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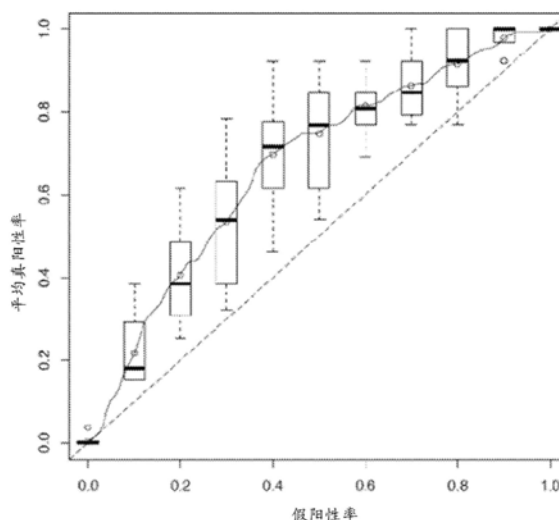
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(54)发明名称

用于评估结肠肿瘤的存在或风险的方法

(57)摘要

公开的方法用于预测或评估患者的结肠肿瘤状态。这些方法可用于确定肿瘤的性质、复发或患者对治疗的反应。该方法的一些实施方案包括生成用于临床管理的报告。本文提供的方法旨在检测技术变化,并允许数据归一化及提高信号检测,以及构建疾病状态和反应的预测性蛋白质谱。



1. 一种以大于70%的灵敏度或大于70%的选择性检测受试者结肠的腺瘤或息肉存在的方法;所述方法包括以下步骤:

- (a) 从受试者获得血液样品;
- (b) 裂解所述血液样品中的蛋白质以提供包含肽的样品;
- (c) 分析所述样品中至少十种肽的存在;
- (d) 将分析所述样品的结果与对照参考值进行比较,从而以大于70%的灵敏度或大于70%的选择性确定存在结肠的腺瘤或息肉的正或负得分。

2. 一种治疗受试者的结肠的腺瘤或息肉的方法,该方法包括:

- (a) 执行权利要求1所述的方法以得到具有存在腺瘤或息肉的正得分的受试者;以及
- (b) 进行用于去除所述受试者的腺瘤或息肉组织的程序。

3. 一种检测受试者的结肠的腺瘤或息肉的存在与否的方法,其中所述受试者没有结肠的腺瘤或息肉的症状或家族史,所述方法包括以下步骤:

- (a) 从所述受试者获得生物样品;
- (b) 对所述生物样品进行关于一种或多种蛋白质和/或肽的存在和量的分析;
- (c) 将来自所述生物样品的一种或多种蛋白质和/或肽的存在和量与对照参考值进行比较;以及
- (d) 将一种或多种蛋白质和/或肽的存在和量与所述受试者的腺瘤或息肉状态相关联。

4. 一种检测在结肠镜检查得到阴性结果的受试者中结肠的腺瘤或息肉的存在与否的方法,所述方法包括以下步骤:

- (a) 从基于结肠镜检查具有腺瘤或息肉的阴性诊断的受试者获得生物样品;
- (b) 对所述生物样品进行关于一种或多种蛋白质和/或肽的存在和量的分析;
- (c) 将来自所述生物样品的一种或多种蛋白质和/或肽的存在和量与对照参考值进行比较;以及
- (d) 将一种或多种蛋白质和/或肽的存在和量与所述受试者的腺瘤或息肉状态相关联。

5. 一种检测先前治疗结肠的腺瘤或息肉的受试者中结肠的腺瘤或息肉的复发或不存在的方法,该方法包括以下步骤:

- (a) 从先前治疗结肠的腺瘤或息肉的受试者获得生物样品;
- (b) 对所述生物样品进行关于一种或多种蛋白质和/或肽的存在和量的分析;
- (c) 将来自所述生物样品的一种或多种蛋白质和/或肽的存在和量与对照参考值进行比较;以及
- (d) 将一种或多种蛋白质和/或肽的存在和量与所述受试者的腺瘤或息肉状态相关联。

6. 一种针对诊断应用的蛋白质和/或肽检测方法,该方法包括以下步骤:

- (a) 从受试者获得生物样品;
 - (b) 对所述生物样品进行关于一种或多种蛋白质和/或肽的存在和量的分析;
 - (c) 将来自所述生物样品的一种或多种蛋白质和/或肽的存在和量与对照参考值进行比较;以及
 - (d) 将一种或多种蛋白质和/或肽的存在和量与所述受试者的诊断相关联;
- 其中所述分析检测下组中的一种或多种的存在和量:

i) 选自SCDC26 (CD26)、CEA分子5 (CEACAM5)、CA195 (CCR5)、CA19-9、M2PK (PKM2)、TIMP1、

P-选择蛋白 (SELPLG)、VEGFA、HcGB (CGB)、绒毛蛋白、TATI (SPINK1)、A-L-岩藻糖苷酶 (FUCA2)、ANXA5、GAPDH、PKM2、ANXA4、GARS、RRBP1、KRT8、SYNCRIP、S100A9、ANXA3、CAPG、HNRNPF、PPA1、NME1、PSME3、AHCY、TPT1、HSPB1和RPSA、和/或图9中的蛋白质,以及它们的一种或多种蛋白质;

ii) SCDC26 (CD26)、CEA分子5 (CEACAM5)、CA195 (CCR5)、CA19-9、M2PK (PKM2)、TIMP1、P-选择蛋白 (SELPLG)、VEGFA、HcGB (CGB)、绒毛蛋白、TATI (SPINK1)、A-L-岩藻糖苷酶 (FUCA2) 和ANXA5、GAPDH、PKM2、ANXA4、GARS、RRBP1、KRT8、SYNCRIP、S100A9、ANXA3、CAPG、HNRNPF、PPA1、NME1、PSME3、AHCY、TPT1、HSPB1和RPSA、和/或图9中的蛋白质,以及它们的组合的一种或多种肽片段;

iii) 与SCDC26 (CD26)、CEA分子5 (CEACAM5)、CA195 (CCR5)、CA19-9、M2PK (PKM2)、TIMP1、P-选择蛋白 (SELPLG)、VEGFA、HcGB (CGB)、绒毛蛋白、TATI (SPINK1)、A-L-岩藻糖苷酶 (FUCA2)、ANXA5、GAPDH、PKM2、ANXA4、GARS、RRBP1、KRT8、SYNCRIP、S100A9、ANXA3、CAPG、HNRNPF、PPA1、NME1、PSME3、AHCY、TPT1、HSPB1和RPSA、和/或图9中的蛋白质,以及它们的组合具有序列同源性的一种或多种肽,其中所述序列同源性选自大于75%、大于80%、大于85%、大于90%、大于95%及大于99%;

iv) SCDC26 (CD26)、CEA分子5 (CEACAM5)、CA195 (CCR5)、CA19-9、M2PK (PKM2)、TIMP1、P-选择蛋白 (SELPLG)、VEGFA、HcGB (CGB)、绒毛蛋白、TATI (SPINK1)、A-L-岩藻糖苷酶 (FUCA2) 和ANXA5、GAPDH、PKM2、ANXA4、GARS、RRBP1、KRT8、SYNCRIP、S100A9、ANXA3、CAPG、HNRNPF、PPA1、NME1、PSME3、AHCY、TPT1、HSPB1和RPSA、和/或图9中的蛋白质,以及它们的组合的一种或多种结合配偶体;以及

v) 从中得到图7或图8中的一个或多个中性质量簇的蛋白质或肽。

7. 一种用于诊断、预测、预后和/或监测受试者的结肠疾病的方法,该方法包括:测量来自所述受试者的生物样品中选自下组的至少一种生物标志物:ACTB、ACTH、ANGT、SAHH、ALDR、AKT1、ALBU、AL1A1、AL1B1、ALDOA、AMY2B、ANXA1、ANXA3、ANXA4、ANXA5、APC、APOA1、APOC1、APOH、GDIR1、ATPB、BANK1、MIC1、CA195、CO3、CO9、CAH1、CAH2、CALR、CAPG、CD24、CD63、CDD、CEAM3、CEAM5、CEAM6、CGHB、CH3L1、KCRB、CLC4D、CLUS、CNN1、COR1C、CRP、CSF1、CTNB1、CATD、CATS、CATZ、CUL1、SYDC、DEF1、DEF3、DESM、DPP4、DPYL2、DYHC1、ECH1、EF2、IF4A3、ENOA、EZRI、NIBL2、SEPR、FBX4、FIBB、FIBG、FHL1、FLNA、FRMD3、FRIH、FRIL、FUCO、GBRA1、G3P、SYG、GDF15、GELS、GSTP1、HABP2、HGF、1A68、HMGB1、ROA1、ROA2、HNRPF、HPT、HS90B、ENPL、GRP75、HSPB1、CH60、SIAL、IFT74、IGF1、IGHA2、IL2RB、IL8、IL9、RASK、K1C19、K2C8、LAMA2、LEG3、LMNB1、MARE1、MCM4、MIF、MMP7、MMP9、CD20、MYL6、MYL9、NDKA、NNMT、A1AG1、PCKGM、PDIA3、PDIA6、PDXK、PEBP1、PIPNA、KPYM、UROK、IPYR、PRDX1、KPCD1、PRL、TMG4、PSME3、PTEN、FAK1、FAK2、RBX1、REG4、RHOA、RHOB、RHOC、RSSA、RRBP1、S10AB、S10AC、S10A8、S109、SAA1、SAA2、SEGN、SDCG3、DHSA、SBP1、SELPL、SEP9、A1AT、AACT、ILEU、SPB6、SF3B3、SKP1、ADT2、ISK1、SPON2、OSTP、SRC、STK11、HNRPQ、TAL1、TRFE、TSP1、TIMP1、TKT、TSG6、TR10B、TNF6B、P53、TPM2、TCTP、TRAP1、THTR、TBB1、UGDH、UGPA、VEGFA、VILI、VIME、VNN1、1433Z、CCR5、FUCO及其组合。

8. 一种用于诊断、预测、预后和/或监测受试者的结肠疾病的方法,该方法包括:测量来自所述受试者的生物样品中选自SPB6、FRIL、P53、1A68、ENOA、TKT及其组合的至少一种生物

标志物。

9. 一种用于诊断、预测、预后和/或监测受试者的结肠疾病的方法,该方法包括:测量来自所述受试者的生物样品中选自SPB6、FRIL、P53、1A68、ENOA、TKT、TSG6、TPM2、ADT2、FHL1、CCR5、CEAM5、SPON2、1A68、RBX1、COR1C、VIME、PSME3及其组合的至少一种生物标志物。

10. 一种用于诊断、预测、预后和/或监测受试者的结肠疾病的方法,该方法包括:测量来自所述受试者的生物样品中选自SPB6、FRIL、P53、1A68、ENOA、TKT、TSG6、TPM2、ADT2、FHL1、CCR5、CEAM5、SPON2、1A68、RBX1、COR1C、VIME、PSME3、MIC1、STK11、IPYR、SBP1、PEBP1、CATD、HPT、ANXA5、ALDOA、LAMA2、CATZ、ACTB、AACT及其组合的至少一种生物标志物。

用于评估结肠肿瘤的存在或风险的方法

本申请是申请日为2013年12月02日、申请号为 201380071930.X、发明名称为“用于评估结肠肿瘤的存在或风险的方法”的中国专利申请(PCT申请号为PCT/US2013/072691,PCT申请日为2013年12月02日)的分案申请。

交叉引用

[0001] 本申请根据35U.S.C.§119(e)要求2012年11月30日提交的美 国临时申请号61/732,024和2013年3月5日提交的美国临时申请号 61/772,979的优先权,所有这些临时申请均通过引用而整体并入本文。

序列表

[0002] 本申请包含序列表,该序列表已经以ASCII格式电子提交,且 通过引用而整体并入于此。所述ASCII副本在2013年11月27日创 建,被命名为36765-703.201_SL.txt,大小为783,936个字节。

发明背景

[0003] 如本领域已知,基因组的信息内容作为DNA而携带。基因表 达的第一步是将DNA转录成mRNA。基因表达的第二步是从mRNA 合成多肽,使得mRNA的每三个核苷酸编码一个将组成多肽的氨基 酸残基。翻译后,多肽通常通过添加不同的化学基团如碳水化合物、脂质和磷酸基团以及通过对特定肽键的蛋白水解裂解进行翻译后修 饰。这些化学修饰使多肽呈现独特的三维构象,从而形成成熟蛋白质。虽然这些翻译后修饰不是由mRNA模板直接编码的,但它们是蛋白 质的关键特质,其通过改变整体构象和可用的相互作用位点来起到调节蛋白质功能的作用。此外,细胞内的蛋白质水平可反映个体是否处 于健康或疾病状态。因此,蛋白质是疾病状态、疾病的早期发作和疾 病风险的非常有价值的生物标志物来源。

[0004] mRNA和蛋白质均通过单独的途径不断地合成并降解。此外, 存在对合成和降解途径的多个水平的调节。鉴于此,在mRNA种类 的丰度与它们编码的蛋白质的实际量之间不存在简单的关联也就不 足为奇了(Anderson和Seilhamer,Electrophoresis 18:533-537; Gygi 等人,Mol.Cell.Biol.19:1720-1730,1999)。因此,尽管通常外推 mRNA水平以指示表达的蛋白质的水平,但蛋白质的最终水平并非必 需通过测量mRNA水平才可获得(Patton, J.Chromatogr.722:203-223, 1999;Patton等人,J.Biol.Chem.270:21404-21410(1995))。

[0005] 因此,需要确定生物样品的蛋白质谱的方法。

发明内容

[0006] 公开了用于以大于70%的灵敏度或大于70%的选择性检测受试 者的结肠的腺瘤、癌症或息肉的存在的方法。在各个实施方案中,所 述方法包括以下步骤:(a)从受试者获得血液样品;(b)裂解所述 血液样品中的蛋白质以提供包含肽的样品;(c)分析所述样品中至 少十种肽的存在;(d)将分析所述样品的结果与对照参考值进行比 较,从而以大于70%的灵敏度或大于70%的选择性确定存在结肠的腺 瘤或息肉的正或负得分。还公开了治疗受试者的结肠的腺瘤、癌症或 息肉的方法,该方法包括:(a)执行如本文所述的检测方法以得到 具有存在腺瘤、癌症或息肉的正得分的受试者;以及(b)进行用于 去除所述受试

者的腺瘤或息肉组织的程序。

[0007] 此外,公开了用于检测受试者的结肠的腺瘤或息肉的存在与否的方法,其中所述受试者没有结肠的腺瘤或息肉的症状或家族史,所述方法包括以下步骤:(a)从所述受试者获得生物样品;(b)对所述生物样品进行关于一种或多种蛋白质和/或肽的存在和量的分析;(c)将来自所述生物样品的一种或多种蛋白质和/或肽的存在和量与对照参考值进行比较;以及(d)将一种或多种蛋白质和/或肽的存在和量与所述受试者的腺瘤、癌症或息肉状态相关联。

[0008] 此外,公开了用于检测在结肠镜检查得到阴性结果的受试者中结肠的腺瘤、癌症或息肉的存在与否的方法,该方法包括以下步骤:(a)从基于结肠镜检查具有腺瘤、癌症或息肉的阴性诊断的受试者获得生物样品;(b)对所述生物样品进行关于一种或多种蛋白质和/或肽的存在和量的分析;(c)将来自所述生物样品的一种或多种蛋白质和/或肽的存在和量与对照参考值进行比较;以及(d)将一种或多种蛋白质和/或肽的存在和量与所述受试者的腺瘤、癌症或息肉状态相关联。

[0009] 公开了用于检测先前治疗结肠的腺瘤、癌症或息肉的受试者中结肠的腺瘤、癌症或息肉的复发或不存在的方法,该方法包括以下步骤:(a)从先前治疗结肠的腺瘤、癌症或息肉的受试者获得生物样品;(b)对所述生物样品进行关于一种或多种蛋白质和/或肽的存在和量的分析;(c)将来自所述生物样品的一种或多种蛋白质和/或肽的存在和量与对照参考值进行比较;以及(d)将一种或多种蛋白质和/或肽的存在和量与所述受试者的腺瘤、癌症或息肉状态相关联。

[0010] 此外,公开了针对诊断应用的蛋白质和/或肽检测方法,该方法包括以下步骤:(a)从受试者获得生物样品;(b)对所述生物样品进行关于一种或多种蛋白质和/或肽的存在和量的分析;(c)将来自所述生物样品的一种或多种蛋白质和/或肽的存在和量与对照参考值进行比较;以及(d)将一种或多种蛋白质和/或肽的存在和量与所述受试者的诊断相关联;其中所述分析检测如本文公开的一种或多种蛋白质、肽或分类器的存在和量。

[0011] 此外,公开了用于执行如本文所述的方法的试剂盒,其中该试剂盒包含:(a)用于从受试者采集样品的容器;(b)用于检测一种或多种蛋白质或肽的工具(means),或用于将所述容器转移至测试设备的工具;以及(c)书面说明书。

[0012] 最后,本公开提供了用于诊断、预测、预后和/或监测结肠疾病的方法。还公开了用于诊断、预测、预后和/或监测受试者的结肠疾病或结肠直肠癌的方法,该方法包括:测量来自受试者的生物样品中选自下组的至少一种生物标志物:ACTB、ACTH、ANGT、SAHH、ALDR、AKT1、ALBU、AL1A1、AL1B1、ALDOA、AMY2B、ANXA1、ANXA3、ANXA4、ANXA5、APC、APOA1、APOC1、APOH、GDIR1、ATPB、BANK1、MIC1、CA195、C03、C09、CAH1、CAH2、CALR、CAPG、CD24、CD63、CDD、CEAM3、CEAM5、CEAM6、CGHB、CH3L1、KCRB、CLC4D、CLUS、CNN1、COR1C、CRP、CSF1、CTNB1、CATD、CATS、CATZ、CUL1、SYDC、DEF1、DEF3、DESM、DPP4、DPYL2、DYHC1、ECH1、EF2、IF4A3、ENOA、EZRI、NIBL2、SEPR、FBX4、FIBB、FIBG、FHL1、FLNA、FRMD3、FRIH、FRIL、FUCO、GBRA1、G3P、SYG、GDF15、GELS、GSTP1、HABP2、HGF、1A68、HMGB1、ROA1、ROA2、HNRPF、HPT、HS90B、ENPL、GRP75、HSPB1、CH60、SIAL、IFT74、IGF1、IGHA2、IL2RB、IL8、IL9、RASK、K1C19、K2C8、LAMA2、LEG3、LMNB1、MARE1、MCM4、MIF、MMP7、MMP9、CD20、MYL6、MYL9、NDKA、NNMT、A1AG1、PCKGM、PDIA3、PDIA6、PDXK、PEBP1、PIPNA、KPYM、UROK、IPYR、PRDX1、KPCD1、PRL、

TMG4、PSME3、PTEN、FAK1、FAK2、RBX1、REG4、RHOA、RHOB、RHOC、RSSA、RRBP1、S10AB、S10AC、S10A8、S109、SAA1、SAA2、SEGN、SDCG3、DHSA、SBP1、SELPL、SEP9、A1AT、AACT、ILEU、SPB6、SF3B3、SKP1、ADT2、ISK1、SPON2、OSTP、SRC、STK11、HNRPQ、TAL1、TRFE、TSP1、TIMP1、TKT、TSG6、TR10B、TNF6B、P53、TPM2、TCTP、TRAP1、THTR、TBB1、UGDH、UGPA、VEGFA、VILI、VIME、VNN1、1433Z、CCR5、FUC0及其组合。

[0013] 还公开了用于诊断、预测、预后和/或监测受试者的结肠疾病或结肠直肠癌的方法，该方法包括：测量来自所述受试者的生物样品中选自SPB6、FRIL、P53、1A68、ENOA、TKT及其组合的至少一种生物标志物。

[0014] 公开了用于诊断、预测、预后和/或监测受试者的结肠疾病或结肠直肠癌的方法，该方法包括：测量来自所述受试者的生物样品中选自SPB6、FRIL、P53、1A68、ENOA、TKT、TSG6、TPM2、ADT2、FHL1、CCR5、CEAM5、SPON2、1A68、RBX1、COR1C、VIME、PSME3及其组合的至少一种生物标志物。

[0015] 公开了用于诊断、预测、预后和/或监测受试者的结肠疾病或结肠直肠癌的方法，该方法包括：测量来自所述受试者的生物样品中选自SPB6、FRIL、P53、1A68、ENOA、TKT、TSG6、TPM2、ADT2、FHL1、CCR5、CEAM5、SPON2、1A68、RBX1、COR1C、VIME、PSME3、MIC1、STK11、IPYR、SBP1、PEBP1、CATD、HPT、ANXA5、ALDOA、LAMA2、CATZ、ACTB、AACT及其组合的至少一种生物标志物。

以下非限制性实施方案提供了本发明的示例性实例，但并不限制本发明的范围。

1. 一种以大于70%的灵敏度或大于70%的选择性检测受试者结肠的腺瘤或息肉存在的方法；所述方法包括以下步骤：

(a) 从受试者获得血液样品；

(b) 裂解所述血液样品中的蛋白质以提供包含肽的样品；

(c) 分析所述样品中至少十种肽的存在；

(d) 将分析所述样品的结果与对照参考值进行比较，从而以大于70%的灵敏度或大于70%的选择性确定存在结肠的腺瘤或息肉的正或负得分。

2. 根据实施方案1所述的方法，其中所述灵敏度选自大于75%、大于80%、大于85%、大于90%、大于95%以及大于99%。

3. 根据实施方案1所述的方法，其中所述选择性选自大于75%、大于80%、大于85%、大于90%、大于95%以及大于99%。

4. 根据实施方案1所述的方法，其中所述选择性和所述灵敏度大于90%。

5. 根据实施方案1所述的方法，其中所述受试者无症状。

6. 根据实施方案1所述的方法，其中所述受试者先前已接受针对结肠息肉的治疗。

7. 根据实施方案1所述的方法，其中所述分析步骤包括光谱分析、质谱法、免疫分析、酶反应性分析及其组合。

8. 根据实施方案1所述的方法，其中所述分析包括质谱法。

9. 根据实施方案1所述的方法，其中所述至少十种肽选自图8的中性质量分类器。

10. 一种治疗受试者的结肠的腺瘤或息肉的方法，该方法包括：

(a) 执行实施方案1所述的方法以得到具有存在腺瘤或息肉的正得分的受试者；以及

(b) 进行用于去除所述受试者的腺瘤或息肉组织的程序。

11. 一种检测受试者的结肠的腺瘤或息肉的存在与否的方法,其中所述受试者没有结肠的腺瘤或息肉的症状或家族史,所述方法包括以下步骤:

- (a) 从所述受试者获得生物样品;
- (b) 对所述生物样品进行关于一种或多种蛋白质和/或肽的存在和量的分析;
- (c) 将来自所述生物样品的一种或多种蛋白质和/或肽的存在和量与对照参考值进行比较;以及
- (d) 将一种或多种蛋白质和/或肽的存在和量与所述受试者的腺瘤或息肉状态相关联。

12. 根据实施方案11所述的方法,其中所述方法实现了选自大于70%、大于75%、大于80%、大于85%、大于90%、大于95%以及大于99%的灵敏度。

13. 根据实施方案11所述的方法,其中所述方法实现了选自大于70%、大于75%、大于80%、大于85%、大于90%、大于95%以及大于99%的特异性。

14. 根据实施方案11所述的方法,其中所述方法实现了各自独立地选自大于70%、大于75%、大于80%、大于85%、大于90%、大于95%以及大于99%的灵敏度和特异性。

15. 根据实施方案11所述的方法,进一步包括准备关于所述受试者的报告,其中所述报告指示腺瘤或息肉的存在与否。

16. 根据实施方案15所述的方法,其中所述报告指示息肉发展的倾向或风险、细胞发育异常的程度、腺瘤性息肉的亚型或良性结肠肿瘤疾病的亚型。

17. 根据实施方案11所述的方法,其中所述方法检测腺瘤的存在与否。

18. 根据实施方案17所述的方法,其中所述腺瘤是腺瘤性息肉或息肉样腺瘤。

19. 根据实施方案18所述的方法,其中所述腺瘤性息肉或息肉样腺瘤选自有蒂息肉和无蒂息肉。

20. 根据实施方案18所述的方法,其中对所述腺瘤性息肉或息肉样腺瘤根据细胞发育异常或恶变前的程度进行表征。

21. 根据实施方案11所述的方法,其中所述方法进一步检测结肠直肠癌的存在与否。

22. 根据实施方案11所述的方法,其中所述方法不检测结肠直肠癌的存在与否。

23. 根据实施方案11所述的方法,其中不对结肠直肠癌的存在与否进行确定。

24. 根据实施方案11所述的方法,其中所述存在与否通过结肠镜检查、成像和/或手术来确认。

25. 根据实施方案11所述的方法,其中所述生物样品选自全血、血清、血浆、血液成分、骨髓、唾液、脸颊拭子、尿、粪便、淋巴液、CNS液和病变渗出物。

26. 根据实施方案25所述的方法,其中所述生物样品选自全血、血清和血浆。

27. 根据实施方案11所述的方法,其中所述受试者无症状。

28. 根据实施方案11所述的方法,其中所述受试者为18至49岁。

29. 根据实施方案11所述的方法,其中所述受试者先前未接受过结肠镜检查。

30. 根据实施方案11所述的方法,其中所述受试者没有结肠直肠癌的症状,没有结肠直肠癌家族史,并且没有经识别的结肠直肠癌风险因素。

31. 根据实施方案11所述的方法,其中所述受试者没有结肠直肠癌的症状,没有结肠直肠癌家族史,并且没有除年龄之外的经识别的结肠直肠癌风险因素。

32. 根据实施方案11所述的方法, 其中步骤(b)中的所述分析 包括选自光谱分析、质谱法、免疫分析和酶反应性分析的方法。

33. 根据实施方案32所述的方法, 其中所述分析为质谱法。

34. 根据实施方案32所述的方法, 其中所述免疫分析包括酶联免疫吸附测定或放射免疫测定。

35. 根据实施方案32所述的方法, 其中所述免疫分析包括免疫印迹、免疫扩散、免疫电泳或免疫沉淀。

36. 根据实施方案32所述的方法, 其中所述免疫分析包括免疫染色和/或流式细胞术分析。

37. 根据实施方案11所述的方法, 其中所述对照参考为相同生物样品中的一组一种或多种非重叠蛋白质和/或肽的存在和量。

38. 根据实施方案11所述的方法, 其中所述对照参考为从一个或多个存在结肠的腺瘤或息肉的受试者获得的重叠的一组蛋白质和/或肽的存在和量。

39. 根据实施方案11所述的方法, 其中所述对照参考为从一个或多个不存在结肠的腺瘤或息肉的受试者获得的重叠的一组蛋白质和/或肽的存在和量。

40. 根据实施方案11所述的方法, 其中所述分析检测一定数目的蛋白质或多肽的存在和量, 其中所述数目选自至少2种、至少5种、至少10种、至少50种、至少100种以及至少1000种。

41. 根据实施方案11所述的方法, 其中所述分析检测下组中的一种或多种的存在和量:

i) 选自SCDC26 (CD26)、CEA分子5 (CEACAM5)、CA195 (CCR5)、CA19-9、M2PK (PKM2)、TIMP1、P-选择蛋白 (SELPLG)、VEGFA、HcGB (CGB)、绒毛蛋白、TATI (SPINK1)、A-L-岩藻糖苷酶 (FUCA2)、ANXA5、GAPDH、PKM2、ANXA4、GARS、RRBP1、KRT8、SYNCRIP、S100A9、ANXA3、CAPG、HNRNPF、PPA1、NME1、PSME3、AHCY、TPT1、HSPB1和RPSA、和/或图9中的蛋白质, 以及它们的组合的一种或多种蛋白质;

ii) SCDC26 (CD26)、CEA分子5 (CEACAM5)、CA195 (CCR5)、CA19-9、M2PK (PKM2)、TIMP1、P-选择蛋白 (SELPLG)、VEGFA、HcGB (CGB)、绒毛蛋白、TATI (SPINK1)、A-L-岩藻糖苷酶 (FUCA2)、ANXA5、GAPDH、PKM2、ANXA4、GARS、RRBP1、KRT8、SYNCRIP、S100A9、ANXA3、CAPG、HNRNPF、PPA1、NME1、PSME3、AHCY、TPT1、HSPB1和RPSA、和/或图9中的蛋白质, 以及它们的组合的一种或多种肽片段;

iii) 与SCDC26 (CD26)、CEA分子5 (CEACAM5)、CA195 (CCR5)、CA19-9、M2PK (PKM2)、TIMP1、P-选择蛋白 (SELPLG)、VEGFA、HcGB (CGB)、绒毛蛋白、TATI (SPINK1)、A-L-岩藻糖苷酶 (FUCA2)、ANXA5、GAPDH、PKM2、ANXA4、GARS、RRBP1、KRT8、SYNCRIP、S100A9、ANXA3、CAPG、HNRNPF、PPA1、NME1、PSME3、AHCY、TPT1、HSPB1和RPSA、和/或图9中的蛋白质, 以及它们的组合具有序列同源性的一种或多种肽, 其中所述序列同源性选自大于75%、大于80%、大于85%、大于90%、大于95%及大于99%; 以及

iv) SCDC26 (CD26)、CEA分子5 (CEACAM5)、CA195 (CCR5)、CA19-9、M2PK (PKM2)、TIMP1、P-选择蛋白 (SELPLG)、VEGFA、HcGB (CGB)、绒毛蛋白、TATI (SPINK1)、A-L-岩藻糖苷酶 (FUCA2)、ANXA5、GAPDH、PKM2、ANXA4、GARS、RRBP1、KRT8、SYNCRIP、S100A9、ANXA3、CAPG、

HNRNPF、PPA1、NME1、PSME3、AHCY、TPT1、HSPB1和RPSA、和/或图9中的蛋白质,以及它们的组合的一种或多种结合配偶体。

42. 根据实施方案11所述的方法,其中所述分析检测图7或图8 中的一个或多个中性质量簇的存在和/或量。

43. 根据实施方案42所述的方法,其中所述分析检测图7或图8 中的一些数目的中性质量簇的存在和/或量,其中所述数目选自至少2 个、至少5个、至少10个、至少50个、至少100个、至少200个、至少500个以及至少1000个。

44. 根据实施方案42所述的方法,其中所述分析检测图7或图8 中的一些数目的中性质量簇的存在和/或量,其中所述数目为至少一个,并选自少于5个、少于10个、少于50个、少于100个、少于200个、少于500个以及少于1000个。

45. 根据实施方案42所述的方法,其中所述分析检测图7或图8 中的一些数目的中性质量簇的存在和/或量,其中所述数目选自10-50 个、60-100个、150-300个、400-600个以及800-1000个,包含端值。

46. 根据实施方案42所述的方法,其中所述中性质量簇在根据针对分割分类器的70/30训练/测试进行测试时具有下述分类器频率,所述分类器频率选自至少3/50、至少10/50、至少20/50、至少30/50以及至少40/50。

47. 根据实施方案42所述的方法,其中所述分析检测从中得到图 7或图8中的一个或多个中性质量簇的蛋白质或肽的存在和/或量。

48. 根据实施方案11所述的方法,进一步包括:

(e) 对所述生物样品进行关于选自代谢物、DNA序列、RNA序列及其组合的一种或多种分析物的存在和量的分析;以及

(f) 将所述分析物的存在和量与对照参考值进行比较;以及

(g) 将所述分析物的存在和量与所述受试者的腺瘤或息肉状态 相关联。

49. 一种检测在结肠镜检查得到阴性结果的受试者中结肠的腺瘤 或息肉的存在与否的方法,所述方法包括以下步骤:

(a) 从基于结肠镜检查具有腺瘤或息肉的阴性诊断的受试者获得 生物样品;

(b) 对所述生物样品进行关于一种或多种蛋白质和/或肽的存在 和量的分析;

(c) 将来自所述生物样品的一种或多种蛋白质和/或肽的存在和 量与对照参考值进行比较;以及

(d) 将一种或多种蛋白质和/或肽的存在和量与所述受试者的腺 瘤或息肉状态相关联。

50. 根据实施方案49所述的方法,其中所述方法实现了选自大于 70%、大于75%、大于80%、大于85%、大于90%、大于95%以及大于99%的灵敏度。

51. 根据实施方案49所述的方法,其中所述方法实现了选自大于 70%、大于75%、大于80%、大于85%、大于90%、大于95%以及大于99%的特异性。

52. 根据实施方案49所述的方法,其中所述方法实现了各自独立 地选自大于70%、大于75%、大于80%、大于85%、大于90%、大于95%以及大于99%的灵敏度和特异性。

53. 根据实施方案49所述的方法,进一步包括准备关于所述受试 者的报告,其中所述报告指示腺瘤或息肉的存在与否。

54. 根据实施方案53所述的方法,其中所述报告指示息肉发展的 倾向或风险、细胞发育异常的程度、腺瘤性息肉的亚型或良性结肠肿 瘤疾病的亚型。

55. 根据实施方案49所述的方法,其中所述方法检测腺瘤的存在 与否。

56. 根据实施方案55所述的方法,其中所述腺瘤是腺瘤性息肉或 息肉样腺瘤。

57. 根据实施方案56所述的方法,其中所述腺瘤性息肉或息肉样 腺瘤选自有蒂息肉和无蒂息肉。

58. 根据实施方案56所述的方法,其中对所述腺瘤性息肉或息肉 样腺瘤根据细胞发育异常或恶变前的程度进行表征。

59. 根据实施方案49所述的方法,其中所述方法进一步检测结肠 直肠癌的存在与否。

60. 根据实施方案49所述的方法,其中所述方法不检测结肠直肠 癌的存在与否。

61. 根据实施方案49所述的方法,其中不对结肠直肠癌的存在与 否进行确定。

62. 根据实施方案49所述的方法,其中所述存在与否通过结肠镜 检查、成像和/或手术来确认。

63. 根据实施方案49所述的方法,其中所述生物样品选自全血、血清、血浆、血液成分、骨髓、唾液、脸颊拭子、尿、粪便、淋巴液、CNS液和病变渗出物。

64. 根据实施方案63所述的方法,其中所述生物样品选自全血、血清和血浆。

65. 根据实施方案49所述的方法,其中所述受试者无症状。

66. 根据实施方案49所述的方法,其中所述受试者为18至49岁。

67. 根据实施方案49所述的方法,其中所述受试者没有结肠直肠 癌的症状,没有结肠直肠癌家族史,并且没有经识别的结肠直肠癌风 险因素。

68. 根据实施方案49所述的方法,其中所述受试者没有结肠直肠 癌的症状,没有结肠直肠癌家族史,并且没有除年龄之外的经识别的 结肠直肠癌风险因素。

69. 根据实施方案49所述的方法,其中步骤(b)中的所述分析 包括选自光谱分析、质谱法、免疫分析和酶反应性分析的方法。

70. 根据实施方案69所述的方法,其中所述分析为质谱法。

71. 根据实施方案69所述的方法,其中所述免疫分析包括酶联免 疫吸附测定或放射免疫测定。

72. 根据实施方案69所述的方法,其中所述免疫分析包括免疫印 迹、免疫扩散、免疫电泳或免疫沉淀。

73. 根据实施方案69所述的方法,其中所述免疫分析包括免疫染 色和/或流式细胞术分析。

74. 根据实施方案49所述的方法,其中所述对照参考为相同生物 样品中的一组一种或多种非重叠蛋白质和/或肽的存在和量。

75. 根据实施方案49所述的方法,其中所述对照参考为从一个或 多个存在结肠的腺瘤或息肉的受试者获得的重叠的一组蛋白质和/或 肽的存在和量。

76. 根据实施方案49所述的方法,其中所述对照参考为从一个或 多个不存在结肠的腺瘤或息肉的受试者获得的重叠的一组蛋白质和/ 或肽的存在和量。

77. 根据实施方案49所述的方法,其中所述分析检测一定数目的 蛋白质或多肽的存在和量,其中所述数目选自至少2种、至少5种、至少10种、至少50种、至少100种以及至少1000

种。

78. 根据实施方案49所述的方法,其中所述分析检测下组中的一种或多种的存在和量:

i) 选自SCDC26 (CD26)、CEA分子5 (CEACAM5)、CA195 (CCR5)、CA19-9、M2PK (PKM2)、TIMP1、P-选择蛋白 (SELPLG)、VEGFA、HcGB (CGB)、绒毛蛋白、TATI (SPINK1)、A-L-岩藻糖苷酶 (FUCA2)、ANXA5、GAPDH、PKM2、ANXA4、GARS、RRBP1、KRT8、SYNCRIP、S100A9、ANXA3、CAPG、HNRNPF、PPA1、NME1、PSME3、AHCY、TPT1、HSPB1和RPSA、和/或图9中的蛋白质,以及它们的组合的一种或多种蛋白质;

ii) SCDC26 (CD26)、CEA分子5 (CEACAM5)、CA195 (CCR5)、CA19-9、M2PK (PKM2)、TIMP1、P-选择蛋白 (SELPLG)、VEGFA、HcGB (CGB)、绒毛蛋白、TATI (SPINK1)、A-L-岩藻糖苷酶 (FUCA2)、ANXA5、GAPDH、PKM2、ANXA4、GARS、RRBP1、KRT8、SYNCRIP、S100A9、ANXA3、CAPG、HNRNPF、PPA1、NME1、PSME3、AHCY、TPT1、HSPB1和RPSA、和/或图9中的蛋白质,以及它们的组合的一种或多种肽片段;

iii) 与SCDC26 (CD26)、CEA分子5 (CEACAM5)、CA195 (CCR5)、CA19-9、M2PK (PKM2)、TIMP1、P-选择蛋白 (SELPLG)、VEGFA、HcGB (CGB)、绒毛蛋白、TATI (SPINK1)、A-L-岩藻糖苷酶 (FUCA2)、ANXA5、GAPDH、PKM2、ANXA4、GARS、RRBP1、KRT8、SYNCRIP、S100A9、ANXA3、CAPG、HNRNPF、PPA1、NME1、PSME3、AHCY、TPT1、HSPB1和RPSA、和/或图9中的蛋白质,以及它们的组合具有序列同源性的一种或多种肽,其中所述序列同源性选自大于75%、大于80%、大于85%、大于90%、大于95%及大于99%;以及

iv) SCDC26 (CD26)、CEA分子5 (CEACAM5)、CA195 (CCR5)、CA19-9、M2PK (PKM2)、TIMP1、P-选择蛋白 (SELPLG)、VEGFA、HcGB (CGB)、绒毛蛋白、TATI (SPINK1)、A-L-岩藻糖苷酶 (FUCA2)、ANXA5、GAPDH、PKM2、ANXA4、GARS、RRBP1、KRT8、SYNCRIP、S100A9、ANXA3、CAPG、HNRNPF、PPA1、NME1、PSME3、AHCY、TPT1、HSPB1和RPSA、和/或图9中的蛋白质以及它们的组合的一种或多种结合配偶体。

79. 根据实施方案49所述的方法,其中所述分析检测图7或图8 中的一个或多个中性质量簇的存在和/或量。

80. 根据实施方案79所述的方法,其中所述分析检测图7或图8 中的一定数目的中性质量簇的存在和/或量,其中所述数目选自至少2 个、至少5个、至少10个、至少50个、至少100个、至少200个、至少500个以及至少1000个。

81. 根据实施方案79所述的方法,其中所述分析检测图7或图8 中的一定数目的中性质量簇的存在和/或量,其中所述数目为至少一个,并选自少于5个、少于10个、少于50个、少于100个、少于200个、少于500个以及少于1000个。

82. 根据实施方案79所述的方法,其中所述分析检测图7或图8 中的一定数目的中性质量簇的存在和/或量,其中所述数目选自10-50 个、60-100个、150-300个、400-600个以及800-1000个,包含端值。

83. 根据实施方案79所述的方法,其中所述中性质量簇在根据针对分割分类器的70/30训练/测试进行测试时具有下述分类器频率,所述分类器频率选自至少3/50、至少10/50、至少20/50、至少30/50以及至少40/50。

84. 根据实施方案79所述的方法,其中所述分析检测从中得到图 7或图8中的一个或多

个中性质量簇的蛋白质或肽的存在和/或量。

85. 根据实施方案79所述的方法,进一步包括:

(e) 对所述生物样品进行关于选自代谢物、DNA序列、RNA序列及其组合的一种或多种分析物的存在和量的分析;以及

(f) 将所述分析物的存在和量与对照参考值进行比较;以及

(g) 将所述分析物的存在和量与所述受试者的腺瘤或息肉状态相关联。

86. 一种检测先前治疗结肠的腺瘤或息肉的受试者中结肠的腺瘤或息肉的复发或不存在的方法,该方法包括以下步骤:

(a) 从先前治疗结肠的腺瘤或息肉的受试者获得生物样品;

(b) 对所述生物样品进行关于一种或多种蛋白质和/或肽的存在和量的分析;

(c) 将来自所述生物样品的一种或多种蛋白质和/或肽的存在和量与对照参考值进行比较;以及

(d) 将一种或多种蛋白质和/或肽的存在和量与所述受试者的腺瘤或息肉状态相关联。

87. 根据实施方案86所述的方法,其中所述方法实现了选自大于70%、大于75%、大于80%、大于85%、大于90%、大于95%以及大于99%的灵敏度。

88. 根据实施方案86所述的方法,其中所述方法实现了选自大于70%、大于75%、大于80%、大于85%、大于90%、大于95%以及大于99%的特异性。

89. 根据实施方案86所述的方法,其中所述方法实现了各自独立地选自大于70%、大于75%、大于80%、大于85%、大于90%、大于95%以及大于99%的灵敏度和特异性。

90. 根据实施方案86所述的方法,进一步包括准备关于所述受试者的报告,其中所述报告指示腺瘤或息肉的存在与否。

91. 根据实施方案90所述的方法,其中所述报告指示息肉发展的倾向或风险、细胞发育异常的程度、腺瘤性息肉的亚型或良性结肠肿瘤疾病的亚型。

92. 根据实施方案86所述的方法,其中所述方法检测腺瘤的存在与否。

93. 根据实施方案92所述的方法,其中所述腺瘤是腺瘤性息肉或息肉样腺瘤。

94. 根据实施方案93所述的方法,其中所述腺瘤性息肉或息肉样腺瘤选自有蒂息肉和无蒂息肉。

95. 根据实施方案93所述的方法,其中对所述腺瘤性息肉或息肉样腺瘤根据细胞发育异常或恶变前的程度进行表征。

96. 根据实施方案86所述的方法,其中所述方法进一步检测结肠直肠癌的存在与否。

97. 根据实施方案86所述的方法,其中所述方法不检测结肠直肠癌的存在与否。

98. 根据实施方案86所述的方法,其中不对结肠直肠癌的存在与否进行确定。

99. 根据实施方案86所述的方法,其中所述存在与否通过结肠镜检查、成像和/或手术来确认。

100. 根据实施方案86所述的方法,其中所述生物样品选自全血、血清、血浆、血液成分、骨髓、唾液、脸颊拭子、尿、粪便、淋巴液、CNS液和病变渗出物。

101. 根据实施方案100所述的方法,其中所述生物样品选自全血、血清和血浆。

102. 根据实施方案86所述的方法,其中所述受试者无症状。

103. 根据实施方案86所述的方法,其中所述受试者为18至49 岁。
104. 根据实施方案86所述的方法,其中所述受试者没有结肠直 肠癌的症状,没有结肠直 肠癌家族史,并且没有经识别的结肠直 肠癌 风险因素。
105. 根据实施方案86所述的方法,其中所述受试者没有结肠直 肠癌的症状,没有结肠直 肠癌家族史,并且没有除年龄之外的经识别 的结肠直 肠癌风险因素。
106. 根据实施方案86所述的方法,其中步骤 (b) 中的所述分析 包括选自光谱分析、质谱法、免疫分析和酶反应性分析的方法。
107. 根据实施方案106所述的方法,其中所述分析为质谱法。
108. 根据实施方案106所述的方法,其中所述免疫分析包括酶联 免疫吸附测定或放射免疫测定。
109. 根据实施方案106所述的方法,其中所述免疫分析包括免疫 印迹、免疫扩散、免疫电泳或免疫沉淀。
110. 根据实施方案106所述的方法,其中所述免疫分析包括免疫 染色和/或流式细胞术分析。
111. 根据实施方案86所述的方法,其中所述对照参考为相同生 物样品中的一组一种或多种非重叠蛋白质和/或肽的存在和量。
112. 根据实施方案86所述的方法,其中所述对照参考为从一个 或多个存在结肠的腺瘤或息肉的受试者获得的重叠的一组蛋白质和/ 或肽的存在和量。
113. 根据实施方案86所述的方法,其中所述对照参考为从一个 或多个不存在结肠的腺瘤或息肉的受试者获得的重叠的一组蛋白质 和/或肽的存在和量。
114. 根据实施方案86所述的方法,其中所述分析检测一定数目 的蛋白质或多肽的存在和量,其中所述数目选自至少2种、至少5种、至少10种、至少50种、至少100种以及至少1000种。
115. 根据实施方案86所述的方法,其中所述分析检测下组中的 一种或多种的存在和量:
- i) 选自SCDC26 (CD26)、CEA分子5 (CEACAM5)、CA195 (CCR5)、CA19-9、M2PK (PKM2)、TIMP1、P-选择蛋白 (SELPLG)、VEGFA、HcGB (CGB)、绒毛蛋白、TATI (SPINK1)、A-L-岩藻糖苷酶 (FUCA2)、ANXA5、GAPDH、PKM2、ANXA4、GARS、RRBP1、KRT8、SYNCRIP、S100A9、ANXA3、CAPG、HNRNPF、PPA1、NME1、PSME3、AHCY、TPT1、HSPB1和RPSA、和/或图9中的蛋白质,以及它们的组合的 一种或多种蛋白质;
 - ii) SCDC26 (CD26)、CEA分子5 (CEACAM5)、CA195 (CCR5)、CA19-9、M2PK (PKM2)、TIMP1、P-选择蛋白 (SELPLG)、VEGFA、HcGB (CGB)、绒毛蛋白、TATI (SPINK1)、A-L-岩藻糖苷酶 (FUCA2)、ANXA5、GAPDH、PKM2、ANXA4、GARS、RRBP1、KRT8、SYNCRIP、S100A9、ANXA3、CAPG、HNRNPF、PPA1、NME1、PSME3、AHCY、TPT1、HSPB1和RPSA、和/或图9中的蛋白质,以及它们的组合的 一种或多种肽片段;
 - iii) 与SCDC26 (CD26)、CEA分子5 (CEACAM5)、CA195 (CCR5)、CA19-9、M2PK (PKM2)、TIMP1、P-选择蛋白 (SELPLG)、VEGFA、HcGB (CGB)、绒毛蛋白、TATI (SPINK1)、A-L-岩藻糖苷酶 (FUCA2)、ANXA5、GAPDH、PKM2、ANXA4、GARS、RRBP1、KRT8、SYNCRIP、S100A9、ANXA3、CAPG、HNRNPF、PPA1、NME1、PSME3、AHCY、TPT1、HSPB1和RPSA、和/或图9中的蛋白质,以及它们的组

合具 有序列同源性的一种或多种肽,其中所述序列同源性选自大于75%、大于80%、大于85%、大于90%、大于95%及大于99%;以及

iv) SCDC26 (CD26)、CEA分子5 (CEACAM5)、CA195 (CCR5)、CA19-9、M2PK (PKM2)、TIMP1、P-选择蛋白 (SELPLG)、VEGFA、HcGB (CGB)、绒毛蛋白、TATI (SPINK1)、A-L-岩藻糖苷酶 (FUCA2) 和ANXA5、GAPDH、PKM2、ANXA4、GARS、RRBP1、KRT8、SYNCRIP、S100A9、ANXA3、CAPG、HNRNPF、PPA1、NME1、PSME3、AHCY、TPT1、HSPB1和RPSA、和/或图9中的蛋白质,以及它们的组合的 一种或多种结合配偶体。

116. 根据实施方案86所述的方法,其中所述分析检测图7或图 8中的一个或多个中性质量簇的存在和/或量。

117. 根据实施方案116所述的方法,其中所述分析检测图7或图8中的一定数目的中性质量簇的存在和/或量,其中所述数目选自至少 2个、至少5个、至少10个、至少50个、至少100个、至少200个、至少500个以及至少1000个。

118. 根据实施方案116所述的方法,其中所述分析检测图7或图 8中的一定数目的中性质量簇的存在和/或量,其中所述数目为至少一 个,并选自少于5个、少于10个、少于50个、少于100个、少于200 个、少于500个以及少于1000个。

119. 根据实施方案116所述的方法,其中所述分析检测图7或图 8中的一定数目的中性质量簇的存在和/或量,其中所述数目选自 10-50个、60-100个、150-300个、400-600个以及800-1000个,包含 端值。

120. 根据实施方案116所述的方法,其中所述中性质量簇在根据 针对分割分类器的70/30训练/测试进行测试时具有下述分类器频率, 所述分类器频率选自至少3/50、至少10/50、至少20/50、至少30/50 以及至少40/50。

121. 根据实施方案116所述的方法,其中所述分析检测从中得到 图7或图8中的一个或多个中性质量簇的蛋白质或肽的存在和/或量。

122. 根据实施方案86所述的方法,进一步包括:

(e) 对所述生物样品进行关于选自代谢物、DNA序列、RNA序 列以及它们的组合的一种或多种分析物的存在和量的分析;

(f) 将所述分析物的存在和量与对照参考值进行比较;以及

(g) 将所述分析物的存在和量与所述受试者的腺瘤或息肉状态 相关联。

123. 根据实施方案86所述的方法,其中所述受试者先前通过去 除息肉而治疗结肠息肉。

124. 根据实施方案86所述的方法,其中所述受试者先前通过从 结肠中去除至少1厘米的组织进行治疗。

125. 一种针对诊断应用的蛋白质和/或肽检测方法,该方法包括 以下步骤:

(a) 从受试者获得生物样品;

(b) 对所述生物样品进行关于一种或多种蛋白质和/或肽的存在 和量的分析;

(c) 将来自所述生物样品的一种或多种蛋白质和/或肽的存在和 量与对照参考值进行比较;以及

(d) 将一种或多种蛋白质和/或肽的存在和量与所述受试者的诊 断相关联;

其中所述分析检测下组中的一种或多种的存在和量:

i) 选自SCDC26 (CD26)、CEA分子5 (CEACAM5)、CA195 (CCR5)、CA19-9、M2PK (PKM2)、TIMP1、P-选择蛋白 (SELPLG)、VEGFA、HcGB (CGB)、绒毛蛋白、TATI (SPINK1)、A-L-岩藻糖苷酶 (FUCA2)、ANXA5、GAPDH、PKM2、ANXA4、GARS、RRBP1、KRT8、SYNCRIP、S100A9、ANXA3、CAPG、HNRNPF、PPA1、NME1、PSME3、AHCY、TPT1、HSPB1和RPSA、和/或图9中的蛋白质,以及它们的组合的一种或多种蛋白质;

ii) SCDC26 (CD26)、CEA分子5 (CEACAM5)、CA195 (CCR5)、CA19-9、M2PK (PKM2)、TIMP1、P-选择蛋白 (SELPLG)、VEGFA、HcGB (CGB)、绒毛蛋白、TATI (SPINK1)、A-L-岩藻糖苷酶 (FUCA2) 和ANXA5、GAPDH、PKM2、ANXA4、GARS、RRBP1、KRT8、SYNCRIP、S100A9、ANXA3、CAPG、HNRNPF、PPA1、NME1、PSME3、AHCY、TPT1、HSPB1和RPSA、和/或图9中的蛋白质,以及它们的组合的一种或多种肽片段;

iii) 与SCDC26 (CD26)、CEA分子5 (CEACAM5)、CA195 (CCR5)、CA19-9、M2PK (PKM2)、TIMP1、P-选择蛋白 (SELPLG)、VEGFA、HcGB (CGB)、绒毛蛋白、TATI (SPINK1)、A-L-岩藻糖苷酶 (FUCA2)、ANXA5、GAPDH、PKM2、ANXA4、GARS、RRBP1、KRT8、SYNCRIP、S100A9、ANXA3、CAPG、HNRNPF、PPA1、NME1、PSME3、AHCY、TPT1、HSPB1和RPSA、和/或图9中的蛋白质,以及它们的组合具有序列同源性的一种或多种肽,其中所述序列同源性选自大于75%、大于80%、大于85%、大于90%、大于95%及大于99%;

iv) SCDC26 (CD26)、CEA分子5 (CEACAM5)、CA195 (CCR5)、CA19-9、M2PK (PKM2)、TIMP1、P-选择蛋白 (SELPLG)、VEGFA、HcGB (CGB)、绒毛蛋白、TATI (SPINK1)、A-L-岩藻糖苷酶 (FUCA2) 和ANXA5、GAPDH、PKM2、ANXA4、GARS、RRBP1、KRT8、SYNCRIP、S100A9、ANXA3、CAPG、HNRNPF、PPA1、NME1、PSME3、AHCY、TPT1、HSPB1和RPSA、和/或图9中的蛋白质,以及它们的组合的一种或多种结合配偶体;以及

v) 从中得到图7或图8中的一个或多个中性质量簇的蛋白质或肽。

126. 根据实施方案125所述的方法,其中所述诊断为选自结肠的 腺瘤、息肉、结肠直肠癌及其组合的病况的存在与否。

127. 根据实施方案125所述的方法,进一步包括通过以下步骤确定步骤(b)中的所述量:

(b1) 使所述生物样品或其部分与对第一肽具有特异性的第一抗 肽抗体接触;

(b2) 使所述生物样品或其部分与对第二肽具有特异性的第二抗 肽抗体接触,其中所述第二抗肽抗体不同于所述第一抗肽抗体;

(b3) 将被所述第一和第二抗肽抗体结合的肽与未结合的肽分离;

(b4) 使用质谱法、流式细胞术、非重叠激发光谱、Western分析、酶联免疫吸附测定、密度测定法或其组合来检测和/或测量被所述 第一和第二抗肽抗体结合的所述肽的量。

128. 根据实施方案127所述的方法,其中所述生物样品或其部分 为所述生物样品的蛋白水解消化物。

129. 根据实施方案127所述的方法,其中步骤(b4) 包括质谱法。

130. 一种用于执行根据实施方案1-129中任一项所述的方法的试 剂盒:

(a) 用于从受试者采集样品的容器;

(b) 用于检测一种或多种蛋白质或肽的工具,或用于将所述容 器转移至测试设备的工具;以及

(c) 书面说明书。

131. 根据实施方案130所述的试剂盒,其中所述用于检测一种或多种蛋白质或肽的工具包含与下组中的一种或多种结合的一种或多种抗体:

i) 选自SCDC26 (CD26)、CEA分子5 (CEACAM5)、CA195 (CCR5)、CA19-9、M2PK (PKM2)、TIMP1、P-选择蛋白 (SELPLG)、VEGFA、HcGB (CGB)、绒毛蛋白、TATI (SPINK1)、A-L-岩藻糖苷酶 (FUCA2)、ANXA5、GAPDH、PKM2、ANXA4、GARS、RRBP1、KRT8、SYNCRIP、S100A9、ANXA3、CAPG、HNRNPF、PPA1、NME1、PSME3、AHCY、TPT1、HSPB1和RPSA、和/或图9中的蛋白质,以及它们的组合的一种或多种蛋白质;

ii) SCDC26 (CD26)、CEA分子5 (CEACAM5)、CA195 (CCR5)、CA19-9、M2PK (PKM2)、TIMP1、P-选择蛋白 (SELPLG)、VEGFA、HcGB (CGB)、绒毛蛋白、TATI (SPINK1)、A-L-岩藻糖苷酶 (FUCA2) 和ANXA5、GAPDH、PKM2、ANXA4、GARS、RRBP1、KRT8、SYNCRIP、S100A9、ANXA3、CAPG、HNRNPF、PPA1、NME1、PSME3、AHCY、TPT1、HSPB1和RPSA、和/或图9中的蛋白质,以及它们的组合的一种或多种肽片段;

iii) 与SCDC26 (CD26)、CEA分子5 (CEACAM5)、CA195 (CCR5)、CA19-9、M2PK (PKM2)、TIMP1、P-选择蛋白 (SELPLG)、VEGFA、HcGB (CGB)、绒毛蛋白、TATI (SPINK1)、A-L-岩藻糖苷酶 (FUCA2)、ANXA5、GAPDH、PKM2、ANXA4、GARS、RRBP1、KRT8、SYNCRIP、S100A9、ANXA3、CAPG、HNRNPF、PPA1、NME1、PSME3、AHCY、TPT1、HSPB1和RPSA、和/或图9中的蛋白质,以及它们的组合具有序列同源性的一种或多种肽,其中所述序列同源性选自大于75%、大于80%、大于85%、大于90%、大于95%及大于99%;

iv) SCDC26 (CD26)、CEA分子5 (CEACAM5)、CA195 (CCR5)、CA19-9、M2PK (PKM2)、TIMP1、P-选择蛋白 (SELPLG)、VEGFA、HcGB (CGB)、绒毛蛋白、TATI (SPINK1)、A-L-岩藻糖苷酶 (FUCA2)、ANXA5、GAPDH、PKM2、ANXA4、GARS、RRBP1、KRT8、SYNCRIP、S100A9、ANXA3、CAPG、HNRNPF、PPA1、NME1、PSME3、AHCY、TPT1、HSPB1和RPSA、和/或图9中的蛋白质,以及它们的组合的一种或多种结合配偶体;以及

v) 从中得到图7或图8中的一个或多个中性质量簇的蛋白质或肽。

132. 根据实施方案131所述的试剂盒,其中一种或多种抗体各自用标记物进行标记。

133. 根据实施方案132所述的试剂盒,其中所述标记物选自放射性标记物、荧光标记物、酶、化学发光标签及其组合。

134. 根据实施方案131所述的试剂盒,其中所述抗体被包装在水性介质中或以冻干形式包装。

135. 根据实施方案130所述的试剂盒,其中所述用于检测一种或多种蛋白质或肽的工具包括酶联免疫吸附测定。

136. 一种用于诊断、预测、预后和/或监测受试者的结肠疾病的方法,该方法包括:测量来自所述受试者的生物样品中选自下组的至少一种生物标志物:ACTB、ACTH、ANGT、SAHH、ALDR、AKT1、ALBU、AL1A1、AL1B1、ALDOA、AMY2B、ANXA1、ANXA3、ANXA4、ANXA5、APC、APOA1、APOC1、APOH、GDIR1、ATPB、BANK1、MIC1、CA195、CO3、CO9、CAH1、CAH2、CALR、CAPG、CD24、CD63、CDD、CEAM3、CEAM5、CEAM6、CGHB、CH3L1、KCRB、CLC4D、CLUS、CNN1、COR1C、CRP、CSF1、CTNB1、CATD、CATS、CATZ、CUL1、SYDC、DEF1、DEF3、DESM、DPP4、DPYL2、DYHC1、ECH1、EF2、IF4A3、ENOA、EZRI、NIBL2、SEPR、FBX4、FIBB、FIBG、FHL1、FLNA、FRMD3、FRIH、FRIL、

FUC0、GBRA1、G3P、SYG、GDF15、GELS、GSTP1、HABP2、HGF、1A68、HMGB1、ROA1、ROA2、HNRPF、HPT、HS90B、ENPL、GRP75、HSPB1、CH60、SIAL、IFT74、IGF1、IGHA2、IL2RB、IL8、IL9、RASK、K1C19、K2C8、LAMA2、LEG3、LMNB1、MARE1、MCM4、MIF、MMP7、MMP9、CD20、MYL6、MYL9、NDKA、NNMT、A1AG1、PCKGM、PDIA3、PDIA6、PDXK、PEBP1、PIPNA、KPYM、UROK、IPYR、PRDX1、KPCD1、PRL、TMG4、PSME3、PTEN、FAK1、FAK2、RBX1、REG4、RHOA、RHOB、RHOC、RSSA、RRBP1、S10AB、S10AC、S10A8、S109、SAA1、SAA2、SEGN、SDCG3、DHSA、SBP1、SELPL、SEP9、A1AT、AACT、ILEU、SPB6、SF3B3、SKP1、ADT2、ISK1、SPON2、OSTP、SRC、STK11、HNRPQ、TAL1、TRFE、TSP1、TIMP1、TKT、TSG6、TR10B、TNF6B、P53、TPM2、TCTP、TRAP1、THTR、TBB1、UGDH、UGPA、VEGFA、VILI、VIME、VNN1、1433Z、CCR5、FUC0及其组合。

137. 一种用于诊断、预测、预后和/或监测受试者的结肠疾病的方法,该方法包括:测量来自所述受试者的生物样品中选自SPB6、FRIL、P53、1A68、ENOA、TKT及其组合的至少一种生物标志物。

138. 一种用于诊断、预测、预后和/或监测受试者的结肠疾病的方法,该方法包括:测量来自所述受试者的生物样品中选自SPB6、FRIL、P53、1A68、ENOA、TKT、TSG6、TPM2、ADT2、FHL1、CCR5、CEAM5、SPON2、1A68、RBX1、COR1C、VIME、PSME3及其组合的至少一种生物标志物。

139. 一种用于诊断、预测、预后和/或监测受试者的结肠疾病的方法,该方法包括:测量来自所述受试者的生物样品中选自SPB6、FRIL、P53、1A68、ENOA、TKT、TSG6、TPM2、ADT2、FHL1、CCR5、CEAM5、SPON2、1A68、RBX1、COR1C、VIME、PSME3、MIC1、STK11、IPYR、SBP1、PEBP1、CATD、HPT、ANXA5、ALDOA、LAMA2、CATZ、ACTB、AACT及其组合的至少一种生物标志物。

援引并入

[0016] 本说明书中提到的所有出版物、专利和专利申请均通过引用以相同的程度并入本文,犹如特别地且单独地指出每个单独的出版物、专利或专利申请通过引用而并入。

附图说明

[0017] 本公开的新颖特征在所附的权利要求书中特别地提出。通过参考以下对利用本公开原理的说明性实施方案加以阐述的详细描述以及附图,将获得对本公开的特征和优点的更好的理解,附图中:

[0018] 图1A示出了显示根据实施例3A的结肠息肉生物标志物谱的预测性能的曲线图。

[0019] 图1B示出了显示根据实施例3B的结肠息肉生物标志物谱的预测性能的曲线图,其中Y轴为平均真阳性率而X轴为假阳性率。

[0020] 图2A示出了实施例3A的测试集性能的验证。

[0021] 图2B示出了实施例3B的测试集性能的验证,其中Y轴为平均真阳性率而X轴为假阳性率。

[0022] 图3示出了实施例3A的特征-频率表的帕累托图(pareto plot)。

[0023] 图4示出了实施例3B的特征-频率表的帕累托图,其中Y轴为特征出现率而X轴为特征等级(feature rank)。

[0024] 图5示出了显示根据实施例3A的具有较小集的结肠息肉的生物标志物谱的预测性能的曲线图。

- [0025] 图6示出了实施例3A的具有较小集测试集性能的验证。
- [0026] 图7示出了实施例3A中组装的分类器中表示的1014个特征的质量,每个特征出现3次或更多次。
- [0027] 图8示出了实施例3B中组装的分类器中表示的206个特征的质量。
- [0028] 图9提供了供包含或排除的附加生物标志物的列表。
- [0029] 图10示出了显示根据实施例4的CRC的生物标志物谱的预测性能的曲线图,其中Y轴为平均真阳性率而X轴为假阳性率。
- [0030] 图11示出了实施例4中组装的特征-频率表的帕累托图。
- [0031] 图12示出了预测实施例4中组装的CRC的分类器中表示的肽片段过渡离子。
- [0032] 图13显示了通用计算机系统1300的各种组件的实施方案。
- [0033] 图14为显示了可与本公开实施方案1400结合使用的计算机系统架构的实施方案的示意图。
- [0034] 图15为显示了可与本公开实施方案1500结合使用的计算机网络的实施方案的示意图。
- [0035] 图16为显示了可与本公开实施方案1600结合使用的计算机系统架构的实施方案的示意图。

具体实施方式

I. 定义

- [0036] 术语“结肠直肠癌状态”是指受试者的疾病状态。结肠直肠癌状态的类型的实例包括但不限于,受试者患包括结肠直肠癌在内的癌症的风险,疾病(例如,息肉或腺癌)的存在与否,患者的疾病阶段(例如,癌),和疾病治疗的疗效。
- [0037] 术语“质谱仪”是指测量可以转变成气相离子的质-荷(m/z)比的参数的气相离子谱仪。质谱仪通常包括离子源和质量分析器。质谱仪的实例为飞行时间(time-of-flight)、扇形磁场(magnetic sector)、四极滤质器、离子阱、离子回旋共振、静电扇形分析器以及这些的混合。“质谱法”是指使用质谱仪对气相离子的检测。
- [0038] 术语“串联质谱仪”是指能够进行基于 m/z 的离子(包括离子混合物中的离子)鉴别或测量的两个连续阶段的任何质谱仪。该词语包括具有两个质量分析器的质谱仪,该质量分析器能够空间串联地进行基于 m/z 的离子鉴别或测量的两个连续阶段。该词语进一步包括具有单个质量分析器的质谱仪,该质量分析器能够时间串联地进行基于 m/z 的离子鉴别或测量的两个连续阶段。该词语因此明确包括 Qq -TOF质谱仪、离子阱质谱仪、离子阱-TOF质谱仪、TOF-TOF质谱仪、傅立叶变换离子回旋共振质谱仪、静电扇形-扇形磁场质谱仪以及它们的组合。
- [0039] 术语“生物芯片”是指具有附着有吸附剂的通常平坦的表面的固体基底。通常,生物芯片的表面包含多个可寻址位置,每个可寻址位置具有与其结合的吸附剂。生物芯片可适应于接合探针界面,并因此起到探针的作用。蛋白质生物芯片适应于捕获多肽并且可包含在可寻址位置附着有色谱或生物特异性吸附剂的表面。微阵列芯片通常用于DNA和RNA基因表达检测。
- [0040] 术语“生物标志物”是指(具有特定的表观分子量的)多肽,与取自对照受试者(例

如,具有阴性诊断或检测不到结肠直肠癌的人,正常或健康的受试者,或者,例如在不同时间点来自同一个体的类似样品相比,该多肽差异性地存在于取自患有人结肠直肠癌的受试者的样品中。术语“生物标志物”可与术语“标志物”互换使用。生物标志物可以是基因,如DNA或RNA或DNA或RNA的遗传变异,它们的结合配偶体、剪接变体。生物标志物可以是蛋白质或蛋白质片段或氨基酸序列的过渡离子,或者蛋白质氨基酸序列上的一种或多种修饰。此外,蛋白质生物标志物可以是蛋白质或蛋白质片段或氨基酸序列的过渡离子的结合配偶体。

[0041] 术语“多肽”、“肽”和“蛋白质”在本文中可互换使用,意指氨基酸残基的聚合物。多肽是通过相邻氨基酸残基的羧基与氨基之间的肽键结合在一起的氨基酸的单个线性聚合物链。多肽可以例如通过加入碳水化合物、磷酸化等来修饰。

[0042] 术语“免疫测定”是使用抗体来特异性地结合抗原(例如,标志物)的测定。免疫测定的特征在于使用特定抗体的特异性结合性质来分离、靶向和/或量化抗原。

[0043] 术语“抗体”是指基本由一个免疫球蛋白基因或多个免疫球蛋白基因或其片段编码的、特异性结合并识别表位的多肽配体。抗体,例如作为完整的免疫球蛋白存在或作为由各种肽酶消化产生的多个良好表征的片段存在。这包括,例如Fab”和F(ab)”₂片段。如本文所用的,术语“抗体”还包括通过整个抗体的修饰产生的抗体片段或使用重组DNA方法从头合成的抗体片段。它还包括多克隆抗体、单克隆抗体、嵌合抗体、人源化抗体或单链抗体。抗体的“Fc”部分是指免疫球蛋白重链的包含一个或多个重链恒定区结构域但不包含重链可变区的部分。

[0044] 术语“肿瘤”是指可由癌性或非癌性细胞形成的、固体或液体填充的病变。术语“肿块”和“结节”经常与“肿瘤”同义使用。肿瘤包括恶性肿瘤或良性肿瘤。恶性肿瘤的实例可以是已知包含转化细胞的癌。

[0045] 术语“息肉”是指从粘膜凸出的组织异常生长。如果它通过狭长的柄附接至表面,则它被称为有蒂息肉。如果不存在柄,则它被称为无蒂息肉。息肉可以是恶性的、癌变前的或良性的。息肉可通过各种程序如手术或者例如在结肠镜检查期间采用息肉切除术而除去。

[0046] 术语“腺瘤性息肉”或“腺瘤”在本文中可互换使用,意指在结肠内衬(lining)上生长并具有增加的癌症风险的息肉。腺瘤性息肉被认为是恶变前的;然而,一些可能发展成结肠癌。管状腺瘤是腺瘤性息肉中最常见的并且它们是最不可能发展成结肠癌的结肠息肉。管状绒毛状腺瘤是另一种类型。绒毛状腺瘤是尺寸通常大于其他两种类型的腺瘤的第三种类型,且它们在所有息肉中具有最高的发病率和死亡率。

[0047] 术语“结合配偶体”是指分子对——通常是表现出特异性结合的生物分子对。蛋白质-蛋白质相互作用可发生在两个或更多个蛋白质之间,当蛋白质结合在一起时,它们通常行使它们的生物功能。蛋白质间的相互作用对大多数生物功能至关重要。例如,来自细胞外部的信号通过信号分子的蛋白质-蛋白质相互作用,经由配体和受体蛋白质被介导至该细胞的内部。例如,分子结合配偶体包括但不限于受体和配体、抗体和抗原、生物素和抗生物素蛋白等。

[0048] 术语“对照参考”是指已知的稳态分子或非患病健康状态,其在其中用作相对标志物以研究波动或比较非稳态分子或正常非患病健康状况,或者它也可以用于对值进行

校准或归一化。在各个实施方案中,对照参考值是由多个因素的组合或因素范围的组合如生物标志物浓度的组合或浓度范围的组合计算的值。

[0049] 术语“受试者”、“个体”或“患者”在本文中可互换使用,其指脊椎动物,优选哺乳动物,更优选人。哺乳动物包括但不限于鼠类、猿、家畜、竞技动物以及宠物。具体的哺乳动物包括大鼠、小鼠、猫、狗、猴子和人。非人类哺乳动物包括除人之外的所有哺乳动物。在体外获得或在体外培养的生物实体的组织、细胞及其后代也涵盖在内。

[0050] 术语“体内”是指发生在受试者身体内的事件。

[0051] 术语“体外”是指发生在受试者身体之外的事件。例如,体外测定包括在受试者之外进行测定的任何测定。体外测定涵盖采用活细胞或死细胞的基于细胞的测定。体外测定还涵盖不采用完整细胞的无细胞测定。

[0052] 术语“测量”意指包括检测样品中的标志物的存在与否、量化样品中的标志物的量和/或定性生物标志物的类型的方法。测量可以通过本领域中已知的方法和本文进一步描述的方法来完成,这些方法包括但不限于质谱法和免疫测定法或可用于检测和测量本文所述的一种或多种标志物的任何合适的方法。

[0053] 术语“检测”是指鉴定待检测的物体的存在、不存在或量。非限制性实例包括但不限于DNA分子、蛋白质、肽、蛋白质复合物、RNA分子或代谢物的检测。

[0054] 术语“差异性存在”是指在取自受试者的样品中存在的标志物与对照参考或对照非患病健康受试者相比在量和/或频率上的差异。标志物可以在量、频率或这两个方面差异性存在。

[0055] 术语“监测”是指记录连续变化参数的改变。

[0056] 术语“诊断的”或“诊断”在本文中可互换使用,意指鉴定病理状况的存在或性质,或病理状况的亚型,即结肠息肉的存在或风险。诊断方法在它们的灵敏度和特异性上不同。诊断方法可不提供状况的确诊;然而,如果该方法提供了有助于诊断的正向指示,那就足够了。

[0057] 术语“预后”在本文中用来指疾病或疾病进展(包括复发和治疗反应)的可能性的预测。

[0058] 术语“预测”在本文中用来指患者将具有特定临床结果(无论是阳性还是阴性)的可能性。本公开的预测方法可以在临床上用来通过为任何特定患者选择最合适的治疗方式来作出治疗决定。

[0059] 术语“报告”是指由本公开的方法提供给医师的不确定的或必要时为确定的打印结果。该报告可指示病理状况的存在、性质或风险。该报告还可指示什么样的治疗是最合适的;例如,不处理、手术、进一步测试或施用治疗剂。

II. 总体概述

[0060] 用于诊断疾病、疾病预后和预测对疾病的药物反应的生物标志物谱的开发对于医学界可能是有用的。

[0061] 本公开提供了通过使用各种测定外加由受计算机可读介质指示的处理器执行的算法以确定生物标志物来分析来自个体的复杂生物样品的方法、组合物、系统和试剂盒,该生物标志物指示临床状态或健康的恶化或改善。通常,该方法使用来自生物系统的多个分子生物学水平(例如,多核苷酸(DNA或RNA)、多肽和代谢物水平)的多种分子来鉴定疾

病如结肠癌、结肠息肉和预期的各种结肠直肠疾病 的生物标志物或生物标志物谱。

[0062] 本公开还提供了可用于诊断、预测、预后或监测个体的结肠息肉或结肠癌的存在或从其恢复的生物标志物和系统。

[0063] 本公开还提供了商业化诊断试剂盒,其通常将包括用于检测本 文所提供的生物标志物的组合物、说明以及指示个体的结肠息肉或结 肠癌的诊断、预测、预后、存在或从其恢复的报告。由该报告提供的 临床预测或状态可指示,例如,尚未在临床上表现出结肠息肉或癌的 个体在某一时间段内或者在给定年龄下,受试者将患有临床上表现的 结肠息肉和结肠癌的可能性、几率或风险。

III. 方法

[0064] 本公开提供了使用通过质谱法获得的数据,基于蛋白质组和/ 或基因组模式的医学诊断方法。该方法允许基于患者的蛋白质组和/ 或基因组模式按照患者的疾病阶段对患者进行分类。

[0065] 结肠直肠癌,也被称为结肠癌、直肠癌或肠癌,是由结肠或直 肠中的不受控的细胞生长而导致的癌症。此外,本公开提供了用于结 肠息肉和结肠直肠癌的医学诊断的新的生物标志物。

[0066] 结肠息肉为在大肠或结肠的内衬上形成的细胞良性块。几乎所 有的息肉最初都是非恶性的。然而,随着时间的推移,一些可能变成 癌性病变。大部分结肠息肉的原因是未知的,但它们常见于成人中。由于结肠息肉是无症状的,因此建议定期筛查结肠息肉。当前,用于 筛查息肉的方法是高度侵入性的且昂贵的。因此,尽管结肠镜检查筛 查在预防和减少结肠癌方面存在益处,但被建议该程序的许多人拒绝 进行此筛查,主要是因为担心成本、不适和不良事件。这类人仅在美 国就有数千万人。

[0067] 有助于对患者具有存在结肠息肉、腺瘤或癌性肿瘤如癌的较高 风险的可能性进行分类的分子测试可帮助医师指导患者关于抗拒进 行结肠镜检查的态度和行为。增加的结肠镜检查筛查依从性将导致早 期检测出癌症或癌变前腺瘤,并减少与结肠癌相关的发病率和死亡率。

[0068] 本公开提供了侵入性低于结肠镜检查并且将确定个体的蛋白质 表达指纹或谱的蛋白质生物标志物测试。在本公开的一些应用中,基 于所预测的个体的息肉状态和/或患有结肠息肉或结肠癌的风险的可 能性而生成报告。因此,本公开提供了提供关于个体的结肠息肉状态 和/或患有结肠息肉或结肠癌的风险的信息的方法、试剂盒、组合物和 系统。

[0069] 在本公开的一个方面,已通过基于LCMS的程序鉴定出一组基 于蛋白质的分类器(例如,生物标志物谱),该程序能够预测关于患 者的结肠息肉、腺瘤或癌的存在与否的结肠镜检查程序结果。

[0070] 在本公开的一个方面,已使用基于LCMS的方法来鉴定基于血 浆-蛋白质的分子特征,该分子特征可包含鉴别更可能患有息肉、腺 瘤或肿瘤的患者中的一个或多个分类器。

[0071] 在本公开的一个方面,分类器用于确定哪些个体不可能患有息 肉、腺瘤或肿瘤,并因此可能无需进行结肠镜检查。

[0072] 在本公开的一个方面,分类器用于通过比较程序之前与之后的 分类器值来测量结肠镜检查期间疑似息肉去除的完成度。

[0073] 在本公开的一个方面,在定期筛查结肠镜检查之间的间隔期间 使用分类器来捕

捉所谓的间期疾病(interval disease)。

[0074] 在本公开的一个方面,分类器用于增加具有升高的风险谱的患者的连续结肠镜检查之间的时间。具有升高的风险谱的患者的实例可包括先前进行过息肉切除术或其他病理操作的患者。

[0075] 本公开提供了在从完整蛋白质衍生的特定片段的大小和序列以及沿全蛋白质多肽链发生酶切(例如,胰蛋白酶消化等)的位置(其为结肠的病变状态的特征)方面生成和分析血液蛋白质片段谱的方法。

[0076] 预期本公开提供的方法、试剂盒、组合物和系统还可根据应用全部或部分自动化。

[0077] A. 基于算法的方法

[0078] 本公开提供了用于预测结肠息肉或结肠癌患者的临床结果的基于算法的诊断测定。可单独使用一种或多种蛋白质生物标志物的表达水平或将其设置成功能子集来计算可用于预测临床结果的可能性的定量得分。

[0079] 本公开的“生物标志物”或“标志物”可以是具有特定表观分子量的多肽,基因如DNA或RNA或DNA或RNA的遗传变异,它们的结合配偶体,剪接变体。生物标志物可以是蛋白质或蛋白质片段或氨基酸序列的过渡离子,或者蛋白质氨基酸序列上的一个或多个修饰。此外,蛋白质生物标志物可以是蛋白质或蛋白质片段或氨基酸序列的过渡离子的结合配偶体。

[0080] 通过实施本公开方法提供的基于算法的测定和相关信息促进了对表现出结肠肿瘤的患者们的最佳治疗决策制定。例如,这样的临床工具将使医师能够鉴定具有患息肉或癌的低可能性并因此无需抗癌治疗的患者,或具有患侵袭性癌症的高可能性并因此将需要抗癌治疗的患者。

[0081] 可通过应用特定算法来确定定量得分。在本文公开的方法中用于计算定量得分的算法可对一种生物标志物或成组生物标志物的表达水平值进行分组。此外,特定一组生物标志物的形成可促进生物标志物或生物标志物子集(例如分类器)的各个表达水平对定量得分的贡献的数学权重。本公开提供了用于计算定量得分的各种算法。

[0082] B. 数据的归一化

[0083] 在本文公开的方法中使用的表达数据可进行归一化。归一化是指对例如所测定的基因的量或蛋白质水平的差异以及所用模板的质量的可变性进行校正,以除去在处理 and 检测基因或蛋白质表达中涉及的不期望的系统变异测量来源的过程。其他的系统变异来源可归因于实验室处理条件。

[0084] 在一些情况下,归一化方法可用于实验室处理条件的归一化。可与本公开的方法一起使用的实验室处理的归一化的非限制性实例包括但不限于:解释在数据生成过程中使用的仪器、试剂和设备之间的系统性差异,和/或在数据采集中的日期和时间或时间消逝。

[0085] 测定可通过并入某些归一化的标准基因或蛋白质的表达来提供归一化,这些归一化的标准基因或蛋白质在相关条件下在表达水平上无显著不同,也就是说,在该特定样品类型中,它们已知具有稳定且一致的表达水平。可在本公开中使用的合适的归一化基因和蛋白质包括持家基因。(参见,例如E.Eisenberg等人,Trends in Genetics 19(7):362-

365 (2003))。在一些应用中,归一化的生物标志物(基因和蛋白质),也被称为参考基因,已知与无结肠息肉的患者相比,不表现出结肠息肉或癌症的在意义上不同的表达水平。在一些应用中,添加可被使用并代表具有已知性质的实体的稳定同位素标记的标准物以用于数据归一化可能是有用的。在其他应用中,标准的固定化样品可与每个分析批次一起进行测量,以解释仪器和日常测量的可变性。

[0086] 在一些应用中,诊断、预后和预测基因可相对于至少2、3、4、5、6、7、8、9、10、15、20、25、30、40或50个或更多个参考基因和蛋白质的平均值进行归一化。归一化可基于所有测定的生物标志物的信号平均值或中值或通过整体生物标志物归一化方法来进行。本领域技术人员将认识到,可以采用许多种方式来实现归一化,并且上述技术仅旨在示例。

[0087] C. 数据的标准化

[0088] 在本文公开的方法中使用的表达数据可以被标准化。标准化是指有效地将所有基因置于可比标度上的过程。因一些基因将比其他基因表现出更多的变异(更广范围的表达)而进行该过程。标准化通过将每个表达值除以其在该基因或蛋白质的所有样品中的标准差来进行。

[0089] D. 临床结果得分

[0090] 用于亚选择鉴别性生物标志物和用于构建分类模型的机器学习算法的使用可用于确定临床结果得分。这些算法包括但不限于,弹性网络、随机森林、支持向量机和逻辑回归。这些算法可对重要的生物标志物特征进行磨砺(hone in)并将基础测量值转换成与例如临床结果、疾病风险、治疗反应和/或疾病状态的分类相关的得分或概率。

[0091] 在一些应用中,定量得分的增加指示不良临床结果、良好临床结果、疾病的高风险、疾病的低风险、完全反应、部分反应、病情稳定、无反应和为疾病管理推荐的治疗的可能性的增加。在一些应用中,定量得分的降低指示不良临床结果、良好临床结果、疾病的高风险、疾病的低风险、完全反应、部分反应、病情稳定、无反应和为疾病管理推荐的治疗的可能性的增加。

[0092] 在一些应用中,来自患者的与参考谱类似的生物标志物谱指示不良临床结果、良好临床结果、疾病的高风险、疾病的低风险、完全反应、部分反应、病情稳定、无反应和为疾病管理推荐的治疗的可能性的增加。在一些应用中,来自患者的与参考谱不同的生物标志物谱表明不良临床结果、良好临床结果、疾病的高风险、疾病的低风险、完全反应、部分反应、病情稳定、无反应和为疾病管理推荐的治疗的可能性的增加。

[0093] 在一些应用中,一个或多个生物标志物阈值的增加指示不良临床结果、良好临床结果、疾病的高风险、疾病的低风险、完全反应、部分反应、病情稳定、无反应和为疾病管理推荐的治疗的可能性的增加。在一些应用中,一个或多个生物标志物阈值的降低指示不良临床结果、良好临床结果、疾病的高风险、疾病的低风险、完全反应、部分反应、病情稳定、无反应和为疾病管理推荐的治疗的可能性的增加。

[0094] 在一些应用中,定量得分、一个或多个生物标志物阈值、类似的生物标志物谱值或其组合的增加指示不良临床结果、良好临床结果、疾病的高风险、疾病的低风险、完全反应、部分反应、病情稳定、无反应和为疾病管理推荐的治疗的可能性的增加。在一些应用中,定量得分、一个或多个生物标志物阈值、类似的生物标志物谱值或其组合的降低指示不良临床结果、良好临床结果、疾病的高风险、疾病的低风险、完全反应、部分反应、病情稳

定、无反应和为疾病管理推荐的 治疗的可能性的增加。

[0095] E. 样品制备和处理

[0096] 在分析样品之前,可能期望对样品进行一个或多个样品制备操作。通常,这些样品制备操作可包括,如从细胞或组织提取和分离细胞内物质等操作,例如,从样品提取核酸、蛋白质或其他大分子。

[0097] 可与本公开的方法一起使用的样品制备包括但不限于,离心、亲和色谱法、磁分离、免疫测定、核酸分析、基于受体的测定、细胞计数测定、比色测定、酶测定、电泳分析、电化学测定、光谱测定、色谱测定、显微检测、地形分析(topographic assay)、量热分析、放射性同位素测定、蛋白质合成分析、组织学测定、培养试验以及它们的组合。

[0098] 样品制备可进一步包括用合适的溶剂和量进行稀释,以确保适当的浓度水平范围通过给定的测定法能检测到。

[0099] 从样品的细胞内空间接近核酸和大分子通常可通过物理、化学方法或二者的组合来进行。在该方法的一些应用中,在分离粗提取物后,通常期望分离核酸、蛋白质、细胞膜颗粒等。在该方法的一些应用中,期望将核酸与其蛋白质和细胞膜颗粒保持在一起。

[0100] 在本文提供的方法的一些应用中,可在使用本公开的方法进行分析之前,从生物样品中提取核酸和蛋白质。提取可通过包括但不限于使用去污剂裂解物、超声处理或采用玻璃珠涡旋的手段进行。

[0101] 在一些应用中,分子可以使用本领域中适合的任何技术进行分离,该技术包括但不限于,使用梯度离心(例如,氯化铯梯度、蔗糖梯度、葡萄糖梯度等)、离心方案、沸腾、纯化试剂盒以及使用采用试剂提取方法(如使用Trizol或DNAzol的方法)的液体提取的技术。

[0102] 可根据期望的检测方法,基于标准生物样品制备法制备样品。例如对于质谱法检测,可以对从患者获得的生物样品进行离心、过滤、通过免疫亲和柱的处理、分离成级分、部分消化以及它们的组合。各种级分可再悬浮于适当的载体中,如缓冲液或用于检测和分析的其他类型的上样溶液,包括LCMS上样缓冲液。

[0103] F. 检测方法

[0104] 本公开提供了用于检测生物样品中的生物标志物的方法。生物标志物可包括但不限于,蛋白质、代谢物、DNA分子和RNA分子。更具体地,本公开基于在患有结肠息肉或可能发展结肠息肉的受试者中差异性表达的蛋白质生物标志物的发现。因此,生物样品中这些差异性表达的生物标志物中的一种或多种的检测提供了关于受试者是否处于结肠息肉的风险下或患有结肠息肉以及该状况的性质或状态的类型的有用信息。任何合适的方法可用于检测本文所述的一种或多种生物标志物。

[0105] 可在本公开中使用的有用的分析物捕获剂包括但不限于,抗体,如含有抗体的粗血清、纯化的抗体、单克隆抗体、多克隆抗体、合成抗体、抗体片段(例如,Fab片段);抗体相互作用剂,如蛋白A、碳水化合物结合蛋白质和其他相互作用物;蛋白质相互作用物(例如,抗生物素蛋白及其衍生物);肽;以及小化学实体,如酶底物、辅因子、金属离子/螯合物和半抗原。可对抗体进行修饰或化学处理,以优化与靶标或固体表面(例如,生物芯片和柱)的结合。

[0106] 在本公开的一个方面,可以使用免疫测定在生物样品中检测生物标志物。免疫测

定是使用特异性结合至或识别抗原(例如,蛋白质或肽上的位点,即生物标志物靶标)的抗体的测定。该方法包括以下步骤:使生物样品与抗体接触,并使该抗体与样品中的抗原形成复合物,洗涤该样品并用检测试剂检测抗体-抗原复合物。在一个实施方案中,识别生物标志物的抗体可以是市售的。在另一个实施方案中,识别生物标志物的抗体可以通过已知的抗体产生方法生成。

[0107] 或者,可以使用间接测定法检测样品中的标志物,其中,例如使用标记的第二抗体来检测结合的标志物-特异性抗体。示例性的可检测标记物包括磁珠(例如, DYNABEADS™)、荧光染料、放射性标记物、酶(例如,辣根过氧化物、碱性磷酸酶以及其他常用的酶)和量热标记物,如胶体金或有色玻璃或塑料珠。可以使用竞争或抑制试验和/或在竞争或抑制试验中检测样品中的标志物,其中,例如,与标志物的不同表位结合的单克隆抗体与该混合物同时孵育。

[0108] 使用免疫测定检测抗原的条件将取决于所用的特定抗体。而且,孵育时间将取决于测定形式、标志物、溶液体积、浓度等。尽管根据所用的抗体,免疫测定可以在诸如10摄氏度到40摄氏度的温度范围进行,但通常免疫测定将在室温下进行。

[0109] 存在本领域中已知的多种类型的免疫测定,其作为起始基础可用于对该测定进行调整以用于检测本公开的生物标志物。有用的测定可包括,例如,酶免疫测定(EIA),诸如酶联免疫吸附测定(ELISA)。存在这些方法的许多变化形式,但这些变化形式都是基于类似的理念。例如,如果抗原可与固体支持物或表面结合,则它可通过使其与特异性抗体反应进行检测,并且该抗体可通过使其与第二抗体反应或者通过将标记物直接引入第一抗体来进行定量。或者,抗体可与固体表面和添加的抗原结合。随后,可添加并检测识别抗原上的不同表位的第二抗体。这通常称为“夹心法测定(sandwich assay)”并通常可用于避免高背景或非特异性反应的问题。这些类型的测定具有足以测定生物样品中低浓度的抗原的灵敏性和重现性。

[0110] 免疫测定可用于确定样品中标志物的存在与否以及样品中的标志物的量。用于测量抗体-标志物复合物的量或存在的方法包括但不限于,荧光法、发光法、化学发光法、吸光度法、反射率法、透射率法、双折射法或折射率法(例如,表面等离子体共振、椭圆测量法、共振镜法、光栅耦合器波导法或干涉法)。通常,这些试剂与光学检测方法如各种形式的显微术、成像方法和非成像方法一起使用。电化学方法包括伏安法和安培法。射频法包括多极共振光谱法。

[0111] 在一个方面,本公开可使用抗体来检测生物标志物。可以使抗体与该测定的生物标志物特异性结合,这样的抗体可使用本领域中已知的标准方法来制备。例如,多克隆抗体可通过将抗原注射至诸如小鼠、大鼠、兔、山羊、绵羊或马等哺乳动物来产生,以用于产生大量抗体。从这些动物中分离的血液含有多克隆抗体——与相同抗原结合的多种抗体。或者,多克隆抗体可以通过将抗原注射至鸡以便在蛋黄中产生多克隆抗体来产生。此外,可以使抗体特异性识别生物标志物的修饰形式,如生物标志物的磷酸化形式,也就是说,它们将识别磷酸化后的酪氨酸或丝氨酸,但在不存在磷酸的情况下不识别。这样,抗体可用于确定特定生物标志物的磷酸化状态。

[0112] 抗体可商购获得或使用已确立的方法产生。为了获得对抗原的单个表位具有特异性的抗体,从动物中分离分泌抗体的淋巴细胞并通过将它们与癌细胞系融合而永生化。

该融合的细胞被称为杂交瘤,并将在培养中持续生长并分泌抗体。单个杂交瘤细胞通过稀释克隆以生成均产生相同抗体的细胞克隆来分离;这些抗体被称为单克隆抗体。

[0113] 多克隆和单克隆抗体可以采用若干种方式进行纯化。例如,可以使用抗原亲和色谱法分离抗体,该抗原亲和色谱法与细菌蛋白质如蛋白A、蛋白G、蛋白L或重组融合蛋白、蛋白A/G偶联,随后通过280nm处的紫外线吸光度来检测洗脱物级分,以确定哪些级分含有所述抗体。蛋白A/G与人IgG的所有亚类结合,从而使它对于纯化其亚类尚未确定的多克隆或单克隆IgG抗体是有用的。另外,它与IgA、IgE、IgM和(在较小程度上)IgD结合。蛋白A/G还与小鼠IgG的所有亚类结合但不结合小鼠IgA、IgM或血清白蛋白。这一特征使得蛋白A/G用于纯化和检测小鼠单克隆IgG抗体,而不受IgA、IgM和血清白蛋白的干扰。

[0114] 抗体可来源于分子的不同类别或同种型,如IgA、IgA IgD、IgE、IgM和IgG。将IgA设计成用于在体液中分泌,而将其他抗体如IgM设计成在细胞表面上表达。在生物研究中最有用的抗体是IgG类别——被制备并分泌并可识别特异性抗原的蛋白质分子。IgG包含两个亚基,包括两个“重”链和两个“轻”链。它们组装成对称结构且每个IgG具有两个相同的抗原识别域。该抗原识别域为来自重链和轻链的氨基酸的组合。该分子的形状大致类似于“Y”,且该分子的臂/尖端包含抗原识别区或Fab(片段,抗原结合)区,而Fc(片段,可结晶)区的茎不参与识别并且相当恒定。恒定区在相同同种型的所有抗体中相同,但在不同同种型的抗体中不同。

[0115] 也可以在通过Western印迹法分级分离之后,使用抗体来检测蛋白质。在一个方面,本公开可使用Western印迹法来检测生物标志物。Western印迹法(蛋白质免疫印迹)是用于检测给定样品或来自样品的蛋白质提取物中的特异性蛋白质的分析技术。它使用凝胶电泳(SDS-PAGE)根据蛋白质的三维结构来分离任一天然蛋白质,或者它可在变性条件下运行以根据蛋白质长度来分离蛋白质。通过凝胶电泳分离后,随后将蛋白质转移到膜(通常为硝酸纤维素或PVDF)上。然后,可将从SDS-PAGE转移到膜上的蛋白质与特定抗体在轻柔搅拌下一起孵育,漂洗以除去非特异性结合物,并且与印迹结合的蛋白质-抗体复合物可使用一步或两步检测法进行检测。一步法包括既识别感兴趣的蛋白质又包含可检测标记物的探针抗体,探针通常对已知的蛋白质标签是可用的。两步检测法包含具有报道酶或与其结合的报道分子的第二抗体。采用适当的参考对照,这种方法可用于测量蛋白质的丰度。

[0116] 在一个方面,本公开的方法可使用流式细胞术。流式细胞术是可用于生物标志物的检测、定量(细胞计数)和细胞分离的基于激光的生物物理技术。该技术常规用于健康病症,尤其是血癌的诊断。在通常情况下,流式细胞术通过下列步骤工作:将单细胞悬浮在液体流中,将单波长光束(通常为激光)导向至液体流上,并由电子检测装置检测由穿过细胞而引起的散射光。荧光激活细胞分选(FACS)是专业型的流式细胞术,其通常借助于荧光标记的抗体来检测细胞上感兴趣的抗原。这一在FACS中使用抗体标记的附加特征提供了基于特定的光散射和每个细胞的荧光特性对荧光标记的细胞的同时多参数分析和定量,并且它提供了感兴趣的细胞群体的物理分离以及传统流式细胞术所实现的那些。

[0117] 很多种荧光团可用作流式细胞术中的标记物。荧光团通常附接至识别细胞之上或之内的靶特征的抗体。合适的荧光标记物的实例包括但不限于:荧光素(FITC),5,6-羧甲基荧光素,德克萨斯红(Texas red),硝基苯-2-氧杂-1,3-二唑-4-基(NBD),以及花青染

料Cy3、CY3.5、Cy5、Cy5.5和Cy7。其他荧光标记物如Alexa Fluor®染料、DNA内容物染料如DAPI、Hoechst染料是本领域中公知的,并且均可从多个商业来源容易地获得。每个荧光团具有特征峰激发和发射波长,并且发射光谱通常重叠。这些荧光标记物的吸收和发射最大值分别为:FITC (490nm;520nm)、Cy3 (554nm;568nm)、Cy3.5 (581nm; 588nm)、Cy5 (652nm; 672nm)、Cy5.5 (682nm;703nm)和Cy7 (755 nm;778nm),因此选择不具有很多光谱重叠的荧光标记物允许它们的同时检测。荧光标记物可以从多个商业来源获得。可区分的荧光标记物的最大数目被认为是约17或18种不同的荧光标记物。这个水平的复杂读出需要进行费时费力的优化以限制伪迹,以及进行复杂的反卷积算法以分离重叠的光谱。量子点因其较窄的发射峰而有时用来代替传统的荧光团。可用于检测的其他方法包括同位素(如镧系元素的同位素)标记的抗体。然而,该技术最终破坏细胞,从而阻止对其回收用于进一步的分析。

[0118] 在一个方面,本公开的方法可以使用免疫组织化学法来检测本公开的生物标志物的表达水平。因此,使用对每个标志物具有特异性的抗体来检测组织样品中所请求保护的生物标志物的表达。该抗体可通过抗体本身的直接标记,例如用放射性标记物、荧光标记物、半抗原标记物如生物素或酶(如辣根过氧化物酶或碱性磷酸酶)标记来检测。或者,将未标记的第一抗体与标记的第二抗体结合使用,该第二抗体包含对第一抗体具有特异性的抗血清、多克隆抗血清或单克隆抗体。免疫组织化学方案是本领域公知的,并且方案和抗体可商购获得。或者,可制备针对如本文公开的生物标志物或生物标志物的修饰形式或结合配偶体的抗体,其对于确定组织样品中的表达水平将是有益的。

[0119] 在一个方面,本公开的方法可使用生物芯片。生物芯片可用于筛选大量大分子。在该技术中,大分子以有序的阵列形式附着到生物芯片的表面。测试区的网格图案允许由成像软件进行分析,以快速且同时量化在分析物的预定位置(地址)处的单个分析物。CCD相机是能够准确地检测并量化芯片上的非常低水平的光的灵敏且高分辨率的传感器。

[0120] 生物芯片可采用固定的核酸分子、全长蛋白质、抗体、亲和体(affibodies)(被工程化为模拟单克隆抗体的小分子)、适体(基于核酸的配体)或化学化合物进行设计。芯片可被设计用于在一个芯片上检测多种大分子类型。例如,芯片可被设计用于在一个芯片上检测核酸分子、蛋白质和代谢物。生物芯片用于并被设计成同时分析单个样品中的一组生物标志物,从而产生这些生物标志物的受试者谱。生物芯片的使用允许进行多个分析,从而减少了总处理时间和所需样品的量。

[0121] 蛋白质微阵列是可在本公开中使用的特定类型的生物芯片。该芯片包含支持表面如载玻片、硝酸纤维素膜、珠子或微量滴定板,捕获蛋白质阵列以阵列的形式结合到固体表面上。蛋白质阵列检测方法必须提供高信号和低背景。将通常用荧光染料标记的检测探针分子添加至阵列。探针与固定的蛋白质之间的任何反应发射出可由激光扫描仪读取的荧光信号。此类蛋白质微阵列是快速、自动化的,并为诊断试验提供高灵敏度的蛋白质生物标志物读出。然而,本领域技术人员将立即理解它们是与该技术一起使用的多种检测方法。

[0122] 存在至少三种类型的当前用于研究蛋白质的生物化学活性的蛋白质微阵列。例如,存在分析微阵列(也称为捕获阵列)、功能性蛋白质微阵列(也称为靶蛋白质阵列)和反相蛋白质微阵列(RPA)。

[0123] 本公开提供了使用分析型蛋白质微阵列对生物标志物的检测。分析型蛋白质微阵列使用抗体、适体或亲和体的文库来构建。该阵列用复杂蛋白质溶液如血液、血清或细胞裂解物进行探查,该复杂蛋白质溶液通过捕获与其特异性结合的蛋白质分子而起作用。使用各种检测系统对所产生的结合反应的分析可提供关于样品中的特定蛋白质的表达水平以及结合亲和性和特异性的测量的信息。这种类型的蛋白质微阵列在比较不同样品中的蛋白质表达方面是特别有用的。

[0124] 在一个方面,本公开的方法可以使用功能性蛋白质微阵列,该功能性蛋白质微阵列通过固定大量的纯化的全长功能性蛋白质或蛋白质结构域而构建,并用于鉴定蛋白质-蛋白质、蛋白质-DNA、蛋白质-RNA、蛋白质-磷脂和蛋白质-小分子相互作用,以测定酶活性以及检测抗体并证明抗体的特异性。这些蛋白质微阵列生物芯片可用于研究样品中的整个蛋白质组的生化活性。

[0125] 在一个方面,本公开的方法可使用反相蛋白质微阵列(RPA)。反相蛋白质微阵列由排列到该微阵列上的组织和细胞裂解物构建,并用针对感兴趣的靶蛋白质的抗体来探查。这些抗体通常用化学发光、荧光或比色测定法进行检测。除了裂解物中的蛋白质外,也将参考对照肽打印在载玻片上,以允许蛋白质定量。RPA允许确定改变的蛋白质或可能是疾病的结果并存在于病变细胞中的其他物质的存在。

[0126] 本公开提供了使用质谱分析法(或者称为质谱法)对生物标志物的检测。质谱法(MS)是测量带电粒子的质荷比的分析技术。它主要用于确定样品或分子的元素组成,并用于解释分子如肽和其他化学化合物的化学结构。MS通过电离化学化合物以产生带电分子或分子片段并测量它们的质荷比而工作。MS仪器通常由以下三个模块组成:(1)离子源,其可将气相样品分子转化为离子(或者,在电喷雾电离的情况下,使溶液中存在的离子移动至气相中);(2)质量分析器,其通过施加电磁场根据离子的质量对其进行分选;以及(3)检测器,其测量指标量(indicator quantity)的值并由此提供数据以供计算存在的每个离子的丰度。

