPMHPQLLGYVVLCLLGAGPLEAQVTQNPRYLITVTGKKLTVTCSQNMNHEYMSWYRQDPGLGLRQIYYSMNV
EVTDKGDVPEGYKVSKEKRNFPILILESPSPNQTSLYFCASSIQQGADTQYFGPGTRLTVLEDLRNVTPPKVSLFE
PSKAEIANKQKATLVCLARGFFPDHVELSWWVNGKEVHSGVCTDPQAYKESNYSYCLSSRLRVSATFWHNPRNHFR
CQVQFHGLSEEDKWPEGSPKPVQTQNISAEAWGRADCGITSASYQQGVLSATILYEILLGKATLYAVLVSTLVVMAM
VKRKNS (SEQ ID NO:587)

[0153] 来自患者4141的4141-TCR1a2的统计数据示于下表4中。

[0154] 表4

[0155]	参数	#	频率
	总孔	96	100%
	CDR3 α	未知(TA TOPO克隆)	不适用
	CDR3 β	58	60.4%

[0156] 实施例2

[0157] 该实施例证实了通过在自体T细胞内共培养被诱导以表达突变的p53的自体APC来鉴定患者4130中的抗-突变的p53 T细胞(“p53热点突变通用筛选”)。

[0158] 如图2针对患者4130所述进行实验。将来自患者4130的TIL片段(F14、F20和F24)与自体APC共培养,所述自体APC(1)用由无关的、WT p53或经突变的p53序列组成的TMG电穿孔,或(2)用肽媒介物(DMSO)或由WT p53-R273序列或经突变的p53-R273H序列组成的经纯化的(>95%,通过HPLC)25个氨基酸的肽脉冲。在37°C下进行共培养过夜。对于淋巴细胞→活细胞(PI阴性)→CD3+(T细胞)设门后,通过流式细胞术评价4-1BB的表达。结果示于图2中。

[0159] 实施例3

[0160] 该实施例证实了通过在自体T细胞内共培养被诱导以表达突变的p53的自体APC来鉴定患者4259中的抗-突变的p53 T细胞(“p53热点突变通用筛选”)。该实施例还证实了从患者4259分离的TCR的分离和特异的反应性。

[0161] 如图3-8和49-53针对患者4259所述进行实验。将来自患者4259的TIL片段(n=18)与用由无关的、WT p53或突变的p53序列组成的TMG电穿孔的自体APC共培养。在37°C下进行共培养过夜。使用ELISPOT测定评价IFN- γ 的分泌。结果示于图3中。对淋巴细胞→活细胞(PI阴性)→CD3+(T细胞)设门后,通过流式细胞术评价4-1BB的表达。结果示于图4-5中。

[0162] 将来自患者4259的TIL片段 (n=18) 与用肽媒介物 (DMSO) 或由WT p53-Y220序列或突变的p53-Y220C序列组成的经纯化的 (>95%, 通过HPLC) 25个氨基酸的肽脉冲的自体APC共培养。在37℃下进行共培养过夜。使用ELISPOT测定评价IFN- γ 的分泌。结果示于图6中。对于淋巴细胞→活细胞 (PI阴性) →CD3+ (T细胞) 设门后, 通过流式细胞术评价4-1BB的表达。结果示于图7-8中。

[0163] 将来自患者4259的TIL片段培养物 (no.6) 与自体APC共培养, 所述自体APC (1) 用由无关、WT p53或经突变的p53序列组成的TMG电穿孔, 或 (2) 用肽媒介物 (DMSO) 或由WT p53-Y220序列或经突变的p53-Y220C序列组成的经纯化的 (>95%, 通过HPLC) 25-个氨基酸的肽脉冲。在37℃下进行共培养过夜。对于淋巴细胞→活细胞 (PI阴性) →CD3+ (T细胞) 设门后, 通过流式细胞术评价4-1BB的表达。结果示于图49中。

[0164] 将自体APC在37℃下用降低浓度的25-个氨基酸的肽 (对应于WT p53-Y220或突变的p53-Y220C序列) 脉冲2小时。将来自患者4259的TIL片段培养物 (no.6) 与肽-脉冲的APC共培养。对于淋巴细胞→活细胞 (PI阴性) →CD3+ (T细胞) 设门后, 通过流式细胞术测定4-1BB的表达。结果示于图50中。

[0165] 将自体抗原呈递细胞在37℃下用DMSO、WT p53-Y220肽RNTFRHSVVVPYE (SEQ ID NO:533) 或突变的p53-Y220C肽RNTFRHSVVVPCE (SEQ ID NO:534) 脉冲2小时。将过量肽冲走。将来自患者4259的对p53-Y220C具有特异性的TIL (片段培养物6) 在37℃下与肽-脉冲的APC共培养过夜。对于淋巴细胞→活细胞 (PI阴性) →CD3+ (T细胞) 设门后, 通过流式细胞术评价4-1BB的表达。结果示于图51中。

[0166] 将Cos7细胞 (每孔 2.5×10^4 个) 涂铺在平底96孔板的孔上。接下来的一天, 将细胞与来自患者4259的单独的HLA等位基因共转染。次日, 将DMSO或p53-Y220C肽RNTFRHSVVVPCE (SEQ ID NO:534) 在经转染的Cos7细胞上脉冲2小时。将过量肽冲走。添加来自患者4259的TIL片段培养物no.6 (10^5 个细胞/孔)。将共培养物在37℃下孵育过夜。对于淋巴细胞→活→CD3+ (T细胞) →CD8-CD4+设门后, 通过流式细胞术测定4-1BB的表达。结果示于图52中。

[0167] 将患者4259自体的APC在37℃下用对应于WT p53-Y220或经突变的p53-Y220C序列的25-个氨基酸的肽脉冲2小时。将过量肽冲走。将表达4259-F6-TCR的T细胞与肽-脉冲的APC在37℃下共培养过夜。对于淋巴细胞→活细胞 (PI阴性) →CD3+ (T细胞) 设门后, 通过流式细胞术评价4-1BB的表达。通过小鼠TCR β (mTCR) 测量导入的TCR。结果示于表5中。

[0168] 表5

[0169]	WT p53-Y220	Mut p53-Y220C
4-1BB+/mTCR+	0.27	5.22
4-1BB-/mTCR-	68.5	73.7
4-1BB+/mTCR-	0.18	1.59
4-1BB-/mTCR+	31.0	19.5

[0170] 肿瘤细胞 (TC) 系由从患者4259切除的异种移植的肿瘤碎片建立, 然后通过免疫受损的小鼠连续传代 (TC#4259)。将TC#4259与表达模拟物 (无TCR) 或p53-Y220C-特异性TCR (4259-F6-TCR) 的T细胞 (10^5) 在37℃下共培养过夜。将单独的TC#4259细胞或者将TC#4259细胞与W6/32泛-HLA I类特异性阻断抗体、IVA12泛-HLA II类特异性阻断抗体或经突变的p53-Y220C肽RNTFRHSVVVPCE (SEQ ID NO:534) 在37℃下孵育2小时。将抗体以5 μ g/mL的终浓

度保存在共培养物中。将肽以10μg/mL孵育,并且孵育后洗涤过量肽。单独的培养基(无TC)及PMA和离子霉素分别为阴性对照和阳性对照。对于淋巴细胞→活细胞(PI阴性)→CD3+(T细胞)设门后,通过流式细胞术评价4-1BB的表达。结果示于图53中。

[0171] 从患者4259分离的TCR 4259-F6-TCR的序列示于以下。从氨基末端开始,第一加下划线的区域是CDR1α (SEQ ID NO:477),第二加下划线的区域是CDR2α (SEQ ID NO:478),第三加下划线的区域是CDR3α (SEQ ID NO:479),第四加下划线的区域是CDR1β (SEQ ID NO:480),第五加下划线的区域是CDR2β (SEQ ID NO:481),和第六加下划线的区域是CDR3β (SEQ ID NO:482)。粗体区是连接子 (SEQ ID NO:26)。从氨基末端开始,第一斜体区是α链恒定区 (SEQ ID NO:23) 并且第二斜体区是β链恒定区 (SEQ ID NO:25)。α链可变区 (SEQ ID NO:483) 包含从氨基末端开始并且就在α链恒定区开始之前结束的序列。β链可变区 (SEQ ID NO:484) 包含在连接子之后立即开始并且就在β链恒定区开始之前结束的序列。全长α链 (SEQ ID NO:485) 包含从氨基末端开始并且就在连接子开始之前结束的序列。全长β链 (SEQ ID NO:486) 包含在连接子之后立即开始并且以羧基末端结束的序列。

[0172] 如下所述鉴定癌症反应性T细胞。如下所述分离TCR。

[0173] TCR名称:4259-F6-TCR

[0174] P53突变的识别:Y220C

[0175] 筛选方法:p53“热点”突变通用筛选

[0176] 共培养以鉴定TCR:共培养4259-F6与p53-Y220C肽,和分选CD4+41BB+T细胞

[0177] 鉴定TCR的方法:单细胞RT-PCR

[0178] 所有配对的TCR中的TCR的丰度:81.1% (在44对中观察到36次)

[0179] TCR取向:α-β

[0180] 表达载体:SB转座子

[0181] MASLRVLLVILWLQLSWVWSQQKEVEQNSGPLSVPEGAIASLNCTYSDRGSQSFFWYRQYSGKSPELI
MFIYSNGDKEDGRFTAQLNKASQYVSLLIRDSQPSDSATYLCAWNSGGSNYKLTFGKGTLLTVNPNIQNPEPAVYQ
LKDPRSQDSTLCLFTDFDSQINVPKTMESGTFITDKCVLDMKAMDSKSNGAIAWSNQTSFTCQDIFKETNATYPSS
DVPCDATLTEKSFETDMNLNFQNLIVIVLRILLKLVAGFNLLMTLRLWSSRAKRSGSGATNFSLLKQAGDVEENPG
PMHLGLLCCGAFSLLWAGPVNAGVTQTPKFRVLKTGQSMTLLCAQDMNHEYMYWYRQDPGMGLRLIHYSVGEGTTA
KGEVPDGYNVSRLLKQNFLLGLESAAPSQTSVYFCASSYSQAWGQPQHFGDGTRLSEILEDLRNVTPPKVSLFEPK
AEIANKQKATLVCLARGFFPDHVELSWWVNGKEVHSGVCTDPQAYKESNYSYCLSSRLRVSATFWHNPRNHFRCQV
QFHGLSEEDKWPEGSPKPVQTQNISAEAWGRADCGITSASYQQGVLSATILYEILLGKATLYAVLVSTLVVMAMVKR
KNS (SEQ ID NO:588)

[0182] 来自患者4259的4259-F6-TCR的统计数据示于下表6中。

[0183] 表6

[0184]	参数	#	频率
	总孔	96	100%

参数	#	频率
CDR3 α	41	42.7%
CDR3 β	47	49.0%
4259-F6-TCR 对	36	37.5%
总配对的 TCR	44	45.8%

[0185] 实施例4

[0186] 该实施例证实了通过在自体T细胞内共培养被诱导表达经突变的p53的自体APC来鉴定患者4127中的抗-突变的p53的T细胞(“p53热点突变通用筛选”)。

[0187] 如图9-10针对患者4127所述进行实验。将来自患者4127的TIL与同种异体的(DRB3*01:01:01或DRB3*02:02:01) APC共培养,所述APC (1) 用由无关、WT p53或经突变的p53序列组成的TMG电穿孔,或(2) 用肽媒介物(DMSO) 或由WT p53-G245序列或经突变的p53-G245S序列组成的经纯化的(>95%,通过HPLC) 25个氨基酸的肽脉冲。在37℃下进行共培养过夜。使用ELISPOT测定评价IFN- γ 的分泌。结果示于图9中。

[0188] 将表达对p53-G245S具有特异性的4127-TCR1的T细胞与同种异体的(DRB3*01:01:01或DRB3*02:02:01) APC共培养,所述APC (1) 用由无关、WT p53或经突变的p53序列组成的TMG电穿孔,或(2) 用肽媒介物(DMSO) 或由WT p53-G245序列或经突变的p53-G245S序列组成的经纯化的(>95%,通过HPLC) 25个氨基酸的肽脉冲。在37℃下进行共培养过夜。使用ELISPOT测定评价IFN- γ 的分泌。结果示于图10中。

[0189] 实施例5

[0190] 通过(i) 诱导患者的自体抗原呈递细胞(APC) 呈递至少一种突变的p53氨基酸序列;(ii) 将患者的自体T细胞与呈递经突变的p53氨基酸序列的自体APC共培养;和(iii) 选择(a) 与呈递经突变的p53氨基酸序列的自体APC共培养的自体T细胞,来筛选来自27名患者的T细胞。表7提供了使用筛选方法进行的T细胞对p53“热点”突变的响应的概述。

[0191] 表7

[0192]

突变	患者数	患者%	测试数	反应数	筛选的反应%
R175H	7	19%	6	4	66.7%
Y220C	3	8%	3	2	66.7%
G245D	1	3%	1	0	0.0%
G245S	2	6%	1	1	100.0%
R248L	0	0%	0	0	不适用
R248Q	6	17%	6	3	50.0%
R248W	6	17%	5	3	60.0%
R249S	0	0%	0	0	不适用
R273C	2	6%	1	0	0.0%
R273H	5	14%	5	1	20.0%
R273L	0	0%	0	0	不适用
R282W	4	11%	3	2	66.7%
总计	36	100%	31	16	51.6%

[0193] 实施例6

[0194] 该实施例证实了通过在自体T细胞内共培养被诱导表达经突变的p53的自体APC来鉴定患者4273中的抗-突变的p53 T细胞(“p53热点突变通用筛选”)。该实施例还证实了从患者4273分离两种抗-突变的p53TCR。

[0195] 如图11-14和33-37针对患者4273所述进行实验。将来自患者4273的TIL片段(F1-F24, n=24)与用由无关、WT p53或经突变的p53序列组成的TMG电穿孔的自体APC共培养。在37℃下进行共培养过夜。使用ELISPOT测定评价IFN- γ 的分泌。结果示于图11中。对于淋巴细胞→活细胞(PI阴性)→CD3+(T细胞)设门后,通过流式细胞术评价4-1BB的表达。结果示于图12中。

[0196] 将来自患者4273的TIL片段(F1-F24, n=24)与用肽媒介物(DMSO)或由WT p53-R248序列或经突变的p53-R248W序列组成的经纯化的(>95%,通过HPLC)25-个氨基酸的肽脉冲的自体APC共培养。在37℃下进行共培养过夜。使用ELISPOT测定评价IFN- γ 的分泌。结果示于图13中。对于淋巴细胞→活细胞(PI阴性)→CD3+(T细胞)设门后,通过流式细胞术评价4-1BB的表达。结果示于图14中。

[0197] 对于患者4273, F15是最有反应性的片段,并且F15对LP和TMG的反应相当并且主要由CD4 T细胞进行。因此,将4273-F15与用R248W LP脉冲的APC共培养,并在第二天我们将CD4+41BB+T细胞作为单细胞分选至96孔PCR板的孔中,每孔一个细胞。PCR板在每个孔中都有RT-PCR溶液,其同一溶液中扩增TCR α 和 β CDR3区。然后将板的孔分至两个96孔PCR板中,

并进行第二轮PCR以分开的反应来扩增CDR3 α 或CDR3 β 。通过Sanger测序对每个孔的PCR产物(总共192种PCR产物,对应至每个孔- α 或 β)进行测序。将核苷酸序列输入IMGT/V-QUEST(imgt.org/IMGT_vquest/vquest?livret=0&Option=humanTcR)、IgBlast(ncbi.nlm.nih.gov/igblast/igblast.cgi?CMD=Web&SEARCH_TYPE=TCR&LINK_LOC=igtab),并由Expasy(web.expasy.org/translate/)翻译。确定可变家族并将其融合至来自经翻译的序列的CDR3和接合点(J或DJ)。可变序列融合至鼠恒定序列,并且重构的TCR α 和TCR β 通过弗林蛋白酶-柔性-P2A(RAKR-SGSG-ATNFSLLKQAGDVEENPGP)(SEQ ID NO:26)连接。然后将该序列从头合成为DNA,并克隆至表达载体(γ 逆转录病毒或SLEEPING BEAUTY(SB)转座子(University of Minnesota,Minneapolis,MN))中。然后使用标准病毒转导或非病毒转座方案使T细胞表达TCR,并针对推定的肽测试表达鼠源化TCR的T细胞(如通过小鼠TCR β 恒定链检测)。

[0198] 用编码无关突变、WT p53序列或经突变的p53序列(包括p53-R248W)的TMG转染自体APC。单独的培养基及PMA和离子霉素分别为阴性对照和阳性对照。将来自患者4273的TIL(片段培养物8和15)与TMG转染的APC在37℃下共培养过夜。对于淋巴细胞 $\rightarrow$ 活细胞(PI阴性) $\rightarrow$ CD3 $^{+}$ (T细胞)设门后,通过流式细胞术评价4-1BB的表达。结果示于图33中。

[0199] 将自体APC在37℃下用对应于WT或经突变的p53-R248W新表位的25个氨基酸的肽脉冲2小时。将来自患者4273的对p53-R248W具有特异性的TIL(片段培养物15)与肽-脉冲的APC在37℃下共培养过夜。DMSO是肽媒介物。对于淋巴细胞 $\rightarrow$ 活细胞(PI阴性) $\rightarrow$ CD3 $^{+}$ (T细胞),设门后,通过流式细胞术评价4-1BB的表达。结果示于图34中。

[0200] 将自体APC用来自p53-R248W新表位的重叠14个氨基酸的15个氨基酸的肽脉冲。将来自患者4273的对p53-R248W具有特异性的TIL与肽-脉冲的APC在37℃下共培养过夜。DMSO是肽媒介物,单独的培养基(仅T细胞)及PMA和离子霉素是对照。25个氨基酸的肽(wt p53-R248和经突变的p53-R248W)是15个氨基酸的肽的另外对照。对于淋巴细胞 $\rightarrow$ 活细胞(PI阴性) $\rightarrow$ CD3 $^{+}$ (T细胞) $\rightarrow$ CD4 $^{+}$ CD8 $^{-}$ 设门后,通过流式细胞术评价4-1BB的表达。结果示于图35中。

[0201] 将Cos7细胞(每孔 2.5×10^4 个)涂铺在平底96孔板的孔上。第二天,将细胞分别与来自患者4273的单独的HLA等位基因以及有或无p53-R248W新抗原的WT或经突变的TP53 TMG共转染。第二天,将来自患者4273的对p53-R248W具有特异性的TIL(片段培养物15)与转染的Cos7细胞在37℃下共培养过夜。通过ELISA评价IFN- γ 的分泌。结果示于图36中。

[0202] 将表达模拟物(无TCR)或4273-TCR1a2的T细胞与自体APC共培养,所述自体APC用肽媒介物(DMSO)或由WT p53-R248序列或经突变的p53-R248W序列组成的经纯化的(>95%,通过HPLC)25个氨基酸的肽脉冲。单独的培养基及PMA和离子霉素分别为阴性对照和阳性对照。在37℃下进行共培养过夜。通过ELISPOT评价IFN- γ 的分泌。结果示于图37中。

[0203] 从患者4273分离的TCR 4273-TP53-R248W-TCR1a1的序列示于下文。从氨基末端开始,第一加下划线区是CDR1 α (SEQ ID NO:437),第二加下划线区是CDR2 α (SEQ ID NO:438),第三加下划线区是CDR3 α (SEQ ID NO:439),第四加下划线区是CDR1 β (SEQ ID NO:440),第五加下划线区是CDR2 β (SEQ ID NO:441),和第六加下划线区是CDR3 β (SEQ ID NO:442)。粗体区是连接子(SEQ ID NO:26)。从氨基末端开始,第一加斜体区是 α 链恒定区(SEQ ID NO:23)并且第二加斜体区是 β 链恒定区(SEQ ID NO:25)。 α 链可变区(SEQ ID NO:443)包含从氨

基末端开始并且就在 α 链恒定区开始之前结束的序列。 β 链可变区 (SEQ ID NO:444) 包含在连接子之后立即开始并且就在 β 链恒定区开始之前结束的序列。全长 α 链 (SEQ ID NO:445) 包含从氨基末端开始并且就在连接子开始之前结束的序列。全长 β 链 (SEQ ID NO:446) 包含在连接子之后立即开始并且以羧基末端结束的序列。

[0204] TCR名称:4273-TP53-R248W-TCR1a1

[0205] P53突变的识别:R248W

[0206] 方法:p53“热点”突变通用筛选

[0207] MASLRVLLVILWLQLSWWSQQKEVEQNSGPLSVPEGAIASLNCTYSDRGSQSFFWYRQYSGKSPELI
MFIYSNGDKEDGRFTAQLNKASQYVSLLIRDSQPSDSATYLCAVTLGGYNKLIFGAGTRLAVHPNIQNPEPAVYQ
LKDPRSQDSTLCLFTDFDSQINVPKTMESGTFITDKCVLDMKAMDSKSNGAIAWSNQTSTFCQDIFKETNATYPSS
DVPCDATLTEKSFETDMNLFQNLIVLRILLKLVAGFNLLMTLRLWSSRAKRSGSGATNFSLLKQAGDVEENPG
PMHNQVLCVVLCFLGANTVDGGITQSPKYLFRKEGQNVTLSCEQNLNHDAMYWYRQDPGQGLRLIYYSQIVNDFQ
KGDIVEGYVSREKKESFPLTVTSAQKNPTAFYLCASSRDYEQYFGGPTRLTVTEDLRNVTPPKVSLFEPSKAEI
ANKQKATLVCLARGFFPDHVELSWVNGKEVHSGVCTDPQAYKESNYSYCLSSRLRVSATFWHNPRNHFRCQVQFH
GLSEEDKWPEGSPKPVTVQNISAEAWGRADCGITSASYQQGVLSATILYEILLGKATLYAVLVSTLVMMAMVKRKN
(SEQ ID NO:563)

[0208] 从患者4273分离的TCR 4273-TP53-R248W-TCR1a2的序列示于下文。从氨基末端开始,第一加下划线区是CDR1 α (SEQ ID NO:447),第二加下划线区是CDR2 α (SEQ ID NO:448),第三加下划线区是CDR3 α (SEQ ID NO:449),第四加下划线区是CDR1 β (SEQ ID NO:450),第五加下划线区是CDR2 β (SEQ ID NO:451),和第六加下划线区是CDR3 β (SEQ ID NO:452)。粗体区是连接子 (SEQ ID NO:26)。从氨基末端开始,第一加斜体区是 α 链恒定区 (SEQ ID NO:23) 并且第二加斜体区是 β 链恒定区 (SEQ ID NO:25)。 α 链可变区 (SEQ ID NO:453) 包含从氨基末端开始并且就在 α 链恒定区的开始之前结束的序列。 β 链可变区 (SEQ ID NO:454) 包含在连接子之后立即开始并且就在 β 链恒定区开始之前结束的序列。全长 α 链 (SEQ ID NO:455) 包含从氨基末端开始并且就在连接子开始之前结束的序列。全长 β 链 (SEQ ID NO:456) 包含在连接子之后立即开始并且以羧基末端结束的序列。

[0209] TCR名称:4273-TP53-R248W-TCR1a2

[0210] P53突变的识别:R248W

[0211] 方法:p53“热点”突变通用筛选

[0212] MASLRVLLVILWLQLSWWSQQKEVEQNSGPLSVPEGAIASLNCTYSDRGSQSFFWYRQYSGKSPELI
MFIYSNGDKEDGRFTAQLNKASQYVSLLIRDSQPSDSATYLCAVTLSGGYNKLIFGAGTRLAVHPNIQNPEPAVYQ
LKDPRSQDSTLCLFTDFDSQINVPKTMESGTFITDKCVLDMKAMDSKSNGAIAWSNQTSTFCQDIFKETNATYPSS
DVPCDATLTEKSFETDMNLFQNLIVLRILLKLVAGFNLLMTLRLWSSRAKRSGSGATNFSLLKQAGDVEENPG
PMHNQVLCVVLCFLGANTVDGGITQSPKYLFRKEGQNVTLSCEQNLNHDAMYWYRQDPGQGLRLIYYSQIVNDFQ
KGDIVEGYVSREKKESFPLTVTSAQKNPTAFYLCASSRDYEQYFGGPTRLTVTEDLRNVTPPKVSLFEPSKAEI
ANKQKATLVCLARGFFPDHVELSWVNGKEVHSGVCTDPQAYKESNYSYCLSSRLRVSATFWHNPRNHFRCQVQFH
GLSEEDKWPEGSPKPVTVQNISAEAWGRADCGITSASYQQGVLSATILYEILLGKATLYAVLVSTLVMMAMVKRKN
(SEQ ID NO:564)

[0213] 下表8列出了患者4273的TCR的统计数据。在表8中,与经突变的p53蛋白 (TMG或肽)

共培养后,总有96个孔用41BB+T细胞分选。77个孔具有生产对(意指具有(1)序列和(2)该序列中没有终止密码子),配对频率为80.2%。那些对中有43个是CDR3A/CDR3B组合,以构成4273-TP53-R248W-TCR1a1(生产对的55.8%)。那些对中有30个是CDR3A/CDR3B组合,以构成4273-TP53-R248W-TCR1a2(生产对的39%)。总体而言,在96个孔中,分别发现了4273-TP53-R248W-TCR1a1的CDR3A和CDR3B 50次和83次。总体而言,在96个孔中,分别发现了4273-TP53-R248W-TCR1a2的CDR3A和CDR3B 33次和83次。

[0214] 表8

[0215]	TCR 名称	4273-TP53-R248W-TCR1a1	4273-TP53-R248W-TCR1a2
	CDR3a	CAVTLCGGYNKLIF (SEQ ID NO: 439)	CAVTLSGGYNKLIF (SEQ ID NO: 449)
	CDR3b	CASSSRDYEQYF (SEQ ID NO: 442)	CASSSRDYEQYF (SEQ ID NO: 452)
	总孔	96	
	总 CDR3a/CDR3b 对	77	
	配对%	80.21%	
	#次数 CDR3a	50	33
	#次数 CDR3b	83	83
	配对的 CDR3a/CDR3b 对的%	43 55.84%	30 38.96%

[0216] 实施例7

[0217] 该实施例证实了在患者4149中抗-突变的p53 T细胞的鉴定。该实施例还证实了从患者4149中分离出一种抗-突变的p53 TCR。

[0218] 如图15-18针对患者4149所述进行实验。使用Tran方法发现了TCR。然后使用TCR来验证“p53热点突变通用筛选”方法。

[0219] 将TCR (4149-TCRa2b1或4149-TCRa2b2) 转座至来自患者4149的自体PBL中,并与自体APC共培养,所述自体APC (1) 用由无关、WT p53或经突变的p53序列组成的TMG电穿孔,或(2) 用肽媒介物(DMSO) 或由WT p53-Y220序列或经突变的p53-Y220C序列组成的经纯化的(>95%,通过HPLC) 25-个氨基酸的肽脉冲。PMA和离子霉素的组合是阳性对照。在37℃下进行共培养过夜。使用ELISPOT测定评价IFN- γ 的分泌。结果示于图15中。对于淋巴细胞→活细胞(PI阴性)→CD3+(T细胞)→CD4+mTCR+(TCR转座的T细胞) 设门后,通过流式细胞术评价4-1BB的表达。结果示于图16中。

[0220] 还进行了通过TCRAD深度测序和TCRB深度测序确定CD4+4-1BB+细胞的百分比。结果示于表9中。

[0221] 表9

[0222]

TCR 名称	CDR3 α (通过 TCRA 深度测序的 CD4+41BB+的%)	CDR3 β (通过 TCRB 深度测序的 CD4+41BB+的%)
4149-TCR-a2b1	20%	66%
4149-TCR-a2b2	20%	18%

[0223] 被4149-F11识别的假定p53^{Y220C}最小表位的作图：将自体DC细胞经肽脉冲(10 μ g/mL)并在粒细胞-巨噬细胞菌落刺激因子(GM-CSF)和IL-4中静置过夜。将TIL在500CU/mL IL-2中静置2-3天。将2 $\times$ 10⁴个TIL和10⁵个靶细胞在37℃下共培养过夜。通过ELISPOT测量IFN- γ 。结果示于表10中。通过FACS用门淋巴细胞\PI (neg) CD3+\CD3+CD4+测量4-1BB表达。结果示于图17中。

[0224] 表10

[0225]

肽 编 号.	ELISPOT 结果 对于 IFN- γ 产生呈 阳性(+)或阴性(-)	肽	SEQ ID NO:
0	-	媒介物	不适用
1	+	DRNTFRHSVVVP <u>C</u> EP	508

[0226]

肽 编 号.	ELISPOT 结果 对于 IFN- γ 产生呈 阳性(+)或阴性(-)	肽	SEQ ID NO:
2	+	RNTFRHSVVVP <u>C</u> EP	509
3	+	NTFRHSVVVP <u>C</u> EPPE	510
4	+	TFRHSVVVP <u>C</u> EPPEV	511
5	+(弱)	FRHSVVVP <u>C</u> EPPEVG	512
6	-	RHSVVVP <u>C</u> EPPEVGS	513
7	-	HSVVVP <u>C</u> EPPEVGSD	514
8	-	SVVVP <u>C</u> EPPEVGSDC	515
9	-	VVVP <u>C</u> EPPEVGSDCT	516
10	-	VVP <u>C</u> EPPEVGSDCTT	517
11	-	VP <u>C</u> EPPEVGSDCTTI	518

[0227] 将Cos7细胞(每孔2.5 $\times$ 10⁴个)涂铺在平底96孔板的孔上。20小时后,将细胞与单独的HLA等位基因在有或无TMG的情况下共转染。20小时后,将自体DC细胞用TMG平行转染。将所有HLA II类等位基因在有或无TMG的情况下共转染一组孔中。将未用TMG转染的细胞在37℃下用10 μ g/mL的p53-Y220C 15-聚体肽脉冲2-3小时。洗涤后,将在第二REP的第14天的4149-TCRa2b2-转座的T细胞(10⁵)添加至孔,并在37℃下共培养过夜。通过ELISA测量IFN-

γ 分泌。结果示于表18中。通过NetMHCIIpan进行预测(表11):cbs.dtu.dk/services/NetMHCIIpan/。

[0228] 表11

	HLA	肽	亲和力, nM	排名
[0229]	DRB3*02:02	NTFRHSVVVP <u>C</u> EPPE (SEQ ID NO: 510)	433.8	17

[0230] 在NCI HLA数据库中的3719名DRB_型患者中有1367名(37%)以及在NCI-SB的9名子宫内膜癌和卵巢癌患者中有5名(56%)检测到DRB3*02表达。DRB3*02等位基因的报道频率非常高。

[0231] 从患者4149分离的TCR 4149TCRa2b2的序列示于下文。从氨基末端开始,第一加下划线区是CDR1 α (SEQ ID NO:57),第二加下划线区是CDR2 α (SEQ ID NO:58),第三加下划线区是CDR3 α (SEQ ID NO:59),第四加下划线区是CDR1 β (SEQ ID NO:60),第五加下划线区是CDR2 β (SEQ ID NO:61),和第六加下划线区是CDR3 β (SEQ ID NO:62)。粗体区是连接子(SEQ ID NO:26)。从氨基末端开始,第一加斜体区是 α 链恒定区(SEQ ID NO:23)并且第二加斜体区是 β 链恒定区(SEQ ID NO:25)。 α 链可变区(SEQ ID NO:63)包含从氨基末端开始并且就在 α 链恒定区的开始之前结束的序列。 β 链可变区(SEQ ID NO:64)包含在连接子之后立即开始并且就在 β 链恒定区开始之前结束的序列。全长 α 链(SEQ ID NO:65)包含从氨基末端开始并且就在连接子开始之前结束的序列。全长 β 链(SEQ ID NO:66)包含在连接子之后立即开始并且以羧基末端结束的序列。

[0232] 癌症反应性T细胞使用下面列出的筛选方法进行鉴定。该患者的p53反应性细胞通过美国申请2017/0224800描述的方法(“Tran方法”)来鉴定。

[0233] TCR名称:4149TCRa2b2

[0234] P53突变的识别:Y220C

[0235] 筛选方法:用于验证p53“热点”突变通用筛选(后者是给定的)

[0236] 共培养以鉴定TCR:共培养4149-F11 TIL片段与p53-Y220C长肽,分选CD4+41BB+T细胞

[0237] 鉴定TCR的方法:频率配对.将CD4+41BB+分选的T细胞在REP中扩增并使所得的T细胞培养物经受Adaptive Biotechnologies的TCRAD(α)和TCRB(β)深度测序。在4种总TCR矩阵中,I使前两种TCR α 与前两种TCR β 配对。第二TCR α 和第二TCR β 是反应性TCR,因此TCRa2b2命名。

[0238] 所有TCR中TCR的丰度:如下

[0239] TCR取向: α - β

[0240] 表达载体:SB转座子

[0241] MASAPISMLAMLFTLSGLRAQSVAPEDQVNVAEGNPLTVKCTYSVSGNPYLFWYVQYPNRGLQFLK
YITGDNLVKGSYGFEAFNKSQTSFHLKKPSALVSDSALYFC AVRVDYKLSFGAGTTVTVRANIQNPEPAVYQLK
DPRSQDSTLCLFTDFDSQINVPKTMESGTFITDKCVLDMKAMDSKSNGAIAWSNQTSTFCQDIFKETNATYPSSDV
PCDATLTEKSFETDMNLFQNLVIVLRILLKLVAGFNLLMTLRLWSSRAKRSGSGATNFSLLKQAGDVEENPGPM

HNQVLCCVVLCLGANTVDGGITQSPKYLFRKEGQNVTLSC EQNLNHDAMYWYRQDPGQGLRLIYYSQIVNDFQKG
DIAEGYSVSREKKESFPLTVTSAQKNPTAFYL CASSISAGGDGYTF GSGTRLTVVEDLRNVTPPKVSLFEPSKAEI
ANKQKATLVCLARGFFPDHVELSWVWNGKEVHSGVCTDPQAYKESNYSYCLSSRLRVSATFWHNPRNHFRCQVQFH
GLSEEDKWPEGSPKPV TQNISAEAWGRADCGITSASYQQGVLSATILYEILLGKATLYAVLVSTLVMMAMVKRKNS
(SEQ ID NO:565)

[0242] 患者4149的TCR 4149TCRa2b2的统计数据示于下表12中。

[0243] 表12

CDR3	独特的生产性 CDR3 的排名	CDR3 计数	CDR3 频率
[0244] A: CAVRVWDYKLSF (SEQ ID NO: 59)	4,308 中的 2	3,309,400 中的 648,707	19.6 %
B: ASSISAGGDGYTF (SEQ ID NO: 62)	3,176 中的 2	578,948 中的 104,325	18.0 %

[0245] 实施例8

[0246] 该实施例证实了通过在自体T细胞内共培养被诱导表达突变的p53的自体APC来鉴定患者4213中的抗-突变的p53 T细胞(“p53热点突变通用筛选”)。该实施例还证实了从患者4213分离12种抗-突变的p53 TCR。

[0247] 如图19-20针对患者4213所述进行实验。

[0248] 将来自患者4213的TIL片段(F2和F24)与用肽媒介物(DMSO)或由经突变的p53-R248Q序列组成的经纯化的(>95%,通过HPLC)25-个氨基酸的肽脉冲的自体APC共培养。在37℃下进行共培养过夜。对于淋巴细胞→活细胞(PI阴性)→CD3+(T细胞)设门后,通过流式细胞术评价4-1BB的表达。结果示于图19中。将CD8+4-1BB+T细胞分选至96孔板的孔中。使用单细胞RT-PCR鉴定TCR。

[0249] CD4+T细胞来自患者4213的外周血淋巴细胞。将CD4+T细胞培养物与用肽媒介物(DMSO)或由经突变的p53-R248Q序列组成的经纯化的(>95%,通过HPLC)25-个氨基酸的肽脉冲的自体APC共培养。在37℃下进行共培养过夜。IFN- γ 的分泌通过ELISPOT评价。对于淋巴细胞→活细胞(PI阴性)→CD3+(T细胞)设门后,通过流式细胞术评价4-1BB的表达。结果示于图20中。将CD4+41BB+T细胞分选至96孔板的孔中。使用单细胞RT-PCR鉴定TCR。

[0250] 从患者4213分离的4213-F2-TCR1的序列示于下文。从氨基末端开始,第一加下划线区是CDR1 α (SEQ ID NO:317),第二加下划线区是CDR2 α (SEQ ID NO:318),第三加下划线区是CDR3 α (SEQ ID NO:319),第四加下划线区是CDR1 β (SEQ ID NO:320),第五加下划线区是CDR2 β (SEQ ID NO:321),和第六加下划线区是CDR3 β (SEQ ID NO:322)。粗体区是连接子(SEQ ID NO:26)。从氨基末端开始,第一加斜体区是 α 链恒定区(SEQ ID NO:23)并且第二加斜体区是 β 链恒定区(SEQ ID NO:25)。 α 链可变区(SEQ ID NO:323)包含从氨基末端开始并且就在 α 链恒定区的开始之前结束的序列。 β 链可变区(SEQ ID NO:324)包含在连接子之后立即开始并且就在 β 链恒定区开始之前结束的序列。全长 α 链(SEQ ID NO:325)包含从氨基

末端开始并且就在连接子开始之前结束的序列。全长 β 链 (SEQ ID NO:326) 包含在连接子之后立即开始并且以羧基末端结束的序列。

[0251] 癌症反应性T细胞使用下面列出的筛选方法进行鉴定。用于分离TCR的方法示于下文。

[0252] TCR名称:4213-F2-TCR1

[0253] P53突变的识别:R248Q

[0254] 筛选方法:p53“热点”突变通用筛选

[0255] 共培养以鉴定TCR:共培养4213-F2与R248Q长肽,分选CD8+41BB+T细胞

[0256] 鉴定TCR的方法:单细胞RT-PCR

[0257] 所有配对的TCR中的TCR的丰度:8.3% (在24对中观察到2次)

[0258] TCR取向: α - β

[0259] 表达载体:SB转座子

[0260] MAMLLGASVLILWLQPDWVNSQQKNDDQQVKQNSPSLSVQEGRISILNCDYTNSMFDYFLWYKKYPAE
GPTFLISISSIKDKNEDGRFTVFLNKS AKHLSLHIVPSQPGDSAVYFCAANTGNQFYFGTGTSLTVIPNIQNPEPA
VYQLKDPRSQDSTLCLFTDFDSQINVPKTMESGTFITDKCVLDMKAMDSKSNGAIAWSNQTSTFCQDIFKETNATY
PSSDVPCDATLTEKSFETDMNLFQNLIVIVLRILLKLVAGFNLLMTLRLWSSRAKRSGSGATNFSLLKQAGDVEE
NPGPMHTRLLCWAALCLLGAELTEAGVAQSPRYKII EKRSVAFWCNPI SGHATLYWYQQILGQGP KLLIQFQNNQ
VVDDSQLPKDRFSAERLKGVDSTLKI QPAKLEDSAVYLCASSHLAGEFYNEQFFGPGTRLTVLEDLRNVT PPKVSL
FEPSKAEIANKQKATLVCLARGFFPDHVELSWVWNGKEVHSGVCTDPQAYKESNYSYCLSSRLRV SATFWHNPRNH
FRCVQVFHGLSEEDKWPEGSPKPV TQNISAEAWGRADCGITSASYQQGVLSATILYEILLGKATLYAVLVSTLVVM
AMVKRKNS (SEQ ID NO:566)

[0261] 患者4213的TCR 4213-F2-TCR1的统计数据示于下表13中。

[0262] 表13

[0263]	参数	#	频率
	总孔	96	100%
	CDR3 α	3	3.1%
	CDR3 β	8	8.3%
	4213-F2-TCR1 对	2	2.1%
	总配对的 TCR	24	25.0%

[0264] 从患者4213分离的4213-F2-TCR2的序列示于下文。从氨基末端开始,第一加下划线区是CDR1 α (SEQ ID NO:327),第二加下划线区是CDR2 α (SEQ ID NO:328),第三加下划线区是CDR3 α (SEQ ID NO:329),第四加下划线区是CDR1 β (SEQ ID NO:330),第五加下划线区是CDR2 β (SEQ ID NO:331),和第六加下划线区是CDR3 β (SEQ ID NO:332)。粗体区是连接子 (SEQ ID NO:26)。从氨基末端开始,第一加斜体区是 α 链恒定区 (SEQ ID NO:23) 并且第二加斜体区是 β 链恒定区 (SEQ ID NO:25)。 α 链可变区 (SEQ ID NO:333) 包含从氨基末端开始并且就在 α 链恒定区的开始之前结束的序列。 β 链可变区 (SEQ ID NO:334) 包含在连接子之后立即开始并且就在 β 链恒定区开始之前结束的序列。全长 α 链 (SEQ ID NO:335) 包含从氨基

末端开始并且就在连接子开始之前结束的序列。全长 β 链 (SEQ ID NO:336) 包含在连接子之后立即开始并且以羧基末端结束的序列。

[0265] 癌症反应性T细胞使用下面列出的筛选方法进行鉴定。用于分离TCR的方法示于下文。

[0266] TCR名称:4213-F2-TCR2

[0267] P53突变的识别:R248Q

[0268] 筛选方法:p53“热点”突变通用筛选

[0269] 共培养以鉴定TCR:共培养4213-F2与R248Q长肽,分选CD8+41BB+T细胞

[0270] 鉴定TCR的方法:单细胞RT-PCR

[0271] 所有配对的TCR中的TCR的丰度:12.5% (在24对中观察到3次)

[0272] TCR取向: α - β

[0273] 表达载体:SB转座子

[0274] MAGAFLLYVSMKMGGTAGQSLEQPSEVTAVEGAIVQINCTYQTSGFYGLSWYQQHDGGAPTFLSYNAL
DGLEETGRFSSFLSRSDSYGYLLLQELQMKDSASYFCAFAYGQNFVFGPGTRLSVLPNIQNPEPAVYQLKDPRSQD
STLCLFTDFDSQINVPKTMESGTFITDKCVLDMKAMDSKSNGAIAWSNQTSFTCQDIFKETNATYPSSDVPCDATL
TEKSFETDMNLFQNLVIVLRILLKLVAGFNLLMTLRLWSSRAKRSGSGATNFSLLKQAGDVEENPGPMHFRLLC
CVAFCLLGAGPVD SGVTQTPKHLITATGQRTVLRCSPRSGDL SVYWYQQSLDQGLQFLIQYYNGEERAKGNILERF
SAQQFPDLHSELNLSSLELGDSALYFCASSPLGDSGNTIYFGECSWLTVVEDLRNVTPPKVSLFEP SKAEIANKQK
ATLVCLARGFFPDHVELSWVWNGKEVHSGVCTDPQAYKESNYSYCLSSRLRV SATFWHNPRNHFR CQVQFHGLSEE
DKWPEGSPKPV TQNISAEAWGRADCGITSASYQQGVLSATILYEILLGKATLYAVLVSTLVVMAMVKRKNS (SEQ
ID NO:567)

[0275] 患者4213的TCR 4213-F2-TCR2的统计数据示于下表14中。

[0276] 表14

参数	#	频率
总孔	96	100%
CDR3 α	4	4.2%
CDR3 β	4	4.2%
4213-F2-TCR2对	3	3.1%
总配对的TCR	24	25.0%

[0278] 从患者4213分离的4213-F2-TCR3的序列示于下文。从氨基末端开始,第一加下划线区是CDR1 α (SEQ ID NO:337),第二加下划线区是CDR2 α (SEQ ID NO:338),第三加下划线区是CDR3 α (SEQ ID NO:339),第四加下划线区是CDR1 β (SEQ ID NO:340),第五加下划线区是CDR2 β (SEQ ID NO:341),并且第六加下划线区是CDR3 β (SEQ ID NO:342)。粗体区是连接子 (SEQ ID NO:26)。从氨基末端开始,第一加斜体区是 α 链恒定区 (SEQ ID NO:23) 并且第二加斜体区是 β 链恒定区 (SEQ ID NO:25)。 α 链可变区 (SEQ ID NO:343) 包含从氨基末端开始并且就在 α 链恒定区的开始之前结束的序列。 β 链可变区 (SEQ ID NO:344) 包含在连接子之后立即开始并且就在 β 链恒定区开始之前结束的序列。全长 α 链 (SEQ ID NO:345) 包含从氨基末端开始并且就在连接子开始之前结束的序列。全长 β 链 (SEQ ID NO:346) 包含在连接子之后立即开始并且以羧基末端结束的序列。

[0279] 癌症反应性T细胞使用下面列出的筛选方法进行鉴定。用于分离TCR的方法示于下文。

[0280] TCR名称:4213-F2-TCR3

[0281] P53突变的识别:R248Q

[0282] 筛选方法:p53“热点”突变通用筛选

[0283] 共培养以鉴定TCR:共培养4213-F2与R248Q长肽,分选CD8+41BB+T细胞

[0284] 鉴定TCR的方法:单细胞RT-PCR

[0285] 所有配对的TCR中的TCR的丰度:70.8% (在24对中观察到17次)

[0286] TCR取向: α - β

[0287] 表达载体:SB转座子

[0288] MATLLGVSLVILWLQLARVNSQQGEEDPQALSIQEGENATMNC SYKTSINN LQWYRQNSGRGLVHLIL
IRSNEREKHSGRRLRVTLDTSKKSSSLITASRAADTASYFCATDAWNNDMRFGAGTRLTVKPNIQNPEPAVYQLKD
PRSQDSTLCLFTLDFDSQINVPKTMESGTFITDKCVLDMKAMDSKSNGAIAWSNQTSTFCQDIFKETNATYPSSDVP
CDATLTEKSFETDMNLNFQNLIVIVLRILLKLVAGFNLLMTLRLWSSRAKRSGSGATNFSLLKQAGDVEENPGPMH
IGLLCCVAFSLLWASPVNAGVTQTPKFQVLKTGQSMTLQCAQDMNHNSMYWYRQDPGMGLRLIYYSASEGTTDKGE
VPNGYNVSRLNKREFSLRLESAAPSQTSVYFCASSESQGNTEAFFGQGTRLTVVEDLRNVTPPKVSLFEPSKAEIA
NKQKATLVCLARGFFPDHVELSWVNGKEVHSGVCTDPQAYKESNYSYCLSSRLRVSATFWHNPRNHFRCQVQFHG
LSEEDKWPEGSPKPVQTQNISAEAWGRADCGITSASYQQGVLSATILYEILLGKATLYAVLVSTLVVMAMVKRKNS
(SEQ ID NO:568)

[0289] 患者4213的TCR 4213-F2-TCR3的统计数据示于下表15中。

[0290] 表15

参数	#	频率
总孔	96	100%
CDR3 α	19	19.8%
CDR3 β	42	43.8%
4213-F2-TCR3对	17	17.7%
总配对的TCR	24	25.0%

[0292] 从患者4213分离的4213-F24-TCR α 1的序列示于下文。从氨基末端开始,第一加下划线区是CDR1 α (SEQ ID NO:347),第二加下划线区是CDR2 α (SEQ ID NO:348),第三加下划线区是CDR3 α (SEQ ID NO:349),第四加下划线区是CDR1 β (SEQ ID NO:350),第五加下划线区是CDR2 β (SEQ ID NO:351),和第六加下划线区是CDR3 β (SEQ ID NO:352)。粗体区是连接子 (SEQ ID NO:26)。从氨基末端开始,第一加斜体区是 α 链恒定区 (SEQ ID NO:23) 并且第二加斜体区是 β 链恒定区 (SEQ ID NO:25)。 α 链可变区 (SEQ ID NO:353) 包含从氨基末端开始并且就在 α 链恒定区的开始之前结束的序列。 β 链可变区 (SEQ ID NO:354) 包含在连接子之后立即开始并且就在 β 链恒定区开始之前结束的序列。全长 α 链 (SEQ ID NO:355) 包含从氨基末端开始并且就在连接子开始之前结束的序列。全长 β 链 (SEQ ID NO:356) 包含在连接子之后立即开始并且以羧基末端结束的序列。

[0293] 癌症反应性T细胞使用下面列出的筛选方法进行鉴定。用于分离TCR的方法示于下文。

[0294] TCR名称:4213-F24-TCRa1

[0295] P53突变的识别:R248Q

[0296] 筛选方法:p53“热点”突变通用筛选

[0297] 共培养以鉴定TCR:共培养4213-F24与R248Q长肽,分选CD8+41BB+T细胞

[0298] 鉴定TCR的方法:单细胞RT-PCR

[0299] 所有配对的TCR中的TCR的丰度:15.9% (在44对中观察到7次)

[0300] TCR取向: α - β

[0301] 表达载体:SB转座子

[0302] MAKHLTTFLVILWLYFYRGNQVEQSPQSLIIILEGKNCTLQCNYTVSPFSNLRWYKQDTGRGPVSL
TIMTFSENTKSNGRYTATLDADTKQSSLHITASQLSDSASYICVVSSYKIIIFGTGTRLHVFPNIQNPEPAVYQLKD
PRSQDSTLCLFTDFDSQINVPKTMESGTFITDKCVLDMKAMDSKSNGAIAWSNQTSTFCQDIFKETNATYPSSDVP
CDATLTEKSFETDMNLNFQNLIVLRIILLKVAGFNLLMTLRLWSSRAKRSGSGATNFSLLKQAGDVEENPGPMH
TRLLFWVAFCLLGAYHTGAGVSQSPSNKVTEKGKDVLRCDPISGHTALYWYRQRLGQGLEFLIYFQGN SAPDKSG
LPSEDRFSAERTGESVSTLTIQRTQQEDSAVYLCASSPIQGENSPLHFGNGTRLTVTEDLRNVTPPKVSLFEPSKAE
IANKQKATLVCLARGFFPDHVELSWVNGKEVHSGVCTDPQAYKESNYSYCLSSRLRVSATFWHNPRNHFRCQVQF
HGLSEEDKWPEGSPKPVTONISAEAWGRADCGITSASYQQGVLSATILYEILLGKATLYAVLVSTLVMMAMVKRKNS
(SEQ ID NO:569)

[0303] 患者4213的TCR 4213-F24-TCRa1的统计数据示于下表16中。

[0304] 表16

参数	#	频率
总孔	96	100%
CDR3 α	7	7.3%
CDR3 β	80	83.3%
4213-F24-TCRa1对	7	7.3%
总配对的TCR	44	45.8%

[0306] 从患者4213分离的4213-F24-TCRa2的序列示于下文。从氨基末端开始,第一加下划线区是CDR1 α (SEQ ID NO:357),第二加下划线区是CDR2 α (SEQ ID NO:358),第三加下划线区是CDR3 α (SEQ ID NO:359),第四加下划线区是CDR1 β (SEQ ID NO:360),第五加下划线区是CDR2 β (SEQ ID NO:361),和第六加下划线区是CDR3 β (SEQ ID NO:362)。粗体区是连接子 (SEQ ID NO:26)。从氨基末端开始,第一加斜体区是 α 链恒定区 (SEQ ID NO:23) 并且第二加斜体区是 β 链恒定区 (SEQ ID NO:25)。 α 链可变区 (SEQ ID NO:363) 包含从氨基末端开始并且就在 α 链恒定区开始之前结束的序列。 β 链可变区 (SEQ ID NO:364) 包含在连接子之后立即开始并且就在 β 链恒定区开始之前结束的序列。全长 α 链 (SEQ ID NO:365) 包含从氨基末端开始并且就在连接子开始之前结束的序列。全长 β 链 (SEQ ID NO:366) 包含在连接子之后立即开始并且以羧基末端结束的序列。

[0307] 癌症反应性T细胞使用下面列出的筛选方法进行鉴定。用于分离TCR的方法示于下文。

[0308] TCR名称:4213-F24-TCRa2

[0309] P53突变的识别:R248Q

[0310] 筛选方法:p53“热点”突变通用筛选

[0311] 共培养以鉴定TCR:共培养4213-F24与R248Q长肽,分选CD8+41BB+T细胞

[0312] 鉴定TCR的方法:单细胞RT-PCR

[0313] 所有配对的TCR中的TCR的丰度:84.1% (在44对中观察到37次)

[0314] TCR取向: α - β

[0315] 表达载体:SB转座子

[0316] MAKHLTTFLVILWLYFYRGNGKNQVEQSPQSLIIILEGKNCTLQCNYTVSPFSNLRWYKQDTGRGPVSL
TIMTFSENTKSNGRYTATLDADTKQSSLHITASQLSDSASYICVVSSYKLIFGTGTRLQVFPNIQNPEPAVYQLKD
PRSQDSTLCLFTDFDSQINVPKTMESGTFITDKCVLDMKAMDSKSNGAIAWSNQTSTFCQDIFKETNATYPSSDVP
CDATLTEKSFETDMNLNFQNLIVIVLRILLKLVAGFNLLMTLRLWSSRAKRSGSGATNFSLLKQAGDVEENPGPMH
TRLLFWVAFCLLGAYHTGAGVSQSPSNKVTEKGKDVELRCDPISGHTALYWYRQRLGQGLEFLIYFQGNSAPDKSG
LPSDRFSARTGESVSTLTIQRTQQEDSAVYLCASSPIQGENSEPLHFGNGTRLTVTEDLRNVTPPKVSLFEPSKAE
IANKQKATLVCLARGFFPDHVELSWVNGKEVHSGVCTDPQAYKESNYSYCLSSRLRVSATFWHNPRNHFRQVQV
HGLSEEDKWPEGSPKPVTONISAEAWGRADCGITSASYQQGVLSATILYEILLGKATLYAVLVSTLVMMVMVKRKN
(SEQ ID NO:570)

[0317] 患者4213的TCR 4213-F24-TCRa2的统计数据示于下表17中。

[0318] 表17

参数	#	频率
总孔	96	100%
CDR3 α	39	40.6%
CDR3 β	80	83.3%
4213-F24-TCRa2对	37	38.5%
总配对的TCR	44	45.8%

[0320] 从患者4213分离的4213-PBL-TCR1的序列示于下文。从氨基末端开始,第一加下划线区是CDR1 α (SEQ ID NO:367),第二加下划线区是CDR2 α (SEQ ID NO:368),第三加下划线区是CDR3 α (SEQ ID NO:369),第四加下划线区是CDR1 β (SEQ ID NO:370),第五加下划线区是CDR2 β (SEQ ID NO:371),和第六加下划线区是CDR3 β (SEQ ID NO:372)。粗体区是连接子 (SEQ ID NO:26)。从氨基末端开始,第一加斜体区是 α 链恒定区 (SEQ ID NO:23) 并且第二加斜体区是 β 链恒定区 (SEQ ID NO:25)。 α 链可变区 (SEQ ID NO:373) 包含从氨基末端开始并且就在 α 链恒定区开始之前结束的序列。 β 链可变区 (SEQ ID NO:374) 包含在连接子之后立即开始并且就在 β 链恒定区开始之前结束的序列。全长 α 链 (SEQ ID NO:375) 包含从氨基末端开始并且就在连接子开始之前结束的序列。全长 β 链 (SEQ ID NO:376) 包含在连接子之后立即开始并且以羧基末端结束的序列。

[0321] 癌症反应性T细胞使用下面列出的筛选方法进行鉴定。用于分离TCR的方法示于下文。

[0322] TCR名称:4213-PBL-TCR1

[0323] P53突变的识别:R248Q

[0324] 筛选方法:p53“热点”突变通用筛选

[0325] 共培养以鉴定TCR:将在用R248Q长肽体外致敏之后的CD4+记忆T细胞与R248Q长肽

共培养,并分选CD4+41BB+T细胞

[0326] 鉴定TCR的方法:单细胞RT-PCR

[0327] 所有配对的TCR中的TCR的丰度:9.5% (在63对中观察到6次)

[0328] TCR取向: α - β

[0329] 表达载体:SB转座子

[0330] MALLLVPAFQVIFTLGGTRAQSVTQLDSQVPVFEEAPVELRCNYSSSVSVYLFWYVQYPNQGLQLLLK
YLSGSTLVESINGFEAEFNKSQTSFHLRKPSVHISDTAEYFCVASKGTGAQKLVFGQGTRLTINPNIQNPEPAVYQ
LKDPRSQDSTLCLFTDFDSQINVPKTMESGTFITDKCVLDMKAMDSKSNGAIAWSNQTSFTCQDIFKETNATYPSS
DVPCDATLTEKSFETDMNLFQNLVIVLRILLKLVAGFNLLMTLRLWSSRAKRSGSGATNFSLLKQAGDVEENPG
PMHNQVLCCVVLFCFLGANTVDGGITQSPKYLFRKEGQNVTLSCQNLNHDAMYWYRQDPGQGLRLIYYSQIVNDFQ
KGDIAEGYSVSREKKESFPLIVTSAQKNPTASYLCASEAFFGQGTRLTVVEDLRNVTPPKVSLFEPSKAEIANKQK
ATLVCLARGFFPDHVELSWVNGKEVHSGVCTDPQAYKESNYSYCLSSRLRVSATFWHNPRNHFRCQVQFHGLSEE
DKWPEGSPKPVTONISAEAWGRADCGITSASYQQGVLSATILYEILLGKATLYAVLVSTLVVMAMVKRKNS (SEQ
ID NO:571)

[0331] 患者4213的TCR 4213-PBL-TCR1的统计数据示于下表18中。

[0332] 表18

[0333]	参数	#	频率
	总孔	192	100%
	CDR3 α	9	4.7%
	CDR3 β	6	3.1%
	4213-PBL-TCR1 对	6	3.1%
	参数	#	频率
	总配对的 TCR	63	32.8%

[0334] 从患者4213分离的4213-PBL-TCR2的序列示于下文。从氨基末端开始,第一加下划线区是CDR1 α (SEQ ID NO:377),第二加下划线区是CDR2 α (SEQ ID NO:378),第三加下划线区是CDR3 α (SEQ ID NO:379),第四加下划线区是CDR1 β (SEQ ID NO:380),第五加下划线区是CDR2 β (SEQ ID NO:381),和第六加下划线区是CDR3 β (SEQ ID NO:382)。粗体区是连接子 (SEQ ID NO:26)。从氨基末端开始,第一加斜体区是 α 链恒定区 (SEQ ID NO:23) 并且第二加斜体区是 β 链恒定区 (SEQ ID NO:25)。 α 链可变区 (SEQ ID NO:383) 包含从氨基末端开始并且在 α 链恒定区开始之前结束的序列。 β 链可变区 (SEQ ID NO:384) 包含在连接子之后立即开始并且就在 β 链恒定区开始之前结束的序列。全长 α 链 (SEQ ID NO:385) 包含从氨基末端开始并且就在连接子开始之前结束的序列。全长 β 链 (SEQ ID NO:386) 包含在连接子之后立即开始并且以羧基末端结束的序列。

[0335] 癌症反应性T细胞使用下面列出的筛选方法进行鉴定。用于分离TCR的方法示于下文。

[0336] TCR名称:4213-PBL-TCR2

[0337] P53突变的识别:R248Q

[0338] 筛选方法:p53“热点”突变通用筛选

[0339] 共培养以鉴定TCR:将在用R248Q长肽体外致敏之后的CD4+记忆T细胞与R248Q长肽共培养,并分选CD4+41BB+T细胞

[0340] 鉴定TCR的方法:单细胞RT-PCR

[0341] 所有配对的TCR中的TCR的丰度:7.9% (在63对中观察到5次)

[0342] TCR取向: α - β

[0343] 表达载体:SB转座子

[0344] MALVTSITVLLSLGIMGDAKTTQPNSMESNEEEPVHLPCNHSTISGTDYIHWRQLPSQGPEYVIHGL
TSNVNNRMASLAIAEDRKSSTLILHRATLRDAVYYCILASGAGSYQLTFGKGTKLSVIPNIQNPEPAVYQLKDPR
SQDSTLCLFTDFDSQINVPKTMESGTFITDKCVLDMKAMDSKSNGAIAWSNQTSTFCQDIFKETNATYPSSDVPCD
ATLTEKSFETDMNLFNQNLIVIVLRILLKLVAGFNLLMTLRLWSSRAKRSGSGATNFSLLKQAGDVEENPGPMHCR
LLCCVVFCLLQAGPLDTAVSQTPKYLVTQMGNKSIKCEQNLGHDTMYWYKQDSKKFLKIMFSYNNKELIINETVP
NRFSPKSPDKAHLNLHINSLELGDSAVYFCASRTIGYNTEAFFGQGTRLTVVEDLRNVTPPKVSLFEPKAEIANK
QKATLVCLARGFFPDHVELSWVNGKEVHSGVCTDPQAYKESNYSYCLSSRLRVSATFWHNPRNHFRCQVQFHGLS
EEDKWPEGSPKPVTONISAEAWGRADCGITSASYQQGVLSATILYEILLGKATLYAVLVSTLVMMAMVKRKNS (SEQ
ID NO:572)

[0345] 患者4213的TCR 4213-PBL-TCR2的统计数据示于下表19中。

[0346] 表19

参数	#	频率
总孔	192	100%
CDR3 α	8	4.2%
CDR3 β	8	4.2%
4213-PBL-TCR2对	5	2.6%
总配对的TCR	63	32.8%

[0348] 从患者4213分离的4213-PBL-TCR3的序列示于下文。从氨基末端开始,第一加下划线区是CDR1 α (SEQ ID NO:387),第二加下划线区是CDR2 α (SEQ ID NO:388),第三加下划线区是CDR3 α (SEQ ID NO:389),第四加下划线区是CDR1 β (SEQ ID NO:390),第五加下划线区是CDR2 β (SEQ ID NO:391),和第六加下划线区是CDR3 β (SEQ ID NO:392)。粗体区是连接子 (SEQ ID NO:26)。从氨基末端开始,第一加斜体区是 α 链恒定区 (SEQ ID NO:23) 并且第二加斜体区是 β 链恒定区 (SEQ ID NO:25)。 α 链可变区 (SEQ ID NO:393) 包含从氨基末端开始并且就在 α 链恒定区开始之前结束的序列。 β 链可变区 (SEQ ID NO:394) 包含在连接子之后立即开始并且就在 β 链恒定区开始之前结束的序列。全长 α 链 (SEQ ID NO:395) 包含从氨基末端开始并且就在连接子开始之前结束的序列。全长 β 链 (SEQ ID NO:396) 包含在连接子之后立即开始并且以羧基末端结束的序列。

[0349] 癌症反应性T细胞使用下面列出的筛选方法进行鉴定。用于分离TCR的方法示于下文。

[0350] TCR名称:4213-PBL-TCR3

[0351] P53突变的识别:R248Q

[0352] 筛选方法:p53“热点”突变通用筛选

[0353] 共培养以鉴定TCR:将在用R248Q长肽体外致敏之后的CD4+记忆T细胞与R248Q长肽共培养,并分选CD4+41BB+T细胞

[0354] 鉴定TCR的方法:单细胞RT-PCR

[0355] 所有配对的TCR中的TCR的丰度:6.3% (在63对中观察到4次)

[0356] TCR取向: α - β

[0357] 表达载体:SB转座子

[0358] MAKIRQFLAILWLQLSCVSAKNEVEQSPQNLTAEQEGFITINCSYSVGVISALHWLQQHPGGGIVSL
FMLSSGKKKHGRLLIATINIQEKHSSLHITASHPRDSAVYICAALSYNTDKLIFGTGTRLQVFPNIQNPEPAVYQLK
DPRSQDSTLCLFTDFDSQINVPKTMESGTFITDKCVLDMKAMDSKSNGAIAWSNQTSTFCQDIFKETNATYPSSDV
PCDATLTEKSFETDMNLFQNLVIVLRILLKLVAGFNLLMTLRLWSSRAKRSRSGSGATNFSLLKQAGDVEENPGPM
HTRLWCWAALCLLGADHTGAGVSQTPSNKVTEKGKYVELRCDPISGHTALYWYRQSLGQGPEFLIYFQGTGAADDS
GLPNDRFFFAVRPEGSVSTLKIQRTERGDSAVYLCASSLSGLLQETQYFGPGTRLLVLEDLRNVTTPKVSLEFESKA
EIANKQKATLVCLARGFFPDHVELSWVWNGKEVHSGVCTDPQAYKESNYSYCLSSRLRVSATFWHNPRNHFRQCQVQ
FHGLSEEDKWPEGSPKPVQTQNISAEAWGRADCGITSASYQQGVLSATILYEILLGKATLYAVLVSTLVMMVMVKRK
NS (SEQ ID NO:573)

[0359] 患者4213的TCR 4213-PBL-TCR3的统计数据示于下表20中。

[0360] 表20

[0361]

参数	#	频率
总孔	192	100%
CDR3 α	4	2.1%
CDR3 β	7	3.6%
4213-PBL-TCR3对	4	2.1%
总配对的TCR	63	32.8%

[0362] 从患者4213分离的4213-PBL-TCR4a1的序列示于下文。从氨基末端开始,第一加下划线区是CDR1 α (SEQ ID NO:397),第二加下划线区是CDR2 α (SEQ ID NO:398),第三加下划线区是CDR3 α (SEQ ID NO:399),第四加下划线区是CDR1 β (SEQ ID NO:400),第五加下划线区是CDR2 β (SEQ ID NO:401),和第六加下划线区是CDR3 β (SEQ ID NO:402)。粗体区是连接子 (SEQ ID NO:26)。从氨基末端开始,第一加斜体区是 α 链恒定区 (SEQ ID NO:23) 并且第二加斜体区是 β 链恒定区 (SEQ ID NO:25)。 α 链可变区 (SEQ ID NO:403) 包含从氨基末端开始并且就在 α 链恒定区的开始之前结束的序列。 β 链可变区 (SEQ ID NO:404) 包含在连接子之后立即开始并且就在 β 链恒定区开始之前结束的序列。全长 α 链 (SEQ ID NO:405) 包含从氨基末端开始并且就在连接子开始之前结束的序列。全长 β 链 (SEQ ID NO:406) 包含在连接子之后立即开始并且以羧基末端结束的序列。

[0363] 癌症反应性T细胞使用下面列出的筛选方法进行鉴定。用于分离TCR的方法示于下文。

[0364] TCR名称:4213-PBL-TCR4a1

[0365] P53突变的识别:R248Q

[0366] 筛选方法:p53“热点”突变通用筛选

[0367] 共培养以鉴定TCR:将在用R248Q长肽体外致敏之后的CD4+记忆T细胞与R248Q长肽共培养并分选CD4+41BB+T细胞

[0368] 鉴定TCR的方法:单细胞RT-PCR

[0369] 所有配对的TCR中的TCR的丰度:3.2% (在63对中观察到2次)

[0370] TCR取向: α - β

[0371] 表达载体:SB转座子

[0372] MAYSPGLVSLILLLLGRTRGNSVTQMEGPVTLSEEAFLTINCTYTATGYPSLFWYVQYPGEGLQLLK
ATKADDKGSNKGFEATYRKETTSFHLEKGSVQVSDSAVYFCALSHTGSSNTGKLIFGQGTRLQVKPNIQNPEPAVY
QLKDPRSQDSTLCLFTDFDSQINVPKTMESGTFITDKCVLDMKAMDSKNGAIAWSNQTSTFCQDIFKETNATYPS
SDVPCDATLTEKSFETDMNLFQNLIVLRIILLKVAGFNLLMTLRLWSSRAKRSGSGATNFSLLKQAGDVEENP
GPMHTRLLCWAALCCLLGAELTEAGVAQSPRYKIIIEKRQSVAFWCNPI SGHATLYWYQQILGQGPKLLIQFNNGVV
DDSQLPKDRFSAERLKGVDSTLKIQPAKLEDSAVYLCASSTGGGRHQPHFGDGTRLSILEDLRNVTPPKVSLFEP
SKAEIANKQKATLVCLARGFFPDHVELSWWVNGKEVHSGVCTDPQAYKESNYSYCLSSRLRVSATFWHNPRNHFR
QVQFHGLSEEDKWPEGSPKPVTONISAEAWGRADCGITSASYQQGVLSATILYEILLGKATLYAVLVSTLVVMAMV
KRKNS (SEQ ID NO:574)

[0373] 患者4213的TCR 4213-PBL-TCR4a1的统计数据示于下表21中。

[0374] 表21

参数	#	频率
总孔	192	100%
CDR3 α	2	1.0%
CDR3 β	36	18.8%
4213-PBL-TCR4a1对	2	1.0%
总配对的TCR	63	32.8%

[0376] 从患者4213分离的4213-PBL-TCR4a2的序列示于下文。从氨基末端开始,第一加下划线区是CDR1 α (SEQ ID NO:407),第二加下划线区是CDR2 α (SEQ ID NO:408),第三加下划线区是CDR3 α (SEQ ID NO:409),第四加下划线区是CDR1 β (SEQ ID NO:410),第五加下划线区是CDR2 β (SEQ ID NO:411),和第六加下划线区是CDR3 β (SEQ ID NO:412)。粗体区是连接子 (SEQ ID NO:26)。从氨基末端开始,第一加斜体区是 α 链恒定区 (SEQ ID NO:23) 并且第二加斜体区是 β 链恒定区 (SEQ ID NO:25)。 α 链可变区 (SEQ ID NO:413) 包含从氨基末端开始并且就在 α 链恒定区开始之前结束的序列。 β 链可变区 (SEQ ID NO:414) 包含在连接子之后立即开始并且就在 β 链恒定区开始之前结束的序列。全长 α 链 (SEQ ID NO:415) 包含从氨基末端开始并且就在连接子开始之前结束的序列。全长 β 链 (SEQ ID NO:416) 包含在连接子之后立即开始并且以羧基末端结束的序列。

[0377] 癌症反应性T细胞使用下面列出的筛选方法进行鉴定。用于分离TCR的方法示于下文。

[0378] TCR名称:4213-PBL-TCR4a2

[0379] P53突变的识别:R248Q

[0380] 筛选方法:p53“热点”突变通用筛选

[0381] 共培养以鉴定TCR:将在用R248Q长肽体外致敏之后的CD4+记忆T细胞与R248Q长肽

共培养并分选CD4+41BB+T细胞

[0382] 鉴定TCR的方法:单细胞RT-PCR

[0383] 所有配对的TCR中的TCR的丰度:3.2% (在63对中观察到2次)

[0384] TCR取向: α - β

[0385] 表达载体:SB转座子

[0386] MAYSPGLVSLILLLLGRTRGNSVTQMEGPVTLSEEAFLTINCTYTATGYPSLFWYVQYPGEGLQLLLK
ATKADDKGSNKGFEATYRKETTSFHLEKGSVQVSDSAVYFCALSQTGSSKTGKLIFGQGTRLQVKPNIQNPEPAVY
QLKDPRSQDSTLCLFTDFDSQINVPKTMESGTFITDKCVLDMKAMDSKSNGAIAWSNQTSFTCQDIFKETNATYPS
SDVPCDATLTEKSFETDMNLFQNLIVILRILLKLVAGFNLLMTLRLWSSRAKRSKSGATNFSLLKQAGDVEENP
GPMHTRLLCWAALCLLGAELTEAGVAQSPRYKIIIEKRQSVAFWCNPI SGHATLYWYQQILGQGPKLLIQFQNNGVV
DDSQLPKDRFSAERLKGVDSTLKIQPAKLEDSAVYLCASSTGGGRHQPHFGDGTRLSILEDLRNVTPPKVSLFEP
SKAEIANKQKATLVCLARGFFPDHVELSWWVNGKEVHSGVCTDPQAYKESNYSYCLSSRLRVSATFWHNPRNHFR
QVQFHGLSEEDKWPEGSPKPVTONISAEAWGRADCGITSASYQQGVLSATILYEILLGKATLYAVLVSTLVVMAMV
KRKNS (SEQ ID NO:575)

[0387] 患者4213的TCR 4213-PBL-TCR4a2的统计数据示于下表22中。

[0388] 表22

[0389]

参数	#	频率
总孔	192	100%
CDR3 α	2	1.0%
CDR3 β	36	18.8%
4213-PBL-TCR4a2对	2	1.0%
总配对的TCR	63	32.8%

[0390] 从患者4213分离的4213-PBL-TCR4a3的序列示于下文。从氨基末端开始,第一加下划线区是CDR1 α (SEQ ID NO:417),第二加下划线区是CDR2 α (SEQ ID NO:418),第三加下划线区是CDR3 α (SEQ ID NO:419),第四加下划线区是CDR1 β (SEQ ID NO:420),第五加下划线区是CDR2 β (SEQ ID NO:421),和第六加下划线区是CDR3 β (SEQ ID NO:422)。粗体区是连接子 (SEQ ID NO:26)。从氨基末端开始,第一加斜体区是 α 链恒定区 (SEQ ID NO:23) 并且第二加斜体区是 β 链恒定区 (SEQ ID NO:25)。 α 链可变区 (SEQ ID NO:423) 包含从氨基末端开始并且就在 α 链恒定区开始之前结束的序列。 β 链可变区 (SEQ ID NO:424) 包含在连接子之后立即开始并且就在 β 链恒定区开始之前结束的序列。全长 α 链 (SEQ ID NO:425) 包含从氨基末端开始并且就在连接子开始之前结束的序列。全长 β 链 (SEQ ID NO:426) 包含在连接子之后立即开始并且以羧基末端结束的序列。

[0391] 癌症反应性T细胞使用下面列出的筛选方法进行鉴定。用于分离TCR的方法示于下文。

[0392] TCR名称:4213-PBL-TCR4a3

[0393] P53突变的识别:R248Q

[0394] 筛选方法:p53“热点”突变通用筛选

[0395] 共培养以鉴定TCR:将在用R248Q长肽体外致敏之后的CD4+记忆T细胞与R248Q长肽共培养并分选CD4+41BB+T细胞

[0396] 鉴定TCR的方法:单细胞RT-PCR

[0397] 所有配对的TCR中的TCR的丰度:4.8% (在63对中观察到3次)

[0398] TCR取向: α - β

[0399] 表达载体:SB转座子

[0400] MAYSPGLVSLILLLLGRTRGNSVTQMEGPVTLSEEAFLTINCTYTATGYPSLFWYVQYPGEGLQLLK
ATKADDKGSNKGFEATYRKETTSFHLEKGSVQVSDSAVYFCALSQTGSSNTGKLIFGQGTRLQVKPNIQNPEPAVY
QLKDPRSQDSTLCLFTDFDSQINVPKTMESGTFITDKCVLDMKAMDSKSNGAIAWSNQTSTFCQDIFKETNATYPS
SDVPCDATLTEKSFETDMNLFQNLIVIVLRILLKLVAGFNLLMTLRLWSSRAKRSGSGATNFSLLKQAGDVEENP
GPMHTRLLCWAALCLLGAELTEAGVAQSPRYKIIIEKRQSVAFWCNPI SGHATLYWYQQILGQGPKLLIQFQNNGVV
DDSQLPKDRFSAERLKGVDSTLKIQPAKLEDSAVYLCASSTGGGRHQPQHFGDGTRLSILEDLRNVTPPKVSLFEP
SKAEIANKQKATLVCLARGFFPDHVELSWWVNGKEVHSGVCTDPQAYKESNYSYCLSSRLRVSATFWHNPRNHFR
QVQFHGLSEEDKWPEGSPKPVTQNISAEAWGRADCGITSASYQQGVLSATILYEILLGKATLYAVLVSTLVVMAMV
KRKNS (SEQ ID NO:576)

[0401] 患者4213的TCR 4213-PBL-TCR4a3的统计数据示于下表23中。

[0402] 表23

[0403]

参数	#	频率
总孔	192	100%
CDR3 α	4	2.1%
CDR3 β	36	18.8%

参数	#	频率
4213-PBL-TCR4a3 对	3	1.6%
总配对的 TCR	63	32.8%

[0404] 从患者4213分离的4213-PBL-TCR4a4的序列示于下文。从氨基末端开始,第一加下划线区是CDR1 α (SEQ ID NO:427),第二加下划线区是CDR2 α (SEQ ID NO:428),第三加下划线区是CDR3 α (SEQ ID NO:429),第四加下划线区是CDR1 β (SEQ ID NO:430),第五加下划线区是CDR2 β (SEQ ID NO:431),和第六加下划线区是CDR3 β (SEQ ID NO:432)。粗体区是连接子 (SEQ ID NO:26)。从氨基末端开始,第一加斜体区是 α 链恒定区 (SEQ ID NO:23) 并且第二加斜体区是 β 链恒定区 (SEQ ID NO:25)。 α 链可变区 (SEQ ID NO:433) 包含从氨基末端开始并且就在 α 链恒定区开始之前结束的序列。 β 链可变区 (SEQ ID NO:434) 包含在连接子之后立即开始并且就在 β 链恒定区开始之前结束的序列。全长 α 链 (SEQ ID NO:435) 包含从氨基末端开始并且就在连接子开始之前结束的序列。全长 β 链 (SEQ ID NO:436) 包含在连接子之后立即开始并且以羧基末端结束的序列。

[0405] 癌症反应性T细胞使用下面列出的筛选方法进行鉴定。用于分离TCR的方法示于下文。

[0406] TCR名称:4213-PBL-TCR4a4

[0407] P53突变的识别:R248Q

[0408] 筛选方法:p53“热点”突变通用筛选

[0409] 共培养以鉴定TCR:将在用R248Q长肽体外致敏之后的CD4+记忆T细胞与R248Q长肽共培养并分选CD4+41BB+T细胞

[0410] 鉴定TCR的方法:单细胞RT-PCR

[0411] 所有配对的TCR中的TCR的丰度:3.2% (在63对中观察到2次)

[0412] TCR取向: α - β

[0413] 表达载体:SB转座子

[0414] MAYSPGLVSLILLLLGRTRGNSVTQMEGPVTLSEEAFLTINCTYTATGYPSLFWYVQYPGEGLQLLK
ATKADDKGSNKGFEATYRKETTSFHLEKGSVQVSDSAVYFCALSTTGSSNTGKLIFGQGTTLVKPNIQNPEPAVY
QLKDPRSQDSTLCLFTDFDSQINVPKTMESGTFITDKCVLDMKAMDSKSNGAIAWSNQTSFTCQDIFKETNATYPS
SDVPCDATLTEKSFETDMNLFQNLLVIVLRILLKLVAGFNLLMTLRLWSSRAKRSRSGATNFSLLKQAGDVEENP
GPMHTRLLCWAALCLLGAELTEAGVAQSPRYKIIIEKRQSVAFWCNPI SGHATLYWYQQILGQGPKLLIQFNNGVV
DDSQLPKDRFSAERLKGVDSTLKIQPAKLEDSAVYLCASSTGGGRHQPHFGDGTRLSILEDLRNVTPPKVSLFEP
SKAEIANKQKATLVCLARGFFPDHVELSWWVNGKEVHSGVCTDPQAYKESNYSYCLSSRLRVSATFWHNPRNHFR
QVQFHGLSEEDKWPEGSPKPVTONISAEAWGRADCGITSASYQQGVLSATILYEILLGKATLYAVLVSTLVVMAMV
KRKNS (SEQ ID NO:577)

[0415] 患者4213的TCR 4213-PBL-TCR4a4的统计数据示于下表24中。

[0416] 表24

参数	#	频率
总孔	192	100%
CDR3 α	2	1.0%
CDR3 β	36	18.8%
4213-PBL-TCR4a3对	2	1.0%
总配对的TCR	63	32.8%

[0418] 实施例9

[0419] 该实施例证实了通过在自体T细胞内共培养被诱导以表达突变的p53的自体APC来鉴定患者4268中的抗-突变的p53 T细胞(“p53热点突变通用筛选”)。该实施例还证实了从患者4268分离五种抗-突变的p53TCR。

[0420] 如针对患者4268的图21-24所述进行实验。

[0421] 将来自患者4268的TIL片段(F1-F24, n=24)与用由无关、WT p53或经突变的p53序列组成的TMG电穿孔的自体APC共培养。在37℃下进行共培养过夜。使用ELISPOT测定评价IFN- γ 的分泌。结果示于图21中。

[0422] 将来自患者4268的TIL片段(F1-F24, n=24)与用肽媒介物(DMSO)或由WT p53-R248序列或经突变的p53-R248Q序列组成的经纯化的(>95%,通过HPLC) 25-个氨基酸的肽脉冲的自体APC共培养。在37℃下进行共培养过夜。使用ELISPOT测定评价IFN- γ 的分泌。结果示于图22中。

[0423] 将来自患者4268的TIL片段(F1-F24, n=24)与用肽媒介物(DMSO)或由wt p53-R248序列或经突变的p53-R248Q序列组成的经纯化的(>95%,通过HPLC) 25-个氨基酸的肽脉冲的自体APC共培养。在37℃下进行共培养过夜。对于淋巴细胞→活细胞(PI阴性)→CD3+

(T细胞)设门后,通过流式细胞术评价4-1BB的表达。结果示于23-24中。TIL片段F18和F19是对CD4+41BB+T细胞进行分选后的TCR的来源。TIL片段F7、F8和F15是对CD8+4-1BB+T细胞进行分选后的TCR的来源。

[0424] 从患者4268分离的4268-TCR1的序列示于下文。从氨基末端开始,第一加下划线区是CDR1 α (SEQ ID NO:137),第二加下划线区是CDR2 α (SEQ ID NO:138),第三加下划线区是CDR3 α (SEQ ID NO:139),第四加下划线区是CDR1 β (SEQ ID NO:140),第五加下划线区是CDR2 β (SEQ ID NO:141),和第六加下划线区是CDR3 β (SEQ ID NO:142)。粗体区是连接子 (SEQ ID NO:26)。从氨基末端开始,第一加斜体区是 α 链恒定区 (SEQ ID NO:23) 并且第二加斜体区是 β 链恒定区 (SEQ ID NO:25)。 α 链可变区 (SEQ ID NO:143) 包含从氨基末端开始并且在 α 链恒定区开始之前就结束的序列。 β 链可变区 (SEQ ID NO:144) 包含在连接子之后立即开始并且在 β 链恒定区开始之前就结束的序列。全长 α 链 (SEQ ID NO:145) 包含从氨基末端开始并且在连接子开始之前就结束的序列。全长 β 链 (SEQ ID NO:146) 包含在连接子之后立即开始并且以羧基末端结束的序列。

[0425] 癌症反应性T细胞使用下面列出的筛选方法进行鉴定。用于分离TCR的方法示于下文。

[0426] TCR名称:4268-TCR1

[0427] P53突变的识别:R248Q

[0428] 方法:p53“热点”突变通用筛选

[0429] 共培养以鉴定TCR:共培养4268-F7和4268-F8与p53-R248Q长肽,分选CD8+41BB+T细胞

[0430] 鉴定TCR的方法:单细胞RT-PCR

[0431] 所有配对的TCR中的TCR的丰度:78.7% (在61对中观察到48次)

[0432] TCR取向: α - β

[0433] 表达载体:SB转座子

[0434] MASLRVLLVILWLQLSWVWSQQKEVEQNSGPLSVPEGAIASLNCTYSDRGSQSFFWYRQYSGKSPELIMFIYSNGDKEDGRFTAQLNKASQYVSLLIRDSQPSDSATYLCVSWYSTLTFGKGTMLLVSPNIQNPEPAVYQLKDPRSQDSTLCLFTDFDSQINVPKTMESGTFITDKCVLDMKAMDSKSNGAIAWSNQTSTFCQDIFKETNATYPSSDVP CDATLTEKSFETDMNLFQNLVIVLRILLKLVAGFNLLMTLRLWSSRAKRS¹SGSGATNFSLLKQAGDVEENPGPMHTRLFFYVALCLLWAGHRDAGITQSPRYKITETGRQVTLMCHQTWSHSYMFWYRQDLGHGLRLIYYSAAADITDKGEVPDGYVVSRSKTENFPLTLESATRSQTSVYFCASSGSRTDTQYFGPGTRLTVLEDLRNVTTPPKVSLFEPSKAEIANKQKATLVCLARGFFPDHVELSWVWNGKEVHSGVCTDPQAYKESNYSYCLSSRLRVSATFWHNPRNHFRQVQFHGLSEEDKWPEGSPKPVQTQNISAEAWGRADCGITSASYQQGVLSATILYEILLGKATLYAVLVSTLVVMAMVVRKNS (SEQ ID NO:578)

[0435] 患者4268的TCR 4268-TCR1的统计数据示于下表25中。

[0436] 表25

[0437]	参数	#	频率
	总孔	96	100%

CDR3 α	54	56.3%
CDR3 β	71	74.0%
4268-TCR1 对	48	50.0%
总配对的 TCR	61	63.5%

[0438] 从患者4268分离的4268-TCR2的序列示于下文。从氨基末端开始,第一加下划线区是CDR1 α (SEQ ID NO:147),第二加下划线区是CDR2 α (SEQ ID NO:148),第三加下划线区是CDR3 α (SEQ ID NO:149),第四加下划线区是CDR1 β (SEQ ID NO:150),第五加下划线区是CDR2 β (SEQ ID NO:151),和第六加下划线区是CDR3 β (SEQ ID NO:152)。粗体区是连接子 (SEQ ID NO:26)。从氨基末端开始,第一加斜体区是 α 链恒定区 (SEQ ID NO:23) 并且第二加斜体区是 β 链恒定区 (SEQ ID NO:25)。 α 链可变区 (SEQ ID NO:153) 包含从氨基末端开始并且在 α 链恒定区开始之前就结束的序列。 β 链可变区 (SEQ ID NO:154) 包含在连接子之后立即开始并且就 β 链恒定区开始之前结束的序列。全长 α 链 (SEQ ID NO:155) 包含从氨基末端开始并且就在连接子开始之前结束的序列。全长 β 链 (SEQ ID NO:156) 包含在连接子之后立即开始并且以羧基末端结束的序列。

[0439] 癌症反应性T细胞使用下面列出的筛选方法进行鉴定。用于分离TCR的方法示于下文。

[0440] TCR名称:4268-TCR2

[0441] P53突变的识别:R248Q

[0442] 方法:p53“热点”突变通用筛选

[0443] 共培养以鉴定TCR:共培养4268-F7和4268-F8与p53-R248Q长肽,分选CD8+41BB+T细胞

[0444] 鉴定TCR的方法:单细胞RT-PCR

[0445] 所有配对的TCR中的TCR的丰度:6.6% (在61对中观察到4次)

[0446] TCR取向: α - β

[0447] 表达载体:SB转座子

[0448] MALKFSVSILWQLAWVSTQLLEQSPQFLSIQEGENLTVYCNSSSVFSSLQWYRQEPGEGPVLLVTVV
TGGEVKKLRLTFQFGDARKDSSLHITAAQPGDTGLYLCAGEFAGNQFYFGTGTSLTVIPNIQNPEPAVYQLKDPR
SQDSTLCLFTDFDSQINVPKTMESGTFITDKCVLDMKAMDSKSNGAIAWSNQTSTFCQDIFKETNATYPSSDVPCD
ATLTEKSFETDMNLNFQNLIVLRILLKLVAGFNLLMTLRLWSSRAKRSGSGATNFSLLKQAGDVEENPGPMHCR
LLCCAVALCLLGAVPIDTEVTQTPKHLVMGMTNKKSLKCEQHMGHRAMYWYKQKAKKPPPELMFVYSYEKLSINESVP
SRFSPECNSSLNLHLHALQPEDSALYLCASSQVGLTYEQYFGPGTRLTVTEDLRNVTTPKVSLFEPKAEIANK
QKATLVCLARGFFPDHVELSWVNGKEVHSGVCTDPQAYKESNYSYCLSSRLRVSATFWHNPRNHFRQCQVQFHGLS
EEDKWPEGSPKPVTONISAEAWGRADCGITSASYQQGVLSATILYEILLGKATLYAVLVSTLVMMAMVKRKN (SEQ
ID NO:579)

[0449] 患者4268的TCR 4268-TCR2的统计数据示于下表26中。

[0450] 表26

[0451]	参数	#	频率

总孔	96	100%
CDR3 α	6	6.3%
CDR3 β	4	4.2%
4268-TCR2对	4	4.2%
总配对的TCR	61	63.5%

[0452] 从患者4268分离的4268-TCR3的序列示于下文。从氨基末端开始,第一加下划线区是CDR1 α (SEQ ID NO:157),第二加下划线区是CDR2 α (SEQ ID NO:158),第三加下划线区是CDR3 α (SEQ ID NO:159),第四加下划线区是CDR1 β (SEQ ID NO:160),第五加下划线区是CDR2 β (SEQ ID NO:161),和第六加下划线区是CDR3 β (SEQ ID NO:162)。粗体区是连接子 (SEQ ID NO:26)。从氨基末端开始,第一加斜体区是 α 链恒定区 (SEQ ID NO:23) 并且第二加斜体区是 β 链恒定区 (SEQ ID NO:25)。 α 链可变区 (SEQ ID NO:163) 包含从氨基末端开始并且在 α 链恒定区开始之前就结束的序列。 β 链可变区 (SEQ ID NO:164) 包含在连接子之后立即开始并且就在 β 链恒定区开始之前就结束的序列。全长 α 链 (SEQ ID NO:165) 包含从氨基末端开始并且就在连接子开始之前就结束的序列。全长 β 链 (SEQ ID NO:166) 包含在连接子之后立即开始并且以羧基末端结束的序列。

[0453] 癌症反应性T细胞使用下面列出的筛选方法进行鉴定。用于分离TCR的方法示于下文。

[0454] TCR名称:4268-TCR3

[0455] P53突变的识别:R248Q

[0456] 方法:p53“热点”突变通用筛选

[0457] 共培养以鉴定TCR:共培养4268-F15与p53-R248Q长肽,分选CD8+41BB+T细胞

[0458] 鉴定TCR的方法:单细胞RT-PCR

[0459] 所有配对的TCR中的TCR的丰度:88.6% (在35对中观察到31次)

[0460] TCR取向: α - β

[0461] 表达载体:SB转座子

[0462] MASAPISMLAMLFTLSGLRAQSVAQPEDQVNVAEGNPLTVKCTYSVSGNPYLFWYVQYPNRGLQFLK
YITGDNLVKGSYGFEAEFNKSQTSFHLKKPSALVSDSALYFC~~AVRDNSGGSNYKLTFGKG~~TLLTVNPNIQNPEPAV
YQLKDPRSQDSTLCLFTDFDSQINVPKTMESGTFITDKCVLDMKAMDSKNGAIAWSNQTSTFCQDIFKETNATYP
SSDVPCDATLTEKSFETDMNLFQNLIVIVLRILLKLVAGFNLLMTLRLWSSRAKRSGSGATNFSLLKQAGDVEEN
PGPMHTRLLCWAALCLLGAELTEAGVAQSPRYKIIIEKRQSVAFWCNPI~~SGHATLYWYQQILGQGP~~KLLIQFQNGV
VDDSQLPKDRFSAERLKGVDSTLKIQPAKLEDSAVYLC~~ASSLGQGQTQYFGPG~~TRLLVLEDLRNVTTPPKVSLFEPS
KAEIANKQKATLVCLARGFFPDHVELSWVNGKEVHSGVCTDPQAYKESNYSYCLSSRLRVSATFWHNPRNHFRCQ
VQFHGLSEEDKWPEGSPKPV~~TQ~~NISAEAWGRADCGITSASYQ~~QGVLSATILYEILLG~~KATLYAVLVSTLVMMAMVK
RKNS (SEQ ID NO:580)

[0463] 患者4268的TCR 4268-TCR3的统计数据示于下表27中。

[0464] 表27

[0465]

参数	#	频率
总孔	96	100%
CDR3 α	42	43.8%

CDR3 β	37	38.5%
4268-TCR3对	31	32.3%
总配对的TCR	35	36.5%

[0466] 从患者4268分离的4268-TCR4的序列示于下文。从氨基末端开始,第一加下划线区是CDR1 α (SEQ ID NO:167),第二加下划线区是CDR2 α (SEQ ID NO:168),第三加下划线区是CDR3 α (SEQ ID NO:169),第四加下划线区是CDR1 β (SEQ ID NO:170),第五加下划线区是CDR2 β (SEQ ID NO:171),和第六加下划线区是CDR3 β (SEQ ID NO:172)。粗体区是连接子 (SEQ ID NO:26)。从氨基末端开始,第一加斜体区是 α 链恒定区 (SEQ ID NO:23) 并且第二加斜体区是 β 链恒定区 (SEQ ID NO:25)。 α 链可变区 (SEQ ID NO:173) 包含从氨基末端开始并且就在 α 链恒定区开始之前结束的序列。 β 链可变区 (SEQ ID NO:174) 包含在连接子之后立即开始并且就在 β 链恒定区开始之前结束的序列。全长 α 链 (SEQ ID NO:175) 包含从氨基末端开始并且在连接子开始之前就结束的序列。全长 β 链 (SEQ ID NO:176) 包含在连接子之后立即开始并且以羧基末端结束的序列。

[0467] 癌症反应性T细胞使用下面列出的筛选方法进行鉴定。用于分离TCR的方法示于下文。

[0468] TCR名称:4268-TCR4

[0469] P53突变的识别:R248Q

[0470] 方法:p53“热点”突变通用筛选

[0471] 共培养以鉴定TCR:共培养4268-F18与p53-R248Q长肽,分选CD4+41BB+T细胞

[0472] 鉴定TCR的方法:单细胞RT-PCR

[0473] 所有配对的TCR中的TCR的丰度:95.2% (在42对中观察到40次)

[0474] TCR取向: α - β

[0475] 表达载体:SB转座子

[0476] MALLLVPAFQVIFTLGGTRAQSVTQLDSQVPVFEEAPVELRCNYSSSVSVYLFWYVQYPNQGLQLLLK
YLSGSTLVESINGFEAEFNKSQTSFHLRKPSVHISDTAEYFCAVRGSSGTYKYIFGTGTRLKVLANIQNPEPAVYQ
LKDPRSQDSTLCLFTDFDSQINVPKTMESGTFITDKCVLDMKAMDSKSNGAIAWSNQTSFTCQDIFKETNATYPSS
DVPCDATLTEKSFETDMNLFQNLVIVLRILLKLVAGFNLLMTLRLWSSRAKRSGSGATNFSLLKQAGDVEENPG
PMHIRLLCRVAFCLAVGLVDVKVTQSSRYLVKRTGEKVFLECVQDMDHENMFWYRQDPGLGLRLIYFSYDVKMKE
KGDIPGYSVSREKKERFSLILESASTNQTSMYLCASKGDQNTAEFFGQGTRLTVVEDLRNVTPPKVSLFEPSKAE
IANKQKATLVCLARGFFPDHVELSWWVNGKEVHSGVCTDPQAYKESNYSYCLSSRLRVSATFWHNPRNHFRQVQF
HGLSEEDKWPEGSPKPVTONISAEAWGRADCGITSASYQQGVLSATILYEILLGKATLYAVLVSTLVMMAMVKRKNS
(SEQ ID NO:581)

