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(56)參考文獻：

期刊 Puskas J., et al., "Development of an attenuated interleukin-2 fusion protein that can be activated by tumour-expressed proteases",Immunology,Vol. 123, 無 2011, page 206-220.

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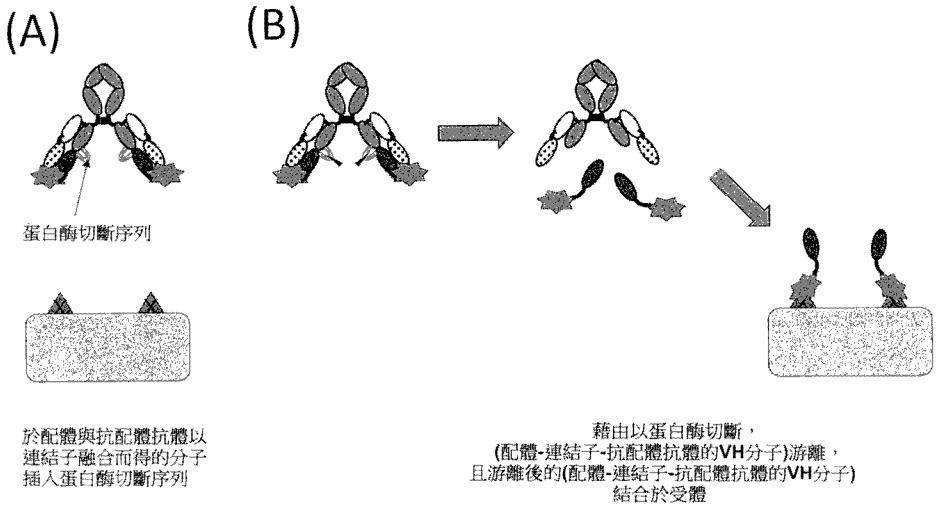
(54)名稱

能夠調節配體結合活性的配體結合分子

(57)摘要

本發明係關於藉由在切斷位點被切斷而減弱對於配體之結合活性之配體結合分子及其製造方法、由該配體結合分子與配體形成之複合體、含有該配體結合分子與配體之融合蛋白質、含有配體結合分子或配體結合分子與配體之融合蛋白質之醫藥組合物。

指定代表圖：



第1圖

I776827

【發明摘要】

【中文發明名稱】　能夠調節配體結合活性的配體結合分子

【中文】

本發明係關於藉由在切斷位點被切斷而減弱對於配體之結合活性之配體結合分子及其製造方法、由該配體結合分子與配體形成之複合體、含有該配體結合分子與配體之融合蛋白質、含有配體結合分子或配體結合分子與配體之融合蛋白質之醫藥組合物。

【指定代表圖】　第（1）圖

【代表圖之符號簡單說明】無。

【發明說明書】

【中文發明名稱】　能夠調節配體結合活性的配體結合分子

【技術領域】

【0001】　本發明提供至少有1個切斷位點且在該切斷位點被切斷之狀態時與配體之結合減弱之配體結合分子、該配體結合分子之製造方法、以及含有該配體結合分子之醫藥組合物。

【先前技術】

【0002】　抗體在血漿中的安定性高、副作用少，故作為醫藥品受到重視。其中IgG1型的抗體醫藥已有多數個上市，現在也有許多抗體醫藥正在開發 (非專利文獻1、及非專利文獻2)。

【0003】　作為使用抗體醫藥之癌治療藥，至今認可的已有對抗CD20抗原之Rituxan、對抗EGFR抗原之Cetuximab、對抗HER2抗原之Herceptin等(非專利文獻3)。該等抗體分子結合於在癌細胞表現的抗原，利用ADCC、信息妨礙等發揮對於癌細胞之傷害活性。

【0004】　又，已知有對於會結合於在癌細胞高表現之癌抗原的抗體分子融合了細胞介素等具生理活性之配體而得的免疫細胞介素，以將配體傳遞到固體癌的方法。利用免疫細胞介素而傳遞到固體癌的細胞介素，藉由活化免疫而發揮抗腫瘤效果。IL2、IL12、TNF為主的細胞介素因為毒性強，該等細胞介素在癌局部作用，所以期待利用抗體而傳遞到癌的局部，藉此減輕副作用並加強效果(非專利文獻4、5、6)，但是它們有:在全身投予皆在臨床未顯示充分的效果、治療窗(therapeutic window)窄、毒性強而無法全身投予等課題，尚未認可作為醫藥品。

【0005】 就其重大原因可列舉:雖是免疫細胞介素但全身投予的細胞介素會暴露於全身，所以可能全身作用而發揮毒性、或為了避免毒性而僅能以極低用量投予。也有人報告於會結合於癌抗原之抗體融合了IL2的免疫細胞介素和於不會結合於癌抗原之抗體融合了IL2的免疫細胞介素，抗腫瘤效果並無不同(非專利文獻7)。

【0006】 就避免上述問題的方法而言，有人報告將細胞介素與細胞介素受體之間以會被在癌中為高表現之蛋白酶切斷之連結子結合而得的分子。細胞介素會因以連結子結合之細胞介素受體而受抑制，但連結子若被蛋白酶切斷則細胞介素會從細胞介素受體游離且成為活性體。舉例而言，有人報告TNF-alpha與TNF-R以會被uPA切斷之連結子結合而得之分子(非專利文獻8)，有人報告IL2與IL2R以會被MMP2切斷之連結子結合而得之分子(非專利文獻9)。但是該等分子雖在連結子切斷前，細胞介素有活性，因連結子之切斷獲致之活性提高僅有約10倍的程度。又，有人報告將IL2R替換為抗IL2 scFv，以會被MMP-2切斷之連結子與IL2結合而得之分子(非專利文獻9)。

[先前技術文獻]

[非專利文獻]

【0007】

[非專利文獻1] Monoclonal antibody successes in the clinic. Janice M Reichert, Clark J Rosensweig, Laura B Faden & Matthew C Dewitz, Nat. Biotechnol. (2005) 23, 1073-1078

[非專利文獻2] The therapeutic antibodies market to 2008. Pavlou AK, Belsey MJ., Eur. J. Pharm. Biopharm. (2005) 59 (3), 389-396

[非專利文獻3] Monoclonal antibodies: versatile platforms for cancer immunotherapy. Weiner LM, Surana R, Wang S., Nat. Rev. Immunol. (2010) 10 (5),

317-327

[非專利文獻4] Cyclophosphamide and tucotuzumab (huKS-IL2) following first-line chemotherapy in responding patients with extensive-disease small-cell lung cancer. Gladkov O, Ramlau R, Serwatowski P, Milanowski J, Tomeczko J, Komarnitsky PB, Kramer D, Krzakowski MJ. Anticancer Drugs. 2015 Nov;26(10):1061-8.

[非專利文獻5] Defining the Pharmacodynamic Profile and Therapeutic Index of NHS-IL12 Immunocytokine in Dogs with Malignant Melanoma. Paoloni M, Mazcko C, Selting K, Lana S, Barber L, Phillips J, Skorupski K, Vail D, Wilson H, Biller B, Avery A, Kiupel M, LeBlanc A, Bernhardt A, Brunkhorst B, Tighe R, Khanna C. PLoS One. 2015 Jun 19;10(6):e0129954.

[非專利文獻6] Isolated limb perfusion with the tumor-targeting human monoclonal antibody-cytokine fusion protein L19-TNF plus melphalan and mild hyperthermia in patients with locally advanced extremity melanoma. Papadia F, Basso V, Patuzzo R, Maurichi A, Di Florio A, Zardi L, Ventura E, Gonzalez-Iglesias R, Lovato V, Giovannoni L, Tasciotti A, Neri D, Santinami M, Menssen HD, De Cian F. J Surg Oncol. 2013 Feb;107(2):173-9.

[非專利文獻7] Antigen specificity can be irrelevant to immunocytokine efficacy and biodistribution. Tzeng A, Kwan BH, Opel CF, Navaratna T, Wittrup KD. Proc Natl Acad Sci U S A. 2015 Mar 17;112(11):3320-5.

[非專利文獻8] Cancer Immunol Immunother. 2006 Dec;55(12):1590-600. Epub 2006 Apr 25. Target-selective activation of a TNF prodrug by urokinase-type plasminogen activator (uPA) mediated proteolytic processing at the cell surface. Gerspach J1, Nemeth J, Munkel S, Wajant H, Pfizenmaier K.

[專利文獻9] Immunology. 2011 Jun;133(2):206-20. doi: 10.1111/j.1365-2567.2011.03428.x. Epub 2011 Mar 23. Development of an attenuated interleukin-2 fusion protein that can be activated by tumour-expressed proteases. Puskas J1, Skrombolas D, Sedlacek A, Lord E, Sullivan M, Frelinger J.

【發明內容】

(發明欲解決之課題)

【0008】 本發明係有鑑於如此的情況而成，目的之一在於提供在標靶組織將細胞介素或趨化介素等配體予以選擇性地活化的配體結合分子、含有該配體結合分子之醫藥組合物、該醫藥組合物及該有效成分之製造方法。

(解決課題之方式)

【0009】 本案發明人等為了達成上述目的而努力銳意研究，結果創作出藉由切斷位點被切斷而減弱對於配體之結合活性的配體結合分子。又，本案發明人等發現該配體結合分子或含有該配體結合分子之醫藥組合物在使用該配體治療病症方面為有用，並發現在包括投予該配體結合分子之步驟之病症之治療有用、及該配體結合分子在製造用以治療病症之醫藥為有用。又，本案發明人等創作出該配體結合分子之製造方法而完成本發明。

【0010】 本發明係基於如此的知見，具體而言包括以下例示性地記載的態樣。

(1) 一種配體結合分子，係能夠結合於配體之分子，該分子係為具有至少1個切斷位點之多胜肽，且於該分子在至少1個切斷位點被切斷之狀態，與配體之結合減弱。

(2) 如(1)之配體結合分子，其中，於前述切斷位點被切斷的狀態，前述配體從前述配體結合分子游離。

(3) 如(1)或(2)之配體結合分子，其中，該切斷位點包括蛋白酶切斷序列。

(4) 如(3)之配體結合分子，其中，該蛋白酶係標靶組織專一性的蛋白酶。

(5) 如(4)之配體結合分子，其中，該標靶組織為癌組織，該標靶組織專一性的蛋白酶係癌組織專一性的蛋白酶。

(6) 如(4)之配體結合分子，其中，該標靶組織為發炎組織，該標靶組織專一性的蛋白酶係發炎組織專一性的蛋白酶。

(7) 如(3)至(6)中任一項之配體結合分子，其中，前述蛋白酶係選自Matriptase、尿激酶(uPA)、及金屬蛋白酶中之至少1種蛋白酶。

(8) 如(3)之配體結合分子，其中，前述蛋白酶切斷序列係含有選自序列編號：3、34、66、70、71、72、73、35、75、76、及345記載之序列中之序列的序列。

(9) 如(3)至(8)中任一項之配體結合分子，其中，在前述蛋白酶切斷序列一端更附加第一可動連結子。

(10) 如(9)之配體結合分子，其中，在前述蛋白酶切斷序列之另一端更附加第二可動連結子。

(11) 如(9)之配體結合分子，其中，前述第一可動連結子係由甘胺酸-絲胺酸聚合物構成之可動連結子。

(12) 如(10)之配體結合分子，其中，前述第二可動連結子係由甘胺酸-絲胺酸聚合物構成之可動連結子。

(13) 如(1)至(12)中任一項之配體結合分子，其中，前述配體結合分子包括抗體VH、抗體VL、及抗體不變區。

(14) 如(13)之配體結合分子，其中，前述切斷位點、或前述蛋白酶切斷序列、或蛋白酶切斷序列與第一可動連結子、或蛋白酶切斷序列與第一可動連結子與第二可動連結子，係位在前述抗體不變區內。

(15) 如(14)之配體結合分子，其中，前述切斷位點、或前述蛋白酶切斷序列、或

蛋白酶切斷序列與第一可動連結子、或蛋白酶切斷序列與第一可動連結子與第二可動連結子，係插入在抗體重鏈不變區118號胺基酸(EU編號)至抗體重鏈不變區140號胺基酸(EU編號)的序列中之任意位置。

(16) 如(14)之配體結合分子，其中，前述切斷位點、或前述蛋白酶切斷序列、或蛋白酶切斷序列與第一可動連結子、或蛋白酶切斷序列與第一可動連結子與第二可動連結子，係插入在抗體輕鏈不變區108號胺基酸(EU編號)(Kabat編號108號)至抗體輕鏈不變區131號胺基酸(EU編號)(Kabat編號131號)之序列中之任意位置。

(17) 如(13)之配體結合分子，其中，前述切斷位點、或前述蛋白酶切斷序列、或蛋白酶切斷序列與第一可動連結子、或蛋白酶切斷序列與第一可動連結子與第二可動連結子，係位在前述抗體VH內或前述抗體VL內。

(18) 如(17)之配體結合分子，其中，前述切斷位點、或前述蛋白酶切斷序列、或蛋白酶切斷序列與第一可動連結子、或蛋白酶切斷序列與第一可動連結子與第二可動連結子，係插入在選自由抗體VH7號胺基酸(Kabat編號)至16號胺基酸(Kabat編號)、40號胺基酸(Kabat編號)至47號胺基酸(Kabat編號)、55號胺基酸(Kabat編號)至69號胺基酸(Kabat編號)、73號胺基酸(Kabat編號)至79號胺基酸(Kabat編號)、83號胺基酸(Kabat編號)至89號胺基酸(Kabat編號)、95號胺基酸(Kabat編號)至99號胺基酸(Kabat編號)、及101號胺基酸(Kabat編號)至113號胺基酸(Kabat編號)構成之群組的序列中之任意位置。

(19) 如(17)之配體結合分子，其中，前述切斷位點、或前述蛋白酶切斷序列、或蛋白酶切斷序列與第一可動連結子、或蛋白酶切斷序列與第一可動連結子與第二可動連結子，係插入在選自由抗體VL7號胺基酸(Kabat編號)至19號胺基酸(Kabat編號)、39號胺基酸(Kabat編號)至46號胺基酸(Kabat編號)、49號胺基酸(Kabat編號)至62號胺基酸(Kabat編號)、及96號胺基酸(Kabat編號)至107號胺基酸

(Kabat編號)構成之群組的序列中之任意位置。

(20)如(13)之配體結合分子，其中，前述切斷位點、或前述蛋白酶切斷序列、或蛋白酶切斷序列與第一可動連結子、或蛋白酶切斷序列與第一可動連結子與第二可動連結子，位在前述抗體不變區與前述抗體VH之交界附近、或/及前述抗體不變區與前述抗體VL之交界附近。

(21)如(20)之配體結合分子，其中，前述切斷位點、或前述蛋白酶切斷序列、或蛋白酶切斷序列與第一可動連結子、或蛋白酶切斷序列與第一可動連結子與第二可動連結子，係插入在抗體VH109號之胺基酸(Kabat編號)至抗體重鏈不變區122號之胺基酸(EU編號)之序列中之任意位置。

(22)如(20)之配體結合分子，其中，前述切斷位點、或前述蛋白酶切斷序列、或蛋白酶切斷序列與第一可動連結子、或蛋白酶切斷序列與第一可動連結子與第二可動連結子，係插入在抗體VL104號之胺基酸(Kabat編號)至抗體輕鏈不變區113號之胺基酸(EU編號)(Kabat編號113位)之序列中之任意位置。

(23) 如(13)至(22)中任一項之配體結合分子，其中，

該配體結合分子中之該抗體VL與該抗體VH係組裝，該組裝因為該切斷位點被切斷而解除、或因為該蛋白酶切斷序列被蛋白酶切斷而解除。

(24)如(1)至(23)中任一項之配體結合分子，其中，前述配體為有生物活性之分子，前述配體結合分子利用與前述配體之結合而抑制前述配體之生物活性。

(25)如(1)至(24)中任一項之配體結合分子，其中，前述配體係細胞介素或趨化介素。

(26)如(1)至(24)中任一項之配體結合分子，其中，前述配體係選自介白素、干擾素、造血因子、TNF超級家族、趨化介素、細胞增殖因子、及TGF-β家族中的配體。

(27)如(1)至(24)中任一項之配體結合分子，其中，前述配體為CXCL10、IL12、

PD1、或IL6R。

(28)如(27)之配體結合分子，其中，前述配體為CXCL10，前述配體結合分子含有抗體VH與抗體VL，該配體結合分子：

(a)具有含有成為序列編號：374之H-CDR1、成為序列編號：375之H-CDR2、成為序列編號:376之H-CDR3之抗體VH，含有成為序列編號：377之L-CDR1、成為序列編號：378之L-CDR2、成為序列編號：379之L-CDR3之抗體VL；或

(b)具有含有成為序列編號：380之H-CDR1、成為序列編號：381之H-CDR2、成為序列編號:382之H-CDR3之抗體VH，含有成為序列編號：383之L-CDR1、成為序列編號：384之L-CDR2、成為序列編號：385之L-CDR3之抗體VL；或

(c) 具有與(a)或(b)競爭之抗體VH與抗體VL；或

(d) 具有會與(a)或(b)結合於同一抗原決定基之抗體VH與抗體VL。

(29)如(28)之配體結合分子，其中，前述配體結合分子係含有選自序列編號：4~14、23~27、33、59、60、356、及367所示序列之抗體重鏈、或選自序列編號：15~22所示序列之抗體輕鏈的抗體。

(30) 如(27)之配體結合分子，其中，前述配體為IL12，前述配體結合分子含有抗體VH與抗體VL，該配體結合分子：

(a)具有含有成為序列編號：386之H-CDR1、成為序列編號：387之H-CDR2、成為序列編號：388之H-CDR3之抗體VH，含有成為序列編號：389之L-CDR1、成為序列編號：390之L-CDR2、成為序列編號：391之L-CDR3之抗體VL；或

(b)具有與(a)競爭之抗體VH與抗體VL；或

(c)與(a)會結合於同一抗原決定基之抗體VH與抗體VL。

(31)如(30)之配體結合分子，其中，前述配體結合分子係含有以序列編號：146表示之抗體重鏈之抗體。

(32)如(27)之配體結合分子，其中，前述配體為PD1，前述配體結合分子含有抗

體VH與抗體VL，該配體結合分子：

(a)具有含有成為序列編號：392之H-CDR1、成為序列編號：393之H-CDR2、成為序列編號：394之H-CDR3之抗體VH、含有成為序列編號：395之R3L-CDR1、成為序列編號：396之L-CDR2、成為序列編號：397之L-CDR3之抗體VL；或

(b)具有與(a)競爭之抗體VH與抗體VL；或

(c)具有會與(a)結合在同一抗原決定基之抗體VH與抗體VL。

(33) 如(32)之配體結合分子，其中，前述配體結合分子係含有選自序列編號：304及305所示序列之抗體重鏈、或選自序列編號：306~315、及322所示序列之抗體輕鏈的抗體。

(34)如(27)之配體結合分子，其中，前述配體為IL-6R(IL-6受體)，前述配體結合分子含有抗體VH與抗體VL，該配體結合分子：

(a)具有含有成為序列編號：398之H-CDR1、成為序列編號：399之H-CDR2、成為序列編號：400之H-CDR3之抗體VH、含有成為序列編號：401之L-CDR1、成為序列編號：402之L-CDR2、成為序列編號：403之L-CDR3之抗體VL；或

(b)具有與(a)競爭之抗體VH與抗體VL；或

(c)具有會與(a)結合在同一抗原決定基之抗體VH與抗體VL。

(35)如(34)之配體結合分子，其中，前述配體結合分子係含有選自序列編號：153~156、157~159、及404~470所示之序列之抗體重鏈、或選自序列編號：471~535所示之序列之抗體輕鏈之抗體。

(36) 如(1)至(35)中任一項之配體結合分子，其中，前述配體結合分子為IgG抗體。

(37) 如(1)至(36)中任一項之配體結合分子，係與前述配體結合。

(38) 如(1)至(36)中任一項之配體結合分子，係與前述配體融合。

(39) 如(38)之配體結合分子，其中，前述配體結合分子於已和配體融合之狀態不會進一步與其他配體結合。

(40) 如(38)或(39)之配體結合分子，其中，前述配體結合分子介隔連結子而與前述配體融合。

(41) 如(40)之配體結合分子，其中，前述連結子不含有蛋白酶切斷序列。

(42) 如(38)至(41)中任一項之配體結合分子，其中，前述配體為CXCL10，前述配體結合分子含有抗體輕鏈與抗體重鏈，前述抗體輕鏈或前述抗體重鏈係與前述配體融合。

(43) 如(42)之配體結合分子，其中，前述切斷位點係在前述抗體輕鏈或前述抗體重鏈中含有。

(44)如(42)或(43)之配體結合分子，其中，前述配體為CXCL10，前述配體結合分子中含有的抗體輕鏈係與前述配體融合，前述配體結合分子：

(a)具有含有成為序列編號：374之H-CDR1、成為序列編號：375之H-CDR2、成為序列編號：376之H-CDR3之抗體重鏈、及含有成為序列編號：377之L-CDR1、成為序列編號：378之L-CDR2、成為序列編號：379之L-CDR3之抗體輕鏈；或

(b)具有含有成為序列編號：380之H-CDR1、成為序列編號：381之H-CDR2、成為序列編號：382之H-CDR3之抗體重鏈、及含有成為序列編號：383之L-CDR1、成為序列編號：384之L-CDR2、成為序列編號：385之L-CDR3之抗體輕鏈。

(45) 如(42)至(44)中任一項之配體結合分子，其中，前述配體為序列編號：370表示之CXCL10改變體。

(46) 如(38)至(41)中任一項之配體結合分子，其中，前述配體為PD1，前述配體結合分子含有抗體輕鏈與抗體重鏈，前述抗體輕鏈或前述抗體重鏈係與前述配體融合。

(47)如(46)之配體結合分子，其中，前述切斷位點係在前述抗體輕鏈或前述抗體

重鏈中含有。

(48) 如(46)或(47)之配體結合分子，其中，前述配體為PD1，前述抗體輕鏈具有成為序列編號：395之R3L-CDR1、成為序列編號：396之L-CDR2、成為序列編號：397之L-CDR3，前述抗體重鏈具有成為序列編號：392之H-CDR1、成為序列編號：393之H-CDR2、成為序列編號：394之H-CDR3。

(49) 如(46)至(48)中任一項之配體結合分子，其中，前述配體為序列編號：320表示之PD1。

(50) 如(46)至(49)中任一項之配體結合分子，其中，前述配體為PD1，前述配體結合分子中含有的抗體重鏈係與前述配體融合，PD1與抗體重鏈融合而得的一系列多胜肽含有選自序列編號：323及324所示之序列中的序列。

(51)如(46)至(49)中任一項之配體結合分子，其中，前述配體為PD1，前述配體結合分子中含有的抗體輕鏈係與前述配體融合，PD1與抗體輕鏈融合而得的一系列多胜肽含有選自序列編號：325~334所示之序列中的序列。

(52) 如(38)至(41)中任一項之配體結合分子，其中，前述配體為IL12，前述配體結合分子含有抗體輕鏈與抗體重鏈，前述抗體輕鏈或前述抗體重鏈係與前述配體融合。

(53)如(52)之配體結合分子，其中，前述切斷位點係在前述抗體輕鏈或前述抗體重鏈中含有。

(54) 如(52)或(53)之配體結合分子，其中，前述配體為IL12，前述抗體輕鏈具有成為序列編號：389之L-CDR1、成為序列編號：390之L-CDR2、成為序列編號：391之L-CDR3，且前述抗體重鏈具有成為序列編號：386之H-CDR1、成為序列編號：387之H-CDR2、成為序列編號：388之H-CDR3。

(55) 如(38)至(41)中任一項之配體結合分子，其中，前述配體為IL-6R，前述配體結合分子含有抗體輕鏈與抗體重鏈，前述抗體輕鏈或前述抗體重鏈係與前述配

體融合。

(56) 如(55)之配體結合分子，其中，前述切斷位點係在前述抗體輕鏈或前述抗體重鏈中含有。

(57) 如(55)或(56)之配體結合分子，其中，前述配體為IL-6R，前述抗體輕鏈具有成為序列編號：401之L-CDR1、成為序列編號：402之L-CDR2、成為序列編號：403之L-CDR3，且前述抗體重鏈具有成為序列編號：398之H-CDR1、成為序列編號：399之H-CDR2、成為序列編號：400之H-CDR3。

(58) 一種複合體，係以前述配體、及與前述配體結合之如(1)至(36)中任一項之配體結合分子形成。

(59) 一種融合蛋白質，前述配體與如(1)至(36)中任一項之配體結合分子係融合。

(60) 如(59)之融合蛋白質，其中，於前述配體結合分子已和配體融合之狀態，不會進一步與其他配體結合。

(61) 如(59)或(60)之融合蛋白質，其中，前述配體結合分子介隔連結子而與前述配體融合。

(62) 如(61)之融合蛋白質，其中，前述連結子不含有蛋白酶切斷序列。

(63) 如(61)或(62)之融合蛋白質，其中，前述連結子係由甘胺酸-絲胺酸聚合物構成之連結子。

(64) 如(59)至(63)中任一項之融合蛋白質，其中，前述配體為CXCL10，前述配體結合分子含有抗體輕鏈與抗體重鏈，前述抗體輕鏈或前述抗體重鏈係與前述配體融合。

(65) 如(64)之融合蛋白質，其中，前述切斷位點係在前述配體結合分子之前述抗體輕鏈或前述抗體重鏈中含有。

(66) 如(64)或(65)之融合蛋白質，其中，前述配體為CXCL10，前述配體結合分子中含有的抗體輕鏈係與前述配體融合，前述配體結合分子：

(a)具有含有成為序列編號：374之H-CDR1、成為序列編號：375之H-CDR2、成為序列編號：376之H-CDR3之抗體重鏈、及含有成為序列編號：377之L-CDR1、成為序列編號：378之L-CDR2、成為序列編號：379之L-CDR3之抗體輕鏈；或

(b)具有含有成為序列編號：380之H-CDR1、成為序列編號：381之H-CDR2、成為序列編號：382之H-CDR3之抗體重鏈、及含有成為序列編號：383之L-CDR1、成為序列編號：384之L-CDR2、成為序列編號：385之L-CDR3之抗體輕鏈。

(67) 如(64)至(66)中任一項之融合蛋白質，其中，前述配體為序列編號：370表示之CXCL10改變體。

(68) 如(59)至(63)中任一項之融合蛋白質，其中，前述配體為PD1，前述配體結合分子含有抗體輕鏈與抗體重鏈，前述抗體輕鏈或前述抗體重鏈係與前述配體融合。

(69) 如(68)之配體結合分子，其中，前述切斷位點係在前述抗體輕鏈或前述抗體重鏈中含有。

(70) 如(68)或(69)之融合蛋白質，其中，前述配體為PD1，前述抗體輕鏈具有成為序列編號：395之R3L-CDR1、成為序列編號：396之L-CDR2、成為序列編號：397之L-CDR3，且前述抗體重鏈具有成為序列編號：392之H-CDR1、成為序列編號：393之H-CDR2、成為序列編號：394之H-CDR3。

(71) 如(68)至(70)中任一項之融合蛋白質，其中，前述配體為序列編號：320表示之PD1。

(72) 如(68)至(71)中任一項之融合蛋白質，其中，前述配體為PD1，前述配體結合分子中含有的抗體重鏈係與前述配體融合，PD1與抗體重鏈融合而得之一系列多胜肽含有選自序列編號：323及324所示之序列中之序列。

(73) 如(68)至(71)中任一項之融合蛋白質，其中，前述配體為PD1，前述配體結合分子中含有的抗體輕鏈係與前述配體融合，PD1與抗體輕鏈融合而得之一系列多胜肽含有選自序列編號：325~334所示之序列中之序列。

(74) 如(59)至(63)中任一項之融合蛋白質，其中，前述配體為IL12，前述配體結合分子含有抗體輕鏈與抗體重鏈，前述抗體輕鏈或前述抗體重鏈係與前述配體融合。

(75) 如(74)之融合蛋白質，其中，前述切斷位點係在前述抗體輕鏈或前述抗體重鏈中含有。

(76) 如(74)或(75)之融合蛋白質，其中，前述配體為IL12，前述抗體輕鏈具有成為序列編號：389之L-CDR1、成為序列編號：390之L-CDR2、成為序列編號：391之L-CDR3，且前述抗體重鏈具有成為序列編號：386之H-CDR1、成為序列編號：387之H-CDR2、成為序列編號：388之H-CDR3。

(77) 如(59)至(63)中任一項之融合蛋白質，其中，前述配體為IL-6R，前述配體結合分子含有抗體輕鏈與抗體重鏈，前述抗體輕鏈或前述抗體重鏈係與前述配體融合。

(78) 如(77)之融合蛋白質，其中，前述切斷位點係在前述抗體輕鏈或前述抗體重鏈中含有。

(79) 如(77)或(78)之融合蛋白質，其中，前述配體為IL-6R，前述抗體輕鏈具有成為序列編號：401之L-CDR1、成為序列編號：402之L-CDR2、成為序列編號：403之L-CDR3，且前述抗體重鏈具有成為序列編號：398之H-CDR1、成為序列編號：399之H-CDR2、成為序列編號：400之H-CDR3。

(80) 一種醫藥組合物，含有如(1)至(57)中任一項之配體結合分子。

(81) 一種醫藥組合物，含有如(1)至(37)中任一項之配體結合分子及配體。

(82) 一種醫藥組合物，含有如(58)之複合體。

(83) 一種醫藥組合物，含有如(59)至(79)中任一項之融合蛋白質。

(84) 一種製造如(1)至(57)中任一項之配體結合分子之方法。

(85) 如(84)之製造方法，包括在可結合於配體之分子中導入蛋白酶切斷序列之步驟。

(86)一種如(59)至(79)中任一項之融合蛋白質之製造方法，包括使具蛋白酶切斷序列之配體結合分子與其配體融合的步驟。

(87) 一種聚核苷酸，編碼如(1)至(57)中任一項之配體結合分子。

(88) 一種載體，含有如(87)之聚核苷酸。

(89) 一種寄主細胞，含有如(87)之聚核苷酸或如(88)之載體。

(90) 一種如(1)至(57)中任一項之配體結合分子之製造方法，包括培養如(89)之寄主細胞之步驟。

(91) 一種聚核苷酸，編碼如(59)至(79)中任一項之融合蛋白質。

(92) 一種載體，含有如(91)之聚核苷酸。

(93) 一種寄主細胞，含有如(91)之聚核苷酸或如(92)之載體。

(94) 一種如(59)至(79)中任一項之融合蛋白質之製造方法，包括培養如(93)之寄主細胞之步驟。

【圖式簡單說明】

【0011】

第1圖揭示於含有標靶組織專一性的游離的配體-連結子-抗配體抗體之VH分子之IgG抗體與配體之融合蛋白質、及其活化之一樣式之圖。配體與抗配體抗體係以連結子連結。

第2圖揭示在標靶組織專一性地使配體游離之IgG抗體、及其活化之一樣式之圖。在VH與CH1之交界附近插入了蛋白酶切斷序列之抗配體抗體與配體係混合

並投予給個體。

第3圖揭示在標靶組織專一性地使配體游離之IgG抗體、及其活化之一樣式之圖。在VH與CH1之交界附近插入了蛋白酶切斷序列之抗配體抗體係投予給個體。被投予的抗體結合於體內原本存在的配體，之後則與第2圖之活化樣式為同樣。

第4圖揭示使用Biacore評價MabCXCL10與人CXCL10之交互作用之結果。

第5A圖揭示藉由在MabCXCL10之抗體可變區與不變區之交界附近插入蛋白酶切斷序列而作成之抗體分子之模型。

第5B圖揭示製作的各重鏈改變體的名稱、插入了蛋白酶切斷序列的位置、已插入的胺基酸序列。插入部位以[insert]代表。

第5C圖揭示製作的各輕鏈改變體的名稱、插入了蛋白酶切斷序列的位置、已插入的胺基酸序列。插入部位以[insert]代表。

第6A圖揭示使用Biacore評價在MabCXCL10之重鏈之可變區與不變區之交界附近插入蛋白酶切斷序列而製作之抗體分子與人CXCL10之交互作用之結果。

第6B圖揭示使用Biacore評價在MabCXCL10之輕鏈之可變區與不變區之交界附近插入蛋白酶切斷序列而製作之抗體分子與人CXCL10之交互作用之結果。

第7-1(A)圖揭示將藉由在MabCXCL10之重鏈可變區與不變區之交界附近插入蛋白酶切斷序列而作成之抗體分子進行蛋白酶(MT-SP1)處理後，以還原SDS-PAGE電泳，並以考馬司亮藍(Coomassie Brilliant Blue，CBB)檢測以評價切斷程度之結果。在利用蛋白酶處理而產生的2條新的譜帶當中，出現在15 kDa附近的譜帶係來自VH的譜帶，出現在25-50 kDa之位置的譜帶係來自不變區的譜帶。

第7-2圖揭示接續(A)，及(B)將藉由在MabCXCL10之輕鏈可變區與不變區插入蛋白酶切斷序列而製作之抗體分子進行蛋白酶(MT-SP1)處理後，以還原SDS-PAGE評價切斷程度之結果。出現了來自經蛋白酶處理切斷之輕鏈的2條新的譜帶。

第7-3圖係接續(B)。

第8圖揭示藉由在MabCXCL10之可變區與不變區之交界附近插入蛋白酶切斷序列與可動連結子序列而製作之各重鏈改變體之名稱、插入了蛋白酶切斷序列與可動連結子序列之位置、已插入的胺基酸序列。插入部位以[insert]表示。

第9圖揭示使用Biacore評價藉由在MabCXCL10之重鏈可變區與不變區之交界附近插入蛋白酶切斷序列與可動連結子序列而作之抗體分子與人CXCL10之交互作用之結果。

第10A圖揭示將藉由在MabCXCL10之重鏈可變區與不變區之交界附近插入蛋白酶切斷序列與連結子序列而製作之抗體分子進行蛋白酶(uPA, MT-SP1)處理後，以還原SDS-PAGE電泳並以CBB檢測來評價切斷程度之結果。因為蛋白酶處理而出現的2條新的譜帶當中，出現在15 kDa 附近的譜帶係來自VH的譜帶，出現在25-50 kDa之位置的譜帶係來自不變區之譜帶。

第10B圖接續第10A圖。

第11A圖揭示評價是否CXCL10會因為將MabCXCL10a與CXCL10之複合體進行蛋白酶(MT-SP1)處理而游離之結果。

第11B圖揭示評價是否CXCL10會因為將EEIVHC006a/EEIVL與CXCL10之複合體進行蛋白酶(MT-SP1)處理而游離之結果。

第12圖揭示將MabCXCL10之可變區與不變區之交界附近之胺基酸序列一部分以蛋白酶切斷序列與可動連結子序列取代而作成之各重鏈之名稱、插入了及改變了胺基酸之部位、插入序列、插入及改變後之胺基酸序列。插入部位以[insert]表示。「插入位置及改變位置」之欄中，取消線代表之胺基酸殘基，在插入插入序列時被除去，亦即被取代為插入序列最C末端側之胺基酸。

第13圖揭示將MabCXCL10之可變區與不變區之交界附近之胺基酸序列一部分以蛋白酶切斷序列與可動連結子取代而製作之抗體分子進行蛋白酶(uPA,

MT-SP1)處理後，以還原SDS-PAGE電泳並以CBB檢測來評價切斷程度之結果。因為蛋白酶處理而出現的2條新譜帶當中，出現在15 kDa 附近的譜帶係來自VH的譜帶，出現在25-50 kDa之位置的譜帶係來自不變區之譜帶。

第14圖係表示螢光素酶活性(發光值)之圖。

第15圖揭示CXCL10-抗CXCL10抗體融合蛋白質以蛋白酶切斷前後之SDS-PAGE之結果。

第16圖係表示螢光素酶活性(發光值)之圖。

第17圖揭示評價導入了蛋白酶切斷序列與可動連結子序列之抗IL-12中和抗體因為蛋白酶所為之切斷之還原SDS-PAGE之圖。

第18圖揭示添加IL-12與抗體時之干擾素gamma之產生之圖。NoAb為不添加抗體僅添加IL-12之樣本，NoIL-12係不添加IL-12也不添加之樣本。

第19A圖揭示抗體利用蛋白酶進行切斷。

第19B圖揭示抗體利用蛋白酶進行切斷。

第20A圖揭示以各種蛋白酶切斷之結果。

第20B圖揭示以各種蛋白酶切斷之結果。

第21圖揭示以各種蛋白酶切斷之結果。

第22A圖揭示MRA改變體以蛋白酶切斷之結果。

第22B圖揭示MRA改變體以蛋白酶切斷之結果。

第22C圖揭示MRA改變體以蛋白酶切斷之結果。

第22D圖揭示MRA改變體以蛋白酶切斷之結果。

第22E圖揭示MRA改變體以蛋白酶切斷之結果。

第22F圖揭示MRA改變體以蛋白酶切斷之結果 。

第22G圖揭示MRA改變體以蛋白酶切斷之結果。

第22H圖揭示MRA改變體以蛋白酶切斷之結果。

第22I圖揭示MRA改變體以蛋白酶切斷之結果。

第23A圖揭示MRA改變體以蛋白酶切斷之結果。

第23B圖揭示MRA改變體以蛋白酶切斷之結果。

第23C圖揭示MRA改變體以蛋白酶切斷之結果。

第24A圖揭示MRA改變體以蛋白酶切斷之結果。

第24B圖揭示MRA改變體以蛋白酶切斷之結果。

第24C圖揭示MRA改變體以蛋白酶切斷之結果。

第24D圖揭示MRA改變體以蛋白酶切斷之結果。

第24E圖揭示MRA改變體以蛋白酶切斷之結果。

第25A圖揭示MRA改變體以蛋白酶切斷之結果。

第25B圖揭示MRA改變體以蛋白酶切斷之結果。

第26圖揭示比較含有經蛋白酶處理之抗體/未經蛋白酶處理之抗體以及PD1之結合評價用樣本中之PD1對於5C4-bio之結合之即時軸之圖。黑色粗線代表含有經蛋白酶處理之抗體之結合評價用樣本、灰色細線代表含有未經蛋白酶處理之抗體之結合評價用樣本。X軸代表測定時間(秒)，測定開始定為0秒。Y軸代表結合。各軸之名稱代表評價用樣本中中含有的抗體，None(僅抗原之)之軸代表只使用抗原作為評價用樣本且不混合抗體。

第27圖係經蛋白酶處理之抗體與未經蛋白酶處理之抗體之電泳結果。Protease(+)泳道為經蛋白酶處理之抗體，protease(-)泳道為未經蛋白酶處理之抗體。

第28圖係揭示比較經蛋白酶處理之抗體與蛋白酶處理未處理抗體對於PD1之結合之即時軸之圖。黑色粗線代表經蛋白酶處理之抗體，灰色細線代表未經蛋白酶處理之抗體。X軸代表測定時間(秒)，測定開始設為0秒。Y軸代表結合。各軸之名稱代表使用之抗體，None之軸僅使用PBS buffer，未使用抗體。

第29圖揭示比較於PD1存在下進行蛋白酶處理之樣本與於PD1存在下未進行蛋

白酶處理之樣本中所存在之游離PD1對於5C4-bio之結合之即時軸之圖。黑色粗線表示已進行蛋白酶處理之樣本、灰色細線代表未進行蛋白酶處理之樣本。X軸表示測定時間(秒)，測定開始設為0秒。Y軸表示結合。各軸名稱代表樣本中含有的抗體，在「抗原與蛋白酶」之軸，樣本中僅含PD1，不含有抗體。

第30圖揭示比較在經蛋白酶處理之融合蛋白質與蛋白酶未處理蛋白質溶液中存在之游離PD1對於5C4-bio之結合之即時軸之圖。黑色粗線代表已進行蛋白酶處理之樣本，灰色細線代表未進行蛋白酶處理之樣本。X軸表示測定時間(秒)，測定開始設為0秒。Y軸代表結合。各軸之名稱代表融合蛋白質中，None(僅抗原)之軸係就評價用樣本而言不使用融合蛋白質，僅使用抗原PD1。5C4H-G1T4/5C4L-KT0之軸係不使用融合蛋白質，僅使用5C4H-G1T4/5C4L-KT0抗體。

第31圖係經蛋白酶處理之抗體-PD1融合蛋白質之電泳結果。Protease(+)泳道係經蛋白酶處理之融合蛋白質，protease(-)泳道係未經蛋白酶處理之融合蛋白質。

【實施方式】

【0012】 本發明中，多胜肽通常係指有4個胺基酸左右以上之長度之胜肽、及蛋白質。又，本發明中，多胜肽通常係由人工設計的序列構成的多胜肽，但不特別限定，例如也可為生物來源的多胜肽。又，也可以是天然多胜肽、或合成多胜肽、重組多胜肽等中任一者。再者，上述多胜肽之斷片也包括在本發明之多胜肽。

【0013】 本說明書中，例如如Ala/A、Leu/L、Arg/R、Lys/K、Asn/N、Met/M、Asp/D、Phe/F、Cys/C、Pro/P、Gln/Q、Ser/S、Glu/E、Thr/T、Gly/G、Trp/W、His/H、Tyr/Y、Ile/I、Val/V，胺基酸以單字母碼或3字母碼、或其兩者表示記載。

【0014】 為了改變多胜肽之胺基酸序列中之胺基酸，可適當採用部位專一

的變異誘發法(Kunkel等(Proc. Natl. Acad. Sci. USA (1985) 82, 488-492))、Overlap extension PCR等公知方法。又，作為取代成天然胺基酸以外之胺基酸的胺基酸改變方法，也有複數個公知方法可採用 (Annu. Rev. Biophys. Biomol. Struct. (2006) 35, 225-249、Proc. Natl. Acad. Sci. U.S.A. (2003) 100 (11), 6353-6357)。例如:含有終止碼之一即UAG密碼子 (Amber codon)的互補amber suppressor tRNA結合了非天然胺基酸而得的tRNA無細胞轉譯系系統(Clover Direct(Protein Express))等亦為理想。

【0015】 本說明書中，表示胺基酸之改變部位時使用之「及/或」之用語之意義，包括「及」與「或」適當組合的各種組合。具體而言，例如「37號、45號、及/或47號之胺基酸經取代」，包括以下胺基酸之改變的變化形；(a) 37號、(b)45號、(c)47號、(d) 37號及45號、(e) 37號及47號、(f) 45號及47號、(g) 37號及45號及47號。

【0016】 本說明書中，又，就表達胺基酸改變的方式，可適當使用在代表特定位置的數字前後加註改變前與改變後之胺基酸之單字母碼或3字母碼的表達方式。例如:於抗體可變區所含之胺基酸施加取代時使用之F37V或Phe37Val這類改變，代表Kabat編號表示之37位之Phe取代成Val。亦即，數字代表Kabat編號表示之胺基酸位置，於其前記載之胺基酸之單字母碼或3字母碼代表取代前之胺基酸、其後記載之胺基酸之單字母碼或3字母碼代表取代後之胺基酸。同樣，對於抗體不變區所含之Fc區施加胺基酸取代時使用的P238A或Pro238Ala這類改變，表示EU編號表示之238位之Pro取代為Ala。亦即，數字代表EU編號表示之胺基酸位置，在其前記載之胺基酸之單字母碼或3字母碼代表取代前之胺基酸、其後記載之胺基酸之單字母碼或3字母碼代表取代後的胺基酸。

【0017】 本發明係關於有切斷位點且於該切斷位點被切斷之狀態時與配體之結合減弱的配體結合分子。本發明之配體結合分子係指為多胜肽且可結合

於配體之分子。

【0018】 本發明之配體結合分子，係可結合於配體之分子，尤其在未切斷的狀態可結合於配體之分子。在此的「結合」。通常指以靜電力、凡得瓦力、氫鍵等非共價鍵為主的交互作用所為之結合。本發明之配體結合分子之配體結合態樣之理想例不僅限於此，例如可列舉抗原結合區、抗原結合分子、抗體、及抗體斷片等會結合於抗原之類的抗原抗體反應。

【0019】 又，可結合於配體，係指配體結合分子與配體即使是不同分子，配體結合分子仍可結合於配體，並不是指利用共價鍵將配體結合分子予以配體連結。例如不是指配體與配體結合分子介隔連結子而共價鍵結為可結合於配體。又，與配體之結合減弱，係指前述可結合之能力減弱。例如配體與配體結合分子介隔連結子而共價鍵結時，其連結子切斷不視為與配體之結合減弱。又，本發明中，只要配體結合分子可結合於配體，則配體結合分子也可介隔連結子等而與配體連接。

【0020】 本發明之配體結合分子僅在於以未切斷狀態和配體結合，只要能以未切斷狀態和目的之配體結合，何種結構的分子皆可使用。配體結合分子，不僅限定如上例，例如:抗體之重鏈可變區(VH)及抗體之輕鏈可變區(VL)、單分域抗體(sdAb)、存在於活體內之細胞膜蛋白質Avimer所含之約35個胺基酸之稱為A分域之模組(WO2004/044011、WO2005/040229)、包含於細胞膜表現之糖蛋白質fibronectin中之蛋白質所結合之域10Fn3分域之Adnectin(WO2002/032925)、以構成由ProteinA之58個胺基酸構成的3個螺旋束(bundle)的IgG結合分域為支架(scaffold)的Affibody(WO1995/001937)、具含33個胺基酸殘基之轉彎(turn)與2個反向並行之螺旋以及迴圈的次單元返覆層疊的構造的ankyrin返覆(ankyrin repeat：AR)之分子表面所露出之區DARPins(Designed Ankyrin Repeat proteins)(WO2002/020565)、將嗜中性球明膠酶結合lipocalin (neutrophil

gelatinase-associated lipocalin(NGAL))等lipocalin分子中高度保守的8個反向並行的股中央方向扭曲成的活塞桶(barrel)構造的單側予以支撐的4個迴圈區Anticalin等(WO2003/029462)、就八目鰻、沼田鰻等無顎類之獲得免疫系統而言不具免疫球蛋白之構造的可變性淋巴球受體(variable lymphocyte receptor(VLR))之富含白胺酸殘基之返覆(leucine-rich-repeat(LRR))模組返覆疊層而獲得之馬蹄形構造之內部之平行型片構造之中空區(WO2008/016854)。

【0021】 本說明書，用語「抗體」係以最廣的含意使用，只要能顯示所望的抗原結合活性即可，並不限於此等，包括單株抗體、多株抗體、多專一性抗體(例如:雙專一性抗體)及抗體斷片各種抗體結構。

【0022】 製作具有所望結合活性之抗體之方法於該技術領域之具有通常知識者為公知。以下列舉製作與IL-6結合之抗體(抗IL-6R抗體)之方法。與IL-6R以外之抗原結合的抗體也可依據下列例示適當製作。

【0023】 抗IL-6R抗體可使用公眾所知方法以多株或單株抗體之形式取得。抗IL-6R抗體，宜製作哺乳動物來源的單株抗體。哺乳動物來源的單株抗體，包含由融合瘤產生者，及由基因工程的方法以含抗體基因之表現載體轉形而得之寄主細胞所產生者等。本發明之言及之抗體包括「人類化抗體」或「嵌合抗體」。

【0024】 單株抗體產生融合瘤，可使用公知技術依例如以下方式製作。亦即，使用IL-6R蛋白質當做感作抗原，依通常之免疫方法將哺乳動物免疫。將獲得之免疫細胞以通常的細胞融合法與公知之親代細胞融合。其次依照通常之篩選法，篩選單株抗體產生細胞，可選擇產生抗IL-6R抗體之融合瘤。

【0025】 具體而言，單株抗體之製作係依例如以下所示方式實行。首先，藉由表現IL-6R基因，取得當做抗體取得之感作抗原使用的IL-6R蛋白質。亦即，藉由將編碼IL-6R之基因序列插入公知之表現載體，而將適當的寄主細胞轉形。

從該寄主細胞中或培養上清中以公知方法精製所望之人類IL-6R蛋白質。為了從培養上清中取得可溶型之IL-6R，例如可使Mullberg等人(J. Immunol. (1994) 152 (10), 4958-4968)之可溶型IL-6R表現。又，經精製的天然IL-6R蛋白質也同樣可當做感作抗原使用。

【0026】 對於哺乳動物免疫時使用之感作抗原，可使用該精製IL-6R蛋白質。IL-6R之部分胜肽也可當做感作抗原使用。於此時，該部分胜肽可利用人類IL-6R之胺基酸序列以化學合成取得。又，也可將IL-6R基因之一部分納入表現載體使表現而取得。再者，使用蛋白質分解酵素將IL-6R蛋白質分解也可取得，但是當做部分胜肽使用之IL-6R胜肽之區域及大小不限於特別之態樣。構成當做感作抗原之胜肽的胺基酸的數目至少為5以上，例如6以上或7以上較佳。更具體而言，可將8～50、較佳為10～30個殘基之胜肽當做感作抗原使用。

【0027】 又，將IL-6R蛋白質之所望之部分多胜肽或胜肽與不同的多胜肽融合成的融合蛋白質可利用為感作抗原。為了製造當做感作抗原使用之融合蛋白質，例如可適當利用抗體之Fc片段或胜肽標籤(tag)等。表現融合蛋白質之載體，可藉由將編碼所望之二種或更多種多胜肽片段之基因於同一讀框(inframe)融合，並將該融合基因以前述方式插入表現載體而製作。融合蛋白質之製作方法記載於Molecular Cloning 2nd ed. (Sambrook,J et al., Molecular Cloning 2nd ed., 9.47-9.58(1989)Cold Spring Harbor Lab. press)。可當做感作抗原使用之IL-6R之取得方法及使用其之免疫方法，在WO2003/000883、WO2004/022754、WO2006/006693等亦有具體記載。

【0028】 以該感作抗原免疫之哺乳動物不限於特定動物，宜考慮與細胞融合使用之親代細胞之間的適合性選擇。一般的嚙齒類動物例如小鼠、大鼠、倉鼠，或兔、猴等較佳。

【0029】 依公知方法將上述動物以感作抗原免疫。例如就一般方法而言，

係藉由將感作抗原對於哺乳動物之腹腔內或皮下投予而投予以實施免疫。具體而言，將以PBS(Phosphate-Buffered Saline)或生理食鹽水等以適當稀釋倍率稀釋過的感作抗原，視所望與通常的佐劑例如佛洛依德完全佐劑混合並乳化後，將該感作抗原對於哺乳動物每4至21日投予數次。又，感作抗原免疫時可以使用適當擔體。尤其使用小分子量之部分胜肽當做感作抗原時，有時以結合有白蛋白、血藍蛋白(keyhole lympet hemocyanin)等擔體蛋白質的該感作抗原胜肽進行免疫為理想。

【0030】 又，產生所望抗體之融合瘤可使用DNA免疫並依以下方式製作。DNA免疫，係指在免疫動物中投予以能表現編碼抗原蛋白質之基因的態樣構建之載體DNA的該免疫動物中，藉由感作抗原在該免疫動物之活體內表現，能提供免疫刺激之免疫方法。比起對於免疫動物投予蛋白質抗原之一般免疫方法，DNA免疫可期待如下的優越性。

-可維持如IL-6R之膜蛋白質之構造而提供免疫刺激

-無需精製免疫抗原

【0031】 為了以DNA免疫獲得本發明之單株抗體，首先將表現IL-6R蛋白質之DNA對於免疫動物投予。編碼IL-6R之DNA可利用PCR等公知方法合成。將獲得之DNA插入適當表現載體並對於免疫動物投予。表現載體例如可以理想地利用pcDNA3.1等市售表現載體。將載體對於活體投予之方法，可使用一般使用之方法。例如，可藉由將吸附有表現載體之金粒子以基因槍導入免疫動物個體之細胞內而實施DNA免疫。再者，認識IL-6R之抗體之製作也可使用國際公開WO2003/104453記載之方法製作。

【0032】 以此方式將哺乳動物免疫，確認血清中與IL-6R結合之抗體力價上升後，從哺乳動物採取免疫細胞以供細胞融合。較佳之免疫細胞尤佳為使用脾細胞。

【0033】 與前述免疫細胞融合之細胞，可使用哺乳動物之骨髓瘤細胞。骨髓瘤細胞宜具有為了篩選的適當選擇標記。選擇標記，係指能於特定培養條件下生存之(或無法生存)之形質。選擇標記中，次黃嘌呤-鳥嘌呤磷酸核糖轉移酶(hypoxanthine-guanine phosphoribosyl transferase)缺損(以下簡稱為HGPRT缺損)、或胸腺嘧啶激酶缺損(以下簡稱為TK缺損)等為公知。具HGPRT或TK缺損之細胞，具有次黃嘌呤-胺基喋呤-胸腺嘧啶感受性(以下簡稱為HAT感受性)。HAT感受性之細胞在HAT選擇培養基中無法合成DNA會死滅，但若與正常細胞融合則會利用正常細胞之補救合成路徑(salvage pathway)繼續合成DNA，故能在HAT選擇培養基中增殖。

【0034】 HGPRT缺損或TK缺損之細胞，各可以含6硫鳥嘌呤(thioguanine)、8氮雜鳥嘌呤(以下簡稱為8AG)、或5'溴去氧尿嘧啶之培養基選擇。於DNA中納入該等嘧啶類似物之正常細胞會死滅。另一方面，未納入該等嘧啶類似物之該等酵素缺損之細胞，能在選擇培養基中生存。其他稱為G418耐受性之選擇標記，係利用新黴素耐受性基因提供對於2-去氧鏈黴胺(streptamine)系抗生物質(慶大黴素(gentamycin類似體)之耐受性。對細胞融合為理想的各種骨髓瘤細胞為公知。

【0035】 如此的骨髓瘤細胞例如可理想地使用例如:P3(P3x63Ag8.653)(J. Immunol.(1979)123 (4), 1548-1550)、P3x63Ag8U.1(Current Topics in Microbiology and Immunology(1978)81, 1-7)、NS-1(C. Eur. J. Immunol.(1976)6 (7), 511-519)、MPC-11(Cell(1976)8 (3), 405-415)、SP2/0(Nature(1978)276 (5685), 269-270)、FO(J. Immunol. Methods(1980)35 (1-2), 1-21)、S194/5.XX0.BU.1(J. Exp. Med.(1978)148 (1), 313-323)、R210(Nature(1979)277 (5692), 131-133)等。

【0036】 基本上可依照公知方法例如Keller與Milstein等人的方法(Methods Enzymol.(1981)73, 3-46)等，實施前述免疫細胞與骨髓瘤細胞之細胞融

合。

更具體而言，可於例如細胞融合促進劑存在下於通常的營養培養液中實施前述細胞融合。融合促進劑可使用例如聚乙二醇(PEG)、仙台病毒 (HVJ)等，為更提高融合效率，可視所望添加使用二甲基亞碸等輔助劑。

【0037】 免疫細胞與骨髓瘤細胞之使用比例可任意設定。例如相對於骨髓瘤細胞將免疫細胞定為1至10倍較佳。前述細胞融合使用之培養液，例如適於前述骨髓瘤細胞株增殖之RPMI1640培養液、MEM培養液、此外，可使用該種細胞培養使用之通常之培養液，再者，可理想地添加胎牛血清(FCS)等血清補液。

【0038】 細胞融合係將前述免疫細胞與骨髓瘤細胞以既定量於前述培養液中充分混合，並且將預先加溫至約37℃之PEG溶液(例如平均分子量1000至6000左右)以通常30至60%(w/v)之濃度添加。藉由將混合液緩慢混合，會形成所望之融合細胞(融合瘤)。接著，逐次添加上述列舉之適當培養液，反複實施離心並去除上清之操作，可將對於融合瘤之生長不利的細胞融合劑等除去。

【0039】 以如此方式獲得之融合瘤，可藉由於通常之選擇培養液，例如HAT培養液(含次黃嘌呤、胺基喋呤、胸腺嘧啶之培養液)培養而選擇。為了使所望之融合瘤以外之細胞(非融合細胞)死滅，可使繼續進行使用上述HAT培養液之培養足夠時間(通常該足夠時間為數日至數週)。其次，以通常之極限稀釋法，實施產生所望抗體之融合瘤之篩選及單一選殖。

【0040】 以如此方式獲得之融合瘤，可利用因應細胞融合使用之骨髓瘤具有之選擇標記的選擇培養液而選擇。例如具HGPRT或TK缺損之細胞，可藉由以HAT培養液(含次黃嘌呤、胺基喋呤及胸腺嘧啶之培養液)培養而選擇。亦即，當使用HAT感受性骨髓瘤細胞於細胞融合時，可在HAT培養液中將成功與正常細胞細胞融合的細胞選擇性增殖。為了使所望融合瘤以外之細胞(非融合細胞)死滅，可以繼續使用上述HAT培養液之培養足夠時間。具體而言，一般可藉由數

日至數週的培養而選擇所望之融合瘤。其次可利用通常之極限稀釋法，實施產生所望之抗體的融合瘤的篩選及單一選殖。

【0041】 所望之抗體之篩選及單一選殖，可依照基於公知抗原抗體反應之篩選方法而理想地實施。例如，結合於IL-6R之單株抗體可以結合於在細胞表面表現的IL-6R。如此的單株抗體例如可藉由FACS(fluorescence activated cell sorting)篩選。FACS係將與螢光抗體接觸之細胞以雷射光解析，並測定各個細胞發出之螢光，而可測定抗體對於細胞表面之結合的系統。

【0042】 為了利用FACS篩選產生本發明之單株抗體的融合瘤，首先要製備表現IL-6R之細胞。用於篩選之較佳細胞為使IL-6R強制表現之哺乳動物細胞。藉由以當做寄主細胞之未經轉形之哺乳動物細胞為對照，可以選擇性檢測抗體對於細胞表面之IL-6R的結合活性。亦即，藉由選擇產生未結合於寄主細胞而結合於IL-6R強制表現細胞的抗體的融合瘤，可以取得產生IL-6R單株抗體之融合瘤。

【0043】 或抗體對於經固定化之IL-6R表現細胞的結合活性可依據ELISA之原理評價。例如，將IL-6R表現細胞固定化在ELISA板的孔。使融合瘤之培養上清接觸孔內之固定化細胞，以檢測結合於固定化細胞的抗體。單株抗體為小鼠來源時，與細胞結合之抗體可利用抗小鼠免疫球蛋白抗體檢測。該等篩選所選擇之產生具有對於抗原之結合能力的所望抗體的融合瘤，可利用極限稀釋法等選殖。

【0044】 以此方式製作之產生單株抗體之融合瘤可在通常之培養液中繼代培養。而且，該融合瘤可於液態氮中長期保存。

【0045】 將該融合瘤依照通常方法培養，可從其培養上清取得所望之單株抗體。或可將融合瘤對於與其具適合性之哺乳動物投予使增殖，並從其腹水獲取單株抗體。前者之方法對於獲得高純度抗體為適當。

【0046】 從該融合瘤等抗體產生細胞選殖的抗體基因所編碼之抗體也可適當利用。藉由將經選殖的抗體基因納入適當載體並導入寄主，可以表現該基因所編碼的抗體。抗體基因之單離與對於載體之導入、及用於將寄主細胞轉形之方法，例如已由Vandamme等人確立 (Eur.J. Biochem.(1990)192 (3), 767-775)。下列所述重組抗體之製造方法亦為公知。

【0047】 例如，可從產生抗IL-6R抗體之融合瘤細胞取得編碼抗IL-6R抗體之可變區(V區)之cDNA。為此，通常首先從融合瘤萃取全體RNA。用於從細胞萃取mRNA之方法，例如可利用如下方法。

-胍(guanidine)超離心法(Biochemistry (1979) 18 (24), 5294-5299)

-AGPC法(Anal. Biochem. (1987) 162 (1), 156-159)

【0048】 萃取到的mRNA可使用mRNA Purification Kit (GE Health care bioscience製)等精製。或如QuickPrep mRNA Purification Kit (GE Health care bioscience製)等，也有用於從細胞直接萃取全體mRNA之市售套組。使用如此的套組，可從融合瘤取得mRNA。從獲得之mRNA使用反轉錄酵素可合成編碼抗體V區之cDNA。cDNA可利用AMV Reverse Transcriptase First-strand cDNA Synthesis Kit(生化學工業社製)等合成。又，為了cDNA之合成及放大，可適當利用SMART RACE cDNA 放大套組(Clontech製)及使用PCR之5'-RACE法(Proc. Natl. Acad. Sci. USA (1988) 85 (23), 8998-9002、Nucleic Acids Res. (1989) 17 (8), 2919-2932)。又，在如此的cDNA合成之過程中，可在cDNA的兩末端導入後述適當的限制酶部位。

【0049】 從獲得之PCR產物精製目的之cDNA片段，其次與載體DNA連結。以如此方式製作重組載體，並導入大腸菌等，選擇群落(colony)後，從形成有該群落之大腸菌製備所望之重組載體。並且針對該重組載體是否具有目的cDNA之鹼基序列，可使用公知之方法例如二去氧核苷酸鏈終結法等確認。

【0050】 為了取得編碼可變區之基因，利用使用可變區基因放大用引子之5'-RACE法係屬簡便。首先，以從融合瘤細胞萃取之RNA當做模板，合成cDNA，獲得5'-RACE cDNA資料庫。5'-RACE cDNA資料庫之合成可適當使用SMART RACE cDNA 放大套組等市售套組。

【0051】 以獲得之5'-RACE cDNA資料庫為模板，以PCR法將抗體基因放大。依據公知之抗體基因序列可設計小鼠抗體基因放大用之引子。此等引子為依免疫球蛋白之次類而各不相同的鹼基序列。因此，次類理想為預先使用Iso Strip小鼠單株抗體同種型決定套組(Roche diagnostics)等市售套組決定。

【0052】 具體而言，當目的為取得例如編碼小鼠IgG之基因時，可利用能將編碼當做重鏈之γ1、γ2a、γ2b、γ3、當做輕鏈之κ鏈與λ鏈的基因放大的引子。為了放大IgG之可變區基因，一般係利用於3'側之引子黏合有相當於接近可變區之不變區之部分的引子。另一方面， 5'側之引子係利用5' RACE cDNA資料庫製作套組所附帶的引子。

【0053】 利用如此放大之PCR產物，可再構成由重鏈與輕鏈之組合而成的免疫球蛋白。以再構成之免疫球蛋白對於IL-6R之結合活性當做指標，可以篩選所望之抗體。例如目的為取得對抗IL-6R之抗體時，抗體對於IL-6R之結合，更佳為專一性的。與IL-6R結合之抗體可藉由例如以下方式篩選；

(1)使從融合瘤獲得之含有由cDNA編碼之V區的抗體接觸IL-6R表現細胞之步驟、

(2)檢測IL-6R表現細胞與抗體之間的結合之步驟、及

(3)選擇與IL-6R表現細胞結合之抗體之步驟。

【0054】 檢測抗體與IL-6R表現細胞之間的結合的方法為公知。具體而言，可利用先前所述FACS等方法，檢測抗體與IL-6R表現細胞間之結合。為了評價抗體之結合活性，可適當利用IL-6R表現細胞之固定標本。

【0055】 以結合活性為指標之抗體之篩選方法，亦宜使用利用噬菌體載體之淘選法。從多株抗體表現細胞群，以重鏈與輕鏈之次類之資料庫的形式取得抗體基因時，利用噬菌體載體之篩選方法係屬有利。編碼重鏈與輕鏈之可變區之基因，可藉由以適當連結子序列連結，而形成單鏈Fv(scFv)。藉由將編碼scFv之基因插入噬菌體載體，可取得於表面表現scFv之噬菌體。該噬菌體與所望抗原接觸後，藉由回收與抗原結合之噬菌體，可以回收編碼具目的結合活性之scFv的DNA。該操作可視需要反複實施，而將具所望之結合活性之scFv濃縮。

【0056】 獲得編碼目的抗IL-6R抗體之V區的cDNA後，將該cDNA以認識插入於該cDNA之兩末端的限制酶部位之限制酶消化。較佳之限制酶，係認識構成抗體基因之鹼基序列中出現頻度低之鹼基序列並消化。再者，為了將1副本的消化片段以正確方向插入載體，宜插入提供附著末端之限制酶。藉由將以上述方式經消化之編碼抗IL-6R抗體之V區的cDNA插入適當表現載體，可以取得抗體表現載體。此時，若將編碼抗體不變區(C區)之基因、與編碼前述V區之基因於同一讀框融合，則可取得嵌合抗體。在此，嵌合抗體係指不變區與可變區之來源不同者。因此，除了小鼠-人類等的異種嵌合抗體，人類-人類同種嵌合抗體也包含在本發明之嵌合抗體。藉由預先在具不變區之表現載體插入前述V區基因，可以構建嵌合抗體表現載體。具體而言，可於例如保持有編碼所望之抗體不變區(C區)之DNA的表現載體之5'側，適當配置消化前述V區基因之限制酶之限制酶認識序列。藉由將以相同組合之限制酶消化過的兩者於同一讀框融合，可以構建嵌合抗體表現載體。

【0057】 為了製造抗IL-6R單株抗體，可以將抗體基因於由表現控制區控制之下表現的方式納入表現載體。用於表現抗體之表現控制區，包含例如增強子或啟動子。又，也可在胺基末端附加適當的信號序列，以使表現的抗體分泌到細胞外。例如係使用具胺基酸序列MGWSCIILFLVATATGVHS(序列編號：

536)之胜肽當做信號序列，但是也可附加其他適當的信號序列。將表現的多胜肽在上述序列之羧基末端部分切斷，切斷的多胜肽可以成熟多胜肽之形式分泌到細胞外。其次，藉由以該表現載體將適當的寄主細胞轉形，可以取得表現編碼抗IL-6R抗體之DNA的重組細胞。

【0058】 「抗體斷片」係指會和完整抗體所結合之抗原結合之該完整抗體之一部分的該完全抗體以外之分子。抗體斷片之例不僅限於此，包括Fv、Fab、Fab'、Fab'-SH、F(ab')2、雙體抗體(diabody)、線狀抗體、單鏈抗體分子(例如:scFv)、及由抗體斷片形成之多專一性抗體。

【0059】 用語「全長抗體」、「完整抗體」、及「全部抗體」，在本說明書可交互替換，係指有實質類似天然型抗體結構的結構、或具有包含在本說明書定義之Fc區域之重鏈之抗體。

【0060】 用語「可變區」或「可變分域」，係指涉及使抗體結合於抗原之抗體之重鏈或輕鏈之分域。抗體之重鏈及輕鏈之可變分域(各為VH及VL)，通常各分域有4個保守的框架區 (FR) 及3個互補性決定區 (CDR) 的類似結構。(例如參照Kindt et al. Kuby Immunology, 6th ed., W.H. Freeman and Co., page 91 (2007)。)能以1個VH或VL分域給予充分的抗原結合專一性。

【0061】 本說明書使用之用語「互補性決定區」或「CDR」，係指序列為超可變，及/或形成結構上指定的圈環(loop)(「超可變圈環(loop)」)及/或抗原接觸殘基(「抗原接觸」)、抗體之可變分域之各區。通常抗體包括6個CDR：3個VH (H1、H2、H3)、及3個VL(L1、L2、L3)。本說明書之例示的CDR包括下列者：

(a) 胺基酸殘基26-32 (L1)、50-52 (L2)、91-96 (L3)、26-32 (H1)、53-55 (H2)、及96-101 (H3)之處產生的超可變圈環(loop) (Chothia and Lesk, J. Mol. Biol. 196:901-917 (1987))；

(b) 胺基酸殘基24-34 (L1)、50-56 (L2)、89-97 (L3)、31-35b (H1)、50-65 (H2)、

及95-102 (H3) 之處產生的CDR (Kabat et al., Sequences of Proteins of Immunological Interest, 5th Ed. Public Health Service, National Institutes of Health, Bethesda, MD (1991))；

(c) 胺基酸殘基27c-36 (L1)、46-55 (L2)、89-96 (L3)、30-35b (H1)、47-58 (H2)、及93-101 (H3) 之處產生的抗原接觸 (MacCallum et al. J. Mol. Biol. 262: 732-745 (1996))；及、

(d)包括 HVR胺基酸殘基46-56 (L2)、47-56 (L2)、48-56 (L2)、49-56 (L2)、26-35 (H1)、26-35b (H1)、49-65 (H2)、93-102 (H3)、及94-102 (H3)之(a)、(b)、及/或(c)之組合。

若無特別限定，CDR殘基及可變分域中之其他殘基(例如:FR殘基)，在本說明書係依照上述Kabat等人賦予編號。

【0062】 「框架」或「FR」，係指互補性決定區(CDR)殘基以外之可變分域殘基。可變分域之FR，通常由4個FR分域：FR1、FR2、FR3、及FR4構成。因應此，CDR及FR之序列通常依下列順序出現在VH(或VL)：FR1-H1(L1)-FR2-H2(L2)-FR3-H3(L3)-FR4。

【0063】 本說明書中，用語「不變區」或「固定區」係指抗體之可變區以外之部分。例如，IgG抗體，係以雙硫鍵鍵結的2個相同輕鏈與2個相同重鏈構成的約150,000道爾吞的雜四聚物糖蛋白，從N末端朝C末端，各重鏈具有也稱為可變重鏈分域或重鏈可變分域的可變區(VH)，然後是含有CH1分域、鉸鏈區、CH2分域、CH3分域之重鏈不變區(CH)。同樣，從N末端朝C末端，各輕鏈具有也稱為可變輕鏈分域或輕鏈可變分域之可變區 (VL)，然後是固定輕鏈(CL)分域。天然型抗體之輕鏈，可依據其固定區之胺基酸序列，歸屬在稱為kappa(κ)及lamda (λ)之2類型中之1個類型。

【0064】 抗體的「類別」，係指抗體之重鏈所具備的固定區或不變區的類

型。抗體有5個主要的類別：IgA、IgD、IgE、IgG、及IgM。並且其中有一些更進一步可區分成次類別(isotype)。例如:IgG1、IgG2、IgG3、IgG4、IgA1、及IgA2。不同類別的免疫球蛋白所對應的重鏈固定區分別稱為α、δ、ε、γ、及μ。

【0065】 本說明書中，用語「Fc區」係為了要定義含有不變區之至少一部分之免疫球蛋白重鏈之C末端區。此用語包括天然型序列Fc區及變異體Fc區。一態樣中，人IgG1的情形，重鏈Fc區從Cys226、或從Pro230，延伸到重鏈的羧基末端。惟Fc區之C末端之離胺酸(Lys447)或甘胺酸-離胺酸(Gly446-Lys447)可存在亦可不存在。本說明書中，若無特別限制，則Fc區或不變區中之胺基酸殘基之編號係依Kabat et al., Sequences of Proteins of Immunological Interest, 5th Ed. Public Health Service, National Institutes of Health, Bethesda, MD 1991 記載之EU編號系統(也稱為EU索引)。

【0066】 本發明之配體結合分子係含有切斷位點之多胜肽。切斷位點例如可利用酵素切斷，但也可利用還原劑予以還原、或光分解。切斷位點，只要能利用切斷而減弱配體結合分子對於配體之結合即可，可以配置在多胜肽中之任意位置。又，多胜肽中含有的切斷位點可為一個也可為多個。

【0067】 又，本發明之配體結合分子，切斷之狀態相較於切斷狀態時，配體結合較弱(亦即減弱)。配體結合分子與配體之結合在抗原抗體反應實施態樣中，配體結合之減弱可利用配體結合分子之配體結合活性予以評價。

【0068】 配體結合分子與配體之結合活性之評價，可依FACS、ELISA格式、ALPHA screen (Amplified Luminescent Proximity Homogeneous Assay)、利用表面電漿子共振(SPR)現象之BIACORE法、BLI(Bio-Layer Interferometry)法(Octet)等周知之方法確認(Proc. Natl. Acad. Sci. USA (2006) 103 (11), 4005-4010)。

ALPHA screen，係利用使用提供者與接受者的2種珠之ALPHA技術，依下列之原理實施。接近於提供者珠之分子會與結合於接受者珠之分子交互作用，

僅在2珠接近的狀態檢測出發光信號。由雷射激發的提供者珠內的光敏劑將周邊的氧變換為激發狀態的單態氧。單態氧擴散到提供者珠周邊，到達接近的接受者珠時會引起珠內之化學發光反應，最終發出光。與提供者珠結合之分子及結合於接受者珠之分子彼此未交互作用時，提供者珠產生之單態氧未到達接受者珠，故不起化學發光反應。

【0069】 例如於提供者珠結合有包括經生物素標記之Fc區之配體結合分子，於接受者珠結合有以麩胱甘肽S轉移酶(GST)標籤化的配體。競爭的含未標記的配體結合分子不存在時，配體結合分子與配體會交互作用並產生520-620 nm的信號。未標籤化的配體結合分子，會與標籤化的配體結合分子在與配體間之交互作用競爭。將競爭結果表示之螢光減少予以定量，可決定相對的結合親和性。抗體等配體結合分子使用Sulfo-NHS-生物素等予以生物素化係為公知。將配體以GST予以標籤化之方法，可適當採用將編碼配體之聚核苷酸與編碼GST之聚核苷酸於同一讀框融合而得之融合基因於保持有可表現之載體的細胞等中表現GST融合配體，並使用麩胱甘肽管柱精製之方法等。獲得之信號可藉由使用例如GRAPHPAD PRISM(GraphPad公司、San Diego)等的軟體以非線性回歸解析之一部位競爭(one-site competition)模型擬合(fitting)而理想地解析。

【0070】 將觀察交互作用之物質的其中之一(配體)固定在感應晶片之金薄膜上，並從感應晶片的背側照射光使在金薄膜與玻璃的交界面發生全反射，則反射光的一部分會形成反射強度下降的部分(SPR信號)。將觀察交互作用之物質的其中另一者(分析物)流過感應晶片的表面並使配體與分析物結合，則經固定化之配體分子的質量增加，感應晶片表面之溶劑之折射率會改變。藉由該折射率的變化，SPR信號的位置會偏移(反之，結合若解離，則回到信號位置)。Biacore系統取上述偏移量，亦即感應晶片表面之質量變化作為縱軸，將質量之時間變化作為測定資料表示(感測圖)。從感測圖的曲線，求出動力學：結合速度常數(ka)

與解離速度常數(kd)，由該常數之比求出解離常數(KD)。BIACORE法也可理想地使用於抑制測定法、平衡值解析法。抑制測定法，例如Proc.Natl.Acad.Sci.USA (2006) 103 (11), 4005-4010，平衡值解析法之例記載於Methods Enzymol. 2000;323:325-40.。

【0071】 配體結合分子與配體結合之功能減弱，係指例如依上述測定方法，比較待驗配體結合分子單位配體結合量相較於對照配體結合分子呈50%以下，較佳為45%以下、40%以下、35%以下、30%以下、20%以下、15%以下，尤佳為10%以下、9%以下、8%以下、7%以下、6%以下、5%以下、4%以下、3%以下、2%以下、或1%以下之結合量。結合活性之指標可適當使用所望的指標，也可使用例如解離常數(KD)。使用解離常數(KD)作為結合活性之評價指標時，若待驗配體結合分子對於配體之解離常數(KD)比起對照配體結合分子對於配體之解離常數(KD)大，則代表待驗配體結合分子對於配體之結合活性比起對照配體結合分子弱。與配體結合之機能減弱，係指例如:待驗配體結合分子對於配體之解離常數(KD)相較於對照配體結合分子對於配體之解離常數(KD)為2倍以上，較佳為5倍以上、10倍以上，尤佳為100倍以上。

對照配體結合分子，例如，未切斷型之配體結合分子。

【0072】 本發明之一實施態樣中，本發明之配體結合分子藉由在切斷位點切斷，配體從配體結合分子游離。在此，配體介隔連結子而與配體結合分子之一部分結合，該連結子無切斷位點時，配體以與配體結合分子之該一部分介隔連結子維持連接的狀態而游離(參照例如第1圖)。如此，配體與配體結合分子之一部分一起游離，只要配體結合分子的超過一半游離，則可說配體已從配體結合分子游離。

【0073】 作為檢測配體因為切斷位點之切斷而從配體結合分子游離之方法，有利用認識配體之配體檢測用抗體等檢測配體之方法。配體結合分子為抗

體斷片時，配體檢測用抗體宜和配體結合分子結合在同樣的抗原決定基較佳。使用配體檢測用抗體之配體之檢測，可利用FACS、ELISA格式、ALPHAscreen(Amplified Luminescent Proximity Homogeneous Assay)、利用了表面電漿子共振(SPR)現象之BIACORE法、BLI(Bio-Layer Interferometry)法(Octet)等周知之方法確認(Proc. Natl. Acad. Sci. USA (2006) 103 (11), 4005-4010)。

例如，使用Octet檢測配體之游離時，可藉由將認識配體之配體檢測用抗體予以生物素化，使其與生物感測器接觸後，測定針對樣本中之配體之結合，以檢測配體之游離。具體而言，針對含有蛋白酶處理前或蛋白酶處理後之配體結合分子與配體之樣本，使用配體檢測抗體測定配體之量，並比較蛋白酶處理前後之樣本中之配體檢測量，藉此可檢測配體之游離。又，針對含有蛋白酶、配體結合分子、以及配體之樣本及不含蛋白酶且含有配體結合分子與配體之樣本，使用配體檢測抗體測定之配體之量，並比較蛋白酶有無之樣本中之配體檢測量，藉此可檢測配體之游離。更具體而言，可依本申請案實施例中之方法檢測配體之游離。當配體結合分子與配體融合且形成融合蛋白質時，針對含有蛋白酶處理前或蛋白酶處理後之融合蛋白質之樣本，使用配體檢測抗體測定配體之量，並比較蛋白酶處理前後之樣本中之配體檢測量，藉此可檢測配體之游離。又，針對含有蛋白酶與融合蛋白質之樣本及不含蛋白酶且含有融合蛋白質之樣本，使用配體檢測抗體測定配體之量，並比較蛋白酶有無之樣本中之配體檢測量，藉此可檢測配體之游離。更具體而言，可依本申請案實施例中之方法檢測配體之游離。

【0074】 又，在與配體結合分子結合時會抑制配體之生理活性之實施態樣中，作為檢測從配體結合分子游離之方法而言，可藉由測定樣本中之配體之生理活性以檢測配體之游離。具體而言，針對含有蛋白酶處理前或蛋白酶處理後之配體結合分子與配體之樣本，測定配體之生理活性並加以比較，藉此可檢測

配體之游離。又，針對含有蛋白酶、配體結合分子、及配體之樣本及不含蛋白酶且含有配體結合分子與配體之樣本，測定並比較配體之生理活性，藉此可檢測配體之游離。當配體結合分子與配體融合並形成融合蛋白質時，針對含有蛋白酶處理前或蛋白酶處理後之融合蛋白質之樣本，測定並比較配體之生理活性，藉此可檢測配體之游離。又，針對含有蛋白酶與融合蛋白質之樣本及不含蛋白酶且含有融合蛋白質之樣本，測定並比較配體之生理活性，藉此可檢測配體之游離。

【0075】 本發明之一實施態樣中，切斷位點包括蛋白酶切斷序列並利用蛋白酶予以切斷。

【0076】 本說明書中，用語「蛋白酶」係水解胜肽鍵之內切胜肽酶或外切胜肽酶等酵素，通常稱為內切胜肽酶。本發明中使用的蛋白酶僅限定於能夠切斷蛋白酶切斷序列，其種類無特殊限制。一些實施態樣中，使用標靶組織專一性的蛋白酶。標靶組織專一性的蛋白酶例如可指下列中的任一者

(1) 在標靶組織中比起在正常組織以更高位準表現之蛋白酶、

(2) 在標靶組織中比起在正常組織有更高活性之蛋白酶、

(3) 在標靶細胞比起在正常細胞以更高位準表現之蛋白酶、

(4) 在標靶細胞比起在正常細胞有更高活性之蛋白酶。

更具體的實施態樣中，使用癌組織專一性的蛋白酶或發炎組織專一性的蛋白酶。

【0077】 本說明書中，用語「標靶組織」意指至少含有1個標靶細胞之組織。本發明之一些實施態樣中，標靶組織係癌組織。本發明之一些實施態樣中，標靶組織係發炎組織。

【0078】 用語「癌組織」，係指至少含有1個癌細胞之組織。因此例如係指以癌組織含有癌細胞與血管之方式，貢獻於包括癌細胞及內皮細胞之腫瘤

(tumor mass)之形成之所有細胞型。本說明書中，腫瘤係指腫瘤組織巢 (a foci of tumor tissue)。「腫瘤」之用語一般言之，係意指良性新生物或惡性新生物。

【0079】 本說明書中，「發炎組織」例如可列舉如下。

・類風濕性關節炎、變形性關節症中之關節

・支氣管氣喘、COPD中的肺(肺泡)

・發炎性腸病症、克隆氏病、潰瘍性大腸炎中的消化器官

・肝臟、腎臟、肺之纖維化症中之纖維化組織

・臟器移植引起排斥反應的組織

・動脈硬化、心臟衰竭之血管、心臟(心肌)

・代謝症候群中之內臟脂肪

・異位性皮膚炎其他皮膚炎中之皮膚組織

・椎間盤突出、慢性腰痛中的脊髓神經

【0080】 一些種類之標靶組織中，已知有專一性的表現或專一性的活化的蛋白酶或據認為和標靶組織病症狀態相關的蛋白酶(標靶組織專一性的蛋白酶)。例如:國際公開WO2013/128194號、國際公開WO2010/081173號、國際公開WO2009/025846號等揭示在癌組織專一性的表現的蛋白酶。又，J Inflamm (Lond). 2010; 7: 45.、Nat Rev Immunol. 2006 Jul;6(7):541-50.、Nat Rev Drug Discov. 2014 Dec;13(12):904-27.、Respir Res. 2016 Mar 4;17:23.、Dis Model Mech. 2014 Feb;7(2):193-203.、Biochim Biophys Acta. 2012 Jan;1824(1):133-45.揭示據認為和發炎相關的蛋白酶。

【0081】 除了在標靶組織專一性的表現的蛋白酶以外，也存在於標靶組織專一性的活化的蛋白酶。例如:蛋白酶有時會以不活化型表現，之後成為活性型，在許多組織存在有抑制活性型蛋白酶之物質，利用活化處理與抑制劑之存在來控制活性 (Nat Rev Cancer. 2003 Jul;3(7):489-501.)。標靶組織中，有時活性型蛋

白酶從受抑制狀態脫逃，而被專一性地活化。

活性型蛋白酶之測定方法，可採用使用認識活化型蛋白酶之抗體之方法(PNAS 2013 Jan 2; 110(1): 93-98.)、將蛋白酶所認識之胜肽予以螢光標識並在切斷前消光(淬滅)，但切斷後發光之方法(Nat Rev Drug Discov. 2010 Sep;9(9):690-701. doi: 10.1038/nrd3053.)進行測定。

【0082】 從一觀點，用語「標靶組織專一性的蛋白酶」可指下列中之任一者:

(i) 在標靶組織比起在正常組織以更高位準表現之蛋白酶、

(ii) 在標靶組織比起在正常組織有更高活性之蛋白酶、

(iii) 在標靶細胞比起在正常細胞以更高位準表現之蛋白酶、

(iv) 在標靶細胞比起在正常細胞有更高活性之蛋白酶。

【0083】 雖不限定解釋，但具體的蛋白酶可列舉，半胱胺酸蛋白酶(包括細胞自溶酶(Cathepsin)家族B、L、S等)、天冬胺醯基蛋白酶(細胞自溶酶D、E、K、O等)、絲胺酸蛋白酶(包括蛋白裂解酶(Matriptase)(包括MT-SP1)、細胞自溶酶A及G、凝血酶、胞漿素、尿激酶(uPA)、組織胞漿素原活化因子(tPA)、彈性蛋白酶、蛋白酶3、凝血酶、激肽釋放素(kallikrein)、中性蛋白酶(tryptase)、凝乳酶(chymase)、金屬蛋白酶(包括膜結合型(MMP14-17及MMP24-25)及分泌型(MMP1-13及MMP18-23及MMP26-28)兩者之金屬蛋白酶(MMP1-28)、蛋白酶之A整合素(disintegrin)及金屬蛋白酶(ADAM)、具有A整合素或血小板反應素(thrombospondin)功能域之金屬蛋白酶(ADAMTS)、Meprin (Meprin α(meprin alpha)、Meprin β(meprin beta)))、CD10(CALLA)、以及前列腺專一性的抗原(PSA)、Legumain、TMPRSS3、TMPRSS4、嗜中性球彈性蛋白酶(HNE)、beta分泌酶(secretase)(BACE)、纖維芽細胞活化蛋白質alpha (FAP)、Granzyme B、胍基苯甲酸酶(guanidino-benzoatase)(GB)、胃蛋白酶、neprilysin、NS3/4A、

HCV-NS3/4、calpain、ADAMDEC1、腎活素(renin)、細胞自溶酶C、細胞自溶酶V/L2、細胞自溶酶 X/Z/P、Cruzipain、otubain2、激肽釋放素關連胜肽酶(KLKs(KLK3、KLK4、KLK5、KLK6、KLK7、KLK8、KLK10、KLK11、KLK13、KLK14))、骨形成蛋白質1(BMP-1)、活化Protein C、血液凝固關連蛋白酶(Factor VIIa、Factor IXa、Factor Xa、Factor XIa、Factor XIIa)、HtrA1、乳鐵蛋白、Marapsin、PACE4、DESC1、二胜肽胜肽酶4(DPP-4)、TMPRSS2、細胞自溶酶F、細胞自溶酶H、細胞自溶酶L2、細胞自溶酶O、細胞自溶酶S、顆粒酶(Granzyme) A、Gepsin calpain 2、麩胺酸羧基胜肽酶2、AMSH-Like Proteases、AMSH、gamma分泌酶(gamma secretase)、A抗胞漿素切斷酵素(APCE)、Decysin 1、N-Acetylated Alpha-Linked Acidic Dipeptidase-Like 1(NAALADL1)、furin(furin)等。

【0084】 從其他觀點，標靶組織專一性的蛋白酶可以指癌組織專一性的蛋白酶或發炎組織專一性的蛋白酶。

【0085】 癌組織專一性的蛋白酶，例如:國際公開WO2013/128194號、國際公開WO2010/081173號、國際公開WO2009/025846號等揭示之在癌組織專一性的表現的蛋白酶。

【0086】 就癌組織專一性的蛋白酶之種類而言，在治療對象之癌組織之表現專一性越高，則越可獲得副作用減低效果。癌組織專一性的蛋白酶，在癌組織之濃度為高出正常組織之濃度之5倍以上較佳，高10倍以上更佳，高100倍以上更理想，高500倍以上特別理想，高1000倍以上最理想。又，癌組織專一性的蛋白酶，在癌組織之活性為高出正常組織之活性之2倍以上較佳，高3倍以上、高4倍以上、高5倍以上、高10倍以上更佳，高100倍以上更理想，高500倍以上特別理想，高1000倍以上最理想。

又，癌組織專一性的蛋白酶，可為結合在癌細胞之細胞膜者，也可為不結合在細胞膜而是分泌到細胞外者。癌組織專一性的蛋白酶未結合在癌細胞之細

胞膜時，利用免疫細胞所為之細胞傷害因為係對於癌細胞有專一性，故癌組織專一性的蛋白酶宜存在於癌組織之內部或附近較佳。本說明書中，「癌組織之附近」，係指癌組織專一性的蛋白酶切斷序列被切斷而發揮配體結合活性之降低效果之範圍內。惟宜儘可能不傷害正常細胞之範圍較佳。

由另一觀點，癌組織專一性的蛋白酶，係下列中之任一者:

(i) 在癌組織比起在正常組織以更高位準表現之蛋白酶、

(ii) 在癌組織比起在正常組織有更高活性之蛋白酶、

(iii) 在癌細胞比起在正常細胞以更高位準表現之蛋白酶、

(iv) 在癌細胞比起在正常細胞有更高活性之蛋白酶。

癌組織專一性的蛋白酶可為單獨1種也可將2種以上組合。癌組織專一性的蛋白酶之種類數，可由該技術領域中有通常知識者考慮治療對象之癌種類而適當設定。

【0087】 由以上之觀點，癌組織專一性的蛋白酶宜為上述例示之蛋白酶中之絲胺酸蛋白酶與金屬蛋白酶較理想，Matriptase(包括MT-SP1)、尿激酶(uPA)與金屬蛋白酶更佳，MT-SP1、uPA、MMP2、MMP9更理想。

【0088】 就發炎組織專一性的蛋白酶的種類而言，在治療對象之發炎組織之表現專一性越高，則越可獲得副作用減低效果。發炎組織專一性的蛋白酶，宜為在發炎組織之濃度為高出在正常組織之濃度之5倍以上較佳，高10倍以上更佳，高100倍以上更理想，高500倍以上特別理想，高1000倍以上最理想。又，發炎組織專一性的蛋白酶，宜為在發炎組織之活性為高出在正常組織之活性之2倍以上較佳，高3倍以上、高4倍以上、高5倍以上、高10倍以上更佳，高100倍以上更理想，高500倍以上特別理想，高1000倍以上最理想。

又，發炎組織專一性的蛋白酶，可為結合在發炎組織之細胞膜者，也可為不結合在細胞膜在而是分泌到細胞外者。發炎組織專一性的蛋白酶未結合在發

炎組織之細胞膜時，利用免疫細胞所為之細胞傷害因為係對於發炎組織有專一性，故發炎組織專一性的蛋白酶宜存在於發炎組織之內部或附近較佳。本說明書中，「發炎組織之附近」，係指發炎組織專一性的蛋白酶切斷序列被切斷而發揮配體結合活性之降低效果之範圍內。惟宜儘可能不傷害正常細胞之範圍較佳。

由其他觀點，發炎組織專一性的蛋白酶，係下列中之任一者:

(i) 在發炎組織比起在正常組織以更高位準表現之蛋白酶、

(ii) 在發炎組織比起在正常組織有更高活性之蛋白酶、

(iii) 在發炎細胞比起在正常細胞以更高位準表現之蛋白酶、

(iv) 在發炎細胞比起在正常細胞有更高活性之蛋白酶。

發炎組織專一性的蛋白酶可為單獨1種也可將2種以上組合。發炎組織專一性的蛋白酶之種類數，可由該技術領域中有通常知識者考慮治療對象之病狀而適當設定。

【0089】 由以上之觀點，發炎組織專一性的蛋白酶宜為上述例示之蛋白酶中之金屬蛋白酶較理想，金屬蛋白酶中之ADAMTS5、MMP2、MMP7、MMP9、MMP13更理想。

【0090】 蛋白酶切斷序列，係當於水溶液中由於標靶組織專一性的蛋白酶而使多胜肽受到水解時，被該標靶組織專一性的蛋白酶專一性的認識的特定胺基酸序列。

蛋白酶切斷序列，考慮減低副作用之觀點，宜為利用在治療對象之標靶組織/細胞較專一性表現、或在治療對象之標靶組織/細胞較專一性的活化的標靶組織專一性的蛋白而以高專一性水解之胺基酸序列較佳。

具體的蛋白酶切斷序列，例如:國際公開WO2013/128194號、國際公開WO2010/081173號、國際公開WO2009/025846號等揭示之在由上述例示之癌組織

專一性的表現的蛋白酶、發炎組織專一性的蛋白酶等所專一性的水解的標靶序列。也可使用對於藉由既知之蛋白酶專一性的水解的標靶序列導入適當胺基酸變異等予以人工改變而得的序列。又，蛋白酶切斷序列也可使用如Nature Biotechnology 19, 661 - 667 (2001)之該技術領域中有通常知識者公知之方法鑑定者。

又，也可使用天然存在的蛋白酶切斷序列。例如可使用TGFβ因接受蛋白酶之切斷而變化為潛在型的這類由於接受蛋白酶之切斷而改變分子形之蛋白質中之接受蛋白酶切斷之序列。

【0091】 蛋白酶切斷序列例雖不僅限定於此，但可使用國際公開WO2015/116933號、國際公開WO2015/048329號、國際公開WO2016/118629號、國際公開WO2016/179257號、國際公開WO2016/179285號、國際公開WO2016/179335號、國際公開WO2016/179003號、國際公開WO2016/046778號、國際公開WO2016/014974號、美國專利公開US2016/0289324號、美國專利公開US2016/0311903號、PNAS (2000) 97: 7754-7759.、Biochemical Journal (2010) 426: 219-228.、Beilstein J Nanotechnol. (2016) 7: 364-373.中例示之序列。

蛋白酶切斷序列，如上述，更宜為利用理想的標靶組織專一性的蛋白酶予以專一性的水解的胺基酸序列更佳。利用標靶組織專一性的蛋白酶予以專一性的水解的胺基酸序列中，以下之胺基酸序列為較佳。

LSGRSDNH(序列編號：3、MT-SP1、可利用uPA切斷)

PLGLAG(序列編號：34、可利用MMP2、MMP9切斷)

VPLSLTMG(序列編號：35、可利用MMP7切斷)

蛋白酶切斷序列也可使用下列的序列。

TSTSGRSANPRG(序列編號：66、MT-SP1、可利用uPA切斷)

ISSGLLSGRSDNH(序列編號：67、MT-SP1、可利用uPA切斷)

AVGLLAPPGGLSGRSDNH(序列編號：68、MT-SP1、可利用uPA切斷)