[0127] 将在本公开中使用的合适的质谱方法包括但不限于以下方法中的一种或多种:电喷雾电离质谱法(ESI-MS)、ESI-MS/MS、ESI-MS/(MS)_n、基质辅助激光解吸电离飞行时间质谱法(MALDI-TOF-MS)、表面增强激光解吸/电离飞行时间质谱法(SELDI-TOF-MS)、串联液相色谱-质谱(LC-MS/MS)质谱法、硅上解吸/电离(DIOS)、二次离子质谱法(SIMS)、四极杆飞行时间(Q-TOF)、大气压化学电离质谱法(APCI-MS)、APCI-MS/MS、APCI-(MS)、大气压光电离质谱法(APPI-MS)、APPI-MS/MS和 APPI-(MS)_n、四极杆质谱法、傅立叶变换质谱法(FTMS)和离子阱质谱法,其中n是大于零的整数。

[0128] 为了深入了解样品的基础蛋白质组,通常使用LC-MS来解析复杂混合物的组分。LC-MS方法通常包括蛋白酶消化和变性(通常涉及蛋白酶如胰蛋白酶,和变性剂,如用于使三级结构变性的尿素和用于为半胱氨酸残基加帽的碘乙酰胺),随后进行具有肽质量指纹分析的LC-MS或LC-MS/MS(串联MS)以获得单个肽的序列。LC-MS/MS最常用于复杂样品的蛋白质组分析,其中即使采用高分辨率质谱仪,肽质量仍可能重叠。复杂生物流体如人血清的样品可首先在SDS-PAGE凝胶或HPLC-SCX上分离并随后在LC-MS/MS中运行,以允许鉴定超过1000种蛋白质。

[0129] 尽管多种质谱方法可与本文所提供的方法一起使用,但在一些应用中,可能期望

量化生物样品中来自所选的感兴趣的蛋白质子集中的蛋白质。可在本公开中使用的一种这样的MS技术是多重反应监测 质谱法 (MRM-MS), 或者可替代地被称为选择反应监测质谱法 (SRM-MS)。

[0130] MRM-MS技术使用三重四极杆 (QQQ, triple quadrupole) 质谱 仪来从感兴趣的肽中选择带正电荷的离子, 使带正电荷的离子片段化, 并随后测量所选带正电荷的片段离子的丰度。这种测量方法通常被称 为过渡法 (transition)。例如, 从该方法得到的过渡离子参见表1。

[0131] 在一些应用中, MRM-MS与高压液相色谱法 (HPLC) 和最近 的超高压液相色谱法 (UHPLC) 耦合。在其他应用中, MRM-MS与 采用QQQ质谱仪的UHPLC耦合, 以对所有感兴趣的肽和蛋白质进 行所需的LC-MS过渡测量。

[0132] 在一些应用中, 可使用四极杆飞行时间 (qTOF) 质谱仪、飞行 时间-飞行时间 (TOF-TOF) 质谱仪、轨道阱质谱仪、四极杆轨道阱 质谱仪或任何四极杆离子阱质谱仪从一种或多种感兴趣的肽中选择 带正电荷的离子。然后, 可测量片段化的带正电荷的离子来确定带正电荷的离子的丰度以用于量化感兴趣的肽或蛋白质。

[0133] 在一些应用中, 可使用飞行时间 (TOF)、四极杆飞行时间 (qTOF) 质谱仪、飞行时 间-飞行时间 (TOF-TOF) 质谱仪、轨道阱质谱仪或 四极杆轨道阱质谱仪来测量来自未片段化的感兴趣的蛋白质的带正 电荷的肽离子的质量和丰度, 以供定量。在本申请中, 分析物 质量测 量的准确度可用作测定的选择标准。具有已知组成和浓度的同位素标 记的内标物可用作质谱定量方法的一部分。

[0134] 在一些应用中, 可使用飞行时间 (TOF)、四极杆飞行时间 (qTOF) 质谱仪、飞行时 间-飞行时间 (TOF-TOF) 质谱仪、轨道阱质谱仪或 四极杆轨道阱质谱仪来测量感兴趣的蛋白质的质量和丰度以供定量。在本申请中, 分析物质量测量的准确度可用作测定的选择标准。任 选 地, 本申请在通过质谱法分析之前, 可使用蛋白质的蛋白水解消化。具有已知组成和浓度的同位素标记的内标物可用作质谱定量方法的一部分。

[0135] 在一些应用中, 各种电离技术可与本文提供的质谱仪耦合, 以 产生所需的信息。可与本公开一起使用的非限制性的示例性电离技术 包括但不限于: 基质辅助激光解吸电离 (MALDI)、解吸电喷雾电离 (DESI)、直接辅助实时 (DART)、表面辅助激光解吸电离 (SALDI) 或电喷雾电离 (ESI)。

[0136] 在一些应用中, HPLC和UHPLC可与质谱仪耦合。在质谱分析 前, 可进行多种其他肽和蛋白质分离技术。可用于从基质背景中分离 所需分析物 (例如, 肽或蛋白质) 的一些示例性分离技术包括但不限 于, 蛋白质或肽的反相液相色谱法 (RP-LC)、MALDI前的离线液 相色谱法 (LC)、一维凝胶分离、二维凝胶分离、强阳离子交换 (SCX) 色谱法、强阴离子交换 (SAX) 色谱法、弱阳离子交换 (WCX) 和弱 阴离子交换 (WAX)。在质谱分析前可使用上述技术中的一种或多 种。

[0137] 在本公开的一个方面, 可使用微阵列检测生物样品中的生物标 志物。还可以使用微阵列技术鉴定或确认差异性基因表达。因此, 可 使用微阵列技术测量新鲜或固定的组织中的表达谱生物标志物。在该 方法中, 将感兴趣的多核苷酸序列 (包括cDNA和寡核苷酸) 铺 在或 排列在微芯片基底上。随后, 将排列的序列与来自感兴趣的细胞或组 织的特异性DNA探针杂交。mRNA的来源通常是从生物样品中分离 的总RNA, 并且可使用相应的正常组织或

细胞系来确定差异性表达。

[0138] 在微阵列技术的具体实施方案中,将PCR扩增的cDNA克隆插入物以密集阵列形式施加至基底。优选将至少10,000个核苷酸序列施加至基底。以每个基底10,000个元件固定在微芯片上的微阵列基因适于严格条件下的杂交。荧光标记的cDNA探针可通过经由从感兴趣组织中提取的RNA的逆转录掺入荧光核苷酸而产生。施加至芯片的标记的cDNA探针与阵列上的每个DNA位点特异性地杂交。严格洗涤以除去非特异性结合的探针后,通过诸如共聚焦激光显微镜的设备或通过诸如CCD相机的另一种检测方法来扫描微阵列芯片。对每个排列的元件的杂交的定量允许评估相应的mRNA丰度。通过采用双色荧光,从两个RNA来源产生的分别标记的cDNA探针与阵列成对杂交。来自两个来源的与每个指定基因相对应的转录物的相对丰度因此同时得以确定。微阵列分析可通过市售设备按照生产商的方案来进行。

[0139] 在本公开的一个方面,生物标志物可使用qRT-PCR在生物样品中进行检测,该生物标志物可用于比较在进行或不进行药物治疗下正常和肿瘤组织中的不同样品群体的mRNA水平,以表征基因表达模式,区分密切相关的mRNA,并分析RNA结构。通过RT-PCR进行基因表达谱分析的第一步是从生物样品中提取RNA,接着将RNA模板逆转录成cDNA,并通过PCR反应进行扩增。逆转录反应步骤通常使用特异性引物、随机六聚体或寡-dT引物根据表达谱分析的目标来引发。两种常用的逆转录酶是禽(avilo)成髓细胞瘤病毒逆转录酶(AMV-RT)和莫洛尼(Moloney)鼠白血病病毒逆转录酶(MLV-RT)。

[0140] 尽管PCR步骤可使用多种热稳定的DNA依赖性DNA聚合酶,但它通常采用Taq DNA聚合酶,Taq DNA聚合酶具有5'-3'核酸酶活性但缺乏3'-5'校正核酸内切酶活性。因此,TaqMan™ PCR通常使用Taq或Tth聚合酶的5'-核酸酶活性来水解与其靶扩增子结合的杂交探针,但具有等效的5'核酸酶活性的任何酶均可以使用。使用两个寡核苷酸引物产生PCR反应的典型扩增子。第三寡核苷酸或探针被设计用于检测位于两个PCR引物之间的核苷酸序列。探针不可由Taq DNA聚合酶延伸,并采用报道荧光染料和猝灭荧光染料进行标记。当报道染料和猝灭染料在探针上位置靠近时,来自报道染料的任何激光诱导的发射被猝灭染料猝灭。在扩增反应过程中,Taq DNA聚合酶以模板依赖性方式裂解探针。所得探针片段在溶液中解离,并且来自释放的报道染料的信号不受第二荧光团的猝灭效应的影响。释放报道染料的一个分子用于每个新合成的分子,并且非猝灭的报道染料的检测提供了数据的定量解释的基础。

[0141] TaqMan™ RT-PCR可使用市售的设备如ABI PRISM 7700™ Sequence Detection System™ (Perkin-Elmer-Applied Biosystems, Foster City, Calif., USA) 或LightCycler™ (Roche Molecular Biochemicals, Mannheim, 德国) 进行。在一个优选的实施方案中,5'核酸酶程序在实时定量PCR设备如ABI PRISM 7700™ Sequence Detection System™上运行。该系统包含热循环仪、激光器、电荷耦合器件(CCD)、照相机和计算机。该系统包含用于运行仪器和用于分析数据的软件。5'-核酸酶测定数据最初表述为Ct或循环阈值。如上所讨论的,在每个循环期间记录荧光值且荧光值代表在扩增反应中扩增至该点的产物的量。首次记录到荧光信号为统计学上显著时的点为循环阈值(Ct)。

[0142] 为了使误差和样品间变化的影响最小化,RT-PCR通常使用内标物进行。理想的内标物在不同组织间以恒定的水平表达并且不受实验处理的影响。最常用于对基因表达模

式进行归一化的RNA是管家基因甘油醛-3-磷酸脱氢酶(GAPDH)和 β -肌动蛋白的mRNA。

[0143] RT-PCR技术的较新变化形式是实时定量PCR,其通过双标记的荧光生成探针(即TaqMan™探针)测量PCR产物累积。实时PCR与定量竞争PCR(其中每个靶序列的内部竞争物均用于归一化)以及定量比较PCR(其使用样品内包含的归一化基因或用于RT-PCR的管家基因)均相容。进一步的细节参见,例如Held等人,Genome Research 6:986-994(1996)。

[0144] G. 数据处理

[0145] 上述测定获得的值可手动计算并存储。或者,上述步骤可完全或部分地由计算机程序产品进行。因此,本公开提供了包括计算机可读存储介质的计算机程序产品,该计算机可读存储介质具有存储在其上的计算机程序。该程序在被计算机读取时,可基于从来自个体的一个或多个生物样品的分析获得的值(例如,基因或蛋白质表达水平、归一化、标准化、取阈和从测定的值到临床结果得分和/或临床状态或阶段的文本或图形描述的转换以及相关信息)来执行相关计算。该计算机程序产品在其中存储用于执行计算的计算机程序。

[0146] 本公开提供了用于执行数据采集和处理或计算上述软件程序的系统,该系统通常包括:a)中央计算环境;b)输入设备,其可操作地连接到所述计算环境,以接收患者数据,其中所述患者数据可以包括,例如基因或蛋白质表达水平或从使用来自患者的生物样品的测定获得的其他值,或质谱数据或由本公开提供的任何测定的数据;c)输出设备,其连接至所述计算环境,以向用户(例如,医务人员)提供信息;以及d)由中央计算环境(例如,处理器)执行的算法,其中该算法基于由所述输入设备接收的数据来执行,并且其中所述算法计算表达得分、取阈或本文描述的其他功能。本公开提供的方法也可以是整体或部分自动化的。

[0147] H. 受试者

[0148] 生物样品从想要确定其患有结肠肿瘤或息肉的可能性的受试者采集。本公开提供了可为健康且无症状的受试者。在各个实施方案中,受试者是健康的、无症状的且年龄在20-50岁之间。在各个实施方案中,受试者是健康且无症状的并且没有腺瘤或息肉的家族史。在各个实施方案中,受试者是健康且无症状的并且从未接受过结肠镜检查。本公开还提供了正在接受作为例行检查的一部分或用于建立生物标志物的基线水平的检测的健康受试者。

[0149] 本公开提供了没有结肠直肠癌的症状、没有结肠直肠癌家族史且没有经识别的结肠直肠癌风险因素的受试者。本公开提供了没有结肠直肠癌的症状、没有结肠直肠癌家族史且没有除年龄之外的经识别的结肠直肠癌风险因素的受试者。

[0150] 生物样品也可以从已根据其家族史确定具有结肠直肠息肉或癌症的高风险、先前曾治疗结肠直肠息肉或癌症和或处于缓解期的受试者采集。生物样品还可从表现出已知与结肠直肠癌相关的身体症状的受试者、通过筛选测定(例如,粪便隐血试验或乙状结肠镜检查)或直肠数字检查(rectal digital exam)或刚性或柔性结肠镜检查或CT扫描或其他X射线技术确认的受试者采集。生物样品也可从目前正在经治疗的受试者采集,以确定他们正在接受的疗法或治疗的有效性。

[0151] I. 生物样品

[0152] 生物标志物可以在不同类型的生物样品中测量。该样品优选来自汇集并概括了

整个系统的生物样品。本公开中有用的生物样品类型的实例包括但不限于以下的一种或多种：尿、粪便、泪液、全血、血清、血浆、血液成分、骨髓、组织、细胞、器官、唾液、脸颊拭子、淋巴液、脑脊髓液、病变渗出物和由身体产生的其他流体。该生物标志物也可从冷冻的、固定的、石蜡包埋的或新鲜的活检样品中提取。

IV. 生物标志物和生物标志物谱

[0153] 本公开的生物标志物允许在健康个体与患有结肠息肉或处于发展结肠息肉的风险下的个体之间以及在结肠息肉的不同状态(例如增生的、恶性的、癌或肿瘤亚型)之间进行区分。具体地,本公开对生物标志物的发现提供了有助于结肠息肉和结肠癌的临床评价和管理的方法、试剂盒。

[0154] 可用于结肠息肉的临床评价和管理的生物标志物包括下列蛋白质(UNIPROTEIN ID号)的全蛋白、肽片段、核酸或过渡离子: SPB6_HUMAN、FRIL_HUMAN、P53_HUMAN、1A68_HUMAN、ENO1_HUMAN、TKT_HUMAN及其组合。

[0155] 可用于结肠息肉的临床评价和管理的生物标志物包括下列蛋白质(UNIPROTEIN ID号)的全蛋白、肽片段、核酸或过渡离子: SPB6_HUMAN、FRIL_HUMAN、P53_HUMAN、1A68_HUMAN、ENO1_HUMAN、TKT_HUMAN、TSG6_HUMAN、TPM2_HUMAN、ADT2_HUMAN、FHL1_HUMAN、CCR5_HUMAN、CEAM5_HUMAN、SPON2_HUMAN、1A68_HUMAN、RBX1_HUMAN、COR1C_HUMAN、VIME_HUMAN、PSME3_HUMAN及其组合。

[0156] 可用于结肠息肉的临床评价和管理的生物标志物包括下列蛋白质(UNIPROTEIN ID号)的全蛋白、肽片段、核酸或过渡离子: SPB6_HUMAN、FRIL_HUMAN、P53_HUMAN、1A68_HUMAN、ENO1_HUMAN和TKT_HUMAN、TSG6_HUMAN、TPM2_HUMAN、ADT2_HUMAN、FHL1_HUMAN、CCR5_HUMAN、CEAM5_HUMAN、SPON2_HUMAN、1A68_HUMAN、RBX1_HUMAN、COR1C_HUMAN、VIME_HUMAN、PSME3_HUMAN、MIC1_HUMAN、STK11_HUMAN、IPYR_HUMAN、SBP1_HUMAN、PEBP1_HUMAN、CATD_HUMAN、HPT_HUMAN、ANXA5_HUMAN、ALDOA_HUMAN、LAMA2_HUMAN、CATZ_HUMAN、ACTB_HUMAN、AACT_HUMAN及其组合。

[0157] 可用于结肠息肉的临床评价和管理的生物标志物包括图12中的过渡离子。

[0158] 通过本公开的方法从全血清中鉴定出的生物标志物包括与下列蛋白质(UNIPROTEIN ID号)相对应的全蛋白、肽片段、核酸或过渡离子: 细胞质肌动蛋白1(ACTB_HUMAN)(SEQ ID NO:1)、肌动蛋白 γ -肠平滑肌前体(ACTH_HUMAN)(SEQ ID NO:2)、血管紧张素原前体(ANGT_HUMAN)(SEQ ID NO:3)、腺苷高半胱氨酸酶(SAHH_HUMAN)(SEQ ID NO:4)、醛糖还原酶(ALDR_HUMAN)(SEQ ID NO:5)、RAC- α 丝氨酸/苏氨酸-蛋白激酶(AKT1_HUMAN)(SEQ ID NO:6)、血清白蛋白前体(ALBU_HUMAN)(SEQ ID NO:7)、视黄醛脱氢酶1(AL1A1_HUMAN)(SEQ ID NO:8)、醛脱氢酶X线粒体前体(AL1B1_HUMAN)(SEQ ID NO:9)、果糖-二磷酸醛缩酶A(ALDOA_HUMAN)(SEQ ID NO:10)、 α -淀粉酶2B前体(AMY2B_HUMAN)(SEQ ID NO:11)、膜联蛋白A1(ANXA1_HUMAN)(SEQ ID NO:12)、膜联蛋白A3(ANXA3_HUMAN)(SEQ ID NO:13)、膜联蛋白A4(ANXA4_HUMAN)(SEQ ID NO:14)、膜联蛋白A5(ANXA5_HUMAN)(SEQ ID NO:15)、腺瘤性结肠息肉病蛋白(APC_HUMAN)(SEQ ID NO:16)、载脂蛋白A-I前体(APOA1_HUMAN)(SEQ ID NO:17)、载脂蛋白C-I前体(APOC1_HUMAN)(SEQ ID NO:18)、 β -2-糖蛋白1前体(APOH_HUMAN)(SEQ ID NO:19)、Rho GDP解离抑制剂1(GDIR1_HUMAN)(SEQ ID NO:20)、ATP合酶 β 亚基线粒体前体(ATPB_HUMAN)(SEQ ID NO:21)、具有锚蛋白重复序

列的 B 细胞支架蛋白 (BANK1_HUMAN) (SEQ ID NO:22)、未表征 的蛋白 C18orf8 (MIC1_HUMAN) (SEQ ID NO:23)、推定的未表 征的蛋白 C1orf195 (CA195_HUMAN) (SEQ ID NO:24)、补体 C3 前体 (C03_HUMAN) (SEQ ID NO:25)、补体成分 C9 前体 (C09_HUMAN) (SEQ ID NO:26)、碳酸酐酶 1 (CAH1_HUMAN) (SEQ ID NO:27)、碳酸酐酶 2 (CAH2_HUMAN) (SEQ ID NO:28)、钙网蛋白前体 (CALR_HUMAN) (SEQ ID NO:29)、巨噬 细胞加帽蛋白 (CAPG_HUMAN) (SEQ ID NO:30)、信号转导蛋 白 CD24 前体 (CD24_HUMAN) (SEQ ID NO:31)、CD63 抗原 (CD63_HUMAN) (SEQ ID NO:32)、胞苷脱氨酶 (CDD_HUMAN) (SEQ ID NO:33)、癌胚抗原相关细胞粘附分子 3 (CEAM3_HUMAN) (SEQ ID NO:34)、癌胚抗原相关细胞粘附分子 5 (CEAM5_HUMAN) (SEQ ID NO:35)、癌胚抗原相关细胞粘附分子 6 (CEAM6_HUMAN) (SEQ ID NO:36)、绒毛膜促性腺激素 β 亚基前体 (CGHB_HUMAN) (SEQ ID NO:37)、几丁质酶-3 样蛋白 1 前体 (CH3L1_HUMAN) (SEQ ID NO:38)、肌酸激酶 B 型 (KCRB_HUMAN) (SEQ ID NO:39)、C 型凝集素结构域家族 4 成员 D (CLC4D_HUMAN) (SEQ ID NO:40)、簇蛋白前体 (CLUS_HUMAN) (SEQ ID NO:41)、钙调理蛋白-1 (CNN1_HUMAN) (SEQ ID NO:42)、冠蛋白-1C (COR1C_HUMAN) (SEQ ID NO:43)、C-反应蛋白前体 (CRP_HUMAN) (SEQ ID NO:44)、巨噬细胞集落刺激因子 1 前 体 (CSF1_HUMAN) (SEQ ID NO:45)、连环蛋白 β -1 (CTNB1_HUMAN) (SEQ ID NO:46)、组织蛋白酶 D 前体 (CATD_HUMAN) (SEQ ID NO:47)、组织蛋白酶 S 前体 (CATS_HUMAN) (SEQ ID NO:48)、组织蛋白酶 Z 前体 (CATZ_HUMAN) (SEQ ID NO:49)、滞蛋白-1 (CUL1_HUMAN) (SEQ ID NO:50)、细胞质天冬氨酸-tRNA 连接酶 (SYDC_HUMAN) (SEQ ID NO:51)、嗜中性粒细胞防御 素 1 (DEF1_HUMAN) (SEQ ID NO:52)、嗜中性粒细胞防御素 3 (DEF3_HUMAN) (SEQ ID NO:53)、结蛋白 (DESM_HUMAN) (SEQ ID NO:54)、二肽基肽酶 4 (DPP4_HUMAN) (SEQ ID NO:55)、二氢嘧啶酶相关蛋白 2 (DPYL2_HUMAN) (SEQ ID NO:56)、细胞质动力蛋白 1 重链 1 (DYHC1_HUMAN) (SEQ ID NO:57)、 $\delta(3,5)-\delta(2,4)$ -二烯酰-CoA 异构酶线粒体前体 (ECH1_HUMAN) (SEQ ID NO:58)、延伸因子 2 (EF2_HUMAN) (SEQ ID NO:59)、真 核起始因子 4A-III (IF4A3_HUMAN) (SEQ ID NO:60)、 α -烯醇 化酶 (ENOA_HUMAN) (SEQ ID NO:61)、埃兹蛋白 (EZRI_HUMAN) (SEQ ID NO:62)、Niban 样蛋白 2 (NIBL2_HUMAN) (SEQ ID NO:63)、Seprase (SEPR_HUMAN) (SEQ ID NO:64)、仅 F 框蛋白 4 (F-box only protein 4) (FBX4_HUMAN) (SEQ ID NO:65)、纤 维蛋白原 β 链前体 (FIBB_HUMAN) (SEQ ID NO:66)、纤维蛋 白原 γ 链 (FIBG_HUMAN) (SEQ ID NO:67)、四个半 LIM 结构域蛋白 1 (FHL1_HUMAN) (SEQ ID NO:68)、细丝蛋白-A (FLNA_HUMAN) (SEQ ID NO:69)、包含 FERM 结构域的蛋白 3 (FRMD3_HUMAN) (SEQ ID NO:70)、铁蛋白重链 (FRIH_HUMAN) (SEQ ID NO:71)、铁蛋白轻链 (FRIL_HUMAN) (SEQ ID NO:72)、组织 α -L-岩藻糖苷酶前体 (FUCO_HUMAN) (SEQ ID NO:73)、 γ -氨基丁酸受体亚基 α -1 前体 (GBRA1_HUMAN) (SEQ ID NO:74)、甘油醛-3-磷酸脱氢酶 (G3P_HUMAN) (SEQ ID NO:75)、甘氨酸-tRNA 连接酶 (SYG_HUMAN) (SEQ ID NO:76)、生长/ 分化因子 15 前体 (GDF15_HUMAN) (SEQ ID NO:77)、凝溶胶 蛋白前体 (GELS_HUMAN) (SEQ ID NO:78)、谷胱甘肽 S-转移 酶 P (GSTP1_HUMAN) (SEQ ID NO:79)、透明质酸结合蛋白 2 前体 (HABP2_HUMAN) (SEQ ID NO:80)、肝细胞生长因子前体 (HGF_HUMAN) (SEQ ID NO:81)、HLA I 类组织相容性抗原 A-68 α 链 (1A68_HUMAN) (SEQ ID NO:82)、高速泳动族蛋白 B1 (HMGB1_HUMAN) (SEQ ID NO:83)、核内不均一核糖核蛋 白 A1 (ROA1_HUMAN) (SEQ ID NO:84)、核内不均一核糖核蛋 白 A2/B1 (ROA2_HUMAN) (SEQ ID NO:85)、核内不均一核糖 核蛋白 F (HNRPF_HUMAN) (SEQ ID NO:86)、触珠蛋白前体 (HPT_HUMAN) (SEQ

ID NO:87)、热休克蛋白HSP 90- β (HS90B_HUMAN) (SEQ ID NO:88)、内质网素 (Endoplasmic reticulum chaperone) 前体 (ENPL_HUMAN) (SEQ ID NO:89)、Stress-70蛋白线粒体 前体 (Stress-70protein, mitochondrial precursor) (GRP75_HUMAN) (SEQ ID NO:90)、热休克蛋白 β -1 (HSPB1_HUMAN) (SEQ ID NO:91)、线粒体60kDa热休克蛋白 (CH60_HUMAN) (SEQ ID NO: 92)、骨唾液蛋白2 (SIAL_HUMAN) (SEQ ID NO:93)、鞭毛内 转运蛋白74同系物 (IFT74_HUMAN) (SEQ ID NO:94)、胰岛素 样生长因子I (IGF1_HUMAN) (SEQ ID NO:95)、Ig α -2链C区 (IGHA2_HUMAN) (SEQ ID NO:96)、白介素-2受体 β 亚基前体 (IL2RB_HUMAN) (SEQ ID NO: 97)、白介素-8 (IL8_HUMAN) (SEQ ID NO:98)、白介素-9 (IL9_HUMAN) (SEQ ID NO:99)、GTP 酶Kras前体 (RASK_HUMAN) (SEQ ID NO:100)、角蛋白 I型细胞骨架19 (K1C19_HUMAN) (SEQ ID NO:101)、角蛋白 II型细胞骨架8 (K2C8_HUMAN) (SEQ ID NO:102)、层粘连蛋 白亚基 α -2 前体 (LAMA2_HUMAN) (SEQ ID NO:103)、半乳凝 集素-3 (LEG3_HUMAN) (SEQ ID NO:104)、核 纤层蛋白-B1前 体 (LMNB1_HUMAN) (SEQ ID NO:105)、微管相关蛋白RP/EB 家族成员1 (MARE1_HUMAN) (SEQ ID NO:106)、DNA复制许 可因子MCM4 (MCM4_HUMAN) (SEQ ID NO:107)、巨噬细胞 游走抑制因子 (MIF_HUMAN) (SEQ ID NO:108)、基质溶解素 前体 (MMP7_HUMAN) (SEQ ID NO:109)、基质金属蛋白酶9 前体 (MMP9_HUMAN) (SEQ ID NO:110)、B淋巴细胞抗原 CD20 (CD20_HUMAN) (SEQ ID NO:111)、肌球蛋白轻链多肽6 (MYL6_HUMAN) (SEQ ID NO: 112)、肌球蛋白调节轻链多肽9 (MYL9_HUMAN) (SEQ ID NO:113)、核苷二磷酸激酶A (NDKA_ HUMAN) (SEQ ID NO:114)、烟酰胺N-甲基转移酶 (NNMT_HUMAN) (SEQ ID NO:115)、 α -1-酸性 糖蛋白1前体 (A1AG1_HUMAN) (SEQ ID NO:116)、磷酸烯醇丙酮酸羧激酶 [GTP]线粒体前体 (PCKGM_HUMAN) (SEQ ID NO:117)、蛋白 质二硫键异构酶A3前体 (PDIA3_HUMAN) (SEQ ID NO:118)、蛋白质二硫键异构酶A6前体 (PDIA6_HUMAN) (SEQ ID NO:119)、吡哆醛激酶 (PDXK_HUMAN) (SEQ ID NO:120)、磷脂酰乙醇胺 结合蛋白1 (PEBP1_HUMAN) (SEQ ID NO: 121)、磷脂酰肌醇转 移蛋白 α 同种型 (PIPNA_HUMAN) (SEQ ID NO:122)、丙酮酸 激酶同工酶 M1/M2 (KPYM_HUMAN) (SEQ ID NO:123)、尿激 酶型纤溶酶原激活剂前体 (UROK_HUMAN) (SEQ ID NO:124)、无机焦磷酸酶 (IPYR_HUMAN) (SEQ ID NO:125)、过氧化物氧 还蛋白-1 (PRDX1_HUMAN) (SEQ ID NO:126)、丝氨酸/苏氨酸 -蛋白激酶D1 (KPCD1_HUMAN) (SEQ ID NO:127)、催乳素 (PRL_HUMAN) (SEQ ID NO:128)、跨膜 γ -羧基谷氨酸蛋白4 前体 (TMG4_ HUMAN) (SEQ ID NO:129)、蛋白酶体激活剂复合 物亚基3 (PSME3_HUMAN) (SEQ ID NO:130)、磷脂酰肌醇3,4,5- 三磷酸3-磷酸酶和双特异性蛋白质磷酸酶PTEN (PTEN_HUMAN) (SEQ ID NO:131)、黏着斑激酶1 (FAK1_HUMAN) (SEQ ID NO: 132)、蛋白质酪氨酸激酶2- β (FAK2_ HUMAN) (SEQ ID NO:133)、E3泛素-蛋白质连接酶RBX1 (RBX1_HUMAN) (SEQ ID NO:134)、再 生胰岛衍生蛋白4前体 (REG4_HUMAN) (SEQ ID NO:135)、转化蛋白RhoA (RHOA_HUMAN) (SEQ ID NO:136)、Rho相关 GTP结合蛋白RhoB (RHOB_HUMAN) (SEQ ID NO:137)、Rho 相关GTP结合 蛋白RhoC (RHOC_HUMAN) (SEQ ID NO:138)、40S核糖体蛋白SA (RSSA_HUMAN) (SEQ ID NO: 139)、核糖 体结合蛋白1 (RRBP1_HUMAN) (SEQ ID NO:140)、蛋白S100-A11 (S10AB_HUMAN) (SEQ ID NO:141)、蛋白S100-A12 (S10AC_HUMAN) (SEQ ID NO:142)、蛋白S100-A8 (S10A8_ HUMAN) (SEQ ID NO:143)、蛋白S100-A9 (S10A9_HUMAN) (SEQ ID NO:144)、血清淀粉样蛋白 A-1蛋 白 (SAA1_HUMAN) (SEQ ID NO:145)、血清淀粉样蛋白A-2蛋 白前体 (SAA2_HUMAN) (SEQ ID NO:146)、促泌素 (SEGN_HUMAN) (SEQ ID NO:147)、血清学定义结肠癌抗原3

(SDCG3_HUMAN) (SEQ ID NO:148)、琥珀酸脱氢酶[泛醌]黄素蛋白亚基线粒体前体 (DHSA_HUMAN) (SEQ ID NO:149)、硒结合蛋白1 (SBP1_HUMAN) (SEQ ID NO:150)、P-选择蛋白糖蛋白配体1前体 (SELPL_HUMAN) (SEQ ID NO:151)、隔蛋白-9 (SEPT9_HUMAN) (SEQ ID NO:152)、 α -1抗胰蛋白酶前体 (A1AT_HUMAN) (SEQ ID NO:153)、 α -1抗胰凝乳蛋白酶前体 (AACT_HUMAN) (SEQ ID NO:154)、白细胞弹性蛋白酶抑制剂 (ILEU_HUMAN) (SEQ ID NO:155)、丝氨酸蛋白酶抑制蛋白B6 (SPB6_HUMAN) (SEQ ID NO:156)、剪接因子3B亚基3 (SF3B3_HUMAN) (SEQ ID NO:157)、S相 激酶相关蛋白1 (SKP1_HUMAN) (SEQ ID NO:158)、ADP/ATP 移位酶2 (ADT2_HUMAN) (SEQ ID NO:159)、胰分泌型胰蛋白酶抑制剂 (ISK1_HUMAN) (SEQ ID NO:160)、脊椎蛋白-2 (SPON2_HUMAN) (SEQ ID NO:161)、骨桥蛋白 (OSTP_HUMAN) (SEQ ID NO:162)、原癌基因酪氨酸蛋白激酶Src (SRC_HUMAN) (SEQ ID NO:163)、丝氨酸/苏氨酸-蛋白激酶STK11 (STK11_HUMAN) (SEQ ID NO:164)、核内不均一核糖核蛋白Q (HNRPQ_HUMAN) (SEQ ID NO:165)、T细胞急性淋巴细胞性白血病蛋白1 (TAL1_HUMAN) (SEQ ID NO:166)、血清铁传递蛋白前体 (TRFE_HUMAN) (SEQ ID NO:167)、血小板反应蛋白-1前体 (TSP1_HUMAN) (SEQ ID NO:168)、金属蛋白酶抑制剂1 (TIMP1_HUMAN) (SEQ ID NO:169)、转酮醇酶 (TKT_HUMAN) (SEQ ID NO:170)、肿瘤坏死因子诱导型基因6蛋白前体 (TSG6_HUMAN) (SEQ ID NO:171)、肿瘤坏死因子受体超家族 成员10B (TR10B_HUMAN) (SEQ ID NO:172)、肿瘤坏死因子 受体超家族成员6B (TNF6B_HUMAN) (SEQ ID NO:173)、细胞肿瘤抗原p53 (P53_HUMAN) (SEQ ID NO:174)、原肌球蛋白 β 链 (TPM2_HUMAN) (SEQ ID NO:175)、翻译控制肿瘤蛋白 (TCTP_HUMAN) (SEQ ID NO:176)、热休克蛋白75kDa线粒体前体 (TRAP1_HUMAN) (SEQ ID NO:177)、硫代硫酸硫基转移酶 (THTR_HUMAN) (SEQ ID NO:178)、微管蛋白 β -1链 (TBB1_HUMAN) (SEQ ID NO:179)、UDP-葡萄糖6-脱氢酶 (UGDH_HUMAN) (SEQ ID NO:180)、UTP-葡萄糖-1-磷酸尿苷 酰转移酶 (UGPA_HUMAN) (SEQ ID NO:181)、血管内皮生长因子A (VEGFA_HUMAN) (SEQ ID NO:182)、绒毛蛋白-1 (VILI_HUMAN) (SEQ ID NO:183)、波形蛋白 (VIME_HUMAN) (SEQ ID NO:184)、泛酰巯基乙胺酶前体 (VNN1_HUMAN) (SEQ ID NO:185)、14-3-3蛋白 ζ/δ (1433Z_HUMAN) (SEQ ID NO:186)、C-C趋化因子受体5型 (CCR5_HUMAN) (SEQ ID NO:187)或血浆 α -L-岩藻糖苷酶 (FUCO2_HUMAN) (SEQ ID NO:188)。本公开的方法预期确定上文提供的至少一种、至少两种、至少三种、至少四种、至少五种、至少六种、至少七种、至少八种、至少九种生物标志物的表达水平。该方法可包括确定上文提供的至少十种、至少十五种或至少二十种生物标志物的表达水平。

[0159] 对于本公开的所有方面,所述方法可进一步包括确定本文提供的至少两种生物标志物的表达水平。进一步预期:本公开的方法可进一步包括确定本文提供的至少三种、至少四种、至少五种、至少六种、至少七种、至少八种、至少九种生物标志物的表达水平。该方法可包括确定本文提供的至少十种、至少十五种或至少二十种生物标志物的表达水平。

[0160] 通过本公开的方法从全血清中鉴定的生物标志物包括与下列蛋白质相对应的肽/蛋白质片段或基因:SCDC26 (CD26)、CEA分子5 (CEACAM5)、CA195 (CCR5)、CA19-9、M2PK (PKM2)、TIMP1、P-选择蛋白 (SELPLG)、VEGFA、HcGB (CGB)、绒毛蛋白 (VILLIN)、TATI (SPINK1)和 α -L-岩藻糖苷酶 (FUCA2)。包括上述蛋白质或基因中的两种、三种、四种、五种、六种、七种、八种、九种、十种、十一种和全部十二种的群组。这样的群组可排除这一组内的

蛋白质或基因,或者可排除另外的蛋白质或基因,或可进一步包含另外的蛋白质。

[0161] 通过本公开的方法从全血清中鉴定的生物标志物包括与下列蛋白质相对应的肽/蛋白质片段或基因:ANXA5、GAPDH、PKM2、ANXA4、GARS、RRBP1、KRT8、SYNCRIP、S100A9、ANXA3、CAPG、HNRNPF、PPA1、NME1、PSME3、AHCY、TPT1、HSPB1 和RPSA。包括上述蛋白质或基因中的两种、三种、四种、五种、六种、七种、八种、九种、十种、十一种、十二种、十三种、十四种、十五种、十六种、十七种、十八种和所有十九种的群组。这样的群组可排除这一组内的蛋白质或基因,或者可排除另外的蛋白质或基因,或可以进一步包含另外的蛋白质。

[0162] 通过本公开的方法从全血清中鉴定的生物标志物包括与图9中鉴定的蛋白质相对应的肽/蛋白质片段或基因。包括上述蛋白质或基因中的两种、三种、四种、五种、六种、七种、八种、九种、十种、十一种、十二种及更多种的群组。这样的群组可排除这一组内的蛋白质或基因,或者可排除另外的蛋白质,或可以进一步包含另外的蛋白质。

[0163] 已知由于蛋白质可以以各种形式缔合以形成各种蛋白质复合物,因此蛋白质通常以多种不同的形式存在于样品中。这些形式可由翻译前和翻译后修饰中的任一种或两种产生。翻译前修饰形式包括等位基因变体、剪接变体和RNA编辑形式。在这样的情况下,已知基因表达产物将与人类数据库中定义的蛋白质呈现各种同源性。因此,本公开认识到,可以存在所定义的生物标志物的各种形式。例如,所述序列同源性选自大于75%、大于80%、大于85%、大于90%、大于95%以及大于99%。此外,可以存在生物标志物的翻译后修饰形式。翻译后修饰形式包括但不限于由蛋白质生物标志物的蛋白水解裂解(例如,亲本蛋白质的片段)、糖基化、磷酸化、脂化、氧化、甲基化、半胱氨酰化(cystinylation)、磺化和乙酰化产生的形式。

[0164] 本公开的生物标志物包括全长蛋白质、它们相应的RNA或DNA及所有的修饰形式。该生物标志物的修饰形式包括,例如所公开的生物标志物和它们相应的编码它们的RNA或DNA的任何剪接变体。在某些情况下,蛋白质或它们相应的RNA或DNA的修饰形式或截短形式可在诊断上表现出比全长蛋白质更好的鉴别能力。

[0165] 蛋白质、多肽或肽的截短形式或片段通常是指所述蛋白质、多肽或肽的N-末端和/或C-末端缺失或截短形式。该术语涵盖通过任何机制,诸如但不限于,通过所述肽、多肽或蛋白质例如在体内或体外的选择性翻译、外切和/或内切蛋白水解和/或降解(例如,通过物理、化学和/或酶促蛋白水解)产生的片段。非限制性地,蛋白质、多肽或肽的截短形式或片段可以代表所述蛋白质、多肽或肽的至少约5%或至少约10%(例如>20%、>30%或>40%,如>50%,例如>60%、>70%或>80%或甚至90%或>95%)的氨基酸序列。

[0166] 非限制性地,蛋白质的截短形式或片段可包含相应全长蛋白质的5个连续氨基酸或10个连续氨基酸或20个连续氨基酸或30个连续氨基酸或多于50个连续氨基酸,例如60、70、80、90、100、200、300、400、500或600个连续氨基酸的序列。

[0167] 在一些情况下,与相应成熟的全长蛋白质或其可溶性或血浆循环形式相比,片段可以是N末端和/或C末端截短1至约20个氨基酸,如1至约15个氨基酸或者1至约10个氨基酸或者1至约5个氨基酸。

[0168] 本公开的任何蛋白质生物标志物如肽、多肽或蛋白质及其片段也可涵盖所述标志物、肽、多肽或蛋白质和片段的修饰形式,如具有表达后修饰,包括但不限于,诸如磷酸化、糖基化、脂化、甲基化、半胱氨酰化、磺化、谷胱甘肽化、乙酰化、甲硫氨酸氧化成甲硫氨

酸 亚砷或甲硫氨酸砷等修饰。

[0169] 在一些情况下,给定蛋白质、多肽或肽的片段可通过所述蛋白质、多肽或肽的体外蛋白水解来实现,以从样品获得可有利地检测的肽。例如,这样的蛋白水解可通过合适的物理、化学和/或酶试剂,例如蛋白酶、优选内切蛋白酶(即,在蛋白质、多肽或肽链内进行内部切割的蛋白酶)来实现。

[0170] 内切蛋白酶的合适的非限制性实例包括但不限于,丝氨酸蛋白酶(EC 3.4.21)、苏氨酸蛋白酶(EC 3.4.25)、半胱氨酸蛋白酶(EC 3.4.22)、天冬氨酸蛋白酶(EC 3.4.23)、金属蛋白酶(EC 3.4.24)和谷氨酸蛋白酶。示例性的非限制性内切蛋白酶包括胰蛋白酶、糜蛋白酶、弹性蛋白酶、产酶溶杆菌内切蛋白酶Lys-C、金黄色葡萄球菌内切蛋白酶Glu-C(肽链内切酶V8)或溶组织梭菌内切蛋白酶Arg-C(梭菌蛋白酶)。

[0171] 优选地,所述蛋白水解可通过胰蛋白酶型的肽链内切酶(EC 3.4.21.4),优选胰蛋白酶,诸如但不限于,来自牛胰脏、人胰脏、猪胰脏的胰蛋白酶、重组胰蛋白酶、Lys-乙酰化的胰蛋白酶、溶液中的胰蛋白酶、固定于固体支持物的胰蛋白酶等的制剂来实现。胰蛋白酶尤其因裂解的高特异性和高效性而特别有用。本公开还提供了任何胰蛋白酶样蛋白酶(即具有与胰蛋白酶的特异性相似的特异性)的使用。另外,化学试剂可用于蛋白水解。仅举例而言,CNBr可在Met处裂解;BNPS-粪臭素可以在Trp处裂解。用于处理的条件,例如蛋白质浓度、酶或化学试剂浓度、pH、缓冲液、温度、时间,可由技术人员根据所用酶或化学试剂来确定。其他已知的或尚未鉴定的酶可基于它们的裂解特异性和频率在本公开中使用,以获得期望的肽形式。

[0172] 在一些情况下,片段化的蛋白质或肽可以是N-末端和/或C-末端截短的,且为N-末端(a、b、c-离子)和/或C-末端(x、y、z-离子)截短的蛋白质或肽的一个或全部过渡离子。例如,如果肽片段由氨基酸序列IAELLSPGSVDPLTR组成,则该肽片段的过渡离子生物标志物可包括表1中提供的下列过渡离子生物标志物中的一种或多种。

[0173] 表1:肽序列IAELLSPGSVDPLTR的所有过渡离子的实例

过渡离子	氨基酸序列
b1	I
b2	IA
b3	IAE
b4	IAEL
b5	IAELL
b6	IAELLS
b7	IAELLSP
b8	IAELLSPG
b9	IAELLSPGS
b10	IAELLSPGSV
b11	IAELLSPGSVD
b12	IAELLSPGSVDP

b13	IAELLSPGSVDPL
b14	IAELLSPGSVDPLT
y14	AELLSPGSVDPLTR
y13	ELLSPGSVDPLTR
y12	LLSPGSVDPLTR
y11	LSPGSVDPLTR
y10	SPGSVDPLTR
y9	PGSVDPLTR
y8	GSVDPLTR
y7	SVDPLTR
y6	VDPLTR
y5	DPLTR
y4	PLTR
y3	LTR
y2	TR
y1	R

[0174] 本公开的生物标志物包括SCDC26 (CD26)、CEA分子5 (CEACAM5)、CA195 (CCR5)、CA19-9、M2PK (PKM2)、TIMP1、P-选择蛋白 (SELPLG)、VEGFA、HcGB (CGB)、绒毛蛋白、TATI (SPINK1) 和A-L-岩藻糖苷酶 (FUCA2) 的结合配偶体。包括上述蛋白质中的两种、三种、四种、五种、六种、七种、八种、九种、十种、十一种和所有十二种的群组。这样的群组可排除这一组内的蛋白质,或可排除另外的蛋白质,或可以进一步包含另外的蛋白质。

[0175] 本公开的生物标志物包括ANXA5、GAPDH、PKM2、ANXA4、GARS、RRBP1、KRT8、SYNCRIP、S100A9、ANXA3、CAPG、HNRNPF、PPA1、NME1、PSME3、AHCY、TPT1、HSPB1和RPSA的结合配偶体。包括上述蛋白质中的两种、三种、四种、五种、六种、七种、八种、九种、十种、十一种、十二种、十三种、十四种、十五种、十六种、十七种、十八种和所有十九种的群组。这样的群组可排除这一组内的蛋白质,或可排除另外的蛋白质,或可以进一步包含另外的蛋白质。

[0176] 如本文所教导的示例性的人标志物、核酸、蛋白质或多肽可以如NCBI Genbank (<http://www.ncbi.nlm.nih.gov/>) 或Swissprot/Uniprot (<http://www.uniprot.org/>) 登录号下所注释的。在一些情况下,所述序列可以是如本文所教导的标志物、核酸、蛋白质或多肽的前体(例如,前蛋白质)的序列,并且可包含从成熟分子加工除去的部分。在一些情况下,虽然可能仅公开一个或多个同种型,但旨在涵盖该序列的所有同种型。

[0177] 本公开的生物标志物包括图9中鉴定的蛋白质的结合配偶体。包括上述蛋白质中的两种、三种、四种、五种、六种、七种、八种、九种、十种、十一种、十二种和更多种的群组。这样的群组可排除这一组内的蛋白质,或可排除另外的蛋白质,或可进一步包含另外的蛋白质。

[0178] 上述鉴定的生物标志物是如根据分子量和部分序列确定的,通过本公开的方法鉴定的生物标志物的实例,并且仅作为说明性实例且并不意在以任何方式限制本公开。可用于检测一种或多种生物标志物或修饰的生物标志物的合适的方法在本文中进行了描述。在某一方面,本公开提供了对生物样品进行关于存在选自代谢物、DNA序列、RNA序列及其组合的一种或多种分析物的附加生物标志物的分析。本文所列出的生物标志物可进一步与其他信息,如遗传分析,例如受试者的全基因组DNA或RNA测序进行组合。

[0179] 本公开的所有方面也可采用有限数目的公开的生物标志物、它们的结合配偶体、剪接变体和相应的DNA和RNA来实施。

[0180] 除了相应的DNA和RNA外,在本公开提供的生物标志物的DNA和RNA内发现的变异也可提供用于区分个体的临床状态的手段。可在本公开的方法中使用的此类DNA和RNA遗传变异标志物的实例包括但不限于限制性片段长度多态性、单核苷酸DNA多态性、单核苷酸cDNA多态性、单核苷酸RNA多态性、单核苷酸RNA多态性、插入、缺失、插入缺失(indel)、微卫星重复(简单序列重复)、小卫星重复(可变数目的串联重复)、短串联重复、转座因子、随机扩增多态性DNA和扩增片段长度多态性。

[0181] 生物标志物谱

[0182] 本公开的方法还提供了将要生成并用于商业医疗诊断产品或试剂盒的生物标志物谱。

[0183] 所述方法提供了将要以多种方式确定的并且可以是使用诸如比例或其他更复杂的关联方法或算法(例如,基于规则的方法)的方法确定的可测量生物标志物或生物标志物的多个方面的组合的生物标志物谱。生物标志物谱可包含至少两个测量值,其中该测量值可对应于相同或不同的生物标志物。生物标志物谱还可包含至少3、4、5、10、15、20、25、30、35、40、45、50、55个或更多个测量值。在一些应用中,生物标志物谱包含数百个或甚至数千个测量值。生物标志物谱可包含仅来自个体或包含来自个体的测量值以及来自已知与个体相关的分层群体或已知与个体无关的分层群体或两者的测量值。

[0184] 此外,生物标志物谱还提供了本文提供的可各自独立地且独立地评估的生物标志物的存在与否或量,或者此类其他生物标志物的存在与否和/或量可包含在本文公开的方法中建立的受试者谱或参考谱内。

V. 生物标志物的应用

[0185] 通常,所述方法至少包括以下步骤:(a)获得生物样品,(b)进行生物样品分析,(c)将该样品与参照对照进行比较,以及(d)将蛋白质的存在或量与受试者的结肠息肉状态相关联。在本公开的一些方面,定量包括将测量值相对于已知处在恒定水平的内标对照进行归一化。在本公开的其他方面,定量包括与来自健康非患病无肿瘤的受试者的参考对照进行比较并确定差异表达。在本公开的其他方面,定量包括与来自患有肿瘤的患病受试者的参考对照进行比较并确定差异表达。从该方法获得的数据可用于创建“谱”,该谱用于预测疾病状态、复发或对治疗的反应。一旦创建了谱,则可将试验结果与标准谱进行比

较,并可得到与反应的相关性。应当理解,通常对描述的谱 进行优化。本公开并不限于这种特定的生物标志物谱的使用。提供有 用信息的一种或多种标志物的任何组合可在本公开的方法中使用。例如,应当理解,可以加入或从签名中减去一种或多种标志物,同时保持该签名产生有用信息的能力。

[0186] 在本公开的一个方面,所有或一些生物标志物或生物标志物的 组合的定量可用于检测受试者中存在结肠息肉的可能性。在本公开的 另一方面,所有或一些生物标志物或生物标志物的组合可用于通过鉴定受试者样品的一种或多种性质来检测结肠肿瘤的性质,包括但不限于,良性的存在、息肉的类型、癌变前的阶段、发育异常的程度、亚 型腺瘤性息肉或良性结肠肿瘤疾病的亚型以及预后。在本公开的一个 方面,所有或一些生物标志物或生物标志物的组合可用于检测患上结 肠肿瘤或息肉的可能性。在本公开的一个方面,所有或一些生物标志物或生物标志物的组合可用于排除结肠肿瘤或息肉的存在,即确定受 试者不存在结肠息肉、癌或两者均不存在。在本公开的另一方面,所 有或一些生物标志物或生物标志物的组合可用于确定肿瘤的性质,即, 它是否是良性肿瘤息肉、恶性肿瘤、腺瘤性息肉、有蒂息肉或无蒂息 肉型。

[0187] 在本公开的一个方面,所有或一些生物标志物或生物标志物的 组合可用于生成报告,该报告有助于结肠直肠癌或结肠肿瘤的临床管 理的下一步骤。在本公开的一个方面,所有或一些生物标志物或生物 标志物的组合可用于监测对结肠直肠癌或结肠肿瘤的各种治疗的反 应性。在本公开的一个方面,所有或一些生物标志物或生物标志物的 组合可用于监测具有患结肠直肠癌或结肠肿瘤的倾向的受试者。在本 公开的一个方面,所有或一些生物标志物或生物标志物的组合可用于 监测受试者的结肠直肠癌或结肠肿瘤的复发。在本公开的一个方面, 所有或一些生物标志物或生物标志物的组合可用于监测受试者的结 肠直肠癌或息肉的复发。

[0188] 在一些实施方案中,所述方法包括鉴定来自受试者的生物样品 的细胞中的生物标志物的谱,其中所述模式与疾病或状况或反应的可 能性相关联。

[0189] 在该方法的一些方面,通过由例如定量免疫荧光或基于ELISA 的测定法、流式细胞术或本文提供的其他免疫测定来对蛋白质表达水 平进行定量来检测一种或多种生物标志物或生物标志物谱。在该方法 的一些方面,通过例如使用特异性扩增与DNA或RNA相对应的生物 标志物的引物组的实时PCR对多核苷酸的表达水平进行定量来检测 生物标志物谱。在本公开的另一方面,该谱由包含生物标志物的捕获 特征(例如,抗体、探针等)的生物芯片来检测。生物芯片可根据生 物样品中或来自受试者的多核苷酸例如mRNA的表达水平或者通过 使用例如抗体检测患者样品中的蛋白质的表达水平来检测生物标志 物谱的存在。在另一些实施方案中,通过使用引物组的实时PCR来 检测肿瘤细胞谱,该引物组特异性地扩增包含癌干细胞签名的基因。在本公开的其他实施方案中,提供了包含多核苷酸或蛋白质(即抗体) 的微阵列,该多核苷酸或蛋白质(即抗体)检测癌干细胞签名的表达 以用于预后。

[0190] 可将生物样品的生物标志物谱与参考谱进行比较并可确定结果。在本公开的一个方面,将从本文所述的试验产生的数据与由谱模型定 义的参考谱进行比较,该谱模型由一个或多个生物样品的测量值得到。可以将试验安排为使得单个患者样品可与考虑到的 这些群体一起查 看并被分配给一个群体或其他群体或者两者的混合,并随后使用这种 与

患者管理、疗法、预后等的相关性。

[0191] 在本公开的一个方面,从本文所述的方法和试剂盒检测产生的数据与可视化手段一起使用,该可视化手段能够指示样品中的所述一种或多种标志物或片段的量是否在某个阈值水平以上或以下,或者样品中的所述一种或多种标志物或片段的量是否偏离或不偏离所述一种或多种标志物或片段的量的参考值,所述参考值表示如本文所教导的疾病或状况的已知诊断、预测或预后。

[0192] 在本公开的一个方面,选择从本文所述的方法或试剂盒检测产生的确定为阈值水平的数据,使得样品中的所述一种或多种标志物和/或片段的量在所述阈值水平以上或以下(取决于标志物以及疾病或状况)指示受试者患有相应的疾病或状况或处于患有相应的疾病或状况的风险下,或者指示受试者的相应的疾病或状况的不良预后,以及样品中的所述一种或多种标志物和/或片段的量在所述阈值水平以下或以上(取决于标志物以及疾病或状况)指示受试者不患有如本文所教导的疾病或状况或不处于患有该疾病或状况的风险下,或者指示受试者的该疾病或状况的良好预后。

[0193] 在本公开的一个方面,从本文所述的方法和试剂盒检测产生的确定样品中的核酸分子或分析物的相对量的数据可有利地表示为相对于所述另一个值,诸如相对于如本文教导的参考值、权重或等级的增加或减少,或表示为倍数增加或倍数减少。在第一和第二参数(例如,第一和第二量)间进行相对比较可以但不是必然需要首先确定所述第一和第二参数的绝对值。例如,测量方法可以产生所述第一和第二参数的可量化读数(例如,信号强度),其中所述读数是所述参数的值的函数,并且其中可以直接比较所述读数,以产生第一参数相对于第二参数的相对值,而实际上无需首先将读数转化为相应参数的绝对值。

A. 灵敏度和特异性

[0194] 灵敏度和特异性是二元分类试验的性能的统计度量。完美的分类预测指标(predictor)被描述为100%灵敏(即,将来自患病组的所 有人预测为患病)和100%特异(即,不将来自健康组的任何人预测 为患病);然而,理论上任何分类预测指标将具有最小误差。(Altman DG, Bland JM (1994). "Diagnostic tests Sensitivity and Specificity". BMJ 308 (6943):1552和Loong T (2003). "Understanding sensitivity and specificity with the right side of the brain". BMJ 327 (7417):716-719)。

[0195] 在本公开方法的一个方面,使用全部或一些生物标志物或生物标志物的组合针对受试者的腺瘤或息肉状态实现了选自大于60%真阳性、70%真阳性、75%真阳性、85%真阳性、90%真阳性、95%真阳性或99%真阳性的灵敏度。在本公开方法的一个方面,使用全部或一些生物标志物或生物标志物的组合针对受试者的腺瘤、癌症或息肉状态实现了选自大于60%真阴性、70%真阴性、75%真阴性、85%真阴性、90%真阴性、95%真阴性或99%真阴性的特异性。在本公开方法的一个方面,使用全部或一些生物标志物或生物标志物的组合排除了 或没有确定结肠直肠癌的存在与否。在本公开方法的一个方面,通过附加试验如结肠镜检查、其他成像方法或诊断试验或手术来确认腺瘤、癌症或息肉状态的存在与否。在本公开方法的一个方面,使用全部或一些生物标志物或生物标志物的组合针对受试者的腺瘤、癌症或息肉状态实现了选自大于70%真阳性和小于30%真阴性、75%真阳性和小于25%真阴性、85%真阳性和小于15%真阴性、90%真阳性和小于10%真阴性、

95%真阳性和小于5%真阴性、或99%真阳性和小于1%真阴性的灵敏度和特异性。

[0196] 在本公开方法的一个方面,使用全部或一些生物标志物或生物标志物的组合针对受试者的结肠直肠癌的存在与否实现了选自大于70%真阳性、75%真阳性、85%真阳性、90%真阳性、95%真阳性或99%真阳性的灵敏度。在本公开方法的一个方面,使用全部或一些生物标志物或生物标志物的组合针对受试者的结肠直肠癌的存在与否实现了选自大于70%真阴性、75%真阴性、85%真阴性、90%真阴性、95%真阴性或99%真阴性的特异性。在本公开方法的一个方面,不检测结肠直肠癌的存在与否。在本公开方法的一个方面,通过附加试验如结肠镜检查、其他成像方法或诊断试验或手术来确认结肠直肠癌的存在与否。在本公开方法的一个方面,使用全部或一些生物标志物或生物标志物的组合针对受试者的结肠直肠癌的存在与否实现了选自大于70%真阳性和小于30%真阴性、75%真阳性和小于25%真阴性、85%真阳性和小于15%真阴性、90%真阳性和小于10%真阴性、95%真阳性和小于5%真阴性、或99%真阳性和小于1%真阴性的灵敏度和特异性。

[0197] 在本公开方法的一个方面,使用全部或一些生物标志物或生物标志物的组合针对受试者的腺瘤性息肉或息肉样腺瘤的存在与否实现了选自大于70%真阳性、75%真阳性、85%真阳性、90%真阳性、95%真阳性或99%真阳性的灵敏度。在本公开方法的一个方面,使用全部或一些生物标志物或生物标志物的组合针对受试者的腺瘤性息肉或息肉样腺瘤的存在与否实现了选自大于70%真阴性、75%真阴性、85%真阴性、90%真阴性、95%真阴性或99%真阴性的特异性。在本公开方法的一个方面,通过附加试验如结肠镜检查、其他成像方法或诊断试验或手术来确认腺瘤性息肉或息肉样腺瘤。在本公开方法的一个方面,使用全部或一些生物标志物或生物标志物的组合针对受试者的腺瘤性息肉或息肉样腺瘤的存在与否实现了选自大于70%真阳性和小于30%真阴性、75%真阳性和小于25%真阴性、85%真阳性和小于15%真阴性、90%真阳性和小于10%真阴性、95%真阳性和小于5%真阴性、或99%真阳性和小于1%真阴性的灵敏度和特异性。

[0198] 在本公开方法的一个方面,使用全部或一些生物标志物或生物标志物的组合针对受试者的有蒂息肉和无蒂息肉的存在与否实现了选自大于70%真阳性、75%真阳性、85%真阳性、90%真阳性、95%真阳性或99%真阳性的灵敏度。在本公开方法的一个方面,使用全部或一些生物标志物或生物标志物的组合针对受试者的有蒂息肉和无蒂息肉的存在与否实现了选自大于70%真阴性、75%真阴性、85%真阴性、90%真阴性、95%真阴性或99%真阴性的特异性。在本公开方法的一个方面,通过附加试验如结肠镜检查、其他成像方法或诊断试验或手术来确认有蒂息肉和无蒂息肉的存在与否。在本公开方法的一个方面,使用全部或一些生物标志物或生物标志物的组合针对受试者的有蒂息肉和无蒂息肉的存在与否实现了选自大于70%真阳性和小于30%真阴性、75%真阳性和小于25%真阴性、85%真阳性和小于15%真阴性、90%真阳性和小于10%真阴性、95%真阳性和小于5%真阴性、或99%真阳性和小于1%真阴性的灵敏度和特异性。

[0199] 在本公开方法的一个方面,使用全部或一些生物标志物或生物标志物的组合针对根据细胞发育异常或恶变前的程度表征的受试者的腺瘤性息肉或息肉样腺瘤实现了选自大于70%真阳性、75%真阳性、85%真阳性、90%真阳性、95%真阳性或99%真阳性的灵敏度。在本公开方法的一个方面,使用全部或一些生物标志物或生物标志物的组合针对根据细胞发育异常或恶变前的程度表征的受试者的腺瘤性息肉或息肉样腺瘤实现了选自

大于70%真阴性、75%真阴性、85%真阴性、90%真阴性、95%真阴性或99%真阴性的特异性。在本公开方法的一个方面,通过附加试验如结肠镜检查、其他成像方法或诊断试验或手术来确认根据细胞发育异常或恶变前的程度表征的腺瘤性息肉或息肉样腺瘤。在本公开方法的一个方面,使用全部或一些生物标志物或生物标志物的组合针对根据细胞发育异常或恶变前的程度表征的受试者的腺瘤性息肉或息肉样腺瘤实现了选自大于70%真阳性和小于30%真阴性、75%真阳性和小于25%真阴性、85%真阳性和小于15%真阴性、90%真阳性和小于10%真阴性、95%真阳性和小于5%真阴性、或99%真阳性和小于1%真阴性的灵敏度和特异性。

VI. 系统

[0200] 本公开的系统和方法基于和/或通过使用一个或多个计算机处理器系统而设计。本公开的计算机系统的实例在下文进行了描述。所述计算机系统的变化形式是可能的,只要它们提供用于本公开的系统和方法的平台。

[0201] 本公开的计算机系统的一个实例显示于图13中。图13中显示的计算机系统1300可被理解为可从介质1311和/或网络端口1305读取指令的逻辑装置,该介质1311和/或网络端口1305可任选地连接到具有固定介质1312的服务器1309。如在图13中所示的系统可包含CPU 1301、磁盘驱动器1303、任选的输入设备(如键盘1315和/或鼠标1316)以及任选的监视器1307。数据通信可通过通往在本地或远程位置的服务器的指定通信介质来实现。通信介质可包括传送和/或接收数据的任何手段。例如,通信介质可以是网络连接、无线连接或因特网连接。这样的连接可提供在万维网上的通信。可以预想到,与本公开相关的数据可以通过这样的网络或连接进行传送,以便由如图13显示的主体1322接收和/或审查。

[0202] 图14为显示了可以与本公开的示例性实施方案结合使用的计算机系统1400的示例性架构的框图。如图14中所示,该示例性的计算机系统可以包括用于处理指令的处理器1402。处理器的非限制性实例包括: Intel Xeon™处理器、AMD Opteron™处理器、Samsung 32-bit RISC ARM 1176JZ(F)-S v1.0™处理器、ARM Cortex-A8 Samsung S5PC100™处理器、ARM Cortex-A8 Apple A4™处理器、Marvell PXA 930™处理器或功能上等同的处理器。多个执行线程可用于并行处理。在本公开的一些方面,也可使用多个处理器或具有多个核的处理器,无论是在单个计算机系统中,在集群中,还是通过包括多个计算机、蜂窝电话和/或个人数据助理设备的网络分布在整个系统上。

[0203] 如图14中所示,高速缓冲存储器1404可以连接到或并入处理器1402以提供处理器1402最近或频繁使用的指令或数据的高速存储器。处理器1402通过处理器总线1408连接到北桥1406。北桥1406通过存储器总线1412连接到随机存取存储器(RAM) 1410,并管理处理器1402对RAM 1410的访问。北桥1406还通过芯片组总线1416连接到南桥1414。南桥1414又连接到外围总线1418。该外围总线可以是,例如,PCI、PCI-X、PCI Express或其他外围总线。北桥和南桥通常称作处理器芯片组,并管理处理器、RAM以及外围总线1418上的外围组件之间的数据传输。在一些可替代的架构中,北桥的功能可并入处理器中而不是使用单独的北桥芯片。在本公开的一些方面,系统100可以包括连接到外围总线1418的加速器卡1422。该加速器可以包括现场可编程门阵列(FPGA)或用于加速某种处理的其他硬件。例如,加速器可以用于自适应数据重组或用于评估在扩展集处理中使用的代数表达式。

[0204] 软件和数据存储在外部存储1424中并且可以加载到RAM 1410 和/或缓存1404中,以供处理器使用。系统1400包括用于管理系统资源的操作系统;操作系统的非限制性实例包括:Linux、Windows™、MACOS™、BlackBerry OS™、iOS™和其他功能等同的操作系统,以及在操作系统的顶端上运行的用于管理数据存储并根据本公开的 示例性实施方案进行优化的应用软件。

[0205] 在这个实例中,系统1400还包括连接至外围总线的网络接口卡 (NIC) 1420和1421,以用于向外部存储如网络附加存储 (NAS) 和 可用于分布式并行处理的其他计算机系统提供网络接口。

[0206] 图15为示出了具有多个计算机系统1502a和1502b、多个蜂窝 电话和个人数字助理1502c以及网络附加存储 (NAS) 1504a和1504b 的网络1500的示意图。在示例性的实施方案中,系统1502a、1502b 和1502c可以管理数据存储并优化存储在网络附加存储 (NAS) 1504a 和1504b中的数据的数据存取。数学模型可用于该数据并使用跨计算 机系统1502a和1502b以及蜂窝电话和个人数字助理系统1502c的分 布式并行处理进行评价。计算机系统1502a和1502b以及蜂窝电话和 个人数字助理系统1502c也可提供用于存储在网络附加存储 (NAS) 1504a和1504b中的数据的自适应数据重组的并行处理。很多种其他 计算机构架和系统可与本公开的各个实施方案结合使用。例如,刀片 式服务器可用于提供并行处理。处理器刀片可以通过底板连接,以提 供并行处理。存储也可通过单独的网络接口连接到底板或作为网络附 加存储 (NAS)。

[0207] 在一些示例性实施方案中,处理器可以保持独立的存储器空间, 并通过网络接口、底板或用于其他处理器进行并行处理的其他连接器 传送数据。在其他实施方案中,一些或所有处理器可使用共享的虚拟 地址存储空间。

[0208] 图16为根据示例性实施方案的使用共享的虚拟地址存储空间 的多处理器计算机系统1600的框图。该系统包括可访问共享的存储 器子系统1604的多个处理器1602a-f。该系统在存储器子系统1604 中并入多个可编程硬件存储算法处理器 (MAP) 1606a-f。每个MAP 1606a-f可包含存储器1608a-f以及一个或多个现场可编程门阵列 (FPGA) 1610a-f。该MAP 提供可配置功能单元,并且特定算法或算 法的一部分可提供给FPGA 1610a-f以用于密切配合相应的处理器进 行处理。例如,该MAP可用于评估关于数据模型的代数表达式并用 于进行示例性实施方案中的自适应数据重组。在该实例中,每个MAP 可由所有处理器进行全局访问以用于这些目的。在一种配置中,每个 MAP可以使用直接存储器存取 (DMA) 来访问相关联的存储器 1608a-f,从而允许它独立于相应的微处理器1602a-f且与相应的微处 理器 1602a-f异步地执行任务。在该配置中,MAP可将结果直接馈送 至另一个MAP,以用于算法的流水线和并行执行。本公开预想计算 机可读存储介质,例如CD-ROM、存储键、闪存卡、软磁 盘或其上存 储有程序的其他有形介质,其在计算环境中执行时,执行自定义算法 以实现如本公开方法所述的所提供的生物样品的预测可能性或评估 的全部或部分结果。在各个实施方案中,该计算机可读存储介质是非 暂时性的。

[0209] 本公开的系统和方法整合了一个或多个实验室设备。

[0210] 在一些实施方案中,该整合在实验室信息管理系统 (LIMS) 或 更低的水平下进行。计算机系统可以运行多个实验室设备。用于实验 室应用的软件和硬件可使用本公开的方法和系统进行整合。在各个实 施方案中,具有共有功能的相似组件在多个实验室设备中重

复使用。

[0211] 计算机系统可控制各个设备中的多个组件,从而创建可用组件 的新的组合。在另一实例中,本公开的计算机系统可通过控制该实验室设备内的泵、传感器或其他组件来控制质谱法、板处理法、液相色谱法。软件可由包括独立的实验室最终用户或任何其他合适的用户在 内的任何人提供。LIMS在整合实验室系统中的使用进一步描述于美国专利申请 7,991,560中,该专利申请通过引用以其整体并入本文。

[0212] 在其中试剂盒提供计算机可读介质的方案中,它将包含用于执行本公开的方法的完整程序。该程序包含用于收集、分析并生成输出的程序指令,并且通常包含用于与本文所述的用户交互、处理该数据 以及分析信息并生成针对该用户独特的印刷或电子介质的计算机可读代码和设备。

[0213] 在其他方面,所述试剂盒提供了仅运行本公开方法的一部分的 有限的计算机可读介质。在这方面,该试剂盒提供了这样的程序,该 程序提供来自用户的数据输入并用于将用户输入(例如,经由因特网, 经由内部网等)的数据传送至在远程地点的计算环境如服务器(在其 上将进行本公开的自定义数学算法)。由用户提供的数据处理的处理 或完成在远程地点进行,并且该服务器也将用来生成报告。在审查报 告并完成提供完整报告所需的任何人工干预后,将完整的报告作为电 子报告或打印的报告传送回用户。

[0214] 根据本公开的包含程序的存储介质可与用于程序安装和使用的 说明或可以从中获得这样的说明的网址一起包装。

VII. 报告

[0215] 当本公开的方法用于商业诊断目的,例如用于医疗领域中时, 通常将生成从该方法获得的信息的报告或汇总。

[0216] 该方法的报告或汇总可包含关于一种或多种基因或蛋白质的表 达水平、息肉或肿瘤的分类、患者的风险水平(如高、中或低)、患 者的预后、治疗选择、治疗建议、生物标志物表达以及如何确定生物 标志物水平、生物标志物谱、临床和病理因素的信息和/或与患者疾病 状态相关的患者或群组的其他标准临床信息。

[0217] 所述方法和报告可存储在数据库中。该方法可以在数据库中创 建受试者的记录并将数据填入该记录。该报告可以是纸质报告、音频 报告或电子记录。该报告可以显示和/或存储在计算设备(例如,手持 设备、台式计算机、智能设备、网站等)上。可以预期,报告将提供 给医师和/或患者。报告的接收可进一步包括建立与包含所述数据和报 告的服务器计算机的网络连接,并从该服务器计算机请求该数据和报 告。

[0218] 在另一方面,本公开提供了生成包含关于从受试者获得的生物 样品的生物标志物信息的报告的方法,该方法包括以下步骤:确定样 品中以下一种或多种生物标志物或其结合配偶体之一的生物标志物 谱表达水平:SCDC26 (CD26)、CEA分子5 (CEACAM5)、CA195 (CCR5)、CA19-9、M2PK (PKM2)、TIMP1、P-选择蛋白 (SELPLG)、VEGFA、HcGB (CGB)、绒毛蛋白、TATI (SPINK1)、A-L-岩藻糖苷 酶 (FUCA2)、ANXA5、GAPDH、PKM2、ANXA4、GARS、RRBP1、KRT8、SYNCRIP、S100A9、ANXA3、CAPG、HNRNPF、PPA1、NME1、PSME3、AHCY、TPT1、HSPB1和RPSA和/或图9中的蛋 白质或它们的修饰形式,并创建汇总它们的表达水平的报告。在一些 方面,该报告可进一步包含将受试者分类成风险组,诸如“低风险”、“中等风险”或“高风险”的分 类。在各个实施方案中,包括上述蛋白质 中的两种、三种、四种、五种、六种、七种、八种、九

种、十种、十一种和全部十二种的群组。这样的群组可排除另外的蛋白质,或可以进一步包含另外的蛋白质。

[0219] 在所述方法的一个方面,如果确定了以下一种或多种生物标志物或其结合配偶体之一的表达增加:SCDC26 (CD26)、CEA分子5 (CEACAM5)、CA195 (CCR5)、CA19-9、M2PK (PKM2)、TIMP1、P-选择蛋白 (SELPLG)、VEGFA、HcGB (CGB)、绒毛蛋白、TATI (SPINK1)、A-L-岩藻糖苷酶 (FUCA2)、ANXA5、GAPDH、PKM2、ANXA4、GARS、RRBP1、KRT8、SYNCRIP、S100A9、ANXA3、CAPG、HNRNPF、PPA1、NME1、PSME3、AHCY、TPT1、HSPB1和RPSA和/或图9中的蛋白质或它们的修饰形式,则所述报告包含关于所述受试者具有患有结肠息肉的增加了的可能性的预测。在各个实施方案中,包括上述蛋白质中的两种、三种、四种、五种、六种、七种、八种、九种、十种、十一种和全部十二种的群组。这样的群组可排除另外的蛋白质,或可以进一步包含另外的蛋白质。

[0220] 在所述方法的另一方面,如果确定了以下一种或多种生物标志物或其结合配偶体之一的表达增加:SCDC26 (CD26)、CEA分子5 (CEACAM5)、CA195 (CCR5)、CA19-9、M2PK (PKM2)、TIMP1、P-选择蛋白 (SELPLG)、VEGFA、HcGB (CGB)、绒毛蛋白、TATI (SPINK1)、A-L-岩藻糖苷酶 (FUCA2)、ANXA5、GAPDH、PKM2、ANXA4、GARS、RRBP1、KRT8、SYNCRIP、S100A9、ANXA3、CAPG、HNRNPF、PPA1、NME1、PSME3、AHCY、TPT1、HSPB1和RPSA和/或图9中的蛋白质或它们的修饰形式,则所述报告包含关于所述受试者具有患有结肠息肉的降低的可能性的预测。在各个实施方案中,包括上述蛋白质中的两种、三种、四种、五种、六种、七种、八种、九种、十种、十一种和全部十二种的群组。这样的群组可排除另外的蛋白质,或可以进一步包含另外的蛋白质。

[0221] 在一个方面,该报告包括支持针对所述患者的治疗建议的信息。例如,该信息可以包括定制诊断试验、结肠镜检查、手术、治疗性治疗中的一个或多个以及不采取进一步的医疗行动的建议,此类治疗的有益得分的可能性,或其他此类数据。在一些实施方案中,该报告进一步包括对所述患者的治疗方式的建议。

[0222] 在本公开的一个方面,所述报告是纸质形式。在本公开的一个方面,所述报告是电子形式,如CD-ROM、闪存驱动器、本领域中已知的其他电子存储设备。在本公开的另一方面,电子报告从有线或无线网络下载到第二计算机设备,如膝上型计算机、移动电话或平板电脑上。

[0223] 在一个方面,所述报告指示,如果确定了以下一种或多种生物标志物或其结合配偶体之一的表达增加:SCDC26 (CD26)、CEA分子5 (CEACAM5)、CA195 (CCR5)、CA19-9、M2PK (PKM2)、TIMP1、P-选择蛋白 (SELPLG)、VEGFA、HcGB (CGB)、绒毛蛋白、TATI (SPINK1)、A-L-岩藻糖苷酶 (FUCA2)、ANXA5、GAPDH、PKM2、ANXA4、GARS、RRBP1、KRT8、SYNCRIP、S100A9、ANXA3、CAPG、HNRNPF、PPA1、NME1、PSME3、AHCY、TPT1、HSPB1和RPSA和/或图9中的蛋白质或它们的修饰形式,则所述报告包含关于所述受试者在5-10年具有结肠息肉或肿瘤复发的增加了的可能性的预测。在各个实施方案中,包括上述蛋白质中的两种、三种、四种、五种、六种、七种、八种、九种、十种、十一种和全部十二种的群组。这样的群组可排除另外的蛋白质,或可以进一步包含另外的蛋白质。

[0224] 在另一方面,所述报告指示,如果确定了以下一种或多种生物标志物或其结合配偶体之一的表达增加:SCDC26 (CD26)、CEA分子5 (CEACAM5)、CA195 (CCR5)、CA19-9、M2PK

(PKM2)、TIMP1、P-选择蛋白 (SELPLG)、VEGFA、HcGB (CGB)、绒毛蛋白、TATI (SPINK1)、A-L-岩藻糖苷酶 (FUCA2)、ANXA5、GAPDH、PKM2、ANXA4、GARS、RRBP1、KRT8、SYNCRIP、S100A9、ANXA3、CAPG、HNRNPF、PPA1、NME1、PSME3、AHCY、TPT1、HSPB1 和RPSA和/或图9中的蛋白质或它们的修饰形式,则所述报告包含关于所述受试者在5-10年具有结肠息肉或肿瘤复发的降低的可能性的预测。在各个实施方案中,包括上述蛋白质中的两种、三种、四种、五种、六种、七种、八种、九种、十种、十一种和全部十二种的群组。这样的群组可排除另外的蛋白质,或可以进一步包含另外的蛋白质。

[0225] 在本公开的一些方面,所述报告进一步包括针对所述患者的结肠疾病的治疗管理的治疗方式的建议。治疗管理选项可包括但不限于,其他诊断试验,如结肠镜检查、可屈性乙状结肠镜检查(flex sigmoidoscopy)、CT结肠成像术、粪便检验、排泄物检验、用治疗剂进一步治疗、手术干预以及不采取进一步行动。

[0226] 本公开还提供了通过以下步骤制备针对患者的个人生物标志物谱的方法:a)确定从受试者t获得的生物样品中以下至少一种或多种的归一化表达水平:SCDC26 (CD26)、CEA分子5 (CEACAM5)、CA195 (CCR5)、CA19-9、M2PK (PKM2)、TIMP1、P-选择蛋白 (SELPLG)、VEGFA、HcGB (CGB)、绒毛蛋白、TATI (SPINK1)、A-L-岩藻糖苷酶 (FUCA2)、ANXA5、GAPDH、PKM2、ANXA4、GARS、RRBP1、KRT8、SYNCRIP、S100A9、ANXA3、CAPG、HNRNPF、PPA1、NME1、PSME3、AHCY、TPT1、HSPB1和RPSA和/或图9中的蛋白质或它们的修饰形式或其表达产物;以及(b)创建报告,该报告汇总了通过基因表达分析获得的数据。在各个实施方案中,包括上述蛋白质中的两种、三种、四种、五种、六种、七种、八种、九种、十种、十一种和全部十二种的群组。这样的群组可排除另外的蛋白质,或可以进一步包含另外的蛋白质。

VIII. 试剂盒

[0227] 用于本公开方法的材料适于根据公知的程序生产的试剂盒的制备。本公开提供的试剂盒销售给医疗服务提供者,包括医师、临床实验室科学家、护士、药剂师、处方人员(formulary official)或直接销售给消费者。

[0228] 试剂盒通常可包含插入材料、组合物、试剂、装置的组件以及关于如何对特定的生物样品类型进行该方法或试验的说明。该试剂盒可进一步包含能够通过各种测定类型(诸如ELISA测定、免疫测定、蛋白质芯片或微阵列、DNA/RNA芯片或微阵列、RT-PCR、核酸测序、质谱法、免疫组织化学法、流式细胞术或高含量细胞筛选)检测生物标志物的试剂。

[0229] 本公开提供了组合物,诸如能够与如本文所教导的生物标志物、肽、多肽或蛋白质及其片段中的任意一种或多种特异性结合的结合剂。结合剂可包括抗体、适体、光适体(photoaptamer)、蛋白质、肽、肽模拟物或小分子。本公开提供的结合剂包括两种特异性结合剂,该特异性结合剂通过与一种或多种期望的分子或分析物结合,诸如与感兴趣的一种或多种蛋白质、多肽或肽或其片段结合(基本上排除随机或不相关的其他分子,并且任选地基本排除结构相似或相关的其他分子)而起作用。术语“特异性结合”并非必需要求结合剂排他地与其预期的靶标结合。例如,如果在结合条件下,结合剂对预期的靶标的亲和力是其对非靶标分子的亲和力的至少约2倍、优选至少约5倍、更优选至少约10倍、更优选至少约25倍、更优选至少约50倍以及甚至更优选至少约100倍或更多倍,则该结合剂可被称为与感兴趣的蛋白质、多肽、肽和/或其片段特异性结合。

[0230] 优选地,所述结合剂可以以此类结合的以下亲和常数(KA)与其预期的靶标结合:

KA $1 \times 10^6 \text{M}^{-1}$ 、更优选KA $1 \times 10^7 \text{M}^{-1}$ 、更优选KA $1 \times 10^8 \text{M}^{-1}$ 、甚至更优选KA $1 \times 10^9 \text{M}^{-1}$ 并且更优选KA $1 \times 10^{10} \text{M}^{-1}$ 或KA $1 \times 10^{11} \text{M}^{-1}$,其中 $\text{KA} = [\text{SBA\_T}] / [\text{SBA}] [1]$,SBA表示特异性结合剂,T 表示预期的靶标。KA的确定可通过本领域中已知的方法进行,例如,使用平衡透析和Scatchard作图分析。

[0231] 在所述方法和试剂盒的一些应用中,结合剂将为免疫结合剂,如抗体。可在本公开中使用的抗体的实例包括本领域中公知的多克隆 和单克隆抗体以及它们的片段。可在本公开的方法和试剂盒中使用的 抗体的另外的实例包括由至少两个完整的抗体形成的多价(例如,2 价、3价或更高价)和/或多特异性抗体(例如,双特异性或多特异性 抗体),以及抗体片段(只要它们表现出期望的生物活性(特别是,特异性结合感兴趣的抗原的能力)),以及这些片段的多价和/或多特 异性复合物。

[0232] 抗体可以是IgA、IgD、IgE、IgG和IgM类中的任意类别,并 优选IgG类抗体。抗体可以是多克隆抗体,例如从其纯化的(例如,亲和纯化的)抗血清或免疫球蛋白。抗体可以是单克隆抗体或单克隆 抗体的混合物。单克隆抗体可以以较高的选择性和重现性靶向抗原 内的特定抗原或特定表位。举例来说,但非限制性地,单克隆抗体可以 通过首先由Kohler等人1975(Nature 256:495)描述的杂交瘤方法来制 备,或者可以通过重组DNA方法(例如,在US 4,816,567中的)来 制备。例如,单克隆抗体还可以使用如Clackson等人1991(Nature 352: 624-628)和Marks等人1991(J Mol Biol 222:581-597)所述的技术从噬 菌体抗体文库中分离。

[0233] 抗体结合剂可以是抗体片段。“抗体片段”包含完整抗体的一部分,包括其抗原结合区或可变区。抗体片段的实例包括Fab、Fab'、F(ab')₂、Fv和scFv片段;双抗体;线性抗体;单链抗体分子;以及 由抗体片段形成的多价和/或多特异性抗体,例如双体、三体和 多体。上述称谓Fab、Fab'、F(ab')₂、Fv、scFv等旨在具有其本领域确定的 含义。

[0234] 制备多克隆和单克隆抗体以及它们的片段的方法是本领域公知 的,如用于制备重组抗体或其片段的方法(参见,例如,Harlow和 Lane,“Antibodies:A Laboratory Manual”,Cold Spring Harbour Laboratory,New York,1988;Harlow和Lane,“Using Antibodies:A Laboratory Manual”,Cold Spring Harbour Laboratory,New York,1999, ISBN 0879695447;“Monoclonal Antibodies:A Manual of Techniques”, Zola编著,CRC Press 1987,ISBN 0849364760;“Monoclonal Antibodies: A Practical Approach”,Dean和Shepherd编著,Oxford University Press 2000,ISBN 0199637229;Methods in Molecular Biology,vol.248: “Antibody Engineering:Methods and Protocols”,Lo编 著,Humana Press 2004,ISBN 1588290921)。

[0235] 本公开的抗体可来源于任何动物物种,优选脊椎动物物种,包 括,例如禽类和哺乳动物,或包含由其衍生的一个或多个部分。非限 制性地,抗体可以是鸡、鸡蛋、火鸡、鹅、鸭、珍珠鸡、鹌鹑或雉鸡 抗体。仍非限制性地,抗体可以是人、鼠(例如,小鼠、大鼠等)、驴、兔、山羊、绵羊、豚鼠、骆驼(例如双峰骆驼(Camelus bactrianus) 和单峰骆驼(Camelus dromaderius))、美洲驼(例如,羊驼(Lama paccos)、大羊驼或骆马)或马抗体。

[0236] 本公开还提供了针对本文提供的生物标志物的抗体,该抗体可 包含一个或多个氨基酸缺失、添加和/或置换(例如,保守置换),只 要这样的改变保持其与相应抗原的结合。抗体还可以包含其组成氨基 酸残基的一个或多个天然或人工修饰(例如,糖基化等)。

[0237] 本公开提供的抗体不限于通过包括免疫的方法产生的抗体,且还包括被制备成包含至少一种能够与感兴趣抗原上的表位特异性结合的互补性决定区(CDR)的任何多肽,例如重组表达的多肽。因此,术语抗体或免疫结合剂适用于此类分子,而不论它们是在体外还是在体内产生。

[0238] 本公开试剂盒中的抗体或免疫结合剂、肽、多肽、蛋白质、生物标志物等可以是各种形式,例如冻干的、在溶液中游离或固定在固相上。抗体或免疫结合剂可以例如在多孔板中或作为阵列或微阵列来提供,或者它们可以单独地和/或分别进行包装。它们可适当地标记以进行检测,如本文所教导的。本文提供的试剂盒可以特别适于进行本公开的测定方法,如免疫测定、ELISA测定、质谱测定、流式细胞术等。

[0239] 在本公开中提供了将由合格的临床科学家递送并使用的试剂盒。在这样的试剂盒中,本公开提供了包含各种试剂的试剂盒,该试剂可包括识别一种或多种所公开的生物标志物的抗体读出检测抗体,用于量化一种或多种所公开的生物标志物的表达的基因特异性或基因选择性探针和/或引物,用于预测结肠肿瘤状态或对治疗的反应的生物标志物的修饰形式或结合配偶体。

[0240] 试剂盒可以进一步包含容器(包括适用于所述方法的自动化实现的微量滴定板)、预制的生物芯片、缓冲液、适当的试剂抗体、探针、酶以进行测定。在本公开的一些方面,试剂盒可包含用于从生物样品中提取蛋白质和核酸的试剂,和/或用于DNA或RNA扩增或蛋白质分级分离或纯化的试剂,以及检测生物标志物的捕获生物芯片。试剂盒中的试剂将具有与它们的使用或进行测定的步骤相关的标识描述或标签或说明。此外,该试剂盒可进一步包含与它们在用于确定结肠息肉/肿瘤状态和复发和治疗反应的可能性的方法中的使用相关的说明,或者也可以组合提供计算机可读存储介质以确定结肠息肉/肿瘤状态和复发和治疗反应的可能性。

[0241] 试剂盒可进一步包含用于数据分析的软件包,其可包含用于比较的参考生物标志物谱。在一些应用中,试剂盒的软件包包含与中心服务器的连接,以进行数据分析,并且其中包含具有对疾病状态的建议、治疗建议或对用于疾病管理的治疗或程序的推荐的报告。

[0242] 试剂盒中提供的报告可以是纸质或电子报告。它可以由试剂盒中提供的计算机软件或者由计算机服务器来生成,其由用户上传至网站,其中该计算机服务器生成该报告。

[0243] 在本公开的一些方面,试剂盒可包含用于评估或量化作为试剂盒的组件的预后、诊断、临床状态或预测信息的数学算法。在一些方面,这将通过计算机可读存储介质递送,并且在本公开的其他方面,这可以通过向用户提供访问包含运行数学算法的逻辑的计算机服务器的密码来给出。

[0244] 试剂盒可以以任何合适的方式进行包装,通常所有元件在单个容器中,并随附用于执行该方法或试验的打印的说明书页。

[0245] 在本公开中提供了将递送给医师的试剂盒。用于此目的的试剂盒将包含供医师提供医疗信息的电子或书面文件,以及粘贴到含有生物样品和任选的固定/防腐试剂的无菌容纳容器上的条形码标签。在一些方面,这样的试剂盒将包含将通过邮件发送以供通过本文提供的方法进行处理的邮寄说明和供给。

实施例

[0246] 实施例1

[0247] 结肠镜检查呈阴性诊断的个体的腺瘤或息肉状态的鉴定

[0248] 通过使用经验证的生物标志物分类器,针对结肠息肉的存在与 否,检测来自基于结肠镜检查为腺瘤或息肉诊断阴性的患者的全血清 进行检测。独立地分析来自每个部位的样品的数据(即,验证数据集 不用于在发现交叉验证中的训练或测试),并继而对结果间的重叠进 行评价。对表E1中的分类器的蛋白质和/或肽进行LC-MS/MS分析。

[0249] 鉴定生物标志物。例如,生物标志物集示于表E1和表E2以及 图7中。

[0250] 表E1

序号	名称 (别名)	
1	SCDC26 (CD26)	二肽基肽酶4, 可溶形式
2	CEA分子5 (CEACAM5)	癌胚抗原相关粘附分子
3	CA195 (CCR5)	C-C趋化因子受体5型
4	CA19-9	碳水化合物抗原19-9
5	M2PK (PKM2)	丙酮酸激酶同工酶M1/M2
6	TIMP1	金属蛋白酶抑制剂1
7	P-选择蛋白(SELPLG)	P-选择蛋白糖蛋白配体1
8	VEGFA	血管内皮生长因子A
9	HcGB (CGB)	绒毛膜促性腺激素 β 亚基
10	绒毛蛋白	上皮细胞特异性Ca ²⁺ 调节的肌动蛋白
11	TATI (SPINK1)	胰分泌型胰蛋白酶抑制剂
12	A-L-岩藻糖苷酶 (FUCA2)	血浆 α -L岩藻糖苷酶

[0251] 表E2

序号	名称 (别名)	
1	ANXA5	膜联蛋白A5
2	GAPDH	甘油醛-3-磷酸脱氢酶
3	PKM2	丙酮酸激酶同工酶M1/M2
4	ANXA4	膜联蛋白A4
5	GARS	甘氨酸-tRNA合成酶
6	RRBP1	核糖体结合蛋白1
7	KRT8	角蛋白II型细胞骨架8
8	SYNCRIP	核内不均一核糖核蛋白Q
9	S100A9	S100A9钙结合蛋白
10	ANXA3	膜联蛋白A3
11	CAPG	巨噬细胞加帽蛋白
12	HNRNPF	核内不均一核糖核蛋白F
13	PPA1	无机焦磷酸酶
14	NME1	核苷二磷酸激酶A

15	PSME3	蛋白酶体激活剂复合物亚基3
16	AHCY	腺苷高半胱氨酸酶
17	TPT1	翻译控制肿瘤蛋白
18	HSPB1	热休克蛋白 β -1
19	RPSA	40S核糖体蛋白SA

[0252] 将这些值与对照参考值进行比较。最后,将分类器谱与低或无 风险、中等风险和高风险的分类器谱进行比较,从而使患者样品以约 90%或更高的准确率与受试者的预测的腺瘤/息肉状态或正常状态相 关联。参见表E3。或者,通过免疫分析如免疫印迹、生物芯片、免 疫染色和/或流式细胞术分析使用生物标志物分类器进行临床检测。

[0253] 表E3

	验证集		发现集	
	正常	息肉	正常	息肉
	n=500	n=600	n=400	n=700
归类为正常 (无息肉)	461	0	387	0
归类为具有 息肉	0	543	0	673
无法归类	39	57	13	27

[0254] 实施例2

[0255] 先前具有结肠息肉的个体的息肉状态复发的鉴定

[0256] 使用具有特异性结合或识别针对表E1和/或表E2中的蛋白质生 物标志物分类器的抗原的抗体的捕获生物芯片以及对照参考对来自 早先具有结肠息肉肿瘤的患者全血清样品中的抗原进行谱分析。

[0257] 筛选样品,以确定患者是否具有结肠息肉或息肉的复发。芯片 与样品在室温下一起孵育,以使抗体与样品中的抗原形成复合物。接 着,用温和的去污剂溶液洗涤芯片,以去除未特异性结合的任何蛋白 质或抗体。添加第二抗体与检测试剂的复合物且使其结合该芯片,并 用温和的洗涤剂进行洗涤。使用阅读器如CCD相机对蛋白质进行定 量。最后,将来自生物芯片读出的分类器谱与低或无风险、中等风险 和高风险复发分类器的谱进行比较,以确定患者的复发状态。

[0258] 实施例3A

[0259] 在本研究中,从即将接受结肠镜检查的患者中采集血液。使用 基于串联质谱法的方法采集关于血浆中存在的基于蛋白质的分子特 征的谱的定量数据,并且使用该数据来鉴定特征,该特征包含能够预 测结肠镜检查程序的结果的分类器。

[0260] 研究设计和患者样品采集

[0261] 为了将血浆蛋白质谱与患者结肠镜检查结果相关联,在他们进行结肠镜检查的当天,从进行结肠镜检查的患者中采集血液样品。入选标准要求患者等于或大于18岁,且愿意并能够签署知情同意书。这是一个“全体愿意参加者(all comers)”研究,其中患者可能经受根据所建议的常规筛查、因先前个人或家族病史而采取的预防措施或对个人健康症状的随访的程序。

[0262] 在结肠镜检查的常规准备(包含过夜禁食、液体限制以及去除粪便物质的肠道准备)后,将血液样品吸至包含作为抗凝剂的EDTA的血浆采集设备。根据制造商的说明,将血液样品混合、离心以分离血浆,并在四小时内收集分离的血浆并将其在-80℃下冷冻。

[0263] 除了血浆样品之外,还收集患者临床数据如年龄、体重、性别、种族、当前的用药和指征以及个人和家族健康史,如同针对任何采集和检查的组织的结肠镜检查程序报告和病理学报告。收集了超过500名患者的样品。在表E4、表E5和表E6中提供了患者人口统计数据。

[0264] 表E4

	排除的	对 照	疾 病			总 计	%总计
		正 常	息 肉	腺瘤和息肉	腺 瘤		
总计	3	73	20	7	49	152	100.00%
常规访视	0	37	6	1	22	66	43.42%
病史	0	14	10	5	15	44	28.95%
症状	3	22	4	1	12	42	27.63%
先前的结肠镜检查	1	41	13	6	25	86	56.58%
男性	2	35	8	4	27	76	50.00%
女性	1	38	12	3	22	76	50.00%
非裔美国人	1	3	2	0	2	8	5.26%
亚洲人	0	0	0	1	0	1	0.66%
高加索人	2	69	16	6	45	138	90.79%
西班牙人	0	1	1	0	2	4	2.63%
印第安人	0	0	1	0	0	1	0.66%
太平洋岛人	0	0	0	0	0	0	0.00%

[0265] 表E5

	对照	疾病
女性	38	37
男性	35	39
		p=0.6808
年龄 (平均值+/-标准差, 岁)	58.8 +/- 9.8	58.9 +/- 9.6
		p=0.9305
常规	37	29
病史或症状	36	47
		p=0.1237

p值来自相关性的卡方检验

[0266] 表E6

状况或用药	在训练组中的人数	有对照	无对照	患病	未患病	卡方 p-值
变态反应	27	15	58	12	64	0.450942
贫血	10	6	67	4	72	0.470814
焦虑性障碍	13	8	65	5	71	0.343321
关节炎	13	6	67	7	69	0.830237
哮喘	16	5	68	10	66	0.199724
便秘	12	4	69	7	69	0.383146
抑郁症	32	19	54	13	63	0.184788
II型糖尿病	25	8	65	15	61	0.137476
憩室病	13	8	65	5	71	0.343321
胃食管反流病 (GERD)	36	13	60	22	54	0.108432
高胆固醇血症	22	11	62	11	65	0.918512
高血脂症	45	16	57	27	49	0.066549
高血压	64	29	44	34	42	0.535918
甲状腺功能减退症	21	8	65	13	63	0.280525
失眠症	13	8	65	5	71	0.343321
肠易激综合征 (IBS)	17	10	63	7	69	0.388888
HCTZ 氢氯噻嗪	14	7	66	6	70	0.714104
ASA 阿司匹林	45	20	53	24	52	0.575854
沙丁胺醇	12	5	68	7	69	0.596230
钙补充剂	26	10	63	16	60	0.236565
鱼油	23	11	62	12	64	0.903077
氟替卡松	15	9	64	6	70	0.368360
激素替代疗法	14	10	63	4	72	0.076930
布洛芬	11	6	67	5	71	0.701900
左旋甲状腺素	18	7	66	11	65	0.359898
立普妥	12	4	69	8	68	0.256630
赖诺普利	17	4	69	12	64	0.041113
二甲双胍	14	4	69	9	67	0.167563
普拉固	11	3	70	8	68	0.132598
奥美拉唑	27	12	61	15	61	0.601195
维生素C	12	5	68	7	69	0.596230
维生素D	25	11	62	13	63	0.735244
维生素D3	10	3	70	7	69	0.211955
舒降之	18	7	66	10	66	0.493048

[0267] 用于血浆蛋白质分析的样品制备

[0268] 选择152个样品 (76个息肉和/或腺瘤和76个对照) 用于分类器分析。患者的息肉和/或腺瘤组随机地选自较大的研究组且与对照在年龄和性别上相匹配。制备患者的血浆蛋白质样品用于如下的LCMS 测量。将血浆样品从-80℃的存储中解冻并通过过滤器离心去除脂质和颗粒。通过基于免疫亲和柱的消耗去除滤出的血浆中的高丰度蛋白质。通过反相HPLC将较低丰度的流过蛋白质分离成级分。将所选择的蛋白质级分 (每个样品6份) 通过胰蛋白酶-TFE消化还原成肽, 并使所得肽再悬浮于乙腈/甲酸LCMS上样缓冲液中。

[0269] LCMS数据采集和蛋白质分子特征量化

[0270] 将来自每个患者的血浆样品的若干级分的再悬浮的肽通过UHPLC注射至串联质谱仪 (Q-TOF) 用于定量分析。分析收集的数据 (保留时间、质/荷比和离子丰度) 以检测观察到的被称为分子特征的峰。三维峰积分算法决定了该分子特征的相对丰度。

[0271] 在使用三次样条算法进行数据集叠加和校准之后比较来自多个患者样品的分子特征数据。仅被确定为以50%或更高的百分比存在于至少一个患者类别 (无或有息肉/腺

瘤)中的特征被考虑用于进一步的 分析。在该集中缺少患者特征数据的情况下,通过对如 在其他样品中 观察到的先验峰位置上的原始离子丰度数据进行积分来估算特征值。来自 152个患者样品中的每个样品的大于145,000个分子特征包含用 于随后的分类器分析的最终数据集。

[0272] 数据归一化、特征选择和分类器组装

[0273] 将来源于单个原始中性质量的不同分子特征的定量数据组合并 汇总。例如,来自 同一母体分子的+2m/z和+3m/z特征通过合并成单 个中性质量簇(NMC)值而进行组合。

[0274] 通过在相同的研究日期以及同一仪器上收集的样品的平均值调 节NMC对来自不同样品的分子特征数据进行归一化。平衡数据采集 以使得在每个仪器-日期组中评价近似 相等数目的无和有息肉/腺瘤样 品。这种方法被定义为簇-仪器-日期(“CID”)归一化。

[0275] 数据的初始分析表明,女性样品的激素替代疗法状态的不平衡 可能是分类器构建中的混杂因素。为了消除这种可能性,将表明与 HRT相关的分子特征通过不同的分类器 组装进行鉴定并从随后的分 析中去除。

[0276] 仅具有来自所有实验级分的完整数据的样品用于分析。在最初 测量的152个样品 中,保留108个完整的样品。对于大多数排除的样 品,6个样品级分中的一个或多个的QC失败导致被排除。

[0277] 使用最终的归一化数据,创建分类器并对它们从息肉和/或腺瘤 样品中鉴别无息肉 和腺瘤的患者样品的能力进行评估。在样品数据的 五十个70/30训练/测试分割 (splits)中的每一个中,使用弹性网络方 法进行特征选择,从而将所考虑的NMC的数目从 多于100,000个减 少至约200-250个。然后,使用这些选定的NMC来构建基于SVM(乙 状结肠-核)的分类器。在五十个训练/测试分割的每次迭代中,确定 如通过ROC图上的AUC测量的 测试数据(灵敏度和特异性的组合测 量)的分类器的性能。所得的平均AUC(0.79+/- 0.08)示于图1A中。根据二等分该图的虚线,该AUC明显不同于0.5——不能达到鉴别能 力的随机测定的值。因此,图1A提供了测试集性能的比较。X轴表 示假阳性率。Y轴表示真阳性 率。

[0278] 为了确认弹性网络/SVM分类器性能的稳健性,对类别分配, 即息肉/腺瘤相比无 息肉/腺瘤进行随机排列,并在整个五十次迭代中 再次进行整个特征选择和分类器组装过 程。所得平均AUC (0.52+/-0.09)示于图2A中,且表明诸如正确分配确定的结果不太 可能 偶然出现。因此,图2A提供了测试集性能的验证。X轴表示假 阳性率。Y轴表示真阳性率。

[0279] 结果的显著性的另外的测量是单个NMC在五十个70/30训练/ 测试分割分类器中 出现的频率的列表。在每一次迭代中,为分类器选 择约200-250个特征;特征在50次迭代中 出现至少3次或更多次是 非偶然预期的结果。特征频率表的帕累托图(排序的直方图)示于 图 3中。该数据指示大量特征被多次选择,从而表明它们参与鉴别分类 器的稳健性。当选择 频率最高的特征(即,不同相关组中的前30个) 并将其用于在嵌套的70(70/30)/30分析 结构中构建分类器时,所得平 均AUC仍然明显不同于随机的。该结果指示存在可由选定的 特征集 构建的多个分类器。