[0477] 患者4268的TCR 4268-TCR4的统计数据示于下表28中。

[0478] 表28

参数	#	频率
总孔	96	100%
CDR3 α	43	44.8%
CDR3 β	53	55.2%
4268-TCR4对	40	41.7%

总配对的TCR	42	43.8%

[0480] 从患者4268分离的4268-TCR5的序列示于下文。从氨基末端开始,第一加下划线区是CDR1 α (SEQ ID NO:177),第二加下划线区是CDR2 α (SEQ ID NO:178),第三加下划线区是CDR3 α (SEQ ID NO:179),第四加下划线区是CDR1 β (SEQ ID NO:180),第五加下划线区是CDR2 β (SEQ ID NO:181),和第六加下划线区是CDR3 β (SEQ ID NO:182)。粗体区是连接子 (SEQ ID NO:26)。从氨基末端开始,第一加斜体区是 α 链恒定区 (SEQ ID NO:23) 并且第二加斜体区是 β 链恒定区 (SEQ ID NO:25)。 α 链可变区 (SEQ ID NO:183) 包含从氨基末端开始并且在 α 链恒定区开始之前就结束的序列。 β 链可变区 (SEQ ID NO:184) 包含在连接子之后立即开始并且就在 β 链恒定区开始之前结束的序列。全长 α 链 (SEQ ID NO:185) 包含从氨基末端开始并且就在连接子开始之前结束的序列。全长 β 链 (SEQ ID NO:186) 包含在连接子之后立即开始并且以羧基末端结束的序列。

[0481] 癌症反应性T细胞使用下面列出的筛选方法进行鉴定。用于分离TCR的方法示于下文。

[0482] TCR名称:4268-TCR5

[0483] P53突变的识别:R248Q

[0484] 方法:p53“热点”突变通用筛选

[0485] 共培养以鉴定TCR:共培养4268-F19与p53-mut-TMG,分选CD4+41BB+T细胞

[0486] 鉴定TCR的方法:单细胞RT-PCR

[0487] 所有配对的TCR中的TCR的丰度:11.8% (在17对中观察到2次)

[0488] TCR取向: α - β

[0489] 表达载体:SB转座子

[0490] MAGVFLLYVSMKMGTTGQNIDQPTMTATEGAIVQINCTYQTSGFNGLFWYQQHAGEAPTFLSYNVL
DGLEEKGRFSSFLSRSGYSYLLKELQMKDSASYLCAVRDLQTGANNLFFGTGTRLTVIPNIQNPEPAVYQLKDP
RSQDSTLCLFTDFDSQINVPKTMESGTFITDKCVLDMKAMDSKSNGAIAWSNQTSTFCQDIFKETNATYPSSDVPC
DATLTEKSFETDMNLFQNLVIVLRILLKLVAGFNLLMTLRLWSSRAKRSGSGATNFSLLKQAGDVEENPGPMHI
RLLCRVAFCLAVGLVDVKVTQSSRYLVKRTGEKVFLECVQDMDHENMFWYRQDPGLGLRLIYFSYDVKMKEKGDI
PEGYSVSREKKERFSLILESASTNQTSMYLCASSLTFGTTEAFFGQGTRLTVVEDLRNVTTPPKVSLFEPSKAEIAN
KQKATLVCLARGFFPDHVELSWVNGKEVHSGVCTDPQAYKESNYSYCLSSRLRVSATFWHNPRNHFRQVQFHGL
SEEDKWPEGSPKPVTQNISAEAWGRADCGITSASYQQGVLSATILYEILLGKATLYAVLVSTLVVMAMVKRKN
(SEQ ID NO:582)

[0491] 患者4268的TCR 4268-TCR5的统计数据示于下表29中。

[0492] 表29

参数	#	频率
总孔	96	100%
CDR3 α	2	2.1%
CDR3 β	87	90.6%
4268-TCR5对	2	2.1%
总配对的TCR	17	17.7%

[0494] 实施例10

[0495] 该实施例证实了通过在自体T细胞内共培养被诱导以表达突变的p53的自体APC来鉴定患者4266中的抗-突变的p53 T细胞(“p53热点突变通用筛选”)。该实施例还证实了从患者4266分离四种抗-突变的p53TCR。

[0496] 如图25-31针对患者4266所述进行实验。

[0497] 将来自患者4266的TIL片段(F1-F24, n=24)与用由无关、WT p53或经突变的p53序列组成的TMG电穿孔的自体APC共培养。在37℃下进行共培养过夜。使用ELISPOT测定评价IFN- γ 的分泌。结果显示于图25中。对于淋巴细胞→活细胞(PI阴性)→CD3+(T细胞)设门后,通过流式细胞术评价4-1BB的表达。结果显示于图26中。

[0498] 将来自患者4266的TIL片段(F1-F24, n=24)与用肽媒介物(DMSO)或由WT p53-R248序列或经突变的p53-R248W序列组成的经纯化的(>95%,通过HPLC)25-个氨基酸的肽脉冲的自体APC共培养。在37℃下进行共培养过夜。使用ELISPOT测定评价IFN- γ 的分泌。结果显示于图27中。对于淋巴细胞→活细胞(PI阴性)→CD3+(T细胞)设门后,通过流式细胞术评价4-1BB的表达。结果显示于图28中。

[0499] 将Cos7细胞(每孔 2.5×10^4 个)涂铺在平底96孔板的各孔上。第二天,将细胞与来自患者4266的单独HLA等位基因共转染。次日,将细胞用无肽、DMSO、WT p53-R248肽SSCMGGMNRR(SEQ ID NO:590)或经突变的p53-R248W肽SSCMGGMNWR(SEQ ID NO:591)在37℃下以1 μ g/mL脉冲2小时。将来自患者4266的TIL培养物(10^5)添加至各孔并在37℃下共培养过夜。对于淋巴细胞→活细胞(PI阴性)→CD3+(T细胞)→CD4-CD8+设门后,通过流式细胞术评价4-1BB的表达。结果显示于图29中。

[0500] 将对从4266-TIL鉴定的p53-R248W具有假定特异性的表达模拟物(无TCR)、4266-TCR1、4266-TCR2、4266-TCR3或4266-TCR4的T细胞与用肽媒介物(DMSO)或由WT p53-R248序列或经突变的p53-R248W序列组成的经纯化的(>95%,通过HPLC)25个氨基酸的肽脉冲的自体APC共培养。单独的培养基及PMA和离子霉素分别为阴性对照和阳性对照。在37℃下进行共培养过夜。对于淋巴细胞→活细胞(PI阴性)→CD3+(T细胞)→CD4-CD8+设门后,通过流式细胞术评价4-1BB的表达。结果显示于图30中。

[0501] 肿瘤细胞(TC)系由从患者4266切除的异种移植的肿瘤碎片建立,然后通过免疫受损的小鼠连续传代(TC#4266)。将TC#4266与表达模拟物(无TCR)或p53-R248W-特异性TCR(4266-TCR2、4266-TCR3或4266-TCR4)的T细胞(10^5)在37℃下共培养过夜。将TC#4266细胞不与任何东西孵育、或者将TC#4266细胞与W6/32泛-HLA I类特异性阻断抗体、IVA12泛-HLA II类特异性阻断抗体或突变的p53-R248W肽SSCMGGMNWR(SEQ ID NO:591)在37℃下孵育2小时。将抗体以5 μ g/mL的终浓度保存在共培养物中。将肽以1 μ g/mL孵育,并且孵育后洗涤过量肽。单独的培养基(无TC)及PMA和离子霉素分别为阴性对照和阳性对照。对于淋巴细胞→活细胞(PI阴性)→CD3+(T细胞)→CD4-CD8+设门后,通过流式细胞术评价4-1BB的表达。结果显示于图31中。

[0502] 从患者4266分离的4266-TCR1的序列示于下文。从氨基末端开始,第一加下划线区是CDR1 α (SEQ ID NO:97),第二加下划线区是CDR2 α (SEQ ID NO:98),第三加下划线区是CDR3 α (SEQ ID NO:99),第四加下划线区是CDR1 β (SEQ ID NO:100),第五加下划线区是CDR2 β (SEQ ID NO:101),和第六加下划线区是CDR3 β (SEQ ID NO:102)。粗体区是连接子(SEQ ID NO:26)。从氨基末端开始,第一加斜体区是 α 链恒定区(SEQ ID NO:23)并且第二加斜体区是

β链恒定区 (SEQ ID NO:25)。α链可变区 (SEQ ID NO:103) 包含从氨基末端开始并且在α链恒定区开始之前就结束的序列。β链可变区 (SEQ ID NO:104) 包含在连接子之后立即开始并且就在β链恒定区开始之前就结束的序列。全长α链 (SEQ ID NO:105) 包含从氨基末端开始并且就在连接子开始之前就结束的序列。全长β链 (SEQ ID NO:106) 包含在连接子之后立即开始并且以羧基末端结束的序列。

[0503] 癌症反应性T细胞使用下面列出的筛选方法进行鉴定。用于分离TCR的方法示于下文。

[0504] TCR名称:4266-TCR1

[0505] P53突变的识别:R248W

[0506] 筛选方法:p53“热点”突变通用筛选

[0507] 共培养以鉴定TCR:共培养4266-F1、4266-F3、4266-F5和4266-F6与p53mutTMG或R248W长肽(两次共培养均检测相同的TCR),分选CD8+41BB+T细胞

[0508] 鉴定TCR的方法:单细胞RT-PCR

[0509] 所有配对的TCR中的TCR的丰度:17.0%(在53对中观察到9次)

[0510] TCR取向:α-β

[0511] 表达载体:SB转座子

[0512] MALLLVPAFQVIFTLGGTRAQSVTQLDSQVPVFEEAPVELRCNYSSSVSVYLFWYVQYPNQGLQLLLK
YLSGSTLVESINGFEAEFNKSQTSFHLRKPSVHISDTAEYFCVSDLVRRDKIIFGKGTSLHILPNIQNPEPAVYQ
LKDPRSQDSTLCLFTDFDSQINVPKTMESGTFITDKCVLDMKAMDSKSNGAIAWSNQTSFTCDIFKETNATYPSS
DVPCDATLTEKSFETDMNLNFQNLVIVLRILLKLVAGFNLLMTLRLWSSRAKRSGSGATNFSLLKQAGDVEENPG
PMHIGLLCCVAFSLLWASPVNAGVTQTPKFQVLKTGQSMTLQCAQDMNHNSMYWYRQDPGMGLRLIYYSASEGTTD
KGEVPNGYNVSRLNKRFSRLRESAAPSQTSVYFCASIGGFEEAFFGQGTSLTVVEDLRNVTPPKVSLFEPKAEIA
NKQKATLVCLARGFFPDHVELSWVNGKEVHSGVCTDPQAYKESNYSYCLSSRLRVSATFWHNPRNHFRCQVQFHG
LSEEDKWPEGSPKPVQTQNISAEAWGRADCGITSASYQQGVLSATILYEILLGKATLYAVLVSTLVMMAMVKRKN
(SEQ ID NO:583)

[0513] 患者4266的TCR 4266-TCR1的统计数据示于下表30中。

[0514] 表30

参数	#	频率
总孔	96	100%
CDR3α	9	9.4%
CDR3β	10	10.4%
4266-TCR1对	9	9.4%
总配对的TCR	53	55.2%

[0516] 从患者4266分离的4266-TCR2的序列示于下文。从氨基末端开始,第一加下划线区是CDR1α (SEQ ID NO:107),第二加下划线区是CDR2α (SEQ ID NO:108),第三加下划线区是CDR3α (SEQ ID NO:109),第四加下划线区是CDR1β (SEQ ID NO:110),第五加下划线区是CDR2β (SEQ ID NO:111),和第六加下划线区是CDR3β (SEQ ID NO:112)。粗体区是连接子 (SEQ ID NO:26)。从氨基末端开始,第一加斜体区是α链恒定区 (SEQ ID NO:23) 并且第二加斜体区是β链恒定区 (SEQ ID NO:25)。α链可变区 (SEQ ID NO:113) 包含从氨基末端开始并

且在 α 链恒定区开始之前就结束的序列。 β 链可变区 (SEQ ID NO:114) 包含在连接子之后立即开始并且在 β 链恒定区开始之前就结束的序列。全长 α 链 (SEQ ID NO:115) 包含从氨基末端开始并且在连接子开始之前就结束的序列。全长 β 链 (SEQ ID NO:116) 包含在连接子之后立即开始并且以羧基末端结束的序列。

[0517] 癌症反应性T细胞使用下面列出的筛选方法进行鉴定。用于分离TCR的方法示于下文。

[0518] TCR名称:4266-TCR2

[0519] P53突变的识别:R248W

[0520] 筛选方法:p53“热点”突变通用筛选

[0521] 共培养以鉴定TCR:共培养4266-F1、4266-F3、4266-F5和4266-F6与p53mutTMG或R248W长肽(两次共培养均检测相同的TCR),分选CD8+41BB+T细胞

[0522] 鉴定TCR的方法:单细胞RT-PCR

[0523] 所有配对的TCR中的TCR的丰度:24.5%(在53对中观察到13次)

[0524] TCR取向: α - β

[0525] 表达载体:SB转座子

[0526] MAGVFLLYVSMKMGTTGQNIDQPTMTATEGAIVQINCTYQTSGFNGLFWYQQHAGEAPTFLSYNVLDGLEEKGRFSSFLSRSGYSYLLKELQMKDSASYLCAVYTGGFKTIFGAGTRLFVKANIQNPEPAVYQLKDPRSQDSTLCLFTDFDSQINVPKTMESGTFITDKCVLDMKAMDSKSNGAIAWSNQTSTFCQDIFKETNATYPSSDVPCDATLTEKSFETDMNLNFQNLVIVLRILLKLVAGFNLLMTLRLWSSRAKRSGSGATNFSLLKQAGDVEENPGPMHTRLLCWAALCCLGAELTEAGVAQSPRYKIIIEKRQSVAFWCNPI SGHATLYWYQQILGQGPKLLIQFQNNGVVDDSQLPKDRFSAERLKGVDSTLKIQPAKLEDSAVYLCASNLGSGSTDTQYFGPGTRLTVLEDLRNVTPPKVSLFEPKAEIANKQKATLVCLARGFFPDHVELSWVWNGKEVHSGVCTDPQAYKESNYSYCLSSRLRVSATFWHNPRNHFRCQVQFHGLSEEDKWPEGSPKPVTTQNISAEAWGRADCGITSASYQQGVLSATILYEILLGKATLYAVLVSTLVMMAMVKRKNS (SEQ ID NO:584)

[0527] 患者4266的TCR 4266-TCR2的统计数据示于下表31中。

[0528] 表31

参数	#	频率
总孔	96	100%
CDR3 α	21	21.9%
CDR3 β	18	18.8%
4266-TCR2对	13	13.5%
总配对的TCR	53	55.2%

[0530] 从患者4266分离的4266-TCR3的序列示于下文。从氨基末端开始,第一加下划线区是CDR1 α (SEQ ID NO:117),第二加下划线区是CDR2 α (SEQ ID NO:118),第三加下划线区是CDR3 α (SEQ ID NO:119),第四加下划线区是CDR1 β (SEQ ID NO:120),第五加下划线区是CDR2 β (SEQ ID NO:121),和第六加下划线区是CDR3 β (SEQ ID NO:122)。粗体区是连接子 (SEQ ID NO:26)。从氨基末端开始,第一加斜体区是 α 链恒定区 (SEQ ID NO:23) 并且第二加斜体区是 β 链恒定区 (SEQ ID NO:25)。 α 链可变区 (SEQ ID NO:123) 包含从氨基末端开始并且在 α 链恒定区开始之前就结束的序列。 β 链可变区 (SEQ ID NO:124) 包含在连接子之后立

即开始并且在β链恒定区开始之前就结束的序列。全长α链(SEQ ID NO:125)包含从氨基末端开始并且就在连接子开始之前结束的序列。全长β链(SEQ ID NO:126)包含在连接子之后立即开始并且以羧基末端结束的序列。

[0531] 癌症反应性T细胞使用下面列出的筛选方法进行鉴定。用于分离TCR的方法示于下文。

[0532] TCR名称:4266-TCR3

[0533] P53突变的识别:R248W

[0534] 筛选方法:p53“热点”突变通用筛选

[0535] 共培养以鉴定TCR:共培养4266-F1、4266-F3、4266-F5和4266-F6与p53mutTMG或R248W长肽(两次共培养均检测相同的TCR),分选CD8+41BB+T细胞

[0536] 鉴定TCR的方法:单细胞RT-PCR

[0537] 所有配对的TCR中的TCR的丰度:34.0%(在53对中观察到18次)

[0538] TCR取向:α-β

[0539] 表达载体:SB转座子

[0540] MAGVFLLYVSMKMGTTGQNIDQPTMTATEGAIVQINCTYQTSGFNGLFWYQQHAGEAPTFLSYNVLDGLEEKGRFSSFLSRSGYSYLLKELQMKDSASYLCAFYYGGSQGNLIFGKGTKLSVKPNIQNPEPAVYQLKDPRSQDSTLCLFTDFDSQINVPKTMESGTFITDKCVLDMKAMDSKSNGAIAWSNQTSFTCQDIFKETNATYPSSDVPCD
ATLTEKSFETDMNLNFQNLVIVLRILLKLVAGFNLLMTLRLWSSRAKRSGSGATNFSLLKQAGDVEENPGPMHTR
LLCWVVLGFLGTDHTGAGVSQSPRYKVAKRGQDVALRCDPISGHVSLFWYQQALGQGPEFLTYFQNEAQLDKSGLP
SDRFFAERPEGSVSTLKIQRTOQEDSAVYLCASSFGSGSTDTQYFGPGTRLTVLEDLRNVTPPKVSLFEPKAEIA
NKQKATLVCLARGFFPDHVELSWVNGKEVHSGVCTDPQAYKESNYSYCLSSRLRVSATFWHNPRNHFRCQVQFHG
LSEEDKWPEGSPKPVTONISAEAWGRADCGITSASYQQGVLSATILYEILLGKATLYAVLVSTLVVMAMVKRKN
(SEQ ID NO:585)

[0541] 患者4266的TCR 4266-TCR3的统计数据示于下表32中。

[0542] 表32

参数	#	频率
总孔	96	100%
CDR3α	19	19.8%
CDR3β	26	27.1
4266-TCR3对	18	18.8%
总配对的TCR	53	55.2%

[0544] 从患者4266分离的4266-TCR4的序列示于下文。从氨基末端开始,第一加下划线区是CDR1α(SEQ ID NO:127),第二加下划线区是CDR2α(SEQ ID NO:128),第三加下划线区是CDR3α(SEQ ID NO:129),第四加下划线区是CDR1β(SEQ ID NO:130),第五加下划线区是CDR2β(SEQ ID NO:131),和第六加下划线区是CDR3β(SEQ ID NO:132)。粗体区是连接子(SEQ ID NO:26)。从氨基末端开始,第一加斜体区是α链恒定区(SEQ ID NO:23)并且第二加斜体区是β链恒定区(SEQ ID NO:25)。α链可变区(SEQ ID NO:133)包含从氨基末端开始并且就在α链恒定区开始之前结束的序列。β链可变区(SEQ ID NO:134)包含在连接子之后立即开始并且就在β链恒定区开始之前结束的序列。全长α链(SEQ ID NO:135)包含从氨基末

端开始并且就在连接子开始之前结束的序列。全长 β 链 (SEQ ID NO:136) 包含在连接子之后立即开始并且以羧基末端结束的序列。

[0545] 癌症反应性T细胞使用下面列出的筛选方法进行鉴定。用于分离TCR的方法示于下文。

[0546] TCR名称:4266-TCR4

[0547] P53突变的识别:R248W

[0548] 筛选方法:p53“热点”突变通用筛选

[0549] 共培养以鉴定TCR:共培养4266-F1、4266-F3、4266-F5和4266-F6与p53mutTMG或R248W长肽(两次共培养均检测相同的TCR),分选CD8+41BB+T细胞

[0550] 鉴定TCR的方法:单细胞RT-PCR

[0551] 所有配对的TCR中的TCR的丰度:9.4%(在53对中观察到5次)

[0552] TCR取向: α - β

[0553] 表达载体:SB转座子

[0554] MAGVFLLYVSMKMGTTGQNIDQPTMTATEGAIVQINCTYQTSGFNGLFWYQQHAGEAPTFLSYNVLDGLEEKGRFSSFLSRSKGYSYLLKELQMKDSASYLCAYPPGGSQGNLIFGKGTKLSVKPNIQNPEPAVYQLKDPRSQDSTLCLFTDFDSQINVPKTMESGTFITDKCVLDMKAMDSKSNGAIAWSNQTSTFCQDIFKETNATYPSSDVPCD
ATLTEKSFETDMNLNLFQNLVIVLRILLKLVAGFNLLMTLRLWSSRAKRSRSGSGATNFSLLKQAGDVEENPGPMHTR
LLCWAALCCLGAELTEAGVAQSPRYKIIIEKRQSVAFWCNPIISGHATLYWYQQILGQGPKLLIQFQNNGVVDDSQLP
KDRFSAERLKGVDSTLKIIPAKLEDSAVYLCASSLGTGSDTQYFGPGTRTLTVLEDLRNVTPPKVSLFEPKAEIA
NKQKATLVCLARGFFPDHVELSWWVNGKEVHSGVCTDPQAYKESNYSYCLSSRLRVSATFWHNPRNHFRCQVQFHG
LSEEDKWPEGPSKPVQTQNISAEAWGRADCGITSASYQQGVLSATILYEILLGKATLYAVLVSTLVVMAMVKRKN
(SEQ ID NO:586)

[0555] 患者4266的TCR 4266-TCR4的统计数据示于下表33中。

[0556] 表33

参数	#	频率
总孔	96	100%
CDR3 α	5	5.2%
CDR3 β	13	13.5
4266-TCR3对	5	5.2%
总配对的TCR	53	55.2%

[0558] 实施例11

[0559] 该实施例证实了通过在自体T细胞内共培养被诱导以表达突变的p53的自体APC来鉴定患者4252中的抗-突变的p53 T细胞(“p53热点突变通用筛选”)。

[0560] TIL片段F1、F3、F7和F19患者4252用作效应器。将T细胞效应器和自体APC(不成熟的DC)的共培养物(1)用由无关、WT p53或经突变的p53序列组成的TMG电穿孔或(2)用肽媒介物(DMSO)或由WT p53-R175序列或突变的p53-R175H序列组成的经纯化的(>95%,通过HPLC)25个氨基酸的肽脉冲。仅T细胞(无靶标)是阴性对照并且PMA和Iono是阳性对照。在37℃下进行共培养过夜。通过流式细胞术评价4-1BB在CD3+CD8-CD4+T细胞上的表达。结果显示于图38中。

[0561] 实施例12

[0562] 该实施例证实了通过在自体T细胞内共培养被诱导以表达突变的p53的自体APC来鉴定患者4270中的抗-突变的p53 T细胞(“p53热点突变通用筛选”)。

[0563] TIL片段F13和F16患者4270用作效应器。与T细胞效应器和自体APC(不成熟的DC)的共培养物(1)用由无关、WT p53或突变的p53序列组成的TMG电穿孔,或(2)用肽媒介物(DMSO)或由WT p53-R282序列或经突变的p53-R282W序列组成的经纯化的(>95%,通过HPLC) 25个氨基酸的肽脉冲。T细胞仅是阴性对照,并且PMA和Iono是阳性对照。在37℃下进行共培养过夜。使用ELISPOT测定评价IFN- γ 的分泌。结果显示于图39中。

[0564] 实施例13

[0565] 该实施例证实了通过在自体T细胞内共培养被诱导以表达突变的p53的自体APC来鉴定患者4285中的抗-突变的p53 T细胞(“p53热点突变通用筛选”)。

[0566] 将来自患者4285的TIL片段(F1-F22和F24, n=18)与用由无关、WT p53或经突变的p53序列组成的TMG电穿孔的自体APC共培养。在37℃下进行共培养过夜。使用ELISPOT测定评价IFN- γ 的分泌。结果显示于图40中。对于淋巴细胞→活细胞(PI阴性)→CD3+(T细胞)设门后,通过流式细胞术评价4-1BB的表达。结果显示于图42中。

[0567] 将来自患者4285的TIL片段(F1-F22和F24, n=18)与用肽媒介物(DMSO)或由WT p53-R175序列或突变的p53-R175H序列组成的经纯化的(>95%,通过HPLC) 25个氨基酸的肽脉冲的自体APC共培养。在37℃下进行共培养过夜。使用ELISPOT测定评价IFN- γ 的分泌。结果显示于图41中。对于淋巴细胞→活细胞(PI阴性)→CD3+(T细胞)设门后,通过流式细胞术评价4-1BB的表达。结果显示于图43中。

[0568] 将自体APC用来自p53-R175H序列(表34中加下划线的氨基酸取代)的重叠14个氨基酸的15个氨基酸的肽脉冲。将对p53-R175H具有特异性的来自患者4285的TIL(片段培养物10、6和9)与肽-脉冲的APC在37℃下共培养过夜。DMSO是肽媒介物。使用ELISPOT测定评价IFN- γ 的分泌。结果显示于表34中。

[0569] 表34

		ELISPOT 结果 对于 IFN- γ 产生呈阳性(+)或阴性(-)		
肽	SEQ ID NO:	4285-F10	4285-F6	4285-F9
无(媒介物)	不适用	-	-	-
YKQSQHMTEVVR <u>H</u> CP	519	-	-	-
KQSQHMTEVVR <u>H</u> CPH	520	-	-	+
QSQHMTEVVR <u>H</u> CPHH	521	-	+	+
SQHMTEVVR <u>H</u> CPHHE	522	+	+	+
QHMTEVVR <u>H</u> CPHHER	523	+	+	+
HMTEVVR <u>H</u> CPHHERC	524	+	+	+
MTEVVR <u>H</u> CPHHERCS	525	+	+	+
TEVVR <u>H</u> CPHHERCSD	526	+	+	+
EVVR <u>H</u> CPHHERCSDS	527	+	+	+
VVR <u>H</u> CPHHERCSDSD	528	+	+	-
VR <u>H</u> CPHHERCSDSDG	529	+	+	-

[0570]

[0571] 将Cos7细胞(每孔 2.5×10^4 个)涂铺在平底96孔板的孔上。第二天,将细胞与来自患者4285的单独HLA等位基因共转染。次日,将细胞用DMSO或经突变的p53-R175H肽YKQSQHMTEVVRHCPHHERCSDSDG(SEQ ID NO:2)在37℃下在10 μ g/mL下脉冲2小时。将来自患者4285的对p53-R175H具有特异性的选定TIL片段培养物(4285-F6、4285-F9和4285-F10)与经转染的Cos7细胞在37℃下共培养过夜。对于淋巴细胞→活→CD3⁺(T细胞)→CD8-CD4⁺设门后,通过流式细胞术测定4-1BB的表达。结果显示于图54中。

[0572] 将自体APC用对应于WT或突变的p53-R175H序列的降低浓度的25-个或15-个氨基酸的肽在37℃下脉冲2小时。将来自患者4285的4285-TCR1转座的T细胞与肽-脉冲的APC在37℃下共培养过夜。对于淋巴细胞→活→CD3⁺(T细胞)→CD8-CD4⁺设门后,通过流式细胞术测定4-1BB的表达。结果显示于图55中。

[0573] 从患者4285分离的4285-TCR1的序列示于下文。从氨基末端开始,第一加下划线区是CDR1 α (SEQ ID NO:487),第二加下划线区是CDR2 α (SEQ ID NO:488),第三加下划线区是CDR3 α (SEQ ID NO:489),第四加下划线区是CDR1 β (SEQ ID NO:490),第五加下划线区是CDR2 β (SEQ ID NO:491),和第六加下划线区是CDR3 β (SEQ ID NO:492)。粗体区是连接子(SEQ ID NO:26)。从氨基末端开始,第一加斜体区是 α 链恒定区(SEQ ID NO:23)并且第二加斜体区是 β 链恒定区(SEQ ID NO:25)。 α 链可变区(SEQ ID NO:493)包含从氨基末端开始并且就在 α 链恒定区开始之前结束的序列。 β 链可变区(SEQ ID NO:494)包含在连接子之后立即开始并且就在 β 链恒定区开始之前结束的序列。全长 α 链(SEQ ID NO:495)包含从氨基末端开始并且就在连接子开始之前结束的序列。全长 β 链(SEQ ID NO:496)包含在连接子之后

立即开始并且以羧基末端结束的序列。

[0574] 癌症反应性T细胞如下所述鉴定。TCR如下所述分离。

[0575] TCR名称:4285-TCR1

[0576] P53突变的识别:R175H

[0577] 筛选方法:p53“热点”突变通用筛选

[0578] 共培养以鉴定TCR:共培养4285-F6与p53-R175H肽和分选CD4+41BB+T细胞

[0579] 鉴定TCR的方法:单细胞RT-PCR

[0580] 所有配对的TCR中的TCR的丰度:81.8% (在44对中观察到36次)

[0581] TCR取向: α - β

[0582] 表达载体:SB转座子

[0583] MAKNPLAAPLLILWFHLDVCSSILNVEQSPQSLHVQEGDSTNFTCSFPSSNFYALHWYRWETAKSPEALFVMTLNGDEKKKGRISATLNTKEGYSLYIKGSQPEDSATYLCALITGGGNKLTFGTGTQLKVELNIQNPEPAVYQLKDPRSQDSTLCLFTDFDSQINVPKTMESGTFITDKCVLDMKAMDSKSNGAIAWSNQTSFTCQDIFKETNATYPS SDVPCDATLTEKSFETDMNLFQNLVIVLRILLKLVAGFNLLMTLRLWSSRAKRSGSGATNFSLLKQAGDVEENP GPMHLGLLCCGAFSLLWAGPVNAGVTQTPKFRVLKTQGSMTLLCAQDMNHEYMYWYRQDPGMGLRLIHYSVGEGETT AKGEVPDGYNVSRLLKKQNFLLGLESAAPSQTSVYFCASRLQGWSNPLHFGNGTRLTVTEDLRNVTPPKVSLFEPSK AEIANKQKATLVCLARGFFPDHVELSWWVNGKEVHSGVCTDPQAYKESNYSYCLSSRLRVSATFWHNPRNHFRQCQV QFHGLSEEDKWPEGSPKPVQTQNISAEAWGRADCGITSASYQQGVLSATILYEILLGKATLYAVLVSTLVVMAMVKR KNS (SEQ ID NO:589)

[0584] 患者4285的4285-TCR1的统计数据示于下表35中。

[0585] 表35

参数	#	频率
总孔	96	100%
CDR3 α	37	39.8%
CDR3 β	39	40.6%
4285-TCR1对	36	37.5%
总配对的TCR	44	45.8%

[0587] 实施例14

[0588] 该实施例证实了T细胞对p53“热点”突变的响应的概述。

[0589] 表36提供了T细胞对p53“热点”突变的响应的概述。表36的第1-15号是一项回顾性研究。表36的第16-33号是一项前瞻性研究。

[0590] 表36

#	肿瘤类型	患者	p53 mut	T 细胞筛选	HLA
1	胃	3446	G245S	n/a	n/a
2	胃食管	3788	Y220C	N	n/a
3	直肠	3942	R273C	n/a	n/a

[0592]

#	肿瘤类型	患者	p53 mut	T 细胞筛选	HLA
4	结肠	4023	R282W	Y	II 类
5	结肠	4095	R282W	n/a	n/a
6	卵巢	4127	G245S	Y	DRB3*02:02
7	乳房	4130	R273H	Y	II 类
8	结肠	4141	R175H	Y	A*02:01
9	卵巢	4149	Y220C	Y	DRB3*02:02
10	结肠	4160	R273H	N	n/a
11	黑素瘤	4165	G245D	N	n/a
12	结肠	4166	R248W	n/a	n/a
13	直肠	4171	R248Q	N	n/a
14	黑素瘤	4187	R273H	N	n/a
15	结肠	4196	R175H	Y	A*02:01
16	结肠	4213	R248Q	Y	两者
17	结肠	4217	R175H	N	n/a
18	胆管癌	4220	R248Q	N	n/a
19	直肠	4235	R273C	N	n/a
20	结肠	4238	R248Q	Y	I 类
21	结肠	4244	R282W	N	n/a
22	结肠	4245	R248Q	N	n/a
23	结肠	4252	R175H	N	n/a
24	黑素瘤	4253	R248W	Y	未知
25	结肠	4254	R273H	N	n/a
26	结肠	4257	R248W	N	n/a
27	内皮	4258	R273H	N	n/a
28	结肠	4259	Y220C	Y	A*02:01, DRB1*04
29	结肠	4266	R248W	Y	A*68:01
30	结肠	4268	R248Q	Y	两者
31	胰腺	4270	R282W	Y	未知
32	直肠	4273	R248W	Y	DPB1*02:01
33	直肠	4274	R175H	n/a	
34	结肠	4283	R175H	N	n/a
35	结肠	4285	R175H	Y	DRB1*13:01
36	结肠	4287	R248W	N	n/a
37	结肠	4312	R175H	N	n/a

[0593] n/a=不适用;N=阴性;Y=确认有反应性;TBS=待筛选。

[0594] 实施例15

[0595] 该实施例证实了用p53突变-反应性TIL治疗患者。

[0596] 表37提供了用p53突变-反应性TIL治疗患者的概述。

[0597] 表37

[0598]

#	肿瘤类型	患者	p53 mut	输液袋筛选	细胞总数 (x10 ⁹)	p53 反应性 TIL%	p53 反应性 TIL 数量 (x10 ⁹)	响应	持续时间 (月)
1	卵巢	4127	G245S	Y	143	2.8	4.0	P.R.	4
2	结肠	4141	R175H	Y	69	0.8	0.6	N.R.	-
3	结肠	4196	R175H	Y	92	3.3	3.0	N.R.	-
4	卵巢	4149	Y220C	Y	37	11.1	4.1	N.R.	-
5	结肠	4213	R248Q	TBS	33			P.R.	4
6	结肠	4238	R248Q	TBS	57			N.R.	
7	结肠	4266	R248W	Y	104	50.8	52.8		
8	结肠	4268	R248Q	**TBS					
9	直肠	4273	R248W	**Y	117	6.8	8.0	N.R.	-
10	结肠	4285	R175H	Y	69.6	2.4	1.7	N.R.	-

[0599] NT=未治疗;TBS=待筛选;N.R.=无响应;P.R.=部分响应;**患者尚未治疗。

[0600] 实施例16

[0601] 该实施例证实了在所有测序的肿瘤中每种错义p53突变的总频率。

[0602] 如下采集样品:从141名癌症患者中收集了肿瘤和PBL。TIL从肿瘤生长。对肿瘤样品进行外显子组和转录组测序。鉴定了Tp53突变。在150个肿瘤中,30%表达WT p53,而70%表达经突变的p53。在表达突变的p53的122个肿瘤样品中,73%表达错义突变,13%表达终止-获得突变,11%表达移码突变,并且3%表达插入缺失突变。

[0603] 图44显示了所有测序肿瘤中每种错义p53突变的总频率。

[0604] 实施例17

[0605] 该实施例证实了实施例1-15的TCR的反应性的概述。

[0606] 将表38的TCR分离,在T细胞中表达并针对相关抗原进行了测试。结果概述显示于表38中。

[0607] 表38

[0608]

TCR 名称	p53 a.a. 取代	测 试 TCR?	p53 突变有反应性?
4127-TP53-G245S-TCR1	G245S	是	是
4149TCRa2b2	Y220C	是	是
4266-TCR1	R248W	是	否
4266-TCR2	R248W	是	是
4266-TCR3	R248W	是	是
4266-TCR4	R248W	是	是
4268-TCR1	R248Q	是	否
4268-TCR2	R248Q	是	否
4268-TCR3	R248Q	是	否
4268-TCR4	R248Q	是	否
4268-TCR5	R248Q	是	否
4273-TP53-R248W-TCR1a1	R248W	是	否

[0609]

TCR 名称	p53 a.a. 取代	测 试 TCR?	p53 突变有反应性?
4273-TP53-R248W-TCR1a2	R248W	是	是
4141-TCR1a2	R175H	是	是
4285-TCR1	R175H	是	是
4259-F6-TCR	Y220C	是	是
4127-O37-TCR	G245S	是	是

[0610] 本文引用的所有参考文献,包括出版物、专利申请和专利,均通过引用并入本文,其程度如同每篇参考文献均被单独且具体地指示为通过引用并入本文并在本文中整体阐述。

[0611] 在描述本发明的上下文中(尤其是在所附权利要求的上下文中)术语“一个”和“一种”和“该”和“至少一种”以及类似指代物的使用应被解释为涵盖了单数和复数两种,除非

本文另有说明或与上下文明显矛盾。术语“至少一种”之后是一项或多项的列表(例如,“A和B中的至少一种”)的使用应理解为意指选自所列项(A或B)的一项或所列项(A和B)的两种或多种的任何组合,除非本文另有说明或与上下文明显矛盾。除非另有说明,否则术语“包含”、“具有”、“包括”和“含有”应被解释为开放式术语(即,意指“包括但不限于”)。除非在本文中另外指出,否则本文中数值范围的叙述仅旨在用作分别指代落入该范围内的每个单独值的简写方法,并且每个单独值都被并入说明书中,就好像它在本文中被单独叙述一样。除非本文另外指出或另外与上下文明显矛盾,否则本文描述的所有方法可以以任何适合的顺序执行。除非另外要求保护,否则本文提供的任何和所有示例或示例性语言(如,“诸如”)的使用仅旨在更好地阐明本发明,并且不对本发明的范围构成限制。说明书中的任何语言都不应解释为指示任何未要求保护的要素对于实施本发明必不可少。

[0612] 本文描述了本发明的优选实施方案,包括发明人已知的用于实施本发明的最佳模式。在阅读前述说明书之后,那些优选实施方案的变型对于本领域普通技术人员而言将变得显而易见。本发明人期望熟练的技术人员适当地采用这样的变型,并且本发明人希望以不同于本文具体描述的方式来实践本发明。因此,本发明包括适用法律所允许的所附权利要求书中记载的主题的所有修改和等同物。此外,除非本文另外指出或另外与上下文明显矛盾,否则本发明涵盖上述要素在其所有可能的变型中的任何组合。

序列表

<110> THE UNITED STATES OF AMERICA, AS REPRESENTED BY THE
SECRETARY, DEPARTMENT OF HEALTH AND HUMAN SERVICES

<120> 分离对P53癌症-特异性突变具有抗原特异性的T细胞的方法

<130> 740175

<150> US 62/565,464

<151> 2017-09-29

<160> 602

<170> PatentIn 3.5版

<210> 1

<211> 393

<212> PRT

<213> 智人(Homo sapiens)

<400> 1

```

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

```

His Leu Ile Arg Val Glu Gly Asn Leu Arg Val Glu Tyr Leu Asp Asp		
195	200	205
Arg Asn Thr Phe Arg His Ser Val Val Val Pro Tyr Glu Pro Pro Glu		
210	215	220
Val Gly Ser Asp Cys Thr Thr Ile His Tyr Asn Tyr Met Cys Asn Ser		
225	230	235
Ser Cys Met Gly Gly Met Asn Arg Arg Pro Ile Leu Thr Ile Ile Thr		
245	250	255
Leu Glu Asp Ser Ser Gly Asn Leu Leu Gly Arg Asn Ser Phe Glu Val		
260	265	270
Arg Val Cys Ala Cys Pro Gly Arg Asp Arg Arg Thr Glu Glu Glu Asn		
275	280	285
Leu Arg Lys Lys Gly Glu Pro His His Glu Leu Pro Pro Gly Ser Thr		
290	295	300
Lys Arg Ala Leu Pro Asn Asn Thr Ser Ser Ser Pro Gln Pro Lys Lys		
305	310	315
Lys Pro Leu Asp Gly Glu Tyr Phe Thr Leu Gln Ile Arg Gly Arg Glu		
325	330	335
Arg Phe Glu Met Phe Arg Glu Leu Asn Glu Ala Leu Glu Leu Lys Asp		
340	345	350
Ala Gln Ala Gly Lys Glu Pro Gly Gly Ser Arg Ala His Ser Ser His		
355	360	365
Leu Lys Ser Lys Lys Gly Gln Ser Thr Ser Arg His Lys Lys Leu Met		
370	375	380
Phe Lys Thr Glu Gly Pro Asp Ser Asp		
385	390	
<210> 2		
<211> 25		
<212> PRT		
<213> 智人(Homo sapiens)		
<400> 2		
Tyr Lys Gln Ser Gln His Met Thr Glu Val Val Arg His Cys Pro His		
1	5	10
His Glu Arg Cys Ser Asp Ser Asp Gly		
20	25	
<210> 3		
<211> 25		
<212> PRT		
<213> 智人(Homo sapiens)		

<400> 3

Ser Gly Asn Leu Leu Gly Arg Asn Ser Phe Glu Val His Val Cys Ala

1 5 10 15

Cys Pro Gly Arg Asp Arg Arg Thr Glu

20 25

<210> 4

<211> 25

<212> PRT

<213> 智人 (Homo sapiens)

<400> 4

Tyr Met Cys Asn Ser Ser Cys Met Gly Gly Met Asn Leu Arg Pro Ile

1 5 10 15

Leu Thr Ile Ile Thr Leu Glu Asp Ser

20 25

<210> 5

<211> 25

<212> PRT

<213> 智人 (Homo sapiens)

<400> 5

Phe Glu Val Arg Val Cys Ala Cys Pro Gly Arg Asp Trp Arg Thr Glu

1 5 10 15

Glu Glu Asn Leu Arg Lys Lys Gly Glu

20 25

<210> 6

<211> 25

<212> PRT

<213> 智人 (Homo sapiens)

<400> 6

Ser Gly Asn Leu Leu Gly Arg Asn Ser Phe Glu Val Cys Val Cys Ala

1 5 10 15

Cys Pro Gly Arg Asp Arg Arg Thr Glu

20 25

<210> 7

<211> 25

<212> PRT

<213> 智人 (Homo sapiens)

<400> 7

His Tyr Asn Tyr Met Cys Asn Ser Ser Cys Met Gly Ser Met Asn Arg

1 5 10 15

Arg Pro Ile Leu Thr Ile Ile Thr Leu
20 25

<210> 8

<211> 25

<212> PRT

<213> 智人(Homo sapiens)

<400> 8

Tyr Met Cys Asn Ser Ser Cys Met Gly Gly Met Asn Gln Arg Pro Ile
1 5 10 15

Leu Thr Ile Ile Thr Leu Glu Asp Ser
20 25

<210> 9

<211> 25

<212> PRT

<213> 智人(Homo sapiens)

<400> 9

His Tyr Asn Tyr Met Cys Asn Ser Ser Cys Met Gly Asp Met Asn Arg
1 5 10 15

Arg Pro Ile Leu Thr Ile Ile Thr Leu
20 25

<210> 10

<211> 25

<212> PRT

<213> 智人(Homo sapiens)

<400> 10

Ser Gly Asn Leu Leu Gly Arg Asn Ser Phe Glu Val Leu Val Cys Ala
1 5 10 15

Cys Pro Gly Arg Asp Arg Arg Thr Glu
20 25

<210> 11

<211> 25

<212> PRT

<213> 智人(Homo sapiens)

<400> 11

Tyr Met Cys Asn Ser Ser Cys Met Gly Gly Met Asn Trp Arg Pro Ile
1 5 10 15

Leu Thr Ile Ile Thr Leu Glu Asp Ser
20 25

<210> 12

<211> 25

<212> PRT

<213> 智人(Homo sapiens)

<400> 12

Asp Arg Asn Thr Phe Arg His Ser Val Val Val Pro Cys Glu Pro Pro

1 5 10 15

Glu Val Gly Ser Asp Cys Thr Thr Ile

20 25

<210> 13

<211> 25

<212> PRT

<213> 智人(Homo sapiens)

<400> 13

Met Cys Asn Ser Ser Cys Met Gly Gly Met Asn Arg Ser Pro Ile Leu

1 5 10 15

Thr Ile Ile Thr Leu Glu Asp Ser Ser

20 25

<210> 14

<211> 300

<212> PRT

<213> 人工序列(Artificial Sequence)

<220>

<223> 合成

<400> 14

Tyr Lys Gln Ser Gln His Met Thr Glu Val Val Arg His Cys Pro His

1 5 10 15

His Glu Arg Cys Ser Asp Ser Asp Gly Ser Gly Asn Leu Leu Gly Arg

20 25 30

Asn Ser Phe Glu Val His Val Cys Ala Cys Pro Gly Arg Asp Arg Arg

35 40 45

Thr Glu Tyr Met Cys Asn Ser Ser Cys Met Gly Gly Met Asn Leu Arg

50 55 60

Pro Ile Leu Thr Ile Ile Thr Leu Glu Asp Ser Phe Glu Val Arg Val

65 70 75 80

Cys Ala Cys Pro Gly Arg Asp Trp Arg Thr Glu Glu Glu Asn Leu Arg

85 90 95

Lys Lys Gly Glu Ser Gly Asn Leu Leu Gly Arg Asn Ser Phe Glu Val

100 105 110

Cys Val Cys Ala Cys Pro Gly Arg Asp Arg Arg Thr Glu His Tyr Asn

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

⟨210⟩ 15

<211> 25

⟨212⟩ PRT

〈213〉 智人 (*Homo sapiens*)

$\langle 400 \rangle$ 15

Tyr Lys Gln Ser Gln His Met Thr Glu Val Val Arg Arg Cys Pro His
1 5 10 15

His Glu Arg Cys Ser Asp Ser Asp Gly
20 25

<210> 16

<211> 25

<212> PRT

〈213〉 智人 (Homo sapiens)

<400> 16

Ser Gly Asn Leu Leu Gly Arg Asn Ser Phe Glu Val Arg Val Cys Ala
1 5 10 15

Cys Pro Gly Arg Asp Arg Arg Thr Glu
20 25

<210> 17

<211> 25

<212> PRT

<213> 智人(Homo sapiens)

<400> 17

Tyr Met Cys Asn Ser Ser Cys Met Gly Gly Met Asn Arg Arg Pro Ile
1 5 10 15

Leu Thr Ile Ile Thr Leu Glu Asp Ser
20 25

<210> 18

<211> 25

<212> PRT

<213> 智人(Homo sapiens)

<400> 18

Phe Glu Val Arg Val Cys Ala Cys Pro Gly Arg Asp Arg Arg Thr Glu
1 5 10 15

Glu Glu Asn Leu Arg Lys Lys Gly Glu
20 25

<210> 19

<211> 25

<212> PRT

<213> 智人(Homo sapiens)

<400> 19

His Tyr Asn Tyr Met Cys Asn Ser Ser Cys Met Gly Gly Met Asn Arg
1 5 10 15

Arg Pro Ile Leu Thr Ile Ile Thr Leu
20 25

<210> 20

<211> 25

<212> PRT

<213> 智人(Homo sapiens)

<400> 20

Asp Arg Asn Thr Phe Arg His Ser Val Val Val Pro Tyr Glu Pro Pro
1 5 10 15

Glu Val Gly Ser Asp Cys Thr Thr Ile
20 25

<210> 21

<211> 25

<212> PRT

<213> 智人(Homo sapiens)

<400> 21

Met Cys Asn Ser Ser Cys Met Gly Gly Met Asn Arg Arg Pro Ile Leu

1 5 10 15

Thr Ile Ile Thr Leu Glu Asp Ser Ser

20 25

<210> 22

<211> 300

<212> PRT

<213> 人工序列(Artificial Sequence)

<220>

<223> 合成

<400> 22

Tyr Lys Gln Ser Gln His Met Thr Glu Val Val Arg Arg Cys Pro His

1 5 10 15

His Glu Arg Cys Ser Asp Ser Asp Gly Ser Gly Asn Leu Leu Gly Arg

20 25 30

Asn Ser Phe Glu Val Arg Val Cys Ala Cys Pro Gly Arg Asp Arg Arg

35 40 45

Thr Glu Tyr Met Cys Asn Ser Ser Cys Met Gly Gly Met Asn Arg Arg

50 55 60

Pro Ile Leu Thr Ile Ile Thr Leu Glu Asp Ser Phe Glu Val Arg Val

65 70 75 80

Cys Ala Cys Pro Gly Arg Asp Arg Arg Thr Glu Glu Glu Asn Leu Arg

85 90 95

Lys Lys Gly Glu Ser Gly Asn Leu Leu Gly Arg Asn Ser Phe Glu Val

100 105 110

Arg Val Cys Ala Cys Pro Gly Arg Asp Arg Arg Thr Glu His Tyr Asn

115 120 125

Tyr Met Cys Asn Ser Ser Cys Met Gly Gly Met Asn Arg Arg Pro Ile

130 135 140

Leu Thr Ile Ile Thr Leu Tyr Met Cys Asn Ser Ser Cys Met Gly Gly

145 150 155 160

Met Asn Arg Arg Pro Ile Leu Thr Ile Ile Thr Leu Glu Asp Ser His

165 170 175

Tyr Asn Tyr Met Cys Asn Ser Ser Cys Met Gly Gly Met Asn Arg Arg

180 185 190

Pro	Ile	Leu	Thr	Ile	Ile	Thr	Leu	Ser	Gly	Asn	Leu	Leu	Gly	Arg	Asn
195				200				205							
Ser	Phe	Glu	Val	Arg	Val	Cys	Ala	Cys	Pro	Gly	Arg	Asp	Arg	Arg	Thr
210				215				220							
Glu	Tyr	Met	Cys	Asn	Ser	Ser	Cys	Met	Gly	Gly	Met	Asn	Arg	Arg	Pro
225				230				235				240			
Ile	Leu	Thr	Ile	Ile	Thr	Leu	Glu	Asp	Ser	Asp	Arg	Asn	Thr	Phe	Arg
				245				250				255			
His	Ser	Val	Val	Val	Pro	Tyr	Glu	Pro	Pro	Glu	Val	Gly	Ser	Asp	Cys
260				265				270							
Thr	Thr	Ile	Met	Cys	Asn	Ser	Ser	Cys	Met	Gly	Gly	Met	Asn	Arg	Arg
275				280				285							
Pro	Ile	Leu	Thr	Ile	Ile	Thr	Leu	Glu	Asp	Ser	Ser				
290				295				300							

<210> 23

<211> 137

<212> PRT

<213> 人工序列(Artificial Sequence)

<220>

<223> 合成

<400> 23

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

<210> 24

<211> 137

<212> PRT

<213> 人工序列(Artificial Sequence)

<220>

<223> 合成

<400> 24

```

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

```

<210> 25

<211> 173

<212> PRT

<213> 人工序列(Artificial Sequence)

<220>

<223> 合成

<400> 25

```

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

```

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

<210> 26

<211> 27

<212> PRT

<213> 人工序列(Artificial Sequence)

<220>

<223> 合成

<400> 26

Arg Ala Lys Arg Ser Gly Ser Gly Ala Thr Asn Phe Ser Leu Leu Lys
1 5 10 15
Gln Ala Gly Asp Val Glu Glu Asn Pro Gly Pro
20 25

<210> 27

<211> 6

<212> PRT

<213> 智人(Homo sapiens)

<400> 27

Tyr Gly Gly Thr Val Asn
1 5

<210> 28

<211> 8

<212> PRT

<213> 智人(Homo sapiens)

<400> 28

Tyr Phe Ser Gly Asp Pro Leu Val

1 5
 <210> 29
 <211> 11
 <212> PRT
 <213> 智人 (Homo sapiens)
 <400> 29
 Cys Ala Val Lys Gly Asp Tyr Lys Leu Ser Phe
 1 5 10
 <210> 30
 <211> 5
 <212> PRT
 <213> 智人 (Homo sapiens)
 <400> 30
 Ser Gly His Ala Thr
 1 5
 <210> 31
 <211> 6
 <212> PRT
 <213> 智人 (Homo sapiens)
 <400> 31
 Phe Gln Asn Asn Gly Val
 1 5
 <210> 32
 <211> 12
 <212> PRT
 <213> 智人 (Homo sapiens)
 <400> 32
 Cys Ala Ser Ser Leu Val Asn Thr Glu Ala Phe Phe
 1 5 10
 <210> 33
 <211> 130
 <212> PRT
 <213> 智人 (Homo sapiens)
 <400> 33
 Met Leu Leu Leu Leu Ile Pro Val Leu Gly Met Ile Phe Ala Leu Arg
 1 5 10 15
 Asp Ala Arg Ala Gln Ser Val Ser Gln His Asn His His Val Ile Leu
 20 25 30
 Ser Glu Ala Ala Ser Leu Glu Leu Gly Cys Asn Tyr Ser Tyr Gly Gly

35	40	45
Thr Val Asn Leu Phe Trp Tyr	Val Gln Tyr Pro Gly Gln His Leu Gln	
50	55	60
Leu Leu Leu Lys Tyr Phe Ser Gly Asp Pro Leu Val Lys Gly Ile Lys		
65	70	75
Gly Phe Glu Ala Glu Phe Ile Lys Ser Lys Phe Ser Phe Asn Leu Arg		
85	90	95
Lys Pro Ser Val Gln Trp Ser Asp Thr Ala Glu Tyr Phe Cys Ala Val		
100	105	110
Lys Gly Asp Tyr Lys Leu Ser Phe Gly Ala Gly Thr Thr Val Thr Val		
115	120	125
Arg Ala		
130		
<210> 34		
<211> 131		
<212> PRT		
<213> 智人 (Homo sapiens)		
<400> 34		
Met Ala Thr Arg Leu Leu Cys Trp Ala Ala Leu Cys Leu Leu Gly Ala		
1	5	10
Glu Leu Thr Glu Ala Gly Val Ala Gln Ser Pro Arg Tyr Lys Ile Ile		
20	25	30
Glu Lys Arg Gln Ser Val Ala Phe Trp Cys Asn Pro Ile Ser Gly His		
35	40	45
Ala Thr Leu Tyr Trp Tyr Gln Gln Ile Leu Gly Gln Gly Pro Lys Leu		
50	55	60
Leu Ile Gln Phe Gln Asn Asn Gly Val Val Asp Asp Ser Gln Leu Pro		
65	70	75
Lys Asp Arg Phe Ser Ala Glu Arg Leu Lys Gly Val Asp Ser Thr Leu		
85	90	95
Lys Ile Gln Pro Ala Lys Leu Glu Asp Ser Ala Val Tyr Leu Cys Ala		
100	105	110
Ser Ser Leu Val Asn Thr Glu Ala Phe Phe Gly Gln Gly Thr Arg Leu		
115	120	125
Thr Val Val		
130		
<210> 35		
<211> 267		
<212> PRT		

<213> 智人 (Homo sapiens)

<400> 35

```

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

```

<210> 36

<211> 304

<212> PRT

<213> 智人 (Homo sapiens)

<400> 36

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

290	295	300
<210> 37		
<211> 7		
<212> PRT		
<213> 智人 (Homo sapiens)		
<400> 37		
Thr Arg Asp Thr Thr Tyr Tyr		
1	5	
<210> 38		
<211> 8		
<212> PRT		
<213> 智人 (Homo sapiens)		
<400> 38		
Arg Asn Ser Phe Asp Glu Gln Asn		
1	5	
<210> 39		
<211> 14		
<212> PRT		
<213> 智人 (Homo sapiens)		
<400> 39		
Cys Ala Leu Ser Glu Gly Gly Ser Asn Tyr Lys Leu Thr Phe		
1	5	10
<210> 40		
<211> 5		
<212> PRT		
<213> 智人 (Homo sapiens)		
<400> 40		
Leu Asn His Asn Val		
1	5	
<210> 41		
<211> 6		
<212> PRT		
<213> 智人 (Homo sapiens)		
<400> 41		
Tyr Tyr Asp Lys Asp Phe		
1	5	
<210> 42		
<211> 14		
<212> PRT		

<213> 智人 (Homo sapiens)

<400> 42

Cys Ala Thr Ser Arg Glu Leu Arg Gly Asn Glu Gln Phe Phe

1 5 10

<210> 43

<211> 135

<212> PRT

<213> 智人 (Homo sapiens)

<400> 43

Met Leu Thr Ala Ser Leu Leu Arg Ala Val Ile Ala Ser Ile Cys Val

1 5 10 15

Val Ser Ser Met Ala Gln Lys Val Thr Gln Ala Gln Thr Glu Ile Ser

20 25 30

Val Val Glu Lys Glu Asp Val Thr Leu Asp Cys Val Tyr Glu Thr Arg

35 40 45

Asp Thr Thr Tyr Tyr Leu Phe Trp Tyr Lys Gln Pro Pro Ser Gly Glu

50 55 60

Leu Val Phe Leu Ile Arg Arg Asn Ser Phe Asp Glu Gln Asn Glu Ile

65 70 75 80

Ser Gly Arg Tyr Ser Trp Asn Phe Gln Lys Ser Thr Ser Ser Phe Asn

85 90 95

Phe Thr Ile Thr Ala Ser Gln Val Val Asp Ser Ala Val Tyr Phe Cys

100 105 110

Ala Leu Ser Glu Gly Gly Ser Asn Tyr Lys Leu Thr Phe Gly Lys Gly

115 120 125

Thr Leu Leu Thr Val Asn Pro

130 135

<210> 44

<211> 132

<212> PRT

<213> 智人 (Homo sapiens)

<400> 44

Met Ala Pro Gly Leu Leu His Trp Met Ala Leu Cys Leu Leu Gly Thr

1 5 10 15

Gly His Gly Asp Ala Met Val Ile Gln Asn Pro Arg Tyr Gln Val Thr

20 25 30

Gln Phe Gly Lys Pro Val Thr Leu Ser Cys Ser Gln Thr Leu Asn His

35 40 45

Asn Val Met Tyr Trp Tyr Gln Gln Lys Ser Ser Gln Ala Pro Lys Leu

50	55	60																	
Leu	Phe	His	Tyr	Tyr	Asp	Lys	Asp	Phe	Asn	Asn	Glu	Ala	Asp	Thr	Pro				
65					70					75					80				
Asp	Asn	Phe	Gln	Ser	Arg	Arg	Pro	Asn	Thr	Ser	Phe	Cys	Phe	Leu	Asp				
				85					90					95					
Ile	Arg	Ser	Pro	Gly	Leu	Gly	Asp	Ala	Ala	Met	Tyr	Leu	Cys	Ala	Thr				
			100					105					110						
Ser	Arg	Glu	Leu	Arg	Gly	Asn	Glu	Gln	Phe	Phe	Gly	Pro	Gly	Thr	Arg				
		115					120					125							
Leu	Thr	Val	Leu																
130																			
<210>	45																		
<211>	272																		
<212>	PRT																		
<213>	智人 (Homo sapiens)																		
<400>	45																		
Met	Leu	Thr	Ala	Ser	Leu	Leu	Arg	Ala	Val	Ile	Ala	Ser	Ile	Cys	Val				
1				5					10					15					
Val	Ser	Ser	Met	Ala	Gln	Lys	Val	Thr	Gln	Ala	Gln	Thr	Glu	Ile	Ser				
			20					25					30						
Val	Val	Glu	Lys	Glu	Asp	Val	Thr	Leu	Asp	Cys	Val	Tyr	Glu	Thr	Arg				
		35					40					45							
Asp	Thr	Thr	Tyr	Tyr	Leu	Phe	Trp	Tyr	Lys	Gln	Pro	Pro	Ser	Gly	Glu				
50					55				60										
Leu	Val	Phe	Leu	Ile	Arg	Arg	Asn	Ser	Phe	Asp	Glu	Gln	Asn	Glu	Ile				
65				70					75					80					
Ser	Gly	Arg	Tyr	Ser	Trp	Asn	Phe	Gln	Lys	Ser	Thr	Ser	Ser	Phe	Asn				
			85					90					95						
Phe	Thr	Ile	Thr	Ala	Ser	Gln	Val	Val	Asp	Ser	Ala	Val	Tyr	Phe	Cys				
			100					105					110						
Ala	Leu	Ser	Glu	Gly	Gly	Ser	Asn	Tyr	Lys	Leu	Thr	Phe	Gly	Lys	Gly				
		115					120					125							
Thr	Leu	Leu	Thr	Val	Asn	Pro	Asn	Ile	Gln	Asn	Pro	Glu	Pro	Ala	Val				
130					135				140										
Tyr	Gln	Leu	Lys	Asp	Pro	Arg	Ser	Gln	Asp	Ser	Thr	Leu	Cys	Leu	Phe				
145				150					155				160						
Thr	Asp	Phe	Asp	Ser	Gln	Ile	Asn	Val	Pro	Lys	Thr	Met	Glu	Ser	Gly				
			165					170				175							
Thr	Phe	Ile	Thr	Asp	Lys	Cys	Val	Leu	Asp	Met	Lys	Ala	Met	Asp	Ser				

180	185	190
Lys Ser Asn Gly Ala Ile Ala Trp Ser Asn Gln Thr Ser Phe Thr Cys		
195	200	205
Gln Asp Ile Phe Lys Glu Thr Asn Ala Thr Tyr Pro Ser Ser Asp Val		
210	215	220
Pro Cys Asp Ala Thr Leu Thr Glu Lys Ser Phe Glu Thr Asp Met Asn		
225	230	235
Leu Asn Phe Gln Asn Leu Leu Val Ile Val Leu Arg Ile Leu Leu Leu		
245	250	255
Lys Val Ala Gly Phe Asn Leu Leu Met Thr Leu Arg Leu Trp Ser Ser		
260	265	270
<210> 46		
<211> 305		
<212> PRT		
<213> 智人(Homo sapiens)		
<400> 46		
Met Ala Pro Gly Leu Leu His Trp Met Ala Leu Cys Leu Leu Gly Thr		
1	5	10
Gly His Gly Asp Ala Met Val Ile Gln Asn Pro Arg Tyr Gln Val Thr		
20	25	30
Gln Phe Gly Lys Pro Val Thr Leu Ser Cys Ser Gln Thr Leu Asn His		
35	40	45
Asn Val Met Tyr Trp Tyr Gln Gln Lys Ser Ser Gln Ala Pro Lys Leu		
50	55	60
Leu Phe His Tyr Tyr Asp Lys Asp Phe Asn Asn Glu Ala Asp Thr Pro		
65	70	75
Asp Asn Phe Gln Ser Arg Arg Pro Asn Thr Ser Phe Cys Phe Leu Asp		
85	90	95
Ile Arg Ser Pro Gly Leu Gly Asp Ala Ala Met Tyr Leu Cys Ala Thr		
100	105	110
Ser Arg Glu Leu Arg Gly Asn Glu Gln Phe Phe Gly Pro Gly Thr Arg		
115	120	125
Leu Thr Val Leu Glu Asp Leu Arg Asn Val Thr Pro Pro Lys Val Ser		
130	135	140
Leu Phe Glu Pro Ser Lys Ala Glu Ile Ala Asn Lys Gln Lys Ala Thr		
145	150	155
Leu Val Cys Leu Ala Arg Gly Phe Phe Pro Asp His Val Glu Leu Ser		
165	170	175
Trp Trp Val Asn Gly Lys Glu Val His Ser Gly Val Cys Thr Asp Pro		

180	185	190
Gln Ala Tyr Lys Glu Ser Asn Tyr Ser Tyr Cys Leu Ser Ser Arg Leu		
195	200	205
Arg Val Ser Ala Thr Phe Trp His Asn Pro Arg Asn His Phe Arg Cys		
210	215	220
Gln Val Gln Phe His Gly Leu Ser Glu Glu Asp Lys Trp Pro Glu Gly		
225	230	235
Ser Pro Lys Pro Val Thr Gln Asn Ile Ser Ala Glu Ala Trp Gly Arg		
245	250	255
Ala Asp Cys Gly Ile Thr Ser Ala Ser Tyr Gln Gln Gly Val Leu Ser		
260	265	270
Ala Thr Ile Leu Tyr Glu Ile Leu Leu Gly Lys Ala Thr Leu Tyr Ala		
275	280	285
Val Leu Val Ser Thr Leu Val Val Met Ala Met Val Lys Arg Lys Asn		
290	295	300
Ser		
305		
<210> 47		
<211> 6		
<212> PRT		
<213> 智人(Homo sapiens)		
<400> 47		
Thr Ser Gly Phe Asn Gly		
1	5	
<210> 48		
<211> 6		
<212> PRT		
<213> 智人(Homo sapiens)		
<400> 48		
Asn Val Leu Asp Gly Leu		
1	5	
<210> 49		
<211> 13		
<212> PRT		
<213> 智人(Homo sapiens)		
<400> 49		
Cys Ala Val Lys Trp Thr Gly Gly Phe Lys Thr Ile Phe		
1	5	10
<210> 50		

<211> 5
 <212> PRT
 <213> 智人 (Homo sapiens)
 <400> 50
 Met Asn His Glu Tyr
 1 5
 <210> 51
 <211> 6
 <212> PRT
 <213> 智人 (Homo sapiens)
 <400> 51
 Ser Val Gly Ala Gly Ile
 1 5
 <210> 52
 <211> 14
 <212> PRT
 <213> 智人 (Homo sapiens)
 <400> 52
 Cys Ala Ser Ser Tyr Arg Glu Ser His Tyr Gly Tyr Thr Phe
 1 5 10
 <210> 53
 <211> 127
 <212> PRT
 <213> 智人 (Homo sapiens)
 <400> 53
 Met Trp Gly Val Phe Leu Leu Tyr Val Ser Met Lys Met Gly Gly Thr
 1 5 10 15
 Thr Gly Gln Asn Ile Asp Gln Pro Thr Glu Met Thr Ala Thr Glu Gly
 20 25 30
 Ala Ile Val Gln Ile Asn Cys Thr Tyr Gln Thr Ser Gly Phe Asn Gly
 35 40 45
 Leu Phe Trp Tyr Gln Gln His Ala Gly Glu Ala Pro Thr Phe Leu Ser
 50 55 60
 Tyr Asn Val Leu Asp Gly Leu Glu Glu Lys Gly Arg Phe Ser Ser Phe
 65 70 75 80
 Leu Ser Arg Ser Lys Gly Tyr Ser Tyr Leu Leu Leu Lys Glu Leu Gln
 85 90 95
 Met Lys Asp Ser Ala Ser Tyr Leu Cys Ala Val Lys Trp Thr Gly Gly
 100 105 110

Phe Lys Thr Ile Phe Gly Ala Gly Thr Arg Leu Phe Val Lys Ala
 115 120 125

<210> 54

<211> 134

<212> PRT

<213> 智人 (Homo sapiens)

<400> 54

Met Ala Met Ser Ile Gly Leu Leu Cys Cys Ala Ala Leu Ser Leu Leu
 1 5 10 15

Trp Ala Gly Pro Val Asn Ala Gly Val Thr Gln Thr Pro Lys Phe Gln
 20 25 30

Val Leu Lys Thr Gly Gln Ser Met Thr Leu Gln Cys Ala Gln Asp Met
 35 40 45

Asn His Glu Tyr Met Ser Trp Tyr Arg Gln Asp Pro Gly Met Gly Leu
 50 55 60

Arg Leu Ile His Tyr Ser Val Gly Ala Gly Ile Thr Asp Gln Gly Glu
 65 70 75 80

Val Pro Asn Gly Tyr Asn Val Ser Arg Ser Thr Thr Glu Asp Phe Pro
 85 90 95

Leu Arg Leu Leu Ser Ala Ala Pro Ser Gln Thr Ser Val Tyr Phe Cys
 100 105 110

Ala Ser Ser Tyr Arg Glu Ser His Tyr Gly Tyr Thr Phe Gly Ser Gly
 115 120 125

Thr Arg Leu Thr Val Val
 130

<210> 55

<211> 264

<212> PRT

<213> 智人 (Homo sapiens)

<400> 55

Met Trp Gly Val Phe Leu Leu Tyr Val Ser Met Lys Met Gly Gly Thr
 1 5 10 15

Thr Gly Gln Asn Ile Asp Gln Pro Thr Glu Met Thr Ala Thr Glu Gly
 20 25 30

Ala Ile Val Gln Ile Asn Cys Thr Tyr Gln Thr Ser Gly Phe Asn Gly
 35 40 45

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

Tyr Asn Val Leu Asp Gly Leu Glu Glu Lys Gly Arg Phe Ser Ser Phe

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

<210> 56

<211> 307

<212> PRT

<213> 智人(Homo sapiens)

<400> 56

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

65	70	75	80
Val Pro Asn Gly Tyr Asn Val Ser Arg Ser Thr Thr Glu Asp Phe Pro			
	85	90	95
Leu Arg Leu Leu Ser Ala Ala Pro Ser Gln Thr Ser Val Tyr Phe Cys			
	100	105	110
Ala Ser Ser Tyr Arg Glu Ser His Tyr Gly Tyr Thr Phe Gly Ser Gly			
	115	120	125
Thr Arg Leu Thr Val Val Glu Asp Leu Arg Asn Val Thr Pro Pro Lys			
	130	135	140
Val Ser Leu Phe Glu Pro Ser Lys Ala Glu Ile Ala Asn Lys Gln Lys			
145	150	155	160
Ala Thr Leu Val Cys Leu Ala Arg Gly Phe Phe Pro Asp His Val Glu			
	165	170	175
Leu Ser Trp Trp Val Asn Gly Lys Glu Val His Ser Gly Val Cys Thr			
	180	185	190
Asp Pro Gln Ala Tyr Lys Glu Ser Asn Tyr Ser Tyr Cys Leu Ser Ser			
	195	200	205
Arg Leu Arg Val Ser Ala Thr Phe Trp His Asn Pro Arg Asn His Phe			
	210	215	220
Arg Cys Gln Val Gln Phe His Gly Leu Ser Glu Glu Asp Lys Trp Pro			
225	230	235	240
Glu Gly Ser Pro Lys Pro Val Thr Gln Asn Ile Ser Ala Glu Ala Trp			
	245	250	255
Gly Arg Ala Asp Cys Gly Ile Thr Ser Ala Ser Tyr Gln Gln Gly Val			
	260	265	270
Leu Ser Ala Thr Ile Leu Tyr Glu Ile Leu Leu Gly Lys Ala Thr Leu			
	275	280	285
Tyr Ala Val Leu Val Ser Thr Leu Val Val Met Ala Met Val Lys Arg			
	290	295	300
Lys Asn Ser			
305			
<210> 57			
<211> 6			
<212> PRT			
<213> 智人 (Homo sapiens)			
<400> 57			
Val Ser Gly Asn Pro Tyr			
1	5		
<210> 58			

<211> 8
<212> PRT
<213> 智人 (Homo sapiens)
<400> 58
Tyr Ile Thr Gly Asp Asn Leu Val
1 5
<210> 59
<211> 12
<212> PRT
<213> 智人 (Homo sapiens)
<400> 59
Cys Ala Val Arg Val Trp Asp Tyr Lys Leu Ser Phe
1 5 10
<210> 60
<211> 5
<212> PRT
<213> 智人 (Homo sapiens)
<400> 60
Leu Asn His Asp Ala
1 5
<210> 61
<211> 6
<212> PRT
<213> 智人 (Homo sapiens)
<400> 61
Ser Gln Ile Val Asn Asp
1 5
<210> 62
<211> 14
<212> PRT
<213> 智人 (Homo sapiens)
<400> 62
Cys Ala Ser Ser Ile Ser Ala Gly Gly Asp Gly Tyr Thr Phe
1 5 10
<210> 63
<211> 131
<212> PRT
<213> 智人 (Homo sapiens)
<400> 63

Met	Ala	Ser	Ala	Pro	Ile	Ser	Met	Leu	Ala	Met	Leu	Phe	Thr	Leu	Ser
1				5					10					15	
Gly	Leu	Arg	Ala	Gln	Ser	Val	Ala	Gln	Pro	Glu	Asp	Gln	Val	Asn	Val
			20					25					30		
Ala	Glu	Gly	Asn	Pro	Leu	Thr	Val	Lys	Cys	Thr	Tyr	Ser	Val	Ser	Gly
			35				40					45			
Asn	Pro	Tyr	Leu	Phe	Trp	Tyr	Val	Gln	Tyr	Pro	Asn	Arg	Gly	Leu	Gln
			50				55				60				
Phe	Leu	Leu	Lys	Tyr	Ile	Thr	Gly	Asp	Asn	Leu	Val	Lys	Gly	Ser	Tyr
65					70					75					80
Gly	Phe	Glu	Ala	Glu	Phe	Asn	Lys	Ser	Gln	Thr	Ser	Phe	His	Leu	Lys
				85					90					95	
Lys	Pro	Ser	Ala	Leu	Val	Ser	Asp	Ser	Ala	Leu	Tyr	Phe	Cys	Ala	Val
			100						105				110		
Arg	Val	Trp	Asp	Tyr	Lys	Leu	Ser	Phe	Gly	Ala	Gly	Thr	Thr	Val	Thr
			115				120						125		
Val	Arg	Ala													
			130												
<210>	64														
<211>	132														
<212>	PRT														
<213>	智人 (Homo sapiens)														
<400>	64														
Met	His	Asn	Gln	Val	Leu	Cys	Cys	Val	Val	Leu	Cys	Phe	Leu	Gly	Ala
1				5					10					15	
Asn	Thr	Val	Asp	Gly	Gly	Ile	Thr	Gln	Ser	Pro	Lys	Tyr	Leu	Phe	Arg
			20					25					30		
Lys	Glu	Gly	Gln	Asn	Val	Thr	Leu	Ser	Cys	Glu	Gln	Asn	Leu	Asn	His
			35				40					45			
Asp	Ala	Met	Tyr	Trp	Tyr	Arg	Gln	Asp	Pro	Gly	Gln	Gly	Leu	Arg	Leu
			50				55				60				
Ile	Tyr	Tyr	Ser	Gln	Ile	Val	Asn	Asp	Phe	Gln	Lys	Gly	Asp	Ile	Ala
65					70					75					80
Glu	Gly	Tyr	Ser	Val	Ser	Arg	Glu	Lys	Lys	Glu	Ser	Phe	Pro	Leu	Thr
				85					90					95	
Val	Thr	Ser	Ala	Gln	Lys	Asn	Pro	Thr	Ala	Phe	Tyr	Leu	Cys	Ala	Ser
			100						105				110		
Ser	Ile	Ser	Ala	Gly	Gly	Asp	Gly	Tyr	Thr	Phe	Gly	Ser	Gly	Thr	Arg
			115				120						125		

Leu Thr Val Val

130

<210> 65

<211> 268

<212> PRT

<213> 智人 (Homo sapiens)

<400> 65

Met Ala Ser Ala Pro Ile Ser Met Leu Ala Met Leu Phe Thr Leu Ser

1 5 10 15

Gly Leu Arg Ala Gln Ser Val Ala Gln Pro Glu Asp Gln Val Asn Val

20 25 30

Ala Glu Gly Asn Pro Leu Thr Val Lys Cys Thr Tyr Ser Val Ser Gly

35 40 45

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

50 55 60

Phe Leu Leu Lys Tyr Ile Thr Gly Asp Asn Leu Val Lys Gly Ser Tyr

65 70 75 80

Gly Phe Glu Ala Glu Phe Asn Lys Ser Gln Thr Ser Phe His Leu Lys

85 90 95

Lys Pro Ser Ala Leu Val Ser Asp Ser Ala Leu Tyr Phe Cys Ala Val

100 105 110

Arg Val Trp Asp Tyr Lys Leu Ser Phe Gly Ala Gly Thr Thr Val Thr

115 120 125

Val Arg Ala Asn Ile Gln Asn Pro Glu Pro Ala Val Tyr Gln Leu Lys

130 135 140

Asp Pro Arg Ser Gln Asp Ser Thr Leu Cys Leu Phe Thr Asp Phe Asp

145 150 155 160

Ser Gln Ile Asn Val Pro Lys Thr Met Glu Ser Gly Thr Phe Ile Thr

165 170 175

Asp Lys Cys Val Leu Asp Met Lys Ala Met Asp Ser Lys Ser Asn Gly

180 185 190

Ala Ile Ala Trp Ser Asn Gln Thr Ser Phe Thr Cys Gln Asp Ile Phe

195 200 205

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

210 215 220

Thr Leu Thr Glu Lys Ser Phe Glu Thr Asp Met Asn Leu Asn Phe Gln

225 230 235 240

Asn Leu Leu Val Ile Val Leu Arg Ile Leu Leu Leu Lys Val Ala Gly

245 250 255

Phe Asn Leu Leu Met Thr Leu Arg Leu Trp Ser Ser
 260 265
 <210> 66
 <211> 305
 <212> PRT
 <213> 智人 (Homo sapiens)
 <400> 66
 Met His Asn Gln Val Leu Cys Cys Val Val Leu Cys Phe Leu Gly Ala
 1 5 10 15
 Asn Thr Val Asp Gly Gly Ile Thr Gln Ser Pro Lys Tyr Leu Phe Arg
 20 25 30
 Lys Glu Gly Gln Asn Val Thr Leu Ser Cys Glu Gln Asn Leu Asn His
 35 40 45
 Asp Ala Met Tyr Trp Tyr Arg Gln Asp Pro Gly Gln Gly Leu Arg Leu
 50 55 60
 Ile Tyr Tyr Ser Gln Ile Val Asn Asp Phe Gln Lys Gly Asp Ile Ala
 65 70 75 80
 Glu Gly Tyr Ser Val Ser Arg Glu Lys Lys Glu Ser Phe Pro Leu Thr
 85 90 95
 Val Thr Ser Ala Gln Lys Asn Pro Thr Ala Phe Tyr Leu Cys Ala Ser
 100 105 110
 Ser Ile Ser Ala Gly Gly Asp Gly Tyr Thr Phe Gly Ser Gly Thr Arg
 115 120 125
 Leu Thr Val Val Glu Asp Leu Arg Asn Val Thr Pro Pro Lys Val Ser
 130 135 140
 Leu Phe Glu Pro Ser Lys Ala Glu Ile Ala Asn Lys Gln Lys Ala Thr
 145 150 155 160
 Leu Val Cys Leu Ala Arg Gly Phe Phe Pro Asp His Val Glu Leu Ser
 165 170 175
 Trp Trp Val Asn Gly Lys Glu Val His Ser Gly Val Cys Thr Asp Pro
 180 185 190
 Gln Ala Tyr Lys Glu Ser Asn Tyr Ser Tyr Cys Leu Ser Ser Arg Leu
 195 200 205
 Arg Val Ser Ala Thr Phe Trp His Asn Pro Arg Asn His Phe Arg Cys
 210 215 220
 Gln Val Gln Phe His Gly Leu Ser Glu Glu Asp Lys Trp Pro Glu Gly
 225 230 235 240
 Ser Pro Lys Pro Val Thr Gln Asn Ile Ser Ala Glu Ala Trp Gly Arg
 245 250 255

Ala Asp Cys Gly Ile Thr Ser Ala Ser Tyr Gln Gln Gly Val Leu Ser
260 265 270
Ala Thr Ile Leu Tyr Glu Ile Leu Leu Gly Lys Ala Thr Leu Tyr Ala
275 280 285
Val Leu Val Ser Thr Leu Val Val Met Ala Met Val Lys Arg Lys Asn
290 295 300

Ser

305

<210> 67

<211> 6

<212> PRT

<213> 智人 (Homo sapiens)

<400> 67

Asn Ser Ala Ser Gln Ser

1 5

<210> 68

<211> 6

<212> PRT

<213> 智人 (Homo sapiens)

<400> 68

Val Tyr Ser Ser Gly Asn

1 5

<210> 69

<211> 13

<212> PRT

<213> 智人 (Homo sapiens)

<400> 69

Cys Val Val Gln Pro Gly Gly Tyr Gln Lys Val Thr Phe

1 5 10

<210> 70

<211> 5

<212> PRT

<213> 智人 (Homo sapiens)

<400> 70

Met Asn His Asn Ser

1 5

<210> 71

<211> 6

<212> PRT

<213> 智人 (Homo sapiens)

<400> 71

Ser Ala Ser Glu Gly Thr

1 5

<210> 72

<211> 16

<212> PRT

<213> 智人 (Homo sapiens)

<400> 72

Cys Ala Ser Ser Glu Gly Leu Trp Gln Val Gly Asp Glu Gln Tyr Phe

1 5 10 15

<210> 73

<211> 131

<212> PRT

<213> 智人 (Homo sapiens)

<400> 73

Met Ile Ser Leu Arg Val Leu Leu Val Ile Leu Trp Leu Gln Leu Ser

1 5 10 15

Trp Val Trp Ser Gln Arg Lys Glu Val Glu Gln Asp Pro Gly Pro Phe

20 25 30

Asn Val Pro Glu Gly Ala Thr Val Ala Phe Asn Cys Thr Tyr Ser Asn

35 40 45

Ser Ala Ser Gln Ser Phe Phe Trp Tyr Arg Gln Asp Cys Arg Lys Glu

50 55 60

Pro Lys Leu Leu Met Ser Val Tyr Ser Ser Gly Asn Glu Asp Gly Arg

65 70 75 80

Phe Thr Ala Gln Leu Asn Arg Ala Ser Gln Tyr Ile Ser Leu Leu Ile

85 90 95

Arg Asp Ser Lys Leu Ser Asp Ser Ala Thr Tyr Leu Cys Val Val Gln

100 105 110

Pro Gly Gly Tyr Gln Lys Val Thr Phe Gly Thr Gly Thr Lys Leu Gln

115 120 125

Val Ile Pro

130

<210> 74

<211> 134

<212> PRT

<213> 智人 (Homo sapiens)

<400> 74

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

<210> 75

<211> 268

<212> PRT

<213> 智人(Homo sapiens)

<400> 75

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

Val Ile Pro Asp Ile Gln Asn Pro Glu Pro Ala Val Tyr Gln Leu Lys		
130	135	140
Asp Pro Arg Ser Gln Asp Ser Thr Leu Cys Leu Phe Thr Asp Phe Asp		
145	150	155
Ser Gln Ile Asn Val Pro Lys Thr Met Glu Ser Gly Thr Phe Ile Thr		
	165	170
Asp Lys Cys Val Leu Asp Met Lys Ala Met Asp Ser Lys Ser Asn Gly		
	180	185
Ala Ile Ala Trp Ser Asn Gln Thr Ser Phe Thr Cys Gln Asp Ile Phe		
	195	200
Lys Glu Thr Asn Ala Thr Tyr Pro Ser Ser Asp Val Pro Cys Asp Ala		
	210	215
Thr Leu Thr Glu Lys Ser Phe Glu Thr Asp Met Asn Leu Asn Phe Gln		
225	230	235
Asn Leu Leu Val Ile Val Leu Arg Ile Leu Leu Leu Lys Val Ala Gly		
	245	250
Phe Asn Leu Leu Met Thr Leu Arg Leu Trp Ser Ser		
	260	265
<210> 76		
<211> 307		
<212> PRT		
<213> 智人 (Homo sapiens)		
<400> 76		
Met Ala Ile Gly Leu Leu Cys Cys Val Ala Phe Ser Leu Leu Trp Ala		
1	5	10
Ser Pro Val Asn Ala Gly Val Thr Gln Thr Pro Lys Phe Gln Val Leu		
	20	25
Lys Thr Gly Gln Ser Met Thr Leu Gln Cys Ala Gln Asp Met Asn His		
	35	40
Asn Ser Met Tyr Trp Tyr Arg Gln Asp Pro Gly Met Gly Leu Arg Leu		
	50	55
Ile Tyr Tyr Ser Ala Ser Glu Gly Thr Thr Asp Lys Gly Glu Val Pro		
65	70	75
Asn Gly Tyr Asn Val Ser Arg Leu Asn Lys Arg Glu Phe Ser Leu Arg		
	85	90
Leu Glu Ser Ala Ala Pro Ser Gln Thr Ser Val Tyr Phe Cys Ala Ser		
	100	105
Ser Glu Gly Leu Trp Gln Val Gly Asp Glu Gln Tyr Phe Gly Pro Gly		
	115	120
		125

Thr Arg Leu Thr Val Thr Glu Asp Leu Arg Asn Val Thr Pro Pro Lys		
130	135	140
Val Ser Leu Phe Glu Pro Ser Lys Ala Glu Ile Ala Asn Lys Gln Lys		
145	150	155
Ala Thr Leu Val Cys Leu Ala Arg Gly Phe Phe Pro Asp His Val Glu		
	165	170
Leu Ser Trp Trp Val Asn Gly Lys Glu Val His Ser Gly Val Cys Thr		
	180	185
Asp Pro Gln Ala Tyr Lys Glu Ser Asn Tyr Ser Tyr Cys Leu Ser Ser		
	195	200
Arg Leu Arg Val Ser Ala Thr Phe Trp His Asn Pro Arg Asn His Phe		
	210	215
Arg Cys Gln Val Gln Phe His Gly Leu Ser Glu Glu Asp Lys Trp Pro		
225	230	235
Glu Gly Ser Pro Lys Pro Val Thr Gln Asn Ile Ser Ala Glu Ala Trp		
	245	250
Gly Arg Ala Asp Cys Gly Ile Thr Ser Ala Ser Tyr Gln Gln Gly Val		
	260	265
Leu Ser Ala Thr Ile Leu Tyr Glu Ile Leu Leu Gly Lys Ala Thr Leu		
	275	280
Tyr Ala Val Leu Val Ser Thr Leu Val Val Met Ala Met Val Lys Arg		
	290	295
Lys Asn Ser		300

Lys Asn Ser

305

<210> 77

<211> 7

<212> PRT

<213> 智人(Homo sapiens)

<400> 77

Thr Ser Glu Asn Asn Tyr Tyr

1

5

<210> 78

<211> 8

<212> PRT

<213> 智人(Homo sapiens)

<400> 78

Gln Glu Ala Tyr Lys Gln Gln Asn

1

5

<210> 79

<211> 16

<212> PRT

<213> 智人 (Homo sapiens)

<400> 79

Cys Ala Phe Met Gly Tyr Ser Gly Ala Gly Ser Tyr Gln Leu Thr Phe

1 5 10 15

<210> 80

<211> 5

<212> PRT

<213> 智人 (Homo sapiens)

<400> 80

Glu Asn His Arg Tyr

1 5

<210> 81

<211> 6

<212> PRT

<213> 智人 (Homo sapiens)

<400> 81

Ser Tyr Gly Val Lys Asp

1 5

<210> 82

<211> 15

<212> PRT

<213> 智人 (Homo sapiens)

<400> 82

Cys Ala Ile Ser Glu Leu Val Thr Gly Asp Ser Pro Leu His Phe

1 5 10 15

<210> 83

<211> 137

<212> PRT

<213> 智人 (Homo sapiens)

<400> 83

Met Thr Arg Val Ser Leu Leu Trp Ala Val Val Val Ser Thr Cys Leu

1 5 10 15

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

20 25 30

Val Gln Glu Ala Glu Thr Val Thr Leu Ser Cys Thr Tyr Asp Thr Ser

35 40 45

Glu Asn Asn Tyr Tyr Leu Phe Trp Tyr Lys Gln Pro Pro Ser Arg Gln

50	55	60
Met Ile Leu Val Ile Arg Gln Glu Ala Tyr Lys Gln Gln Asn Ala Thr		
65	70	75
Glu Asn Arg Phe Ser Val Asn Phe Gln Lys Ala Ala Lys Ser Phe Ser		80
	85	90
Leu Lys Ile Ser Asp Ser Gln Leu Gly Asp Thr Ala Met Tyr Phe Cys		95
	100	105
Ala Phe Met Gly Tyr Ser Gly Ala Gly Ser Tyr Gln Leu Thr Phe Gly		110
	115	120
Lys Gly Thr Lys Leu Ser Val Ile Pro		125
130	135	
<210> 84		
<211> 133		
<212> PRT		
<213> 智人(Homo sapiens)		
<400> 84		
Met Ala Thr Arg Leu Phe Phe Tyr Val Ala Leu Cys Leu Leu Trp Thr		
1	5	10
Gly His Met Asp Ala Gly Ile Thr Gln Ser Pro Arg His Lys Val Thr		15
	20	25
Glu Thr Gly Thr Pro Val Thr Leu Arg Cys His Gln Thr Glu Asn His		30
	35	40
Arg Tyr Met Tyr Trp Tyr Arg Gln Asp Pro Gly His Gly Leu Arg Leu		45
50	55	60
Ile His Tyr Ser Tyr Gly Val Lys Asp Thr Asp Lys Gly Glu Val Ser		
65	70	75
Asp Gly Tyr Ser Val Ser Arg Ser Lys Thr Glu Asp Phe Leu Leu Thr		80
	85	90
Leu Glu Ser Ala Thr Ser Ser Gln Thr Ser Val Tyr Phe Cys Ala Ile		95
	100	105
Ser Glu Leu Val Thr Gly Asp Ser Pro Leu His Phe Gly Asn Gly Thr		110
	115	120
Arg Leu Thr Val Thr		125
130		
<210> 85		
<211> 274		
<212> PRT		
<213> 智人(Homo sapiens)		
<400> 85		

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

Ser Ser
 <210> 86
 <211> 306
 <212> PRT
 <213> 智人 (Homo sapiens)

<400> 86

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

Asn Ser

305

<210> 87

<211> 6

<212> PRT

<213> 智人(Homo sapiens)

<400> 87

Asn Tyr Ser Pro Ala Tyr

1 5

<210> 88

<211> 7

<212> PRT

<213> 智人(Homo sapiens)

<400> 88

Ile Arg Glu Asn Glu Lys Glu

1 5

<210> 89

<211> 12

<212> PRT

<213> 智人(Homo sapiens)

<400> 89

Cys Ala Leu Asp Ile Tyr Pro His Asp Met Arg Phe

1 5 10

<210> 90

<211> 5

<212> PRT

<213> 智人(Homo sapiens)

<400> 90

Ser Gly His Ala Thr

1 5

<210> 91

<211> 6

<212> PRT

<213> 智人(Homo sapiens)

<400> 91

Phe Gln Asn Asn Gly Val

1 5

<210> 92

<211> 15

<212> PRT

<213> 智人 (Homo sapiens)

<400> 92

Cys Ala Ser Ser Leu Asp Pro Gly Asp Thr Gly Glu Leu Phe Phe
 1 5 10 15

<210> 93

<211> 131

<212> PRT

<213> 智人 (Homo sapiens)

<400> 93

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

<210> 94

<211> 134

<212> PRT

<213> 智人 (Homo sapiens)

<400> 94

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

Ala Thr Leu Tyr Trp Tyr Gln Gln Ile Leu Gly Gln Gly Pro Lys Leu
 50 55 60
 Leu Ile Gln Phe Gln Asn Asn Gly Val Val Asp Asp Ser Gln Leu Pro
 65 70 75 80
 Lys Asp Arg Phe Ser Ala Glu Arg Leu Lys Gly Val Asp Ser Thr Leu
 85 90 95
 Lys Ile Gln Pro Ala Lys Leu Glu Asp Ser Ala Val Tyr Leu Cys Ala
 100 105 110
 Ser Ser Leu Asp Pro Gly Asp Thr Gly Glu Leu Phe Phe Gly Glu Gly
 115 120 125
 Ser Arg Leu Thr Val Leu
 130
 <210> 95
 <211> 268
 <212> PRT
 <213> 智人(Homo sapiens)
 <400> 95
 Met Glu Ser Phe Leu Gly Gly Val Leu Leu Ile Leu Trp Leu Gln Val
 1 5 10 15
 Asp Trp Val Lys Ser Gln Lys Ile Glu Gln Asn Ser Glu Ala Leu Asn
 20 25 30
 Ile Gln Glu Gly Lys Thr Ala Thr Leu Thr Cys Asn Tyr Thr Asn Tyr
 35 40 45
 Ser Pro Ala Tyr Leu Gln Trp Tyr Arg Gln Asp Pro Gly Arg Gly Pro
 50 55 60
 Val Phe Leu Leu Leu Ile Arg Glu Asn Glu Lys Glu Lys Arg Lys Glu
 65 70 75 80
 Arg Leu Lys Val Thr Phe Asp Thr Thr Leu Lys Gln Ser Leu Phe His
 85 90 95
 Ile Thr Ala Ser Gln Pro Ala Asp Ser Ala Thr Tyr Leu Cys Ala Leu
 100 105 110
 Asp Ile Tyr Pro His Asp Met Arg Phe Gly Ala Gly Thr Arg Leu Thr
 115 120 125
 Val Lys Pro Asp Ile Gln Asn Pro Glu Pro Ala Val Tyr Gln Leu Lys
 130 135 140
 Asp Pro Arg Ser Gln Asp Ser Thr Leu Cys Leu Phe Thr Asp Phe Asp
 145 150 155 160
 Ser Gln Ile Asn Val Pro Lys Thr Met Glu Ser Gly Thr Phe Ile Thr
 165 170 175

Asp	Lys	Cys	Val	Leu	Asp	Met	Lys	Ala	Met	Asp	Ser	Lys	Ser	Asn	Gly
			180					185					190		
Ala	Ile	Ala	Trp	Ser	Asn	Gln	Thr	Ser	Phe	Thr	Cys	Gln	Asp	Ile	Phe
			195				200					205			
Lys	Glu	Thr	Asn	Ala	Thr	Tyr	Pro	Ser	Ser	Asp	Val	Pro	Cys	Asp	Ala
			210				215				220				
Thr	Leu	Thr	Glu	Lys	Ser	Phe	Glu	Thr	Asp	Met	Asn	Leu	Asn	Phe	Gln
225						230				235					240
Asn	Leu	Leu	Val	Ile	Val	Leu	Arg	Ile	Leu	Leu	Leu	Lys	Val	Ala	Gly
				245					250					255	
Phe	Asn	Leu	Leu	Met	Thr	Leu	Arg	Leu	Trp	Ser	Ser				
			260					265							

<210> 96
 <211> 307
 <212> PRT
 <213> 智人(Homo sapiens)
 <400> 96

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

Leu Ser Trp Trp Val Asn Gly Lys Glu Val His Ser Gly Val Cys Thr
 180 185 190
 Asp Pro Gln Ala Tyr Lys Glu Ser Asn Tyr Ser Tyr Cys Leu Ser Ser
 195 200 205
 Arg Leu Arg Val Ser Ala Thr Phe Trp His Asn Pro Arg Asn His Phe
 210 215 220
 Arg Cys Gln Val Gln Phe His Gly Leu Ser Glu Glu Asp Lys Trp Pro
 225 230 235 240
 Glu Gly Ser Pro Lys Pro Val Thr Gln Asn Ile Ser Ala Glu Ala Trp
 245 250 255
 Gly Arg Ala Asp Cys Gly Ile Thr Ser Ala Ser Tyr Gln Gln Gly Val
 260 265 270
 Leu Ser Ala Thr Ile Leu Tyr Glu Ile Leu Leu Gly Lys Ala Thr Leu
 275 280 285
 Tyr Ala Val Leu Val Ser Thr Leu Val Val Met Ala Met Val Lys Arg
 290 295 300
 Lys Asn Ser
 305
 <210> 97
 <211> 6
 <212> PRT
 <213> 智人 (Homo sapiens)
 <400> 97
 Ser Ser Val Ser Val Tyr
 1 5
 <210> 98
 <211> 8
 <212> PRT
 <213> 智人 (Homo sapiens)
 <400> 98
 Tyr Leu Ser Gly Ser Thr Leu Val
 1 5
 <210> 99
 <211> 14
 <212> PRT
 <213> 智人 (Homo sapiens)
 <400> 99
 Cys Ala Val Ser Asp Leu Val Arg Asp Asp Lys Ile Ile Phe
 1 5 10