GAGVPMSMRGGAG(序列編號：69、可利用MMP1切斷)

GAGIPVSLRSGAG(序列編號：70、可利用MMP2切斷)

GPLGIAGQ(序列編號：71、可利用MMP2切斷)

GGPLGMLSQS(序列編號：72、可利用MMP2切斷)

PLGLWA(序列編號：73、可利用MMP2切斷)

GAGRPFSMIMGAG(序列編號：74、可利用MMP3切斷)

GAGVPLSLTMGAG(序列編號：75、可利用MMP7切斷)

GAGVPLSLYSGAG(序列編號：76、可利用MMP9切斷)

AANLRN(序列編號：77、可利用MMP11切斷)

AQAYVK(序列編號：78、可利用MMP11切斷)

AANYMR(序列編號：79、可利用MMP11切斷)

AAALTR(序列編號：80、可利用MMP11切斷)

AQNLMR(序列編號：81、可利用MMP11切斷)

AANYTK(序列編號：82、可利用MMP11切斷)

GAGPQGLAGQRGIVAG(序列編號：83、可利用MMP13切斷)

PRFKIIGG(序列編號：84、可利用尿激酶原切斷)

PRFRIIGG(序列編號：85、可利用尿激酶原切斷)

GAGSGRSAG(序列編號：86、可利用uPA切斷)

SGRSA(序列編號：87、可利用uPA切斷)

GSGRSA(序列編號：88、可利用uPA切斷)

SGKSA(序列編號：89、可利用uPA切斷)

SGRSS(序列編號：90、可利用uPA切斷)

SGRRA(序列編號：91、可利用uPA切斷)

SGRNA(序列編號：92、可利用uPA切斷)

SGRKA(序列編號：93、可利用uPA切斷)

QRGRSA(序列編號：94、可利用tPA切斷)

GAGSLLKSRMVPNFNAG(序列編號：95、可利用細胞自溶酶B切斷)

TQGAAA(序列編號：96、可利用細胞自溶酶B切斷)

GAAAAA(序列編號：97、可利用細胞自溶酶B切斷)

GAGAAG(序列編號：98、可利用細胞自溶酶B切斷)

AAAAAG(序列編號：99、可利用細胞自溶酶B切斷)

LCGAAI(序列編號：100、可利用細胞自溶酶B切斷)

FAQALG(序列編號：101、可利用細胞自溶酶B切斷)

LLQANP(序列編號：102、可利用細胞自溶酶B切斷)

LAAANP(序列編號：103、可利用細胞自溶酶B切斷)

LYGAQF(序列編號：104、可利用細胞自溶酶B切斷)

LSQAQG(序列編號：105、可利用細胞自溶酶B切斷)

ASAASG(序列編號：106、可利用細胞自溶酶B切斷)

FLGASL(序列編號：107、可利用細胞自溶酶B切斷)

AYGATG(序列編號：108、可利用細胞自溶酶B切斷)

LAQATG(序列編號：109、可利用細胞自溶酶B切斷)

GAGSGVVIATVIVITAG(序列編號：110、可利用細胞自溶酶L切斷)

APMAEGGG(序列編號：111、可利用Meprinα、Meprinβ切斷)

EAQGDKII(序列編號：112、可利用Meprinα、Meprinβ切斷)

LAFSDAGP(序列編號：113、可利用Meprinα、Meprinβ切斷)

YVADAPK(序列編號：114、可利用Meprinα、Meprinβ切斷)

RRRRR(序列編號：115、可利用furin切斷)

RRRRRR(序列編號：116、可利用furin切斷)

GQSSRHRRAL(序列編號：117、可利用furin切斷)

SSRHRRALD(序列編號：118)

RKSSIIIRMRDVVL(序列編號：119、可利用胞漿素原(Plasminogen)切斷)

SSSFDKGKYKKGDDA(序列編號：120、可利用Staphylokinase切斷)

SSSFDKGKYKRGDDA(序列編號：121、可利用Staphylokinase切斷)

IEGR(序列編號：122、可利用FactorIXa切斷)

IDGR(序列編號：123、可利用FactorIXa切斷)

GGSIDGR(序列編號：124、可利用FactorIXa切斷)

GPQGIAGQ(序列編號：125、可利用膠原蛋白酶切斷)

GPQGLLGA(序列編號：126、可利用膠原蛋白酶切斷)

GIAGQ(序列編號：127、可利用膠原蛋白酶切斷)

GPLGIAG(序列編號：128、可利用膠原蛋白酶切斷)

GPEGLRVG(序列編號：129、可利用膠原蛋白酶切斷)

YGAGLGVV(序列編號：130、可利用膠原蛋白酶切斷)

AGLGVVER(序列編號：131、可利用膠原蛋白酶切斷)

AGLGISST(序列編號：132、可利用膠原蛋白酶切斷)

EPQALAMS(序列編號：133、可利用膠原蛋白酶切斷)

QALAMSAI(序列編號：134、可利用膠原蛋白酶切斷)

AAYHLVSQ(序列編號：135、可利用膠原蛋白酶切斷)

MDAFLESS(序列編號：136、可利用膠原蛋白酶切斷)

ESLPVVAV(序列編號：137、可利用膠原蛋白酶切斷)

SAPAVESE(序列編號：138、可利用膠原蛋白酶切斷)

DVAQFVLT(序列編號：139、可利用膠原蛋白酶切斷)

VAQFVLTE(序列編號：140、可利用膠原蛋白酶切斷)

AQFVLTEG(序列編號：141、可利用膠原蛋白酶切斷)

PVQPIGPQ(序列編號：142、可利用膠原蛋白酶切斷)

LVPRGS(序列編號：143、可利用凝血酶切斷)

TSTSGRSANPRG(序列編號：345)

【0092】 本發明之一實施態樣中，可於蛋白酶切斷序列的一端或兩端更附加可動連結子。蛋白酶切斷序列一端之可動連結子可稱呼為第一可動連結子，另一端之可動連結子可稱呼為第二可動連結子。於特定之實施形態，蛋白酶切斷序列與可動連結子包括下式中之一者。

(蛋白酶切斷序列)

(第一可動連結子)-(蛋白酶切斷序列)

(蛋白酶切斷序列)-(第二可動連結子)

(第一可動連結子)-(蛋白酶切斷序列)-(第二可動連結子)

本實施態樣中，可動連結子宜為胜肽連結子較佳。第一可動連結子與第二可動連結子，係各自獨立且任意地存在且含有至少1個可撓性胺基酸(Gly等)之相同或不同之可動連結子。例如:含有蛋白酶切斷序列會獲得所望之蛋白酶接近性之程度之充分數目的殘基(從Arg、Ile、Gln、Glu、Cys、Tyr、Trp、Thr、Val、His、Phe、Pro、Met、Lys、Gly、Ser、Asp、Asn、Ala等任意選擇的胺基酸、尤其Gly、Ser、Asp、Asn、Ala，進而Gly及Ser，尤其Gly等)。

【0093】 適合使用在蛋白酶切斷序列兩端之可動連結子，通常係會增進蛋白酶對於蛋白酶切斷序列之接近且提升蛋白酶之切斷效率者。理想的可動連結子可輕易地選擇，可從1個胺基酸(Gly等)至20個胺基酸、2個胺基酸至15個胺基酸或4個胺基酸至10個胺基酸、5個胺基酸至9個胺基酸、6個胺基酸至8個胺基酸或7個胺基酸至8個胺基酸為主而從3個胺基酸至12個胺基酸等不同長度當中選

擇理想者者。本發明之一些實施態樣中，可動連結子係1至7個胺基酸之胜肽連結子。

【0094】 可動連結子，例如下列但不限定，例如:甘胺酸聚合物(G)n、甘胺酸-絲胺酸聚合物(例如包括 (GS)n、(GSGGS：序列編號：45)n及(GGGS：序列編號：36)n，n為至少1之整數)、甘胺酸-丙胺酸聚合物、丙胺酸-絲胺酸聚合物、習知技術周知之其他可動連結子。

其中，甘胺酸及甘胺酸-絲胺酸聚合物受重視，理由是該等胺基酸相對地較不結構化，容易作為成分間之中性繫鏈的作用。

由甘胺酸-絲胺酸聚合物構成之可動連結子，例如以下但不限定，例如：

Ser

Gly・Ser(GS)

Ser・Gly(SG)

Gly・Gly・Ser(GGS)

Gly・Ser・Gly(GSG)

Ser・Gly・Gly(SGG)

Gly・Ser・Ser(GSS)

Ser・Ser・Gly(SSG)

Ser・Gly・Ser(SGS)

Gly・Gly・Gly・Ser(GGGS、序列編號：36)

Gly・Gly・Ser・Gly(GGSG、序列編號：37)

Gly・Ser・Gly・Gly(GSGG、序列編號：38)

Ser・Gly・Gly・Gly(SGGG、序列編號：39)

Gly・Ser・Ser・Gly(GSSG、序列編號：40)

Gly・Gly・Gly・Gly・Ser(GGGGS、序列編號：41)

Gly・Gly・Gly・Ser・Gly(GGGSG、序列編號：42)

Gly・Gly・Ser・Gly・Gly(GGSGG、序列編號：43)

Gly・Ser・Gly・Gly・Gly(GSGGG、序列編號：44)

Gly・Ser・Gly・Gly・Ser(GSGGS、序列編號：45)

Ser・Gly・Gly・Gly・Gly(SGGGG、序列編號：46)

Gly・Ser・Ser・Gly・Gly(GSSGG、序列編號：47)

Gly・Ser・Gly・Ser・Gly(GSGSG、序列編號：48)

Ser・Gly・Gly・Ser・Gly(SGGSG、序列編號：49)

Gly・Ser・Ser・Ser・Gly(GSSSG、序列編號：50)

Gly・Gly・Gly・Gly・Gly・Ser(GGGGGS、序列編號：51)

Ser・Gly・Gly・Gly・Gly・Gly(SGGGGG、序列編號：52)

Gly・Gly・Gly・Gly・Gly・Gly・Ser(GGGGGGS、序列編號：53)

Ser・Gly・Gly・Gly・Gly・Gly・Gly(SGGGGGG、序列編號：54)

(Gly・Gly・Gly・Gly・Ser(GGGGS、序列編號：41))n

(Ser・Gly・Gly・Gly・Gly(SGGGG、序列編號：46))n

[n為1以上之整數]等。惟胜肽連結子之長度、序列可因應目的由該技術區中有通常知識者適當選擇。

【0095】 本發明之一些實施態樣中，配體結合分子包括抗體VH與抗體VL。包括VH與VL之配體結合分子，例如但不限於Fv、scFv、Fab、Fab'、Fab'-SH、F(ab')2、完全抗體等。

【0096】 本發明之一些實施態樣中，配體結合分子包括Fc區。使用IgG抗體之Fc區時，其種類不限定，可使用IgG1、IgG2、IgG3、IgG4等Fc區。例如可使用包括選自序列編號：55、56、57、58表示之胺基酸序列中之一個序列之Fc區、或對於該等Fc區施加了改變之Fc區變異體。又，本發明之一些實施態樣中，

配體結合分子包括抗體不變區。

【0097】 本發明之更具體的一些實施態樣中，配體結合分子為抗體。使用抗體作為配體結合分子時，對於配體之結合係由可變區實現。更具體的一些實施態樣中，配體結合分子為IgG抗體。使用IgG抗體作為配體結合分子時，其種類不限定，可使用IgG1、IgG2、IgG3、IgG4等。使用IgG抗體作為配體結合分子時，對於配體之結合亦由可變區實現，IgG抗體之二個可變區中之一者或二者皆可實現對於配體之結合。

【0098】 本發明之一些實施態樣中，藉由將配體結合分子中之切斷位點/蛋白酶切斷序列切斷，配體結合分子中之具配體結合活性之分域被分割切斷，對於配體之結合減弱。例如:使用IgG抗體作為配體結合分子時，抗體可變區中設置切斷位點/蛋白酶切斷序列，於切斷狀態時，不能形成完全的抗體可變區，而是對於配體之結合減弱之實施態樣。

【0099】 本說明書中，「組裝」可代換為例如，2個以上之多胜肽區交互作用之狀態。一般而言，成為對象之多胜肽區之間，形成疏水鍵、氫鍵、離子鍵等而形成組裝體。常見的組裝的一例已知在以天然型抗體為代表之抗體中，重鏈可變區(VH)與輕鏈可變區(VL)利用兩者間之非共價鍵等而保持配對結構。

【0100】 本發明之一些實施態樣中，配體結合分子中含有的VH與VL係組裝。又，抗體VH與抗體VL之組裝例如可利用切斷位點/蛋白酶切斷序列切斷解除。組裝之解除，例如可代換為2個以上之多胜肽區之交互作用狀態之全部或一部分解除。VH與VL之組裝之解除，可為VH與VL之交互作用全部解除，也可為VH與VL之交互作用之中之一部分解除。

本發明之配體結合分子中，包括，配體結合分子中之抗體VL或其一部分與抗體VH或其一部分之組裝，藉由將切斷位點切斷而解除、或蛋白酶切斷序列被蛋白酶切斷而解除之配體結合分子。

【0101】 本發明之一些實施態樣中，配體結合分子包括抗體VH與抗體VL，配體結合分子之切斷位點/蛋白酶切斷序列未被切斷之狀態，配體結合分子中之抗體VH與抗體VL係組裝，藉由切斷位點/蛋白酶切斷序列切斷，配體結合分子中之抗體VH與抗體VL之組裝解除。配體結合分子中之切斷位點/蛋白酶切斷序列，只要是因切斷而配體結合分子對於配體之結合能力減弱，則可配置在配體結合分子中之任意位置。

【0102】 本發明之更進一步的一些實施態樣中，配體結合分子包括抗體VH、抗體VL及抗體不變區。

抗體之VH與VL、CH與CL，依Rothlisberger等人(J Mol Biol. 2005 Apr 8;347(4):773-89.)所述，已知在分域間介隔多數胺基酸側鏈而交互作用。VH-CH1與VL-CL已知就Fab分域而言能形成安定的結構，但如有人所報告，VH與VL之間之胺基酸側鏈一般而言係以10^{-5}M至10^{-8}M範圍的解離常數交互作用，僅存在VH分域與VL分域時，據認為形成組裝狀態之比例少。

【0103】 本發明之一些實施態樣中，設計了:在含有抗體VH與抗體VL之配體結合分子設置切斷位點/蛋白酶切斷序列，切斷前在Fab結構的重鏈-輕鏈交互作用皆存在於二個胜肽間，但於已將切斷位點/蛋白酶切斷序列切斷時，包括VH(或VH之一部份)之胜肽與包括VL(或VL之一部份)之胜肽之間之交互作用減弱，VH與VL之組裝解除的配體結合分子。

【0104】 本發明之一實施態樣中，切斷位點/蛋白酶切斷序列位在抗體不變區內。更具體的實施態樣中，切斷位點/蛋白酶切斷序列，位在比起抗體重鏈不變區中之140號(EU編號)胺基酸更靠可變區側，較佳為比起抗體重鏈不變區中之122號(EU編號)胺基酸更靠可變區側。於一些具體的實施態樣中，切斷位點/蛋白酶切斷序列插入在抗體重鏈不變區118號胺基酸(EU編號)至抗體重鏈不變區140號胺基酸(EU編號)之序列中之任意位置。於其他更具體的實施態樣中，切

斷位點/蛋白酶切斷序列，位在比起抗體輕鏈不變區中之130號(EU編號)(Kabat編號130號)胺基酸更靠可變區側，較佳為比起抗體輕鏈不變區中之113號(EU編號)(Kabat編號113號)胺基酸更靠可變區側、比起抗體輕鏈不變區中之112號(EU編號)(Kabat編號112號)胺基酸更靠可變區側。於一些具體的實施態樣中，切斷位點/蛋白酶切斷序列，插入在從抗體輕鏈不變區108號胺基酸(EU編號)(Kabat編號108號)到抗體輕鏈不變區131號胺基酸(EU編號)(Kabat編號131號)之序列中之任意位置。

【0105】 本發明之一實施態樣中，切斷位點/蛋白酶切斷序列位在抗體VH內或抗體VL內。更具體的實施態樣中，切斷位點/蛋白酶切斷序列，位在比起抗體VH之7號(Kabat編號)胺基酸更靠抗體不變區側，較佳為比起抗體VH之40號(Kabat編號)胺基酸更靠抗體不變區側，更佳為比起抗體VH之101號(Kabat編號)胺基酸更靠抗體不變區側，又更佳為比起抗體VH之109號(Kabat編號)胺基酸更靠抗體不變區側，比起抗體VH之111號(Kabat編號)胺基酸更靠抗體不變區側。更具體的實施態樣中，切斷位點/蛋白酶切斷序列，位在比起抗體VL之7號(Kabat編號)胺基酸更靠抗體不變區側，較佳為比起抗體VL之39號(Kabat編號)胺基酸更靠抗體不變區側，更佳為比起抗體VL之96號(Kabat編號)胺基酸更靠抗體不變區側，又更佳為比起抗體VL之104號(Kabat編號)胺基酸更靠抗體不變區側，比起抗體VL之105號(Kabat編號)胺基酸更靠抗體不變區側。

於一些更具體的實施態樣中，切斷位點/蛋白酶切斷序列，插入在形成抗體VH或抗體VL中之圈環結構之殘基及靠近圈環結構之殘基之位置。抗體VH或抗體VL中之圈環結構，係指在抗體VH或抗體VL之中未形成α-螺旋、β-板片等二級結構之部分。形成圈環結構之殘基及靠近圈環結構之殘基之位置，具體而言，可指抗體VH7號胺基酸(Kabat編號)至16號胺基酸(Kabat編號)、40號胺基酸(Kabat編號)至47號胺基酸(Kabat編號)、55號胺基酸(Kabat編號)至69號胺基酸(Kabat編

號)、73號胺基酸(Kabat編號)至79號胺基酸(Kabat編號)、83號胺基酸(Kabat編號)至89號胺基酸(Kabat編號)、95號胺基酸(Kabat編號)至99號胺基酸(Kabat編號)、101號胺基酸(Kabat編號)至113號胺基酸(Kabat編號)、抗體VL7號胺基酸(Kabat編號)至19號胺基酸(Kabat編號)、39號胺基酸(Kabat編號)至46號胺基酸(Kabat編號)、49號胺基酸(Kabat編號)至62號胺基酸(Kabat編號)、96號胺基酸(Kabat編號)至107號胺基酸(Kabat編號)之範圍。

於一些更具體的實施態樣中，切斷位點/蛋白酶切斷序列係插入到抗體VH7號胺基酸(Kabat編號)至16號胺基酸(Kabat編號)、40號胺基酸(Kabat編號)至47號胺基酸(Kabat編號)、55號胺基酸(Kabat編號)至69號胺基酸(Kabat編號)、73號胺基酸(Kabat編號)至79號胺基酸(Kabat編號)、83號胺基酸(Kabat編號)至89號胺基酸(Kabat編號)、95號胺基酸(Kabat編號)至99號胺基酸(Kabat編號)、101號胺基酸(Kabat編號)至113號胺基酸(Kabat編號)之序列中之任意位置。

於一些更具體的實施態樣中，切斷位點/蛋白酶切斷序列，係插入到從抗體VL7號胺基酸(Kabat編號)至19號胺基酸(Kabat編號)、從39號胺基酸(Kabat編號)至46號胺基酸(Kabat編號)、從49號胺基酸(Kabat編號)至62號胺基酸(Kabat編號)、從96號胺基酸(Kabat編號)至107號胺基酸(Kabat編號)之序列中之任意位置。

【0106】 本發明之一實施態樣中，切斷位點/蛋白酶切斷序列位在抗體VH與抗體不變區之交界附近。抗體VH與抗體重鏈不變區之交界附近，可指抗體VH之101號(Kabat編號)之胺基酸至抗體重鏈不變區140號(EU編號)之胺基酸之間，較佳可指從抗體VH之109號(Kabat編號)之胺基酸至抗體重鏈不變區122號(EU編號)之胺基酸之間、或從抗體VH之111號(Kabat編號)之胺基酸至抗體重鏈不變區122號(EU編號)之胺基酸之間。又，抗體VH與抗體輕鏈不變區連結時，抗體VH與抗體輕鏈不變區之交界附近，可指從抗體VH之101號(Kabat編號)之胺基酸至抗體輕鏈不變區130號(EU編號(Kabat編號130號))之胺基酸之間，較佳可指從抗

體VH之109號(Kabat編號)之胺基酸至抗體輕鏈不變區113號(EU編號)(Kabat編號113號)之胺基酸之間、或從抗體VH之111號(Kabat編號)之胺基酸至抗體輕鏈不變區112號(EU編號)(Kabat編號112號)之胺基酸之間。

【0107】 一實施態樣中，切斷位點/蛋白酶切斷序列位在抗體VL與抗體不變區之交界附近。抗體VL與抗體輕鏈不變區之交界附近，可指從抗體VL之96號(Kabat編號)之胺基酸至抗體輕鏈不變區130號(EU編號)(Kabat編號130號)之胺基酸之間，較佳為可指從抗體VL之104號(Kabat編號)之胺基酸至抗體輕鏈不變區113號(EU編號)(Kabat編號113號)之胺基酸之間，或從抗體VL之105號(Kabat編號)之胺基酸至抗體輕鏈不變區112號(EU編號)(Kabat編號112號)之胺基酸之間。抗體VL與抗體重鏈不變區連結時，抗體VL與抗體重鏈不變區之交界附近，可指抗體VL之96號(Kabat編號)之胺基酸至抗體重鏈不變區140號(EU編號)之胺基酸之間，較佳為可指抗體VL之104號(Kabat編號)之胺基酸至抗體重鏈不變區122號(EU編號)之胺基酸之間，或抗體VL之105號(Kabat編號)之胺基酸至抗體重鏈不變區122號(EU編號)之胺基酸之間。

【0108】 切斷位點/蛋白酶切斷序列，在配體分子中可以設置多數個，例如可在抗體不變區內、抗體VH內、抗體VL內、抗體VH與抗體不變區之交界附近、抗體VL與抗體不變區之交界附近中選出的多數處設置。又，若為接觸本發明之該技術領域中有通常知識者，則可替換抗體VH與抗體VL等、變更含有抗體VH與抗體VL與抗體不變區之分子之形，該分子形也不脫離本發明之範圍。

【0109】 本說明書中，用語「配體」係有生物活性之分子。有生物活性之分子通常會和細胞表面之受體交互作用，藉此調節生物學性的刺激、抑制、或其他樣式而作用，據認為它們通常涉及保有前述受體之細胞內之信號傳遞路徑。

【0110】 本說明書中，配體包括藉由與生物體分子交互作用而發揮生物活性之所望分子。例如配體不僅指與受體交互作用之分子，藉由與該分子交互作

用而發揮生物活性之分子亦為配體，例如與該分子交互作用之受體、其結合斷片等也包括在配體。例如:已知作為受體之蛋白質之配體結合部位、含有該受體與其他分子交互作用之部位之蛋白質，包括在本發明之配體。具體而言，可溶性受體、受體之可溶性斷片、膜貫通型受體之細胞外分域、及含有它們的多胜肽等，包括在本發明之配體。

【0111】 本發明之配體，通常藉由結合於一或多數個結合伙伴而發揮所望的生物活性。配體之結合伙伴，可以為細胞外、細胞內、或膜貫通蛋白質。一個實施形態中，配體之其結合伙伴，為細胞外蛋白質，例如可溶性受體。於其他實施形態中，配體之結合伙伴為膜結合型受體。

本發明之配體能夠以10μM、1μM、100nM、50nM、10nM、5nM、1nM、500pM、400pM、350pM、300pM、250pM、200pM、150pM、100pM、50pM、25pM、10pM、5pM、1pM、0.5pM、或0.1pM以下之解離常數(KD)專一性的結合於其結合伙伴。

【0112】 作為有生物活性之分子，例如但不限於細胞介素、趨化介素、多胜肽激素、成長因子、細胞凋亡誘導因子、PAMPs、DAMPs、核酸、或它們的斷片。詳細的實施形態中，可使用介白素、干擾素、造血因子、TNF超級家族、趨化介素、細胞增殖因子、TGF-β家族、myokine、adipokine、或神經營養因子作為配體。更詳細的實施形態中，可使用CXCL10、IL-2、IL-7、IL-12、IL-15、IL-18、IL-21、IFN-α、IFN-β、IFN-g、MIG、I-TAC、RANTES、MIP-1a、或MIP-1b作為配體。

【0113】 趨化介素係7~16kDa之間之均質的血清蛋白質的家族，特徵為誘導白血球之游走的能力。大部分的趨化介素有4個特徵的半胱胺酸(Cys)，由最初2個半胱胺酸所示之功能域而分類在CXC、或alpha、CC或beta、C或gamma及CX3C或delta之趨化介素類別。2個雙硫鍵，係形成在第1與第3半胱胺酸之間、及第2

與第4半胱胺酸之間。一般而言，需要雙硫交聯，Clark-Lewis與共同研究者們報告，至少針對CXCL10，雙硫鍵對於趨化介素活性係有決定性(Clark-Lewis et al., J. Biol. Chem. 269:16075-16081, 1994)。對於有4個半胱胺酸之唯一例外，係lymphotactin，僅有2個半胱胺酸殘基。因此lymphotactin，利用僅1個的雙硫鍵而保持了有功能的結構。

再者，CXC或alpha之次家族，因為存在較第1半胱胺酸先行之ELR功能域(Glu-Leu-Arg)而分類為2個群：ELR-CXC趨化介素及非ELR-CXC趨化介素(例如Clark-Lewis, 上述，及Belperio et al., "CXC Chemokines in Angiogenesis(脈管形成之CXC趨化介素)," J. Leukoc. Biol. 68:1-8, 2000)。

【0114】 干擾素誘導性之蛋白質-10(IP-10或CXCL10)，係由干擾素-γ及TNF-α誘導，由角化細胞、內皮細胞、纖維母細胞及單核球產生。IP-10，據認為擔當朝向組織發炎部位之活化T細胞之增援的作用(Dufour, et al., "IFN-gamma-inducible protein 10 (IP-10; CXCL10)-deficient mice reveal a role for IP-10 in effector T cell generation and trafficking(可誘導IFNγ之蛋白質-10(IP-10：CXCL10)缺損小鼠，解明在效應子T細胞之生成及輸送時IP-10之作用)," J Immunol., 168:3195-204, 2002)。再者，IP-10可能負責過敏反應。又，也可能負責在發炎性脫髓神經障礙之發生(Kieseier, et al., "Chemokines and chemokine receptors in inflammatory demyelinating neuropathies: a central role for IP-10(發炎性脫髓神經障礙之趨化介素及趨化介素受體：IP-10之中心作用)," Brain 125:823-34, 2002)。

【0115】 研究顯示IP-10對於接續移植之幹細胞之植入(Nagasawa, T., Int. J. Hematol. 72:408-11, 2000)、幹細胞之增援(Gazitt, Y., J. Hematother Stem Cell Res 10:229-36, 2001; Hattori et al., Blood 97:3354-59, 2001)及抗腫瘤免疫之亢進(Nomura et al., Int. J. Cancer 91:597-606, 2001; Mach and Dranoff, Curr. Opin.

Immunol. 12:571-75, 2000)可能有用。例如在該技術領域中有通常知識者已知之報告之中，有人討論趨化介素之生物活性(Bruce, L. et al., "Radiolabeled Chemokine binding assays(放射性標識趨化介素結合分析)," Methods in Molecular Biology (2000) vol. 138, pp129-134, Raphaele, B. et al. "Calcium Mobilization," Methods in Molecular Biology (2000) vol. 138, pp143-148, Paul D. Ponath et al., "Transwell Chemotaxis," Methods in Molecular Biology (2000) vol. 138, pp113-120 Humana Press. Totowa, New Jersey)。

【0116】 CXCL10之生物活性例如對於CXCL10受體(CXCR3)之結合、CXCL10誘導性鈣流、CXCL10誘導性細胞趨化性、CXCL10對於醣胺聚糖之結合及CXCL10寡聚物化。

測CXCL10之生理活性之方法可列舉測定CXCL10之細胞游走活性之方法、使用CXCR3安定表現細胞株之Reporter assay(參照PLoS One. 2010 Sep 13;5(9):e12700.)、利用在GPCR信號傳遞初期誘導之B-Arrestin recruitment之PathHunter™ β-Arrestin recruitment assay等。

【0117】 介白素12(IL-12)，係由以雙硫醚鍵結的30與40kD之糖苷化多胜肽鏈構成的雜二量物的細胞介素。細胞介素，由包括樹狀細胞、單核球、巨噬體、B細胞、蘭氏細胞及角化細胞及天然殺手(NK)細胞之抗原提示細胞合成並分泌。IL-12中介各種生物學的處理，並且涉及NK細胞刺激因子(NKSF)、T細胞刺激因子、細胞障礙T淋巴球成熟因子及經EBV轉形的B細胞系因子。

【0118】 介白素12藉由和在細胞(例如:T細胞、NK細胞)之細胞質膜表現之IL-12受體結合而可改變生物學的處理(例如:開始、阻止)。例如: IL-12對於IL-12受體之結合，會刺激前活化之T細胞及NK細胞之增殖，並增進細胞障礙性之T細胞(CTL)、NK細胞及LAK(淋巴因子活化殺手)細胞之細胞溶解活性，誘導T細胞及NK細胞產生γ干擾素(IFNγ)，並進而誘導初始Th0細胞(naive Th0 cell)分化為產

生IFNγ及IL-2之Th1細胞。尤其IL-12對於設定細胞溶解細胞(例如NK、CTL)之生成及細胞性免疫應答(例如:Th1細胞媒介之免疫應答)係絕對必要。總之，IL-12在預防免疫(例如:感染症之根絕)及病理學的免疫應答(例如:自體免疫)兩者的生成及調節係絕對重要。

【0119】 作為測定IL12之生理活性之方法，可列舉IL12之細胞增殖活性之測定、STAT4 報告基因分析、測定利用IL12所為之細胞活化(細胞表面標記表現、細胞介素產生等)、利用IL12所為之細胞分化之促進等之方法。

【0120】 蛋白質之Programmed Death 1(PD-1)，係CD28家族受體之抑制成員，CD28家族尚包括CD28、CTLA-4、ICOS及BTLA。PD-1會在活化B細胞、T細胞及骨髓細胞上表現(Okazaki等人(2002)Curr.Opin.Immunol. 14：391779-82、Bennett等人(2003)J Immunol 170：711-8)。該家族之最初之成員CD28及ICOS，係因為對於單株抗體添加後之T細胞增殖上昇帶來的功能的影響發現(Hutloff等人(1999)Nature 397：263-266、Hansen等人(1980)Immunogenics 10：247-260)。PD-1，係利用篩選細胞凋亡細胞中之不同表現而發現到(Ishida等人(1992)EMBO J. 11：3887-95)。該家族之其他成員CTLA-4與BTLA，各利用篩選細胞傷害性T淋巴球與TH1細胞中之不同表現而發現到。CD28、ICOS及CTLA-4皆有不成對的半胱胺酸殘基，它們可以同聚物化。對照而言，據認為PD-1係以單體形式存在，不具有其他CD28家族成員之特徵之不成對的半胱胺酸。

【0121】 PD-1基因，係為Ig基因超級家族之一部份的55kDa之I型膜貫通蛋白質。PD-1，包括膜近位免疫受體酪胺酸抑制功能域(ITIM)及膜遠位之酪胺酸鹼開關功能域(ITSM)。PD-1與CTLA-4在結構上類似，但是缺少對於B7-1及B7-2結合為重要的MYPPPY功能域(序列編號：537)。已鑑節出針對PD-1之2個配體PD-L1及PD-L2，若結合於PD-1則會負控制T細胞活化 (Freeman等人(2000)J Exp Med 192：1027-34、Latchman等人(2001)Nat Immunol 2：261-8、Carter等人

(2002)Eur J Immunol 32：634-43)。PD-L1及PD-L2兩者，皆係會結合於PD-1，且不結合於其他CD28家族成員之B7同系物。PD-1之一個配體PD-L1，於各種人癌當中豐富地存在(Dong等人(2002)Nat.Med. 8：787-9)。PD-1與PD-L1交互作用之結果，會發生腫瘤浸潤性淋巴球之減少、T細胞受體媒介性增殖之降低、及利用癌性細胞所為之免疫回避(Dong等人(2003)J.Mol.Med. 81：281-7、Blank等人(2005)Cancer Immunol.Immunother. 54：307-314、Konishi等人(2004)Clin.Cancer Res. 10：5094-100)。免疫抑制能夠利用抑制PD-L1與PD-1之局部交互作用而回復，當同樣地抑制PD-L2與PD-2之交互作用時，其效果係加成的(Iwai等人(2002)Proc.Nat' l.Acad.Sci. USA 99：12293-7、Brown等人(2003)J.Immunol. 170：1257-66)。

【0122】 PD-1係在活化B細胞、T細胞及骨髓細胞上表現之CD28家族之抑制成員。PD-1缺損動物，會發生自體免疫性心肌症及伴隨關節炎及腎炎之類紅斑狼瘡症候群之各種自體免疫性表現型病症(Nishimura等人(1999)Immunity 11：141-51、Nishimura等人(2001)Science 291：319-22)。再者，已知PD-1對於自體免疫性腦脊髓炎、全身性紅斑性狼瘡、移植片對寄主病(GVHD)、I型糖尿病及類風濕性關節炎發揮重要的作用(Salama等人(2003)J Exp Med 198：71-78、Prokunia及Alarcon-Riquelme(2004)Hum Mol Genet 13：R143、Nielsen等人(2004)Lupus 13：510)。已知小鼠B細胞腫瘤株中，PD-1之ITSM在BCR媒介Ca^{2+}之流向及下游效應子分子之酪胺酸磷酸化抑制時為必要(Okazaki等(2001)PNAS 98：13866-71)。

【0123】 本發明之一些實施態樣中，配體為細胞介素。

細胞介素係涉及免疫調節性及發炎性之過程之分泌型細胞信號傳遞蛋白質之家族，其由神經系之神經膠細胞及免疫系之多數細胞分泌。細胞介素可分類為蛋白質、胜肽或糖蛋白質，包括大而多樣的調節因子家族。細胞介素會結合於細胞表面受體而誘發細胞內信號傳遞，藉此調節酵素活性、一些基因及其轉

錄因子之上方調控或下方調控、或回饋的妨礙等。

一些實施態樣中，本發明之細胞介素包括介白素(IL)及干擾素(IFN)等免疫調節因子。適合的細胞介素可包括下列類型的1或多數來源的蛋白質：4個α-螺旋束家族(其包括IL-2次家族、IFN次家族及IL-10次家族); IL-1家族(其包括IL-1及IL-8)、以及IL-17家族。細胞介素也可包括分類為增強細胞免疫反應之1型細胞介素(例如:IFN-γ、TGF-β等)、或對於抗體反應有利地作用的2型細胞介素(例如:IL-4、IL-10、IL-13等)者。

【0124】 本發明之一些實施態樣中，配體為趨化介素。趨化介素一般作為使免疫效應子細胞增援到趨化介素表現部位之化學誘引物質。其據認為為了使其他免疫系成分增援到治療部位，和特定趨化介素基因例如細胞介素基因一起表現為有益。如此的趨化介素包括CXCL10、RANTES、MCAF、MIP1-α、MIP1-β。該技術領域中有通常知識者已知某種細胞介素也有化學誘引作用，據認為可將它們以趨化介素的用語分類。

【0125】 又，本發明之一些實施態樣中，配體可以使用細胞介素、趨化介素等改變體(例：Annu Rev Immunol. 2015;33:139-67.)、包括它們的融合蛋白質(例：Stem Cells Transl Med. 2015 Jan; 4(1): 66-73.)。

【0126】 本發明之一些實施態樣中，配體係選自CXCL10、PD1、IL12、IL6R。前述CXCL10、PD1、IL12、IL6R可以和天然存在的CXCL10、PD1、IL12、IL6R有相同序列，也可為和天然存在之CXCL10、PD1、IL12、IL6R有不同序列但是保持具對應之天然配體之生理活性的改變體。為了要取得配體之改變體，可以因應各式各樣的目的加入人為的配體序列，較佳為藉由加入不受蛋白酶切斷(蛋白酶抵抗性之)改變以取得配體之改變體。

【0127】 本發明之一些實施態樣中，配體藉由與未切斷之配體結合分子結合而抑制其生物活性。配體之生物活性受抑制的實施態樣不限定，其之例子例

如，未切斷之配體結合分子與配體之結合會實質上或顯著地妨礙或競爭配體與其結合伙伴之結合的實施態樣。使用有配體中和活性之抗體或其斷片作為配體結合分子時，與配體結合之配體結合分子藉由發揮其中和活性，可以抑制配體之生物活性。

【0128】 本發明之一實施態樣中，未切斷的配體結合分子宜能藉由和配體結合以將配體之生物活性充分中和較佳。亦即，與未切斷的配體結合分子結合之配體之生物活性宜比起未和未切斷的配體結合分子結合之配體之生物活性低為較佳。並不限定於此限定，但例如與未切斷的配體結合分子結合之配體之生物活性，相較於未與未切斷的配體結合分子結合之配體之生物活性，可為90%以下，較佳為80%以下、70%以下、60%以下、50%以下、40%以下、30%以下，尤佳為20%以下、10%以下、9%以下、8%以下、7%以下、6%以下、5%以下、4%以下、3%以下、2%以下、或1%以下。藉由將配體之生物活性予以充分中和，當投予配體結合分子時，可以期待配體防止在到達標靶組織前發揮生物活性。

【0129】 本發明之一實施態樣中，被切斷之配體結合分子對於配體之結合活性，宜比起針對配體之生物體內之天然之結合伙伴(例如針對配體之天然受體)對於配體之結合活性為低較佳。並不限定於此，但例如被切斷之配體結合分子與配體之結合活性，相較於在生物體內之天然結合伙伴與配體之結合量(每單位結合伙伴)，顯示90%以下，較佳為80%以下、70%以下、60%以下、50%以下、40%以下、30%以下，尤佳為20%以下、10%以下、9%以下、8%以下、7%以下、6%以下、5%以下、4%以下、3%以下、2%以下、或1%以下之結合量。結合活性的指標可使用適當理想的指標，例如可使用解離常數(KD)。使用解離常數(KD)作為結合活性之評價指標時，被切斷的配體結合分子對於配體之解離常數(KD)，相較於生物體內的天然之結合伙伴對於配體之解離常數(KD)為大的話，則被切斷之配體結合分子對於配體之結合活性相較於生物體內之天然結合伙伴

顯示會較弱。切斷之配體結合分子對於配體之解離常數(KD)，相較於在生物體內之天然結合伙伴對於配體之解離常數(KD)，例如1.1倍以上，較佳為1.5倍以上、2倍以上、5倍以上、10倍以上，尤佳為100倍以上。藉由切斷後之配體結合分子對於配體僅保持低結合活性、或對於配體幾乎不具結合活性，會確保配體結合分子被切斷後使配體游離，且可期待與其他配體分子再度結合。

【0130】 配體結合分子被切斷後，希望受抑制之配體之生物活性會回復。希望藉由被切斷之配體結合分子對於配體之結合減弱，配體結合分子之配體生物活性抑制功能也減弱。該技術領域中有通常知識者可利用既知之方法，例如檢測配體與其結合伙伴之結合之方法來確認配體之生物活性。

【0131】 本發明之一些實施態樣中，未切斷狀態之配體結合分子會藉由抗原抗體結合而和配體形成複合體。更具體的實施態樣中，配體結合分子與配體之複合體，可利用配體結合分子與配體之非共價鍵，例如抗原抗體結合形成。

【0132】 本發明之一些實施態樣中，未切斷狀態之配體結合分子與配體融合且形成融合蛋白質後，該融合蛋白質內之配體結合分子部分與配體部分會進一步利用抗原抗體結合而交互作用。配體結合分子與配體可介隔連結子或不介隔連結子而融合。融合蛋白質中之配體結合分子與配體介隔或不介隔連結子而融合的情形下，配體結合分子部分與配體部分之間之非共價鍵仍然存在。換言之，在配體結合分子與配體融合之實施態樣中，配體結合分子部分與配體部分之間之非共價鍵，類似於配體結合分子與配體未融合的實施態樣。藉由配體結合分子被切斷，其非共價鍵減弱。亦即，配體結合分子與配體之結合變得減弱。

本發明之一理想實施態樣中，配體結合分子與配體介隔連結子而融合。配體結合分子與配體融合時可使用之連結子，可以使用能利用基因工程導入的任意胜肽連結子、或合成化合物連結子(參照例如:Protein Engineering, 9 (3), 299-305, 1996)揭示之連結子等，但在本實施態樣宜為胜肽連結子較佳。胜肽連

結子之長度不特別限定，可由該技術領域中有通常知識者因應目的適當選擇。舉例但不限於此，例如，胜肽連結子的情形可列舉：

Ser

Gly・Ser(GS)

Ser・Gly(SG)

Gly・Gly・Ser(GGS)

Gly・Ser・Gly(GSG)

Ser・Gly・Gly(SGG)

Gly・Ser・Ser(GSS)

Ser・Ser・Gly(SSG)

Ser・Gly・Ser(SGS)

Gly・Gly・Gly・Ser(GGGS、序列編號：36)

Gly・Gly・Ser・Gly(GGSG、序列編號：37)

Gly・Ser・Gly・Gly(GSGG、序列編號：38)

Ser・Gly・Gly・Gly(SGGG、序列編號：39)

Gly・Ser・Ser・Gly(GSSG、序列編號：40)

Gly・Gly・Gly・Gly・Ser(GGGGS、序列編號：41)

Gly・Gly・Gly・Ser・Gly(GGGSG、序列編號：42)

Gly・Gly・Ser・Gly・Gly(GGSGG、序列編號：43)

Gly・Ser・Gly・Gly・Gly(GSGGG、序列編號：44)

Gly・Ser・Gly・Gly・Ser(GSGGS、序列編號：45)

Ser・Gly・Gly・Gly・Gly(SGGGG、序列編號：46)

Gly・Ser・Ser・Gly・Gly(GSSGG、序列編號：47)

Gly・Ser・Gly・Ser・Gly(GSGSG、序列編號：48)

Ser・Gly・Gly・Ser・Gly(SGGSG、序列編號：49)

Gly・Ser・Ser・Ser・Gly(GSSSG、序列編號：50)

Gly・Gly・Gly・Gly・Gly・Ser(GGGGGS、序列編號：51)

Ser・Gly・Gly・Gly・Gly・Gly(SGGGGG、序列編號：52)

Gly・Gly・Gly・Gly・Gly・Gly・Ser(GGGGGGS、序列編號：53)

Ser・Gly・Gly・Gly・Gly・Gly・Gly(SGGGGGG、序列編號：54)

(Gly・Gly・Gly・Gly・Ser(GGGGS、序列編號：41))n

(Ser・Gly・Gly・Gly・Gly(SGGGG、序列編號：46))n

[n為1以上之整數]等。惟胜肽連結子之長度、序列可以由該技術領域中有通常知識者因應目的而適當選擇。

【0133】 合成化學物連結子(化學交聯劑)，為胜肽交聯通常使用之交聯劑，例如N-羥基琥珀醯亞胺(NHS)、辛二酸二琥珀醯亞胺酯(DSS)、辛二酸二(硫琥珀醯亞胺基)酯(BS 3)、二硫雙(琥珀醯亞胺基丙酸酯)(DSP)、二硫雙(硫琥珀醯亞胺基丙酸酯)(DTSSP)、乙二醇雙(琥珀醯亞胺基琥珀酸酯)(EGS)、乙二醇雙(硫琥珀醯亞胺基琥珀酸酯)(硫-EGS)、二琥珀醯亞胺基酒石酸鹽(DST)、二硫琥珀醯亞胺基 酒石酸鹽(硫-DST)、雙[2-(琥珀醯亞胺氧羰基氧)乙基]碸(BSOCOES)、雙[2-(硫琥珀醯亞胺氧羰基氧)乙基]碸(硫-BSOCOES) 等，該等交聯劑在市面上可購得。

【0134】 本發明也係關於包括本發明之配體結合分子及醫藥上可容許之擔體之醫藥組合物(藥劑)、包括本發明之配體結合分子、配體、及醫藥上可容許之擔體之醫藥組合物(藥劑)、包括本發明之配體結合分子與配體融合而得之融合蛋白質、及醫藥上可容許之擔體之醫藥組合物(藥劑)。

【0135】 本說明書使用之「治療」(及其在文法上之衍生語，例如「治療之」、「治療之事」等)，係指企圖改變受治療之個體之自然過程的臨床性介入，

在為了預防、在臨床的病態之過程之間都可實施。理想的治療效果不僅限於此，但包括防止病症發生或再發、症狀之減輕、減弱因病症所致任意之直接的或間接的病理的影響、防止轉移、減低病症進行速度、病症狀態之回復或緩和、及預後之寬解或改善。一些實施態樣中，本發明之配體結合分子可以控制配體之生物活性，用在延遲病症之發作、或減慢病症之進行。

【0136】 本發明中，醫藥組合物通常係指為了病症之治療或預防、或檢查・診斷的藥劑。

又，本發明中，「包括配體結合分子之醫藥組合物」的用語，也可代換為「包括將配體結合分子投予給治療對象之步驟的病症的治療方法」，也可代換為「為了製造治療病症之醫藥之配體結合分子之用途」。「包括配體結合分子之醫藥組合物」，也可代換為「為了治療病症之配體結合分子之用途」。

「包括配體結合分子與配體之醫藥組合物」之用語，也可以代換為「包括將配體結合分子與配體投予給治療對象之步驟之病症之治療方法」，也可以代換為「為了製造治療病症之醫藥之配體結合分子與配體之用途」。「包括配體結合分子與配體之醫藥組合物」之用語，也可以代換為「為了治療病症之配體結合分子與配體之用途」。

「包括融合蛋白質之醫藥組合物」之用語，也可以代換為「包括將融合蛋白質投予給治療對象之步驟之病症之治療方法」，也可以代換為「為了製造治療病症之醫藥之融合蛋白質之用途」。「包括融合蛋白質之醫藥組合物」之用語也可以代換為「為了治療病症之融合蛋白質之用途」。

【0137】 本發明之一些實施態樣中，可以將包括配體結合分子之組合物對於個體投予。已對於個體投予之配體結合分子會在個體內，例如:血中，組織中等，與個體內原本存在的配體結合，並以和配體結合的狀態進一步運送到生物體內。被運送到標靶組織的配體結合分子，於標靶組織被切斷，對於配體之結

合減弱，且可在標靶組織釋放已結合的配體。被釋放的配體會在標靶組織發揮生物活性，並治療起因於標靶組織之病症。在配體結合分子已和配體結合時，會抑制配體之生物活性，且配體結合分子於標靶組織專一性的被切斷的實施態樣，運送時不會使配體之生物活性發揮，而是在標靶組織切斷後方使配體之生物活性發揮，並可治療病症、抑制全身副作用。

【0138】 本發明之一些實施態樣中，可以將包括配體結合分子之組合物、及包括配體之組合物個別或同時地對於個體投予。又，也可將包括配體結合分子與配體之兩者的組合物對於個體投予。當將包括配體結合分子與配體之兩者之組合物對於個體投予時，該組合物中之配體結合分子與配體可形成複合體。當投予配體結合分子與配體之兩者給個體時，配體結合分子會與已投予給個體的配體結合，並且維持結合了配體的狀態運送到生物體內。被運送到標靶組織的配體結合分子，在標靶組織被切斷，對於配體之結合減弱，且可在標靶組織釋放已結合的配體。被釋放的配體會在標靶組織發揮生物活性，並治療起因於標靶組織之病症。在配體結合分子已和配體結合時，會抑制配體之生物活性，且配體結合分子於標靶組織專一性的被切斷的實施態樣，運送時不會使配體之生物活性發揮，而是在標靶組織切斷後方使配體之生物活性發揮，並可治療病症、抑制全身副作用。已投予給個體的配體結合分子，除了會和已投予給個體的配體結合以外，也可能和個體內原本存在的配體結合，可維持和個體內原本存在的配體或投予給個體的配體結合的狀態運送到生物體內。

【0139】 本發明之一些實施態樣中，可將配體結合分子與配體融合而得的融合蛋白質投予給個體。該一些實施態樣中，融合蛋白質中之配體結合分子與配體介隔或不介隔連結子而形成融合蛋白質，但配體結合分子部分與配體部分之間之非共價鍵仍然存在。當配體結合分子與配體融合而得的融合蛋白質投予給個體時，融合蛋白質會在生物體內被運送，於標靶組織中，融合蛋白質中之

配體結合分子部分被切斷，藉此，配體結合分子部分對於配體之非共價鍵減弱，配體及配體結合分子之一部分從融合蛋白質被釋放。被釋放的配體及配體結合分子之一部分會在標靶組織發揮配體之生物活性，可治療起因於標靶組織之病症。在配體結合分子已和配體結合時，會抑制配體之生物活性，且配體結合分子於標靶組織專一性的被切斷的實施態樣，運送時不會使融合蛋白質中之配體之生物活性發揮，而是在標靶組織切斷後方使配體之生物活性發揮，並可治療病症、抑制全身副作用。

【0140】 本發明之醫藥組成物，能以該技術領域之人士公知之方法製劑化。例如，能以與水或其他藥學上可容許之液體的無菌性溶液、或懸浮液劑之注射劑之形式以非經口的使用。例如:藥理學上可容許之擔體或介質，具體而言，可考慮適當組合滅菌水或生理食鹽水、植物油、乳化劑、懸浮劑、界面活性劑、安定劑、香味劑、賦形劑、運載劑、防腐劑、黏結劑等，以一般認可的製藥實務要求的單位用量形態混合而製劑化。該等製劑中的有效成分量，可設定為可獲得指示範圍之適當容量。

【0141】 用於注射之無菌組成物，可使用如注射用蒸餾水之運載劑而依通常之製劑實務配方。注射用之水溶液，例如生理食鹽水、葡萄糖或含其他輔助藥(例如D-山梨醇、D-甘露糖、D-甘露醇、氯化鈉)之等張液。也可併用適當的溶解輔助劑，例如醇(乙醇等)、多元醇(丙二醇、聚乙二醇等)、非離子性界面活性劑(聚山梨糖醇酸酯80(TM)、HCO-50等)。

【0142】 油性液，例如麻油、黃豆油，溶解輔助劑可併用苯甲酸苄酯及/或苯甲醇。又，也可摻合緩衝劑(例如:磷酸鹽緩衝液及乙酸鈉緩衝液)、止痛劑(例如，鹽酸普羅卡因)、安定劑(例如，苯甲醇及酚)、抗氧化劑。製備的注射液通常充填在適當的安瓿。

【0143】 本發明之醫藥組成物較佳為以非經口投予。例如可製成注射劑

型、經鼻投予劑型、經肺投予劑型、經皮投予型之組成物。例如可利用靜脈內注射、肌肉內注射、腹腔內注射、皮下注射等對於全身或局部投予。

【0144】 投予方法可視患者之年齡、症狀適當選擇。含配體結合分子之醫藥組成物之投予量，例如可設定為每次體重1 kg為0.0001 mg至1000 mg之範圍。或，可定為例如每位患者為0.001~100000 mg之投予量，但本發明不一定限於該等數值。投予量及投予方法，視患者之體重、年齡、症狀等而變動，但如為該技術區之人士，可考慮該等條件，設定適當的投予量及投予方法。

【0145】 本發明也係關於製造在被切斷之狀態對於配體之結合減弱之配體結合分子、或該配體結合分子與配體融合而得之融合蛋白質之方法。本發明之一實施態樣中，提供包括在可和配體結合之分子中導入蛋白酶切斷序列之步驟的配體結合分子或融合蛋白質之製造方法。

【0146】 作為在可和配體結合之分子中導入蛋白酶切斷序列之方法之例，可以列舉在可和配體結合之多胜肽之胺基酸序列中插入蛋白酶切斷序列之方法、將可和配體結合之多胜肽之胺基酸序列的一部分置換為蛋白酶切斷序列之方法等。

【0147】 作為取得可和配體結合之分子之方法，例如取得具有和配體結合之能力之配體結合區之方法。配體結合區，例如可使用公知之抗體之製作方法的方法獲得。

利用該製作方法獲得之抗體可直接用在配體結合區，也可僅用在獲得之抗體中的Fv區，當該Fv區能以單鏈(也稱為「sc」。)認識抗原時，亦可僅使用該單鏈。又，也可使用包括Fv區之Fab區。

【0148】 具體的抗體之製作方法為該技術領域中有通常知識者週知，例如單株抗體的情形，可利用融合瘤法(Kohler and Milstein, Nature 256:495 (1975))、重組方法(美國專利第4,816,567號)製造。又，可以從噬菌體抗體庫單離 (Clackson

et al., Nature 352:624-628 (1991) ; Marks et al., J.Mol.Biol. 222:581-597 (1991))。又，也可以從單一的B細胞選殖體單離 (N. Biotechnol. 28(5): 253-457 (2011))。

【0149】 人化抗體也可稱為再構成(reshaped)人抗體。具體而言，人以外之動物，例如小鼠抗體之CDR移植到人抗體而得的人化抗體等係公知。為了獲得人化抗體的一般的基因重組方法亦為已知。具體而言，用以將小鼠之抗體之CDR移植到人之FR的方法，例如Overlap Extension PCR為公知。

【0150】 藉由將編碼3個CDR與4個FR連結而得的抗體可變區的DNA與編碼人抗體不變區之DNA於讀框內融合的方式插入到表現載體中，可以製作出人化抗體表現用載體。將該重組載體導入到寄主並建立重組細胞後，培養該重組細胞，使編碼該人化抗體之DNA表現，可藉此於該培養細胞之培養物中產生該人化抗體 (參照歐洲專利申請案公開第239400號說明書、國際公開第1996/002576號)。

【0151】 也可因應需要，以構成人抗體之CDR會形成適當抗原結合部位的方式取代FR之胺基酸殘基。例如:可應用小鼠CDR移植到人FR所使用之PCR法，而對於FR導入胺基酸序列變異。

【0152】 可將具有人抗體基因之全部曲目的基因轉殖動物(參照國際公開第1993/012227號、國際公開第1992/003918號、國際公開第1994/002602號、國際公開第1994/025585號、國際公開第1996/034096號、國際公開第1996/033735號)作為免疫動物，以DNA免疫取得所望的人抗體。

【0153】 再者，使用人抗體庫，以淘選(panning)取得人抗體的技術亦為已知。例如:將人抗體之Fv區以單鏈抗體(亦稱為「scFv」。)的形式，依噬菌體提示法表現在噬菌體之表面。可以選擇表現與抗原結合之scFv的噬菌體。藉由解析選出的噬菌體的基因，可以定出編碼與抗原結合之人抗體之Fv區之DNA的序列。決定了與抗原結合之scFv之DNA序列後，使該Fv區序列與所望之人抗體C區之序

列於讀框內融合，之後插入到適当的表現載體，可以製作表現載體。藉由將該表現載體導入到上述列舉的理想表現細胞中，並使編碼該人抗體之基因表現，可取得該人抗體。該等方法已為公知(參照國際公開第1992/001047號、國際公開第1992/020791號、國際公開第1993/006213號、國際公開第1993/011236號、國際公開第1993/019172號、國際公開第1995/001438號、國際公開第1995/015388號)。

【0154】 於可結合於配體之分子導入了蛋白酶切斷序列的分子，成為本發明之配體結合分子。可以針對配體結合分子，確認是否任意地利用對應於該蛋白酶切斷序列之蛋白酶之處理會將配體結合分子切斷。例如:使對於可與配體結合之分子導入了蛋白酶切斷序列的分子與蛋白酶接觸，並以SDS-PAGE等電泳法確認蛋白酶處理後產物之分子量，可以藉此確認蛋白酶切斷序列是否被切斷。

【0155】 又，本發明也係關於編碼於被切斷之狀態對於配體之結合減弱之配體結合分子的聚核苷酸、或編碼該配體結合分子與配體融合而得之融合蛋白質的聚核苷酸。

【0156】 又，本發明之中聚核苷酸通常被載持(插入)於適當載體並導入寄主細胞。該載體只要可安定地保持插入之核酸即不特別限定，例如寄主使用大腸菌則選殖用載體較佳為pBluescript載體(Stratagene社製)等，可利用市售之各種載體。為了生產本發明之配體結合分子或融合蛋白質而使用載體之情形，尤以表現載體為有用的。表現載體只要是在試管內、大腸菌內、培養細胞內、生物個體內表現配體結合分子之載體即不特別限制，例如如於試管內表現，較佳為pBEST載體(Promega社製)、於大腸菌則較佳為pET載體(Invitrogen社製)、於培養細胞則較佳為pME18S-FL3載體(GenBank Accession No. AB009864)、於生物個體則較佳為pME18S載體(Mol Cell Biol. 8:466-472(1988))等。本發明之DNA插入載體可依常法，例如利用使用限制酶部位之接合酶反應來進行(Current protocols in Molecular Biology edit. Ausubel et al. (1987) Publish. John Wiley & Sons.Section

11.4-11.11)。

【0157】 上述寄主細胞不特別限定，可視目的使用各種寄主細胞。用於表現配體結合分子或融合蛋白質之細胞，例如:細菌細胞(例：鏈球菌、葡萄球菌、大腸菌、鏈黴菌、枯草菌)、真菌細胞(例：酵母、麴菌)、昆蟲細胞(例：果蠅S2、斜紋夜蛾(Spodoptera)SF9)、動物細胞(例：CHO、COS、HeLa、C127、3T3、BHK、HEK293、Bowes黑色瘤(Melanoma)細胞)及植物細胞。載體對寄主細胞之導入，例如可利用磷酸鈣沉澱法、電脈衝穿孔法(Current protocols in Molecular Biology edit. Ausubel et al. (1987) Publish. John Wiley & Sons.Section 9.1-9.9)、脂質體(Lipofectamine)法(GIBCO-BRL社製)、微注射法等公知之方法進行。

【0158】 為了使寄主細胞之中表現之配體結合分子或融合蛋白質分泌至微胞體之內腔、細胞周邊腔或細胞外之環境，可將適當之分泌信號嵌入目的配體結合分子或融合蛋白質。該等信號對於目的配體結合分子或融合蛋白質可為內因性也可為異種信號。

【0159】 上述製造方法之中，配體結合分子或融合蛋白質之回收當本發明之配體結合分子或融合蛋白質分泌至培養基之情形，將培養基回收。當本發明之配體結合分子或融合蛋白質產生於細胞內時，先將該細胞溶解之後將配體結合分子或融合蛋白質回收。

【0160】 自重組細胞培養物將本發明之配體結合分子或融合蛋白質回收並精製時，可利用包含硫酸銨或乙醇沉澱、酸萃取、陰離子或陽離子交換層析、磷酸纖維素層析、疏水性交互作用層析、親和層析、羥基磷灰石層析及凝集素(lectin)層析之公知方法。

【0161】 本說明書記載之一或多數實施態樣予以任意組合而得者，只要基於該技術領域中有通常知識者之技術常識在技術方面不矛盾，則該技術領域中有通常知識者當然可理解為包括在本發明中。又，本發明除了本說明書記載之

一或多數實施態樣予以任意組合而得者以外的發明，只要基於該技術領域中有通常知識者之技術常識在技術上不矛盾，也應視為本說明書記載的發明。

【實施例】

【0162】 以下為本發明之方法及組合物之實施例。當可理解依上述一般的記載，有各種其他態樣可以實施。

【0163】 實施例1 已報導之免疫細胞介素及蛋白酶活化細胞介素之課題

以在癌組織表現之抗原作為標靶的免疫細胞介素，一般係藉由在標靶的IgG、scFv的末端融合目的的細胞介素而製作(Expert Opin Investig Drugs. 2009 Jul;18(7):991-1000.、Curr Opin Immunol. 2016 Jun;40:96-102.)。IL2、IL12、TNF為主的細胞介素因為毒性強，為了使該等細胞介素在癌局部作用，利用抗體遞送到癌局部，期待可減輕副作用並且加強效果(非專利文獻4、5、6)，但有它們皆在全身投予時於臨床未顯示充分的效果、治療窗(therapeutic window)窄、毒性強而無法全身投予等課題。其重大原因可列舉因為即使是免疫細胞介素，全身投予的細胞介素係暴露於全身，所以於全身作用並可能發揮毒性、或為了避免毒性而僅能以極低用量投予。又，與癌抗原結合之免疫細胞介素，在腫瘤中內化到癌細胞而消失掉，因此視情形難以將細胞介素暴露在腫瘤局部。也已報導於與癌抗原結合之抗體融合了IL2之免疫細胞介素和於不與癌抗原結合之抗體融合了IL2之免疫細胞介素，抗腫瘤效果並無不同(非專利文獻7)。

【0164】 作為使係免疫細胞介素之重大課題的全身性作用減低的方法而言，已報導將細胞介素與細胞介素受體之間利用於癌為高表現之蛋白酶切斷的連結子予以結合的分子。細胞介素因為以連結子結合的細胞介素受體而受抑制，但是連結子若被蛋白酶切斷，則細胞介素受體游離，細胞介素成為活性體。舉例而言，有人報告TNFalpha與TNFR利用以uPA切斷之連結子結合之分子(非專利文獻8)、IL2與IL2R利用以MMP2切斷之連結子結合之分子(非專利文獻9)等。

但是該等分子即使在連結子之切斷前，細胞介素仍有生物活性，經由連結子之切斷，活性僅提高約10倍左右。

就其原因而言，舉出下列兩點：細胞介素與細胞介素受體之親和性不強，所以即使蛋白酶切斷前，細胞介素仍有某程度之活性、或即使利用蛋白酶將連結子切斷後，細胞介素受體仍可結合於細胞介素，所以會抑制細胞介素之生物活性。

【0165】 已報導將IL2R替換成抗IL2 scFv，介隔利用以MMP-2切斷之連結子而與IL2結合而得的分子(非專利文獻9)。此IL2與抗IL2 scFv介隔蛋白酶切斷連結子結合而得的分子，亦如同細胞介素與細胞介素受體結合而得的分子，若考慮連結子切斷時使IL2游離的情事，當然會使用IL2親和性不強的抗IL2 scFv。

又，該等報告的蛋白酶活化細胞介素，不同於上述IgG-IL2融合物(fusion)，因不具Fc區，預測半減期為短，難維持高暴露。藉由蛋白酶切斷活化前後之細胞介素之藥物動態無重大差別(半減期皆短)，難以加寬治療窗(therapeutic window)。

【0166】 實施例2 趨化介素在癌免疫療法之應用之課題

趨化介素(Nature Immunology 9, 949 - 952 (2008))，係經由G蛋白質共軛受體而表現其作用的鹼性蛋白質，為細胞介素之一群。作用於表現受體之特定白血球，並有使白血球游走於此物質之濃度梯度的方向的活性(趨化性) (Nat Cell Biol. 2016 Jan;18(1):43-53.)。趨化介素已知會在發炎部大量產生，使白血球從血管內游走到發炎組織內。

藉由控制趨化介素，能夠控制白血球之游走，所以據認為可以活用在癌免疫療法。若能夠使T細胞、抗原提示細胞、M1巨噬體等游走在固體癌的局部，據認為可引起抗腫瘤效果。細胞介素利用全身投予亦能發揮作用，但是趨化介素會因濃度梯度而使細胞游走到濃度較高的組織，即使將趨化介素全身投予也

無法獲得期待的效果。所以，利用趨化介素之全身投予所為的癌免疫療法(趨化介素療法)據認為並不實際。

【0167】 實施例3 能夠使導入了蛋白酶切斷序列之標靶組織專一性的配體釋放的配體結合分子的概念

如實施例1、2所示，已有人報告之細胞介素・趨化介素療法存在下列課題。

1.免疫細胞介素，即使利用抗體將細胞介素標靶到固體癌，仍因細胞介素會在全身作用，故會產生副作用、或為了避免副作用而僅能以低用量投予，所以無法在腫瘤中高暴露。

2.細胞介素受體(或抗體)與細胞介素以能利用蛋白酶切斷之連結子連結之經蛋白酶活化之細胞介素，細胞介素活性之中和不足，即使在蛋白酶切斷前，細胞介素仍有某程度之活性。

3.經蛋白酶活化之細胞介素中，利用蛋白酶將連結子切斷後，細胞介素受體(或抗體)仍可結合於細胞介素，故會抑制細胞介素之生物活性。

4.經蛋白酶活化之細胞介素中，不活化性型細胞介素之半減期短，血中滯留時間短，因此必要的投予量多。

【0168】 為了解決此課題，據認為符合下列條件係重要。

1.在全身，細胞介素或趨化介素等配體會因為配體結合分子而充分受抑制(生物活性最小化)

2.由於蛋白酶所為之切斷，配體之生物活性會回復(成為活性型配體)

3.由於蛋白酶所為之切斷，配體結合分子喪失配體結合活性

4.相較於接受蛋白酶所為之切斷前已結合於配體結合分子之配體，接受蛋白酶所為之切斷而成為活性型的配體有較短的半減期

【0169】 符合上述條件之醫藥組合物，據認為是經由切斷位點被切斷而對於配體之結合減弱的分子。可藉由首先取得針對配體之結合分子，然後於結合

分子中插入切斷位點以製作配體結合分子。

【0170】 實施例4 導入了蛋白酶切斷序列之抗配體抗體之例

第1、2、3圖顯示使用抗體作為對於配體結合之分子之分子之例。該等例中，首先取得針對配體之中和抗體。然後，在抗配體中和抗體之可變區(VH或VL)與不變區(CH1或CL)之交界附近插入蛋白酶切斷序列。確認該抗配體抗體於蛋白酶切斷序列插入後仍保持著配體結合活性。於配體結合於抗配體中和抗體之狀態，經由利用蛋白酶切斷，確認配體解離。

確認已解離的配體會發揮生物活性。

第1圖中，配體之C末端與抗配體抗體之VH之N末端介隔連結子而結合，並在VH與CH1之交界附近插入了蛋白酶切斷序列。抗配體抗體對於配體之親和性若足夠強，則配體之生物活性會被充分抑制。此配體-抗配體抗體融合體即使全身投予，配體亦會被中和，故不發揮其生物活性，且配體-抗配體抗體融合體因為有Fc區，故具有長的半減期。經全身投予之配體-抗配體抗體融合體，若因為在腫瘤組織高表現之蛋白酶而切斷了VH與CH1之交界附近之蛋白酶切斷序列，則配體-連結子-抗配體抗體之VH分子會游離。VH或VL單獨無法結合於配體(為了結合於配體需要VH與VL兩者)，配體之中和會解除，於腫瘤組織能發揮生物學的作用。又，此釋放出的配體-連結子-抗配體抗體的VH分子不具Fc區，分子量小，所以具有非常短的半減期，會快速地從全身消失，能夠使由於配體所致之全身性副作用最小化。

第2圖中，配體與抗配體抗體不像第1圖般以連結子結合，而是在VH與CH1之交界附近插入了蛋白酶切斷序列的抗配體抗體與配體混合投予。若抗配體抗體對於配體之親和性充分強，抗配體抗體相對於配體濃度足夠，可將配體之生物活性充分地抑制。即使將此配體-抗配體抗體複合體全身投予，配體仍可被中和，故其生物活性不會發揮，且配體-抗配體抗體複合體因為有Fc區，具有長的

半減期。被全身投予的配體-抗配體抗體複合體，若由於在腫瘤組織高表現的蛋白酶而將VH與CH1之交界附近之蛋白酶切斷序列切斷，則抗配體抗體之VH分子會游離。VH或VL單獨無法結合於配體(為了結合於配體需要VH與VL兩者)，配體之中和被解除，可在腫瘤組織發揮生物學的作用。又，此釋出的配體分子沒有Fc區，分子量小，所以具有非常短的半減期，會快速地從全身消失，因此能使配體所致之全身性副作用最小化。

第3圖中，VH與CH1之交界附近插入了蛋白酶切斷序列而得的抗配體抗體被全身投予。被投予的抗體和體內原本存在的配體結合，之後則與第2圖之上述記載同樣。

如此方式，藉由使用在VH與CH1之交界附近插入了蛋白酶切斷序列的抗配體抗體，配體會在表現蛋白酶的組織中選擇性地釋出，並發揮其生物學的作用。配體若為細胞介素，則能使細胞介素在表現蛋白酶之組織中選擇性地作用。配體若為趨化介素，則趨化介素在表現蛋白酶之組織中以高濃度存在，於末梢血則趨化介素濃度降低，所以能使表現趨化介素受體之細胞向表現蛋白酶之組織游走。

【0171】　實施例5　CXCL10釋放抗體之製作與評價

5-1.對於抗CXCL10中和抗體導入蛋白酶切斷序列

CXCL10係對於效應子T細胞有游走作用的趨化介素之一。以該技術領域中有通常知識者公知之方法製備針對係人CXCL10 之中和抗體MabCXCL10(重鏈：EEIVH(序列編號：1)、輕鏈：EEIVL(序列編號：2))的表現載體，並使用FreeStyle 293(Life Technology)以該技術領域中有通常知識者公知之方法進行表現、精製。MabCXCL10中含有的CDR序列如下：H-CDR1(NNGMH、序列編號：380)、H-CDR2(VIWFDGMNKFYVDSVKG、序列編號：381)、H-CDR3(EGDGSGIYYYYGMDV、序列編號：382)、L-CDR1(RASQSVSSSYLA、

序列編號：383)、L-CDR2(GASSRAT、序列編號：384)、L-CDR3(QQYGSSPIFT、序列編號：385)。

使用Biacore評價MabCXCL10與人CXCL10(266-IP-010/CF , R&D Systems)的交互作用。具體而言，依照使用NHS・EDC之胺偶聯法在CM3感測晶片(BR100536, GE Healthcare)固定R PROTEIN A (SURE) (28-4018-60, GE Healthcare)，並使用20mM ACES, 0.05% Tween20, 200mM NaCl, pH 7.4作為電泳緩衝液，於捕捉了抗體的狀態，將1.563 nM的人CXCL10作為分析物使其流動，評價抗體對於抗原於37℃之結合。第4圖顯示取僅以電泳緩衝液作為分析物與對照組(blank)之差的經時的結合量的傳感圖。將分析物開始流過的時間作為橫軸的開始點。分析物開始流過的時間的回應為0時之各時間之回應(結合量)為縱軸。如第4圖之傳感圖所示，確認了MabCXCL10對於人CXCL10的結合。

進行於MabCXCL10之重鏈或輕鏈之可變區與不變區之交界附近插入蛋白酶切斷序列的探討。設計將據報告會被在癌專一性的表現的尿激酶（uPA）及Matriptase(MT-SP1)切斷的序列胜肽序列A(序列編號：3)插入到重鏈或輕鏈之可變區與不變區之交界附近的7處的第5圖所示的重鏈及輕鏈。也設計不會伴隨切斷序列插入發生糖鎖加成的改變體。依該技術領域中有通常知識者公知之方法製作編碼重鏈改變體EEIVHA(序列編號：4)、EEIVHB(序列編號：5)、EEIVHC(序列編號：6)、EEIVHD(序列編號：7)、EEIVHE(序列編號：8)、EEIVHF(序列編號：9)、EEIVHG(序列編號：10)、EEIVHBG(序列編號：11)、EEIVHCG(序列編號：12)、EEIVHDG(序列編號：13)、EEIVHEG(序列編號：14)、及輕鏈改變體EEIVLA(序列編號：15)、EEIVLB(序列編號：16)、EEIVLC(序列編號：17)、EEIVLD(序列編號：18)、EEIVLE(序列編號：19)、EEIVLF(序列編號：20)、EEIVLG(序列編號：21)、EEIVLEG(序列編號：22)的表現載體。

將該等重鏈改變體與天然型輕鏈組合、或將天然型重鏈與輕鏈改變體組

合，並在重鏈之可變區與不變區之交界附近插入了蛋白酶切斷序列之下列之IgG1抗體：EEIVHA/EEIVL(重鏈序列編號：4、輕鏈序列編號：2)、EEIVHB/EEIVL(重鏈序列編號：5、輕鏈序列編號：2)、EEIVHC/EEIVL(重鏈序列編號：6、輕鏈序列編號：2)、EEIVHD/EEIVL(重鏈序列編號：7、輕鏈序列編號:2)、EEIVHE/EEIVL(重鏈序列編號:8、輕鏈序列編號:2)、EEIVHF/EEIVL(重鏈序列編號：9、輕鏈序列編號：2)、EEIVHG/EEIVL(重鏈序列編號：10、輕鏈序列編號：2)、EEIVHBG/EEIVL(重鏈序列編號：11、輕鏈序列編號：2)、EEIVHCG/EEIVL(重鏈序列編號：12、輕鏈序列編號：2)、EEIVHDG/EEIVL(重鏈序列編號：13、輕鏈序列編號：2)、EEIVHEG/EEIVL(重鏈序列編號：14、輕鏈序列編號：2)、及在輕鏈之可變區與不變區之交界附近插入了蛋白酶切斷序列之下列之IgG1抗體：EEIVH/EEIVLA(重鏈序列編號：1、輕鏈序列編號：15)、EEIVH/EEIVLB(重鏈序列編號：1、輕鏈序列編號：16)、EEIVH/EEIVLC(重鏈序列編號：1、輕鏈序列編號：17)、EEIVH/EEIVLD(重鏈序列編號：1、輕鏈序列編號：18)、EEIVH/EEIVLE(重鏈序列編號：1、輕鏈序列編號：19)、EEIVH/EEIVLF(重鏈序列編號：1、輕鏈序列編號：20)、EEIVH/EEIVLG(重鏈序列編號：1、輕鏈序列編號：21)、EEIVH/EEIVLEG(重鏈序列編號：1、輕鏈序列編號：22)，依該技術領域中有通常知識者公知之方法利用使用了FreeStyle 293 (Life Technologies)之暫時性表現予以表現，並依使用了Protein A之該技術領域中有通常知識者公知之方法進行精製。

【0172】 5-2.導入了蛋白酶切斷序列之抗CXCL10中和抗體之結合活性之評價

將在5-1製備之抗體與人CXCL10(266-IP-010/CF , R&D Systems)之交互作用使用Biacore評價之結果示於第6圖。具體而言，依照使用了NHS・EDC之胺偶聯法於CM3感測晶片 (BR100536, GE Healthcare)固定R PROTEIN A (SURE)

(28-4018-60, GE Healthcare)，並使用20mM ACES, 0.05% Tween20, 150mM NaCl, pH 7.4作為電泳緩衝液，將抗體以捕捉的狀態流過3.125, 1.563, 0.781 nM 之人CXCL10作為分析物，評價抗體對於抗原於25℃之結合。第6圖顯示取僅以電泳緩衝液作為分析物與對照組(blank)之差的經時的結合量的傳感圖。將分析物開始流過的時間作為橫軸的開始點。分析物開始流過的時間的回應為0時之各時間之回應(結合量)為縱軸。如第6圖之傳感圖所示，任一抗體皆會對於人CXCL10結合。亦即，可不喪失對於抗原之結合活性，而在抗體可變區與不變區之交界附近插入蛋白酶切斷序列。

【0173】 5-3.導入了蛋白酶切斷序列之抗CXCL10中和抗體之利用蛋白酶所為之切斷之評價

檢驗於5-1製備之抗體是否會被蛋白酶切斷。使用重組人Matriptase/ST14 觸媒分域(MT-SP1) (R&D Systems, 3946-SE-010)作為蛋白酶，於蛋白酶 20nM、抗體 60或100μg/mL、PBS、37℃之條件下進行20小時反應後，利用還原SDS-PAGE評價利用蛋白酶所為之切斷，結果示於第7圖。其結果，EEIVHA/EEIVL、EEIVHE/EEIVL、EEIVHF/EEIVL、EEIVHG/EEIVL、EEIVHEG/EEIVL、EEIVHBG/EEIVL因為蛋白酶處理而在25kDa至50kDa之間生出了新的譜帶。再者，EEIVH/EEIVLEG、EEIVH/EEIVLF、EEIVH/EEIVLG因為蛋白酶處理而在25kDa以下生出譜帶。因此確認了EEIVHA/EEIVL、EEIVHE/EEIVL、EEIVHF/EEIVL、EEIVHG/EEIVL、EEIVHEG/EEIVL、EEIVHBG/EEIVL、EEIVH/EEIVLEG、EEIVH/EEIVLF、EEIVH/EEIVLG中，抗體被蛋白酶切斷。

【0174】 5-4.導入了蛋白酶切斷序列之抗CXCL10中和抗體之蛋白酶切斷序列附近導入可動連結子序列

探討在5-3未因重組人Matriptase/ST14(MT-SP1) 觸媒分域 (R&D Systems,

3946-SE-010)受切斷之EEIVHC/EEIVL之蛋白酶切斷序列附近插入包括由甘胺酸-絲胺酸聚合物構成之連結子之序列。設計第8圖所示之5種重鏈。依該技術領域中有通常知識者公知之方法製作編碼重鏈改變體EEIVHC002(序列編號：23)、EEIVHC003(序列編號：24)、EEIVHC004(序列編號：25)、EEIVHC005(序列編號：26)、EEIVHC006(序列編號：27)之表現載體。

將該等重鏈改變體與天然型輕鏈組合，並在重鏈之可變區與不變區之交界附近插入了蛋白酶切斷序列之下列IgG1抗體：EEIVHC002/EEIVL(重鏈序列編號：23、輕鏈序列編號：2)、EEIVHC003/EEIVL(重鏈序列編號：24、輕鏈序列編號：2)、EEIVHC004/EEIVL(重鏈序列編號：25、輕鏈序列編號：2)、EEIVHC005/EEIVL(重鏈序列編號：26、輕鏈序列編號：2)、EEIVHC006/EEIVL(重鏈序列編號：27、輕鏈序列編號：2)，依該技術領域中有通常知識者公知之方法利用使用了FreeStyle 293 (Life Technologies)之暫時性表現予以表現，並依使用了Protein A之該技術領域中有通常知識者公知之方法進行精製。

【0175】 5-5.導入了蛋白酶切斷序列與可動連結子序列之抗CXCL10中和抗體之結合活性之評價

使用Biacore評價於5-4製備之抗體與人CXCL10(266-IP-010/CF , R&D Systems)之交互作用，結果示於第9圖。具體而言，依使用了NHS・EDC之胺偶聯法在CM3感測晶片 (BR100536, GE Healthcare) 固定R PROTEIN A (SURE) (28-4018-60, GE Healthcare)，並使用20mM ACES, 0.05% Tween20, 300mM NaCl, pH 7.4作為電泳緩衝液，於捕捉了抗體的狀態，流過6.25, 3.125, 1.563, 0.781 nM之人CXCL10作為分析物，評價抗體對於抗原在25℃之結合。第9圖顯示取僅以電泳緩衝液作為分析物與對照組(blank)之差的經時的結合量的傳感圖。將分析物開始流過的時間作為橫軸的開始點。分析物開始流過的時間的回應為0時之各時間之回應(結合量)為縱軸。如第9圖之傳感圖所示，任一抗體皆對於人CXCL10結

合。亦即，可不失去對於抗原之結合活性而在抗體可變區與不變區之交界附近插入蛋白酶切斷序列與可動連結子序列。

【0176】 5-6.導入了蛋白酶切斷序列與可動連結子序列之抗CXCL10中和抗體之利用蛋白酶所為之切斷之評價

檢驗於5-5製備之抗體是否會被蛋白酶切斷。使用人尿激酶(uPA)(R&D Systems, 1310-SE-010)、重組人Matriptase/ST14 觸媒分域(MT-SP1) (R&D Systems, 3946-SE-010)作為蛋白酶，於蛋白酶12.5nM、抗體 133μg/mL、PBS、37℃之條件下進行2、20小時反應後，利用還原SDS-PAGE評價利用蛋白酶所為之切斷，結果示於第10圖。其結果，EEIVHC002/EEIVL、EEIVHC003/EEIVL、EEIVHC004/EEIVL、EEIVHC005/EEIVL、EEIVHEC006/EEIVL因為蛋白酶處理而在25kDa至50kDa之間生出新的譜帶。因此確認了EEIVHC002/EEIVL、EEIVHC003/EEIVL、EEIVHC004/EEIVL、EEIVHC005/EEIVL、EEIVHEC006/EEIVL中，抗體被蛋白酶切斷。

由該等結果顯示，即使是像EEIVHC/EEIVL般僅將蛋白酶切斷位點導入到可變區與不變區之交界附近的情形下不會被蛋白酶切斷的抗體，仍可藉由在切斷序列附近導入可動連結子序列而製出能被蛋白酶切斷的分子。因此，顯示可藉由將蛋白酶切斷序列與可動連結子任意組合以製作會被蛋白酶切斷的抗體。

【0177】 5-7.CXCL10-抗CXCL10中和抗體之利用蛋白酶切斷所為之配體之活化

然後使用Biacore評價接合於5-5製備之抗體的人CXCL10是否會因蛋白酶處理而游離。具體而言，使用5-5製備之抗體EEIVHC006a/EEIVL(重鏈序列編號：33、輕鏈序列編號：2)，分別準備有抗原/有蛋白酶之分析物、無抗原/有蛋白酶之分析物、有抗原/無蛋白酶之分析物。有抗原/有蛋白酶之分析物，係使用在抗體與人CXCL10結合後以20nM之重組人Matriptase/ST14 觸媒分域

(MT-SP1)(R&D Systems, 3946-SE-010)進行了20小時處置者。無抗原/有蛋白酶之分析物，係使用僅將抗體以20nM之重組人Matriptase/ST14 觸媒分域(MT-SP1)(R&D Systems, 3946-SE-010)進行了20小時處置者。有抗原/無蛋白酶之分析物，使用抗體與人CXCL10結合者。又，準備僅有CXCL10作為抗原之分析物，作為確認CXCL10之結合所為之回應之系統之對照組。將抗CXCL10抗體以該技術領域中有通常知識者公知之方法固定在CM5感測晶片 (BR100530, GE Healthcare)，使用20mM ACES, 0.05% Tween20, pH 7.4作為電泳緩衝液，分別流過有抗原/有蛋白酶之分析物、無抗原/有蛋白酶之分析物、有抗原/無蛋白酶之分析物、僅抗原之分析物的4種分析物，評價感測晶片上之抗CXCL10抗體與人CXCL10於25℃之結合。

又，使用與不具蛋白酶切斷序列之抗體MabCXCL10帶有同樣Fab區之MabCXCL10a(重鏈：EEIVHa(序列編號：65)、輕鏈：EEIVL(序列編號：2))，與抗體EEIVHC006a/EEIVL同樣準備有抗原/有蛋白酶之分析物、無抗原/有蛋白酶之分析物、有抗原/無蛋白酶之分析物。同樣地，依該技術領域中有通常知識者公知之方法在CM5感測晶片 (BR100530, GE Healthcare)固定抗CXCL10抗體，並使用20mM ACES, 0.05% Tween20, pH 7.4作為電泳緩衝液，分別流過有抗原/有蛋白酶之分析物、無抗原/有蛋白酶之分析物、有抗原/無蛋白酶之分析物、僅抗原之分析物(CXCL10)之4種分析物，評價感測晶片上之抗CXCL10抗體與人CXCL10於25℃之結合。

表示取和未固定抗CXCL10抗體之流通槽(flow cell)之差的經時的結合量的傳感圖，示於第11圖。將開始流過分析物之時間作為縱軸之開始點。縱軸表示分析物開始流過時之回應設為100時之各時間之回應。其結果，如第11圖(A)所示，未插入切斷序列之MabCXCL10a即使進行蛋白酶處理，CXCL10仍不游離，但如第11圖(B)所示，藉由EEIVHC006a/EEIVL以蛋白酶處理，確認CXCL10游離。

【0178】 5-8. 抗體可變區與不變區之交界附近之胺基酸序列的一部分取代為蛋白酶切斷序列與可動連結子之序列的一部分而得的抗CXCL10中和抗體之製作與利用蛋白酶所為之切斷之評價

探討將MabCXCL10之重鏈之可變區與不變區之交界附近之胺基酸序列的一部分取代為蛋白酶切斷序列與可動連結子之序列的一部分。設計據報告會被在癌專一性表現之尿激酶 (uPA) 及Matriptase(MT-SP1)切斷之序列即胜肽序列A(序列編號：3)取代為重鏈之一部分胺基酸而得的第12圖所示之重鏈。依該技術領域中有通常知識者公知之方法製作編碼重鏈改變體EESVHA009(序列編號：59)、EESVHA012(序列編號：60)之表現載體。

將該等重鏈改變體與天然型輕鏈組合，將下列IgG1抗體：EESVHA009/EEIVL(重鏈序列編號：59、輕鏈序列編號：2)、EESVHA012/EEIVL(重鏈序列編號：60、輕鏈序列編號：2)依該技術領域中有通常知識者公知之方法以使用FreeStyle 293 (Life Technologies)之暫時性表現予以表現，並依使用了Protein A之該技術領域中有通常知識者公知之方法進行精製。

檢查EESVHA009/EEIVL、EESVHA012/EEIVL是否會被蛋白酶切斷。使用人尿激酶(uPA)(R&D Systems, 1310-SE-010)、重組人Matriptase/ST14 觸媒分域 (MT-SP1) (R&D Systems, 3946-SE-010)作為蛋白酶，於蛋白酶12.5nM、抗體100μg/mL、PBS、37℃之條件下進行20小時反應後，利用還原SDS-PAGE評價利用蛋白酶所為之切斷，結果示於第13圖。其結果，EESVHA009/EEIVL、EESVHA012/EEIVL因為蛋白酶處理而在25kDa至50kDa之間生出新的譜帶。因此確認了EESVHA009/EEIVL、EESVHA012/EEIVL中，抗體會被蛋白酶切斷。

【0179】 實施例6 關於為了使因為蛋白酶切斷而失去抗原結合能力之切斷序列插入容許部位之考察

已報導關於在人IgG1抗體之重鏈216號天冬胺酸之正前插入了蛋白酶切斷

序列之抗體之製作及試管內(in vitro)之功能評價(國際公開WO2004/021861A2)。實驗數據未記載，但主張若將此抗體與抗原混合後以含有對應蛋白酶之培養基處置，則抗原會從抗原抗體複合體游離。

該報告中主張之插入了蛋白酶切斷序列之人IgG1抗體之重鏈第216號之胺基酸，在依Kabat, E. et al. Sequences of Proteins of Immunological Interest 5th edition記載之Kabat編號、EU編號、OU編號中之任一編號系統皆不是天冬胺酸。而若參照不同的文獻，人IgG1抗體之重鏈216號胺基酸據認為是於重鏈與輕鏈之間形成雙硫鍵之半胱胺酸之正後之天冬胺酸(Nature 344, 667 - 670 (12 April 1990), Kabat, E. et al. Sequences of Proteins of Immunological Interest 4th edition)。在此216號之天冬胺酸之正前插入蛋白酶切斷序列時，據認為會形成和從接受蛋白酶所為之切斷之抗體因木瓜蛋白酶而在抗體之鉸鏈區受切斷時同樣的Fab區。一般認為利用木瓜蛋白酶所為之抗體之鉸鏈區之切斷不易喪失抗原結合能力，所以據認為即使將此於216號之天冬胺酸之正前插入了蛋白酶切斷序列之抗體以對應的蛋白酶切斷，仍不會失去抗原結合能力。

也探討假設在Kabat, E. et al. Sequences of Proteins of Immunological Interest 5th edition記載之Kabat編號中之人IgG1抗體之重鏈第216號之胺基酸(Kabat編號)之正前插入了蛋白酶切斷序列的情形。此部位存在於比起於重鏈與輕鏈之間形成雙硫鍵之第220號半胱胺酸(Kabat編號)還更靠N末端側有數個胺基酸。所以，於此部位引起之蛋白酶所為之重鏈之切斷所帶來的影響，據推測和失去於重鏈與輕鏈之間形成之雙硫鍵時帶來的影響同樣。依過去的文獻，即使是無法形成重鏈與輕鏈之間之雙硫鍵的Fab區，也不易失去抗原結合 (MAbs. 2014 Jan-Feb;6(1):204-18.)。所以Kabat, E. et al. Sequences of Proteins of Immunological Interest 5th edition記載之Kabat編號之人IgG1抗體之重鏈第216號之胺基酸(Kabat編號)之正前插入了蛋白酶切斷序列的情形，據認為不會因蛋白酶切斷而失去抗

原結合能力。

【0180】 實施例7 導入了蛋白酶切斷序列之抗CXCL10中和抗體/CXCL10複合體之伴隨蛋白酶切斷之游走活性評價

評價將實施例5製作之導入了蛋白酶切斷序列之CXCL10中和抗體與CXCL10形成之複合體是否會因蛋白酶切斷而使CXCL10游離，且CXCL10發揮細胞游走活性。

CXCL10之細胞游走活性，係製作表現小鼠CXCR3(mCXCR3)之Ba/F3轉染細胞 (以下稱為BaF3/mCXCR3)，使用此細胞與HTS Transwell™-96 Permeable Support with 5.0μm Pore Polycarbonate Membrane (Cat. 3387、Corning)評價。準備CXCL10+ 蛋白酶、EEIVHC006a/EEIVL + CXCL10、EEIVHC006a/EEIVL+CXCL10+ 蛋白酶、EEIVHC006a/EEIVL+ 蛋白酶、MabCXCL10+CXCL10+蛋白酶之5種分析物。在PROTEOSAVE SS 1.5mL微型管(Cat. MS-4265M、住友電木)中裝入終濃度10 μg/mL之抗體(MabCXCL10或EEIVHC006a/EEIVL)、終濃度100 ng/mL 之hCXCL10 (Cat. 300-12、Peprotech)、或抗體與hCXCL10兩者，於常溫放置30分鐘，針對有蛋白酶之分析物，於前述反應後更添加mouse MT-SP1 (mMT-SP1 、Cat. 4735-SE-010、R&D Systems)使其終濃度成為12.5 nM。

將各分析物235 μL移到下腔體，於上腔體接種BaF3/mCXCR3細胞75 μL/孔，使成為2.0×10^5 細胞/孔，並反應6小時。反應於5%二氧化碳、37℃條件下進行。反應6小時後，將下腔體中之溶液100 μL移到螢光冷光96孔板(Cat. 3912、Corning)，加入CellTiter-Glo™ Luminescent Cell Viability Assay溶液(Cat. G7571、Promega) 100 μL。於室溫反應10分鐘後，以SpectraMax M3 多模式微板讀取儀(Molecular Devices)測定發光值，評價細胞向下腔體之游走度。其結果示於第14圖。

相較於CXCL10+蛋白酶之分析物，添加EEIVHC006a/EEIVL+CXCL10之分析物時，發光強度減少。發光強度係反應游走的細胞的量，所以可知EEIVHC006a/EEIVL與CXCL10形成複合體，且中和掉CXCL10的作用。另一方面，添加EEIVHC006a/EEIVL+CXCL10+蛋白酶之分析物時，相較於添加了EEIVHC006a/EEIVL+CXCL10之分析物時，發光強度回復，顯示與添加CXCL10+蛋白酶之分析物時同樣使細胞游走。添加了使用不具切斷序列之MabCXCL10抗體之MabCXCL10+CXCL10+蛋白酶之分析物時，未見發光強度之回復。由此結果，顯示EEIVHC006a/EEIVL伴隨利用蛋白酶所為之抗體切斷，CXCL10之中和能力降低。

【0181】 實施例8 導入了蛋白酶切斷序列之抗CXCL10中和抗體-CXCL10融合蛋白質之伴隨蛋白酶切斷之游走活性評價

8-1 抗CXCL10中和抗體-CXCL10融合蛋白質之製作及蛋白酶切斷評價

使用針對人CXCL10之中和抗體即MabCXCL10_G7(重鏈：G7H-G1T4(序列編號：368)、輕鏈：G7L-LT0(序列編號：369))之輕鏈，在該輕鏈之N末端介隔由甘胺酸-絲胺酸聚合物構成的連結子序列，連接變異成耐受蛋白酶之人CXCL10變異體hCXCL10R75A (序列編號：370)，而設計出配體融合輕鏈hCXCL10R75A.G4SGGGG.G7L-LT0(序列編號：371)。將配體融合輕鏈與MabCXCL10_G7重鏈之G7H-G1T4組合，將融合蛋白質：G7H-G1T4/hCXCL10R75A.G4SGGGG.G7L-LT0(重鏈序列編號：368、配體融合輕鏈序列編號：371)依照該技術領域中有通常知識者公知之方法利用使用了Expi293 (Life Technologies)之暫時性表現予以表現，並依使用了Protein A之該技術領域中有通常知識者公知之方法精製。MabCXCL10_G7之CDR序列如下：H-CDR1(SFSIT、序列編號：374)、H-CDR2(EITPMFGIANYAQKFQG、序列編號：375)、H-CDR3(DGRFDVSDLLTDKPKVTINYNGMDV、序列編號：376)、

L-CDR1(SGSSSNIGSNTVN、序列編號：377)、L-CDR2(NNDQRPS、序列編號：378)、L-CDR3(ASWDDSLNGRV、序列編號：379)。