[0280] 分类器分子特征的子集

[0281] 通过外循环/内循环策略来鉴定分类器特征的较小子集。在该方 法中,样品分成 50个外循环70/30分割和500个内循环70/30分割。进行多个内循环用于特征选择,计算SVM

分类器内部测试的ROC AUC,并且选择500次迭代中最好的5%并保留所包含的特征。使用弹性网络选择最终的一组特征,以构建外循环SVM分类器。对于不同大小的分类器,使用来自选定的内循环的特征的频率等级来确定特征的优先顺序(例如,频率最高的10、20、30个等)。基于外循环测试集评估所得分类器,且测量性能AUC。图5示出了50次外循环迭代的平均ROC,且表明大小为30的分类器保留了显著的预测值($AUC=0.645\pm0.092$)。在图5中,Y轴显示真阳性率而X轴显示假阳性率。由于确认该结果不能偶然得到,因此对50个不同的样品集(其中样品类别分配已随机重新分配)执行该程序。所得AUC(0.502 ± 0.101 ,如图6中所示)是随机的,从而确认了正确的类别分配结果的稳健性。在图6中,Y轴显示真阳性率而X轴显示假阳性率。表E7表明已用大小为10个特征或NMC的分类器证明了显著性能的类似迹象。

[0282] 表E7

大小	AUC	sd
100	0.70	0.08
50	0.66	0.09
40	0.65	0.09
30	0.64	0.09
20	0.63	0.09
10	0.60	0.09

[0283] 分类器分子特征的鉴定

[0284] 通过质谱法进行的分子特征的质量测定足够准确和精确地提供唯一的鉴定。在本实施例中组装的分类器中表示的1014个特征(每个特征出现3次或更多次)的质量在如图7的附表中列出。准确的质量对于分子特征是固有唯一地鉴定性的,因此可以确定这些特征的一级氨基酸序列和任何翻译后修饰以便将它们的测量值转化为可替代的表示。

[0285] 实施例3B

[0286] 研究设计对应于实施例3A的研究设计,并具有以下附加细节。

[0287] LCMS数据采集和蛋白质分子特征量化

[0288] 经由UHPLC将来自每个患者的血浆样品的若干级分的再悬浮的肽注射至串联质谱仪(Q-TOF),以用于定量分析。对收集的数据(保留时间、质/荷比和离子丰度)进行分析,以检测所观察到的被称为分子特征的峰。三维峰积分算法确定了分子特征的相对丰度。平均来说,从每个血浆样品中检测并定量出约364,000个分子特征。

[0289] 在使用三次样条算法进行数据集叠加和校准之后比较来自多个患者样品的分子特征数据。仅被确定为以50%或更高的百分比存在于至少一个患者类别(无或有息肉/腺瘤)中的特征被考虑用于进一步的分析。在该集中缺失患者特征数据的情况下,通过对如在其他样品中观察到的先验峰位置上的原始离子丰度数据进行积分来估算特征值。来自152个患者样品中的每个样品的约149,000个分子特征包含用于随后的分类器分析的最终数据集。

[0290] 数据归一化、特征选择和分类器组装

[0291] 将来源于单个原始中性质量的不同分子特征的定量数据组合并汇总。例如,来自同一母体分子的+2m/z和+3m/z特征通过合并成单个中性质量簇(NMC)值而进行组合。NMC

的总数目为约105,000 个。

[0292] 细节如实施例3A中所述。此外,通过用于指示较高鉴定概率 的参数对特征进行过滤;例如,仅考虑电荷状态大于1 ($z>1$) 的特征。这将用于分类器分析的NMC的总数目减少至约47,000个。

[0293] 进一步参考对实施例3A的分析,在该分析中,使用十轮10折 交叉验证来选择特征并构建分类器。在每一轮中,90%的数据用于使 用弹性网络回归算法来选择特征,基于所确定的特征系数的排序来选 择前20个特征,并随后构建具有线性核的SVM分类器。然后,基 于 所给倍数的测试集中提供的10%的样品对这个最终的分类器进行评 估。因此,在每一轮的10折交叉验证中,每一个样品在测试集中仅 出现一次。使用来自每一个样品的分类器的预测测试集值来构建该轮 的ROC图,其中每个样品一个点。对十个ROC图(每一轮一个)进 行平均化并绘图。针对分析中使用的108个完整的样品,以及通过使 用原始结肠镜检查确定的诊断作为比较物,得到20个特征分类器的 中值AUC为0.91。平均AUC为 0.91 ± 0.021 。图1B。

[0294] 为了确认分类器性能的稳健性,对类别分配,即息肉/腺瘤相比 无息肉/腺瘤进行随机排列,并在整个十轮的10折交叉验证中再次进 行整个特征选择和分类器组装过程,如 本文所述。中值AUC (0.52) 和平均AUC (0.52 ± 0.033) (图2B) 表明诸如正确分配确定的结果 (AUC 0.91) 不大可能偶然出现。

[0295] 结果的显著性的另外的测量是单个NMC在十轮的10折交叉验 证中创建的100个分类器中出现的频率的列表。在每一次迭代中,选 择20个特征用于分类器;特征在多个分类器中的出现指示特征选择 和分类器过程的稳健性。通过使用原始诊断构建分类器(如在图 1B 中观察到的),多数特征被选择了不止一次。最频繁被选的特征从100 个分类器中的99 个中选择。参见图4。相比之下,通过使用随机特征 选择,最频繁被选的特征仅被选择了三次。总之,206个特征在100 个20特征分类器中的一个或多个中出现。

[0296] 分类器分子特征的鉴定

[0297] 通过质谱法进行的分子特征的质量测定足够准确和精确地提供 唯一的鉴定。在本实施例中组装的分类器中表示的206个特征的质量 在如图8的附表中列出。准确的质量对于分子特征是固有唯一地鉴定 性的,因此可以确定这些特征的一级氨基酸序列和任何翻译后修饰以 便将它们的测量值转化为可替代的表示。

[0298] 实施例4

[0299] MRM测定发展

[0300] 最初,对先前报道为与结肠直肠癌具有关联的188种蛋白质在 计算机上进行查询以揭示用于靶向蛋白质组谱分析的潜在肽候选物。从成千上万个潜在的胰蛋白酶肽中,选 择初步的一组1056个用于实 验验证。从实验验证中选择最终一组337个肽(代表187种蛋白 质),以包含最终的多反应监测(MRM) 试验。此外,将用重(全部为C13) 精氨酸(R)或赖氨酸(K) 标记的具有确切序列组成的337个补充 肽作为内标物而并入,以在最终分析中用作归 一化参考。

[0301] 用于血浆蛋白质分析的样品制备

[0302] 根据两种方法(称为稀释和消耗)制备用于MRM LCMS测量 的患者血浆蛋白质样 品。

[0303] 在稀释方法中,将血浆样品从-80℃存储中解冻并通过过滤器离心去除脂质和颗粒。将剩余的蛋白质通过胰蛋白酶-TFE消化还原成肽,并使所得肽再悬浮于乙腈/甲酸MRM LCMS上样缓冲液中。

[0304] 在消耗方法中,将血浆样品从-80℃存储中解冻并通过过滤器离心去除脂质和颗粒。通过基于免疫亲和柱的消耗去除滤出的血浆中的高丰度蛋白质。将较低丰度的流过蛋白质用胰蛋白酶-TFE消化还原成肽,并使所得肽再悬浮于乙腈/甲酸MRM LCMS上样缓冲液中。

[0305] LCMS数据采集和过渡特征量化

[0306] 经由UHPLC将来自每个患者的血浆样品的再悬浮的肽注射至三重四极杆质谱仪(QQQ),以用于定量分析。对收集的数据(保留时间、前体质量、碎片质量和离子丰度)进行分析,以检测所观察到的被称为过渡的峰。

[0307] 采用二维峰积分算法来确定每个过渡峰的曲线下面积(AUC)。

[0308] 将用重(全部为C13)精氨酸(R)或赖氨酸(K)标记的具有确切序列组成的补充肽用作676个靶向过渡中的每一个的内标物。采用补充的内标AUC值对过渡AUC值进行归一化,以得到每个过渡的浓度值。

[0309] 数据归一化、特征选择和分类器组装

[0310] 对于分类器组装和性能评估,基于原始肽峰面积与相关联的标记的标准肽原始峰面积的比值来使用特征浓度值。不对其原始峰面积应用归一化。将过渡的缺失值设置为0。

[0311] 使用10×10折交叉验证过程来评估分类器模型和相关的分类性能。在该过程中,首先应用特征选择来减少所使用的特征的数目,接着是分类器模型的开发以及随后的分类性能评估。对于每轮10折交叉验证,将数据分成10个分割份,每个包含90%的样品作为训练集而剩余10%的样品作为测试集。在该过程中,总共95个样品中的每一个在测试集中评估一次。仅使用训练集进行特征选择和模型组装过程,并且随后将这些模型应用于测试集以评估分类器性能。

[0312] 为了进一步评估分类性能的概括,将该整个10折交叉验证程序重复10次,每次具有训练集和测试集的不同取样。

[0313] 用于分类器分析的过渡特征的总数目为674。为了探索具有较少数目的特征的分类性能,在构建分类模型之前应用弹性网络特征选择。在该过程中,构建了弹性网络模型并在分类模型的开发中使用给出20个过渡特征的模型。由于交叉-折回验证过程的每一折具有它自己的特征选择步骤,因此每一折可选择不同的特征,从而在整个10×10折交叉验证过程的模型中使用的特征的总数目将大于或等于20。

[0314] 在特征选择步骤之后,使用具有线性核的支持向量机(SVM)算法构建分类器模型。在构建训练集的分类器模型后,将其在未经修改的情况下直接应用于测试集,并且产生相关的受试者工作特征(ROC)曲线,从该曲线计算曲线下面积(AUC)。在10×10折交叉验证过程中,得到平均测试集AUC(0.76+/-0.035),图10指示了分类模型鉴别结肠直肠癌和正常患者样品的能力。为了进一步评估特征选择过程中选定的特征,提供了频率/等级图(图11)。该图显示了若干特征,这些特征在全部或几乎全部的交叉验证折中被选定,突出了它们区分结肠直肠癌与正常样品的效用。通过分类过程鉴定的特征的列表在图12中

列出。

[0315] 研究设计和患者样品采集

	对照	CRC疾病
女性	24	23
男性	24	24
		p=1
年龄	65.0+/-9.7	65.5+/-9.6
(平均值+/-标准差,岁)		
		p=0.82

[0316] 尽管本文中已经示出并描述了本公开的优选实施方案,但对本 领域技术人员显而易见的是这样的实施方案仅通过示例的方式提供。本领域技术人员在不脱离本公开的情况下现将想到许多变化、改变和 替换。应当理解,本文所述的本公开实施方案的各种替代方案均可用 于实施本公开。其意图在于以下述权利要求限定本公开的范围并由此 涵盖这些权利要求范围内的方法和结构及其等同物。

序列表

<110> 迪森德克斯公司

<120> 用于评估结肠肿瘤的存在或风险的方法

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<151> 2013-03-05

<150> 61/732,024

<151> 2012-11-30

<160> 188

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

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Gln	Glu	Met	Ala	Thr	Ala	Ala	Ser	Ser	Ser	Ser	Leu	Glu	Lys	Ser	Tyr																		
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	100	105
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	195	200
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	210	215
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30

Gly Asp Arg Val Tyr Ile His Pro Phe His Leu Val Ile His Asn Glu

35

40

45

Ser Thr Cys Glu Gln Leu Ala Lys Ala Asn Ala Gly Lys Pro Lys Asp

50

55

60

Pro Thr Phe Ile Pro Ala Pro Ile Gln Ala Lys Thr Ser Pro Val Asp

65

70

75

80

Glu Lys Ala Leu Gln Asp Gln Leu Val Leu Val Ala Ala Lys Leu Asp

85

90

95

Thr Glu Asp Lys Leu Arg Ala Ala Met Val Gly Met Leu Ala Asn Phe

100

105

110

Leu Gly Phe Arg Ile Tyr Gly Met His Ser Glu Leu Trp Gly Val Val

115

120

125

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

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135

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Ser Leu Tyr Leu Gly Ala Leu Asp His Thr Ala Asp Arg Leu Gln Ala

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155

160

Ile Leu Gly Val Pro Trp Lys Asp Lys Asn Cys Thr Ser Arg Leu Asp

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175

Ala His Lys Val Leu Ser Ala Leu Gln Ala Val Gln Gly Leu Leu Val

180

185

190

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

195

200

205

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

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215

220

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

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

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

Ile Thr Pro Pro Asp Gln Asp Asp Ser Met Glu Cys Val Asp Ser Glu			
450	455	460	
Arg Arg Pro His Phe Pro Gln Phe Ser Tyr Ser Ala Ser Gly Thr Ala			
465	470	475	480
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His Arg Phe Lys Asp Leu Gly Glu Glu Asn Phe Lys Ala Leu Val Leu			
35	40	45	
Ile Ala Phe Ala Gln Tyr Leu Gln Gln Cys Pro Phe Glu Asp His Val			
50	55	60	
Lys Leu Val Asn Glu Val Thr Glu Phe Ala Lys Thr Cys Val Ala Asp			
65	70	75	80
Glu Ser Ala Glu Asn Cys Asp Lys Ser Leu His Thr Leu Phe Gly Asp			
85	90	95	
Lys Leu Cys Thr Val Ala Thr Leu Arg Glu Thr Tyr Gly Glu Met Ala			
100	105	110	
Asp Cys Cys Ala Lys Gln Glu Pro Glu Arg Asn Glu Cys Phe Leu Gln			
115	120	125	
His Lys Asp Asp Asn Pro Asn Leu Pro Arg Leu Val Arg Pro Glu Val			
130	135	140	
Asp Val Met Cys Thr Ala Phe His Asp Asn Glu Glu Thr Phe Leu Lys			
145	150	155	160
Lys Tyr Leu Tyr Glu Ile Ala Arg Arg His Pro Tyr Phe Tyr Ala Pro			
165	170	175	
Glu Leu Leu Phe Phe Ala Lys Arg Tyr Lys Ala Ala Phe Thr Glu Cys			
180	185	190	
Cys Gln Ala Ala Asp Lys Ala Ala Cys Leu Leu Pro Lys Leu Asp Glu			
195	200	205	
Leu Arg Asp Glu Gly Lys Ala Ser Ser Ala Lys Gln Arg Leu Lys Cys			
210	215	220	
Ala Ser Leu Gln Lys Phe Gly Glu Arg Ala Phe Lys Ala Trp Ala Val			
225	230	235	240

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

545	550	555	560
Pro Lys Ala Thr Lys Glu Gln Leu Lys Ala Val Met Asp Asp Phe Ala			
	565	570	575
Ala Phe Val Glu Lys Cys Cys Lys Ala Asp Asp Lys Glu Thr Cys Phe			
	580	585	590
Ala Glu Glu Gly Lys Lys Leu Val Ala Ala Ser Gln Ala Ala Leu Gly			
	595	600	605
Leu			
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Met Ser Ser Ser Gly Thr Pro Asp Leu Pro Val Leu Leu Thr Asp Leu			
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Lys Ile Gln Tyr Thr Lys Ile Phe Ile Asn Asn Glu Trp His Asp Ser			
	20	25	30
Val Ser Gly Lys Lys Phe Pro Val Phe Asn Pro Ala Thr Glu Glu Glu			
	35	40	45
Leu Cys Gln Val Glu Glu Gly Asp Lys Glu Asp Val Asp Lys Ala Val			
	50	55	60
Lys Ala Ala Arg Gln Ala Phe Gln Ile Gly Ser Pro Trp Arg Thr Met			
65	70	75	80
Asp Ala Ser Glu Arg Gly Arg Leu Leu Tyr Lys Leu Ala Asp Leu Ile			
	85	90	95
Glu Arg Asp Arg Leu Leu Leu Ala Thr Met Glu Ser Met Asn Gly Gly			
	100	105	110
Lys Leu Tyr Ser Asn Ala Tyr Leu Asn Asp Leu Ala Gly Cys Ile Lys			
	115	120	125
Thr Leu Arg Tyr Cys Ala Gly Trp Ala Asp Lys Ile Gln Gly Arg Thr			
	130	135	140
Ile Pro Ile Asp Gly Asn Phe Phe Thr Tyr Thr Arg His Glu Pro Ile			
145	150	155	160
Gly Val Cys Gly Gln Ile Ile Pro Trp Asn Phe Pro Leu Val Met Leu			
	165	170	175
Ile Trp Lys Ile Gly Pro Ala Leu Ser Cys Gly Asn Thr Val Val Val			
	180	185	190
Lys Pro Ala Glu Gln Thr Pro Leu Thr Ala Leu His Val Ala Ser Leu			
	195	200	205

Ile Lys Glu Ala Gly Phe Pro Pro Gly Val Val Asn Ile Val Pro Gly		
210	215	220
Tyr Gly Pro Thr Ala Gly Ala Ala Ile Ser Ser His Met Asp Ile Asp		
225	230	235 240
Lys Val Ala Phe Thr Gly Ser Thr Glu Val Gly Lys Leu Ile Lys Glu		
	245	250 255
Ala Ala Gly Lys Ser Asn Leu Lys Arg Val Thr Leu Glu Leu Gly Gly		
	260	265 270
Lys Ser Pro Cys Ile Val Leu Ala Asp Ala Asp Leu Asp Asn Ala Val		
	275	280 285
Glu Phe Ala His His Gly Val Phe Tyr His Gln Gly Gln Cys Cys Ile		
	290	295 300
Ala Ala Ser Arg Ile Phe Val Glu Glu Ser Ile Tyr Asp Glu Phe Val		
305	310	315 320
Arg Arg Ser Val Glu Arg Ala Lys Lys Tyr Ile Leu Gly Asn Pro Leu		
	325	330 335
Thr Pro Gly Val Thr Gln Gly Pro Gln Ile Asp Lys Glu Gln Tyr Asp		
	340	345 350
Lys Ile Leu Asp Leu Ile Glu Ser Gly Lys Lys Glu Gly Ala Lys Leu		
	355	360 365
Glu Cys Gly Gly Gly Pro Trp Gly Asn Lys Gly Tyr Phe Val Gln Pro		
370	375	380
Thr Val Phe Ser Asn Val Thr Asp Glu Met Arg Ile Ala Lys Glu Glu		
385	390	395 400
Ile Phe Gly Pro Val Gln Gln Ile Met Lys Phe Lys Ser Leu Asp Asp		
	405	410 415
Val Ile Lys Arg Ala Asn Asn Thr Phe Tyr Gly Leu Ser Ala Gly Val		
	420	425 430
Phe Thr Lys Asp Ile Asp Lys Ala Ile Thr Ile Ser Ser Ala Leu Gln		
	435	440 445
Ala Gly Thr Val Trp Val Asn Cys Tyr Gly Val Val Ser Ala Gln Cys		
450	455	460
Pro Phe Gly Gly Phe Lys Met Ser Gly Asn Gly Arg Glu Leu Gly Glu		
465	470	475 480
Tyr Gly Phe His Glu Tyr Thr Glu Val Lys Thr Val Thr Val Lys Ile		
	485	490 495
Ser Gln Lys Asn Ser		
	500	

<210> 9

<211> 517

<212> PRT

<213> 智人

<400> 9

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

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275	280	285
Lys Ser Pro Ser Ile Val	Leu Ala Asp Ala Asp Met	Glu His Ala Val
290	295	300
Glu Gln Cys His Glu Ala	Leu Phe Phe Asn Met Gly	Gln Cys Cys Cys
305	310	315
Ala Gly Ser Arg Thr Phe	Val Glu Glu Ser Ile Tyr	Asn Glu Phe Leu
325	330	335
Glu Arg Thr Val Glu Lys	Ala Lys Gln Arg Lys Val	Gly Asn Pro Phe
340	345	350
Glu Leu Asp Thr Gln Gln	Gly Pro Gln Val Asp Lys	Glu Gln Phe Glu
355	360	365
Arg Val Leu Gly Tyr Ile	Gln Leu Gly Gln Lys Glu	Gly Ala Lys Leu
370	375	380
Leu Cys Gly Gly Glu Arg	Phe Gly Glu Arg Gly Phe	Phe Ile Lys Pro
385	390	395
Thr Val Phe Gly Gly Val	Gln Asp Asp Met Arg Ile	Ala Lys Glu Glu
405	410	415
Ile Phe Gly Pro Val Gln	Pro Leu Phe Lys Phe Lys	Lys Ile Glu Glu
420	425	430
Val Val Glu Arg Ala Asn	Asn Thr Arg Tyr Gly Leu	Ala Ala Ala Val
435	440	445
Phe Thr Arg Asp Leu Asp	Lys Ala Met Tyr Phe Thr	Gln Ala Leu Gln
450	455	460
Ala Gly Thr Val Trp Val	Asn Thr Tyr Asn Ile Val	Thr Cys His Thr
465	470	475
Pro Phe Gly Gly Phe Lys	Glu Ser Gly Asn Gly Arg	Glu Leu Gly Glu
485	490	495
Asp Gly Leu Lys Ala Tyr	Thr Glu Val Lys Thr Val	Thr Ile Lys Val
500	505	510
Pro Gln Lys Asn Ser		
515		
<210> 10		
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Ser Asp Ile Ala His Arg	Ile Val Ala Pro Gly Lys	Gly Ile Leu Ala

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

Leu Ala Cys Gln Gly Lys Tyr Thr Pro Ser Gly Gln Ala Gly Ala Ala
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 Ala Ser Glu Ser Leu Phe Val Ser Asn His Ala Tyr
 355 360
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 Tyr Ser Pro Asn Thr Gln Gln Gly Arg Thr Ser Ile Val His Leu Phe
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 Glu Trp Arg Trp Val Asp Ile Ala Leu Glu Cys Glu Arg Tyr Leu Ala
 35 40 45
 Pro Lys Gly Phe Gly Gly Val Gln Val Ser Pro Pro Asn Glu Asn Val
 50 55 60
 Ala Ile His Asn Pro Phe Arg Pro Trp Trp Glu Arg Tyr Gln Pro Val
 65 70 75 80
 Ser Tyr Lys Leu Cys Thr Arg Ser Gly Asn Glu Asp Glu Phe Arg Asn
 85 90 95
 Met Val Thr Arg Cys Asn Asn Val Gly Val Arg Ile Tyr Val Asp Ala
 100 105 110
 Val Ile Asn His Met Ser Gly Asn Ala Val Ser Ala Gly Thr Ser Ser
 115 120 125
 Thr Cys Gly Ser Tyr Phe Asn Pro Gly Ser Arg Asp Phe Pro Ala Val
 130 135 140
 Pro Tyr Ser Gly Trp Asp Phe Asn Asp Gly Lys Cys Lys Thr Gly Ser
 145 150 155 160
 Gly Asp Ile Glu Asn Tyr Asn Asp Ala Thr Gln Val Arg Asp Cys Arg
 165 170 175
 Leu Val Gly Leu Leu Asp Leu Ala Leu Glu Lys Asp Tyr Val Arg Ser
 180 185 190
 Lys Ile Ala Glu Tyr Met Asn His Leu Ile Asp Ile Gly Val Ala Gly
 195 200 205
 Phe Arg Leu Asp Ala Ser Lys His Met Trp Pro Gly Asp Ile Lys Ala
 210 215 220
 Ile Leu Asp Lys Leu His Asn Leu Asn Ser Asn Trp Phe Pro Ala Gly
 225 230 235 240

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

<210> 12

<211> 346

<212> PRT

<213> 智人

<400> 12

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

305	310	315	320
Ile Ser Leu Cys Gln Ala Ile Leu Asp Glu Thr Lys Gly Asp Tyr Glu			
	325	330	335
Lys Ile Leu Val Ala Leu Cys Gly Gly Asn			
	340	345	
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Asp Phe Ser Pro Ser Val Asp Ala Glu Ala Ile Gln Lys Ala Ile Arg			
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Gly Ile Gly Thr Asp Glu Lys Met Leu Ile Ser Ile Leu Thr Glu Arg			
	35	40	45
Ser Asn Ala Gln Arg Gln Leu Ile Val Lys Glu Tyr Gln Ala Ala Tyr			
	50	55	60
Gly Lys Glu Leu Lys Asp Asp Leu Lys Gly Asp Leu Ser Gly His Phe			
65	70	75	80
Glu His Leu Met Val Ala Leu Val Thr Pro Pro Ala Val Phe Asp Ala			
	85	90	95
Lys Gln Leu Lys Lys Ser Met Lys Gly Ala Gly Thr Asn Glu Asp Ala			
	100	105	110
Leu Ile Glu Ile Leu Thr Thr Arg Thr Ser Arg Gln Met Lys Asp Ile			
	115	120	125
Ser Gln Ala Tyr Tyr Thr Val Tyr Lys Lys Ser Leu Gly Asp Asp Ile			
	130	135	140
Ser Ser Glu Thr Ser Gly Asp Phe Arg Lys Ala Leu Leu Thr Leu Ala			
145	150	155	160
Asp Gly Arg Arg Asp Glu Ser Leu Lys Val Asp Glu His Leu Ala Lys			
	165	170	175
Gln Asp Ala Gln Ile Leu Tyr Lys Ala Gly Glu Asn Arg Trp Gly Thr			
	180	185	190
Asp Glu Asp Lys Phe Thr Glu Ile Leu Cys Leu Arg Ser Phe Pro Gln			
	195	200	205
Leu Lys Leu Thr Phe Asp Glu Tyr Arg Asn Ile Ser Gln Lys Asp Ile			
	210	215	220
Val Asp Ser Ile Lys Gly Glu Leu Ser Gly His Phe Glu Asp Leu Leu			

225	230	235	240
Leu Ala Ile Val Asn Cys Val Arg Asn Thr Pro Ala Phe Leu Ala Glu			
	245	250	255
Arg Leu His Arg Ala Leu Lys Gly Ile Gly Thr Asp Glu Phe Thr Leu			
	260	265	270
Asn Arg Ile Met Val Ser Arg Ser Glu Ile Asp Leu Leu Asp Ile Arg			
	275	280	285
Thr Glu Phe Lys Lys His Tyr Gly Tyr Ser Leu Tyr Ser Ala Ile Lys			
	290	295	300
Ser Asp Thr Ser Gly Asp Tyr Glu Ile Thr Leu Leu Lys Ile Cys Gly			
305	310	315	320
Gly Asp Asp			
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<213> 智人			
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Met Ala Thr Lys Gly Gly Thr Val Lys Ala Ala Ser Gly Phe Asn Ala			
1	5	10	15
Met Glu Asp Ala Gln Thr Leu Arg Lys Ala Met Lys Gly Leu Gly Thr			
	20	25	30
Asp Glu Asp Ala Ile Ile Ser Val Leu Ala Tyr Arg Asn Thr Ala Gln			
	35	40	45
Arg Gln Glu Ile Arg Thr Ala Tyr Lys Ser Thr Ile Gly Arg Asp Leu			
	50	55	60
Ile Asp Asp Leu Lys Ser Glu Leu Ser Gly Asn Phe Glu Gln Val Ile			
65	70	75	80
Val Gly Met Met Thr Pro Thr Val Leu Tyr Asp Val Gln Glu Leu Arg			
	85	90	95
Arg Ala Met Lys Gly Ala Gly Thr Asp Glu Gly Cys Leu Ile Glu Ile			
	100	105	110
Leu Ala Ser Arg Thr Pro Glu Glu Ile Arg Arg Ile Ser Gln Thr Tyr			
	115	120	125
Gln Gln Gln Tyr Gly Arg Ser Leu Glu Asp Asp Ile Arg Ser Asp Thr			
	130	135	140
Ser Phe Met Phe Gln Arg Val Leu Val Ser Leu Ser Ala Gly Gly Arg			
145	150	155	160
Asp Glu Gly Asn Tyr Leu Asp Asp Ala Leu Val Arg Gln Asp Ala Gln			
	165	170	175

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

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

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

385	390	395	400
Arg Arg Glu Ile Arg Val Leu His Leu Leu Glu Gln Ile Arg Ala Tyr			
	405	410	415
Cys Glu Thr Cys Trp Glu Trp Gln Glu Ala His Glu Pro Gly Met Asp			
	420	425	430
Gln Asp Lys Asn Pro Met Pro Ala Pro Val Glu His Gln Ile Cys Pro			
	435	440	445
Ala Val Cys Val Leu Met Lys Leu Ser Phe Asp Glu Glu His Arg His			
	450	455	460
Ala Met Asn Glu Leu Gly Gly Leu Gln Ala Ile Ala Glu Leu Leu Gln			
465	470	475	480
Val Asp Cys Glu Met Tyr Gly Leu Thr Asn Asp His Tyr Ser Ile Thr			
	485	490	495
Leu Arg Arg Tyr Ala Gly Met Ala Leu Thr Asn Leu Thr Phe Gly Asp			
	500	505	510
Val Ala Asn Lys Ala Thr Leu Cys Ser Met Lys Gly Cys Met Arg Ala			
	515	520	525
Leu Val Ala Gln Leu Lys Ser Glu Ser Glu Asp Leu Gln Gln Val Ile			
	530	535	540
Ala Ser Val Leu Arg Asn Leu Ser Trp Arg Ala Asp Val Asn Ser Lys			
545	550	555	560
Lys Thr Leu Arg Glu Val Gly Ser Val Lys Ala Leu Met Glu Cys Ala			
	565	570	575
Leu Glu Val Lys Lys Glu Ser Thr Leu Lys Ser Val Leu Ser Ala Leu			
	580	585	590
Trp Asn Leu Ser Ala His Cys Thr Glu Asn Lys Ala Asp Ile Cys Ala			
	595	600	605
Val Asp Gly Ala Leu Ala Phe Leu Val Gly Thr Leu Thr Tyr Arg Ser			
	610	615	620
Gln Thr Asn Thr Leu Ala Ile Ile Glu Ser Gly Gly Gly Ile Leu Arg			
625	630	635	640
Asn Val Ser Ser Leu Ile Ala Thr Asn Glu Asp His Arg Gln Ile Leu			
	645	650	655
Arg Glu Asn Asn Cys Leu Gln Thr Leu Leu Gln His Leu Lys Ser His			
	660	665	670
Ser Leu Thr Ile Val Ser Asn Ala Cys Gly Thr Leu Trp Asn Leu Ser			
	675	680	685
Ala Arg Asn Pro Lys Asp Gln Glu Ala Leu Trp Asp Met Gly Ala Val			
690	695	700	

Ser Met Leu Lys Asn Leu Ile His Ser Lys His Lys Met Ile Ala Met			
705	710	715	720
Gly Ser Ala Ala Ala Leu Arg Asn Leu Met Ala Asn Arg Pro Ala Lys			
	725	730	735
Tyr Lys Asp Ala Asn Ile Met Ser Pro Gly Ser Ser Leu Pro Ser Leu			
	740	745	750
His Val Arg Lys Gln Lys Ala Leu Glu Ala Glu Leu Asp Ala Gln His			
	755	760	765
Leu Ser Glu Thr Phe Asp Asn Ile Asp Asn Leu Ser Pro Lys Ala Ser			
	770	775	780
His Arg Ser Lys Gln Arg His Lys Gln Ser Leu Tyr Gly Asp Tyr Val			
785	790	795	800
Phe Asp Thr Asn Arg His Asp Asp Asn Arg Ser Asp Asn Phe Asn Thr			
	805	810	815
Gly Asn Met Thr Val Leu Ser Pro Tyr Leu Asn Thr Thr Val Leu Pro			
	820	825	830
Ser Ser Ser Ser Ser Arg Gly Ser Leu Asp Ser Ser Arg Ser Glu Lys			
	835	840	845
Asp Arg Ser Leu Glu Arg Glu Arg Gly Ile Gly Leu Gly Asn Tyr His			
	850	855	860
Pro Ala Thr Glu Asn Pro Gly Thr Ser Ser Lys Arg Gly Leu Gln Ile			
865	870	875	880
Ser Thr Thr Ala Ala Gln Ile Ala Lys Val Met Glu Glu Val Ser Ala			
	885	890	895
Ile His Thr Ser Gln Glu Asp Arg Ser Ser Gly Ser Thr Thr Glu Leu			
	900	905	910
His Cys Val Thr Asp Glu Arg Asn Ala Leu Arg Arg Ser Ser Ala Ala			
	915	920	925
His Thr His Ser Asn Thr Tyr Asn Phe Thr Lys Ser Glu Asn Ser Asn			
	930	935	940
Arg Thr Cys Ser Met Pro Tyr Ala Lys Leu Glu Tyr Lys Arg Ser Ser			
945	950	955	960
Asn Asp Ser Leu Asn Ser Val Ser Ser Ser Asp Gly Tyr Gly Lys Arg			
	965	970	975
Gly Gln Met Lys Pro Ser Ile Glu Ser Tyr Ser Glu Asp Asp Glu Ser			
	980	985	990
Lys Phe Cys Ser Tyr Gly Gln Tyr Pro Ala Asp Leu Ala His Lys Ile			
	995	1000	1005
His Ser Ala Asn His Met Asp Asp Asn Asp Gly Glu Leu Asp Thr			

1010	1015	1020
Pro Ile Asn Tyr Ser Leu	Lys Tyr Ser Asp Glu	Gln Leu Asn Ser
1025	1030	1035
Gly Arg Gln Ser Pro Ser	Gln Asn Glu Arg Trp	Ala Arg Pro Lys
1040	1045	1050
His Ile Ile Glu Asp Glu	Ile Lys Gln Ser Glu	Gln Arg Gln Ser
1055	1060	1065
Arg Asn Gln Ser Thr Thr	Tyr Pro Val Tyr Thr	Glu Ser Thr Asp
1070	1075	1080
Asp Lys His Leu Lys Phe	Gln Pro His Phe Gly	Gln Gln Glu Cys
1085	1090	1095
Val Ser Pro Tyr Arg Ser	Arg Gly Ala Asn Gly	Ser Glu Thr Asn
1100	1105	1110
Arg Val Gly Ser Asn His	Gly Ile Asn Gln Asn	Val Ser Gln Ser
1115	1120	1125
Leu Cys Gln Glu Asp Asp	Tyr Glu Asp Asp Lys	Pro Thr Asn Tyr
1130	1135	1140
Ser Glu Arg Tyr Ser Glu	Glu Glu Gln His Glu	Glu Glu Glu Arg
1145	1150	1155
Pro Thr Asn Tyr Ser Ile	Lys Tyr Asn Glu Glu	Lys Arg His Val
1160	1165	1170
Asp Gln Pro Ile Asp Tyr	Ser Leu Lys Tyr Ala	Thr Asp Ile Pro
1175	1180	1185
Ser Ser Gln Lys Gln Ser	Phe Ser Phe Ser Lys	Ser Ser Ser Gly
1190	1195	1200
Gln Ser Ser Lys Thr Glu	His Met Ser Ser Ser	Ser Glu Asn Thr
1205	1210	1215
Ser Thr Pro Ser Ser Asn	Ala Lys Arg Gln Asn	Gln Leu His Pro
1220	1225	1230
Ser Ser Ala Gln Ser Arg	Ser Gly Gln Pro Gln	Lys Ala Ala Thr
1235	1240	1245
Cys Lys Val Ser Ser Ile	Asn Gln Glu Thr Ile	Gln Thr Tyr Cys
1250	1255	1260
Val Glu Asp Thr Pro Ile	Cys Phe Ser Arg Cys	Ser Ser Leu Ser
1265	1270	1275
Ser Leu Ser Ser Ala Glu	Asp Glu Ile Gly Cys	Asn Gln Thr Thr
1280	1285	1290
Gln Glu Ala Asp Ser Ala	Asn Thr Leu Gln Ile	Ala Glu Ile Lys
1295	1300	1305

Glu Lys Ile Gly Thr Arg Ser Ala Glu Asp Pro Val Ser Glu Val		
1310	1315	1320
Pro Ala Val Ser Gln His Pro Arg Thr Lys Ser Ser Arg Leu Gln		
1325	1330	1335
Gly Ser Ser Leu Ser Ser Glu Ser Ala Arg His Lys Ala Val Glu		
1340	1345	1350
Phe Ser Ser Gly Ala Lys Ser Pro Ser Lys Ser Gly Ala Gln Thr		
1355	1360	1365
Pro Lys Ser Pro Pro Glu His Tyr Val Gln Glu Thr Pro Leu Met		
1370	1375	1380
Phe Ser Arg Cys Thr Ser Val Ser Ser Leu Asp Ser Phe Glu Ser		
1385	1390	1395
Arg Ser Ile Ala Ser Ser Val Gln Ser Glu Pro Cys Ser Gly Met		
1400	1405	1410
Val Ser Gly Ile Ile Ser Pro Ser Asp Leu Pro Asp Ser Pro Gly		
1415	1420	1425
Gln Thr Met Pro Pro Ser Arg Ser Lys Thr Pro Pro Pro Pro Pro		
1430	1435	1440
Gln Thr Ala Gln Thr Lys Arg Glu Val Pro Lys Asn Lys Ala Pro		
1445	1450	1455
Thr Ala Glu Lys Arg Glu Ser Gly Pro Lys Gln Ala Ala Val Asn		
1460	1465	1470
Ala Ala Val Gln Arg Val Gln Val Leu Pro Asp Ala Asp Thr Leu		
1475	1480	1485
Leu His Phe Ala Thr Glu Ser Thr Pro Asp Gly Phe Ser Cys Ser		
1490	1495	1500
Ser Ser Leu Ser Ala Leu Ser Leu Asp Glu Pro Phe Ile Gln Lys		
1505	1510	1515
Asp Val Glu Leu Arg Ile Met Pro Pro Val Gln Glu Asn Asp Asn		
1520	1525	1530
Gly Asn Glu Thr Glu Ser Glu Gln Pro Lys Glu Ser Asn Glu Asn		
1535	1540	1545
Gln Glu Lys Glu Ala Glu Lys Thr Ile Asp Ser Glu Lys Asp Leu		
1550	1555	1560
Leu Asp Asp Ser Asp Asp Asp Asp Ile Glu Ile Leu Glu Glu Cys		
1565	1570	1575
Ile Ile Ser Ala Met Pro Thr Lys Ser Ser Arg Lys Ala Lys Lys		
1580	1585	1590
Pro Ala Gln Thr Ala Ser Lys Leu Pro Pro Pro Val Ala Arg Lys		

1595	1600	1605
Pro Ser Gln Leu Pro Val	Tyr Lys Leu Leu Pro	Ser Gln Asn Arg
1610	1615	1620
Leu Gln Pro Gln Lys His	Val Ser Phe Thr Pro	Gly Asp Asp Met
1625	1630	1635
Pro Arg Val Tyr Cys Val	Glu Gly Thr Pro Ile	Asn Phe Ser Thr
1640	1645	1650
Ala Thr Ser Leu Ser Asp	Leu Thr Ile Glu Ser	Pro Pro Asn Glu
1655	1660	1665
Leu Ala Ala Gly Glu Gly	Val Arg Gly Gly Ala	Gln Ser Gly Glu
1670	1675	1680
Phe Glu Lys Arg Asp Thr	Ile Pro Thr Glu Gly	Arg Ser Thr Asp
1685	1690	1695
Glu Ala Gln Gly Gly Lys	Thr Ser Ser Val Thr	Ile Pro Glu Leu
1700	1705	1710
Asp Asp Asn Lys Ala Glu	Glu Gly Asp Ile Leu	Ala Glu Cys Ile
1715	1720	1725
Asn Ser Ala Met Pro Lys	Gly Lys Ser His Lys	Pro Phe Arg Val
1730	1735	1740
Lys Lys Ile Met Asp Gln	Val Gln Gln Ala Ser	Ala Ser Ser Ser
1745	1750	1755
Ala Pro Asn Lys Asn Gln	Leu Asp Gly Lys Lys	Lys Lys Pro Thr
1760	1765	1770
Ser Pro Val Lys Pro Ile	Pro Gln Asn Thr Glu	Tyr Arg Thr Arg
1775	1780	1785
Val Arg Lys Asn Ala Asp	Ser Lys Asn Asn Leu	Asn Ala Glu Arg
1790	1795	1800
Val Phe Ser Asp Asn Lys	Asp Ser Lys Lys Gln	Asn Leu Lys Asn
1805	1810	1815
Asn Ser Lys Val Phe Asn	Asp Lys Leu Pro Asn	Asn Glu Asp Arg
1820	1825	1830
Val Arg Gly Ser Phe Ala	Phe Asp Ser Pro His	His Tyr Thr Pro
1835	1840	1845
Ile Glu Gly Thr Pro Tyr	Cys Phe Ser Arg Asn	Asp Ser Leu Ser
1850	1855	1860
Ser Leu Asp Phe Asp Asp	Asp Asp Val Asp Leu	Ser Arg Glu Lys
1865	1870	1875
Ala Glu Leu Arg Lys Ala	Lys Glu Asn Lys Glu	Ser Glu Ala Lys
1880	1885	1890

Val Thr Ser His Thr Glu Leu Thr Ser Asn Gln Gln Ser Ala Asn		
1895	1900	1905
Lys Thr Gln Ala Ile Ala Lys Gln Pro Ile Asn Arg Gly Gln Pro		
1910	1915	1920
Lys Pro Ile Leu Gln Lys Gln Ser Thr Phe Pro Gln Ser Ser Lys		
1925	1930	1935
Asp Ile Pro Asp Arg Gly Ala Ala Thr Asp Glu Lys Leu Gln Asn		
1940	1945	1950
Phe Ala Ile Glu Asn Thr Pro Val Cys Phe Ser His Asn Ser Ser		
1955	1960	1965
Leu Ser Ser Leu Ser Asp Ile Asp Gln Glu Asn Asn Asn Lys Glu		
1970	1975	1980
Asn Glu Pro Ile Lys Glu Thr Glu Pro Pro Asp Ser Gln Gly Glu		
1985	1990	1995
Pro Ser Lys Pro Gln Ala Ser Gly Tyr Ala Pro Lys Ser Phe His		
2000	2005	2010
Val Glu Asp Thr Pro Val Cys Phe Ser Arg Asn Ser Ser Leu Ser		
2015	2020	2025
Ser Leu Ser Ile Asp Ser Glu Asp Asp Leu Leu Gln Glu Cys Ile		
2030	2035	2040
Ser Ser Ala Met Pro Lys Lys Lys Lys Pro Ser Arg Leu Lys Gly		
2045	2050	2055
Asp Asn Glu Lys His Ser Pro Arg Asn Met Gly Gly Ile Leu Gly		
2060	2065	2070
Glu Asp Leu Thr Leu Asp Leu Lys Asp Ile Gln Arg Pro Asp Ser		
2075	2080	2085
Glu His Gly Leu Ser Pro Asp Ser Glu Asn Phe Asp Trp Lys Ala		
2090	2095	2100
Ile Gln Glu Gly Ala Asn Ser Ile Val Ser Ser Leu His Gln Ala		
2105	2110	2115
Ala Ala Ala Ala Cys Leu Ser Arg Gln Ala Ser Ser Asp Ser Asp		
2120	2125	2130
Ser Ile Leu Ser Leu Lys Ser Gly Ile Ser Leu Gly Ser Pro Phe		
2135	2140	2145
His Leu Thr Pro Asp Gln Glu Glu Lys Pro Phe Thr Ser Asn Lys		
2150	2155	2160
Gly Pro Arg Ile Leu Lys Pro Gly Glu Lys Ser Thr Leu Glu Thr		
2165	2170	2175
Lys Lys Ile Glu Ser Glu Ser Lys Gly Ile Lys Gly Gly Lys Lys		

2180	2185	2190
Val Tyr Lys Ser Leu Ile	Thr Gly Lys Val Arg	Ser Asn Ser Glu
2195	2200	2205
Ile Ser Gly Gln Met Lys	Gln Pro Leu Gln Ala	Asn Met Pro Ser
2210	2215	2220
Ile Ser Arg Gly Arg Thr	Met Ile His Ile Pro	Gly Val Arg Asn
2225	2230	2235
Ser Ser Ser Ser Thr Ser	Pro Val Ser Lys Lys	Gly Pro Pro Leu
2240	2245	2250
Lys Thr Pro Ala Ser Lys	Ser Pro Ser Glu Gly	Gln Thr Ala Thr
2255	2260	2265
Thr Ser Pro Arg Gly Ala	Lys Pro Ser Val Lys	Ser Glu Leu Ser
2270	2275	2280
Pro Val Ala Arg Gln Thr	Ser Gln Ile Gly Gly	Ser Ser Lys Ala
2285	2290	2295
Pro Ser Arg Ser Gly Ser	Arg Asp Ser Thr Pro	Ser Arg Pro Ala
2300	2305	2310
Gln Gln Pro Leu Ser Arg	Pro Ile Gln Ser Pro	Gly Arg Asn Ser
2315	2320	2325
Ile Ser Pro Gly Arg Asn	Gly Ile Ser Pro Pro	Asn Lys Leu Ser
2330	2335	2340
Gln Leu Pro Arg Thr Ser	Ser Pro Ser Thr Ala	Ser Thr Lys Ser
2345	2350	2355
Ser Gly Ser Gly Lys Met	Ser Tyr Thr Ser Pro	Gly Arg Gln Met
2360	2365	2370
Ser Gln Gln Asn Leu Thr	Lys Gln Thr Gly Leu	Ser Lys Asn Ala
2375	2380	2385
Ser Ser Ile Pro Arg Ser	Glu Ser Ala Ser Lys	Gly Leu Asn Gln
2390	2395	2400
Met Asn Asn Gly Asn Gly	Ala Asn Lys Lys Val	Glu Leu Ser Arg
2405	2410	2415
Met Ser Ser Thr Lys Ser	Ser Gly Ser Glu Ser	Asp Arg Ser Glu
2420	2425	2430
Arg Pro Val Leu Val Arg	Gln Ser Thr Phe Ile	Lys Glu Ala Pro
2435	2440	2445
Ser Pro Thr Leu Arg Arg	Lys Leu Glu Glu Ser	Ala Ser Phe Glu
2450	2455	2460
Ser Leu Ser Pro Ser Ser	Arg Pro Ala Ser Pro	Thr Arg Ser Gln
2465	2470	2475

Ala Gln Thr Pro Val Leu Ser Pro Ser Leu Pro Asp Met Ser Leu		
2480	2485	2490
Ser Thr His Ser Ser Val Gln Ala Gly Gly Trp Arg Lys Leu Pro		
2495	2500	2505
Pro Asn Leu Ser Pro Thr Ile Glu Tyr Asn Asp Gly Arg Pro Ala		
2510	2515	2520
Lys Arg His Asp Ile Ala Arg Ser His Ser Glu Ser Pro Ser Arg		
2525	2530	2535
Leu Pro Ile Asn Arg Ser Gly Thr Trp Lys Arg Glu His Ser Lys		
2540	2545	2550
His Ser Ser Ser Leu Pro Arg Val Ser Thr Trp Arg Arg Thr Gly		
2555	2560	2565
Ser Ser Ser Ser Ile Leu Ser Ala Ser Ser Glu Ser Ser Glu Lys		
2570	2575	2580
Ala Lys Ser Glu Asp Glu Lys His Val Asn Ser Ile Ser Gly Thr		
2585	2590	2595
Lys Gln Ser Lys Glu Asn Gln Val Ser Ala Lys Gly Thr Trp Arg		
2600	2605	2610
Lys Ile Lys Glu Asn Glu Phe Ser Pro Thr Asn Ser Thr Ser Gln		
2615	2620	2625
Thr Val Ser Ser Gly Ala Thr Asn Gly Ala Glu Ser Lys Thr Leu		
2630	2635	2640
Ile Tyr Gln Met Ala Pro Ala Val Ser Lys Thr Glu Asp Val Trp		
2645	2650	2655
Val Arg Ile Glu Asp Cys Pro Ile Asn Asn Pro Arg Ser Gly Arg		
2660	2665	2670
Ser Pro Thr Gly Asn Thr Pro Pro Val Ile Asp Ser Val Ser Glu		
2675	2680	2685
Lys Ala Asn Pro Asn Ile Lys Asp Ser Lys Asp Asn Gln Ala Lys		
2690	2695	2700
Gln Asn Val Gly Asn Gly Ser Val Pro Met Arg Thr Val Gly Leu		
2705	2710	2715
Glu Asn Arg Leu Asn Ser Phe Ile Gln Val Asp Ala Pro Asp Gln		
2720	2725	2730
Lys Gly Thr Glu Ile Lys Pro Gly Gln Asn Asn Pro Val Pro Val		
2735	2740	2745
Ser Glu Thr Asn Glu Ser Ser Ile Val Glu Arg Thr Pro Phe Ser		
2750	2755	2760
Ser Ser Ser Ser Ser Lys His Ser Ser Pro Ser Gly Thr Val Ala		

2765	2770	2775
Ala Arg Val Thr Pro Phe	Asn Tyr Asn Pro Ser	Pro Arg Lys Ser
2780	2785	2790
Ser Ala Asp Ser Thr Ser	Ala Arg Pro Ser Gln	Ile Pro Thr Pro
2795	2800	2805
Val Asn Asn Asn Thr Lys	Lys Arg Asp Ser Lys	Thr Asp Ser Thr
2810	2815	2820
Glu Ser Ser Gly Thr Gln	Ser Pro Lys Arg His	Ser Gly Ser Tyr
2825	2830	2835
Leu Val Thr Ser Val		
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<213> 智人		
<400> 17		
Met Lys Ala Ala Val Leu Thr Leu Ala Val Leu Phe Leu Thr Gly Ser		
1	5	10
Gln Ala Arg His Phe Trp Gln Gln Asp Glu Pro Pro Gln Ser Pro Trp		
20	25	30
Asp Arg Val Lys Asp Leu Ala Thr Val Tyr Val Asp Val Leu Lys Asp		
35	40	45
Ser Gly Arg Asp Tyr Val Ser Gln Phe Glu Gly Ser Ala Leu Gly Lys		
50	55	60
Gln Leu Asn Leu Lys Leu Leu Asp Asn Trp Asp Ser Val Thr Ser Thr		
65	70	75
Phe Ser Lys Leu Arg Glu Gln Leu Gly Pro Val Thr Gln Glu Phe Trp		
85	90	95
Asp Asn Leu Glu Lys Glu Thr Glu Gly Leu Arg Gln Glu Met Ser Lys		
100	105	110
Asp Leu Glu Glu Val Lys Ala Lys Val Gln Pro Tyr Leu Asp Asp Phe		
115	120	125
Gln Lys Lys Trp Gln Glu Glu Met Glu Leu Tyr Arg Gln Lys Val Glu		
130	135	140
Pro Leu Arg Ala Glu Leu Gln Glu Gly Ala Arg Gln Lys Leu His Glu		
145	150	155
Leu Gln Glu Lys Leu Ser Pro Leu Gly Glu Glu Met Arg Asp Arg Ala		
165	170	175
Arg Ala His Val Asp Ala Leu Arg Thr His Leu Ala Pro Tyr Ser Asp		

180	185	190
Glu Leu Arg Gln Arg Leu Ala Ala Arg Leu Glu Ala Leu Lys Glu Asn		
195	200	205
Gly Gly Ala Arg Leu Ala Glu Tyr His Ala Lys Ala Thr Glu His Leu		
210	215	220
Ser Thr Leu Ser Glu Lys Ala Lys Pro Ala Leu Glu Asp Leu Arg Gln		
225	230	235
Gly Leu Leu Pro Val Leu Glu Ser Phe Lys Val Ser Phe Leu Ser Ala		
245	250	255
Leu Glu Glu Tyr Thr Lys Lys Leu Asn Thr Gln		
260	265	
<210> 18		
<211> 83		
<212> PRT		
<213> 智人		
<400> 18		
Met Arg Leu Phe Leu Ser Leu Pro Val Leu Val Val Val Leu Ser Ile		
1	5	10
Val Leu Glu Gly Pro Ala Pro Ala Gln Gly Thr Pro Asp Val Ser Ser		
20	25	30
Ala Leu Asp Lys Leu Lys Glu Phe Gly Asn Thr Leu Glu Asp Lys Ala		
35	40	45
Arg Glu Leu Ile Ser Arg Ile Lys Gln Ser Glu Leu Ser Ala Lys Met		
50	55	60
Arg Glu Trp Phe Ser Glu Thr Phe Gln Lys Val Lys Glu Lys Leu Lys		
65	70	75
Ile Asp Ser		
<210> 19		
<211> 345		
<212> PRT		
<213> 智人		
<400> 19		
Met Ile Ser Pro Val Leu Ile Leu Phe Ser Ser Phe Leu Cys His Val		
1	5	10
Ala Ile Ala Gly Arg Thr Cys Pro Lys Pro Asp Asp Leu Pro Phe Ser		
20	25	30
Thr Val Val Pro Leu Lys Thr Phe Tyr Glu Pro Gly Glu Glu Ile Thr		
35	40	45
Tyr Ser Cys Lys Pro Gly Tyr Val Ser Arg Gly Gly Met Arg Lys Phe		

50	55	60
Ile Cys Pro Leu Thr Gly	Leu Trp Pro Ile Asn Thr	Leu Lys Cys Thr
65	70	75
Pro Arg Val Cys Pro Phe	Ala Gly Ile Leu Glu Asn Gly	Ala Val Arg
85	90	95
Tyr Thr Thr Phe Glu Tyr	Pro Asn Thr Ile Ser Phe Ser	Cys Asn Thr
100	105	110
Gly Phe Tyr Leu Asn Gly	Ala Asp Ser Ala Lys Cys Thr	Glu Glu Gly
115	120	125
Lys Trp Ser Pro Glu Leu	Pro Val Cys Ala Pro Ile Ile	Cys Pro Pro
130	135	140
Pro Ser Ile Pro Thr Phe	Ala Thr Leu Arg Val Tyr Lys	Pro Ser Ala
145	150	155
Gly Asn Asn Ser Leu Tyr	Arg Asp Thr Ala Val Phe Glu	Cys Leu Pro
165	170	175
Gln His Ala Met Phe Gly	Asn Asp Thr Ile Thr Cys Thr	Thr His Gly
180	185	190
Asn Trp Thr Lys Leu Pro	Glu Cys Arg Glu Val Lys Cys	Pro Phe Pro
195	200	205
Ser Arg Pro Asp Asn Gly	Phe Val Asn Tyr Pro Ala Lys	Pro Thr Leu
210	215	220
Tyr Tyr Lys Asp Lys Ala	Thr Phe Gly Cys His Asp Gly	Tyr Ser Leu
225	230	235
Asp Gly Pro Glu Glu Ile	Glu Cys Thr Lys Leu Gly Asn	Trp Ser Ala
245	250	255
Met Pro Ser Cys Lys Ala	Ser Cys Lys Val Pro Val Lys	Lys Ala Thr
260	265	270
Val Val Tyr Gln Gly Glu	Arg Val Lys Ile Gln Glu Lys	Phe Lys Asn
275	280	285
Gly Met Leu His Gly Asp	Lys Val Ser Phe Phe Cys Lys	Asn Lys Glu
290	295	300
Lys Lys Cys Ser Tyr Thr	Glu Asp Ala Gln Cys Ile Asp	Gly Thr Ile
305	310	315
Glu Val Pro Lys Cys Phe	Lys Glu His Ser Ser Leu Ala	Phe Trp Lys
325	330	335
Thr Asp Ala Ser Asp Val	Lys Pro Cys	
340	345	
<210> 20		
<211> 204		

<212> PRT

<213> 智人

<400> 20

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

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<210> 21

<211> 529

<212> PRT

<213> 智人

<400> 21

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Met Leu Gly Phe Val Gly Arg Val Ala Ala Ala Pro Ala Ser Gly Ala
1           5           10           15
Leu Arg Arg Leu Thr Pro Ser Ala Ser Leu Pro Pro Ala Gln Leu Leu
           20           25           30
Leu Arg Ala Ala Pro Thr Ala Val His Pro Val Arg Asp Tyr Ala Ala

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

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

Ser

<210> 22

<211> 785

<212> PRT

<213> 智人

<400> 22

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

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

Phe Ser Ile Gln Glu Ile Asp Ile Asn Asn Glu Gln Glu Asn Asp Tyr		
405	410	415
Glu Glu Asp Ile Ala Ser Phe Ser Thr Tyr Ile Pro Ser Thr Gln Asn		
420	425	430
Pro Ala Phe His His Glu Ser Arg Lys Thr Tyr Gly Gln Ser Ala Asp		
435	440	445
Gly Ala Glu Ala Asn Glu Met Glu Gly Glu Gly Lys Gln Asn Gly Ser		
450	455	460
Gly Met Glu Thr Lys His Ser Pro Leu Glu Val Gly Ser Glu Ser Ser		
465	470	475
Glu Asp Gln Tyr Asp Asp Leu Tyr Val Phe Ile Pro Gly Ala Asp Pro		
485	490	495
Glu Asn Asn Ser Gln Glu Pro Leu Met Ser Ser Arg Pro Pro Leu Pro		
500	505	510
Pro Pro Arg Pro Val Ala Asn Ala Phe Gln Leu Glu Arg Pro His Phe		
515	520	525
Thr Leu Pro Gly Thr Met Val Glu Gly Gln Met Glu Arg Ser Gln Asn		
530	535	540
Trp Gly His Pro Gly Val Arg Gln Glu Thr Gly Asp Glu Pro Lys Gly		
545	550	555
Glu Lys Glu Lys Lys Glu Glu Glu Lys Glu Gln Glu Glu Glu Glu Asp		
565	570	575
Pro Tyr Thr Phe Ala Glu Ile Asp Asp Ser Glu Tyr Asp Met Ile Leu		
580	585	590
Ala Asn Leu Ser Ile Lys Lys Lys Thr Gly Ser Arg Ser Phe Ile Ile		
595	600	605
Asn Arg Pro Pro Ala Pro Thr Pro Arg Pro Thr Ser Ile Pro Pro Lys		
610	615	620
Glu Glu Thr Thr Pro Tyr Ile Ala Gln Val Phe Gln Gln Lys Thr Ala		
625	630	635
Arg Arg Gln Ser Asp Asp Asp Lys Phe Cys Gly Leu Pro Lys Lys Gln		
645	650	655
Asp Arg Ala Arg Ile Glu Ser Pro Ala Phe Ser Thr Leu Arg Gly Cys		
660	665	670
Leu Thr Asp Gly Gln Glu Glu Leu Ile Leu Leu Gln Glu Lys Val Lys		
675	680	685
Asn Gly Lys Met Ser Met Asp Glu Ala Leu Glu Lys Phe Lys His Trp		
690	695	700
Gln Met Gly Lys Ser Gly Leu Glu Met Ile Gln Gln Glu Lys Leu Arg		

705	710	715	720
Gln Leu Arg Asp Cys Ile Ile Gly Lys Arg Pro Glu Glu Glu Asn Val			
	725	730	735
Tyr Asn Lys Leu Thr Ile Val His His Pro Gly Gly Lys Glu Thr Ala			
	740	745	750
His Asn Glu Asn Lys Phe Tyr Asn Val His Phe Ser Asn Lys Leu Pro			
	755	760	765
Ala Arg Pro Gln Val Glu Lys Glu Phe Gly Phe Cys Cys Lys Lys Asp			
	770	775	780
His			
785			
<210> 23			
<211> 657			
<212> PRT			
<213> 智人			
<400> 23			
Met Gly Glu Glu Asp Tyr Tyr Leu Glu Leu Cys Glu Arg Pro Val Gln			
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Phe Glu Lys Ala Asn Pro Val Asn Cys Val Phe Phe Asp Glu Ala Asn			
	20	25	30
Lys Gln Val Phe Ala Val Arg Ser Gly Gly Ala Thr Gly Val Val Val			
	35	40	45
Lys Gly Pro Asp Asp Arg Asn Pro Ile Ser Phe Arg Met Asp Asp Lys			
	50	55	60
Gly Glu Val Lys Cys Ile Lys Phe Ser Leu Glu Asn Lys Ile Leu Ala			
65	70	75	80
Val Gln Arg Thr Ser Lys Thr Val Asp Phe Cys Asn Phe Ile Pro Asp			
	85	90	95
Asn Ser Gln Leu Glu Tyr Thr Gln Glu Cys Lys Thr Lys Asn Ala Asn			
	100	105	110
Ile Leu Gly Phe Cys Trp Thr Ser Ser Thr Glu Ile Val Phe Ile Thr			
	115	120	125
Asp Gln Gly Ile Glu Phe Tyr Gln Val Leu Pro Glu Lys Arg Ser Leu			
	130	135	140
Lys Leu Leu Lys Ser His Asn Leu Asn Val Asn Trp Tyr Met Tyr Cys			
145	150	155	160
Pro Glu Ser Ala Val Ile Leu Leu Ser Thr Thr Val Leu Glu Asn Val			
	165	170	175
Leu Gln Pro Phe His Phe Arg Ala Gly Thr Met Ser Lys Leu Pro Lys			

	180						185						190					
Phe	Glu	Ile	Glu	Leu	Pro	Ala	Ala	Pro	Lys	Ser	Thr	Lys	Pro	Ser	Leu			
	195						200						205					
Ser	Glu	Arg	Asp	Ile	Ala	Met	Ala	Thr	Ile	Tyr	Gly	Gln	Leu	Tyr	Val			
	210						215						220					
Leu	Phe	Leu	Arg	His	His	Ser	Arg	Thr	Ser	Asn	Ser	Thr	Gly	Ala	Glu			
225					230					235					240			
Val	Val	Leu	Tyr	His	Leu	Pro	Arg	Glu	Gly	Ala	Cys	Lys	Lys	Met	His			
	245						250						255					
Ile	Leu	Lys	Leu	Asn	Arg	Thr	Gly	Lys	Phe	Ala	Leu	Asn	Val	Val	Asp			
	260						265						270					
Asn	Leu	Val	Val	Val	His	His	Gln	Asp	Thr	Glu	Thr	Ser	Val	Ile	Phe			
	275						280						285					
Asp	Ile	Lys	Leu	Arg	Gly	Glu	Phe	Asp	Gly	Ser	Val	Thr	Phe	His	His			
	290						295						300					
Pro	Val	Leu	Pro	Ala	Arg	Ser	Ile	Gln	Pro	Tyr	Gln	Ile	Pro	Ile	Thr			
305					310					315					320			
Gly	Pro	Ala	Ala	Val	Thr	Ser	Gln	Ser	Pro	Val	Pro	Cys	Lys	Leu	Tyr			
	325						330						335					
Ser	Ser	Ser	Trp	Ile	Val	Phe	Gln	Pro	Asp	Ile	Ile	Ile	Ser	Ala	Ser			
	340						345						350					
Gln	Gly	Tyr	Leu	Trp	Asn	Leu	Gln	Val	Lys	Leu	Glu	Pro	Ile	Val	Asn			
	355						360						365					
Leu	Leu	Pro	Asp	Lys	Gly	Arg	Leu	Met	Asp	Phe	Leu	Leu	Gln	Arg	Lys			
	370						375						380					
Glu	Cys	Lys	Met	Val	Ile	Leu	Ser	Val	Cys	Ser	Gln	Met	Leu	Ser	Glu			
385					390					395					400			
Ser	Asp	Arg	Ala	Ser	Leu	Pro	Val	Ile	Ala	Thr	Val	Phe	Asp	Lys	Leu			
	405						410						415					
Asn	His	Glu	Tyr	Lys	Lys	Tyr	Leu	Asp	Ala	Glu	Gln	Ser	Tyr	Ala	Met			
	420						425						430					
Ala	Val	Glu	Ala	Gly	Gln	Ser	Arg	Ser	Ser	Pro	Leu	Leu	Lys	Arg	Pro			
	435						440						445					
Val	Arg	Thr	Gln	Ala	Val	Leu	Asp	Gln	Ser	Asp	Val	Tyr	Thr	His	Val			
	450						455						460					
Leu	Ser	Ala	Phe	Val	Glu	Lys	Lys	Glu	Met	Pro	His	Lys	Phe	Val	Ile			
465					470					475					480			
Ala	Val	Leu	Met	Glu	Tyr	Ile	Arg	Ser	Leu	Asn	Gln	Phe	Gln	Ile	Ala			
	485						490						495					

Val	Gln	His	Tyr	Leu	His	Glu	Leu	Val	Ile	Lys	Thr	Leu	Val	Gln	His
500				505				510							
Asn	Leu	Phe	Tyr	Met	Leu	His	Gln	Phe	Leu	Gln	Tyr	His	Val	Leu	Ser
515				520				525							
Asp	Ser	Lys	Pro	Leu	Ala	Cys	Leu	Leu	Leu	Ser	Leu	Glu	Ser	Phe	Tyr
530				535				540							
Pro	Pro	Ala	His	Gln	Leu	Ser	Leu	Asp	Met	Leu	Lys	Arg	Leu	Ser	Thr
545				550				555				560			
Ala	Asn	Asp	Glu	Ile	Val	Glu	Val	Leu	Leu	Ser	Lys	His	Gln	Val	Leu
565				570				575							
Ala	Ala	Leu	Arg	Phe	Ile	Arg	Gly	Ile	Gly	Gly	His	Asp	Asn	Ile	Ser
580				585				590							
Ala	Arg	Lys	Phe	Leu	Asp	Ala	Ala	Lys	Gln	Thr	Glu	Asp	Asn	Met	Leu
595				600				605							
Phe	Tyr	Thr	Ile	Phe	Arg	Phe	Phe	Glu	Gln	Arg	Asn	Gln	Arg	Leu	Arg
610				615				620							
Gly	Ser	Pro	Asn	Phe	Thr	Pro	Gly	Glu	His	Cys	Glu	Glu	His	Val	Ala
625				630				635				640			
Phe	Phe	Lys	Gln	Ile	Phe	Gly	Asp	Gln	Ala	Leu	Met	Arg	Pro	Thr	Thr
645				650				655							

Phe

<210> 24

<211> 126

<212> PRT

<213> 智人

<400> 24

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

	100		105		110
Ser Val Val	Leu Pro Ala	Ser Asn His	Lys Thr Lys	Gly Gln	
	115		120		125
<210>	25				
<211>	1663				
<212>	PRT				
<213>	智人				
<400>	25				
Met Gly Pro Thr Ser Gly Pro Ser Leu Leu Leu Leu Leu Thr His					
1	5		10		15
Leu Pro Leu Ala Leu Gly Ser Pro Met Tyr Ser Ile Ile Thr Pro Asn					
	20		25		30
Ile Leu Arg Leu Glu Ser Glu Glu Thr Met Val Leu Glu Ala His Asp					
	35		40		45
Ala Gln Gly Asp Val Pro Val Thr Val Thr Val His Asp Phe Pro Gly					
	50		55		60
Lys Lys Leu Val Leu Ser Ser Glu Lys Thr Val Leu Thr Pro Ala Thr					
65	70		75		80
Asn His Met Gly Asn Val Thr Phe Thr Ile Pro Ala Asn Arg Glu Phe					
	85		90		95
Lys Ser Glu Lys Gly Arg Asn Lys Phe Val Thr Val Gln Ala Thr Phe					
	100		105		110
Gly Thr Gln Val Val Glu Lys Val Val Leu Val Ser Leu Gln Ser Gly					
	115		120		125
Tyr Leu Phe Ile Gln Thr Asp Lys Thr Ile Tyr Thr Pro Gly Ser Thr					
	130		135		140
Val Leu Tyr Arg Ile Phe Thr Val Asn His Lys Leu Leu Pro Val Gly					
145	150		155		160
Arg Thr Val Met Val Asn Ile Glu Asn Pro Glu Gly Ile Pro Val Lys					
	165		170		175
Gln Asp Ser Leu Ser Ser Gln Asn Gln Leu Gly Val Leu Pro Leu Ser					
	180		185		190
Trp Asp Ile Pro Glu Leu Val Asn Met Gly Gln Trp Lys Ile Arg Ala					
	195		200		205
Tyr Tyr Glu Asn Ser Pro Gln Gln Val Phe Ser Thr Glu Phe Glu Val					
	210		215		220
Lys Glu Tyr Val Leu Pro Ser Phe Glu Val Ile Val Glu Pro Thr Glu					
225	230		235		240
Lys Phe Tyr Tyr Ile Tyr Asn Glu Lys Gly Leu Glu Val Thr Ile Thr					

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

Gly Ser Leu Val Val Lys Ser Gly Gln Ser Glu Asp Arg Gln Pro Val		
565	570	575
Pro Gly Gln Gln Met Thr Leu Lys Ile Glu Gly Asp His Gly Ala Arg		
580	585	590
Val Val Leu Val Ala Val Asp Lys Gly Val Phe Val Leu Asn Lys Lys		
595	600	605
Asn Lys Leu Thr Gln Ser Lys Ile Trp Asp Val Val Glu Lys Ala Asp		
610	615	620
Ile Gly Cys Thr Pro Gly Ser Gly Lys Asp Tyr Ala Gly Val Phe Ser		
625	630	635
Asp Ala Gly Leu Thr Phe Thr Ser Ser Ser Gly Gln Gln Thr Ala Gln		
645	650	655
Arg Ala Glu Leu Gln Cys Pro Gln Pro Ala Ala Arg Arg Arg Arg Ser		
660	665	670
Val Gln Leu Thr Glu Lys Arg Met Asp Lys Val Gly Lys Tyr Pro Lys		
675	680	685
Glu Leu Arg Lys Cys Cys Glu Asp Gly Met Arg Glu Asn Pro Met Arg		
690	695	700
Phe Ser Cys Gln Arg Arg Thr Arg Phe Ile Ser Leu Gly Glu Ala Cys		
705	710	715
Lys Lys Val Phe Leu Asp Cys Cys Asn Tyr Ile Thr Glu Leu Arg Arg		
725	730	735
Gln His Ala Arg Ala Ser His Leu Gly Leu Ala Arg Ser Asn Leu Asp		
740	745	750
Glu Asp Ile Ile Ala Glu Glu Asn Ile Val Ser Arg Ser Glu Phe Pro		
755	760	765
Glu Ser Trp Leu Trp Asn Val Glu Asp Leu Lys Glu Pro Pro Lys Asn		
770	775	780
Gly Ile Ser Thr Lys Leu Met Asn Ile Phe Leu Lys Asp Ser Ile Thr		
785	790	795
Thr Trp Glu Ile Leu Ala Val Ser Met Ser Asp Lys Lys Gly Ile Cys		
805	810	815
Val Ala Asp Pro Phe Glu Val Thr Val Met Gln Asp Phe Phe Ile Asp		
820	825	830
Leu Arg Leu Pro Tyr Ser Val Val Arg Asn Glu Gln Val Glu Ile Arg		
835	840	845
Ala Val Leu Tyr Asn Tyr Arg Gln Asn Gln Glu Leu Lys Val Arg Val		
850	855	860
Glu Leu Leu His Asn Pro Ala Phe Cys Ser Leu Ala Thr Thr Lys Arg		

865	870	875	880
Arg His Gln Gln Thr Val Thr Ile Pro Pro Lys Ser Ser Leu Ser Val			
	885	890	895
Pro Tyr Val Ile Val Pro Leu Lys Thr Gly Leu Gln Glu Val Glu Val			
	900	905	910
Lys Ala Ala Val Tyr His His Phe Ile Ser Asp Gly Val Arg Lys Ser			
	915	920	925
Leu Lys Val Val Pro Glu Gly Ile Arg Met Asn Lys Thr Val Ala Val			
	930	935	940
Arg Thr Leu Asp Pro Glu Arg Leu Gly Arg Glu Gly Val Gln Lys Glu			
945	950	955	960
Asp Ile Pro Pro Ala Asp Leu Ser Asp Gln Val Pro Asp Thr Glu Ser			
	965	970	975
Glu Thr Arg Ile Leu Leu Gln Gly Thr Pro Val Ala Gln Met Thr Glu			
	980	985	990
Asp Ala Val Asp Ala Glu Arg Leu Lys His Leu Ile Val Thr Pro Ser			
	995	1000	1005
Gly Cys Gly Glu Gln Asn Met Ile Gly Met Thr Pro Thr Val Ile			
	1010	1015	1020
Ala Val His Tyr Leu Asp Glu Thr Glu Gln Trp Glu Lys Phe Gly			
	1025	1030	1035
Leu Glu Lys Arg Gln Gly Ala Leu Glu Leu Ile Lys Lys Gly Tyr			
	1040	1045	1050
Thr Gln Gln Leu Ala Phe Arg Gln Pro Ser Ser Ala Phe Ala Ala			
	1055	1060	1065
Phe Val Lys Arg Ala Pro Ser Thr Trp Leu Thr Ala Tyr Val Val			
	1070	1075	1080
Lys Val Phe Ser Leu Ala Val Asn Leu Ile Ala Ile Asp Ser Gln			
	1085	1090	1095
Val Leu Cys Gly Ala Val Lys Trp Leu Ile Leu Glu Lys Gln Lys			
	1100	1105	1110
Pro Asp Gly Val Phe Gln Glu Asp Ala Pro Val Ile His Gln Glu			
	1115	1120	1125
Met Ile Gly Gly Leu Arg Asn Asn Asn Glu Lys Asp Met Ala Leu			
	1130	1135	1140
Thr Ala Phe Val Leu Ile Ser Leu Gln Glu Ala Lys Asp Ile Cys			
	1145	1150	1155
Glu Glu Gln Val Asn Ser Leu Pro Gly Ser Ile Thr Lys Ala Gly			
	1160	1165	1170

Asp Phe Leu Glu Ala Asn Tyr Met Asn Leu Gln Arg Ser Tyr Thr		
1175	1180	1185
Val Ala Ile Ala Gly Tyr Ala Leu Ala Gln Met Gly Arg Leu Lys		
1190	1195	1200
Gly Pro Leu Leu Asn Lys Phe Leu Thr Thr Ala Lys Asp Lys Asn		
1205	1210	1215
Arg Trp Glu Asp Pro Gly Lys Gln Leu Tyr Asn Val Glu Ala Thr		
1220	1225	1230
Ser Tyr Ala Leu Leu Ala Leu Leu Gln Leu Lys Asp Phe Asp Phe		
1235	1240	1245
Val Pro Pro Val Val Arg Trp Leu Asn Glu Gln Arg Tyr Tyr Gly		
1250	1255	1260
Gly Gly Tyr Gly Ser Thr Gln Ala Thr Phe Met Val Phe Gln Ala		
1265	1270	1275
Leu Ala Gln Tyr Gln Lys Asp Ala Pro Asp His Gln Glu Leu Asn		
1280	1285	1290
Leu Asp Val Ser Leu Gln Leu Pro Ser Arg Ser Ser Lys Ile Thr		
1295	1300	1305
His Arg Ile His Trp Glu Ser Ala Ser Leu Leu Arg Ser Glu Glu		
1310	1315	1320
Thr Lys Glu Asn Glu Gly Phe Thr Val Thr Ala Glu Gly Lys Gly		
1325	1330	1335
Gln Gly Thr Leu Ser Val Val Thr Met Tyr His Ala Lys Ala Lys		
1340	1345	1350
Asp Gln Leu Thr Cys Asn Lys Phe Asp Leu Lys Val Thr Ile Lys		
1355	1360	1365
Pro Ala Pro Glu Thr Glu Lys Arg Pro Gln Asp Ala Lys Asn Thr		
1370	1375	1380
Met Ile Leu Glu Ile Cys Thr Arg Tyr Arg Gly Asp Gln Asp Ala		
1385	1390	1395
Thr Met Ser Ile Leu Asp Ile Ser Met Met Thr Gly Phe Ala Pro		
1400	1405	1410
Asp Thr Asp Asp Leu Lys Gln Leu Ala Asn Gly Val Asp Arg Tyr		
1415	1420	1425
Ile Ser Lys Tyr Glu Leu Asp Lys Ala Phe Ser Asp Arg Asn Thr		
1430	1435	1440
Leu Ile Ile Tyr Leu Asp Lys Val Ser His Ser Glu Asp Asp Cys		
1445	1450	1455
Leu Ala Phe Lys Val His Gln Tyr Phe Asn Val Glu Leu Ile Gln		

1460						1465						1470					
Pro	Gly	Ala	Val	Lys	Val	Tyr	Ala	Tyr	Tyr	Asn	Leu	Glu	Glu	Ser			
1475						1480						1485					
Cys	Thr	Arg	Phe	Tyr	His	Pro	Glu	Lys	Glu	Asp	Gly	Lys	Leu	Asn			
1490						1495						1500					
Lys	Leu	Cys	Arg	Asp	Glu	Leu	Cys	Arg	Cys	Ala	Glu	Glu	Asn	Cys			
1505						1510						1515					
Phe	Ile	Gln	Lys	Ser	Asp	Asp	Lys	Val	Thr	Leu	Glu	Glu	Arg	Leu			
1520						1525						1530					
Asp	Lys	Ala	Cys	Glu	Pro	Gly	Val	Asp	Tyr	Val	Tyr	Lys	Thr	Arg			
1535						1540						1545					
Leu	Val	Lys	Val	Gln	Leu	Ser	Asn	Asp	Phe	Asp	Glu	Tyr	Ile	Met			
1550						1555						1560					
Ala	Ile	Glu	Gln	Thr	Ile	Lys	Ser	Gly	Ser	Asp	Glu	Val	Gln	Val			
1565						1570						1575					
Gly	Gln	Gln	Arg	Thr	Phe	Ile	Ser	Pro	Ile	Lys	Cys	Arg	Glu	Ala			
1580						1585						1590					
Leu	Lys	Leu	Glu	Glu	Lys	Lys	His	Tyr	Leu	Met	Trp	Gly	Leu	Ser			
1595						1600						1605					
Ser	Asp	Phe	Trp	Gly	Glu	Lys	Pro	Asn	Leu	Ser	Tyr	Ile	Ile	Gly			
1610						1615						1620					
Lys	Asp	Thr	Trp	Val	Glu	His	Trp	Pro	Glu	Glu	Asp	Glu	Cys	Gln			
1625						1630						1635					
Asp	Glu	Glu	Asn	Gln	Lys	Gln	Cys	Gln	Asp	Leu	Gly	Ala	Phe	Thr			
1640						1645						1650					
Glu	Ser	Met	Val	Val	Phe	Gly	Cys	Pro	Asn								
1655						1660											
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<211> 559																	
<212> PRT																	
<213> 智人																	
<400> 26																	
Met	Ser	Ala	Cys	Arg	Ser	Phe	Ala	Val	Ala	Ile	Cys	Ile	Leu	Glu	Ile		
1				5				10				15					
Ser	Ile	Leu	Thr	Ala	Gln	Tyr	Thr	Thr	Ser	Tyr	Asp	Pro	Glu	Leu	Thr		
			20				25				30						
Glu	Ser	Ser	Gly	Ser	Ala	Ser	His	Ile	Asp	Cys	Arg	Met	Ser	Pro	Trp		
			35				40				45						
Ser	Glu	Trp	Ser	Gln	Cys	Asp	Pro	Cys	Leu	Arg	Gln	Met	Phe	Arg	Ser		

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

Arg Lys Gly Val Glu Leu Lys Asp Ile Lys Arg Cys Leu Gly Tyr His		
370	375	380
Leu Asp Val Ser Leu Ala Phe Ser Glu Ile Ser Val Gly Ala Glu Phe		
385	390	395 400
Asn Lys Asp Asp Cys Val Lys Arg Gly Glu Gly Arg Ala Val Asn Ile		
405	410	415
Thr Ser Glu Asn Leu Ile Asp Asp Val Val Ser Leu Ile Arg Gly Gly		
420	425	430
Thr Arg Lys Tyr Ala Phe Glu Leu Lys Glu Lys Leu Leu Arg Gly Thr		
435	440	445
Val Ile Asp Val Thr Asp Phe Val Asn Trp Ala Ser Ser Ile Asn Asp		
450	455	460
Ala Pro Val Leu Ile Ser Gln Lys Leu Ser Pro Ile Tyr Asn Leu Val		
465	470	475 480
Pro Val Lys Met Lys Asn Ala His Leu Lys Lys Gln Asn Leu Glu Arg		
485	490	495
Ala Ile Glu Asp Tyr Ile Asn Glu Phe Ser Val Arg Lys Cys His Thr		
500	505	510
Cys Gln Asn Gly Gly Thr Val Ile Leu Met Asp Gly Lys Cys Leu Cys		
515	520	525
Ala Cys Pro Phe Lys Phe Glu Gly Ile Ala Cys Glu Ile Ser Lys Gln		
530	535	540
Lys Ile Ser Glu Gly Leu Pro Ala Leu Glu Phe Pro Asn Glu Lys		
545	550	555
<210> 27		
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<213> 智人		
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Met Ala Ser Pro Asp Trp Gly Tyr Asp Asp Lys Asn Gly Pro Glu Gln		
1	5	10 15
Trp Ser Lys Leu Tyr Pro Ile Ala Asn Gly Asn Asn Gln Ser Pro Val		
20	25	30
Asp Ile Lys Thr Ser Glu Thr Lys His Asp Thr Ser Leu Lys Pro Ile		
35	40	45
Ser Val Ser Tyr Asn Pro Ala Thr Ala Lys Glu Ile Ile Asn Val Gly		
50	55	60
His Ser Phe His Val Asn Phe Glu Asp Asn Asp Asn Arg Ser Val Leu		
65	70	75 80

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

<210> 28

<211> 260

<212> PRT

<213> 智人

<400> 28

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

Gly	Gly	Pro	Leu	Asp	Gly	Thr	Tyr	Arg	Leu	Ile	Gln	Phe	His	Phe	His
				85					90					95	
Trp	Gly	Ser	Leu	Asp	Gly	Gln	Gly	Ser	Glu	His	Thr	Val	Asp	Lys	Lys
			100					105					110		
Lys	Tyr	Ala	Ala	Glu	Leu	His	Leu	Val	His	Trp	Asn	Thr	Lys	Tyr	Gly
			115				120					125			
Asp	Phe	Gly	Lys	Ala	Val	Gln	Gln	Pro	Asp	Gly	Leu	Ala	Val	Leu	Gly
			130				135					140			
Ile	Phe	Leu	Lys	Val	Gly	Ser	Ala	Lys	Pro	Gly	Leu	Gln	Lys	Val	Val
145					150					155					160
Asp	Val	Leu	Asp	Ser	Ile	Lys	Thr	Lys	Gly	Lys	Ser	Ala	Asp	Phe	Thr
				165					170					175	
Asn	Phe	Asp	Pro	Arg	Gly	Leu	Leu	Pro	Glu	Ser	Leu	Asp	Tyr	Trp	Thr
			180					185					190		
Tyr	Pro	Gly	Ser	Leu	Thr	Thr	Pro	Pro	Leu	Leu	Glu	Cys	Val	Thr	Trp
			195					200					205		
Ile	Val	Leu	Lys	Glu	Pro	Ile	Ser	Val	Ser	Ser	Glu	Gln	Val	Leu	Lys
			210					215				220			
Phe	Arg	Lys	Leu	Asn	Phe	Asn	Gly	Glu	Gly	Glu	Pro	Glu	Glu	Leu	Met
225					230					235					240
Val	Asp	Asn	Trp	Arg	Pro	Ala	Gln	Pro	Leu	Lys	Asn	Arg	Gln	Ile	Lys
				245					250					255	
Ala	Ser	Phe	Lys												
			260												
<210>	29														
<211>	417														
<212>	PRT														
<213>	智人														
<400>	29														
Met	Leu	Leu	Ser	Val	Pro	Leu	Leu	Leu	Gly	Leu	Leu	Gly	Leu	Ala	Val
1				5					10					15	
Ala	Glu	Pro	Ala	Val	Tyr	Phe	Lys	Glu	Gln	Phe	Leu	Asp	Gly	Asp	Gly
			20					25					30		
Trp	Thr	Ser	Arg	Trp	Ile	Glu	Ser	Lys	His	Lys	Ser	Asp	Phe	Gly	Lys
			35					40					45		
Phe	Val	Leu	Ser	Ser	Gly	Lys	Phe	Tyr	Gly	Asp	Glu	Glu	Lys	Asp	Lys
			50				55				60				
Gly	Leu	Gln	Thr	Ser	Gln	Asp	Ala	Arg	Phe	Tyr	Ala	Leu	Ser	Ala	Ser
65					70					75					80

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

385	390	395	400
Lys Glu Glu Asp	Glu Glu Glu Asp Val	Pro Gly Gln Ala Lys	Asp Glu
	405	410	415
Leu			
<210> 30			
<211> 348			
<212> PRT			
<213> 智人			
<400> 30			
Met Tyr Thr Ala Ile	Pro Gln Ser Gly Ser	Pro Phe Pro Gly Ser	Val
1	5	10	15
Gln Asp Pro Gly Leu	His Val Trp Arg Val	Glu Lys Leu Lys Pro	Val
	20	25	30
Pro Val Ala Gln Glu	Asn Gln Gly Val Phe	Phe Ser Gly Asp Ser	Tyr
	35	40	45
Leu Val Leu His Asn	Gly Pro Glu Glu Val	Ser His Leu His Leu	Trp
	50	55	60
Ile Gly Gln Gln Ser	Ser Arg Asp Glu Gln	Gly Ala Cys Ala Val	Leu
65	70	75	80
Ala Val His Leu Asn	Thr Leu Leu Gly Glu	Arg Pro Val Gln His	Arg
	85	90	95
Glu Val Gln Gly Asn	Glu Ser Asp Leu Phe	Met Ser Tyr Phe Pro	Arg
	100	105	110
Gly Leu Lys Tyr Gln	Glu Gly Gly Val Glu	Ser Ala Phe His Lys	Thr
	115	120	125
Ser Thr Gly Ala Pro	Ala Ala Ile Lys Lys	Leu Tyr Gln Val Lys	Gly
	130	135	140
Lys Lys Asn Ile Arg	Ala Thr Glu Arg Ala	Leu Asn Trp Asp Ser	Phe
145	150	155	160
Asn Thr Gly Asp Cys	Phe Ile Leu Asp Leu	Gly Gln Asn Ile Phe	Ala
	165	170	175
Trp Cys Gly Gly Lys	Ser Asn Ile Leu Glu	Arg Asn Lys Ala Arg	Asp
	180	185	190
Leu Ala Leu Ala Ile	Arg Asp Ser Glu Arg	Gln Gly Lys Ala Gln	Val
	195	200	205
Glu Ile Val Thr Asp	Gly Glu Glu Pro Ala	Glu Met Ile Gln Val	Leu
	210	215	220
Gly Pro Lys Pro Ala	Leu Lys Glu Gly Asn	Pro Glu Glu Asp Leu	Thr
225	230	235	240

Ala Asp Lys Ala Asn Ala Gln Ala Ala Ala Leu Tyr Lys Val Ser Asp		
245	250	255
Ala Thr Gly Gln Met Asn Leu Thr Lys Val Ala Asp Ser Ser Pro Phe		
260	265	270
Ala Leu Glu Leu Leu Ile Ser Asp Asp Cys Phe Val Leu Asp Asn Gly		
275	280	285
Leu Cys Gly Lys Ile Tyr Ile Trp Lys Gly Arg Lys Ala Asn Glu Lys		
290	295	300
Glu Arg Gln Ala Ala Leu Gln Val Ala Glu Gly Phe Ile Ser Arg Met		
305	310	315
Gln Tyr Ala Pro Asn Thr Gln Val Glu Ile Leu Pro Gln Gly His Glu		
325	330	335
Ser Pro Ile Phe Lys Gln Phe Phe Lys Asp Trp Lys		
340	345	

<210> 31

<211> 80

<212> PRT

<213> 智人

<400> 31

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

<210> 32

<211> 238

<212> PRT

<213> 智人

<400> 32

Met Ala Val Glu Gly Gly Met Lys Cys Val Lys Phe Leu Leu Tyr Val		
1	5	10
Leu Leu Leu Ala Phe Cys Ala Cys Ala Val Gly Leu Ile Ala Val Gly		
20	25	30
Val Gly Ala Gln Leu Val Leu Ser Gln Thr Ile Ile Gln Gly Ala Thr		

35	40	45
Pro Gly Ser Leu Leu Pro Val Val Ile Ile Ala Val Gly Val Phe Leu		
50	55	60
Phe Leu Val Ala Phe Val Gly Cys Cys Gly Ala Cys Lys Glu Asn Tyr		
65	70	75
Cys Leu Met Ile Thr Phe Ala Ile Phe Leu Ser Leu Ile Met Leu Val		
85	90	95
Glu Val Ala Ala Ala Ile Ala Gly Tyr Val Phe Arg Asp Lys Val Met		
100	105	110
Ser Glu Phe Asn Asn Asn Phe Arg Gln Gln Met Glu Asn Tyr Pro Lys		
115	120	125
Asn Asn His Thr Ala Ser Ile Leu Asp Arg Met Gln Ala Asp Phe Lys		
130	135	140
Cys Cys Gly Ala Ala Asn Tyr Thr Asp Trp Glu Lys Ile Pro Ser Met		
145	150	155
Ser Lys Asn Arg Val Pro Asp Ser Cys Cys Ile Asn Val Thr Val Gly		
165	170	175
Cys Gly Ile Asn Phe Asn Glu Lys Ala Ile His Lys Glu Gly Cys Val		
180	185	190
Glu Lys Ile Gly Gly Trp Leu Arg Lys Asn Val Leu Val Val Ala Ala		
195	200	205
Ala Ala Leu Gly Ile Ala Phe Val Glu Val Leu Gly Ile Val Phe Ala		
210	215	220
Cys Cys Leu Val Lys Ser Ile Arg Ser Gly Tyr Glu Val Met		
225	230	235
<210> 33		
<211> 146		
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<213> 智人		
<400> 33		
Met Ala Gln Lys Arg Pro Ala Cys Thr Leu Lys Pro Glu Cys Val Gln		
1	5	10
Gln Leu Leu Val Cys Ser Gln Glu Ala Lys Lys Ser Ala Tyr Cys Pro		
20	25	30
Tyr Ser His Phe Pro Val Gly Ala Ala Leu Leu Thr Gln Glu Gly Arg		
35	40	45
Ile Phe Lys Gly Cys Asn Ile Glu Asn Ala Cys Tyr Pro Leu Gly Ile		
50	55	60
Cys Ala Glu Arg Thr Ala Ile Gln Lys Ala Val Ser Glu Gly Tyr Lys		

65	70	75	80
Asp Phe Arg Ala Ile	Ala Ile Ala Ser Asp	Met Gln Asp Asp	Phe Ile
	85	90	95
Ser Pro Cys Gly Ala	Cys Arg Gln Val	Met Arg Glu Phe	Gly Thr Asn
	100	105	110
Trp Pro Val Tyr Met	Thr Lys Pro Asp	Gly Thr Tyr Ile	Val Met Thr
	115	120	125
Val Gln Glu Leu Leu	Pro Ser Ser Phe	Gly Pro Glu Asp	Leu Gln Lys
	130	135	140
Thr Gln			
145			
<210> 34			
<211> 252			
<212> PRT			
<213> 智人			
<400> 34			
Met Gly Pro Pro Ser	Ala Ser Pro His	Arg Glu Cys Ile	Pro Trp Gln
1	5	10	15
Gly Leu Leu Leu Thr	Ala Ser Leu Leu	Asn Phe Trp Asn	Pro Pro Thr
	20	25	30
Thr Ala Lys Leu Thr	Ile Glu Ser Met	Pro Leu Ser Val	Ala Glu Gly
	35	40	45
Lys Glu Val Leu Leu	Leu Val His Asn	Leu Pro Gln His	Leu Phe Gly
	50	55	60
Tyr Ser Trp Tyr Lys	Gly Glu Arg Val	Asp Gly Asn Ser	Leu Ile Val
65	70	75	80
Gly Tyr Val Ile Gly	Thr Gln Gln Ala	Thr Pro Gly Ala	Ala Tyr Ser
	85	90	95
Gly Arg Glu Thr Ile	Tyr Thr Asn Ala	Ser Leu Leu Ile	Gln Asn Val
	100	105	110
Thr Gln Asn Asp Ile	Gly Phe Tyr Thr	Leu Gln Val Ile	Lys Ser Asp
	115	120	125
Leu Val Asn Glu Glu	Ala Thr Gly Gln	Phe His Val Tyr	Gln Glu Asn
	130	135	140
Ala Pro Gly Leu Pro	Val Gly Ala Val	Ala Gly Ile Val	Thr Gly Val
145	150	155	160
Leu Val Gly Val Ala	Leu Val Ala Ala	Leu Val Cys Phe	Leu Leu Leu
	165	170	175
Ala Lys Thr Gly Arg	Thr Ser Ile Gln	Arg Asp Leu Lys	Glu Gln Gln

	180					185					190				
Pro	Gln	Ala	Leu	Ala	Pro	Gly	Arg	Gly	Pro	Ser	His	Ser	Ser	Ala	Phe
	195					200					205				
Ser	Met	Ser	Pro	Leu	Ser	Thr	Ala	Gln	Ala	Pro	Leu	Pro	Asn	Pro	Arg
	210					215					220				
Thr	Ala	Ala	Ser	Ile	Tyr	Glu	Glu	Leu	Leu	Lys	His	Asp	Thr	Asn	Ile
225					230					235					240
Tyr	Cys	Arg	Met	Asp	His	Lys	Ala	Glu	Val	Ala	Ser				
				245					250						
<210>	35														
<211>	702														
<212>	PRT														
<213>	智人														
<400>	35														
Met	Glu	Ser	Pro	Ser	Ala	Pro	Pro	His	Arg	Trp	Cys	Ile	Pro	Trp	Gln
1			5					10					15		
Arg	Leu	Leu	Leu	Thr	Ala	Ser	Leu	Leu	Thr	Phe	Trp	Asn	Pro	Pro	Thr
	20					25					30				
Thr	Ala	Lys	Leu	Thr	Ile	Glu	Ser	Thr	Pro	Phe	Asn	Val	Ala	Glu	Gly
	35					40					45				
Lys	Glu	Val	Leu	Leu	Leu	Val	His	Asn	Leu	Pro	Gln	His	Leu	Phe	Gly
	50					55					60				
Tyr	Ser	Trp	Tyr	Lys	Gly	Glu	Arg	Val	Asp	Gly	Asn	Arg	Gln	Ile	Ile
65				70				75						80	
Gly	Tyr	Val	Ile	Gly	Thr	Gln	Gln	Ala	Thr	Pro	Gly	Pro	Ala	Tyr	Ser
	85					90					95				
Gly	Arg	Glu	Ile	Ile	Tyr	Pro	Asn	Ala	Ser	Leu	Leu	Ile	Gln	Asn	Ile
	100					105					110				
Ile	Gln	Asn	Asp	Thr	Gly	Phe	Tyr	Thr	Leu	His	Val	Ile	Lys	Ser	Asp
	115					120					125				
Leu	Val	Asn	Glu	Glu	Ala	Thr	Gly	Gln	Phe	Arg	Val	Tyr	Pro	Glu	Leu
	130					135					140				
Pro	Lys	Pro	Ser	Ile	Ser	Ser	Asn	Asn	Ser	Lys	Pro	Val	Glu	Asp	Lys
145				150				155						160	
Asp	Ala	Val	Ala	Phe	Thr	Cys	Glu	Pro	Glu	Thr	Gln	Asp	Ala	Thr	Tyr
	165					170					175				
Leu	Trp	Trp	Val	Asn	Asn	Gln	Ser	Leu	Pro	Val	Ser	Pro	Arg	Leu	Gln
	180					185					190				
Leu	Ser	Asn	Gly	Asn	Arg	Thr	Leu	Thr	Leu	Phe	Asn	Val	Thr	Arg	Asn

195	200	205
Asp Thr Ala Ser Tyr Lys Cys Glu Thr Gln Asn Pro Val Ser Ala Arg		
210	215	220
Arg Ser Asp Ser Val Ile Leu Asn Val Leu Tyr Gly Pro Asp Ala Pro		
225	230	235
Thr Ile Ser Pro Leu Asn Thr Ser Tyr Arg Ser Gly Glu Asn Leu Asn		
245	250	255
Leu Ser Cys His Ala Ala Ser Asn Pro Pro Ala Gln Tyr Ser Trp Phe		
260	265	270
Val Asn Gly Thr Phe Gln Gln Ser Thr Gln Glu Leu Phe Ile Pro Asn		
275	280	285
Ile Thr Val Asn Asn Ser Gly Ser Tyr Thr Cys Gln Ala His Asn Ser		
290	295	300
Asp Thr Gly Leu Asn Arg Thr Thr Val Thr Thr Ile Thr Val Tyr Ala		
305	310	315
Glu Pro Pro Lys Pro Phe Ile Thr Ser Asn Asn Ser Asn Pro Val Glu		
325	330	335
Asp Glu Asp Ala Val Ala Leu Thr Cys Glu Pro Glu Ile Gln Asn Thr		
340	345	350
Thr Tyr Leu Trp Trp Val Asn Asn Gln Ser Leu Pro Val Ser Pro Arg		
355	360	365
Leu Gln Leu Ser Asn Asp Asn Arg Thr Leu Thr Leu Leu Ser Val Thr		
370	375	380
Arg Asn Asp Val Gly Pro Tyr Glu Cys Gly Ile Gln Asn Lys Leu Ser		
385	390	395
Val Asp His Ser Asp Pro Val Ile Leu Asn Val Leu Tyr Gly Pro Asp		
405	410	415
Asp Pro Thr Ile Ser Pro Ser Tyr Thr Tyr Tyr Arg Pro Gly Val Asn		
420	425	430
Leu Ser Leu Ser Cys His Ala Ala Ser Asn Pro Pro Ala Gln Tyr Ser		
435	440	445
Trp Leu Ile Asp Gly Asn Ile Gln Gln His Thr Gln Glu Leu Phe Ile		
450	455	460
Ser Asn Ile Thr Glu Lys Asn Ser Gly Leu Tyr Thr Cys Gln Ala Asn		
465	470	475
Asn Ser Ala Ser Gly His Ser Arg Thr Thr Val Lys Thr Ile Thr Val		
485	490	495
Ser Ala Glu Leu Pro Lys Pro Ser Ile Ser Ser Asn Asn Ser Lys Pro		
500	505	510

Val Glu Asp Lys Asp Ala Val Ala Phe Thr Cys Glu Pro Glu Ala Gln		
515	520	525
Asn Thr Thr Tyr Leu Trp Trp Val Asn Gly Gln Ser Leu Pro Val Ser		
530	535	540
Pro Arg Leu Gln Leu Ser Asn Gly Asn Arg Thr Leu Thr Leu Phe Asn		
545	550	555
Val Thr Arg Asn Asp Ala Arg Ala Tyr Val Cys Gly Ile Gln Asn Ser		
565	570	575
Val Ser Ala Asn Arg Ser Asp Pro Val Thr Leu Asp Val Leu Tyr Gly		
580	585	590
Pro Asp Thr Pro Ile Ile Ser Pro Pro Asp Ser Ser Tyr Leu Ser Gly		
595	600	605
Ala Asn Leu Asn Leu Ser Cys His Ser Ala Ser Asn Pro Ser Pro Gln		
610	615	620
Tyr Ser Trp Arg Ile Asn Gly Ile Pro Gln Gln His Thr Gln Val Leu		
625	630	635
Phe Ile Ala Lys Ile Thr Pro Asn Asn Asn Gly Thr Tyr Ala Cys Phe		
645	650	655
Val Ser Asn Leu Ala Thr Gly Arg Asn Asn Ser Ile Val Lys Ser Ile		
660	665	670
Thr Val Ser Ala Ser Gly Thr Ser Pro Gly Leu Ser Ala Gly Ala Thr		
675	680	685
Val Gly Ile Met Ile Gly Val Leu Val Gly Val Ala Leu Ile		
690	695	700
<210> 36		
<211> 344		
<212> PRT		
<213> 智人		
<400> 36		
Met Gly Pro Pro Ser Ala Pro Pro Cys Arg Leu His Val Pro Trp Lys		
1	5	10
Glu Val Leu Leu Thr Ala Ser Leu Leu Thr Phe Trp Asn Pro Pro Thr		
20	25	30
Thr Ala Lys Leu Thr Ile Glu Ser Thr Pro Phe Asn Val Ala Glu Gly		
35	40	45
Lys Glu Val Leu Leu Leu Ala His Asn Leu Pro Gln Asn Arg Ile Gly		
50	55	60
Tyr Ser Trp Tyr Lys Gly Glu Arg Val Asp Gly Asn Ser Leu Ile Val		
65	70	75
		80