<210> 100
 <211> 5
 <212> PRT
 <213> 智人 (Homo sapiens)
 <400> 100
 Met Asn His Asn Ser
 1 5
 <210> 101
 <211> 6
 <212> PRT
 <213> 智人 (Homo sapiens)
 <400> 101
 Ser Ala Ser Glu Gly Thr
 1 5
 <210> 102
 <211> 11
 <212> PRT
 <213> 智人 (Homo sapiens)
 <400> 102
 Cys Ala Ser Ile Gly Gly Phe Glu Ala Phe Phe
 1 5 10
 <210> 103
 <211> 133
 <212> PRT
 <213> 智人 (Homo sapiens)
 <400> 103
 Met Ala Leu Leu Leu Val Pro Ala Phe Gln Val Ile Phe Thr Leu Gly
 1 5 10 15
 Gly Thr Arg Ala Gln Ser Val Thr Gln Leu Asp Ser Gln Val Pro Val
 20 25 30
 Phe Glu Glu Ala Pro Val Glu Leu Arg Cys Asn Tyr Ser Ser Ser Val
 35 40 45
 Ser Val Tyr Leu Phe Trp Tyr Val Gln Tyr Pro Asn Gln Gly Leu Gln
 50 55 60
 Leu Leu Leu Lys Tyr Leu Ser Gly Ser Thr Leu Val Glu Ser Ile Asn
 65 70 75 80
 Gly Phe Glu Ala Glu Phe Asn Lys Ser Gln Thr Ser Phe His Leu Arg
 85 90 95
 Lys Pro Ser Val His Ile Ser Asp Thr Ala Glu Tyr Phe Cys Ala Val

100	105	110
Ser Asp Leu Val Arg Asp Asp Lys Ile Ile Phe Gly Lys Gly Thr Arg		
115	120	125
Leu His Ile Leu Pro		
130		
<210> 104		
<211> 129		
<212> PRT		
<213> 智人 (Homo sapiens)		
<400> 104		
Met His Ile Gly Leu Leu Cys Cys Val Ala Phe Ser Leu Leu Trp Ala		
1 5 10 15		
Ser Pro Val Asn Ala Gly Val Thr Gln Thr Pro Lys Phe Gln Val Leu		
20 25 30		
Lys Thr Gly Gln Ser Met Thr Leu Gln Cys Ala Gln Asp Met Asn His		
35 40 45		
Asn Ser Met Tyr Trp Tyr Arg Gln Asp Pro Gly Met Gly Leu Arg Leu		
50 55 60		
Ile Tyr Tyr Ser Ala Ser Glu Gly Thr Thr Asp Lys Gly Glu Val Pro		
65 70 75 80		
Asn Gly Tyr Asn Val Ser Arg Leu Asn Lys Arg Glu Phe Ser Leu Arg		
85 90 95		
Leu Glu Ser Ala Ala Pro Ser Gln Thr Ser Val Tyr Phe Cys Ala Ser		
100 105 110		
Ile Gly Gly Phe Glu Ala Phe Phe Gly Gln Gly Thr Arg Leu Thr Val		
115 120 125		
Val		
<210> 105		
<211> 270		
<212> PRT		
<213> 智人 (Homo sapiens)		
<400> 105		
Met Ala Leu Leu Leu Val Pro Ala Phe Gln Val Ile Phe Thr Leu Gly		
1 5 10 15		
Gly Thr Arg Ala Gln Ser Val Thr Gln Leu Asp Ser Gln Val Pro Val		
20 25 30		
Phe Glu Glu Ala Pro Val Glu Leu Arg Cys Asn Tyr Ser Ser Ser Val		
35 40 45		
Ser Val Tyr Leu Phe Trp Tyr Val Gln Tyr Pro Asn Gln Gly Leu Gln		

50	55	60													
Leu	Leu	Leu	Lys	Tyr	Leu	Ser	Gly	Ser	Thr	Leu	Val	Glu	Ser	Ile	Asn
65					70					75					80
Gly	Phe	Glu	Ala	Glu	Phe	Asn	Lys	Ser	Gln	Thr	Ser	Phe	His	Leu	Arg
				85						90					95
Lys	Pro	Ser	Val	His	Ile	Ser	Asp	Thr	Ala	Glu	Tyr	Phe	Cys	Ala	Val
			100						105					110	
Ser	Asp	Leu	Val	Arg	Asp	Asp	Lys	Ile	Ile	Phe	Gly	Lys	Gly	Thr	Arg
		115						120					125		
Leu	His	Ile	Leu	Pro	Asn	Ile	Gln	Asn	Pro	Glu	Pro	Ala	Val	Tyr	Gln
		130					135					140			
Leu	Lys	Asp	Pro	Arg	Ser	Gln	Asp	Ser	Thr	Leu	Cys	Leu	Phe	Thr	Asp
145					150					155					160
Phe	Asp	Ser	Gln	Ile	Asn	Val	Pro	Lys	Thr	Met	Glu	Ser	Gly	Thr	Phe
				165						170					175
Ile	Thr	Asp	Lys	Cys	Val	Leu	Asp	Met	Lys	Ala	Met	Asp	Ser	Lys	Ser
			180						185					190	
Asn	Gly	Ala	Ile	Ala	Trp	Ser	Asn	Gln	Thr	Ser	Phe	Thr	Cys	Gln	Asp
		195						200					205		
Ile	Phe	Lys	Glu	Thr	Asn	Ala	Thr	Tyr	Pro	Ser	Ser	Asp	Val	Pro	Cys
		210					215					220			
Asp	Ala	Thr	Leu	Thr	Glu	Lys	Ser	Phe	Glu	Thr	Asp	Met	Asn	Leu	Asn
225					230					235					240
Phe	Gln	Asn	Leu	Leu	Val	Ile	Val	Leu	Arg	Ile	Leu	Leu	Leu	Lys	Val
				245						250					255
Ala	Gly	Phe	Asn	Leu	Leu	Met	Thr	Leu	Arg	Leu	Trp	Ser	Ser		
			260						265				270		
<210> 106															
<211> 302															
<212> PRT															
<213> 智人 (Homo sapiens)															
<400> 106															
Met	His	Ile	Gly	Leu	Leu	Cys	Cys	Val	Ala	Phe	Ser	Leu	Leu	Trp	Ala
1				5					10					15	
Ser	Pro	Val	Asn	Ala	Gly	Val	Thr	Gln	Thr	Pro	Lys	Phe	Gln	Val	Leu
				20					25					30	
Lys	Thr	Gly	Gln	Ser	Met	Thr	Leu	Gln	Cys	Ala	Gln	Asp	Met	Asn	His
			35					40					45		
Asn	Ser	Met	Tyr	Trp	Tyr	Arg	Gln	Asp	Pro	Gly	Met	Gly	Leu	Arg	Leu

50	55	60
Ile Tyr Tyr Ser Ala Ser Glu Gly Thr Thr Asp Lys Gly Glu Val Pro		
65	70	75
Asn Gly Tyr Asn Val Ser Arg Leu Asn Lys Arg Glu Phe Ser Leu Arg		
85	90	95
Leu Glu Ser Ala Ala Pro Ser Gln Thr Ser Val Tyr Phe Cys Ala Ser		
100	105	110
Ile Gly Gly Phe Glu Ala Phe Phe Gly Gln Gly Thr Arg Leu Thr Val		
115	120	125
Val Glu Asp Leu Arg Asn Val Thr Pro Pro Lys Val Ser Leu Phe Glu		
130	135	140
Pro Ser Lys Ala Glu Ile Ala Asn Lys Gln Lys Ala Thr Leu Val Cys		
145	150	155
Leu Ala Arg Gly Phe Phe Pro Asp His Val Glu Leu Ser Trp Trp Val		
165	170	175
Asn Gly Lys Glu Val His Ser Gly Val Cys Thr Asp Pro Gln Ala Tyr		
180	185	190
Lys Glu Ser Asn Tyr Ser Tyr Cys Leu Ser Ser Arg Leu Arg Val Ser		
195	200	205
Ala Thr Phe Trp His Asn Pro Arg Asn His Phe Arg Cys Gln Val Gln		
210	215	220
Phe His Gly Leu Ser Glu Glu Asp Lys Trp Pro Glu Gly Ser Pro Lys		
225	230	235
Pro Val Thr Gln Asn Ile Ser Ala Glu Ala Trp Gly Arg Ala Asp Cys		
245	250	255
Gly Ile Thr Ser Ala Ser Tyr Gln Gln Gly Val Leu Ser Ala Thr Ile		
260	265	270
Leu Tyr Glu Ile Leu Leu Gly Lys Ala Thr Leu Tyr Ala Val Leu Val		
275	280	285
Ser Thr Leu Val Val Met Ala Met Val Lys Arg Lys Asn Ser		
290	295	300
<210> 107		
<211> 6		
<212> PRT		
<213> 智人 (Homo sapiens)		
<400> 107		
Thr Ser Gly Phe Asn Gly		
1	5	
<210> 108		

<211> 6
<212> PRT
<213> 智人 (Homo sapiens)
<400> 108
Asn Val Leu Asp Gly Leu
1 5
<210> 109
<211> 12
<212> PRT
<213> 智人 (Homo sapiens)
<400> 109
Cys Ala Val Tyr Thr Gly Gly Phe Lys Thr Ile Phe
1 5 10
<210> 110
<211> 5
<212> PRT
<213> 智人 (Homo sapiens)
<400> 110
Ser Gly His Ala Thr
1 5
<210> 111
<211> 6
<212> PRT
<213> 智人 (Homo sapiens)
<400> 111
Phe Gln Asn Asn Gly Val
1 5
<210> 112
<211> 15
<212> PRT
<213> 智人 (Homo sapiens)
<400> 112
Cys Ala Ser Asn Leu Gly Gly Gly Ser Thr Asp Thr Gln Tyr Phe
1 5 10 15
<210> 113
<211> 126
<212> PRT
<213> 智人 (Homo sapiens)
<400> 113

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

<210> 114

<211> 134

<212> PRT

<213> 智人(Homo sapiens)

<400> 114

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

<210> 115

<211> 263

<212> PRT

<213> 智人(Homo sapiens)

<400> 115

```

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

```

<210> 116

<211> 307

<212> PRT

<213> 智人(Homo sapiens)

<400> 116

```

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

```

Leu Ser Ala Thr Ile Leu Tyr Glu Ile Leu Leu Gly Lys Ala Thr Leu
275 280 285
Tyr Ala Val Leu Val Ser Thr Leu Val Val Met Ala Met Val Lys Arg
290 295 300
Lys Asn Ser
305
<210> 117
<211> 6
<212> PRT
<213> 智人 (Homo sapiens)
<400> 117
Thr Ser Gly Phe Asn Gly
1 5
<210> 118
<211> 6
<212> PRT
<213> 智人 (Homo sapiens)
<400> 118
Asn Val Leu Asp Gly Leu
1 5
<210> 119
<211> 14
<212> PRT
<213> 智人 (Homo sapiens)
<400> 119
Cys Ala Phe Tyr Tyr Gly Gly Ser Gln Gly Asn Leu Ile Phe
1 5 10
<210> 120
<211> 5
<212> PRT
<213> 智人 (Homo sapiens)
<400> 120
Ser Gly His Val Ser
1 5
<210> 121
<211> 6
<212> PRT
<213> 智人 (Homo sapiens)
<400> 121

Phe Gln Asn Glu Ala Gln

1 5

<210> 122

<211> 15

<212> PRT

<213> 智人(Homo sapiens)

<400> 122

Cys Ala Ser Ser Phe Gly Ser Gly Ser Thr Asp Thr Gln Tyr Phe

1 5 10 15

<210> 123

<211> 128

<212> PRT

<213> 智人(Homo sapiens)

<400> 123

Met Ala Gly Val Phe Leu Leu Tyr Val Ser Met Lys Met Gly Gly Thr

1 5 10 15

Thr Gly Gln Asn Ile Asp Gln Pro Thr Glu Met Thr Ala Thr Glu Gly

20 25 30

Ala Ile Val Gln Ile Asn Cys Thr Tyr Gln Thr Ser Gly Phe Asn Gly

35 40 45

Leu Phe Trp Tyr Gln Gln His Ala Gly Glu Ala Pro Thr Phe Leu Ser

50 55 60

Tyr Asn Val Leu Asp Gly Leu Glu Glu Lys Gly Arg Phe Ser Ser Phe

65 70 75 80

Leu Ser Arg Ser Lys Gly Tyr Ser Tyr Leu Leu Leu Lys Glu Leu Gln

85 90 95

Met Lys Asp Ser Ala Ser Tyr Leu Cys Ala Phe Tyr Tyr Gly Gly Ser

100 105 110

Gln Gly Asn Leu Ile Phe Gly Lys Gly Thr Lys Leu Ser Val Lys Pro

115 120 125

<210> 124

<211> 134

<212> PRT

<213> 智人(Homo sapiens)

<400> 124

Met His Thr Arg Leu Leu Cys Trp Val Val Leu Gly Phe Leu Gly Thr

1 5 10 15

Asp His Thr Gly Ala Gly Val Ser Gln Ser Pro Arg Tyr Lys Val Ala

20 25 30

Lys Arg Gly Gln Asp Val Ala Leu Arg Cys Asp Pro Ile Ser Gly His
 35 40 45
 Val Ser Leu Phe Trp Tyr Gln Gln Ala Leu Gly Gln Gly Pro Glu Phe
 50 55 60
 Leu Thr Tyr Phe Gln Asn Glu Ala Gln Leu Asp Lys Ser Gly Leu Pro
 65 70 75 80
 Ser Asp Arg Phe Phe Ala Glu Arg Pro Glu Gly Ser Val Ser Thr Leu
 85 90 95
 Lys Ile Gln Arg Thr Gln Gln Glu Asp Ser Ala Val Tyr Leu Cys Ala
 100 105 110
 Ser Ser Phe Gly Ser Gly Ser Thr Asp Thr Gln Tyr Phe Gly Pro Gly
 115 120 125
 Thr Arg Leu Thr Val Leu
 130
 <210> 125
 <211> 265
 <212> PRT
 <213> 智人(Homo sapiens)
 <400> 125
 Met Ala Gly Val Phe Leu Leu Tyr Val Ser Met Lys Met Gly Gly Thr
 1 5 10 15
 Thr Gly Gln Asn Ile Asp Gln Pro Thr Glu Met Thr Ala Thr Glu Gly
 20 25 30
 Ala Ile Val Gln Ile Asn Cys Thr Tyr Gln Thr Ser Gly Phe Asn Gly
 35 40 45
 Leu Phe Trp Tyr Gln Gln His Ala Gly Glu Ala Pro Thr Phe Leu Ser
 50 55 60
 Tyr Asn Val Leu Asp Gly Leu Glu Glu Lys Gly Arg Phe Ser Ser Phe
 65 70 75 80
 Leu Ser Arg Ser Lys Gly Tyr Ser Tyr Leu Leu Leu Lys Glu Leu Gln
 85 90 95
 Met Lys Asp Ser Ala Ser Tyr Leu Cys Ala Phe Tyr Tyr Gly Gly Ser
 100 105 110
 Gln Gly Asn Leu Ile Phe Gly Lys Gly Thr Lys Leu Ser Val Lys Pro
 115 120 125
 Asn Ile Gln Asn Pro Glu Pro Ala Val Tyr Gln Leu Lys Asp Pro Arg
 130 135 140
 Ser Gln Asp Ser Thr Leu Cys Leu Phe Thr Asp Phe Asp Ser Gln Ile
 145 150 155 160

Asn Val Pro Lys Thr Met Glu Ser Gly Thr Phe Ile Thr Asp Lys Cys		
165	170	175
Val Leu Asp Met Lys Ala Met Asp Ser Lys Ser Asn Gly Ala Ile Ala		
180	185	190
Trp Ser Asn Gln Thr Ser Phe Thr Cys Gln Asp Ile Phe Lys Glu Thr		
195	200	205
Asn Ala Thr Tyr Pro Ser Ser Asp Val Pro Cys Asp Ala Thr Leu Thr		
210	215	220
Glu Lys Ser Phe Glu Thr Asp Met Asn Leu Asn Phe Gln Asn Leu Leu		
225	230	235
Val Ile Val Leu Arg Ile Leu Leu Leu Lys Val Ala Gly Phe Asn Leu		
245	250	255
Leu Met Thr Leu Arg Leu Trp Ser Ser		
260	265	
<210> 126		
<211> 307		
<212> PRT		
<213> 智人(Homo sapiens)		
<400> 126		
Met His Thr Arg Leu Leu Cys Trp Val Val Leu Gly Phe Leu Gly Thr		
1	5	10
Asp His Thr Gly Ala Gly Val Ser Gln Ser Pro Arg Tyr Lys Val Ala		
20	25	30
Lys Arg Gly Gln Asp Val Ala Leu Arg Cys Asp Pro Ile Ser Gly His		
35	40	45
Val Ser Leu Phe Trp Tyr Gln Gln Ala Leu Gly Gln Gly Pro Glu Phe		
50	55	60
Leu Thr Tyr Phe Gln Asn Glu Ala Gln Leu Asp Lys Ser Gly Leu Pro		
65	70	75
Ser Asp Arg Phe Phe Ala Glu Arg Pro Glu Gly Ser Val Ser Thr Leu		
85	90	95
Lys Ile Gln Arg Thr Gln Gln Glu Asp Ser Ala Val Tyr Leu Cys Ala		
100	105	110
Ser Ser Phe Gly Ser Gly Ser Thr Asp Thr Gln Tyr Phe Gly Pro Gly		
115	120	125
Thr Arg Leu Thr Val Leu Glu Asp Leu Arg Asn Val Thr Pro Pro Lys		
130	135	140
Val Ser Leu Phe Glu Pro Ser Lys Ala Glu Ile Ala Asn Lys Gln Lys		
145	150	155
		160

Ala Thr Leu Val Cys Leu Ala Arg Gly Phe Phe Pro Asp His Val Glu		
165	170	175
Leu Ser Trp Trp Val Asn Gly Lys Glu Val His Ser Gly Val Cys Thr		
180	185	190
Asp Pro Gln Ala Tyr Lys Glu Ser Asn Tyr Ser Tyr Cys Leu Ser Ser		
195	200	205
Arg Leu Arg Val Ser Ala Thr Phe Trp His Asn Pro Arg Asn His Phe		
210	215	220
Arg Cys Gln Val Gln Phe His Gly Leu Ser Glu Glu Asp Lys Trp Pro		
225	230	235
Glu Gly Ser Pro Lys Pro Val Thr Gln Asn Ile Ser Ala Glu Ala Trp		
245	250	255
Gly Arg Ala Asp Cys Gly Ile Thr Ser Ala Ser Tyr Gln Gln Gly Val		
260	265	270
Leu Ser Ala Thr Ile Leu Tyr Glu Ile Leu Leu Gly Lys Ala Thr Leu		
275	280	285
Tyr Ala Val Leu Val Ser Thr Leu Val Val Met Ala Met Val Lys Arg		
290	295	300
Lys Asn Ser		
305		
<210> 127		
<211> 6		
<212> PRT		
<213> 智人 (Homo sapiens)		
<400> 127		
Thr Ser Gly Phe Asn Gly		
1	5	
<210> 128		
<211> 6		
<212> PRT		
<213> 智人 (Homo sapiens)		
<400> 128		
Asn Val Leu Asp Gly Leu		
1	5	
<210> 129		
<211> 14		
<212> PRT		
<213> 智人 (Homo sapiens)		
<400> 129		

Cys Ala Val Tyr Pro Gly Gly Ser Gln Gly Asn Leu Ile Phe
1 5 10

<210> 130

<211> 5

<212> PRT

<213> 智人(Homo sapiens)

<400> 130

Ser Gly His Ala Thr

1 5

<210> 131

<211> 6

<212> PRT

<213> 智人(Homo sapiens)

<400> 131

Phe Gln Asn Asn Gly Val

1 5

<210> 132

<211> 15

<212> PRT

<213> 智人(Homo sapiens)

<400> 132

Cys Ala Ser Ser Leu Gly Thr Gly Ser Thr Asp Thr Gln Tyr Phe

1 5 10 15

<210> 133

<211> 128

<212> PRT

<213> 智人(Homo sapiens)

<400> 133

Met Ala Gly Val Phe Leu Leu Tyr Val Ser Met Lys Met Gly Gly Thr

1 5 10 15

Thr Gly Gln Asn Ile Asp Gln Pro Thr Glu Met Thr Ala Thr Glu Gly

20 25 30

Ala Ile Val Gln Ile Asn Cys Thr Tyr Gln Thr Ser Gly Phe Asn Gly

35 40 45

Leu Phe Trp Tyr Gln Gln His Ala Gly Glu Ala Pro Thr Phe Leu Ser

50 55 60

Tyr Asn Val Leu Asp Gly Leu Glu Glu Lys Gly Arg Phe Ser Ser Phe

65 70 75 80

Leu Ser Arg Ser Lys Gly Tyr Ser Tyr Leu Leu Leu Lys Glu Leu Gln

				85					90					95		
Met	Lys	Asp	Ser	Ala	Ser	Tyr	Leu	Cys	Ala	Val	Tyr	Pro	Gly	Gly	Ser	
			100					105					110			
Gln	Gly	Asn	Leu	Ile	Phe	Gly	Lys	Gly	Thr	Lys	Leu	Ser	Val	Lys	Pro	
		115					120					125				
<210>	134															
<211>	134															
<212>	PRT															
<213>	智人 (Homo sapiens)															
<400>	134															
Met	His	Thr	Arg	Leu	Leu	Cys	Trp	Ala	Ala	Leu	Cys	Leu	Leu	Gly	Ala	
1				5				10						15		
Glu	Leu	Thr	Glu	Ala	Gly	Val	Ala	Gln	Ser	Pro	Arg	Tyr	Lys	Ile	Ile	
			20					25					30			
Glu	Lys	Arg	Gln	Ser	Val	Ala	Phe	Trp	Cys	Asn	Pro	Ile	Ser	Gly	His	
		35					40					45				
Ala	Thr	Leu	Tyr	Trp	Tyr	Gln	Gln	Ile	Leu	Gly	Gln	Gly	Pro	Lys	Leu	
	50					55					60					
Leu	Ile	Gln	Phe	Gln	Asn	Asn	Gly	Val	Val	Asp	Asp	Ser	Gln	Leu	Pro	
65				70						75					80	
Lys	Asp	Arg	Phe	Ser	Ala	Glu	Arg	Leu	Lys	Gly	Val	Asp	Ser	Thr	Leu	
				85					90					95		
Lys	Ile	Gln	Pro	Ala	Lys	Leu	Glu	Asp	Ser	Ala	Val	Tyr	Leu	Cys	Ala	
			100					105					110			
Ser	Ser	Leu	Gly	Thr	Gly	Ser	Thr	Asp	Thr	Gln	Tyr	Phe	Gly	Pro	Gly	
		115					120					125				
Thr	Arg	Leu	Thr	Val	Leu											
	130															
<210>	135															
<211>	265															
<212>	PRT															
<213>	智人 (Homo sapiens)															
<400>	135															
Met	Ala	Gly	Val	Phe	Leu	Leu	Tyr	Val	Ser	Met	Lys	Met	Gly	Gly	Thr	
1				5				10						15		
Thr	Gly	Gln	Asn	Ile	Asp	Gln	Pro	Thr	Glu	Met	Thr	Ala	Thr	Glu	Gly	
			20					25					30			
Ala	Ile	Val	Gln	Ile	Asn	Cys	Thr	Tyr	Gln	Thr	Ser	Gly	Phe	Asn	Gly	
		35					40					45				

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

<210> 136

<211> 307

<212> PRT

<213> 智人 (Homo sapiens)

<400> 136

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

Ala Thr Leu Tyr Trp Tyr Gln Gln Ile Leu Gly Gln Gly Pro Lys Leu		
50	55	60
Leu Ile Gln Phe Gln Asn Asn Gly Val Val Asp Asp Ser Gln Leu Pro		
65	70	75 80
Lys Asp Arg Phe Ser Ala Glu Arg Leu Lys Gly Val Asp Ser Thr Leu		
	85	90 95
Lys Ile Gln Pro Ala Lys Leu Glu Asp Ser Ala Val Tyr Leu Cys Ala		
	100	105 110
Ser Ser Leu Gly Thr Gly Ser Thr Asp Thr Gln Tyr Phe Gly Pro Gly		
	115	120 125
Thr Arg Leu Thr Val Leu Glu Asp Leu Arg Asn Val Thr Pro Pro Lys		
	130	135 140
Val Ser Leu Phe Glu Pro Ser Lys Ala Glu Ile Ala Asn Lys Gln Lys		
145	150	155 160
Ala Thr Leu Val Cys Leu Ala Arg Gly Phe Phe Pro Asp His Val Glu		
	165	170 175
Leu Ser Trp Trp Val Asn Gly Lys Glu Val His Ser Gly Val Cys Thr		
	180	185 190
Asp Pro Gln Ala Tyr Lys Glu Ser Asn Tyr Ser Tyr Cys Leu Ser Ser		
	195	200 205
Arg Leu Arg Val Ser Ala Thr Phe Trp His Asn Pro Arg Asn His Phe		
	210	215 220
Arg Cys Gln Val Gln Phe His Gly Leu Ser Glu Glu Asp Lys Trp Pro		
225	230	235 240
Glu Gly Ser Pro Lys Pro Val Thr Gln Asn Ile Ser Ala Glu Ala Trp		
	245	250 255
Gly Arg Ala Asp Cys Gly Ile Thr Ser Ala Ser Tyr Gln Gln Gly Val		
	260	265 270
Leu Ser Ala Thr Ile Leu Tyr Glu Ile Leu Leu Gly Lys Ala Thr Leu		
	275	280 285
Tyr Ala Val Leu Val Ser Thr Leu Val Val Met Ala Met Val Lys Arg		
	290	295 300
Lys Asn Ser		
305		
<210> 137		
<211> 6		
<212> PRT		
<213> 智人 (Homo sapiens)		
<400> 137		

Asp Arg Gly Ser Gln Ser

1 5

<210> 138

<211> 6

<212> PRT

<213> 智人(Homo sapiens)

<400> 138

Ile Tyr Ser Asn Gly Asp

1 5

<210> 139

<211> 11

<212> PRT

<213> 智人(Homo sapiens)

<400> 139

Cys Ala Val Ser Trp Tyr Ser Thr Leu Thr Phe

1 5 10

<210> 140

<211> 5

<212> PRT

<213> 智人(Homo sapiens)

<400> 140

Trp Ser His Ser Tyr

1 5

<210> 141

<211> 6

<212> PRT

<213> 智人(Homo sapiens)

<400> 141

Ser Ala Ala Ala Asp Ile

1 5

<210> 142

<211> 13

<212> PRT

<213> 智人(Homo sapiens)

<400> 142

Cys Ala Ser Ser Gly Ser Arg Thr Asp Thr Gln Tyr Phe

1 5 10

<210> 143

<211> 130

<212> PRT

<213> 智人(Homo sapiens)

<400> 143

```

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

```

Ser Pro

130

<210> 144

<211> 131

<212> PRT

<213> 智人(Homo sapiens)

<400> 144

```

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

```

	100		105		110
Ser Gly Ser Arg Thr Asp Thr Gln Tyr Phe Gly Pro Gly Thr Arg Leu					
	115		120		125
Thr Val Leu					
	130				
<210> 145					
<211> 267					
<212> PRT					
<213> 智人 (Homo sapiens)					
<400> 145					
Met Ala Ser Leu Arg Val Leu Leu Val Ile Leu Trp Leu Gln Leu Ser					
1	5		10		15
Trp Val Trp Ser Gln Gln Lys Glu Val Glu Gln Asn Ser Gly Pro Leu					
	20		25		30
Ser Val Pro Glu Gly Ala Ile Ala Ser Leu Asn Cys Thr Tyr Ser Asp					
	35		40		45
Arg Gly Ser Gln Ser Phe Phe Trp Tyr Arg Gln Tyr Ser Gly Lys Ser					
	50		55		60
Pro Glu Leu Ile Met Phe Ile Tyr Ser Asn Gly Asp Lys Glu Asp Gly					
65	70		75		80
Arg Phe Thr Ala Gln Leu Asn Lys Ala Ser Gln Tyr Val Ser Leu Leu					
	85		90		95
Ile Arg Asp Ser Gln Pro Ser Asp Ser Ala Thr Tyr Leu Cys Ala Val					
	100		105		110
Ser Trp Tyr Ser Thr Leu Thr Phe Gly Lys Gly Thr Met Leu Leu Val					
	115		120		125
Ser Pro Asn Ile Gln Asn Pro Glu Pro Ala Val Tyr Gln Leu Lys Asp					
	130		135		140
Pro Arg Ser Gln Asp Ser Thr Leu Cys Leu Phe Thr Asp Phe Asp Ser					
145	150		155		160
Gln Ile Asn Val Pro Lys Thr Met Glu Ser Gly Thr Phe Ile Thr Asp					
	165		170		175
Lys Cys Val Leu Asp Met Lys Ala Met Asp Ser Lys Ser Asn Gly Ala					
	180		185		190
Ile Ala Trp Ser Asn Gln Thr Ser Phe Thr Cys Gln Asp Ile Phe Lys					
	195		200		205
Glu Thr Asn Ala Thr Tyr Pro Ser Ser Asp Val Pro Cys Asp Ala Thr					
	210		215		220
Leu Thr Glu Lys Ser Phe Glu Thr Asp Met Asn Leu Asn Phe Gln Asn					

225	230	235	240
Leu Leu Val Ile Val Leu Arg Ile Leu Leu Leu Lys Val Ala Gly Phe			
	245	250	255
Asn Leu Leu Met Thr Leu Arg Leu Trp Ser Ser			
260	265		
<210> 146			
<211> 304			
<212> PRT			
<213> 智人 (Homo sapiens)			
<400> 146			
Met His Thr Arg Leu Phe Phe Tyr Val Ala Leu Cys Leu Leu Trp Ala			
1	5	10	15
Gly His Arg Asp Ala Gly Ile Thr Gln Ser Pro Arg Tyr Lys Ile Thr			
20	25	30	
Glu Thr Gly Arg Gln Val Thr Leu Met Cys His Gln Thr Trp Ser His			
35	40	45	
Ser Tyr Met Phe Trp Tyr Arg Gln Asp Leu Gly His Gly Leu Arg Leu			
50	55	60	
Ile Tyr Tyr Ser Ala Ala Ala Asp Ile Thr Asp Lys Gly Glu Val Pro			
65	70	75	80
Asp Gly Tyr Val Val Ser Arg Ser Lys Thr Glu Asn Phe Pro Leu Thr			
85	90	95	
Leu Glu Ser Ala Thr Arg Ser Gln Thr Ser Val Tyr Phe Cys Ala Ser			
100	105	110	
Ser Gly Ser Arg Thr Asp Thr Gln Tyr Phe Gly Pro Gly Thr Arg Leu			
115	120	125	
Thr Val Leu Glu Asp Leu Arg Asn Val Thr Pro Pro Lys Val Ser Leu			
130	135	140	
Phe Glu Pro Ser Lys Ala Glu Ile Ala Asn Lys Gln Lys Ala Thr Leu			
145	150	155	160
Val Cys Leu Ala Arg Gly Phe Phe Pro Asp His Val Glu Leu Ser Trp			
165	170	175	
Trp Val Asn Gly Lys Glu Val His Ser Gly Val Cys Thr Asp Pro Gln			
180	185	190	
Ala Tyr Lys Glu Ser Asn Tyr Ser Tyr Cys Leu Ser Ser Arg Leu Arg			
195	200	205	
Val Ser Ala Thr Phe Trp His Asn Pro Arg Asn His Phe Arg Cys Gln			
210	215	220	
Val Gln Phe His Gly Leu Ser Glu Glu Asp Lys Trp Pro Glu Gly Ser			

225	230	235	240
Pro Lys Pro Val Thr Gln Asn Ile Ser Ala Glu Ala Trp Gly Arg Ala			
	245	250	255
Asp Cys Gly Ile Thr Ser Ala Ser Tyr Gln Gln Gly Val Leu Ser Ala			
	260	265	270
Thr Ile Leu Tyr Glu Ile Leu Leu Gly Lys Ala Thr Leu Tyr Ala Val			
	275	280	285
Leu Val Ser Thr Leu Val Val Met Ala Met Val Lys Arg Lys Asn Ser			
	290	295	300

<210> 147

<211> 5

<212> PRT

<213> 智人(Homo sapiens)

<400> 147

Ser Val Phe Ser Ser

1 5

<210> 148

<211> 7

<212> PRT

<213> 智人(Homo sapiens)

<400> 148

Val Val Thr Gly Gly Glu Val

1 5

<210> 149

<211> 12

<212> PRT

<213> 智人(Homo sapiens)

<400> 149

Cys Ala Gly Glu Phe Ala Gly Asn Gln Phe Tyr Phe

1 5 10

<210> 150

<211> 5

<212> PRT

<213> 智人(Homo sapiens)

<400> 150

Met Gly His Arg Ala

1 5

<210> 151

<211> 6

<212> PRT

<213> 智人 (Homo sapiens)

<400> 151

Tyr Ser Tyr Glu Lys Leu

1 5

<210> 152

<211> 14

<212> PRT

<213> 智人 (Homo sapiens)

<400> 152

Cys Ala Ser Ser Gln Val Gly Leu Thr Tyr Glu Gln Tyr Phe

1 5 10

<210> 153

<211> 128

<212> PRT

<213> 智人 (Homo sapiens)

<400> 153

Met Ala Leu Lys Phe Ser Val Ser Ile Leu Trp Ile Gln Leu Ala Trp

1 5 10 15

Val Ser Thr Gln Leu Leu Glu Gln Ser Pro Gln Phe Leu Ser Ile Gln

20 25 30

Glu Gly Glu Asn Leu Thr Val Tyr Cys Asn Ser Ser Ser Val Phe Ser

35 40 45

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

50 55 60

Val Thr Val Val Thr Gly Gly Glu Val Lys Lys Leu Lys Arg Leu Thr

65 70 75 80

Phe Gln Phe Gly Asp Ala Arg Lys Asp Ser Ser Leu His Ile Thr Ala

85 90 95

Ala Gln Pro Gly Asp Thr Gly Leu Tyr Leu Cys Ala Gly Glu Phe Ala

100 105 110

Gly Asn Gln Phe Tyr Phe Gly Thr Gly Thr Ser Leu Thr Val Ile Pro

115 120 125

<210> 154

<211> 132

<212> PRT

<213> 智人 (Homo sapiens)

<400> 154

Met His Cys Arg Leu Leu Cys Cys Ala Val Leu Cys Leu Leu Gly Ala

1	5	10	15
Val Pro Ile Asp Thr Glu Val Thr Gln Thr Pro Lys His Leu Val Met			
20	25	30	
Gly Met Thr Asn Lys Lys Ser Leu Lys Cys Glu Gln His Met Gly His			
35	40	45	
Arg Ala Met Tyr Trp Tyr Lys Gln Lys Ala Lys Lys Pro Pro Glu Leu			
50	55	60	
Met Phe Val Tyr Ser Tyr Glu Lys Leu Ser Ile Asn Glu Ser Val Pro			
65	70	75	80
Ser Arg Phe Ser Pro Glu Cys Pro Asn Ser Ser Leu Leu Asn Leu His			
85	90	95	
Leu His Ala Leu Gln Pro Glu Asp Ser Ala Leu Tyr Leu Cys Ala Ser			
100	105	110	
Ser Gln Val Gly Leu Thr Tyr Glu Gln Tyr Phe Gly Pro Gly Thr Arg			
115	120	125	
Leu Thr Val Thr			
130			
<210> 155			
<211> 265			
<212> PRT			
<213> 智人(Homo sapiens)			
<400> 155			
Met Ala Leu Lys Phe Ser Val Ser Ile Leu Trp Ile Gln Leu Ala Trp			
1	5	10	15
Val Ser Thr Gln Leu Leu Glu Gln Ser Pro Gln Phe Leu Ser Ile Gln			
20	25	30	
Glu Gly Glu Asn Leu Thr Val Tyr Cys Asn Ser Ser Ser Val Phe Ser			
35	40	45	
Ser Leu Gln Trp Tyr Arg Gln Glu Pro Gly Glu Gly Pro Val Leu Leu			
50	55	60	
Val Thr Val Val Thr Gly Gly Glu Val Lys Lys Leu Lys Arg Leu Thr			
65	70	75	80
Phe Gln Phe Gly Asp Ala Arg Lys Asp Ser Ser Leu His Ile Thr Ala			
85	90	95	
Ala Gln Pro Gly Asp Thr Gly Leu Tyr Leu Cys Ala Gly Glu Phe Ala			
100	105	110	
Gly Asn Gln Phe Tyr Phe Gly Thr Gly Thr Ser Leu Thr Val Ile Pro			
115	120	125	
Asn Ile Gln Asn Pro Glu Pro Ala Val Tyr Gln Leu Lys Asp Pro Arg			

130	135	140
Ser Gln Asp Ser Thr Leu Cys Leu Phe Thr Asp Phe Asp Ser Gln Ile		
145	150	155
Asn Val Pro Lys Thr Met Glu Ser Gly Thr Phe Ile Thr Asp Lys Cys		
165	170	175
Val Leu Asp Met Lys Ala Met Asp Ser Lys Ser Asn Gly Ala Ile Ala		
180	185	190
Trp Ser Asn Gln Thr Ser Phe Thr Cys Gln Asp Ile Phe Lys Glu Thr		
195	200	205
Asn Ala Thr Tyr Pro Ser Ser Asp Val Pro Cys Asp Ala Thr Leu Thr		
210	215	220
Glu Lys Ser Phe Glu Thr Asp Met Asn Leu Asn Phe Gln Asn Leu Leu		
225	230	235
Val Ile Val Leu Arg Ile Leu Leu Leu Lys Val Ala Gly Phe Asn Leu		
245	250	255
Leu Met Thr Leu Arg Leu Trp Ser Ser		
260	265	
<210> 156		
<211> 305		
<212> PRT		
<213> 智人(Homo sapiens)		
<400> 156		
Met His Cys Arg Leu Leu Cys Cys Ala Val Leu Cys Leu Leu Gly Ala		
1	5	10
Val Pro Ile Asp Thr Glu Val Thr Gln Thr Pro Lys His Leu Val Met		
20	25	30
Gly Met Thr Asn Lys Lys Ser Leu Lys Cys Glu Gln His Met Gly His		
35	40	45
Arg Ala Met Tyr Trp Tyr Lys Gln Lys Ala Lys Lys Pro Pro Glu Leu		
50	55	60
Met Phe Val Tyr Ser Tyr Glu Lys Leu Ser Ile Asn Glu Ser Val Pro		
65	70	75
Ser Arg Phe Ser Pro Glu Cys Pro Asn Ser Ser Leu Leu Asn Leu His		
85	90	95
Leu His Ala Leu Gln Pro Glu Asp Ser Ala Leu Tyr Leu Cys Ala Ser		
100	105	110
Ser Gln Val Gly Leu Thr Tyr Glu Gln Tyr Phe Gly Pro Gly Thr Arg		
115	120	125
Leu Thr Val Thr Glu Asp Leu Arg Asn Val Thr Pro Pro Lys Val Ser		

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

Ser

305

<210> 157

<211> 6

<212> PRT

<213> 智人(Homo sapiens)

<400> 157

Val Ser Gly Asn Pro Tyr

1

5

<210> 158

<211> 8

<212> PRT

<213> 智人(Homo sapiens)

<400> 158

Tyr Ile Thr Gly Asp Asn Leu Val

1

5

<210> 159

<211> 16

<212> PRT

<213> 智人 (Homo sapiens)

<400> 159

Cys	Ala	Val	Arg	Asp	Asn	Ser	Gly	Gly	Ser	Asn	Tyr	Lys	Leu	Thr	Phe
1				5					10					15	

<210> 160

<211> 5

<212> PRT

<213> 智人 (Homo sapiens)

<400> 160

Ser	Gly	His	Ala	Thr
1			5	

<210> 161

<211> 6

<212> PRT

<213> 智人 (Homo sapiens)

<400> 161

Phe	Gln	Asn	Asn	Gly	Val
1			5		

<210> 162

<211> 13

<212> PRT

<213> 智人 (Homo sapiens)

<400> 162

Cys	Ala	Ser	Ser	Leu	Gly	Gln	Gly	Gln	Thr	Gln	Tyr	Phe
1				5					10			

<210> 163

<211> 135

<212> PRT

<213> 智人 (Homo sapiens)

<400> 163

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

Met Ala Ser Ala Pro Ile Ser Met Leu Ala Met Leu Phe Thr Leu Ser

1	5	10	15
Gly Leu Arg Ala Gln Ser Val Ala Gln Pro Glu Asp Gln Val Asn Val			
20	25	30	
Ala Glu Gly Asn Pro Leu Thr Val Lys Cys Thr Tyr Ser Val Ser Gly			
35	40	45	
Asn Pro Tyr Leu Phe Trp Tyr Val Gln Tyr Pro Asn Arg Gly Leu Gln			
50	55	60	
Phe Leu Leu Lys Tyr Ile Thr Gly Asp Asn Leu Val Lys Gly Ser Tyr			
65	70	75	80
Gly Phe Glu Ala Glu Phe Asn Lys Ser Gln Thr Ser Phe His Leu Lys			
85	90	95	
Lys Pro Ser Ala Leu Val Ser Asp Ser Ala Leu Tyr Phe Cys Ala Val			
100	105	110	
Arg Asp Asn Ser Gly Gly Ser Asn Tyr Lys Leu Thr Phe Gly Lys Gly			
115	120	125	
Thr Leu Leu Thr Val Asn Pro Asn Ile Gln Asn Pro Glu Pro Ala Val			
130	135	140	
Tyr Gln Leu Lys Asp Pro Arg Ser Gln Asp Ser Thr Leu Cys Leu Phe			
145	150	155	160
Thr Asp Phe Asp Ser Gln Ile Asn Val Pro Lys Thr Met Glu Ser Gly			
165	170	175	
Thr Phe Ile Thr Asp Lys Cys Val Leu Asp Met Lys Ala Met Asp Ser			
180	185	190	
Lys Ser Asn Gly Ala Ile Ala Trp Ser Asn Gln Thr Ser Phe Thr Cys			
195	200	205	
Gln Asp Ile Phe Lys Glu Thr Asn Ala Thr Tyr Pro Ser Ser Asp Val			
210	215	220	
Pro Cys Asp Ala Thr Leu Thr Glu Lys Ser Phe Glu Thr Asp Met Asn			
225	230	235	240
Leu Asn Phe Gln Asn Leu Leu Val Ile Val Leu Arg Ile Leu Leu Leu			
245	250	255	
Lys Val Ala Gly Phe Asn Leu Leu Met Thr Leu Arg Leu Trp Ser Ser			
260	265	270	
<210> 166			
<211> 305			
<212> PRT			
<213> 智人(Homo sapiens)			
<400> 166			
Met His Thr Arg Leu Leu Cys Trp Ala Ala Leu Cys Leu Leu Gly Ala			

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

<210> 167
<211> 6
<212> PRT
<213> 智人 (Homo sapiens)
<400> 167
Ser Ser Val Ser Val Tyr
1 5
<210> 168
<211> 8
<212> PRT
<213> 智人 (Homo sapiens)
<400> 168
Tyr Leu Ser Gly Ser Thr Leu Val
1 5
<210> 169
<211> 14
<212> PRT
<213> 智人 (Homo sapiens)
<400> 169
Cys Ala Val Arg Gly Ser Ser Gly Thr Tyr Lys Tyr Ile Phe
1 5 10
<210> 170
<211> 5
<212> PRT
<213> 智人 (Homo sapiens)
<400> 170
Met Asp His Glu Asn
1 5
<210> 171
<211> 6
<212> PRT
<213> 智人 (Homo sapiens)
<400> 171
Ser Tyr Asp Val Lys Met
1 5
<210> 172
<211> 13
<212> PRT
<213> 智人 (Homo sapiens)

<400> 172

Cys Ala Ser Lys Gly Asp Gln Asn Thr Glu Ala Phe Phe

1 5 10

<210> 173

<211> 133

<212> PRT

<213> 智人(Homo sapiens)

<400> 173

Met Ala Leu Leu Leu Val Pro Ala Phe Gln Val Ile Phe Thr Leu Gly

1 5 10 15

Gly Thr Arg Ala Gln Ser Val Thr Gln Leu Asp Ser Gln Val Pro Val

20 25 30

Phe Glu Glu Ala Pro Val Glu Leu Arg Cys Asn Tyr Ser Ser Ser Val

35 40 45

Ser Val Tyr Leu Phe Trp Tyr Val Gln Tyr Pro Asn Gln Gly Leu Gln

50 55 60

Leu Leu Leu Lys Tyr Leu Ser Gly Ser Thr Leu Val Glu Ser Ile Asn

65 70 75 80

Gly Phe Glu Ala Glu Phe Asn Lys Ser Gln Thr Ser Phe His Leu Arg

85 90 95

Lys Pro Ser Val His Ile Ser Asp Thr Ala Glu Tyr Phe Cys Ala Val

100 105 110

Arg Gly Ser Ser Gly Thr Tyr Lys Tyr Ile Phe Gly Thr Gly Thr Arg

115 120 125

Leu Lys Val Leu Ala

130

<210> 174

<211> 131

<212> PRT

<213> 智人(Homo sapiens)

<400> 174

Met His Ile Arg Leu Leu Cys Arg Val Ala Phe Cys Phe Leu Ala Val

1 5 10 15

Gly Leu Val Asp Val Lys Val Thr Gln Ser Ser Arg Tyr Leu Val Lys

20 25 30

Arg Thr Gly Glu Lys Val Phe Leu Glu Cys Val Gln Asp Met Asp His

35 40 45

Glu Asn Met Phe Trp Tyr Arg Gln Asp Pro Gly Leu Gly Leu Arg Leu

50 55 60

Ile Tyr Phe Ser Tyr Asp Val Lys Met Lys Glu Lys Gly Asp Ile Pro			
65	70	75	80
Glu Gly Tyr Ser Val Ser Arg Glu Lys Lys Glu Arg Phe Ser Leu Ile			
	85	90	95
Leu Glu Ser Ala Ser Thr Asn Gln Thr Ser Met Tyr Leu Cys Ala Ser			
	100	105	110
Lys Gly Asp Gln Asn Thr Glu Ala Phe Phe Gly Gln Gly Thr Arg Leu			
	115	120	125
Thr Val Val			
130			
<210> 175			
<211> 270			
<212> PRT			
<213> 智人(Homo sapiens)			
<400> 175			
Met Ala Leu Leu Leu Val Pro Ala Phe Gln Val Ile Phe Thr Leu Gly			
1	5	10	15
Gly Thr Arg Ala Gln Ser Val Thr Gln Leu Asp Ser Gln Val Pro Val			
	20	25	30
Phe Glu Glu Ala Pro Val Glu Leu Arg Cys Asn Tyr Ser Ser Ser Val			
	35	40	45
Ser Val Tyr Leu Phe Trp Tyr Val Gln Tyr Pro Asn Gln Gly Leu Gln			
	50	55	60
Leu Leu Leu Lys Tyr Leu Ser Gly Ser Thr Leu Val Glu Ser Ile Asn			
65	70	75	80
Gly Phe Glu Ala Glu Phe Asn Lys Ser Gln Thr Ser Phe His Leu Arg			
	85	90	95
Lys Pro Ser Val His Ile Ser Asp Thr Ala Glu Tyr Phe Cys Ala Val			
	100	105	110
Arg Gly Ser Ser Gly Thr Tyr Lys Tyr Ile Phe Gly Thr Gly Thr Arg			
	115	120	125
Leu Lys Val Leu Ala Asn Ile Gln Asn Pro Glu Pro Ala Val Tyr Gln			
	130	135	140
Leu Lys Asp Pro Arg Ser Gln Asp Ser Thr Leu Cys Leu Phe Thr Asp			
145	150	155	160
Phe Asp Ser Gln Ile Asn Val Pro Lys Thr Met Glu Ser Gly Thr Phe			
	165	170	175
Ile Thr Asp Lys Cys Val Leu Asp Met Lys Ala Met Asp Ser Lys Ser			
	180	185	190

Asn Gly Ala Ile Ala Trp Ser Asn Gln Thr Ser Phe Thr Cys Gln Asp		
195	200	205
Ile Phe Lys Glu Thr Asn Ala Thr Tyr Pro Ser Ser Asp Val Pro Cys		
210	215	220
Asp Ala Thr Leu Thr Glu Lys Ser Phe Glu Thr Asp Met Asn Leu Asn		
225	230	235
Phe Gln Asn Leu Leu Val Ile Val Leu Arg Ile Leu Leu Leu Lys Val		
	245	250
Ala Gly Phe Asn Leu Leu Met Thr Leu Arg Leu Trp Ser Ser		
	260	265
		270
<210> 176		
<211> 304		
<212> PRT		
<213> 智人 (Homo sapiens)		
<400> 176		
Met His Ile Arg Leu Leu Cys Arg Val Ala Phe Cys Phe Leu Ala Val		
1	5	10
Gly Leu Val Asp Val Lys Val Thr Gln Ser Ser Arg Tyr Leu Val Lys		
	20	25
Arg Thr Gly Glu Lys Val Phe Leu Glu Cys Val Gln Asp Met Asp His		
	35	40
Glu Asn Met Phe Trp Tyr Arg Gln Asp Pro Gly Leu Gly Leu Arg Leu		
	50	55
Ile Tyr Phe Ser Tyr Asp Val Lys Met Lys Glu Lys Gly Asp Ile Pro		
65	70	75
Glu Gly Tyr Ser Val Ser Arg Glu Lys Lys Glu Arg Phe Ser Leu Ile		
	85	90
Leu Glu Ser Ala Ser Thr Asn Gln Thr Ser Met Tyr Leu Cys Ala Ser		
	100	105
Lys Gly Asp Gln Asn Thr Glu Ala Phe Phe Gly Gln Gly Thr Arg Leu		
	115	120
Thr Val Val Glu Asp Leu Arg Asn Val Thr Pro Pro Lys Val Ser Leu		
	130	135
Phe Glu Pro Ser Lys Ala Glu Ile Ala Asn Lys Gln Lys Ala Thr Leu		
145	150	155
Val Cys Leu Ala Arg Gly Phe Phe Pro Asp His Val Glu Leu Ser Trp		
	165	170
Trp Val Asn Gly Lys Glu Val His Ser Gly Val Cys Thr Asp Pro Gln		
	180	185
		190

Ala Tyr Lys Glu Ser Asn Tyr Ser Tyr Cys Leu Ser Ser Arg Leu Arg		
195	200	205
Val Ser Ala Thr Phe Trp His Asn Pro Arg Asn His Phe Arg Cys Gln		
210	215	220
Val Gln Phe His Gly Leu Ser Glu Glu Asp Lys Trp Pro Glu Gly Ser		
225	230	235
Pro Lys Pro Val Thr Gln Asn Ile Ser Ala Glu Ala Trp Gly Arg Ala		
	245	250
Asp Cys Gly Ile Thr Ser Ala Ser Tyr Gln Gln Gly Val Leu Ser Ala		
	260	265
Thr Ile Leu Tyr Glu Ile Leu Leu Gly Lys Ala Thr Leu Tyr Ala Val		
	275	280
Leu Val Ser Thr Leu Val Val Met Ala Met Val Lys Arg Lys Asn Ser		
	290	295
		300

<210> 177

<211> 6

<212> PRT

<213> 智人(Homo sapiens)

<400> 177

Thr Ser Gly Phe Asn Gly

1 5

<210> 178

<211> 6

<212> PRT

<213> 智人(Homo sapiens)

<400> 178

Asn Val Leu Asp Gly Leu

1 5

<210> 179

<211> 15

<212> PRT

<213> 智人(Homo sapiens)

<400> 179

Cys Ala Val Arg Asp Leu Gln Thr Gly Ala Asn Asn Leu Phe Phe

1 5 10 15

<210> 180

<211> 5

<212> PRT

<213> 智人(Homo sapiens)

<400> 180

Met Asp His Glu Asn

1 5

<210> 181

<211> 6

<212> PRT

<213> 智人 (Homo sapiens)

<400> 181

Ser Tyr Asp Val Lys Met

1 5

<210> 182

<211> 14

<212> PRT

<213> 智人 (Homo sapiens)

<400> 182

Cys Ala Ser Ser Leu Thr Phe Gly Thr Thr Glu Ala Phe Phe

1 5 10

<210> 183

<211> 129

<212> PRT

<213> 智人 (Homo sapiens)

<400> 183

Met Ala Gly Val Phe Leu Leu Tyr Val Ser Met Lys Met Gly Gly Thr

1 5 10 15

Thr Gly Gln Asn Ile Asp Gln Pro Thr Glu Met Thr Ala Thr Glu Gly

20 25 30

Ala Ile Val Gln Ile Asn Cys Thr Tyr Gln Thr Ser Gly Phe Asn Gly

35 40 45

Leu Phe Trp Tyr Gln Gln His Ala Gly Glu Ala Pro Thr Phe Leu Ser

50 55 60

Tyr Asn Val Leu Asp Gly Leu Glu Glu Lys Gly Arg Phe Ser Ser Phe

65 70 75 80

Leu Ser Arg Ser Lys Gly Tyr Ser Tyr Leu Leu Leu Lys Glu Leu Gln

85 90 95

Met Lys Asp Ser Ala Ser Tyr Leu Cys Ala Val Arg Asp Leu Gln Thr

100 105 110

Gly Ala Asn Asn Leu Phe Phe Gly Thr Gly Thr Arg Leu Thr Val Ile

115 120 125

Pro

<210> 184

<211> 132

<212> PRT

<213> 智人(Homo sapiens)

<400> 184

```

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

```

<210> 185

<211> 266

<212> PRT

<213> 智人(Homo sapiens)

<400> 185

```

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

```

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

<210> 186

<211> 305

<212> PRT

<213> 智人(Homo sapiens)

<400> 186

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

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

Ser

305

<210> 187

<211> 6

<212> PRT

<213> 智人 (Homo sapiens)

<400> 187

Val Thr Asn Phe Arg Ser

1

5

<210> 188

<211> 7

<212> PRT

<213> 智人 (Homo sapiens)

<400> 188

Leu Thr Ser Ser Gly Ile Glu

1 5

<210> 189

<211> 15

<212> PRT

<213> 智人 (Homo sapiens)

<400> 189

Cys Ala Gly Gln Asn Tyr Gly Gly Ser Gln Gly Asn Leu Ile Phe

1 5 10 15

<210> 190

<211> 5

<212> PRT

<213> 智人 (Homo sapiens)

<400> 190

Ser Asn His Leu Tyr

1 5

<210> 191

<211> 6

<212> PRT

<213> 智人 (Homo sapiens)

<400> 191

Phe Tyr Asn Asn Glu Ile

1 5

<210> 192

<211> 12

<212> PRT

<213> 智人 (Homo sapiens)

<400> 192

Cys Ala Ser Arg Asp Pro Ala Tyr Glu Gln Tyr Phe

1 5 10

<210> 193

<211> 134

<212> PRT

<213> 智人 (Homo sapiens)

<400> 193

Met Ala Lys Cys Pro Gln Ala Leu Leu Ala Ile Phe Trp Leu Leu Leu

1 5 10 15

Ser Trp Val Ser Ser Glu Asp Lys Val Val Gln Ser Pro Leu Ser Leu
 20 25 30
 Val Val His Glu Gly Asp Thr Val Thr Leu Asn Cys Ser Tyr Glu Val
 35 40 45
 Thr Asn Phe Arg Ser Leu Leu Trp Tyr Lys Gln Glu Lys Lys Ala Pro
 50 55 60
 Thr Phe Leu Phe Met Leu Thr Ser Ser Gly Ile Glu Lys Lys Ser Gly
 65 70 75 80
 Arg Leu Ser Ser Ile Leu Asp Lys Lys Glu Leu Ser Ser Ile Leu Asn
 85 90 95
 Ile Thr Ala Thr Gln Thr Gly Asp Ser Ala Ile Tyr Leu Cys Ala Gly
 100 105 110
 Gln Asn Tyr Gly Gly Ser Gln Gly Asn Leu Ile Phe Gly Lys Gly Thr
 115 120 125
 Lys Leu Ser Val Lys Pro
 130
 <210> 194
 <211> 131
 <212> PRT
 <213> 智人(Homo sapiens)
 <400> 194
 Met His Thr Trp Leu Val Cys Trp Ala Ile Phe Ser Leu Leu Lys Ala
 1 5 10 15
 Gly Leu Thr Glu Pro Glu Val Thr Gln Thr Pro Ser His Gln Val Thr
 20 25 30
 Gln Met Gly Gln Glu Val Ile Leu Arg Cys Val Pro Ile Ser Asn His
 35 40 45
 Leu Tyr Phe Tyr Trp Tyr Arg Gln Ile Leu Gly Gln Lys Val Glu Phe
 50 55 60
 Leu Val Ser Phe Tyr Asn Asn Glu Ile Ser Glu Lys Ser Glu Ile Phe
 65 70 75 80
 Asp Asp Gln Phe Ser Val Glu Arg Pro Asp Gly Ser Asn Phe Thr Leu
 85 90 95
 Lys Ile Arg Ser Thr Lys Leu Glu Asp Ser Ala Met Tyr Phe Cys Ala
 100 105 110
 Ser Arg Asp Pro Ala Tyr Glu Gln Tyr Phe Gly Pro Gly Thr Arg Leu
 115 120 125
 Thr Val Thr
 130

<210> 195

<211> 271

<212> PRT

<213> 智人(Homo sapiens)

<400> 195

```

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

```


<210> 196

<211> 304

<212> PRT

<213> 智人(Homo sapiens)

<400> 196

```

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

```

Thr Ile Leu Tyr Glu Ile Leu Leu Gly Lys Ala Thr Leu Tyr Ala Val
275 280 285
Leu Val Ser Thr Leu Val Val Met Ala Met Val Lys Arg Lys Asn Ser
290 295 300
<210> 197
<211> 6
<212> PRT
<213> 智人 (Homo sapiens)
<400> 197
Asp Arg Gly Ser Gln Ser
1 5
<210> 198
<211> 6
<212> PRT
<213> 智人 (Homo sapiens)
<400> 198
Ile Tyr Ser Asn Gly Asp
1 5
<210> 199
<211> 16
<212> PRT
<213> 智人 (Homo sapiens)
<400> 199
Cys Ala Val Asn Pro Pro Val Lys Thr Ser Tyr Asp Lys Val Ile Phe
1 5 10 15
<210> 200
<211> 5
<212> PRT
<213> 智人 (Homo sapiens)
<400> 200
Ser Gly His Val Ser
1 5
<210> 201
<211> 6
<212> PRT
<213> 智人 (Homo sapiens)
<400> 201
Phe Asn Tyr Glu Ala Gln
1 5

<210> 202

<211> 15

<212> PRT

<213> 智人(Homo sapiens)

<400> 202

Cys Ala Ser Ser His Arg Glu Pro His Thr Gly Glu Leu Phe Phe

1 5 10 15

<210> 203

<211> 135

<212> PRT

<213> 智人(Homo sapiens)

<400> 203

Met Ala Ser Leu Arg Val Leu Leu Val Ile Leu Trp Leu Gln Leu Ser

1 5 10 15

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

20 25 30

Ser Val Pro Glu Gly Ala Ile Ala Ser Leu Asn Cys Thr Tyr Ser Asp

35 40 45

Arg Gly Ser Gln Ser Phe Phe Trp Tyr Arg Gln Tyr Ser Gly Lys Ser

50 55 60

Pro Glu Leu Ile Met Phe Ile Tyr Ser Asn Gly Asp Lys Glu Asp Gly

65 70 75 80

Arg Phe Thr Ala Gln Leu Asn Lys Ala Ser Gln Tyr Val Ser Leu Leu

85 90 95

Ile Arg Asp Ser Gln Pro Ser Asp Ser Ala Thr Tyr Leu Cys Ala Val

100 105 110

Asn Pro Pro Val Lys Thr Ser Tyr Asp Lys Val Ile Phe Gly Pro Gly

115 120 125

Thr Ser Leu Ser Val Ile Pro

130 135

<210> 204

<211> 134

<212> PRT

<213> 智人(Homo sapiens)

<400> 204

Met His Thr Ser Leu Leu Cys Trp Val Val Leu Gly Phe Leu Gly Thr

1 5 10 15

Asp His Thr Gly Ala Gly Val Ser Gln Ser Pro Arg Tyr Lys Val Thr

20 25 30

Lys Arg Gly Gln Asp Val Ala Leu Arg Cys Asp Pro Ile Ser Gly His
 35 40 45
 Val Ser Leu Tyr Trp Tyr Arg Gln Ala Leu Gly Gln Gly Pro Glu Phe
 50 55 60
 Leu Thr Tyr Phe Asn Tyr Glu Ala Gln Gln Asp Lys Ser Gly Leu Pro
 65 70 75 80
 Asn Asp Arg Phe Ser Ala Glu Arg Pro Glu Gly Ser Ile Ser Thr Leu
 85 90 95
 Thr Ile Gln Arg Thr Glu Gln Arg Asp Ser Ala Met Tyr Arg Cys Ala
 100 105 110
 Ser Ser His Arg Glu Pro His Thr Gly Glu Leu Phe Phe Gly Glu Gly
 115 120 125
 Ser Arg Leu Thr Val Leu
 130
 <210> 205
 <211> 272
 <212> PRT
 <213> 智人(Homo sapiens)
 <400> 205
 Met Ala Ser Leu Arg Val Leu Leu Val Ile Leu Trp Leu Gln Leu Ser
 1 5 10 15
 Trp Val Trp Ser Gln Gln Lys Glu Val Glu Gln Asn Ser Gly Pro Leu
 20 25 30
 Ser Val Pro Glu Gly Ala Ile Ala Ser Leu Asn Cys Thr Tyr Ser Asp
 35 40 45
 Arg Gly Ser Gln Ser Phe Phe Trp Tyr Arg Gln Tyr Ser Gly Lys Ser
 50 55 60
 Pro Glu Leu Ile Met Phe Ile Tyr Ser Asn Gly Asp Lys Glu Asp Gly
 65 70 75 80
 Arg Phe Thr Ala Gln Leu Asn Lys Ala Ser Gln Tyr Val Ser Leu Leu
 85 90 95
 Ile Arg Asp Ser Gln Pro Ser Asp Ser Ala Thr Tyr Leu Cys Ala Val
 100 105 110
 Asn Pro Pro Val Lys Thr Ser Tyr Asp Lys Val Ile Phe Gly Pro Gly
 115 120 125
 Thr Ser Leu Ser Val Ile Pro Asn Ile Gln Asn Pro Glu Pro Ala Val
 130 135 140
 Tyr Gln Leu Lys Asp Pro Arg Ser Gln Asp Ser Thr Leu Cys Leu Phe
 145 150 155 160

Thr	Asp	Phe	Asp	Ser	Gln	Ile	Asn	Val	Pro	Lys	Thr	Met	Glu	Ser	Gly
					165				170					175	
Thr	Phe	Ile	Thr	Asp	Lys	Cys	Val	Leu	Asp	Met	Lys	Ala	Met	Asp	Ser
					180				185					190	
Lys	Ser	Asn	Gly	Ala	Ile	Ala	Trp	Ser	Asn	Gln	Thr	Ser	Phe	Thr	Cys
					195				200					205	
Gln	Asp	Ile	Phe	Lys	Glu	Thr	Asn	Ala	Thr	Tyr	Pro	Ser	Ser	Asp	Val
					210				215					220	
Pro	Cys	Asp	Ala	Thr	Leu	Thr	Glu	Lys	Ser	Phe	Glu	Thr	Asp	Met	Asn
225					230					235				240	
Leu	Asn	Phe	Gln	Asn	Leu	Leu	Val	Ile	Val	Leu	Arg	Ile	Leu	Leu	Leu
					245					250				255	
Lys	Val	Ala	Gly	Phe	Asn	Leu	Leu	Met	Thr	Leu	Arg	Leu	Trp	Ser	Ser
					260				265					270	
<210> 206															
<211> 307															
<212> PRT															
<213> 智人(Homo sapiens)															
<400> 206															
Met	His	Thr	Ser	Leu	Leu	Cys	Trp	Val	Val	Leu	Gly	Phe	Leu	Gly	Thr
1				5					10					15	
Asp	His	Thr	Gly	Ala	Gly	Val	Ser	Gln	Ser	Pro	Arg	Tyr	Lys	Val	Thr
				20				25					30		
Lys	Arg	Gly	Gln	Asp	Val	Ala	Leu	Arg	Cys	Asp	Pro	Ile	Ser	Gly	His
				35				40					45		
Val	Ser	Leu	Tyr	Trp	Tyr	Arg	Gln	Ala	Leu	Gly	Gln	Gly	Pro	Glu	Phe
				50			55				60				
Leu	Thr	Tyr	Phe	Asn	Tyr	Glu	Ala	Gln	Gln	Asp	Lys	Ser	Gly	Leu	Pro
65				70					75					80	
Asn	Asp	Arg	Phe	Ser	Ala	Glu	Arg	Pro	Glu	Gly	Ser	Ile	Ser	Thr	Leu
				85					90					95	
Thr	Ile	Gln	Arg	Thr	Glu	Gln	Arg	Asp	Ser	Ala	Met	Tyr	Arg	Cys	Ala
				100					105					110	
Ser	Ser	His	Arg	Glu	Pro	His	Thr	Gly	Glu	Leu	Phe	Phe	Gly	Glu	Gly
				115					120					125	
Ser	Arg	Leu	Thr	Val	Leu	Glu	Asp	Leu	Arg	Asn	Val	Thr	Pro	Pro	Lys
				130				135					140		
Val	Ser	Leu	Phe	Glu	Pro	Ser	Lys	Ala	Glu	Ile	Ala	Asn	Lys	Gln	Lys
145					150					155					160

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

Lys Asn Ser

305

<210> 207

<211> 7

<212> PRT

<213> 智人 (Homo sapiens)

<400> 207

Thr Arg Asp Thr Thr Tyr Tyr

1

5

<210> 208

<211> 8

<212> PRT

<213> 智人 (Homo sapiens)

<400> 208

Arg Asn Ser Phe Asp Glu Gln Asn

1

5

<210> 209

<211> 15

<212> PRT

<213> 智人 (Homo sapiens)

<400> 209

Cys Ala Leu Ser Glu Val Asp Ser Gly Asn Thr Pro Leu Val Phe
 1 5 10 15

<210> 210

<211> 5

<212> PRT

<213> 智人(Homo sapiens)

<400> 210

Ser Gly Asp Leu Ser

1 5

<210> 211

<211> 6

<212> PRT

<213> 智人(Homo sapiens)

<400> 211

Tyr Tyr Asn Gly Glu Glu

1 5

<210> 212

<211> 16

<212> PRT

<213> 智人(Homo sapiens)

<400> 212

Cys Ala Ser Ser Val Gly Ser Ser Ser Ser Thr Asp Thr Gln Tyr Phe

1 5 10 15

<210> 213

<211> 136

<212> PRT

<213> 智人(Homo sapiens)

<400> 213

Met Ala Thr Ala Ser Leu Leu Arg Ala Val Ile Ala Ser Ile Cys Val

1 5 10 15

Val Ser Ser Met Ala Gln Lys Val Thr Gln Ala Gln Thr Glu Ile Ser

20 25 30

Val Val Glu Lys Glu Asp Val Thr Leu Asp Cys Val Tyr Glu Thr Arg

35 40 45

Asp Thr Thr Tyr Tyr Leu Phe Trp Tyr Lys Gln Pro Pro Ser Gly Glu

50 55 60

Leu Val Phe Leu Ile Arg Arg Asn Ser Phe Asp Glu Gln Asn Glu Ile

65 70 75 80

Ser Gly Arg Tyr Ser Trp Asn Phe Gln Lys Ser Thr Ser Ser Phe Asn

85								90				95					
Phe	Thr	Ile	Thr	Ala	Ser	Gln	Val	Val	Asp	Ser	Ala	Val	Tyr	Phe	Cys		
100								105				110					
Ala	Leu	Ser	Glu	Val	Asp	Ser	Gly	Asn	Thr	Pro	Leu	Val	Phe	Gly	Lys		
115								120				125					
Gly	Thr	Arg	Leu	Ser	Val	Ile	Ala										
130								135									
<210> 214																	
<211> 134																	
<212> PRT																	
<213> 智人 (Homo sapiens)																	
<400> 214																	
Met	His	Phe	Arg	Leu	Leu	Cys	Cys	Val	Ala	Phe	Cys	Leu	Leu	Gly	Ala		
1				5				10						15			
Gly	Pro	Val	Asp	Ser	Gly	Val	Thr	Gln	Thr	Pro	Lys	His	Leu	Ile	Thr		
20								25				30					
Ala	Thr	Gly	Gln	Arg	Val	Thr	Leu	Arg	Cys	Ser	Pro	Arg	Ser	Gly	Asp		
35								40				45					
Leu	Ser	Val	Tyr	Trp	Tyr	Gln	Gln	Ser	Leu	Asp	Gln	Gly	Leu	Gln	Phe		
50								55				60					
Leu	Ile	Gln	Tyr	Tyr	Asn	Gly	Glu	Glu	Arg	Ala	Lys	Gly	Asn	Ile	Leu		
65	70								75				80				
Glu	Arg	Phe	Ser	Ala	Gln	Gln	Phe	Pro	Asp	Leu	His	Ser	Glu	Leu	Asn		
85								90				95					
Leu	Ser	Ser	Leu	Glu	Leu	Gly	Asp	Ser	Ala	Leu	Tyr	Phe	Cys	Ala	Ser		
100								105				110					
Ser	Val	Gly	Ser	Ser	Ser	Ser	Thr	Asp	Thr	Gln	Tyr	Phe	Gly	Pro	Gly		
115								120				125					
Thr	Arg	Leu	Thr	Val	Leu												
130																	
<210> 215																	
<211> 273																	
<212> PRT																	
<213> 智人 (Homo sapiens)																	
<400> 215																	
Met	Ala	Thr	Ala	Ser	Leu	Leu	Arg	Ala	Val	Ile	Ala	Ser	Ile	Cys	Val		
1				5				10						15			
Val	Ser	Ser	Met	Ala	Gln	Lys	Val	Thr	Gln	Ala	Gln	Thr	Glu	Ile	Ser		
20								25				30					

Val	Val	Glu	Lys	Glu	Asp	Val	Thr	Leu	Asp	Cys	Val	Tyr	Glu	Thr	Arg
	35						40					45			
Asp	Thr	Thr	Tyr	Tyr	Leu	Phe	Trp	Tyr	Lys	Gln	Pro	Pro	Ser	Gly	Glu
	50					55					60				
Leu	Val	Phe	Leu	Ile	Arg	Arg	Asn	Ser	Phe	Asp	Glu	Gln	Asn	Glu	Ile
65					70					75					80
Ser	Gly	Arg	Tyr	Ser	Trp	Asn	Phe	Gln	Lys	Ser	Thr	Ser	Ser	Phe	Asn
				85					90					95	
Phe	Thr	Ile	Thr	Ala	Ser	Gln	Val	Val	Asp	Ser	Ala	Val	Tyr	Phe	Cys
				100					105					110	
Ala	Leu	Ser	Glu	Val	Asp	Ser	Gly	Asn	Thr	Pro	Leu	Val	Phe	Gly	Lys
				115					120					125	
Gly	Thr	Arg	Leu	Ser	Val	Ile	Ala	Asn	Ile	Gln	Asn	Pro	Glu	Pro	Ala
						130			135					140	
Val	Tyr	Gln	Leu	Lys	Asp	Pro	Arg	Ser	Gln	Asp	Ser	Thr	Leu	Cys	Leu
145					150					155					160
Phe	Thr	Asp	Phe	Asp	Ser	Gln	Ile	Asn	Val	Pro	Lys	Thr	Met	Glu	Ser
					165					170				175	
Gly	Thr	Phe	Ile	Thr	Asp	Lys	Cys	Val	Leu	Asp	Met	Lys	Ala	Met	Asp
					180					185				190	
Ser	Lys	Ser	Asn	Gly	Ala	Ile	Ala	Trp	Ser	Asn	Gln	Thr	Ser	Phe	Thr
				195					200					205	
Cys	Gln	Asp	Ile	Phe	Lys	Glu	Thr	Asn	Ala	Thr	Tyr	Pro	Ser	Ser	Asp
				210					215					220	
Val	Pro	Cys	Asp	Ala	Thr	Leu	Thr	Glu	Lys	Ser	Phe	Glu	Thr	Asp	Met
225					230					235					240
Asn	Leu	Asn	Phe	Gln	Asn	Leu	Leu	Val	Ile	Val	Leu	Arg	Ile	Leu	Leu
					245					250				255	
Leu	Lys	Val	Ala	Gly	Phe	Asn	Leu	Leu	Met	Thr	Leu	Arg	Leu	Trp	Ser
				260					265					270	
Ser															
<210>	216														
<211>	307														
<212>	PRT														
<213>	智人 (Homo sapiens)														
<400>	216														
Met	His	Phe	Arg	Leu	Leu	Cys	Cys	Val	Ala	Phe	Cys	Leu	Leu	Gly	Ala
1				5					10					15	
Gly	Pro	Val	Asp	Ser	Gly	Val	Thr	Gln	Thr	Pro	Lys	His	Leu	Ile	Thr

20	25	30
Ala Thr Gly Gln Arg Val Thr	Leu Arg Cys Ser Pro Arg	Ser Gly Asp
35	40	45
Leu Ser Val Tyr Trp Tyr Gln	Gln Ser Leu Asp Gln Gly	Leu Gln Phe
50	55	60
Leu Ile Gln Tyr Tyr Asn Gly	Glu Glu Arg Ala Lys Gly	Asn Ile Leu
65	70	75
Glu Arg Phe Ser Ala Gln Gln	Phe Pro Asp Leu His Ser	Glu Leu Asn
85	90	95
Leu Ser Ser Leu Glu Leu Gly	Asp Ser Ala Leu Tyr Phe	Cys Ala Ser
100	105	110
Ser Val Gly Ser Ser Ser Ser	Thr Asp Thr Gln Tyr Phe	Gly Pro Gly
115	120	125
Thr Arg Leu Thr Val Leu Glu	Asp Leu Arg Asn Val Thr	Pro Pro Lys
130	135	140
Val Ser Leu Phe Glu Pro Ser	Lys Ala Glu Ile Ala Asn	Lys Gln Lys
145	150	155
Ala Thr Leu Val Cys Leu Ala	Arg Gly Phe Phe Pro Asp	His Val Glu
165	170	175
Leu Ser Trp Trp Val Asn Gly	Lys Glu Val His Ser Gly	Val Cys Thr
180	185	190
Asp Pro Gln Ala Tyr Lys Glu	Ser Asn Tyr Ser Tyr Cys	Leu Ser Ser
195	200	205
Arg Leu Arg Val Ser Ala Thr	Phe Trp His Asn Pro Arg	Asn His Phe
210	215	220
Arg Cys Gln Val Gln Phe His	Gly Leu Ser Glu Glu Asp	Lys Trp Pro
225	230	235
Glu Gly Ser Pro Lys Pro Val	Thr Gln Asn Ile Ser Ala	Glu Ala Trp
245	250	255
Gly Arg Ala Asp Cys Gly Ile	Thr Ser Ala Ser Tyr Gln	Gln Gly Val
260	265	270
Leu Ser Ala Thr Ile Leu Tyr	Glu Ile Leu Leu Gly Lys	Ala Thr Leu
275	280	285
Tyr Ala Val Leu Val Ser Thr	Leu Val Val Met Ala Met	Val Lys Arg
290	295	300
Lys Asn Ser		
305		
<210> 217		
<211> 7		

<212> PRT

<213> 智人 (Homo sapiens)

<400> 217

Thr Arg Asp Thr Thr Tyr Tyr

1 5

<210> 218

<211> 8

<212> PRT

<213> 智人 (Homo sapiens)

<400> 218

Arg Asn Ser Phe Asp Glu Gln Asn

1 5

<210> 219

<211> 15

<212> PRT

<213> 智人 (Homo sapiens)

<400> 219

Cys Ala Leu Ser Glu Val Asp Ser Gly Asn Thr Pro Leu Val Phe

1 5 10 15

<210> 220

<211> 5

<212> PRT

<213> 智人 (Homo sapiens)

<400> 220

Ser Gly Asp Leu Ser

1 5

<210> 221

<211> 6

<212> PRT

<213> 智人 (Homo sapiens)

<400> 221

Tyr Tyr Asn Gly Glu Glu

1 5

<210> 222

<211> 16

<212> PRT

<213> 智人 (Homo sapiens)

<400> 222

Cys Ala Ser Ser Val Gly Ser Ser Ser Ser Thr Asp Thr Gln Tyr Phe

1	5	10	15
<210> 223			
<211> 136			
<212> PRT			
<213> 智人(Homo sapiens)			
<400> 223			
Met Ala Thr Ala Ser Leu Leu Arg Ala Val Ile Ala Ser Ile Cys Val			
1	5	10	15
Val Ser Ser Met Ala Gln Lys Val Thr Gln Ala Gln Thr Glu Ile Ser			
20	25	30	
Val Val Glu Lys Glu Asp Val Thr Leu Asp Cys Val Tyr Glu Thr Arg			
35	40	45	
Asp Thr Thr Tyr Tyr Leu Phe Trp Tyr Lys Gln Pro Pro Ser Gly Glu			
50	55	60	
Leu Val Phe Leu Ile Arg Arg Asn Ser Phe Asp Glu Gln Asn Glu Ile			
65	70	75	80
Ser Gly Arg Tyr Ser Trp Asn Phe Gln Lys Ser Thr Ser Ser Phe Asn			
85	90	95	
Phe Thr Ile Thr Ala Ser Gln Val Val Asp Ser Ala Val Tyr Phe Cys			
100	105	110	
Ala Leu Ser Glu Val Asp Ser Gly Asn Thr Pro Leu Val Phe Gly Lys			
115	120	125	
Gly Thr Arg Leu Ser Val Ile Ala			
130	135		
<210> 224			
<211> 134			
<212> PRT			
<213> 智人(Homo sapiens)			
<400> 224			
Met His Phe Arg Leu Leu Cys Cys Val Ala Phe Cys Leu Leu Gly Ala			
1	5	10	15
Gly Pro Val Asp Ser Gly Val Thr Gln Thr Pro Lys His Leu Ile Thr			
20	25	30	
Ala Thr Gly Gln Arg Val Thr Leu Arg Cys Ser Pro Arg Ser Gly Asp			
35	40	45	
Leu Ser Val Tyr Trp Tyr Gln Gln Ser Leu Asp Gln Gly Leu Gln Phe			
50	55	60	
Leu Ile His Tyr Tyr Asn Gly Glu Glu Arg Ala Lys Gly Asn Ile Leu			
65	70	75	80

Glu Arg Phe Ser Ala Gln Gln Phe Pro Asp Leu His Ser Glu Leu Asn
 85 90 95
 Leu Ser Ser Leu Glu Leu Gly Asp Ser Ala Leu Tyr Phe Cys Ala Ser
 100 105 110
 Ser Val Gly Ser Ser Ser Ser Thr Asp Thr Gln Tyr Phe Gly Pro Gly
 115 120 125
 Thr Arg Leu Thr Val Leu
 130
 <210> 225
 <211> 273
 <212> PRT
 <213> 智人 (Homo sapiens)
 <400> 225
 Met Ala Thr Ala Ser Leu Leu Arg Ala Val Ile Ala Ser Ile Cys Val
 1 5 10 15
 Val Ser Ser Met Ala Gln Lys Val Thr Gln Ala Gln Thr Glu Ile Ser
 20 25 30
 Val Val Glu Lys Glu Asp Val Thr Leu Asp Cys Val Tyr Glu Thr Arg
 35 40 45
 Asp Thr Thr Tyr Tyr Leu Phe Trp Tyr Lys Gln Pro Pro Ser Gly Glu
 50 55 60
 Leu Val Phe Leu Ile Arg Arg Asn Ser Phe Asp Glu Gln Asn Glu Ile
 65 70 75 80
 Ser Gly Arg Tyr Ser Trp Asn Phe Gln Lys Ser Thr Ser Ser Phe Asn
 85 90 95
 Phe Thr Ile Thr Ala Ser Gln Val Val Asp Ser Ala Val Tyr Phe Cys
 100 105 110
 Ala Leu Ser Glu Val Asp Ser Gly Asn Thr Pro Leu Val Phe Gly Lys
 115 120 125
 Gly Thr Arg Leu Ser Val Ile Ala Asn Ile Gln Asn Pro Glu Pro Ala
 130 135 140
 Val Tyr Gln Leu Lys Asp Pro Arg Ser Gln Asp Ser Thr Leu Cys Leu
 145 150 155 160
 Phe Thr Asp Phe Asp Ser Gln Ile Asn Val Pro Lys Thr Met Glu Ser
 165 170 175
 Gly Thr Phe Ile Thr Asp Lys Cys Val Leu Asp Met Lys Ala Met Asp
 180 185 190
 Ser Lys Ser Asn Gly Ala Ile Ala Trp Ser Asn Gln Thr Ser Phe Thr
 195 200 205

Cys	Gln	Asp	Ile	Phe	Lys	Glu	Thr	Asn	Ala	Thr	Tyr	Pro	Ser	Ser	Asp
210						215					220				
Val	Pro	Cys	Asp	Ala	Thr	Leu	Thr	Glu	Lys	Ser	Phe	Glu	Thr	Asp	Met
225						230				235					240
Asn	Leu	Asn	Phe	Gln	Asn	Leu	Leu	Val	Ile	Val	Leu	Arg	Ile	Leu	Leu
				245					250					255	
Leu	Lys	Val	Ala	Gly	Phe	Asn	Leu	Leu	Met	Thr	Leu	Arg	Leu	Trp	Ser
			260					265						270	
Ser															
<210>	226														
<211>	307														
<212>	PRT														
<213>	智人 (Homo sapiens)														
<400>	226														
Met	His	Phe	Arg	Leu	Leu	Cys	Cys	Val	Ala	Phe	Cys	Leu	Leu	Gly	Ala
1				5					10					15	
Gly	Pro	Val	Asp	Ser	Gly	Val	Thr	Gln	Thr	Pro	Lys	His	Leu	Ile	Thr
			20					25					30		
Ala	Thr	Gly	Gln	Arg	Val	Thr	Leu	Arg	Cys	Ser	Pro	Arg	Ser	Gly	Asp
			35					40					45		
Leu	Ser	Val	Tyr	Trp	Tyr	Gln	Gln	Ser	Leu	Asp	Gln	Gly	Leu	Gln	Phe
			50					55			60				
Leu	Ile	His	Tyr	Tyr	Asn	Gly	Glu	Glu	Arg	Ala	Lys	Gly	Asn	Ile	Leu
65					70				75					80	
Glu	Arg	Phe	Ser	Ala	Gln	Gln	Phe	Pro	Asp	Leu	His	Ser	Glu	Leu	Asn
				85					90					95	
Leu	Ser	Ser	Leu	Glu	Leu	Gly	Asp	Ser	Ala	Leu	Tyr	Phe	Cys	Ala	Ser
			100					105					110		
Ser	Val	Gly	Ser	Ser	Ser	Ser	Thr	Asp	Thr	Gln	Tyr	Phe	Gly	Pro	Gly
		115						120				125			
Thr	Arg	Leu	Thr	Val	Leu	Glu	Asp	Leu	Arg	Asn	Val	Thr	Pro	Pro	Lys
		130						135				140			
Val	Ser	Leu	Phe	Glu	Pro	Ser	Lys	Ala	Glu	Ile	Ala	Asn	Lys	Gln	Lys
145					150				155					160	
Ala	Thr	Leu	Val	Cys	Leu	Ala	Arg	Gly	Phe	Phe	Pro	Asp	His	Val	Glu
				165					170					175	
Leu	Ser	Trp	Trp	Val	Asn	Gly	Lys	Glu	Val	His	Ser	Gly	Val	Cys	Thr
			180						185					190	
Asp	Pro	Gln	Ala	Tyr	Lys	Glu	Ser	Asn	Tyr	Ser	Tyr	Cys	Leu	Ser	Ser

195	200	205
Arg Leu Arg Val Ser Ala Thr Phe Trp His Asn Pro Arg Asn His Phe		
210	215	220
Arg Cys Gln Val Gln Phe His Gly Leu Ser Glu Glu Asp Lys Trp Pro		
225	230	235
Glu Gly Ser Pro Lys Pro Val Thr Gln Asn Ile Ser Ala Glu Ala Trp		
245	250	255
Gly Arg Ala Asp Cys Gly Ile Thr Ser Ala Ser Tyr Gln Gln Gly Val		
260	265	270
Leu Ser Ala Thr Ile Leu Tyr Glu Ile Leu Leu Gly Lys Ala Thr Leu		
275	280	285
Tyr Ala Val Leu Val Ser Thr Leu Val Val Met Ala Met Val Lys Arg		
290	295	300
Lys Asn Ser		
305		
<210> 227		
<211> 6		
<212> PRT		
<213> 智人(Homo sapiens)		
<400> 227		
Asn Ser Ala Phe Gln Tyr		
1	5	
<210> 228		
<211> 6		
<212> PRT		
<213> 智人(Homo sapiens)		
<400> 228		
Thr Tyr Ser Ser Gly Asn		
1	5	
<210> 229		
<211> 14		
<212> PRT		
<213> 智人(Homo sapiens)		
<400> 229		
Cys Ala Met Thr Ser Pro Tyr Asn Asn Asn Asp Met Arg Phe		
1	5	10
<210> 230		
<211> 6		
<212> PRT		

<213> 智人 (Homo sapiens)

<400> 230

Asp Phe Gln Ala Thr Thr

1 5

<210> 231

<211> 7

<212> PRT

<213> 智人 (Homo sapiens)

<400> 231

Ser Asn Glu Gly Ser Lys Ala

1 5

<210> 232

<211> 13

<212> PRT

<213> 智人 (Homo sapiens)

<400> 232

Cys Ser Gly Gly Leu Glu Glu Ala Ala Arg Gln Phe Ile

1 5 10

<210> 233

<211> 134

<212> PRT

<213> 智人 (Homo sapiens)

<400> 233

Met Ala Lys Ser Leu Arg Val Leu Leu Val Ile Leu Trp Leu Gln Leu

1 5 10 15

Ser Trp Val Trp Ser Gln Gln Lys Glu Val Glu Gln Asp Pro Gly Pro

20 25 30

Leu Ser Val Pro Glu Gly Ala Ile Val Ser Leu Asn Cys Thr Tyr Ser

35 40 45

Asn Ser Ala Phe Gln Tyr Phe Met Trp Tyr Arg Gln Tyr Ser Arg Lys

50 55 60

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

65 70 75 80

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

85 90 95

Phe Ile Arg Asp Ser Gln Pro Ser Asp Ser Ala Thr Tyr Leu Cys Ala

100 105 110

Met Thr Ser Pro Tyr Asn Asn Asn Asp Met Arg Phe Gly Ala Gly Thr

115 120 125

Arg Leu Thr Val Lys Pro

130

<210> 234

<211> 140

<212> PRT

<213> 智人(Homo sapiens)

<400> 234

Met His Leu Leu Leu Leu Leu Leu Gly Pro Gly Ile Ser Leu Leu Leu

1 5 10 15

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

20 25 30

Pro Ser Trp Val Ile Cys Lys Ser Gly Thr Ser Val Lys Ile Glu Cys

35 40 45

Arg Ser Leu Asp Phe Gln Ala Thr Thr Met Phe Trp Tyr Arg Gln Phe

50 55 60

Pro Lys Gln Ser Leu Met Leu Met Ala Thr Ser Asn Glu Gly Ser Lys

65 70 75 80

Ala Thr Tyr Glu Gln Gly Val Glu Lys Asp Lys Phe Leu Ile Asn His

85 90 95

Ala Ser Leu Thr Leu Ser Thr Leu Thr Val Thr Ser Ala His Pro Glu

100 105 110

Asp Ser Ser Phe Tyr Ile Cys Ser Gly Gly Leu Glu Glu Ala Ala Arg

115 120 125

Gln Phe Ile Gly Pro Gly Thr Arg Leu Thr Val Leu

130 135 140

<210> 235

<211> 271

<212> PRT

<213> 智人(Homo sapiens)

<400> 235

Met Ala Lys Ser Leu Arg Val Leu Leu Val Ile Leu Trp Leu Gln Leu

1 5 10 15

Ser Trp Val Trp Ser Gln Gln Lys Glu Val Glu Gln Asp Pro Gly Pro

20 25 30

Leu Ser Val Pro Glu Gly Ala Ile Val Ser Leu Asn Cys Thr Tyr Ser

35 40 45

Asn Ser Ala Phe Gln Tyr Phe Met Trp Tyr Arg Gln Tyr Ser Arg Lys

50 55 60

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

65	70	75	80
Gly Arg Phe Thr Ala Gln Val Asp Lys Ser Ser Lys Tyr Ile Ser Leu			
	85	90	95
Phe Ile Arg Asp Ser Gln Pro Ser Asp Ser Ala Thr Tyr Leu Cys Ala			
	100	105	110
Met Thr Ser Pro Tyr Asn Asn Asn Asp Met Arg Phe Gly Ala Gly Thr			
	115	120	125
Arg Leu Thr Val Lys Pro Asn Ile Gln Asn Pro Glu Pro Ala Val Tyr			
	130	135	140
Gln Leu Lys Asp Pro Arg Ser Gln Asp Ser Thr Leu Cys Leu Phe Thr			
145	150	155	160
Asp Phe Asp Ser Gln Ile Asn Val Pro Lys Thr Met Glu Ser Gly Thr			
	165	170	175
Phe Ile Thr Asp Lys Cys Val Leu Asp Met Lys Ala Met Asp Ser Lys			
	180	185	190
Ser Asn Gly Ala Ile Ala Trp Ser Asn Gln Thr Ser Phe Thr Cys Gln			
	195	200	205
Asp Ile Phe Lys Glu Thr Asn Ala Thr Tyr Pro Ser Ser Asp Val Pro			
	210	215	220
Cys Asp Ala Thr Leu Thr Glu Lys Ser Phe Glu Thr Asp Met Asn Leu			
225	230	235	240
Asn Phe Gln Asn Leu Leu Val Ile Val Leu Arg Ile Leu Leu Leu Lys			
	245	250	255
Val Ala Gly Phe Asn Leu Leu Met Thr Leu Arg Leu Trp Ser Ser			
	260	265	270
<210> 236			
<211> 313			
<212> PRT			
<213> 智人 (Homo sapiens)			
<400> 236			
Met His Leu Leu Leu Leu Leu Gly Pro Gly Ile Ser Leu Leu Leu			
1	5	10	15
Pro Gly Ser Leu Ala Gly Ser Gly Leu Gly Ala Val Val Ser Gln His			
	20	25	30
Pro Ser Trp Val Ile Cys Lys Ser Gly Thr Ser Val Lys Ile Glu Cys			
	35	40	45
Arg Ser Leu Asp Phe Gln Ala Thr Thr Met Phe Trp Tyr Arg Gln Phe			
	50	55	60
Pro Lys Gln Ser Leu Met Leu Met Ala Thr Ser Asn Glu Gly Ser Lys			

65	70	75	80
Ala Thr Tyr Glu Gln Gly Val Glu Lys Asp Lys Phe Leu Ile Asn His			
	85	90	95
Ala Ser Leu Thr Leu Ser Thr Leu Thr Val Thr Ser Ala His Pro Glu			
	100	105	110
Asp Ser Ser Phe Tyr Ile Cys Ser Gly Gly Leu Glu Glu Ala Ala Arg			
	115	120	125
Gln Phe Ile Gly Pro Gly Thr Arg Leu Thr Val Leu Glu Asp Leu Arg			
	130	135	140
Asn Val Thr Pro Pro Lys Val Ser Leu Phe Glu Pro Ser Lys Ala Glu			
145	150	155	160
Ile Ala Asn Lys Gln Lys Ala Thr Leu Val Cys Leu Ala Arg Gly Phe			
	165	170	175
Phe Pro Asp His Val Glu Leu Ser Trp Trp Val Asn Gly Lys Glu Val			
	180	185	190
His Ser Gly Val Cys Thr Asp Pro Gln Ala Tyr Lys Glu Ser Asn Tyr			
	195	200	205
Ser Tyr Cys Leu Ser Ser Arg Leu Arg Val Ser Ala Thr Phe Trp His			
	210	215	220
Asn Pro Arg Asn His Phe Arg Cys Gln Val Gln Phe His Gly Leu Ser			
225	230	235	240
Glu Glu Asp Lys Trp Pro Glu Gly Ser Pro Lys Pro Val Thr Gln Asn			
	245	250	255
Ile Ser Ala Glu Ala Trp Gly Arg Ala Asp Cys Gly Ile Thr Ser Ala			
	260	265	270
Ser Tyr Gln Gln Gly Val Leu Ser Ala Thr Ile Leu Tyr Glu Ile Leu			
	275	280	285
Leu Gly Lys Ala Thr Leu Tyr Ala Val Leu Val Ser Thr Leu Val Val			
	290	295	300
Met Ala Met Val Lys Arg Lys Asn Ser			
305	310		
<210> 237			
<211> 6			
<212> PRT			
<213> 智人 (Homo sapiens)			
<400> 237			
Asn Ser Ala Phe Gln Tyr			
1	5		
<210> 238			

<211> 6
<212> PRT
<213> 智人 (Homo sapiens)
<400> 238
Thr Tyr Ser Ser Gly Asn
1 5
<210> 239
<211> 14
<212> PRT
<213> 智人 (Homo sapiens)
<400> 239
Cys Ala Met Thr Ser Pro Tyr Asn Asn Asn Asp Met Arg Phe
1 5 10
<210> 240
<211> 6
<212> PRT
<213> 智人 (Homo sapiens)
<400> 240
Asp Phe Gln Ala Thr Thr
1 5
<210> 241
<211> 7
<212> PRT
<213> 智人 (Homo sapiens)
<400> 241
Ser Asn Glu Gly Ser Lys Ala
1 5
<210> 242
<211> 13
<212> PRT
<213> 智人 (Homo sapiens)
<400> 242
Cys Ser Gly Gly Leu Glu Glu Ala Ala Arg Gln Phe Ile
1 5 10
<210> 243
<211> 134
<212> PRT
<213> 智人 (Homo sapiens)
<400> 243