檢查此融合蛋白質是否會被蛋白酶切斷。使用來自人的尿激酶(human uPA, huPA)(R&D Systems, 1310-SE-010)作為蛋白酶。利用還原SDS-PAGE評價利用蛋白酶所為之融合蛋白質之切斷。對於融合蛋白質0.1 mg/ml使30 nM huPA於37℃作用1小時後，利用還原SDS-PAGE評價融合蛋白質之切斷。其結果，G7H-G1T4/hCXCL10R75A.G4SGGGG.G7L-LT0未被蛋白酶處理切斷(第15圖)。

【0182】 8-2 抗CXCL10中和抗體-CXCL10融合蛋白質之伴隨蛋白酶切斷之游走活性評價

評價導入了蛋白酶切斷序列之抗CXCL10中和抗體與CXCL10融合而得的抗CXCL10中和抗體-CXCL10融合蛋白質是否會因蛋白酶切斷而使CXCL10游離並引起細胞游走。

依下列方法製作、精製僅表現出hCXCL10R75A之活性之hCXCL10R75A-His(序列編號：373)以作為從融合蛋白質游離之hCXCL10R75A之活性比較對象。在變異成耐受蛋白酶的人CXCL10變異體hCXCL10R75A(序列編號：370)的C末端附加組胺酸標籤，製作成附加了組胺酸標籤之人CXCL10變異體hCXCL10R75A-His (序列編號：373)。hCXCL10R75A-His(序列編號：373)依該技術領域中有通常知識者公知之方法利用使用了Expi293 (Life Technologies)之暫時性表現予以表現，並依使用了Ni-sepharose之該技術領域中有通常知識者公知之方法精製。

細胞游走活性，係製作表現小鼠CXCR3(mCXCR3)之Ba/F3轉染細胞(以下稱為BaF3/mCXCR3)，使用此細胞與HTS Transwell™-96 Permeable Support with 5.0μm Pore Polycarbonate Membrane (Cat. 3387、Corning) 評價。

就uPA(+)之分析物而言，在2.0mL 96孔深孔盤(Cat. P-DW-20-C-S、Axygen)

中加入hCXCL10R75A-His 0.15 μg/mL、對於沒有蛋白酶切斷序列之融合蛋白質G7H-G1T4/ hCXCL10R75A.G4SGGGG.G7L-LT0 1.5 μg/mL添加了重組huPA (Cat. 1310-SE、R&D systems)使終濃度成為30 nM以準備。G7H-G1T4/ hCXCL10R75A.G4SGGGG.G7L-LT0 1.5 μg/mL含有0.15 μg/mL相當量之hCXCL10R75A。uPA(-)之分析物，使用hCXCL10R75A-His 0.15 μg/mL、沒有蛋白酶切斷序列之融合蛋白質G7H-G1T4/ hCXCL10R75A.G4SGGGG.G7L-LT0 1.5 μg/mL。

將成為分析對象之各溶液各235 μL移到下腔體，於上腔體接種BaF3/mCXCR3細胞75 μL/孔，以使其成為2.0×10^5細胞/孔，反應6小時。反應係於5%二氧化碳、37℃條件下進行。6小時反應後，將下腔體中之溶液100 μL移到OptiPlate-96(Cat. 6005299、PerkinElmer)，加入CellTiter-Glo™ Luminescent Cell Viability Assay溶液(Cat. G7571、Promega)100 μL。於室溫反應10分鐘後，以SpectraMax M3多模式微板讀取儀(Molecular Devices)測定發光值，評價細胞向下腔體之游走度。其結果示於第16圖。相較於添加CXCL10R75A-His之情形，沒有切斷序列之G7H-G1T4/hCXCL10R75A.G4SGGGG.G7L-LT0即使進行蛋白酶處理，也未觀察到發光強度回復。

【0183】 8-3 導入了蛋白酶切斷序列之抗CXCL10中和抗體-CXCL10融合蛋白質之建構與伴隨蛋白酶切斷之游走活性評價

設計胺基酸序列，以使在8-1建構之配體融合輕鏈hCXCL10R75A.G4SGGGG.G7L-LT0(序列編號：371)之可變區與不變區之交界附近含有蛋白酶切斷序列。將導入了蛋白酶切斷序列之配體融合輕鏈與MabCXCL10_G7重鏈之G7H-G1T4組合，將融合蛋白質依該技術領域中有通常知識者公知之方法利用使用Expi293 (Life Technologies)之暫時性表現予以表現，並依使用了Protein A之該技術領域中有通常知識者公知之方法精製。

檢查該等融合蛋白質是否會被蛋白酶切斷。使用來自人之尿激酶(human uPA, huPA)(R&D Systems, 1310-SE-010)作為蛋白酶。利用還原SDS-PAGE評價利用蛋白酶所為之融合蛋白質之切斷。相對於融合蛋白質0.1 mg/ml使30 nM huPA於37℃作用1小時後，利用還原SDS-PAGE評價融合蛋白質之切斷。

評價導入了蛋白酶切斷序列之抗CXCL10中和抗體與CXCL10融合而得之抗CXCL10中和抗體-CXCL10融合蛋白質是否會因蛋白酶切斷而使CXCL10游離，並引起細胞游走。細胞游走活性，係製作表現小鼠CXCR3(mCXCR3)之Ba/F3轉染細胞(以下稱為BaF3/mCXCR3)，並使用此細胞與HTS Transwell™-96 Permeable Support with 5.0μm Pore Polycarbonate Membrane (Cat. 3387、Corning) 評價。

就uPA(+)之分析物而言，在2.0mL 96孔深孔盤(Cat. P-DW-20-C-S、Axygen)中加入8-2製備之hCXCL10R75A-His 0.15 μg/mL、或對於導入了蛋白酶切斷序列之融合蛋白質1.5 μg/mL添加了重組huPA (Cat. 1310-SE、R&D systems)使終濃度成為30 nM以準備。有蛋白酶切斷序列之融合蛋白質 1.5 μg/mL含有0.15 μg/mL相當量之hCXCL10R75A。uPA(-)之分析物，使用hCXCL10R75A-His 0.15 μg/mL、或有蛋白酶切斷序列之融合蛋白質1.5 μg/mL。

將成為分析對象之各溶液各235 μL移到下腔體，於上腔體接種BaF3/mCXCR3細胞75 μL/孔，使其成為2.0×10^5細胞/1孔，反應6小時。反應於5%二氧化碳、37℃條件下進行。6小時反應後，將下腔體中之溶液100 μL移到OptiPlate-96(Cat. 6005299、PerkinElmer)，加入CellTiter-Glo™ Luminescent Cell Viability Assay溶液(Cat. G7571、Promega)100 μL。於室溫反應10分鐘後，以SpectraMax M3 多模式微板讀取儀(Molecular Devices)測定發光值，評價細胞向下腔體之游走度。能以發光強度評價游走活性之評價。

【0184】 實施例9 導入了蛋白酶切斷序列與可動連結子序列之抗IL-12中和抗體之製作與伴隨蛋白酶切斷之IL-12活化之評價

9-1. 導入了蛋白酶切斷序列與可動連結子序列之抗IL-12中和抗體之製作

IL-12係具有免疫活化作用之細胞介素之一。IL-12藉由使免疫細胞活化而發揮抗腫瘤效果，但據報導同時會因全身暴露而引起嚴重的副作用(Nat Immunol. 2012 Jul 19;13(8):722-8.)。

在具有和針對人IL-12之中和抗體Ustekinumab有同樣可變區之抗IL12抗體之重鏈 (UstkH-G1T4, 重鏈序列編號：144)之可變區與不變區之交界附近插入含有由據報導會被尿激酶(uPA)及Matriptase(MT-SP1)切斷之由胜肽序列A(序列編號：3)及甘胺酸-絲胺酸聚合物構成可動連結子之序列，設計Ustekinumab之重鏈之改變體UstkH-G1T4CYTM1inP1(序列編號：146)，並與Ustekinumab之輕鏈(UstkL-kT0、序列編號：145)組合，依該技術領域中有通常知識者公知之方法製作編碼Ustekinumab之改變體UstkH-G1T4CYTM1inP1/UstkL-kT0(重鏈序列編號：146、輕鏈序列編號：145)的表現載體。將此Ustekinumab之改變體UstkH-G1T4CYTM1inP1/UstkL-kT0依該技術領域中有通常知識者公知之方法，利用使用了FreeStyle 293 (Life Technologies)之暫時性表現予以表現，並依使用了Protein A之該技術領域中有通常知識者公知之方法精製。本實施例中之抗IL12抗體及其改變體中含有的CDR序列如下：H-CDR1(TYWLG、序列編號：386)、H-CDR2(IMSPVDSDIRYSPSFQG、序列編號：387)、H-CDR3(RRPGQGYFDF、序列編號：388)、L-CDR1(RASQGISSWLA、序列編號：389)、L-CDR2(AASSLQS、序列編號：390)、L-CDR3(QQYNIYPYT、序列編號：391)。

【0185】 9-2. 導入了蛋白酶切斷序列與可動連結子序列之抗IL-12中和抗體之蛋白酶切斷

檢查前述9-1製備之抗體是否會被蛋白酶切斷。使用來自人之重組人Matriptase/ST14 觸媒分域 (human MT-SP1, hMT-SP1) (R&D Systems, 3946-SE-010)、來自小鼠之重組小鼠Matriptase/ST14 觸媒分域(mouse MT-SP1,

mMT-SP1) (R&D Systems, 4735-SE-010)、及來自人之尿激酶(human uPA, huPA)(R&D Systems, 1310-SE-010)作為蛋白酶。蛋白酶處理，係對於Ustekinumab(UstkH-G1T4/ UstkL-kT0)、或Ustekinumab之改變體UstkH-G1T4CYTM1inP1/UstkL-kT0添加hMT-SP1、mMT-SP1、或huPA使最終濃度成為10.1, 16.9, 9.17 μM，於37℃進行一晚反應。

【0186】 9-3. 已導入切斷之蛋白酶切斷序列與可動連結子序列之抗IL-12中和抗體之切斷之確認與IL-12活化之評價

利用還原SDS-PAGE評價利用蛋白酶所為之抗體之切斷。其結果，UstkH-G1T4/ UstkL-kT0未受各蛋白酶切斷，反觀插入了蛋白酶切斷序列及可動連結子之UstkH-G1T4CYTM1inP1/UstkL-kT0，因各蛋白酶處理而在25kDa至50kDa之間生出了新的譜帶(第17圖)。因此確認了導入了蛋白酶切斷序列與可動連結子序列之抗IL-12中和抗體(UstkH-G1T4CYTM1inP1/UstkL-kT0)會被蛋白酶切斷。

然後，評價當利用蛋白酶切斷了抗體時，IL-12是否會從與抗體之複合體游離並發揮生理活性。IL-12之生理活性係依據NK92人細胞株之IFN-γ(也記載為干擾素gamma、IFN-g)產生來評價。在96孔細胞培養盤接種NK92細胞1×10^5 細胞/孔。添加10 ng/mL之IL-12與實施了蛋白酶處理之抗體(UstkH-G1T4/ UstkL-kT0或UstkH-G1T4CYTM1inP1/UstkL-kT0，20、4、0.8、0.16、0.032、0.0054、0.0013 μg/mL之各濃度)，以ELISA測定48小時後之IFN-γ產生量。為了評價抗體對於IL12活性之影響，也進行不添加抗體僅添加經蛋白酶處理完畢的IL12的實驗(No Ab)。第18圖係測定干擾素gamma之濃度之結果。經各種蛋白酶處理之UstkH-G1T4/ UstkL-kT0(不具蛋白酶切斷序列)，會抑制IL-12所為之干擾素gamma之產生(稱為中和)，抗體為0.8μg/mL時和未添加IL-12時(No IL-12)成為同程度。另一方面，經各種蛋白酶處理之UstkH-G1T4CYTM1inP1/UstkL-kT0(包括

蛋白酶切斷序列)，在任一抗體濃度，皆相較於添加了不具蛋白酶切斷序列之UstkH-G1T4/ UstkL-kT0之情形，產生較多干擾素gamma。由此結果可確認:UstkH-G1T4CYTM1inP1/UstkL-kT0因為伴隨切斷而使對於IL-12之中和能力減弱，使IL-12作用於細胞。

【0187】 實施例10 於抗人CXCL10中和抗體導入了蛋白酶切斷序列之抗體之評價

10-1.對於抗人CXCL10中和抗體導入蛋白酶切斷序列

依該技術領域中有通常知識者公知之方法製備中和CXCL10之抗體MabCXCL10(重鏈：EEIVH(序列編號：1)、輕鏈：EEIVL(序列編號：2))與MabCXCL10_G7(重鏈：G7H-G1T4(序列編號：368)、輕鏈：G7L-LT0(序列編號：369))之表現載體，使用FreeStyle293細胞 (Invitrogen) 或Expi293細胞 (Life technologies)依該技術領域中有通常知識者公知之方法表現、精製。

在MabCXCL10或MabCXCL10_G7之重鏈之可變區與不變區之交界附近分別插入以序列編號：345表示之切斷序列，製作MabCXCL10改變重鏈EldHA0003-G1T4(序列編號：356)與MabCXCL10_G7改變重鏈G7H.12aa-G1T4(序列編號：367)。

【0188】 將上述2種改變重鏈與輕鏈組合，依該技術領域中有通常知識者公知之方法將MabCXCL10改變體EldHA0003(重鏈序列編號：356、輕鏈序列編號：2)及MabCXCL10_G7改變體G7H.12aa(重鏈序列編號：367、輕鏈序列編號：369)使用 FreeStyle293細胞 (Invitrogen) 或Expi293細胞 (Life technologies)以暫時性表現予以表現，並依使用了Protein A之該技術領域中有通常知識者公知之方法精製。

【0189】 10-2.蛋白酶切斷序列導入到重鏈區之抗人CXCL10中和抗體之利用蛋白酶所為之切斷之評價

檢查10-1製備之抗體是否會被蛋白酶切斷。使用重組人Matriptase/ST14 觸媒分域(human MT-SP1, hMT-SP1) (R&D Systems, 3946-SE-010)作為蛋白酶，於蛋白酶 10nM、抗體 50μg/mL、PBS、37℃之條件下反應20小時後，供還原SDS-PAGE。結果示於第19A圖、第19B圖。MabCXCL10改變體EldHA0003與MabCXCL10_G7改變體G7H.12aa，皆因hMT-SP1處理而在37kDa附近生出新的譜帶。亦即確認以序列編號：345表示之蛋白酶切斷序列會被hMT-SP1切斷。又，依類似的方法也確認以序列編號：345表示之蛋白酶切斷序列也會被人uPA, 小鼠uPA切斷。

【0190】 實施例11 導入了多樣的蛋白酶的切斷序列的多胜肽之製作與評價

11-1 導入了多樣的蛋白酶的認識序列的多胜肽之製作

依該技術領域中有通常知識者公知之方法製備針對人IL6R之中和抗體MRA(重鏈：MRAH-G1T4(序列編號：147)、輕鏈：MRAL-k0(序列編號：148))之表現載體。MRA之CDR序列如下：H-CDR1(SDHAWS、序列編號：398)、H-CDR2(YISYSGITTYNPSLKS、序列編號：399)、H-CDR3(SLARTTAMDY、序列編號：400)、L-CDR1(RASQDISSYLN、序列編號：401)、L-CDR2(YTSRLHS、序列編號：402)、L-CDR3(QQGNTLPYT、序列編號：403)。

已知會被MMP-2、MMP-7、MMP-9切斷之胜肽序列及在此等序列附近含有由甘胺酸-絲胺酸聚合物構成之可動連結子的胜肽序列，示於表4。

【0191】 【表1】

蛋白酶	插入序列	序列編號
MMP-2 MMP-9	PLGLAG	３４
MMP-2	GAGIPVSLRSGAG	７０
MMP-2	GPLGIAGQ	７１
MMP-2	GGPLGMLSQS	７２
MMP-2	PLGLWA	７３
MMP-7	VPLSLTMG	３５
MMP-7	GAGVPLSLTMGAG	７５
MMP-9	GAGVPLSLYSGAG	７６
MMP-2 MMP-9	GGGGSPLGLAGGGGGS	149
MMP-2	GGGGSGPLGIAGQGGGGS	150
MMP-2	GGGGSPLGLWAGGGGS	151
MMP-9	GGGGSGAGVPLSLYSGAGGGGGS	152

【0192】 設計將該等插入序列插入到MRA抗體之重鏈可變區與不變區之交界附近而得的改變重鏈MEIVHG4SMP2MP9G4S-MEIVHG4SMP2MP9G4SG1T4(序列編號：153)、MEIVHG4SMP2.2G4S-MEIVHG4SMP2.2G4SG1T4(序列編號：154)、MEIVHG4SMP2.4G4S-MEIVHG4SMP2.4G4SG1T4(序列編號：155)、MEIVHG4SMP9G4S-MEIVHG4SMP9G4SG1T4(序列編號：156)、MEIVHMP2.1-MEIVHMP2.1G1T4 (序列編號：157)、MEIVHMP2.3-MEIVHMP2.3G1T4 (序列編號：158)、MEIVHMP7.2-MEIVHMP7.2G1T4 (重鏈序列編號：159)，依該技術領域中有通常知識者公知之方法製作編碼該等改變重鏈之表現載體。

將該等改變重鏈與MRA輕鏈組合，將表5所示之MRA改變體依該技術領域中有通常知識者公知之方法利用使用了FreeStyle293細胞 (Invitrogen) 或Expi293細胞 (Life technologies)之暫時性表現予以表現，並依使用了Protein A之該技術領

域中有通常知識者公知之方法精製。

【0193】 【表2】

MRA改變體

蛋白酶	抗體名	重鏈 序列編號	輕鏈 序列編號
MMP-2	MEIVHG4SMP2MP9G4S-MEICHG4SMP2MP9G4SG1T4 /MRAL-k0	153	148
MMP-2	MEIVHG4SMP2.2G4S-MEICHG4SMP2.2G4SG1T4 /MRAL-k0	154	148
MMP-2	MEIVHG4SMP2.4G4S-MEICHG4SMP2.4G4SG1T4 /MRAL-k0	155	148
MMP-9	MEIVHG4SMP2MP9G4S-MEICHG4SMP2MP9G4SG1T4 /MRAL-k0	153	148
MMP-9	MEIVHG4SMP9G4S-MEICHG4SMP9G4SG1T4 /MRAL-k0	156	148
MMP-2	MEIVHMP2.1-MEIVHMP2.1G1T4/MRAL-k0	157	148
MMP-2	MEIVHMP2.3-MEIVHMP2.3G1T4/MRAL-k0	158	148
MMP-7	MEIVHMP7.2-MEIVHMP7.2G1T4/MRAL-k0	159	148

【0194】 11-2.導入了多樣的蛋白酶的認識序列的多胜肽之利用蛋白酶所為之切斷之評價

檢查於11-1製備之MRA改變體是否會被蛋白酶切斷。使用重組人MMP-2(R&D Systems, 902-MP-010)、重組人MMP-7(R&D Systems, 907-MP-010)、重組人MMP-9(R&D Systems, 911-MP-010)作為蛋白酶。又，蛋白酶係與1 mM對氨基苯汞乙酸鹽(p-aminophenylmercuric acetate) (APMA; abcam, ab112146) 混合，於37℃各活化1、24小時活化後使用。使蛋白酶 50 nM、100 nM、或 500 nM、抗體 50μg/mL 、 assay buffer(以 MMP Activity Assay Kit(Fluorometric - Green) (ab112146), Component C: Assay Buffer)實施。))或 20 mM Tris-HCl, 150 mM NaCl, 5 mM $CaCl_2$, pH 7.2 (以下稱為Tris)在37℃之條件下反應20小時後，利用還原

SDS-PAGE評價利用蛋白酶所為之切斷，結果示於第20A圖、第20B圖、第21圖。MRA改變體抗體各與表5所示之蛋白酶反應。MMP-2中，觀察到MEIVHG4SMP2MP9G4S-MEIVHG4SMP2MP9G4SG1T4/MRAL-k0, MEIVHG4SMP2.2G4S-MEIVHG4SMP2.2G4SG1T4/MRAL-k0, MEIVHG4SMP2.4G4S-MEIVHG4SMP2.4G4SG1T4/MRAL-k0,MEIVHMP2.1-MEIVHMP2.1G1T4/MRAL-k0, MEIVHMP2.3-MEIVHMP2.3G1T4/MRAL-k0之切斷，MMP-7中，觀察到MEIVHMP7.2-MEIVHMP7.2G1T4/MRAL-k0之切斷，MMP-9中，觀察到MEIVHG4SMP2MP9G4S-MEIVHG4SMP2MP9G4SG1T4/MRAL-k0, MEIVHG4SMP9G4S-MEIVHG4SMP9G4SG1T4/MRAL-k0之切斷。

【0195】 實施例12 於重鏈之多樣的位置導入了蛋白酶切斷序列之抗體之評價

12-1 於重鏈之多樣的位置導入了蛋白酶切斷序列之抗體之製作

將據報告會被尿激酶（uPA）及Matriptase（MT-SP1）切斷之胜肽序列B(序列編號：160)各插入到MRA重鏈可變區(MRAH、序列編號：161)內之不同位置，製得表6所示之MRA重鏈可變區之改變體。使該等MRA重鏈可變區之改變體與各MRA重鏈不變區(G1T4、序列編號：162)連結，製作出MRA重鏈改變體之，並依該技術領域中有通常知識者公知之方法製作編碼對應之基因之表現載體。又，將胜肽序列B(序列編號：160)插入到MRA重鏈不變區(G1T4、序列編號：162)內之不同位置，製作出表7所示之MRA重鏈不變區之改變體。使該等MRA重鏈不變區之改變體與各MRA重鏈可變區(MRAH、序列編號：161)連結，製作出MRA重鏈改變體，並依該技術領域中有通常知識者公知之方法製作編碼對應基因之表現載體。製作的MRA重鏈可變區之改變體及MRA重鏈不變區之改變體中，蛋白酶切斷序列插入位置也示於表6、7。表6之插入處，係指抗體重鏈可變區中之記載位置(Kabat編號)之不變區側鄰，表7之插入處，係指抗體重鏈不變區中之記

載位置 (EU編號)之可變區側鄰。

【0196】 【表3】

MRA重鏈可變區之改變體及蛋白酶切斷序列插入位置

MRA重鏈可變區之改變體	蛋白酶切斷序列插入位置 (Kabat編號)	序列編號
MRAVH007.12aa	7 號	163
MRAVH008.12aa	8 號	164
MRAVH009.12aa	9 號	165
MRAVH010.12aa	10 號	166
MRAVH011.12aa	11 號	167
MRAVH012.12aa	12 號	168
MRAVH013.12aa	13 號	169
MRAVH014.12aa	14 號	170
MRAVH015.12aa	15 號	171
MRAVH041.12aa	40 號	172
MRAVH042.12aa	41 號	173
MRAVH043.12aa	42 號	174
MRAVH044.12aa	43 號	175
MRAVH045.12aa	44 號	176
MRAVH046.12aa	45 號	177
MRAVH056.12aa	55 號	178
MRAVH057.12aa	56 號	179
MRAVH058.12aa	57 號	180
MRAVH059.12aa	58 號	181
MRAVH060.12aa	59 號	182
MRAVH061.12aa	60 號	183
MRAVH062.12aa	61 號	184
MRAVH063.12aa	62 號	185
MRAVH064.12aa	63 號	186
MRAVH065.12aa	64 號	187
MRAVH066.12aa	65 號	188
MRAVH067.12aa	66 號	189
MRAVH068.12aa	67 號	190
MRAVH069.12aa	68 號	191
MRAVH074.12aa	73 號	192
MRAVH075.12aa	74 號	193
MRAVH076.12aa	75 號	194

MRAVH077.12aa	76號	195
MRAVH078.12aa	77號	196
MRAVH087.12aa	83號	197
MRAVH088.12aa	84號	198
MRAVH089.12aa	85號	199
MRAVH099.12aa	95號	200
MRAVH100.12aa	96號	201
MRAVH101.12aa	97號	202
MRAVH102.12aa	98號	203
MRAVH109.12aa	103號	204
MRAVH110.12aa	104號	205
MRAVH111.12aa	105號	206
MRAVH112.12aa	106號	207
MRAVH113.12aa	107號	208
MRAVH114.12aa	108號	209
MRAVH115.12aa	109號	210
MRAVH116.12aa	110號	211
MRAVH117.12aa	111號	212
MRAVH118.12aa	112號	213
MRAVH119.12aa	113號	214

【0197】 【表4】

MRA重鏈不變區之改變體及蛋白酶切斷序列插入位置

MRA重鏈不變區之改變體	蛋白酶切斷序列插入位置 (EU 編號)	序列編號
G1T4.118.12aa	119 號	215
G1T4.119.12aa	120 號	216
G1T4.120.12aa	121 號	217
G1T4.121.12aa	122 號	218
G1T4.122.12aa	123 號	219
G1T4.123.12aa	124 號	220
G1T4.124.12aa	125 號	221
G1T4.129.12aa	130 號	222
G1T4.130.12aa	131 號	223
G1T4.131.12aa	132 號	224
G1T4.132.12aa	133 號	225
G1T4.134.12aa	135 號	226
G1T4.135.12aa	136 號	227
G1T4.137.12aa	138 號	228
G1T4.139.12aa	140 號	229

【0198】 將上述製作之MRA重鏈改變體與MRA輕鏈組合，將表8所示之MRA改變體依該技術領域中有通常知識者公知之方法利用使用了FreeStyle293細胞 (Invitrogen) 或Expi293細胞 (Life technologies)之暫時性表現予以表現，並依使用了Protein A之該技術領域中有通常知識者公知之方法精製。

【0199】 【表5】

MRA改變體

抗體名	重鏈序列編號	輕鏈序列編號
MRAVH007.12aa-G1T4/MRAL-k0	404	148
MRAVH008.12aa-G1T4/MRAL-k0	405	148
MRAVH009.12aa-G1T4/MRAL-k0	406	148
MRAVH010.12aa-G1T4/MRAL-k0	407	148
MRAVH011.12aa-G1T4/MRAL-k0	408	148
MRAVH012.12aa-G1T4/MRAL-k0	409	148
MRAVH013.12aa-G1T4/MRAL-k0	410	148
MRAVH014.12aa-G1T4/MRAL-k0	411	148
MRAVH015.12aa-G1T4/MRAL-k0	412	148
MRAVH041.12aa-G1T4/MRAL-k0	413	148
MRAVH042.12aa-G1T4/MRAL-k0	414	148
MRAVH043.12aa-G1T4/MRAL-k0	415	148
MRAVH044.12aa-G1T4/MRAL-k0	416	148
MRAVH045.12aa-G1T4/MRAL-k0	417	148
MRAVH046.12aa-G1T4/MRAL-k0	418	148
MRAVH056.12aa-G1T4/MRAL-k0	419	148
MRAVH057.12aa-G1T4/MRAL-k0	420	148
MRAVH058.12aa-G1T4/MRAL-k0	421	148
MRAVH059.12aa-G1T4/MRAL-k0	422	148
MRAVH060.12aa-G1T4/MRAL-k0	423	148
MRAVH061.12aa-G1T4/MRAL-k0	424	148
MRAVH062.12aa-G1T4/MRAL-k0	425	148
MRAVH063.12aa-G1T4/MRAL-k0	426	148
MRAVH064.12aa-G1T4/MRAL-k0	427	148
MRAVH065.12aa-G1T4/MRAL-k0	428	148
MRAVH066.12aa-G1T4/MRAL-k0	429	148
MRAVH067.12aa-G1T4/MRAL-k0	430	148
MRAVH068.12aa-G1T4/MRAL-k0	431	148
MRAVH069.12aa-G1T4/MRAL-k0	432	148
MRAVH074.12aa-G1T4/MRAL-k0	433	148
MRAVH075.12aa-G1T4/MRAL-k0	434	148
MRAVH076.12aa-G1T4/MRAL-k0	435	148
MRAVH077.12aa-G1T4/MRAL-k0	436	148

MRAVH078.12aa-G1T4/MRAL-k0	437	148
MRAVH087.12aa-G1T4/MRAL-k0	438	148
MRAVH088.12aa-G1T4/MRAL-k0	439	148
MRAVH089.12aa-G1T4/MRAL-k0	440	148
MRAVH099.12aa-G1T4/MRAL-k0	441	148
MRAVH100.12aa-G1T4/MRAL-k0	442	148
MRAVH101.12aa-G1T4/MRAL-k0	443	148
MRAVH102.12aa-G1T4/MRAL-k0	444	148
MRAVH109.12aa-G1T4/MRAL-k0	445	148
MRAVH110.12aa-G1T4/MRAL-k0	446	148
MRAVH111.12aa-G1T4/MRAL-k0	447	148
MRAVH112.12aa-G1T4/MRAL-k0	448	148
MRAVH113.12aa-G1T4/MRAL-k0	449	148
MRAVH114.12aa-G1T4/MRAL-k0	450	148
MRAVH115.12aa-G1T4/MRAL-k0	451	148
MRAVH116.12aa-G1T4/MRAL-k0	452	148
MRAVH117.12aa-G1T4/MRAL-k0	453	148
MRAVH118.12aa-G1T4/MRAL-k0	454	148
MRAVH119.12aa-G1T4/MRAL-k0	455	148
MRAH-G1T4.118.12aa/MRAL-k0	456	148
MRAH-G1T4.119.12aa/MRAL-k0	457	148
MRAH-G1T4.120.12aa/MRAL-k0	458	148
MRAH-G1T4.121.12aa/MRAL-k0	459	148
MRAH-G1T4.122.12aa/MRAL-k0	460	148
MRAH-G1T4.123.12aa/MRAL-k0	461	148
MRAH-G1T4.124.12aa/MRAL-k0	462	148
MRAH-G1T4.129.12aa/MRAL-k0	463	148
MRAH-G1T4.130.12aa/MRAL-k0	464	148
MRAH-G1T4.131.12aa/MRAL-k0	465	148
MRAH-G1T4.132.12aa/MRAL-k0	466	148
MRAH-G1T4.134.12aa/MRAL-k0	467	148
MRAH-G1T4.135.12aa/MRAL-k0	468	148
MRAH-G1T4.137.12aa/MRAL-k0	469	148
MRAH-G1T4.139.12aa/MRAL-k0	470	148

【0200】 12-2.蛋白酶切斷序列導入到抗體重鏈而得之抗人IL6R中和抗體之利用蛋白酶所為之切斷之評價

檢查12-1製備之MRA改變體是否會被蛋白酶切斷。使用重組人Matriptase/ST14 觸媒分域(human MT-SP1, hMT-SP1) (R&D Systems, 3946-SE-010)作為蛋白酶，於蛋白酶 10nM、抗體 50μg/mL、PBS、37℃之條件下反應20小時後，供還原SDS-PAGE。結果示於第22A、22B、22C、22D、22E、22F、22G、22H、22I、23A、23B、23C圖。蛋白酶處理後之MRA改變體，相較於重鏈被切斷、未受蛋白酶處理之MRA改變體之重鏈(圖中之MT-SP1(-)泳道(lane)之50kDa附近出現之譜帶)，在分子量更小的位置出現重鏈譜帶。由此結果可以確認於12-1製備之MRA改變體會被hMT-SP1切斷。

【0201】 實施例13 於輕鏈之多樣的位置導入了蛋白酶切斷序列之抗體之評價

13-1 於輕鏈之多樣的位置導入了蛋白酶切斷序列之抗體之製作

將據報告會被尿激酶 (uPA)及Matriptase(MT-SP1)切斷之胜肽序列B(序列編號：160)分別插入到MRA輕鏈可變區(MRAL、序列編號：230)內的不同位置，製出表9所示之MRA輕鏈可變區之改變體。使該等MRA輕鏈可變區之改變體各與MRA輕鏈不變區(k0、序列編號：231)連結，製作出MRA輕鏈改變體之，並依該技術領域中有通常知識者公知之方法製作編碼對應基因之表現載體。又，將胜肽序列B(序列編號：160)各插入到MRA輕鏈不變區(k0、序列編號：231)內之不同位置，製出表10所示之MRA輕鏈不變區之改變體。使該等MRA輕鏈不變區之改變體與各MRA輕鏈可變區(MRAL、序列編號：230)連結，製作MRA輕鏈改變體，並依該技術領域中有通常知識者公知之方法製作對應之編碼基因之表現載體。製作的MRA輕鏈可變區之改變體及MRA輕鏈不變區之改變體中的蛋白酶切斷序列插入位置也示於表9、10。表9之插入處，係抗體輕鏈可變區中之記載

胺基酸(Kabat編號)之不變區側鄰，表10之插入處係指抗體輕鏈不變區中之記載胺基酸(EU編號)之可變區側鄰。

【0202】 【表6】

MRA輕鏈可變區之改變體及蛋白酶切斷序列插入位置

MRA輕鏈可變區之改變體	蛋白酶切斷序列插入位置 (Kabat編號)	序列編號
MRAVL007.12aa	7號	232
MRAVL008.12aa	8號	233
MRAVL009.12aa	9號	234
MRAVL010.12aa	10號	235
MRAVL011.12aa	11號	236
MRAVL012.12aa	12號	237
MRAVL013.12aa	13號	238
MRAVL014.12aa	14號	239
MRAVL015.12aa	15號	240
MRAVL016.12aa	16號	241
MRAVL017.12aa	17號	242
MRAVL018.12aa	18號	243
MRAVL039.12aa	39號	244
MRAVL040.12aa	40號	245
MRAVL041.12aa	41號	246
MRAVL042.12aa	42號	247
MRAVL043.12aa	43號	248
MRAVL044.12aa	44號	249
MRAVL045.12aa	45號	250
MRAVL049.12aa	49號	251
MRAVL050.12aa	50號	252
MRAVL051.12aa	51號	253
MRAVL052.12aa	52號	254
MRAVL053.12aa	53號	255
MRAVL054.12aa	54號	256
MRAVL055.12aa	55號	257
MRAVL056.12aa	56號	258
MRAVL057.12aa	57號	259
MRAVL058.12aa	58號	260
MRAVL059.12aa	59號	261
MRAVL060.12aa	60號	262
MRAVL096.12aa	96號	263

MRAVL097.12aa	97號	264
MRAVL098.12aa	98號	265
MRAVL099.12aa	99號	266
MRAVL100.12aa	100號	267
MRAVL101.12aa	101號	268
MRAVL102.12aa	102號	269
MRAVL103.12aa	103號	270
MRAVL104.12aa	104號	271
MRAVL105.12aa	105號	272
MRAVL106.12aa	106號	273
MRAVL107.12aa	107號	274

【0203】 【表7】

MRA輕鏈可變區之改變體及蛋白酶切斷序列插入位置

MRA輕鏈不變區之改變體	蛋白酶切斷序列插入位置 (EU編號)	序列編號
k0.108.12aa	109號 (Kabat 編號 109號)	275
k0.109.12aa	110號 (Kabat 編號 110號)	276
k0.110.12aa	111號 (Kabat 編號 111號)	277
k0.111.12aa	112號 (Kabat 編號 112號)	278
k0.112.12aa	113號 (Kabat 編號 113號)	279
k0.113.12aa	114號 (Kabat 編號 114號)	280
k0.115.12aa	116號 (Kabat 編號 116號)	281
k0.116.12aa	117號 (Kabat 編號 117號)	282
k0.117.12aa	118號 (Kabat 編號 118號)	283
k0.118.12aa	119號 (Kabat 編號 119號)	284
k0.119.12aa	120號 (Kabat 編號 120號)	285
k0.120.12aa	121號 (Kabat 編號 121號)	286
k0.121.12aa	122號 (Kabat 編號 122號)	287
k0.122.12aa	123號 (Kabat 編號 123號)	288
k0.123.12aa	124號 (Kabat 編號 124號)	289
k0.124.12aa	125號 (Kabat 編號 125號)	290
k0.125.12aa	126號 (Kabat 編號 126號)	291
k0.126.12aa	127號 (Kabat 編號 127號)	292
k0.127.12aa	128號 (Kabat 編號 128號)	293
k0.128.12aa	129號 (Kabat 編號 129號)	294
k0.129.12aa	130號 (Kabat 編號 130號)	295
k0.130.12aa	131號 (Kabat 編號 131號)	296

【0204】 將上述製作之MRA輕鏈改變體與MRA重鏈組合，並將表11所示之MRA改變體依該技術領域中有通常知識者公知之方法以使用了FreeStyle293細胞 (Invitrogen) 或Expi293細胞 (Life technologies)之暫時性表現予以表現，並依使用了Protein A之該技術領域中有通常知識者公知之方法精製。

【0205】 【表8】

MRA改變體

抗體名	重鏈序列編號	輕鏈序列編號
MRAH-G1T4/MRAVL007.12aa-k0	147	471
MRAH-G1T4/MRAVL008.12aa-k0	147	472
MRAH-G1T4/MRAVL009.12aa-k0	147	473
MRAH-G1T4/MRAVL010.12aa-k0	147	474
MRAH-G1T4/MRAVL011.12aa-k0	147	475
MRAH-G1T4/MRAVL012.12aa-k0	147	476
MRAH-G1T4/MRAVL013.12aa-k0	147	477
MRAH-G1T4/MRAVL014.12aa-k0	147	478
MRAH-G1T4/MRAVL015.12aa-k0	147	479
MRAH-G1T4/MRAVL016.12aa-k0	147	480
MRAH-G1T4/MRAVL017.12aa-k0	147	481
MRAH-G1T4/MRAVL018.12aa-k0	147	482
MRAH-G1T4/MRAVL039.12aa-k0	147	483
MRAH-G1T4/MRAVL040.12aa-k0	147	484
MRAH-G1T4/MRAVL041.12aa-k0	147	485
MRAH-G1T4/MRAVL042.12aa-k0	147	486
MRAH-G1T4/MRAVL043.12aa-k0	147	487
MRAH-G1T4/MRAVL044.12aa-k0	147	488
MRAH-G1T4/MRAVL045.12aa-k0	147	489
MRAH-G1T4/MRAVL049.12aa-k0	147	490
MRAH-G1T4/MRAVL050.12aa-k0	147	491
MRAH-G1T4/MRAVL051.12aa-k0	147	492
MRAH-G1T4/MRAVL052.12aa-k0	147	493
MRAH-G1T4/MRAVL053.12aa-k0	147	494
MRAH-G1T4/MRAVL054.12aa-k0	147	495
MRAH-G1T4/MRAVL055.12aa-k0	147	496
MRAH-G1T4/MRAVL056.12aa-k0	147	497
MRAH-G1T4/MRAVL057.12aa-k0	147	498
MRAH-G1T4/MRAVL058.12aa-k0	147	499
MRAH-G1T4/MRAVL059.12aa-k0	147	500
MRAH-G1T4/MRAVL060.12aa-k0	147	501
MRAH-G1T4/MRAVL096.12aa-k0	147	502
MRAH-G1T4/MRAVL097.12aa-k0	147	503

MRAH-G1T4/MRAVL098.12aa-k0	147	504
MRAH-G1T4/MRAVL099.12aa-k0	147	505
MRAH-G1T4/MRAVL100.12aa-k0	147	506
MRAH-G1T4/MRAVL101.12aa-k0	147	507
MRAH-G1T4/MRAVL102.12aa-k0	147	508
MRAH-G1T4/MRAVL103.12aa-k0	147	509
MRAH-G1T4/MRAVL104.12aa-k0	147	510
MRAH-G1T4/MRAVL105.12aa-k0	147	511
MRAH-G1T4/MRAVL106.12aa-k0	147	512
MRAH-G1T4/MRAVL107.12aa-k0	147	513
MRAH-G1T4/MRAL-k0.108.12aa	147	514
MRAH-G1T4/MRAL-k0.109.12aa	147	515
MRAH-G1T4/MRAL-k0.110.12aa	147	516
MRAH-G1T4/MRAL-k0.111.12aa	147	517
MRAH-G1T4/MRAL-k0.112.12aa	147	518
MRAH-G1T4/MRAL-k0.113.12aa	147	519
MRAH-G1T4/MRAL-k0.115.12aa	147	520
MRAH-G1T4/MRAL-k0.116.12aa	147	521
MRAH-G1T4/MRAL-k0.117.12aa	147	522
MRAH-G1T4/MRAL-k0.118.12aa	147	523
MRAH-G1T4/MRAL-k0.119.12aa	147	524
MRAH-G1T4/MRAL-k0.120.12aa	147	525
MRAH-G1T4/MRAL-k0.121.12aa	147	526
MRAH-G1T4/MRAL-k0.122.12aa	147	527
MRAH-G1T4/MRAL-k0.123.12aa	147	528
MRAH-G1T4/MRAL-k0.124.12aa	147	529
MRAH-G1T4/MRAL-k0.125.12aa	147	530
MRAH-G1T4/MRAL-k0.126.12aa	147	531
MRAH-G1T4/MRAL-k0.127.12aa	147	532
MRAH-G1T4/MRAL-k0.128.12aa	147	533
MRAH-G1T4/MRAL-k0.129.12aa	147	534
MRAH-G1T4/MRAL-k0.130.12aa	147	535

【0206】 13-2.蛋白酶切斷序列導入到抗體輕鏈可變區而得的抗人IL6R中和抗體的利用蛋白酶所為之切斷之評價

檢查於13-1製備之MRA改變體是否會被蛋白酶切斷。使用重組人Matriptase/ST14 觸媒分域(MT-SP1) (R&D Systems, 3946-SE-010)作為蛋白酶，於蛋白酶 10nM、抗體 50μg/mL、PBS、37℃之條件下反應20小時之後，供還原SDS-PAGE。結果示於第24A、第24B、第24C、第24D、第24E、第25A、第25B圖。蛋白酶處理後切斷的MRA改變體，相較於未接受蛋白酶處理之MRA改變體之輕鏈(在圖中MT-SP1(-)泳道之25kDa附近出願的譜帶)，於分子量較小的位置出現輕鏈譜帶。

【0207】 實施例14 導入了蛋白酶切斷序列之抗人PD1中和抗體之製作及對於人PD1之結合評價

14-1.對於抗人PD1中和抗體導入蛋白酶切斷序列

於針對人PD1之中和抗體5C4H-G1T4/5C4L-KT0(重鏈5C4H-G1T4、序列編號：297；重鏈可變區5C4H、序列編號：300；重鏈不變區G1T4、序列編號：301；輕鏈5C4L-KT0、序列編號：298；輕鏈可變區5C4L、序列編號：302；輕鏈不變區 KT0 、序列編號：303; H-CDR1(NSGMH 、序列編號：392) 、H-CDR2(VIWYDGSKRYYADSVKG、序列編號：393)、H-CDR3(NDDY、序列編號：394)、L-CDR1(RASQSVSSYLA、序列編號：395)、L-CDR2(DASNRAT、序列編號：396)、L-CDR3(QQSSNWPRT、序列編號：397))之重鏈或輕鏈插入蛋白酶切斷序列，製作導入了蛋白酶切斷序列之抗體。

首先將據報導會被在癌專一性的表現之Matriptase(MT-SP1)切斷的胜肽序列(序列編號：299)插入到前述抗體之重鏈5C4H-G1T4或輕鏈5C4L-KT0，製作表12所示之重鏈改變體與表13所示之輕鏈改變體，以該技術領域中有通常知識者公知之方法使其表現。

【0208】 【表9】

抗人PD1中和抗體之重鏈改變體

重鏈改變體	序列編號	蛋白酶切斷序列插入位置
5C4HA12aa-G1T4	304	可變區113號(Kabat編號)與不變區118號(EU編號)之間
5C4HA12aa-G1T4E	305	不變區118號與119號之間(EU編號)

【0209】 【表10】

抗人PD1中和抗體之輕鏈改變體

輕鏈改變體	序列編號	蛋白酶切斷序列插入位置
5C4LI12aa-KT0	306	可變區104號與105號之間(Kabat編號)
5C4LC12aa-KT0	307	可變區105號與106號之間(Kabat編號)
5C4LD12aa-KT0	308	可變區106號與107號之間(Kabat編號)
5C4LA12aa-KT0	309	可變區107號(Kabat編號)與不變區108號(EU編號)(不變區Kabat編號108號)之間
5C4LE12aa-KT0E	310	不變區108號與109號之間(EU編號)(不變區Kabat編號108號與不變區Kabat編號109號之間)
5C4LB12aa-KT0B	311	不變區109號與110號之間(EU編號)(不變區Kabat編號109號與不變區Kabat編號110號之間)
5C4LF12aa-KT0F	312	不變區110號與111號之間(EU編號)(不變區Kabat編號110號與不變區Kabat編號111號之間)
5C4LG12aa-KT0G	313	不變區111號與112號之間(EU編號)(不變區Kabat編號111號與不變區Kabat編號112號之間)
5C4LJ12aa-KT0J	314	不變區112號與113號之間(EU編號)(不變區Kabat編號112號與不變區Kabat編號113號之間)
5C4LK12aa-KT0K	315	不變區113號與114號之間(EU編號)(不變區Kabat編號113號與不變區Kabat編號114號之間)

【0210】 將表12之重鏈改變體與輕鏈5C4L-KT0、或表13之輕鏈改變體與重鏈5C4H-G1T4組合，並導入了蛋白酶切斷序列的IgG1抗體(表14)利用該技術領域中有通常知識者公知之方法以使用了Expi293 (Life Technologies)之暫時性表現予以表現，並依使用了Protein A之該技術領域中有通常知識者公知之方法精製。又，將不含蛋白酶切斷序列之作為對照抗體之5C4H-G1T4/5C4L-KT0(重鏈序列編號：297、輕鏈序列編號：298)進行表現及精製。

【0211】 【表11】

導入了蛋白酶切斷序列之抗體

導入了蛋白酶切斷序列之抗體	重鏈序列編號	輕鏈序列編號
5C4HA12aa-G1T4/5C4L-KT0	304	298
5C4HE12aa-G1T4E/5C4L-KT0	305	298
5C4H-G1T4/5C4LI12aa-KT0	297	306
5C4H-G1T4/5C4LC12aa-KT0	297	307
5C4H-G1T4/5C4LD12aa-KT0	297	308
5C4H-G1T4/5C4LA12aa-KT0	297	309
5C4H-G1T4/5C4LE12aa-KT0E	297	310
5C4H-G1T4/5C4LB12aa-KT0B	297	311
5C4H-G1T4/5C4LF12aa-KT0F	297	312
5C4H-G1T4/5C4LG12aa-KT0G	297	313
5C4H-G1T4/5C4LJ12aa-KT0J	297	314
5C4H-G1T4/5C4LK12aa-KT0K	297	315

【0212】 14-2.導入了蛋白酶切斷序列之抗人PD1中和抗體之對於人PD1之結合評價

14-2-1 蛋白酶處理

經蛋白酶處理之抗體，係在14-1製備之抗體(終濃度0.111mg/mL)中加入以PBS製備為1.8μg/mL之Recombinant Human Matriptase/ST14 Catalytic Domain (hMT-SP1, R&D systems 3946-SE-010) 10μL。未經蛋白酶處理之抗體，係於14-1製備之抗體(終濃度0.111mg/mL) 僅加入PBS10μL。反應時之樣本體積為90μL，蛋白酶之終濃度為0.2μg/mL。各樣本於37℃保溫12小時。

【0213】 14-2-2 生物素化抗人PD1中和抗體之製備

製備與5C4H-G1T4/5C4L-KT0有相同可變區之序列之生物素化抗人PD1中和抗體。具體而言，製備編碼在重鏈可變區5C4H(序列編號：300)附加抗體之重

鏈不變區與生物素(AviTag序列、序列編號：316)之5C4VH-G1dGSBAP(序列編號：317)的基因斷片，以該技術領域中有通常知識者公知之方法導入到動物細胞表現用載體。將建構之表現載體與表現輕鏈5C4L-KT0B(序列編號：298)之載體使用293 Fectin (Invitrogen)導入到FreeStyle293細胞 (Invitrogen)。此時，係將表現EBNA1(序列編號：318)之基因及表現生物素連接酶(BirA、序列編號：319)之基因同時導入，並以生物素標識之目的添加生物素。將已導入基因之細胞於37℃、8% CO_2培養，使目的之生物素化抗人PD1中和抗體(5C4-bio)分泌到培養上清中。從培養上清以該技術領域中有通常知識者公知之方法精製5C4-bio。

【0214】 14-2-3 蛋白酶處理前後之各抗體之對於人PD1之結合評價

於14-2-1製備之經蛋白酶處理之抗體/未經蛋白酶處理之抗體80μL添加人PD1使終濃度成為0.67μM，於室溫使其結合30分鐘，製備結合評價用樣本。藉由評價未與抗體結合之PD1之量，以評價抗體之蛋白酶處理/未處理時之對於PD1之結合。

具體而言，使用實施例14-2-2製備之生物素化抗人PD1中和抗體 (5C4-bio) 以BioLayer Interferometry (BLI法)評價未與抗體結合之PD1之量。

將結合評價用樣本、5C4-bio、PBS分別注入到Tilted bottom (TW384) Micro plates(ForteBio、18-5076)的不同的孔內。使用PBS將鏈黴親和素生物感測器(ForteBio, 18-0009)水合，以30℃之設定以Octet RED 384實施測定。於裝有PBS之孔實施30秒基線測定，之後使5C4-bio結合於鏈黴親和素感測器200秒。再度以裝有PBS的孔實施30秒基線測定，之後以裝有結合評價用樣本之孔測定180秒結合，並以裝有PBS之孔測定180秒解離。顯示結合的狀態的即時結合軸示於第26圖。如第26圖所示，於已導入了蛋白酶切斷序列的抗體的情形，相較於含有未經蛋白酶處理之抗體之結合評價用樣本，以含有經蛋白酶處理之抗體之結合評價用樣本測定時之結合於5C4-bio之人PD1之量比較多。亦即導入了蛋白酶切斷

序列的各抗體，因為蛋白酶處理而對於PD1之結合活性減弱，PD1游離且結合於5C4-bio。

【0215】 14-2-4 抗體之蛋白酶切斷確認(SDS-PAGE)

以SDS-PAGE確認14-2-3使用之抗體是否被蛋白酶處理切斷。將14-2-3製備之蛋白酶切斷抗體/未經蛋白酶處理之抗體當中的10μL與3.3μL之樣本緩衝液混合，並於95℃保溫5分鐘。然後使用Mini-PROTEAN TGX gel (4-20% 15well) (Bio-Rad #456-1096)進行電泳，以Sample Blue Safe Stain (novex, LC6065)將蛋白質染色。其結果示於第27圖。如第27圖所示，導入了蛋白酶切斷序列之各抗體，已被蛋白酶處理切斷。

【0216】 14-2-5 蛋白酶處理前後之抗體之PD1結合評價

也依其他方法測定已導入了蛋白酶切斷序列之各抗體在蛋白酶處理前後之對於PD1之結合活性。

將14-2-1製備之經蛋白酶處理之抗體或未經蛋白酶處理之抗體10μL與PBS 70μL混合，作為PD1結合測定樣本。樣本之PD1結合評價以BioLayer Interferometry (BLI法)評價。將14-2-1製備之經蛋白酶處理之抗體/未經蛋白酶處理之抗體與人PD1 (250nM)分別注入到Tilted bottom (TW384) Microplates(ForteBio、18-5076)的不同孔。使用PBS來水合Protein G感測器(ForteBio, 18-0022)，以30℃之設定以Octet RED 384實施測定。以裝有PBS之孔實施30秒基線測定，之後使抗體結合於Protein G感測器200秒。再度以裝有PBS之孔實施30秒基線測定，之後以裝有人PD1之孔測定180秒結合，以裝有PBS之孔測定180秒解離。顯示結合狀態的即時結合軸示於第28圖。如第28圖所示，使用已導入了蛋白酶切斷序列之各抗體時，相較於未經蛋白酶處理之抗體，經蛋白酶處理之抗體之人PD1結合量減少。

【0217】 14-3.導入了蛋白酶切斷序列之抗人PD1中和抗體與配體(人PD1)

之複合體中，利用蛋白酶所為之配體釋放評價

14-3-1　配體存在下之蛋白酶處理

於14-1製備之抗體(終濃度0.100mg/mL)中添加10μL以PBS製備成6.67μM之人PD1，製備成抗體-PD1複合體液。蛋白酶處理樣本，係於抗體-PD1複合體液中加入10μL 之以PBS製備為5.28μg/mL之重組之人Matriptase/ST14 Catalytic Domain (hMT-SP1, R&D systems 3946-SE-010) ，蛋白酶非處理樣本，則僅添加PBS10μL。反應時蛋白酶之終濃度為0.528μg/mL。將各樣本於37℃保溫12小時。

【0218】　14-3-2　蛋白酶處理後之PD1釋放之評價

使用實施例14-2-2製備之生物素化抗人PD1中和抗體 (5C4-bio)，以BioLayer Interferometry(BLI法)來評價未與抗體形成複合體之PD1之量。

將14-3-1製備之各樣本、5C4-bio、PBS分別注入到Tilted bottom (TW384) Micro plates(ForteBio、18-5076)之不同孔。使用PBS將鏈黴親和素生物感測器(ForteBio, 18-0009)水合，於30℃之設定以Octet RED 384測定。以裝有PBS之孔實施30秒基線測定，之後使5C4-bio結合於鏈黴親和素感測器200秒。再度以裝有PBS的孔實施30秒基線測定，以裝有蛋白酶處理樣本或蛋白酶未處理樣本之孔測定180秒結合，並以裝有PBS之孔測定180秒解離。顯示結合狀態之即時結合軸示於第29圖。如第29圖所示，導入了蛋白酶切斷序列之各抗體之情形，相較於蛋白酶未處理樣本，蛋白酶處理樣本中，結合於5C4-bio之人PD1之量增加。亦即，由於蛋白酶處理使各抗體對於PD1之結合活性減弱，PD1從抗體-PD1複合體游離並釋放。

【0219】　實施例15　已導入蛋白酶切斷序列之抗人PD1中和抗體與人PD1之融合蛋白質(抗PD1中和抗體-PD1融合蛋白質)之製作及評價

15-1.抗人PD1中和抗體與人PD1之融合蛋白質之製作

在實施例14-1製作之抗體之重鏈或重鏈改變體之N末端，介隔由甘胺酸-絲胺

酸聚合物(序列編號：321)構成之可動連結子來連接人PD1序列(序列編號：320)，製出PD1融合重鏈(表15)。

【0220】 【表12】

PD1融合重鏈

重鏈/重鏈改變體	有無插入蛋白酶切斷序列	PD1融合重鏈
5C4HA12aa-G1T4 (序列編號 ：304)	有	hPD15C4HA12aa-G1T4 (序列編號 ：323)
5C4HE12aa-G1T4E (重鏈序列編號 ：305)	有	hPD15C4HE12aa-G1T4E (序列編號 ：324)

【0221】 又，於實施例14-1製作之抗體之輕鏈或輕鏈改變體之N末端，介隔由甘胺酸-絲胺酸聚合物(序列編號：321)構成之可動連結子來連接人PD1序列(序列編號：320)，製作成PD1融合輕鏈 (表16)。

【0222】 【表13】

PD1融合輕鏈

輕鏈/輕鏈改變體	有無插入蛋白酶切斷序列	PD1融合輕鏈
5C4LH12aa-KT0 (序列編號 ：322)	無	hPD15C4LH12aa-KT0 (序列編號 ：325)
5C4LI12aa-KT0 (序列編號 ：306)	有	hPD15C4LI12aa-KT0 (序列編號 ：326)
5C4LC12aa-KT0 (序列編號 ：307)	有	hPD15C4LC12aa-KT0 (序列編號 ：327)
5C4LD12aa-KT0 (序列編號 ：308)	有	hPD15C4LD12aa-KT0 (序列編號 ：328)
5C4LE12aa-KT0E (序列編號 ：310)	有	hPD15C4LE12aa-KT0E (序列編號 ：329)
5C4LB12aa-KT0B (序列編號 ：311)	有	hPD15C4LB12aa-KT0B (序列編號 ：330)
5C4LF12aa-KT0F (序列編號 ：312)	有	hPD15C4LF12aa-KT0F (序列編號 ：331)
5C4LG12aa-KT0G (序列編號 ：313)	有	hPD15C4LG12aa-KT0G (序列編號 ：332)
5C4LJ12aa-KT0J (序列編號 ：314)	有	hPD15C4LJ12aa-KT0J (序列編號 ：333)
5C4LK12aa-KT0K (序列編號 ：315)	有	hPD15C4LK12aa-KT0K (序列編號 ：334)

【0223】 將表15之PD1融合重鏈與輕鏈5C4L-KT0、或表16之PD1融合輕鏈與重鏈5C4H-G1T4組合而得的下列之抗PD1中和抗體-PD1融合蛋白質：

hPD15C4HA12aa-G1T4/5C4L-KT0(PD1融合重鏈序列編號：323、輕鏈序列編號：298)

hPD15C4HE12aa-G1T4E/5C4L-KT0(PD1融合重鏈序列編號：324、輕鏈序列編號：298)

5C4H-G1T4/hPD15C4LH12aa-KT0(重鏈序列編號：297、輕鏈序列編號：325)

5C4H-G1T4/hPD15C4LI12aa-KT0(重鏈序列編號：297、PD1融合輕鏈序列編

號：326)

5C4H-G1T4/hPD15C4LC12aa-KT0(重鏈序列編號：297、PD1融合輕鏈序列編號：327)

5C4H-G1T4/hPD15C4LD12aa-KT0(重鏈序列編號：297、PD1融合輕鏈序列編號：328)

5C4H-G1T4/hPD15C4LE12aa-KT0E(重鏈序列編號：297、PD1融合輕鏈序列編號：329)

5C4H-G1T4/hPD15C4LB12aa-KT0B(重鏈序列編號：297、PD1融合輕鏈序列編號：330)

5C4H-G1T4/hPD15C4LF12aa-KT0F(重鏈序列編號：297、PD1融合輕鏈序列編號：331)

5C4H-G1T4/hPD15C4LG12aa-KT0G(重鏈序列編號：297、PD1融合輕鏈序列編號：332)

5C4H-G1T4/hPD15C4LJ12aa-KT0J(重鏈序列編號：297、PD1融合輕鏈序列編號：333)

5C4H-G1T4/hPD15C4LK12aa-KT0K(重鏈序列編號：297、PD1融合輕鏈序列編號：334)

依該技術領域中有通常知識者公知之方法以使用了Expi293 (Life Technologies)的暫時性表現予以表現，並依使用了Protein A之該技術領域中有通常知識者公知之方法精製。又，針對不含蛋白酶切斷序列之作為對照抗體之5C4H-G1T4/5C4L-KT0(重鏈序列編號：297、輕鏈序列編號：298))，同樣地表現及精製。

【0224】 15-2.抗PD1中和抗體-PD1融合蛋白質之利用蛋白酶所為之切斷評價

15-2-1　蛋白酶處理

經蛋白酶處理之融合蛋白質，係於15-1製備之融合蛋白質30μg加入4.9μL 之以PBS製備為16.7μg/mL之Recombinant Human Matriptase/ST14 Catalytic Domain (hMT-SP1, R&D systems 3946-SE-010)。未經蛋白酶處理之融合蛋白質，係在15-1製備之融合蛋白質30μg僅加入4.9μL 之PBS。經蛋白酶處理之融合蛋白質或未經蛋白酶處理之融合蛋白質於37℃保溫12小時。

【0225】　15-2-2　利用蛋白酶處理所為之PD1之游離評價

使用實施例14-2-2製備之生物素化抗人PD1中和抗體 (5C4-bio) 以BioLayer Interferometry (BLI法)來評價利用蛋白酶處理所為之PD1游離。

將15-2-1製備之經蛋白酶處理之融合蛋白質、未經蛋白酶處理之融合蛋白質、5C4-bio、PBS分別注入到Tilted bottom (TW384) Micro plates(ForteBio、18-5076)的不同孔。使用PBS將鏈黴親和素生物感測器(ForteBio, 18-0009)水合，以30℃之設定以Octet RED 384實施測定。於裝有PBS之孔實施30秒基線測定，之後，使5C4-bio結合於鏈黴親和素感測器200秒。再度於裝有PBS之孔實施30秒基線測定之後，以裝有經蛋白酶處理之融合蛋白質或未經蛋白酶處理之融合蛋白質之孔測定180秒結合，以裝有PBS之孔測定180秒解離。顯示結合狀態之即時結合軸示於第30圖。如第30圖所示，含有導入了蛋白酶切斷序列之抗體之抗體-PD1融合蛋白質之情形，相較於蛋白酶未處理樣本，蛋白酶處理樣本中，結合於5C4-bio之人PD1之量增加。亦即，由於蛋白酶處理使融合蛋白質中之抗體對於PD1之結合活性減弱，PD1從融合蛋白質游離。

【0226】　15-2-3　抗PD1中和抗體-PD1融合蛋白質之切斷之確認 (SDS-PAGE)

以SDS-PAGE確認15-2-1製備之經蛋白酶處理之融合蛋白質是否被蛋白酶處理切斷。將15-2-1製備之經蛋白酶處理之融合蛋白質或未經蛋白酶處理之融合

蛋白質中的10μL與3.3μL之樣本緩衝液混合，於95℃保溫5分鐘。然後使用Mini-PROTEAN TGX gel(4-20% 15孔) (Bio-Rad #456-1096)進行電泳，以Sample Blue Safe Stain(novex, LC6065)將蛋白質染色。其結果示於第31圖。如第31圖所示，含有導入了蛋白酶切斷序列之抗體之融合蛋白質，已被蛋白酶處理切斷。

【0227】 前述發明已為了幫助明確的理解使用實例及例示詳細記載，但是本說明書之記載及例示不應解釋為限定本發明之範圍。本說明書引用的全部專利文獻及科學文獻的揭示，其全體以參照明示的納入到本說明書內。

[產業利用性]

【0228】 本發明之配體結合分子，以結合配體的狀態運送到生物體內，在病症組織被切斷而減弱對於配體之結合，能將配體以病症組織專一性的釋放，故可將病症組織專一性的暴露於配體。又，該配體結合分子在運送時會抑制配體之生物活性，所以配體全身性作用的可能性減少，在病症治療方面極有用。

【符號說明】

無。

【序列表】

<110> 中外製藥股份有線公司(CHUGAI SEIYAKU KABUSHIKI KAISHA)

<120> 能夠調節配體結合活性的配體結合分子

<130> C1-A1615-TW

<150> JP 2016-229882
<151> 2016-11-28

<160> 537

<170> PatentIn version 3.5

<210> 1
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20 25 30

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

Ala Val Ile Trp Phe Asp Gly Met Asn Lys Phe Tyr Val Asp Ser Val
50 55 60

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

65 70 75 80

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

Ala Arg Glu Gly Asp Gly Ser Gly Ile Tyr Tyr Tyr Tyr Gly Met Asp
100 105 110

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

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

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

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

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

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

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

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

Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp

245 250 255

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

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
275 280 285

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn
290 295 300

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
305 310 315 320

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro
325 330 335

Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
340 345 350

Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn
355 360 365

Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
370 375 380

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

Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys
405 410 415

Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys

420 425 430

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
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Ser Leu Ser Pro
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20 25 30

Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu
35 40 45

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

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

Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr Gly Ser Ser Pro
85 90 95

Ile Phe Thr Phe Gly Pro Gly Thr Lys Val Asp Ile Lys Arg Thr Val
100 105 110

Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys
115 120 125

Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg
130 135 140

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

Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser
165 170 175

Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys
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Lys Ser Phe Asn Arg Gly Glu Cys
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<212> PRT
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<220>
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<400> 4

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

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

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

Ala Val Ile Trp Phe Asp Gly Met Asn Lys Phe Tyr Val Asp Ser Val
50 55 60

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

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

Ala Arg Glu Gly Asp Gly Ser Gly Ile Tyr Tyr Tyr Tyr Gly Met Asp
100 105 110

Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Leu Ser Gly Arg
115 120 125

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

<210> 5
<211> 460
<212> PRT

<213> 人造序列

<220>
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<400> 5

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

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

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

Ala Val Ile Trp Phe Asp Gly Met Asn Lys Phe Tyr Val Asp Ser Val
    50                  55                  60

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

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

Ala Arg Glu Gly Asp Gly Ser Gly Ile Tyr Tyr Tyr Tyr Gly Met Asp
            100                 105                 110

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

Gly Arg Ser Asp Asn His Thr Lys Gly Pro Ser Val Phe Pro Leu Ala
    130                 135                 140

Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu
```

145 150 155 160

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

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

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

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

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

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

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

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

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

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

Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys

325 330 335

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

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

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

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

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

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

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

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

<210> 6
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<213> 人造序列

<220>
<223> 人造的合成序列

<400> 6

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

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

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

Ala Val Ile Trp Phe Asp Gly Met Asn Lys Phe Tyr Val Asp Ser Val
    50                  55                  60

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

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

Ala Arg Glu Gly Asp Gly Ser Gly Ile Tyr Tyr Tyr Tyr Gly Met Asp
            100                 105                 110

Val Trp Gly Gln Gly Thr Thr Val Thr Val Leu Ser Gly Arg Ser Asp
        115                 120                 125

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

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

Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly
                165                 170                 175
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Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser
180 185 190

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

<210> 7
<211> 460
<212> PRT
<213> 人造序列

<220>
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<400> 7

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

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

20 25 30

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

Ala Val Ile Trp Phe Asp Gly Met Asn Lys Phe Tyr Val Asp Ser Val
50 55 60

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

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

Ala Arg Glu Gly Asp Gly Ser Gly Ile Tyr Tyr Tyr Tyr Gly Met Asp
100 105 110

Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Leu Ser Gly Arg Ser
115 120 125

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

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

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

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

Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu

195 200 205

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

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

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

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

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

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

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

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

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

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

Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val

370 375 380

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

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

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

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

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

<210> 8
<211> 460
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 8

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

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

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

Ala Val Ile Trp Phe Asp Gly Met Asn Lys Phe Tyr Val Asp Ser Val
50 55 60

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

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

Ala Arg Glu Gly Asp Gly Ser Gly Ile Tyr Tyr Tyr Tyr Gly Met Asp
100 105 110

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

Arg Ser Asp Asn His Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala
130 135 140

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

<210> 9
<211> 460
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 9

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

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

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

Ala Val Ile Trp Phe Asp Gly Met Asn Lys Phe Tyr Val Asp Ser Val
50 55 60

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

65 70 75 80

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

Ala Arg Glu Gly Asp Gly Ser Gly Ile Tyr Tyr Tyr Tyr Gly Met Asp
100 105 110

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

Ser Gly Arg Ser Asp Asn His Lys Gly Pro Ser Val Phe Pro Leu Ala
130 135 140

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

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

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

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

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

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

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

245 250 255

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

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

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

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

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

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

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

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

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

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

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

420 425 430

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

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

<210> 10
<211> 460
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 10

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

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

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

Ala Val Ile Trp Phe Asp Gly Met Asn Lys Phe Tyr Val Asp Ser Val
50 55 60

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

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

Ala Arg Glu Gly Asp Gly Ser Gly Ile Tyr Tyr Tyr Tyr Gly Met Asp
100 105 110

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

Leu Ser Gly Arg Ser Asp Asn His Gly Pro Ser Val Phe Pro Leu Ala
130 135 140

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

<210> 11
<211> 460
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 11

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

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

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

Ala Val Ile Trp Phe Asp Gly Met Asn Lys Phe Tyr Val Asp Ser Val
50 55 60

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

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

Ala Arg Glu Gly Asp Gly Ser Gly Ile Tyr Tyr Tyr Tyr Gly Met Asp
100 105 110

Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Ala Ser Leu Ser

115 120 125

Gly Arg Ser Asp Asn His Gly Lys Gly Pro Ser Val Phe Pro Leu Ala
130 135 140

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

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

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

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

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

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

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

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

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

Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr

290 295 300

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

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

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

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

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

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

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

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

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

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

<210> 12

<211> 460
<212> PRT
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<220>
<223> 人造的合成序列

<400> 12

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

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

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

Ala Val Ile Trp Phe Asp Gly Met Asn Lys Phe Tyr Val Asp Ser Val
50 55 60

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

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

Ala Arg Glu Gly Asp Gly Ser Gly Ile Tyr Tyr Tyr Tyr Gly Met Asp
100 105 110

Val Trp Gly Gln Gly Thr Thr Val Thr Val Leu Ser Gly Arg Ser Asp
115 120 125

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

<210> 13
<211> 460
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 13

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

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

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

Ala Val Ile Trp Phe Asp Gly Met Asn Lys Phe Tyr Val Asp Ser Val
    50                  55                  60

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

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

Ala Arg Glu Gly Asp Gly Ser Gly Ile Tyr Tyr Tyr Tyr Gly Met Asp
            100                 105                 110

Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Leu Ser Gly Arg Ser
        115                 120                 125

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

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

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

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

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

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

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

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

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

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

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

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

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

Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser

340 345 350

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

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

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

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

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

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

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

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<400> 14

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

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

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

Ala Val Ile Trp Phe Asp Gly Met Asn Lys Phe Tyr Val Asp Ser Val
    50                  55                  60

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

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

Ala Arg Glu Gly Asp Gly Ser Gly Ile Tyr Tyr Tyr Tyr Gly Met Asp
            100                 105                 110

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

Arg Ser Asp Asn His Gly Thr Lys Gly Pro Ser Val Phe Pro Leu Ala
    130                 135                 140

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

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

Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser
            180                 185                 190
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Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu
195 200 205

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Ser
20 25 30

Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu

35 40 45

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

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

Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr Gly Ser Ser Pro
85 90 95

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

Arg Ser Asp Asn His Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe
115 120 125

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

Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val
145 150 155 160

Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln
165 170 175

Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser
180 185 190

Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala Cys Glu Val Thr His
195 200 205

Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys

210 215 220

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<400> 16

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

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Ser
20 25 30

Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu
35 40 45

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

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

Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr Gly Ser Ser Pro
85 90 95

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

Ser Gly Arg Ser Asp Asn His Val Ala Ala Pro Ser Val Phe Ile Phe
115 120 125

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

Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val
145 150 155 160

Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln
165 170 175

Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser
180 185 190

Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala Cys Glu Val Thr His
195 200 205

Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
210 215 220

<210> 17
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<400> 17

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

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Ser
20 25 30

Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu

35 40 45

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

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

Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr Gly Ser Ser Pro
85 90 95

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

Asp Asn His Ile Lys Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe
115 120 125

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

Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val
145 150 155 160

Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln
165 170 175

Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser
180 185 190

Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala Cys Glu Val Thr His
195 200 205

Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys

210 215 220

<210> 18
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<400> 18

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

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Ser
20 25 30

Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu
35 40 45

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

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

Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr Gly Ser Ser Pro
85 90 95

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

Ser Asp Asn His Lys Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe
115 120 125

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

Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val
145 150 155 160

Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln
165 170 175

Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser
180 185 190

Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala Cys Glu Val Thr His
195 200 205

Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
210 215 220

<210> 19
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<400> 19

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

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Ser
20 25 30

Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu

35 40 45

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

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

Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr Gly Ser Ser Pro
85 90 95

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

Gly Arg Ser Asp Asn His Thr Val Ala Ala Pro Ser Val Phe Ile Phe
115 120 125

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

Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val
145 150 155 160

Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln
165 170 175

Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser
180 185 190

Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala Cys Glu Val Thr His
195 200 205

Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys

210 215 220

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<400> 20

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

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Ser
20 25 30

Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu
35 40 45

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

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

Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr Gly Ser Ser Pro
85 90 95

Ile Phe Thr Phe Gly Pro Gly Thr Lys Val Asp Ile Lys Arg Thr Val
100 105 110

Leu Ser Gly Arg Ser Asp Asn His Ala Ala Pro Ser Val Phe Ile Phe
115 120 125

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

Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val
145 150 155 160

Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln
165 170 175

Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser
180 185 190

Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala Cys Glu Val Thr His
195 200 205

Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
210 215 220

<210> 21
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<220>
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<400> 21

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

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Ser
20 25 30

Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu

35 40 45

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

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

Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr Gly Ser Ser Pro
85 90 95

Ile Phe Thr Phe Gly Pro Gly Thr Lys Val Asp Ile Lys Arg Thr Val
100 105 110

Ala Leu Ser Gly Arg Ser Asp Asn His Ala Pro Ser Val Phe Ile Phe
115 120 125

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

Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val
145 150 155 160

Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln
165 170 175

Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser
180 185 190

Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala Cys Glu Val Thr His
195 200 205

Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys

210 215 220

<210> 22
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<400> 22

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

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Ser
20 25 30

Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu
35 40 45

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

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

Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr Gly Ser Ser Pro
85 90 95

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

Gly Arg Ser Asp Asn His Gly Val Ala Ala Pro Ser Val Phe Ile Phe
115 120 125

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

Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val
145 150 155 160

Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln
165 170 175

Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser
180 185 190

Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala Cys Glu Val Thr His
195 200 205

Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
210 215 220

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<400> 23

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

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

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

35 40 45

Ala Val Ile Trp Phe Asp Gly Met Asn Lys Phe Tyr Val Asp Ser Val
50 55 60

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

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

Ala Arg Glu Gly Asp Gly Ser Gly Ile Tyr Tyr Tyr Tyr Gly Met Asp
100 105 110

Val Trp Gly Gln Gly Thr Thr Val Thr Val Gly Leu Ser Gly Arg Ser
115 120 125

Asp Asn His Gly Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro
130 135 140

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

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

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

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

Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser

210 215 220

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

His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser
245 250 255

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

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

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

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

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

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

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

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

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

385 390 395 400

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

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

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

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

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<211> 464
<212> PRT
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<220>
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<400> 24

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

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

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

Ala Val Ile Trp Phe Asp Gly Met Asn Lys Phe Tyr Val Asp Ser Val
50 55 60

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

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

Ala Arg Glu Gly Asp Gly Ser Gly Ile Tyr Tyr Tyr Tyr Gly Met Asp
100 105 110

Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Gly Leu Ser Gly Arg
115 120 125

Ser Asp Asn His Gly Ser Ser Ser Ala Ser Thr Lys Gly Pro Ser Val
130 135 140

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

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

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

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

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

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

Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly
245 250 255

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

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

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

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

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

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

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

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

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

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

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

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

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

<210> 25
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<400> 25

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

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

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

Ala Val Ile Trp Phe Asp Gly Met Asn Lys Phe Tyr Val Asp Ser Val
50 55 60

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

Leu Glu Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Ile Tyr Tyr Cys

85 90 95

Ala Arg Glu Gly Asp Gly Ser Gly Ile Tyr Tyr Tyr Tyr Gly Met Asp
100 105 110

Val Trp Gly Gln Gly Thr Thr Val Thr Val Gly Ser Gly Leu Ser Gly
115 120 125

Arg Ser Asp Asn His Gly Ser Ser Ser Ser Ala Ser Thr Lys Gly Pro
130 135 140

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

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

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

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

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

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

Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu
245 250 255

Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu

260 265 270

Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser
275 280 285

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

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

Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn
325 330 335

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

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

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

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

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

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

Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val

435 440 445

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

Ser Pro
465

<210> 26
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<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 26

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

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

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

Ala Val Ile Trp Phe Asp Gly Met Asn Lys Phe Tyr Val Asp Ser Val
50 55 60

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

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

Ala Arg Glu Gly Asp Gly Ser Gly Ile Tyr Tyr Tyr Tyr Gly Met Asp
100 105 110

Val Trp Gly Gln Gly Thr Thr Val Thr Val Gly Gly Ser Gly Leu Ser
115 120 125

Gly Arg Ser Asp Asn His Gly Ser Ser Gly Ser Ser Ala Ser Thr Lys
130 135 140

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

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

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

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

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

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

Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu
245 250 255

Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
260 265 270

Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp
275 280 285

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

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn
305 310 315 320

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
325 330 335

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

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

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

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

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

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

Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
435 440 445

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

Ser Leu Ser Pro
465

<210> 27
<211> 470
<212> PRT
<213> 人造序列

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<400> 27

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

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

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

Ala Val Ile Trp Phe Asp Gly Met Asn Lys Phe Tyr Val Asp Ser Val
50 55 60

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

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

Ala Arg Glu Gly Asp Gly Ser Gly Ile Tyr Tyr Tyr Tyr Gly Met Asp

100 105 110

Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Gly Gly Ser Gly Leu
115 120 125

Ser Gly Arg Ser Asp Asn His Gly Ser Ser Gly Thr Ser Ser Ala Ser
130 135 140

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

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

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

His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser
195 200 205

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

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

Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala
245 250 255

Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro
260 265 270

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

275 280 285

Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val
290 295 300

Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln
305 310 315 320

Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln
325 330 335

Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala
340 345 350

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

Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr
370 375 380

Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser
385 390 395 400

Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr
405 410 415

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

Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe
435 440 445

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

450 455 460

Ser Leu Ser Leu Ser Pro
465 470

<210> 28
<211> 10
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 28

Gly Leu Ser Gly Arg Ser Asp Asn His Gly
1 5 10

<210> 29
<211> 12
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 29

Ser Gly Leu Ser Gly Arg Ser Asp Asn His Gly Ser
1 5 10

<210> 30
<211> 14
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 30

Gly Ser Gly Leu Ser Gly Arg Ser Asp Asn His Gly Ser Ser
1 5 10

<210> 31
<211> 16
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 31

Gly Gly Ser Gly Leu Ser Gly Arg Ser Asp Asn His Gly Ser Ser Gly
1 5 10 15

<210> 32
<211> 18
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 32

Ser Gly Gly Ser Gly Leu Ser Gly Arg Ser Asp Asn His Gly Ser Ser
1 5 10 15

Gly Thr

<210> 33
<211> 472
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 33

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

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

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

Ala Val Ile Trp Phe Asp Gly Met Asn Lys Phe Tyr Val Asp Ser Val
50 55 60

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

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

Ala Arg Glu Gly Asp Gly Ser Gly Ile Tyr Tyr Tyr Tyr Gly Met Asp
100 105 110

Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Gly Gly Ser Gly Leu
115 120 125

Ser Gly Arg Ser Asp Asn His Gly Ser Ser Gly Thr Ser Ser Ala Ser
130 135 140

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

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

165 170 175

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

His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser
195 200 205

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

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

Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala
245 250 255

Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro
260 265 270

Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val
275 280 285

Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val
290 295 300

Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln
305 310 315 320

Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln
325 330 335

Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala

340 345 350

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

Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr
370 375 380

Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser
385 390 395 400

Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr
405 410 415

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

Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe
435 440 445

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

Ser Leu Ser Leu Ser Pro Gly Lys
465 470

<210> 34
<211> 6
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 34

Pro Leu Gly Leu Ala Gly
1 5

<210> 35
<211> 8
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 35

Val Pro Leu Ser Leu Thr Met Gly
1 5

<210> 36
<211> 4
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 36

Gly Gly Gly Ser
1

<210> 37
<211> 4
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 37

Gly Gly Ser Gly

1

<210> 38
<211> 4
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 38

Gly Ser Gly Gly
1

<210> 39
<211> 4
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 39

Ser Gly Gly Gly
1

<210> 40
<211> 4
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 40

Gly Ser Ser Gly
1

<210> 41
<211> 5
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 41

Gly Gly Gly Gly Ser
1 5

<210> 42
<211> 5
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 42

Gly Gly Gly Ser Gly
1 5

<210> 43
<211> 5
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 43

Gly Gly Ser Gly Gly
1 5

<210> 44

<211> 5
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 44

Gly Ser Gly Gly Gly
1 5

<210> 45
<211> 5
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 45

Gly Ser Gly Gly Ser
1 5

<210> 46
<211> 5
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 46

Ser Gly Gly Gly Gly
1 5

<210> 47
<211> 5
<212> PRT

<213> 人造序列

<220>
<223> 人造的合成序列

<400> 47

Gly Ser Ser Gly Gly
1 5

<210> 48
<211> 5
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 48

Gly Ser Gly Ser Gly
1 5

<210> 49
<211> 5
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 49

Ser Gly Gly Ser Gly
1 5

<210> 50
<211> 5
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 50

Gly Ser Ser Ser Gly
1 5

<210> 51
<211> 6
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 51

Gly Gly Gly Gly Gly Ser
1 5

<210> 52
<211> 6
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 52

Ser Gly Gly Gly Gly Gly
1 5

<210> 53
<211> 7
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 53

Gly Gly Gly Gly Gly Gly Ser
1 5

<210> 54
<211> 7
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 54

Ser Gly Gly Gly Gly Gly Gly
1 5

<210> 55
<211> 330
<212> PRT
<213> 智人(Homo sapiens)

<400> 55

Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys
1 5 10 15

Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr
20 25 30

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

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

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

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

Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys
100 105 110

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

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

Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp
145 150 155 160

Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu
165 170 175

Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu
180 185 190

His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn
195 200 205

Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly
210 215 220

Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu
225 230 235 240

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

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

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

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

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

Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
325 330

<210> 56
<211> 326
<212> PRT
<213> 智人(Homo sapiens)

<400> 56

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

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

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

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

50 55 60

Leu Ser Ser Val Val Thr Val Pro Ser Ser Asn Phe Gly Thr Gln Thr
65 70 75 80

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

Thr Val Glu Arg Lys Cys Cys Val Glu Cys Pro Pro Cys Pro Ala Pro
100 105 110

Pro Val Ala Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
115 120 125

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

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

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

Ser Thr Phe Arg Val Val Ser Val Leu Thr Val Val His Gln Asp Trp
180 185 190

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro
195 200 205

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

Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn

225 230 235 240

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

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

Thr Pro Pro Met Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys
275 280 285

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

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

Ser Leu Ser Pro Gly Lys
325

<210> 57
<211> 377
<212> PRT
<213> 智人(Homo sapiens)

<400> 57

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

Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr
20 25 30

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

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

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

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

Arg Val Glu Leu Lys Thr Pro Leu Gly Asp Thr Thr His Thr Cys Pro
            100                 105                 110

Arg Cys Pro Glu Pro Lys Ser Cys Asp Thr Pro Pro Pro Cys Pro Arg
        115                 120                 125

Cys Pro Glu Pro Lys Ser Cys Asp Thr Pro Pro Pro Cys Pro Arg Cys
    130                 135                 140

Pro Glu Pro Lys Ser Cys Asp Thr Pro Pro Pro Cys Pro Arg Cys Pro
145                 150                 155                 160

Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys
                165                 170                 175

Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val
            180                 185                 190

Val Val Asp Val Ser His Glu Asp Pro Glu Val Gln Phe Lys Trp Tyr
        195                 200                 205

Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu
    210                 215                 220
```

Gln Tyr Asn Ser Thr Phe Arg Val Val Ser Val Leu Thr Val Leu His
225 230 235 240

Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys
245 250 255

Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Thr Lys Gly Gln
260 265 270

Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met
275 280 285

Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro
290 295 300

Ser Asp Ile Ala Val Glu Trp Glu Ser Ser Gly Gln Pro Glu Asn Asn
305 310 315 320

Tyr Asn Thr Thr Pro Pro Met Leu Asp Ser Asp Gly Ser Phe Phe Leu
325 330 335

Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Ile
340 345 350

Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn Arg Phe Thr Gln
355 360 365

Lys Ser Leu Ser Leu Ser Pro Gly Lys
370 375

<210> 58
<211> 327

<212> PRT
<213> 智人(Homo sapiens)

<400> 58

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

Leu Ser Leu Ser Leu Gly Lys
                325
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<210> 59
<211> 462
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 59

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

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

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

Ala Val Ile Trp Phe Asp Gly Met Asn Lys Phe Tyr Val Asp Ser Val
50 55 60

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

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

Ala Arg Glu Gly Asp Gly Ser Gly Ile Tyr Tyr Tyr Tyr Gly Met Asp
100 105 110

Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Leu Ser Gly
115 120 125

Arg Ser Asp Asn His Gly Ser Ser Thr Lys Gly Pro Ser Val Phe Pro

130 135 140

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

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

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

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

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

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

His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser
245 250 255

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

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

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

Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val

305 310 315 320

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

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

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

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

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

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

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

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

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

<210> 60
<211> 468
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 60

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

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

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

Ala Val Ile Trp Phe Asp Gly Met Asn Lys Phe Tyr Val Asp Ser Val
50 55 60

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

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

Ala Arg Glu Gly Asp Gly Ser Gly Ile Tyr Tyr Tyr Tyr Gly Met Asp
100 105 110

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

Leu Ser Gly Arg Ser Asp Asn His Gly Ser Ser Gly Thr Ser Thr Lys
130 135 140

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

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

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

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

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

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

Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu
245 250 255

Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
260 265 270

Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp
275 280 285

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

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn
305 310 315 320

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
325 330 335

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

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

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

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

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

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

Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
435 440 445

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

Ser Leu Ser Pro
465

<210> 61
<211> 11
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 61

Gly Leu Ser Gly Arg Ser Asp Asn His Gly Ser
1 5 10

<210> 62
<211> 20
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 62

Thr Val Ser Ser Gly Leu Ser Gly Arg Ser Asp Asn His Gly Ser Ser
1 5 10 15

Thr Lys Gly Pro
20

<210> 63
<211> 17
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 63

Gly Gly Ser Gly Leu Ser Gly Arg Ser Asp Asn His Gly Ser Ser Gly
1 5 10 15

Thr

<210> 64

<211> 26
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 64

Thr Val Ser Ser Gly Gly Ser Gly Leu Ser Gly Arg Ser Asp Asn His
1 5 10 15

Gly Ser Ser Gly Thr Ser Thr Lys Gly Pro
20 25

<210> 65
<211> 454
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 65

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

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

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

Ala Val Ile Trp Phe Asp Gly Met Asn Lys Phe Tyr Val Asp Ser Val
50 55 60

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

65 70 75 80

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

Ala Arg Glu Gly Asp Gly Ser Gly Ile Tyr Tyr Tyr Tyr Gly Met Asp
100 105 110

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

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

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

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

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

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

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

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

Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp

245 250 255

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

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
275 280 285

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn
290 295 300

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
305 310 315 320

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro
325 330 335

Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
340 345 350

Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn
355 360 365

Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
370 375 380

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

Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys
405 410 415

Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys

420 425 430

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
435 440 445

Ser Leu Ser Pro Gly Lys
450

<210> 66
<211> 12
<212> PRT
<213> 人造序列

<220>
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<400> 66

Thr Ser Thr Ser Gly Arg Ser Ala Asn Pro Arg Gly
1 5 10

<210> 67
<211> 13
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 67

Ile Ser Ser Gly Leu Leu Ser Gly Arg Ser Asp Asn His
1 5 10

<210> 68
<211> 18
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 68

Ala Val Gly Leu Leu Ala Pro Pro Gly Gly Leu Ser Gly Arg Ser Asp
1 5 10 15

Asn His

<210> 69
<211> 13
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 69

Gly Ala Gly Val Pro Met Ser Met Arg Gly Gly Ala Gly
1 5 10

<210> 70
<211> 13
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 70

Gly Ala Gly Ile Pro Val Ser Leu Arg Ser Gly Ala Gly
1 5 10

<210> 71
<211> 8
<212> PRT

<213> 人造序列

<220>
<223> 人造的合成序列

<400> 71

Gly Pro Leu Gly Ile Ala Gly Gln
1 5

<210> 72
<211> 10
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 72

Gly Gly Pro Leu Gly Met Leu Ser Gln Ser
1 5 10

<210> 73
<211> 6
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 73

Pro Leu Gly Leu Trp Ala
1 5

<210> 74
<211> 13
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 74

Gly Ala Gly Arg Pro Phe Ser Met Ile Met Gly Ala Gly
1 5 10

<210> 75
<211> 13
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 75

Gly Ala Gly Val Pro Leu Ser Leu Thr Met Gly Ala Gly
1 5 10

<210> 76
<211> 13
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 76

Gly Ala Gly Val Pro Leu Ser Leu Tyr Ser Gly Ala Gly
1 5 10

<210> 77
<211> 6
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 77

Ala Ala Asn Leu Arg Asn
1 5

<210> 78
<211> 6
<212> PRT
<213> 人造序列

<220>
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<400> 78

Ala Gln Ala Tyr Val Lys
1 5

<210> 79
<211> 6
<212> PRT
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<220>
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<400> 79

Ala Ala Asn Tyr Met Arg
1 5

<210> 80
<211> 6
<212> PRT
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<220>
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<400> 80

Ala Ala Ala Leu Thr Arg
1 5

<210> 81
<211> 6
<212> PRT
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<220>
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<400> 81

Ala Gln Asn Leu Met Arg
1 5

<210> 82
<211> 6
<212> PRT
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<220>
<223> 人造的合成序列

<400> 82

Ala Ala Asn Tyr Thr Lys
1 5

<210> 83
<211> 16
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 83

Gly Ala Gly Pro Gln Gly Leu Ala Gly Gln Arg Gly Ile Val Ala Gly

1 5 10 15

<210> 84
<211> 8
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 84

Pro Arg Phe Lys Ile Ile Gly Gly
1 5

<210> 85
<211> 8
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 85

Pro Arg Phe Arg Ile Ile Gly Gly
1 5

<210> 86
<211> 9
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 86

Gly Ala Gly Ser Gly Arg Ser Ala Gly
1 5

<210> 87
<211> 5
<212> PRT
<213> 人造序列

<220>
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<400> 87

Ser Gly Arg Ser Ala
1 5

<210> 88
<211> 6
<212> PRT
<213> 人造序列

<220>
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<400> 88

Gly Ser Gly Arg Ser Ala
1 5

<210> 89
<211> 5
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 89

Ser Gly Lys Ser Ala
1 5

<210> 90

<211> 5
<212> PRT
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<220>
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<400> 90

Ser Gly Arg Ser Ser
1 5

<210> 91
<211> 5
<212> PRT
<213> 人造序列

<220>
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<400> 91

Ser Gly Arg Arg Ala
1 5

<210> 92
<211> 5
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<220>
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<400> 92

Ser Gly Arg Asn Ala
1 5

<210> 93
<211> 5
<212> PRT

<213> 人造序列

<220>
<223> 人造的合成序列

<400> 93

Ser Gly Arg Lys Ala
1 5

<210> 94
<211> 6
<212> PRT
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<220>
<223> 人造的合成序列

<400> 94

Gln Arg Gly Arg Ser Ala
1 5

<210> 95
<211> 17
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 95

Gly Ala Gly Ser Leu Leu Lys Ser Arg Met Val Pro Asn Phe Asn Ala
1 5 10 15

Gly

<210> 96

<211> 6
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 96

Thr Gln Gly Ala Ala Ala
1 5

<210> 97
<211> 6
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 97

Gly Ala Ala Ala Ala Ala
1 5

<210> 98
<211> 6
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 98

Gly Ala Gly Ala Ala Gly
1 5

<210> 99
<211> 6
<212> PRT

<213> 人造序列

<220>
<223> 人造的合成序列

<400> 99

Ala Ala Ala Ala Ala Gly
1 5

<210> 100
<211> 6
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 100

Leu Cys Gly Ala Ala Ile
1 5

<210> 101
<211> 6
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 101

Phe Ala Gln Ala Leu Gly
1 5

<210> 102
<211> 6
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 102

Leu Leu Gln Ala Asn Pro
1 5

<210> 103
<211> 6
<212> PRT
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<220>
<223> 人造的合成序列

<400> 103

Leu Ala Ala Ala Asn Pro
1 5

<210> 104
<211> 6
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 104

Leu Tyr Gly Ala Gln Phe
1 5

<210> 105
<211> 6
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 105

Leu Ser Gln Ala Gln Gly
1 5

<210> 106
<211> 6
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 106

Ala Ser Ala Ala Ser Gly
1 5

<210> 107
<211> 6
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 107

Phe Leu Gly Ala Ser Leu
1 5

<210> 108
<211> 6
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 108

Ala Tyr Gly Ala Thr Gly
1 5

<210> 109
<211> 6
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 109

Leu Ala Gln Ala Thr Gly
1 5

<210> 110
<211> 17
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 110

Gly Ala Gly Ser Gly Val Val Ile Ala Thr Val Ile Val Ile Thr Ala
1 5 10 15

Gly

<210> 111
<211> 8
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 111

Ala Pro Met Ala Glu Gly Gly Gly
1 5

<210> 112
<211> 8
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 112

Glu Ala Gln Gly Asp Lys Ile Ile
1 5

<210> 113
<211> 8
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 113

Leu Ala Phe Ser Asp Ala Gly Pro
1 5

<210> 114
<211> 7
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 114

Tyr Val Ala Asp Ala Pro Lys
1 5

<210> 115
<211> 5
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 115

Arg Arg Arg Arg Arg
1 5

<210> 116
<211> 6
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 116

Arg Arg Arg Arg Arg Arg
1 5

<210> 117
<211> 10
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 117

Gly Gln Ser Ser Arg His Arg Arg Ala Leu

1 5 10

<210> 118
<211> 9
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 118

Ser Ser Arg His Arg Arg Ala Leu Asp
1 5

<210> 119
<211> 14
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 119

Arg Lys Ser Ser Ile Ile Ile Arg Met Arg Asp Val Val Leu
1 5 10

<210> 120
<211> 15
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 120

Ser Ser Ser Phe Asp Lys Gly Lys Tyr Lys Lys Gly Asp Asp Ala
1 5 10 15

<210> 121
<211> 15
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 121

Ser Ser Ser Phe Asp Lys Gly Lys Tyr Lys Arg Gly Asp Asp Ala
1 5 10 15

<210> 122
<211> 4
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 122

Ile Glu Gly Arg
1

<210> 123
<211> 4
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 123

Ile Asp Gly Arg
1

<210> 124

<211> 7
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 124

Gly Gly Ser Ile Asp Gly Arg
1 5

<210> 125
<211> 8
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 125

Gly Pro Gln Gly Ile Ala Gly Gln
1 5

<210> 126
<211> 8
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 126

Gly Pro Gln Gly Leu Leu Gly Ala
1 5

<210> 127
<211> 5
<212> PRT

<213> 人造序列

<220>
<223> 人造的合成序列

<400> 127

Gly Ile Ala Gly Gln
1 5

<210> 128
<211> 7
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 128

Gly Pro Leu Gly Ile Ala Gly
1 5

<210> 129
<211> 8
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 129

Gly Pro Glu Gly Leu Arg Val Gly
1 5

<210> 130
<211> 8
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 130

Tyr Gly Ala Gly Leu Gly Val Val
1 5

<210> 131
<211> 8
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 131

Ala Gly Leu Gly Val Val Glu Arg
1 5

<210> 132
<211> 8
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 132

Ala Gly Leu Gly Ile Ser Ser Thr
1 5

<210> 133
<211> 8
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 133

Glu Pro Gln Ala Leu Ala Met Ser
1 5

<210> 134
<211> 8
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 134

Gln Ala Leu Ala Met Ser Ala Ile
1 5

<210> 135
<211> 8
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 135

Ala Ala Tyr His Leu Val Ser Gln
1 5

<210> 136
<211> 8
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 136

Met Asp Ala Phe Leu Glu Ser Ser
1 5

<210> 137
<211> 8
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 137

Glu Ser Leu Pro Val Val Ala Val
1 5

<210> 138
<211> 8
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 138

Ser Ala Pro Ala Val Glu Ser Glu
1 5

<210> 139
<211> 8
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 139

Asp Val Ala Gln Phe Val Leu Thr

1 5

<210> 140
<211> 8
<212> PRT
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<220>
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<400> 140