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

<210> 37

<211> 165

<212> PRT

<213> 智人

<400> 37

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

<210> 38

<211> 383

<212> PRT

<213> 智人

<400> 38

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

Gly Gly Trp Asn Phe Gly Ser Gln Arg Phe Ser Lys Ile Ala Ser Asn		
100	105	110
Thr Gln Ser Arg Arg Thr Phe Ile Lys Ser Val Pro Pro Phe Leu Arg		
115	120	125
Thr His Gly Phe Asp Gly Leu Asp Leu Ala Trp Leu Tyr Pro Gly Arg		
130	135	140
Arg Asp Lys Gln His Phe Thr Thr Leu Ile Lys Glu Met Lys Ala Glu		
145	150	155
Phe Ile Lys Glu Ala Gln Pro Gly Lys Lys Gln Leu Leu Leu Ser Ala		
165	170	175
Ala Leu Ser Ala Gly Lys Val Thr Ile Asp Ser Ser Tyr Asp Ile Ala		
180	185	190
Lys Ile Ser Gln His Leu Asp Phe Ile Ser Ile Met Thr Tyr Asp Phe		
195	200	205
His Gly Ala Trp Arg Gly Thr Thr Gly His His Ser Pro Leu Phe Arg		
210	215	220
Gly Gln Glu Asp Ala Ser Pro Asp Arg Phe Ser Asn Thr Asp Tyr Ala		
225	230	235
Val Gly Tyr Met Leu Arg Leu Gly Ala Pro Ala Ser Lys Leu Val Met		
245	250	255
Gly Ile Pro Thr Phe Gly Arg Ser Phe Thr Leu Ala Ser Ser Glu Thr		
260	265	270
Gly Val Gly Ala Pro Ile Ser Gly Pro Gly Ile Pro Gly Arg Phe Thr		
275	280	285
Lys Glu Ala Gly Thr Leu Ala Tyr Tyr Glu Ile Cys Asp Phe Leu Arg		
290	295	300
Gly Ala Thr Val His Arg Ile Leu Gly Gln Gln Val Pro Tyr Ala Thr		
305	310	315
Lys Gly Asn Gln Trp Val Gly Tyr Asp Asp Gln Glu Ser Val Lys Ser		
325	330	335
Lys Val Gln Tyr Leu Lys Asp Arg Gln Leu Ala Gly Ala Met Val Trp		
340	345	350
Ala Leu Asp Leu Asp Asp Phe Gln Gly Ser Phe Cys Gly Gln Asp Leu		
355	360	365
Arg Phe Pro Leu Thr Asn Ala Ile Lys Asp Ala Leu Ala Ala Thr		
370	375	380
<210> 39		
<211> 381		
<212> PRT		

<213> 智人

<400> 39

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

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290	295	300
His Glu Lys Phe Ser Glu Val Leu Lys Arg Leu Arg Leu Gln Lys Arg		
305	310	315
Gly Thr Gly Gly Val Asp Thr Ala Ala Val Gly Gly Val Phe Asp Val		
325	330	335
Ser Asn Ala Asp Arg Leu Gly Phe Ser Glu Val Glu Leu Val Gln Met		
340	345	350
Val Val Asp Gly Val Lys Leu Leu Ile Glu Met Glu Gln Arg Leu Glu		
355	360	365
Gln Gly Gln Ala Ile Asp Asp Leu Met Pro Ala Gln Lys		
370	375	380
<210> 40		
<211> 215		
<212> PRT		
<213> 智人		
<400> 40		
Met Gly Leu Glu Lys Pro Gln Ser Lys Leu Glu Gly Gly Met His Pro		
1	5	10
Gln Leu Ile Pro Ser Val Ile Ala Val Val Phe Ile Leu Leu Leu Ser		
20	25	30
Val Cys Phe Ile Ala Ser Cys Leu Val Thr His His Asn Phe Ser Arg		
35	40	45
Cys Lys Arg Gly Thr Gly Val His Lys Leu Glu His His Ala Lys Leu		
50	55	60
Lys Cys Ile Lys Glu Lys Ser Glu Leu Lys Ser Ala Glu Gly Ser Thr		
65	70	75
Trp Asn Cys Cys Pro Ile Asp Trp Arg Ala Phe Gln Ser Asn Cys Tyr		
85	90	95
Phe Pro Leu Thr Asp Asn Lys Thr Trp Ala Glu Ser Glu Arg Asn Cys		
100	105	110
Ser Gly Met Gly Ala His Leu Met Thr Ile Ser Thr Glu Ala Glu Gln		
115	120	125
Asn Phe Ile Ile Gln Phe Leu Asp Arg Arg Leu Ser Tyr Phe Leu Gly		
130	135	140
Leu Arg Asp Glu Asn Ala Lys Gly Gln Trp Arg Trp Val Asp Gln Thr		
145	150	155
Pro Phe Asn Pro Arg Arg Val Phe Trp His Lys Asn Glu Pro Asp Asn		
165	170	175
Ser Gln Gly Glu Asn Cys Val Val Leu Val Tyr Asn Gln Asp Lys Trp		

	180		185		190
Ala Trp Asn Asp Val Pro Cys Asn Phe Glu Ala Ser Arg Ile Cys Lys					
195		200		205	
Ile Pro Gly Thr Thr Leu Asn					
210		215			
<210> 41					
<211> 449					
<212> PRT					
<213> 智人					
<400> 41					
Met Met Lys Thr Leu Leu Leu Phe Val Gly Leu Leu Leu Thr Trp Glu					
1	5		10		15
Ser Gly Gln Val Leu Gly Asp Gln Thr Val Ser Asp Asn Glu Leu Gln					
20		25		30	
Glu Met Ser Asn Gln Gly Ser Lys Tyr Val Asn Lys Glu Ile Gln Asn					
35		40		45	
Ala Val Asn Gly Val Lys Gln Ile Lys Thr Leu Ile Glu Lys Thr Asn					
50		55		60	
Glu Glu Arg Lys Thr Leu Leu Ser Asn Leu Glu Glu Ala Lys Lys Lys					
65		70		75	80
Lys Glu Asp Ala Leu Asn Glu Thr Arg Glu Ser Glu Thr Lys Leu Lys					
85		90		95	
Glu Leu Pro Gly Val Cys Asn Glu Thr Met Met Ala Leu Trp Glu Glu					
100		105		110	
Cys Lys Pro Cys Leu Lys Gln Thr Cys Met Lys Phe Tyr Ala Arg Val					
115		120		125	
Cys Arg Ser Gly Ser Gly Leu Val Gly Arg Gln Leu Glu Glu Phe Leu					
130		135		140	
Asn Gln Ser Ser Pro Phe Tyr Phe Trp Met Asn Gly Asp Arg Ile Asp					
145		150		155	160
Ser Leu Leu Glu Asn Asp Arg Gln Gln Thr His Met Leu Asp Val Met					
165		170		175	
Gln Asp His Phe Ser Arg Ala Ser Ser Ile Ile Asp Glu Leu Phe Gln					
180		185		190	
Asp Arg Phe Phe Thr Arg Glu Pro Gln Asp Thr Tyr His Tyr Leu Pro					
195		200		205	
Phe Ser Leu Pro His Arg Arg Pro His Phe Phe Phe Pro Lys Ser Arg					
210		215		220	
Ile Val Arg Ser Leu Met Pro Phe Ser Pro Tyr Glu Pro Leu Asn Phe					

225	230	235	240
His Ala Met Phe Gln Pro Phe Leu Glu Met Ile His Glu Ala Gln Gln			
	245	250	255
Ala Met Asp Ile His Phe His Ser Pro Ala Phe Gln His Pro Pro Thr			
	260	265	270
Glu Phe Ile Arg Glu Gly Asp Asp Asp Arg Thr Val Cys Arg Glu Ile			
	275	280	285
Arg His Asn Ser Thr Gly Cys Leu Arg Met Lys Asp Gln Cys Asp Lys			
	290	295	300
Cys Arg Glu Ile Leu Ser Val Asp Cys Ser Thr Asn Asn Pro Ser Gln			
305	310	315	320
Ala Lys Leu Arg Arg Glu Leu Asp Glu Ser Leu Gln Val Ala Glu Arg			
	325	330	335
Leu Thr Arg Lys Tyr Asn Glu Leu Leu Lys Ser Tyr Gln Trp Lys Met			
	340	345	350
Leu Asn Thr Ser Ser Leu Leu Glu Gln Leu Asn Glu Gln Phe Asn Trp			
	355	360	365
Val Ser Arg Leu Ala Asn Leu Thr Gln Gly Glu Asp Gln Tyr Tyr Leu			
	370	375	380
Arg Val Thr Thr Val Ala Ser His Thr Ser Asp Ser Asp Val Pro Ser			
385	390	395	400
Gly Val Thr Glu Val Val Val Lys Leu Phe Asp Ser Asp Pro Ile Thr			
	405	410	415
Val Thr Val Pro Val Glu Val Ser Arg Lys Asn Pro Lys Phe Met Glu			
	420	425	430
Thr Val Ala Glu Lys Ala Leu Gln Glu Tyr Arg Lys Lys His Arg Glu			
	435	440	445
Glu			
<210> 42			
<211> 297			
<212> PRT			
<213> 智人			
<400> 42			
Met Ser Ser Ala His Phe Asn Arg Gly Pro Ala Tyr Gly Leu Ser Ala			
1	5	10	15
Glu Val Lys Asn Lys Leu Ala Gln Lys Tyr Asp His Gln Arg Glu Gln			
	20	25	30
Glu Leu Arg Glu Trp Ile Glu Gly Val Thr Gly Arg Arg Ile Gly Asn			
	35	40	45

Asn Phe Met Asp Gly Leu Lys Asp Gly Ile Ile Leu Cys Glu Phe Ile		
50	55	60
Asn Lys Leu Gln Pro Gly Ser Val Lys Lys Ile Asn Glu Ser Thr Gln		
65	70	75 80
Asn Trp His Gln Leu Glu Asn Ile Gly Asn Phe Ile Lys Ala Ile Thr		
85	90	95
Lys Tyr Gly Val Lys Pro His Asp Ile Phe Glu Ala Asn Asp Leu Phe		
100	105	110
Glu Asn Thr Asn His Thr Gln Val Gln Ser Thr Leu Leu Ala Leu Ala		
115	120	125
Ser Met Ala Lys Thr Lys Gly Asn Lys Val Asn Val Gly Val Lys Tyr		
130	135	140
Ala Glu Lys Gln Glu Arg Lys Phe Glu Pro Gly Lys Leu Arg Glu Gly		
145	150	155 160
Arg Asn Ile Ile Gly Leu Gln Met Gly Thr Asn Lys Phe Ala Ser Gln		
165	170	175
Gln Gly Met Thr Ala Tyr Gly Thr Arg Arg His Leu Tyr Asp Pro Lys		
180	185	190
Leu Gly Thr Asp Gln Pro Leu Asp Gln Ala Thr Ile Ser Leu Gln Met		
195	200	205
Gly Thr Asn Lys Gly Ala Ser Gln Ala Gly Met Thr Ala Pro Gly Thr		
210	215	220
Lys Arg Gln Ile Phe Glu Pro Gly Leu Gly Met Glu His Cys Asp Thr		
225	230	235 240
Leu Asn Val Ser Leu Gln Met Gly Ser Asn Lys Gly Ala Ser Gln Arg		
245	250	255
Gly Met Thr Val Tyr Gly Leu Pro Arg Gln Val Tyr Asp Pro Lys Tyr		
260	265	270
Cys Leu Thr Pro Glu Tyr Pro Glu Leu Gly Glu Pro Ala His Asn His		
275	280	285
His Ala His Asn Tyr Tyr Asn Ser Ala		
290	295	
<210> 43		
<211> 474		
<212> PRT		
<213> 智人		
<400> 43		
Met Arg Arg Val Val Arg Gln Ser Lys Phe Arg His Val Phe Gly Gln		
1	5	10 15

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

				325				330				335			
Lys	Leu	His	Glu	Arg	Lys	Cys	Glu	Pro	Ile	Ile	Met	Thr	Val	Pro	Arg
				340				345				350			
Lys	Ser	Asp	Leu	Phe	Gln	Asp	Asp	Leu	Tyr	Pro	Asp	Thr	Ala	Gly	Pro
				355				360				365			
Glu	Ala	Ala	Leu	Glu	Ala	Glu	Glu	Trp	Phe	Glu	Gly	Lys	Asn	Ala	Asp
				370				375				380			
Pro	Ile	Leu	Ile	Ser	Leu	Lys	His	Gly	Tyr	Ile	Pro	Gly	Lys	Asn	Arg
385				390				395				400			
Asp	Leu	Lys	Val	Val	Lys	Lys	Asn	Ile	Leu	Asp	Ser	Lys	Pro	Thr	Ala
				405				410				415			
Asn	Lys	Lys	Cys	Asp	Leu	Ile	Ser	Ile	Pro	Lys	Lys	Thr	Thr	Asp	Thr
				420				425				430			
Ala	Ser	Val	Gln	Asn	Glu	Ala	Lys	Leu	Asp	Glu	Ile	Leu	Lys	Glu	Ile
				435				440				445			
Lys	Ser	Ile	Lys	Asp	Thr	Ile	Cys	Asn	Gln	Asp	Glu	Arg	Ile	Ser	Lys
450				455				460							
Leu	Glu	Gln	Gln	Met	Ala	Lys	Ile	Ala	Ala						
465				470											
<210> 44															
<211> 224															
<212> PRT															
<213> 智人															
<400> 44															
Met	Glu	Lys	Leu	Leu	Cys	Phe	Leu	Val	Leu	Thr	Ser	Leu	Ser	His	Ala
1				5				10				15			
Phe	Gly	Gln	Thr	Asp	Met	Ser	Arg	Lys	Ala	Phe	Val	Phe	Pro	Lys	Glu
				20				25				30			
Ser	Asp	Thr	Ser	Tyr	Val	Ser	Leu	Lys	Ala	Pro	Leu	Thr	Lys	Pro	Leu
				35				40				45			
Lys	Ala	Phe	Thr	Val	Cys	Leu	His	Phe	Tyr	Thr	Glu	Leu	Ser	Ser	Thr
50				55				60							
Arg	Gly	Tyr	Ser	Ile	Phe	Ser	Tyr	Ala	Thr	Lys	Arg	Gln	Asp	Asn	Glu
65				70				75				80			
Ile	Leu	Ile	Phe	Trp	Ser	Lys	Asp	Ile	Gly	Tyr	Ser	Phe	Thr	Val	Gly
				85				90				95			
Gly	Ser	Glu	Ile	Leu	Phe	Glu	Val	Pro	Glu	Val	Thr	Val	Ala	Pro	Val
				100				105				110			
His	Ile	Cys	Thr	Ser	Trp	Glu	Ser	Ala	Ser	Gly	Ile	Val	Glu	Phe	Trp

115	120	125
Val Asp Gly Lys Pro Arg	Val Arg Lys Ser Leu	Lys Lys Gly Tyr Thr
130	135	140
Val Gly Ala Glu Ala Ser	Ile Ile Leu Gly Gln	Glu Gln Asp Ser Phe
145	150	155
Gly Gly Asn Phe Glu Gly	Ser Gln Ser Leu Val	Gly Asp Ile Gly Asn
165	170	175
Val Asn Met Trp Asp Phe	Val Leu Ser Pro Asp	Glu Ile Asn Thr Ile
180	185	190
Tyr Leu Gly Gly Pro Phe	Ser Pro Asn Val Leu	Asn Trp Arg Ala Leu
195	200	205
Lys Tyr Glu Val Gln Gly	Glu Val Phe Thr Lys	Pro Gln Leu Trp Pro
210	215	220
<210> 45		
<211> 554		
<212> PRT		
<213> 智人		
<400> 45		
Met Thr Ala Pro Gly Ala	Ala Gly Arg Cys Pro	Pro Thr Thr Trp Leu
1	5	10
Gly Ser Leu Leu Leu Leu	Val Cys Leu Leu Ala	Ser Arg Ser Ile Thr
20	25	30
Glu Glu Val Ser Glu Tyr	Cys Ser His Met Ile	Gly Ser Gly His Leu
35	40	45
Gln Ser Leu Gln Arg Leu	Ile Asp Ser Gln Met	Glu Thr Ser Cys Gln
50	55	60
Ile Thr Phe Glu Phe Val	Asp Gln Glu Gln Leu	Lys Asp Pro Val Cys
65	70	75
Tyr Leu Lys Lys Ala Phe	Leu Leu Val Gln Asp	Ile Met Glu Asp Thr
85	90	95
Met Arg Phe Arg Asp Asn	Thr Pro Asn Ala Ile	Ala Ile Val Gln Leu
100	105	110
Gln Glu Leu Ser Leu Arg	Leu Lys Ser Cys Phe	Thr Lys Asp Tyr Glu
115	120	125
Glu His Asp Lys Ala Cys	Val Arg Thr Phe Tyr	Glu Thr Pro Leu Gln
130	135	140
Leu Leu Glu Lys Val Lys	Asn Val Phe Asn Glu	Thr Lys Asn Leu Leu
145	150	155
Asp Lys Asp Trp Asn Ile	Phe Ser Lys Asn Cys	Asn Asn Ser Phe Ala

				165					170					175			
Glu	Cys	Ser	Ser	Gln	Asp	Val	Val	Thr	Lys	Pro	Asp	Cys	Asn	Cys	Leu		
				180					185					190			
Tyr	Pro	Lys	Ala	Ile	Pro	Ser	Ser	Asp	Pro	Ala	Ser	Val	Ser	Pro	His		
				195					200					205			
Gln	Pro	Leu	Ala	Pro	Ser	Met	Ala	Pro	Val	Ala	Gly	Leu	Thr	Trp	Glu		
				210					215					220			
Asp	Ser	Glu	Gly	Thr	Glu	Gly	Ser	Ser	Leu	Leu	Pro	Gly	Glu	Gln	Pro		
225					230					235					240		
Leu	His	Thr	Val	Asp	Pro	Gly	Ser	Ala	Lys	Gln	Arg	Pro	Pro	Arg	Ser		
				245					250					255			
Thr	Cys	Gln	Ser	Phe	Glu	Pro	Pro	Glu	Thr	Pro	Val	Val	Lys	Asp	Ser		
				260					265					270			
Thr	Ile	Gly	Gly	Ser	Pro	Gln	Pro	Arg	Pro	Ser	Val	Gly	Ala	Phe	Asn		
				275					280					285			
Pro	Gly	Met	Glu	Asp	Ile	Leu	Asp	Ser	Ala	Met	Gly	Thr	Asn	Trp	Val		
				290					295					300			
Pro	Glu	Glu	Ala	Ser	Gly	Glu	Ala	Ser	Glu	Ile	Pro	Val	Pro	Gln	Gly		
305					310					315					320		
Thr	Glu	Leu	Ser	Pro	Ser	Arg	Pro	Gly	Gly	Gly	Ser	Met	Gln	Thr	Glu		
				325					330					335			
Pro	Ala	Arg	Pro	Ser	Asn	Phe	Leu	Ser	Ala	Ser	Ser	Pro	Leu	Pro	Ala		
				340					345					350			
Ser	Ala	Lys	Gly	Gln	Gln	Pro	Ala	Asp	Val	Thr	Gly	Thr	Ala	Leu	Pro		
				355					360					365			
Arg	Val	Gly	Pro	Val	Arg	Pro	Thr	Gly	Gln	Asp	Trp	Asn	His	Thr	Pro		
				370					375					380			
Gln	Lys	Thr	Asp	His	Pro	Ser	Ala	Leu	Leu	Arg	Asp	Pro	Pro	Glu	Pro		
385					390					395					400		
Gly	Ser	Pro	Arg	Ile	Ser	Ser	Leu	Arg	Pro	Gln	Gly	Leu	Ser	Asn	Pro		
				405					410					415			
Ser	Thr	Leu	Ser	Ala	Gln	Pro	Gln	Leu	Ser	Arg	Ser	His	Ser	Ser	Gly		
				420					425					430			
Ser	Val	Leu	Pro	Leu	Gly	Glu	Leu	Glu	Gly	Arg	Arg	Ser	Thr	Arg	Asp		
				435					440					445			
Arg	Arg	Ser	Pro	Ala	Glu	Pro	Glu	Gly	Gly	Pro	Ala	Ser	Glu	Gly	Ala		
				450					455					460			
Ala	Arg	Pro	Leu	Pro	Arg	Phe	Asn	Ser	Val	Pro	Leu	Thr	Asp	Thr	Gly		
465					470					475					480		

His Glu Arg Gln Ser Glu Gly Ser Phe Ser Pro Gln Leu Gln Glu Ser
 485 490 495
 Val Phe His Leu Leu Val Pro Ser Val Ile Leu Val Leu Leu Ala Val
 500 505 510
 Gly Gly Leu Leu Phe Tyr Arg Trp Arg Arg Arg Ser His Gln Glu Pro
 515 520 525
 Gln Arg Ala Asp Ser Pro Leu Glu Gln Pro Glu Gly Ser Pro Leu Thr
 530 535 540
 Gln Asp Asp Arg Gln Val Glu Leu Pro Val
 545 550
 <210> 46
 <211> 781
 <212> PRT
 <213> 智人
 <400> 46
 Met Ala Thr Gln Ala Asp Leu Met Glu Leu Asp Met Ala Met Glu Pro
 1 5 10 15
 Asp Arg Lys Ala Ala Val Ser His Trp Gln Gln Gln Ser Tyr Leu Asp
 20 25 30
 Ser Gly Ile His Ser Gly Ala Thr Thr Thr Ala Pro Ser Leu Ser Gly
 35 40 45
 Lys Gly Asn Pro Glu Glu Glu Asp Val Asp Thr Ser Gln Val Leu Tyr
 50 55 60
 Glu Trp Glu Gln Gly Phe Ser Gln Ser Phe Thr Gln Glu Gln Val Ala
 65 70 75 80
 Asp Ile Asp Gly Gln Tyr Ala Met Thr Arg Ala Gln Arg Val Arg Ala
 85 90 95
 Ala Met Phe Pro Glu Thr Leu Asp Glu Gly Met Gln Ile Pro Ser Thr
 100 105 110
 Gln Phe Asp Ala Ala His Pro Thr Asn Val Gln Arg Leu Ala Glu Pro
 115 120 125
 Ser Gln Met Leu Lys His Ala Val Val Asn Leu Ile Asn Tyr Gln Asp
 130 135 140
 Asp Ala Glu Leu Ala Thr Arg Ala Ile Pro Glu Leu Thr Lys Leu Leu
 145 150 155 160
 Asn Asp Glu Asp Gln Val Val Val Asn Lys Ala Ala Val Met Val His
 165 170 175
 Gln Leu Ser Lys Lys Glu Ala Ser Arg His Ala Ile Met Arg Ser Pro
 180 185 190

Gln Met Val Ser Ala Ile Val Arg Thr Met Gln Asn Thr Asn Asp Val		
195	200	205
Glu Thr Ala Arg Cys Thr Ala Gly Thr Leu His Asn Leu Ser His His		
210	215	220
Arg Glu Gly Leu Leu Ala Ile Phe Lys Ser Gly Gly Ile Pro Ala Leu		
225	230	235 240
Val Lys Met Leu Gly Ser Pro Val Asp Ser Val Leu Phe Tyr Ala Ile		
	245	250 255
Thr Thr Leu His Asn Leu Leu Leu His Gln Glu Gly Ala Lys Met Ala		
	260	265 270
Val Arg Leu Ala Gly Gly Leu Gln Lys Met Val Ala Leu Leu Asn Lys		
	275	280 285
Thr Asn Val Lys Phe Leu Ala Ile Thr Thr Asp Cys Leu Gln Ile Leu		
290	295	300
Ala Tyr Gly Asn Gln Glu Ser Lys Leu Ile Ile Leu Ala Ser Gly Gly		
305	310	315 320
Pro Gln Ala Leu Val Asn Ile Met Arg Thr Tyr Thr Tyr Glu Lys Leu		
	325	330 335
Leu Trp Thr Thr Ser Arg Val Leu Lys Val Leu Ser Val Cys Ser Ser		
	340	345 350
Asn Lys Pro Ala Ile Val Glu Ala Gly Gly Met Gln Ala Leu Gly Leu		
	355	360 365
His Leu Thr Asp Pro Ser Gln Arg Leu Val Gln Asn Cys Leu Trp Thr		
370	375	380
Leu Arg Asn Leu Ser Asp Ala Ala Thr Lys Gln Glu Gly Met Glu Gly		
385	390	395 400
Leu Leu Gly Thr Leu Val Gln Leu Leu Gly Ser Asp Asp Ile Asn Val		
	405	410 415
Val Thr Cys Ala Ala Gly Ile Leu Ser Asn Leu Thr Cys Asn Asn Tyr		
	420	425 430
Lys Asn Lys Met Met Val Cys Gln Val Gly Gly Ile Glu Ala Leu Val		
	435	440 445
Arg Thr Val Leu Arg Ala Gly Asp Arg Glu Asp Ile Thr Glu Pro Ala		
450	455	460
Ile Cys Ala Leu Arg His Leu Thr Ser Arg His Gln Glu Ala Glu Met		
465	470	475 480
Ala Gln Asn Ala Val Arg Leu His Tyr Gly Leu Pro Val Val Val Lys		
	485	490 495
Leu Leu His Pro Pro Ser His Trp Pro Leu Ile Lys Ala Thr Val Gly		

500	505	510
Leu Ile Arg Asn Leu Ala Leu Cys Pro Ala Asn His Ala Pro Leu Arg		
515	520	525
Glu Gln Gly Ala Ile Pro Arg Leu Val Gln Leu Leu Val Arg Ala His		
530	535	540
Gln Asp Thr Gln Arg Arg Thr Ser Met Gly Gly Thr Gln Gln Gln Phe		
545	550	555
Val Glu Gly Val Arg Met Glu Glu Ile Val Glu Gly Cys Thr Gly Ala		
565	570	575
Leu His Ile Leu Ala Arg Asp Val His Asn Arg Ile Val Ile Arg Gly		
580	585	590
Leu Asn Thr Ile Pro Leu Phe Val Gln Leu Leu Tyr Ser Pro Ile Glu		
595	600	605
Asn Ile Gln Arg Val Ala Ala Gly Val Leu Cys Glu Leu Ala Gln Asp		
610	615	620
Lys Glu Ala Ala Glu Ala Ile Glu Ala Glu Gly Ala Thr Ala Pro Leu		
625	630	635
Thr Glu Leu Leu His Ser Arg Asn Glu Gly Val Ala Thr Tyr Ala Ala		
645	650	655
Ala Val Leu Phe Arg Met Ser Glu Asp Lys Pro Gln Asp Tyr Lys Lys		
660	665	670
Arg Leu Ser Val Glu Leu Thr Ser Ser Leu Phe Arg Thr Glu Pro Met		
675	680	685
Ala Trp Asn Glu Thr Ala Asp Leu Gly Leu Asp Ile Gly Ala Gln Gly		
690	695	700
Glu Pro Leu Gly Tyr Arg Gln Asp Asp Pro Ser Tyr Arg Ser Phe His		
705	710	715
Ser Gly Gly Tyr Gly Gln Asp Ala Leu Gly Met Asp Pro Met Met Glu		
725	730	735
His Glu Met Gly Gly His His Pro Gly Ala Asp Tyr Pro Val Asp Gly		
740	745	750
Leu Pro Asp Leu Gly His Ala Gln Asp Leu Met Asp Gly Leu Pro Pro		
755	760	765
Gly Asp Ser Asn Gln Leu Ala Trp Phe Asp Thr Asp Leu		
770	775	780

<210> 47

<211> 412

<212> PRT

<213> 智人

<400> 47

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

Val	Asp	Glu	Val	Arg	Glu	Leu	Gln	Lys	Ala	Ile	Gly	Ala	Val	Pro	Leu
305					310					315					320
Ile	Gln	Gly	Glu	Tyr	Met	Ile	Pro	Cys	Glu	Lys	Val	Ser	Thr	Leu	Pro
				325					330					335	
Ala	Ile	Thr	Leu	Lys	Leu	Gly	Gly	Lys	Gly	Tyr	Lys	Leu	Ser	Pro	Glu
			340					345					350		
Asp	Tyr	Thr	Leu	Lys	Val	Ser	Gln	Ala	Gly	Lys	Thr	Leu	Cys	Leu	Ser
			355				360					365			
Gly	Phe	Met	Gly	Met	Asp	Ile	Pro	Pro	Pro	Ser	Gly	Pro	Leu	Trp	Ile
	370					375					380				
Leu	Gly	Asp	Val	Phe	Ile	Gly	Arg	Tyr	Tyr	Thr	Val	Phe	Asp	Arg	Asp
385					390					395					400
Asn	Asn	Arg	Val	Gly	Phe	Ala	Glu	Ala	Ala	Arg	Leu				
			405						410						

<210> 48

<211> 331

<212> PRT

<213> 智人

<400> 48

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

Ser Leu Ser Ala Gln Asn Leu Val Asp Cys Ser Thr Glu Lys Tyr Gly
 165 170 175
 Asn Lys Gly Cys Asn Gly Gly Phe Met Thr Thr Ala Phe Gln Tyr Ile
 180 185 190
 Ile Asp Asn Lys Gly Ile Asp Ser Asp Ala Ser Tyr Pro Tyr Lys Ala
 195 200 205
 Met Asp Gln Lys Cys Gln Tyr Asp Ser Lys Tyr Arg Ala Ala Thr Cys
 210 215 220
 Ser Lys Tyr Thr Glu Leu Pro Tyr Gly Arg Glu Asp Val Leu Lys Glu
 225 230 235 240
 Ala Val Ala Asn Lys Gly Pro Val Ser Val Gly Val Asp Ala Arg His
 245 250 255
 Pro Ser Phe Phe Leu Tyr Arg Ser Gly Val Tyr Tyr Glu Pro Ser Cys
 260 265 270
 Thr Gln Asn Val Asn His Gly Val Leu Val Val Gly Tyr Gly Asp Leu
 275 280 285
 Asn Gly Lys Glu Tyr Trp Leu Val Lys Asn Ser Trp Gly His Asn Phe
 290 295 300
 Gly Glu Glu Gly Tyr Ile Arg Met Ala Arg Asn Lys Gly Asn His Cys
 305 310 315 320
 Gly Ile Ala Ser Phe Pro Ser Tyr Pro Glu Ile
 325 330

<210> 49

<211> 303

<212> PRT

<213> 智人

<400> 49

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

Ser Thr Ser Ala Met Ala Asp Arg Ile Asn Ile Lys Arg Lys Gly Ala		
100	105	110
Trp Pro Ser Thr Leu Leu Ser Val Gln Asn Val Ile Asp Cys Gly Asn		
115	120	125
Ala Gly Ser Cys Glu Gly Gly Asn Asp Leu Ser Val Trp Asp Tyr Ala		
130	135	140
His Gln His Gly Ile Pro Asp Glu Thr Cys Asn Asn Tyr Gln Ala Lys		
145	150	155
Asp Gln Glu Cys Asp Lys Phe Asn Gln Cys Gly Thr Cys Asn Glu Phe		
165	170	175
Lys Glu Cys His Ala Ile Arg Asn Tyr Thr Leu Trp Arg Val Gly Asp		
180	185	190
Tyr Gly Ser Leu Ser Gly Arg Glu Lys Met Met Ala Glu Ile Tyr Ala		
195	200	205
Asn Gly Pro Ile Ser Cys Gly Ile Met Ala Thr Glu Arg Leu Ala Asn		
210	215	220
Tyr Thr Gly Gly Ile Tyr Ala Glu Tyr Gln Asp Thr Thr Tyr Ile Asn		
225	230	235
His Val Val Ser Val Ala Gly Trp Gly Ile Ser Asp Gly Thr Glu Tyr		
245	250	255
Trp Ile Val Arg Asn Ser Trp Gly Glu Pro Trp Gly Glu Arg Gly Trp		
260	265	270
Leu Arg Ile Val Thr Ser Thr Tyr Lys Asp Gly Lys Gly Ala Arg Tyr		
275	280	285
Asn Leu Ala Ile Glu Glu His Cys Thr Phe Gly Asp Pro Ile Val		
290	295	300
<210> 50		
<211> 776		
<212> PRT		
<213> 智人		
<400> 50		
Met Ser Ser Thr Arg Ser Gln Asn Pro His Gly Leu Lys Gln Ile Gly		
1	5	10
Leu Asp Gln Ile Trp Asp Asp Leu Arg Ala Gly Ile Gln Gln Val Tyr		
20	25	30
Thr Arg Gln Ser Met Ala Lys Ser Arg Tyr Met Glu Leu Tyr Thr His		
35	40	45
Val Tyr Asn Tyr Cys Thr Ser Val His Gln Ser Asn Gln Ala Arg Gly		
50	55	60

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

370	375	380
Phe Asn Asn Asp Ala Gly	Phe Val Ala Ala Leu	Asp Lys Ala Cys Gly
385	390	395
Arg Phe Ile Asn Asn Asn	Ala Val Thr Lys Met	Ala Gln Ser Ser Ser
405	410	415
Lys Ser Pro Glu Leu Leu	Ala Arg Tyr Cys Asp	Ser Leu Leu Lys Lys
420	425	430
Ser Ser Lys Asn Pro Glu	Glu Ala Glu Leu Glu	Asp Thr Leu Asn Gln
435	440	445
Val Met Val Val Phe Lys	Tyr Ile Glu Asp Lys	Asp Val Phe Gln Lys
450	455	460
Phe Tyr Ala Lys Met Leu	Ala Lys Arg Leu Val	His Gln Asn Ser Ala
465	470	475
Ser Asp Asp Ala Glu Ala	Ser Met Ile Ser Lys	Leu Lys Gln Ala Cys
485	490	495
Gly Phe Glu Tyr Thr Ser	Lys Leu Gln Arg Met	Phe Gln Asp Ile Gly
500	505	510
Val Ser Lys Asp Leu Asn	Glu Gln Phe Lys Lys	His Leu Thr Asn Ser
515	520	525
Glu Pro Leu Asp Leu Asp	Phe Ser Ile Gln Val	Leu Ser Ser Gly Ser
530	535	540
Trp Pro Phe Gln Gln Ser	Cys Thr Phe Ala Leu	Pro Ser Glu Leu Glu
545	550	555
Arg Ser Tyr Gln Arg Phe	Thr Ala Phe Tyr Ala	Ser Arg His Ser Gly
565	570	575
Arg Lys Leu Thr Trp Leu	Tyr Gln Leu Ser Lys	Gly Glu Leu Val Thr
580	585	590
Asn Cys Phe Lys Asn Arg	Tyr Thr Leu Gln Ala	Ser Thr Phe Gln Met
595	600	605
Ala Ile Leu Leu Gln Tyr	Asn Thr Glu Asp Ala	Tyr Thr Val Gln Gln
610	615	620
Leu Thr Asp Ser Thr Gln	Ile Lys Met Asp Ile	Leu Ala Gln Val Leu
625	630	635
Gln Ile Leu Leu Lys Ser	Lys Leu Leu Val Leu	Glu Asp Glu Asn Ala
645	650	655
Asn Val Asp Glu Val Glu	Leu Lys Pro Asp Thr	Leu Ile Lys Leu Tyr
660	665	670
Leu Gly Tyr Lys Asn Lys	Lys Leu Arg Val Asn	Ile Asn Val Pro Met
675	680	685

Lys Thr Glu Gln Lys Gln Glu Gln Glu Thr Thr His Lys Asn Ile Glu			
690	695	700	
Glu Asp Arg Lys Leu Leu Ile Gln Ala Ala Ile Val Arg Ile Met Lys			
705	710	715	720
Met Arg Lys Val Leu Lys His Gln Gln Leu Leu Gly Glu Val Leu Thr			
	725	730	735
Gln Leu Ser Ser Arg Phe Lys Pro Arg Val Pro Val Ile Lys Lys Cys			
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Ile Asp Ile Leu Ile Glu Lys Glu Tyr Leu Glu Arg Val Asp Gly Glu			
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Lys Asp Thr Tyr Ser Tyr Leu Ala			
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	35	40	45
Arg Asp Leu Thr Ile Gln Lys Ala Asp Glu Val Val Trp Val Arg Ala			
	50	55	60
Arg Val His Thr Ser Arg Ala Lys Gly Lys Gln Cys Phe Leu Val Leu			
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Arg Gln Gln Gln Phe Asn Val Gln Ala Leu Val Ala Val Gly Asp His			
	85	90	95
Ala Ser Lys Gln Met Val Lys Phe Ala Ala Asn Ile Asn Lys Glu Ser			
	100	105	110
Ile Val Asp Val Glu Gly Val Val Arg Lys Val Asn Gln Lys Ile Gly			
	115	120	125
Ser Cys Thr Gln Gln Asp Val Glu Leu His Val Gln Lys Ile Tyr Val			
	130	135	140
Ile Ser Leu Ala Glu Pro Arg Leu Pro Leu Gln Leu Asp Asp Ala Val			
145	150	155	160
Arg Pro Glu Ala Glu Gly Glu Glu Glu Gly Arg Ala Thr Val Asn Gln			
	165	170	175

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

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Lys Arg Leu Thr Pro			
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Pro Glu Gln Ile Ala Ala Asp Ile Pro Glu Val Val Val Ser Leu Ala			
35 40 45			
Trp Asp Glu Ser Leu Ala Pro Lys His Pro Gly Ser Arg Lys Asn Met			
50 55 60			
Ala Cys Tyr Cys Arg Ile Pro Ala Cys Ile Ala Gly Glu Arg Arg Tyr			
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Gly Thr Cys Ile Tyr Gln Gly Arg Leu Trp Ala Phe Cys Cys			
85 90			
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Ala Gln Ala Glu Pro Leu Gln Ala Arg Ala Asp Glu Val Ala Ala Ala			
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Pro Glu Gln Ile Ala Ala Asp Ile Pro Glu Val Val Val Ser Leu Ala			
35 40 45			
Trp Asp Glu Ser Leu Ala Pro Lys His Pro Gly Ser Arg Lys Asn Met			
50 55 60			
Asp Cys Tyr Cys Arg Ile Pro Ala Cys Ile Ala Gly Glu Arg Arg Tyr			
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Gly Thr Cys Ile Tyr Gln Gly Arg Leu Trp Ala Phe Cys Cys			
85 90			
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<212> PRT

<213> 智人

<400> 54

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

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Ile Ser Glu Ala Glu Glu Trp Tyr Lys Ser Lys Val Ser Asp Leu Thr															
290								295						300	
Gln Ala Ala Asn Lys Asn Asn Asp Ala Leu Arg Gln Ala Lys Gln Glu															
305							310					315			320
Met Met Glu Tyr Arg His Gln Ile Gln Ser Tyr Thr Cys Glu Ile Asp															
						325					330				335
Ala Leu Lys Gly Thr Asn Asp Ser Leu Met Arg Gln Met Arg Glu Leu															
						340					345				350
Glu Asp Arg Phe Ala Ser Glu Ala Ser Gly Tyr Gln Asp Asn Ile Ala															
						355					360				365
Arg Leu Glu Glu Glu Ile Arg His Leu Lys Asp Glu Met Ala Arg His															
						370					375				380
Leu Arg Glu Tyr Gln Asp Leu Leu Asn Val Lys Met Ala Leu Asp Val															
385						390					395				400
Glu Ile Ala Thr Tyr Arg Lys Leu Leu Glu Gly Glu Glu Ser Arg Ile															
						405					410				415
Asn Leu Pro Ile Gln Thr Tyr Ser Ala Leu Asn Phe Arg Glu Thr Ser															
						420					425				430
Pro Glu Gln Arg Gly Ser Glu Val His Thr Lys Lys Thr Val Met Ile															
						435					440				445
Lys Thr Ile Glu Thr Arg Asp Gly Glu Val Val Ser Glu Ala Thr Gln															
						450					455				460
Gln Gln His Glu Val Leu															
465															470
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Leu Val Thr Ile Ile Thr Val Pro Val Val Leu Leu Asn Lys Gly Thr															
						20					25				30
Asp Asp Ala Thr Ala Asp Ser Arg Lys Thr Tyr Thr Leu Thr Asp Tyr															
						35					40				45
Leu Lys Asn Thr Tyr Arg Leu Lys Leu Tyr Ser Leu Arg Trp Ile Ser															
						50					55				60
Asp His Glu Tyr Leu Tyr Lys Gln Glu Asn Asn Ile Leu Val Phe Asn															
65											70				75
															80

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

385	390	395	400
Thr Trp Glu Val Ile Gly Ile Glu Ala Leu Thr Ser Asp Tyr Leu Tyr			
	405	410	415
Tyr Ile Ser Asn Glu Tyr Lys Gly Met Pro Gly Gly Arg Asn Leu Tyr			
	420	425	430
Lys Ile Gln Leu Ser Asp Tyr Thr Lys Val Thr Cys Leu Ser Cys Glu			
	435	440	445
Leu Asn Pro Glu Arg Cys Gln Tyr Tyr Ser Val Ser Phe Ser Lys Glu			
	450	455	460
Ala Lys Tyr Tyr Gln Leu Arg Cys Ser Gly Pro Gly Leu Pro Leu Tyr			
465	470	475	480
Thr Leu His Ser Ser Val Asn Asp Lys Gly Leu Arg Val Leu Glu Asp			
	485	490	495
Asn Ser Ala Leu Asp Lys Met Leu Gln Asn Val Gln Met Pro Ser Lys			
	500	505	510
Lys Leu Asp Phe Ile Ile Leu Asn Glu Thr Lys Phe Trp Tyr Gln Met			
	515	520	525
Ile Leu Pro Pro His Phe Asp Lys Ser Lys Lys Tyr Pro Leu Leu Leu			
	530	535	540
Asp Val Tyr Ala Gly Pro Cys Ser Gln Lys Ala Asp Thr Val Phe Arg			
545	550	555	560
Leu Asn Trp Ala Thr Tyr Leu Ala Ser Thr Glu Asn Ile Ile Val Ala			
	565	570	575
Ser Phe Asp Gly Arg Gly Ser Gly Tyr Gln Gly Asp Lys Ile Met His			
	580	585	590
Ala Ile Asn Arg Arg Leu Gly Thr Phe Glu Val Glu Asp Gln Ile Glu			
	595	600	605
Ala Ala Arg Gln Phe Ser Lys Met Gly Phe Val Asp Asn Lys Arg Ile			
	610	615	620
Ala Ile Trp Gly Trp Ser Tyr Gly Gly Tyr Val Thr Ser Met Val Leu			
625	630	635	640
Gly Ser Gly Ser Gly Val Phe Lys Cys Gly Ile Ala Val Ala Pro Val			
	645	650	655
Ser Arg Trp Glu Tyr Tyr Asp Ser Val Tyr Thr Glu Arg Tyr Met Gly			
	660	665	670
Leu Pro Thr Pro Glu Asp Asn Leu Asp His Tyr Arg Asn Ser Thr Val			
	675	680	685
Met Ser Arg Ala Glu Asn Phe Lys Gln Val Glu Tyr Leu Leu Ile His			
	690	695	700

Gly	Thr	Ala	Asp	Asp	Asn	Val	His	Phe	Gln	Gln	Ser	Ala	Gln	Ile	Ser
705					710				715					720	
Lys	Ala	Leu	Val	Asp	Val	Gly	Val	Asp	Phe	Gln	Ala	Met	Trp	Tyr	Thr
				725					730					735	
Asp	Glu	Asp	His	Gly	Ile	Ala	Ser	Ser	Thr	Ala	His	Gln	His	Ile	Tyr
			740					745				750			
Thr	His	Met	Ser	His	Phe	Ile	Lys	Gln	Cys	Phe	Ser	Leu	Pro		
		755					760					765			
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Leu	Leu	Ile	Lys	Gly	Gly	Lys	Ile	Val	Asn	Asp	Asp	Gln	Ser	Phe	Tyr
			20					25				30			
Ala	Asp	Ile	Tyr	Met	Glu	Asp	Gly	Leu	Ile	Lys	Gln	Ile	Gly	Glu	Asn
			35				40					45			
Leu	Ile	Val	Pro	Gly	Gly	Val	Lys	Thr	Ile	Glu	Ala	His	Ser	Arg	Met
		50				55				60					
Val	Ile	Pro	Gly	Gly	Ile	Asp	Val	His	Thr	Arg	Phe	Gln	Met	Pro	Asp
65				70					75					80	
Gln	Gly	Met	Thr	Ser	Ala	Asp	Asp	Phe	Phe	Gln	Gly	Thr	Lys	Ala	Ala
				85					90					95	
Leu	Ala	Gly	Gly	Thr	Thr	Met	Ile	Ile	Asp	His	Val	Val	Pro	Glu	Pro
			100					105					110		
Gly	Thr	Ser	Leu	Leu	Ala	Ala	Phe	Asp	Gln	Trp	Arg	Glu	Trp	Ala	Asp
		115					120					125			
Ser	Lys	Ser	Cys	Cys	Asp	Tyr	Ser	Leu	His	Val	Asp	Ile	Ser	Glu	Trp
		130				135					140				
His	Lys	Gly	Ile	Gln	Glu	Glu	Met	Glu	Ala	Leu	Val	Lys	Asp	His	Gly
145				150					155					160	
Val	Asn	Ser	Phe	Leu	Val	Tyr	Met	Ala	Phe	Lys	Asp	Arg	Phe	Gln	Leu
				165					170					175	
Thr	Asp	Cys	Gln	Ile	Tyr	Glu	Val	Leu	Ser	Val	Ile	Arg	Asp	Ile	Gly
			180					185					190		
Ala	Ile	Ala	Gln	Val	His	Ala	Glu	Asn	Gly	Asp	Ile	Ile	Ala	Glu	Glu
			195					200					205		

Gln	Gln	Arg	Ile	Leu	Asp	Leu	Gly	Ile	Thr	Gly	Pro	Glu	Gly	His	Val
210			215			220									
Leu	Ser	Arg	Pro	Glu	Glu	Val	Glu	Ala	Glu	Ala	Val	Asn	Arg	Ala	Ile
225			230			235			240						
Thr	Ile	Ala	Asn	Gln	Thr	Asn	Cys	Pro	Leu	Tyr	Ile	Thr	Lys	Val	Met
245			250			255									
Ser	Lys	Ser	Ser	Ala	Glu	Val	Ile	Ala	Gln	Ala	Arg	Lys	Lys	Gly	Thr
260			265			270									
Val	Val	Tyr	Gly	Glu	Pro	Ile	Thr	Ala	Ser	Leu	Gly	Thr	Asp	Gly	Ser
275			280			285									
His	Tyr	Trp	Ser	Lys	Asn	Trp	Ala	Lys	Ala	Ala	Ala	Phe	Val	Thr	Ser
290			295			300									
Pro	Pro	Leu	Ser	Pro	Asp	Pro	Thr	Thr	Pro	Asp	Phe	Leu	Asn	Ser	Leu
305			310			315			320						
Leu	Ser	Cys	Gly	Asp	Leu	Gln	Val	Thr	Gly	Ser	Ala	His	Cys	Thr	Phe
325			330			335									
Asn	Thr	Ala	Gln	Lys	Ala	Val	Gly	Lys	Asp	Asn	Phe	Thr	Leu	Ile	Pro
340			345			350									
Glu	Gly	Thr	Asn	Gly	Thr	Glu	Glu	Arg	Met	Ser	Val	Ile	Trp	Asp	Lys
355			360			365									
Ala	Val	Val	Thr	Gly	Lys	Met	Asp	Glu	Asn	Gln	Phe	Val	Ala	Val	Thr
370			375			380									
Ser	Thr	Asn	Ala	Ala	Lys	Val	Phe	Asn	Leu	Tyr	Pro	Arg	Lys	Gly	Arg
385			390			395			400						
Ile	Ala	Val	Gly	Ser	Asp	Ala	Asp	Leu	Val	Ile	Trp	Asp	Pro	Asp	Ser
405			410			415									
Val	Lys	Thr	Ile	Ser	Ala	Lys	Thr	His	Asn	Ser	Ser	Leu	Glu	Tyr	Asn
420			425			430									
Ile	Phe	Glu	Gly	Met	Glu	Cys	Arg	Gly	Ser	Pro	Leu	Val	Val	Ile	Ser
435			440			445									
Gln	Gly	Lys	Ile	Val	Leu	Glu	Asp	Gly	Thr	Leu	His	Val	Thr	Glu	Gly
450			455			460									
Ser	Gly	Arg	Tyr	Ile	Pro	Arg	Lys	Pro	Phe	Pro	Asp	Phe	Val	Tyr	Lys
465			470			475			480						
Arg	Ile	Lys	Ala	Arg	Ser	Arg	Leu	Ala	Glu	Leu	Arg	Gly	Val	Pro	Arg
485			490			495									
Gly	Leu	Tyr	Asp	Gly	Pro	Val	Cys	Glu	Val	Ser	Val	Thr	Pro	Lys	Thr
500			505			510									
Val	Thr	Pro	Ala	Ser	Ser	Ala	Lys	Thr	Ser	Pro	Ala	Lys	Gln	Gln	Ala

515	520	525
Pro Pro Val Arg Asn Leu His Gln Ser Gly Phe Ser Leu Ser Gly Ala		
530	535	540
Gln Ile Asp Asp Asn Ile Pro Arg Arg Thr Thr Gln Arg Ile Val Ala		
545	550	555
Pro Pro Gly Gly Arg Ala Asn Ile Thr Ser Leu Gly		560
565	570	
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Glu Val Ser Ala Val Gln Asn Val Ala Asp Val Ser Val Leu Gln Lys		15
20	25	30
His Leu Arg Lys Leu Val Pro Leu Leu Leu Glu Asp Gly Gly Glu Ala		
35	40	45
Pro Ala Ala Leu Glu Ala Ala Leu Glu Glu Lys Ser Ala Leu Glu Gln		
50	55	60
Met Arg Lys Phe Leu Ser Asp Pro Gln Val His Thr Val Leu Val Glu		
65	70	75
Arg Ser Thr Leu Lys Glu Asp Val Gly Asp Glu Gly Glu Glu Glu Lys		80
85	90	95
Glu Phe Ile Ser Tyr Asn Ile Asn Ile Asp Ile His Tyr Gly Val Lys		
100	105	110
Ser Asn Ser Leu Ala Phe Ile Lys Arg Thr Pro Val Ile Asp Ala Asp		
115	120	125
Lys Pro Val Ser Ser Gln Leu Arg Val Leu Thr Leu Ser Glu Asp Ser		
130	135	140
Pro Tyr Glu Thr Leu His Ser Phe Ile Ser Asn Ala Val Ala Pro Phe		
145	150	155
Phe Lys Ser Tyr Ile Arg Glu Ser Gly Lys Ala Asp Arg Asp Gly Asp		160
165	170	175
Lys Met Ala Pro Ser Val Glu Lys Lys Ile Ala Glu Leu Glu Met Gly		
180	185	190
Leu Leu His Leu Gln Gln Asn Ile Glu Ile Pro Glu Ile Ser Leu Pro		
195	200	205
Ile His Pro Met Ile Thr Asn Val Ala Lys Gln Cys Tyr Glu Arg Gly		

210	215	220
Glu Lys Pro Lys Val Thr Asp Phe Gly Asp Lys Val Glu Asp Pro Thr		
225	230	235
Phe Leu Asn Gln Leu Gln Ser Gly Val Asn Arg Trp Ile Arg Glu Ile		240
	245	250
Gln Lys Val Thr Lys Leu Asp Arg Asp Pro Ala Ser Gly Thr Ala Leu		255
	260	265
Gln Glu Ile Ser Phe Trp Leu Asn Leu Glu Arg Ala Leu Tyr Arg Ile		270
	275	280
Gln Glu Lys Arg Glu Ser Pro Glu Val Leu Leu Thr Leu Asp Ile Leu		285
290	295	300
Lys His Gly Lys Arg Phe His Ala Thr Val Ser Phe Asp Thr Asp Thr		
305	310	315
Gly Leu Lys Gln Ala Leu Glu Thr Val Asn Asp Tyr Asn Pro Leu Met		320
	325	330
Lys Asp Phe Pro Leu Asn Asp Leu Leu Ser Ala Thr Glu Leu Asp Lys		335
	340	345
Ile Arg Gln Ala Leu Val Ala Ile Phe Thr His Leu Arg Lys Ile Arg		350
	355	360
Asn Thr Lys Tyr Pro Ile Gln Arg Ala Leu Arg Leu Val Glu Ala Ile		365
370	375	380
Ser Arg Asp Leu Ser Ser Gln Leu Leu Lys Val Leu Gly Thr Arg Lys		
385	390	395
Leu Met His Val Ala Tyr Glu Glu Phe Glu Lys Val Met Val Ala Cys		400
	405	410
Phe Glu Val Phe Gln Thr Trp Asp Asp Glu Tyr Glu Lys Leu Gln Val		415
	420	425
Leu Leu Arg Asp Ile Val Lys Arg Lys Arg Glu Glu Asn Leu Lys Met		430
	435	440
Val Trp Arg Ile Asn Pro Ala His Arg Lys Leu Gln Ala Arg Leu Asp		445
	450	455
Gln Met Arg Lys Phe Arg Arg Gln His Glu Gln Leu Arg Ala Val Ile		460
465	470	475
Val Arg Val Leu Arg Pro Gln Val Thr Ala Val Ala Gln Gln Asn Gln		480
	485	490
Gly Glu Val Pro Glu Pro Gln Asp Met Lys Val Ala Glu Val Leu Phe		495
	500	505
Asp Ala Ala Asp Ala Asn Ala Ile Glu Glu Val Asn Leu Ala Tyr Glu		510
515	520	525

Asn Val Lys Glu Val Asp Gly Leu Asp Val Ser Lys Glu Gly Thr Glu		
530	535	540
Ala Trp Glu Ala Ala Met Lys Arg Tyr Asp Glu Arg Ile Asp Arg Val		
545	550	555 560
Glu Thr Arg Ile Thr Ala Arg Leu Arg Asp Gln Leu Gly Thr Ala Lys		
	565	570 575
Asn Ala Asn Glu Met Phe Arg Ile Phe Ser Arg Phe Asn Ala Leu Phe		
	580	585 590
Val Arg Pro His Ile Arg Gly Ala Ile Arg Glu Tyr Gln Thr Gln Leu		
	595	600 605
Ile Gln Arg Val Lys Asp Asp Ile Glu Ser Leu His Asp Lys Phe Lys		
	610	615 620
Val Gln Tyr Pro Gln Ser Gln Ala Cys Lys Met Ser His Val Arg Asp		
625	630	635 640
Leu Pro Pro Val Ser Gly Ser Ile Ile Trp Ala Lys Gln Ile Asp Arg		
	645	650 655
Gln Leu Thr Ala Tyr Met Lys Arg Val Glu Asp Val Leu Gly Lys Gly		
	660	665 670
Trp Glu Asn His Val Glu Gly Gln Lys Leu Lys Gln Asp Gly Asp Ser		
	675	680 685
Phe Arg Met Lys Leu Asn Thr Gln Glu Ile Phe Asp Asp Trp Ala Arg		
690	695	700
Lys Val Gln Gln Arg Asn Leu Gly Val Ser Gly Arg Ile Phe Thr Ile		
705	710	715 720
Glu Ser Thr Arg Val Arg Gly Arg Thr Gly Asn Val Leu Lys Leu Lys		
	725	730 735
Val Asn Phe Leu Pro Glu Ile Ile Thr Leu Ser Lys Glu Val Arg Asn		
	740	745 750
Leu Lys Trp Leu Gly Phe Arg Val Pro Leu Ala Ile Val Asn Lys Ala		
	755	760 765
His Gln Ala Asn Gln Leu Tyr Pro Phe Ala Ile Ser Leu Ile Glu Ser		
770	775	780
Val Arg Thr Tyr Glu Arg Thr Cys Glu Lys Val Glu Glu Arg Asn Thr		
785	790	795 800
Ile Ser Leu Leu Val Ala Gly Leu Lys Lys Glu Val Gln Ala Leu Ile		
	805	810 815
Ala Glu Gly Ile Ala Leu Val Trp Glu Ser Tyr Lys Leu Asp Pro Tyr		
	820	825 830
Val Gln Arg Leu Ala Glu Thr Val Phe Asn Phe Gln Glu Lys Val Asp		

835	840	845
Asp Leu Leu Ile Ile Glu Glu Lys Ile Asp Leu Glu Val Arg Ser Leu		
850	855	860
Glu Thr Cys Met Tyr Asp His Lys Thr Phe Ser Glu Ile Leu Asn Arg		
865	870	875
Val Gln Lys Ala Val Asp Asp Leu Asn Leu His Ser Tyr Ser Asn Leu		880
885	890	895
Pro Ile Trp Val Asn Lys Leu Asp Met Glu Ile Glu Arg Ile Leu Gly		
900	905	910
Val Arg Leu Gln Ala Gly Leu Arg Ala Trp Thr Gln Val Leu Leu Gly		
915	920	925
Gln Ala Glu Asp Lys Ala Glu Val Asp Met Asp Thr Asp Ala Pro Gln		
930	935	940
Val Ser His Lys Pro Gly Gly Glu Pro Lys Ile Lys Asn Val Val His		
945	950	955
Glu Leu Arg Ile Thr Asn Gln Val Ile Tyr Leu Asn Pro Pro Ile Glu		
965	970	975
Glu Cys Arg Tyr Lys Leu Tyr Gln Glu Met Phe Ala Trp Lys Met Val		
980	985	990
Val Leu Ser Leu Pro Arg Ile Gln Ser Gln Arg Tyr Gln Val Gly Val		
995	1000	1005
His Tyr Glu Leu Thr Glu Glu Glu Lys Phe Tyr Arg Asn Ala Leu		
1010	1015	1020
Thr Arg Met Pro Asp Gly Pro Val Ala Leu Glu Glu Ser Tyr Ser		
1025	1030	1035
Ala Val Met Gly Ile Val Ser Glu Val Glu Gln Tyr Val Lys Val		
1040	1045	1050
Trp Leu Gln Tyr Gln Cys Leu Trp Asp Met Gln Ala Glu Asn Ile		
1055	1060	1065
Tyr Asn Arg Leu Gly Glu Asp Leu Asn Lys Trp Gln Ala Leu Leu		
1070	1075	1080
Val Gln Ile Arg Lys Ala Arg Gly Thr Phe Asp Asn Ala Glu Thr		
1085	1090	1095
Lys Lys Glu Phe Gly Pro Val Val Ile Asp Tyr Gly Lys Val Gln		
1100	1105	1110
Ser Lys Val Asn Leu Lys Tyr Asp Ser Trp His Lys Glu Val Leu		
1115	1120	1125
Ser Lys Phe Gly Gln Met Leu Gly Ser Asn Met Thr Glu Phe His		
1130	1135	1140

Ser Gln Ile Ser Lys Ser Arg Gln Glu Leu Glu Gln His Ser Val		
1145	1150	1155
Asp Thr Ala Ser Thr Ser Asp Ala Val Thr Phe Ile Thr Tyr Val		
1160	1165	1170
Gln Ser Leu Lys Arg Lys Ile Lys Gln Phe Glu Lys Gln Val Glu		
1175	1180	1185
Leu Tyr Arg Asn Gly Gln Arg Leu Leu Glu Lys Gln Arg Phe Gln		
1190	1195	1200
Phe Pro Pro Ser Trp Leu Tyr Ile Asp Asn Ile Glu Gly Glu Trp		
1205	1210	1215
Gly Ala Phe Asn Asp Ile Met Arg Arg Lys Asp Ser Ala Ile Gln		
1220	1225	1230
Gln Gln Val Ala Asn Leu Gln Met Lys Ile Val Gln Glu Asp Arg		
1235	1240	1245
Ala Val Glu Ser Arg Thr Thr Asp Leu Leu Thr Asp Trp Glu Lys		
1250	1255	1260
Thr Lys Pro Val Thr Gly Asn Leu Arg Pro Glu Glu Ala Leu Gln		
1265	1270	1275
Ala Leu Thr Ile Tyr Glu Gly Lys Phe Gly Arg Leu Lys Asp Asp		
1280	1285	1290
Arg Glu Lys Cys Ala Lys Ala Lys Glu Ala Leu Glu Leu Thr Asp		
1295	1300	1305
Thr Gly Leu Leu Ser Gly Ser Glu Glu Arg Val Gln Val Ala Leu		
1310	1315	1320
Glu Glu Leu Gln Asp Leu Lys Gly Val Trp Ser Glu Leu Ser Lys		
1325	1330	1335
Val Trp Glu Gln Ile Asp Gln Met Lys Glu Gln Pro Trp Val Ser		
1340	1345	1350
Val Gln Pro Arg Lys Leu Arg Gln Asn Leu Asp Ala Leu Leu Asn		
1355	1360	1365
Gln Leu Lys Ser Phe Pro Ala Arg Leu Arg Gln Tyr Ala Ser Tyr		
1370	1375	1380
Glu Phe Val Gln Arg Leu Leu Lys Gly Tyr Met Lys Ile Asn Met		
1385	1390	1395
Leu Val Ile Glu Leu Lys Ser Glu Ala Leu Lys Asp Arg His Trp		
1400	1405	1410
Lys Gln Leu Met Lys Arg Leu His Val Asn Trp Val Val Ser Glu		
1415	1420	1425
Leu Thr Leu Gly Gln Ile Trp Asp Val Asp Leu Gln Lys Asn Glu		

1430	1435	1440
Ala Ile Val Lys Asp Val	Leu Leu Val Ala Gln	Gly Glu Met Ala
1445	1450	1455
Leu Glu Glu Phe Leu Lys	Gln Ile Arg Glu Val	Trp Asn Thr Tyr
1460	1465	1470
Glu Leu Asp Leu Val Asn	Tyr Gln Asn Lys Cys	Arg Leu Ile Arg
1475	1480	1485
Gly Trp Asp Asp Leu Phe	Asn Lys Val Lys Glu	His Ile Asn Ser
1490	1495	1500
Val Ser Ala Met Lys Leu	Ser Pro Tyr Tyr Lys	Val Phe Glu Glu
1505	1510	1515
Asp Ala Leu Ser Trp Glu	Asp Lys Leu Asn Arg	Ile Met Ala Leu
1520	1525	1530
Phe Asp Val Trp Ile Asp	Val Gln Arg Arg Trp	Val Tyr Leu Glu
1535	1540	1545
Gly Ile Phe Thr Gly Ser	Ala Asp Ile Lys His	Leu Leu Pro Val
1550	1555	1560
Glu Thr Gln Arg Phe Gln	Ser Ile Ser Thr Glu	Phe Leu Ala Leu
1565	1570	1575
Met Lys Lys Val Ser Lys	Ser Pro Leu Val Met	Asp Val Leu Asn
1580	1585	1590
Ile Gln Gly Val Gln Arg	Ser Leu Glu Arg Leu	Ala Asp Leu Leu
1595	1600	1605
Gly Lys Ile Gln Lys Ala	Leu Gly Glu Tyr Leu	Glu Arg Glu Arg
1610	1615	1620
Ser Ser Phe Pro Arg Phe	Tyr Phe Val Gly Asp	Glu Asp Leu Leu
1625	1630	1635
Glu Ile Ile Gly Asn Ser	Lys Asn Val Ala Lys	Leu Gln Lys His
1640	1645	1650
Phe Lys Lys Met Phe Ala	Gly Val Ser Ser Ile	Ile Leu Asn Glu
1655	1660	1665
Asp Asn Ser Val Val Leu	Gly Ile Ser Ser Arg	Glu Gly Glu Glu
1670	1675	1680
Val Met Phe Lys Thr Pro	Val Ser Ile Thr Glu	His Pro Lys Ile
1685	1690	1695
Asn Glu Trp Leu Thr Leu	Val Glu Lys Glu Met	Arg Val Thr Leu
1700	1705	1710
Ala Lys Leu Leu Ala Glu	Ser Val Thr Glu Val	Glu Ile Phe Gly
1715	1720	1725

Lys Ala Thr Ser Ile Asp Pro Asn Thr Tyr Ile Thr Trp Ile Asp		
1730	1735	1740
Lys Tyr Gln Ala Gln Leu Val Val Leu Ser Ala Gln Ile Ala Trp		
1745	1750	1755
Ser Glu Asn Val Glu Thr Ala Leu Ser Ser Met Gly Gly Gly Gly		
1760	1765	1770
Asp Ala Ala Pro Leu His Ser Val Leu Ser Asn Val Glu Val Thr		
1775	1780	1785
Leu Asn Val Leu Ala Asp Ser Val Leu Met Glu Gln Pro Pro Leu		
1790	1795	1800
Arg Arg Arg Lys Leu Glu His Leu Ile Thr Glu Leu Val His Gln		
1805	1810	1815
Arg Asp Val Thr Arg Ser Leu Ile Lys Ser Lys Ile Asp Asn Ala		
1820	1825	1830
Lys Ser Phe Glu Trp Leu Ser Gln Met Arg Phe Tyr Phe Asp Pro		
1835	1840	1845
Lys Gln Thr Asp Val Leu Gln Gln Leu Ser Ile Gln Met Ala Asn		
1850	1855	1860
Ala Lys Phe Asn Tyr Gly Phe Glu Tyr Leu Gly Val Gln Asp Lys		
1865	1870	1875
Leu Val Gln Thr Pro Leu Thr Asp Arg Cys Tyr Leu Thr Met Thr		
1880	1885	1890
Gln Ala Leu Glu Ala Arg Leu Gly Gly Ser Pro Phe Gly Pro Ala		
1895	1900	1905
Gly Thr Gly Lys Thr Glu Ser Val Lys Ala Leu Gly His Gln Leu		
1910	1915	1920
Gly Arg Phe Val Leu Val Phe Asn Cys Asp Glu Thr Phe Asp Phe		
1925	1930	1935
Gln Ala Met Gly Arg Ile Phe Val Gly Leu Cys Gln Val Gly Ala		
1940	1945	1950
Trp Gly Cys Phe Asp Glu Phe Asn Arg Leu Glu Glu Arg Met Leu		
1955	1960	1965
Ser Ala Val Ser Gln Gln Val Gln Cys Ile Gln Glu Ala Leu Arg		
1970	1975	1980
Glu His Ser Asn Pro Asn Tyr Asp Lys Thr Ser Ala Pro Ile Thr		
1985	1990	1995
Cys Glu Leu Leu Asn Lys Gln Val Lys Val Ser Pro Asp Met Ala		
2000	2005	2010
Ile Phe Ile Thr Met Asn Pro Gly Tyr Ala Gly Arg Ser Asn Leu		

2015	2020	2025
Pro Asp Asn Leu Lys Lys	Leu Phe Arg Ser Leu	Ala Met Thr Lys
2030	2035	2040
Pro Asp Arg Gln Leu Ile	Ala Gln Val Met Leu	Tyr Ser Gln Gly
2045	2050	2055
Phe Arg Thr Ala Glu Val	Leu Ala Asn Lys Ile	Val Pro Phe Phe
2060	2065	2070
Lys Leu Cys Asp Glu Gln	Leu Ser Ser Gln Ser	His Tyr Asp Phe
2075	2080	2085
Gly Leu Arg Ala Leu Lys	Ser Val Leu Val Ser	Ala Gly Asn Val
2090	2095	2100
Lys Arg Glu Arg Ile Gln	Lys Ile Lys Arg Glu	Lys Glu Glu Arg
2105	2110	2115
Gly Glu Ala Val Asp Glu	Gly Glu Ile Ala Glu	Asn Leu Pro Glu
2120	2125	2130
Gln Glu Ile Leu Ile Gln	Ser Val Cys Glu Thr	Met Val Pro Lys
2135	2140	2145
Leu Val Ala Glu Asp Ile	Pro Leu Leu Phe Ser	Leu Leu Ser Asp
2150	2155	2160
Val Phe Pro Gly Val Gln	Tyr His Arg Gly Glu	Met Thr Ala Leu
2165	2170	2175
Arg Glu Glu Leu Lys Lys	Val Cys Gln Glu Met	Tyr Leu Thr Tyr
2180	2185	2190
Gly Asp Gly Glu Glu Val	Gly Gly Met Trp Val	Glu Lys Val Leu
2195	2200	2205
Gln Leu Tyr Gln Ile Thr	Gln Ile Asn His Gly	Leu Met Met Val
2210	2215	2220
Gly Pro Ser Gly Ser Gly	Lys Ser Met Ala Trp	Arg Val Leu Leu
2225	2230	2235
Lys Ala Leu Glu Arg Leu	Glu Gly Val Glu Gly	Val Ala His Ile
2240	2245	2250
Ile Asp Pro Lys Ala Ile	Ser Lys Asp His Leu	Tyr Gly Thr Leu
2255	2260	2265
Asp Pro Asn Thr Arg Glu	Trp Thr Asp Gly Leu	Phe Thr His Val
2270	2275	2280
Leu Arg Lys Ile Ile Asp	Ser Val Arg Gly Glu	Leu Gln Lys Arg
2285	2290	2295
Gln Trp Ile Val Phe Asp	Gly Asp Val Asp Pro	Glu Trp Val Glu
2300	2305	2310

Asn Leu Asn Ser Val Leu Asp Asp Asn Lys Leu Leu Thr Leu Pro		
2315	2320	2325
Asn Gly Glu Arg Leu Ser Leu Pro Pro Asn Val Arg Ile Met Phe		
2330	2335	2340
Glu Val Gln Asp Leu Lys Tyr Ala Thr Leu Ala Thr Val Ser Arg		
2345	2350	2355
Cys Gly Met Val Trp Phe Ser Glu Asp Val Leu Ser Thr Asp Met		
2360	2365	2370
Ile Phe Asn Asn Phe Leu Ala Arg Leu Arg Ser Ile Pro Leu Asp		
2375	2380	2385
Glu Gly Glu Asp Glu Ala Gln Arg Arg Arg Lys Gly Lys Glu Asp		
2390	2395	2400
Glu Gly Glu Glu Ala Ala Ser Pro Met Leu Gln Ile Gln Arg Asp		
2405	2410	2415
Ala Ala Thr Ile Met Gln Pro Tyr Phe Thr Ser Asn Gly Leu Val		
2420	2425	2430
Thr Lys Ala Leu Glu His Ala Phe Gln Leu Glu His Ile Met Asp		
2435	2440	2445
Leu Thr Arg Leu Arg Cys Leu Gly Ser Leu Phe Ser Met Leu His		
2450	2455	2460
Gln Ala Cys Arg Asn Val Ala Gln Tyr Asn Ala Asn His Pro Asp		
2465	2470	2475
Phe Pro Met Gln Ile Glu Gln Leu Glu Arg Tyr Ile Gln Arg Tyr		
2480	2485	2490
Leu Val Tyr Ala Ile Leu Trp Ser Leu Ser Gly Asp Ser Arg Leu		
2495	2500	2505
Lys Met Arg Ala Glu Leu Gly Glu Tyr Ile Arg Arg Ile Thr Thr		
2510	2515	2520
Val Pro Leu Pro Thr Ala Pro Asn Ile Pro Ile Ile Asp Tyr Glu		
2525	2530	2535
Val Ser Ile Ser Gly Glu Trp Ser Pro Trp Gln Ala Lys Val Pro		
2540	2545	2550
Gln Ile Glu Val Glu Thr His Lys Val Ala Ala Pro Asp Val Val		
2555	2560	2565
Val Pro Thr Leu Asp Thr Val Arg His Glu Ala Leu Leu Tyr Thr		
2570	2575	2580
Trp Leu Ala Glu His Lys Pro Leu Val Leu Cys Gly Pro Pro Gly		
2585	2590	2595
Ser Gly Lys Thr Met Thr Leu Phe Ser Ala Leu Arg Ala Leu Pro		

2600	2605	2610
Asp Met Glu Val Val Gly	Leu Asn Phe Ser Ser	Ala Thr Thr Pro
2615	2620	2625
Glu Leu Leu Leu Lys Thr	Phe Asp His Tyr Cys	Glu Tyr Arg Arg
2630	2635	2640
Thr Pro Asn Gly Val Val	Leu Ala Pro Val Gln	Leu Gly Lys Trp
2645	2650	2655
Leu Val Leu Phe Cys Asp	Glu Ile Asn Leu Pro	Asp Met Asp Lys
2660	2665	2670
Tyr Gly Thr Gln Arg Val	Ile Ser Phe Ile Arg	Gln Met Val Glu
2675	2680	2685
His Gly Gly Phe Tyr Arg	Thr Ser Asp Gln Thr	Trp Val Lys Leu
2690	2695	2700
Glu Arg Ile Gln Phe Val	Gly Ala Cys Asn Pro	Pro Thr Asp Pro
2705	2710	2715
Gly Arg Lys Pro Leu Ser	His Arg Phe Leu Arg	His Val Pro Val
2720	2725	2730
Val Tyr Val Asp Tyr Pro	Gly Pro Ala Ser Leu	Thr Gln Ile Tyr
2735	2740	2745
Gly Thr Phe Asn Arg Ala	Met Leu Arg Leu Ile	Pro Ser Leu Arg
2750	2755	2760
Thr Tyr Ala Glu Pro Leu	Thr Ala Ala Met Val	Glu Phe Tyr Thr
2765	2770	2775
Met Ser Gln Glu Arg Phe	Thr Gln Asp Thr Gln	Pro His Tyr Ile
2780	2785	2790
Tyr Ser Pro Arg Glu Met	Thr Arg Trp Val Arg	Gly Ile Phe Glu
2795	2800	2805
Ala Leu Arg Pro Leu Glu	Thr Leu Pro Val Glu	Gly Leu Ile Arg
2810	2815	2820
Ile Trp Ala His Glu Ala	Leu Arg Leu Phe Gln	Asp Arg Leu Val
2825	2830	2835
Glu Asp Glu Glu Arg Arg	Trp Thr Asp Glu Asn	Ile Asp Thr Val
2840	2845	2850
Ala Leu Lys His Phe Pro	Asn Ile Asp Arg Glu	Lys Ala Met Ser
2855	2860	2865
Arg Pro Ile Leu Tyr Ser	Asn Trp Leu Ser Lys	Asp Tyr Ile Pro
2870	2875	2880
Val Asp Gln Glu Glu Leu	Arg Asp Tyr Val Lys	Ala Arg Leu Lys
2885	2890	2895

Val Phe Tyr Glu Glu Glu Leu Asp Val Pro Leu Val Leu Phe Asn		
2900	2905	2910
Glu Val Leu Asp His Val Leu Arg Ile Asp Arg Ile Phe Arg Gln		
2915	2920	2925
Pro Gln Gly His Leu Leu Leu Ile Gly Val Ser Gly Ala Gly Lys		
2930	2935	2940
Thr Thr Leu Ser Arg Phe Val Ala Trp Met Asn Gly Leu Ser Val		
2945	2950	2955
Tyr Gln Ile Lys Val His Arg Lys Tyr Thr Gly Glu Asp Phe Asp		
2960	2965	2970
Glu Asp Leu Arg Thr Val Leu Arg Arg Ser Gly Cys Lys Asn Glu		
2975	2980	2985
Lys Ile Ala Phe Ile Met Asp Glu Ser Asn Val Leu Asp Ser Gly		
2990	2995	3000
Phe Leu Glu Arg Met Asn Thr Leu Leu Ala Asn Gly Glu Val Pro		
3005	3010	3015
Gly Leu Phe Glu Gly Asp Glu Tyr Ala Thr Leu Met Thr Gln Cys		
3020	3025	3030
Lys Glu Gly Ala Gln Lys Glu Gly Leu Met Leu Asp Ser His Glu		
3035	3040	3045
Glu Leu Tyr Lys Trp Phe Thr Ser Gln Val Ile Arg Asn Leu His		
3050	3055	3060
Val Val Phe Thr Met Asn Pro Ser Ser Glu Gly Leu Lys Asp Arg		
3065	3070	3075
Ala Ala Thr Ser Pro Ala Leu Phe Asn Arg Cys Val Leu Asn Trp		
3080	3085	3090
Phe Gly Asp Trp Ser Thr Glu Ala Leu Tyr Gln Val Gly Lys Glu		
3095	3100	3105
Phe Thr Ser Lys Met Asp Leu Glu Lys Pro Asn Tyr Ile Val Pro		
3110	3115	3120
Asp Tyr Met Pro Val Val Tyr Asp Lys Leu Pro Gln Pro Pro Ser		
3125	3130	3135
His Arg Glu Ala Ile Val Asn Ser Cys Val Phe Val His Gln Thr		
3140	3145	3150
Leu His Gln Ala Asn Ala Arg Leu Ala Lys Arg Gly Gly Arg Thr		
3155	3160	3165
Met Ala Ile Thr Pro Arg His Tyr Leu Asp Phe Ile Asn His Tyr		
3170	3175	3180
Ala Asn Leu Phe His Glu Lys Arg Ser Glu Leu Glu Glu Gln Gln		

3185	3190	3195
Met His Leu Asn Val Gly	Leu Arg Lys Ile Lys	Glu Thr Val Asp
3200	3205	3210
Gln Val Glu Glu Leu Arg	Arg Asp Leu Arg Ile	Lys Ser Gln Glu
3215	3220	3225
Leu Glu Val Lys Asn Ala	Ala Ala Asn Asp Lys	Leu Lys Lys Met
3230	3235	3240
Val Lys Asp Gln Gln Glu	Ala Glu Lys Lys Lys	Val Met Ser Gln
3245	3250	3255
Glu Ile Gln Glu Gln Leu	His Lys Gln Gln Glu	Val Ile Ala Asp
3260	3265	3270
Lys Gln Met Ser Val Lys	Glu Asp Leu Asp Lys	Val Glu Pro Ala
3275	3280	3285
Val Ile Glu Ala Gln Asn	Ala Val Lys Ser Ile	Lys Lys Gln His
3290	3295	3300
Leu Val Glu Val Arg Ser	Met Ala Asn Pro Pro	Ala Ala Val Lys
3305	3310	3315
Leu Ala Leu Glu Ser Ile	Cys Leu Leu Leu Gly	Glu Ser Thr Thr
3320	3325	3330
Asp Trp Lys Gln Ile Arg	Ser Ile Ile Met Arg	Glu Asn Phe Ile
3335	3340	3345
Pro Thr Ile Val Asn Phe	Ser Ala Glu Glu Ile	Ser Asp Ala Ile
3350	3355	3360
Arg Glu Lys Met Lys Lys	Asn Tyr Met Ser Asn	Pro Ser Tyr Asn
3365	3370	3375
Tyr Glu Ile Val Asn Arg	Ala Ser Leu Ala Cys	Gly Pro Met Val
3380	3385	3390
Lys Trp Ala Ile Ala Gln	Leu Asn Tyr Ala Asp	Met Leu Lys Arg
3395	3400	3405
Val Glu Pro Leu Arg Asn	Glu Leu Gln Lys Leu	Glu Asp Asp Ala
3410	3415	3420
Lys Asp Asn Gln Gln Lys	Ala Asn Glu Val Glu	Gln Met Ile Arg
3425	3430	3435
Asp Leu Glu Ala Ser Ile	Ala Arg Tyr Lys Glu	Glu Tyr Ala Val
3440	3445	3450
Leu Ile Ser Glu Ala Gln	Ala Ile Lys Ala Asp	Leu Ala Ala Val
3455	3460	3465
Glu Ala Lys Val Asn Arg	Ser Thr Ala Leu Leu	Lys Ser Leu Ser
3470	3475	3480

Ala Glu Arg Glu Arg Trp Glu Lys Thr Ser Glu Thr Phe Lys Asn		
3485	3490	3495
Gln Met Ser Thr Ile Ala Gly Asp Cys Leu Leu Ser Ala Ala Phe		
3500	3505	3510
Ile Ala Tyr Ala Gly Tyr Phe Asp Gln Gln Met Arg Gln Asn Leu		
3515	3520	3525
Phe Thr Thr Trp Ser His His Leu Gln Gln Ala Asn Ile Gln Phe		
3530	3535	3540
Arg Thr Asp Ile Ala Arg Thr Glu Tyr Leu Ser Asn Ala Asp Glu		
3545	3550	3555
Arg Leu Arg Trp Gln Ala Ser Ser Leu Pro Ala Asp Asp Leu Cys		
3560	3565	3570
Thr Glu Asn Ala Ile Met Leu Lys Arg Phe Asn Arg Tyr Pro Leu		
3575	3580	3585
Ile Ile Asp Pro Ser Gly Gln Ala Thr Glu Phe Ile Met Asn Glu		
3590	3595	3600
Tyr Lys Asp Arg Lys Ile Thr Arg Thr Ser Phe Leu Asp Asp Ala		
3605	3610	3615
Phe Arg Lys Asn Leu Glu Ser Ala Leu Arg Phe Gly Asn Pro Leu		
3620	3625	3630
Leu Val Gln Asp Val Glu Ser Tyr Asp Pro Val Leu Asn Pro Val		
3635	3640	3645
Leu Asn Arg Glu Val Arg Arg Thr Gly Gly Arg Val Leu Ile Thr		
3650	3655	3660
Leu Gly Asp Gln Asp Ile Asp Leu Ser Pro Ser Phe Val Ile Phe		
3665	3670	3675
Leu Ser Thr Arg Asp Pro Thr Val Glu Phe Pro Pro Asp Leu Cys		
3680	3685	3690
Ser Arg Val Thr Phe Val Asn Phe Thr Val Thr Arg Ser Ser Leu		
3695	3700	3705
Gln Ser Gln Cys Leu Asn Glu Val Leu Lys Ala Glu Arg Pro Asp		
3710	3715	3720
Val Asp Glu Lys Arg Ser Asp Leu Leu Lys Leu Gln Gly Glu Phe		
3725	3730	3735
Gln Leu Arg Leu Arg Gln Leu Glu Lys Ser Leu Leu Gln Ala Leu		
3740	3745	3750
Asn Glu Val Lys Gly Arg Ile Leu Asp Asp Asp Thr Ile Ile Thr		
3755	3760	3765
Thr Leu Glu Asn Leu Lys Arg Glu Ala Ala Glu Val Thr Arg Lys		

3770	3775	3780
Val Glu Glu Thr Asp Ile	Val Met Gln Glu Val	Glu Thr Val Ser
3785	3790	3795
Gln Gln Tyr Leu Pro Leu	Ser Thr Ala Cys Ser	Ser Ile Tyr Phe
3800	3805	3810
Thr Met Glu Ser Leu Lys	Gln Ile His Phe Leu	Tyr Gln Tyr Ser
3815	3820	3825
Leu Gln Phe Phe Leu Asp	Ile Tyr His Asn Val	Leu Tyr Glu Asn
3830	3835	3840
Pro Asn Leu Lys Gly Val	Thr Asp His Thr Gln	Arg Leu Ser Ile
3845	3850	3855
Ile Thr Lys Asp Leu Phe	Gln Val Ala Phe Asn	Arg Val Ala Arg
3860	3865	3870
Gly Met Leu His Gln Asp	His Ile Thr Phe Ala	Met Leu Leu Ala
3875	3880	3885
Arg Ile Lys Leu Lys Gly	Thr Val Gly Glu Pro	Thr Tyr Asp Ala
3890	3895	3900
Glu Phe Gln His Phe Leu	Arg Gly Asn Glu Ile	Val Leu Ser Ala
3905	3910	3915
Gly Ser Thr Pro Arg Ile	Gln Gly Leu Thr Val	Glu Gln Ala Glu
3920	3925	3930
Ala Val Val Arg Leu Ser	Cys Leu Pro Ala Phe	Lys Asp Leu Ile
3935	3940	3945
Ala Lys Val Gln Ala Asp	Glu Gln Phe Gly Ile	Trp Leu Asp Ser
3950	3955	3960
Ser Ser Pro Glu Gln Thr	Val Pro Tyr Leu Trp	Ser Glu Glu Thr
3965	3970	3975
Pro Ala Thr Pro Ile Gly	Gln Ala Ile His Arg	Leu Leu Leu Ile
3980	3985	3990
Gln Ala Phe Arg Pro Asp	Arg Leu Leu Ala Met	Ala His Met Phe
3995	4000	4005
Val Ser Thr Asn Leu Gly	Glu Ser Phe Met Ser	Ile Met Glu Gln
4010	4015	4020
Pro Leu Asp Leu Thr His	Ile Val Gly Thr Glu	Val Lys Pro Asn
4025	4030	4035
Thr Pro Val Leu Met Cys	Ser Val Pro Gly Tyr	Asp Ala Ser Gly
4040	4045	4050
His Val Glu Asp Leu Ala	Ala Glu Gln Asn Thr	Gln Ile Thr Ser
4055	4060	4065

Ile Ala Ile Gly Ser Ala Glu Gly Phe Asn Gln Ala Asp Lys Ala		
4070	4075	4080
Ile Asn Thr Ala Val Lys Ser Gly Arg Trp Val Met Leu Lys Asn		
4085	4090	4095
Val His Leu Ala Pro Gly Trp Leu Met Gln Leu Glu Lys Lys Leu		
4100	4105	4110
His Ser Leu Gln Pro His Ala Cys Phe Arg Leu Phe Leu Thr Met		
4115	4120	4125
Glu Ile Asn Pro Lys Val Pro Val Asn Leu Leu Arg Ala Gly Arg		
4130	4135	4140
Ile Phe Val Phe Glu Pro Pro Pro Gly Val Lys Ala Asn Met Leu		
4145	4150	4155
Arg Thr Phe Ser Ser Ile Pro Val Ser Arg Ile Cys Lys Ser Pro		
4160	4165	4170
Asn Glu Arg Ala Arg Leu Tyr Phe Leu Leu Ala Trp Phe His Ala		
4175	4180	4185
Ile Ile Gln Glu Arg Leu Arg Tyr Ala Pro Leu Gly Trp Ser Lys		
4190	4195	4200
Lys Tyr Glu Phe Gly Glu Ser Asp Leu Arg Ser Ala Cys Asp Thr		
4205	4210	4215
Val Asp Thr Trp Leu Asp Asp Thr Ala Lys Gly Arg Gln Asn Ile		
4220	4225	4230
Ser Pro Asp Lys Ile Pro Trp Ser Ala Leu Lys Thr Leu Met Ala		
4235	4240	4245
Gln Ser Ile Tyr Gly Gly Arg Val Asp Asn Glu Phe Asp Gln Arg		
4250	4255	4260
Leu Leu Asn Thr Phe Leu Glu Arg Leu Phe Thr Thr Arg Ser Phe		
4265	4270	4275
Asp Ser Glu Phe Lys Leu Ala Cys Lys Val Asp Gly His Lys Asp		
4280	4285	4290
Ile Gln Met Pro Asp Gly Ile Arg Arg Glu Glu Phe Val Gln Trp		
4295	4300	4305
Val Glu Leu Leu Pro Asp Thr Gln Thr Pro Ser Trp Leu Gly Leu		
4310	4315	4320
Pro Asn Asn Ala Glu Arg Val Leu Leu Thr Thr Gln Gly Val Asp		
4325	4330	4335
Met Ile Ser Lys Met Leu Lys Met Gln Met Leu Glu Asp Glu Asp		
4340	4345	4350
Asp Leu Ala Tyr Ala Glu Thr Glu Lys Lys Thr Arg Thr Asp Ser		

4355	4360	4365
Thr Ser Asp Gly Arg Pro	Ala Trp Met Arg Thr	Leu His Thr Thr
4370	4375	4380
Ala Ser Asn Trp Leu His	Leu Ile Pro Gln Thr	Leu Ser His Leu
4385	4390	4395
Lys Arg Thr Val Glu Asn	Ile Lys Asp Pro Leu	Phe Arg Phe Phe
4400	4405	4410
Glu Arg Glu Val Lys Met	Gly Ala Lys Leu Leu	Gln Asp Val Arg
4415	4420	4425
Gln Asp Leu Ala Asp Val	Val Gln Val Cys Glu	Gly Lys Lys Lys
4430	4435	4440
Gln Thr Asn Tyr Leu Arg	Thr Leu Ile Asn Glu	Leu Val Lys Gly
4445	4450	4455
Ile Leu Pro Arg Ser Trp	Ser His Tyr Thr Val	Pro Ala Gly Met
4460	4465	4470
Thr Val Ile Gln Trp Val	Ser Asp Phe Ser Glu	Arg Ile Lys Gln
4475	4480	4485
Leu Gln Asn Ile Ser Leu	Ala Ala Ala Ser Gly	Gly Ala Lys Glu
4490	4495	4500
Leu Lys Asn Ile His Val	Cys Leu Gly Gly Leu	Phe Val Pro Glu
4505	4510	4515
Ala Tyr Ile Thr Ala Thr	Arg Gln Tyr Val Ala	Gln Ala Asn Ser
4520	4525	4530
Trp Ser Leu Glu Glu Leu	Cys Leu Glu Val Asn	Val Thr Thr Ser
4535	4540	4545
Gln Gly Ala Thr Leu Asp	Ala Cys Ser Phe Gly	Val Thr Gly Leu
4550	4555	4560
Lys Leu Gln Gly Ala Thr	Cys Asn Asn Asn Lys	Leu Ser Leu Ser
4565	4570	4575
Asn Ala Ile Ser Thr Ala	Leu Pro Leu Thr Gln	Leu Arg Trp Val
4580	4585	4590
Lys Gln Thr Asn Thr Glu	Lys Lys Ala Ser Val	Val Thr Leu Pro
4595	4600	4605
Val Tyr Leu Asn Phe Thr	Arg Ala Asp Leu Ile	Phe Thr Val Asp
4610	4615	4620
Phe Glu Ile Ala Thr Lys	Glu Asp Pro Arg Ser	Phe Tyr Glu Arg
4625	4630	4635
Gly Val Ala Val Leu Cys	Thr Glu	
4640	4645	

<210> 58

<211> 328

<212> PRT

<213> 智人

<400> 58

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

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Gln Ser Thr Lys Val Asn Leu Leu Tyr Ser Arg Asp His Ser Val Ala
275 280 285
Glu Ser Leu Asn Tyr Val Ala Ser Trp Asn Met Ser Met Leu Gln Thr
290 295 300
Gln Asp Leu Val Lys Ser Val Gln Ala Thr Thr Glu Asn Lys Glu Leu
305 310 315 320
Lys Thr Val Thr Phe Ser Lys Leu
325

<210> 59

<211> 858

<212> PRT

<213> 智人

<400> 59

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

Leu Gly Thr Val Gly Phe Gly Ser Gly Leu His Gly Trp Ala Phe Thr			
210	215	220	
Leu Lys Gln Phe Ala Glu Met Tyr Val Ala Lys Phe Ala Ala Lys Gly			
225	230	235	240
Glu Gly Gln Leu Gly Pro Ala Glu Arg Ala Lys Lys Val Glu Asp Met			
	245	250	255
Met Lys Lys Leu Trp Gly Asp Arg Tyr Phe Asp Pro Ala Asn Gly Lys			
	260	265	270
Phe Ser Lys Ser Ala Thr Ser Pro Glu Gly Lys Lys Leu Pro Arg Thr			
	275	280	285
Phe Cys Gln Leu Ile Leu Asp Pro Ile Phe Lys Val Phe Asp Ala Ile			
290	295	300	
Met Asn Phe Lys Lys Glu Glu Thr Ala Lys Leu Ile Glu Lys Leu Asp			
305	310	315	320
Ile Lys Leu Asp Ser Glu Asp Lys Asp Lys Glu Gly Lys Pro Leu Leu			
	325	330	335
Lys Ala Val Met Arg Arg Trp Leu Pro Ala Gly Asp Ala Leu Leu Gln			
	340	345	350
Met Ile Thr Ile His Leu Pro Ser Pro Val Thr Ala Gln Lys Tyr Arg			
	355	360	365
Cys Glu Leu Leu Tyr Glu Gly Pro Pro Asp Asp Glu Ala Ala Met Gly			
370	375	380	
Ile Lys Ser Cys Asp Pro Lys Gly Pro Leu Met Met Tyr Ile Ser Lys			
385	390	395	400
Met Val Pro Thr Ser Asp Lys Gly Arg Phe Tyr Ala Phe Gly Arg Val			
	405	410	415
Phe Ser Gly Leu Val Ser Thr Gly Leu Lys Val Arg Ile Met Gly Pro			
	420	425	430
Asn Tyr Thr Pro Gly Lys Lys Glu Asp Leu Tyr Leu Lys Pro Ile Gln			
	435	440	445
Arg Thr Ile Leu Met Met Gly Arg Tyr Val Glu Pro Ile Glu Asp Val			
450	455	460	
Pro Cys Gly Asn Ile Val Gly Leu Val Gly Val Asp Gln Phe Leu Val			
465	470	475	480
Lys Thr Gly Thr Ile Thr Thr Phe Glu His Ala His Asn Met Arg Val			
	485	490	495
Met Lys Phe Ser Val Ser Pro Val Val Arg Val Ala Val Glu Ala Lys			
	500	505	510
Asn Pro Ala Asp Leu Pro Lys Leu Val Glu Gly Leu Lys Arg Leu Ala			

515	520	525
Lys Ser Asp Pro Met Val Gln Cys Ile Ile Glu Glu Ser Gly Glu His		
530	535	540
Ile Ile Ala Gly Ala Gly Glu Leu His Leu Glu Ile Cys Leu Lys Asp		
545	550	555
Leu Glu Glu Asp His Ala Cys Ile Pro Ile Lys Lys Ser Asp Pro Val		
565	570	575
Val Ser Tyr Arg Glu Thr Val Ser Glu Glu Ser Asn Val Leu Cys Leu		
580	585	590
Ser Lys Ser Pro Asn Lys His Asn Arg Leu Tyr Met Lys Ala Arg Pro		
595	600	605
Phe Pro Asp Gly Leu Ala Glu Asp Ile Asp Lys Gly Glu Val Ser Ala		
610	615	620
Arg Gln Glu Leu Lys Gln Arg Ala Arg Tyr Leu Ala Glu Lys Tyr Glu		
625	630	635
Trp Asp Val Ala Glu Ala Arg Lys Ile Trp Cys Phe Gly Pro Asp Gly		
645	650	655
Thr Gly Pro Asn Ile Leu Thr Asp Ile Thr Lys Gly Val Gln Tyr Leu		
660	665	670
Asn Glu Ile Lys Asp Ser Val Val Ala Gly Phe Gln Trp Ala Thr Lys		
675	680	685
Glu Gly Ala Leu Cys Glu Glu Asn Met Arg Gly Val Arg Phe Asp Val		
690	695	700
His Asp Val Thr Leu His Ala Asp Ala Ile His Arg Gly Gly Gly Gln		
705	710	715
Ile Ile Pro Thr Ala Arg Arg Cys Leu Tyr Ala Ser Val Leu Thr Ala		
725	730	735
Gln Pro Arg Leu Met Glu Pro Ile Tyr Leu Val Glu Ile Gln Cys Pro		
740	745	750
Glu Gln Val Val Gly Gly Ile Tyr Gly Val Leu Asn Arg Lys Arg Gly		
755	760	765
His Val Phe Glu Glu Ser Gln Val Ala Gly Thr Pro Met Phe Val Val		
770	775	780
Lys Ala Tyr Leu Pro Val Asn Glu Ser Phe Gly Phe Thr Ala Asp Leu		
785	790	795
Arg Ser Asn Thr Gly Gly Gln Ala Phe Pro Gln Cys Val Phe Asp His		
805	810	815
Trp Gln Ile Leu Pro Gly Asp Pro Phe Asp Asn Ser Ser Arg Pro Ser		
820	825	830

Gln Val Val Ala Glu Thr Arg Lys Arg Lys Gly Leu Lys Glu Gly Ile
 835 840 845
 Pro Ala Leu Asp Asn Phe Leu Asp Lys Leu
 850 855
 <210> 60
 <211> 411
 <212> PRT
 <213> 智人
 <400> 60
 Met Ala Thr Thr Ala Thr Met Ala Thr Ser Gly Ser Ala Arg Lys Arg
 1 5 10 15
 Leu Leu Lys Glu Glu Asp Met Thr Lys Val Glu Phe Glu Thr Ser Glu
 20 25 30
 Glu Val Asp Val Thr Pro Thr Phe Asp Thr Met Gly Leu Arg Glu Asp
 35 40 45
 Leu Leu Arg Gly Ile Tyr Ala Tyr Gly Phe Glu Lys Pro Ser Ala Ile
 50 55 60
 Gln Gln Arg Ala Ile Lys Gln Ile Ile Lys Gly Arg Asp Val Ile Ala
 65 70 75 80
 Gln Ser Gln Ser Gly Thr Gly Lys Thr Ala Thr Phe Ser Ile Ser Val
 85 90 95
 Leu Gln Cys Leu Asp Ile Gln Val Arg Glu Thr Gln Ala Leu Ile Leu
 100 105 110
 Ala Pro Thr Arg Glu Leu Ala Val Gln Ile Gln Lys Gly Leu Leu Ala
 115 120 125
 Leu Gly Asp Tyr Met Asn Val Gln Cys His Ala Cys Ile Gly Gly Thr
 130 135 140
 Asn Val Gly Glu Asp Ile Arg Lys Leu Asp Tyr Gly Gln His Val Val
 145 150 155 160
 Ala Gly Thr Pro Gly Arg Val Phe Asp Met Ile Arg Arg Arg Ser Leu
 165 170 175
 Arg Thr Arg Ala Ile Lys Met Leu Val Leu Asp Glu Ala Asp Glu Met
 180 185 190
 Leu Asn Lys Gly Phe Lys Glu Gln Ile Tyr Asp Val Tyr Arg Tyr Leu
 195 200 205
 Pro Pro Ala Thr Gln Val Val Leu Ile Ser Ala Thr Leu Pro His Glu
 210 215 220
 Ile Leu Glu Met Thr Asn Lys Phe Met Thr Asp Pro Ile Arg Ile Leu
 225 230 235 240

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

<210> 61

<211> 434

<212> PRT

<213> 智人

<400> 61

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

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

	405		410		415
Leu Gly Ser Lys Ala Lys Phe Ala Gly Arg Asn Phe Arg Asn Pro Leu					
	420		425		430
Ala Lys					
<210> 62					
<211> 586					
<212> PRT					
<213> 智人					
<400> 62					
Met Pro Lys Pro Ile Asn Val Arg Val Thr Thr Met Asp Ala Glu Leu					
1	5		10		15
Glu Phe Ala Ile Gln Pro Asn Thr Thr Gly Lys Gln Leu Phe Asp Gln					
	20		25		30
Val Val Lys Thr Ile Gly Leu Arg Glu Val Trp Tyr Phe Gly Leu His					
	35		40		45
Tyr Val Asp Asn Lys Gly Phe Pro Thr Trp Leu Lys Leu Asp Lys Lys					
	50		55		60
Val Ser Ala Gln Glu Val Arg Lys Glu Asn Pro Leu Gln Phe Lys Phe					
65	70		75		80
Arg Ala Lys Phe Tyr Pro Glu Asp Val Ala Glu Glu Leu Ile Gln Asp					
	85		90		95
Ile Thr Gln Lys Leu Phe Phe Leu Gln Val Lys Glu Gly Ile Leu Ser					
	100		105		110
Asp Glu Ile Tyr Cys Pro Pro Glu Thr Ala Val Leu Leu Gly Ser Tyr					
	115		120		125
Ala Val Gln Ala Lys Phe Gly Asp Tyr Asn Lys Glu Val His Lys Ser					
	130		135		140
Gly Tyr Leu Ser Ser Glu Arg Leu Ile Pro Gln Arg Val Met Asp Gln					
145	150		155		160
His Lys Leu Thr Arg Asp Gln Trp Glu Asp Arg Ile Gln Val Trp His					
	165		170		175
Ala Glu His Arg Gly Met Leu Lys Asp Asn Ala Met Leu Glu Tyr Leu					
	180		185		190
Lys Ile Ala Gln Asp Leu Glu Met Tyr Gly Ile Asn Tyr Phe Glu Ile					
	195		200		205
Lys Asn Lys Lys Gly Thr Asp Leu Trp Leu Gly Val Asp Ala Leu Gly					
	210		215		220
Leu Asn Ile Tyr Glu Lys Asp Asp Lys Leu Thr Pro Lys Ile Gly Phe					
225	230		235		240

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

545	550	555	560
Gly Arg Asp Lys Tyr Lys Thr Leu Arg Gln Ile Arg Gln Gly Asn Thr			
	565	570	575
Lys Gln Arg Ile Asp Glu Phe Glu Ala Leu			
	580	585	
<210> 63			
<211> 697			
<212> PRT			
<213> 智人			
<400> 63			
Met Gly Pro Asp Arg Lys Glu Val Pro Leu Ser Arg Gly Thr Gln Ala			
1	5	10	15
Val Val Val Gly Lys Gly Arg Gly Ala Pro Gly Asp Asp Ser Ser Met			
	20	25	30
Gly Gly Arg Pro Ser Ser Pro Leu Asp Lys Gln Gln Arg Gln His Leu			
	35	40	45
Arg Gly Gln Val Asp Thr Leu Leu Arg Asn Phe Leu Pro Cys Tyr Arg			
	50	55	60
Gly Gln Leu Ala Ala Ser Val Leu Arg Gln Ile Ser Arg Glu Leu Gly			
65	70	75	80
Pro Gln Glu Pro Thr Gly Ser Gln Leu Leu Arg Ser Lys Lys Leu Pro			
	85	90	95
Arg Val Arg Glu His Arg Gly Pro Leu Thr Gln Leu Arg Gly His Pro			
	100	105	110
Pro Arg Trp Gln Pro Ile Phe Cys Val Leu Arg Gly Asp Gly Arg Leu			
	115	120	125
Glu Trp Phe Ser His Lys Glu Glu Tyr Glu Asn Gly Gly His Cys Leu			
	130	135	140
Gly Ser Thr Ala Leu Thr Gly Tyr Thr Leu Leu Thr Ser Gln Arg Glu			
145	150	155	160
Tyr Leu Arg Leu Leu Asp Ala Leu Cys Pro Glu Ser Leu Gly Asp His			
	165	170	175
Thr Gln Glu Glu Pro Asp Ser Leu Leu Glu Val Pro Val Ser Phe Pro			
	180	185	190
Leu Phe Leu Gln His Pro Phe Arg Arg His Leu Cys Phe Ser Ala Ala			
	195	200	205
Thr Arg Glu Ala Gln His Ala Trp Arg Leu Ala Leu Gln Gly Gly Ile			
210	215	220	
Arg Leu Gln Gly Ile Val Leu Gln Arg Ser Gln Ala Pro Ala Ala Arg			