Val Leu
 130
 <210> 245
 <211> 271
 <212> PRT
 <213> 智人(Homo sapiens)
 <400> 245
 Met Ala Lys Ser Leu Arg Val Leu Leu Val Ile Leu Trp Leu Gln Leu
 1 5 10 15
 Ser Trp Val Trp Ser Gln Gln Lys Glu Val Glu Gln Asp Pro Gly Pro
 20 25 30
 Leu Ser Val Pro Glu Gly Ala Ile Val Ser Leu Asn Cys Thr Tyr Ser
 35 40 45
 Asn Ser Ala Phe Gln Tyr Phe Met Trp Tyr Arg Gln Tyr Ser Arg Lys
 50 55 60
 Gly Pro Glu Leu Leu Met Tyr Thr Tyr Ser Ser Gly Asn Lys Glu Asp
 65 70 75 80
 Gly Arg Phe Thr Ala Gln Val Asp Lys Ser Ser Lys Tyr Ile Ser Leu
 85 90 95
 Phe Ile Arg Asp Ser Gln Pro Ser Asp Ser Ala Thr Tyr Leu Cys Ala
 100 105 110
 Met Thr Ser Pro Tyr Asn Asn Asn Asp Met Arg Phe Gly Ala Gly Thr
 115 120 125
 Arg Leu Thr Val Lys Pro Asn Ile Gln Asn Pro Glu Pro Ala Val Tyr
 130 135 140
 Gln Leu Lys Asp Pro Arg Ser Gln Asp Ser Thr Leu Cys Leu Phe Thr
 145 150 155 160
 Asp Phe Asp Ser Gln Ile Asn Val Pro Lys Thr Met Glu Ser Gly Thr
 165 170 175
 Phe Ile Thr Asp Lys Cys Val Leu Asp Met Lys Ala Met Asp Ser Lys
 180 185 190
 Ser Asn Gly Ala Ile Ala Trp Ser Asn Gln Thr Ser Phe Thr Cys Gln
 195 200 205
 Asp Ile Phe Lys Glu Thr Asn Ala Thr Tyr Pro Ser Ser Asp Val Pro
 210 215 220
 Cys Asp Ala Thr Leu Thr Glu Lys Ser Phe Glu Thr Asp Met Asn Leu
 225 230 235 240
 Asn Phe Gln Asn Leu Leu Val Ile Val Leu Arg Ile Leu Leu Leu Lys
 245 250 255

Val	Ala	Gly	Phe	Asn	Leu	Leu	Met	Thr	Leu	Arg	Leu	Trp	Ser	Ser		
					260				265					270		
<210> 246																
<211> 303																
<212> PRT																
<213> 智人(Homo sapiens)																
<400> 246																
Met	His	Leu	Leu	Leu	Leu	Leu	Leu	Gly	Pro	Ala	Gly	Ser	Gly	Leu	Gly	
1				5					10					15		
Ala	Val	Val	Ser	Gln	His	Pro	Ser	Arg	Val	Ile	Cys	Lys	Ser	Gly	Thr	
			20					25					30			
Ser	Val	Lys	Ile	Glu	Cys	Arg	Ser	Leu	Asp	Phe	Gln	Ala	Thr	Thr	Met	
		35					40					45				
Phe	Trp	Tyr	Arg	Gln	Phe	Pro	Lys	Gln	Ser	Leu	Met	Leu	Met	Ala	Thr	
	50					55				60						
Ser	Asn	Glu	Gly	Ser	Lys	Ala	Thr	Tyr	Glu	Gln	Gly	Val	Glu	Lys	Asp	
65					70				75					80		
Lys	Phe	Leu	Ile	Asn	His	Ala	Ser	Leu	Thr	Leu	Ser	Thr	Leu	Thr	Val	
			85					90					95			
Thr	Ser	Ala	His	Pro	Glu	Asp	Ser	Ser	Phe	Tyr	Ile	Cys	Ser	Gly	Gly	
		100						105					110			
Leu	Glu	Glu	Ala	Ala	Arg	Gln	Phe	Ile	Gly	Pro	Gly	Thr	Arg	Leu	Thr	
	115					120						125				
Val	Leu	Glu	Asp	Leu	Arg	Asn	Val	Thr	Pro	Pro	Lys	Val	Ser	Leu	Phe	
	130					135					140					
Glu	Pro	Ser	Lys	Ala	Glu	Ile	Ala	Asn	Lys	Gln	Lys	Ala	Thr	Leu	Val	
145				150					155					160		
Cys	Leu	Ala	Arg	Gly	Phe	Phe	Pro	Asp	His	Val	Glu	Leu	Ser	Trp	Trp	
			165					170					175			
Val	Asn	Gly	Lys	Glu	Val	His	Ser	Gly	Val	Cys	Thr	Asp	Pro	Gln	Ala	
		180						185				190				
Tyr	Lys	Glu	Ser	Asn	Tyr	Ser	Tyr	Cys	Leu	Ser	Ser	Arg	Leu	Arg	Val	
	195					200						205				
Ser	Ala	Thr	Phe	Trp	His	Asn	Pro	Arg	Asn	His	Phe	Arg	Cys	Gln	Val	
	210					215					220					
Gln	Phe	His	Gly	Leu	Ser	Glu	Glu	Asp	Lys	Trp	Pro	Glu	Gly	Ser	Pro	
225				230					235					240		
Lys	Pro	Val	Thr	Gln	Asn	Ile	Ser	Ala	Glu	Ala	Trp	Gly	Arg	Ala	Asp	
			245					250					255			

Cys Gly Ile Thr Ser Ala Ser Tyr Gln Gln Gly Val Leu Ser Ala Thr
260 265 270
Ile Leu Tyr Glu Ile Leu Leu Gly Lys Ala Thr Leu Tyr Ala Val Leu
275 280 285
Val Ser Thr Leu Val Val Met Ala Met Val Lys Arg Lys Asn Ser
290 295 300

<210> 247

<211> 7

<212> PRT

<213> 智人 (Homo sapiens)

<400> 247

Thr Ile Ser Gly Asn Glu Tyr

1 5

<210> 248

<211> 5

<212> PRT

<213> 智人 (Homo sapiens)

<400> 248

Gly Leu Lys Asn Asn

1 5

<210> 249

<211> 11

<212> PRT

<213> 智人 (Homo sapiens)

<400> 249

Cys Ile Val Pro Asn Asp Tyr Lys Leu Ser Phe

1 5 10

<210> 250

<211> 5

<212> PRT

<213> 智人 (Homo sapiens)

<400> 250

Met Asp His Glu Asn

1 5

<210> 251

<211> 6

<212> PRT

<213> 智人 (Homo sapiens)

<400> 251

Ser Tyr Asp Val Lys Met

1 5

<210> 252

<211> 16

<212> PRT

<213> 智人(Homo sapiens)

<400> 252

Cys Ala Ser Ser Phe Gly Thr Gly Ser Ile Gln Glu Thr Gln Tyr Phe

1 5 10 15

<210> 253

<211> 125

<212> PRT

<213> 智人(Homo sapiens)

<400> 253

Met Ala Leu Val Ala Arg Val Thr Val Phe Leu Thr Phe Gly Thr Ile

1 5 10 15

Ile Asp Ala Lys Thr Thr Gln Pro Pro Ser Met Asp Cys Ala Glu Gly

20 25 30

Arg Ala Ala Asn Leu Pro Cys Asn His Ser Thr Ile Ser Gly Asn Glu

35 40 45

Tyr Val Tyr Trp Tyr Arg Gln Ile His Ser Gln Gly Pro Gln Tyr Ile

50 55 60

Ile His Gly Leu Lys Asn Asn Glu Thr Asn Glu Met Ala Ser Leu Ile

65 70 75 80

Ile Thr Glu Asp Arg Lys Ser Ser Thr Leu Ile Leu Pro His Ala Thr

85 90 95

Leu Arg Asp Thr Ala Val Tyr Tyr Cys Ile Val Pro Asn Asp Tyr Lys

100 105 110

Leu Ser Phe Gly Ala Gly Thr Thr Val Thr Val Arg Ala

115 120 125

<210> 254

<211> 134

<212> PRT

<213> 智人(Homo sapiens)

<400> 254

Met His Ile Arg Leu Leu Cys Arg Val Ala Phe Cys Phe Leu Ala Val

1 5 10 15

Gly Leu Val Asp Val Lys Val Thr Gln Ser Ser Arg Tyr Leu Val Lys

20 25 30

Arg	Thr	Gly	Glu	Lys	Val	Phe	Leu	Glu	Cys	Val	Gln	Asp	Met	Asp	His
	35						40					45			
Glu	Asn	Met	Phe	Trp	Tyr	Arg	Gln	Asp	Pro	Gly	Leu	Gly	Leu	Arg	Leu
	50					55					60				
Ile	Tyr	Phe	Ser	Tyr	Asp	Val	Lys	Met	Lys	Glu	Lys	Gly	Asp	Ile	Pro
65					70					75				80	
Glu	Gly	Tyr	Ser	Val	Ser	Arg	Glu	Lys	Lys	Glu	Arg	Phe	Ser	Leu	Ile
				85					90					95	
Leu	Glu	Ser	Ala	Ser	Thr	Asn	Gln	Thr	Ser	Met	Tyr	Leu	Cys	Ala	Ser
			100					105					110		
Ser	Phe	Gly	Thr	Gly	Ser	Ile	Gln	Glu	Thr	Gln	Tyr	Phe	Gly	Pro	Gly
	115						120					125			
Thr	Arg	Leu	Leu	Val	Leu										
	130														
<210>	255														
<211>	262														
<212>	PRT														
<213>	智人 (Homo sapiens)														
<400>	255														
Met	Ala	Leu	Val	Ala	Arg	Val	Thr	Val	Phe	Leu	Thr	Phe	Gly	Thr	Ile
1			5						10					15	
Ile	Asp	Ala	Lys	Thr	Thr	Gln	Pro	Pro	Ser	Met	Asp	Cys	Ala	Glu	Gly
		20					25					30			
Arg	Ala	Ala	Asn	Leu	Pro	Cys	Asn	His	Ser	Thr	Ile	Ser	Gly	Asn	Glu
	35						40					45			
Tyr	Val	Tyr	Trp	Tyr	Arg	Gln	Ile	His	Ser	Gln	Gly	Pro	Gln	Tyr	Ile
	50					55					60				
Ile	His	Gly	Leu	Lys	Asn	Asn	Glu	Thr	Asn	Glu	Met	Ala	Ser	Leu	Ile
65					70					75				80	
Ile	Thr	Glu	Asp	Arg	Lys	Ser	Ser	Thr	Leu	Ile	Leu	Pro	His	Ala	Thr
				85					90					95	
Leu	Arg	Asp	Thr	Ala	Val	Tyr	Tyr	Cys	Ile	Val	Pro	Asn	Asp	Tyr	Lys
			100					105					110		
Leu	Ser	Phe	Gly	Ala	Gly	Thr	Thr	Val	Thr	Val	Arg	Ala	Asn	Ile	Gln
	115						120					125			
Asn	Pro	Glu	Pro	Ala	Val	Tyr	Gln	Leu	Lys	Asp	Pro	Arg	Ser	Gln	Asp
	130						135				140				
Ser	Thr	Leu	Cys	Leu	Phe	Thr	Asp	Phe	Asp	Ser	Gln	Ile	Asn	Val	Pro
145					150					155				160	

Lys Thr Met Glu Ser Gly Thr Phe Ile Thr Asp Lys Cys Val Leu Asp
 165 170 175
 Met Lys Ala Met Asp Ser Lys Ser Asn Gly Ala Ile Ala Trp Ser Asn
 180 185 190
 Gln Thr Ser Phe Thr Cys Gln Asp Ile Phe Lys Glu Thr Asn Ala Thr
 195 200 205
 Tyr Pro Ser Ser Asp Val Pro Cys Asp Ala Thr Leu Thr Glu Lys Ser
 210 215 220
 Phe Glu Thr Asp Met Asn Leu Asn Phe Gln Asn Leu Leu Val Ile Val
 225 230 235 240
 Leu Arg Ile Leu Leu Leu Lys Val Ala Gly Phe Asn Leu Leu Met Thr
 245 250 255
 Leu Arg Leu Trp Ser Ser
 260
 <210> 256
 <211> 307
 <212> PRT
 <213> 智人(Homo sapiens)
 <400> 256
 Met His Ile Arg Leu Leu Cys Arg Val Ala Phe Cys Phe Leu Ala Val
 1 5 10 15
 Gly Leu Val Asp Val Lys Val Thr Gln Ser Ser Arg Tyr Leu Val Lys
 20 25 30
 Arg Thr Gly Glu Lys Val Phe Leu Glu Cys Val Gln Asp Met Asp His
 35 40 45
 Glu Asn Met Phe Trp Tyr Arg Gln Asp Pro Gly Leu Gly Leu Arg Leu
 50 55 60
 Ile Tyr Phe Ser Tyr Asp Val Lys Met Lys Glu Lys Gly Asp Ile Pro
 65 70 75 80
 Glu Gly Tyr Ser Val Ser Arg Glu Lys Lys Glu Arg Phe Ser Leu Ile
 85 90 95
 Leu Glu Ser Ala Ser Thr Asn Gln Thr Ser Met Tyr Leu Cys Ala Ser
 100 105 110
 Ser Phe Gly Thr Gly Ser Ile Gln Glu Thr Gln Tyr Phe Gly Pro Gly
 115 120 125
 Thr Arg Leu Leu Val Leu Glu Asp Leu Arg Asn Val Thr Pro Pro Lys
 130 135 140
 Val Ser Leu Phe Glu Pro Ser Lys Ala Glu Ile Ala Asn Lys Gln Lys
 145 150 155 160

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

Lys Asn Ser

305

<210> 257

<211> 6

<212> PRT

<213> 智人 (Homo sapiens)

<400> 257

Ala Thr Gly Tyr Pro Ser

1

5

<210> 258

<211> 7

<212> PRT

<213> 智人 (Homo sapiens)

<400> 258

Ala Thr Lys Ala Asp Asp Lys

1

5

<210> 259

<211> 17

<212> PRT

<213> 智人 (Homo sapiens)

<400> 259

Cys Ala Leu Asn Pro Asn Ala Gly Gly Thr Ser Tyr Gly Lys Leu Thr
 1 5 10 15
 Phe
 <210> 260
 <211> 5
 <212> PRT
 <213> 智人 (Homo sapiens)
 <400> 260
 Ser Gly His Thr Ser
 1 5
 <210> 261
 <211> 6
 <212> PRT
 <213> 智人 (Homo sapiens)
 <400> 261
 Tyr Asp Glu Gly Glu Glu
 1 5
 <210> 262
 <211> 20
 <212> PRT
 <213> 智人 (Homo sapiens)
 <400> 262
 Cys Ala Ser Ser Ser Pro Gly Ala Thr Ser Gly Gly Ala Asn Thr Gly
 1 5 10 15
 Glu Leu Phe Phe
 20
 <210> 263
 <211> 135
 <212> PRT
 <213> 智人 (Homo sapiens)
 <400> 263
 Met Ala Tyr Ser Pro Gly Leu Val Ser Leu Ile Leu Leu Leu Leu Gly
 1 5 10 15
 Arg Thr Arg Gly Asn Ser Val Thr Gln Met Glu Gly Pro Val Thr Leu
 20 25 30
 Ser Glu Glu Ala Phe Leu Thr Ile Asn Cys Thr Tyr Thr Ala Thr Gly
 35 40 45
 Tyr Pro Ser Leu Phe Trp Tyr Val Gln Tyr Pro Gly Glu Gly Leu Gln
 50 55 60

Met Ala Tyr Ser Pro Gly Leu Val Ser Leu Ile Leu Leu Leu Leu Gly

1	5	10	15
Arg Thr Arg Gly Asn Ser Val Thr Gln Met Glu Gly Pro Val Thr Leu			
20	25	30	
Ser Glu Glu Ala Phe Leu Thr Ile Asn Cys Thr Tyr Thr Ala Thr Gly			
35	40	45	
Tyr Pro Ser Leu Phe Trp Tyr Val Gln Tyr Pro Gly Glu Gly Leu Gln			
50	55	60	
Leu Leu Leu Lys Ala Thr Lys Ala Asp Asp Lys Gly Ser Asn Lys Gly			
65	70	75	80
Phe Glu Ala Thr Tyr Arg Lys Glu Thr Thr Ser Phe His Leu Glu Lys			
85	90	95	
Gly Ser Val Gln Val Ser Asp Ser Ala Val Tyr Phe Cys Ala Leu Asn			
100	105	110	
Pro Asn Ala Gly Gly Thr Ser Tyr Gly Lys Leu Thr Phe Gly Gln Gly			
115	120	125	
Thr Ile Leu Thr Val His Pro Asn Ile Gln Asn Pro Glu Pro Ala Val			
130	135	140	
Tyr Gln Leu Lys Asp Pro Arg Ser Gln Asp Ser Thr Leu Cys Leu Phe			
145	150	155	160
Thr Asp Phe Asp Ser Gln Ile Asn Val Pro Lys Thr Met Glu Ser Gly			
165	170	175	
Thr Phe Ile Thr Asp Lys Cys Val Leu Asp Met Lys Ala Met Asp Ser			
180	185	190	
Lys Ser Asn Gly Ala Ile Ala Trp Ser Asn Gln Thr Ser Phe Thr Cys			
195	200	205	
Gln Asp Ile Phe Lys Glu Thr Asn Ala Thr Tyr Pro Ser Ser Asp Val			
210	215	220	
Pro Cys Asp Ala Thr Leu Thr Glu Lys Ser Phe Glu Thr Asp Met Asn			
225	230	235	240
Leu Asn Phe Gln Asn Leu Leu Val Ile Val Leu Arg Ile Leu Leu Leu			
245	250	255	
Lys Val Ala Gly Phe Asn Leu Leu Met Thr Leu Arg Leu Trp Ser Ser			
260	265	270	
<210> 266			
<211> 311			
<212> PRT			
<213> 智人(Homo sapiens)			
<400> 266			
Met His Pro Arg Leu Leu Phe Trp Ala Leu Leu Cys Leu Leu Gly Thr			

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

<210> 267

<211> 6

<212> PRT

<213> 智人 (Homo sapiens)

<400> 267

Asp Ser Ser Ser Thr Tyr

1 5

<210> 268

<211> 7

<212> PRT

<213> 智人 (Homo sapiens)

<400> 268

Ile Phe Ser Asn Met Asp Met

1 5

<210> 269

<211> 17

<212> PRT

<213> 智人 (Homo sapiens)

<400> 269

Cys Ala Glu Ile Pro Arg Asp Ser Gly Gly Gly Ala Asp Gly Leu Thr

1 5 10 15

Phe

<210> 270

<211> 6

<212> PRT

<213> 智人 (Homo sapiens)

<400> 270

Asp Phe Gln Ala Thr Thr

1 5

<210> 271

<211> 7

<212> PRT

<213> 智人 (Homo sapiens)

<400> 271

Ser Asn Glu Gly Ser Lys Ala

1 5

<210> 272

<211> 14

<212> PRT

<213> 智人 (Homo sapiens)

<400> 272

Cys Ser Ala Arg Asp Leu Gln Arg Ser Tyr Glu Gln Tyr Phe

1 5 10

<210> 273

<211> 136

<212> PRT

<213> 智人 (Homo sapiens)

<400> 273

Met Ala Thr Phe Ala Gly Phe Ser Phe Leu Phe Leu Trp Leu Gln Leu

1 5 10 15

Asp Cys Met Ser Arg Gly Glu Asp Val Glu Gln Ser Leu Phe Leu Ser

20 25 30

Val Arg Glu Gly Asp Ser Ser Val Ile Asn Cys Thr Tyr Thr Asp Ser

35 40 45

Ser Ser Thr Tyr Leu Tyr Trp Tyr Lys Gln Glu Pro Gly Ala Gly Leu

50 55 60

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

65 70 75 80

Arg Leu Thr Val Leu Leu Asn Lys Lys Asp Lys His Leu Ser Leu Arg

85 90 95

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

100 105 110

Ile Pro Arg Asp Ser Gly Gly Gly Ala Asp Gly Leu Thr Phe Gly Lys

115 120 125

Gly Thr His Leu Ile Ile Gln Pro

130 135

<210> 274

<211> 141

<212> PRT

<213> 智人 (Homo sapiens)

<400> 274

Met His Leu Leu Leu Leu Leu Gly Pro Gly Ile Ser Leu Leu Leu

1 5 10 15

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

20 25 30

Pro Ser Trp Val Ile Cys Lys Ser Gly Thr Ser Val Lys Ile Glu Cys

35 40 45

Arg Ser Leu Asp Phe Gln Ala Thr Thr Met Phe Trp Tyr Arg Gln Phe

50	55	60
Pro Lys Gln Ser Leu Met	Leu Met Ala Thr Ser Asn Glu Gly Ser Lys	
65	70	75
Ala Thr Tyr Glu Gln Gly Val Glu Lys Asp Lys Phe Leu Ile Asn His		80
	85	90
Ala Ser Leu Thr Leu Ser Thr Leu Thr Val Thr Ser Ala His Pro Glu		95
	100	105
Asp Ser Ser Phe Tyr Ile Cys Ser Ala Arg Asp Leu Gln Arg Ser Tyr		110
	115	120
Glu Gln Tyr Phe Gly Pro Gly Thr Arg Leu Thr Val Thr		125
	130	135
		140
<210> 275		
<211> 273		
<212> PRT		
<213> 智人(Homo sapiens)		
<400> 275		
Met Ala Thr Phe Ala Gly Phe Ser Phe Leu Phe Leu Trp Leu Gln Leu		
1	5	10
Asp Cys Met Ser Arg Gly Glu Asp Val Glu Gln Ser Leu Phe Leu Ser		15
	20	25
Val Arg Glu Gly Asp Ser Ser Val Ile Asn Cys Thr Tyr Thr Asp Ser		30
	35	40
Ser Ser Thr Tyr Leu Tyr Trp Tyr Lys Gln Glu Pro Gly Ala Gly Leu		45
	50	55
Gln Leu Leu Thr Tyr Ile Phe Ser Asn Met Asp Met Lys Gln Asp Gln		60
65	70	75
Arg Leu Thr Val Leu Leu Asn Lys Lys Asp Lys His Leu Ser Leu Arg		80
	85	90
Ile Ala Asp Thr Gln Thr Gly Asp Ser Ala Ile Tyr Phe Cys Ala Glu		95
	100	105
Ile Pro Arg Asp Ser Gly Gly Gly Ala Asp Gly Leu Thr Phe Gly Lys		110
	115	120
Gly Thr His Leu Ile Ile Gln Pro Asn Ile Gln Asn Pro Glu Pro Ala		125
	130	135
Val Tyr Gln Leu Lys Asp Pro Arg Ser Gln Asp Ser Thr Leu Cys Leu		140
145	150	155
Phe Thr Asp Phe Asp Ser Gln Ile Asn Val Pro Lys Thr Met Glu Ser		160
	165	170
Gly Thr Phe Ile Thr Asp Lys Cys Val Leu Asp Met Lys Ala Met Asp		175

	180					185					190				
Ser	Lys	Ser	Asn	Gly	Ala	Ile	Ala	Trp	Ser	Asn	Gln	Thr	Ser	Phe	Thr
	195					200					205				
Cys	Gln	Asp	Ile	Phe	Lys	Glu	Thr	Asn	Ala	Thr	Tyr	Pro	Ser	Ser	Asp
	210					215					220				
Val	Pro	Cys	Asp	Ala	Thr	Leu	Thr	Glu	Lys	Ser	Phe	Glu	Thr	Asp	Met
225				230				235						240	
Asn	Leu	Asn	Phe	Gln	Asn	Leu	Leu	Val	Ile	Val	Leu	Arg	Ile	Leu	Leu
	245					250					255				
Leu	Lys	Val	Ala	Gly	Phe	Asn	Leu	Leu	Met	Thr	Leu	Arg	Leu	Trp	Ser
	260					265					270				
Ser															
<210> 276															
<211> 314															
<212> PRT															
<213> 智人 (Homo sapiens)															
<400> 276															
Met	His	Leu	Leu	Leu	Leu	Leu	Leu	Gly	Pro	Gly	Ile	Ser	Leu	Leu	Leu
1			5					10					15		
Pro	Gly	Ser	Leu	Ala	Gly	Ser	Gly	Leu	Gly	Ala	Val	Val	Ser	Gln	His
	20					25					30				
Pro	Ser	Trp	Val	Ile	Cys	Lys	Ser	Gly	Thr	Ser	Val	Lys	Ile	Glu	Cys
	35					40					45				
Arg	Ser	Leu	Asp	Phe	Gln	Ala	Thr	Thr	Met	Phe	Trp	Tyr	Arg	Gln	Phe
	50					55					60				
Pro	Lys	Gln	Ser	Leu	Met	Leu	Met	Ala	Thr	Ser	Asn	Glu	Gly	Ser	Lys
65				70				75						80	
Ala	Thr	Tyr	Glu	Gln	Gly	Val	Glu	Lys	Asp	Lys	Phe	Leu	Ile	Asn	His
	85					90					95				
Ala	Ser	Leu	Thr	Leu	Ser	Thr	Leu	Thr	Val	Thr	Ser	Ala	His	Pro	Glu
	100					105					110				
Asp	Ser	Ser	Phe	Tyr	Ile	Cys	Ser	Ala	Arg	Asp	Leu	Gln	Arg	Ser	Tyr
	115					120					125				
Glu	Gln	Tyr	Phe	Gly	Pro	Gly	Thr	Arg	Leu	Thr	Val	Thr	Glu	Asp	Leu
	130					135					140				
Arg	Asn	Val	Thr	Pro	Pro	Lys	Val	Ser	Leu	Phe	Glu	Pro	Ser	Lys	Ala
145				150				155						160	
Glu	Ile	Ala	Asn	Lys	Gln	Lys	Ala	Thr	Leu	Val	Cys	Leu	Ala	Arg	Gly
	165					170					175				

Phe Phe Pro Asp His Val Glu Leu Ser Trp Trp Val Asn Gly Lys Glu
 180 185 190
 Val His Ser Gly Val Cys Thr Asp Pro Gln Ala Tyr Lys Glu Ser Asn
 195 200 205
 Tyr Ser Tyr Cys Leu Ser Ser Arg Leu Arg Val Ser Ala Thr Phe Trp
 210 215 220
 His Asn Pro Arg Asn His Phe Arg Cys Gln Val Gln Phe His Gly Leu
 225 230 235 240
 Ser Glu Glu Asp Lys Trp Pro Glu Gly Ser Pro Lys Pro Val Thr Gln
 245 250 255
 Asn Ile Ser Ala Glu Ala Trp Gly Arg Ala Asp Cys Gly Ile Thr Ser
 260 265 270
 Ala Ser Tyr Gln Gln Gly Val Leu Ser Ala Thr Ile Leu Tyr Glu Ile
 275 280 285
 Leu Leu Gly Lys Ala Thr Leu Tyr Ala Val Leu Val Ser Thr Leu Val
 290 295 300
 Val Met Ala Met Val Lys Arg Lys Asn Ser
 305 310
 <210> 277
 <211> 6
 <212> PRT
 <213> 智人 (Homo sapiens)
 <400> 277
 Asp Ser Ser Ser Thr Tyr
 1 5
 <210> 278
 <211> 7
 <212> PRT
 <213> 智人 (Homo sapiens)
 <400> 278
 Ile Phe Ser Asn Met Asp Met
 1 5
 <210> 279
 <211> 17
 <212> PRT
 <213> 智人 (Homo sapiens)
 <400> 279
 Cys Ala Glu Ile Pro Arg Asp Ser Gly Gly Gly Ala Asp Gly Leu Thr
 1 5 10 15

Phe

<210> 280

<211> 6

<212> PRT

<213> 智人(Homo sapiens)

<400> 280

Asp Phe Gln Ala Thr Thr

1 5

<210> 281

<211> 7

<212> PRT

<213> 智人(Homo sapiens)

<400> 281

Ser Asn Glu Gly Ser Lys Ala

1 5

<210> 282

<211> 14

<212> PRT

<213> 智人(Homo sapiens)

<400> 282

Cys Ser Ala Arg Asp Leu Gln Arg Ser Tyr Glu Gln Tyr Phe

1 5 10

<210> 283

<211> 136

<212> PRT

<213> 智人(Homo sapiens)

<400> 283

Met Ala Thr Phe Ala Gly Phe Ser Phe Leu Phe Leu Trp Leu Gln Leu

1 5 10 15

Asp Cys Met Ser Arg Gly Glu Asp Val Glu Gln Ser Leu Phe Leu Ser

20 25 30

Val Arg Glu Gly Asp Ser Ser Val Ile Asn Cys Thr Tyr Thr Asp Ser

35 40 45

Ser Ser Thr Tyr Leu Tyr Trp Tyr Lys Gln Glu Pro Gly Ala Gly Leu

50 55 60

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

65 70 75 80

Arg Leu Thr Val Leu Leu Asn Lys Lys Asp Lys His Leu Ser Leu Arg

85 90 95

Ile Ala Asp Thr Gln Thr Gly Asp Ser Ala Ile Tyr Phe Cys Ala Glu
 100 105 110
 Ile Pro Arg Asp Ser Gly Gly Gly Ala Asp Gly Leu Thr Phe Gly Lys
 115 120 125
 Gly Thr His Leu Ile Ile Gln Pro
 130 135

<210> 284

<211> 131

<212> PRT

<213> 智人 (Homo sapiens)

<400> 284

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

<210> 285

<211> 273

<212> PRT

<213> 智人 (Homo sapiens)

<400> 285

Met Ala Thr Phe Ala Gly Phe Ser Phe Leu Phe Leu Trp Leu Gln Leu
 1 5 10 15
 Asp Cys Met Ser Arg Gly Glu Asp Val Glu Gln Ser Leu Phe Leu Ser
 20 25 30
 Val Arg Glu Gly Asp Ser Ser Val Ile Asn Cys Thr Tyr Thr Asp Ser

35	40	45
Ser Ser Thr Tyr Leu Tyr Trp Tyr Lys Gln Glu Pro Gly Ala Gly Leu		
50	55	60
Gln Leu Leu Thr Tyr Ile Phe Ser Asn Met Asp Met Lys Gln Asp Gln		
65	70	75
Arg Leu Thr Val Leu Leu Asn Lys Lys Asp Lys His Leu Ser Leu Arg		
85	90	95
Ile Ala Asp Thr Gln Thr Gly Asp Ser Ala Ile Tyr Phe Cys Ala Glu		
100	105	110
Ile Pro Arg Asp Ser Gly Gly Gly Ala Asp Gly Leu Thr Phe Gly Lys		
115	120	125
Gly Thr His Leu Ile Ile Gln Pro Asn Ile Gln Asn Pro Glu Pro Ala		
130	135	140
Val Tyr Gln Leu Lys Asp Pro Arg Ser Gln Asp Ser Thr Leu Cys Leu		
145	150	155
Phe Thr Asp Phe Asp Ser Gln Ile Asn Val Pro Lys Thr Met Glu Ser		
165	170	175
Gly Thr Phe Ile Thr Asp Lys Cys Val Leu Asp Met Lys Ala Met Asp		
180	185	190
Ser Lys Ser Asn Gly Ala Ile Ala Trp Ser Asn Gln Thr Ser Phe Thr		
195	200	205
Cys Gln Asp Ile Phe Lys Glu Thr Asn Ala Thr Tyr Pro Ser Ser Asp		
210	215	220
Val Pro Cys Asp Ala Thr Leu Thr Glu Lys Ser Phe Glu Thr Asp Met		
225	230	235
Asn Leu Asn Phe Gln Asn Leu Leu Val Ile Val Leu Arg Ile Leu Leu		
245	250	255
Leu Lys Val Ala Gly Phe Asn Leu Leu Met Thr Leu Arg Leu Trp Ser		
260	265	270
Ser		
<210> 286		
<211> 304		
<212> PRT		
<213> 智人 (Homo sapiens)		
<400> 286		
Met His Leu Leu Leu Leu Leu Gly Pro Ala Gly Ser Gly Leu Gly		
1	5	10
Ala Val Val Ser Gln His Pro Ser Arg Val Ile Cys Lys Ser Gly Thr		
20	25	30

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

<210> 287
 <211> 6
 <212> PRT
 <213> 智人 (Homo sapiens)
 <400> 287

Asn Ser Ala Ser Asp Tyr

1 5

<210> 288

<211> 7

<212> PRT

<213> 智人(Homo sapiens)

<400> 288

Ile Arg Ser Asn Met Asp Lys

1 5

<210> 289

<211> 16

<212> PRT

<213> 智人(Homo sapiens)

<400> 289

Cys Ala Glu Pro Val Gly Gly Leu Asn Ser Gly Tyr Ala Leu Asn Phe

1 5 10 15

<210> 290

<211> 5

<212> PRT

<213> 智人(Homo sapiens)

<400> 290

Ser Gly His Lys Ser

1 5

<210> 291

<211> 6

<212> PRT

<213> 智人(Homo sapiens)

<400> 291

Tyr Tyr Glu Lys Glu Glu

1 5

<210> 292

<211> 16

<212> PRT

<213> 智人(Homo sapiens)

<400> 292

Cys Ala Ser Ser Gly Gly Arg Thr Ser Gly Ala Tyr Glu Gln Phe Phe

1 5 10 15

<210> 293

<211> 135

<212> PRT

<213> 智人(Homo sapiens)

<400> 293

```

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

```

<210> 294

<211> 134

<212> PRT

<213> 智人(Homo sapiens)

<400> 294

```

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

```

	100		105		110
Ser Gly Gly Arg Thr Ser Gly Ala Tyr Glu Gln Phe Phe Gly Pro Gly					
	115		120		125
Thr Arg Leu Thr Val Leu					
	130				
<210> 295					
<211> 272					
<212> PRT					
<213> 智人 (Homo sapiens)					
<400> 295					
Met Ala Gly Ile Arg Ala Leu Phe Met Tyr Leu Trp Leu Gln Leu Asp					
1	5		10		15
Trp Val Ser Arg Gly Glu Ser Val Gly Leu His Leu Pro Thr Leu Ser					
	20		25		30
Val Gln Glu Gly Asp Asn Ser Ile Ile Asn Cys Ala Tyr Ser Asn Ser					
	35		40		45
Ala Ser Asp Tyr Phe Ile Trp Tyr Lys Gln Glu Ser Gly Lys Gly Pro					
	50		55		60
Gln Phe Ile Ile Asp Ile Arg Ser Asn Met Asp Lys Arg Gln Gly Gln					
65	70		75		80
Arg Val Thr Val Leu Leu Asn Lys Thr Val Lys His Leu Ser Leu Gln					
	85		90		95
Ile Ala Ala Thr Gln Pro Gly Asp Ser Ala Val Tyr Phe Cys Ala Glu					
	100		105		110
Pro Val Gly Gly Leu Asn Ser Gly Tyr Ala Leu Asn Phe Gly Lys Gly					
	115		120		125
Thr Ser Leu Leu Val Thr Pro Asn Ile Gln Asn Pro Glu Pro Ala Val					
	130		135		140
Tyr Gln Leu Lys Asp Pro Arg Ser Gln Asp Ser Thr Leu Cys Leu Phe					
145	150		155		160
Thr Asp Phe Asp Ser Gln Ile Asn Val Pro Lys Thr Met Glu Ser Gly					
	165		170		175
Thr Phe Ile Thr Asp Lys Cys Val Leu Asp Met Lys Ala Met Asp Ser					
	180		185		190
Lys Ser Asn Gly Ala Ile Ala Trp Ser Asn Gln Thr Ser Phe Thr Cys					
	195		200		205
Gln Asp Ile Phe Lys Glu Thr Asn Ala Thr Tyr Pro Ser Ser Asp Val					
210	215		220		
Pro Cys Asp Ala Thr Leu Thr Glu Lys Ser Phe Glu Thr Asp Met Asn					

225	230	235	240
Leu Asn Phe Gln Asn Leu Leu Val Ile Val Leu Arg Ile Leu Leu Leu			
	245	250	255
Lys Val Ala Gly Phe Asn Leu Leu Met Thr Leu Arg Leu Trp Ser Ser			
	260	265	270
<210> 296			
<211> 307			
<212> PRT			
<213> 智人 (Homo sapiens)			
<400> 296			
Met His Pro Gly Leu Leu Cys Trp Val Leu Leu Cys Leu Leu Gly Ala			
1	5	10	15
Gly Pro Val Asp Ala Gly Val Thr Gln Ser Pro Thr His Leu Ile Lys			
	20	25	30
Thr Arg Gly Gln Gln Val Thr Leu Arg Cys Ser Pro Ile Ser Gly His			
	35	40	45
Lys Ser Val Ser Trp Tyr Gln Gln Val Leu Gly Gln Gly Pro Gln Phe			
	50	55	60
Ile Phe Gln Tyr Tyr Glu Lys Glu Glu Arg Gly Arg Gly Asn Phe Pro			
65	70	75	80
Asp Arg Phe Ser Ala Arg Gln Phe Pro Asn Tyr Ser Ser Glu Leu Asn			
	85	90	95
Val Asn Ala Leu Leu Leu Gly Asp Ser Ala Leu Tyr Leu Cys Ala Ser			
	100	105	110
Ser Gly Gly Arg Thr Ser Gly Ala Tyr Glu Gln Phe Phe Gly Pro Gly			
	115	120	125
Thr Arg Leu Thr Val Leu Glu Asp Leu Arg Asn Val Thr Pro Pro Lys			
	130	135	140
Val Ser Leu Phe Glu Pro Ser Lys Ala Glu Ile Ala Asn Lys Gln Lys			
145	150	155	160
Ala Thr Leu Val Cys Leu Ala Arg Gly Phe Phe Pro Asp His Val Glu			
	165	170	175
Leu Ser Trp Trp Val Asn Gly Lys Glu Val His Ser Gly Val Cys Thr			
	180	185	190
Asp Pro Gln Ala Tyr Lys Glu Ser Asn Tyr Ser Tyr Cys Leu Ser Ser			
	195	200	205
Arg Leu Arg Val Ser Ala Thr Phe Trp His Asn Pro Arg Asn His Phe			
	210	215	220
Arg Cys Gln Val Gln Phe His Gly Leu Ser Glu Glu Asp Lys Trp Pro			

225	230	235	240
Glu Gly Ser Pro Lys Pro Val Thr Gln Asn Ile Ser Ala Glu Ala Trp			
	245	250	255
Gly Arg Ala Asp Cys Gly Ile Thr Ser Ala Ser Tyr Gln Gln Gly Val			
	260	265	270
Leu Ser Ala Thr Ile Leu Tyr Glu Ile Leu Leu Gly Lys Ala Thr Leu			
	275	280	285
Tyr Ala Val Leu Val Ser Thr Leu Val Val Met Ala Met Val Lys Arg			
290	295	300	
Lys Asn Ser			
305			
<210> 297			
<211> 6			
<212> PRT			
<213> 智人 (Homo sapiens)			
<400> 297			
Val Ser Gly Leu Arg Gly			
1	5		
<210> 298			
<211> 7			
<212> PRT			
<213> 智人 (Homo sapiens)			
<400> 298			
Leu Tyr Ser Ala Gly Glu Glu			
1	5		
<210> 299			
<211> 16			
<212> PRT			
<213> 智人 (Homo sapiens)			
<400> 299			
Cys Ala Val Thr Ala His Arg Gly Ser Thr Leu Gly Arg Leu Tyr Phe			
1	5	10	15
<210> 300			
<211> 5			
<212> PRT			
<213> 智人 (Homo sapiens)			
<400> 300			
Ser Gly His Asp Thr			
1	5		

<210> 301

<211> 6

<212> PRT

<213> 智人(Homo sapiens)

<400> 301

Tyr Tyr Glu Glu Glu Glu

1 5

<210> 302

<211> 15

<212> PRT

<213> 智人(Homo sapiens)

<400> 302

Cys Ala Ser Ser Arg Arg Gly Gly Ala Tyr Asn Glu Gln Phe Phe

1 5 10 15

<210> 303

<211> 134

<212> PRT

<213> 智人(Homo sapiens)

<400> 303

Met Ala Lys Met Leu Glu Cys Ala Phe Ile Val Leu Trp Leu Gln Leu

1 5 10 15

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

20 25 30

Arg Leu Gln Glu Gly Glu Ser Ser Ser Leu Asn Cys Ser Tyr Thr Val

35 40 45

Ser Gly Leu Arg Gly Leu Phe Trp Tyr Arg Gln Asp Pro Gly Lys Gly

50 55 60

Pro Glu Phe Leu Phe Thr Leu Tyr Ser Ala Gly Glu Glu Lys Glu Lys

65 70 75 80

Glu Arg Leu Lys Ala Thr Leu Thr Lys Lys Glu Ser Phe Leu His Ile

85 90 95

Thr Ala Pro Lys Pro Glu Asp Ser Ala Thr Tyr Leu Cys Ala Val Thr

100 105 110

Ala His Arg Gly Ser Thr Leu Gly Arg Leu Tyr Phe Gly Arg Gly Thr

115 120 125

Gln Leu Thr Val Trp Pro

130

<210> 304

<211> 133

<212> PRT

<213> 智人(Homo sapiens)

<400> 304

```

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

```

<210> 305

<211> 271

<212> PRT

<213> 智人(Homo sapiens)

<400> 305

```

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

```


100	105	110
Ala His Arg Gly Ser Thr Leu Gly Arg Leu Tyr Phe Gly Arg Gly Thr		
115	120	125
Gln Leu Thr Val Trp Pro Asn Ile Gln Asn Pro Glu Pro Ala Val Tyr		
130	135	140
Gln Leu Lys Asp Pro Arg Ser Gln Asp Ser Thr Leu Cys Leu Phe Thr		
145	150	155
Asp Phe Asp Ser Gln Ile Asn Val Pro Lys Thr Met Glu Ser Gly Thr		
165	170	175
Phe Ile Thr Asp Lys Cys Val Leu Asp Met Lys Ala Met Asp Ser Lys		
180	185	190
Ser Asn Gly Ala Ile Ala Trp Ser Asn Gln Thr Ser Phe Thr Cys Gln		
195	200	205
Asp Ile Phe Lys Glu Thr Asn Ala Thr Tyr Pro Ser Ser Asp Val Pro		
210	215	220
Cys Asp Ala Thr Leu Thr Glu Lys Ser Phe Glu Thr Asp Met Asn Leu		
225	230	235
Asn Phe Gln Asn Leu Leu Val Ile Val Leu Arg Ile Leu Leu Leu Lys		
245	250	255
Val Ala Gly Phe Asn Leu Leu Met Thr Leu Arg Leu Trp Ser Ser		
260	265	270
<210> 306		
<211> 306		
<212> PRT		
<213> 智人(Homo sapiens)		
<400> 306		
Met His Pro Gly Leu Leu Cys Trp Ala Leu Leu Cys Leu Leu Gly Ala		
1	5	10
Gly Leu Val Asp Ala Gly Val Thr Gln Ser Pro Thr His Leu Ile Lys		
20	25	30
Thr Arg Gly Gln Gln Val Thr Leu Arg Cys Ser Pro Lys Ser Gly His		
35	40	45
Asp Thr Val Ser Trp Tyr Gln Gln Ala Leu Gly Gln Gly Pro Gln Phe		
50	55	60
Ile Phe Gln Tyr Tyr Glu Glu Glu Glu Arg Gln Arg Gly Asn Phe Pro		
65	70	75
Asp Arg Phe Ser Gly His Gln Phe Pro Asn Tyr Ser Ser Glu Leu Asn		
85	90	95
Val Asn Ala Leu Leu Leu Gly Asp Ser Ala Leu Tyr Leu Cys Ala Ser		

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

Asn Ser

305

<210> 307

<211> 6

<212> PRT

<213> 智人 (Homo sapiens)

<400> 307

Ser Ser Asn Phe Tyr Ala

1

5

<210> 308

<211> 7

<212> PRT

<213> 智人 (Homo sapiens)

<400> 308

Met Thr Leu Asn Gly Asp Glu

1 5

<210> 309

<211> 13

<212> PRT

<213> 智人(Homo sapiens)

<400> 309

Cys Ala Ser Val Gly Gly Gly Ala Asp Gly Leu Thr Phe

1 5 10

<210> 310

<211> 5

<212> PRT

<213> 智人(Homo sapiens)

<400> 310

Ser Gly His Thr Ala

1 5

<210> 311

<211> 6

<212> PRT

<213> 智人(Homo sapiens)

<400> 311

Phe Gln Gly Asn Ser Ala

1 5

<210> 312

<211> 15

<212> PRT

<213> 智人(Homo sapiens)

<400> 312

Cys Ala Ser Thr Trp Asp Arg Gly Ser Tyr Asn Glu Gln Phe Phe

1 5 10 15

<210> 313

<211> 134

<212> PRT

<213> 智人(Homo sapiens)

<400> 313

Met Ala Lys Asn Pro Leu Ala Ala Pro Leu Leu Ile Leu Trp Phe His

1 5 10 15

Leu Asp Cys Val Ser Ser Ile Leu Asn Val Glu Gln Ser Pro Gln Ser

20 25 30

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

<210> 314

<211> 134

<212> PRT

<213> 智人(Homo sapiens)

<400> 314

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

<210> 315

<211> 271

<212> PRT

<213> 智人(Homo sapiens)

<400> 315

```

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

```

<210> 316

<211> 307

<212> PRT

<213> 智人(Homo sapiens)

<400> 316

```

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

```

Tyr Ala Val Leu Val Ser Thr Leu Val Val Met Ala Met Val Lys Arg
290 295 300

Lys Asn Ser
305

<210> 317
<211> 6
<212> PRT
<213> 智人 (Homo sapiens)
<400> 317

Asn Ser Met Phe Asp Tyr
1 5

<210> 318
<211> 7
<212> PRT
<213> 智人 (Homo sapiens)
<400> 318

Ile Ser Ser Ile Lys Asp Lys
1 5

<210> 319
<211> 11
<212> PRT
<213> 智人 (Homo sapiens)
<400> 319

Cys Ala Ala Asn Thr Gly Asn Gln Phe Tyr Phe
1 5 10

<210> 320
<211> 5
<212> PRT
<213> 智人 (Homo sapiens)
<400> 320

Ser Gly His Ala Thr
1 5

<210> 321
<211> 6
<212> PRT
<213> 智人 (Homo sapiens)
<400> 321

Phe Gln Asn Asn Gly Val
1 5

<210> 322

<211> 16

<212> PRT

<213> 智人(Homo sapiens)

<400> 322

Cys Ala Ser Ser His Leu Ala Gly Glu Phe Tyr Asn Glu Gln Phe Phe
 1 5 10 15

<210> 323

<211> 136

<212> PRT

<213> 智人(Homo sapiens)

<400> 323

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

Asp Trp Val Asn Ser Gln Gln Lys Asn Asp Asp Gln Gln Val Lys Gln
 20 25 30

Asn Ser Pro Ser Leu Ser Val Gln Glu Gly Arg Ile Ser Ile Leu Asn
 35 40 45

Cys Asp Tyr Thr Asn Ser Met Phe Asp Tyr Phe Leu Trp Tyr Lys Lys
 50 55 60

Tyr Pro Ala Glu Gly Pro Thr Phe Leu Ile Ser Ile Ser Ser Ile Lys
 65 70 75 80

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

Lys His Leu Ser Leu His Ile Val Pro Ser Gln Pro Gly Asp Ser Ala
 100 105 110

Val Tyr Phe Cys Ala Ala Asn Thr Gly Asn Gln Phe Tyr Phe Gly Thr
 115 120 125

Gly Thr Ser Leu Thr Val Ile Pro
 130 135

<210> 324

<211> 135

<212> PRT

<213> 智人(Homo sapiens)

<400> 324

Met His Thr Arg Leu Leu Cys Trp Ala Ala Leu Cys Leu Leu Gly Ala
 1 5 10 15

Glu Leu Thr Glu Ala Gly Val Ala Gln Ser Pro Arg Tyr Lys Ile Ile
 20 25 30

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

<210> 325

<211> 273

<212> PRT

<213> 智人(Homo sapiens)

<400> 325

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

Phe Thr Asp Phe Asp Ser Gln Ile Asn Val Pro Lys Thr Met Glu Ser		
	165	170 175
Gly Thr Phe Ile Thr Asp Lys Cys Val Leu Asp Met Lys Ala Met Asp		
	180	185 190
Ser Lys Ser Asn Gly Ala Ile Ala Trp Ser Asn Gln Thr Ser Phe Thr		
	195	200 205
Cys Gln Asp Ile Phe Lys Glu Thr Asn Ala Thr Tyr Pro Ser Ser Asp		
	210	215 220
Val Pro Cys Asp Ala Thr Leu Thr Glu Lys Ser Phe Glu Thr Asp Met		
225	230	235 240
Asn Leu Asn Phe Gln Asn Leu Leu Val Ile Val Leu Arg Ile Leu Leu		
	245	250 255
Leu Lys Val Ala Gly Phe Asn Leu Leu Met Thr Leu Arg Leu Trp Ser		
	260	265 270
Ser		
<210> 326		
<211> 308		
<212> PRT		
<213> 智人(Homo sapiens)		
<400> 326		
Met His Thr Arg Leu Leu Cys Trp Ala Ala Leu Cys Leu Leu Gly Ala		
1	5	10 15
Glu Leu Thr Glu Ala Gly Val Ala Gln Ser Pro Arg Tyr Lys Ile Ile		
	20	25 30
Glu Lys Arg Gln Ser Val Ala Phe Trp Cys Asn Pro Ile Ser Gly His		
	35	40 45
Ala Thr Leu Tyr Trp Tyr Gln Gln Ile Leu Gly Gln Gly Pro Lys Leu		
	50	55 60
Leu Ile Gln Phe Gln Asn Asn Gly Val Val Asp Asp Ser Gln Leu Pro		
65	70	75 80
Lys Asp Arg Phe Ser Ala Glu Arg Leu Lys Gly Val Asp Ser Thr Leu		
	85	90 95
Lys Ile Gln Pro Ala Lys Leu Glu Asp Ser Ala Val Tyr Leu Cys Ala		
	100	105 110
Ser Ser His Leu Ala Gly Glu Phe Tyr Asn Glu Gln Phe Phe Gly Pro		
	115	120 125
Gly Thr Arg Leu Thr Val Leu Glu Asp Leu Arg Asn Val Thr Pro Pro		
	130	135 140
Lys Val Ser Leu Phe Glu Pro Ser Lys Ala Glu Ile Ala Asn Lys Gln		

145	150	155	160
Lys Ala Thr Leu Val Cys Leu Ala Arg Gly Phe Phe Pro Asp His Val			
	165	170	175
Glu Leu Ser Trp Trp Val Asn Gly Lys Glu Val His Ser Gly Val Cys			
	180	185	190
Thr Asp Pro Gln Ala Tyr Lys Glu Ser Asn Tyr Ser Tyr Cys Leu Ser			
	195	200	205
Ser Arg Leu Arg Val Ser Ala Thr Phe Trp His Asn Pro Arg Asn His			
	210	215	220
Phe Arg Cys Gln Val Gln Phe His Gly Leu Ser Glu Glu Asp Lys Trp			
225	230	235	240
Pro Glu Gly Ser Pro Lys Pro Val Thr Gln Asn Ile Ser Ala Glu Ala			
	245	250	255
Trp Gly Arg Ala Asp Cys Gly Ile Thr Ser Ala Ser Tyr Gln Gln Gly			
	260	265	270
Val Leu Ser Ala Thr Ile Leu Tyr Glu Ile Leu Leu Gly Lys Ala Thr			
	275	280	285
Leu Tyr Ala Val Leu Val Ser Thr Leu Val Val Met Ala Met Val Lys			
	290	295	300
Arg Lys Asn Ser			
305			
<210> 327			
<211> 6			
<212> PRT			
<213> 智人 (Homo sapiens)			
<400> 327			
Thr Ser Gly Phe Tyr Gly			
1	5		
<210> 328			
<211> 6			
<212> PRT			
<213> 智人 (Homo sapiens)			
<400> 328			
Asn Ala Leu Asp Gly Leu			
1	5		
<210> 329			
<211> 11			
<212> PRT			
<213> 智人 (Homo sapiens)			

<400> 329

Cys Ala Phe Ala Tyr Gly Gln Asn Phe Val Phe

1 5 10

<210> 330

<211> 5

<212> PRT

<213> 智人(Homo sapiens)

<400> 330

Ser Gly Asp Leu Ser

1 5

<210> 331

<211> 6

<212> PRT

<213> 智人(Homo sapiens)

<400> 331

Tyr Tyr Asn Gly Glu Glu

1 5

<210> 332

<211> 15

<212> PRT

<213> 智人(Homo sapiens)

<400> 332

Cys Ala Ser Ser Pro Leu Gly Asp Ser Gly Asn Thr Ile Tyr Phe

1 5 10 15

<210> 333

<211> 125

<212> PRT

<213> 智人(Homo sapiens)

<400> 333

Met Ala Gly Ala Phe Leu Leu Tyr Val Ser Met Lys Met Gly Gly Thr

1 5 10 15

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

20 25 30

Ala Ile Val Gln Ile Asn Cys Thr Tyr Gln Thr Ser Gly Phe Tyr Gly

35 40 45

Leu Ser Trp Tyr Gln Gln His Asp Gly Gly Ala Pro Thr Phe Leu Ser

50 55 60

Tyr Asn Ala Leu Asp Gly Leu Glu Glu Thr Gly Arg Phe Ser Ser Phe

65 70 75 80

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

<210> 336

<211> 306

<212> PRT

<213> 智人 (Homo sapiens)

<400> 336

Met His Phe Arg Leu Leu Cys Cys Val Ala Phe Cys Leu Leu Gly Ala
1 5 10 15
Gly Pro Val Asp Ser Gly Val Thr Gln Thr Pro Lys His Leu Ile Thr
20 25 30
Ala Thr Gly Gln Arg Val Thr Leu Arg Cys Ser Pro Arg Ser Gly Asp

35	40	45
Leu Ser Val Tyr Trp Tyr Gln Gln Ser Leu Asp Gln Gly Leu Gln Phe		
50	55	60
Leu Ile Gln Tyr Tyr Asn Gly Glu Glu Arg Ala Lys Gly Asn Ile Leu		
65	70	75
Glu Arg Phe Ser Ala Gln Gln Phe Pro Asp Leu His Ser Glu Leu Asn		
85	90	95
Leu Ser Ser Leu Glu Leu Gly Asp Ser Ala Leu Tyr Phe Cys Ala Ser		
100	105	110
Ser Pro Leu Gly Asp Ser Gly Asn Thr Ile Tyr Phe Gly Glu Gly Ser		
115	120	125
Trp Leu Thr Val Val Glu Asp Leu Arg Asn Val Thr Pro Pro Lys Val		
130	135	140
Ser Leu Phe Glu Pro Ser Lys Ala Glu Ile Ala Asn Lys Gln Lys Ala		
145	150	155
Thr Leu Val Cys Leu Ala Arg Gly Phe Phe Pro Asp His Val Glu Leu		
165	170	175
Ser Trp Trp Val Asn Gly Lys Glu Val His Ser Gly Val Cys Thr Asp		
180	185	190
Pro Gln Ala Tyr Lys Glu Ser Asn Tyr Ser Tyr Cys Leu Ser Ser Arg		
195	200	205
Leu Arg Val Ser Ala Thr Phe Trp His Asn Pro Arg Asn His Phe Arg		
210	215	220
Cys Gln Val Gln Phe His Gly Leu Ser Glu Glu Asp Lys Trp Pro Glu		
225	230	235
Gly Ser Pro Lys Pro Val Thr Gln Asn Ile Ser Ala Glu Ala Trp Gly		
245	250	255
Arg Ala Asp Cys Gly Ile Thr Ser Ala Ser Tyr Gln Gln Gly Val Leu		
260	265	270
Ser Ala Thr Ile Leu Tyr Glu Ile Leu Leu Gly Lys Ala Thr Leu Tyr		
275	280	285
Ala Val Leu Val Ser Thr Leu Val Val Met Ala Met Val Lys Arg Lys		
290	295	300
Asn Ser		
305		
<210> 337		
<211> 5		
<212> PRT		
<213> 智人 (Homo sapiens)		

<400> 337
Thr Ser Ile Asn Asn
1 5
<210> 338
<211> 7
<212> PRT
<213> 智人 (Homo sapiens)
<400> 338
Ile Arg Ser Asn Glu Arg Glu
1 5
<210> 339
<211> 12
<212> PRT
<213> 智人 (Homo sapiens)
<400> 339
Cys Ala Thr Asp Ala Trp Asn Asn Asp Met Arg Phe
1 5 10
<210> 340
<211> 5
<212> PRT
<213> 智人 (Homo sapiens)
<400> 340
Met Asn His Asn Ser
1 5
<210> 341
<211> 6
<212> PRT
<213> 智人 (Homo sapiens)
<400> 341
Ser Ala Ser Glu Gly Thr
1 5
<210> 342
<211> 14
<212> PRT
<213> 智人 (Homo sapiens)
<400> 342
Cys Ala Ser Ser Glu Ser Gln Gly Asn Thr Glu Ala Phe Phe
1 5 10
<210> 343

<211> 130

<212> PRT

<213> 智人(Homo sapiens)

<400> 343

```

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

```

Lys Pro

130

<210> 344

<211> 132

<212> PRT

<213> 智人(Homo sapiens)

<400> 344

```

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

```

Leu	Glu	Ser	Ala	Ala	Pro	Ser	Gln	Thr	Ser	Val	Tyr	Phe	Cys	Ala	Ser
100					105					110					
Ser	Glu	Ser	Gln	Gly	Asn	Thr	Glu	Ala	Phe	Phe	Gly	Gln	Gly	Thr	Arg
115					120					125					
Leu	Thr	Val	Val												
130															
<210> 345															
<211> 267															
<212> PRT															
<213> 智人 (Homo sapiens)															
<400> 345															
Met	Ala	Thr	Leu	Leu	Gly	Val	Ser	Leu	Val	Ile	Leu	Trp	Leu	Gln	Leu
1		5				10				15					
Ala	Arg	Val	Asn	Ser	Gln	Gln	Gly	Glu	Glu	Asp	Pro	Gln	Ala	Leu	Ser
20					25					30					
Ile	Gln	Glu	Gly	Glu	Asn	Ala	Thr	Met	Asn	Cys	Ser	Tyr	Lys	Thr	Ser
35				40				45							
Ile	Asn	Asn	Leu	Gln	Trp	Tyr	Arg	Gln	Asn	Ser	Gly	Arg	Gly	Leu	Val
50			55				60								
His	Leu	Ile	Leu	Ile	Arg	Ser	Asn	Glu	Arg	Glu	Lys	His	Ser	Gly	Arg
65		70				75				80					
Leu	Arg	Val	Thr	Leu	Asp	Thr	Ser	Lys	Lys	Ser	Ser	Ser	Leu	Leu	Ile
85					90					95					
Thr	Ala	Ser	Arg	Ala	Ala	Asp	Thr	Ala	Ser	Tyr	Phe	Cys	Ala	Thr	Asp
100					105					110					
Ala	Trp	Asn	Asn	Asp	Met	Arg	Phe	Gly	Ala	Gly	Thr	Arg	Leu	Thr	Val
115				120				125							
Lys	Pro	Asn	Ile	Gln	Asn	Pro	Glu	Pro	Ala	Val	Tyr	Gln	Leu	Lys	Asp
130				135				140							
Pro	Arg	Ser	Gln	Asp	Ser	Thr	Leu	Cys	Leu	Phe	Thr	Asp	Phe	Asp	Ser
145		150				155					160				
Gln	Ile	Asn	Val	Pro	Lys	Thr	Met	Glu	Ser	Gly	Thr	Phe	Ile	Thr	Asp
165					170					175					
Lys	Cys	Val	Leu	Asp	Met	Lys	Ala	Met	Asp	Ser	Lys	Ser	Asn	Gly	Ala
180				185				190							
Ile	Ala	Trp	Ser	Asn	Gln	Thr	Ser	Phe	Thr	Cys	Gln	Asp	Ile	Phe	Lys
195				200				205							
Glu	Thr	Asn	Ala	Thr	Tyr	Pro	Ser	Ser	Asp	Val	Pro	Cys	Asp	Ala	Thr
210			215				220								

Leu Thr Glu Lys Ser Phe Glu Thr Asp Met Asn Leu Asn Phe Gln Asn
 225 230 235 240
 Leu Leu Val Ile Val Leu Arg Ile Leu Leu Lys Val Ala Gly Phe
 245 250 255
 Asn Leu Leu Met Thr Leu Arg Leu Trp Ser Ser
 260 265
 <210> 346
 <211> 305
 <212> PRT
 <213> 智人 (Homo sapiens)
 <400> 346
 Met His Ile Gly Leu Leu Cys Cys Val Ala Phe Ser Leu Leu Trp Ala
 1 5 10 15
 Ser Pro Val Asn Ala Gly Val Thr Gln Thr Pro Lys Phe Gln Val Leu
 20 25 30
 Lys Thr Gly Gln Ser Met Thr Leu Gln Cys Ala Gln Asp Met Asn His
 35 40 45
 Asn Ser Met Tyr Trp Tyr Arg Gln Asp Pro Gly Met Gly Leu Arg Leu
 50 55 60
 Ile Tyr Tyr Ser Ala Ser Glu Gly Thr Thr Asp Lys Gly Glu Val Pro
 65 70 75 80
 Asn Gly Tyr Asn Val Ser Arg Leu Asn Lys Arg Glu Phe Ser Leu Arg
 85 90 95
 Leu Glu Ser Ala Ala Pro Ser Gln Thr Ser Val Tyr Phe Cys Ala Ser
 100 105 110
 Ser Glu Ser Gln Gly Asn Thr Glu Ala Phe Phe Gly Gln Gly Thr Arg
 115 120 125
 Leu Thr Val Val Glu Asp Leu Arg Asn Val Thr Pro Pro Lys Val Ser
 130 135 140
 Leu Phe Glu Pro Ser Lys Ala Glu Ile Ala Asn Lys Gln Lys Ala Thr
 145 150 155 160
 Leu Val Cys Leu Ala Arg Gly Phe Phe Pro Asp His Val Glu Leu Ser
 165 170 175
 Trp Trp Val Asn Gly Lys Glu Val His Ser Gly Val Cys Thr Asp Pro
 180 185 190
 Gln Ala Tyr Lys Glu Ser Asn Tyr Ser Tyr Cys Leu Ser Ser Arg Leu
 195 200 205
 Arg Val Ser Ala Thr Phe Trp His Asn Pro Arg Asn His Phe Arg Cys
 210 215 220

Gln Val Gln Phe His Gly Leu Ser Glu Glu Asp Lys Trp Pro Glu Gly
 225 230 235 240
 Ser Pro Lys Pro Val Thr Gln Asn Ile Ser Ala Glu Ala Trp Gly Arg
 245 250 255
 Ala Asp Cys Gly Ile Thr Ser Ala Ser Tyr Gln Gln Gly Val Leu Ser
 260 265 270
 Ala Thr Ile Leu Tyr Glu Ile Leu Leu Gly Lys Ala Thr Leu Tyr Ala
 275 280 285
 Val Leu Val Ser Thr Leu Val Val Met Ala Met Val Lys Arg Lys Asn
 290 295 300

Ser

305

<210> 347

<211> 6

<212> PRT

<213> 智人 (Homo sapiens)

<400> 347

Val Ser Pro Phe Ser Asn

1 5

<210> 348

<211> 7

<212> PRT

<213> 智人 (Homo sapiens)

<400> 348

Met Thr Phe Ser Glu Asn Thr

1 5

<210> 349

<211> 10

<212> PRT

<213> 智人 (Homo sapiens)

<400> 349

Cys Val Val Ser Ser Tyr Lys Ile Ile Phe

1 5 10

<210> 350

<211> 5

<212> PRT

<213> 智人 (Homo sapiens)

<400> 350

Ser Gly His Thr Ala

1 5
 <210> 351
 <211> 6
 <212> PRT
 <213> 智人 (Homo sapiens)
 <400> 351
 Phe Gln Gly Asn Ser Ala
 1 5
 <210> 352
 <211> 15
 <212> PRT
 <213> 智人 (Homo sapiens)
 <400> 352
 Cys Ala Ser Ser Pro Ile Gln Gly Glu Asn Ser Pro Leu His Phe
 1 5 10 15
 <210> 353
 <211> 130
 <212> PRT
 <213> 智人 (Homo sapiens)
 <400> 353
 Met Ala Lys His Leu Thr Thr Phe Leu Val Ile Leu Trp Leu Tyr Phe
 1 5 10 15
 Tyr Arg Gly Asn Gly Lys Asn Gln Val Glu Gln Ser Pro Gln Ser Leu
 20 25 30
 Ile Ile Leu Glu Gly Lys Asn Cys Thr Leu Gln Cys Asn Tyr Thr Val
 35 40 45
 Ser Pro Phe Ser Asn Leu Arg Trp Tyr Lys Gln Asp Thr Gly Arg Gly
 50 55 60
 Pro Val Ser Leu Thr Ile Met Thr Phe Ser Glu Asn Thr Lys Ser Asn
 65 70 75 80
 Gly Arg Tyr Thr Ala Thr Leu Asp Ala Asp Thr Lys Gln Ser Ser Leu
 85 90 95
 His Ile Thr Ala Ser Gln Leu Ser Asp Ser Ala Ser Tyr Ile Cys Val
 100 105 110
 Val Ser Ser Tyr Lys Ile Ile Phe Gly Thr Gly Thr Arg Leu His Val
 115 120 125
 Phe Pro
 130
 <210> 354

<211> 134

<212> PRT

<213> 智人(Homo sapiens)

<400> 354

```

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

```

<210> 355

<211> 267

<212> PRT

<213> 智人(Homo sapiens)

<400> 355

```

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

```

His Ile Thr Ala Ser Gln Leu Ser Asp Ser Ala Ser Tyr Ile Cys Val		
100	105	110
Val Ser Ser Tyr Lys Ile Ile Phe Gly Thr Gly Thr Arg Leu His Val		
115	120	125
Phe Pro Asn Ile Gln Asn Pro Glu Pro Ala Val Tyr Gln Leu Lys Asp		
130	135	140
Pro Arg Ser Gln Asp Ser Thr Leu Cys Leu Phe Thr Asp Phe Asp Ser		
145	150	155
Gln Ile Asn Val Pro Lys Thr Met Glu Ser Gly Thr Phe Ile Thr Asp		
165	170	175
Lys Cys Val Leu Asp Met Lys Ala Met Asp Ser Lys Ser Asn Gly Ala		
180	185	190
Ile Ala Trp Ser Asn Gln Thr Ser Phe Thr Cys Gln Asp Ile Phe Lys		
195	200	205
Glu Thr Asn Ala Thr Tyr Pro Ser Ser Asp Val Pro Cys Asp Ala Thr		
210	215	220
Leu Thr Glu Lys Ser Phe Glu Thr Asp Met Asn Leu Asn Phe Gln Asn		
225	230	235
Leu Leu Val Ile Val Leu Arg Ile Leu Leu Leu Lys Val Ala Gly Phe		
245	250	255
Asn Leu Leu Met Thr Leu Arg Leu Trp Ser Ser		
260	265	
<210> 356		
<211> 307		
<212> PRT		
<213> 智人(Homo sapiens)		
<400> 356		
Met His Thr Arg Leu Leu Phe Trp Val Ala Phe Cys Leu Leu Gly Ala		
1	5	10
Tyr His Thr Gly Ala Gly Val Ser Gln Ser Pro Ser Asn Lys Val Thr		
20	25	30
Glu Lys Gly Lys Asp Val Glu Leu Arg Cys Asp Pro Ile Ser Gly His		
35	40	45
Thr Ala Leu Tyr Trp Tyr Arg Gln Arg Leu Gly Gln Gly Leu Glu Phe		
50	55	60
Leu Ile Tyr Phe Gln Gly Asn Ser Ala Pro Asp Lys Ser Gly Leu Pro		
65	70	75
Ser Asp Arg Phe Ser Ala Glu Arg Thr Gly Glu Ser Val Ser Thr Leu		
85	90	95

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

Lys Asn Ser

305

<210> 357

<211> 6

<212> PRT

<213> 智人 (Homo sapiens)

<400> 357

Val Ser Pro Phe Ser Asn

1

5

<210> 358

<211> 7

<212> PRT

<213> 智人 (Homo sapiens)

<400> 358

Met Thr Phe Ser Glu Asn Thr

1 5

<210> 359

<211> 11

<212> PRT

<213> 智人 (Homo sapiens)

<400> 359

Ile Cys Val Val Ser Ser Tyr Lys Leu Ile Phe

1 5 10

<210> 360

<211> 5

<212> PRT

<213> 智人 (Homo sapiens)

<400> 360

Ser Gly His Thr Ala

1 5

<210> 361

<211> 6

<212> PRT

<213> 智人 (Homo sapiens)

<400> 361

Phe Gln Gly Asn Ser Ala

1 5

<210> 362

<211> 15

<212> PRT

<213> 智人 (Homo sapiens)

<400> 362

Cys Ala Ser Ser Pro Ile Gln Gly Glu Asn Ser Pro Leu His Phe

1 5 10 15

<210> 363

<211> 130

<212> PRT

<213> 智人 (Homo sapiens)

<400> 363

Met Ala Lys His Leu Thr Thr Phe Leu Val Ile Leu Trp Leu Tyr Phe

1 5 10 15

Tyr Arg Gly Asn Gly Lys Asn Gln Val Glu Gln Ser Pro Gln Ser Leu

20	25	30
Ile Ile Leu Glu Gly Lys Asn Cys Thr Leu Gln Cys Asn Tyr Thr Val		
35	40	45
Ser Pro Phe Ser Asn Leu Arg Trp Tyr Lys Gln Asp Thr Gly Arg Gly		
50	55	60
Pro Val Ser Leu Thr Ile Met Thr Phe Ser Glu Asn Thr Lys Ser Asn		
65	70	75
Gly Arg Tyr Thr Ala Thr Leu Asp Ala Asp Thr Lys Gln Ser Ser Leu		
85	90	95
His Ile Thr Ala Ser Gln Leu Ser Asp Ser Ala Ser Tyr Ile Cys Val		
100	105	110
Val Ser Ser Tyr Lys Leu Ile Phe Gly Thr Gly Thr Arg Leu Gln Val		
115	120	125
Phe Pro		
130		
<210> 364		
<211> 134		
<212> PRT		
<213> 智人(Homo sapiens)		
<400> 364		
Met His Thr Arg Leu Leu Phe Trp Val Ala Phe Cys Leu Leu Gly Ala		
1	5	10
Tyr His Thr Gly Ala Gly Val Ser Gln Ser Pro Ser Asn Lys Val Thr		
20	25	30
Glu Lys Gly Lys Asp Val Glu Leu Arg Cys Asp Pro Ile Ser Gly His		
35	40	45
Thr Ala Leu Tyr Trp Tyr Arg Gln Arg Leu Gly Gln Gly Leu Glu Phe		
50	55	60
Leu Ile Tyr Phe Gln Gly Asn Ser Ala Pro Asp Lys Ser Gly Leu Pro		
65	70	75
Ser Asp Arg Phe Ser Ala Glu Arg Thr Gly Glu Ser Val Ser Thr Leu		
85	90	95
Thr Ile Gln Arg Thr Gln Gln Glu Asp Ser Ala Val Tyr Leu Cys Ala		
100	105	110
Ser Ser Pro Ile Gln Gly Glu Asn Ser Pro Leu His Phe Gly Asn Gly		
115	120	125
Thr Arg Leu Thr Val Thr		
130		
<210> 365		

<211> 267

<212> PRT

<213> 智人(Homo sapiens)

<400> 365

```

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

```

<210> 366

<211> 307

<212> PRT

<213> 智人(Homo sapiens)

<400> 366

```

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

```

275	280	285
Tyr Ala Val Leu Val Ser Thr	Leu Val Val Met	Ala Met Val Lys Arg
290	295	300
Lys Asn Ser		
305		
<210> 367		
<211> 6		
<212> PRT		
<213> 智人 (Homo sapiens)		
<400> 367		
Ser Ser Val Ser Val Tyr		
1	5	
<210> 368		
<211> 8		
<212> PRT		
<213> 智人 (Homo sapiens)		
<400> 368		
Tyr Leu Ser Gly Ser Thr Leu Val		
1	5	
<210> 369		
<211> 14		
<212> PRT		
<213> 智人 (Homo sapiens)		
<400> 369		
Cys Ala Val Ser Lys Gly Thr Gly Ala Gln Lys Leu Val Phe		
1	5	10
<210> 370		
<211> 5		
<212> PRT		
<213> 智人 (Homo sapiens)		
<400> 370		
Leu Asn His Asp Ala		
1	5	
<210> 371		
<211> 6		
<212> PRT		
<213> 智人 (Homo sapiens)		
<400> 371		
Ser Gln Ile Val Asn Asp		

1 5
 <210> 372
 <211> 7
 <212> PRT
 <213> 智人 (Homo sapiens)
 <400> 372
 Cys Ala Ser Glu Ala Phe Phe
 1 5
 <210> 373
 <211> 133
 <212> PRT
 <213> 智人 (Homo sapiens)
 <400> 373
 Met Ala Leu Leu Leu Val Pro Ala Phe Gln Val Ile Phe Thr Leu Gly
 1 5 10 15
 Gly Thr Arg Ala Gln Ser Val Thr Gln Leu Asp Ser Gln Val Pro Val
 20 25 30
 Phe Glu Glu Ala Pro Val Glu Leu Arg Cys Asn Tyr Ser Ser Ser Val
 35 40 45
 Ser Val Tyr Leu Phe Trp Tyr Val Gln Tyr Pro Asn Gln Gly Leu Gln
 50 55 60
 Leu Leu Leu Lys Tyr Leu Ser Gly Ser Thr Leu Val Glu Ser Ile Asn
 65 70 75 80
 Gly Phe Glu Ala Glu Phe Asn Lys Ser Gln Thr Ser Phe His Leu Arg
 85 90 95
 Lys Pro Ser Val His Ile Ser Asp Thr Ala Glu Tyr Phe Cys Ala Val
 100 105 110
 Ser Lys Gly Thr Gly Ala Gln Lys Leu Val Phe Gly Gln Gly Thr Arg
 115 120 125
 Leu Thr Ile Asn Pro
 130
 <210> 374
 <211> 125
 <212> PRT
 <213> 智人 (Homo sapiens)
 <400> 374
 Met His Asn Gln Val Leu Cys Cys Val Val Leu Cys Phe Leu Gly Ala
 1 5 10 15
 Asn Thr Val Asp Gly Gly Ile Thr Gln Ser Pro Lys Tyr Leu Phe Arg

227

	165		170		175
Ile Thr Asp Lys Cys Val Leu Asp Met Lys Ala Met Asp Ser Lys Ser					
	180		185		190
Asn Gly Ala Ile Ala Trp Ser Asn Gln Thr Ser Phe Thr Cys Gln Asp					
	195		200		205
Ile Phe Lys Glu Thr Asn Ala Thr Tyr Pro Ser Ser Asp Val Pro Cys					
	210		215		220
Asp Ala Thr Leu Thr Glu Lys Ser Phe Glu Thr Asp Met Asn Leu Asn					
225		230		235	240
Phe Gln Asn Leu Leu Val Ile Val Leu Arg Ile Leu Leu Leu Lys Val					
	245		250		255
Ala Gly Phe Asn Leu Leu Met Thr Leu Arg Leu Trp Ser Ser					
	260		265		270
<210> 376					
<211> 298					
<212> PRT					
<213> 智人 (Homo sapiens)					
<400> 376					
Met His Asn Gln Val Leu Cys Cys Val Val Leu Cys Phe Leu Gly Ala					
1	5		10		15
Asn Thr Val Asp Gly Gly Ile Thr Gln Ser Pro Lys Tyr Leu Phe Arg					
	20		25		30
Lys Glu Gly Gln Asn Val Thr Leu Ser Cys Glu Gln Asn Leu Asn His					
	35		40		45
Asp Ala Met Tyr Trp Tyr Arg Gln Asp Pro Gly Gln Gly Leu Arg Leu					
50		55		60	
Ile Tyr Tyr Ser Gln Ile Val Asn Asp Phe Gln Lys Gly Asp Ile Ala					
65		70		75	80
Glu Gly Tyr Ser Val Ser Arg Glu Lys Lys Glu Ser Phe Pro Leu Ile					
	85		90		95
Val Thr Ser Ala Gln Lys Asn Pro Thr Ala Ser Tyr Leu Cys Ala Ser					
	100		105		110
Glu Ala Phe Phe Gly Gln Gly Thr Arg Leu Thr Val Val Glu Asp Leu					
	115		120		125
Arg Asn Val Thr Pro Pro Lys Val Ser Leu Phe Glu Pro Ser Lys Ala					
	130		135		140
Glu Ile Ala Asn Lys Gln Lys Ala Thr Leu Val Cys Leu Ala Arg Gly					
145		150		155	160
Phe Phe Pro Asp His Val Glu Leu Ser Trp Trp Val Asn Gly Lys Glu					

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

<210> 377

<211> 7

<212> PRT

<213> 智人(Homo sapiens)

<400> 377

Thr Ile Ser Gly Thr Asp Tyr

1 5

<210> 378

<211> 5

<212> PRT

<213> 智人(Homo sapiens)

<400> 378

Gly Leu Thr Ser Asn

1 5

<210> 379

<211> 14

<212> PRT

<213> 智人(Homo sapiens)

<400> 379

Cys Ile Leu Ala Ser Gly Ala Gly Ser Tyr Gln Leu Thr Phe

1 5 10

<210> 380

<211> 5
 <212> PRT
 <213> 智人(Homo sapiens)
 <400> 380
 Leu Gly His Asp Thr
 1 5
 <210> 381
 <211> 6
 <212> PRT
 <213> 智人(Homo sapiens)
 <400> 381
 Tyr Asn Asn Lys Glu Leu
 1 5
 <210> 382
 <211> 14
 <212> PRT
 <213> 智人(Homo sapiens)
 <400> 382
 Cys Ala Ser Arg Thr Ile Gly Tyr Asn Thr Glu Ala Phe Phe
 1 5 10
 <210> 383
 <211> 128
 <212> PRT
 <213> 智人(Homo sapiens)
 <400> 383
 Met Ala Leu Val Thr Ser Ile Thr Val Leu Leu Ser Leu Gly Ile Met
 1 5 10 15
 Gly Asp Ala Lys Thr Thr Gln Pro Asn Ser Met Glu Ser Asn Glu Glu
 20 25 30
 Glu Pro Val His Leu Pro Cys Asn His Ser Thr Ile Ser Gly Thr Asp
 35 40 45
 Tyr Ile His Trp Tyr Arg Gln Leu Pro Ser Gln Gly Pro Glu Tyr Val
 50 55 60
 Ile His Gly Leu Thr Ser Asn Val Asn Asn Arg Met Ala Ser Leu Ala
 65 70 75 80
 Ile Ala Glu Asp Arg Lys Ser Ser Thr Leu Ile Leu His Arg Ala Thr
 85 90 95
 Leu Arg Asp Ala Ala Val Tyr Tyr Cys Ile Leu Ala Ser Gly Ala Gly
 100 105 110

Ser Tyr Gln Leu Thr Phe Gly Lys Gly Thr Lys Leu Ser Val Ile Pro
 115 120 125

<210> 384

<211> 132

<212> PRT

<213> 智人 (Homo sapiens)

<400> 384

Met His Cys Arg Leu Leu Cys Cys Val Val Phe Cys Leu Leu Gln Ala
 1 5 10 15

Gly Pro Leu Asp Thr Ala Val Ser Gln Thr Pro Lys Tyr Leu Val Thr
 20 25 30

Gln Met Gly Asn Asp Lys Ser Ile Lys Cys Glu Gln Asn Leu Gly His
 35 40 45

Asp Thr Met Tyr Trp Tyr Lys Gln Asp Ser Lys Lys Phe Leu Lys Ile
 50 55 60

Met Phe Ser Tyr Asn Asn Lys Glu Leu Ile Ile Asn Glu Thr Val Pro
 65 70 75 80

Asn Arg Phe Ser Pro Lys Ser Pro Asp Lys Ala His Leu Asn Leu His
 85 90 95

Ile Asn Ser Leu Glu Leu Gly Asp Ser Ala Val Tyr Phe Cys Ala Ser
 100 105 110

Arg Thr Ile Gly Tyr Asn Thr Glu Ala Phe Phe Gly Gln Gly Thr Arg
 115 120 125

Leu Thr Val Val
 130

<210> 385

<211> 265

<212> PRT

<213> 智人 (Homo sapiens)

<400> 385

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

Gly Asp Ala Lys Thr Thr Gln Pro Asn Ser Met Glu Ser Asn Glu Glu
 20 25 30

Glu Pro Val His Leu Pro Cys Asn His Ser Thr Ile Ser Gly Thr Asp
 35 40 45

Tyr Ile His Trp Tyr Arg Gln Leu Pro Ser Gln Gly Pro Glu Tyr Val
 50 55 60

Ile His Gly Leu Thr Ser Asn Val Asn Asn Arg Met Ala Ser Leu Ala

65	70	75	80
Ile Ala Glu Asp Arg Lys Ser Ser Thr Leu Ile Leu His Arg Ala Thr			
	85	90	95
Leu Arg Asp Ala Ala Val Tyr Tyr Cys Ile Leu Ala Ser Gly Ala Gly			
	100	105	110
Ser Tyr Gln Leu Thr Phe Gly Lys Gly Thr Lys Leu Ser Val Ile Pro			
	115	120	125
Asn Ile Gln Asn Pro Glu Pro Ala Val Tyr Gln Leu Lys Asp Pro Arg			
	130	135	140
Ser Gln Asp Ser Thr Leu Cys Leu Phe Thr Asp Phe Asp Ser Gln Ile			
145	150	155	160
Asn Val Pro Lys Thr Met Glu Ser Gly Thr Phe Ile Thr Asp Lys Cys			
	165	170	175
Val Leu Asp Met Lys Ala Met Asp Ser Lys Ser Asn Gly Ala Ile Ala			
	180	185	190
Trp Ser Asn Gln Thr Ser Phe Thr Cys Gln Asp Ile Phe Lys Glu Thr			
	195	200	205
Asn Ala Thr Tyr Pro Ser Ser Asp Val Pro Cys Asp Ala Thr Leu Thr			
	210	215	220
Glu Lys Ser Phe Glu Thr Asp Met Asn Leu Asn Phe Gln Asn Leu Leu			
225	230	235	240
Val Ile Val Leu Arg Ile Leu Leu Leu Lys Val Ala Gly Phe Asn Leu			
	245	250	255
Leu Met Thr Leu Arg Leu Trp Ser Ser			
	260	265	
<210> 386			
<211> 305			
<212> PRT			
<213> 智人 (Homo sapiens)			
<400> 386			
Met His Cys Arg Leu Leu Cys Cys Val Val Phe Cys Leu Leu Gln Ala			
1	5	10	15
Gly Pro Leu Asp Thr Ala Val Ser Gln Thr Pro Lys Tyr Leu Val Thr			
	20	25	30
Gln Met Gly Asn Asp Lys Ser Ile Lys Cys Glu Gln Asn Leu Gly His			
	35	40	45
Asp Thr Met Tyr Trp Tyr Lys Gln Asp Ser Lys Lys Phe Leu Lys Ile			
	50	55	60
Met Phe Ser Tyr Asn Asn Lys Glu Leu Ile Ile Asn Glu Thr Val Pro			

65	70	75	80
Asn Arg Phe Ser Pro Lys Ser Pro Asp Lys Ala His Leu Asn Leu His			
	85	90	95
Ile Asn Ser Leu Glu Leu Gly Asp Ser Ala Val Tyr Phe Cys Ala Ser			
	100	105	110
Arg Thr Ile Gly Tyr Asn Thr Glu Ala Phe Phe Gly Gln Gly Thr Arg			
	115	120	125
Leu Thr Val Val Glu Asp Leu Arg Asn Val Thr Pro Pro Lys Val Ser			
	130	135	140
Leu Phe Glu Pro Ser Lys Ala Glu Ile Ala Asn Lys Gln Lys Ala Thr			
145	150	155	160
Leu Val Cys Leu Ala Arg Gly Phe Phe Pro Asp His Val Glu Leu Ser			
	165	170	175
Trp Trp Val Asn Gly Lys Glu Val His Ser Gly Val Cys Thr Asp Pro			
	180	185	190
Gln Ala Tyr Lys Glu Ser Asn Tyr Ser Tyr Cys Leu Ser Ser Arg Leu			
	195	200	205
Arg Val Ser Ala Thr Phe Trp His Asn Pro Arg Asn His Phe Arg Cys			
	210	215	220
Gln Val Gln Phe His Gly Leu Ser Glu Glu Asp Lys Trp Pro Glu Gly			
225	230	235	240
Ser Pro Lys Pro Val Thr Gln Asn Ile Ser Ala Glu Ala Trp Gly Arg			
	245	250	255
Ala Asp Cys Gly Ile Thr Ser Ala Ser Tyr Gln Gln Gly Val Leu Ser			
	260	265	270
Ala Thr Ile Leu Tyr Glu Ile Leu Leu Gly Lys Ala Thr Leu Tyr Ala			
	275	280	285
Val Leu Val Ser Thr Leu Val Val Met Ala Met Val Lys Arg Lys Asn			
	290	295	300
Ser			
305			
<210> 387			
<211> 5			
<212> PRT			
<213> 智人 (Homo sapiens)			
<400> 387			
Val Gly Ile Ser Ala			
1	5		
<210> 388			

<211> 5
<212> PRT
<213> 智人 (Homo sapiens)
<400> 388
Leu Ser Ser Gly Lys
1 5
<210> 389
<211> 13
<212> PRT
<213> 智人 (Homo sapiens)
<400> 389
Cys Ala Ala Leu Ser Tyr Asn Thr Asp Lys Leu Ile Phe
1 5 10
<210> 390
<211> 5
<212> PRT
<213> 智人 (Homo sapiens)
<400> 390
Ser Gly His Thr Ala
1 5
<210> 391
<211> 6
<212> PRT
<213> 智人 (Homo sapiens)
<400> 391
Phe Gln Gly Thr Gly Ala
1 5
<210> 392
<211> 15
<212> PRT
<213> 智人 (Homo sapiens)
<400> 392
Cys Ala Ser Ser Leu Ser Gly Leu Leu Gln Glu Thr Gln Tyr Phe
1 5 10 15
<210> 393
<211> 131
<212> PRT
<213> 智人 (Homo sapiens)
<400> 393

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

<210> 394

<211> 134

<212> PRT

<213> 智人(Homo sapiens)

<400> 394

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

Thr Arg Leu Leu Val Leu

130

<210> 395

<211> 268

<212> PRT

<213> 智人(Homo sapiens)

<400> 395

Met Ala Lys Ile Arg Gln Phe Leu Leu Ala Ile Leu Trp Leu Gln Leu

1 5 10 15

Ser Cys Val Ser Ala Ala Lys Asn Glu Val Glu Gln Ser Pro Gln Asn

20 25 30

Leu Thr Ala Gln Glu Gly Glu Phe Ile Thr Ile Asn Cys Ser Tyr Ser

35 40 45

Val Gly Ile Ser Ala Leu His Trp Leu Gln Gln His Pro Gly Gly Gly

50 55 60

Ile Val Ser Leu Phe Met Leu Ser Ser Gly Lys Lys Lys His Gly Arg

65 70 75 80

Leu Ile Ala Thr Ile Asn Ile Gln Glu Lys His Ser Ser Leu His Ile

85 90 95

Thr Ala Ser His Pro Arg Asp Ser Ala Val Tyr Ile Cys Ala Ala Leu

100 105 110

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

115 120 125

Val Phe Pro Asn Ile Gln Asn Pro Glu Pro Ala Val Tyr Gln Leu Lys

130 135 140

Asp Pro Arg Ser Gln Asp Ser Thr Leu Cys Leu Phe Thr Asp Phe Asp

145 150 155 160

Ser Gln Ile Asn Val Pro Lys Thr Met Glu Ser Gly Thr Phe Ile Thr

165 170 175

Asp Lys Cys Val Leu Asp Met Lys Ala Met Asp Ser Lys Ser Asn Gly

180 185 190

Ala Ile Ala Trp Ser Asn Gln Thr Ser Phe Thr Cys Gln Asp Ile Phe

195 200 205

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

210 215 220

Thr Leu Thr Glu Lys Ser Phe Glu Thr Asp Met Asn Leu Asn Phe Gln

225 230 235 240

Asn Leu Leu Val Ile Val Leu Arg Ile Leu Leu Leu Lys Val Ala Gly

245 250 255

Phe Asn Leu Leu Met Thr Leu Arg Leu Trp Ser Ser
 260 265
 <210> 396
 <211> 307
 <212> PRT
 <213> 智人 (Homo sapiens)
 <400> 396
 Met His Thr Arg Leu Leu Cys Trp Ala Ala Leu Cys Leu Leu Gly Ala
 1 5 10 15
 Asp His Thr Gly Ala Gly Val Ser Gln Thr Pro Ser Asn Lys Val Thr
 20 25 30
 Glu Lys Gly Lys Tyr Val Glu Leu Arg Cys Asp Pro Ile Ser Gly His
 35 40 45
 Thr Ala Leu Tyr Trp Tyr Arg Gln Ser Leu Gly Gln Gly Pro Glu Phe
 50 55 60
 Leu Ile Tyr Phe Gln Gly Thr Gly Ala Ala Asp Asp Ser Gly Leu Pro
 65 70 75 80
 Asn Asp Arg Phe Phe Ala Val Arg Pro Glu Gly Ser Val Ser Thr Leu
 85 90 95
 Lys Ile Gln Arg Thr Glu Arg Gly Asp Ser Ala Val Tyr Leu Cys Ala
 100 105 110
 Ser Ser Leu Ser Gly Leu Leu Gln Glu Thr Gln Tyr Phe Gly Pro Gly
 115 120 125
 Thr Arg Leu Leu Val Leu Glu Asp Leu Arg Asn Val Thr Pro Pro Lys
 130 135 140
 Val Ser Leu Phe Glu Pro Ser Lys Ala Glu Ile Ala Asn Lys Gln Lys
 145 150 155 160
 Ala Thr Leu Val Cys Leu Ala Arg Gly Phe Phe Pro Asp His Val Glu
 165 170 175
 Leu Ser Trp Trp Val Asn Gly Lys Glu Val His Ser Gly Val Cys Thr
 180 185 190
 Asp Pro Gln Ala Tyr Lys Glu Ser Asn Tyr Ser Tyr Cys Leu Ser Ser
 195 200 205
 Arg Leu Arg Val Ser Ala Thr Phe Trp His Asn Pro Arg Asn His Phe
 210 215 220
 Arg Cys Gln Val Gln Phe His Gly Leu Ser Glu Glu Asp Lys Trp Pro
 225 230 235 240
 Glu Gly Ser Pro Lys Pro Val Thr Gln Asn Ile Ser Ala Glu Ala Trp
 245 250 255

Gly Arg Ala Asp Cys Gly Ile Thr Ser Ala Ser Tyr Gln Gln Gly Val
 260 265 270

Leu Ser Ala Thr Ile Leu Tyr Glu Ile Leu Leu Gly Lys Ala Thr Leu
 275 280 285

Tyr Ala Val Leu Val Ser Thr Leu Val Val Met Ala Met Val Lys Arg
 290 295 300

Lys Asn Ser
 305

<210> 397

<211> 6

<212> PRT

<213> 智人 (Homo sapiens)

<400> 397

Ala Thr Gly Tyr Pro Ser

1 5

<210> 398

<211> 7

<212> PRT

<213> 智人 (Homo sapiens)

<400> 398

Ala Thr Lys Ala Asp Asp Lys

1 5

<210> 399

<211> 16

<212> PRT

<213> 智人 (Homo sapiens)

<400> 399

Cys Ala Leu Ser His Thr Gly Ser Ser Asn Thr Gly Lys Leu Ile Phe

1 5 10 15

<210> 400

<211> 5

<212> PRT

<213> 智人 (Homo sapiens)

<400> 400

Ser Gly His Ala Thr

1 5

<210> 401

<211> 6

<212> PRT

<213> 智人 (Homo sapiens)

<400> 401

Phe Gln Asn Asn Gly Val

1 5

<210> 402

<211> 15

<212> PRT

<213> 智人 (Homo sapiens)

<400> 402

Cys Ala Ser Ser Thr Gly Gly Gly Arg His Gln Pro Gln His Phe

1 5 10 15

<210> 403

<211> 134

<212> PRT

<213> 智人 (Homo sapiens)

<400> 403

Met Ala Tyr Ser Pro Gly Leu Val Ser Leu Ile Leu Leu Leu Gly

1 5 10 15

Arg Thr Arg Gly Asn Ser Val Thr Gln Met Glu Gly Pro Val Thr Leu

20 25 30

Ser Glu Glu Ala Phe Leu Thr Ile Asn Cys Thr Tyr Thr Ala Thr Gly

35 40 45

Tyr Pro Ser Leu Phe Trp Tyr Val Gln Tyr Pro Gly Glu Gly Leu Gln

50 55 60

Leu Leu Leu Lys Ala Thr Lys Ala Asp Asp Lys Gly Ser Asn Lys Gly

65 70 75 80

Phe Glu Ala Thr Tyr Arg Lys Glu Thr Thr Ser Phe His Leu Glu Lys

85 90 95

Gly Ser Val Gln Val Ser Asp Ser Ala Val Tyr Phe Cys Ala Leu Ser

100 105 110

His Thr Gly Ser Ser Asn Thr Gly Lys Leu Ile Phe Gly Gln Gly Thr

115 120 125

Arg Leu Gln Val Lys Pro

130

<210> 404

<211> 134

<212> PRT

<213> 智人 (Homo sapiens)

<400> 404

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

<210> 405

<211> 271

<212> PRT

<213> 智人(Homo sapiens)