Val Ala Gln Phe Val Leu Thr Glu
1 5

<210> 141
<211> 8
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 141

Ala Gln Phe Val Leu Thr Glu Gly
1 5

<210> 142
<211> 8
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 142

Pro Val Gln Pro Ile Gly Pro Gln
1 5

<210> 143
<211> 6
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 143

Leu Val Pro Arg Gly Ser
1 5

<210> 144
<211> 447
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 144

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

Ser Leu Lys Ile Ser Cys Lys Gly Ser Gly Tyr Ser Phe Thr Thr Tyr
20 25 30

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

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

Gln Gly Gln Val Thr Met Ser Val Asp Lys Ser Ile Thr Thr Ala Tyr
65 70 75 80

Leu Gln Trp Asn Ser Leu Lys Ala Ser Asp Thr Ala Met Tyr Tyr Cys
85 90 95

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

Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe
115 120 125

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

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

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

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

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

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

Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Arg Arg Gly Pro
225 230 235 240

Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser
245 250 255

Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp
260 265 270

Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn
275 280 285

Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val
290 295 300

Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu
305 310 315 320

Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys
325 330 335

Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr
340 345 350

Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr
355 360 365

Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu
370 375 380

Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu
385 390 395 400

Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys
405 410 415

Ser Arg Trp Gln Glu Gly Asn Val Phe Ser Cys Ser Val Met His Glu
420 425 430

Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
435 440 445

<210> 145
<211> 214
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 145

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

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

Leu Ala Trp Tyr Gln Gln Lys Pro Glu Lys Ala Pro Lys Ser Leu Ile
35 40 45

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

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Asn Ile Tyr Pro Tyr
85 90 95

Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys Arg Thr Val Ala Ala
100 105 110

Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly
115 120 125

Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala
130 135 140

Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln
145 150 155 160

Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser
165 170 175

Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr
180 185 190

Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser
195 200 205

Phe Asn Arg Gly Glu Cys
210

<210> 146
<211> 461
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 146

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

Ser Leu Lys Ile Ser Cys Lys Gly Ser Gly Tyr Ser Phe Thr Thr Tyr
20 25 30

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

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

Gln Gly Gln Val Thr Met Ser Val Asp Lys Ser Ile Thr Thr Ala Tyr
65 70 75 80

Leu Gln Trp Asn Ser Leu Lys Ala Ser Asp Thr Ala Met Tyr Tyr Cys
85 90 95

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

Thr Leu Val Thr Val Ser Ser Ala Ser Gly Ser Gly Leu Ser Gly Arg
115 120 125

Ser Asp Asn His Gly Ser Ser Thr Lys Gly Pro Ser Val Phe Pro Leu
130 135 140

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

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

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

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

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

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

Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Arg Arg Gly Pro Ser Val
245 250 255

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

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

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

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

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

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

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

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

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

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

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

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

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

<210> 147
<211> 447
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 147

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

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

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

Ile Gly Tyr Ile Ser Tyr Ser Gly Ile Thr Thr Tyr Asn Pro Ser Leu
50 55 60

Lys Ser Arg Val Thr Met Leu Arg Asp Thr Ser Lys Asn Gln Phe Ser
65 70 75 80

Leu Arg Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Ser Leu Ala Arg Thr Thr Ala Met Asp Tyr Trp Gly Gln Gly
100 105 110

Ser Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe
115 120 125

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

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

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

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

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

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

Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Arg Arg Gly Pro
225 230 235 240

```
Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser
                245                 250                 255

Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp
            260                 265                 270

Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn
        275                 280                 285

Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val
    290                 295                 300

Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu
305                 310                 315                 320

Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys
                325                 330                 335

Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr
            340                 345                 350

Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr
        355                 360                 365

Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu
    370                 375                 380

Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu
385                 390                 395                 400

Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys
                405                 410                 415
```

Ser Arg Trp Gln Glu Gly Asn Val Phe Ser Cys Ser Val Met His Glu
420 425 430

Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
435 440 445

<210> 148
<211> 214
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 148

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

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

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

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

Ser Gly Ser Gly Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Ile Ala Thr Tyr Tyr Cys Gln Gln Gly Asn Thr Leu Pro Tyr
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala
100 105 110

Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly
115 120 125

Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala
130 135 140

Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln
145 150 155 160

Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser
165 170 175

Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr
180 185 190

Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser
195 200 205

Phe Asn Arg Gly Glu Cys
210

<210> 149
<211> 16
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 149

Gly Gly Gly Gly Ser Pro Leu Gly Leu Ala Gly Gly Gly Gly Gly Ser
1 5 10 15

<210> 150
<211> 18
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 150

Gly Gly Gly Gly Ser Gly Pro Leu Gly Ile Ala Gly Gln Gly Gly Gly
1 5 10 15

Gly Ser

<210> 151
<211> 16
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 151

Gly Gly Gly Gly Ser Pro Leu Gly Leu Trp Ala Gly Gly Gly Gly Ser
1 5 10 15

<210> 152
<211> 23
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 152

Gly Gly Gly Gly Ser Gly Ala Gly Val Pro Leu Ser Leu Tyr Ser Gly
1 5 10 15

Ala Gly Gly Gly Gly Gly Ser
20

<210> 153
<211> 463
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 153

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

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

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

Ile Gly Tyr Ile Ser Tyr Ser Gly Ile Thr Thr Tyr Asn Pro Ser Leu
50 55 60

Lys Ser Arg Val Thr Met Leu Arg Asp Thr Ser Lys Asn Gln Phe Ser
65 70 75 80

Leu Arg Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Ser Leu Ala Arg Thr Thr Ala Met Asp Tyr Trp Gly Gln Gly
100 105 110

Ser Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Pro Leu Gly Leu
115 120 125

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

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

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

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

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

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

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

Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Arg Arg Gly Pro
245 250 255

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

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

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

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

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

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

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

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

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

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

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

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

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

<210> 154
<211> 465
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 154

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

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

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

Ile Gly Tyr Ile Ser Tyr Ser Gly Ile Thr Thr Tyr Asn Pro Ser Leu
    50                  55                  60

Lys Ser Arg Val Thr Met Leu Arg Asp Thr Ser Lys Asn Gln Phe Ser
65                  70                  75                  80

Leu Arg Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Ser Leu Ala Arg Thr Thr Ala Met Asp Tyr Trp Gly Gln Gly
            100                 105                 110

Ser Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Pro Leu Gly
        115                 120                 125
```

Ile Ala Gly Gln Gly Gly Gly Gly Ser Ala Ser Thr Lys Gly Pro Ser
130 135 140

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

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

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

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

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

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

Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Arg Arg
245 250 255

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

Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His
275 280 285

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

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

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

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

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

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

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

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

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

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

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

Pro
465

<210> 155
<211> 463
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 155

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

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

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

Ile Gly Tyr Ile Ser Tyr Ser Gly Ile Thr Thr Tyr Asn Pro Ser Leu
    50                  55                  60

Lys Ser Arg Val Thr Met Leu Arg Asp Thr Ser Lys Asn Gln Phe Ser
65                  70                  75                  80

Leu Arg Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Ser Leu Ala Arg Thr Thr Ala Met Asp Tyr Trp Gly Gln Gly
            100                 105                 110

Ser Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Pro Leu Gly Leu
        115                 120                 125

Trp Ala Gly Gly Gly Gly Ser Ala Ser Thr Lys Gly Pro Ser Val Phe
    130                 135                 140
```

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

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

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

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

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

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

Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Arg Arg Gly Pro
245 250 255

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

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

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

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

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

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

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

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

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

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

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

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

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

<210> 156
<211> 470
<212> PRT
<213> 人造序列

<220>

<223> 人造的合成序列

<400> 156

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

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

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

Ile Gly Tyr Ile Ser Tyr Ser Gly Ile Thr Thr Tyr Asn Pro Ser Leu
    50                  55                  60

Lys Ser Arg Val Thr Met Leu Arg Asp Thr Ser Lys Asn Gln Phe Ser
65                  70                  75                  80

Leu Arg Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Ser Leu Ala Arg Thr Thr Ala Met Asp Tyr Trp Gly Gln Gly
            100                 105                 110

Ser Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Ala Gly Val
        115                 120                 125

Pro Leu Ser Leu Tyr Ser Gly Ala Gly Gly Gly Gly Gly Ser Ala Ser
    130                 135                 140

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

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

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

His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser
195 200 205

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

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

Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala
245 250 255

Pro Glu Leu Arg Arg Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro
260 265 270

Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val
275 280 285

Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val
290 295 300

Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln
305 310 315 320

Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln
325 330 335

Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly
340 345 350

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

Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr
370 375 380

Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser
385 390 395 400

Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr
405 410 415

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

Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Glu Gly Asn Val Phe
435 440 445

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

Ser Leu Ser Leu Ser Pro
465 470

<210> 157
<211> 460
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 157

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

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

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

Ile Gly Tyr Ile Ser Tyr Ser Gly Ile Thr Thr Tyr Asn Pro Ser Leu
50 55 60

Lys Ser Arg Val Thr Met Leu Arg Asp Thr Ser Lys Asn Gln Phe Ser
65 70 75 80

Leu Arg Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Ser Leu Ala Arg Thr Thr Ala Met Asp Tyr Trp Gly Gln Gly
100 105 110

Ser Leu Val Thr Val Ser Ser Gly Ala Gly Ile Pro Val Ser Leu Arg
115 120 125

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

<210> 158
<211> 457
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 158

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

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

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

Ile Gly Tyr Ile Ser Tyr Ser Gly Ile Thr Thr Tyr Asn Pro Ser Leu
50 55 60

Lys Ser Arg Val Thr Met Leu Arg Asp Thr Ser Lys Asn Gln Phe Ser
65 70 75 80

Leu Arg Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Ser Leu Ala Arg Thr Thr Ala Met Asp Tyr Trp Gly Gln Gly
100 105 110

Ser Leu Val Thr Val Ser Ser Gly Gly Pro Leu Gly Met Leu Ser Gln
115 120 125

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

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

Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr
165 170 175

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

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

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

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

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

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

Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn
275 280 285

Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg
290 295 300

Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val
305 310 315 320

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

Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys
340 345 350

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

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

Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu
385 390 395 400

Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe
405 410 415

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

Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr
435 440 445

Thr Gln Lys Ser Leu Ser Leu Ser Pro
450 455

<210> 159
<211> 460
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 159

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

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

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

```
Ile Gly Tyr Ile Ser Tyr Ser Gly Ile Thr Thr Tyr Asn Pro Ser Leu
    50                  55                  60

Lys Ser Arg Val Thr Met Leu Arg Asp Thr Ser Lys Asn Gln Phe Ser
65                  70                  75                  80

Leu Arg Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Ser Leu Ala Arg Thr Thr Ala Met Asp Tyr Trp Gly Gln Gly
            100                 105                 110

Ser Leu Val Thr Val Ser Ser Gly Ala Gly Val Pro Leu Ser Leu Thr
        115                 120                 125

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

<210> 160
<211> 12
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 160

Thr Ser Thr Ser Gly Arg Ser Ala Asn Pro Arg Gly
1 5 10

<210> 161
<211> 119
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 161

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

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

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

Ile Gly Tyr Ile Ser Tyr Ser Gly Ile Thr Thr Tyr Asn Pro Ser Leu
50 55 60

Lys Ser Arg Val Thr Met Leu Arg Asp Thr Ser Lys Asn Gln Phe Ser
65 70 75 80

Leu Arg Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Ser Leu Ala Arg Thr Thr Ala Met Asp Tyr Trp Gly Gln Gly
100 105 110

Ser Leu Val Thr Val Ser Ser
115

<210> 162
<211> 328
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 162

Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys
1 5 10 15

Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr
20 25 30

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

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

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

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

Arg Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys
100 105 110

Pro Ala Pro Glu Leu Arg Arg Gly Pro Ser Val Phe Leu Phe Pro Pro
115 120 125

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

Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp
145 150 155 160

Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu
165 170 175

Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu
180 185 190

```
His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn
        195                 200                 205

Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly
    210                 215                 220

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

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

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

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

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

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

Gln Lys Ser Leu Ser Leu Ser Pro
                325
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<210> 163
<211> 131
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 163

```
Gln Val Gln Leu Gln Glu Ser Thr Ser Thr Ser Gly Arg Ser Ala Asn
1               5                  10                  15

Pro Arg Gly Gly Pro Gly Leu Val Arg Pro Ser Gln Thr Leu Ser Leu
            20                  25                  30

Thr Cys Thr Val Ser Gly Tyr Ser Ile Thr Ser Asp His Ala Trp Ser
        35                  40                  45

Trp Val Arg Gln Pro Pro Gly Arg Gly Leu Glu Trp Ile Gly Tyr Ile
    50                  55                  60

Ser Tyr Ser Gly Ile Thr Thr Tyr Asn Pro Ser Leu Lys Ser Arg Val
65                  70                  75                  80

Thr Met Leu Arg Asp Thr Ser Lys Asn Gln Phe Ser Leu Arg Leu Ser
                85                  90                  95

Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala Arg Ser Leu
            100                 105                 110

Ala Arg Thr Thr Ala Met Asp Tyr Trp Gly Gln Gly Ser Leu Val Thr
        115                 120                 125

Val Ser Ser
    130
```

<210> 164
<211> 131
<212> PRT
<213> 人造序列

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<223> 人造的合成序列

<400> 164

```
Gln Val Gln Leu Gln Glu Ser Gly Thr Ser Thr Ser Gly Arg Ser Ala
1               5                  10                  15

Asn Pro Arg Gly Pro Gly Leu Val Arg Pro Ser Gln Thr Leu Ser Leu
            20                  25                  30

Thr Cys Thr Val Ser Gly Tyr Ser Ile Thr Ser Asp His Ala Trp Ser
        35                  40                  45

Trp Val Arg Gln Pro Pro Gly Arg Gly Leu Glu Trp Ile Gly Tyr Ile
    50                  55                  60

Ser Tyr Ser Gly Ile Thr Thr Tyr Asn Pro Ser Leu Lys Ser Arg Val
65                  70                  75                  80

Thr Met Leu Arg Asp Thr Ser Lys Asn Gln Phe Ser Leu Arg Leu Ser
                85                  90                  95

Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala Arg Ser Leu
            100                 105                 110

Ala Arg Thr Thr Ala Met Asp Tyr Trp Gly Gln Gly Ser Leu Val Thr
        115                 120                 125

Val Ser Ser
    130
```

<210> 165
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<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 165

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

Ala Asn Pro Arg Gly Gly Leu Val Arg Pro Ser Gln Thr Leu Ser Leu
20 25 30

Thr Cys Thr Val Ser Gly Tyr Ser Ile Thr Ser Asp His Ala Trp Ser
35 40 45

Trp Val Arg Gln Pro Pro Gly Arg Gly Leu Glu Trp Ile Gly Tyr Ile
50 55 60

Ser Tyr Ser Gly Ile Thr Thr Tyr Asn Pro Ser Leu Lys Ser Arg Val
65 70 75 80

Thr Met Leu Arg Asp Thr Ser Lys Asn Gln Phe Ser Leu Arg Leu Ser
85 90 95

Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala Arg Ser Leu
100 105 110

Ala Arg Thr Thr Ala Met Asp Tyr Trp Gly Gln Gly Ser Leu Val Thr
115 120 125

Val Ser Ser
130

<210> 166
<211> 131

<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 166

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

Ser Ala Asn Pro Arg Gly Leu Val Arg Pro Ser Gln Thr Leu Ser Leu
            20                  25                  30

Thr Cys Thr Val Ser Gly Tyr Ser Ile Thr Ser Asp His Ala Trp Ser
        35                  40                  45

Trp Val Arg Gln Pro Pro Gly Arg Gly Leu Glu Trp Ile Gly Tyr Ile
    50                  55                  60

Ser Tyr Ser Gly Ile Thr Thr Tyr Asn Pro Ser Leu Lys Ser Arg Val
65                  70                  75                  80

Thr Met Leu Arg Asp Thr Ser Lys Asn Gln Phe Ser Leu Arg Leu Ser
                85                  90                  95

Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala Arg Ser Leu
            100                 105                 110

Ala Arg Thr Thr Ala Met Asp Tyr Trp Gly Gln Gly Ser Leu Val Thr
        115                 120                 125

Val Ser Ser
    130
```

<210> 167
<211> 131
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 167

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

Arg Ser Ala Asn Pro Arg Gly Val Arg Pro Ser Gln Thr Leu Ser Leu
20 25 30

Thr Cys Thr Val Ser Gly Tyr Ser Ile Thr Ser Asp His Ala Trp Ser
35 40 45

Trp Val Arg Gln Pro Pro Gly Arg Gly Leu Glu Trp Ile Gly Tyr Ile
50 55 60

Ser Tyr Ser Gly Ile Thr Thr Tyr Asn Pro Ser Leu Lys Ser Arg Val
65 70 75 80

Thr Met Leu Arg Asp Thr Ser Lys Asn Gln Phe Ser Leu Arg Leu Ser
85 90 95

Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala Arg Ser Leu
100 105 110

Ala Arg Thr Thr Ala Met Asp Tyr Trp Gly Gln Gly Ser Leu Val Thr
115 120 125

Val Ser Ser
130

<210> 168
<211> 131
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 168

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

Gly Arg Ser Ala Asn Pro Arg Gly Arg Pro Ser Gln Thr Leu Ser Leu
            20                  25                  30

Thr Cys Thr Val Ser Gly Tyr Ser Ile Thr Ser Asp His Ala Trp Ser
        35                  40                  45

Trp Val Arg Gln Pro Pro Gly Arg Gly Leu Glu Trp Ile Gly Tyr Ile
    50                  55                  60

Ser Tyr Ser Gly Ile Thr Thr Tyr Asn Pro Ser Leu Lys Ser Arg Val
65                  70                  75                  80

Thr Met Leu Arg Asp Thr Ser Lys Asn Gln Phe Ser Leu Arg Leu Ser
                85                  90                  95

Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala Arg Ser Leu
            100                 105                 110

Ala Arg Thr Thr Ala Met Asp Tyr Trp Gly Gln Gly Ser Leu Val Thr
        115                 120                 125
```

Val Ser Ser
130

<210> 169
<211> 131
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 169

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

Ser Gly Arg Ser Ala Asn Pro Arg Gly Pro Ser Gln Thr Leu Ser Leu
20 25 30

Thr Cys Thr Val Ser Gly Tyr Ser Ile Thr Ser Asp His Ala Trp Ser
35 40 45

Trp Val Arg Gln Pro Pro Gly Arg Gly Leu Glu Trp Ile Gly Tyr Ile
50 55 60

Ser Tyr Ser Gly Ile Thr Thr Tyr Asn Pro Ser Leu Lys Ser Arg Val
65 70 75 80

Thr Met Leu Arg Asp Thr Ser Lys Asn Gln Phe Ser Leu Arg Leu Ser
85 90 95

Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala Arg Ser Leu
100 105 110

Ala Arg Thr Thr Ala Met Asp Tyr Trp Gly Gln Gly Ser Leu Val Thr
115 120 125

Val Ser Ser
130

<210> 170
<211> 131
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 170

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

Thr Ser Gly Arg Ser Ala Asn Pro Arg Gly Ser Gln Thr Leu Ser Leu
20 25 30

Thr Cys Thr Val Ser Gly Tyr Ser Ile Thr Ser Asp His Ala Trp Ser
35 40 45

Trp Val Arg Gln Pro Pro Gly Arg Gly Leu Glu Trp Ile Gly Tyr Ile
50 55 60

Ser Tyr Ser Gly Ile Thr Thr Tyr Asn Pro Ser Leu Lys Ser Arg Val
65 70 75 80

Thr Met Leu Arg Asp Thr Ser Lys Asn Gln Phe Ser Leu Arg Leu Ser
85 90 95

Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala Arg Ser Leu
100 105 110

Ala Arg Thr Thr Ala Met Asp Tyr Trp Gly Gln Gly Ser Leu Val Thr
115 120 125

Val Ser Ser
130

<210> 171
<211> 131
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 171

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

Ser Thr Ser Gly Arg Ser Ala Asn Pro Arg Gly Gln Thr Leu Ser Leu
20 25 30

Thr Cys Thr Val Ser Gly Tyr Ser Ile Thr Ser Asp His Ala Trp Ser
35 40 45

Trp Val Arg Gln Pro Pro Gly Arg Gly Leu Glu Trp Ile Gly Tyr Ile
50 55 60

Ser Tyr Ser Gly Ile Thr Thr Tyr Asn Pro Ser Leu Lys Ser Arg Val
65 70 75 80

Thr Met Leu Arg Asp Thr Ser Lys Asn Gln Phe Ser Leu Arg Leu Ser
85 90 95

Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala Arg Ser Leu
100 105 110

Ala Arg Thr Thr Ala Met Asp Tyr Trp Gly Gln Gly Ser Leu Val Thr
115 120 125

Val Ser Ser
130

<210> 172
<211> 131
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 172

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

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

His Ala Trp Ser Trp Val Arg Gln Pro Thr Ser Thr Ser Gly Arg Ser
35 40 45

Ala Asn Pro Arg Gly Pro Gly Arg Gly Leu Glu Trp Ile Gly Tyr Ile
50 55 60

Ser Tyr Ser Gly Ile Thr Thr Tyr Asn Pro Ser Leu Lys Ser Arg Val
65 70 75 80

Thr Met Leu Arg Asp Thr Ser Lys Asn Gln Phe Ser Leu Arg Leu Ser
85 90 95

Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala Arg Ser Leu
100 105 110

Ala Arg Thr Thr Ala Met Asp Tyr Trp Gly Gln Gly Ser Leu Val Thr
115 120 125

Val Ser Ser
130

<210> 173
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<223> 人造的合成序列

<400> 173

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

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

His Ala Trp Ser Trp Val Arg Gln Pro Pro Thr Ser Thr Ser Gly Arg
35 40 45

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

Ser Tyr Ser Gly Ile Thr Thr Tyr Asn Pro Ser Leu Lys Ser Arg Val
65 70 75 80

Thr Met Leu Arg Asp Thr Ser Lys Asn Gln Phe Ser Leu Arg Leu Ser
85 90 95

Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala Arg Ser Leu
100 105 110

Ala Arg Thr Thr Ala Met Asp Tyr Trp Gly Gln Gly Ser Leu Val Thr
115 120 125

Val Ser Ser
130

<210> 174
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<220>
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<400> 174

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

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

His Ala Trp Ser Trp Val Arg Gln Pro Pro Gly Thr Ser Thr Ser Gly
35 40 45

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

Ser Tyr Ser Gly Ile Thr Thr Tyr Asn Pro Ser Leu Lys Ser Arg Val
65 70 75 80

Thr Met Leu Arg Asp Thr Ser Lys Asn Gln Phe Ser Leu Arg Leu Ser
85 90 95

Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala Arg Ser Leu
100 105 110

Ala Arg Thr Thr Ala Met Asp Tyr Trp Gly Gln Gly Ser Leu Val Thr
115 120 125

Val Ser Ser
130

<210> 175
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<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 175

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

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

His Ala Trp Ser Trp Val Arg Gln Pro Pro Gly Arg Thr Ser Thr Ser
35 40 45

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

Ser Tyr Ser Gly Ile Thr Thr Tyr Asn Pro Ser Leu Lys Ser Arg Val
65 70 75 80

Thr Met Leu Arg Asp Thr Ser Lys Asn Gln Phe Ser Leu Arg Leu Ser
85 90 95

Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala Arg Ser Leu
100 105 110

Ala Arg Thr Thr Ala Met Asp Tyr Trp Gly Gln Gly Ser Leu Val Thr
115 120 125

Val Ser Ser
130

<210> 176
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<212> PRT
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<220>
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<400> 176

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

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

His Ala Trp Ser Trp Val Arg Gln Pro Pro Gly Arg Gly Thr Ser Thr
35 40 45

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

Ser Tyr Ser Gly Ile Thr Thr Tyr Asn Pro Ser Leu Lys Ser Arg Val
65 70 75 80

Thr Met Leu Arg Asp Thr Ser Lys Asn Gln Phe Ser Leu Arg Leu Ser
85 90 95

Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala Arg Ser Leu
100 105 110

Ala Arg Thr Thr Ala Met Asp Tyr Trp Gly Gln Gly Ser Leu Val Thr
115 120 125

Val Ser Ser
130

<210> 177
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<212> PRT
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<220>
<223> 人造的合成序列

<400> 177

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

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

His Ala Trp Ser Trp Val Arg Gln Pro Pro Gly Arg Gly Leu Thr Ser
35 40 45

Thr Ser Gly Arg Ser Ala Asn Pro Arg Gly Glu Trp Ile Gly Tyr Ile
50 55 60

Ser Tyr Ser Gly Ile Thr Thr Tyr Asn Pro Ser Leu Lys Ser Arg Val
65 70 75 80

Thr Met Leu Arg Asp Thr Ser Lys Asn Gln Phe Ser Leu Arg Leu Ser
85 90 95

Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala Arg Ser Leu
100 105 110

Ala Arg Thr Thr Ala Met Asp Tyr Trp Gly Gln Gly Ser Leu Val Thr
115 120 125

Val Ser Ser
130

<210> 178
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<212> PRT
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<220>
<223> 人造的合成序列

<400> 178

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

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

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

Ile Gly Tyr Ile Ser Tyr Ser Gly Thr Ser Thr Ser Gly Arg Ser Ala
50 55 60

Asn Pro Arg Gly Ile Thr Thr Tyr Asn Pro Ser Leu Lys Ser Arg Val
65 70 75 80

Thr Met Leu Arg Asp Thr Ser Lys Asn Gln Phe Ser Leu Arg Leu Ser
85 90 95

Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala Arg Ser Leu
100 105 110

Ala Arg Thr Thr Ala Met Asp Tyr Trp Gly Gln Gly Ser Leu Val Thr
115 120 125

Val Ser Ser
130

<210> 179
<211> 131
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 179

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

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

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

Ile Gly Tyr Ile Ser Tyr Ser Gly Ile Thr Ser Thr Ser Gly Arg Ser
50 55 60

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

Thr Met Leu Arg Asp Thr Ser Lys Asn Gln Phe Ser Leu Arg Leu Ser
85 90 95

Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala Arg Ser Leu
100 105 110

Ala Arg Thr Thr Ala Met Asp Tyr Trp Gly Gln Gly Ser Leu Val Thr
115 120 125

Val Ser Ser
130

<210> 180
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<220>
<223> 人造的合成序列

<400> 180

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

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

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

Ile Gly Tyr Ile Ser Tyr Ser Gly Ile Thr Thr Ser Thr Ser Gly Arg
50 55 60

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

Thr Met Leu Arg Asp Thr Ser Lys Asn Gln Phe Ser Leu Arg Leu Ser
85 90 95

Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala Arg Ser Leu
100 105 110

Ala Arg Thr Thr Ala Met Asp Tyr Trp Gly Gln Gly Ser Leu Val Thr
115 120 125

Val Ser Ser
130

<210> 181
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<220>
<223> 人造的合成序列

<400> 181

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

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

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

Ile Gly Tyr Ile Ser Tyr Ser Gly Ile Thr Thr Thr Ser Thr Ser Gly
50 55 60

Arg Ser Ala Asn Pro Arg Gly Tyr Asn Pro Ser Leu Lys Ser Arg Val
65 70 75 80

Thr Met Leu Arg Asp Thr Ser Lys Asn Gln Phe Ser Leu Arg Leu Ser
85 90 95

Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala Arg Ser Leu
100 105 110

Ala Arg Thr Thr Ala Met Asp Tyr Trp Gly Gln Gly Ser Leu Val Thr
115 120 125

Val Ser Ser
130

<210> 182
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<400> 182

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

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

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

Ile Gly Tyr Ile Ser Tyr Ser Gly Ile Thr Thr Tyr Thr Ser Thr Ser
50 55 60

Gly Arg Ser Ala Asn Pro Arg Gly Asn Pro Ser Leu Lys Ser Arg Val
65 70 75 80

Thr Met Leu Arg Asp Thr Ser Lys Asn Gln Phe Ser Leu Arg Leu Ser
85 90 95

Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala Arg Ser Leu
100 105 110

Ala Arg Thr Thr Ala Met Asp Tyr Trp Gly Gln Gly Ser Leu Val Thr
115 120 125

Val Ser Ser
130

<210> 183
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<220>
<223> 人造的合成序列

<400> 183

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

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

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

Ile Gly Tyr Ile Ser Tyr Ser Gly Ile Thr Thr Tyr Asn Thr Ser Thr
50 55 60

Ser Gly Arg Ser Ala Asn Pro Arg Gly Pro Ser Leu Lys Ser Arg Val
65 70 75 80

Thr Met Leu Arg Asp Thr Ser Lys Asn Gln Phe Ser Leu Arg Leu Ser
85 90 95

Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala Arg Ser Leu
100 105 110

Ala Arg Thr Thr Ala Met Asp Tyr Trp Gly Gln Gly Ser Leu Val Thr
115 120 125

Val Ser Ser
130

<210> 184
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<220>
<223> 人造的合成序列

<400> 184

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

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

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

Ile Gly Tyr Ile Ser Tyr Ser Gly Ile Thr Thr Tyr Asn Pro Thr Ser
50 55 60

Thr Ser Gly Arg Ser Ala Asn Pro Arg Gly Ser Leu Lys Ser Arg Val
65 70 75 80

Thr Met Leu Arg Asp Thr Ser Lys Asn Gln Phe Ser Leu Arg Leu Ser
85 90 95

Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala Arg Ser Leu
100 105 110

Ala Arg Thr Thr Ala Met Asp Tyr Trp Gly Gln Gly Ser Leu Val Thr
115 120 125

Val Ser Ser
130

<210> 185
<211> 131
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 185

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

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

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

Ile Gly Tyr Ile Ser Tyr Ser Gly Ile Thr Thr Tyr Asn Pro Ser Thr
    50                  55                  60

Ser Thr Ser Gly Arg Ser Ala Asn Pro Arg Gly Leu Lys Ser Arg Val
65                  70                  75                  80

Thr Met Leu Arg Asp Thr Ser Lys Asn Gln Phe Ser Leu Arg Leu Ser
                85                  90                  95

Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala Arg Ser Leu
            100                 105                 110

Ala Arg Thr Thr Ala Met Asp Tyr Trp Gly Gln Gly Ser Leu Val Thr
        115                 120                 125

Val Ser Ser
    130
```

<210> 186
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<223> 人造的合成序列

<400> 186

```
Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Arg Pro Ser Gln
1               5                  10                  15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Tyr Ser Ile Thr Ser Asp
            20                  25                  30

His Ala Trp Ser Trp Val Arg Gln Pro Pro Gly Arg Gly Leu Glu Trp
        35                  40                  45

Ile Gly Tyr Ile Ser Tyr Ser Gly Ile Thr Thr Tyr Asn Pro Ser Leu
    50                  55                  60

Thr Ser Thr Ser Gly Arg Ser Ala Asn Pro Arg Gly Lys Ser Arg Val
65                  70                  75                  80

Thr Met Leu Arg Asp Thr Ser Lys Asn Gln Phe Ser Leu Arg Leu Ser
                85                  90                  95

Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala Arg Ser Leu
            100                 105                 110

Ala Arg Thr Thr Ala Met Asp Tyr Trp Gly Gln Gly Ser Leu Val Thr
        115                 120                 125

Val Ser Ser
    130
```

<210> 187
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<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 187

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Arg Pro Ser Gln
1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Tyr Ser Ile Thr Ser Asp
20 25 30

His Ala Trp Ser Trp Val Arg Gln Pro Pro Gly Arg Gly Leu Glu Trp
35 40 45

Ile Gly Tyr Ile Ser Tyr Ser Gly Ile Thr Thr Tyr Asn Pro Ser Leu
50 55 60

Lys Thr Ser Thr Ser Gly Arg Ser Ala Asn Pro Arg Gly Ser Arg Val
65 70 75 80

Thr Met Leu Arg Asp Thr Ser Lys Asn Gln Phe Ser Leu Arg Leu Ser
85 90 95

Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala Arg Ser Leu
100 105 110

Ala Arg Thr Thr Ala Met Asp Tyr Trp Gly Gln Gly Ser Leu Val Thr
115 120 125

Val Ser Ser
130

<210> 188
<211> 131

<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 188

```
Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Arg Pro Ser Gln
1               5                  10                  15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Tyr Ser Ile Thr Ser Asp
            20                  25                  30

His Ala Trp Ser Trp Val Arg Gln Pro Pro Gly Arg Gly Leu Glu Trp
        35                  40                  45

Ile Gly Tyr Ile Ser Tyr Ser Gly Ile Thr Thr Tyr Asn Pro Ser Leu
    50                  55                  60

Lys Ser Thr Ser Thr Ser Gly Arg Ser Ala Asn Pro Arg Gly Arg Val
65                  70                  75                  80

Thr Met Leu Arg Asp Thr Ser Lys Asn Gln Phe Ser Leu Arg Leu Ser
                85                  90                  95

Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala Arg Ser Leu
            100                 105                 110

Ala Arg Thr Thr Ala Met Asp Tyr Trp Gly Gln Gly Ser Leu Val Thr
        115                 120                 125

Val Ser Ser
    130
```

<210> 189
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<212> PRT
<213> 人造序列

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<223> 人造的合成序列

<400> 189

```
Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Arg Pro Ser Gln
1               5                  10                  15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Tyr Ser Ile Thr Ser Asp
            20                  25                  30

His Ala Trp Ser Trp Val Arg Gln Pro Pro Gly Arg Gly Leu Glu Trp
        35                  40                  45

Ile Gly Tyr Ile Ser Tyr Ser Gly Ile Thr Thr Tyr Asn Pro Ser Leu
    50                  55                  60

Lys Ser Arg Thr Ser Thr Ser Gly Arg Ser Ala Asn Pro Arg Gly Val
65                  70                  75                  80

Thr Met Leu Arg Asp Thr Ser Lys Asn Gln Phe Ser Leu Arg Leu Ser
                85                  90                  95

Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala Arg Ser Leu
            100                 105                 110

Ala Arg Thr Thr Ala Met Asp Tyr Trp Gly Gln Gly Ser Leu Val Thr
        115                 120                 125

Val Ser Ser
    130
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<220>
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<400> 190

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Arg Pro Ser Gln
1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Tyr Ser Ile Thr Ser Asp
20 25 30

His Ala Trp Ser Trp Val Arg Gln Pro Pro Gly Arg Gly Leu Glu Trp
35 40 45

Ile Gly Tyr Ile Ser Tyr Ser Gly Ile Thr Thr Tyr Asn Pro Ser Leu
50 55 60

Lys Ser Arg Val Thr Ser Thr Ser Gly Arg Ser Ala Asn Pro Arg Gly
65 70 75 80

Thr Met Leu Arg Asp Thr Ser Lys Asn Gln Phe Ser Leu Arg Leu Ser
85 90 95

Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala Arg Ser Leu
100 105 110

Ala Arg Thr Thr Ala Met Asp Tyr Trp Gly Gln Gly Ser Leu Val Thr
115 120 125

Val Ser Ser
130

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<400> 191

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Arg Pro Ser Gln
1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Tyr Ser Ile Thr Ser Asp
20 25 30

His Ala Trp Ser Trp Val Arg Gln Pro Pro Gly Arg Gly Leu Glu Trp
35 40 45

Ile Gly Tyr Ile Ser Tyr Ser Gly Ile Thr Thr Tyr Asn Pro Ser Leu
50 55 60

Lys Ser Arg Val Thr Thr Ser Thr Ser Gly Arg Ser Ala Asn Pro Arg
65 70 75 80

Gly Met Leu Arg Asp Thr Ser Lys Asn Gln Phe Ser Leu Arg Leu Ser
85 90 95

Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala Arg Ser Leu
100 105 110

Ala Arg Thr Thr Ala Met Asp Tyr Trp Gly Gln Gly Ser Leu Val Thr
115 120 125

Val Ser Ser
130

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<400> 192

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Arg Pro Ser Gln
1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Tyr Ser Ile Thr Ser Asp
20 25 30

His Ala Trp Ser Trp Val Arg Gln Pro Pro Gly Arg Gly Leu Glu Trp
35 40 45

Ile Gly Tyr Ile Ser Tyr Ser Gly Ile Thr Thr Tyr Asn Pro Ser Leu
50 55 60

Lys Ser Arg Val Thr Met Leu Arg Asp Thr Thr Ser Thr Ser Gly Arg
65 70 75 80

Ser Ala Asn Pro Arg Gly Ser Lys Asn Gln Phe Ser Leu Arg Leu Ser
85 90 95

Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala Arg Ser Leu
100 105 110

Ala Arg Thr Thr Ala Met Asp Tyr Trp Gly Gln Gly Ser Leu Val Thr
115 120 125

Val Ser Ser
130

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<400> 193

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Arg Pro Ser Gln
1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Tyr Ser Ile Thr Ser Asp
20 25 30

His Ala Trp Ser Trp Val Arg Gln Pro Pro Gly Arg Gly Leu Glu Trp
35 40 45

Ile Gly Tyr Ile Ser Tyr Ser Gly Ile Thr Thr Tyr Asn Pro Ser Leu
50 55 60

Lys Ser Arg Val Thr Met Leu Arg Asp Thr Ser Thr Ser Thr Ser Gly
65 70 75 80

Arg Ser Ala Asn Pro Arg Gly Lys Asn Gln Phe Ser Leu Arg Leu Ser
85 90 95

Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala Arg Ser Leu
100 105 110

Ala Arg Thr Thr Ala Met Asp Tyr Trp Gly Gln Gly Ser Leu Val Thr
115 120 125

Val Ser Ser
130

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<400> 194

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Arg Pro Ser Gln
1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Tyr Ser Ile Thr Ser Asp
20 25 30

His Ala Trp Ser Trp Val Arg Gln Pro Pro Gly Arg Gly Leu Glu Trp
35 40 45

Ile Gly Tyr Ile Ser Tyr Ser Gly Ile Thr Thr Tyr Asn Pro Ser Leu
50 55 60

Lys Ser Arg Val Thr Met Leu Arg Asp Thr Ser Lys Thr Ser Thr Ser
65 70 75 80

Gly Arg Ser Ala Asn Pro Arg Gly Asn Gln Phe Ser Leu Arg Leu Ser
85 90 95

Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala Arg Ser Leu
100 105 110

Ala Arg Thr Thr Ala Met Asp Tyr Trp Gly Gln Gly Ser Leu Val Thr
115 120 125

Val Ser Ser
130

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<400> 195

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Arg Pro Ser Gln
1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Tyr Ser Ile Thr Ser Asp
20 25 30

His Ala Trp Ser Trp Val Arg Gln Pro Pro Gly Arg Gly Leu Glu Trp
35 40 45

Ile Gly Tyr Ile Ser Tyr Ser Gly Ile Thr Thr Tyr Asn Pro Ser Leu
50 55 60

Lys Ser Arg Val Thr Met Leu Arg Asp Thr Ser Lys Asn Thr Ser Thr
65 70 75 80

Ser Gly Arg Ser Ala Asn Pro Arg Gly Gln Phe Ser Leu Arg Leu Ser
85 90 95

Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala Arg Ser Leu
100 105 110

Ala Arg Thr Thr Ala Met Asp Tyr Trp Gly Gln Gly Ser Leu Val Thr
115 120 125

Val Ser Ser
130

<210> 196
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<400> 196

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Arg Pro Ser Gln
1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Tyr Ser Ile Thr Ser Asp
20 25 30

His Ala Trp Ser Trp Val Arg Gln Pro Pro Gly Arg Gly Leu Glu Trp
35 40 45

Ile Gly Tyr Ile Ser Tyr Ser Gly Ile Thr Thr Tyr Asn Pro Ser Leu
50 55 60

Lys Ser Arg Val Thr Met Leu Arg Asp Thr Ser Lys Asn Gln Thr Ser
65 70 75 80

Thr Ser Gly Arg Ser Ala Asn Pro Arg Gly Phe Ser Leu Arg Leu Ser
85 90 95

Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala Arg Ser Leu
100 105 110

Ala Arg Thr Thr Ala Met Asp Tyr Trp Gly Gln Gly Ser Leu Val Thr
115 120 125

Val Ser Ser
130

<210> 197
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<400> 197

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Arg Pro Ser Gln
1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Tyr Ser Ile Thr Ser Asp
20 25 30

His Ala Trp Ser Trp Val Arg Gln Pro Pro Gly Arg Gly Leu Glu Trp
35 40 45

Ile Gly Tyr Ile Ser Tyr Ser Gly Ile Thr Thr Tyr Asn Pro Ser Leu
50 55 60

Lys Ser Arg Val Thr Met Leu Arg Asp Thr Ser Lys Asn Gln Phe Ser
65 70 75 80

Leu Arg Leu Ser Ser Val Thr Thr Ser Thr Ser Gly Arg Ser Ala Asn
85 90 95

Pro Arg Gly Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala Arg Ser Leu
100 105 110

Ala Arg Thr Thr Ala Met Asp Tyr Trp Gly Gln Gly Ser Leu Val Thr
115 120 125

Val Ser Ser
130

<210> 198
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<220>
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<400> 198

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Arg Pro Ser Gln
1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Tyr Ser Ile Thr Ser Asp
20 25 30

His Ala Trp Ser Trp Val Arg Gln Pro Pro Gly Arg Gly Leu Glu Trp
35 40 45

Ile Gly Tyr Ile Ser Tyr Ser Gly Ile Thr Thr Tyr Asn Pro Ser Leu
50 55 60

Lys Ser Arg Val Thr Met Leu Arg Asp Thr Ser Lys Asn Gln Phe Ser
65 70 75 80

Leu Arg Leu Ser Ser Val Thr Ala Thr Ser Thr Ser Gly Arg Ser Ala
85 90 95

Asn Pro Arg Gly Ala Asp Thr Ala Val Tyr Tyr Cys Ala Arg Ser Leu
100 105 110

Ala Arg Thr Thr Ala Met Asp Tyr Trp Gly Gln Gly Ser Leu Val Thr
115 120 125

Val Ser Ser
130

<210> 199
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<220>
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<400> 199

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Arg Pro Ser Gln
1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Tyr Ser Ile Thr Ser Asp
20 25 30

His Ala Trp Ser Trp Val Arg Gln Pro Pro Gly Arg Gly Leu Glu Trp
35 40 45

Ile Gly Tyr Ile Ser Tyr Ser Gly Ile Thr Thr Tyr Asn Pro Ser Leu
50 55 60

Lys Ser Arg Val Thr Met Leu Arg Asp Thr Ser Lys Asn Gln Phe Ser
65 70 75 80

Leu Arg Leu Ser Ser Val Thr Ala Ala Thr Ser Thr Ser Gly Arg Ser
85 90 95

Ala Asn Pro Arg Gly Asp Thr Ala Val Tyr Tyr Cys Ala Arg Ser Leu
100 105 110

Ala Arg Thr Thr Ala Met Asp Tyr Trp Gly Gln Gly Ser Leu Val Thr
115 120 125

Val Ser Ser
130

<210> 200
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<212> PRT
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<400> 200

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Arg Pro Ser Gln
1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Tyr Ser Ile Thr Ser Asp
20 25 30

His Ala Trp Ser Trp Val Arg Gln Pro Pro Gly Arg Gly Leu Glu Trp
35 40 45

```
Ile Gly Tyr Ile Ser Tyr Ser Gly Ile Thr Thr Tyr Asn Pro Ser Leu
    50                  55                  60

Lys Ser Arg Val Thr Met Leu Arg Asp Thr Ser Lys Asn Gln Phe Ser
65                  70                  75                  80

Leu Arg Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Ser Thr Ser Thr Ser Gly Arg Ser Ala Asn Pro Arg Gly Leu
            100                 105                 110

Ala Arg Thr Thr Ala Met Asp Tyr Trp Gly Gln Gly Ser Leu Val Thr
        115                 120                 125

Val Ser Ser
    130
```

<210> 201
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<400> 201

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Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Arg Pro Ser Gln
1               5                   10                  15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Tyr Ser Ile Thr Ser Asp
            20                  25                  30

His Ala Trp Ser Trp Val Arg Gln Pro Pro Gly Arg Gly Leu Glu Trp
        35                  40                  45
```

Ile Gly Tyr Ile Ser Tyr Ser Gly Ile Thr Thr Tyr Asn Pro Ser Leu
50 55 60

Lys Ser Arg Val Thr Met Leu Arg Asp Thr Ser Lys Asn Gln Phe Ser
65 70 75 80

Leu Arg Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Ser Leu Thr Ser Thr Ser Gly Arg Ser Ala Asn Pro Arg Gly
100 105 110

Ala Arg Thr Thr Ala Met Asp Tyr Trp Gly Gln Gly Ser Leu Val Thr
115 120 125

Val Ser Ser
130

<210> 202
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<212> PRT
<213> 人造序列

<220>
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<400> 202

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Arg Pro Ser Gln
1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Tyr Ser Ile Thr Ser Asp
20 25 30

His Ala Trp Ser Trp Val Arg Gln Pro Pro Gly Arg Gly Leu Glu Trp
35 40 45

Ile Gly Tyr Ile Ser Tyr Ser Gly Ile Thr Thr Tyr Asn Pro Ser Leu
50 55 60

Lys Ser Arg Val Thr Met Leu Arg Asp Thr Ser Lys Asn Gln Phe Ser
65 70 75 80

Leu Arg Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Ser Leu Ala Thr Ser Thr Ser Gly Arg Ser Ala Asn Pro Arg
100 105 110

Gly Arg Thr Thr Ala Met Asp Tyr Trp Gly Gln Gly Ser Leu Val Thr
115 120 125

Val Ser Ser
130

<210> 203
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<212> PRT
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<220>
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<400> 203

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Arg Pro Ser Gln
1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Tyr Ser Ile Thr Ser Asp
20 25 30

His Ala Trp Ser Trp Val Arg Gln Pro Pro Gly Arg Gly Leu Glu Trp
35 40 45

Ile Gly Tyr Ile Ser Tyr Ser Gly Ile Thr Thr Tyr Asn Pro Ser Leu
50 55 60

Lys Ser Arg Val Thr Met Leu Arg Asp Thr Ser Lys Asn Gln Phe Ser
65 70 75 80

Leu Arg Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Ser Leu Ala Arg Thr Ser Thr Ser Gly Arg Ser Ala Asn Pro
100 105 110

Arg Gly Thr Thr Ala Met Asp Tyr Trp Gly Gln Gly Ser Leu Val Thr
115 120 125

Val Ser Ser
130

<210> 204
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<220>
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<400> 204

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Arg Pro Ser Gln
1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Tyr Ser Ile Thr Ser Asp
20 25 30

His Ala Trp Ser Trp Val Arg Gln Pro Pro Gly Arg Gly Leu Glu Trp
35 40 45

Ile Gly Tyr Ile Ser Tyr Ser Gly Ile Thr Thr Tyr Asn Pro Ser Leu
50 55 60

Lys Ser Arg Val Thr Met Leu Arg Asp Thr Ser Lys Asn Gln Phe Ser
65 70 75 80

Leu Arg Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Ser Leu Ala Arg Thr Thr Ala Met Asp Tyr Trp Thr Ser Thr
100 105 110

Ser Gly Arg Ser Ala Asn Pro Arg Gly Gly Gln Gly Ser Leu Val Thr
115 120 125

Val Ser Ser
130

<210> 205
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<220>
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<400> 205

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Arg Pro Ser Gln
1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Tyr Ser Ile Thr Ser Asp
20 25 30

His Ala Trp Ser Trp Val Arg Gln Pro Pro Gly Arg Gly Leu Glu Trp
35 40 45

Ile Gly Tyr Ile Ser Tyr Ser Gly Ile Thr Thr Tyr Asn Pro Ser Leu
50 55 60

Lys Ser Arg Val Thr Met Leu Arg Asp Thr Ser Lys Asn Gln Phe Ser
65 70 75 80

Leu Arg Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Ser Leu Ala Arg Thr Thr Ala Met Asp Tyr Trp Gly Thr Ser
100 105 110

Thr Ser Gly Arg Ser Ala Asn Pro Arg Gly Gln Gly Ser Leu Val Thr
115 120 125

Val Ser Ser
130

<210> 206
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<220>
<223> 人造的合成序列

<400> 206

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Arg Pro Ser Gln
1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Tyr Ser Ile Thr Ser Asp
20 25 30

His Ala Trp Ser Trp Val Arg Gln Pro Pro Gly Arg Gly Leu Glu Trp
35 40 45

Ile Gly Tyr Ile Ser Tyr Ser Gly Ile Thr Thr Tyr Asn Pro Ser Leu
50 55 60

Lys Ser Arg Val Thr Met Leu Arg Asp Thr Ser Lys Asn Gln Phe Ser
65 70 75 80

Leu Arg Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Ser Leu Ala Arg Thr Thr Ala Met Asp Tyr Trp Gly Gln Thr
100 105 110

Ser Thr Ser Gly Arg Ser Ala Asn Pro Arg Gly Gly Ser Leu Val Thr
115 120 125

Val Ser Ser
130

<210> 207
<211> 131
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<213> 人造序列

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<400> 207

```
Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Arg Pro Ser Gln
1               5                  10                  15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Tyr Ser Ile Thr Ser Asp
            20                  25                  30

His Ala Trp Ser Trp Val Arg Gln Pro Pro Gly Arg Gly Leu Glu Trp
        35                  40                  45

Ile Gly Tyr Ile Ser Tyr Ser Gly Ile Thr Thr Tyr Asn Pro Ser Leu
    50                  55                  60

Lys Ser Arg Val Thr Met Leu Arg Asp Thr Ser Lys Asn Gln Phe Ser
65                  70                  75                  80

Leu Arg Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Ser Leu Ala Arg Thr Thr Ala Met Asp Tyr Trp Gly Gln Gly
            100                 105                 110

Thr Ser Thr Ser Gly Arg Ser Ala Asn Pro Arg Gly Ser Leu Val Thr
        115                 120                 125

Val Ser Ser
    130
```

<210> 208
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<220>

<223> 人造的合成序列

<400> 208

```
Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Arg Pro Ser Gln
1               5                  10                  15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Tyr Ser Ile Thr Ser Asp
            20                  25                  30

His Ala Trp Ser Trp Val Arg Gln Pro Pro Gly Arg Gly Leu Glu Trp
        35                  40                  45

Ile Gly Tyr Ile Ser Tyr Ser Gly Ile Thr Thr Tyr Asn Pro Ser Leu
    50                  55                  60

Lys Ser Arg Val Thr Met Leu Arg Asp Thr Ser Lys Asn Gln Phe Ser
65                  70                  75                  80

Leu Arg Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Ser Leu Ala Arg Thr Thr Ala Met Asp Tyr Trp Gly Gln Gly
            100                 105                 110

Ser Thr Ser Thr Ser Gly Arg Ser Ala Asn Pro Arg Gly Leu Val Thr
        115                 120                 125

Val Ser Ser
    130
```

<210> 209
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<400> 209

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Arg Pro Ser Gln
1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Tyr Ser Ile Thr Ser Asp
20 25 30

His Ala Trp Ser Trp Val Arg Gln Pro Pro Gly Arg Gly Leu Glu Trp
35 40 45

Ile Gly Tyr Ile Ser Tyr Ser Gly Ile Thr Thr Tyr Asn Pro Ser Leu
50 55 60

Lys Ser Arg Val Thr Met Leu Arg Asp Thr Ser Lys Asn Gln Phe Ser
65 70 75 80

Leu Arg Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Ser Leu Ala Arg Thr Thr Ala Met Asp Tyr Trp Gly Gln Gly
100 105 110

Ser Leu Thr Ser Thr Ser Gly Arg Ser Ala Asn Pro Arg Gly Val Thr
115 120 125

Val Ser Ser
130

<210> 210
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<400> 210

```
Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Arg Pro Ser Gln
1               5                  10                  15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Tyr Ser Ile Thr Ser Asp
            20                  25                  30

His Ala Trp Ser Trp Val Arg Gln Pro Pro Gly Arg Gly Leu Glu Trp
        35                  40                  45

Ile Gly Tyr Ile Ser Tyr Ser Gly Ile Thr Thr Tyr Asn Pro Ser Leu
    50                  55                  60

Lys Ser Arg Val Thr Met Leu Arg Asp Thr Ser Lys Asn Gln Phe Ser
65                  70                  75                  80

Leu Arg Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Ser Leu Ala Arg Thr Thr Ala Met Asp Tyr Trp Gly Gln Gly
            100                 105                 110

Ser Leu Val Thr Ser Thr Ser Gly Arg Ser Ala Asn Pro Arg Gly Thr
        115                 120                 125

Val Ser Ser
    130
```

<210> 211
<211> 131
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<220>
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<400> 211

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Arg Pro Ser Gln
1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Tyr Ser Ile Thr Ser Asp
20 25 30

His Ala Trp Ser Trp Val Arg Gln Pro Pro Gly Arg Gly Leu Glu Trp
35 40 45

Ile Gly Tyr Ile Ser Tyr Ser Gly Ile Thr Thr Tyr Asn Pro Ser Leu
50 55 60

Lys Ser Arg Val Thr Met Leu Arg Asp Thr Ser Lys Asn Gln Phe Ser
65 70 75 80

Leu Arg Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Ser Leu Ala Arg Thr Thr Ala Met Asp Tyr Trp Gly Gln Gly
100 105 110

Ser Leu Val Thr Thr Ser Thr Ser Gly Arg Ser Ala Asn Pro Arg Gly
115 120 125

Val Ser Ser
130

<210> 212
<211> 131
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<220>
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<400> 212

```
Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Arg Pro Ser Gln
1               5                  10                  15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Tyr Ser Ile Thr Ser Asp
            20                  25                  30

His Ala Trp Ser Trp Val Arg Gln Pro Pro Gly Arg Gly Leu Glu Trp
        35                  40                  45

Ile Gly Tyr Ile Ser Tyr Ser Gly Ile Thr Thr Tyr Asn Pro Ser Leu
    50                  55                  60

Lys Ser Arg Val Thr Met Leu Arg Asp Thr Ser Lys Asn Gln Phe Ser
65                  70                  75                  80

Leu Arg Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Ser Leu Ala Arg Thr Thr Ala Met Asp Tyr Trp Gly Gln Gly
            100                 105                 110

Ser Leu Val Thr Val Thr Ser Thr Ser Gly Arg Ser Ala Asn Pro Arg
        115                 120                 125
```

Gly Ser Ser
130

<210> 213
<211> 131
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 213

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Arg Pro Ser Gln
1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Tyr Ser Ile Thr Ser Asp
20 25 30

His Ala Trp Ser Trp Val Arg Gln Pro Pro Gly Arg Gly Leu Glu Trp
35 40 45

Ile Gly Tyr Ile Ser Tyr Ser Gly Ile Thr Thr Tyr Asn Pro Ser Leu
50 55 60

Lys Ser Arg Val Thr Met Leu Arg Asp Thr Ser Lys Asn Gln Phe Ser
65 70 75 80

Leu Arg Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Ser Leu Ala Arg Thr Thr Ala Met Asp Tyr Trp Gly Gln Gly
100 105 110

Ser Leu Val Thr Val Ser Thr Ser Thr Ser Gly Arg Ser Ala Asn Pro
115 120 125

Arg Gly Ser
130

<210> 214
<211> 131
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 214

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Arg Pro Ser Gln
1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Tyr Ser Ile Thr Ser Asp
20 25 30

His Ala Trp Ser Trp Val Arg Gln Pro Pro Gly Arg Gly Leu Glu Trp
35 40 45

Ile Gly Tyr Ile Ser Tyr Ser Gly Ile Thr Thr Tyr Asn Pro Ser Leu
50 55 60

Lys Ser Arg Val Thr Met Leu Arg Asp Thr Ser Lys Asn Gln Phe Ser
65 70 75 80

Leu Arg Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Ser Leu Ala Arg Thr Thr Ala Met Asp Tyr Trp Gly Gln Gly
100 105 110

Ser Leu Val Thr Val Ser Ser Thr Ser Thr Ser Gly Arg Ser Ala Asn
115 120 125

Pro Arg Gly
130

<210> 215
<211> 340
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 215

Ala Thr Ser Thr Ser Gly Arg Ser Ala Asn Pro Arg Gly Ser Thr Lys
1 5 10 15

Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly
20 25 30

Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro
35 40 45

Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr
50 55 60

Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val
65 70 75 80

Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn
85 90 95

Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro
100 105 110

Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu
115 120 125

Leu Arg Arg Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
130 135 140

Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp
145 150 155 160

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
165 170 175

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn
180 185 190

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
195 200 205

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro
210 215 220

Ser Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
225 230 235 240

Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn
245 250 255

Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
260 265 270

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
275 280 285

Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys
290 295 300

Leu Thr Val Asp Lys Ser Arg Trp Gln Glu Gly Asn Val Phe Ser Cys
305 310 315 320

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
325 330 335

Ser Leu Ser Pro
340

<210> 216
<211> 340
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 216

Ala Ser Thr Ser Thr Ser Gly Arg Ser Ala Asn Pro Arg Gly Thr Lys
1 5 10 15

Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly
20 25 30

Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro
35 40 45

Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr
50 55 60

Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val
65 70 75 80

Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn
85 90 95

Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro
100 105 110

Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu
115 120 125

Leu Arg Arg Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
130 135 140

Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp
145 150 155 160

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
165 170 175

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn
180 185 190

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
195 200 205

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro
210 215 220

Ser Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
225 230 235 240

Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn
245 250 255

Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
260 265 270

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
275 280 285

Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys
290 295 300

Leu Thr Val Asp Lys Ser Arg Trp Gln Glu Gly Asn Val Phe Ser Cys
305 310 315 320

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
325 330 335

Ser Leu Ser Pro
340

<210> 217
<211> 340
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 217

Ala Ser Thr Thr Ser Thr Ser Gly Arg Ser Ala Asn Pro Arg Gly Lys
1 5 10 15

Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly
20 25 30

Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro
35 40 45

Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr
50 55 60

Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val
65 70 75 80

Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn
85 90 95

Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro
100 105 110

Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu
115 120 125

Leu Arg Arg Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
130 135 140

Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp
145 150 155 160

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
165 170 175

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn
180 185 190

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
195 200 205

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro
210 215 220

Ser Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
225 230 235 240

Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn
245 250 255

Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
260 265 270

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
275 280 285

Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys
290 295 300

Leu Thr Val Asp Lys Ser Arg Trp Gln Glu Gly Asn Val Phe Ser Cys
305 310 315 320

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
325 330 335

Ser Leu Ser Pro
340

<210> 218
<211> 340
<212> PRT
<213> 人造序列

<220>

<223> 人造的合成序列

<400> 218

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Ala Ser Thr Lys Thr Ser Thr Ser Gly Arg Ser Ala Asn Pro Arg Gly
1               5                  10                  15

Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly
            20                  25                  30

Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro
        35                  40                  45

Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr
    50                  55                  60

Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val
65                  70                  75                  80

Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn
                85                  90                  95

Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro
            100                 105                 110

Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu
        115                 120                 125

Leu Arg Arg Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
    130                 135                 140

Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp
145                 150                 155                 160
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Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
165 170 175

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn
180 185 190

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
195 200 205

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro
210 215 220

Ser Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
225 230 235 240

Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn
245 250 255

Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
260 265 270

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
275 280 285

Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys
290 295 300

Leu Thr Val Asp Lys Ser Arg Trp Gln Glu Gly Asn Val Phe Ser Cys
305 310 315 320

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
325 330 335

Ser Leu Ser Pro
340

<210> 219
<211> 340
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 219

Ala Ser Thr Lys Gly Thr Ser Thr Ser Gly Arg Ser Ala Asn Pro Arg
1 5 10 15

Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly
20 25 30

Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro
35 40 45

Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr
50 55 60

Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val
65 70 75 80

Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn
85 90 95

Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro
100 105 110

Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu
115 120 125

Leu Arg Arg Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
130 135 140

Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp
145 150 155 160

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
165 170 175

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn
180 185 190

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
195 200 205

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro
210 215 220

Ser Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
225 230 235 240

Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn
245 250 255

Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
260 265 270

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
275 280 285

Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys
290 295 300

Leu Thr Val Asp Lys Ser Arg Trp Gln Glu Gly Asn Val Phe Ser Cys
305 310 315 320

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
325 330 335

Ser Leu Ser Pro
340

<210> 220
<211> 340
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 220

Ala Ser Thr Lys Gly Pro Thr Ser Thr Ser Gly Arg Ser Ala Asn Pro
1 5 10 15

Arg Gly Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly
20 25 30

Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro
35 40 45

Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr
50 55 60

Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val
65 70 75 80

Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn
85 90 95

Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro
100 105 110

Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu
115 120 125

Leu Arg Arg Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
130 135 140

Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp
145 150 155 160

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
165 170 175

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn
180 185 190

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
195 200 205

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro
210 215 220

Ser Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
225 230 235 240

Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn
245 250 255

Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
260 265 270

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
275 280 285

Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys
290 295 300

Leu Thr Val Asp Lys Ser Arg Trp Gln Glu Gly Asn Val Phe Ser Cys
305 310 315 320

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
325 330 335

Ser Leu Ser Pro
340

<210> 221
<211> 340
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 221

Ala Ser Thr Lys Gly Pro Ser Thr Ser Thr Ser Gly Arg Ser Ala Asn
1 5 10 15

Pro Arg Gly Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly
20 25 30

Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro
35 40 45

Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr
50 55 60

Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val
65 70 75 80

Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn
85 90 95

Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro
100 105 110

Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu
115 120 125

Leu Arg Arg Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
130 135 140

Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp
145 150 155 160

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
165 170 175

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn
180 185 190

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
195 200 205

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro
210 215 220

Ser Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
225 230 235 240

Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn
245 250 255

Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
260 265 270

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
275 280 285

Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys
290 295 300

Leu Thr Val Asp Lys Ser Arg Trp Gln Glu Gly Asn Val Phe Ser Cys
305 310 315 320

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
325 330 335

Ser Leu Ser Pro
340

<210> 222
<211> 340
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 222

Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Thr Ser Thr Ser
1 5 10 15

Gly Arg Ser Ala Asn Pro Arg Gly Pro Ser Ser Lys Ser Thr Ser Gly
20 25 30

Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro
35 40 45

Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr
50 55 60

Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val
65 70 75 80

Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn
85 90 95

Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro
100 105 110

Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu
115 120 125

Leu Arg Arg Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
130 135 140

Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp
145 150 155 160

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
165 170 175

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn
180 185 190

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
195 200 205

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro
210 215 220

Ser Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
225 230 235 240

Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn
245 250 255

Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
260 265 270

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
275 280 285

Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys
290 295 300

Leu Thr Val Asp Lys Ser Arg Trp Gln Glu Gly Asn Val Phe Ser Cys
305 310 315 320

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
325 330 335

Ser Leu Ser Pro
340

<210> 223
<211> 340
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 223

Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Thr Ser Thr
1 5 10 15

Ser Gly Arg Ser Ala Asn Pro Arg Gly Ser Ser Lys Ser Thr Ser Gly
20 25 30

Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro
35 40 45

Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr
50 55 60

Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val
65 70 75 80

Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn
85 90 95

Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro
100 105 110

Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu
115 120 125

Leu Arg Arg Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
130 135 140

```
Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp
145                 150                 155                 160

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
                165                 170                 175

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn
            180                 185                 190

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
        195                 200                 205

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro
    210                 215                 220

Ser Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
225                 230                 235                 240

Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn
                245                 250                 255

Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
            260                 265                 270

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
        275                 280                 285

Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys
    290                 295                 300

Leu Thr Val Asp Lys Ser Arg Trp Gln Glu Gly Asn Val Phe Ser Cys
305                 310                 315                 320
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Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
325 330 335

Ser Leu Ser Pro
340

<210> 224
<211> 340
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 224

Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Thr Ser
1 5 10 15

Thr Ser Gly Arg Ser Ala Asn Pro Arg Gly Ser Lys Ser Thr Ser Gly
20 25 30

Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro
35 40 45

Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr
50 55 60

Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val
65 70 75 80

Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn
85 90 95

Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro
100 105 110

Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu
115 120 125

Leu Arg Arg Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
130 135 140

Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp
145 150 155 160

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
165 170 175

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn
180 185 190

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
195 200 205

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro
210 215 220

Ser Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
225 230 235 240

Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn
245 250 255

Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
260 265 270

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
275 280 285

Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys
290 295 300

Leu Thr Val Asp Lys Ser Arg Trp Gln Glu Gly Asn Val Phe Ser Cys
305 310 315 320

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
325 330 335

Ser Leu Ser Pro
340

<210> 225
<211> 340
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 225

Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Thr
1 5 10 15

Ser Thr Ser Gly Arg Ser Ala Asn Pro Arg Gly Lys Ser Thr Ser Gly
20 25 30

Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro
35 40 45

Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr
50 55 60

Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val
65 70 75 80

Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn
85 90 95

Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro
100 105 110

Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu
115 120 125

Leu Arg Arg Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
130 135 140

Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp
145 150 155 160

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
165 170 175

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn
180 185 190

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
195 200 205

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro
210 215 220

Ser Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
225 230 235 240

Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn
245 250 255

Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
260 265 270

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
275 280 285

Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys
290 295 300

Leu Thr Val Asp Lys Ser Arg Trp Gln Glu Gly Asn Val Phe Ser Cys
305 310 315 320

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
325 330 335

Ser Leu Ser Pro
340

<210> 226
<211> 340
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 226

Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys
1 5 10 15

Ser Thr Ser Thr Ser Gly Arg Ser Ala Asn Pro Arg Gly Thr Ser Gly
20 25 30

Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro
35 40 45

Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr
50 55 60

Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val
65 70 75 80

Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn
85 90 95

Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro
100 105 110

Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu
115 120 125

Leu Arg Arg Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
130 135 140

Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp
145 150 155 160

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
165 170 175

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn
180 185 190

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
195 200 205

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro
210 215 220

Ser Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
225 230 235 240

Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn
245 250 255

Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
260 265 270

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
275 280 285

Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys
290 295 300

Leu Thr Val Asp Lys Ser Arg Trp Gln Glu Gly Asn Val Phe Ser Cys
305 310 315 320

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
325 330 335

Ser Leu Ser Pro
340

<210> 227
<211> 340
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 227

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Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys
1               5                  10                  15

Ser Thr Thr Ser Thr Ser Gly Arg Ser Ala Asn Pro Arg Gly Ser Gly
            20                  25                  30

Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro
        35                  40                  45

Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr
    50                  55                  60

Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val
65                  70                  75                  80

Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn
                85                  90                  95

Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro
            100                 105                 110

Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu
        115                 120                 125

Leu Arg Arg Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
    130                 135                 140

Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp
145                 150                 155                 160
```

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
165 170 175

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn
180 185 190

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
195 200 205

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro
210 215 220

Ser Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
225 230 235 240

Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn
245 250 255

Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
260 265 270

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
275 280 285

Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys
290 295 300

Leu Thr Val Asp Lys Ser Arg Trp Gln Glu Gly Asn Val Phe Ser Cys
305 310 315 320

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
325 330 335

Ser Leu Ser Pro
340

<210> 228
<211> 340
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 228

Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys
1 5 10 15

Ser Thr Ser Gly Thr Ser Thr Ser Gly Arg Ser Ala Asn Pro Arg Gly
20 25 30

Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro
35 40 45

Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr
50 55 60

Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val
65 70 75 80

Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn
85 90 95

Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro
100 105 110

Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu
115 120 125

Leu Arg Arg Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
130 135 140

Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp
145 150 155 160

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
165 170 175

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn
180 185 190

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
195 200 205

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro
210 215 220

Ser Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
225 230 235 240

Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn
245 250 255

Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
260 265 270

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
275 280 285

Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys
290 295 300

Leu Thr Val Asp Lys Ser Arg Trp Gln Glu Gly Asn Val Phe Ser Cys
305 310 315 320

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
325 330 335

Ser Leu Ser Pro
340

<210> 229
<211> 340
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 229

Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys
1 5 10 15

Ser Thr Ser Gly Gly Thr Thr Ser Thr Ser Gly Arg Ser Ala Asn Pro
20 25 30

Arg Gly Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro
35 40 45

Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr
50 55 60

Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val
65 70 75 80

Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn
85 90 95

Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro
100 105 110

Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu
115 120 125

Leu Arg Arg Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
130 135 140

Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp
145 150 155 160

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
165 170 175

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn
180 185 190

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
195 200 205

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro
210 215 220

Ser Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
225 230 235 240

Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn
245 250 255

Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
260 265 270

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
275 280 285

Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys
290 295 300

Leu Thr Val Asp Lys Ser Arg Trp Gln Glu Gly Asn Val Phe Ser Cys
305 310 315 320

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
325 330 335

Ser Leu Ser Pro
340

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<223> 人造的合成序列

<400> 230

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asp Ile Ser Ser Tyr
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Tyr Thr Ser Arg Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Ile Ala Thr Tyr Tyr Cys Gln Gln Gly Asn Thr Leu Pro Tyr
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
100 105

<210> 231
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<212> PRT
<213> 人造序列

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<400> 231

Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu
1 5 10 15

Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe
20 25 30

Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln
35 40 45

Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser
50 55 60

```
Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu
65                  70                  75                  80

Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser
                85                  90                  95

Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
            100                 105
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<400> 232

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Asp Ile Gln Met Thr Gln Ser Thr Ser Thr Ser Gly Arg Ser Ala Asn
1               5                   10                  15

Pro Arg Gly Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr
            20                  25                  30

Ile Thr Cys Arg Ala Ser Gln Asp Ile Ser Ser Tyr Leu Asn Trp Tyr
        35                  40                  45

Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Tyr Thr Ser
    50                  55                  60

Arg Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly
65                  70                  75                  80
```

Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Gln Pro Glu Asp Ile Ala
85 90 95

Thr Tyr Tyr Cys Gln Gln Gly Asn Thr Leu Pro Tyr Thr Phe Gly Gln
100 105 110

Gly Thr Lys Val Glu Ile Lys
115

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<400> 233

Asp Ile Gln Met Thr Gln Ser Pro Thr Ser Thr Ser Gly Arg Ser Ala
1 5 10 15

Asn Pro Arg Gly Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr
20 25 30

Ile Thr Cys Arg Ala Ser Gln Asp Ile Ser Ser Tyr Leu Asn Trp Tyr
35 40 45

Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Tyr Thr Ser
50 55 60

Arg Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly
65 70 75 80

Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Gln Pro Glu Asp Ile Ala
85 90 95

Thr Tyr Tyr Cys Gln Gln Gly Asn Thr Leu Pro Tyr Thr Phe Gly Gln
100 105 110

Gly Thr Lys Val Glu Ile Lys
115

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<400> 234

Asp Ile Gln Met Thr Gln Ser Pro Ser Thr Ser Thr Ser Gly Arg Ser
1 5 10 15

Ala Asn Pro Arg Gly Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr
20 25 30

Ile Thr Cys Arg Ala Ser Gln Asp Ile Ser Ser Tyr Leu Asn Trp Tyr
35 40 45

Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Tyr Thr Ser
50 55 60

Arg Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly
65 70 75 80

Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Gln Pro Glu Asp Ile Ala
85 90 95

Thr Tyr Tyr Cys Gln Gln Gly Asn Thr Leu Pro Tyr Thr Phe Gly Gln
100 105 110

Gly Thr Lys Val Glu Ile Lys
115

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<400> 235

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Thr Ser Thr Ser Gly Arg
1 5 10 15

Ser Ala Asn Pro Arg Gly Leu Ser Ala Ser Val Gly Asp Arg Val Thr
20 25 30

Ile Thr Cys Arg Ala Ser Gln Asp Ile Ser Ser Tyr Leu Asn Trp Tyr
35 40 45

Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Tyr Thr Ser
50 55 60

Arg Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly
65 70 75 80

Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Gln Pro Glu Asp Ile Ala
85 90 95

Thr Tyr Tyr Cys Gln Gln Gly Asn Thr Leu Pro Tyr Thr Phe Gly Gln
100 105 110

Gly Thr Lys Val Glu Ile Lys
115

<210> 236
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<223> 人造的合成序列

<400> 236

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Thr Ser Thr Ser Gly
1 5 10 15

Arg Ser Ala Asn Pro Arg Gly Ser Ala Ser Val Gly Asp Arg Val Thr
20 25 30

Ile Thr Cys Arg Ala Ser Gln Asp Ile Ser Ser Tyr Leu Asn Trp Tyr
35 40 45

Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Tyr Thr Ser
50 55 60

Arg Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly
65 70 75 80

Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Gln Pro Glu Asp Ile Ala
85 90 95

Thr Tyr Tyr Cys Gln Gln Gly Asn Thr Leu Pro Tyr Thr Phe Gly Gln
100 105 110

Gly Thr Lys Val Glu Ile Lys
115

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<400> 237

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Thr Ser Thr Ser
1 5 10 15

Gly Arg Ser Ala Asn Pro Arg Gly Ala Ser Val Gly Asp Arg Val Thr
20 25 30

Ile Thr Cys Arg Ala Ser Gln Asp Ile Ser Ser Tyr Leu Asn Trp Tyr
35 40 45

Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Tyr Thr Ser
50 55 60

Arg Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly
65 70 75 80

Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Gln Pro Glu Asp Ile Ala
85 90 95

Thr Tyr Tyr Cys Gln Gln Gly Asn Thr Leu Pro Tyr Thr Phe Gly Gln
100 105 110

Gly Thr Lys Val Glu Ile Lys
115

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<211> 119
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<223> 人造的合成序列

<400> 238

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Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Thr Ser Thr
1               5                  10                  15

Ser Gly Arg Ser Ala Asn Pro Arg Gly Ser Val Gly Asp Arg Val Thr
            20                  25                  30

Ile Thr Cys Arg Ala Ser Gln Asp Ile Ser Ser Tyr Leu Asn Trp Tyr
        35                  40                  45

Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Tyr Thr Ser
    50                  55                  60

Arg Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly
65                  70                  75                  80

Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Gln Pro Glu Asp Ile Ala
                85                  90                  95

Thr Tyr Tyr Cys Gln Gln Gly Asn Thr Leu Pro Tyr Thr Phe Gly Gln
            100                 105                 110

Gly Thr Lys Val Glu Ile Lys
        115
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<400> 239

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Thr Ser
1 5 10 15

Thr Ser Gly Arg Ser Ala Asn Pro Arg Gly Val Gly Asp Arg Val Thr
20 25 30

Ile Thr Cys Arg Ala Ser Gln Asp Ile Ser Ser Tyr Leu Asn Trp Tyr
35 40 45

Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Tyr Thr Ser
50 55 60

Arg Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly
65 70 75 80

Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Gln Pro Glu Asp Ile Ala
85 90 95

Thr Tyr Tyr Cys Gln Gln Gly Asn Thr Leu Pro Tyr Thr Phe Gly Gln
100 105 110

Gly Thr Lys Val Glu Ile Lys
115

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<400> 240

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Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Thr
1               5                  10                  15

Ser Thr Ser Gly Arg Ser Ala Asn Pro Arg Gly Gly Asp Arg Val Thr
            20                  25                  30

Ile Thr Cys Arg Ala Ser Gln Asp Ile Ser Ser Tyr Leu Asn Trp Tyr
        35                  40                  45

Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Tyr Thr Ser
    50                  55                  60

Arg Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly
65                  70                  75                  80

Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Gln Pro Glu Asp Ile Ala
                85                  90                  95

Thr Tyr Tyr Cys Gln Gln Gly Asn Thr Leu Pro Tyr Thr Phe Gly Gln
            100                 105                 110

Gly Thr Lys Val Glu Ile Lys
        115
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<400> 241

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Thr Ser Thr Ser Gly Arg Ser Ala Asn Pro Arg Gly Asp Arg Val Thr
20 25 30

Ile Thr Cys Arg Ala Ser Gln Asp Ile Ser Ser Tyr Leu Asn Trp Tyr
35 40 45

Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Tyr Thr Ser
50 55 60

Arg Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly
65 70 75 80

Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Gln Pro Glu Asp Ile Ala
85 90 95

Thr Tyr Tyr Cys Gln Gln Gly Asn Thr Leu Pro Tyr Thr Phe Gly Gln
100 105 110

Gly Thr Lys Val Glu Ile Lys
115

<210> 242
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<400> 242

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Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1               5                  10                  15

Asp Thr Ser Thr Ser Gly Arg Ser Ala Asn Pro Arg Gly Arg Val Thr
            20                  25                  30

Ile Thr Cys Arg Ala Ser Gln Asp Ile Ser Ser Tyr Leu Asn Trp Tyr
        35                  40                  45

Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Tyr Thr Ser
    50                  55                  60

Arg Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly
65                  70                  75                  80

Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Gln Pro Glu Asp Ile Ala
                85                  90                  95

Thr Tyr Tyr Cys Gln Gln Gly Asn Thr Leu Pro Tyr Thr Phe Gly Gln
            100                 105                 110

Gly Thr Lys Val Glu Ile Lys
        115
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<400> 243

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Thr Ser Thr Ser Gly Arg Ser Ala Asn Pro Arg Gly Val Thr
20 25 30

Ile Thr Cys Arg Ala Ser Gln Asp Ile Ser Ser Tyr Leu Asn Trp Tyr
35 40 45

Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Tyr Thr Ser
50 55 60

Arg Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly
65 70 75 80

Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Gln Pro Glu Asp Ile Ala
85 90 95

Thr Tyr Tyr Cys Gln Gln Gly Asn Thr Leu Pro Tyr Thr Phe Gly Gln
100 105 110

Gly Thr Lys Val Glu Ile Lys
115

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<400> 244

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asp Ile Ser Ser Tyr
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Thr Ser Thr Ser Gly Arg Ser Ala Asn
35 40 45

Pro Arg Gly Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Tyr Thr Ser
50 55 60

Arg Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly
65 70 75 80

Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Gln Pro Glu Asp Ile Ala
85 90 95

Thr Tyr Tyr Cys Gln Gln Gly Asn Thr Leu Pro Tyr Thr Phe Gly Gln
100 105 110

Gly Thr Lys Val Glu Ile Lys
115

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<400> 245

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asp Ile Ser Ser Tyr
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Thr Ser Thr Ser Gly Arg Ser Ala
35 40 45

Asn Pro Arg Gly Gly Lys Ala Pro Lys Leu Leu Ile Tyr Tyr Thr Ser
50 55 60

Arg Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly
65 70 75 80

Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Gln Pro Glu Asp Ile Ala
85 90 95

Thr Tyr Tyr Cys Gln Gln Gly Asn Thr Leu Pro Tyr Thr Phe Gly Gln
100 105 110

Gly Thr Lys Val Glu Ile Lys
115

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<400> 246

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asp Ile Ser Ser Tyr
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Thr Ser Thr Ser Gly Arg Ser
35 40 45

Ala Asn Pro Arg Gly Lys Ala Pro Lys Leu Leu Ile Tyr Tyr Thr Ser
50 55 60

Arg Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly
65 70 75 80

Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Gln Pro Glu Asp Ile Ala
85 90 95

Thr Tyr Tyr Cys Gln Gln Gly Asn Thr Leu Pro Tyr Thr Phe Gly Gln
100 105 110

Gly Thr Lys Val Glu Ile Lys
115

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<400> 247

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asp Ile Ser Ser Tyr
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Thr Ser Thr Ser Gly Arg
35 40 45

Ser Ala Asn Pro Arg Gly Ala Pro Lys Leu Leu Ile Tyr Tyr Thr Ser
50 55 60

Arg Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly
65 70 75 80

Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Gln Pro Glu Asp Ile Ala
85 90 95

Thr Tyr Tyr Cys Gln Gln Gly Asn Thr Leu Pro Tyr Thr Phe Gly Gln
100 105 110

Gly Thr Lys Val Glu Ile Lys
115

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<400> 248

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asp Ile Ser Ser Tyr
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Thr Ser Thr Ser Gly
35 40 45

Arg Ser Ala Asn Pro Arg Gly Pro Lys Leu Leu Ile Tyr Tyr Thr Ser
50 55 60

Arg Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly
65 70 75 80

Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Gln Pro Glu Asp Ile Ala
85 90 95

Thr Tyr Tyr Cys Gln Gln Gly Asn Thr Leu Pro Tyr Thr Phe Gly Gln
100 105 110

Gly Thr Lys Val Glu Ile Lys
115

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<400> 249

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asp Ile Ser Ser Tyr
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Thr Ser Thr Ser
35 40 45

Gly Arg Ser Ala Asn Pro Arg Gly Lys Leu Leu Ile Tyr Tyr Thr Ser
50 55 60

Arg Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly
65 70 75 80

Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Gln Pro Glu Asp Ile Ala
85 90 95

Thr Tyr Tyr Cys Gln Gln Gly Asn Thr Leu Pro Tyr Thr Phe Gly Gln
100 105 110

Gly Thr Lys Val Glu Ile Lys
115

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<400> 250

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asp Ile Ser Ser Tyr
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Thr Ser Thr
35 40 45

Ser Gly Arg Ser Ala Asn Pro Arg Gly Leu Leu Ile Tyr Tyr Thr Ser
50 55 60

Arg Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly
65 70 75 80

Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Gln Pro Glu Asp Ile Ala
85 90 95

Thr Tyr Tyr Cys Gln Gln Gly Asn Thr Leu Pro Tyr Thr Phe Gly Gln
100 105 110

Gly Thr Lys Val Glu Ile Lys
115

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<400> 251

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asp Ile Ser Ser Tyr
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Thr Ser Thr Ser Gly Arg Ser Ala Asn Pro Arg Gly Tyr Thr Ser
50 55 60

Arg Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly
65 70 75 80

Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Gln Pro Glu Asp Ile Ala
85 90 95

Thr Tyr Tyr Cys Gln Gln Gly Asn Thr Leu Pro Tyr Thr Phe Gly Gln
100 105 110

Gly Thr Lys Val Glu Ile Lys
115

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<400> 252

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asp Ile Ser Ser Tyr
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Tyr Thr Ser Thr Ser Gly Arg Ser Ala Asn Pro Arg Gly Thr Ser
50 55 60

Arg Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly
65 70 75 80

Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Gln Pro Glu Asp Ile Ala
85 90 95

Thr Tyr Tyr Cys Gln Gln Gly Asn Thr Leu Pro Tyr Thr Phe Gly Gln
100 105 110

Gly Thr Lys Val Glu Ile Lys
115

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<400> 253

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asp Ile Ser Ser Tyr
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Tyr Thr Thr Ser Thr Ser Gly Arg Ser Ala Asn Pro Arg Gly Ser
50 55 60

Arg Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly
65 70 75 80

Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Gln Pro Glu Asp Ile Ala
85 90 95

Thr Tyr Tyr Cys Gln Gln Gly Asn Thr Leu Pro Tyr Thr Phe Gly Gln
100 105 110

Gly Thr Lys Val Glu Ile Lys
115

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<400> 254

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asp Ile Ser Ser Tyr
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Tyr Thr Ser Thr Ser Thr Ser Gly Arg Ser Ala Asn Pro Arg Gly
50 55 60

Arg Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly
65 70 75 80

Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Gln Pro Glu Asp Ile Ala
85 90 95

Thr Tyr Tyr Cys Gln Gln Gly Asn Thr Leu Pro Tyr Thr Phe Gly Gln
100 105 110

Gly Thr Lys Val Glu Ile Lys
115

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<400> 255

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asp Ile Ser Ser Tyr
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Tyr Thr Ser Arg Thr Ser Thr Ser Gly Arg Ser Ala Asn Pro Arg
50 55 60

Gly Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly
65 70 75 80

Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Gln Pro Glu Asp Ile Ala
85 90 95

Thr Tyr Tyr Cys Gln Gln Gly Asn Thr Leu Pro Tyr Thr Phe Gly Gln
100 105 110

Gly Thr Lys Val Glu Ile Lys
115

<210> 256
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<400> 256

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asp Ile Ser Ser Tyr
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Tyr Thr Ser Arg Leu Thr Ser Thr Ser Gly Arg Ser Ala Asn Pro
50 55 60

Arg Gly His Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly
65 70 75 80

Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Gln Pro Glu Asp Ile Ala
85 90 95

Thr Tyr Tyr Cys Gln Gln Gly Asn Thr Leu Pro Tyr Thr Phe Gly Gln
100 105 110

Gly Thr Lys Val Glu Ile Lys
115

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<400> 257

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asp Ile Ser Ser Tyr
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Tyr Thr Ser Arg Leu His Thr Ser Thr Ser Gly Arg Ser Ala Asn
50 55 60

Pro Arg Gly Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly
65 70 75 80

Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Gln Pro Glu Asp Ile Ala
85 90 95

Thr Tyr Tyr Cys Gln Gln Gly Asn Thr Leu Pro Tyr Thr Phe Gly Gln
100 105 110

Gly Thr Lys Val Glu Ile Lys
115

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<400> 258

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asp Ile Ser Ser Tyr
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Tyr Thr Ser Arg Leu His Ser Thr Ser Thr Ser Gly Arg Ser Ala
50 55 60

Asn Pro Arg Gly Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly
65 70 75 80

Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Gln Pro Glu Asp Ile Ala
85 90 95

Thr Tyr Tyr Cys Gln Gln Gly Asn Thr Leu Pro Tyr Thr Phe Gly Gln
100 105 110

Gly Thr Lys Val Glu Ile Lys
115

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Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asp Ile Ser Ser Tyr
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Tyr Thr Ser Arg Leu His Ser Gly Thr Ser Thr Ser Gly Arg Ser
50 55 60

Ala Asn Pro Arg Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly
65 70 75 80

Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Gln Pro Glu Asp Ile Ala
85 90 95

Thr Tyr Tyr Cys Gln Gln Gly Asn Thr Leu Pro Tyr Thr Phe Gly Gln
100 105 110

Gly Thr Lys Val Glu Ile Lys
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Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asp Ile Ser Ser Tyr
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Tyr Thr Ser Arg Leu His Ser Gly Val Thr Ser Thr Ser Gly Arg
50 55 60

Ser Ala Asn Pro Arg Gly Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly
65 70 75 80

Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Gln Pro Glu Asp Ile Ala
85 90 95

Thr Tyr Tyr Cys Gln Gln Gly Asn Thr Leu Pro Tyr Thr Phe Gly Gln
100 105 110

Gly Thr Lys Val Glu Ile Lys
115

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Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1               5                  10                  15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asp Ile Ser Ser Tyr
            20                  25                  30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35                  40                  45

Tyr Tyr Thr Ser Arg Leu His Ser Gly Val Pro Thr Ser Thr Ser Gly
    50                  55                  60

Arg Ser Ala Asn Pro Arg Gly Ser Arg Phe Ser Gly Ser Gly Ser Gly
65                  70                  75                  80

Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Gln Pro Glu Asp Ile Ala
                85                  90                  95

Thr Tyr Tyr Cys Gln Gln Gly Asn Thr Leu Pro Tyr Thr Phe Gly Gln
            100                 105                 110

Gly Thr Lys Val Glu Ile Lys
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<400> 262

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asp Ile Ser Ser Tyr
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Tyr Thr Ser Arg Leu His Ser Gly Val Pro Ser Thr Ser Thr Ser
50 55 60

Gly Arg Ser Ala Asn Pro Arg Gly Arg Phe Ser Gly Ser Gly Ser Gly
65 70 75 80

Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Gln Pro Glu Asp Ile Ala
85 90 95

Thr Tyr Tyr Cys Gln Gln Gly Asn Thr Leu Pro Tyr Thr Phe Gly Gln
100 105 110

Gly Thr Lys Val Glu Ile Lys
115

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<400> 263

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asp Ile Ser Ser Tyr
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Tyr Thr Ser Arg Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Ile Ala Thr Tyr Tyr Cys Gln Gln Gly Asn Thr Leu Pro Tyr
85 90 95

Thr Ser Thr Ser Gly Arg Ser Ala Asn Pro Arg Gly Thr Phe Gly Gln
100 105 110

Gly Thr Lys Val Glu Ile Lys
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<400> 264

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Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1               5                  10                  15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asp Ile Ser Ser Tyr
            20                  25                  30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35                  40                  45

Tyr Tyr Thr Ser Arg Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60

Ser Gly Ser Gly Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80

Glu Asp Ile Ala Thr Tyr Tyr Cys Gln Gln Gly Asn Thr Leu Pro Tyr
                85                  90                  95

Thr Thr Ser Thr Ser Gly Arg Ser Ala Asn Pro Arg Gly Phe Gly Gln
            100                 105                 110

Gly Thr Lys Val Glu Ile Lys
        115
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Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asp Ile Ser Ser Tyr
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Tyr Thr Ser Arg Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Ile Ala Thr Tyr Tyr Cys Gln Gln Gly Asn Thr Leu Pro Tyr
85 90 95

Thr Phe Thr Ser Thr Ser Gly Arg Ser Ala Asn Pro Arg Gly Gly Gln
100 105 110

Gly Thr Lys Val Glu Ile Lys
115

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Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asp Ile Ser Ser Tyr
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Tyr Thr Ser Arg Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Ile Ala Thr Tyr Tyr Cys Gln Gln Gly Asn Thr Leu Pro Tyr
85 90 95

Thr Phe Gly Thr Ser Thr Ser Gly Arg Ser Ala Asn Pro Arg Gly Gln
100 105 110

Gly Thr Lys Val Glu Ile Lys
115

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Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asp Ile Ser Ser Tyr
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Tyr Thr Ser Arg Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Ile Ala Thr Tyr Tyr Cys Gln Gln Gly Asn Thr Leu Pro Tyr
85 90 95

Thr Phe Gly Gln Thr Ser Thr Ser Gly Arg Ser Ala Asn Pro Arg Gly
100 105 110

Gly Thr Lys Val Glu Ile Lys
115

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Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asp Ile Ser Ser Tyr
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Tyr Thr Ser Arg Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Ile Ala Thr Tyr Tyr Cys Gln Gln Gly Asn Thr Leu Pro Tyr
85 90 95

Thr Phe Gly Gln Gly Thr Ser Thr Ser Gly Arg Ser Ala Asn Pro Arg
100 105 110

Gly Thr Lys Val Glu Ile Lys
115

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Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asp Ile Ser Ser Tyr
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Tyr Thr Ser Arg Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Ile Ala Thr Tyr Tyr Cys Gln Gln Gly Asn Thr Leu Pro Tyr
85 90 95

Thr Phe Gly Gln Gly Thr Thr Ser Thr Ser Gly Arg Ser Ala Asn Pro
100 105 110

Arg Gly Lys Val Glu Ile Lys
115

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Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asp Ile Ser Ser Tyr
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Tyr Thr Ser Arg Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Ile Ala Thr Tyr Tyr Cys Gln Gln Gly Asn Thr Leu Pro Tyr
85 90 95

Thr Phe Gly Gln Gly Thr Lys Thr Ser Thr Ser Gly Arg Ser Ala Asn
100 105 110

Pro Arg Gly Val Glu Ile Lys
115

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Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asp Ile Ser Ser Tyr
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Tyr Thr Ser Arg Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Ile Ala Thr Tyr Tyr Cys Gln Gln Gly Asn Thr Leu Pro Tyr
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Thr Ser Thr Ser Gly Arg Ser Ala
100 105 110

Asn Pro Arg Gly Glu Ile Lys
115

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<400> 272

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asp Ile Ser Ser Tyr
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Tyr Thr Ser Arg Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Ile Ala Thr Tyr Tyr Cys Gln Gln Gly Asn Thr Leu Pro Tyr
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Thr Ser Thr Ser Gly Arg Ser
100 105 110

Ala Asn Pro Arg Gly Ile Lys
115

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<400> 273

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asp Ile Ser Ser Tyr
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Tyr Thr Ser Arg Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Ile Ala Thr Tyr Tyr Cys Gln Gln Gly Asn Thr Leu Pro Tyr
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Thr Ser Thr Ser Gly Arg
100 105 110

Ser Ala Asn Pro Arg Gly Lys
115

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<400> 274

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asp Ile Ser Ser Tyr
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Tyr Thr Ser Arg Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Ile Ala Thr Tyr Tyr Cys Gln Gln Gly Asn Thr Leu Pro Tyr
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Thr Ser Thr Ser Gly
100 105 110

Arg Ser Ala Asn Pro Arg Gly
115

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<400> 275

Arg Thr Ser Thr Ser Gly Arg Ser Ala Asn Pro Arg Gly Thr Val Ala
1 5 10 15

Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser
20 25 30

Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu
35 40 45

Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser
50 55 60

Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu
65 70 75 80

Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val
85 90 95

Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys
100 105 110

Ser Phe Asn Arg Gly Glu Cys
115

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<400> 276

Arg Thr Thr Ser Thr Ser Gly Arg Ser Ala Asn Pro Arg Gly Val Ala
1 5 10 15

Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser
20 25 30

Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu
35 40 45

Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser
50 55 60

Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu
65 70 75 80

Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val
85 90 95

Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys
100 105 110

Ser Phe Asn Arg Gly Glu Cys
115

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<400> 277

Arg Thr Val Thr Ser Thr Ser Gly Arg Ser Ala Asn Pro Arg Gly Ala
1 5 10 15

Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser
20 25 30

Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu
35 40 45

Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser
50 55 60

Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu
65 70 75 80

Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val
85 90 95

Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys
100 105 110

Ser Phe Asn Arg Gly Glu Cys
115

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<400> 278

Arg Thr Val Ala Thr Ser Thr Ser Gly Arg Ser Ala Asn Pro Arg Gly
1 5 10 15

Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser
20 25 30

Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu
35 40 45

Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser
50 55 60

Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu
65 70 75 80

Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val
85 90 95

Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys
100 105 110

Ser Phe Asn Arg Gly Glu Cys
115

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<400> 279

Arg Thr Val Ala Ala Thr Ser Thr Ser Gly Arg Ser Ala Asn Pro Arg
1 5 10 15

Gly Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser
20 25 30

Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu
35 40 45

Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser
50 55 60

Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu
65 70 75 80

Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val
85 90 95

Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys
100 105 110

Ser Phe Asn Arg Gly Glu Cys
115

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<400> 280

Arg Thr Val Ala Ala Pro Thr Ser Thr Ser Gly Arg Ser Ala Asn Pro
1 5 10 15

Arg Gly Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser
20 25 30

Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu
35 40 45

Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser
50 55 60

Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu
65 70 75 80

Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val
85 90 95

Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys
100 105 110

Ser Phe Asn Arg Gly Glu Cys
115

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<400> 281

Arg Thr Val Ala Ala Pro Ser Val Thr Ser Thr Ser Gly Arg Ser Ala
1 5 10 15

Asn Pro Arg Gly Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser
20 25 30

Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu
35 40 45

Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser
50 55 60

Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu
65 70 75 80

Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val
85 90 95

Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys
100 105 110

Ser Phe Asn Arg Gly Glu Cys
115

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<400> 282

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Arg Thr Val Ala Ala Pro Ser Val Phe Thr Ser Thr Ser Gly Arg Ser
1               5                  10                  15

Ala Asn Pro Arg Gly Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser
            20                  25                  30

Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu
        35                  40                  45

Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser
    50                  55                  60

Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu
65                  70                  75                  80

Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val
                85                  90                  95

Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys
            100                 105                 110

Ser Phe Asn Arg Gly Glu Cys
        115
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<400> 283

Arg Thr Val Ala Ala Pro Ser Val Phe Ile Thr Ser Thr Ser Gly Arg
1 5 10 15

Ser Ala Asn Pro Arg Gly Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser
20 25 30

Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu
35 40 45

Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser
50 55 60

Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu
65 70 75 80

Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val
85 90 95

Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys
100 105 110

Ser Phe Asn Arg Gly Glu Cys
115

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<400> 284

Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Thr Ser Thr Ser Gly
1 5 10 15

Arg Ser Ala Asn Pro Arg Gly Pro Pro Ser Asp Glu Gln Leu Lys Ser
20 25 30

Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu
35 40 45

Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser
50 55 60

Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu
65 70 75 80

Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val
85 90 95

Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys
100 105 110

Ser Phe Asn Arg Gly Glu Cys
115

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<400> 285

Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Thr Ser Thr Ser
1 5 10 15

Gly Arg Ser Ala Asn Pro Arg Gly Pro Ser Asp Glu Gln Leu Lys Ser
20 25 30

Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu
35 40 45

Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser
50 55 60

Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu
65 70 75 80

Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val
85 90 95

Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys
100 105 110

Ser Phe Asn Arg Gly Glu Cys
115

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<400> 286