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

Pro Gly Cys Lys Lys Glu Leu Pro Glu Phe Glu Gly Asp Val Leu Ala			
545	550	555	560
Val Gly Ser Gln Ala Leu Thr Thr Glu Gly Ile Tyr Glu Asp Val Ile			
	565	570	575
Arg Gly Cys Leu Leu Gln Arg Ile Asp Gln Glu Leu Lys Lys Thr Leu			
	580	585	590
Gly Ala Asn Asp Val Ser Cys Thr Leu Asp Gly Cys Leu Glu Val Pro			
	595	600	605
Trp Glu Gln Glu Gly Ala Ala Pro Asn Leu Asn Leu Val Ser Ser Phe			
	610	615	620
Leu Ala Gly Arg Gln Ala Phe Thr Asp Phe Leu Cys Leu Pro Ala Lys			
625	630	635	640
Ser Ser Ala Asn Trp Ile Leu Ala Ala Ser Leu Leu Ser Cys Ser Cys			
	645	650	655
Phe Arg Ser Gly Phe His Arg Asp Ser Arg Val Phe Leu Val Gln Leu			
	660	665	670
Ala Glu Gly Leu Ser His Ser Leu Glu Thr Val Ser Ser His Ser Val			
	675	680	685
Trp Ser Phe Arg Pro Thr Pro Arg Gln			
	690	695	
<210> 64			
<211> 760			
<212> PRT			
<213> 智人			
<400> 64			
Met Lys Thr Trp Val Lys Ile Val Phe Gly Val Ala Thr Ser Ala Val			
1	5	10	15
Leu Ala Leu Leu Val Met Cys Ile Val Leu Arg Pro Ser Arg Val His			
	20	25	30
Asn Ser Glu Glu Asn Thr Met Arg Ala Leu Thr Leu Lys Asp Ile Leu			
	35	40	45
Asn Gly Thr Phe Ser Tyr Lys Thr Phe Phe Pro Asn Trp Ile Ser Gly			
	50	55	60
Gln Glu Tyr Leu His Gln Ser Ala Asp Asn Asn Ile Val Leu Tyr Asn			
65	70	75	80
Ile Glu Thr Gly Gln Ser Tyr Thr Ile Leu Ser Asn Arg Thr Met Lys			
	85	90	95
Ser Val Asn Ala Ser Asn Tyr Gly Leu Ser Pro Asp Arg Gln Phe Val			
	100	105	110

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

420	425	430
Pro Pro Ser Lys Lys Cys Val Thr Cys His Leu Arg Lys Glu Arg Cys		
435	440	445
Gln Tyr Tyr Thr Ala Ser Phe Ser Asp Tyr Ala Lys Tyr Tyr Ala Leu		
450	455	460
Val Cys Tyr Gly Pro Gly Ile Pro Ile Ser Thr Leu His Asp Gly Arg		
465	470	475
Thr Asp Gln Glu Ile Lys Ile Leu Glu Glu Asn Lys Glu Leu Glu Asn		
485	490	495
Ala Leu Lys Asn Ile Gln Leu Pro Lys Glu Glu Ile Lys Lys Leu Glu		
500	505	510
Val Asp Glu Ile Thr Leu Trp Tyr Lys Met Ile Leu Pro Pro Gln Phe		
515	520	525
Asp Arg Ser Lys Lys Tyr Pro Leu Leu Ile Gln Val Tyr Gly Gly Pro		
530	535	540
Cys Ser Gln Ser Val Arg Ser Val Phe Ala Val Asn Trp Ile Ser Tyr		
545	550	555
Leu Ala Ser Lys Glu Gly Met Val Ile Ala Leu Val Asp Gly Arg Gly		
565	570	575
Thr Ala Phe Gln Gly Asp Lys Leu Leu Tyr Ala Val Tyr Arg Lys Leu		
580	585	590
Gly Val Tyr Glu Val Glu Asp Gln Ile Thr Ala Val Arg Lys Phe Ile		
595	600	605
Glu Met Gly Phe Ile Asp Glu Lys Arg Ile Ala Ile Trp Gly Trp Ser		
610	615	620
Tyr Gly Gly Tyr Val Ser Ser Leu Ala Leu Ala Ser Gly Thr Gly Leu		
625	630	635
Phe Lys Cys Gly Ile Ala Val Ala Pro Val Ser Ser Trp Glu Tyr Tyr		
645	650	655
Ala Ser Val Tyr Thr Glu Arg Phe Met Gly Leu Pro Thr Lys Asp Asp		
660	665	670
Asn Leu Glu His Tyr Lys Asn Ser Thr Val Met Ala Arg Ala Glu Tyr		
675	680	685
Phe Arg Asn Val Asp Tyr Leu Leu Ile His Gly Thr Ala Asp Asp Asn		
690	695	700
Val His Phe Gln Asn Ser Ala Gln Ile Ala Lys Ala Leu Val Asn Ala		
705	710	715
Gln Val Asp Phe Gln Ala Met Trp Tyr Ser Asp Gln Asn His Gly Leu		
725	730	735

Ser Gly Leu Ser Thr Asn His Leu Tyr Thr His Met Thr His Phe Leu
 740 745 750
 Lys Gln Cys Phe Ser Leu Ser Asp
 755 760
 <210> 65
 <211> 387
 <212> PRT
 <213> 智人
 <400> 65
 Met Ala Gly Ser Glu Pro Arg Ser Gly Thr Asn Ser Pro Pro Pro Pro
 1 5 10 15
 Phe Ser Asp Trp Gly Arg Leu Glu Ala Ala Ile Leu Ser Gly Trp Lys
 20 25 30
 Thr Phe Trp Gln Ser Val Ser Lys Glu Arg Val Ala Arg Thr Thr Ser
 35 40 45
 Arg Glu Glu Val Asp Glu Ala Ala Ser Thr Leu Thr Arg Leu Pro Ile
 50 55 60
 Asp Val Gln Leu Tyr Ile Leu Ser Phe Leu Ser Pro His Asp Leu Cys
 65 70 75 80
 Gln Leu Gly Ser Thr Asn His Tyr Trp Asn Glu Thr Val Arg Asp Pro
 85 90 95
 Ile Leu Trp Arg Tyr Phe Leu Leu Arg Asp Leu Pro Ser Trp Ser Ser
 100 105 110
 Val Asp Trp Lys Ser Leu Pro Asp Leu Glu Ile Leu Lys Lys Pro Ile
 115 120 125
 Ser Glu Val Thr Asp Gly Ala Phe Phe Asp Tyr Met Ala Val Tyr Arg
 130 135 140
 Met Cys Cys Pro Tyr Thr Arg Arg Ala Ser Lys Ser Ser Arg Pro Met
 145 150 155 160
 Tyr Gly Ala Val Thr Ser Phe Leu His Ser Leu Ile Ile Gln Asn Glu
 165 170 175
 Pro Arg Phe Ala Met Phe Gly Pro Gly Leu Glu Glu Leu Asn Thr Ser
 180 185 190
 Leu Val Leu Ser Leu Met Ser Ser Glu Glu Leu Cys Pro Thr Ala Gly
 195 200 205
 Leu Pro Gln Arg Gln Ile Asp Gly Ile Gly Ser Gly Val Asn Phe Gln
 210 215 220
 Leu Asn Asn Gln His Lys Phe Asn Ile Leu Ile Leu Tyr Ser Thr Thr
 225 230 235 240

Arg	Lys	Glu	Arg	Asp	Arg	Ala	Arg	Glu	Glu	His	Thr	Ser	Ala	Val	Asn
				245				250				255			
Lys	Met	Phe	Ser	Arg	His	Asn	Glu	Gly	Asp	Asp	Gln	Gln	Gly	Ser	Arg
				260				265				270			
Tyr	Ser	Val	Ile	Pro	Gln	Ile	Gln	Lys	Val	Cys	Glu	Val	Val	Asp	Gly
				275				280				285			
Phe	Ile	Tyr	Val	Ala	Asn	Ala	Glu	Ala	His	Lys	Arg	His	Glu	Trp	Gln
				290				295				300			
Asp	Glu	Phe	Ser	His	Ile	Met	Ala	Met	Thr	Asp	Pro	Ala	Phe	Gly	Ser
305				310				315				320			
Ser	Gly	Arg	Pro	Leu	Leu	Val	Leu	Ser	Cys	Ile	Ser	Gln	Gly	Asp	Val
				325				330				335			
Lys	Arg	Met	Pro	Cys	Phe	Tyr	Leu	Ala	His	Glu	Leu	His	Leu	Asn	Leu
				340				345				350			
Leu	Asn	His	Pro	Trp	Leu	Val	Gln	Asp	Thr	Glu	Ala	Glu	Thr	Leu	Thr
				355				360				365			
Gly	Phe	Leu	Asn	Gly	Ile	Glu	Trp	Ile	Leu	Glu	Glu	Val	Glu	Ser	Lys
370				375				380							
Arg Ala Arg															
385															
<210> 66															
<211> 491															
<212> PRT															
<213> 智人															
<400> 66															
Met	Lys	Arg	Met	Val	Ser	Trp	Ser	Phe	His	Lys	Leu	Lys	Thr	Met	Lys
1		5				10				15					
His	Leu	Leu	Leu	Leu	Leu	Leu	Cys	Val	Phe	Leu	Val	Lys	Ser	Gln	Gly
				20				25				30			
Val	Asn	Asp	Asn	Glu	Glu	Gly	Phe	Phe	Ser	Ala	Arg	Gly	His	Arg	Pro
				35				40				45			
Leu	Asp	Lys	Lys	Arg	Glu	Glu	Ala	Pro	Ser	Leu	Arg	Pro	Ala	Pro	Pro
50				55				60							
Pro	Ile	Ser	Gly	Gly	Gly	Tyr	Arg	Ala	Arg	Pro	Ala	Lys	Ala	Ala	Ala
65				70				75				80			
Thr	Gln	Lys	Lys	Val	Glu	Arg	Lys	Ala	Pro	Asp	Ala	Gly	Gly	Cys	Leu
				85				90				95			
His	Ala	Asp	Pro	Asp	Leu	Gly	Val	Leu	Cys	Pro	Thr	Gly	Cys	Gln	Leu
				100				105				110			

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

420						425						430							
Trp	Tyr	Asn	Arg	Cys	His	Ala	Ala	Asn	Pro	Asn	Gly	Arg	Tyr	Tyr	Trp				
435						440						445							
Gly	Gly	Gln	Tyr	Thr	Trp	Asp	Met	Ala	Lys	His	Gly	Thr	Asp	Asp	Gly				
450						455						460							
Val	Val	Trp	Met	Asn	Trp	Lys	Gly	Ser	Trp	Tyr	Ser	Met	Arg	Lys	Met				
465						470						475						480	
Ser	Met	Lys	Ile	Arg	Pro	Phe	Phe	Pro	Gln	Gln									
485						490													
<210> 67																			
<211> 453																			
<212> PRT																			
<213> 智人																			
<400> 67																			
Met	Ser	Trp	Ser	Leu	His	Pro	Arg	Asn	Leu	Ile	Leu	Tyr	Phe	Tyr	Ala				
1				5				10				15							
Leu	Leu	Phe	Leu	Ser	Ser	Thr	Cys	Val	Ala	Tyr	Val	Ala	Thr	Arg	Asp				
20						25						30							
Asn	Cys	Cys	Ile	Leu	Asp	Glu	Arg	Phe	Gly	Ser	Tyr	Cys	Pro	Thr	Thr				
35						40						45							
Cys	Gly	Ile	Ala	Asp	Phe	Leu	Ser	Thr	Tyr	Gln	Thr	Lys	Val	Asp	Lys				
50						55						60							
Asp	Leu	Gln	Ser	Leu	Glu	Asp	Ile	Leu	His	Gln	Val	Glu	Asn	Lys	Thr				
65						70						75				80			
Ser	Glu	Val	Lys	Gln	Leu	Ile	Lys	Ala	Ile	Gln	Leu	Thr	Tyr	Asn	Pro				
85						90						95							
Asp	Glu	Ser	Ser	Lys	Pro	Asn	Met	Ile	Asp	Ala	Ala	Thr	Leu	Lys	Ser				
100						105						110							
Arg	Lys	Met	Leu	Glu	Glu	Ile	Met	Lys	Tyr	Glu	Ala	Ser	Ile	Leu	Thr				
115						120						125							
His	Asp	Ser	Ser	Ile	Arg	Tyr	Leu	Gln	Glu	Ile	Tyr	Asn	Ser	Asn	Asn				
130						135						140							
Gln	Lys	Ile	Val	Asn	Leu	Lys	Glu	Lys	Val	Ala	Gln	Leu	Glu	Ala	Gln				
145						150						155				160			
Cys	Gln	Glu	Pro	Cys	Lys	Asp	Thr	Val	Gln	Ile	His	Asp	Ile	Thr	Gly				
165						170						175							
Lys	Asp	Cys	Gln	Asp	Ile	Ala	Asn	Lys	Gly	Ala	Lys	Gln	Ser	Gly	Leu				
180						185						190							
Tyr	Phe	Ile	Lys	Pro	Leu	Lys	Ala	Asn	Gln	Gln	Phe	Leu	Val	Tyr	Cys				

195	200	205
Glu Ile Asp Gly Ser Gly Asn Gly Trp Thr Val Phe Gln Lys Arg Leu		
210	215	220
Asp Gly Ser Val Asp Phe Lys Lys Asn Trp Ile Gln Tyr Lys Glu Gly		
225	230	235
Phe Gly His Leu Ser Pro Thr Gly Thr Thr Glu Phe Trp Leu Gly Asn		
245	250	255
Glu Lys Ile His Leu Ile Ser Thr Gln Ser Ala Ile Pro Tyr Ala Leu		
260	265	270
Arg Val Glu Leu Glu Asp Trp Asn Gly Arg Thr Ser Thr Ala Asp Tyr		
275	280	285
Ala Met Phe Lys Val Gly Pro Glu Ala Asp Lys Tyr Arg Leu Thr Tyr		
290	295	300
Ala Tyr Phe Ala Gly Gly Asp Ala Gly Asp Ala Phe Asp Gly Phe Asp		
305	310	315
Phe Gly Asp Asp Pro Ser Asp Lys Phe Phe Thr Ser His Asn Gly Met		
325	330	335
Gln Phe Ser Thr Trp Asp Asn Asp Asn Asp Lys Phe Glu Gly Asn Cys		
340	345	350
Ala Glu Gln Asp Gly Ser Gly Trp Trp Met Asn Lys Cys His Ala Gly		
355	360	365
His Leu Asn Gly Val Tyr Tyr Gln Gly Gly Thr Tyr Ser Lys Ala Ser		
370	375	380
Thr Pro Asn Gly Tyr Asp Asn Gly Ile Ile Trp Ala Thr Trp Lys Thr		
385	390	395
Arg Trp Tyr Ser Met Lys Lys Thr Thr Met Lys Ile Ile Pro Phe Asn		
405	410	415
Arg Leu Thr Ile Gly Glu Gly Gln Gln His His Leu Gly Gly Ala Lys		
420	425	430
Gln Val Arg Pro Glu His Pro Ala Glu Thr Glu Tyr Asp Ser Leu Tyr		
435	440	445
Pro Glu Asp Asp Leu		
450		
<210> 68		
<211> 323		
<212> PRT		
<213> 智人		
<400> 68		
Met Ala Glu Lys Phe Asp Cys His Tyr Cys Arg Asp Pro Leu Gln Gly		

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

Asn Ala Pro
 <210> 69
 <211> 2647
 <212> PRT
 <213> 智人
 <400> 69
 Met Ser Ser Ser His Ser Arg Ala Gly Gln Ser Ala Ala Gly Ala Ala
 1 5 10 15
 Pro Gly Gly Gly Val Asp Thr Arg Asp Ala Glu Met Pro Ala Thr Glu
 20 25 30
 Lys Asp Leu Ala Glu Asp Ala Pro Trp Lys Lys Ile Gln Gln Asn Thr
 35 40 45
 Phe Thr Arg Trp Cys Asn Glu His Leu Lys Cys Val Ser Lys Arg Ile
 50 55 60
 Ala Asn Leu Gln Thr Asp Leu Ser Asp Gly Leu Arg Leu Ile Ala Leu
 65 70 75 80
 Leu Glu Val Leu Ser Gln Lys Lys Met His Arg Lys His Asn Gln Arg
 85 90 95
 Pro Thr Phe Arg Gln Met Gln Leu Glu Asn Val Ser Val Ala Leu Glu
 100 105 110
 Phe Leu Asp Arg Glu Ser Ile Lys Leu Val Ser Ile Asp Ser Lys Ala
 115 120 125
 Ile Val Asp Gly Asn Leu Lys Leu Ile Leu Gly Leu Ile Trp Thr Leu
 130 135 140
 Ile Leu His Tyr Ser Ile Ser Met Pro Met Trp Asp Glu Glu Glu Asp
 145 150 155 160
 Glu Glu Ala Lys Lys Gln Thr Pro Lys Gln Arg Leu Leu Gly Trp Ile
 165 170 175
 Gln Asn Lys Leu Pro Gln Leu Pro Ile Thr Asn Phe Ser Arg Asp Trp
 180 185 190
 Gln Ser Gly Arg Ala Leu Gly Ala Leu Val Asp Ser Cys Ala Pro Gly
 195 200 205
 Leu Cys Pro Asp Trp Asp Ser Trp Asp Ala Ser Lys Pro Val Thr Asn
 210 215 220
 Ala Arg Glu Ala Met Gln Gln Ala Asp Asp Trp Leu Gly Ile Pro Gln
 225 230 235 240
 Val Ile Thr Pro Glu Glu Ile Val Asp Pro Asn Val Asp Glu His Ser
 245 250 255
 Val Met Thr Tyr Leu Ser Gln Phe Pro Lys Ala Lys Leu Lys Pro Gly

260	265	270
Ala Pro Leu Arg Pro Lys Leu Asn Pro Lys Lys Ala Arg Ala Tyr Gly		
275	280	285
Pro Gly Ile Glu Pro Thr Gly Asn Met Val Lys Lys Arg Ala Glu Phe		
290	295	300
Thr Val Glu Thr Arg Ser Ala Gly Gln Gly Glu Val Leu Val Tyr Val		
305	310	315
Glu Asp Pro Ala Gly His Gln Glu Glu Ala Lys Val Thr Ala Asn Asn		
325	330	335
Asp Lys Asn Arg Thr Phe Ser Val Trp Tyr Val Pro Glu Val Thr Gly		
340	345	350
Thr His Lys Val Thr Val Leu Phe Ala Gly Gln His Ile Ala Lys Ser		
355	360	365
Pro Phe Glu Val Tyr Val Asp Lys Ser Gln Gly Asp Ala Ser Lys Val		
370	375	380
Thr Ala Gln Gly Pro Gly Leu Glu Pro Ser Gly Asn Ile Ala Asn Lys		
385	390	395
Thr Thr Tyr Phe Glu Ile Phe Thr Ala Gly Ala Gly Thr Gly Glu Val		
405	410	415
Glu Val Val Ile Gln Asp Pro Met Gly Gln Lys Gly Thr Val Glu Pro		
420	425	430
Gln Leu Glu Ala Arg Gly Asp Ser Thr Tyr Arg Cys Ser Tyr Gln Pro		
435	440	445
Thr Met Glu Gly Val His Thr Val His Val Thr Phe Ala Gly Val Pro		
450	455	460
Ile Pro Arg Ser Pro Tyr Thr Val Thr Val Gly Gln Ala Cys Asn Pro		
465	470	475
Ser Ala Cys Arg Ala Val Gly Arg Gly Leu Gln Pro Lys Gly Val Arg		
485	490	495
Val Lys Glu Thr Ala Asp Phe Lys Val Tyr Thr Lys Gly Ala Gly Ser		
500	505	510
Gly Glu Leu Lys Val Thr Val Lys Gly Pro Lys Gly Glu Glu Arg Val		
515	520	525
Lys Gln Lys Asp Leu Gly Asp Gly Val Tyr Gly Phe Glu Tyr Tyr Pro		
530	535	540
Met Val Pro Gly Thr Tyr Ile Val Thr Ile Thr Trp Gly Gly Gln Asn		
545	550	555
Ile Gly Arg Ser Pro Phe Glu Val Lys Val Gly Thr Glu Cys Gly Asn		
565	570	575

Gln Lys Val Arg Ala Trp Gly Pro Gly Leu Glu Gly Gly Val Val Gly		
580	585	590
Lys Ser Ala Asp Phe Val Val Glu Ala Ile Gly Asp Asp Val Gly Thr		
595	600	605
Leu Gly Phe Ser Val Glu Gly Pro Ser Gln Ala Lys Ile Glu Cys Asp		
610	615	620
Asp Lys Gly Asp Gly Ser Cys Asp Val Arg Tyr Trp Pro Gln Glu Ala		
625	630	635
Gly Glu Tyr Ala Val His Val Leu Cys Asn Ser Glu Asp Ile Arg Leu		
645	650	655
Ser Pro Phe Met Ala Asp Ile Arg Asp Ala Pro Gln Asp Phe His Pro		
660	665	670
Asp Arg Val Lys Ala Arg Gly Pro Gly Leu Glu Lys Thr Gly Val Ala		
675	680	685
Val Asn Lys Pro Ala Glu Phe Thr Val Asp Ala Lys His Gly Gly Lys		
690	695	700
Ala Pro Leu Arg Val Gln Val Gln Asp Asn Glu Gly Cys Pro Val Glu		
705	710	715
Ala Leu Val Lys Asp Asn Gly Asn Gly Thr Tyr Ser Cys Ser Tyr Val		
725	730	735
Pro Arg Lys Pro Val Lys His Thr Ala Met Val Ser Trp Gly Gly Val		
740	745	750
Ser Ile Pro Asn Ser Pro Phe Arg Val Asn Val Gly Ala Gly Ser His		
755	760	765
Pro Asn Lys Val Lys Val Tyr Gly Pro Gly Val Ala Lys Thr Gly Leu		
770	775	780
Lys Ala His Glu Pro Thr Tyr Phe Thr Val Asp Cys Ala Glu Ala Gly		
785	790	795
Gln Gly Asp Val Ser Ile Gly Ile Lys Cys Ala Pro Gly Val Val Gly		
805	810	815
Pro Ala Glu Ala Asp Ile Asp Phe Asp Ile Ile Arg Asn Asp Asn Asp		
820	825	830
Thr Phe Thr Val Lys Tyr Thr Pro Arg Gly Ala Gly Ser Tyr Thr Ile		
835	840	845
Met Val Leu Phe Ala Asp Gln Ala Thr Pro Thr Ser Pro Ile Arg Val		
850	855	860
Lys Val Glu Pro Ser His Asp Ala Ser Lys Val Lys Ala Glu Gly Pro		
865	870	875
Gly Leu Ser Arg Thr Gly Val Glu Leu Gly Lys Pro Thr His Phe Thr		

				885					890					895			
Val	Asn	Ala	Lys	Ala	Ala	Gly	Lys	Gly	Lys	Leu	Asp	Val	Gln	Phe	Ser		
				900					905					910			
Gly	Leu	Thr	Lys	Gly	Asp	Ala	Val	Arg	Asp	Val	Asp	Ile	Ile	Asp	His		
				915					920					925			
His	Asp	Asn	Thr	Tyr	Thr	Val	Lys	Tyr	Thr	Pro	Val	Gln	Gln	Gly	Pro		
				930					935					940			
Val	Gly	Val	Asn	Val	Thr	Tyr	Gly	Gly	Asp	Pro	Ile	Pro	Lys	Ser	Pro		
945							950				955				960		
Phe	Ser	Val	Ala	Val	Ser	Pro	Ser	Leu	Asp	Leu	Ser	Lys	Ile	Lys	Val		
				965					970					975			
Ser	Gly	Leu	Gly	Glu	Lys	Val	Asp	Val	Gly	Lys	Asp	Gln	Glu	Phe	Thr		
				980					985					990			
Val	Lys	Ser	Lys	Gly	Ala	Gly	Gly	Gln	Gly	Lys	Val	Ala	Ser	Lys	Ile		
				995					1000					1005			
Val	Gly	Pro	Ser	Gly	Ala	Ala	Val	Pro	Cys	Lys	Val	Glu	Pro	Gly			
				1010					1015					1020			
Leu	Gly	Ala	Asp	Asn	Ser	Val	Val	Arg	Phe	Leu	Pro	Arg	Glu	Glu			
				1025					1030					1035			
Gly	Pro	Tyr	Glu	Val	Glu	Val	Thr	Tyr	Asp	Gly	Val	Pro	Val	Pro			
				1040					1045					1050			
Gly	Ser	Pro	Phe	Pro	Leu	Glu	Ala	Val	Ala	Pro	Thr	Lys	Pro	Ser			
				1055					1060					1065			
Lys	Val	Lys	Ala	Phe	Gly	Pro	Gly	Leu	Gln	Gly	Gly	Ser	Ala	Gly			
				1070					1075					1080			
Ser	Pro	Ala	Arg	Phe	Thr	Ile	Asp	Thr	Lys	Gly	Ala	Gly	Thr	Gly			
				1085					1090					1095			
Gly	Leu	Gly	Leu	Thr	Val	Glu	Gly	Pro	Cys	Glu	Ala	Gln	Leu	Glu			
				1100					1105					1110			
Cys	Leu	Asp	Asn	Gly	Asp	Gly	Thr	Cys	Ser	Val	Ser	Tyr	Val	Pro			
				1115					1120					1125			
Thr	Glu	Pro	Gly	Asp	Tyr	Asn	Ile	Asn	Ile	Leu	Phe	Ala	Asp	Thr			
				1130					1135					1140			
His	Ile	Pro	Gly	Ser	Pro	Phe	Lys	Ala	His	Val	Val	Pro	Cys	Phe			
				1145					1150					1155			
Asp	Ala	Ser	Lys	Val	Lys	Cys	Ser	Gly	Pro	Gly	Leu	Glu	Arg	Ala			
				1160					1165					1170			
Thr	Ala	Gly	Glu	Val	Gly	Gln	Phe	Gln	Val	Asp	Cys	Ser	Ser	Ala			
				1175					1180					1185			

Gly Ser Ala Glu Leu Thr Ile Glu Ile Cys Ser Glu Ala Gly Leu		
1190	1195	1200
Pro Ala Glu Val Tyr Ile Gln Asp His Gly Asp Gly Thr His Thr		
1205	1210	1215
Ile Thr Tyr Ile Pro Leu Cys Pro Gly Ala Tyr Thr Val Thr Ile		
1220	1225	1230
Lys Tyr Gly Gly Gln Pro Val Pro Asn Phe Pro Ser Lys Leu Gln		
1235	1240	1245
Val Glu Pro Ala Val Asp Thr Ser Gly Val Gln Cys Tyr Gly Pro		
1250	1255	1260
Gly Ile Glu Gly Gln Gly Val Phe Arg Glu Ala Thr Thr Glu Phe		
1265	1270	1275
Ser Val Asp Ala Arg Ala Leu Thr Gln Thr Gly Gly Pro His Val		
1280	1285	1290
Lys Ala Arg Val Ala Asn Pro Ser Gly Asn Leu Thr Glu Thr Tyr		
1295	1300	1305
Val Gln Asp Arg Gly Asp Gly Met Tyr Lys Val Glu Tyr Thr Pro		
1310	1315	1320
Tyr Glu Glu Gly Leu His Ser Val Asp Val Thr Tyr Asp Gly Ser		
1325	1330	1335
Pro Val Pro Ser Ser Pro Phe Gln Val Pro Val Thr Glu Gly Cys		
1340	1345	1350
Asp Pro Ser Arg Val Arg Val His Gly Pro Gly Ile Gln Ser Gly		
1355	1360	1365
Thr Thr Asn Lys Pro Asn Lys Phe Thr Val Glu Thr Arg Gly Ala		
1370	1375	1380
Gly Thr Gly Gly Leu Gly Leu Ala Val Glu Gly Pro Ser Glu Ala		
1385	1390	1395
Lys Met Ser Cys Met Asp Asn Lys Asp Gly Ser Cys Ser Val Glu		
1400	1405	1410
Tyr Ile Pro Tyr Glu Ala Gly Thr Tyr Ser Leu Asn Val Thr Tyr		
1415	1420	1425
Gly Gly His Gln Val Pro Gly Ser Pro Phe Lys Val Pro Val His		
1430	1435	1440
Asp Val Thr Asp Ala Ser Lys Val Lys Cys Ser Gly Pro Gly Leu		
1445	1450	1455
Ser Pro Gly Met Val Arg Ala Asn Leu Pro Gln Ser Phe Gln Val		
1460	1465	1470
Asp Thr Ser Lys Ala Gly Val Ala Pro Leu Gln Val Lys Val Gln		

1475	1480	1485
Gly Pro Lys Gly Leu Val	Glu Pro Val Asp Val	Val Asp Asn Ala
1490	1495	1500
Asp Gly Thr Gln Thr Val	Asn Tyr Val Pro Ser	Arg Glu Gly Pro
1505	1510	1515
Tyr Ser Ile Ser Val Leu	Tyr Gly Asp Glu Glu	Val Pro Arg Ser
1520	1525	1530
Pro Phe Lys Val Lys Val	Leu Pro Thr His Asp	Ala Ser Lys Val
1535	1540	1545
Lys Ala Ser Gly Pro Gly	Leu Asn Thr Thr Gly	Val Pro Ala Ser
1550	1555	1560
Leu Pro Val Glu Phe Thr	Ile Asp Ala Lys Asp	Ala Gly Glu Gly
1565	1570	1575
Leu Leu Ala Val Gln Ile	Thr Asp Pro Glu Gly	Lys Pro Lys Lys
1580	1585	1590
Thr His Ile Gln Asp Asn	His Asp Gly Thr Tyr	Thr Val Ala Tyr
1595	1600	1605
Val Pro Asp Val Thr Gly	Arg Tyr Thr Ile Leu	Ile Lys Tyr Gly
1610	1615	1620
Gly Asp Glu Ile Pro Phe	Ser Pro Tyr Arg Val	Arg Ala Val Pro
1625	1630	1635
Thr Gly Asp Ala Ser Lys	Cys Thr Val Thr Val	Ser Ile Gly Gly
1640	1645	1650
His Gly Leu Gly Ala Gly	Ile Gly Pro Thr Ile	Gln Ile Gly Glu
1655	1660	1665
Glu Thr Val Ile Thr Val	Asp Thr Lys Ala Ala	Gly Lys Gly Lys
1670	1675	1680
Val Thr Cys Thr Val Cys	Thr Pro Asp Gly Ser	Glu Val Asp Val
1685	1690	1695
Asp Val Val Glu Asn Glu	Asp Gly Thr Phe Asp	Ile Phe Tyr Thr
1700	1705	1710
Ala Pro Gln Pro Gly Lys	Tyr Val Ile Cys Val	Arg Phe Gly Gly
1715	1720	1725
Glu His Val Pro Asn Ser	Pro Phe Gln Val Thr	Ala Leu Ala Gly
1730	1735	1740
Asp Gln Pro Ser Val Gln	Pro Pro Leu Arg Ser	Gln Gln Leu Ala
1745	1750	1755
Pro Gln Tyr Thr Tyr Ala	Gln Gly Gly Gln Gln	Thr Trp Ala Pro
1760	1765	1770

Glu Arg Pro Leu Val Gly Val Asn Gly Leu Asp Val Thr Ser Leu		
1775	1780	1785
Arg Pro Phe Asp Leu Val Ile Pro Phe Thr Ile Lys Lys Gly Glu		
1790	1795	1800
Ile Thr Gly Glu Val Arg Met Pro Ser Gly Lys Val Ala Gln Pro		
1805	1810	1815
Thr Ile Thr Asp Asn Lys Asp Gly Thr Val Thr Val Arg Tyr Ala		
1820	1825	1830
Pro Ser Glu Ala Gly Leu His Glu Met Asp Ile Arg Tyr Asp Asn		
1835	1840	1845
Met His Ile Pro Gly Ser Pro Leu Gln Phe Tyr Val Asp Tyr Val		
1850	1855	1860
Asn Cys Gly His Val Thr Ala Tyr Gly Pro Gly Leu Thr His Gly		
1865	1870	1875
Val Val Asn Lys Pro Ala Thr Phe Thr Val Asn Thr Lys Asp Ala		
1880	1885	1890
Gly Glu Gly Gly Leu Ser Leu Ala Ile Glu Gly Pro Ser Lys Ala		
1895	1900	1905
Glu Ile Ser Cys Thr Asp Asn Gln Asp Gly Thr Cys Ser Val Ser		
1910	1915	1920
Tyr Leu Pro Val Leu Pro Gly Asp Tyr Ser Ile Leu Val Lys Tyr		
1925	1930	1935
Asn Glu Gln His Val Pro Gly Ser Pro Phe Thr Ala Arg Val Thr		
1940	1945	1950
Gly Asp Asp Ser Met Arg Met Ser His Leu Lys Val Gly Ser Ala		
1955	1960	1965
Ala Asp Ile Pro Ile Asn Ile Ser Glu Thr Asp Leu Ser Leu Leu		
1970	1975	1980
Thr Ala Thr Val Val Pro Pro Ser Gly Arg Glu Glu Pro Cys Leu		
1985	1990	1995
Leu Lys Arg Leu Arg Asn Gly His Val Gly Ile Ser Phe Val Pro		
2000	2005	2010
Lys Glu Thr Gly Glu His Leu Val His Val Lys Lys Asn Gly Gln		
2015	2020	2025
His Val Ala Ser Ser Pro Ile Pro Val Val Ile Ser Gln Ser Glu		
2030	2035	2040
Ile Gly Asp Ala Ser Arg Val Arg Val Ser Gly Gln Gly Leu His		
2045	2050	2055
Glu Gly His Thr Phe Glu Pro Ala Glu Phe Ile Ile Asp Thr Arg		

2060	2065	2070
Asp Ala Gly Tyr Gly Gly	Leu Ser Leu Ser Ile	Glu Gly Pro Ser
2075	2080	2085
Lys Val Asp Ile Asn Thr	Glu Asp Leu Glu Asp	Gly Thr Cys Arg
2090	2095	2100
Val Thr Tyr Cys Pro Thr	Glu Pro Gly Asn Tyr	Ile Ile Asn Ile
2105	2110	2115
Lys Phe Ala Asp Gln His	Val Pro Gly Ser Pro	Phe Ser Val Lys
2120	2125	2130
Val Thr Gly Glu Gly Arg	Val Lys Glu Ser Ile	Thr Arg Arg Arg
2135	2140	2145
Arg Ala Pro Ser Val Ala	Asn Val Gly Ser His	Cys Asp Leu Ser
2150	2155	2160
Leu Lys Ile Pro Glu Ile	Ser Ile Gln Asp Met	Thr Ala Gln Val
2165	2170	2175
Thr Ser Pro Ser Gly Lys	Thr His Glu Ala Glu	Ile Val Glu Gly
2180	2185	2190
Glu Asn His Thr Tyr Cys	Ile Arg Phe Val Pro	Ala Glu Met Gly
2195	2200	2205
Thr His Thr Val Ser Val	Lys Tyr Lys Gly Gln	His Val Pro Gly
2210	2215	2220
Ser Pro Phe Gln Phe Thr	Val Gly Pro Leu Gly	Glu Gly Gly Ala
2225	2230	2235
His Lys Val Arg Ala Gly	Gly Pro Gly Leu Glu	Arg Ala Glu Ala
2240	2245	2250
Gly Val Pro Ala Glu Phe	Ser Ile Trp Thr Arg	Glu Ala Gly Ala
2255	2260	2265
Gly Gly Leu Ala Ile Ala	Val Glu Gly Pro Ser	Lys Ala Glu Ile
2270	2275	2280
Ser Phe Glu Asp Arg Lys	Asp Gly Ser Cys Gly	Val Ala Tyr Val
2285	2290	2295
Val Gln Glu Pro Gly Asp	Tyr Glu Val Ser Val	Lys Phe Asn Glu
2300	2305	2310
Glu His Ile Pro Asp Ser	Pro Phe Val Val Pro	Val Ala Ser Pro
2315	2320	2325
Ser Gly Asp Ala Arg Arg	Leu Thr Val Ser Ser	Leu Gln Glu Ser
2330	2335	2340
Gly Leu Lys Val Asn Gln	Pro Ala Ser Phe Ala	Val Ser Leu Asn
2345	2350	2355

Gly Ala Lys Gly Ala Ile Asp Ala Lys Val His Ser Pro Ser Gly		
2360	2365	2370
Ala Leu Glu Glu Cys Tyr Val Thr Glu Ile Asp Gln Asp Lys Tyr		
2375	2380	2385
Ala Val Arg Phe Ile Pro Arg Glu Asn Gly Val Tyr Leu Ile Asp		
2390	2395	2400
Val Lys Phe Asn Gly Thr His Ile Pro Gly Ser Pro Phe Lys Ile		
2405	2410	2415
Arg Val Gly Glu Pro Gly His Gly Gly Asp Pro Gly Leu Val Ser		
2420	2425	2430
Ala Tyr Gly Ala Gly Leu Glu Gly Gly Val Thr Gly Asn Pro Ala		
2435	2440	2445
Glu Phe Val Val Asn Thr Ser Asn Ala Gly Ala Gly Ala Leu Ser		
2450	2455	2460
Val Thr Ile Asp Gly Pro Ser Lys Val Lys Met Asp Cys Gln Glu		
2465	2470	2475
Cys Pro Glu Gly Tyr Arg Val Thr Tyr Thr Pro Met Ala Pro Gly		
2480	2485	2490
Ser Tyr Leu Ile Ser Ile Lys Tyr Gly Gly Pro Tyr His Ile Gly		
2495	2500	2505
Gly Ser Pro Phe Lys Ala Lys Val Thr Gly Pro Arg Leu Val Ser		
2510	2515	2520
Asn His Ser Leu His Glu Thr Ser Ser Val Phe Val Asp Ser Leu		
2525	2530	2535
Thr Lys Ala Thr Cys Ala Pro Gln His Gly Ala Pro Gly Pro Gly		
2540	2545	2550
Pro Ala Asp Ala Ser Lys Val Val Ala Lys Gly Leu Gly Leu Ser		
2555	2560	2565
Lys Ala Tyr Val Gly Gln Lys Ser Ser Phe Thr Val Asp Cys Ser		
2570	2575	2580
Lys Ala Gly Asn Asn Met Leu Leu Val Gly Val His Gly Pro Arg		
2585	2590	2595
Thr Pro Cys Glu Glu Ile Leu Val Lys His Val Gly Ser Arg Leu		
2600	2605	2610
Tyr Ser Val Ser Tyr Leu Leu Lys Asp Lys Gly Glu Tyr Thr Leu		
2615	2620	2625
Val Val Lys Trp Gly Asp Glu His Ile Pro Gly Ser Pro Tyr Arg		
2630	2635	2640
Val Val Val Pro		

2645
 <210> 70
 <211> 597
 <212> PRT
 <213> 智人
 <400> 70
 Met Phe Ala Ser Cys His Cys Val Pro Arg Gly Arg Arg Thr Met Lys
 1 5 10 15
 Met Ile His Phe Arg Ser Ser Ser Val Lys Ser Leu Ser Gln Glu Met
 20 25 30
 Arg Cys Thr Ile Arg Leu Leu Asp Asp Ser Glu Ile Ser Cys His Ile
 35 40 45
 Gln Arg Glu Thr Lys Gly Gln Phe Leu Ile Asp His Ile Cys Asn Tyr
 50 55 60
 Tyr Ser Leu Leu Glu Lys Asp Tyr Phe Gly Ile Arg Tyr Val Asp Pro
 65 70 75 80
 Glu Lys Gln Arg His Trp Leu Glu Pro Asn Lys Ser Ile Phe Lys Gln
 85 90 95
 Met Lys Thr His Pro Pro Tyr Thr Met Cys Phe Arg Val Lys Phe Tyr
 100 105 110
 Pro His Glu Pro Leu Lys Ile Lys Glu Glu Leu Thr Arg Tyr Leu Leu
 115 120 125
 Tyr Leu Gln Ile Lys Arg Asp Ile Phe His Gly Arg Leu Leu Cys Ser
 130 135 140
 Phe Ser Asp Ala Ala Tyr Leu Gly Ala Cys Ile Val Gln Ala Glu Leu
 145 150 155 160
 Gly Asp Tyr Asp Pro Asp Glu His Pro Glu Asn Tyr Ile Ser Glu Phe
 165 170 175
 Glu Ile Phe Pro Lys Gln Ser Gln Lys Leu Glu Arg Lys Ile Val Glu
 180 185 190
 Ile His Lys Asn Glu Leu Arg Gly Gln Ser Pro Pro Val Ala Glu Phe
 195 200 205
 Asn Leu Leu Leu Lys Ala His Thr Leu Glu Thr Tyr Gly Val Asp Pro
 210 215 220
 His Pro Cys Lys Asp Ser Thr Gly Thr Thr Thr Phe Leu Gly Phe Thr
 225 230 235 240
 Ala Ala Gly Phe Val Val Phe Gln Gly Asn Lys Arg Ile His Leu Ile
 245 250 255
 Lys Trp Pro Asp Val Cys Lys Leu Lys Phe Glu Gly Lys Thr Phe Tyr

260	265	270
Val Ile Gly Thr Gln Lys Glu Lys Lys Ala Met Leu Ala Phe His Thr		
275	280	285
Ser Thr Pro Ala Ala Cys Lys His Leu Trp Lys Cys Gly Val Glu Asn		
290	295	300
Gln Ala Phe Tyr Lys Tyr Ala Lys Ser Ser Gln Ile Lys Thr Val Ser		
305	310	315
Ser Ser Lys Ile Phe Phe Lys Gly Ser Arg Phe Arg Tyr Ser Gly Lys		
325	330	335
Val Ala Lys Glu Val Val Glu Ala Ser Ser Lys Ile Gln Arg Glu Pro		
340	345	350
Pro Glu Val His Arg Ala Asn Ile Thr Gln Ser Arg Ser Ser His Ser		
355	360	365
Leu Asn Lys Gln Leu Ile Ile Asn Met Glu Pro Leu Gln Pro Leu Leu		
370	375	380
Pro Ser Pro Ser Glu Gln Glu Glu Glu Leu Pro Leu Gly Glu Gly Val		
385	390	395
Pro Leu Pro Lys Glu Glu Asn Ile Ser Ala Pro Leu Ile Ser Ser Ser		
405	410	415
Pro Val Lys Ala Ala Arg Glu Tyr Glu Asp Pro Pro Ser Glu Glu Glu		
420	425	430
Asp Lys Ile Lys Glu Glu Pro Leu Thr Ile Ser Glu Leu Val Tyr Asn		
435	440	445
Pro Ser Ala Ser Leu Leu Pro Thr Pro Val Asp Asp Asp Glu Ile Asp		
450	455	460
Met Leu Phe Asp Cys Pro Ser Arg Leu Glu Leu Glu Arg Glu Asp Thr		
465	470	475
Asp Ser Phe Glu Asp Leu Glu Ala Asp Glu Asn Ala Phe Leu Ile Ala		
485	490	495
Glu Glu Glu Glu Leu Lys Glu Ala Arg Arg Ala Leu Ser Trp Ser Tyr		
500	505	510
Asp Ile Leu Thr Gly His Ile Arg Val Asn Pro Leu Val Lys Ser Phe		
515	520	525
Ser Arg Leu Leu Val Val Gly Leu Gly Leu Leu Leu Phe Val Phe Pro		
530	535	540
Leu Leu Leu Leu Leu Leu Glu Ser Gly Ile Asp Leu Ser Phe Leu Cys		
545	550	555
Glu Ile Arg Gln Thr Pro Glu Phe Glu Gln Phe His Tyr Glu Tyr Tyr		
565	570	575

Cys Pro Leu Lys Glu Trp Val Ala Gly Lys Val His Leu Ile Leu Tyr
 580 585 590

Met Leu Gly Cys Ser
 595

<210> 71

<211> 183

<212> PRT

<213> 智人

<400> 71

Met Thr Thr Ala Ser Thr Ser Gln Val Arg Gln Asn Tyr His Gln Asp
 1 5 10 15

Ser Glu Ala Ala Ile Asn Arg Gln Ile Asn Leu Glu Leu Tyr Ala Ser
 20 25 30

Tyr Val Tyr Leu Ser Met Ser Tyr Tyr Phe Asp Arg Asp Asp Val Ala
 35 40 45

Leu Lys Asn Phe Ala Lys Tyr Phe Leu His Gln Ser His Glu Glu Arg
 50 55 60

Glu His Ala Glu Lys Leu Met Lys Leu Gln Asn Gln Arg Gly Gly Arg
 65 70 75 80

Ile Phe Leu Gln Asp Ile Lys Lys Pro Asp Cys Asp Asp Trp Glu Ser
 85 90 95

Gly Leu Asn Ala Met Glu Cys Ala Leu His Leu Glu Lys Asn Val Asn
 100 105 110

Gln Ser Leu Leu Glu Leu His Lys Leu Ala Thr Asp Lys Asn Asp Pro
 115 120 125

His Leu Cys Asp Phe Ile Glu Thr His Tyr Leu Asn Glu Gln Val Lys
 130 135 140

Ala Ile Lys Glu Leu Gly Asp His Val Thr Asn Leu Arg Lys Met Gly
 145 150 155 160

Ala Pro Glu Ser Gly Leu Ala Glu Tyr Leu Phe Asp Lys His Thr Leu
 165 170 175

Gly Asp Ser Asp Asn Glu Ser
 180

<210> 72

<211> 175

<212> PRT

<213> 智人

<400> 72

Met Ser Ser Gln Ile Arg Gln Asn Tyr Ser Thr Asp Val Glu Ala Ala

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

<210> 73

<211> 466

<212> PRT

<213> 智人

<400> 73

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

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

Ser Thr Thr Lys Ile Thr Met Leu Gly Ile Gln Gly Asp Leu Lys Trp
 420 425 430
 Ser Thr Asp Pro Asp Lys Gly Leu Phe Ile Ser Leu Pro Gln Leu Pro
 435 440 445
 Pro Ser Ala Val Pro Ala Glu Phe Ala Trp Thr Ile Lys Leu Thr Gly
 450 455 460
 Val Lys
 465
 <210> 74
 <211> 456
 <212> PRT
 <213> 智人
 <400> 74
 Met Arg Lys Ser Pro Gly Leu Ser Asp Cys Leu Trp Ala Trp Ile Leu
 1 5 10 15
 Leu Leu Ser Thr Leu Thr Gly Arg Ser Tyr Gly Gln Pro Ser Leu Gln
 20 25 30
 Asp Glu Leu Lys Asp Asn Thr Thr Val Phe Thr Arg Ile Leu Asp Arg
 35 40 45
 Leu Leu Asp Gly Tyr Asp Asn Arg Leu Arg Pro Gly Leu Gly Glu Arg
 50 55 60
 Val Thr Glu Val Lys Thr Asp Ile Phe Val Thr Ser Phe Gly Pro Val
 65 70 75 80
 Ser Asp His Asp Met Glu Tyr Thr Ile Asp Val Phe Phe Arg Gln Ser
 85 90 95
 Trp Lys Asp Glu Arg Leu Lys Phe Lys Gly Pro Met Thr Val Leu Arg
 100 105 110
 Leu Asn Asn Leu Met Ala Ser Lys Ile Trp Thr Pro Asp Thr Phe Phe
 115 120 125
 His Asn Gly Lys Lys Ser Val Ala His Asn Met Thr Met Pro Asn Lys
 130 135 140
 Leu Leu Arg Ile Thr Glu Asp Gly Thr Leu Leu Tyr Thr Met Arg Leu
 145 150 155 160
 Thr Val Arg Ala Glu Cys Pro Met His Leu Glu Asp Phe Pro Met Asp
 165 170 175
 Ala His Ala Cys Pro Leu Lys Phe Gly Ser Tyr Ala Tyr Thr Arg Ala
 180 185 190
 Glu Val Val Tyr Glu Trp Thr Arg Glu Pro Ala Arg Ser Val Val Val
 195 200 205

Ala	Glu	Asp	Gly	Ser	Arg	Leu	Asn	Gln	Tyr	Asp	Leu	Leu	Gly	Gln	Thr
210						215					220				
Val	Asp	Ser	Gly	Ile	Val	Gln	Ser	Ser	Thr	Gly	Glu	Tyr	Val	Val	Met
225						230				235					240
Thr	Thr	His	Phe	His	Leu	Lys	Arg	Lys	Ile	Gly	Tyr	Phe	Val	Ile	Gln
					245				250					255	
Thr	Tyr	Leu	Pro	Cys	Ile	Met	Thr	Val	Ile	Leu	Ser	Gln	Val	Ser	Phe
			260					265					270		
Trp	Leu	Asn	Arg	Glu	Ser	Val	Pro	Ala	Arg	Thr	Val	Phe	Gly	Val	Thr
			275					280					285		
Thr	Val	Leu	Thr	Met	Thr	Thr	Leu	Ser	Ile	Ser	Ala	Arg	Asn	Ser	Leu
290							295				300				
Pro	Lys	Val	Ala	Tyr	Ala	Thr	Ala	Met	Asp	Trp	Phe	Ile	Ala	Val	Cys
305						310				315					320
Tyr	Ala	Phe	Val	Phe	Ser	Ala	Leu	Ile	Glu	Phe	Ala	Thr	Val	Asn	Tyr
					325				330					335	
Phe	Thr	Lys	Arg	Gly	Tyr	Ala	Trp	Asp	Gly	Lys	Ser	Val	Val	Pro	Glu
			340					345						350	
Lys	Pro	Lys	Lys	Val	Lys	Asp	Pro	Leu	Ile	Lys	Lys	Asn	Asn	Thr	Tyr
			355					360						365	
Ala	Pro	Thr	Ala	Thr	Ser	Tyr	Thr	Pro	Asn	Leu	Ala	Arg	Gly	Asp	Pro
			370					375					380		
Gly	Leu	Ala	Thr	Ile	Ala	Lys	Ser	Ala	Thr	Ile	Glu	Pro	Lys	Glu	Val
385						390				395					400
Lys	Pro	Glu	Thr	Lys	Pro	Pro	Glu	Pro	Lys	Lys	Thr	Phe	Asn	Ser	Val
					405				410					415	
Ser	Lys	Ile	Asp	Arg	Leu	Ser	Arg	Ile	Ala	Phe	Pro	Leu	Leu	Phe	Gly
			420					425						430	
Ile	Phe	Asn	Leu	Val	Tyr	Trp	Ala	Thr	Tyr	Leu	Asn	Arg	Glu	Pro	Gln
			435					440					445		
Leu	Lys	Ala	Pro	Thr	Pro	His	Gln								
450							455								
<210>	75														
<211>	335														
<212>	PRT														
<213>	智人														
<400>	75														
Met	Gly	Lys	Val	Lys	Val	Gly	Val	Asn	Gly	Phe	Gly	Arg	Ile	Gly	Arg
1				5					10					15	

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

	325	330	335
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<211> 739			
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<213> 智人			
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Met Pro Ser Pro Arg Pro Val Leu Leu Arg Gly Ala Arg Ala Ala Leu			
1	5	10	15
Leu Leu Leu Leu Pro Pro Arg Leu Leu Ala Arg Pro Ser Leu Leu Leu			
	20	25	30
Arg Arg Ser Leu Ser Ala Ala Ser Cys Pro Pro Ile Ser Leu Pro Ala			
	35	40	45
Ala Ala Ser Arg Ser Ser Met Asp Gly Ala Gly Ala Glu Glu Val Leu			
	50	55	60
Ala Pro Leu Arg Leu Ala Val Arg Gln Gln Gly Asp Leu Val Arg Lys			
65	70	75	80
Leu Lys Glu Asp Lys Ala Pro Gln Val Asp Val Asp Lys Ala Val Ala			
	85	90	95
Glu Leu Lys Ala Arg Lys Arg Val Leu Glu Ala Lys Glu Leu Ala Leu			
	100	105	110
Gln Pro Lys Asp Asp Ile Val Asp Arg Ala Lys Met Glu Asp Thr Leu			
	115	120	125
Lys Arg Arg Phe Phe Tyr Asp Gln Ala Phe Ala Ile Tyr Gly Gly Val			
	130	135	140
Ser Gly Leu Tyr Asp Phe Gly Pro Val Gly Cys Ala Leu Lys Asn Asn			
145	150	155	160
Ile Ile Gln Thr Trp Arg Gln His Phe Ile Gln Glu Glu Gln Ile Leu			
	165	170	175
Glu Ile Asp Cys Thr Met Leu Thr Pro Glu Pro Val Leu Lys Thr Ser			
	180	185	190
Gly His Val Asp Lys Phe Ala Asp Phe Met Val Lys Asp Val Lys Asn			
	195	200	205
Gly Glu Cys Phe Arg Ala Asp His Leu Leu Lys Ala His Leu Gln Lys			
	210	215	220
Leu Met Ser Asp Lys Lys Cys Ser Val Glu Lys Lys Ser Glu Met Glu			
225	230	235	240
Ser Val Leu Ala Gln Leu Asp Asn Tyr Gly Gln Gln Glu Leu Ala Asp			
	245	250	255
Leu Phe Val Asn Tyr Asn Val Lys Ser Pro Ile Thr Gly Asn Asp Leu			

260	265	270
Ser Pro Pro Val Ser Phe Asn Leu Met Phe Lys Thr Phe Ile Gly Pro		
275	280	285
Gly Gly Asn Met Pro Gly Tyr Leu Arg Pro Glu Thr Ala Gln Gly Ile		
290	295	300
Phe Leu Asn Phe Lys Arg Leu Leu Glu Phe Asn Gln Gly Lys Leu Pro		
305	310	315
Phe Ala Ala Ala Gln Ile Gly Asn Ser Phe Arg Asn Glu Ile Ser Pro		
325	330	335
Arg Ser Gly Leu Ile Arg Val Arg Glu Phe Thr Met Ala Glu Ile Glu		
340	345	350
His Phe Val Asp Pro Ser Glu Lys Asp His Pro Lys Phe Gln Asn Val		
355	360	365
Ala Asp Leu His Leu Tyr Leu Tyr Ser Ala Lys Ala Gln Val Ser Gly		
370	375	380
Gln Ser Ala Arg Lys Met Arg Leu Gly Asp Ala Val Glu Gln Gly Val		
385	390	395
Ile Asn Asn Thr Val Leu Gly Tyr Phe Ile Gly Arg Ile Tyr Leu Tyr		
405	410	415
Leu Thr Lys Val Gly Ile Ser Pro Asp Lys Leu Arg Phe Arg Gln His		
420	425	430
Met Glu Asn Glu Met Ala His Tyr Ala Cys Asp Cys Trp Asp Ala Glu		
435	440	445
Ser Lys Thr Ser Tyr Gly Trp Ile Glu Ile Val Gly Cys Ala Asp Arg		
450	455	460
Ser Cys Tyr Asp Leu Ser Cys His Ala Arg Ala Thr Lys Val Pro Leu		
465	470	475
Val Ala Glu Lys Pro Leu Lys Glu Pro Lys Thr Val Asn Val Val Gln		
485	490	495
Phe Glu Pro Ser Lys Gly Ala Ile Gly Lys Ala Tyr Lys Lys Asp Ala		
500	505	510
Lys Leu Val Met Glu Tyr Leu Ala Ile Cys Asp Glu Cys Tyr Ile Thr		
515	520	525
Glu Met Glu Met Leu Leu Asn Glu Lys Gly Glu Phe Thr Ile Glu Thr		
530	535	540
Glu Gly Lys Thr Phe Gln Leu Thr Lys Asp Met Ile Asn Val Lys Arg		
545	550	555
Phe Gln Lys Thr Leu Tyr Val Glu Glu Val Val Pro Asn Val Ile Glu		
565	570	575

Pro Ser Phe Gly Leu Gly Arg Ile Met Tyr Thr Val Phe Glu His Thr
 580 585 590
 Phe His Val Arg Glu Gly Asp Glu Gln Arg Thr Phe Phe Ser Phe Pro
 595 600 605
 Ala Val Val Ala Pro Phe Lys Cys Ser Val Leu Pro Leu Ser Gln Asn
 610 615 620
 Gln Glu Phe Met Pro Phe Val Lys Glu Leu Ser Glu Ala Leu Thr Arg
 625 630 635 640
 His Gly Val Ser His Lys Val Asp Asp Ser Ser Gly Ser Ile Gly Arg
 645 650 655
 Arg Tyr Ala Arg Thr Asp Glu Ile Gly Val Ala Phe Gly Val Thr Ile
 660 665 670
 Asp Phe Asp Thr Val Asn Lys Thr Pro His Thr Ala Thr Leu Arg Asp
 675 680 685
 Arg Asp Ser Met Arg Gln Ile Arg Ala Glu Ile Ser Glu Leu Pro Ser
 690 695 700
 Ile Val Gln Asp Leu Ala Asn Gly Asn Ile Thr Trp Ala Asp Val Glu
 705 710 715 720
 Ala Arg Tyr Pro Leu Phe Glu Gly Gln Glu Thr Gly Lys Lys Glu Thr
 725 730 735
 Ile Glu Glu
 <210> 77
 <211> 308
 <212> PRT
 <213> 智人
 <400> 77
 Met Pro Gly Gln Glu Leu Arg Thr Val Asn Gly Ser Gln Met Leu Leu
 1 5 10 15
 Val Leu Leu Val Leu Ser Trp Leu Pro His Gly Gly Ala Leu Ser Leu
 20 25 30
 Ala Glu Ala Ser Arg Ala Ser Phe Pro Gly Pro Ser Glu Leu His Ser
 35 40 45
 Glu Asp Ser Arg Phe Arg Glu Leu Arg Lys Arg Tyr Glu Asp Leu Leu
 50 55 60
 Thr Arg Leu Arg Ala Asn Gln Ser Trp Glu Asp Ser Asn Thr Asp Leu
 65 70 75 80
 Val Pro Ala Pro Ala Val Arg Ile Leu Thr Pro Glu Val Arg Leu Gly
 85 90 95
 Ser Gly Gly His Leu His Leu Arg Ile Ser Arg Ala Ala Leu Pro Glu

100	105	110
Gly Leu Pro Glu Ala Ser Arg	Leu His Arg Ala Leu Phe	Arg Leu Ser
115	120	125
Pro Thr Ala Ser Arg Ser Trp	Asp Val Thr Arg Pro Leu	Arg Arg Gln
130	135	140
Leu Ser Leu Ala Arg Pro Gln	Ala Pro Ala Leu His Leu	Arg Leu Ser
145	150	155
Pro Pro Pro Ser Gln Ser Asp	Gln Leu Leu Ala Glu Ser	Ser Ser Ala
165	170	175
Arg Pro Gln Leu Glu Leu His	Leu Arg Pro Gln Ala Ala	Arg Gly Arg
180	185	190
Arg Arg Ala Arg Ala Arg Asn	Gly Asp His Cys Pro Leu	Gly Pro Gly
195	200	205
Arg Cys Cys Arg Leu His Thr	Val Arg Ala Ser Leu Glu	Asp Leu Gly
210	215	220
Trp Ala Asp Trp Val Leu Ser	Pro Arg Glu Val Gln Val	Thr Met Cys
225	230	235
Ile Gly Ala Cys Pro Ser Gln	Phe Arg Ala Ala Asn Met	His Ala Gln
245	250	255
Ile Lys Thr Ser Leu His Arg	Leu Lys Pro Asp Thr Val	Pro Ala Pro
260	265	270
Cys Cys Val Pro Ala Ser Tyr	Asn Pro Met Val Leu Ile	Gln Lys Thr
275	280	285
Asp Thr Gly Val Ser Leu Gln	Thr Tyr Asp Asp Leu Leu	Ala Lys Asp
290	295	300
Cys His Cys Ile		
305		
<210> 78		
<211> 782		
<212> PRT		
<213> 智人		
<400> 78		
Met Ala Pro His Arg Pro Ala	Pro Ala Leu Leu Cys Ala	Leu Ser Leu
1	5	10
Ala Leu Cys Ala Leu Ser Leu	Pro Val Arg Ala Ala Thr	Ala Ser Arg
20	25	30
Gly Ala Ser Gln Ala Gly Ala	Pro Gln Gly Arg Val Pro	Glu Ala Arg
35	40	45
Pro Asn Ser Met Val Val Glu	His Pro Glu Phe Leu Lys	Ala Gly Lys

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

Met Asp Tyr Pro Lys Gln Thr Gln Val Ser Val Leu Pro Glu Gly Gly		
370	375	380
Glu Thr Pro Leu Phe Lys Gln Phe Phe Lys Asn Trp Arg Asp Pro Asp		
385	390	395 400
Gln Thr Asp Gly Leu Gly Leu Ser Tyr Leu Ser Ser His Ile Ala Asn		
	405	410 415
Val Glu Arg Val Pro Phe Asp Ala Ala Thr Leu His Thr Ser Thr Ala		
	420	425 430
Met Ala Ala Gln His Gly Met Asp Asp Asp Gly Thr Gly Gln Lys Gln		
	435	440 445
Ile Trp Arg Ile Glu Gly Ser Asn Lys Val Pro Val Asp Pro Ala Thr		
	450	455 460
Tyr Gly Gln Phe Tyr Gly Gly Asp Ser Tyr Ile Ile Leu Tyr Asn Tyr		
465	470	475 480
Arg His Gly Gly Arg Gln Gly Gln Ile Ile Tyr Asn Trp Gln Gly Ala		
	485	490 495
Gln Ser Thr Gln Asp Glu Val Ala Ala Ser Ala Ile Leu Thr Ala Gln		
	500	505 510
Leu Asp Glu Glu Leu Gly Gly Thr Pro Val Gln Ser Arg Val Val Gln		
	515	520 525
Gly Lys Glu Pro Ala His Leu Met Ser Leu Phe Gly Gly Lys Pro Met		
530	535	540
Ile Ile Tyr Lys Gly Gly Thr Ser Arg Glu Gly Gly Gln Thr Ala Pro		
545	550	555 560
Ala Ser Thr Arg Leu Phe Gln Val Arg Ala Asn Ser Ala Gly Ala Thr		
	565	570 575
Arg Ala Val Glu Val Leu Pro Lys Ala Gly Ala Leu Asn Ser Asn Asp		
	580	585 590
Ala Phe Val Leu Lys Thr Pro Ser Ala Ala Tyr Leu Trp Val Gly Thr		
	595	600 605
Gly Ala Ser Glu Ala Glu Lys Thr Gly Ala Gln Glu Leu Leu Arg Val		
610	615	620
Leu Arg Ala Gln Pro Val Gln Val Ala Glu Gly Ser Glu Pro Asp Gly		
625	630	635 640
Phe Trp Glu Ala Leu Gly Gly Lys Ala Ala Tyr Arg Thr Ser Pro Arg		
	645	650 655
Leu Lys Asp Lys Lys Met Asp Ala His Pro Pro Arg Leu Phe Ala Cys		
	660	665 670
Ser Asn Lys Ile Gly Arg Phe Val Ile Glu Glu Val Pro Gly Glu Leu		

675	680	685
Met Gln Glu Asp Leu Ala Thr Asp Asp Val Met Leu Leu Asp Thr Trp		
690	695	700
Asp Gln Val Phe Val Trp Val Gly Lys Asp Ser Gln Glu Glu Glu Lys		
705	710	715
Thr Glu Ala Leu Thr Ser Ala Lys Arg Tyr Ile Glu Thr Asp Pro Ala		
725	730	735
Asn Arg Asp Arg Arg Thr Pro Ile Thr Val Val Lys Gln Gly Phe Glu		
740	745	750
Pro Pro Ser Phe Val Gly Trp Phe Leu Gly Trp Asp Asp Asp Tyr Trp		
755	760	765
Ser Val Asp Pro Leu Asp Arg Ala Met Ala Glu Leu Ala Ala		
770	775	780
<210> 79		
<211> 210		
<212> PRT		
<213> 智人		
<400> 79		
Met Pro Pro Tyr Thr Val Val Tyr Phe Pro Val Arg Gly Arg Cys Ala		
1	5	10
Ala Leu Arg Met Leu Leu Ala Asp Gln Gly Gln Ser Trp Lys Glu Glu		
20	25	30
Val Val Thr Val Glu Thr Trp Gln Glu Gly Ser Leu Lys Ala Ser Cys		
35	40	45
Leu Tyr Gly Gln Leu Pro Lys Phe Gln Asp Gly Asp Leu Thr Leu Tyr		
50	55	60
Gln Ser Asn Thr Ile Leu Arg His Leu Gly Arg Thr Leu Gly Leu Tyr		
65	70	75
Gly Lys Asp Gln Gln Glu Ala Ala Leu Val Asp Met Val Asn Asp Gly		
85	90	95
Val Glu Asp Leu Arg Cys Lys Tyr Ile Ser Leu Ile Tyr Thr Asn Tyr		
100	105	110
Glu Ala Gly Lys Asp Asp Tyr Val Lys Ala Leu Pro Gly Gln Leu Lys		
115	120	125
Pro Phe Glu Thr Leu Leu Ser Gln Asn Gln Gly Gly Lys Thr Phe Ile		
130	135	140
Val Gly Asp Gln Ile Ser Phe Ala Asp Tyr Asn Leu Leu Asp Leu Leu		
145	150	155
Leu Ile His Glu Val Leu Ala Pro Gly Cys Leu Asp Ala Phe Pro Leu		

				165						170					175				
Leu	Ser	Ala	Tyr	Val	Gly	Arg	Leu	Ser	Ala	Arg	Pro	Lys	Leu	Lys	Ala				
				180						185					190				
Phe	Leu	Ala	Ser	Pro	Glu	Tyr	Val	Asn	Leu	Pro	Ile	Asn	Gly	Asn	Gly				
				195						200					205				
Lys	Gln																		
	210																		
<210>	80																		
<211>	560																		
<212>	PRT																		
<213>	智人																		
<400>	80																		
Met	Phe	Ala	Arg	Met	Ser	Asp	Leu	His	Val	Leu	Leu	Leu	Met	Ala	Leu				
1				5					10					15					
Val	Gly	Lys	Thr	Ala	Cys	Gly	Phe	Ser	Leu	Met	Ser	Leu	Leu	Glu	Ser				
				20					25					30					
Leu	Asp	Pro	Asp	Trp	Thr	Pro	Asp	Gln	Tyr	Asp	Tyr	Ser	Tyr	Glu	Asp				
				35				40					45						
Tyr	Asn	Gln	Glu	Glu	Asn	Thr	Ser	Ser	Thr	Leu	Thr	His	Ala	Glu	Asn				
	50							55				60							
Pro	Asp	Trp	Tyr	Tyr	Thr	Glu	Asp	Gln	Ala	Asp	Pro	Cys	Gln	Pro	Asn				
65						70				75					80				
Pro	Cys	Glu	His	Gly	Gly	Asp	Cys	Leu	Val	His	Gly	Ser	Thr	Phe	Thr				
				85					90					95					
Cys	Ser	Cys	Leu	Ala	Pro	Phe	Ser	Gly	Asn	Lys	Cys	Gln	Lys	Val	Gln				
				100					105					110					
Asn	Thr	Cys	Lys	Asp	Asn	Pro	Cys	Gly	Arg	Gly	Gln	Cys	Leu	Ile	Thr				
				115					120					125					
Gln	Ser	Pro	Pro	Tyr	Tyr	Arg	Cys	Val	Cys	Lys	His	Pro	Tyr	Thr	Gly				
				130					135					140					
Pro	Ser	Cys	Ser	Gln	Val	Val	Pro	Val	Cys	Arg	Pro	Asn	Pro	Cys	Gln				
145						150				155					160				
Asn	Gly	Ala	Thr	Cys	Ser	Arg	His	Lys	Arg	Arg	Ser	Lys	Phe	Thr	Cys				
				165						170					175				
Ala	Cys	Pro	Asp	Gln	Phe	Lys	Gly	Lys	Phe	Cys	Glu	Ile	Gly	Ser	Asp				
				180						185					190				
Asp	Cys	Tyr	Val	Gly	Asp	Gly	Tyr	Ser	Tyr	Arg	Gly	Lys	Met	Asn	Arg				
				195						200					205				
Thr	Val	Asn	Gln	His	Ala	Cys	Leu	Tyr	Trp	Asn	Ser	His	Leu	Leu	Leu				

210	215	220
Gln Glu Asn Tyr Asn Met Phe Met Glu Asp Ala Glu Thr His Gly Ile		
225	230	235
Gly Glu His Asn Phe Cys Arg Asn Pro Asp Ala Asp Glu Lys Pro Trp		240
	245	250
Cys Phe Ile Lys Val Thr Asn Asp Lys Val Lys Trp Glu Tyr Cys Asp		255
	260	265
Val Ser Ala Cys Ser Ala Gln Asp Val Ala Tyr Pro Glu Glu Ser Pro		270
	275	280
Thr Glu Pro Ser Thr Lys Leu Pro Gly Phe Asp Ser Cys Gly Lys Thr		285
290	295	300
Glu Ile Ala Glu Arg Lys Ile Lys Arg Ile Tyr Gly Gly Phe Lys Ser		
305	310	315
Thr Ala Gly Lys His Pro Trp Gln Ala Ser Leu Gln Ser Ser Leu Pro		320
	325	330
Leu Thr Ile Ser Met Pro Gln Gly His Phe Cys Gly Gly Ala Leu Ile		335
	340	345
His Pro Cys Trp Val Leu Thr Ala Ala His Cys Thr Asp Ile Lys Thr		350
355	360	365
Arg His Leu Lys Val Val Leu Gly Asp Gln Asp Leu Lys Lys Glu Glu		
370	375	380
Phe His Glu Gln Ser Phe Arg Val Glu Lys Ile Phe Lys Tyr Ser His		
385	390	395
Tyr Asn Glu Arg Asp Glu Ile Pro His Asn Asp Ile Ala Leu Leu Lys		400
	405	410
Leu Lys Pro Val Asp Gly His Cys Ala Leu Glu Ser Lys Tyr Val Lys		415
	420	425
Thr Val Cys Leu Pro Asp Gly Ser Phe Pro Ser Gly Ser Glu Cys His		430
	435	440
Ile Ser Gly Trp Gly Val Thr Glu Thr Gly Lys Gly Ser Arg Gln Leu		445
450	455	460
Leu Asp Ala Lys Val Lys Leu Ile Ala Asn Thr Leu Cys Asn Ser Arg		
465	470	475
Gln Leu Tyr Asp His Met Ile Asp Asp Ser Met Ile Cys Ala Gly Asn		480
	485	490
Leu Gln Lys Pro Gly Gln Asp Thr Cys Gln Gly Asp Ser Gly Gly Pro		495
	500	505
Leu Thr Cys Glu Lys Asp Gly Thr Tyr Tyr Val Tyr Gly Ile Val Ser		510
515	520	525

Trp Gly Leu Glu Cys Gly Lys Arg Pro Gly Val Tyr Thr Gln Val Thr			
530	535	540	
Lys Phe Leu Asn Trp Ile Lys Ala Thr Ile Lys Ser Glu Ser Gly Phe			
545	550	555	560
<210> 81			
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<212> PRT			
<213> 智人			
<400> 81			
Met Trp Val Thr Lys Leu Leu Pro Ala Leu Leu Leu Gln His Val Leu			
1	5	10	15
Leu His Leu Leu Leu Leu Pro Ile Ala Ile Pro Tyr Ala Glu Gly Gln			
20	25	30	
Arg Lys Arg Arg Asn Thr Ile His Glu Phe Lys Lys Ser Ala Lys Thr			
35	40	45	
Thr Leu Ile Lys Ile Asp Pro Ala Leu Lys Ile Lys Thr Lys Lys Val			
50	55	60	
Asn Thr Ala Asp Gln Cys Ala Asn Arg Cys Thr Arg Asn Lys Gly Leu			
65	70	75	80
Pro Phe Thr Cys Lys Ala Phe Val Phe Asp Lys Ala Arg Lys Gln Cys			
85	90	95	
Leu Trp Phe Pro Phe Asn Ser Met Ser Ser Gly Val Lys Lys Glu Phe			
100	105	110	
Gly His Glu Phe Asp Leu Tyr Glu Asn Lys Asp Tyr Ile Arg Asn Cys			
115	120	125	
Ile Ile Gly Lys Gly Arg Ser Tyr Lys Gly Thr Val Ser Ile Thr Lys			
130	135	140	
Ser Gly Ile Lys Cys Gln Pro Trp Ser Ser Met Ile Pro His Glu His			
145	150	155	160
Ser Phe Leu Pro Ser Ser Tyr Arg Gly Lys Asp Leu Gln Glu Asn Tyr			
165	170	175	
Cys Arg Asn Pro Arg Gly Glu Glu Gly Gly Pro Trp Cys Phe Thr Ser			
180	185	190	
Asn Pro Glu Val Arg Tyr Glu Val Cys Asp Ile Pro Gln Cys Ser Glu			
195	200	205	
Val Glu Cys Met Thr Cys Asn Gly Glu Ser Tyr Arg Gly Leu Met Asp			
210	215	220	
His Thr Glu Ser Gly Lys Ile Cys Gln Arg Trp Asp His Gln Thr Pro			
225	230	235	240

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

545	550	555	560
Cys Lys Gln Val Leu Asn Val Ser Gln Leu Val Tyr Gly Pro Glu Gly			
	565	570	575
Ser Asp Leu Val Leu Met Lys Leu Ala Arg Pro Ala Val Leu Asp Asp			
	580	585	590
Phe Val Ser Thr Ile Asp Leu Pro Asn Tyr Gly Cys Thr Ile Pro Glu			
	595	600	605
Lys Thr Ser Cys Ser Val Tyr Gly Trp Gly Tyr Thr Gly Leu Ile Asn			
	610	615	620
Tyr Asp Gly Leu Leu Arg Val Ala His Leu Tyr Ile Met Gly Asn Glu			
625	630	635	640
Lys Cys Ser Gln His His Arg Gly Lys Val Thr Leu Asn Glu Ser Glu			
	645	650	655
Ile Cys Ala Gly Ala Glu Lys Ile Gly Ser Gly Pro Cys Glu Gly Asp			
	660	665	670
Tyr Gly Gly Pro Leu Val Cys Glu Gln His Lys Met Arg Met Val Leu			
	675	680	685
Gly Val Ile Val Pro Gly Arg Gly Cys Ala Ile Pro Asn Arg Pro Gly			
	690	695	700
Ile Phe Val Arg Val Ala Tyr Tyr Ala Lys Trp Ile His Lys Ile Ile			
705	710	715	720
Leu Thr Tyr Lys Val Pro Gln Ser			
	725		

<210> 82

<211> 365

<212> PRT

<213> 智人

<400> 82

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

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

<210> 83

<211> 215

<212> PRT

<213> 智人

<400> 83

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

<210> 84

<211> 372

<212> PRT

<213> 智人

<400> 84

Met Ser Lys Ser Glu Ser Pro Lys Glu Pro Glu Gln Leu Arg Lys Leu
 1 5 10 15
 Phe Ile Gly Gly Leu Ser Phe Glu Thr Thr Asp Glu Ser Leu Arg Ser
 20 25 30
 His Phe Glu Gln Trp Gly Thr Leu Thr Asp Cys Val Val Met Arg Asp

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

Asn	Gln	Gly	Gly	Tyr	Gly	Gly	Ser	Ser	Ser	Ser	Ser	Ser	Tyr	Gly	Ser
355				360				365							
Gly	Arg	Arg	Phe												
370															
<210> 85															
<211> 353															
<212> PRT															
<213> 智人															
<400> 85															
Met	Glu	Lys	Thr	Leu	Glu	Thr	Val	Pro	Leu	Glu	Arg	Lys	Lys	Arg	Glu
1		5		10		15									
Lys	Glu	Gln	Phe	Arg	Lys	Leu	Phe	Ile	Gly	Gly	Leu	Ser	Phe	Glu	Thr
20				25				30							
Thr	Glu	Glu	Ser	Leu	Arg	Asn	Tyr	Tyr	Glu	Gln	Trp	Gly	Lys	Leu	Thr
35				40				45							
Asp	Cys	Val	Val	Met	Arg	Asp	Pro	Ala	Ser	Lys	Arg	Ser	Arg	Gly	Phe
50		55		60											
Gly	Phe	Val	Thr	Phe	Ser	Ser	Met	Ala	Glu	Val	Asp	Ala	Ala	Met	Ala
65		70		75		80									
Ala	Arg	Pro	His	Ser	Ile	Asp	Gly	Arg	Val	Val	Glu	Pro	Lys	Arg	Ala
85				90				95							
Val	Ala	Arg	Glu	Glu	Ser	Gly	Lys	Pro	Gly	Ala	His	Val	Thr	Val	Lys
100				105				110							
Lys	Leu	Phe	Val	Gly	Gly	Ile	Lys	Glu	Asp	Thr	Glu	Glu	His	His	Leu
115				120				125							
Arg	Asp	Tyr	Phe	Glu	Glu	Tyr	Gly	Lys	Ile	Asp	Thr	Ile	Glu	Ile	Ile
130				135				140							
Thr	Asp	Arg	Gln	Ser	Gly	Lys	Lys	Arg	Gly	Phe	Gly	Phe	Val	Thr	Phe
145		150		155		160									
Asp	Asp	His	Asp	Pro	Val	Asp	Lys	Ile	Val	Leu	Gln	Lys	Tyr	His	Thr
165				170				175							
Ile	Asn	Gly	His	Asn	Ala	Glu	Val	Arg	Lys	Ala	Leu	Ser	Arg	Gln	Glu
180				185				190							
Met	Gln	Glu	Val	Gln	Ser	Ser	Arg	Ser	Gly	Arg	Gly	Gly	Asn	Phe	Gly
195		200		205											
Phe	Gly	Asp	Ser	Arg	Gly	Gly	Gly	Gly	Asn	Phe	Gly	Pro	Gly	Pro	Gly
210		215		220											
Ser	Asn	Phe	Arg	Gly	Gly	Ser	Asp	Gly	Tyr	Gly	Ser	Gly	Arg	Gly	Phe
225		230		235		240									

Gly Asp Gly Tyr Asn Gly Tyr Gly Gly Gly Pro Gly Gly Gly Asn Phe
 245 250 255
 Gly Gly Ser Pro Gly Tyr Gly Gly Gly Arg Gly Gly Tyr Gly Gly Gly
 260 265 270
 Gly Pro Gly Tyr Gly Asn Gln Gly Gly Gly Tyr Gly Gly Gly Tyr Asp
 275 280 285
 Asn Tyr Gly Gly Gly Asn Tyr Gly Ser Gly Asn Tyr Asn Asp Phe Gly
 290 295 300
 Asn Tyr Asn Gln Gln Pro Ser Asn Tyr Gly Pro Met Lys Ser Gly Asn
 305 310 315 320
 Phe Gly Gly Ser Arg Asn Met Gly Gly Pro Tyr Gly Gly Gly Asn Tyr
 325 330 335
 Gly Pro Gly Gly Ser Gly Gly Ser Gly Gly Tyr Gly Gly Arg Ser Arg
 340 345 350
 Tyr
 <210> 86
 <211> 415
 <212> PRT
 <213> 智人
 <400> 86
 Met Met Leu Gly Pro Glu Gly Gly Glu Gly Phe Val Val Lys Leu Arg
 1 5 10 15
 Gly Leu Pro Trp Ser Cys Ser Val Glu Asp Val Gln Asn Phe Leu Ser
 20 25 30
 Asp Cys Thr Ile His Asp Gly Ala Ala Gly Val His Phe Ile Tyr Thr
 35 40 45
 Arg Glu Gly Arg Gln Ser Gly Glu Ala Phe Val Glu Leu Gly Ser Glu
 50 55 60
 Asp Asp Val Lys Met Ala Leu Lys Lys Asp Arg Glu Ser Met Gly His
 65 70 75 80
 Arg Tyr Ile Glu Val Phe Lys Ser His Arg Thr Glu Met Asp Trp Val
 85 90 95
 Leu Lys His Ser Gly Pro Asn Ser Ala Asp Ser Ala Asn Asp Gly Phe
 100 105 110
 Val Arg Leu Arg Gly Leu Pro Phe Gly Cys Thr Lys Glu Glu Ile Val
 115 120 125
 Gln Phe Phe Ser Gly Leu Glu Ile Val Pro Asn Gly Ile Thr Leu Pro
 130 135 140
 Val Asp Pro Glu Gly Lys Ile Thr Gly Glu Ala Phe Val Gln Phe Ala

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

<210> 87

<211> 406

<212> PRT

<213> 智人

<400> 87

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

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

Lys Lys Thr Pro Lys Ser Pro Val Gly Val Gln Pro Ile Leu Asn Glu
 325 330 335
 His Thr Phe Cys Ala Gly Met Ser Lys Tyr Gln Glu Asp Thr Cys Tyr
 340 345 350
 Gly Asp Ala Gly Ser Ala Phe Ala Val His Asp Leu Glu Glu Asp Thr
 355 360 365
 Trp Tyr Ala Thr Gly Ile Leu Ser Phe Asp Lys Ser Cys Ala Val Ala
 370 375 380
 Glu Tyr Gly Val Tyr Val Lys Val Thr Ser Ile Gln Asp Trp Val Gln
 385 390 395 400
 Lys Thr Ile Ala Glu Asn
 405

<210> 88

<211> 724

<212> PRT

<213> 智人

<400> 88

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

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

				485				490				495			
Ser	Ala	Phe	Val	Glu	Arg	Val	Arg	Lys	Arg	Gly	Phe	Glu	Val	Val	Tyr
				500				505				510			
Met	Thr	Glu	Pro	Ile	Asp	Glu	Tyr	Cys	Val	Gln	Gln	Leu	Lys	Glu	Phe
				515				520				525			
Asp	Gly	Lys	Ser	Leu	Val	Ser	Val	Thr	Lys	Glu	Gly	Leu	Glu	Leu	Pro
				530				535				540			
Glu	Asp	Glu	Glu	Glu	Lys	Lys	Lys	Met	Glu	Glu	Ser	Lys	Ala	Lys	Phe
545				550				555				560			
Glu	Asn	Leu	Cys	Lys	Leu	Met	Lys	Glu	Ile	Leu	Asp	Lys	Lys	Val	Glu
				565				570				575			
Lys	Val	Thr	Ile	Ser	Asn	Arg	Leu	Val	Ser	Ser	Pro	Cys	Cys	Ile	Val
				580				585				590			
Thr	Ser	Thr	Tyr	Gly	Trp	Thr	Ala	Asn	Met	Glu	Arg	Ile	Met	Lys	Ala
				595				600				605			
Gln	Ala	Leu	Arg	Asp	Asn	Ser	Thr	Met	Gly	Tyr	Met	Met	Ala	Lys	Lys
				610				615				620			
His	Leu	Glu	Ile	Asn	Pro	Asp	His	Pro	Ile	Val	Glu	Thr	Leu	Arg	Gln
625				630				635				640			
Lys	Ala	Glu	Ala	Asp	Lys	Asn	Asp	Lys	Ala	Val	Lys	Asp	Leu	Val	Val
				645				650				655			
Leu	Leu	Phe	Glu	Thr	Ala	Leu	Leu	Ser	Ser	Gly	Phe	Ser	Leu	Glu	Asp
				660				665				670			
Pro	Gln	Thr	His	Ser	Asn	Arg	Ile	Tyr	Arg	Met	Ile	Lys	Leu	Gly	Leu
				675				680				685			
Gly	Ile	Asp	Glu	Asp	Glu	Val	Ala	Ala	Glu	Glu	Pro	Asn	Ala	Ala	Val
				690				695				700			
Pro	Asp	Glu	Ile	Pro	Pro	Leu	Glu	Gly	Asp	Glu	Asp	Ala	Ser	Arg	Met
705				710				715				720			
Glu Glu Val Asp															
<210> 89															
<211> 803															
<212> PRT															
<213> 智人															
<400> 89															
Met	Arg	Ala	Leu	Trp	Val	Leu	Gly	Leu	Cys	Cys	Val	Leu	Leu	Thr	Phe
1				5				10				15			
Gly	Ser	Val	Arg	Ala	Asp	Asp	Glu	Val	Asp	Val	Asp	Gly	Thr	Val	Glu
				20				25				30			

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

340	345	350
Asp Glu Tyr Lys Ala Phe Tyr Lys Ser Phe Ser Lys Glu Ser Asp Asp		
355	360	365
Pro Met Ala Tyr Ile His Phe Thr Ala Glu Gly Glu Val Thr Phe Lys		
370	375	380
Ser Ile Leu Phe Val Pro Thr Ser Ala Pro Arg Gly Leu Phe Asp Glu		
385	390	395
Tyr Gly Ser Lys Lys Ser Asp Tyr Ile Lys Leu Tyr Val Arg Arg Val		
405	410	415
Phe Ile Thr Asp Asp Phe His Asp Met Met Pro Lys Tyr Leu Asn Phe		
420	425	430
Val Lys Gly Val Val Asp Ser Asp Asp Leu Pro Leu Asn Val Ser Arg		
435	440	445
Glu Thr Leu Gln Gln His Lys Leu Leu Lys Val Ile Arg Lys Lys Leu		
450	455	460
Val Arg Lys Thr Leu Asp Met Ile Lys Lys Ile Ala Asp Asp Lys Tyr		
465	470	475
Asn Asp Thr Phe Trp Lys Glu Phe Gly Thr Asn Ile Lys Leu Gly Val		
485	490	495
Ile Glu Asp His Ser Asn Arg Thr Arg Leu Ala Lys Leu Leu Arg Phe		
500	505	510
Gln Ser Ser His His Pro Thr Asp Ile Thr Ser Leu Asp Gln Tyr Val		
515	520	525
Glu Arg Met Lys Glu Lys Gln Asp Lys Ile Tyr Phe Met Ala Gly Ser		
530	535	540
Ser Arg Lys Glu Ala Glu Ser Ser Pro Phe Val Glu Arg Leu Leu Lys		
545	550	555
Lys Gly Tyr Glu Val Ile Tyr Leu Thr Glu Pro Val Asp Glu Tyr Cys		
565	570	575
Ile Gln Ala Leu Pro Glu Phe Asp Gly Lys Arg Phe Gln Asn Val Ala		
580	585	590
Lys Glu Gly Val Lys Phe Asp Glu Ser Glu Lys Thr Lys Glu Ser Arg		
595	600	605
Glu Ala Val Glu Lys Glu Phe Glu Pro Leu Leu Asn Trp Met Lys Asp		
610	615	620
Lys Ala Leu Lys Asp Lys Ile Glu Lys Ala Val Val Ser Gln Arg Leu		
625	630	635
Thr Glu Ser Pro Cys Ala Leu Val Ala Ser Gln Tyr Gly Trp Ser Gly		
645	650	655

Asn Met Glu Arg Ile Met Lys Ala Gln Ala Tyr Gln Thr Gly Lys Asp			
660	665	670	
Ile Ser Thr Asn Tyr Tyr Ala Ser Gln Lys Lys Thr Phe Glu Ile Asn			
675	680	685	
Pro Arg His Pro Leu Ile Arg Asp Met Leu Arg Arg Ile Lys Glu Asp			
690	695	700	
Glu Asp Asp Lys Thr Val Leu Asp Leu Ala Val Val Leu Phe Glu Thr			
705	710	715	720
Ala Thr Leu Arg Ser Gly Tyr Leu Leu Pro Asp Thr Lys Ala Tyr Gly			
725	730	735	
Asp Arg Ile Glu Arg Met Leu Arg Leu Ser Leu Asn Ile Asp Pro Asp			
740	745	750	
Ala Lys Val Glu Glu Glu Pro Glu Glu Glu Pro Glu Glu Thr Ala Glu			
755	760	765	
Asp Thr Thr Glu Asp Thr Glu Gln Asp Glu Asp Glu Glu Met Asp Val			
770	775	780	
Gly Thr Asp Glu Glu Glu Glu Thr Ala Lys Glu Ser Thr Ala Glu Lys			
785	790	795	800
Asp Glu Leu			
<210> 90			
<211> 679			
<212> PRT			
<213> 智人			
<400> 90			
Met Ile Ser Ala Ser Arg Ala Ala Ala Ala Arg Leu Val Gly Ala Ala			
1	5	10	15
Ala Ser Arg Gly Pro Thr Ala Ala Arg His Gln Asp Ser Trp Asn Gly			
20	25	30	
Leu Ser His Glu Ala Phe Arg Leu Val Ser Arg Arg Asp Tyr Ala Ser			
35	40	45	
Glu Ala Ile Lys Gly Ala Val Val Gly Ile Asp Leu Gly Thr Thr Asn			
50	55	60	
Ser Cys Val Ala Val Met Glu Gly Lys Gln Ala Lys Val Leu Glu Asn			
65	70	75	80
Ala Glu Gly Ala Arg Thr Thr Pro Ser Val Val Ala Phe Thr Ala Asp			
85	90	95	
Gly Glu Arg Leu Val Gly Met Pro Ala Lys Arg Gln Ala Val Thr Asn			
100	105	110	
Pro Asn Asn Thr Phe Tyr Ala Thr Lys Arg Leu Ile Gly Arg Arg Tyr			

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

Thr Asp Val Leu Leu Leu Asp Val Thr Pro Leu Ser Leu Gly Ile Glu
435 440 445
Thr Leu Gly Gly Val Phe Thr Lys Leu Ile Asn Arg Asn Thr Thr Ile
450 455 460
Pro Thr Lys Lys Ser Gln Val Phe Ser Thr Ala Ala Asp Gly Gln Thr
465 470 475 480
Gln Val Glu Ile Lys Val Cys Gln Gly Glu Arg Glu Met Ala Gly Asp
485 490 495
Asn Lys Leu Leu Gly Gln Phe Thr Leu Ile Gly Ile Pro Pro Ala Pro
500 505 510
Arg Gly Val Pro Gln Ile Glu Val Thr Phe Asp Ile Asp Ala Asn Gly
515 520 525
Ile Val His Val Ser Ala Lys Asp Lys Gly Thr Gly Arg Glu Gln Gln
530 535 540
Ile Val Ile Gln Ser Ser Gly Gly Leu Ser Lys Asp Asp Ile Glu Asn
545 550 555 560
Met Val Lys Asn Ala Glu Lys Tyr Ala Glu Glu Asp Arg Arg Lys Lys
565 570 575
Glu Arg Val Glu Ala Val Asn Met Ala Glu Gly Ile Ile His Asp Thr
580 585 590
Glu Thr Lys Met Glu Glu Phe Lys Asp Gln Leu Pro Ala Asp Glu Cys
595 600 605
Asn Lys Leu Lys Glu Glu Ile Ser Lys Met Arg Glu Leu Leu Ala Arg
610 615 620
Lys Asp Ser Glu Thr Gly Glu Asn Ile Arg Gln Ala Ala Ser Ser Leu
625 630 635 640
Gln Gln Ala Ser Leu Lys Leu Phe Glu Met Ala Tyr Lys Lys Met Ala
645 650 655
Ser Glu Arg Glu Gly Ser Gly Ser Ser Gly Thr Gly Glu Gln Lys Glu
660 665 670
Asp Gln Lys Glu Glu Lys Gln
675
<210> 91
<211> 205
<212> PRT
<213> 智人
<400> 91
Met Thr Glu Arg Arg Val Pro Phe Ser Leu Leu Arg Gly Pro Ser Trp
1 5 10 15

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

<210> 92

<211> 573

<212> PRT

<213> 智人

<400> 92

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

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

385	390	395	400
Val Ala Val Leu Lys	Val Gly Gly Thr Ser	Asp Val Glu Val Asn Glu	
	405	410	415
Lys Lys Asp Arg Val Thr	Asp Ala Leu Asn Ala Thr	Arg Ala Ala Val	
	420	425	430
Glu Glu Gly Ile Val Leu	Gly Gly Gly Cys Ala Leu	Leu Arg Cys Ile	
	435	440	445
Pro Ala Leu Asp Ser Leu	Thr Pro Ala Asn Glu Asp	Gln Lys Ile Gly	
	450	455	460
Ile Glu Ile Ile Lys Arg	Thr Leu Lys Ile Pro Ala	Met Thr Ile Ala	
465	470	475	480
Lys Asn Ala Gly Val Glu	Gly Ser Leu Ile Val Glu	Lys Ile Met Gln	
	485	490	495
Ser Ser Ser Glu Val Gly	Tyr Asp Ala Met Ala Gly	Asp Phe Val Asn	
	500	505	510
Met Val Glu Lys Gly Ile	Ile Asp Pro Thr Lys Val	Val Arg Thr Ala	
	515	520	525
Leu Leu Asp Ala Ala Gly	Val Ala Ser Leu Leu Thr	Thr Ala Glu Val	
	530	535	540
Val Val Thr Glu Ile Pro	Lys Glu Glu Lys Asp Pro	Gly Met Gly Ala	
545	550	555	560
Met Gly Gly Met Gly Gly	Gly Met Gly Gly Met Phe		
	565	570	

<210> 93

<211> 317

<212> PRT

<213> 智人

<400> 93

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

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

<210> 94

<211> 600

<212> PRT

<213> 智人

<400> 94

Met Ala Ser Asn His Lys Ser Ser Ala Ala Arg Pro Val Ser Arg Gly					
1		5		10	
Gly Val Gly Leu Thr Gly Arg Pro Pro Ser Gly Ile Arg Pro Leu Ser					
20		25		30	
Gly Asn Ile Arg Val Ala Thr Ala Met Pro Pro Gly Thr Ala Arg Pro					

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

Glu Met Asn Gln Lys Tyr Lys Glu Leu Lys Lys Arg Glu Glu His Met			
355	360	365	
Asp Thr Phe Ile Glu Thr Phe Glu Glu Thr Lys Asn Gln Glu Leu Lys			
370	375	380	
Arg Lys Ala Gln Ile Glu Ala Asn Ile Val Ala Leu Leu Glu His Cys			
385	390	395	400
Ser Arg Asn Ile Asn Arg Ile Glu Gln Ile Ser Ser Ile Thr Asn Gln			
405	410	415	
Glu Leu Lys Met Met Gln Asp Asp Leu Asn Phe Lys Ser Thr Glu Val			
420	425	430	
Gln Lys Ser Gln Ser Thr Ala Gln Asn Leu Thr Ser Asp Ile Gln Arg			
435	440	445	
Leu Gln Leu Asp Leu Gln Lys Met Glu Leu Leu Glu Ser Lys Met Thr			
450	455	460	
Glu Glu Gln His Ser Leu Lys Ser Lys Ile Lys Gln Met Thr Thr Asp			
465	470	475	480
Leu Glu Ile Tyr Asn Asp Leu Pro Ala Leu Lys Ser Ser Gly Glu Glu			
485	490	495	
Lys Ile Lys Lys Leu His Gln Glu Arg Met Ile Leu Ser Thr His Arg			
500	505	510	
Asn Ala Phe Lys Lys Ile Met Glu Lys Gln Asn Ile Glu Tyr Glu Ala			
515	520	525	
Leu Lys Thr Gln Leu Gln Glu Asn Glu Thr His Ser Gln Leu Thr Asn			
530	535	540	
Leu Glu Arg Lys Trp Gln His Leu Glu Gln Asn Asn Phe Ala Met Lys			
545	550	555	560
Glu Phe Ile Ala Thr Lys Ser Gln Glu Ser Asp Tyr Gln Pro Ile Lys			
565	570	575	
Lys Asn Val Thr Lys Gln Ile Ala Glu Tyr Asn Lys Thr Ile Val Asp			
580	585	590	
Ala Leu His Ser Thr Ser Gly Asn			
595	600		
<210> 95			
<211> 195			
<212> PRT			
<213> 智人			
<400> 95			
Met Gly Lys Ile Ser Ser Leu Pro Thr Gln Leu Phe Lys Cys Cys Phe			
1	5	10	15

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

<210> 96

<211> 340

<212> PRT

<213> 智人

<400> 96

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

$\langle 210 \rangle$	97
$\langle 211 \rangle$	551
$\langle 212 \rangle$	PRT
$\langle 213 \rangle$	智人
$\langle 400 \rangle$	97

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

305	310	315	320
Glu Ile Ser Pro Leu Glu Val Leu Glu Arg Asp Lys Val Thr Gln Leu			
	325	330	335
Leu Leu Gln Gln Asp Lys Val Pro Glu Pro Ala Ser Leu Ser Ser Asn			
	340	345	350
His Ser Leu Thr Ser Cys Phe Thr Asn Gln Gly Tyr Phe Phe Phe His			
	355	360	365
Leu Pro Asp Ala Leu Glu Ile Glu Ala Cys Gln Val Tyr Phe Thr Tyr			
	370	375	380
Asp Pro Tyr Ser Glu Glu Asp Pro Asp Glu Gly Val Ala Gly Ala Pro			
385	390	395	400
Thr Gly Ser Ser Pro Gln Pro Leu Gln Pro Leu Ser Gly Glu Asp Asp			
	405	410	415
Ala Tyr Cys Thr Phe Pro Ser Arg Asp Asp Leu Leu Leu Phe Ser Pro			
	420	425	430
Ser Leu Leu Gly Gly Pro Ser Pro Pro Ser Thr Ala Pro Gly Gly Ser			
	435	440	445
Gly Ala Gly Glu Glu Arg Met Pro Pro Ser Leu Gln Glu Arg Val Pro			
	450	455	460
Arg Asp Trp Asp Pro Gln Pro Leu Gly Pro Pro Thr Pro Gly Val Pro			
465	470	475	480
Asp Leu Val Asp Phe Gln Pro Pro Pro Glu Leu Val Leu Arg Glu Ala			
	485	490	495
Gly Glu Glu Val Pro Asp Ala Gly Pro Arg Glu Gly Val Ser Phe Pro			
	500	505	510
Trp Ser Arg Pro Pro Gly Gln Gly Glu Phe Arg Ala Leu Asn Ala Arg			
	515	520	525
Leu Pro Leu Asn Thr Asp Ala Tyr Leu Ser Leu Gln Glu Leu Gln Gly			
	530	535	540
Gln Asp Pro Thr His Leu Val			
545	550		
<210> 98			
<211> 99			
<212> PRT			
<213> 智人			
<400> 98			
Met Thr Ser Lys Leu Ala Val Ala Leu Leu Ala Ala Phe Leu Ile Ser			
1	5	10	15
Ala Ala Leu Cys Glu Gly Ala Val Leu Pro Arg Ser Ala Lys Glu Leu			

20																25								30							
Arg	Cys	Gln	Cys	Ile	Lys	Thr	Tyr	Ser	Lys	Pro	Phe	His	Pro	Lys	Phe																
35								40								45															
Ile	Lys	Glu	Leu	Arg	Val	Ile	Glu	Ser	Gly	Pro	His	Cys	Ala	Asn	Thr																
50								55								60															
Glu	Ile	Ile	Val	Lys	Leu	Ser	Asp	Gly	Arg	Glu	Leu	Cys	Leu	Asp	Pro																
65								70								75								80							
Lys	Glu	Asn	Trp	Val	Gln	Arg	Val	Val	Glu	Lys	Phe	Leu	Lys	Arg	Ala																
85								90								95															
Glu Asn Ser																															
<210> 99																															
<211> 144																															
<212> PRT																															
<213> 智人																															
<400> 99																															
Met	Leu	Leu	Ala	Met	Val	Leu	Thr	Ser	Ala	Leu	Leu	Leu	Cys	Ser	Val																
1				5				10								15															
Ala	Gly	Gln	Gly	Cys	Pro	Thr	Leu	Ala	Gly	Ile	Leu	Asp	Ile	Asn	Phe																
20								25								30															
Leu	Ile	Asn	Lys	Met	Gln	Glu	Asp	Pro	Ala	Ser	Lys	Cys	His	Cys	Ser																
35								40								45															
Ala	Asn	Val	Thr	Ser	Cys	Leu	Cys	Leu	Gly	Ile	Pro	Ser	Asp	Asn	Cys																
50								55								60															
Thr	Arg	Pro	Cys	Phe	Ser	Glu	Arg	Leu	Ser	Gln	Met	Thr	Asn	Thr	Thr																
65								70								75								80							
Met	Gln	Thr	Arg	Tyr	Pro	Leu	Ile	Phe	Ser	Arg	Val	Lys	Lys	Ser	Val																
85								90								95															
Glu	Val	Leu	Lys	Asn	Asn	Lys	Cys	Pro	Tyr	Phe	Ser	Cys	Glu	Gln	Pro																
100								105								110															
Cys	Asn	Gln	Thr	Thr	Ala	Gly	Asn	Ala	Leu	Thr	Phe	Leu	Lys	Ser	Leu																
115								120								125															
Leu	Glu	Ile	Phe	Gln	Lys	Glu	Lys	Met	Arg	Gly	Met	Arg	Gly	Lys	Ile																
130								135								140															
<210> 100																															
<211> 189																															
<212> PRT																															
<213> 智人																															
<400> 100																															
Met	Thr	Glu	Tyr	Lys	Leu	Val	Val	Val	Gly	Ala	Gly	Gly	Val	Gly	Lys																