<400> 405

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

Arg	Leu	Gln	Val	Lys	Pro	Asn	Ile	Gln	Asn	Pro	Glu	Pro	Ala	Val	Tyr
130						135					140				
Gln	Leu	Lys	Asp	Pro	Arg	Ser	Gln	Asp	Ser	Thr	Leu	Cys	Leu	Phe	Thr
145					150					155					160
Asp	Phe	Asp	Ser	Gln	Ile	Asn	Val	Pro	Lys	Thr	Met	Glu	Ser	Gly	Thr
				165						170					175
Phe	Ile	Thr	Asp	Lys	Cys	Val	Leu	Asp	Met	Lys	Ala	Met	Asp	Ser	Lys
			180							185					190
Ser	Asn	Gly	Ala	Ile	Ala	Trp	Ser	Asn	Gln	Thr	Ser	Phe	Thr	Cys	Gln
		195							200						205
Asp	Ile	Phe	Lys	Glu	Thr	Asn	Ala	Thr	Tyr	Pro	Ser	Ser	Asp	Val	Pro
		210							215						220
Cys	Asp	Ala	Thr	Leu	Thr	Glu	Lys	Ser	Phe	Glu	Thr	Asp	Met	Asn	Leu
225						230						235			240
Asn	Phe	Gln	Asn	Leu	Leu	Val	Ile	Val	Leu	Arg	Ile	Leu	Leu	Leu	Lys
						245						250			255
Val	Ala	Gly	Phe	Asn	Leu	Leu	Met	Thr	Leu	Arg	Leu	Trp	Ser	Ser	
				260								265			270
<210> 406															
<211> 307															
<212> PRT															
<213> 智人 (Homo sapiens)															
<400> 406															
Met	His	Thr	Arg	Leu	Leu	Cys	Trp	Ala	Ala	Leu	Cys	Leu	Leu	Gly	Ala
1				5						10				15	
Glu	Leu	Thr	Glu	Ala	Gly	Val	Ala	Gln	Ser	Pro	Arg	Tyr	Lys	Ile	Ile
			20					25					30		
Glu	Lys	Arg	Gln	Ser	Val	Ala	Phe	Trp	Cys	Asn	Pro	Ile	Ser	Gly	His
		35						40					45		
Ala	Thr	Leu	Tyr	Trp	Tyr	Gln	Gln	Ile	Leu	Gly	Gln	Gly	Pro	Lys	Leu
		50						55				60			
Leu	Ile	Gln	Phe	Gln	Asn	Asn	Gly	Val	Val	Asp	Asp	Ser	Gln	Leu	Pro
65					70					75					80
Lys	Asp	Arg	Phe	Ser	Ala	Glu	Arg	Leu	Lys	Gly	Val	Asp	Ser	Thr	Leu
				85						90					95
Lys	Ile	Gln	Pro	Ala	Lys	Leu	Glu	Asp	Ser	Ala	Val	Tyr	Leu	Cys	Ala
			100							105				110	
Ser	Ser	Thr	Gly	Gly	Gly	Arg	His	Gln	Pro	Gln	His	Phe	Gly	Asp	Gly
			115							120					125

Thr Arg Leu Ser Ile Leu Glu Asp Leu Arg Asn Val Thr Pro Pro Lys
130 135 140
Val Ser Leu Phe Glu Pro Ser Lys Ala Glu Ile Ala Asn Lys Gln Lys
145 150 155 160
Ala Thr Leu Val Cys Leu Ala Arg Gly Phe Phe Pro Asp His Val Glu
165 170 175
Leu Ser Trp Trp Val Asn Gly Lys Glu Val His Ser Gly Val Cys Thr
180 185 190
Asp Pro Gln Ala Tyr Lys Glu Ser Asn Tyr Ser Tyr Cys Leu Ser Ser
195 200 205
Arg Leu Arg Val Ser Ala Thr Phe Trp His Asn Pro Arg Asn His Phe
210 215 220
Arg Cys Gln Val Gln Phe His Gly Leu Ser Glu Glu Asp Lys Trp Pro
225 230 235 240
Glu Gly Ser Pro Lys Pro Val Thr Gln Asn Ile Ser Ala Glu Ala Trp
245 250 255
Gly Arg Ala Asp Cys Gly Ile Thr Ser Ala Ser Tyr Gln Gln Gly Val
260 265 270
Leu Ser Ala Thr Ile Leu Tyr Glu Ile Leu Leu Gly Lys Ala Thr Leu
275 280 285
Tyr Ala Val Leu Val Ser Thr Leu Val Val Met Ala Met Val Lys Arg
290 295 300
Lys Asn Ser
305
<210> 407
<211> 6
<212> PRT
<213> 智人(Homo sapiens)
<400> 407
Ala Thr Gly Tyr Pro Ser
1 5
<210> 408
<211> 7
<212> PRT
<213> 智人(Homo sapiens)
<400> 408
Ala Thr Lys Ala Asp Asp Lys
1 5
<210> 409

<211> 16

<212> PRT

<213> 智人 (Homo sapiens)

<400> 409

Cys Ala Leu Ser Gln Thr Gly Ser Ser Lys Thr Gly Lys Leu Ile Phe

1 5 10 15

<210> 410

<211> 5

<212> PRT

<213> 智人 (Homo sapiens)

<400> 410

Ser Gly His Ala Thr

1 5

<210> 411

<211> 6

<212> PRT

<213> 智人 (Homo sapiens)

<400> 411

Phe Gln Asn Asn Gly Val

1 5

<210> 412

<211> 15

<212> PRT

<213> 智人 (Homo sapiens)

<400> 412

Cys Ala Ser Ser Thr Gly Gly Gly Arg His Gln Pro Gln His Phe

1 5 10 15

<210> 413

<211> 134

<212> PRT

<213> 智人 (Homo sapiens)

<400> 413

Met Ala Tyr Ser Pro Gly Leu Val Ser Leu Ile Leu Leu Leu Gly

1 5 10 15

Arg Thr Arg Gly Asn Ser Val Thr Gln Met Glu Gly Pro Val Thr Leu

20 25 30

Ser Glu Glu Ala Phe Leu Thr Ile Asn Cys Thr Tyr Thr Ala Thr Gly

35 40 45

Tyr Pro Ser Leu Phe Trp Tyr Val Gln Tyr Pro Gly Glu Gly Leu Gln

50	55	60
Leu Leu Leu Lys Ala Thr	Lys Ala Asp Asp Lys Gly Ser Asn Lys Gly	
65	70	75
Phe Glu Ala Thr Tyr Arg	Lys Glu Thr Thr Ser Phe His Leu Glu Lys	80
	85	90
Gly Ser Val Gln Val Ser	Asp Ser Ala Val Tyr Phe Cys Ala Leu Ser	95
	100	105
Gln Thr Gly Ser Ser Lys	Thr Gly Lys Leu Ile Phe Gly Gln Gly Thr	110
	115	120
Arg Leu Gln Val Lys Pro		125
130		
<210> 414		
<211> 134		
<212> PRT		
<213> 智人 (Homo sapiens)		
<400> 414		
Met His Thr Arg Leu Leu Cys Trp	Ala Ala Leu Cys Leu Leu Gly Ala	
1	5	10
Glu Leu Thr Glu Ala Gly Val	Ala Gln Ser Pro Arg Tyr Lys Ile Ile	15
	20	25
Glu Lys Arg Gln Ser Val	Ala Phe Trp Cys Asn Pro Ile Ser Gly His	30
	35	40
Ala Thr Leu Tyr Trp Tyr	Gln Gln Ile Leu Gly Gln Gly Pro Lys Leu	45
50	55	60
Leu Ile Gln Phe Gln Asn Asn	Gly Val Val Asp Asp Ser Gln Leu Pro	
65	70	75
Lys Asp Arg Phe Ser Ala	Glu Arg Leu Lys Gly Val Asp Ser Thr Leu	80
	85	90
Lys Ile Gln Pro Ala Lys	Leu Glu Asp Ser Ala Val Tyr Leu Cys Ala	95
	100	105
Ser Ser Thr Gly Gly Gly	Arg His Gln Pro Gln His Phe Gly Asp Gly	110
	115	120
Thr Arg Leu Ser Ile Leu		125
130		
<210> 415		
<211> 271		
<212> PRT		
<213> 智人 (Homo sapiens)		
<400> 415		

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

<210> 416
 <211> 307
 <212> PRT
 <213> 智人 (Homo sapiens)
 <400> 416

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

305

<210> 417

<211> 6

<212> PRT

<213> 智人 (Homo sapiens)

<400> 417

Ala Thr Gly Tyr Pro Ser

1 5

<210> 418

<211> 7

<212> PRT

<213> 智人 (Homo sapiens)

<400> 418

Ala Thr Lys Ala Asp Asp Lys

1 5

<210> 419

<211> 16

<212> PRT

<213> 智人 (Homo sapiens)

<400> 419

Cys Ala Leu Ser Gln Thr Gly Ser Ser Asn Thr Gly Lys Leu Ile Phe

1 5 10 15

<210> 420

<211> 5

<212> PRT

<213> 智人 (Homo sapiens)

<400> 420

Ser Gly His Ala Thr

1 5

<210> 421

<211> 6

<212> PRT

<213> 智人 (Homo sapiens)

<400> 421

Phe Gln Asn Asn Gly Val

1 5

<210> 422

<211> 15

<212> PRT

<213> 智人 (Homo sapiens)

<400> 422

Cys Ala Ser Ser Thr Gly Gly Gly Arg His Gln Pro Gln His Phe
1 5 10 15

<210> 423

<211> 134

<212> PRT

<213> 智人 (Homo sapiens)

<400> 423

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

<210> 424

<211> 134

<212> PRT

<213> 智人 (Homo sapiens)

<400> 424

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

50	55	60
Leu Ile Gln Phe Gln Asn Asn Gly Val Val Asp Asp Ser Gln Leu Pro		
65	70	75
Lys Asp Arg Phe Ser Ala Glu Arg Leu Lys Gly Val Asp Ser Thr Leu		
85	90	95
Lys Ile Gln Pro Ala Lys Leu Glu Asp Ser Ala Val Tyr Leu Cys Ala		
100	105	110
Ser Ser Thr Gly Gly Gly Arg His Gln Pro Gln His Phe Gly Asp Gly		
115	120	125
Thr Arg Leu Ser Ile Leu		
130		
<210> 425		
<211> 271		
<212> PRT		
<213> 智人(Homo sapiens)		
<400> 425		
Met Ala Tyr Ser Pro Gly Leu Val Ser Leu Ile Leu Leu Leu Gly		
1	5	10
Arg Thr Arg Gly Asn Ser Val Thr Gln Met Glu Gly Pro Val Thr Leu		
20	25	30
Ser Glu Glu Ala Phe Leu Thr Ile Asn Cys Thr Tyr Thr Ala Thr Gly		
35	40	45
Tyr Pro Ser Leu Phe Trp Tyr Val Gln Tyr Pro Gly Glu Gly Leu Gln		
50	55	60
Leu Leu Leu Lys Ala Thr Lys Ala Asp Asp Lys Gly Ser Asn Lys Gly		
65	70	75
Phe Glu Ala Thr Tyr Arg Lys Glu Thr Thr Ser Phe His Leu Glu Lys		
85	90	95
Gly Ser Val Gln Val Ser Asp Ser Ala Val Tyr Phe Cys Ala Leu Ser		
100	105	110
Gln Thr Gly Ser Ser Asn Thr Gly Lys Leu Ile Phe Gly Gln Gly Thr		
115	120	125
Arg Leu Gln Val Lys Pro Asn Ile Gln Asn Pro Glu Pro Ala Val Tyr		
130	135	140
Gln Leu Lys Asp Pro Arg Ser Gln Asp Ser Thr Leu Cys Leu Phe Thr		
145	150	155
Asp Phe Asp Ser Gln Ile Asn Val Pro Lys Thr Met Glu Ser Gly Thr		
165	170	175
Phe Ile Thr Asp Lys Cys Val Leu Asp Met Lys Ala Met Asp Ser Lys		

180	185	190
Ser Asn Gly Ala Ile Ala Trp	Ser Asn Gln Thr Ser Phe Thr Cys Gln	
195	200	205
Asp Ile Phe Lys Glu Thr Asn Ala Thr Tyr Pro Ser Ser Asp Val Pro		
210	215	220
Cys Asp Ala Thr Leu Thr Glu Lys Ser Phe Glu Thr Asp Met Asn Leu		
225	230	235
Asn Phe Gln Asn Leu Leu Val Ile Val Leu Arg Ile Leu Leu Leu Lys		
245	250	255
Val Ala Gly Phe Asn Leu Leu Met Thr Leu Arg Leu Trp Ser Ser		
260	265	270
<210> 426		
<211> 307		
<212> PRT		
<213> 智人 (Homo sapiens)		
<400> 426		
Met His Thr Arg Leu Leu Cys Trp Ala Ala Leu Cys Leu Leu Gly Ala		
1	5	10
Glu Leu Thr Glu Ala Gly Val Ala Gln Ser Pro Arg Tyr Lys Ile Ile		
20	25	30
Glu Lys Arg Gln Ser Val Ala Phe Trp Cys Asn Pro Ile Ser Gly His		
35	40	45
Ala Thr Leu Tyr Trp Tyr Gln Gln Ile Leu Gly Gln Gly Pro Lys Leu		
50	55	60
Leu Ile Gln Phe Gln Asn Asn Gly Val Val Asp Asp Ser Gln Leu Pro		
65	70	75
Lys Asp Arg Phe Ser Ala Glu Arg Leu Lys Gly Val Asp Ser Thr Leu		
85	90	95
Lys Ile Gln Pro Ala Lys Leu Glu Asp Ser Ala Val Tyr Leu Cys Ala		
100	105	110
Ser Ser Thr Gly Gly Gly Arg His Gln Pro Gln His Phe Gly Asp Gly		
115	120	125
Thr Arg Leu Ser Ile Leu Glu Asp Leu Arg Asn Val Thr Pro Pro Lys		
130	135	140
Val Ser Leu Phe Glu Pro Ser Lys Ala Glu Ile Ala Asn Lys Gln Lys		
145	150	155
Ala Thr Leu Val Cys Leu Ala Arg Gly Phe Phe Pro Asp His Val Glu		
165	170	175
Leu Ser Trp Trp Val Asn Gly Lys Glu Val His Ser Gly Val Cys Thr		

180	185	190
Asp Pro Gln Ala Tyr Lys Glu Ser Asn Tyr Ser Tyr Cys Leu Ser Ser		
195	200	205
Arg Leu Arg Val Ser Ala Thr Phe Trp His Asn Pro Arg Asn His Phe		
210	215	220
Arg Cys Gln Val Gln Phe His Gly Leu Ser Glu Glu Asp Lys Trp Pro		
225	230	235
240		240
Glu Gly Ser Pro Lys Pro Val Thr Gln Asn Ile Ser Ala Glu Ala Trp		
245	250	255
Gly Arg Ala Asp Cys Gly Ile Thr Ser Ala Ser Tyr Gln Gln Gly Val		
260	265	270
Leu Ser Ala Thr Ile Leu Tyr Glu Ile Leu Leu Gly Lys Ala Thr Leu		
275	280	285
Tyr Ala Val Leu Val Ser Thr Leu Val Val Met Ala Met Val Lys Arg		
290	295	300
Lys Asn Ser		
305		
<210> 427		
<211> 6		
<212> PRT		
<213> 智人(Homo sapiens)		
<400> 427		
Ala Thr Gly Tyr Pro Ser		
1	5	
<210> 428		
<211> 7		
<212> PRT		
<213> 智人(Homo sapiens)		
<400> 428		
Ala Thr Lys Ala Asp Asp Lys		
1	5	
<210> 429		
<211> 16		
<212> PRT		
<213> 智人(Homo sapiens)		
<400> 429		
Cys Ala Leu Ser Thr Thr Gly Ser Ser Asn Thr Gly Lys Leu Ile Phe		
1	5	10
		15
<210> 430		

<211> 5
 <212> PRT
 <213> 智人 (Homo sapiens)
 <400> 430
 Ser Gly His Ala Thr
 1 5
 <210> 431
 <211> 6
 <212> PRT
 <213> 智人 (Homo sapiens)
 <400> 431
 Phe Gln Asn Asn Gly Val
 1 5
 <210> 432
 <211> 15
 <212> PRT
 <213> 智人 (Homo sapiens)
 <400> 432
 Cys Ala Ser Ser Thr Gly Gly Gly Arg His Gln Pro Gln His Phe
 1 5 10 15
 <210> 433
 <211> 134
 <212> PRT
 <213> 智人 (Homo sapiens)
 <400> 433
 Met Ala Tyr Ser Pro Gly Leu Val Ser Leu Ile Leu Leu Leu Leu Gly
 1 5 10 15
 Arg Thr Arg Gly Asn Ser Val Thr Gln Met Glu Gly Pro Val Thr Leu
 20 25 30
 Ser Glu Glu Ala Phe Leu Thr Ile Asn Cys Thr Tyr Thr Ala Thr Gly
 35 40 45
 Tyr Pro Ser Leu Phe Trp Tyr Val Gln Tyr Pro Gly Glu Gly Leu Gln
 50 55 60
 Leu Leu Leu Lys Ala Thr Lys Ala Asp Asp Lys Gly Ser Asn Lys Gly
 65 70 75 80
 Phe Glu Ala Thr Tyr Arg Lys Glu Thr Thr Ser Phe His Leu Glu Lys
 85 90 95
 Gly Ser Val Gln Val Ser Asp Ser Ala Val Tyr Phe Cys Ala Leu Ser
 100 105 110

Thr Thr Gly Ser Ser Asn Thr Gly Lys Leu Ile Phe Gly Gln Gly Thr
 115 120 125

Thr Leu Gln Val Lys Pro
 130

<210> 434

<211> 134

<212> PRT

<213> 智人 (Homo sapiens)

<400> 434

Met His Thr Arg Leu Leu Cys Trp Ala Ala Leu Cys Leu Leu Gly Ala
 1 5 10 15

Glu Leu Thr Glu Ala Gly Val Ala Gln Ser Pro Arg Tyr Lys Ile Ile
 20 25 30

Glu Lys Arg Gln Ser Val Ala Phe Trp Cys Asn Pro Ile Ser Gly His
 35 40 45

Ala Thr Leu Tyr Trp Tyr Gln Gln Ile Leu Gly Gln Gly Pro Lys Leu
 50 55 60

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

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

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

Ser Ser Thr Gly Gly Gly Arg His Gln Pro Gln His Phe Gly Asp Gly
 115 120 125

Thr Arg Leu Ser Ile Leu
 130

<210> 435

<211> 271

<212> PRT

<213> 智人 (Homo sapiens)

<400> 435

Met Ala Tyr Ser Pro Gly Leu Val Ser Leu Ile Leu Leu Leu Gly
 1 5 10 15

Arg Thr Arg Gly Asn Ser Val Thr Gln Met Glu Gly Pro Val Thr Leu
 20 25 30

Ser Glu Glu Ala Phe Leu Thr Ile Asn Cys Thr Tyr Thr Ala Thr Gly
 35 40 45

Tyr Pro Ser Leu Phe Trp Tyr Val Gln Tyr Pro Gly Glu Gly Leu Gln

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

<210> 436

<211> 307

<212> PRT

<213> 智人 (Homo sapiens)

<400> 436

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

50	55	60
Leu Ile Gln Phe Gln Asn Asn Gly Val Val Asp Asp Ser Gln Leu Pro		
65	70	75
Lys Asp Arg Phe Ser Ala Glu Arg Leu Lys Gly Val Asp Ser Thr Leu		80
	85	90
Lys Ile Gln Pro Ala Lys Leu Glu Asp Ser Ala Val Tyr Leu Cys Ala		95
	100	105
Ser Ser Thr Gly Gly Gly Arg His Gln Pro Gln His Phe Gly Asp Gly		110
	115	120
Thr Arg Leu Ser Ile Leu Glu Asp Leu Arg Asn Val Thr Pro Pro Lys		125
	130	135
Val Ser Leu Phe Glu Pro Ser Lys Ala Glu Ile Ala Asn Lys Gln Lys		140
145	150	155
Ala Thr Leu Val Cys Leu Ala Arg Gly Phe Phe Pro Asp His Val Glu		160
	165	170
Leu Ser Trp Trp Val Asn Gly Lys Glu Val His Ser Gly Val Cys Thr		175
	180	185
Asp Pro Gln Ala Tyr Lys Glu Ser Asn Tyr Ser Tyr Cys Leu Ser Ser		190
	195	200
Arg Leu Arg Val Ser Ala Thr Phe Trp His Asn Pro Arg Asn His Phe		205
	210	215
Arg Cys Gln Val Gln Phe His Gly Leu Ser Glu Glu Asp Lys Trp Pro		220
225	230	235
Glu Gly Ser Pro Lys Pro Val Thr Gln Asn Ile Ser Ala Glu Ala Trp		240
	245	250
Gly Arg Ala Asp Cys Gly Ile Thr Ser Ala Ser Tyr Gln Gln Gly Val		255
	260	265
Leu Ser Ala Thr Ile Leu Tyr Glu Ile Leu Leu Gly Lys Ala Thr Leu		270
	275	280
Tyr Ala Val Leu Val Ser Thr Leu Val Val Met Ala Met Val Lys Arg		285
	290	295
Lys Asn Ser		300
305		
<210> 437		
<211> 6		
<212> PRT		
<213> 智人(Homo sapiens)		
<400> 437		
Asp Arg Gly Ser Gln Ser		

1 5
<210> 438
<211> 6
<212> PRT
<213> 智人 (Homo sapiens)
<400> 438
Ile Tyr Ser Asn Gly Asp
1 5
<210> 439
<211> 14
<212> PRT
<213> 智人 (Homo sapiens)
<400> 439
Cys Ala Val Thr Leu Cys Gly Gly Tyr Asn Lys Leu Ile Phe
1 5 10
<210> 440
<211> 5
<212> PRT
<213> 智人 (Homo sapiens)
<400> 440
Leu Asn His Asp Ala
1 5
<210> 441
<211> 6
<212> PRT
<213> 智人 (Homo sapiens)
<400> 441
Ser Gln Ile Val Asn Asp
1 5
<210> 442
<211> 12
<212> PRT
<213> 智人 (Homo sapiens)
<400> 442
Cys Ala Ser Ser Ser Arg Asp Tyr Glu Gln Tyr Phe
1 5 10
<210> 443
<211> 133
<212> PRT

<213> 智人 (Homo sapiens)

<400> 443

```

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

```

<210> 444

<211> 130

<212> PRT

<213> 智人 (Homo sapiens)

<400> 444

```

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

```

Ser Ser Arg Asp Tyr Glu Gln Tyr Phe Gly Pro Gly Thr Arg Leu Thr
 115 120 125
 Val Thr
 130
 <210> 445
 <211> 270
 <212> PRT
 <213> 智人 (Homo sapiens)
 <400> 445
 Met Ala Ser Leu Arg Val Leu Leu Val Ile Leu Trp Leu Gln Leu Ser
 1 5 10 15
 Trp Val Trp Ser Gln Gln Lys Glu Val Glu Gln Asn Ser Gly Pro Leu
 20 25 30
 Ser Val Pro Glu Gly Ala Ile Ala Ser Leu Asn Cys Thr Tyr Ser Asp
 35 40 45
 Arg Gly Ser Gln Ser Phe Phe Trp Tyr Arg Gln Tyr Ser Gly Lys Ser
 50 55 60
 Pro Glu Leu Ile Met Phe Ile Tyr Ser Asn Gly Asp Lys Glu Asp Gly
 65 70 75 80
 Arg Phe Thr Ala Gln Leu Asn Lys Ala Ser Gln Tyr Val Ser Leu Leu
 85 90 95
 Ile Arg Asp Ser Gln Pro Ser Asp Ser Ala Thr Tyr Leu Cys Ala Val
 100 105 110
 Thr Leu Cys Gly Gly Tyr Asn Lys Leu Ile Phe Gly Ala Gly Thr Arg
 115 120 125
 Leu Ala Val His Pro Asn Ile Gln Asn Pro Glu Pro Ala Val Tyr Gln
 130 135 140
 Leu Lys Asp Pro Arg Ser Gln Asp Ser Thr Leu Cys Leu Phe Thr Asp
 145 150 155 160
 Phe Asp Ser Gln Ile Asn Val Pro Lys Thr Met Glu Ser Gly Thr Phe
 165 170 175
 Ile Thr Asp Lys Cys Val Leu Asp Met Lys Ala Met Asp Ser Lys Ser
 180 185 190
 Asn Gly Ala Ile Ala Trp Ser Asn Gln Thr Ser Phe Thr Cys Gln Asp
 195 200 205
 Ile Phe Lys Glu Thr Asn Ala Thr Tyr Pro Ser Ser Asp Val Pro Cys
 210 215 220
 Asp Ala Thr Leu Thr Glu Lys Ser Phe Glu Thr Asp Met Asn Leu Asn
 225 230 235 240

Phe	Gln	Asn	Leu	Leu	Val	Ile	Val	Leu	Arg	Ile	Leu	Leu	Leu	Lys	Val		
				245				250				255					
Ala	Gly	Phe	Asn	Leu	Leu	Met	Thr	Leu	Arg	Leu	Trp	Ser	Ser				
				260				265				270					
<210> 446																	
<211> 303																	
<212> PRT																	
<213> 智人(Homo sapiens)																	
<400> 446																	
Met	His	Asn	Gln	Val	Leu	Cys	Cys	Val	Val	Leu	Cys	Phe	Leu	Gly	Ala		
				5				10				15					
Asn	Thr	Val	Asp	Gly	Gly	Ile	Thr	Gln	Ser	Pro	Lys	Tyr	Leu	Phe	Arg		
				20				25				30					
Lys	Glu	Gly	Gln	Asn	Val	Thr	Leu	Ser	Cys	Glu	Gln	Asn	Leu	Asn	His		
				35				40				45					
Asp	Ala	Met	Tyr	Trp	Tyr	Arg	Gln	Asp	Pro	Gly	Gln	Gly	Leu	Arg	Leu		
				50				55				60					
Ile	Tyr	Tyr	Ser	Gln	Ile	Val	Asn	Asp	Phe	Gln	Lys	Gly	Asp	Ile	Val		
				65				70				75				80	
Glu	Gly	Tyr	Ser	Val	Ser	Arg	Glu	Lys	Lys	Glu	Ser	Phe	Pro	Leu	Thr		
				85				90				95					
Val	Thr	Ser	Ala	Gln	Lys	Asn	Pro	Thr	Ala	Phe	Tyr	Leu	Cys	Ala	Ser		
				100				105				110					
Ser	Ser	Arg	Asp	Tyr	Glu	Gln	Tyr	Phe	Gly	Pro	Gly	Thr	Arg	Leu	Thr		
				115				120				125					
Val	Thr	Glu	Asp	Leu	Arg	Asn	Val	Thr	Pro	Pro	Lys	Val	Ser	Leu	Phe		
				130				135				140					
Glu	Pro	Ser	Lys	Ala	Glu	Ile	Ala	Asn	Lys	Gln	Lys	Ala	Thr	Leu	Val		
				145				150				155				160	
Cys	Leu	Ala	Arg	Gly	Phe	Phe	Pro	Asp	His	Val	Glu	Leu	Ser	Trp	Trp		
				165				170				175					
Val	Asn	Gly	Lys	Glu	Val	His	Ser	Gly	Val	Cys	Thr	Asp	Pro	Gln	Ala		
				180				185				190					
Tyr	Lys	Glu	Ser	Asn	Tyr	Ser	Tyr	Cys	Leu	Ser	Ser	Arg	Leu	Arg	Val		
				195				200				205					
Ser	Ala	Thr	Phe	Trp	His	Asn	Pro	Arg	Asn	His	Phe	Arg	Cys	Gln	Val		
				210				215				220					
Gln	Phe	His	Gly	Leu	Ser	Glu	Glu	Asp	Lys	Trp	Pro	Glu	Gly	Ser	Pro		
				225				230				235				240	

Lys Pro Val Thr Gln Asn Ile Ser Ala Glu Ala Trp Gly Arg Ala Asp
245 250 255
Cys Gly Ile Thr Ser Ala Ser Tyr Gln Gln Gly Val Leu Ser Ala Thr
260 265 270
Ile Leu Tyr Glu Ile Leu Leu Gly Lys Ala Thr Leu Tyr Ala Val Leu
275 280 285
Val Ser Thr Leu Val Val Met Ala Met Val Lys Arg Lys Asn Ser
290 295 300

<210> 447

<211> 6

<212> PRT

<213> 智人 (Homo sapiens)

<400> 447

Asp Arg Gly Ser Gln Ser

1 5

<210> 448

<211> 6

<212> PRT

<213> 智人 (Homo sapiens)

<400> 448

Ile Tyr Ser Asn Gly Asp

1 5

<210> 449

<211> 14

<212> PRT

<213> 智人 (Homo sapiens)

<400> 449

Cys Ala Val Thr Leu Ser Gly Gly Tyr Asn Lys Leu Ile Phe

1 5 10

<210> 450

<211> 5

<212> PRT

<213> 智人 (Homo sapiens)

<400> 450

Leu Asn His Asp Ala

1 5

<210> 451

<211> 6

<212> PRT

<213> 智人 (Homo sapiens)

<400> 451

Ser Gln Ile Val Asn Asp

1 5

<210> 452

<211> 12

<212> PRT

<213> 智人 (Homo sapiens)

<400> 452

Cys Ala Ser Ser Ser Arg Asp Tyr Glu Gln Tyr Phe

1 5 10

<210> 453

<211> 133

<212> PRT

<213> 智人 (Homo sapiens)

<400> 453

Met Ala Ser Leu Arg Val Leu Leu Val Ile Leu Trp Leu Gln Leu Ser

1 5 10 15

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

20 25 30

Ser Val Pro Glu Gly Ala Ile Ala Ser Leu Asn Cys Thr Tyr Ser Asp

35 40 45

Arg Gly Ser Gln Ser Phe Phe Trp Tyr Arg Gln Tyr Ser Gly Lys Ser

50 55 60

Pro Glu Leu Ile Met Phe Ile Tyr Ser Asn Gly Asp Lys Glu Asp Gly

65 70 75 80

Arg Phe Thr Ala Gln Leu Asn Lys Ala Ser Gln Tyr Val Ser Leu Leu

85 90 95

Ile Arg Asp Ser Gln Pro Ser Asp Ser Ala Thr Tyr Leu Cys Ala Val

100 105 110

Thr Leu Ser Gly Gly Tyr Asn Lys Leu Ile Phe Gly Ala Gly Thr Arg

115 120 125

Leu Ala Val His Pro

130

<210> 454

<211> 130

<212> PRT

<213> 智人 (Homo sapiens)

<400> 454

Met	His	Asn	Gln	Val	Leu	Cys	Cys	Val	Val	Leu	Cys	Phe	Leu	Gly	Ala
1				5						10				15	
Asn	Thr	Val	Asp	Gly	Gly	Ile	Thr	Gln	Ser	Pro	Lys	Tyr	Leu	Phe	Arg
			20					25					30		
Lys	Glu	Gly	Gln	Asn	Val	Thr	Leu	Ser	Cys	Glu	Gln	Asn	Leu	Asn	His
			35				40					45			
Asp	Ala	Met	Tyr	Trp	Tyr	Arg	Gln	Asp	Pro	Gly	Gln	Gly	Leu	Arg	Leu
		50				55				60					
Ile	Tyr	Tyr	Ser	Gln	Ile	Val	Asn	Asp	Phe	Gln	Lys	Gly	Asp	Ile	Val
65					70					75				80	
Glu	Gly	Tyr	Ser	Val	Ser	Arg	Glu	Lys	Lys	Glu	Ser	Phe	Pro	Leu	Thr
				85				90					95		
Val	Thr	Ser	Ala	Gln	Lys	Asn	Pro	Thr	Ala	Phe	Tyr	Leu	Cys	Ala	Ser
			100					105				110			
Ser	Ser	Arg	Asp	Tyr	Glu	Gln	Tyr	Phe	Gly	Pro	Gly	Thr	Arg	Leu	Thr
		115				120						125			
Val	Thr														
	130														
<210>	455														
<211>	270														
<212>	PRT														
<213>	智人 (Homo sapiens)														
<400>	455														
Met	Ala	Ser	Leu	Arg	Val	Leu	Leu	Val	Ile	Leu	Trp	Leu	Gln	Leu	Ser
1				5					10					15	
Trp	Val	Trp	Ser	Gln	Gln	Lys	Glu	Val	Glu	Gln	Asn	Ser	Gly	Pro	Leu
			20					25					30		
Ser	Val	Pro	Glu	Gly	Ala	Ile	Ala	Ser	Leu	Asn	Cys	Thr	Tyr	Ser	Asp
			35				40					45			
Arg	Gly	Ser	Gln	Ser	Phe	Phe	Trp	Tyr	Arg	Gln	Tyr	Ser	Gly	Lys	Ser
		50				55				60					
Pro	Glu	Leu	Ile	Met	Phe	Ile	Tyr	Ser	Asn	Gly	Asp	Lys	Glu	Asp	Gly
65					70					75				80	
Arg	Phe	Thr	Ala	Gln	Leu	Asn	Lys	Ala	Ser	Gln	Tyr	Val	Ser	Leu	Leu
				85				90					95		
Ile	Arg	Asp	Ser	Gln	Pro	Ser	Asp	Ser	Ala	Thr	Tyr	Leu	Cys	Ala	Val
			100					105				110			
Thr	Leu	Ser	Gly	Gly	Tyr	Asn	Lys	Leu	Ile	Phe	Gly	Ala	Gly	Thr	Arg
		115				120						125			

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

<210> 456
 <211> 303
 <212> PRT
 <213> 智人 (Homo sapiens)
 <400> 456

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

Val Thr Glu Asp Leu Arg Asn Val Thr Pro Pro Lys Val Ser Leu Phe		
130	135	140
Glu Pro Ser Lys Ala Glu Ile Ala Asn Lys Gln Lys Ala Thr Leu Val		
145	150	155
Cys Leu Ala Arg Gly Phe Phe Pro Asp His Val Glu Leu Ser Trp Trp		
	165	170
Val Asn Gly Lys Glu Val His Ser Gly Val Cys Thr Asp Pro Gln Ala		
	180	185
Tyr Lys Glu Ser Asn Tyr Ser Tyr Cys Leu Ser Ser Arg Leu Arg Val		
	195	200
Ser Ala Thr Phe Trp His Asn Pro Arg Asn His Phe Arg Cys Gln Val		
	210	215
Gln Phe His Gly Leu Ser Glu Glu Asp Lys Trp Pro Glu Gly Ser Pro		
225	230	235
Lys Pro Val Thr Gln Asn Ile Ser Ala Glu Ala Trp Gly Arg Ala Asp		
	245	250
Cys Gly Ile Thr Ser Ala Ser Tyr Gln Gln Gly Val Leu Ser Ala Thr		
	260	265
Ile Leu Tyr Glu Ile Leu Leu Gly Lys Ala Thr Leu Tyr Ala Val Leu		
	275	280
Val Ser Thr Leu Val Val Met Ala Met Val Lys Arg Lys Asn Ser		
	290	300

<210> 457

<211> 6

<212> PRT

<213> 智人(Homo sapiens)

<400> 457

Asp Arg Gly Ser Gln Ser

1 5

<210> 458

<211> 6

<212> PRT

<213> 智人(Homo sapiens)

<400> 458

Ile Tyr Ser Asn Gly Asp

1 5

<210> 459

<211> 12

<212> PRT

<213> 智人 (Homo sapiens)

<400> 459

Cys Ala Val Asn Asp Ala Gly Asn Met Leu Thr Phe

1 5 10

<210> 460

<211> 6

<212> PRT

<213> 智人 (Homo sapiens)

<400> 460

Asp Phe Gln Ala Thr Thr

1 5

<210> 461

<211> 7

<212> PRT

<213> 智人 (Homo sapiens)

<400> 461

Ser Asn Glu Gly Ser Lys Ala

1 5

<210> 462

<211> 13

<212> PRT

<213> 智人 (Homo sapiens)

<400> 462

Cys Ser Ala Ala Gly Gln Ala Asn Thr Glu Ala Phe Phe

1 5 10

<210> 463

<211> 131

<212> PRT

<213> 智人 (Homo sapiens)

<400> 463

Met His Ser Leu Arg Val Leu Leu Val Ile Leu Trp Leu Gln Leu Ser

1 5 10 15

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

20 25 30

Ser Val Pro Glu Gly Ala Ile Ala Ser Leu Asn Cys Thr Tyr Ser Asp

35 40 45

Arg Gly Ser Gln Ser Phe Phe Trp Tyr Arg Gln Tyr Ser Gly Lys Ser

50 55 60

Pro Glu Leu Ile Met Phe Ile Tyr Ser Asn Gly Asp Lys Glu Asp Gly

65	70	75	80
Arg Phe Thr Ala Gln Leu Asn Lys Ala Ser Gln Tyr Val Ser Leu Leu			
	85	90	95
Ile Arg Asp Ser Gln Pro Ser Asp Ser Ala Thr Tyr Leu Cys Ala Val			
	100	105	110
Asn Asp Ala Gly Asn Met Leu Thr Phe Gly Gly Gly Thr Arg Leu Met			
	115	120	125
Val Lys Pro			
130			

<210> 464

<211> 140

<212> PRT

<213> 智人(Homo sapiens)

<400> 464

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

<210> 465

<211> 268

<212> PRT

<213> 智人(Homo sapiens)

<400> 465

Met His Ser Leu Arg Val Leu Leu Val Ile Leu Trp Leu Gln Leu Ser			
1	5	10	15

267

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

<210> 467

<211> 6
<212> PRT
<213> 智人 (Homo sapiens)
<400> 467
Asp Ser Ala Ser Asn Tyr
1 5
<210> 468
<211> 7
<212> PRT
<213> 智人 (Homo sapiens)
<400> 468
Ile Arg Ser Asn Val Gly Glu
1 5
<210> 469
<211> 18
<212> PRT
<213> 智人 (Homo sapiens)
<400> 469
Cys Ala Ala Ser Lys Ser Ala Ile Met Val Val Leu Gln Thr Ser Ser
1 5 10 15
Ser Leu
<210> 470
<211> 5
<212> PRT
<213> 智人 (Homo sapiens)
<400> 470
Met Asn His Glu Tyr
1 5
<210> 471
<211> 6
<212> PRT
<213> 智人 (Homo sapiens)
<400> 471
Ser Met Asn Val Glu Val
1 5
<210> 472
<211> 14
<212> PRT
<213> 智人 (Homo sapiens)

<400> 472

Cys Ala Ser Ser Ile Gln Gln Gly Ala Asp Thr Gln Tyr Phe
 1 5 10

<210> 473

<211> 137

<212> PRT

<213> 智人(Homo sapiens)

<400> 473

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

<210> 474

<211> 132

<212> PRT

<213> 智人(Homo sapiens)

<400> 474

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

Ile Tyr Tyr Ser Met Asn Val Glu Val Thr Asp Lys Gly Asp Val Pro			
65	70	75	80
Glu Gly Tyr Lys Val Ser Arg Lys Glu Lys Arg Asn Phe Pro Leu Ile			
	85	90	95
Leu Glu Ser Pro Ser Pro Asn Gln Thr Ser Leu Tyr Phe Cys Ala Ser			
	100	105	110
Ser Ile Gln Gln Gly Ala Asp Thr Gln Tyr Phe Gly Pro Gly Thr Arg			
	115	120	125
Leu Thr Val Leu			
130			
<210> 475			
<211> 274			
<212> PRT			
<213> 智人(Homo sapiens)			
<400> 475			
Met Ala Ser Ile Arg Ala Val Phe Ile Phe Leu Trp Leu Gln Leu Asp			
1	5	10	15
Leu Val Asn Gly Glu Asn Val Glu Gln His Pro Ser Thr Leu Ser Val			
	20	25	30
Gln Glu Gly Asp Ser Ala Val Ile Lys Cys Thr Tyr Ser Asp Ser Ala			
	35	40	45
Ser Asn Tyr Phe Pro Trp Tyr Lys Gln Glu Leu Gly Lys Gly Pro Gln			
	50	55	60
Leu Ile Ile Asp Ile Arg Ser Asn Val Gly Glu Lys Lys Asp Gln Arg			
65	70	75	80
Ile Ala Val Thr Leu Asn Lys Thr Ala Lys His Phe Ser Leu His Ile			
	85	90	95
Thr Glu Thr Gln Pro Glu Asp Ser Ala Val Tyr Phe Cys Ala Ala Ser			
	100	105	110
Lys Ser Ala Ile Met Val Val Leu Gln Thr Ser Ser Ser Leu Glu Leu			
	115	120	125
Ala Leu Cys Leu Leu Ser Ser Gln Val Asn Ile Gln Asn Pro Glu Pro			
	130	135	140
Ala Val Tyr Gln Leu Lys Asp Pro Arg Ser Gln Asp Ser Thr Leu Cys			
145	150	155	160
Leu Phe Thr Asp Phe Asp Ser Gln Ile Asn Val Pro Lys Thr Met Glu			
	165	170	175
Ser Gly Thr Phe Ile Thr Asp Lys Cys Val Leu Asp Met Lys Ala Met			
	180	185	190

Asp Ser Lys Ser Asn Gly Ala Ile Ala Trp Ser Asn Gln Thr Ser Phe		
195	200	205
Thr Cys Gln Asp Ile Phe Lys Glu Thr Asn Ala Thr Tyr Pro Ser Ser		
210	215	220
Asp Val Pro Cys Asp Ala Thr Leu Thr Glu Lys Ser Phe Glu Thr Asp		
225	230	235
Met Asn Leu Asn Phe Gln Asn Leu Leu Val Ile Val Leu Arg Ile Leu		
	245	250
		255
Leu Leu Lys Val Ala Gly Phe Asn Leu Leu Met Thr Leu Arg Leu Trp		
	260	265
		270
Ser Ser		
<210> 476		
<211> 305		
<212> PRT		
<213> 智人(Homo sapiens)		
<400> 476		
Met His Pro Gln Leu Leu Gly Tyr Val Val Leu Cys Leu Leu Gly Ala		
1	5	10
Gly Pro Leu Glu Ala Gln Val Thr Gln Asn Pro Arg Tyr Leu Ile Thr		
	20	25
		30
Val Thr Gly Lys Lys Leu Thr Val Thr Cys Ser Gln Asn Met Asn His		
	35	40
		45
Glu Tyr Met Ser Trp Tyr Arg Gln Asp Pro Gly Leu Gly Leu Arg Gln		
	50	55
		60
Ile Tyr Tyr Ser Met Asn Val Glu Val Thr Asp Lys Gly Asp Val Pro		
65	70	75
		80
Glu Gly Tyr Lys Val Ser Arg Lys Glu Lys Arg Asn Phe Pro Leu Ile		
	85	90
		95
Leu Glu Ser Pro Ser Pro Asn Gln Thr Ser Leu Tyr Phe Cys Ala Ser		
	100	105
		110
Ser Ile Gln Gln Gly Ala Asp Thr Gln Tyr Phe Gly Pro Gly Thr Arg		
	115	120
		125
Leu Thr Val Leu Glu Asp Leu Arg Asn Val Thr Pro Pro Lys Val Ser		
	130	135
		140
Leu Phe Glu Pro Ser Lys Ala Glu Ile Ala Asn Lys Gln Lys Ala Thr		
145	150	155
		160
Leu Val Cys Leu Ala Arg Gly Phe Phe Pro Asp His Val Glu Leu Ser		
	165	170
		175
Trp Trp Val Asn Gly Lys Glu Val His Ser Gly Val Cys Thr Asp Pro		

180	185	190
Gln Ala Tyr Lys Glu Ser Asn Tyr Ser Tyr Cys Leu Ser Ser Arg Leu		
195	200	205
Arg Val Ser Ala Thr Phe Trp His Asn Pro Arg Asn His Phe Arg Cys		
210	215	220
Gln Val Gln Phe His Gly Leu Ser Glu Glu Asp Lys Trp Pro Glu Gly		
225	230	235
Ser Pro Lys Pro Val Thr Gln Asn Ile Ser Ala Glu Ala Trp Gly Arg		
245	250	255
Ala Asp Cys Gly Ile Thr Ser Ala Ser Tyr Gln Gln Gly Val Leu Ser		
260	265	270
Ala Thr Ile Leu Tyr Glu Ile Leu Leu Gly Lys Ala Thr Leu Tyr Ala		
275	280	285
Val Leu Val Ser Thr Leu Val Val Met Ala Met Val Lys Arg Lys Asn		
290	295	300
Ser		
305		
<210> 477		
<211> 6		
<212> PRT		
<213> 智人(Homo sapiens)		
<400> 477		
Asp Arg Gly Ser Gln Ser		
1	5	
<210> 478		
<211> 6		
<212> PRT		
<213> 智人(Homo sapiens)		
<400> 478		
Ile Tyr Ser Asn Gly Asp		
1	5	
<210> 479		
<211> 14		
<212> PRT		
<213> 智人(Homo sapiens)		
<400> 479		
Cys Ala Trp Asn Ser Gly Gly Ser Asn Tyr Lys Leu Thr Phe		
1	5	10
<210> 480		

<211> 5
 <212> PRT
 <213> 智人 (Homo sapiens)
 <400> 480
 Met Asn His Glu Tyr
 1 5
 <210> 481
 <211> 6
 <212> PRT
 <213> 智人 (Homo sapiens)
 <400> 481
 Ser Val Gly Glu Gly Thr
 1 5
 <210> 482
 <211> 15
 <212> PRT
 <213> 智人 (Homo sapiens)
 <400> 482
 Cys Ala Ser Ser Tyr Ser Gln Ala Trp Gly Gln Pro Gln His Phe
 1 5 10 15
 <210> 483
 <211> 133
 <212> PRT
 <213> 智人 (Homo sapiens)
 <400> 483
 Met Ala Ser Leu Arg Val Leu Leu Val Ile Leu Trp Leu Gln Leu Ser
 1 5 10 15
 Trp Val Trp Ser Gln Gln Lys Glu Val Glu Gln Asn Ser Gly Pro Leu
 20 25 30
 Ser Val Pro Glu Gly Ala Ile Ala Ser Leu Asn Cys Thr Tyr Ser Asp
 35 40 45
 Arg Gly Ser Gln Ser Phe Phe Trp Tyr Arg Gln Tyr Ser Gly Lys Ser
 50 55 60
 Pro Glu Leu Ile Met Phe Ile Tyr Ser Asn Gly Asp Lys Glu Asp Gly
 65 70 75 80
 Arg Phe Thr Ala Gln Leu Asn Lys Ala Ser Gln Tyr Val Ser Leu Leu
 85 90 95
 Ile Arg Asp Ser Gln Pro Ser Asp Ser Ala Thr Tyr Leu Cys Ala Trp
 100 105 110

Asn Ser Gly Gly Ser Asn Tyr Lys Leu Thr Phe Gly Lys Gly Thr Leu
 115 120 125

Leu Thr Val Asn Pro
 130

<210> 484

<211> 133

<212> PRT

<213> 智人 (Homo sapiens)

<400> 484

Met His Leu Gly Leu Leu Cys Cys Gly Ala Phe Ser Leu Leu Trp Ala
 1 5 10 15

Gly Pro Val Asn Ala Gly Val Thr Gln Thr Pro Lys Phe Arg Val Leu
 20 25 30

Lys Thr Gly Gln Ser Met Thr Leu Leu Cys Ala Gln Asp Met Asn His
 35 40 45

Glu Tyr Met Tyr Trp Tyr Arg Gln Asp Pro Gly Met Gly Leu Arg Leu
 50 55 60

Ile His Tyr Ser Val Gly Glu Gly Thr Thr Ala Lys Gly Glu Val Pro
 65 70 75 80

Asp Gly Tyr Asn Val Ser Arg Leu Lys Lys Gln Asn Phe Leu Leu Gly
 85 90 95

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

Ser Tyr Ser Gln Ala Trp Gly Gln Pro Gln His Phe Gly Asp Gly Thr
 115 120 125

Arg Leu Ser Ile Leu
 130

<210> 485

<211> 270

<212> PRT

<213> 智人 (Homo sapiens)

<400> 485

Met Ala Ser Leu Arg Val Leu Leu Val Ile Leu Trp Leu Gln Leu Ser
 1 5 10 15

Trp Val Trp Ser Gln Gln Lys Glu Val Glu Gln Asn Ser Gly Pro Leu
 20 25 30

Ser Val Pro Glu Gly Ala Ile Ala Ser Leu Asn Cys Thr Tyr Ser Asp
 35 40 45

Arg Gly Ser Gln Ser Phe Phe Trp Tyr Arg Gln Tyr Ser Gly Lys Ser

50	55	60
Pro Glu Leu Ile Met Phe	Ile Tyr Ser Asn Gly	Asp Lys Glu Asp Gly
65	70	75
Arg Phe Thr Ala Gln Leu	Asn Lys Ala Ser Gln	Tyr Val Ser Leu Leu
85	90	95
Ile Arg Asp Ser Gln Pro	Ser Asp Ser Ala Thr	Tyr Leu Cys Ala Trp
100	105	110
Asn Ser Gly Gly Ser Asn	Tyr Lys Leu Thr Phe	Gly Lys Gly Thr Leu
115	120	125
Leu Thr Val Asn Pro Asn	Ile Gln Asn Pro Glu	Pro Ala Val Tyr Gln
130	135	140
Leu Lys Asp Pro Arg Ser	Gln Asp Ser Thr Leu	Cys Leu Phe Thr Asp
145	150	155
Phe Asp Ser Gln Ile Asn	Val Pro Lys Thr Met	Glu Ser Gly Thr Phe
165	170	175
Ile Thr Asp Lys Cys Val	Leu Asp Met Lys Ala	Met Asp Ser Lys Ser
180	185	190
Asn Gly Ala Ile Ala Trp	Ser Asn Gln Thr Ser	Phe Thr Cys Gln Asp
195	200	205
Ile Phe Lys Glu Thr Asn	Ala Thr Tyr Pro Ser	Ser Asp Val Pro Cys
210	215	220
Asp Ala Thr Leu Thr Glu	Lys Ser Phe Glu Thr	Asp Met Asn Leu Asn
225	230	235
Phe Gln Asn Leu Leu Val	Ile Val Leu Arg Ile	Leu Leu Leu Lys Val
245	250	255
Ala Gly Phe Asn Leu Leu	Met Thr Leu Arg Leu	Trp Ser Ser
260	265	270
<210> 486		
<211> 306		
<212> PRT		
<213> 智人 (Homo sapiens)		
<400> 486		
Met His Leu Gly Leu Leu	Cys Cys Gly Ala Phe	Ser Leu Leu Trp Ala
1	5	10
Gly Pro Val Asn Ala Gly	Val Thr Gln Thr Pro	Lys Phe Arg Val Leu
20	25	30
Lys Thr Gly Gln Ser Met	Thr Leu Leu Cys Ala	Gln Asp Met Asn His
35	40	45
Glu Tyr Met Tyr Trp Tyr	Arg Gln Asp Pro Gly	Met Gly Leu Arg Leu

50	55	60
Ile His Tyr Ser Val Gly Glu Gly Thr Thr Ala Lys Gly Glu Val Pro		
65	70	75
Asp Gly Tyr Asn Val Ser Arg Leu Lys Lys Gln Asn Phe Leu Leu Gly		80
	85	90
Leu Glu Ser Ala Ala Pro Ser Gln Thr Ser Val Tyr Phe Cys Ala Ser		95
	100	105
Ser Tyr Ser Gln Ala Trp Gly Gln Pro Gln His Phe Gly Asp Gly Thr		110
	115	120
Arg Leu Ser Ile Leu Glu Asp Leu Arg Asn Val Thr Pro Pro Lys Val		125
	130	135
Ser Leu Phe Glu Pro Ser Lys Ala Glu Ile Ala Asn Lys Gln Lys Ala		140
145	150	155
Thr Leu Val Cys Leu Ala Arg Gly Phe Phe Pro Asp His Val Glu Leu		160
	165	170
Ser Trp Trp Val Asn Gly Lys Glu Val His Ser Gly Val Cys Thr Asp		175
	180	185
Pro Gln Ala Tyr Lys Glu Ser Asn Tyr Ser Tyr Cys Leu Ser Ser Arg		190
	195	200
Leu Arg Val Ser Ala Thr Phe Trp His Asn Pro Arg Asn His Phe Arg		205
	210	215
Cys Gln Val Gln Phe His Gly Leu Ser Glu Glu Asp Lys Trp Pro Glu		220
225	230	235
Gly Ser Pro Lys Pro Val Thr Gln Asn Ile Ser Ala Glu Ala Trp Gly		240
	245	250
Arg Ala Asp Cys Gly Ile Thr Ser Ala Ser Tyr Gln Gln Gly Val Leu		255
	260	265
Ser Ala Thr Ile Leu Tyr Glu Ile Leu Leu Gly Lys Ala Thr Leu Tyr		270
	275	280
Ala Val Leu Val Ser Thr Leu Val Val Met Ala Met Val Lys Arg Lys		285
	290	295
Asn Ser		300
305		
<210> 487		
<211> 6		
<212> PRT		
<213> 智人(Homo sapiens)		
<400> 487		
Ser Ser Asn Phe Tyr Ala		

1 5
<210> 488
<211> 7
<212> PRT
<213> 智人 (Homo sapiens)
<400> 488
Met Thr Leu Asn Gly Asp Glu
1 5
<210> 489
<211> 13
<212> PRT
<213> 智人 (Homo sapiens)
<400> 489
Cys Ala Leu Ile Thr Gly Gly Gly Asn Lys Leu Thr Phe
1 5 10
<210> 490
<211> 5
<212> PRT
<213> 智人 (Homo sapiens)
<400> 490
Met Asn His Glu Tyr
1 5
<210> 491
<211> 6
<212> PRT
<213> 智人 (Homo sapiens)
<400> 491
Ser Val Gly Glu Gly Thr
1 5
<210> 492
<211> 14
<212> PRT
<213> 智人 (Homo sapiens)
<400> 492
Cys Ala Ser Arg Leu Gln Gly Trp Asn Ser Pro Leu His Phe
1 5 10
<210> 493
<211> 134
<212> PRT

<213> 智人 (Homo sapiens)

<400> 493

```

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

```

<210> 494

<211> 132

<212> PRT

<213> 智人 (Homo sapiens)

<400> 494

```

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

```

Arg Leu Gln Gly Trp Asn Ser Pro Leu His Phe Gly Asn Gly Thr Arg
 115 120 125
 Leu Thr Val Thr
 130
 <210> 495
 <211> 271
 <212> PRT
 <213> 智人(Homo sapiens)
 <400> 495
 Met Ala Lys Asn Pro Leu Ala Ala Pro Leu Leu Ile Leu Trp Phe His
 1 5 10 15
 Leu Asp Cys Val Ser Ser Ile Leu Asn Val Glu Gln Ser Pro Gln Ser
 20 25 30
 Leu His Val Gln Glu Gly Asp Ser Thr Asn Phe Thr Cys Ser Phe Pro
 35 40 45
 Ser Ser Asn Phe Tyr Ala Leu His Trp Tyr Arg Trp Glu Thr Ala Lys
 50 55 60
 Ser Pro Glu Ala Leu Phe Val Met Thr Leu Asn Gly Asp Glu Lys Lys
 65 70 75 80
 Lys Gly Arg Ile Ser Ala Thr Leu Asn Thr Lys Glu Gly Tyr Ser Tyr
 85 90 95
 Leu Tyr Ile Lys Gly Ser Gln Pro Glu Asp Ser Ala Thr Tyr Leu Cys
 100 105 110
 Ala Leu Ile Thr Gly Gly Gly Asn Lys Leu Thr Phe Gly Thr Gly Thr
 115 120 125
 Gln Leu Lys Val Glu Leu Asn Ile Gln Asn Pro Glu Pro Ala Val Tyr
 130 135 140
 Gln Leu Lys Asp Pro Arg Ser Gln Asp Ser Thr Leu Cys Leu Phe Thr
 145 150 155 160
 Asp Phe Asp Ser Gln Ile Asn Val Pro Lys Thr Met Glu Ser Gly Thr
 165 170 175
 Phe Ile Thr Asp Lys Cys Val Leu Asp Met Lys Ala Met Asp Ser Lys
 180 185 190
 Ser Asn Gly Ala Ile Ala Trp Ser Asn Gln Thr Ser Phe Thr Cys Gln
 195 200 205
 Asp Ile Phe Lys Glu Thr Asn Ala Thr Tyr Pro Ser Ser Asp Val Pro
 210 215 220
 Cys Asp Ala Thr Leu Thr Glu Lys Ser Phe Glu Thr Asp Met Asn Leu
 225 230 235 240

Asn	Phe	Gln	Asn	Leu	Leu	Val	Ile	Val	Leu	Arg	Ile	Leu	Leu	Leu	Lys
				245				250				255			
Val	Ala	Gly	Phe	Asn	Leu	Leu	Met	Thr	Leu	Arg	Leu	Trp	Ser	Ser	
				260				265				270			
<210> 496															
<211> 305															
<212> PRT															
<213> 智人(Homo sapiens)															
<400> 496															
Met	His	Leu	Gly	Leu	Leu	Cys	Cys	Gly	Ala	Phe	Ser	Leu	Leu	Trp	Ala
1				5				10				15			
Gly	Pro	Val	Asn	Ala	Gly	Val	Thr	Gln	Thr	Pro	Lys	Phe	Arg	Val	Leu
				20				25				30			
Lys	Thr	Gly	Gln	Ser	Met	Thr	Leu	Leu	Cys	Ala	Gln	Asp	Met	Asn	His
				35				40				45			
Glu	Tyr	Met	Tyr	Trp	Tyr	Arg	Gln	Asp	Pro	Gly	Met	Gly	Leu	Arg	Leu
50				55				60							
Ile	His	Tyr	Ser	Val	Gly	Glu	Gly	Thr	Thr	Ala	Lys	Gly	Glu	Val	Pro
65				70				75				80			
Asp	Gly	Tyr	Asn	Val	Ser	Arg	Leu	Lys	Lys	Gln	Asn	Phe	Leu	Leu	Gly
				85				90				95			
Leu	Glu	Ser	Ala	Ala	Pro	Ser	Gln	Thr	Ser	Val	Tyr	Phe	Cys	Ala	Ser
				100				105				110			
Arg	Leu	Gln	Gly	Trp	Asn	Ser	Pro	Leu	His	Phe	Gly	Asn	Gly	Thr	Arg
115				120				125							
Leu	Thr	Val	Thr	Glu	Asp	Leu	Arg	Asn	Val	Thr	Pro	Pro	Lys	Val	Ser
130				135				140							
Leu	Phe	Glu	Pro	Ser	Lys	Ala	Glu	Ile	Ala	Asn	Lys	Gln	Lys	Ala	Thr
145				150				155				160			
Leu	Val	Cys	Leu	Ala	Arg	Gly	Phe	Phe	Pro	Asp	His	Val	Glu	Leu	Ser
				165				170				175			
Trp	Trp	Val	Asn	Gly	Lys	Glu	Val	His	Ser	Gly	Val	Cys	Thr	Asp	Pro
				180				185				190			
Gln	Ala	Tyr	Lys	Glu	Ser	Asn	Tyr	Ser	Tyr	Cys	Leu	Ser	Ser	Arg	Leu
195				200				205							
Arg	Val	Ser	Ala	Thr	Phe	Trp	His	Asn	Pro	Arg	Asn	His	Phe	Arg	Cys
210				215				220							
Gln	Val	Gln	Phe	His	Gly	Leu	Ser	Glu	Glu	Asp	Lys	Trp	Pro	Glu	Gly
225				230				235				240			

Ser Pro Lys Pro Val Thr Gln Asn Ile Ser Ala Glu Ala Trp Gly Arg
245 250 255
Ala Asp Cys Gly Ile Thr Ser Ala Ser Tyr Gln Gln Gly Val Leu Ser
260 265 270
Ala Thr Ile Leu Tyr Glu Ile Leu Leu Gly Lys Ala Thr Leu Tyr Ala
275 280 285
Val Leu Val Ser Thr Leu Val Val Met Ala Met Val Lys Arg Lys Asn
290 295 300

Ser

305

<210> 497

<211> 15

<212> PRT

<213> 智人 (Homo sapiens)

<400> 497

His Tyr Asn Tyr Met Cys Asn Ser Ser Cys Met Gly Ser Met Asn
1 5 10 15

<210> 498

<211> 15

<212> PRT

<213> 智人 (Homo sapiens)

<400> 498

Tyr Asn Tyr Met Cys Asn Ser Ser Cys Met Gly Ser Met Asn Arg
1 5 10 15

<210> 499

<211> 15

<212> PRT

<213> 智人 (Homo sapiens)

<400> 499

Asn Tyr Met Cys Asn Ser Ser Cys Met Gly Ser Met Asn Arg Arg
1 5 10 15

<210> 500

<211> 15

<212> PRT

<213> 智人 (Homo sapiens)

<400> 500

Tyr Met Cys Asn Ser Ser Cys Met Gly Ser Met Asn Arg Arg Pro
1 5 10 15

<210> 501

<211> 15
<212> PRT
<213> 智人(Homo sapiens)
<400> 501
Met Cys Asn Ser Ser Cys Met Gly Ser Met Asn Arg Arg Pro Ile
1 5 10 15
<210> 502
<211> 15
<212> PRT
<213> 智人(Homo sapiens)
<400> 502
Cys Asn Ser Ser Cys Met Gly Ser Met Asn Arg Arg Pro Ile Leu
1 5 10 15
<210> 503
<211> 15
<212> PRT
<213> 智人(Homo sapiens)
<400> 503
Asn Ser Ser Cys Met Gly Ser Met Asn Arg Arg Pro Ile Leu Thr
1 5 10 15
<210> 504
<211> 15
<212> PRT
<213> 智人(Homo sapiens)
<400> 504
Ser Ser Cys Met Gly Ser Met Asn Arg Arg Pro Ile Leu Thr Ile
1 5 10 15
<210> 505
<211> 15
<212> PRT
<213> 智人(Homo sapiens)
<400> 505
Ser Cys Met Gly Ser Met Asn Arg Arg Pro Ile Leu Thr Ile Ile
1 5 10 15
<210> 506
<211> 15
<212> PRT
<213> 智人(Homo sapiens)
<400> 506

Cys Met Gly Ser Met Asn Arg Arg Pro Ile Leu Thr Ile Ile Thr
1 5 10 15
<210> 507
<211> 15
<212> PRT
<213> 智人 (Homo sapiens)
<400> 507
Met Gly Ser Met Asn Arg Arg Pro Ile Leu Thr Ile Ile Thr Leu
1 5 10 15
<210> 508
<211> 15
<212> PRT
<213> 智人 (Homo sapiens)
<400> 508
Asp Arg Asn Thr Phe Arg His Ser Val Val Val Pro Cys Glu Pro
1 5 10 15
<210> 509
<211> 15
<212> PRT
<213> 智人 (Homo sapiens)
<400> 509
Arg Asn Thr Phe Arg His Ser Val Val Val Pro Cys Glu Pro Pro
1 5 10 15
<210> 510
<211> 15
<212> PRT
<213> 智人 (Homo sapiens)
<400> 510
Asn Thr Phe Arg His Ser Val Val Val Pro Cys Glu Pro Pro Glu
1 5 10 15
<210> 511
<211> 15
<212> PRT
<213> 智人 (Homo sapiens)
<400> 511
Thr Phe Arg His Ser Val Val Val Pro Cys Glu Pro Pro Glu Val
1 5 10 15
<210> 512
<211> 15

<212> PRT

<213> 智人 (Homo sapiens)

<400> 512

Phe	Arg	His	Ser	Val	Val	Val	Pro	Cys	Glu	Pro	Pro	Glu	Val	Gly
1				5					10					15

<210> 513

<211> 15

<212> PRT

<213> 智人 (Homo sapiens)

<400> 513

Arg	His	Ser	Val	Val	Val	Pro	Cys	Glu	Pro	Pro	Glu	Val	Gly	Ser
1				5					10					15

<210> 514

<211> 15

<212> PRT

<213> 智人 (Homo sapiens)

<400> 514

His	Ser	Val	Val	Val	Pro	Cys	Glu	Pro	Pro	Glu	Val	Gly	Ser	Asp
1				5					10					15

<210> 515

<211> 15

<212> PRT

<213> 智人 (Homo sapiens)

<400> 515

Ser	Val	Val	Val	Pro	Cys	Glu	Pro	Pro	Glu	Val	Gly	Ser	Asp	Cys
1				5					10					15

<210> 516

<211> 15

<212> PRT

<213> 智人 (Homo sapiens)

<400> 516

Val	Val	Val	Pro	Cys	Glu	Pro	Pro	Glu	Val	Gly	Ser	Asp	Cys	Thr
1				5					10					15

<210> 517

<211> 15

<212> PRT

<213> 智人 (Homo sapiens)

<400> 517

Val	Val	Pro	Cys	Glu	Pro	Pro	Glu	Val	Gly	Ser	Asp	Cys	Thr	Thr

1	5	10	15
<210> 518			
<211> 15			
<212> PRT			
<213> 智人(Homo sapiens)			
<400> 518			
Val Pro Cys Glu Pro Pro Glu Val Gly Ser Asp Cys Thr Thr Ile			
1	5	10	15
<210> 519			
<211> 15			
<212> PRT			
<213> 智人(Homo sapiens)			
<400> 519			
Tyr Lys Gln Ser Gln His Met Thr Glu Val Val Arg His Cys Pro			
1	5	10	15
<210> 520			
<211> 15			
<212> PRT			
<213> 智人(Homo sapiens)			
<400> 520			
Lys Gln Ser Gln His Met Thr Glu Val Val Arg His Cys Pro His			
1	5	10	15
<210> 521			
<211> 15			
<212> PRT			
<213> 智人(Homo sapiens)			
<400> 521			
Gln Ser Gln His Met Thr Glu Val Val Arg His Cys Pro His His			
1	5	10	15
<210> 522			
<211> 15			
<212> PRT			
<213> 智人(Homo sapiens)			
<400> 522			
Ser Gln His Met Thr Glu Val Val Arg His Cys Pro His His Glu			
1	5	10	15
<210> 523			
<211> 15			
<212> PRT			

<213> 智人 (Homo sapiens)

<400> 523

Gln His Met Thr Glu Val Val Arg His Cys Pro His His Glu Arg

1 5 10 15

<210> 524

<211> 15

<212> PRT

<213> 智人 (Homo sapiens)

<400> 524

His Met Thr Glu Val Val Arg His Cys Pro His His Glu Arg Cys

1 5 10 15

<210> 525

<211> 15

<212> PRT

<213> 智人 (Homo sapiens)

<400> 525

Met Thr Glu Val Val Arg His Cys Pro His His Glu Arg Cys Ser

1 5 10 15

<210> 526

<211> 15

<212> PRT

<213> 智人 (Homo sapiens)

<400> 526

Thr Glu Val Val Arg His Cys Pro His His Glu Arg Cys Ser Asp

1 5 10 15

<210> 527

<211> 15

<212> PRT

<213> 智人 (Homo sapiens)

<400> 527

Glu Val Val Arg His Cys Pro His His Glu Arg Cys Ser Asp Ser

1 5 10 15

<210> 528

<211> 15

<212> PRT

<213> 智人 (Homo sapiens)

<400> 528

Val Val Arg His Cys Pro His His Glu Arg Cys Ser Asp Ser Asp

1 5 10 15

<210> 529

<211> 15

<212> PRT

<213> 智人 (Homo sapiens)

<400> 529

Val Arg His Cys Pro His His Glu Arg Cys Ser Asp Ser Asp Gly

1 5 10 15

<210> 530

<211> 9

<212> PRT

<213> 智人 (Homo sapiens)

<400> 530

His Met Thr Glu Val Val Arg His Cys

1 5

<210> 531

<211> 10

<212> PRT

<213> 智人 (Homo sapiens)

<400> 531

Ser Gln His Met Thr Glu Val Val Arg His

1 5 10

<210> 532

<211> 9

<212> PRT

<213> 智人 (Homo sapiens)

<400> 532

His Met Thr Glu Val Val Arg Arg Cys

1 5

<210> 533

<211> 13

<212> PRT

<213> 智人 (Homo sapiens)

<400> 533

Arg Asn Thr Phe Arg His Ser Val Val Val Pro Tyr Glu

1 5 10

<210> 534

<211> 13

<212> PRT

<213> 智人 (Homo sapiens)

<400> 534

Arg Asn Thr Phe Arg His Ser Val Val Val Pro Cys Glu

1 5 10

<210> 535

<211> 341

<212> PRT

<213> 智人(Homo sapiens)

<400> 535

Met Glu Glu Pro Gln Ser Asp Pro Ser Val Glu Pro Pro Leu Ser Gln

1 5 10 15

Glu Thr Phe Ser Asp Leu Trp Lys Leu Leu Pro Glu Asn Asn Val Leu

20 25 30

Ser Pro Leu Pro Ser Gln Ala Met Asp Asp Leu Met Leu Ser Pro Asp

35 40 45

Asp Ile Glu Gln Trp Phe Thr Glu Asp Pro Gly Pro Asp Glu Ala Pro

50 55 60

Arg Met Pro Glu Ala Ala Pro Pro Val Ala Pro Ala Pro Ala Ala Pro

65 70 75 80

Thr Pro Ala Ala Pro Ala Pro Ala Pro Ser Trp Pro Leu Ser Ser Ser

85 90 95

Val Pro Ser Gln Lys Thr Tyr Gln Gly Ser Tyr Gly Phe Arg Leu Gly

100 105 110

Phe Leu His Ser Gly Thr Ala Lys Ser Val Thr Cys Thr Tyr Ser Pro

115 120 125

Ala Leu Asn Lys Met Phe Cys Gln Leu Ala Lys Thr Cys Pro Val Gln

130 135 140

Leu Trp Val Asp Ser Thr Pro Pro Pro Gly Thr Arg Val Arg Ala Met

145 150 155 160

Ala Ile Tyr Lys Gln Ser Gln His Met Thr Glu Val Val Arg Arg Cys

165 170 175

Pro His His Glu Arg Cys Ser Asp Ser Asp Gly Leu Ala Pro Pro Gln

180 185 190

His Leu Ile Arg Val Glu Gly Asn Leu Arg Val Glu Tyr Leu Asp Asp

195 200 205

Arg Asn Thr Phe Arg His Ser Val Val Val Pro Tyr Glu Pro Pro Glu

210 215 220

Val Gly Ser Asp Cys Thr Thr Ile His Tyr Asn Tyr Met Cys Asn Ser

225 230 235 240

Ser Cys Met Gly Gly Met Asn Arg Arg Pro Ile Leu Thr Ile Ile Thr

245																250																255																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																						
Leu	Glu	Asp	Ser	Ser	Gly	Asn	Leu	Leu	Gly	Arg	Asn	Ser	Phe	Glu	Val																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																							

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

<210> 537

<211> 354

<212> PRT

<213> 智人(Homo sapiens)

<400> 537

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

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

Ser Asp

<210> 538

<211> 302

<212> PRT

<213> 智人 (Homo sapiens)

<400> 538

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

<210> 539

<211> 307

<212> PRT

<213> 智人(Homo sapiens)

<400> 539

```

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

```

275	280	285
Phe Thr Leu Gln Met Leu Leu Asp Leu Arg Trp Cys Tyr Phe Leu Ile		
290	295	300
Asn Ser Ser		
305		
<210> 540		
<211> 261		
<212> PRT		
<213> 智人 (Homo sapiens)		
<400> 540		
Met Phe Cys Gln Leu Ala Lys Thr Cys Pro Val Gln Leu Trp Val Asp		
1	5	10
Ser Thr Pro Pro Pro Gly Thr Arg Val Arg Ala Met Ala Ile Tyr Lys		
20	25	30
Gln Ser Gln His Met Thr Glu Val Val Arg Arg Cys Pro His His Glu		
35	40	45
Arg Cys Ser Asp Ser Asp Gly Leu Ala Pro Pro Gln His Leu Ile Arg		
50	55	60
Val Glu Gly Asn Leu Arg Val Glu Tyr Leu Asp Asp Arg Asn Thr Phe		
65	70	75
Arg His Ser Val Val Val Pro Tyr Glu Pro Pro Glu Val Gly Ser Asp		
85	90	95
Cys Thr Thr Ile His Tyr Asn Tyr Met Cys Asn Ser Ser Cys Met Gly		
100	105	110
Gly Met Asn Arg Arg Pro Ile Leu Thr Ile Ile Thr Leu Glu Asp Ser		
115	120	125
Ser Gly Asn Leu Leu Gly Arg Asn Ser Phe Glu Val Arg Val Cys Ala		
130	135	140
Cys Pro Gly Arg Asp Arg Arg Thr Glu Glu Glu Asn Leu Arg Lys Lys		
145	150	155
Gly Glu Pro His His Glu Leu Pro Pro Gly Ser Thr Lys Arg Ala Leu		
165	170	175
Pro Asn Asn Thr Ser Ser Ser Pro Gln Pro Lys Lys Lys Pro Leu Asp		
180	185	190
Gly Glu Tyr Phe Thr Leu Gln Ile Arg Gly Arg Glu Arg Phe Glu Met		
195	200	205
Phe Arg Glu Leu Asn Glu Ala Leu Glu Leu Lys Asp Ala Gln Ala Gly		
210	215	220
Lys Glu Pro Gly Gly Ser Arg Ala His Ser Ser His Leu Lys Ser Lys		

225	230	235	240
Lys Gly Gln Ser Thr	Ser Arg His Lys Lys	Leu Met Phe Lys Thr	Glu
	245	250	255
Gly Pro Asp Ser Asp			
260			
<210> 541			
<211> 209			
<212> PRT			
<213> 智人 (Homo sapiens)			
<400> 541			
Met Phe Cys Gln Leu Ala Lys Thr Cys Pro Val Gln Leu Trp Val Asp			
1	5	10	15
Ser Thr Pro Pro Pro Gly Thr Arg Val Arg Ala Met Ala Ile Tyr Lys			
20	25	30	
Gln Ser Gln His Met Thr Glu Val Val Arg Arg Cys Pro His His Glu			
35	40	45	
Arg Cys Ser Asp Ser Asp Gly Leu Ala Pro Pro Gln His Leu Ile Arg			
50	55	60	
Val Glu Gly Asn Leu Arg Val Glu Tyr Leu Asp Asp Arg Asn Thr Phe			
65	70	75	80
Arg His Ser Val Val Val Pro Tyr Glu Pro Pro Glu Val Gly Ser Asp			
85	90	95	
Cys Thr Thr Ile His Tyr Asn Tyr Met Cys Asn Ser Ser Cys Met Gly			
100	105	110	
Gly Met Asn Arg Arg Pro Ile Leu Thr Ile Ile Thr Leu Glu Asp Ser			
115	120	125	
Ser Gly Asn Leu Leu Gly Arg Asn Ser Phe Glu Val Arg Val Cys Ala			
130	135	140	
Cys Pro Gly Arg Asp Arg Arg Thr Glu Glu Glu Asn Leu Arg Lys Lys			
145	150	155	160
Gly Glu Pro His His Glu Leu Pro Pro Gly Ser Thr Lys Arg Ala Leu			
165	170	175	
Pro Asn Asn Thr Ser Ser Ser Pro Gln Pro Lys Lys Lys Pro Leu Asp			
180	185	190	
Gly Glu Tyr Phe Thr Leu Gln Asp Gln Thr Ser Phe Gln Lys Glu Asn			
195	200	205	
Cys			
<210> 542			
<211> 214			

<212> PRT

<213> 智人 (Homo sapiens)

<400> 542

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

<210> 543

<211> 598

<212> PRT

<213> 人工序列 (Artificial Sequence)

<220>

<223> 合成

<400> 543

Met Ala Thr Arg Leu Leu Cys Trp Ala Ala Leu Cys Leu Leu Gly Ala

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

Gln Ala Gly Asp Val Glu Glu Asn Pro Gly Pro Met Leu Leu Leu Leu		
325	330	335
Ile Pro Val Leu Gly Met Ile Phe Ala Leu Arg Asp Ala Arg Ala Gln		
340	345	350
Ser Val Ser Gln His Asn His His Val Ile Leu Ser Glu Ala Ala Ser		
355	360	365
Leu Glu Leu Gly Cys Asn Tyr Ser Tyr Gly Gly Thr Val Asn Leu Phe		
370	375	380
Trp Tyr Val Gln Tyr Pro Gly Gln His Leu Gln Leu Leu Leu Lys Tyr		
385	390	395
Phe Ser Gly Asp Pro Leu Val Lys Gly Ile Lys Gly Phe Glu Ala Glu		
405	410	415
Phe Ile Lys Ser Lys Phe Ser Phe Asn Leu Arg Lys Pro Ser Val Gln		
420	425	430
Trp Ser Asp Thr Ala Glu Tyr Phe Cys Ala Val Lys Gly Asp Tyr Lys		
435	440	445
Leu Ser Phe Gly Ala Gly Thr Thr Val Thr Val Arg Ala Asn Ile Gln		
450	455	460
Asn Pro Glu Pro Ala Val Tyr Gln Leu Lys Asp Pro Arg Ser Gln Asp		
465	470	475
Ser Thr Leu Cys Leu Phe Thr Asp Phe Asp Ser Gln Ile Asn Val Pro		
485	490	495
Lys Thr Met Glu Ser Gly Thr Phe Ile Thr Asp Lys Cys Val Leu Asp		
500	505	510
Met Lys Ala Met Asp Ser Lys Ser Asn Gly Ala Ile Ala Trp Ser Asn		
515	520	525
Gln Thr Ser Phe Thr Cys Gln Asp Ile Phe Lys Glu Thr Asn Ala Thr		
530	535	540
Tyr Pro Ser Ser Asp Val Pro Cys Asp Ala Thr Leu Thr Glu Lys Ser		
545	550	555
Phe Glu Thr Asp Met Asn Leu Asn Phe Gln Asn Leu Leu Val Ile Val		
565	570	575
Leu Arg Ile Leu Leu Leu Lys Val Ala Gly Phe Asn Leu Leu Met Thr		
580	585	590
Leu Arg Leu Trp Ser Ser		
595		
<210> 544		
<211> 604		
<212> PRT		

<213> 人工序列(Artificial Sequence)

<220>

<223> 合成

<400> 544

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

275	280	285
Val Leu Val Ser Thr Leu	Val Val Met Ala Met	Val Lys Arg Lys Asn
290	295	300
Ser Arg Ala Lys Arg Ser Gly	Ser Gly Ala Thr Asn Phe	Ser Leu Leu
305	310	315
Lys Gln Ala Gly Asp Val Glu Glu	Asn Pro Gly Pro Met Leu Thr Ala	
325	330	335
Ser Leu Leu Arg Ala Val Ile Ala	Ser Ile Cys Val Val Ser Ser Met	
340	345	350
Ala Gln Lys Val Thr Gln Ala Gln	Thr Glu Ile Ser Val Val Glu Lys	
355	360	365
Glu Asp Val Thr Leu Asp Cys Val Tyr	Glu Thr Arg Asp Thr Thr Tyr	
370	375	380
Tyr Leu Phe Trp Tyr Lys Gln Pro Pro	Ser Gly Glu Leu Val Phe Leu	
385	390	395
Ile Arg Arg Asn Ser Phe Asp Glu Gln	Asn Glu Ile Ser Gly Arg Tyr	
405	410	415
Ser Trp Asn Phe Gln Lys Ser Thr Ser	Ser Phe Asn Phe Thr Ile Thr	
420	425	430
Ala Ser Gln Val Val Asp Ser Ala Val	Tyr Phe Cys Ala Leu Ser Glu	
435	440	445
Gly Gly Ser Asn Tyr Lys Leu Thr Phe	Gly Lys Gly Thr Leu Leu Thr	
450	455	460
Val Asn Pro Asn Ile Gln Asn Pro Glu	Pro Ala Val Tyr Gln Leu Lys	
465	470	475
Asp Pro Arg Ser Gln Asp Ser Thr Leu	Cys Leu Phe Thr Asp Phe Asp	
485	490	495
Ser Gln Ile Asn Val Pro Lys Thr Met	Glu Ser Gly Thr Phe Ile Thr	
500	505	510
Asp Lys Cys Val Leu Asp Met Lys Ala	Met Asp Ser Lys Ser Asn Gly	
515	520	525
Ala Ile Ala Trp Ser Asn Gln Thr Ser	Phe Thr Cys Gln Asp Ile Phe	
530	535	540
Lys Glu Thr Asn Ala Thr Tyr Pro Ser	Ser Asp Val Pro Cys Asp Ala	
545	550	555
Thr Leu Thr Glu Lys Ser Phe Glu Thr	Asp Met Asn Leu Asn Phe Gln	
565	570	575
Asn Leu Leu Val Ile Val Leu Arg Ile	Leu Leu Leu Lys Val Ala Gly	
580	585	590

Phe Asn Leu Leu Met Thr Leu Arg Leu Trp Ser Ser
595 600

<210> 545

<211> 598

<212> PRT

<213> 人工序列(Artificial Sequence)

<220>

<223> 合成

<400> 545

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

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

545	550	555	560
Phe Glu Thr Asp Met Asn Leu Asn Phe Gln Asn Leu Leu Val Ile Val			
	565	570	575
Leu Arg Ile Leu Leu Leu Lys Val Ala Gly Phe Asn Leu Leu Met Thr			
	580	585	590
Leu Arg Leu Trp Ser Ser			
595			
<210> 546			
<211> 608			
<212> PRT			
<213> 人工序列(Artificial Sequence)			
<220>			
<223> 合成			
<400> 546			
Met Ala Leu Leu Leu Leu Leu Leu Gly Pro Gly Ile Ser Leu Leu Leu			
1 5 10 15			
Pro Gly Ser Leu Ala Gly Ser Gly Leu Gly Ala Val Val Ser Gln His			
20 25 30			
Pro Ser Trp Val Ile Cys Lys Ser Gly Thr Ser Val Lys Ile Glu Cys			
35 40 45			
Arg Ser Leu Asp Phe Gln Ala Thr Thr Met Phe Trp Tyr Arg Gln Phe			
50 55 60			
Pro Lys Gln Ser Leu Met Leu Met Ala Thr Ser Asn Glu Gly Ser Lys			
65 70 75 80			
Ala Thr Tyr Glu Gln Gly Val Glu Lys Asp Lys Phe Leu Ile Asn His			
85 90 95			
Ala Ser Leu Thr Leu Ser Thr Leu Thr Val Thr Ser Ala His Pro Glu			
100 105 110			
Asp Ser Ser Phe Tyr Ile Cys Ser Ala Ala Gly Gln Ala Asn Thr Glu			
115 120 125			
Ala Phe Phe Gly Gln Gly Thr Arg Leu Thr Val Val Glu Asp Leu Arg			
130 135 140			
Asn Val Thr Pro Pro Lys Val Ser Leu Phe Glu Pro Ser Lys Ala Glu			
145 150 155 160			
Ile Ala Asn Lys Gln Lys Ala Thr Leu Val Cys Leu Ala Arg Gly Phe			
165 170 175			
Phe Pro Asp His Val Glu Leu Ser Trp Trp Val Asn Gly Lys Glu Val			
180 185 190			
His Ser Gly Val Cys Thr Asp Pro Gln Ala Tyr Lys Glu Ser Asn Tyr			

195	200	205
Ser Tyr Cys Leu Ser Ser Arg	Leu Arg Val Ser Ala Thr Phe Trp His	
210	215	220
Asn Pro Arg Asn His Phe Arg Cys Gln Val Gln Phe His Gly Leu Ser		
225	230	235
Glu Glu Asp Lys Trp Pro Glu Gly Ser Pro Lys Pro Val Thr Gln Asn		
245	250	255
Ile Ser Ala Glu Ala Trp Gly Arg Ala Asp Cys Gly Ile Thr Ser Ala		
260	265	270
Ser Tyr Gln Gln Gly Val Leu Ser Ala Thr Ile Leu Tyr Glu Ile Leu		
275	280	285
Leu Gly Lys Ala Thr Leu Tyr Ala Val Leu Val Ser Thr Leu Val Val		
290	295	300
Met Ala Met Val Lys Arg Lys Asn Ser Arg Ala Lys Arg Ser Gly Ser		
305	310	315
Gly Ala Thr Asn Phe Ser Leu Leu Lys Gln Ala Gly Asp Val Glu Glu		
325	330	335
Asn Pro Gly Pro Met His Ser Leu Arg Val Leu Leu Val Ile Leu Trp		
340	345	350
Leu Gln Leu Ser Trp Val Trp Ser Gln Gln Lys Glu Val Glu Gln Asn		
355	360	365
Ser Gly Pro Leu Ser Val Pro Glu Gly Ala Ile Ala Ser Leu Asn Cys		
370	375	380
Thr Tyr Ser Asp Arg Gly Ser Gln Ser Phe Phe Trp Tyr Arg Gln Tyr		
385	390	395
Ser Gly Lys Ser Pro Glu Leu Ile Met Phe Ile Tyr Ser Asn Gly Asp		
405	410	415
Lys Glu Asp Gly Arg Phe Thr Ala Gln Leu Asn Lys Ala Ser Gln Tyr		
420	425	430
Val Ser Leu Leu Ile Arg Asp Ser Gln Pro Ser Asp Ser Ala Thr Tyr		
435	440	445
Leu Cys Ala Val Asn Asp Ala Gly Asn Met Leu Thr Phe Gly Gly Gly		
450	455	460
Thr Arg Leu Met Val Lys Pro Asn Ile Gln Asn Pro Glu Pro Ala Val		
465	470	475
Tyr Gln Leu Lys Asp Pro Arg Ser Gln Asp Ser Thr Leu Cys Leu Phe		
485	490	495
Thr Asp Phe Asp Ser Gln Ile Asn Val Pro Lys Thr Met Glu Ser Gly		
500	505	510

Thr Phe Ile Thr Asp Lys Cys Val Leu Asp Met Lys Ala Met Asp Ser		
515	520	525
Lys Ser Asn Gly Ala Ile Ala Trp Ser Asn Gln Thr Ser Phe Thr Cys		
530	535	540
Gln Asp Ile Phe Lys Glu Thr Asn Ala Thr Tyr Pro Ser Ser Asp Val		
545	550	555
Pro Cys Asp Ala Thr Leu Thr Glu Lys Ser Phe Glu Thr Asp Met Asn		
565	570	575
Leu Asn Phe Gln Asn Leu Leu Val Ile Val Leu Arg Ile Leu Leu Leu		
580	585	590
Lys Val Ala Gly Phe Asn Leu Leu Met Thr Leu Arg Leu Trp Ser Ser		
595	600	605
<210> 547		
<211> 602		
<212> PRT		
<213> 人工序列(Artificial Sequence)		
<220>		
<223> 合成		
<400> 547		
Met Ala Ile Gly Leu Leu Cys Cys Val Ala Phe Ser Leu Leu Trp Ala		
1	5	10
Ser Pro Val Asn Ala Gly Val Thr Gln Thr Pro Lys Phe Gln Val Leu		
20	25	30
Lys Thr Gly Gln Ser Met Thr Leu Gln Cys Ala Gln Asp Met Asn His		
35	40	45
Asn Ser Met Tyr Trp Tyr Arg Gln Asp Pro Gly Met Gly Leu Arg Leu		
50	55	60
Ile Tyr Tyr Ser Ala Ser Glu Gly Thr Thr Asp Lys Gly Glu Val Pro		
65	70	75
Asn Gly Tyr Asn Val Ser Arg Leu Asn Lys Arg Glu Phe Ser Leu Arg		
85	90	95
Leu Glu Ser Ala Ala Pro Ser Gln Thr Ser Val Tyr Phe Cys Ala Ser		
100	105	110
Ser Glu Gly Leu Trp Gln Val Gly Asp Glu Gln Tyr Phe Gly Pro Gly		
115	120	125
Thr Arg Leu Thr Val Thr Glu Asp Leu Arg Asn Val Thr Pro Pro Lys		
130	135	140
Val Ser Leu Phe Glu Pro Ser Lys Ala Glu Ile Ala Asn Lys Gln Lys		
145	150	155
		160

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

465	470	475	480
Arg Ser Gln Asp Ser Thr Leu Cys Leu Phe Thr Asp Phe Asp Ser Gln			
	485	490	495
Ile Asn Val Pro Lys Thr Met Glu Ser Gly Thr Phe Ile Thr Asp Lys			
	500	505	510
Cys Val Leu Asp Met Lys Ala Met Asp Ser Lys Ser Asn Gly Ala Ile			
	515	520	525
Ala Trp Ser Asn Gln Thr Ser Phe Thr Cys Gln Asp Ile Phe Lys Glu			
	530	535	540
Thr Asn Ala Thr Tyr Pro Ser Ser Asp Val Pro Cys Asp Ala Thr Leu			
545	550	555	560
Thr Glu Lys Ser Phe Glu Thr Asp Met Asn Leu Asn Phe Gln Asn Leu			
	565	570	575
Leu Val Ile Val Leu Arg Ile Leu Leu Leu Lys Val Ala Gly Phe Asn			
	580	585	590
Leu Leu Met Thr Leu Arg Leu Trp Ser Ser			
	595	600	
<210> 548			
<211> 607			
<212> PRT			
<213> 人工序列(Artificial Sequence)			
<220>			
<223> 合成			
<400> 548			
Met Ala Thr Arg Leu Phe Phe Tyr Val Ala Leu Cys Leu Leu Trp Thr			
1	5	10	15
Gly His Met Asp Ala Gly Ile Thr Gln Ser Pro Arg His Lys Val Thr			
	20	25	30
Glu Thr Gly Thr Pro Val Thr Leu Arg Cys His Gln Thr Glu Asn His			
	35	40	45
Arg Tyr Met Tyr Trp Tyr Arg Gln Asp Pro Gly His Gly Leu Arg Leu			
	50	55	60
Ile His Tyr Ser Tyr Gly Val Lys Asp Thr Asp Lys Gly Glu Val Ser			
65	70	75	80
Asp Gly Tyr Ser Val Ser Arg Ser Lys Thr Glu Asp Phe Leu Leu Thr			
	85	90	95
Leu Glu Ser Ala Thr Ser Ser Gln Thr Ser Val Tyr Phe Cys Ala Ile			
	100	105	110
Ser Glu Leu Val Thr Gly Asp Ser Pro Leu His Phe Gly Asn Gly Thr			

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

Ser Asp Ser Gln Leu Gly Asp Thr Ala Met Tyr Phe Cys Ala Phe Met		
435	440	445
Gly Tyr Ser Gly Ala Gly Ser Tyr Gln Leu Thr Phe Gly Lys Gly Thr		
450	455	460
Lys Leu Ser Val Ile Pro Asp Ile Gln Asn Pro Glu Pro Ala Val Tyr		
465	470	475
Gln Leu Lys Asp Pro Arg Ser Gln Asp Ser Thr Leu Cys Leu Phe Thr		
	485	490
Asp Phe Asp Ser Gln Ile Asn Val Pro Lys Thr Met Glu Ser Gly Thr		
	500	505
Phe Ile Thr Asp Lys Cys Val Leu Asp Met Lys Ala Met Asp Ser Lys		
	515	520
Ser Asn Gly Ala Ile Ala Trp Ser Asn Gln Thr Ser Phe Thr Cys Gln		
	530	535
Asp Ile Phe Lys Glu Thr Asn Ala Thr Tyr Pro Ser Ser Asp Val Pro		
545	550	555
Cys Asp Ala Thr Leu Thr Glu Lys Ser Phe Glu Thr Asp Met Asn Leu		
	565	570
Asn Phe Gln Asn Leu Leu Val Ile Val Leu Arg Ile Leu Leu Leu Lys		
	580	585
Val Ala Gly Phe Asn Leu Leu Met Thr Leu Arg Leu Trp Ser Ser		
	595	600
<210> 549		
<211> 602		
<212> PRT		
<213> 人工序列(Artificial Sequence)		
<220>		
<223> 合成		
<400> 549		
Met Ala Thr Arg Leu Leu Cys Trp Ala Ala Leu Cys Leu Leu Gly Ala		
1	5	10
Glu Leu Thr Glu Ala Gly Val Ala Gln Ser Pro Arg Tyr Lys Ile Ile		
	20	25
Glu Lys Arg Gln Ser Val Ala Phe Trp Cys Asn Pro Ile Ser Gly His		
	35	40
Ala Thr Leu Tyr Trp Tyr Gln Gln Ile Leu Gly Gln Gly Pro Lys Leu		
	50	55
Leu Ile Gln Phe Gln Asn Asn Gly Val Val Asp Asp Ser Gln Leu Pro		
65	70	75
		80

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

385	390	395	400
Leu Leu Leu Ile Arg Glu Asn Glu Lys Glu Lys Arg Lys Glu Arg Leu			
	405	410	415
Lys Val Thr Phe Asp Thr Thr Leu Lys Gln Ser Leu Phe His Ile Thr			
	420	425	430
Ala Ser Gln Pro Ala Asp Ser Ala Thr Tyr Leu Cys Ala Leu Asp Ile			
	435	440	445
Tyr Pro His Asp Met Arg Phe Gly Ala Gly Thr Arg Leu Thr Val Lys			
	450	455	460
Pro Asp Ile Gln Asn Pro Glu Pro Ala Val Tyr Gln Leu Lys Asp Pro			
465	470	475	480
Arg Ser Gln Asp Ser Thr Leu Cys Leu Phe Thr Asp Phe Asp Ser Gln			
	485	490	495
Ile Asn Val Pro Lys Thr Met Glu Ser Gly Thr Phe Ile Thr Asp Lys			
	500	505	510
Cys Val Leu Asp Met Lys Ala Met Asp Ser Lys Ser Asn Gly Ala Ile			
	515	520	525
Ala Trp Ser Asn Gln Thr Ser Phe Thr Cys Gln Asp Ile Phe Lys Glu			
	530	535	540
Thr Asn Ala Thr Tyr Pro Ser Ser Asp Val Pro Cys Asp Ala Thr Leu			
545	550	555	560
Thr Glu Lys Ser Phe Glu Thr Asp Met Asn Leu Asn Phe Gln Asn Leu			
	565	570	575
Leu Val Ile Val Leu Arg Ile Leu Leu Lys Val Ala Gly Phe Asn			
	580	585	590
Leu Leu Met Thr Leu Arg Leu Trp Ser Ser			
	595	600	
<210> 550			
<211> 607			
<212> PRT			
<213> 人工序列(Artificial Sequence)			
<220>			
<223> 合成			
<400> 550			
Met Ala Thr Ala Ser Leu Leu Arg Ala Val Ile Ala Ser Ile Cys Val			
1	5	10	15
Val Ser Ser Met Ala Gln Lys Val Thr Gln Ala Gln Thr Glu Ile Ser			
	20	25	30
Val Val Glu Lys Glu Asp Val Thr Leu Asp Cys Val Tyr Glu Thr Arg			