```
Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Thr Ser Thr
1               5                  10                  15

Ser Gly Arg Ser Ala Asn Pro Arg Gly Ser Asp Glu Gln Leu Lys Ser
            20                  25                  30

Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu
        35                  40                  45

Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser
    50                  55                  60

Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu
65                  70                  75                  80

Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val
                85                  90                  95

Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys
            100                 105                 110

Ser Phe Asn Arg Gly Glu Cys
        115
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<400> 287

Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Thr Ser
1 5 10 15

Thr Ser Gly Arg Ser Ala Asn Pro Arg Gly Asp Glu Gln Leu Lys Ser
20 25 30

Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu
35 40 45

Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser
50 55 60

Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu
65 70 75 80

Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val
85 90 95

Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys
100 105 110

Ser Phe Asn Arg Gly Glu Cys
115

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<400> 288

```
Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Thr
1               5                  10                  15

Ser Thr Ser Gly Arg Ser Ala Asn Pro Arg Gly Glu Gln Leu Lys Ser
            20                  25                  30

Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu
        35                  40                  45

Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser
    50                  55                  60

Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu
65                  70                  75                  80

Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val
                85                  90                  95

Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys
            100                 105                 110

Ser Phe Asn Arg Gly Glu Cys
        115
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<210> 289
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<400> 289

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Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu
1               5                  10                  15
```

Thr Ser Thr Ser Gly Arg Ser Ala Asn Pro Arg Gly Gln Leu Lys Ser
20 25 30

Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu
35 40 45

Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser
50 55 60

Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu
65 70 75 80

Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val
85 90 95

Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys
100 105 110

Ser Phe Asn Arg Gly Glu Cys
115

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<220>
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<400> 290

Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu
1 5 10 15

Gln Thr Ser Thr Ser Gly Arg Ser Ala Asn Pro Arg Gly Leu Lys Ser
20 25 30

Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu
35 40 45

Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser
50 55 60

Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu
65 70 75 80

Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val
85 90 95

Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys
100 105 110

Ser Phe Asn Arg Gly Glu Cys
115

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<400> 291

Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu
1 5 10 15

Gln Leu Thr Ser Thr Ser Gly Arg Ser Ala Asn Pro Arg Gly Lys Ser
20 25 30

Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu
35 40 45

Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser
50 55 60

Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu
65 70 75 80

Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val
85 90 95

Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys
100 105 110

Ser Phe Asn Arg Gly Glu Cys
115

<210> 292
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<400> 292

Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu
1 5 10 15

Gln Leu Lys Thr Ser Thr Ser Gly Arg Ser Ala Asn Pro Arg Gly Ser
20 25 30

Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu
35 40 45

Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser
50 55 60

Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu
65 70 75 80

Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val
85 90 95

Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys
100 105 110

Ser Phe Asn Arg Gly Glu Cys
115

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<400> 293

Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu
1 5 10 15

Gln Leu Lys Ser Thr Ser Thr Ser Gly Arg Ser Ala Asn Pro Arg Gly
20 25 30

Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu
35 40 45

Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser
50 55 60

Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu
65 70 75 80

Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val
85 90 95

Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys
100 105 110

Ser Phe Asn Arg Gly Glu Cys
115

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<400> 294

Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu
1 5 10 15

Gln Leu Lys Ser Gly Thr Ser Thr Ser Gly Arg Ser Ala Asn Pro Arg
20 25 30

Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu
35 40 45

Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser
50 55 60

Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu
65 70 75 80

Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val
85 90 95

Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys
100 105 110

Ser Phe Asn Arg Gly Glu Cys
115

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<400> 295

Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu
1 5 10 15

Gln Leu Lys Ser Gly Thr Thr Ser Thr Ser Gly Arg Ser Ala Asn Pro
20 25 30

Arg Gly Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu
35 40 45

Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser
50 55 60

Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu
65 70 75 80

Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val
85 90 95

Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys
100 105 110

Ser Phe Asn Arg Gly Glu Cys
115

<210> 296
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<400> 296

Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu
1 5 10 15

Gln Leu Lys Ser Gly Thr Ala Thr Ser Thr Ser Gly Arg Ser Ala Asn
20 25 30

Pro Arg Gly Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu
35 40 45

Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser
50 55 60

Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu
65 70 75 80

Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val
85 90 95

Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys
100 105 110

Ser Phe Asn Arg Gly Glu Cys
115

<210> 297
<211> 441
<212> PRT
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<220>
<223> 人造的合成序列

<400> 297

Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg
1 5 10 15

Ser Leu Arg Leu Asp Cys Lys Ala Ser Gly Ile Thr Phe Ser Asn Ser
20 25 30

Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ala Val Ile Trp Tyr Asp Gly Ser Lys Arg Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Phe
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Thr Asn Asp Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser
100 105 110

Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser
115 120 125

Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp
130 135 140

Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr
145 150 155 160

Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr
165 170 175

Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln
180 185 190

Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp
195 200 205

Lys Arg Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro
210 215 220

Cys Pro Ala Pro Glu Leu Arg Arg Gly Pro Ser Val Phe Leu Phe Pro
225 230 235 240

Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr
245 250 255

Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn
260 265 270

Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg
275 280 285

Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val
290 295 300

Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser
305 310 315 320

Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys
325 330 335

Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu
340 345 350

Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe
355 360 365

Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu
370 375 380

Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe
385 390 395 400

Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Glu Gly
405 410 415

Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr
420 425 430

Thr Gln Lys Ser Leu Ser Leu Ser Pro
435 440

<210> 298
<211> 214
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 298

Glu Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
1 5 10 15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Tyr
20 25 30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile
35 40 45

Tyr Asp Ala Ser Asn Arg Ala Thr Gly Ile Pro Ala Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Glu Pro
65 70 75 80

Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Ser Ser Asn Trp Pro Arg
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala
100 105 110

Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly
115 120 125

Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala
130 135 140

Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln
145 150 155 160

Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser
165 170 175

Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr
180 185 190

Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser
195 200 205

Phe Asn Arg Gly Glu Cys
210

<210> 299
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<212> PRT
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<220>
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<400> 299

Thr Ser Thr Ser Gly Arg Ser Ala Asn Pro Arg Gly
1 5 10

<210> 300
<211> 113

<212> PRT
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<400> 300

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Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg
1               5                  10                  15

Ser Leu Arg Leu Asp Cys Lys Ala Ser Gly Ile Thr Phe Ser Asn Ser
            20                  25                  30

Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Ala Val Ile Trp Tyr Asp Gly Ser Lys Arg Tyr Tyr Ala Asp Ser Val
    50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Phe
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Thr Asn Asp Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser
            100                 105                 110

Ser
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<210> 301
<211> 328
<212> PRT
<213> 人造序列

<220>
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<400> 301

Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys
1 5 10 15

Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr
20 25 30

Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser
35 40 45

Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser
50 55 60

Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr
65 70 75 80

Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys
85 90 95

Arg Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys
100 105 110

Pro Ala Pro Glu Leu Arg Arg Gly Pro Ser Val Phe Leu Phe Pro Pro
115 120 125

Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys
130 135 140

Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp
145 150 155 160

Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu
165 170 175

Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu
180 185 190

His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn
195 200 205

Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly
210 215 220

Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu
225 230 235 240

Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr
245 250 255

Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn
260 265 270

Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe
275 280 285

Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Glu Gly Asn
290 295 300

Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr
305 310 315 320

Gln Lys Ser Leu Ser Leu Ser Pro
325

<210> 302
<211> 107
<212> PRT
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<400> 302

Glu Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
1 5 10 15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Tyr
20 25 30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile
35 40 45

Tyr Asp Ala Ser Asn Arg Ala Thr Gly Ile Pro Ala Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Glu Pro
65 70 75 80

Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Ser Ser Asn Trp Pro Arg
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
100 105

<210> 303
<211> 107
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 303

Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu
1 5 10 15

Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe
20 25 30

Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln
35 40 45

Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser
50 55 60

Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu
65 70 75 80

Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser
85 90 95

Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
100 105

<210> 304
<211> 453
<212> PRT
<213> 人造序列

<220>
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<400> 304

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Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg
1               5                  10                  15

Ser Leu Arg Leu Asp Cys Lys Ala Ser Gly Ile Thr Phe Ser Asn Ser
            20                  25                  30

Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Ala Val Ile Trp Tyr Asp Gly Ser Lys Arg Tyr Tyr Ala Asp Ser Val
    50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Phe
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Thr Asn Asp Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser
            100                 105                 110

Ser Thr Ser Thr Ser Gly Arg Ser Ala Asn Pro Arg Gly Ala Ser Thr
        115                 120                 125

Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser
    130                 135                 140

Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu
145                 150                 155                 160

Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His
                165                 170                 175
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Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser
180 185 190

Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys
195 200 205

Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu
210 215 220

Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro
225 230 235 240

Glu Leu Arg Arg Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys
245 250 255

Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val
260 265 270

Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp
275 280 285

Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr
290 295 300

Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp
305 310 315 320

Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu
325 330 335

Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg
340 345 350

Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys
355 360 365

Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp
370 375 380

Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys
385 390 395 400

Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser
405 410 415

Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Glu Gly Asn Val Phe Ser
420 425 430

Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser
435 440 445

Leu Ser Leu Ser Pro
450

<210> 305
<211> 453
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 305

Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg
1 5 10 15

Ser Leu Arg Leu Asp Cys Lys Ala Ser Gly Ile Thr Phe Ser Asn Ser
20 25 30

```
Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Ala Val Ile Trp Tyr Asp Gly Ser Lys Arg Tyr Tyr Ala Asp Ser Val
    50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Phe
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Thr Asn Asp Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser
            100                 105                 110

Ser Ala Thr Ser Thr Ser Gly Arg Ser Ala Asn Pro Arg Gly Ser Thr
        115                 120                 125

Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser
    130                 135                 140

Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu
145                 150                 155                 160

Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His
                165                 170                 175

Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser
            180                 185                 190

Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys
        195                 200                 205
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Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu
    210                 215                 220

Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro
225                 230                 235                 240

Glu Leu Arg Arg Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys
                245                 250                 255

Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val
            260                 265                 270

Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp
        275                 280                 285

Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr
    290                 295                 300

Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp
305                 310                 315                 320

Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu
                325                 330                 335

Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg
            340                 345                 350

Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys
        355                 360                 365

Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp
    370                 375                 380
```

Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys
385 390 395 400

Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser
405 410 415

Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Glu Gly Asn Val Phe Ser
420 425 430

Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser
435 440 445

Leu Ser Leu Ser Pro
450

<210> 306
<211> 226
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 306

Glu Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
1 5 10 15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Tyr
20 25 30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile
35 40 45

Tyr Asp Ala Ser Asn Arg Ala Thr Gly Ile Pro Ala Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Glu Pro
65 70 75 80

Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Ser Ser Asn Trp Pro Arg
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Thr Ser Thr Ser Gly Arg Ser Ala
100 105 110

Asn Pro Arg Gly Glu Ile Lys Arg Thr Val Ala Ala Pro Ser Val Phe
115 120 125

Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr Ala Ser Val
130 135 140

Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp
145 150 155 160

Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser Val Thr
165 170 175

Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr
180 185 190

Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala Cys Glu Val
195 200 205

Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe Asn Arg Gly
210 215 220

Glu Cys
225

<210> 307
<211> 226
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 307

Glu Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
1 5 10 15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Tyr
20 25 30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile
35 40 45

Tyr Asp Ala Ser Asn Arg Ala Thr Gly Ile Pro Ala Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Glu Pro
65 70 75 80

Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Ser Ser Asn Trp Pro Arg
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Thr Ser Thr Ser Gly Arg Ser
100 105 110

Ala Asn Pro Arg Gly Ile Lys Arg Thr Val Ala Ala Pro Ser Val Phe
115 120 125

Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr Ala Ser Val
130 135 140

Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp
145 150 155 160

Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser Val Thr
165 170 175

Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr
180 185 190

Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala Cys Glu Val
195 200 205

Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe Asn Arg Gly
210 215 220

Glu Cys
225

<210> 308
<211> 226
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 308

Glu Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
1 5 10 15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Tyr
20 25 30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile
35 40 45

Tyr Asp Ala Ser Asn Arg Ala Thr Gly Ile Pro Ala Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Glu Pro
65 70 75 80

Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Ser Ser Asn Trp Pro Arg
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Thr Ser Thr Ser Gly Arg
100 105 110

Ser Ala Asn Pro Arg Gly Lys Arg Thr Val Ala Ala Pro Ser Val Phe
115 120 125

Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr Ala Ser Val
130 135 140

Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp
145 150 155 160

Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser Val Thr
165 170 175

Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr
180 185 190

Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala Cys Glu Val
195 200 205

Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe Asn Arg Gly
210 215 220

Glu Cys
225

<210> 309
<211> 226
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 309

Glu Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
1 5 10 15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Tyr
20 25 30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile
35 40 45

Tyr Asp Ala Ser Asn Arg Ala Thr Gly Ile Pro Ala Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Glu Pro
65 70 75 80

Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Ser Ser Asn Trp Pro Arg
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Thr Ser Thr Ser Gly
100 105 110

Arg Ser Ala Asn Pro Arg Gly Arg Thr Val Ala Ala Pro Ser Val Phe
115 120 125

Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr Ala Ser Val
130 135 140

Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp
145 150 155 160

Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser Val Thr
165 170 175

Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr
180 185 190

Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala Cys Glu Val
195 200 205

Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe Asn Arg Gly
210 215 220

Glu Cys
225

<210> 310
<211> 226
<212> PRT
<213> 人造序列

<220>

<223> 人造的合成序列

<400> 310

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Glu Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
1               5                  10                  15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Tyr
            20                  25                  30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile
        35                  40                  45

Tyr Asp Ala Ser Asn Arg Ala Thr Gly Ile Pro Ala Arg Phe Ser Gly
    50                  55                  60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Glu Pro
65                  70                  75                  80

Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Ser Ser Asn Trp Pro Arg
                85                  90                  95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg Thr Ser Thr Ser
            100                 105                 110

Gly Arg Ser Ala Asn Pro Arg Gly Thr Val Ala Ala Pro Ser Val Phe
        115                 120                 125

Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr Ala Ser Val
    130                 135                 140

Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp
145                 150                 155                 160
```

Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser Val Thr
165 170 175

Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr
180 185 190

Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala Cys Glu Val
195 200 205

Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe Asn Arg Gly
210 215 220

Glu Cys
225

<210> 311
<211> 226
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 311

Glu Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
1 5 10 15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Tyr
20 25 30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile
35 40 45

Tyr Asp Ala Ser Asn Arg Ala Thr Gly Ile Pro Ala Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Glu Pro
65 70 75 80

Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Ser Ser Asn Trp Pro Arg
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg Thr Thr Ser Thr
100 105 110

Ser Gly Arg Ser Ala Asn Pro Arg Gly Val Ala Ala Pro Ser Val Phe
115 120 125

Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr Ala Ser Val
130 135 140

Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp
145 150 155 160

Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser Val Thr
165 170 175

Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr
180 185 190

Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala Cys Glu Val
195 200 205

Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe Asn Arg Gly
210 215 220

Glu Cys
225

<210> 312
<211> 226
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 312

Glu Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
1 5 10 15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Tyr
20 25 30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile
35 40 45

Tyr Asp Ala Ser Asn Arg Ala Thr Gly Ile Pro Ala Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Glu Pro
65 70 75 80

Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Ser Ser Asn Trp Pro Arg
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg Thr Val Thr Ser
100 105 110

Thr Ser Gly Arg Ser Ala Asn Pro Arg Gly Ala Ala Pro Ser Val Phe
115 120 125

Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr Ala Ser Val
130 135 140

Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp
145 150 155 160

Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser Val Thr
165 170 175

Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr
180 185 190

Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala Cys Glu Val
195 200 205

Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe Asn Arg Gly
210 215 220

Glu Cys
225

<210> 313
<211> 226
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 313

Glu Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
1 5 10 15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Tyr
20 25 30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile
35 40 45

Tyr Asp Ala Ser Asn Arg Ala Thr Gly Ile Pro Ala Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Glu Pro
65 70 75 80

Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Ser Ser Asn Trp Pro Arg
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Thr
100 105 110

Ser Thr Ser Gly Arg Ser Ala Asn Pro Arg Gly Ala Pro Ser Val Phe
115 120 125

Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr Ala Ser Val
130 135 140

Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp
145 150 155 160

Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser Val Thr
165 170 175

Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr
180 185 190

Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala Cys Glu Val
195 200 205

Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe Asn Arg Gly
210 215 220

Glu Cys
225

<210> 314
<211> 226
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 314

Glu Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
1 5 10 15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Tyr
20 25 30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile
35 40 45

Tyr Asp Ala Ser Asn Arg Ala Thr Gly Ile Pro Ala Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Glu Pro
65 70 75 80

Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Ser Ser Asn Trp Pro Arg
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala
100 105 110

Thr Ser Thr Ser Gly Arg Ser Ala Asn Pro Arg Gly Pro Ser Val Phe
115 120 125

Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr Ala Ser Val
130 135 140

Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp
145 150 155 160

Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser Val Thr
165 170 175

Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr
180 185 190

Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala Cys Glu Val
195 200 205

Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe Asn Arg Gly
210 215 220

Glu Cys
225

<210> 315
<211> 226
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 315

```
Glu Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
1               5                  10                  15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Tyr
            20                  25                  30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile
        35                  40                  45

Tyr Asp Ala Ser Asn Arg Ala Thr Gly Ile Pro Ala Arg Phe Ser Gly
    50                  55                  60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Glu Pro
65                  70                  75                  80

Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Ser Ser Asn Trp Pro Arg
                85                  90                  95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala
            100                 105                 110

Pro Thr Ser Thr Ser Gly Arg Ser Ala Asn Pro Arg Gly Ser Val Phe
        115                 120                 125

Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr Ala Ser Val
    130                 135                 140

Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp
145                 150                 155                 160

Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser Val Thr
                165                 170                 175
```

Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr
180 185 190

Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala Cys Glu Val
195 200 205

Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe Asn Arg Gly
210 215 220

Glu Cys
225

<210> 316
<211> 15
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 316

Gly Leu Asn Asp Ile Phe Glu Ala Gln Lys Ile Glu Trp His Glu
1 5 10 15

<210> 317
<211> 461
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 317

Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg
1 5 10 15

Ser Leu Arg Leu Asp Cys Lys Ala Ser Gly Ile Thr Phe Ser Asn Ser
20 25 30

Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ala Val Ile Trp Tyr Asp Gly Ser Lys Arg Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Phe
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Thr Asn Asp Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser
100 105 110

Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser
115 120 125

Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp
130 135 140

Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr
145 150 155 160

Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr
165 170 175

Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln
180 185 190

Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp
195 200 205

Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro
210 215 220

Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro
225 230 235 240

Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr
245 250 255

Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn
260 265 270

Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg
275 280 285

Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val
290 295 300

Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser
305 310 315 320

Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys
325 330 335

Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp
340 345 350

Glu Leu Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe
355 360 365

Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu
370 375 380

Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe
385 390 395 400

Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly
405 410 415

Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr
420 425 430

Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Gly Gly Gly Ser Gly Leu
435 440 445

Asn Asp Ile Phe Glu Ala Gln Lys Ile Glu Trp His Glu
450 455 460

<210> 318
<211> 641
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 318

Met Ser Asp Glu Gly Pro Gly Thr Gly Pro Gly Asn Gly Leu Gly Glu
1 5 10 15

Lys Gly Asp Thr Ser Gly Pro Glu Gly Ser Gly Gly Ser Gly Pro Gln
20 25 30

Arg Arg Gly Gly Asp Asn His Gly Arg Gly Arg Gly Arg Gly Arg Gly
35 40 45

Arg Gly Gly Gly Arg Pro Gly Ala Pro Gly Gly Ser Gly Ser Gly Pro
50 55 60

Arg His Arg Asp Gly Val Arg Arg Pro Gln Lys Arg Pro Ser Cys Ile
65 70 75 80

Gly Cys Lys Gly Thr His Gly Gly Thr Gly Ala Gly Ala Gly Ala Gly
85 90 95

Gly Ala Gly Ala Gly Gly Ala Gly Ala Gly Gly Gly Ala Gly Ala Gly
100 105 110

Gly Gly Ala Gly Gly Ala Gly Gly Ala Gly Gly Ala Gly Ala Gly Gly
115 120 125

Gly Ala Gly Ala Gly Gly Gly Ala Gly Gly Ala Gly Gly Ala Gly Ala
130 135 140

Gly Gly Gly Ala Gly Ala Gly Gly Gly Ala Gly Gly Ala Gly Ala Gly
145 150 155 160

Gly Gly Ala Gly Gly Ala Gly Gly Ala Gly Ala Gly Gly Gly Ala Gly
165 170 175

Ala Gly Gly Gly Ala Gly Gly Ala Gly Ala Gly Gly Gly Ala Gly Gly
180 185 190

Ala Gly Gly Ala Gly Ala Gly Gly Gly Ala Gly Ala Gly Gly Ala Gly
195 200 205

Gly Ala Gly Gly Ala Gly Ala Gly Gly Ala Gly Ala Gly Gly Gly Ala
210 215 220

Gly Gly Ala Gly Gly Ala Gly Ala Gly Gly Ala Gly Ala Gly Gly Ala
225 230 235 240

Gly Ala Gly Gly Ala Gly Ala Gly Gly Ala Gly Gly Ala Gly Ala Gly
245 250 255

Gly Ala Gly Gly Ala Gly Ala Gly Gly Ala Gly Gly Ala Gly Ala Gly
260 265 270

Gly Gly Ala Gly Gly Ala Gly Ala Gly Gly Gly Ala Gly Gly Ala Gly
275 280 285

Ala Gly Gly Ala Gly Gly Ala Gly Ala Gly Gly Ala Gly Gly Ala Gly
290 295 300

Ala Gly Gly Ala Gly Gly Ala Gly Ala Gly Gly Gly Ala Gly Ala Gly
305 310 315 320

Gly Ala Gly Ala Gly Gly Gly Gly Arg Gly Arg Gly Gly Ser Gly Gly
325 330 335

Arg Gly Arg Gly Gly Ser Gly Gly Arg Gly Arg Gly Gly Ser Gly Gly
340 345 350

Arg Arg Gly Arg Gly Arg Glu Arg Ala Arg Gly Gly Ser Arg Glu Arg
355 360 365

Ala Arg Gly Arg Gly Arg Gly Arg Gly Glu Lys Arg Pro Arg Ser Pro
370 375 380

Ser Ser Gln Ser Ser Ser Ser Gly Ser Pro Pro Arg Arg Pro Pro Pro
385 390 395 400

Gly Arg Arg Pro Phe Phe His Pro Val Gly Glu Ala Asp Tyr Phe Glu
405 410 415

Tyr His Gln Glu Gly Gly Pro Asp Gly Glu Pro Asp Val Pro Pro Gly
420 425 430

Ala Ile Glu Gln Gly Pro Ala Asp Asp Pro Gly Glu Gly Pro Ser Thr
435 440 445

Gly Pro Arg Gly Gln Gly Asp Gly Gly Arg Arg Lys Lys Gly Gly Trp
450 455 460

Phe Gly Lys His Arg Gly Gln Gly Gly Ser Asn Pro Lys Phe Glu Asn
465 470 475 480

Ile Ala Glu Gly Leu Arg Ala Leu Leu Ala Arg Ser His Val Glu Arg
485 490 495

Thr Thr Asp Glu Gly Thr Trp Val Ala Gly Val Phe Val Tyr Gly Gly
500 505 510

Ser Lys Thr Ser Leu Tyr Asn Leu Arg Arg Gly Thr Ala Leu Ala Ile
515 520 525

Pro Gln Cys Arg Leu Thr Pro Leu Ser Arg Leu Pro Phe Gly Met Ala
530 535 540

Pro Gly Pro Gly Pro Gln Pro Gly Pro Leu Arg Glu Ser Ile Val Cys
545 550 555 560

Tyr Phe Met Val Phe Leu Gln Thr His Ile Phe Ala Glu Val Leu Lys
565 570 575

Asp Ala Ile Lys Asp Leu Val Met Thr Lys Pro Ala Pro Thr Cys Asn
580 585 590

Ile Arg Val Thr Val Cys Ser Phe Asp Asp Gly Val Asp Leu Pro Pro
595 600 605

Trp Phe Pro Pro Met Val Glu Gly Ala Ala Ala Glu Gly Asp Asp Gly
610 615 620

Asp Asp Gly Asp Glu Gly Gly Asp Gly Asp Glu Gly Glu Glu Gly Gln
625 630 635 640

Glu

<210> 319
<211> 347
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 319

Met Val Leu Ala Ser Ser Thr Thr Ser Ile His Thr Met Leu Leu Leu
1 5 10 15

Leu Leu Met Leu Ala Gln Pro Ala Met Ala Met Lys Asp Asn Thr Val
20 25 30

Pro Leu Lys Leu Ile Ala Leu Leu Ala Asn Gly Glu Phe His Ser Gly
35 40 45

Glu Gln Leu Gly Glu Thr Leu Gly Met Ser Arg Ala Ala Ile Asn Lys
50 55 60

His Ile Gln Thr Leu Arg Asp Trp Gly Val Asp Val Phe Thr Val Pro
65 70 75 80

Gly Lys Gly Tyr Ser Leu Pro Glu Pro Ile Gln Leu Leu Asn Ala Lys
85 90 95

Gln Ile Leu Gly Gln Leu Asp Gly Gly Ser Val Ala Val Leu Pro Val
100 105 110

Ile Asp Ser Thr Asn Gln Tyr Leu Leu Asp Arg Ile Gly Glu Leu Lys
115 120 125

Ser Gly Asp Ala Cys Ile Ala Glu Tyr Gln Gln Ala Gly Arg Gly Arg
130 135 140

Arg Gly Arg Lys Trp Phe Ser Pro Phe Gly Ala Asn Leu Tyr Leu Ser
145 150 155 160

Met Phe Trp Arg Leu Glu Gln Gly Pro Ala Ala Ala Ile Gly Leu Ser
165 170 175

Leu Val Ile Gly Ile Val Met Ala Glu Val Leu Arg Lys Leu Gly Ala
180 185 190

Asp Lys Val Arg Val Lys Trp Pro Asn Asp Leu Tyr Leu Gln Asp Arg
195 200 205

Lys Leu Ala Gly Ile Leu Val Glu Leu Thr Gly Lys Thr Gly Asp Ala
210 215 220

```
Ala Gln Ile Val Ile Gly Ala Gly Ile Asn Met Ala Met Arg Arg Val
225                 230                 235                 240

Glu Glu Ser Val Val Asn Gln Gly Trp Ile Thr Leu Gln Glu Ala Gly
                245                 250                 255

Ile Asn Leu Asp Arg Asn Thr Leu Ala Ala Met Leu Ile Arg Glu Leu
            260                 265                 270

Arg Ala Ala Leu Glu Leu Phe Glu Gln Glu Gly Leu Ala Pro Tyr Leu
        275                 280                 285

Ser Arg Trp Glu Lys Leu Asp Asn Phe Ile Asn Arg Pro Val Lys Leu
    290                 295                 300

Ile Ile Gly Asp Lys Glu Ile Phe Gly Ile Ser Arg Gly Ile Asp Lys
305                 310                 315                 320

Gln Gly Ala Leu Leu Leu Glu Gln Asp Gly Ile Ile Lys Pro Trp Met
                325                 330                 335

Gly Gly Glu Ile Ser Leu Arg Ser Ala Glu Lys
            340                 345
```

<210> 320
<211> 147
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 320

Pro Gly Trp Phe Leu Asp Ser Pro Asp Arg Pro Trp Asn Pro Pro Thr
1 5 10 15

Phe Ser Pro Ala Leu Leu Val Val Thr Glu Gly Asp Asn Ala Thr Phe
20 25 30

Thr Cys Ser Phe Ser Asn Thr Ser Glu Ser Phe Val Leu Asn Trp Tyr
35 40 45

Arg Met Ser Pro Ser Asn Gln Thr Asp Lys Leu Ala Ala Phe Pro Glu
50 55 60

Asp Arg Ser Gln Pro Gly Gln Asp Cys Arg Phe Arg Val Thr Gln Leu
65 70 75 80

Pro Asn Gly Arg Asp Phe His Met Ser Val Val Arg Ala Arg Arg Asn
85 90 95

Asp Ser Gly Thr Tyr Leu Cys Gly Ala Ile Ser Leu Ala Pro Lys Ala
100 105 110

Gln Ile Lys Glu Ser Leu Arg Ala Glu Leu Arg Val Thr Glu Arg Arg
115 120 125

Ala Glu Val Pro Thr Ala His Pro Ser Pro Ser Pro Arg Pro Ala Gly
130 135 140

Gln Phe Gln
145

<210> 321
<211> 25
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 321

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
1 5 10 15

Gly Gly Gly Ser Gly Gly Gly Gly Ser
20 25

<210> 322
<211> 226
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 322

Glu Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
1 5 10 15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Tyr
20 25 30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile
35 40 45

Tyr Asp Ala Ser Asn Arg Ala Thr Gly Ile Pro Ala Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Glu Pro
65 70 75 80

Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Ser Ser Asn Trp Pro Arg
85 90 95

Thr Phe Gly Gln Gly Thr Lys Thr Ser Thr Ser Gly Arg Ser Ala Asn
100 105 110

Pro Arg Gly Val Glu Ile Lys Arg Thr Val Ala Ala Pro Ser Val Phe
115 120 125

Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr Ala Ser Val
130 135 140

Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp
145 150 155 160

Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser Val Thr
165 170 175

Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr
180 185 190

Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala Cys Glu Val
195 200 205

Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe Asn Arg Gly
210 215 220

Glu Cys
225

<210> 323
<211> 625
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 323

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Pro Gly Trp Phe Leu Asp Ser Pro Asp Arg Pro Trp Asn Pro Pro Thr
1               5                  10                  15

Phe Ser Pro Ala Leu Leu Val Val Thr Glu Gly Asp Asn Ala Thr Phe
            20                  25                  30

Thr Cys Ser Phe Ser Asn Thr Ser Glu Ser Phe Val Leu Asn Trp Tyr
        35                  40                  45

Arg Met Ser Pro Ser Asn Gln Thr Asp Lys Leu Ala Ala Phe Pro Glu
    50                  55                  60

Asp Arg Ser Gln Pro Gly Gln Asp Cys Arg Phe Arg Val Thr Gln Leu
65                  70                  75                  80

Pro Asn Gly Arg Asp Phe His Met Ser Val Val Arg Ala Arg Arg Asn
                85                  90                  95

Asp Ser Gly Thr Tyr Leu Cys Gly Ala Ile Ser Leu Ala Pro Lys Ala
            100                 105                 110

Gln Ile Lys Glu Ser Leu Arg Ala Glu Leu Arg Val Thr Glu Arg Arg
        115                 120                 125

Ala Glu Val Pro Thr Ala His Pro Ser Pro Ser Pro Arg Pro Ala Gly
    130                 135                 140

Gln Phe Gln Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly
145                 150                 155                 160
```

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Val Gln Leu
165 170 175

Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg Ser Leu Arg Leu
180 185 190

Asp Cys Lys Ala Ser Gly Ile Thr Phe Ser Asn Ser Gly Met His Trp
195 200 205

Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala Val Ile Trp
210 215 220

Tyr Asp Gly Ser Lys Arg Tyr Tyr Ala Asp Ser Val Lys Gly Arg Phe
225 230 235 240

Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Phe Leu Gln Met Asn
245 250 255

Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Thr Asn Asp
260 265 270

Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Thr Ser Thr
275 280 285

Ser Gly Arg Ser Ala Asn Pro Arg Gly Ala Ser Thr Lys Gly Pro Ser
290 295 300

Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala
305 310 315 320

Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val
325 330 335

Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala
340 345 350

Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val
355 360 365

Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His
370 375 380

Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys
385 390 395 400

Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Arg Arg
405 410 415

Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
420 425 430

Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His
435 440 445

Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val
450 455 460

His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr
465 470 475 480

Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly
485 490 495

Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ser Ser Ile
500 505 510

Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val
515 520 525

Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser
530 535 540

Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu
545 550 555 560

Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro
565 570 575

Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val
580 585 590

Asp Lys Ser Arg Trp Gln Glu Gly Asn Val Phe Ser Cys Ser Val Met
595 600 605

His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser
610 615 620

Pro
625

<210> 324
<211> 625
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 324

```
Pro Gly Trp Phe Leu Asp Ser Pro Asp Arg Pro Trp Asn Pro Pro Thr
1               5                  10                  15

Phe Ser Pro Ala Leu Leu Val Val Thr Glu Gly Asp Asn Ala Thr Phe
            20                  25                  30

Thr Cys Ser Phe Ser Asn Thr Ser Glu Ser Phe Val Leu Asn Trp Tyr
        35                  40                  45

Arg Met Ser Pro Ser Asn Gln Thr Asp Lys Leu Ala Ala Phe Pro Glu
    50                  55                  60

Asp Arg Ser Gln Pro Gly Gln Asp Cys Arg Phe Arg Val Thr Gln Leu
65                  70                  75                  80

Pro Asn Gly Arg Asp Phe His Met Ser Val Val Arg Ala Arg Arg Asn
                85                  90                  95

Asp Ser Gly Thr Tyr Leu Cys Gly Ala Ile Ser Leu Ala Pro Lys Ala
            100                 105                 110

Gln Ile Lys Glu Ser Leu Arg Ala Glu Leu Arg Val Thr Glu Arg Arg
        115                 120                 125

Ala Glu Val Pro Thr Ala His Pro Ser Pro Ser Pro Arg Pro Ala Gly
    130                 135                 140

Gln Phe Gln Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly
145                 150                 155                 160

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Val Gln Leu
                165                 170                 175
```

Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg Ser Leu Arg Leu
180 185 190

Asp Cys Lys Ala Ser Gly Ile Thr Phe Ser Asn Ser Gly Met His Trp
195 200 205

Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala Val Ile Trp
210 215 220

Tyr Asp Gly Ser Lys Arg Tyr Tyr Ala Asp Ser Val Lys Gly Arg Phe
225 230 235 240

Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Phe Leu Gln Met Asn
245 250 255

Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Thr Asn Asp
260 265 270

Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Thr Ser
275 280 285

Thr Ser Gly Arg Ser Ala Asn Pro Arg Gly Ser Thr Lys Gly Pro Ser
290 295 300

Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala
305 310 315 320

Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val
325 330 335

Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala
340 345 350

Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val
355 360 365

Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His
370 375 380

Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys
385 390 395 400

Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Arg Arg
405 410 415

Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
420 425 430

Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His
435 440 445

Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val
450 455 460

His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr
465 470 475 480

Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly
485 490 495

Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ser Ser Ile
500 505 510

Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val
515 520 525

Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser
530 535 540

Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu
545 550 555 560

Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro
565 570 575

Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val
580 585 590

Asp Lys Ser Arg Trp Gln Glu Gly Asn Val Phe Ser Cys Ser Val Met
595 600 605

His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser
610 615 620

Pro
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Phe Ser Pro Ala Leu Leu Val Val Thr Glu Gly Asp Asn Ala Thr Phe
20 25 30

Thr Cys Ser Phe Ser Asn Thr Ser Glu Ser Phe Val Leu Asn Trp Tyr
35 40 45

Arg Met Ser Pro Ser Asn Gln Thr Asp Lys Leu Ala Ala Phe Pro Glu
50 55 60

Asp Arg Ser Gln Pro Gly Gln Asp Cys Arg Phe Arg Val Thr Gln Leu
65 70 75 80

Pro Asn Gly Arg Asp Phe His Met Ser Val Val Arg Ala Arg Arg Asn
85 90 95

Asp Ser Gly Thr Tyr Leu Cys Gly Ala Ile Ser Leu Ala Pro Lys Ala
100 105 110

Gln Ile Lys Glu Ser Leu Arg Ala Glu Leu Arg Val Thr Glu Arg Arg
115 120 125

Ala Glu Val Pro Thr Ala His Pro Ser Pro Ser Pro Arg Pro Ala Gly
130 135 140

Gln Phe Gln Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly
145 150 155 160

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Ile Val Leu
165 170 175

Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr
180 185 190

Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Tyr Leu Ala Trp Tyr
195 200 205

Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr Asp Ala Ser
210 215 220

Asn Arg Ala Thr Gly Ile Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly
225 230 235 240

Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Glu Pro Glu Asp Phe Ala
245 250 255

Val Tyr Tyr Cys Gln Gln Ser Ser Asn Trp Pro Arg Thr Phe Gly Gln
260 265 270

Gly Thr Lys Thr Ser Thr Ser Gly Arg Ser Ala Asn Pro Arg Gly Val
275 280 285

Glu Ile Lys Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro
290 295 300

Ser Asp Glu Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu
305 310 315 320

Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn
325 330 335

Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser
340 345 350

Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala
355 360 365

Asp Tyr Glu Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly
370 375 380

Leu Ser Ser Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
385 390 395

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Phe Ser Pro Ala Leu Leu Val Val Thr Glu Gly Asp Asn Ala Thr Phe
20 25 30

Thr Cys Ser Phe Ser Asn Thr Ser Glu Ser Phe Val Leu Asn Trp Tyr
35 40 45

Arg Met Ser Pro Ser Asn Gln Thr Asp Lys Leu Ala Ala Phe Pro Glu
50 55 60

Asp Arg Ser Gln Pro Gly Gln Asp Cys Arg Phe Arg Val Thr Gln Leu
65 70 75 80

Pro Asn Gly Arg Asp Phe His Met Ser Val Val Arg Ala Arg Arg Asn
85 90 95

Asp Ser Gly Thr Tyr Leu Cys Gly Ala Ile Ser Leu Ala Pro Lys Ala
100 105 110

Gln Ile Lys Glu Ser Leu Arg Ala Glu Leu Arg Val Thr Glu Arg Arg
115 120 125

Ala Glu Val Pro Thr Ala His Pro Ser Pro Ser Pro Arg Pro Ala Gly
130 135 140

Gln Phe Gln Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly
145 150 155 160

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Ile Val Leu
165 170 175

Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr
180 185 190

Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Tyr Leu Ala Trp Tyr
195 200 205

Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr Asp Ala Ser
210 215 220

Asn Arg Ala Thr Gly Ile Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly
225 230 235 240

Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Glu Pro Glu Asp Phe Ala
245 250 255

Val Tyr Tyr Cys Gln Gln Ser Ser Asn Trp Pro Arg Thr Phe Gly Gln
260 265 270

Gly Thr Lys Val Thr Ser Thr Ser Gly Arg Ser Ala Asn Pro Arg Gly
275 280 285

Glu Ile Lys Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro
290 295 300

Ser Asp Glu Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu
305 310 315 320

Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn
325 330 335

Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser
340 345 350

Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala
355 360 365

Asp Tyr Glu Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly
370 375 380

Leu Ser Ser Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
385 390 395

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Phe Ser Pro Ala Leu Leu Val Val Thr Glu Gly Asp Asn Ala Thr Phe
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Thr Cys Ser Phe Ser Asn Thr Ser Glu Ser Phe Val Leu Asn Trp Tyr
35 40 45

Arg Met Ser Pro Ser Asn Gln Thr Asp Lys Leu Ala Ala Phe Pro Glu
50 55 60

Asp Arg Ser Gln Pro Gly Gln Asp Cys Arg Phe Arg Val Thr Gln Leu
65 70 75 80

Pro Asn Gly Arg Asp Phe His Met Ser Val Val Arg Ala Arg Arg Asn
85 90 95

Asp Ser Gly Thr Tyr Leu Cys Gly Ala Ile Ser Leu Ala Pro Lys Ala
100 105 110

Gln Ile Lys Glu Ser Leu Arg Ala Glu Leu Arg Val Thr Glu Arg Arg
115 120 125

Ala Glu Val Pro Thr Ala His Pro Ser Pro Ser Pro Arg Pro Ala Gly
130 135 140

Gln Phe Gln Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly
145 150 155 160

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Ile Val Leu
165 170 175

Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr
180 185 190

Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Tyr Leu Ala Trp Tyr
195 200 205

Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr Asp Ala Ser
210 215 220

Asn Arg Ala Thr Gly Ile Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly
225 230 235 240

Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Glu Pro Glu Asp Phe Ala
245 250 255

Val Tyr Tyr Cys Gln Gln Ser Ser Asn Trp Pro Arg Thr Phe Gly Gln
260 265 270

Gly Thr Lys Val Glu Thr Ser Thr Ser Gly Arg Ser Ala Asn Pro Arg
275 280 285

Gly Ile Lys Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro
290 295 300

Ser Asp Glu Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu
305 310 315 320

Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn
325 330 335

Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser
340 345 350

Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala
355 360 365

Asp Tyr Glu Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly
370 375 380

Leu Ser Ser Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
385 390 395

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Pro Gly Trp Phe Leu Asp Ser Pro Asp Arg Pro Trp Asn Pro Pro Thr
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Phe Ser Pro Ala Leu Leu Val Val Thr Glu Gly Asp Asn Ala Thr Phe
20 25 30

Thr Cys Ser Phe Ser Asn Thr Ser Glu Ser Phe Val Leu Asn Trp Tyr
35 40 45

Arg Met Ser Pro Ser Asn Gln Thr Asp Lys Leu Ala Ala Phe Pro Glu
50 55 60

Asp Arg Ser Gln Pro Gly Gln Asp Cys Arg Phe Arg Val Thr Gln Leu
65 70 75 80

Pro Asn Gly Arg Asp Phe His Met Ser Val Val Arg Ala Arg Arg Asn
85 90 95

Asp Ser Gly Thr Tyr Leu Cys Gly Ala Ile Ser Leu Ala Pro Lys Ala
100 105 110

Gln Ile Lys Glu Ser Leu Arg Ala Glu Leu Arg Val Thr Glu Arg Arg
115 120 125

Ala Glu Val Pro Thr Ala His Pro Ser Pro Ser Pro Arg Pro Ala Gly
130 135 140

Gln Phe Gln Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly
145 150 155 160

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Ile Val Leu
165 170 175

Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr
180 185 190

Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Tyr Leu Ala Trp Tyr
195 200 205

Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr Asp Ala Ser
210 215 220

Asn Arg Ala Thr Gly Ile Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly
225 230 235 240

Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Glu Pro Glu Asp Phe Ala
245 250 255

Val Tyr Tyr Cys Gln Gln Ser Ser Asn Trp Pro Arg Thr Phe Gly Gln
260 265 270

Gly Thr Lys Val Glu Ile Thr Ser Thr Ser Gly Arg Ser Ala Asn Pro
275 280 285

Arg Gly Lys Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro
290 295 300

Ser Asp Glu Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu
305 310 315 320

Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn
325 330 335

Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser
340 345 350

Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala
355 360 365

Asp Tyr Glu Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly
370 375 380

Leu Ser Ser Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
385 390 395

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Phe Ser Pro Ala Leu Leu Val Val Thr Glu Gly Asp Asn Ala Thr Phe
20 25 30

Thr Cys Ser Phe Ser Asn Thr Ser Glu Ser Phe Val Leu Asn Trp Tyr
35 40 45

Arg Met Ser Pro Ser Asn Gln Thr Asp Lys Leu Ala Ala Phe Pro Glu
50 55 60

Asp Arg Ser Gln Pro Gly Gln Asp Cys Arg Phe Arg Val Thr Gln Leu
65 70 75 80

Pro Asn Gly Arg Asp Phe His Met Ser Val Val Arg Ala Arg Arg Asn
85 90 95

Asp Ser Gly Thr Tyr Leu Cys Gly Ala Ile Ser Leu Ala Pro Lys Ala
100 105 110

Gln Ile Lys Glu Ser Leu Arg Ala Glu Leu Arg Val Thr Glu Arg Arg
115 120 125

Ala Glu Val Pro Thr Ala His Pro Ser Pro Ser Pro Arg Pro Ala Gly
130 135 140

Gln Phe Gln Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly
145 150 155 160

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Ile Val Leu
165 170 175

Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr
180 185 190

Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Tyr Leu Ala Trp Tyr
195 200 205

Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr Asp Ala Ser
210 215 220

Asn Arg Ala Thr Gly Ile Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly
225 230 235 240

Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Glu Pro Glu Asp Phe Ala
245 250 255

Val Tyr Tyr Cys Gln Gln Ser Ser Asn Trp Pro Arg Thr Phe Gly Gln
260 265 270

Gly Thr Lys Val Glu Ile Lys Arg Thr Ser Thr Ser Gly Arg Ser Ala
275 280 285

Asn Pro Arg Gly Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro
290 295 300

Ser Asp Glu Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu
305 310 315 320

Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn
325 330 335

Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser
340 345 350

Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala
355 360 365

Asp Tyr Glu Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly
370 375 380

Leu Ser Ser Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
385 390 395

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Pro Gly Trp Phe Leu Asp Ser Pro Asp Arg Pro Trp Asn Pro Pro Thr
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Phe Ser Pro Ala Leu Leu Val Val Thr Glu Gly Asp Asn Ala Thr Phe
20 25 30

Thr Cys Ser Phe Ser Asn Thr Ser Glu Ser Phe Val Leu Asn Trp Tyr
35 40 45

Arg Met Ser Pro Ser Asn Gln Thr Asp Lys Leu Ala Ala Phe Pro Glu
50 55 60

Asp Arg Ser Gln Pro Gly Gln Asp Cys Arg Phe Arg Val Thr Gln Leu
65 70 75 80

Pro Asn Gly Arg Asp Phe His Met Ser Val Val Arg Ala Arg Arg Asn
85 90 95

Asp Ser Gly Thr Tyr Leu Cys Gly Ala Ile Ser Leu Ala Pro Lys Ala
100 105 110

Gln Ile Lys Glu Ser Leu Arg Ala Glu Leu Arg Val Thr Glu Arg Arg
115 120 125

Ala Glu Val Pro Thr Ala His Pro Ser Pro Ser Pro Arg Pro Ala Gly
130 135 140

Gln Phe Gln Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly
145 150 155 160

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Ile Val Leu
165 170 175

Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr
180 185 190

Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Tyr Leu Ala Trp Tyr
195 200 205

Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr Asp Ala Ser
210 215 220

Asn Arg Ala Thr Gly Ile Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly
225 230 235 240

Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Glu Pro Glu Asp Phe Ala
245 250 255

Val Tyr Tyr Cys Gln Gln Ser Ser Asn Trp Pro Arg Thr Phe Gly Gln
260 265 270

Gly Thr Lys Val Glu Ile Lys Arg Thr Thr Ser Thr Ser Gly Arg Ser
275 280 285

Ala Asn Pro Arg Gly Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro
290 295 300

Ser Asp Glu Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu
305 310 315 320

Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn
325 330 335

Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser
340 345 350

Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala
355 360 365

Asp Tyr Glu Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly
370 375 380

Leu Ser Ser Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
385 390 395

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Pro Gly Trp Phe Leu Asp Ser Pro Asp Arg Pro Trp Asn Pro Pro Thr
1 5 10 15

Phe Ser Pro Ala Leu Leu Val Val Thr Glu Gly Asp Asn Ala Thr Phe
20 25 30

Thr Cys Ser Phe Ser Asn Thr Ser Glu Ser Phe Val Leu Asn Trp Tyr
35 40 45

Arg Met Ser Pro Ser Asn Gln Thr Asp Lys Leu Ala Ala Phe Pro Glu
50 55 60

Asp Arg Ser Gln Pro Gly Gln Asp Cys Arg Phe Arg Val Thr Gln Leu
65 70 75 80

Pro Asn Gly Arg Asp Phe His Met Ser Val Val Arg Ala Arg Arg Asn
85 90 95

Asp Ser Gly Thr Tyr Leu Cys Gly Ala Ile Ser Leu Ala Pro Lys Ala
100 105 110

Gln Ile Lys Glu Ser Leu Arg Ala Glu Leu Arg Val Thr Glu Arg Arg
115 120 125

Ala Glu Val Pro Thr Ala His Pro Ser Pro Ser Pro Arg Pro Ala Gly
130 135 140

Gln Phe Gln Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly
145 150 155 160

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Ile Val Leu
165 170 175

Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr
180 185 190

Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Tyr Leu Ala Trp Tyr
195 200 205

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Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr Asp Ala Ser
    210                 215                 220

Asn Arg Ala Thr Gly Ile Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly
225                 230                 235                 240

Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Glu Pro Glu Asp Phe Ala
                245                 250                 255

Val Tyr Tyr Cys Gln Gln Ser Ser Asn Trp Pro Arg Thr Phe Gly Gln
            260                 265                 270

Gly Thr Lys Val Glu Ile Lys Arg Thr Val Thr Ser Thr Ser Gly Arg
        275                 280                 285

Ser Ala Asn Pro Arg Gly Ala Ala Pro Ser Val Phe Ile Phe Pro Pro
    290                 295                 300

Ser Asp Glu Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu
305                 310                 315                 320

Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn
                325                 330                 335

Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser
            340                 345                 350

Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala
        355                 360                 365

Asp Tyr Glu Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly
    370                 375                 380
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Leu Ser Ser Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
385 390 395

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Pro Gly Trp Phe Leu Asp Ser Pro Asp Arg Pro Trp Asn Pro Pro Thr
1 5 10 15

Phe Ser Pro Ala Leu Leu Val Val Thr Glu Gly Asp Asn Ala Thr Phe
20 25 30

Thr Cys Ser Phe Ser Asn Thr Ser Glu Ser Phe Val Leu Asn Trp Tyr
35 40 45

Arg Met Ser Pro Ser Asn Gln Thr Asp Lys Leu Ala Ala Phe Pro Glu
50 55 60

Asp Arg Ser Gln Pro Gly Gln Asp Cys Arg Phe Arg Val Thr Gln Leu
65 70 75 80

Pro Asn Gly Arg Asp Phe His Met Ser Val Val Arg Ala Arg Arg Asn
85 90 95

Asp Ser Gly Thr Tyr Leu Cys Gly Ala Ile Ser Leu Ala Pro Lys Ala
100 105 110

Gln Ile Lys Glu Ser Leu Arg Ala Glu Leu Arg Val Thr Glu Arg Arg
115 120 125

Ala Glu Val Pro Thr Ala His Pro Ser Pro Ser Pro Arg Pro Ala Gly
130 135 140

Gln Phe Gln Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly
145 150 155 160

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Ile Val Leu
165 170 175

Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr
180 185 190

Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Tyr Leu Ala Trp Tyr
195 200 205

Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr Asp Ala Ser
210 215 220

Asn Arg Ala Thr Gly Ile Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly
225 230 235 240

Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Glu Pro Glu Asp Phe Ala
245 250 255

Val Tyr Tyr Cys Gln Gln Ser Ser Asn Trp Pro Arg Thr Phe Gly Gln
260 265 270

Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Thr Ser Thr Ser Gly
275 280 285

Arg Ser Ala Asn Pro Arg Gly Ala Pro Ser Val Phe Ile Phe Pro Pro
290 295 300

Ser Asp Glu Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu
305 310 315 320

Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn
325 330 335

Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser
340 345 350

Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala
355 360 365

Asp Tyr Glu Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly
370 375 380

Leu Ser Ser Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
385 390 395

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Pro Gly Trp Phe Leu Asp Ser Pro Asp Arg Pro Trp Asn Pro Pro Thr
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Phe Ser Pro Ala Leu Leu Val Val Thr Glu Gly Asp Asn Ala Thr Phe
20 25 30

Thr Cys Ser Phe Ser Asn Thr Ser Glu Ser Phe Val Leu Asn Trp Tyr
35 40 45

Arg Met Ser Pro Ser Asn Gln Thr Asp Lys Leu Ala Ala Phe Pro Glu
50 55 60

Asp Arg Ser Gln Pro Gly Gln Asp Cys Arg Phe Arg Val Thr Gln Leu
65 70 75 80

Pro Asn Gly Arg Asp Phe His Met Ser Val Val Arg Ala Arg Arg Asn
85 90 95

Asp Ser Gly Thr Tyr Leu Cys Gly Ala Ile Ser Leu Ala Pro Lys Ala
100 105 110

Gln Ile Lys Glu Ser Leu Arg Ala Glu Leu Arg Val Thr Glu Arg Arg
115 120 125

Ala Glu Val Pro Thr Ala His Pro Ser Pro Ser Pro Arg Pro Ala Gly
130 135 140

Gln Phe Gln Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly
145 150 155 160

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Ile Val Leu
165 170 175

Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr
180 185 190

Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Tyr Leu Ala Trp Tyr
195 200 205

Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr Asp Ala Ser
210 215 220

Asn Arg Ala Thr Gly Ile Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly
225 230 235 240

Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Glu Pro Glu Asp Phe Ala
245 250 255

Val Tyr Tyr Cys Gln Gln Ser Ser Asn Trp Pro Arg Thr Phe Gly Gln
260 265 270

Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala Thr Ser Thr Ser
275 280 285

Gly Arg Ser Ala Asn Pro Arg Gly Pro Ser Val Phe Ile Phe Pro Pro
290 295 300

Ser Asp Glu Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu
305 310 315 320

Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn
325 330 335

Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser
340 345 350

Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala
355 360 365

Asp Tyr Glu Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly
370 375 380

Leu Ser Ser Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
385 390 395

<210> 334
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Pro Gly Trp Phe Leu Asp Ser Pro Asp Arg Pro Trp Asn Pro Pro Thr
1 5 10 15

Phe Ser Pro Ala Leu Leu Val Val Thr Glu Gly Asp Asn Ala Thr Phe
20 25 30

Thr Cys Ser Phe Ser Asn Thr Ser Glu Ser Phe Val Leu Asn Trp Tyr
35 40 45

Arg Met Ser Pro Ser Asn Gln Thr Asp Lys Leu Ala Ala Phe Pro Glu
50 55 60

Asp Arg Ser Gln Pro Gly Gln Asp Cys Arg Phe Arg Val Thr Gln Leu
65 70 75 80

Pro Asn Gly Arg Asp Phe His Met Ser Val Val Arg Ala Arg Arg Asn
85 90 95

Asp Ser Gly Thr Tyr Leu Cys Gly Ala Ile Ser Leu Ala Pro Lys Ala
100 105 110

Gln Ile Lys Glu Ser Leu Arg Ala Glu Leu Arg Val Thr Glu Arg Arg
115 120 125

Ala Glu Val Pro Thr Ala His Pro Ser Pro Ser Pro Arg Pro Ala Gly
130 135 140

Gln Phe Gln Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly
145 150 155 160

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Ile Val Leu
165 170 175

Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr
180 185 190

Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Tyr Leu Ala Trp Tyr
195 200 205

Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr Asp Ala Ser
210 215 220

Asn Arg Ala Thr Gly Ile Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly
225 230 235 240

Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Glu Pro Glu Asp Phe Ala
245 250 255

Val Tyr Tyr Cys Gln Gln Ser Ser Asn Trp Pro Arg Thr Phe Gly Gln
260 265 270

Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala Pro Thr Ser Thr
275 280 285

Ser Gly Arg Ser Ala Asn Pro Arg Gly Ser Val Phe Ile Phe Pro Pro
290 295 300

Ser Asp Glu Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu
305 310 315 320

Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn
325 330 335

Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser
340 345 350

Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala
355 360 365

Asp Tyr Glu Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly
370 375 380

Leu Ser Ser Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
385 390 395

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Thr Ser Thr Ser Gly Arg Ser Ala Asn Pro Arg Gly
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<400> 356

Gln Met Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg
1 5 10 15

Ser Leu Arg Leu Ser Cys Thr Ala Ser Gly Phe Thr Phe Ser Asn Asn
20 25 30

Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ala Val Ile Trp Phe Asp Gly Met Asn Lys Phe Tyr Val Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Glu Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Ile Tyr Tyr Cys
85 90 95

```
Ala Arg Glu Gly Asp Gly Ser Gly Ile Tyr Tyr Tyr Tyr Gly Met Asp
            100                 105                 110

Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Thr Ser Thr Ser
        115                 120                 125

Gly Arg Ser Ala Asn Pro Arg Gly Ala Ser Thr Lys Gly Pro Ser Val
    130                 135                 140

Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala
145                 150                 155                 160

Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser
                165                 170                 175

Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val
            180                 185                 190

Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro
        195                 200                 205

Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys
    210                 215                 220

Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp
225                 230                 235                 240

Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Arg Arg Gly
                245                 250                 255

Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile
            260                 265                 270
```

Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu
275 280 285

Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His
290 295 300

Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg
305 310 315 320

Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys
325 330 335

Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu
340 345 350

Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr
355 360 365

Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu
370 375 380

Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp
385 390 395 400

Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val
405 410 415

Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp
420 425 430

Lys Ser Arg Trp Gln Glu Gly Asn Val Phe Ser Cys Ser Val Met His
435 440 445

Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
450 455 460

<210> 357

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<210> 367
<211> 474
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<213> 人造序列

<220>
<223> 人造的合成序列

<400> 367

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ser
1 5 10 15

Ser Val Thr Val Ser Cys Lys Ala Ser Gly Gly Thr Phe Ser Ser Phe
20 25 30

Ser Ile Thr Trp Leu Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Glu Ile Thr Pro Met Phe Gly Ile Ala Asn Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Ile Ser Ala Asp Glu Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Gly Leu Thr Ser Glu Asp Thr Ala Met Tyr Tyr Cys
85 90 95

```
Ala Arg Asp Gly Arg Phe Asp Val Ser Asp Leu Leu Thr Asp Lys Pro
            100                 105                 110

Lys Val Thr Ile Asn Tyr Asn Gly Met Asp Val Trp Gly Gln Gly Thr
        115                 120                 125

Thr Val Thr Val Ser Ser Thr Ser Thr Ser Gly Arg Ser Ala Asn Pro
    130                 135                 140

Arg Gly Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser
145                 150                 155                 160

Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys
                165                 170                 175

Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu
            180                 185                 190

Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu
        195                 200                 205

Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr
    210                 215                 220

Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val
225                 230                 235                 240

Asp Lys Arg Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro
                245                 250                 255

Pro Cys Pro Ala Pro Glu Leu Arg Arg Gly Pro Ser Val Phe Leu Phe
            260                 265                 270
```

Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val
275 280 285

Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe
290 295 300

Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro
305 310 315 320

Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr
325 330 335

Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val
340 345 350

Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys Ala
355 360 365

Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg
370 375 380

Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly
385 390 395 400

Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro
405 410 415

Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser
420 425 430

Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Glu
435 440 445

Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His
450 455 460

Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
465 470

<210> 368
<211> 462
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 368

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ser
1 5 10 15

Ser Val Thr Val Ser Cys Lys Ala Ser Gly Gly Thr Phe Ser Ser Phe
20 25 30

Ser Ile Thr Trp Leu Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Glu Ile Thr Pro Met Phe Gly Ile Ala Asn Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Ile Ser Ala Asp Glu Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Gly Leu Thr Ser Glu Asp Thr Ala Met Tyr Tyr Cys
85 90 95

Ala Arg Asp Gly Arg Phe Asp Val Ser Asp Leu Leu Thr Asp Lys Pro
100 105 110

Lys Val Thr Ile Asn Tyr Asn Gly Met Asp Val Trp Gly Gln Gly Thr
115 120 125

Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro
130 135 140

Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly
145 150 155 160

Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn
165 170 175

Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln
180 185 190

Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser
195 200 205

Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser
210 215 220

Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp Lys Thr
225 230 235 240

His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Arg Arg Gly Pro Ser
245 250 255

Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg
260 265 270

Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro
275 280 285

Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala
290 295 300

Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val
305 310 315 320

Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr
325 330 335

Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr
340 345 350

Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu
355 360 365

Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys
370 375 380

Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser
385 390 395 400

Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp
405 410 415

Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser
420 425 430

Arg Trp Gln Glu Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala
435 440 445

Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
450 455 460

<210> 369
<211> 216
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 369

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Gln Ser Val Leu Thr Gln Pro Pro Ser Ala Ser Gly Thr Pro Gly Gln
1               5                  10                  15

Arg Val Thr Ile Ser Cys Ser Gly Ser Ser Ser Asn Ile Gly Ser Asn
            20                  25                  30

Thr Val Asn Trp Tyr Gln Arg Leu Pro Gly Ala Ala Pro Gln Leu Leu
        35                  40                  45

Ile Tyr Asn Asn Asp Gln Arg Pro Ser Gly Ile Pro Asp Arg Phe Ser
    50                  55                  60

Gly Ser Lys Ser Gly Thr Ser Gly Ser Leu Val Ile Ser Gly Leu Gln
65                  70                  75                  80

Ser Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Ser Trp Asp Asp Ser Leu
                85                  90                  95

Asn Gly Arg Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly Gln
            100                 105                 110

Pro Lys Ala Ala Pro Ser Val Thr Leu Phe Pro Pro Ser Ser Glu Glu
        115                 120                 125
```

Leu Gln Ala Asn Lys Ala Thr Leu Val Cys Leu Ile Ser Asp Phe Tyr
130 135 140

Pro Gly Ala Val Thr Val Ala Trp Lys Ala Asp Ser Ser Pro Val Lys
145 150 155 160

Ala Gly Val Glu Thr Thr Thr Pro Ser Lys Gln Ser Asn Asn Lys Tyr
165 170 175

Ala Ala Ser Ser Tyr Leu Ser Leu Thr Pro Glu Gln Trp Lys Ser His
180 185 190

Arg Ser Tyr Ser Cys Gln Val Thr His Glu Gly Ser Thr Val Glu Lys
195 200 205

Thr Val Ala Pro Thr Glu Cys Ser
210 215

<210> 370
<211> 77
<212> PRT
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<220>
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<400> 370

Val Pro Leu Ser Arg Thr Val Arg Cys Thr Cys Ile Ser Ile Ser Asn
1 5 10 15

Gln Pro Val Asn Pro Arg Ser Leu Glu Lys Leu Glu Ile Ile Pro Ala
20 25 30

Ser Gln Phe Cys Pro Arg Val Glu Ile Ile Ala Thr Met Lys Lys Lys
35 40 45

Gly Glu Lys Arg Cys Leu Asn Pro Glu Ser Lys Ala Ile Lys Asn Leu
50 55 60

Leu Lys Ala Val Ser Lys Glu Arg Ser Lys Ala Ser Pro
65 70 75

<210> 371
<211> 302
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 371

Val Pro Leu Ser Arg Thr Val Arg Cys Thr Cys Ile Ser Ile Ser Asn
1 5 10 15

Gln Pro Val Asn Pro Arg Ser Leu Glu Lys Leu Glu Ile Ile Pro Ala
20 25 30

Ser Gln Phe Cys Pro Arg Val Glu Ile Ile Ala Thr Met Lys Lys Lys
35 40 45

Gly Glu Lys Arg Cys Leu Asn Pro Glu Ser Lys Ala Ile Lys Asn Leu
50 55 60

Leu Lys Ala Val Ser Lys Glu Arg Ser Lys Ala Ser Pro Gly Gly Gly
65 70 75 80

Gly Ser Gly Gly Gly Gly Gln Ser Val Leu Thr Gln Pro Pro Ser Ala
85 90 95

Ser Gly Thr Pro Gly Gln Arg Val Thr Ile Ser Cys Ser Gly Ser Ser
100 105 110

Ser Asn Ile Gly Ser Asn Thr Val Asn Trp Tyr Gln Arg Leu Pro Gly
115 120 125

Ala Ala Pro Gln Leu Leu Ile Tyr Asn Asn Asp Gln Arg Pro Ser Gly
130 135 140

Ile Pro Asp Arg Phe Ser Gly Ser Lys Ser Gly Thr Ser Gly Ser Leu
145 150 155 160

Val Ile Ser Gly Leu Gln Ser Glu Asp Glu Ala Asp Tyr Tyr Cys Ala
165 170 175

Ser Trp Asp Asp Ser Leu Asn Gly Arg Val Phe Gly Gly Gly Thr Lys
180 185 190

Leu Thr Val Leu Gly Gln Pro Lys Ala Ala Pro Ser Val Thr Leu Phe
195 200 205

Pro Pro Ser Ser Glu Glu Leu Gln Ala Asn Lys Ala Thr Leu Val Cys
210 215 220

Leu Ile Ser Asp Phe Tyr Pro Gly Ala Val Thr Val Ala Trp Lys Ala
225 230 235 240

Asp Ser Ser Pro Val Lys Ala Gly Val Glu Thr Thr Thr Pro Ser Lys
245 250 255

Gln Ser Asn Asn Lys Tyr Ala Ala Ser Ser Tyr Leu Ser Leu Thr Pro
260 265 270

Glu Gln Trp Lys Ser His Arg Ser Tyr Ser Cys Gln Val Thr His Glu
275 280 285

Gly Ser Thr Val Glu Lys Thr Val Ala Pro Thr Glu Cys Ser
290 295 300

<210> 372

<400> 372
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<210> 373
<211> 85
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 373

Val Pro Leu Ser Arg Thr Val Arg Cys Thr Cys Ile Ser Ile Ser Asn
1 5 10 15

Gln Pro Val Asn Pro Arg Ser Leu Glu Lys Leu Glu Ile Ile Pro Ala
20 25 30

Ser Gln Phe Cys Pro Arg Val Glu Ile Ile Ala Thr Met Lys Lys Lys
35 40 45

Gly Glu Lys Arg Cys Leu Asn Pro Glu Ser Lys Ala Ile Lys Asn Leu
50 55 60

Leu Lys Ala Val Ser Lys Glu Arg Ser Lys Ala Ser Pro His His His
65 70 75 80

His His His His His

<210> 374
<211> 5
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 374

Ser Phe Ser Ile Thr
1 5

<210> 375
<211> 17
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 375

Glu Ile Thr Pro Met Phe Gly Ile Ala Asn Tyr Ala Gln Lys Phe Gln
1 5 10 15

Gly

<210> 376
<211> 25
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 376

Asp Gly Arg Phe Asp Val Ser Asp Leu Leu Thr Asp Lys Pro Lys Val
1 5 10 15

Thr Ile Asn Tyr Asn Gly Met Asp Val
20 25

<210> 377
<211> 13
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 377

Ser Gly Ser Ser Ser Asn Ile Gly Ser Asn Thr Val Asn
1 5 10

<210> 378
<211> 7
<212> PRT
<213> 人造序列

<220>
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<400> 378

Asn Asn Asp Gln Arg Pro Ser
1 5

<210> 379
<211> 11
<212> PRT
<213> 人造序列

<220>
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<400> 379

Ala Ser Trp Asp Asp Ser Leu Asn Gly Arg Val
1 5 10

<210> 380
<211> 5
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 380

Asn Asn Gly Met His
1 5

<210> 381
<211> 17
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 381

Val Ile Trp Phe Asp Gly Met Asn Lys Phe Tyr Val Asp Ser Val Lys
1 5 10 15

Gly

<210> 382
<211> 15
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 382

Glu Gly Asp Gly Ser Gly Ile Tyr Tyr Tyr Tyr Gly Met Asp Val
1 5 10 15

<210> 383
<211> 12
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 383

Arg Ala Ser Gln Ser Val Ser Ser Ser Tyr Leu Ala
1 5 10

<210> 384
<211> 7
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 384

Gly Ala Ser Ser Arg Ala Thr
1 5

<210> 385
<211> 10
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 385

Gln Gln Tyr Gly Ser Ser Pro Ile Phe Thr
1 5 10

<210> 386
<211> 5
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 386

Thr Tyr Trp Leu Gly
1 5

<210> 387
<211> 17
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 387

Ile Met Ser Pro Val Asp Ser Asp Ile Arg Tyr Ser Pro Ser Phe Gln
1 5 10 15

Gly

<210> 388
<211> 10
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 388

Arg Arg Pro Gly Gln Gly Tyr Phe Asp Phe
1 5 10

<210> 389
<211> 11
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 389

Arg Ala Ser Gln Gly Ile Ser Ser Trp Leu Ala
1 5 10

<210> 390
<211> 7
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 390

Ala Ala Ser Ser Leu Gln Ser
1 5

<210> 391
<211> 9
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 391

Gln Gln Tyr Asn Ile Tyr Pro Tyr Thr
1 5

<210> 392
<211> 5
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 392

Asn Ser Gly Met His
1 5

<210> 393
<211> 17
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 393

Val Ile Trp Tyr Asp Gly Ser Lys Arg Tyr Tyr Ala Asp Ser Val Lys
1 5 10 15

Gly

<210> 394
<211> 4
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 394

Asn Asp Asp Tyr
1

<210> 395
<211> 11
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 395

Arg Ala Ser Gln Ser Val Ser Ser Tyr Leu Ala
1 5 10

<210> 396
<211> 7
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 396

Asp Ala Ser Asn Arg Ala Thr
1 5

<210> 397
<211> 9
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 397

Gln Gln Ser Ser Asn Trp Pro Arg Thr
1 5

<210> 398
<211> 6
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 398

Ser Asp His Ala Trp Ser
1 5

<210> 399
<211> 16
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 399

Tyr Ile Ser Tyr Ser Gly Ile Thr Thr Tyr Asn Pro Ser Leu Lys Ser
1 5 10 15

<210> 400
<211> 10
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 400

Ser Leu Ala Arg Thr Thr Ala Met Asp Tyr
1 5 10

<210> 401
<211> 11
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 401

Arg Ala Ser Gln Asp Ile Ser Ser Tyr Leu Asn
1 5 10

<210> 402
<211> 7
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 402

Tyr Thr Ser Arg Leu His Ser
1 5

<210> 403
<211> 9
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 403

Gln Gln Gly Asn Thr Leu Pro Tyr Thr

1 5

<210> 404
<211> 459
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 404

Gln Val Gln Leu Gln Glu Ser Thr Ser Thr Ser Gly Arg Ser Ala Asn
1 5 10 15

Pro Arg Gly Gly Pro Gly Leu Val Arg Pro Ser Gln Thr Leu Ser Leu
20 25 30

Thr Cys Thr Val Ser Gly Tyr Ser Ile Thr Ser Asp His Ala Trp Ser
35 40 45

Trp Val Arg Gln Pro Pro Gly Arg Gly Leu Glu Trp Ile Gly Tyr Ile
50 55 60

Ser Tyr Ser Gly Ile Thr Thr Tyr Asn Pro Ser Leu Lys Ser Arg Val
65 70 75 80

Thr Met Leu Arg Asp Thr Ser Lys Asn Gln Phe Ser Leu Arg Leu Ser
85 90 95

Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala Arg Ser Leu
100 105 110

Ala Arg Thr Thr Ala Met Asp Tyr Trp Gly Gln Gly Ser Leu Val Thr
115 120 125

Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro
130 135 140

Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val
145 150 155 160

Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala
165 170 175

Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly
180 185 190

Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly
195 200 205

Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys
210 215 220

Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys
225 230 235 240

Pro Pro Cys Pro Ala Pro Glu Leu Arg Arg Gly Pro Ser Val Phe Leu
245 250 255

Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu
260 265 270

Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys
275 280 285

Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys
290 295 300

```
Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu
305                 310                 315                 320

Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys
                325                 330                 335

Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys
            340                 345                 350

Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser
        355                 360                 365

Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys
    370                 375                 380

Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln
385                 390                 395                 400

Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly
                405                 410                 415

Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln
            420                 425                 430

Glu Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
        435                 440                 445

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
    450                 455
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<210> 405
<211> 459
<212> PRT

<213> 人造序列

<220>
<223> 人造的合成序列

<400> 405

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Gln Val Gln Leu Gln Glu Ser Gly Thr Ser Thr Ser Gly Arg Ser Ala
1               5                  10                  15

Asn Pro Arg Gly Pro Gly Leu Val Arg Pro Ser Gln Thr Leu Ser Leu
            20                  25                  30

Thr Cys Thr Val Ser Gly Tyr Ser Ile Thr Ser Asp His Ala Trp Ser
        35                  40                  45

Trp Val Arg Gln Pro Pro Gly Arg Gly Leu Glu Trp Ile Gly Tyr Ile
    50                  55                  60

Ser Tyr Ser Gly Ile Thr Thr Tyr Asn Pro Ser Leu Lys Ser Arg Val
65                  70                  75                  80

Thr Met Leu Arg Asp Thr Ser Lys Asn Gln Phe Ser Leu Arg Leu Ser
                85                  90                  95

Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala Arg Ser Leu
            100                 105                 110

Ala Arg Thr Thr Ala Met Asp Tyr Trp Gly Gln Gly Ser Leu Val Thr
        115                 120                 125

Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro
    130                 135                 140

Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val
```

145 150 155 160

Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala
165 170 175

Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly
180 185 190

Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly
195 200 205

Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys
210 215 220

Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys
225 230 235 240

Pro Pro Cys Pro Ala Pro Glu Leu Arg Arg Gly Pro Ser Val Phe Leu
245 250 255

Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu
260 265 270

Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys
275 280 285

Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys
290 295 300

Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu
305 310 315 320

Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys

325 330 335

Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys
340 345 350

Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser
355 360 365

Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys
370 375 380

Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln
385 390 395 400

Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly
405 410 415

Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln
420 425 430

Glu Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
435 440 445

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
450 455

<210> 406
<211> 459
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 406

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Gln Val Gln Leu Gln Glu Ser Gly Pro Thr Ser Thr Ser Gly Arg Ser
1               5                  10                  15

Ala Asn Pro Arg Gly Gly Leu Val Arg Pro Ser Gln Thr Leu Ser Leu
            20                  25                  30

Thr Cys Thr Val Ser Gly Tyr Ser Ile Thr Ser Asp His Ala Trp Ser
        35                  40                  45

Trp Val Arg Gln Pro Pro Gly Arg Gly Leu Glu Trp Ile Gly Tyr Ile
    50                  55                  60

Ser Tyr Ser Gly Ile Thr Thr Tyr Asn Pro Ser Leu Lys Ser Arg Val
65                  70                  75                  80

Thr Met Leu Arg Asp Thr Ser Lys Asn Gln Phe Ser Leu Arg Leu Ser
                85                  90                  95

Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala Arg Ser Leu
            100                 105                 110

Ala Arg Thr Thr Ala Met Asp Tyr Trp Gly Gln Gly Ser Leu Val Thr
        115                 120                 125

Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro
    130                 135                 140

Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val
145                 150                 155                 160

Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala
                165                 170                 175
```

Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly
180 185 190

Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly
195 200 205

Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys
210 215 220

Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys
225 230 235 240

Pro Pro Cys Pro Ala Pro Glu Leu Arg Arg Gly Pro Ser Val Phe Leu
245 250 255

Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu
260 265 270

Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys
275 280 285

Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys
290 295 300

Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu
305 310 315 320

Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys
325 330 335

Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys
340 345 350

Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser
355 360 365

Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys
370 375 380

Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln
385 390 395 400

Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly
405 410 415

Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln
420 425 430

Glu Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
435 440 445

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
450 455

<210> 407
<211> 459
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 407

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Thr Ser Thr Ser Gly Arg
1 5 10 15

Ser Ala Asn Pro Arg Gly Leu Val Arg Pro Ser Gln Thr Leu Ser Leu

20 25 30

Thr Cys Thr Val Ser Gly Tyr Ser Ile Thr Ser Asp His Ala Trp Ser
35 40 45

Trp Val Arg Gln Pro Pro Gly Arg Gly Leu Glu Trp Ile Gly Tyr Ile
50 55 60

Ser Tyr Ser Gly Ile Thr Thr Tyr Asn Pro Ser Leu Lys Ser Arg Val
65 70 75 80

Thr Met Leu Arg Asp Thr Ser Lys Asn Gln Phe Ser Leu Arg Leu Ser
85 90 95

Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala Arg Ser Leu
100 105 110

Ala Arg Thr Thr Ala Met Asp Tyr Trp Gly Gln Gly Ser Leu Val Thr
115 120 125

Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro
130 135 140

Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val
145 150 155 160

Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala
165 170 175

Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly
180 185 190

Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly

195 200 205

Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys
210 215 220

Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys
225 230 235 240

Pro Pro Cys Pro Ala Pro Glu Leu Arg Arg Gly Pro Ser Val Phe Leu
245 250 255

Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu
260 265 270

Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys
275 280 285

Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys
290 295 300

Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu
305 310 315 320

Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys
325 330 335

Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys
340 345 350

Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser
355 360 365

Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys

370 375 380

Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln
385 390 395 400

Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly
405 410 415

Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln
420 425 430

Glu Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
435 440 445

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
450 455

<210> 408
<211> 459
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 408

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Thr Ser Thr Ser Gly
1 5 10 15

Arg Ser Ala Asn Pro Arg Gly Val Arg Pro Ser Gln Thr Leu Ser Leu
20 25 30

Thr Cys Thr Val Ser Gly Tyr Ser Ile Thr Ser Asp His Ala Trp Ser
35 40 45

```
Trp Val Arg Gln Pro Pro Gly Arg Gly Leu Glu Trp Ile Gly Tyr Ile
    50                  55                  60

Ser Tyr Ser Gly Ile Thr Thr Tyr Asn Pro Ser Leu Lys Ser Arg Val
65                  70                  75                  80

Thr Met Leu Arg Asp Thr Ser Lys Asn Gln Phe Ser Leu Arg Leu Ser
                85                  90                  95

Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala Arg Ser Leu
            100                 105                 110

Ala Arg Thr Thr Ala Met Asp Tyr Trp Gly Gln Gly Ser Leu Val Thr
        115                 120                 125

Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro
    130                 135                 140

Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val
145                 150                 155                 160

Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala
                165                 170                 175

Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly
            180                 185                 190

Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly
        195                 200                 205

Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys
    210                 215                 220
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Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys
225 230 235 240

Pro Pro Cys Pro Ala Pro Glu Leu Arg Arg Gly Pro Ser Val Phe Leu
245 250 255

Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu
260 265 270

Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys
275 280 285

Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys
290 295 300

Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu
305 310 315 320

Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys
325 330 335

Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys
340 345 350

Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser
355 360 365

Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys
370 375 380

Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln
385 390 395 400

Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly
405 410 415

Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln
420 425 430

Glu Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
435 440 445

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
450 455

<210> 409
<211> 459
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 409

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Thr Ser Thr Ser
1 5 10 15

Gly Arg Ser Ala Asn Pro Arg Gly Arg Pro Ser Gln Thr Leu Ser Leu
20 25 30

Thr Cys Thr Val Ser Gly Tyr Ser Ile Thr Ser Asp His Ala Trp Ser
35 40 45

Trp Val Arg Gln Pro Pro Gly Arg Gly Leu Glu Trp Ile Gly Tyr Ile
50 55 60

Ser Tyr Ser Gly Ile Thr Thr Tyr Asn Pro Ser Leu Lys Ser Arg Val

65 70 75 80

Thr Met Leu Arg Asp Thr Ser Lys Asn Gln Phe Ser Leu Arg Leu Ser
85 90 95

Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala Arg Ser Leu
100 105 110

Ala Arg Thr Thr Ala Met Asp Tyr Trp Gly Gln Gly Ser Leu Val Thr
115 120 125

Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro
130 135 140

Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val
145 150 155 160

Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala
165 170 175

Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly
180 185 190

Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly
195 200 205

Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys
210 215 220

Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys
225 230 235 240

Pro Pro Cys Pro Ala Pro Glu Leu Arg Arg Gly Pro Ser Val Phe Leu

245 250 255

Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu
260 265 270

Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys
275 280 285

Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys
290 295 300

Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu
305 310 315 320

Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys
325 330 335

Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys
340 345 350

Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser
355 360 365

Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys
370 375 380

Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln
385 390 395 400

Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly
405 410 415

Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln

420 425 430

Glu Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
435 440 445

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
450 455

<210> 410
<211> 459
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 410

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Arg Thr Ser Thr
1 5 10 15

Ser Gly Arg Ser Ala Asn Pro Arg Gly Pro Ser Gln Thr Leu Ser Leu
20 25 30

Thr Cys Thr Val Ser Gly Tyr Ser Ile Thr Ser Asp His Ala Trp Ser
35 40 45

Trp Val Arg Gln Pro Pro Gly Arg Gly Leu Glu Trp Ile Gly Tyr Ile
50 55 60

Ser Tyr Ser Gly Ile Thr Thr Tyr Asn Pro Ser Leu Lys Ser Arg Val
65 70 75 80

Thr Met Leu Arg Asp Thr Ser Lys Asn Gln Phe Ser Leu Arg Leu Ser
85 90 95

```
Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala Arg Ser Leu
            100                 105                 110

Ala Arg Thr Thr Ala Met Asp Tyr Trp Gly Gln Gly Ser Leu Val Thr
        115                 120                 125

Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro
    130                 135                 140

Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val
145                 150                 155                 160

Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala
                165                 170                 175

Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly
            180                 185                 190

Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly
        195                 200                 205

Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys
    210                 215                 220

Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys
225                 230                 235                 240

Pro Pro Cys Pro Ala Pro Glu Leu Arg Arg Gly Pro Ser Val Phe Leu
                245                 250                 255

Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu
            260                 265                 270
```

Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys
275 280 285

Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys
290 295 300

Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu
305 310 315 320

Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys
325 330 335

Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys
340 345 350

Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser
355 360 365

Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys
370 375 380

Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln
385 390 395 400

Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly
405 410 415

Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln
420 425 430

Glu Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
435 440 445

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
450 455

<210> 411
<211> 459
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 411

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Arg Pro Thr Ser
1 5 10 15

Thr Ser Gly Arg Ser Ala Asn Pro Arg Gly Ser Gln Thr Leu Ser Leu
20 25 30

Thr Cys Thr Val Ser Gly Tyr Ser Ile Thr Ser Asp His Ala Trp Ser
35 40 45

Trp Val Arg Gln Pro Pro Gly Arg Gly Leu Glu Trp Ile Gly Tyr Ile
50 55 60

Ser Tyr Ser Gly Ile Thr Thr Tyr Asn Pro Ser Leu Lys Ser Arg Val
65 70 75 80

Thr Met Leu Arg Asp Thr Ser Lys Asn Gln Phe Ser Leu Arg Leu Ser
85 90 95

Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala Arg Ser Leu
100 105 110

Ala Arg Thr Thr Ala Met Asp Tyr Trp Gly Gln Gly Ser Leu Val Thr

115 120 125

Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro
130 135 140

Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val
145 150 155 160

Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala
165 170 175

Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly
180 185 190

Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly
195 200 205

Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys
210 215 220

Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys
225 230 235 240

Pro Pro Cys Pro Ala Pro Glu Leu Arg Arg Gly Pro Ser Val Phe Leu
245 250 255

Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu
260 265 270

Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys
275 280 285

Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys

290 295 300

Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu
305 310 315 320

Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys
325 330 335

Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys
340 345 350

Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser
355 360 365

Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys
370 375 380

Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln
385 390 395 400

Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly
405 410 415

Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln
420 425 430

Glu Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
435 440 445

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
450 455

<210> 412

<211> 459
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 412

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Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Arg Pro Ser Thr
1               5                  10                  15

Ser Thr Ser Gly Arg Ser Ala Asn Pro Arg Gly Gln Thr Leu Ser Leu
            20                  25                  30

Thr Cys Thr Val Ser Gly Tyr Ser Ile Thr Ser Asp His Ala Trp Ser
        35                  40                  45

Trp Val Arg Gln Pro Pro Gly Arg Gly Leu Glu Trp Ile Gly Tyr Ile
    50                  55                  60

Ser Tyr Ser Gly Ile Thr Thr Tyr Asn Pro Ser Leu Lys Ser Arg Val
65                  70                  75                  80

Thr Met Leu Arg Asp Thr Ser Lys Asn Gln Phe Ser Leu Arg Leu Ser
                85                  90                  95

Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala Arg Ser Leu
            100                 105                 110

Ala Arg Thr Thr Ala Met Asp Tyr Trp Gly Gln Gly Ser Leu Val Thr
        115                 120                 125

Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro
    130                 135                 140
```

Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val
145 150 155 160

Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala
165 170 175

Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly
180 185 190

Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly
195 200 205

Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys
210 215 220

Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys
225 230 235 240

Pro Pro Cys Pro Ala Pro Glu Leu Arg Arg Gly Pro Ser Val Phe Leu
245 250 255

Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu
260 265 270

Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys
275 280 285

Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys
290 295 300

Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu
305 310 315 320

Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys
325 330 335

Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys
340 345 350

Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser
355 360 365

Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys
370 375 380

Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln
385 390 395 400

Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly
405 410 415

Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln
420 425 430

Glu Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
435 440 445

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
450 455

<210> 413
<211> 459
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 413

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Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Arg Pro Ser Gln
1               5                  10                  15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Tyr Ser Ile Thr Ser Asp
            20                  25                  30

His Ala Trp Ser Trp Val Arg Gln Pro Thr Ser Thr Ser Gly Arg Ser
        35                  40                  45

Ala Asn Pro Arg Gly Pro Gly Arg Gly Leu Glu Trp Ile Gly Tyr Ile
    50                  55                  60

Ser Tyr Ser Gly Ile Thr Thr Tyr Asn Pro Ser Leu Lys Ser Arg Val
65                  70                  75                  80

Thr Met Leu Arg Asp Thr Ser Lys Asn Gln Phe Ser Leu Arg Leu Ser
                85                  90                  95

Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala Arg Ser Leu
            100                 105                 110

Ala Arg Thr Thr Ala Met Asp Tyr Trp Gly Gln Gly Ser Leu Val Thr
        115                 120                 125

Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro
    130                 135                 140

Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val
145                 150                 155                 160

Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala
```

165 170 175

Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly
180 185 190

Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly
195 200 205

Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys
210 215 220

Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys
225 230 235 240

Pro Pro Cys Pro Ala Pro Glu Leu Arg Arg Gly Pro Ser Val Phe Leu
245 250 255

Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu
260 265 270

Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys
275 280 285

Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys
290 295 300

Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu
305 310 315 320

Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys
325 330 335

Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys

340 345 350

Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser
355 360 365

Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys
370 375 380

Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln
385 390 395 400

Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly
405 410 415

Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln
420 425 430

Glu Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
435 440 445

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
450 455

<210> 414
<211> 459
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 414

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Arg Pro Ser Gln
1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Tyr Ser Ile Thr Ser Asp
20 25 30

His Ala Trp Ser Trp Val Arg Gln Pro Pro Thr Ser Thr Ser Gly Arg
35 40 45

Ser Ala Asn Pro Arg Gly Gly Arg Gly Leu Glu Trp Ile Gly Tyr Ile
50 55 60

Ser Tyr Ser Gly Ile Thr Thr Tyr Asn Pro Ser Leu Lys Ser Arg Val
65 70 75 80

Thr Met Leu Arg Asp Thr Ser Lys Asn Gln Phe Ser Leu Arg Leu Ser
85 90 95

Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala Arg Ser Leu
100 105 110

Ala Arg Thr Thr Ala Met Asp Tyr Trp Gly Gln Gly Ser Leu Val Thr
115 120 125

Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro
130 135 140

Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val
145 150 155 160

Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala
165 170 175

Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly
180 185 190

Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly
195 200 205

Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys
210 215 220

Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys
225 230 235 240

Pro Pro Cys Pro Ala Pro Glu Leu Arg Arg Gly Pro Ser Val Phe Leu
245 250 255

Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu
260 265 270

Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys
275 280 285

Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys
290 295 300

Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu
305 310 315 320

Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys
325 330 335

Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys
340 345 350

Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser
355 360 365

Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys
370 375 380

Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln
385 390 395 400

Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly
405 410 415

Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln
420 425 430

Glu Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
435 440 445

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
450 455

<210> 415
<211> 459
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 415

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Arg Pro Ser Gln
1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Tyr Ser Ile Thr Ser Asp
20 25 30

His Ala Trp Ser Trp Val Arg Gln Pro Pro Gly Thr Ser Thr Ser Gly

35 40 45

Arg Ser Ala Asn Pro Arg Gly Arg Gly Leu Glu Trp Ile Gly Tyr Ile
50 55 60

Ser Tyr Ser Gly Ile Thr Thr Tyr Asn Pro Ser Leu Lys Ser Arg Val
65 70 75 80

Thr Met Leu Arg Asp Thr Ser Lys Asn Gln Phe Ser Leu Arg Leu Ser
85 90 95

Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala Arg Ser Leu
100 105 110

Ala Arg Thr Thr Ala Met Asp Tyr Trp Gly Gln Gly Ser Leu Val Thr
115 120 125

Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro
130 135 140

Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val
145 150 155 160

Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala
165 170 175

Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly
180 185 190

Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly
195 200 205

Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys

210 215 220

Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys
225 230 235 240

Pro Pro Cys Pro Ala Pro Glu Leu Arg Arg Gly Pro Ser Val Phe Leu
245 250 255

Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu
260 265 270

Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys
275 280 285

Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys
290 295 300

Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu
305 310 315 320

Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys
325 330 335

Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys
340 345 350

Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser
355 360 365

Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys
370 375 380

Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln

385 390 395 400

Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly
405 410 415

Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln
420 425 430

Glu Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
435 440 445

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
450 455

<210> 416
<211> 459
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 416

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Arg Pro Ser Gln
1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Tyr Ser Ile Thr Ser Asp
20 25 30

His Ala Trp Ser Trp Val Arg Gln Pro Pro Gly Arg Thr Ser Thr Ser
35 40 45

Gly Arg Ser Ala Asn Pro Arg Gly Gly Leu Glu Trp Ile Gly Tyr Ile
50 55 60

Ser Tyr Ser Gly Ile Thr Thr Tyr Asn Pro Ser Leu Lys Ser Arg Val
65 70 75 80

Thr Met Leu Arg Asp Thr Ser Lys Asn Gln Phe Ser Leu Arg Leu Ser
85 90 95

Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala Arg Ser Leu
100 105 110

Ala Arg Thr Thr Ala Met Asp Tyr Trp Gly Gln Gly Ser Leu Val Thr
115 120 125

Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro
130 135 140

Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val
145 150 155 160

Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala
165 170 175

Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly
180 185 190

Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly
195 200 205

Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys
210 215 220

Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys
225 230 235 240

Pro Pro Cys Pro Ala Pro Glu Leu Arg Arg Gly Pro Ser Val Phe Leu
245 250 255

Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu
260 265 270

Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys
275 280 285

Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys
290 295 300

Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu
305 310 315 320

Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys
325 330 335

Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys
340 345 350

Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser
355 360 365

Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys
370 375 380

Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln
385 390 395 400

Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly
405 410 415

Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln
420 425 430

Glu Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
435 440 445

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
450 455

<210> 417
<211> 459
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 417

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Arg Pro Ser Gln
1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Tyr Ser Ile Thr Ser Asp
20 25 30

His Ala Trp Ser Trp Val Arg Gln Pro Pro Gly Arg Gly Thr Ser Thr
35 40 45

Ser Gly Arg Ser Ala Asn Pro Arg Gly Leu Glu Trp Ile Gly Tyr Ile
50 55 60

Ser Tyr Ser Gly Ile Thr Thr Tyr Asn Pro Ser Leu Lys Ser Arg Val
65 70 75 80

Thr Met Leu Arg Asp Thr Ser Lys Asn Gln Phe Ser Leu Arg Leu Ser

85 90 95

Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala Arg Ser Leu
100 105 110

Ala Arg Thr Thr Ala Met Asp Tyr Trp Gly Gln Gly Ser Leu Val Thr
115 120 125

Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro
130 135 140

Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val
145 150 155 160

Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala
165 170 175

Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly
180 185 190

Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly
195 200 205

Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys
210 215 220

Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys
225 230 235 240

Pro Pro Cys Pro Ala Pro Glu Leu Arg Arg Gly Pro Ser Val Phe Leu
245 250 255

Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu

260 265 270

Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys
275 280 285

Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys
290 295 300

Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu
305 310 315 320

Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys
325 330 335

Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys
340 345 350

Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser
355 360 365

Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys
370 375 380

Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln
385 390 395 400

Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly
405 410 415

Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln
420 425 430

Glu Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn

435 440 445

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
450 455

<210> 418
<211> 459
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 418

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Arg Pro Ser Gln
1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Tyr Ser Ile Thr Ser Asp
20 25 30

His Ala Trp Ser Trp Val Arg Gln Pro Pro Gly Arg Gly Leu Thr Ser
35 40 45

Thr Ser Gly Arg Ser Ala Asn Pro Arg Gly Glu Trp Ile Gly Tyr Ile
50 55 60

Ser Tyr Ser Gly Ile Thr Thr Tyr Asn Pro Ser Leu Lys Ser Arg Val
65 70 75 80

Thr Met Leu Arg Asp Thr Ser Lys Asn Gln Phe Ser Leu Arg Leu Ser
85 90 95

Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala Arg Ser Leu
100 105 110

Ala Arg Thr Thr Ala Met Asp Tyr Trp Gly Gln Gly Ser Leu Val Thr
115 120 125

Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro
130 135 140

Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val
145 150 155 160

Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala
165 170 175

Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly
180 185 190

Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly
195 200 205

Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys
210 215 220

Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys
225 230 235 240

Pro Pro Cys Pro Ala Pro Glu Leu Arg Arg Gly Pro Ser Val Phe Leu
245 250 255

Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu
260 265 270

Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys
275 280 285