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

<210> 101

<211> 400

<212> PRT

<213> 智人

<400> 101

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

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

<210> 102

<211> 483

<212> PRT

<213> 智人

<400> 102

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

Arg Ser Arg Ala Glu Ala Glu Ser Met Tyr Gln Ile Lys Tyr Glu Glu			
275	280	285	
Leu Gln Ser Leu Ala Gly Lys His Gly Asp Asp Leu Arg Arg Thr Lys			
290	295	300	
Thr Glu Ile Ser Glu Met Asn Arg Asn Ile Ser Arg Leu Gln Ala Glu			
305	310	315	320
Ile Glu Gly Leu Lys Gly Gln Arg Ala Ser Leu Glu Ala Ala Ile Ala			
	325	330	335
Asp Ala Glu Gln Arg Gly Glu Leu Ala Ile Lys Asp Ala Asn Ala Lys			
	340	345	350
Leu Ser Glu Leu Glu Ala Ala Leu Gln Arg Ala Lys Gln Asp Met Ala			
	355	360	365
Arg Gln Leu Arg Glu Tyr Gln Glu Leu Met Asn Val Lys Leu Ala Leu			
370	375	380	
Asp Ile Glu Ile Ala Thr Tyr Arg Lys Leu Leu Glu Gly Glu Glu Ser			
385	390	395	400
Arg Leu Glu Ser Gly Met Gln Asn Met Ser Ile His Thr Lys Thr Thr			
	405	410	415
Ser Gly Tyr Ala Gly Gly Leu Ser Ser Ala Tyr Gly Gly Leu Thr Ser			
	420	425	430
Pro Gly Leu Ser Tyr Ser Leu Gly Ser Ser Phe Gly Ser Gly Ala Gly			
	435	440	445
Ser Ser Ser Phe Ser Arg Thr Ser Ser Ser Arg Ala Val Val Val Lys			
	450	455	460
Lys Ile Glu Thr Arg Asp Gly Lys Leu Val Ser Glu Ser Ser Asp Val			
465	470	475	480
Leu Pro Lys			
<210> 103			
<211> 3122			
<212> PRT			
<213> 智人			
<400> 103			
Met Pro Gly Ala Ala Gly Val Leu Leu Leu Leu Leu Ser Gly Gly			
1	5	10	15
Leu Gly Gly Val Gln Ala Gln Arg Pro Gln Gln Gln Arg Gln Ser Gln			
	20	25	30
Ala His Gln Gln Arg Gly Leu Phe Pro Ala Val Leu Asn Leu Ala Ser			
	35	40	45
Asn Ala Leu Ile Thr Thr Asn Ala Thr Cys Gly Glu Lys Gly Pro Glu			

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

Arg Gly Lys Tyr Ile Gly Gly Gly Val Cys Ile Asn Cys Thr Gln Asn		
370	375	380
Thr Ala Gly Ile Asn Cys Glu Thr Cys Thr Asp Gly Phe Phe Arg Pro		
385	390	395 400
Lys Gly Val Ser Pro Asn Tyr Pro Arg Pro Cys Gln Pro Cys His Cys		
	405	410 415
Asp Pro Ile Gly Ser Leu Asn Glu Val Cys Val Lys Asp Glu Lys His		
	420	425 430
Ala Arg Arg Gly Leu Ala Pro Gly Ser Cys His Cys Lys Thr Gly Phe		
	435	440 445
Gly Gly Val Ser Cys Asp Arg Cys Ala Arg Gly Tyr Thr Gly Tyr Pro		
	450	455 460
Asp Cys Lys Ala Cys Asn Cys Ser Gly Leu Gly Ser Lys Asn Glu Asp		
465	470	475 480
Pro Cys Phe Gly Pro Cys Ile Cys Lys Glu Asn Val Glu Gly Gly Asp		
	485	490 495
Cys Ser Arg Cys Lys Ser Gly Phe Phe Asn Leu Gln Glu Asp Asn Trp		
	500	505 510
Lys Gly Cys Asp Glu Cys Phe Cys Ser Gly Val Ser Asn Arg Cys Gln		
	515	520 525
Ser Ser Tyr Trp Thr Tyr Gly Lys Ile Gln Asp Met Ser Gly Trp Tyr		
	530	535 540
Leu Thr Asp Leu Pro Gly Arg Ile Arg Val Ala Pro Gln Gln Asp Asp		
545	550	555 560
Leu Asp Ser Pro Gln Gln Ile Ser Ile Ser Asn Ala Glu Ala Arg Gln		
	565	570 575
Ala Leu Pro His Ser Tyr Tyr Trp Ser Ala Pro Ala Pro Tyr Leu Gly		
	580	585 590
Asn Lys Leu Pro Ala Val Gly Gly Gln Leu Thr Phe Thr Ile Ser Tyr		
	595	600 605
Asp Leu Glu Glu Glu Glu Glu Asp Thr Glu Arg Val Leu Gln Leu Met		
	610	615 620
Ile Ile Leu Glu Gly Asn Asp Leu Ser Ile Ser Thr Ala Gln Asp Glu		
625	630	635 640
Val Tyr Leu His Pro Ser Glu Glu His Thr Asn Val Leu Leu Leu Lys		
	645	650 655
Glu Glu Ser Phe Thr Ile His Gly Thr His Phe Pro Val Arg Arg Lys		
	660	665 670
Glu Phe Met Thr Val Leu Ala Asn Leu Lys Arg Val Leu Leu Gln Ile		

675	680	685
Thr Tyr Ser Phe Gly Met Asp	Ala Ile Phe Arg Leu Ser Ser Val Asn	
690	695	700
Leu Glu Ser Ala Val Ser Tyr Pro Thr Asp Gly Ser Ile Ala Ala Ala		
705	710	715
Val Glu Val Cys Gln Cys Pro Pro Gly Tyr Thr Gly Ser Ser Cys Glu		
725	730	735
Ser Cys Trp Pro Arg His Arg Arg Val Asn Gly Thr Ile Phe Gly Gly		
740	745	750
Ile Cys Glu Pro Cys Gln Cys Phe Gly His Ala Glu Ser Cys Asp Asp		
755	760	765
Val Thr Gly Glu Cys Leu Asn Cys Lys Asp His Thr Gly Gly Pro Tyr		
770	775	780
Cys Asp Lys Cys Leu Pro Gly Phe Tyr Gly Glu Pro Thr Lys Gly Thr		
785	790	795
Ser Glu Asp Cys Gln Pro Cys Ala Cys Pro Leu Asn Ile Pro Ser Asn		
805	810	815
Asn Phe Ser Pro Thr Cys His Leu Asp Arg Ser Leu Gly Leu Ile Cys		
820	825	830
Asp Gly Cys Pro Val Gly Tyr Thr Gly Pro Arg Cys Glu Arg Cys Ala		
835	840	845
Glu Gly Tyr Phe Gly Gln Pro Ser Val Pro Gly Gly Ser Cys Gln Pro		
850	855	860
Cys Gln Cys Asn Asp Asn Leu Asp Phe Ser Ile Pro Gly Ser Cys Asp		
865	870	875
Ser Leu Ser Gly Ser Cys Leu Ile Cys Lys Pro Gly Thr Thr Gly Arg		
885	890	895
Tyr Cys Glu Leu Cys Ala Asp Gly Tyr Phe Gly Asp Ala Val Asp Ala		
900	905	910
Lys Asn Cys Gln Pro Cys Arg Cys Asn Ala Gly Gly Ser Phe Ser Glu		
915	920	925
Val Cys His Ser Gln Thr Gly Gln Cys Glu Cys Arg Ala Asn Val Gln		
930	935	940
Gly Gln Arg Cys Asp Lys Cys Lys Ala Gly Thr Phe Gly Leu Gln Ser		
945	950	955
Ala Arg Gly Cys Val Pro Cys Asn Cys Asn Ser Phe Gly Ser Lys Ser		
965	970	975
Phe Asp Cys Glu Glu Ser Gly Gln Cys Trp Cys Gln Pro Gly Val Thr		
980	985	990

Gly Lys Lys Cys Asp Arg Cys Ala His Gly Tyr Phe Asn Phe Gln Glu		
995	1000	1005
Gly Gly Cys Thr Ala Cys Glu Cys Ser His Leu Gly Asn Asn Cys		
1010	1015	1020
Asp Pro Lys Thr Gly Arg Cys Ile Cys Pro Pro Asn Thr Ile Gly		
1025	1030	1035
Glu Lys Cys Ser Lys Cys Ala Pro Asn Thr Trp Gly His Ser Ile		
1040	1045	1050
Thr Thr Gly Cys Lys Ala Cys Asn Cys Ser Thr Val Gly Ser Leu		
1055	1060	1065
Asp Phe Gln Cys Asn Val Asn Thr Gly Gln Cys Asn Cys His Pro		
1070	1075	1080
Lys Phe Ser Gly Ala Lys Cys Thr Glu Cys Ser Arg Gly His Trp		
1085	1090	1095
Asn Tyr Pro Arg Cys Asn Leu Cys Asp Cys Phe Leu Pro Gly Thr		
1100	1105	1110
Asp Ala Thr Thr Cys Asp Ser Glu Thr Lys Lys Cys Ser Cys Ser		
1115	1120	1125
Asp Gln Thr Gly Gln Cys Thr Cys Lys Val Asn Val Glu Gly Ile		
1130	1135	1140
His Cys Asp Arg Cys Arg Pro Gly Lys Phe Gly Leu Asp Ala Lys		
1145	1150	1155
Asn Pro Leu Gly Cys Ser Ser Cys Tyr Cys Phe Gly Thr Thr Thr		
1160	1165	1170
Gln Cys Ser Glu Ala Lys Gly Leu Ile Arg Thr Trp Val Thr Leu		
1175	1180	1185
Lys Ala Glu Gln Thr Ile Leu Pro Leu Val Asp Glu Ala Leu Gln		
1190	1195	1200
His Thr Thr Thr Lys Gly Ile Val Phe Gln His Pro Glu Ile Val		
1205	1210	1215
Ala His Met Asp Leu Met Arg Glu Asp Leu His Leu Glu Pro Phe		
1220	1225	1230
Tyr Trp Lys Leu Pro Glu Gln Phe Glu Gly Lys Lys Leu Met Ala		
1235	1240	1245
Tyr Gly Gly Lys Leu Lys Tyr Ala Ile Tyr Phe Glu Ala Arg Glu		
1250	1255	1260
Glu Thr Gly Phe Ser Thr Tyr Asn Pro Gln Val Ile Ile Arg Gly		
1265	1270	1275
Gly Thr Pro Thr His Ala Arg Ile Ile Val Arg His Met Ala Ala		

1280	1285	1290
Pro Leu Ile Gly Gln Leu Thr Arg His Glu Ile Glu Met Thr Glu		
1295	1300	1305
Lys Glu Trp Lys Tyr Tyr Gly Asp Asp Pro Arg Val His Arg Thr		
1310	1315	1320
Val Thr Arg Glu Asp Phe Leu Asp Ile Leu Tyr Asp Ile His Tyr		
1325	1330	1335
Ile Leu Ile Lys Ala Thr Tyr Gly Asn Phe Met Arg Gln Ser Arg		
1340	1345	1350
Ile Ser Glu Ile Ser Met Glu Val Ala Glu Gln Gly Arg Gly Thr		
1355	1360	1365
Thr Met Thr Pro Pro Ala Asp Leu Ile Glu Lys Cys Asp Cys Pro		
1370	1375	1380
Leu Gly Tyr Ser Gly Leu Ser Cys Glu Ala Cys Leu Pro Gly Phe		
1385	1390	1395
Tyr Arg Leu Arg Ser Gln Pro Gly Gly Arg Thr Pro Gly Pro Thr		
1400	1405	1410
Leu Gly Thr Cys Val Pro Cys Gln Cys Asn Gly His Ser Ser Leu		
1415	1420	1425
Cys Asp Pro Glu Thr Ser Ile Cys Gln Asn Cys Gln His His Thr		
1430	1435	1440
Ala Gly Asp Phe Cys Glu Arg Cys Ala Leu Gly Tyr Tyr Gly Ile		
1445	1450	1455
Val Lys Gly Leu Pro Asn Asp Cys Gln Gln Cys Ala Cys Pro Leu		
1460	1465	1470
Ile Ser Ser Ser Asn Asn Phe Ser Pro Ser Cys Val Ala Glu Gly		
1475	1480	1485
Leu Asp Asp Tyr Arg Cys Thr Ala Cys Pro Arg Gly Tyr Glu Gly		
1490	1495	1500
Gln Tyr Cys Glu Arg Cys Ala Pro Gly Tyr Thr Gly Ser Pro Gly		
1505	1510	1515
Asn Pro Gly Gly Ser Cys Gln Glu Cys Glu Cys Asp Pro Tyr Gly		
1520	1525	1530
Ser Leu Pro Val Pro Cys Asp Pro Val Thr Gly Phe Cys Thr Cys		
1535	1540	1545
Arg Pro Gly Ala Thr Gly Arg Lys Cys Asp Gly Cys Lys His Trp		
1550	1555	1560
His Ala Arg Glu Gly Trp Glu Cys Val Phe Cys Gly Asp Glu Cys		
1565	1570	1575

Thr Gly Leu Leu Leu Gly Asp Leu Ala Arg Leu Glu Gln Met Val		
1580	1585	1590
Met Ser Ile Asn Leu Thr Gly Pro Leu Pro Ala Pro Tyr Lys Met		
1595	1600	1605
Leu Tyr Gly Leu Glu Asn Met Thr Gln Glu Leu Lys His Leu Leu		
1610	1615	1620
Ser Pro Gln Arg Ala Pro Glu Arg Leu Ile Gln Leu Ala Glu Gly		
1625	1630	1635
Asn Leu Asn Thr Leu Val Thr Glu Met Asn Glu Leu Leu Thr Arg		
1640	1645	1650
Ala Thr Lys Val Thr Ala Asp Gly Glu Gln Thr Gly Gln Asp Ala		
1655	1660	1665
Glu Arg Thr Asn Thr Arg Ala Lys Ser Leu Gly Glu Phe Ile Lys		
1670	1675	1680
Glu Leu Ala Arg Asp Ala Glu Ala Val Asn Glu Lys Ala Ile Lys		
1685	1690	1695
Leu Asn Glu Thr Leu Gly Thr Arg Asp Glu Ala Phe Glu Arg Asn		
1700	1705	1710
Leu Glu Gly Leu Gln Lys Glu Ile Asp Gln Met Ile Lys Glu Leu		
1715	1720	1725
Arg Arg Lys Asn Leu Glu Thr Gln Lys Glu Ile Ala Glu Asp Glu		
1730	1735	1740
Leu Val Ala Ala Glu Ala Leu Leu Lys Lys Val Lys Lys Leu Phe		
1745	1750	1755
Gly Glu Ser Arg Gly Glu Asn Glu Glu Met Glu Lys Asp Leu Arg		
1760	1765	1770
Glu Lys Leu Ala Asp Tyr Lys Asn Lys Val Asp Asp Ala Trp Asp		
1775	1780	1785
Leu Leu Arg Glu Ala Thr Asp Lys Ile Arg Glu Ala Asn Arg Leu		
1790	1795	1800
Phe Ala Val Asn Gln Lys Asn Met Thr Ala Leu Glu Lys Lys Lys		
1805	1810	1815
Glu Ala Val Glu Ser Gly Lys Arg Gln Ile Glu Asn Thr Leu Lys		
1820	1825	1830
Glu Gly Asn Asp Ile Leu Asp Glu Ala Asn Arg Leu Ala Asp Glu		
1835	1840	1845
Ile Asn Ser Ile Ile Asp Tyr Val Glu Asp Ile Gln Thr Lys Leu		
1850	1855	1860
Pro Pro Met Ser Glu Glu Leu Asn Asp Lys Ile Asp Asp Leu Ser		

1865	1870	1875
Gln Glu Ile Lys Asp Arg	Lys Leu Ala Glu Lys	Val Ser Gln Ala
1880	1885	1890
Glu Ser His Ala Ala Gln	Leu Asn Asp Ser Ser	Ala Val Leu Asp
1895	1900	1905
Gly Ile Leu Asp Glu Ala	Lys Asn Ile Ser Phe	Asn Ala Thr Ala
1910	1915	1920
Ala Phe Lys Ala Tyr Ser	Asn Ile Lys Asp Tyr	Ile Asp Glu Ala
1925	1930	1935
Glu Lys Val Ala Lys Glu	Ala Lys Asp Leu Ala	His Glu Ala Thr
1940	1945	1950
Lys Leu Ala Thr Gly Pro	Arg Gly Leu Leu Lys	Glu Asp Ala Lys
1955	1960	1965
Gly Cys Leu Gln Lys Ser	Phe Arg Ile Leu Asn	Glu Ala Lys Lys
1970	1975	1980
Leu Ala Asn Asp Val Lys	Glu Asn Glu Asp His	Leu Asn Gly Leu
1985	1990	1995
Lys Thr Arg Ile Glu Asn	Ala Asp Ala Arg Asn	Gly Asp Leu Leu
2000	2005	2010
Arg Thr Leu Asn Asp Thr	Leu Gly Lys Leu Ser	Ala Ile Pro Asn
2015	2020	2025
Asp Thr Ala Ala Lys Leu	Gln Ala Val Lys Asp	Lys Ala Arg Gln
2030	2035	2040
Ala Asn Asp Thr Ala Lys	Asp Val Leu Ala Gln	Ile Thr Glu Leu
2045	2050	2055
His Gln Asn Leu Asp Gly	Leu Lys Lys Asn Tyr	Asn Lys Leu Ala
2060	2065	2070
Asp Ser Val Ala Lys Thr	Asn Ala Val Val Lys	Asp Pro Ser Lys
2075	2080	2085
Asn Lys Ile Ile Ala Asp	Ala Asp Ala Thr Val	Lys Asn Leu Glu
2090	2095	2100
Gln Glu Ala Asp Arg Leu	Ile Asp Lys Leu Lys	Pro Ile Lys Glu
2105	2110	2115
Leu Glu Asp Asn Leu Lys	Lys Asn Ile Ser Glu	Ile Lys Glu Leu
2120	2125	2130
Ile Asn Gln Ala Arg Lys	Gln Ala Asn Ser Ile	Lys Val Ser Val
2135	2140	2145
Ser Ser Gly Gly Asp Cys	Ile Arg Thr Tyr Lys	Pro Glu Ile Lys
2150	2155	2160

Lys Gly Ser Tyr Asn Asn Ile Val Val Asn Val Lys Thr Ala Val		
2165	2170	2175
Ala Asp Asn Leu Leu Phe Tyr Leu Gly Ser Ala Lys Phe Ile Asp		
2180	2185	2190
Phe Leu Ala Ile Glu Met Arg Lys Gly Lys Val Ser Phe Leu Trp		
2195	2200	2205
Asp Val Gly Ser Gly Val Gly Arg Val Glu Tyr Pro Asp Leu Thr		
2210	2215	2220
Ile Asp Asp Ser Tyr Trp Tyr Arg Ile Val Ala Ser Arg Thr Gly		
2225	2230	2235
Arg Asn Gly Thr Ile Ser Val Arg Ala Leu Asp Gly Pro Lys Ala		
2240	2245	2250
Ser Ile Val Pro Ser Thr His His Ser Thr Ser Pro Pro Gly Tyr		
2255	2260	2265
Thr Ile Leu Asp Val Asp Ala Asn Ala Met Leu Phe Val Gly Gly		
2270	2275	2280
Leu Thr Gly Lys Leu Lys Lys Ala Asp Ala Val Arg Val Ile Thr		
2285	2290	2295
Phe Thr Gly Cys Met Gly Glu Thr Tyr Phe Asp Asn Lys Pro Ile		
2300	2305	2310
Gly Leu Trp Asn Phe Arg Glu Lys Glu Gly Asp Cys Lys Gly Cys		
2315	2320	2325
Thr Val Ser Pro Gln Val Glu Asp Ser Glu Gly Thr Ile Gln Phe		
2330	2335	2340
Asp Gly Glu Gly Tyr Ala Leu Val Ser Arg Pro Ile Arg Trp Tyr		
2345	2350	2355
Pro Asn Ile Ser Thr Val Met Phe Lys Phe Arg Thr Phe Ser Ser		
2360	2365	2370
Ser Ala Leu Leu Met Tyr Leu Ala Thr Arg Asp Leu Arg Asp Phe		
2375	2380	2385
Met Ser Val Glu Leu Thr Asp Gly His Ile Lys Val Ser Tyr Asp		
2390	2395	2400
Leu Gly Ser Gly Met Ala Ser Val Val Ser Asn Gln Asn His Asn		
2405	2410	2415
Asp Gly Lys Trp Lys Ser Phe Thr Leu Ser Arg Ile Gln Lys Gln		
2420	2425	2430
Ala Asn Ile Ser Ile Val Asp Ile Asp Thr Asn Gln Glu Glu Asn		
2435	2440	2445
Ile Ala Thr Ser Ser Ser Gly Asn Asn Phe Gly Leu Asp Leu Lys		

2450	2455	2460
Ala Asp Asp Lys Ile Tyr Phe Gly Gly Leu Pro Thr Leu Arg Asn		
2465	2470	2475
Leu Ser Met Lys Ala Arg Pro Glu Val Asn Leu Lys Lys Tyr Ser		
2480	2485	2490
Gly Cys Leu Lys Asp Ile Glu Ile Ser Arg Thr Pro Tyr Asn Ile		
2495	2500	2505
Leu Ser Ser Pro Asp Tyr Val Gly Val Thr Lys Gly Cys Ser Leu		
2510	2515	2520
Glu Asn Val Tyr Thr Val Ser Phe Pro Lys Pro Gly Phe Val Glu		
2525	2530	2535
Leu Ser Pro Val Pro Ile Asp Val Gly Thr Glu Ile Asn Leu Ser		
2540	2545	2550
Phe Ser Thr Lys Asn Glu Ser Gly Ile Ile Leu Leu Gly Ser Gly		
2555	2560	2565
Gly Thr Pro Ala Pro Pro Arg Arg Lys Arg Arg Gln Thr Gly Gln		
2570	2575	2580
Ala Tyr Tyr Ala Ile Leu Leu Asn Arg Gly Arg Leu Glu Val His		
2585	2590	2595
Leu Ser Thr Gly Ala Arg Thr Met Arg Lys Ile Val Ile Arg Pro		
2600	2605	2610
Glu Pro Asn Leu Phe His Asp Gly Arg Glu His Ser Val His Val		
2615	2620	2625
Glu Arg Thr Arg Gly Ile Phe Thr Val Gln Val Asp Glu Asn Arg		
2630	2635	2640
Arg Tyr Met Gln Asn Leu Thr Val Glu Gln Pro Ile Glu Val Lys		
2645	2650	2655
Lys Leu Phe Val Gly Gly Ala Pro Pro Glu Phe Gln Pro Ser Pro		
2660	2665	2670
Leu Arg Asn Ile Pro Pro Phe Glu Gly Cys Ile Trp Asn Leu Val		
2675	2680	2685
Ile Asn Ser Val Pro Met Asp Phe Ala Arg Pro Val Ser Phe Lys		
2690	2695	2700
Asn Ala Asp Ile Gly Arg Cys Ala His Gln Lys Leu Arg Glu Asp		
2705	2710	2715
Glu Asp Gly Ala Ala Pro Ala Glu Ile Val Ile Gln Pro Glu Pro		
2720	2725	2730
Val Pro Thr Pro Ala Phe Pro Thr Pro Thr Pro Val Leu Thr His		
2735	2740	2745

Gly Pro Cys Ala Ala Glu Ser Glu Pro Ala Leu Leu Ile Gly Ser		
2750	2755	2760
Lys Gln Phe Gly Leu Ser Arg Asn Ser His Ile Ala Ile Ala Phe		
2765	2770	2775
Asp Asp Thr Lys Val Lys Asn Arg Leu Thr Ile Glu Leu Glu Val		
2780	2785	2790
Arg Thr Glu Ala Glu Ser Gly Leu Leu Phe Tyr Met Ala Arg Ile		
2795	2800	2805
Asn His Ala Asp Phe Ala Thr Val Gln Leu Arg Asn Gly Leu Pro		
2810	2815	2820
Tyr Phe Ser Tyr Asp Leu Gly Ser Gly Asp Thr His Thr Met Ile		
2825	2830	2835
Pro Thr Lys Ile Asn Asp Gly Gln Trp His Lys Ile Lys Ile Met		
2840	2845	2850
Arg Ser Lys Gln Glu Gly Ile Leu Tyr Val Asp Gly Ala Ser Asn		
2855	2860	2865
Arg Thr Ile Ser Pro Lys Lys Ala Asp Ile Leu Asp Val Val Gly		
2870	2875	2880
Met Leu Tyr Val Gly Gly Leu Pro Ile Asn Tyr Thr Thr Arg Arg		
2885	2890	2895
Ile Gly Pro Val Thr Tyr Ser Ile Asp Gly Cys Val Arg Asn Leu		
2900	2905	2910
His Met Ala Glu Ala Pro Ala Asp Leu Glu Gln Pro Thr Ser Ser		
2915	2920	2925
Phe His Val Gly Thr Cys Phe Ala Asn Ala Gln Arg Gly Thr Tyr		
2930	2935	2940
Phe Asp Gly Thr Gly Phe Ala Lys Ala Val Gly Gly Phe Lys Val		
2945	2950	2955
Gly Leu Asp Leu Leu Val Glu Phe Glu Phe Arg Thr Thr Thr Thr		
2960	2965	2970
Thr Gly Val Leu Leu Gly Ile Ser Ser Gln Lys Met Asp Gly Met		
2975	2980	2985
Gly Ile Glu Met Ile Asp Glu Lys Leu Met Phe His Val Asp Asn		
2990	2995	3000
Gly Ala Gly Arg Phe Thr Ala Val Tyr Asp Ala Gly Val Pro Gly		
3005	3010	3015
His Leu Cys Asp Gly Gln Trp His Lys Val Thr Ala Asn Lys Ile		
3020	3025	3030
Lys His Arg Ile Glu Leu Thr Val Asp Gly Asn Gln Val Glu Ala		

3035	3040	3045
Gln Ser Pro Asn Pro Ala	Ser Thr Ser Ala Asp	Thr Asn Asp Pro
3050	3055	3060
Val Phe Val Gly Gly Phe	Pro Asp Asp Leu Lys	Gln Phe Gly Leu
3065	3070	3075
Thr Thr Ser Ile Pro Phe	Arg Gly Cys Ile Arg	Ser Leu Lys Leu
3080	3085	3090
Thr Lys Gly Thr Gly Lys	Pro Leu Glu Val Asn	Phe Ala Lys Ala
3095	3100	3105
Leu Glu Leu Arg Gly Val	Gln Pro Val Ser Cys	Pro Ala Asn
3110	3115	3120
<210> 104		
<211> 250		
<212> PRT		
<213> 智人		
<400> 104		
Met Ala Asp Asn Phe Ser Leu His	Asp Ala Leu Ser Gly Ser Gly Asn	
1	5	10
Pro Asn Pro Gln Gly Trp Pro Gly	Ala Trp Gly Asn Gln Pro Ala Gly	
20	25	30
Ala Gly Gly Tyr Pro Gly Ala Ser	Tyr Pro Gly Ala Tyr Pro Gly Gln	
35	40	45
Ala Pro Pro Gly Ala Tyr Pro Gly	Gln Ala Pro Pro Gly Ala Tyr Pro	
50	55	60
Gly Ala Pro Gly Ala Tyr Pro Gly	Ala Pro Ala Pro Gly Val Tyr Pro	
65	70	75
Gly Pro Pro Ser Gly Pro Gly Ala	Tyr Pro Ser Ser Gly Gln Pro Ser	
85	90	95
Ala Thr Gly Ala Tyr Pro Ala Thr	Gly Pro Tyr Gly Ala Pro Ala Gly	
100	105	110
Pro Leu Ile Val Pro Tyr Asn Leu	Pro Leu Pro Gly Gly Val Val Pro	
115	120	125
Arg Met Leu Ile Thr Ile Leu Gly	Thr Val Lys Pro Asn Ala Asn Arg	
130	135	140
Ile Ala Leu Asp Phe Gln Arg Gly	Asn Asp Val Ala Phe His Phe Asn	
145	150	155
Pro Arg Phe Asn Glu Asn Asn Arg	Arg Val Ile Val Cys Asn Thr Lys	
165	170	175
Leu Asp Asn Asn Trp Gly Arg Glu	Glu Arg Gln Ser Val Phe Pro Phe	

	180		185		190
Glu Ser Gly Lys Pro Phe Lys Ile Gln Val Leu Val Glu Pro Asp His					
195		200		205	
Phe Lys Val Ala Val Asn Asp Ala His Leu Leu Gln Tyr Asn His Arg					
210		215		220	
Val Lys Lys Leu Asn Glu Ile Ser Lys Leu Gly Ile Ser Gly Asp Ile					
225		230		235	240
Asp Leu Thr Ser Ala Ser Tyr Thr Met Ile					
	245		250		
<210> 105					
<211> 586					
<212> PRT					
<213> 智人					
<400> 105					
Met Ala Thr Ala Thr Pro Val Pro Pro Arg Met Gly Ser Arg Ala Gly					
1	5		10		15
Gly Pro Thr Thr Pro Leu Ser Pro Thr Arg Leu Ser Arg Leu Gln Glu					
	20		25		30
Lys Glu Glu Leu Arg Glu Leu Asn Asp Arg Leu Ala Val Tyr Ile Asp					
	35		40		45
Lys Val Arg Ser Leu Glu Thr Glu Asn Ser Ala Leu Gln Leu Gln Val					
	50		55		60
Thr Glu Arg Glu Glu Val Arg Gly Arg Glu Leu Thr Gly Leu Lys Ala					
65		70		75	80
Leu Tyr Glu Thr Glu Leu Ala Asp Ala Arg Arg Ala Leu Asp Asp Thr					
	85		90		95
Ala Arg Glu Arg Ala Lys Leu Gln Ile Glu Leu Gly Lys Cys Lys Ala					
	100		105		110
Glu His Asp Gln Leu Leu Leu Asn Tyr Ala Lys Lys Glu Ser Asp Leu					
	115		120		125
Asn Gly Ala Gln Ile Lys Leu Arg Glu Tyr Glu Ala Ala Leu Asn Ser					
	130		135		140
Lys Asp Ala Ala Leu Ala Thr Ala Leu Gly Asp Lys Lys Ser Leu Glu					
145		150		155	160
Gly Asp Leu Glu Asp Leu Lys Asp Gln Ile Ala Gln Leu Glu Ala Ser					
	165		170		175
Leu Ala Ala Ala Lys Lys Gln Leu Ala Asp Glu Thr Leu Leu Lys Val					
	180		185		190
Asp Leu Glu Asn Arg Cys Gln Ser Leu Thr Glu Asp Leu Glu Phe Arg					

195	200	205
Lys Ser Met Tyr Glu Glu Glu Ile Asn Glu Thr Arg Arg Lys His Glu		
210	215	220
Thr Arg Leu Val Glu Val Asp Ser Gly Arg Gln Ile Glu Tyr Glu Tyr		
225	230	235
Lys Leu Ala Gln Ala Leu His Glu Met Arg Glu Gln His Asp Ala Gln		240
245	250	255
Val Arg Leu Tyr Lys Glu Glu Leu Glu Gln Thr Tyr His Ala Lys Leu		
260	265	270
Glu Asn Ala Arg Leu Ser Ser Glu Met Asn Thr Ser Thr Val Asn Ser		
275	280	285
Ala Arg Glu Glu Leu Met Glu Ser Arg Met Arg Ile Glu Ser Leu Ser		
290	295	300
Ser Gln Leu Ser Asn Leu Gln Lys Glu Ser Arg Ala Cys Leu Glu Arg		
305	310	315
Ile Gln Glu Leu Glu Asp Leu Leu Ala Lys Glu Lys Asp Asn Ser Arg		
325	330	335
Arg Met Leu Thr Asp Lys Glu Arg Glu Met Ala Glu Ile Arg Asp Gln		
340	345	350
Met Gln Gln Gln Leu Asn Asp Tyr Glu Gln Leu Leu Asp Val Lys Leu		
355	360	365
Ala Leu Asp Met Glu Ile Ser Ala Tyr Arg Lys Leu Leu Glu Gly Glu		
370	375	380
Glu Glu Arg Leu Lys Leu Ser Pro Ser Pro Ser Ser Arg Val Thr Val		
385	390	395
Ser Arg Ala Ser Ser Ser Arg Ser Val Arg Thr Thr Arg Gly Lys Arg		
405	410	415
Lys Arg Val Asp Val Glu Glu Ser Glu Ala Ser Ser Ser Val Ser Ile		
420	425	430
Ser His Ser Ala Ser Ala Thr Gly Asn Val Cys Ile Glu Glu Ile Asp		
435	440	445
Val Asp Gly Lys Phe Ile Arg Leu Lys Asn Thr Ser Glu Gln Asp Gln		
450	455	460
Pro Met Gly Gly Trp Glu Met Ile Arg Lys Ile Gly Asp Thr Ser Val		
465	470	475
Ser Tyr Lys Tyr Thr Ser Arg Tyr Val Leu Lys Ala Gly Gln Thr Val		
485	490	495
Thr Ile Trp Ala Ala Asn Ala Gly Val Thr Ala Ser Pro Pro Thr Asp		
500	505	510

Leu Ile Trp Lys Asn Gln Asn Ser Trp Gly Thr Gly Glu Asp Val Lys
515 520 525
Val Ile Leu Lys Asn Ser Gln Gly Glu Glu Val Ala Gln Arg Ser Thr
530 535 540
Val Phe Lys Thr Thr Ile Pro Glu Glu Glu Glu Glu Glu Glu Ala
545 550 555 560
Ala Gly Val Val Val Glu Glu Glu Leu Phe His Gln Gln Gly Thr Pro
565 570 575
Arg Ala Ser Asn Arg Ser Cys Ala Ile Met
580 585
<210> 106
<211> 268
<212> PRT
<213> 智人
<400> 106
Met Ala Val Asn Val Tyr Ser Thr Ser Val Thr Ser Asp Asn Leu Ser
1 5 10 15
Arg His Asp Met Leu Ala Trp Ile Asn Glu Ser Leu Gln Leu Asn Leu
20 25 30
Thr Lys Ile Glu Gln Leu Cys Ser Gly Ala Ala Tyr Cys Gln Phe Met
35 40 45
Asp Met Leu Phe Pro Gly Ser Ile Ala Leu Lys Lys Val Lys Phe Gln
50 55 60
Ala Lys Leu Glu His Glu Tyr Ile Gln Asn Phe Lys Ile Leu Gln Ala
65 70 75 80
Gly Phe Lys Arg Met Gly Val Asp Lys Ile Ile Pro Val Asp Lys Leu
85 90 95
Val Lys Gly Lys Phe Gln Asp Asn Phe Glu Phe Val Gln Trp Phe Lys
100 105 110
Lys Phe Phe Asp Ala Asn Tyr Asp Gly Lys Asp Tyr Asp Pro Val Ala
115 120 125
Ala Arg Gln Gly Gln Glu Thr Ala Val Ala Pro Ser Leu Val Ala Pro
130 135 140
Ala Leu Asn Lys Pro Lys Lys Pro Leu Thr Ser Ser Ser Ala Ala Pro
145 150 155 160
Gln Arg Pro Ile Ser Thr Gln Arg Thr Ala Ala Ala Pro Lys Ala Gly
165 170 175
Pro Gly Val Val Arg Lys Asn Pro Gly Val Gly Asn Gly Asp Asp Glu
180 185 190

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

<210> 107

<211> 863

<212> PRT

<213> 智人

<400> 107

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

Tyr Met Gln Arg Leu Gly Glu Ile Asn Val Ile Gly Glu Pro Phe Leu		
195	200	205
Asn Val Asn Cys Glu His Ile Lys Ser Phe Asp Lys Asn Leu Tyr Arg		
210	215	220
Gln Leu Ile Ser Tyr Pro Gln Glu Val Ile Pro Thr Phe Asp Met Ala		
225	230	235
Val Asn Glu Ile Phe Phe Asp Arg Tyr Pro Asp Ser Ile Leu Glu His		
	245	250
Gln Ile Gln Val Arg Pro Phe Asn Ala Leu Lys Thr Lys Asn Met Arg		
	260	265
Asn Leu Asn Pro Glu Asp Ile Asp Gln Leu Ile Thr Ile Ser Gly Met		
	275	280
Val Ile Arg Thr Ser Gln Leu Ile Pro Glu Met Gln Glu Ala Phe Phe		
290	295	300
Gln Cys Gln Val Cys Ala His Thr Thr Arg Val Glu Met Asp Arg Gly		
305	310	315
Arg Ile Ala Glu Pro Ser Val Cys Gly Arg Cys His Thr Thr His Ser		
	325	330
Met Ala Leu Ile His Asn Arg Ser Leu Phe Ser Asp Lys Gln Met Ile		
	340	345
Lys Leu Gln Glu Ser Pro Glu Asp Met Pro Ala Gly Gln Thr Pro His		
	355	360
Thr Val Ile Leu Phe Ala His Asn Asp Leu Val Asp Lys Val Gln Pro		
370	375	380
Gly Asp Arg Val Asn Val Thr Gly Ile Tyr Arg Ala Val Pro Ile Arg		
385	390	395
Val Asn Pro Arg Val Ser Asn Val Lys Ser Val Tyr Lys Thr His Ile		
	405	410
Asp Val Ile His Tyr Arg Lys Thr Asp Ala Lys Arg Leu His Gly Leu		
	420	425
Asp Glu Glu Ala Glu Gln Lys Leu Phe Ser Glu Lys Arg Val Glu Leu		
	435	440
Leu Lys Glu Leu Ser Arg Lys Pro Asp Ile Tyr Glu Arg Leu Ala Ser		
	450	455
Ala Leu Ala Pro Ser Ile Tyr Glu His Glu Asp Ile Lys Lys Gly Ile		
465	470	475
Leu Leu Gln Leu Phe Gly Gly Thr Arg Lys Asp Phe Ser His Thr Gly		
	485	490
Arg Gly Lys Phe Arg Ala Glu Ile Asn Ile Leu Leu Cys Gly Asp Pro		

	500		505		510
Gly Thr Ser Lys Ser Gln Leu Leu Gln Tyr Val Tyr Asn Leu Val Pro					
515		520		525	
Arg Gly Gln Tyr Thr Ser Gly Lys Gly Ser Ser Ala Val Gly Leu Thr					
530		535		540	
Ala Tyr Val Met Lys Asp Pro Glu Thr Arg Gln Leu Val Leu Gln Thr					
545		550		555	560
Gly Ala Leu Val Leu Ser Asp Asn Gly Ile Cys Cys Ile Asp Glu Phe					
565		570		575	
Asp Lys Met Asn Glu Ser Thr Arg Ser Val Leu His Glu Val Met Glu					
580		585		590	
Gln Gln Thr Leu Ser Ile Ala Lys Ala Gly Ile Ile Cys Gln Leu Asn					
595		600		605	
Ala Arg Thr Ser Val Leu Ala Ala Ala Asn Pro Ile Glu Ser Gln Trp					
610		615		620	
Asn Pro Lys Lys Thr Thr Ile Glu Asn Ile Gln Leu Pro His Thr Leu					
625		630		635	640
Leu Ser Arg Phe Asp Leu Ile Phe Leu Leu Leu Asp Pro Gln Asp Glu					
645		650		655	
Ala Tyr Asp Arg Arg Leu Ala His His Leu Val Ala Leu Tyr Tyr Gln					
660		665		670	
Ser Glu Glu Gln Ala Glu Glu Glu Leu Leu Asp Met Ala Val Leu Lys					
675		680		685	
Asp Tyr Ile Ala Tyr Ala His Ser Thr Ile Met Pro Arg Leu Ser Glu					
690		695		700	
Glu Ala Ser Gln Ala Leu Ile Glu Ala Tyr Val Asp Met Arg Lys Ile					
705		710		715	720
Gly Ser Ser Arg Gly Met Val Ser Ala Tyr Pro Arg Gln Leu Glu Ser					
725		730		735	
Leu Ile Arg Leu Ala Glu Ala His Ala Lys Val Arg Leu Ser Asn Lys					
740		745		750	
Val Glu Ala Ile Asp Val Glu Glu Ala Lys Arg Leu His Arg Glu Ala					
755		760		765	
Leu Lys Gln Ser Ala Thr Asp Pro Arg Thr Gly Ile Val Asp Ile Ser					
770		775		780	
Ile Leu Thr Thr Gly Met Ser Ala Thr Ser Arg Lys Arg Lys Glu Glu					
785		790		795	800
Leu Ala Glu Ala Leu Lys Lys Leu Ile Leu Ser Lys Gly Lys Thr Pro					
805		810		815	

Ala Leu Lys Tyr Gln Gln Leu Phe Glu Asp Ile Arg Gly Gln Ser Asp
820 825 830

Ile Ala Ile Thr Lys Asp Met Phe Glu Glu Ala Leu Arg Ala Leu Ala
835 840 845

Asp Asp Asp Phe Leu Thr Val Thr Gly Lys Thr Val Arg Leu Leu
850 855 860

<210> 108

<211> 115

<212> PRT

<213> 智人

<400> 108

Met Pro Met Phe Ile Val Asn Thr Asn Val Pro Arg Ala Ser Val Pro
1 5 10 15

Asp Gly Phe Leu Ser Glu Leu Thr Gln Gln Leu Ala Gln Ala Thr Gly
20 25 30

Lys Pro Pro Gln Tyr Ile Ala Val His Val Val Pro Asp Gln Leu Met
35 40 45

Ala Phe Gly Gly Ser Ser Glu Pro Cys Ala Leu Cys Ser Leu His Ser
50 55 60

Ile Gly Lys Ile Gly Gly Ala Gln Asn Arg Ser Tyr Ser Lys Leu Leu
65 70 75 80

Cys Gly Leu Leu Ala Glu Arg Leu Arg Ile Ser Pro Asp Arg Val Tyr
85 90 95

Ile Asn Tyr Tyr Asp Met Asn Ala Ala Asn Val Gly Trp Asn Asn Ser
100 105 110

Thr Phe Ala
115

<210> 109

<211> 267

<212> PRT

<213> 智人

<400> 109

Met Arg Leu Thr Val Leu Cys Ala Val Cys Leu Leu Pro Gly Ser Leu
1 5 10 15

Ala Leu Pro Leu Pro Gln Glu Ala Gly Gly Met Ser Glu Leu Gln Trp
20 25 30

Glu Gln Ala Gln Asp Tyr Leu Lys Arg Phe Tyr Leu Tyr Asp Ser Glu
35 40 45

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

50	55	60
Phe Phe Gly Leu Pro Ile Thr Gly Met Leu Asn Ser Arg Val Ile Glu		
65	70	75
Ile Met Gln Lys Pro Arg Cys Gly Val Pro Asp Val Ala Glu Tyr Ser		80
	85	90
Leu Phe Pro Asn Ser Pro Lys Trp Thr Ser Lys Val Val Thr Tyr Arg		95
	100	105
Ile Val Ser Tyr Thr Arg Asp Leu Pro His Ile Thr Val Asp Arg Leu		110
	115	120
Val Ser Lys Ala Leu Asn Met Trp Gly Lys Glu Ile Pro Leu His Phe		125
	130	135
Arg Lys Val Val Trp Gly Thr Ala Asp Ile Met Ile Gly Phe Ala Arg		140
145	150	155
Gly Ala His Gly Asp Ser Tyr Pro Phe Asp Gly Pro Gly Asn Thr Leu		160
	165	170
Ala His Ala Phe Ala Pro Gly Thr Gly Leu Gly Gly Asp Ala His Phe		175
	180	185
Asp Glu Asp Glu Arg Trp Thr Asp Gly Ser Ser Leu Gly Ile Asn Phe		190
	195	200
Leu Tyr Ala Ala Thr His Glu Leu Gly His Ser Leu Gly Met Gly His		205
	210	215
Ser Ser Asp Pro Asn Ala Val Met Tyr Pro Thr Tyr Gly Asn Gly Asp		220
225	230	235
Pro Gln Asn Phe Lys Leu Ser Gln Asp Asp Ile Lys Gly Ile Gln Lys		240
	245	250
Leu Tyr Gly Lys Arg Ser Asn Ser Arg Lys Lys		255
	260	265
<210> 110		
<211> 707		
<212> PRT		
<213> 智人		
<400> 110		
Met Ser Leu Trp Gln Pro Leu Val Leu Val Leu Leu Val Leu Gly Cys		
1	5	10
Cys Phe Ala Ala Pro Arg Gln Arg Gln Ser Thr Leu Val Leu Phe Pro		15
	20	25
Gly Asp Leu Arg Thr Asn Leu Thr Asp Arg Gln Leu Ala Glu Glu Tyr		30
	35	40
Leu Tyr Arg Tyr Gly Tyr Thr Arg Val Ala Glu Met Arg Gly Glu Ser		45

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

Gly Arg Leu Trp Cys Ala Thr Thr Ser Asn Phe Asp Ser Asp Lys Lys		
370	375	380
Trp Gly Phe Cys Pro Asp Gln Gly Tyr Ser Leu Phe Leu Val Ala Ala		
385	390	395
His Glu Phe Gly His Ala Leu Gly Leu Asp His Ser Ser Val Pro Glu		
	405	410
Ala Leu Met Tyr Pro Met Tyr Arg Phe Thr Glu Gly Pro Pro Leu His		
	420	425
Lys Asp Asp Val Asn Gly Ile Arg His Leu Tyr Gly Pro Arg Pro Glu		
	435	440
Pro Glu Pro Arg Pro Pro Thr Thr Thr Thr Pro Gln Pro Thr Ala Pro		
	450	455
Pro Thr Val Cys Pro Thr Gly Pro Pro Thr Val His Pro Ser Glu Arg		
465	470	475
Pro Thr Ala Gly Pro Thr Gly Pro Pro Ser Ala Gly Pro Thr Gly Pro		
	485	490
Pro Thr Ala Gly Pro Ser Thr Ala Thr Thr Val Pro Leu Ser Pro Val		
	500	505
Asp Asp Ala Cys Asn Val Asn Ile Phe Asp Ala Ile Ala Glu Ile Gly		
	515	520
Asn Gln Leu Tyr Leu Phe Lys Asp Gly Lys Tyr Trp Arg Phe Ser Glu		
	530	535
Gly Arg Gly Ser Arg Pro Gln Gly Pro Phe Leu Ile Ala Asp Lys Trp		
545	550	555
Pro Ala Leu Pro Arg Lys Leu Asp Ser Val Phe Glu Glu Arg Leu Ser		
	565	570
Lys Lys Leu Phe Phe Phe Ser Gly Arg Gln Val Trp Val Tyr Thr Gly		
	580	585
Ala Ser Val Leu Gly Pro Arg Arg Leu Asp Lys Leu Gly Leu Gly Ala		
	595	600
Asp Val Ala Gln Val Thr Gly Ala Leu Arg Ser Gly Arg Gly Lys Met		
	610	615
Leu Leu Phe Ser Gly Arg Arg Leu Trp Arg Phe Asp Val Lys Ala Gln		
625	630	635
Met Val Asp Pro Arg Ser Ala Ser Glu Val Asp Arg Met Phe Pro Gly		
	645	650
Val Pro Leu Asp Thr His Asp Val Phe Gln Tyr Arg Glu Lys Ala Tyr		
	660	665
Phe Cys Gln Asp Arg Phe Tyr Trp Arg Val Ser Ser Arg Ser Glu Leu		

675	680	685
Asn Gln Val Asp Gln Val Gly Tyr Val Thr Tyr Asp Ile Leu Gln Cys		
690	695	700
Pro Glu Asp		
705		
<210> 111		
<211> 297		
<212> PRT		
<213> 智人		
<400> 111		
Met Thr Thr Pro Arg Asn Ser Val Asn Gly Thr Phe Pro Ala Glu Pro		
1	5	10
Met Lys Gly Pro Ile Ala Met Gln Ser Gly Pro Lys Pro Leu Phe Arg		
20	25	30
Arg Met Ser Ser Leu Val Gly Pro Thr Gln Ser Phe Phe Met Arg Glu		
35	40	45
Ser Lys Thr Leu Gly Ala Val Gln Ile Met Asn Gly Leu Phe His Ile		
50	55	60
Ala Leu Gly Gly Leu Leu Met Ile Pro Ala Gly Ile Tyr Ala Pro Ile		
65	70	75
Cys Val Thr Val Trp Tyr Pro Leu Trp Gly Gly Ile Met Tyr Ile Ile		
85	90	95
Ser Gly Ser Leu Leu Ala Ala Thr Glu Lys Asn Ser Arg Lys Cys Leu		
100	105	110
Val Lys Gly Lys Met Ile Met Asn Ser Leu Ser Leu Phe Ala Ala Ile		
115	120	125
Ser Gly Met Ile Leu Ser Ile Met Asp Ile Leu Asn Ile Lys Ile Ser		
130	135	140
His Phe Leu Lys Met Glu Ser Leu Asn Phe Ile Arg Ala His Thr Pro		
145	150	155
Tyr Ile Asn Ile Tyr Asn Cys Glu Pro Ala Asn Pro Ser Glu Lys Asn		
165	170	175
Ser Pro Ser Thr Gln Tyr Cys Tyr Ser Ile Gln Ser Leu Phe Leu Gly		
180	185	190
Ile Leu Ser Val Met Leu Ile Phe Ala Phe Phe Gln Glu Leu Val Ile		
195	200	205
Ala Gly Ile Val Glu Asn Glu Trp Lys Arg Thr Cys Ser Arg Pro Lys		
210	215	220
Ser Asn Ile Val Leu Leu Ser Ala Glu Glu Lys Lys Glu Gln Thr Ile		

225	230	235	240
Glu Ile Lys Glu Glu Val Val Gly Leu Thr Glu Thr Ser Ser Gln Pro			
	245	250	255
Lys Asn Glu Glu Asp Ile Glu Ile Ile Pro Ile Gln Glu Glu Glu Glu			
	260	265	270
Glu Glu Thr Glu Thr Asn Phe Pro Glu Pro Pro Gln Asp Gln Glu Ser			
	275	280	285
Ser Pro Ile Glu Asn Asp Ser Ser Pro			
290	295		
<210> 112			
<211> 151			
<212> PRT			
<213> 智人			
<400> 112			
Met Cys Asp Phe Thr Glu Asp Gln Thr Ala Glu Phe Lys Glu Ala Phe			
1	5	10	15
Gln Leu Phe Asp Arg Thr Gly Asp Gly Lys Ile Leu Tyr Ser Gln Cys			
	20	25	30
Gly Asp Val Met Arg Ala Leu Gly Gln Asn Pro Thr Asn Ala Glu Val			
	35	40	45
Leu Lys Val Leu Gly Asn Pro Lys Ser Asp Glu Met Asn Val Lys Val			
	50	55	60
Leu Asp Phe Glu His Phe Leu Pro Met Leu Gln Thr Val Ala Lys Asn			
65	70	75	80
Lys Asp Gln Gly Thr Tyr Glu Asp Tyr Val Glu Gly Leu Arg Val Phe			
	85	90	95
Asp Lys Glu Gly Asn Gly Thr Val Met Gly Ala Glu Ile Arg His Val			
	100	105	110
Leu Val Thr Leu Gly Glu Lys Met Thr Glu Glu Glu Val Glu Met Leu			
	115	120	125
Val Ala Gly His Glu Asp Ser Asn Gly Cys Ile Asn Tyr Glu Ala Phe			
	130	135	140
Val Arg His Ile Leu Ser Gly			
145	150		
<210> 113			
<211> 172			
<212> PRT			
<213> 智人			
<400> 113			

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

<210> 114

<211> 152

<212> PRT

<213> 智人

<400> 114

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

Ala Asp Ser Lys Pro Gly Thr Ile Arg Gly Asp Phe Cys Ile Gln Val		
100	105	110
Gly Arg Asn Ile Ile His Gly Ser Asp Ser Val Glu Ser Ala Glu Lys		
115	120	125
Glu Ile Gly Leu Trp Phe His Pro Glu Glu Leu Val Asp Tyr Thr Ser		
130	135	140
Cys Ala Gln Asn Trp Ile Tyr Glu		
145	150	
<210> 115		
<211> 264		
<212> PRT		
<213> 智人		
<400> 115		
Met Glu Ser Gly Phe Thr Ser Lys Asp Thr Tyr Leu Ser His Phe Asn		
1	5	10
Pro Arg Asp Tyr Leu Glu Lys Tyr Tyr Lys Phe Gly Ser Arg His Ser		
20	25	30
Ala Glu Ser Gln Ile Leu Lys His Leu Leu Lys Asn Leu Phe Lys Ile		
35	40	45
Phe Cys Leu Asp Gly Val Lys Gly Asp Leu Leu Ile Asp Ile Gly Ser		
50	55	60
Gly Pro Thr Ile Tyr Gln Leu Leu Ser Ala Cys Glu Ser Phe Lys Glu		
65	70	75
Ile Val Val Thr Asp Tyr Ser Asp Gln Asn Leu Gln Glu Leu Glu Lys		
85	90	95
Trp Leu Lys Lys Glu Pro Glu Ala Phe Asp Trp Ser Pro Val Val Thr		
100	105	110
Tyr Val Cys Asp Leu Glu Gly Asn Arg Val Lys Gly Pro Glu Lys Glu		
115	120	125
Glu Lys Leu Arg Gln Ala Val Lys Gln Val Leu Lys Cys Asp Val Thr		
130	135	140
Gln Ser Gln Pro Leu Gly Ala Val Pro Leu Pro Pro Ala Asp Cys Val		
145	150	155
Leu Ser Thr Leu Cys Leu Asp Ala Ala Cys Pro Asp Leu Pro Thr Tyr		
165	170	175
Cys Arg Ala Leu Arg Asn Leu Gly Ser Leu Leu Lys Pro Gly Gly Phe		
180	185	190
Leu Val Ile Met Asp Ala Leu Lys Ser Ser Tyr Tyr Met Ile Gly Glu		
195	200	205

Gln Lys Phe Ser Ser Leu Pro Leu Gly Arg Glu Ala Val Glu Ala Ala
210 215 220
Val Lys Glu Ala Gly Tyr Thr Ile Glu Trp Phe Glu Val Ile Ser Gln
225 230 235 240
Ser Tyr Ser Ser Thr Met Ala Asn Asn Glu Gly Leu Phe Ser Leu Val
245 250 255
Ala Arg Lys Leu Ser Arg Pro Leu
260
<210> 116
<211> 201
<212> PRT
<213> 智人
<400> 116
Met Ala Leu Ser Trp Val Leu Thr Val Leu Ser Leu Leu Pro Leu Leu
1 5 10 15
Glu Ala Gln Ile Pro Leu Cys Ala Asn Leu Val Pro Val Pro Ile Thr
20 25 30
Asn Ala Thr Leu Asp Gln Ile Thr Gly Lys Trp Phe Tyr Ile Ala Ser
35 40 45
Ala Phe Arg Asn Glu Glu Tyr Asn Lys Ser Val Gln Glu Ile Gln Ala
50 55 60
Thr Phe Phe Tyr Phe Thr Pro Asn Lys Thr Glu Asp Thr Ile Phe Leu
65 70 75 80
Arg Glu Tyr Gln Thr Arg Gln Asp Gln Cys Ile Tyr Asn Thr Thr Tyr
85 90 95
Leu Asn Val Gln Arg Glu Asn Gly Thr Ile Ser Arg Tyr Val Gly Gly
100 105 110
Gln Glu His Phe Ala His Leu Leu Ile Leu Arg Asp Thr Lys Thr Tyr
115 120 125
Met Leu Ala Phe Asp Val Asn Asp Glu Lys Asn Trp Gly Leu Ser Val
130 135 140
Tyr Ala Asp Lys Pro Glu Thr Thr Lys Glu Gln Leu Gly Glu Phe Tyr
145 150 155 160
Glu Ala Leu Asp Cys Leu Arg Ile Pro Lys Ser Asp Val Val Tyr Thr
165 170 175
Asp Trp Lys Lys Asp Lys Cys Glu Pro Leu Glu Lys Gln His Glu Lys
180 185 190
Glu Arg Lys Gln Glu Glu Gly Glu Ser
195 200

<210> 117

<211> 640

<212> PRT

<213> 智人

<400> 117

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

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Ala Arg Asp Glu Gly Trp Leu Ala Glu His Met Leu Ile Leu Gly Ile		
275	280	285
Thr Ser Pro Ala Gly Lys Lys Arg Tyr Val Ala Ala Ala Phe Pro Ser		
290	295	300
Ala Cys Gly Lys Thr Asn Leu Ala Met Met Arg Pro Ala Leu Pro Gly		
305	310	315
Trp Lys Val Glu Cys Val Gly Asp Asp Ile Ala Trp Met Arg Phe Asp		
	325	330
Ser Glu Gly Arg Leu Arg Ala Ile Asn Pro Glu Asn Gly Phe Phe Gly		
	340	345
Val Ala Pro Gly Thr Ser Ala Thr Thr Asn Pro Asn Ala Met Ala Thr		
	355	360
Ile Gln Ser Asn Thr Ile Phe Thr Asn Val Ala Glu Thr Ser Asp Gly		
370	375	380
Gly Val Tyr Trp Glu Gly Ile Asp Gln Pro Leu Pro Pro Gly Val Thr		
385	390	395
Val Thr Ser Trp Leu Gly Lys Pro Trp Lys Pro Gly Asp Lys Glu Pro		
	405	410
Cys Ala His Pro Asn Ser Arg Phe Cys Ala Pro Ala Arg Gln Cys Pro		
	420	425
Ile Met Asp Pro Ala Trp Glu Ala Pro Glu Gly Val Pro Ile Asp Ala		
435	440	445
Ile Ile Phe Gly Gly Arg Arg Pro Lys Gly Val Pro Leu Val Tyr Glu		
450	455	460
Ala Phe Asn Trp Arg His Gly Val Phe Val Gly Ser Ala Met Arg Ser		
465	470	475
Glu Ser Thr Ala Ala Ala Glu His Lys Gly Lys Ile Ile Met His Asp		
	485	490
Pro Phe Ala Met Arg Pro Phe Phe Gly Tyr Asn Phe Gly His Tyr Leu		
	500	505
Glu His Trp Leu Ser Met Glu Gly Arg Lys Gly Ala Gln Leu Pro Arg		
	515	520
Ile Phe His Val Asn Trp Phe Arg Arg Asp Glu Ala Gly His Phe Leu		
530	535	540
Trp Pro Gly Phe Gly Glu Asn Ala Arg Val Leu Asp Trp Ile Cys Arg		
545	550	555
Arg Leu Glu Gly Glu Asp Ser Ala Arg Glu Thr Pro Ile Gly Leu Val		
	565	570
Pro Lys Glu Gly Ala Leu Asp Leu Ser Gly Leu Arg Ala Ile Asp Thr		

276

210	215	220
Gln Lys Met Thr Ser Gly Lys Ile Lys Lys Phe Ile Gln Glu Asn Ile		
225	230	235
Phe Gly Ile Cys Pro His Met Thr Glu Asp Asn Lys Asp Leu Ile Gln		240
	245	250
Gly Lys Asp Leu Leu Ile Ala Tyr Tyr Asp Val Asp Tyr Glu Lys Asn		255
	260	265
Ala Lys Gly Ser Asn Tyr Trp Arg Asn Arg Val Met Met Val Ala Lys		270
	275	280
Lys Phe Leu Asp Ala Gly His Lys Leu Asn Phe Ala Val Ala Ser Arg		285
290	295	300
Lys Thr Phe Ser His Glu Leu Ser Asp Phe Gly Leu Glu Ser Thr Ala		
305	310	315
Gly Glu Ile Pro Val Val Ala Ile Arg Thr Ala Lys Gly Glu Lys Phe		320
	325	330
Val Met Gln Glu Glu Phe Ser Arg Asp Gly Lys Ala Leu Glu Arg Phe		335
	340	345
Leu Gln Asp Tyr Phe Asp Gly Asn Leu Lys Arg Tyr Leu Lys Ser Glu		350
355	360	365
Pro Ile Pro Glu Ser Asn Asp Gly Pro Val Lys Val Val Val Ala Glu		
370	375	380
Asn Phe Asp Glu Ile Val Asn Asn Glu Asn Lys Asp Val Leu Ile Glu		
385	390	395
Phe Tyr Ala Pro Trp Cys Gly His Cys Lys Asn Leu Glu Pro Lys Tyr		400
	405	410
Lys Glu Leu Gly Glu Lys Leu Ser Lys Asp Pro Asn Ile Val Ile Ala		415
	420	425
Lys Met Asp Ala Thr Ala Asn Asp Val Pro Ser Pro Tyr Glu Val Arg		430
	435	440
Gly Phe Pro Thr Ile Tyr Phe Ser Pro Ala Asn Lys Lys Leu Asn Pro		445
450	455	460
Lys Lys Tyr Glu Gly Gly Arg Glu Leu Ser Asp Phe Ile Ser Tyr Leu		
465	470	475
Gln Arg Glu Ala Thr Asn Pro Pro Val Ile Gln Glu Glu Lys Pro Lys		480
	485	490
Lys Lys Lys Lys Ala Gln Glu Asp Leu		495
	500	505
<210> 119		
<211> 440		

<212> PRT

<213> 智人

<400> 119

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

Arg Thr Cys Glu Glu His Gln Leu Cys Val Val Ala Val Leu Pro His		
290	295	300
Ile Leu Asp Thr Gly Ala Ala Gly Arg Asn Ser Tyr Leu Glu Val Leu		
305	310	315 320
Leu Lys Leu Ala Asp Lys Tyr Lys Lys Lys Met Trp Gly Trp Leu Trp		
	325	330 335
Thr Glu Ala Gly Ala Gln Ser Glu Leu Glu Thr Ala Leu Gly Ile Gly		
	340	345 350
Gly Phe Gly Tyr Pro Ala Met Ala Ala Ile Asn Ala Arg Lys Met Lys		
	355	360 365
Phe Ala Leu Leu Lys Gly Ser Phe Ser Glu Gln Gly Ile Asn Glu Phe		
	370	375 380
Leu Arg Glu Leu Ser Phe Gly Arg Gly Ser Thr Ala Pro Val Gly Gly		
385	390	395 400
Gly Ala Phe Pro Thr Ile Val Glu Arg Glu Pro Trp Asp Gly Arg Asp		
	405	410 415
Gly Glu Leu Pro Val Glu Asp Asp Ile Asp Leu Ser Asp Val Glu Leu		
	420	425 430
Asp Asp Leu Gly Lys Asp Glu Leu		
	435	440
<210> 120		
<211> 312		
<212> PRT		
<213> 智人		
<400> 120		
Met Glu Glu Glu Cys Arg Val Leu Ser Ile Gln Ser His Val Ile Arg		
1	5	10 15
Gly Tyr Val Gly Asn Arg Ala Ala Thr Phe Pro Leu Gln Val Leu Gly		
	20	25 30
Phe Glu Ile Asp Ala Val Asn Ser Val Gln Phe Ser Asn His Thr Gly		
	35	40 45
Tyr Ala His Trp Lys Gly Gln Val Leu Asn Ser Asp Glu Leu Gln Glu		
	50	55 60
Leu Tyr Glu Gly Leu Arg Leu Asn Asn Met Asn Lys Tyr Asp Tyr Val		
65	70	75 80
Leu Thr Gly Tyr Thr Arg Asp Lys Ser Phe Leu Ala Met Val Val Asp		
	85	90 95
Ile Val Gln Glu Leu Lys Gln Gln Asn Pro Arg Leu Val Tyr Val Cys		
	100	105 110

Asp Pro Val Leu Gly Asp Lys Trp Asp Gly Glu Gly Ser Met Tyr Val		
115	120	125
Pro Glu Asp Leu Leu Pro Val Tyr Lys Glu Lys Val Val Pro Leu Ala		
130	135	140
Asp Ile Ile Thr Pro Asn Gln Phe Glu Ala Glu Leu Leu Ser Gly Arg		
145	150	155
Lys Ile His Ser Gln Glu Glu Ala Leu Arg Val Met Asp Met Leu His		
	165	170
Ser Met Gly Pro Asp Thr Val Val Ile Thr Ser Ser Asp Leu Pro Ser		
	180	185
Pro Gln Gly Ser Asn Tyr Leu Ile Val Leu Gly Ser Gln Arg Arg Arg		
	195	200
Asn Pro Ala Gly Ser Val Val Met Glu Arg Ile Arg Met Asp Ile Arg		
	210	215
Lys Val Asp Ala Val Phe Val Gly Thr Gly Asp Leu Phe Ala Ala Met		
225	230	235
Leu Leu Ala Trp Thr His Lys His Pro Asn Asn Leu Lys Val Ala Cys		
	245	250
Glu Lys Thr Val Ser Thr Leu His His Val Leu Gln Arg Thr Ile Gln		
	260	265
Cys Ala Lys Ala Gln Ala Gly Glu Gly Val Arg Pro Ser Pro Met Gln		
	275	280
Leu Glu Leu Arg Met Val Gln Ser Lys Arg Asp Ile Glu Asp Pro Glu		
	290	295
Ile Val Val Gln Ala Thr Val Leu		
305	310	
<210> 121		
<211> 187		
<212> PRT		
<213> 智人		
<400> 121		
Met Pro Val Asp Leu Ser Lys Trp Ser Gly Pro Leu Ser Leu Gln Glu		
1	5	10
Val Asp Glu Gln Pro Gln His Pro Leu His Val Thr Tyr Ala Gly Ala		
	20	25
Ala Val Asp Glu Leu Gly Lys Val Leu Thr Pro Thr Gln Val Lys Asn		
	35	40
Arg Pro Thr Ser Ile Ser Trp Asp Gly Leu Asp Ser Gly Lys Leu Tyr		
	50	55
		60

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

<210> 122

<211> 270

<212> PRT

<213> 智人

<400> 122

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

Asp	Arg	Ser	Gln	Val	Leu	Ser	Lys	Asp	Tyr	Lys	Ala	Glu	Glu	Asp	Pro
145					150					155					160
Ala	Lys	Phe	Lys	Ser	Ile	Lys	Thr	Gly	Arg	Gly	Pro	Leu	Gly	Pro	Asn
					165					170					175
Trp	Lys	Gln	Glu	Leu	Val	Asn	Gln	Lys	Asp	Cys	Pro	Tyr	Met	Cys	Ala
					180					185					190
Tyr	Lys	Leu	Val	Thr	Val	Lys	Phe	Lys	Trp	Trp	Gly	Leu	Gln	Asn	Lys
					195					200					205
Val	Glu	Asn	Phe	Ile	His	Lys	Gln	Glu	Arg	Arg	Leu	Phe	Thr	Asn	Phe
His	Arg	Gln	Leu	Phe	Cys	Trp	Leu	Asp	Lys	Trp	Val	Asp	Leu	Thr	Met
225															
Asp	Asp	Ile	Arg	Arg	Met	Glu	Glu	Glu	Thr	Lys	Arg	Gln	Leu	Asp	Glu
Met	Arg	Gln	Lys	Asp	Pro	Val	Lys	Gly	Met	Thr	Ala	Asp	Asp		

<210> 123

<211> 531

<212> PRT

<213> 智人

<400> 123

Met	Ser	Lys	Pro	His	Ser	Glu	Ala	Gly	Thr	Ala	Phe	Ile	Gln	Thr	Gln
1					5				10					15	
Gln	Leu	His	Ala	Ala	Met	Ala	Asp	Thr	Phe	Leu	Glu	His	Met	Cys	Arg
Leu	Asp	Ile	Asp	Ser	Pro	Pro	Ile	Thr	Ala	Arg	Asn	Thr	Gly	Ile	Ile
Cys	Thr	Ile	Gly	Pro	Ala	Ser	Arg	Ser	Val	Glu	Thr	Leu	Lys	Glu	Met
Ile	Lys	Ser	Gly	Met	Asn	Val	Ala	Arg	Leu	Asn	Phe	Ser	His	Gly	Thr
65															
His	Glu	Tyr	His	Ala	Glu	Thr	Ile	Lys	Asn	Val	Arg	Thr	Ala	Thr	Glu
Ser	Phe	Ala	Ser	Asp	Pro	Ile	Leu	Tyr	Arg	Pro	Val	Ala	Val	Ala	Leu
Asp	Thr	Lys	Gly	Pro	Glu	Ile	Arg	Thr	Gly	Leu	Ile	Lys	Gly	Ser	Gly
Thr	Ala	Glu	Val	Glu	Leu	Lys	Lys	Gly	Ala	Thr	Leu	Lys	Ile	Thr	Leu

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

450	455	460
Leu Tyr Arg Gly Ile Phe Pro Val Leu Cys Lys Asp Pro Val Gln Glu		
465	470	475
Ala Trp Ala Glu Asp Val Asp Leu Arg Val Asn Phe Ala Met Asn Val		
485	490	495
Gly Lys Ala Arg Gly Phe Phe Lys Lys Gly Asp Val Val Ile Val Leu		
500	505	510
Thr Gly Trp Arg Pro Gly Ser Gly Phe Thr Asn Thr Met Arg Val Val		
515	520	525
Pro Val Pro		
530		
<210> 124		
<211> 431		
<212> PRT		
<213> 智人		
<400> 124		
Met Arg Ala Leu Leu Ala Arg Leu Leu Leu Cys Val Leu Val Val Ser		
1	5	10
Asp Ser Lys Gly Ser Asn Glu Leu His Gln Val Pro Ser Asn Cys Asp		
20	25	30
Cys Leu Asn Gly Gly Thr Cys Val Ser Asn Lys Tyr Phe Ser Asn Ile		
35	40	45
His Trp Cys Asn Cys Pro Lys Lys Phe Gly Gly Gln His Cys Glu Ile		
50	55	60
Asp Lys Ser Lys Thr Cys Tyr Glu Gly Asn Gly His Phe Tyr Arg Gly		
65	70	75
Lys Ala Ser Thr Asp Thr Met Gly Arg Pro Cys Leu Pro Trp Asn Ser		
85	90	95
Ala Thr Val Leu Gln Gln Thr Tyr His Ala His Arg Ser Asp Ala Leu		
100	105	110
Gln Leu Gly Leu Gly Lys His Asn Tyr Cys Arg Asn Pro Asp Asn Arg		
115	120	125
Arg Arg Pro Trp Cys Tyr Val Gln Val Gly Leu Lys Pro Leu Val Gln		
130	135	140
Glu Cys Met Val His Asp Cys Ala Asp Gly Lys Lys Pro Ser Ser Pro		
145	150	155
Pro Glu Glu Leu Lys Phe Gln Cys Gly Gln Lys Thr Leu Arg Pro Arg		
165	170	175
Phe Lys Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp		

180	185	190
Phe Ala Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Val Thr Tyr Val		
195	200	205
Cys Gly Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His		
210	215	220
Cys Phe Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly		
225	230	235
Arg Ser Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val		
245	250	255
Glu Asn Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Leu Ala His		
260	265	270
His Asn Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys		
275	280	285
Ala Gln Pro Ser Arg Thr Ile Gln Thr Ile Cys Leu Pro Ser Met Tyr		
290	295	300
Asn Asp Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys		
305	310	315
Glu Asn Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val		
325	330	335
Val Lys Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly		
340	345	350
Ser Glu Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys		
355	360	365
Thr Asp Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu		
370	375	380
Gln Gly Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys		
385	390	395
Ala Leu Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu		
405	410	415
Pro Trp Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu		
420	425	430
<210> 125		
<211> 289		
<212> PRT		
<213> 智人		
<400> 125		
Met Ser Gly Phe Ser Thr Glu Glu Arg Ala Ala Pro Phe Ser Leu Glu		
1	5	10
Tyr Arg Val Phe Leu Lys Asn Glu Lys Gly Gln Tyr Ile Ser Pro Phe		

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

Asn

<210> 126

<211> 199

<212> PRT

<213> 智人

<400> 126

Met	Ser	Ser	Gly	Asn	Ala	Lys	Ile	Gly	His	Pro	Ala	Pro	Asn	Phe	Lys
1				5					10					15	
Ala	Thr	Ala	Val	Met	Pro	Asp	Gly	Gln	Phe	Lys	Asp	Ile	Ser	Leu	Ser
			20					25					30		
Asp	Tyr	Lys	Gly	Lys	Tyr	Val	Val	Phe	Phe	Phe	Tyr	Pro	Leu	Asp	Phe
		35					40						45		
Thr	Phe	Val	Cys	Pro	Thr	Glu	Ile	Ile	Ala	Phe	Ser	Asp	Arg	Ala	Glu
		50					55					60			
Glu	Phe	Lys	Lys	Leu	Asn	Cys	Gln	Val	Ile	Gly	Ala	Ser	Val	Asp	Ser
65					70					75				80	
His	Phe	Cys	His	Leu	Ala	Trp	Val	Asn	Thr	Pro	Lys	Lys	Gln	Gly	Gly
				85					90					95	
Leu	Gly	Pro	Met	Asn	Ile	Pro	Leu	Val	Ser	Asp	Pro	Lys	Arg	Thr	Ile
			100					105					110		
Ala	Gln	Asp	Tyr	Gly	Val	Leu	Lys	Ala	Asp	Glu	Gly	Ile	Ser	Phe	Arg
		115						120					125		
Gly	Leu	Phe	Ile	Ile	Asp	Asp	Lys	Gly	Ile	Leu	Arg	Gln	Ile	Thr	Val
		130					135					140			
Asn	Asp	Leu	Pro	Val	Gly	Arg	Ser	Val	Asp	Glu	Thr	Leu	Arg	Leu	Val
145					150					155				160	
Gln	Ala	Phe	Gln	Phe	Thr	Asp	Lys	His	Gly	Glu	Val	Cys	Pro	Ala	Gly
				165					170					175	
Trp	Lys	Pro	Gly	Ser	Asp	Thr	Ile	Lys	Pro	Asp	Val	Gln	Lys	Ser	Lys
			180					185					190		
Glu	Tyr	Phe	Ser	Lys	Gln	Lys									
			195												
<210>	127														
<211>	912														
<212>	PRT														
<213>	智人														
<400>	127														
Met	Ser	Ala	Pro	Pro	Val	Leu	Arg	Pro	Pro	Ser	Pro	Leu	Leu	Pro	Val
1					5					10				15	
Ala	Ala	Ala	Ala	Ala	Ala	Ala	Ala	Ala	Ala	Leu	Val	Pro	Gly	Ser	Gly
			20						25				30		
Pro	Gly	Pro	Ala	Pro	Phe	Leu	Ala	Pro	Val	Ala	Ala	Pro	Val	Gly	Gly
		35					40					45			
Ile	Ser	Phe	His	Leu	Gln	Ile	Gly	Leu	Ser	Arg	Glu	Pro	Val	Leu	Leu
		50					55					60			

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

370	375	380
Pro Asp Pro Asp His Glu Asp Ala Asn Arg Thr Ile Ser Pro Ser Thr		
385	390	395
Ser Asn Asn Ile Pro Leu Met Arg Val Val Gln Ser Val Lys His Thr		400
	405	410
Lys Arg Lys Ser Ser Thr Val Met Lys Glu Gly Trp Met Val His Tyr		415
	420	425
Thr Ser Lys Asp Thr Leu Arg Lys Arg His Tyr Trp Arg Leu Asp Ser		430
	435	440
Lys Cys Ile Thr Leu Phe Gln Asn Asp Thr Gly Ser Arg Tyr Tyr Lys		445
450	455	460
Glu Ile Pro Leu Ser Glu Ile Leu Ser Leu Glu Pro Val Lys Thr Ser		465
	470	475
Ala Leu Ile Pro Asn Gly Ala Asn Pro His Cys Phe Glu Ile Thr Thr		480
	485	490
Ala Asn Val Val Tyr Tyr Val Gly Glu Asn Val Val Asn Pro Ser Ser		495
	500	505
Pro Ser Pro Asn Asn Ser Val Leu Thr Ser Gly Val Gly Ala Asp Val		510
	515	520
Ala Arg Met Trp Glu Ile Ala Ile Gln His Ala Leu Met Pro Val Ile		525
	530	535
Pro Lys Gly Ser Ser Val Gly Thr Gly Thr Asn Leu His Arg Asp Ile		540
545	550	555
Ser Val Ser Ile Ser Val Ser Asn Cys Gln Ile Gln Glu Asn Val Asp		560
	565	570
Ile Ser Thr Val Tyr Gln Ile Phe Pro Asp Glu Val Leu Gly Ser Gly		575
	580	585
Gln Phe Gly Ile Val Tyr Gly Gly Lys His Arg Lys Thr Gly Arg Asp		590
	595	600
Val Ala Ile Lys Ile Ile Asp Lys Leu Arg Phe Pro Thr Lys Gln Glu		605
	610	615
Ser Gln Leu Arg Asn Glu Val Ala Ile Leu Gln Asn Leu His His Pro		620
625	630	635
Gly Val Val Asn Leu Glu Cys Met Phe Glu Thr Pro Glu Arg Val Phe		640
	645	650
Val Val Met Glu Lys Leu His Gly Asp Met Leu Glu Met Ile Leu Ser		655
	660	665
Ser Glu Lys Gly Arg Leu Pro Glu His Ile Thr Lys Phe Leu Ile Thr		670
	675	680
		685

Gln	Ile	Leu	Val	Ala	Leu	Arg	His	Leu	His	Phe	Lys	Asn	Ile	Val	His		
690					695					700							
Cys	Asp	Leu	Lys	Pro	Glu	Asn	Val	Leu	Leu	Ala	Ser	Ala	Asp	Pro	Phe		
705					710					715						720	
Pro	Gln	Val	Lys	Leu	Cys	Asp	Phe	Gly	Phe	Ala	Arg	Ile	Ile	Gly	Glu		
725					730					735							
Lys	Ser	Phe	Arg	Arg	Ser	Val	Val	Gly	Thr	Pro	Ala	Tyr	Leu	Ala	Pro		
740					745					750							
Glu	Val	Leu	Arg	Asn	Lys	Gly	Tyr	Asn	Arg	Ser	Leu	Asp	Met	Trp	Ser		
755					760					765							
Val	Gly	Val	Ile	Ile	Tyr	Val	Ser	Leu	Ser	Gly	Thr	Phe	Pro	Phe	Asn		
770					775					780							
Glu	Asp	Glu	Asp	Ile	His	Asp	Gln	Ile	Gln	Asn	Ala	Ala	Phe	Met	Tyr		
785					790					795						800	
Pro	Pro	Asn	Pro	Trp	Lys	Glu	Ile	Ser	His	Glu	Ala	Ile	Asp	Leu	Ile		
805					810					815							
Asn	Asn	Leu	Leu	Gln	Val	Lys	Met	Arg	Lys	Arg	Tyr	Ser	Val	Asp	Lys		
820					825					830							
Thr	Leu	Ser	His	Pro	Trp	Leu	Gln	Asp	Tyr	Gln	Thr	Trp	Leu	Asp	Leu		
835					840					845							
Arg	Glu	Leu	Glu	Cys	Lys	Ile	Gly	Glu	Arg	Tyr	Ile	Thr	His	Glu	Ser		
850					855					860							
Asp	Asp	Leu	Arg	Trp	Glu	Lys	Tyr	Ala	Gly	Glu	Gln	Gly	Leu	Gln	Tyr		
865					870					875						880	
Pro	Thr	His	Leu	Ile	Asn	Pro	Ser	Ala	Ser	His	Ser	Asp	Thr	Pro	Glu		
885					890					895							
Thr	Glu	Glu	Thr	Glu	Met	Lys	Ala	Leu	Gly	Glu	Arg	Val	Ser	Ile	Leu		
900					905					910							

⟨210⟩ 128

<211> 227

<212> PRT

〈213〉 智人

<400> 128

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

Arg Ala Val Val Leu Ser His Tyr Ile His Asn Leu Ser Ser Glu Met		
50	55	60
Phe Ser Glu Phe Asp Lys Arg Tyr Thr His Gly Arg Gly Phe Ile Thr		
65	70	75 80
Lys Ala Ile Asn Ser Cys His Thr Ser Ser Leu Ala Thr Pro Glu Asp		
	85	90 95
Lys Glu Gln Ala Gln Gln Met Asn Gln Lys Asp Phe Leu Ser Leu Ile		
	100	105 110
Val Ser Ile Leu Arg Ser Trp Asn Glu Pro Leu Tyr His Leu Val Thr		
	115	120 125
Glu Val Arg Gly Met Gln Glu Ala Pro Glu Ala Ile Leu Ser Lys Ala		
	130	135 140
Val Glu Ile Glu Glu Gln Thr Lys Arg Leu Leu Glu Gly Met Glu Leu		
145	150	155 160
Ile Val Ser Gln Val His Pro Glu Thr Lys Glu Asn Glu Ile Tyr Pro		
	165	170 175
Val Trp Ser Gly Leu Pro Ser Leu Gln Met Ala Asp Glu Glu Ser Arg		
	180	185 190
Leu Ser Ala Tyr Tyr Asn Leu Leu His Cys Leu Arg Arg Asp Ser His		
	195	200 205
Lys Ile Asp Asn Tyr Leu Lys Leu Leu Lys Cys Arg Ile Ile His Asn		
210	215	220
Asn Asn Cys		
225		
<210> 129		
<211> 226		
<212> PRT		
<213> 智人		
<400> 129		
Met Phe Thr Leu Leu Val Leu Leu Ser Gln Leu Pro Thr Val Thr Leu		
1	5	10 15
Gly Phe Pro His Cys Ala Arg Gly Pro Lys Ala Ser Lys His Ala Gly		
	20	25 30
Glu Glu Val Phe Thr Ser Lys Glu Glu Ala Asn Phe Phe Ile His Arg		
	35	40 45
Arg Leu Leu Tyr Asn Arg Phe Asp Leu Glu Leu Phe Thr Pro Gly Asn		
50	55	60
Leu Glu Arg Glu Cys Asn Glu Glu Leu Cys Asn Tyr Glu Glu Ala Arg		
65	70	75 80

Glu	Ile	Phe	Val	Asp	Glu	Asp	Lys	Thr	Ile	Ala	Phe	Trp	Gln	Glu	Tyr
				85					90					95	
Ser	Ala	Lys	Gly	Pro	Thr	Thr	Lys	Ser	Asp	Gly	Asn	Arg	Glu	Lys	Ile
			100					105					110		
Asp	Val	Met	Gly	Leu	Leu	Thr	Gly	Leu	Ile	Ala	Ala	Gly	Val	Phe	Leu
			115					120					125		
Val	Ile	Phe	Gly	Leu	Leu	Gly	Tyr	Tyr	Leu	Cys	Ile	Thr	Lys	Cys	Asn
			130					135					140		
Arg	Leu	Gln	His	Pro	Cys	Ser	Ser	Ala	Val	Tyr	Glu	Arg	Gly	Arg	His
145					150					155					160
Thr	Pro	Ser	Ile	Ile	Phe	Arg	Arg	Pro	Glu	Glu	Ala	Ala	Leu	Ser	Pro
					165					170					175
Leu	Pro	Pro	Ser	Val	Glu	Asp	Ala	Gly	Leu	Pro	Ser	Tyr	Glu	Gln	Ala
			180					185						190	
Val	Ala	Leu	Thr	Arg	Lys	His	Ser	Val	Ser	Pro	Pro	Pro	Pro	Tyr	Pro
			195					200						205	
Gly	His	Thr	Lys	Gly	Phe	Arg	Val	Phe	Lys	Lys	Ser	Met	Ser	Leu	Pro
			210					215						220	
Ser	His														
225															
<210>	130														
<211>	254														
<212>	PRT														
<213>	智人														
<400>	130														
Met	Ala	Ser	Leu	Leu	Lys	Val	Asp	Gln	Glu	Val	Lys	Leu	Lys	Val	Asp
1				5					10					15	
Ser	Phe	Arg	Glu	Arg	Ile	Thr	Ser	Glu	Ala	Glu	Asp	Leu	Val	Ala	Asn
			20					25					30		
Phe	Phe	Pro	Lys	Lys	Leu	Leu	Glu	Leu	Asp	Ser	Phe	Leu	Lys	Glu	Pro
			35					40					45		
Ile	Leu	Asn	Ile	His	Asp	Leu	Thr	Gln	Ile	His	Ser	Asp	Met	Asn	Leu
			50					55					60		
Pro	Val	Pro	Asp	Pro	Ile	Leu	Leu	Thr	Asn	Ser	His	Asp	Gly	Leu	Asp
65					70					75					80
Gly	Pro	Thr	Tyr	Lys	Lys	Arg	Arg	Leu	Asp	Glu	Cys	Glu	Glu	Ala	Phe
				85						90					95
Gln	Gly	Thr	Lys	Val	Phe	Val	Met	Pro	Asn	Gly	Met	Leu	Lys	Ser	Asn
			100						105						110

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

<210> 131

<211> 403

<212> PRT

<213> 智人

<400> 131

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

Gly Arg Thr Gly Val Met Ile Cys Ala Tyr Leu Leu His Arg Gly Lys		
130	135	140
Phe Leu Lys Ala Gln Glu Ala Leu Asp Phe Tyr Gly Glu Val Arg Thr		
145	150	155 160
Arg Asp Lys Lys Gly Val Thr Ile Pro Ser Gln Arg Arg Tyr Val Tyr		
165	170	175
Tyr Tyr Ser Tyr Leu Leu Lys Asn His Leu Asp Tyr Arg Pro Val Ala		
180	185	190
Leu Leu Phe His Lys Met Met Phe Glu Thr Ile Pro Met Phe Ser Gly		
195	200	205
Gly Thr Cys Asn Pro Gln Phe Val Val Cys Gln Leu Lys Val Lys Ile		
210	215	220
Tyr Ser Ser Asn Ser Gly Pro Thr Arg Arg Glu Asp Lys Phe Met Tyr		
225	230	235 240
Phe Glu Phe Pro Gln Pro Leu Pro Val Cys Gly Asp Ile Lys Val Glu		
245	250	255
Phe Phe His Lys Gln Asn Lys Met Leu Lys Lys Asp Lys Met Phe His		
260	265	270
Phe Trp Val Asn Thr Phe Phe Ile Pro Gly Pro Glu Glu Thr Ser Glu		
275	280	285
Lys Val Glu Asn Gly Ser Leu Cys Asp Gln Glu Ile Asp Ser Ile Cys		
290	295	300
Ser Ile Glu Arg Ala Asp Asn Asp Lys Glu Tyr Leu Val Leu Thr Leu		
305	310	315 320
Thr Lys Asn Asp Leu Asp Lys Ala Asn Lys Asp Lys Ala Asn Arg Tyr		
325	330	335
Phe Ser Pro Asn Phe Lys Val Lys Leu Tyr Phe Thr Lys Thr Val Glu		
340	345	350
Glu Pro Ser Asn Pro Glu Ala Ser Ser Ser Thr Ser Val Thr Pro Asp		
355	360	365
Val Ser Asp Asn Glu Pro Asp His Tyr Arg Tyr Ser Asp Thr Thr Asp		
370	375	380
Ser Asp Pro Glu Asn Glu Pro Phe Asp Glu Asp Gln His Thr Gln Ile		
385	390	395 400
Thr Lys Val		
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<212> PRT		
<213> 智人		

<400> 132

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

Ser Asn Ser Glu Asp Lys Asp Arg Lys Gly Met Leu Gln Leu Lys Ile			
305	310	315	320
Ala Gly Ala Pro Glu Pro Leu Thr Val Thr Ala Pro Ser Leu Thr Ile			
	325	330	335
Ala Glu Asn Met Ala Asp Leu Ile Asp Gly Tyr Cys Arg Leu Val Asn			
	340	345	350
Gly Thr Ser Gln Ser Phe Ile Ile Arg Pro Gln Lys Glu Gly Glu Arg			
	355	360	365
Ala Leu Pro Ser Ile Pro Lys Leu Ala Asn Ser Glu Lys Gln Gly Met			
	370	375	380
Arg Thr His Ala Val Ser Val Ser Glu Thr Asp Asp Tyr Ala Glu Ile			
385	390	395	400
Ile Asp Glu Glu Asp Thr Tyr Thr Met Pro Ser Thr Arg Asp Tyr Glu			
	405	410	415
Ile Gln Arg Glu Arg Ile Glu Leu Gly Arg Cys Ile Gly Glu Gly Gln			
	420	425	430
Phe Gly Asp Val His Gln Gly Ile Tyr Met Ser Pro Glu Asn Pro Ala			
	435	440	445
Leu Ala Val Ala Ile Lys Thr Cys Lys Asn Cys Thr Ser Asp Ser Val			
	450	455	460
Arg Glu Lys Phe Leu Gln Glu Ala Leu Thr Met Arg Gln Phe Asp His			
465	470	475	480
Pro His Ile Val Lys Leu Ile Gly Val Ile Thr Glu Asn Pro Val Trp			
	485	490	495
Ile Ile Met Glu Leu Cys Thr Leu Gly Glu Leu Arg Ser Phe Leu Gln			
	500	505	510
Val Arg Lys Tyr Ser Leu Asp Leu Ala Ser Leu Ile Leu Tyr Ala Tyr			
	515	520	525
Gln Leu Ser Thr Ala Leu Ala Tyr Leu Glu Ser Lys Arg Phe Val His			
	530	535	540
Arg Asp Ile Ala Ala Arg Asn Val Leu Val Ser Ser Asn Asp Cys Val			
545	550	555	560
Lys Leu Gly Asp Phe Gly Leu Ser Arg Tyr Met Glu Asp Ser Thr Tyr			
	565	570	575
Tyr Lys Ala Ser Lys Gly Lys Leu Pro Ile Lys Trp Met Ala Pro Glu			
	580	585	590
Ser Ile Asn Phe Arg Arg Phe Thr Ser Ala Ser Asp Val Trp Met Phe			
	595	600	605
Gly Val Cys Met Trp Glu Ile Leu Met His Gly Val Lys Pro Phe Gln			

610	615	620
Gly Val Lys Asn Asn Asp	Val Ile Gly Arg Ile Glu Asn Gly Glu Arg	
625	630	635
Leu Pro Met Pro Pro Asn Cys Pro Pro Thr Leu Tyr Ser Leu Met Thr		640
	645	650
Lys Cys Trp Ala Tyr Asp Pro Ser Arg Arg Pro Arg Phe Thr Glu Leu		655
	660	665
Lys Ala Gln Leu Ser Thr Ile Leu Glu Glu Glu Lys Ala Gln Gln Glu		670
	675	680
Glu Arg Met Arg Met Glu Ser Arg Arg Gln Ala Thr Val Ser Trp Asp		685
690	695	700
Ser Gly Gly Ser Asp Glu Ala Pro Pro Lys Pro Ser Arg Pro Gly Tyr		705
	710	715
Pro Ser Pro Arg Ser Ser Glu Gly Phe Tyr Pro Ser Pro Gln His Met		720
	725	730
Val Gln Thr Asn His Tyr Gln Val Ser Gly Tyr Pro Gly Ser His Gly		735
	740	745
Ile Thr Ala Met Ala Gly Ser Ile Tyr Pro Gly Gln Ala Ser Leu Leu		750
	755	760
Asp Gln Thr Asp Ser Trp Asn His Arg Pro Gln Glu Ile Ala Met Trp		765
770	775	780
Gln Pro Asn Val Glu Asp Ser Thr Val Leu Asp Leu Arg Gly Ile Gly		785
	790	795
Gln Val Leu Pro Thr His Leu Met Glu Glu Arg Leu Ile Arg Gln Gln		800
	805	810
Gln Glu Met Glu Glu Asp Gln Arg Trp Leu Glu Lys Glu Glu Arg Phe		815
	820	825
Leu Lys Pro Asp Val Arg Leu Ser Arg Gly Ser Ile Asp Arg Glu Asp		830
	835	840
Gly Ser Leu Gln Gly Pro Ile Gly Asn Gln His Ile Tyr Gln Pro Val		845
	850	855
Gly Lys Pro Asp Pro Ala Ala Pro Pro Lys Lys Pro Pro Arg Pro Gly		860
865	870	875
Ala Pro Gly His Leu Gly Ser Leu Ala Ser Leu Ser Ser Pro Ala Asp		880
	885	890
Ser Tyr Asn Glu Gly Val Lys Leu Gln Pro Gln Glu Ile Ser Pro Pro		895
	900	905
Pro Thr Ala Asn Leu Asp Arg Ser Asn Asp Lys Val Tyr Glu Asn Val		910
	915	920
		925

Thr Gly Leu Val Lys Ala Val Ile Glu Met Ser Ser Lys Ile Gln Pro		
930	935	940
Ala Pro Pro Glu Glu Tyr Val Pro Met Val Lys Glu Val Gly Leu Ala		
945	950	955 960
Leu Arg Thr Leu Leu Ala Thr Val Asp Glu Thr Ile Pro Leu Leu Pro		
	965	970 975
Ala Ser Thr His Arg Glu Ile Glu Met Ala Gln Lys Leu Leu Asn Ser		
	980	985 990
Asp Leu Gly Glu Leu Ile Asn Lys Met Lys Leu Ala Gln Gln Tyr Val		
	995	1000 1005
Met Thr Ser Leu Gln Gln Glu Tyr Lys Lys Gln Met Leu Thr Ala		
	1010	1015 1020
Ala His Ala Leu Ala Val Asp Ala Lys Asn Leu Leu Asp Val Ile		
	1025	1030 1035
Asp Gln Ala Arg Leu Lys Met Leu Gly Gln Thr Arg Pro His		
	1040	1045 1050
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Met Ser Gly Val Ser Glu Pro Leu Ser Arg Val Lys Leu Gly Thr Leu		
1	5	10 15
Arg Arg Pro Glu Gly Pro Ala Glu Pro Met Val Val Val Pro Val Asp		
	20	25 30
Val Glu Lys Glu Asp Val Arg Ile Leu Lys Val Cys Phe Tyr Ser Asn		
	35	40 45
Ser Phe Asn Pro Gly Lys Asn Phe Lys Leu Val Lys Cys Thr Val Gln		
	50	55 60
Thr Glu Ile Arg Glu Ile Ile Thr Ser Ile Leu Leu Ser Gly Arg Ile		
65	70	75 80
Gly Pro Asn Ile Arg Leu Ala Glu Cys Tyr Gly Leu Arg Leu Lys His		
	85	90 95
Met Lys Ser Asp Glu Ile His Trp Leu His Pro Gln Met Thr Val Gly		
	100	105 110
Glu Val Gln Asp Lys Tyr Glu Cys Leu His Val Glu Ala Glu Trp Arg		
	115	120 125
Tyr Asp Leu Gln Ile Arg Tyr Leu Pro Glu Asp Phe Met Glu Ser Leu		
	130	135 140

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

450	455	460
Leu Asp Asn Lys Glu Lys Phe Met Ser Glu Ala Val Ile Met Lys Asn		
465	470	475
Leu Asp His Pro His Ile Val Lys Leu Ile Gly Ile Ile Glu Glu Glu		480
	485	490
Pro Thr Trp Ile Ile Met Glu Leu Tyr Pro Tyr Gly Glu Leu Gly His		495
	500	505
Tyr Leu Glu Arg Asn Lys Asn Ser Leu Lys Val Leu Thr Leu Val Leu		510
	515	520
Tyr Ser Leu Gln Ile Cys Lys Ala Met Ala Tyr Leu Glu Ser Ile Asn		525
	530	535
Cys Val His Arg Asp Ile Ala Val Arg Asn Ile Leu Val Ala Ser Pro		540
545	550	555
Glu Cys Val Lys Leu Gly Asp Phe Gly Leu Ser Arg Tyr Ile Glu Asp		560
	565	570
Glu Asp Tyr Tyr Lys Ala Ser Val Thr Arg Leu Pro Ile Lys Trp Met		575
	580	585
Ser Pro Glu Ser Ile Asn Phe Arg Arg Phe Thr Thr Ala Ser Asp Val		590
	595	600
Trp Met Phe Ala Val Cys Met Trp Glu Ile Leu Ser Phe Gly Lys Gln		605
	610	615
Pro Phe Phe Trp Leu Glu Asn Lys Asp Val Ile Gly Val Leu Glu Lys		620
625	630	635
Gly Asp Arg Leu Pro Lys Pro Asp Leu Cys Pro Pro Val Leu Tyr Thr		640
	645	650
Leu Met Thr Arg Cys Trp Asp Tyr Asp Pro Ser Asp Arg Pro Arg Phe		655
	660	665
Thr Glu Leu Val Cys Ser Leu Ser Asp Val Tyr Gln Met Glu Lys Asp		670
	675	680
Ile Ala Met Glu Gln Glu Arg Asn Ala Arg Tyr Arg Thr Pro Lys Ile		685
	690	695
Leu Glu Pro Thr Ala Phe Gln Glu Pro Pro Pro Lys Pro Ser Arg Pro		700
705	710	715
Lys Tyr Arg Pro Pro Pro Gln Thr Asn Leu Leu Ala Pro Lys Leu Gln		720
	725	730
Phe Gln Val Pro Glu Gly Leu Cys Ala Ser Ser Pro Thr Leu Thr Ser		735
	740	745
Pro Met Glu Tyr Pro Ser Pro Val Asn Ser Leu His Thr Pro Pro Leu		750
	755	760
		765

His Arg His Asn Val Phe Lys Arg His Ser Met Arg Glu Glu Asp Phe			
770	775	780	
Ile Gln Pro Ser Ser Arg Glu Glu Ala Gln Gln Leu Trp Glu Ala Glu			
785	790	795	800
Lys Val Lys Met Arg Gln Ile Leu Asp Lys Gln Gln Lys Gln Met Val			
	805	810	815
Glu Asp Tyr Gln Trp Leu Arg Gln Glu Glu Lys Ser Leu Asp Pro Met			
	820	825	830
Val Tyr Met Asn Asp Lys Ser Pro Leu Thr Pro Glu Lys Glu Val Gly			
	835	840	845
Tyr Leu Glu Phe Thr Gly Pro Pro Gln Lys Pro Pro Arg Leu Gly Ala			
	850	855	860
Gln Ser Ile Gln Pro Thr Ala Asn Leu Asp Arg Thr Asp Asp Leu Val			
865	870	875	880
Tyr Leu Asn Val Met Glu Leu Val Arg Ala Val Leu Glu Leu Lys Asn			
	885	890	895
Glu Leu Cys Gln Leu Pro Pro Glu Gly Tyr Val Val Val Val Lys Asn			
	900	905	910
Val Gly Leu Thr Leu Arg Lys Leu Ile Gly Ser Val Asp Asp Leu Leu			
	915	920	925
Pro Ser Leu Pro Ser Ser Ser Arg Thr Glu Ile Glu Gly Thr Gln Lys			
	930	935	940
Leu Leu Asn Lys Asp Leu Ala Glu Leu Ile Asn Lys Met Arg Leu Ala			
945	950	955	960
Gln Gln Asn Ala Val Thr Ser Leu Ser Glu Glu Cys Lys Arg Gln Met			
	965	970	975
Leu Thr Ala Ser His Thr Leu Ala Val Asp Ala Lys Asn Leu Leu Asp			
	980	985	990
Ala Val Asp Gln Ala Lys Val Leu Ala Asn Leu Ala His Pro Pro Ala			
	995	1000	1005
Glu			
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<211> 108			
<212> PRT			
<213> 智人			
<400> 134			
Met Ala Ala Ala Met Asp Val Asp Thr Pro Ser Gly Thr Asn Ser Gly			
1	5	10	15
Ala Gly Lys Lys Arg Phe Glu Val Lys Lys Trp Asn Ala Val Ala Leu			

<212> PRT

<213> 智人

<400> 136

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

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Leu

<210> 137

<211> 196

<212> PRT

<213> 智人

<400> 137

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

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50	55	60
Asp Tyr Asp Arg Leu Arg Pro Leu Ser Tyr Pro Asp Thr Asp Val Ile		
65	70	75
Leu Met Cys Phe Ser Val Asp Ser Pro Asp Ser Leu Glu Asn Ile Pro		80
	85	90
Glu Lys Trp Val Pro Glu Val Lys His Phe Cys Pro Asn Val Pro Ile		95
	100	105
Ile Leu Val Ala Asn Lys Lys Asp Leu Arg Ser Asp Glu His Val Arg		110
	115	120
Thr Glu Leu Ala Arg Met Lys Gln Glu Pro Val Arg Thr Asp Asp Gly		125
	130	135
Arg Ala Met Ala Val Arg Ile Gln Ala Tyr Asp Tyr Leu Glu Cys Ser		140
145	150	155
Ala Lys Thr Lys Glu Gly Val Arg Glu Val Phe Glu Thr Ala Thr Arg		160
	165	170
Ala Ala Leu Gln Lys Arg Tyr Gly Ser Gln Asn Gly Cys Ile Asn Cys		175
	180	185
Cys Lys Val Leu		190
	195	
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<212> PRT		
<213> 智人		
<400> 138		
Met Ala Ala Ile Arg Lys Lys Leu Val Ile Val Gly Asp Gly Ala Cys		
1	5	10
Gly Lys Thr Cys Leu Leu Ile Val Phe Ser Lys Asp Gln Phe Pro Glu		15
	20	25
Val Tyr Val Pro Thr Val Phe Glu Asn Tyr Ile Ala Asp Ile Glu Val		30
	35	40
Asp Gly Lys Gln Val Glu Leu Ala Leu Trp Asp Thr Ala Gly Gln Glu		45
50	55	60
Asp Tyr Asp Arg Leu Arg Pro Leu Ser Tyr Pro Asp Thr Asp Val Ile		
65	70	75
Leu Met Cys Phe Ser Ile Asp Ser Pro Asp Ser Leu Glu Asn Ile Pro		80
	85	90
Glu Lys Trp Thr Pro Glu Val Lys His Phe Cys Pro Asn Val Pro Ile		95
	100	105
Ile Leu Val Gly Asn Lys Lys Asp Leu Arg Gln Asp Glu His Thr Arg		110