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

Trp Tyr Gln Gln Ser Leu Asp Gln Gly Leu Gln Phe Leu Ile Gln Tyr		
355	360	365
Tyr Asn Gly Glu Glu Arg Ala Lys Gly Asn Ile Leu Glu Arg Phe Ser		
370	375	380
Ala Gln Gln Phe Pro Asp Leu His Ser Glu Leu Asn Leu Ser Ser Leu		
385	390	395
Glu Leu Gly Asp Ser Ala Leu Tyr Phe Cys Ala Ser Ser Val Gly Ser		
	405	410
Ser Ser Ser Thr Asp Thr Gln Tyr Phe Gly Pro Gly Thr Arg Leu Thr		
	420	425
Val Leu Glu Asp Leu Arg Asn Val Thr Pro Pro Lys Val Ser Leu Phe		
	435	440
Glu Pro Ser Lys Ala Glu Ile Ala Asn Lys Gln Lys Ala Thr Leu Val		
450	455	460
Cys Leu Ala Arg Gly Phe Phe Pro Asp His Val Glu Leu Ser Trp Trp		
465	470	475
Val Asn Gly Lys Glu Val His Ser Gly Val Cys Thr Asp Pro Gln Ala		
	485	490
Tyr Lys Glu Ser Asn Tyr Ser Tyr Cys Leu Ser Ser Arg Leu Arg Val		
	500	505
Ser Ala Thr Phe Trp His Asn Pro Arg Asn His Phe Arg Cys Gln Val		
	515	520
Gln Phe His Gly Leu Ser Glu Glu Asp Lys Trp Pro Glu Gly Ser Pro		
530	535	540
Lys Pro Val Thr Gln Asn Ile Ser Ala Glu Ala Trp Gly Arg Ala Asp		
545	550	555
Cys Gly Ile Thr Ser Ala Ser Tyr Gln Gln Gly Val Leu Ser Ala Thr		
	565	570
Ile Leu Tyr Glu Ile Leu Leu Gly Lys Ala Thr Leu Tyr Ala Val Leu		
	580	585
Val Ser Thr Leu Val Val Met Ala Met Val Lys Arg Lys Asn Ser		
	595	600
<210> 551		
<211> 607		
<212> PRT		
<213> 人工序列(Artificial Sequence)		
<220>		
<223> 合成		
<400> 551		

Met	Ala	Thr	Ala	Ser	Leu	Leu	Arg	Ala	Val	Ile	Ala	Ser	Ile	Cys	Val
1				5					10					15	
Val	Ser	Ser	Met	Ala	Gln	Lys	Val	Thr	Gln	Ala	Gln	Thr	Glu	Ile	Ser
				20					25					30	
Val	Val	Glu	Lys	Glu	Asp	Val	Thr	Leu	Asp	Cys	Val	Tyr	Glu	Thr	Arg
				35					40					45	
Asp	Thr	Thr	Tyr	Tyr	Leu	Phe	Trp	Tyr	Lys	Gln	Pro	Pro	Ser	Gly	Glu
				50					55					60	
Leu	Val	Phe	Leu	Ile	Arg	Arg	Asn	Ser	Phe	Asp	Glu	Gln	Asn	Glu	Ile
65					70					75					80
Ser	Gly	Arg	Tyr	Ser	Trp	Asn	Phe	Gln	Lys	Ser	Thr	Ser	Ser	Phe	Asn
					85					90					95
Phe	Thr	Ile	Thr	Ala	Ser	Gln	Val	Val	Asp	Ser	Ala	Val	Tyr	Phe	Cys
				100						105					110
Ala	Leu	Ser	Glu	Val	Asp	Ser	Gly	Asn	Thr	Pro	Leu	Val	Phe	Gly	Lys
				115						120					125
Gly	Thr	Arg	Leu	Ser	Val	Ile	Ala	Asn	Ile	Gln	Asn	Pro	Glu	Pro	Ala
										135					140
Val	Tyr	Gln	Leu	Lys	Asp	Pro	Arg	Ser	Gln	Asp	Ser	Thr	Leu	Cys	Leu
145										150					160
Phe	Thr	Asp	Phe	Asp	Ser	Gln	Ile	Asn	Val	Pro	Lys	Thr	Met	Glu	Ser
										165					175
Gly	Thr	Phe	Ile	Thr	Asp	Lys	Cys	Val	Leu	Asp	Met	Lys	Ala	Met	Asp
										180					190
Ser	Lys	Ser	Asn	Gly	Ala	Ile	Ala	Trp	Ser	Asn	Gln	Thr	Ser	Phe	Thr
										195					205
Cys	Gln	Asp	Ile	Phe	Lys	Glu	Thr	Asn	Ala	Thr	Tyr	Pro	Ser	Ser	Asp
										210					220
Val	Pro	Cys	Asp	Ala	Thr	Leu	Thr	Glu	Lys	Ser	Phe	Glu	Thr	Asp	Met
225										230					240
Asn	Leu	Asn	Phe	Gln	Asn	Leu	Leu	Val	Ile	Val	Leu	Arg	Ile	Leu	Leu
										245					255
Leu	Lys	Val	Ala	Gly	Phe	Asn	Leu	Leu	Met	Thr	Leu	Arg	Leu	Trp	Ser
										260					270
Ser	Arg	Ala	Lys	Arg	Ser	Gly	Ser	Gly	Ala	Thr	Asn	Phe	Ser	Leu	Leu
										275					285
Lys	Gln	Ala	Gly	Asp	Val	Glu	Glu	Asn	Pro	Gly	Pro	Met	His	Phe	Arg
										290					300
Leu	Leu	Cys	Cys	Val	Ala	Phe	Cys	Leu	Leu	Gly	Ala	Gly	Pro	Val	Asp

305	310	315	320
Ser Gly Val Thr Gln Thr Pro Lys His Leu Ile Thr Ala Thr Gly Gln			
	325	330	335
Arg Val Thr Leu Arg Cys Ser Pro Arg Ser Gly Asp Leu Ser Val Tyr			
	340	345	350
Trp Tyr Gln Gln Ser Leu Asp Gln Gly Leu Gln Phe Leu Ile His Tyr			
	355	360	365
Tyr Asn Gly Glu Glu Arg Ala Lys Gly Asn Ile Leu Glu Arg Phe Ser			
	370	375	380
Ala Gln Gln Phe Pro Asp Leu His Ser Glu Leu Asn Leu Ser Ser Leu			
385	390	395	400
Glu Leu Gly Asp Ser Ala Leu Tyr Phe Cys Ala Ser Ser Val Gly Ser			
	405	410	415
Ser Ser Ser Thr Asp Thr Gln Tyr Phe Gly Pro Gly Thr Arg Leu Thr			
	420	425	430
Val Leu Glu Asp Leu Arg Asn Val Thr Pro Pro Lys Val Ser Leu Phe			
	435	440	445
Glu Pro Ser Lys Ala Glu Ile Ala Asn Lys Gln Lys Ala Thr Leu Val			
	450	455	460
Cys Leu Ala Arg Gly Phe Phe Pro Asp His Val Glu Leu Ser Trp Trp			
465	470	475	480
Val Asn Gly Lys Glu Val His Ser Gly Val Cys Thr Asp Pro Gln Ala			
	485	490	495
Tyr Lys Glu Ser Asn Tyr Ser Tyr Cys Leu Ser Ser Arg Leu Arg Val			
	500	505	510
Ser Ala Thr Phe Trp His Asn Pro Arg Asn His Phe Arg Cys Gln Val			
	515	520	525
Gln Phe His Gly Leu Ser Glu Glu Asp Lys Trp Pro Glu Gly Ser Pro			
	530	535	540
Lys Pro Val Thr Gln Asn Ile Ser Ala Glu Ala Trp Gly Arg Ala Asp			
545	550	555	560
Cys Gly Ile Thr Ser Ala Ser Tyr Gln Gln Gly Val Leu Ser Ala Thr			
	565	570	575
Ile Leu Tyr Glu Ile Leu Leu Gly Lys Ala Thr Leu Tyr Ala Val Leu			
	580	585	590
Val Ser Thr Leu Val Val Met Ala Met Val Lys Arg Lys Asn Ser			
	595	600	605
<210> 552			
<211> 611			

<212> PRT

<213> 人工序列(Artificial Sequence)

<220>

<223> 合成

<400> 552

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

Ala Lys Arg Ser Gly Ser Gly	Ala Thr Asn Phe Ser	Leu Leu Lys Gln
275	280	285
Ala Gly Asp Val Glu Glu Asn Pro Gly Pro Met His	Leu Leu Leu Leu	
290	295	300
Leu Leu Gly Pro Gly Ile Ser Leu Leu Leu Pro Gly Ser Leu Ala Gly		
305	310	315 320
Ser Gly Leu Gly Ala Val Val Ser Gln His Pro Ser Trp Val Ile Cys		
	325	330 335
Lys Ser Gly Thr Ser Val Lys Ile Glu Cys Arg Ser Leu Asp Phe Gln		
	340	345 350
Ala Thr Thr Met Phe Trp Tyr Arg Gln Phe Pro Lys Gln Ser Leu Met		
	355	360 365
Leu Met Ala Thr Ser Asn Glu Gly Ser Lys Ala Thr Tyr Glu Gln Gly		
	370	375 380
Val Glu Lys Asp Lys Phe Leu Ile Asn His Ala Ser Leu Thr Leu Ser		
385	390	395 400
Thr Leu Thr Val Thr Ser Ala His Pro Glu Asp Ser Ser Phe Tyr Ile		
	405	410 415
Cys Ser Gly Gly Leu Glu Glu Ala Ala Arg Gln Phe Ile Gly Pro Gly		
	420	425 430
Thr Arg Leu Thr Val Leu Glu Asp Leu Arg Asn Val Thr Pro Pro Lys		
	435	440 445
Val Ser Leu Phe Glu Pro Ser Lys Ala Glu Ile Ala Asn Lys Gln Lys		
	450	455 460
Ala Thr Leu Val Cys Leu Ala Arg Gly Phe Phe Pro Asp His Val Glu		
465	470	475 480
Leu Ser Trp Trp Val Asn Gly Lys Glu Val His Ser Gly Val Cys Thr		
	485	490 495
Asp Pro Gln Ala Tyr Lys Glu Ser Asn Tyr Ser Tyr Cys Leu Ser Ser		
	500	505 510
Arg Leu Arg Val Ser Ala Thr Phe Trp His Asn Pro Arg Asn His Phe		
	515	520 525
Arg Cys Gln Val Gln Phe His Gly Leu Ser Glu Glu Asp Lys Trp Pro		
	530	535 540
Glu Gly Ser Pro Lys Pro Val Thr Gln Asn Ile Ser Ala Glu Ala Trp		
545	550	555 560
Gly Arg Ala Asp Cys Gly Ile Thr Ser Ala Ser Tyr Gln Gln Gly Val		
	565	570 575
Leu Ser Ala Thr Ile Leu Tyr Glu Ile Leu Leu Gly Lys Ala Thr Leu		

	580					585					590				
Tyr	Ala	Val	Leu	Val	Ser	Thr	Leu	Val	Val	Met	Ala	Met	Val	Lys	Arg
	595					600					605				
Lys	Asn	Ser													
	610														
<210>	553														
<211>	601														
<212>	PRT														
<213>	人工序列(Artificial Sequence)														
<220>															
<223>	合成														
<400>	553														
Met	Ala	Lys	Ser	Leu	Arg	Val	Leu	Leu	Val	Ile	Leu	Trp	Leu	Gln	Leu
1				5					10					15	
Ser	Trp	Val	Trp	Ser	Gln	Gln	Lys	Glu	Val	Glu	Gln	Asp	Pro	Gly	Pro
			20					25					30		
Leu	Ser	Val	Pro	Glu	Gly	Ala	Ile	Val	Ser	Leu	Asn	Cys	Thr	Tyr	Ser
		35					40					45			
Asn	Ser	Ala	Phe	Gln	Tyr	Phe	Met	Trp	Tyr	Arg	Gln	Tyr	Ser	Arg	Lys
	50					55					60				
Gly	Pro	Glu	Leu	Leu	Met	Tyr	Thr	Tyr	Ser	Ser	Gly	Asn	Lys	Glu	Asp
65				70						75				80	
Gly	Arg	Phe	Thr	Ala	Gln	Val	Asp	Lys	Ser	Ser	Lys	Tyr	Ile	Ser	Leu
			85						90					95	
Phe	Ile	Arg	Asp	Ser	Gln	Pro	Ser	Asp	Ser	Ala	Thr	Tyr	Leu	Cys	Ala
		100						105					110		
Met	Thr	Ser	Pro	Tyr	Asn	Asn	Asn	Asp	Met	Arg	Phe	Gly	Ala	Gly	Thr
		115					120					125			
Arg	Leu	Thr	Val	Lys	Pro	Asn	Ile	Gln	Asn	Pro	Glu	Pro	Ala	Val	Tyr
	130					135					140				
Gln	Leu	Lys	Asp	Pro	Arg	Ser	Gln	Asp	Ser	Thr	Leu	Cys	Leu	Phe	Thr
145				150						155				160	
Asp	Phe	Asp	Ser	Gln	Ile	Asn	Val	Pro	Lys	Thr	Met	Glu	Ser	Gly	Thr
			165						170					175	
Phe	Ile	Thr	Asp	Lys	Cys	Val	Leu	Asp	Met	Lys	Ala	Met	Asp	Ser	Lys
		180						185					190		
Ser	Asn	Gly	Ala	Ile	Ala	Trp	Ser	Asn	Gln	Thr	Ser	Phe	Thr	Cys	Gln
	195					200						205			
Asp	Ile	Phe	Lys	Glu	Thr	Asn	Ala	Thr	Tyr	Pro	Ser	Ser	Asp	Val	Pro

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

Glu Glu Asp Lys Trp Pro Glu Gly Ser Pro Lys Pro Val Thr Gln Asn
 530 535 540
 Ile Ser Ala Glu Ala Trp Gly Arg Ala Asp Cys Gly Ile Thr Ser Ala
 545 550 555 560
 Ser Tyr Gln Gln Gly Val Leu Ser Ala Thr Ile Leu Tyr Glu Ile Leu
 565 570 575
 Leu Gly Lys Ala Thr Leu Tyr Ala Val Leu Val Ser Thr Leu Val Val
 580 585 590
 Met Ala Met Val Lys Arg Lys Asn Ser
 595 600

<210> 554

<211> 596

<212> PRT

<213> 人工序列(Artificial Sequence)

<220>

<223> 合成

<400> 554

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

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

	485		490		495
Ser Arg Leu Arg Val Ser Ala Thr Phe Trp His Asn Pro Arg Asn His					
500		505		510	
Phe Arg Cys Gln Val Gln Phe His Gly Leu Ser Glu Glu Asp Lys Trp					
515		520		525	
Pro Glu Gly Ser Pro Lys Pro Val Thr Gln Asn Ile Ser Ala Glu Ala					
530		535		540	
Trp Gly Arg Ala Asp Cys Gly Ile Thr Ser Ala Ser Tyr Gln Gln Gly					
545		550		555	560
Val Leu Ser Ala Thr Ile Leu Tyr Glu Ile Leu Leu Gly Lys Ala Thr					
565		570		575	
Leu Tyr Ala Val Leu Val Ser Thr Leu Val Val Met Ala Met Val Lys					
580		585		590	
Arg Lys Asn Ser					
595					
<210> 555					
<211> 610					
<212> PRT					
<213> 人工序列(Artificial Sequence)					
<220>					
<223> 合成					
<400> 555					
Met Ala Tyr Ser Pro Gly Leu Val Ser Leu Ile Leu Leu Leu Gly					
1	5	10	15		
Arg Thr Arg Gly Asn Ser Val Thr Gln Met Glu Gly Pro Val Thr Leu					
20	25	30			
Ser Glu Glu Ala Phe Leu Thr Ile Asn Cys Thr Tyr Thr Ala Thr Gly					
35	40	45			
Tyr Pro Ser Leu Phe Trp Tyr Val Gln Tyr Pro Gly Glu Gly Leu Gln					
50	55	60			
Leu Leu Leu Lys Ala Thr Lys Ala Asp Asp Lys Gly Ser Asn Lys Gly					
65	70	75	80		
Phe Glu Ala Thr Tyr Arg Lys Glu Thr Thr Ser Phe His Leu Glu Lys					
85	90	95			
Gly Ser Val Gln Val Ser Asp Ser Ala Val Tyr Phe Cys Ala Leu Asn					
100	105	110			
Pro Asn Ala Gly Gly Thr Ser Tyr Gly Lys Leu Thr Phe Gly Gln Gly					
115	120	125			
Thr Ile Leu Thr Val His Pro Asn Ile Gln Asn Pro Glu Pro Ala Val					

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

Ser Leu Phe Glu Pro Ser Lys Ala Glu Ile Ala Asn Lys Gln Lys Ala
 450 455 460
 Thr Leu Val Cys Leu Ala Arg Gly Phe Phe Pro Asp His Val Glu Leu
 465 470 475 480
 Ser Trp Trp Val Asn Gly Lys Glu Val His Ser Gly Val Cys Thr Asp
 485 490 495
 Pro Gln Ala Tyr Lys Glu Ser Asn Tyr Ser Tyr Cys Leu Ser Ser Arg
 500 505 510
 Leu Arg Val Ser Ala Thr Phe Trp His Asn Pro Arg Asn His Phe Arg
 515 520 525
 Cys Gln Val Gln Phe His Gly Leu Ser Glu Glu Asp Lys Trp Pro Glu
 530 535 540
 Gly Ser Pro Lys Pro Val Thr Gln Asn Ile Ser Ala Glu Ala Trp Gly
 545 550 555 560
 Arg Ala Asp Cys Gly Ile Thr Ser Ala Ser Tyr Gln Gln Gly Val Leu
 565 570 575
 Ser Ala Thr Ile Leu Tyr Glu Ile Leu Leu Gly Lys Ala Thr Leu Tyr
 580 585 590
 Ala Val Leu Val Ser Thr Leu Val Val Met Ala Met Val Lys Arg Lys
 595 600 605
 Asn Ser
 610
 <210> 556
 <211> 614
 <212> PRT
 <213> 人工序列(Artificial Sequence)
 <220>
 <223> 合成
 <400> 556
 Met Ala Thr Phe Ala Gly Phe Ser Phe Leu Phe Leu Trp Leu Gln Leu
 1 5 10 15
 Asp Cys Met Ser Arg Gly Glu Asp Val Glu Gln Ser Leu Phe Leu Ser
 20 25 30
 Val Arg Glu Gly Asp Ser Ser Val Ile Asn Cys Thr Tyr Thr Asp Ser
 35 40 45
 Ser Ser Thr Tyr Leu Tyr Trp Tyr Lys Gln Glu Pro Gly Ala Gly Leu
 50 55 60
 Gln Leu Leu Thr Tyr Ile Phe Ser Asn Met Asp Met Lys Gln Asp Gln
 65 70 75 80

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

385	390	395	400
Leu Ser Thr Leu Thr Val Thr Ser Ala His Pro Glu Asp Ser Ser Phe			
	405	410	415
Tyr Ile Cys Ser Ala Arg Asp Leu Gln Arg Ser Tyr Glu Gln Tyr Phe			
	420	425	430
Gly Pro Gly Thr Arg Leu Thr Val Thr Glu Asp Leu Arg Asn Val Thr			
	435	440	445
Pro Pro Lys Val Ser Leu Phe Glu Pro Ser Lys Ala Glu Ile Ala Asn			
	450	455	460
Lys Gln Lys Ala Thr Leu Val Cys Leu Ala Arg Gly Phe Phe Pro Asp			
465	470	475	480
His Val Glu Leu Ser Trp Trp Val Asn Gly Lys Glu Val His Ser Gly			
	485	490	495
Val Cys Thr Asp Pro Gln Ala Tyr Lys Glu Ser Asn Tyr Ser Tyr Cys			
	500	505	510
Leu Ser Ser Arg Leu Arg Val Ser Ala Thr Phe Trp His Asn Pro Arg			
	515	520	525
Asn His Phe Arg Cys Gln Val Gln Phe His Gly Leu Ser Glu Glu Asp			
	530	535	540
Lys Trp Pro Glu Gly Ser Pro Lys Pro Val Thr Gln Asn Ile Ser Ala			
545	550	555	560
Glu Ala Trp Gly Arg Ala Asp Cys Gly Ile Thr Ser Ala Ser Tyr Gln			
	565	570	575
Gln Gly Val Leu Ser Ala Thr Ile Leu Tyr Glu Ile Leu Leu Gly Lys			
	580	585	590
Ala Thr Leu Tyr Ala Val Leu Val Ser Thr Leu Val Val Met Ala Met			
	595	600	605
Val Lys Arg Lys Asn Ser			
610			
<210> 557			
<211> 604			
<212> PRT			
<213> 人工序列 (Artificial Sequence)			
<220>			
<223> 合成			
<400> 557			
Met Ala Thr Phe Ala Gly Phe Ser Phe Leu Phe Leu Trp Leu Gln Leu			
1	5	10	15
Asp Cys Met Ser Arg Gly Glu Asp Val Glu Gln Ser Leu Phe Leu Ser			

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

Glu Cys Arg Ser Leu Asp Phe Gln Ala Thr Thr Met Phe Trp Tyr Arg		
340	345	350
Gln Phe Pro Lys Gln Ser Leu Met Leu Met Ala Thr Ser Asn Glu Gly		
355	360	365
Ser Lys Ala Thr Tyr Glu Gln Gly Val Glu Lys Asp Lys Phe Leu Ile		
370	375	380
Asn His Ala Ser Leu Thr Leu Ser Thr Leu Thr Val Thr Ser Ala His		
385	390	395
Pro Glu Asp Ser Ser Phe Tyr Ile Cys Ser Ala Arg Asp Leu Gln Arg		
405	410	415
Ser Tyr Glu Gln Tyr Phe Gly Pro Gly Thr Arg Leu Thr Val Thr Glu		
420	425	430
Asp Leu Arg Asn Val Thr Pro Pro Lys Val Ser Leu Phe Glu Pro Ser		
435	440	445
Lys Ala Glu Ile Ala Asn Lys Gln Lys Ala Thr Leu Val Cys Leu Ala		
450	455	460
Arg Gly Phe Phe Pro Asp His Val Glu Leu Ser Trp Trp Val Asn Gly		
465	470	475
Lys Glu Val His Ser Gly Val Cys Thr Asp Pro Gln Ala Tyr Lys Glu		
485	490	495
Ser Asn Tyr Ser Tyr Cys Leu Ser Ser Arg Leu Arg Val Ser Ala Thr		
500	505	510
Phe Trp His Asn Pro Arg Asn His Phe Arg Cys Gln Val Gln Phe His		
515	520	525
Gly Leu Ser Glu Glu Asp Lys Trp Pro Glu Gly Ser Pro Lys Pro Val		
530	535	540
Thr Gln Asn Ile Ser Ala Glu Ala Trp Gly Arg Ala Asp Cys Gly Ile		
545	550	555
Thr Ser Ala Ser Tyr Gln Gln Gly Val Leu Ser Ala Thr Ile Leu Tyr		
565	570	575
Glu Ile Leu Leu Gly Lys Ala Thr Leu Tyr Ala Val Leu Val Ser Thr		
580	585	590
Leu Val Val Met Ala Met Val Lys Arg Lys Asn Ser		
595	600	
<210>	558	
<211>	606	
<212>	PRT	
<213>	人工序列 (Artificial Sequence)	
<220>		

<223> 合成

<400> 558

```

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

```

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

<210> 559

<211> 604

<212> PRT

<213> 人工序列(Artificial Sequence)

<220>

<223> 合成

<400> 559

```

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

```


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

	565		570		575
Glu Ile Leu Leu Gly Lys Ala Thr Leu Tyr Ala Val Leu Val Ser Thr					
	580		585		590
Leu Val Val Met Ala Met Val Lys Arg Lys Asn Ser					
	595		600		
<210> 560					
<211> 605					
<212> PRT					
<213> 人工序列(Artificial Sequence)					
<220>					
<223> 合成					
<400> 560					
Met Ala Lys Asn Pro Leu Ala Ala Pro Leu Leu Ile Leu Trp Phe His					
1	5		10		15
Leu Asp Cys Val Ser Ser Ile Leu Asn Val Glu Gln Ser Pro Gln Ser					
	20		25		30
Leu His Val Gln Glu Gly Asp Ser Thr Asn Phe Thr Cys Ser Phe Pro					
	35		40		45
Ser Ser Asn Phe Tyr Ala Leu His Trp Tyr Arg Trp Glu Thr Ala Lys					
	50		55		60
Ser Pro Glu Ala Leu Phe Val Met Thr Leu Asn Gly Asp Glu Lys Lys					
65	70		75		80
Lys Gly Arg Ile Ser Ala Thr Leu Asn Thr Lys Glu Gly Tyr Ser Tyr					
	85		90		95
Leu Tyr Ile Lys Gly Ser Gln Pro Glu Asp Ser Ala Thr Tyr Leu Cys					
	100		105		110
Ala Ser Val Gly Gly Gly Ala Asp Gly Leu Thr Phe Gly Lys Gly Thr					
	115		120		125
His Leu Ile Ile Gln Pro Asn Ile Gln Asn Pro Glu Pro Ala Val Tyr					
	130		135		140
Gln Leu Lys Asp Pro Arg Ser Gln Asp Ser Thr Leu Cys Leu Phe Thr					
145	150		155		160
Asp Phe Asp Ser Gln Ile Asn Val Pro Lys Thr Met Glu Ser Gly Thr					
	165		170		175
Phe Ile Thr Asp Lys Cys Val Leu Asp Met Lys Ala Met Asp Ser Lys					
	180		185		190
Ser Asn Gly Ala Ile Ala Trp Ser Asn Gln Thr Ser Phe Thr Cys Gln					
	195		200		205
Asp Ile Phe Lys Glu Thr Asn Ala Thr Tyr Pro Ser Ser Asp Val Pro					

210	215	220
Cys Asp Ala Thr Leu Thr Glu Lys Ser Phe Glu Thr Asp Met Asn Leu		
225	230	235
Asn Phe Gln Asn Leu Leu Val Ile Val Leu Arg Ile Leu Leu Leu Lys		240
245	250	255
Val Ala Gly Phe Asn Leu Leu Met Thr Leu Arg Leu Trp Ser Ser Arg		
260	265	270
Ala Lys Arg Ser Gly Ser Gly Ala Thr Asn Phe Ser Leu Leu Lys Gln		
275	280	285
Ala Gly Asp Val Glu Glu Asn Pro Gly Pro Met His Thr Arg Leu Leu		
290	295	300
Phe Trp Val Ala Phe Cys Leu Leu Gly Ala Asp His Thr Gly Ala Gly		
305	310	315
Val Ser Gln Ser Pro Ser Asn Lys Val Thr Glu Lys Gly Lys Asp Val		
325	330	335
Glu Leu Arg Cys Asp Pro Ile Ser Gly His Thr Ala Leu Tyr Trp Tyr		
340	345	350
Arg Gln Ser Leu Gly Gln Gly Leu Glu Phe Leu Ile Tyr Phe Gln Gly		
355	360	365
Asn Ser Ala Pro Asp Lys Ser Gly Leu Pro Ser Asp Arg Phe Ser Ala		
370	375	380
Glu Arg Thr Gly Gly Ser Val Ser Thr Leu Thr Ile Gln Arg Thr Gln		
385	390	395
Gln Glu Asp Ser Ala Val Tyr Leu Cys Ala Ser Thr Trp Asp Arg Gly		
405	410	415
Ser Tyr Asn Glu Gln Phe Phe Gly Pro Gly Thr Arg Leu Thr Val Leu		
420	425	430
Glu Asp Leu Arg Asn Val Thr Pro Pro Lys Val Ser Leu Phe Glu Pro		
435	440	445
Ser Lys Ala Glu Ile Ala Asn Lys Gln Lys Ala Thr Leu Val Cys Leu		
450	455	460
Ala Arg Gly Phe Phe Pro Asp His Val Glu Leu Ser Trp Trp Val Asn		
465	470	475
Gly Lys Glu Val His Ser Gly Val Cys Thr Asp Pro Gln Ala Tyr Lys		
485	490	495
Glu Ser Asn Tyr Ser Tyr Cys Leu Ser Ser Arg Leu Arg Val Ser Ala		
500	505	510
Thr Phe Trp His Asn Pro Arg Asn His Phe Arg Cys Gln Val Gln Phe		
515	520	525

His Gly Leu Ser Glu Glu Asp Lys Trp Pro Glu Gly Ser Pro Lys Pro		
530	535	540
Val Thr Gln Asn Ile Ser Ala Glu Ala Trp Gly Arg Ala Asp Cys Gly		
545	550	555
Ile Thr Ser Ala Ser Tyr Gln Gln Gly Val Leu Ser Ala Thr Ile Leu		
	565	570
Tyr Glu Ile Leu Leu Gly Lys Ala Thr Leu Tyr Ala Val Leu Val Ser		
	580	585
Thr Leu Val Val Met Ala Met Val Lys Arg Lys Asn Ser		
	595	600
		605
<210> 561		
<211> 602		
<212> PRT		
<213> 人工序列(Artificial Sequence)		
<220>		
<223> 合成		
<400> 561		
Met Ala Lys Cys Pro Gln Ala Leu Leu Ala Ile Phe Trp Leu Leu Leu		
1	5	10
Ser Trp Val Ser Ser Glu Asp Lys Val Val Gln Ser Pro Leu Ser Leu		
	20	25
Val Val His Glu Gly Asp Thr Val Thr Leu Asn Cys Ser Tyr Glu Val		
	35	40
Thr Asn Phe Arg Ser Leu Leu Trp Tyr Lys Gln Glu Lys Lys Ala Pro		
	50	55
Thr Phe Leu Phe Met Leu Thr Ser Ser Gly Ile Glu Lys Lys Ser Gly		
65	70	75
Arg Leu Ser Ser Ile Leu Asp Lys Lys Glu Leu Ser Ser Ile Leu Asn		
	85	90
Ile Thr Ala Thr Gln Thr Gly Asp Ser Ala Ile Tyr Leu Cys Ala Gly		
	100	105
Gln Asn Tyr Gly Gly Ser Gln Gly Asn Leu Ile Phe Gly Lys Gly Thr		
	115	120
Lys Leu Ser Val Lys Pro Asn Ile Gln Asn Pro Glu Pro Ala Val Tyr		
	130	135
Gln Leu Lys Asp Pro Arg Ser Gln Asp Ser Thr Leu Cys Leu Phe Thr		
145	150	155
Asp Phe Asp Ser Gln Ile Asn Val Pro Lys Thr Met Glu Ser Gly Thr		
	165	170
		175

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

				485					490					495			
Tyr	Ser	Tyr	Cys	Leu	Ser	Ser	Arg	Leu	Arg	Val	Ser	Ala	Thr	Phe	Trp		
				500					505					510			
His	Asn	Pro	Arg	Asn	His	Phe	Arg	Cys	Gln	Val	Gln	Phe	His	Gly	Leu		
				515					520					525			
Ser	Glu	Glu	Asp	Lys	Trp	Pro	Glu	Gly	Ser	Pro	Lys	Pro	Val	Thr	Gln		
				530					535					540			
Asn	Ile	Ser	Ala	Glu	Ala	Trp	Gly	Arg	Ala	Asp	Cys	Gly	Ile	Thr	Ser		
545									550					555			560
Ala	Ser	Tyr	Gln	Gln	Gly	Val	Leu	Ser	Ala	Thr	Ile	Leu	Tyr	Glu	Ile		
				565					570					575			
Leu	Leu	Gly	Lys	Ala	Thr	Leu	Tyr	Ala	Val	Leu	Val	Ser	Thr	Leu	Val		
				580					585					590			
Val	Met	Ala	Met	Val	Lys	Arg	Lys	Asn	Ser								
				595					600								
<210> 562																	
<211> 606																	
<212> PRT																	
<213> 人工序列(Artificial Sequence)																	
<220>																	
<223> 合成																	
<400> 562																	
Met	Ala	Ser	Leu	Arg	Val	Leu	Leu	Val	Ile	Leu	Trp	Leu	Gln	Leu	Ser		
1				5					10					15			
Trp	Val	Trp	Ser	Gln	Gln	Lys	Glu	Val	Glu	Gln	Asn	Ser	Gly	Pro	Leu		
				20					25					30			
Ser	Val	Pro	Glu	Gly	Ala	Ile	Ala	Ser	Leu	Asn	Cys	Thr	Tyr	Ser	Asp		
				35					40					45			
Arg	Gly	Ser	Gln	Ser	Phe	Phe	Trp	Tyr	Arg	Gln	Tyr	Ser	Gly	Lys	Ser		
				50					55					60			
Pro	Glu	Leu	Ile	Met	Phe	Ile	Tyr	Ser	Asn	Gly	Asp	Lys	Glu	Asp	Gly		
65				70					75					80			
Arg	Phe	Thr	Ala	Gln	Leu	Asn	Lys	Ala	Ser	Gln	Tyr	Val	Ser	Leu	Leu		
				85					90					95			
Ile	Arg	Asp	Ser	Gln	Pro	Ser	Asp	Ser	Ala	Thr	Tyr	Leu	Cys	Ala	Val		
				100					105					110			
Asn	Pro	Pro	Val	Lys	Thr	Ser	Tyr	Asp	Lys	Val	Ile	Phe	Gly	Pro	Gly		
				115					120					125			
Thr	Ser	Leu	Ser	Val	Ile	Pro	Asn	Ile	Gln	Asn	Pro	Glu	Pro	Ala	Val		

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

Pro Ser Lys Ala Glu Ile Ala Asn Lys Gln Lys Ala Thr Leu Val Cys
 450 455 460
 Leu Ala Arg Gly Phe Phe Pro Asp His Val Glu Leu Ser Trp Trp Val
 465 470 475 480
 Asn Gly Lys Glu Val His Ser Gly Val Cys Thr Asp Pro Gln Ala Tyr
 485 490 495
 Lys Glu Ser Asn Tyr Ser Tyr Cys Leu Ser Ser Arg Leu Arg Val Ser
 500 505 510
 Ala Thr Phe Trp His Asn Pro Arg Asn His Phe Arg Cys Gln Val Gln
 515 520 525
 Phe His Gly Leu Ser Glu Glu Asp Lys Trp Pro Glu Gly Ser Pro Lys
 530 535 540
 Pro Val Thr Gln Asn Ile Ser Ala Glu Ala Trp Gly Arg Ala Asp Cys
 545 550 555 560
 Gly Ile Thr Ser Ala Ser Tyr Gln Gln Gly Val Leu Ser Ala Thr Ile
 565 570 575
 Leu Tyr Glu Ile Leu Leu Gly Lys Ala Thr Leu Tyr Ala Val Leu Val
 580 585 590
 Ser Thr Leu Val Val Met Ala Met Val Lys Arg Lys Asn Ser
 595 600 605
 <210> 563
 <211> 600
 <212> PRT
 <213> 人工序列(Artificial Sequence)
 <220>
 <223> 合成
 <400> 563
 Met Ala Ser Leu Arg Val Leu Leu Val Ile Leu Trp Leu Gln Leu Ser
 1 5 10 15
 Trp Val Trp Ser Gln Gln Lys Glu Val Glu Gln Asn Ser Gly Pro Leu
 20 25 30
 Ser Val Pro Glu Gly Ala Ile Ala Ser Leu Asn Cys Thr Tyr Ser Asp
 35 40 45
 Arg Gly Ser Gln Ser Phe Phe Trp Tyr Arg Gln Tyr Ser Gly Lys Ser
 50 55 60
 Pro Glu Leu Ile Met Phe Ile Tyr Ser Asn Gly Asp Lys Glu Asp Gly
 65 70 75 80
 Arg Phe Thr Ala Gln Leu Asn Lys Ala Ser Gln Tyr Val Ser Leu Leu
 85 90 95

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

	405	410	415
Tyr Phe Gly Pro Gly Thr Arg Leu Thr Val Thr Glu Asp Leu Arg Asn			
	420	425	430
Val Thr Pro Pro Lys Val Ser Leu Phe Glu Pro Ser Lys Ala Glu Ile			
	435	440	445
Ala Asn Lys Gln Lys Ala Thr Leu Val Cys Leu Ala Arg Gly Phe Phe			
	450	455	460
Pro Asp His Val Glu Leu Ser Trp Trp Val Asn Gly Lys Glu Val His			
465	470	475	480
Ser Gly Val Cys Thr Asp Pro Gln Ala Tyr Lys Glu Ser Asn Tyr Ser			
	485	490	495
Tyr Cys Leu Ser Ser Arg Leu Arg Val Ser Ala Thr Phe Trp His Asn			
	500	505	510
Pro Arg Asn His Phe Arg Cys Gln Val Gln Phe His Gly Leu Ser Glu			
	515	520	525
Glu Asp Lys Trp Pro Glu Gly Ser Pro Lys Pro Val Thr Gln Asn Ile			
	530	535	540
Ser Ala Glu Ala Trp Gly Arg Ala Asp Cys Gly Ile Thr Ser Ala Ser			
545	550	555	560
Tyr Gln Gln Gly Val Leu Ser Ala Thr Ile Leu Tyr Glu Ile Leu Leu			
	565	570	575
Gly Lys Ala Thr Leu Tyr Ala Val Leu Val Ser Thr Leu Val Val Met			
	580	585	590
Ala Met Val Lys Arg Lys Asn Ser			
	595	600	
<210> 564			
<211> 600			
<212> PRT			
<213> 人工序列(Artificial Sequence)			
<220>			
<223> 合成			
<400> 564			
Met Ala Ser Leu Arg Val Leu Leu Val Ile Leu Trp Leu Gln Leu Ser			
1	5	10	15
Trp Val Trp Ser Gln Gln Lys Glu Val Glu Gln Asn Ser Gly Pro Leu			
	20	25	30
Ser Val Pro Glu Gly Ala Ile Ala Ser Leu Asn Cys Thr Tyr Ser Asp			
	35	40	45
Arg Gly Ser Gln Ser Phe Phe Trp Tyr Arg Gln Tyr Ser Gly Lys Ser			

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

Asn Asp Phe Gln Lys Gly Asp Ile Val Glu Gly Tyr Ser Val Ser Arg			
370	375	380	
Glu Lys Lys Glu Ser Phe Pro Leu Thr Val Thr Ser Ala Gln Lys Asn			
385	390	395	400
Pro Thr Ala Phe Tyr Leu Cys Ala Ser Ser Ser Arg Asp Tyr Glu Gln			
405	410	415	
Tyr Phe Gly Pro Gly Thr Arg Leu Thr Val Thr Glu Asp Leu Arg Asn			
420	425	430	
Val Thr Pro Pro Lys Val Ser Leu Phe Glu Pro Ser Lys Ala Glu Ile			
435	440	445	
Ala Asn Lys Gln Lys Ala Thr Leu Val Cys Leu Ala Arg Gly Phe Phe			
450	455	460	
Pro Asp His Val Glu Leu Ser Trp Trp Val Asn Gly Lys Glu Val His			
465	470	475	480
Ser Gly Val Cys Thr Asp Pro Gln Ala Tyr Lys Glu Ser Asn Tyr Ser			
485	490	495	
Tyr Cys Leu Ser Ser Arg Leu Arg Val Ser Ala Thr Phe Trp His Asn			
500	505	510	
Pro Arg Asn His Phe Arg Cys Gln Val Gln Phe His Gly Leu Ser Glu			
515	520	525	
Glu Asp Lys Trp Pro Glu Gly Ser Pro Lys Pro Val Thr Gln Asn Ile			
530	535	540	
Ser Ala Glu Ala Trp Gly Arg Ala Asp Cys Gly Ile Thr Ser Ala Ser			
545	550	555	560
Tyr Gln Gln Gly Val Leu Ser Ala Thr Ile Leu Tyr Glu Ile Leu Leu			
565	570	575	
Gly Lys Ala Thr Leu Tyr Ala Val Leu Val Ser Thr Leu Val Val Met			
580	585	590	
Ala Met Val Lys Arg Lys Asn Ser			
595	600		
<210> 565			
<211> 600			
<212> PRT			
<213> 人工序列(Artificial Sequence)			
<220>			
<223> 合成			
<400> 565			
Met Ala Ser Ala Pro Ile Ser Met Leu Ala Met Leu Phe Thr Leu Ser			
1	5	10	15

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

				325				330				335			
Cys	Glu	Gln	Asn	Leu	Asn	His	Asp	Ala	Met	Tyr	Trp	Tyr	Arg	Gln	Asp
				340				345				350			
Pro	Gly	Gln	Gly	Leu	Arg	Leu	Ile	Tyr	Tyr	Ser	Gln	Ile	Val	Asn	Asp
				355				360				365			
Phe	Gln	Lys	Gly	Asp	Ile	Ala	Glu	Gly	Tyr	Ser	Val	Ser	Arg	Glu	Lys
				370				375				380			
Lys	Glu	Ser	Phe	Pro	Leu	Thr	Val	Thr	Ser	Ala	Gln	Lys	Asn	Pro	Thr
385				390				395				400			
Ala	Phe	Tyr	Leu	Cys	Ala	Ser	Ser	Ile	Ser	Ala	Gly	Gly	Asp	Gly	Tyr
				405				410				415			
Thr	Phe	Gly	Ser	Gly	Thr	Arg	Leu	Thr	Val	Val	Glu	Asp	Leu	Arg	Asn
				420				425				430			
Val	Thr	Pro	Pro	Lys	Val	Ser	Leu	Phe	Glu	Pro	Ser	Lys	Ala	Glu	Ile
				435				440				445			
Ala	Asn	Lys	Gln	Lys	Ala	Thr	Leu	Val	Cys	Leu	Ala	Arg	Gly	Phe	Phe
450				455				460							
Pro	Asp	His	Val	Glu	Leu	Ser	Trp	Trp	Val	Asn	Gly	Lys	Glu	Val	His
465				470				475				480			
Ser	Gly	Val	Cys	Thr	Asp	Pro	Gln	Ala	Tyr	Lys	Glu	Ser	Asn	Tyr	Ser
				485				490				495			
Tyr	Cys	Leu	Ser	Ser	Arg	Leu	Arg	Val	Ser	Ala	Thr	Phe	Trp	His	Asn
				500				505				510			
Pro	Arg	Asn	His	Phe	Arg	Cys	Gln	Val	Gln	Phe	His	Gly	Leu	Ser	Glu
				515				520				525			
Glu	Asp	Lys	Trp	Pro	Glu	Gly	Ser	Pro	Lys	Pro	Val	Thr	Gln	Asn	Ile
				530				535				540			
Ser	Ala	Glu	Ala	Trp	Gly	Arg	Ala	Asp	Cys	Gly	Ile	Thr	Ser	Ala	Ser
545				550				555				560			
Tyr	Gln	Gln	Gly	Val	Leu	Ser	Ala	Thr	Ile	Leu	Tyr	Glu	Ile	Leu	Leu
				565				570				575			
Gly	Lys	Ala	Thr	Leu	Tyr	Ala	Val	Leu	Val	Ser	Thr	Leu	Val	Val	Met
				580				585				590			
Ala	Met	Val	Lys	Arg	Lys	Asn	Ser								
595				600											
<210>	566														
<211>	608														
<212>	PRT														
<213>	人工序列(Artificial Sequence)														

<220>

<223> 合成

<400> 566

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

Lys	Gln	Ala	Gly	Asp	Val	Glu	Glu	Asn	Pro	Gly	Pro	Met	His	Thr	Arg
290						295				300					
Leu	Leu	Cys	Trp	Ala	Ala	Leu	Cys	Leu	Leu	Gly	Ala	Glu	Leu	Thr	Glu
305					310					315					320
Ala	Gly	Val	Ala	Gln	Ser	Pro	Arg	Tyr	Lys	Ile	Ile	Glu	Lys	Arg	Gln
				325					330					335	
Ser	Val	Ala	Phe	Trp	Cys	Asn	Pro	Ile	Ser	Gly	His	Ala	Thr	Leu	Tyr
		340						345					350		
Trp	Tyr	Gln	Gln	Ile	Leu	Gly	Gln	Gly	Pro	Lys	Leu	Leu	Ile	Gln	Phe
	355					360					365				
Gln	Asn	Asn	Gly	Val	Val	Asp	Asp	Ser	Gln	Leu	Pro	Lys	Asp	Arg	Phe
370						375				380					
Ser	Ala	Glu	Arg	Leu	Lys	Gly	Val	Asp	Ser	Thr	Leu	Lys	Ile	Gln	Pro
385				390						395					400
Ala	Lys	Leu	Glu	Asp	Ser	Ala	Val	Tyr	Leu	Cys	Ala	Ser	Ser	His	Leu
			405						410					415	
Ala	Gly	Glu	Phe	Tyr	Asn	Glu	Gln	Phe	Phe	Gly	Pro	Gly	Thr	Arg	Leu
		420						425					430		
Thr	Val	Leu	Glu	Asp	Leu	Arg	Asn	Val	Thr	Pro	Pro	Lys	Val	Ser	Leu
	435						440					445			
Phe	Glu	Pro	Ser	Lys	Ala	Glu	Ile	Ala	Asn	Lys	Gln	Lys	Ala	Thr	Leu
450					455					460					
Val	Cys	Leu	Ala	Arg	Gly	Phe	Phe	Pro	Asp	His	Val	Glu	Leu	Ser	Trp
465				470						475					480
Trp	Val	Asn	Gly	Lys	Glu	Val	His	Ser	Gly	Val	Cys	Thr	Asp	Pro	Gln
			485						490				495		
Ala	Tyr	Lys	Glu	Ser	Asn	Tyr	Ser	Tyr	Cys	Leu	Ser	Ser	Arg	Leu	Arg
		500						505					510		
Val	Ser	Ala	Thr	Phe	Trp	His	Asn	Pro	Arg	Asn	His	Phe	Arg	Cys	Gln
	515					520						525			
Val	Gln	Phe	His	Gly	Leu	Ser	Glu	Glu	Asp	Lys	Trp	Pro	Glu	Gly	Ser
530					535					540					
Pro	Lys	Pro	Val	Thr	Gln	Asn	Ile	Ser	Ala	Glu	Ala	Trp	Gly	Arg	Ala
545					550					555					560
Asp	Cys	Gly	Ile	Thr	Ser	Ala	Ser	Tyr	Gln	Gln	Gly	Val	Leu	Ser	Ala
			565						570				575		
Thr	Ile	Leu	Tyr	Glu	Ile	Leu	Leu	Gly	Lys	Ala	Thr	Leu	Tyr	Ala	Val
		580						585				590			
Leu	Val	Ser	Thr	Leu	Val	Val	Met	Ala	Met	Val	Lys	Arg	Lys	Asn	Ser

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

Leu Ser Ala Thr Ile Leu Tyr Glu Ile Leu Leu Gly Lys Ala Thr Leu
 565 570 575
 Tyr Ala Val Leu Val Ser Thr Leu Val Val Met Ala Met Val Lys Arg
 580 585 590
 Lys Asn Ser
 595
 <210> 568
 <211> 599
 <212> PRT
 <213> 人工序列(Artificial Sequence)
 <220>
 <223> 合成
 <400> 568
 Met Ala Thr Leu Leu Gly Val Ser Leu Val Ile Leu Trp Leu Gln Leu
 1 5 10 15
 Ala Arg Val Asn Ser Gln Gln Gly Glu Glu Asp Pro Gln Ala Leu Ser
 20 25 30
 Ile Gln Glu Gly Glu Asn Ala Thr Met Asn Cys Ser Tyr Lys Thr Ser
 35 40 45
 Ile Asn Asn Leu Gln Trp Tyr Arg Gln Asn Ser Gly Arg Gly Leu Val
 50 55 60
 His Leu Ile Leu Ile Arg Ser Asn Glu Arg Glu Lys His Ser Gly Arg
 65 70 75 80
 Leu Arg Val Thr Leu Asp Thr Ser Lys Lys Ser Ser Ser Leu Leu Ile
 85 90 95
 Thr Ala Ser Arg Ala Ala Asp Thr Ala Ser Tyr Phe Cys Ala Thr Asp
 100 105 110
 Ala Trp Asn Asn Asp Met Arg Phe Gly Ala Gly Thr Arg Leu Thr Val
 115 120 125
 Lys Pro Asn Ile Gln Asn Pro Glu Pro Ala Val Tyr Gln Leu Lys Asp
 130 135 140
 Pro Arg Ser Gln Asp Ser Thr Leu Cys Leu Phe Thr Asp Phe Asp Ser
 145 150 155 160
 Gln Ile Asn Val Pro Lys Thr Met Glu Ser Gly Thr Phe Ile Thr Asp
 165 170 175
 Lys Cys Val Leu Asp Met Lys Ala Met Asp Ser Lys Ser Asn Gly Ala
 180 185 190
 Ile Ala Trp Ser Asn Gln Thr Ser Phe Thr Cys Gln Asp Ile Phe Lys
 195 200 205

Glu Thr Asn Ala Thr Tyr Pro Ser Ser Asp Val Pro Cys Asp Ala Thr		
210	215	220
Leu Thr Glu Lys Ser Phe Glu Thr Asp Met Asn Leu Asn Phe Gln Asn		
225	230	235 240
Leu Leu Val Ile Val Leu Arg Ile Leu Leu Lys Val Ala Gly Phe		
	245	250 255
Asn Leu Leu Met Thr Leu Arg Leu Trp Ser Ser Arg Ala Lys Arg Ser		
	260	265 270
Gly Ser Gly Ala Thr Asn Phe Ser Leu Leu Lys Gln Ala Gly Asp Val		
	275	280 285
Glu Glu Asn Pro Gly Pro Met His Ile Gly Leu Leu Cys Cys Val Ala		
	290	295 300
Phe Ser Leu Leu Trp Ala Ser Pro Val Asn Ala Gly Val Thr Gln Thr		
305	310	315 320
Pro Lys Phe Gln Val Leu Lys Thr Gly Gln Ser Met Thr Leu Gln Cys		
	325	330 335
Ala Gln Asp Met Asn His Asn Ser Met Tyr Trp Tyr Arg Gln Asp Pro		
	340	345 350
Gly Met Gly Leu Arg Leu Ile Tyr Tyr Ser Ala Ser Glu Gly Thr Thr		
	355	360 365
Asp Lys Gly Glu Val Pro Asn Gly Tyr Asn Val Ser Arg Leu Asn Lys		
	370	375 380
Arg Glu Phe Ser Leu Arg Leu Glu Ser Ala Ala Pro Ser Gln Thr Ser		
385	390	395 400
Val Tyr Phe Cys Ala Ser Ser Glu Ser Gln Gly Asn Thr Glu Ala Phe		
	405	410 415
Phe Gly Gln Gly Thr Arg Leu Thr Val Val Glu Asp Leu Arg Asn Val		
	420	425 430
Thr Pro Pro Lys Val Ser Leu Phe Glu Pro Ser Lys Ala Glu Ile Ala		
	435	440 445
Asn Lys Gln Lys Ala Thr Leu Val Cys Leu Ala Arg Gly Phe Phe Pro		
	450	455 460
Asp His Val Glu Leu Ser Trp Trp Val Asn Gly Lys Glu Val His Ser		
465	470	475 480
Gly Val Cys Thr Asp Pro Gln Ala Tyr Lys Glu Ser Asn Tyr Ser Tyr		
	485	490 495
Cys Leu Ser Ser Arg Leu Arg Val Ser Ala Thr Phe Trp His Asn Pro		
	500	505 510
Arg Asn His Phe Arg Cys Gln Val Gln Phe His Gly Leu Ser Glu Glu		

515	520	525
Asp Lys Trp Pro Glu Gly Ser	Pro Lys Pro Val Thr Gln Asn Ile Ser	
530	535	540
Ala Glu Ala Trp Gly Arg Ala Asp Cys Gly Ile Thr Ser Ala Ser Tyr		
545	550	555
Gln Gln Gly Val Leu Ser Ala Thr Ile Leu Tyr Glu Ile Leu Leu Gly		560
565	570	575
Lys Ala Thr Leu Tyr Ala Val Leu Val Ser Thr Leu Val Val Met Ala		
580	585	590
Met Val Lys Arg Lys Asn Ser		
595		
<210> 569		
<211> 601		
<212> PRT		
<213> 人工序列(Artificial Sequence)		
<220>		
<223> 合成		
<400> 569		
Met Ala Lys His Leu Thr Thr Phe Leu Val Ile Leu Trp Leu Tyr Phe		
1	5	10
Tyr Arg Gly Asn Gly Lys Asn Gln Val Glu Gln Ser Pro Gln Ser Leu		
20	25	30
Ile Ile Leu Glu Gly Lys Asn Cys Thr Leu Gln Cys Asn Tyr Thr Val		
35	40	45
Ser Pro Phe Ser Asn Leu Arg Trp Tyr Lys Gln Asp Thr Gly Arg Gly		
50	55	60
Pro Val Ser Leu Thr Ile Met Thr Phe Ser Glu Asn Thr Lys Ser Asn		
65	70	75
Gly Arg Tyr Thr Ala Thr Leu Asp Ala Asp Thr Lys Gln Ser Ser Leu		
85	90	95
His Ile Thr Ala Ser Gln Leu Ser Asp Ser Ala Ser Tyr Ile Cys Val		
100	105	110
Val Ser Ser Tyr Lys Ile Ile Phe Gly Thr Gly Thr Arg Leu His Val		
115	120	125
Phe Pro Asn Ile Gln Asn Pro Glu Pro Ala Val Tyr Gln Leu Lys Asp		
130	135	140
Pro Arg Ser Gln Asp Ser Thr Leu Cys Leu Phe Thr Asp Phe Asp Ser		
145	150	155
Gln Ile Asn Val Pro Lys Thr Met Glu Ser Gly Thr Phe Ile Thr Asp		160

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

His Ser Gly Val Cys Thr Asp Pro Gln Ala Tyr Lys Glu Ser Asn Tyr		
	485	490 495
Ser Tyr Cys Leu Ser Ser Arg Leu Arg Val Ser Ala Thr Phe Trp His		
	500	505 510
Asn Pro Arg Asn His Phe Arg Cys Gln Val Gln Phe His Gly Leu Ser		
	515	520 525
Glu Glu Asp Lys Trp Pro Glu Gly Ser Pro Lys Pro Val Thr Gln Asn		
	530	535 540
Ile Ser Ala Glu Ala Trp Gly Arg Ala Asp Cys Gly Ile Thr Ser Ala		
545	550	555 560
Ser Tyr Gln Gln Gly Val Leu Ser Ala Thr Ile Leu Tyr Glu Ile Leu		
	565	570 575
Leu Gly Lys Ala Thr Leu Tyr Ala Val Leu Val Ser Thr Leu Val Val		
	580	585 590
Met Ala Met Val Lys Arg Lys Asn Ser		
	595	600
<210> 570		
<211> 601		
<212> PRT		
<213> 人工序列(Artificial Sequence)		
<220>		
<223> 合成		
<400> 570		
Met Ala Lys His Leu Thr Thr Phe Leu Val Ile Leu Trp Leu Tyr Phe		
1	5	10 15
Tyr Arg Gly Asn Gly Lys Asn Gln Val Glu Gln Ser Pro Gln Ser Leu		
	20	25 30
Ile Ile Leu Glu Gly Lys Asn Cys Thr Leu Gln Cys Asn Tyr Thr Val		
	35	40 45
Ser Pro Phe Ser Asn Leu Arg Trp Tyr Lys Gln Asp Thr Gly Arg Gly		
	50	55 60
Pro Val Ser Leu Thr Ile Met Thr Phe Ser Glu Asn Thr Lys Ser Asn		
65	70	75 80
Gly Arg Tyr Thr Ala Thr Leu Asp Ala Asp Thr Lys Gln Ser Ser Leu		
	85	90 95
His Ile Thr Ala Ser Gln Leu Ser Asp Ser Ala Ser Tyr Ile Cys Val		
	100	105 110
Val Ser Ser Tyr Lys Leu Ile Phe Gly Thr Gly Thr Arg Leu Gln Val		
	115	120 125

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

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

Pro	Thr	Ala	Ser	Tyr	Leu	Cys	Ala	Ser	Glu	Ala	Phe	Phe	Gly	Gln	Gly
				405				410				415			
Thr	Arg	Leu	Thr	Val	Val	Glu	Asp	Leu	Arg	Asn	Val	Thr	Pro	Pro	Lys
				420				425				430			
Val	Ser	Leu	Phe	Glu	Pro	Ser	Lys	Ala	Glu	Ile	Ala	Asn	Lys	Gln	Lys
				435				440				445			
Ala	Thr	Leu	Val	Cys	Leu	Ala	Arg	Gly	Phe	Phe	Pro	Asp	His	Val	Glu
				450				455				460			
Leu	Ser	Trp	Trp	Val	Asn	Gly	Lys	Glu	Val	His	Ser	Gly	Val	Cys	Thr
465				470				475				480			
Asp	Pro	Gln	Ala	Tyr	Lys	Glu	Ser	Asn	Tyr	Ser	Tyr	Cys	Leu	Ser	Ser
				485				490				495			
Arg	Leu	Arg	Val	Ser	Ala	Thr	Phe	Trp	His	Asn	Pro	Arg	Asn	His	Phe
				500				505				510			
Arg	Cys	Gln	Val	Gln	Phe	His	Gly	Leu	Ser	Glu	Glu	Asp	Lys	Trp	Pro
				515				520				525			
Glu	Gly	Ser	Pro	Lys	Pro	Val	Thr	Gln	Asn	Ile	Ser	Ala	Glu	Ala	Trp
				530				535				540			
Gly	Arg	Ala	Asp	Cys	Gly	Ile	Thr	Ser	Ala	Ser	Tyr	Gln	Gln	Gly	Val
545				550				555				560			
Leu	Ser	Ala	Thr	Ile	Leu	Tyr	Glu	Ile	Leu	Leu	Gly	Lys	Ala	Thr	Leu
				565				570				575			
Tyr	Ala	Val	Leu	Val	Ser	Thr	Leu	Val	Val	Met	Ala	Met	Val	Lys	Arg
				580				585				590			
Lys	Asn	Ser													
595															
<210>				572											
<211>				597											
<212>				PRT											
<213>				人工序列(Artificial Sequence)											
<220>															
<223>				合成											
<400>				572											
Met	Ala	Leu	Val	Thr	Ser	Ile	Thr	Val	Leu	Leu	Ser	Leu	Gly	Ile	Met
1				5				10				15			
Gly	Asp	Ala	Lys	Thr	Thr	Gln	Pro	Asn	Ser	Met	Glu	Ser	Asn	Glu	Glu
				20				25				30			
Glu	Pro	Val	His	Leu	Pro	Cys	Asn	His	Ser	Thr	Ile	Ser	Gly	Thr	Asp
				35				40				45			

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

355	360	365
Glu Thr Val Pro Asn Arg Phe	Ser Pro Lys Ser Pro	Asp Lys Ala His
370	375	380
Leu Asn Leu His Ile Asn Ser	Leu Glu Leu Gly Asp Ser	Ala Val Tyr
385	390	395
Phe Cys Ala Ser Arg Thr Ile	Gly Tyr Asn Thr Glu Ala	Phe Phe Gly
405	410	415
Gln Gly Thr Arg Leu Thr Val	Val Glu Asp Leu Arg Asn	Val Thr Pro
420	425	430
Pro Lys Val Ser Leu Phe Glu	Pro Ser Lys Ala Glu Ile	Ala Asn Lys
435	440	445
Gln Lys Ala Thr Leu Val Cys	Leu Ala Arg Gly Phe Phe	Pro Asp His
450	455	460
Val Glu Leu Ser Trp Trp Val	Asn Gly Lys Glu Val His	Ser Gly Val
465	470	475
Cys Thr Asp Pro Gln Ala Tyr	Lys Glu Ser Asn Tyr Ser	Tyr Cys Leu
485	490	495
Ser Ser Arg Leu Arg Val Ser	Ala Thr Phe Trp His Asn	Pro Arg Asn
500	505	510
His Phe Arg Cys Gln Val Gln	Phe His Gly Leu Ser Glu	Glu Asp Lys
515	520	525
Trp Pro Glu Gly Ser Pro Lys	Pro Val Thr Gln Asn Ile	Ser Ala Glu
530	535	540
Ala Trp Gly Arg Ala Asp Cys	Gly Ile Thr Ser Ala Ser	Tyr Gln Gln
545	550	555
Gly Val Leu Ser Ala Thr Ile	Leu Tyr Glu Ile Leu Leu	Gly Lys Ala
565	570	575
Thr Leu Tyr Ala Val Leu Val	Ser Thr Leu Val Val Met	Ala Met Val
580	585	590
Lys Arg Lys Asn Ser		
595		
<210> 573		
<211> 602		
<212> PRT		
<213> 人工序列 (Artificial Sequence)		
<220>		
<223> 合成		
<400> 573		
Met Ala Lys Ile Arg Gln Phe	Leu Leu Ala Ile Leu Trp	Leu Gln Leu

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

Thr	Pro	Ser	Asn	Lys	Val	Thr	Glu	Lys	Gly	Lys	Tyr	Val	Glu	Leu	Arg			
																325	330	335
Cys	Asp	Pro	Ile	Ser	Gly	His	Thr	Ala	Leu	Tyr	Trp	Tyr	Arg	Gln	Ser			
																340	345	350
Leu	Gly	Gln	Gly	Pro	Glu	Phe	Leu	Ile	Tyr	Phe	Gln	Gly	Thr	Gly	Ala			
																355	360	365
Ala	Asp	Asp	Ser	Gly	Leu	Pro	Asn	Asp	Arg	Phe	Phe	Ala	Val	Arg	Pro			
																370	375	380
Glu	Gly	Ser	Val	Ser	Thr	Leu	Lys	Ile	Gln	Arg	Thr	Glu	Arg	Gly	Asp			
																385	390	400
Ser	Ala	Val	Tyr	Leu	Cys	Ala	Ser	Ser	Leu	Ser	Gly	Leu	Leu	Gln	Glu			
																405	410	415
Thr	Gln	Tyr	Phe	Gly	Pro	Gly	Thr	Arg	Leu	Leu	Val	Leu	Glu	Asp	Leu			
																420	425	430
Arg	Asn	Val	Thr	Pro	Pro	Lys	Val	Ser	Leu	Phe	Glu	Pro	Ser	Lys	Ala			
																435	440	445
Glu	Ile	Ala	Asn	Lys	Gln	Lys	Ala	Thr	Leu	Val	Cys	Leu	Ala	Arg	Gly			
																450	455	460
Phe	Phe	Pro	Asp	His	Val	Glu	Leu	Ser	Trp	Trp	Val	Asn	Gly	Lys	Glu			
																465	470	480
Val	His	Ser	Gly	Val	Cys	Thr	Asp	Pro	Gln	Ala	Tyr	Lys	Glu	Ser	Asn			
																485	490	495
Tyr	Ser	Tyr	Cys	Leu	Ser	Ser	Arg	Leu	Arg	Val	Ser	Ala	Thr	Phe	Trp			
																500	505	510
His	Asn	Pro	Arg	Asn	His	Phe	Arg	Cys	Gln	Val	Gln	Phe	His	Gly	Leu			
																515	520	525
Ser	Glu	Glu	Asp	Lys	Trp	Pro	Glu	Gly	Ser	Pro	Lys	Pro	Val	Thr	Gln			
																530	535	540
Asn	Ile	Ser	Ala	Glu	Ala	Trp	Gly	Arg	Ala	Asp	Cys	Gly	Ile	Thr	Ser			
																545	550	560
Ala	Ser	Tyr	Gln	Gln	Gly	Val	Leu	Ser	Ala	Thr	Ile	Leu	Tyr	Glu	Ile			
																565	570	575
Leu	Leu	Gly	Lys	Ala	Thr	Leu	Tyr	Ala	Val	Leu	Val	Ser	Thr	Leu	Val			
																580	585	590
Val	Met	Ala	Met	Val	Lys	Arg	Lys	Asn	Ser									
																595	600	

<210> 574
 <211> 605
 <212> PRT

<213> 人工序列(Artificial Sequence)

<220>

<223> 合成

<400> 574

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

275	280	285
Ala Gly Asp Val Glu Glu Asn Pro Gly Pro Met His Thr Arg Leu Leu		
290	295	300
Cys Trp Ala Ala Leu Cys Leu Leu Gly Ala Glu Leu Thr Glu Ala Gly		
305	310	315
Val Ala Gln Ser Pro Arg Tyr Lys Ile Ile Glu Lys Arg Gln Ser Val		
325	330	335
Ala Phe Trp Cys Asn Pro Ile Ser Gly His Ala Thr Leu Tyr Trp Tyr		
340	345	350
Gln Gln Ile Leu Gly Gln Gly Pro Lys Leu Leu Ile Gln Phe Gln Asn		
355	360	365
Asn Gly Val Val Asp Asp Ser Gln Leu Pro Lys Asp Arg Phe Ser Ala		
370	375	380
Glu Arg Leu Lys Gly Val Asp Ser Thr Leu Lys Ile Gln Pro Ala Lys		
385	390	395
Leu Glu Asp Ser Ala Val Tyr Leu Cys Ala Ser Ser Thr Gly Gly Gly		
405	410	415
Arg His Gln Pro Gln His Phe Gly Asp Gly Thr Arg Leu Ser Ile Leu		
420	425	430
Glu Asp Leu Arg Asn Val Thr Pro Pro Lys Val Ser Leu Phe Glu Pro		
435	440	445
Ser Lys Ala Glu Ile Ala Asn Lys Gln Lys Ala Thr Leu Val Cys Leu		
450	455	460
Ala Arg Gly Phe Phe Pro Asp His Val Glu Leu Ser Trp Trp Val Asn		
465	470	475
Gly Lys Glu Val His Ser Gly Val Cys Thr Asp Pro Gln Ala Tyr Lys		
485	490	495
Glu Ser Asn Tyr Ser Tyr Cys Leu Ser Ser Arg Leu Arg Val Ser Ala		
500	505	510
Thr Phe Trp His Asn Pro Arg Asn His Phe Arg Cys Gln Val Gln Phe		
515	520	525
His Gly Leu Ser Glu Glu Asp Lys Trp Pro Glu Gly Ser Pro Lys Pro		
530	535	540
Val Thr Gln Asn Ile Ser Ala Glu Ala Trp Gly Arg Ala Asp Cys Gly		
545	550	555
Ile Thr Ser Ala Ser Tyr Gln Gln Gly Val Leu Ser Ala Thr Ile Leu		
565	570	575
Tyr Glu Ile Leu Leu Gly Lys Ala Thr Leu Tyr Ala Val Leu Val Ser		
580	585	590

Thr Leu Val Val Met Ala Met Val Lys Arg Lys Asn Ser
 595 600 605
 <210> 575
 <211> 605
 <212> PRT
 <213> 人工序列(Artificial Sequence)
 <220>
 <223> 合成
 <400> 575
 Met Ala Tyr Ser Pro Gly Leu Val Ser Leu Ile Leu Leu Leu Gly
 1 5 10 15
 Arg Thr Arg Gly Asn Ser Val Thr Gln Met Glu Gly Pro Val Thr Leu
 20 25 30
 Ser Glu Glu Ala Phe Leu Thr Ile Asn Cys Thr Tyr Thr Ala Thr Gly
 35 40 45
 Tyr Pro Ser Leu Phe Trp Tyr Val Gln Tyr Pro Gly Glu Gly Leu Gln
 50 55 60
 Leu Leu Leu Lys Ala Thr Lys Ala Asp Asp Lys Gly Ser Asn Lys Gly
 65 70 75 80
 Phe Glu Ala Thr Tyr Arg Lys Glu Thr Thr Ser Phe His Leu Glu Lys
 85 90 95
 Gly Ser Val Gln Val Ser Asp Ser Ala Val Tyr Phe Cys Ala Leu Ser
 100 105 110
 Gln Thr Gly Ser Ser Lys Thr Gly Lys Leu Ile Phe Gly Gln Gly Thr
 115 120 125
 Arg Leu Gln Val Lys Pro Asn Ile Gln Asn Pro Glu Pro Ala Val Tyr
 130 135 140
 Gln Leu Lys Asp Pro Arg Ser Gln Asp Ser Thr Leu Cys Leu Phe Thr
 145 150 155 160
 Asp Phe Asp Ser Gln Ile Asn Val Pro Lys Thr Met Glu Ser Gly Thr
 165 170 175
 Phe Ile Thr Asp Lys Cys Val Leu Asp Met Lys Ala Met Asp Ser Lys
 180 185 190
 Ser Asn Gly Ala Ile Ala Trp Ser Asn Gln Thr Ser Phe Thr Cys Gln
 195 200 205
 Asp Ile Phe Lys Glu Thr Asn Ala Thr Tyr Pro Ser Ser Asp Val Pro
 210 215 220
 Cys Asp Ala Thr Leu Thr Glu Lys Ser Phe Glu Thr Asp Met Asn Leu
 225 230 235 240

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

545	550	555	560
Ile Thr Ser Ala Ser Tyr Gln Gln Gly Val Leu Ser Ala Thr Ile Leu			
	565	570	575
Tyr Glu Ile Leu Leu Gly Lys Ala Thr Leu Tyr Ala Val Leu Val Ser			
	580	585	590
Thr Leu Val Val Met Ala Met Val Lys Arg Lys Asn Ser			
	595	600	605
<210> 576			
<211> 605			
<212> PRT			
<213> 人工序列(Artificial Sequence)			
<220>			
<223> 合成			
<400> 576			
Met Ala Tyr Ser Pro Gly Leu Val Ser Leu Ile Leu Leu Leu Gly			
1 5 10 15			
Arg Thr Arg Gly Asn Ser Val Thr Gln Met Glu Gly Pro Val Thr Leu			
20 25 30			
Ser Glu Glu Ala Phe Leu Thr Ile Asn Cys Thr Tyr Thr Ala Thr Gly			
35 40 45			
Tyr Pro Ser Leu Phe Trp Tyr Val Gln Tyr Pro Gly Glu Gly Leu Gln			
50 55 60			
Leu Leu Leu Lys Ala Thr Lys Ala Asp Asp Lys Gly Ser Asn Lys Gly			
65 70 75 80			
Phe Glu Ala Thr Tyr Arg Lys Glu Thr Thr Ser Phe His Leu Glu Lys			
85 90 95			
Gly Ser Val Gln Val Ser Asp Ser Ala Val Tyr Phe Cys Ala Leu Ser			
100 105 110			
Gln Thr Gly Ser Ser Asn Thr Gly Lys Leu Ile Phe Gly Gln Gly Thr			
115 120 125			
Arg Leu Gln Val Lys Pro Asn Ile Gln Asn Pro Glu Pro Ala Val Tyr			
130 135 140			
Gln Leu Lys Asp Pro Arg Ser Gln Asp Ser Thr Leu Cys Leu Phe Thr			
145 150 155 160			
Asp Phe Asp Ser Gln Ile Asn Val Pro Lys Thr Met Glu Ser Gly Thr			
165 170 175			
Phe Ile Thr Asp Lys Cys Val Leu Asp Met Lys Ala Met Asp Ser Lys			
180 185 190			
Ser Asn Gly Ala Ile Ala Trp Ser Asn Gln Thr Ser Phe Thr Cys Gln			

195	200	205
Asp Ile Phe Lys Glu Thr Asn Ala Thr Tyr Pro Ser Ser Asp Val Pro		
210	215	220
Cys Asp Ala Thr Leu Thr Glu Lys Ser Phe Glu Thr Asp Met Asn Leu		
225	230	235
Asn Phe Gln Asn Leu Leu Val Ile Val Leu Arg Ile Leu Leu Leu Lys		
245	250	255
Val Ala Gly Phe Asn Leu Leu Met Thr Leu Arg Leu Trp Ser Ser Arg		
260	265	270
Ala Lys Arg Ser Gly Ser Gly Ala Thr Asn Phe Ser Leu Leu Lys Gln		
275	280	285
Ala Gly Asp Val Glu Glu Asn Pro Gly Pro Met His Thr Arg Leu Leu		
290	295	300
Cys Trp Ala Ala Leu Cys Leu Leu Gly Ala Glu Leu Thr Glu Ala Gly		
305	310	315
Val Ala Gln Ser Pro Arg Tyr Lys Ile Ile Glu Lys Arg Gln Ser Val		
325	330	335
Ala Phe Trp Cys Asn Pro Ile Ser Gly His Ala Thr Leu Tyr Trp Tyr		
340	345	350
Gln Gln Ile Leu Gly Gln Gly Pro Lys Leu Leu Ile Gln Phe Gln Asn		
355	360	365
Asn Gly Val Val Asp Asp Ser Gln Leu Pro Lys Asp Arg Phe Ser Ala		
370	375	380
Glu Arg Leu Lys Gly Val Asp Ser Thr Leu Lys Ile Gln Pro Ala Lys		
385	390	395
Leu Glu Asp Ser Ala Val Tyr Leu Cys Ala Ser Ser Thr Gly Gly Gly		
405	410	415
Arg His Gln Pro Gln His Phe Gly Asp Gly Thr Arg Leu Ser Ile Leu		
420	425	430
Glu Asp Leu Arg Asn Val Thr Pro Pro Lys Val Ser Leu Phe Glu Pro		
435	440	445
Ser Lys Ala Glu Ile Ala Asn Lys Gln Lys Ala Thr Leu Val Cys Leu		
450	455	460
Ala Arg Gly Phe Phe Pro Asp His Val Glu Leu Ser Trp Trp Val Asn		
465	470	475
Gly Lys Glu Val His Ser Gly Val Cys Thr Asp Pro Gln Ala Tyr Lys		
485	490	495
Glu Ser Asn Tyr Ser Tyr Cys Leu Ser Ser Arg Leu Arg Val Ser Ala		
500	505	510

Thr	Phe	Trp	His	Asn	Pro	Arg	Asn	His	Phe	Arg	Cys	Gln	Val	Gln	Phe
515				520				525							
His	Gly	Leu	Ser	Glu	Glu	Asp	Lys	Trp	Pro	Glu	Gly	Ser	Pro	Lys	Pro
530				535				540							
Val	Thr	Gln	Asn	Ile	Ser	Ala	Glu	Ala	Trp	Gly	Arg	Ala	Asp	Cys	Gly
545				550				555				560			
Ile	Thr	Ser	Ala	Ser	Tyr	Gln	Gln	Gly	Val	Leu	Ser	Ala	Thr	Ile	Leu
				565				570				575			
Tyr	Glu	Ile	Leu	Leu	Gly	Lys	Ala	Thr	Leu	Tyr	Ala	Val	Leu	Val	Ser
				580				585				590			
Thr	Leu	Val	Val	Met	Ala	Met	Val	Lys	Arg	Lys	Asn	Ser			
595				600				605							

<210> 577
 <211> 605
 <212> PRT
 <213> 人工序列(Artificial Sequence)
 <220>
 <223> 合成
 <400> 577

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

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

465	470	475	480
Gly Lys Glu Val His Ser Gly Val Cys Thr Asp Pro Gln Ala Tyr Lys			
	485	490	495
Glu Ser Asn Tyr Ser Tyr Cys Leu Ser Ser Arg Leu Arg Val Ser Ala			
500	505	510	
Thr Phe Trp His Asn Pro Arg Asn His Phe Arg Cys Gln Val Gln Phe			
515	520	525	
His Gly Leu Ser Glu Glu Asp Lys Trp Pro Glu Gly Ser Pro Lys Pro			
530	535	540	
Val Thr Gln Asn Ile Ser Ala Glu Ala Trp Gly Arg Ala Asp Cys Gly			
545	550	555	560
Ile Thr Ser Ala Ser Tyr Gln Gln Gly Val Leu Ser Ala Thr Ile Leu			
565	570	575	
Tyr Glu Ile Leu Leu Gly Lys Ala Thr Leu Tyr Ala Val Leu Val Ser			
580	585	590	
Thr Leu Val Val Met Ala Met Val Lys Arg Lys Asn Ser			
595	600	605	
<210> 578			
<211> 598			
<212> PRT			
<213> 人工序列(Artificial Sequence)			
<220>			
<223> 合成			
<400> 578			
Met Ala Ser Leu Arg Val Leu Leu Val Ile Leu Trp Leu Gln Leu Ser			
1	5	10	15
Trp Val Trp Ser Gln Gln Lys Glu Val Glu Gln Asn Ser Gly Pro Leu			
20	25	30	
Ser Val Pro Glu Gly Ala Ile Ala Ser Leu Asn Cys Thr Tyr Ser Asp			
35	40	45	
Arg Gly Ser Gln Ser Phe Phe Trp Tyr Arg Gln Tyr Ser Gly Lys Ser			
50	55	60	
Pro Glu Leu Ile Met Phe Ile Tyr Ser Asn Gly Asp Lys Glu Asp Gly			
65	70	75	80
Arg Phe Thr Ala Gln Leu Asn Lys Ala Ser Gln Tyr Val Ser Leu Leu			
85	90	95	
Ile Arg Asp Ser Gln Pro Ser Asp Ser Ala Thr Tyr Leu Cys Ala Val			
100	105	110	
Ser Trp Tyr Ser Thr Leu Thr Phe Gly Lys Gly Thr Met Leu Leu Val			

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

Pro Pro Lys Val Ser Leu Phe Glu Pro Ser Lys Ala Glu Ile Ala Asn
 435 440 445
 Lys Gln Lys Ala Thr Leu Val Cys Leu Ala Arg Gly Phe Phe Pro Asp
 450 455 460
 His Val Glu Leu Ser Trp Trp Val Asn Gly Lys Glu Val His Ser Gly
 465 470 475 480
 Val Cys Thr Asp Pro Gln Ala Tyr Lys Glu Ser Asn Tyr Ser Tyr Cys
 485 490 495
 Leu Ser Ser Arg Leu Arg Val Ser Ala Thr Phe Trp His Asn Pro Arg
 500 505 510
 Asn His Phe Arg Cys Gln Val Gln Phe His Gly Leu Ser Glu Glu Asp
 515 520 525
 Lys Trp Pro Glu Gly Ser Pro Lys Pro Val Thr Gln Asn Ile Ser Ala
 530 535 540
 Glu Ala Trp Gly Arg Ala Asp Cys Gly Ile Thr Ser Ala Ser Tyr Gln
 545 550 555 560
 Gln Gly Val Leu Ser Ala Thr Ile Leu Tyr Glu Ile Leu Leu Gly Lys
 565 570 575
 Ala Thr Leu Tyr Ala Val Leu Val Ser Thr Leu Val Val Met Ala Met
 580 585 590
 Val Lys Arg Lys Asn Ser
 595
 <210> 579
 <211> 597
 <212> PRT
 <213> 人工序列(Artificial Sequence)
 <220>
 <223> 合成
 <400> 579
 Met Ala Leu Lys Phe Ser Val Ser Ile Leu Trp Ile Gln Leu Ala Trp
 1 5 10 15
 Val Ser Thr Gln Leu Leu Glu Gln Ser Pro Gln Phe Leu Ser Ile Gln
 20 25 30
 Glu Gly Glu Asn Leu Thr Val Tyr Cys Asn Ser Ser Ser Val Phe Ser
 35 40 45
 Ser Leu Gln Trp Tyr Arg Gln Glu Pro Gly Glu Gly Pro Val Leu Leu
 50 55 60
 Val Thr Val Val Thr Gly Gly Glu Val Lys Lys Leu Lys Arg Leu Thr
 65 70 75 80

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

385	390	395	400
Leu Cys Ala Ser Ser Gln Val Gly Leu Thr Tyr Glu Gln Tyr Phe Gly			
	405	410	415
Pro Gly Thr Arg Leu Thr Val Thr Glu Asp Leu Arg Asn Val Thr Pro			
	420	425	430
Pro Lys Val Ser Leu Phe Glu Pro Ser Lys Ala Glu Ile Ala Asn Lys			
	435	440	445
Gln Lys Ala Thr Leu Val Cys Leu Ala Arg Gly Phe Phe Pro Asp His			
	450	455	460
Val Glu Leu Ser Trp Trp Val Asn Gly Lys Glu Val His Ser Gly Val			
465	470	475	480
Cys Thr Asp Pro Gln Ala Tyr Lys Glu Ser Asn Tyr Ser Tyr Cys Leu			
	485	490	495
Ser Ser Arg Leu Arg Val Ser Ala Thr Phe Trp His Asn Pro Arg Asn			
	500	505	510
His Phe Arg Cys Gln Val Gln Phe His Gly Leu Ser Glu Glu Asp Lys			
	515	520	525
Trp Pro Glu Gly Ser Pro Lys Pro Val Thr Gln Asn Ile Ser Ala Glu			
	530	535	540
Ala Trp Gly Arg Ala Asp Cys Gly Ile Thr Ser Ala Ser Tyr Gln Gln			
545	550	555	560
Gly Val Leu Ser Ala Thr Ile Leu Tyr Glu Ile Leu Leu Gly Lys Ala			
	565	570	575
Thr Leu Tyr Ala Val Leu Val Ser Thr Leu Val Val Met Ala Met Val			
	580	585	590
Lys Arg Lys Asn Ser			
	595		
<210> 580			
<211> 604			
<212> PRT			
<213> 人工序列(Artificial Sequence)			
<220>			
<223> 合成			
<400> 580			
Met Ala Ser Ala Pro Ile Ser Met Leu Ala Met Leu Phe Thr Leu Ser			
1	5	10	15
Gly Leu Arg Ala Gln Ser Val Ala Gln Pro Glu Asp Gln Val Asn Val			
	20	25	30
Ala Glu Gly Asn Pro Leu Thr Val Lys Cys Thr Tyr Ser Val Ser Gly			

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

Tyr	Gln	Gln	Ile	Leu	Gly	Gln	Gly	Pro	Lys	Leu	Leu	Ile	Gln	Phe	Gln
355				360				365							
Asn	Asn	Gly	Val	Val	Asp	Asp	Ser	Gln	Leu	Pro	Lys	Asp	Arg	Phe	Ser
370				375				380							
Ala	Glu	Arg	Leu	Lys	Gly	Val	Asp	Ser	Thr	Leu	Lys	Ile	Gln	Pro	Ala
385				390				395				400			
Lys	Leu	Glu	Asp	Ser	Ala	Val	Tyr	Leu	Cys	Ala	Ser	Ser	Leu	Gly	Gln
				405				410				415			
Gly	Gln	Thr	Gln	Tyr	Phe	Gly	Pro	Gly	Thr	Arg	Leu	Leu	Val	Leu	Glu
				420				425				430			
Asp	Leu	Arg	Asn	Val	Thr	Pro	Pro	Lys	Val	Ser	Leu	Phe	Glu	Pro	Ser
				435				440				445			
Lys	Ala	Glu	Ile	Ala	Asn	Lys	Gln	Lys	Ala	Thr	Leu	Val	Cys	Leu	Ala
450				455				460							
Arg	Gly	Phe	Phe	Pro	Asp	His	Val	Glu	Leu	Ser	Trp	Trp	Val	Asn	Gly
465				470				475				480			
Lys	Glu	Val	His	Ser	Gly	Val	Cys	Thr	Asp	Pro	Gln	Ala	Tyr	Lys	Glu
				485				490				495			
Ser	Asn	Tyr	Ser	Tyr	Cys	Leu	Ser	Ser	Arg	Leu	Arg	Val	Ser	Ala	Thr
500				505				510							
Phe	Trp	His	Asn	Pro	Arg	Asn	His	Phe	Arg	Cys	Gln	Val	Gln	Phe	His
515				520				525							
Gly	Leu	Ser	Glu	Glu	Asp	Lys	Trp	Pro	Glu	Gly	Ser	Pro	Lys	Pro	Val
530				535				540							
Thr	Gln	Asn	Ile	Ser	Ala	Glu	Ala	Trp	Gly	Arg	Ala	Asp	Cys	Gly	Ile
545				550				555				560			
Thr	Ser	Ala	Ser	Tyr	Gln	Gln	Gly	Val	Leu	Ser	Ala	Thr	Ile	Leu	Tyr
				565				570				575			
Glu	Ile	Leu	Leu	Gly	Lys	Ala	Thr	Leu	Tyr	Ala	Val	Leu	Val	Ser	Thr
580				585				590							
Leu	Val	Val	Met	Ala	Met	Val	Lys	Arg	Lys	Asn	Ser				
595				600											

<210> 581
 <211> 601
 <212> PRT
 <213> 人工序列(Artificial Sequence)
 <220>
 <223> 合成
 <400> 581

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

305	310	315	320
Thr Gln Ser Ser Arg Tyr Leu Val Lys Arg Thr Gly Glu Lys Val Phe			
	325	330	335
Leu Glu Cys Val Gln Asp Met Asp His Glu Asn Met Phe Trp Tyr Arg			
	340	345	350
Gln Asp Pro Gly Leu Gly Leu Arg Leu Ile Tyr Phe Ser Tyr Asp Val			
	355	360	365
Lys Met Lys Glu Lys Gly Asp Ile Pro Glu Gly Tyr Ser Val Ser Arg			
	370	375	380
Glu Lys Lys Glu Arg Phe Ser Leu Ile Leu Glu Ser Ala Ser Thr Asn			
385	390	395	400
Gln Thr Ser Met Tyr Leu Cys Ala Ser Lys Gly Asp Gln Asn Thr Glu			
	405	410	415
Ala Phe Phe Gly Gln Gly Thr Arg Leu Thr Val Val Glu Asp Leu Arg			
	420	425	430
Asn Val Thr Pro Pro Lys Val Ser Leu Phe Glu Pro Ser Lys Ala Glu			
	435	440	445
Ile Ala Asn Lys Gln Lys Ala Thr Leu Val Cys Leu Ala Arg Gly Phe			
	450	455	460
Phe Pro Asp His Val Glu Leu Ser Trp Trp Val Asn Gly Lys Glu Val			
465	470	475	480
His Ser Gly Val Cys Thr Asp Pro Gln Ala Tyr Lys Glu Ser Asn Tyr			
	485	490	495
Ser Tyr Cys Leu Ser Ser Arg Leu Arg Val Ser Ala Thr Phe Trp His			
	500	505	510
Asn Pro Arg Asn His Phe Arg Cys Gln Val Gln Phe His Gly Leu Ser			
	515	520	525
Glu Glu Asp Lys Trp Pro Glu Gly Ser Pro Lys Pro Val Thr Gln Asn			
	530	535	540
Ile Ser Ala Glu Ala Trp Gly Arg Ala Asp Cys Gly Ile Thr Ser Ala			
545	550	555	560
Ser Tyr Gln Gln Gly Val Leu Ser Ala Thr Ile Leu Tyr Glu Ile Leu			
	565	570	575
Leu Gly Lys Ala Thr Leu Tyr Ala Val Leu Val Ser Thr Leu Val Val			
	580	585	590
Met Ala Met Val Lys Arg Lys Asn Ser			
	595	600	
<210> 582			
<211> 598			

<212> PRT

<213> 人工序列(Artificial Sequence)

<220>

<223> 合成

<400> 582

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

Ser Gly Ala Thr Asn Phe Ser Leu Leu Lys Gln Ala Gly Asp Val Glu		
275	280	285
Glu Asn Pro Gly Pro Met His Ile Arg Leu Leu Cys Arg Val Ala Phe		
290	295	300
Cys Phe Leu Ala Val Gly Leu Val Asp Val Lys Val Thr Gln Ser Ser		
305	310	315
Arg Tyr Leu Val Lys Arg Thr Gly Glu Lys Val Phe Leu Glu Cys Val		
	325	330
Gln Asp Met Asp His Glu Asn Met Phe Trp Tyr Arg Gln Asp Pro Gly		
	340	345
Leu Gly Leu Arg Leu Ile Tyr Phe Ser Tyr Asp Val Lys Met Lys Glu		
	355	360
Lys Gly Asp Ile Pro Glu Gly Tyr Ser Val Ser Arg Glu Lys Lys Glu		
	370	375
Arg Phe Ser Leu Ile Leu Glu Ser Ala Ser Thr Asn Gln Thr Ser Met		
385	390	395
Tyr Leu Cys Ala Ser Ser Leu Thr Phe Gly Thr Thr Glu Ala Phe Phe		
	405	410
Gly Gln Gly Thr Arg Leu Thr Val Val Glu Asp Leu Arg Asn Val Thr		
	420	425
Pro Pro Lys Val Ser Leu Phe Glu Pro Ser Lys Ala Glu Ile Ala Asn		
	435	440
Lys Gln Lys Ala Thr Leu Val Cys Leu Ala Arg Gly Phe Phe Pro Asp		
	450	455
His Val Glu Leu Ser Trp Trp Val Asn Gly Lys Glu Val His Ser Gly		
465	470	475
Val Cys Thr Asp Pro Gln Ala Tyr Lys Glu Ser Asn Tyr Ser Tyr Cys		
	485	490
Leu Ser Ser Arg Leu Arg Val Ser Ala Thr Phe Trp His Asn Pro Arg		
	500	505
Asn His Phe Arg Cys Gln Val Gln Phe His Gly Leu Ser Glu Glu Asp		
	515	520
Lys Trp Pro Glu Gly Ser Pro Lys Pro Val Thr Gln Asn Ile Ser Ala		
	530	535
Glu Ala Trp Gly Arg Ala Asp Cys Gly Ile Thr Ser Ala Ser Tyr Gln		
545	550	555
Gln Gly Val Leu Ser Ala Thr Ile Leu Tyr Glu Ile Leu Leu Gly Lys		
	565	570
Ala Thr Leu Tyr Ala Val Leu Val Ser Thr Leu Val Val Met Ala Met		

580	585	590
Val Lys Arg Lys Asn Ser		
595		
<210> 583		
<211> 599		
<212> PRT		
<213> 人工序列(Artificial Sequence)		
<220>		
<223> 合成		
<400> 583		
Met Ala Leu Leu Leu Val Pro Ala Phe Gln Val Ile Phe Thr Leu Gly		
1 5 10 15		
Gly Thr Arg Ala Gln Ser Val Thr Gln Leu Asp Ser Gln Val Pro Val		
20 25 30		
Phe Glu Glu Ala Pro Val Glu Leu Arg Cys Asn Tyr Ser Ser Ser Val		
35 40 45		
Ser Val Tyr Leu Phe Trp Tyr Val Gln Tyr Pro Asn Gln Gly Leu Gln		
50 55 60		
Leu Leu Leu Lys Tyr Leu Ser Gly Ser Thr Leu Val Glu Ser Ile Asn		
65 70 75 80		
Gly Phe Glu Ala Glu Phe Asn Lys Ser Gln Thr Ser Phe His Leu Arg		
85 90 95		
Lys Pro Ser Val His Ile Ser Asp Thr Ala Glu Tyr Phe Cys Ala Val		
100 105 110		
Ser Asp Leu Val Arg Asp Asp Lys Ile Ile Phe Gly Lys Gly Thr Arg		
115 120 125		
Leu His Ile Leu Pro Asn Ile Gln Asn Pro Glu Pro Ala Val Tyr Gln		
130 135 140		
Leu Lys Asp Pro Arg Ser Gln Asp Ser Thr Leu Cys Leu Phe Thr Asp		
145 150 155 160		
Phe Asp Ser Gln Ile Asn Val Pro Lys Thr Met Glu Ser Gly Thr Phe		
165 170 175		
Ile Thr Asp Lys Cys Val Leu Asp Met Lys Ala Met Asp Ser Lys Ser		
180 185 190		
Asn Gly Ala Ile Ala Trp Ser Asn Gln Thr Ser Phe Thr Cys Gln Asp		
195 200 205		
Ile Phe Lys Glu Thr Asn Ala Thr Tyr Pro Ser Ser Asp Val Pro Cys		
210 215 220		
Asp Ala Thr Leu Thr Glu Lys Ser Phe Glu Thr Asp Met Asn Leu Asn		

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

Ala Glu Ala Trp Gly Arg Ala Asp Cys Gly Ile Thr Ser Ala Ser Tyr
 545 550 555 560
 Gln Gln Gly Val Leu Ser Ala Thr Ile Leu Tyr Glu Ile Leu Leu Gly
 565 570 575
 Lys Ala Thr Leu Tyr Ala Val Leu Val Ser Thr Leu Val Val Met Ala
 580 585 590
 Met Val Lys Arg Lys Asn Ser
 595

<210> 584

<211> 597

<212> PRT

<213> 人工序列(Artificial Sequence)

<220>

<223> 合成

<400> 584

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

Asn Gln Thr Ser Phe Thr Cys Gln Asp Ile Phe Lys Glu Thr Asn Ala		
195	200	205
Thr Tyr Pro Ser Ser Asp Val Pro Cys Asp Ala Thr Leu Thr Glu Lys		
210	215	220
Ser Phe Glu Thr Asp Met Asn Leu Asn Phe Gln Asn Leu Leu Val Ile		
225	230	235
Val Leu Arg Ile Leu Leu Leu Lys Val Ala Gly Phe Asn Leu Leu Met		
	245	250
Thr Leu Arg Leu Trp Ser Ser Arg Ala Lys Arg Ser Gly Ser Gly Ala		
	260	265
Thr Asn Phe Ser Leu Leu Lys Gln Ala Gly Asp Val Glu Glu Asn Pro		
	275	280
Gly Pro Met His Thr Arg Leu Leu Cys Trp Ala Ala Leu Cys Leu Leu		
	290	295
Gly Ala Glu Leu Thr Glu Ala Gly Val Ala Gln Ser Pro Arg Tyr Lys		
305	310	315
Ile Ile Glu Lys Arg Gln Ser Val Ala Phe Trp Cys Asn Pro Ile Ser		
	325	330
Gly His Ala Thr Leu Tyr Trp Tyr Gln Gln Ile Leu Gly Gln Gly Pro		
	340	345
Lys Leu Leu Ile Gln Phe Gln Asn Asn Gly Val Val Asp Asp Ser Gln		
	355	360
Leu Pro Lys Asp Arg Phe Ser Ala Glu Arg Leu Lys Gly Val Asp Ser		
	370	375
Thr Leu Lys Ile Gln Pro Ala Lys Leu Glu Asp Ser Ala Val Tyr Leu		
385	390	395
Cys Ala Ser Asn Leu Gly Gly Gly Ser Thr Asp Thr Gln Tyr Phe Gly		
	405	410
Pro Gly Thr Arg Leu Thr Val Leu Glu Asp Leu Arg Asn Val Thr Pro		
	420	425
Pro Lys Val Ser Leu Phe Glu Pro Ser Lys Ala Glu Ile Ala Asn Lys		
	435	440
Gln Lys Ala Thr Leu Val Cys Leu Ala Arg Gly Phe Phe Pro Asp His		
	450	455
Val Glu Leu Ser Trp Trp Val Asn Gly Lys Glu Val His Ser Gly Val		
465	470	475
Cys Thr Asp Pro Gln Ala Tyr Lys Glu Ser Asn Tyr Ser Tyr Cys Leu		
	485	490
Ser Ser Arg Leu Arg Val Ser Ala Thr Phe Trp His Asn Pro Arg Asn		