```
Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys
    290                 295                 300

Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu
305                 310                 315                 320

Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys
                325                 330                 335

Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys
            340                 345                 350

Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser
        355                 360                 365

Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys
    370                 375                 380

Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln
385                 390                 395                 400

Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly
                405                 410                 415

Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln
            420                 425                 430

Glu Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
        435                 440                 445

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
    450                 455
```

<210> 419
<211> 459
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 419

```
Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Arg Pro Ser Gln
1               5                  10                  15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Tyr Ser Ile Thr Ser Asp
            20                  25                  30

His Ala Trp Ser Trp Val Arg Gln Pro Pro Gly Arg Gly Leu Glu Trp
        35                  40                  45

Ile Gly Tyr Ile Ser Tyr Ser Gly Thr Ser Thr Ser Gly Arg Ser Ala
    50                  55                  60

Asn Pro Arg Gly Ile Thr Thr Tyr Asn Pro Ser Leu Lys Ser Arg Val
65                  70                  75                  80

Thr Met Leu Arg Asp Thr Ser Lys Asn Gln Phe Ser Leu Arg Leu Ser
                85                  90                  95

Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala Arg Ser Leu
            100                 105                 110

Ala Arg Thr Thr Ala Met Asp Tyr Trp Gly Gln Gly Ser Leu Val Thr
        115                 120                 125

Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro
```

130 135 140

Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val
145 150 155 160

Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala
165 170 175

Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly
180 185 190

Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly
195 200 205

Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys
210 215 220

Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys
225 230 235 240

Pro Pro Cys Pro Ala Pro Glu Leu Arg Arg Gly Pro Ser Val Phe Leu
245 250 255

Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu
260 265 270

Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys
275 280 285

Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys
290 295 300

Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu

305 310 315 320

Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys
325 330 335

Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys
340 345 350

Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser
355 360 365

Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys
370 375 380

Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln
385 390 395 400

Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly
405 410 415

Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln
420 425 430

Glu Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
435 440 445

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
450 455

<210> 420
<211> 459
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 420

```
Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Arg Pro Ser Gln
1               5                  10                  15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Tyr Ser Ile Thr Ser Asp
            20                  25                  30

His Ala Trp Ser Trp Val Arg Gln Pro Pro Gly Arg Gly Leu Glu Trp
        35                  40                  45

Ile Gly Tyr Ile Ser Tyr Ser Gly Ile Thr Ser Thr Ser Gly Arg Ser
    50                  55                  60

Ala Asn Pro Arg Gly Thr Thr Tyr Asn Pro Ser Leu Lys Ser Arg Val
65                  70                  75                  80

Thr Met Leu Arg Asp Thr Ser Lys Asn Gln Phe Ser Leu Arg Leu Ser
                85                  90                  95

Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala Arg Ser Leu
            100                 105                 110

Ala Arg Thr Thr Ala Met Asp Tyr Trp Gly Gln Gly Ser Leu Val Thr
        115                 120                 125

Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro
    130                 135                 140

Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val
145                 150                 155                 160
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Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala
165 170 175

Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly
180 185 190

Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly
195 200 205

Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys
210 215 220

Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys
225 230 235 240

Pro Pro Cys Pro Ala Pro Glu Leu Arg Arg Gly Pro Ser Val Phe Leu
245 250 255

Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu
260 265 270

Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys
275 280 285

Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys
290 295 300

Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu
305 310 315 320

Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys
325 330 335

Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys
340 345 350

Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser
355 360 365

Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys
370 375 380

Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln
385 390 395 400

Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly
405 410 415

Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln
420 425 430

Glu Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
435 440 445

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
450 455

<210> 421
<211> 459
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 421

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Arg Pro Ser Gln

1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Tyr Ser Ile Thr Ser Asp
20 25 30

His Ala Trp Ser Trp Val Arg Gln Pro Pro Gly Arg Gly Leu Glu Trp
35 40 45

Ile Gly Tyr Ile Ser Tyr Ser Gly Ile Thr Thr Ser Thr Ser Gly Arg
50 55 60

Ser Ala Asn Pro Arg Gly Thr Tyr Asn Pro Ser Leu Lys Ser Arg Val
65 70 75 80

Thr Met Leu Arg Asp Thr Ser Lys Asn Gln Phe Ser Leu Arg Leu Ser
85 90 95

Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala Arg Ser Leu
100 105 110

Ala Arg Thr Thr Ala Met Asp Tyr Trp Gly Gln Gly Ser Leu Val Thr
115 120 125

Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro
130 135 140

Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val
145 150 155 160

Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala
165 170 175

Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly

180 185 190

Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly
195 200 205

Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys
210 215 220

Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys
225 230 235 240

Pro Pro Cys Pro Ala Pro Glu Leu Arg Arg Gly Pro Ser Val Phe Leu
245 250 255

Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu
260 265 270

Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys
275 280 285

Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys
290 295 300

Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu
305 310 315 320

Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys
325 330 335

Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys
340 345 350

Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser

355 360 365

Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys
370 375 380

Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln
385 390 395 400

Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly
405 410 415

Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln
420 425 430

Glu Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
435 440 445

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
450 455

<210> 422
<211> 459
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 422

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Arg Pro Ser Gln
1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Tyr Ser Ile Thr Ser Asp
20 25 30

```
His Ala Trp Ser Trp Val Arg Gln Pro Pro Gly Arg Gly Leu Glu Trp
        35                  40                  45

Ile Gly Tyr Ile Ser Tyr Ser Gly Ile Thr Thr Thr Ser Thr Ser Gly
    50                  55                  60

Arg Ser Ala Asn Pro Arg Gly Tyr Asn Pro Ser Leu Lys Ser Arg Val
65                  70                  75                  80

Thr Met Leu Arg Asp Thr Ser Lys Asn Gln Phe Ser Leu Arg Leu Ser
                85                  90                  95

Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala Arg Ser Leu
            100                 105                 110

Ala Arg Thr Thr Ala Met Asp Tyr Trp Gly Gln Gly Ser Leu Val Thr
        115                 120                 125

Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro
    130                 135                 140

Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val
145                 150                 155                 160

Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala
                165                 170                 175

Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly
            180                 185                 190

Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly
        195                 200                 205
```

Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys
210 215 220

Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys
225 230 235 240

Pro Pro Cys Pro Ala Pro Glu Leu Arg Arg Gly Pro Ser Val Phe Leu
245 250 255

Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu
260 265 270

Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys
275 280 285

Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys
290 295 300

Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu
305 310 315 320

Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys
325 330 335

Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys
340 345 350

Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser
355 360 365

Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys
370 375 380

Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln
385 390 395 400

Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly
405 410 415

Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln
420 425 430

Glu Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
435 440 445

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
450 455

<210> 423
<211> 459
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 423

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Arg Pro Ser Gln
1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Tyr Ser Ile Thr Ser Asp
20 25 30

His Ala Trp Ser Trp Val Arg Gln Pro Pro Gly Arg Gly Leu Glu Trp
35 40 45

Ile Gly Tyr Ile Ser Tyr Ser Gly Ile Thr Thr Tyr Thr Ser Thr Ser

50 55 60

Gly Arg Ser Ala Asn Pro Arg Gly Asn Pro Ser Leu Lys Ser Arg Val
65 70 75 80

Thr Met Leu Arg Asp Thr Ser Lys Asn Gln Phe Ser Leu Arg Leu Ser
85 90 95

Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala Arg Ser Leu
100 105 110

Ala Arg Thr Thr Ala Met Asp Tyr Trp Gly Gln Gly Ser Leu Val Thr
115 120 125

Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro
130 135 140

Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val
145 150 155 160

Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala
165 170 175

Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly
180 185 190

Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly
195 200 205

Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys
210 215 220

Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys

225 230 235 240

Pro Pro Cys Pro Ala Pro Glu Leu Arg Arg Gly Pro Ser Val Phe Leu
245 250 255

Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu
260 265 270

Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys
275 280 285

Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys
290 295 300

Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu
305 310 315 320

Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys
325 330 335

Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys
340 345 350

Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser
355 360 365

Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys
370 375 380

Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln
385 390 395 400

Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly

405 410 415

Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln
420 425 430

Glu Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
435 440 445

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
450 455

<210> 424
<211> 459
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 424

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Arg Pro Ser Gln
1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Tyr Ser Ile Thr Ser Asp
20 25 30

His Ala Trp Ser Trp Val Arg Gln Pro Pro Gly Arg Gly Leu Glu Trp
35 40 45

Ile Gly Tyr Ile Ser Tyr Ser Gly Ile Thr Thr Tyr Asn Thr Ser Thr
50 55 60

Ser Gly Arg Ser Ala Asn Pro Arg Gly Pro Ser Leu Lys Ser Arg Val
65 70 75 80

```
Thr Met Leu Arg Asp Thr Ser Lys Asn Gln Phe Ser Leu Arg Leu Ser
                85                  90                  95

Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala Arg Ser Leu
            100                 105                 110

Ala Arg Thr Thr Ala Met Asp Tyr Trp Gly Gln Gly Ser Leu Val Thr
        115                 120                 125

Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro
    130                 135                 140

Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val
145                 150                 155                 160

Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala
                165                 170                 175

Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly
            180                 185                 190

Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly
        195                 200                 205

Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys
    210                 215                 220

Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys
225                 230                 235                 240

Pro Pro Cys Pro Ala Pro Glu Leu Arg Arg Gly Pro Ser Val Phe Leu
                245                 250                 255
```

```
Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu
            260                 265                 270

Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys
        275                 280                 285

Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys
    290                 295                 300

Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu
305                 310                 315                 320

Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys
                325                 330                 335

Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys
            340                 345                 350

Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser
        355                 360                 365

Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys
    370                 375                 380

Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln
385                 390                 395                 400

Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly
                405                 410                 415

Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln
            420                 425                 430
```

Glu Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
435 440 445

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
450 455

<210> 425
<211> 459
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 425

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Arg Pro Ser Gln
1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Tyr Ser Ile Thr Ser Asp
20 25 30

His Ala Trp Ser Trp Val Arg Gln Pro Pro Gly Arg Gly Leu Glu Trp
35 40 45

Ile Gly Tyr Ile Ser Tyr Ser Gly Ile Thr Thr Tyr Asn Pro Thr Ser
50 55 60

Thr Ser Gly Arg Ser Ala Asn Pro Arg Gly Ser Leu Lys Ser Arg Val
65 70 75 80

Thr Met Leu Arg Asp Thr Ser Lys Asn Gln Phe Ser Leu Arg Leu Ser
85 90 95

Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala Arg Ser Leu

100 105 110

Ala Arg Thr Thr Ala Met Asp Tyr Trp Gly Gln Gly Ser Leu Val Thr
115 120 125

Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro
130 135 140

Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val
145 150 155 160

Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala
165 170 175

Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly
180 185 190

Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly
195 200 205

Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys
210 215 220

Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys
225 230 235 240

Pro Pro Cys Pro Ala Pro Glu Leu Arg Arg Gly Pro Ser Val Phe Leu
245 250 255

Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu
260 265 270

Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys

275 280 285

Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys
290 295 300

Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu
305 310 315 320

Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys
325 330 335

Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys
340 345 350

Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser
355 360 365

Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys
370 375 380

Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln
385 390 395 400

Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly
405 410 415

Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln
420 425 430

Glu Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
435 440 445

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro

450 455

<210> 426
<211> 459
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 426

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Arg Pro Ser Gln
1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Tyr Ser Ile Thr Ser Asp
20 25 30

His Ala Trp Ser Trp Val Arg Gln Pro Pro Gly Arg Gly Leu Glu Trp
35 40 45

Ile Gly Tyr Ile Ser Tyr Ser Gly Ile Thr Thr Tyr Asn Pro Ser Thr
50 55 60

Ser Thr Ser Gly Arg Ser Ala Asn Pro Arg Gly Leu Lys Ser Arg Val
65 70 75 80

Thr Met Leu Arg Asp Thr Ser Lys Asn Gln Phe Ser Leu Arg Leu Ser
85 90 95

Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala Arg Ser Leu
100 105 110

Ala Arg Thr Thr Ala Met Asp Tyr Trp Gly Gln Gly Ser Leu Val Thr
115 120 125

Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro
130 135 140

Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val
145 150 155 160

Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala
165 170 175

Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly
180 185 190

Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly
195 200 205

Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys
210 215 220

Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys
225 230 235 240

Pro Pro Cys Pro Ala Pro Glu Leu Arg Arg Gly Pro Ser Val Phe Leu
245 250 255

Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu
260 265 270

Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys
275 280 285

Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys
290 295 300

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Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu
305                 310                 315                 320

Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys
                325                 330                 335

Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys
            340                 345                 350

Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser
        355                 360                 365

Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys
    370                 375                 380

Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln
385                 390                 395                 400

Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly
                405                 410                 415

Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln
            420                 425                 430

Glu Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
        435                 440                 445

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
    450                 455
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<210> 427
<211> 459
<212> PRT

<213> 人造序列

<220>
<223> 人造的合成序列

<400> 427

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Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Arg Pro Ser Gln
1               5                  10                  15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Tyr Ser Ile Thr Ser Asp
            20                  25                  30

His Ala Trp Ser Trp Val Arg Gln Pro Pro Gly Arg Gly Leu Glu Trp
        35                  40                  45

Ile Gly Tyr Ile Ser Tyr Ser Gly Ile Thr Thr Tyr Asn Pro Ser Leu
    50                  55                  60

Thr Ser Thr Ser Gly Arg Ser Ala Asn Pro Arg Gly Lys Ser Arg Val
65                  70                  75                  80

Thr Met Leu Arg Asp Thr Ser Lys Asn Gln Phe Ser Leu Arg Leu Ser
                85                  90                  95

Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala Arg Ser Leu
            100                 105                 110

Ala Arg Thr Thr Ala Met Asp Tyr Trp Gly Gln Gly Ser Leu Val Thr
        115                 120                 125

Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro
    130                 135                 140

Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val
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145 150 155 160

Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala
165 170 175

Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly
180 185 190

Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly
195 200 205

Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys
210 215 220

Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys
225 230 235 240

Pro Pro Cys Pro Ala Pro Glu Leu Arg Arg Gly Pro Ser Val Phe Leu
245 250 255

Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu
260 265 270

Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys
275 280 285

Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys
290 295 300

Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu
305 310 315 320

Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys

325 330 335

Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys
340 345 350

Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser
355 360 365

Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys
370 375 380

Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln
385 390 395 400

Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly
405 410 415

Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln
420 425 430

Glu Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
435 440 445

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
450 455

<210> 428
<211> 459
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 428

```
Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Arg Pro Ser Gln
1               5                  10                  15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Tyr Ser Ile Thr Ser Asp
            20                  25                  30

His Ala Trp Ser Trp Val Arg Gln Pro Pro Gly Arg Gly Leu Glu Trp
        35                  40                  45

Ile Gly Tyr Ile Ser Tyr Ser Gly Ile Thr Thr Tyr Asn Pro Ser Leu
    50                  55                  60

Lys Thr Ser Thr Ser Gly Arg Ser Ala Asn Pro Arg Gly Ser Arg Val
65                  70                  75                  80

Thr Met Leu Arg Asp Thr Ser Lys Asn Gln Phe Ser Leu Arg Leu Ser
                85                  90                  95

Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala Arg Ser Leu
            100                 105                 110

Ala Arg Thr Thr Ala Met Asp Tyr Trp Gly Gln Gly Ser Leu Val Thr
        115                 120                 125

Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro
    130                 135                 140

Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val
145                 150                 155                 160

Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala
                165                 170                 175
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Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly
            180                 185                 190

Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly
        195                 200                 205

Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys
    210                 215                 220

Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys
225                 230                 235                 240

Pro Pro Cys Pro Ala Pro Glu Leu Arg Arg Gly Pro Ser Val Phe Leu
                245                 250                 255

Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu
            260                 265                 270

Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys
        275                 280                 285

Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys
    290                 295                 300

Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu
305                 310                 315                 320

Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys
                325                 330                 335

Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys
            340                 345                 350
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Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser
355 360 365

Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys
370 375 380

Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln
385 390 395 400

Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly
405 410 415

Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln
420 425 430

Glu Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
435 440 445

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
450 455

<210> 429
<211> 459
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 429

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Arg Pro Ser Gln
1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Tyr Ser Ile Thr Ser Asp

20 25 30

His Ala Trp Ser Trp Val Arg Gln Pro Pro Gly Arg Gly Leu Glu Trp
35 40 45

Ile Gly Tyr Ile Ser Tyr Ser Gly Ile Thr Thr Tyr Asn Pro Ser Leu
50 55 60

Lys Ser Thr Ser Thr Ser Gly Arg Ser Ala Asn Pro Arg Gly Arg Val
65 70 75 80

Thr Met Leu Arg Asp Thr Ser Lys Asn Gln Phe Ser Leu Arg Leu Ser
85 90 95

Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala Arg Ser Leu
100 105 110

Ala Arg Thr Thr Ala Met Asp Tyr Trp Gly Gln Gly Ser Leu Val Thr
115 120 125

Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro
130 135 140

Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val
145 150 155 160

Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala
165 170 175

Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly
180 185 190

Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly

195 200 205

Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys
210 215 220

Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys
225 230 235 240

Pro Pro Cys Pro Ala Pro Glu Leu Arg Arg Gly Pro Ser Val Phe Leu
245 250 255

Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu
260 265 270

Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys
275 280 285

Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys
290 295 300

Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu
305 310 315 320

Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys
325 330 335

Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys
340 345 350

Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser
355 360 365

Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys

370 375 380

Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln
385 390 395 400

Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly
405 410 415

Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln
420 425 430

Glu Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
435 440 445

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
450 455

<210> 430
<211> 459
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 430

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Arg Pro Ser Gln
1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Tyr Ser Ile Thr Ser Asp
20 25 30

His Ala Trp Ser Trp Val Arg Gln Pro Pro Gly Arg Gly Leu Glu Trp
35 40 45

Ile Gly Tyr Ile Ser Tyr Ser Gly Ile Thr Thr Tyr Asn Pro Ser Leu
50 55 60

Lys Ser Arg Thr Ser Thr Ser Gly Arg Ser Ala Asn Pro Arg Gly Val
65 70 75 80

Thr Met Leu Arg Asp Thr Ser Lys Asn Gln Phe Ser Leu Arg Leu Ser
85 90 95

Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala Arg Ser Leu
100 105 110

Ala Arg Thr Thr Ala Met Asp Tyr Trp Gly Gln Gly Ser Leu Val Thr
115 120 125

Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro
130 135 140

Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val
145 150 155 160

Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala
165 170 175

Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly
180 185 190

Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly
195 200 205

Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys
210 215 220

Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys
225 230 235 240

Pro Pro Cys Pro Ala Pro Glu Leu Arg Arg Gly Pro Ser Val Phe Leu
245 250 255

Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu
260 265 270

Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys
275 280 285

Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys
290 295 300

Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu
305 310 315 320

Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys
325 330 335

Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys
340 345 350

Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser
355 360 365

Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys
370 375 380

Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln
385 390 395 400

Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly
405 410 415

Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln
420 425 430

Glu Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
435 440 445

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
450 455

<210> 431
<211> 459
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 431

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Arg Pro Ser Gln
1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Tyr Ser Ile Thr Ser Asp
20 25 30

His Ala Trp Ser Trp Val Arg Gln Pro Pro Gly Arg Gly Leu Glu Trp
35 40 45

Ile Gly Tyr Ile Ser Tyr Ser Gly Ile Thr Thr Tyr Asn Pro Ser Leu
50 55 60

Lys Ser Arg Val Thr Ser Thr Ser Gly Arg Ser Ala Asn Pro Arg Gly

65 70 75 80

Thr Met Leu Arg Asp Thr Ser Lys Asn Gln Phe Ser Leu Arg Leu Ser
85 90 95

Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala Arg Ser Leu
100 105 110

Ala Arg Thr Thr Ala Met Asp Tyr Trp Gly Gln Gly Ser Leu Val Thr
115 120 125

Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro
130 135 140

Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val
145 150 155 160

Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala
165 170 175

Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly
180 185 190

Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly
195 200 205

Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys
210 215 220

Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys
225 230 235 240

Pro Pro Cys Pro Ala Pro Glu Leu Arg Arg Gly Pro Ser Val Phe Leu

245 250 255

Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu
260 265 270

Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys
275 280 285

Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys
290 295 300

Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu
305 310 315 320

Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys
325 330 335

Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys
340 345 350

Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser
355 360 365

Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys
370 375 380

Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln
385 390 395 400

Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly
405 410 415

Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln

420 425 430

Glu Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
435 440 445

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
450 455

<210> 432
<211> 459
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 432

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Arg Pro Ser Gln
1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Tyr Ser Ile Thr Ser Asp
20 25 30

His Ala Trp Ser Trp Val Arg Gln Pro Pro Gly Arg Gly Leu Glu Trp
35 40 45

Ile Gly Tyr Ile Ser Tyr Ser Gly Ile Thr Thr Tyr Asn Pro Ser Leu
50 55 60

Lys Ser Arg Val Thr Thr Ser Thr Ser Gly Arg Ser Ala Asn Pro Arg
65 70 75 80

Gly Met Leu Arg Asp Thr Ser Lys Asn Gln Phe Ser Leu Arg Leu Ser
85 90 95

Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala Arg Ser Leu
100 105 110

Ala Arg Thr Thr Ala Met Asp Tyr Trp Gly Gln Gly Ser Leu Val Thr
115 120 125

Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro
130 135 140

Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val
145 150 155 160

Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala
165 170 175

Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly
180 185 190

Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly
195 200 205

Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys
210 215 220

Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys
225 230 235 240

Pro Pro Cys Pro Ala Pro Glu Leu Arg Arg Gly Pro Ser Val Phe Leu
245 250 255

Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu
260 265 270

Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys
275 280 285

Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys
290 295 300

Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu
305 310 315 320

Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys
325 330 335

Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys
340 345 350

Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser
355 360 365

Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys
370 375 380

Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln
385 390 395 400

Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly
405 410 415

Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln
420 425 430

Glu Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
435 440 445

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
450 455

<210> 433
<211> 459
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 433

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Arg Pro Ser Gln
1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Tyr Ser Ile Thr Ser Asp
20 25 30

His Ala Trp Ser Trp Val Arg Gln Pro Pro Gly Arg Gly Leu Glu Trp
35 40 45

Ile Gly Tyr Ile Ser Tyr Ser Gly Ile Thr Thr Tyr Asn Pro Ser Leu
50 55 60

Lys Ser Arg Val Thr Met Leu Arg Asp Thr Thr Ser Thr Ser Gly Arg
65 70 75 80

Ser Ala Asn Pro Arg Gly Ser Lys Asn Gln Phe Ser Leu Arg Leu Ser
85 90 95

Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala Arg Ser Leu
100 105 110

Ala Arg Thr Thr Ala Met Asp Tyr Trp Gly Gln Gly Ser Leu Val Thr

115 120 125

Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro
130 135 140

Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val
145 150 155 160

Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala
165 170 175

Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly
180 185 190

Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly
195 200 205

Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys
210 215 220

Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys
225 230 235 240

Pro Pro Cys Pro Ala Pro Glu Leu Arg Arg Gly Pro Ser Val Phe Leu
245 250 255

Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu
260 265 270

Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys
275 280 285

Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys

290 295 300

Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu
305 310 315 320

Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys
325 330 335

Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys
340 345 350

Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser
355 360 365

Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys
370 375 380

Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln
385 390 395 400

Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly
405 410 415

Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln
420 425 430

Glu Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
435 440 445

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
450 455

<210> 434

<211> 459
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 434

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Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Arg Pro Ser Gln
1               5                  10                  15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Tyr Ser Ile Thr Ser Asp
            20                  25                  30

His Ala Trp Ser Trp Val Arg Gln Pro Pro Gly Arg Gly Leu Glu Trp
        35                  40                  45

Ile Gly Tyr Ile Ser Tyr Ser Gly Ile Thr Thr Tyr Asn Pro Ser Leu
    50                  55                  60

Lys Ser Arg Val Thr Met Leu Arg Asp Thr Ser Thr Ser Thr Ser Gly
65                  70                  75                  80

Arg Ser Ala Asn Pro Arg Gly Lys Asn Gln Phe Ser Leu Arg Leu Ser
                85                  90                  95

Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala Arg Ser Leu
            100                 105                 110

Ala Arg Thr Thr Ala Met Asp Tyr Trp Gly Gln Gly Ser Leu Val Thr
        115                 120                 125

Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro
    130                 135                 140
```

Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val
145 150 155 160

Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala
165 170 175

Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly
180 185 190

Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly
195 200 205

Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys
210 215 220

Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys
225 230 235 240

Pro Pro Cys Pro Ala Pro Glu Leu Arg Arg Gly Pro Ser Val Phe Leu
245 250 255

Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu
260 265 270

Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys
275 280 285

Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys
290 295 300

Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu
305 310 315 320

```
Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys
                325                 330                 335

Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys
            340                 345                 350

Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser
        355                 360                 365

Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys
    370                 375                 380

Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln
385                 390                 395                 400

Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly
                405                 410                 415

Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln
            420                 425                 430

Glu Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
        435                 440                 445

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
    450                 455
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<210> 435
<211> 459
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 435

```
Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Arg Pro Ser Gln
1               5                  10                  15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Tyr Ser Ile Thr Ser Asp
            20                  25                  30

His Ala Trp Ser Trp Val Arg Gln Pro Pro Gly Arg Gly Leu Glu Trp
        35                  40                  45

Ile Gly Tyr Ile Ser Tyr Ser Gly Ile Thr Thr Tyr Asn Pro Ser Leu
    50                  55                  60

Lys Ser Arg Val Thr Met Leu Arg Asp Thr Ser Lys Thr Ser Thr Ser
65                  70                  75                  80

Gly Arg Ser Ala Asn Pro Arg Gly Asn Gln Phe Ser Leu Arg Leu Ser
                85                  90                  95

Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala Arg Ser Leu
            100                 105                 110

Ala Arg Thr Thr Ala Met Asp Tyr Trp Gly Gln Gly Ser Leu Val Thr
        115                 120                 125

Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro
    130                 135                 140

Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val
145                 150                 155                 160

Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala
```

165 170 175

Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly
180 185 190

Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly
195 200 205

Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys
210 215 220

Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys
225 230 235 240

Pro Pro Cys Pro Ala Pro Glu Leu Arg Arg Gly Pro Ser Val Phe Leu
245 250 255

Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu
260 265 270

Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys
275 280 285

Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys
290 295 300

Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu
305 310 315 320

Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys
325 330 335

Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys

340 345 350

Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser
355 360 365

Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys
370 375 380

Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln
385 390 395 400

Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly
405 410 415

Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln
420 425 430

Glu Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
435 440 445

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
450 455

<210> 436
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<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 436

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Arg Pro Ser Gln
1 5 10 15

```
Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Tyr Ser Ile Thr Ser Asp
            20                  25                  30

His Ala Trp Ser Trp Val Arg Gln Pro Pro Gly Arg Gly Leu Glu Trp
        35                  40                  45

Ile Gly Tyr Ile Ser Tyr Ser Gly Ile Thr Thr Tyr Asn Pro Ser Leu
    50                  55                  60

Lys Ser Arg Val Thr Met Leu Arg Asp Thr Ser Lys Asn Thr Ser Thr
65                  70                  75                  80

Ser Gly Arg Ser Ala Asn Pro Arg Gly Gln Phe Ser Leu Arg Leu Ser
                85                  90                  95

Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala Arg Ser Leu
            100                 105                 110

Ala Arg Thr Thr Ala Met Asp Tyr Trp Gly Gln Gly Ser Leu Val Thr
        115                 120                 125

Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro
    130                 135                 140

Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val
145                 150                 155                 160

Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala
                165                 170                 175

Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly
            180                 185                 190
```

Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly
195 200 205

Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys
210 215 220

Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys
225 230 235 240

Pro Pro Cys Pro Ala Pro Glu Leu Arg Arg Gly Pro Ser Val Phe Leu
245 250 255

Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu
260 265 270

Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys
275 280 285

Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys
290 295 300

Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu
305 310 315 320

Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys
325 330 335

Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys
340 345 350

Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser
355 360 365

```
Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys
    370                 375                 380

Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln
385                 390                 395                 400

Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly
                405                 410                 415

Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln
            420                 425                 430

Glu Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
        435                 440                 445

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
    450                 455
```

<210> 437
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<212> PRT
<213> 人造序列

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<223> 人造的合成序列

<400> 437

```
Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Arg Pro Ser Gln
1               5                   10                  15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Tyr Ser Ile Thr Ser Asp
            20                  25                  30

His Ala Trp Ser Trp Val Arg Gln Pro Pro Gly Arg Gly Leu Glu Trp
```

35 40 45

Ile Gly Tyr Ile Ser Tyr Ser Gly Ile Thr Thr Tyr Asn Pro Ser Leu
50 55 60

Lys Ser Arg Val Thr Met Leu Arg Asp Thr Ser Lys Asn Gln Thr Ser
65 70 75 80

Thr Ser Gly Arg Ser Ala Asn Pro Arg Gly Phe Ser Leu Arg Leu Ser
85 90 95

Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala Arg Ser Leu
100 105 110

Ala Arg Thr Thr Ala Met Asp Tyr Trp Gly Gln Gly Ser Leu Val Thr
115 120 125

Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro
130 135 140

Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val
145 150 155 160

Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala
165 170 175

Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly
180 185 190

Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly
195 200 205

Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys

210 215 220

Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys
225 230 235 240

Pro Pro Cys Pro Ala Pro Glu Leu Arg Arg Gly Pro Ser Val Phe Leu
245 250 255

Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu
260 265 270

Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys
275 280 285

Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys
290 295 300

Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu
305 310 315 320

Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys
325 330 335

Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys
340 345 350

Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser
355 360 365

Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys
370 375 380

Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln

385 390 395 400

Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly
405 410 415

Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln
420 425 430

Glu Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
435 440 445

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
450 455

<210> 438
<211> 459
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 438

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Arg Pro Ser Gln
1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Tyr Ser Ile Thr Ser Asp
20 25 30

His Ala Trp Ser Trp Val Arg Gln Pro Pro Gly Arg Gly Leu Glu Trp
35 40 45

Ile Gly Tyr Ile Ser Tyr Ser Gly Ile Thr Thr Tyr Asn Pro Ser Leu
50 55 60

```
Lys Ser Arg Val Thr Met Leu Arg Asp Thr Ser Lys Asn Gln Phe Ser
65                  70                  75                  80

Leu Arg Leu Ser Ser Val Thr Thr Ser Thr Ser Gly Arg Ser Ala Asn
                85                  90                  95

Pro Arg Gly Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala Arg Ser Leu
            100                 105                 110

Ala Arg Thr Thr Ala Met Asp Tyr Trp Gly Gln Gly Ser Leu Val Thr
        115                 120                 125

Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro
    130                 135                 140

Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val
145                 150                 155                 160

Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala
                165                 170                 175

Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly
            180                 185                 190

Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly
        195                 200                 205

Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys
    210                 215                 220

Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys
225                 230                 235                 240
```

Pro Pro Cys Pro Ala Pro Glu Leu Arg Arg Gly Pro Ser Val Phe Leu
245 250 255

Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu
260 265 270

Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys
275 280 285

Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys
290 295 300

Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu
305 310 315 320

Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys
325 330 335

Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys
340 345 350

Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser
355 360 365

Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys
370 375 380

Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln
385 390 395 400

Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly
405 410 415

Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln
420 425 430

Glu Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
435 440 445

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
450 455

<210> 439
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<212> PRT
<213> 人造序列

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<223> 人造的合成序列

<400> 439

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Arg Pro Ser Gln
1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Tyr Ser Ile Thr Ser Asp
20 25 30

His Ala Trp Ser Trp Val Arg Gln Pro Pro Gly Arg Gly Leu Glu Trp
35 40 45

Ile Gly Tyr Ile Ser Tyr Ser Gly Ile Thr Thr Tyr Asn Pro Ser Leu
50 55 60

Lys Ser Arg Val Thr Met Leu Arg Asp Thr Ser Lys Asn Gln Phe Ser
65 70 75 80

Leu Arg Leu Ser Ser Val Thr Ala Thr Ser Thr Ser Gly Arg Ser Ala

85 90 95

Asn Pro Arg Gly Ala Asp Thr Ala Val Tyr Tyr Cys Ala Arg Ser Leu
100 105 110

Ala Arg Thr Thr Ala Met Asp Tyr Trp Gly Gln Gly Ser Leu Val Thr
115 120 125

Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro
130 135 140

Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val
145 150 155 160

Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala
165 170 175

Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly
180 185 190

Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly
195 200 205

Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys
210 215 220

Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys
225 230 235 240

Pro Pro Cys Pro Ala Pro Glu Leu Arg Arg Gly Pro Ser Val Phe Leu
245 250 255

Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu

260 265 270

Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys
275 280 285

Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys
290 295 300

Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu
305 310 315 320

Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys
325 330 335

Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys
340 345 350

Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser
355 360 365

Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys
370 375 380

Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln
385 390 395 400

Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly
405 410 415

Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln
420 425 430

Glu Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn

435 440 445

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
450 455

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<220>
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<400> 440

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Arg Pro Ser Gln
1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Tyr Ser Ile Thr Ser Asp
20 25 30

His Ala Trp Ser Trp Val Arg Gln Pro Pro Gly Arg Gly Leu Glu Trp
35 40 45

Ile Gly Tyr Ile Ser Tyr Ser Gly Ile Thr Thr Tyr Asn Pro Ser Leu
50 55 60

Lys Ser Arg Val Thr Met Leu Arg Asp Thr Ser Lys Asn Gln Phe Ser
65 70 75 80

Leu Arg Leu Ser Ser Val Thr Ala Ala Thr Ser Thr Ser Gly Arg Ser
85 90 95

Ala Asn Pro Arg Gly Asp Thr Ala Val Tyr Tyr Cys Ala Arg Ser Leu
100 105 110

```
Ala Arg Thr Thr Ala Met Asp Tyr Trp Gly Gln Gly Ser Leu Val Thr
        115                 120                 125

Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro
    130                 135                 140

Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val
145                 150                 155                 160

Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala
                165                 170                 175

Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly
            180                 185                 190

Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly
        195                 200                 205

Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys
    210                 215                 220

Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys
225                 230                 235                 240

Pro Pro Cys Pro Ala Pro Glu Leu Arg Arg Gly Pro Ser Val Phe Leu
                245                 250                 255

Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu
            260                 265                 270

Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys
        275                 280                 285
```

Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys
290 295 300

Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu
305 310 315 320

Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys
325 330 335

Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys
340 345 350

Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser
355 360 365

Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys
370 375 380

Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln
385 390 395 400

Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly
405 410 415

Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln
420 425 430

Glu Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
435 440 445

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
450 455

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```
Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Arg Pro Ser Gln
1               5                  10                  15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Tyr Ser Ile Thr Ser Asp
            20                  25                  30

His Ala Trp Ser Trp Val Arg Gln Pro Pro Gly Arg Gly Leu Glu Trp
        35                  40                  45

Ile Gly Tyr Ile Ser Tyr Ser Gly Ile Thr Thr Tyr Asn Pro Ser Leu
    50                  55                  60

Lys Ser Arg Val Thr Met Leu Arg Asp Thr Ser Lys Asn Gln Phe Ser
65                  70                  75                  80

Leu Arg Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Ser Thr Ser Thr Ser Gly Arg Ser Ala Asn Pro Arg Gly Leu
            100                 105                 110

Ala Arg Thr Thr Ala Met Asp Tyr Trp Gly Gln Gly Ser Leu Val Thr
        115                 120                 125

Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro
```

130 135 140

Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val
145 150 155 160

Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala
165 170 175

Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly
180 185 190

Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly
195 200 205

Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys
210 215 220

Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys
225 230 235 240

Pro Pro Cys Pro Ala Pro Glu Leu Arg Arg Gly Pro Ser Val Phe Leu
245 250 255

Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu
260 265 270

Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys
275 280 285

Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys
290 295 300

Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu

305 310 315 320

Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys
325 330 335

Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys
340 345 350

Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser
355 360 365

Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys
370 375 380

Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln
385 390 395 400

Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly
405 410 415

Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln
420 425 430

Glu Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
435 440 445

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
450 455

<210> 442
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<212> PRT
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<400> 442

```
Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Arg Pro Ser Gln
1               5                  10                  15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Tyr Ser Ile Thr Ser Asp
            20                  25                  30

His Ala Trp Ser Trp Val Arg Gln Pro Pro Gly Arg Gly Leu Glu Trp
        35                  40                  45

Ile Gly Tyr Ile Ser Tyr Ser Gly Ile Thr Thr Tyr Asn Pro Ser Leu
    50                  55                  60

Lys Ser Arg Val Thr Met Leu Arg Asp Thr Ser Lys Asn Gln Phe Ser
65                  70                  75                  80

Leu Arg Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Ser Leu Thr Ser Thr Ser Gly Arg Ser Ala Asn Pro Arg Gly
            100                 105                 110

Ala Arg Thr Thr Ala Met Asp Tyr Trp Gly Gln Gly Ser Leu Val Thr
        115                 120                 125

Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro
    130                 135                 140

Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val
145                 150                 155                 160
```

```
Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala
                165                 170                 175

Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly
            180                 185                 190

Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly
        195                 200                 205

Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys
    210                 215                 220

Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys
225                 230                 235                 240

Pro Pro Cys Pro Ala Pro Glu Leu Arg Arg Gly Pro Ser Val Phe Leu
                245                 250                 255

Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu
            260                 265                 270

Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys
        275                 280                 285

Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys
    290                 295                 300

Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu
305                 310                 315                 320

Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys
                325                 330                 335
```

Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys
340 345 350

Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser
355 360 365

Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys
370 375 380

Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln
385 390 395 400

Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly
405 410 415

Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln
420 425 430

Glu Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
435 440 445

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
450 455

<210> 443
<211> 459
<212> PRT
<213> 人造序列

<220>
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<400> 443

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Arg Pro Ser Gln

1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Tyr Ser Ile Thr Ser Asp
20 25 30

His Ala Trp Ser Trp Val Arg Gln Pro Pro Gly Arg Gly Leu Glu Trp
35 40 45

Ile Gly Tyr Ile Ser Tyr Ser Gly Ile Thr Thr Tyr Asn Pro Ser Leu
50 55 60

Lys Ser Arg Val Thr Met Leu Arg Asp Thr Ser Lys Asn Gln Phe Ser
65 70 75 80

Leu Arg Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Ser Leu Ala Thr Ser Thr Ser Gly Arg Ser Ala Asn Pro Arg
100 105 110

Gly Arg Thr Thr Ala Met Asp Tyr Trp Gly Gln Gly Ser Leu Val Thr
115 120 125

Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro
130 135 140

Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val
145 150 155 160

Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala
165 170 175

Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly

180 185 190

Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly
195 200 205

Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys
210 215 220

Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys
225 230 235 240

Pro Pro Cys Pro Ala Pro Glu Leu Arg Arg Gly Pro Ser Val Phe Leu
245 250 255

Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu
260 265 270

Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys
275 280 285

Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys
290 295 300

Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu
305 310 315 320

Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys
325 330 335

Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys
340 345 350

Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser

355 360 365

Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys
370 375 380

Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln
385 390 395 400

Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly
405 410 415

Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln
420 425 430

Glu Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
435 440 445

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
450 455

<210> 444
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<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 444

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Arg Pro Ser Gln
1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Tyr Ser Ile Thr Ser Asp
20 25 30

His Ala Trp Ser Trp Val Arg Gln Pro Pro Gly Arg Gly Leu Glu Trp
35 40 45

Ile Gly Tyr Ile Ser Tyr Ser Gly Ile Thr Thr Tyr Asn Pro Ser Leu
50 55 60

Lys Ser Arg Val Thr Met Leu Arg Asp Thr Ser Lys Asn Gln Phe Ser
65 70 75 80

Leu Arg Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Ser Leu Ala Arg Thr Ser Thr Ser Gly Arg Ser Ala Asn Pro
100 105 110

Arg Gly Thr Thr Ala Met Asp Tyr Trp Gly Gln Gly Ser Leu Val Thr
115 120 125

Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro
130 135 140

Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val
145 150 155 160

Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala
165 170 175

Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly
180 185 190

Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly
195 200 205

Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys
210 215 220

Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys
225 230 235 240

Pro Pro Cys Pro Ala Pro Glu Leu Arg Arg Gly Pro Ser Val Phe Leu
245 250 255

Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu
260 265 270

Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys
275 280 285

Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys
290 295 300

Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu
305 310 315 320

Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys
325 330 335

Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys
340 345 350

Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser
355 360 365

Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys
370 375 380

Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln
385 390 395 400

Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly
405 410 415

Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln
420 425 430

Glu Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
435 440 445

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
450 455

<210> 445
<211> 459
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 445

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Arg Pro Ser Gln
1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Tyr Ser Ile Thr Ser Asp
20 25 30

His Ala Trp Ser Trp Val Arg Gln Pro Pro Gly Arg Gly Leu Glu Trp
35 40 45

Ile Gly Tyr Ile Ser Tyr Ser Gly Ile Thr Thr Tyr Asn Pro Ser Leu

50 55 60

Lys Ser Arg Val Thr Met Leu Arg Asp Thr Ser Lys Asn Gln Phe Ser
65 70 75 80

Leu Arg Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Ser Leu Ala Arg Thr Thr Ala Met Asp Tyr Trp Thr Ser Thr
100 105 110

Ser Gly Arg Ser Ala Asn Pro Arg Gly Gly Gln Gly Ser Leu Val Thr
115 120 125

Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro
130 135 140

Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val
145 150 155 160

Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala
165 170 175

Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly
180 185 190

Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly
195 200 205

Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys
210 215 220

Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys

225 230 235 240

Pro Pro Cys Pro Ala Pro Glu Leu Arg Arg Gly Pro Ser Val Phe Leu
245 250 255

Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu
260 265 270

Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys
275 280 285

Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys
290 295 300

Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu
305 310 315 320

Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys
325 330 335

Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys
340 345 350

Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser
355 360 365

Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys
370 375 380

Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln
385 390 395 400

Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly

405 410 415

Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln
420 425 430

Glu Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
435 440 445

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
450 455

<210> 446
<211> 459
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 446

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Arg Pro Ser Gln
1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Tyr Ser Ile Thr Ser Asp
20 25 30

His Ala Trp Ser Trp Val Arg Gln Pro Pro Gly Arg Gly Leu Glu Trp
35 40 45

Ile Gly Tyr Ile Ser Tyr Ser Gly Ile Thr Thr Tyr Asn Pro Ser Leu
50 55 60

Lys Ser Arg Val Thr Met Leu Arg Asp Thr Ser Lys Asn Gln Phe Ser
65 70 75 80

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Leu Arg Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Ser Leu Ala Arg Thr Thr Ala Met Asp Tyr Trp Gly Thr Ser
            100                 105                 110

Thr Ser Gly Arg Ser Ala Asn Pro Arg Gly Gln Gly Ser Leu Val Thr
        115                 120                 125

Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro
    130                 135                 140

Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val
145                 150                 155                 160

Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala
                165                 170                 175

Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly
            180                 185                 190

Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly
        195                 200                 205

Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys
    210                 215                 220

Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys
225                 230                 235                 240

Pro Pro Cys Pro Ala Pro Glu Leu Arg Arg Gly Pro Ser Val Phe Leu
                245                 250                 255
```

Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu
260 265 270

Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys
275 280 285

Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys
290 295 300

Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu
305 310 315 320

Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys
325 330 335

Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys
340 345 350

Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser
355 360 365

Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys
370 375 380

Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln
385 390 395 400

Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly
405 410 415

Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln
420 425 430

Glu Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
435 440 445

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
450 455

<210> 447
<211> 459
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 447

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Arg Pro Ser Gln
1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Tyr Ser Ile Thr Ser Asp
20 25 30

His Ala Trp Ser Trp Val Arg Gln Pro Pro Gly Arg Gly Leu Glu Trp
35 40 45

Ile Gly Tyr Ile Ser Tyr Ser Gly Ile Thr Thr Tyr Asn Pro Ser Leu
50 55 60

Lys Ser Arg Val Thr Met Leu Arg Asp Thr Ser Lys Asn Gln Phe Ser
65 70 75 80

Leu Arg Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Ser Leu Ala Arg Thr Thr Ala Met Asp Tyr Trp Gly Gln Thr

100 105 110

Ser Thr Ser Gly Arg Ser Ala Asn Pro Arg Gly Gly Ser Leu Val Thr
115 120 125

Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro
130 135 140

Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val
145 150 155 160

Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala
165 170 175

Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly
180 185 190

Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly
195 200 205

Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys
210 215 220

Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys
225 230 235 240

Pro Pro Cys Pro Ala Pro Glu Leu Arg Arg Gly Pro Ser Val Phe Leu
245 250 255

Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu
260 265 270

Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys

275 280 285

Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys
290 295 300

Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu
305 310 315 320

Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys
325 330 335

Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys
340 345 350

Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser
355 360 365

Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys
370 375 380

Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln
385 390 395 400

Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly
405 410 415

Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln
420 425 430

Glu Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
435 440 445

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro

450 455

<210> 448
<211> 459
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 448

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Arg Pro Ser Gln
1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Tyr Ser Ile Thr Ser Asp
20 25 30

His Ala Trp Ser Trp Val Arg Gln Pro Pro Gly Arg Gly Leu Glu Trp
35 40 45

Ile Gly Tyr Ile Ser Tyr Ser Gly Ile Thr Thr Tyr Asn Pro Ser Leu
50 55 60

Lys Ser Arg Val Thr Met Leu Arg Asp Thr Ser Lys Asn Gln Phe Ser
65 70 75 80

Leu Arg Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Ser Leu Ala Arg Thr Thr Ala Met Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Ser Thr Ser Gly Arg Ser Ala Asn Pro Arg Gly Ser Leu Val Thr
115 120 125

Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro
130 135 140

Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val
145 150 155 160

Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala
165 170 175

Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly
180 185 190

Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly
195 200 205

Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys
210 215 220

Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys
225 230 235 240

Pro Pro Cys Pro Ala Pro Glu Leu Arg Arg Gly Pro Ser Val Phe Leu
245 250 255

Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu
260 265 270

Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys
275 280 285

Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys
290 295 300

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Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu
305                 310                 315                 320

Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys
                325                 330                 335

Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys
            340                 345                 350

Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser
        355                 360                 365

Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys
    370                 375                 380

Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln
385                 390                 395                 400

Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly
                405                 410                 415

Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln
            420                 425                 430

Glu Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
        435                 440                 445

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
    450                 455
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<210> 449
<211> 459
<212> PRT

<213> 人造序列

<220>
<223> 人造的合成序列

<400> 449

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Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Arg Pro Ser Gln
1               5                  10                  15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Tyr Ser Ile Thr Ser Asp
            20                  25                  30

His Ala Trp Ser Trp Val Arg Gln Pro Pro Gly Arg Gly Leu Glu Trp
        35                  40                  45

Ile Gly Tyr Ile Ser Tyr Ser Gly Ile Thr Thr Tyr Asn Pro Ser Leu
    50                  55                  60

Lys Ser Arg Val Thr Met Leu Arg Asp Thr Ser Lys Asn Gln Phe Ser
65                  70                  75                  80

Leu Arg Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Ser Leu Ala Arg Thr Thr Ala Met Asp Tyr Trp Gly Gln Gly
            100                 105                 110

Ser Thr Ser Thr Ser Gly Arg Ser Ala Asn Pro Arg Gly Leu Val Thr
        115                 120                 125

Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro
    130                 135                 140

Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val
```

145 150 155 160

Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala
165 170 175

Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly
180 185 190

Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly
195 200 205

Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys
210 215 220

Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys
225 230 235 240

Pro Pro Cys Pro Ala Pro Glu Leu Arg Arg Gly Pro Ser Val Phe Leu
245 250 255

Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu
260 265 270

Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys
275 280 285

Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys
290 295 300

Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu
305 310 315 320

Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys

325 330 335

Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys
340 345 350

Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser
355 360 365

Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys
370 375 380

Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln
385 390 395 400

Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly
405 410 415

Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln
420 425 430

Glu Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
435 440 445

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
450 455

<210> 450
<211> 459
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 450

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Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Arg Pro Ser Gln
1               5                  10                  15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Tyr Ser Ile Thr Ser Asp
            20                  25                  30

His Ala Trp Ser Trp Val Arg Gln Pro Pro Gly Arg Gly Leu Glu Trp
        35                  40                  45

Ile Gly Tyr Ile Ser Tyr Ser Gly Ile Thr Thr Tyr Asn Pro Ser Leu
    50                  55                  60

Lys Ser Arg Val Thr Met Leu Arg Asp Thr Ser Lys Asn Gln Phe Ser
65                  70                  75                  80

Leu Arg Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Ser Leu Ala Arg Thr Thr Ala Met Asp Tyr Trp Gly Gln Gly
            100                 105                 110

Ser Leu Thr Ser Thr Ser Gly Arg Ser Ala Asn Pro Arg Gly Val Thr
        115                 120                 125

Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro
    130                 135                 140

Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val
145                 150                 155                 160

Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala
                165                 170                 175
```

Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly
180 185 190

Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly
195 200 205

Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys
210 215 220

Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys
225 230 235 240

Pro Pro Cys Pro Ala Pro Glu Leu Arg Arg Gly Pro Ser Val Phe Leu
245 250 255

Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu
260 265 270

Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys
275 280 285

Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys
290 295 300

Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu
305 310 315 320

Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys
325 330 335

Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys
340 345 350

Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser
355 360 365

Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys
370 375 380

Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln
385 390 395 400

Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly
405 410 415

Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln
420 425 430

Glu Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
435 440 445

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
450 455

<210> 451
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<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 451

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Arg Pro Ser Gln
1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Tyr Ser Ile Thr Ser Asp

20 25 30

His Ala Trp Ser Trp Val Arg Gln Pro Pro Gly Arg Gly Leu Glu Trp
35 40 45

Ile Gly Tyr Ile Ser Tyr Ser Gly Ile Thr Thr Tyr Asn Pro Ser Leu
50 55 60

Lys Ser Arg Val Thr Met Leu Arg Asp Thr Ser Lys Asn Gln Phe Ser
65 70 75 80

Leu Arg Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Ser Leu Ala Arg Thr Thr Ala Met Asp Tyr Trp Gly Gln Gly
100 105 110

Ser Leu Val Thr Ser Thr Ser Gly Arg Ser Ala Asn Pro Arg Gly Thr
115 120 125

Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro
130 135 140

Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val
145 150 155 160

Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala
165 170 175

Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly
180 185 190

Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly

195 200 205

Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys
210 215 220

Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys
225 230 235 240

Pro Pro Cys Pro Ala Pro Glu Leu Arg Arg Gly Pro Ser Val Phe Leu
245 250 255

Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu
260 265 270

Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys
275 280 285

Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys
290 295 300

Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu
305 310 315 320

Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys
325 330 335

Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys
340 345 350

Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser
355 360 365

Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys

370 375 380

Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln
385 390 395 400

Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly
405 410 415

Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln
420 425 430

Glu Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
435 440 445

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
450 455

<210> 452
<211> 459
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 452

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Arg Pro Ser Gln
1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Tyr Ser Ile Thr Ser Asp
20 25 30

His Ala Trp Ser Trp Val Arg Gln Pro Pro Gly Arg Gly Leu Glu Trp
35 40 45

```
Ile Gly Tyr Ile Ser Tyr Ser Gly Ile Thr Thr Tyr Asn Pro Ser Leu
    50                  55                  60

Lys Ser Arg Val Thr Met Leu Arg Asp Thr Ser Lys Asn Gln Phe Ser
65                  70                  75                  80

Leu Arg Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Ser Leu Ala Arg Thr Thr Ala Met Asp Tyr Trp Gly Gln Gly
            100                 105                 110

Ser Leu Val Thr Thr Ser Thr Ser Gly Arg Ser Ala Asn Pro Arg Gly
        115                 120                 125

Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro
    130                 135                 140

Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val
145                 150                 155                 160

Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala
                165                 170                 175

Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly
            180                 185                 190

Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly
        195                 200                 205

Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys
    210                 215                 220
```

Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys
225 230 235 240

Pro Pro Cys Pro Ala Pro Glu Leu Arg Arg Gly Pro Ser Val Phe Leu
245 250 255

Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu
260 265 270

Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys
275 280 285

Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys
290 295 300

Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu
305 310 315 320

Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys
325 330 335

Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys
340 345 350

Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser
355 360 365

Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys
370 375 380

Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln
385 390 395 400

Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly
405 410 415

Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln
420 425 430

Glu Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
435 440 445

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
450 455

<210> 453
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<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 453

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Arg Pro Ser Gln
1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Tyr Ser Ile Thr Ser Asp
20 25 30

His Ala Trp Ser Trp Val Arg Gln Pro Pro Gly Arg Gly Leu Glu Trp
35 40 45

Ile Gly Tyr Ile Ser Tyr Ser Gly Ile Thr Thr Tyr Asn Pro Ser Leu
50 55 60

Lys Ser Arg Val Thr Met Leu Arg Asp Thr Ser Lys Asn Gln Phe Ser

65 70 75 80

Leu Arg Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Ser Leu Ala Arg Thr Thr Ala Met Asp Tyr Trp Gly Gln Gly
100 105 110

Ser Leu Val Thr Val Thr Ser Thr Ser Gly Arg Ser Ala Asn Pro Arg
115 120 125

Gly Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro
130 135 140

Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val
145 150 155 160

Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala
165 170 175

Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly
180 185 190

Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly
195 200 205

Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys
210 215 220

Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys
225 230 235 240

Pro Pro Cys Pro Ala Pro Glu Leu Arg Arg Gly Pro Ser Val Phe Leu

245 250 255

Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu
260 265 270

Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys
275 280 285

Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys
290 295 300

Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu
305 310 315 320

Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys
325 330 335

Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys
340 345 350

Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser
355 360 365

Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys
370 375 380

Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln
385 390 395 400

Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly
405 410 415

Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln

420 425 430

Glu Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
435 440 445

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
450 455

<210> 454
<211> 459
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 454

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Arg Pro Ser Gln
1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Tyr Ser Ile Thr Ser Asp
20 25 30

His Ala Trp Ser Trp Val Arg Gln Pro Pro Gly Arg Gly Leu Glu Trp
35 40 45

Ile Gly Tyr Ile Ser Tyr Ser Gly Ile Thr Thr Tyr Asn Pro Ser Leu
50 55 60

Lys Ser Arg Val Thr Met Leu Arg Asp Thr Ser Lys Asn Gln Phe Ser
65 70 75 80

Leu Arg Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys
85 90 95

```
Ala Arg Ser Leu Ala Arg Thr Thr Ala Met Asp Tyr Trp Gly Gln Gly
            100                 105                 110

Ser Leu Val Thr Val Ser Thr Ser Thr Ser Gly Arg Ser Ala Asn Pro
        115                 120                 125

Arg Gly Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro
    130                 135                 140

Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val
145                 150                 155                 160

Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala
                165                 170                 175

Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly
            180                 185                 190

Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly
        195                 200                 205

Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys
    210                 215                 220

Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys
225                 230                 235                 240

Pro Pro Cys Pro Ala Pro Glu Leu Arg Arg Gly Pro Ser Val Phe Leu
                245                 250                 255

Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu
            260                 265                 270
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Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys
275 280 285

Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys
290 295 300

Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu
305 310 315 320

Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys
325 330 335

Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys
340 345 350

Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser
355 360 365

Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys
370 375 380

Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln
385 390 395 400

Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly
405 410 415

Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln
420 425 430

Glu Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
435 440 445

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
450 455

<210> 455
<211> 459
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 455

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Arg Pro Ser Gln
1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Tyr Ser Ile Thr Ser Asp
20 25 30

His Ala Trp Ser Trp Val Arg Gln Pro Pro Gly Arg Gly Leu Glu Trp
35 40 45

Ile Gly Tyr Ile Ser Tyr Ser Gly Ile Thr Thr Tyr Asn Pro Ser Leu
50 55 60

Lys Ser Arg Val Thr Met Leu Arg Asp Thr Ser Lys Asn Gln Phe Ser
65 70 75 80

Leu Arg Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Ser Leu Ala Arg Thr Thr Ala Met Asp Tyr Trp Gly Gln Gly
100 105 110

Ser Leu Val Thr Val Ser Ser Thr Ser Thr Ser Gly Arg Ser Ala Asn

115 120 125

Pro Arg Gly Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro
130 135 140

Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val
145 150 155 160

Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala
165 170 175

Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly
180 185 190

Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly
195 200 205

Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys
210 215 220

Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys
225 230 235 240

Pro Pro Cys Pro Ala Pro Glu Leu Arg Arg Gly Pro Ser Val Phe Leu
245 250 255

Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu
260 265 270

Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys
275 280 285

Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys

290 295 300

Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu
305 310 315 320

Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys
325 330 335

Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys
340 345 350

Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser
355 360 365

Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys
370 375 380

Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln
385 390 395 400

Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly
405 410 415

Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln
420 425 430

Glu Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
435 440 445

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
450 455

<210> 456

<211> 459
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 456

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Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Arg Pro Ser Gln
1               5                  10                  15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Tyr Ser Ile Thr Ser Asp
            20                  25                  30

His Ala Trp Ser Trp Val Arg Gln Pro Pro Gly Arg Gly Leu Glu Trp
        35                  40                  45

Ile Gly Tyr Ile Ser Tyr Ser Gly Ile Thr Thr Tyr Asn Pro Ser Leu
    50                  55                  60

Lys Ser Arg Val Thr Met Leu Arg Asp Thr Ser Lys Asn Gln Phe Ser
65                  70                  75                  80

Leu Arg Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Ser Leu Ala Arg Thr Thr Ala Met Asp Tyr Trp Gly Gln Gly
            100                 105                 110

Ser Leu Val Thr Val Ser Ser Ala Thr Ser Thr Ser Gly Arg Ser Ala
        115                 120                 125

Asn Pro Arg Gly Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro
    130                 135                 140
```

Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val
145 150 155 160

Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala
165 170 175

Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly
180 185 190

Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly
195 200 205

Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys
210 215 220

Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys
225 230 235 240

Pro Pro Cys Pro Ala Pro Glu Leu Arg Arg Gly Pro Ser Val Phe Leu
245 250 255

Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu
260 265 270

Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys
275 280 285

Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys
290 295 300

Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu
305 310 315 320

Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys
325 330 335

Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys
340 345 350

Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser
355 360 365

Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys
370 375 380

Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln
385 390 395 400

Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly
405 410 415

Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln
420 425 430

Glu Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
435 440 445

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
450 455

<210> 457
<211> 459
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 457

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Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Arg Pro Ser Gln
1               5                  10                  15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Tyr Ser Ile Thr Ser Asp
            20                  25                  30

His Ala Trp Ser Trp Val Arg Gln Pro Pro Gly Arg Gly Leu Glu Trp
        35                  40                  45

Ile Gly Tyr Ile Ser Tyr Ser Gly Ile Thr Thr Tyr Asn Pro Ser Leu
    50                  55                  60

Lys Ser Arg Val Thr Met Leu Arg Asp Thr Ser Lys Asn Gln Phe Ser
65                  70                  75                  80

Leu Arg Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Ser Leu Ala Arg Thr Thr Ala Met Asp Tyr Trp Gly Gln Gly
            100                 105                 110

Ser Leu Val Thr Val Ser Ser Ala Ser Thr Ser Thr Ser Gly Arg Ser
        115                 120                 125

Ala Asn Pro Arg Gly Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro
    130                 135                 140

Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val
145                 150                 155                 160

Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala
```

165 170 175

Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly
180 185 190

Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly
195 200 205

Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys
210 215 220

Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys
225 230 235 240

Pro Pro Cys Pro Ala Pro Glu Leu Arg Arg Gly Pro Ser Val Phe Leu
245 250 255

Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu
260 265 270

Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys
275 280 285

Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys
290 295 300

Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu
305 310 315 320

Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys
325 330 335

Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys

340 345 350

Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser
355 360 365

Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys
370 375 380

Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln
385 390 395 400

Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly
405 410 415

Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln
420 425 430

Glu Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
435 440 445

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
450 455

<210> 458
<211> 459
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 458

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Arg Pro Ser Gln
1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Tyr Ser Ile Thr Ser Asp
20 25 30

His Ala Trp Ser Trp Val Arg Gln Pro Pro Gly Arg Gly Leu Glu Trp
35 40 45

Ile Gly Tyr Ile Ser Tyr Ser Gly Ile Thr Thr Tyr Asn Pro Ser Leu
50 55 60

Lys Ser Arg Val Thr Met Leu Arg Asp Thr Ser Lys Asn Gln Phe Ser
65 70 75 80

Leu Arg Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Ser Leu Ala Arg Thr Thr Ala Met Asp Tyr Trp Gly Gln Gly
100 105 110

Ser Leu Val Thr Val Ser Ser Ala Ser Thr Thr Ser Thr Ser Gly Arg
115 120 125

Ser Ala Asn Pro Arg Gly Lys Gly Pro Ser Val Phe Pro Leu Ala Pro
130 135 140

Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val
145 150 155 160

Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala
165 170 175

Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly
180 185 190

Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly
195 200 205

Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys
210 215 220

Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys
225 230 235 240

Pro Pro Cys Pro Ala Pro Glu Leu Arg Arg Gly Pro Ser Val Phe Leu
245 250 255

Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu
260 265 270

Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys
275 280 285

Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys
290 295 300

Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu
305 310 315 320

Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys
325 330 335

Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys
340 345 350

Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser
355 360 365

Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys
370 375 380

Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln
385 390 395 400

Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly
405 410 415

Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln
420 425 430

Glu Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
435 440 445

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
450 455

<210> 459
<211> 459
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 459

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Arg Pro Ser Gln
1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Tyr Ser Ile Thr Ser Asp
20 25 30

His Ala Trp Ser Trp Val Arg Gln Pro Pro Gly Arg Gly Leu Glu Trp

35 40 45

Ile Gly Tyr Ile Ser Tyr Ser Gly Ile Thr Thr Tyr Asn Pro Ser Leu
50 55 60

Lys Ser Arg Val Thr Met Leu Arg Asp Thr Ser Lys Asn Gln Phe Ser
65 70 75 80

Leu Arg Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Ser Leu Ala Arg Thr Thr Ala Met Asp Tyr Trp Gly Gln Gly
100 105 110

Ser Leu Val Thr Val Ser Ser Ala Ser Thr Lys Thr Ser Thr Ser Gly
115 120 125

Arg Ser Ala Asn Pro Arg Gly Gly Pro Ser Val Phe Pro Leu Ala Pro
130 135 140

Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val
145 150 155 160

Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala
165 170 175

Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly
180 185 190

Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly
195 200 205

Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys

210 215 220

Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys
225 230 235 240

Pro Pro Cys Pro Ala Pro Glu Leu Arg Arg Gly Pro Ser Val Phe Leu
245 250 255

Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu
260 265 270

Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys
275 280 285

Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys
290 295 300

Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu
305 310 315 320

Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys
325 330 335

Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys
340 345 350

Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser
355 360 365

Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys
370 375 380

Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln

385 390 395 400

Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly
405 410 415

Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln
420 425 430

Glu Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
435 440 445

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
450 455

<210> 460
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<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 460

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Arg Pro Ser Gln
1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Tyr Ser Ile Thr Ser Asp
20 25 30

His Ala Trp Ser Trp Val Arg Gln Pro Pro Gly Arg Gly Leu Glu Trp
35 40 45

Ile Gly Tyr Ile Ser Tyr Ser Gly Ile Thr Thr Tyr Asn Pro Ser Leu
50 55 60

```
Lys Ser Arg Val Thr Met Leu Arg Asp Thr Ser Lys Asn Gln Phe Ser
65                  70                  75                  80

Leu Arg Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Ser Leu Ala Arg Thr Thr Ala Met Asp Tyr Trp Gly Gln Gly
            100                 105                 110

Ser Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Thr Ser Thr Ser
        115                 120                 125

Gly Arg Ser Ala Asn Pro Arg Gly Pro Ser Val Phe Pro Leu Ala Pro
    130                 135                 140

Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val
145                 150                 155                 160

Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala
                165                 170                 175

Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly
            180                 185                 190

Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly
        195                 200                 205

Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys
    210                 215                 220

Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys
225                 230                 235                 240
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Pro Pro Cys Pro Ala Pro Glu Leu Arg Arg Gly Pro Ser Val Phe Leu
245 250 255

Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu
260 265 270

Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys
275 280 285

Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys
290 295 300

Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu
305 310 315 320

Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys
325 330 335

Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys
340 345 350

Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser
355 360 365

Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys
370 375 380

Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln
385 390 395 400

Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly
405 410 415

Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln
420 425 430

Glu Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
435 440 445

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
450 455

<210> 461
<211> 459
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 461

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Arg Pro Ser Gln
1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Tyr Ser Ile Thr Ser Asp
20 25 30

His Ala Trp Ser Trp Val Arg Gln Pro Pro Gly Arg Gly Leu Glu Trp
35 40 45

Ile Gly Tyr Ile Ser Tyr Ser Gly Ile Thr Thr Tyr Asn Pro Ser Leu
50 55 60

Lys Ser Arg Val Thr Met Leu Arg Asp Thr Ser Lys Asn Gln Phe Ser
65 70 75 80

Leu Arg Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys

85 90 95

Ala Arg Ser Leu Ala Arg Thr Thr Ala Met Asp Tyr Trp Gly Gln Gly
100 105 110

Ser Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Thr Ser Thr
115 120 125

Ser Gly Arg Ser Ala Asn Pro Arg Gly Ser Val Phe Pro Leu Ala Pro
130 135 140

Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val
145 150 155 160

Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala
165 170 175

Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly
180 185 190

Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly
195 200 205

Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys
210 215 220

Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys
225 230 235 240

Pro Pro Cys Pro Ala Pro Glu Leu Arg Arg Gly Pro Ser Val Phe Leu
245 250 255

Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu

260 265 270

Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys
275 280 285

Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys
290 295 300

Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu
305 310 315 320

Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys
325 330 335

Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys
340 345 350

Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser
355 360 365

Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys
370 375 380

Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln
385 390 395 400

Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly
405 410 415

Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln
420 425 430

Glu Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn

435 440 445

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
450 455

<210> 462
<211> 459
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 462

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Arg Pro Ser Gln
1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Tyr Ser Ile Thr Ser Asp
20 25 30

His Ala Trp Ser Trp Val Arg Gln Pro Pro Gly Arg Gly Leu Glu Trp
35 40 45

Ile Gly Tyr Ile Ser Tyr Ser Gly Ile Thr Thr Tyr Asn Pro Ser Leu
50 55 60

Lys Ser Arg Val Thr Met Leu Arg Asp Thr Ser Lys Asn Gln Phe Ser
65 70 75 80

Leu Arg Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Ser Leu Ala Arg Thr Thr Ala Met Asp Tyr Trp Gly Gln Gly
100 105 110

Ser Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Thr Ser
115 120 125

Thr Ser Gly Arg Ser Ala Asn Pro Arg Gly Val Phe Pro Leu Ala Pro
130 135 140

Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val
145 150 155 160

Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala
165 170 175

Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly
180 185 190

Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly
195 200 205

Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys
210 215 220

Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys
225 230 235 240

Pro Pro Cys Pro Ala Pro Glu Leu Arg Arg Gly Pro Ser Val Phe Leu
245 250 255

Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu
260 265 270

Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys
275 280 285

Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys
290 295 300

Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu
305 310 315 320

Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys
325 330 335

Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys
340 345 350

Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser
355 360 365

Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys
370 375 380

Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln
385 390 395 400

Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly
405 410 415

Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln
420 425 430

Glu Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
435 440 445

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
450 455

<210> 463
<211> 459
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 463

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Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Arg Pro Ser Gln
1               5                  10                  15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Tyr Ser Ile Thr Ser Asp
            20                  25                  30

His Ala Trp Ser Trp Val Arg Gln Pro Pro Gly Arg Gly Leu Glu Trp
        35                  40                  45

Ile Gly Tyr Ile Ser Tyr Ser Gly Ile Thr Thr Tyr Asn Pro Ser Leu
    50                  55                  60

Lys Ser Arg Val Thr Met Leu Arg Asp Thr Ser Lys Asn Gln Phe Ser
65                  70                  75                  80

Leu Arg Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Ser Leu Ala Arg Thr Thr Ala Met Asp Tyr Trp Gly Gln Gly
            100                 105                 110

Ser Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe
        115                 120                 125

Pro Leu Ala Thr Ser Thr Ser Gly Arg Ser Ala Asn Pro Arg Gly Pro
```

130 135 140

Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val
145 150 155 160

Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala
165 170 175

Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly
180 185 190

Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly
195 200 205

Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys
210 215 220

Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys
225 230 235 240

Pro Pro Cys Pro Ala Pro Glu Leu Arg Arg Gly Pro Ser Val Phe Leu
245 250 255

Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu
260 265 270

Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys
275 280 285

Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys
290 295 300

Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu

305 310 315 320

Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys
325 330 335

Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys
340 345 350

Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser
355 360 365

Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys
370 375 380

Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln
385 390 395 400

Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly
405 410 415

Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln
420 425 430

Glu Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
435 440 445

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
450 455

<210> 464
<211> 459
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 464

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Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Arg Pro Ser Gln
1               5                  10                  15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Tyr Ser Ile Thr Ser Asp
            20                  25                  30

His Ala Trp Ser Trp Val Arg Gln Pro Pro Gly Arg Gly Leu Glu Trp
        35                  40                  45

Ile Gly Tyr Ile Ser Tyr Ser Gly Ile Thr Thr Tyr Asn Pro Ser Leu
    50                  55                  60

Lys Ser Arg Val Thr Met Leu Arg Asp Thr Ser Lys Asn Gln Phe Ser
65                  70                  75                  80

Leu Arg Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Ser Leu Ala Arg Thr Thr Ala Met Asp Tyr Trp Gly Gln Gly
            100                 105                 110

Ser Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe
        115                 120                 125

Pro Leu Ala Pro Thr Ser Thr Ser Gly Arg Ser Ala Asn Pro Arg Gly
    130                 135                 140

Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val
145                 150                 155                 160
```

Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala
165 170 175

Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly
180 185 190

Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly
195 200 205

Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys
210 215 220

Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys
225 230 235 240

Pro Pro Cys Pro Ala Pro Glu Leu Arg Arg Gly Pro Ser Val Phe Leu
245 250 255

Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu
260 265 270

Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys
275 280 285

Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys
290 295 300

Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu
305 310 315 320

Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys
325 330 335

Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys
340 345 350

Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser
355 360 365

Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys
370 375 380

Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln
385 390 395 400

Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly
405 410 415

Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln
420 425 430

Glu Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
435 440 445

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
450 455

<210> 465
<211> 459
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 465

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Arg Pro Ser Gln

1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Tyr Ser Ile Thr Ser Asp
20 25 30

His Ala Trp Ser Trp Val Arg Gln Pro Pro Gly Arg Gly Leu Glu Trp
35 40 45

Ile Gly Tyr Ile Ser Tyr Ser Gly Ile Thr Thr Tyr Asn Pro Ser Leu
50 55 60

Lys Ser Arg Val Thr Met Leu Arg Asp Thr Ser Lys Asn Gln Phe Ser
65 70 75 80

Leu Arg Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Ser Leu Ala Arg Thr Thr Ala Met Asp Tyr Trp Gly Gln Gly
100 105 110

Ser Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe
115 120 125

Pro Leu Ala Pro Ser Thr Ser Thr Ser Gly Arg Ser Ala Asn Pro Arg
130 135 140

Gly Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val
145 150 155 160

Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala
165 170 175

Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly

180 185 190

Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly
195 200 205

Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys
210 215 220

Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys
225 230 235 240

Pro Pro Cys Pro Ala Pro Glu Leu Arg Arg Gly Pro Ser Val Phe Leu
245 250 255

Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu
260 265 270

Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys
275 280 285

Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys
290 295 300

Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu
305 310 315 320

Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys
325 330 335

Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys
340 345 350

Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser

355 360 365

Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys
370 375 380

Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln
385 390 395 400

Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly
405 410 415

Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln
420 425 430

Glu Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
435 440 445

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
450 455

<210> 466
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<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 466

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Arg Pro Ser Gln
1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Tyr Ser Ile Thr Ser Asp
20 25 30

```
His Ala Trp Ser Trp Val Arg Gln Pro Pro Gly Arg Gly Leu Glu Trp
        35                  40                  45

Ile Gly Tyr Ile Ser Tyr Ser Gly Ile Thr Thr Tyr Asn Pro Ser Leu
    50                  55                  60

Lys Ser Arg Val Thr Met Leu Arg Asp Thr Ser Lys Asn Gln Phe Ser
65                  70                  75                  80

Leu Arg Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Ser Leu Ala Arg Thr Thr Ala Met Asp Tyr Trp Gly Gln Gly
            100                 105                 110

Ser Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe
        115                 120                 125

Pro Leu Ala Pro Ser Ser Thr Ser Thr Ser Gly Arg Ser Ala Asn Pro
    130                 135                 140

Arg Gly Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val
145                 150                 155                 160

Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala
                165                 170                 175

Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly
            180                 185                 190

Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly
        195                 200                 205
```

```
Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys
    210                 215                 220

Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys
225                 230                 235                 240

Pro Pro Cys Pro Ala Pro Glu Leu Arg Arg Gly Pro Ser Val Phe Leu
                245                 250                 255

Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu
            260                 265                 270

Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys
        275                 280                 285

Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys
    290                 295                 300

Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu
305                 310                 315                 320

Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys
                325                 330                 335

Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys
            340                 345                 350

Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser
        355                 360                 365

Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys
    370                 375                 380
```

Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln
385 390 395 400

Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly
405 410 415

Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln
420 425 430

Glu Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
435 440 445

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
450 455

<210> 467
<211> 459
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 467

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Arg Pro Ser Gln
1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Tyr Ser Ile Thr Ser Asp
20 25 30

His Ala Trp Ser Trp Val Arg Gln Pro Pro Gly Arg Gly Leu Glu Trp
35 40 45

Ile Gly Tyr Ile Ser Tyr Ser Gly Ile Thr Thr Tyr Asn Pro Ser Leu

50 55 60

Lys Ser Arg Val Thr Met Leu Arg Asp Thr Ser Lys Asn Gln Phe Ser
65 70 75 80

Leu Arg Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Ser Leu Ala Arg Thr Thr Ala Met Asp Tyr Trp Gly Gln Gly
100 105 110

Ser Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe
115 120 125

Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Thr Ser Gly Arg Ser Ala
130 135 140

Asn Pro Arg Gly Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val
145 150 155 160

Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala
165 170 175

Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly
180 185 190

Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly
195 200 205

Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys
210 215 220

Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys

225 230 235 240

Pro Pro Cys Pro Ala Pro Glu Leu Arg Arg Gly Pro Ser Val Phe Leu
245 250 255

Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu
260 265 270

Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys
275 280 285

Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys
290 295 300

Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu
305 310 315 320

Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys
325 330 335

Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys
340 345 350

Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser
355 360 365

Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys
370 375 380

Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln
385 390 395 400

Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly

405 410 415

Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln
420 425 430

Glu Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
435 440 445

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
450 455

<210> 468
<211> 459
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 468

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Arg Pro Ser Gln
1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Tyr Ser Ile Thr Ser Asp
20 25 30

His Ala Trp Ser Trp Val Arg Gln Pro Pro Gly Arg Gly Leu Glu Trp
35 40 45

Ile Gly Tyr Ile Ser Tyr Ser Gly Ile Thr Thr Tyr Asn Pro Ser Leu
50 55 60

Lys Ser Arg Val Thr Met Leu Arg Asp Thr Ser Lys Asn Gln Phe Ser
65 70 75 80

```
Leu Arg Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Ser Leu Ala Arg Thr Thr Ala Met Asp Tyr Trp Gly Gln Gly
            100                 105                 110

Ser Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe
        115                 120                 125

Pro Leu Ala Pro Ser Ser Lys Ser Thr Thr Ser Thr Ser Gly Arg Ser
    130                 135                 140

Ala Asn Pro Arg Gly Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val
145                 150                 155                 160

Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala
                165                 170                 175

Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly
            180                 185                 190

Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly
        195                 200                 205

Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys
    210                 215                 220

Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys
225                 230                 235                 240

Pro Pro Cys Pro Ala Pro Glu Leu Arg Arg Gly Pro Ser Val Phe Leu
                245                 250                 255
```

```
Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu
            260                 265                 270

Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys
        275                 280                 285

Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys
    290                 295                 300

Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu
305                 310                 315                 320

Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys
                325                 330                 335

Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys
            340                 345                 350

Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser
        355                 360                 365

Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys
    370                 375                 380

Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln
385                 390                 395                 400

Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly
                405                 410                 415

Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln
            420                 425                 430
```

Glu Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
435 440 445

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
450 455

<210> 469
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<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 469

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Arg Pro Ser Gln
1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Tyr Ser Ile Thr Ser Asp
20 25 30

His Ala Trp Ser Trp Val Arg Gln Pro Pro Gly Arg Gly Leu Glu Trp
35 40 45

Ile Gly Tyr Ile Ser Tyr Ser Gly Ile Thr Thr Tyr Asn Pro Ser Leu
50 55 60

Lys Ser Arg Val Thr Met Leu Arg Asp Thr Ser Lys Asn Gln Phe Ser
65 70 75 80

Leu Arg Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Ser Leu Ala Arg Thr Thr Ala Met Asp Tyr Trp Gly Gln Gly

100 105 110

Ser Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe
115 120 125

Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Thr Ser Thr Ser Gly
130 135 140

Arg Ser Ala Asn Pro Arg Gly Gly Thr Ala Ala Leu Gly Cys Leu Val
145 150 155 160

Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala
165 170 175

Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly
180 185 190

Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly
195 200 205

Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys
210 215 220

Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys
225 230 235 240

Pro Pro Cys Pro Ala Pro Glu Leu Arg Arg Gly Pro Ser Val Phe Leu
245 250 255

Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu
260 265 270

Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys

275 280 285

Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys
290 295 300

Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu
305 310 315 320

Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys
325 330 335

Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys
340 345 350

Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser
355 360 365

Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys
370 375 380

Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln
385 390 395 400

Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly
405 410 415

Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln
420 425 430

Glu Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
435 440 445

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro

450 455

<210> 470
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<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 470

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Arg Pro Ser Gln
1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Tyr Ser Ile Thr Ser Asp
20 25 30

His Ala Trp Ser Trp Val Arg Gln Pro Pro Gly Arg Gly Leu Glu Trp
35 40 45

Ile Gly Tyr Ile Ser Tyr Ser Gly Ile Thr Thr Tyr Asn Pro Ser Leu
50 55 60

Lys Ser Arg Val Thr Met Leu Arg Asp Thr Ser Lys Asn Gln Phe Ser
65 70 75 80

Leu Arg Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Ser Leu Ala Arg Thr Thr Ala Met Asp Tyr Trp Gly Gln Gly
100 105 110

Ser Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe
115 120 125

```
Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Thr Ser Thr
    130                 135                 140

Ser Gly Arg Ser Ala Asn Pro Arg Gly Ala Ala Leu Gly Cys Leu Val
145                 150                 155                 160

Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala
                165                 170                 175

Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly
            180                 185                 190

Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly
        195                 200                 205

Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys
    210                 215                 220

Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys
225                 230                 235                 240

Pro Pro Cys Pro Ala Pro Glu Leu Arg Arg Gly Pro Ser Val Phe Leu
                245                 250                 255

Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu
            260                 265                 270

Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys
        275                 280                 285

Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys
    290                 295                 300
```

```
Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu
305                 310                 315                 320

Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys
                325                 330                 335

Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys
            340                 345                 350

Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser
        355                 360                 365

Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys
    370                 375                 380

Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln
385                 390                 395                 400

Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly
                405                 410                 415

Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln
            420                 425                 430

Glu Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
        435                 440                 445

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
    450                 455
```

<210> 471
<211> 226
<212> PRT

<213> 人造序列

<220>
<223> 人造的合成序列

<400> 471

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Asp Ile Gln Met Thr Gln Ser Thr Ser Thr Ser Gly Arg Ser Ala Asn
1               5                  10                  15

Pro Arg Gly Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr
            20                  25                  30

Ile Thr Cys Arg Ala Ser Gln Asp Ile Ser Ser Tyr Leu Asn Trp Tyr
        35                  40                  45

Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Tyr Thr Ser
    50                  55                  60

Arg Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly
65                  70                  75                  80

Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Gln Pro Glu Asp Ile Ala
                85                  90                  95

Thr Tyr Tyr Cys Gln Gln Gly Asn Thr Leu Pro Tyr Thr Phe Gly Gln
            100                 105                 110

Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala Pro Ser Val Phe
        115                 120                 125

Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr Ala Ser Val
    130                 135                 140

Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp
```

145 150 155 160

Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser Val Thr
165 170 175

Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr
180 185 190

Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala Cys Glu Val
195 200 205

Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe Asn Arg Gly
210 215 220

Glu Cys
225

<210> 472
<211> 226
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 472

Asp Ile Gln Met Thr Gln Ser Pro Thr Ser Thr Ser Gly Arg Ser Ala
1 5 10 15

Asn Pro Arg Gly Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr
20 25 30

Ile Thr Cys Arg Ala Ser Gln Asp Ile Ser Ser Tyr Leu Asn Trp Tyr
35 40 45

```
Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Tyr Thr Ser
    50                  55                  60

Arg Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly
65                  70                  75                  80

Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Gln Pro Glu Asp Ile Ala
                85                  90                  95

Thr Tyr Tyr Cys Gln Gln Gly Asn Thr Leu Pro Tyr Thr Phe Gly Gln
            100                 105                 110

Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala Pro Ser Val Phe
        115                 120                 125

Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr Ala Ser Val
    130                 135                 140

Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp
145                 150                 155                 160

Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser Val Thr
                165                 170                 175

Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr
            180                 185                 190

Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala Cys Glu Val
        195                 200                 205

Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe Asn Arg Gly
    210                 215                 220
```

Glu Cys
225

<210> 473
<211> 226
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 473

Asp Ile Gln Met Thr Gln Ser Pro Ser Thr Ser Thr Ser Gly Arg Ser
1 5 10 15

Ala Asn Pro Arg Gly Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr
20 25 30

Ile Thr Cys Arg Ala Ser Gln Asp Ile Ser Ser Tyr Leu Asn Trp Tyr
35 40 45

Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Tyr Thr Ser
50 55 60

Arg Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly
65 70 75 80

Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Gln Pro Glu Asp Ile Ala
85 90 95

Thr Tyr Tyr Cys Gln Gln Gly Asn Thr Leu Pro Tyr Thr Phe Gly Gln
100 105 110

Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala Pro Ser Val Phe

115 120 125

Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr Ala Ser Val
130 135 140

Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp
145 150 155 160

Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser Val Thr
165 170 175

Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr
180 185 190

Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala Cys Glu Val
195 200 205

Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe Asn Arg Gly
210 215 220

Glu Cys
225

<210> 474
<211> 226
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 474

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Thr Ser Thr Ser Gly Arg
1 5 10 15

Ser Ala Asn Pro Arg Gly Leu Ser Ala Ser Val Gly Asp Arg Val Thr
20 25 30

Ile Thr Cys Arg Ala Ser Gln Asp Ile Ser Ser Tyr Leu Asn Trp Tyr
35 40 45

Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Tyr Thr Ser
50 55 60

Arg Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly
65 70 75 80

Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Gln Pro Glu Asp Ile Ala
85 90 95

Thr Tyr Tyr Cys Gln Gln Gly Asn Thr Leu Pro Tyr Thr Phe Gly Gln
100 105 110

Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala Pro Ser Val Phe
115 120 125

Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr Ala Ser Val
130 135 140

Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp
145 150 155 160

Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser Val Thr
165 170 175

Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr
180 185 190

Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala Cys Glu Val
195 200 205

Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe Asn Arg Gly
210 215 220

Glu Cys
225

<210> 475
<211> 226
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<400> 475

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Thr Ser Thr Ser Gly
1 5 10 15

Arg Ser Ala Asn Pro Arg Gly Ser Ala Ser Val Gly Asp Arg Val Thr
20 25 30

Ile Thr Cys Arg Ala Ser Gln Asp Ile Ser Ser Tyr Leu Asn Trp Tyr
35 40 45

Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Tyr Thr Ser
50 55 60

Arg Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly
65 70 75 80

Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Gln Pro Glu Asp Ile Ala

85 90 95

Thr Tyr Tyr Cys Gln Gln Gly Asn Thr Leu Pro Tyr Thr Phe Gly Gln
100 105 110

Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala Pro Ser Val Phe
115 120 125

Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr Ala Ser Val
130 135 140

Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp
145 150 155 160

Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser Val Thr
165 170 175

Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr
180 185 190

Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala Cys Glu Val
195 200 205

Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe Asn Arg Gly
210 215 220

Glu Cys
225

<210> 476
<211> 226
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<213> 人造序列

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<400> 476

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Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Thr Ser Thr Ser
1               5                  10                  15

Gly Arg Ser Ala Asn Pro Arg Gly Ala Ser Val Gly Asp Arg Val Thr
            20                  25                  30

Ile Thr Cys Arg Ala Ser Gln Asp Ile Ser Ser Tyr Leu Asn Trp Tyr
        35                  40                  45

Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Tyr Thr Ser
    50                  55                  60

Arg Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly
65                  70                  75                  80

Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Gln Pro Glu Asp Ile Ala
                85                  90                  95

Thr Tyr Tyr Cys Gln Gln Gly Asn Thr Leu Pro Tyr Thr Phe Gly Gln
            100                 105                 110

Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala Pro Ser Val Phe
        115                 120                 125

Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr Ala Ser Val
    130                 135                 140

Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp
145                 150                 155                 160
```

Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser Val Thr
165 170 175

Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr
180 185 190

Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala Cys Glu Val
195 200 205

Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe Asn Arg Gly
210 215 220

Glu Cys
225

<210> 477
<211> 226
<212> PRT
<213> 人造序列

<220>
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<400> 477

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Thr Ser Thr
1 5 10 15

Ser Gly Arg Ser Ala Asn Pro Arg Gly Ser Val Gly Asp Arg Val Thr
20 25 30

Ile Thr Cys Arg Ala Ser Gln Asp Ile Ser Ser Tyr Leu Asn Trp Tyr
35 40 45

Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Tyr Thr Ser

50 55 60

Arg Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly
65 70 75 80

Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Gln Pro Glu Asp Ile Ala
85 90 95

Thr Tyr Tyr Cys Gln Gln Gly Asn Thr Leu Pro Tyr Thr Phe Gly Gln
100 105 110

Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala Pro Ser Val Phe
115 120 125

Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr Ala Ser Val
130 135 140

Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp
145 150 155 160

Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser Val Thr
165 170 175

Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr
180 185 190

Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala Cys Glu Val
195 200 205

Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe Asn Arg Gly
210 215 220

Glu Cys

225

<210> 478
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<212> PRT
<213> 人造序列

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<400> 478

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Thr Ser
1 5 10 15

Thr Ser Gly Arg Ser Ala Asn Pro Arg Gly Val Gly Asp Arg Val Thr
20 25 30

Ile Thr Cys Arg Ala Ser Gln Asp Ile Ser Ser Tyr Leu Asn Trp Tyr
35 40 45

Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Tyr Thr Ser
50 55 60

Arg Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly
65 70 75 80

Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Gln Pro Glu Asp Ile Ala
85 90 95

Thr Tyr Tyr Cys Gln Gln Gly Asn Thr Leu Pro Tyr Thr Phe Gly Gln
100 105 110

Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala Pro Ser Val Phe
115 120 125

```
Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr Ala Ser Val
    130                 135                 140

Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp
145                 150                 155                 160

Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser Val Thr
                165                 170                 175

Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr
            180                 185                 190

Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala Cys Glu Val
        195                 200                 205

Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe Asn Arg Gly
    210                 215                 220

Glu Cys
225
```

<210> 479
<211> 226
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<213> 人造序列

<220>
<223> 人造的合成序列

<400> 479

```
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Thr
1               5                   10                  15

Ser Thr Ser Gly Arg Ser Ala Asn Pro Arg Gly Gly Asp Arg Val Thr
```

20 25 30

Ile Thr Cys Arg Ala Ser Gln Asp Ile Ser Ser Tyr Leu Asn Trp Tyr
35 40 45

Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Tyr Thr Ser
50 55 60

Arg Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly
65 70 75 80

Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Gln Pro Glu Asp Ile Ala
85 90 95

Thr Tyr Tyr Cys Gln Gln Gly Asn Thr Leu Pro Tyr Thr Phe Gly Gln
100 105 110

Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala Pro Ser Val Phe
115 120 125

Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr Ala Ser Val
130 135 140

Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp
145 150 155 160

Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser Val Thr
165 170 175

Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr
180 185 190

Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala Cys Glu Val

195 200 205

Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe Asn Arg Gly
210 215 220

Glu Cys
225

<210> 480
<211> 226
<212> PRT
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<220>
<223> 人造的合成序列

<400> 480

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Thr Ser Thr Ser Gly Arg Ser Ala Asn Pro Arg Gly Asp Arg Val Thr
20 25 30

Ile Thr Cys Arg Ala Ser Gln Asp Ile Ser Ser Tyr Leu Asn Trp Tyr
35 40 45

Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Tyr Thr Ser
50 55 60

Arg Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly
65 70 75 80

Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Gln Pro Glu Asp Ile Ala
85 90 95

Thr Tyr Tyr Cys Gln Gln Gly Asn Thr Leu Pro Tyr Thr Phe Gly Gln
100 105 110

Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala Pro Ser Val Phe
115 120 125

Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr Ala Ser Val
130 135 140

Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp
145 150 155 160

Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser Val Thr
165 170 175

Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr
180 185 190

Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala Cys Glu Val
195 200 205

Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe Asn Arg Gly
210 215 220

Glu Cys
225

<210> 481
<211> 226
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 481

```
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1               5                  10                  15

Asp Thr Ser Thr Ser Gly Arg Ser Ala Asn Pro Arg Gly Arg Val Thr
            20                  25                  30

Ile Thr Cys Arg Ala Ser Gln Asp Ile Ser Ser Tyr Leu Asn Trp Tyr
        35                  40                  45

Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Tyr Thr Ser
    50                  55                  60

Arg Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly
65                  70                  75                  80

Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Gln Pro Glu Asp Ile Ala
                85                  90                  95

Thr Tyr Tyr Cys Gln Gln Gly Asn Thr Leu Pro Tyr Thr Phe Gly Gln
            100                 105                 110

Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala Pro Ser Val Phe
        115                 120                 125

Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr Ala Ser Val
    130                 135                 140

Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp
145                 150                 155                 160

Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser Val Thr
```

165 170 175

Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr
180 185 190

Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala Cys Glu Val
195 200 205

Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe Asn Arg Gly
210 215 220

Glu Cys
225

<210> 482
<211> 226
<212> PRT
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<220>
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<400> 482

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Thr Ser Thr Ser Gly Arg Ser Ala Asn Pro Arg Gly Val Thr
20 25 30

Ile Thr Cys Arg Ala Ser Gln Asp Ile Ser Ser Tyr Leu Asn Trp Tyr
35 40 45

Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Tyr Thr Ser
50 55 60