115	120	125
Arg Glu Leu Ala Lys Met Lys Gln Glu Pro Val Arg Ser Glu Glu Gly		
130	135	140
Arg Asp Met Ala Asn Arg Ile Ser Ala Phe Gly Tyr Leu Glu Cys Ser		
145	150	155
Ala Lys Thr Lys Glu Gly Val Arg Glu Val Phe Glu Met Ala Thr Arg		
165	170	175
Ala Gly Leu Gln Val Arg Lys Asn Lys Arg Arg Arg Gly Cys Pro Ile		
180	185	190
Leu		
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<211> 295		
<212> PRT		
<213> 智人		
<400> 139		
Met Ser Gly Ala Leu Asp Val Leu Gln Met Lys Glu Glu Asp Val Leu		
1	5	10
Lys Phe Leu Ala Ala Gly Thr His Leu Gly Gly Thr Asn Leu Asp Phe		
20	25	30
Gln Met Glu Gln Tyr Ile Tyr Lys Arg Lys Ser Asp Gly Ile Tyr Ile		
35	40	45
Ile Asn Leu Lys Arg Thr Trp Glu Lys Leu Leu Leu Ala Ala Arg Ala		
50	55	60
Ile Val Ala Ile Glu Asn Pro Ala Asp Val Ser Val Ile Ser Ser Arg		
65	70	75
Asn Thr Gly Gln Arg Ala Val Leu Lys Phe Ala Ala Ala Thr Gly Ala		
85	90	95
Thr Pro Ile Ala Gly Arg Phe Thr Pro Gly Thr Phe Thr Asn Gln Ile		
100	105	110
Gln Ala Ala Phe Arg Glu Pro Arg Leu Leu Val Val Thr Asp Pro Arg		
115	120	125
Ala Asp His Gln Pro Leu Thr Glu Ala Ser Tyr Val Asn Leu Pro Thr		
130	135	140
Ile Ala Leu Cys Asn Thr Asp Ser Pro Leu Arg Tyr Val Asp Ile Ala		
145	150	155
Ile Pro Cys Asn Asn Lys Gly Ala His Ser Val Gly Leu Met Trp Trp		
165	170	175
Met Leu Ala Arg Glu Val Leu Arg Met Arg Gly Thr Ile Ser Arg Glu		
180	185	190

His	Pro	Trp	Glu	Val	Met	Pro	Asp	Leu	Tyr	Phe	Tyr	Arg	Asp	Pro	Glu	
195				200				205								
Glu	Ile	Glu	Lys	Glu	Glu	Gln	Ala	Ala	Ala	Glu	Lys	Ala	Val	Thr	Lys	
210				215				220								
Glu	Glu	Phe	Gln	Gly	Glu	Trp	Thr	Ala	Pro	Ala	Pro	Glu	Phe	Thr	Ala	
225				230				235				240				
Thr	Gln	Pro	Glu	Val	Ala	Asp	Trp	Ser	Glu	Gly	Val	Gln	Val	Pro	Ser	
				245				250				255				
Val	Pro	Ile	Gln	Gln	Phe	Pro	Thr	Glu	Asp	Trp	Ser	Ala	Gln	Pro	Ala	
				260				265				270				
Thr	Glu	Asp	Trp	Ser	Ala	Ala	Pro	Thr	Ala	Gln	Ala	Thr	Glu	Trp	Val	
				275				280				285				
Gly	Ala	Thr	Thr	Asp	Trp	Ser										
290				295												
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<211> 1410																
<212> PRT																
<213> 智人																
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Met	Asp	Ile	Tyr	Asp	Thr	Gln	Thr	Leu	Gly	Val	Val	Val	Phe	Gly	Gly	
1		5				10				15						
Phe	Met	Val	Val	Ser	Ala	Ile	Gly	Ile	Phe	Leu	Val	Ser	Thr	Phe	Ser	
20				25				30								
Met	Lys	Glu	Thr	Ser	Tyr	Glu	Glu	Ala	Leu	Ala	Asn	Gln	Arg	Lys	Glu	
35				40				45								
Met	Ala	Lys	Thr	His	His	Gln	Lys	Val	Glu	Lys	Lys	Lys	Lys	Glu	Lys	
50				55				60								
Thr	Val	Glu	Lys	Lys	Gly	Lys	Thr	Lys	Lys	Lys	Glu	Glu	Lys	Pro	Asn	
65		70				75				80						
Gly	Lys	Ile	Pro	Asp	His	Asp	Pro	Ala	Pro	Asn	Val	Thr	Val	Leu	Leu	
				85				90				95				
Arg	Glu	Pro	Val	Arg	Ala	Pro	Ala	Val	Ala	Val	Ala	Pro	Thr	Pro	Val	
100				105				110								
Gln	Pro	Pro	Ile	Ile	Val	Ala	Pro	Val	Ala	Thr	Val	Pro	Ala	Met	Pro	
115				120				125								
Gln	Glu	Lys	Leu	Ala	Ser	Ser	Pro	Lys	Asp	Lys	Lys	Lys	Lys	Glu	Lys	
130				135				140								
Lys	Val	Ala	Lys	Val	Glu	Pro	Ala	Val	Ser	Ser	Val	Val	Asn	Ser	Ile	
145		150				155				160						

Gln Val Leu Thr Ser Lys Ala Ala Ile Leu Glu Thr Ala Pro Lys Glu		
165	170	175
Val Pro Met Val Val Val Pro Pro Val Gly Ala Lys Gly Asn Thr Pro		
180	185	190
Ala Thr Gly Thr Thr Gln Gly Lys Lys Ala Glu Gly Thr Gln Asn Gln		
195	200	205
Ser Lys Lys Ala Glu Gly Ala Pro Asn Gln Gly Arg Lys Ala Glu Gly		
210	215	220
Thr Pro Asn Gln Gly Lys Lys Thr Glu Gly Thr Pro Asn Gln Gly Lys		
225	230	235
Lys Ala Glu Gly Thr Pro Asn Gln Gly Lys Lys Ala Glu Gly Thr Pro		
245	250	255
Asn Gln Gly Lys Lys Ala Glu Gly Ala Gln Asn Gln Gly Lys Lys Val		
260	265	270
Asp Thr Thr Pro Asn Gln Gly Lys Lys Val Glu Gly Ala Pro Thr Gln		
275	280	285
Gly Arg Lys Ala Glu Gly Ala Gln Asn Gln Ala Lys Lys Val Glu Gly		
290	295	300
Ala Gln Asn Gln Gly Lys Lys Ala Glu Gly Ala Gln Asn Gln Gly Lys		
305	310	315
Lys Gly Glu Gly Ala Gln Asn Gln Gly Lys Lys Ala Glu Gly Ala Gln		
325	330	335
Asn Gln Gly Lys Lys Ala Glu Gly Ala Gln Asn Gln Gly Lys Lys Ala		
340	345	350
Glu Gly Ala Gln Asn Gln Gly Lys Lys Ala Glu Gly Ala Gln Asn Gln		
355	360	365
Gly Lys Lys Ala Glu Gly Ala Gln Asn Gln Gly Lys Lys Ser Glu Gly		
370	375	380
Ala Gln Asn Gln Gly Lys Lys Val Glu Gly Ala Gln Asn Gln Gly Lys		
385	390	395
Lys Ala Glu Gly Ala Gln Asn Gln Gly Lys Lys Ala Glu Gly Ala Gln		
405	410	415
Asn Gln Gly Lys Lys Ala Glu Gly Ala Gln Asn Gln Gly Lys Lys Ala		
420	425	430
Glu Gly Ala Gln Asn Gln Gly Lys Lys Ala Glu Gly Ala Gln Asn Gln		
435	440	445
Gly Lys Lys Ala Glu Gly Ala Gln Asn Gln Gly Lys Lys Ala Glu Gly		
450	455	460
Ala Gln Asn Gln Gly Lys Lys Val Glu Gly Ala Gln Asn Gln Gly Lys		

465	470	475	480
Lys Ala Glu Gly	Ala Gln Asn Gln Gly	Lys Lys Ala Glu Gly	Ala Gln
	485	490	495
Asn Gln Gly Lys	Lys Ala Glu Gly	Ala Gln Asn Gln Gly	Gln Lys Gly
	500	505	510
Glu Gly Ala Gln	Asn Gln Gly Lys	Lys Thr Glu Gly	Ala Gln Gly Lys
	515	520	525
Lys Ala Glu Arg	Ser Pro Asn Gln Gly	Lys Lys Gly Glu Gly	Ala Pro
	530	535	540
Ile Gln Gly Lys	Lys Ala Asp Ser Val	Ala Asn Gln Gly	Thr Lys Val
545	550	555	560
Glu Gly Ile Thr	Asn Gln Gly Lys	Lys Ala Glu Gly	Ser Pro Ser Glu
	565	570	575
Gly Lys Lys Ala	Glu Gly Ser Pro	Asn Gln Gly Lys	Lys Lys Ala Asp Ala
	580	585	590
Ala Ala Asn Gln	Gly Lys Lys Thr	Glu Ser Ala Ser	Val Gln Gly Arg
	595	600	605
Asn Thr Asp Val	Ala Gln Ser Pro	Glu Ala Pro Lys	Gln Glu Ala Pro
	610	615	620
Ala Lys Lys Lys	Ser Gly Ser Lys	Lys Lys Gly Glu	Pro Gly Pro Pro
625	630	635	640
Asp Ala Asp Gly	Pro Leu Tyr Leu	Pro Tyr Lys Thr	Leu Val Ser Thr
	645	650	655
Val Gly Ser Met	Val Phe Asn Glu	Gly Glu Ala Gln	Arg Leu Ile Glu
	660	665	670
Ile Leu Ser Glu	Lys Ala Gly Ile	Ile Gln Asp Thr	Trp His Lys Ala
	675	680	685
Thr Gln Lys Gly	Asp Pro Val Ala	Ile Leu Lys Arg	Gln Leu Glu Glu
	690	695	700
Lys Glu Lys Leu	Leu Ala Thr Glu	Gln Glu Asp Ala	Ala Val Ala Lys
705	710	715	720
Ser Lys Leu Arg	Glu Leu Asn Lys	Glu Met Ala Ala	Glu Lys Ala Lys
	725	730	735
Ala Ala Ala Gly	Glu Ala Lys Val	Lys Lys Gln Leu	Val Ala Arg Glu
	740	745	750
Gln Glu Ile Thr	Ala Val Gln Ala	Arg Met Gln Ala	Ser Tyr Arg Glu
	755	760	765
His Val Lys Glu	Val Gln Gln Leu	Gln Gly Lys Ile	Arg Thr Leu Gln
	770	775	780

Glu Gln Leu Glu Asn Gly Pro Asn Thr Gln Leu Ala Arg Leu Gln Gln			
785	790	795	800
Glu Asn Ser Ile Leu Arg Asp Ala Leu Asn Gln Ala Thr Ser Gln Val			
	805	810	815
Glu Ser Lys Gln Asn Ala Glu Leu Ala Lys Leu Arg Gln Glu Leu Ser			
	820	825	830
Lys Val Ser Lys Glu Leu Val Glu Lys Ser Glu Ala Val Arg Gln Asp			
	835	840	845
Glu Gln Gln Arg Lys Ala Leu Glu Ala Lys Ala Ala Ala Phe Glu Lys			
	850	855	860
Gln Val Leu Gln Leu Gln Ala Ser His Arg Glu Ser Glu Glu Ala Leu			
865	870	875	880
Gln Lys Arg Leu Asp Glu Val Ser Arg Glu Leu Cys His Thr Gln Ser			
	885	890	895
Ser His Ala Ser Leu Arg Ala Asp Ala Glu Lys Ala Gln Glu Gln Gln			
	900	905	910
Gln Gln Met Ala Glu Leu His Ser Lys Leu Gln Ser Ser Glu Ala Glu			
	915	920	925
Val Arg Ser Lys Cys Glu Glu Leu Ser Gly Leu His Gly Gln Leu Gln			
	930	935	940
Glu Ala Arg Ala Glu Asn Ser Gln Leu Thr Glu Arg Ile Arg Ser Ile			
945	950	955	960
Glu Ala Leu Leu Glu Ala Gly Gln Ala Arg Asp Ala Gln Asp Val Gln			
	965	970	975
Ala Ser Gln Ala Glu Ala Asp Gln Gln Gln Thr Arg Leu Lys Glu Leu			
	980	985	990
Glu Ser Gln Val Ser Gly Leu Glu Lys Glu Ala Ile Glu Leu Arg Glu			
	995	1000	1005
Ala Val Glu Gln Gln Lys Val Lys Asn Asn Asp Leu Arg Glu Lys			
	1010	1015	1020
Asn Trp Lys Ala Met Glu Ala Leu Ala Thr Ala Glu Gln Ala Cys			
	1025	1030	1035
Lys Glu Lys Leu Leu Ser Leu Thr Gln Ala Lys Glu Glu Ser Glu			
	1040	1045	1050
Lys Gln Leu Cys Leu Ile Glu Ala Gln Thr Met Glu Ala Leu Leu			
	1055	1060	1065
Ala Leu Leu Pro Glu Leu Ser Val Leu Ala Gln Gln Asn Tyr Thr			
	1070	1075	1080
Glu Trp Leu Gln Asp Leu Lys Glu Lys Gly Pro Thr Leu Leu Lys			

1085	1090	1095
His Pro Pro Ala Pro Ala	Glu Pro Ser Ser Asp	Leu Ala Ser Lys
1100	1105	1110
Leu Arg Glu Ala Glu Glu	Thr Gln Ser Thr Leu	Gln Ala Glu Cys
1115	1120	1125
Asp Gln Tyr Arg Ser Ile	Leu Ala Glu Thr Glu	Gly Met Leu Arg
1130	1135	1140
Asp Leu Gln Lys Ser Val	Glu Glu Glu Glu Gln	Val Trp Arg Ala
1145	1150	1155
Lys Val Gly Ala Ala Glu	Glu Glu Leu Gln Lys	Ser Arg Val Thr
1160	1165	1170
Val Lys His Leu Glu Glu	Ile Val Glu Lys Leu	Lys Gly Glu Leu
1175	1180	1185
Glu Ser Ser Asp Gln Val	Arg Glu His Thr Ser	His Leu Glu Ala
1190	1195	1200
Glu Leu Glu Lys His Met	Ala Ala Ala Ser Ala	Glu Cys Gln Asn
1205	1210	1215
Tyr Ala Lys Glu Val Ala	Gly Leu Arg Gln Leu	Leu Leu Glu Ser
1220	1225	1230
Gln Ser Gln Leu Asp Ala	Ala Lys Ser Glu Ala	Gln Lys Gln Ser
1235	1240	1245
Asp Glu Leu Ala Leu Val	Arg Gln Gln Leu Ser	Glu Met Lys Ser
1250	1255	1260
His Val Glu Asp Gly Asp	Ile Ala Gly Ala Pro	Ala Ser Ser Pro
1265	1270	1275
Glu Ala Pro Pro Ala Glu	Gln Asp Pro Val Gln	Leu Lys Thr Gln
1280	1285	1290
Leu Glu Trp Thr Glu Ala	Ile Leu Glu Asp Glu	Gln Thr Gln Arg
1295	1300	1305
Gln Lys Leu Thr Ala Glu	Phe Glu Glu Ala Gln	Thr Ser Ala Cys
1310	1315	1320
Arg Leu Gln Glu Glu Leu	Glu Lys Leu Arg Thr	Ala Gly Pro Leu
1325	1330	1335
Glu Ser Ser Glu Thr Glu	Glu Ala Ser Gln Leu	Lys Glu Arg Leu
1340	1345	1350
Glu Lys Glu Lys Lys Leu	Thr Ser Asp Leu Gly	Arg Ala Ala Thr
1355	1360	1365
Arg Leu Gln Glu Leu Leu	Lys Thr Thr Gln Glu	Gln Leu Ala Arg
1370	1375	1380

Glu Lys Asp Thr Val Lys Lys Leu Gln Glu Gln Leu Glu Lys Ala
 1385 1390 1395

Glu Asp Gly Ser Ser Ser Lys Glu Gly Thr Ser Val
 1400 1405 1410

<210> 141

<211> 105

<212> PRT

<213> 智人

<400> 141

Met Ala Lys Ile Ser Ser Pro Thr Glu Thr Glu Arg Cys Ile Glu Ser
 1 5 10 15

Leu Ile Ala Val Phe Gln Lys Tyr Ala Gly Lys Asp Gly Tyr Asn Tyr
 20 25 30

Thr Leu Ser Lys Thr Glu Phe Leu Ser Phe Met Asn Thr Glu Leu Ala
 35 40 45

Ala Phe Thr Lys Asn Gln Lys Asp Pro Gly Val Leu Asp Arg Met Met
 50 55 60

Lys Lys Leu Asp Thr Asn Ser Asp Gly Gln Leu Asp Phe Ser Glu Phe
 65 70 75 80

Leu Asn Leu Ile Gly Gly Leu Ala Met Ala Cys His Asp Ser Phe Leu
 85 90 95

Lys Ala Val Pro Ser Gln Lys Arg Thr
 100 105

<210> 142

<211> 92

<212> PRT

<213> 智人

<400> 142

Met Thr Lys Leu Glu Glu His Leu Glu Gly Ile Val Asn Ile Phe His
 1 5 10 15

Gln Tyr Ser Val Arg Lys Gly His Phe Asp Thr Leu Ser Lys Gly Glu
 20 25 30

Leu Lys Gln Leu Leu Thr Lys Glu Leu Ala Asn Thr Ile Lys Asn Ile
 35 40 45

Lys Asp Lys Ala Val Ile Asp Glu Ile Phe Gln Gly Leu Asp Ala Asn
 50 55 60

Gln Asp Glu Gln Val Asp Phe Gln Glu Phe Ile Ser Leu Val Ala Ile
 65 70 75 80

Ala Leu Lys Ala Ala His Tyr His Thr His Lys Glu

<210>	144																
<211>	114																
<212>	PRT																
<213>	智人																
<400>	144																
Met	Thr	Cys	Lys	Met	Ser	Gln	Leu	Glu	Arg	Asn	Ile	Glu	Thr	Ile	Ile		
1				5					10					15			
Asn	Thr	Phe	His	Gln	Tyr	Ser	Val	Lys	Leu	Gly	His	Pro	Asp	Thr	Leu		
			20					25					30				
Asn	Gln	Gly	Glu	Phe	Lys	Glu	Leu	Val	Arg	Lys	Asp	Leu	Gln	Asn	Phe		
		35					40					45					
Leu	Lys	Lys	Glu	Asn	Lys	Asn	Glu	Lys	Val	Ile	Glu	His	Ile	Met	Glu		
	50					55					60						
Asp	Leu	Asp	Thr	Asn	Ala	Asp	Lys	Gln	Leu	Ser	Phe	Glu	Glu	Phe	Ile		
65					70					75					80		
Met	Leu	Met	Ala	Arg	Leu	Thr	Trp	Ala	Ser	His	Glu	Lys	Met	His	Glu		
				85					90					95			
Gly	Asp	Glu	Gly	Pro	Gly	His	His	His	Lys	Pro	Gly	Leu	Gly	Glu	Gly		
			100					105					110				
Thr	Pro																
<210>	145																

<211> 122

<212> PRT

<213> 智人

<400> 145

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

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<210> 146

<211> 122

<212> PRT

<213> 智人

<400> 146

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

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Phe Arg Pro Ala Gly Leu Pro Glu Lys Tyr
 115 120
 <210> 147
 <211> 276
 <212> PRT
 <213> 智人
 <400> 147
 Met Asp Ser Ser Arg Glu Pro Thr Leu Gly Arg Leu Asp Ala Ala Gly
 1 5 10 15
 Phe Trp Gln Val Trp Gln Arg Phe Asp Ala Asp Glu Lys Gly Tyr Ile
 20 25 30
 Glu Glu Lys Glu Leu Asp Ala Phe Phe Leu His Met Leu Met Lys Leu
 35 40 45
 Gly Thr Asp Asp Thr Val Met Lys Ala Asn Leu His Lys Val Lys Gln
 50 55 60
 Gln Phe Met Thr Thr Gln Asp Ala Ser Lys Asp Gly Arg Ile Arg Met
 65 70 75 80
 Lys Glu Leu Ala Gly Met Phe Leu Ser Glu Asp Glu Asn Phe Leu Leu
 85 90 95
 Leu Phe Arg Arg Glu Asn Pro Leu Asp Ser Ser Val Glu Phe Met Gln
 100 105 110
 Ile Trp Arg Lys Tyr Asp Ala Asp Ser Ser Gly Phe Ile Ser Ala Ala
 115 120 125
 Glu Leu Arg Asn Phe Leu Arg Asp Leu Phe Leu His His Lys Lys Ala
 130 135 140
 Ile Ser Glu Ala Lys Leu Glu Glu Tyr Thr Gly Thr Met Met Lys Ile
 145 150 155 160
 Phe Asp Arg Asn Lys Asp Gly Arg Leu Asp Leu Asn Asp Leu Ala Arg
 165 170 175
 Ile Leu Ala Leu Gln Glu Asn Phe Leu Leu Gln Phe Lys Met Asp Ala
 180 185 190
 Cys Ser Thr Glu Glu Arg Lys Arg Asp Phe Glu Lys Ile Phe Ala Tyr
 195 200 205
 Tyr Asp Val Ser Lys Thr Gly Ala Leu Glu Gly Pro Glu Val Asp Gly
 210 215 220
 Phe Val Lys Asp Met Met Glu Leu Val Gln Pro Ser Ile Ser Gly Val
 225 230 235 240
 Asp Leu Asp Lys Phe Arg Glu Ile Leu Leu Arg His Cys Asp Val Asn
 245 250 255

Lys Asp Gly Lys Ile Gln Lys Ser Glu Leu Ala Leu Cys Leu Gly Leu
 260 265 270
 Lys Ile Asn Pro
 275
 <210> 148
 <211> 435
 <212> PRT
 <213> 智人
 <400> 148
 Met Ser Gly Tyr Gln Arg Arg Pro Gly Ala Thr Pro Leu Ser Arg Ala
 1 5 10 15
 Arg Ser Leu Ala Ile Pro Asp Ala Pro Ala Phe Tyr Glu Arg Arg Ser
 20 25 30
 Cys Leu Pro Gln Leu Asn Cys Glu Arg Pro His Gly Arg Asp Leu Asp
 35 40 45
 Ser Pro Phe Phe Gly Ile Arg Pro Ala Phe Met Cys Tyr Val Pro Ser
 50 55 60
 Pro Val Leu Ala Ser Val Gly Asp Thr Asp Phe Gly Tyr Gly Lys Gly
 65 70 75 80
 Lys Cys Ser Lys Gln Ser Pro Ser Gly Ala His Gly Thr His Phe Gly
 85 90 95
 Asp Asp Arg Phe Glu Asp Leu Glu Glu Ala Asn Pro Phe Ser Phe Arg
 100 105 110
 Glu Phe Leu Lys Thr Lys Asn Leu Gly Leu Ser Lys Glu Asp Pro Ala
 115 120 125
 Ser Arg Ile Tyr Ala Lys Glu Ala Ser Arg His Ser Leu Gly Leu Asp
 130 135 140
 His Asn Ser Pro Pro Ser Gln Thr Gly Gly Tyr Gly Leu Glu Tyr Gln
 145 150 155 160
 Gln Pro Phe Phe Glu Asp Pro Thr Gly Ala Gly Asp Leu Leu Asp Glu
 165 170 175
 Glu Glu Asp Glu Asp Thr Gly Trp Ser Gly Ala Tyr Leu Pro Ser Ala
 180 185 190
 Ile Glu Gln Thr His Pro Glu Arg Val Pro Ala Gly Thr Ser Pro Cys
 195 200 205
 Ser Thr Tyr Leu Ser Phe Phe Ser Thr Pro Ser Glu Leu Ala Gly Pro
 210 215 220
 Glu Ser Leu Pro Ser Trp Ala Leu Ser Asp Thr Asp Ser Arg Val Ser
 225 230 235 240

Pro Ala Ser Pro Ala Gly Ser Pro Ser Ala Asp Phe Ala Val His Gly
 245 250 255
 Glu Ser Leu Gly Asp Arg His Leu Arg Thr Leu Gln Ile Ser Tyr Asp
 260 265 270
 Ala Leu Lys Asp Glu Asn Ser Lys Leu Arg Arg Lys Leu Asn Glu Val
 275 280 285
 Gln Ser Phe Ser Glu Ala Gln Thr Glu Met Val Arg Thr Leu Glu Arg
 290 295 300
 Lys Leu Glu Ala Lys Met Ile Lys Glu Glu Ser Asp Tyr His Asp Leu
 305 310 315 320
 Glu Ser Val Val Gln Gln Val Glu Gln Asn Leu Glu Leu Met Thr Lys
 325 330 335
 Arg Ala Val Lys Ala Glu Asn His Val Val Lys Leu Lys Gln Glu Ile
 340 345 350
 Ser Leu Leu Gln Ala Gln Val Ser Asn Phe Gln Arg Glu Asn Glu Ala
 355 360 365
 Leu Arg Cys Gly Gln Gly Ala Ser Leu Thr Val Val Lys Gln Asn Ala
 370 375 380
 Asp Val Ala Leu Gln Asn Leu Arg Val Val Met Asn Ser Ala Gln Ala
 385 390 395 400
 Ser Ile Lys Gln Leu Val Ser Gly Ala Glu Thr Leu Asn Leu Val Ala
 405 410 415
 Glu Ile Leu Lys Ser Ile Asp Arg Ile Ser Glu Val Lys Asp Glu Glu
 420 425 430
 Glu Asp Ser
 435
 <210> 149
 <211> 664
 <212> PRT
 <213> 智人
 <400> 149
 Met Ser Gly Val Arg Gly Leu Ser Arg Leu Leu Ser Ala Arg Arg Leu
 1 5 10 15
 Ala Leu Ala Lys Ala Trp Pro Thr Val Leu Gln Thr Gly Thr Arg Gly
 20 25 30
 Phe His Phe Thr Val Asp Gly Asn Lys Arg Ala Ser Ala Lys Val Ser
 35 40 45
 Asp Ser Ile Ser Ala Gln Tyr Pro Val Val Asp His Glu Phe Asp Ala
 50 55 60

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

370	375	380
Glu Thr Ala Met Ile Phe	Ala Gly Val Asp Val	Thr Lys Glu Pro Ile
385	390	395
Pro Val Leu Pro Thr Val	His Tyr Asn Met Gly Gly	Ile Pro Thr Asn
405	410	415
Tyr Lys Gly Gln Val Leu	Arg His Val Asn Gly Gln	Asp Gln Ile Val
420	425	430
Pro Gly Leu Tyr Ala Cys	Gly Glu Ala Ala Cys Ala	Ser Val His Gly
435	440	445
Ala Asn Arg Leu Gly Ala	Asn Ser Leu Leu Asp Leu	Val Val Phe Gly
450	455	460
Arg Ala Cys Ala Leu Ser	Ile Glu Glu Ser Cys Arg	Pro Gly Asp Lys
465	470	475
Val Pro Pro Ile Lys Pro	Asn Ala Gly Glu Glu Ser	Val Met Asn Leu
485	490	495
Asp Lys Leu Arg Phe Ala	Asp Gly Ser Ile Arg Thr	Ser Glu Leu Arg
500	505	510
Leu Ser Met Gln Lys Ser	Met Gln Asn His Ala Ala	Val Phe Arg Val
515	520	525
Gly Ser Val Leu Gln Glu	Gly Cys Gly Lys Ile Ser	Lys Leu Tyr Gly
530	535	540
Asp Leu Lys His Leu Lys	Thr Phe Asp Arg Gly Met	Val Trp Asn Thr
545	550	555
Asp Leu Val Glu Thr Leu	Glu Leu Gln Asn Leu Met	Leu Cys Ala Leu
565	570	575
Gln Thr Ile Tyr Gly Ala	Glu Ala Arg Lys Glu Ser	Arg Gly Ala His
580	585	590
Ala Arg Glu Asp Tyr Lys	Val Arg Ile Asp Glu Tyr	Asp Tyr Ser Lys
595	600	605
Pro Ile Gln Gly Gln Gln	Lys Lys Pro Phe Glu Glu	His Trp Arg Lys
610	615	620
His Thr Leu Ser Tyr Val	Asp Val Gly Thr Gly Lys	Val Thr Leu Glu
625	630	635
Tyr Arg Pro Val Ile Asp	Lys Thr Leu Asn Glu Ala	Asp Cys Ala Thr
645	650	655
Val Pro Pro Ala Ile Arg	Ser Tyr	
660		

<210> 150

<211> 472

<212> PRT

<213> 智人

<400> 150

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

Lys Val Ile Gln Val Pro Pro Lys Lys Val Lys Gly Trp Leu Leu Pro			
290	295	300	
Glu Met Pro Gly Leu Ile Thr Asp Ile Leu Leu Ser Leu Asp Asp Arg			
305	310	315	320
Phe Leu Tyr Phe Ser Asn Trp Leu His Gly Asp Leu Arg Gln Tyr Asp			
	325	330	335
Ile Ser Asp Pro Gln Arg Pro Arg Leu Thr Gly Gln Leu Phe Leu Gly			
	340	345	350
Gly Ser Ile Val Lys Gly Gly Pro Val Gln Val Leu Glu Asp Glu Glu			
	355	360	365
Leu Lys Ser Gln Pro Glu Pro Leu Val Val Lys Gly Lys Arg Val Ala			
	370	375	380
Gly Gly Pro Gln Met Ile Gln Leu Ser Leu Asp Gly Lys Arg Leu Tyr			
385	390	395	400
Ile Thr Thr Ser Leu Tyr Ser Ala Trp Asp Lys Gln Phe Tyr Pro Asp			
	405	410	415
Leu Ile Arg Glu Gly Ser Val Met Leu Gln Val Asp Val Asp Thr Val			
	420	425	430
Lys Gly Gly Leu Lys Leu Asn Pro Asn Phe Leu Val Asp Phe Gly Lys			
	435	440	445
Glu Pro Leu Gly Pro Ala Leu Ala His Glu Leu Arg Tyr Pro Gly Gly			
450	455	460	
Asp Cys Ser Ser Asp Ile Trp Ile			
465	470		
<210> 151			
<211> 412			
<212> PRT			
<213> 智人			
<400> 151			
Met Pro Leu Gln Leu Leu Leu Leu Leu Ile Leu Leu Gly Pro Gly Asn			
1	5	10	15
Ser Leu Gln Leu Trp Asp Thr Trp Ala Asp Glu Ala Glu Lys Ala Leu			
	20	25	30
Gly Pro Leu Leu Ala Arg Asp Arg Arg Gln Ala Thr Glu Tyr Glu Tyr			
	35	40	45
Leu Asp Tyr Asp Phe Leu Pro Glu Thr Glu Pro Pro Glu Met Leu Arg			
50	55	60	
Asn Ser Thr Asp Thr Thr Pro Leu Thr Gly Pro Gly Thr Pro Glu Ser			
65	70	75	80

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

385	390	395	400
Glu Gly Asp Asp Leu Thr Leu His Ser Phe Leu Pro			
	405	410	
<210> 152			
<211> 586			
<212> PRT			
<213> 智人			
<400> 152			
Met Lys Lys Ser Tyr Ser Gly Gly Thr Arg Thr Ser Ser Gly Arg Leu			
1	5	10	15
Arg Arg Leu Gly Asp Ser Ser Gly Pro Ala Leu Lys Arg Ser Phe Glu			
	20	25	30
Val Glu Glu Val Glu Thr Pro Asn Ser Thr Pro Pro Arg Arg Val Gln			
	35	40	45
Thr Pro Leu Leu Arg Ala Thr Val Ala Ser Ser Thr Gln Lys Phe Gln			
	50	55	60
Asp Leu Gly Val Lys Asn Ser Glu Pro Ser Ala Arg His Val Asp Ser			
65	70	75	80
Leu Ser Gln Arg Ser Pro Lys Ala Ser Leu Arg Arg Val Glu Leu Ser			
	85	90	95
Gly Pro Lys Ala Ala Glu Pro Val Ser Arg Arg Thr Glu Leu Ser Ile			
	100	105	110
Asp Ile Ser Ser Lys Gln Val Glu Asn Ala Gly Ala Ile Gly Pro Ser			
	115	120	125
Arg Phe Gly Leu Lys Arg Ala Glu Val Leu Gly His Lys Thr Pro Glu			
	130	135	140
Pro Ala Pro Arg Arg Thr Glu Ile Thr Ile Val Lys Pro Gln Glu Ser			
145	150	155	160
Ala His Arg Arg Met Glu Pro Pro Ala Ser Lys Val Pro Glu Val Pro			
	165	170	175
Thr Ala Pro Ala Thr Asp Ala Ala Pro Lys Arg Val Glu Ile Gln Met			
	180	185	190
Pro Lys Pro Ala Glu Ala Pro Thr Ala Pro Ser Pro Ala Gln Thr Leu			
	195	200	205
Glu Asn Ser Glu Pro Ala Pro Val Ser Gln Leu Gln Ser Arg Leu Glu			
	210	215	220
Pro Lys Pro Gln Pro Pro Val Ala Glu Ala Thr Pro Arg Ser Gln Glu			
225	230	235	240
Ala Thr Glu Ala Ala Pro Ser Cys Val Gly Asp Met Ala Asp Thr Pro			

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

Arg	Val	Lys	Arg	Leu	Asn	Glu	Gly	Ser	Ser	Ala	Met	Ala	Asn	Gly	Met		
				565					570					575			
Glu	Glu	Lys	Glu	Pro	Glu	Ala	Pro	Glu	Met								
				580					585								
<210> 153																	
<211> 418																	
<212> PRT																	
<213> 智人																	
<400> 153																	
Met	Pro	Ser	Ser	Val	Ser	Trp	Gly	Ile	Leu	Leu	Leu	Ala	Gly	Leu	Cys		
1				5				10				15					
Cys	Leu	Val	Pro	Val	Ser	Leu	Ala	Glu	Asp	Pro	Gln	Gly	Asp	Ala	Ala		
				20					25					30			
Gln	Lys	Thr	Asp	Thr	Ser	His	His	Asp	Gln	Asp	His	Pro	Thr	Phe	Asn		
				35					40					45			
Lys	Ile	Thr	Pro	Asn	Leu	Ala	Glu	Phe	Ala	Phe	Ser	Leu	Tyr	Arg	Gln		
				50					55					60			
Leu	Ala	His	Gln	Ser	Asn	Ser	Thr	Asn	Ile	Phe	Phe	Ser	Pro	Val	Ser		
65					70					75					80		
Ile	Ala	Thr	Ala	Phe	Ala	Met	Leu	Ser	Leu	Gly	Thr	Lys	Ala	Asp	Thr		
				85					90					95			
His	Asp	Glu	Ile	Leu	Glu	Gly	Leu	Asn	Phe	Asn	Leu	Thr	Glu	Ile	Pro		
				100					105					110			
Glu	Ala	Gln	Ile	His	Glu	Gly	Phe	Gln	Glu	Leu	Leu	Arg	Thr	Leu	Asn		
				115					120					125			
Gln	Pro	Asp	Ser	Gln	Leu	Gln	Leu	Thr	Thr	Gly	Asn	Gly	Leu	Phe	Leu		
				130					135					140			
Ser	Glu	Gly	Leu	Lys	Leu	Val	Asp	Lys	Phe	Leu	Glu	Asp	Val	Lys	Lys		
145					150					155					160		
Leu	Tyr	His	Ser	Glu	Ala	Phe	Thr	Val	Asn	Phe	Gly	Asp	Thr	Glu	Glu		
				165					170					175			
Ala	Lys	Lys	Gln	Ile	Asn	Asp	Tyr	Val	Glu	Lys	Gly	Thr	Gln	Gly	Lys		
				180					185					190			
Ile	Val	Asp	Leu	Val	Lys	Glu	Leu	Asp	Arg	Asp	Thr	Val	Phe	Ala	Leu		
				195					200					205			
Val	Asn	Tyr	Ile	Phe	Phe	Lys	Gly	Lys	Trp	Glu	Arg	Pro	Phe	Glu	Val		
				210					215					220			
Lys	Asp	Thr	Glu	Glu	Glu	Asp	Phe	His	Val	Asp	Gln	Val	Thr	Thr	Val		
225					230					235					240		

Lys Val Pro Met Met Lys Arg Leu Gly Met Phe Asn Ile Gln His Cys
 245 250 255
 Lys Lys Leu Ser Ser Trp Val Leu Leu Met Lys Tyr Leu Gly Asn Ala
 260 265 270
 Thr Ala Ile Phe Phe Leu Pro Asp Glu Gly Lys Leu Gln His Leu Glu
 275 280 285
 Asn Glu Leu Thr His Asp Ile Ile Thr Lys Phe Leu Glu Asn Glu Asp
 290 295 300
 Arg Arg Ser Ala Ser Leu His Leu Pro Lys Leu Ser Ile Thr Gly Thr
 305 310 315 320
 Tyr Asp Leu Lys Ser Val Leu Gly Gln Leu Gly Ile Thr Lys Val Phe
 325 330 335
 Ser Asn Gly Ala Asp Leu Ser Gly Val Thr Glu Glu Ala Pro Leu Lys
 340 345 350
 Leu Ser Lys Ala Val His Lys Ala Val Leu Thr Ile Asp Glu Lys Gly
 355 360 365
 Thr Glu Ala Ala Gly Ala Met Phe Leu Glu Ala Ile Pro Met Ser Ile
 370 375 380
 Pro Pro Glu Val Lys Phe Asn Lys Pro Phe Val Phe Leu Met Ile Glu
 385 390 395 400
 Gln Asn Thr Lys Ser Pro Leu Phe Met Gly Lys Val Val Asn Pro Thr
 405 410 415
 Gln Lys
 <210> 154
 <211> 423
 <212> PRT
 <213> 智人
 <400> 154
 Met Glu Arg Met Leu Pro Leu Leu Ala Leu Gly Leu Leu Ala Ala Gly
 1 5 10 15
 Phe Cys Pro Ala Val Leu Cys His Pro Asn Ser Pro Leu Asp Glu Glu
 20 25 30
 Asn Leu Thr Gln Glu Asn Gln Asp Arg Gly Thr His Val Asp Leu Gly
 35 40 45
 Leu Ala Ser Ala Asn Val Asp Phe Ala Phe Ser Leu Tyr Lys Gln Leu
 50 55 60
 Val Leu Lys Ala Pro Asp Lys Asn Val Ile Phe Ser Pro Leu Ser Ile
 65 70 75 80
 Ser Thr Ala Leu Ala Phe Leu Ser Leu Gly Ala His Asn Thr Thr Leu

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

Met Ile Ile Val Pro Thr Asp Thr Gln Asn Ile Phe Phe Met Ser Lys
 405 410 415

Val Thr Asn Pro Lys Gln Ala
 420

<210> 155
 <211> 379
 <212> PRT
 <213> 智人
 <400> 155

Met Glu Gln Leu Ser Ser Ala Asn Thr Arg Phe Ala Leu Asp Leu Phe
 1 5 10 15

Leu Ala Leu Ser Glu Asn Asn Pro Ala Gly Asn Ile Phe Ile Ser Pro
 20 25 30

Phe Ser Ile Ser Ser Ala Met Ala Met Val Phe Leu Gly Thr Arg Gly
 35 40 45

Asn Thr Ala Ala Gln Leu Ser Lys Thr Phe His Phe Asn Thr Val Glu
 50 55 60

Glu Val His Ser Arg Phe Gln Ser Leu Asn Ala Asp Ile Asn Lys Arg
 65 70 75 80

Gly Ala Ser Tyr Ile Leu Lys Leu Ala Asn Arg Leu Tyr Gly Glu Lys
 85 90 95

Thr Tyr Asn Phe Leu Pro Glu Phe Leu Val Ser Thr Gln Lys Thr Tyr
 100 105 110

Gly Ala Asp Leu Ala Ser Val Asp Phe Gln His Ala Ser Glu Asp Ala
 115 120 125

Arg Lys Thr Ile Asn Gln Trp Val Lys Gly Gln Thr Glu Gly Lys Ile
 130 135 140

Pro Glu Leu Leu Ala Ser Gly Met Val Asp Asn Met Thr Lys Leu Val
 145 150 155 160

Leu Val Asn Ala Ile Tyr Phe Lys Gly Asn Trp Lys Asp Lys Phe Met
 165 170 175

Lys Glu Ala Thr Thr Asn Ala Pro Phe Arg Leu Asn Lys Lys Asp Arg
 180 185 190

Lys Thr Val Lys Met Met Tyr Gln Lys Lys Lys Phe Ala Tyr Gly Tyr
 195 200 205

Ile Glu Asp Leu Lys Cys Arg Val Leu Glu Leu Pro Tyr Gln Gly Glu
 210 215 220

Glu Leu Ser Met Val Ile Leu Leu Pro Asp Asp Ile Glu Asp Glu Ser
 225 230 235 240

Thr Gly Leu Lys Lys Ile Glu Glu Gln Leu Thr Leu Glu Lys Leu His			
245	250	255	
Glu Trp Thr Lys Pro Glu Asn Leu Asp Phe Ile Glu Val Asn Val Ser			
260	265	270	
Leu Pro Arg Phe Lys Leu Glu Glu Ser Tyr Thr Leu Asn Ser Asp Leu			
275	280	285	
Ala Arg Leu Gly Val Gln Asp Leu Phe Asn Ser Ser Lys Ala Asp Leu			
290	295	300	
Ser Gly Met Ser Gly Ala Arg Asp Ile Phe Ile Ser Lys Ile Val His			
305	310	315	320
Lys Ser Phe Val Glu Val Asn Glu Glu Gly Thr Glu Ala Ala Ala Ala			
325	330	335	
Thr Ala Gly Ile Ala Thr Phe Cys Met Leu Met Pro Glu Glu Asn Phe			
340	345	350	
Thr Ala Asp His Pro Phe Leu Phe Phe Ile Arg His Asn Ser Ser Gly			
355	360	365	
Ser Ile Leu Phe Leu Gly Arg Phe Ser Ser Pro			
370	375		
<210> 156			
<211> 376			
<212> PRT			
<213> 智人			
<400> 156			
Met Asp Val Leu Ala Glu Ala Asn Gly Thr Phe Ala Leu Asn Leu Leu			
1	5	10	15
Lys Thr Leu Gly Lys Asp Asn Ser Lys Asn Val Phe Phe Ser Pro Met			
20	25	30	
Ser Met Ser Cys Ala Leu Ala Met Val Tyr Met Gly Ala Lys Gly Asn			
35	40	45	
Thr Ala Ala Gln Met Ala Gln Ile Leu Ser Phe Asn Lys Ser Gly Gly			
50	55	60	
Gly Gly Asp Ile His Gln Gly Phe Gln Ser Leu Leu Thr Glu Val Asn			
65	70	75	80
Lys Thr Gly Thr Gln Tyr Leu Leu Arg Met Ala Asn Arg Leu Phe Gly			
85	90	95	
Glu Lys Ser Cys Asp Phe Leu Ser Ser Phe Arg Asp Ser Cys Gln Lys			
100	105	110	
Phe Tyr Gln Ala Glu Met Glu Glu Leu Asp Phe Ile Ser Ala Val Glu			
115	120	125	

Lys Ser Arg Lys His Ile Asn Thr Trp Val Ala Glu Lys Thr Glu Gly			
130	135	140	
Lys Ile Ala Glu Leu Leu Ser Pro Gly Ser Val Asp Pro Leu Thr Arg			
145	150	155	160
Leu Val Leu Val Asn Ala Val Tyr Phe Arg Gly Asn Trp Asp Glu Gln			
	165	170	175
Phe Asp Lys Glu Asn Thr Glu Glu Arg Leu Phe Lys Val Ser Lys Asn			
	180	185	190
Glu Glu Lys Pro Val Gln Met Met Phe Lys Gln Ser Thr Phe Lys Lys			
	195	200	205
Thr Tyr Ile Gly Glu Ile Phe Thr Gln Ile Leu Val Leu Pro Tyr Val			
	210	215	220
Gly Lys Glu Leu Asn Met Ile Ile Met Leu Pro Asp Glu Thr Thr Asp			
225	230	235	240
Leu Arg Thr Val Glu Lys Glu Leu Thr Tyr Glu Lys Phe Val Glu Trp			
	245	250	255
Thr Arg Leu Asp Met Met Asp Glu Glu Glu Val Glu Val Ser Leu Pro			
	260	265	270
Arg Phe Lys Leu Glu Glu Ser Tyr Asp Met Glu Ser Val Leu Arg Asn			
	275	280	285
Leu Gly Met Thr Asp Ala Phe Glu Leu Gly Lys Ala Asp Phe Ser Gly			
	290	295	300
Met Ser Gln Thr Asp Leu Ser Leu Ser Lys Val Val His Lys Ser Phe			
305	310	315	320
Val Glu Val Asn Glu Glu Gly Thr Glu Ala Ala Ala Ala Thr Ala Ala			
	325	330	335
Ile Met Met Met Arg Cys Ala Arg Phe Val Pro Arg Phe Cys Ala Asp			
	340	345	350
His Pro Phe Leu Phe Phe Ile Gln His Ser Lys Thr Asn Gly Ile Leu			
	355	360	365
Phe Cys Gly Arg Phe Ser Ser Pro			
	370	375	
<210> 157			
<211> 1217			
<212> PRT			
<213> 智人			
<400> 157			
Met Phe Leu Tyr Asn Leu Thr Leu Gln Arg Ala Thr Gly Ile Ser Phe			
1	5	10	15

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

				325					330					335			
Ala	Ala	Met	Cys	Val	Leu	Lys	Thr	Gly	Phe	Leu	Phe	Val	Ala	Ser	Glu		
				340					345					350			
Phe	Gly	Asn	His	Tyr	Leu	Tyr	Gln	Ile	Ala	His	Leu	Gly	Asp	Asp	Asp		
				355					360					365			
Glu	Glu	Pro	Glu	Phe	Ser	Ser	Ala	Met	Pro	Leu	Glu	Glu	Gly	Asp	Thr		
				370					375					380			
Phe	Phe	Phe	Gln	Pro	Arg	Pro	Leu	Lys	Asn	Leu	Val	Leu	Val	Asp	Glu		
385							390							395			400
Leu	Asp	Ser	Leu	Ser	Pro	Ile	Leu	Phe	Cys	Gln	Ile	Ala	Asp	Leu	Ala		
				405					410					415			
Asn	Glu	Asp	Thr	Pro	Gln	Leu	Tyr	Val	Ala	Cys	Gly	Arg	Gly	Pro	Arg		
				420					425					430			
Ser	Ser	Leu	Arg	Val	Leu	Arg	His	Gly	Leu	Glu	Val	Ser	Glu	Met	Ala		
				435					440					445			
Val	Ser	Glu	Leu	Pro	Gly	Asn	Pro	Asn	Ala	Val	Trp	Thr	Val	Arg	Arg		
				450					455					460			
His	Ile	Glu	Asp	Glu	Phe	Asp	Ala	Tyr	Ile	Ile	Val	Ser	Phe	Val	Asn		
465							470							475			480
Ala	Thr	Leu	Val	Leu	Ser	Ile	Gly	Glu	Thr	Val	Glu	Glu	Val	Thr	Asp		
				485					490					495			
Ser	Gly	Phe	Leu	Gly	Thr	Thr	Pro	Thr	Leu	Ser	Cys	Ser	Leu	Leu	Gly		
				500					505					510			
Asp	Asp	Ala	Leu	Val	Gln	Val	Tyr	Pro	Asp	Gly	Ile	Arg	His	Ile	Arg		
				515					520					525			
Ala	Asp	Lys	Arg	Val	Asn	Glu	Trp	Lys	Thr	Pro	Gly	Lys	Lys	Thr	Ile		
				530					535					540			
Val	Lys	Cys	Ala	Val	Asn	Gln	Arg	Gln	Val	Val	Ile	Ala	Leu	Thr	Gly		
545							550							555			560
Gly	Glu	Leu	Val	Tyr	Phe	Glu	Met	Asp	Pro	Ser	Gly	Gln	Leu	Asn	Glu		
				565					570					575			
Tyr	Thr	Glu	Arg	Lys	Glu	Met	Ser	Ala	Asp	Val	Val	Cys	Met	Ser	Leu		
				580					585					590			
Ala	Asn	Val	Pro	Pro	Gly	Glu	Gln	Arg	Ser	Arg	Phe	Leu	Ala	Val	Gly		
				595					600					605			
Leu	Val	Asp	Asn	Thr	Val	Arg	Ile	Ile	Ser	Leu	Asp	Pro	Ser	Asp	Cys		
				610					615					620			
Leu	Gln	Pro	Leu	Ser	Met	Gln	Ala	Leu	Pro	Ala	Gln	Pro	Glu	Ser	Leu		
625							630							635			640

Cys Ile Val Glu Met Gly Gly Thr Glu Lys Gln Asp Glu Leu Gly Glu		
645	650	655
Arg Gly Ser Ile Gly Phe Leu Tyr Leu Asn Ile Gly Leu Gln Asn Gly		
660	665	670
Val Leu Leu Arg Thr Val Leu Asp Pro Val Thr Gly Asp Leu Ser Asp		
675	680	685
Thr Arg Thr Arg Tyr Leu Gly Ser Arg Pro Val Lys Leu Phe Arg Val		
690	695	700
Arg Met Gln Gly Gln Glu Ala Val Leu Ala Met Ser Ser Arg Ser Trp		
705	710	715
Leu Ser Tyr Ser Tyr Gln Ser Arg Phe His Leu Thr Pro Leu Ser Tyr		
725	730	735
Glu Thr Leu Glu Phe Ala Ser Gly Phe Ala Ser Glu Gln Cys Pro Glu		
740	745	750
Gly Ile Val Ala Ile Ser Thr Asn Thr Leu Arg Ile Leu Ala Leu Glu		
755	760	765
Lys Leu Gly Ala Val Phe Asn Gln Val Ala Phe Pro Leu Gln Tyr Thr		
770	775	780
Pro Arg Lys Phe Val Ile His Pro Glu Ser Asn Asn Leu Ile Ile Ile		
785	790	795
Glu Thr Asp His Asn Ala Tyr Thr Glu Ala Thr Lys Ala Gln Arg Lys		
805	810	815
Gln Gln Met Ala Glu Glu Met Val Glu Ala Ala Gly Glu Asp Glu Arg		
820	825	830
Glu Leu Ala Ala Glu Met Ala Ala Ala Phe Leu Asn Glu Asn Leu Pro		
835	840	845
Glu Ser Ile Phe Gly Ala Pro Lys Ala Gly Asn Gly Gln Trp Ala Ser		
850	855	860
Val Ile Arg Val Met Asn Pro Ile Gln Gly Asn Thr Leu Asp Leu Val		
865	870	875
Gln Leu Glu Gln Asn Glu Ala Ala Phe Ser Val Ala Val Cys Arg Phe		
885	890	895
Ser Asn Thr Gly Glu Asp Trp Tyr Val Leu Val Gly Val Ala Lys Asp		
900	905	910
Leu Ile Leu Asn Pro Arg Ser Val Ala Gly Gly Phe Val Tyr Thr Tyr		
915	920	925
Lys Leu Val Asn Asn Gly Glu Lys Leu Glu Phe Leu His Lys Thr Pro		
930	935	940
Val Glu Glu Val Pro Ala Ala Ile Ala Pro Phe Gln Gly Arg Val Leu		

945	950	955	960
Ile Gly Val Gly Lys Leu Leu Arg Val Tyr Asp Leu Gly Lys Lys Lys			
	965	970	975
Leu Leu Arg Lys Cys Glu Asn Lys His Ile Ala Asn Tyr Ile Ser Gly			
	980	985	990
Ile Gln Thr Ile Gly His Arg Val Ile Val Ser Asp Val Gln Glu Ser			
	995	1000	1005
Phe Ile Trp Val Arg Tyr Lys Arg Asn Glu Asn Gln Leu Ile Ile			
	1010	1015	1020
Phe Ala Asp Asp Thr Tyr Pro Arg Trp Val Thr Thr Ala Ser Leu			
	1025	1030	1035
Leu Asp Tyr Asp Thr Val Ala Gly Ala Asp Lys Phe Gly Asn Ile			
	1040	1045	1050
Cys Val Val Arg Leu Pro Pro Asn Thr Asn Asp Glu Val Asp Glu			
	1055	1060	1065
Asp Pro Thr Gly Asn Lys Ala Leu Trp Asp Arg Gly Leu Leu Asn			
	1070	1075	1080
Gly Ala Ser Gln Lys Ala Glu Val Ile Met Asn Tyr His Val Gly			
	1085	1090	1095
Glu Thr Val Leu Ser Leu Gln Lys Thr Thr Leu Ile Pro Gly Gly			
	1100	1105	1110
Ser Glu Ser Leu Val Tyr Thr Thr Leu Ser Gly Gly Ile Gly Ile			
	1115	1120	1125
Leu Val Pro Phe Thr Ser His Glu Asp His Asp Phe Phe Gln His			
	1130	1135	1140
Val Glu Met His Leu Arg Ser Glu His Pro Pro Leu Cys Gly Arg			
	1145	1150	1155
Asp His Leu Ser Phe Arg Ser Tyr Tyr Phe Pro Val Lys Asn Val			
	1160	1165	1170
Ile Asp Gly Asp Leu Cys Glu Gln Phe Asn Ser Met Glu Pro Asn			
	1175	1180	1185
Lys Gln Lys Asn Val Ser Glu Glu Leu Asp Arg Thr Pro Pro Glu			
	1190	1195	1200
Val Ser Lys Lys Leu Glu Asp Ile Arg Thr Arg Tyr Ala Phe			
	1205	1210	1215
<210> 158			
<211> 163			
<212> PRT			
<213> 智人			

<400> 158

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

<210> 159

<211> 298

<212> PRT

<213> 智人

<400> 159

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

Gln Ile Phe Leu Gly Gly Val Asp Lys Arg Thr Gln Phe Trp Leu Tyr																			
100																			
Phe Ala Gly Asn Leu Ala Ser Gly Gly Ala Ala Gly Ala Thr Ser Leu																			
115																			
Cys Phe Val Tyr Pro Leu Asp Phe Ala Arg Thr Arg Leu Ala Ala Asp																			
130																			
Val Gly Lys Ala Gly Ala Glu Arg Glu Phe Arg Gly Leu Gly Asp Cys																			
145																			
Leu Val Lys Ile Tyr Lys Ser Asp Gly Ile Lys Gly Leu Tyr Gln Gly																			
165																			
Phe Asn Val Ser Val Gln Gly Ile Ile Ile Tyr Arg Ala Ala Tyr Phe																			
180																			
Gly Ile Tyr Asp Thr Ala Lys Gly Met Leu Pro Asp Pro Lys Asn Thr																			
195																			
His Ile Val Ile Ser Trp Met Ile Ala Gln Thr Val Thr Ala Val Ala																			
210																			
Gly Leu Thr Ser Tyr Pro Phe Asp Thr Val Arg Arg Arg Met Met Met																			
225																			
Gln Ser Gly Arg Lys Gly Thr Asp Ile Met Tyr Thr Gly Thr Leu Asp																			
245																			
Cys Trp Arg Lys Ile Ala Arg Asp Glu Gly Gly Lys Ala Phe Phe Lys																			
260																			
Gly Ala Trp Ser Asn Val Leu Arg Gly Met Gly Gly Ala Phe Val Leu																			
275																			
Val Leu Tyr Asp Glu Ile Lys Lys Tyr Thr																			
290																			
<210> 160																			
<211> 79																			
<212> PRT																			
<213> 智人																			
<400> 160																			
Met Lys Val Thr Gly Ile Phe Leu Leu Ser Ala Leu Ala Leu Leu Ser																			
1																			
5																			
10																			
15																			
Leu Ser Gly Asn Thr Gly Ala Asp Ser Leu Gly Arg Glu Ala Lys Cys																			
20																			
25																			
30																			
Tyr Asn Glu Leu Asn Gly Cys Thr Lys Ile Tyr Asp Pro Val Cys Gly																			
35																			
40																			
45																			
Thr Asp Gly Asn Thr Tyr Pro Asn Glu Cys Val Leu Cys Phe Glu Asn																			
50																			
55																			
60																			

Arg Lys Arg Gln Thr Ser Ile Leu Ile Gln Lys Ser Gly Pro Cys
 65 70 75
 <210> 161
 <211> 331
 <212> PRT
 <213> 智人
 <400> 161
 Met Glu Asn Pro Ser Pro Ala Ala Ala Leu Gly Lys Ala Leu Cys Ala
 1 5 10 15
 Leu Leu Leu Ala Thr Leu Gly Ala Ala Gly Gln Pro Leu Gly Gly Glu
 20 25 30
 Ser Ile Cys Ser Ala Arg Ala Leu Ala Lys Tyr Ser Ile Thr Phe Thr
 35 40 45
 Gly Lys Trp Ser Gln Thr Ala Phe Pro Lys Gln Tyr Pro Leu Phe Arg
 50 55 60
 Pro Pro Ala Gln Trp Ser Ser Leu Leu Gly Ala Ala His Ser Ser Asp
 65 70 75 80
 Tyr Ser Met Trp Arg Lys Asn Gln Tyr Val Ser Asn Gly Leu Arg Asp
 85 90 95
 Phe Ala Glu Arg Gly Glu Ala Trp Ala Leu Met Lys Glu Ile Glu Ala
 100 105 110
 Ala Gly Glu Ala Leu Gln Ser Val His Glu Val Phe Ser Ala Pro Ala
 115 120 125
 Val Pro Ser Gly Thr Gly Gln Thr Ser Ala Glu Leu Glu Val Gln Arg
 130 135 140
 Arg His Ser Leu Val Ser Phe Val Val Arg Ile Val Pro Ser Pro Asp
 145 150 155 160
 Trp Phe Val Gly Val Asp Ser Leu Asp Leu Cys Asp Gly Asp Arg Trp
 165 170 175
 Arg Glu Gln Ala Ala Leu Asp Leu Tyr Pro Tyr Asp Ala Gly Thr Asp
 180 185 190
 Ser Gly Phe Thr Phe Ser Ser Pro Asn Phe Ala Thr Ile Pro Gln Asp
 195 200 205
 Thr Val Thr Glu Ile Thr Ser Ser Ser Pro Ser His Pro Ala Asn Ser
 210 215 220
 Phe Tyr Tyr Pro Arg Leu Lys Ala Leu Pro Pro Ile Ala Arg Val Thr
 225 230 235 240
 Leu Val Arg Leu Arg Gln Ser Pro Arg Ala Phe Ile Pro Pro Ala Pro
 245 250 255

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

<210> 162

<211> 314

<212> PRT

<213> 智人

<400> 162

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

Met Glu Ser Glu Glu Leu Asn Gly Ala Tyr Lys Ala Ile Pro Val Ala		
195	200	205
Gln Asp Leu Asn Ala Pro Ser Asp Trp Asp Ser Arg Gly Lys Asp Ser		
210	215	220
Tyr Glu Thr Ser Gln Leu Asp Asp Gln Ser Ala Glu Thr His Ser His		
225	230	235 240
Lys Gln Ser Arg Leu Tyr Lys Arg Lys Ala Asn Asp Glu Ser Asn Glu		
	245	250 255
His Ser Asp Val Ile Asp Ser Gln Glu Leu Ser Lys Val Ser Arg Glu		
	260	265 270
Phe His Ser His Glu Phe His Ser His Glu Asp Met Leu Val Val Asp		
	275	280 285
Pro Lys Ser Lys Glu Glu Asp Lys His Leu Lys Phe Arg Ile Ser His		
	290	295 300
Glu Leu Asp Ser Ala Ser Ser Glu Val Asn		
305	310	
<210> 163		
<211> 536		
<212> PRT		
<213> 智人		
<400> 163		
Met Gly Ser Asn Lys Ser Lys Pro Lys Asp Ala Ser Gln Arg Arg Arg		
1	5	10 15
Ser Leu Glu Pro Ala Glu Asn Val His Gly Ala Gly Gly Ala Phe		
	20	25 30
Pro Ala Ser Gln Thr Pro Ser Lys Pro Ala Ser Ala Asp Gly His Arg		
	35	40 45
Gly Pro Ser Ala Ala Phe Ala Pro Ala Ala Glu Pro Lys Leu Phe		
	50	55 60
Gly Gly Phe Asn Ser Ser Asp Thr Val Thr Ser Pro Gln Arg Ala Gly		
65	70	75 80
Pro Leu Ala Gly Gly Val Thr Thr Phe Val Ala Leu Tyr Asp Tyr Glu		
	85	90 95
Ser Arg Thr Glu Thr Asp Leu Ser Phe Lys Lys Gly Glu Arg Leu Gln		
	100	105 110
Ile Val Asn Asn Thr Glu Gly Asp Trp Trp Leu Ala His Ser Leu Ser		
	115	120 125
Thr Gly Gln Thr Gly Tyr Ile Pro Ser Asn Tyr Val Ala Pro Ser Asp		
	130	135 140

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

450	455	460
Pro Tyr Pro Gly Met Val Asn Arg Glu Val Leu Asp Gln Val Glu Arg		
465	470	475
Gly Tyr Arg Met Pro Cys Pro Pro Glu Cys Pro Glu Ser Leu His Asp		
485	490	495
Leu Met Cys Gln Cys Trp Arg Lys Glu Pro Glu Glu Arg Pro Thr Phe		
500	505	510
Glu Tyr Leu Gln Ala Phe Leu Glu Asp Tyr Phe Thr Ser Thr Glu Pro		
515	520	525
Gln Tyr Gln Pro Gly Glu Asn Leu		
530	535	
<210> 164		
<211> 536		
<212> PRT		
<213> 智人		
<400> 164		
Met Gly Ser Asn Lys Ser Lys Pro Lys Asp Ala Ser Gln Arg Arg Arg		
1	5	10
Ser Leu Glu Pro Ala Glu Asn Val His Gly Ala Gly Gly Gly Ala Phe		
20	25	30
Pro Ala Ser Gln Thr Pro Ser Lys Pro Ala Ser Ala Asp Gly His Arg		
35	40	45
Gly Pro Ser Ala Ala Phe Ala Pro Ala Ala Ala Glu Pro Lys Leu Phe		
50	55	60
Gly Gly Phe Asn Ser Ser Asp Thr Val Thr Ser Pro Gln Arg Ala Gly		
65	70	75
Pro Leu Ala Gly Gly Val Thr Thr Phe Val Ala Leu Tyr Asp Tyr Glu		
85	90	95
Ser Arg Thr Glu Thr Asp Leu Ser Phe Lys Lys Gly Glu Arg Leu Gln		
100	105	110
Ile Val Asn Asn Thr Glu Gly Asp Trp Trp Leu Ala His Ser Leu Ser		
115	120	125
Thr Gly Gln Thr Gly Tyr Ile Pro Ser Asn Tyr Val Ala Pro Ser Asp		
130	135	140
Ser Ile Gln Ala Glu Glu Trp Tyr Phe Gly Lys Ile Thr Arg Arg Glu		
145	150	155
Ser Glu Arg Leu Leu Leu Asn Ala Glu Asn Pro Arg Gly Thr Phe Leu		
165	170	175
Val Arg Glu Ser Glu Thr Thr Lys Gly Ala Tyr Cys Leu Ser Val Ser		

			180				185				190				
Asp	Phe	Asp	Asn	Ala	Lys	Gly	Leu	Asn	Val	Lys	His	Tyr	Lys	Ile	Arg
			195				200				205				
Lys	Leu	Asp	Ser	Gly	Gly	Phe	Tyr	Ile	Thr	Ser	Arg	Thr	Gln	Phe	Asn
			210				215				220				
Ser	Leu	Gln	Gln	Leu	Val	Ala	Tyr	Tyr	Ser	Lys	His	Ala	Asp	Gly	Leu
225			230				235				240				
Cys	His	Arg	Leu	Thr	Thr	Val	Cys	Pro	Thr	Ser	Lys	Pro	Gln	Thr	Gln
			245				250				255				
Gly	Leu	Ala	Lys	Asp	Ala	Trp	Glu	Ile	Pro	Arg	Glu	Ser	Leu	Arg	Leu
			260				265				270				
Glu	Val	Lys	Leu	Gly	Gln	Gly	Cys	Phe	Gly	Glu	Val	Trp	Met	Gly	Thr
			275				280				285				
Trp	Asn	Gly	Thr	Thr	Arg	Val	Ala	Ile	Lys	Thr	Leu	Lys	Pro	Gly	Thr
290			295				300								
Met	Ser	Pro	Glu	Ala	Phe	Leu	Gln	Glu	Ala	Gln	Val	Met	Lys	Lys	Leu
305			310				315				320				
Arg	His	Glu	Lys	Leu	Val	Gln	Leu	Tyr	Ala	Val	Val	Ser	Glu	Glu	Pro
			325				330				335				
Ile	Tyr	Ile	Val	Thr	Glu	Tyr	Met	Ser	Lys	Gly	Ser	Leu	Leu	Asp	Phe
			340				345				350				
Leu	Lys	Gly	Glu	Thr	Gly	Lys	Tyr	Leu	Arg	Leu	Pro	Gln	Leu	Val	Asp
			355				360				365				
Met	Ala	Ala	Gln	Ile	Ala	Ser	Gly	Met	Ala	Tyr	Val	Glu	Arg	Met	Asn
370			375				380								
Tyr	Val	His	Arg	Asp	Leu	Arg	Ala	Ala	Asn	Ile	Leu	Val	Gly	Glu	Asn
385			390				395				400				
Leu	Val	Cys	Lys	Val	Ala	Asp	Phe	Gly	Leu	Ala	Arg	Leu	Ile	Glu	Asp
			405				410				415				
Asn	Glu	Tyr	Thr	Ala	Arg	Gln	Gly	Ala	Lys	Phe	Pro	Ile	Lys	Trp	Thr
			420				425				430				
Ala	Pro	Glu	Ala	Ala	Leu	Tyr	Gly	Arg	Phe	Thr	Ile	Lys	Ser	Asp	Val
			435				440				445				
Trp	Ser	Phe	Gly	Ile	Leu	Leu	Thr	Glu	Leu	Thr	Thr	Lys	Gly	Arg	Val
450			455				460								
Pro	Tyr	Pro	Gly	Met	Val	Asn	Arg	Glu	Val	Leu	Asp	Gln	Val	Glu	Arg
465			470				475				480				
Gly	Tyr	Arg	Met	Pro	Cys	Pro	Pro	Glu	Cys	Pro	Glu	Ser	Leu	His	Asp
			485				490				495				

Leu Met Cys Gln Cys Trp Arg Lys Glu Pro Glu Glu Arg Pro Thr Phe
 500 505 510
 Glu Tyr Leu Gln Ala Phe Leu Glu Asp Tyr Phe Thr Ser Thr Glu Pro
 515 520 525
 Gln Tyr Gln Pro Gly Glu Asn Leu
 530 535
 <210> 165
 <211> 623
 <212> PRT
 <213> 智人
 <400> 165
 Met Ala Thr Glu His Val Asn Gly Asn Gly Thr Glu Glu Pro Met Asp
 1 5 10 15
 Thr Thr Ser Ala Val Ile His Ser Glu Asn Phe Gln Thr Leu Leu Asp
 20 25 30
 Ala Gly Leu Pro Gln Lys Val Ala Glu Lys Leu Asp Glu Ile Tyr Val
 35 40 45
 Ala Gly Leu Val Ala His Ser Asp Leu Asp Glu Arg Ala Ile Glu Ala
 50 55 60
 Leu Lys Glu Phe Asn Glu Asp Gly Ala Leu Ala Val Leu Gln Gln Phe
 65 70 75 80
 Lys Asp Ser Asp Leu Ser His Val Gln Asn Lys Ser Ala Phe Leu Cys
 85 90 95
 Gly Val Met Lys Thr Tyr Arg Gln Arg Glu Lys Gln Gly Thr Lys Val
 100 105 110
 Ala Asp Ser Ser Lys Gly Pro Asp Glu Ala Lys Ile Lys Ala Leu Leu
 115 120 125
 Glu Arg Thr Gly Tyr Thr Leu Asp Val Thr Thr Gly Gln Arg Lys Tyr
 130 135 140
 Gly Gly Pro Pro Pro Asp Ser Val Tyr Ser Gly Gln Gln Pro Ser Val
 145 150 155 160
 Gly Thr Glu Ile Phe Val Gly Lys Ile Pro Arg Asp Leu Phe Glu Asp
 165 170 175
 Glu Leu Val Pro Leu Phe Glu Lys Ala Gly Pro Ile Trp Asp Leu Arg
 180 185 190
 Leu Met Met Asp Pro Leu Thr Gly Leu Asn Arg Gly Tyr Ala Phe Val
 195 200 205
 Thr Phe Cys Thr Lys Glu Ala Ala Gln Glu Ala Val Lys Leu Tyr Asn
 210 215 220

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

530	535	540
Gln Arg Gly Arg Gly Val Arg Gly Ala Arg Gly Gly Arg Gly Gly Asn		
545	550	555
Val Gly Gly Lys Arg Lys Ala Asp Gly Tyr Asn Gln Pro Asp Ser Lys		
565	570	575
Arg Arg Gln Thr Asn Asn Gln Asn Trp Gly Ser Gln Pro Ile Ala Gln		
580	585	590
Gln Pro Leu Gln Gly Gly Asp His Ser Gly Asn Tyr Gly Tyr Lys Ser		
595	600	605
Glu Asn Gln Glu Phe Tyr Gln Asp Thr Phe Gly Gln Gln Trp Lys		
610	615	620
<210> 166		
<211> 331		
<212> PRT		
<213> 智人		
<400> 166		
Met Thr Glu Arg Pro Pro Ser Glu Ala Ala Arg Ser Asp Pro Gln Leu		
1	5	10
Glu Gly Arg Asp Ala Ala Glu Ala Ser Met Ala Pro Pro His Leu Val		
20	25	30
Leu Leu Asn Gly Val Ala Lys Glu Thr Ser Arg Ala Ala Ala Ala Glu		
35	40	45
Pro Pro Val Ile Glu Leu Gly Ala Arg Gly Gly Pro Gly Gly Gly Pro		
50	55	60
Ala Gly Gly Gly Gly Ala Ala Arg Asp Leu Lys Gly Arg Asp Ala Ala		
65	70	75
Thr Ala Glu Ala Arg His Arg Val Pro Thr Thr Glu Leu Cys Arg Pro		
85	90	95
Pro Gly Pro Ala Pro Ala Pro Ala Pro Ala Ser Val Thr Ala Glu Leu		
100	105	110
Pro Gly Asp Gly Arg Met Val Gln Leu Ser Pro Pro Ala Leu Ala Ala		
115	120	125
Pro Ala Ala Pro Gly Arg Ala Leu Leu Tyr Ser Leu Ser Gln Pro Leu		
130	135	140
Ala Ser Leu Gly Ser Gly Phe Phe Gly Glu Pro Asp Ala Phe Pro Met		
145	150	155
Phe Thr Thr Asn Asn Arg Val Lys Arg Arg Pro Ser Pro Tyr Glu Met		
165	170	175
Glu Ile Thr Asp Gly Pro His Thr Lys Val Val Arg Arg Ile Phe Thr		

<400> 167

345

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

$\langle 210 \rangle$	168
$\langle 211 \rangle$	1170
$\langle 212 \rangle$	PRT
$\langle 213 \rangle$	智人
$\langle 400 \rangle$	168

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

305	310	315	320
Asn Gly Val Gln Tyr Arg Asn Asn Glu Glu Trp Thr Val Asp Ser Cys			
	325	330	335
Thr Glu Cys His Cys Gln Asn Ser Val Thr Ile Cys Lys Lys Val Ser			
	340	345	350
Cys Pro Ile Met Pro Cys Ser Asn Ala Thr Val Pro Asp Gly Glu Cys			
	355	360	365
Cys Pro Arg Cys Trp Pro Ser Asp Ser Ala Asp Asp Gly Trp Ser Pro			
	370	375	380
Trp Ser Glu Trp Thr Ser Cys Ser Thr Ser Cys Gly Asn Gly Ile Gln			
385	390	395	400
Gln Arg Gly Arg Ser Cys Asp Ser Leu Asn Asn Arg Cys Glu Gly Ser			
	405	410	415
Ser Val Gln Thr Arg Thr Cys His Ile Gln Glu Cys Asp Lys Arg Phe			
	420	425	430
Lys Gln Asp Gly Gly Trp Ser His Trp Ser Pro Trp Ser Ser Cys Ser			
	435	440	445
Val Thr Cys Gly Asp Gly Val Ile Thr Arg Ile Arg Leu Cys Asn Ser			
	450	455	460
Pro Ser Pro Gln Met Asn Gly Lys Pro Cys Glu Gly Glu Ala Arg Glu			
465	470	475	480
Thr Lys Ala Cys Lys Lys Asp Ala Cys Pro Ile Asn Gly Gly Trp Gly			
	485	490	495
Pro Trp Ser Pro Trp Asp Ile Cys Ser Val Thr Cys Gly Gly Gly Val			
	500	505	510
Gln Lys Arg Ser Arg Leu Cys Asn Asn Pro Thr Pro Gln Phe Gly Gly			
	515	520	525
Lys Asp Cys Val Gly Asp Val Thr Glu Asn Gln Ile Cys Asn Lys Gln			
	530	535	540
Asp Cys Pro Ile Asp Gly Cys Leu Ser Asn Pro Cys Phe Ala Gly Val			
545	550	555	560
Lys Cys Thr Ser Tyr Pro Asp Gly Ser Trp Lys Cys Gly Ala Cys Pro			
	565	570	575
Pro Gly Tyr Ser Gly Asn Gly Ile Gln Cys Thr Asp Val Asp Glu Cys			
	580	585	590
Lys Glu Val Pro Asp Ala Cys Phe Asn His Asn Gly Glu His Arg Cys			
	595	600	605
Glu Asn Thr Asp Pro Gly Tyr Asn Cys Leu Pro Cys Pro Pro Arg Phe			
610	615	620	

Thr Gly Ser Gln Pro Phe Gly Gln Gly Val Glu His Ala Thr Ala Asn			
625	630	635	640
Lys Gln Val Cys Lys Pro Arg Asn Pro Cys Thr Asp Gly Thr His Asp			
	645	650	655
Cys Asn Lys Asn Ala Lys Cys Asn Tyr Leu Gly His Tyr Ser Asp Pro			
	660	665	670
Met Tyr Arg Cys Glu Cys Lys Pro Gly Tyr Ala Gly Asn Gly Ile Ile			
	675	680	685
Cys Gly Glu Asp Thr Asp Leu Asp Gly Trp Pro Asn Glu Asn Leu Val			
	690	695	700
Cys Val Ala Asn Ala Thr Tyr His Cys Lys Lys Asp Asn Cys Pro Asn			
705	710	715	720
Leu Pro Asn Ser Gly Gln Glu Asp Tyr Asp Lys Asp Gly Ile Gly Asp			
	725	730	735
Ala Cys Asp Asp Asp Asp Asp Asn Asp Lys Ile Pro Asp Asp Arg Asp			
	740	745	750
Asn Cys Pro Phe His Tyr Asn Pro Ala Gln Tyr Asp Tyr Asp Arg Asp			
	755	760	765
Asp Val Gly Asp Arg Cys Asp Asn Cys Pro Tyr Asn His Asn Pro Asp			
	770	775	780
Gln Ala Asp Thr Asp Asn Asn Gly Glu Gly Asp Ala Cys Ala Ala Asp			
785	790	795	800
Ile Asp Gly Asp Gly Ile Leu Asn Glu Arg Asp Asn Cys Gln Tyr Val			
	805	810	815
Tyr Asn Val Asp Gln Arg Asp Thr Asp Met Asp Gly Val Gly Asp Gln			
	820	825	830
Cys Asp Asn Cys Pro Leu Glu His Asn Pro Asp Gln Leu Asp Ser Asp			
	835	840	845
Ser Asp Arg Ile Gly Asp Thr Cys Asp Asn Asn Gln Asp Ile Asp Glu			
	850	855	860
Asp Gly His Gln Asn Asn Leu Asp Asn Cys Pro Tyr Val Pro Asn Ala			
865	870	875	880
Asn Gln Ala Asp His Asp Lys Asp Gly Lys Gly Asp Ala Cys Asp His			
	885	890	895
Asp Asp Asp Asn Asp Gly Ile Pro Asp Asp Lys Asp Asn Cys Arg Leu			
	900	905	910
Val Pro Asn Pro Asp Gln Lys Asp Ser Asp Gly Asp Gly Arg Gly Asp			
	915	920	925
Ala Cys Lys Asp Asp Phe Asp His Asp Ser Val Pro Asp Ile Asp Asp			

930	935	940
Ile Cys Pro Glu Asn Val Asp Ile Ser Glu Thr Asp Phe Arg Arg Phe		
945	950	955
Gln Met Ile Pro Leu Asp Pro Lys Gly Thr Ser Gln Asn Asp Pro Asn		
965	970	975
Trp Val Val Arg His Gln Gly Lys Glu Leu Val Gln Thr Val Asn Cys		
980	985	990
Asp Pro Gly Leu Ala Val Gly Tyr Asp Glu Phe Asn Ala Val Asp Phe		
995	1000	1005
Ser Gly Thr Phe Phe Ile Asn Thr Glu Arg Asp Asp Asp Tyr Ala		
1010	1015	1020
Gly Phe Val Phe Gly Tyr Gln Ser Ser Ser Arg Phe Tyr Val Val		
1025	1030	1035
Met Trp Lys Gln Val Thr Gln Ser Tyr Trp Asp Thr Asn Pro Thr		
1040	1045	1050
Arg Ala Gln Gly Tyr Ser Gly Leu Ser Val Lys Val Val Asn Ser		
1055	1060	1065
Thr Thr Gly Pro Gly Glu His Leu Arg Asn Ala Leu Trp His Thr		
1070	1075	1080
Gly Asn Thr Pro Gly Gln Val Arg Thr Leu Trp His Asp Pro Arg		
1085	1090	1095
His Ile Gly Trp Lys Asp Phe Thr Ala Tyr Arg Trp Arg Leu Ser		
1100	1105	1110
His Arg Pro Lys Thr Gly Phe Ile Arg Val Val Met Tyr Glu Gly		
1115	1120	1125
Lys Lys Ile Met Ala Asp Ser Gly Pro Ile Tyr Asp Lys Thr Tyr		
1130	1135	1140
Ala Gly Gly Arg Leu Gly Leu Phe Val Phe Ser Gln Glu Met Val		
1145	1150	1155
Phe Phe Ser Asp Leu Lys Tyr Glu Cys Arg Asp Pro		
1160	1165	1170
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<211> 207		
<212> PRT		
<213> 智人		
<400> 169		
Met Ala Pro Phe Glu Pro Leu Ala Ser Gly Ile Leu Leu Leu Leu Trp		
1	5	10
Leu Ile Ala Pro Ser Arg Ala Cys Thr Cys Val Pro Pro His Pro Gln		15

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

<210> 170

<211> 623

<212> PRT

<213> 智人

<400> 170

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

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

Arg Met Ala Ala Ile Ser Glu Ser Asn Ile Asn Leu Cys Gly Ser His			
405	410	415	
Cys Gly Val Ser Ile Gly Glu Asp Gly Pro Ser Gln Met Ala Leu Glu			
420	425	430	
Asp Leu Ala Met Phe Arg Ser Val Pro Thr Ser Thr Val Phe Tyr Pro			
435	440	445	
Ser Asp Gly Val Ala Thr Glu Lys Ala Val Glu Leu Ala Ala Asn Thr			
450	455	460	
Lys Gly Ile Cys Phe Ile Arg Thr Ser Arg Pro Glu Asn Ala Ile Ile			
465	470	475	480
Tyr Asn Asn Asn Glu Asp Phe Gln Val Gly Gln Ala Lys Val Val Leu			
485	490	495	
Lys Ser Lys Asp Asp Gln Val Thr Val Ile Gly Ala Gly Val Thr Leu			
500	505	510	
His Glu Ala Leu Ala Ala Ala Glu Leu Leu Lys Lys Glu Lys Ile Asn			
515	520	525	
Ile Arg Val Leu Asp Pro Phe Thr Ile Lys Pro Leu Asp Arg Lys Leu			
530	535	540	
Ile Leu Asp Ser Ala Arg Ala Thr Lys Gly Arg Ile Leu Thr Val Glu			
545	550	555	560
Asp His Tyr Tyr Glu Gly Gly Ile Gly Glu Ala Val Ser Ser Ala Val			
565	570	575	
Val Gly Glu Pro Gly Ile Thr Val Thr His Leu Ala Val Asn Arg Val			
580	585	590	
Pro Arg Ser Gly Lys Pro Ala Glu Leu Leu Lys Met Phe Gly Ile Asp			
595	600	605	
Arg Asp Ala Ile Ala Gln Ala Val Arg Gly Leu Ile Thr Lys Ala			
610	615	620	
<210> 171			
<211> 277			
<212> PRT			
<213> 智人			
<400> 171			
Met Ile Ile Leu Ile Tyr Leu Phe Leu Leu Leu Trp Glu Asp Thr Gln			
1	5	10	15
Gly Trp Gly Phe Lys Asp Gly Ile Phe His Asn Ser Ile Trp Leu Glu			
20	25	30	
Arg Ala Ala Gly Val Tyr His Arg Glu Ala Arg Ser Gly Lys Tyr Lys			
35	40	45	

Leu Thr Tyr Ala Glu Ala Lys Ala Val Cys Glu Phe Glu Gly Gly His		
50	55	60
Leu Ala Thr Tyr Lys Gln Leu Glu Ala Ala Arg Lys Ile Gly Phe His		
65	70	75 80
Val Cys Ala Ala Gly Trp Met Ala Lys Gly Arg Val Gly Tyr Pro Ile		
85	90	95
Val Lys Pro Gly Pro Asn Cys Gly Phe Gly Lys Thr Gly Ile Ile Asp		
100	105	110
Tyr Gly Ile Arg Leu Asn Arg Ser Glu Arg Trp Asp Ala Tyr Cys Tyr		
115	120	125
Asn Pro His Ala Lys Glu Cys Gly Gly Val Phe Thr Asp Pro Lys Gln		
130	135	140
Ile Phe Lys Ser Pro Gly Phe Pro Asn Glu Tyr Glu Asp Asn Gln Ile		
145	150	155 160
Cys Tyr Trp His Ile Arg Leu Lys Tyr Gly Gln Arg Ile His Leu Ser		
165	170	175
Phe Leu Asp Phe Asp Leu Glu Asp Asp Pro Gly Cys Leu Ala Asp Tyr		
180	185	190
Val Glu Ile Tyr Asp Ser Tyr Asp Asp Val His Gly Phe Val Gly Arg		
195	200	205
Tyr Cys Gly Asp Glu Leu Pro Asp Asp Ile Ile Ser Thr Gly Asn Val		
210	215	220
Met Thr Leu Lys Phe Leu Ser Asp Ala Ser Val Thr Ala Gly Gly Phe		
225	230	235 240
Gln Ile Lys Tyr Val Ala Met Asp Pro Val Ser Lys Ser Ser Gln Gly		
245	250	255
Lys Asn Thr Ser Thr Thr Ser Thr Gly Asn Lys Asn Phe Leu Ala Gly		
260	265	270
Arg Phe Ser His Leu		
275		
<210> 172		
<211> 440		
<212> PRT		
<213> 智人		
<400> 172		
Met Glu Gln Arg Gly Gln Asn Ala Pro Ala Ala Ser Gly Ala Arg Lys		
1	5	10 15
Arg His Gly Pro Gly Pro Arg Glu Ala Arg Gly Ala Arg Pro Gly Pro		
20	25	30

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

			340					345					350			
Ser	Trp	Glu	Pro	Leu	Met	Arg	Lys	Leu	Gly	Leu	Met	Asp	Asn	Glu	Ile	
		355					360					365				
Lys	Val	Ala	Lys	Ala	Glu	Ala	Ala	Gly	His	Arg	Asp	Thr	Leu	Tyr	Thr	
	370					375					380					
Met	Leu	Ile	Lys	Trp	Val	Asn	Lys	Thr	Gly	Arg	Asp	Ala	Ser	Val	His	
385					390					395					400	
Thr	Leu	Leu	Asp	Ala	Leu	Glu	Thr	Leu	Gly	Glu	Arg	Leu	Ala	Lys	Gln	
			405					410					415			
Lys	Ile	Glu	Asp	His	Leu	Leu	Ser	Ser	Gly	Lys	Phe	Met	Tyr	Leu	Glu	
		420					425					430				
Gly	Asn	Ala	Asp	Ser	Ala	Met	Ser									
	435					440										
<210>	173															
<211>	300															
<212>	PRT															
<213>	智人															
<400>	173															
Met	Arg	Ala	Leu	Glu	Gly	Pro	Gly	Leu	Ser	Leu	Leu	Cys	Leu	Val	Leu	
1			5					10					15			
Ala	Leu	Pro	Ala	Leu	Leu	Pro	Val	Pro	Ala	Val	Arg	Gly	Val	Ala	Glu	
		20					25					30				
Thr	Pro	Thr	Tyr	Pro	Trp	Arg	Asp	Ala	Glu	Thr	Gly	Glu	Arg	Leu	Val	
	35					40					45					
Cys	Ala	Gln	Cys	Pro	Pro	Gly	Thr	Phe	Val	Gln	Arg	Pro	Cys	Arg	Arg	
	50					55					60					
Asp	Ser	Pro	Thr	Thr	Cys	Gly	Pro	Cys	Pro	Pro	Arg	His	Tyr	Thr	Gln	
65					70					75					80	
Phe	Trp	Asn	Tyr	Leu	Glu	Arg	Cys	Arg	Tyr	Cys	Asn	Val	Leu	Cys	Gly	
		85					90					95				
Glu	Arg	Glu	Glu	Glu	Ala	Arg	Ala	Cys	His	Ala	Thr	His	Asn	Arg	Ala	
	100					105					110					
Cys	Arg	Cys	Arg	Thr	Gly	Phe	Phe	Ala	His	Ala	Gly	Phe	Cys	Leu	Glu	
	115					120					125					
His	Ala	Ser	Cys	Pro	Pro	Gly	Ala	Gly	Val	Ile	Ala	Pro	Gly	Thr	Pro	
	130					135					140					
Ser	Gln	Asn	Thr	Gln	Cys	Gln	Pro	Cys	Pro	Pro	Gly	Thr	Phe	Ser	Ala	
145				150					155					160		
Ser	Ser	Ser	Ser	Ser	Glu	Gln	Cys	Gln	Pro	His	Arg	Asn	Cys	Thr	Ala	

	165		170		175
Leu Gly Leu Ala Leu Asn Val Pro Gly Ser Ser Ser His Asp Thr Leu					
	180		185		190
Cys Thr Ser Cys Thr Gly Phe Pro Leu Ser Thr Arg Val Pro Gly Ala					
	195		200		205
Glu Glu Cys Glu Arg Ala Val Ile Asp Phe Val Ala Phe Gln Asp Ile					
	210		215		220
Ser Ile Lys Arg Leu Gln Arg Leu Leu Gln Ala Leu Glu Ala Pro Glu					
225		230		235	240
Gly Trp Gly Pro Thr Pro Arg Ala Gly Arg Ala Ala Leu Gln Leu Lys					
	245		250		255
Leu Arg Arg Arg Leu Thr Glu Leu Leu Gly Ala Gln Asp Gly Ala Leu					
	260		265		270
Leu Val Arg Leu Leu Gln Ala Leu Arg Val Ala Arg Met Pro Gly Leu					
	275		280		285
Glu Arg Ser Val Arg Glu Arg Phe Leu Pro Val His					
	290		295		300
<210> 174					
<211> 393					
<212> PRT					
<213> 智人					
<400> 174					
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
Ala Ile Tyr Lys Gln Ser Gln His Met Thr Glu Val Val Arg Arg Cys		160
	165	170
Pro His His Glu Arg Cys Ser Asp Ser Asp Gly Leu Ala Pro Pro Gln		175
	180	185
His Leu Ile Arg Val Glu Gly Asn Leu Arg Val Glu Tyr Leu Asp Asp		190
	195	200
Arg Asn Thr Phe Arg His Ser Val Val Val Pro Tyr Glu Pro Pro Glu		205
	210	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		240
	245	250
Leu Glu Asp Ser Ser Gly Asn Leu Leu Gly Arg Asn Ser Phe Glu Val		255
	260	265
Arg Val Cys Ala Cys Pro Gly Arg Asp Arg Arg Thr Glu Glu Glu Asn		270
	275	280
Leu Arg Lys Lys Gly Glu Pro His His Glu Leu Pro Pro Gly Ser Thr		285
	290	295
Lys Arg Ala Leu Pro Asn Asn Thr Ser Ser Ser Pro Gln Pro Lys Lys		300
305	310	315
Lys Pro Leu Asp Gly Glu Tyr Phe Thr Leu Gln Ile Arg Gly Arg Glu		320
	325	330
Arg Phe Glu Met Phe Arg Glu Leu Asn Glu Ala Leu Glu Leu Lys Asp		335
	340	345
Ala Gln Ala Gly Lys Glu Pro Gly Gly Ser Arg Ala His Ser Ser His		350
	355	360
Leu Lys Ser Lys Lys Gly Gln Ser Thr Ser Arg His Lys Lys Leu Met		365
	370	375
Phe Lys Thr Glu Gly Pro Asp Ser Asp		380
385	390	
<210> 175		
<211> 284		
<212> PRT		
<213> 智人		
<400> 175		
Met Asp Ala Ile Lys Lys Lys Met Gln Met Leu Lys Leu Asp Lys Glu		

1	5	10	15
Asn Ala Ile Asp Arg Ala Glu Gln Ala Glu Ala Asp Lys Lys Gln Ala			
20	25	30	
Glu Asp Arg Cys Lys Gln Leu Glu Glu Glu Gln Gln Ala Leu Gln Lys			
35	40	45	
Lys Leu Lys Gly Thr Glu Asp Glu Val Glu Lys Tyr Ser Glu Ser Val			
50	55	60	
Lys Glu Ala Gln Glu Lys Leu Glu Gln Ala Glu Lys Lys Ala Thr Asp			
65	70	75	80
Ala Glu Ala Asp Val Ala Ser Leu Asn Arg Arg Ile Gln Leu Val Glu			
85	90	95	
Glu Glu Leu Asp Arg Ala Gln Glu Arg Leu Ala Thr Ala Leu Gln Lys			
100	105	110	
Leu Glu Glu Ala Glu Lys Ala Ala Asp Glu Ser Glu Arg Gly Met Lys			
115	120	125	
Val Ile Glu Asn Arg Ala Met Lys Asp Glu Glu Lys Met Glu Leu Gln			
130	135	140	
Glu Met Gln Leu Lys Glu Ala Lys His Ile Ala Glu Asp Ser Asp Arg			
145	150	155	160
Lys Tyr Glu Glu Val Ala Arg Lys Leu Val Ile Leu Glu Gly Glu Leu			
165	170	175	
Glu Arg Ser Glu Glu Arg Ala Glu Val Ala Glu Ser Lys Cys Gly Asp			
180	185	190	
Leu Glu Glu Glu Leu Lys Ile Val Thr Asn Asn Leu Lys Ser Leu Glu			
195	200	205	
Ala Gln Ala Asp Lys Tyr Ser Thr Lys Glu Asp Lys Tyr Glu Glu Glu			
210	215	220	
Ile Lys Leu Leu Glu Glu Lys Leu Lys Glu Ala Glu Thr Arg Ala Glu			
225	230	235	240
Phe Ala Glu Arg Ser Val Ala Lys Leu Glu Lys Thr Ile Asp Asp Leu			
245	250	255	
Glu Asp Glu Val Tyr Ala Gln Lys Met Lys Tyr Lys Ala Ile Ser Glu			
260	265	270	
Glu Leu Asp Asn Ala Leu Asn Asp Ile Thr Ser Leu			
275	280		
<210> 176			
<211> 172			
<212> PRT			
<213> 智人			

<400> 176

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

<210> 177

<211> 704

<212> PRT

<213> 智人

<400> 177

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

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

Ser Arg Glu Leu Leu Gln Glu Ser Ala Leu Ile Arg Lys Leu Arg Asp		
405	410	415
Val Leu Gln Gln Arg Leu Ile Lys Phe Phe Ile Asp Gln Ser Lys Lys		
420	425	430
Asp Ala Glu Lys Tyr Ala Lys Phe Phe Glu Asp Tyr Gly Leu Phe Met		
435	440	445
Arg Glu Gly Ile Val Thr Ala Thr Glu Gln Glu Val Lys Glu Asp Ile		
450	455	460
Ala Lys Leu Leu Arg Tyr Glu Ser Ser Ala Leu Pro Ser Gly Gln Leu		
465	470	475
Thr Ser Leu Ser Glu Tyr Ala Ser Arg Met Arg Ala Gly Thr Arg Asn		
485	490	495
Ile Tyr Tyr Leu Cys Ala Pro Asn Arg His Leu Ala Glu His Ser Pro		
500	505	510
Tyr Tyr Glu Ala Met Lys Lys Lys Asp Thr Glu Val Leu Phe Cys Phe		
515	520	525
Glu Gln Phe Asp Glu Leu Thr Leu Leu His Leu Arg Glu Phe Asp Lys		
530	535	540
Lys Lys Leu Ile Ser Val Glu Thr Asp Ile Val Val Asp His Tyr Lys		
545	550	555
Glu Glu Lys Phe Glu Asp Arg Ser Pro Ala Ala Glu Cys Leu Ser Glu		
565	570	575
Lys Glu Thr Glu Glu Leu Met Ala Trp Met Arg Asn Val Leu Gly Ser		
580	585	590
Arg Val Thr Asn Val Lys Val Thr Leu Arg Leu Asp Thr His Pro Ala		
595	600	605
Met Val Thr Val Leu Glu Met Gly Ala Ala Arg His Phe Leu Arg Met		
610	615	620
Gln Gln Leu Ala Lys Thr Gln Glu Glu Arg Ala Gln Leu Leu Gln Pro		
625	630	635
Thr Leu Glu Ile Asn Pro Arg His Ala Leu Ile Lys Lys Leu Asn Gln		
645	650	655
Leu Arg Ala Ser Glu Pro Gly Leu Ala Gln Leu Leu Val Asp Gln Ile		
660	665	670
Tyr Glu Asn Ala Met Ile Ala Ala Gly Leu Val Asp Asp Pro Arg Ala		
675	680	685
Met Val Gly Arg Leu Asn Glu Leu Leu Val Lys Ala Leu Glu Arg His		
690	695	700

<210> 178

<211> 297

<212> PRT

<213> 智人

<400> 178

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

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275	280	285
Val Ser Gln Gly Lys Ser Glu Lys Ala		
290	295	
<210> 179		
<211> 451		
<212> PRT		
<213> 智人		
<400> 179		
Met Arg Glu Ile Val His Ile Gln Ile Gly Gln Cys Gly Asn Gln Ile		
1	5	10
Gly Ala Lys Phe Trp Glu Met Ile Gly Glu Glu His Gly Ile Asp Leu		
20	25	30
Ala Gly Ser Asp Arg Gly Ala Ser Ala Leu Gln Leu Glu Arg Ile Ser		
35	40	45
Val Tyr Tyr Asn Glu Ala Tyr Gly Arg Lys Tyr Val Pro Arg Ala Val		
50	55	60
Leu Val Asp Leu Glu Pro Gly Thr Met Asp Ser Ile Arg Ser Ser Lys		
65	70	75
Leu Gly Ala Leu Phe Gln Pro Asp Ser Phe Val His Gly Asn Ser Gly		
85	90	95
Ala Gly Asn Asn Trp Ala Lys Gly His Tyr Thr Glu Gly Ala Glu Leu		
100	105	110
Ile Glu Asn Val Leu Glu Val Val Arg His Glu Ser Glu Ser Cys Asp		
115	120	125
Cys Leu Gln Gly Phe Gln Ile Val His Ser Leu Gly Gly Gly Thr Gly		
130	135	140
Ser Gly Met Gly Thr Leu Leu Met Asn Lys Ile Arg Glu Glu Tyr Pro		
145	150	155
Asp Arg Ile Met Asn Ser Phe Ser Val Met Pro Ser Pro Lys Val Ser		
165	170	175
Asp Thr Val Val Glu Pro Tyr Asn Ala Val Leu Ser Ile His Gln Leu		
180	185	190
Ile Glu Asn Ala Asp Ala Cys Phe Cys Ile Asp Asn Glu Ala Leu Tyr		
195	200	205
Asp Ile Cys Phe Arg Thr Leu Lys Leu Thr Thr Pro Thr Tyr Gly Asp		
210	215	220
Leu Asn His Leu Val Ser Leu Thr Met Ser Gly Ile Thr Thr Ser Leu		
225	230	235
Arg Phe Pro Gly Gln Leu Asn Ala Asp Leu Arg Lys Leu Ala Val Asn		

	245		250		255
Met Val Pro Phe	Pro Arg Leu His Phe	Phe Met Pro Gly	Phe Ala Pro		
	260		265		270
Leu Thr Ala Gln	Gly Ser Gln Gln Tyr Arg	Ala Leu Ser Val	Ala Glu		
	275		280		285
Leu Thr Gln Gln	Met Phe Asp Ala Arg Asn Thr	Met Ala Ala Cys	Asp		
	290		295		300
Leu Arg Arg Gly	Arg Tyr Leu Thr Val Ala Cys	Ile Phe Arg Gly	Lys		
305		310		315	320
Met Ser Thr Lys	Glu Val Asp Gln Gln Leu Leu	Ser Val Gln Thr	Arg		
	325		330		335
Asn Ser Ser Cys	Phe Val Glu Trp Ile Pro Asn	Asn Val Lys Val	Ala		
	340		345		350
Val Cys Asp Ile	Pro Pro Arg Gly Leu Ser Met	Ala Ala Thr Phe	Ile		
	355		360		365
Gly Asn Asn Thr	Ala Ile Gln Glu Ile Phe Asn	Arg Val Ser Glu	His		
	370		375		380
Phe Ser Ala Met	Phe Lys Arg Lys Ala Phe Val	His Trp Tyr Thr	Ser		
385		390		395	400
Glu Gly Met Asp	Ile Asn Glu Phe Gly Glu Ala	Glu Asn Asn Ile	His		
	405		410		415
Asp Leu Val Ser	Glu Tyr Gln Gln Phe Gln Asp	Ala Lys Ala Val	Leu		
	420		425		430
Glu Glu Asp Glu	Glu Val Thr Glu Glu Ala Glu	Met Glu Pro Glu	Asp		
	435		440		445
Lys Gly His					
450					
<210> 180					
<211> 494					
<212> PRT					
<213> 智人					
<400> 180					
Met Phe Glu Ile	Lys Lys Ile Cys Cys Ile	Gly Ala Gly Tyr	Val Gly		
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Gly Pro Thr Cys	Ser Val Ile Ala His Met	Cys Pro Glu Ile	Arg Val		
	20		25		30
Thr Val Val Asp	Val Asn Glu Ser Arg Ile	Asn Ala Trp Asn	Ser Pro		
	35		40		45
Thr Leu Pro Ile	Tyr Glu Pro Gly Leu Lys	Glu Val Val Glu	Ser Cys		

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

Pro Lys Val Pro Arg Glu Gln Ile Val Val Asp Leu Ser His Pro Gly
 370 375 380
 Val Ser Glu Asp Asp Gln Val Ser Arg Leu Val Thr Ile Ser Lys Asp
 385 390 395 400
 Pro Tyr Glu Ala Cys Asp Gly Ala His Ala Val Val Ile Cys Thr Glu
 405 410 415
 Trp Asp Met Phe Lys Glu Leu Asp Tyr Glu Arg Ile His Lys Lys Met
 420 425 430
 Leu Lys Pro Ala Phe Ile Phe Asp Gly Arg Arg Val Leu Asp Gly Leu
 435 440 445
 His Asn Glu Leu Gln Thr Ile Gly Phe Gln Ile Glu Thr Ile Gly Lys
 450 455 460
 Lys Val Ser Ser Lys Arg Ile Pro Tyr Ala Pro Ser Gly Glu Ile Pro
 465 470 475 480
 Lys Phe Ser Leu Gln Asp Pro Pro Asn Lys Lys Pro Lys Val
 485 490