500	505	510
His Phe Arg Cys Gln Val Gln Phe	His Gly Leu Ser Glu Glu Asp Lys	
515	520	525
Trp Pro Glu Gly Ser Pro Lys Pro	Val Thr Gln Asn Ile Ser Ala Glu	
530	535	540
Ala Trp Gly Arg Ala Asp Cys Gly	Ile Thr Ser Ala Ser Tyr Gln Gln	
545	550	555
Gly Val Leu Ser Ala Thr Ile Leu Tyr	Glu Ile Leu Leu Gly Lys Ala	
565	570	575
Thr Leu Tyr Ala Val Leu Val Ser Thr	Leu Val Val Met Ala Met Val	
580	585	590
Lys Arg Lys Asn Ser		
595		
<210> 585		
<211> 599		
<212> PRT		
<213> 人工序列(Artificial Sequence)		
<220>		
<223> 合成		
<400> 585		
Met Ala Gly Val Phe Leu Leu Tyr Val	Ser Met Lys Met Gly Gly Thr	
1	5	10
Thr Gly Gln Asn Ile Asp Gln Pro Thr	Glu Met Thr Ala Thr Glu Gly	
20	25	30
Ala Ile Val Gln Ile Asn Cys Thr Tyr	Gln Thr Ser Gly Phe Asn Gly	
35	40	45
Leu Phe Trp Tyr Gln Gln His Ala Gly	Glu Ala Pro Thr Phe Leu Ser	
50	55	60
Tyr Asn Val Leu Asp Gly Leu Glu Glu	Lys Gly Arg Phe Ser Ser Phe	
65	70	75
Leu Ser Arg Ser Lys Gly Tyr Ser Tyr	Leu Leu Leu Lys Glu Leu Gln	
85	90	95
Met Lys Asp Ser Ala Ser Tyr Leu Cys	Ala Phe Tyr Tyr Gly Gly Ser	
100	105	110
Gln Gly Asn Leu Ile Phe Gly Lys Gly	Thr Lys Leu Ser Val Lys Pro	
115	120	125
Asn Ile Gln Asn Pro Glu Pro Ala Val	Tyr Gln Leu Lys Asp Pro Arg	
130	135	140
Ser Gln Asp Ser Thr Leu Cys Leu Phe	Thr Asp Phe Asp Ser Gln Ile	

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

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

<210> 586

<211> 599

<212> PRT

<213> 人工序列(Artificial Sequence)

<220>

<223> 合成

<400> 586

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

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

420	425	430
Thr Pro Pro Lys Val Ser Leu Phe	Glu Pro Ser Lys Ala Glu Ile Ala	
435	440	445
Asn Lys Gln Lys Ala Thr Leu Val	Cys Leu Ala Arg Gly Phe Phe Pro	
450	455	460
Asp His Val Glu Leu Ser Trp Trp	Val Asn Gly Lys Glu Val His Ser	
465	470	475
Gly Val Cys Thr Asp Pro Gln Ala	Tyr Lys Glu Ser Asn Tyr Ser Tyr	
485	490	495
Cys Leu Ser Ser Arg Leu Arg Val	Ser Ala Thr Phe Trp His Asn Pro	
500	505	510
Arg Asn His Phe Arg Cys Gln Val	Gln Phe His Gly Leu Ser Glu Glu	
515	520	525
Asp Lys Trp Pro Glu Gly Ser Pro	Lys Pro Val Thr Gln Asn Ile Ser	
530	535	540
Ala Glu Ala Trp Gly Arg Ala Asp	Cys Gly Ile Thr Ser Ala Ser Tyr	
545	550	555
Gln Gln Gly Val Leu Ser Ala Thr	Ile Leu Tyr Glu Ile Leu Leu Gly	
565	570	575
Lys Ala Thr Leu Tyr Ala Val Leu	Val Ser Thr Leu Val Val Met Ala	
580	585	590
Met Val Lys Arg Lys Asn Ser		
595		
<210> 587		
<211> 606		
<212> PRT		
<213> 人工序列(Artificial Sequence)		
<220>		
<223> 合成		
<400> 587		
Met Ala Ser Ile Arg Ala Val Phe	Ile Phe Leu Trp Leu Gln Leu Asp	
1	5	10
Leu Val Asn Gly Glu Asn Val Glu	Gln His Pro Ser Thr Leu Ser Val	
20	25	30
Gln Glu Gly Asp Ser Ala Val Ile	Lys Cys Thr Tyr Ser Asp Ser Ala	
35	40	45
Ser Asn Tyr Phe Pro Trp Tyr Lys	Gln Glu Leu Gly Lys Gly Pro Gln	
50	55	60
Leu Ile Ile Asp Ile Arg Ser Asn	Val Gly Glu Lys Lys Asp Gln Arg	

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

Lys Val Ser Arg Lys Glu Lys Arg Asn Phe Pro Leu Ile Leu Glu Ser			
385	390	395	400
Pro Ser Pro Asn Gln Thr Ser Leu Tyr Phe Cys Ala Ser Ser Ile Gln			
	405	410	415
Gln Gly Ala Asp Thr Gln Tyr Phe Gly Pro Gly Thr Arg Leu Thr Val			
	420	425	430
Leu Glu Asp Leu Arg Asn Val Thr Pro Pro Lys Val Ser Leu Phe Glu			
	435	440	445
Pro Ser Lys Ala Glu Ile Ala Asn Lys Gln Lys Ala Thr Leu Val Cys			
	450	455	460
Leu Ala Arg Gly Phe Phe Pro Asp His Val Glu Leu Ser Trp Trp Val			
465	470	475	480
Asn Gly Lys Glu Val His Ser Gly Val Cys Thr Asp Pro Gln Ala Tyr			
	485	490	495
Lys Glu Ser Asn Tyr Ser Tyr Cys Leu Ser Ser Arg Leu Arg Val Ser			
	500	505	510
Ala Thr Phe Trp His Asn Pro Arg Asn His Phe Arg Cys Gln Val Gln			
	515	520	525
Phe His Gly Leu Ser Glu Glu Asp Lys Trp Pro Glu Gly Ser Pro Lys			
	530	535	540
Pro Val Thr Gln Asn Ile Ser Ala Glu Ala Trp Gly Arg Ala Asp Cys			
545	550	555	560
Gly Ile Thr Ser Ala Ser Tyr Gln Gln Gly Val Leu Ser Ala Thr Ile			
	565	570	575
Leu Tyr Glu Ile Leu Leu Gly Lys Ala Thr Leu Tyr Ala Val Leu Val			
	580	585	590
Ser Thr Leu Val Val Met Ala Met Val Lys Arg Lys Asn Ser			
	595	600	605
<210> 588			
<211> 603			
<212> PRT			
<213> 人工序列(Artificial Sequence)			
<220>			
<223> 合成			
<400> 588			
Met Ala Ser Leu Arg Val Leu Leu Val Ile Leu Trp Leu Gln Leu Ser			
1	5	10	15
Trp Val Trp Ser Gln Gln Lys Glu Val Glu Gln Asn Ser Gly Pro Leu			
	20	25	30

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

340	345	350
Gln Asp Pro Gly Met Gly Leu Arg Leu Ile His Tyr Ser Val Gly Glu		
355	360	365
Gly Thr Thr Ala Lys Gly Glu Val Pro Asp Gly Tyr Asn Val Ser Arg		
370	375	380
Leu Lys Lys Gln Asn Phe Leu Leu Gly Leu Glu Ser Ala Ala Pro Ser		
385	390	395
Gln Thr Ser Val Tyr Phe Cys Ala Ser Ser Tyr Ser Gln Ala Trp Gly		
405	410	415
Gln Pro Gln His Phe Gly Asp Gly Thr Arg Leu Ser Ile Leu Glu Asp		
420	425	430
Leu Arg Asn Val Thr Pro Pro Lys Val Ser Leu Phe Glu Pro Ser Lys		
435	440	445
Ala Glu Ile Ala Asn Lys Gln Lys Ala Thr Leu Val Cys Leu Ala Arg		
450	455	460
Gly Phe Phe Pro Asp His Val Glu Leu Ser Trp Trp Val Asn Gly Lys		
465	470	475
Glu Val His Ser Gly Val Cys Thr Asp Pro Gln Ala Tyr Lys Glu Ser		
485	490	495
Asn Tyr Ser Tyr Cys Leu Ser Ser Arg Leu Arg Val Ser Ala Thr Phe		
500	505	510
Trp His Asn Pro Arg Asn His Phe Arg Cys Gln Val Gln Phe His Gly		
515	520	525
Leu Ser Glu Glu Asp Lys Trp Pro Glu Gly Ser Pro Lys Pro Val Thr		
530	535	540
Gln Asn Ile Ser Ala Glu Ala Trp Gly Arg Ala Asp Cys Gly Ile Thr		
545	550	555
Ser Ala Ser Tyr Gln Gln Gly Val Leu Ser Ala Thr Ile Leu Tyr Glu		
565	570	575
Ile Leu Leu Gly Lys Ala Thr Leu Tyr Ala Val Leu Val Ser Thr Leu		
580	585	590
Val Val Met Ala Met Val Lys Arg Lys Asn Ser		
595	600	

<210> 589

<211> 603

<212> PRT

<213> 人工序列(Artificial Sequence)

<220>

<223> 合成

<400> 589

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

Cys Cys Gly Ala Phe Ser Leu Leu Trp Ala Gly Pro Val Asn Ala Gly			
305	310	315	320
Val Thr Gln Thr Pro Lys Phe Arg Val Leu Lys Thr Gly Gln Ser Met			
	325	330	335
Thr Leu Leu Cys Ala Gln Asp Met Asn His Glu Tyr Met Tyr Trp Tyr			
	340	345	350
Arg Gln Asp Pro Gly Met Gly Leu Arg Leu Ile His Tyr Ser Val Gly			
	355	360	365
Glu Gly Thr Thr Ala Lys Gly Glu Val Pro Asp Gly Tyr Asn Val Ser			
	370	375	380
Arg Leu Lys Lys Gln Asn Phe Leu Leu Gly Leu Glu Ser Ala Ala Pro			
385	390	395	400
Ser Gln Thr Ser Val Tyr Phe Cys Ala Ser Arg Leu Gln Gly Trp Asn			
	405	410	415
Ser Pro Leu His Phe Gly Asn Gly Thr Arg Leu Thr Val Thr Glu Asp			
	420	425	430
Leu Arg Asn Val Thr Pro Pro Lys Val Ser Leu Phe Glu Pro Ser Lys			
	435	440	445
Ala Glu Ile Ala Asn Lys Gln Lys Ala Thr Leu Val Cys Leu Ala Arg			
	450	455	460
Gly Phe Phe Pro Asp His Val Glu Leu Ser Trp Trp Val Asn Gly Lys			
465	470	475	480
Glu Val His Ser Gly Val Cys Thr Asp Pro Gln Ala Tyr Lys Glu Ser			
	485	490	495
Asn Tyr Ser Tyr Cys Leu Ser Ser Arg Leu Arg Val Ser Ala Thr Phe			
	500	505	510
Trp His Asn Pro Arg Asn His Phe Arg Cys Gln Val Gln Phe His Gly			
	515	520	525
Leu Ser Glu Glu Asp Lys Trp Pro Glu Gly Ser Pro Lys Pro Val Thr			
	530	535	540
Gln Asn Ile Ser Ala Glu Ala Trp Gly Arg Ala Asp Cys Gly Ile Thr			
545	550	555	560
Ser Ala Ser Tyr Gln Gln Gly Val Leu Ser Ala Thr Ile Leu Tyr Glu			
	565	570	575
Ile Leu Leu Gly Lys Ala Thr Leu Tyr Ala Val Leu Val Ser Thr Leu			
	580	585	590
Val Val Met Ala Met Val Lys Arg Lys Asn Ser			
	595	600	
<210>	590		

<211> 10
<212> PRT
<213> 智人 (Homo sapiens)
<400> 590
Ser Ser Cys Met Gly Gly Met Asn Arg Arg
1 5 10
<210> 591
<211> 10
<212> PRT
<213> 智人 (Homo sapiens)
<400> 591
Ser Ser Cys Met Gly Gly Met Asn Trp Arg
1 5 10
<210> 592
<211> 15
<212> PRT
<213> 智人 (Homo sapiens)
<400> 592
Tyr Met Cys Asn Ser Ser Cys Met Gly Gly Met Asn Trp Arg Pro
1 5 10 15
<210> 593
<211> 15
<212> PRT
<213> 智人 (Homo sapiens)
<400> 593
Met Cys Asn Ser Ser Cys Met Gly Gly Met Asn Trp Arg Pro Ile
1 5 10 15
<210> 594
<211> 15
<212> PRT
<213> 智人 (Homo sapiens)
<400> 594
Cys Asn Ser Ser Cys Met Gly Gly Met Asn Trp Arg Pro Ile Leu
1 5 10 15
<210> 595
<211> 15
<212> PRT
<213> 智人 (Homo sapiens)
<400> 595

Asn Ser Ser Cys Met Gly Gly Met Asn Trp Arg Pro Ile Leu Thr
1 5 10 15

<210> 596

<211> 15

<212> PRT

<213> 智人 (Homo sapiens)

<400> 596

Ser Ser Cys Met Gly Gly Met Asn Trp Arg Pro Ile Leu Thr Ile
1 5 10 15

<210> 597

<211> 15

<212> PRT

<213> 智人 (Homo sapiens)

<400> 597

Ser Cys Met Gly Gly Met Asn Trp Arg Pro Ile Leu Thr Ile Ile
1 5 10 15

<210> 598

<211> 15

<212> PRT

<213> 智人 (Homo sapiens)

<400> 598

Cys Met Gly Gly Met Asn Trp Arg Pro Ile Leu Thr Ile Ile Thr
1 5 10 15

<210> 599

<211> 15

<212> PRT

<213> 智人 (Homo sapiens)

<400> 599

Met Gly Gly Met Asn Trp Arg Pro Ile Leu Thr Ile Ile Thr Leu
1 5 10 15

<210> 600

<211> 15

<212> PRT

<213> 智人 (Homo sapiens)

<400> 600

Gly Gly Met Asn Trp Arg Pro Ile Leu Thr Ile Ile Thr Leu Glu
1 5 10 15

<210> 601

<211> 15

<212> PRT

<213> 智人 (Homo sapiens)

<400> 601

Gly Met Asn Trp Arg Pro Ile Leu Thr Ile Ile Thr Leu Glu Asp

1 5 10 15

<210> 602

<211> 15

<212> PRT

<213> 智人 (Homo sapiens)