```
Arg Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly
65                  70                  75                  80

Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Gln Pro Glu Asp Ile Ala
                85                  90                  95

Thr Tyr Tyr Cys Gln Gln Gly Asn Thr Leu Pro Tyr Thr Phe Gly Gln
            100                 105                 110

Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala Pro Ser Val Phe
        115                 120                 125

Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr Ala Ser Val
    130                 135                 140

Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp
145                 150                 155                 160

Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser Val Thr
                165                 170                 175

Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr
            180                 185                 190

Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala Cys Glu Val
        195                 200                 205

Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe Asn Arg Gly
    210                 215                 220

Glu Cys
225
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<210> 483
<211> 226
<212> PRT
<213> 人造序列

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<400> 483

```
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1               5                  10                  15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asp Ile Ser Ser Tyr
            20                  25                  30

Leu Asn Trp Tyr Gln Gln Lys Thr Ser Thr Ser Gly Arg Ser Ala Asn
        35                  40                  45

Pro Arg Gly Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Tyr Thr Ser
    50                  55                  60

Arg Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly
65                  70                  75                  80

Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Gln Pro Glu Asp Ile Ala
                85                  90                  95

Thr Tyr Tyr Cys Gln Gln Gly Asn Thr Leu Pro Tyr Thr Phe Gly Gln
            100                 105                 110

Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala Pro Ser Val Phe
        115                 120                 125

Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr Ala Ser Val
```

130 135 140

Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp
145 150 155 160

Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser Val Thr
165 170 175

Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr
180 185 190

Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala Cys Glu Val
195 200 205

Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe Asn Arg Gly
210 215 220

Glu Cys
225

<210> 484
<211> 226
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 484

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asp Ile Ser Ser Tyr
20 25 30

```
Leu Asn Trp Tyr Gln Gln Lys Pro Thr Ser Thr Ser Gly Arg Ser Ala
        35                  40                  45

Asn Pro Arg Gly Gly Lys Ala Pro Lys Leu Leu Ile Tyr Tyr Thr Ser
    50                  55                  60

Arg Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly
65                  70                  75                  80

Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Gln Pro Glu Asp Ile Ala
                85                  90                  95

Thr Tyr Tyr Cys Gln Gln Gly Asn Thr Leu Pro Tyr Thr Phe Gly Gln
            100                 105                 110

Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala Pro Ser Val Phe
        115                 120                 125

Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr Ala Ser Val
    130                 135                 140

Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp
145                 150                 155                 160

Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser Val Thr
                165                 170                 175

Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr
            180                 185                 190

Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala Cys Glu Val
        195                 200                 205
```

Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe Asn Arg Gly
210 215 220

Glu Cys
225

<210> 485
<211> 226
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 485

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asp Ile Ser Ser Tyr
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Thr Ser Thr Ser Gly Arg Ser
35 40 45

Ala Asn Pro Arg Gly Lys Ala Pro Lys Leu Leu Ile Tyr Tyr Thr Ser
50 55 60

Arg Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly
65 70 75 80

Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Gln Pro Glu Asp Ile Ala
85 90 95

Thr Tyr Tyr Cys Gln Gln Gly Asn Thr Leu Pro Tyr Thr Phe Gly Gln

100 105 110

Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala Pro Ser Val Phe
115 120 125

Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr Ala Ser Val
130 135 140

Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp
145 150 155 160

Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser Val Thr
165 170 175

Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr
180 185 190

Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala Cys Glu Val
195 200 205

Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe Asn Arg Gly
210 215 220

Glu Cys
225

<210> 486
<211> 226
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 486

```
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1               5                  10                  15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asp Ile Ser Ser Tyr
            20                  25                  30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Thr Ser Thr Ser Gly Arg
        35                  40                  45

Ser Ala Asn Pro Arg Gly Ala Pro Lys Leu Leu Ile Tyr Tyr Thr Ser
    50                  55                  60

Arg Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly
65                  70                  75                  80

Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Gln Pro Glu Asp Ile Ala
                85                  90                  95

Thr Tyr Tyr Cys Gln Gln Gly Asn Thr Leu Pro Tyr Thr Phe Gly Gln
            100                 105                 110

Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala Pro Ser Val Phe
        115                 120                 125

Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr Ala Ser Val
    130                 135                 140

Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp
145                 150                 155                 160

Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser Val Thr
                165                 170                 175
```

Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr
180 185 190

Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala Cys Glu Val
195 200 205

Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe Asn Arg Gly
210 215 220

Glu Cys
225

<210> 487
<211> 226
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 487

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asp Ile Ser Ser Tyr
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Thr Ser Thr Ser Gly
35 40 45

Arg Ser Ala Asn Pro Arg Gly Pro Lys Leu Leu Ile Tyr Tyr Thr Ser
50 55 60

Arg Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly

65 70 75 80

Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Gln Pro Glu Asp Ile Ala
85 90 95

Thr Tyr Tyr Cys Gln Gln Gly Asn Thr Leu Pro Tyr Thr Phe Gly Gln
100 105 110

Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala Pro Ser Val Phe
115 120 125

Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr Ala Ser Val
130 135 140

Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp
145 150 155 160

Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser Val Thr
165 170 175

Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr
180 185 190

Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala Cys Glu Val
195 200 205

Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe Asn Arg Gly
210 215 220

Glu Cys
225

<210> 488

<211> 226
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 488

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asp Ile Ser Ser Tyr
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Thr Ser Thr Ser
35 40 45

Gly Arg Ser Ala Asn Pro Arg Gly Lys Leu Leu Ile Tyr Tyr Thr Ser
50 55 60

Arg Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly
65 70 75 80

Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Gln Pro Glu Asp Ile Ala
85 90 95

Thr Tyr Tyr Cys Gln Gln Gly Asn Thr Leu Pro Tyr Thr Phe Gly Gln
100 105 110

Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala Pro Ser Val Phe
115 120 125

Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr Ala Ser Val
130 135 140

Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp
145 150 155 160

Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser Val Thr
165 170 175

Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr
180 185 190

Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala Cys Glu Val
195 200 205

Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe Asn Arg Gly
210 215 220

Glu Cys
225

<210> 489
<211> 226
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 489

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asp Ile Ser Ser Tyr
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Thr Ser Thr

35 40 45

Ser Gly Arg Ser Ala Asn Pro Arg Gly Leu Leu Ile Tyr Tyr Thr Ser
50 55 60

Arg Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly
65 70 75 80

Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Gln Pro Glu Asp Ile Ala
85 90 95

Thr Tyr Tyr Cys Gln Gln Gly Asn Thr Leu Pro Tyr Thr Phe Gly Gln
100 105 110

Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala Pro Ser Val Phe
115 120 125

Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr Ala Ser Val
130 135 140

Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp
145 150 155 160

Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser Val Thr
165 170 175

Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr
180 185 190

Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala Cys Glu Val
195 200 205

Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe Asn Arg Gly

210 215 220

Glu Cys
225

<210> 490
<211> 226
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 490

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asp Ile Ser Ser Tyr
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Thr Ser Thr Ser Gly Arg Ser Ala Asn Pro Arg Gly Tyr Thr Ser
50 55 60

Arg Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly
65 70 75 80

Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Gln Pro Glu Asp Ile Ala
85 90 95

Thr Tyr Tyr Cys Gln Gln Gly Asn Thr Leu Pro Tyr Thr Phe Gly Gln
100 105 110

Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala Pro Ser Val Phe
115 120 125

Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr Ala Ser Val
130 135 140

Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp
145 150 155 160

Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser Val Thr
165 170 175

Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr
180 185 190

Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala Cys Glu Val
195 200 205

Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe Asn Arg Gly
210 215 220

Glu Cys
225

<210> 491
<211> 226
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 491

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly

1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asp Ile Ser Ser Tyr
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Tyr Thr Ser Thr Ser Gly Arg Ser Ala Asn Pro Arg Gly Thr Ser
50 55 60

Arg Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly
65 70 75 80

Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Gln Pro Glu Asp Ile Ala
85 90 95

Thr Tyr Tyr Cys Gln Gln Gly Asn Thr Leu Pro Tyr Thr Phe Gly Gln
100 105 110

Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala Pro Ser Val Phe
115 120 125

Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr Ala Ser Val
130 135 140

Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp
145 150 155 160

Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser Val Thr
165 170 175

Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr

180 185 190

Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala Cys Glu Val
195 200 205

Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe Asn Arg Gly
210 215 220

Glu Cys
225

<210> 492
<211> 226
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 492

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asp Ile Ser Ser Tyr
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Tyr Thr Thr Ser Thr Ser Gly Arg Ser Ala Asn Pro Arg Gly Ser
50 55 60

Arg Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly
65 70 75 80

```
Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Gln Pro Glu Asp Ile Ala
                85                  90                  95

Thr Tyr Tyr Cys Gln Gln Gly Asn Thr Leu Pro Tyr Thr Phe Gly Gln
            100                 105                 110

Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala Pro Ser Val Phe
        115                 120                 125

Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr Ala Ser Val
    130                 135                 140

Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp
145                 150                 155                 160

Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser Val Thr
                165                 170                 175

Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr
            180                 185                 190

Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala Cys Glu Val
        195                 200                 205

Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe Asn Arg Gly
    210                 215                 220

Glu Cys
225
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<400> 493

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asp Ile Ser Ser Tyr
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Tyr Thr Ser Thr Ser Thr Ser Gly Arg Ser Ala Asn Pro Arg Gly
50 55 60

Arg Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly
65 70 75 80

Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Gln Pro Glu Asp Ile Ala
85 90 95

Thr Tyr Tyr Cys Gln Gln Gly Asn Thr Leu Pro Tyr Thr Phe Gly Gln
100 105 110

Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala Pro Ser Val Phe
115 120 125

Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr Ala Ser Val
130 135 140

Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp

145 150 155 160

Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser Val Thr
165 170 175

Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr
180 185 190

Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala Cys Glu Val
195 200 205

Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe Asn Arg Gly
210 215 220

Glu Cys
225

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<400> 494

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asp Ile Ser Ser Tyr
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Tyr Thr Ser Arg Thr Ser Thr Ser Gly Arg Ser Ala Asn Pro Arg
50 55 60

Gly Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly
65 70 75 80

Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Gln Pro Glu Asp Ile Ala
85 90 95

Thr Tyr Tyr Cys Gln Gln Gly Asn Thr Leu Pro Tyr Thr Phe Gly Gln
100 105 110

Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala Pro Ser Val Phe
115 120 125

Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr Ala Ser Val
130 135 140

Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp
145 150 155 160

Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser Val Thr
165 170 175

Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr
180 185 190

Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala Cys Glu Val
195 200 205

Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe Asn Arg Gly
210 215 220

Glu Cys
225

<210> 495
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Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asp Ile Ser Ser Tyr
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Tyr Thr Ser Arg Leu Thr Ser Thr Ser Gly Arg Ser Ala Asn Pro
50 55 60

Arg Gly His Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly
65 70 75 80

Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Gln Pro Glu Asp Ile Ala
85 90 95

Thr Tyr Tyr Cys Gln Gln Gly Asn Thr Leu Pro Tyr Thr Phe Gly Gln
100 105 110

Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala Pro Ser Val Phe

115 120 125

Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr Ala Ser Val
130 135 140

Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp
145 150 155 160

Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser Val Thr
165 170 175

Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr
180 185 190

Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala Cys Glu Val
195 200 205

Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe Asn Arg Gly
210 215 220

Glu Cys
225

<210> 496
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Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

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Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asp Ile Ser Ser Tyr
            20                  25                  30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35                  40                  45

Tyr Tyr Thr Ser Arg Leu His Thr Ser Thr Ser Gly Arg Ser Ala Asn
    50                  55                  60

Pro Arg Gly Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly
65                  70                  75                  80

Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Gln Pro Glu Asp Ile Ala
                85                  90                  95

Thr Tyr Tyr Cys Gln Gln Gly Asn Thr Leu Pro Tyr Thr Phe Gly Gln
            100                 105                 110

Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala Pro Ser Val Phe
        115                 120                 125

Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr Ala Ser Val
    130                 135                 140

Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp
145                 150                 155                 160

Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser Val Thr
                165                 170                 175

Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr
            180                 185                 190
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Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala Cys Glu Val
195 200 205

Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe Asn Arg Gly
210 215 220

Glu Cys
225

<210> 497
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<400> 497

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asp Ile Ser Ser Tyr
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Tyr Thr Ser Arg Leu His Ser Thr Ser Thr Ser Gly Arg Ser Ala
50 55 60

Asn Pro Arg Gly Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly
65 70 75 80

Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Gln Pro Glu Asp Ile Ala

85 90 95

Thr Tyr Tyr Cys Gln Gln Gly Asn Thr Leu Pro Tyr Thr Phe Gly Gln
100 105 110

Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala Pro Ser Val Phe
115 120 125

Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr Ala Ser Val
130 135 140

Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp
145 150 155 160

Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser Val Thr
165 170 175

Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr
180 185 190

Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala Cys Glu Val
195 200 205

Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe Asn Arg Gly
210 215 220

Glu Cys
225

<210> 498
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<400> 498

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Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1               5                  10                  15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asp Ile Ser Ser Tyr
            20                  25                  30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35                  40                  45

Tyr Tyr Thr Ser Arg Leu His Ser Gly Thr Ser Thr Ser Gly Arg Ser
    50                  55                  60

Ala Asn Pro Arg Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly
65                  70                  75                  80

Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Gln Pro Glu Asp Ile Ala
                85                  90                  95

Thr Tyr Tyr Cys Gln Gln Gly Asn Thr Leu Pro Tyr Thr Phe Gly Gln
            100                 105                 110

Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala Pro Ser Val Phe
        115                 120                 125

Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr Ala Ser Val
    130                 135                 140

Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp
145                 150                 155                 160
```

Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser Val Thr
165 170 175

Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr
180 185 190

Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala Cys Glu Val
195 200 205

Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe Asn Arg Gly
210 215 220

Glu Cys
225

<210> 499
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<220>
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<400> 499

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asp Ile Ser Ser Tyr
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Tyr Thr Ser Arg Leu His Ser Gly Val Thr Ser Thr Ser Gly Arg

50 55 60

Ser Ala Asn Pro Arg Gly Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly
65 70 75 80

Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Gln Pro Glu Asp Ile Ala
85 90 95

Thr Tyr Tyr Cys Gln Gln Gly Asn Thr Leu Pro Tyr Thr Phe Gly Gln
100 105 110

Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala Pro Ser Val Phe
115 120 125

Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr Ala Ser Val
130 135 140

Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp
145 150 155 160

Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser Val Thr
165 170 175

Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr
180 185 190

Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala Cys Glu Val
195 200 205

Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe Asn Arg Gly
210 215 220

Glu Cys

225

<210> 500
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<220>
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<400> 500

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asp Ile Ser Ser Tyr
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Tyr Thr Ser Arg Leu His Ser Gly Val Pro Thr Ser Thr Ser Gly
50 55 60

Arg Ser Ala Asn Pro Arg Gly Ser Arg Phe Ser Gly Ser Gly Ser Gly
65 70 75 80

Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Gln Pro Glu Asp Ile Ala
85 90 95

Thr Tyr Tyr Cys Gln Gln Gly Asn Thr Leu Pro Tyr Thr Phe Gly Gln
100 105 110

Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala Pro Ser Val Phe
115 120 125

Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr Ala Ser Val
130 135 140

Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp
145 150 155 160

Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser Val Thr
165 170 175

Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr
180 185 190

Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala Cys Glu Val
195 200 205

Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe Asn Arg Gly
210 215 220

Glu Cys
225

<210> 501
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<400> 501

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asp Ile Ser Ser Tyr

20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Tyr Thr Ser Arg Leu His Ser Gly Val Pro Ser Thr Ser Thr Ser
50 55 60

Gly Arg Ser Ala Asn Pro Arg Gly Arg Phe Ser Gly Ser Gly Ser Gly
65 70 75 80

Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Gln Pro Glu Asp Ile Ala
85 90 95

Thr Tyr Tyr Cys Gln Gln Gly Asn Thr Leu Pro Tyr Thr Phe Gly Gln
100 105 110

Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala Pro Ser Val Phe
115 120 125

Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr Ala Ser Val
130 135 140

Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp
145 150 155 160

Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser Val Thr
165 170 175

Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr
180 185 190

Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala Cys Glu Val

195 200 205

Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe Asn Arg Gly
210 215 220

Glu Cys
225

<210> 502
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<212> PRT
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<220>
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<400> 502

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asp Ile Ser Ser Tyr
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Tyr Thr Ser Arg Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Ile Ala Thr Tyr Tyr Cys Gln Gln Gly Asn Thr Leu Pro Tyr
85 90 95

Thr Ser Thr Ser Gly Arg Ser Ala Asn Pro Arg Gly Thr Phe Gly Gln
100 105 110

Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala Pro Ser Val Phe
115 120 125

Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr Ala Ser Val
130 135 140

Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp
145 150 155 160

Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser Val Thr
165 170 175

Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr
180 185 190

Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala Cys Glu Val
195 200 205

Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe Asn Arg Gly
210 215 220

Glu Cys
225

<210> 503
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<212> PRT
<213> 人造序列

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<400> 503

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Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1               5                  10                  15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asp Ile Ser Ser Tyr
            20                  25                  30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35                  40                  45

Tyr Tyr Thr Ser Arg Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60

Ser Gly Ser Gly Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80

Glu Asp Ile Ala Thr Tyr Tyr Cys Gln Gln Gly Asn Thr Leu Pro Tyr
                85                  90                  95

Thr Thr Ser Thr Ser Gly Arg Ser Ala Asn Pro Arg Gly Phe Gly Gln
            100                 105                 110

Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala Pro Ser Val Phe
        115                 120                 125

Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr Ala Ser Val
    130                 135                 140

Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp
145                 150                 155                 160

Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser Val Thr
```

165 170 175

Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr
180 185 190

Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala Cys Glu Val
195 200 205

Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe Asn Arg Gly
210 215 220

Glu Cys
225

<210> 504
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<213> 人造序列

<220>
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<400> 504

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asp Ile Ser Ser Tyr
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Tyr Thr Ser Arg Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Ile Ala Thr Tyr Tyr Cys Gln Gln Gly Asn Thr Leu Pro Tyr
85 90 95

Thr Phe Thr Ser Thr Ser Gly Arg Ser Ala Asn Pro Arg Gly Gly Gln
100 105 110

Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala Pro Ser Val Phe
115 120 125

Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr Ala Ser Val
130 135 140

Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp
145 150 155 160

Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser Val Thr
165 170 175

Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr
180 185 190

Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala Cys Glu Val
195 200 205

Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe Asn Arg Gly
210 215 220

Glu Cys
225

<210> 505
<211> 226
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<220>
<223> 人造的合成序列

<400> 505

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asp Ile Ser Ser Tyr
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Tyr Thr Ser Arg Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Ile Ala Thr Tyr Tyr Cys Gln Gln Gly Asn Thr Leu Pro Tyr
85 90 95

Thr Phe Gly Thr Ser Thr Ser Gly Arg Ser Ala Asn Pro Arg Gly Gln
100 105 110

Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala Pro Ser Val Phe
115 120 125

Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr Ala Ser Val

130 135 140

Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp
145 150 155 160

Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser Val Thr
165 170 175

Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr
180 185 190

Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala Cys Glu Val
195 200 205

Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe Asn Arg Gly
210 215 220

Glu Cys
225

<210> 506
<211> 226
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 506

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asp Ile Ser Ser Tyr
20 25 30

```
Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35                  40                  45

Tyr Tyr Thr Ser Arg Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60

Ser Gly Ser Gly Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80

Glu Asp Ile Ala Thr Tyr Tyr Cys Gln Gln Gly Asn Thr Leu Pro Tyr
                85                  90                  95

Thr Phe Gly Gln Thr Ser Thr Ser Gly Arg Ser Ala Asn Pro Arg Gly
            100                 105                 110

Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala Pro Ser Val Phe
        115                 120                 125

Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr Ala Ser Val
    130                 135                 140

Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp
145                 150                 155                 160

Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser Val Thr
                165                 170                 175

Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr
            180                 185                 190

Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala Cys Glu Val
        195                 200                 205
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Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe Asn Arg Gly
210 215 220

Glu Cys
225

<210> 507
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<220>
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<400> 507

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asp Ile Ser Ser Tyr
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Tyr Thr Ser Arg Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Ile Ala Thr Tyr Tyr Cys Gln Gln Gly Asn Thr Leu Pro Tyr
85 90 95

Thr Phe Gly Gln Gly Thr Ser Thr Ser Gly Arg Ser Ala Asn Pro Arg

100 105 110

Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala Pro Ser Val Phe
115 120 125

Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr Ala Ser Val
130 135 140

Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp
145 150 155 160

Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser Val Thr
165 170 175

Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr
180 185 190

Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala Cys Glu Val
195 200 205

Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe Asn Arg Gly
210 215 220

Glu Cys
225

<210> 508
<211> 226
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 508

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Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1               5                  10                  15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asp Ile Ser Ser Tyr
            20                  25                  30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35                  40                  45

Tyr Tyr Thr Ser Arg Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60

Ser Gly Ser Gly Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80

Glu Asp Ile Ala Thr Tyr Tyr Cys Gln Gln Gly Asn Thr Leu Pro Tyr
                85                  90                  95

Thr Phe Gly Gln Gly Thr Thr Ser Thr Ser Gly Arg Ser Ala Asn Pro
            100                 105                 110

Arg Gly Lys Val Glu Ile Lys Arg Thr Val Ala Ala Pro Ser Val Phe
        115                 120                 125

Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr Ala Ser Val
    130                 135                 140

Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp
145                 150                 155                 160

Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser Val Thr
                165                 170                 175
```

Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr
180 185 190

Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala Cys Glu Val
195 200 205

Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe Asn Arg Gly
210 215 220

Glu Cys
225

<210> 509
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<212> PRT
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<220>
<223> 人造的合成序列

<400> 509

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asp Ile Ser Ser Tyr
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Tyr Thr Ser Arg Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Gln Pro

65 70 75 80

Glu Asp Ile Ala Thr Tyr Tyr Cys Gln Gln Gly Asn Thr Leu Pro Tyr
85 90 95

Thr Phe Gly Gln Gly Thr Lys Thr Ser Thr Ser Gly Arg Ser Ala Asn
100 105 110

Pro Arg Gly Val Glu Ile Lys Arg Thr Val Ala Ala Pro Ser Val Phe
115 120 125

Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr Ala Ser Val
130 135 140

Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp
145 150 155 160

Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser Val Thr
165 170 175

Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr
180 185 190

Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala Cys Glu Val
195 200 205

Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe Asn Arg Gly
210 215 220

Glu Cys
225

<210> 510

<211> 226
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 510

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Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1               5                  10                  15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asp Ile Ser Ser Tyr
            20                  25                  30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35                  40                  45

Tyr Tyr Thr Ser Arg Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60

Ser Gly Ser Gly Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80

Glu Asp Ile Ala Thr Tyr Tyr Cys Gln Gln Gly Asn Thr Leu Pro Tyr
                85                  90                  95

Thr Phe Gly Gln Gly Thr Lys Val Thr Ser Thr Ser Gly Arg Ser Ala
            100                 105                 110

Asn Pro Arg Gly Glu Ile Lys Arg Thr Val Ala Ala Pro Ser Val Phe
        115                 120                 125

Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr Ala Ser Val
    130                 135                 140
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Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp
145 150 155 160

Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser Val Thr
165 170 175

Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr
180 185 190

Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala Cys Glu Val
195 200 205

Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe Asn Arg Gly
210 215 220

Glu Cys
225

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Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asp Ile Ser Ser Tyr
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile

35 40 45

Tyr Tyr Thr Ser Arg Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Ile Ala Thr Tyr Tyr Cys Gln Gln Gly Asn Thr Leu Pro Tyr
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Thr Ser Thr Ser Gly Arg Ser
100 105 110

Ala Asn Pro Arg Gly Ile Lys Arg Thr Val Ala Ala Pro Ser Val Phe
115 120 125

Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr Ala Ser Val
130 135 140

Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp
145 150 155 160

Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser Val Thr
165 170 175

Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr
180 185 190

Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala Cys Glu Val
195 200 205

Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe Asn Arg Gly

210 215 220

Glu Cys
225

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Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asp Ile Ser Ser Tyr
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Tyr Thr Ser Arg Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Ile Ala Thr Tyr Tyr Cys Gln Gln Gly Asn Thr Leu Pro Tyr
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Thr Ser Thr Ser Gly Arg
100 105 110

Ser Ala Asn Pro Arg Gly Lys Arg Thr Val Ala Ala Pro Ser Val Phe
115 120 125

Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr Ala Ser Val
130 135 140

Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp
145 150 155 160

Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser Val Thr
165 170 175

Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr
180 185 190

Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala Cys Glu Val
195 200 205

Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe Asn Arg Gly
210 215 220

Glu Cys
225

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Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly

1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asp Ile Ser Ser Tyr
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Tyr Thr Ser Arg Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Ile Ala Thr Tyr Tyr Cys Gln Gln Gly Asn Thr Leu Pro Tyr
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Thr Ser Thr Ser Gly
100 105 110

Arg Ser Ala Asn Pro Arg Gly Arg Thr Val Ala Ala Pro Ser Val Phe
115 120 125

Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr Ala Ser Val
130 135 140

Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp
145 150 155 160

Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser Val Thr
165 170 175

Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr

180 185 190

Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala Cys Glu Val
195 200 205

Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe Asn Arg Gly
210 215 220

Glu Cys
225

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Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asp Ile Ser Ser Tyr
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Tyr Thr Ser Arg Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Ile Ala Thr Tyr Tyr Cys Gln Gln Gly Asn Thr Leu Pro Tyr
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg Thr Ser Thr Ser
100 105 110

Gly Arg Ser Ala Asn Pro Arg Gly Thr Val Ala Ala Pro Ser Val Phe
115 120 125

Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr Ala Ser Val
130 135 140

Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp
145 150 155 160

Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser Val Thr
165 170 175

Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr
180 185 190

Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala Cys Glu Val
195 200 205

Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe Asn Arg Gly
210 215 220

Glu Cys
225

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Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1               5                  10                  15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asp Ile Ser Ser Tyr
            20                  25                  30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35                  40                  45

Tyr Tyr Thr Ser Arg Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60

Ser Gly Ser Gly Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80

Glu Asp Ile Ala Thr Tyr Tyr Cys Gln Gln Gly Asn Thr Leu Pro Tyr
                85                  90                  95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg Thr Thr Ser Thr
            100                 105                 110

Ser Gly Arg Ser Ala Asn Pro Arg Gly Val Ala Ala Pro Ser Val Phe
        115                 120                 125

Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr Ala Ser Val
    130                 135                 140

Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp
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145 150 155 160

Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser Val Thr
165 170 175

Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr
180 185 190

Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala Cys Glu Val
195 200 205

Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe Asn Arg Gly
210 215 220

Glu Cys
225

<210> 516
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Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asp Ile Ser Ser Tyr
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

```
Tyr Tyr Thr Ser Arg Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60

Ser Gly Ser Gly Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80

Glu Asp Ile Ala Thr Tyr Tyr Cys Gln Gln Gly Asn Thr Leu Pro Tyr
                85                  90                  95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg Thr Val Thr Ser
            100                 105                 110

Thr Ser Gly Arg Ser Ala Asn Pro Arg Gly Ala Ala Pro Ser Val Phe
        115                 120                 125

Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr Ala Ser Val
    130                 135                 140

Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp
145                 150                 155                 160

Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser Val Thr
                165                 170                 175

Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr
            180                 185                 190

Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala Cys Glu Val
        195                 200                 205

Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe Asn Arg Gly
    210                 215                 220
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Glu Cys
225

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Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asp Ile Ser Ser Tyr
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Tyr Thr Ser Arg Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Ile Ala Thr Tyr Tyr Cys Gln Gln Gly Asn Thr Leu Pro Tyr
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Thr
100 105 110

Ser Thr Ser Gly Arg Ser Ala Asn Pro Arg Gly Ala Pro Ser Val Phe

115 120 125

Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr Ala Ser Val
130 135 140

Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp
145 150 155 160

Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser Val Thr
165 170 175

Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr
180 185 190

Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala Cys Glu Val
195 200 205

Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe Asn Arg Gly
210 215 220

Glu Cys
225

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Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asp Ile Ser Ser Tyr
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Tyr Thr Ser Arg Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Ile Ala Thr Tyr Tyr Cys Gln Gln Gly Asn Thr Leu Pro Tyr
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala
100 105 110

Thr Ser Thr Ser Gly Arg Ser Ala Asn Pro Arg Gly Pro Ser Val Phe
115 120 125

Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr Ala Ser Val
130 135 140

Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp
145 150 155 160

Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser Val Thr
165 170 175

Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr
180 185 190

Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala Cys Glu Val
195 200 205

Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe Asn Arg Gly
210 215 220

Glu Cys
225

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Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asp Ile Ser Ser Tyr
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Tyr Thr Ser Arg Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Ile Ala Thr Tyr Tyr Cys Gln Gln Gly Asn Thr Leu Pro Tyr

85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala
100 105 110

Pro Thr Ser Thr Ser Gly Arg Ser Ala Asn Pro Arg Gly Ser Val Phe
115 120 125

Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr Ala Ser Val
130 135 140

Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp
145 150 155 160

Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser Val Thr
165 170 175

Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr
180 185 190

Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala Cys Glu Val
195 200 205

Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe Asn Arg Gly
210 215 220

Glu Cys
225

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Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1               5                  10                  15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asp Ile Ser Ser Tyr
            20                  25                  30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35                  40                  45

Tyr Tyr Thr Ser Arg Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60

Ser Gly Ser Gly Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80

Glu Asp Ile Ala Thr Tyr Tyr Cys Gln Gln Gly Asn Thr Leu Pro Tyr
                85                  90                  95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala
            100                 105                 110

Pro Ser Val Thr Ser Thr Ser Gly Arg Ser Ala Asn Pro Arg Gly Phe
        115                 120                 125

Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr Ala Ser Val
    130                 135                 140

Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp
145                 150                 155                 160
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Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser Val Thr
165 170 175

Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr
180 185 190

Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala Cys Glu Val
195 200 205

Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe Asn Arg Gly
210 215 220

Glu Cys
225

<210> 521
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Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asp Ile Ser Ser Tyr
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Tyr Thr Ser Arg Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly

50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Ile Ala Thr Tyr Tyr Cys Gln Gln Gly Asn Thr Leu Pro Tyr
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala
100 105 110

Pro Ser Val Phe Thr Ser Thr Ser Gly Arg Ser Ala Asn Pro Arg Gly
115 120 125

Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr Ala Ser Val
130 135 140

Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp
145 150 155 160

Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser Val Thr
165 170 175

Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr
180 185 190

Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala Cys Glu Val
195 200 205

Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe Asn Arg Gly
210 215 220

Glu Cys

225

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Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asp Ile Ser Ser Tyr
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Tyr Thr Ser Arg Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Ile Ala Thr Tyr Tyr Cys Gln Gln Gly Asn Thr Leu Pro Tyr
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala
100 105 110

Pro Ser Val Phe Ile Thr Ser Thr Ser Gly Arg Ser Ala Asn Pro Arg
115 120 125

Gly Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr Ala Ser Val
130 135 140

Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp
145 150 155 160

Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser Val Thr
165 170 175

Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr
180 185 190

Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala Cys Glu Val
195 200 205

Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe Asn Arg Gly
210 215 220

Glu Cys
225

<210> 523
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Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asp Ile Ser Ser Tyr

20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Tyr Thr Ser Arg Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Ile Ala Thr Tyr Tyr Cys Gln Gln Gly Asn Thr Leu Pro Tyr
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala
100 105 110

Pro Ser Val Phe Ile Phe Thr Ser Thr Ser Gly Arg Ser Ala Asn Pro
115 120 125

Arg Gly Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr Ala Ser Val
130 135 140

Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp
145 150 155 160

Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser Val Thr
165 170 175

Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr
180 185 190

Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala Cys Glu Val

195 200 205

Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe Asn Arg Gly
210 215 220

Glu Cys
225

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<400> 524

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asp Ile Ser Ser Tyr
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Tyr Thr Ser Arg Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Ile Ala Thr Tyr Tyr Cys Gln Gln Gly Asn Thr Leu Pro Tyr
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala
100 105 110

Pro Ser Val Phe Ile Phe Pro Thr Ser Thr Ser Gly Arg Ser Ala Asn
115 120 125

Pro Arg Gly Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr Ala Ser Val
130 135 140

Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp
145 150 155 160

Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser Val Thr
165 170 175

Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr
180 185 190

Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala Cys Glu Val
195 200 205

Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe Asn Arg Gly
210 215 220

Glu Cys
225

<210> 525
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<400> 525

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asp Ile Ser Ser Tyr
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Tyr Thr Ser Arg Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Ile Ala Thr Tyr Tyr Cys Gln Gln Gly Asn Thr Leu Pro Tyr
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala
100 105 110

Pro Ser Val Phe Ile Phe Pro Pro Thr Ser Thr Ser Gly Arg Ser Ala
115 120 125

Asn Pro Arg Gly Ser Asp Glu Gln Leu Lys Ser Gly Thr Ala Ser Val
130 135 140

Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp
145 150 155 160

Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser Val Thr

165 170 175

Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr
180 185 190

Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala Cys Glu Val
195 200 205

Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe Asn Arg Gly
210 215 220

Glu Cys
225

<210> 526
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<400> 526

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asp Ile Ser Ser Tyr
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Tyr Thr Ser Arg Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

```
Ser Gly Ser Gly Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80

Glu Asp Ile Ala Thr Tyr Tyr Cys Gln Gln Gly Asn Thr Leu Pro Tyr
                85                  90                  95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala
            100                 105                 110

Pro Ser Val Phe Ile Phe Pro Pro Ser Thr Ser Thr Ser Gly Arg Ser
        115                 120                 125

Ala Asn Pro Arg Gly Asp Glu Gln Leu Lys Ser Gly Thr Ala Ser Val
    130                 135                 140

Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp
145                 150                 155                 160

Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser Val Thr
                165                 170                 175

Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr
            180                 185                 190

Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala Cys Glu Val
        195                 200                 205

Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe Asn Arg Gly
    210                 215                 220

Glu Cys
225
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<210> 527
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Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1               5                  10                  15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asp Ile Ser Ser Tyr
            20                  25                  30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35                  40                  45

Tyr Tyr Thr Ser Arg Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60

Ser Gly Ser Gly Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80

Glu Asp Ile Ala Thr Tyr Tyr Cys Gln Gln Gly Asn Thr Leu Pro Tyr
                85                  90                  95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala
            100                 105                 110

Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Thr Ser Thr Ser Gly Arg
        115                 120                 125

Ser Ala Asn Pro Arg Gly Glu Gln Leu Lys Ser Gly Thr Ala Ser Val
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130 135 140

Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp
145 150 155 160

Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser Val Thr
165 170 175

Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr
180 185 190

Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala Cys Glu Val
195 200 205

Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe Asn Arg Gly
210 215 220

Glu Cys
225

<210> 528
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<212> PRT
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<220>
<223> 人造的合成序列

<400> 528

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asp Ile Ser Ser Tyr
20 25 30

```
Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35                  40                  45

Tyr Tyr Thr Ser Arg Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60

Ser Gly Ser Gly Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80

Glu Asp Ile Ala Thr Tyr Tyr Cys Gln Gln Gly Asn Thr Leu Pro Tyr
                85                  90                  95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala
            100                 105                 110

Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Thr Ser Thr Ser Gly
        115                 120                 125

Arg Ser Ala Asn Pro Arg Gly Gln Leu Lys Ser Gly Thr Ala Ser Val
    130                 135                 140

Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp
145                 150                 155                 160

Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser Val Thr
                165                 170                 175

Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr
            180                 185                 190

Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala Cys Glu Val
        195                 200                 205
```

Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe Asn Arg Gly
210 215 220

Glu Cys
225

<210> 529
<211> 226
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 529

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asp Ile Ser Ser Tyr
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Tyr Thr Ser Arg Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Ile Ala Thr Tyr Tyr Cys Gln Gln Gly Asn Thr Leu Pro Tyr
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala

100 105 110

Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Thr Ser Thr Ser
115 120 125

Gly Arg Ser Ala Asn Pro Arg Gly Leu Lys Ser Gly Thr Ala Ser Val
130 135 140

Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp
145 150 155 160

Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser Val Thr
165 170 175

Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr
180 185 190

Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala Cys Glu Val
195 200 205

Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe Asn Arg Gly
210 215 220

Glu Cys
225

<210> 530
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<400> 530

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Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1               5                  10                  15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asp Ile Ser Ser Tyr
            20                  25                  30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35                  40                  45

Tyr Tyr Thr Ser Arg Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60

Ser Gly Ser Gly Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80

Glu Asp Ile Ala Thr Tyr Tyr Cys Gln Gln Gly Asn Thr Leu Pro Tyr
                85                  90                  95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala
            100                 105                 110

Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Thr Ser Thr
        115                 120                 125

Ser Gly Arg Ser Ala Asn Pro Arg Gly Lys Ser Gly Thr Ala Ser Val
    130                 135                 140

Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp
145                 150                 155                 160

Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser Val Thr
                165                 170                 175
```

Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr
180 185 190

Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala Cys Glu Val
195 200 205

Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe Asn Arg Gly
210 215 220

Glu Cys
225

<210> 531
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<212> PRT
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<400> 531

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asp Ile Ser Ser Tyr
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Tyr Thr Ser Arg Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Gln Pro

65 70 75 80

Glu Asp Ile Ala Thr Tyr Tyr Cys Gln Gln Gly Asn Thr Leu Pro Tyr
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala
100 105 110

Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Thr Ser
115 120 125

Thr Ser Gly Arg Ser Ala Asn Pro Arg Gly Ser Gly Thr Ala Ser Val
130 135 140

Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp
145 150 155 160

Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser Val Thr
165 170 175

Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr
180 185 190

Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala Cys Glu Val
195 200 205

Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe Asn Arg Gly
210 215 220

Glu Cys
225

<210> 532

<211> 226
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<220>
<223> 人造的合成序列

<400> 532

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Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1               5                  10                  15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asp Ile Ser Ser Tyr
            20                  25                  30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35                  40                  45

Tyr Tyr Thr Ser Arg Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60

Ser Gly Ser Gly Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80

Glu Asp Ile Ala Thr Tyr Tyr Cys Gln Gln Gly Asn Thr Leu Pro Tyr
                85                  90                  95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala
            100                 105                 110

Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Thr
        115                 120                 125