<210> 181

<211> 508

<212> PRT

<213> 智人

<400> 181

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

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

450	455	460
Thr Phe Gly Lys Asn Val Ser Leu Lys Gly Thr Val Ile Ile Ile Ala		
465	470	475
Asn His Gly Asp Arg Ile Asp Ile Pro Pro Gly Ala Val Leu Glu Asn		480
	485	490
Lys Ile Val Ser Gly Asn Leu Arg Ile Leu Asp His		495
500	505	
<210> 182		
<211> 232		
<212> PRT		
<213> 智人		
<400> 182		
Met Asn Phe Leu Leu Ser Trp Val His Trp Ser Leu Ala Leu Leu Leu		
1	5	10
Tyr Leu His His Ala Lys Trp Ser Gln Ala Ala Pro Met Ala Glu Gly		15
	20	25
Gly Gly Gln Asn His His Glu Val Val Lys Phe Met Asp Val Tyr Gln		30
	35	40
Arg Ser Tyr Cys His Pro Ile Glu Thr Leu Val Asp Ile Phe Gln Glu		45
50	55	60
Tyr Pro Asp Glu Ile Glu Tyr Ile Phe Lys Pro Ser Cys Val Pro Leu		
65	70	75
Met Arg Cys Gly Gly Cys Cys Asn Asp Glu Gly Leu Glu Cys Val Pro		80
	85	90
Thr Glu Glu Ser Asn Ile Thr Met Gln Ile Met Arg Ile Lys Pro His		95
	100	105
Gln Gly Gln His Ile Gly Glu Met Ser Phe Leu Gln His Asn Lys Cys		110
	115	120
Glu Cys Arg Pro Lys Lys Asp Arg Ala Arg Gln Glu Lys Lys Ser Val		125
130	135	140
Arg Gly Lys Gly Lys Gly Gln Lys Arg Lys Arg Lys Lys Ser Arg Tyr		
145	150	155
Lys Ser Trp Ser Val Tyr Val Gly Ala Arg Cys Cys Leu Met Pro Trp		160
	165	170
Ser Leu Pro Gly Pro His Pro Cys Gly Pro Cys Ser Glu Arg Arg Lys		175
	180	185
His Leu Phe Val Gln Asp Pro Gln Thr Cys Lys Cys Ser Cys Lys Asn		190
195	200	205
Thr Asp Ser Arg Cys Lys Ala Arg Gln Leu Glu Leu Asn Glu Arg Thr		

210	215	220
Cys Arg Cys Asp Lys Pro Arg Arg		
225	230	
<210> 183		
<211> 827		
<212> PRT		
<213> 智人		
<400> 183		
Met Thr Lys Leu Ser Ala Gln Val Lys Gly Ser Leu Asn Ile Thr Thr		
1	5	10
Pro Gly Leu Gln Ile Trp Arg Ile Glu Ala Met Gln Met Val Pro Val		
20	25	30
Pro Ser Ser Thr Phe Gly Ser Phe Phe Asp Gly Asp Cys Tyr Ile Ile		
35	40	45
Leu Ala Ile His Lys Thr Ala Ser Ser Leu Ser Tyr Asp Ile His Tyr		
50	55	60
Trp Ile Gly Gln Asp Ser Ser Leu Asp Glu Gln Gly Ala Ala Ala Ile		
65	70	75
Tyr Thr Thr Gln Met Asp Asp Phe Leu Lys Gly Arg Ala Val Gln His		
85	90	95
Arg Glu Val Gln Gly Asn Glu Ser Glu Ala Phe Arg Gly Tyr Phe Lys		
100	105	110
Gln Gly Leu Val Ile Arg Lys Gly Gly Val Ala Ser Gly Met Lys His		
115	120	125
Val Glu Thr Asn Ser Tyr Asp Val Gln Arg Leu Leu His Val Lys Gly		
130	135	140
Lys Arg Asn Val Val Ala Gly Glu Val Glu Met Ser Trp Lys Ser Phe		
145	150	155
Asn Arg Gly Asp Val Phe Leu Leu Asp Leu Gly Lys Leu Ile Ile Gln		
165	170	175
Trp Asn Gly Pro Glu Ser Thr Arg Met Glu Arg Leu Arg Gly Met Thr		
180	185	190
Leu Ala Lys Glu Ile Arg Asp Gln Glu Arg Gly Gly Arg Thr Tyr Val		
195	200	205
Gly Val Val Asp Gly Glu Asn Glu Leu Ala Ser Pro Lys Leu Met Glu		
210	215	220
Val Met Asn His Val Leu Gly Lys Arg Arg Glu Leu Lys Ala Ala Val		
225	230	235
Pro Asp Thr Val Val Glu Pro Ala Leu Lys Ala Ala Leu Lys Leu Tyr		240

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

Gly Cys Ser Gly Asp Glu Arg Glu Met Ala Lys Met Val Ala Asp Thr		
	565	570 575
Ile Ser Arg Thr Glu Lys Gln Val Val Val Glu Gly Gln Glu Pro Ala		
	580	585 590
Asn Phe Trp Met Ala Leu Gly Gly Lys Ala Pro Tyr Ala Asn Thr Lys		
	595	600 605
Arg Leu Gln Glu Glu Asn Leu Val Ile Thr Pro Arg Leu Phe Glu Cys		
	610	615 620
Ser Asn Lys Thr Gly Arg Phe Leu Ala Thr Glu Ile Pro Asp Phe Asn		
625	630	635 640
Gln Asp Asp Leu Glu Glu Asp Asp Val Phe Leu Leu Asp Val Trp Asp		
	645	650 655
Gln Val Phe Phe Trp Ile Gly Lys His Ala Asn Glu Glu Glu Lys Lys		
	660	665 670
Ala Ala Ala Thr Thr Ala Gln Glu Tyr Leu Lys Thr His Pro Ser Gly		
	675	680 685
Arg Asp Pro Glu Thr Pro Ile Ile Val Val Lys Gln Gly His Glu Pro		
690	695	700
Pro Thr Phe Thr Gly Trp Phe Leu Ala Trp Asp Pro Phe Lys Trp Ser		
705	710	715 720
Asn Thr Lys Ser Tyr Glu Asp Leu Lys Ala Glu Leu Gly Asn Ser Arg		
	725	730 735
Asp Trp Ser Gln Ile Thr Ala Glu Val Thr Ser Pro Lys Val Asp Val		
	740	745 750
Phe Asn Ala Asn Ser Asn Leu Ser Ser Gly Pro Leu Pro Ile Phe Pro		
	755	760 765
Leu Glu Gln Leu Val Asn Lys Pro Val Glu Glu Leu Pro Glu Gly Val		
	770	775 780
Asp Pro Ser Arg Lys Glu Glu His Leu Ser Ile Glu Asp Phe Thr Gln		
785	790	795 800
Ala Phe Gly Met Thr Pro Ala Ala Phe Ser Ala Leu Pro Arg Trp Lys		
	805	810 815
Gln Gln Asn Leu Lys Lys Glu Lys Gly Leu Phe		
	820	825

<210> 184

<211> 466

<212> PRT

<213> 智人

<400> 184

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

305	310	315	320
Arg Gln Val Gln Ser Leu Thr Cys Glu Val Asp Ala Leu Lys Gly Thr			
	325	330	335
Asn Glu Ser Leu Glu Arg Gln Met Arg Glu Met Glu Glu Asn Phe Ala			
	340	345	350
Val Glu Ala Ala Asn Tyr Gln Asp Thr Ile Gly Arg Leu Gln Asp Glu			
	355	360	365
Ile Gln Asn Met Lys Glu Glu Met Ala Arg His Leu Arg Glu Tyr Gln			
	370	375	380
Asp Leu Leu Asn Val Lys Met Ala Leu Asp Ile Glu Ile Ala Thr Tyr			
385	390	395	400
Arg Lys Leu Leu Glu Gly Glu Glu Ser Arg Ile Ser Leu Pro Leu Pro			
	405	410	415
Asn Phe Ser Ser Leu Asn Leu Arg Glu Thr Asn Leu Asp Ser Leu Pro			
	420	425	430
Leu Val Asp Thr His Ser Lys Arg Thr Leu Leu Ile Lys Thr Val Glu			
	435	440	445
Thr Arg Asp Gly Gln Val Ile Asn Glu Thr Ser Gln His His Asp Asp			
	450	455	460
Leu Glu			
465			
<210> 185			
<211> 513			
<212> PRT			
<213> 智人			
<400> 185			
Met Thr Thr Gln Leu Pro Ala Tyr Val Ala Ile Leu Leu Phe Tyr Val			
1	5	10	15
Ser Arg Ala Ser Cys Gln Asp Thr Phe Thr Ala Ala Val Tyr Glu His			
	20	25	30
Ala Ala Ile Leu Pro Asn Ala Thr Leu Thr Pro Val Ser Arg Glu Glu			
	35	40	45
Ala Leu Ala Leu Met Asn Arg Asn Leu Asp Ile Leu Glu Gly Ala Ile			
	50	55	60
Thr Ser Ala Ala Asp Gln Gly Ala His Ile Ile Val Thr Pro Glu Asp			
65	70	75	80
Ala Ile Tyr Gly Trp Asn Phe Asn Arg Asp Ser Leu Tyr Pro Tyr Leu			
	85	90	95
Glu Asp Ile Pro Asp Pro Glu Val Asn Trp Ile Pro Cys Asn Asn Arg			

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

Thr	Ala	Ser	Thr	Arg	Phe	Glu	Met	Phe	Ser	Leu	Ser	Gly	Thr	Phe	Gly
420				425				430							
Thr	Gln	Tyr	Val	Phe	Pro	Glu	Val	Leu	Leu	Ser	Glu	Asn	Gln	Leu	Ala
435				440				445							
Pro	Gly	Glu	Phe	Gln	Val	Ser	Thr	Asp	Gly	Arg	Leu	Phe	Ser	Leu	Lys
450				455				460							
Pro	Thr	Ser	Gly	Pro	Val	Leu	Thr	Val	Thr	Leu	Phe	Gly	Arg	Leu	Tyr
465				470				475				480			
Glu	Lys	Asp	Trp	Ala	Ser	Asn	Ala	Ser	Ser	Gly	Leu	Thr	Ala	Gln	Ala
485				490				495							
Arg	Ile	Ile	Met	Leu	Ile	Val	Ile	Ala	Pro	Ile	Val	Cys	Ser	Leu	Ser
500				505				510							

Trp
 <210> 186
 <211> 245
 <212> PRT
 <213> 智人
 <400> 186

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

				165					170					175			
Phe	Tyr	Tyr	Glu	Ile	Leu	Asn	Ser	Pro	Glu	Lys	Ala	Cys	Ser	Leu	Ala		
				180					185					190			
Lys	Thr	Ala	Phe	Asp	Glu	Ala	Ile	Ala	Glu	Leu	Asp	Thr	Leu	Ser	Glu		
				195					200					205			
Glu	Ser	Tyr	Lys	Asp	Ser	Thr	Leu	Ile	Met	Gln	Leu	Leu	Arg	Asp	Asn		
				210					215					220			
Leu	Thr	Leu	Trp	Thr	Ser	Asp	Thr	Gln	Gly	Asp	Glu	Ala	Glu	Ala	Gly		
225							230				235				240		
Glu	Gly	Gly	Glu	Asn													
				245													
<210> 187																	
<211> 352																	
<212> PRT																	
<213> 智人																	
<400> 187																	
Met	Asp	Tyr	Gln	Val	Ser	Ser	Pro	Ile	Tyr	Asp	Ile	Asn	Tyr	Tyr	Thr		
1				5					10					15			
Ser	Glu	Pro	Cys	Gln	Lys	Ile	Asn	Val	Lys	Gln	Ile	Ala	Ala	Arg	Leu		
				20					25					30			
Leu	Pro	Pro	Leu	Tyr	Ser	Leu	Val	Phe	Ile	Phe	Gly	Phe	Val	Gly	Asn		
				35					40					45			
Met	Leu	Val	Ile	Leu	Ile	Leu	Ile	Asn	Cys	Lys	Arg	Leu	Lys	Ser	Met		
				50					55					60			
Thr	Asp	Ile	Tyr	Leu	Leu	Asn	Leu	Ala	Ile	Ser	Asp	Leu	Phe	Phe	Leu		
65						70				75					80		
Leu	Thr	Val	Pro	Phe	Trp	Ala	His	Tyr	Ala	Ala	Ala	Gln	Trp	Asp	Phe		
				85					90					95			
Gly	Asn	Thr	Met	Cys	Gln	Leu	Leu	Thr	Gly	Leu	Tyr	Phe	Ile	Gly	Phe		
				100					105					110			
Phe	Ser	Gly	Ile	Phe	Phe	Ile	Ile	Leu	Leu	Thr	Ile	Asp	Arg	Tyr	Leu		
				115					120					125			
Ala	Val	Val	His	Ala	Val	Phe	Ala	Leu	Lys	Ala	Arg	Thr	Val	Thr	Phe		
				130					135					140			
Gly	Val	Val	Thr	Ser	Val	Ile	Thr	Trp	Val	Val	Ala	Val	Phe	Ala	Ser		
145						150				155				160			
Leu	Pro	Gly	Ile	Ile	Phe	Thr	Arg	Ser	Gln	Lys	Glu	Gly	Leu	His	Tyr		
						165				170				175			
Thr	Cys	Ser	Ser	His	Phe	Pro	Tyr	Ser	Gln	Tyr	Gln	Phe	Trp	Lys	Asn		

180	185	190
Phe Gln Thr Leu Lys Ile Val	Ile Leu Gly Leu Val	Leu Pro Leu Leu
195	200	205
Val Met Val Ile Cys Tyr Ser	Gly Ile Leu Lys Thr	Leu Leu Arg Cys
210	215	220
Arg Asn Glu Lys Lys Arg His	Arg Ala Val Arg Leu Ile	Phe Thr Ile
225	230	235
240	245	250
Met Ile Val Tyr Phe Leu Phe	Trp Ala Pro Tyr Asn Ile	Val Leu Leu
255	260	265
Leu Asn Thr Phe Gln Glu Phe	Phe Gly Leu Asn Asn Cys	Ser Ser Ser
270	275	280
Asn Arg Leu Asp Gln Ala Met	Gln Val Thr Glu Thr Leu	Gly Met Thr
285	290	295
His Cys Cys Ile Asn Pro Ile	Ile Tyr Ala Phe Val Gly	Glu Lys Phe
300	305	310
Arg Asn Tyr Leu Leu Val Phe	Phe Gln Lys His Ile Ala	Lys Arg Phe
315	320	325
Cys Lys Cys Cys Ser Ile Phe	Gln Gln Glu Ala Pro Glu	Arg Ala Ser
330	335	340
Ser Val Tyr Thr Arg Ser Thr	Gly Glu Gln Glu Ile Ser	Val Gly Leu
345	350	

<210> 188

<211> 467

<212> PRT

<213> 智人

<400> 188

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

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

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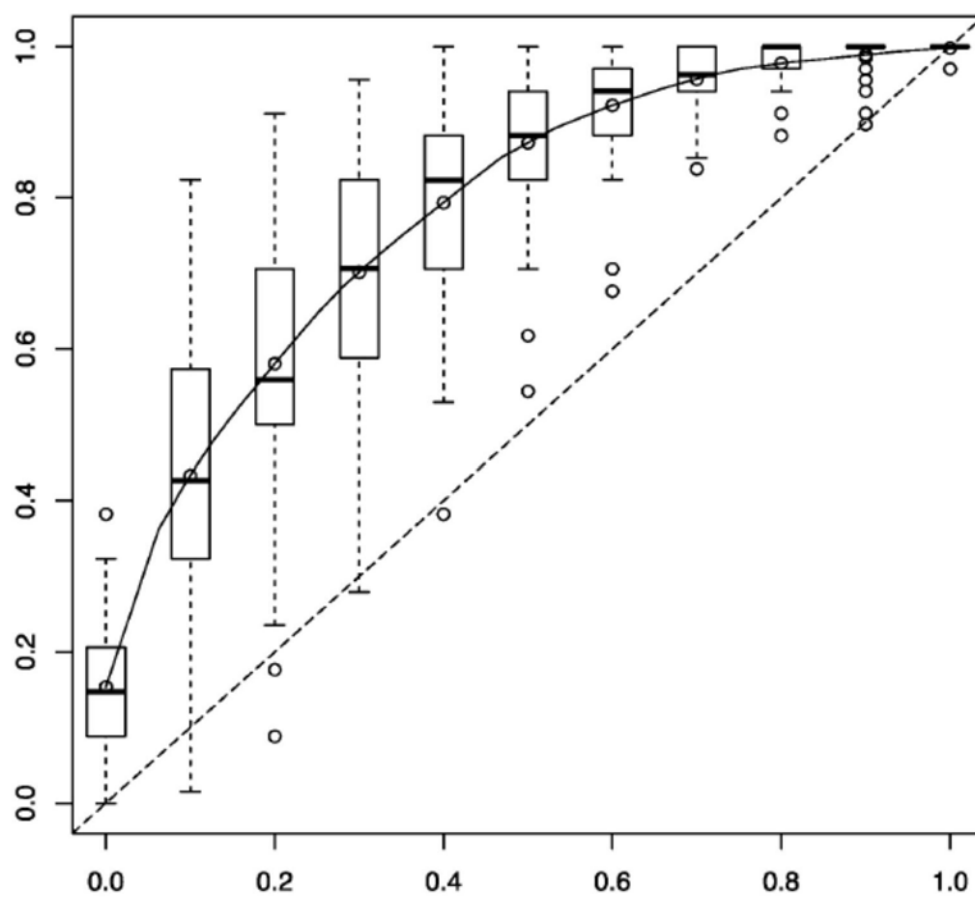


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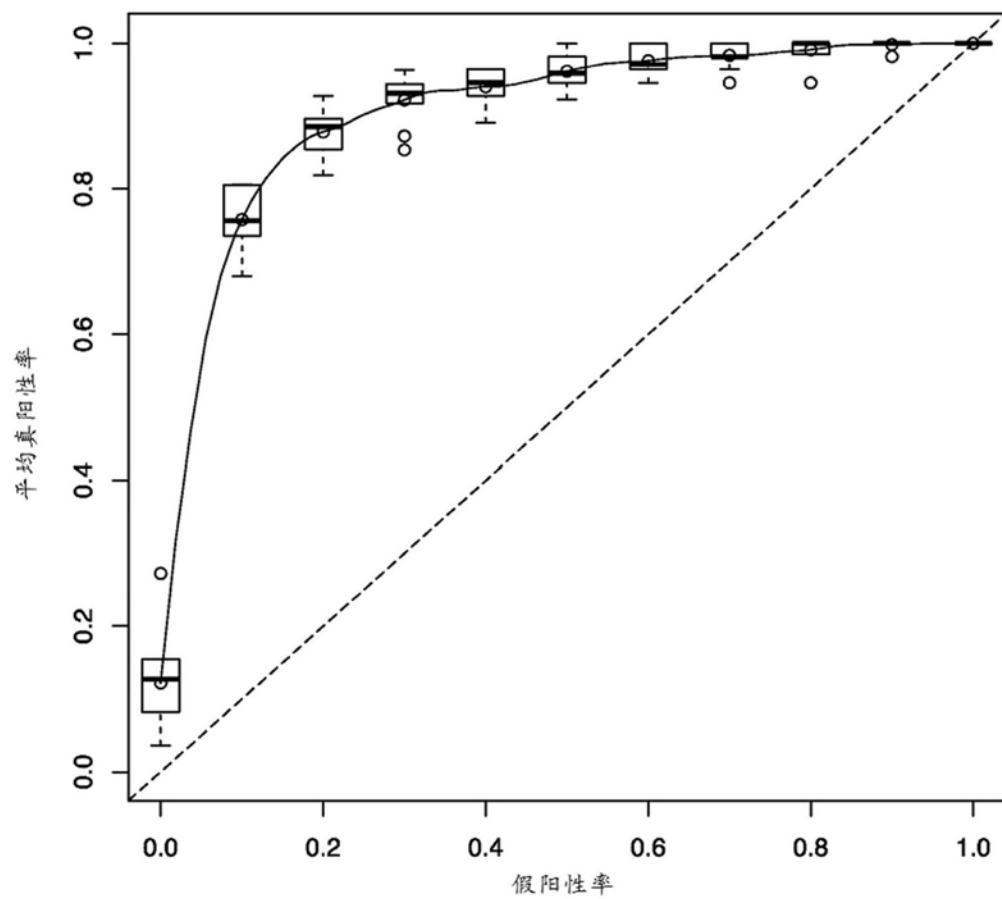


图1B

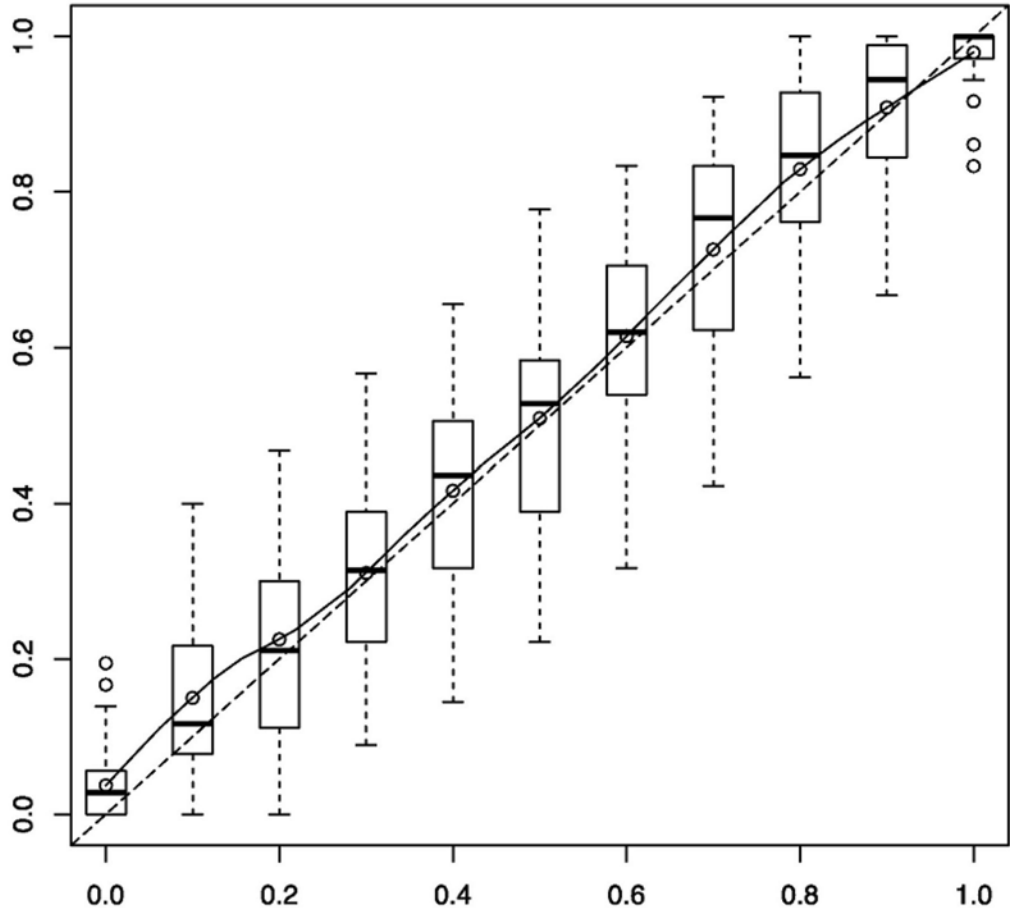


图2A

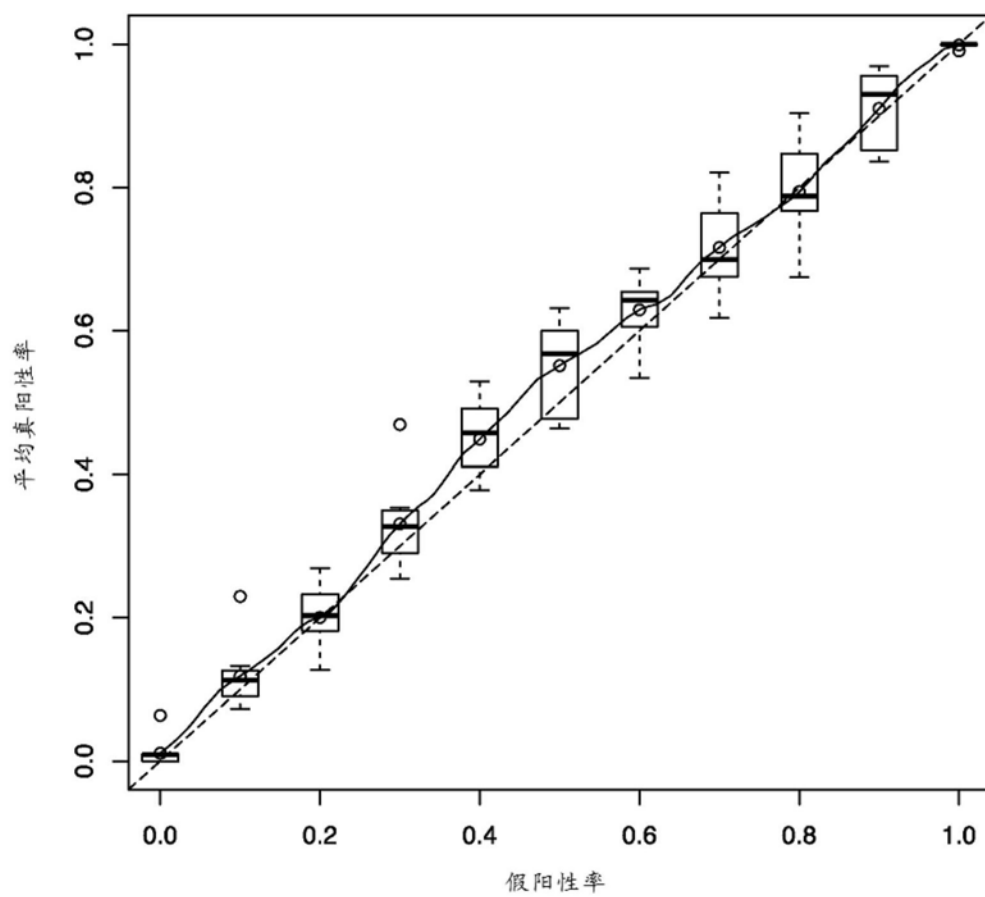


图2B

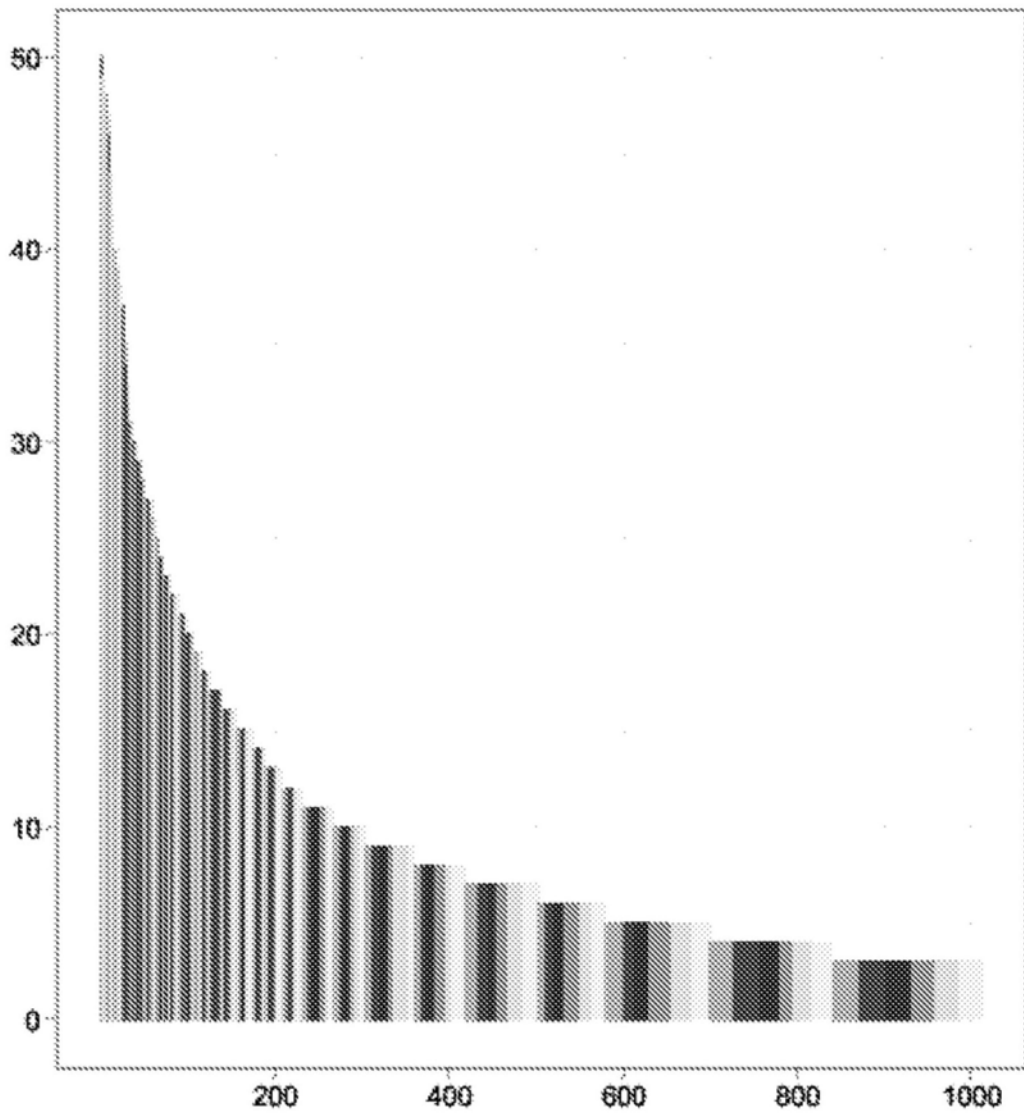


图3

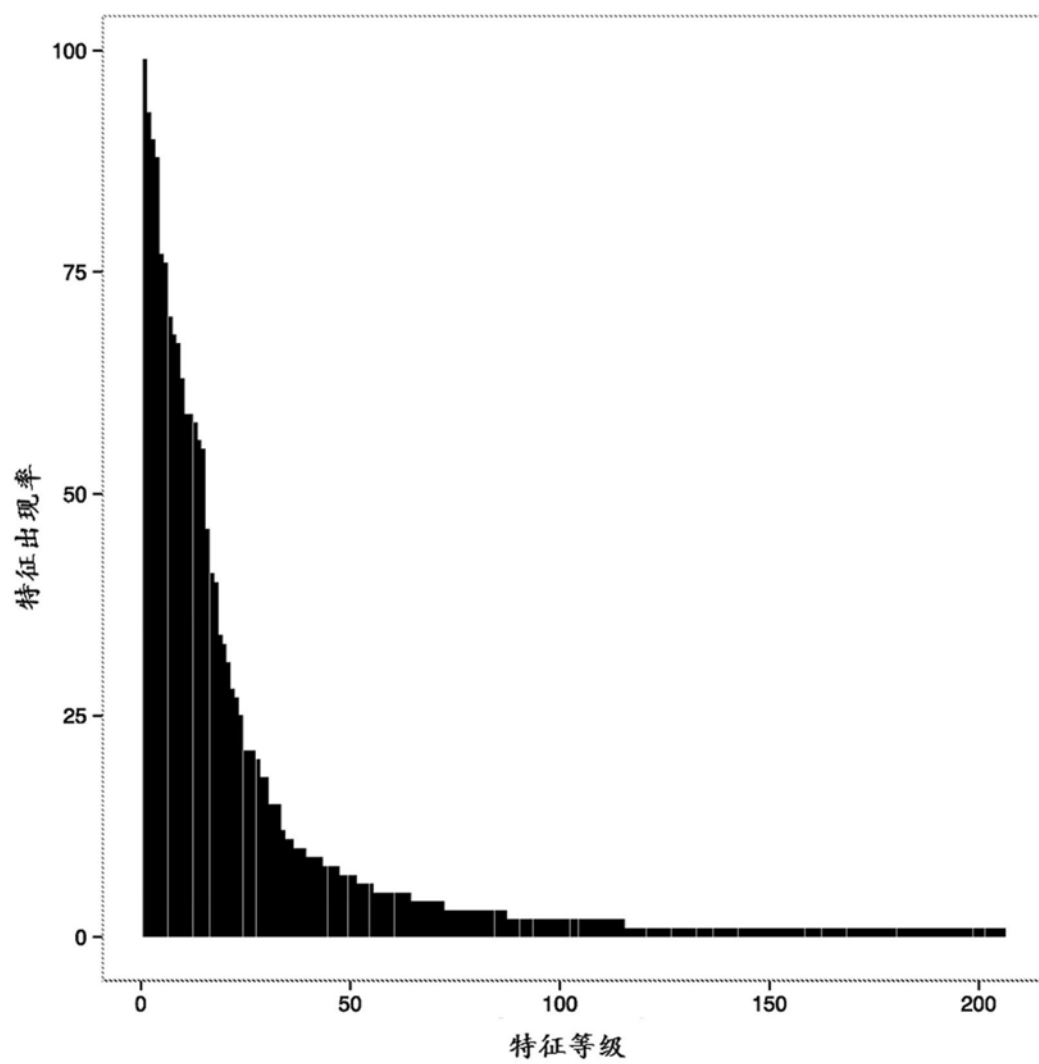


图4

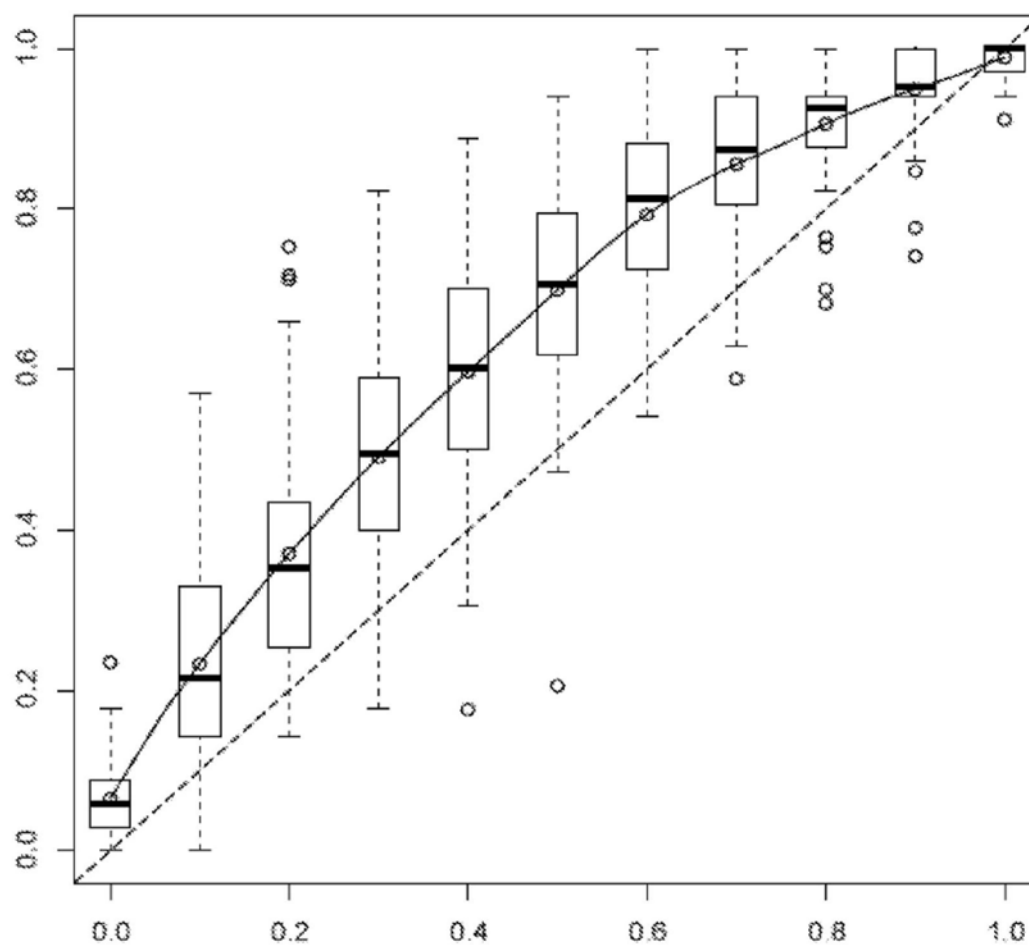


图5

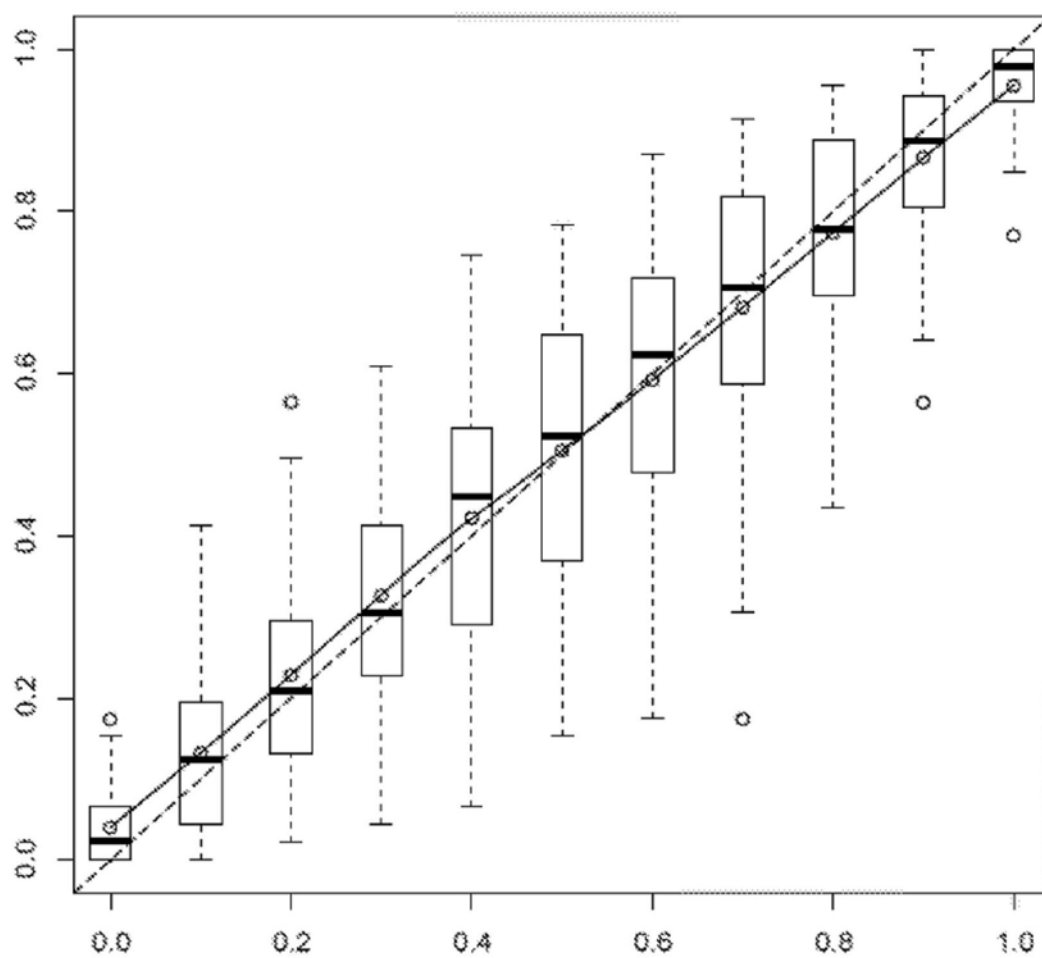


图6

中性质量	分类器 频率				
1280.859291	50	930.4880521	30	1515.251442	22
1239.135649	49	2182.996603	30	2007.080071	22
1985.956097	49	1103.146186	29	3411.472434	22
2477.254682	49	1695.40379	29	2499.220722	22
1678.43676	49	2499.004523	29	1464.287383	22
828.0340546	49	588.3466599	28	727.8597579	22
3038.549902	48	651.3352566	28	1816.822377	22
1105.247979	47	1423.689546	28	1413.512843	22
1456.618686	46	2285.002747	28	1242.715861	21
1684.943282	44	1127.785206	28	344.2206758	21
1985.464468	44	1615.702692	28	3038.141022	21
1020.530256	43	957.5184233	27	1377.334925	21
707.13519	43	1700.844794	27	2033.559716	21
2912.732248	42	1125.64933	27	2571.994949	21
440.9806659	42	1522.808276	27	1219.605149	21
1337.835994	40	2093.351988	27	1582.001996	21
1476.761392	40	3217.768912	27	1309.599756	20
1146.561252	39	3535.95808	27	3000.593189	20
1818.760439	39	1656.897164	26	1473.696014	20
1531.353896	39	1387.255205	26	2697.454242	20
819.3393507	38	1042.455695	26	1066.477284	20
1628.704305	38	3812.577464	26	1989.985366	20
2946.47777	38	960.2116197	26	1261.703826	20
494.0646707	38	1817.159874	26	2948.432217	20
2524.19249	37	2178.965074	25	711.4583118	20
1679.261452	37	1200.527528	25	2636.679097	19
308.129724	37	2786.354169	25	1032.527911	19
422.2197066	35	2477.27019	24	893.4954426	19
3022.572148	34	1740.755479	24	1703.919962	19
3054.518133	33	2658.169206	24	2131.050072	19
1954.007725	32	984.2836764	24	1432.805134	19
2514.631558	32	1598.849716	24	1173.576204	19
1803.350451	31	718.8415383	24	705.4194027	19
1527.658305	31	2750.576737	23	1805.939025	19
1741.829691	31	2033.908003	23	1858.167945	19
1179.567226	31	3038.544735	23	728.3716681	18
2345.226012	30	1793.818251	23	493.2656827	18
2135.110474	30	761.4358638	23	771.6575623	18
1285.828757	30	386.182813	23	920.3557768	18
		1527.661981	23	1187.559054	18
		477.2390672	23	919.4614047	18
		2705.810237	22	2360.178399	18

图7

653.8098853	18	1489.688009	15	934.4464616	12
704.2321796	18	2419.924489	15	2306.104719	12
2506.17666	17	1195.63612	15	816.3960753	12
1593.789468	17	1955.951603	15	1265.696286	12
584.8024263	17	1666.807875	15	2722.698224	12
1594.936404	17	1826.487704	15	2804.333903	12
1786.905847	17	1188.630959	15	2069.753131	12
1816.825774	17	1671.775622	15	3026.313863	12
504.2580006	17	1498.803682	14	1030.469647	12
1280.769213	17	2400.077335	14	823.4257554	12
1815.795709	17	1195.603817	14	1958.918846	12
1925.26736	17	3821.960734	14	1586.623048	12
1402.646882	17	768.4683292	14	821.4124091	12
3014.194029	17	1826.897269	14	584.3738522	12
863.4861578	17	2924.447956	14	1747.783535	12
1271.199658	17	1772.772289	14	1375.556966	12
1623.975402	17	2454.999295	14	2060.881933	12
1595.849587	17	2768.043757	14	797.9211875	12
1163.592202	16	2315.16076	14	2513.339943	12
2793.251034	16	1960.018855	14	3430.57265	12
1613.890795	16	1735.714578	14	911.6157399	12
948.0663086	16	2092.909019	14	2088.108877	11
1792.847081	16	1439.725612	13	2007.370937	11
1195.612435	16	2715.328682	13	1814.622166	11
937.5333487	16	1098.637536	13	1440.668445	11
957.4246968	16	2739.342741	13	2097.746504	11
1474.674777	16	1108.545977	13	323.1812761	11
876.4693839	16	1318.379556	13	2983.510241	11
1764.027106	16	1196.599894	13	1727.896543	11
1471.564652	16	1894.928752	13	1676.117941	11
3385.620472	16	2783.03585	13	2501.183652	11
491.5615299	16	1206.543207	13	1407.711204	11
739.3925383	16	4132.787873	13	2052.9864	11
1178.697069	16	657.6284765	13	2623.17241	11
1598.7649	15	1160.538887	13	1581.771638	11
1476.958498	15	1047.080084	13	1950.374257	11
1110.547752	15	2735.321042	13	1905.795577	11
1694.841276	15	1368.685333	13	2726.071081	11
1303.640891	15	876.4488121	13	2400.496006	11
3605.670842	15	1347.705373	13	1057.507955	11
2967.573707	15	1812.384263	13	1574.36094	11
3089.114621	15	914.38315	13	3324.537295	11
1278.524418	15	654.4064948	13	2173.984642	11
718.0305511	15	1714.823278	12	1895.857411	11

图7 (续)

733.3253316	11	1751.874038	10	708.3710889	9
2150.07399	11	2220.101483	10	1658.764618	9
1667.970072	11	1602.685209	10	1271.187282	9
703.3636979	11	1241.620676	10	2185.457825	9
1990.982964	11	2020.73667	10	387.0141783	9
1179.693455	11	1966.928305	9	608.0503383	9
696.6799279	11	2159.206079	9	835.4977623	9
1118.461963	11	2244.081281	9	1084.544297	9
1747.734027	11	2309.114741	9	2245.067759	9
367.9914374	11	1806.971398	9	1707.747831	9
1682.821575	11	1372.658204	9	779.5412333	9
1060.539151	11	1482.678068	9	1552.656162	9
358.5316953	11	1319.271229	9	710.3428871	9
1080.429863	10	1817.162925	9	1706.048938	9
2831.291513	10	584.3540933	9	2266.064273	9
1607.95233	10	2006.908553	9	1423.68518	9
3437.665567	10	1521.851615	9	1682.834131	9
1224.918332	10	1559.341793	9	3910.86499	8
2137.224005	10	1194.476506	9	2775.829557	8
1553.802219	10	2124.512024	9	1820.876214	8
2251.022525	10	1184.830837	9	2195.919415	8
1916.343771	10	1636.206887	9	2222.147335	8
1170.633806	10	3209.098078	9	1060.554029	8
1368.225854	10	1764.867221	9	1534.673104	8
3734.59818	10	980.2696122	9	1136.497353	8
1536.730485	10	1047.507197	9	2307.571451	8
2052.342523	10	2194.944232	9	985.4844472	8
2856.521794	10	1402.657795	9	1013.870137	8
1368.563507	10	2020.995171	9	1550.109659	8
1473.691067	10	1607.799751	9	2253.166848	8
1653.44164	10	922.4371266	9	2424.683086	8
1258.295692	10	854.4266041	9	956.4093041	8
2121.131033	10	454.0304485	9	664.3678849	8
676.3574456	10	900.4553512	9	2429.102366	8
3183.496838	10	2249.985587	9	784.8656644	8
1455.583346	10	351.0089894	9	2092.905666	8
1280.755177	10	1554.790653	9	1202.59327	8
2088.113556	10	707.4043254	9	1227.997244	8
1312.910345	10	2601.11815	9	1602.804553	8
1004.571226	10	810.4639788	9	2450.256718	8
798.4157028	10	1939.94005	9	2077.956139	8
2057.364926	10	1474.401121	9	3045.126925	8
471.0146187	10	2834.430176	9	1431.737104	8
1953.956195	10	1328.628575	9	784.4779713	8

图7 (续)

1064.485131	8	812.3975109	7	1587.667066	7
1000.621993	8	1225.248412	7	324.1345984	7
1950.97234	8	1828.785329	7	1079.976033	7
498.1605339	8	1319.594317	7	1122.546573	7
864.4392203	8	2116.107252	7	1137.468423	7
2278.113732	8	1728.872456	7	1728.963084	7
930.5547303	8	1863.828871	7	760.4241916	7
906.3131218	8	1585.653154	7	1080.774434	7
1424.655793	8	1280.575613	7	1514.234311	7
1265.288057	8	2075.067729	7	2282.266671	7
1254.634092	8	3587.91521	7	1316.659239	7
648.3611414	8	306.1163962	7	1387.826928	7
2200.032681	8	1522.371234	7	2104.965173	7
2244.081059	8	960.4072128	7	1559.789808	7
2919.333904	8	763.4469317	7	414.2590501	7
1205.613525	8	2272.168208	7	613.3967363	7
2198.073183	8	1779.806365	7	1638.841843	7
1080.470377	8	980.4035868	7	867.5912787	7
2221.190757	8	2945.323519	7	1280.617782	7
762.4664058	8	1187.836917	7	621.2222873	7
1205.694353	8	1219.232042	7	1825.156071	7
1548.741637	8	1325.616869	7	784.4098098	7
2158.447532	8	1102.077981	7	1581.66774	7
468.1876847	8	829.4562194	7	1111.114842	7
2692.127921	8	922.412735	7	1804.931648	7
2020.94582	8	1558.665482	7	1240.568222	7
882.3832467	8	2328.169627	7	1412.394226	7
3248.638568	8	2813.325097	7	2721.28938	7
1522.698415	8	1882.807354	7	1196.611575	6
1970.433056	8	2252.077728	7	2572.273634	6
1319.584412	8	3049.454318	7	1465.898146	6
1789.845924	8	2246.090539	7	1678.861022	6
2153.178069	7	1952.04901	7	1390.235581	6
2714.202314	7	836.3889703	7	2831.136747	6
1271.521648	7	1464.767821	7	952.4466364	6
2978.6174	7	1067.486806	7	1686.793021	6
2388.188926	7	433.6838883	7	3188.576592	6
967.7284891	7	1464.945542	7	1522.705903	6
1289.924817	7	1253.710646	7	2793.562436	6
1124.609902	7	2251.05848	7	1062.629846	6
728.4159353	7	2736.404077	7	825.082693	6
2466.628146	7	2692.121934	7	2562.285431	6
2092.905349	7	1924.761793	7	1740.774143	6
1969.841542	7	4581.040704	7	1385.674398	6

图7 (续)

1298.182675	6	1058.563161	6	1278.306387	5
1552.715079	6	821.4386902	6	1197.61264	5
2760.072956	6	2443.00922	6	2116.208463	5
1483.661202	6	1459.275347	6	1696.701416	5
2404.191094	6	787.348936	6	3271.403035	5
1418.718477	6	1464.966906	6	1611.797286	5
1643.681184	6	1582.336667	6	1457.697677	5
511.0573767	6	1728.815336	6	598.3006898	5
1193.552359	6	597.3618075	6	1553.75725	5
802.4651672	6	409.0531778	6	1633.066531	5
1517.086169	6	558.0135703	6	3089.304879	5
2232.058561	6	1150.547456	6	1806.941122	5
882.8805922	6	649.813554	6	2166.948172	5
476.1447173	6	423.302692	6	2349.030802	5
1939.017361	6	508.0470685	6	1225.652059	5
1706.219211	6	1855.911299	6	2029.882351	5
1735.713361	6	1673.443167	6	1073.47078	5
1683.421891	6	1947.848898	5	2454.113875	5
821.4135719	6	1337.941266	5	2715.224983	5
1741.291892	6	3016.536555	5	1385.255327	5
1956.909617	6	2015.840267	5	1904.403068	5
1078.632339	6	2199.059313	5	812.4009802	5
2768.039218	6	2228.095052	5	1865.902954	5
1705.951729	6	498.2814125	5	1943.817228	5
953.9306905	6	2750.165495	5	1115.491588	5
408.2068081	6	1924.774485	5	586.3788332	5
1105.581567	6	482.2054014	5	1038.433681	5
2172.053747	6	1585.652818	5	1778.690006	5
348.1806168	6	2506.136724	5	2238.993623	5
2240.145035	6	1116.025473	5	898.4217621	5
1489.689479	6	1134.539807	5	562.369265	5
1571.526159	6	1392.64386	5	1458.941578	5
1482.820666	6	2059.093981	5	2136.035951	5
1636.776318	6	2479.148233	5	942.4591629	5
914.4373764	6	1157.61132	5	1806.943641	5
1271.52331	6	810.4701928	5	1458.526209	5
2150.080808	6	1043.283245	5	1984.216015	5
403.03199	6	2336.074025	5	849.4740621	5
1325.536346	6	895.4441149	5	1008.345191	5
1294.635295	6	1600.720266	5	1952.400077	5
550.2630003	6	3150.616201	5	3109.351257	5
1729.704265	6	475.2329518	5	1953.957878	5
1509.718758	6	2612.409811	5	2262.078784	5
1753.811503	6	3770.564522	5	1365.648371	5

图7(续)

336.1055586	5	722.4820901	5	382.1510044	4
1432.841048	5	1534.803775	5	1772.920568	4
1606.115429	5	2337.263856	5	1392.696324	4
706.3862112	5	895.5367915	5	2088.220479	4
2309.0673	5	1463.616556	4	1577.924237	4
588.347913	5	1392.682122	4	1522.035985	4
1888.258293	5	1140.56337	4	1156.513561	4
597.257281	5	1018.864142	4	617.350504	4
1371.623975	5	1290.263212	4	871.6471187	4
2059.866272	5	1869.92372	4	2158.63072	4
399.198574	5	1369.705109	4	2682.206655	4
1636.799974	5	1112.556136	4	2136.049487	4
1382.60319	5	707.4027247	4	427.3021592	4
2082.281689	5	3378.70373	4	3748.584278	4
1520.973646	5	979.1456566	4	984.2830268	4
837.4292788	5	802.8575909	4	1008.438389	4
1460.632733	5	2360.188004	4	944.5485886	4
1509.038743	5	3605.664088	4	1600.750062	4
2150.169986	5	3990.761139	4	1619.788604	4
2207.051728	5	1097.154075	4	2085.873535	4
1079.582353	5	1078.636943	4	3428.463039	4
882.4158446	5	1328.64222	4	1097.264849	4
1284.629852	5	1930.821661	4	2070.882507	4
1068.474677	5	1598.852704	4	462.3209129	4
1068.619217	5	1290.714688	4	2669.051931	4
1286.072442	5	1679.834832	4	1782.801802	4
3827.631272	5	1737.781929	4	1362.647391	4
1482.628713	5	1205.200738	4	733.4204086	4
1038.569473	5	1622.700913	4	1482.633228	4
976.5514941	5	1605.393545	4	1583.736038	4
1508.770682	5	1504.815825	4	1834.914942	4
1603.991597	5	1797.930087	4	1155.595396	4
2477.243186	5	1428.666497	4	2229.936248	4
3113.513773	5	1001.536294	4	2654.168525	4
1908.843836	5	1411.882737	4	1731.866029	4
1273.572888	5	442.2172439	4	1643.854285	4
509.1697042	5	1259.391298	4	2306.151953	4
1179.697725	5	2195.92968	4	2402.172348	4
1260.60432	5	2143.998639	4	1821.804237	4
875.9540154	5	1298.552723	4	1340.984543	4
785.4663035	5	590.247069	4	1659.800026	4
955.6035675	5	739.3886054	4	1488.775812	4
3313.679157	5	2919.479234	4	1877.821619	4
1747.447671	5	1360.618282	4	1974.012972	4

图7(续)

3139.383071	4	1593.705163	4	1204.571185	3
1474.675473	4	1142.787629	4	1671.732926	3
2992.481318	4	1953.999973	4	1558.771543	3
2349.079109	4	829.3705634	4	530.2769133	3
1712.75831	4	1176.623083	4	744.8456525	3
2158.024334	4	1714.41394	4	486.0057662	3
2971.391247	4	890.541987	4	1684.760451	3
1176.314031	4	1471.65187	4	2942.543754	3
1467.805878	4	317.0417319	4	1593.248626	3
2005.98819	4	312.1538262	4	2067.054012	3
1824.869186	4	626.334424	4	694.2740564	3
1280.57281	4	1509.954373	4	1443.393733	3
1349.652837	4	2549.38392	4	1618.670229	3
877.4726661	4	1918.414611	4	1233.853606	3
1266.630526	4	2418.574258	3	4058.214976	3
1790.850342	4	1677.713603	3	1774.01086	3
1125.918913	4	1887.94821	3	3361.718475	3
2350.078136	4	1137.59999	3	1482.699397	3
3248.517395	4	1940.057024	3	2274.236403	3
1308.613261	4	1054.547419	3	1928.937403	3
1802.873863	4	1655.678295	3	1156.541147	3
2488.212136	4	602.3338682	3	2315.01287	3
1508.373659	4	871.5136371	3	1177.497576	3
1420.701755	4	1044.003374	3	888.4498869	3
1946.763111	4	875.9571532	3	617.0585567	3
1766.762478	4	1570.667173	3	440.1539494	3
1495.275821	4	1261.705234	3	444.2398136	3
1271.690267	4	1617.814914	3	1165.544695	3
2099.129825	4	2181.191677	3	2160.06669	3
1492.717533	4	2951.531648	3	3363.480648	3
2254.912852	4	3183.504962	3	1872.940111	3
370.1858478	4	1098.492108	3	795.8580008	3
2033.914169	4	1369.743122	3	1516.637208	3
2072.467285	4	2729.296945	3	1188.175448	3
563.257074	4	1796.832914	3	1629.763759	3
1400.670896	4	3470.721763	3	1846.910751	3
1217.557764	4	1097.680902	3	2163.17881	3
723.3466866	4	1179.610068	3	903.5465302	3
1703.76068	4	2556.19933	3	1954.437292	3
3494.4887	4	2126.025425	3	1273.633235	3
1418.667349	4	1044.136622	3	3381.416499	3
1542.811358	4	1745.844374	3	3718.737385	3
3194.260872	4	1096.5528	3	2082.931277	3
1564.768646	4	2675.156445	3	1257.867522	3

图7(续)

1378.587172	3	1040.671037	3	542.7340532	3
2311.545148	3	1683.220528	3	2407.945379	3
3069.411004	3	2523.347622	3	1696.647798	3
805.8934017	3	2329.878791	3	762.463039	3
2185.480584	3	2251.937416	3	1509.27719	3
1233.603324	3	567.9934426	3	425.9930884	3
2598.01642	3	2957.378373	3	1335.060653	3
717.8581098	3	2707.256826	3	1316.668112	3
1358.677603	3	568.6011113	3	2988.524358	3
1531.791439	3	2827.232752	3	1091.578089	3
1789.228382	3	1729.48511	3	966.6273457	3
1003.531248	3	2675.817991	3	1644.426577	3
2667.206219	3	1331.356918	3	1657.488012	3
4848.363443	3	2948.441045	3	1409.213525	3
2259.228315	3	1412.539611	3	1542.680219	3
600.2783787	3	3270.50955	3	2036.938778	3
1382.654292	3	1200.508199	3	1177.470252	3
2598.190466	3	1676.912138	3	554.3445036	3
2706.176516	3	535.3415708	3	1813.300887	3
1123.602954	3	2856.526452	3	1311.90907	3
906.3368054	3	1402.68831	3	1078.57678	3
2092.811796	3	1083.529348	3	1713.38049	3
406.0304723	3	1232.624375	3	2971.424773	3
2460.021453	3	849.4682922	3	2464.535358	3
3177.44115	3	1090.216953	3	1768.799889	3
1157.681776	3	1098.175282	3	932.4388026	3
2813.341777	3	1955.945428	3	855.511109	3
904.4490305	3	1732.825795	3	1709.033507	3
3350.513506	3	2599.727559	3	665.427559	3
3570.607889	3	773.4321059	3		
990.3076074	3	1262.903496	3		
1374.24927	3	1720.76919	3		
403.2062371	3	1665.424322	3		
493.7622045	3	1528.655314	3		
2369.060931	3	2272.53957	3		

图7 (续)

频率等级	平均中性质量	中性质量标准偏差
1	2514.631	0.01
2	1628.705	0.033
3	1200.5275	0.0095
4	1985.956	0.0093
5	1741.8297	0.0049
6	1239.135	0.028
7	1368.683	0.012
8	1020.5302	0.0053
9	2831.291	0.015
10	1558.665	0.012
11	1146.5611	0.0076
12	1531.3539	0.0073
13	3313.679	0.023
14	1594.9364	0.0078
15	2477.254	0.065
16	2706.173	0.055
17	2786.354	0.022
18	3535.957	0.026
19	2285.002	0.023
20	2501.176	0.013
21	2060.881	0.016
22	1679.2614	0.0089
23	1439.725	0.012
24	1509.7188	0.0093
25	2813.325	0.013
26	2606.289	0.02
27	788.3559	0.0053
28	1527.661	0.016
29	1527.658	0.013
30	2282.266	0.013
31	1280.6178	0.0087
32	1124.6099	0.0048
33	3821.96	0.017
34	2499.0045	0.0093
35	1598.8497	0.0098
36	2131.05	0.014
37	2033.908	0.03
38	1607.799	0.021
39	2534.132	0.042
40	1205.6948	0.0066
41	1833.376	0.012
42	2983.51	0.015
43	2146.859	0.01
44	2149.04	0.013
45	3014.194	0.03
46	2521.183	0.01
47	2178.9649	0.0099
48	4064.252	0.055
49	1686.793	0.0098
50	1280.7548	0.0071
51	2443.009	0.044
52	2211.06	0.03
53	1195.6124	0.0085

图8

54	711.4583	0.0046
55	2272.168	0.01
56	1372.6582	0.0076
57	1500.717	0.014
58	2072.467	0.017
59	2059.094	0.048
60	1233.6033	0.005
61	1713.839	0.011
62	1219.6051	0.0064
63	2400.077	0.01
64	1595.849	0.017
65	1924.761	0.032
66	1392.682	0.01
67	1611.822	0.018
68	1402.6469	0.0061
69	2006.7983	0.009
70	1731.866	0.0096
71	1407.711	0.012
72	1985.464	0.01
73	1569.7434	0.0082
74	2159.205	0.019
75	2988.524	0.012
76	1989.985	0.015
77	2092.9057	0.007
78	1474.6748	0.0059
79	2193.11	0.01
80	2137.223	0.015
81	3748.584	0.01
82	1552.714	0.011
83	2116.107	0.01

84	3038.549	0.011
85	2359.135	0.032
86	1935.866	0.012
87	4132.788	0.013
88	1294.6353	0.0089
89	3055.456	0.022
90	2323.092	0.011
91	2156.087	0.022
92	1482.6287	0.0096
93	2841.328	0.013
94	947.4632	0.0047
95	2179.975	0.012
96	2088.108	0.014
97	2339.142	0.013
98	1365.648	0.012
99	1408.616	0.023
100	2245.067	0.012
101	2302.07	0.025
102	3183.496	0.02
103	2088.113	0.016
104	1956.909	0.035
105	1593.789	0.02
106	2318.131	0.023
107	1666.808	0.01
108	2721.292	0.026
109	2057.364	0.012
110	2546.197	0.02
111	3437.665	0.048
112	1684.943	0.016
113	1644.807	0.034

图8(续)

114	3430.572	0.026	144	1173.576	0.022
115	1598.7648	0.009	145	1526.7146	0.0099
116	2624.749	0.016	146	2479.148	0.023
117	1043.6006	0.0094	147	2844.508	0.016
118	2735.32	0.02	148	1559.7897	0.0062
119	2157.039	0.021	149	1432.8051	0.0087
120	3126.56	0.025	150	1805.9391	0.0056
121	1123.603	0.0045	151	1875.0415	0.0084
122	2975.432	0.016	152	1488.7758	0.0073
123	2164.0213	0.0072	153	1179.693	0.01
124	1902.875	0.011	154	1833.8703	0.0097
125	1411.6631	0.007	155	1110.5477	0.008
126	1428.6665	0.0088	156	1794.4397	0.0079
127	1194.4768	0.0095	157	2079.043	0.013
128	1483.661	0.016	158	876.4686	0.0067
129	972.504	0.014	159	1844.8443	0.009
130	802.465	0.01	160	2563.5673	0.0081
131	1413.5127	0.0085	161	3113.513	0.015
132	3139.383	0.015	162	1410.769	0.011
133	1964.85	0.01	163	2585.187	0.017
134	3035.284	0.017	164	1290.7147	0.0085
135	2513.339	0.011	165	2245.0142	0.0094
136	1686.816	0.0065	166	1778.801	0.018
137	957.4247	0.006	167	2992.481	0.061
138	2246.0905	0.0096	168	1553.755	0.014
139	3115.433	0.016	169	1178.698	0.014
140	1534.5889	0.0064	170	1554.79	0.012
141	2971.426	0.045	171	2417.611	0.035
142	1067.486	0.017	172	2027.916	0.011
143	2938.371	0.015	173	1253.7095	0.0075

图8 (续)

174	1587.6671	0.007
175	2198.13	0.013
176	1140.5988	0.0071
177	2849.298	0.019
178	1242.6024	0.0073
179	3217.768	0.019
180	1392.643	0.015
181	1489.688	0.01
182	1464.767	0.036
183	4990.334	0.018
184	2549.203	0.01
185	1108.5459	0.0047
186	1575.7613	0.0064
187	1105.581	0.013
188	2651.119	0.017
189	1832.027	0.013
190	3031.42	0.014

191	1947.848	0.023
192	1482.633	0.011
193	1496.745	0.01
194	1436.1266	0.0093
195	3439.628	0.015
196	1612.2466	0.006
197	1727.8966	0.0062
198	2315.157	0.016
199	1728.815	0.012
200	1628.847	0.011
201	3605.67	0.013
202	1187.6058	0.0067
203	3004.502	0.025
204	2001.5719	0.0091
205	3072.301	0.011
206	1384.6283	0.0075

图8 (续)

基因名称	蛋白质
IFT74	鞭毛内转运蛋白质74同源物
YWHAZ	14-3-3蛋白质 ζ/δ
RPSA	40S 核糖体蛋白质SA
HSPD1	60 kDa 线粒体热休克蛋白质
ACTB	细胞质1肌动蛋白
ACTG2	γ -肠平滑肌肌动蛋白
C3a-desArg	酰化刺激蛋白质
APC	腺瘤性结肠息肉病蛋白质
AHCY	腺苷高半胱氨酸酶
SLC25A5	ADP/ATP移位酶2
ALDH1B1	线粒体醛脱氢酶X
AKR1B1	醛糖还原酶
ORM1	α -1-酸糖蛋白1
SERPINA1	α -1-抗胰蛋白酶
AMY2B	α -淀粉酶2B
ENO1	α -烯醇酶
FUCA1	α -L-岩藻糖苷酶
SERPINA1	α 1抗胰蛋白酶
AGT	血管紧张素原
ANXA1	膜联蛋白A1
ANXA3	膜联蛋白A3
ANXA4	膜联蛋白A4
ANXA5	膜联蛋白A5
APOA1	载脂蛋白A-1
APOC1	载脂蛋白C1
DARS	细胞质天冬氨酰-tRNA合成酶
ATP5B	线粒体ATP合成酶 β 亚基
BCNP1	B细胞新型蛋白质1
BANK1	具有锚蛋白重复序列的B细胞支架蛋白质
CTTNB1	β 连环蛋白
APOH	β -2-糖蛋白1
BSP	骨唾液蛋白
CRP	C反应蛋白
CA195	C-C趋化因子受体5型
CLEC4D	C型凝集素结构域家族4成员D
CNN1	钙调节蛋白-1
CALR	钙网蛋白
CA 19-9	碳水化合物抗原 19-9
CA1	碳酸酐酶1

图9

CA2	碳酸酐酶2
CEA	癌胚抗原
CTSD	组织蛋白酶D
CTSS	组织蛋白酶S
CTSZ	组织蛋白酶Z
MS4A1	CD20
CD63	CD63抗原(黑色素瘤1抗原)
CHI3L1	甲壳酶3类1(软骨糖蛋白-39)
CGB	绒毛膜促性腺激素 β
CLU	丛生蛋白
CRMP2	脑表反应调节蛋白-2
CCSA-2	结肠癌特异性抗原2
CCSA-3	结肠癌特异性抗原3
CCSA-4	结肠癌特异性抗原4
MIC 1	与结肠癌相关的蛋白质 Mic1
CSF1	集落刺激因子1(巨噬细胞)
C3A	补体c3a成分
C9	补体9成分
C3	补体C3成分
CORO1C	冠蛋白-1C
CKB	肌酸激酶B型
CDA	胞苷脱氨酶
CYFRA 21-1	细胞角蛋白19片段
DYNC1H1	细胞质动力蛋白
ECH1	线粒体 $\delta(3,5)$ - $\delta(2,4)$ -二烯酰-CoA异构酶
DES	结蛋白
CRMP-2	与二氢嘧啶酶相关的蛋白质2
EEF2	延伸因子2
HSP90B1	内质网素
EIF4A3	真核起始因子4A-III
EZR	埃兹蛋白
FERR	铁蛋白
FTL	铁蛋白轻链
FGB	纤维蛋白原 β 链[裂解成:纤维蛋白肽B]
FGG A	纤维蛋白原 γ 链
Seprase	纤维母细胞活化蛋白质 α
FLNA	细丝蛋白-A
FHL1	四又二分之一LIM结构域蛋白质1
MGC20553	FRMD3
ALDOA	果糖-二磷酸醛缩酶
GABRA1	γ -氨基丁酸(GABA) A受体 $\alpha 1$

图9(续)

GSN	钙结合微丝蛋白
GSTP1	谷胱甘肽S-转移酶P
GAPDH	3-磷酸甘油醛脱氢酶
GARS	甘氨酸-tRNA合成酶
GDF15	生长分化因子15
HP	热休克蛋白[裂解成: [热休克蛋白 α 链; 热休克蛋白 β 链]
HSP60	热休克蛋白质 60kDa
TRAP1	线粒体热休克蛋白质 75kDa
HSPB1	热休克蛋白质 β -1
HGF	肝细胞生长因子
HNRNPA1	异质核糖核蛋白A1
HNRNPF	异质核糖核蛋白F
SYNCRIP	异质核糖核蛋白Q
HNRNPA2B1	异质核糖核蛋白A2/B1
HMGB1	高迁移率族蛋白B1
HLA_A	HLA 1类组织相容性抗原 A68 α 链
HSP90AB1	HSP90AB1 蛋白质
HNP 1	人嗜中性粒细胞防御素1
HNP 3	人嗜中性粒细胞防御素3
HABP2	透明质酸结合蛋白2
PPA1	无机焦磷酸酶
IGF-1	胰岛素样生长因子1
IL2RB	白介素2受体 β
IL-8	白介素8
IL-9	白介素9
CYFRA 21-1	I型细胞支架19角蛋白
KRT8	II型细胞支架8角蛋白
LMNB1	核纤层蛋白B1
LAMA2	层粘连蛋白 α 2
LGALS3	可溶性半乳糖凝集素3
SERPINB1	白细胞弹性蛋白酶抑制剂
M-CSF	巨噬细胞集落刺激因子1
MIF	巨噬细胞迁移抑制因子
CAPG	巨噬细胞加帽蛋白
MMP7	基质金属蛋白酶-7
MMP9	基质金属蛋白酶9
TIMP 1	金属蛋白酶抑制剂1
MAPRE1	微管相关的蛋白质RP/EB家族成员1
MCM4	微小染色体维持复合体组分4
MYL6	肌球蛋白轻多肽6

图9 (续)

MYL9	肌球蛋白调节轻多肽9
NNMT	烟酰胺N甲基转移酶
NME1	核苷二磷酸激酶A
OPN	骨桥蛋白
TATI	胰分泌型胰蛋白酶抑制型
PRDX1	过氧化氧化还原蛋白-1
PTEN	磷酸酶和张力蛋白同源物
PEBP1	磷脂酰乙醇胺结合蛋白质1
PITPNA	磷脂酰肌醇转移蛋白质 α 同种型
PCK2	线粒体磷酸烯醇丙酮酸羧基酶[GTP]
PLAU	尿激酶型纤维蛋白酶原激活剂
Prolactin	催乳素
PRRG4	脯氨酸富Gla 4
PSME3	蛋白酶体激活剂复合体3亚基
PDIA3	蛋白质二硫化物异构酶A3
PDIA6	蛋白质二硫化物异构酶A6
PKD	蛋白质激酶D
PTK2B	蛋白质酪氨酸激酶2 β
SRC	原癌基因酪氨酸蛋白激酶Src
DKFZp686M08189	推定的未表征的蛋白质DKFZp686M08189
PDXK	吡哆醛激酶
PKM2	丙酮酸激酶同工酶M1/M2
M2-PK	丙酮酸激酶同工酶M1/M2
RhoA	Ras同源物家族成员A
RhoB	Ras同源物家族成员B
RhoC	Ras同源物家族成员C
REG4	再生胰岛衍生蛋白质4
ALDH1A1	视黄醛脱氢酶1
RHGDIA	Rho GDP-相关性抑制剂1
RRBP1	核糖体结合蛋白质1
S100A11	S100 A11 钙结合蛋白质
S100A12	S100 A12 钙结合蛋白质
S100A8	S100 A8钙结合蛋白质
S100A9	S100 A9钙结合蛋白质
SCGN	促泌素
SELPLG	选择蛋白P配体
SELENBP1	硒结合蛋白质1
SEPT9	胞裂蛋白9
SERPINA3	丝氨酸蛋白酶抑制剂, 分化枝A, 成员3
LKB1/STK11	丝氨酸/苏氨酸激酶11
TF	血清铁传递蛋白/铁转蛋白

图9(续)

SERPINB6	丝氨酸蛋白酶抑制蛋白B6
ALB	血清白蛋白
SAA	血清淀粉样A
SAA2	血清淀粉样A2
sCD26	血清可溶性CD26/二肽基肽酶IV
SCF	包含Skp、Cullin、F-box的复合体（多蛋白质复合体）
CD24	小细胞肺癌膜4抗原
SF3B3	剪接因子3B亚基3
Spondin-2	脊椎蛋白-2
HSPA9	线粒体应激70蛋白质
SDHA	线粒体琥珀酸脱氢酶[泛醌]黄素蛋白亚基
TAL1	T-细胞急性淋巴细胞白血病蛋白质1
TST	硫代硫酸硫转移酶
THBS1	凝血酶敏感蛋白-1
TKT	转酮醇酶
TPT1	翻译控制的肿瘤蛋白质
TPM2	原肌球蛋白β链
TUBB1	微管蛋白β-1链
Trail-R2	肿瘤坏死因子受体超家族成员10b
DcR3	肿瘤坏死因子受体超家族成员6b, 诱感物
TNFAIP6	肿瘤坏死因子α诱导的蛋白质6
TP53	肿瘤蛋白质53
UGDH	UDP-右旋糖6-脱氢酶
UGP2	UDP-右旋糖-1-磷酸尿苷酰转移酶
KRAS	v-Ki-ras2克里斯丁大鼠肉瘤病毒癌基因同源物
VNN1	Vanin 1
VEGF	血管内皮生长因子
VIL1	绒毛蛋白-1
VIM	波形蛋白
RAC	

图9 (续)

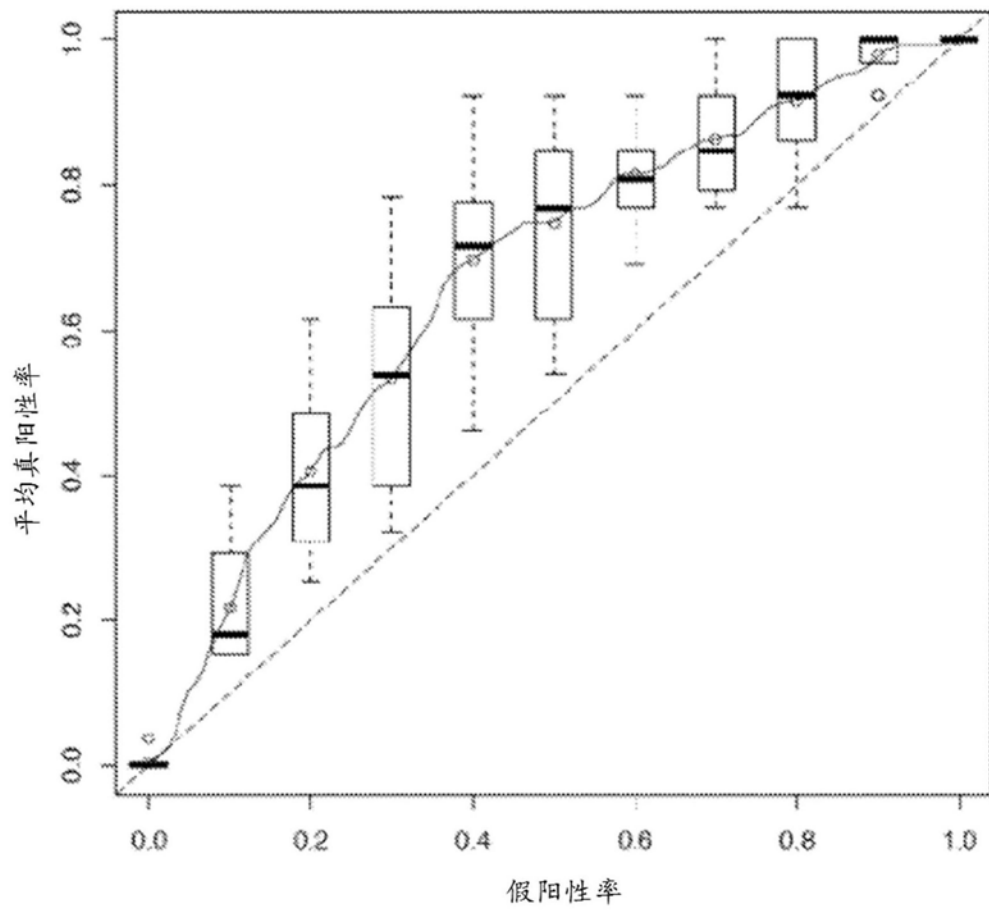


图10

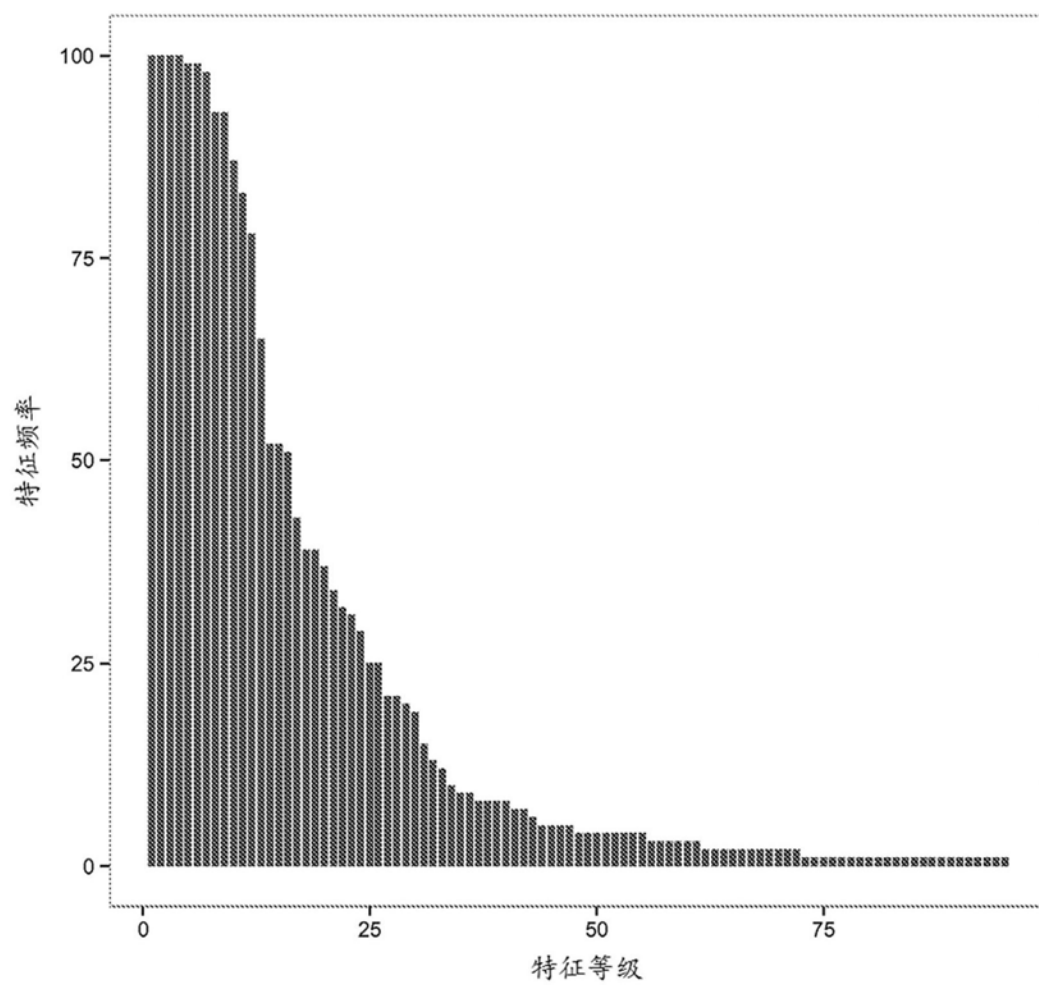


图11

过渡离子	UNIPRO 蛋白质ID	频率排序
IAELLSPGSVDPLTR_b5	SPB6_HUMAN	1
KPAEDEWGK_y8	FRIL_HUMAN	2
VEYLDDR_y6	P53_HUMAN	3
WVAVVPSGQEQR_y7	1A68_HUMAN	4
DATNVGDEGGFAPNILENK_b5	ENOA_HUMAN	5
KPAEDEWGK_y3	FRIL_HUMAN	6
AVELAANTK_y5	TKT_HUMAN	7
FLSDASVTAGGFQIK_y6	TSG6_HUMAN	8
SLEAQADK_y6	TPM2_HUMAN	9
IYKSDGIK_b2	ADT2_HUMAN	10
QVIGTGSFFPK_y8	FHL1_HUMAN	11
YLAVVHAVFALKAR_y8	CCR5_HUMAN	12
INGIPQQHTQVLFIK_b3	CEAM5_HUMAN	13
HSLVSFVVR_y7	SPON2_HUMAN	14
WVAVVPSGQEQR_b3	1A68_HUMAN	15
EWEFQK_b3	RBX1_HUMAN	16
VGIVAWHPTAR_y6	COR1C_HUMAN	17
FADLSEAANR_b3	VIME_HUMAN	18
ITSEAEDLVANFFPK_y7	PSME3_HUMAN	19
FEIELPAAPK_y8	MIC1_HUMAN	20
LFENIGK_y5	STK11_HUMAN	21
DPLNPIKQDVK_y7	IPYR_HUMAN	22
EPLGPALAHCLR_y8	SBP1_HUMAN	23
LYTLVLTPDAPSR_y8	PEBP1_HUMAN	24
QPGITFIAAK_y5	CATD_HUMAN	25
TEGDGVYTLNNEK_b3	HPT_HUMAN	26
VLTEIIASR_y6	ANXA5_HUMAN	27

图12

ALQASALK_y3	ALDOA_HUMAN	28
NSHIAIAFDDTK_b3	LAMA2_HUMAN	29
VGDYGSLSGR_y6	CATZ_HUMAN	30
GYSFTTTAER_b3	ACTB_HUMAN	31
GKITDLIK_y3	AACT_HUMAN	32
EIFVDEDK_y4	TMG4_HUMAN	33
DGAGDVAFVK_y8	TRFE_HUMAN	34
VLSIQSHVIR_y7	PDXK_HUMAN	35
LRISPDR_b3	MIF_HUMAN	36
ISRAALPEGLPEASR_b6	GDF15_HUMAN	37
EHSSLAFWK_y7	APOH_HUMAN	38
SERPVLVR_b3	APC_HUMAN	39
KIEEQLTLEK_y8	ILEU_HUMAN	40
LIQQTFR_y6	FAK1_HUMAN	41
QAVTNPNNTFYATK_b3	GRP75_HUMAN	42
TVDAAASR_y6	VEGFA_HUMAN	43
DFDFVPPVVR_y5	CO3_HUMAN	44
GYSIFSYATK_y8	CRP_HUMAN	45
GADVWFK_b3	S10A8_HUMAN	46
TGIIDYGIR_y6	TSG6_HUMAN	47
NALLSLAK_y5	ANXA1_HUMAN	48
ADEGISFR_y3	PRDX1_HUMAN	49
AFVFDK_y3	HGF_HUMAN	50
EGNPEEDLTADK_y9	CAPG_HUMAN	51
LRDLLTR_b3	ECH1_HUMAN	52
YFLHQSHEER_y7	FRIH_HUMAN	53
FTAFYASR_y3	CUL1_HUMAN	54
LSKNEILR_y5	TAL1_HUMAN	55
AVSEGYK_y5	CDD_HUMAN	56
QVTNAVLK_y6	CUL1_HUMAN	57

图12(续)

LGANSLDLVVFGFGR_y8	DHSA_HUMAN	58
LAADVKGAGAER_y5	ADT2_HUMAN	59
NVDGVNYASITR_y9	CATZ_HUMAN	60
LLNLLADLVER_y6	AL1B1_HUMAN	61
GHFDTLSK_y5	S10AC_HUMAN	62
SPPGQVTEAVK_y8	ALDR_HUMAN	63
DLILNPR_y4	SF3B3_HUMAN	64
LGVEVEDQITAVR_y10	SEPR_HUMAN	65
KAFVFPK_y5	CRP_HUMAN	66
FGSYAYTR_y3	GBRA1_HUMAN	67
QIDNPDK_y4	CALR_HUMAN	68
TLIGHVPDQR_y5	PCKGM_HUMAN	69
PSISSNNSNPK_y6	CEAM3_HUMAN	70
DPGVLDLDR_y5	S10AB_HUMAN	71
LGANSLDLVVFGFGR_y5	DHSA_HUMAN	72
LFQVQGTGANNTK_b3	VILI_HUMAN	73
TLAILAAILLVALQAQAEPLQAR_y8	DEF1_HUMAN	74
EAFQLFDR_b4	MYL6_HUMAN	75
LEGLTDEINFLR_y7	K2C8_HUMAN	76
PEYDEAGPSIVHR_y9	ACTH_HUMAN	77
ALQASALK_y6	ALDOA_HUMAN	78
YHTINGHNAEVR_b3	ROA2_HUMAN	79
SFEDIHHYR_y6	RASK_HUMAN	80
FEIELPAAPK_y6	MIC1_HUMAN	81
ISELTTEVNK_y6	IFT74_HUMAN	82
FGSYAYTR_y5	GBRA1_HUMAN	83
FIDPLAK_y4	MCM4_HUMAN	84
DITSDTSGDFR_b3	ANXA1_HUMAN	85
IEDSEENGVEFK_y7	SIAL_HUMAN	86
LQAILGVPWK_b3	ANGT_HUMAN	87

图12(续)

AAGDSNLK_y7	AL1B1_HUMAN	88
LRDLLTR_y5	ECH1_HUMAN	89
LTIESTPFNVAEGK_b5	CEAM6_HUMAN	90
VTIDSSYDIAK_y9	CH3L1_HUMAN	91
SGYLLPDTK_b3	ENPL_HUMAN	92
GGRALFQDIK_b3	FRIL_HUMAN	93
NQYVSNGLR_b3	SPON2_HUMAN	94
VVDLLAPYAK_y7	ATPB_HUMAN	95

图12(续)

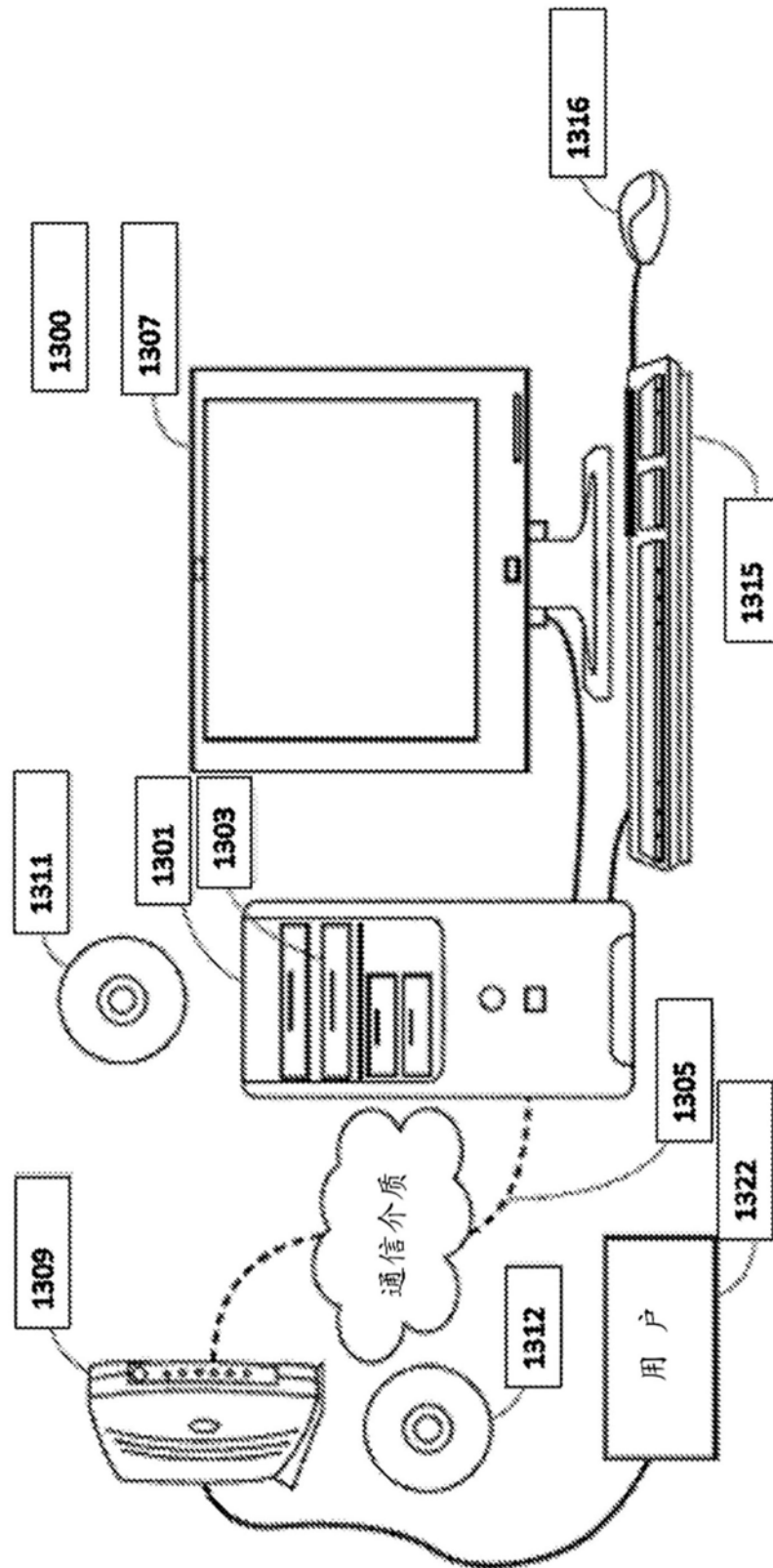


图13

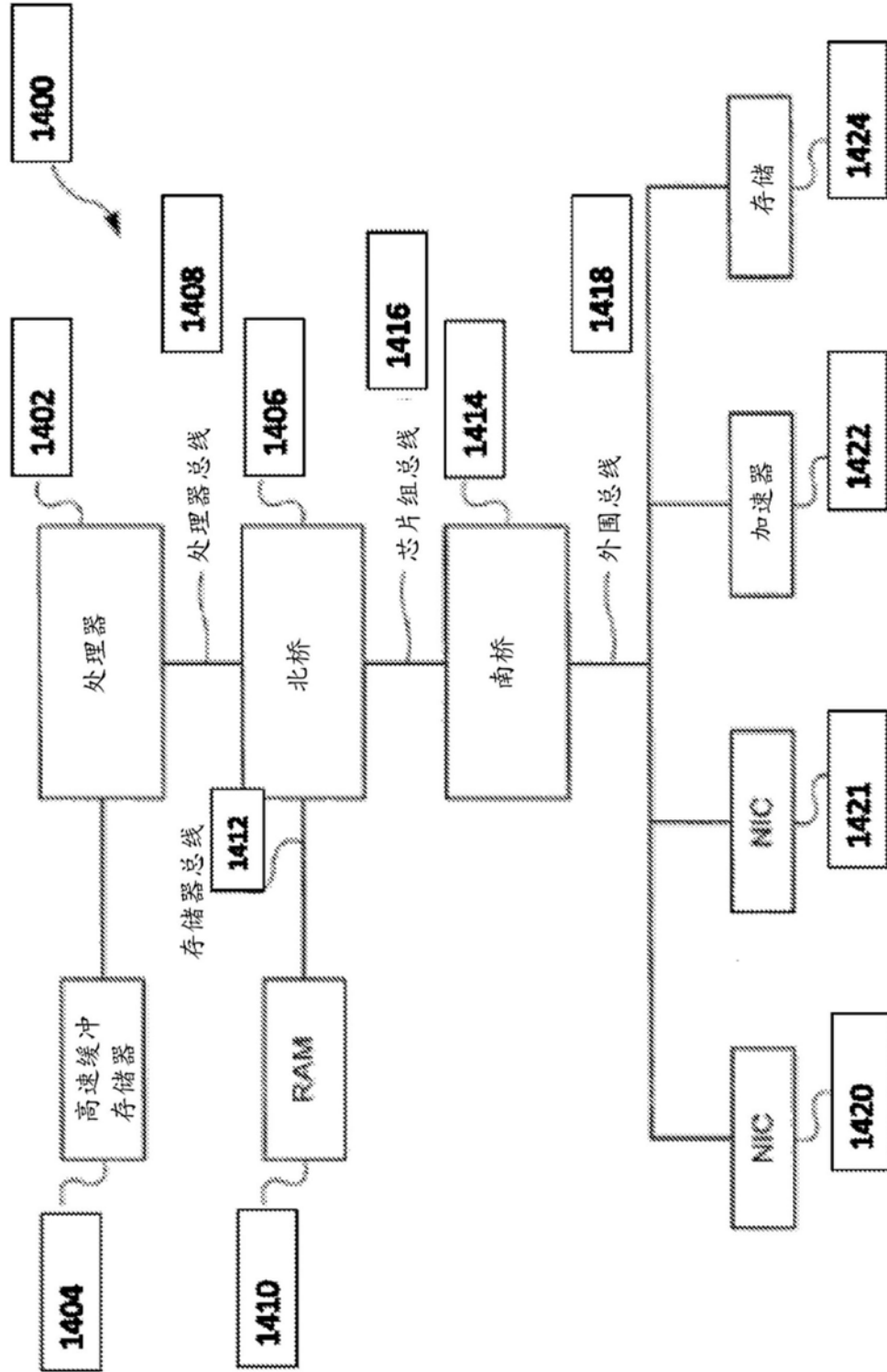


图14

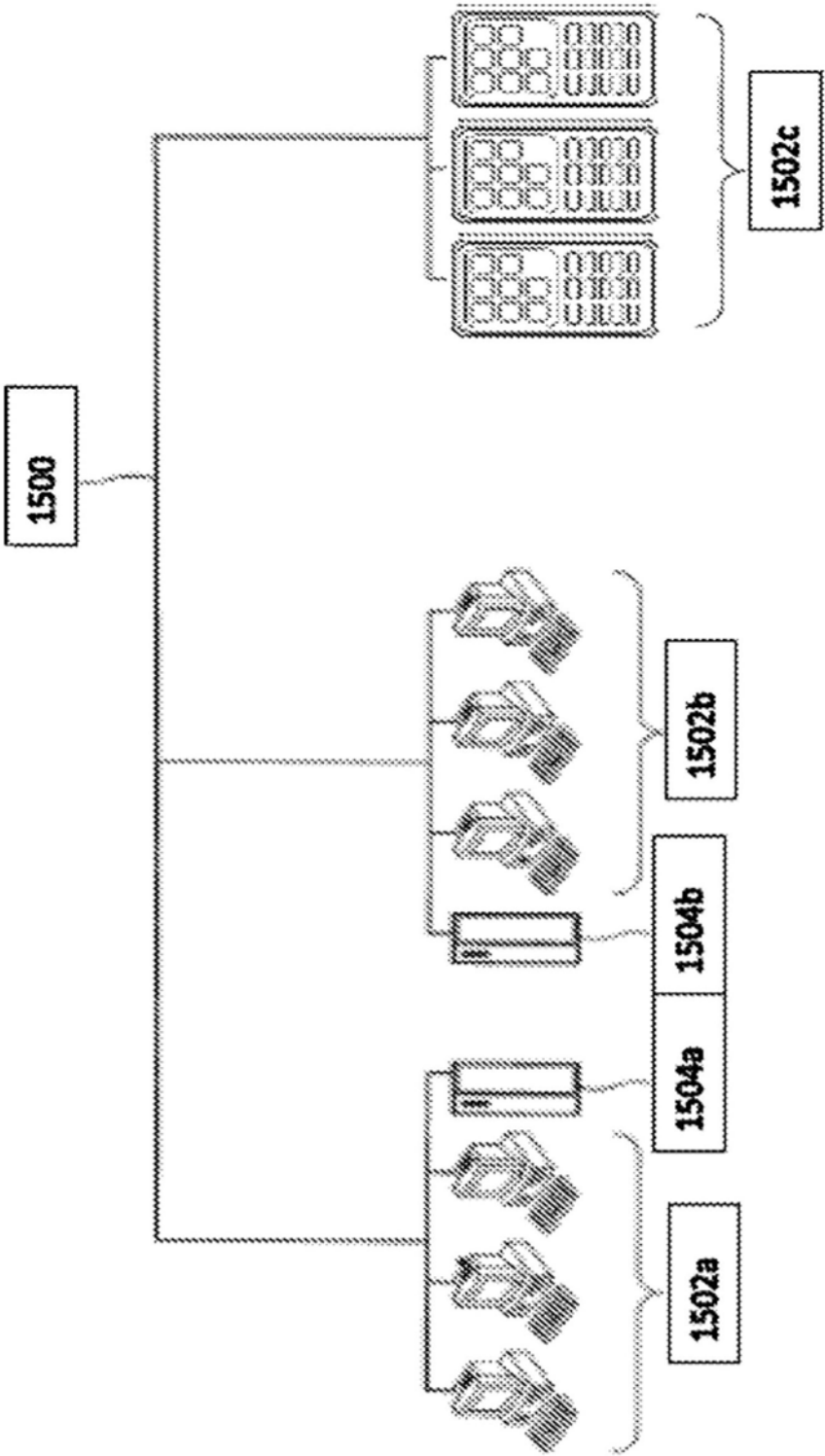


图15

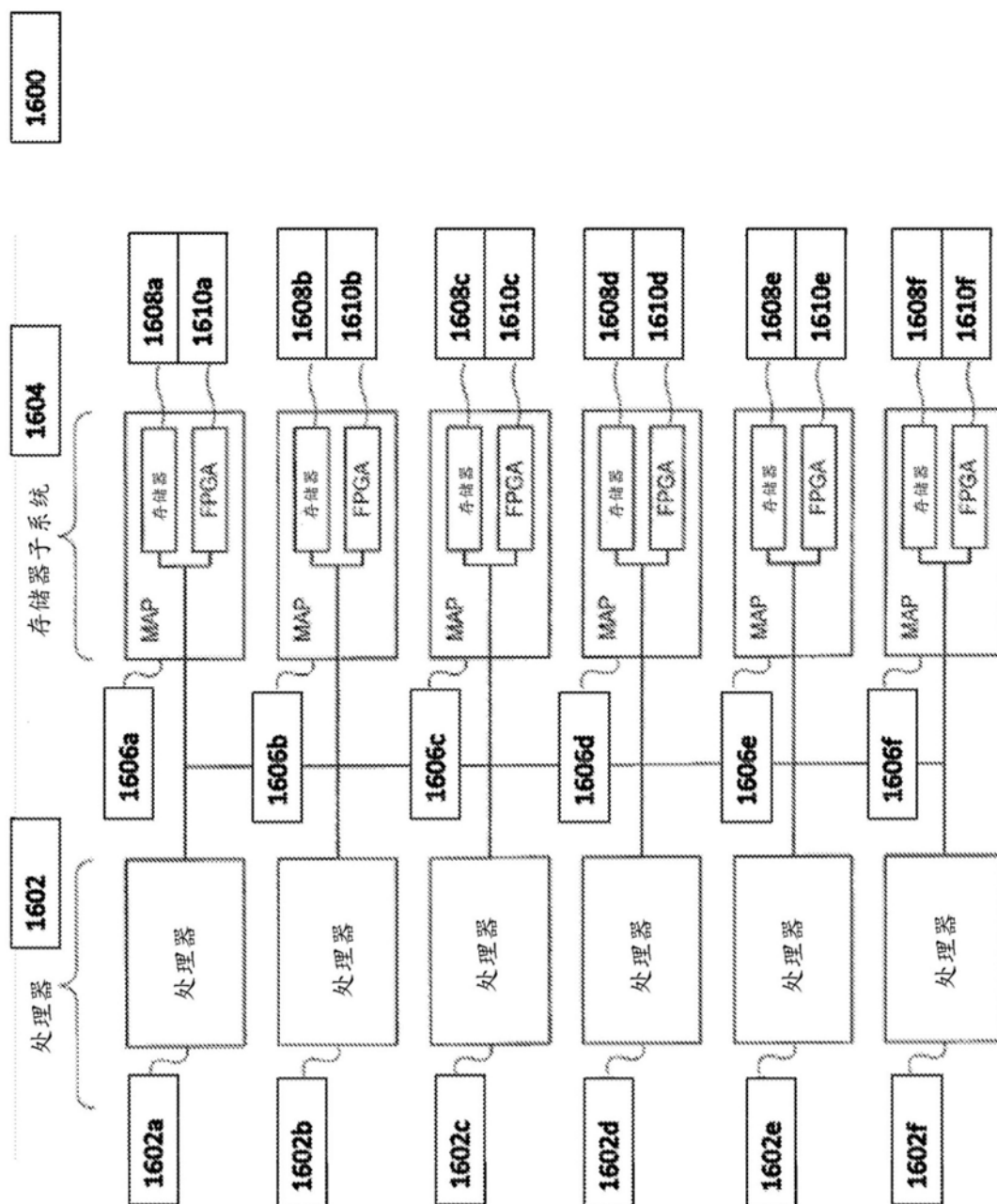


图16