<400> 602

Met Asn Trp Arg Pro Ile Leu Thr Ile Ile Thr Leu Glu Asp Ser

1 5 10 15

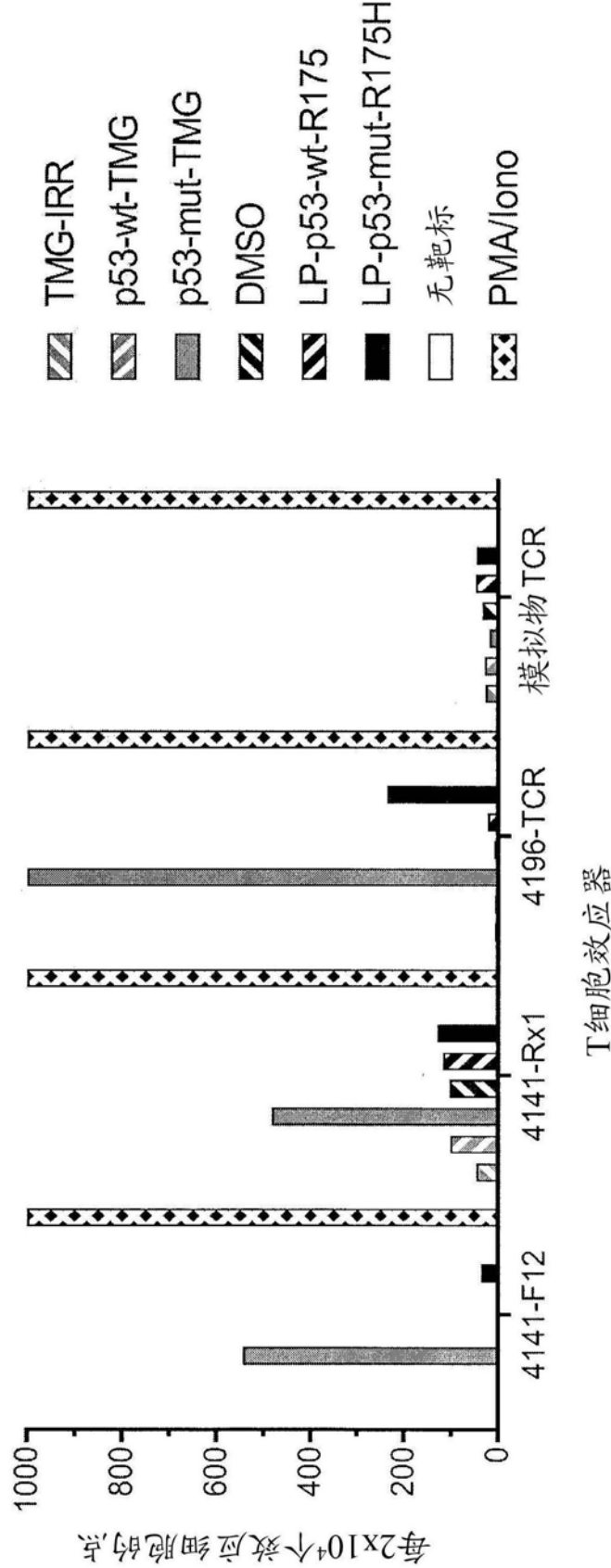


图1

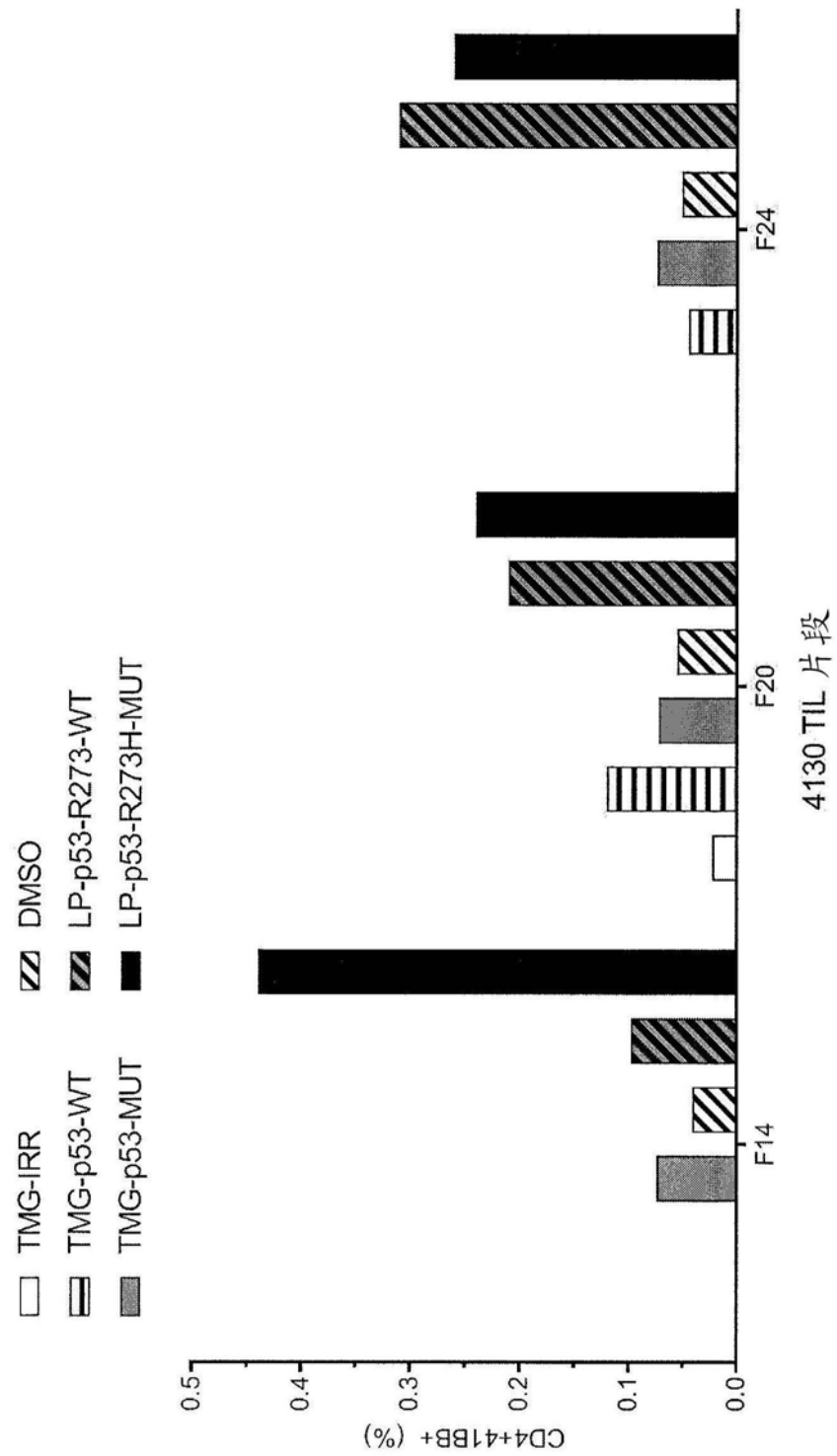


图2

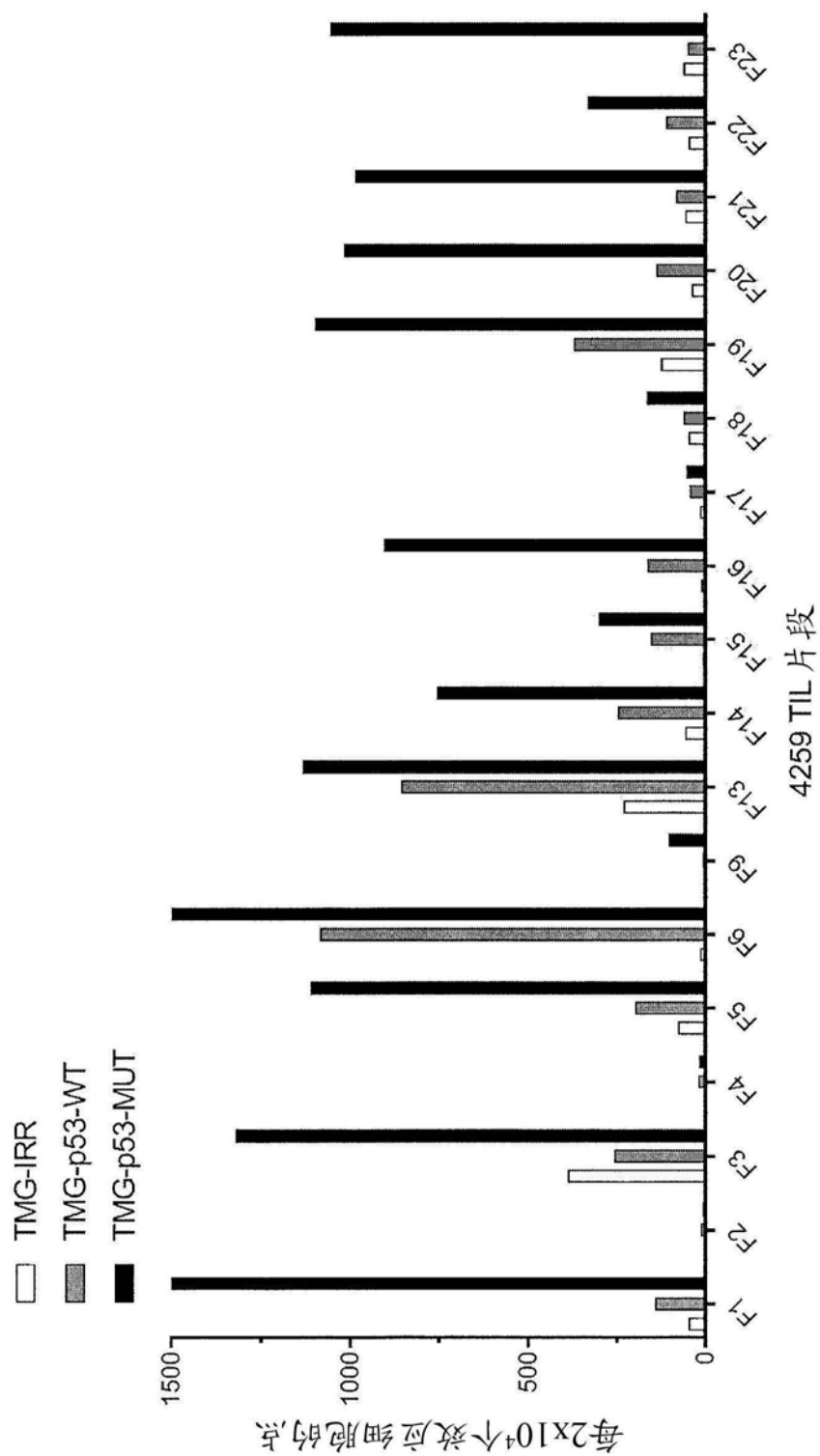


图3

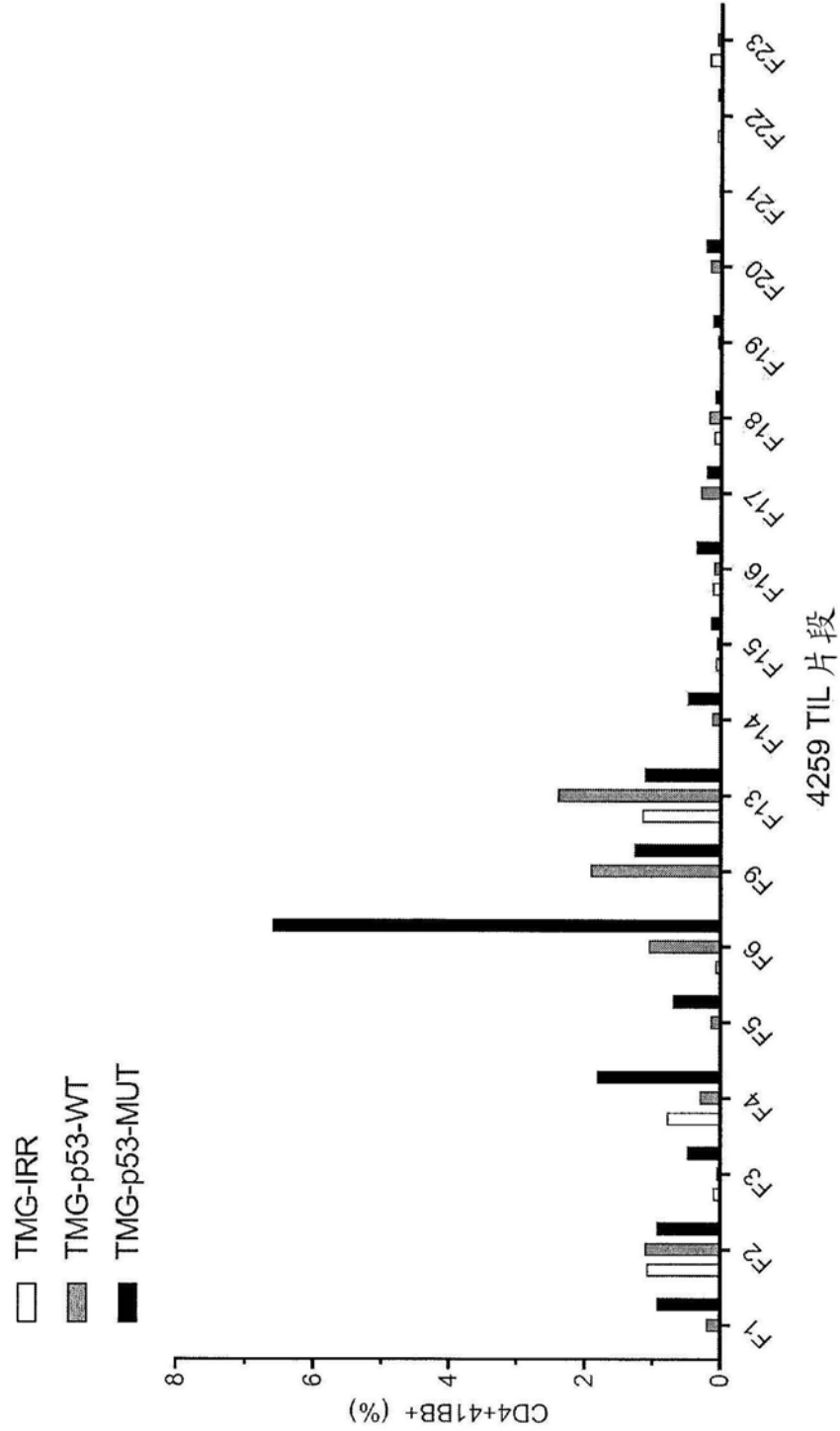


图4

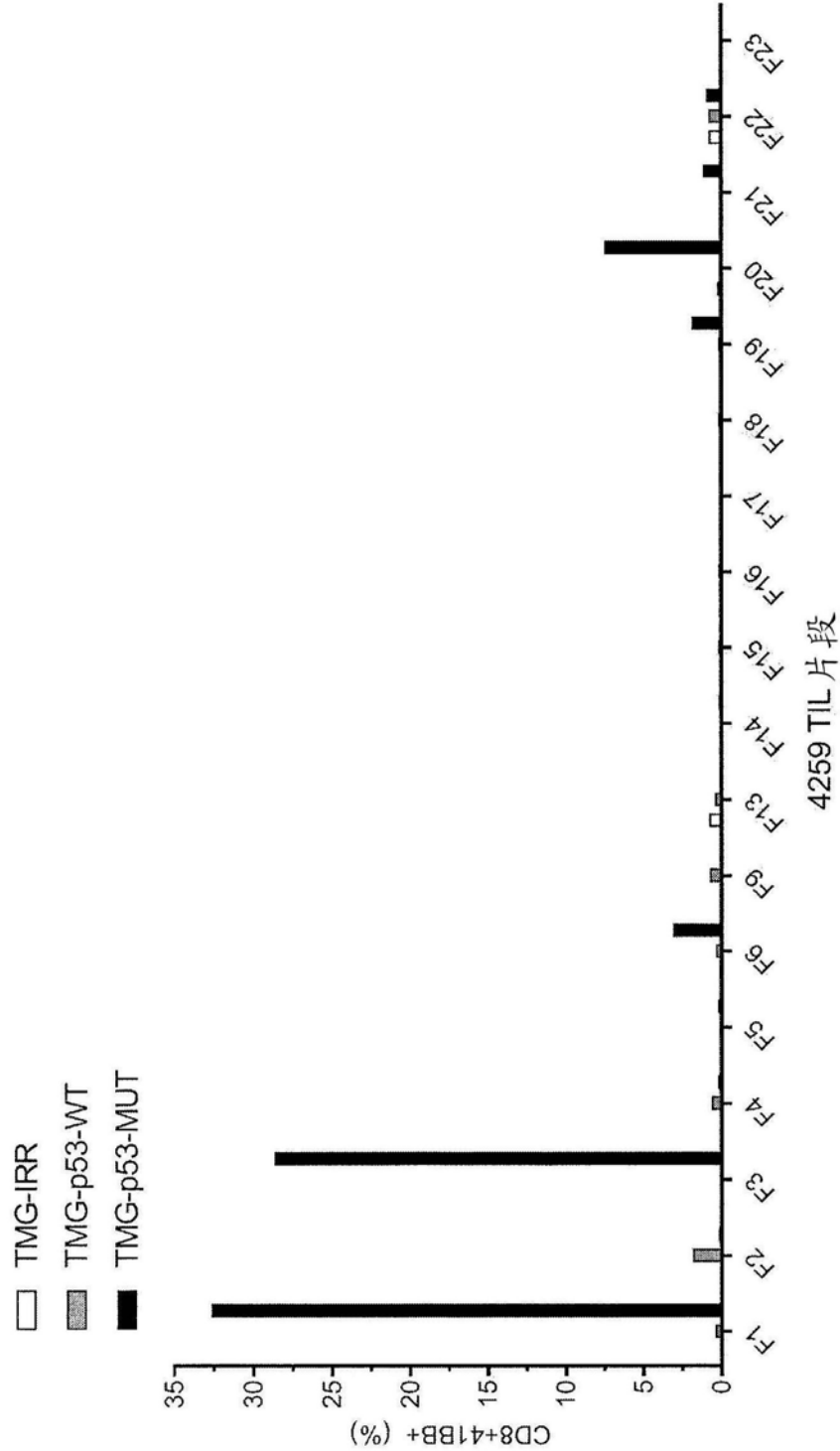


图5

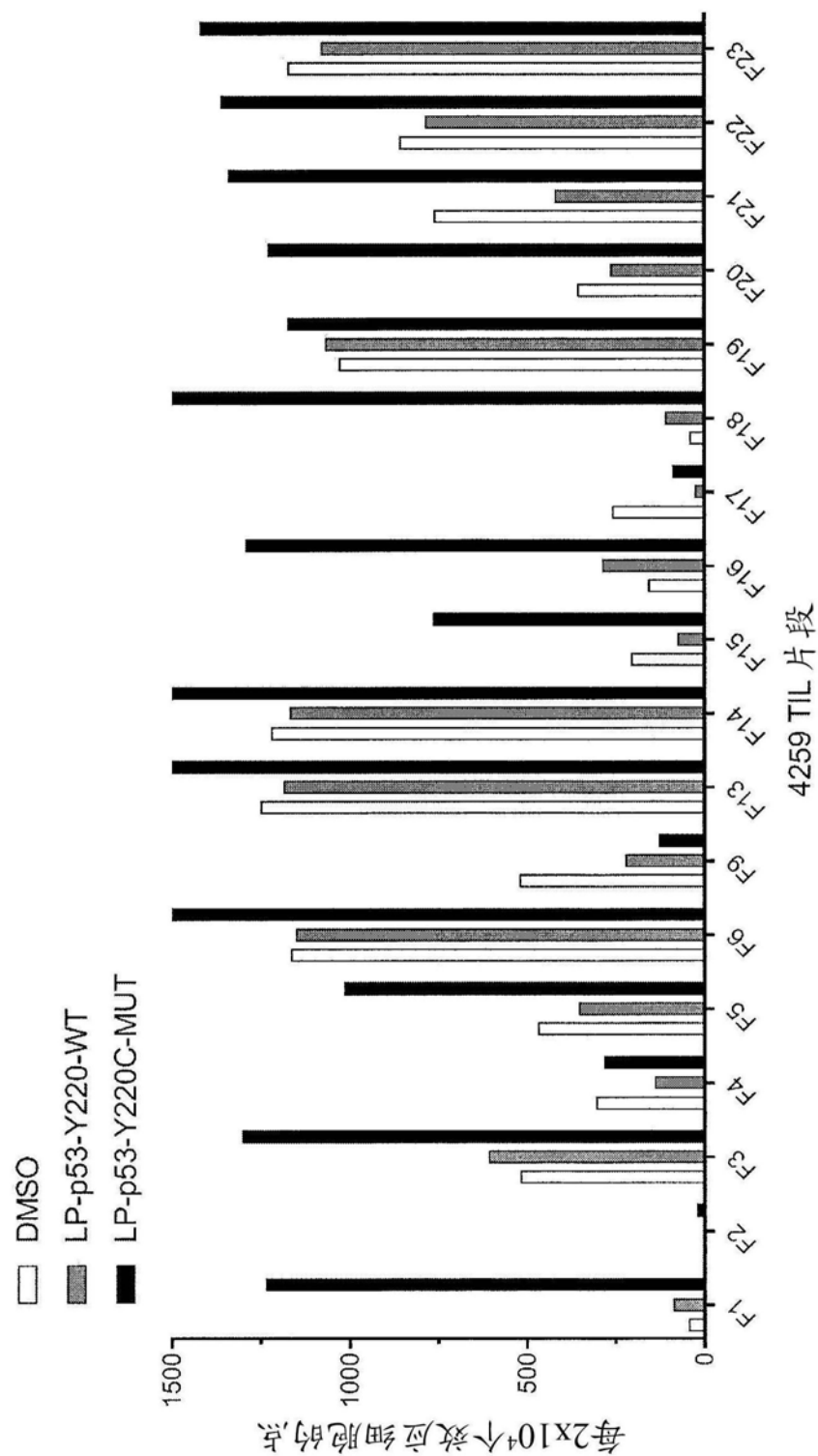


图6

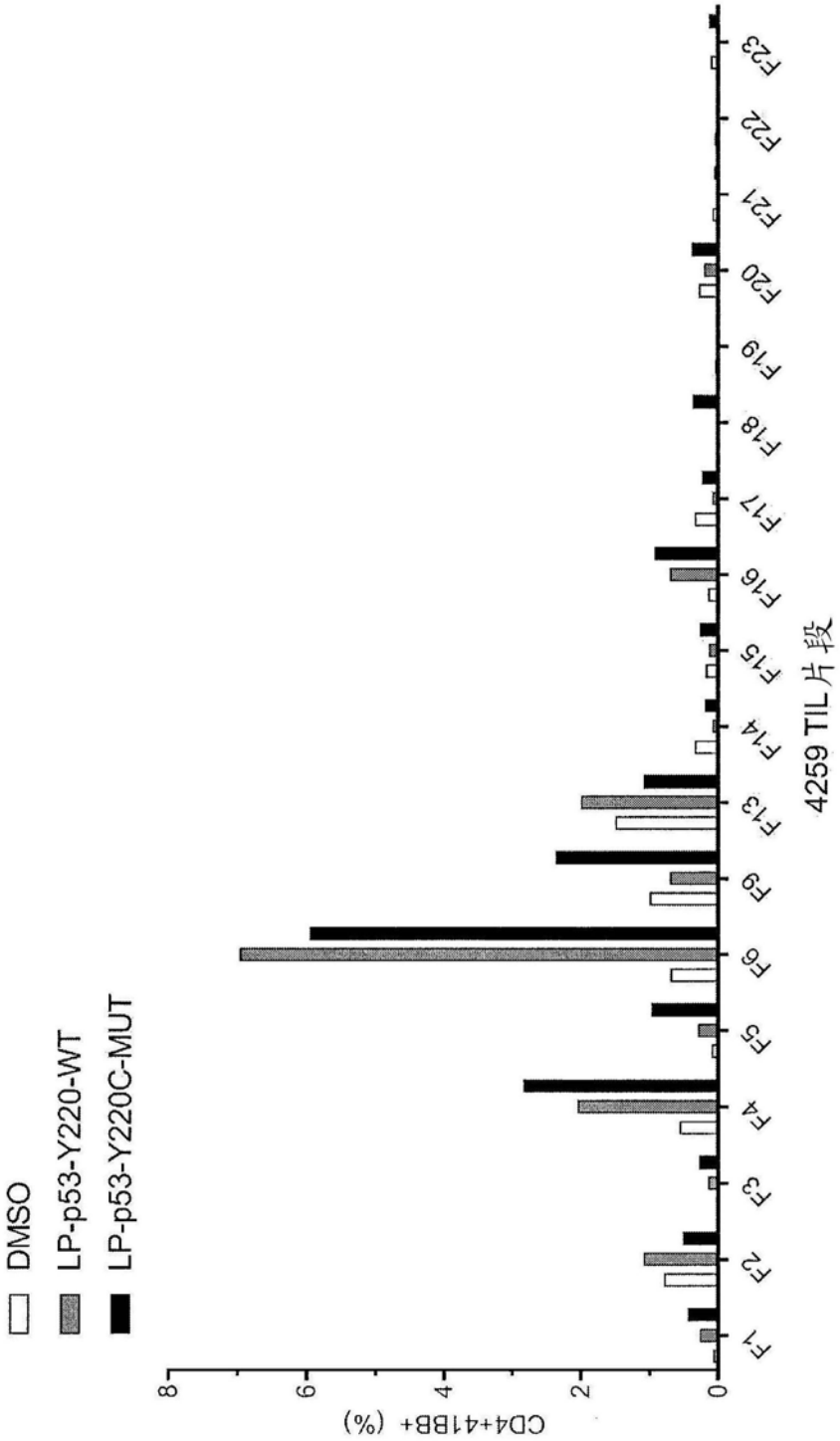


图7

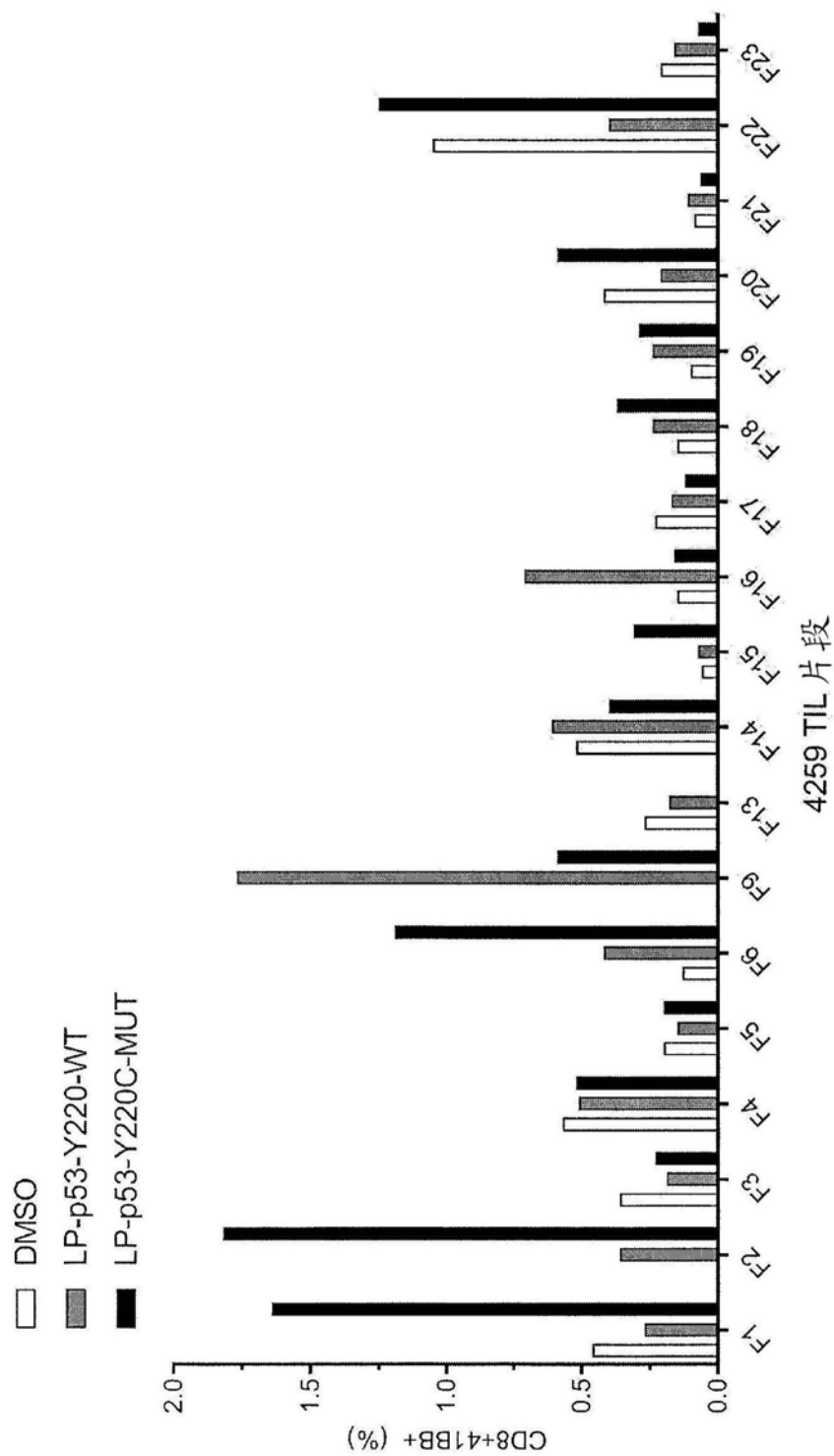


图8

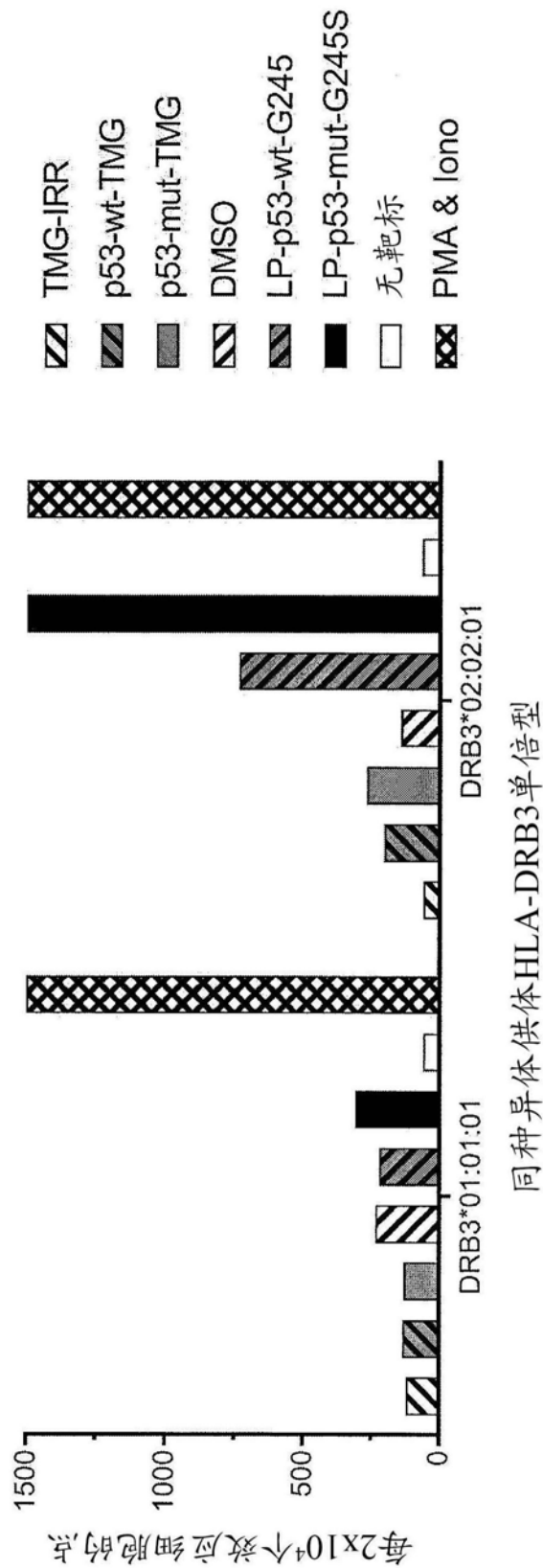


图9

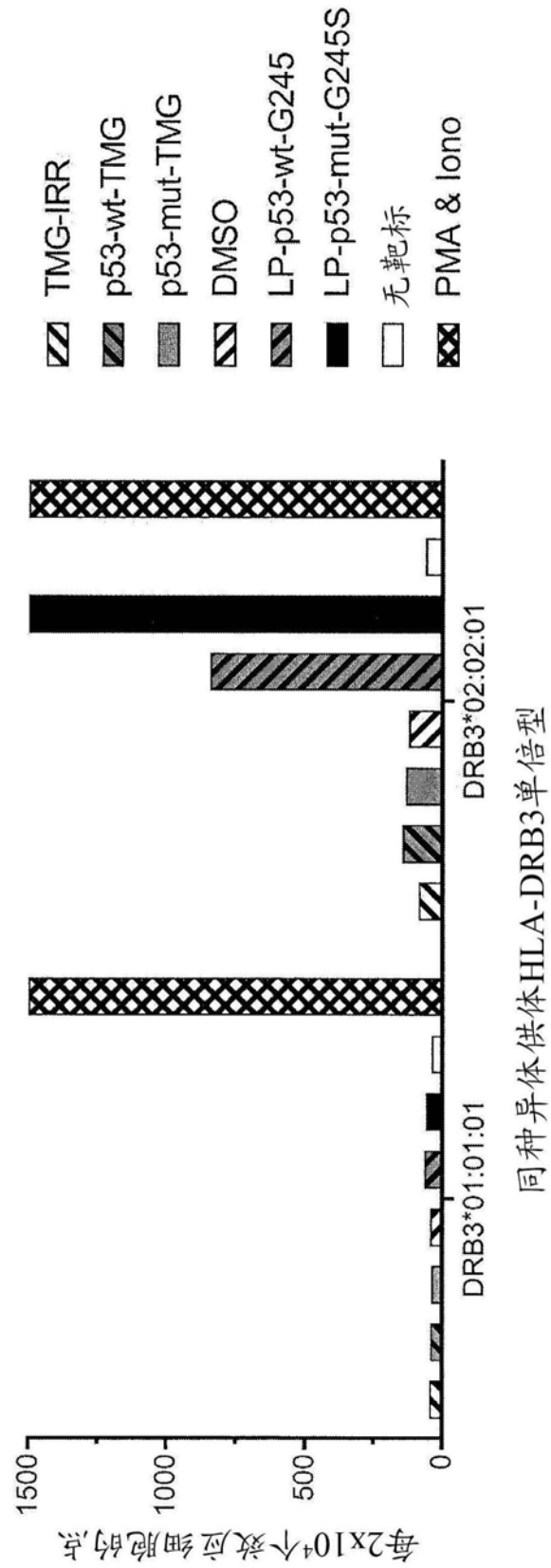


图10

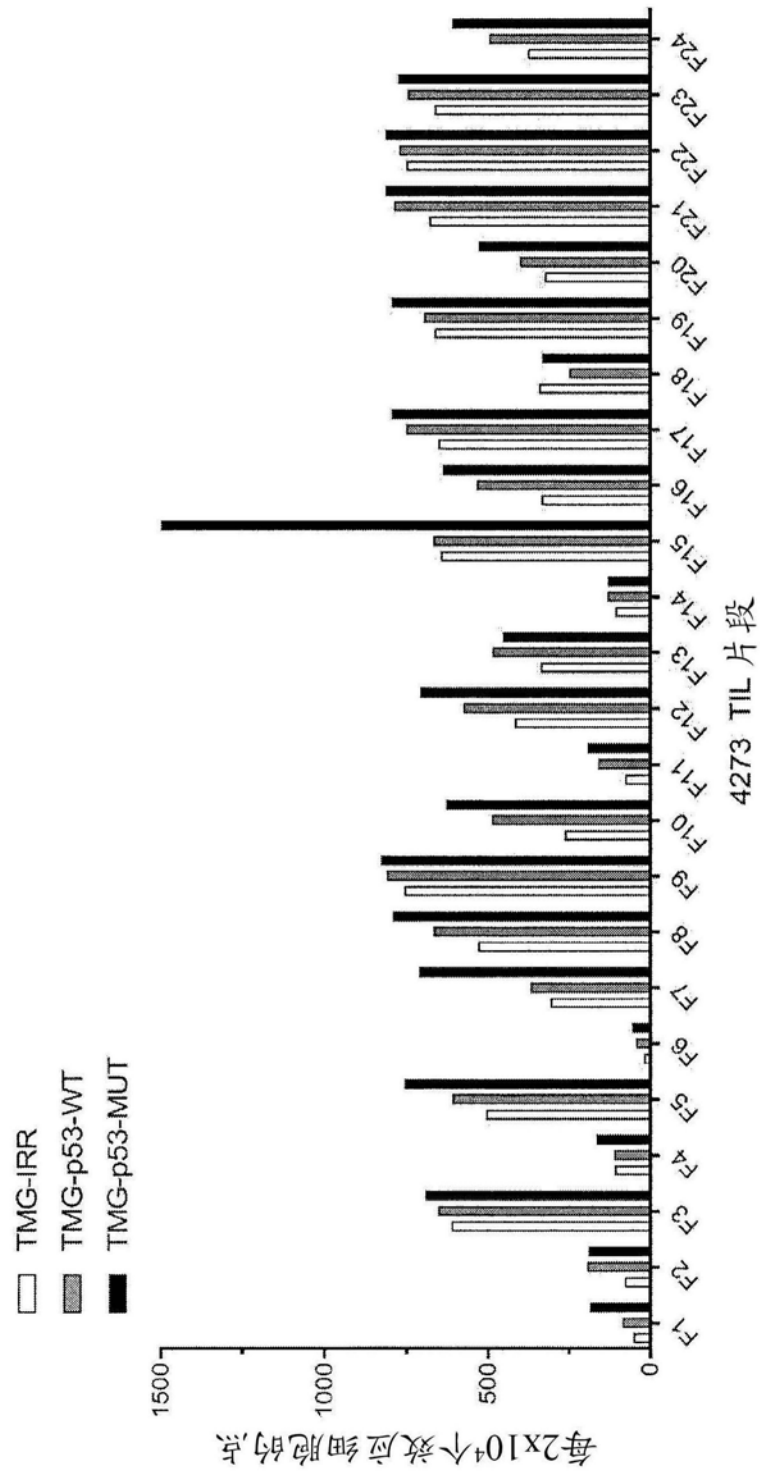


图11

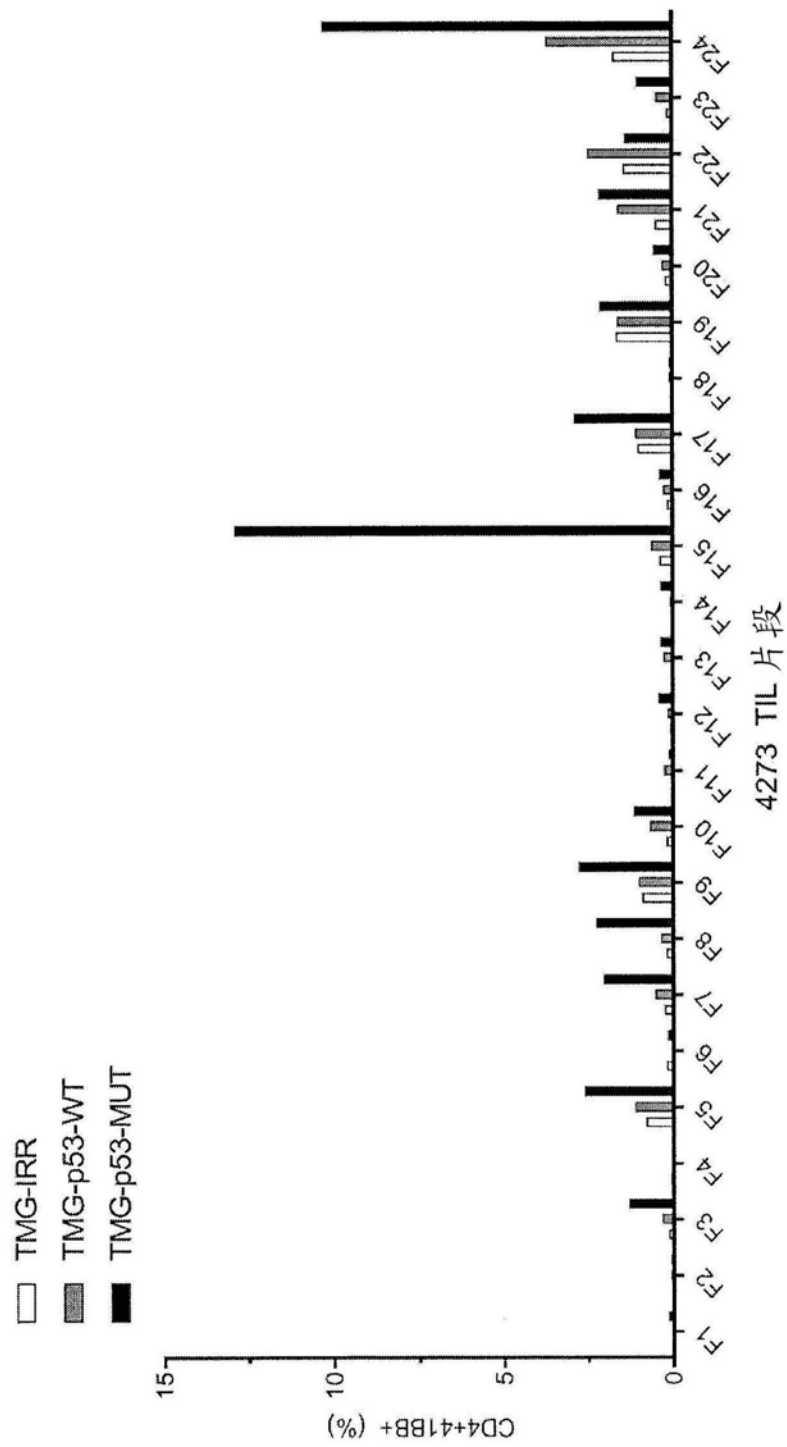


图12

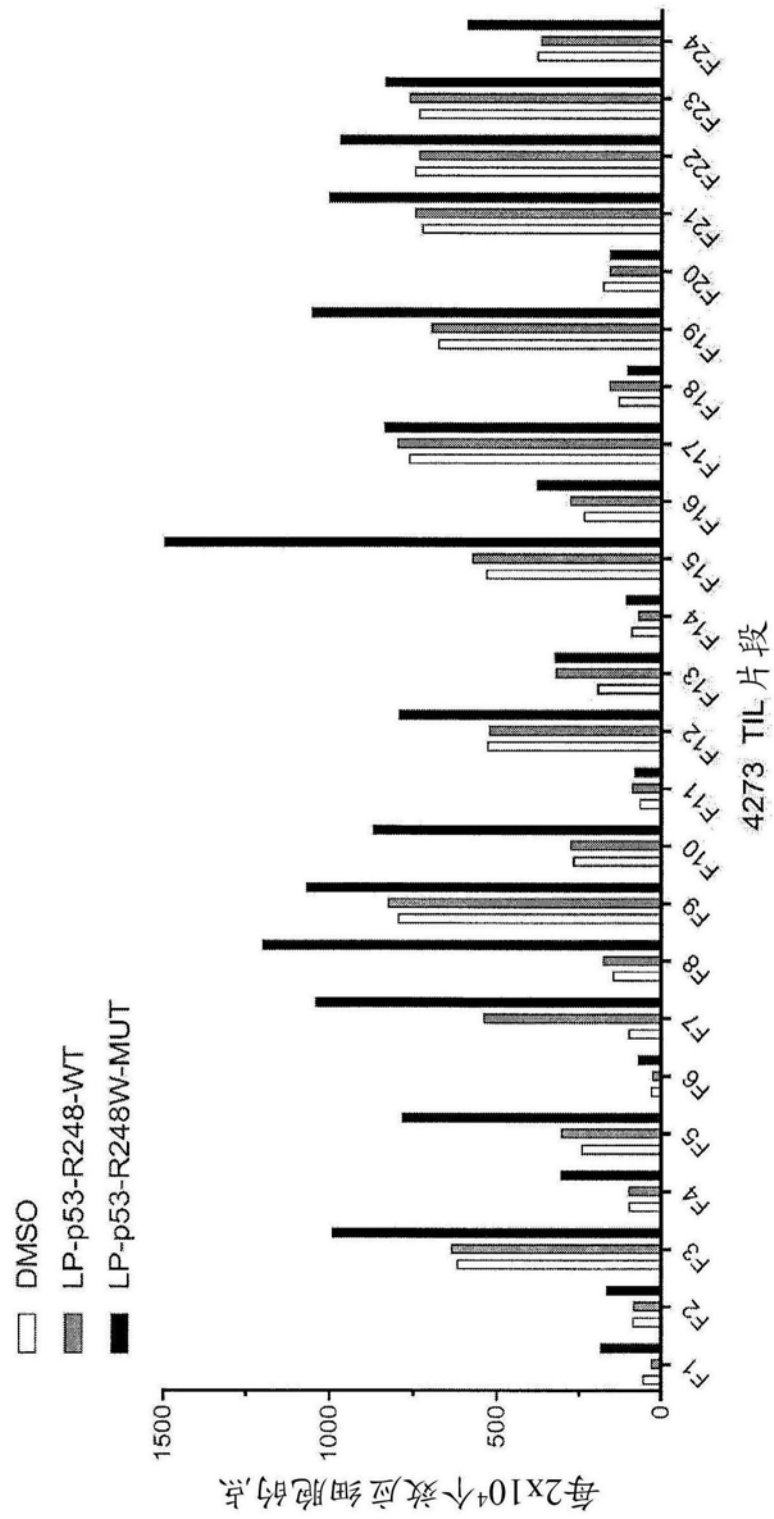


图13

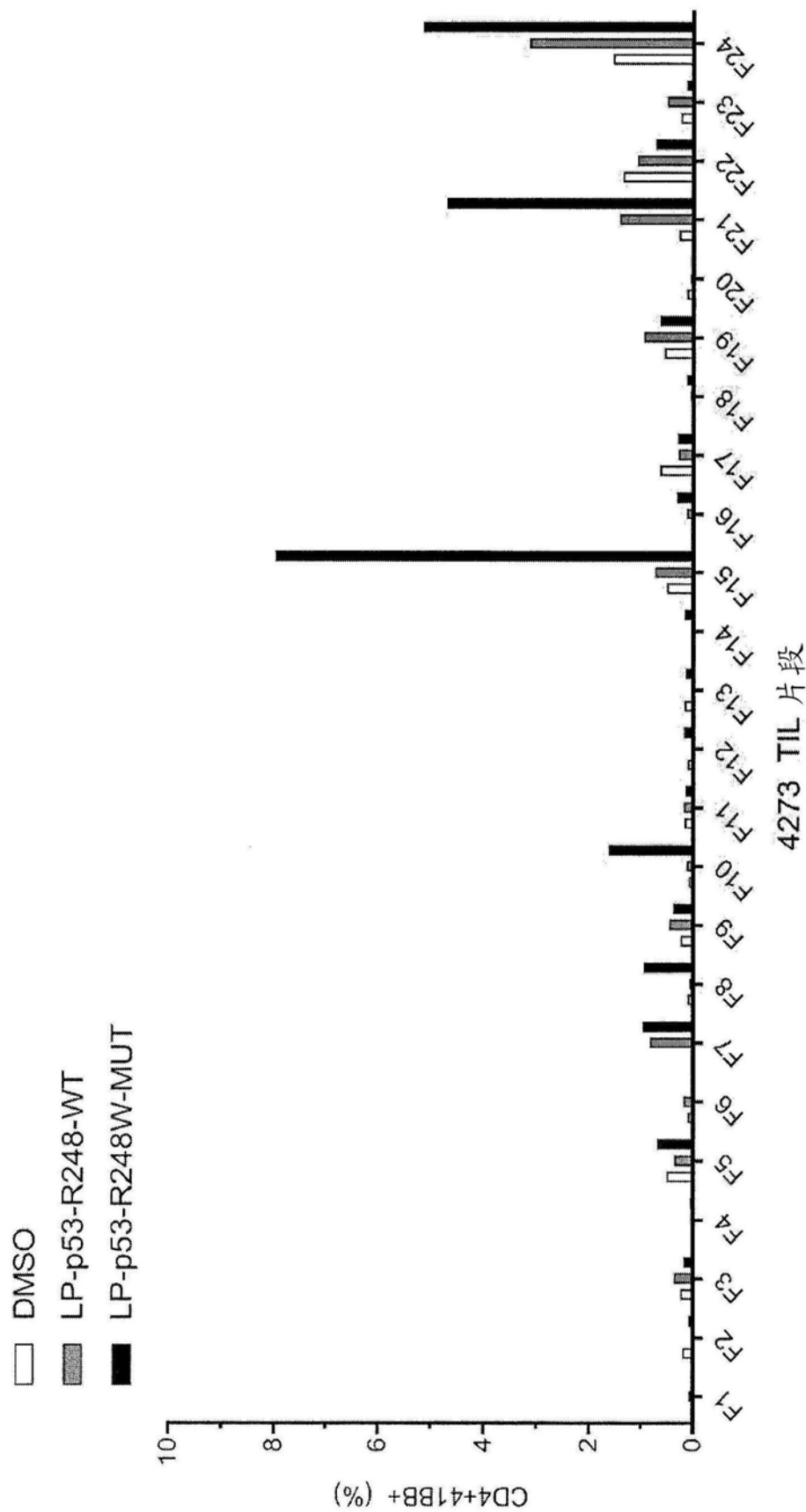


图14

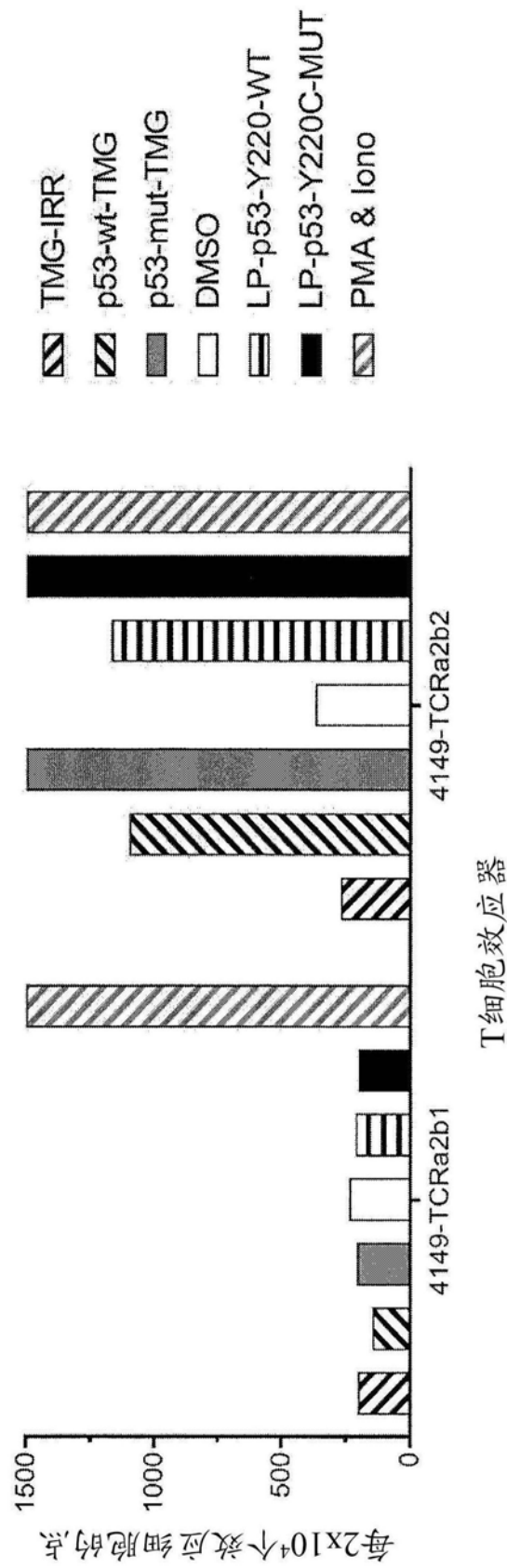


图15

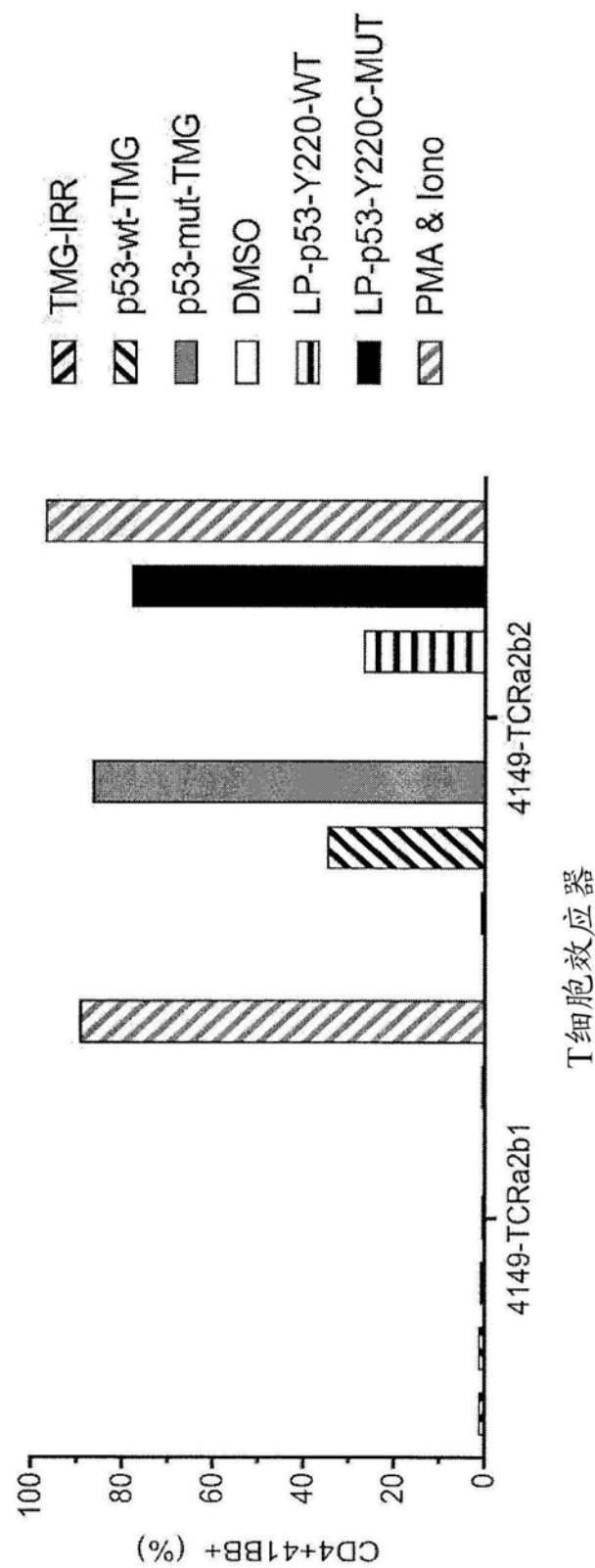


图16

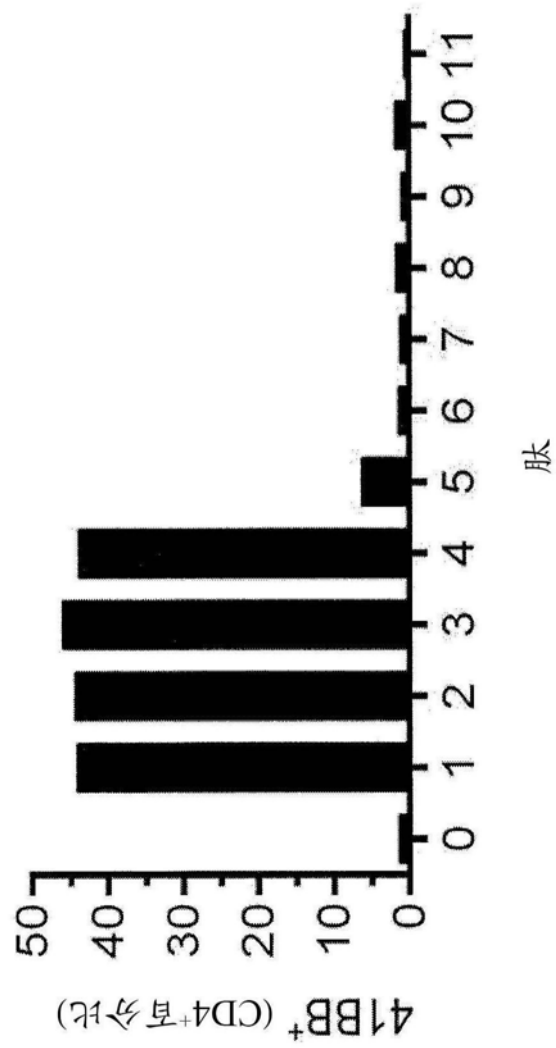


图17

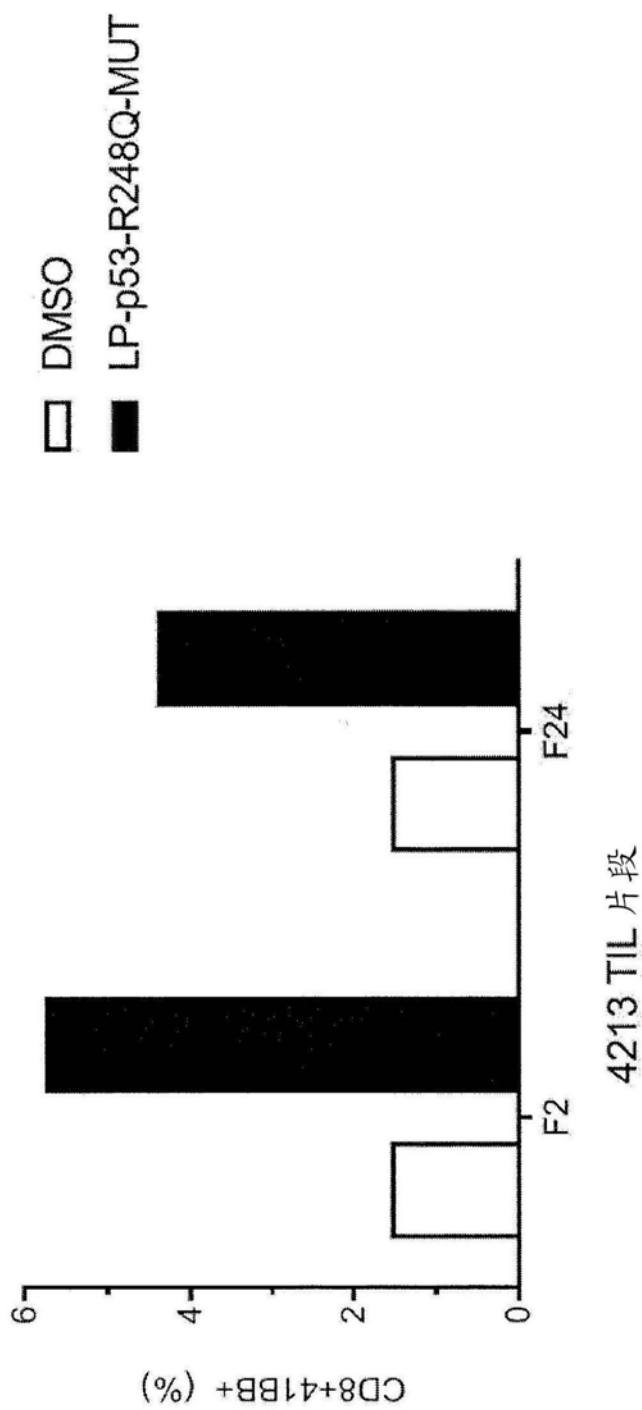


图19

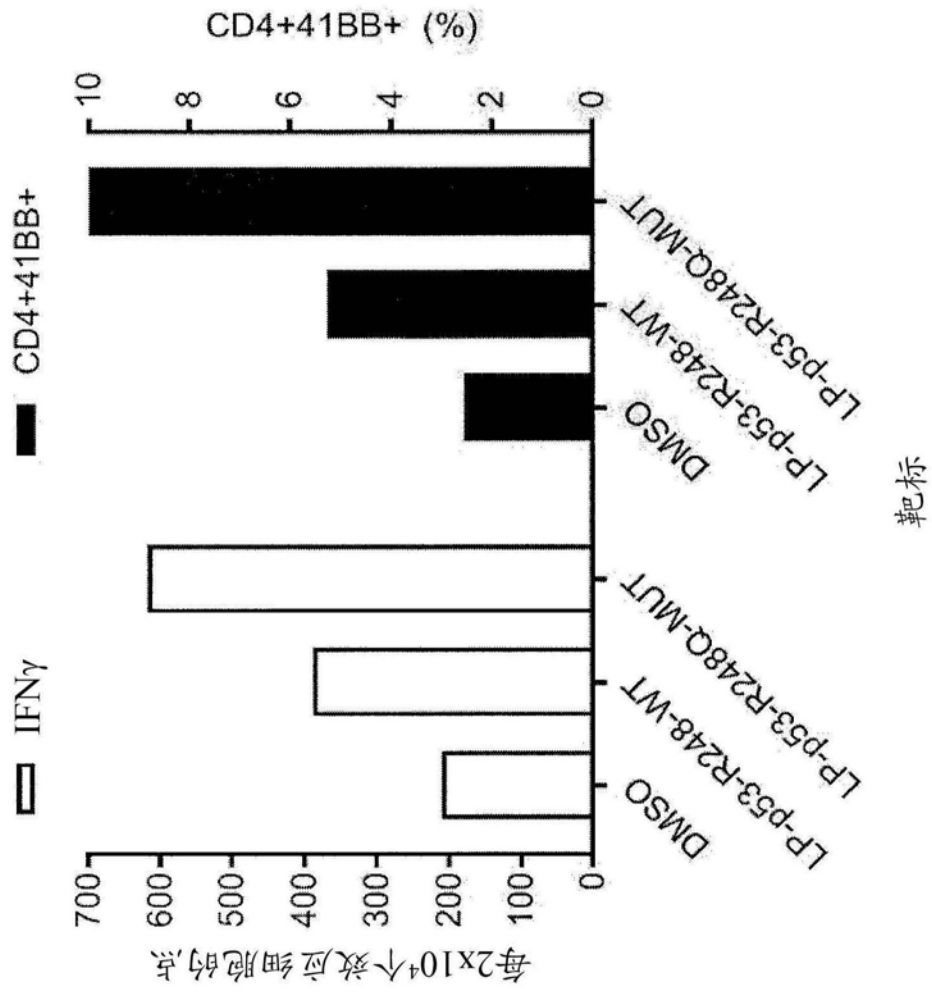


图20

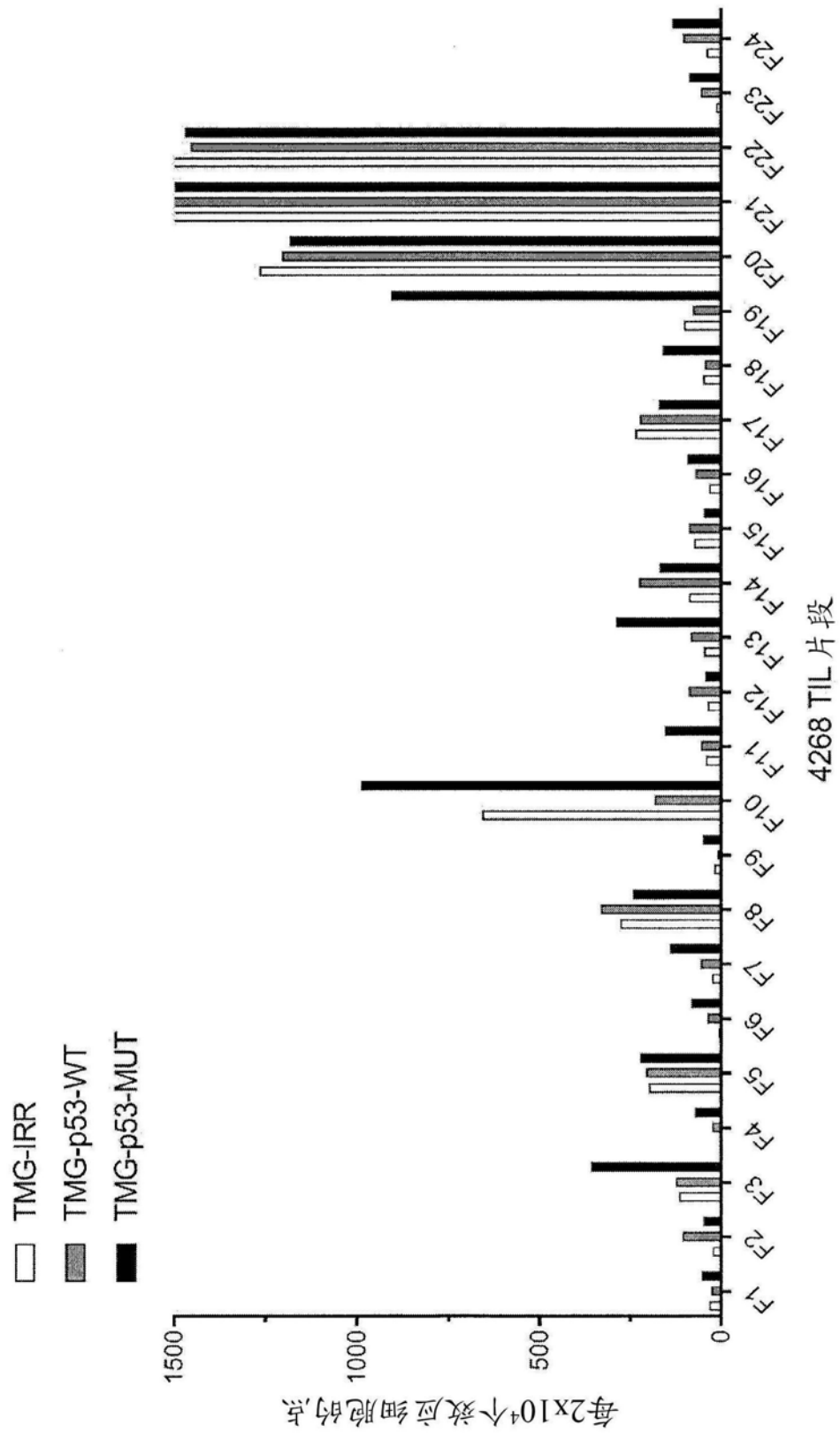


图21

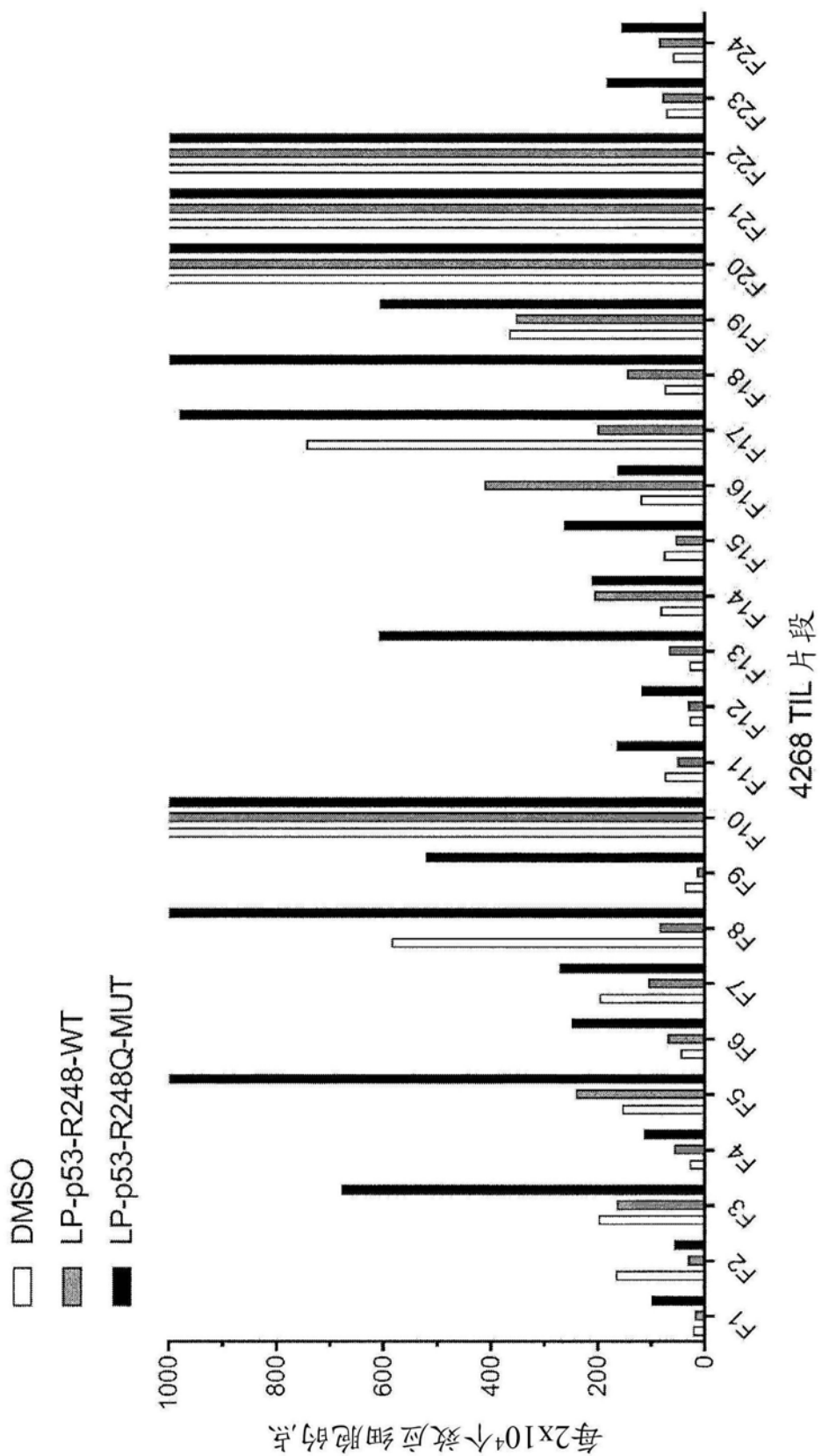


图22

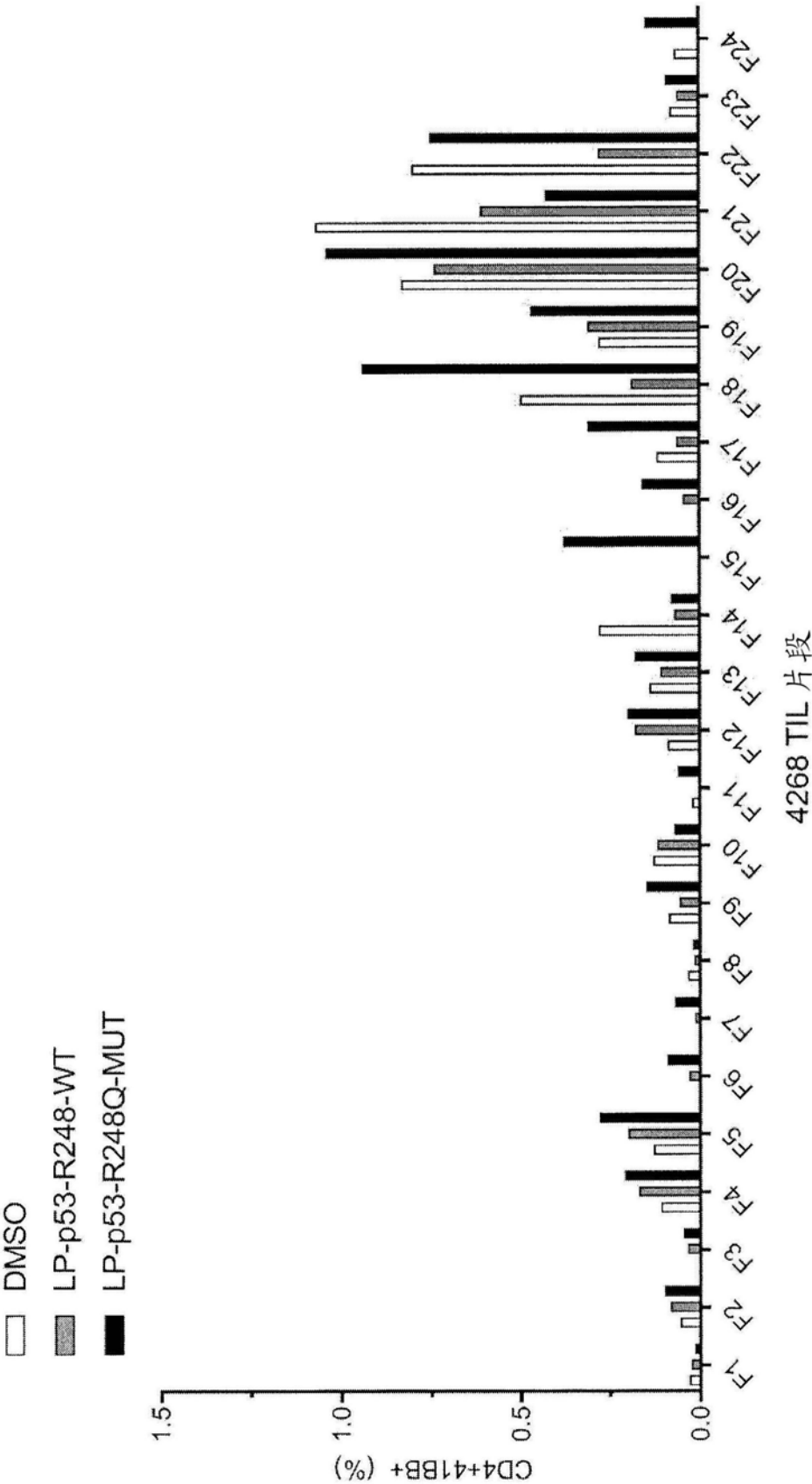


图23

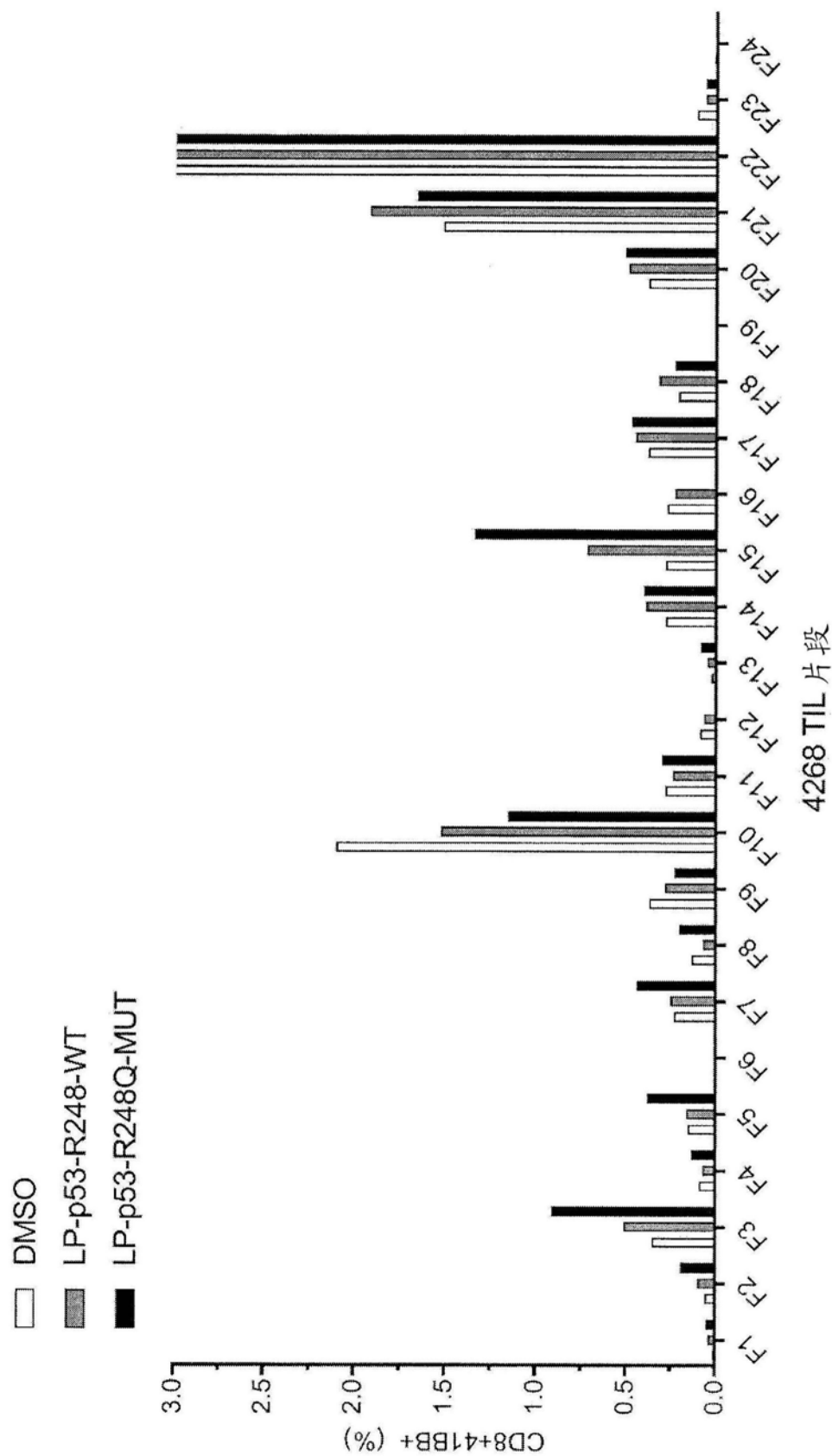


图24

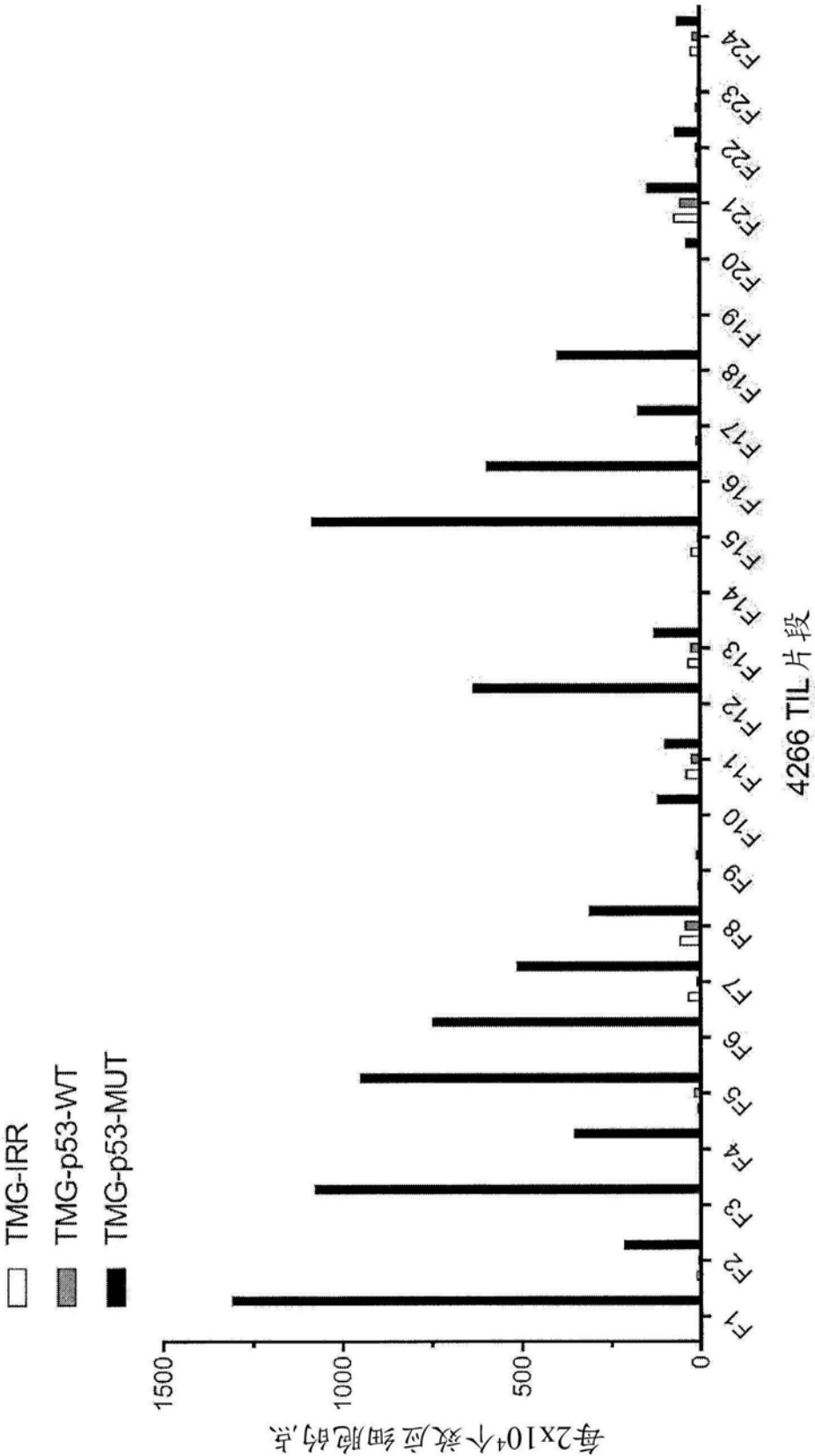


图25

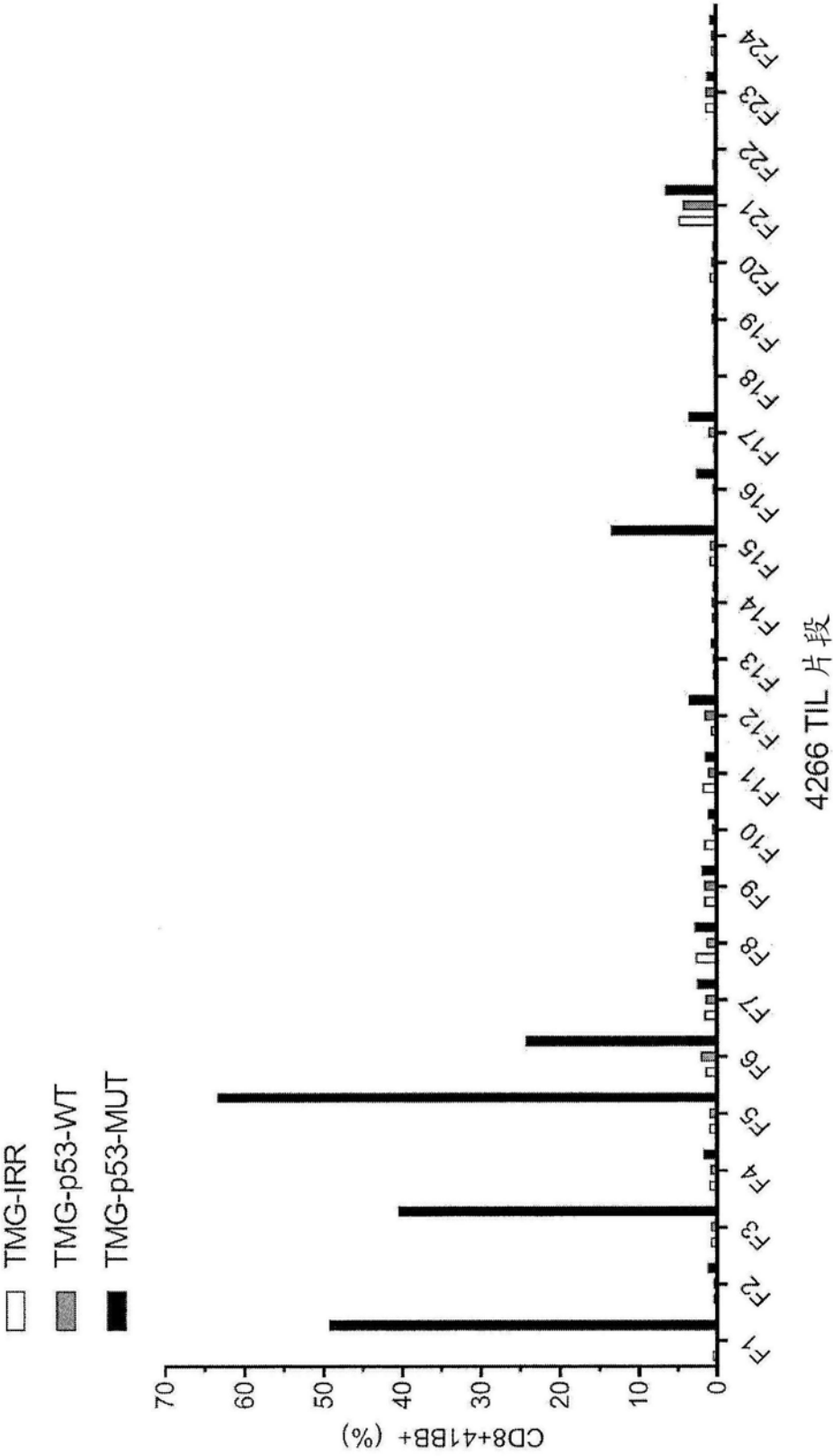


图26

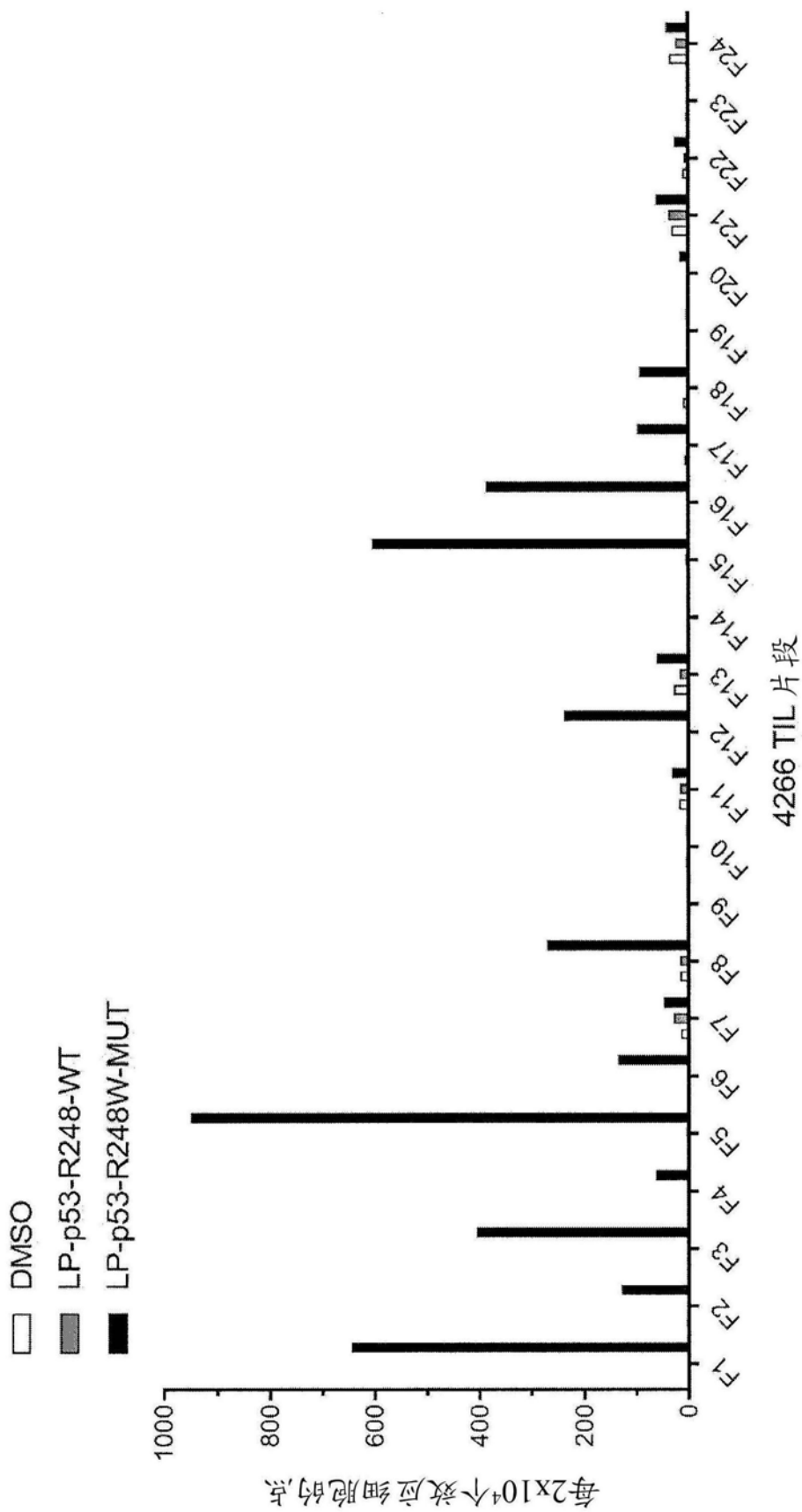


图27

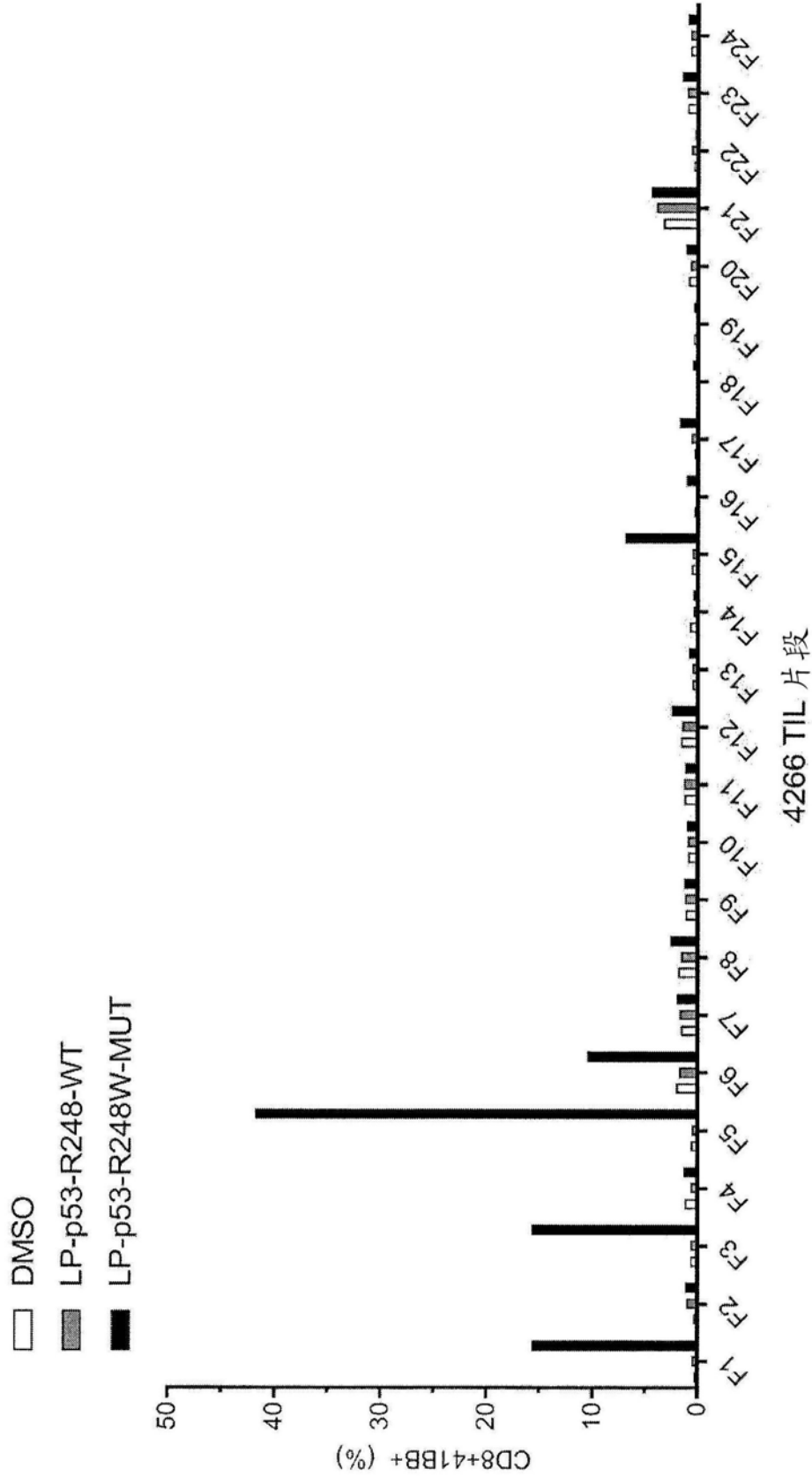


图28

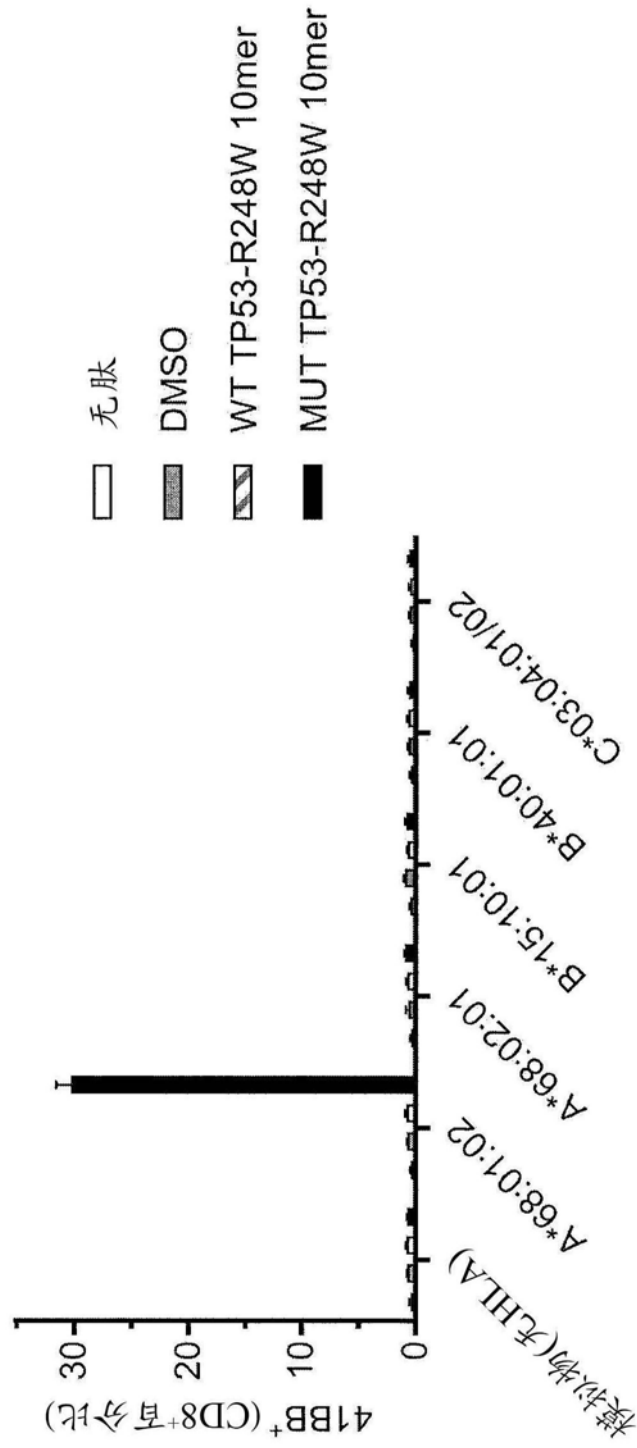


图29

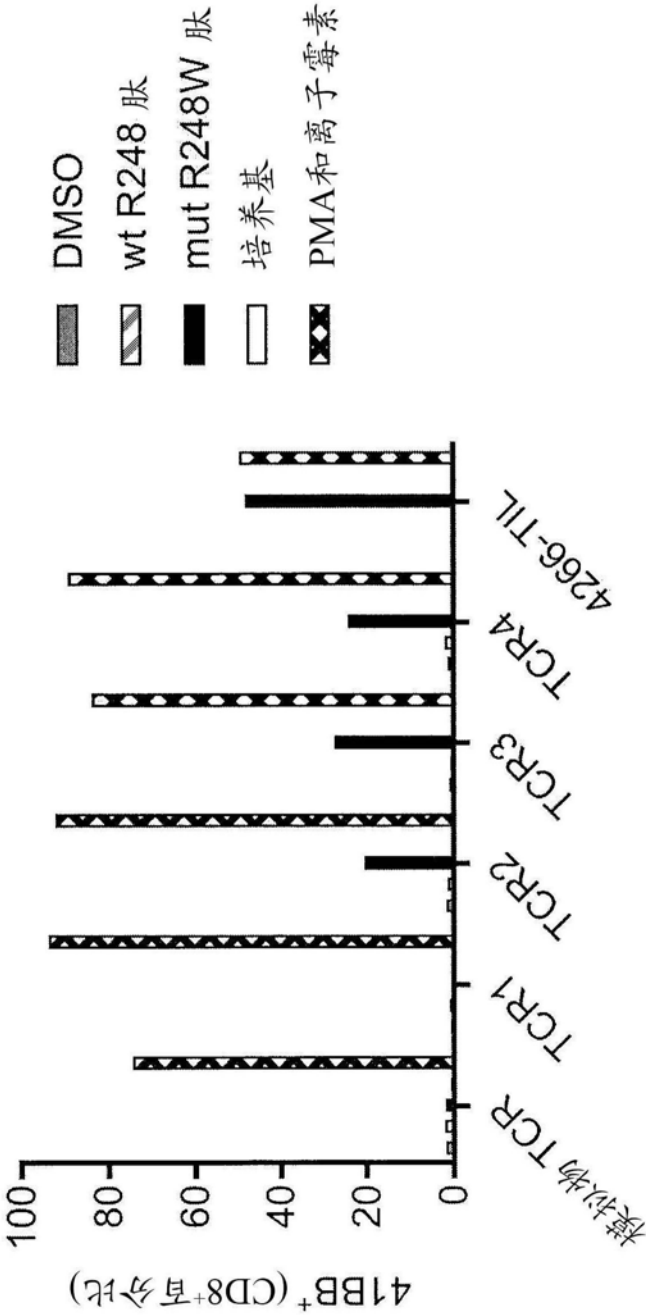


图30

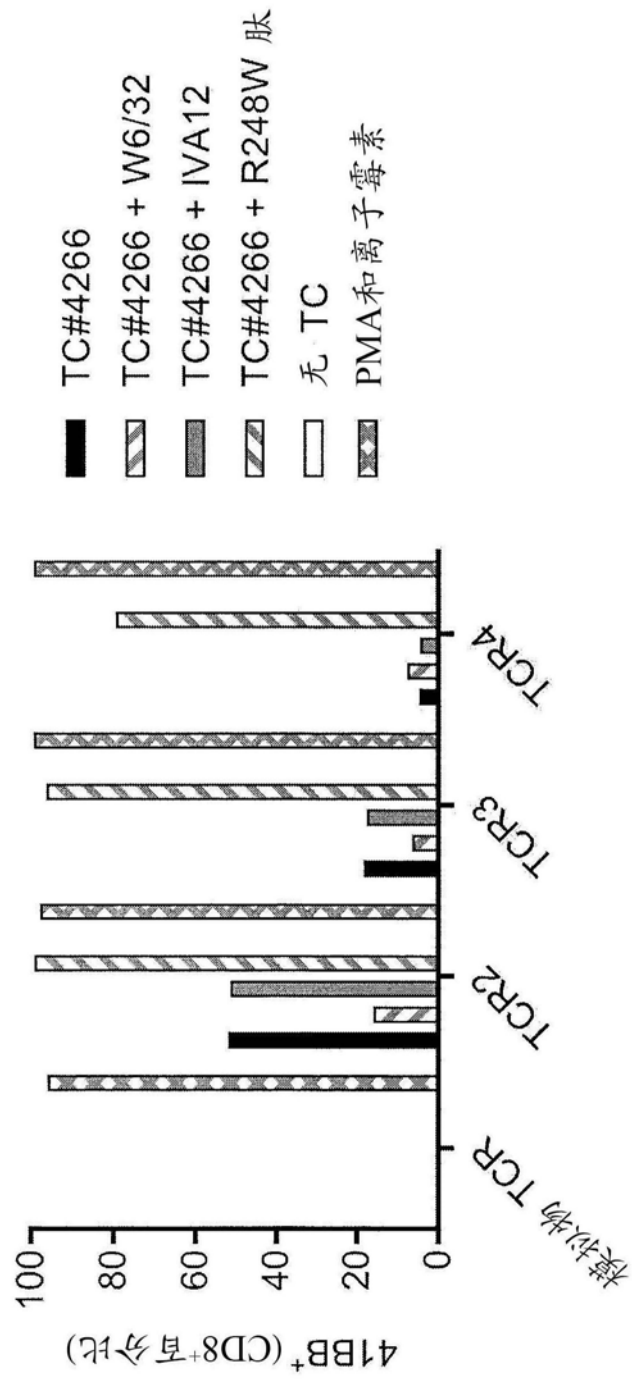


图31

CLUSTAL D(1.2.4) 多序列比对

```

SP|P04637|P53_HUMAN  MEEPQSDPSVEPPLSQETFSOLWKLLPENNVLSPPLSQAMDDLMLSPDDIEQWFTEDPGP 60
SP|P04637-2|P53_HUMAN MEEPQSDPSVEPPLSQETFSOLWKLLPENNVLSPPLSQAMDDLMLSPDDIEQWFTEDPGP 60
SP|P04637-3|P53_HUMAN MEEPQSDPSVEPPLSQETFSOLWKLLPENNVLSPPLSQAMDDLMLSPDDIEQWFTEDPGP 60
SP|P04637-4|P53_HUMAN -----MDDLMLSPDDIEQWFTEDPGP 21
SP|P04637-5|P53_HUMAN -----MDDLMLSPDDIEQWFTEDPGP 21
SP|P04637-6|P53_HUMAN -----MDDLMLSPDDIEQWFTEDPGP 21
SP|P04637-7|P53_HUMAN -----
SP|P04637-8|P53_HUMAN -----
SP|P04637-9|P53_HUMAN -----

SP|P04637|P53_HUMAN  DEAPRMPEAAPPVAPAPAAPTAAPAPAPSWPLSSSVPSQKTYQGSYGFRLGFLHSGTAK 120
SP|P04637-2|P53_HUMAN DEAPRMPEAAPPVAPAPAAPTAAPAPAPSWPLSSSVPSQKTYQGSYGFRLGFLHSGTAK 120
SP|P04637-3|P53_HUMAN DEAPRMPEAAPPVAPAPAAPTAAPAPAPSWPLSSSVPSQKTYQGSYGFRLGFLHSGTAK 120
SP|P04637-4|P53_HUMAN DEAPRMPEAAPPVAPAPAAPTAAPAPAPSWPLSSSVPSQKTYQGSYGFRLGFLHSGTAK 81
SP|P04637-5|P53_HUMAN DEAPRMPEAAPPVAPAPAAPTAAPAPAPSWPLSSSVPSQKTYQGSYGFRLGFLHSGTAK 81
SP|P04637-6|P53_HUMAN DEAPRMPEAAPPVAPAPAAPTAAPAPAPSWPLSSSVPSQKTYQGSYGFRLGFLHSGTAK 81
SP|P04637-7|P53_HUMAN -----
SP|P04637-8|P53_HUMAN -----
SP|P04637-9|P53_HUMAN -----

SP|P04637|P53_HUMAN  SVTCTYSPALNKMFCQLAKTCPVQLWVDSTPPPGTRVRAMAIYKQSQHMTVEVRRCPHHE 180
SP|P04637-2|P53_HUMAN SVTCTYSPALNKMFCQLAKTCPVQLWVDSTPPPGTRVRAMAIYKQSQHMTVEVRRCPHHE 180
SP|P04637-3|P53_HUMAN SVTCTYSPALNKMFCQLAKTCPVQLWVDSTPPPGTRVRAMAIYKQSQHMTVEVRRCPHHE 180
SP|P04637-4|P53_HUMAN SVTCTYSPALNKMFCQLAKTCPVQLWVDSTPPPGTRVRAMAIYKQSQHMTVEVRRCPHHE 141
SP|P04637-5|P53_HUMAN SVTCTYSPALNKMFCQLAKTCPVQLWVDSTPPPGTRVRAMAIYKQSQHMTVEVRRCPHHE 141
SP|P04637-6|P53_HUMAN SVTCTYSPALNKMFCQLAKTCPVQLWVDSTPPPGTRVRAMAIYKQSQHMTVEVRRCPHHE 141
SP|P04637-7|P53_HUMAN -----MFCQLAKTCPVQLWVDSTPPPGTRVRAMAIYKQSQHMTVEVRRCPHHE 48
SP|P04637-8|P53_HUMAN -----MFCQLAKTCPVQLWVDSTPPPGTRVRAMAIYKQSQHMTVEVRRCPHHE 48
SP|P04637-9|P53_HUMAN -----MFCQLAKTCPVQLWVDSTPPPGTRVRAMAIYKQSQHMTVEVRRCPHHE 48
*****

SP|P04637|P53_HUMAN  RCSDSGLAPPQHLIRVEGNLRVEYLDNRNTRHSSVVVPYEPPEVGSDCCTTIHYNMNCNS 240
SP|P04637-2|P53_HUMAN RCSDSGLAPPQHLIRVEGNLRVEYLDNRNTRHSSVVVPYEPPEVGSDCCTTIHYNMNCNS 240
SP|P04637-3|P53_HUMAN RCSDSGLAPPQHLIRVEGNLRVEYLDNRNTRHSSVVVPYEPPEVGSDCCTTIHYNMNCNS 240
SP|P04637-4|P53_HUMAN RCSDSGLAPPQHLIRVEGNLRVEYLDNRNTRHSSVVVPYEPPEVGSDCCTTIHYNMNCNS 201
SP|P04637-5|P53_HUMAN RCSDSGLAPPQHLIRVEGNLRVEYLDNRNTRHSSVVVPYEPPEVGSDCCTTIHYNMNCNS 201
SP|P04637-6|P53_HUMAN RCSDSGLAPPQHLIRVEGNLRVEYLDNRNTRHSSVVVPYEPPEVGSDCCTTIHYNMNCNS 201
SP|P04637-7|P53_HUMAN RCSDSGLAPPQHLIRVEGNLRVEYLDNRNTRHSSVVVPYEPPEVGSDCCTTIHYNMNCNS 108
SP|P04637-8|P53_HUMAN RCSDSGLAPPQHLIRVEGNLRVEYLDNRNTRHSSVVVPYEPPEVGSDCCTTIHYNMNCNS 108
SP|P04637-9|P53_HUMAN RCSDSGLAPPQHLIRVEGNLRVEYLDNRNTRHSSVVVPYEPPEVGSDCCTTIHYNMNCNS 108
*****

SP|P04637|P53_HUMAN  SCMGGMNRRPILTIITLEDSSGNLLGRNSFEVRVCACPGDRRTEENLRKKGEPHHELP 300
SP|P04637-2|P53_HUMAN SCMGGMNRRPILTIITLEDSSGNLLGRNSFEVRVCACPGDRRTEENLRKKGEPHHELP 300
SP|P04637-3|P53_HUMAN SCMGGMNRRPILTIITLEDSSGNLLGRNSFEVRVCACPGDRRTEENLRKKGEPHHELP 300
SP|P04637-4|P53_HUMAN SCMGGMNRRPILTIITLEDSSGNLLGRNSFEVRVCACPGDRRTEENLRKKGEPHHELP 261
SP|P04637-5|P53_HUMAN SCMGGMNRRPILTIITLEDSSGNLLGRNSFEVRVCACPGDRRTEENLRKKGEPHHELP 261
SP|P04637-6|P53_HUMAN SCMGGMNRRPILTIITLEDSSGNLLGRNSFEVRVCACPGDRRTEENLRKKGEPHHELP 261
SP|P04637-7|P53_HUMAN SCMGGMNRRPILTIITLEDSSGNLLGRNSFEVRVCACPGDRRTEENLRKKGEPHHELP 168
SP|P04637-8|P53_HUMAN SCMGGMNRRPILTIITLEDSSGNLLGRNSFEVRVCACPGDRRTEENLRKKGEPHHELP 168
SP|P04637-9|P53_HUMAN SCMGGMNRRPILTIITLEDSSGNLLGRNSFEVRVCACPGDRRTEENLRKKGEPHHELP 168
*****

SP|P04637|P53_HUMAN  PGSTKRALPNNTSSSPQPKKKPLDGEYFTLQIRGRERFEMFRELNEALELQDAQAGKEPG 360
SP|P04637-2|P53_HUMAN PGSTKRALPNNTSSSPQPKKKPLDGEYFTLQDQTSFQKENC----- 341
SP|P04637-3|P53_HUMAN PGSTKRALPNNTSSSPQPKKKPLDGEYFTLQMLLDLRWCYFLINSS----- 346
SP|P04637-4|P53_HUMAN PGSTKRALPNNTSSSPQPKKKPLDGEYFTLQIRGRERFEMFRELNEALELQDAQAGKEPG 321
SP|P04637-5|P53_HUMAN PGSTKRALPNNTSSSPQPKKKPLDGEYFTLQDQTSFQKENC----- 302
SP|P04637-6|P53_HUMAN PGSTKRALPNNTSSSPQPKKKPLDGEYFTLQMLLDLRWCYFLINSS----- 307
SP|P04637-7|P53_HUMAN PGSTKRALPNNTSSSPQPKKKPLDGEYFTLQIRGRERFEMFRELNEALELQDAQAGKEPG 228
SP|P04637-8|P53_HUMAN PGSTKRALPNNTSSSPQPKKKPLDGEYFTLQDQTSFQKENC----- 209
SP|P04637-9|P53_HUMAN PGSTKRALPNNTSSSPQPKKKPLDGEYFTLQMLLDLRWCYFLINSS----- 214
*****

SP|P04637|P53_HUMAN  GSRAHSSHLKSKKGQSTSRHKLMFKTEGPDS 393
SP|P04637-2|P53_HUMAN -----
SP|P04637-3|P53_HUMAN -----
SP|P04637-4|P53_HUMAN GSRAHSSHLKSKKGQSTSRHKLMFKTEGPDS 354
SP|P04637-5|P53_HUMAN -----
SP|P04637-6|P53_HUMAN -----
SP|P04637-7|P53_HUMAN GSRAHSSHLKSKKGQSTSRHKLMFKTEGPDS 261
SP|P04637-8|P53_HUMAN -----
SP|P04637-9|P53_HUMAN -----

```

图32

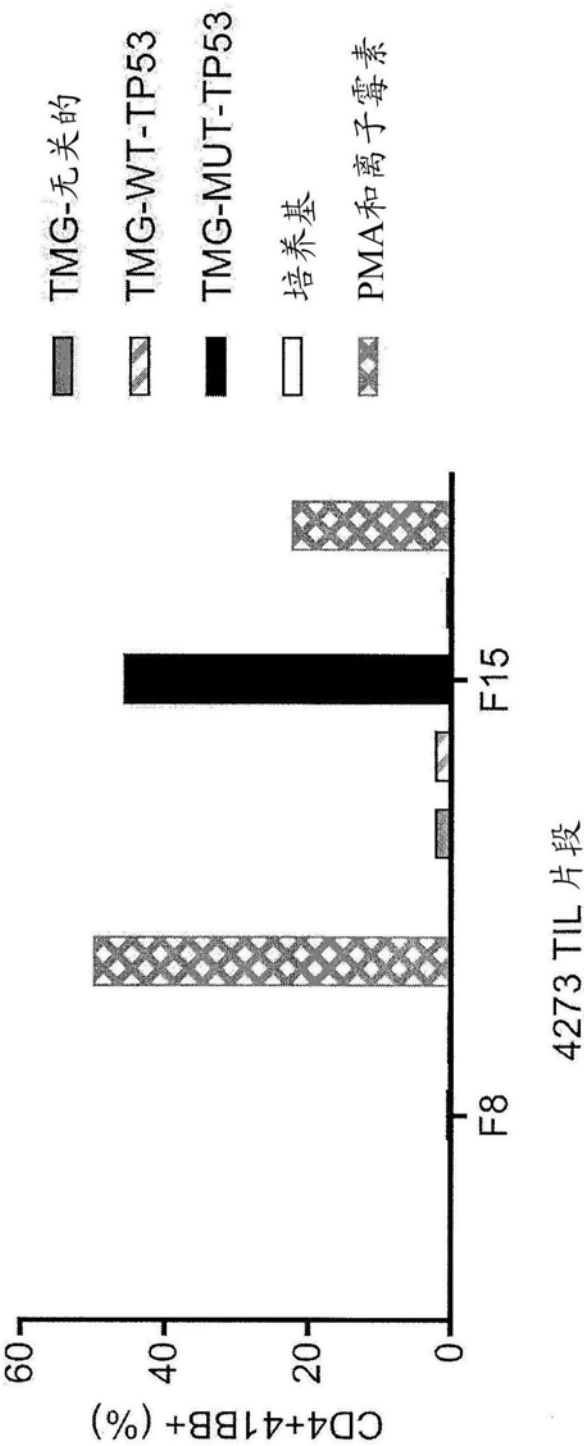


图33

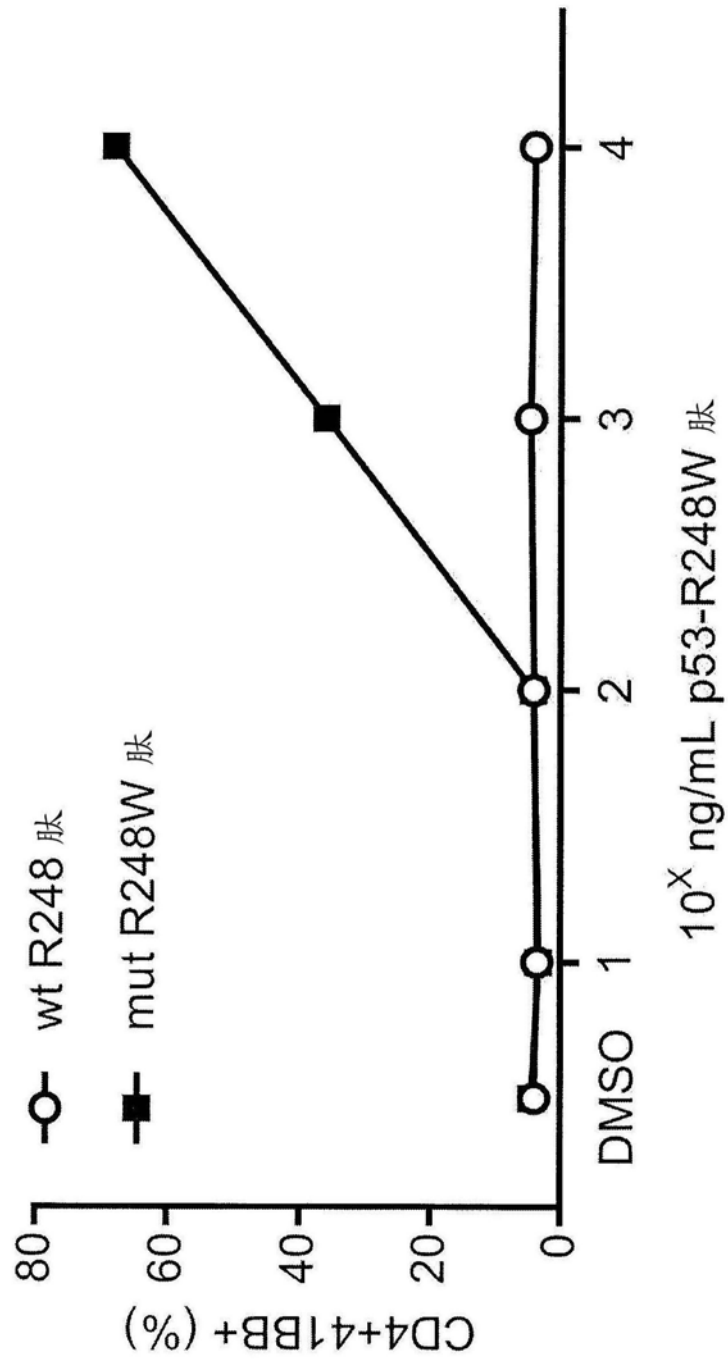


图34

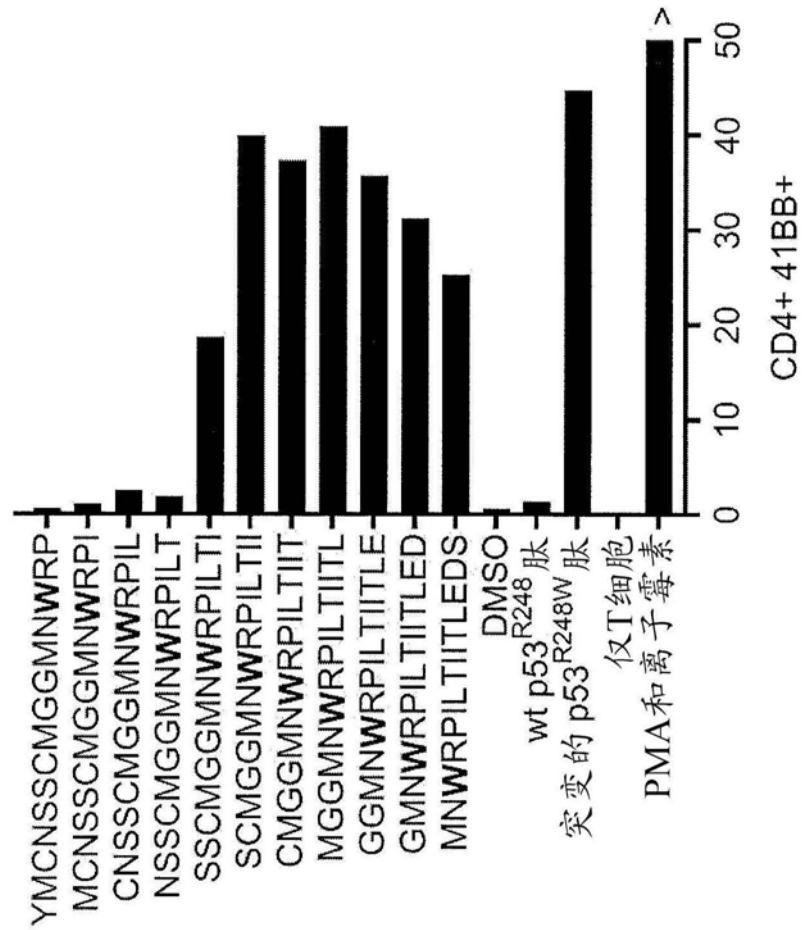


图35

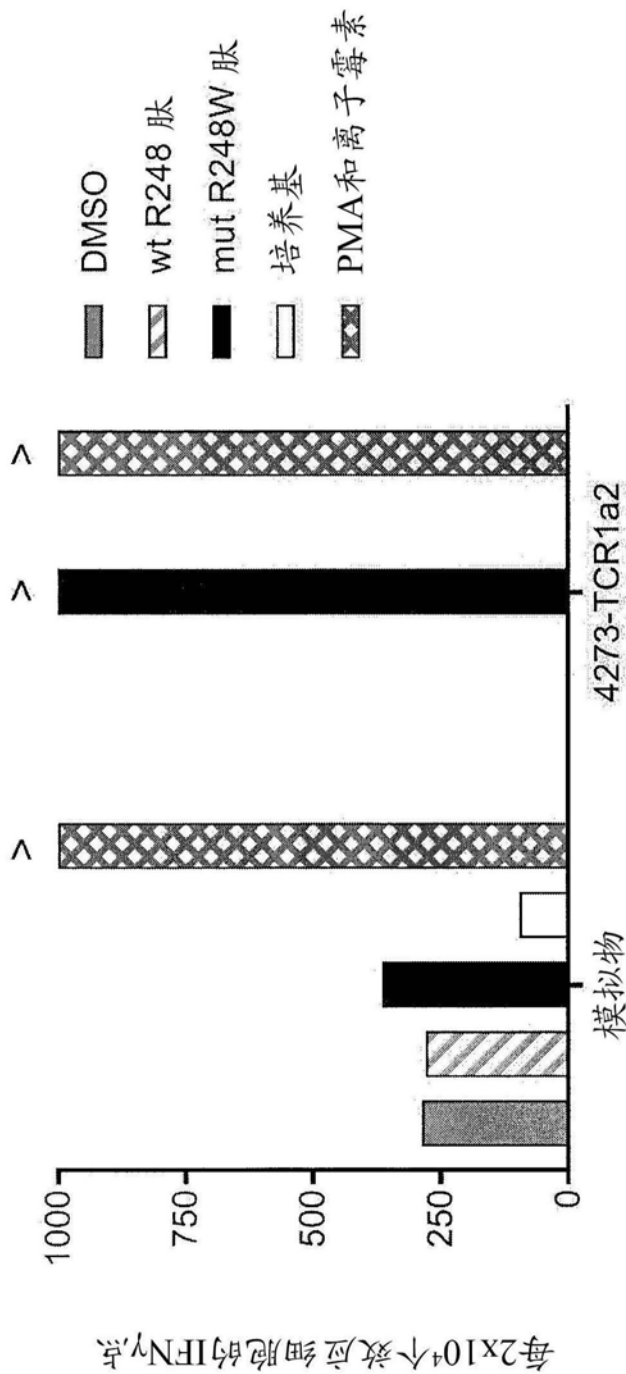


图37

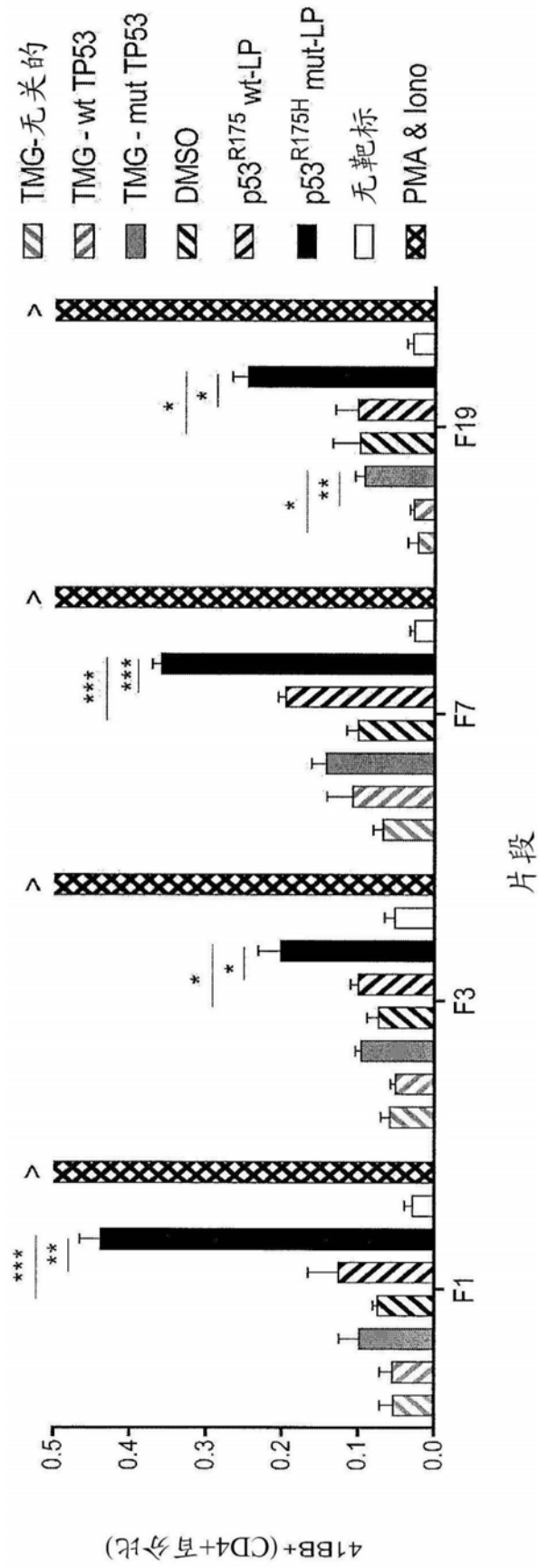


图38

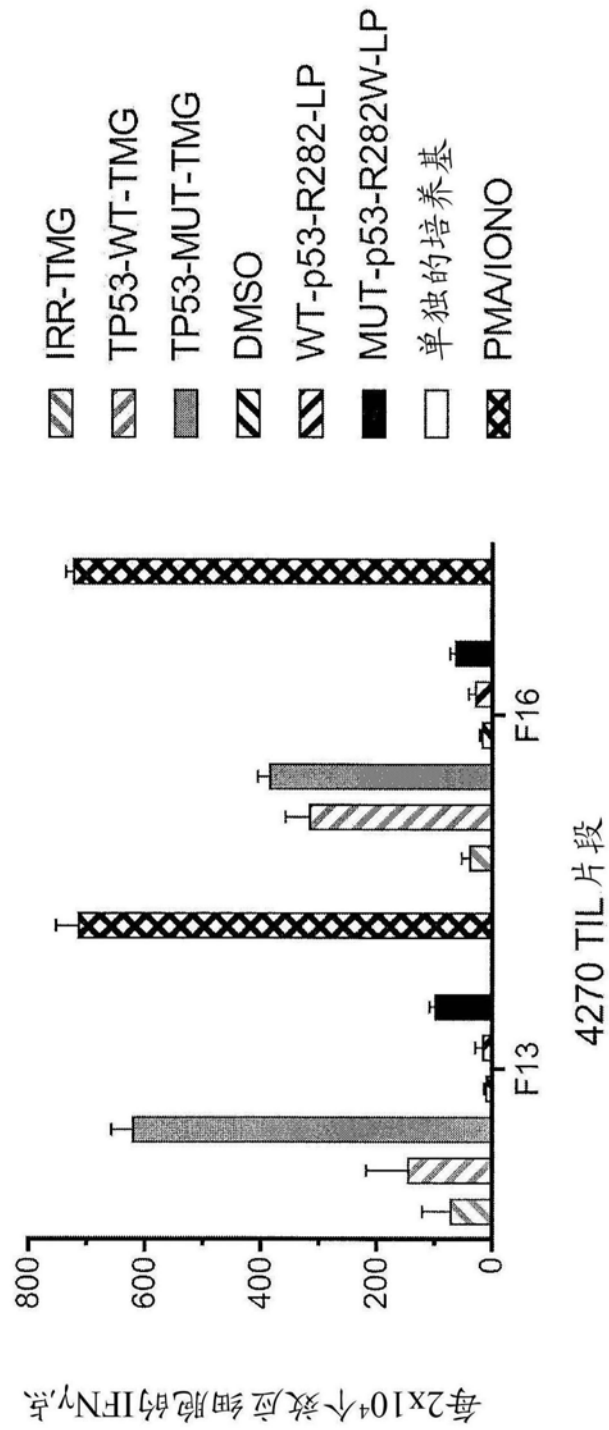


图39

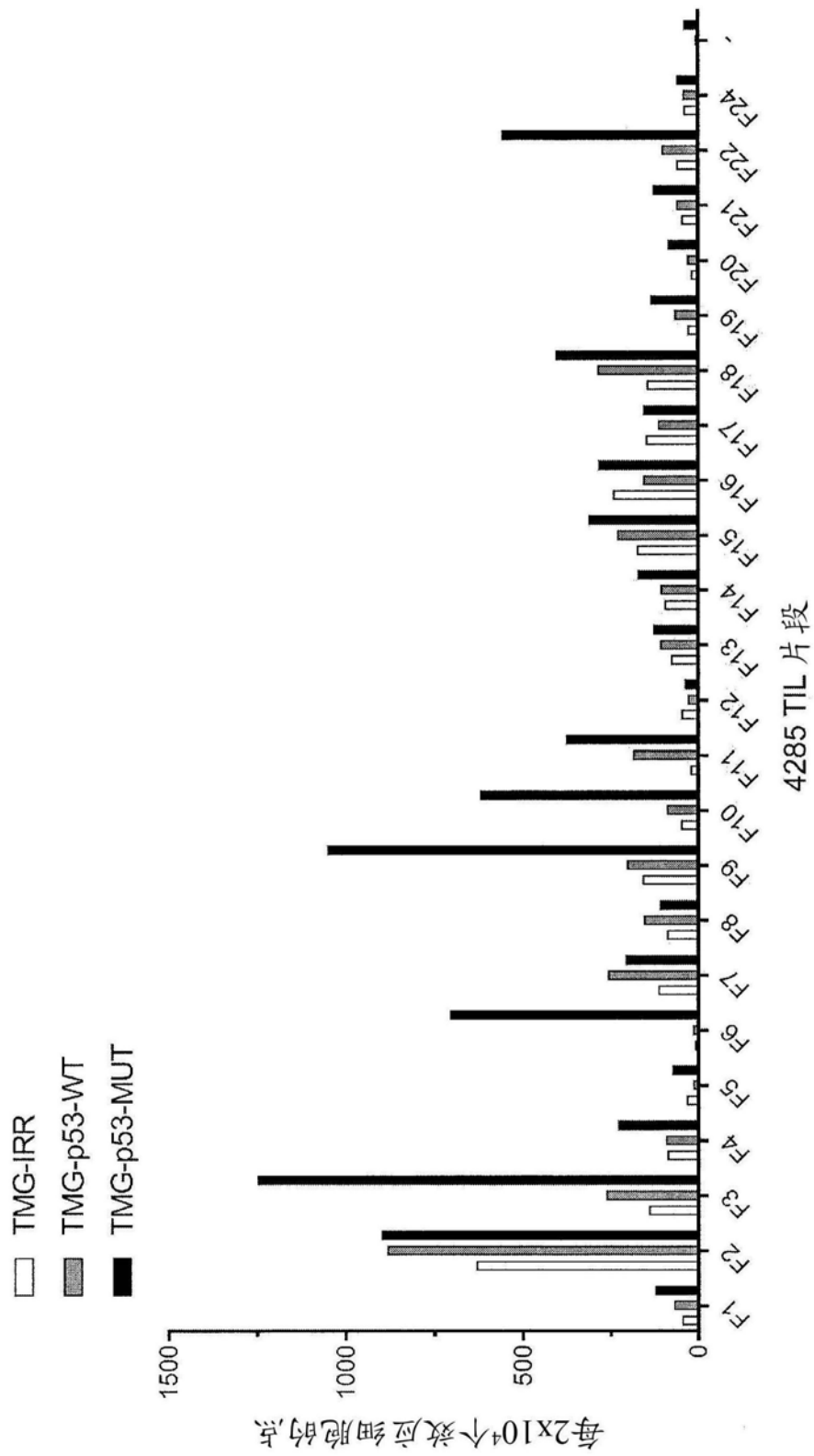


图40

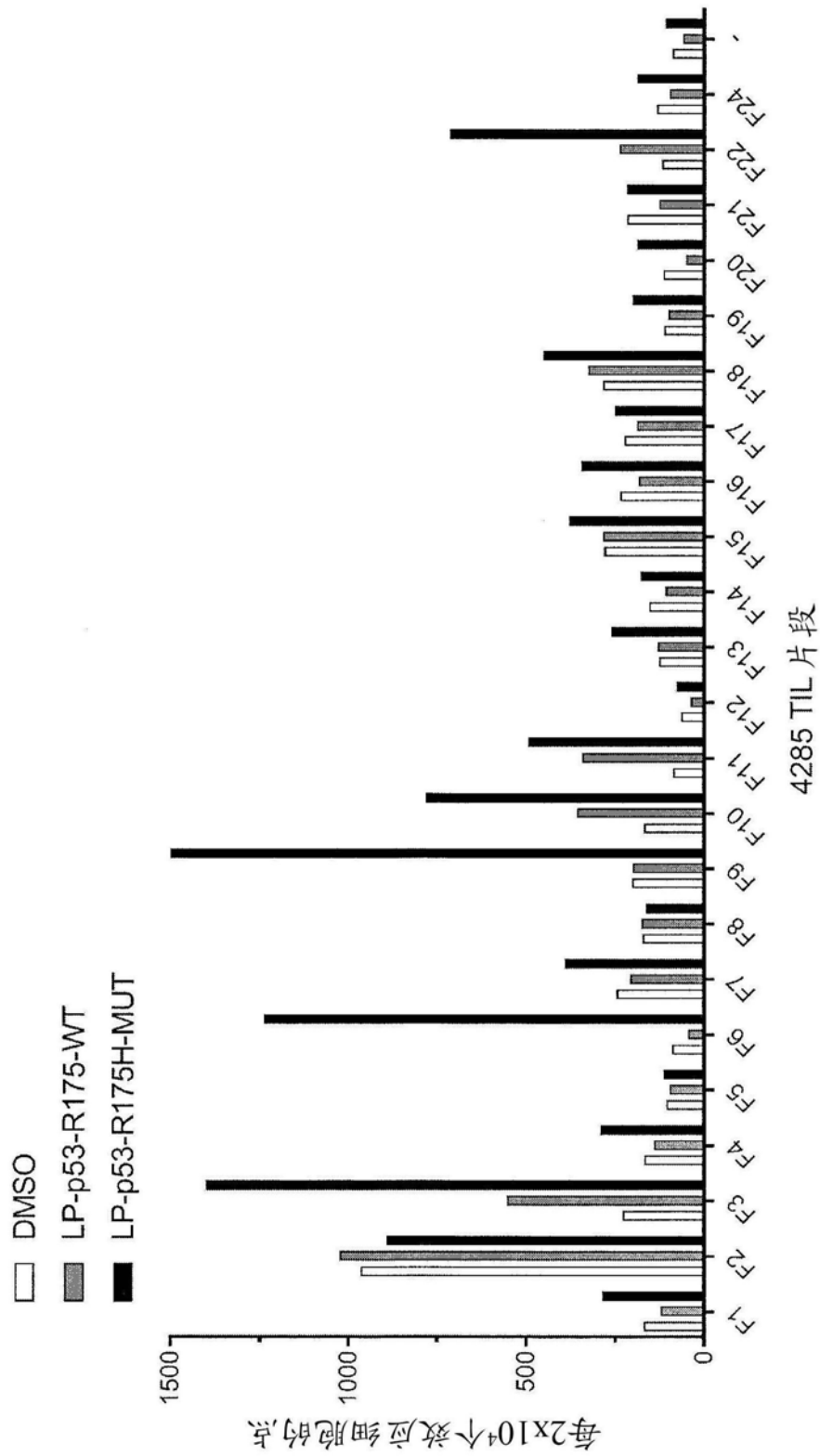


图41

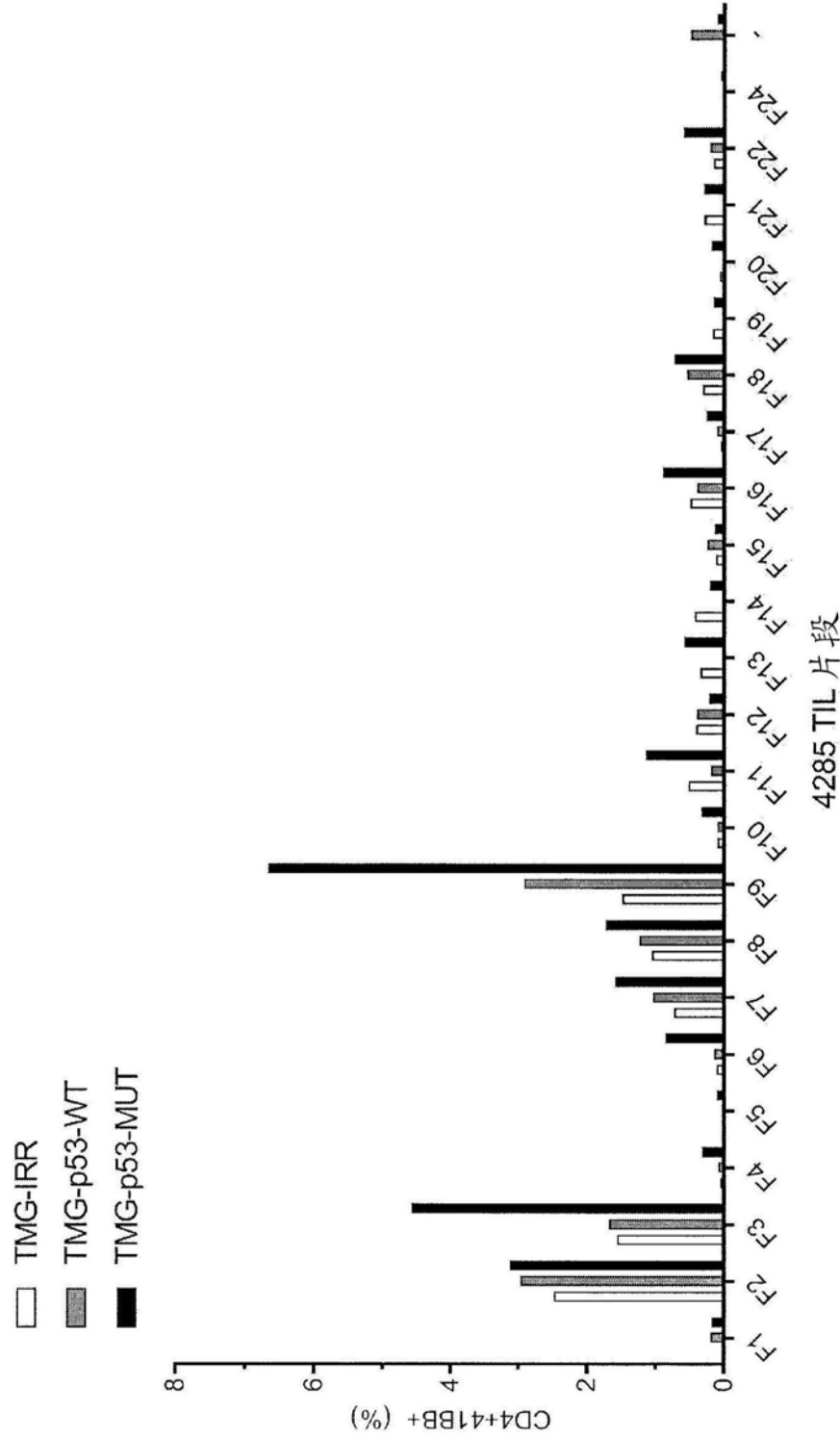


图42

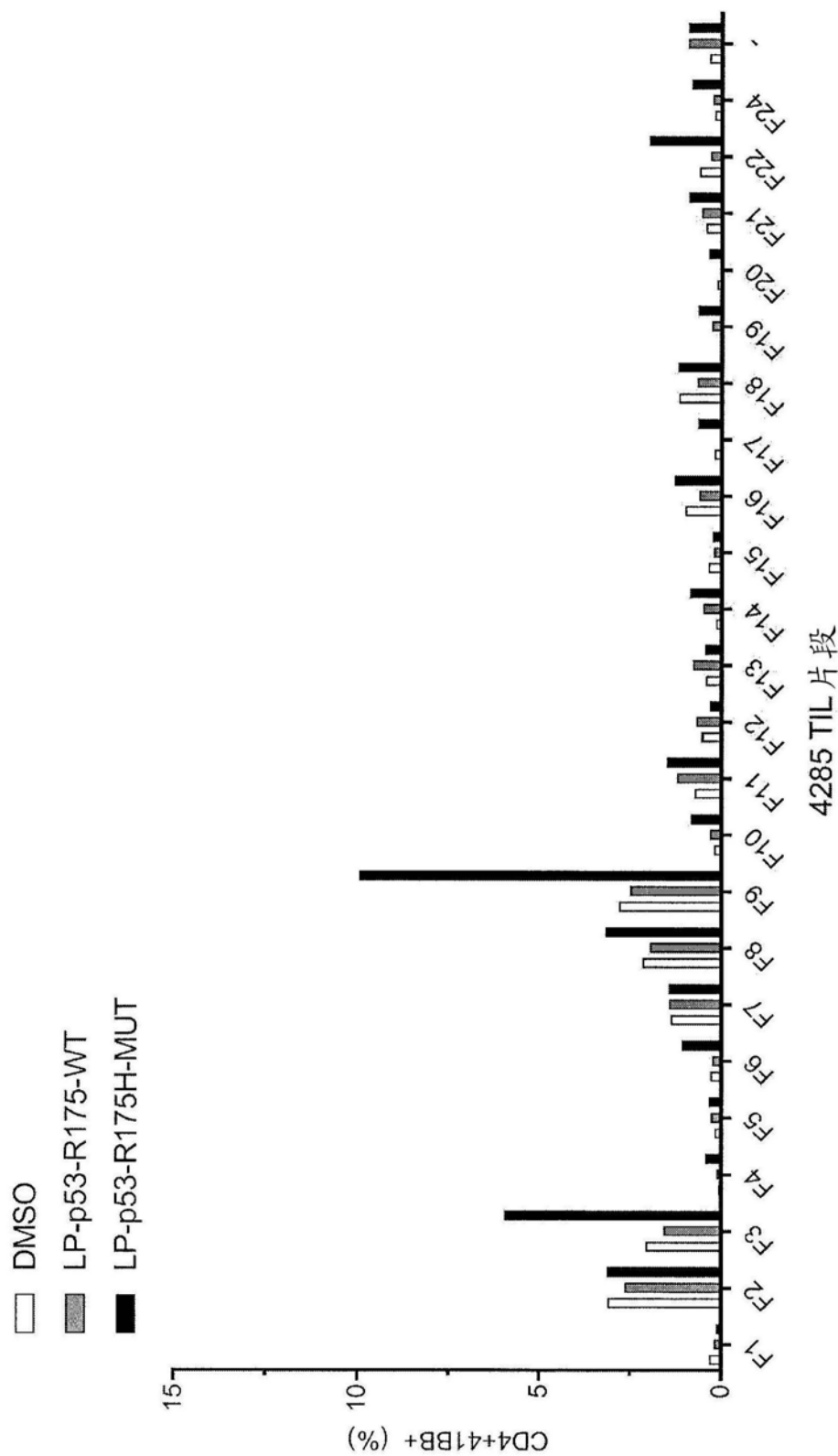


图43

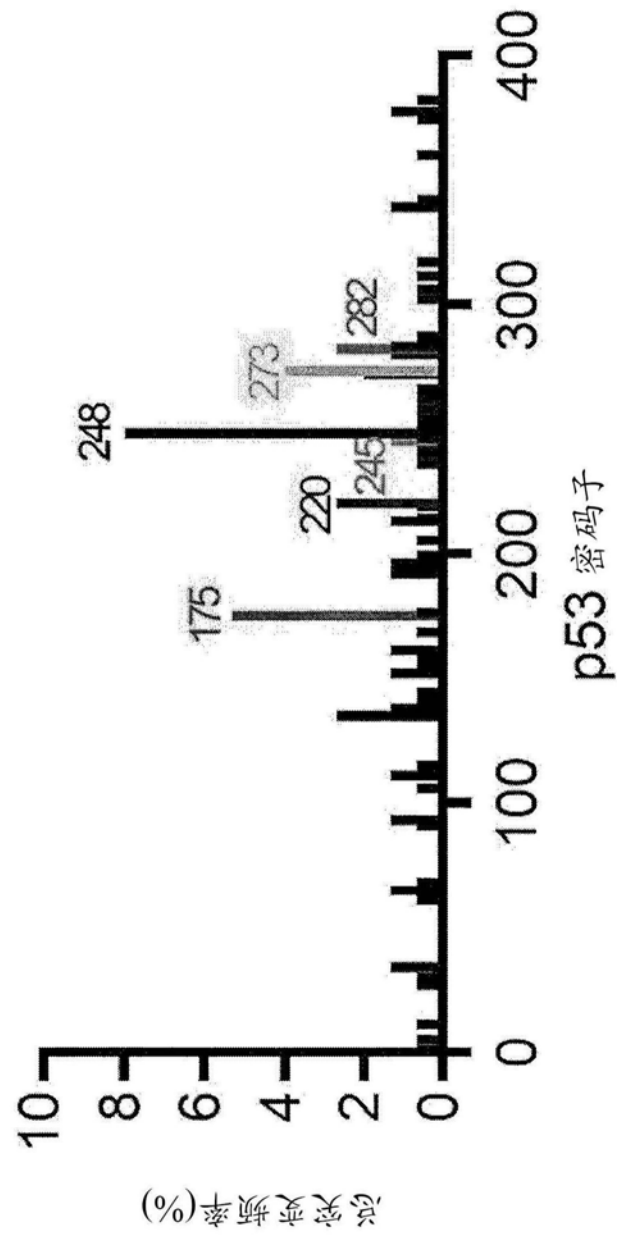


图44

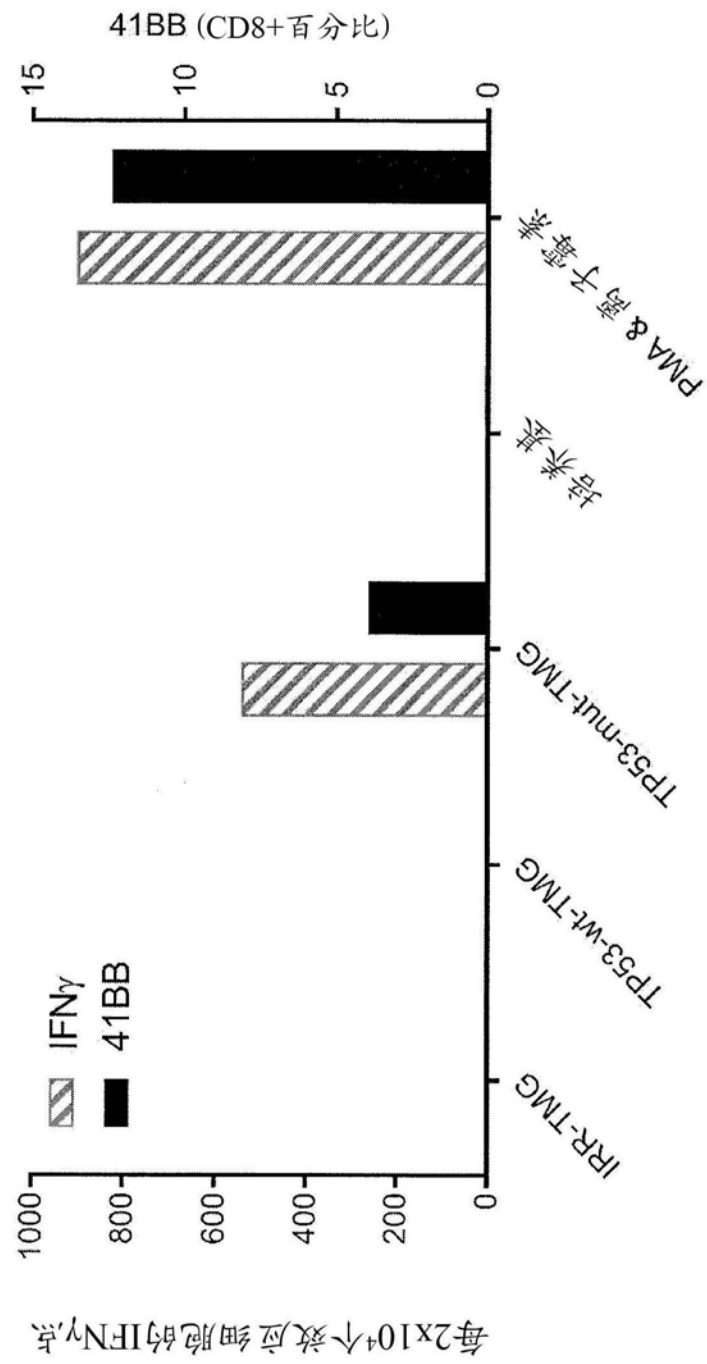


图45

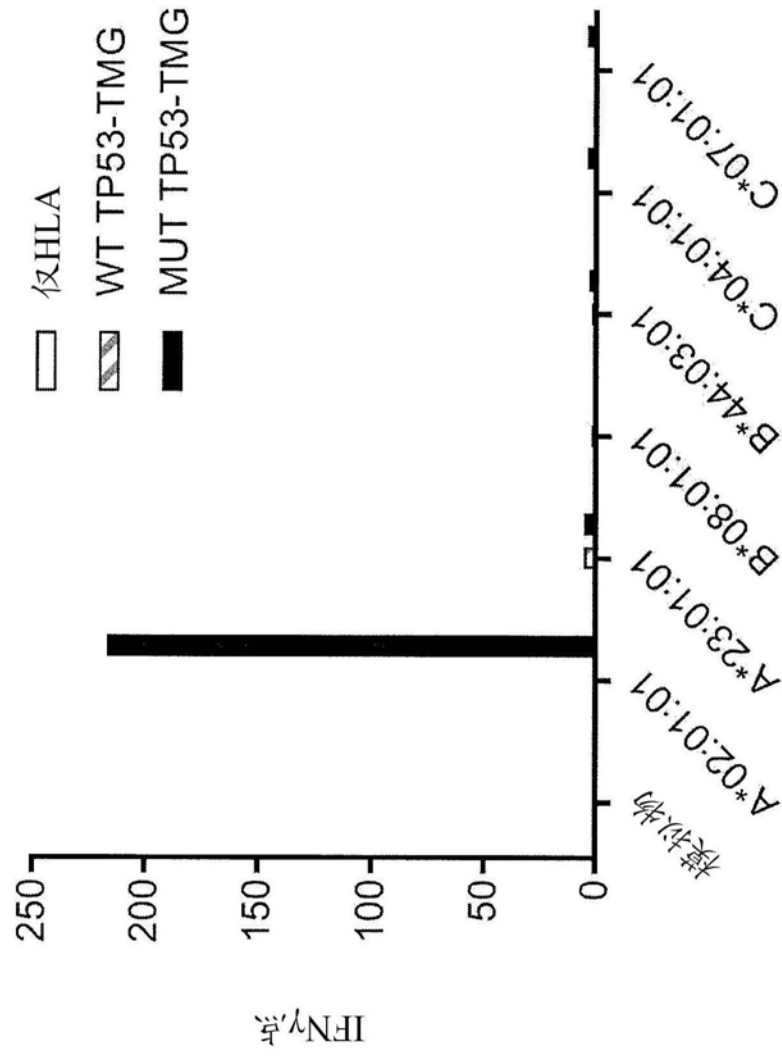


图46

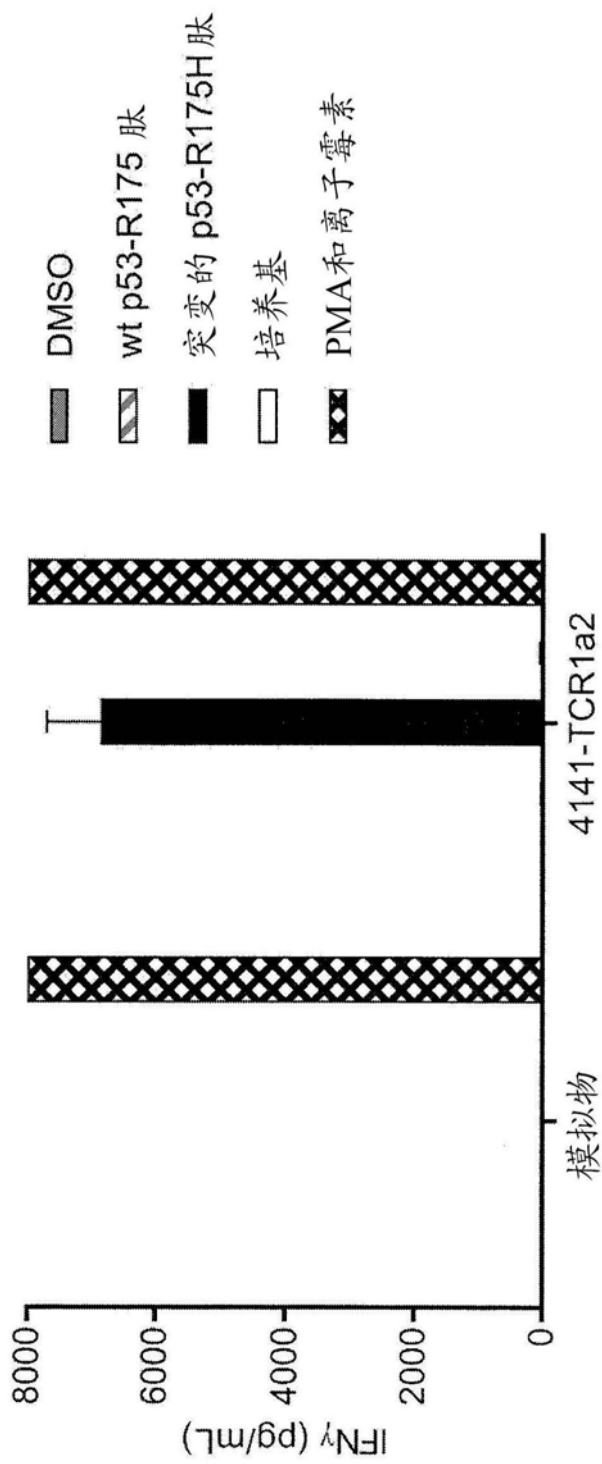


图47

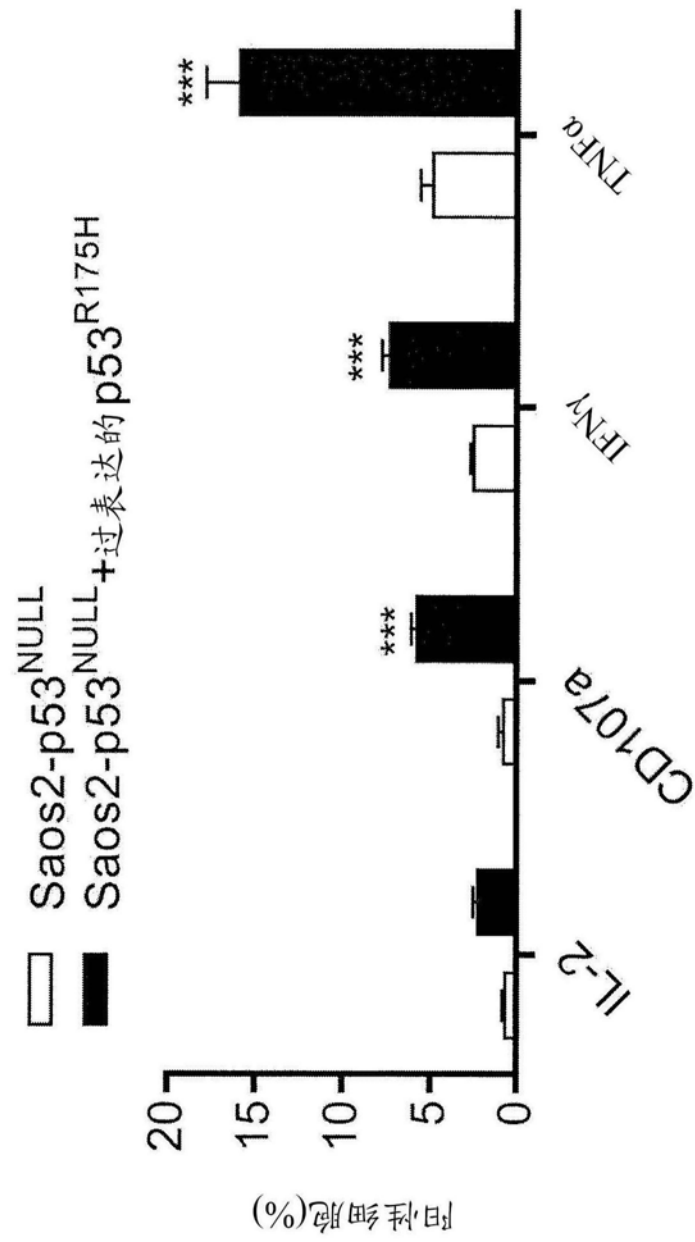


图48

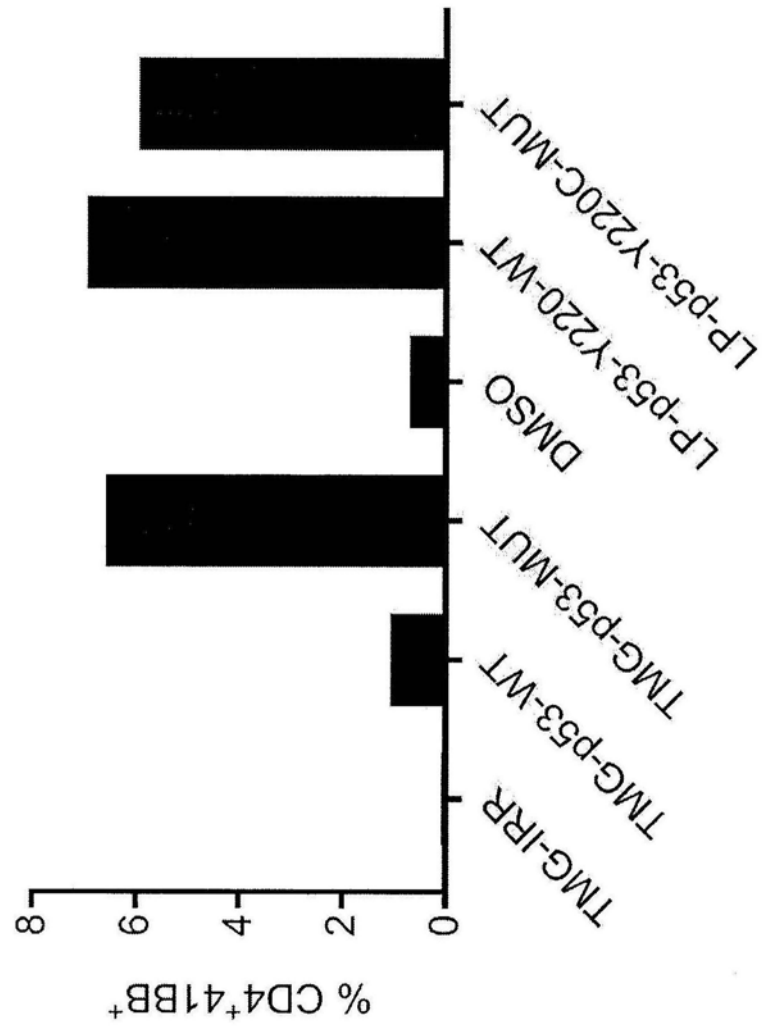


图49

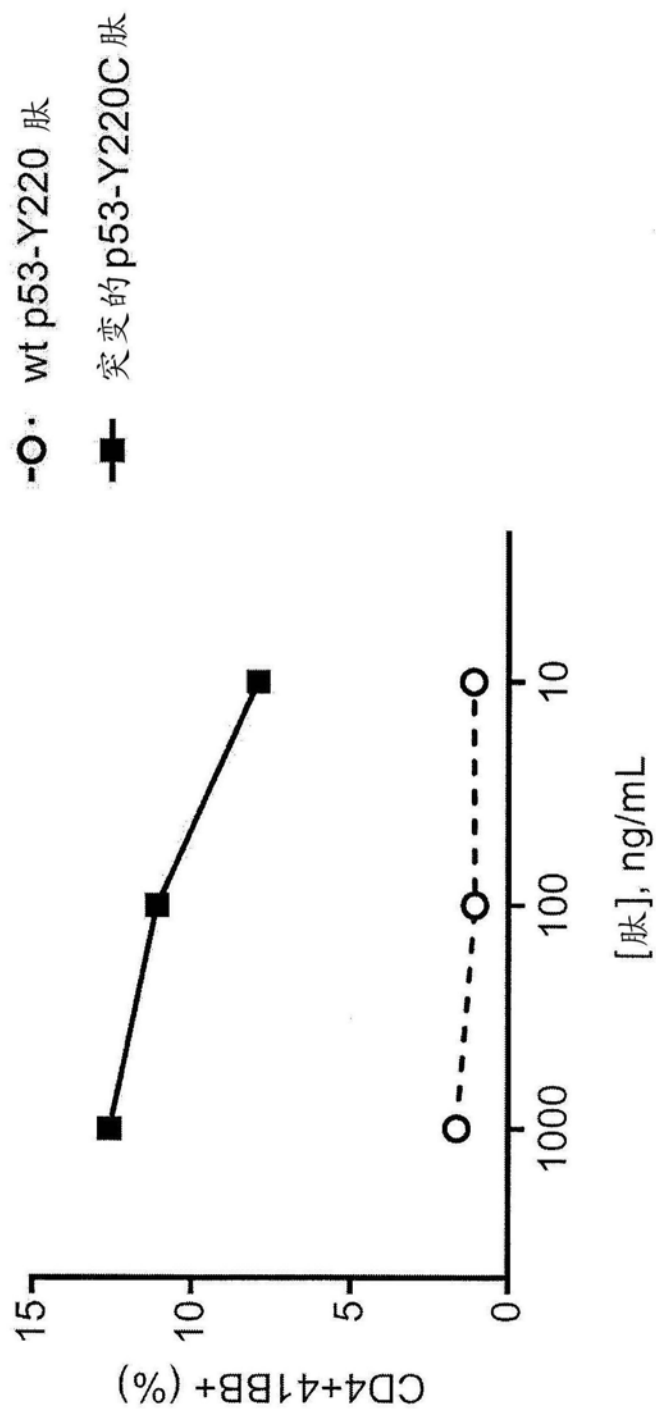


图50

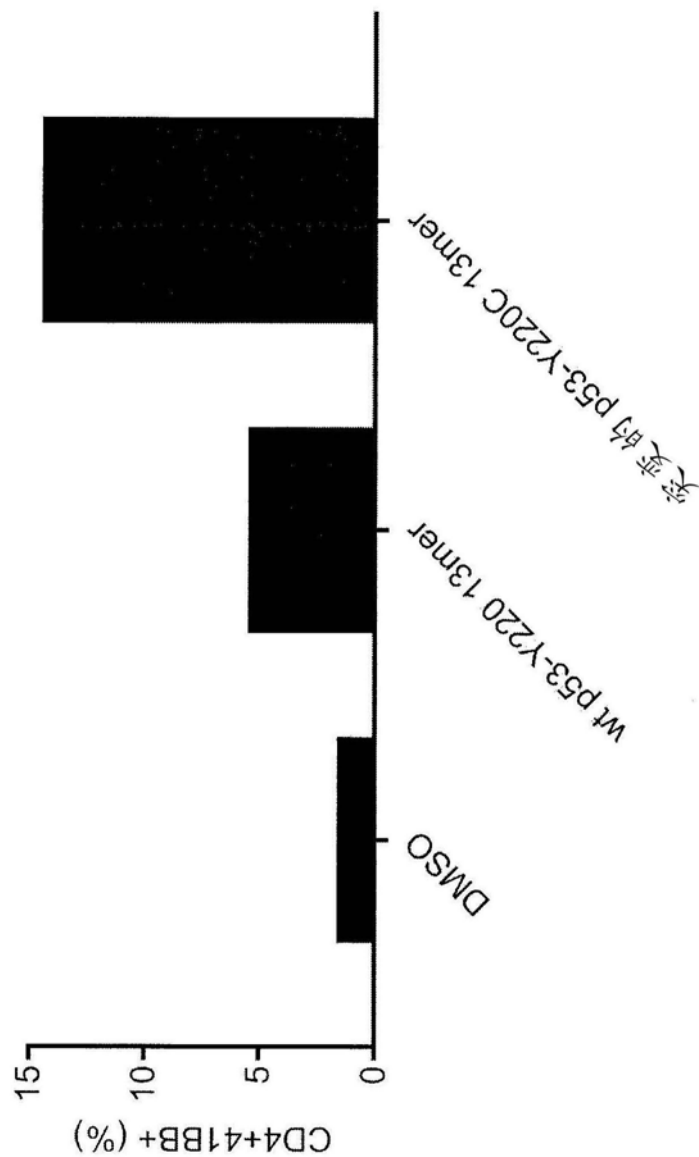


图51

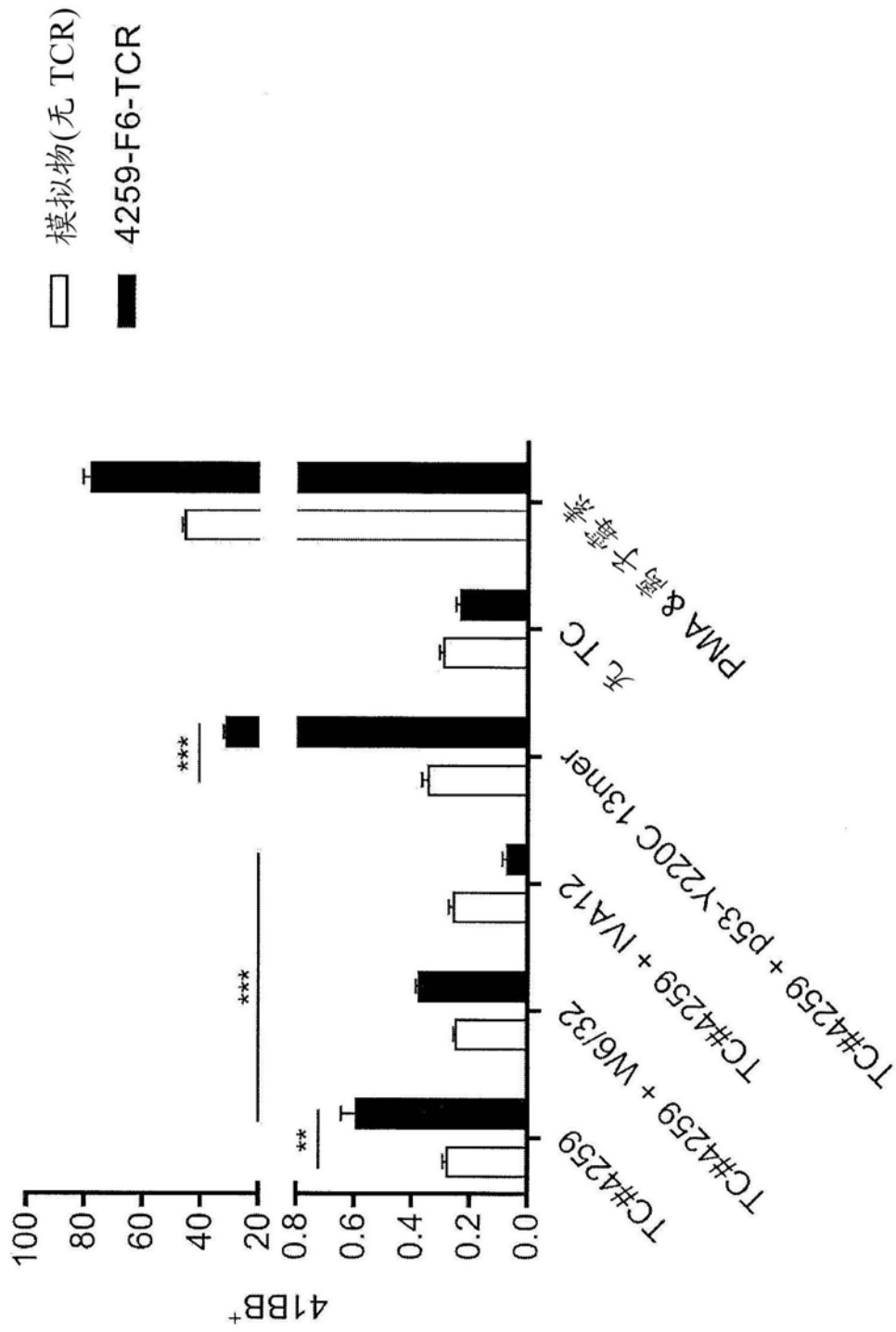


图53

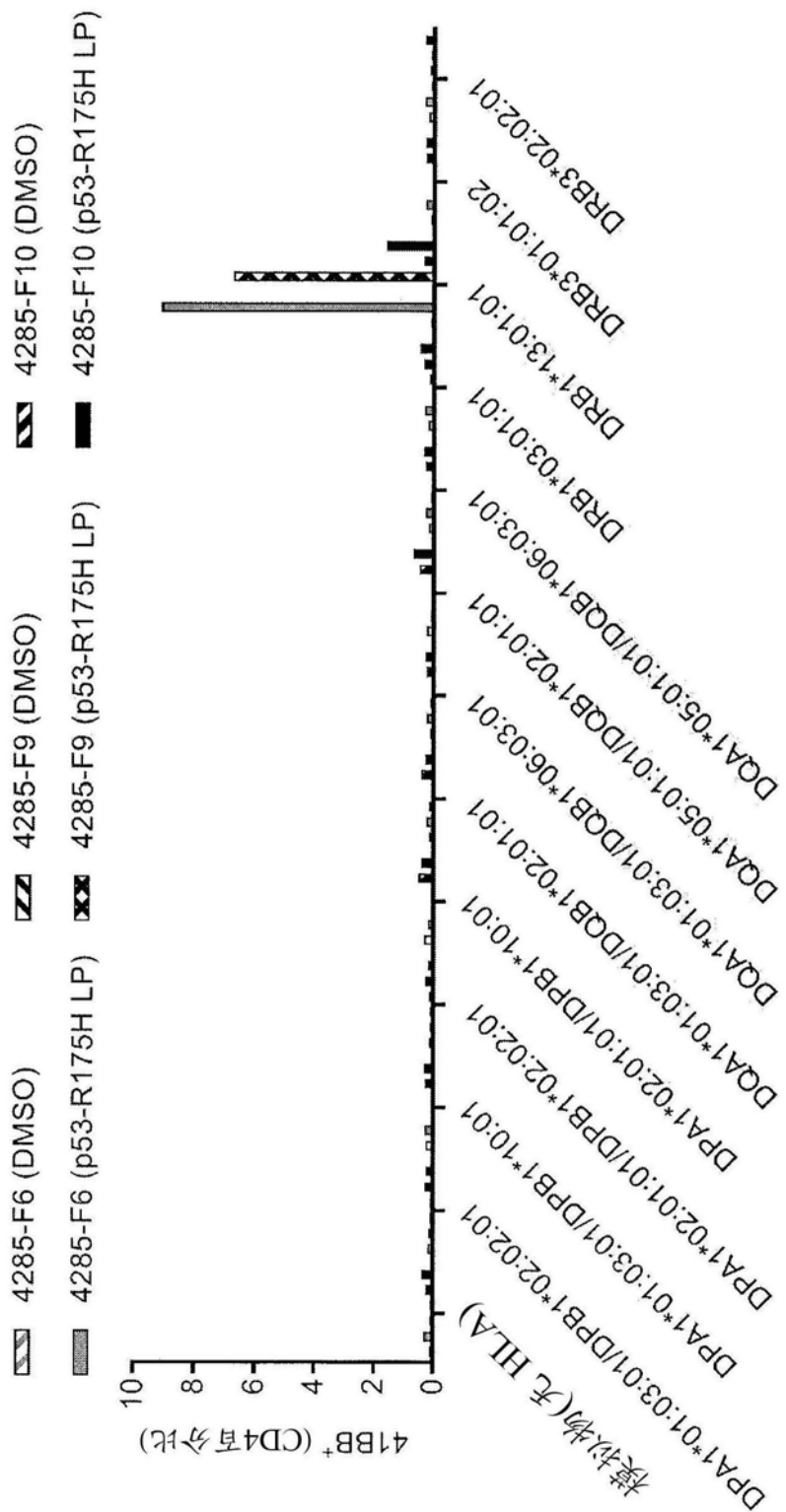


图54

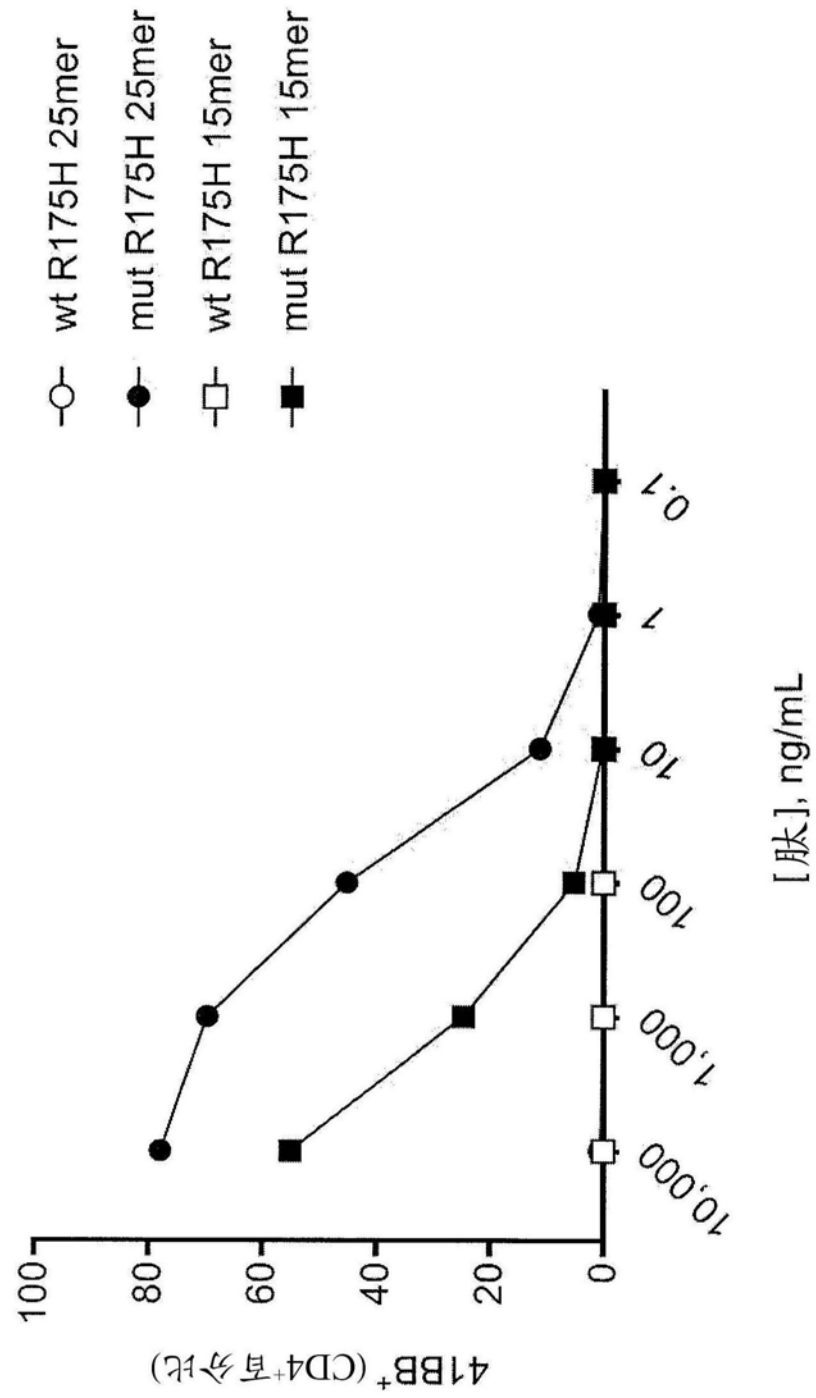


图55