Ser Thr Ser Gly Arg Ser Ala Asn Pro Arg Gly Gly Thr Ala Ser Val
    130                 135                 140
```

Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp
145 150 155 160

Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser Val Thr
165 170 175

Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr
180 185 190

Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala Cys Glu Val
195 200 205

Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe Asn Arg Gly
210 215 220

Glu Cys
225

<210> 533
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Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asp Ile Ser Ser Tyr
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile

35 40 45

Tyr Tyr Thr Ser Arg Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Ile Ala Thr Tyr Tyr Cys Gln Gln Gly Asn Thr Leu Pro Tyr
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala
100 105 110

Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly
115 120 125

Thr Ser Thr Ser Gly Arg Ser Ala Asn Pro Arg Gly Thr Ala Ser Val
130 135 140

Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp
145 150 155 160

Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser Val Thr
165 170 175

Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr
180 185 190

Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala Cys Glu Val
195 200 205

Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe Asn Arg Gly

210 215 220

Glu Cys
225

<210> 534
<211> 226
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 534

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asp Ile Ser Ser Tyr
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Tyr Thr Ser Arg Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Ile Ala Thr Tyr Tyr Cys Gln Gln Gly Asn Thr Leu Pro Tyr
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala
100 105 110

Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly
115 120 125

Thr Thr Ser Thr Ser Gly Arg Ser Ala Asn Pro Arg Gly Ala Ser Val
130 135 140

Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp
145 150 155 160

Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser Val Thr
165 170 175

Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr
180 185 190

Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala Cys Glu Val
195 200 205

Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe Asn Arg Gly
210 215 220

Glu Cys
225

<210> 535
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<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 535

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly

1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asp Ile Ser Ser Tyr
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Tyr Thr Ser Arg Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Ile Ala Thr Tyr Tyr Cys Gln Gln Gly Asn Thr Leu Pro Tyr
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala
100 105 110

Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly
115 120 125

Thr Ala Thr Ser Thr Ser Gly Arg Ser Ala Asn Pro Arg Gly Ser Val
130 135 140

Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp
145 150 155 160

Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser Val Thr
165 170 175

Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr

180 185 190

Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala Cys Glu Val
195 200 205

Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe Asn Arg Gly
210 215 220

Glu Cys
225

<210> 536
<211> 19
<212> PRT
<213> 人造序列

<220>
<223> 人造的合成序列

<400> 536

Met Gly Trp Ser Cys Ile Ile Leu Phe Leu Val Ala Thr Ala Thr Gly
1 5 10 15

Val His Ser

<210> 537
<211> 6
<212> PRT
<213> 智人(Homo sapiens)

<400> 537

Met Tyr Pro Pro Pro Tyr
1 5

【發明申請專利範圍】

【第1項】 一種配體結合分子，係能夠結合於配體之分子，該分子係為具有至少1個切斷位點之多胜肽，且於該分子在至少1個切斷位點被切斷之狀態，與配體之結合減弱，

其中該配體結合分子包括抗體VH、抗體VL、及抗體不變區，

且其中該切斷位點位在該抗體不變區與該抗體VH之交界附近、或/及該抗體不變區與該抗體VL之交界附近。

【第2項】 如申請專利範圍第1項之配體結合分子，其中，該切斷位點包括蛋白酶切斷序列。

【第3項】 如申請專利範圍第2項之配體結合分子，其中該切斷位點為該蛋白酶切斷序列或附加可動連結子的該蛋白酶切斷序列。

【第4項】 如申請專利範圍第2項之配體結合分子，其中，該蛋白酶切斷序列係被標靶組織專一性的蛋白酶所切斷。

【第5項】 如申請專利範圍第2項之配體結合分子，其中，該蛋白酶切斷序列係被癌症組織專一性的蛋白酶所切斷，或係被發炎組織專一性的蛋白酶所切斷。

【第6項】 如申請專利範圍第2項之配體結合分子，其中，該蛋白酶切斷序列係被選自蛋白裂解酶(Matriptase)、尿激酶(uPA)、及金屬蛋白酶中之至少一種蛋白酶所切斷。

【第7項】 如申請專利範圍第1項之配體結合分子，其中，

該配體結合分子中之該抗體VL與該抗體VH係組裝，該組裝經由該切斷位點被切斷而解除、或經由該蛋白酶切斷序列被蛋白酶切斷而解除。

【第8項】 如申請專利範圍第1至3項中任一項之配體結合分子，其中，該配體係有生物活性之分子，該配體結合分子藉由和該配體結合而抑制該配體之

生物活性。

【第9項】 如申請專利範圍第1至3項中任一項之配體結合分子，其中，該配體為細胞介素或趨化介素。

【第10項】如申請專利範圍第1至3項中任一項之配體結合分子，其中，該配體結合分子為IgG抗體。

【第11項】如申請專利範圍第1至3項中任一項之配體結合分子，係結合了該配體。

【第12項】如申請專利範圍第1至3項中任一項之配體結合分子，係融合了該配體。

【第13項】一種醫藥組合物，包含如申請專利範圍第1至12項中任一項之配體結合分子。

【第14項】一種醫藥組合物，包含如申請專利範圍第1至11項中任一項之配體結合分子與配體。

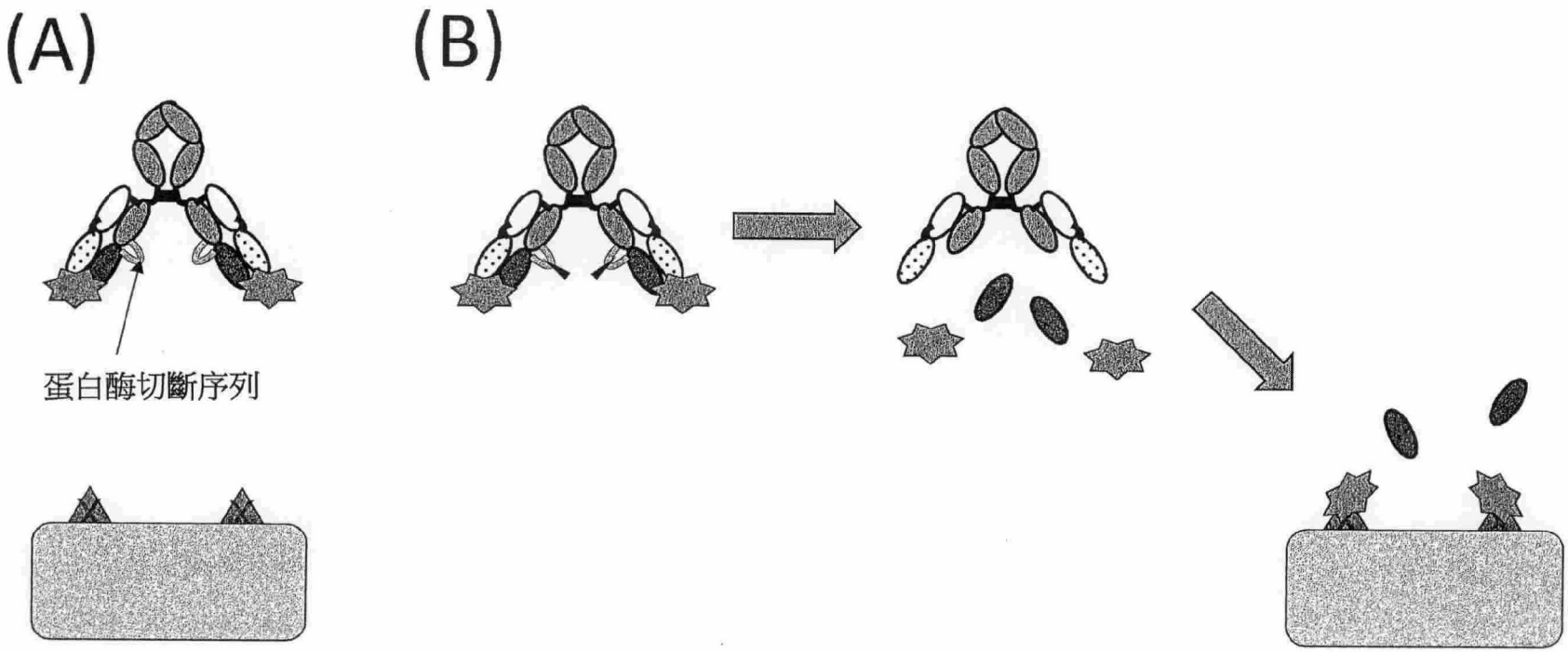
【第15項】一種醫藥組合物，包含融合了如申請專利範圍第1至10項中任一項之配體結合分子與配體的融合蛋白質。

【第16項】一種方法，係製造如申請專利範圍第1至12項中任一項之配體結合分子之方法。

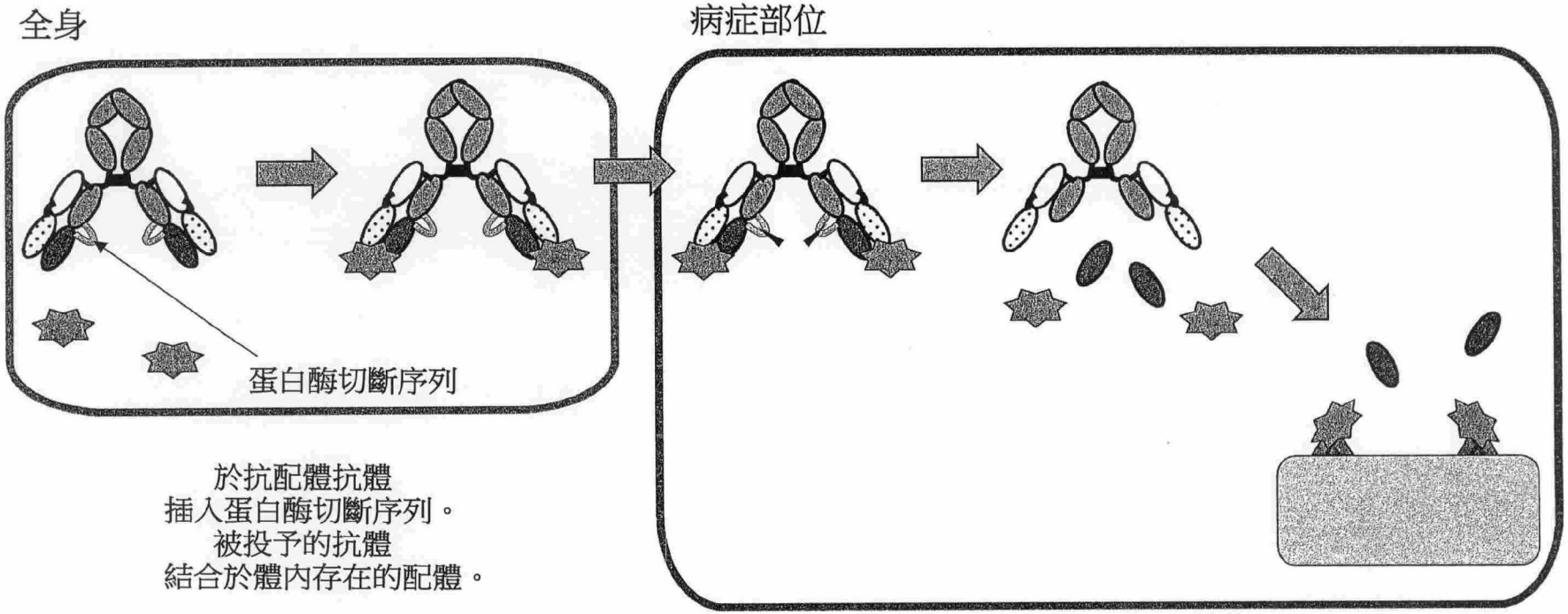
【發明圖式】

(A)
蛋白酶切斷序列
於配體與抗配體抗體以
連結子融合而得的分子
插入蛋白酶切斷序列
(B)
藉由以蛋白酶切斷，
(配體-連結子-抗配體抗體的VH分子)游離，
且游離後的(配體-連結子-抗配體抗體的VH分子)
結合於受體

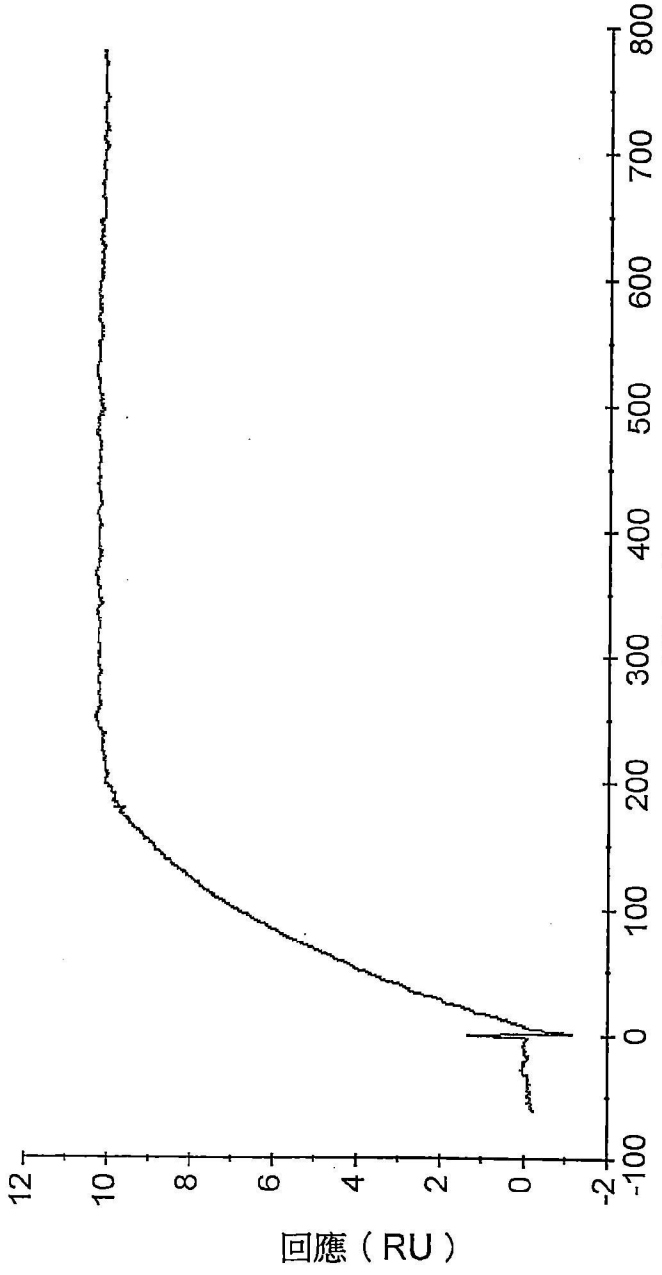
第1圖


(A)
(B)
蛋白酶切斷序列
藉於抗配體抗體
插入蛋白酶切斷序列
藉由以蛋白酶切斷，
配體-抗配體抗體複合體的配體與VH分子
游離，且游離後的配體結合於受體

第2圖


全身
病症部位
蛋白酶切斷序列
於抗配體抗體
插入蛋白酶切斷序列。
被投予的抗體
結合於體內存在的配體。
藉由以蛋白酶切斷，
配體-抗配體抗體複合體的配體與VH分子
游離，且游離後的配體結合於受體

第3圖



第4圖

(A)

在可變區與不變區的插入位置名**A~G**的各位置插入了蛋白酶切斷序列

第5A圖

（B） 重鏈

重鏈改變體名	蛋白酶切斷序列插入位置	插入序列
EEIVHA	TVSS [insert] ASTKGP	LSGRSDNH（序列編號：3）
EEIVHB	TVSSAS [insert] TKGP	LSGRSDNH（序列編號：3）
EEIVHC	TV [insert] SSASTKGP	LSGRSDNH（序列編號：3）
EEIVHD	TVS [insert] SASTKGP	LSGRSDNH（序列編號：3）
EEIVHE	TVSSA [insert] STKGP	LSGRSDNH（序列編號：3）
EEIVHF	TVSSAST [insert] KGP	LSGRSDNH（序列編號：3）
EEIVHG	TVSSASTK [insert] GP	LSGRSDNH（序列編號：3）
EEIVHBG	TVSSAS [insert] GKGP	LSGRSDNH（序列編號：3）
EEIVHCG	TV [insert] GSASTKGP	LSGRSDNH（序列編號：3）
EEIVHDG	TVS [insert] GASTKGP	LSGRSDNH（序列編號：3）
EEIVHEG	TVSSA [insert] GTKGP	LSGRSDNH（序列編號：3）

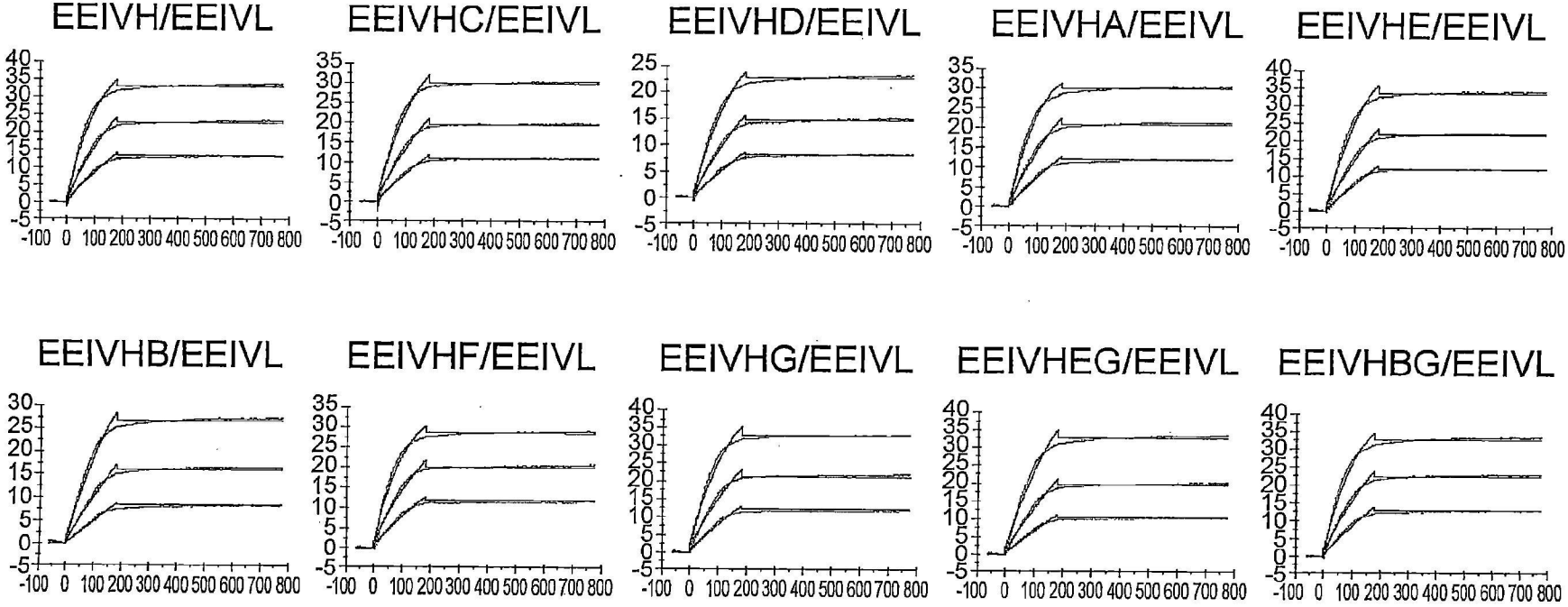
第5B圖

（C）輕鏈

輕鏈改變體名	蛋白酶切斷序列插入位置	插入序列
EEIVLA	VDIK [insert] RTVAAP	LSGRSDNH（序列編號：3）
EEIVLB	VDIKRT [insert] VAAP	LSGRSDNH（序列編號：3）
EEIVLC	VD [insert] IKRTVAAP	LSGRSDNH（序列編號：3）
EEIVLD	VDI [insert] KRTVAAP	LSGRSDNH（序列編號：3）
EEIVLE	VDIKR [insert] TVAAP	LSGRSDNH（序列編號：3）
EEIVLF	VDIKRTV [insert] AAP	LSGRSDNH（序列編號：3）
EEIVLG	VDIKRTVA [insert] AP	LSGRSDNH（序列編號：3）
EEIVLEG	VDIKR [insert] GVAAP	LSGRSDNH（序列編號：3）

第5C圖

(A)

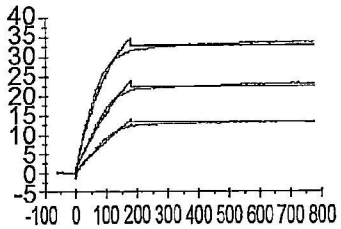


縱軸: 回應(RU)
橫軸: 時間(秒)

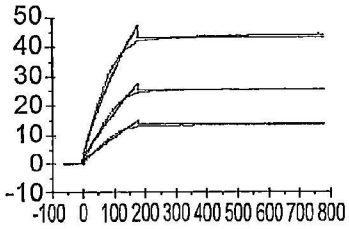
第6A圖

(B)

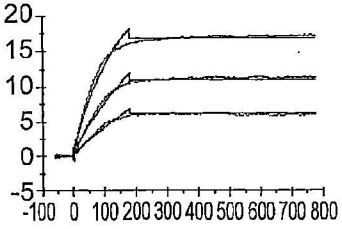
EEIVH/EEIVL



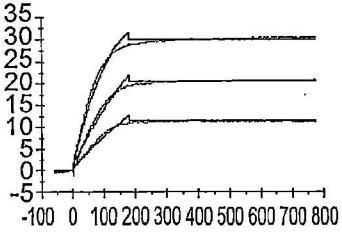
EEIVH/EEIVLC



EEIVH/EEIVLD



EEIVH/EEIVLA



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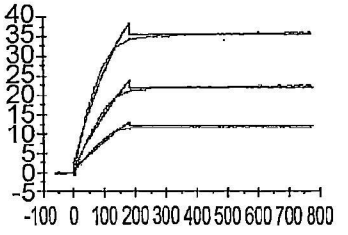
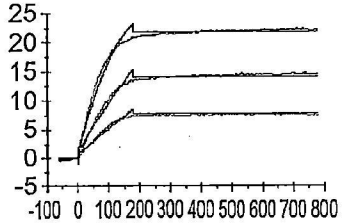
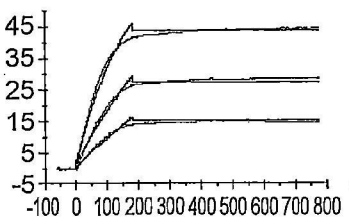


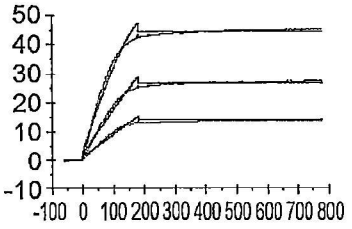
EEIVH/EEIVLB



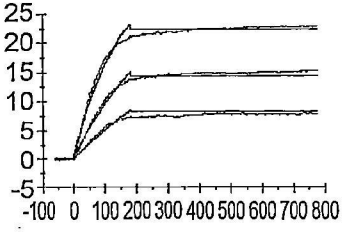
EEIVH/EEIVLF



EEIVH/EEIVLG

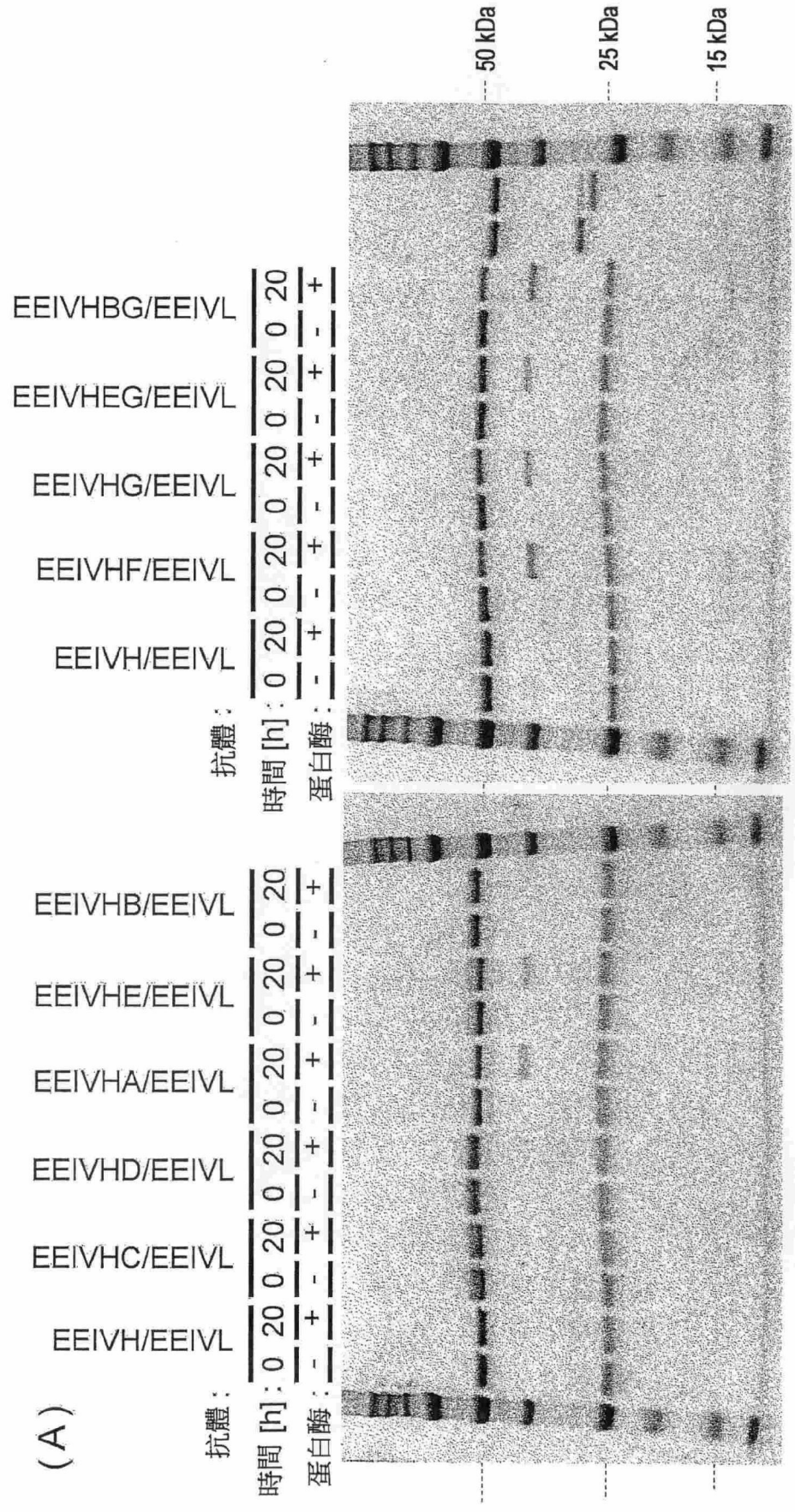


EEIVH/EEIVLEG

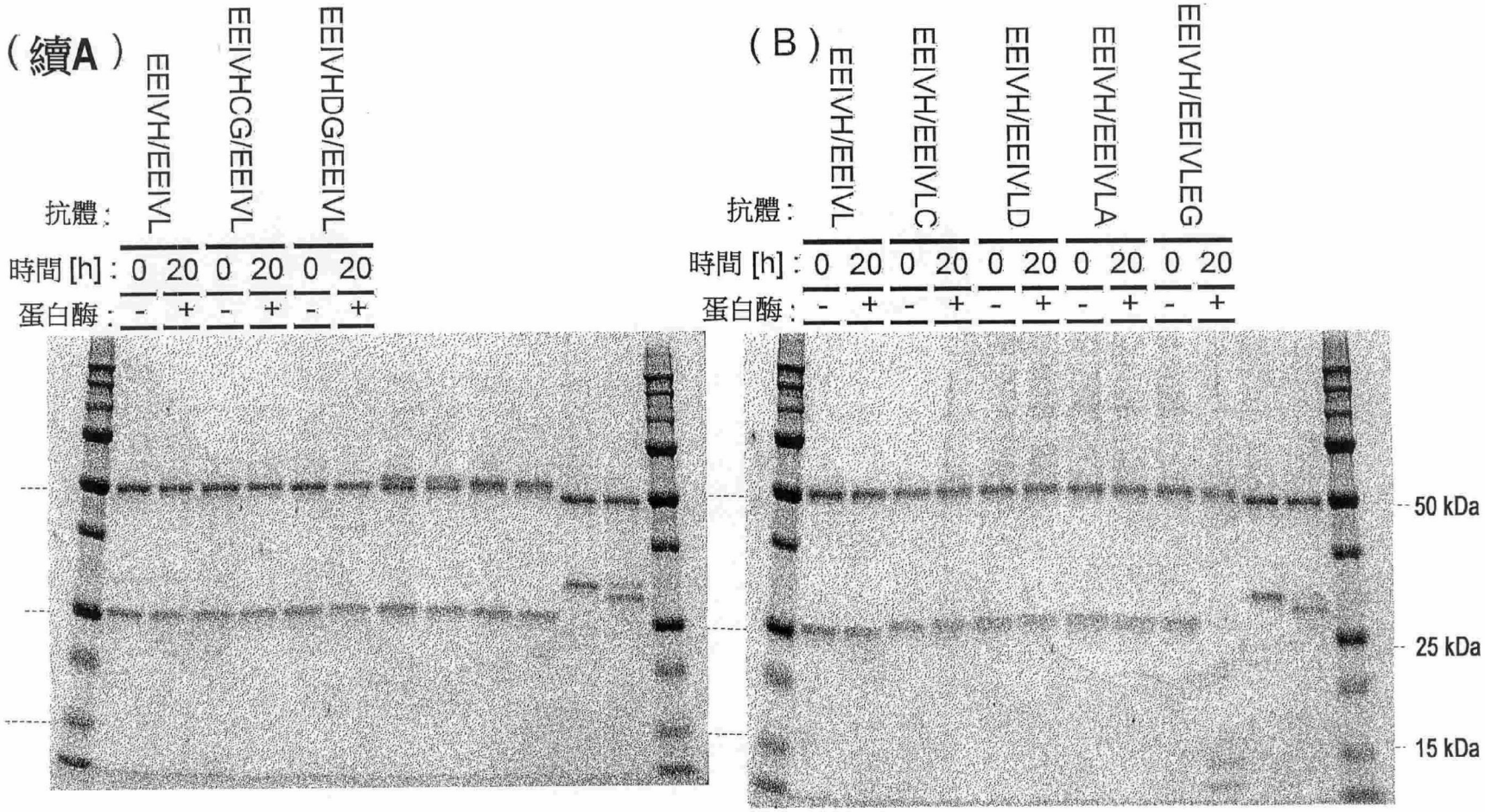


縱軸: 回應 (RU)
橫軸: 時間 (秒)

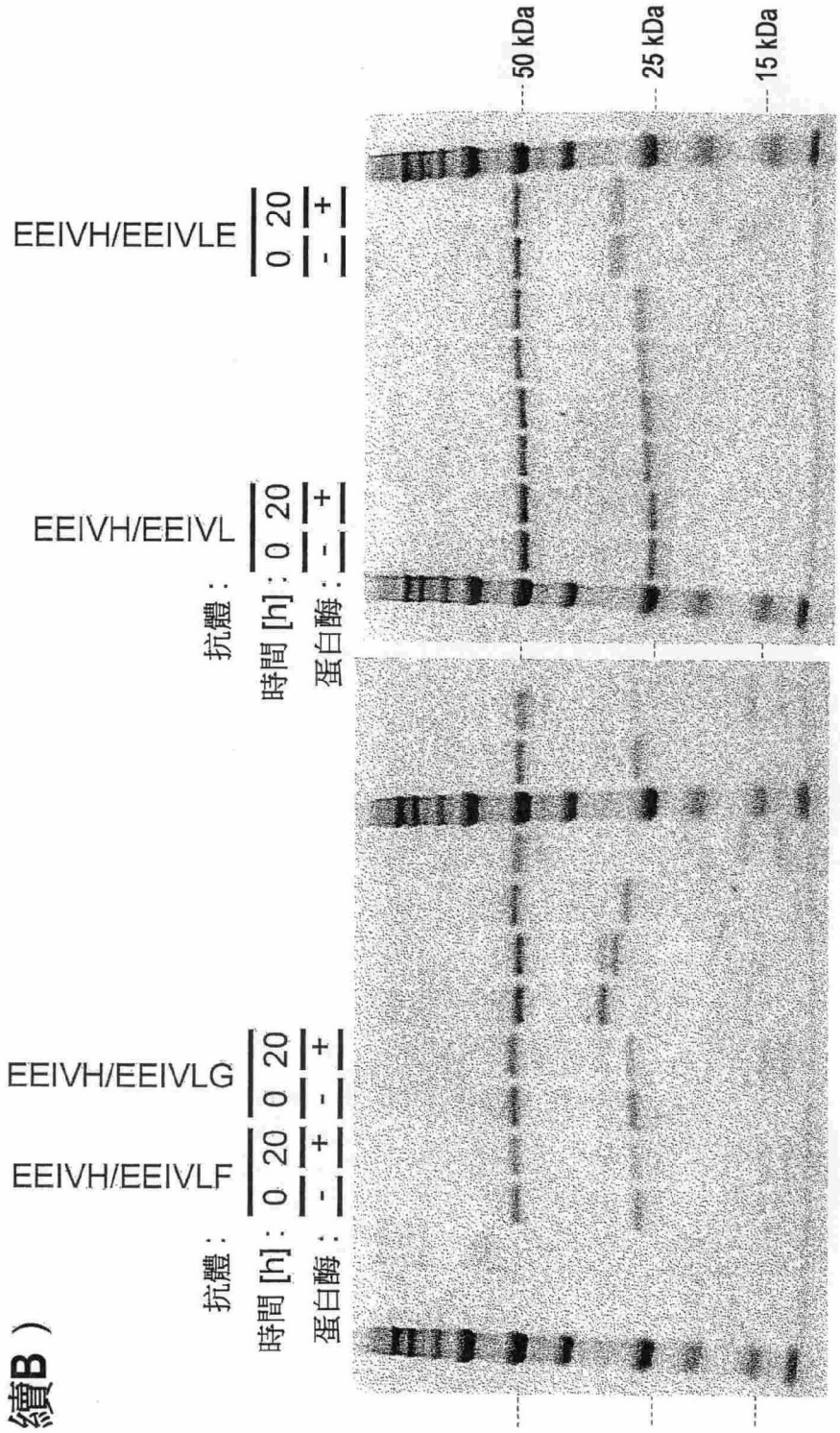
第6B圖


(A)
抗體：
時間 [h]：
蛋白酶：
EEIVH/EEIVL
EEIVHC/EEIVL
EEIVHD/EEIVL
EEIVHA/EEIVL
EEIVHE/EEIVL
EEIVHB/EEIVL
EEIVH/EEIVL
EEIVHF/EEIVL
EEIVHG/EEIVL
EEIVHEG/EEIVL
EEIVHBG/EEIVL
50 kDa
25 kDa
15 kDa

第7-1圖


(續A)
EEIVH/EEIVL
EEIVHCG/EEIVL
EEIVHDG/EEIVL
抗體:
時間 [h]: 0 20 0 20 0 20
蛋白酶: - + - + - +
(B)
EEIVH/EEIVL
EEIVH/EEIVLC
EEIVH/EEIVLD
EEIVH/EEIVLA
EEIVH/EEIVLEG
抗體:
時間 [h]: 0 20 0 20 0 20 0 20 0 20
蛋白酶: - + - + - + - + - +
50 kDa
25 kDa
15 kDa

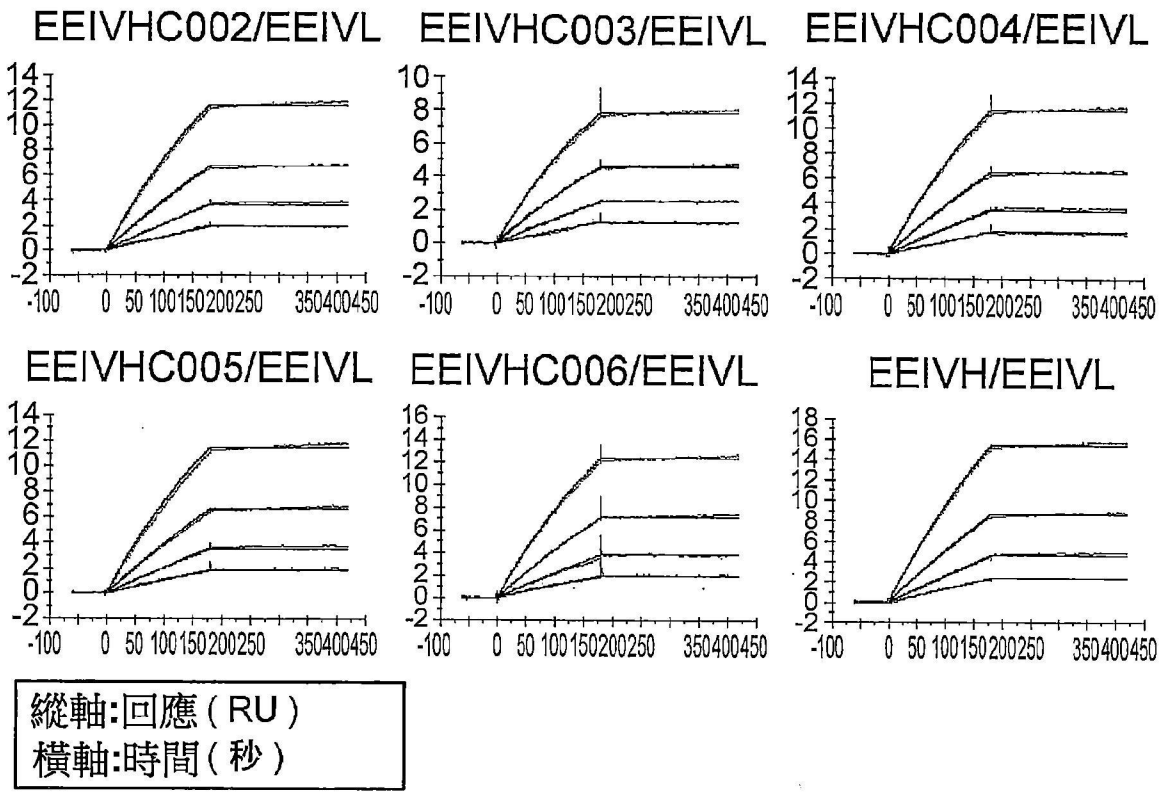
第7-2圖


(續B)
抗體：
時間 [h]：
蛋白酶：
EEIVH/EEIVLF
EEIVH/EEIVLG
EEIVH/EEIVL
EEIVH/EEIVLE
0 20 0 20
- + - +
0 20
- +
0 20
- +
50 kDa
25 kDa
15 kDa

第7-3圖

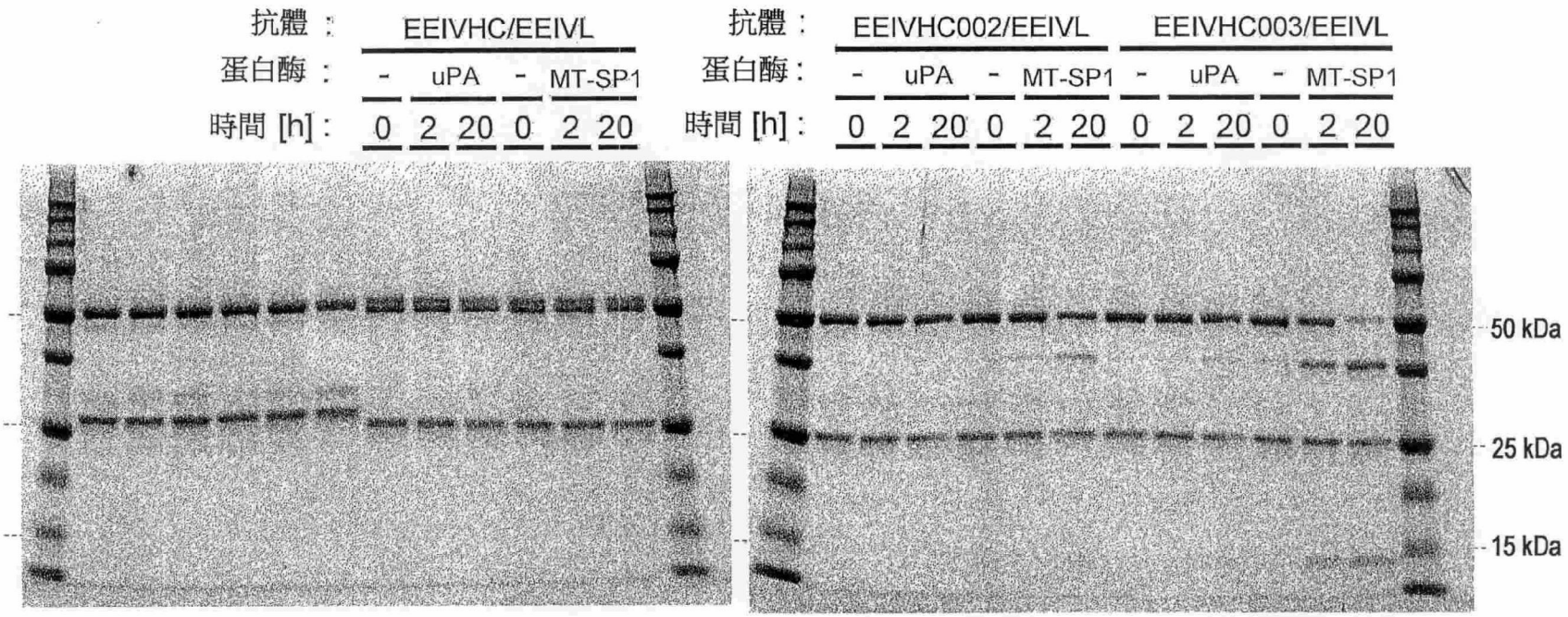
重鏈改變體名	蛋白酶切斷序列插入位置	插入序列
EEIVHC	TV [insert] SSASTKGP	LSGRSDNH（序列編號：3）
EEIVHC002	TV [insert] SSASTKGP	GLSGRSDNHG（序列編號：28）
EEIVHC003	TV [insert] SSASTKGP	SGLSGRSDNHGS（序列編號：29）
EEIVHC004	TV [insert] SSASTKGP	GSGLSGRSDNHGSS（序列編號：30）
EEIVHC005	TV [insert] SSASTKGP	GGSGLSGRSDNHGSSG（序列編號：31）
EEIVHC006	TV [insert] SSASTKGP	SGGSGLSGRSDNHGSSGT（序列編號：32）

第8圖


EEIVHC002/EEIVL
EEIVHC003/EEIVL
EEIVHC004/EEIVL
EEIVHC005/EEIVL
EEIVHC006/EEIVL
EEIVH/EEIVL
-100 0 50 100 150 200 250 350 400 450
縱軸:回應(RU)
橫軸:時間(秒)

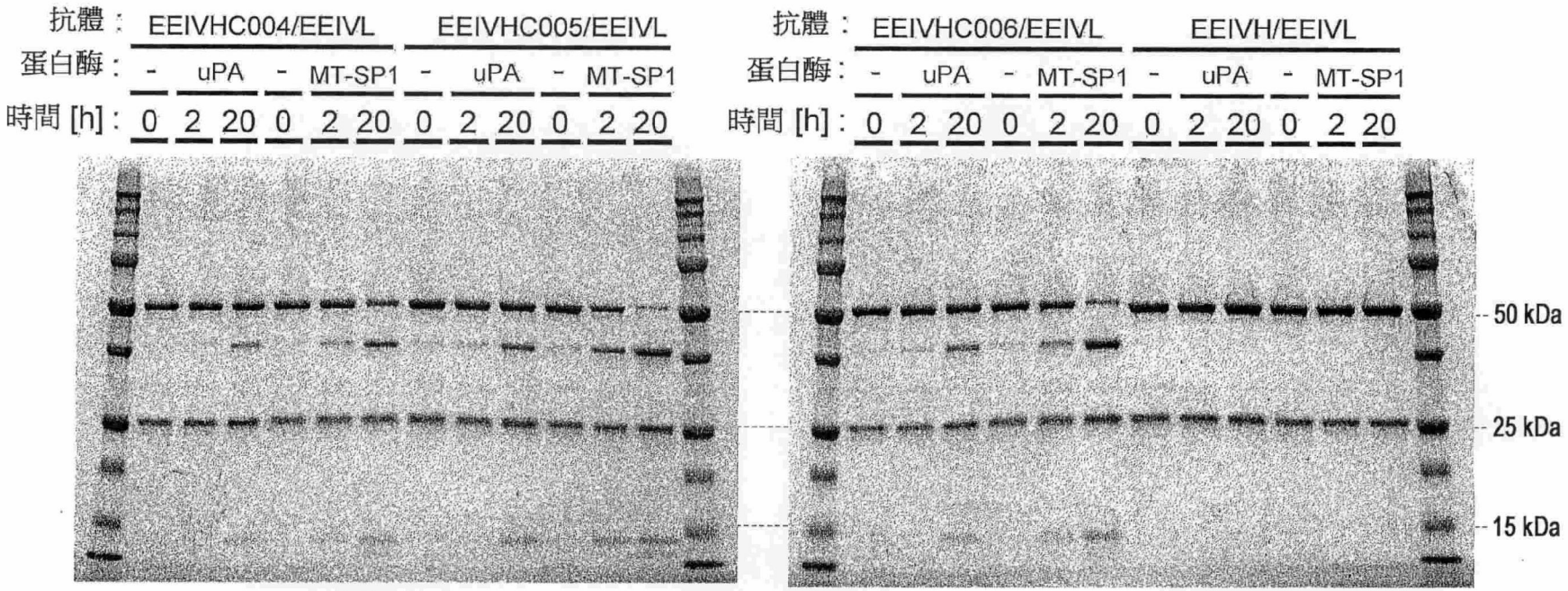
第9圖

(A)

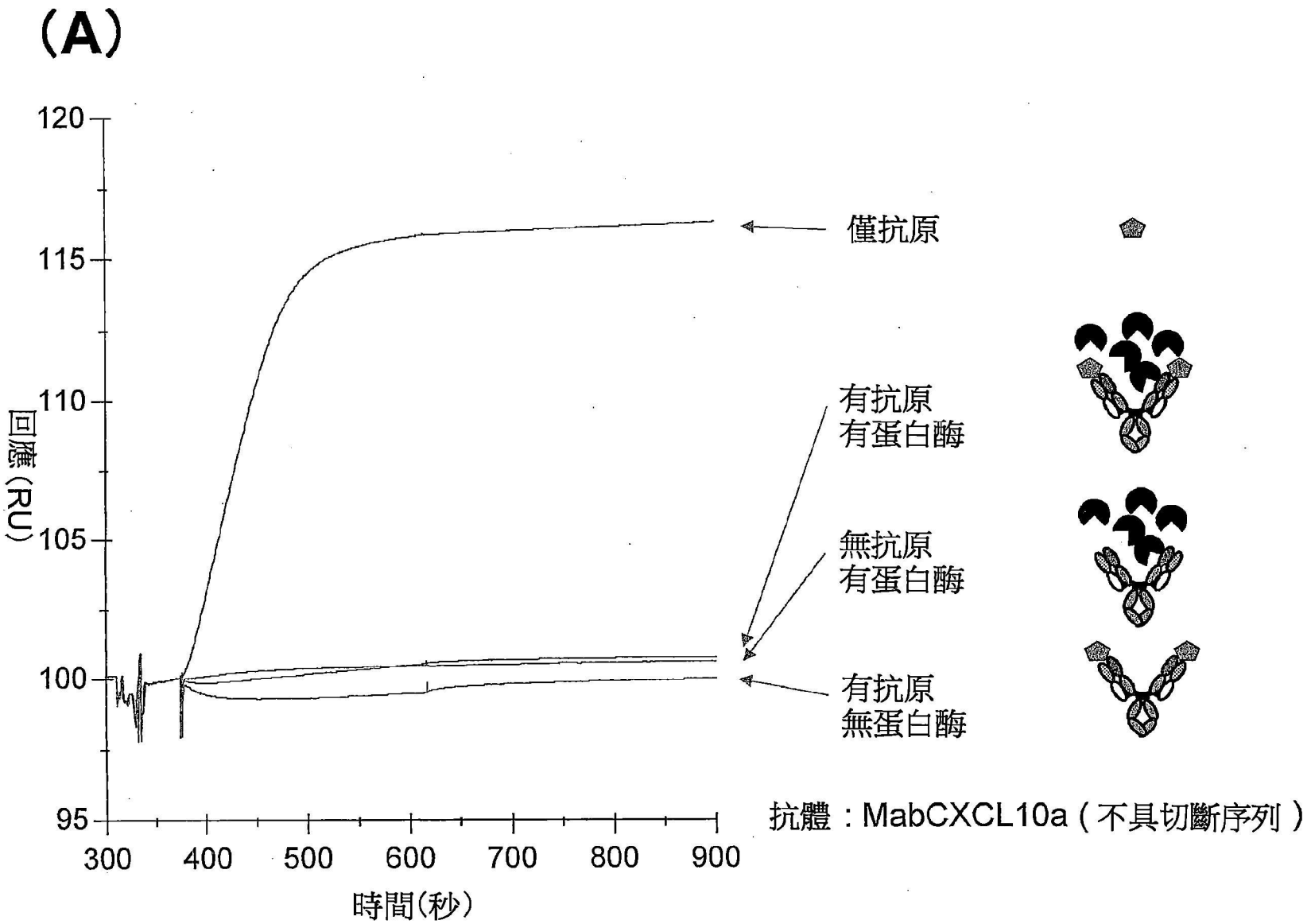

抗體：
EEIVHC/EEIVL
蛋白酶：
-
uPA
-
MT-SP1
時間 [h]：
0 2 20 0 2 20
抗體：
EEIVHC002/EEIVL
EEIVHC003/EEIVL
蛋白酶：
-
uPA
-
MT-SP1
-
uPA
-
MT-SP1
時間 [h]：
0 2 20 0 2 20 0 2 20 0 2 20
50 kDa
25 kDa
15 kDa

第10A圖

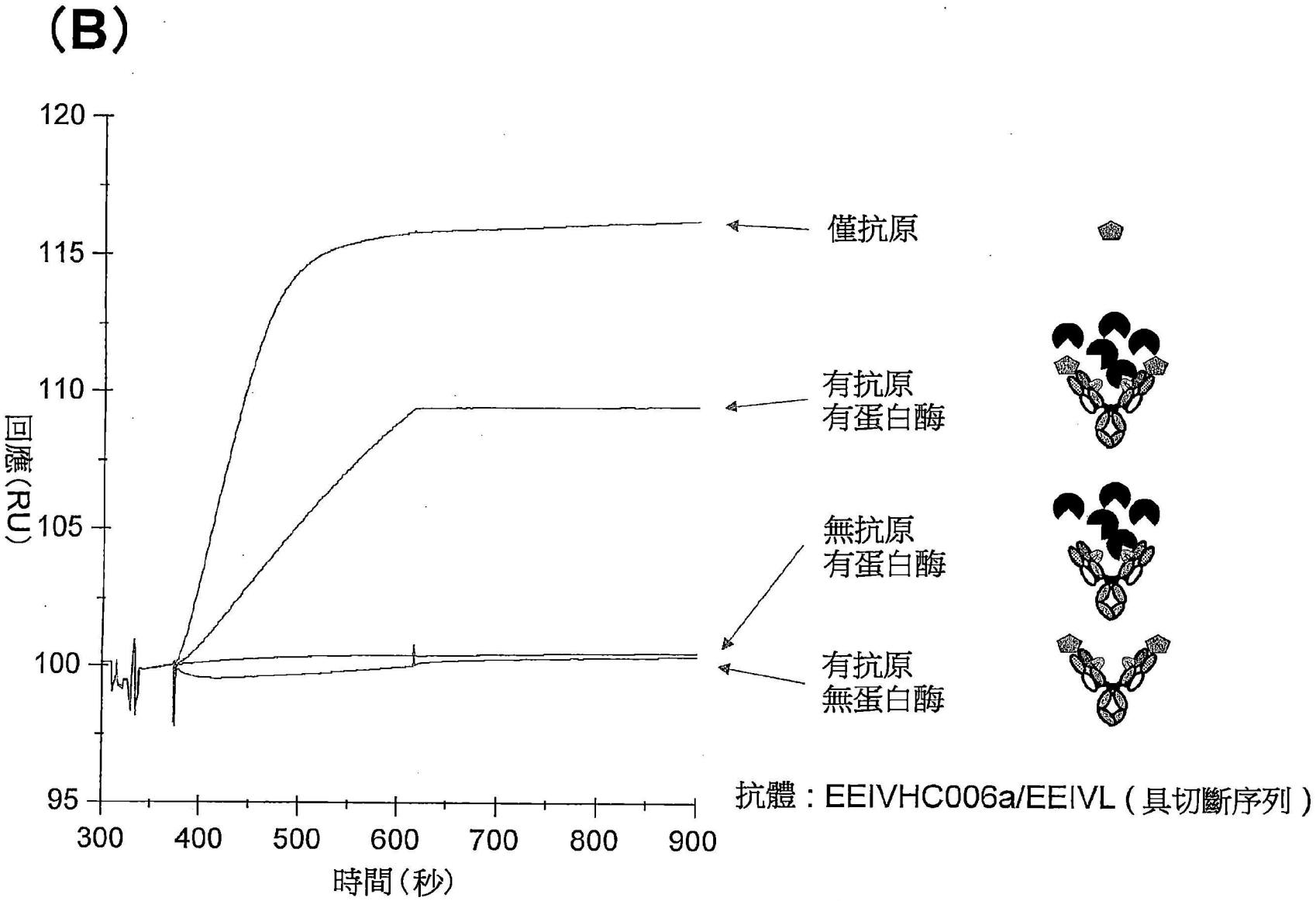
(B)


抗體：
EEIVHC004/EEIVL
EEIVHC005/EEIVL
蛋白酶：
-
uPA
-
MT-SP1
-
uPA
-
MT-SP1
時間 [h]：
0 2 20 0 2 20 0 2 20 0 2 20
抗體：
EEIVHC006/EEIVL
EEIVH/EEIVL
蛋白酶：
-
uPA
-
MT-SP1
-
uPA
-
MT-SP1
時間 [h]：
0 2 20 0 2 20 0 2 20 0 2 20
50 kDa
25 kDa
15 kDa

第10B圖


(A)
120
115
110
105
100
95
回應(RU)
300
400
500
600
700
800
900
時間(秒)
僅抗原
有抗原
有蛋白酶
無抗原
有蛋白酶
有抗原
無蛋白酶
抗體：MabCXCL10a（不具切斷序列）

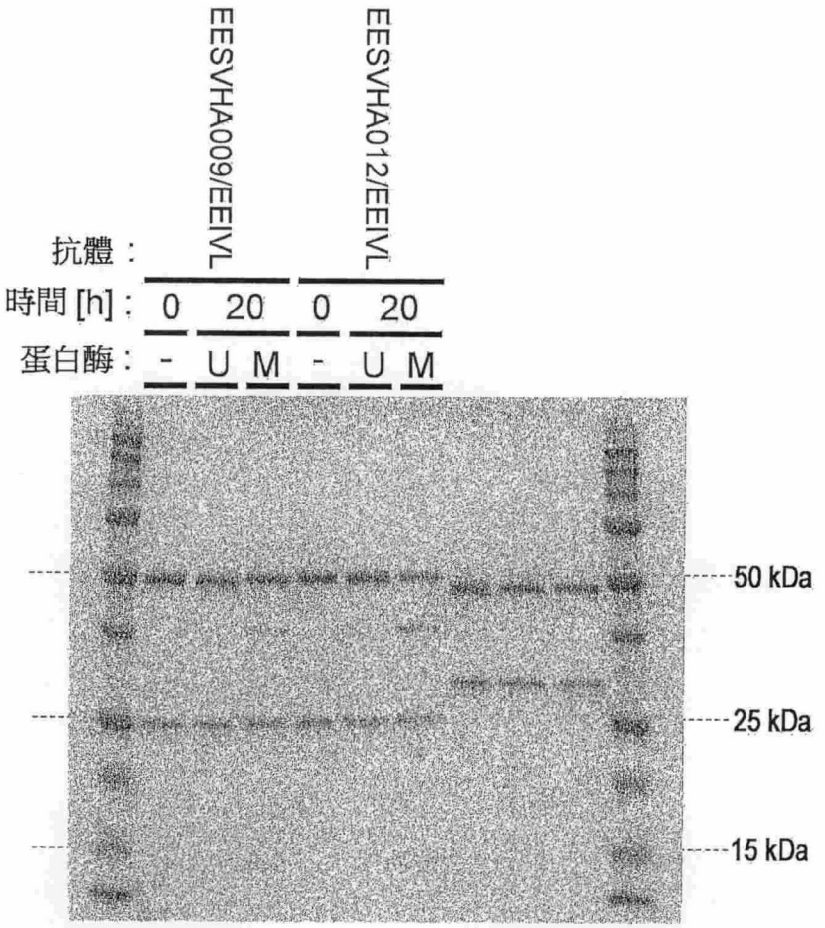
第11A圖


(B)
120
115
110
105
100
95
回應(RU)
300
400
500
600
700
800
900
時間(秒)
僅抗原
有抗原
有蛋白酶
無抗原
有蛋白酶
有抗原
無蛋白酶
抗體：EEIVHC006a/EEIVL（具切斷序列）

第11B圖

重鏈改變體名	插入位置及改變位置	插入序列	插入及改變後的序列
EESVHA009	TVSS [insert] ~~A~~ STKGP	GLSGRSDNHGS （序列編號：61）	TVSSGLSGRSDNHGS STKGP （序列編號：62）
EESVHA012	TVSS [insert] ~~A~~ STKGP	GGSGLSGRSDNHGSSGT （序列編號：63）	TVSSGGSGLSGRSDNHGSS GTSTKGP （序列編號：64）

第12圖

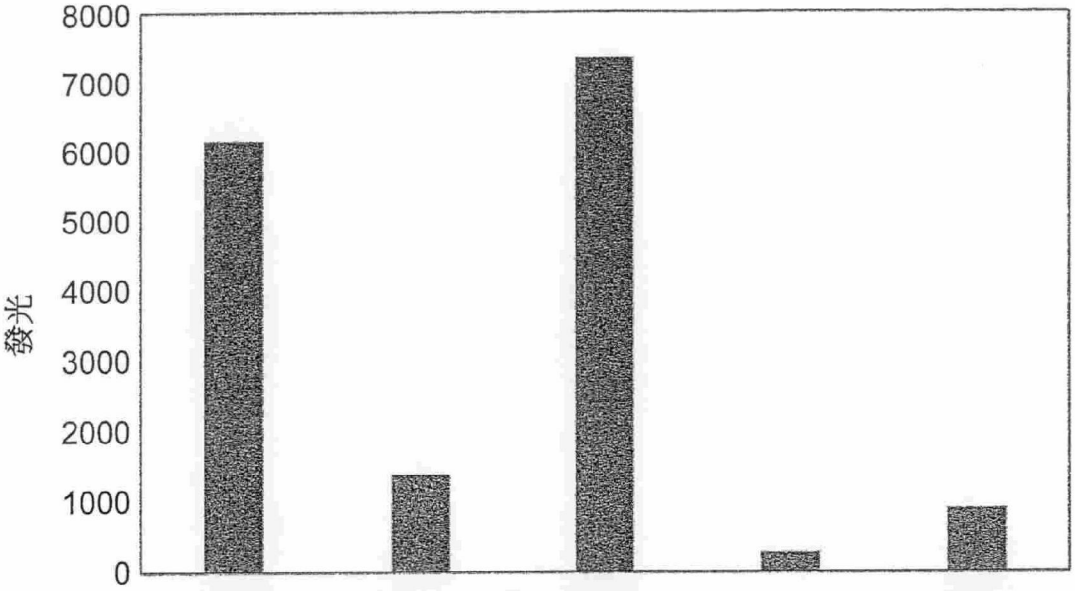


蛋白酶

U : uPA

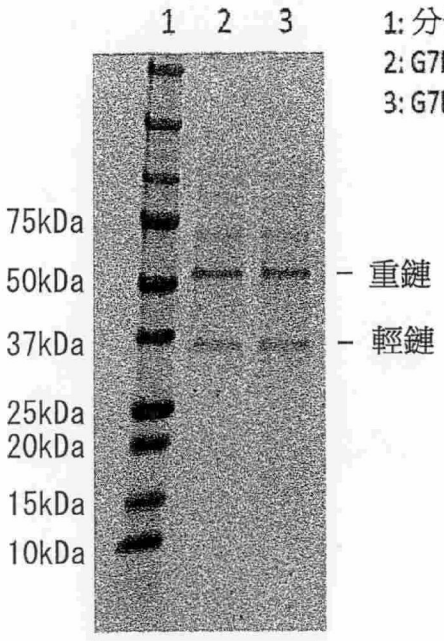
M : MT-SP1

第13圖



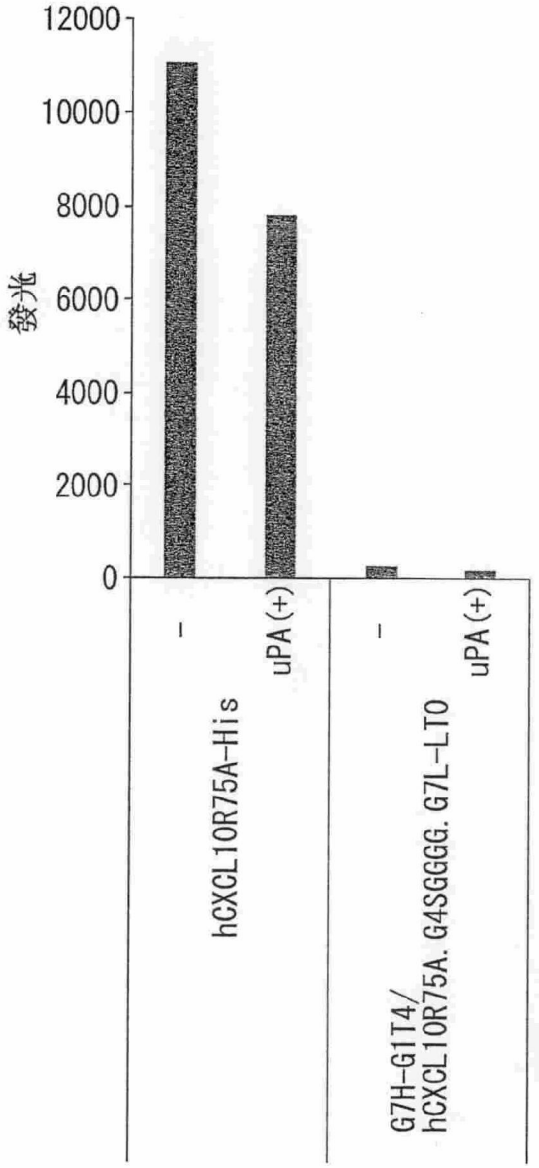
抗體	-	EEIVHC006a/EEIVL			MabCXCL10
CXCL10	+	+	+	-	+
mMT-SP1	+	-	+	+	+

第14圖

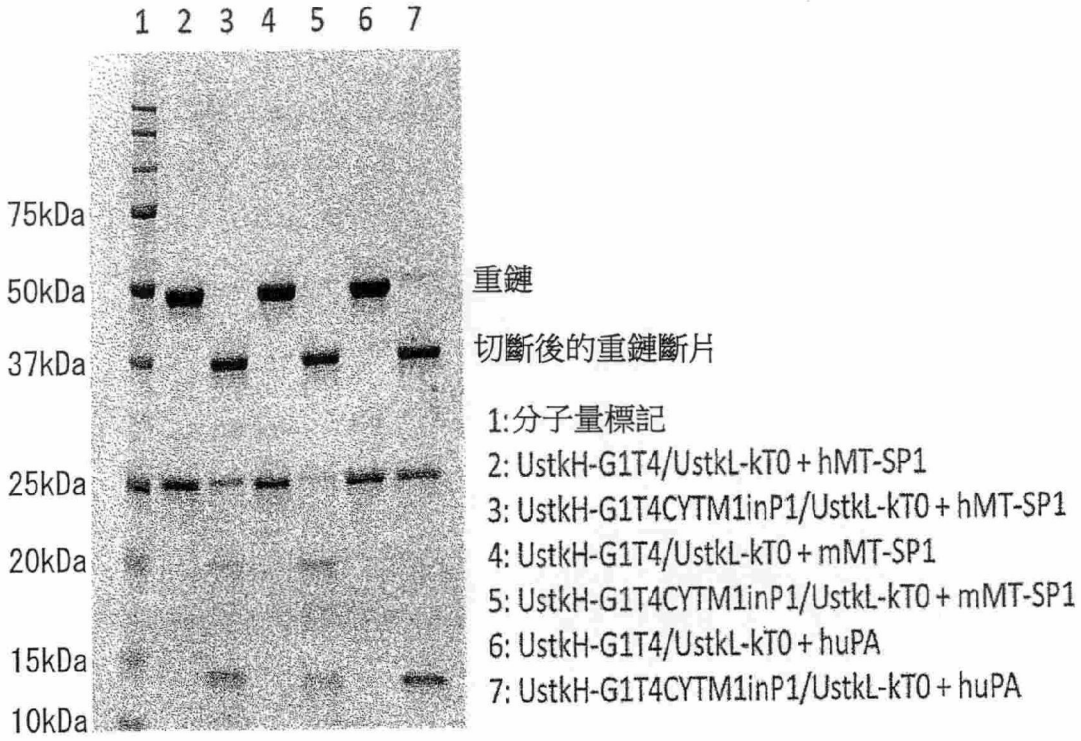


1: 分子量標記
2: G7H-G1T4/ hCXCL10R75A.G4SGGGG.G7L-LT0
3: G7H-G1T4/ hCXCL10R75A.G4SGGGG.G7L-LT0 +huPA

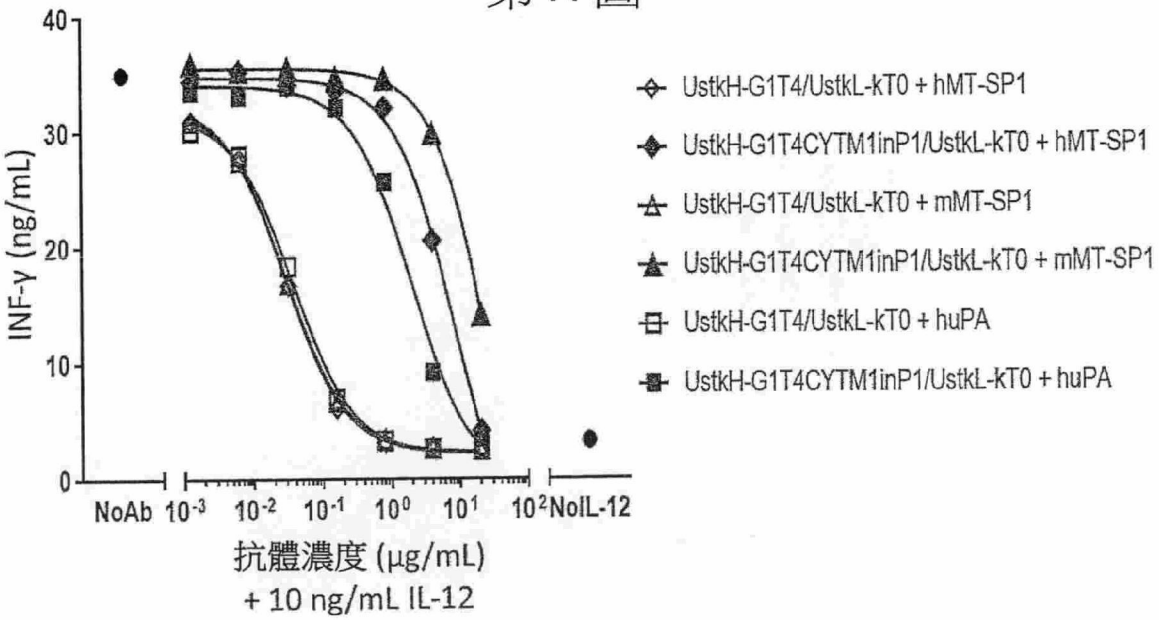
第15圖


12000
10000
8000
6000
4000
2000
0
發光
-
uPA (+)
hCXCL10R75A-His
-
uPA (+)
G7H-G1T4/
hCXCL10R75A. G4SGGGG. G7L-LTO

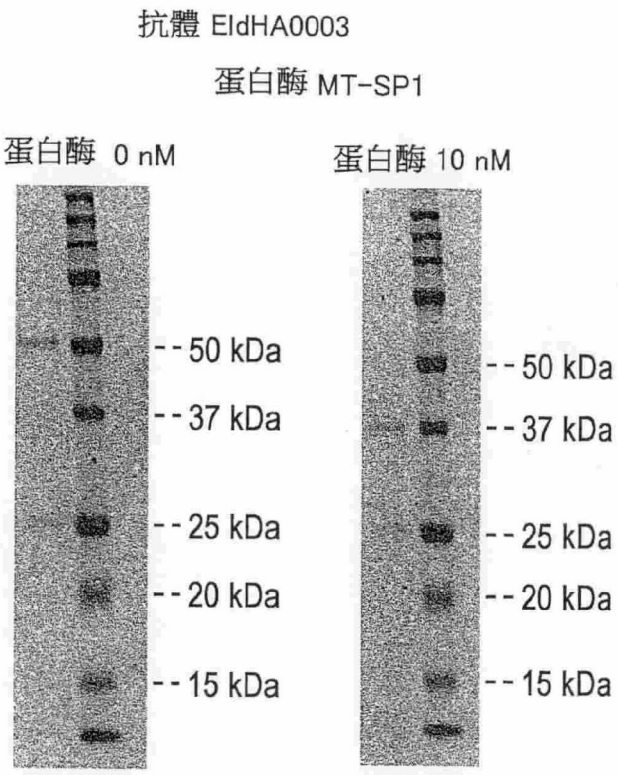
第16圖


1 2 3 4 5 6 7
75kDa
50kDa
37kDa
25kDa
20kDa
15kDa
10kDa
重鏈
切斷後的重鏈斷片
1:分子量標記
2: UstkH-G1T4/UstkL-kT0 + hMT-SP1
3: UstkH-G1T4CYTM1inP1/UstkL-kT0 + hMT-SP1
4: UstkH-G1T4/UstkL-kT0 + mMT-SP1
5: UstkH-G1T4CYTM1inP1/UstkL-kT0 + mMT-SP1
6: UstkH-G1T4/UstkL-kT0 + huPA
7: UstkH-G1T4CYTM1inP1/UstkL-kT0 + huPA

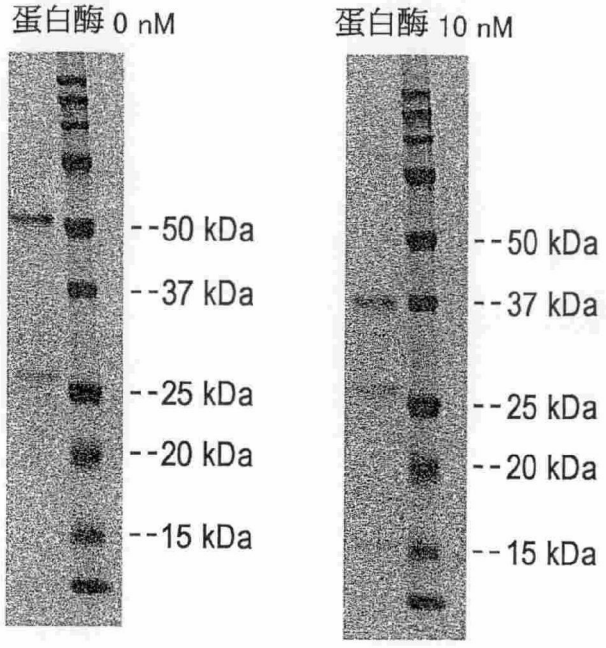
第17圖


INF-γ (ng/mL)
40
30
20
10
0
NoAb
10-3
10-2
10-1
100
101
102
NoIL-12
抗體濃度 (μg/mL)
+ 10 ng/mL IL-12
UstkH-G1T4/UstkL-kT0 + hMT-SP1
UstkH-G1T4CYTM1inP1/UstkL-kT0 + hMT-SP1
UstkH-G1T4/UstkL-kT0 + mMT-SP1
UstkH-G1T4CYTM1inP1/UstkL-kT0 + mMT-SP1
UstkH-G1T4/UstkL-kT0 + huPA
UstkH-G1T4CYTM1inP1/UstkL-kT0 + huPA

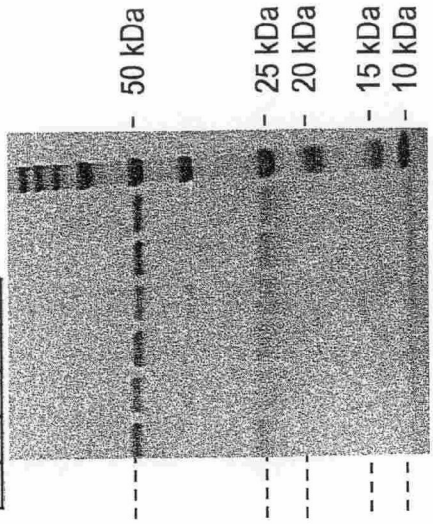
第18圖


抗體 EIdHA0003
蛋白酶 MT-SP1
蛋白酶 0 nM
蛋白酶 10 nM
50 kDa
37 kDa
25 kDa
20 kDa
15 kDa
50 kDa
37 kDa
25 kDa
20 kDa
15 kDa

第19A圖

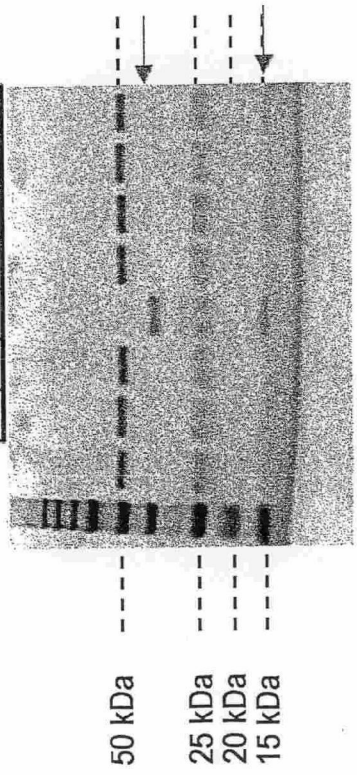

抗體 G7H.12aa
蛋白酶 MT-SP1
蛋白酶 0 nM
蛋白酶 10 nM
50 kDa
37 kDa
25 kDa
20 kDa
15 kDa
50 kDa
37 kDa
25 kDa
20 kDa
15 kDa

第19B圖



抗體	緩衝液	蛋白酶	
MEIVHG4SMP2.4G4S-MEICHG4SMP2.4G4SG1T4/MRAL-k0	Tris	MMP-2	100 nM
			0 nM
MEIVHG4SMP2.2G4S-MEICHG4SMP2.2G4SG1T4/MRAL-k0	Tris	MMP-2	100 nM
			0 nM

第20A圖



抗體	緩衝液	蛋白酶	
MEIVHG4SMP9G4S-MEICHG4SMP9G4SG1T4/MRAL-k0	Tris	MMP-9	500 nM
			0 nM
MEIVHG4SMP2MP9G4S-MEICHG4SMP2MP9G4SG1T4/MRAL-k0	Tris	MMP-9	500 nM
			0 nM
MEIVHG4SMP2MP9G4S-MEICHG4SMP2MP9G4SG1T4/MRAL-k0	Tris	MMP-2	500 nM
			0 nM

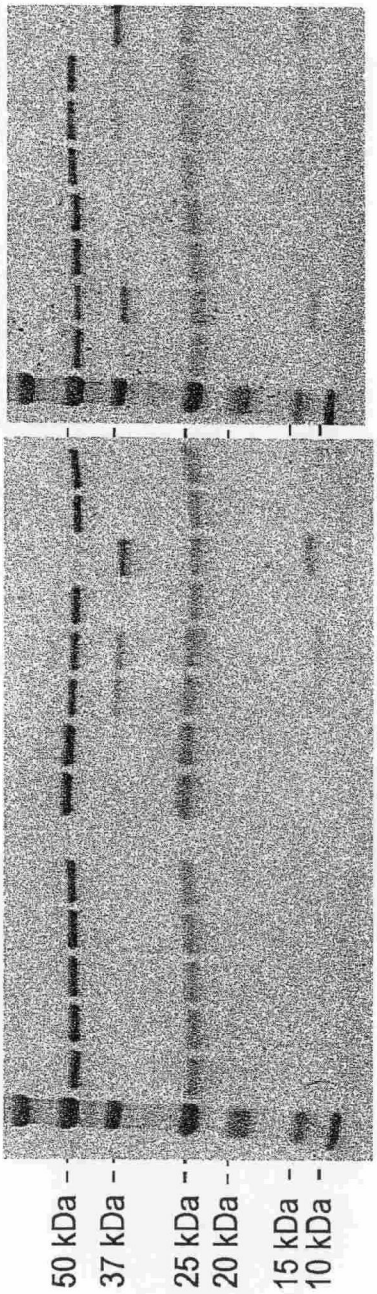
第20B圖

MEIVHMP7.2-MEIVHMP7.2G1T4/MRAL-k0	Assay buffer	MMP-7	50 nM
			0 nM
樣本	緩衝液	蛋白酶	

MEIVHMP2.3-MEIVHMP2.3G1T4/MRAL-k0	assay buffer	MMP-2	50 nM
			0 nM
樣本	緩衝液	蛋白酶	

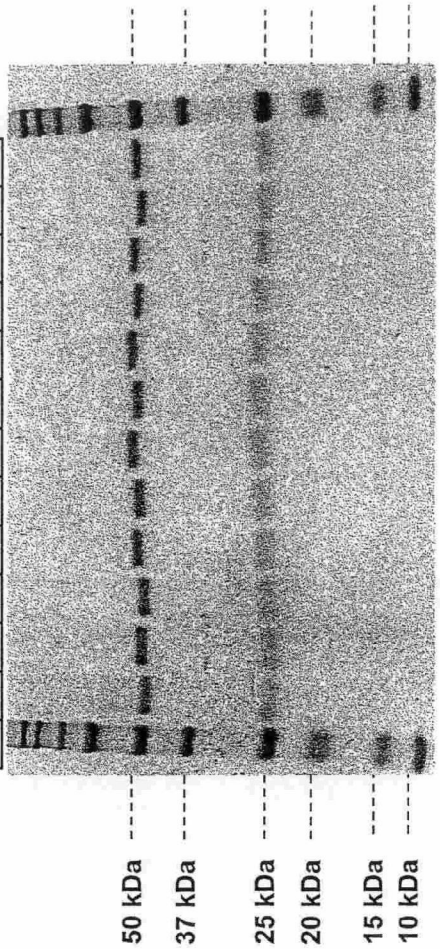
MEIVHMP2.1-MEIVHMP2.1G1T4/MRAL-k0	Assay buffer	MMP-2	50 nM
			0 nM
樣本	緩衝液	蛋白酶	

MRAH-G1T4/MRAL-k0	assay buffer	MMP-9	50 nM
		MMP-7	50 nM
		MMP-2	50 nM
			0 nM
樣本	緩衝液	蛋白酶	



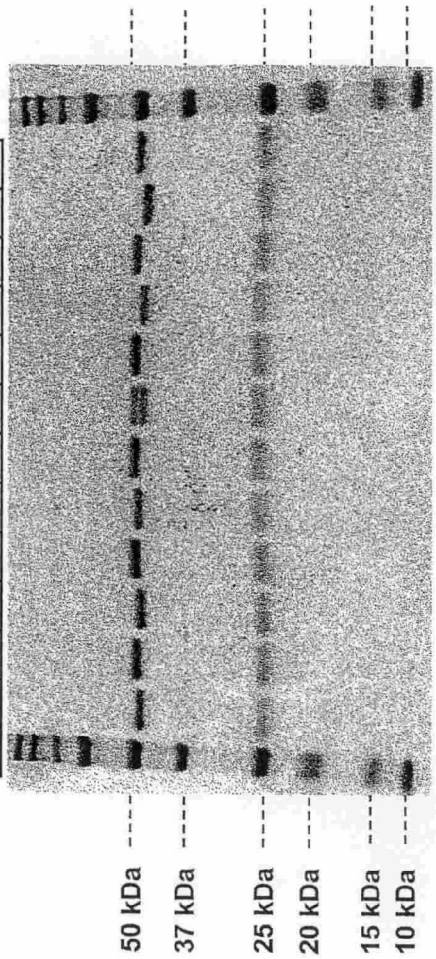
第21圖

MRAVH012.12aa-G1T4 /MRAL-k0	-
	+
MRAVH011.12aa-G1T4 /MRAL-k0	-
	+
MRAVH010.12aa-G1T4 /MRAL-k0	-
	+
MRAVH009.12aa-G1T4 /MRAL-k0	-
	+
MRAVH008.12aa-G1T4 /MRAL-k0	-
	+
MRAVH007.12aa-G1T4 /MRAL-k0	-
	+
抗體	MT-SP1



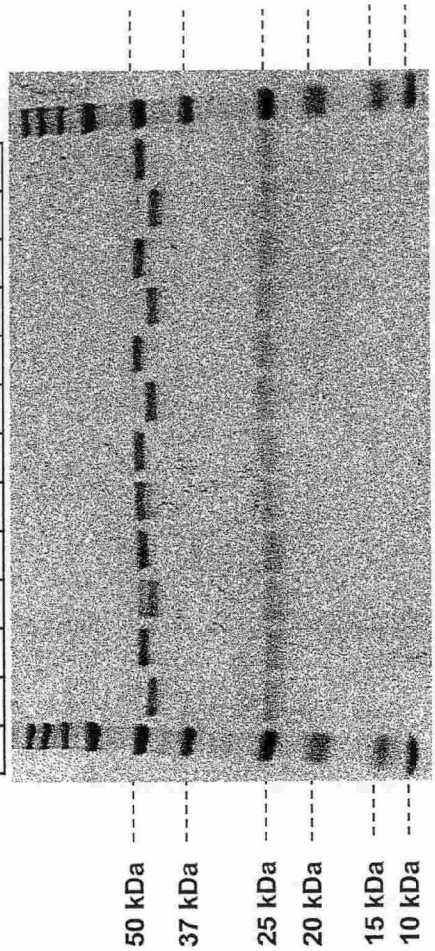
第22A圖

MRAVH043.12aa-G1T4 /MRAL-k0	-
	+
MRAVH042.12aa-G1T4 /MRAL-k0	-
	+
MRAVH041.12aa-G1T4 /MRAL-k0	-
	+
MRAVH015.12aa-G1T4 /MRAL-k0	-
	+
MRAVH014.12aa-G1T4 /MRAL-k0	-
	+
MRAVH013.12aa-G1T4 /MRAL-k0	-
	+
抗體	MT-SP1



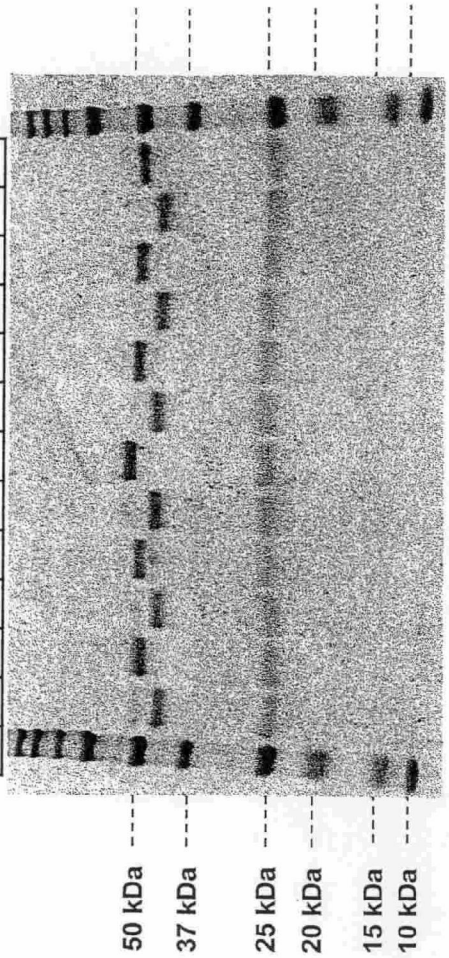
第22B圖

MRAVH058.12aa-G1T4 /MRAL-k0	-
	+
MRAVH057.12aa-G1T4 /MRAL-k0	-
	+
MRAVH056.12aa-G1T4 /MRAL-k0	-
	+
MRAVH046.12aa-G1T4 /MRAL-k0	-
	+
MRAVH045.12aa-G1T4 /MRAL-k0	-
	+
MRAVH044.12aa-G1T4 /MRAL-k0	-
	+
抗體	MT-SP1

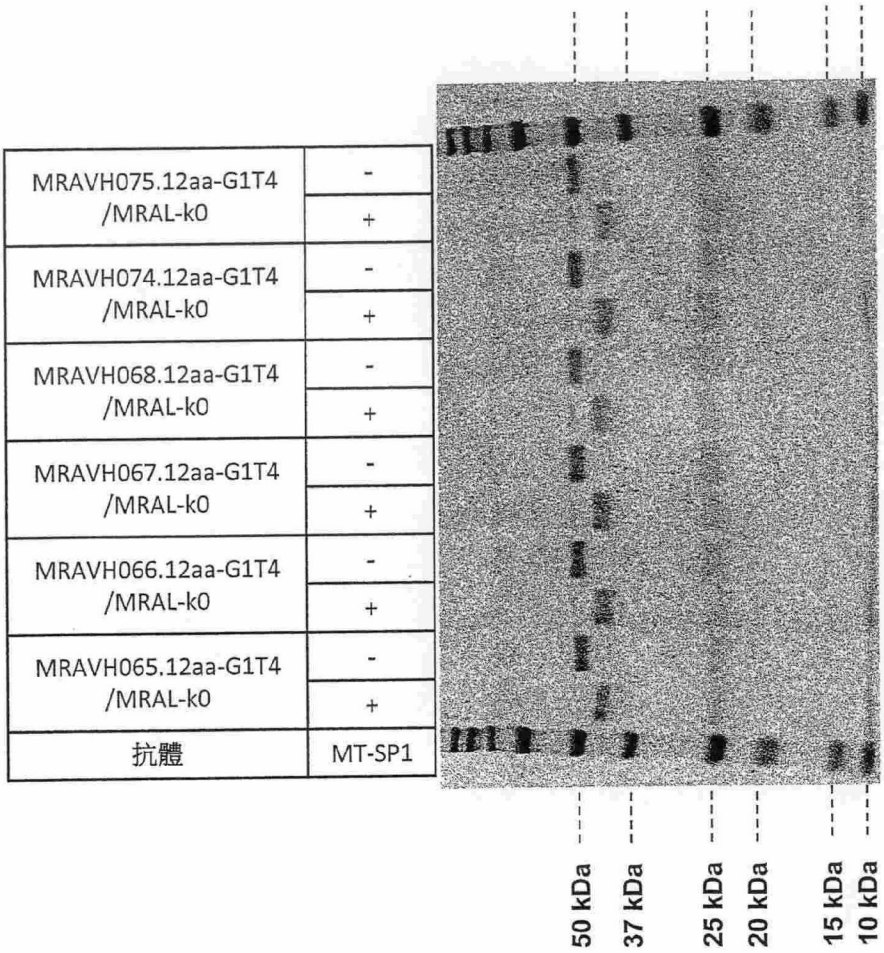


第22C圖

MRAVH064.12aa-G1T4 /MRAL-k0	-
	+
MRAVH063.12aa-G1T4 /MRAL-k0	-
	+
MRAVH062.12aa-G1T4 /MRAL-k0	-
	+
MRAVH061.12aa-G1T4 /MRAL-k0	-
	+
MRAVH060.12aa-G1T4 /MRAL-k0	-
	+
MRAVH059.12aa-G1T4 /MRAL-k0	-
	+
抗體	MT-SP1

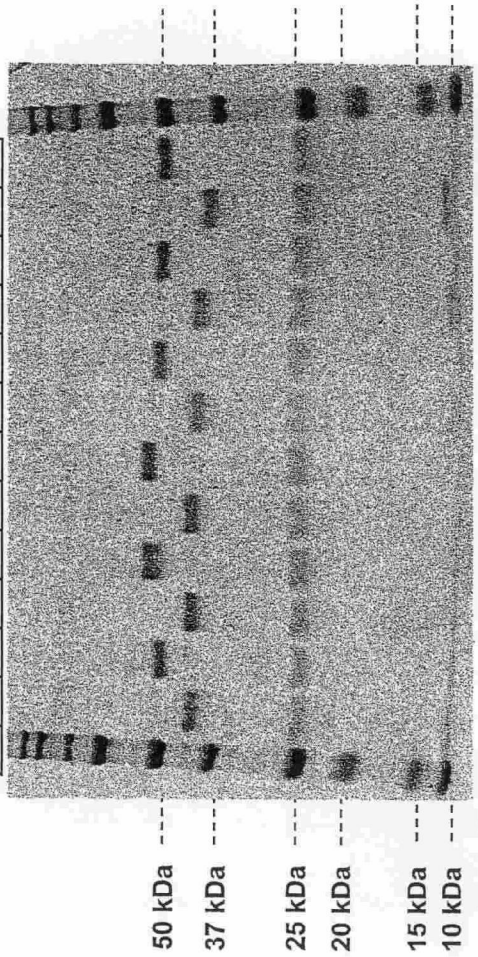


第22D圖

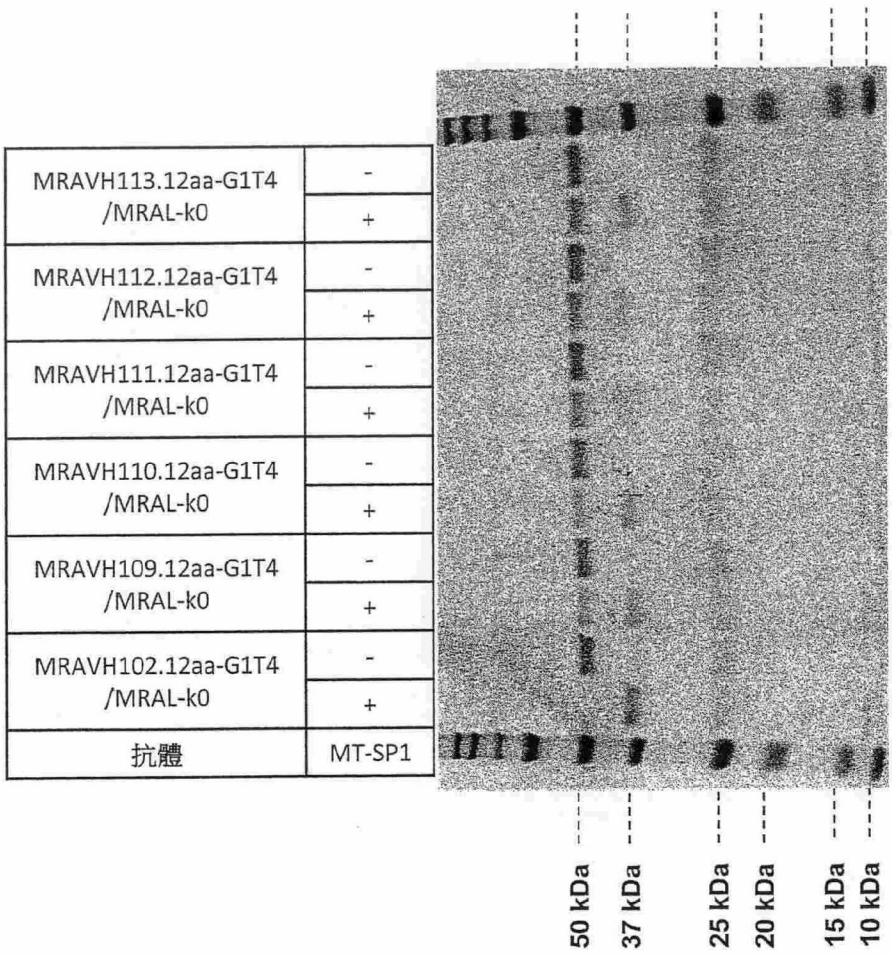

MRAVH075.12aa-G1T4 /MRAL-k0
-
+
MRAVH074.12aa-G1T4 /MRAL-k0
-
+
MRAVH068.12aa-G1T4 /MRAL-k0
-
+
MRAVH067.12aa-G1T4 /MRAL-k0
-
+
MRAVH066.12aa-G1T4 /MRAL-k0
-
+
MRAVH065.12aa-G1T4 /MRAL-k0
-
+
抗體
MT-SP1
50 kDa
37 kDa
25 kDa
20 kDa
15 kDa
10 kDa

第22E圖

MRAVH101.12aa-G1T4 /MRAL-k0	-
	+
MRAVH088.12aa-G1T4 /MRAL-k0	-
	+
MRAVH087.12aa-G1T4 /MRAL-k0	-
	+
MRAVH078.12aa-G1T4 /MRAL-k0	-
	+
MRAVH077.12aa-G1T4 /MRAL-k0	-
	+
MRAVH076.12aa-G1T4 /MRAL-k0	-
	+
抗體	MT-SP1

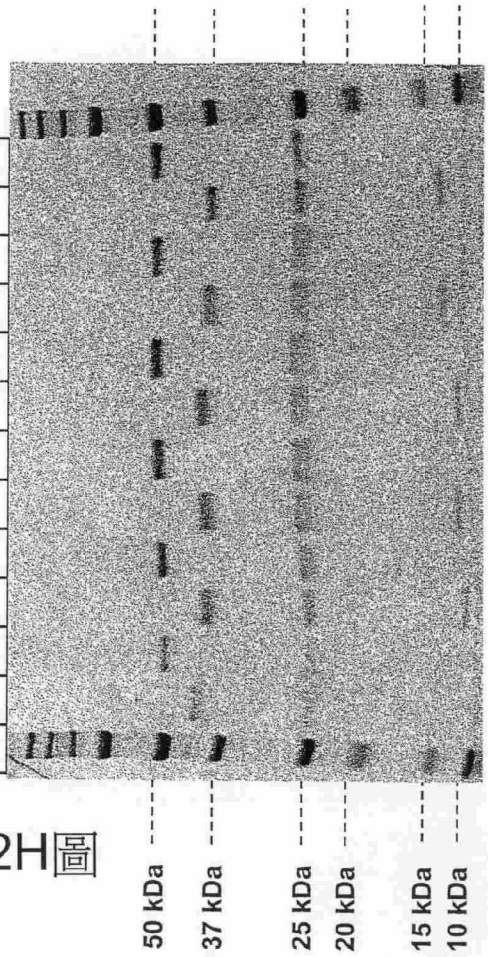


第22F圖


MRAVH113.12aa-G1T4 /MRAL-k0
-
+
MRAVH112.12aa-G1T4 /MRAL-k0
-
+
MRAVH111.12aa-G1T4 /MRAL-k0
-
+
MRAVH110.12aa-G1T4 /MRAL-k0
-
+
MRAVH109.12aa-G1T4 /MRAL-k0
-
+
MRAVH102.12aa-G1T4 /MRAL-k0
-
+
抗體
MT-SP1
50 kDa
37 kDa
25 kDa
20 kDa
15 kDa
10 kDa

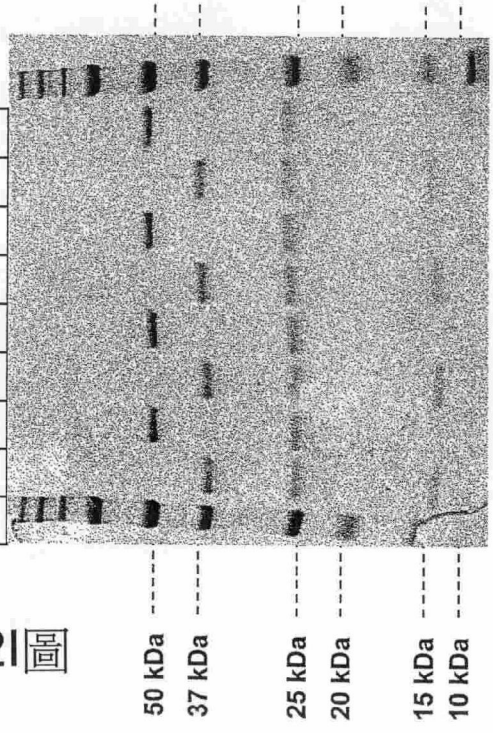
第22G圖

MRAVH115.12aa-G1T4 /MRAL-k0	-
	+
MRAVH114.12aa-G1T4 /MRAL-k0	-
	+
MRAVH100.12aa-G1T4 /MRAL-k0	-
	+
MRAVH099.12aa-G1T4 /MRAL-k0	-
	+
MRAVH089.12aa-G1T4 /MRAL-k0	-
	+
MRAVH069.12aa-G1T4 /MRAL-k0	-
	+
抗體	MT-SP1



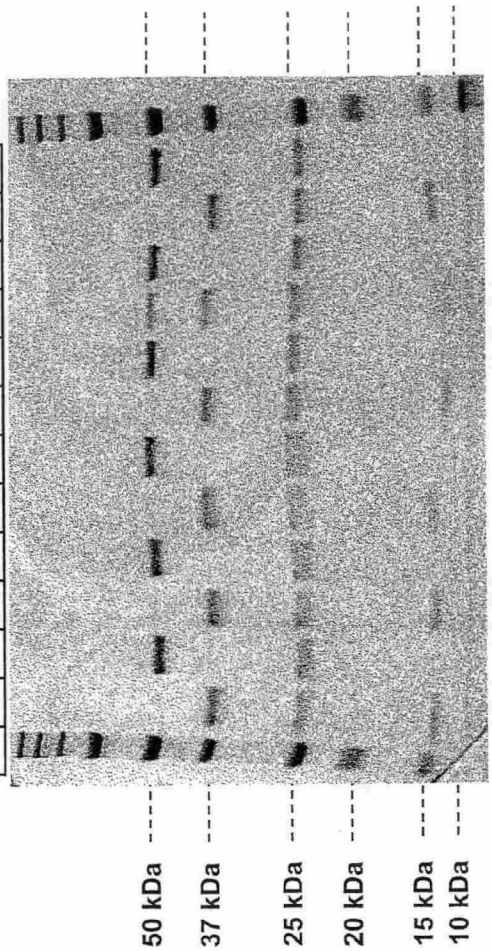
第22H圖

MRAVH119.12aa-G1T4 /MRAL-k0	-
	+
MRAVH118.12aa-G1T4 /MRAL-k0	-
	+
MRAVH117.12aa-G1T4 /MRAL-k0	-
	+
MRAVH116.12aa-G1T4 /MRAL-k0	-
	+
抗體	MT-SP1



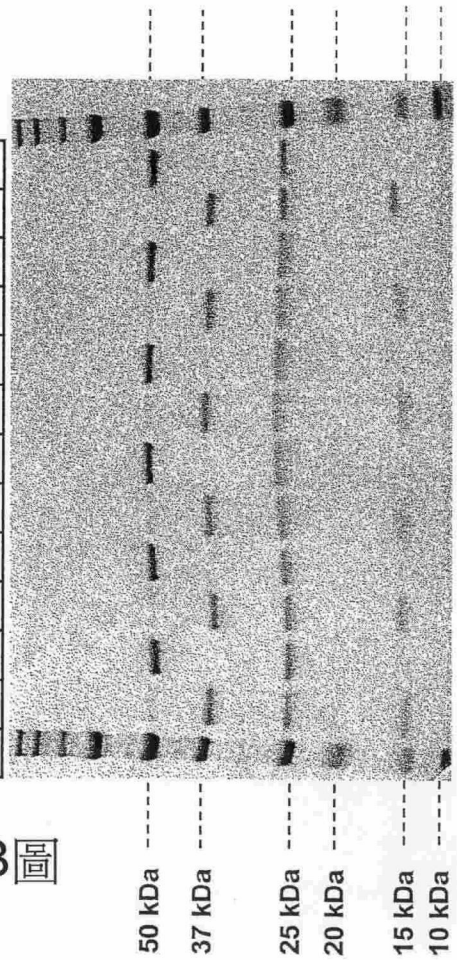
第22I圖

MRAH-G1T4.123.12aa /MRAL-k0	-
	+
MRAH-G1T4.122.12aa /MRAL-k0	-
	+
MRAH-G1T4.121.12aa /MRAL-k0	-
	+
MRAH-G1T4.120.12aa /MRAL-k0	-
	+
MRAH-G1T4.119.12aa /MRAL-k0	-
	+
MRAH-G1T4.118.12aa /MRAL-k0	-
	+
抗體	MT-SP1



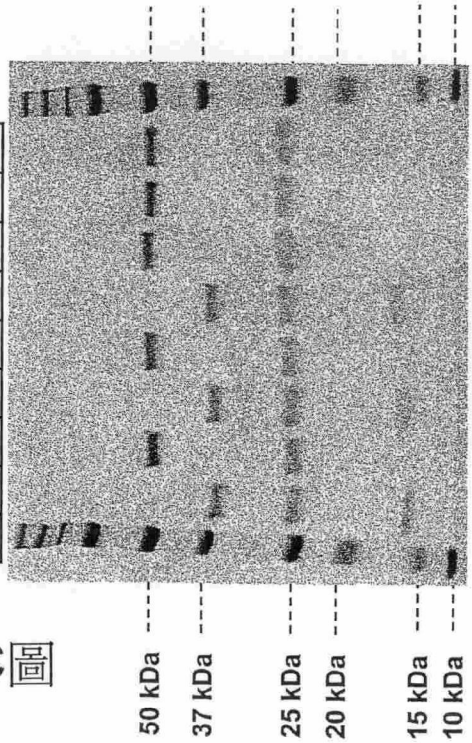
第23A圖

MRAH-G1T4.134.12aa /MRAL-k0	-
	+
MRAH-G1T4.132.12aa /MRAL-k0	-
	+
MRAH-G1T4.131.12aa /MRAL-k0	-
	+
MRAH-G1T4.130.12aa /MRAL-k0	-
	+
MRAH-G1T4.129.12aa /MRAL-k0	-
	+
MRAH-G1T4.124.12aa /MRAL-k0	-
	+
抗體	MT-SP1



第23B圖

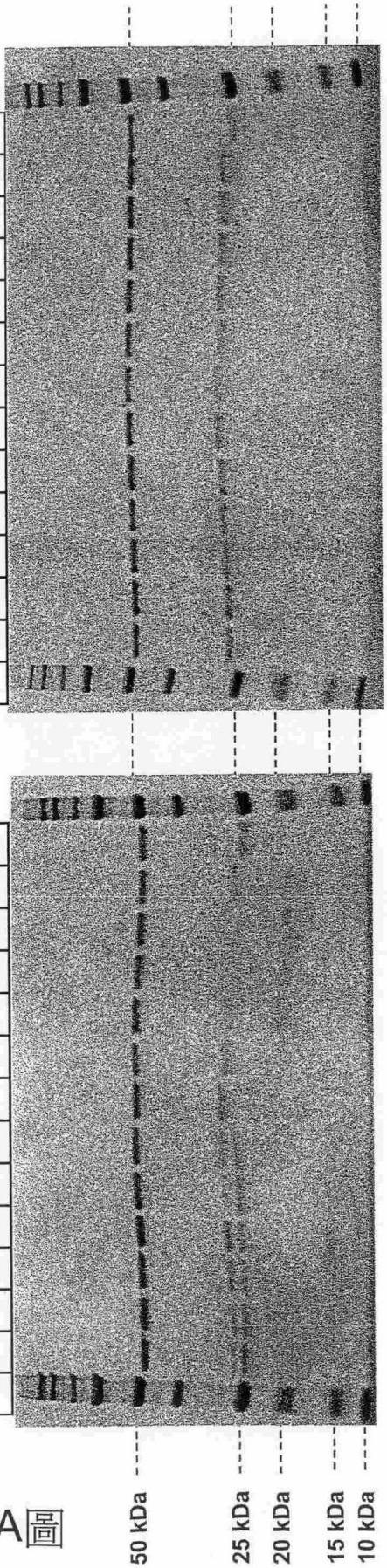
MRAH-G1T4 /MRAL-k0	-
	+
MRAH-G1T4.139.12aa /MRAL-k0	-
	+
MRAH-G1T4.137.12aa /MRAL-k0	-
	+
MRAH-G1T4.135.12aa /MRAL-k0	-
	+
抗体	MT-SP1



第23C圖

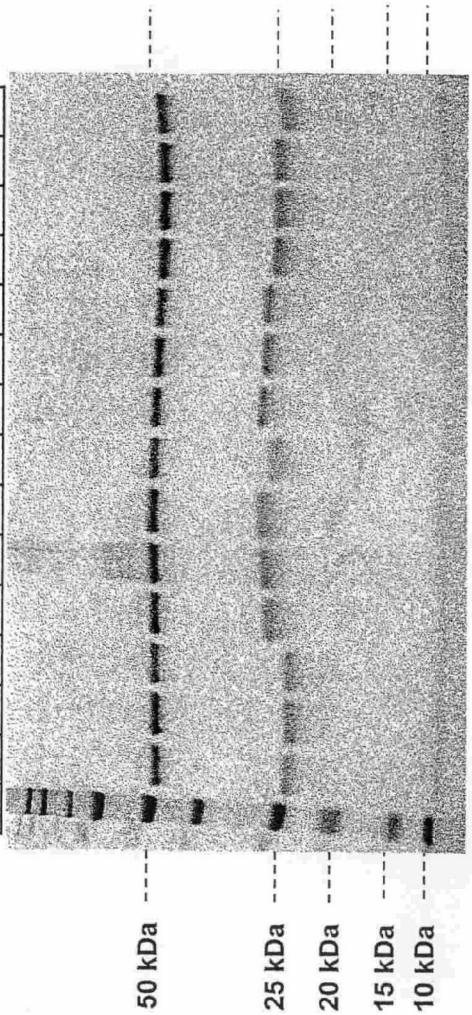
MRAH-G1T4/MRAL-k0	-
MRAH-G1T4/MRAVL052.12aa-k0	-
MRAH-G1T4/MRAVL051.12aa-k0	-
MRAH-G1T4/MRAVL050.12aa-k0	-
MRAH-G1T4/MRAVL049.12aa-k0	-
MRAH-G1T4/MRAVL041.12aa-k0	-
MRAH-G1T4/MRAVL013.12aa-k0	-
MRAH-G1T4/MRAVL012.12aa-k0	-
MRAH-G1T4/MRAVL011.12aa-k0	-
MRAH-G1T4/MRAVL010.12aa-k0	-
MRAH-G1T4/MRAVL009.12aa-k0	-
MRAH-G1T4/MRAVL008.12aa-k0	-
MRAH-G1T4/MRAVL007.12aa-k0	-
抗體	MT-SP1

MRAH-G1T4/MRAL-k0	+
MRAH-G1T4/MRAVL052.12aa-k0	+
MRAH-G1T4/MRAVL051.12aa-k0	+
MRAH-G1T4/MRAVL050.12aa-k0	+
MRAH-G1T4/MRAVL049.12aa-k0	+
MRAH-G1T4/MRAVL041.12aa-k0	+
MRAH-G1T4/MRAVL013.12aa-k0	+
MRAH-G1T4/MRAVL012.12aa-k0	+
MRAH-G1T4/MRAVL011.12aa-k0	+
MRAH-G1T4/MRAVL010.12aa-k0	+
MRAH-G1T4/MRAVL009.12aa-k0	+
MRAH-G1T4/MRAVL008.12aa-k0	+
MRAH-G1T4/MRAVL007.12aa-k0	+
抗体	MT-SP1



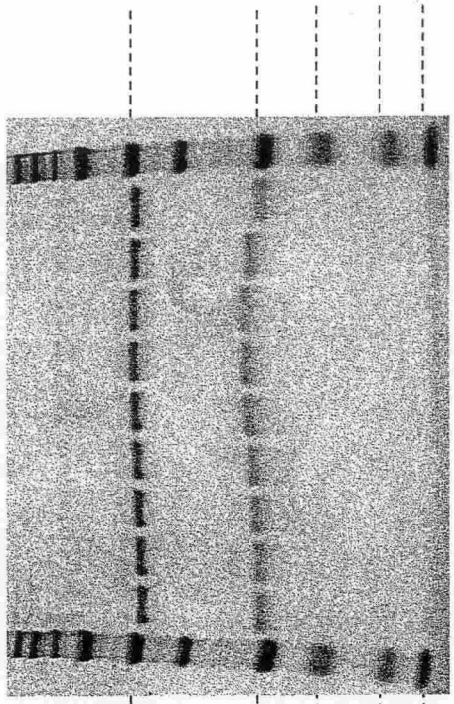
第24A圖

MRAH-G1T4/MRAL-k0	-
MRAH-G1T4/MRAVL044.12aa-k0	-
MRAH-G1T4/MRAVL042.12aa-k0	-
MRAH-G1T4/MRAVL040.12aa-k0	-
MRAH-G1T4/MRAVL017.12aa-k0	-
MRAH-G1T4/MRAVL016.12aa-k0	-
MRAH-G1T4/MRAVL014.12aa-k0	-
MRAH-G1T4/MRAL-k0	+
MRAH-G1T4/MRAVL044.12aa-k0	+
MRAH-G1T4/MRAVL042.12aa-k0	+
MRAH-G1T4/MRAVL040.12aa-k0	+
MRAH-G1T4/MRAVL017.12aa-k0	+
MRAH-G1T4/MRAVL016.12aa-k0	+
MRAH-G1T4/MRAVL014.12aa-k0	+
抗體	MT-SP1

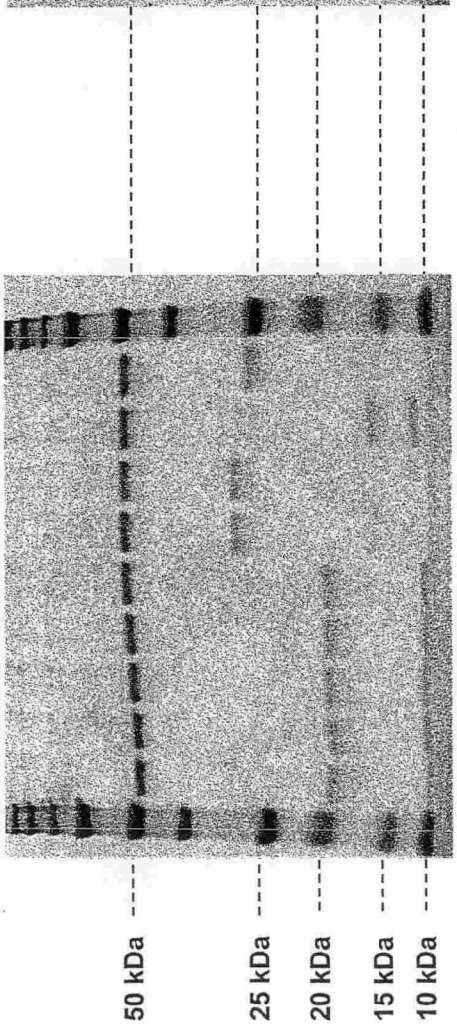


第24B圖

MRAH-G1T4/MRAL-k0	-
MRAH-G1T4/MRAVL098.12aa-k0	-
MRAH-G1T4/MRAVL097.12aa-k0	-
MRAH-G1T4/MRAVL096.12aa-k0	-
MRAH-G1T4/MRAVL059.12aa-k0	-
MRAH-G1T4/MRAVL058.12aa-k0	-
MRAH-G1T4/MRAVL057.12aa-k0	-
MRAH-G1T4/MRAVL056.12aa-k0	-
MRAH-G1T4/MRAVL054.12aa-k0	-
抗體	MT-SP1



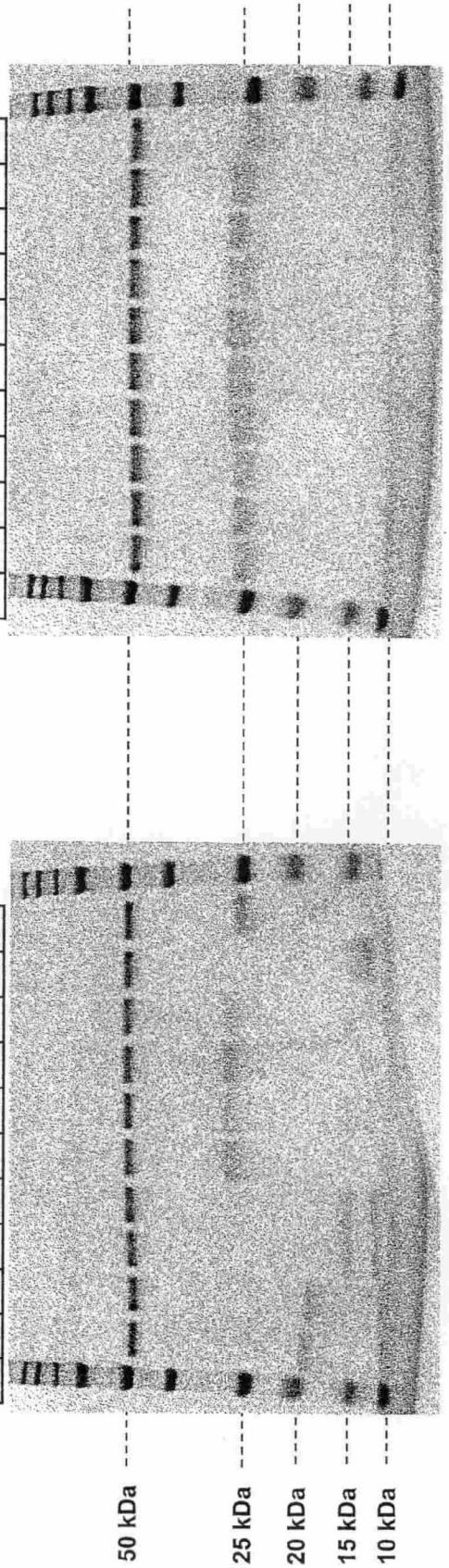
MRAH-G1T4/MRAL-k0	+
MRAH-G1T4/MRAVL098.12aa-k0	+
MRAH-G1T4/MRAVL097.12aa-k0	+
MRAH-G1T4/MRAVL096.12aa-k0	+
MRAH-G1T4/MRAVL059.12aa-k0	+
MRAH-G1T4/MRAVL058.12aa-k0	+
MRAH-G1T4/MRAVL057.12aa-k0	+
MRAH-G1T4/MRAVL056.12aa-k0	+
MRAH-G1T4/MRAVL054.12aa-k0	+
抗体	MT-SP1



第24C圖

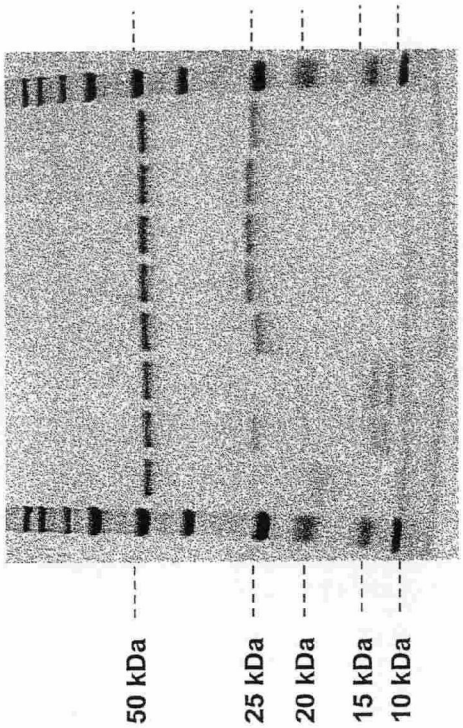
MRAH-G1T4/MRAL-k0	-
MRAH-G1T4/MRAVL106.12aa-k0	-
MRAH-G1T4/MRAVL104.12aa-k0	-
MRAH-G1T4/MRAVL103.12aa-k0	-
MRAH-G1T4/MRAVL102.12aa-k0	-
MRAH-G1T4/MRAVL101.12aa-k0	-
MRAH-G1T4/MRAVL100.12aa-k0	-
MRAH-G1T4/MRAVL099.12aa-k0	-
MRAH-G1T4/MRAVL060.12aa-k0	-
MRAH-G1T4/MRAVL055.12aa-k0	-
抗體	MT-SP1

MRAH-G1T4/MRAL-k0	+
MRAH-G1T4/MRAVL106.12aa-k0	+
MRAH-G1T4/MRAVL104.12aa-k0	+
MRAH-G1T4/MRAVL103.12aa-k0	+
MRAH-G1T4/MRAVL102.12aa-k0	+
MRAH-G1T4/MRAVL101.12aa-k0	+
MRAH-G1T4/MRAVL100.12aa-k0	+
MRAH-G1T4/MRAVL099.12aa-k0	+
MRAH-G1T4/MRAVL060.12aa-k0	+
MRAH-G1T4/MRAVL055.12aa-k0	+
抗體	MT-SP1



第24D圖

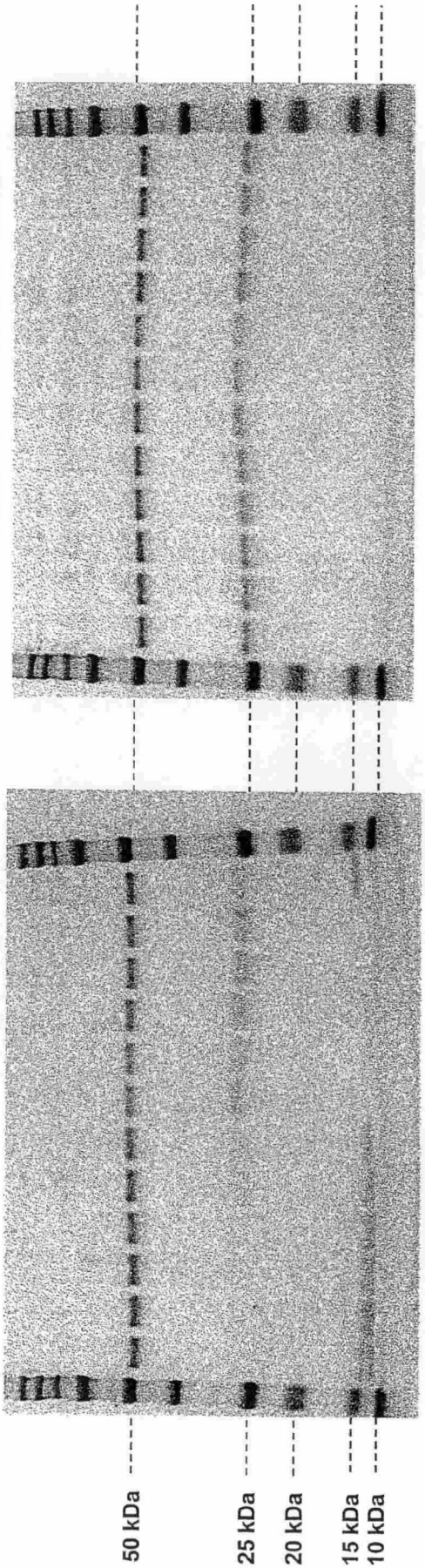
MRAH-G1T4/MRAL-k0	-
MRAH-G1T4/MRAVL107.12aa-k0	-
MRAH-G1T4/MRAVL105.12aa-k0	-
MRAH-G1T4/MRAVL053.12aa-k0	-
MRAH-G1T4/MRAL-k0	+
MRAH-G1T4/MRAVL107.12aa-k0	+
MRAH-G1T4/MRAVL105.12aa-k0	+
MRAH-G1T4/MRAVL053.12aa-k0	+
抗體	MT-SP1



第24E圖

MRAH-G1T4/MRAL-k0.120.12aa	-
MRAH-G1T4/MRAL-k0.119.12aa	-
MRAH-G1T4/MRAL-k0.118.12aa	-
MRAH-G1T4/MRAL-k0.117.12aa	-
MRAH-G1T4/MRAL-k0.116.12aa	-
MRAH-G1T4/MRAL-k0.115.12aa	-
MRAH-G1T4/MRAL-k0.113.12aa	-
MRAH-G1T4/MRAL-k0.112.12aa	-
MRAH-G1T4/MRAL-k0.111.12aa	-
MRAH-G1T4/MRAL-k0.110.12aa	-
MRAH-G1T4/MRAL-k0.109.12aa	-
MRAH-G1T4/MRAL-k0.108.12aa	-
抗體	MT-SP1

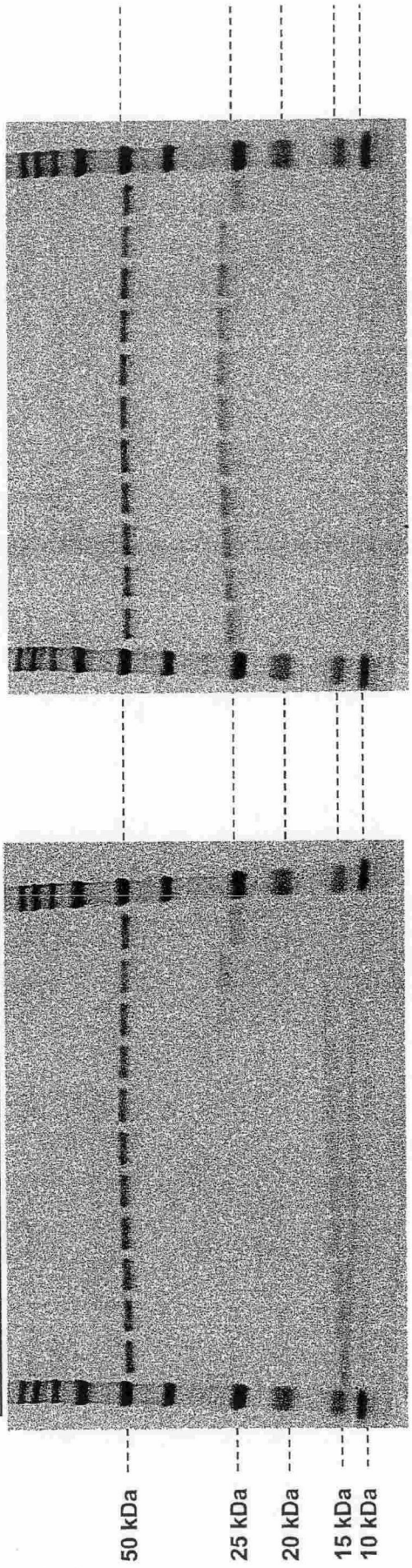
MRAH-G1T4/MRAL-k0.120.12aa	+
MRAH-G1T4/MRAL-k0.119.12aa	+
MRAH-G1T4/MRAL-k0.118.12aa	+
MRAH-G1T4/MRAL-k0.117.12aa	+
MRAH-G1T4/MRAL-k0.116.12aa	+
MRAH-G1T4/MRAL-k0.115.12aa	+
MRAH-G1T4/MRAL-k0.113.12aa	+
MRAH-G1T4/MRAL-k0.112.12aa	+
MRAH-G1T4/MRAL-k0.111.12aa	+
MRAH-G1T4/MRAL-k0.110.12aa	+
MRAH-G1T4/MRAL-k0.109.12aa	+
MRAH-G1T4/MRAL-k0.108.12aa	+
抗體	MT-SP1



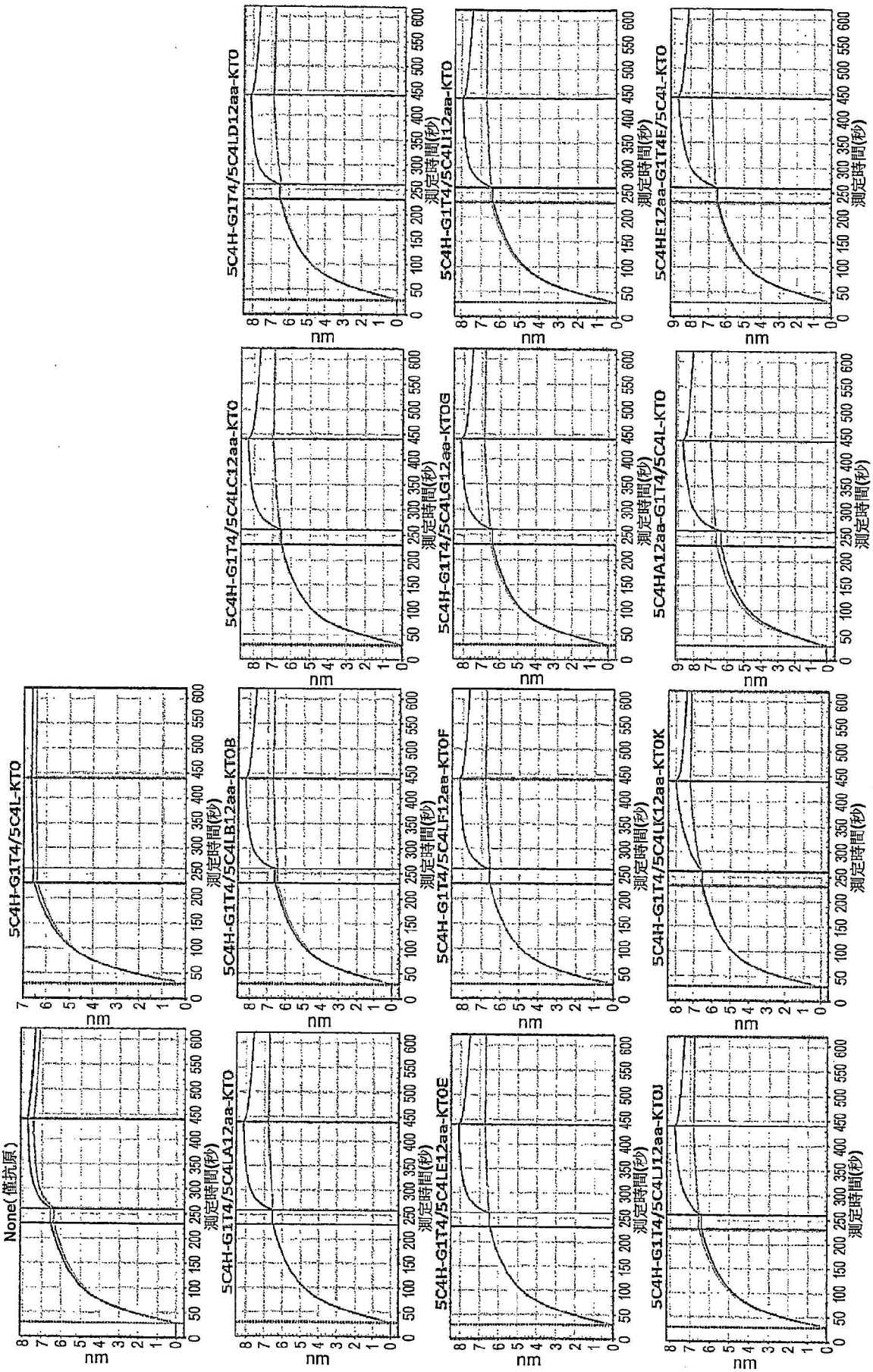
第25A圖

MRAH-G1T4/MRAL-k0	-
MRAH-G1T4/MRAL-k0.130.12aa	-
MRAH-G1T4/MRAL-k0.129.12aa	-
MRAH-G1T4/MRAL-k0.128.12aa	-
MRAH-G1T4/MRAL-k0.127.12aa	-
MRAH-G1T4/MRAL-k0.126.12aa	-
MRAH-G1T4/MRAL-k0.125.12aa	-
MRAH-G1T4/MRAL-k0.124.12aa	-
MRAH-G1T4/MRAL-k0.123.12aa	-
MRAH-G1T4/MRAL-k0.122.12aa	-
MRAH-G1T4/MRAL-k0.121.12aa	-
抗體	MT-SP1

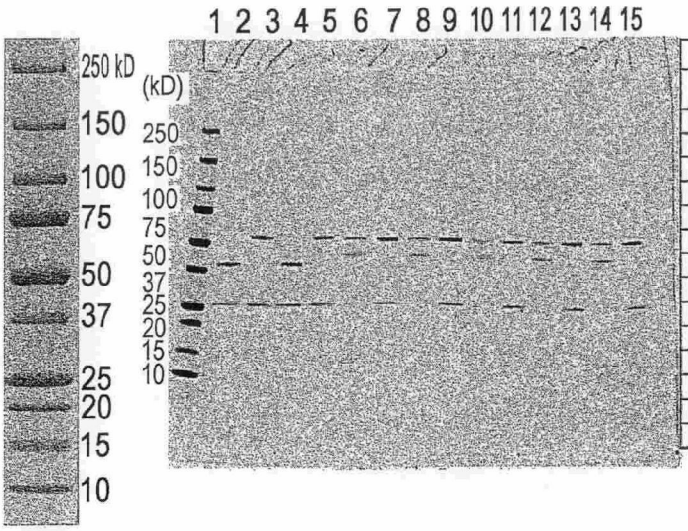
MRAH-G1T4/MRAL-k0	+
MRAH-G1T4/MRAL-k0.130.12aa	+
MRAH-G1T4/MRAL-k0.129.12aa	+
MRAH-G1T4/MRAL-k0.128.12aa	+
MRAH-G1T4/MRAL-k0.127.12aa	+
MRAH-G1T4/MRAL-k0.126.12aa	+
MRAH-G1T4/MRAL-k0.125.12aa	+
MRAH-G1T4/MRAL-k0.124.12aa	+
MRAH-G1T4/MRAL-k0.123.12aa	+
MRAH-G1T4/MRAL-k0.122.12aa	+
MRAH-G1T4/MRAL-k0.121.12aa	+
抗體	MT-SP1



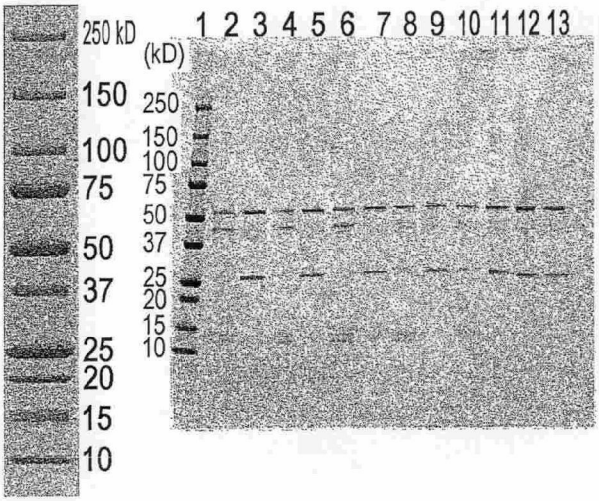
第25B圖


None(僅抗原)
5C4H-G1T4/5C4L-KTO
5C4H-G1T4/5C4LA12aa-KTO
5C4H-G1T4/5C4LB12aa-KTOB
5C4H-G1T4/5C4LC12aa-KTO
5C4H-G1T4/5C4LD12aa-KTO
5C4H-G1T4/5C4LE12aa-KTOE
5C4H-G1T4/5C4LF12aa-KTOF
5C4H-G1T4/5C4LG12aa-KTOG
5C4H-G1T4/5C4LI12aa-KTO
5C4H-G1T4/5C4LJ12aa-KTOJ
5C4H-G1T4/5C4LK12aa-KTOK
5C4HA12aa-G1T4/5C4L-KTO
5C4HE12aa-G1T4E/5C4L-KTO
nm
測定時間(秒)

第26圖

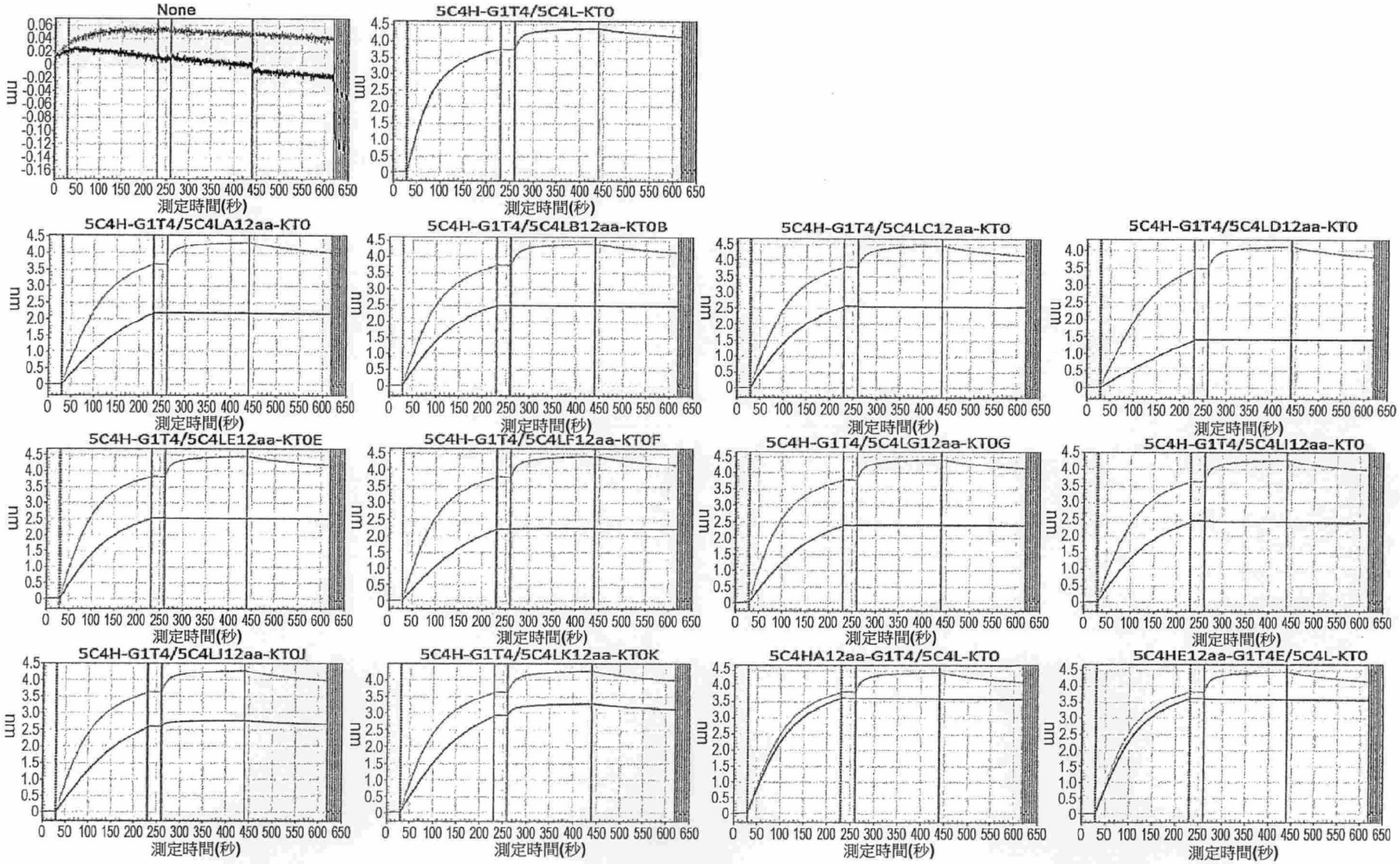


泳道	蛋白酶	樣本
1	-	M.W.Marker (Precision Plus(All Blue) (Bio-Rad #161-0373))
2	+	5C4HA12aa-G1T4/5C4L-KT0
3	-	
4	+	5C4HE12aa-G1T4E/5C4L-KT0
5	-	
6	+	5C4H-G1T4/5C4LI12aa-KT0
7	-	
8	+	5C4H-G1T4/5C4LC12aa-KT0
9	-	
10	+	5C4H-G1T4/5C4LD12aa-KT0
11	-	
12	+	5C4H-G1T4/5C4LA12aa-KT0
13	-	
14	+	5C4H-G1T4/5C4LE12aa-KT0E
15	-	



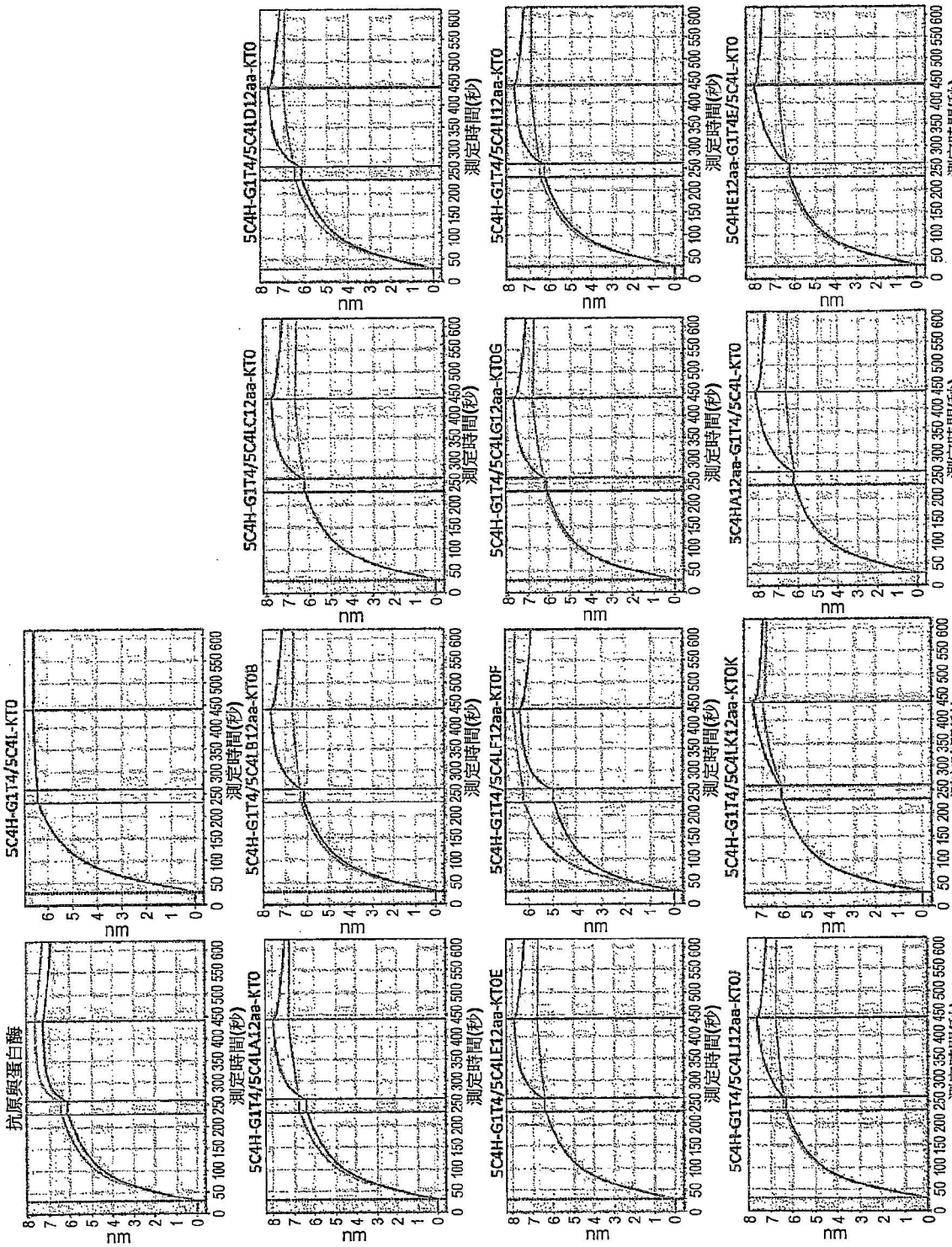
泳道	蛋白酶	樣本
1	-	M.W.Marker (Precision Plus(All Blue) (Bio-Rad #161-0373))
2	+	5C4H-G1T4/5C4LB12aa-KT0B
3	-	
4	+	5C4H-G1T4/5C4LF12aa-KT0F
5	-	
6	+	5C4H-G1T4/5C4LG12aa-KT0G
7	-	
8	+	5C4H-G1T4/5C4LJ12aa-KT0J
9	-	
10	+	5C4H-G1T4/5C4LK12aa-KT0K
11	-	
12	+	5C4H-G1T4/5C4L-KT0
13	-	

第27圖


None
5C4H-G1T4/5C4L-KT0
5C4H-G1T4/5C4LA12aa-KT0
5C4H-G1T4/5C4LB12aa-KT0B
5C4H-G1T4/5C4LC12aa-KT0
5C4H-G1T4/5C4LD12aa-KT0
5C4H-G1T4/5C4LE12aa-KT0E
5C4H-G1T4/5C4LF12aa-KT0F
5C4H-G1T4/5C4LG12aa-KT0G
5C4H-G1T4/5C4LI12aa-KT0
5C4H-G1T4/5C4LJ12aa-KT0J
5C4H-G1T4/5C4LK12aa-KT0K
5C4HA12aa-G1T4/5C4L-KT0
5C4HE12aa-G1T4E/5C4L-KT0
nm
測定時間(秒)

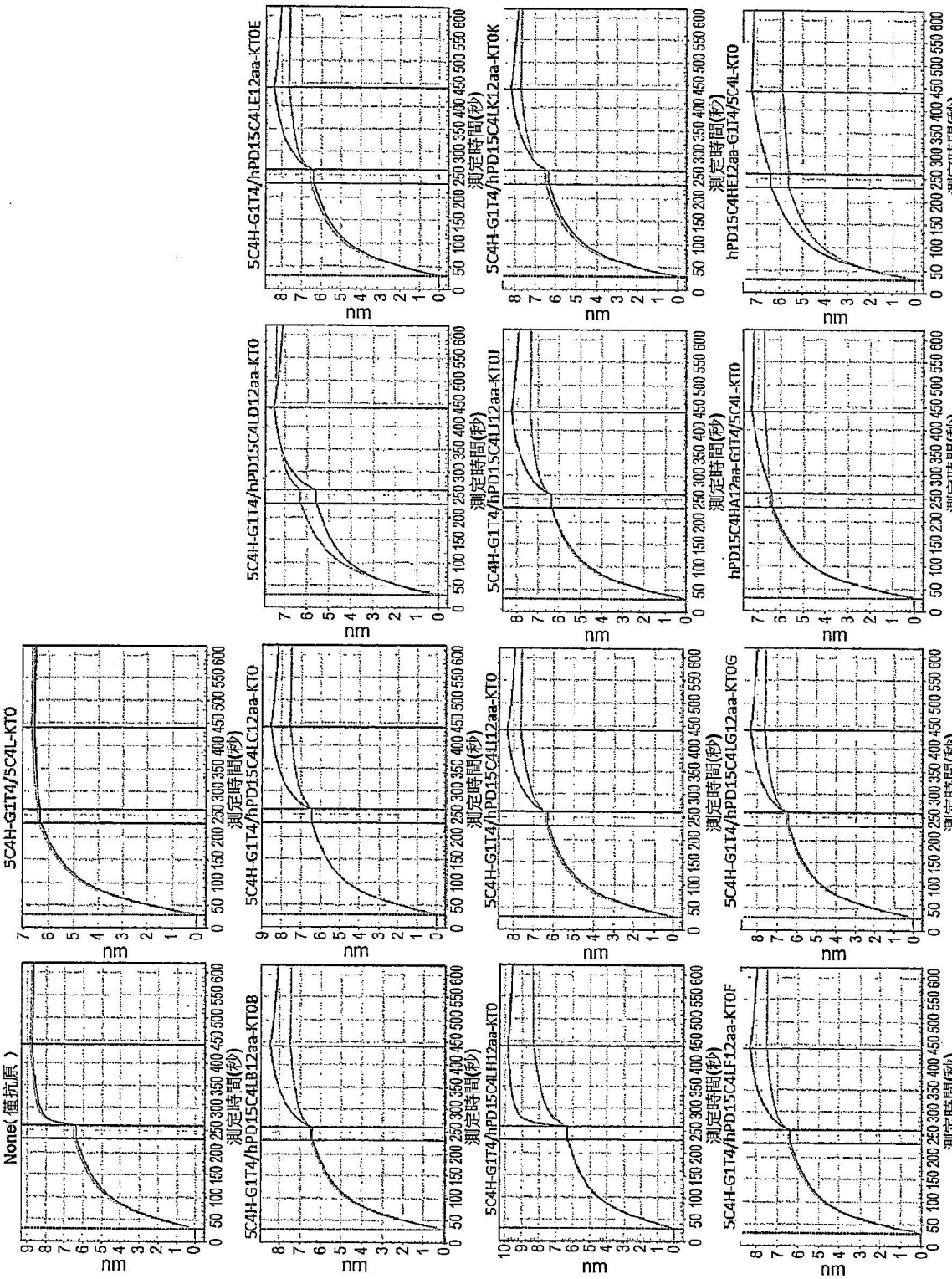
第28圖

I776827

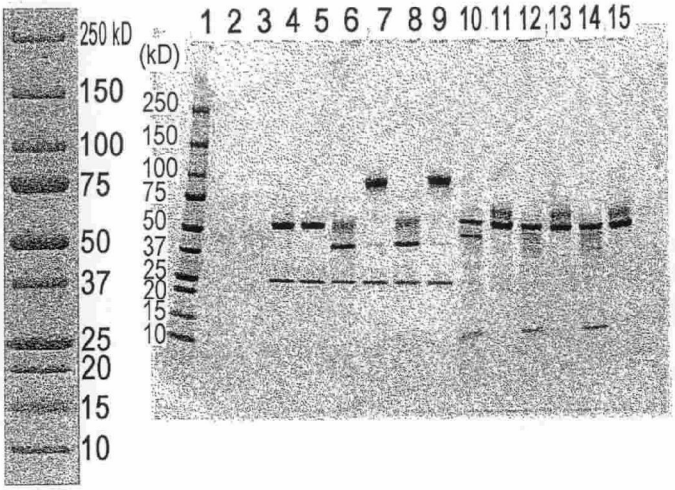


第29圖

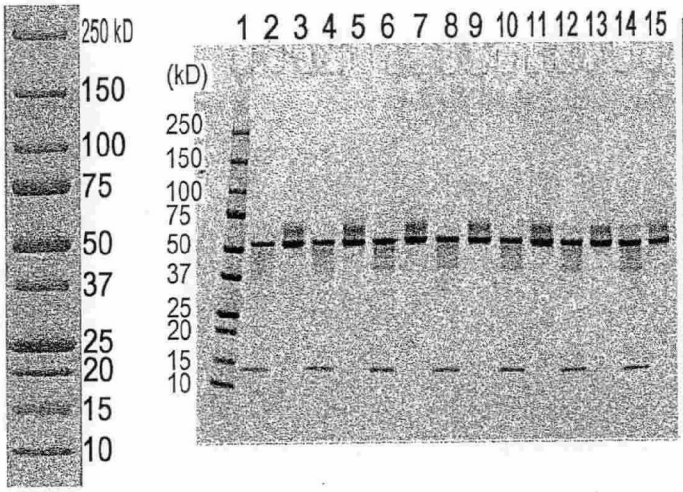
I776827



第30圖



泳道	蛋白酶	樣本
1	-	M.W.Marker(Precision Plus(All Blue) (Bio-Rad #161-0373))
2	+	PD1
3	-	
4	+	5C4H-G1T4/5C4L-KT0
5	-	
6	+	hPD15C4HA12aa-G1T4/5C4L-KT0
7	-	
8	+	hPD15C4HE12aa-G1T4E/5C4L-KT0
9	-	
10	+	5C4H-G1T4/hPD15C4LH12aa-KT0
11	-	
12	+	5C4H-G1T4/hPD15C4LI12aa-KT0
13	-	
14	+	5C4H-G1T4/hPD15C4LC12aa-KT0
15	-	



泳道	蛋白酶	樣本
1	-	M.W.Marker (Precision Plus(All Blue) (Bio-Rad #161-0373))
2	+	5C4H-G1T4/hPD15C4LD12aa-KT0
3	-	
4	+	5C4H-G1T4/hPD15C4LE12aa-KT0E
5	-	
6	+	5C4H-G1T4/hPD15C4LB12aa-KT0B
7	-	
8	+	5C4H-G1T4/hPD15C4LF12aa-KT0F
9	-	
10	+	5C4H-G1T4/hPD15C4LG12aa-KT0G
11	-	
12	+	5C4H-G1T4/hPD15C4LJ12aa-KT0J
13	-	
14	+	5C4H-G1T4/hPD15C4LK12aa-KT0K
15	-	

第31圖